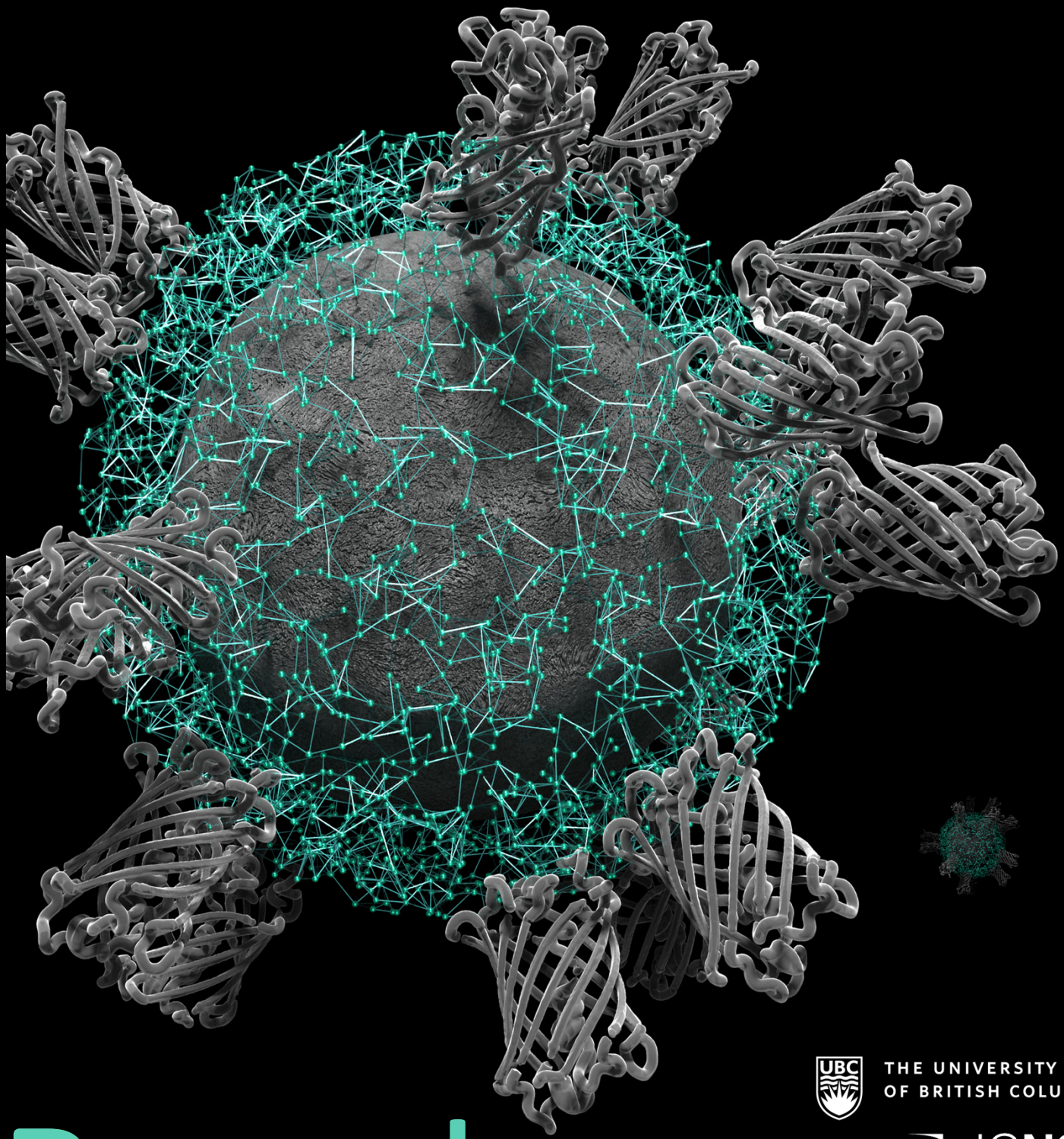
14th International Conference on the Scientific and Clinical Applications of Magnetic Carriers



THE UNIVERSITY OF BRITISH COLUMBIA

ICN2 Institut Català de Nanociència i Nanotecnologia

INMA INSTITUTO DE NANOCIENCIA Y MATERIALES DE ARAGÓN

icmm Instituto de Ciencia de Materiales de Madrid

Barcelona

June 17-21, 2024

Alejandro G. Roca, Lucía Gutiérrez, Puerto Morales, Urs Hafeli

www.magneticmicrosphere.com

Coffee mug design © 2024 by **Ilaria Armenia** (University of Zaragoza) and **Gianluca Tomasello** (3D protein imaging studio - 3Dproteinimaging.com).

Welcome Message – Benvinguts!

It is our great pleasure to welcome you all to the 14th International Conference on the Scientific and Clinical Applications of Magnetic Carriers. It is wonderful to again meet you all in person, to discuss all kinds of magnetic particles with all you experts from the fields of chemistry, physics, medicine, biology, engineering, materials sciences, and more. New materials may come and go - but no other material like magnetic (nano)particles has stayed at the forefront of technology for so long, constantly reinventing itself to become the most valuable material of all.

This time we are meeting in the beautiful Catalan City of Barcelona. It is not only the Centre of lots of colorful art (Gaudi, Picasso, Miro), buildings and parks, excellent shopping (La Rambla, Mercat de Sant Antoni) or the beaches and Montjuic, it also houses the excellent Universidad Autonoma de Barcelona (UAB). We will meet first at its beautiful downtown location, the Casa de Convalescència, for the reception, and then at its main campus between Bellaterra and Sabadell in the town of Cerdanyola del Valles for all the talks and poster sessions.

As in the past, we wish to cultivate discussions and a familiar atmosphere not only during the talks, but also during breaks, lunches and a boat trip on the Mediterranean Sea with a magical sunset. There is no better way to have fun, discuss new and old research with your colleagues, and begin new collaborations. This will advance our field even more!

We are counting on you for a successful and interesting conference and wish you a very special week, both professionally and personally. Enjoy!

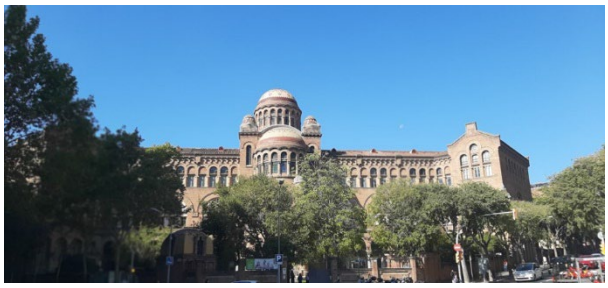
Your organizers,

Alejandro G. Roca, Catalan Institute of Nanoscience and Nanotechnology (ICN2), Barcelona, Spain
Lucia Gutierrez, Instituto de Nanociencia y Materiales de Aragón (INMA/CSIC), Zaragoza, Spain
Puerto Morales, Instituto de Ciencia de Materiales de Madrid (ICMM/CSIC), Spain
Urs Hafeli, University of British Columbia (UBC), Vancouver, Canada

Social Program

As always, we will not let science prevent us from learning new stuff, having fun together and enjoying Barcelona to the fullest.

Monday, June 17
Our meeting will start in downtown Barcelona at 19:00 (7 PM) with a reception at the Universitat Autonoma de Barcelona (UAB)'s Casa de Convalescencia.
The reception is generously sponsored by micromod.



Tuesday, June 18
In the evening, the first poster session with Pretzels and beer will take place at the UAB Bellaterra campus. *The poster session is generously sponsored by Nanomedicine CSIC, the nanomedicine hub in Spain.*

Wednesday, June 19
During the day, we will have a **spouse tour** starting at 9:00 (9 AM). This tour is complimentary and always fun!
There will be a second poster session in the late afternoon. And then we will have a Pizza Party for all - should be lots of fun!
It is sponsored by INMA, the Instituto de Nanociencia y Materiales de Aragon.

Thursday, June 20
On this evening, we will have our **traditional boat trip** on the Balearic Sea. We will take the bus from UAB to the boat and board at 18:30 (6:30 PM) with take off at 19:00 (7:00 PM). Make sure you are all there on time!

Friday, June 21
The meeting will end at 13:00 (1 PM). Please take the opportunity and explore beautiful Barcelona on your own after the end of the conference!
There are so many things to see. Check for example here: https://ticketshop.barcelona/

Conference Location & Maps

Our 14th meeting will take place at **Universidad Autonoma de Barcelona** (UAB) which is situated in the metropolitan area of Barcelona between Bellaterra and Sabadell in the town of Cerdanyola del Vallès, about 20 kilometers from downtown Barcelona.

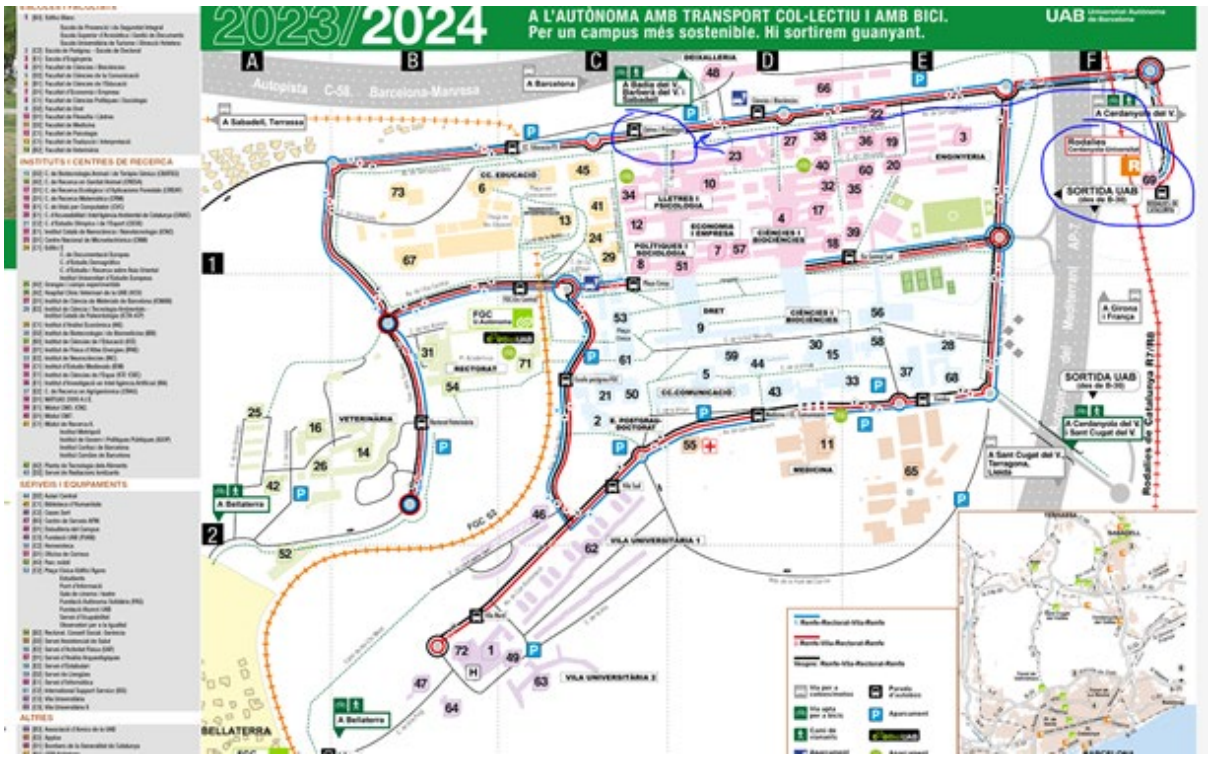
The exact location is "Carrer de la Fortuna, 08193, Barcelona, Spain", and we are in the "Auditori de Filosofia i Lletres (UAB)".

You can find the routes to get to the UAB campus here in this website (https://www.uab.cat/web/means-of-transport-1345796335052.html).

There are two types of train to get to the UAB campus:

1. Rodalies-RENFE:

To get from downtown Barcelona to the UAB campus by train, you can take the train in Sant Andreu Arenal Station (line R7) and you get the UAB campus in 20 minutes. Please, take into account the frequency is every 30 minutes. Once you get to Cerdanyola-Universitat train Station, there are buses at the exit of the train station, please take Bus Line 1 (blue color) to get to the conference venue (Facultat de Filosofia I Lletres).



2. Ferrocarrils de la Generalitat Catalana (FGC)

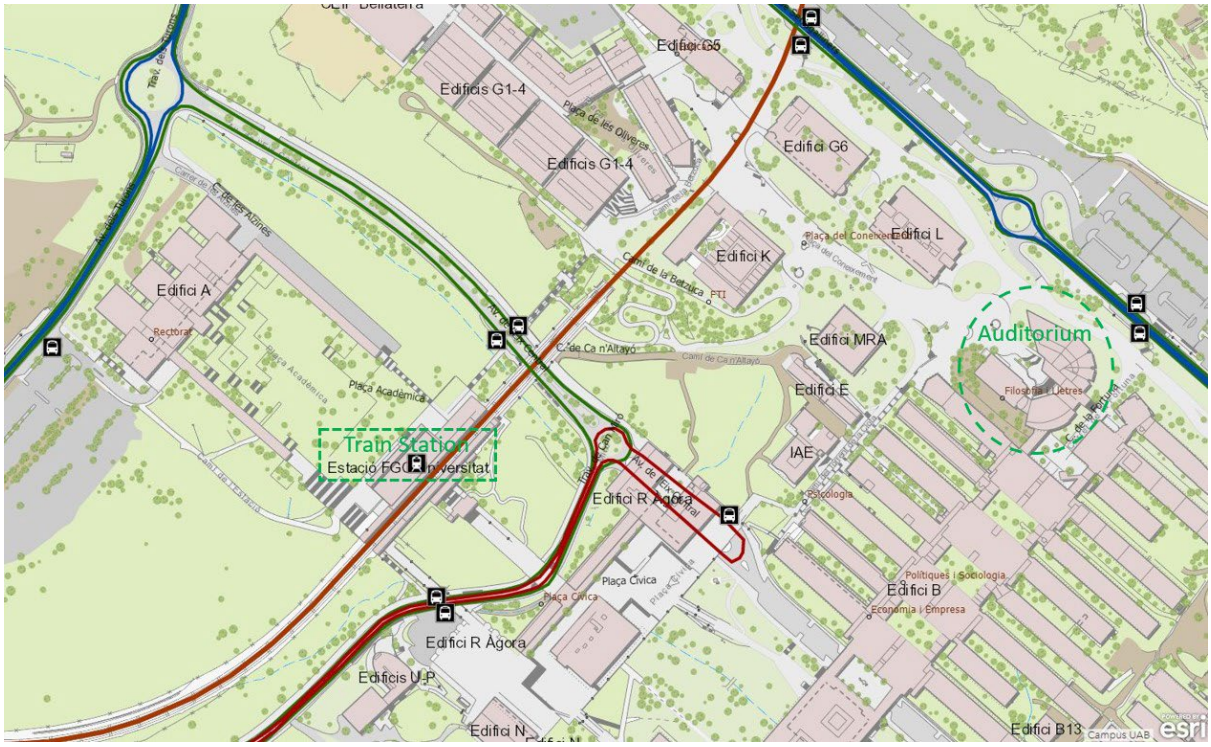
Wherever you are in Barcelona, you can take the Barcelona Metro (Subway) and connect to the FGC train lines. An easy journey is going to Plaza Catalunya which connects Barcelona Metro (Line 1 or Line 3) with FGC (and also RENFE Rodalies).

Once you are at a station that connects to the FGC lines, transfer to the appropriate FGC line that goes towards the UAB campus (Universitat Autonoma Station). The light green (below) S2 line typically serve this route. The journey from Plaza de Catalunya to Universitat Autonoma takes approximately 40 minutes and it runs every 6-8 minutes during the day and 15 minutes in peak-off hours. You can consult the timetable here. Once you get to the FGC station at "Universitat Autonoma", the conference venue is a 5 minute walk away.

You can buy the tickets only for FGC (Billets FGC) from € 2.55 if you come from Barcelona downtown) or combined with Barcelona Metro (Billets Integrats). If you buy a booklet of 10 tickets it is much cheaper.

Campus Map

Registration will take place outside the Faculty of Arts & Humanities auditorium, an excellent facility for our conference. The registration desks will be open from 8:30 AM on during each conference day.



14th International Conference on the Scientific and Clinical Applications of Magnetic Carriers

Monday, June 17, 2024				
18:00	**Registration desk opens at the Casa de Convalescencia, Calle de St. Antoni Maria Claret, 171 - this reception is sponsored by micromod.**			
19:00	Opening of the conference and welcome address			
19:15	Opening of the buffet			
22:00	End of Reception			

Tuesday, June 18, 2024				
8:30	**Registration desk opens in the Faculty of Arts & Humanities auditorium [Auditorium Filosofia y Letras, UAB, Calle de la Fortuna, Bellaterra]**			
9:00	Organization committee	Opening of the conference and welcome address by the organization committee	Bellaterra, Spain	Intro
9:10	Hafeli, Urs	Short review of the last 2 years of magnetic carriers research	Vancouver, BC, Canada	Talk 0
	Session 1		*Chair: Cordula Gruettner*	
9:30	Zabow, Gary	Magnetic control via magnetically microprinted microparticles	Boulder, U.S.A.	Talk 1
9:45	Baumgarten, Daniel	A portable system for unshielded magnetorelaxometry imaging of magnetic nanoparticles	Hall i.T., Austria	Talk 2
10:00	Rivera-Llabres, Victor	Micropatterning of aligned pores as directional cues in granular PEG composite scaffolds using magnetic porogens	Gainesville, U.S.A.	Talk 3
10:15	**Coffee break**			
	Session 2: Magnetic Drug Delivery		*Chair: Borja Sepulveda*	
10:45	Ma, Yunn-Hwa	Translational Assessment of Magnetic Nanotherapeutics for Target Thrombolysis	Tao-Yuan, Taiwan	Talk 4
11:00	Alferiev, Ivan	Nanocarriers for Dual-Targeted Therapy of In-Stent Restenosis	Philadelphia, U.S.A.	Talk 5
11:15	Garcia-Gabilondo, Miguel	Endovascular Delivery and Magnetic Retention Enhance Brain Targeting of PLGA Nanocarriers in Large Cerebral Vascular Models	Barcelona, Spain	Talk 6
11:30	Bakenecker, Anna	Magnetic-enzymatic nanomotors depicting a collective swarming behavior and directional navigation abilities	Lübeck, Germany	Talk 7
11:45	Pané, Salvador	Magnetic Small-Scale Robots for Biomedical Applications	Zurich, Switzerland	Invited Talk 1
12:30	**Lunch**			
	Session 3: Biosensors / Diagnostic Tests		*Chair: Isbel Gessner*	
13:45	Wang, Jian-Ping	Optimization of Volumetric Magnetic Particle Spectroscopy (MPS) Biosensor for 5-Minute Ultrafast Detection of SARS-CoV-2 Spike Protein	Minneapolis, U.S.A.	Talk 8
14:00	Sack, Rebecca	Next generation magnetic circuits for the detection of nucleic acid biomarkers	Braunschweig, Germany	Talk 9
14:15	Mikelez-Alonso, Idoia	One-step and wash-free magnetic method for direct SARS-CoV-2 virus detection in patient samples	Villacastin, Spain	Talk 10
14:30	Salvador, Maria	Magnetic Nanoclusters with Twofold Functionality in Lateral Flow Immunoassays to detect Pneumococcal Pneumonia: Analyte Concentrators and Detection Reporters	Gijon, Spain	Talk 11
14:45	Berret, Jean-Francois	Cytoplasmic Viscosity is a Potential Biomarker for Metastatic Breast Cancer Cells	Paris, France	Talk 12
15:00	**Coffee break**			
	Session 4: Magnetic Characterizations / Methods / Analytics		*Chair: Aidan Lak*	
15:30	Moya, Carlos	Unveiling the 3D Magnetic Vortex Texture of Iron Oxide Nanoflowers	Barcelona, Spain	Talk 13
15:45	Günther, Johanna	COMPASS: A trailblazing technology for rapid in vitro bioassays based on MNPs	Würzburg, Germany	Talk 14
16:00	Martinez-Pedrero, Fernando	Transportation of Magnetic Colloidal Particles via Driven and Ratchet Mechanisms on Self-Assembled Colloidal Tracks	Madrid, Spain	Talk 15
16:15	Novikau, Ivan	Wobbling in Nanogel Rheological and Magnetic Responses	Vienna, Austria	Talk 16
16:30	Bikulov, Timur	Multicontrast binding state analysis using frequency mixing magnetic detection	Jülich, Germany	Talk 17
16:45	Zhong, Jing	The combination of frequency- and spatial-space for Magnetic Particle Imaging	Beijing, China	Talk 18
17:00	Lopez-Lopez, Modesto	Engineering Magnetic Hydrogels for Tissue Engineering and Remote Actuation	Granada, Spain	Invited Talk 2
17:45	**Poster session I (Posters 1-82) - with Beer and Pretzels generously sponsored by Nanomedicine CSIS, the nanomedicine hub in Spain**			
19:30	**Free evening - go and get collaborations going!**			

Wednesday, June 19, 2024				
8:30	**Registration desk opens in UAB's Faculty of Arts & Humanities auditorium [Auditorium Filosofia y Letras, Calle de la Fortuna, Bellaterra]**			
9:00	Gutierrez, Lucia	On the Biology (and Related Subjects) From the Point of View of a Magnetic Nanoparticle	Zaragoza, Spain	Tutorial 1
	Session 5: Basic Magnetic Particle and Force Studies		*Chair: Ondrej Hovorka*	
9:30	Kantorovich, Sofia	Mixtures of Superpara- and Ferro-magnetic Multicore Nanoparticles: Microstructure and Magnetic Response from Experiment & Simulations	Vienna, Austria	Talk 19
9:45	Livesey, Karen	The "interaction temperature" of magnetic nanoparticle systems	Callaghan, Australia	Talk 20
10:00	Rodriguez-Barroso, Alejandr	Use of a variable inductance coil for high-frequency field sweeping in suspensions of magnetic colloidal particles: self-assembly and rheology	Granada, Spain	Talk 21
10:15	**Coffee break**			
	Session 6: Magnetic Separation		*Chair: Karen Livesey*	
10:45	Tierno, Pietro	Magnetically driven micro-propellers: from travelling carpets to hydrodynamic bound states	Barcelona, Spain	Talk 22
11:00	Kuzhir, Pavel	Self-assembling magnetic nanoparticles: can they be useful for biomedical applications?	Nice, France	Talk 23
11:15	Efremova, Mariia	AFM Cantilever Magnetometry for Measuring Femto-Nm Torques Generated by Single Magnetic Particles for Cell Actuation	Eindhoven, Netherlands	Talk 24
11:30	Pividori, Maria Isabel	Magnetic Separation of Exosomes with Tailored Magnetic Particles and Downstream Application	Bellaterra, Spain	Talk 25
11:45	Wilhelm, Claire	Magnetic Nanoparticles as Instructive Tools for Engineering, Stimulation, and Treatment of Model Tissues	Paris, France	Invited Talk 3
12:30	**Lunch**			
	Session 7: Nanoparticle Synthesis and Properties		*Chair: Thompson Mefford*	
13:45	Velazquez-Albino, Ambar	Enhancing MPI Performance: Probing post-synthesis oxidation and correlations to nanoparticle properties	Gainesville, U.S.A.	Talk 26
14:00	Zahn, Diana	High coercivity cobalt ferrite nanoparticles for heating applications	Ilmenau, Germany	Talk 27
14:15	Saladino, Giovanni	Enhanced Functionalities of Magnetic Supramolecular Assemblies for Biomedical and Environmental Applications	Stockholm, Sweden	Talk 28
14:30	Bleul, Regina	Process analytical technology in continuous manufacturing of nanohybrids for advanced theranostics	Mainz, Germany	Talk 29
14:45	Estrader, Marta	Disentangling the layer(s) composition and its indiviual magnetic contribution in bi-magnetic core@shell nanoparticles	Barcelona, Spain	Talk 30
15:00	**Coffee break**			
	Session 8: Nanoparticle Synthesis and Properties		*Chair: Erzsebet Illes*	
15:30	Gorka, Salas	Multicore magnetic nanoparticles for magnetic hyperthermia and combination therapy against cancer	Madrid, Spain	Talk 31
15:45	Simeonidis, Konstantinos	A microwave-assisted automated system for sustainable synthesis of magnetic nanoparticles	Thessaloniki, Greece	Talk 32
16:00	Hadadian, Yaser	A Novel Seed-Mediated Growth Approach for Synthesizing Core@shell CoFe2O4@BaTiO3 Magnetoelectric Nanoparticles	Gwangju, South Korea	Talk 33
16:15	Serantes, David	Decreasing the anisotropy of magnetite nanoparticles doping with Co?	Santiago de Compostela, Spain	Talk 34
16:30	Diaz Ufano, Carlos	The impact of Coating Zero-Valent Iron Nanoparticles on Advanced Oxidative Processes	Madrid, Spain	Talk 35
16:45	Leliaert, Jonathan	Advanced analysis of magnetic nanoflower measurements to leverage their use in biomedicine	Gent, Belgium	Talk 36
17:00	Telling, Neil	Evaluating the Effect of Nanomagnetic Forces on Neuronal Cells: Towards Magnetically Guided Nerve Regeneration	Keele, U.K.	Invited Talk 4
17:45	**Poster session II (Posters 83-164) - with Pizza and Beer generously sponsored by INMA, the Instituto de Nanociencia y Materiales de Aragon**			
19:30	**Free evening - go and get collaborations going!**			

Thursday, June 20, 2024				
8:30	**Registration desk opens in the Faculty of Arts & Humanities auditorium [Auditorium Filosofia y Letras, UAB, Calle de la Fortuna, Bellaterra]**			
9:00	Gutierrez, Lucia	On the Biology (and Related Subjects) From the Point of View of a Magnetic Nanoparticle	Zaragoza, Spain	Tutorial 2
	Session 9: Magnetic Particle Imaging		*Chair: Raluca Fratila*	
9:30	Mayr, Erik	Disk Shaped Magnetic Thin-Film Nanoparticles Tailored for Optimal MPI Signal Generation	Zurich, Switzerland	Talk 37
9:45	Ackers, Justin	Imaging performance of thin-film disk particles tailored for optimal MPI signal generation	Lübeck, Germany	Talk 38
10:00	Good, Hayden	Understanding the Partial Volume Effect in MPI: A study of object size impact on signal distribution and quantification accuracy	Gainesville, U.S.A.	Talk 39
10:15	**Coffee break**			
	Session 10: Magnetic Particle Imaging		*Chair: Elin Winkler*	
10:45	Rösch, Esther	Advancing MPI with SMART RHESINs: A novel hollow nanosphere tracer design for viscosity-independent relaxation	Karlsruhe, Germany	Talk 40
11:00	Thanh, Nguyen	Ultra-small Iron Oxide Nanoparticles to Replace Gd Complexes as T1 Contrast Agents for MRI	London, U.K.	Talk 41
11:15	Kosch, Olaf	Imaging of the flow diverter stent insertion into a patient-specific cerebral aneurysm phantom by Magnetic Particle Imaging	Berlin, Germany	Talk 42
11:30	Franke, Jochen	Theranostics: Magnetic Particle Imaging based planning & controlling of highly localized Magnetic Fluid Hyperthermia	Ettlingen, Germany	Talk 43
11:45	Rinaldi Ramos, Carlos	Magnetic Particle Imaging (MPI) of Dendritic Cell Migration in Cancer Therapy	Gainesville, FL, U.S.A.	Invited Talk 5

12:30	**Lunch**			
	Session 11: Magnetic Hyperthermia		*Chair: David Serantes*	
13:45	Yoon, Jungwon	A Pilot Study on the Possibility of Using MPI for Monitoring the Magnetic Nanoparticles Uptake in Brain Due to Hyperthermia	Gwangju, South Korea	Talk 44
14:00	Mefford, O. Thompson	Measurement of the Differences Between Bulk Heating and Magnetic Hyperthermia via Catalytic Reactions	Clemson, U.S.A.	Talk 45
14:15	Pankhurst, Quentin	An Alternative to the Brezovich Criterion in Magnetic Field Hyperthermia	London, U.K.	Talk 46
14:30	Rizzo, Giusy	Scale-up Syntheses of Ferrite Nanoparticles of Different Shapes with Improved Magnetic Properties for Magnetic Hyperthermia and MPI	Genoa, Italy	Talk 47
14:45	Fernandez-Afonso, Yilian	Reversible alignment of nanoparticles and intracellular vesicles during magnetic hyperthermia experiments	Zaragoza, Spain	Talk 48
15:00	**Coffee break**			
	Session 12: Magnetic Hyperthermia		*Chair: Kostas Simeonidis*	
15:30	Ruta, Sergiu	A device-independent approach to evaluate the heating performance during magnetic hyperthermia: peak analysis and zigzag protocol	Sheffield, U.K.	Talk 49
15:45	Millan, Angel	Local temperature gradients and induced cell death in intracellular magnetic hyperthermia	Zaragoza, Spain	Talk 50
16:00	Schoenen, Max	Towards image-guided therapies with nanomodified stents	Aachen, Germany	Talk 51
16:15	Christiansen, Michael	Localized Electric Fields Induced by Magnetic Nanoparticles	Zurich, Switzerland	Talk 52
16:30	Fratila, Raluca	Plasma membrane localized magnetic hyperthermia promotes intracellular delivery of cell-impermeant probes	Zaragoza, Spain	Talk 53
16:45	Abasolo Olaortua, Ibane	Iron Oxide Nanoparticles for Magnetic Hyperthermia in Pancreatic Cancer, from Preclinical Testing to Clinical Translation	Barcelona, Spain	Invited Talk 6
17:30	Removal of posters			
18:00	**Bus trip to the boat**			
19:00	**Boat tour with dinner**			
22:30	**Return to the Pier**			

Friday, June 21, 2024				
8:30	**Registration desk opens in the Faculty of Arts & Humanities auditorium**			
9:00	Gutierrez, Lucia	On the Biology (and Related Subjects) From the Point of View of a Magnetic Nanoparticle	Zaragoza, Spain	Tutorial 3
	Session 13: Biological Applications		*Chair: Esther Rösch*	
9:30	Herraiz Pérez, Aitor	Who needs chelators? Iron oxide as universal platform for multimodal imaging and therapy with radioisotopes	Madrid, Spain	Talk 54
9:45	Katewongsa, Kanlaya	Protein corona and in vitro studies of magnetic nanoparticles for breast cancer delivery	Bangkok, Thailand	Talk 55
10:00	Mickoleit, Frank	Bacterial Magnetosomes as Innovative, Versatile Platform Technology for Biotechnological and Biomedical Applications	Bayreuth, Germany	Talk 56
10:15	Lafuente, Aritz	Ferromagnetic biodegradable nanocapsules for externally controlled and non-invasively monitored nanotherapies	Barcelona, Spain	Talk 57
10:30	**Coffee break**			
	Session 14: Biological Applications		*Chair: Regina Bleul*	
11:00	Moros, Maria	Remote Magneto-Thermal Modulation of Reactive Oxygen Species Balance Enhances Tissue Regeneration in vivo	Zaragoza, Spain	Talk 58
11:15	Demri, Noam	Magnetic bioprinting of a clip-on muscle tissue	Paris, France	Talk 59
11:30	Grazu, Valeria	Spatio-temporal Selectivity in Chemotherapy: Remote Activation of Enzymatic Nanohybrids for Prodrug Therapy	Zaragoza, Spain	Talk 60
11:45	Viereck, Thilo	Integrated system with magnetic particle imaging and magnetic hyperthermia for localized drug release applications	Braunschweig, Germany	Talk 61
12:00	Del Sol-Fernandez, Susel	Remote Magneto-Mechanical Gating of Endogenous Piezo1 Channel	Zaragoza, Spain	Talk 62
12:15	Perret, Melody	Intracellular proteins targeting with bi-functionalized magnetic nanoparticles	Paris, France	Talk 63
12:30	Joisten, Helene	Mechanobiological responses of cells induced by magneto-mechanical stimulation	Grenoble, France	Talk 64
12:45	Serrano, Maria Concepcion	Exploring magnetic collagen hydrogels for neural regeneration in hemisected rats	Madrid, Spain	Talk 65
13:00	**Announcement of the next Magnetic Carrier Meeting 2026**			
13:15	**End of the Meeting**			

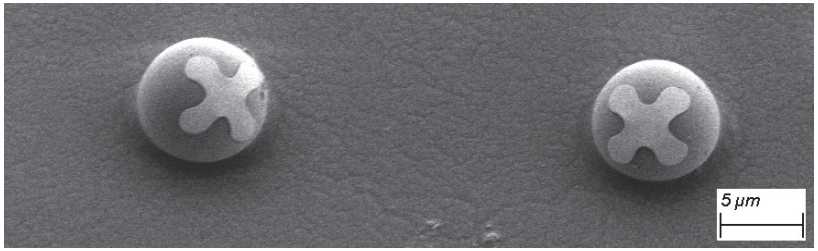
Magnetic control via magnetically microprinted microparticles

Gary Zabow

National Institute of Standards and Technology (NIST), Boulder, Colorado, 80305, USA
Email: zabow@boulder.nist.gov

A key to the popularity of magnetic nano and microparticles is their capacity for remote control. Externally applied fields can translate, rotate, and even reconfigure various microparticles and microparticle assemblies, with applications in drug delivery, microrobotics, and beyond. Generally, such magnetic control is a function of particle size, shape, and magnetization; less commonly, it may also be determined by the particle surface coating such as in the case of Janus microparticles where a layer of magnetic material is evaporated over one side / hemisphere of a particle. Even though such coatings comprise just a thin layer of magnetic material, they allow efficient control of the underlying particle because microparticles possess large surface-area-to-volume ratios. By extension, therefore, different types of surface patternings, beyond Janus coatings, should allow similarly efficient, yet different, new forms of magnetic control. Yet defining arbitrary magnetic patternings beyond simple single-sided/hemisphere coatings on microsphere surfaces, has previously been hard to achieve.

As is well known from the microchip industry, however, intricate micropatternings are readily possible on planar surfaces. A recently introduced new transfer microprinting technique [1], now allows such patternings to be transferred to non-planar surfaces, including those of microparticles (e.g. see figure below). While such transfers have previously comprised mainly non-magnetic materials, this presentation will introduce new examples of both magnetic and magnetizable micropatterns wrapped onto the surfaces of microparticles. The processing involved in the creation of such particles will also be presented as well as examples of the magnetic control that such surface patterning allows, with implications for novel remote control processes, chaining geometries, and magnetically self-assembled microparticle constructions.



Micropatterned microparticles. Side-angled view, scanning electron micrograph (SEM) of microparticles with micropatterned surfaces via microtransfer printing.

Reference:

1. G.Z., "Reflow transfer for conformal 3-dimensional microprinting", *Science* **378**, 894-898, 2022

A portable system for unshielded magnetorelaxometry imaging of magnetic nanoparticles

Aaron Jaufenthaler[1*] and Daniel Baumgarten[1]

[1]Institute of Electrical and Biomedical Engineering, UMIT TIROL - Private University For Health Sciences and Health Technology, Hall in Tirol, Austria
[*]Email: aaron.jaufenthaler@umit-tirol.at

Magnetic hyperthermia with magnetic nanoparticles (MNP) demands an accurate quantitative imaging method to ensure a safe and efficient treatment [1]. Quantitative spatial information about the MNP distribution can be gathered by means of magnetorelaxometry imaging (MRXI), where the MNP's relaxation after previous magnetization by excitation coils is measured using high sensitivity magnetometers. In combination with a mathematical model of the imaging system, the MNP distribution can be reconstructed. Current MRXI systems are rarely exploited due to the need of magnetic shielding [2]. Here, we demonstrate our work towards a portable, tabletop MRXI system for unshielded MRXI. The main challenges lie in the environmental field and gradient control, as well as in appropriate noise removal techniques

Our setup (Fig. 1) is composed of a triaxial magnetic field and magnetic field gradient compensation system, two dual channel scalar optically pumped magnetometers (OMG, Twinleaf), and 32 excitation coils. A 3D printed mouse phantom is enriched with a point-like MNP source of gypsum immobilized MNP (RCL, 850 µg iron). Our approach for environmental field and gradient control includes background magnetic field steering to define the pseudo vectorial sensitive axis of the sensors. Noise removal is achieved using feed forward techniques and Main's synchronized averaging.

With our setup, we were successfully able to reconstruct point-like sources within the region of interest. The experimental results are in line with expectations derived from previously conducted simulations. The imaging parameters of the system are currently analyzed.

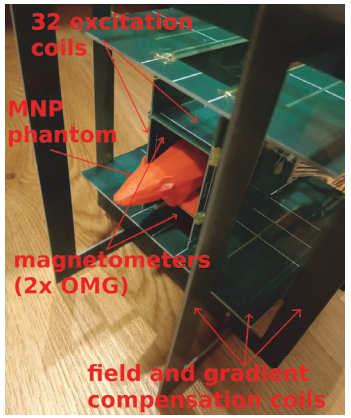


Fig. 1. Experimental proof of principle portable MRXI system for unshielded environments.

Acknowledgements
Financial support by the Austrian Science Fund (FWF), grant I 4357-B is gratefully acknowledged.
References
[1] S. Healyet et al., Clinical magnetic hyperthermia requires integrated magnetic particle imaging. W. Int. Rev.: Nanomed. and Nanobiotech., p. e1779, 2022.
[2] A. Jaufenthaler et al., Human head sized magnetorelaxometry imaging of magnetic nanoparticles with optically pumped magnetometers — A feasibility study. J. Magn. Magn. Mater., 596, p. 171983, 2024.

Micropatterning of aligned pores as directional cues in granular PEG composite scaffolds using magnetic porogens

Victor Rivera-Llabres[1], Laurel Lapish[2], Zoe Fields[1], Michael Cline[1], Carlos Rinaldi-Ramos[1,2]

[1]Department of Chemical Engineering, University of Florida, Gainesville FL, USA 32611

[2]J. Crayton Pruitt Family Department of Biomedical Engineering, university of Florida, Gainesville FL, USA 32611

Magnetic templating is a hydrogel micropatterning technique developed in our laboratory which consists of dispersing and aligning a sacrificial magnetic microparticle in a hydrogel precursor. Upon alignment of the microparticles, the hydrogel is photopolymerized and the sacrificial particle cleared out leaving an aligned pore chain suitable for providing contact guidance cues to cells. Hydrogel microparticles, or microgels, have found increasing use as components in tissue engineering, drug delivery, and wound healing. They are formulated as granular biomaterial scaffolds composed of crosslinked microgels upon their packing or as composite granular biomaterials in which microgels are embedded in a polymer matrix. The use of microgel building blocks brings benefits over traditional bulk hydrogels. For example, they exhibit controllable rheological behavior including shear-thinning, making them injectable, and upon packing, create an inherently microporous network. These benefits of granular materials have been leveraged to improve cell infiltration in tissues, enhance molecule diffusion, and even modulate immune response of the body. However, in some cases an aligned pore is preferred as a randomly distributed porosity may not be enough to induce cellular organization and cells would benefit from higher order organization of porosity scales.

We have combined our previously established magnetic templating technique with the added benefits of microgel-based biomaterials to generate a templated PEG composite scaffold incorporating PEG microgels within a PEG interstitial hydrogel and with aligned pores obtained using magnetic alginate microparticles as sacrificial porogens. Precursor is prepared by mixing microgels and interstitial matrix at different volume ratios with MAMs suspended at 2.2% v/v, aligned for 30 min, and subsequently crosslinked under 20 mW/cm^2 UV intensity (365 nm). The templated composites are then placed in an EDTA clearing solution for 6 days. Rheological characterization shows that as microgel to interstitial ratio decreases, the storage modulus, yield stress, and viscosity of the pre-crosslinked solution also decreases, and this has led to qualitatively better porogen alignment. Mechanical indentation of composites reveals the inclusion of microgels into the composite scaffolds improves the mechanical strength of the scaffold compared to pure bulk PEG hydrogels. Furthermore, the templating process reduces the mechanical properties of non-templated composite scaffolds. The results show that magnetic templating of a PEG composite scaffolds could achieve formulation of micropatterned modular scaffolds with the potential to enhance cell infiltration and organization.

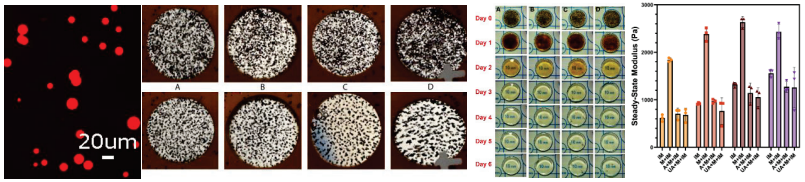


Figure 1. (Far left) Representative fluorescent image of formulated microgels. (Middle left) Representative images of pre-aligned (top) and post-aligned (bottom) magnetically templated microgel/hydrogel composites with A) 50%, B) 60%, C) 70%, and D) 80% v/v interstitial matrix. (Middle right) Day by day clearance of composites made with conditions A, B, C, and D. (Far right) Steady-state relaxation modulus of pure bulk (IM), composite (M+IM), aligned templated composite (A+M+IM), and unaligned templated composite (UA+M+IM) hydrogels post-clearance.

carlos.rinaldi@ufl.edu (corresponding author)

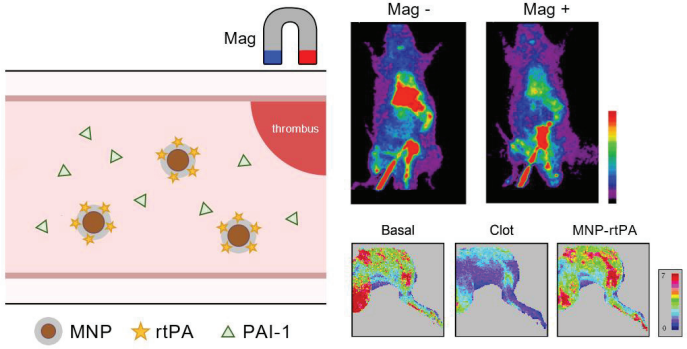
Translational Assessment of Magnetic Nanotherapeutics for Target Thrombolysis

Yunn-Hwa Ma

Department of Physiology and Pharmacology, College of Medicine, Chang Gung University, Taoyuan, Taiwan, Republic of China

Email: yhma@mail.cgu.edu.tw

Plasminogen activators, such as recombinant tissue-type plasminogen activator (rtPA), while effective in treating thromboembolic diseases often induce hemorrhagic complications due to non-specific enzyme activities in the systemic circulation. This study evaluated the targeting effect, efficacy, biodistribution, and potential toxicity of rtPA covalently immobilized on chitosan-coated magnetic nanoparticles (chi-tosan-MNP-rtPA). The thrombolytic activity of chitosan-MNP-rtPA was preserved by protection from endogenous plaminogen inhibitor-1 (PAI-1) in whole blood after circulation *in vivo*, as examined by thromboelastometry. Single-photon emission computed tomography (SPECT)/ computed tomography (CT) demonstrated real-time retention of ^{99m}Tc-MNP-rtPA induced by magnet application in a rat embolic model; an 80% rtPA dosage reduction for chitosan-MNP-rtPA with magnetic guidance was shown to restore blood flow. After treatment, iron deposition was observed in the reticuloendothelial systems, with portal edema and neutrophil infiltration in the liver at a 10-fold higher dose, not the regular dose. Nevertheless, no liver or renal toxicity was observed at this higher dose. In conclusion, the liver may still be the major deposit site of rtPA nanocomposites after targeted delivery; chitosan-coated MNPs are potentially amenable to target therapeutics with parenteral administration.



Nanocarriers for Dual-Targeted Therapy of In-Stent Restenosis

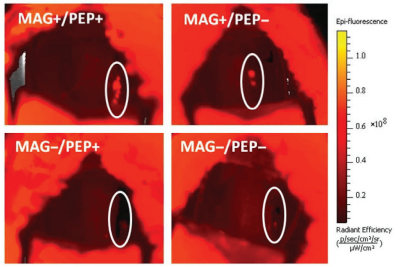
Ivan S. Alferiev, Kehan Zhang, Zoë Folchman-Wagner, Richard F. Adamo, David Guerrero, Ilia Fishbein, Robert J. Levy, Michael Chorny

Division of Cardiology, The Children's Hospital of Philadelphia, and Department of Pediatrics, Perelman School of Medicine, Philadelphia, PA 19104, USA

Injury-triggered reocclusion (restenosis) of arteries treated with angioplasty to relieve atherosclerotic obstruction remains a challenge due to a lack of therapies combining adequate efficacy and safety. While delivery of antiproliferative agents from vascular stents (i.e. drug eluting stents, DES) has reduced the incidence of restenosis in coronary artery disease patients with non-complex lesions, the long-term safety of DES remains compromised by delayed healing, hypersensitivity, and local inflammation, all contributing to neointimal hyperplasia and neoatherosclerosis. As a result, the long-term risk of in-stent restenosis remains significant even with the newest DES devices available today. Therefore, despite the ongoing development and optimization of the stent technology, a need remains for conceptually different drug delivery strategies.

In the present studies, we evaluated feasibility of a site-specific delivery approach combining magnetic guidance with affinity binding to enhance localization and retention of magnetic nanoparticles (MNP) in stented arteries. A two-source magnetic targeting scheme we used to guide magnetizable particles to the region of stent implantation involves a coordinated action of two field sources: a primary source, such as an MRI scanner or a magnetic navigation system, which provides a strong, uniform, and deep-penetrating magnetizing field, and a secondary (dependent) source, such as a vascular stent made of a reversibly magnetizable alloy, positioned in the injured arterial segment and focusing the magnetic force by creating a region of highly localized and strong field gradients. As the stent configured in thin intersecting struts becomes magnetized, its geometry makes it highly efficient for guiding MNP to the region of stent deployment by creating strong field gradients in its vicinity.

To endow MNP with binding affinity for injured blood vessels we functionalized the particle surface with a fibrin α-chain N-terminal short peptide that binds to the C-terminal portion of the fibrin γ-chain with high avidity due to > 10^{15} binding sites per mg fibrin protein. The efficiency of dual-targeted nanocarrier delivery was tested in a rat carotid stenting model, in combination with a brief exposure to a uniform field (1,000 G) generated across the stented region using paired electromagnets. The strong magnetic responsiveness and the multivalent binding mechanism of MNP accommodating up to 4×10^4 peptide residues per particle contributed to stable anchorage of the carriers in stented arteries, resulting in several-fold higher levels of fluorescently labeled MNP detected 3 and 7 days post-treatment per the results of live animal fluorescent imaging (see figure below) and fluorimetric analysis. Importantly, the enhanced arterial localization of dual-targeted MNP was paralleled by markedly reduced particle distribution to non-target tissues: negligible amounts of MNP were detected in the contralateral (control) artery, lungs, or kidneys. Furthermore, the weight-normalized MNP amounts in the stented arteries markedly exceeded those found in the spleen and liver (180±53 ng, 62±7 ng, and 14±2 ng per mg tissue, respectively). In contrast, the single targeting groups (MNP either non-functionalized or applied in the absence of the magnetic exposure: MAG+/PEP- and MAG-/PEP+, respectively) were not significantly different from the untargeted MAG-/PEP- controls exhibiting 0.3±0.1 and 0.8±0.2 target/spleen and target/liver ratios, respectively.



Unlike singly targeted or untargeted MNP formulated with paclitaxel, drug-loaded carriers delivered using the integrated magnetic guidance/affinity targeting scheme achieved a marked reduction in arterial restenosis (p = 0.03 and 0.04 for neointima/media ratio and % stenosis, respectively). The remarkable enhancement in site specificity and the potent mitigation of the injury-triggered arterial renarrowing observed in our study warrant further optimization of dual-targeted delivery using surface-functionalized magnetic nanocarriers as a new modality for treating restenosis and other proliferative vascular diseases.

Endovascular Delivery and Magnetic Retention Enhance Brain Targeting of PLGA Nanocarriers in Large Cerebral Vascular Models

García-Gabilondo M[1], Grayston A[1], Solé A[2], de la Torre-Sánchez, I[1], Otero-Fornés N[1], Mekseriwattana W[2], Timko M[3], Kovac J[3], Kopcansky P[3], Li J[4], Tiberi R[4], Esteves M[5], Tomasello A[4], Hernández D[4], Ribó M[4], Roig A[2], Rosell A[1].*

[1] Neurovascular Research Laboratory, Vall d'Hebron Institut de Recerca, Universitat Autònoma de Barcelona (VHIR-UAB), Barcelona, Spain. [2] Nanoparticles and Nanocomposites Group, Institut de Ciència de Materials de Barcelona (ICMAB-CSIC), Bellaterra, Spain. [3] Department of Magnetism, Institute of Experimental Physics, SAS, Kosice, Slovakia. [4] Stroke Unit & Stroke Research Group, Vall d'Hebron University Hospital-VHIR, Barcelona, Spain. [5] Experimental Surgery Unit, Vall d'Hebron Institut de Recerca. *Corresponding author: Anna Rosell Novel; anna.rosell@vhir.org

Ischemic stroke is one of the leading causes of death and disability and is characterized by an interruption of cerebral blood flow due to the presence of a clot in blood vessels. Nowadays, mechanical thrombectomy has become an available reperfusion treatment and has opened the opportunity to use the intraarterial endovascular route for brain delivery of therapeutic agents to improve brain targeting.

We have previously worked with polymeric PLGA nanocapsules (NC) as biocompatible nanocarriers that can be upgraded by including iron particles for magnetic guidance and fluorescent moieties such as Cy5 for imaging. We have already proven in rodents the safe and targeted delivery of NCs into ischemic brain areas through intraarterial administration in combination with magnetic guidance. Now, as a step towards translation, we aimed to assess the feasibility of the same strategy in large cerebral circulation models, which are more extrapolative to the human anatomy.

In vivo, brain targeting was studied in pigs (*Sus domesticus*) after intraarterial infusion of the NC using a micro-catheter through the femoral vein as conducted in the clinical practice, while intravenous administration was performed through the marginal ear vein (n=4-5/group). The brains were observed by *ex-vivo* fluorescent molecular imaging (FMI) showing that the endovascular approach enhanced brain delivery with a higher accumulation in the hemisphere of administration compared to intravenous administration (p=0.01), confirmed by the presence of Cy5 fluorescence in brain microvessels.

In addition, to assess the efficacy of magnetic retention, we used a 3D-printed model of the human supra-aortic cerebral vasculature to test the effect of magnetic retention after endovascular infusion of NCs (n=4-5/group). A focused magnet tailored to fit the human anatomy was positioned on the administration side, enhancing NC accumulation in the targeted middle cerebral artery versus the control without magnet (p=0.06).

This study demonstrates the feasibility of a clinically-relevant endovascular approach in pigs and the efficacy of the magnet device to improve local retention in the 3D-printed human vascular model. The PLGA nanoformulations designed to deliver therapeutic drugs show promise for targeted delivery into ischemic brain areas to enhance tissue repair.

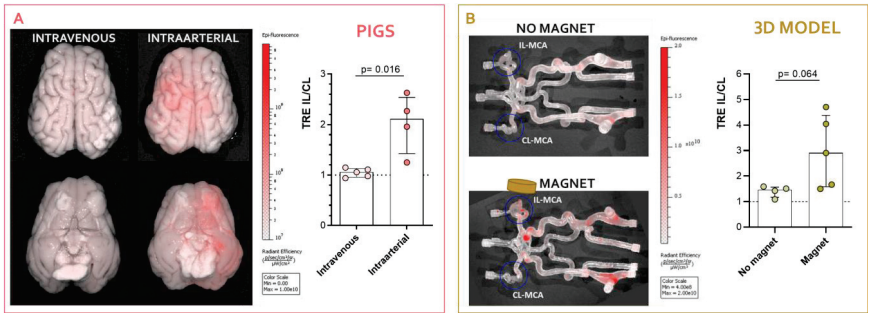


Figure. **A** Ex-vivo FMI imaging of pig brains after intraarterial/intravenous NC infusion and Total Radiant Efficiency (TRE) ratio of the administration side / opposite side (IL/CL). **B** FMI of the 3D printed model with or without magnetic retention near the middle cerebral artery (MCA) during NC administration and TRE ratio of the IL/CL MCAs. Graphs represent median with interquartile range and p-values of Mann-Whitney tests.

Magnetic-enzymatic nanomotors depicting a collective swarming behavior and directional navigation abilities

Anna C. Bakenecker[1,2*], Xavier Arqué[1], Juan C. Fraire[1], Huimin Wei[2], Heiko Lemcke[2], Paul Soto Rodriguez[3], Sandra Prévéral[3], Damien Faivre[3], and Samuel Sánchez[1,4*]

[1]Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Baldiri i Reixac 10-12, 08028 Barcelona, Spain

[2]Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering IMTE, Mönkhofer Weg 239a, 23562 Lübeck, Germany

[3]Aix-Marseille University, CNRS, CEA, BIAM, Saint-Paul-lez-Durance, 13115 France

[4]Catalan Institute for Research and Advanced Studies (ICREA), Passeig de Lluís Companys 23, 08010 Barcelona, Spain

*E-Mail: anna.bakenecker@imte.fraunhofer.de, ssanchez@ibecbarcelona.eu

Many treatments are based on the systemic administration of high amounts of therapeutic drugs, which leads to side effects and limited accumulation at the target side. Therefore, methods to efficiently administer, penetrate and locally release the drugs such as smart nanoparticles (NPs) for precision medicine are highly needed. For this, NPs with self-propelling properties, which are called nanomotors, have been proposed as drug delivery systems able to overcome these limitations [1].

Nanomotors show self-propelling behavior due to the catalytic reaction of enzymes decorated on the NPs surface. The propulsion mechanism is based on the consumption of an enzyme-specific substrate serving as fuel. On a single particle level, enhanced diffusion coefficients have been reported. For drug delivery approaches however, many particles are needed and therefore the collective swarming effect of nanomotors has been brought into focus [2]. It has been recently shown that actively propelled nanomotors can cross extracellular barriers [3], show enhanced penetration into tumor tissue [4] and enable the movement through complex media such as the synovial fluid [5].

On the other hand, several approaches have been demonstrated of using magnetic NPs for an enhanced administration of drugs by applying magnetic fields and steering the particles towards their targeted site. Also, for the actuation of magnetic NPs, the collective behavior has attracted interest [6].

To combine the properties of active self-propulsion and magnetic guidance, we present enzymatic functionalized magnetic NPs. These magnetic-enzymatic nanomotors show, on one hand, an active swarming behavior due to the catalytic reaction of the enzymes and, on the other hand, the magnetic properties allow for a directional steering of the nanomotors in magnetic gradient fields. The figure shows representative snapshots of the video taken from nanomotors, which were pipetted into a petri dish either containing water or fuel. Furthermore, these nanomotors have the potential to be visualized by means of Magnetic Particle Imaging (MPI) as well as to be used for Hyperthermia treatments.

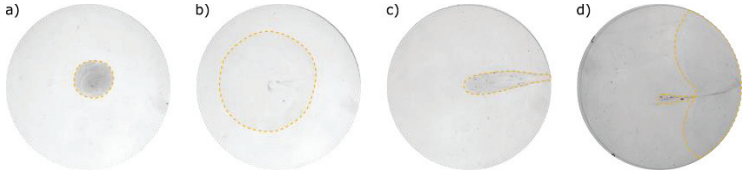


Figure: Representative snapshots of the dispersion behavior of magnetic-enzymatic nanomotors in a) water b) fuel c) water + magnetic force (pointing towards right side) d) fuel + magnetic force (pointing towards right side). The area occupied by nanomotors is encircled in yellow for better visibility.

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INVITED TALK

Magnetic Small-Scale Robots for Biomedical Applications

Salvador Pané
Multi-Scale Robotics Lab, ETH Zürich, Tannenstrasse 3, CLA H9, 8092, Zürich, Switzerland
E-mail: vidalp@ethz.ch

Magnetic micro- and nanorobots are small-scale devices that have the ability to move through fluids using external magnetic fields, and have the potential to deliver drugs and perform other medical tasks within confined spaces of the human body. The recent advancements in magnetic small-scale robotics can be largely attributed to progress in material science and manufacturing. While numerous applications have been demonstrated, there are still several areas that require further research, including complex locomotion, multifunctionality, biocompatibility, and biodegradability. As a result, new material-based concepts, innovative fabrication techniques are urgently needed to address these challenges and improve the field of small-scale robotics. This discussion will explore various material-based concepts and innovative fabrication techniques aimed at overcoming translational hurdles and further enhancing the capabilities of small-scale robotics. In the first part of the talk, we will show how 3D printed microtemplates can be exploited to produce complex robotic microstructures made of electrodeposited rigid metals, soft polymers and combinations of these. As a result, topologically complex metal-organic structures can be realized with sub-micrometric resolution. I will also demonstrate that metal-organic interlocked micromachines can solve several practical challenges in small-scale robotics. We will show that high magnetic responsiveness, drug loading capabilities, biocompatibility, on-demand shape transformation, and multi-locomotion modes can be embedded in a single microrobotic machine. In the second part of my talk, we will show how to achieve multifunctional microrobots using magnetoelectric multiferroic composites. These materials have the ability to generate an electric field under the application of an external magnetic field. The magnetoelectric small-scale swimmers comprise a magnetostrictive component that allows for both the magnetic locomotion of the device, and also for the activation of the piezoelectric component. This wireless polarization can then be used for cell electrostimulation and differentiation.

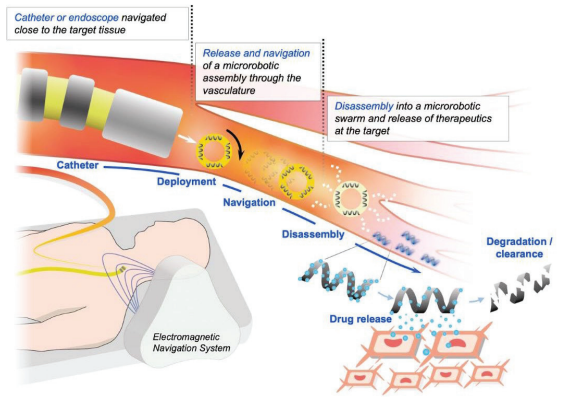

Figure. A potential medical procedure with microrobots involves delivering them via a catheter or endoscope to target areas like tumors or blood clots. These microrobots travel through the bloodstream to their destination, where they precisely release therapeutic agents. Once their task is complete, the microrobots degrade and are naturally eliminated from the body.

Optimization of Volumetric Magnetic Particle Spectroscopy (MPS) Biosensor for Five-Minute Ultrafast Detection of SARS-CoV-2 Spike Protein

Kai Wu[1,2], Vinit Kumar Chugh[1], Venkatramana D Krishna[3], Maxim C-J Cheeran[3], Jian-Ping Wang[1,*]
[1]Department of Electrical and Computer Engineering, University of Minnesota, Minneapolis, MN 55455, United States
[2]Department of Electrical and Computer Engineering, Texas Tech University, Lubbock, TX 79409, United States
[3]Department of Veterinary Population Medicine, University of Minnesota, St. Paul, MN 55108, United States
*Presenter and corresponding author, E-mail: jpwang@umn.edu (J.-P. W)

The coronavirus disease 2019 (COVID-19) pandemic has brought forward an urgent need for rapid, convenient, and widely deployable diagnosis tools for the surveillance of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), in a joint effort to mitigate its spread within and across communities. A rapid and sensitive method for the detection of SARS-CoV-2 is critical for controlling the spread of COVID-19 by proper containment procedures as well as for reducing morbidity and mortality by facilitating early treatment. Currently, the fastest on-site detection techniques such as lateral flow assays and ID Now can detect COVID-19 in 15–30 min. For most on-site diagnosis platforms, the bioassay time varies from 1 to 12 hours. As a result, the long turnaround time has severely hindered COVID-19 surveillance and impeded pandemic control measures. In this work, we report a 5-min magnetic particle spectroscopy (MPS)-based bioassay strategy. In our approach, surface-functionalized magnetic nanoparticles are incubated with target analytes at 37 °C with agitation for 3 min, and the MPS reading is then taken at the fifth minute, as shown in Fig. 1. We demonstrated 5 min ultrafast detection of SARS-CoV-2 spike protein and achieved a detection limit below 5 nM (0.2 pmol). Our proposed 5-min bioassay strategy may be applied to reduce the assay time for other liquid-phase, volumetric biosensors such as nuclear magnetic resonance (NMR), quantum dots, fluorescent biosensors, etc.

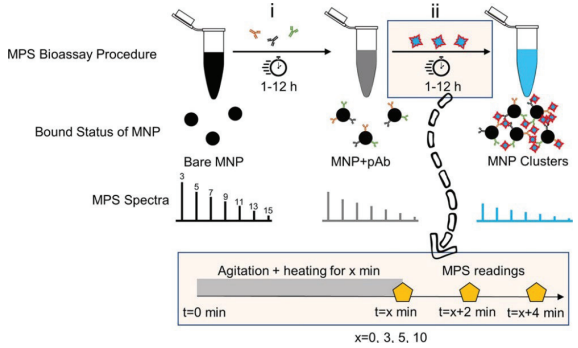

Fig.1. Traditional MPS bioassays as well as other volumetric-based assay platforms require 1–12 hours of incubation time as shown in step ii. Herein, incubation conditions (agitation and heating) are applied during the incubation step to result in ultrafast MPS bioassay (top row). (i) MNP surface functionalization with polyclonal antibodies. (ii) Surface-functionalized MNPs incubating with target analytes. Figure from Ref. [1].

References

[1]ACS Applied Nano Materials 2022, 5, 12, 17503–17507

Next generation magnetic circuits for the detection of nucleic acid biomarkers

Rebecca Sack*, Enja L. Rösch, Florian Wolgast, Frank Ludwig, Meinhard Schilling, Thilo Viereck, Aidin Lak

Institute for Electrical Measurement Science and Fundamental Electrical Engineering and Laboratory for Emerging Nanometrology (LENA), TU Braunschweig, Germany
*E-Mail: rebecca.sack@tu-braunschweig.de

Magnetic biosensing concepts have recently made significant progress towards detecting pathogen-specific nucleic acid sequences such as Malaria DNA [1] and SARS-CoV-2 RNA [2] in complex samples, utilizing a novel approach of declustering bio-responsive magnetic clusters upon detecting the target. While enzyme-mediated magnetic bioassays offer high sensitivity and short assay time [1], enzymes are expensive and require extremely low temperature storage and transportation. Our enzyme-free magnetic diagnostic cascades, that are based on toehold-mediated DNA strand displacement (TM-DSD), provide high sensitivity and specificity. However, the assay incubation time takes 24 hours. In homogeneous and volume-based magnetic bioassays, few target DNA strands have to search for binding sites within the clusters in a large volume before the DSD-mediated declustering can occur, which is a stochastical process governed by several factors. Therefore, it is highly challenging to combine high assay sensitivity and short incubation time in a mix-and-measure assay.

Here we exploit three major concepts from DNA nanotechnology, namely toehold-exchange, destabilizing mismatches and concentration driven TM-DSD, and translate them into our magnetic diagnostic circuit to design highly sensitive and rapid bioassays. During the toehold-exchange reaction a DNA target first displaces a branch migration (BM) domain of an incumbent DNA (Figure 1a). Next, domain TH_2 (blue) dissociates spontaneously to expose a toehold (TH_2*) for a fuel DNA and enable recycling of the target by reverse TM-DSD. This unique feature facilitates multiple declustering reactions by one target strand and enhances the sensitivity of our assays. We study the influence of the properties of TH_2, along with the concentration of added DNA strands and magnesium ions on the performance of our assay. Utilizing Alternating Current Susceptometry (ACS) and Magnetic Particle Spectroscopy (MPS) measurements, we found that the highest declustering rate is achieved for a TH_2 length of 6 nucleotides with a mismatched base pair at position 6 (Figure 1b). We further improved the target recycling rate by feeding more fuel DNA to the assay to harness concentration driven TM-DSD. The combination of these two effects results in the limit of detection (LOD) of 58.5 pM of target DNA after 4 h assay time, falling within the similar range of LOD of 27 pM obtained in our previous work [2], yet after 24 h assay time.

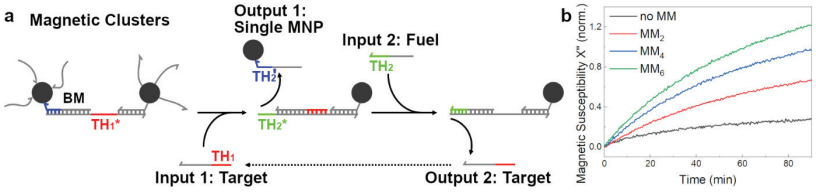

Figure 1: (a) Schematic visualization of DNA target recycling via toehold exchange, including spontaneous dissociation of TH_2' (blue), releasing a previously bound Magnetic Nanoparticle (MNP), and reverse TM-DSD via a fuel DNA to release the target strand. (b) ACS measurement at 120 Hz for clusters with a mismatch MM_x at different base-pair positions x proximal to the MNP, for a TH_2 length of 6 nucleotides, 1 nM of target and 100 mM Mg^{2+}.

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One-step and wash-free magnetic method for direct SARS-CoV-2 virus detection in patient samples

I. Mikelez-Alonso,[1] J. Sanchez-Martínez,[2,3] C. Martinez-Boubeta,[1] I. Sanz-Muñoz,[2,3,4]

A.L. Cortajarena[5,6] and F.J. Terán[1,7]

[1] Nanotech Solutions, Ctra Madrid 23, 40150 Villacastín, Spain
[2] National Influenza Centre, Hospital Clinico Universitario de Valladolid, Valladolid, Spain
[3] Instituto de Estudios de Ciencias de la Salud de Castilla y León, ICSCYL, Soria, Spain
[4] CIBER INFEC, Instituto de Salud Carlos III, Madrid, Spain
[5] CIC biomaGUNE, Paseo de Miramón 194, 20014, Donostia-San Sebastián, Spain
[6] Ikerbasque, Basque Foundation for Science, Bilbao, Spain
[7] iMdea Nanociencia, Ciudad Universitaria de Cantoblanco, 28049 Madrid, Spain

Recent COVID-19 pandemic has remarkably boosted the research on *in vitro* diagnosis immunoassays for biomarker detection in biological fluids. Although specificity and sensitivity are mandatory for accurate clinical outcomes, simplicity and minimal sample processing are key points to render faster and cheaper the next generations of *in vitro* diagnostic assays. Taking advantage of the outstanding progress on material science, high quality nanoparticles with customized physical properties can be currently employed for efficient sensing transduction in liquid media. One example is given by magnetic nanoparticles (MNPs), which have been extensively used in distinct biosensing methodologies in liquids. Here, we report on a novel biosensing method for direct and simple SARS-CoV-2 virus detection in nasopharyngeal patient samples dispersed in virus transport media (VTM). The proposed magnetic labeling method (MLM) is based on the changes of AC magnetic hysteresis area obtained from bioconjugated cobalt ferrite nanoflowers (b-MNPs). These AC magnetization variations follow biomolecular recognition of SARS-CoV-2 virus specimens present in PCR diagnosed patient samples (n=11). Conjugated receptors covalently bounded onto b-MNP surface are commercial anti-spike antibodies, which specifically interacts with SARS-CoV-2 virus. MLM recognition takes place during 30 minutes incubation of b-MNPs dispersed in non-purified nor processed patient samples dispersed in VTM at room temperature. Later, we observe the variations of AC magnetic hysteresis cycles observed in viral transport media (virus free) and patient samples (with CoV+ virus) tightly depend on AC magnetic field conditions, virus and b-MNP concentrations. Interestingly, the MLM time requested for virus detection in less than 45 minutes. Our study provides significant insights on the potential of AC magnetometry for one-step, wash-free and direct virus detection in minimally manipulated patient samples in less than one hour.

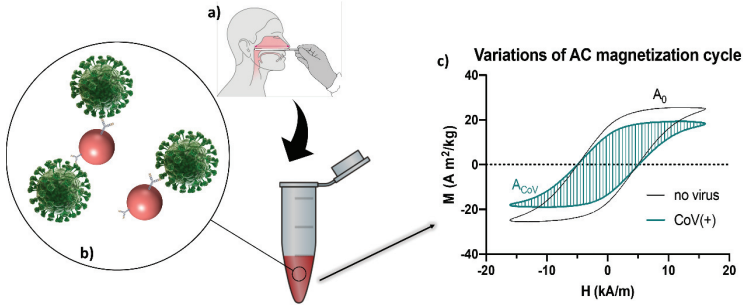

Figure. a) Nasopharyngeal sample extraction, b) Scheme of the biomolecular recognition of the virus by MNPs, c) Comparison of the AC hysteresis cycles measured at 30 kHz and 16 kA/m from b-MNPs dispersed in media virus free or SARS-CoV-2 virus at 0.1 gram of magnetic elements per liter.

Magnetic Nanoclusters with Twofold Functionality in Lateral Flow Immunoassays to detect Pneumococcal Pneumonia: Analyte Concentrators and Detection Reporters

María Salvador[1], José Luis Marqués-Fernández[1], Alexander Bunge[2], José Carlos Martínez-García[1], Vanessa Pilatti[1], Rodica Turcu[2], Davide Peddis[3], M. del Mar García-Suárez[4], M. Dolores Cima-Cabal[4], Montserrat Rivas[1*]

[1]Department of Physics & IUTA, University of Oviedo, Spain
[2]National Institute for Research and Development of Isotopic and Molecular Technologies, Romania
[3]Department of Chemistry and Industrial Chemistry, Università degli Studi di Genova, Italy
[4]Escuela Superior de Ingeniería y Tecnología (ESIT), Universidad Internacional de la Rioja, Spain
*Email: rivas@uniovi.es

Pneumonia is the leading cause of death from infectious diseases globally, significantly affecting the elderly and children [1]. In fact, among children, it emerges as the foremost cause of mortality following the neonatal stage. Various pathogens can instigate this illness, underscoring the importance of accurate identification to facilitate appropriate treatment. *Streptococcus pneumoniae* bacteria is the leading pathogen responsible for most community-acquired pneumonia and other respiratory and systemic infections However, the current diagnostic methods for this bacterium still require enhancement, as sample collection proves challenging, time-consuming, and necessitates sophisticated equipment typically housed in centralized laboratory settings.

This work shows the development of a rapid diagnostic test to detect pneumolysin (PLY). This protein is an ideal diagnostic target that is present in readily accessible urine samples. PLY quantification was developed via a combination of magnetic labelling in a lateral flow immunoassay and an inductive sensor. The magnetic labels, synthesized via a polyol method, comprised iron oxide nanoparticles approximately 8 nm in size, which agglomerated into spherical clusters with mean diameters of 89 nm. The polyacrylic acid on their surface enables their biofunctionalization with a monoclonal antibody for the specific recognition of the PLY. The lateral flow test was calibrated using various standard PLY solutions, and its readout was dual: magnetic, utilizing the inductive sensor, and optical, employing image analysis via a smartphone camera. Both methods showed remarkable figures of merit, with the inductive reader exhibiting a wider linear range, superior correlation factor, and lower limits of detection and quantification. Finally, we proved the ability of the nanoclusters to concentrate diluted samples thanks to their magnetic character. Thanks to this simple technique, we considerably improved the limit of detection for both the inductive and optical sensors at 0.2 ng/mL and 0.6 ng/mL, respectively.

Acknowledgments

We acknowledge the Ministry of Science and Innovation of the Spanish Government (PLEC2022-009490), the IUTA (SV-22-GIJON-18), and the Government of the Principality of Asturias (FICYT/IDI/2021/000100, FICYT/IDI/2021/00027). M.S. was supported by a Margarita Salas fellowship financed by the European Union-Next Generation EU and the Plan for Recovery, Transformation, and Resilience.

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Cytoplasmic Viscosity is a Potential Biomarker for Metastatic Breast Cancer Cells

Marie Dessard[1,2] Jean-Baptiste Manneville[1] and Jean-François Berret[1]*
[1]*Université Paris Cité, CNRS, Matière et systèmes complexes, 75013 Paris, France*
[2]*CNRS, INSERM, CIML, Luminy Campus, Aix-Marseille University, 13009 Marseille, France*
Email : jean-francois.berret@u-paris.fr

Cancer is responsible for 25% of deaths worldwide. To stem the high mortality rate, it is essential to develop new diagnostic methods for the early detection of cancerous and metastatic cells. A common idea is that the metastatic potential of cancer cells correlates with their deformability, pointing to the possibility of using specific mechanical properties as biomarkers of malignancy and cancer aggressiveness [1]. These findings rely on measuring the apparent Young modulus of whole cells using primarily atomic force microscopy [2]. The present study aims to explore whether alternative mechanical parameters have discriminating features with regard to metastatic potential. Magnetic rotational spectroscopy (MRS) is employed in the examination of mammary epithelial cell lines, MCF-7 and MDA-MB-231, representing low and high metastatic potential, alongside normal-like MCF-10A cells. MRS utilizes active micron-sized magnetic wires in a rotating mag netic field to measure the viscosity and elastic modulus of the cytoplasm [3,4]. All three cell lines display viscoelastic behavior, with cytoplasmic viscosities ranging from 10-70 Pa s and elastic moduli from 30-80 Pa. Our findings indicate that MCF-10A normal breast cells exhibit the highest viscosity and elasticity, while MDA-MB-231 breast tumor cells with high metastatic potential display the lowest viscosity and elasticity (Figure 1). Importantly, our study highlights that Young modulus is not the sole characteristic affected by the breast cancer phenotype [5]. To differentiate cells with low and high malignancy, viscosity emerges as the more discriminating parameter, as MCF-7 exhibits a 5 times higher viscosity as compared to MDA-MB-231. This study hence suggests that static viscosity, instead of the elastic or Young modulus, could be used as a potential marker for invasive and metastatic cancer cells.

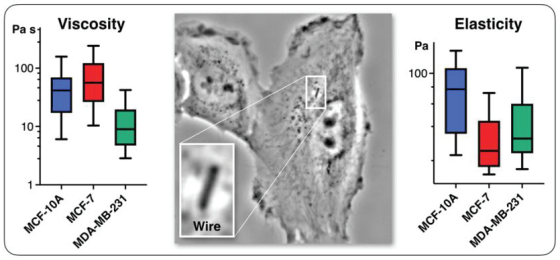

***Figure 1**: **a)** Static viscosity for MCF-10A, MCF-7 and MDA-MB-231 epithelial breast cells. **b)** Phase-contrast optical microscopy images of MCF-10A cells showing an internalized magnetic wire (inset). **c)** Elastic modulus for MCF-10A, MCF-7 and MDA-MB-231 cells.*

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Unveiling the 3D Magnetic Vortex Texture of Iron Oxide Nanoflowers

Carlos Moya,[1,2] Mariona Escoda-Torroella, [1,2] Javier Rodríguez-Álvarez, [1,2] Adriana Figueroa, [1,2] Íker García,[1] Inés Batalla Ferrer-Vidal,[1] A. Gallo-Cordova,[3] M. Puerto Morales,[3] Lucía Aballe,[4] Arantxa Fraile Rodríguez,[1,2] Amílcar Labarta,[1,2] and Xavier Batlle[1,2]

[1]Departament de Física de la Matèria Condensada, Universitat de Barcelona, Martí i Franquès 1, 08028 Barcelona, Spain
[2]Institut de Nanociència i Nanotecnologia (IN2UB), Universitat de Barcelona, 08028 Barcelona, Spain
[3]Department of Nanoscience and Nanotechnology, Instituto de Ciencia de Materiales de Madrid (ICMM-CSIC), Sor Juana Inés de la Cruz 3, 28049 Madrid, Spain
[4]ALBA Synchrotron Light Facility, CELLS, 08290 Barcelona, Spain

***e-mail of presenting author:** carlosmoyaalvarez@ub.edu

Magnetic iron oxide Nanoflowers (IONF) have been drawing much attention because of their superior magnetic performance compared to single-core magnetic nanoparticles.[1] Despite the large sizes of IONF, these aggregates show almost zero remanences and nearly vanishing coercivities, while preserving high saturation magnetization.[2] This seemingly effective superparamagnetic behavior has motivated their use in biomedical and environmental applications since the net magnetization can be controlled at will by an external magnetic field so that the particle agglomeration is effectively reduced. Some authors have attributed this phenomenology to the existence of some exchange coupling among the cores, leading to a super ferromagnetic state of the whole aggregate.[3] However, the effect of the crystal texture on the nearly demagnetized remnant state of these systems is still unclear. This study reports on how the local magnetic texture, originating from crystalline correlations among the cores, governs the unique magnetic properties of individual IONF in sizes ranging from 40 to 400 nm.[4] Despite size variations, all samples exhibit consistent crystalline correlations extending beyond the IONF cores. A nearly zero remnant magnetization, a persistently blocked state, and temperature-independent magnetization support the existence of a 3D magnetic texture throughout IONF. Magnetic transmission X-ray microscopy confirms nearly demagnetized states caused by magnetic texture vorticity. Moreover, micromagnetic simulations show vortex-like spin configurations with partial topological protection, stabilized by inter-core exchange coupling and demagnetizing fields at low magnetic fields (see Fig. 1). Overall, this study provides valuable insights into the impact of crystalline texture on the magnetic properties of IONF over a wide size range.

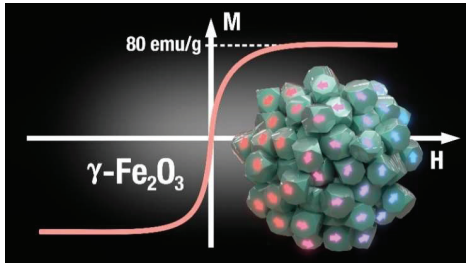

Figure 1. The hysteresis loop shows the effective superparamagnetic behaviour in IONF caused by the near demagnetized state driven by the high vorticity of the core moment texture at low magnetic fields as shown in the inset.

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COMPASS: A trailblazing technology for rapid in vitro bioassays based on MNPs

J. Günther[1*], M.A. Rückert[1], B. Friedrich[2], R. Tietze[2], L. Heinen[2], E. Hausen[2], S. Lyer[2], K. Knies[4], T. Reichl[1], T. Kampf[1,5], L. Dölken[3,4], C. Alexiou[2], V.C. Behr[1], P. Vogel[1,6]

[1] Department of Experimental Physics 5 (Biophysics), Julius-Maximilians-University Würzburg, Germany. [2] Department of Otorhinolaryngology, Head and Neck Surgery, Section of Experimental Oncology and Nanomedicine (SEON), Else Kröner-Fresenius-Stiftung-Professorship, University Hospital Erlangen, Germany, [3] Helmholtz Institute for RNA-based Infection Research, Helmholtz-Center for Infection Research, Würzburg, Germany. [4] Institute for Virology and Immunobiology, Julius-Maximilians-University Würzburg, Germany. [5] Department of Diagnostic and Interventional Neuroradiology, University Hospital Würzburg, Germany. [6] Pure Devices GmbH, Rimpar, Germany.
*E-Mail: Johanna.Guenther1@uni-wuerzburg.de.

Critical offset magnetic particle spectroscopy (COMPASS) is a novel approach to characterize the properties of magnetic nanoparticles (MNP) within seconds and with an outstanding precision [1]. The method is based on a critical effect, that is highly sensitive to changes in particle mobility. This has a high relevance for applications of magnetic nanoparticles as bioassays for detecting biomolecules like antibodies or biomarkers. In this work we present the successful detection of SARS-CoV 2 antibodies using the COMPASS method combined with specifically functionalized MNP reaching a sensitivity in the pico-molar range.

Compared to classical magnetic particle spectroscopy (MPS) COMPASS is complemented with a static offset field H_{DC} additionally to the oscillating field H_{AC} to excite the particles. By sweeping through different H_{DC} field strengths a critical effect occurs for specific field combinations of H_{DC} and H_{AC}. At these so-called critical points (CP) the signal of a higher harmonic in the nonlinear magnetization response of the MNP is suppressed leading to a significant jump-like behavior of the phase that is highly sensitive to changes in particle mobility. Such changes can be induced, e.g., by binding antibodies on the functionalized MNP surface causing an increase of the particle's hydrodynamic diameter.

The hardware equipment needed for such a COMPASS measurement can be reduced to a fairly small and portable device. The effect itself is independent of MNP concentration, thus the sample handling is much simpler and more robust as known from methods like ACS (ac-susceptometry) or MPS [2], [3]. The measurement time itself can be reduced to less than 1s.

With this device the proof of concept for highly sensitive detection of biomolecules was performed on the example of SARS-CoV 2 antibodies reaching a validated sensitivity of 0.33 fmol per 50 µl sample volume (≙7 pM). This result shows that the COMPASS method is competitive with the sensitivity of commonly used ELISA or flow cytometry tests. However, the COMPASS method stands out by its additional features of being more flexible due to the small portable device and more rapid since a complete measurement including sample conjugation, mixing and incubation times can be performed in less than a minute.

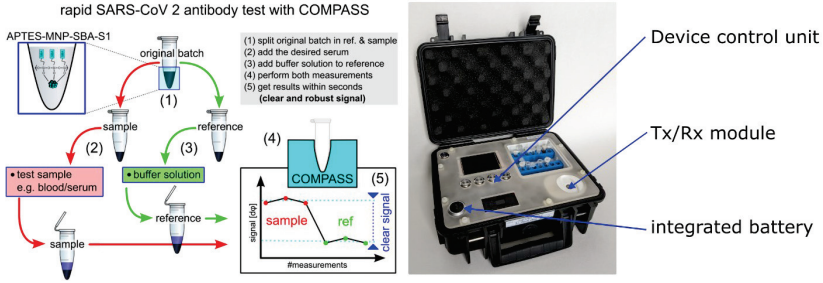

Fig. 1: Left: COMPASS rapid test routine on the example of SARS-CoV 2 antibodies. Right: Portable COMPASS measurement device.

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Transportation of Magnetic Colloidal Particles via Driven and Ratchet Mechanisms on Self-Assembled Colloidal Tracks

Fernando Martínez-Pedrero[1,*], Francisco Ortega[1], Chantal Valeriani[2], Ramón G. Rubio[1], and José Martín-Roca[2]

[1]Facultad de Ciencias Químicas, Universidad Complutense de Madrid, Madrid, Spain.
[2]Facultad de Ciencias Físicas, Universidad Complutense de Madrid, Madrid, Spain.
Email: fernandm@ucm.es. Mobile: 0034-686-03-39-76

The non-diffusive transport of micro-cargoes, spanning colloids, cells, microcapsules, and liposomes, holds paramount importance across biomedicine, nanotechnology, and fundamental biological processes. Notably, molecular walkers like dynein, myosin, and kinesin play pivotal roles in actively ferrying vesicles and organelles along dynamic self-assembled microtubules. Within this framework, a primary objective of contemporary technology is the development of nano/micrometer-scale robots boasting dependable performance. To this end, scientists have devised strategies to emulate motor proteins, facilitating directional transport at the nanoscale along specific pathways. These advancements hold the potential to revolutionize various fields, encompassing bio-detection, theragnosis, drug delivery, single-cell manipulation, microsurgery, filtration, molecular separation, size analysis, and point-of-care diagnostics.

While fully functional small-scale actuated robots are commonly crafted at the millimeter scale, achieving effective actuation at smaller length scales presents notable challenges. Directed transport through a viscous fluid encounters limitations due to thermal fluctuations, constraints dictated by the scallop theorem, and influences stemming from external flows, obstacles, confinements, and interfaces. In our study, we leverage the inherent microstructured magnetic properties found in diverse magnetic colloidal self-assemblies anchored to a solid substrate. Through the application of rotating or pulsating magnetic fields, these engineered tracks induce traveling or on/off switching potentials, thereby facilitating driven or ratchet transport of adjacent non-adsorbed magnetic colloids. These methodologies not only facilitate material conveyance under diverse conditions but also furnish invaluable models for dissecting and comprehending the intricacies of such transport mechanisms.

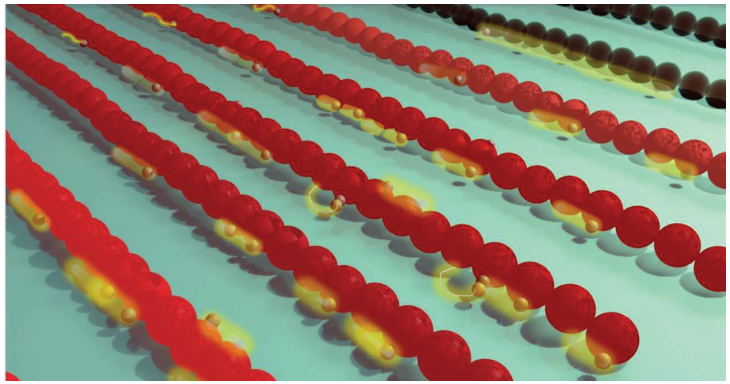

Figure. The infographic depicts a swarm of small, non-adsorbed superparamagnetic spheres being propelled along parallel tracks formed by larger magnetic colloids that are adsorbed on a solid surface. The non-adsorbed spheres are transported by the influence of a magnetic field that rotates parallel to the confining plane.

Wobbling in Nanogel Rheological and Magnetic Responses

Ivan S. Novikau[1], and Sofia S. Kantorovich[1,2]

[1] Faculty of Physics, University of Vienna, Boltzmanngasse 5, 1090 Vienna, Austria
[2] Research Platform MMM, University of Vienna, Oskar-Morgenstern-Platz 1, 1090 Vienna, Austria
*Email: ivan.novikau@univie.ac.at

In the past decade, nano- and microgels have garnered significant attention due to their unique physical properties and promising medical and technological applications. Recent research has focused on incorporating magnetic nanoparticles (MNPs) into nanogels for targeted drug delivery, enhanced uptake by tumor cells, and advancements in medical imaging and therapy. The potential for remote control of the rheology and internal structure of these soft colloids with external stimuli, particularly magnetic fields, makes magnetic nanogels (MNGs), shown in Figure, highly attractive for bio-compatible regulation. However, to fully unlock MNG-based applications, a deep understanding of magnetodynamics and rheology is crucial.

Our study explores the dynamics of MNGs, examining the influence of polymer matrix morphology, MNP coupling, and concentration on shape, stiffness, hydrodynamics, and dynamic magnetic response. Leveraging Molecular Dynamics and Lattice-Boltzmann Methods, we establish a strong correlation between cross-linker and monomer densities, and elastic energy. Demonstrating how these factors enhance magneto-controllability, especially in shear flow with an external magnetic field, our findings introduce novel wobbling dynamics resulting from polymer mesh relaxations. Additionally, we elucidate MNG's dynamic magnetic susceptibility, bridging experimental observations with theoretical predictions of high-frequency wobbling and low-frequency gel rotation. Our methodology provides a flexible and industry-relevant framework for precisely tuning magnetic properties in nanogel-based systems.

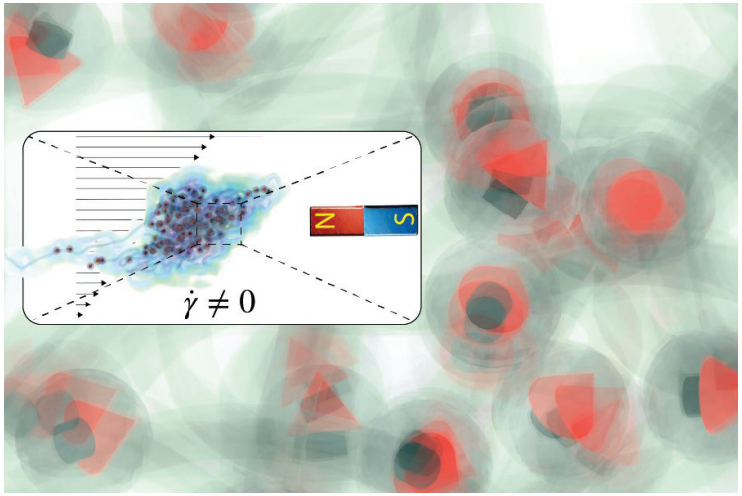

Figure. Left inset: Magnetic nanogel subjected to shear flow, covered with an iso-surface of the perturbed hydrodynamic velocity field. The magnet demonstrates an external uniform magnetic field switched on along the flow direction. Main figure: Dynamics of MNPs within the polymer matrix of the gel, showcasing their movement and interactions.

Multicontrast binding state analysis using frequency mixing magnetic detection

Timur Bikulov[1,2], Ali Mohammad Pourshahidi[1], Abdalhalim Abuawad[1], Andreas Offenhäusser[1,2] and Hans-Joachim Krause[1]

[1]Institute of Biological Information Processing, Bioelectronics (IBI-3), Forschungszentrum Jülich, Germany,
[2]Faculty of Mathematics, Computer Science and Natural Sciences, RWTH Aachen University, 52062 Aachen, Germany
e-mail: timur.bikulov@rwth-aachen.de

Keywords: Magnetic nanoparticles, Frequency mixing magnetic detection, Magnetic Immunoassay, core size characterization, Multi-contrast assay, Magnetic moment characterization

Unique nonlinear magnetic properties of magnetic nanoparticles (MNPs) enable applications beyond a contrast agent, i.e., remote spatiotemporal temperature/viscosity measurement or multi-contrast bioassay. Frequency Mixing Magnetic Detection is a technique that probes the nonlinear properties of the magnetization curve with a dual-tone excitation field [1]. Earlier, we demonstrated multi-contrast reconstruction as a linear combination of original constituents [2]. Recently, we proposed a principle [3] and a measurement technique [4] that allows independent read-out of several contrast agents by determining magnetic moment distribution without any assumptions about the original constituents. In this work, we reconstruct constituent concentration of binary and ternary mixtures of commercially available magnetic particles (SynomagD 50 nm, SynomagD 70 nm, and Perimag 130 nm) and extract additional dynamic information of their binding state by selective agglomeration with a linker molecule. We systematically correlate the FMMD response with static and dynamic magnetic property characterization methods.

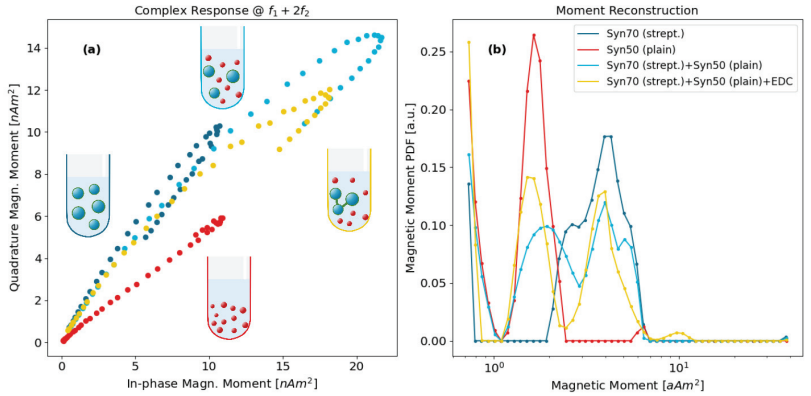

Figure 1. Binary mixture measurement. a) Frequency mixing response @ f_1+$2f_2$ (f_1=40 kHz, f_2=10 Hz) on complex plane of Synomag-D® 70 nm (streptavidin) and Synomag-D® 50 nm (plane) MNPs, their mixture with and without EDC linker across varying ranges of low-frequency excitation field strengths (0-26 mT @ 10 Hz). b) Reconstructed magnetic moment distributions

Acknowledgements:
This work was funded by German Ministry of Food and Agriculture (BMEL), contract 2818710C19.

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The combination of frequency- and spatial-space for Magnetic Particle Imaging

Jing Zhong[1,*], Rui Zhang[1], Shaoqi Sun, Shijie Sun, and Lijun Xu

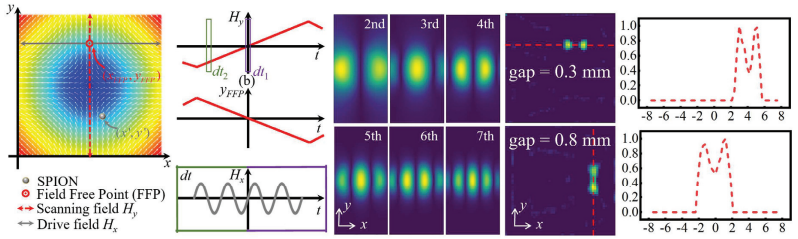
[1]School of Instrumentation Science and Optoelectronic Engineering, Beihang University, Beijing, China

*Email: zhongjing@buaa.edu.cn

Magnetic particle imaging (MPI) directly measures the nonlinear magnetic response of magnetic nanoparticles (MNPs) for quantitative visualization of the MNPs. General MPI contains frequency-space (*f*-space) and spatial-space (*x*-space) imaging approaches. For instance, the *f*-space MPI uses a system matrix that contains rich harmonics of the MNPs for reconstruction. It allows very high spatial resolution and temperal resolution. However, the hardware efforts, including 2D/3D drive magnetic fields and decoupling between the drive coils, are huge while it's really time consuming to measure the system matrix. The *x*-space MPI allows for direct imaging of the MNPs with the measured signal vs. the FFP position. However, current literatures indicate the spatial resolution is comparably low.

This study proposes a new approach of mixing-space MPI based on the combination of the frequency- and spatial-space. Figure 1(a) shows the schematic of the mixing-space MPI. A drive magnetic field is generated to drive the MNPs and to scan the FFP in *x*-direction whereas a low-frequency scanning magnetic field is generated to scan the FFP in y-direction. The MNP spectra in *x*-direction and its dependence on the FFP position in y-direction are measured to contruct the system matrix for recontruction, which allows to deblur the image in both *x*- and *y*-direction.

An MPI scaner is designed and built with a gradient of 1.14 T/m in *x*- and *y*-direction. The MNPs of Perimag® plain, purchased from micromod GmbH (Rostock, Germany), are used for phantom experiments. A drive magnetic field with 10 kHz and a triangule-wave scanning magnetic field are applied in *x*- and *y*-direction, respectively. The 2D imaging speed is 1 frame per second (FPS). The time-domain signal is segmented according to the scanning of the FFP position in *y*-direction. Totally, 25 harmonics (2nd to 26th) of a spot MNP sample are measured to contruct the system matrix. Figure 1(b) shows the measured system matrix of some individual harmoincs (8th to 26th harmonics not presented). Several phantoms of two spot MNP samples with different gaps are used to determine the spatial resolution. Figure 1(c) shows the reconstructed 2D images, and their 1D curves along the red dashed lines in the 2D images. It indicates that the proposed method allows a spatial resolution of 0.3 mm in x-direction and 0.8 mm in y-direction, respectively. With the proposed approach, the consuming time for the measurement of system matrix is significantly reduced. Moreover, the proposed approach significantly reduces the hardware efforts by 2 fold (only 1D high-frequency drive magnetic field), but still allows for very nice spatial resolution.



(a) Schematic of the mixing-space MPI (b) System matrix of individual harmonics (c) 2D reconstructed images and the curve along the red dashed line

Figure 1. The principle of mixing-space MPI, the measured system matrix of some individual harmonics, and the reconstructed 2D images, as well as its 1D curves along the red dashed lines.

INVITED TALK

Engineering Magnetic Hydrogels for Tissue Engineering and Remote Actuation

Francisco J. Vazquez-Perez[1,2], Alberto Leon-Cecilla[1,2], Cristina Gila-Vilchez[1,2], James E. Martin,[3] Modesto T. Lopez-Lopez[1,2,*]

[1] Universidad de Granada, Departamento de Física Aplicada, Granada 18071, Spain
[2] Instituto de Investigación Biosanitaria Ibs.GRANADA, Granada 18012, Spain
[3] Sandia National Laboratories, Albuquerque, New Mexico 87059, United States
*Email: modesto@ugr.es

Hydrogels are unique systems characterized by a soft solid-like macroscopic appearance and a highly porous microscopic structure. Structurally, they consist of three-dimensional, hydrophilic networks of flexible polymer chains swollen by water or biological fluids. Due to their resemblance to the extracellular matrix of living tissues, hydrogels are subject to intense research in the biomedical field. By doping hydrogels with magnetic particles, magnetic hydrogels are created, combining softness with magnetic properties, a characteristic not found in natural materials.

Embedded magnetic particles provide a powerful tool to manipulate the internal structure of hydrogels, thereby modifying their macroscopic properties and enhancing their applicability. For instance, magnetic field-induced particle chaining can be utilized to induce anisotropy in magnetic hydrogels, more accurately mimicking the hierarchical architecture of many biological systems compared to nonmagnetic hydrogels, which typically exhibit isotropic structures.

This talk will review recent findings from our research group on engineering magnetic hydrogels for various applications, with a focus on tissue engineering and smart actuation. Prior to gelation, magnetic particles in the pre-gel mixture are free to migrate and aggregate. This property can be utilized to aggregate particles along defined patterns, including chiral domains, and to modify the gelling process, resulting in distinct arrangements of the polymer fibers. The interaction between magnetic particles and polymer strands can also enhance the stability of resulting magnetic hydrogels, preventing degradation in tissue engineering applications. Once the gel point is reached, particle structures become fixed within the polymer network of the hydrogel, making it possible to complete gelation in different shapes while maintaining the preexisting particle structures. This allows for the fabrication of shape-memory hydrogels by leveraging the tendency of magnetic particle structures to align with magnetic fields. Through a combination of hydrogel geometry with magnetic particle arrangement, remotely controlled actuators capable of executing virtually any complex movement—such as locomotion, bending, twisting, and even exhibiting hysteretic behaviors—can be realized. These magnetic hydrogel actuators hold considerable potential for a multitude of applications, including fluidics, pumping, cargo delivery, and biomimicry (see Figure), offering promising prospects for advancements in the biomedical field.

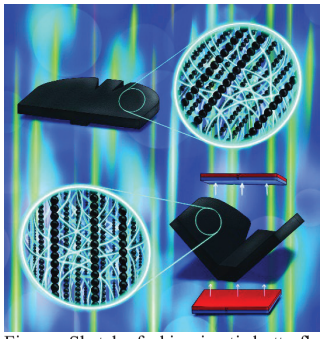


Figure. Sketch of a biomimetic butterfly actuator with magnetic particle structures depicted as chains of black circles. When subjected to a uniform magnetic field, the actual actuator mimics wing motion, resulting in hoping and locomotion.

Acknowledgments: This study was supported by grant PID2020-118498GB-I00 funded by MCIN/AEI/10.13039/501100011033, Spain. Ms. Laura Quesada de la Torre is acknowledged for her assistance with the artistic design of the figure.

Mixtures of Superpara- and Ferro-magnetic Multicore Nanoparticles: Microstructure and Magnetic Response from Experiment and Simulations

Sofia Kantorovich[1], Malika Khefallah[2], Amelie Juhin[2], Claire Carvallo[2], Ekaterina Novak[2], Aleksey Ivanov[2]

[1] Computational and Soft Matter Physics, University of Vienna, Vienna, Austria

[2] Institut de Minéralogie, de Physique des Matériaux et de Cosmochimie, Sorbonne Université, Paris, France

[3] Ural Federal University, Ekaterinburg, Russia

* Email:sofia.kantorovich@univie.ac.at.

Magnetic nanoparticles possess the inherent ability to self-organise into chains, rings and branched structures owing to strong dipole-dipole interactions. This intricate behaviour holds significant promise for modelling novel ferrofluids that exhibit distinctive magnetic responses to external magnetic fields, with implications spanning biomedical applications, mechanical properties, and optics.

To effectively synthesise and model new materials with desired properties, it is imperative to comprehend and manipulate these nanoscale structures and investigate the interactions between nanoparticles. Experimental ferrofluids are inherently polydisperse, necessitating theoretical studies focusing on bidisperse systems, where nanoparticles possess two distinct sizes, representing an initial approximation for polydisperse ferrofluids [1].

Alternatively, creating binary systems using different magnetic components results in magnetically bidisperse systems, such as combinations of ferrimagnets and paramagnets or hard and soft ferrimagnets. Such binary ferrofluids serve as fundamental models for exploring interactions between particles within ferrofluids, thereby enabling more realistic constraints for future theoretical models. Moreover, these composite formulations lay the groundwork for crafting complex materials with significant implications for emerging magneto-optical applications [2].

In this contribution, we utilise experimental techniques alongside computer simulations to investigate a binary ferrofluid composed of nanoflowers of CoFe2O4 and γ-Fe2O3. The nanoparticles in this ferrofluid exhibit distinct magnetic anisotropy and moments. Through a comprehensive examination involving FORC diagrams, bulk magnetometry, structural properties, and dynamic magnetic response, both experimentally and via simulations, we reveal significant disparities in both the structure, as illustrated in the accompanying figure, and the magnetic properties of such binary mixtures compared to conventional magnetic nanoparticle suspensions.

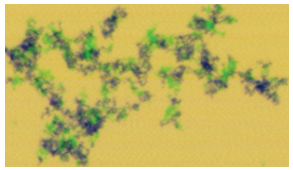


Figure. A cluster found by element-selective X-ray microscopy. Blue/purple nanoparticles are MnFeO , green nanoparticles are CoFeO with ratio 1:2.

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The "interaction temperature" of magnetic nanoparticle systems

Robert E. Camley,[1,2] Rair Macêdo,[3] and Karen L. Livesey[4,1]

[1]UCCS Biofrontiers Center, University of Colorado – Colorado Springs, CO 80918, USA

[2]Center for Magnetism and Magnetic Materials, Department of Physics and Energy Science, University of Colorado – Colorado Springs, CO 80918, USA

[3]James Watt School of Engineering, Electronics and Nanoscale Engineering Division, University of Glasgow, Glasgow G12 8QQ, United Kingdom

[4]School of Information and Physical Sciences, University of Newcastle, Callaghan NSW 2308, Australia

A key issue for the use of magnetic nanoparticles in applications is their proper characterization. A commonly used tool to measure the dipolar interactions between particles is based on the Curie-Weiss law, which applies to superparamagnetic particles that are weakly interacting. One finds that the inverse magnetic susceptibility ($1/\chi$) measured as a function of temperature T forms a straight line, with the temperature intercept θ of the linear fit indicating the strength of the interactions (see the Figure for an illustration). Hence, θ is referred to as the "interaction temperature" or the "ordering temperature".

Here, we show through theoretical calculations that an interaction temperature can arise due to alignment of the magnetocrystalline anisotropy easy axes of nanoparticles, when there are in fact *no interactions* between particles in the system (see dots and dashed line fit in the Figure). We also show that in dilute systems, no interaction temperature is expected unless particles form local clusters.

These calculations show that nanoscale details of magnetic nanoparticle systems must be known in order to correctly interpret whether the interaction temperature θ is indeed due to interactions, or if it is instead due to other energy contributions that affect the net magnetization response to a field.

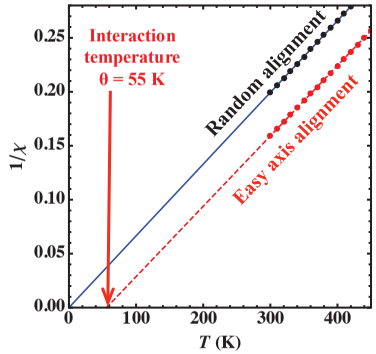

Figure: Inverse susceptibility versus temperature for 4 nm diameter magnetite nanoparticles that are non-interacting. The black dots are for random easy axes alignment, and the red dots are for full alignment of the anisotropy easy axes along the applied field direction. With random alignment the interaction temperature θ=0 (solid line intercept), however when the easy axes are aligned one sees that θ=55 K (dashed line intercept).

On the use of a variable inductance coil for high-frequency field sweeping in suspensions of magnetic colloidal particles: self-assembly and rheology

Alejandro Rodriguez-Barroso, Javier Ruiz-Nievas, Carlos Ruiz-Pelegrina, Oscar Martinez-Cano, Guillermo Camacho and Juan de Vicente

Magnetic Soft Matter Group, Department of Applied Physics, University of Granada, and Modelling Nature Excellence Unit
*email: arguezbarroso@ugr.es

Magnetic colloids, constituted by dispersions of magnetic multidomain particles in a Newtonian liquid carrier, self-assemble under the presence of magnetic fields. The mechanism for (chain-like) structure formation has been extensively investigated in the case of uniaxial steady fields. However, the case of triaxial unsteady fields is largely unknown [1]. When the frequency of the time-varying field is small, the structures try to follow the field. However, when the frequency is large the viscosity of the carrier restricts their movement and as a result, of time-averaged interactions, exotic structures are formed including sheets, foams, spirals and vortexes. The relationship between magnetic and hydrodynamic forces is expressed by the dimensionless Mason number [2] and the associated time scale is typically emplaced between magnetic relaxation at particle level (micromagnetic problem) and the shear/elongation-induced deformation (rheological problem).

In order to get sufficiently strong fields (for self-assembly) at high frequencies (for the particles to experience time-averaged interactions) resonant RLC circuits employing capacitor banks can be used [3]. Unfortunately, these devices do not allow a continuous sweep in the field frequency because the signal generation needs to be stopped for the capacitance to be changed. In this communication we propose a solution to this problem involving the use of a variable inductor, based on a movable high permeability core within a coil, to tune the resonance peak of the circuit. With this, continuous frequency sweeps can be generated to study the self-assembly at the magnetic particle level and the rheological behavior of the suspensions [4].

The device is designed, constructed and validated with high-frequency perturbation fields (uniaxial DC + alternating AC in the orthogonal direction) at a range of duty ratios $\xi = t_{on}/(t_{on} + t_{off})$. Figure 1 shows the measured torque of a magnetic suspension in a torsional parallel-plate rheometer at an oscillatory shear of 5 Hz for different ξ. As expected, the rheological response is very similar for large ξ ($\xi \geq 0.5$). However, for $\xi \leq 0.3$ the capacitor bank switching strongly impacts the rheological performance and therefore the inner microstructure within the self-assembled structures. Moreover, Figure 2 compares the results obtained in a frequency sweep using the classical capacitor control (blue) and the proposed variable inductor control (red). As desired, a smooth curve is measured using the inductor control in striking contrast to the use of the capacitor that clearly shows deep valleys associated to bank switching events.

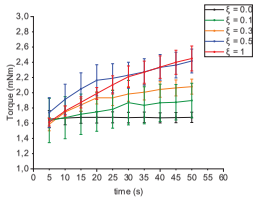

Figure 1

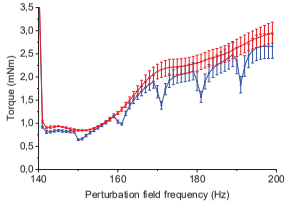

Figure 2

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Magnetically driven micro-propellers: from travelling carpets to hydrodynamic bound states

Fernando Martinez-Pedrero[1], Helena Massana-Cid[1], Ignacio Pagonabarraga Mora[2,3], and Pietro Tierno[1,2,3]

[1] Departament de Física de la Matèria Condensada, Universitat de Barcelona, Barcelona, Spain.,
[2] Universitat de Barcelona Institute of Complex Systems (UBICS), Universitat de Barcelona, Barcelona, Spain
3Institut de Nanociència i Nanotecnologia, IN2UB, Universitat de Barcelona, Barcelona, Spain.

In this talk, I will explain different results obtained in my group related to the controlled assembly and transport of paramagnetic colloidal particles subjected to time dependent magnetic field. In the first part of the talk, I will demonstrate a general method to assemble and propel highly maneuverable colloidal carpets which can be steered via remote control in any direction of the plane. These colloidal micropropellers are composed by an ensemble of spinning rotors and can be readily used to entrap, transport, and release biological cargos on command via a hydrodynamic conveyor-belt effect. An efficient control of the cargo transportation combined with remarkable “healing” ability to surpass obstacles demonstrate a great potential towards development of multifunctional smart devices at the microscale [1,2].

In the second part of the talk, I will explain the emergence of hydrodynamic interactions (HIs) between colloidal micropropellers [1] confined above a plane and driven in a viscous fluid via application of a circularly polarized rotating magnetic field [2]. The applied field torques the particles, which translate close to the surface due to the HIs with the bounding plate. At high driving frequencies, the strong flow generated by the spinning particles makes HIs dominating over magnetic dipolar ones, and close propelling particles form bound states by temporarily adjusting their translational speed to optimize the transport of the couple. I will introduce a theoretical model which shows quantitative agreement with the direct experimental data. In dense suspension, these bound states can be extended to metastable 1D array of particles assembled by the sole HIs. These results also demonstrate the importance of the boundary surface in the interaction and dynamics of con fined propelling microswimmers.

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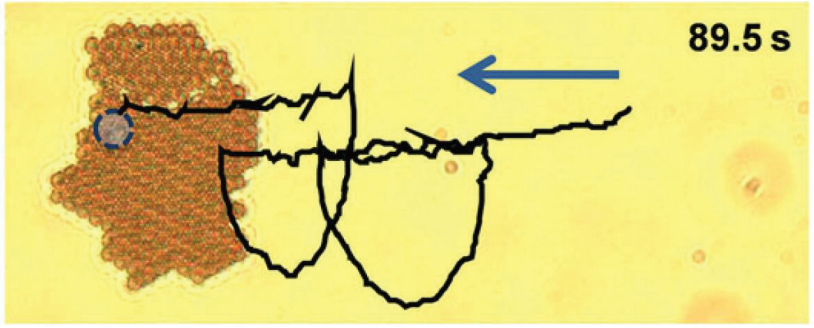

Figure. Optical microscope image showing a carpet of paramagnetic colloidal particles the transport of one yeast cell by combining translation and rotation of the carpet. The position of the tracked cell is superimposed as a black line.

Self-assembling magnetic nanoparticles: can they be useful for biomedical applications?

P. Kuzhir[1]*, M. Raboisson-Michel[1], J. Q. Campos[1], J. Lagouarde[1], G. Godeau[1], G.Verger-Dubois[2]

[1]Université Côte d'Azur, CNRS UMR 7010, Institute of Physics of Nice, 17, rue Julien Lauprêtre, Nice 06200 France
[2]Axlepios Biomedical - 1st Avenue 5th Street, 06510 Carros, France

*Email: pavel.kuzhir@univ-cotedazur.fr

Superparamagnetic iron oxide nanoparticles (IONPs), as small as ~10 nm in size, are smart platforms for various biomedical applications. However, their *in vitro* or *in vivo* manipulation by external magnetic fields is quite challenging, if not impossible, because of strong Brownian motion and weak magnetic forces scaling with the 3rd power of their diameter. As an example, a single 10 nm-sized magnetite nanoparticle moves in a quiescent blood plasma at a speed of ~3 nm/s in very strong magnetic fields (B~1 T) and magnetic field gradients (∇B~100 T/m). Fortunately, the nature itself has found a smart solution to overcome this serious limitation: in most cases, once dispersed in physiological media, nanoparticles self-assemble into so-called primary aggregates because of various reasons (screened electrostatics, hydrophobic interactions, bridging flocculation, etc.). These primary aggregates are further self-assembled into micron-sized filaments under applied magnetic fields. This allows an easy manipulation (translation, rotation, separation from the solvent) of small nanoparticles constituting large (but reversible) filaments using magnetic fields as low as B~5-10 mT.

In this work, we focus on physical background of the enhanced manipulation of self-assembling IONPs and explore a few examples mimicking their possible biomedical applications. First, we demonstrate an extreme enhancement of the magnetophoretic mobility and efficiency of magneto-microfluidic separation of IONPs loaded by either curcumin or antibodies, these effects being potentially useful for drug delivery and immunoassays. Second, we show that under external low-frequency rotating magnetic fields, the filaments of self-assembled IONPs can generate macroscopic flows in a stagnant blood plasma in a microfluidic channel mimicking a blood vessel blocked by a clot. These flows considerably enhance the transport of a dissolution agent towards *in-situ* generated proxy clot allowing for its full dissolution within a time lapse of 10 min. Finally, the same filaments can be used as micro-swimmers rolling along the walls of the branched fluidic network and transporting a drug towards a therapeutic target, with a speed achieving ~1 mm/s. We argue that a broad field of possible applications of self-assembling IONPs is covered by similar physical grounds, as summarized in the recent work [1].

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AFM Cantilever Magnetometry for Measuring Femto-Nm Torques Generated by Single Magnetic Particles for Cell Actuation

Mariia Efremova[1§*], Lotte Boer[1§], Jianing Li[1], Laurenz Edelmann[1], Lieke Ruijs[1], Marc A. Verschuuren[2], and Reinoud Lavrijsen[1]

[1]Department of Applied Physics and Science Education, Eindhoven University of Technology, the Netherlands
[2]SCIL Nanoimprint Solutions, Philips Group Innovation, the Netherlands
*Email: m.efremova@tue.nl; Mobile: +49(174)5955342; § equal contribution

Spatiotemporal remote modulation of mechanical forces is of great interest for new cancer therapies – for example, applying ~0.1 nN force is enough to rupture the cancer cell membrane [1]. Magnetomechanical cancer treatments rely on forces or torques (typically in the femto-Nm range) generated by magnetic particles (MPs) via their mechanical movement in an external magnetic field [2]. However, these torques are only theoretically estimated and then correlated with the observations of cancer cell viability change. In this work, we had a challenging aim to directly measure the torques generated by single MPs, which allows for a better understanding of how magnetomechanical cell actuation works in an actual experiment.

MPs were placed on a cantilever for Atomic Force Microscopy (AFM) and installed in an AFM setup with a magnet underneath (Figure 1a). The forces generated by MPs led to the cantilever deflection and resulted in an AFM signal, which can be converted into the torque, knowing the properties of a cantilever and MPs themselves. In our setup, we investigated synthetic antiferromagnetic platelets (SAFs) with 1.88 µm diameter and 52 nm thickness [3]. The basic SAFs stack (repeated 5 times in a platelet) has two ferromagnetic CoFeB layers with opposite magnetization directions, resulting in 'off' SAFs (with no magnetic moment) at a zero field and 'on' SAFs upon the application of a magnetic field above a ~150 mT threshold (Figure 1b). Importantly, due to a high out-of-plane magnetic anisotropy, the platelet induces a mechanical torque (force) to align with the applied field direction.

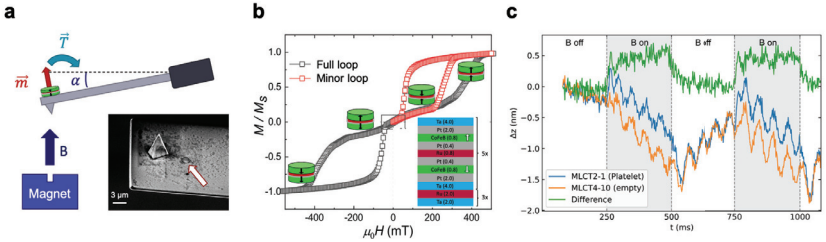

Figure 1. Torque magnetometry of SAFs: a) the working principle of the setup: the SAF MP (green) is placed on an AFM cantilever. Due to the angle α between the SAF magnetic moment m and the horizontal, the MP generates a torque T proportional to m, α, and external magnetic field B. Inset: the SEM image of a cantilever with a single SAF MP (indicated by a white arrow); b) the out-of-plane hysteresis loop of SAFs MP ensemble (SQUID measurement) [3]. Inset: the layer stack of a SAF MP with the layers' thicknesses in nm between parentheses; c) the AFM signal generated in 200 ms pulses of 373 mT field for an empty cantilever (orange), cantilever with a single SAF MP (blue), and the difference isolating the signal from the single MP (green).

In an AFM experiment, the magnetic field was applied in 200 ms pulses of the same magnitude. After averaging and subtracting the signal of an empty cantilever from the cantilever with a single SAF MP, we observed a clear cantilever deflection when the field was turned on (green trace in Figure 1c). This way, we measure torques between ~ 0.25 and $1.5 \cdot 10^{-15}$ Nm generated by a single 1.88 µm-diameter SAF platelet in a 75-373 mT field, respectively. This naively translates into a ~1 nN force generated by single SAF MPs using their radius as an arm (900 nm), making them promising candidates for magnetomechanical cell actuation. Importantly, it also shows the applicability of our technique for measuring the torques generated by other MPs (e.g., [4]), which potential for magnetomechanical cancer treatment is being explored now.

Acknowledgments: This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement no. 899987.

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Magnetic Separation of Exosomes with Tailored Magnetic Particles and Downstream Application

María Isabel Pividori[1,2]

[1]*Grup de Sensors i Biosensors, Departament de Química, Universitat Autònoma de Barcelona, Bellaterra, 08193, Spain.*
[2]*Biosensing and Bioanalysis Group, Institute of Biotechnology and Biomedicine, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain*
E-mail: isabel.pividori@uab.es; webpage: https://isabelpividori.net

Exosomes are membrane encapsulated biological nanometric particles of endocytic origin, which are released by all types of cells[1]. Due to their low concentration, conventional procedures for extracellular vesicle (EV) detection usually require relatively large sample volumes, involving preliminary purification or preconcentration steps from complex specimens. Here, we describe the separation and preconcentration in magnetic particles of extracellular vesicles from breast cancer, human fetal osteoblastic, and human neuroblastoma cell lines, as well as exosomes from human serum. The first approach involves the covalent immobilization for the exosomes directly on micro (4.5 µm)-sized magnetic particles. The second approach is based on tailored magnetic particles modified with antibodies for further immunomagnetic separation of the exosomes. In these instances, micro (4.5 µm)-sized magnetic particles are modified with different commercial antibodies against selected receptors, including the general tetraspanins CD9, CD63, and CD81 and the specific receptors (CD24, CD44, CD54, CD326, CD340, and CD171). The magnetic separation can be easily coupled with downstream characterization and quantification methods, including molecular biology techniques, confocal microscopy, or flow cytometry. This work also addresses different biosensing strategies for the quantification of exosomes in breast cancer patients (Figure 1).

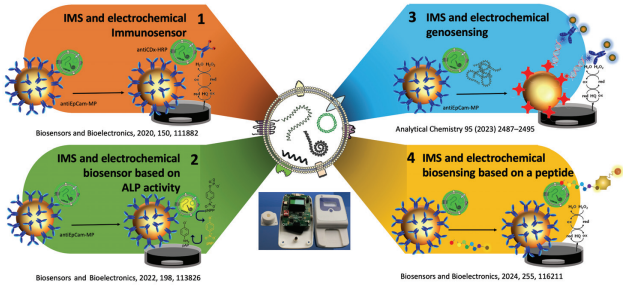

Figure 1. Schematic representation of the magneto electrochemical biosensors for the detection of exosomes

Three key cross-cutting technological challenges that have been identified as technology bottlenecks in biosensing of exosomes which are considered here, including (i) the isolation of exosomes from complex specimens by magnetic particles amenable with biosensing platforms[2] (ii) the enhancement of the analytical signal by amplification techniques of nucleic acid targets[3] and (iii) the analytical simplification[4,5]. Hand-held electrochemical magneto biosensors operated by batteries are presented for quantitative results. In all cases the biosensing approaches discussed here provide low complexity and affordable platforms requiring minimal training for final users, but without any lost in the diagnostic accuracy.

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INVITED TALK

Magnetic Nanoparticles as Instructive Tools for Engineering, Stimulation, and Treatment of Model Tissues

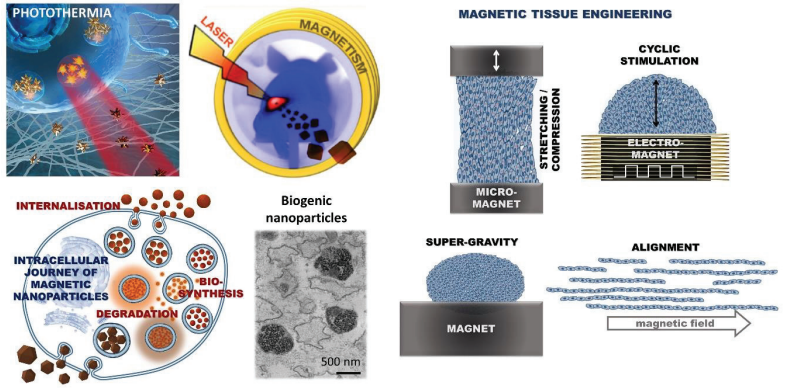
Claire Wilhelm[1]

[1] *PCC laboratory, CNRS UMR168, Institut Curie, Sorbonne University, PSL University, 75005 Paris, France.*

Magnetic nanoparticles providing multiples functions paved the way to tailor-made therapeutic prescriptions and theranostics functionalities. In cancer therapy, they have raised the prospect of thermal treatments that have few if any adverse effects. We compared the heating potential of magnetic nanoparticles under magnetic hyperthermia or photothermia, of plasmonic nanoparticles under photothermia, or the combination of both, towards synergistic solutions to complete cancer cell destruction. Different pre-clinical studies were showcased, exploring in vivo these nanoparticles-based modalities. For instance biosynthesized magnetosomes combined with a genetically encoded targeting unit were able to achieve enhanced photo-thermal treatment following intravenous injection.

Besides, the magnetism of iron oxide - based nanoparticles also provide cells with sufficient magnetization to manipulate them. Magnetic nanoparticles thus appear as a promising tool for tissue engineering opening up challenging perspectives. We developed magnetic-based methods to manipulate cells, towards the goal to provide magnetic artificial tissue replacements, that can be stimulated on demand. For instance, it could induce mechanically stem cells differentiation. Similarly, it allows to magnetically compress cancer spheroids alongside their genesis or drug testing and even nanoparticles-mediated therapy, then in an all-in-one actor/probe action of the magnetic nanoparticles.

The therapeutic use of nanoparticles regenerative medicine application still raises the more general issue of intracellular nanoparticle long-term fate. Cell spheroids models and magnetic tools were developed to monitor long-term nanomaterials intracellular integrity. It evidenced a massive intracellular degradation, which could be prevented by a polymeric coating or an inert gold shell. Remarkably, human cells could also biosynthesize their own magnetic nanoparticles, with longer persistence, and limited toxicity.



Fundings: European Research Council (ERC-2019-CoG project NanoBioMade 865629) & ANR (2019, project SuperMagStemCells).

Enhancing MPI Performance: Probing post-synthesis oxidation and correlations to nanoparticle properties

Ambar C. Velazquez-Albino[1], Aniela Nozka[2], Andrii Melnyk[1], Hayden J. Good[1], Carlos M. Rinaldi-Ramos[1,3*]

[1]Department of Chemical Engineering, University of Florida, Gainesville, FL, United States
[2]Department of Bioengineering, Clemson University, Clemson, SC, United States
[3]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, U.S.
*email: carlos.rinaldi@ufl.edu

Tailoring magnetic nanoparticle tracers for magnetic particle imaging (MPI), a novel imaging modality with tremendous potential in diagnostic imaging and theranostics, is a challenging problem. Achieving this requires improved control of nanoparticle physical and magnetic properties, as well as synthesis reproducibility, which are well-known problems in the field. This study investigates the impact of post-synthesis oxidation on superparamagnetic iron oxide nanoparticles (SPIONs) synthesized via thermal decomposition of iron oleate, the most often used method for synthesis of high-quality MPI tracers. A custom platform was designed to carry out eight simultaneous reactions as replicates per synthesis condition to apply statistical analysis. MPI performance is gauged via signal intensity and resolution using a MOMENTUM™ scanner and is correlated to physical and magnetic properties. Post-synthesis oxidation did not alter physical attributes like size and shape, but significantly enhanced magnetic properties. Saturation magnetization increased from 52% to 93% of the bulk value for magnetite, leading to better MPI performance. Deviations from the Langevin model predictions, the ideal model describing superparamagnetic behavior, elucidate the need for considering factors like the discrepancy between physical and magnetic diameters (D_p-D_m), and shape anisotropy, here gauged as the aspect ratio (AR). The findings underscore the potential of post-synthesis oxidation as a method to tune magnetic properties of SPIONs and improve MPI performance, while also highlighting MPI's sensitivity to the tracer's properties and increasing relaxation effects. MPI needs reproducible synthesis methods that afford finely tuned control of nanoparticle size, shape, and magnetic properties.

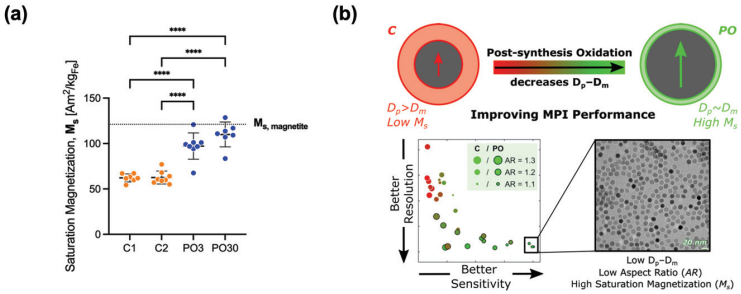


Figure. **Post-synthesis oxidation (PO) improves tracer magnetic properties and MPI performance.** (a) Saturation magnetization (M_s) increases with PO treatment compared to control (C) groups, $p < 0.0001$ (****). (b) Tracers with the best MPI performance have high M_s and minimized discrepancy between physical and magnetic diameters (D_p-D_m) due to PO treatment, as well as a low aspect ratio (AR) indicating lower shape anisotropy.
Adapted from Velazquez-Albino *et al. ACS Applied Nano Materials* **2024** *7* (1), 279-291

High coercivity cobalt ferrite nanoparticles for heating applications

Diana Zahn[1,†], Joachim Landers[2,†], Marco Diegel[3], Soma Salamon[2], Heiko Wende[2], Jan Dellith[3] and Silvio Dutz[1,4]

[1] *Institute of biomedical engineering and informatics, TU Ilmenau, Ilmenau, Germany*
[2] *Faculty of Physics and CENIDE University of Duisburg-Essen, Duisburg, Germany*
[3] *Leibniz Institute of Photonic Technology, Jena, Germany*
[4] *Westsächsische Hochschule Zwickau, Zwickau, Germany*
[†] *These authors contributed equally to this work*
***E-mail:** diana.zahn@tu-ilmenau.de

Optimizing magnetic nanoparticles for heating purposes in (bio-)technological applications, the safety limits restricting the external magnetic field used in a medical scenario do not need to be met. Therefore, we synthesized and characterized high coercivity cobalt ferrite nanoparticles for applications in high magnetic fields. Particles were synthesized with a precipitation method. In a first study, the synthesis parameters duration of addition of the base (d_{add}), addition temperature (T_{add}), duration of reaction (d_{react}), end temperature (T_{end}) and the atmosphere (O_2 or N_2) were systematically varied. In a second study, the ratio of Co^{2+} to Fe^{2+} was varied, tuning the particles' composition from magnetite to cobalt ferrite. The cobalt fraction x in $Co_xFe_{3-x}O_4$ was varied from 0 to 1. Particles were characterized using transmission electron microscopy, magnetometry, X-ray diffraction spectroscopy, Mössbauer spectroscopy and calorimetric measurements.
In the first study, thresholds for synthesis parameters were identified, that, if not met, lead to the formation of impurity phases apart from $CoFe_2O_4$. Akageneite, an iron hydroxide, was identified by XRD as well as in Mössbauer spectra. This hydroxide diminishes the particles' magnetization, resulting in higher magnetization value for particles synthesized under N_2, what seems to prevent the hydroxide formation. Some correlations of synthesis parameters with magnetic or structural properties were found: Increasing d_{add} leads to higher coercivities and decreasing magnetization, while a longer duration of reaction d_{react} increases crystallinity, e.g. In the second study, a correlation between cobalt fraction x and coercivity was found (see Fig. (b)). With increasing x, H_C increases with a maximum of 37 kA/m at 300 K for x = 0.8 – 0.9. The magnetization values M_{9T} are rather constant with a slight drop for very high cobalt ratios (see Fig. (a)). The heating power was specified using SAR values, that can be seen in Fig. (c). A maximum was found for the sample with x = 0.3, since higher values of x lead to coercivities that are already too hard magnetic for efficient heating in the used magnetic field of 56 kA/m.

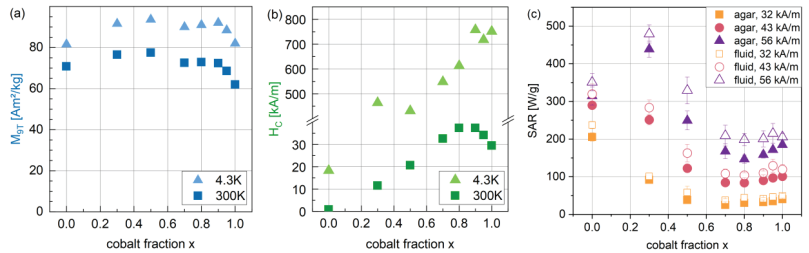


Figure: Magnetization at 9 T (a) and coercivity (b) for different x at 4.3 K and 300 K. SAR values for different x in agar and fluid samples (c).

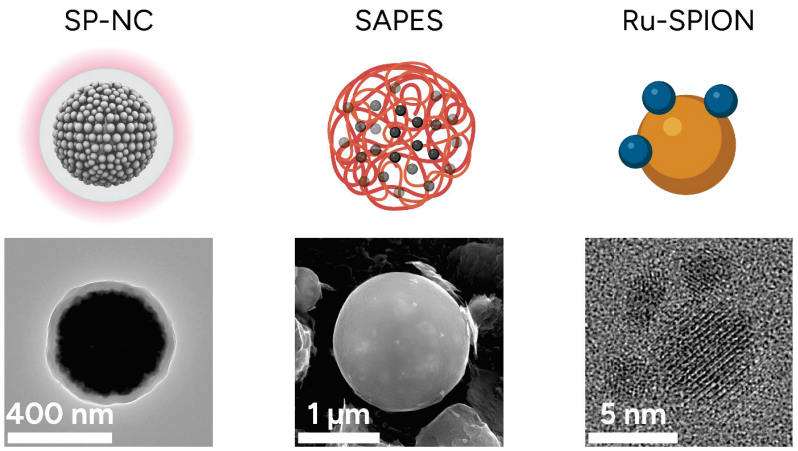
Acknowledgements
This work was funded within the "Central Innovation Program for small and medium-sized enterprises" by the Federal Ministry for Economic Affairs and Climate Action of Germany in the project "NanoTherMagS (16KN081337)" and by the "Thüringer Innovationszentrum für Medizintechnik-Lösungen (ThIMEDOP; FKZ 2018 IZN 004). DFG provided funding within the SFB 1278 "PolyTarget" (project number 316213987, project B04), via the CRC/TRR 247 (Project-ID 388390466, sub-project B02) and for the TEM facilities together with the European Fonds for Regional Development (EFRE).

Enhanced Functionalities of Magnetic Supramolecular Assemblies for Biomedical and Environmental Applications

Giovanni M. Saladino, Hans M. Hertz, and Muhammet S. Toprak

Department of Applied Physics, KTH Royal Institute of Technology, 10691 Stockholm, Sweden

Superparamagnetic iron oxide nanoparticles (SPIONs) have gained significant attention in biomedical and environmental applications due to their unique properties and versatile functionalities, including magnetic resonance imaging (MRI), magnetic hyperthermia (MHT), and magnetic separation. SPIONs can form supramolecular assemblies using various strategies to create complex structures with multifunctionality. In our work, we designed micron-sized superparamagnetic nanoclusters (SP-NCs) and self-assembled poly-electrolytic spheres (SAPES), for MHT and magnetic separation, respectively. Both the assemblies exhibit high unit magnetization owing to their supramolecular nature, while additional functionality was provided by a dye-doped silica shell on the SP-NCs for optical fluorescence and by the bio-conjugated Moringa oleifera coagulant protein (MOCP) for turbidity removal from water with SAPES. A third approach was based on decorating the SPION surface with Ru nanoparticles (NPs), which constituted together hybrid nanostructures (Ru-SPIONs) enabling dual-mode imaging with MRI and X-ray fluorescence imaging (XFI), a novel bioimaging technique. SPIONs were chosen for their known role as T_2 contrast agents for MRI, while Ru NPs constituted the XFI contrast agents, with the Ru absorption edge matching the X-ray source energy (24 keV) for Kα fluorescence emission. Ru-SPIONs were tested *in vivo* for correlative XFI-MRI, highlighting the complementarity of the two techniques. Altogether, these three approaches demonstrated the enhanced functionalities provided by magnetic supramolecular assemblies for biomedical and environmental applications.



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Process analytical technology in continuous manufacturing of nanohybrids for advanced theranostics

Alexander-Nicolas Egler-Kemmerer[1], Eilien Heinrich[1], Christina Wenck[1], Nils Meier[1], Frank Wiekhorst[2], Regina Bleul[1*]

[1] Fraunhofer Institute for Microengineering and Microsystems IMM, Carl Zeiss Straße 18 20, 55129 Mainz, Germany
[2] Physikalisch-Technische Bundesanstalt, Abbestraße 2-12, 10587 Berlin, Germany
*Email: regina.bleul@imm.fraunhofer.de

Current guidelines of the European and US regulation authorities (FDA, EMA) suggest supporting the transition from batch processing towards continuous manufacturing (CM) in pharmaceutic production. For batch processes the quality assurance of intermediate and end products is usually performed by time consuming and often delayed off-line testing. New tools of Process Analytical Technology (PAT) are obviously advantageous to monitor the critical quality attributes of continuously produced (nano)pharmaceutics in real time, enabling direct feedback control during the continuous manufacturing process.

Theranostic systems combine therapeutic and diagnostic features into a single nanohybrid. These multifunctional nanosystems are generally complex and challenging regarding their quality control and the compliance of their quality attributes is crucial for a successful clinical translation. Magnetic nanoparticles as theranostic agent can both support therapeutic efficacy, e.g., by magnetic fluid hyperthermia or temperature-triggered drug release, and enable online monitoring and in vivo tracking of the drug carrier on their way to the site of action.

In this work we present continuous manufacturing of size controlled magnetic iron oxide nanoparticles as well as continuously prepared hybrid systems such as protein coated single core magnetic nanoparticles or magnetic liposomes exploiting the controlled self-assembly in micromixers. This continuous manufacturing set-up enables additionally a dual loading with drugs and magnetic agent to create a theranostic nanohybrid. Different tools of PAT have been used to control the nanoparticle and nanohybrid synthesis including downstream processing via tangential flow filtration and in flow magnetic separation. Exemplarily, an inhouse-developed and patented technology for flow dynamic light scatting measurements of the hydrodynamic size as well as a sensitive bench-top, inline magnetic particle spectroscopy to analyze in situ magnetic properties during the process was presented as suitable PAT to accelerate the development of theranostic nanohybrids.

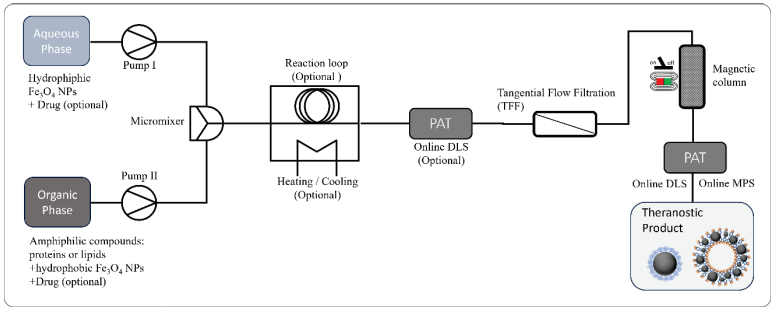

Figure 1: Schematic illustration of continuous manufacturing of theranostic nanohybrids using process analytical technology to control and monitor the process.

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Disentangling the layer(s) composition and its indiviual magnetic contribution in bi-magnetic core@shell nanoparticles

M. Estrader[*1], A. G. Roca[2], A. López-Ortega[3], R. U. Ichikawa[4], X. Turrillas[5], D. del-Pozo-Bueno[6], M. Varela[7], F. Peiró[6], S. Estradé[6], I.V. Golosovsky[8], I.A. Kibalin[9], A. Gukasov[9], M. Vasilakaki[10], K.N. Trohidou[10], T.C. Hansen[11], I. Puente-Orench[11], A. Lelièvre-Berna[11], and J. Nogués[2,12]*

[1]Departament de Química Inorgànica i Orgànica, Universitat de Barcelona and Institute of Nanoscience and Nanotechnology of the University of Barcelona (IN2UB), E-08028 Barcelona, Spain,
[2]Catalan Institute of Nanoscience and Nanotechnology (ICN2), Campus UAB, Bellaterra, E-08193, Spain
[3]Departamento de Ciencias and Institute for Advanced Materials and Mathematics INAMAT, Universidad Pública de Navarra, 31006 Pamplona, Spain
[4]Nuclear and Energy Research Institute (IPEN/CNEN-SP), SP 05508-000 São Paulo, Brazil
[5]Institut de Ciència de Materials de Barcelona- CSIC, UAB Campus, E-08193 Barcelona, Spain
[6]LENS-MIND, Departament Enginyeries Electrònica i Biomèdica and Institute of Nanoscience and Nanotechnology of the University of Barcelona (IN2UB), E-08028 Barcelona, Spain
[7]Departamento de Física de Materiales, Universidad Complutense de Madrid, 28040 Spain
[8]National Research "Kurchatov Institute", Petersburg Nuclear Physics Institute, 188300 Gatchina, Russia.
[9]Laboratoire Léon Brillouin, CEA-CNRS, CE-Saclay, 91191 Gif-sur-Yvette, France.
[10]Institute of Nanoscience and Nanotechnology, NCSR "Demokritos", 15310 Agia Paraskevi, Attiki, Greece.
[11]Institut Laue Langevin, 71 avenue des Martyrs, 38000 Grenoble, France.
[12]ICREA, E-08010 Barcelona, Spain
*martaestrader@gmail.com

Bimagnetic core/shell nanoparticles (NPs) are a subject of considerable current interest both due to their appealing magnetic properties and their potential applications (e.g., magnetic hyperthermia, magnetic bioassays, microwave absorbers, anode materials for Li-ion batteries, or solar hydrogen production via water splitting). In this work I will briefly present the main features we discovered for FeO/Fe_3O_4 and Fe_3O_4/Mn_3O_4 core/shell nanoparticles in the last few years. As both core and shell exhibit magnetic properties, then, not only the structural/morphological interface is important, but also the magnetic arrangement at the interface can play a crucial role in the properties and performance of the NPs. **1) In the case of FeO/Fe_3O_4 NPs** we have revealed two important features to understand their magnetic properties: *i)* the temporal evolution over four years of the oxidation front which leads to a final onion-like structure with a graded composition[1] and *ii)* the concomitant appearance of a graded magnetic structure[2]. We have demonstrated that the oxidation process reaches to a 'stand-by' state owing to the passivation character of the Fe_3O_4 shell and that the magnetic moment being largest at the surface decreases towards the inner part of the NP. **2) Regarding Fe_3O_4/Mn_3O_4 NPs** we showed some years ago the existence of antiferromagnetic (AFM) coupling (being, so far, the ferromagnetic (FM) exchange the most common coupling observed) at the interface between the core and the shell.[3] Recently, we have successfully proved by Polarized Neutron Powder Diffraction (PNPD) that this AFM coupling has its origin on the canted magnetic arrangement of the Mn_3O_4 lattice at low applied magnetic fields. In contrast, this canting evolves towards a collinear arrangement at higher magnetic fields, thus leading a FM alignment.[4] The elucidation of all these results has been addressed by a careful multicharacterization approach using several techniques: X-ray diffraction (Whole Powder Pattern Modeling-WPPM, Rietveld refinement, Pair Distribution Function-PDF), Electron Energy Loss Spectroscopy (EELS) and electron Magnetic Circular Dichroism (e-MCD) techniques, X-ray magnetic circular dichroism (XMCD) and PNPD.

Acknowledgements
M.E. and A. G. R acknowledges the grants RYC2018-024396-I and RYC2019-027449-I, respectively, funded by MCIN/AEI/ 10.13039/501100011033 and by "ESF Investing in your future'' and grants PID2019-106165GB-C22, PID2019-106165GB-C21 and RTI2018-095495-J-I00 funded by MCIN/AEI/ 10.13039/501100011033 and by "ERDF A way of making Europe".

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Multicore magnetic nanoparticles for magnetic hyperthermia and combination therapy against cancer

David García-Soriano,[1,‡] Paula Milán-Rois,[1,‡] Nuria Lafuente-Gómez[1], Ciro Rodríguez-Díaz[1], Cristina Navío,[1] Álvaro Somoza,[1,2] and Gorka Salas[1,2,3,*]

[1] *Instituto Madrileño de Estudios Avanzados en Nanociencia, Campus Universitario de Cantoblanco, 28049 Madrid, Spain*

[2] *Unidad Asociada de Nanobiotecnología (CNB-CSIC e IMDEA Nanociencia), 28049 Madrid, Spain*

[3] *Unidad de Nanomateriales Avanzados, IMDEA Nanociencia (Unidad de I+D+I Asociada al Instituto de Ciencia de Materiales de Madrid, CSIC), 28049 Madrid, Spain*

* e-mail: gorka.salas@imdea.org

Multicore iron oxide nanoparticles (IONPs), including the so called nanoflowers, are among the best candidates for magnetic hyperthermia applications against cancer [1]. However, reports on their efficacy in cell cultures are scarce. In this work, we have synthesized multicore IONPs (Fig. 1) adapting a seeded-growth approach previously employed in the preparation of other hybrid nanomaterials [2,3]. Their cytotoxicity, cell uptake, and the efficacy of the magnetic hyperthermia approach have been studied employing six cancer cell lines as models of pancreatic carcinoma, uveal melanoma, breast adenocarcinoma, triple-negative breast cancer line, lung cancer, and colon cancer. In addition, IONPs have been modified with a chemotherapeutic drug and tumor suppressor microRNAs. Our results show that this combination dramatically enhances the efficacy of magnetic hyperthermia.

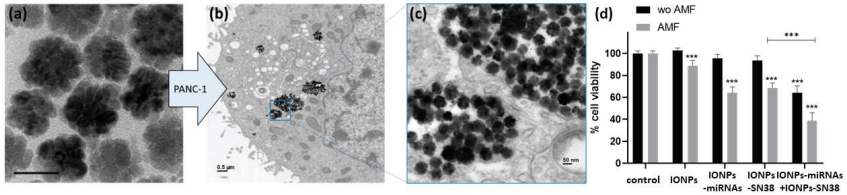

Figure 1. Multicore IONPs (a) as-prepared, (b,c) internalized in PANC-1 cells after incubation, (d) cell viability without and with application of alternating magnetic field (AMF) in A549 cells incubated with IONPs functionalized and non-functionalized.

Acknowledgments

This work has been supported by the Ministerio de Ciencia e Innovación (PID2019-106301RB-I00 and PID2020-119352RB-I00) and Comunidad de Madrid (P2022/BMD-7403 RENIM-CM). PMR and NLG acknowledge Ministerio de Economía y Competitividad and Ministerio de Ciencia (BES-2017-082521 and FPU18/02323 fellowships). IMDEA Nanociencia acknowledges support from the 'Severo Ochoa' Programme for Centres of Excellence (Ministerio de Ciencia e Innovación, CEX2020-001039-S).

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A microwave-assisted automated system for sustainable synthesis of magnetic nanoparticles

K. Simeonidis[1*], M.P. Morales[2], T. Damartzis[1], N. Maniotis[1], S. Veintemillas-Verdaguer[2]

[1]Department of Chemical Engineering, Aristotle University of Thessaloniki, Thessaloniki, Greece
[2]Materials for Medicine and Biotechnology Group, Instituto de Ciencia de Materiales de Madrid, CSIC, Madrid, Spain
[*]Email: ksime@physics.auth.gr

As the demand for magnetic nanoparticles in developing biomedical and environmental applications is exponentially growing, the need to transfer laboratory knowledge into large-scale production schemes is getting more intense. At the same time, promoting methodologies which secure minimum involvement of toxic reagents, by-products and energy are in line with recent guidelines for sustainable development. An interesting alternative for the production of uniform iron oxide nanoparticles following a green route is the oxidative hydrolysis of Fe^{2+} in aqueous media through the intermediate formation of green rust [1]. This work refers to the operation of a small-sized automated system for the fast production of Fe_3O_4 nanoparticles based on the adoption of continuous oxidative precipitation of green rust in a plug-flow reactor placed inside a microwave heater. The setup was capable to provide well-defined nanoparticles within less than 5 min enabling also the direct discharge of reaction residuals at the end of the process using an attached linear magnetic separator and combined washing streams. Importantly, the technoeconomic figures of representative cases and the life cycle assessment were analyzed to indicate the viability and the sustainability of the presented process with respect to the conventional batch method.

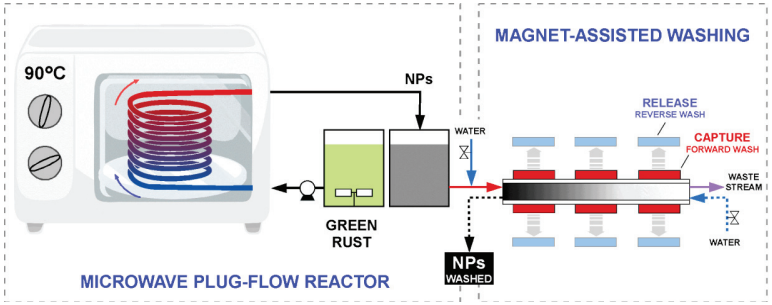

Figure 1. Continuous flow synthesis and washing of Fe_3O_4 nanoparticles through green rust precipitation using a plug-flow microwave heated reactor.

Acknowledgments
The research project was supported by the Hellenic Foundation for Research and Innovation (H.F.R.I.) under the "2nd Call for H.F.R.I. Research Projects to support Post-Doctoral Researchers" (Project Number: 00046 MagnoSorb). Research was held in the frame of the IMAGINE: Implementing MAgnetic targeting of nano-Guided ImmuNE cells project funded by European Science Foundation Fight Kids Cancer 2020 programme.

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A Novel Seed-Mediated Growth Approach for Synthesizing Core@shell $CoFe_2O_4$@$BaTiO_3$ Magnetoelectric Nanoparticles

Yaser Hadadian[1,*], Chiseon Ryu[2], Jae Young Lee[2], and Jungwon Yoon[1,*]
[1]School of Integrated Technology, Gwangju Institute of Science and Technology, Gwangju, South Korea
[2]School of Materials Science and Engineering, Gwangju Institute of Science and Technology, Gwangju, South Korea
Emails: yaser.hadadian@outlook.com & jyoon@gist.ac.kr

Magnetoelectrics (ME) have recently emerged as transformative technological materials, and as promising candidates for electrical stimulation (ES) in biomedical application [1]. Of particular interest are core@shell structure magnetoelectric nanoparticles (MENPs) that combine piezoelectric and ferromagnetic behaviours simultaneously. The presence of a coupling between the piezoelectric (or ferroelectric) and ferromagnetic properties enables the control of the piezoelectric properties of the ME materials by simply using a variable magnetic field (and vice versa). The most common MENPs for biomedical application is cobalt ferrite@barium titanate (CFO@BTO) structure.

Almost in all reports, thus far, on MENs [2], the piezoelectric shell is grown using sol-gel methods [3]. There are at least two major obstacles in the use of MENPs produced by this method for biomedical applications. First, since the MENPs are obtained after annealing at high temperatures, usually >700 °C, colloidal stability of the NPs becomes very challenging, because organic surfactants that render MENPs dispersed in solution are destroyed at temperatures beyond 200 °C. Second, sol-gel does not allow a control over the morphology of the resulting MENPs. Typically, the NPs are highly aggregated and appear as large clusters. Moreover, the piezoelectric shell thickness is not homogeneous among the resulting NPs or even within each NP. Often, a mixed-phase composite of CFO and BTO instead of a core@shell structure is obtained [4]. Using such unstable and highly aggregated MENPs lead to a lower ME coefficient and an inaccurate assessment of MENPs' toxicity, affect the cellular uptake, exposure locations or pathways, and thus resulting in misleading conclusions [5].

Here, we introduce a novel approach for synthesizing CFO@BTO MENPs. Monodispersed CFO NPs synthesised by a one-pot thermal decomposition were employed as seeds for the growth of the BTO shells in a solvothermal reaction. Two distinct surfactants, oleic acid (OA) and decanoic acid (DA), were utilized to obtain spherical and cubic CFO NPs. For BTO shell growth, CFOs, covered by OA or DA, were subsequently introduced in a standard solvothermal reaction at 180 °C for 24 hours [6] using OA or DA interchangeably. The amount of the precursors for the BTO shell was chosen based on the seed sizes and the typical yield of the solvothermal reaction [6].

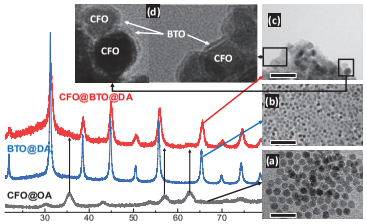

Fig. 1. XRD patterns and TEM images of a) CFO, b) BTO, and c) CFO@BTO. The scale bar is 25 nm.

From the TEM images of the samples and their corresponding XRD data (Fig. 1), it is clear that BTO shell can be successfully grown on the CFO NPs at a significantly lower temperature compared to that in sol-gel method. In [6], OA was used as surfactant and the resultant BTO NPs were cubic. Here, we examined the possibility of obtaining crystalized BTO NPs using DA and, interestingly, truly monodispersed spherical BTO NPs (Fig. 1b) were synthesized. Therefore, for BTO shell growth on the spherical CFO@OA NPs, we utilized DA in the solvothermal reaction. The peak intensities for both BTO NPs and shell are significantly higher than those of CFO nanoparticles. This makes it difficult to clearly observer the peaks associated with the spinel structure in CFO@BTO NPs. However, the peaks associated to (311), (511), and (400) planes of CFO crystal structure have appeared as either small bumps or a shift in (211) peak of the tetragonal structure in BTO shell. Although agglomeration in CFO@BTO NPs are evident in TEM image, this may be due to TEM sample preparation, as a simple drop casting methods was used for as-synthesized NPs. However, further studies for optimizing the synthesis condition and better control over the morphology of the particles are in progress.

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Decreasing the anisotropy of magnetite nanoparticles doping with Co?

David Serantes,[1]• Daniel Faílde,[2] Adolfo O. Fumega,[3] Víctor Pardo,[1] Daniel Baldomir,[1] Beatriz Pelaz,[4] Pablo del Pino,[4] and Roy W. Chantrell[5]

[1]Appl. Phys. Dept. and iMATUS, Universidade de Santiago de Compostela, Santiago de Compostela, Spain.
[2]Centro de Supercomputación de Galicia (CESGA), 15782 Santiago de Compostela, Spain
[3]Department of Applied Physics, Aalto University, 02150 Espoo, Finland
[4] Particle Phys. Dept. and CiQUS, Universidade de Santiago de Compostela, Santiago de Compostela, Spain
[5] Department of Physics, University of York, United Kingdom
*Email: david.serantes@usc.gal

Due to their good biocompatibility, iron oxide nanoparticles are the most common candidates for biomedical applications. Such applications require a great control of the magnetic properties, which may be obtained by adjusting particle size and shape. Additional fine-tuning can be achieved by doping with other elements as Co, Zn, Mn, etc. In this regard, doping with Co is usually considered a straightforward way to make them magnetically harder (i.e. to increase their anisotropy). However, when considering the broad picture of the $Co_xFe_{3-x}O_4$ series, it is noted that this exhibits a sign change of the magnetocrystalline anisotropy: while the x=0 case (magnetite) has a cubic and negative constant, $K_C<0$, the x=1 one (Co ferrite) has a cubic and positive one, $K_C>0$. This scenario raises an apparently naïve question: what happens for intermediate compositions? (see Figure 1). In this work we present a simple model, based on the macrospín approximation, that considers the resultant effective anisotropy to be directly proportional to the amount of Co. The change of sign of the anisotropy at the ends of the series implies that a composition should exist at which the change occurs; remarkably, that implies that the initial range of Co-doping leads to a decrease of the anisotropy, until becoming zero (at around 0.05% Co-doping). Such an unexpected result -that doping with Co may decrease the anisotropy- is also supported by *ab initio* electronic structure calculations and, furthermore, confirmed with our own experiments with spherical $Co_xFe_{3-x}O_4$ particles with an unprecedented level of control of both Co-doping content, and particle shape (to diminish shape contributions to the effective anisotropy).

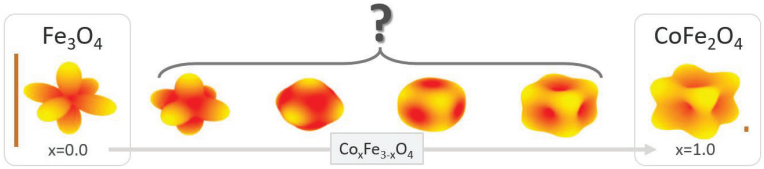

Figure 1. Scheme illustrating the transition from magnetite (x=0, $K_C < 0$) to Co-ferrite (x=1, $K_C>0$), and raising the question of what might be occurring for intermediate compositions.

The impact of Coating Zero-Valent Iron Nanoparticles on Advanced Oxidative Processes

Carlos Díaz-Ufano[1], Nahuel Nuñez[2], Elin Winkler[2], María del Puerto Morales[1], Sabino Veintemillas-Verdaguer[1]

[1]Instituto de Ciencia de Materiales de Madrid, ICMM/CSIC, 28049 Madrid, Spain

[2]Laboratorio de Resonancias Magnéticas, Gerencia de Física, Centro Atómico Bariloche, Av. Bustillo 9500, (8400) S. C. de Bariloche (RN), Argentina

Stabilized zero-valent iron nanoparticles (ZVIN) have become essential in several catalytic processes, particularly in driving Fenton-like reactions with interesting applications in advanced oxidation processes for water purification [1]. These reactions that take place at the nanoparticle surface generate reactive oxygen species (ROS) essential for breaking down organic compounds into smaller fragments or oxidizing them into CO_2. Effective control over the reactivity of the nanoparticle surface holds the key to regulating the generation of ROS over time.

Here, the synthesis of zero-valent iron nanoparticles was achieved using the polyol method in a highly alkaline environment. This method has been refined to enable the direct reduction of iron (II) salts to iron (0) without the need for any additional reducing agents. This optimization has resulted in the production of well-defined cubic nanoparticles with sizes below 100 nm [2]. The ZVIN were coated with a thin layer of metal hydroxides such us $Ni(OH)_2$ and $Mn(OH)_2$ by heterogeneous precipitation and an organic polymer such as PVP introduced during the synthesis (Figure 1a-d). The oxidation of the ZVIN particles with time was followed by electron paramagnetic resonance (EPR), analyzing the ROS generation. It was concluded that Fe^0 nanoparticles coated with manganese hydroxide produce practically the same amount of ROS after being suspended in water at pH 4 for one week. However, Fe^0 nanoparticles coated with nickel hydroxide exhibited highest ROS levels at shorter times, although they decayed rapidly afterwards (Figure 1f). Magnetic characterization conducted at room temperature on the particles prepared one month ago revealed that manganese-coated particles exhibited less oxidation compared to those coated with nickel and PVP (Figure 1e). This suggests that manganese coating effectively slow down the oxidation of the ZVIN and controls the reactivity at the surface.

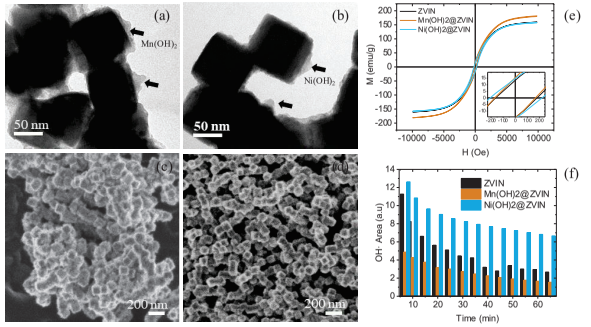

Figure 1. TEM and SEM micrographs of the zero-valent iron nanoparticles coated with $Mn(OH)_2$ (a,c) and $Ni(OH)_2$ (b,d). Hysteresis loops at RT (e) and OH· production with time measured by EPR (f).

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Advanced analysis of magnetic nanoflower measurements to leverage their use in biomedicine

Jonathan Leliaert[1*], Augustas Karpavičius[1], Philipp Bender[2], Annelies Coene[3]

[1] Dept. of Solid State Sciences, Ghent University, Ghent, Belgium
[2] Dept. of Physics and Materials Science, University of Luxembourg, Luxembourg, Grand Duchy of Luxembourg
[3] Dept. of Electromechanical, Systems and Metal Engineering, Ghent University, Ghent Belgium
*Email: jonathan.leliaert@ugent.be

Magnetic nanoparticles are an important asset in many biomedical applications ranging from the local heating of tumours[1] to targeted drug delivery towards diseased sites[2]. Recently, magnetic nanoflowers showed a remarkable heating performance[3,4] in hyperthermia experiments thanks to their complex structure leading to a broad range of magnetic dynamics.

To grasp their full potential and to better understand the origin of this unexpected heating performance, we propose the use of Kaczmarz' algorithm[5] in interpreting magnetic characterisation measurements[6]. It has the advantage that no *a priori* assumptions need to be made on the particle size distribution, contrasting current magnetic interpretation methods that often assume a lognormal size distribution.

In this work[7], both approaches are compared on DC magnetometry, magnetorelaxometry and AC susceptibility characterisation measurements of the nanoflowers. We report that the lognormal distribution parameters vary significantly between data sets, whereas Kaczmarz' approach achieves a consistent and accurate characterisation for all measurement sets. Additionally, we introduce a methodology to use Kaczmarz' approach on distinct measurement data sets simultaneously. It has the advantage that the strengths of the individual characterisation techniques are combined and their weaknesses reduced, further improving characterisation accuracy. Our findings are important for biomedical applications as Kaczmarz' algorithm allows to pinpoint multiple, smaller peaks in the nanostructure's size distribution compared to the monomodal lognormal distribution. The smaller peaks permit to fine-tune biomedical applications with respect to these peaks to e.g. boost heating or to reduce blurring effects in images. Furthermore, the Kaczmarz algorithm allows for a standardised data analysis for a broad range of magnetic nanoparticle samples. Thus, our approach can improve the safety and efficiency of biomedical applications of magnetic nanoparticles, paving the way towards their clinical use.

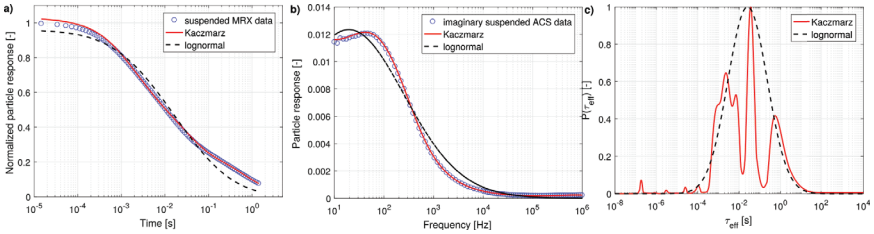

Fig. 1: Best combined fit to a) the magnetorelaxometry measurement data and b) imaginary part of the AC-susceptibility measurement data of suspended nanoflowers using a lognormal distribution and using Kaczmarz' method. c) The obtained relaxation time distributions corresponding to the fits in panel a) and b).

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INVITED TALK

Evaluating the Effect of Nanomagnetic Forces on Neuronal Cells: Towards Magnetically Guided Nerve Regeneration

T. Nahar[1], M. Gates[1,2], E. Secret[3], J.M. Siaugue[3], J. Fresnais[3], M. Rotherham[1,4], A.J. El-Haj[4] and Neil D. Telling[1*]

[1]School of Pharmacy and Bioengineering, Keele University, Staffordshire, UK
[2]School of Medicine, Keele University, Staffordshire, UK
[3]Sorbonne Université, CNRS, Physico-Chimie des Électrolytes et Nanosystèmes Interfaciaux, PHENIX, 75005, Paris, France
[4]Healthcare Technology Institute, Institute of Translational Medicine, University of Birmingham, Birmingham, United Kingdom
*Email: n.d.telling@keele.ac.uk

The central nervous system (CNS) consists of both the brain and spinal cord and is responsible for co-ordinating activity across our entire body. Such co-ordination requires the precise connections of billions of neurons (nerve cells) by axons, sometimes across distances of up to 0.5 metres long. Unfortunately, the ability of axons in the CNS to naturally regenerate is extremely limited, and so functional deficits resulting from damage to the brain or spinal cord can persist indefinitely.

We are investigating how magnetic force can be utilized to direct outgrowth in neuronal cells to facilitate the regeneration of axons. To do this we use magnetic nanoparticles sequestered within intracellular compartments known as endosomes. The forces effective on these 'magnetic endosomes' are significantly larger than those for individual nanoparticles and can be manipulated by applying suitable magnetic field gradients to the cells to create locally varying 3D force vectors (Fig. 1(a)). The average direction of resulting neurite outgrowth in different cell regions was quantified using a 2D Fourier transform analysis (an example of which is shown in Fig. 1(b), (c)), and showed excellent agreement with the derived magnetic force vectors from the applied magnetic field configuration. Significantly, the control of orientation was found to be effective over areas >1cm^2 using only modest forces of ~10s fN per endosome, apparently limited only by the local population density of cells. Furthermore, in regions where the force vectors converged, large (~100 µm) nanoparticle loaded spherically shaped cell aggregates were seen to form, connected by unusually thick and artificially linear neurite fibres. This suggests a magnetically driven enhancement of cellular aggregation, with the resulting (magnetic) spheres themselves appearing to contribute to the local forces that direct outgrowth. Such structures, which have not been previously observed, could provide new insights into the development and possible enhancement of neural circuitry.

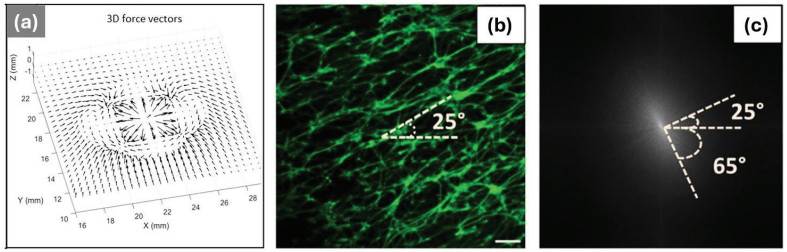

Figure 1: (a) 3D magnetic force vectors derived from measurements of the local magnetic field gradients from a magnet array system in contact with cell culture plates. (b) Low magnification fluorescence microscopy image of neuronal cells stained for β-III tubulin (scale bar=100 µm). (c) 2D Fourier transform of the fluorescence image, showing preferred orientation along an axis (the angle was determined from a corresponding radial sum plot – not shown).

Disk Shaped Magnetic Thin-Film Nanoparticles Tailored for Optimal MPI Signal Generation

Erik M. Mayr † [1,2,3], Justin Ackers [6], Alex Gogos [2], Subas Scheibler [1,2,3], Matthias Graeser [6,7], Michał Krupiński [8], Inge K. Herrmann [1,2,4], Hans J. Hug [3,5]

[1] Nanoparticle Systems Engineering Laboratory, Institute of Energy and Process Engineering, Department of Mechanical and Process Engineering, ETH Zurich, Zurich, Switzerland.
[2] Laboratory for Particles Biology Interactions, Department Materials Meet Life, Swiss Federal Laboratories for Materials Science and Technology (Empa), St. Gallen, Switzerland.
[3] Magnetic and Functional Thin Film Laboratory, Department Materials Meet Life, Swiss Federal Laboratories for Materials Science and Technology (Empa), Dübendorf, Switzerland.
[4] The Ingenuity Lab Zurich, Balgrist University Hospital, University of Zurich, Zurich, Switzerland.
[5] Department of Physics, Faculty of Science, University of Basel, Basel, Switzerland
[6] Fraunhofer IMTE, Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering, Lübeck, Germany
[7] Institute for Medical Engineering, University of Lübeck, Lübeck, Germany
[8] Institute of Nuclear Physics, Polish Academy of Sciences, Kraków, Poland
† corresponding author, email: ermayr@ethz.ch

Magnetic Particle Imaging (MPI) generates signals through the nonlinear magnetization response of magnetic nanoparticle tracers to an external magnetic field. The common tracers used so far are superparamagnetic iron oxide (SPIO) nanoparticles. These particles exhibit a Langevin-type magnetization curve with a modest saturation magnetization, restricting their susceptibility $\chi = \mathrm{dM/dH}$. Consequently, this leads to a limited generation of higher harmonic signals in magnetic drive field oscillations, thereby affecting the sensitivity and spatial resolution achievable in MPI setups.

In our research, we apply a top-down approach to fabricate disk shaped magnetic nanoparticles out of discontinuous metal-insulator multilayers (DMIMs), which are fabricated by sputter-deposition on 2″ silicon wafers. In these $Co_{40}Fe_{60}$ / Al_2O_3 DMIMs, a magnetic metal alloy film of low nominal thickness forms a discontinuous layer, consisting of superparamagnetic islands. By tuning the respective thicknesses of the magnetic and non-magnetic layers, we can induce a collective superferromagnetic behaviour of the islands in the discontinuous layers, resulting in a M(H) loop of the multilayer system characterized by a large saturation magnetization and a very high susceptibility around a small coercive field of around 0.5 mT. The recorded magnetic particle spectra of the DMIM system and the resulting disk-shaped magnetic nanoparticles showed a significant enhancement in the amplitudes of the higher harmonics when compared to Perimag particles, the current gold standard for SPIO MPI tracers, translating to an improvement in signal-to-noise ratio, as well as spatial resolution.

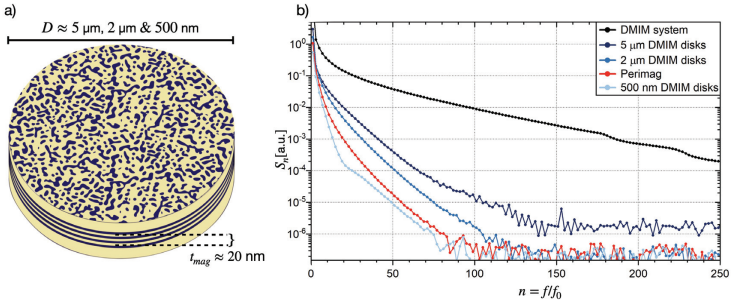

Figure 1: a) Schematic representation of fabricated disk-shaped DMIM particles, showcasing the multilayer structure and the discontinuous nature of the magnetic layers. For the chosen DMIM system, the effective magnetic thickness is given by $t_{mag} \approx 20$ nm. Particles with a diameter of around 5 µm, 2 µm and 500 nm are investigated. b) The signal spectra of the DMIM system on a wafer, the resulting tracer particles with different disk diameters and Perimag are shown. The DMIM system outperforms Perimag by 3 to 4 orders of magnitude in terms of signal amplitude in the higher harmonics. The signal intensity drops as particle diameter decreases. For larger disk diameters, signal intensity still outperforms Perimag, while the 500 nm DMIM disks generate weaker signal.

Imaging performance of thin-film disk particles tailored for optimal MPI signal generation

Justin Ackers[1*], Erik Mayr[2], Michal Krupiński[3], Inge K. Herrmann[2,4], Hans Josef Hug[2] and Matthias Graeser[1,5]

[1] Fraunhofer IMTE, Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering, Lübeck, Germany
[2] Empa, Swiss Federal Laboratories for Materials Science and Technology, Dübendorf/St.Gallen, Switzerland
[3] The Henryk Niewodniczanski Institute of Nuclear Physics, Kraków, Poland
[4] ETH Zürich, Zürich, Switzerland
[5] Institute of Medical Engineering, University of Lübeck, Lübeck, Germany
E-Mail: {justin.ackers, matthias.graeser}@imte.fraunhofer.de

The imaging performance of a Magnetic Particle Imaging (MPI) scanner is fundamentally constrained by the magnetic characteristics of the employed tracer. The achievable spatial resolution depends on the magnetic particle used, particularly on its magnetic moment's reaction to the applied oscillatory field, which, for commonly used superparamagnetic particles, is limited by their Langevin-type magnetization behavior. An optimal nanoparticle would demonstrate a high magnetic moment and a step-like magnetization response to the magnetic field oscillations. This sharp response leads to a narrow point spread function and improves the achievable imaging resolution, by making more higher harmonics detectable above measurement noise.

In this study, we utilized magnetic disk particles fabricated via a top-down approach forming discontinuous metal-insulator multilayers (DMIMs). With this method of fabrication, the optimization of the particles' magnetic properties is not constrained by chemical synthesis limitations resulting in a magnetization behavior closer to the optimum. We analyzed the imaging performance of these particles by employing multi-dimensional (one-, two-, and three-dimensional) excitations and determining the system matrices using a multi-dimensional magnetic particle spectrometer. These results were then benchmarked against Perimag (micromod Partikeltechnologie GmbH, Rostock, Germany), the established gold standard MPI tracer. The system matrices of the disk particles revealed significantly stronger signals, especially noticeable in the high-order harmonics encoding the higher spatial frequencies. Furthermore, the structure of these one- and two-dimensional matrices closely resemble Chebyshev polynomials, without the typical vignette effects visible for existing MPI tracers. Using these system matrices, hybrid software phantoms were reconstructed to quantify the resolution improvement to 50% compared to Perimag (3.4 mm vs 2.2 mm at 1 T/m). Finally, the real-world imaging performance is analyzed in a preclinical MPI scanner showing the potential for future applications based on the presented manufacturing approach.

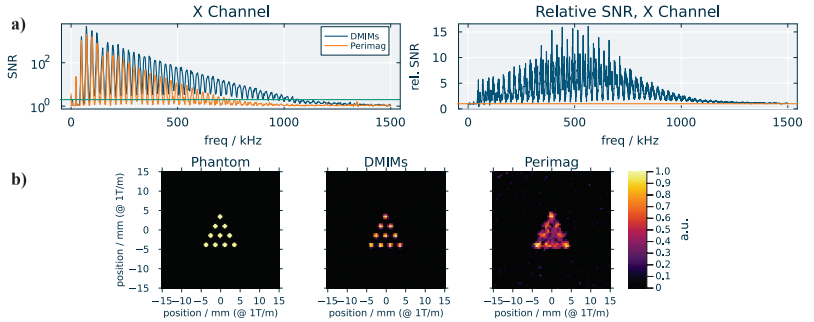

Figure 1: a) Signal-to-noise ratio (SNR) comparison between disk-particles and Perimag for 2D excitation showing improved SNR at higher frequencies, **b)** corresponding hybrid reconstruction with significant improvement in image resolution

Understanding the Partial Volume Effect in Magnetic Particle Imaging (MPI): A study of object size impact on signal distribution and quantification accuracy

Hayden J. Good[1], Sarah N. Parrett[2], Sebastian A. Montero[1], Andrii Melnyk[1], Eric Imhoff[1], A. Rahman Mohtasebzadeh[3], Toby Sanders[3], Patrick W. Goodwill[3], and Carlos M. Rinaldi-Ramos[1,2,*]

[1]Department of Chemical Engineering, University of Florida, Gainesville, FL

[2]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL

3. Magnetic Insight, Inc. Alameda, CA

*Email: carlos.rinaldi@ufl.edu

Magnetic Particle Imaging (MPI) is a new imaging modality that has garnered interest for biomedical applications due to its quantitative nature and high resolution. However, quantification errors arise for large sample volumes that some authors have attributed to the partial volume effect (PVE). In other imaging modalities, such as positron emission tomography, the PVE arises due to the finite resolution of the imaging modality and is manifested by signal suppression for samples close to or below the spatial resolution of imaging, resulting in quantification errors for small sample volumes. This study aims to systematically characterize the Partial Volume Effect (PVE) in MPI by probing the effect of object size on the ability of MPI to measure superparamagnetic iron oxide nanoparticle (SPION) distributions in hollow phantoms. Apparent tracer concentration, the relationship between image and object size, and accuracy in iron estimation were measured as a function of object size.

3D printed millimeter scale hollow phantoms were filled with commercially available VivoTrax+ tracer and scanned in the MPI under different conditions. Results show image size estimations closely match true object size for large models, but deviate for small models, suggesting the true limit of resolution. Signal suppression was apparent for small models, while signal plateaued and saturated for large models. To understand how the ratio of reference volume to sample volume impacts quantification, models with constant mass in varying volume were compared against small or large reference sample volumes. Results show that accuracy of estimation depends on relative sizes of the test and reference sample volumes.

The work to be presented lays a foundation for future studies aiming to correct the consequences of PVE in MPI. Importantly, it demonstrates that test sample to reference sample volume ratio must be considered for accurate iron estimation and image resolution. Current MPI research dogma predicates use of microliter reference samples to quantify unknown masses in larger test volumes. The results to be presented suggest that this approach is flawed. Suggestions to mitigate these effects will be presented.

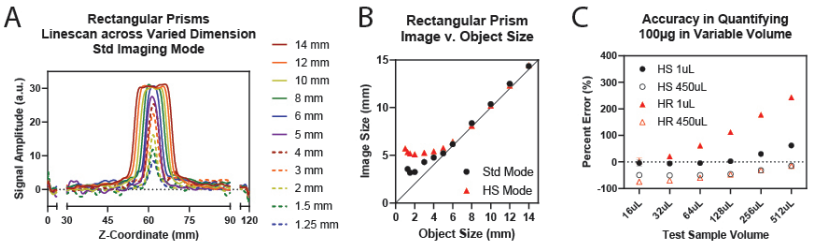

Figure. A) Linescans across the varied dimension of rectangular prisms, demonstrating signal suppression for small samples and plateau for large samples. B) Image size, calculated by full width at half-maximum, plotted against object size, demonstrating resolution limit. C) Accuracy in quantifying 100µg$_{Fe}$ in varying test volumes using small or large reference volumes, demonstrating the impact of reference volume in quantification error.

Advancing magnetic particle imaging (MPI) with SMART RHESINs: A novel hollow nanosphere tracer design for viscosity-independent relaxation

Julia Feye [a,b], Jochen Franke [c], Jens Treptow[b], Claus Feldmann[b], Peter W. Roesky[b], Esther S. Rösch [a*]

[a] Faculty of Engineering, Baden-Württemberg Cooperative State University Karlsruhe, Germany

[b] Insititute for Inorganic Chemistry, Karlsruhe Institute of Technology (KIT), Germany

[c] Bruker BioSpin MRI GmbH, Ettlingen, Germany

[*] Corresponding author, email: esther.roesch@dhbw-karlsruhe.de

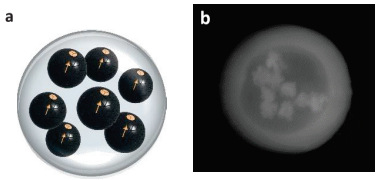

Figure 1: a) Illustration of the SMART RHESIN design. **b**) TEM image of synomag-D-filled SMART RHESIN.

Magnetic particle imaging (MPI) is a promising modality in medical imaging that utilizes the magnetic properties of nanoparticles. So far, mainly commercially available or core/shell nanoparticles have been used, but the development of specific MPI tracers promises a better signal detection and opens up new possibilities in biomedicine. In our study, we introduce SMART RHESINs[1] (**Figure 1 a**), an innovative tracer architecture specifically designed for MPI. In SMART RHESINs, magnetic nanoparticles (MNPs) are encapsulated in a hollow nanosphere (**Figure 1 b**), protecting the MNPs from external influences such as changes in viscosity and thus enabling potential signal quantification independent of the properties of the surrounding media. Further MPS studies confirmed that the phase Φ_k of encapsulated synomag-D remains nearly unaffected by varying media viscosities (**Figure 2 b**), unlike native synomag-D (**Figure 2 a**). MPI image reconstruction of immobilized synomag-D cannot be performed using the system matrix from mobile synomag-D in water (**Figure 2 c, d** - successful and artifact, respectively). As expected, successful reconstructions of SMART RHESINs (containing encapsulated synomag-D) in water and agar-agar use the system matrix of SMART RHESINs in water (**Figure 2 e, f**). In conclusion, the protective shell of SMART RHESINs ensures constant effective relaxation, showcased in MPS and MPI. The SMART RHESIN approach keeps the effective relaxation constant in contrast to classical core/shell NPs and offers a highly versatile platform. These findings open avenues for versatile theranostic MPI tracers from hollow nanospheres, enhancing quantitative MPI techniques.

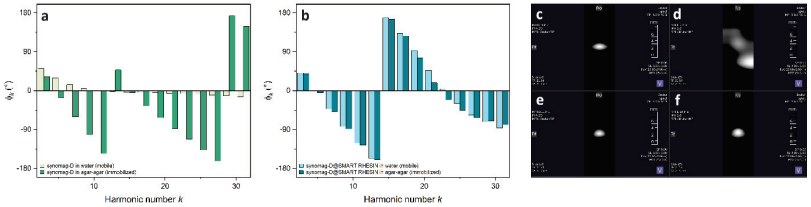

Figure 2: Odd harmonics of the MPS phase spectra Φ_k **a**) synomag-D in water (light green) and synomag-D in agar-agar (dark green) and **b**) synomag-D encapsulated in SMART RHESINs in water (light blue) and synomag-D encapsulated in SMART RHESINs in agar-agar (dark blue) at 20 mT drive field excitation at 25.25 kHz. MPI image reconstruction of synomag-D **c**) in water (mobile) and **d**) in agar-agar (immobilized) with the system matrix of synomag-D in water. Image reconstruction of SMART RHESINs **e**) in water (mobile) and **f**) in agar-agar (immobilized) with the system matrix of SMART RHESINs in water. MPI: commercial preclinical MPI system (MPI 25/20FF, Bruker BioSpin GmbH, Ettlingen, Germany). Gradient field strength was 2.5 T/m in z-direction and 1.25 T/m in x- and y-direction. Drive field frequency was 24.51 kHz in x-direction, drive field amplitude was 14 mT. Mobile samples were measured in deionized H_2O. For immobilization measurements, the samples were embedded in 10 mg/mL agar-agar.

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Ultra-small Iron Oxide Nanoparticles to Replace Gd Complexes as T_1 Contrast Agents for MRI

Liudmyla Storozhuk,[a,b] Maximilian O. Besenhard,[c] Céline Kiefer,[d] Sylvie Begin,[d] Damien Mertz,[d] Asterios Gavriilidis,[c] Nguyen Thi Kim Thanh.[a,b,*]

[a]UCL Healthcare Biomagnetics and Nanomaterials Laboratories, 21 Albemarle Street, London, W1S 4BS, U.K.
[b]Biophysics group, Department of Physics and Astronomy, University College London, London, WC1E 6BT, U.K.
[c]Department of Chemical Engineering, University College London, London, WC1E 7JE, U.K.
[d]Institut de Physique et Chimie des Matériaux de Strasbourg, BP 43, 67034, Strasbourg, France
Email: ntk.thanh@ucl.ac.uk, http://www.ntk-thanh.co.uk

Gadolinium-based contrast agents (GBCAs) are frequently used to enhance magnetic resonance imaging (MRI) contrast, which is particularly helpful in visualizing vascular structures and identifying breakdowns in the blood-brain barrier caused by conditions like tumours, abscesses, or inflammatory tissue. However, GBCAs can cause severe side effects like nephrogenic systemic fibrosis, which can lead to skin contractures, fractures, or even death. As a result, researchers are working to develop alternative T_1 contrast agents that are safer for human.

Iron oxide nanoparticles (IONPs) have emerged as a promising material for T_1 contrast agents, offering immense potential to improve the accuracy of MRI scans. However, IONPs have some challenges, including the need for clinical expertise in interpreting IONP-enhanced MR images and the potential for toxicity at high doses or prolonged exposure.

Using a multistage flow reactor, we developed a simple and cost-effective approach to synthesize various ultra-small single-phase iron oxide nanoparticles via the co-precipitation method. We used the principle of quenching the growth of IONPs during a fast co-precipitation synthesis combined with a partly dissolving precursor iron solution to obtain ultra small IONPs (USIONPs) with sizes down to 1.7 nm. It was found that USIONPs, particularly those less than 5 nm in size (2.7 nm and 1.7 nm), had higher r_1 values than 5 nm particles in positive contrast MRI. The r_2/r_1 ratio was approximately similar for 5 nm and 2.7 nm particles, reaching 3.4, and r_2/r_1 was 2.88 for 1.7 nm particles. These values for USIONP are in the same range as those for commercial GBCAs.

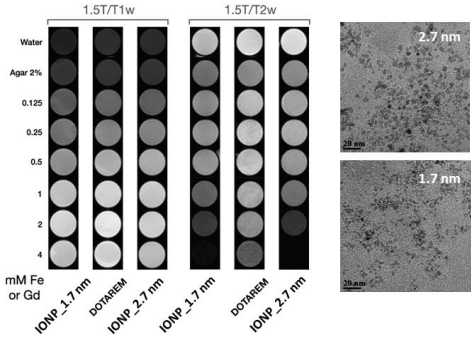

Figure 1. Phantom MR imaging of 1,7 nm IONPs, Dotarem and 2.7 nm IONPs with different concentration in range 0.125 - 4 mM Fe at 1.5 T/T_1w and 1.5 T/ T_2w (left) and TEM images of 2.7 and 1.7 nm IONPs (right).

Reference:

Besenhard M. O., et al., (2021) Small Iron Oxide Nanoparticles as MRI T_1 Contrast Agent: Scalable Inexpensive Water-Based Synthesis Using a Flow Reactor. Nanoscale. 13: 8795-8805. https://doi.org/10.1039/D1NR00877C

Imaging of the flow diverter stent insertion into a patient-specific cerebral aneurysm phantom by Magnetic Particle Imaging

O. Kosch[1*], A. F. Sanches[2], Y. Özpeynirci[2], T. Liebig[2], and F. Wiekhorst[1]
[1] *Department 8.2 Biosignals, Physikalisch-Technische Bundesanstalt, Berlin, Germany*
[2] *Institute for Diagnostic and Interventional Neuroradiology, University Hospital LMU Munich, Germany,*
*Email: olaf.kosch@ptb.de

Undetected asymptomatic brain aneurysms have a high risk of progressive expansion [1] that in about 80% can lead to rupture, bleeding, and death. Therefore, imaging techniques to assess the state of aneurysms and the success of their treatment are of great importance. To this end, we manufactured patient-specific phantoms of cerebral artery including aneurysm using 3D silicon printing using MRI data sets of patient-specific cerebral aneurysms. One phantom was "treated" with a flow diverter (FD) stent while the other was not. By Magnetic Particle Imaging (MPI), a biomedical imaging modality with high temporal and spatial resolution utilizing magnetic nanoparticles (MNP) as tracer, we studied the flow characteristics of MNP in 3D printed phantoms using a preclinical MPI system (MPI 25/20 FF, Bruker Biospin, GER) equipped with an additional gradiometric receive-only coil. The full setup and measurement details will be presented at the conference. Dynamic MPI flow measurements of the artery and the treated artery containing the FD-stent were compared to evaluate the efficacy of stent treating of aneurysms. The flow in the untreated artery is exemplified Fig. 1, top row, where a stable vortex flow is observed with a long afterglow in the MPI images. Driven by the main flow in the cerebral artery, the circulation of the vortex flow starts in the lower part of the aneurysm, s. Fig. 1 top row, t= 8 s, and moves up to the upper part of the aneurysm. At t= 40 s and t= 83 s, the flow returns to the main arterial flow in the upper left outside the dashed red circle.

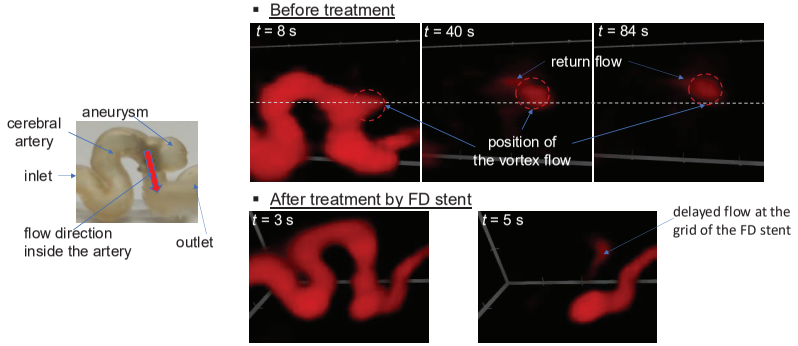

Figure 1: Imaging of the cerebral artery including aneurysm; **Left side:** View of the patient-specific phantom, **Right, top row:** Vortex flow in the aneurysm at time points t= 8 s, t= 40 s and t= 83 s. **Right, bottom row**: Imaging of the cerebral aneurysm after treatment with FD stent;

Following treatment, the FD stent suppresses the vortex flow in the aneurysm (s. Fig.1, bottom row, t= 3 s), allowing arterial flow to reach only a small region outside the grid of the stent. MPI sensitivity to detecting such small flow turbulences, as here at the grid, is evident. Our results provide valuable information on the capabilities and prospects of MPI imaging of vascular structures and the detection and quantification of flow changes in untreated and treated aneurysms for future *in vivo* applications.

Reference:

[1] K. D. Dennis, T. L. Rossman, D. F. Kallmes, and D. Dragomir-Daescu, "Intra-aneurysmal flow rates are reduced by two flow diverters: an experiment using tomographic particle image velocimetry in an aneurysm model," doi: 10.1136/neurintsurg-2014-011323.

Theranostics: Magnetic Particle Imaging based planning & controlling of highly localized Magnetic Fluid Hyperthermia

Jochen Franke[1], Oliver Buchholz[1], Huimin Wei[2], Matthias Graeser[2], Ulrich G. Hofmann[3]
[1] Bruker BioSpin GmbH & Co. KG, [2] Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering,
[3] Section for Neuroelectronic Systems University Medical Center Freiburg
email: Jochen.Franke@Bruker.com

Introduction: Specialized nanomaterials featuring dedicated responses to external magnetic fields are not only crucial for molecular imaging, but also open the door to the development of magnetism based therapeutic strategies [1]. Leveraging the diagnostic value of imaging techniques in combination with therapeutic strategies, called theranostics, gains attention as such systems can push the boundaries for future therapeutic processes. A unique setting of theranostics exists in the domain of Magnetic Particle Imaging (MPI) [2,3] in combination with Magnetic Fluid Hyperthermia (MFH). Each modality contributes to the overall therapeutic process from a different perspective and both methods complement each other. Thus, such a theranostic platform permits to minimize the multidimensional area of conflicting therapeutic processes.

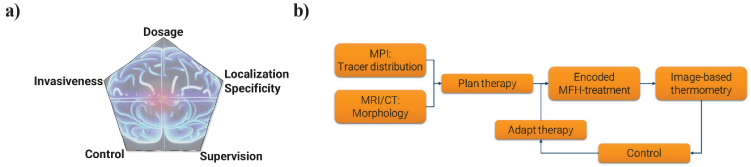

Figure 1: a) Multidimensional area of conflicting therapeutic processes b) Theranostic approach leveraging MPI to plan and encode MFH-applications as well as for MPI-based thermometry to actively control the therapy.

- MPI provides the quantitative distribution of iron-oxides or magnetically labelled drugs, which is the basis for precise iron concentration-dependent therapy planning. In addition, MPI can estimate the temperature of the magnetically labelled drugs, which enables an image-based control mechanism for MFH therapy.
- MFH provides non-invasive and depth-independent energy deposition by exploiting magnetization losses within the iron-oxides. This thermal stimulus eventually provokes drug release of thermo-sensitive compounds or is utilized directly by means of therapeutic heat generation. In addition, the magnetic gradient field of a MPI system can be used to confine the energy deposition to a very small volume easily shifted to any target location in the body.

Method: To demonstrate the theranostic benefit, an in-situ prototype combining MPI and MFH has been reported recently [4]. A MPI system featuring a magnetic gradient field up to 2.5 T/m and field-free-point topology (MPI 25/20 FF, Bruker BioSpin, Ettlingen, Germany) served as basis, while a custom-made MFH-insert [5], adequate for rat-sized rodents, has been integrated. Various tracer materials have been evaluated with respect to their specific-absorption-rate at the given insert field's parameters (f_{MFH}=700 kHz, A_{MFH}=10 mT_{pk}). Furthermore, the specificity of magnetically localized MFH applications, MFH efficacy under flow condition and MPI-based thermometry has been reported, too [4,6].

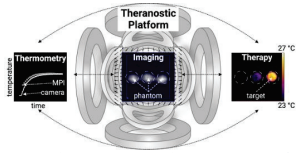

Figure 2: Theranostic platform combining MPI and MFH in a single device, permitting for in situ and localized theranostic applications complemented with MPI-based thermometry as control mechanism. Source: https://www.thno.org/v14p0324

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Funding: German Federal Ministry of Research project FKZ:13GW0230A,B,C

INVITED TALK

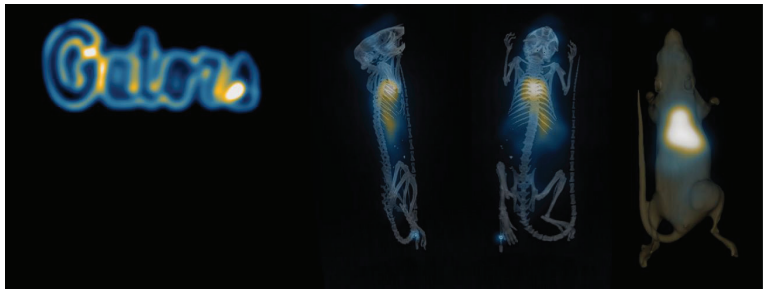
Magnetic Particle Imaging of Dendritic Cell Migration in Cancer Therapy

Carlos M. Rinaldi-Ramos

Department of Chemical Engineering and J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL 32611 U.S.A.

Email: carlos.rinaldi@ufl.edu

Magnetic Particle Imaging (MPI) is a new molecular imaging technology capable of unambiguous and quantitative tomographic imaging of the distribution of superparamagnetic nanoparticle tracers in vivo. While the acronym MPI may be easily confused with that for Magnetic Resonance Imaging (MRI), the two rely on distinct physics. In MPI, a tomographic image of the distribution of superparamagnetic nanoparticles is constructed by scanning a so-called field free region (FFR) through the domain of interest. Outside the FFR there is a quasi-static bias field strong enough to saturate the magnetic moments of the nanoparticles. But inside the FFR the dipole moments of the nanoparticles respond to the superimposed alternating excitation field. The signal used to construct an image in MPI arises due to the non-linear dynamic magnetization response of the nanoparticle dipole moments to the excitation field inside the FFR. At the field amplitudes and frequencies used in MPI there is no appreciable attenuation in signal strength due to tissue. Further, while there are magnetic species in the body (e.g., ferritin), they do not contribute an appreciable signal for MPI, allowing for unambiguous imaging of the distribution of one of the superparamagnetic nanoparticle tracers. This talk will explain image generation in MPI and discuss work developing tracers and using MPI to quantitatively track biodistribution of dendritic cell cancer therapy.



A Pilot Study on the Possibility of Using Magnetic Particle Imaging for Monitoring the Magnetic Nanoparticles Uptake in Brain Due to Hyperthermia

Hafiz Ashfaq Ahmad[1], Seungjun Oh[1], Muhammad Umar Tahir[1], Hohyeon Kim[1], Gawtak Kim[1], Jihye Kim[2], Kangho Choi[2,*] and Jungwon Yoon[1,*]
[1] *School of Integrated Technology, Gwangju Institute of Science and Technology, Gwangju , South Korea*
[2] *Department of Neurology, Chonnam National University Hospital and Medical School, Gwangju 501-757, South Korea*
* Email: ckhchoikang@hanmail.net, jyoon@gist.ac.kr

Delivering drugs to the brain remains a major challenge due to the highly selective nature of the blood-brain barrier (BBB). This barrier, composed of tightly interconnected endothelial cells lining cerebral vessels, prevents harmful substances from entering the brain. This even limits the effectiveness of many drugs and therapeutics for brain disease.

Magnetic particle imaging (MPI) as a highly sensitive, real-time, with the potential for submillimeter resolution biomedical imaging, not only enables imaging of the concentration and distribution of magnetic nanoparticles (MNPs), but has also been utilized in several other applications such as cell tracking, virus detection, and drug release monitoring. The diverse possibilities offered by MPI have attracted substantial attention from the biomedical community in seeking new applications. It has been previously shown that heat generated through magnetic hyperthermia (MH) can induce substantial but reversible opening of the BBB. This change in the permeability of BBB was verified using the fluorescent Evans Blue dye [1, 2].

Based on these studies, we hypothesized that if MH can transiently open BBB, some MNPs may penetrate the barrier. Therefore, we utilized MPI to test this hypothesis in a pilot study on 8 naive Sprague Dawley rats (8 weeks old). The rats were divided into two groups and administered a 70µL injection of Synomag-D (PEG-coated iron oxide NPs, 30 mg_{Fe}/mL) through the common carotid artery. Immediately after the injection, an MPS scan was acquired as a reference and the rats' heads in group 1 were placed in a solenoid coil generating an AC field of 8 mT at 595 kHz for 30 minutes. 3D MPI and MPS scans (were then acquired immediately post- MH, and at 24h, and 72h intervals. In group 2, MPS and MPI scans were acquired at the same intervals as in group 1 and rats were allowed to rest for 30 minutes post-injection instead of the MH procedure.

Fig. 1a shows a typical slice of 3D MPI from groups 1 and 2 and Fig. 1b shows the percentage change in the MPS signals by time. It can be seen from both data that in group 1, the amount of MNPs remaining in the brain is higher than in group 2. This might be due to the change in the permeability of the BBB in response to elevated temperature. This may be considered a preliminary result of the usefulness of MPI for monitoring the MNPs uptake in the brain due to MH.

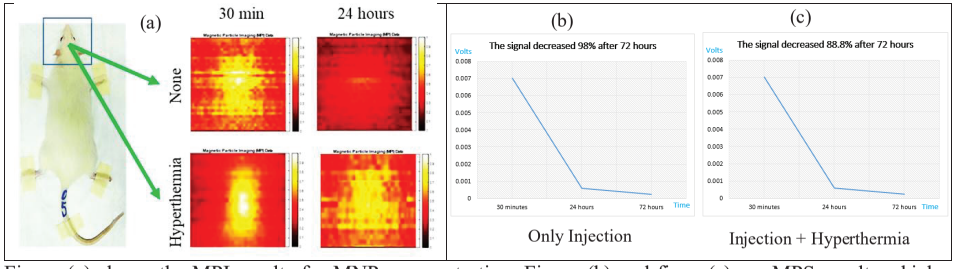


Figure (a) shows the MPI results for MNPs concentration. Figure (b) and figure(c) are MPS results which shows the voltages produced by exciting the MNPs in brain of the rat.

1. Tabatabaei, S. N.; Girouard, H.; Carret, A.-S.; Martel, S., *J. Controlled Release* **2015,** *206*, 49-57. DOI https://doi.org/10.1016/j.jconrel.2015.02.027.
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Measurement of the Differences Between Bulk Heating and Magnetic Hyperthermia via Catalytic Reactions

Alexander Adogwa[a], Ewa Chukwu[a], Alexander Malaj[b], Venkata R. Punyapu[c], Rachel B. Getman[c], Ming Yang[a], O. Thompson Mefford[b*]

[a]Chemical and Biomolecular Engineering, Clemson University, Clemson, South Carolina 29634, United States
[b]Materials Science and Engineering, Clemson University, Clemson, South Carolina 29634, United States
[c]Chemical and Biomolecular Engineering, Ohio State University, Columbus, Ohio 43210-1226
*Corresponding author: mefford@clemson.edu

Magnetic hyperthermia has long been proposed as a method to deliver thermal energy to cells to induce cell apoptosis. This "heating within" has been described as equivalent to a localized heat. Alternatively, others have discussed the idea of "cold hyperthermia", or the observation of significant cell death, with no observable bulk heating.[1] Here in, we demonstrate significant differences between traditional bulk heating and magnetic induction heating of ferromagnetic catalyst particles. We show that the MIH-triggered reaction could go beyond standard thermal catalysis. Specifically, by probing the representative Pt/Fe_3O_4 catalysts with CO oxidation in both thermal and MIH modes with consistent temperature profiles and catalyst structures, we found that the MIH mode boosts the reactivity more than 25 times by modifying Pt−FeOx interfacial synergies and promoting facile oxidation of the adsorbed carbonyl species by atomic oxygen. As we preliminarily observed, this beneficial MIH catalysis can be translational to other thermal reactions, potentially paving the way to launch MIH catalysis as a distinct reaction category. Further, characterization of these cataylized surface reactions could provide additional insight towards the mechanism of cell death in magnetic hyperthermia systems.

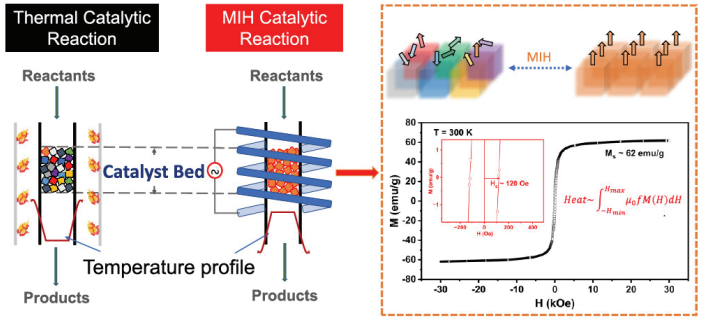

Figure: Reactor schematics of standard thermal vs MIH reactions. In the MIH mode, heating occurs through the periodic alignment of the catalyst's magnetic moment in response to the applied dynamic magnetic field (inset, top). The typical magnetic properties of the Pt/Fe3O4 catalyst via vibrating sample magnetometry (inset, bottom).[2]

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(2) Adogwa, A.; Chukwu, E.; Malaj, A.; Punyapu, V. R.; Chamness, O.; Glisson, N.; Bruce, B.; Lee, S.; Zachman, M. J.; Bruce, D. A. Catalytic Reaction Triggered by Magnetic Induction Heating Mechanistically Distinguishes Itself from the Standard Thermal Reaction. *ACS Catalysis* **2024**, *14*, 4008-4017.

An Alternative to the Brezovich Criterion in Magnetic Field Hyperthermia

Martin K. Y. Kwok[1], Cliona C. J. Maley[1], Asher Dworkin[1], Simon Hattersley[2], Paul Southern[2], and Quentin A. Pankhurst[1,2,*]

[1] Healthcare Biomagnetics Laboratory, University College London, 21 Albemarle Street, London, UK;
[2] Resonant Circuits Limited, 21 Albemarle Street, London, UK; *E-mail: q.pankhurst@ucl.ac.uk

We suggest a new approach to the definition and use of clinical tolerability metrics associated with nonspecific eddy current heating in magnetic field hyperthermia (MFH). Currently, the most often cited metric is the "Brezovich criterion" – $H_o f \geq 485$ MAm^{-1}s^{-1} – which was determined for axial time-varying magnetic fields $H(t) = H_o \sin(2\pi ft)$ and the human torso. Although the criterion in its intended form is entirely correct, it is frequently misinterpreted and misused as a holistic measure of acceptability in MFH.

We propose as an alternative metric the "maximal specific absorption rate" (SAR_{max}) of eddy-current-induced power absorbed per unit mass of tissue. With reference to published clinical data and human volunteer studies in our laboratory (Figure 1), we show that the SAR_{max} metric is both suitable and reliable for use in MFH. We also show that the metric may be extracted from *in silico* finite element models of confounding effects such as anatomical hot spots and non-axial- field geometries, and that as such it has a prospective as well as an experimental/validatory utility.

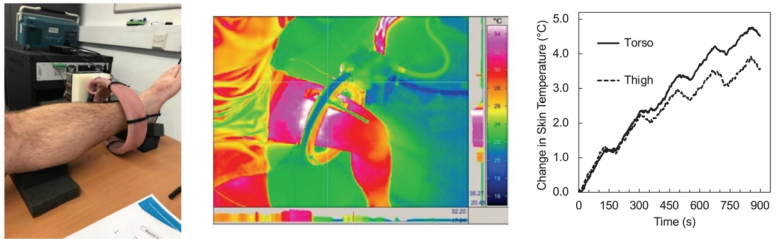

Figure 1: Nonspecific eddy current heating experiments were performed on 25 volunteers. (Left) Set-up for fields applied to the ankle; fields were also applied to the wrist, forearm, calf, thigh, and torso. (Middle) Thermal image showing local skin temperature increases in the thigh. (Right) Recorded temperature-time hot-spot data for the thigh and torso – data averaged over 15 individuals.

We further note a parallel with the "local *SAR*" metric used in magnetic resonance imaging (MRI). This is a standardised metric (formalised in IEC 60601-2-33) with well-established limits for clinical use: *viz*. that the local *SAR*, averaged over 10 g of tissue and 6 min of treatment, should not exceed 20 mWg^{-1} in the torso or head, and should not exceed 40 mWg^{-1} in the limbs. We suggest these values might be regarded as a good starting point for the design of future MFH interventions and be used alongside the SAR_{max} metric in the development of clinically safe and tolerable MFH equipment.

For more details see: Kwok *et al.*, Appl. Phys. Lett. **122** 240502 (2023).

Scale-up Syntheses of Magnetic Ferrite Nanoparticles with different Shapes with Improved Magnetic Properties for Magnetic Hyperthermia Treatment and Magnetic Particle Imaging

Giusy Maria Rita Rizzo[1,2,*], Nabila Jarmouni[1], Niccolò Silvestri[1], Helena Gavilan[1], Anna Cristina Samia[3], Teresa Pellegrino[1,*]

[1] Istituto Italiano di Tecnologia, via Morego 30, 16163 Genoa, Italy
[2] Dipartimento di Chimica e Chimica Industriale, Università di Genova, via Dodecaneso 31, 16146 Genoa, Italy
[3] Department of Chemistry, Case Western Reserve University, Cleveland, OH, 44106, USA
* giusy.rizzo@iit.it; teresa.pellegrino@iit.it

Magnetic iron oxide nanoparticles (IONPs) have found applications in various fields of nanomedicine, including Magnetic Hyperthermia Treatment (MHT) and Magnetic Particles imaging (MPI). The performances of IONPs for these specific applications are strictly related to their shape, size, crystallinity, magnetic volume and saturation magnetization. Various synthetic pathways have been explored to precisely control the final structure of IONPs. However, production of high-quality NPs is in general set at mg scale, a value which falls far short for clinical requirements. In this work, we aimed to scale-up the production of IONPs of different shape to gram scale using the solvothermal method. Our synthesis solution incorporates an alcohol solvent, carboxylic acid, amine, iron precursor and a shape-directing agent. We have discovered that benzaldehyde and its derivatives promote the formation of cubic-like nanoparticles, while aliphatic aldehydes yield spherical and hexagonal shapes. Furthermore, substituting primary amines with secondary or tertiary amines favors the formation of star-like shapes. These different shapes were evaluated for their magnetic properties and heating performance for MHT (Gavilán et al., Nature Protocols 2023, 18 (3), 783-809). By modifying a similar protocol with a similar synthetic route, we set a new synthesis to produce novel shape nanoparticles which we named Rubik-like cubes (NRKs). These nanostructures are hybrid between multicore-like nanoparticles and cubic shaped iron oxide nanoparticles. They exhibit enhanced magnetic features with outstanding performances as heaters for MHT and as tracers for MPI, opening to promising outcomes in the oncological field of imaging and therapy.

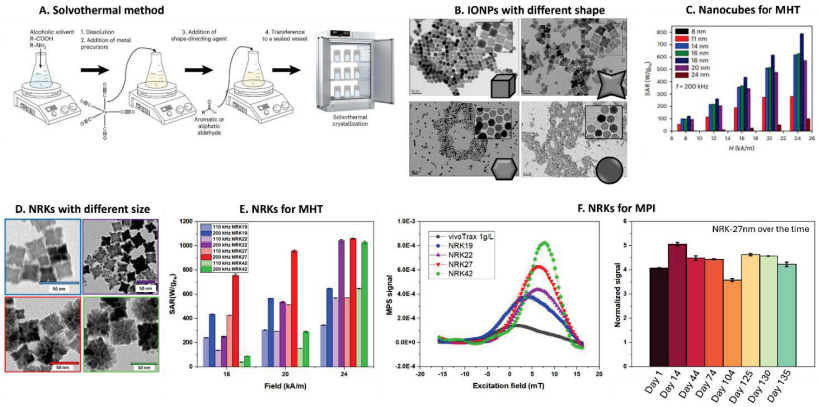

Figure. (A) Scheme of the solvothermal method here developed. (B) TEM images of different shape of IONPs and (C) heating performance expressed in specific adsorption rate (SAR) values of IONPs with cubic shape with different size. (D) TEM images of novel shape nanoparticles named Rubik-like cubes (NRKs) at different sizes and their E) SAR values and (F) MPS signals.

Reversible alignment of nanoparticles and intracellular vesicles during magnetic hyperthermia experiments

Yilian Fernández-Afonso*[1,2], Sergiu Ruta[3], Amira Páez-Rodríguez[1], Thomas S. van Zanten[1], Sian Glead-hall[3], Raluca M. Fratila[1], María Moros[1], M. Puerto Morales[2], Akira Satoh[4], Roy W. Chantrell[5], David Serantes[6], Lucía Gutiérrez[1]

[1]*Instituto de Nanociencia y Materiales de Aragón (INMA, CSIC/UNIZAR) and CIBER- BN, Zaragoza, Spain.* [2]*Materials Science Institute of Madrid (ICMM/CSIC), Spain.* [3]*College of Business, Technology and Engineering, Sheffield Hallam University, United Kingdom.* [4]*Akita Prefectural University, Japan.* [5]*Department of Physics, University of York, United Kingdom.* [6]*Applied Physics Department and Instituto de Materiais (iMATUS), Universidade de Santiago de Compostela, Spain.*

email: yfdezafonso@gmail.com

The use of magnetic nanoparticles (MNPs) to generate heat when exposed to an alternating current (AC) magnetic field has grown significantly in recent years. One overlooked aspect of the physical phenomenon occurring when the MNPs are exposed to the AC magnetic field is their assembly into elongated structures, which can strongly affect the heating properties of the material. However, this behavior has been largely unexplored both in colloids and in biological environments.

In this work we have studied, in colloids, the dynamic processes that occur when MNPs are exposed to an AC magnetic field. We have observed the MNPs alignment parallel to the field when the magnetic field is on and the fast disassembly of such structures when the field is switched off. The impact that such transformation has on their heating properties has also been assessed. This observation can help understanding discrepancies in literature results regarding the heating properties of the particles.

Moreover, we have investigated in vitro, in a macrophage cell line, whether similar assembly processes occur. We have found that the AC magnetic field is able to produce the alignment of vesicles containing the MNPs within the cells while the cells are exposed to the field, but this process is reversible and the alignment quickly disappears. This observation opens many questions about the mechanical forces generated by such movements within the cells during the magnetic field exposure.

Finally, our results suggest the observed alignment (of MNPs or intracellular vesicles (Figure 1)) might be something much more common than expected in usual hyperthermia experiments, but that is not usually reported because the structures formed under the AC magnetic field exposure rapidly disappear once the field is switched off.

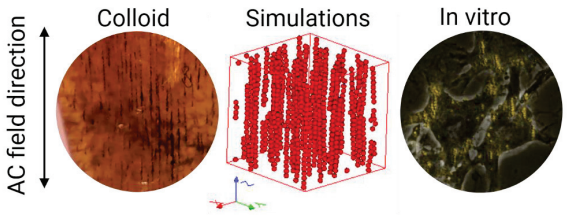

Figure 1. Study of the dynamic processes that occur when the magnetic nanoparticles are exposed to an AC magnetic field in different scenarios: in colloids, in vitro (within intracellular vesicles) and simulations. Aligned structures parallel to the field when the magnetic field is on are observed and a fast disassembly of such structures occurs upon field removal.

A device-independent approach to evaluate the heating performance during magnetic hyperthermia experiments: peak analysis and zigzag protocol

Sergiu Ruta[1], Yilian F. Afonso[2],Samuel E. Rannala[3],Sabino Veintemillas-Verdaguer[4], M. Puerto Morales[4], David Serantes[5], Lucía Gutiérrez[2], Roy W Chantrell[3]

[1]*College of Business, Technology and Engineering, Sheffield Hallam University, UK*
[2]*Department of Analytical Chemistry, Universidad de Zaragoza, Spain*
[3]*Department of Physics, University of York, United Kingdom*
[4]*Materials Science Institute of Madrid (ICMM/CSIC), Spain*
[5]*Applied Physics Department, Universidade de Santiago de Compostela, Spain*

In recent years hyperthermia has been proposed to help a range of biomedical applications such as a non-invasive alternative for cancer treatment. Accurate assessment of the heating performance of magnetic nanoparticles (MNPs) under alternating current (AC) fields is vital for advancing hyperthermia-mediated applications. Usually, the heating efficiency reported in terms of the *specific loss power* (SLP) is obtained from the temperature variation (ΔT) *vs.* time (t) curve. Most methods estimate SLP based on the initial temperature variation to minimise thermal losses. Such estimates are subjected to huge uncertainty due to dynamic changes in the sample or even from the measurement device/environment. For example, large variations in the heating efficiency of a given batch of particles have been reported when measured in different laboratories [1], under *a priori* in the same experimental conditions.

To overcome this challenge, we introduce a device-independent approach to calculate SLP values for MNP suspensions [2]. The observed variation in heat loss mechanisms during heating and cooling as illustrated by changes in the heat loss coefficients (denoted as a and b in Figure 1), emphasizes the necessity for a shift in the data analysis approach: from the initial slope measured in classical methods to the peak generated when the field is switched off.

The variation of heat lost mechanism as illustrated by the change in the heat lost coefficient (a and b in figure 1), suggest the need to shift the data that is going to be analyzed: from the the initial slope measured in the classical methods, to the peak generated when the field is switched off. This method represents an important shift in SLP measurement grounded in fundamental physics principles. The approach ensures adherence to Newton's law of cooling, minimizing the influence of diverse heat dissipation channels and enhancing SLP determination reliability. Additionally, the application of the peak analysis method (PAM) to a series of swift field on/off transitions, resulting in a *zigzag*-like $\Delta T(t)$ curve—termed the zigzag protocol—allows for the assessment of potential variations in SLP values over time or temperature.

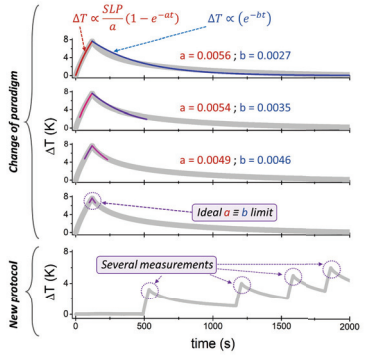

Figure 1: Scheme illustration of the advantages of the Peak Analysis Method and the zigzag protocol. Shifting the data analysis to the temperature peak leads to similar heat loss mechanisms during the heating and the cooling phases. Repeating the on/off switches several times in a zigzag way allows for quickly tracking the evolution of the SLP.

To validate the protocol, simulation have been performed based on the heat diffusion equation considering the liquid, sample holder and surrounding environment (air). The results indicate a significant improvement in the determination of the SLP value. Finally the method is tested on experimental measurement performed on 3 different devices in difference laboratories. The results are compare with existing methods such as initial slope method, Box-Lucas method and Corrected Slope Method.

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(2) Ruta, S.; Fernández-Afonso, Y.; Rannala, S. E.; Morales, M.; Veintemillas-Verdaguer, S.; Jones, C.; Gutiérrez, L.; Chantrell, R. W.; Serantes, D. *arXiv preprint arXiv:2307.11521* **2023**.

Local temperature gradients and induced cell death in intracellular magnetic hyperthermia

Angel Millán,[1*] Yuanyu Gu,[1,2] Rafael Piñol,[1] Raquel Moreno-Loshuertos,[3] Carlos D.S. Brites,[4] Justyna Zeler,[4,5] Abelardo Martínez,[6] Guillaume Maurin,[1] Patricio Fernández-Silva,[3] Joaquín Marco-Brualla,[3] Pedro Téllez,[1] Rafael Cases,[1] Rafael Navarro Belsué,[1] Débora Bonvin,[7] Luís D. Carlos[4*]

[1] INMA, Institute of Nanoscience and Materials of Aragon, CSIC-University of Zaragoza, Zaragoza, Spain,
[2] School of Materials Science and Engineering. Nanjing Tech University, 210009, Nanjing PR China,
[3] Departamento de Bioquímica, Biología Molecular y Celular, and Instituto de Biocomputación y Física de Sistemas Complejos. University of Zaragoza, C/ Pedro Cerbuna 10, 50006 Zaragoza (Spain),
[4] Phantom-g, CICECO-Aveiro Institute of Materials, Department of Physics, University of Aveiro Campus de Santiago, 3810-193 Aveiro, Portugal,
[5] Faculty of Chemistry, University of Wroclaw, 14. F. Joliot-Curie Street, 50-383 Wroclaw, Poland
[6] Departamento de Electrónica de Potencia. I3A. Universidad de Zaragoza 50018 Zaragoza, Spain
[7] Powder Technology Laboratory, Institute of Materials, Ecole Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland

*Email:amillan@unizar.es Mobile: +34 672312859

Heat transport in cells is a subject of intense debate in recent times. While theoreticians predict that it is not physically possible to reach substantial temperature increments on exogenous or endogenous nanoheaters, some experimental results point out to the possibility of large temperature gradients in the cell interior. This issue could be of critical importance in magnetic hyperthermia therapy of cancer since a high temperature increase in the nanoparticle surroundings could cause local cell damage deriving in cell apoptosis and cell death with a small heat supply, even a negligible global cell temperature. We have placed a luminescence molecular thermometer on the coating of magnetic nanoparticles, and we monitored the variation of the temperature of the nanoparticles inside the cells while being exposed to alternating magnetic fields.[1] In another set of experiments, we have used thermometric micelles[2] to measure the temperature during magnetic hyperthermia at intracellular sites close to the magnetic heaters, and that on the outside of the cell membrane. Temperature increments near 10 ºC have been found on the nanoparticle surface for moderate magnetic fields (Hf=2.4×10^9 A·m^{-1}·s^{-1}, H=30 mT, f=100 kHz), still far from the human healthy limit. This temperature increase was reduced at some distance from the nanoheaters, and it dropped to zero at the cell membrane, thus indicating that the heat input was too small to increase of the global cell temperature. Then we studied the cell death generated by the local magnetic hyperthermia and it was found that these local temperature increments were sufficient to produce noticeable cell apoptosis. Moreover, when the intensity and frequency of the magnetic field were increased to Hf values close to the healthy limit (4.8×10^9 A·m^{-1}·s^{-1}, H=60 mT, f=100 kHz), the apoptosis ratio exceed a 60%, which is already relevant for therapeutical purpose. It can be concluded that the local magnetic hyperthermia could be feasible as an improved therapeutical approach in comparison to the actual global tumor heating treatment.

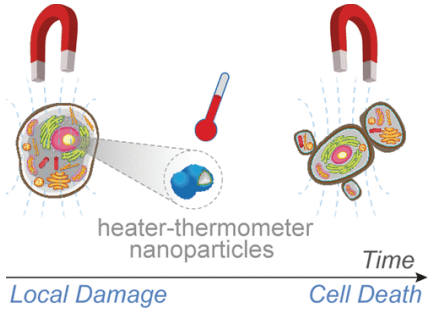

Figure 1. Local temperature variation on the magnetic nanoparticle (T_1) surface, at some distance in the cytoplasm (T_2), and on the exterior of the cell membrane (T_3), during the application of an alternating magnetic field to a cell culture. Taken from reference 1.

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Towards image-guided therapies with nanomodified stents

Max Schoenen[1], Benedict Bauer[2], Lennart Göpfert[1], Caroline Emonts[2], Thomas Gries[2], Thomas Schmitz-Rode[1], Anjali Röth[3], Ioana Slabu[1*]

[1]Institute of Applied Medical Engineering, Helmholtz Institute, Medical Faculty, RWTH Aachen University, Pauwelsstr. 20, 52074 Aachen, Germany
[2]Institut für Textiltechnik, RWTH Aachen University, Otto-Blumenthal-Str. 1, 52074 Aachen, Germany
[3]Department of General, Visceral and Transplant Surgery, RWTH Aachen University Hospital, 52074 Aachen, Germany
Email: *slabu@ame.rwth-aachen.de

The clinical relevance of magnetic nanoparticles (MNP) as tracers in magnetic particle imaging (MPI) and heating agents in magnetic hyperthermia (MH) is significantly increasing. Also, advancements in the development of multimodal devices by combination of MPI and MH accelerate the generation of new theranostic approaches.

Recently, we developed a technology that enables MH treatment of hollow organ tumors. The technology is based on a nanomodified polymer stent with incorporated MNP, which is implanted inside the hollow organ to open the occluded area and is then magnetically actuated to generate local heating and destroy the tumor. For therapy planning and monitoring, MPI promises to provide useful information paving the way towards magnetic image-guided therapies. Here, we present MH and MPI measurements of different stent types and analyse the effects of concentration, MNP agglomeration and orientation inside the fibers of the stents on their performance as heating and tracer agents. For this, we used a costum-built MH setup and an Bruker MPI system. Significant differences were detected for MNP oriented in chain-like structures. For both, MH and MPI, performance enhancing effects could be attained. Stochastic Langevin simulations confirmed the experimental data. The simulations have shown to be a useful tool in predicting heating and imaging performance.

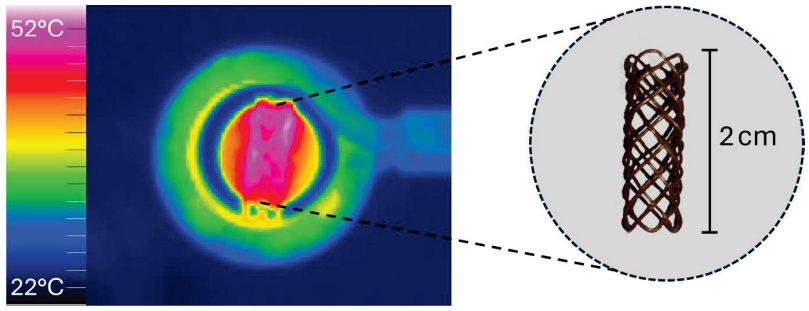

Figure 1: Photo (right) and thermographic image of a nanomodied stent heated in a the coil of a hyperthermia setup (left).

Localized Electric Fields Induced by Magnetic Nanoparticles

Michael G. Christiansen[1*], Nima Mirkhani[1], William Hornslien[2], Simone Schuerle[1†]
[1] Dept. of Health Sciences and Technology, ETH Zurich, 8092, Switzerland
[2]Dept. of Mathematical Sciences, Norwegian University of Science and Technology, 7034, Norway
*michael.christiansen@hest.ethz.ch, † simone.schuerle@hest.ethz.ch

Heat dissipated by magnetic nanoparticles while undergoing high frequency hysteresis has been envisioned as a means to wirelessly trigger biological responses or modulate catalysis. Many independent groups tacitly or explicitly assume the existence of nanoscale temperature gradients in their design concepts and have experimentally observed effects they attribute to them. Nevertheless, this assumption is controversial. Nanoscale temperature gradients are not anticipated theoretically in these systems and recent experiments seeking evidence of nanoscale heating have returned null results.[1-3] Could some other nanoscale phenomenon associated with hysteresis or magnetization dynamics help to explain observations attributed to nanoscale heating?

In this theoretical study,[4] we critically examine the hypothesis that the dynamic magnetization behavior in nanoparticles might induce electric fields sufficient to exert an influence over biological or chemical processes. We select two important case studies where the influence of hysteresis heating has been claimed to play a role, yet is difficult to explain: 1) ferritin-based magnetogenetics[5-6] (**Fig A**) and 2) enhancement of electrolysis by iron carbide nanoparticles[7] (**Fig B**). Using reported magnetic properties, we employ the stochastic Landau-Lifshitz-Gilbert equation to simulate magnetization dynamics. Finite element modelling is then used to predict the resulting induced electric fields. Our analysis suggests electric fields with peak values in the low 100s of V/m that oscillate at dominant frequencies in the GHz. This is far too rapid for the accumulation of interfacial charge in an electrolyte, and the electric fields required to directly perturb chemical or biological processes are anticipated to be much larger (**Fig C**). In addition, we find that in nanoparticles well suited for hysteresis heating, peak values of the electric field are reached during reversal. While induced electric fields apparently cannot explain the effects observed in the case studies, our results cast light on a physical phenomenon that has seldom been considered in the context of magnetic nanoparticles.

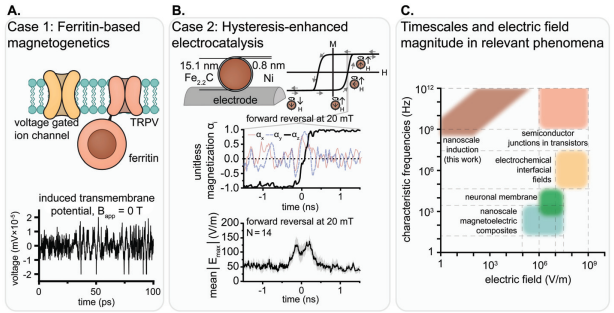

Figure. (A) Case study for transmembrane potential induced by a dynamical magnetization model of ferritin. The potential is too small to realistically perturb the voltage gated ion channel. **(B)** Case study of enhanced electrocatalysis from magnetic nanoparticle heating. The electric field peaks during reversal but is too small to influence the reaction. **(C)** A parameter space comparing relevant timescales and electric field magnitudes for relevant phenomena.

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Plasma membrane localized magnetic hyperthermia promotes intracellular delivery of cell-impermeant probes

Javier Idiago-López[1,2], María Moros, Jesús Martínez de la Fuente[1,2], Raluca M. Fratila[1,2*]

[1] Instituto de Nanociencia y Materiales de Aragón, INMA (CSIC-Universidad de Zaragoza), C/ Pedro Cerbuna 12, 50009, Zaragoza, Spain. [2] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain
*Email: rfratila@unizar.es

Magnetic nanoparticles (MNPs) have been widely exploited for diverse biomedical applications, including imaging, drug delivery, separation, and therapeutic hyperthermia. Magnetic hyperthermia (MH) is based on the ability of certain magnetic materials to generate heat when exposed to an alternating magnetic field (AMF). In the frame of traditional MH, the purpose is to raise the temperature of the targeted tissue to a level that can induce therapeutic effects. Beyond classical MH, the localized heat generated in the vicinity of MNPs (known also as the "hot-spot effect") can be harnessed for triggered release of drugs from thermoresponsive matrices, or for the remote activation of thermosensitive ion channels and enzymes. We are particularly interested in the use of MNPs immobilized on living cell membranes as nanoscale heaters able to induce the thermal disruption of the plasma membrane. Such an effect could be a valuable tool for exploring fundamental aspects of membrane biophysics or for developing new strategies for direct cytosolic delivery of biomolecules, drugs and nanoparticles. However, studying this effect on living cell membranes is not trivial, as the immobilization of MNPs is a challenging task due to the dynamic nature of the cell plasma membrane.

We have recently proposed the use of bioorthogonal chemistry as universal tool for cell surface engineering with MNPs, using the strain-promoted click azide–alkyne cycloaddition (SPAAC) reaction [1]. Here, we show that 13-nm iron oxide MNPs immobilized on the cell membrane act as localized heating sources and promote the internalization of cell-impermeant probes, such as YO-PRO®-1, a fluorescent small molecule that cannot cross intact cell membranes. We also demonstrate that our approach for the thermal disruption of the plasma membrane does not trigger cell death, oxidative stress and alterations of the cell cycle, although cells are able to sense and respond to the thermal stimulus through the expression of different types of heat shock proteins (HSPs). Moreover, the expression of the HSPs studied was different, depending on the nature and location of the heat shock agent, and associated with the role and preferential localization and site of action of each type of HSP studied.

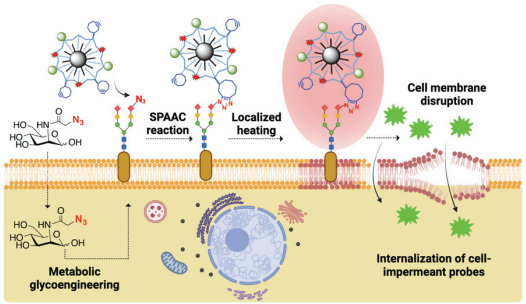

Figure 1: General concept for MH-mediated intracellular delivery using MNPs immobilized on the cell membrane via SPAAC bioorthogonal chemistry. The MNPs functionalized with cyclooctyne moieties are attached to the membrane of cells previously engineered to express azide bioorthogonal reporters.

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INVITED TALK

Iron oxide nanoparticles for magnetic hyperthermia in pancreatic cancer, from preclinical testing to clinical translation

Ibane Abasolo[1,2,3*], Florence Gazeau[4], Álvaro Somoza[5], Ángel Del Pozo[6], Teresa Macarulla[7], Quentin Pankhurst[8]

[1]CB-DDT and FVPR/U20 ICTS Nanbiosis at Vall d'Hebron Institute of Research (VHIR), Barcelona. [2]Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Barcelona, Spain, [3]Institute of Advance Chemistry of Catalonia (IQAC-CSIC), Barcelona, Spain. [4]CNRS, Université Paris Diderot, Paris, France [5]IMDEA Nanociencia, Madrid, Spain. [6]Biokeralty Research Institute, Álava, Spain. [7]Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain. [8]Resonant Circuits Limited, London, U.K.

*Email: ibane.abasolo@iqac.csic.es

Pancreatic ductal adenocarcinoma (PDAC) is characterized by a dense desmoplastic stroma that inhibits drug penetration and limits treatment success. The combination of chemotherapy with hyperthermia (HT) has been proposed as a way to circumvent this obstacle and improve the treatment of PDAC patients. Previous studies showed that iron oxide magnetic nanoparticles (MNP) exposed to alternating magnetic fields (AMFs), inhibited the growth of pancreatic cancers in animal models. Based on this work, we hace advanced towards the clinical use of these MNP, namely NoCanTher ThermoTherapy (NTT) agent, by providing evidence on the safety and efficacy of the NTT agent in combination with first line PDAC chemotherapy with gemcitabine and Nab-Paclitaxel.

We first studied the in vitro behavior of NTT (10 nm iron oxide cores embedded in ca. 130 nm dextran particles) and we observed that that combination of low doses of NTT with chemotherapeutic agents were highly synergic, especially in the BxPC-3 human PDAC cell line. In vivo, biodistribution assays showed that NTT agent remained mainly the tumor after intratumoral administration, concentrated around areas with high stromal component. Moreover, the combination of HT treatment with sub-optimal doses of the standard of care (SoC) in BxPC-3 subcutaneous tumors, showed clear advantages over the use of chemotherapy alone, probably due to the direct effect of HT in the disruption of the interstitial stroma. In vivo assays also helped stablishing that a pulsed protocol of the AMF was more efficient that the standard continuous heating of the tumor and that the use of HT before (and not after) the chemotherapy allowed a better accumulation of the drugs in the tumor. Based on these results the clinical investigation of the NTT agent and the magnetic field generator, as Class III medical device, was approved.

So far 6 patients with locally advanced PDAC have completed the protocol, that consisted in the intratumoral administration of 1.5 mL of NTT (ca. 75 mgFe/mL) by ultrasound guided transgastric endoscopy. One day after NTT administration, patients received the AMF treatment right before the chemotherapy administration. Treatment was repeated for 2 additional weeks. No HT-associated adverse events or complications were identified with any of the patients treated. In all cases an analgesic effect was noted, with the patients reporting pain alleviation from day 1 (1x), day 8 (2x) and day 15 (1x), which is earlier than usual for similar patients at Vall d'Hebron. In 1 case, after 4 months, biopsy results showed less active tumour margins and the patient was moved to surgical resection; in all other cases the patients completed their SoC courses successfully.

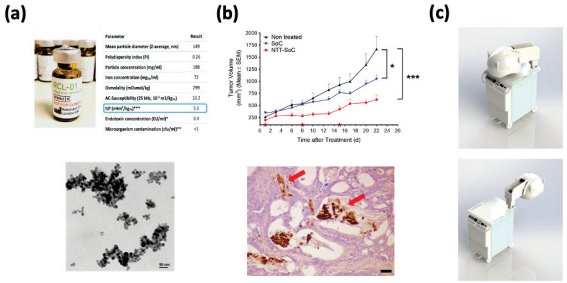

Figure. (a) Iron oxide nanoparticles (NTT agent). (b) Efficacy of the NTT over SoC in preclinical subcutaneous tumors of BxPC-3 cells. (c) Clinical generator of AMF.

Acknowledgments: We thank the many members of the oncology, preclinical, and enabling teams that made this study possible; and the EU Horizon 2020 program for support of the NOCANTHER (no. 685795) and SAFE-N-MEDTECH (no. 814607) projects.

Who needs chelators? Iron oxide as universal platform for multimodal imaging and therapy with radioisotopes

Aitor Herraiz[1], Juan Pellico[2], Unai Cossío[3], Eduardo Romero-Sanz[4], Rafael T.M. De Rosales[2], Jesús Ruiz- Cabello[3, 5], Miguel A. Morcillo-Alonso[4], Fernando Herranz[1, 5]

[1]Instituto de Química Médica (IQM/CSIC), Grupo de Nanomedicina e Imagen Molecular, Madrid, Spain
[2]King's College London, School of Biomedical Engineering & Imaging Sciences, London, United Kingdom
[3] CIC biomaGUNE, Molecular and Functional Biomarkers Lab, Donostia, Spain
[4]CIEMAT, Unidad de Aplicaciones Biomédicas y Farmacocinética, Madrid, Spain
[5]CIBER Enfermedades Respiratorias, (CIBERES), Madrid, Spain

Radiopharmaceuticals combine biological targeting with therapeutic radioisotopes for cancer treatment and imaging. A key aspect in their development is chelate design.[1] An ideal chelate should show excellent *in vivo* stability, easy conjugation to biomolecules, and a wide spectrum of radiometals that can be used.
In this work we show that extremely small magnetic iron oxide nanomaterials are excellent candidates to be considered universal "chelates" for diagnostic and therapeutic radiometales
Using a core-doping synthesis approach, we incorporated eight different radioisotopes in the core of iron oxide nanomaterials (Figure 1). For the synthesis of single- and double-doped xxM-IONPs, a fast and microwave-driven methodology was employed.[2] The radiolabeling yield, radiochemical purity, and stability in human serum were evaluated for all the synthesised nanoparticles. *In vivo* multimodal imaging was conducted with double doped 68Ga177Lu-IONP, these nanoparticles were injected into healthy mice, and PET/SPECT/CT images were acquired 1 h post-injection (Figure 1).

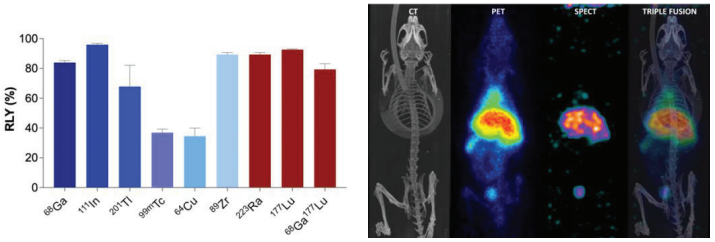

Figure 1. Radiolabelling yield for the incorporation of radiometals into the IONP core (left). PET/SPECT/CT triple imaging of ^{68}Ga/^{177}Lu-IONP in mice.

We carried out a systematic study on the radiometal core doping of iron oxide nanoparticles. Eight different radioisotopes were successfully incorporated, and double doping was demonstrated to be feasible. The *in vivo* dual imaging behaviour and efficiency were assessed with ^{68}Ga/^{177}Lu-IONP, which is suitable for being used for theranostic purposes.

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Protein corona and *in vitro* studies of magnetic nanoparticles for breast cancer delivery

Wid Mekseriwattana[1], Sopon Nuchpun[2], Onrapak Reamtong[3], Theerapong Puangmali[4], Anna Roig[5], and Kanlaya Katewongsa[1,2,*]

[1] School of Materials Science and Innovation, Faculty of Science, Mahidol University, Bangkok 10400, Thailand
[2] Department of Biochemistry, Faculty of Science, Mahidol University, Bangkok 10400, Thailand
[3] Department of Molecular Tropical Medicine and Genetics, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand
[4] Department of Physics, Faculty of Science, Khon Kaen University, Khon Kaen 40002, Thailand
[5] Institut de Ciència de Materials de Barcelona (ICMAB-CSIC), Campus UAB, Bellaterra 08193, Spain
*E-mail: Kanlaya.pra@mahidol.edu

Breast cancer is the most common cancer in women worldwide. Early diagnosis is a crucial step in increasing the survival rate. In this regard, increasing numbers of superparamagnetic iron oxide nanoparticles (SPIONs) are being used as a tool in the advancement of contrast agents and magnetic hyperthermia (MH) for the diagnosis and treatment of cancers.

To achieve successful delivery of SPIONs to breast cancer cells, here we investigated the surface functionalization of SPIONs with riboflavin (Rf) as shown in Figure 1. Rf can be transported via riboflavin carrier protein (RCP) or Rf transporters (RFVTs). It has been shown that both RCP and RFVTs are overexpressed in breast cancer, making Rf a promising ligand to enhance the affinity of NPs towards the cancer cells. The obtained Rf functionalized SPIONs (Rf-SPIONs) formed stable clusters of approximately 100 nm and provided enhanced colloidal stability and high targeting potential of SPIONs to breast cancer cells (MDA-MB231 and MCF-7 cells) with minimal uptake in normal cells (MCF-10A). The Rf-SPIONs demonstrated specific, entropy-driven binding to a riboflavin carrier protein (RCP) assessed by isothermal titration calorimetry. However, in the presence of serum proteins (fetal bovine serum and human serum), they exhibited decreased affinity. The overall corona proteins were evaluated, and the molecular dynamic simulation was used to explain the behavior of NPs in this complex milieu. Furthermore, to assess their potential as a theranostic tool, MRI and MH responses were determined. The overall characterization of the Rf-SPIONs highlighted the excellent performance of this platform for theranostic applications in breast cancer.

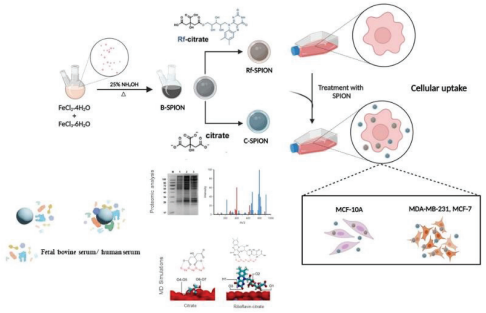

Figure 1. Scheme of synthesis of magnetic nanoparticles, cell studies, proteomic analysis, and molecular dynamic simulation.

Bacterial Magnetosomes as Innovative, Versatile Platform Technology for Biotechnological and Biomedical Applications

Frank Mickoleit*, and Dirk Schüler

Department of Microbiology, University of Bayreuth, D-95447 Bayreuth, Germany
*Email: frank.mickoleit@uni-bayreuth.de

Magnetosomes represent a remarkable novel class of magnetic iron oxide nanoparticles that are biosynthesized by magnetotactic bacteria. In the model organism *Magnetospirillum gryphiswaldense* they consist of a cuboctahedral core of chemically pure magnetite (Fe_3O_4) that is surrounded by a biological membrane of phospholipids and proteins. Subtle control on each step of biomineralization generates core-shell nanoparticles with extraordinary characteristics, i.e. high crystallinity, strong magnetization, uniform particle geometry, and narrow size distribution.[1] As magnetosome biosynthesis is accessible to genetic engineering, particles of different size classes and thus, adjustable magnetic properties can be produced, ranging from superparamagnetic to ferrimagnetic magnetosomes. In addition, our genetic toolkit enables the selective and highly controllable functionalization of the particle surface by the display of foreign protein cargo as translational fusion to highly abundant magnetosome proteins. Because of these features magnetosomes have been envisioned promising alternatives to chemically synthesized nanoparticles for many applications in the biotechnological and biomedical field.[2]

For instance, the magnetosome membrane can be functionalized with enzyme proteins for the generation of highly active nano-biocatalysts for e.g. flow reactor systems. The display of molecular connectors turns the particle surface into a flexible adapter scaffold for the immobilization of (therapeutic) drugs or the entrapment of any complementary tagged structures. Moreover, genetically engineered magnetosomes were successfully tested as contrast agents for magnetic imaging techniques (magnetic resonance imaging *MRI*, magnetic particle imaging *MPI*), or as agents for magnetic hyperthermia. In both cases, magnetosomes exhibited characteristics superior compared to those of chemically synthesized nanoparticle formulations. Overall, with the particle mass production having been established, magnetosomes might therefore represent versatile theranostic agents for the biomedical field, e.g. for the treatment of cancer.

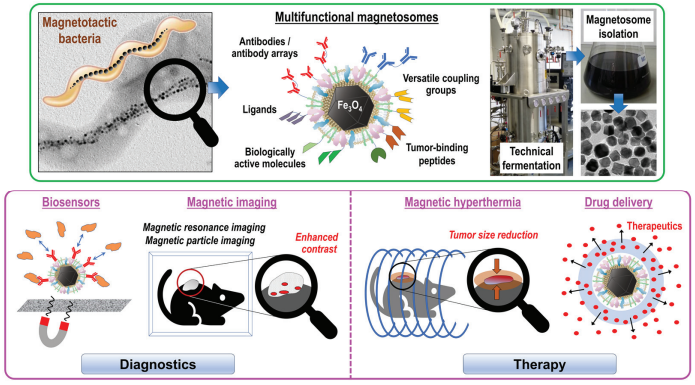

Figure - Biosynthesis and mass production of genetically engineered / functionalized magnetosomes by magnetotactic bacteria. Due to their extraordinary material characteristics, isolated magnetosomes have been successfully tested for a variety of applications in the biomedical field.

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Ferromagnetic biodegradable nanocapsules for externally controlled and non-invasively monitored nanotherapies.

Aritz Lafuente[1], Alejandro G.Roca[1], Borja Sepúlveda[2], Josep Nogues[1]

1 Catalan Institute of Nanoscience and Nanotechnology (ICN2), Bellaterra, Spain
2 Instituto de Microelectrónica de Barcelona (IMB-CNM, CSIC), Bellaterra, Spain

Email: aritz.lafuente@icn2.cat

Cancer nanotherapies require new tools to locally enhance their efficacy, this need could be achieved by nanomaterials enabling external control of the accumulation and non-invasive visualization and detection of the therapeutic action. Here we present magnetoplasmonic biodegradable nanocarriers based on metallic iron semishells merging highly efficient external actuation and manipulation with magnetic fields and near infrared light to locally boost the therapeutic action. [1,2]

The nanocapsules are engineered by a combination of bottom-up and top-down techniques. Briefly, monodisperse poly-lactic-co-glycolic-acid (PLGA) cores of around 150 nm, fabricated by nanoprecipitation, are partially coated by Fe/X (X=SiO2, Au) by combining colloidal self-assembly and physical vapour deposition giving a nanodome (ND) shape. The outer layer can be tuned to exploit different effects such as X-ray imaging or enhanced photothermal efficiency (**Figure 1**).

The magnetic properties of the NDs can be easily tuned with the iron layer thickness from superparamagnetic behaviour (10 nm) to vortex configuration (20 nm-30nm). Moreover, NDs also exhibit very intense r2 relaxivity (up to 370 mM-1s-1) in magnetic resonance imaging enabling non-invasive monitoring of the therapy. The metal Fe semishell exhibits highly damped plasmonic behaviour with intense broadband absorbance in the near infrared (NIR), which allows excellent photothermal conversion efficiencies in the 1st and 2nd biological windows.

This combination of properties allows the nanocapsules to operate as nanothermometers in tand monitor the induced temperature increase by laser heating. The temperature monitoring is based on the detection of the modulated light by nanodomes rotating in viscous media evaluating the phase lag between the driving magnetic field and the optical signal. (**Figure 1**B, **1**D) [3].

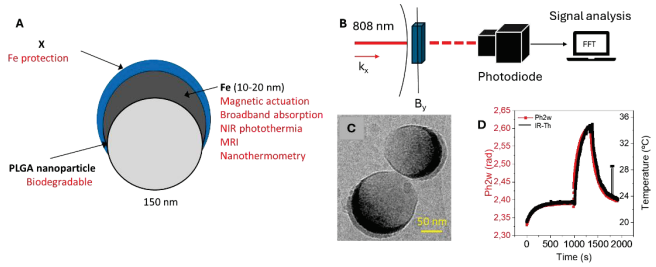

Figure 1: (A) Scheme of the ND structure and functions and (B) nanothermometry set up. (C) TEM image of the synthesized NDs and (D) demonstration of the use of the NDs as nanothermometres.

Acknowledgments

We acknowledge the financial support from the Spanish Ministerio de Ciencia, Innovación y Universidades (MICINN) through the PDC2022-133036-I00, PID2019-106229RB-I00 funded by MCIN/AEI/10.13039/501100011033 and Ramon Areces foundation through grant CIVP19A5922.

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Remote Magneto-Thermal Modulation of Reactive Oxygen Species Balance Enhances Tissue Regeneration *in vivo*

Giuseppina Tommasini,[a] Susel Del Sol-Fernández,[a] Ana Cristina Flavián-Lázaro, [a] Anna Lewinska, [b] Maciej Wnuk, [b] Claudia Tortiglione,[c] María Moros[a,d]

[a] Instituto de Nanociencia y Materiales de Aragón, INMA (CSIC-Universidad de Zaragoza), C/ Pedro Cerbuna 12, 50009, Zaragoza, Spain; [b] Institute of Biotechnology, College of Natural Sciences, University of Rzeszow, Pigonia 1, 35-310 Rzeszow, Poland; [c] Istituto di Scienze Applicate e Sistemi Intelligenti "E. Caianiello", Consiglio Nazionale delle Ricerche, Via Campi Flegrei 34, 80078 Pozzuoli, Italy; [d] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain.

One of the hallmarks of tissue repair is the production of reactive oxygen species (ROS), which modulate processes such as cell proliferation. Although several attempts have been made to manipulate ROS levels to increase tissue repair, the lack of techniques able to remotely manipulate the redox homeostasis with spatio-temporal fashion has hindered its progress. Herein, we present a new approach for tuning the ROS levels using magnetic nanoparticles (MNPs) that act as nanoheaters when exposed to an alternating magnetic field. We designed two $Mn_xFe_{3-x}O_4$ MNPs (with a low and a high Mn^{2+}content) and probed the possibility to modulate the ROS balance by magneto-thermal stimulation in the invertebrate model organism *Hydra vulgaris*, able to fully regenerate. By evaluating the expression of selected genes involved in the maintenance of ROS homeostasis and proliferation pathways, we found a biphasic modulation of the ROS levels played by the MNPs (Figure 1). While MNPs with the lower Mn^{2+} content are able to positively modulate the regeneration potential under magnetostimulation, MNPs with the higher Mn^{2+} content cause a different redox imbalance, negatively affecting the regeneration dynamic. This innovative approach reveals a new way for manipulating redox homeostasis that could advance in the field of tissue engineering.

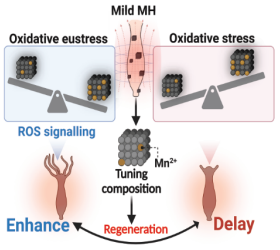

Figure 1. MNPs can be used to enhance tissue regeneration after the application of an alternating magnetic field. The redox imbalance caused by different MNPs can lead to oxidative eustress or stress, promoting or inhibiting this tissue regeneration.

Magnetic bioprinting of a clip-on muscle tissue

Noam Demri[1]*, Lise Morizur[2], Simon Dumas[1], Giacomo Gropplero[1], Cécile Martinat[2], Stéphanie Descroix[1], Claire Wilhelm[1]

[1]Laboratoire Physico Chimie Curie, PCC, CNRS UMR168, Institut Curie, Paris, France
[2]I-Stem, INSERM U861, Corbeil-Essonnes, France
*Email: noam.demri@curie.fr

Generating tissues with precise control over both their macroscopic shape and microscopic cellular architecture remains a pivotal challenge in tissue engineering. This is especially relevant to skeletal muscle tissue, where inducing an anisotropic organization is key for appropriate cell differentiation[1]. Consequently, new techniques, such as extrusion based bioprinting[2], are being developed to impose a given tissue shape. **In this work, we showcase the engineering of 3D mature muscle tissue using magnetic forces, that are employed (1) to precisely bioprint the tissue in any given shape without any matrix, and (2) to maintain its shape, or even stretch it, to favor muscle maturation.** To do so, cells were initially labelled with iron oxide nanoparticles, and optimization led to about 20 pg of iron internalized per cell, with no impact on cell metabolic activity or capacity to differentiate[3]. Thanks to photolithography and NiFe-electrodeposition, we have achieved fine control over the shape of microfabricated magnets (Fig. A), which could then attract the magnetically labelled cells to form a cohesive centimetric tissue in the same shape after only 3 hours (Fig. B). Herein, the chosen shape resembles a wrench, featuring a central fiber mimicking the skeletal muscle's architecture, along with two clamps for functional purposes. Indeed, leveraging both the shape and the magnetic nature of the tissue enabled to trap it between two magnetic needles (Fig. C), turning it into a clip-on magnetic tissue. Besides, we designed the system so that the distance between the two needles could be varied. This could stretch the tissue by up to 100% (Fig. D), which could then be cultured over a week in this configuration. The entire process was tested with mouse C2C12 myoblasts and myoblasts derived from human induced pluripotent stem cells (iPS). In both cases, trapping the tissue between the needles not only preserved its overall shape, but also significantly aligned the cells within the tissue. Differentiation indicators, such as cell fusion or the presence of myogenin-positive cells, were markedly increased compared to those observed in 2D cultures. Remarkably, human iPS-derived myoblasts even showcased spontaneous contractions after only three days of differentiation. Alignment and differentiation were further enhanced in tissues stretched by 100%, as depicted in Figure E, highlighting the importance of mechanical cues in myogenesis. Overall, this work underscores the considerable potential of magnetic engineering techniques in building tissues.

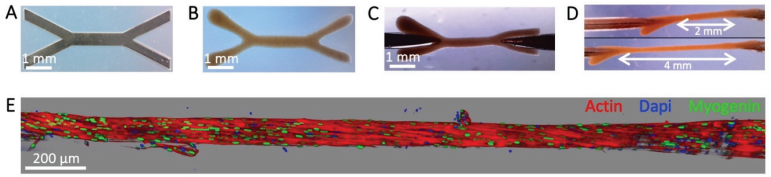

Figure. Wrench shaped magnet (A) to pattern a cohesive muscle tissue (B) that will be trapped between two magnetic needles (C) and stretched by 100% (D). 3D reconstruction of a 3-day old fiber, stretched by 100%, composed of myoblasts derived from human iPS cells (E).

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3. Demri … Wilhelm, Advanced functional materials 2022, 2204850

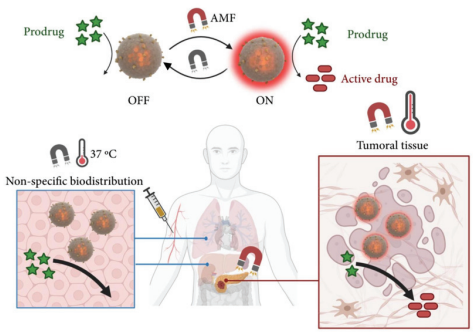
Spatio-temporal Selectivity in Chemotherapy: Remote Activation of Enzymatic Nanohybrids for Prodrug Therapy

Beatriz Torres-Herrero[1], Ilaria Armenia[1], Maria Alleva[1], Laura Asín[1], Lucía Gutiérrez[1], Jesús M. de la Fuente[1,3], Lorena Betancor[2], and **Valeria Grazú[1,3]***

[1]BioNanoSurf Group, Instituto de Nanociencia y Materiales de Aragón, 50018, Zaragoza, Spain.
[2]Departamento de Biotecnología, Facultad de Ingeniería, Universidad ORT-Uruguay, Montevideo, Uruguay.
[3]Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Madrid, Spain

A nanometric carrier that combines magnetic nanoparticles with enzymes has been developed as an innovative solution to revolutionize enzyme therapies against cancer[1]. This involved optimizing the co-encapsulation of magnetic nanoparticles (MNPs) with horseradish peroxidase (HRP) using biomimetic silica as an entrapment matrix to obtain nanosized hybrids (nHs ~150 nm). The goal of this approach is to selectively activate the production of a toxic drug (chemotherapeutic) from a nontoxic pro-drug, exclusively within the tumor without affecting healthy cells.

The selected enzyme is a thermophilic enzyme, requiring higher temperatures than body temperature to efficiently activate drug production, and remains "dormant" until activated by an alternating magnetic field applied to the tumor. This magnetic field transforms the magnetic nanoparticles embedded in the nanocarrier into nanoheaters, raising the temperature of the nanocarrier and initiating cancer cell death through enzyme conversion of the prodrug indole-3-acetic acid (3IAA) into peroxylated radicals. Notably, it was demonstrated for the first time that enzyme nanoactuation is possible with MNPs even without covalent binding. Following extensive physicochemical and magnetic characterization, the spatial location of each component of the nH was deciphered, suggesting an insulating role of the silica matrix as critical for introducing remote control over HRP.



The effectiveness and remote activation capability of this treatment have been demonstrated in pancreatic cancer models. Cytotoxicity resulting from prodrug bioconversion into toxic oxidative species was confirmed as the sole consequence of remotely triggered enzyme activity, leading to cell death *in vitro* using MIA PaCa-2 2D cell cultures. Notably, exposure of cells to nHs and prodrug without the application of an alternating magnetic field (AMF), or exposure to nHs with AMF application, did not result in a significant decrease in cell viability. Moreover, *in vivo* experiments showed higher reductions in the tumor volume growth in those animals treated with nHs in the presence of 3IAA when exposed to AMF.

While this treatment could potentially be applied to various tumor types, pancreatic cancer was prioritized due to its low survival rate, limited eligibility for surgery, and the palliative nature of current chemotherapy. This innovative therapeutic strategy holds promise for significantly reducing the side effects associated with traditional systemic chemotherapy, which often negatively impact patient quality of life and survival by causing severe chronic problems in healthy organs.

[1]*"Remote Activation of Enzyme Nanohybrids for Cancer Prodrug Therapy Controlled by Magnetic Heating" ACS Nano 2023, 17, 13, 12358–12373.*

Integrated system with magnetic particle imaging and magnetic hyperthermia for localized drug release applications

Thilo Viereck, Kai Luenne, Klaas-Julian Janssen, Meinhard Schilling, and Frank Ludwig

Institute for Electrical Measurement Science and Fundamental Electrical Engineering and
Laboratory for Emerging Nanometrology (LENA), TU Braunschweig, Braunschweig, Germany

in collaboration
Franziska Kenneweg and Thomas Thum, Institute of Molecular and Translational Therapeutic Strategies (IMTTS),
Hannover Medical School (MHH), Hannover, Germany

Corresponding author: t.viereck@tu-braunschweig.de

With Magnetic Particle Imaging (MPI) we have an evolving technology available for fast and sensitive diagnostic imaging based on a magnetic nanoparticle (MNP) tracer. In combination with a suitable drug conjugate, which binds an xRNA compound to a magnetic nanoparticle via a thermo-sensitive linker, a novel theranostic platform can be realized. By heating the particle core in an alternating magnetic field and subsequent heat transport into the surrounding medium, the thermo-linker bound onto the particle shell is triggered to locally release the xRNA drug without side effects in off-target organs. The xRNA inhibitor is ineffective as long as it is covalently bound to the MNP conjugate. Local MNP enrichment, as is necessary for heat-induced apoptosis of tissue in conventional magnetic hyperthermia, is not strictly necessary, but can be used with the <200 nm capillary-permeable agent to enhance efficacy. Magnetic Particle Imaging is then utilized to monitor the spatial distribution and thermal release kinetics of the MNP conjugate. Heating of the nanoparticle agent by localized magnetic fields in the MPI selection field enables organ-selective drug release. Initial data for heart-specific delivery confirms that sufficient heat is generated around the magnetic nanoparticles to trigger release of an effective xRNA drug but without thermal damage to cells due to excess tissue heating of the tissue. MNP-local heating requires fast and precise temperature monitoring and feedback to meet the designated release temperature. Our newly developed, integrated MPI prototype (Fig. 1) is built as a compact and cost-effective system for simultaneous heating and spatial imaging, which will enable monitoring and treatment in localized drug release studies soon.

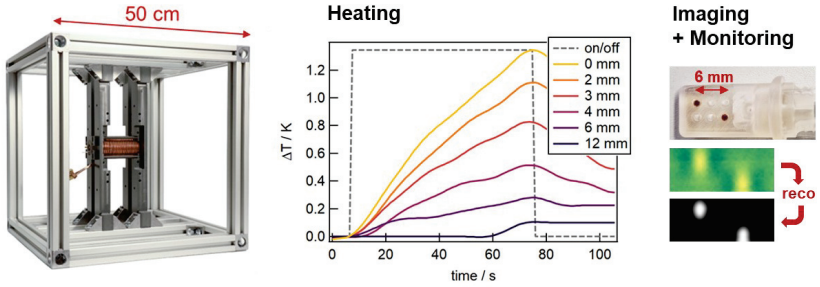


Figure 1: Integrated MPI and magnetic hyperthermia prototype system (left) enables localized magnetic particle heating (middle) and high-resolution imaging of the therapeutic agent (right) for drug delivery applications.

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Remote Magneto-Mechanical Gating of Endogenous Piezo1 Channel

Susel Del Sol-Fernández[1*], Pablo Martínez Vicente[1], Pilar Gomollón-Zueco[1], Giuseppina Tommasini[1], Thomas S. van Zanten[1] and Maria Moros[1,2]

[1]*Instituto de Nanociencia y Materiales de Aragón, INMA (CSIC-Universidad de Zaragoza), C/ Pedro Cerbuna 12, 50009, Zaragoza, Spain*

[2]*Centro de Investigación Biomédica en red en Bioingenieria, Biomateriales y Nanomedicina (CIBER-BBN),Zaragoza, Spain.*

*Email: sdelsol@unizar.es

In a process called mechanotransduction, our cells use a set of molecules capable of sensing mechanical forces from their environment and convert them into electrochemical signals, triggering crucial cellular responses. As pivotal mechanosensors, mechanosensitive (MS) ion channels have a critical role for fast signalling in living cells. Among them, the Piezo channel family (which includes Piezo1 and Piezo2 in mammals) has emerged as the bona fide mechanically activated cation channels that can open in response to different types of stimuli such as shear stress, allowing Ca^{2+} influx. Piezos transduce mechanical forces in a wide range of physiological processes that require exquisite control such as touch, perception of pain, regulation of blood pressure, cell migration, heart valve development, angiogenesis and stem cell differentiation among others. Due to their importance, expression of Piezo channels is needed for survival in vertebrates, and mutations are associated with diseases, like hereditary Xerocytosis and the development of certain tumours. Therefore, they hold great promise as potential novel therapeutic targets. While the succesful manipulation of Piezo channels has been accomplished using MNPs, the previous modification of the cell with exogenous receptors can hamper its translation into the clinics.

This work aims to develop and validate a novel platform that uses small magnetic nanoparticles (MNPs) to study mechanotransduction linked to Piezo1 channels in endothelial cells through remote magnetic stimulation, obtaining real-time responses (**Figure 1**). To do so, octahedral mixed ferrites ($ZnMnFe_2O_4$) were synthesized following the one-step thermal decomposition method. The obtained MNPs were transferred to water and fully characterized with a diversity of spectroscopies and physico-chemical techniques. Theoretical calculations were performed to assess the force exerted by MNPs upon magnetic simulation with a homemade magnetic applicator. Moreover, direct oriented Piezo1 antibody conjugation on optimized MNPs surface was achieved via carbodiimide chemistry. Endogenous Piezo1 expression was studied in different cell lines by several techniques, including immunofluorescence (IF), flow cytometry (FC), and quantitative real-time PCR (qRT-PCR). Then, the *in vitro* magneto-mechanical activation of Piezo1 by MNPs upon magnetic stimulation was studied by real time calcium imaging using fluorescence microscopy. Additionally, the increase of calcium influx was confirmed via early response gene activation by immunofluorescence. This opens the path, for the first time, for the manipulation of endogenous Piezo1 channels using small MNPs without modifying the cells.

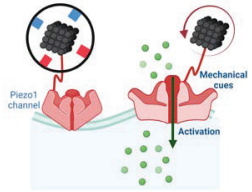

Figure 1. Schematic representation of the aim of the work based on the magnetomechanical activation of Piezo1 channel *in vitro*.

INTRACELLULAR PROTEINS TARGETING WITH BI-FUNCTIONALIZED MAGNETIC NANOPARTICLES

Mélody Perret[1], Estelle Pineda[1], Aude Michel[1], Françoise Illien[2], Jean-Michel Siaugue[1], Christine Menager[1], Fabienne Burlina[2], Emilie Secret[1]

[1] Physicochimie des Electrolytes et Nanosystèmes Interfaciaux PHENIX, Sorbonne-Université CNRS UMR 8234 Paris, France
[2] Laboratoire des Biomolécules LBM, Sorbonne-Université CNRS UMR 7203 Paris, France

Contact: melody.perret@sorbonne-universite.fr

For many applications in nanomedecine, such as cancer therapy by magnetic hyperthermia, cellular engineering or magnetogenetics[1], it can be interesting for magnetic nanoparticles (MNPs) to target intracellular proteins or organites. However, most MNPs, when in contact with cells, are internalized through endocytosis[2] and then trapped inside endosomal vesicles which prevents them from targeting intracellular components and decreases their heating capacities.

Here we will present a strategy that relies on an original bi-functionalization of MNPs with polyhistidines peptides (PHP), allowing the endosomal escape of the MNPs through a proton sponge effect[3,4], and with antibodies, allowing for the first time the targeting of specific proteins once MNPs are in the cytosol. In order to do that, γ-Fe_2O_3@SiO_2 MNPs with diameter smaller than 50 nm, were functionalized with zwitterionic moieties as well as with thiol groups at their surface. These sulfhydryl groups were used to graft PHP through a labile link, allowing the peptide to be detached from the surface of the MNPs once in the cytosol. This severing avoids any interaction between these peptides and intracellular components, which could hinder the MNPs' intracellular mobility. A second functionalization of the MNPs with targeting antibodies through a non-labile link was then performed, so the MNPs can target specific intracellular proteins once the cytosol has been reached.

In a first demonstration of this concept, MNPs functionalized with both PHP and anti-HSP27 antibodies were able to efficiently target intracellular HSP27 (Fig. 1) without micro-injecting particles in the cell, opening the door to new biomedical applications of MNPs.

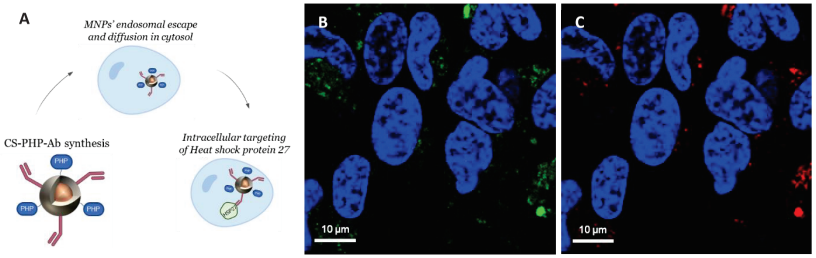

Figure 1. (**A**) Magnetic core-shell nanoparticles bi-functionalized with polyhistidines peptide and anti-HSP27 antibody (CS-PHP-Ab) bypassing endosomal entrapment to reach intracellular thermosensitive proteins HSP27. (**B**-**C**): Confocal microscopy images on SH-SY5Y cell line, observed 24 h after incubation of CS-PHP-Ab. (**B**) HSP27s appear in green and (**C**) MNPs in red. After particles' endosomal escape, 84 % of MNPs were colocalized with the protein of interest. Cell nuclei are in blue (Hoechst dye 33342).

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Mechanobiological responses of cells induced by magneto-mechanical stimulation

H.Joisten[1], C.Naud[1], A.Visona[1,2], R.Morel[1], A.Nicolas[2], Y.Hou[3], M.Carriere[3], S.Belin[4], F.Berger[5], B.Dieny[1]
[1] Univ. Grenoble Alpes, CEA, CNRS, IRIG, SPINTEC, Grenoble, France; [2] Univ. Grenoble Alpes, CNRS/LTM, Grenoble, France, [3] Univ. Grenoble Alpes, CEA, CNRS, IRIG, SYMMES, Grenoble, France; [4] Univ. Grenoble Alpes, INSERM, CHU, Grenoble Institut Neurosciences, Grenoble, France; [5] Univ. Grenoble Alpes, INSERM/Brain Tech Lab, Grenoble, France,
* Email: helene.joisten@cea.fr

The study of the influence of mechanical forces and stresses on living organisms, and in particular on biological molecules, cells and tissues, is a field of research that has considerably grown over the last two decades. In this recent discipline, known as mechanobiology, magnetic micro- or nanoparticles are particularly well suited for generating very local mechanical forces, remotely controlled by the application of a static or low frequency alternating magnetic field (AMF), on living cells or tissues.

The magnetic nanoparticles (Nps) that we developed take the form in particular of magnetic microdisks with diameter of 1 µm and thicknesses of a few tens of nanometers (such as 60-100nm). Various compositions [1] were studied, including synthetic antiferromagnetic multilayers (SAF), magnetite with antiphase boundaries, and permalloy (NiFe) layers in magnetic vortex state (Fig.1a) - the vortex being the ones we currently use, with a gold coating for their biocompatibility. Designed to be superparamagnetic-like to prevent their agglomeration in solution (key property of superparamagnetic iron oxides nanoparticles (SPIONs)), these micro-disks exert larger forces by magnetic field gradients, due to their larger volume (pN instead of fN for SPIONs), and more efficient magnetic torques via rotating fields, thanks to their anisotropy (yielding forces ~ nN).

Since the pioneering study by Kim et al [2], showing the destruction of cancer cells by magneto-mechanical vibration of vortex-Nps, driven by low-frequency AMF (20 Hz), promising effects have been explored [3]. We have demonstrated the ability to induce cell death (apoptosis or necrosis) of renal [4] and glioma cancer cells by these purely mechanical effects, without heat generation, using vortex-Nps vibration (2-20 Hz). Recently, we focused on the cell viability, motility, proliferation and cytoskeleton disorganization (Fig.1b-c), after AMF treatments. The cell reactions are studied versus the actuation conditions (amplitude, frequency, direction of AMF, Nps size), interaction of Nps with cells (internal or external), and influence of the microenvironment (e.g. substrate stiffness). Tests on cells were carried out in vitro in 2D, in vivo and in vitro in 3D spheroids closer to in vivo conditions.

Furthermore, we showed in vitro that this AMF-mediated Nps actuation technique is capable of stimulating the cellular functions in pancreatic cells, increasing insulin secretion (Fig.1d) [5-6]. The use of magnetic vortices is also being considered for neuroregeneration to favor neuronal growth after spinal cord lesion.
These studies demonstrate the interest and effectiveness of anisotropic magnetic nanoparticles in the field of mechanobiology, to be explored for potential future medical treatments.

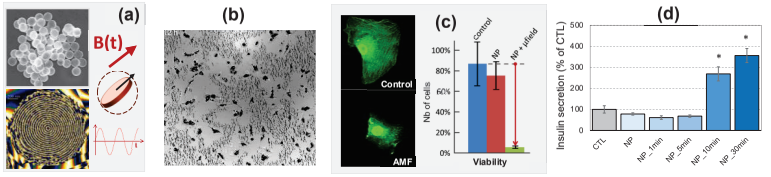

Fig.1. a. Magnetic vortex microdisks (Nps); **b.** U87 cancer cells + vortex particles after 12 h, cells "fond" of magnetic particles (dark spots) absorbed them; **c.** U87 cytoskeleton disorganization after 24h, & cells viability, following AMF; **d.** Stimulation of insulin secretion on INS-1E pancreatic cells, by Nps actuated by AMF (2-20 Hz).

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Exploring magnetic collagen hydrogels for neural regeneration in hemisected rats

Esther Benayas,[1] Julia Martínez-Ramírez,[1] Yasmina Hernández,[2] Cristina Rosas,[2] Elisa López-Dolado,[2,3] María C. Serrano[1,]*

[1]Instituto de Ciencia de Materiales de Madrid, CSIC, Calle Sor Juana Inés de la Cruz 3, 28047 Madrid, Spain; [2]Hospital Nacional de Parapléjicos (HNP), Finca La Peraleda s/n, 45071 Toledo, Spain; [3]Design and development of biomaterials for neural regeneration, HNP, Associated Unit to CSIC through ICMM, Finca La Peraleda s/n, 45071 Toledo, Spain

The combination of hydrogels and magnetic nanoparticles offers a wide range of possibilities for innovative therapies in tissue engineering, although it has been scarcely explored to date. We have recently designed a hybrid 3D collagen matrix integrating chitosan-coated iron oxide nanoparticles to provide a soft and flexible 3D network mimicking the extracellular matrix of natural tissues. After detailed characterization of both nanoparticles and hydrogels,[1] these scaffolds have been first explored with primary neural cells *in vitro* and then challenged to interface the injured spinal cord in hemisected rats. Results demonstrate highly fibrous and porous collagen hydrogels homogeneously loaded with magnetic nanoparticles responsible for their responsive behavior to magnetic stimulation. These hydrogels maintain high neural cell viability and sustain the formation of highly interconnected and differentiated neuronal networks *in vitro*. When explored *in vivo*, hemisected rats show promising behavioral and histological features indicative of repair after 30 days of implantation. However, fast scaffold biodegradation rates hamper the positive progression of these features at longer time points (120 days).

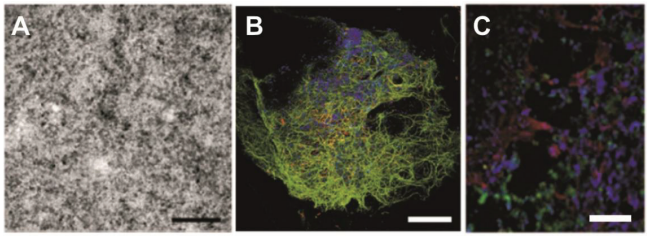


Figure 1. Magnetic collagen hydrogels characterized **(A**; TEM image**)** and explored both *in vitro* with primary neural cultures **(B**; MAP-2/vimentin labelling**)** and *in vivo* in an experimental model of spinal cord injury in rats **(C**; ED1/GAP-43 labelling**)**.

Funding acknowledgement: This work has received funding from the European Union's Horizon Europe research and Innovation Programme under grant agreement No. 101098597.

References: (1) Martínez-Ramírez *et al.* Acta Biomaterialia **2024**, *176*, 156-172.

Poster Session I - Tuesday, June 18, 2024

	First Author	Title	City, Country	Corresponding Author
1	Ahmad, Hafiz	Potential of Magnetic Particle Spectroscopy in Diagnosis of Pancreatic Cancer Biomarkers in the Blood Sample	Gwangju, South Korea	Yoon, Jungwon
2	Ahmed, Yusra	Biocompatible Barium Hexaferrite Nanoparticle Composite Matrix	Cardiff, U.K.	Zabek, Daniel
3	Arsalani, Soudabeh	Towards Quantitative Imaging of Magnetic Nanoparticle Flow by MRXI	Berlin, Germany	Arsalani, Soudabeh
4	Baradoke, Ausra	Enhancing Sensing by Using Magnetic Nanoflowers for Screen-Printed Electrodes	Vilnius, Lithuania	Baradoke, Ausra
5	Bielas, Rafal	Pickering droplets and liquid marbles exposed to an alternating magnetic field for capsule formation	Poznan, Poland	Bielas, Rafal
6	Bilous, Oksana	Non-monotonous Diffusion in Ferrogranulate Layer Induced by Tuning Interactions	Vienna, Austria	Bilous, Oksana
7	Boelens, Peter	On the use of biotechnologically functionalized magnetic nanoparticles for the recycling of valuable ultrafine powders from electronic waste	Dresden, Germany	Boelens, Peter
8	Brero, Francesca	Exploring the Impact of Shape, Size, and Coating on the Efficacy of Iron-Oxide Nanoparticles in Magnetic Resonance Imaging and Hyperthermia	Pavia, Italy	Brero, Francesca
9	Castro-Hinojosa, Christian	Controlled Preparation of Cadherin-Magnetic Nanoparticle Bioconjugates for Remote Cellular Manipulation	Zaragoza, Spain	Castro, Christian
10	Chen, Changyou	Guidance of magnetotactic bacteria to tumors for targeted therapy	Beijing, China	Chen, Changyou
11	Cheng, Ximin	Quantitative Dual-Color Magnetic Particle Imaging	Beijing, China	Zhong, Jing
12	Cicuendez, Monica	A new versatile nanoformulation to remotely trigger mechanotransduction for bone regeneration	Madrid, Spain	Izquierdo-Barba, Isabel
13	Duceac, Ioana	Magnetic Hybrid Materials with Polysaccharide Matrix for MRI and 5-Fluorouracil Delivery	Iasi, Romania	Duceac, Ioana
14	Chen, Ziwei	Enhanced Sensitivity in Magnetic Particle Spectroscopy Through Phase Inversion Signal Processing	Beijing, China	Chen, Ziwei
15	Everaert, Katrijn	Characterizing magnetic nanoparticle ensembles with thermal noise magnetometry	College Park, U.S.A.	Everaert, Katrijn
16	Feoktystov, Artem	Impact of Coating Type on Structural and Magnetic Properties of Superparamagnetic Iron Oxide Nanoparticles for Theranostics	Garching, Germany	Feoktystov, Artem
17	Gallo-Cordova, Alvaro	Magnetic Harvesting of Microplastics Using Multicore Iron Oxide Nanoparticles prepared by a Scaled-up Procedure	Madrid, Spain	Gallo Cordova, Alvaro
18	Gandarias, Lucia	Enhancing the diagnostic capabilities of magnetotactic bacteria via the incorporation of terbium and gadolinium	Saint-Paul-Lez-Durance, France	Gandarias, Lucia
19	Gessner, Isabel	From bench to bedside: engineering magnetic particles for cancer diagnostics and therapy from industry perspective	Bergisch Gladbach, Germany	Gessner, Isabel
20	Gimenez-Aguilar, Rafael	Automatic Dimension Measurement of Magnetic Nanoparticles on Electron Microscope Images using Deep Neural Networks	Madrid, Spain	Gimenez-Aguilar, Rafael
21	Gonzalez Gomez, Manuel Antonio	Hybrid contrast nanomaterials for advanced therapy tracking via multimodal imaging	Santiago de Compostela, Spain	Gonzalez Gomez, Manuel Antonio
22	Göpfert, Lennart	Towards size optimization of magnetic nanoparticles in a continuous production process by applying machine-learning based models	Aachen, Germany	Slabu, Ioana
23	Gröger, Roman	Atomistic Studies of Magnetization Reversal in Magnetite Nanoparticles	Brno, Czech Republic	Groger, Roman
24	Gubieda, Alicia	Temporal and spatial resolution of magnetosome degradation at the subcellular level in a 3D lung carcinoma model	Leioa, Spain	Gascon Gubieda, Alicia
25	Günther, Johanna	COMPASS based stability monitoring of magnetic nanoparticles exemplified on bacterial magnetosomes	Würzburg, Germany	Gunther, Johanna
26	Iglesias, Oscar	Critical Role of the Magnetocrystalline Anisotropy on the Frequency-dependent Hyperthermia Performance of Magnetite Nanoparticles	Barcelona, Spain	Iglesias, Oscar
27	Illes, Erzsbet	Carboxylated nanomagnets for biomedical use: influence of shell composition	Szeged, Hungary	Illes, Erzsbet
28	Illes, Erzsbet	Magnetic nanoflowers for biomedical purposes	Szeged, Hungary	Illes, Erzsbet
29	Ivanov, Alexey	Static Magnetic Response of Intracellular Clusters of Superparamagnetic Nanoparticles	Ekaterinburg, Russia	Ivanov, Alexey
30	Kafash Hoshiar, Ali	Predictive Modelling for Enhanced Precision in Microswarm Steering under Rotating Magnetic Fields	Colchester, U.K.	Kafash Hoshiar, Ali
31	Kampen, Lena	Unraveling nanoparticle-cell surface interactions: Insights into SynC uptake dynamics	Berlin, Germany	Kampen, Lena

32	Kmita, Angelika	New Encapsulated Magnetic Systems Based On Nano Ferrites For Biological and Hyperthermia Applications	Krakow, Poland	Kmita, Angelika
33	Kottenbrock, Kenzington	Magnetic Mapping of Bio-Inspired Clusters of Iron Oxide Nanoparticles	Columbus, U.S.A.	Kottenbrock, Kenzington
34	Lak, Aidin	Amplification- and Enzyme-Free Magnetic Diagnostics Circuit for Whole-Genome Detection of SARS-CoV-2 RNA	Braunschweig, Germany	Lak, Aidin
35	Leon-Cecilla, Alberto	Differential swelling of IPNs for multi-stimuli soft actuation	Granada, Spain	Leon-Cecilla, Alberto
36	Lopez-Mendez, Rosalia	Multifunctional magnetic nanoplatforms for combined chemo-hyperthermia treatment	Madrid, Spain	Lopez-Mendez, Rosalia
37	Maduabuchi, Wisdom	Local Magnetic Hyperthermia and Systemic Chemotherapy Triggers Neo-angiogenesis without Involvement of Auto/Paracrine Tumour Cell VEGF Signalling and Hypoxia	Jena, Germany	Hilger, Ingrid
38	Marfa, Jennifer	Magnetic Molecularly Imprinted Polymer for The Detection of Pathogenic Bacteria	Bellaterra, Spain	Marfa, Jennifer
39	Mefford, O. Thompson	Using Computational Tools to Guide the Synthesis of Substituted Magnetic Nanoparticles to Target Specific of Magnetic Saturation and Magneticocrystalline Anisotropy Values	Clemson, U.S.A.	Mefford, O. Thompson
40	Meier, Nils	Preparation and investigation of casein-coated magnetic nanoparticles for theranostic applications	Mainz, Germany	Bleul, Regina
41	Mejia Carmona, Karen	Cerium surface-doped magnetic Iron Oxide Nanoparticles: Synthesis, Characterization and Catalytic Activity	Barcelona, Spain	Mejia Carmona, Karen
42	Ozel-Okcu, Sedef	Novel magnetic transduction methodology for DNA detection in liquids	Villacastin, Spain	Teran, Francisco Jose
43	Mohandes, Fatemeh	Magnetic Nanoparticles Coated by Fluorescent Carbon Dots as T2 contrast agent	Barcelona, Spain	Mohandes, Fatemeh
44	Moore, Charles	Microfluidic Poiseuille Flow Induced by Magnetically Actuated Microscopic Cilia	Paris, France	Moore, Charles
45	Morales Ovalle, Marco	Impact of complex iron oxide nanoparticles phases on cellular responses and toxicity	San Carlos de Bariloche, Argentina	Morales Ovalle, Marco Antonio
46	Moya, Carlos	Calix[4]arene-PEI Coated Iron Oxide Nanoparticles: A Multifunctional Approach for Recovery of Precious Metals and DNA Strands	Barcelona, Spain	Moya, Carlos
47	Natividad, Eva	Exploring the fabrication and performance of non-crosslinked PNIPAM-Fe3O4 nanospheres	Zaragoza, Spain	Natividad, Eva
48	Nunez, Nahuel	Bifunctional Magnetic Nanozymes: Synergy between Catalytic Activity and Magnetic Hyperthermia	San Carlos de Bariloche, Argentina	Nunez, Nahuel
49	Pabshettiwar, Chinmay	Probing the microstructure properties of soft magnetic polymer hybrid materials	Stuttgart, Germany	Weeber, Rudolf
50	Parekh, Kinnari	Engineering Suitable Biocompatible Magnetic Fluid for Magnetic Fluid Hyperthermia from Synthesis to in vitro investigation	Changa, India	Parekh, Kinnari
51	Patri, Sofia	Magnetic nanogels for combined hyperthermia and chemotherapy of prostate cancer	London, U.K.	Patri, Sofia
52	Porru, Margherita	Iron-Oxide Magnetic Nanoparticles: Manganese and Zinc Doping Effects on Relaxometric Properties	Pavia, Italy	Porru, Margherita
53	Pourshahidi, Ali Mohammad	Magnetic nanoparticles in viscous media from the view of Frequency mixing magnetic detection	Jülich, Germany	Pourshahidi, Ali Mohammad
54	Radon, Patricia	Verifying the MNP dissolution in photo-spectrometric iron concentration determination by magnetic particle spectroscopy	Berlin, Germany	Radon, Patricia
55	Riahi, Kalthoum	Shapes tailored magnetic nanoparticles for magnetic nanoparticle-based hyperthermia for cancer treatment	Darmstadt, Germany	Riahi, Kalthoum
56	Salamzadeh, Sadaf	Impact of temperature on AC magnetic susceptibility of MNPs	Enschede, Netherlands	Alic, Lejla
57	Schütz, Patrick	Preparation of Multi-Responsive Hydrogels Based on Magnetoplasmonic Nanoparticles in a Thermo-Responsive Polymer Matrix	Hamburg, Germany	Schütz, Patrick
58	Seino, Satoshi	Designing Magnetic Nanoparticles for Intranasal Administration : Targeted Delivery to the Brain	Suita, Japan	Seino, Satoshi
59	Serea Abu, Esraa	Enhancement and Tunability of Plasmonic-Magnetic Hyperthermia through Shape and Size Control of Au:Fe3O4 Janus Nanoparticles	Bilbao, Spain	Reguera, Javier
60	Shaterabadi, Zhila	Enhanced magnetic hyperthermia performance by magnetite nanorods: The effect of aspect ratio and synthesis method	Granada, Spain	Shaterabadi, Zhila
61	Storozhuk, Liudmyla	Synthesis and characterisation of doped iron oxide nanoflower seeds for magnetic hyperthermia cancer treatment	London, U.K.	Storozhuk, Liudmyla
62	Strbak, Oliver	Ferritin derivatives as a valuable tool in the research of neurodegenerative disorders	Martin, Slovak Republic	Oliver, Strbak
63	Sun, Shaoqi	Mixing-Frequency Spectra for Magnetic Particle Imaging	Beijing, China	Zhong, Jing
64	Tahir, Muhammad Umar	A Novel Coil Configuration Setup for Noninvasive Focused Brain Stimulation Using Magnetoelectric Nanoparticles: A Simulation Study	Gwangju, South Korea	Yoon, Jungwon
65	Takemura, Yasushi	Human Head Receive Coil-Coupled Magnetoresistive Sensor for Magnetic Particle Imaging	Yokohama, Japan	Takemura, Yasushi
66	Tietze, Rainer	Rapid analysis of microbiological contaminants in 2 stages (RAMICO2)	Erlangen, Germany	Tietze, Rainer
67	Torres, Teobaldo	Enzymatic-like Activity and Specific Loss Power Joining Forces for Vanadium Ferrite Theranostic Applications	Zaragoza, Spain	Torres, Teobaldo
68	Gavilan, Helena	Synthesis of Hybrid Nanomaterials Based on MXene/Magnetic Nanoparticles for Photo-Magnetic Hyperthermia Applications	Madrid, Spain	Gavilan, Helena
69	Villanueva Alvaro, Danny Yosmar	Unravelling the potential of Magnetospirillum gryphiswaldense as nanorobot, a detailed motility study	Bilbao, Spain	Villanueva Alvaro, Danny Yosmar

70	Adhikari, Samyog	Strong exchange bias effect in cobalt oxide@cobalt ferrite core-shell nanoparticles	London, U.K.	Thanh, Nguyen
71	Adhikari, Samyog	Synthesis and characterisation of (Co, Ni) Fe2O4 - BaTiO3 magnetodielectric nanocomposites.	London, U.K.	Thanh, Nguyen
72	Wang, Yueqi	Quantitative visualization of transferrin receptor-mediated iron uptake in Hepatocellular carcinoma using MPI/NIR-II photomagnetic multimodal imaging	Beijing, China	Wang, yueqi
73	Wei, Huimin	Enzyme-Powered Magnetic Nanomotors for Magnetic Particle Imaging and Magnetic Fluid Hyperthermia	Lübeck, Germany	Wei, Huimin
74	Weidner, Andreas	Preparation and characterization of hybrid magnetic nanoparticles featuring a "hard" biomolecular corona for medical applications	Ilmenau, Germany	Weidner, Andreas
75	Weisspflog, Maria	Non-Stoichiometric Cobalt Ferrite Nanoparticles by Green Hydrothermal Synthesis and their Potential for Hyperthermia Applications	Hamburg, Germany	Weisspflog, Maria
76	Winkler, Elin	Ferrite Nanoparticles Nanocatalysts: Unveiling Free Radical Generation and Assessing Environmental Impact on Algal Toxicity	San Carlos de Bariloche, Argentina	Winkler, Elin
77	Wolgast, Florian	Using adjustable DC offset fields in Magnetic Particle Spectroscopy towards sensitive immunoassays	Braunschweig, Germany	Wolgast, Florian
78	Yimeng, Li	Modified Jiles-Atherton model for dynamic magnetization and reconstruction in magnetic particle imaging	Beijing, China	Yimeng, Li
79	Yoshida, Takashi	Quantitative Estimation of Solid and Liquid Phase Magnetic Nanoparticles for Magnetic Immunoassay	Fukuoka, Japan	Yoshida, Takashi
80	Zhu, Tao	Excitation parameters selection for coaxial frequency-mixing magnetic particle imaging	Beijing, China	Tao, Zhu
81	Zurbano, Raquel	Vortex-State Magnetic Nanodisks in Melanoma Cell Cultures: A Potential Approach for Cancer Treatment	Bilbao, Spain	Zurbano, Raquel
82	Shih, Kun-Yauh	Effect of Microwave Hydrothermal Time on the Synthesis and Magnetic Properties of CoFe2O4/rGO Nanocomposites	Pingtung, Taiwan	Shih, Kun-Yauh

Poster Session II - Wednesday, June 18, 2024

#	First Author	Title	City, Country	Corresponding Author
83	Vogel, Patrick	MPI, MNPs and the long way to clinical routine	Würzburg, Germany	Vogel, Patrick
84	Vogel, Patrick	Keep your Camel healthy with COMPASS	Würzburg, Germany	Vogel, Patrick
85	Horcajo, Manuela	Optimizing Magnetic Nanoparticle Design for Effective Thermal Cancer Therapies	Madrid, Spain	Horcajo, Manuela
86	Amin, Rabia	Controlling Morphology and Magnetization of Magnetic Nanoparticles through Solvent-Ligand Chemistry	Braunschweig, Germany	Amin, Rabia
87	Del Valle Peña, Anaixis	A magnetosensing-based Rapid Screening Test for Streptococcus agalactiae Infections: Expanding Global Efforts in Addressing Perinatal Sepsis	Cerdanyola del Valles, Spain	Pividori, Maria Isabel
88	Andryskova, Natalia	Coaxial electrospun nanofibers with encapsulated titanium dioxide and magnetic nanoparticles for photo-stabilization and magnetically controlled release of betamethasone-17 valerate	Bratislava, Slovak Republic	Andryskova, Natalia
89	Antal, Iryna	Preparation and characterization of poly-L-lysine coated magnetic nanoparticles and evaluation of their peroxidase-like activity	Kosice, Slovak Republic	Antal, Iryna
90	de la Presa, Patricia	Heading Towards Standardizing Photothermal Measurements of Iron Oxide Nanoparticles Across Two Biological Windows	Madrid, Spain	de la Presa, Patricia
91	Bermudez-Berrios, Esteban	Sentinel Lymph Node Mapping Using Magnetic Particle Imaging	Gainesville, FL, U.S.A.	Rinaldi-Ramos, Carlos
92	Bhalerao, Smriti	Microscopic Imaging of Magnetic Particles in Flow using Nitrogen-Vacancy Centers in Diamond	College Park, U.S.A.	Bhalerao, Smriti
93	Chowdhury, Mohammad Suman	Organic Molecular Glues to Design Three-Dimensional Cubic Nano-assemblies of Magnetic Nanoparticles	Braunschweig, Germany	Chowdhury, Mohammad Suman
94	Das, Arpita	Polymer-coated Magnetic Nanoparticles (CoFe2O4) for targeted delivery of Intra articular gel for pain management	Kolkatta, India	Das, Arpita
95	Egea-Benavente, David	Microwave-assisted magnetic nanoparticles synthesis and functionalization with antibody 92R: The importance of a controlled MNPs-cell interaction for the correct development of magnetic hyperthermia therapy combined with immunotherapy	Madrid, Spain	Egea-Benavente, David
96	Espinosa, Ana	Exploring the Structural Characterization of Magnetic-based Nanoparticles inside Cells Using Hard X-ray Absorption Spectroscopy	Madrid, Spain	Espinosa, Ana
97	Eswaran, Neel	Formulation of PEG-coated MPI tailored tracers using nitroDOPA anchoring groups	Gainesville, U.S.A.	Rinaldi-Ramos, Carlos
98	Feye, Julia	Analyzing Reaction Parameters on Structural Characteristics of SMART RHESIN Hollow Nanospheres for Magnetic Particle Imaging Applications	Karlsruhe, Germany	Rösch, Esther
99	Garcia-Maestre, Maria	Bottom-up fabrication of filaments based on PLA and Fe3O4 suitable for 3D printing	Zaragoza, Spain	Natividad, Eva
100	Garcia, Ana	Easy synthesis of mesoporous silica nanoparticles doped with nickel oxide for biomedical applications	Madrid, Spain	Garcia, Ana
101	Gombos, Jan	Preparation, characterization, toxicity and usability of reconstructed ferritin and magnetoferritin for biomedical applications	Martin, Slovak Republic	Gombos, Jan
102	Good, Hayden	Impact of Object Size on Magnetic Particle Imaging (MPI) Signal Distribution	Gainesville, U.S.A.	Rinaldi-Ramos, Carlos

103	Goto, Haruki	Measurement of magnetic relaxation time of magnetic nanoparticles in wide time range	Hamamatu, Japan	Ota, Satoshi
104	Garcia Recaredo, Lucia	Functionalization of E-cadherin fragments on magnetic microparticles as a novel tool to study mechanotransduction	Zaragoza, Spain	Moros, Maria
105	Harvell-Smith, Stanley	Synthesis and Characterisation of Zn- and Mn-Doped Iron Oxide Nanocubes for Combined Magnetic Particle Imaging-Magnetic Fluid Hyperthermia Application	London, U.K.	Harvell-Smith, Stanley
106	Herrera Gomez, Roger	Development of Core-Shell Nanoparticles for Singlet Oxygen Storage and in situ Release Through Magnetic Hyperthermia for a Multi-Approach Cancer Treatment	Bellaterra, Spain	Herrera Gomez, Roger
107	Herrera-Aquino, Rafael	Scalability and Reproducibility of Iron Oxide Nanoflowers by the Polyol Method: Comparison of Solvothermal and Microwave Heating	Madrid, Spain	Herrera Aquino, Rafael
108	Hovorka, Ondrej	Developing nanorobotics for healthcare	Southampton, U.K.	Hovorka, Ondrej
109	Hu, Xinkai	Integrating Lipidic Cisplatin Prodrug and Magnetic Nanoflowers for Hyperthermia Cancer Treatment	London, U.K.	Nguyen, Thanh
110	Imhoff, Eric	Characterization of Commercial Magnetic Nanoparticles for Magnetic Particle Imaging	Gainesville, U.S.A.	Rinaldi-Ramos, Carlos
111	Jameel, Bassam	Pickering droplets stabilized by magnetic nanoparticles for optimizing ultrasound heating in tissue-like medium	Poznan, Poland	Jameel, Bassam
112	Jozefczak, Arkadiusz	Textile modified by magnetic nanoparticles	Poznan, Poland	Jozefczak, Arkadiusz
113	Khmara, Iryna	The peroxidase-like activity of magnetic iron oxide nanoparticles functionalized with amino acids	Kosice, Slovak Republic	Khmara, Iryna
114	Kim, Gawtak	Towards Accurate Prediction of Magnetoelectric Coefficient in Spherical Core@Shell CoFe2O4@BaTiO3 Nanoparticle for Brain Stimulation	Gwangju, South Korea	Yoon, Jungwon
115	Kizek, Rene	Spectroscopic and microscopic analysis of the effect of vancomycin-modified SPIONS on methicillin-sensitive and resistant Staphylococcus aureus strains	Prague, Czech Republic	Kizek, Rene
116	Kolesnichenko, Vladimir	Development of ultrasmall superparamagnetic nanoparticles for imaging applications	New Orleans, U.S.A.	Kolesnichenko, Vladimir
117	Kralj, Slavko	Magnetic Nanostructures with Hollow Compartments: A Tunable Acid-Etching Approach	Ljubljana, Slovenia	Kralj, Slavko
118	Kuznetsov, Andrey	Transport properties of active Brownian particles with magnetically-controlled rotation	Vienna, Austria	Kuznetsov, Andrey
119	Lachowicz, Dorota	Carbon Nanofiber-Based Magnetic Mats for Non-Invasive Heating	Krakow, Poland	Lachowicz, Dorota
120	Lagouarde, Julie	Field-induced recirculation flow using magnetic nanoparticles to mimic drug transport in an occluded vessel	Nice, France	Lagouarde, Julie
121	Livesey, Karen	Field-dependent magnetic relaxation times of magnetic nanoparticle systems	Callaghan, Australia	Livesey, Karen
122	Malhotra, Ankit	Actuation of Magnetic Nanoparticles inside a cochlea phantom	Lübeck, Germany	Malhotra, Ankit
123	Markert, Simon	Enhancing protein corona formation on bacterial magnetosomes by genetic engineering	Bayreuth, Germany	Schüler, Dirk
124	Martina, Kubovcikova	Heating efficiency study of amino acid coated iron oxide nanoparticles	Kosice, Slovak Republic	Martina, Kubovcikova
125	Mesas, Melania	Traffic light-based point-of-care test for the rapid stratification of fever syndromes	Barcelona, Spain	Mesas, Melania
126	Mickoleit, Frank	Long-term-stability and biocompatibility of bacterial magnetosomes from Magnetospirillum gryphiswaldense	Bayreuth, Germany	Mickoleit, Frank
127	Minuti, Anca	New protocol for observing adherence of magnetic particles and nanowires on cell surfaces using scanning electron microscopy imaging	Iasi, Romania	Minuti, Anca
128	Mohammed Mustafa, Mohammed Sahinsha	Design, Fabrication, and Biological Evaluation of Polyphenol Loaded Smart Magnetic Nanocarriers for Targeted Breast Cancer Therapy	Tiruchirappalli, India	Palanisamy, Selvamani
129	Mosafer, Jafar	Simultaneous therapeutic and diagnostic applications of magnetic PLGA nanoparticles loaded with doxorubicin in rabbit	Torbat Heydariyeh, Iran	Mosafer, Jafar
130	Musial, Jakub	Optimizing magnetic nanoparticle heating in tumor phantoms using rotating magnetic fields	Poznan, Poland	Musial, Jakub
131	Nagarajan, Krishnanand	Real Time Image Guided Magnetic Theranostic System for Targeted Cancer Therapy via 5 Fluorouracil Loaded Nanoliposomes	Tiruchirappalli, India	Palanisamy, Selvamani
132	Nistor, Mirela	In vitro Evaluation of F127@magnetite on Glioblastoma Cell Lines	Iasi, Romania	Dragoi, Brindusa
133	Novak, Ekaterina	Role of Depletant in Binary Mixtures of Shape-Anisotropic Magnetic Particles	Ekaterinburg, Russia	Novak, Ekaterina
134	Nozka, Aniela	Scalable formulation of magnetic particle imaging tracers via flash nanoprecipitation	Gainesville, U.S.A.	Rinaldi-Ramos, Carlos
135	Ognjanovic, Milos	Unveiling the impact of the chemical composition of ternary ferrites on specific loss power	Belgrade, Serbia	Ognjanovic, Milos
136	Ota, Satoshi	Evaluation of in vivo magnetization dynamics of magnetic nanoparticles in living tumor	Hamamatsu, Japan	Ota, Satoshi
137	Paez, Amira	Influence of anisotropy on the evolution of chains formed by magnetic nanoparticles under an applied magnetic field	Zaragoza, Spain	Paez, Amira
138	Palanisamy, Selvamani	Fabrication of Magnetic Nanoemulsion Loaded with Letrozole for Targeted Oncotherapy	Tiruchirappalli, India	Latha, Subbiah
139	Pansegrau, Kerstin	Temperature Effects on Magnetorelaxometry Parameters of Immobilized Magnetic Nanoparticles	Hall in Tirol, Austria	Pansegrau, Kerstin

140	Ployart, Olifie	Local temperature around iron oxide nanoparticles during hyperthermia	Paris, France	Ployart, Olifie
141	Porras Marichal, Juan Carlos	Portable medical device based on magneto immunosensor for the diagnosis of celiac disorder.	Cerdanyola del Valles, Spain	Pividori Gurgo, Maria Isabel
142	Pourshahidi, Ali Mohammad	Development of high-throughput magnetic tweezers platform with three poles	Jülich, Germany	Pourshahidi, Ali Mohammad
143	Queiros Campos, Jordy	Improvement of magneto-microfluidic separation of nanoparticles by molecular adsorption	Nice, France	Queiros Campos, Jordy
144	Raboisson-Michel, Maxime	Magnetic Micro Vortex for Molecule Convective Transport: Towards a Biomedical Application	Nice, France	Raboisson-Michel, Maxime
145	Ratajczak, Filip	The influence of administration of magnetic carriers on heating efficiency in tissue-mimicking phantoms	Poznan, Poland	Ratajczak, Filip
146	Remmo, Amani	Viability monitoring of cells using magnetic particle imaging	Berlin, Germany	Remmo, Amani
147	Rossi, Rosanna	Magnetic particles immunosensors for early diagnosis of alzheimer's disease	Cerdanyola del Valles, Spain	Pividori, Maria Isabel
148	Santana Otero, Antonio	Novel permalloys nanoparticles for CO2 capture and conversion by magnetic hyperthermia	Madrid, Spain	Santana Otero, Antonio
149	Santander, Sergio	Synthesis of Fe@C core-shell nanoparticles for dual magnetic hyperthermia and photothermal cancer treatment	Singapore, Singapore	Santander, Sergio
150	Selzer, Solange	Iron oxide nanoparticles for biotechnological applications	Cordoba, Argentina	Selzer, Solange
151	Hlukhaniuk, Anna	Preparation and Colloidal Stability of Magnetic Drug Delivery Nanoassemblies for Cancer Treatment	Prague, Czech Republic	Hlukhaniuk, Anna
152	Shlapa, Yuliia	Biocompatible Fe3O4@CeO2 Nanocomposites Synthesized via â€œLayer-by-Layerâ€ Deposition	Kyiv, Ukraine	Shlapa, Yuliia
153	Siska, Zuzana	Magnetic Cubic Nanoparticles Based on Iron Oxide Doped by Metal Ions for Enhancing Magnetic Performance	Brno, Czech Republic	Siska, Zuzana
154	Souiade, Lilia	Testing The Efficacy Of Magnetic Hyperthermia Using Non-Harmonic Electromagnetic Fields In Combination With Chemotherapeutic Drugs (5-Fluorouracil) : An In Vitro Study On Melanoma And Glioblastoma Multiforme Cell Lines	Pozuelo de Alarcon, Spain	Serrano-Olmedo, Jose-Javier
155	Bian, Zhongwei	A novel method for improving sensitivity of MPI based on modulation of offset field and even harmonic signal	Beijing, China	Tian, Jie
156	Stavila, Cristina	Fe-Cr-Nb-B magnetic particles for targeted chemotherapy	Iasi, Romania	Stavila, Cristina
157	Subbiah, Latha	Formulation Optimization, Evaluation of Magnetically Targeted Pantoprazole Effervescent Tablets for Enhanced Anti-Ulcer Therapy	Tiruchirappalli, India	Subbiah, Latha
158	Vas, Anna	Graphite oxide/nickel ferrite nanocomposites for magnetic hyperthermia	Szeged, Hungary	Illes, Erzsebet
159	Veintemillas-Verdaguer, Sabino	Studies of the magnetophoresis of magnetic labelled cells using a constant gradient separation device	Madrid, Spain	Veintemillas-Verdaguer, Sabino
160	Washino, Masaomi	Dynamic Monitoring of Magnetic Nanoparticle Translocation into Monkey Brain via Intranasal Administration Using MRI	Amagasaki, Japan	Washino, Masaomi
161	Wolfschwenger, Manuel	Molecular Dynamics Simulation of Interacting Magnetic Nanoparticles using a Hybrid Approach of Langevin dynamics and Monte Carlo Simulations	Hall in Tirol, Austria	Wolfschwenger, Manuel
162	Zara-Danceanu, Camelia Mihaela	Biocompatibility and Cytotoxic Evaluation of Cobalt Doped Magnetite (Co-Fe3O4) Nanoparticles on Breast Cancer Cells	Iasi, Romania	Dragoi, Brindusa
163	Zaragoza-Medina, Moises Gilberto	Is it Possible to Explain SAR in Nanoparticle-Mediated Magnetic Hyperthermia As The Linear Sum Of Harmonic Contributions When Using Pulsed Alternating Magnetic Fields?	Pozuelo de Alarcon, Spain	Serrano-Olmedo, Jose-Javier
164	Zheng, Mingyi	Stability studies of ultrasmall iron oxide nanoparticles for MRI T1 contrast agent	London, U.K.	Thanh, Nguyen
165	Lei, Siao	Quantification Results of Targeted Magnetic Particles In vivo and In vitro Human Tissues Based on Self-developed FFL-MPI	Beijing, China	Tian, Jie

Potential of Magnetic Particle Spectroscopy in Diagnosis of Pancreatic Cancer Biomarkers in the Blood Sample

Hafiz Ashfaq Ahmad[1] , Ali Dinari[1] , Yun-Hee Kim[2], M. Umar Tahir[1], and Jungwon Yoon[1*]

[1] School of Integrated Technology, Gwangju Institute of Science and Technology, Gwangju 61005, Republic of Korea

[2]National Cancer Center, Goyang-si, Gyeonggi-do,10408, Republic of Korea

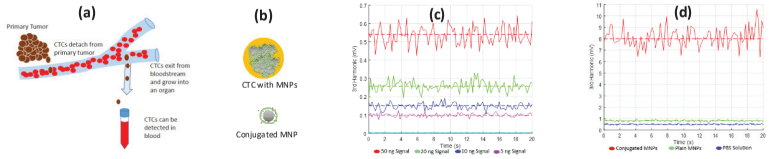
** Email:* jyoon@gist.ac.kr

Precise detection is pivotal for the therapy of diseases. In fact, detection is the first step and affects the therapy process. Magnetic particle spectroscopy (MPS), is a new modality used to trace magnetic nanoparticles (MNPs). It utilizes oscillating magnetic fields to analyze changes in MNPs, offering an easy and rapid method for detection. This versatility makes MPS valuable for various bioassays [1]. Pancreatic ductal adenocarcinoma (PDAC), the most aggressive type of pancreatic cancer, has difficulty in diagnosis. Metastatic stages which are almost close to death can represent pancreatic cancer symptoms. In this study, we applied our newly designed MPS device to detect the PDAC candidate biomarkers in combination with functionalized MNPs. In this regard, circulating tumor cells (CTCs) of pancreatic cancer act as biomarkers. Through applied the mesothelin-conjugated MNPs (M-MNPs) in the blood samples, the presence of CTCs was detected by the MPS device.

In this regard, we designed an MPS system with optimized excitation coils to ensure uniform magnetic field generation (100 mm length, 20 mm diameter, 75 turns, 140/46 Litz wire) for efficient nanoparticle response. Highly sensitive receiver coils (24 mm length, 12 mm diameter, 88 turns, 10/46 Litz wire) capture the emitted signals from MNPs. A 2 mT excitation field at 24.36 kHz frequency was applied, and the third harmonic signal was measured as the output. Amplification and filtration steps further enhanced signal quality by mitigating unwanted noise and interference. This optimized MPS system achieved a detection limit of 5 ng.

For the preparation of conjugated MNPs by using synomag®-D, the mesothelin protein was the desired antibody. Based on previous research, the expression of mesothelin will increase in pancreatic cancer [2]. The mesothelin-conjugated MNPs can attached to the CTCs of pancreatic cancer. In order to follow the experiment, the blood samples of pancreatic cancer model mice were collected, treated with conjugated MNPs (concentration 2.1 mg/ml), and shaken for two hours. In the next, samples were centrifuged (2500 rpm) for 7 minutes and washed (this procedure was repeated three times). In the final, the samples were suspended in phosphate-buffered saline (PBS), put in an MPS coil and the signals were recorded. The obtained results showed that samples with different amounts of CTCs presented different signals. The recorded signals are related to the presence of CTCs in the PDAC blood samples.

This study presents a novel approach to pancreatic cancer detection. While this initial investigation demonstrates the potential of the method, further validation is necessary. This research is in the process and will be updated by comprehensive analysis. The accuracy of CTC detection, and the presence of MNPs which specifically bound to CTCs have to be approved by complementary analytical techniques.



In figure (a) represents the CTCs circulation, isolation and detection. Figure(b) shows the conjugated MNPs and attached with CTCs. Figure(c) shows the detection limit of MPS. Figure(d) shows the results of the detection of CTCs for pancreatic cancer.

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Biocompatible Barium Hexaferrite Nanoparticle Composite Matrix

[1]Yusra Ahmed, [2]Ben Ward, and [1]Daniel Zabek.*

1School of Engineering, Cardiff University, CF24 3AA, Cardiff, United Kingdom.

2School of Chemistry, Cardiff University, CF10 3AT, Cardiff, United Kingdom.

*Zabekd@cardiff.ac.uk

Ferrofluids are stable colloidal dispersions of magnetic particles suspended in a carrier fluid exhibiting rheological and magnetic properties[1]. Non – spherical magnetic particles such as nanoplatelets or thin disks are of great interest due to their high level of shape anisotropy, distinct magnetic properties, and high aspect ratio. Hexagonal ferrites such as barium hexaferrite (BHF) magnetic nanoparticles have a high magnetic coercivity and magnetocrystalline anisotropy which allows BHF and its derivatives to be used for permanent magnets, magnetic recording, and microwave applications. In particular, their easy axis is oriented along the c – direction, i.e. perpendicular to the nanoplatelet basal surface, this makes them good candidates for non – thermic magneto – mechanical cancer treatment where the mechanical rotation of the nanoparticles creates a shear in an alternating magnetic field which can be used to damage cancer cells. We have previously developed a hexadecyltrimethylammonium bromide (CTAB) surfactant assisted manufacturing method which allows a stable dispersion of BHF nanoparticles in ethylene glycol[2]. This produces a ferromagnetic – ferrofluid which we have subsequently polymerised using an in – situ condensation polymerisation reaction between the ethylene glycol based ferrofluid and succinic acid. The polymerised ferrofluid becomes a polymer composite composed of a polyester matrix with magnetic BHF nanoparticles homogenously embedded throughout the polyester matrix. This polymer composite exhibits anisotropic magnetic properties and is magnetically characterised by Vibrating Sample Magnetometry (VSM). The polymer synthesis is optimised for reaction temperature, reaction time as well as chain length and molecular weight through Gas Chromatography (GS – MS) and Nuclear Magnetic Resonance (NMR). The polymer composite molecular weight was found to be approximately 1000 g/mol with a monomer to polymer conversion of 74% while the surface hardness of the resulting polymer is measured and found to be 98 Shore A. This polymer composite matrix is a promising biodegradable and biocompatible polyester and is widely used in different biomedical applications. Aliphatic polyesters as such have been extensively studied for drug delivery systems, functional materials, and artificial implants in tissue engineering. Our polymer composite matrix is a polyethylene succinate (PES) polyester which has comparable biocompatibility and biodegradability to polymers such as polylactic acid (PLA) and polycaprolactone (PCL)[3].

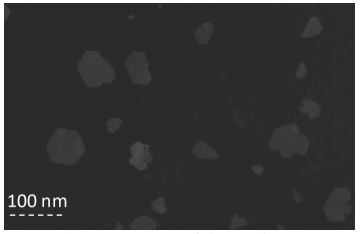

Figure 1: TEM image of dry surfactant coated Barium Hexaferrite nanoparticles on carbon substrate with a size (diameter) range between 10 – 200 nm.

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Towards Quantitative Imaging of Magnetic Nanoparticle Flow by MRXI

Soudabeh Arsalani[1], Frank Wiekhorst[1], Daniel Baumgarten[2] and Rainer Körber[1]*
[1]Physikalisch-Technische Bundesanstalt, Abbestrasse 2-12, D-10587 Berlin, Germany
[2]Institute of Electrical and Biomedical Engineering, UMIT TIROL-Private University for Health Sciences and Health Technology, Hall in Tirol, Austria
* email:soudabeh.arsalani@ptb.de

Magnetic nanoparticles (MNPs) have shown excellent potential for biomedical applications such as cancer diagnosis and therapy. Therapy applications, drug delivery and magnetic hyperthermia, require the localization and quantification of the MNP distribution inside a specific body region (e.g., brain, breast, prostate etc.) before and after treatment. There are several techniques, such as magnetorelaxometry imaging (MRXI), magnetic particle imaging (MPI) and magnetic resonance imaging (MRI), that are capable to provide this information [1]. In our pervious work, we have demonstrated the high capability of MRXI to quantify immobilized MNP distributions in a human head phantom [2]. However, imaging a flow of magnetic nanoparticles is equally important for monitoring the distribution of MNPs after injection into the blood vessels.

In preliminary experiments, our MRXI setup made use of a modular 72 channel SQUID system which is tolerant to pulsed magnetic fields of up to tens of millitesla. It detected the relaxation signal after the flow sample has been magnetized sequentially using six spiral excitation coils. The multichannel recordings monitored the flow of MNPs in a tubular phantom with a diameter of 2.2 mm, see Figure 1. The flow was realized by connecting the phantom to a syringe pump and injecting a bolus of about 90 µL of iron oxide nanoparticles (Micromod Partikeltechnologie, Germany). In this work we investigated the effect of the iron concentration, ranging from 20 to 100 mmol/L, with different flow rates of 0.6 to 1.7 mL/min in reconstructed images of MNPs. We could successfully visualise and reconstruct the MNP bolus movements in the tubular phantom for high iron concentrations.

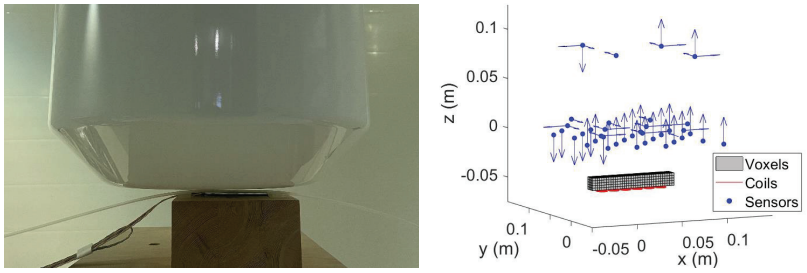

Figure 1. Left: Picture of the MRXI setup with flow phantom underneath the multichannel SQUID system. Right: Simulation setup showing the individual sensors (blue dots with arrows) together with the excitation coils (red) and the region of interest (gray voxels).

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Enhancing Sensing by Using Magnetic Nanoflowers for Screen-Printed Electrodes

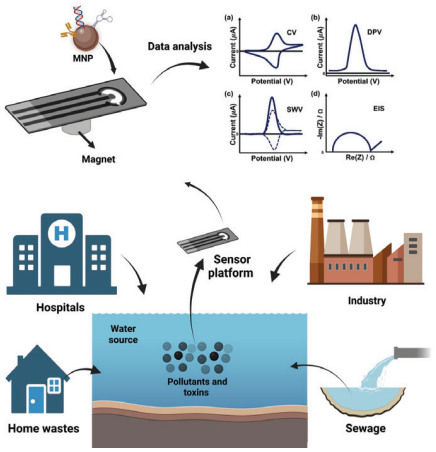
Augustas Rinkevicius[1], Almodather Soheim[6], Paulina Morkyte[1,5], Luka Barzdaite[1,4], Liudmyla Storozhuk[2,3], and Ausra Baradoke[1,5]*

[1]Deep Scientific, Sauletekio ave., 15-316, Vilnius, 10224, Lithuania
[2]UCL Healthcare Biomagnetic and Nanomaterials Laboratories, London, W1S 4BS, UK
[3]London Centre for Nanotechnology, UCL, London, WC1H 0AH, UK
[4]School of biology, University of St Andrews, St Andrews, KY16 9TH, UK
[5]Life Sciences Center, Vilnius University, Sauletekio al. 7, Vilnius, 10257, Lithuania
[6]Assiut University, Faculty of Pharmacy, Libraries Street, Markaz Assiut, Assiut Governorate

*email: info@deepscientific.eu

Abstract:

Green technology and sustainable environmental management require innovative detection technologies with improved sensitivity and specificity to monitor and reduce pollutants [1]. This study introduces a novel method to improve screen-printed carbon ink electrodes (SPCE) for water toxicity electrochemical detection. We have used Polyethylene glycol (PEG) coated magnetic iron oxide nano-flowers (MNP) with a size of 200 nm, prepared during synthesis in an autoclave at 200°C for 10 hours [2]. Optimization of screen-printed carbon electrodes (SPCE) using MNPs and a strategically placed magnet below the electrode increases their surface area, as a novel approach. This development greatly enhances electrochemical detection of a wide range of environmental toxins in water, advancing green technology efforts to reduce global pollution. Cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), Transmission Electron Microscopy (TEM), and Scanning Electron Microscopy (SEM) were used to evaluate added MNPs performance and SPCE structural alterations. These results showed that increasing surface area, surface shape, and magnetic particle dispersion improve environmental pollutant detection. Adding magnetic particles and a magnet underneath SPCE increases their sensitivity and allows them to detect lower water pollutants.



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PICKERING DROPLETS AND LIQUID MARBLES EXPOSED TO AN ALTERNATING MAGNETIC FIELD FOR CAPSULE FORMATION

Rafał Bielas*, Tomasz Kubiak and Arkadiusz Józefczak

Faculty of Physics, Adam Mickiewicz University in Poznań
Uniwersytetu Poznańskiego 2, 61-614 Poznań, Poland
*e-mail: rafal.bielas@amu.edu.pl

Both Pickering droplets, which are droplets coated with solid particles and immersed in another liquid phase, and liquid marbles (droplets coated with solid particles at the air-liquid interface), demonstrate potential for biomedical applications. These systems can be directly employed for the controlled delivery and release of substances, including drugs. Significantly, droplets stabilized by a particle shell can serve as precursors for capsule fabrication if the shell becomes rigid through processes such as magnetic heating [1,2].

Here, we present findings on the thermo-responsive behavior of Pickering droplets and liquid marbles under the application of an alternating magnetic field (AMF). In both scenarios, magnetic nanoparticles generate heat through relaxation and hysteresis loss mechanisms, resulting in partial sintering of the particle shell. For liquid marbles, this heat facilitates the evaporation of the droplet's inside, leaving a reinforced polymer shell with magnetic material integrated into its structure. This shell can then be refilled with various liquids, for instance, an antibiotic dispersed in biocompatible linseed oil. Moreover, the droplet core can consist of a hydrogel embedded with bacteria-based magnetic nanoparticles (magnetosomes) coated with a bio-layer. When subjected to magnetic heating, the shell structure does not strengthen; instead, turmeric microparticles used as a coating absorb the aqueous core, leaving a magnetic shell enriched with the integrated magnetosomes [3].

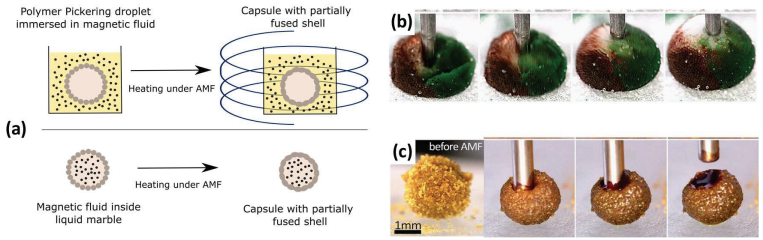

Fig. 1 (a) The scheme of the formation of rigid particle shell around the droplets when exposed to AMF.
(b) Re-functionalization of rigidified polymer shell by filling with antibiotic dispersion in linen oil.
(c) Liquid marbles with incorporated magnetosome nanoparticles re-filled with magnetic fluid.

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Acknowledgments

This work was supported by the project no. 2019/35/N/ST5/00402 (PRELUDIUM) of the Polish National Science Centre.

Non-monotonous Diffusion in Ferrogranulate Layer Induced by Tuning Interactions

Oksana Bilous[1], Kirill Okrugin[1], Pedro Sánchez[1], Ali Lakkis[2], Reinhard Richter[2] and Sofia Kantorovich[1]

[1] Computational and Soft Matter Physics, University of Vienna, Vienna, Austria
[2] Experimental Physics 5, University of Bayreuth, Bayreuth, Germany

*Email:oksana.bilous@univie.ac.at.Mobile:+380503905997

We explore Brownian motion in a quasi-two-dimensional ferrogranulate system through molecular dynamics simulations. The system comprises millimeter-sized magnetic and glass spheres with different diameters $\sigma_m = 3$ and $\sigma_g = 4$ is modelled as a combination of Stockmayer and Week-Chandler-Andersen particles and the shaking amplitude simulated by a thermostat.

Our investigation uncovers complex, non-monotonous diffusion behavior across various area fractions of magnetic and glass spheres and three external magnetic field strengths (B_{z0}=0.0, B_{z1}=0.5, B_{z2}=1.0) perpendicular to the monolayer, leading to transitions between different Brownian dynamics regimes.

By analysis of mean square displacement (MSD) for four different particle configurations, including magnetic particles in clusters, singular magnetic particles, total magnetic particles, and glass particles, we uncover three distinct regimes of Brownian dynamics. These regimes encompass ballistic motion, superdiffusion, and a transition to either subdiffusion or continued superdiffusion, depending on particle type and configuration. We observe that normal diffusion is attained by maximizing both external magnetic field strength and area fraction, except for magnetic particles clustered together.

Additionally, our investigation highlights a differential linear reduction over increasing an area fractions in diffusion coefficient specifically for total magnetic particles under increasing external magnetic field strength, as shown in the Figure.

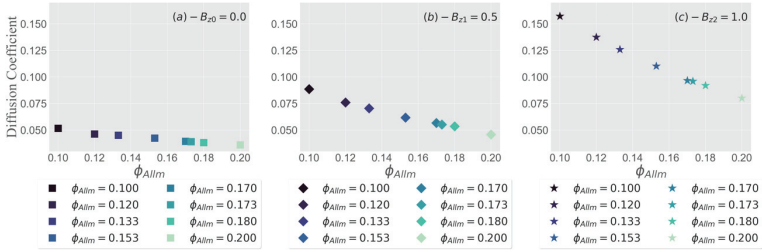

Figure. The diffusion coefficient varies with the total area fractions of magnetic particles in the final simulation time setup representing the third regime of Brownian dynamics under different external field strengths (a)-(c), respectively.

This finding underscores the nuanced interplay between magnetic susceptibility and viscoelastic properties, which significantly influence particle dynamics within the ferrogranulate system.

Furthermore, our analysis showcases the complexity of interactions within ferrogranulate system, providing valuable insights into the fundamental mechanisms governing non-monotonous diffusion phenomena. This study paves the way for further exploration and understanding of particle dynamics in ferrogranulate layers, with implications for various scientific and technological applications.

On the use of biotechnologically functionalized magnetic nanoparticles for the recycling of valuable ultrafine powders from electronic waste

Peter Boelens[1*], Mélody Perret[2], Emma Pustlauk[1], Sirine El Mousli[2], Jean-Michel Siaugue[2], Emilie Secret[2] and Franziska Lederer[1]

[1] Helmholtz-Zentrum Dresden-Rossendorf, Helmholtz Institute Freiberg for Resource Technology, Freiberg, Germany

[2] Physicochimie des Electrolytes et Nanosystèmes Interfaciaux PHENIX, Sorbonne Université CNRS UMR 8234 Paris, France

*Email: p.boelens@hzdr.de

Electronic waste contains high amounts of valuable metals in the form of ultrafine (<10 µm) inorganic powders [1]. Currently, only a minor fraction of these metals is recycled economically. Separation of the inorganic powders would strongly enhance the recyclability of these secondary resources. However, the most prominent particle separation (froth flotation, gravity, magnetic and electric separation) processes were developed by the mining industry for primary particles [2,3]. These processes are only partially suitable for secondary resources and face challenges with regards to the ultrafine particle sizes and the high complexity (typically, >60 elements are present in electronic waste).

In a novel approach, we propose the use of magnetic carriers derived from various life science applications (such as magnetic drug delivery, purification, hyperthermia, imaging, etc. [4]) for the magnetic separation of critical raw materials from electronic waste. Magnetic nanoparticles (MNPs) exhibit excellent properties and can be synthesized cost-effectively. The small size and high specific surface area of ultrafine powders provide benefits for the attachment of MNPs, as opposed to their hindrance of conventional separation processes. Achieving attachment selectivity of MNPs to the desired target powders is crucial for the selectivity of the separation process. This draws inspiration from the common practice of MNP functionalization with biomolecules in the aforementioned fields of life science[5].

In this presentation, we discuss a case study involving biotechnologically functionalized MNPs for the carrier magnetic separation of rare-earth element-containing phosphors from fluorescent lamps Figure 1 [6,7]. We provide a comprehensive overview of MNP synthesis and functionalization, determination of their interaction affinity with various phosphors, application in magnetic separation, as well as post-separation detachment and MNP reuse. Special emphasis is placed on MNP colloidal stability and magnetic field gradient.

Our work presents a novel approach to recycling rare-earth elements from fluorescent lamps. More broadly, it represents a significant advancement in the utilization of biotechnologically functionalized MNPs for the recycling of ultrafine inorganic powders from electronic waste.

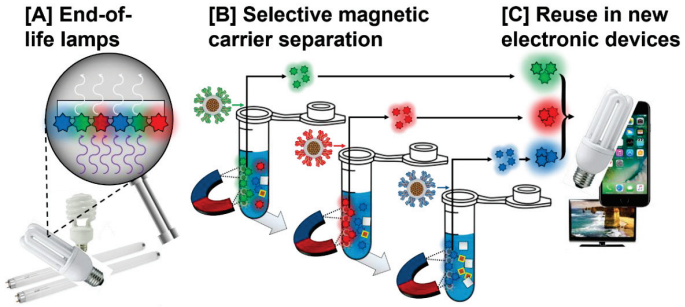

Figure 1 Overview of a case study involving biotechnologically functionalized MNPs for the carrier magnetic separation of rare-earth element-containing phosphors from fluorescent lamps. [A] The blue ($BaMgAl_{10}O_{17}$: Eu^{2+}), green ($LaPO_4$: Ce^{3+}, Tb^{3+} or $CeMgAl_{11}O_{19}$: Tb^{3+}) and red (Y_2O_3:Eu^{3+}) phosphors coated as ultrafine particles on the inner surface of a glass tube. [B] Sequential separation of the phosphors after grinding of the lamps by utilizing selective magnetic carriers. [C] Low carbon-footprint reuse of the critical raw materials in new electronic devices.

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Exploring the Impact of Shape, Size, and Coating on the Efficacy of Iron-Oxide Nanoparticles in Magnetic Resonance Imaging and Hyperthermia

Francesca Brero[1,2,*], Margherita Porru[1,2], Alvaro Gallo-Cordova[3], Manuel Mariani[2,4], Rafael Herrera Aquino[3], Francesco Orsini[4,5], Paolo Arosio[4,5], Alessandro Lascialfari[1,2], Maria del Puerto Morales[3]

[1] Department of Physics, University of Pavia, Pavia 27100, Italy
[2] National Institute of Nuclear Physics-INFN, Pavia 27100, Italy
[3]Instituto de Ciencia de Materiales de Madrid, ICMM/CSIC, Madrid 28049, Spain
[4]National Institute of Nuclear Physics-INFN, Milano 20133, Italy
[5]Department of Physics, University of Milano, Milano 20133, Italy
*Email: francesca.brero@unipv.it. Mobile: +39 0382 987483

Iron oxide-based magnetic nanoparticles (MNPs) offer a dual functionality, serving as contrast agents in magnetic resonance imaging (MRI) and as hyperthermic agents for tumor treatment via Magnetic Fluid Hyperthermia (MFH) [1].
To maximize their efficacy, it's crucial to fine-tune their morpho-structural characteristics including shape, dimensions, core type, magnetic ion, and coating.

This study delves into two sets of core-shell MNPs - nanospheres and nanoflowers (composed of nanospheres) - with variations in ferrite-core diameter. These MNPs are coated with biocompatible layers like dimercaptosuccinic acid (DMSA), polyacrylic acid (PAA), and carboxymethyl-dextran (CM-dextran).

Morpho-structural characterizations were conducted using AFM, DLS, TEM, XRD, IR, and TG analyses.
Exploration of MNPs' relaxation properties involved ^{1}H-NMR measurements of longitudinal (T_1) and transversal (T_2) nuclear relaxation times across varying Larmor frequencies. The resulting nuclear longitudinal r_1 and transverse r_2 relaxivities indicate contrast efficiency.

Morpho-structural investigations yielded magnetic core and hydrodynamic sizes, and surface charge measurements, revealing core diameters ranging from 11 to 35 nm and coating thicknesses of 1-2 nm. Notably, MNPs' shape, size, and coating significantly influenced ^{1}H-NMRD frequency profiles, impacting nuclear relaxation mechanisms.
At a clinical field strength of 1.5 T, particles exhibit r_2 values surpassing those of the Endorem® compound [2]. Furthermore, the study identified shape and size-dependent heating release mechanisms and values (Specific Absorption Rate, SAR), aligning with existing literature models.

In summary, diverse size, coating, and shape configurations lead to distinct spin dynamics. Understanding these mechanisms aids in optimizing morpho-structural and magnetic parameters, maximizing efficiency in both MRI contrast and MFH heat release.

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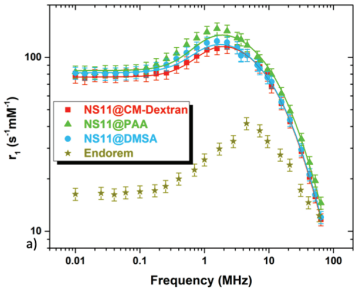

Figure. Longitudinal relaxation profiles of 11-nm nanospheres (coated with CM-dextran, PAA and DMSA) adapted to the heuristic model of Roch-Müller-Gillis [3]. The Endorem's longitudinal profile is also shown.

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Controlled Preparation of Cadherin-Magnetic Nanoparticle Bioconjugates for Remote Cellular Manipulation

Christian Castro-Hinojosa[1], Susel Del Sol-Fernández[1], Lucia García Recaredo[1], Pilar Gomollón[1], Pablo Martínez-Vicente[1], Yilian Fernández-Afonso[1], Raluca M. Fratila[1, 2], María Moros[1, 2].

[1]Institute of Nanoscience and Materials of Aragon (INMA-CSIC), University of Zaragoza- Zaragoza (Spain). [2]Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN) - Madrid (Spain).

Magnetic nanoparticles (MNPs) are extensively studied in nanomedicine due to their unique features including a comparable size to biomolecules and their responsiveness to remote magnetic fields, enabling them to induce heat or tractional forces. By targeting MNPs to cell membranes, remote magnetic stimulation can directly exert pulling forces at the cellular level, providing versatile platforms for precise cellular manipulation. In addition, magnetic fields application presents several benefits, including the ability to penetrate deep tissues and the potential to apply a diverse spectrum of forces (ranging from fN to nN) without causing harm to the sample. We are interested in using MNP to stimulate cellular E-cadherins in order to understand and modulate remotely important intracellular signals connected with them. E-cadherin is a calcium-dependent cell adhesion protein involved in important cellular processes, such as mechanotransduction, cell morphogenesis or tissue growth and repair. To do so, we functionalize MNPs with cadherin fragments, so that they can further interact with cellular cadherins.

The specific targeting of the MNPs to cellular receptors requires the control of factors like biomolecule orientation and density on the MNP surfaces, which often requires expensive or timeconsuming bioconjugation approaches. In this work, we present a versatile bioconjugation strategy for the oriented immobilization of His-tagged E-cadherin on MNPs by metal affinity binding using as linker Nα,Nα-bis(carboxymethyl)-L-lysine hydrate (NTA). To do so, 14-nm manganese-iron oxide MNPs were grafted with polyethylene glycol (PEG) chains and functionalized with previously formed, ready-to-use NTA-Me^{2+} complexes in a single step. The here-presented strategy allows a faster and modulable functionalization controlling the NTA-Me^{2+} incorporated on the MNPs and with that the number of proteins/MNP.[1]

By controlling the number and orientation of cadherins over the MNPs surface, the specific interaction of these MNPs with cells expressing E-cadherin was obtained. To evaluate the potential activation of mechanotransduction pathways mediated by E-cadherin stimulation, a Madin-Darby Kidney cell line (MDCK) was modified with a luciferase reporter designed to monitor the Wnt pathway activation. Wnt constitutes an important mechanotransduction pathway and can be directly linked to E-cadherin, resulting essential to study, and potentially providing new insights into how functionalized MNPs could be used to understand and modulate important intracellular signals associated with mechanoreceptors.

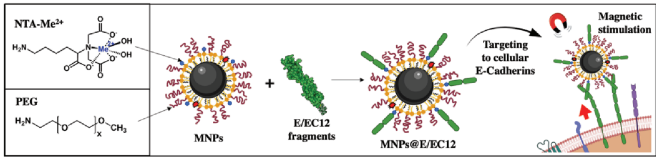

Figure 1: Scheme of the oriented immobilization of E-cadherin fragments (E/EC12) containing a His-tag for cell labeling and a posterior remote magnetic stimulation.

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Aknowledges: This work was supported by the SIROCCO project which has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 853468).

Guidance of magnetotactic bacteria to tumors for targeted therapy

Changyou Chen[1,2] *, Qingmeng Wang[1,2], Haitao Chen[1,2], Pingping Wang[1,2], Tao Song[1,2,3] *

[1] Beijing Key Laboratory of Bioelectromagnetism, Institute of Electrical Engineering, Chinese Academy of Sciences, Beijing 100190, China.

[2] France-China International Laboratory of Evolution and Development of Magnetotactic Multicellular Organisms, Beijing, China.

[3] University of Chinese Academy of Sciences, Beijing 100049, China.

* Email: songtao@mail.iee.ac.cn, chchy@mail.iee.ac.cn. Mobile: 86-01-82547164

Magnetotactic bacteria (MTB) are ubiquitous microorganisms in nature that synthesize chain-like intracellular magnetite nanoparticles called magnetosomes in a gene-controlled way. Due to magnetosomes, they are very responsive to and actively migrate along with magnetic fields, an ability called magnetotaxis. Basing on the existed magnetosomes and magnetotaxis, MTB hold significant potential in biomedical applications. Our previous studies demonstrated that intact AMB-1 was used as a natural magnetic hyperthermia. However, how to guide MTB to reach deep tumor sites still faces challenges and their targeting ability in vivo is also opaque.

In this paper, we designed and developed a three-dimensional focusing magnetic field (fMF)-producing device that physically guided MTB to the tumor site. With the guidance of fMF, polar MO-1 cells and axial AMB-1 bacteria were able to gather at the focusing center both in vitro and in vivo. Polar MO-1 bacteria exhibit a bit superior targeting and aggregation properties compared to axial AMB-1. However, the culture of polar MO-1 is much more difficult, axial AMB-1 was chosen as a magnetic carrier for magnetic targeted hyperthermia in the future.

Besides physical guidance by fMF, biological method was able to navigate AMB-1 to tumor site. After modified with positively-charged glycol chitosan via electrostatic adsorption, the AMB-1 carries a positive charge, which could then combine with nanovesicles derived from tumor cells. The nanovesicles also assisted AMB-1 cells to target tumor in a biological manner. These findings suggest that MTB has enormous promise for tumor targeted therapy.

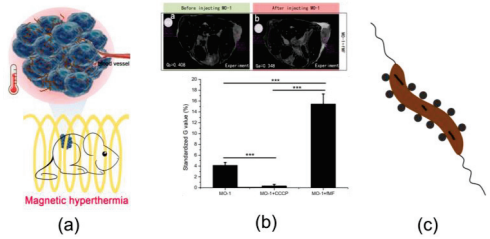

Figure. (a) Intact AMB-1-mediated magnetic hyperthermia. (b) The targeting ability of polar MO-1 bacteria under the control of a fMF to the tumor site in mice. (c) Nanovesicles derived from tumor cells assisted AMB-1 cells to target tumor in a biological manner.

Quantitative Dual-Color Magnetic Particle Imaging

Ximin Cheng[1], Shijie Sun[1], Lijun Xu[1] and Jing Zhong[1,*]

[1]School of Instrumentation and Optoelectronic Engineering, Beihang University, Beijing, China

*Email: zhongjing@buaa.edu.cn

Magnetic particle imaging (MPI) is a novel imaging modality that allows for quantitative imaging of magnetic nanoparticles (MNPs) based on the measurement of their dynamic magnetization. When considering the relaxation dependent dynamic magnetization of the MNPs, it allows to distinguish different MNPs to realize color MPI, which is of great importance to disease theranostics. However, the cross-talk between different colors may prevent complete separation of the different MNPs, thus causing artifact between different colors and poor quantification. Therefore, it is of great importance and interest to investigate a new approach of color MPI to improve the cross-talk and quantification for color MPI.

This study proposes a new approach of dual-color MPI with single-harmonic-based narrow-band MPI approach to quantitatively visualize the spatial distribution of two different MNPs. Only the 3rd harmonics are measured for image reconstruction in the narrow-band MPI. For dual-color imaging, the measured complex 3rd harmonics of the two different MNPs are separated into real and imaginary parts to construct the system matrix for dual-color reconstruction.

In this study, Perimag® plain and Synomag® D-50, purchased from Micromod GmbH (Rostock, Germany), are used as experimental samples. The two types of MNPs are mixed with different volume percentages. Figure 1(a) shows the reconstructed 2D images of the two different MNPs. The first (second) row shows the reconstructed concentration image C_{Perimag} (C_{Synomag}) of Perimag (Synomag) MNPs while the third row shows the overlay images. From the 1st to the 3rd column, the volume percentage of Perimag (Synomag) MNPs decreases (increases). It indicates that the image intensity qualitatively increases with increasing the volume concentration. The maximum image intensity of the reconstructed images is normalized to that of the 100% C_{Perimag} or C_{Synomag} and presented in Figure 1(b). The experimental results are fitted with a linear line, showing R-square better than 99%. It indicates that the proposed approach allows for quantitative imaging of two different MNPs. Moreover, the fitted parameter k is equal to 1.03 for Perimag and 0.983 for Synomag, respectively. It indicates that the proposed approach allows to determine the concentration of the Perimag/Synomag MNPs very accurately.

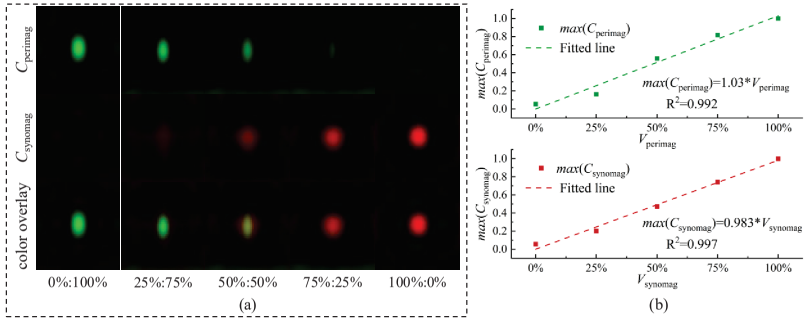

Figure 1. (a) C_{perimag} (upper row), C_{synomag} (middle row) and color overlay (lower row) for different ratio of V_{synomag} : V_{perimag}, (1) 0%:100%, (2) 25%:75%, (3) 50%:50%, (4) 75%:25%, and (5) 100%:0%, respectively; (b) $Max(C_{synomag})$ versus V_{synomag} and $max(C_{perimag})$ versus V_{perimag}. The dashed line represents the fitted linear regression curve.

A new versatile nanoformulation to remotely trigger mechanotransduction for bone regeneration

Manuel Estévez[1,2], Mónica Cicuéndez[1,3]*, Montserrat Colilla[1,2,4], María Vallet-Regí[1,2,4], Blanca González[1,2,4], Isabel Izquierdo-Barba[1,2,4]

[1] Dpto. de Química en Ciencias Farmacéuticas, Facultad de Farmacia, Universidad Complutense de Madrid, Plaza Ramón y Cajal s/n, 28040 Madrid, Spain. [2] Instituto de Investigación Sanitaria, Hospital 12 de Octubre i+12. [3] Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC). [4] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain.

**Email: mcicuendez@ucm.es*

The prevalence of bone diseases among the world older adults, such as osteoporosis, requires the development of new strategies for bone regeneration. Mechanotransduction has irrupted into this scenario bringing up promising opportunities in bone tissue engineering.

Herein, we evaluated the efficacy of new colloidal nanoformulations based on superparamagnetic iron oxide nanoparticles (SPIONs) after exposure to an external magnetic field (EMF) for mechanotransduction in human bone marrow-derived mesenchymal stem cells (hBM-MSCs) [1]. To this aim, SPIONs of *ca.* 13 nm were prepared by the thermal decomposition method, coated with dimercaptosuccinic acid (DMSA) by ligand exchange (affording SPIONs-DMSA), and finally functionalized with an Arg-Gly-Asp (RGD) peptide as targeting ligands towards integrin receptors of the cell membrane (affording SPIONs-DMSA-RGD). Both targeted and non-targeted nanocolloids were submitted to a comparative bioanalytical characterization in terms of biocompatibility, cell uptake pathways and mechanotransduction effect. SPIONs-DMSA-RGD promoted the osteogenic differentiation of hBM-MSCs upon application of an EMF (250 mT, 1 Hz) after 30 min of incubation, *i.e.*, when the nanoparticles are located in the cell membrane surface to initiate endocytic pathway, as evidenced by the increase in the expression of osteogenic genes Runx2 and ALP, and also in ALP activity (Figure).

This study augurs the local administration of nanoformulations combined with the application of an EMF as a promising approach to design new drug-free, controlled, remote and minimally invasive nanotherapy for bone tissue regeneration.

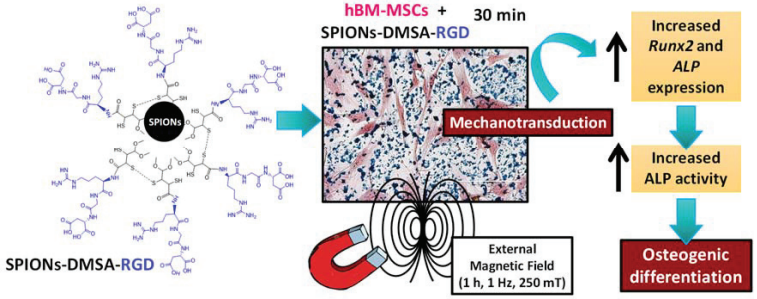

Figure. Scheme of the experimental process using SPIONs for osteogenic differentiation.

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Acknowledgements: European Union's Horizon 2020 Research and Innovation Program under grant agreement No 814410 (GIOTTO) and ERC-2015-AdG (VERDI) Proposal No. 694160, and the Fundación Ramón Areces FD5/22_01 (Nano4Infection) grants.

Magnetic Hybrid Materials with Polysaccharide Matrix for MRI and 5-Fluorouracil Delivery

Duceac I.A.*[1,2], Uritu C.M.[3], Stiufiuc R.I.[2,4], Dragoi B.[2,5], Coseri S.[1]

1 Polyaddition and Photochemistry Department, "Petru Poni" Institute of Macromolecular Chemistry, 700487 Iasi, Romania
2 Nanotechnology Laboratory, TRANSCEND Research Center, Regional Institute of Oncology, 700483 Iasi, Romania
3 Advanced Centre for Research-Development in Experimental Medicine, Grigore T. Popa University of Medicine and Pharmacy, 700259 Iasi, Romania
4 Department of Nanobiophysics, MedFuture Research Center for Advanced Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy, 400337 Cluj-Napoca, Romania
5 Faculty of Chemistry, "Alexandru Ioan Cuza" University of Iași, 700506 Iași, Romania
*duceac.ioana@icmpp.ro

Magnetic nanoparticles (MNPs) remain first-in-class agents for tailor-made theranostic functions. MNPs open perspectives for multiple treatment options with minimal adverse effects in cancer therapy. Iron oxide nanoparticles, such as magnetite, can find practical applications in cancer management as MRI contrast agents, local hyperthermia, and localized drug delivery systems with external control due to their unique properties. On a practical level, superparamagnetic nanoparticles tend to agglomerate and often are not helpful unless stabilized or incorporated into a polymer matrix. This study aimed to explore the structural organization of some magnetic hybrid materials based on a crosslinked matrix of selectively functionalized polysaccharides reinforced with MNPs stabilized with oleic acid. Subsequently, we assessed their applicative potential as drug delivery systems and contrast agents for medical imaging.

To that aim, polysaccharide/MNP hybrids were obtained under different preparation conditions while maintaining constant composition parameters. Previously, chitosan and pullulan were selected and modified by grafting and selective oxidation, respectively, to enable optimal physical and chemical interactions. The successful preparation of the two derivatives was confirmed by the changes in NMR and FTIR spectra. The incorporation of MNPs into the polymeric matrix was performed in solution or emulsion, followed by freeze-drying. FTIR spectroscopy was used for an in-depth analysis of the resulting magnetic hybrid materials, confirming both polysaccharide crosslinking and magnetite incorporation. Electron microscopy images offered information on sample morphology, which depended greatly on the preparation method. Elemental analysis by energy-dispersive X-ray spectroscopy confirmed the inclusion of magnetite inside the polysaccharide matrix. Mass magnetization curves and thermogravimetric analysis provided additional information about magnetite incorporation and nanocomposite organization.

Drug loading in nanocarriers, drug delivery, and controlled release at the target site are particularly challenging for cancer therapy. The possibility of using these magnetic hybrid materials for this application was explored with 5-fluorouracil, a pyrimidine nucleoside analog used for cancer treatment. In addition, these materials were evaluated as contrast agents for MRI diagnosis purposes based on relaxivity measurements in agarose phantoms. The results revealed that the MNPs/polysaccharide hybrids are fine T2-contrast agents that, along with the ability to release FU in a controlled manner, hold promise for future theranostic applications.

Acknowledgment: H2020–ERA-Chair, no 952390 and PN-III-P3-3.6-H2020-2020-0105/35/2021 (UEFISCDI).

Enhanced Sensitivity in Magnetic Particle Spectroscopy Through Phase Inversion Signal Processing

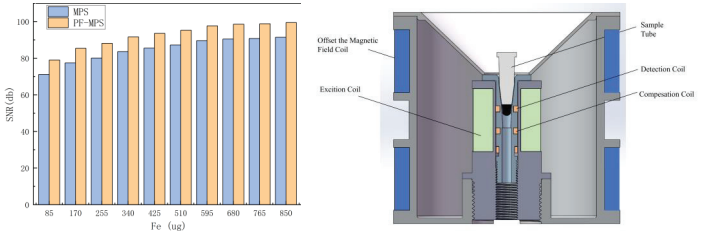
Ziwei Chen[1,2], Zhongwei Bian[1,2], Yu An[1, 2*], and Jie Tian[1,2*]

1 School of Biological Science and Medical Engineering, Beihang University, Beijing, China
2 key Laboratory of Big Data-Based Precision Medicine (Beihang University), Ministry of Industry and Information Technology of the People's Republic of China, Beijing, 100191, China
*Email: tian@ieee.org

Magnetic particle spectroscopy (MPS) is a kind of detection equipment used to characterize the properties of magnetic particles. MPS has been widely used to measure the concentration, temperature and viscosity of magnetic nanoparticle (MNP) suspensions. Among them, concentration measurement is an important basis for the quantitative application of MPS in targeted drug delivery. Maximization of signal-to-noise ratio (SNR) and detection sensitivity is the key of MPS system design.

In this work, we propose a method to enhance the sensitivity of magnetic particles using phase-reversal signals. This method employs the combined action of a static offset magnetic field with a specific amplitude and an excitation magnetic field acting on the magnetic particles, resulting in harmonic signals with phases opposite to the original signals. Due to the application of a static bias magnetic field with a specific amplitude, the phase of the harmonic signal generated is opposite to that of the original signal, while the phase of the interference signal remains unchanged. Therefore, by performing differential calculations on the measurement signals before and after the inversion, it is possible to simultaneously suppress the interference signal and enhance the signal strength, thereby improving the SNR. As depicted in Figure, experimental comparisons were conducted using our equipment, indicating that the method yields higher sensitivity measurements compared to traditional MPS across varying particle concentrations. The results show an approximate 8 dB increase in SNR.

In the future, with more optimized engineering technology, it will be possible to detect the concentration of drug carriers more effectively. In addition, the method can also be applied to nanoparticle imaging, which can not only improve the signal-to-noise ratio, but also have the function of replacing the background reduction.



(a) **(b)**

Figure. **(a)** Comparison of signal-to-noise ratio between conventional MPS and phase-flipped MPS (PF-MPS). **(b)** Device schematic: The system incorporates a traditional MPS; a uniform static bias magnetic field is generated with a pair of Helmholtz coils.

Characterizing magnetic nanoparticle ensembles with thermal noise magnetometry

Katrijn Everaert[1,2,3*], Bartel Van Waeyenberge[1], Frank Wiekhorst[2], Jonathan Leliaert[1]
[1]*Department of Solid State Sciences, Ghent University, 9000 Ghent, Belgium*
[2]*Physikalisch-Technische Bundesanstalt, Abbestraße 2-12, D-10587 Berlin, Germany*
[3]*Department of Physics, University of Maryland, College Park, Maryland, 20742, USA*
[*]*Email: everaert@umd.edu*

Accurate characterization of magnetic nanoparticles (MNPs) is essential for effective and save biomedical applications, such as magnetic particle hyperthermia, magnetic fluid imaging, and drug targeting. Most magnetic methods characterize MNPs by measuring their response to an externally applied excitation field. This field can affect the state of the particles in the ensemble, e.g., via MNP chain formation, thereby complicating the characterization of the individual particle properties. Recently, thermal noise magnetometry (TNM) has been developed as an alternative characterization method that captures the fluctuations in the magnetization in thermal equilibrium without external excitation [1]. This purely observative measurement reduces the impact of external influences on the measurement results to a minimum, thereby giving further insights into the system's fundamental magnetization dynamics.

In this contribution, we present TNM as a magnetic characterization method and highlight our recent advances to turn this emerging technique into a more practical and accessible method. It is shown how sample parameters such as the number of particles in an ensemble and the individual magnetic domain sizes affect the thermal noise, and how these scaling laws offer an intrinsic advantage to monitor MNP aggregation and clustering events in biological environments [2, 3]. Several methodological advances were made, such as the development of an optimized sample holder geometry [2] and the comparison of different sensor systems [3]. The counter intuitive impact of temperature on the magnetization fluctuations, as shown in the figure, is explained [4], and finally, we compare the MNP's magnetization fluctuations with the dissipation under a magnetic AC excitation [5].

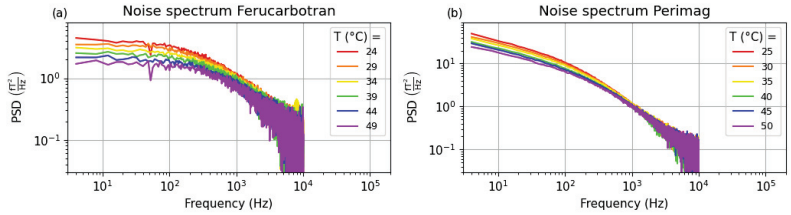


Figure: Power spectral density of the fluctuations in the magnetization as a function of temperature of a Ferucarbotran sample (a) and a Perimag sample (b).

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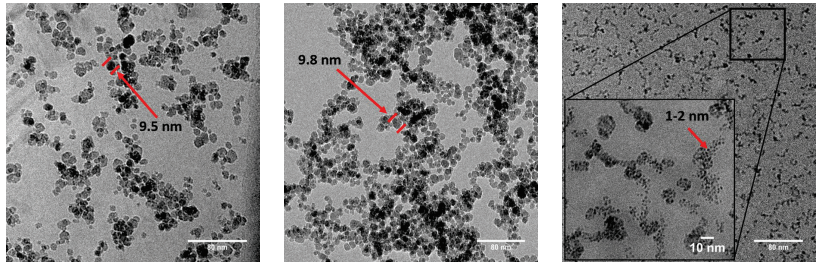
Impact of Coating Type on Structural and Magnetic Properties of Superparamagnetic Iron Oxide Nanoparticles for Theranostics

Amal Nasser[1,2], Asma Qdemat[3], Harald Unterweger[4], Rainer Tietze[4], Xiao Sun[5], Joachim Landers[6], Juri Kopp[6], Baohu Wu[2], Marie-Sousai Appavou[2], AnastasiiaMurmiliuk[2], Elliot Paul Gilbert[7], Oleg Petracic[3], and Artem Feoktystov[2*]

[1] Department of Physics, Technical University Munich (TUM), Garching, Germany
[2] Forschungszentrum Jülich GmbH, Jülich Centre for Neutron Science JCNS at MLZ, Garching, Germany
[3] Forschungszentrum Jülich GmbH, Jülich Centre for Neutron Science JCNS-2, Jülich, Germany
[4] ENT Department, Section of Experimental Oncology and Nanomedicine (SEON), Else Kroener-Fresenius-Stiftung-Professorship, University Hospital Erlangen, Germany
[5] Deutsches Elektronen-Synchrotron DESY, Hamburg, Germany
[6] Faculty of Physics and Center for Nanointegration Duisburg-Essen (CENIDE), University of Duisburg-Essen, Duisburg, Germany
[7] Australian Centre for Neutron Scattering, Australian Nuclear Science and Technology Organisation, Lucas Heights, Australia
*Email: a.feoktystov@fz-juelich.de

Superparamagnetic iron oxide nanoparticles (SPIONs) are promising nano-vehicles for biomedical applications such as drug delivery, imaging, and magnetic hyperthermia. However, one of the limitations of these systems is their tendency to agglomerate, which has a direct impact on the efficiency of their performance. One way to overcome this limitation is to apply a coating during synthesis. In this work, we have investigated the effect of three biocompatible coatings on controlling the agglomeration of iron oxide nanoparticles. The biocompatible coatings used are sodium citrate, (3-aminopropyl)triethoxysilane (APTES), and dextran. The structural and magnetic properties of the coated nanoparticles are characterized using various experimental techniques, including cryogenic transmission electron microscopy (cryo-TEM), magnetometry, Mössbauer spectroscopy, and small-angle X-ray and neutron scattering. The results show that the coatings effectively stabilize the nanoparticles, and lead to clusters of different sizes which then modifies their magnetic behaviour due to magnetic inter-particle interactions. We also investigated the oxidation kinetics of the nanoparticles prepared with the various coating materials as a function of time to characterize the oxidation behaviour and stability. This research provides valuable insights into the design of an optimized nanoparticle functionalization strategy for biomedical applications.



(a) (b) (c)

Figure. Cryo-TEM images of SPIONs with **(a)** sodium citrate, **(b)** APTES and **(c)** dextrane coating. Red arrows indicate single nanoparticles in the clusters. The size of the single nanoparticles is given exemplarily.

Magnetic Harvesting of Microplastics Using Multicore Iron Oxide Nanoparticles prepared by a Scaled-up Procedure

Alvaro Gallo-Cordova*, Belén Corrales-Pérez, Sabino Veintemillas-Verdaguer, Jesús G. Ovejero, and María del Puerto Morales

Materials for Medicine and Biotechnology Group, Institute of Materials Science of Madrid (ICMM/CSIC), C/ Sor Juana Inés de la Cruz 3, 28049, Madrid, Spain

*email: alvaro.gallo@csic.es

The rise of emerging contaminants presents notable ecological hazards and endangers human health. Recent findings reveal that numerous facial and body scrubs contain excessive amounts of primary microplastics (MPs) used as micro-exfoliants. These MPs are irresponsibly released into domestic water systems, becoming vehicles for the bioaccumulation of toxins (*e.g.* organic pollutants and heavy metals) [1]. It is crucial to develop reproducible and scalable materials and technologies to mitigate these adverse effects.

The present work demonstrates the performance of multicore flowered-shaped nanoparticles (NFs) of 40 nm in diameter for the magnetic retrieval of polyethylene MPs originated from cosmetics in water samples. One of the key highlights of this study is the successful scaling up of the polyol synthesis method for producing these NFs to a gram-scale based on a previous study on their formation mechanism [2]. This achievement is underscored by the comprehensive analysis across colloidal, structural and magnetic properties, yielding a 91% of mean reproducibility, particularly noteworthy considering the scale of mass production involved [3].

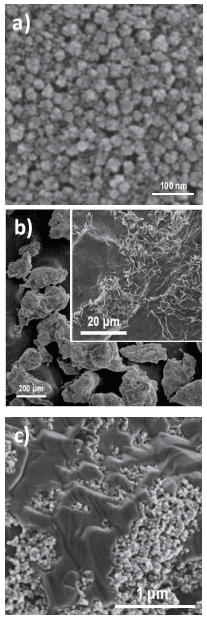


Fig. 1. SEM micrographs of a) NFs, b) MP and c) NFs@MPs

Furthermore, this work demonstrates the practical application of these NFs in addressing the challenge of MPs removal from water sources. For this purpose, the upscaled NFs were directly affixed to the surface of MPs via ultrasonic treatment, as displayed in Fig.1, with variations in conditions such as pH (3, 7, and 10), contact time (5, 30, and 120 min), and NFs to MPs weight-to-weight ratio (0.2, 1, and 4). The findings demonstrate that using a permanent magnet with a field strength of 320 kA/m enables the complete removal of MPs in all cases. Under optimal conditions (pH 7, 10 mg NFs, 30 min), the maximum removal capacity of MPs was determined to be 1000 mg_{MP}/g_{NF}. Lastly, the magnetophoretic mobility of NFs@MPs was evaluated, revealing a limiting velocity of $1.2x10^{-3}$ m/s, representing a velocity ten times faster than that of single-core particles of similar size [3].

These findings underscore the potential of these materials in addressing the challenges associated with emerging contaminants.

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Enhancing the diagnostic capabilities of magnetotactic bacteria *via* the incorporation of terbium and gadolinium

Lucía Gandarias[1,2*], Elizabeth M. Jefremovas[3,4], David Gandia[5], Lourdes Marcano[5,6,7], Virginia Martínez-Martínez[8], Pedro Ramos-Cabrer[9,10], Daniel M. Chevrier[11], Sergio Valencia[6], Luis Fernández Barquín[3], Mª Luisa Fdez-Gubieda[5], Javier Alonso[3], Ana García-Prieto[11], Alicia Muela[1]

[1]Dpto. Inmunología, Microbiología y Parasitología, Universidad del País Vasco (UPV/EHU), Leioa, Spain; [2]Aix-Marseille Université, CEA, CNRS, BIAM, Saint-Paul-lez-Durance, France; [3]CITIMAC, Universidad de Cantabria, Santander, Spain; [4]Institut für Physik, Johannes Gutenberg Universität, Mainz, Germany; [5]Dpto. Electricidad y Electrónica, Universidad del País Vasco (UPV/EHU), Leioa, Spain; [6]Helmholtz-Zentrum Berlin für Materialien und Energie, Berlin, Germany; [7]Departmento de Física, Universidad de Oviedo, Oviedo, Spain; [8]Dpto. Química Física, Universidad del País Vasco (UPV/EHU), Leioa, Spain; [9]Center for Cooperative Research in Biomaterials (CIC BiomaGUNE), Donostia-San Sebastian, Spain; [10]IKERBASQUE, Basque Foundation for Science, Bilbao, Spain; [11]Dpto. Física Aplicada, Universidad del País Vasco (UPV/EHU), Bilbao, Spain

*email: lucia.gandarias@cea.fr

Magnetotactic bacteria are non-pathogenic aquatic microorganisms that intracellularly synthesize magnetic nanoparticles named magnetosomes. Due to their magnetic behavior, their intrinsic motility and their ability to sense and respond to chemical signals, magnetotactic bacteria are envisaged as biological nanorobots [1]. In fact, they have been successfully tested as drug delivery carriers [2] and as heating agents in magnetic hyperthermia cancer treatment [3].

In this work we go a step further by adding extra functionalities to the magnetotactic bacterium *Magnetospirillum gryphiswaldense* MSR-1 using a simple yet effective method: the addition of terbium and gadolinium ions to the culture media [4]. First, the incorporation of terbium and gadolinium into the bacteria and the magnetosomes was verified and their distribution was analyzed by means of X-ray absorption near-edge structure (XANES) spectroscopy and by scanning X-ray fluorescence (XRF) imaging. Then, we studied the extra functionalities added to the modified bacteria. Terbium confers luminescent properties to MSR-1, which makes this bacterium a potential biomarker (Figure 1). On the other hand, gadolinium turns MSR-1 into a dual contrast agent for magnetic resonance imaging (MRI), adding T_1 contrast to the already existing T_2 contrast due to the magnetite nanoparticles inside the bacteria (Figure 1). Finally, given their potential clinical applications, the diagnostic ability of the modified MSR-1 was successfully tested *in vitro* in two cell models, confirming its suitability as fluorescent markers for bacteria incorporating terbium, and as dual contrast agents for MRI in the case of bacteria incorporating gadolinium.

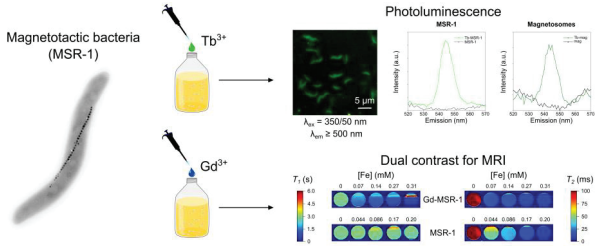

Figure 1. Summary of the performed study. MSR-1 magnetotactic bacteria were grown in the presence of terbium and gadolinium which conferred them additional diagnostic functionalities as biomarkers and as dual contrast agents in MRI, respectively.

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From bench to bedside: engineering magnetic particles for cancer diagnostics and therapy from industry perspective

Isabel Gessner [1,*], Jonathan Fauerbach [1]

[1] Miltenyi Biotec, R&D Reagents, Bergisch Gladbach, Germany

* corresponding/presenting author

Magnetic particles have found widespread application in imaging, therapy and diagnostics. At Miltenyi Biotec, we develop tailored magnetic particles in our research laboratories and optimize their use in biomedical applications. I will give an insight on how magnetic particle research and product development is happening in an industrial setting and showcase some interesting examples of how magnetic particles can be used with patients to diagnose or treat cancer. Examples include cell separation and activation of immune cells from patient samples.

Automatic Dimension Measurement of Magnetic Nanoparticles on Electron Microscope Images using Deep Neural Networks

Rafael C. Giménez-Aguilar[1*], Raúl Alonso-Calvo[1], Antón Cid-Mejías[1], M. Puerto Morales[2], Helena Gavilán[2], José Crespo[1], and Víctor Maojo[1]

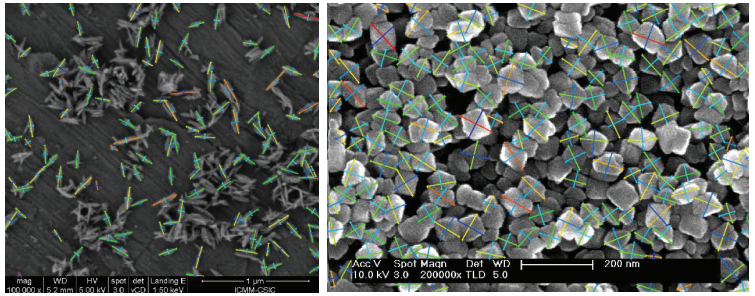
[1] Biomedical Informatics Group (GIB), Escuela Técnica Superior de Ingenieros Informáticos, Universidad Politécnica de Madrid, Campus de Montegancedo S/N, Madrid 28660, Spain
[2] Instituto de Ciencia de Materiales de Madrid, ICMM/CSIC, Sor Juana Inés de la Cruz 3, Madrid 28049, Spain
*Email: rafael.gimenez@upm.es

Magnetic colloids are widely used in biomedical applications such as Magnetic Resonance Imaging and Magnetic Hyperthermia treatments. Small variations in magnetic nanoparticle size, geometry, structure, or orientation strongly affect its magnetic properties, and thus its effectiveness and safety. Therefore, particle characterization constitutes a pivotal task in the advancement of such applications.

Said characterization is often done manually or semi-automatically through Electron Microscopy images. These methods, however, tend to be repetitive and labor-intensive tasks and can suffer from operator-related bias even when following set measurement standards. Recent contributions have shown increased interest in fully automatic methods for nanoparticle characterization, with most steering towards machine learning approaches employing annotated training datasets. In this paper, we present an approach to automatically determine the diameter and width of magnetic nanoparticles of varying morphologies in Electron Microscopy images. This was accomplished through the generation of a synthetic training dataset through 3D rendering, which was then used to train a well-established instance segmentation architecture, Mask R-CNN. The resulting model output binary masks are then processed following the set ISO 13322-1 standard.

The proposed method's measurements show small deviations in width and diameter when compared to manual annotations, being most consistent when presented with images that fit the ISO 13322-1 recommendations, i.e., samples with high resolution and few overlapping particles.

A sample of the output measurements on Scanning Electron Microscopy images is presented in the figure below, where Figure (a) contains needle-shaped nanoparticles and Figure (b) shows octahedral-shaped ones.



(a) (b)

Figure. Automatically generated measurements on a Scanning Electron Microscopy image containing **(a)** needle-shaped and **(b)** octahedral-shaped magnetic nanoparticles.

Hybrid contrast nanomaterials for advanced therapy tracking via multimodal imaging

Manuel A. González Gómez[1,2*], Yolanda Piñeiro[1], Francis Leonard Deepak[2] and José Rivas[1]

[1]NANOMAG Laboratory, Applied Physics Department, Materials Institute (iMATUS) and Health Research Institute of Santiago de Compostela (IDIS), Universidade de Santiago de Compostela, Santiago de Compostela, 15706, Spain
[2]Nanostructured Materials Group, International Iberian Nanotechnology Laboratory (INL), Avenida Mestre Jose Veiga, Braga 4715-330, Portugal
E-mail manuelantonio.gonzalez@usc.es

Early detection and monitoring of diseases, along with personalized precision medicine, are crucial for public health. Advanced research on nanomaterials shows promise for clinical use in therapeutics and medical imaging. Despite this progress, there are still unresolved challenges in precision medicine [1].

Magnetic nanoparticles based on superparamagnetic iron oxide nanoparticles (SPIONs) have demonstrated considerable potential across various biomedical applications. They encompass magnetic resonance imaging (^{1}H-MRI) and offer the possibility of coupling with radioisotopes (such as ^{18}F or ^{89}Zr) for positron emission tomography (PET) imaging. This hybridization of MRI and PET enables bimodal diagnostic imaging capabilities, enhancing the precision and depth of medical diagnostics. Additionally, SPIONs are utilized for targeted delivery of therapeutic agents or genetic material and for magnetic hyperthermia.

These nanoparticles possess favorable traits such as biocompatibility, biodegradability, readily modifiable surfaces for bioagent attachment, and high saturation magnetization, enabling remote magnetic control. Moreover, iron oxide-based nanoparticles have received approval from the Food and Drug Administration (FDA) and are presently employed clinically as contrast agents owing to their robust contrast activity and well-tolerated performance in vivo.

Additionally, SPIONs can be combined with other materials, such as fluorescent agents or natural protein biopolymers (e.g., gelatin shells). These combinations are being intensively investigated as carriers for long-term drug delivery, cell tracking, gene therapy, and other biological applications [2].

In this work, we present the combined capabilities of fluorescent multi-core@shell magnetic gelatin nanostructures as a robust multimodal platform for cutting-edge imaging modalities and revolutionary gene therapy applications.

Acknowledgment
This work was partially supported by the CARTsol project, (PLEC2022-009217 funded by MICINN/AEI/under NextGenerationEU/PRTR program), BOW project, Grant 952183 (FETPROACTEIC-05-2019) and the Xunta de Galicia (Spain) for the Postdoctoral Fellowship Grant (reference ED481B Call 2023).

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Towards size optimization of magnetic nanoparticles in a continuous production process by applying machine-learning based models

Lennart Göpfert[†], Lukas Glänzer[†], Eva Miriam Buhl[‡], Thomas Schmitz-Rode[†] and Ioana Slabu[†]

[†]Institute of Applied Medical Engineering, Helmholtz Institute, Medical Faculty, RWTH Aachen University, Pauwelsstr. 20, 52074 Aachen, Germany

[‡]Institute of Pathology, Electron Microscopy Facility, RWTH University Hospital Aachen, Pauwelsstr. 30, 52074 Aachen, Germany

Email: slabu@ame.rwth-aachen.de

The breakthrough in translation of magnetic scaffolds for applications in, e.g., regenerative medicine and tumor therapy depends to a high extent on the availability of controlled upscaled production of magnetic nanoparticles (MNP) with tailored properties. As an example, tailoring MNP size was shown to be beneficial in enhancing the performance of MNP in magnetic fluid hyperthermia, magnetic resonance imaging, and magnetic particle imaging. For this, continuous production processes are particularly suitable, as they enable the synthesis of MNP in high quantities under standardized reaction conditions (e.g. temperature gradient and mixing time) leading to e.g. narrower MNP size distribution. However, continuous processes cannot reach the outmost of their capability to produce MNP with tailored properties to fulfill the requirements on the quality of resulting MNP (e.g. specific core size). This is due to the lack of reliable kinetic information for chemical process design (e.g., for nucleation and crystal growth). As a result, the selection of appropriate MNP synthesis parameters is challenging because they cannot be directly derived from kinetic data. A wide range of parameters can be varied to continuously produce MNP: Besides reactant type for iron core synthesis and coating agent, mixing and residence time play a major role in tailoring MNP size. Machine-learning based models (such as support vector regression and gradient boosting) promise to predict the synthesis parameters that lead to tailored MNP sizes. Based on established continuous synthesis experiments varying the above-mentioned parameters, the prediction accuracy of such models is tested (cf. Figure 1). In future applications, such models can be integrated in feed-back loops for autonomous MNP size optimization during production.

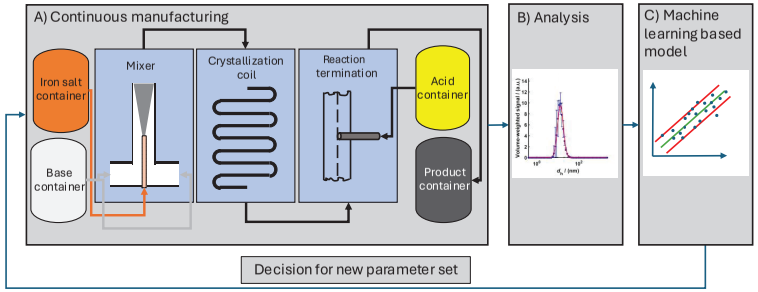

Figure 1: Sketch of the continuous modularly built MNP manufacturing, using a mixer, crystallization coil and reaction termination unit (A). Analysis of the MNP size via dynamic light scattering (B). Adjustment of the experimental parameters of continuous manufacturing (A) according to the machine-learning based models (C). New experimental parameters are obtained based on the results from C.

Atomistic Studies of Magnetization Reversal in Magnetite Nanoparticles

Roman Gröger[1*], Ondrej Hovorka[2]

[1]Institute of Physics of Materials & CEITEC IPM, Czech Academy of Sciences, Žižkova 22, 61600 Brno, Czech Republic
[2]University of Southampton, Faculty of Engineering and Physical Sciences, Southampton SO17 1BJ, United Kingdom
[*]E-mail: groger@ipm.cz, Tel.: +420 532 290 448

In magnetic hyperthermia, superparamagnetic nanoparticles are subjected to an alternating magnetic field that reorients the magnetic moments of individual magnetic ions. Due to the large surface-to-volume ratio a significant fraction of these magnetic moments corresponds to surface ions that are not constrained by magnetocrystalline anisotropy. The alternating magnetic field forces the magnetic moments on individual magnetic ions into the direction of the field and thus facilitates the magnetization reversal. During this process, the energy of the system changes from a local minimum over a maximum to another minimum. For materials with uniaxial anisotropy, as assumed in the widely used Stoner-Wolfarth model [1], this energy barrier is proportional to $\sin^2\theta$, where θ is the orientation of the magnetic field relative to one of the low-energy orientations of magnetic moments. An extension of this model to nanoparticles requires more systematic studies of the process of magnetization reversal and, especially, determining the shape of the barrier that the system has to overcome while reversing the external field. These simulations have to be made using atomistic models that take into account both ionic and spin degrees of freedom [2, 3].

In this work, we determine the shape of the energy barrier for reversing the magnetization in a single-domain nanoparticle of magnetite. The particle is initially a truncated cube [4] but its precise shape at 300 K is determined by molecular dynamics within the NPT ensemble. The orientations of magnetic moments are determined by coupling the motion of individual ions with spin dynamics described by the Landau-Lifshitz-Gilbert equation. Investigation of the process of magnetization reversal is started by first orienting the magnetic moments into one of the easy directions using a large magnetic field. A similar calculation is done on a replica of the same particle to orient the moments using the field applied in the opposite direction. The minimum energy path of the system between these two configurations is determined using the geodesic nudged elastic band method [5] in the configurational space of dimension $5N$ spanned by the positions of all ions and orientations of magnetic moments. This calculation provides not only the shape of the barrier that the system has to overcome when reversing the direction of magnetic field but also the mechanism by which the magnetic moments of individual ions change their orientations. These results allow a direct generalization of the Stoner-Wolfarth model to single-domain magnetite nanocubes. Moreover, they set the stage for more accurate studies of magnetization reversal in systems of interacting nanoparticles.

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Temporal and spatial resolution of magnetosome degradation at the subcellular level in a 3D lung carcinoma model

Alicia G. Gubieda [1*], Lucía Gandarias [1], Mihály Pósfai [2,3], Ajith Pattammattel [4], M. Luisa Fdez-Gubieda [5], Ana Abad Díaz de Cerio [1], Ana García-Prieto [6]

[1] Dep. of Immunology, Microbiology and Parasitology, University of the Basque Country (UPV/EHU), Spain
[2] Research Centre of Biomolecular and Chemical Engineering, University of Pannonia Veszprém, Hungary
[3] HUN-REN-PE Environmental Mineralogy Research Group, Veszprém, Hungary
[4] National Synchrotron Light Source II, Brookhaven National Laboratory, Upton, NY 11973, USA
[5] Department of Electricity and Electronics, University of the Basque Country (UPV/EHU), Spain
[6] Department of Applied Physics, University of the Basque Country (UPV/EHU), Spain
** Email: Alicia.gascon@ehu.eus*

Magnetotactic bacteria are a group of bacteria that can align themselves along the earth's magnetic field thanks to organelles called magnetosomes. Magnetosomes are magnetic nanoparticles enveloped by a lipid bilayer membrane that can be made of magnetite (Fe_3O_4) or greigrite (Fe_3S_4) of high chemical purity, and have very uniform morphology and a narrow size distribution. These properties, together with their low toxicity and their bio-compatibility make them good candidates for many biomedical applications, such as magnetic hyperthermia [1,2].

Despite the biomedical potential of magnetosomes, very little is known about their degradation in human cells, and even less so of their degradation within tumours, which are the target of many intended treatments. Three-dimensional tumours present characteristics that might affect the degradation process of magnetosomes: tight cell interactions that could affect nanoparticle excretion, and acidic microenvironment that could accelerate degradation, and a state of cell-cycle arrest inside the tumours that could slow down the degradation process. In an effort to explore the potential of magnetosomes for cancer treatment, we have investigated their degradation process of magnetosomes, isolated from *Magnetospirillum gryphiswaldense*, in 3D human lung carcinoma model over 36 days after internalisation.

We describe the degradation process at the subcellular level and with nanometre resolution, using state of the art hard X-ray probes, nano-XANES and nano-XRF. The spatial resolution of these methods allows for the detection of iron phases even if they are minoritary within the global sample. Our results reveal two different processes with spatial and temporal resolution. On the one hand, we observed an oxidation of magnetosomes to maghemite, which occurred mainly during the first 10 days and then the magnetite/maghemite content continued stable with maghemite taking up to 36% of the iron of the cell. On the other hand, we detected the *de novo* mineralisation of small particles of magnetite and ferrihydrite by ferritin. Therefore, the low degradation rate of magnetosomes within tumours and their ability to biosynthesise magnetite suggests that low magnetosome dosages could be used for prolonged periods for magnetic hyperthermia cancer treatments.

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COMPASS based stability monitoring of magnetic nanoparticles exemplified on bacterial magnetosomes

J. Günther[1*], T. Kampf[2], M.A. Rückert[1], T. Reichl[1], S. Markert[3], S. Rosenfeldt[4], D. Schüler[3], A.S. Schenk[4], F. Mickoleit[3], V.C. Behr[1], P. Vogel[1,5]

[1] Experimental Physics 5 (Biophysics) University of Würzburg, Germany. [2] Diagnostic and Interventional Neuroradiology, University Hospital Würzburg, Germany. [3] Department of Microbiology, University of Bayreuth, Germany. [4] Department of Physical Chemistry, University of Bayreuth, Germany. [5] Pure Devices GmbH, Germany.
*E-Mail: Johanna.Guenther1@uni-wuerzburg.de

Magnetosomes are a promising type of magnetite-based magnetic nanoparticles (MNP), that are biosynthesized by magnetotactic bacteria. Using synthetic biology, the particles can be precisely engineered with regard to controlling the particle size and thus, their magnetic properties as well as the surface characteristics. Thereby, the genetic approach enables the selective functionalization of the magnetosomes by targeted binding of foreign molecules on the MNP surface [1]. To characterize these properties, highly sensitive and robust measurement techniques are of high interest. A novel and promising method to provide information about the characteristics of a particle dispersion is Critical Offset Magnetic PArticle SpectroScopy (COMPASS), which is highly sensitive towards changes of the particle mobility inside a fluid [2].

To gain reliable information about a particle system, a two-dimensional COMPASS fingerprint was evaluated. This measurement is based on a critical phase effect occurring in the signal of a single higher harmonic in the nonlinear magnetization response when an oscillating excitation field H_{AC} is combined with a static offset field H_{DC}. This critical effect only occurs for specific ratios of H_{AC} and H_{DC}, that are referred to as critical points (CP). By collecting the signal of a single harmonic for different combinations of H_{AC} and H_{DC} between 0 and a maximum field value (here 25 mT), one can achieve two-dimensional patterns visualizing the occurring critical points for the measured field range. It has been shown that these patterns are characteristic for particle properties like size or shape, but also properties of the surrounding media like viscosity or temperature.

Comparing the COMPASS fingerprints allows a classification of MNP systems regarding their stability allowing monitoring of the MNP and their surroundings. This concept has been verified by comparing magnetosomes and their behavior in different buffer solutions. As shown in Figure 1, the fingerprints of magnetosomes in water and in HEPES/EDTA show significant differences. While the magnetosomes in water show linear structures of the CP, in HEPES/EDTA a more curved behavior of the CP on the fingerprint pattern is observed. Via a simulation, these curved patterns were qualitatively reproduced by mixing two types of nanoparticles of a different size distribution. Thus, the change of the fingerprint of magnetosomes in HEPES/EDTA suggests, that a part of the particles tended to form clusters, indicating a lower colloidal stability of the MNP.

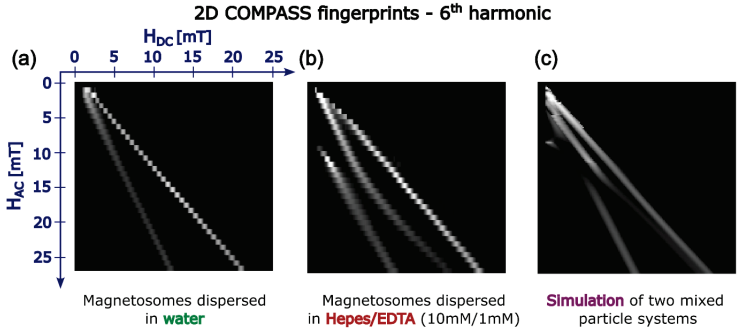

Fig. 1: (a), (b): Measurement of 2D COMPASS fingerprints of magnetosomes in water and in HEPES/EDTA. (c): Simulation of two mixed MNP systems of different size distribution.

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Critical Role of the Magnetocrystalline Anisotropy on the Frequency-dependent Hyperthermia Performance of Magnetite Nanoparticles

Daniel Failde[1], Víctor Ocampo[2], David Serantes[2], and Òscar Iglesias[3*]

[1]Centro de Supercomputación de Galicia (CESGA), Santiago de Compostela, Spain
[2]Applied Physics Dept.and Instituto de Materiais (iMATUS), Univ. de Santiago de Compostela, 15782 Santiago de Compostela, Spain
[3] Dpt. de Física de la Matèria Condensada and IN2UB, Univ. de Barcelona, Martí i Franquès 1, 08028 Barcelona, Spain
*Email: oscariglesias@ub.edu, Mobile: +34 680390126

The role of the magnetocrystalline anisotropy is usually not properly considered when studying the heat release of magnetic nanoparticles (NPs) under AC magnetic fields, building the interpretation of the results upon the assumption that an *effective* uniaxial anisotropy can be a correct description. However, magnetite NPs, which are used in multiple biomedical applications, are characterized by a negative cubic magnetocrystalline anisotropy constant $K_C<0$. Recent works [1,2] have evidenced that the contribution of this kind of anisotropy is non-negligible. With this motivation, we have carried out a theoretical study using simulations based on the LLG equation, computing hysteresis loops to extract the Specific Absorption Rate (SAR) of magnetite NPs. The role of K_C on the SAR of NPs with different aspects ratios (and, therefore, different shape uniaxial anisotropy constants K_U) and sizes has been studied as a function of the frequency f and amplitude of the applied field H_{max}. The results show a complex scenario, with an essentially linear dependence of the SAR on f for the large NPs (cubic with 22 nm side) when H_{max} is large enough to ensure major loop conditions. Significant deviations from the f-independent Stoner-Wohlfarth like behavior (f-independent) are obtained in the entire 0.1-1.0 MHz range, which become more marked the smaller the K_U contribution. Strikingly, when studying the H_{max}·f conditions satisfying either the Brezovich or the Thiesen-Jordan criteria, the magnetocrystalline contribution is shown to play a key role in reaching significant heating, as shown in Fig. 1. Work supported by Spanish MINECO (PID2019-109514RJ-I00, PID2021-127397NB-I00), Catalan DURSI (2021SGR0032). We thank CESGA for computing support.

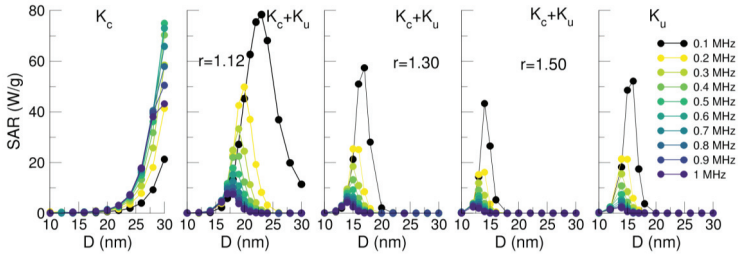

Fig. 1: *SAR vs. f, for H_{max}-f conditions satisfying the Brezovich criteria. Results shown for: only cubic, only uniaxial anisotropy and combined anisotropies for NPs of different aspect ratios r.*

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Carboxylated nanomagnets for biomedical use: influence of shell composition

Erzsébet Illés[1*], Etelka Tombácz[2], Vladan Kusigerski[3], Ana Mrakovič[3], Davide Peddis[4]

[1] Department of Food Engineering, University of Szeged, Szeged, Hungary
[2] Soós Ernő Water Techn. Research and Development Center, University of Pannonia, Hungary
[3] The Vinča Institute of Nuclear Sciences, Mike Petrovića Alasa 12-14, 11351 Belgrade, Serbia
[4] Dept. of Chemistry and Industrial Chemistry, Università degli Studi di Genova, Genova Italy
E-mail: erzsebet.illes@mk.u-szeged.hu

Superparamagnetic iron oxide nanoparticles (SPIONs) serve as multifunctional nanoplatforms for various applications in biomedicine (e.g. magnetic hyperthermia and controlled drug release) and catalysis due to their unique magnetic properties. Magnetically induced heating of SPIONs is influenced by amplitude/frequency of the applied AC field and by the magnetic properties and anisotropy, i.e. size and shape, of nanoparticles. We report here a comparative study on magnetic and structural features of several coated SPIONs with the same magnetic core but with different shell composition designed for biomedical application.

Spherical nanomagnets (d_{TEM} ~10 nm) were synthesized by chemical coprecipitation as magnetic core and double layer of oleic acid (OA-OA), polyethylene glycol with oleic acid (PEG-OA), polyacrylic acid (PAA), polygallic acid (PGA) and a carboxylated PEG copolymer (P(PEGMA-AA)) were applied as biocompatible shell. All samples consist of interacting single-domain SPIONs based on magnetization measurements (ZFC, FC, TRM). It was also shown that the dipolar interparticle interactions were reduced after coating (i.e. the interparticle distance was increased), as T_{max} decreased from ~250 K to ~230 K, but they are still dominating over the exchange interactions. Although, IONPs are in the superparamagnetic state at room temperature in all samples, the polycarboxylate shell enhance the saturation magnetization (M_S), while the oleate layers induce a clear decrease in M_S. AC magnetic hyperthermia studies (252-808 kHz, 50-250 Gauss) showed that PAA, PGA and P(PEGMA-AA) coated SPIONs produced similar temperature increase as the bare ones, while OA content in the shell led to significant reduction in heat release. Beyond the improved magnetic properties, the preliminary colloid stability, hemocompatibility and MRI results indicated that PAA, PGA and P(PEGMA-AA) coated SPIONs are promising candidates for biomedical use.

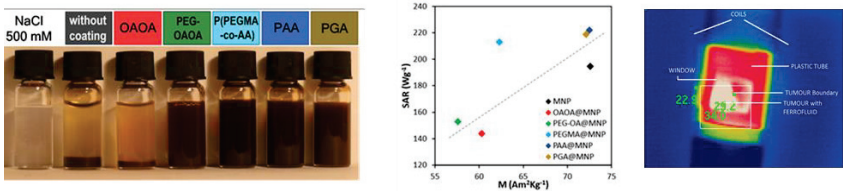

Figure 1 Salt tolerance (left) and hyperthermic efficiency of the coated nanomagnets (centre and right)

Acknowledgments: This work was supported by the National Research, Development, and Innovation Fund of Hungary (FK 131739) and the János Bolyai Research Scholarship of the HAS.

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Magnetic nanoflowers for biomedical purposes

Viktória Varga[1], Erzsébet Illés[2*]

[1] Department of Physical Chemistry and Materials Science, University of Szeged, Szeged, Hungary
[2] Department of Food Engineering, University of Szeged, Szeged, Hungary
E-mail: erzsebet.illes@mk.u-szeged.hu

The colloid aqueous dispersion of superparamagnetic iron oxide nanoparticles (SPIONs) is very popular partly due to their potential theranostic application. Their favorable magnetic properties can be further improved by preparing flower-like structures. There have been some studies in recent years, aiming to prepare magnetite nanoflowers (MNF), however, the preparation conditions are quite different and lack detailed stability experiments. In this study, the MNFs were prepared both in an autoclave and in a round-bottom flask (either with or without continuous mixing) in diethylene glycol (DEG) and N-methyl-diethanolamine (NMDA) mixture. The results verified the crucial importance of some preparation conditions, such as the composition of the reaction solvent mixture, reaction time and rate of heating and cooling. Transmission electron microscopic images (TEM) of the nanoparticles revealed that as an effect of mixing, more fluffy structures with an average particle diameter of 18.3 ± 2.3 nm were obtained (Figure 1).

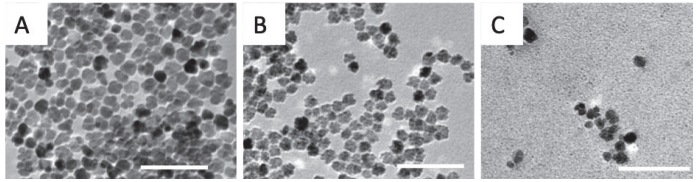

Figure 1. TEM images of MNF prepared without (A), with continuous mixing (B), and *in situ* stabilized by PAA (C). The scale-bar above represent 100 nm.

The magnetite structure was verified by X-ray diffraction measurements. With the variation of synthesis parameters, it has been revealed that the cooling rate plays a crucial part in the resulting NPs with an average particle diameter ranging from about 72 nm to ~20 nm. As a stabilizing agent, poly(acrylic acid-co-maleic acid) (PAM) and poly(acrylic acid) (PAA) was applied both during and after synthesis. The optimal pH and amount of stabilizing polymer were confirmed by both zeta-potential and dynamic light scattering measurements. As for the hyperthermia result, our MNFs unquestionably possess a high effect, underlying the morphology suggestion for increased effect of the cooperation of small magnetic individuals. As a result, our NPs define the requirement of stabile flower structures with increased hyperthermia effect.

Acknowledgments: This research was supported by the Hungarian National Research Development and Innovation Office (NRDIH) through the FK131739 project and by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.

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Static Magnetic Response of Intracellular Clusters of Superparamagnetic Nanoparticles

Alexey O. Ivanov[1*], Anna Yu. Solovyova[1], Sergey A. Sokolsky[1], Elena V. Grokhotova[1], and Ekaterina A. Elfimova[1]

[1] Institute of Nature Sciences and Mathematics, Ural Federal University, Lenin Av. 51, Ekaterinburg 620000, Russia
*Email: Alexey.Ivanov@urfu.ru

Currently, there is a lack of clear information on the magnetic properties of nanoparticles confined within biological cells. Based on indirect evidence, it is frequently observed that magnetic nanoparticles tend to lose mobility and become immobilized at specific locations once they enter cells. Moreover, it is highly probable that nanoparticles aggregate into clusters during the immobilization process, with the topology and sizes of these clusters potentially varying significantly. Hence, predicting the magnetic behavior of these clusters theoretically necessitates incorporating predefined information regarding their properties.

In this research, we model a cell, containing a cluster of magnetic nanoparticles, as a multicore particle (MCP), with the magnetic nanocores located in a fixed configuration. The nanocores are considered to be small (~ 10 nm), so the energy barrier of magnetic anisotropy, which prevents the spontaneous reorientation of the SPP magnetic moment due to thermal fluctuations, is not higher than the thermal energy. Hence, we assume the nanocore as a spherical superparamagnetic particle (SPP), allowing the magnetic moment to rotate freely within the immobilized SPP.

Here, our focus is on theoretical examining the response of the MCP to a static uniform magnetic field. The key-point of our study is the consideration of rather small MCP, containing only few SPPs. We trace the dependence of the MCP magnetic response on the orientation structure, forming in the clusters of SPPs due to the interparticle dipole–dipole interaction. For this, we consider two arrangements of the SPPs within the cubic lattice, differently oriented relative to a magnetic field [1]. To maintain the spherical symmetry of the MCP we use the smallest possible numbers of the SPPs as 7 and 8. By means of the Monte Carlo computer simulations we investigate the orientation probability density for the SPP magnetic moments, and we discovered the different orientation behavior for the SPPs located in various parts of the MCP. We suggest the rough classification, namely, the ‘tip’, the ‘internal’ and the ‘surface’ SPPs, according their reaction to the field. The ‘tip’ SPPs are the most sensitive, while the ‘surface’ SPP magnetic moments can form the ring-like orientation texture with closed magnetic flux, and the ‘internal’ SPPs magnetic moments might be considered as ‘frozen’ due to intensive interparticle interaction with the magnetic moments of surrounding SPPs.

In addition, we simulate the magnetic response of the small MCP with randomly located SPPs. The simulated orientation probability densities demonstrate that all basic ‘tip’, ‘surface’ and ‘internal’ classification types of SPPs can be identified for each random MCP configuration. We calculate also the averaged magnetization over the ensemble of random MCP configurations, and this magnetization is described rather accurately by the continuous media magnetostatics. We hypothesize that this effect is due to the fact that the averaging over the ensemble of random configurations of the SPPs inside MCP leads to formation of some effective MCP medium.

The research was supported by the Russian Science Foundation, Grant No. 23-12-00039.

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Predictive Modelling for Enhanced Precision in Microswarm Steering under Rotating Magnetic Fields

Benjamin W. Jarvis[1+], Daryoush Nasirian[2+], Kiana Abolfathi[1], Mohammad Reza Hairi Yazdi[2], Ali Kafash Hoshiar[1*]

[1] School of Computer Science and Electronic Engineering, University of Essex, Colchester CO4 3SQ, UK

[2] School of Mechanical Engineering, University of Tehran, Tehran 1439955961, Iran

[+] B. W. Jarvis and D. Nasirian equally contributed to this work

*Email: a.kafashhoshiar@Essex.ac.uk, Phone:+44 (0)1206 872932

Abstract:

Magnetic nanoparticle (MNP)-based microrobots represent a promising technology in drug delivery systems with the potential to revolutionize the medical field within this decade. The MNPs can be effectively steered collectively, forming a microswarm, through the application of rotating magnetic fields. As illustrated in Fig. 1 (a), diverse modes exist for manipulating these microswarms using rotating fields. Recent studies have categorized the navigation behaviours of microswarms under rotating magnetic fields, showing that microswarms forming chain-like structures exhibit lower dispersion and achieve higher velocities compared to others under similar conditions. This insight underscores the significance of swarm morphology in optimizing navigational efficiency and precision. As shown, this research focuses on identifying and modelling the most effective steering mechanisms under these conditions using experimental set-up shown in Fig. 1 (b). Our goal is to develop a predictive modelling approach that identifies and optimizes the steering mechanisms of MNPs, ensuring precise and efficient navigation of microswarm. The experiment set-up depicted in Fig. 1(b) are designed to characterize the key parameters influencing the steering behavior of these microswarms. While previous studies have explored swarm formation, the detailed modelling for steering behavior under rotating magnetic fields remains underexplored. To address this, we employ mathematical models that capture the behavior of the particles, based on the forces illustrated in Fig. 1(a). These predictive models are then validated against experimental data. Finally, a comprehensive parametric study under a variety of conditions will be performed. This approach will enhance our understanding of microswarm navigation and lays the groundwork for refining and optimizing steering mechanisms using comprehensive models presented in this work.

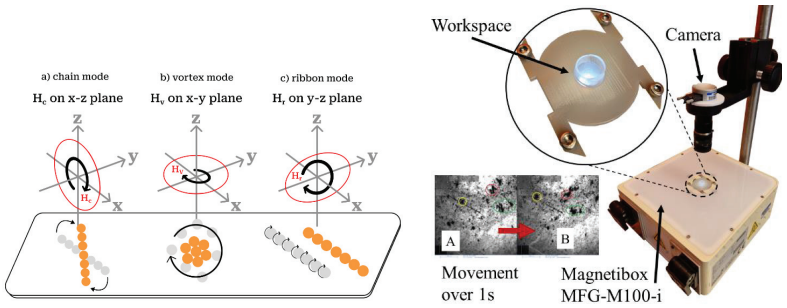

Fig.1(a) shows the various motion modes under each rotational magnetic field orientation employed to navigate the microswarm, (b) illustrates the experimental setup designed for steering microswarm and conducting studies on their navigation (image A and B show the swarm clusters to move over a 1 second time interval).

Unraveling nanoparticle-cell surface interactions: Insights into SynC uptake dynamics

Lena Kampen[1], Amani Remmo[2], Nike Fiebig[1], Olaf Kosch[2], Shailey Twamley[1], Norbert Löwa[2], Frank Wiekhorst[2], Antje Ludwig[1]

[1] Deutsches Herzzentrum der Charité, Charitéplatz 1, 10117 Berlin, Germany.
[2] Physikalisch-Technische Bundesanstalt, Abbestr. 2-12, 10587 Berlin, Germany.
*Corresponding author: Lena Kampen, lena.kampen@dhzc-charite.de

Citrate-coated Synomag® nanoparticles (SynC) have proven suitable for magnetic particle imaging (MPI)-based cell tracking of THP-1 monocytes due to their high magnetic moment, biocompatibility, and rapid uptake [1]. Before internalization, magnetic nanoparticles (MNP) must pass the extracellular glycocalyx. Cell-surface glycosaminoglycans (GAGs) were recently identified as a regulator for nanoparticle uptake [2]. With this work, we investigate whether the rapid uptake of SynC can be explained by interaction with cell-surface GAGs.

To determine whether SynC nanoparticles bind to GAGs before their uptake, we labeled extracellular GAGs using click-chemistry. The intracellular fluorescence did not increase upon adding SynC, indicating that SynC binding to labeled extracellular structures did not accelerate their turnover. To validate our findings, we used GAG-deficient cells and measured the effects of GAGs on the magnetic properties of SynC using real-time magnetic particle spectroscopy (MPS). MPS provides a high-temporal resolution method to unravel interactions between MNPs and cells [3]. GAG-proficient and GAG-deficient cells induced similar magnetic behavior changes in SynC during the initial seconds of cell contact, indicating that GAGs do not directly interact with SynC in a manner that affects their magnetic properties.

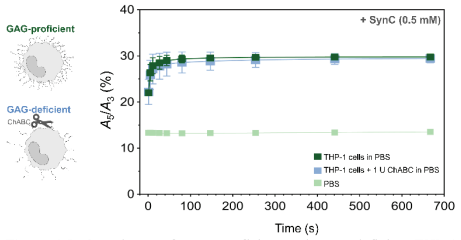

Figure 1 Left: Scheme of GAG-proficient and GAG-deficient THP-1 cells treated with Chondroitinase ABC (ChABC). **Right:** MPS of SynC in the presence of GAG-proficient and GAG-deficient cells. B = 12 mT, B_{off} = 0.05 mT at 37°C. Mean ± SD (n=3).

Our work presents a significant advancement in the study of nanoparticle-glycocalyx interactions by integrating real-time MPS and click-chemistry-based labeling of GAGs. By employing MPS, we can capture the initial seconds of nanoparticle interaction with cells, inaccessible with conventional methods. Based on our work, we propose that the absence of GAG-based repulsion for SynC explains its rapid uptake. This discovery has significant implications for MPI-based cell tracking with SynC, allowing efficient labeling of cell types lacking GAG-based repulsion of SynC. Moving forward, we aim to correlate the matrix profile of endothelial cells cultivated under atherosclerotic risk conditions with SynC uptake dynamics using MPI.

1. Remmo, A., et al., *Counting cells in motion by quantitative real-time magnetic particle imaging.* Scientific Reports, 2024. **14**(1): p. 4253.
2. Olivieri, P.H., et al., *Cell-surface glycosaminoglycans regulate the cellular uptake of charged polystyrene nanoparticles.* Nanoscale, 2022. **14**(19): p. 7350-7363.
3. Poller, W.C., et al., *Initial interaction of citrate-coated iron oxide nanoparticles with the glycocalyx of THP-1 monocytes assessed by real-time magnetic particle spectroscopy and electron microscopy.* Scientific Reports, 2020. **10**(1): p. 3591.

New Encapsulated Magnetic Systems Based On Nano Ferrites For Biological and Hyperthermia Applications.

Angelika Kmita[1]*, Marta Stolińska[1], Dorota Lachowicz[1], Jan Żukrowski[1], Katarzyna Nowicka-Dunal[2], Marcin Sikora[1]
[1]AGH University of Krakow, Academic Centre for Materials and Nanotechnology, A. Mickiewicza 30 St., 30-059 Krakow, Poland,
[2]AGH University of Krakow, Faculty of Materials Science and Ceramics, A. Mickiewicza 30 St., 30-059 Krakow, Poland,
*corresponding author: **akmita@agh.edu.pl**

Ferrite nanoparticles with spinel structure are the subject of intensive research due to low toxicity, photocatalytic activity and tunable electronic and magnetic properties. Ferrite nanoparticles (FN) based on Co, Ni, Mn, and Zn has shown potential for real-life applications due to high magnetic anisotropy and biocompatibility. The aim of the research is design, synthesis and characteristics of new encapsulated magnetic systems based on functional ferrite nanoparticles (FN): e.g. stoichiometric zinc ferrite nanoparticles (ZFNs), non-stoichiometric (ZFNn), cobalt ferrite nanoparticles (CFN) or manganese ferrite nanoparticles (MFN) (Figure (a)) with sodium alginate (SA). The temperature influence on structural and physical-chemical changes occurring in these nanoparticles were determined. The hyperthermic effect of the (FN) systems (Figure (c) was investigated using the apparatus for induction heating of nanoparticle solutions based on Ambrell EasyHeat source (Figure (b)).

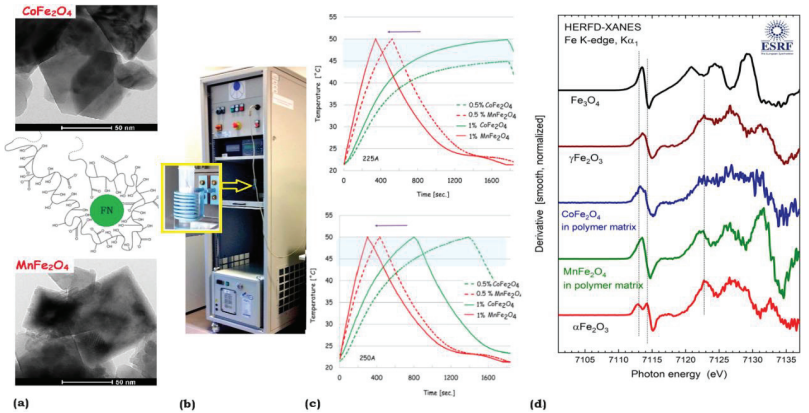

Figure. (a) New Encapsulated Magnetic Systems like CFN@SA or MFN@SA (b) Apparatus for nanoparticle hyperthermia research. (c) Temperature dependence from heating time for samples with different concentration of (FN) in polymer matrix: 0.5% or 1% (the intensity of the electromagnetic power (AC current): 250A and 250A). **(d)** Iron 1s2p HERFD-XANES spectra from the (FN) in polymer matrix (were collected at ID26 beamline of European Synchrotron Radiation Facility (ESRF)).

Vibrating Sample Magnetometer (VSM) systems are used to measure the magnetic properties of (FN) as a function of magnetic field and temperature. Additional temperatures of the (FN) decomposition and profiles of oxygen liberation during their thermal decomposition were tested. The decomposition degree of (ZG) and products of its decomposition as well as the activation energy (E_a) of this process were determined. The mechanism of the thermal decomposition of (FN), taking into account the degree of their non-stoichiometry, was also proposed. Modern equipment was used for the research, including synchrotron radiation (XAS-XANES) (Figure (d), Mössbauer spectroscopy (MS), X-Ray Photoelectron Spectroscopy (XPS) and many others.

Magnetic Mapping of Bio-Inspired Clusters of Iron Oxide Nanoparticles

Kenzington Kottenbrock[1], Sierra Reis[1], Samuel Oberdick[2,3], Gunjan Agarwal[1]
The Ohio State University[1], National Institute of Standards and Technology[2], University of Colorado[3]

Iron oxide nanoparticles (IONs) are of significance in many biological applications. Living organisms store natural reservoirs of iron using the metalloprotein ferritin, which is comprised of an iron oxide core surrounded by a protein shell. Synthetic IONs can be used to label, sort and track cells as well as facilitate hyperthermia and targeted drug delivery. Therefore, the quantification and spatial localization of both naturally occurring and synthetic IONs is important to health and disease applications.

IONs have a magnetic moment that is defined by the size of the particle and its composition. While the magnetic moment of single IONs is relatively weak, clusters of particles can act collectively, such that their structure at an intermediate mesoscale level can ultimately affect their magnetization. The magnetization of nanoparticle cluster can be complex, since it arises from interactions between many individual nanoparticles and is therefore a function of cluster geometry and composition. The overall goal of this study was to investigate how the clustering of IONs on the mesoscale (< 1µm) affects their overall magnetic properties.

Synthetic ION clusters with well-defined size, shape and density were generated using a top-down microfabrication approach. Various imaging modalities were utilized to characterize the ION clusters: scanning electron microscopy (SEM) (Figure 1a,b), magnetic force microscopy (MFM) (Figure 1d-g) and super-conducting quantum interference device (SQUID) magnetometry. We also created identical micropatterns of solid iron thin films.

Our results indicate that mesoscale clustering of synthetically produced IONs can significantly affect their magnetic properties. The clustering effects the phase signal from MFM and is dependent on lift height. Additionally, the magnetic fields of the clusters begin to collectively contribute to the phase signal when they are <1µm apart. These aspects can thus serve as an important parameter in interpreting the magnetic signal arising from an ensemble of IONs in biological samples.

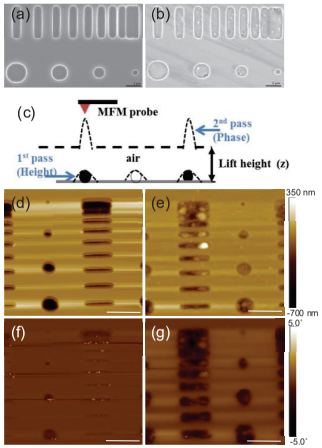

Figure 1: SEM images of micropatterned (a) empty wells and (b) wells filled with Fe_3O_4 NP. (c) In MFM, a magnetically coated probe takes two passes, during the first, it takes a topographical scan, and the second pass detects magnetic interactions at a specific lift height (z) above the samples. Topography images of micropatterned (d) empty wells and (e) wells filled with Fe_3O_4 NP. MFM phase images at (f,g) 100 nm lift height.

Amplification- and Enzyme-Free Magnetic Diagnostics Circuit for Whole-Genome Detection of SARS-CoV-2 RNA

Enja Laureen Rösch[1], Rebecca Sack[1], Mohammad Suman Chowdhury[1], Florian Wolgast[1], Margarete Zaborski[2], Frank Ludwig[1], Meinhard Schilling[1], Thilo Viereck[1], Ulfert Rand[2], Aidin Lak[1]*

[1]Institute for Electrical Measurement Science and Fundamental Electrical Engineering and Laboratory for Emerging Nanometrology (LENA), TU Braunschweig, Germany
[2]Leibniz Institute, German Collection of Microorganisms and Cell Cultures GmbH (DSMZ)
Inhoffenstr. 7b, Braunschweig, 38124, Germany
*E-Mail: a.lak@tu-braunschweig.de

Highly specific and sensitive detection of nucleic acids-based disease biomarkers such as viral DNA/RNA, circulating tumor DNA, and microRNA has gained enormous attention in the past few decades. Reverse transcription polymerase chain reaction (RT-PCR), digital PCR, and droplet digital PCR are used for viral DNA/RNA detection. However, PCR requires well-equipped labs and sophisticated equipment. Among various nanoparticles-based bioassays developed during the COVID-19 pandemic, magnetic nanoparticles (MNPs)-based assays offer a highly promising biosensing platform. Magnetic bioassays (MAs) harness magnetic relaxation dynamics that is highly sensitive to molecular interactions between MNPs and targeting analytes, making them wash-free, inherently quantitative, and allows assays directly on non-processed biofluids. Significant improvements regarding the assay sensitivity and miniaturization were achieved when magnetic particle spectroscopy (MPS) had been transformed into a highly sensitive and cost-effective technique. Yet, the specificity of clustering-based MAs is largely compromised by unspecific clustering of MNPs through various interactions. Additionally, they suffer from low sensitivity, since each target is used irreversibly and thus such approaches cannot offer any target recycling.

Here we propose a declustering-based approach using a so-called **M**agnetic signal **A**mplification **C**ircuit (MAC) to address these two major shortcomings. The MAC combines the specificity of toehold-mediated strand displacement (TM-DSD) reactions and sensitivity of MPS harmonics to the state of clustering/declustering of MNPs. In the MAC, responsive magnetic clusters (RMCs) disintegrate into their building block MNPs upon detecting target nucleic acids [1]. The continuous disintegration of RMCs amplifies the MPS harmonics amplitudes, and thus increases the assay sensitivity. Using MAC, we showcase the detection of N gene of whole genome of SARS-CoV-2 via a mix-and-measure assay workflow with minimal sample processing (Figure 1). The assay is performed in one-pot, at 25 °C, and the measurements are performed on a low-cost benchtop MPS device. Our MAC platform can be highly beneficial in "low-income" settings for detection of various nucleic acid biomarkers, where thermal cycling and enzymatic reactions are not esteemed.

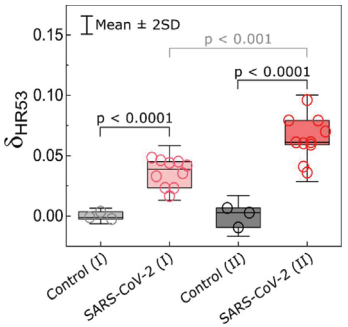

Figure 1: Relative changes in the MPS harmonics ratio upon sensing two sets of SARS-CoV-2 RNA genome samples. The control samples contain exactly the same components as the test samples without the target. Validation of MAC assay by qPCR and ddPCR and obtaining the qPCR Ct values between 26 and 22 for a typical aliquot from set (I) and (II), respectively.

[1] E. Rösch et al., Amplification and extraction free quantitative detection of viral nucleic acids and single-base mismatches using magnetic signal amplification circuit, *Biorxiv* (2022).

Differential swelling of IPNs for multi-stimuli soft actuation

Alberto Leon-Cecilla[1,2*], Mingchao Zhang[3], Metin Sitti[3,4,5], Modesto T. Lopez-Lopez[1,2]

[1] Universidad de Granada, Escuela de Doctorado de Ciencias, Tecnologías e Ingenierías, Departamento de Física Aplicada, Granada 18071, Spain
[2] Instituto de Investigación Biosanitaria Ibs.GRANADA, Granada 18012, Spain
[3] Physical Intelligence Department, Max Planck Institute for Intelligent Systems, Stuttgart, Germany
[4] Institute for Biomedical Engineering, ETH Zürich, Zürich, Switzerland
[5] School of Medicine and College of Engineering, Koç University, Istanbul, Turkey
*Email: alcecilla@ugr.es

The field of soft robots and actuators continues to expand, driven by the potential of soft materials in technological and biomedical applications. To meet the demands of such applications, the development of novel materials capable of responding to diverse stimuli while possessing high toughness is essential. Hydrogels, with their soft consistency, innate responsiveness to stimuli, and capacity to incorporate solid inclusions within the polymeric network, are particularly interesting. However, many hydrogels fall short of the required characteristics, prompting the exploration of alternative strategies such as interpenetrating polymer networks (IPNs). IPNs combine the properties of two or more polymeric networks, resulting in multi-responsiveness and enhanced toughness.

This study presents magnetic interpenetrating hydrogel sheets composed of acrylamide (chemically cross-linked) and sodium alginate, which is physically cross-linked with a diffusion-controlled gradient along the sheet thickness. Neodymium (NdFeB) microparticles are embedded within the polymeric network. The physicochemical properties of this matrix make it responsive to pH changes and the application of a magnetic field. The gradient in the cross-linking density within the alginate network leads to differential swelling along the sheet thickness, offering programmability for actuators. Differential swelling changes the material's shape, which is subsequently recorded on the material by applying a magnetic field that magnetizes the NdFeB particles. The reapplication of a magnetic field to the deswollen gel restores its previous shape (Figure A).

The mechanical anisotropy, the swelling capacity as a function of pH, the gel curvature as a function of the cross-linking gradient and sheet thickness, and the microscopic structure were characterized to elucidate the role of the cross-linking gradient in the material's behaviour. As a proof of concept, a magnetic pumping valve capable of pumping water and mixing the surrounding medium upon application of an alternating magnetic field was designed (Figure B).

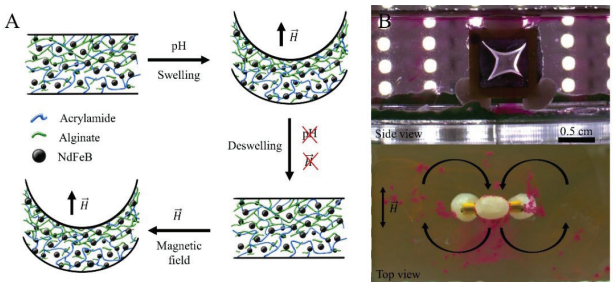

Figure. (A) Sketch of the programming procedure. (B) Magnetic pumping valve.

Acknowledgments: This study was supported by grant PID2020-118498GB-I00 funded by MCIN/AEI/10.13039/501100011033, Spain. A.L.-C. acknowledges grant FPU19/01801 funded by MCIN/AEI/10.13039/501100011033 and "ESF Investing in your future", Spain. Laura Quesada de la Torre is acknowledged for drawing the graphics in Figure A.

Multifunctional magnetic nanoplatforms for combined chemo-hyperthermia treatment

Rosalía López-Méndez[1], Nuria Lafuente-Gómez[1], Marina París[1,2], Yurena Luengo[1], Aida Serrano[2], Julio Camarero[1,3], Gorka Salas[1,4], Álvaro Somoza[1] and Ana Espinosa[5,1]

[1]IMDEA Nanociencia, C/ Faraday 9, 28049 Madrid, Spain
[2]Departamento de Electrocerámica, Instituto de Cerámica y Vidrio, ICV-CSIC, Kelsen 5, 28049 Madrid, Spain
[3]Departamento de Física de la Materia Condensada and Instituto 'Nicolás Cabrera', Universidad Autónoma de Madrid, 28049 Madrid, Spain
[4]Nanobiotecnología (IMDEA-Nanociencia), Unidad Asociada al Centro Nacional de Biotecnología (CSIC), 28049 Madrid, Spain
[5]Instituto de Ciencia de Materiales de Madrid, ICMM-CSIC, 28049 Madrid, Spain

E-mail: rosalia.lopez@imdea.org

The emergence of nanomedicine promises revolutionary advancements in the diagnosis and treatment of diseases through the utilization of nanomaterials. Nanoparticles can penetrate cell membranes and be remotely manipulated to elicit healing effects, enabling the progression to safer and more effective therapeutic approaches [1]. Hyperthermia therapy is an anticancer clinical practice based on elevation of the tumor temperature, driving malignant cells and tissues up to the cytotoxic level, that is, 43-48 °C. In addition, cell resistance against traditional treatments, such as chemotherapy or radiotherapy, can be temporally reduced [2]. Among nanomaterials, magnetic nanoparticles stand out as a prominent class due to their high potential in biomedicine, serving as efficient agents for hyperthermia treatment, drug delivery and magnetic resonance imaging [3-4]. In this work, we report the synthesis of a multifunctional drug delivery system comprising magnetic iron oxide nanoparticles (IONPs) combined with a chemotherapeutic agent, doxorubicin (DOX), for multimodal hyperthermia-based anticancer treatments. The stability of these DOX-loaded IONPs in the tumor environment has been characterized by X-ray absorption spectroscopy (XAS) at the Fe K-edge (7112 eV), concluding that DOX-loaded IONPs are highly stable when internalized into tumor cells. Finally, nanoparticle and doxorubicin co-localization was studied pre- and post-thermal treatment, analyzing drug release and the internalization of doxorubicin into the nucleus.

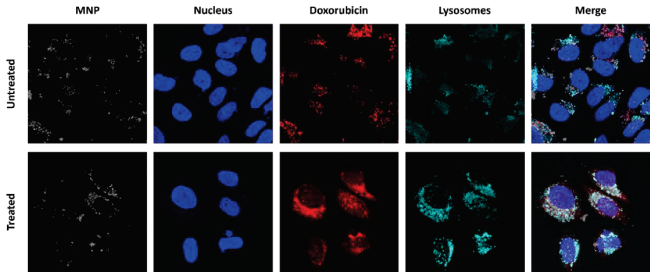

Figure. Confocal images illustrating the simultaneous study of NP localization and doxorubicin before and after combined hyperthermia treatment. Depicted in white (nanoparticles), blue (nucleus), red (doxorubicin), cyan (lysosomes), and merge represents the combination of all signals.

[1] Espinosa, A., et al. (2018) Adv. Funct. Mater. 28 (11), 1803660.
[2] Espinosa, A., et al. (2021) Nano Letters. 21 (1), 769-777.
[3] Lafuente-Gómez N. et al. (2021) Chem. Comm. 7, 13662–13677.
[4] Lafuente-Gómez, N. et al. (2021). Cancers. 13 (16), 4095.

Local Magnetic Hyperthermia and Systemic Chemotherapy Triggers Neo-angiogenesis without Involvement of Auto/Paracrine Tumour Cell VEGF Signalling and Hypoxia

Wisdom O. Maduabuchi [1], Felista L. Tansi [1], Bernd Faenger [1], Paul Southern [2,3], Quentin A. Pankhurst [2,3], Frank Steiniger [4], Martin Westermann [4] and Ingrid Hilger [1,*]

[1]Department of Experimental Radiology, Institute of Diagnostic and Interventional Radiology, Jena, University Hospital, Friedrich Schiller University Jena, Am Klinikum 1, 07747 Jena, Germany
[2]Resonant Circuits Limited, 21 Albemarle Street, London W1S 4BS
[3]Healthcare Biomagnetics Laboratory, University College London, 21 Albemarle St., London W1S 4BS, UK
[4]Center for Electron Microscopy, Jena University Hospital, Friedrich Schiller University Jena, Ziegelmühlenweg 1, 07743 Jena, Germany

There is a growing interest in exploring the therapeutically mediated modulation of tumor vascularization of pancreatic cancer, which is known for its poorly perfused tumor microenvironment limiting the delivery of therapeutic agents to the tumor site. Here, we assessed how magnetic hyperthermia in combination with chemotherapy selectively affects growth, the vascular compartment of tumors, and the presence of tumor cells expressing key regulators of angiogenesis.

To that purpose, a female nude mouse orthotopic PANC-1 (fluorescent human pancreatic adenocarcinoma) tumor model (Rj:Athym-Foxn1nu/nu) was used. Magnetic hyperthermia was applied alone or in combination with systemic chemotherapy (gemcitabine 50 mg/kg body weight (BW), nab-paclitaxel 30 mg/kg BW) on days 1 and 7 following magnetic nanoparticle application (dose: 1 mg per 100 mm3 of tumor, day 0). We used ultrasound imaging, immunohistochemistry, multi-spectral optoacoustic tomography (MSOT), and hematology to assess the biological parameters mentioned above.

We found that magnetic hyperthermia combined with systemic chemotherapy was able to impact tumor growth (decreased volumes and Ki67 expression) and to trigger neo-angiogenesis (increased small vessel diameter). The applied stressors activated specific pro-angiogenic mechanisms, which differed from those seen in hypoxic conditions involving HIF-1α, since (a) treated tumors showed a significant decrease of cells expressing VEGF, CD31, HIF-1α, and neuropilin-1; and (b) the total tumor blood volume and oxygen level remained un-changed.

We deduce that magnetic hyperthermia in combination with gemcitabine/nab-paclitaxel chemotherapy is able to trigger neo-angiogenesis in orthotopic pancreatic tumors in mice, presumably by mechanisms not directly associated with autocrine and paracrine VEGF signaling. Such mechanisms seem to be induced by therapeutic cell damage and cell stress in tumors that subsequently activate specific pro-angiogenic mechanisms, which differ from those seen in hypoxic conditions where HIF1a is typically involved. The therapeutically induced neo-angiogenesis is related to the activation of cell stress pathways, like the MAPK pathway. Furthermore, damaged/stressed tumor cells release specific pro-angiogenic factors other than VEGF or they induce pro-inflammatory responses via the secretion of inflammatory cytokines. The major contributor to the neo-angiogenic process during the bimodal therapy seems to be the magnetic hyperthermia modality. Since the interplay between various biological factors and pathways is complex in relation to the mechanisms underlying angiogenesis in pancreatic tumor cells, further studies are needed. In the long term, the bimodal modality of magnetic hyperthermia and gemcitabine/nab-paclitaxel chemotherapy of pancreatic tumors could serve as a useful tool to prevent severe desmoplasia and reduce tumor resistance during oncological treatments.

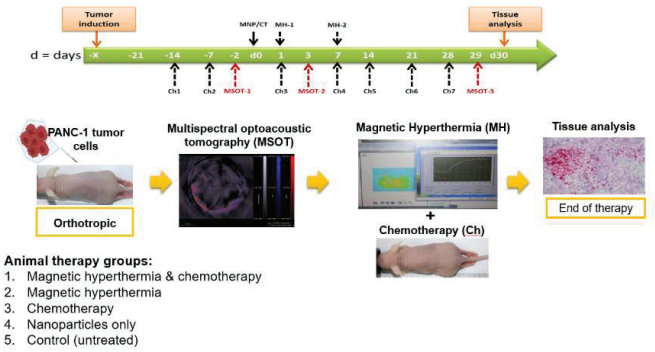

Figure 1. Timeline for therapy of orthotopic PANC-1 tumors in mice with magnetic hyperthermia and chemotherapy.

Magnetic Molecularly Imprinted Polymer for The Detection of Pathogenic Bacteria

J. Marfà[1,2], M.I. Pividori[1,2*]

[1]*Biosensing and Bioanalysis Group, Institute of Biotechnology and Biomedicine, Universitat Autònoma de Barcelona*
[2]*Grup de Sensors i Biosensors, Departament de Química, Universitat Autònoma de Barcelona Bellaterra, 08193, Spain*
[*]*Email: isabel.pividori@uab.cat*

The detection of target molecules at extremely low concentrations within complex biological or environmental samples remains a challenge in current rapid detection methods. A promising solution involves developing solid-phase preconcentration techniques that seamlessly integrate into emerging technologies. Biologically-modified magnetic particles (MPs) serve as powerful and versatile preconcentration tools for a variety of applications, their effectiveness is limited by high costs and poor stability under adverse conditions. To overcome these drawbacks, magneto-actuated molecularly imprinted polymers (m-MIPs) have emerged as a promising alternative. Although MIPs can exhibit lower affinity and selectivity compared to their biological counterparts, they offer distinct advantages such as cost-effectiveness, large-scale synthesis without animal involvement, and enhanced chemical and mechanical stability, allowing their use in harsh environments. Moreover, m-MIPs can be stored at room temperature without compromising analytical performance.

This study focuses on the synthesis of m-MIPs towards biotin and biotinylated biomolecules and their integration into a magneto-actuated platform. Specifically, commercial streptavidin-MPs were replaced with m-MIPs in magneto-actuated enzyme-linked immunosorbent assays (m-ELISA) to develop quantitative assays for various target analytes. Comparative binding studies were conducted using biotinylated biomolecules labeled with horseradish peroxidase (HRP) as an optical reporter to assess the specificity and selectivity of the m-MIPs against non-imprinted polymers and conventional MPs. Moreover, the viability of a one-step m-ELISA was evaluated, taking as a model the detection of the double-tagged PCR amplicons from the waterborne pathogen *E. coli*.

The results demonstrate that the integration of m-MIPs into m-ELISA, emerges as a cost-effective and robust alternative to commercial MPs, showcasing exceptional analytical features, achieving a limit of detection of 0.161 ng mL^{-1} (**Fig. 1**). The integration of m-MIPs into m-ELISA presents a significant opportunity to enhance the sensitivity, specificity, and reliability of target analyte detection, underscoring their suitability in sample pretreatment approaches and elevating the overall performance of the detection process.

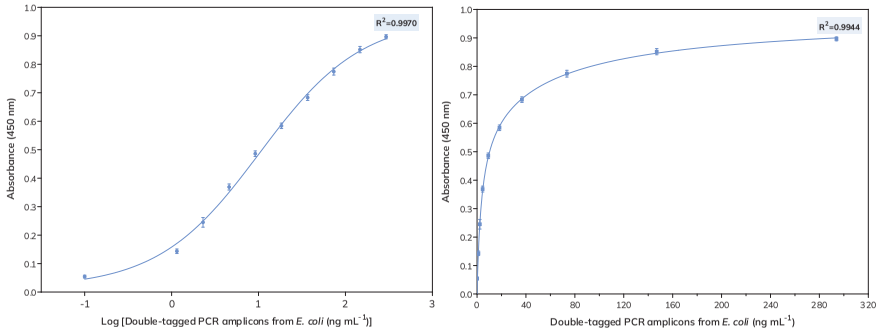

Figure 1. Characterization of the binding of the double-tagged DNA from *E. coli* O157:H7 on the m-MIP by magneto-actuated immunoassay in one step, in a concentration range from 0 to 294 ng mL^{-1}, 0.16 mg m-MIP and 10 mU mL^{-1} antiDIG-HRP. The negative controls are also shown (n=4). Error bars illustrate the standard deviation for the samples (n = 3).

Using Computational Tools to Guide the Synthesis of Substituted Magnetic Nanoparticles to Target Specific of Magnetic Saturation and Magneticocrystalline Anisotropy Values

Alex Malaj[a], Venkata Rohit Punyapu[b], Suvra Laha[a], Rachel B. Getman[b], O. Thompson Mefford,[a]*

[a]Department of Materials Science and Engineering, Clemson University, Clemson, SC 29634, USA
[b]William G. Lowrie Department of Chemical and Biomolecular Engineering, The Ohio State University, Columbus, OH 43210, USA
*Corresponding author: mefford@clemson.edu

Central to this project is the hypothesis that substituted metal ferrites can be produced with superior energy conversion properties, which we used to guide the design of such materials using methods in molecular simulations. Working under the assumption that particles bound in a cellular environment, we can focus on the Néel relaxation, and thus utilize predictive numerical simulations of Carrey et al. comparing the three leading theoretical models for the energy conversion in magnetic hyperthermia for single domain particles.[1] Given the applied field used in magnetic hyperthermia, the group was able to provide calculations for the ideal combination of the effective magnetic anisotropy (K_{eff}) and saturation magnetization (M_s).

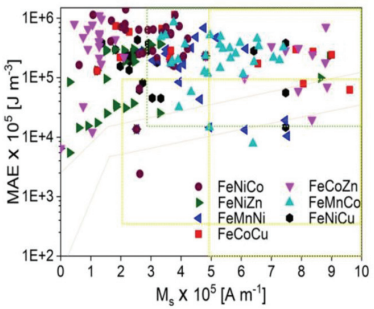

Figure: Calculated Ms and K_{eff} (listed as MAE)

Experimentally, synthesis and characterization of magnetic materials is time consuming. To create insight to help guide synthesis, we compute the relationship between ferrite composition and magnetic properties using density functional theory (DFT). Specifically, we compute Ms and K_{eff} for 571 ferrite structures with the formulae $M1_xM2_yFe_{3-x-y}O_4$, where M1 and M2 can be Mn, Ni, Co, Cu and/or Zn and $0 \leq x \leq 1$ and $y = 1 - x$. By varying composition, we were able to vary calculated values of Ms and K_{eff} by up to 9.6×10^5 A/m and 14.08×10^5 J m^{-3}, respectively (see figure). Our results suggest that composition can be used to optimize magnetic properties for applications in heating, imaging, and recording. This is mainly achieved by varying Ms, as these applications are more sensitive to variation in Ms than K_{eff}.

Utilizing this information, a series of particles were synthesized with varying substitutions of Mn and Co to optimize energy loss at a field at 32 kA/m @ 205 kHz. Particles were characterized via TEM, XRD, and DLS to demonstrate that their size was uniform across the series. Magnetometry revealed shifts in Ms than K_{eff} based on composition.

(1) Carrey, J.; Mehdaoui, B.; Respaud, M. Simple models for dynamic hysteresis loop calculations of magnetic single-domain nanoparticles: Application to magnetic hyperthermia optimization. *Journal of Applied Physics* **2011**, *109* (8), 083921. DOI: 10.1063/1.3551582.

Preparation and investigation of casein-coated magnetic nanoparticles for theranostic applications

Nils Meier[1], Christina Wenck[1], Eilien Heinrich[1], Frank Wiekhorst[2], Regina Bleul[1]*

[1] Fraunhofer Institute for Microengineering and Microsystems IMM, Carl Zeiss Straße 18 20, 55129 Mainz, Germany
[2] Physikalisch-Technische Bundesanstalt, Abbestraße 2-12, 10587 Berlin, Germany
*Email: regina.bleul@imm.fraunhofer.de

Magnetic nanoparticles (MNP) have been intensively studied in the biomedical field. They can be used as biosensors, for magnetic resonance imaging (MRI), for magnetic particle imaging (MPI) or as a hyperthermia treatment in cancer therapy. However, often they exhibit low stability in physiological medium or toxicity in such applications. Thus, a surface modification of the MNP is applied to enhance their stability and biocompatibility.[1] Casein is an abundant, amphiphilic protein that has unique drug release capabilities especially for hydrophobic or poorly soluble substances.[2] In this study we present the continuous production of single core iron oxide nanoparticles and their subsequent surface modification with casein as hydrophobic release layer.
The MNP were continuously produced by alkaline precipitation in a micromixer set-up and preliminary stabilized with tannic acid.[3] After magnetic separation the MNP were coated with Na-caseinate to improve their stability and further functionalize them with a hydrophobic release layer. A subsequent enzymatic crosslinking with transglutaminase was performed to further enhance coating properties.
The casein coated MNPs have been thoroughly investigated. The stability against salt induced aggregation improved and their magnetic behavior hardly declined even after immobilization. A hydrophobic model drug could successfully be encapsulated into the casein layer with encapsulation efficiency up to 74%. In cell viability test no negative influence of the casein coated MNP was distinguishable and the uptake into cell could be observed by fluorescent microscopy.
With the possibility of tracing the MNP with MPI and simultaneously delivering a pharmaceutical substance a huge step towards a theragnostic anti-cancer agent was made. Future studies will focus on encapsulating an anticancer drug and investigating the delivery and its effectiveness.

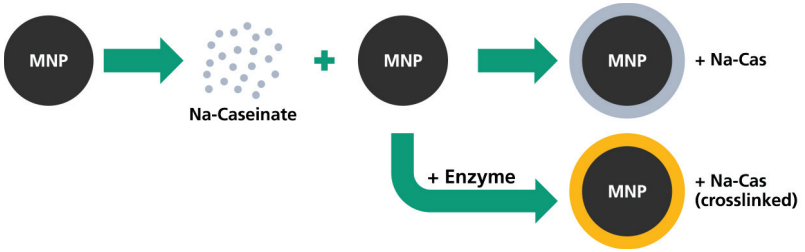

Figure 1 Schematic illustration of the MNP coating process with Na-caseinate and the preparation of MNP+Na-Cas and MNP+Na-Cas (crosslinked).

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Cerium surface-doped magnetic Iron Oxide Nanoparticles: Synthesis, Characterization and Catalytic Activity

Karen Mejía-Carmona[1,2] *, Neus G. Bastús [1], Víctor F. Puntes[1,2,3] *

[1] Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and BIST, Campus UAB, Bellaterra, 08193 Barcelona, Spain
[2] Universitat Autònoma de Barcelona (UAB), Campus UAB, Bellaterra, 08193 Barcelona, Spain.
[3] Vall d'Hebron Institut de Recerca (VHIR), 08035 Barcelona, Spain.
E-mail: karen.mejia@icn2.cat, victor.puntes@icn2.cat

Magnetic iron oxide nanoparticles (IONPs), particularly magnetite and maghemite NPs, have attracted significant interest because of their several nano- and biotechnological applications, particularly in the fields of biomedicine and biology.[1] The magnetic and chemical properties of IONPs, and consequently, their applications, are highly dependent on their size, morphology, atomic composition (such as doping), and surface.[2,3]

In this study, single crystal Cerium surface-doped Iron Oxide Nanoparticles (Ce@IONPs) of different sizes (up to 46 nm) were synthesized by a co-precipitation method in the presence of a cerium-citrate complex in aqueous media at room temperature. By adjusting the cerium-citrate concentration ratio, it was possible to achieve controlled growth and tune the size of the Ce@IONPs. Ce@IONPs were stable in aqueous media at a physiological pH. Ce@IONPs were successfully characterized using high-resolution scanning transmission electron microscopy (HR-STEM), powder X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS), and magnetometry. Finally, the obtained Ce@IONPs were tested as catalysts for mimicking peroxidase activity in the oxidation of 3,3´,5,5´-tetramethylbenzidine (TMB) by H_2O_2, showing an improved catalytic activity compared to the non-doped IONPs.

The versatility of this synthetic procedure was demonstrated by expanding its use with other lanthanide ions, thereby demonstrating its capability to obtain similar Ln@IONPs and its potential for a wide range of applications.

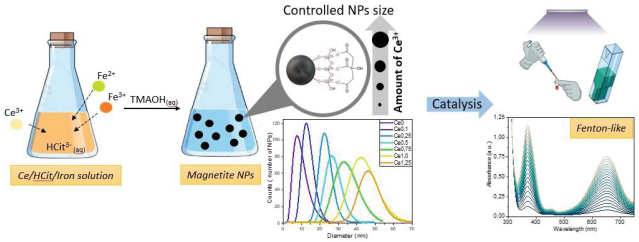

Figure 1. Schematic illustration of Ce@IONPs synthesis and oxidation of TMB by H_2O_2 in the Fenton-like reaction.

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Novel magnetic transduction methodology for DNA detection in liquids

Sedef Ozel-Okcu,[1*] M. J. Valle-Pastor,[2] P. Palacios-Alonso,[1,3] I. Mikelez-Alonso,[1] A. L. Cortajarena,[4] R. Delgado-Buscalioni,[3] and F. J. Terán[1,2]

[1] *Nanotech Solutions SL, Ctra Madrid, 23, 40150 Villacastin, Spain*

[2] *iMdea Nanociencia, C Faraday 9, Cantoblanco, 28049 Madrid, Spain*

[3] *Dpto Física Teórica Materia Condensada, Universidad Autónoma de Madrid, 28049 Madrid, Spain*

[4] *CIC biomaGUNE-BRTA, Paseo de Miramón 194, 20014 Donostia-San Sebastián, Spain*

**Email: sedef.ozel@ntsol.es*

In recent years, magnetic nanoparticles (MNPs) have been extensively employed for applied research in different disciplines thanks to their interesting dynamical magnetization properties. Biosensing is one application example exploiting MNPs magnetization dynamics to transduce biomolecular recognition phenomena to detect the presence of biomarkers in liquid samples. Recent works reported on a novel methodology based on variation of AC magnetization cycles of MNPs conjugated with receptors in absence or presence of the targeted biomolecule [1]. Here, we report on the latest methodology to detect DNA molecules in buffer saline solutions. Biotinylated DNA of different pair bases ranging from 8 up to 88 with persistent length were incubated with streptavidin conjugated cobalt ferrite nanoflowers (bs-MNPs) for 60 min at room temperature to unveil the sensitivity of this methodology. The AC magnetization cycles of bs-MNPs were analyzed in absence and presence of DNA molecules at different AC magnetic field conditions ranging from 5 up to 100 kHz and field intensities up to 32 kA/m. Different parameters such as MNPs concentration, number of streptavidin per bs-MNPs, and field conditions were explored to modulate the detection sensitivity by AC magnetometry. As shown in the Figure, molecular recognition phenomena between bs-MNPs and DNA chains result in multiple DNA chains bounded to individual bs-MNPs. Such specific interactions strongly influence the MNPs diffusion, which tightly depends on the number of streptavidin per bs-MNPs, DNA length and concentration. As shown in figure, AC magnetic area (A) varies up to 25% when MNPs surface is fully modified (i.e. bs-MNPs + 3 mM), or 12% when no DNA chains are bounded to streptavidin receptors (i.e. bs-MNPs + 0 mM) with respect to bare surface (i.e. MNPs). Hence, the distinct capacity of MNPs to bind DNA molecules results in different variation of AC magnetic area. This change can be adequately employed to detect DNA chains of distinct length and concentration in liquids. This approach provides optimal detection conditions for quantifying single DNA strands by simply modelling the dynamical magnetization behavior of individual bs-MNPs.

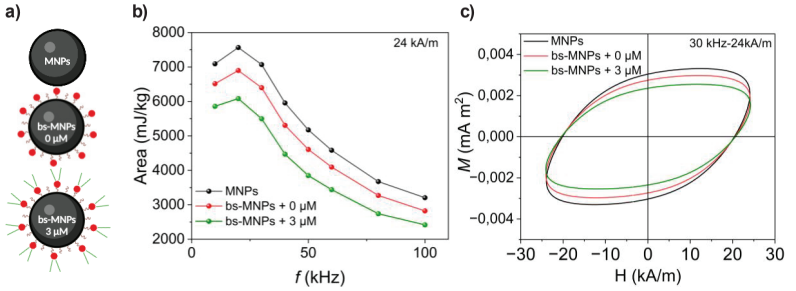

Figure: a) Schematic representation of the studied nanoparticle formulations; b) Frequency dependence of AC magnetic hysteresis area at 24 kA/m for different MNPs formulations at 1 g/L dispersed in 25 mM Tris solution; c) Comparison of AC magnetization cycles obtained from suspensions of different MNPs formulations at 30 kHz and 24 kA/m and 1 g/L.

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Funding: Authors acknowledge the financial support from STRIKE Project (GA Num. 101072462) funded by European Union HORIZON-MSCA-2021-DN-01.

Magnetic Nanoparticles Coated by Fluorescent Carbon Dots as T_2 contrast agent

Fatemeh Mohandes[1], Hamed Dehghani[2,3], Abdolreza Simchi[1]

[1]Department of Materials Science and Engineering, Sharif University of Technology, Tehran, Iran
[2]Biomedical Engineering and Medical Physics Group, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[3]Neuroimaging and Analysis Group (NIAG), Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
*Email: mohandes@ub.edu

In clinical diagnostics, magnetic nanoparticles with uniform particle size, high superparamagnetic moment, and high colloidal stability as contrast agent enhance image contrast by shortening longitudinal (T_1) and transverse (T_2) relaxation times between cancer and normal tissues in magnetic resonance imaging (MRI). Although the non-invasive character of MRI allows the repeated imaging to further interrogate tissues, the lack of resolution at a cellular level is considered as a limitation of MRI. Fluorescence microscopy unlike the MRI technique can provide greater resolution at the cellular level. Therefore, the combination of magnetic and fluorescent properties in one compound introduces new bimodal "two-in-one" magnetic-fluorescent materials to provide accurate delineation of normal and abnormal tissues. This work presents ferrites nanoparticles covered with nitrogen-doped graphene quantum dots (N-GQDs) for MRI and fluorescent dual mode imaging of cancerous tumors. Thermolysis of metal oxalates and phenylenediamine in organic solvents allows to facile synthesize hybrid magneto-fluorescent nanoparticles with average size of 55 nm and PL emission at about 600 nm. Figure 1 shows magnetic hysteresis loops of NPs as superparamagnetic particles. *In vivo* dispersion and biosafety of the hybrid nanoparticles have been improved by a polymer-coating strategy with the aid of polysorbate. *In vitro* studies for *SK-OV-3* cells revealed that the magneto-fluorescent particles are not toxic up to a high concentration of 125 µg/mL. The fluorescence intensity in the tumor tissue region appears to increase over time, and the tumor becomes clearly visible after 60 min *in vivo*. The MRI of phantoms and animal cases also indicate the high efficiency of the particles as an T_2 contrast agent in clinical diagnosis. As a result, the introduced nanoparticles offer great potential for dual mode imaging of malignant tumors.

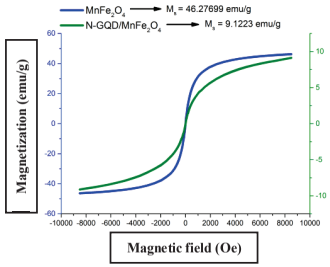

Fig. 1. Magnetic hysteresis loops of pure ferrites nanoparticles and covered with N-GQDs at room temperature.

Microfluidic Poiseuille Flow Induced by Magnetically Actuated Microscopic Cilia

Charles Paul Moore[1*], Marine Le Goas[2], Stefan Rouach[1,2], Jean-François Berret[2] and Jérôme Fresnais[1]
1 : Laboratoire PHENIX, Sorbonne Université, Paris, France
2 : Laboratoire Matière et Systèmes Complexes, Université Paris Cité, Paris, France
*Contact : charles.moore@sorbonne-universite.fr

Lungs are lined with a thin layer of mucus which aids in clearing away foreign particulate. To remove this dirty mucus from the lung, bronchi are lined with cilia: small hair-like structures which beat, forcing the mucus to flow upwards. One approach to studying cilia has been the use of artificial microfabricated cilia, which actuate under a varying magnetic field[1].

Our cilia, see Fig. 1, use soft lithography in order to fill moulds with iron microparticles, as well as polydimethylsiloxane, which is then cured[2]. We characterized these cilia by measuring their bending due to the magnetic field gradient of a permanent magnetic wand. These results are supplemented by simulated bending under the magnetic field. Simulated and measured deflection are in good agreement, exceeding 60° from upright. The simulation demonstrated that cilia with narrower bases, and greater iron concentration near the tip, experienced greater bending. Furthermore, cilia were sensitive to even microscale movement of the magnetic field.

By creating a rotating magnetic field, we are able to asymmetrically actuate our cilia. The cilia motion comprises a whipping active stroke, which is capable of pushing fluid forward, coupled with a recovery stroke, where the cilium slowly swings around to its original position, as illustrated in Fig. 2. We measured the pumping capacity of these actuated cilia by particle tracking velocimetry in closed channels. The asymmetric movement of the cilia results in pulsatile flow within the channel[3]. The flow profile within the channel was approximately parabolic, indicating the cilia created a pressure gradient which is driving the flow.

1 2

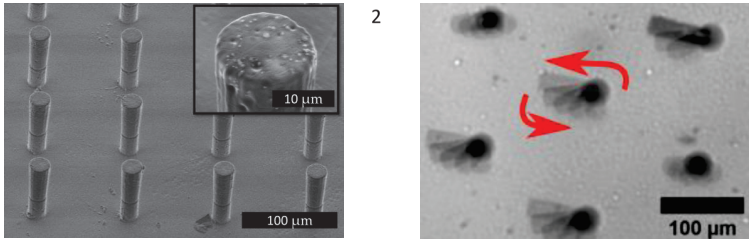

Figure (1) A scanning electron microscope image of magnetic cilia, at a 45° angle to the base. The inset shows a further magnification of the cilia tip, showing some imbedded iron microparticles. Scans were taken at 1 and 3 kV respectively. (2) Superimposed micrographs showing the active and recovery stroke of magnetic cilia under a rotating magnetic field.

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Impact of complex iron oxide nanoparticles phases on cellular responses and toxicity

***Marco A. Morales[1,2,6], *Iza Rozman[3,4,5], Alja Štern[3,4,5], Bojana Žegura[3,4,5], Enio Jr. Lima[2], Elin L. Winkler[1,2], Marcelo Vasquez[2] and Gerardo F. Goya[6,7]**

[1]Instituto Balseiro, Centro Atómico Bariloche, Av. Bustillo 9500, 8400 S. C. de Bariloche, Argentina

[2]Instituto de Nanociencia y Nanotecnología, CNEA, CONICET, Centro Atómico Bariloche, Av. Bustillo 9500, 8400 S. C. de Bariloche, Argentina

[3]National Institute of Biology, Department of Genetic Toxicology and Cancer Biology, Večna pot 121, 1000 Ljubljana, Slovenia

[4]University of Ljubljana, Kongresni Trg 12, 1000 Ljubljana, Slovenia

[5]Biotechnical Faculty, University of Ljubljana, Jamnikarjeva ulica 101, 1000 Ljubljana, Slovenia

[6]Universidad de Zaragoza, Departamento de Materia Condensada, C/ Pedro Cerbuna 12, 50009 Zaragoza, Spain

[7]Instituto de Nanociencia y Materiales de Aragón, CSIC-Universidad de Zaragoza, C/Mariana Esquillos S/N, 50018 Zaragoza, Spain

*Email: marco.morales@ib.edu.ar, iza.rozman@nib.si

The use of iron oxide nanoparticles in different bio-applications, such as nuclear magnetic resonance and anemia treatment, has raised concerns due to evidence of their potential to induce oxidative stress. This concern is amplified by the existence of different phases of iron oxide nanoparticles (e. g., wüstite, magnetite, maghemite) that exhibit distinct iron oxidation states and therefore surface catalytic reactions that may impact cell pathways by producing free radicals and reactive oxygen species (ROS).

Wustite-Magnetite Core-Shell nanoparticles (CS-NPs) represent a system of iron oxides where a large amount of electrons are available to carry out Fenton reactions and produce free radicals for a longer time compared to magnetite as a single phase. To study the effect of this two-phase system, CS-NPs of (9.6 +/ 0.5) nm were synthesized by thermal decomposition of organometallic metals and coated with glucose. In vitro cyto- and genotoxicity of CS-NPs were assessed using CellTiter-Glo® Luminescent Cell Viability Assay, and the Comet Assay, respectively, in an in vitro 3D cell model (spheroids) established from the human hepatocellular carcinoma (HepG2) cell line.

Spheroids were exposed to graded concentrations of tested CS-NPs for 24 and 96 hours. The results showed that tested CS-NPs reduced cell viability in a dose-dependent manner (tested up to 200 µg/mL) at both exposure times (Figure, left panel), while no significant increase in DNA damage was observed (Figure. right panel). The results of our study are a first step in the safety assessment of the potential health risks that studied NPs could cause in humans, which is a crucial step before these types of nanomaterials can be used in biomedical or clinical applications.

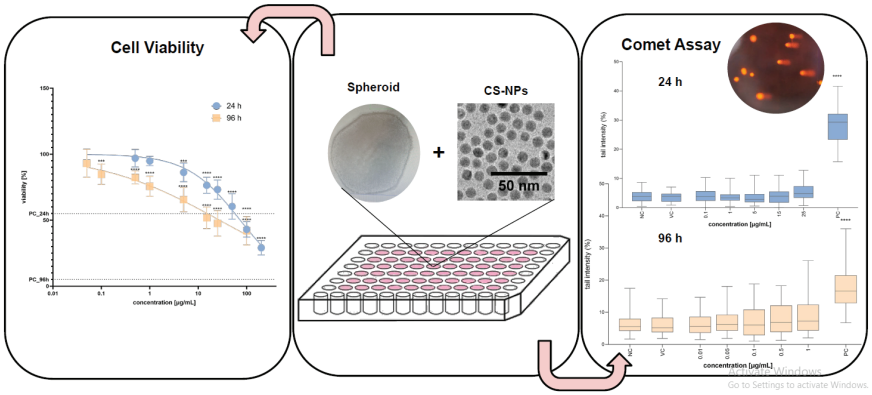

Figure. Viability of HepG2 cells in spheroids after the exposure to CS-NPs (0.5, 1, 5, 15, 25, 50, 100 and 200 μg/mL) for 24 and 96 hours determined by CellTiter-Glo® assay (left panel); DNA damage induced by CS-NPs (0.01, 0.05, 0.1, 0.5, 1, 5, 15 and 25 μg/mL) after 24 and 96 hours determined with the Comet Assay. Data are presented as quantile box plots. The edges of the box represent the 25th and 75th percentiles, the median is a solid line through the box, and the error bars represent 95% confidence intervals (right panel). A statistically significant difference (Kruskal-Wallis, and Dunn's post-test) between NPs-exposed cells and the vehicle control is indicated by ***P < 0.001, and ****P < 0.0001.

Funding: This research was partially funded by H2020-MSCA NESTOR project (101007629), the HE CutCancer project (101079113), ARIS P1-0245, ARIS J1-4395 and ARIS MR grant to IR.

Calix[4]arene-PEI Coated Iron Oxide Nanoparticles: A Multifunctional Approach for Recovery of Precious Metals and DNA Strands

Carlos Moya,[1-3*] Natacha Brion,[4] Joost Brancart,[5] Ludovic Troian-Gautier,[6] Ivan Jabin,[7] Gilles Bruylants[1]

[1] Engineering of Molecular NanoSystems, Ecole Polytechnique de Bruxelles, Université libre de Bruxelles, Brussels 1050, Belgium

[2] Departament de Física de la Matèria Condensada, Universitat de Barcelona, Martí i Franquès 1, 08028 Barcelona, Spain

[3] Institut de Nanociència i Nanotecnologia (IN2UB), Universitat de Barcelona, 08028 Barcelona, Spain

[4] Analytical and Environmental Geochemistry (AMGC), Vrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels, Belgium

[5] Physical Chemistry and Polymer Science, Materials and Chemistry Department, Vrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels, Belgium

[6] Institute of Condensed Matter and Nanosciences, Molecules, Solids and Reactivity (IMCN/MOST), Université catholique de Louvain, Place Louis Pasteur 1, 1348 Louvain-la-Neuve, Belgium

[7] Laboratoire de Chimie Organique, Université libre de Bruxelles, Avenue F.D. Roosevelt, 50 B-1050 Brussels, Belgium

***e-mail of presenting author:** carlosmoyaalvarez@ub.edu

Magnetic removal and recovery of precious metals and deoxyribonucleic acid (DNA) strands from complex biological media pose significant challenges due to the need for efficient, selective, and stable materials [1]. This work reports a methodology for the synthesis of iron oxide nanoparticles (IONPs) coated with a robust polyethyleneimine (PEI) layer, mediated by the covalent grafting of a calix[4]arene-tetraacid (X4C4)-tetra-diazonium layer onto the particles in reducing conditions, to address this challenge [2]. This method relies on the electrostatic attraction between the negatively charged carboxylate groups of the X4C4 and the positively charged PEI polymers, resulting in a synergistic interaction that significantly improves the durability of the PEI coating. In contrast to citrate, previously utilized as an attachment layer for PEI, the reductive grafting of X4C4-tetra-diazonium salts onto IONPs results in a considerably more stable coating that proves to be an excellent substrate for the adsorption of PEI [3]. This enhanced anchoring effectively prevents PEI detachment and maintains the particles in a dispersed state. The stability of the resulting IONPs@X4C4@PEI particles is demonstrated by their ability to withstand both acidic and alkaline conditions without significant particle aggregation or loss of magnetic properties. Moreover, these particles exhibit exceptional magnetic reusability, retaining their selectivity and recovery efficiency over multiple separation cycles. Specifically, the particles exhibit a high affinity for Au and Pt ions due to specific interactions between the metal ions and the PEI coating, allowing for their efficient recovery from complex solutions. Interestingly, the absorbed precious metals can be effectively released with the addition of thiourea. Furthermore, the particles' selectivity for DNA strands is attributed to strong electrostatic interactions that facilitate DNA strand elution from IONPs@X4C4@PEIDNA precipitates by adjusting the pH in PBS solutions, achieving optimal, non-degrading release at basic pH levels. Recovery rates markedly increase from pH 10 to 12, underscoring a successful 5-step DNA extraction cycle.

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Exploring the fabrication and performance of non-crosslinked PNIPAM-Fe_3O_4 nanospheres

Eva Natividad* and María García-Maestre

Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC - Universidad de Zaragoza
Campus Río Ebro, María de Luna, 3, 50018 Zaragoza, Spain
*Email: evanat@unizar.es

The biocompatible polymer poly(N-isopropylacrylamide) (PNIPAM) is widely known for its thermo-responsivity. This ability is based on its lower critical solution temperature (LCST), since water-soluble PNIPAM chains become insoluble at crossing it upon heating, and vice versa, giving rise to the so-called coil-to-globule transition. The LCST of PNIPAM is typically 32ºC, but can be tuned through several strategies (*e.g.* copolymerization), making it very attractive for biomedical applications such as drug release or tissue engineering. The majority of these applications rely on microgels, *i.e.*, PNIPAM network micro/nanobeads, mostly synthesized through polymerization of NIPAM monomers in the presence of a chemical crosslinker. These microgels are able of swelling/shrinking their network at crossing the LCST.

In this contribution, we report the fabrication of non-crosslinked PNIPAM-Fe_3O_4 nanosphere colloids through miniemulsion, solvent evaporation and subsequent separation techniques, starting from already polymerized PNIPAM chains, Fe_3O_4 magnetic nanoparticles, and with the help of water-insoluble polymers and/or surfactants.

Nanosphere characterization was performed using dynamic light scattering (DLS), zeta potential, transmission electron microscopy (TEM and cryo-TEM), differential scanning calorimetry (DSC) and SQUID magnetometry. Nanospheres display reversible size reduction/increase, with reductions upon heating down to 42% of their initial size. Obtained colloids are stable over months with identical size reduction/increase behavior. In addition, size reduction can be tuned by varying either the ratio between polymers, or the heating rate across the LCST. Nanospheres are able to uptake a high concentration of Fe_3O_4 nanoparticles. Eventually, the heating behavior of nanospheres upon alternating magnetic field application is evaluated, with a view to use them for hyperthermia and/or heat-assisted drug release.

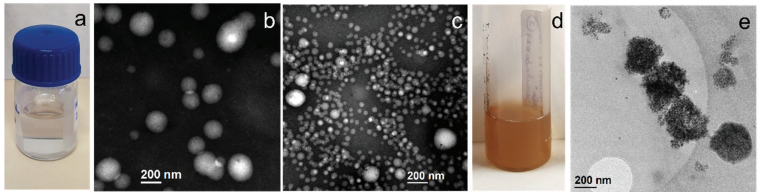

Figure. (a) Image of PNIPAM nanosphere colloidal dispersion after 26 months storage. Negatively stained TEM micrographs of: (b) PNIPAM nanospheres dried at room temperature; (c) PNIPAM nanospheres dried on hot plate at 70ºC. (d) Image of PNIPAM-Fe_3O_4 nanosphere colloidal dispersion after 16 months storage. (e) Cryo-TEM micrograph of PNIPAM-Fe_3O_4 nanospheres.

Bifunctional Magnetic Nanozymes: Synergy between Catalytic Activity and Magnetic Hyperthermia

Nahuel Nuñez[1*], Enio Lima Jr. [1], Marcelo Vasquez Mansilla[1], Alvaro Gallo-Córdova[2], Carlos Díaz-Ufano[2], María del Puerto Morales[2], Elin Lilian Winkler[1]
***Corresponding author**: nahuel.nunez@ib.edu.ar
[1] Instituto de Nanociencia y Nanotecnología (CNEA-CONICET), Nodo Bariloche, Av. Bustillo 9500, (8400) S. C. de Bariloche (RN), Argentina.
[2] Instituto de Ciencia de Materiales de Madrid, ICMM/CSIC, C/ Sor Juana Inés de la Cruz 3, 28049 Madrid, Spain

Nanozymes, synthetic nanostructures with enzyme-like catalytic activity, have emerged as versatile tools in various biomedical and environmental applications. The use of nanozymes with peroxidase-like activity has been proposed for cancer therapy [1]. In these treatments, nanocatalysts are designed to selectively target and eradicate cancer cells through the generation of reactive oxygen species (ROS) or other cytotoxic intermediates. Nanozymes based on magnetic nanoparticles offer various advantages, such as the possibility of enhancing catalytic activity through heat generation in magnetic hyperthermia processes. To improve this synergic effect, nanozymes with good response to elevated temperatures are crucial [2].

In the present work, we designed bifunctional nanozymes based on magnetic nanoparticles with high temperature-optimized peroxidase-like activity, and capable of heating in magnetic hyperthermia processes. For this, we first synthesized magnetite and copper doped iron oxide nanoparticles, varying the copper content and iron oxidation state, and studied their catalytic activity under different reaction conditions. The generation of free radicals was measured by Electronic Paramagnetic Resonance Spectroscopy and the oxidizing capability was assessed calorimetrically by degrading the model compound methylene blue. Our findings reveal that while magnetite displays the highest activity at room temperature, its efficacy diminishes rapidly as it oxidizes. Conversely, copper ferrite demonstrates lower activity compared to magnetite at room temperature but exhibits copper-dependent enhanced performance at elevated temperatures. This experiments suggest that copper catalysts are better for high temperature catalytic applications.

To obtain the bifunctional compound, we synthesized $Zn_{0.4}Fe_{2.6}O_4$ nanoparticles optimized to heat when exposed to an alternating magnetic field. After that, a copper phase was grown over the surface. The free radical production and the oxidizing capability of core and core/shell systems were tested at different temperatures. The magnetic induction heating-assisted catalytic activity was studied and the efficiency compared with conventional heating methods is discussed. The design of these bifunctional materials, with negligible activity in normal conditions but highly catalytic under magnetic hyperthermia heating, is the first step to fabricate magnetically activated nanozymes. This method enables remote control of catalytic activity, offering precise activation of nanozymes at specific locations and times, especially useful in biomedical applications where fine control over enzymatic processes is required.

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Probing the microstructure properties of soft magnetic polymer hybrid materials

Chinmay Pabshettiwar, Patrick Kreissl, Christian Holm, Rudolf Weeber

Institute for Computational Physics, University of Stuttgart
rudolf.weeber@icp.uni-stuttgart.de

Embedding magnetic nanoparticles within a polymer hydrogel results in materials combining magnetic and viscoelastic properties [1, 2], making them promising candidates for engineering and biomedical applications. To tailor the materials for those applications, it is essential to understand the coupling between magnetic nanoparticles and polymers and its effect on mechano-elastic properties. Experimentally, this is studied by analyzing the frequency-dependent magnetic susceptibility. From the susceptibility spectrum, the local viscoelastic moduli around the nanoparticles can be calculated using the Gemant-DiMarzio-Bishop theory[3]. In our study, we model this approach using computer simulations combining coarse-grained molecular dynamics and Lattice-Boltzmann hydrodynamics[4]. Using such simulations, it is possible to switch on specific interactions, such as magnetic, steric, van der Waals, the effects of surface roughness or hydrodynamic, individually. Hence, their influence on nanoparticle-polymer coupling can be studied. In experiments, oscillating external fields of different frequencies are applied consecutively to obtain the AC susceptibility spectrum. While possible, this is not the best approach in simulations. Instead, we obtain the AC susceptibility spectrum by analyzing the thermal fluctuation spectrum of the magnetization in the absence of an external magnetic field. This is called a Green-Kubo approach[5, 6].

Using this technique, in our contribution, we study the effect of the hydrogel's mesh size on the magnetic relaxation behaviour of the nanoparticles. We compare different interaction potentials between the nanoparticle and the polymer chains. For a purely repulsive interaction, we observe a faster magnetic relaxation for larger mesh sizes. This trend, however, largely disappears when we apply an attractive interaction between the nanoparticle and the polymers. We attribute this to differences in the hydrodynamic coupling between magnetic nanoparticles and polymer chains: the polymer density profile around the magnetic nanoparticle differs between the cases with and without an attractive interaction. When an attractive interaction is used, polymer chains are always close to the surface of the magnetic nanoparticle, independent of the mesh width. For a purely repulsive potential, on the other hand, the average distance between nanoparticles and polymers grows with increasing mesh width.

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Engineering Suitable Biocompatible Magnetic Fluid for Magnetic Fluid Hyperthermia from Synthesis to in vitro investigation

Kinnari Parekh[1,*], Neeraj Jain[1], Arshad Pathan[1], and Tushar Patel[1,2]

[1] Dr. K C Patel R & D Centre, Charotar University of Science and Technology, Changa-388421, Gujarat, India
[2] P D Patel Institute of Applied Sciences, Charotar University of Science and Technology, Changa-388421, Gujarat, India.
*Email: kinnariparekh.rnd@charusat.ac.in
Mobile:+91-9426950505

A temperature sensitive magnetic fluid containing $Mn_{0.9}Zn_{0.1}Fe_2O_4$ ferrite nanoparticles (A91) is appearing as a promising material for magnetic fluid hyperthermia due to its combined properties of controlling magnetic response with the change in temperature and a better biocompatibility. The main concerns for using high-quality $Mn_{0.9}Zn_{0.1}Fe_2O_4$ ferrite nanoparticles in magnetic fluid hyperthermia lie in their ability to regulate the temperature window between 42-46 °C, good dispersion in water, their long term stability and low cytotoxicity. The effectiveness of the fluid sample comes from optimizing the specific absorption rate of the dispersed magnetic nanoparticles with their lowest minimum concentration.

The present study encompasses a facile synthesis of $Mn_{0.9}Zn_{0.1}Fe_2O_4$ ferrite nanoparticles based magnetic fluid with polyacrylic acid (PAA) coating and its hyperthermia study investigated under a safety limit of magnetic field amplitude, frequency, and concentration of magnetic nanoparticles. The structure and magnetic properties of the particles are analyzed using X-ray diffraction (XRD) and VSM. TGA and FTIR are used to study the nature of coating and its percentage binding on the particle surface. The stability of the sample is confirmed using the particle size analyzer and zeta potential analyzer. The induction heating capacity of the fluid was investigated using Embrell Easy Heat model LA6310 at 330 kHz frequency.

An in vitro study on breast cancer cells, MCF-7, is carried out for different concentrations of A91 PAA coated magnetic fluids by performing MTT assay. The findings as revealed from Figure 1 shows that even 2.4 mg/mL concentration of A91 PAA coated particle is showing cell viability of 70%. The study also extended to observe the uptake of these particles as a function of time and it is observed that the uptake begins at 1 hour and within 12 hrs a complete uptake of PAA coated sample is seen. The findings of this study hold significant practical value for exploring the potential biomedical applications of $Mn_{0.9}Zn_{0.1}Fe_2O_4$ ferrite nanoparticles.

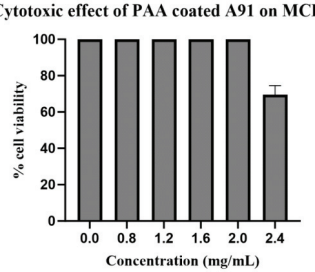

Figure 1: Cytotoxic effect of PAA coated A91 magnetic fluid on breast cancer cells (MCF-7).

Acknowledgement: Authors are thankful to SERB, New Delhi for providing financial support for the study vide ref. no. SERB/CRG/2021/001587. Tushar Patel (2021013010) acknowledge Government of Gujarat for providing SHODH fellowship.

Magnetic nanogels for combined hyperthermia and chemotherapy of prostate cancer

Sofia Patri[1], Nguyen T.K. Thanh[2]*, Nazila Kamaly[3]*

[1] Department of Materials, Imperial College London, London, UK; email: sofia.patri18@imperial.co.uk
http://www.ntk-thanh.co.uk
[2] Healthcare Bio-magnetic and Nanomaterials Laboratories, Department of Physics and Astronomy, University College London, London, UK: ntk.thanh@ucl.ac.uk
[3] Department of Chemistry, Imperial College London, London, UK.

Chemotherapy patients suffer severe side effects from the medications and hyperthermia can be an invasive treatment[1]. In recent years, clinical trials have demonstrated that hyperthermia can enhance the action of chemotherapy drugs[2] as cancer cells are susceptible to heat[1]. Combining the two therapies allows to establish synergistic actions and minimise their individual drawbacks.

The superparamagnetic iron oxide nanoflowers (IONFs) are known to have excellent heating abilities[3]. Nanogels are biocompatible 3D networks of crosslinked polymer chains. Nanogels encapsulate water, cargo and provide drug-carrier properties for smart delivery. In this work, we are developing a combined hyperthermia and chemotherapy treatments for prostate cancer with iron oxide magnetic nanogels.

A surface-active phosphate monomer was anchored to the IONFs; then, the monomer was polymerised to form a nanogel around the IONFs to prevent leakage of the IONFs over time[4]. The anchoring of the ligand was proven with x-ray photoelectron spectroscopy (XPS) with a 15.37 : 84.63 ratio of P : Fe. The IONFs increased slightly after ligand exchange (d_{DLS}= 98.8 nm and d_{TEM}= 61.98 nm for IONFs; d_{DLS}= 125.6 nm and d_{TEM}=67.93 nm for IONFs-ligand).

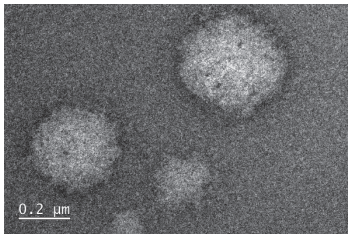

Figure 1 Magnetic nanogels under TEM, negative stain, 20k.

After the polymerisation, the iron signal in the XPS disappeared due to the formation of a thick organic shell. The nanogels were observed after negative stain treatment under transmission electron microscopy (TEM), with d_{TEM}= 363 nm (Figure 1). The hydrodynamic size of the nanogels d_{DLS}= 408 nm was recorded. The iron content inside the nanogels was 79.50% (determined by inductively coupled plasma - optical emission spectrometry ICP-OES). Finally, the magnetic hysteresis loop was recorded with the superconducting quantum interference device (SQUID); the results showed IONFs still superparamagnetic. In a magnetic field with amplitude 16 kA/m and frequency 350 kHz, the specific absorption rate (SAR) was 537 W/g_{Fe} and the intrinsic loss parameter (ILP) was be 6 nHm^2/kg_{Fe}.

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Iron-Oxide Magnetic Nanoparticles: Manganese and Zinc Doping Effects on Relaxometric Properties

Margherita Porru[1,2], Francesca Brero[1,2], Manuel Mariani[1,3], Paolo Arosio[4,3], Francesco Orsini[4,3], Maria del Puerto Morales[5], Alessandro Lascialfari[1,2]

[1] Department of Physics, University of Pavia, Pavia 27100, Italy
[2] National Institute of Nuclear Physics-INFN, Pavia 27100, Italy
[3] National Institute of Nuclear Physics-INFN, Milano 20133, Italy
[4] Department of Physics, University of Milano, Milano 20133, Italy
[5] Instituto de Ciencia de Materiales de Madrid, ICMM/CSIC, Madrid 28049, Spain

*Email: margherita.porru01@universitadipavia.it. Mobile: +39 0382 987483

Iron oxide-based magnetic nanoparticles (MNPs) have gained significant attention in biomedicine, particularly in diagnostics and therapeutics [1,2]. Within biological tissues, these nanoparticles influence the dynamic behavior of adjacent ^{1}H nuclei through their magnetic properties. This interaction induces fluctuations in the hyperfine field at nuclear sites, leading to the shortening of spin-lattice (T_1) and spin-spin (T_2) nuclear relaxation times. Consequently, the contrast observed in MRI images, quantified by the longitudinal and transverse nuclear relaxivity ($r_{1,2}$), increases. Notably, the physical mechanisms underlying the contrast enhancement in MRI are strongly influenced by factors such as core size, shape, coating, and doping.

This study delves into the impact of core composition (specifically magnetic ions) and particle size modifications on MNPs' relaxivities. Two sets of magnetite-based MNPs ($Mn_xZn_yFe_{3-x-y}O_4$), distinguished by core diameters of approximately 4 nm and 15 nm and synthesized by the polyol microwave-assisted method [3] were explored. Within the smallest set, comprising a total of 7 samples, one is undoped, while the others are doped with varying concentrations of Zn^{2+} ions (0.1, 0.7, 0.9). Additionally, three samples maintain a constant Zn^{2+} concentration while gradually introducing Mn^{2+} ions (Zn^{2+}: 0.5, Mn^{2+}: 0.1, 0.2, 0.4). The largest set includes one undoped sample, three samples with increasing concentrations of Zn^{2+} (0.1, 0.3, 0.5) and three samples that maintain a constant Zn^{2+} concentration (0.3) while incrementally introducing Mn^{2+} ions (0.1, 0.2, 0.3). Both sets of MNPs were coated with CM-Dextran and polyacrylic acid-PAA to ensure stability and functionality. Morpho-structural analyses, including ICP-OES, AFM, DLS, TEM, XRD, IR, and TG, were employed for characterization. Additionally, the frequency-dependent nuclear relaxivities were investigated through ^{1}H-NMRD relaxation times in a frequency range of 0.01-64 MHz.

The study demonstrates how the spin dynamics is influenced by the morpho-structural characteristics and the level of Zn^{2+}/Mn^{2+} doping in the nanoparticles. We compare these findings with existing literature models for the variation of $r_{1,2}$ values versus frequency. These results should aid in refining the chemical and physical properties of ferrite-based nanoparticles for MRI contrast agent applications.

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Magnetic nanoparticles in viscous media from the view of Frequency mixing magnetic detection

Ali Mohammad Pourshahidi[1*], Amirreza Gholivand[2,4] , Andreas Offenhäusser[1] and Hans-Joachim Krause[1, 3*]

[1]Institute of Biological Information Processing, Bioelectronics (IBI-3), Forschungszentrum Jülich, Germany,
[2]Institute of Biological Information Processing, Bioelectronics (IBI-5), Forschungszentrum Jülich, Germany,
[3]Institute of Nano- and Biotechnologies (INB), FH Aachen University of Applied Sciences, 52428 Jülich, Germany,
[4]Laboratory for Soft Matter and Biophysics, KU Leuven, B-3001 Leuven, Belgium,
e-mail: a.pourshahidi@fz-juelich.de, h.-j.krause@fz-juelich.de

Keywords : Magnetic nanoparticles, Frequency mixing magnetic detection, Viscometer, Magnetorheology,

The viscosity of the medium plays a pivotal role in the dynamic magnetic properties of superparamagnetic iron oxide nanoparticles (SPIONs), offering significant insights for advancements in biosensing and diagnostics. Our research focuses on Frequency Mixing Magnetic Detection (FMMD) [1], a technique that exploits the nonlinear magnetization of SPIONs induced by dual-frequency magnetic excitation. This methodology employs simultaneous low and high-frequency magnetic fields. The magnetic response at mixing harmonics, representing both the sum and difference of the original frequencies, allows for quantification and a deeper understanding of SPION behavior [2], [3]. This research aims to illustrate the effects of different types of commercially available magnetic nanoparticles in viscous media on the FMMD signal. Particles under study (BNF 80 nm, SynomagD 70 nm, and SynomagD 50 nm from Micromod, Rostock, Germany) have been mixed into media made of glycerin-water mixtures with viscosities ranging from 0.8 to 612 mPa·s. Analysis of even and odd mixing harmonics through scanning of the Low-frequency amplitude modulation and also offset-dependent frequency mixing signals have been performed. Both methods show a clear dependence of the measurement signals on the viscosity of the solutions.

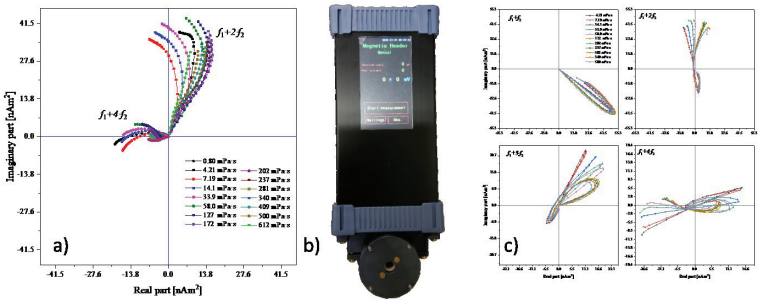

Figure 1 a) Complex representation of frequency mixing signals $f_1+2\cdot f_2$ and $f_1+4\cdot f_2$ of particle BNF80 at different viscosities by low-frequency magnetic field amplitude scanning method. b) Portable FMMD Device c) Complex representation of frequency mixing signals $f_1+n\cdot f_2$ (n=1,2,3,4) of particle BNF80 at different viscosities by static offset magnetic field scanning method.

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Verifying the MNP dissolution in photo-spectrometric iron concentration determination by magnetic particle spectroscopy

Patricia Radon[1], Philipp Kyri[1,2], Amani Remmo[1], Frank Wiekhorst[1]

[1]Physikalisch-Technische Bundesanstalt, Abbestr. 2-12, 10587 Berlin, Germany.
[2]Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health; Institut für Radiologie, Campus Mitte, Charitéplatz 1, 10117, Berlin, Germany.
*Corresponding author: Patricia Radon, patricia.radon@ptb.de

The precise and reliable determination of the magnetic nanoparticle (MNP) concentration (for iron oxide MNP typically the iron concentration c(Fe) is preferred) is of utmost importance for their magnetic characterization, e.g., to determine specific magnetic parameters such as saturation magnetization, susceptibility, or specific heating power – all values that are obtained by normalizing to the iron amount of the sample under investigation.

Besides ICP mass spectroscopy, photo-spectrometric methods are used to determine c(Fe) of the MNP for which the particles are first broken down into atomic components in a strong hydrochloric acid (HCl), followed by the absorption measurement at $\lambda = 510$ nm after complexation (formation of an iron (II) phenanthroline complex $[Fe(phen)_3]^{2+}$ with 1.10-phenanthroline solution) using a photometer. The HCl-decomposition of MNP into its Fe-ions and therefore the accuracy of the c(Fe) determination crucially depends on the robustness of the particle coating/shell against acid exposure. MNP coatings containing silica are known to be rather inert against acid dissolution making the c(Fe) determination cumbersome. Here, we present magnetic particle spectroscopy (MPS) as a tool to control the success of HCl dissolution of MNP using a commercial MPS device (Bruker BioSpin, Germany) operated at $f_0 = 25$ kHz with a high sensitivity for magnetic moment detection down to $5\cdot10^{-12}$ Am^2.

Several MNP systems (10 µL volume) with different shells (plain, PEG, silica) were dissolved in 20 µL of 37% HCl and measured repeatedly by MPS over a time interval of 1000 minutes. We utilized the third harmonic A_3 of the recorded MPS spectra to assess the existence and amount of magnetic iron in the samples, see Fig 1.

Most MNP systems show a decrease in A_3 after the addition of HCl until the signal amplitudes reach the MPS detection limit within about 25 min acid exposure. After this time interval, it can be assumed that the MNP systems are completely dissociated into ionic components. For the MNP system with silica coating, merely a MPS reduction by a factor of 10 was observed where the spectra still exhibited strong magnetic nanoparticle behavior after 24 h.

It is concluded that the excellent sensitivity compared with the huge dynamic range of MPS makes this technique ideally suited to enhance the accuracy of the photometric iron concentration determination of MNP systems.

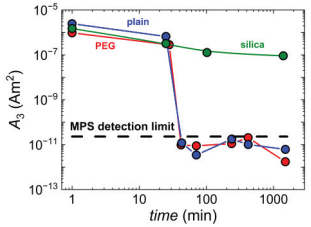


Fig. 1: Monitoring of hydrochloric acid dissolution of different MNP systems by MPS.

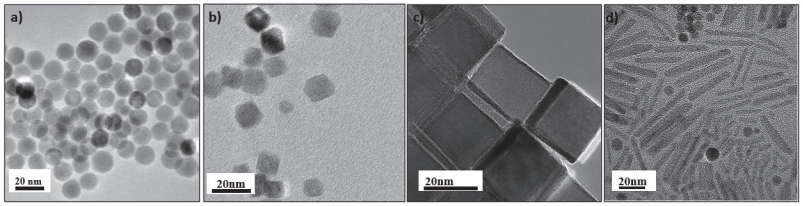
Shapes tailored magnetic nanoparticles for magnetic nanoparticle-based hyperthermia for cancer treatment

K. Riahi[a*], N. Sommer[a], I. Dirba[a], Alina. Filatova[b], E. Adabifiroozjaei [c], L. Molina-Luna [c], U. A. Nuber[b] and O. Gutfleisch[a]

[a] Functional Materials, Institute of Materials Science, Technical University of Darmstadt, Peter-Grünberg-Str. 16, 64287 Darmstadt, Germany
[b] Stem Cell and Developmental Biology, Technical University of Darmstadt, 64287 Darmstadt, Germany
[c] Advanced Electron Microscopy Division, Institute of Materials Science, Technical University of Darmstadt, Peter-Grünberg-Str. 22, 64287 Darmstadt, Germany

e-mail: kalthoumriahi@tu.darmstadt.de

Understanding the correlation between the shape of magnetic nanoparticles, their internalization in cancer cells, and their effects on magnetic heating applications is a challenging task due to the difficulties in designing and synthesizing compositions of similar sizes while controlling the shape[1]. The objective of our work is to assess the performance of various shapes of iron oxide nanoparticles while maintaining the same composition and evaluate their suitability for potential use in magnetic hyperthermia therapy [2]. We have successfully synthesized various shapes of Fe_3O_4 nanoparticles (nano-cubes, nanospheres, nano-hexagons, and nanorods) using an adjusted solvothermal process [3]. Shape-directing agents, aldehydes, were used in the synthesis of nanoparticles. Oleic acid served as a surfactant in all reactions. Particularly, in the fabrication of nano-cubes, a combination of benzaldehyde and hexadecylamine was utilized. Nano-hexagons were synthesized using oleylamine and benzaldehyde, while pentanal and hexadecylamine were used in the synthesis of nanospheres. All samples consisting of iron oxide nanoparticles were characterized using magnetic measurements, X-ray diffraction, thermogravimetric analysis, High-resolution transmission electron microscopy, Inductively Coupled Plasma – Optical Emission Spectroscopy, and AC magnetic hyperthermia measurements. Furthermore, we investigated the cellular uptake of differently shaped magnetic nanoparticles with cancer cells in *vitro*. The calculated intrinsic loss power which has been calculated from the specific absorption rate indicated that the spherical particles show the best heating performance.



Acknowledgements:
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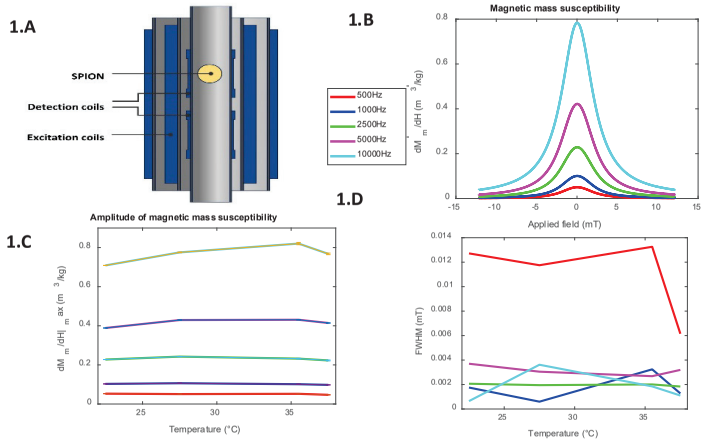
Impact of temperature on AC magnetic susceptibility of MNPs

S. Salamzadeh, H. J. G. Krooshoop, C. Comendant, B. ten Haken, L. Alic*
Magnetic Detection and Imaging group, Technical Medical Centre, University of Twente, the Netherlands
* Corresponding author, email: l.alic@utwente.nl

Magnetic nanoparticles (MNPs) have wide range of applications in industry and healthcare including diagnosis (imaging, biosensors,) and treatment (hyperthermia, drug/gen delivery, tissue engineering)[1]. Given the impact of magnetic behavior on the efficiency of MNPs, their characterization stands as a critical procedure that should be guided by end-user requirements according to the specific application. The absence of standard criteria for characterization of MNPs, coupled with variations in synthesis technique, temperature, pressure, and raw material contamination, poses challenges to achieving consistent quality[2]. For both MNP producers and end-users, the availability of a user-friendly instrument to assess their magnetic properties provide significant value. Therefore, we aim to provide an alternative approach to assess MNPs in terms of morphology (e.g. particle diameter) on top of assessment of magnetic, temperature, and relativity. AC susceptibility (ACS) used to analyze magnetic behavior of particles depends on frequency of applied field and relaxation time of MNPs which are influenced by temperature of magnetic suspension[3].
We used in house built-in device, Super Paramagnetic Quantifier (SPaQ) illustrated in Fig 1.A[4] to acquire differential magnetic (DMS), $\chi_m = dM_m/dH$, of nanoflower-shaped MNPs with hydrodynamic diameter of 70nm (Synomag-D70®, micromod Partikeltechnologie GmbH). AC applied field in SPaQ is generated by combination of two excitation sequences utilizing both low and high frequencies. The magnetization alternation per applied field, ranging from -12 to +12 mT, is measured by pickup coils. To investigate MNPs behavior in various temperatures, a sample of 150µl of Synomag-D70®, which contains 3 mg of iron, was subjected to heating in an ultrasonic bath at four different temperature settings: 22.5°C, 27.5°C, 35.5°C, and 37.5°C. Uder a sinusoidal AC magnetic field, the excitation frequency was set to 0.5, 1, 2.5, 5 and 10 kHz in five separate measurements, repeated three times. Fig 1.B illustrate DMS for different applied frequencies at a temperature of 35.5°C. DMS parameters as amplitude and full width at half maximum (FWHM) for different temperatures are illustrated in Fig 1.C and Fig 1.D, respectively.



Increasing the frequency enhances the DMS of MNPs. An increase in the amplitude of DMS occurs with rising temperature. However, this impact becomes notable at higher frequencies, particularly nearing body temperature. An elevated temperature reduces the sample viscosity. Consequently, decreases the Brownian relaxation time, which then becomes the dominant factor in particles relaxation time.

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Preparation of Multi-Responsive Hydrogels Based on Magnetoplasmonic Nanoparticles in a Thermo-Responsive Polymer Matrix

Patrick Schütz[1], Maria Weißpflog[1], Sascha Benedict Lemich[1], Paul Körner[1], Volker Abetz[1,2*], and Birgit Hankiewicz[1*]

[1]Institute of Physical Chemistry, University of Hamburg, Grindelallee 117, 20146 Hamburg, Germany.
[2]Institute of Membrane Research, Helmholtz-Zentrum Hereon, Max-Planck-Straße 1, 21502 Geesthacht, Germany.
E-Mail: birgit.hankiewicz@uni-hamburg.de; volker.abetz@uni-hamburg.de

Optimized nanomaterials for biomedical applications like targeted drug delivery or hyperthermia, need to fulfill multiple functions e.g. enabling biocompatibility, targeting specific areas, producing heat, or releasing a substance as a response to an external stimulus. Magnetoplasmonic nanoparticles (MNPs), which are a hybrid material based on a magnetic NP core and a plasmonic gold shell, are interesting platforms for these multi-responsive materials. Due to the magnetic core, the MNPs can be moved using magnetic fields, while the gold shell adds optical properties and chemical stability to the system. Besides the MNP system, the ligands or matrix, in which they are embedded are an essential factor in creating optimized materials since they cannot only stabilize the MNPs but can also be utilized to add more functionalities to the system.

In this work, we present a novel synthesis route to obtain multi-responsive hydrogels, which are based on MNPs in a thermo-responsive polymer matrix as shown in Figure 1. The MNPs are based on $CoFe_2O_4$-NPs (CF-NPs) as magnetic cores, which were encapsulated with gold. The synthesis of the MNPs was performed in an aqueous medium using the amino acid L-cysteine as a non-toxic ligand. The MNPs were then functionalized with a double thermo-responsive *graft*-copolymer consisting of a poly[oligo(ethylene glycol) methacrylate] (POEGMA) backbone and multiple poly(*N*-isopropyl acrylamide) (PNIPAM) side chains. Due to the used synthesis method, each polymer chain was terminated with trithiocarbonate groups, which could be anchored to the gold surface of the MNPs. These CF@Au@Polymer-MNPs were characterized regarding their magnetic, optical, and thermo-responsive properties to demonstrate that the properties of each component were present in the hybrid material.

Finally, the CF@Au@Polymer-MNPs were crosslinked to obtain hydrogels that show temperature-dependent swelling behavior. To fully utilize the thermo-responsive behavior of the hydrogel, photothermal heating was investigated using NIR irradiation in the first optical window (800 nm). Additionally to the targeted heating capabilities, this allows a controlled release of a substance, which can be dispersed in the water phase.

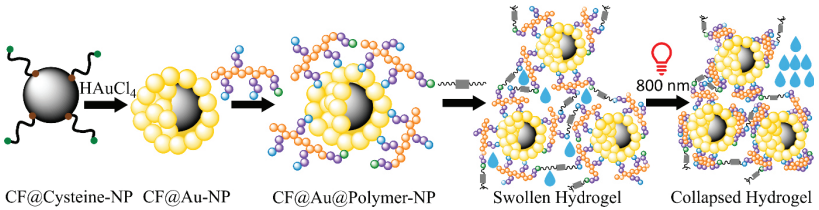

Figure 1: Schematic of the synthesis route of the multi-responsive hydrogel and the swelling behavior of the hydrogel which can be remotely triggered using NIR irradiation. The synthesis route starts from L-cysteine functionalized CF-NPs, which are encapsulated in gold, functionalized with polymers, and crosslinked to obtain the hydrogel.

Designing Magnetic Nanoparticles for Intranasal Administration : Targeted Delivery to the Brain

Satoshi Seino[1*], Tomohiro Umeda[2], Takami Tomiyama[2], Akiko Tanaka[3], Toshiyasu Sakane[3], Toshihiko Kiwa[4], Masaomi Washino[5], Kota Nomura[1,5], Shun Tonooka[5] and Takashi Nakagawa[1]
[1]Graduate School of Engineering, Osaka University
[2] Department of Translational Neuroscience, Osaka Metropolitan University Graduate School of Medicine
[3] Department of Pharmaceutical Technology, Kobe Pharmaceutical University
[4] Graduate School of Interdisciplinary Science and Engineering in Health Systems, Okayama University
[5] Advanced Technology R&D Center, Mitsubishi Electric Corp.

*Email: seino@mit.eng.osaka-u.ac.jp Tel: +81-6-6879-7887

The application of magnetic nanoparticles as contrast agents in biomedical imaging techniques has garnered particular attention. In the realm of Drug Delivery Systems utilizing magnetic nanoparticles as diagnostic agents, intravenous administration has conventionally been the preferred route, as commonly adopted in prior research. By intravenously administering magnetic nanoparticles modified with PEG to impart stealthiness within the body, accumulation in target disease areas (e.g., cancer tumors) via the Enhanced Permeability and Retention effect can enable imaging diagnosis via MRI or MPI. However, when considering the brain as the diagnostic target, delivery of magnetic nanoparticles via intravenous administration becomes exceedingly challenging. The cerebral vasculature harbors a robust defense mechanism known as the Blood-Brain Barrier (BBB), which prevents impurities from entering the brain tissue. Consequently, delivering diagnostically significant quantities of magnetic nanoparticles to target brain regions has been deemed practically unattainable. Thus, our attention turns to a technique known as intranasal administration. It has been recognized that within the nasal cavity exists a route through which administered substances directly traverse to the cerebrospinal fluid or brain without traversing the BBB, hence serving as a drug delivery pathway circumventing the BBB [1]. Intranasal administration studies have traditionally focused on molecular therapeutics. However, applying this approach to facilitate brain delivery of inorganic materials such as magnetic nanoparticles represent a profoundly challenging endeavor undertaken by our research group [2].

We depict a schematic diagram of the magnetic nanoparticles we designed in Figure 1. Ferucarbotran was utilized as the iron oxide core. After conjugating it with gold nanoparticles, PEGylation of the surface was achieved utilizing Au-S bonding. Furthermore, to confer specificity towards the target, amyloid β, functional groups introduced at the PEG terminus were utilized for the modification of Probe molecules. The evaluation of brain penetrance of the designed magnetic nanoparticles was validated through animal experiments employing mice. The migration of the designed PEGylated magnetic nanoparticles into the brain post intranasal administration was confirmed through magnetization measurements. Additionally, using probe molecules immobilized at the PEG terminus, we demonstrated the accumulation of these nanoparticles at specific target sites. Thus, the effectiveness of delivering magnetic nanoparticles to the brain via intranasal administration was demonstrated in this study.

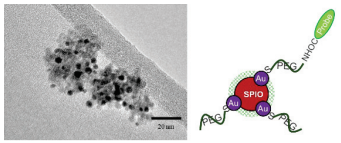

Fig.1 Magnetic nanoparticles designed for intranasal administration. TEM (left) and schematic diagram (right)

Acknowledgements
This work was supported by AMED under grant numbers JP20hm0102073, JP21hm0102073, and JP22hm0102073.

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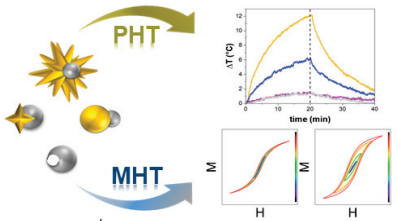
Enhancement and Tunability of Plasmonic-Magnetic Hyperthermia through Shape and Size Control of Au:Fe_3O_4 Janus Nanoparticles

Esraa Samy Abu Serea,[1] Iñaki Orue,[2] José Ángel García,[3] Senentxu Lanceros-Méndez,[1,4] and Javier Reguera[1,*]

[1] BCMaterials, Basque Center for Materials, Applications, and Nanostructures, UPV/EHU Science Park, Leioa 48940, Spain.
[2] SGIker Medidas Magnéticas, Universidad del País Vasco (UPV/EHU), 48940 Leioa, Spain.
[3] Departamento de Física, Universidad del País Vasco (UPV/EHU), 48940 Leioa, Spain.
[4] Ikerbasque, Basque Foundation for Science Bilbao, 48009 Bilbao, Spain.
*Email: javier.reguera@bcmaterials.net

Nanohyperthermia therapies have appeared as a promising alternative for the treatment of diverse cancer tumors. Multifunctional nanosystems offer a step forward in these therapies. They harness more efficient and multistimuli hyperthermia for low-dose application, as well as supplementary functions for imaging, targeting, controlled release, and sensing. Among them, Janus Au:Fe_3O_4 nanoparticles (JNPs) are highly versatile and a prominent example for dual photo- and magneto-thermia capabilities. To achieve the highest efficiencies of these nanomaterials, which allow low-dose applications, optimization in terms of size and shape is imperative. Here, we have expanded the synthesis of Janus nanostructures and carried out a systematic study to understand the structure–performance relationship and improve their hyperthermia efficiency. JNPs were synthesized by seed-mediated growth processes to obtain Janus nanostars (JNSs) and Janus nanospheres (JNSphs) with controlled sizes, together with initial heterodimers and indented Fe_3O_4 NPs. The hyperthermia abilities were then evaluated using AC magnetometry and under near-infrared laser irradiation. The results showed a clear effect of size and shape on the tuning of both magnetothermia and photothermia. Iron oxide size showed the biggest effect on magnetothermia, which could be tuned by the size and shape of the gold component. Likewise, for photothermia, JNSs offered the best performance and a clear correlation between the proximity of the plasmonic band to the irradiation source and their photothermal performance, modulated by the presence of iron oxide. A SARmax of 3 kW g^{-1} for the strongest field and frequency tested, 0.48 kW g^{-1} for biological safety limits in magnetothermia, and 8.3 kW g^{-1} per W cm^{-2} of applied light for photothermia were obtained. The acquired results support the proper selection of the best JNPs for dual hyperthermia and allow one to set up the design rules for obtaining more efficient multifunctional nanosystems, opening new avenues toward advanced heating-based therapies.



Abu Serea, E. S., Orue, I., García, J. Á., Lanceros-Méndez, S., & Reguera, J. (2023). Enhancement and Tunability of Plasmonic-Magnetic Hyperthermia through Shape and Size Control of Au: Fe3O4 Janus Nanoparticles. *ACS Applied Nano Materials*, *6*(19), 18466-18479.

Enhanced magnetic hyperthermia performance by magnetite nanorods: The effect of aspect ratio and synthesis method

Zhila Shaterabadi [1, 2 *], Ángel Delgado [1, 2], Guillermo R. Iglesias [1, 2]

[1] NanoMag Laboratory, Department of Applied Physics, Edificio I+D Josefina Castro, University of Granada, Av. de Madrid, 28 (18012), Spain
[2] Instituto de Investigación Biosanitaria ibs. GRANADA, Spain

[*]e-mail of presenting author: Zhila@ugr.es

Magnetite nanorods (MNRs) have recently drawn considerable attention in magnetic hyperthermia therapy (MHT). The considerable influence of the one-dimensional (1D) structure on their physicochemical properties has made them to show significant heating efficiencies in the MHT. However, the synthesis of nanorods is more challenging than their spherical counterparts because the surface energy favors the formation of isotropic spherical structures [1, 2].

In this study, the MNRs were synthesized through solvotherrmal (MNRs1) and hydrolysis (MNRs2) methods and then investigated by different characterization methods. The results show that the MNRs1 are more uniform in size and have a higher aspect ratio than that of the MNRs2 (Figure 1). Moreover, the MNRs were investigated as heat-generating nanoagents in the MHT. The findings reveal although both synthesized MNRs show enhanced specific absorption rate (SAR) values in the biologically-safe magnetic field irradiation range, the MNRs1 present the more excellent performance thanks to having higher aspect ratios. However, the MNRs2 act as more suitable candidates in the MHT because of their excellent aqueous dispersity.

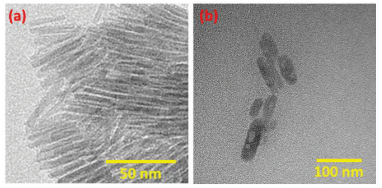


Figure 1. HRTEM images of the (a) MNRs1, and (b) MNRs2

Acknowledgements
This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No. 101064263. Z. Shaterabadi and GR. Iglesias acknowledge the European Union. G.R Iglesias acknowledges funding from Junta de Andalucía, Spain, Consejería de Economía y Conocimiento/Proyectos de I + D + I del Plan Andaluz de Investigacíon, Desarrollo e Innovación/Grants P20_00346 and A-FQM-492- UGR20. G.R.I thanks also for the grant TED2021-131855BI00/Unión Europea Next Generation EU/PRTR.

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Synthesis and characterisation of doped iron oxide nanoflower seeds for magnetic hyperthermia cancer treatment

Liudmyla Storozhuk,[a,b]* **Maximilian O. Besenhard**,[c] **Sayan Pal**,[c] **Asterios Gavriilidis**,[c] **Nguyen Thi Kim Thanh**.[a,b]*

[a] UCL Healthcare Biomagnetic and Nanomaterials Laboratories, 21 Albemarle Street, London, W1S 4BS, U.K.
[b] Biophysics Group, Department of Physics and Astronomy, University College London, London, WC1E 6BT, U.K.
[c] Department of Chemical Engineering, University College London, London, WC1E 7JE, U.K.

Email : ntk.thanh@ucl.ac.uk, http://www.ntk-thanh.co.uk, l.storozhuk@ucl.ac.uk

Cancer treatment is a crucial healthcare challenge that often results in severe side effects. Novel approaches are therefore necessary to address this issue. Superparamagnetic iron oxide nanoparticles (IONPs) have emerged as a promising option for cancer treatment. However, commercial IONPs have certain limitations that restrict their effectiveness, including the requirement for high doses that can be both toxic and expensive. There is a need for the development of more efficient and cost-effective IONPs that are scalable and can be used to treat a broader range of cancer patients. Our recently published method demonstrated a novel approach for synthesising iron oxide nanoflowers (IONFs) with a unique morphological structure [1].

To increase even further magnetic heating efficiency, we synthesised Zn, Co, and Cu-doped nanoflowers using our protocol with additional metal precursors. The synthesised doped IONFs were then compared with their undoped counterpart. As expected, the IONF seeds heating ability increased with the presence of doped metals in the samples: from IONF seeds (ILP = 3.0 nH m^2/kg_{Fe}) to an ILP of 7.42 nH m^2/kg_{Fe} for Zn-doped IONF seeds and ILP of 4.41 nH m^2/kg_{Fe} for Cu-doped IONFs (Figure 1). The suggested growth mechanisms imply that for longer reaction times, a further increase in IONF size >> 10 nm may be possible, and this could lead to higher heating efficiency of the final product. Our approach offers a promising synthesis of IONFs doped with various metals rather changing their morphologies. Our doped IONFs will have great potential in clinical translations for hyperthermia cancer treatment.

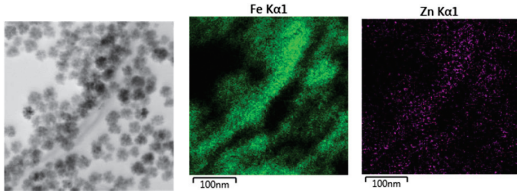

Figure 1. Analysis using STEM and elemental mapping of Zn doped IONFs (green: Fe, magenta: Zn).

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Ferritin derivatives as a valuable tool in the research of neurodegenerative disorders

Oliver Strbak[1*], **Jan Gombos**[1], **Jana Vojtova**[1], **Andrej Krafcik**[2], **Daniel Gogola**[2], **Ladislav Baciak**[3], **Martin Skratek**[2], **Matus Molcan**[4], **Michal Rajnak**[4], **Martin Kopani**[5], **Lucia Balejcikova**[6], **Kristina Zolochevska**[4], **Peter Kopcansky**[4]

[1] Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Martin, Slovakia
[2] Institute of Measurement Science, Slovak Academy of Sciences, Bratislava, Slovakia
[3] Faculty of Chemical and Food Technology, Slovak University of Technology, Bratislava, Slovakia
[4] Institute of Experimental Physics, Slovak Academy of Sciences, Kosice, Slovakia
[5] Faculty of Medicine, Comenius University, Bratislava, Slovakia
[6] Institute of Hydrology, Slovak Academy of Sciences, Bratislava, Slovakia
[*] Email: oliver.strbak@centrum.cz

Synthetic magnetite nanoparticles attract much attention due to their numerous practical applications in biomedical research [1]. However, the biogenic magnetite nanoparticles found in human tissue also possess promising diagnostic and therapeutic potential for various iron-related diseases [2]. The reason is that biogenic iron accumulation and magnetite mineralization are associated with various pathological processes, including neurodegeneration (ND), neuroinflammation, disorders of the liver, heart, and lungs, and even cancer [2]. The most described and studied is magnetite mineralization in ND [3]. It is generally assumed that ferritin is a precursor of iron accumulation and pathological magnetite mineralization due to disrupted iron homeostasis in ND [2]. However, it is still unclear whether these processes are the cause or consequence of pathology.

To clarify this question and reveal the biomedically beneficial properties of mineralized accumulated iron, we use ferritin derivatives: reconstructed ferritin (RF) as a model system of physiological ferritin with ferrihydrite mineral core and magnetoferritin (MF) as a model system of pathological ferritin with magnetite mineral core. We employed various techniques to investigate and characterize the RF and MF's physicochemical properties (e.g., DLS, magnetization measurements, Mossbauer and EDX spectroscopy, SEM, etc.). The prepared ferritin derivatives were also analyzed by magnetic resonance relaxometry to determine visibility thresholds and relaxivity values for different magnetic field strengths: 0.2, 4.7, and 7 T (**Fig. 1**). Accumulated biogenic iron in the form of magnetite nanoparticles is believed to be a non-invasive biomarker for early diagnostics of ND using MRI techniques [4]. In addition, we performed in-silico simulations of RF and MF relaxations at different magnetic field strengths to support experimental relaxivity findings. Finally, we analyzed the viability of model neuronal cells in the presence of ferritin derivatives, which can clarify the effect of accumulated iron on cell survival. Our previous study revealed that MF can induce higher oxidative stress through the increased release of biologically toxic ferrous ions in the presence of vitamins C and B_2 [5], which we have now supplemented by the viability MTT test. These could help answer the question of the "iron cause or consequence in the ND" and support the emergence of new therapeutic and diagnostic options.

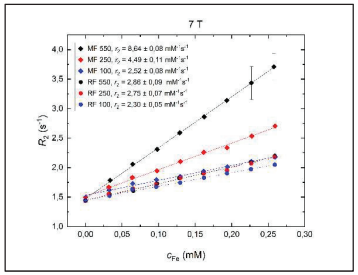

Fig. 1: Relaxivity values of RF and MF at 7 T MRI.

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Mixing-Frequency Spectra for Magnetic Particle Imaging

Shaoqi Sun[1], Shijie Sun[1], Lijun Xu[1] and Jing Zhong[1,*]

[1]School of Instrumentation and Optoelectronic Engineering, Beihang University, Beijing, China.

[*]Email: zhongjing@buaa.edu.cn

Magnetic particle imaging (MPI) is an innovative medical imaging modality that allows for three-dimensional quantitative visualization of magnetic nanoparticles (MNPs). Due to its radiation-free, high sensitivity, and high spatial resolution, MPI has shown great promise in biomedical applications, such as stem cell tracking, cancer imaging, and angiocardiography. In this study, we propose a new approach of MPI based on the mixing-frequency spectra of the MNPs in mixing-frequency magnetic fields. In MPI based on mixing-frequency spectra, e.g. 2D imaging cases, a 2D mixing-frequency magnetic field is used to excite the MNPs, which is composed of a high-frequency ($f = f_H$) drive magnetic field in x-direction and a low-frequency ($f = f_{Ly}$) scanning magnetic field in y-direction. The field free point (FFP) is driven by the mixing-frequency field to sweep in a Lissajous curve trajectory in the x-y plane, which causes the MNPs within the field of view (FOV) to generate mixing-frequency magnetization spectra. Within the spectra, main harmonics at $i \times f_H$ characterize the MNPs' magnetization in the drive field, while mixed harmonics at $i \times f_H \pm k f_{Ly}$ characterize the magnetization in the scanning field. The spectra of all harmonics are used to decode the position and concentration information to reconstruct a 2D image.

To verify the MPI based on mixing-frequency spectra, we have designed and built an MPI system. The system schematic is shown in Figure 1a. A pair of permanent magnets is used to generate the FFP, providing (0.62, 1.28, 0.64) T/m gradient field in (x-, y-, z-) directions. A solenoid coil is designed to generate the high-frequency drive magnetic field (H_H = 10 mT, f_H = 4980 Hz) in x-direction to determine the main harmonics of MPI. To excite the MNPs for mixed harmonics, a pair of saddle coils are designed to generate the low-frequency scanning magnetic field in y-direction (H_{Ly} = 10 mT, f_{Ly} = 97 Hz). Besides, gradiometric detection coils are designed to measure the mixing-frequency spectra of the MNPs for imaging. Figure 1b shows the mixing-frequency spectra and 2D system matrix (extracted from components of the system matrix at $9f_H \pm 5f_{Ly}$) measured from a single-dot phantom (diameter d = 1.5 mm, 4 μL Perimag® Plain, c_{Fe} = 8.5 mg/mL) by the MPI system. The experimental results show that when at higher mixing-frequency index, the MPI signal decreases in intensity, but reflects stronger volatility x- and y-directions.

Based on the imaging experiments, 2D reconstructed images of dual-dot phantoms (2×4 μL Perimag® Plain, c_{Fe} = 8.5 mg/mL) are presented in Figure 1c. The mixing-frequency MPI method attains spatial resolution better than 4 mm in x-direction and 3 mm in y-direction. In conclusion, the proposed MPI approach based on mixing-frequency spectra has showcased significant potential for high-resolution 3D imaging.

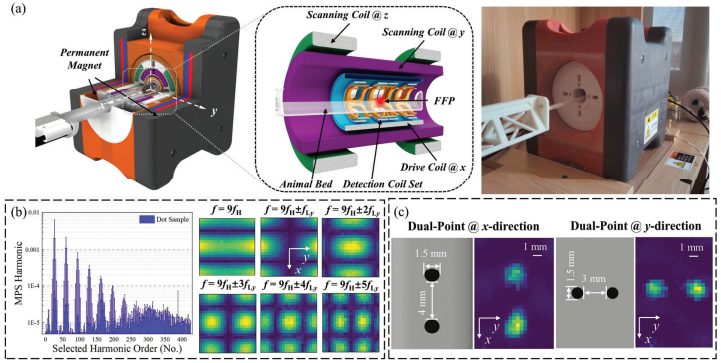

Figure 1. (a) Mixing frequency MPI system schematic with a high-frequency drive coil in x-direction, low-frequency scanning coils in y-direction and a detection coil set. (b) 2D mixing-frequency MPS harmonics and 2D system matrix are measured and analyzed. (c) Dual-dot phantoms with MNPs in x- and y-directions are imaged by the system using mixing-frequency method, showing a robust spatial resolution of 4 mm in x-direction and 3 mm in y-direction.

A Novel Coil Configuration Setup for Noninvasive Focused Brain Stimulation Using Magnetoelectric Nanoparticles: A Simulation Study

Muhammad Umar Tahir[1], Yaser Hadadian[1], Cao Thanh Luu[1], Hafiz Ashfaq Ahmad[1] and Jungwon Yoon[1*]

[1] School of Integrated Technology, Gwangju Institute of Science and Technology, Gwangju 61005, South Korea,

[*]Email: jyoon@gist.ac.kr

Magnetoelectric nanoparticles (MENPs) can facilitate functional stimulation based on the magnetic core, and piezoelectric coating enables them to have unique characteristics that ensure their non-invasive potential for stimulation. MENPs-based brain stimulation can be controlled with an externally controlled magnetic field non-invasively, unlike other conventional noninvasive stimulation techniques like transcranial electric stimulation (TES) and transcranial magnetic stimulation (TMS) which employ electrodes and coils to apply electric or magnetic forces to the human scalp, potentially resulting in both acute and neuroplastic alterations in cortical excitability. Additionally, MENPs can be controlled for drug delivery, can navigate towards the targeted region with localization, and have the potential for a blood-brain barrier (BBB) opening due to their unique ability to capitalize on their structural properties in the presence of the externally controlled field.

The magnetic core of MENPs, coated with piezoelectric $BaTiO_3$ and composed of magneto-resistive $CoFe_2O_4$ nanoparticles, can stretch in the presence of a high DC magnetic field, and can vibrate in the presence of a low-magnitude AC magnetic field. The vibration caused by the magnetic core will be transferred to the piezoelectric material, which will produce the electric potential for electric field required for stimulation purposes, and this controlled vibration has the potential to facilitate the BBB opening. Traditionally, MENP-based brain stimulation involves exposing the entire brain region to a combination of magnetic fields. However, for targeted stimulation, focused magnetic field at specific brain regions is necessary.

In this study, a focused magnetic field system for the MENPs stimulation was designed and simulated. The equipment configuration is shown in Figure 1. (a). Two pairs of permanent magnets (NdFeB) with upward magnetization were used to generate a uniform magnetic field in the upward direction. A Helmholtz pair of cylindrical coil configuration with narrow tips, with a soft iron core inside to concentrate the magnetic flux inside, was used to concentrate the magnetic field in the downward direction to form a narrower beam. A pair of external circular Halbach arrays with K3 configuration using permanent magnetics was utilized to concentrate the magnetic field towards the center. A pair of pancake-type AC magnetic field coils were utilized to generate a low amplitude with low-frequency magnetic field. The simulation results of magnetic field focusing, and AC magnetic field peak magnetic field are shown in Figure 1. (b). The MENPs will observe the 200 mT DC magnetic field with an additional 5 mT AC magnetic field with the frequency of 150 Hz to 200 Hz for simulation purposes at the focused region under 5 mm to generate the desired electric field for brain stimulation.

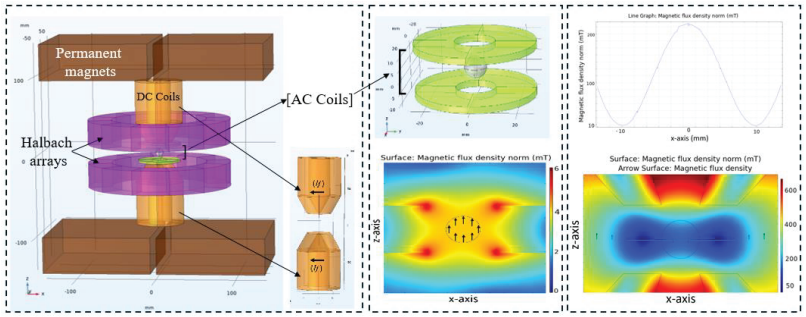

Figure 1. **(a)** Magnetic field focusing system with high amplitude DC and low amplitude AC magnetic fields. Permanent magnets and Helmholtz configuration DC electromagnet with soft iron core-filled coils with narrow tips are used to generate a DC magnetic field with 2D focusing. Permanent magnet based Halbach cylindrical array configuration to enhance focusing. **(b)** Pancake-type AC electromagnetic coils are used to generate a small AC magnetic field to ensure the desired magnetic field is in the focused region. **(c)** The results for the focused DC magnetic field to ensure the desired magnetic field required for stimulation.

Human Head Receive Coil-Coupled Magnetoresistive Sensor for Magnetic Particle Imaging

Suko Bagus Trisnanto[1*], Tamon Kasajima[2], Tomohiko Shibuya[2], Yasushi Takemura[1]

[1]Department of Electrical and Computer Engineering, Yokohama National University, Yokohama, Japan
[2]Technology and Intellectual Property HQ, TDK Corporation, Tokyo, Japan
*E-Mail: suko-trisnanto-zt@ynu.ac.jp

Magnetic particle imaging (MPI) is a promising method for brain diagnostics to examine the risk of neurovascular and neurodegenerative diseases by employing magnetic nanoparticles as tracers [1]. Therefore, human brain MPI scanner demands high sensitivity to probe low magnetic signals from allowable tracer dosage. One may optionally use a high inductance receive coil to multiply magnetization signal. However, an open-circuit voltage of such coil can be noisy due to self-resonance. In comparison to a standard signal filtering, we alternatively employed magnetoresistive (MR) sensor to couple with gradiometric human head coil via flux transformer. This current-sensitive detection expects an amplified MPI signal with low noise level to detect low tracer concentration [2].

We built a magnetometric system consisting of a 334-turns head receive coil with 20 and 18 cm conjugate diameters inside an excitation coil. The corresponding inductance was 9.9 mH to achieve 71.5 mV/µT coil sensitivity. Figure (a) shows that typical low-pass filtering was insufficient to deal with noisy V_R receive output, while detecting synthetic Langevin signal from a 1-mm coil. In contrast, flux transformer with MR sensor recognized a clean V_{SR} signal of 10.8 μg_{Fe} equivalent iron mass. Here, mini coil imitated magnetization response of Ferucarbotran (Resovist®) sample under 5 mT/μ_0 from shaping i_0 current waveforms. Upon combination with cancel coils into an asymmetric split gradiometer, Figure (b) further concludes the mass sensitivity limit reaching below 1 μg_{Fe}.

Owing to a considerable feed-through suppression under 5 mT/μ_0 at 2.0 kHz, it was preliminarily possible to detect third harmonic response of at least 0.7 mg_{Fe} Ferucarbotran sample with 0.1 ml volume [Figure (c)]. However, flux transformer-based receive chain might have a higher iron-mass sensitivity to consider signal averaging in the practical imaging protocols. Thus, this scenario leaves possibility to process raw MPI signal into better signal quality.

Acknowledgement: This work was partially supported by JSPS KAKENHI Grant Numbers 20H05652 and 22K14268.

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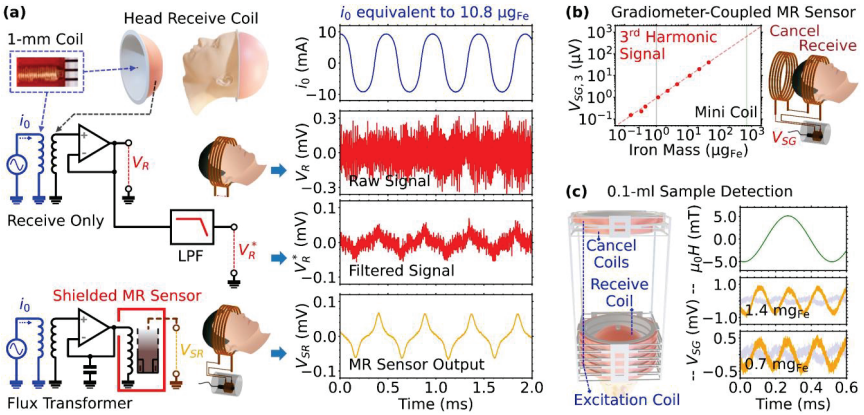

Figure. **(a)** Signal characteristics of a human-head receive coil coupled to MR sensor via flux transformer (V_{SR}) in comparison with typical low-pass filtering (V_R^*). A 9.4-mA current (i_0) at 2.0 kHz drives a 1-mm coil to generate Langevin signal equivalent to magnetization response of 10.8 μg_{Fe} Ferucarbotran nanoparticle sample under 5 mT/μ_0 excitation field (H). **(b)** Iron mass sensitivity limit of an asymmetric split gradiometer-coupled MR sensor corresponding to the detectable third harmonic signal ($V_{SG,3}$) from i_0-controlled mini coil. Here, additional cancel coils were phase compensated relative to the head receive coil before connecting to the flux transformer circuit. **(c)** The third harmonic signal detection of 0.1 ml Ferucarbotran sample for a given $\mu_0 H = 5$ mT. Blue and orange lines correspond to the sample-free and magnetization signals, respectively.

Rapid analysis of microbiological contaminants in 2 stages (RAMICO²)

Rainer Tietze[1*], Patrick Vogel[2], Johanna Günther[2], Emily Hausen, Lukas Heinen, Christoph Alexiou[1], Stefan Lyer[1]

[1]: *Department of Otorhinolaryngology, Head and Neck Surgery, Section of Experimental Oncology and Nanomedicine (SEON), Else Kröner-Fresenius-Stiftung-Professorship, Universitätsklinikum Erlangen, Germany. Erlangen, Germany.*[1]
[2]: *Department of Experimental Physics 5 (Biophysics), Julius-Maximilians-University Würzburg, Germany*
*E-mail: rainer.tietze@uk-erlangen.de

Careful monitoring of microbiological contaminants, which takes place at various points in the processing of food and feed, serves to ensure the safety of supply with food. A complete newly designed analytical method for a much faster, more sensitive and more selective detection of pathogenic microorganisms, which is at the same time robust and easy to handle, could make an important contribution here. The technological basis for this is (I) peptide-functionalized magnetic nanoparticles (SPION-Pep), which can bind a wide variety of microorganisms via a unique biomimetic mechanism. The basis for the efficient separation of microorganisms is the salivary protein GP340, which can bind many gram-positive and gram-negative bacteria and even fungi. The pattern recognition receptor GP340 binds to phosphorylated or sulfated cell wall components, but leaves the microorganisms intact and viable. The binding property is mediated by a short peptide of GP340, which we can bind to magnetic SPIONs (SPION-Pep). We were able to show that pathogenic microorganisms can be efficiently extracted from various substrates. Through this separation with the SPION-Pep, the pathogens remain intact and can then be detected extremely sensitively using a (II) newly developed magnetic spectroscopic measuring device (COMPASS). The underlying measurement principle, called Critical Offset Magnetic PArticle SpectroScopy (COMPASS), reacts sensitively to minimal changes in the mobility of magnetic SPIONs ensembles that can be caused by conjugation of biological compounds on the particle surface. The high sensitivity is achieved by measuring the jump-like behavior of the phase for specific combinations of static and dynamic excitation fields, which are referred to as critical points. Through certain capture structures, SPIONs become specific probes for the detection of e.g. microorganisms.

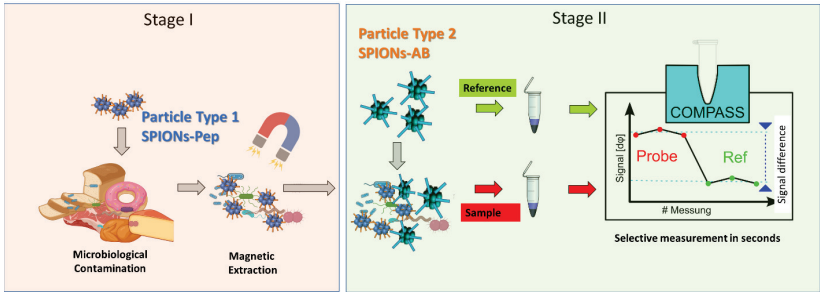

Figure1: Principle of two-stage detection of foodborn pathogenic microorganisms.

Acknowledgement: This work is supported by the Bavarian Ministry of Economic Affairs, Regional Development and Energy (StMWi).

Enzymatic-like Activity and Specific Loss Power Joining Forces for Vanadium Ferrite Theranostic Applications.

Teobaldo Enrique Torres,* [1, 2, 3,4] Daniela Paola Valdés, [5] Simon Hettler, [1,3] Joshua Brandon Stein, [4] Callan Daniel McLoughlin ,[4] Gerardo Fabián Goya [1, 2], Ki Bum Lee [4] and Raul Arenal.[1, 2, 3,6]

[1] Instituto de Nanociencia & Materiales de Aragón (INMA), CSIC- Universidad de Zaragoza, 50018 Zaragoza, Spain.
[2] Departamento de Física de la Materia Condensada, Facultad de Ciencias Universidad de Zaragoza, 50018, Zaragoza, Spain
[3] Laboratorio de Microscopías Avanzadas (LMA), Universidad de Zaragoza, Calle Mariano Esquillor, 50018, Zaragoza, Spain
[4] Department of Chemistry and Chemical Biology, Rutgers, The State University of New Jersey, 123 Bevier Road, Piscataway, 08854, NJ, USA
[5] Instituto de Nanociencia y Nanotecnología CNEA-CONICET, Av. E. Bustillo 9500, 8400, S. C. Bariloche, RN, Argentina.
[6] ARAID Foundation, 50018, Zaragoza, Spain *E-mail: teo@unizar.es

One of the main perspectives of nanocatalytic medicine in tumor therapy is to produce abundant intratumoral Reactive Oxygen Species (ROS) using sensitizers activated by exogenous stimulations such as ultrasound, magnetic fields, or by responding to the specific tumor micro-environment. Magnetic nanoparticles (MNPs) are one of the best example of sensitizers as they can also act as heating agents for magnetic fluid hyperthermia (MFH) applications. Nowadays, there is a great interest to optimize the synergistic effects between heating and enzymatic-like activity for cancer therapies. Vanadium compounds have been investigated as potential therapeutic agents for the treatment of various major health issues, including, atherosclerosis, diabetes and cancer. Many studies suggest a close relationship between vanadium toxicity and ROS, promoting the initiation for mitochondria-mediated cell apoptosis, signal transduction, etc. In this work, a series of $Fe_{3-x}V_xO_4$ MNPs with mean diameters <d> between 8 and 30 nm was studied. A detailed characterization have been carried out, including XPS, HRTEM, STEM-EELS, SQUID and MFH experiments in samples fixed in polyacrilamide gels, kinetic analysis of the peroxidase (POD) mimetic activity on TMB, and citotoxicity assays on RAW 264,7 macrophage cell. A saturation magnetization M_S up to 80 emu/g and SLP values up to 300 W/g at f= 374 kHz and H_{app}= 24kA/m were obtanied. Chemical composition maps performed on indivual particles reflect that vanadium is found with an increased intensity at the border of the MNPs and is distributed inhomogeneously. Colorimetric assays for POD-like activity show an increasing towards intense blue color as the concentration of the MNPs increase. Finally, viability assays reflect an optimal concentration of 50 μg/ml for viability after 16 hrs of incubation. Mitochondrial membrane potential assays are being carried out as a complement to the viability studies.
In conclusion, Vanadium ferrites are a viable material for medical applications, including ROS production and MFH with a great performance.

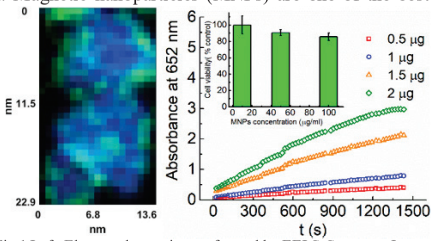

Fig 1 Left. Elemental mapping performed by EELS-Spectrum Image on a couple MNPs for sample with <d>= 11 nm. V in green, Fe in blue. Right. Reaction–time curves of TMB colorimetric reaction catalyzed by sample with <d>= 24 nm. Inset. Cell viability by sample with <d> = 30 nm carried out by Preston blue in Raw 264,7 incubated up 16 hrs.

Synthesis of Hybrid Nanomaterials Based on MXene/Magnetic Nanoparticles for Photo- Magnetic Hyperthermia Applications

Zhu P. Shen,[1] Helena Gavilán,[*,1,2] Álvaro Gallo-Cordova,[3] Lucía Gutiérrez,[4] Yílian Fernández-Afonso,[4] María B. Serrano[*,1] and Juan C. Cabanelas[1]

1 Department of Materials Science and Engineering, Universidad Carlos III de Madrid, Leganés, Madrid, 28911, Spain;
2 Department of Physical Chemistry, Universidad Complutense de Madrid, Madrid, 28040, Spain;
3 Department of Nanoscience and Nanotechnology, Instituto de Ciencia de Materiales de Madrid (ICMM-CSIC), 28049, Spain;
4 Instituto de Nanociencia y Materiales de Aragón (INMA) CSIC-Universidad de Zaragoza, Zaragoza, 50018, Spain

MXenes are two-dimensional transition metal carbides that have emerged as versatile nanomaterials. Their distinctive physicochemical properties and surface characteristics make them ideal platforms for engineering hybrid nanomaterials. The combination of MXenes and magnetic nanoparticles (MNPs) into single nano-object leads to materials with interesting properties (ferrimagnetism, mechanical strength, and conductivity, etc.) for a broad range of applications. In particular, MXenes exhibit good compatibility and excellent photothermal (PTT) properties; while MNPs, particularly iron oxide nanoparticles (IONPs), are exploited for biomedical applications like cancer treatment through magnetic hyperthermia (MHT).

This work focuses on the fabrication of hybrid nanomaterials based of MXenes and MNPs. The surface of delaminated MXenes (dMXenes) sheets was decorated with oleic acid-coated IONPs of 14–15 nm. We have systematically varied the concentration of MNPs on the surface of the MXenes, tuning the MXene/MNPs mass ratios (10/90, 30/70, 50/50, 70/30 and 90/10). The potential of the hybrids for photo- magnetic hyperthermia was evaluated using near-infrared (NIR) light (1064 nm, 1 W) and alternating magnetic fields (AMFs) of 9.5–17.0 kA/m and 282 kHz, determining their specific absorption rates (SAR) values. While for MHT, SAR values are up to 130–150 W/g (Fe_3O_4) for 50/50 hybrids, the characterization of this new nanomaterial revealed a synergistic behavior in PTT, achieving SAR values up to 577 and 1106 W/g (hybrid), for 50/50 and 70/30 mass ratio hybrids, respectively. This work demonstrates the heat dissipation capability of MXene/MNPs nanohybrids through exposure to AMFs and via laser excitation.

Unravelling the potential of *Magnetospirillum gryphiswaldense* as nanorobot, a detailed motility study.

Danny Villanueva-Alvaro[1*], Alicia G. Gubieda[2], Alfredo García-Arribas[1,3], Ana Abad[2], Jorge Feuchtwanger[1,4], David de Cos[5], Mª Luisa Fdez-Gubieda[1,3]

[1]Dpto. Electricidad y Electrónica, Universidad del País Vasco (UPV/EHU),48940 Leioa, Spain.
[2]Dpto. Inmunología, Microbiología y Parasitología, Universidad del País Vasco (UPV/EHU),48940 Leioa, Spain.
[3]Basque Center for Materials Applications and Nanostructures (BCMaterials), 48940 Leioa, Spain.
[4]Ikerbasque, Basque Foundation for Science, 48009 Bilbao, Spain.
[5]Dpto. de Física, Universidad del País Vasco (UPV/EHU), Spain.
* Email: dannyyosmar.villanueva@ehu.eus , Mobile:+34 677 82 95 51

Magnetotactic bacteria (MTB) are aquatic microorganisms with the ability to align and navigate with the earth's magnetic field lines due to the presence of a chain of magnetic nanoparticles. MTB features, such as self-propulsion, magnetic guidance and their capability to grow and proliferate in hypoxic regions, make them unique as nanobiorobots for potential antitumor applications [1-3].
Trying to shed light on the motility of MTB under magnetic field, we set up a three-axis Helmholtz coil system, which allows us to define a precise 3D magnetic field vector with different time-varying configurations. In addition, we have developed software algorithms for the automatic detection and simultaneous tracking of a large number of MTB trajectories by applying image-sequencing techniques to the analysis of videos acquired by optical microscopy. We have performed a detailed motility study of a *Magnetospirillum gryphiswaldense* (MSR-1) strain, in which we evaluate the navigation direction, swimming velocity, aligned bacteria population and response times for different configurations of the applied magnetic field. As an example, Figure 1 shows the motility response of MSR-1 under a rotating magnetic field of 0.1 mT with a constant frequency of 0.2 Hz. Under these conditions, bacteria follow the direction of the magnetic field, describing elliptical trajectories, Figure 1a. The overall behaviour is revealed by analysing swimming direction of the MSR-1 population with time as it shown in the Figure 1b where each coloured square represents an MSR-1 population amount. First, there is a relatively uniform bacteria population (blue) that moves randomly (≈ 20% total population). Second, there are other well-defined populations of bacteria, which form sloped bands in Figure 1b, whose swimming direction increases linearly with time (≈ 80% total population). Finally, we find that half of the working population moves parallel to the magnetic field and the other half antiparallel to it, Figure 1c.

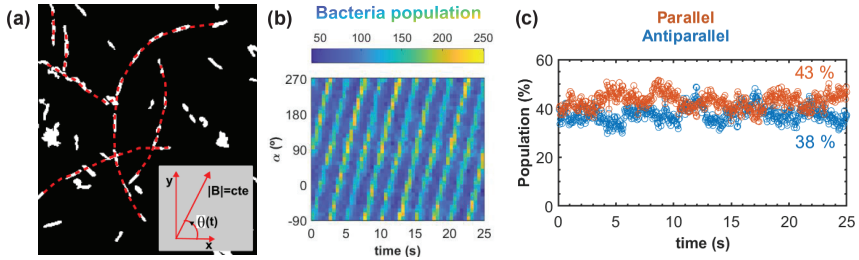

Figure 1: Swimming behaviour of MSR-1 under a rotating magnetic field of 0.1 mT with a frequency of 0.2 Hz, (a) Elliptical trajectories, (b) swimming navigation direction with time and (b) Bacteria population with time swimming parallel and antiparallel with the external applied magnetic field within an arc of 30º.

Acknowledgments
Grant PID2020-115704RB-C31 funded by MCIN/AEI/ 10.13039/501100011033 and, as appropriate, by ESF Investing in your future.

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Strong exchange bias effect in cobalt oxide-cobalt ferrite core-shell nanoparticles

Samyog Adhikari, Vlado Lazarov, Roger Johnson, Leonardo Lari, Le Duc Tung and Nguyen TK Thanh*

*ntk.thanh@ucl.ac.uk, http://www.ntk-thanh.co.uk

Biophysics Group, Department of Physics & Astronomy University College London, Gower Street, London WC1E 6BT, UK and UCL Healthcare Biomagnetics and Nanomaterials Laboratories, 21 Albemarle Street, London W1S 4BS

Exchange bias or exchange anisotropy occurs when there is a coupling between antiferromagnetic and ferromagnetic materials. Here, the hard magnetisation behavior of the antiferromagnet causes a shift in the soft magnetization curve of the ferromagnet along a field axis generally in the opposite direction to the cooling field.[1] To observe the shift in hysteresis, the Curie temperature (T_C) of the ferro/ferrimagnet has to be larger than the Neel temperature (T_N) of the antiferromagnet and the cooling field should be applied at higher T_N temperature.[1] We have synthesised monodisperse composite core-shell nanoparticles that display strong exchange bias between antiferromagnetic cobalt oxide (CoO) and ferrimagnetic cobalt ferrite ($CoFe_2O_4$).

The core-shell nanoparticles are synthesised with a one-step thermal decomposition technique. As a comparison, pure $CoFe_2O_4$ and CoO nanoparticles are synthesised separately. The individually synthesised CoO adopts a mixed cubic (Fm-3m) and hexagonal (P63mc) crystal system, whereas $CoFe_2O_4$ a cubic (Fd-3m) crystal system. The transmission electron microscopy (TEM) results show the monodispersity of synthesised nanoparticles. The SQUID magnetometry results show a superparamagnetic response at room temperature. At low temperatures, the magnetic hysteresis exhibits enhanced coercivity and magnetic hysteresis loop shift of up to 11 kOe in the negative direction. The exchange bias disappears above ~120K. We have performed several other characterisations including Raman, UV-Visible spectroscopy, high-resolution TEM, DLS, FTIR, and neutron diffraction to investigate its chemical, magnetic, and structural information for its potential applications in biomedicine and spintronics.

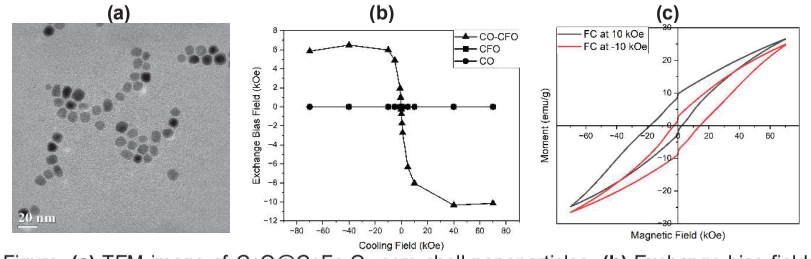

Figure. **(a)** TEM image of CoO@$CoFe_2O_4$ core-shell nanoparticles. **(b)** Exchange-bias field measured against cooling fields. The maximum shift in the hysteresis loop was observed with a cooling field of 40 kOe. **(c)** The shift in magnetic hysteresis loop after a cooling field of 10 kOe and -10 kOe at 5 K.

Reference:

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Synthesis and characterisation of (Co, Ni) Fe_2O_4 – $BaTiO_3$ magnetodielectric nanocomposites.

Samyog Adhikari, Ali Khaleghi, Muhammad Imran Arshad, Le Duc Tung, and Nguyen TK Thanh*

*ntk.thanh@ucl.ac.uk, http://www.ntk-thanh.co.uk

Biophysics Group, Department of Physics & Astronomy University College London, Gower Street, London WC1E 6BT, UK and UCL Healthcare Biomagnetics and Nanomaterials Laboratories, 21 Albemarle Street, London W1S 4BS

The magnetoelectric (ME) and magnetodielectric (MDE) effects are obtained through the coupling of magnetic and electric properties such as ferromagnetism and ferroelectricity. These materials are of significant interest for application in biomedical, microwave devices, data storage, and sensors amongst others as the coupling between the two properties will allow direct control of ferroelectricity and magnetism.[1,2] Although there are several ways of achieving the ME and MDE effects, combining a magnetic material with a ferroelectric one in a core-shell structure has gained significant interest in recent years. Ferrites are used as the magnetic phase due to their high magnetostrictive coefficient and perovskite such as barium titanate ($BaTiO_3$) as the ferroelectric phase due to its high piezoelectric coefficient.[3,4] When a magnetic field is applied, the magnetic phase undergoes magnetostriction which causes the material to strain and elongate. This mechanical energy is transferred to the perovskite which then exhibits electric polarisation. This is called strain-mediated magnetoelectric coupling (figure 1a).

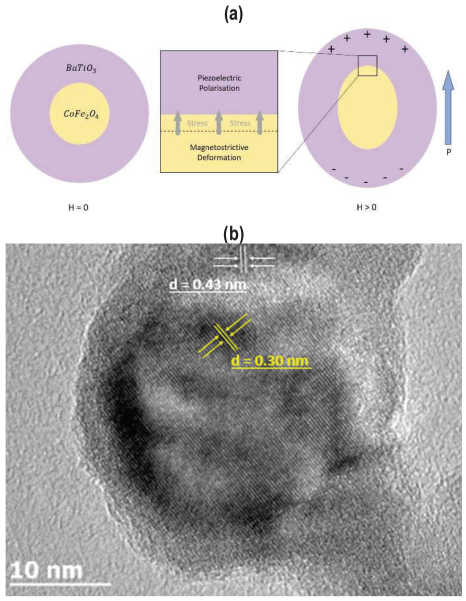

Figure 1. **(a)** Schematic of magnetoelectric coupling causing the direct magnetoelectric effect. **(b)** TEM image of ferrite-perovskite core-shell-like nanocomposite. Interplanar distance (d) for the ferrite and perovskite is 0.30 and 0.43 nm respectively.

We synthesised the (Co, Ni) ferrites using the solvothermal technique. To establish a physical connection between the two phases, the coating of the $BaTiO_3$ was performed using the sol-gel method. The X-ray diffraction data shows the formation of correct phases without significant impurities. Raman spectroscopy was used to confirm tetragonal phase in the $BaTiO_3$ phase. The transmission electron microscope (TEM) shows a mixed core-shell and alloy-like nanostructure. The elemental mapping image obtained using a scanning TEM shows the presence of barium, titanium, cobalt, nickel, and iron as a composite. Several electrical parameters such as conductivity, permittivity, and capacitance of the sample were measured using an LCR meter with and without an alternating magnetic field (AMF). Under an AMF, capacitance and permittivity were decreased, whereas the conductivity was unchanged.

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Quantitative visualization of transferrin receptor-mediated iron uptake in Hepatocellular carcinoma using MPI/NIR-II photomagnetic multimodal imaging

Yueqi Wang[1*], Changjian Li[2], Jie Tian[1, 2]

[1] CAS Key Laboratory of Molecular Imaging, Beijing Key Laboratory of Molecular Imaging, the State Key Laboratory of Management and Control for Complex Systems, Institute of Automation, Chinese Academy of Sciences, Beijing, 100190, China.

[2] School of Engineering Medicine, Beihang University, Beijing 100191, China.

[*] Corresponding author, email: yueqi.wang@ia.ac.cn

Abstract: Transferrin receptor (TfR)-mediated abnormal iron uptake occurs during the early development of liver fibrosis (FIB) and hepatocellular carcinoma (HCC), but there is currently a lack of molecular imaging methods for its quantitative visualization. In clinical practice, 80-90% of HCC is accompanied by FIB, and visualization of iron uptake helps to clearly delineate the boundary of FIB-tumor and detect micronodules in early HCC. The long-term monitoring of iron uptake in FIB-HCC requires high sensitivity, penetration depth and resolution. The Magnetic nanoparticle imaging (MPI)/second near-infrared window (NIR-II) fluorescence multimodal imaging combines the above advantages. MPI is a new tomographic technique that detects changes in the electronic magnetization of iron and allows non-invasive quantitative monitoring of marker biodistribution without the use of ionizing radiation. Therefore, it is very suitable for the quantitative detection of TfR changes in vivo. The NIR-II fluorescent molecular imaging is a novel technique, which has broad application prospects in tumor surgical navigation. The combination of MPI and NIR-II fluorescent imaging complements each other because MPI has a relatively low spatial resolution. We have designed multi-targeting MPI/NIR-II probe (GC NPs) for specific monitoring of TfR-mediated iron uptake in FIB-HCC. GC NPs consists of superparamagnetic iron oxide nanoparticles (SPIO), glypican-3-targeting peptides, TfR-targeting peptides, and indocyanine green. SPIO, as a stable nanocarrier and MPI imaging tracer, does not interfere with TfR-mediated iron uptake and NIR-II imaging. At different time points within 0-72 hours after tail vein injection, the specificity and sensitivity of GC NPs in FIB-HCC mouse models were evaluated using MPI/NIR-II fluorescent multimodal imaging. The MPI and NIR-II fluorescent signal of GC NPs was peaked at 48 hours after tail vein injection in vivo. Compared with non-targeted probes, GC NPs increased the tumor liver background ratio in FIB-HCC by 2.3 times with non-invasive in vivo imaging and highlight micronodules of HCC (<1mm) during surgery. This MPI/NIR-II imaging strategy promotes the application of iron uptake molecular visualization for early tumor detection and precise intraoperative navigation.

Enzyme-Powered Magnetic Nanomotors for Magnetic Particle Imaging and Magnetic Fluid Hyperthermia

Huimin Wei[1*], Justin Ackers[1], Heiko Lemcke[1], Juan C. Fraire[2], Samuel Sánchez [2,3], Thorsten M. Buzug[1,4], Matthias Graeser[1,4], and Anna C. Bakenecker[1]

[1] Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering, IMTE, Lübeck, Germany
[2]Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[3]Catalan Institute for Research and Advanced Studies (ICREA), Barcelona, Spain
[4] Institute of Medical Engineering, University of Lübeck, Lübeck, Germany
Email: huimin.wei@imte.fraunhofer.de

To improve the efficiency of magnetic fluid hyperthermia therapy, it is beneficial to have magnetic materials which has good penetration and diffusion properties to increase their accumulation in the targeted tissue. Self-propelled nanoparticles, usually called nanomotors, have shown great potential in enhancing these properties since they obtain the energy to self-propel from catalytic reactions [1]. Recently, it has been demonstrated that urease-powered nanomotors with self-propelling capacity show an increased accumulation in the tumor and leverage the efficiency of radiotherapy with radiolabeled nanomotors [2]. MFH is a promising cancer therapy which dissipates heat to the malignant regions through hysteresis losses in magnetic materials such as magnetic nanoparticles. Magnetic particle imaging (MPI) helps to provides accurate control of MFH therapy by enabling precisely localized heating to a specific target temperature deep in the tissue as well as visualization of the distribution and quantification of the temperature of magnetic nanoparticle [3,4]. As an imaging technique, MPI also provides the real-time 3D visualization of the distribution of the nanomotors topographically, which allows for 3D motion analysis of the nanomotors.

In this work, we present a self-propelled urease-powered magnetic nanomotor which can serve as tracer for MPI imaging as well as magnetic material for hyperthermia. It can be used in MPI-assisted MFH and with efficient penetration and diffusion and improved heating effect in biological environments. The urease-powered magnetic nanomotors are synthesized using commercial magnetic nanoparticles, which feature good properties as tracer for MPI and magnetic hyperthermia (Synomag, Micromod, Rostock, Germany) [4]. These were functionalized with urease. The behavior in urea solution of the nanomotors is compared to the passive particles under optical microscopy (Figure 1) and the nanomotors are used to obtain 3D MPI images on a preclinical MPI scanner (MPI 25/20 FF, Bruker BioSpin, Ettlingen, Germany). Furthermore, the magnetic nanomotors are evaluated with respect to their specific-absorption-rate as well as ex-vivo MFH treatment using a custom-made magnetic hyperthermia device at field parameters comply to the biological discomfort level (f=302 kHz, A_{MFH}=30 mT_{pk}) [5].

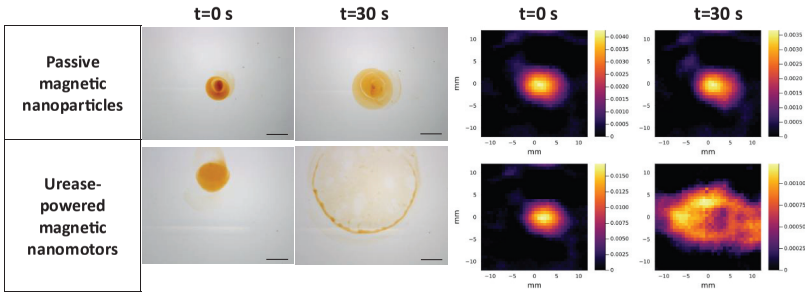

Figure 1: Comparison of active magnetic nanomotors and passive magnetic nanoparticles. Left: behaviour in 300 mM urea. The nanomotors diffused to cover a larger area than the passive nanoparticles. Scale bar 2 mm. Right: xy-plane slice of the 3D MPI image volume showing the spread of nanomotors. Colorbar signal intensity.

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Preparation and characterization of hybrid magnetic nanoparticles featuring a "hard" biomolecular corona for medical applications

Andreas Weidner[1], D. Eberbeck[2], J.H. Clement[3], S. Dutz[4,5]

[1] *Electrochemistry and Electroplating group, Technische Universität Ilmenau, Ilmenau, Germany*
[2] *Physikalisch-Technische Bundesanstalt Berlin, Berlin, Germany*
[3] *Abteilung Hämatologie und Internistische Onkologie, Universitätsklinikum Jena, Jena, Germany*
[4] *Institute of Biomedical Engineering and Informatics, Technische Universität Ilmenau, Ilmenau, Germany*
[5] *Leupold Institute for Applied Natural Sciences (LIAN), Westsächsische Hochschule Zwickau, Zwickau, Germany*
E-mail: andreas.weidner@tu-ilmenau.de

Magnetic nanoparticles (NPs) are promising materials for medical application, e.g. drug delivery or magnetic heating. Applied in a biological system, they instantly interact with biomolecules and form a biomolecular corona (biocorona) as interface with a "soft" (removable by washing) and a "hard" part (remains after washing). To avoid unwanted reactions in the body (e.g. clotting, immune response) it is of major importance to control its properties. The approach presented here, is to prepare colloidally stable, biocompatible magnetic hybrid NPs featuring a controlled preformed "hard" biocorona.

Iron oxide multicore NPs with anchor layers featuring different stabilization mechanisms and surface charges were produced (diethylaminoethyl-dextran (DEAE), carboxymethyl-dextran (CMD), starch (St); see fig.1, 1st and 2nd). Protocols to transform these core-shell NPs into hybrid NPs featuring a "hard" biocorona with applicable properties (polydispersity index (PDI) ≤ 0.100, $\beta \geq 1.0$ mg/mL) were successfully developed and implemented. Therefore, the core-shell NPs were controlled incubated in 90 % (v/v) fetal calf serum (FCS) at 37 °C for 10 min in a water bath and 4x magnetically washed. The resulting hybrid NPs were fractionated by centrifugation (5,000 g, 1 min). Batches with a PDI < 0.100 were selected, homogenized and characterized with focus on colloidal stability, cytotoxicity and the "hard" biocorona.

DEAE-hybrid NPs showed the most profound "hard" biocorona followed by CMD- and St-hybrid NPs. It was possible with specific models (e.g. multi-core single-domain model (MCSDM)) to quantitatively estimate their thickness using a combination of thermogravimetric analysis (TGA), vibration sample magnetometry (VSM), dynamic light scattering (DLS) and AC-susceptibility (ACS) (see fig.1, 3rd).
The protein composition of their "hard" biocoronas was analyzed by gel electrophoresis (SDS-PAGE, see fig.1 3rd). A dependence on the absolute values of the zeta-potential of the underlaying anchor layers (see fig.1, 2nd) due to attachment of small proteins (M_w < 30 kDa) could be determined.
In stability experiments only DEAE-hybrid NPs were colloidally stable after incubation 1:10 (v/v) in FCS for min. 7 d, what could be interpreted with less crosslinking due to the profound biocorona. The thickness of the "soft" biocorona could be determined by ACS (see fig.1, 3rd). CMD- and St-hybrid NPs were colloidally instable, what could be due to crosslinking and could be quantitatively estimated by ACS.
Cytotoxicity experiments (Celltiter Glo® on BeWo cells up to 100 µg/cm² ≙ β = 0.378 mg/mL) showed moderate to no toxicity *in vitro* for all hybrid NPs. Biocompatibility *in vivo* (shell-less *ex ovo* chicken egg model HET-CAV, β = 1 mg/mL), preservation by freeze drying and sterilization with UV-C light for DEAE-hybrid NPs were presented before [1].

Thus, we were able to successfully develop a ready-to-use protocol to prepare colloidally stable, biocompatible DEAE-hybrid-NPs, that are promising for a futher development towards a medical application.

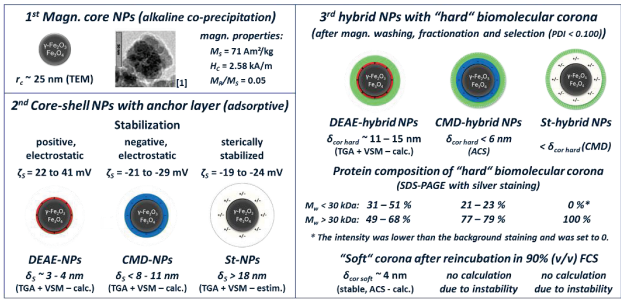

Figure 1) Properties of core, core-shell and hybrid NPs with focus on the biocorona.

Acknowledgements

This work was supported by Deutsche Forschungsgemeinschaft (DFG) by the priority program 1681 (CL202/3-1, CL202/3-2, CL202/3-3, DU1293/4-1, DU1293/4-2, DU1293/7-3, SCHA1640/7-1; FKZ).

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Non-Stoichiometric Cobalt Ferrite Nanoparticles by Green Hydrothermal Synthesis and their Potential for Hyperthermia Applications

Maria Weißpflog[1*], Ngoc Nguyen[1], Nils Sobania[1], and Birgit Hankiewicz[1]

[1]University of Hamburg, Institute of Physical Chemistry, Grindelallee 117, 20146 Hamburg, Germany
[*]Email: maria.weisspflog@uni-hamburg.de, Phone: +49 40 42838-3428

In hyperthermia applications, magnetic nanoparticles (MNP) with high saturation magnetization values and Brownian relaxation behavior are exposed to an alternating magnetic field, whereby heat is generated in the surrounding media to destroy tumor cells locally. Among different types of ferrites, magnetite has the highest magnetic moment, which results in high saturation magnetization values. However, iron oxide tends to oxidize and is a soft magnetic material, and therefore, relaxes according to the Néelian mechanism for particle diameters up to 20 nm. On the other hand, cobalt ferrite nanoparticles (CFNPs) have shown promise as they exhibit a higher magneto-crystalline anisotropy than iron oxide and show hard magnetic properties. Due to that, the Brownian relaxation mechanism is possible for CFNPs larger than 7 nm.

Therefore, our research focuses on the synthesis of non-stoichiometric CFNPs, where reduced concentrations of Co^{2+} ions lead to high saturation magnetization values combined with a Brownian relaxation mechanism. By utilizing a two-step method involving akaganeite nanorod precursors followed by an aqueous hydrothermal reaction without harmful surfactants or solvents, we were able to synthesize cubic and spherical $Co_xFe_{3-x}O_4$ nanoparticles with $0.25 < x < 0.45$ as shown in Figure 1A. The saturation magnetization values of 50 to 75 Am^2/kg are comparable to near-stoichiometric CFNPs ($x = 0.81$) produced by basic coprecipitation.

The hyperthermia-induced temperature change of up to 9.9 K within 10 minutes at 10 kHz and 24.4 mT has significant implications for medical applications such as magnetic particle imaging and cancer treatment. By optimizing the excitation values, we achieved a temperature increase of 43 K/10 min at 150.5 kHz and 19.0 mT without surpassing the biological limit for non-selective heating. The specific absorption rates (SAR, Figure 1B) ranged from 42 to 58 W/g_{MNP} for lower cobalt contents of 50 to 60%. In conclusion, this work is of great importance for the greener aqueous synthesis of magnetic CFNPs, as the cobalt content can be reduced without negatively affecting the hyperthermia and SAR values.

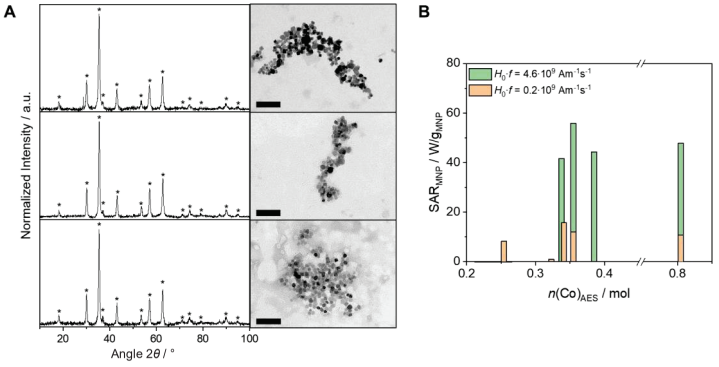

Figure 1. (A) X-ray diffractograms and TEM images of the non-stoichiometric cobalt ferrite nanoparticles synthesized with a molar ratio of akaganeite to metal salts of 2 (top), 1 (middle), and 0.5 (bottom). All the observed diffraction reflexes are in good agreement with the cubic spinel structure of $CoFe_2O_4$ (stars, JCPDS no. 00-003-0864). The scale bars show 100 nm for all micrographs. **(B)** SAR values of non-stoichiometric CFNPs are displayed in dependency on the cobalt amount in the crystal lattice.

Acknowledgment: This work was funded by the Deutsche Forschungsgemeinschaft (DFG) project "GRK 2536".

Ferrite Nanoparticles Nanocatalysts: Unveiling Free Radical Generation and Assessing Environmental Impact on Algal Toxicity

Carolina Bagnato[1], Gisela Ferraro[1], Enio Lima Jr.[2], Nahuel Nuñez[2], Marcelo Vasquez Mansilla[2], Alvaro Gallo Córdova[3], M. Puerto Morales[3], Elin L. Winkler[2]

[1] Instituto de Energía y Desarrollo Sustentable (IEDS), CNEA, Centro Atómico Bariloche, San Carlos de Bariloche, Argentina.
[2] Laboratorio de Resonancias Magnéticas, Gerencia de Física, Centro Atómico Bariloche, Av. Bustillo 9500, (8400) S. C. de Bariloche (RN), Argentina
[3] Instituto de Ciencia de Materiales de Madrid, ICMM/CSIC, C/ Sor Juana Inés de la Cruz 3, 28049 Madrid, Spain

The disposal of organic contaminants into water basins causes serious environmental damage, impacting human health and drinking water sources. Currently, various physical, chemical, and biological techniques are combined to treat the decomposition of dyes and phenolic compounds found in wastewater. Among these approaches, engineering iron oxide nanoparticles proves to be highly effective in degrading organic contaminants through advanced oxidation processes [1,2]. This process involves the generation of highly oxidative radicals, catalyzed on the nanoparticle surface in the presence of oxidant agents such as H_2O_2, which oxidize or degrade organic molecules. Furthermore, the development of magnetic nanocatalysts stands out for their ability to be recovered and reused through magnetic harvesting. However, the high potential and increasing demand for these materials require a deeper evaluation of their impact on the environment to select efficient nanocatalysts for degrading organic contaminants while avoiding the production of toxic systems.

In this context, we synthesized different ferrite nanoparticles (AFe_2O_4, where A = Fe, Mn, Zn) with an average size of ~15 nm and evaluated the production of free radicals, particularly •OH and •OOH, in the presence of H_2O_2 at different pH conditions. We found that the concentration and nature of the free radicals depend on the surface nanoparticle composition, with •OH being the dominant species produced by magnetite, while maghemite and manganese ferrite mostly produced •OOH. Conversely, zinc ferrite showed almost negligible activity when the experiment was conducted under acidic conditions.

The potential toxicity of these nanoparticles and their impact on living organisms were evaluated using the alga Chlamydomonas as a model system. Analysis of the algae population growth rate revealed that while manganese ferrite and maghemite exhibited cytotoxicity when incubated with the nanoparticles, magnetite and zinc oxide ferrite did not significantly affect the population compared to the control system. Transmission electron microscopy (TEM) images revealed that the interaction between the cells and the nanoparticles depends on their composition, leading to different impacts on the physiology and morphology of the algae. We discuss the possible origins of the interaction between the nanoparticles and the algae, the effects of free radical production, and the oxidative stress induced in these living organisms.

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Using adjustable DC offset fields in Magnetic Particle Spectroscopy towards sensitive immunoassays

Florian Wolgast*, Eike Wendt, Frank Ludwig, Meinhard Schilling, Thilo Viereck

Institute for Electrical Measurement Science and Fundamental Electrical Engineering and Laboratory for Emerging Nanometrology (LENA), TU Braunschweig, Germany
*E-Mail: f.wolgast@tu-braunschweig.de

The application of magnetic biosensing concepts allows the versatile detection of e.g. antigens, antibodies, or specific nucleic acid sequences [1-3]. A promising approach for the realization of such magnetic immunoassays (MIAs) is Magnetic Particle Spectroscopy (MPS), as it allows the realization of homogeneous, volume-based assays in opaque media with high sensitivity and thus it enables easy-to-handle MIAs. In addition, the signal is not affected by dia- or paramagnetic background signals. In MPS, the magnetic nanoparticles (MNPs) are repeatedly driven into saturation by a sinusoidal magnetic field and their magnetization response, which contains higher harmonics in addition to the fundamental, is measured. The evaluation is performed independently of MNP concentration by using the ratio of two harmonics. Improving the sensitivity of such MPS-based bioassays is of particular importance in order to reach the clinically relevant analyte range. A common approach is the application of an additional DC offset field, which is superimposed on the alternating excitation field and which generates additional even harmonics with large amplitude [3,4]. An adjustable DC offset field (ADOF) provides a further degree of freedom and can be adapted to the given particle system to further increase sensitivity.

Here we present the advantages of using an ADOF in MPS to obtain harmonic ratios that have both higher harmonic amplitudes and a large change upon analyte binding. For this purpose, different particle systems are simulated as well as measured under ADOF using the successor of our low-cost immunoMPS [5]. The change in the binding state is first mimicked using suspensions with various viscosity. In the next step, the principle is applied to streptavidin-biotin binding reactions and compared with the results we previously achieved with our immunoMPS.

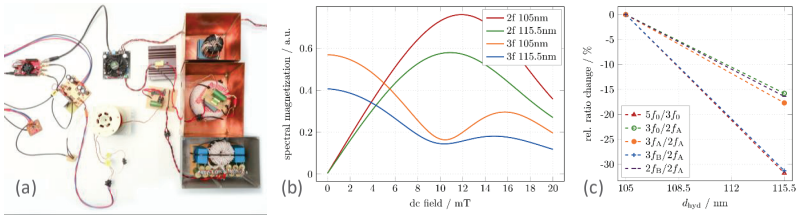

Figure 1: (a) Setup of our new generation immunoMPS to measure (b) the DC field dependence of the second and the third harmonic magnitude from BNF-Starch particles with 80 nm diameter (micromod Partikeltechnik GmbH) at two different viscosities resulting in hydrodynamic sizes of 105 nm and 115.5 nm. For the excitation a field of 15 mT and 2 kHz is used. (c) Exemplary resulting harmonic ratios for different operating points of the DC offset.

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Modified Jiles-Atherton model for dynamic magnetization and reconstruction in magnetic particle imaging

Yimeng Li[1,*], and Yu An[1], and Jie Tian[1]
[1]School of Biology Science and Medical Engineering, Beihang University, Beijing, China
[*] Email: 14031002@buaa.edu.cn

Magnetic particle imaging (MPI) is a promising medical modality with high resolution and sensitivity. In recent years, there has been a remarkable focus within the MPI community on modeling the magnetization behavior of superparamagnetic iron-oxide nanoparticle (SPIO). Our research aims to accurately describe the dynamic magnetization of SPIO by proposing a modified Jiles-Atherton (MJA) model that considers the relaxation effect. The accuracy and robustness of the MJA model have been validated through comprehensive magnetic particle spectrometry experiments. Building upon this magnetization model, we have explored its application in the MPI reconstruction process. There are two main reconstruction algorithms in the MPI area: the system matrix (SM) method, and the x-space method. In the case of the SM method, the MJA model proves valuable as it replaces the time-consuming and noise-containing SM measurement procedure, significantly reducing the overall time required for MPI reconstruction. As for the x-space method, integrating the MJA model into the reconstruction process enhances the spatial resolution of the reconstructed images. These advancements have been tested and validated using our self-developed MPI scanner. Moving forward, we intend to explore the potential of the MJA model in multi-contrast imaging and preclinical applications, further expanding its capabilities in the field of MPI. Overall, our research contributes to the advancement of modeling techniques in MPI and demonstrates the potential impact of the MJA model in improving the accuracy and efficiency of MPI reconstruction processes.

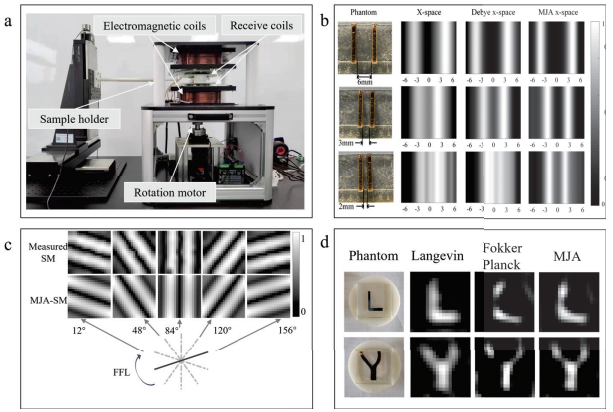

Figure 1. Some of our key findings: (a) our homemade MPI scanner serves as a vital experimental platform for our research; (b) the reconstruction results by integrating the MJA model into the x-space algorithm, and the spatial resolution is improved; (c) the SM calculated by the MJA model, providing an efficient alternative to the traditional measurement procedure; (d) the reconstruction results using MJA model-based SM.

Quantitative Estimation of Solid and Liquid Phase Magnetic Nanoparticles for Magnetic Immunoassay

T. Yoshida, T. Mizuki, I. Matsuzaki, and T. Sasayama

Department of Electrical Engineering, Kyushu University, Motooka 744, Nishi-ku, Fukuoka 819-0385, Japan.
E-mail : t_yoshi@ees.kyushu-u.ac.jp

Magnetic immunoassay using magnetic nanoparticles (MNPs) and magnetic particle imaging (MPI) are novel diagnostic techniques that detect magnetization signals from MNPs. In these applications, quantitative estimation of the binding states of MNPs to biomarkers is the key for practical applications.

In this study, we used a mixture of solid and liquid MNPs samples to simulate whether MNPs bind to biomarkers, and quantitatively estimated the iron contents of the solid and liquid MNPs using the magnetization harmonics from the MNPs sample. Perimag®-plain (micromod, Germany) was used as a MNPs sample and each iron content of solid and liquid MNPs, was calculated by solving the inverse problem of the following equation.

$$\boldsymbol{v} = [v_{m1} \quad v_{m2} \quad \cdots \quad v_{mn}]^{\mathrm{T}} = \boldsymbol{A}[w_L \quad w_S]^{\mathrm{T}} = \boldsymbol{A}\boldsymbol{w}. \tag{1}$$

Here, $v_{m1}, v_{m2}, \cdots, v_{mn}$ are measured voltages corresponding to the magnetization harmonics of MNPs, $A \in \mathbf{R}^{n\times 2}$ is the system matrix, w_L and w_S are the iron contents in the liquid and solid phase samples, respectively. When the measured voltage noise $\Delta\boldsymbol{v}$ is included in the measured voltage, eq. (1) can be rewritten as

$$\boldsymbol{v} + \Delta\boldsymbol{v} = \boldsymbol{A}(\boldsymbol{w} + \Delta\boldsymbol{w}) = \boldsymbol{A}\tilde{\boldsymbol{w}}. \tag{2}$$

Here, $\Delta\boldsymbol{w}$ is the error of the estimated weight vector. By performing the singular value decomposition to $\boldsymbol{A}$ and using some properties of orthogonal matrices, we obtain the following relationship between $\Delta\boldsymbol{w}$ and $\Delta\boldsymbol{v}$ using the smallest singlar value λ_2.

$$\|\Delta\boldsymbol{w}\| \leq \|\Delta\boldsymbol{v}\|/\lambda_2. \tag{3}$$

Based on eq. (3), the harmonic components used were determined to minimize $\Delta\boldsymbol{w}$. In the experiment, 3 harmonic components, $M_{3\mathrm{I}}$, $M_{5\mathrm{R}}$, and $M_{7\mathrm{R}}$ were used for the estimation of each iron content. Here, the subscript figures represent the harmonic order, and the subscript characters "R" and "I" correspond to the real and imaginary parts of the harmonics. Figure 1 shows the estimated results of the iron content in the solid and liquid MNPs for five mixture samples (S0, S25, S50, S75, S100) with different iron content ratios (total iron content for each sample was fixed to 42.5 μg). As shown, the estimated error was below few μg in terms of iron content for both the liquid and solid MNPs.

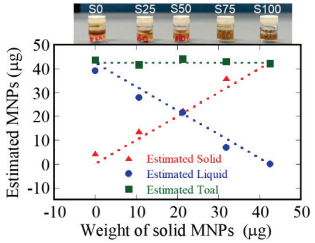

Figure 1 Estimation results of the iron contents of liquid and solid MNPs.

Excitation parameters selection for coaxial frequency-mixing magnetic particle imaging

Tao Zhu[1,2,3], Zechen Wei[1,2,3], Xin Yang[1,2,3], Jie Tian[1,2,4,5,6] and Hui Hui[1,2,3*]

[1] CAS Key Laboratory of Molecular Imaging, Institute of Automation, Beijing, China,
[2] Beijing Key Laboratory of Molecular Imaging, Beijing, China,
[3] The University of Chinese Academy of Sciences, Beijing, China,
[4] School of Engineering Medicine & School of Biological Science and Medical Engineering, Beihang University, Beijing, China,
[5] Key Laboratory of Big Data-Based Precision Medicine (Beihang University), Ministry of Industry and InformationTechnology of the People's Republic of China, Beijing, China,
[6] Zhuhai Precision Medical Center, Zhuhai People's Hospital, affiliated with Jinan University, Zhuhai, China.
*Email: hui.hui@ia.ac.cn

Magnetic nanoparticles (MNPs) are widely used in biomedical imaging and therapy. Magnetic particle imaging (MPI) utilizes the nonlinear response signal of MNPs under alternating excitation magnetic fields to enable highly sensitive quantitative imaging. For conventional MPI, electromagnetic coils are set up along the x/y/z direction in Cartesian coordinates, and a single frequency of current is passed through each set of coils to generate a spatially alternating magnetic field to excite the MNPs. Under three-dimensional excitation, MNPs can generate rich spectral response signals for feature analysis and image reconstruction. However, in some specific scenarios, such as single-side MPI and open-side MPI scanners, the excitation coil is usually placed in only one direction in order to pursue one or more spatial dimensions of unrestricted [1,2]. In practice, the spectral response signals of MNPs are enriched by applying currents at two frequencies in one set of coils (Denote by coaxial frequency-mixing excitation in this abstract) [1]. Considering the physical limitations of the solenoid, it is unrealistic to add two sinusoidal currents of arbitrary frequency and amplitude in one set of coils. Therefore, in this abstract, we explore the excitation parameters selection of coaxial frequency-mixing MPI.

A self-developed MPI scanner was used in the experiment, the main excitation frequency (f_1) is 10 kHz and the maximum magnetic field that can be generated by the excitation coil is 30 mT (A_{max}). The parameter selection method designed in this abstract consists of two steps: frequency selection and amplitude selection. First, the amplitudes of the two frequencies A_1, A_2 are fixed and the frequency f_2 is adjusted to screen out the better frequency; then, the frequencies f_1, f_2 are fixed and the amplitude combination of A_1, A_2 is adjusted to screen out the better value. The 1D system matrix was measured for each parameter combination during all selection processes. The optimal parameters were selected by comparing the number of high-SNR frequencies and the system function at the highest high-SNR frequency, which are favorable for stable image reconstruction and high-resolution reconstruction.

As shown in Fig. 1(a), in frequency selection, the f_2 was selected in [0, 200, 500, 1000, 1500, 2000] Hz, corresponding to the group [1-1, 1-2, 1-3, 1-4, 1-5, 1-6]. And $f_1 = 10\mathrm{kHz}$, $A_1 + A_2 = A_{max}$ are satisfied in this stage. Due to the rich high-SNR frequencies and high-resolution system function, $f_2 =$ 500 Hz was selected. Then, as shown in Fig. 1(b), a better amplitude combination was selected. A_2 was selected in [3, 4, 5, 6, 7, 10] mT and $A_1 = A_{max} - A_2$, corresponding to the group [2-1, 2-2, 2-3, 2-4, 2-5, 2-6] in Fig. 1(b). Here, based on the selection of the previous step, $f_1 = 10kHz$, $f_2 = 500Hz$. According to the results, A_2 in the range of [5~7] mT are appropriate. Hence, for our scanner, $f_1 = 10kHz$, $f_2 = 500Hz$ and $A_1 = 20mT$, $A_2 = 5mT$ are used to obtain high quality MNPs response signal. We believe that this approach is generally applicable to other coaxial frequency-mixing excitation MPI devices as well.

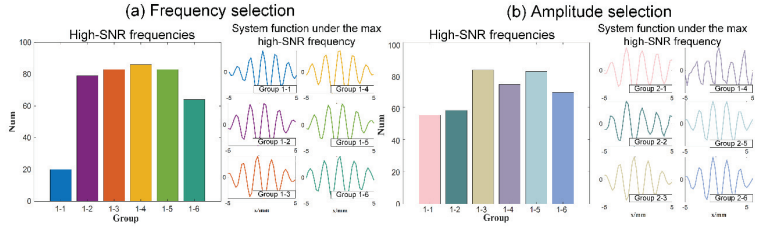

Figure 1. The selection of excitation parameters for coaxial frequency-mixing MPI

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Vortex-State Magnetic Nanodisks in Melanoma Cell Cultures: A Potential Approach for Cancer Treatment

R. Zurbano,[1*] C. Redondo, [1] I. Solozabal,[1] M. D. Boyano,[2,3] and R. Morales[4,5]

[1] Department of Physical Chemistry, University of the Basque Country UPV/EHU, 48940 Leioa, Spain.
[2] Department of Cell Biology and Histology, University of the Basque Country UPV/EHU, 48940 Leioa, Spain.
[3] Biocruces Health Research Institute, 48903 Barakaldo, Spain.
[4] Department of Physical Chemistry, University of the Basque Country UPV/EHU & BCMaterials, 48940 Leioa, Spain.
[5] IKERBASQUE, Basque Foundation for Science, 48011 Bilbao, Spain.
*Email: **raquel.zurbano@ehu.eus**

Current developments in biomedicine using nanotechnology have introduced innovative possibilities and magnetic particles have garnered significant interest in the field. This interest is due to their unique physical properties, which enable cell manipulation, targeted drug release, the development of innovative diagnostic techniques, and the exploration of promising therapies for diseases like cancer.

A novel kind of particle for biomedical applications is a disk-shaped nanostructure or magnetic nanodisk (MND). For certain dimensions, these nanomagnets exhibit a distinctive spin configuration known as vortex state, responding to oscillatory magnetic fields capable of inducing cancer cell death or neuron stimulation.[1, 2] In this study, we produce $Ni_{80}Fe_{20}$ nanodisks in vortex state with diameters of 700 nm and 300 nm combining interference lithography with electron beam evaporation. (Fig. 1A). Additionally, two protective layers of gold were deposited to shield the magnetic material, preventing oxidation and augmenting the biocompatibility of the MNDs.

It was demonstrated that MNDs do not produce direct cytotoxicity on the cells without the application of the magnetic field, thereby minimizing side effects on healthy cells and allowing targeted treatment. The interaction between cells and disks was investigated for various cell lines using SQUID (superconducting quantum interference device) magnetometry and imaging techniques (Fig. 1B). It was observed that the interaction and dynamics of the disks with cells depends on both the morphology of the disk and the characteristics of the cell type. Melanoma cells were capable of internalizing 300 and 700 nm disks, but only externalizing the smaller ones. Macrophages internalized a larger quantity of MND of both sizes without externalizing them. While melanocytes require a longer time to achieve a significant interaction with MND. With this information, a magnetic field treatment was programmed with oscillatory external fields at low frequency (10 Hz). Tumor cell annihilation was observed for treatments of 90 min, validating the great potential of the technique with submicrometer nanomagnets. Work supported by PID2022-136784NB-C22 funded by MCIN/AEI/ 10.13039/501100011033 and by "ERDF A way of making Europe", by the "European Union" and Basque Country grant No IT1491-22.

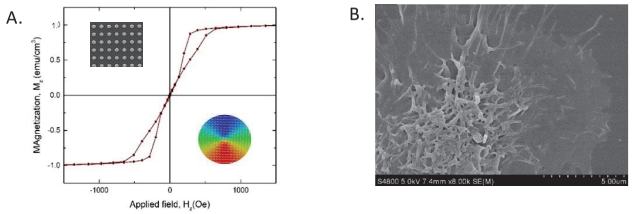

Fig. 1. A. Magnetization as a function of applied field for MNDs 300 nm in diameter measured by SQUID. SEM image of the disk array (upper inset) and vortex state diagram (lower inset). B. Scanning electron microscopy images of a A2058 cell interacting with MNDs of 700 nm.

[1] L. Peixoto et al. *Appl. Phys. Rev.* **7**, 011310 (2020) https://doi.org/10.1063/1.5121702
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Effect of Microwave Hydrothermal Time on the Synthesis and Magnetic Properties of $CoFe_2O_4$/rGO Nanocomposites

Kun-Yauh Shih[1*], Yi-Shu Wang[1]

[1] Department of Applied Chemistry, National Pingtung University, Pintung, Taiwan,

*Email: hello2sky@gmail.com

$CoFe_2O_4$/rGO composite materials, known for their magnetic properties, were synthesized via microwave-assisted methods in this study to explore the influence of varying microwave durations on composite formation, crystalline structure, and magnetic characteristics. Graphene oxide was synthesized using Hummer's method, followed by microwave treatment to produce reduced graphene oxide (rGO), which was then impregnated with numerous cobalt ironate nanoparticles. Molecular vibration and rotation modes were analyzed using Raman spectroscopy, while X-ray diffraction (XRD) was employed to identify crystalline phases. Functional group analysis was conducted using Fourier transform infrared (FTIR) spectroscopy. The impact of rGO addition on sample morphology was investigated using transmission electron microscopy (TEM). Magnetic properties were assessed via vibrating sample magnetometry (VSM), while thermo-gravimetric analysis (TGA) was utilized to monitor sample weight changes at specific temperatures.

The results demonstrated successful synthesis of $CoFe_2O_4$/rGO composite material, with XRD patterns revealing peaks corresponding to the cubic spinel structure of $CoFe_2O_4$ (JCPDS#22-1086). Raman spectra exhibited characteristic D-band and G-band peaks at approximately 1343 cm^{-1} and 1605 cm^{-1}, respectively, confirming effective complexation between $CoFe_2O_4$ and rGO. TEM analysis indicated suppression of metal particle aggregation following rGO incorporation. VSM measurements at room temperature indicated that coercivity was influenced by microstructural properties, such as defects, surface effects, and particle size. Additionally, varying microwave durations led to differences in the degree of $CoFe_2O_4$ composite formation, consequently affecting sample saturation magnetization. This phenomenon was attributed to non-magnetic graphene doping disrupting the long-range magnetic ordering of ferrite particles, thus altering the composite material's magnetic properties.

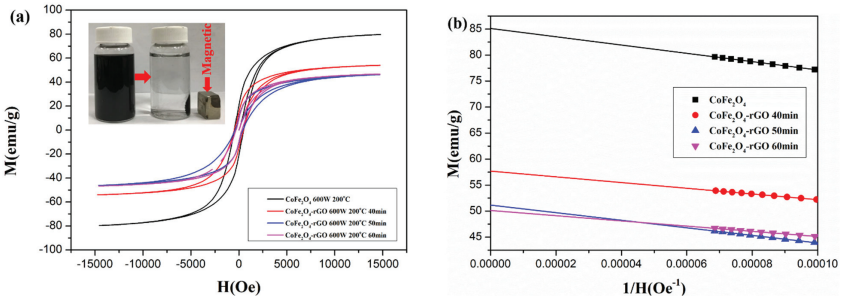

Figure 1 VSM curves (a) and the law of approach to saturation graph (b) for $CoFe_2O_4$/rGO at various synthesis times

MPI, MNPs and the long way to clinical routine

P. Vogel[1,4*], M.A. Rückert[1], J. Günther[1], T. Reichl[1], T. Kampf[1,2], V. Hartung[3], T.A. Bley[3], V.C. Behr[1], and S. Herz[3,5]

[1] Department of Expermental Physics 5 (Biophysics), Julius-Maximilians University Würzburg, [2] Department of Diagnostic and Interventional Neuroradiology, University Hospital Würzburg, [3] Department of Diagnostic and Interventional Radiology, University Hospital Würzburg, [4] Pure Devices GmbH, Rimpar, [5] Radiologie Augsburg Friedberg, Augsburg
* Patrick.Vogel@physik.uni-wuerzburg.de

Human-sized Magnetic Particle Imaging (MPI) scanners are of high interest in cardiovascular medicine as they represent a promising radiation-free alternative to the gold-standard method for treating patients with cardiovascular disease (CVD), where patients and medical personnel are exposed to ionizing radiation [1]. MPI is a tool for real-time functional and molecular imaging and since it is based on the nonlinear magnetization response of magnetic nanoparticles (MNPs), it uses a radiation-free tracer. The major issue with the translation to the clinical field is the upscaling to scanners with sufficient bore size operating with real-time visualization.

Fig. 1 shows our human-sized MPI scanner which was developed for intervention on human extremities. Since the iMPI scanner is lightweight and portable, it can be used within a catheter lab simultaneously with a conventional X-ray machine providing images from both worlds. With a temporal resolution of 4 images per second, an experimental MPI-guided PTA (percutaneous transluminal angioplasty) is feasible [2]. The FOV covered here is 11x12 cm² within the scanners bore size of 20 cm. The pulsatile peak flow velocity in the experimental vessel system was 50 cm/s. For angiography, a 1 ml bolus of mixed iodine contrast agent and iron-oxide based tracer (Perimag) with an iron concentration of 8.5 mg/ml was injected.

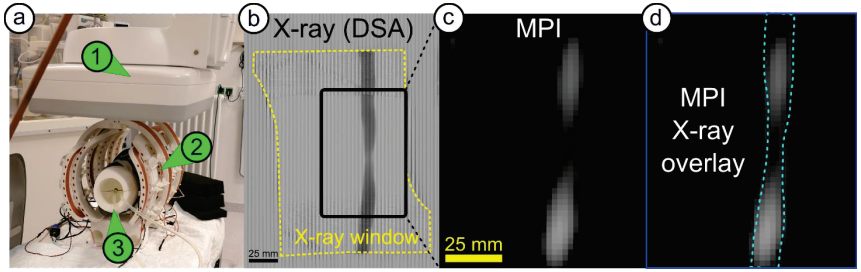

Figure: Interventional Magnetic Particle Imaging (iMPI) (2) scanner in a catheter lab next to a conventional X-ray angiography device for interventional procedure (2). In the FOV of both systems, a human-sized leg phantom consisting of a tubular vessel with an artificial stenosis can be imaged simultaneously. A bolus of iron-oxide nanoparticles and iodine contrast agent is used to visualize the stenosis in both modalities.

[1] Roth, G. A. et al., J. Am. Coll. Cardiol. 76(25), 2982–3021 (2020). [2] Vogel, P. et al., Sci Rep 13, 10472 (2023).

The work was supported by the German Research Council (DFG), grant numbers: VO-2288/1-1, VO-2288/3-1, and BE 5293/1-2.

Keep your Camel healthy with COMPASS

Patrick Vogel[2,6]*, Bernhard Friedrich[1], Martin A Rückert[2], Stefan Lyer[1,5], Johanna Günther[2], Teresa Reichl[2], Ulrich Wernery[3], Sunitha Joseph[3], Judith Müller[4], Volker C. Behr[2], Christoph Alexiou[1] and Rainer Tietze[1]

[1] Department of Otorhinolaryngology, Head and Neck Surgery, Section of Experimental Oncology and Nanomedicine (SEON), Else Kröner-Fresenius-Stiftung Professorship, University Hospital Erlangen, Erlangen, Germany. [2] Department of Experimental Physics 5 (Biophysics), Julius-Maximilians-University Würzburg, Germany. [3] Central Veterinary Research Laboratory, P.O. Box 597, Dubai, UAE. [4] Generatio - Center for Animal Genetics, Heidelberg, Germany. [5] Department of Otorhinolaryngology, Head and Neck Surgery, Section of Experimental Oncology and Nanomedicine (SEON), Professorship for AI-Controlled Nanomaterials, University Hospital Erlangen, Erlangen, Germany. [6] Pure Devices GmbH, Rimpar, Germany.
* Patrick.Vogel@physik.uni-wuerzburg.de

The increasing trade of camels and camel products increases the risk of virus transmission to humans and animals due to their role as reservoirs and carriers of coronavirus strains [1]. Screening for antibodies against infections is usually done in the laboratory using expensive and time-consuming immunochemical methods like ELISA. To avoid delays in case of acute events, easy-to-use and robust POC testing methods such as **C**ritical **O**ffset **M**agnetic **PA**rticle **S**pectro**S**copy (COMPASS) are of high interest [2]. This novel method is based on the highly sensitive measurement of changes in mobility of functionalized iron-oxide based magnetic nanoparticles (MNPs), e.g., by changing the hydrodynamic diameter. For that, a specific ratio of static and dynamic magnetic fields is used to exploit phase shifts in the vicinity of so-called critical points. By controlled engineering of specific surface properties (functionalization), MNPs become special probes for the detection of binding analytes, e.g., antibodies [3].
Three different sera of immunized camels were screened within a portable COMPASS device with different functionalized MNPs and compared with standard ELISA and FACS that confirmed the results of the MNP-based measurements (following the protocol in Fig.1).

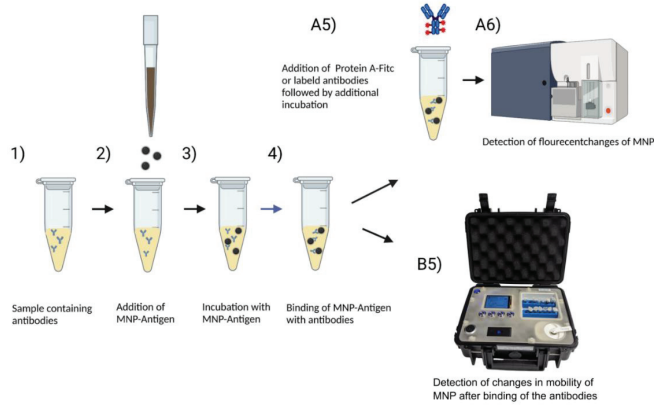

Fig.1: Scheme of MNP-antigen-based detection using FACS or COMPASS analysis. To samples that contain antibodies (1) the matching MNP-antigen are added (2). After incubation (3–4), the samples can be directly measured using COMPASS (B5) or have to undergo a second incubation step with fluorescent antibodies (A5) before measuring using flow cytometry (FACS).

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The work was supported by the German Research Council (DFG), grant numbers: VO-2288/1-1, VO-2288/3-1, and BE 5293/1-2., Manfred-Roth-Stiftung, Fürth (Germany), and Forschungsstiftung Medizin am Universitätsklinikum Erlangen, Hans Wormser, Herzogenaurach (Germany).

Optimizing Magnetic Nanoparticle Design for Effective Thermal Cancer Therapies

Manuel Horcajo[1*] and Patricia de la Presa[1]

[1] Instituto de Magnetismo Aplicado Salvador Velayos (UCM-ADIF), A6 km. 22.5 Las Rozas (Madrid).
*Email: mhorcajo@ucm.es. Mobile: +34647282323

The use of magnetic nanoparticles in thermal therapies for tumour treatment is of great interest due to their ability to precisely direct treatment, thus reducing damage to healthy tissues and overcoming drug resistance. In the design of these nanoparticles, it is crucial to optimize their stability in aqueous media and their cellular penetration capacity. This involves controlling the size and aggregation of the nanoparticles, which not only limits their application in biomedicine but also affects their heat-emitting capability [1,2]. This study investigates the design of a photothermal therapy (PTT) system utilizing iron oxide nanoparticles, which have shown great promise for this therapy, alongside their biocompatibility and ease of functionalization for employment in multifunctional systems.

The samples studied were obtained by modifying a coprecipitation synthesis method [3]. Variation in the medium's basicity, the amount of iron precursors, and the solvent ratio has altered the size of the nanoparticles and the formation of aggregates in aqueous media, affecting their stability in solution and their calorimetric potential. The structure and morphology were analysed using DRX and HRTEM, while the calorimetric efficiency of the system was evaluated with a continuous 808 nm laser [4]. The hydrodynamic radius (R_H) of aggregates and their stability in solution were analysed using Dynamic Light Scattering (DLS). Figure 1 depicts the specific absorption rate (SAR) calculated for different sizes of nanoparticle aggregates obtained and their stability in aqueous solution, as measured by their Zeta potential. It is observed that altering the nanoparticle size modifies the aggregate size, influencing their stability in water and the SAR response for PTT.

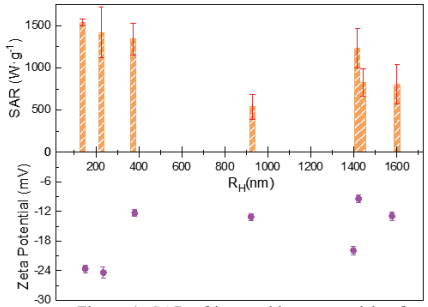

Figure 1: SAR of iron oxide nanoparticles for PTT and their Z potential as a function of R_H.

Acknowledgement: This work was supported by PID2021-123112OB-C21 and TED2021-129688B-C21.

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Controlling Morphology and Magnetization of Magnetic Nanoparticles through Solvent-Ligand Chemistry

Rabia Amin[1], Yihao Wang[1], Susanne Kempter[2], Meinhard Schilling[1], Frank Ludwig[1], Mohammad Suman Chowdhury[1], Aidin Lak[1]

[1]Institute for Electrical Measurement Science and Fundamental Electrical Engineering and Laboratory for Emerging Nanometrology (LENA), TU Braunschweig, Hans-Sommer-Str. 66, Braunschweig, 38106, Germany
[2]Department of Physics and Center for NanoScience, LMU Munich, Amalienstrasse 54, 80539 Munich, Germany
Email: rabia.amin@tu-braunschweig.de

The successful synthesis of magnetic nanoparticles (MNPs) with controlled morphologies via solution-phase synthesis is still a significant challenge. The complexity originates from a complex and intertwined role that ligands and solvents play in determining the morphology of MNPs. Understanding the influence of ligand-solvent chemistry on morphology can help in effectively manipulating these factors and synthesizing MNPs with properties optimized for bio-applications, particularly MNP-based biosensing.

Dibenzyl ether (DBE) is the most commonly used solvent for synthesis via thermal decomposition, yet prone to oxidation over time. Despite being considered as a non-coordinating solvent, DBE's oxidation by-products can influence the morphology of the synthesized MNPs.[1] Building upon our previous procedure for the synthesis of tri-component ferrites (MNPs),[2] here we aim to understand how the nature of solvents and ligands and their interactions dictate the morphology and magnetization of MNPs.

We obtained truncated octahedral nanoparticles when synthesizing with either naturally oxidized (O-DBE) or fresh DBE (F-DBE) with only oleic acid (OA) as ligand (Fig. 1a). Introducing sodium oleate (SO) as a co-ligand in F-DBE results in a preferential binding of oleate ions (OL^-) to {100} facets, promoting growth on {111} facets, thus leading to the formation of nanocubes (Fig. 1b). In contrast, conducting the same synthesis with naturally O-DBE, with SO and OA as ligands, results in the formation of complex morphologies such as octahedron, tetrahedron with truncated vertices, and hexagonal discs (Fig. 1c, 1d, and 1e). The formation of tetrahedra with truncated vertices and discs suggests a growth process in which symmetry is broken, most likely by kinetically driven mechanisms.[3,4]

Our findings reveal distinct morphologies transitioning from nanocubes to nanodiscs when employing ligands in conjugation with naturally O-DBE and F-DBE. The complex variations in morphologies observed with naturally O-DBE can be attributed to the oxidation by-products of DBE, which gradually alter the solvent's chemical composition. Our study elucidates the importance of oxidation state of solvent and how alterations in solvent composition over time can yield a variety of thermodynamically- and kinetically-controlled morphologies. The correlation between particle morphology and magnetization will be discussed thoroughly.

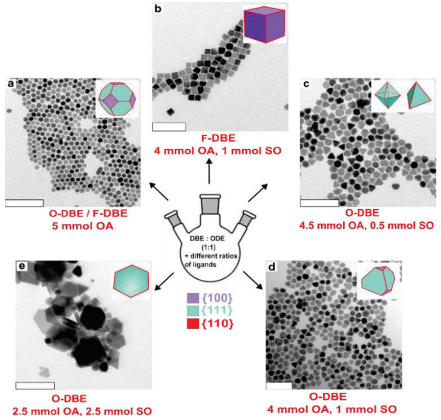

Figure 1: TEM images of MNPs depicting the influence of solvent and ligand chemistry on particle morphologies. The inset shows the corresponding 3-D models of the as-synthesized MNPs. All the scale bars correspond to 100 nm.

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A magnetosensing-based Rapid Screening Test for Streptococcus agalactiae Infections: Expanding Global Efforts in Addressing Perinatal Sepsis

A del Valle[3,4], M. Mesas[3,4], C. Fernández-Senac[3,4], A. Pallarès-Rusiñol[2], M. Martí[3], B. Baró[1], J. Ferrer-Dalmau[2], Q. Bassat[1], M.I. Pividori[3,4]

[1] *ISGlobal, Barcelona Institute for Global Health, Hospital Clínic, Universitat de Barcelona*
[2] *BioEclosion SL, Avda. Can Domènech, Edifici Eureka, Campus de la Universitat Autònoma de Barcelona*
[3] *Biosensing and Bioanalysis Group, Institute of Biotechnology and Biomedicine, Universitat Autònoma de Barcelona.*
[4] *Grup de Sensors i Biosensors, Departament de Química, Universitat Autònoma de Barcelona, Bellaterra, Spain*
Corresponding author: isabel.pividori@uab.cat

Streptococcus agalactiae (GBS) is currently the main cause of neonatal infections, affecting pregnant mothers and their offspring. GBS´s infection affects 18% of the pregnant women worldwide, leading to a spectrum of diseases, including maternal infection, stillbirth, and early- and late-onset sepsis in newborns. Additionally, GBS may contribute to preterm delivery and hypoxic ischemic encephalopathy [1].

Nowadays, a proactive administration of preventive antibiotics to the mother during delivery is initiated upon positive detection of GBS. This measure aims to prevent vertical transmission during childbirth, minimizing risks to the baby [2]. However, current detection methods rely on culturing techniques, resulting in long turnaround times for results and sophisticated laboratory infrastructure and training. Diagnosing GBS in newborns is even more challenging, as it requires a minimum volume of blood and/or Cerebrospinal Fluid for successful culture that can be difficult to obtain from patients. Moreover, the time required for obtaining results can span several days. Considering these limitations, this work addresses the development of a point-of-care rapid screening test based on a hand-held thermocycler to perform double tagging end-point PCR in combination with an electrochemical biosensing detection (Fig.1) [3,4]. A conventional PCR with a novel thermostable DNA polymerase, targeting a GBS specific gene, a screening of several bacterial lysis methods, a methodology specificity determination, and a Limit of detection were performed. Our results demonstrate a simple, specific, and promising system for detecting the presence of GBS in patients. Further work will involve the testing on different matrices, (blood, vaginorectal swabs) to explore the assay´s sensitivity. The development of this device holds the potential to improve the current protocols for GBS detection, allowing for rapid point-of-care screening both in expectant mothers and at the newborn's side. Such a breakthrough could significantly reduce the global burden of GBS disease, with impact in low-income countries, due the challenges of implementing microbiological cultures in these settings [5].

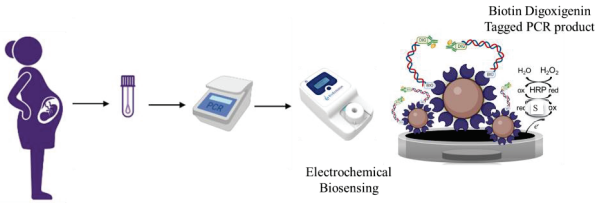

Fig. 1. Schematic representation of the proposal includes the combination of the conventional PCR with the double-tagged primers with an electrochemical Biosensing to detect the amplicons from *S. agalactiae*.

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Coaxial electrospun nanofibers with encapsulated titanium dioxide and magnetic nanoparticles for photo-stabilization and magnetically controlled release of betamethasone-17 valerate

Natália Andrýsková [1]*, Melánia Babincová [2], and Mária Šimaljaková [1]

[1] Department of Dermatovenereology, Faculty of Medicine, Comenius University and Bratislava University Hospital, Mickiewiczova 13, 813 69 Bratislava, Slovakia
[2]Department of Nuclear Physics and Biophysics, Faculty of Mathematics, Physics and Informatics, Comenius University, Mlynská dolina F1, 842 48 Bratislava, Slovakia
*Email: nat.babincova@gmail.com

Betamethasone-17 valerate is a potent synthetic glucocorticoid used in a variety of allergic and inflammatory skin disorders. The drug is applied to the skin in the form of cream, gel, ointment, lotion, or solution. It has been shown to decompose extensively under UV light through a rearrangement of the cyclohexadienone moiety involving a radical mechanism. The reduction in anti-inflammatory activity of the drug upon exposure to UVB light has also been shown in the same study. It has been established that photodegraded products of the drug are toxic/phototoxic, and the toxicity increases with further irradiation. In this study investigated the use of coaxial nanofibers with titanium dioxide nanoparticles in the sheath part and magnetic nanoparticles with drug in the core part. This combination aimed to enhance the photostability of betamethasone while enabling controlled drug release through an external radio-frequency field. The presence of titanium dioxide nanoparticles in the sheath of the nanofibers helped to increase the photostability of betamethasone by protecting it from degradation when exposed to light. Additionally, incorporating magnetic nanoparticles in the core allowed for non-invasive and remotely controlled drug release through the generation of heat by applying a radio-frequency field. More specifically we have used coaxial electrospinning (Figure 1a), a process in which two concentric spinnerets can receive two different polymers. For the purposes of betamethasone photo stabilization, we prepared the coaxial nanofiber with a core-sheath structure [(Betamethasone &MN)@PCL]/[TiO_2@PVA] which consists of two distinct layers (Figure 1b). The core layer is composed of a mixture of the hydrophobic drug betamethasone and PCL-covered magnetic nanoparticles embedded in the PCL polymer matrix. The sheath layer is composed of TiO_2 nanoparticles embedded in PVA (the polyvinyl alcohol polymer matrix which serves as a UV blocker protecting the betamethasone in the core). When TiO_2 is included in a sheath layer, it acts as a physical barrier that prevents UV radiation from reaching the drug in the core. This helps to ensure that the betamethasone remains stable and effective over time. The coaxial structure allows for the remote-controlled release of betamethasone from the core layer under the control of an alternating magnetic field.

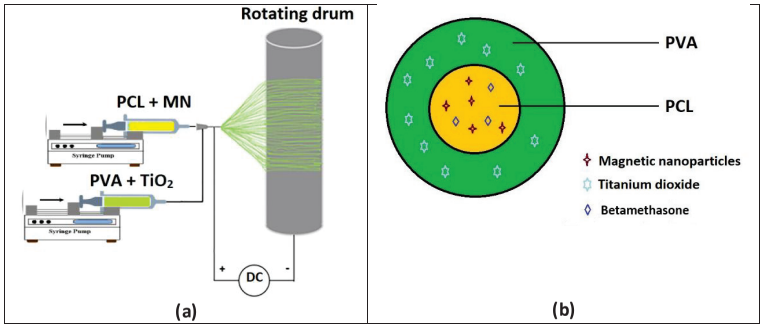

Figure 1. ***(a)*** *Coaxial electrospinning of functionalized PCL/PVA core-sheath nanofibers.* ***(b)*** *Schematic structure of prepared coaxial nanofiber with betamethasone.*

Andrýsková, N.; Sourivong, P.; Babincová, M.; Babinec, P.; Šimaljaková, M. Electrospun PCL/PVA Coaxial Nanofibers with Embedded Titanium Dioxide and Magnetic Nanoparticles for Stabilization and Controlled Release of Dithranol for Therapy of Psoriasis. *Magnetochemistry* 2023, *9*, 187.

Preparation and characterization of poly-L-lysine coated magnetic nanoparticles and evaluation of their peroxidase-like activity

Iryna Antal*, Iryna Khmara, Martina Kubovcikova, Alena Jurikova, Vlasta Zavisova, Martina Koneracka

Institute of Experimental Physics, Slovak Academy of Sciences, Watsonova 47, Kosice, Slovakia
* Email: iryna.antal@saske.sk

The potential of magnetic nanoparticles (MNPs) in various biomedical applications has been the focus of scientific interest for the last few decades. These applications include drug delivery systems, magnetic hyperthermia, and magnetic resonance imaging for clinical diagnosis. Additionally, recent findings have shown that magnetic iron oxide nanoparticles can act as artificial inorganic peroxidase.

Designing superparamagnetic nanoparticles for biomedical applications requires surface derivatization to ensure hydrophilicity and biocompatibility. In our research, we describe a simple synthesis of poly-L-lysine (PLL) coated magnetite nanoparticles, their physicochemical characterization, and evaluate and compare the peroxidase-like activity of both bare MNPs and poly-L-lysine-coated magnetic nanoparticles (PLL-MNPs).

Our study demonstrates successful coating of magnetite nanoparticles with poly-L-lysine, resulting in the formation of a stable magnetic fluid. This stabilization occurs through the interaction of lysine residues of poly-L-lysine with the surface of magnetite nanoparticles. The optimal weight ratio of poly-L-lysine to MNPs in the PLL-MNPs sample was determined to be 1.3 ($PLL_{1.3}$-MNPs sample) using various analytical techniques.

Additionally, we established a correlation between the ζ-potential and hydrodynamic size of the nanoparticles at different pH values. Dynamic light scattering analysis revealed no aggregation during the poly-L-lysine coating process, even up to a pH of 9, in the $PLL_{1.3}$-MNPs sample. Transmission electron microscope images of magnetic nanoparticles showed uniform sizes, with most nanoparticles being approximately spherical and having mean diameters of 9-13 nm. Furthermore, magnetization measurements indicate that the nanoparticles maintain their magnetic properties following modification with poly-L-lysine.

To investigate the peroxidase-like activity of bare and PLL-MNPs, we employed a colorimetric method using starch-sodium iodide reagent as the chromogenic substrate. The results confirmed the peroxidase-like activity of both bare and PLL-MNPs, as they catalytically oxidize the substrate with H_2O_2 to produce a typical blue-colored complex (starch-I_2). However, the PLL coating was found to slightly decrease catalytic activity compared to bare MNPs at pH 3.0.

Acknowledgements
This work was supported by the Slovak Research and Development Agency under the contract no. APVV-DS-FR-22-0037; Slovak Grant Agency VEGA 02/0049/23; the Operational Program Integrated Infrastructure funded by the ERDF ITMS2014+: 3130011AUW7 (NANOVIR).

Heading Towards Standardizing Photothermal Measurements of Iron Oxide Nanoparticles across Two Biological Windows

Daniel Arranz[1,2], Rosa Weigan[2], and Patricia de la Presa[1*]

[1] Institute of Applied Magnetism, UCM-ADIF, A6 22,500 Km, 28230Las Rozas, Spain
[2] Department of Optic, Faculty of Physical Science, Plaza de Ciencias 1, 28040 Madrid, Spain
*Email: pmpresa@ucm.es. Mobile:+34 620 785 501

This work is an investigation into the heating efficiency of Fe_3O_4 colloid under laser irradiation, exploring the impact of vessel volume, laser power, and spot size on photothermal curves. Our findings reveal that these parameters can indeed influence the photothermal behavior, indicating the need for careful consideration when interpreting results in terms of nanoparticle properties (1). Experiments were conducted at 800 nm and 1053 nm, corresponding to two biological windows. We observed that SARs remained independent of vessel size for volumes exceeding 100 µL, regardless of wavelength. Notably, the size of the laser spot emerged as a critical factor; larger spot sizes led to secondary effects influencing the heating curves, causing SAR to vary with laser spot size at constant intensity (see Figure). Moreover, measurements conducted in Eppendorf tubes affected the heating curves and resulting SAR values.

Our findings underscore the impact of geometric parameters on the photothermal characterization of Fe_3O_4 colloids, hindering comparisons between studies and understanding of underlying physical properties. To address this challenge, we advocate for the use of a molecular system capable of releasing heat within the two biological windows, allowing authors to standardize their results against a reference under consistent experimental conditions.

An attractive candidate for this purpose is the commercial IRA 980B as a reference probe. We propose reporting SAR results as the ratio of nanoparticle SAR to IRA 980B SAR. Additionally, we recommend documenting temperature rise, focusing on the irradiated surface, and providing detailed information on colloidal volume, laser power, and spot size to ensure comprehensive understanding of measurement conditions.

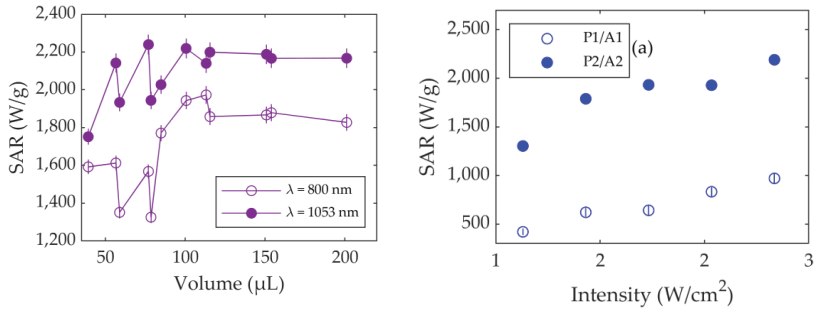

Figure. **(left)** SAR vs. volume for Fe3O4 using lasers at 800 nm and 1053 nm. Errors are represented as vertical bars. **(right)** SAR vs. intensity for Fe3O4 using lasers at 800 nm. P_i /A_i indicates different values of the power and the spot area, but the same intensity.

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Sentinel Lymph Node Mapping Using Magnetic Particle Imaging

Esteban Bermudez-Berrios[1], Ginger Moore[2,3], Ambar Velazquez-Albino[4], Eric Daniel Imhoff[4], Bo Yu[4], Carlos Rinaldi-Ramos[1,4,*]

[1]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, USA
[2]Preston A. Wells Center for Brain Tumor Therapy, University of Florida, Gainesville, FL, USA
[3]Lillian S. Wells Department of Neurosurgery, University of Florida, Gainesville, FL, USA
[4]Department of Chemical Engineering, University of Florida, Gainesville, FL, USA

Magnetic nanoparticles have gained importance in biomedical applications due to the development of imaging systems that harness their physical properties. Magnetic particle imaging (MPI) is a modality that relies on the nonlinear magnetization response of superparamagnetic iron oxide nanoparticles (SPIONs) in a strong alternating magnetic field. Some advantages of MPI are that the signal is unambiguous, as no structures naturally in an organism exhibit the magnetic properties necessary for this type of imaging, and the signal is proportional to the magnetic iron mass in the sample. In our lab, SPIONs tailored for MPI have been developed achieving a peak intensity signal of 91 mV/mgFe that is indicative of sensitivity, and a full-width-at-half-maximum (FWHM) of 10 mT that correlates with an expected spatial resolution of 1.75 mm in a 5.7 T/m gradient field. These particles were coated with a poly(maleic anhydride-1-alt-octadecene) (PMAO) and conjugated with fluoresceinamine for identification under microscopy.

Sentinel lymph node (SLN) is a term that refers to the draining lymph node that is nearest to a tumor. Research has suggested that metastasizing cancers travel through lymphatics to reach other organs throughout the body. Thus, being able to localize and identify lymph nodes when a patient has been diagnosed with cancer can be a method to determine the progression of the disease. By accurately detecting the lymph node, a biopsy may be performed to obtain a sample from the correct anatomical structures, while minimizing unnecessary invasive procedures.

In this study, we used MPI to observe the trafficking of PMAO-coated SPIONs within lymphatic vessels. To do this, we injected mice with RL-1 subcutaneously in the footpad ($n = 6$). Mice were imaged using a Momentum MPI scanner over a 6-day period (**Figure 1**). On day 4 after injection, 4 out of 6 mice showed a visible signal of particles in the popliteal lymph node *in vivo*. Often, when substances are administered to an organism, the substances can only be localized and identified after a biopsy is extracted or in *ex vivo* analysis after euthanasia. Our results support the use of MPI to visualize the trafficking of nanoparticles through the lymphatic system in real-time, non-invasively, and tomographically.

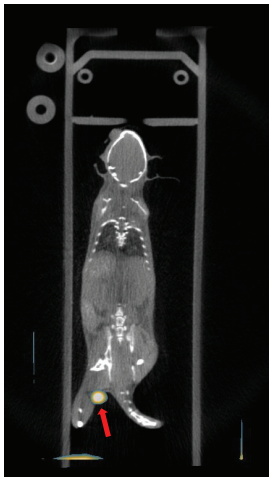


Figure 1: Representative image of a mouse 4 days after footpad SPION administration. The MPI scan is overlayed on a CT scan of the mouse for anatomical reference of the popliteal lymph node into which the SPIONs have trafficked, indicated by the red arrow.

Microscopic Imaging of Magnetic Particles in Flow using Nitrogen-Vacancy Centers in Diamond

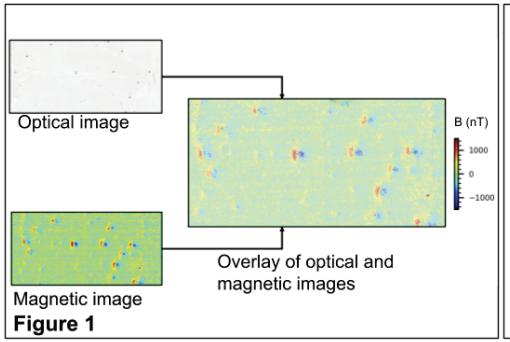
Smriti Bhalerao[1*], Katrijn Everaert[2,3], Jiashen Tang[2,3], Zechuan Yin[3,4], John W. Blanchard[3,4], Connor A. Hart[3], Ronald L. Walsworth[2,3,4]

[1]Fischell Department of Bioengineering, University of Maryland, College Park, Maryland 20742, USA
[2]Department of Physics, University of Maryland, College Park, Maryland 20742, USA
[3]Quantum Technology Center, University of Maryland, College Park, Maryland 20742, USA
[4]Department of Electrical Engineering and Computer Science, University of Maryland, College Park, Maryland 20742, USA
*Email: smritib@umd.edu

Iron-oxide magnetic particles enable precise micron-scale sensing and imaging of biological cells and pathogens in physiological conditions through ligand-based labeling. Moreover, their compatibility with microfluidic systems and trivial background signal make them suitable for studying subcellular processes and developing point-of-care diagnostic tools. Traditionally, SQUIDs and atomic magnetometers are favored for their high sensitivity in the fT Hz^{-1/2} range in studying magnetic particles. However, emerging alternatives like nitrogen-vacancy (NV) centers in diamond are gaining traction for offering micron-scale spatial resolution, nT Hz^{-1/2} sensitivity, and wide-field imaging capabilities at room temperature.

NV centers, which are point defects in diamond, are sensitive to external magnetic fields due to the Zeeman effect and offer optical readout of magnetic information using a laser. The biocompatibility of diamond allows for short stand-off distance between the sample and the sensor, thereby offering high (micron-scale) spatial resolution. NV centers have been used in several studies involving magnetic particles, including quantitative detection of static magnetic nanoparticles within biological cells at single-cell resolution [1] and detecting a suspended magnetic particle within a microfluidic device using a single NV center [2]. Yet to be performed is time-resolved magnetic imaging of multiple magnetic particles flowing in a microfluidic channel using NV magnetometry. Realization of this technology would pave the way for developing point-of-care diagnostic tools and studying organ-on-a-chip systems at the micron scale.

Recently, our group demonstrated wide-field NV magnetic imaging based on the Ramsey sensing protocol to achieve sub-millisecond temporal resolution, <10-micron spatial resolution, and 4.1 nT Hz^{-1/2} sensitivity over a 270 x 270 um^2 field-of-view [3]. To verify the systems' capabilities of imaging particles in flow, we image static beads of 1 and 3 microns in diameter on the diamond surface under a 4 mT bias field. The overlay of the optical and magnetic image is shown in Figure 1. To conduct dynamic imaging of magnetic particles in flow, we integrate a microfluidic system into our existing imaging setup, shown in Figure 2.



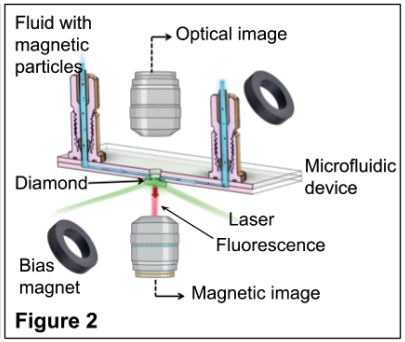


Figure 1: Optical and magnetic images of a mixture of 1 and 3 micron beads using the wide-field NV setup.
Figure 2: NV-diamond microscope for imaging of magnetic particles flowing through a microfluidic channel.

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Organic Molecular Glues to Design Three-Dimensional Cubic Nano-assemblies of Magnetic Nanoparticles

Mohammad Suman Chowdhury[a], Daniel Arenas Esteban[b], Rabia Amin[a], Claudia Román-Freijeiro[c], Enja Laureen Rösch[a], Markus Etzkorn[d], Meinhard Schilling[a], Frank Ludwig[a], Sara Bals[b], Verónica Salgueiriño[c], Aidin Lak[*a]

[a]*Institute for Electrical Measurement Science and Fundamental Electrical Engineering and Laboratory for Emerging Nanometrology (LENA), Hans-Sommer-Str. 66, Braunschweig, 38106, Germany*

[b]*EMAT, University of Antwerp, Groenenborgerlaan 171, B-2020 Antwerp, Belgium*

[c]*CINBIO, Universidade de Vigo, 36310 Vigo, Spain*

[d]*Institute of Applied Physics, TU Braunschweig, Mendelssohnstraße 2, 38106, Braunschweig, Germany*

Email: m.chowdhury@tu-bs.de

Self-assembled magnetic nanoparticles offer next-generation materials that allow harnessing their physicochemical properties for many applications. However, how three-dimensional nano-assemblies of magnetic nanoparticles can be synthesized in one-pot synthesis without excessive post-synthesis processes is still a bottleneck. Here, we propose a panel of small organic molecules that glue nanoparticle crystallites during the growth of particles to form large nano-assembled nanoparticles (NANs). We find that both carbonyl and carboxyl functional groups, presenting in benzaldehyde and benzoic acid, respectively, are needed to anchor with metal ions, while aromatic rings are needed to create NANs through π-π stacking. When benzyl alcohol, lacking carbonyl and carboxyl groups, is employed, no NANs are formed. NANs doped with benzoic acid reveal a unique combination of high magnetization and coercivity; whereas NANs doped with benzaldehyde show the largest exchange bias reported in nanoparticles. Surprisingly, our NANs show unconventional colloidal stability due to their unique mesoporous architectures.

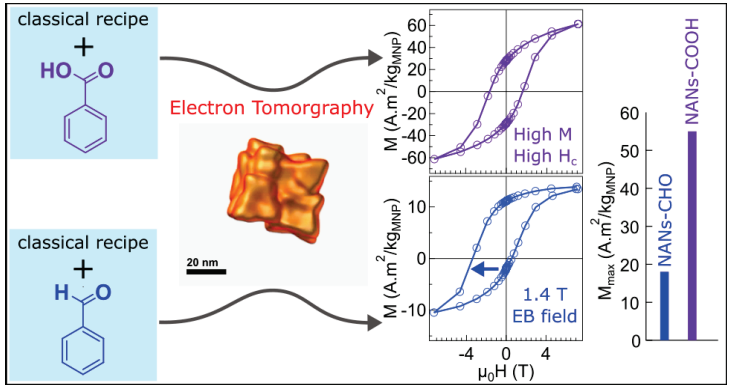

Figure 1. Influence of small organic molecules on the morphology and magnetic properties of magnetic nanoparticles.

Acknowledgement:
We acknowledge the financial support by Graduate Colleague Program "NanoMet" and Junior Research Group "Metrology4life".

Polymer-coated Magnetic Nanoparticles ($CoFe_2O_4$) for targeted delivery of Intra articular gel for pain management

Arpita Das[1], Pankaj Kumar[2], Rohit Srivastava[2]

[1] CRNN, University of Calcutta, Kolkata,700098, India

[2] Department of Biosciences and Bioengineering, IIT Bombay, Mumbai, 400076, India.

E-mail address (corresponding author): *arpitadas166@gmail.com*

Abstract: In today's world, osteoarthritis and rheumatoid arthritis are, some of the most common chronic inflammatory joint problems that affect a large number of the population. Intra-articular injections are applied for the treatment with different therapeutic remedies. In recent years nanoparticles have been used for pain management in the intra-articular injection for effective drug release. In this work, cobalt ferrite nanoparticles were used to deliver diclofenac sodium drugs for pain management in hyperthermic conditions. The particles were synthesized by the wet-chemical coprecipitation method and have been functionalized with chitosan to reduce the toxicity. The particles were tested in the U87 glioblastoma cell line. MTT assay was done to ensure the reduction in toxicity. The particles were characterized by XRD, FTIR, and TEM methods for morphological and size analysis. The drug is added to the functionalized particles. Magnetic analysis of the particle is done to check the ferromagnetic response after the drug attachment. The release of the drug is studied in hyperthermic conditions (elevated temperature). Finally, the particles were infused inside the sodium alginate gel and the release was checked from the gel in the hyperthermic condition. The successful release of pain-relieving drugs makes the chitosan functionalized particles most suitable for intra-articular gel injection.

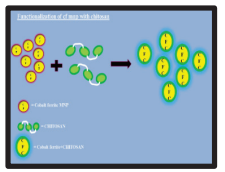

Figure 1: graphical representation of chitosan functionalized nanoparticle

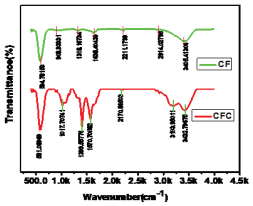

Figure 2: comparative FTIR analysis of bare and functionalized nanoparticle

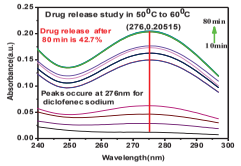

Figure 3: drug release study in hyperthermic condition with respect to time

Microwave-assisted magnetic nanoparticles synthesis and functionalization with antibody 92R: The importance of a controlled MNPs-cell interaction for the correct development of magnetic hyperthermia therapy combined with immunotherapy

David Egea-Benavente[1*], Isabel Corraliza-Gorjon[1], Leonor Kremer[1], Domingo F. Barber[1]
[1] Department of Immunology and Oncology, Centro Nacional de Biotecnología (CNB), Consejo Superior de Investigaciones Científicas (CSIC), 28049, Madrid, Spain
*Email: degea@cnb.csic.es

Magnetic Hyperthermia Therapy (MHT) emerges as a very hopeful alternative to cancer therapy, particularly in combination with other traditional therapies, where synergic effects have been demonstrated. Specifically, the benefits of MHT have been studied in some phase I and II clinical trials for glioblastoma and prostate cancer, with very promising results. MHT is based on the intrinsic ability of magnetic nanoparticles (MNPs) to respond to alternating magnetic fields (AMFs) by releasing heat. This phenomenon is due to two physical mechanisms: Néel and Brown relaxation. Heat release is highly dependent on the intrinsic properties of the MNPs (size and shape, mainly) and their interaction with the medium, which in turn involve monodispersity of the MNPs and the characteristics of the dispersing medium (such as the viscosity). Therefore, in water, heat release in response to AMFs works properly. However, in an *in vitro* context, the efficacy of the treatment could be compromised because of the increased viscosity of the cellular environment and the physical aggregation that MNPs could suffer when interacting with cellular or medium compounds. This could promote a Brown relaxation block, which in turn leads to a dramatic decrease in the heat released by the MNPs.

One approach to improve the heating capacity of MNPs would be to reduce the aggregation between them on the cell surface, which we think could be achieved by changing the way nanoparticles interact with cells. In this study we have analyzed how aggregation and the generation of hyperthermia vary depending on whether the MNPs interact non-specifically with the cell membrane (via their coating molecules) or interact via a membrane receptor, using MNPs functionalized with an antibody that recognizes a cell surface receptor. CCR9 is a seven-transmembrane extracellular receptor with a low internalization rate present on different types of tumors, mainly in hematopoietic cancers. Taking into account this characteristic we have proposed to design a therapeutic strategy based on the functionalization of MNPs with the monoclonal antibody 92R (MNPs-92R), which binds specifically to the human receptor CCR9. In this way, MNPs-92R would specifically recognize CCR9$^+$ cells, such as those of the human T-cell acute lymphoblastic leukemia cell line MOLT-4. This interaction would take place through a spatially defined interaction with the outer part of the cell membrane and in a monodisperse manner, so that Brown's relaxation would be maintained during AMFs application. Consequently, this would be an optimal scenario for the development of a MHT.

In this work, when AMFs were applied to 12 nm spherical MNPs synthesized through microwaves, a high heat release was achieved, which was maintained after functionalization with the 92R antibody, even in culture medium with serum. Several controls were used to demonstrate that the expected effects would be due to the specific binding of MNPs-92R to MOLT-4 (CCR9$^+$) through CCR9, and to the monodisperse spatial location of the MNPs on the cell membrane. The controls employed involved using a MOLT-4 cell line knock-out for CCR9 (MOLT-KO; CCR9$^-$), among other methods. Notably, a significant increase in AMFs-induced cell death was only observed when *in vitro* MHT was applied to unmodified MOLT-4 cells treated with MNPs-92R.

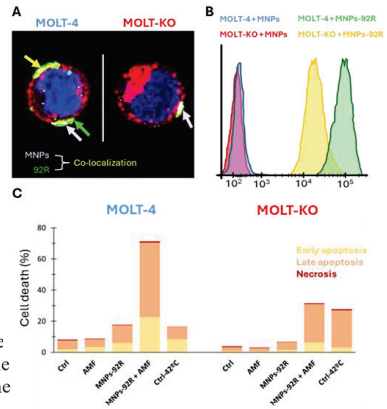

Figura 1. (A) Confocal microscopy of MOLT-4 (CCR9$^+$) and MOLT-KO (CCR9$^-$). MNPs in white and 92R antibody in green. Colocalization in yellow. **(B)** IgG Alexa488 flow cytometry assay of MOLT-4 + MNPs (blue), MOLT-4 + MNPs-92R (green), MOLT-KO + MNPs (red), and MOLT-KO + MNPs-92R (yellow). **(C)** *In vitro* MHT-induced cell death through annexin V-PI flow cytometry

Exploring the Structural Characterization of Magnetic-based Nanoparticles inside Cells Using Hard X-ray Absorption Spectroscopy

Rosalía López-Méndez[1], Javier Reguera[2], Claire Wilhelm[3], Álvaro Muñoz-Noval[4], Ana Espinosa[5]
[1] IMDEA Nanociencia, c/ Faraday, 9, 28049 Madrid, Spain
[2] BCMaterials, Basque Center Centre for Materials, Applications and Nanostructures, UPV/EHU Science Park, 48940 Leioa, Spain
[3] Laboratoire Physico Chimie Curie, PCC, CNRS UMR168, Institut Curie, Sorbonne University, PSL University, Paris, 75005 France
[4] Dpto. Física Materiales, Facultad CC. Físicas, Universidad Complutense de Madrid, 28040 Madrid, Spain
[5] Instituto de Ciencia de Materiales de Madrid, ICMM-CSIC, 28049 Madrid, Spain
Email: ana.espinosa@csic.es

This work describes the capabilities of X-ray absorption spectroscopies—X-ray absorption near-edge structure (XANES) and extended X-ray absorption fine structure (EXAFS)—for the characterization of magnetic nanoparticle (NP) systems in cell environments for biomedical applications. These techniques constitute very useful methods for directly and selectively examining the electronic state and local structure of atoms composing the particle once they are internalized in cells, as well as the transformations they undergo in the biological environment [1]. Moreover, this technique has emerged as a very sensitive and direct nanothermal probe for detecting the temperature of nanoparticles subjected to hyperthermia conditions, serving as a label-free new nanothermometric method [2,3]. Magnetic-based nanoparticles for magneto- and photothermal applications are explored both in solution and in tumor cells using this technique.

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Formulation of PEG-coated MPI tailored tracers using nitroDOPA anchoring groups

Neel Eswaran[1], Hayden Good[2], Eric D. Imhoff[2], Ambar Velazquez-Albino[2] and Carlos M. Rinaldi Ramos[2,3] (Email: carlos.rinaldi@ufl.edu)

[1] Department of Material Science & Engineering, University of Florida, Gainesville, FL, 32611

[2] Department of Chemical Engineering, University of Florida, Gainesville, FL, 32611

[3] J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, 32611

Superparamagnetic iron oxide nanoparticles (SPIONs) are of interest in emerging technologies such as magnetic particle imaging (MPI). MPI is used in applications such as blood pool imaging and cell tracking, which require the SPIONs to have excellent colloidal stability in biological environments to maintain resolution and sensitivity. A large body of work has explored phase transfer methods previously in the context of applications such as hyperthermia and magnetic resonance imaging contrast. However, MPI tracer requirements differ significantly from the tracers used in these applications. The literature suggests that the use of 6-nitro-L-3,4 dihydroxyphenylalanine (nitroDOPA) anchor groups for the SPION coating yields excellent colloidal stability. However, much of the literature evaluating these anchoring groups focuses on SPIONs with a core diameter of 6-10 nm, whereas SPIONs tailored for MPI applications are required to have a core size of 20-25 nm. The resulting increase in magnetization can impact colloidal stability during the coating process and subsequently in biological media.

Herein, we demonstrate ligand exchange conditions used to coat MPI tailored tracers using polyethylene glycol conjugated nitroDOPA (nD-PEG) and that yield monodisperse SPIONs with high colloidal stability. We explore how different variables in the process impact the stability of SPIONs in aqueous and biological media. We also explore the use of different media (e.g., PBS) and conditions (e.g., temperature) that can be used in conjunction with dynamic light scattering (DLS) to screen nD-PEG coated SPION formulations for desired colloidal stability. Furthermore, we demonstrate the MPI performance of nD-PEG coated SPIONs in mice *in vivo*, with results to date demonstrating a circulation half-life of over 2 hours. Ongoing work seeks to establish a correlation between *in vitro* stability tests and the *in vivo* circulation half-life, thus providing an effective screening technique for tracers suitable for *in vivo* applications.

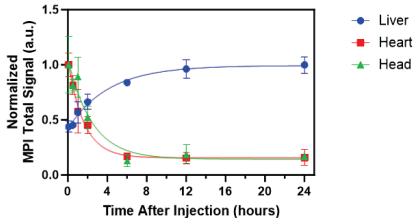

Figure 1: *In vivo* circulation half-life of nD-PEG coated tracers demonstrated in C57BL/6naive mice. MPI signal from the head, heart and liver has been shown separately and is normalized to the largest value in the dataset (0h timepoint for head & heart, 24hr timepoint for liver.)

Analyzing Reaction Parameters on Structural Characteristics of SMART RHESIN Hollow Nanospheres for Magnetic Particle Imaging Applications

Julia Feye[a,b], David Rudolph[b], Jens Treptow[b], Luan Passini[c], Aritz Lafuente[d], Frank Mickoleit[e], Sophia Tessaro[c], René Uebe[e], Dirk Schüler[e], Alejandro G. Roca[d], Clément Roux[c], Claus Feldmann[b], Peter W. Roesky[b], Esther S. Rösch[a]*

[a] Faculty of Engineering, Baden-Württemberg Cooperative State University Karlsruhe, Germany
[b] Institute of Inorganic Chemistry, Karlsruhe Institute of Technology (KIT), Germany
[c] Laboratoire Softmat, Université Toulouse III - Paul Sabatier, France
[d] Catalan Institute of Nanoscience and Nanotechnology, Campus UAB, Spain
[e] Department of Microbiology, University of Bayreuth, Germany
* Corresponding author, email: esther.roesch@dhbw-karlsruhe.de

Medical imaging, including emerging techniques such as Magnetic Particle Imaging (MPI), is advancing rapidly.[1] MPI, which is a novel non-invasive, ionizing-radiation-free imaging modality, offers intrinsic quantification and uses magnetic nanoparticles (NPs) for artefact-free detection, particularly in deep tissues.[2] Variations in NP magnetisation, for example due to viscosity changes, can directly affect signal acquisition.[3] To diminish this, NPs are encapsulated in hollow nanospheres, which provide a stable environment. This study investigates how reaction parameters affect the structural properties of hollow nanospheres filled with core/shell magnetic nanoparticles (CSNPs), termed SMART RHESINs, for potential biomedical MPI applications.[4] Five sets of experiments are investigated, including screening for optimal reaction conditions, different CSNP encapsulation (varying shape, size and shell), influence of CSNP concentration on SMART RHESIN loading, co-encapsulation of different CSNP types and inclusion of a polymer additive in the micelle-forming solution (Figure 1). The SMART RHESIN approach demonstrates robustness to variations in reaction parameters, positioning it as a versatile platform for tailoring nanospheres for various biomedical and physical applications, in particular as MPI contrast agents. This study lays the groundwork for future tailoring of SMART RHESINs for MPI applications.

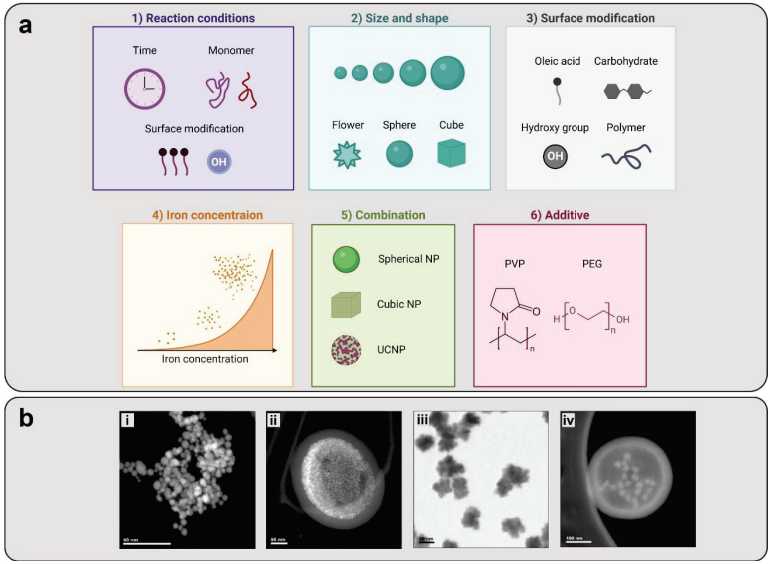

Figure 1: a) Overview of the different reaction series. Series 1: Optimization of reaction conditions by varying phenolic monomer, CSNP shell, CSNP concentration, and mixing time of micelle forming solution. Series 2: Encapsulation of divers CSNP types by using NPs with different sizes, shapes and shells. Series 3: CSNP loading dependence on SMART RHESINs by utilizing three different types of CSNPs at varying concentrations. Series 4: Co-encapsulation of two distinct CSNP types. Series 5: Incorporation of polymer additives during micelle formation by using PVP and PEG at two concentrations, to adjust size and shell thickness of SMART RHESINs. b) Demonstration of two different SMART RHESINs (ii, iv) prepared by using various CSNPs (i, iii).

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Bottom-up fabrication of filaments based on PLA and Fe_3O_4 suitable for 3D printing

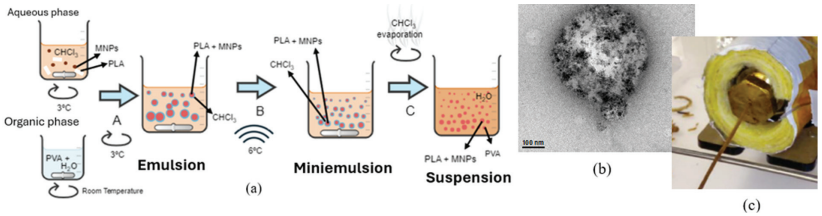
María García-Maestre and Eva Natividad*

Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC - Universidad de Zaragoza
Campus Río Ebro, María de Luna, 3, 50018 Zaragoza, Spain
*Email: evanat@unizar.es

Magnetic nanoparticles are known for their ability to dissipate heat when subjected to an alternating magnetic field in the radiofrequency range. Polylactic acid (PLA) is a synthetic but renewable-resource based polymer that combines biocompatibility, biodegradability and processability through extrusion. Accordingly, the formers are suitable for localized magnetic hyperthermia or heat-assisted drug release, and the latter is of interest in biomedical applications such as resorbable sutures, bone tissue scaffolds or drug delivery systems, especially where additive manufacturing (3D printing) is involved. Combining both materials results in particulate composite materials aiming for the unique integration of their properties. However, a common issue in these materials is that nanoparticles can easily agglomerate when added to the polymer matrix, giving rise to inhomogeneous composites with unwanted performance.

In this contribution, we report the bottom-up fabrication of composite PLA-Fe_3O_4 filaments from PLA nanospheres loaded with Fe_3O_4 nanoparticles. This approach aims at controlling nanoparticle distribution inside the polymer matrix. For the proper formation of nanospheres, a method combining miniemulsion and solvent evaporation was optimized from the point of view of type and quantity of surfactant, scaling, etc. From the obtained colloidal water suspensions, nanospheres were extracted through different methods, such as film formation upon water evaporation or freeze drying. Extracted nanospheres were used as feeding material for an extruder that provides filaments suitable for subsequent 3D printing. Regarding the extrusion process, the thermal behavior of the precursor material was studied to select an optimal extrusion temperature, a fundamental parameter in the process, which depends on both the polymer matrix (PLA and surfactant) and the Fe_3O_4 nanoparticles. Filaments with a constant cross-section were obtained, minimizing both surface and internal defects.

For property determination, colloids were analyzed by dynamic light scattering (DLS). Nanospheres and the resulting multifunctional filaments underwent micro/nanostructural (TEM, FESEM), thermal (DSC), magnetic (SQUID) and magnetothermal (SAR, specific absorption rate) characterization. Finally, filaments were subjected to mechanical characterization by tensile tests.



(a) Scheme of the synthesis of magnetic/polymeric nanospheres. (b) TEM image of polymeric nanospheres loaded with MNPs. (c) Extrusion process of the multifunctional filament.

Easy synthesis of mesoporous silica nanoparticles doped with nickel oxide for biomedical applications

Ana García[1,2]*, Marina Luna-Martínez[1], Blanca González[1,2], Isabel Izquierdo-Barba[1,2]

[1] Dpto. de Química en Ciencias Farmacéuticas, Facultad de Farmacia, Universidad Complutense de Madrid, Instituto de Investigación Sanitaria, Hospital 12 de Octubre i+12, Plaza Ramón y Cajal s/n, 28040 Madrid, Spain.
[2] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain.
**Email: anagfontecha@ucm.es*

In recent decades, research on nanoparticles (NPs) in the medicine field has increases exponentially, as they are a good therapeutic alternative to improve current traditional treatments. In this sense, mesoporous silica nanoparticles (MSNs) exhibit exceptional structural and textural characteristics that make them ideal nanocarriers to host, protect and transport different therapeutic agents to the target tissues or cells [1]. Additionally, nickel oxide exhibits magnetic [2] and antibacterial [3] properties that could be used for the treatment of bacterial infection processes.

A facile synthesis of mesoporous silica nanoparticles containing nickel oxide (MSN-NiO) by microemulsion-assisted sol-gel method is described, in which by adding soluble metal salts ($Ni(NO_3)_2 \cdot 6H_2O$) to the microemulsion droplets formed by ethyl acetate (EA), cetyltrimethylammonium bromide (CTAB) and water, that acted as a soft template for MSNs formation, nickel oxide (NiO) is incorporated after a calcination at 600 ºC. MSN-NiO nanoparticles display a spherical morphology (ϕ_{TEM} ≈110-135 nm) with radial mesoporosity and the presence of small aciculi embedded in the silica matrix, which are assigned to NiO (Figure 1). Its textural properties are excellent, with a high surface area (~700 m^2/g), a large pore volume (~1 cm^3/g) and a pore diameter close to 6 nm. A degradation study of MSN-NiO in physiological medium (PBS 1×) reveals that the nanosystem is reactive, releasing silicon and nickel ions into the medium as it degrades.

Degradation behaviour together with the rest of its physicochemical properties indicates that MSN-NiO could be a good candidate for biomedical applications as a drug delivery system, and for the bacterial infections treatment due to the bactericidal properties of NiO.

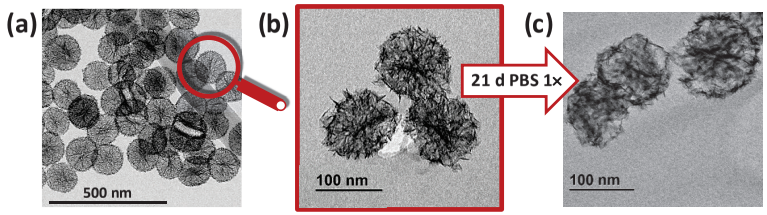


Figure 1. TEM images of MSN-NiO nanosystem before (a,b) and after (c) 21 days soaking in PBS 1×.

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Acknowledgements: European Union's Horizon 2020 Research and Innovation Program under grant agreement No 814410 (GIOTTO) and the Fundación Ramón Areces FD5/22_01 (Nano4Infection) grants.

Preparation, characterization, toxicity and usability of reconstructed ferritin and magnetoferritin for biomedical applications

Jan Gombos[1*], Martin Skratek[2], Michal Rajnak[3], Matus Molcan[3], Martin Kopani[4], Lucia Balejcikova[5], Jana Vojtova[1], Kristina Zolochevska[3], Peter Kopcansky[3], Oliver Strbak[1]

[1] Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Martin, Slovakia
[2] Institute of Measurement, Slovak Academy of Sciences, Bratislava, Slovakia
[3] Institute of Experimental Physics, Slovak Academy of Sciences, Kosice, Slovakia
[4] Faculty of Medicine, Comenius University, Bratislava, Slovakia
[5] Institute of Hydrology, Slovak Academy of Sciences, Bratislava, Slovakia
[*] Email: gombos8@uniba.sk

Iron accumulation, inflammation, or oxidative stress are linked to a number of human pathological conditions [1]. There has been a suggestion that ferritin, one of the main iron storage proteins, is a precursor to iron accumulation in pathological human tissue as well as pathological magnetite mineralization due to disrupted iron homeostasis in neurodegenerative diseases [2,3]. However, functionalized ferritin nanoparticles have also been widely used in biomedical applications, including drug delivery systems, bioassays, contrast agents, and molecular diagnostics probes [4,5].

To study the ferritin nanoparticles for biomedical applications, we prepared so-called ferritin derivatives: 1) reconstructed ferritin (RF) with ferrihydrite mineral core and 2) magnetoferritin (MF) with magnetite mineral core. We used our modified procedure to prepare ferritin derivatives, which is already described in detail in [6]. Such, we can synthesize ferritin particles with various loading factors (LF). LF represents the average amount of iron atoms stored in the core of nanoparticles. To determine the physico-chemical properties and the mineral core composition of nanoparticles, we used various methods, including UV/VIS spectrometry, DLS, SQUID magnetometry, Mössbauer and EDX spectroscopy, etc. The main goal of our work is to characterize in detail the prepared ferritin derivatives' unique properties and to employ these characteristics for biomedical applications. Accordingly, we also analyzed the toxicity of reconstructed ferritin and magnetoferritin using model neuronal cell line SH-SY5Y (**Figure 1**). The viability of cells was analyzed by standardized MTT protocol [7]. Toxicity evaluation reveals suitable biomedical usability and clarifies the effect of different iron mineral phases on cell survival. We believe that our outcomes have the potential to boost the applicability of ferritin-derived nanoparticles in various biomedical fields of research.

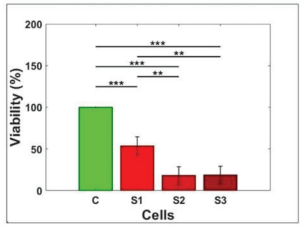

Figure 1: *Viability of SH-SY5Y cell line after 24h incubation with MF for three LFs (S1 – 550, S2 – 730, S3 – 830).*

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Impact of Object Size on Magnetic Particle Imaging (MPI) Signal Distribution

Hayden J. Good[1], Andrii Melnyk[1], Eric Imhoff[1], A. Rahman Mohtasebzadeh[2], Toby Sanders[2], Patrick W. Goodwill[2], Carlos M. Rinaldi-Ramos[1,3,*]

[1]Department of Chemical Engineering, University of Florida, Gainesville, FL
[2]Magnetic Insight Inc, Alameda, CA
[3]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL
*Email:carlos.rinaldi@ufl.edu

Magnetic Particle Imaging (MPI) is a new imaging modality that has garnered interest for biomedical applications due to its quantitative nature and high resolution. However, quantification errors arise for large sample volumes that some authors have attributed to a partial volume effect (PVE). In other imaging modalities, such as positron emission tomography, the PVE arises due to the finite resolution of the imaging modality and is manifested by signal suppression for samples close to or below the spatial resolution of imaging, resulting in quantification errors for small sample volumes. This study aims to systematically characterize the PVE in MPI. The effect of object size on signal spatial distribution and magnitude for superparamagnetic iron oxide nanoparticle (SPIONs) distributions in hollow phantoms was studied. Apparent tracer concentration and the relationship between image and object size, were measured as a function of object size for three instrument resolutions and several object shapes.

3D printed millimeter scale hollow phantoms were filled with constant concentration of commercially available VivoTrax+ tracers. The primary phantom sets of interest were (i) rectangular prisms with varying length dimensions, and (ii) cylindrical prisms with varying radial dimensions. Results show image size estimations closely match true object size for large models but deviate for small models where image size asymptotically approaches a constant value, suggesting the true limit of resolution. Additionally, apparent SPION concentration in an image is depressed for small models, while it saturates for large models. These results were validated at two different MOMENTUM^{TM} imagers, one at the University of Florida and another at Magnetic Insight, Inc., and demonstrate the presence of the PVE in MPI. These results are novel and exciting, motivating research to focus on improving and resolving this effect for accurate quantification and resolution estimations in MPI.

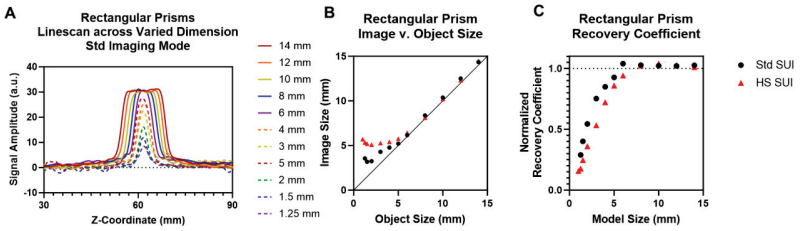

Figure. A) Line scans across the varied dimension of rectangular prisms, demonstrating signal suppression. B) Image size, calculated by full width at half-maximum, plotted against true object size, demonstrating image resolution limits. C) Recovery coefficient calculation, demonstrating the suppression of signal, and a possible correction factor.

Measurement of magnetic relaxation time of magnetic nanoparticles in wide time range

Haruki Goto [1], Masato Futagawa [2], Yasushi Takemura [3], and Satoshi Ota [2,*]

[1] Department of Optoelectronics and Nanostructure Science, Graduate School of Science and Technology, Shizuoka University, Hamamatsu, Japan
[2] Department of Electrical and Electronic Engineering, Shizuoka University, Hamamatsu, Japan
[3] Department of Electrical and Computer Engineering, Yokohama National University, Yokohama, Japan
*E-Mail: ota.s@shizuoka.ac.jp

Magnetic relaxation is important characteristics in biomedical application using magnetic nanoparticles (MNPs) such as hyperthermia and magnetic particle imaging [1]. Magnetic relaxation of MNPs is described in terms of two mechanisms, the Néel and Brownian relaxations. It is important to experimentally reveal the relationships between magnetic relaxation and parameter of MNPs such as size and magnetic anisotropy. In this research, the magnetic relaxation of commercially dispersed MNPs was observed by using a pulsed magnetic field [2] and analyzed by using following equation

$$M(t) = M_{\max} \sum_i A_i \left\{ 1 - \exp\left(-\frac{t}{\tau_{\mathrm{R},i}} \right) \right\}, \qquad (1)$$

where $\tau_{\mathrm{R},i}$, A_i and $M_{\max}$ denote that relaxation time, distribution density of τ_{R} and maximum magnetization when magnetization completely rotated along the applied magnetic field. i is the index for each τ_{R}.

Iron oxide MNPs of SHA-20 (Ocean NanoTech, San Diego, CA, USA), Synomag®-D (Micromod Partikeltechnologie GmbH, Rostock, Germany), and Resovist® (PDR pharma Co. Ltd, Tokyo, Japan) were measured in viscous fluid and solid at the concentration of 20 mg-Fe/mL. Viscous fluids were prepared in the viscosity η= 0.89, 5.4, and 12.4 mPa·s, which were adjusted by mixing diluted water with glycerol. MNPs were solidified with an epoxy resin as the solid sample.

Figure 1 shows the magnetization response by applying a pulsed magnetic field. With respect to SHA-20 and Resovist®, the magnetic relaxation time increased with increasing the viscosity because the Brownian relaxation time was proportional to the viscosity. On the other hand, in Synomag®-D, the relaxation time is unaffected by the Brownian relaxation time, and slightly decreased with increasing viscosity. In the presentation, we will explain in detail not only the magnetic relaxation process but also the magnetic relaxation time distribution calculated from Eq. (1), the frequency dependence of susceptibility under alternating magnetic field, and the particle size estimated from the magnetization curve.

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This work was partially supported by JSPS KAKENHI grant numbers 20H02163, 20H05652, and 23H01419, and JST ACT-X grant number JPMJAX21A5.

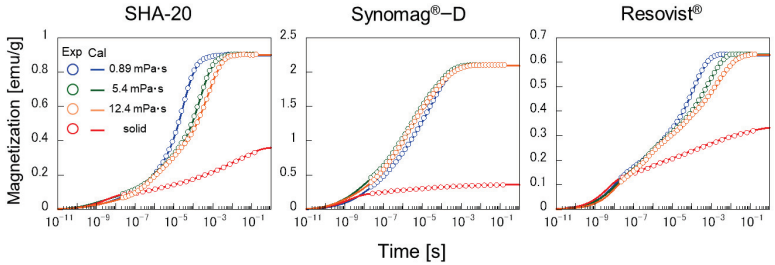

Fig. 1 Time evolution of magnetization response by applying a pulsed magnetic field.

Functionalization of E-cadherin fragments on magnetic microparticles as a novel tool to study mechanotransduction

Lucía García Recaredo[1], Christian Castro-Hinojosa[1], Susel Del Sol-Fernández[1], Yilian Fernández-Afonso[1], Pilar Gomollón-Zueco[1], Pablo Martínez-Vicente[1], María Moros[1,2]

[1] Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza, Pedro Cerbuna No. 12, 50009, Zaragoza, Spain. [2] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain.
mamoros@unizar.es

Promoting tissue repair and regeneration by manipulating intracellular pathways is currently a hot topic in biomedicine research. Cadherins are crucial cell membrane proteins that promote cell-cell adhesion through their calcium-dependent homophilic interactions. In addition, cadherins are important mechanosensors which induce intracellular cascades in order to activate collective epithelial remodeling during tissue repair. Thus, cadherins are an attractive target to manipulate intracellular pathways implicated in these processes.

To manipulate intracellular pathways through the cellular cadherins and promote tissue repair we propose the use of magnetic microparticles (MMPs) functionalized with E-cadherin fragments, as magnetic actuators. Magnetic particles specifically anchored to membrane proteins can be used to precisely manipulate forces on these mechanoreceptors when a magnetic field is applied. Indeed, over the past decades magnetic microparticles and magnetic tweezers have been widely used to demonstrate how mechanical cues can regulate biological processes. The use of magnetic fields offers some advantages such as deep-tissue penetration, the ability to apply a wide range of stresses and forces (fN to nN) without damaging live samples, and the possibility to manipulate the receptors remotely.

To reach this ambitious goal, we have designed a toolbox composed by cadherin fragments bound to MMPs and reporter cell lines following these steps:

A) Production and purification of different engineered E-cadherin fragments, in which mutations have been introduced to modulate their binding affinity. The cadherin fragments present a histidine tag at the C-terminus to allow their oriented attachment to NTA-Cobalt-MMPs.
B) Functionalization of the MMPs with E-cadherin fragments, verifying their density and the correct orientation through the His-tag by antibody staining and an innovative analysis by flow cytometry.
C) Production of reporter cell lines. Through lentiviral transduction and conventional plasmid transfection, we have obtained different cell systems to study if important intracellular pathways related to cadherin mechanotransduction could be activated.

In addition, to mimic the natural cell mechanical-environment we have generated polyacrylamide gels with different stiffness, for subsequent use in cell assays. Finally, we have immobilized the E-cadherin-MMPs on the membrane of living cells that express E-cadherin, stablishing the optimal conditions of membrane labelling without MMP internalization. With this fine-tuning of the MMPs-cell interaction assays, the next step will be the activation of mechanotransduction processes using different configurations of magnets and polyacrylamide gels.

Acknowledges: This work was supported by the SIROCCO project which has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 853468).

Synthesis and Characterisation of Zn- and Mn-Doped Iron Oxide Nanocubes for Combined Magnetic Particle Imaging-Magnetic Fluid Hyperthermia Application

S. Harvell-Smith[1,2] and Nguyễn T. K. Thanh[1,2*]

[1] Biophysics Group, Department of Physics and Astronomy, University College London, London WC1E 6BT, UK
[2] UCL Healthcare Biomagnetics and Nanomaterials Laboratories, University College London, London W1S 4BS, UK
*Corresponding Author: ntk.thanh@ucl.ac.uk, http://www.ntk-thanh.co.uk

Magnetic particle imaging (MPI) is a tracer-based imaging modality that facilitates real-time detection of the response of magnetic nanoparticle (MNP) tracers to an external alternating magnetic field.[1] This produces a signal, leading to image generation. MPI also implements a static gradient field with strong field gradients which permits spatial encoding of this signal. The unique arrangement of magnetic fields enables advantages in various biomedical applications of clinical interest, including MPI in combination with magnetic fluid hyperthermia (MFH), termed MPI-MFH. MPI-MFH addresses several important technical challenges encountered by standard MFH application paradigms. For effective performance here, MNPs must be synthesised with properties tailored towards optimal imaging and heating performance, individually. Due to the infancy of this technique, research on MNPs specifically designed for MPI-MFH application remains scarce.

Single-core superparamagnetic (SPM) iron oxide nanocubes (IONCs) were chosen as the MNP system for investigation. As an initial focus, the thermal decomposition synthetic procedure was optimised to produce monodisperse MNPs reproducibly. Following this, IONCs with ranging core sizes were synthesised. This was carried out through alteration of heating rates, reaction precursors, and solvent ratios. Each parameter independently plays an important role in the synthesis and here, can finely tune the IONC core size to many different sizes between 7 and 58 nm, each with a homogenous cubic shape. For further MPI-MFH performance enhancement, the IONCs were systematically doped with differing quantities of Zn and Mn, each MNP with a variation of a $Zn_xMn_yFe_{3-x-y}O_4$ core structure. This is the first example of IONCs doped with both Zn and Mn in the same core structure. Finally, a ligand exchange with dimercaptosuccinic acid (DMSA) was performed on the optimal co-doped IONCs to allow stable dispersion in water. These MNPs have an average diameter of 22.8 ± 2.0 nm, with an excellent polydispersity of 8.7%, confirmed SPM with a very large saturation magnetisation of 157 emu/$g_{Zn,Mn,Fe}$. Impressive specific absorption rate (SAR) and intrinsic loss parameter (ILP) values for these MNPs were established, at 942.0 W/$g_{Zn,Mn,Fe}$ (24 kA/m, 300 kHz) and 5.5 nHm^2/kg_{Fe}, respectively. MPI capability was determined through magnetic particle spectroscopy (MPS) analysis. With MPS, the magnitude of the 3rd harmonic (A_3*) indicates MPI sensitivity characteristics, and the ratio between the magnitude of the 5th and 3rd harmonic (A_5/A_3), MPI resolution. A high A_3* of 29.4 Am^2/$kg_{Zn,Mn,Fe}$ (25 mT, 25 kHz), and A_5/A_3 of 35.1% were demonstrated. These values compare very favourably to those of the standard MPI tracer, Resovist, where for the same field values, A_3* is 8.7 Am^2/$kg_{Zn,Mn,Fe}$, and A_5/A_3 is 26.1%.

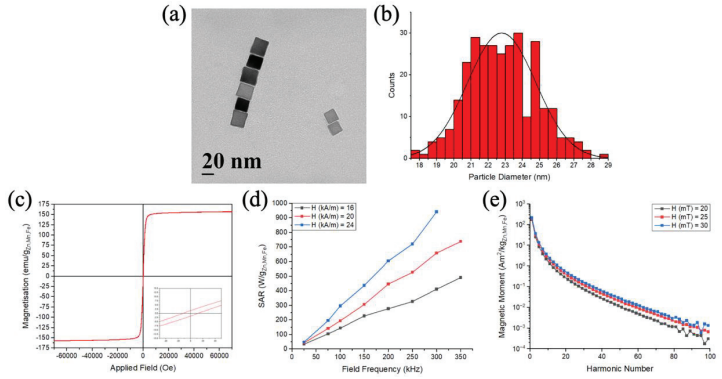

Fig. 1. *Characterisation of the optimal Zn,Mn-doped IONCs following ligand exchange. (a) TEM image. (b) Size distribution. (c) MH loop at 300 K. (d) SAR values at varied field amplitudes and frequencies. (e) MPS amplitude spectrum at different field amplitudes and a frequency of 25 kHz.*

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Development of Core-Shell Nanoparticles for Singlet Oxygen Storage and *in situ* Release Through Magnetic Hyperthermia for a Multi-Approach Cancer Treatment

[1]Roger Gómez Herrera, [1]Daniel Ruiz Molina, [3]Pablo Guardia Girós, [2]Tamara Fernandez Cabada, [2]Julia lorenzo Rivera

[1]Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and BIST, Campus UAB, Bellaterra, 08193 Barcelona, Spain, [2] Institut de Biotecnologia i de Biomedicina, Departament de Bioquimica i Biologia Molecular, Universitat Autònoma de Barcelona, 08193 Cerdanyola del Vallès, Barcelona, Spain,[3]Institut de Ciència de materials de Barcelona (ICMAB-CSIC) Campus UAB, Bellaterra, 08193 Barcelona, Spain

Photodynamic therapy (PDT) is an approach to cancer treatment that useas a combination of oxygen, light, and photosensitizers that has been receiving great attention thanks to it's potential to overcome the weaknesses of existing therapies like surgery, radiation therapy, and chemotherapy.[1] Nanocarriers in the field of PDT has also been recently gaining traction, with the incorporation of nanomaterials that allow for encapsulation of photosensitizer molecules that benefit from enhanced permeability retention (EPR) for tumour accumulation.[2] However, PDT presents some sever limitations in implementation like the difficulty to efficiently photoexcite photosensitizers deeper than 1 cm from the surface due to endogenous biomolecules absorption of a broad part of the light spectrum, small focal area of cutting edge technologies like optical fiber in biomedicine applications, and lack of oxygen in hypoxic tumour environment to conduct type II photodynamic therapy.[3]

Herein, we report the development of core shell nanoparticles that consist of a super paramagnetic iron oxide (SPION) core coated in a coordination polymer based on functionalized 9,10-dyphenilantrhacene (**DPA**) bridging ligands coordinated with zirconium as coordination node.

These nanoparticles combine the capability to store oxygen under UV irradiation due to DPA capability to form *endo*-peroxides under such conditions, with the capability to release this oxygen in the form of singlet oxygen under thermal stimulus provided by the SPION core through magnetic hyperthermia.

This combination allows to release singlet oxygen under hypoxic environments, while at the same time circumventing poor photoexcitation efficiency from classical PDT drugs.

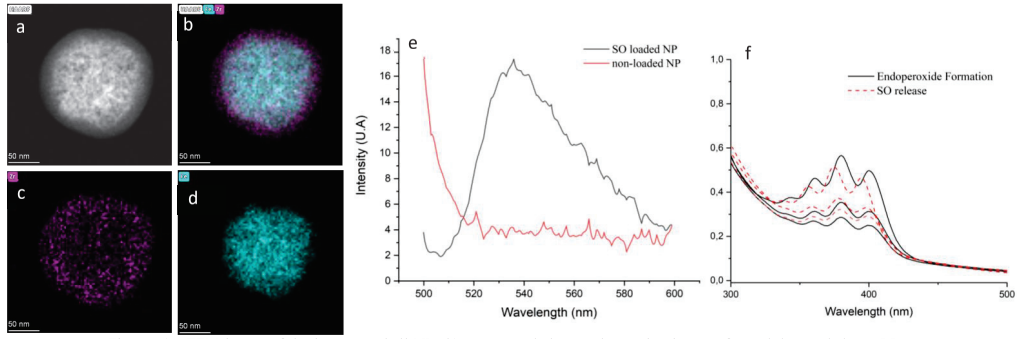

Figure. a) STEM image of the iron core-shell NPs b) superposed elemental mapping image of c and d recorded at ALBA synchrotron facilities c) Elemental distribution of Zirconium in the NP d)Elemental distribution of iron in the NP e) Fluorescence emission of sensor green singlet oxygen fluorescent prove when; in black - reacted with the singlet oxygen of a NP that was previously loaded and induced to release the SO cargo, and in red- no fluorescence detected from a NP that wasn't loaded with SO f) Absorption spectra of a NP that has been loaded with SO over time (black lines) and absorption spectra of a NP recovering the original absorption while releasing SO cargo.

Scalability and Reproducibility of Iron Oxide Nanoflowers by the Polyol Method: Comparison of Solvothermal and Microwave Heating

Rafael Herrera Aquino*, María del Puerto Morales, and Álvaro Gallo-Córdova

Instituto de Ciencia de Materiales de Madrid, ICMM/CSIC, C/ Sor Juana Inés de la Cruz 3, 28049 Madrid, Spain.

*Email: rafael.herrera@icmm.csi.es

Many studies have demonstrated synthesis of nanoparticles with good homogeneity and narrow size distributions. However, it is rare for any of them to produce more than one-gram particle and just a few of these studies have conducted a comprehensive investigation into the reproducibility of such scaled-up procedures [1]. As for now, the sole industrial method capable of generating magnetic nanoparticles (MNPs) in substantial amounts is coprecipitation from aqueous solutions but methods like the polyol are yet to be studied for large-scale production of MNPs. In previous research, the effect of an amined co-solvent in polyol was analyzed in the non-classical formation mechanism of iron oxide nanoflowers (NFs). It was possible to determine an intermediate stage where the NFs presented a crystallographically arrangement of smaller cores leading to a high magnetic moment per particle and a cooperative magnetic behavior, responsible for a highly efficient magnetic heating [2].

In this work, we go further these previous analyses and deep into the scalability and reproducibility of the NFs considering two distinct heating methods: solvothermal and microwave. For the solvothermal synthesis, we performed the reaction in a much larger reactor (1000 mL) while for microwave-assisted heating we considered the batch-to-batch production using an autosampler. In both cases, several synthesis batches were performed and the comprehensive analysis of the reproducibility of colloidal, structural and magnetic parameters was accomplished. Specifically, for the synthesis using an autoclave, we mixed the iron salt precursors in a basic medium and then deposit them in a Teflon-lined autoclave reactor of 1000 mL for heating to 190 ºC/16 h with a yielding product within a gram-scale range. Five different batches were performed and the reproducibility assessment analyzed. The results showed NFs formation (Fig 1, green label) with a mean particle size of 33 ± 4 nm, composed of 8 ± 1 nm cores. Structural, colloidal and magnetic parameters present high reproducibility for all batches, over 90 % (Fig 1, green label).

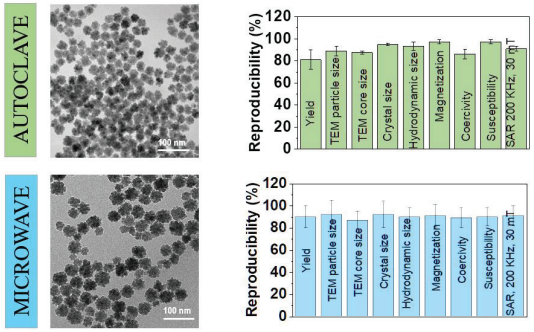

Fig 1. TEM images and reproducibility of NFs prepared by solvothermal (green) and microwave (blue) heating.

Furthermore, the synthesis of NFs was also carried out in a microwave, where temperature gradients are reduced dramatically due to the "in-situ" heating, leading to shorter reaction times and less energy consumption. In this sense, it was possible to synthesize 40 ± 6 nm NFs with core size of 8 ± 1 nm (Fig 1, blue label) in 40 min only, which is quite impressive compared to the 16 h solvothermal reaction. Remarkably, an average reproducibility for all the studied parameters of 95 % was achieved (Fig 1, blue label), indicating a promising avenue for NF production and suggesting potential for large-scale industrial applications [3].

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Developing nanorobotics for healthcare

O. Hovorka
Faculty of Engineering and Physical Sciences, University of Southampton, Southampton, UK
Email: o.hovorka@soton.ac.uk

M. A. Ramos-Docampo, B. Städler
Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Gustav Wieds Vej 14, 8000 Aarhus, Denmark

Nanorobotics deals with the applications of robotic concepts at the nanoscale. Nanorobots are autonomous nanoscale structures capable of self-powered transport and navigation through complex environments with a high degree of intelligent control. Several promising applications are being developed, such as targeted drug delivery to specific cells or tissue in the body, early-stage disease detection by detecting biomolecular anomalies at the cellular level, microsurgery for removing cancerous cells, repairing damaged tissue, or clearing blockages in blood vessels, for example.

In this work, we will address our recent contribution to the development of this field [1, 2], with a focus on heat-assisted cancer therapy. We will highlight nanorobot design with magnetic control and heat delivery, and demonstrate computational modelling, data-driven methods, and machine learning approaches suitable for guiding nanorobot design in complex biological environments. We will also briefly overview the commercialization and clinical status of nanorobotic healthcare technologies.

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Integrating Lipidic Cisplatin Prodrug and Magnetic Nanoflowers for Hyperthermia Cancer Treatment

Xinkai Hu,[a,b] ,Martin Forster,[c] Nazila Kamaly,[d] Nguyen Thi Kim Thanh,[a,b]*

[a]*Biophysics group, Department of Physics and Astronomy, University College London, London, WC1E 6BT, U.K.*
[b]*UCL Healthcare Biomagnetics and Nanomaterials Laboratories, 21 Albemarle Street, London, W1S 4BS, U.K.*
[c]*Department of Medical Oncology, UCL Cancer Institute/UCLH, London, WC1E 6AG, U.K.*
[d]*Department of Chemistry, Molecular Sciences Research Hub, Imperial College London, London, W12 0BZ, U.K.*
Email: ntk.thanh@ucl.ac.uk, http://www.ntk-thanh.co.uk

Magnetic fluid hyperthermia (MFH) using iron oxide nanoparticles (IONPs) holds promise for cancer therapy. However, limited heating efficiency and suboptimal antitumor efficacy of traditional IONPs hinder clinical translation. This study presents a novel approach to address these challenges by developing thermally responsive magnetoliposomes (MLPs). Our previous research demonstrated that engineering IONPs into nanoflower structures significantly improves their magnetic thermal efficiency [1]. Furthermore, the successful encapsulation of thermosensitive liposomes loaded with a hydrophobic cisplatin prodrug ($CisPt_{IV}$) within the nanoflowers creates MLPs capable of synergistic chemo-thermal therapy, shown in Fig 1.

Our synthesis yielded MLPs with a mean hydrodynamic diameter of 142.2 ± 2.4 nm and a mean zeta potential of 20.6 ± 2.0 mV. Notably, these MLPs exhibited a high specific absorption rate (SAR) of 405.7 ± 8.3 W/g_{Fe} or intrinsic loss power (ILP) of 5.3 ± 0.1 nHm^2/kg, which demonstrated stronger heating capacity compared to other MLPs reported. These findings suggest this novel platform offers a promising strategy for effective cancer treatment through combined hyperthermia and targeted cisplatin delivery.

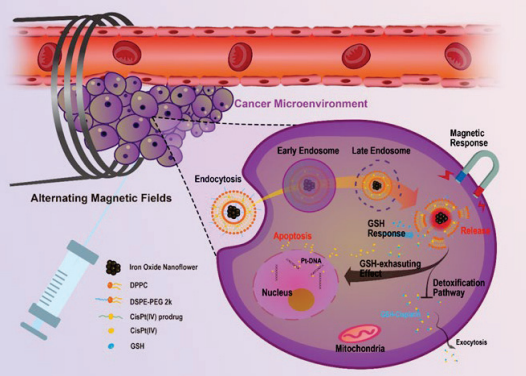

Fig 1. Schematic of magneto-thermal responsive cisPt(IV)@magnetoliposomes ingested into cancer cells for drug release therapy.

Acknowledgement: China Scholarship Council-UCL

Reference:

[1] Storozhuk, Liudmyla, et al. "Stable iron oxide nanoflowers with exceptional magnetic heating efficiency: simple and fast polyol synthesis." ACS Applied Materials & Interfaces 13.38 (2021): 45870-45880.

Characterization of Commercial Magnetic Nanoparticles for Magnetic Particle Imaging

Eric Daniel Imhoff[1], Ambar C. Velazquez-Albino[1], Andrii Melnyk[1], Carlos M. Rinaldi-Ramos[1,2*]

[1]Department of Chemical Engineering, University of Florida, Gainesville, FL, United States
[2]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, U.S.
*email: carlos.rinaldi@ufl.edu

Magnetic particle imaging (MPI) is a novel imaging modality with opportunity for use in several applications in imaging and theranostics. Although commercially available magnetic nanoparticles tracers exist, most are not optimized for use in MPI as they were typically formulated for other purposes. However, due to their wide availability they are still useful as benchmarks for MPI performance, especially comparing relative sensitivity. This study characterizes the MPI performance and relevant physical and magnetic properties of 5 commonly used commercial particles: Ferucarbotran, Perimag, Synomag-D, Vivotrax, and Vivotrax Plus in a Magnetic Insight MOMENTUM™ imager. This data will serve as a reference for other researchers using these commercial particles in MPI.

Tracer performance in x-space MPI is commonly evaluated by measuring the point spread function of the material, which provides information on the sensitivity and resolution of a tracer based on the peak height and full width at half maximum (FWHM) respectively. However, measurements are typically reported as a single value despite the inherent variability present. As illustrated in Figure 1, multiple RELAX measurements of the same sample result in a distribution of FWHM values which highlights the need for statistical analysis of MPI data to ensure accurate characterization when comparing tracers. Based on the largest standard deviation observed in a sample, collecting 5 replicate RELAX measurements allows for the statistical differentiation of 0.45 mT or 0.08 mm for a 5.7 T/m gradient field, several times smaller than the pixel size of a MOMENTUM™ scanner. In this study, commercial particles are comparatively evaluated for their MPI performance using RELAX measurements and 2D scans of point sources incorporating statistical analyses. Additionally, detailed physical and magnetic characterization of the particles for properties such as size distribution and stability in various media will be reported as reference for researchers to use in application-focused work.

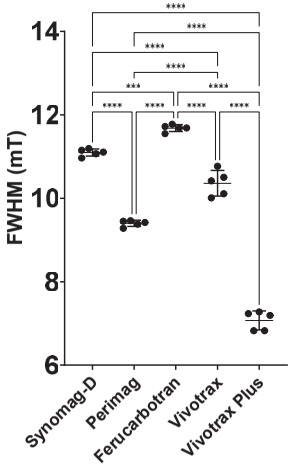

Figure 1. Comparison of FWHM of commercial particles from multiple RELAX measurements of the same sample. Because of the variability between measurements, multiple evaluations are required to accurately compare the different tracers.

PICKERING DROPLETS STABILIZED BY MAGNETIC NANOPARTICLES FOR OPTIMIZING ULTRASOUND HEATING IN A TISSUE-LIKE MEDIUM

Bassam Jameel*, Rafał Bielas, Yaroslav Harkavyi, and Arkadiusz Józefczak

Faculty of Physics, Adam Mickiewicz University in Poznań
Uniwersytetu Poznańskiego 2, 61-614 Poznań, Poland
*e-mail: basjam@amu.edu.pl

Ultrasound-induced heat is generated through the absorption of ultrasound waves. The efficacy of ultrasound heating can be enhanced and controlled by using so-called sonosensitizers, agents that effectively increase the temperature elevation in tissues by manipulating the ultrasound absorption. We propose to use Pickering droplets stabilized by magnetic nanoparticles for this purpose as the increased number of controllable parameters could significantly enhance the precision of optimizing ultrasound heating procedures.

In this research, the core–shell model was employed to replicate the acoustic properties of Pickering droplets. Liquid oil droplets were modeled as stabilized by magnetic and silica nanoparticles and dispersed in an agar gel. As a result, we obtained distinct ultrasound attenuation values, illustrating the contrast between nano and micro-sized Pickering droplets as shown in **Fig 1**. The same model was recently utilized to analyze experimental results from ultrasound spectroscopy [1]. The COMSOL simulation results showed the change in the temperature and penetration depth in the system when using Pickering droplets. The possibility of adjusting their parameters when incorporated into agar phantoms holds the potential to optimize ultrasound heating, for instance, to obtain temperature elevation more locally without using complex focused-ultrasound devices.

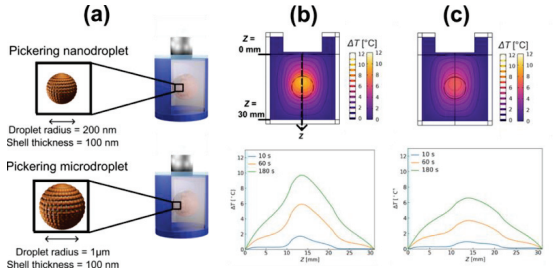

Fig. 1 (a) The scheme of the simulation designed for testing the pure agar phantom incorporated with spherical inclusion doped with nano and micro-Pickering droplets. COMSOL simulation results for the inclusion doped with **(b)** Pickering nanodroplets and **(c)** Pickering microdroplets stabilized by magnetic nanoparticles.

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Acknowledgments

This work was supported by the project no. 2019/35/O/ST3/00503 (PRELUDIUM BIS) of the Polish National Science Centre.

Textile modified by magnetic nanoparticles

Arkadiusz Józefczak[1,*], Rafał Bielas[1], Ivo Šafařík [2], Peter Kopčanský[3]

[1]Faculty of Physics, Adam Mickiewicz University in Poznań,
Uniwersytetu Poznańskiego 2, 61-614 Poznań, Poland

[2]Department of Nanobiotechnology, Biology Centre, ISBB, Czech Academy of Sciences,
Na Sádkách 7, 370 05 České Budějovice, Czech Republic

[3]Institute of Experimental Physics, Slovak Academy of Sciences,
Watsonova 47, 040 01, Košice, Slovakia

*e-mail: arkadiusz.jozefczak@amu.edu.pl

Textiles are materials made of interlocking bundles of yarns or threads. The inherent flexibility of the textile materials opens the possibilities for their functionalization. The space between the single fibers and their surface can carry additives of different functionalities, such as magnetic nanoparticles and drug molecules. Magneto-responsive textiles have emerged lately as an important carrier in various applications, including those in biomedical fields such as drug delivery, tissue engineering, and regenerative medicine. We designed and characterized simple woven and non-woven textile materials with magnetic properties that can become potential candidates for a smart magnetic platform for hyperthermia treatments [1]. When the heat was induced by magneto-responsive textiles under the influence of a high-frequency alternating magnetic field, the temperature increase in tissue-mimicking phantoms depended on several factors, such as the type of basic textile material, the type of materials used for textile surface modification (magnetic fluids, magnetic Pickering emulsion), and the number of layers covering the phantom. The temperature elevation values, achieved with magnetic textiles, are sufficient for potential application in magnetic hyperthermia therapies and as heating patches or bandages. Controlled release of substances and/or nano-sized objects from the textiles triggered by high-intensity ultrasound is also possible. This paves the way for the potential use of the proposed textile materials in the theranostics paradigm.

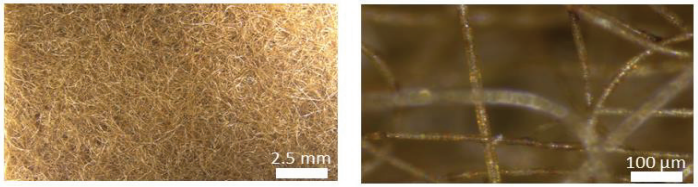

Fig. 1 Optical microscopy images of the magnetic textile with different magnifications [1].

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The peroxidase-like activity of magnetic iron oxide nanoparticles functionalized with amino acids

Iryna Khmara[1*], Martina Kubovcikova[1], Iryna Antal[1], Vlasta Zavisova[1], Martina Koneracka[1]
[1]Institute of Experimental Physics SAS, Watsonova 47, 04001 Kosice, Slovakia
*Email: khmara@saske.sk

Today, iron oxide nanoparticles (IONPs, such as Fe_3O_4) as a type of nanoscale material are of great interest in targeted drug delivery, protein isolation and purification, magnetic resonance imaging, and magnetic hyperthermia due to their extremely small size, low toxicity, superparamagnetic properties, biocompatibility, biological degradation, large surface area per unit volume, and the ability to be excreted from the body naturally. In addition, IONPs have an intrinsic peroxidase-like activity, which makes it possible to use them as a tool for detecting and visualizing tumor tissue. Furthermore, IONPs have almost unchanged catalytic activity in a wide range of temperatures and pH and are also significantly more stable compared to natural enzyme peroxidases. This allows IONPs to be used as natural peroxidase enzymes or to replace natural peroxidase enzymes in applications based on the detection of hydrogen peroxide.

In our work, we studied the influence of amino acids (AA) as stabilizing materials on the peroxidase-like activity of IONPs. Different types of IONPs were prepared – bare IONPs, electrostatically stabilized IONPs by $HClO_4$ (MF), and MF modified with AA such as proline (Pro-MF) and tryptophan (Trp-MF). The comprehensive physicochemical characterization of samples was carried out to determine their structure, morphology, and magnetic properties. The obtained data showed that their hydrodynamic diameters ranged from 32 nm to 49 nm, and the zeta potential from 23.8 mV to 49 mV. Moreover, the classical starch-sodium iodide reagent was utilized as the chromogenic substrate to evaluate the peroxidase-like activity of all samples. Under the catalysis of peroxidase-like nano-enzymes, iodide ion (I^-) is oxidized by H_2O_2 to produce a blue color complex (starch-I_2), and the color reaction is completed within 5 min at room temperature (25 °C). The absorbance at 588 nm (see Fig.) was used for quantitative analysis. As observed from Fig., among the peroxidase-like nano-enzymes tested, MF display the best catalytic performance for the coloration reaction under the same conditions. Moreover, the AA coating was found to slightly decrease catalytic activity compared to MF at pH 3.0 but Pro-MF activity is somewhat better than that of Trp-MF and bare IONPs.

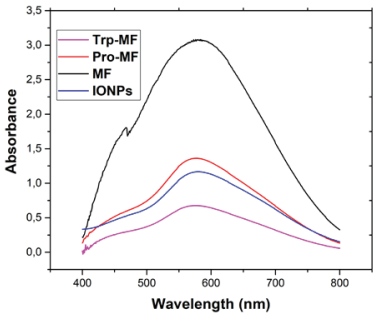

Fig. Absorption spectra of starch-NaI solution under the catalysis of nano-enzyme bare IONPs, MF, Pro-MF, and Trp-MF. Condition: Fe_3O_4 nanoparticles (200 μg mL^{-1}), NaI (2.27 mM), starch (2.27 mM), HAc-NaAc buffer (100 mM, pH 3.0), H_2O_2 (100 μM)

Acknowledgements: This work was supported by the Slovak Research and Development Agency under the contract no. DS-FR-22-0037, and Slovak Grant Agency VEGA 02/0049/23; the Operational Program Integrated Infrastructure funded by the ERDF ITMS2014+: 313011AVG3 (BIOVID).

Towards Accurate Prediction of Magnetoelectric Coefficient in Spherical Core@Shell $CoFe_2O_4$@$BaTiO_3$ Nanoparticle for Brain Stimulation

Gawtak Kim[1], Yaser Hadadian[1], and Jungwon Yoon[1*]

[1] School of Integrated Technology, Gwangju Institute of Science and Technology, Gwangju, Republic of Korea.

*Email: jyoon@gist.ac.kr

Electrical stimulation (ES) has found a broad range of application, spanning from modulating the electrical activity of biological systems to clinical therapeutic. Magnetoelectrics (ME) have recently emerged as transformative technological materials, and as promising candidates for ES. Magnetoelectric refers to a class of materials that combine piezoelectric and ferromagnetic behaviours simultaneously. The presence of a coupling between the piezoelectric (or ferroelectric) and ferromagnetic properties enables the control of the piezoelectric properties of ME materials by simply using a variable magnetic field (and vice versa). The most essential property of ME materials, particularly ME nanoparticles (MENs), is the coupling coefficient, which is the amount of produced voltage per unit of MEN's thickness per unit of the applied magnetic field (in $V.cm^{-1}.Oe^{-1}$).

The most common method for determining ME coefficient uses MENs powder samples, which may not accurately reflect the actual value for a single MEN. In this method, a disc-shaped sample is created by mechanical compressing the MENs powder, and the collective ME coefficient is determined by measuring the voltage of electrodes that sandwich the disc using lock-in technique. This method is not only prone to charge leakage, but also parameters such as the pressure for creating the disc, its morphology, and orientation of the particles can significantly affect the resultant ME coefficient. Due to these challenges ME coupling coefficients usually theoretically predicted, but in many cases the coefficient is significantly over-estimated [1]. Therefore, developing a method for accurate estimation of ME coefficient is of crucial importance.

In this study, we analyzed the electric field and the voltage generated by a single perfect spherical core-shell structure of $CoFe_2O_4$@$BaTiO_3$ (CFO@BTO) MEN with a total diameter of 30 nm (core diameter of 24 nm) in cerebrospinal fluid medium through COMSOL Multiphysics® 6.1 software. We used *AC/DC module* and *Structural Mechanics module* through *Multiphysics Coupling* function. The material parameters were selected from COMSOL materials library and previous studies. We fitted the magnetic hysteresis of our computational MEN model to that of our synthesized MENs sample. The 2D axisymmetric simulation model is shown in Fig. (a) with the MEN located at the center (r = 0, z = 0). A homogeneous DC magnetic field of 1000 Oe in the z-direction was superimposed with a 100Hz AC field of 10 to 100 Oe.

Fig. (a) shows the typical electric field lines and electric potential generated by a single MEN at AC field of 50 Oe. Interestingly, our predicted values in Fig. (b) are very close to the ME coefficients measured using scanning tunneling microscope (STM) probe for single MENs of similar sizes and at similar field conditions [2]. This demonstrates the accurate estimation of ME coefficient of MENs through a straightforward computational modeling, providing a reliable framework for precisely tuning their properties during synthesis.

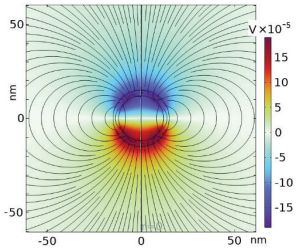

Fig. (a)

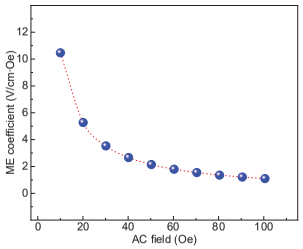

Fig. (b)

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Spectroscopic and microscopic analysis of the effect of vancomycin-modified SPIONS on methicillin-sensitive and resistant Staphylococcus aureus strains

Julia Werle[1], Jakub Podhajsky[1], Kristyna Buresova[1], Agnes Phlosi[2], Katerina Dunovska[1], Eva Klapkova[1], Jana Cepova[1], Vedha Hari B Narayanan[3], Karel Kotaska[1], Carlos Fernandez[4], Joe Modise[2], Richard Prusa[1] and Rene Kizek[1]

[1]Department of Medical Chemistry and Clinical Biochemistry, Second Faculty of Medicine, Charles University in Prague and Motol University Hospital, V Úvalu 84, 150 06 Prague 5, Czechia
[2]Vaal University of Technology, Andries Potgieter boulevard, Vanderbijlpark, 1900, South Africa
[3]Pharmaceutical Technology Lab, SASTRA Deemed University, Thanjavur-613401, India
[4]School of Pharmacy and Life Sciences, Robert Gordon University, Garthdee Road, Aberdeen AB107QB, Aberdeen, United Kingdom
*Email: kizek@sci.muni.cz

It has been nearly a century since the discovery of the antibacterial properties of penicillin. Its integration into clinical practice has significantly advanced the treatment of infectious diseases. Subsequently, these substances found utility in agricultural production as well. However, in recent decades, the emergence of bacterial resistance [1] has become an escalating concern, particularly within hospital environments where nosocomial infections caused by resistant strains pose significant clinical challenges, sometimes with fatal consequences. Thus, there is a crucial need for research of novel antibacterial compounds and methodologies. One of the objectives of nanomedicine is to overcome these resistant bacterial strains. Specially engineered nanoparticles (NPs) affect bacterial metabolism through various mechanisms, including enzymatic degradation, interaction with the bacterial cell wall and cytoplasmic membrane, the formation of oxygen radicals, and binding to DNA structure, thereby overall altering replication and transcription. The objective of this study is to develop novel nanomaterials to improve the effectiveness of antibacterial therapy.

For this purpose, SPIONS were prepared using standard procedures, which were then purified on a magnet and lyophilized for 48 hours at -80 °C. The NPs were resuspended by ultrasound for 5 minutes at 100 W. Furthermore, SPIONs were modified with 125 mM chitosan for 24 hours at 300 rpm and 25°C, and then purified on a magnet. Subsequently, SPIONs/Chito were modified with 100 mM vancomycin for 6 hours at 300 rpm and 25°C. After washing the particles with phosphate buffer at pH 7, the particles were modified with vancomycin (100 μg/mL) resulting in SPIONs/Chito/VANCO NPs. UV-Vis analysis showed maxima at 220, 250 and 400 nm. FTIR analysis demonstrated the presence of both Chito and VANCO on the surface of the nanomaterial through band comparison. TEM and SEM analysis revealed a spherical structure with a particle size of approximately 140-180 nm. The analysis of magnetic properties was performed, and the modification of the nanotransporter resulted in a shift of the zeta potential to positive. The presence of Chito (RT 4.5 min) and VANCO (10.1 min) was demonstrated through their release from the nanoparticles via chromatography. The release of VANCO was studied in various environments, and it was shown that the release decreased with increasing pH (approximately 10% per pH unit). The bacterial culture's growth was monitored using growth curves and evaluated as their integral ($AUC_{0\text{-}24h}$). The average AUC of SA1 was 1900±200, and the total biomass was 21 g/l. For SA2, the average AUC was 2200±250, and the total biomass was 23 g/l. Lastly, for SA3, the average AUC was 1800±150, and the total biomass was 17 g/l.

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Acknowledgements: The project is being implemented under the grant project Liga proti rakovině Praha (2399011548).

DEVELOPMENT OF ULTRASMALL SUPERPARAMAGNETIC NANOPARTICLES FOR IMAGING APPLICATIONS

Vladimir Kolesnichenko[1]*, Galina Goloverda[1], Carl Boateng[1], Caleb Womack[1], Elena Skripnikova[2], and Thomas Wiese[2]

[1] Department of Chemistry, Xavier University, New Orleans, Louisiana 70125, USA

[2] College of Pharmacy, Xavier University, New Orleans, Louisiana 70125, USA

*Email: vkolesni@xula.edu

Nanotechnology offers new pathways for the development of hybrid inorganic/organic materials with a broad range of applications in medicine. Nanoparticulate materials, containing magnetic core, can be used as imaging agents for the cell and biomolecule labeling, contrast agents for MRI, or therapies as delivery or hyperthermia agents. Performance of these materials as theranostic agents heavily relies on the properties of each component of the nanoparticulate assembly. Nanocrystalline core provides essential physical functions, such as magnetic and NMR relaxivity properties, and/or Specific Loss Power (SLP). An organic shell stabilizes the nanoparticulate assembly in a colloidal form, alleviates toxicity, facilitates bioconjugation and provides the desired pharmacokinetic properties.

In this project we focus on the design and synthesis of each component of the nanoparticulate inorganic-organic hybrid. Our strategy is in using organic oligomers covalently attached to the inorganic core on one end and to biomolecule of interest (drug, vector, fluorescent dye, etc.) on another. The composition and the structure of both ends, as well as oligomeric spacer, are optimized for efficient linkage, hydrolytic stability, affinity to the medium and size of the assembled nanoparticles. Optimal size helps control particles' pharmacokinetic properties: small particles with hydrodynamic diameter 20-30 nm can avoid renal and macrophages clearance mechanisms and would stay in the vascular system long enough to be detected by imaging methods.

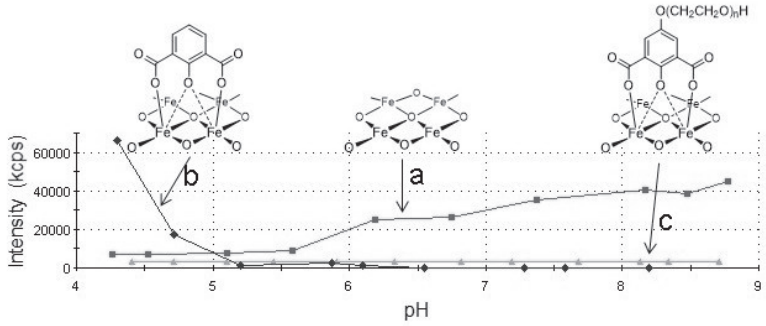

Fig. 1. Light scattering as a function of pH in Fe_2O_3 (4.5 nm) aqueous colloids: the original ligand-free colloid (a), a colloid with nanoparticles coated with tenacic acid (b), and a colloid containing particles coated with tenacic acid-PEG600 conjugate (c). Note: higher light scattering intensity is due to a greater aggregation.

Magnetic Nanostructures with Hollow Compartments: A Tunable Acid-Etching Approach

Sebastjan Nemec[1,2] and Slavko Kralj[1,2,3*]

[1] Department for Materials Synthesis, Jožef Stefan Institute, Jamova 39, 1000 Ljubljana, Slovenia,
[2] Faculty of Pharmacy, University of Ljubljana, Aškerčeva cesta 7, 1000 Ljubljana, Slovenia,
[3] Nanos SCI, Nanos Scientificae d.o.o., Teslova 30, 1000 Ljubljana, Slovenia
*Email: slavko.kralj@ijs.si

Nanostructures with hollow core(s) and porous shell are an exciting type of nanoparticles. Such compartments offer a space available for the incorporation of various functional cargo, such as drugs, catalysts, etc. However, a wider applicability of the hollow nanostructures is delayed due to challenging synthetic procedures needed to obtain them. Thus far, various approaches have been utilized to prepare hollow nanostructures. The most widely used etching methods rely on the synthesis of nanoparticles which have a shell and a sacrificial core, which can be selectively removed while the shell is kept intact. When the removal of the sacrificial core is only partial, we obtain a partially hollow structure, commonly referred to as yolk-shell or rattle-type nanostructures. These partially hollow nanostructures are also attractive as they offer combined functionalities of the shell and the residual core part. The procedures for the preparation of partially hollow nanostructures are generally more challenging than obtaining completely hollow nanostructures, as the core removal process needs to be precisely controlled and should offer the possibility for rapid termination of the core removal. An elegant way to control the core removal process is to utilize core-shell nanoparticles, where the shell and the sacrificial core are composed of chemically different materials. This way we can achieve a selective core removal and, importantly, the core removal rate can be nicely controlled by changing the thickness and morphology (porosity) of the shell.

In our work, we synthesized hollow and partially hollow magnetic silica nanostructures (Figure). These structures were prepared from silica-coated magnetic nanoparticles and nanochains by using an acid etching method to partially dissolve iron oxide cores. The iron oxide cores were either completely or partially dissolved using hydrochloric acid. Iron oxide dissolves readily in the hydrochloric acid while the silica shell remains intact. The silica shell porosity and thickness affect the rate of the iron oxide removal. In our investigation, the protective ability of silica shells with different thicknesses (ranging from ~3 nm to ~60 nm) and morphologies (low-porous and mesoporous) were systematically studied by evaluation of different durations of the etchings and different hydrochloric acid concentrations used. We have figured out differences in the protective ability of different silica shells towards the acid dissolution of iron oxide cores. Our findings can be further applied to efficiently adjust the preparation procedures for obtaining partially hollow magnetic nanostructures for drug delivery systems.

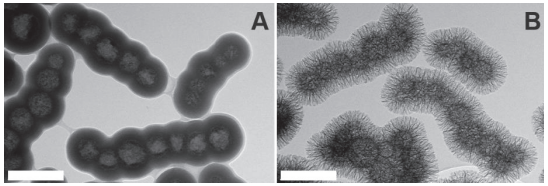

Figure. Transmission electron microscope micrographs of hollow silica nanostructures. **(A)** ~60 nm thick low-porous silica shells, **(B)** ~70 nm mesoporous silica shells. All scale bars are 200 nm.

Acknowledgments: ARIS program and projects: P2-0089, J2-3043, J2-3046, J3-3079, J7-4420, J2-3040

Transport properties of active Brownian particles with magnetically-controlled rotation

Andrey A. Kuznetsov[1*], Vittoria Sposini[1] and Sofia S. Kantorovich[1]
[1]University of Vienna, Vienna, Austria
*E-mail: andrey.kuznetsov@univie.ac.at

Active matter is a class of out-of-equilibrium systems with the ability to transform environmental energy into kinetic one. This unique feature is sought after in multiple fields of science, at different length scales. At micro- and nanoscales, an important challenge lies in overpowering the reorientation of active particles ("swimmers") due to thermal fluctuations. One way of dealing with this issue is the use of magnetic swimmers, whose orientation can be controlled with the applied magnetic field. The simplest and the most common model for studying magnetic active matter is the model of "dipolar active particles". Magnetic swimmers in this framework are represented by active Brownian particles with a point-like magnetic dipole embedded in its center. It is typically assumed that the dipole is "frozen" within the particle body and can only rotate along with it. In this contribution, we generalize the model to make it more suitable for magnetically soft materials such as magnetite. Namely, we explicitly consider the internal orientational fluctuations of the magnetic moment. We assume that each particle possesses a uniaxial magnetic anisotropy, and the moment can randomly flip between two equilibrium orientations, with the rate of flipping depending both on temperature and the magnitude of the field. Using theory and Langevin dynamics simulations, we explore how these internal fluctuations will affect the particle translational diffusion, mean-square displacement curves and displacement distributions (see Figure).

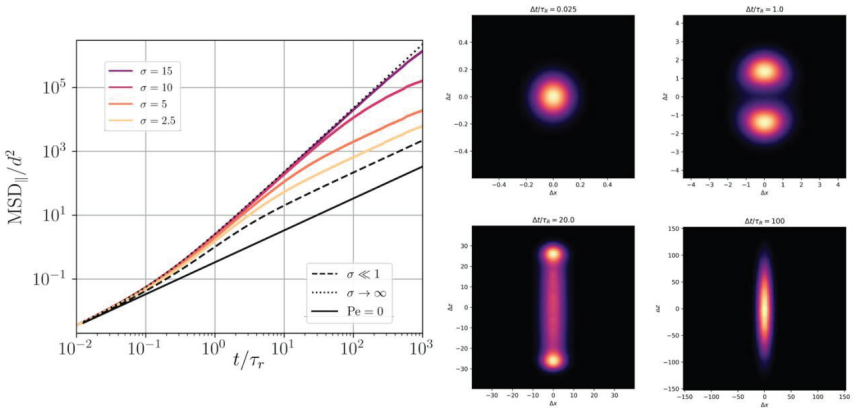

Figure. Left: mean-square displacement of particles in the field direction as a function of time at different values of the dimensionless anisotropy parameter σ. Right: corresponding concentration profiles of particles at different times in the plane, parallel to the field (σ = 5)

Carbon Nanofiber-Based Magnetic Mats for Non-Invasive Heating

D.Lachowicz[a] *, K.Sokołowski[a], K.Berent[a], M.Gajewska[a], M.Sikora[a], S.Zapotoczny[a,b]

[a]AGH University of Science and Technology, Academic Centre for Materials and Nanotechnology, al. A. Mickiewicza 30, 30-059 Krakow, Poland
[b] Faculty of Chemistry, Jagiellonian University, Gronostajowa 2, 30-387 Krakow, Poland
*Email:dorota.bielska@agh.edu.pl .Mobile: +48 12 617 52 74

The clinical use of magnetic hyperthermia (MH) shows great potential due to its very local effect and minimal side effects. Due to their high magnetization values in the saturated state, superparamagnetic iron oxide nanoparticles (SPIONs) are promising candidates for MH. However, under biological conditions, and the influence of physiological fluids, aggregation and instability of nanoparticles (i.e. oxidation) sometimes occur. Therefore, our work presents an innovative methodology for producing a composite material (mats) in the form of SPION nanoparticles deposited on carbon nanofibers (Fig.1.).

We demonstrate that the size and composition of the resulting SPION nanoparticles as well as the thickness of their protective carbon layer can be controlled by selecting the concentrations of precursors and surfactants, as well as the surface area of the carbon fibre. The nanoparticles showed a stronger interaction with the surface of the CNF nanofibers, even after long-term exposure to a strong magnetic field, no release of particles from the fibre surface was observed.

To determine the effectiveness of heating the mats at the target site, tests were performed on phantoms imitating tissue. A clear increase in the temperature of the tissue-imitating phantoms was recorded during the heat induction process in the produced magnetic mats. This increase depended on several factors, such as the concentration of the organometallic precursor used to synthesize magnetic nanoparticles on the fibre surface, the roughness of the fibres, and the number of fibres in the mat (weave density). The temperature increase values obtained using CNF nanofiber mats modified with magnetic nanoparticles are sufficient for potential use in magnetic hyperthermia therapies or warming dressings.

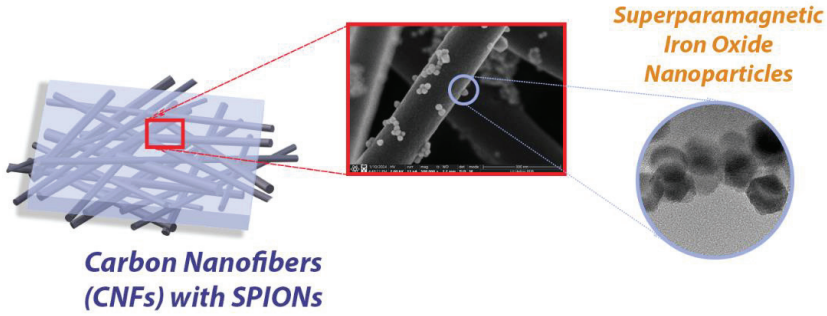

Figure 1. Composite material in the form of mat made of SPION-coated nanofibers.

Field-induced recirculation flow using magnetic nanoparticles to mimic drug transport in an occluded vessel

J. Lagouarde[1]*, G. Verger-Dubois[2], G. Godeau[1] et P. Kuzhir[1]

[1] Université Côte d'Azur, CNRS UMR 7010, Institute of Physics of Nice, 17 rue Julien Lauprêtre, 06200 Nice, France,
[2] Axlepios Biomedical, 1ere Avenue 5eme rue, 06510 Carros, France
*Email: julie.lagouarde@unice.fr

Magnetic iron oxide nanoparticles (IONPs) can be highly effective to create a microfluidic flow that can be used in medicine, for example to dissolve a blood clot during a stroke. Indeed, there is a blood stagnation near the clot that prevents the drug from acting and dissolving it quickly. The idea is to use IONPs to accelerate the transport of the therapeutic agent and accelerate its action [1,2]. For that, it is necessary to generate a collective rotation of the elongated nanoparticle aggregates using an oscillating magnetic field applied via external electric coils.

In view of the intended application, non-toxic IONPs stable in physiological conditions were first developed. They were synthesized by co-precipitation method and functionalized using PEGsilane. Structural and magnetic properties were characterized by DLS, FTIR, TGA, VSM and their biocompatibility was confirmed by *in vitro* cytotoxicity assays. Then, to mimic the environment in a blocked blood vessel, closed microfluidic channel was used. Inside it, the nanoparticles are able to self-assemble reversibly into elongated aggregates (Fig. 1a) and rotate collectively under the action of a rotating magnetic field [3,4]. The first observations of recirculation flows are promising (Fig. 1b,c), encouraging us to optimize them in order to achieve our therapeutic objective.

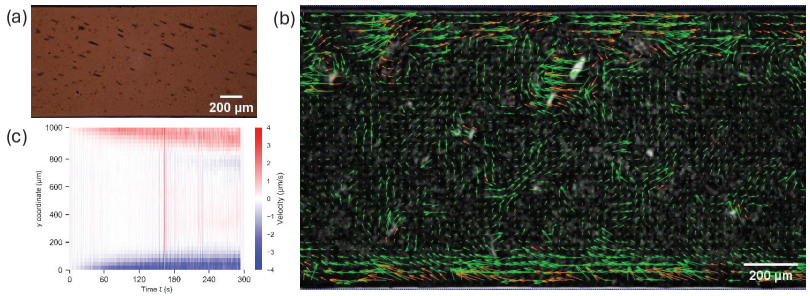

Figure 1. Solution of biocompatible IONPs dispersed in pig plasma at 0.4%vol during rotating magnetic field application of H ~ 9kA/m and f = 5Hz: (a) Snapshot of field-induced aggregates at t = 80 s after the moment of switching on the field; (b) velocity vector field deduced from particle image velocimetry (PIV) analysis taken at t = 280 s; (c) spatiotemporal velocity profile $v_x(y,t)$ of the field-induced recirculation flow

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Field-dependent magnetic relaxation times of magnetic nanoparticle systems

Jonathon C. Davidson,[1] Nicholas R. Anderson,[1] and Karen L. Livesey[2,1]
[1]UCCS Biofrontiers Center and Department of Physics, University of Colorado – Colorado Springs, CO 80918, USA
[2]School of Information and Physical Sciences, University of Newcastle, Callaghan NSW 2308, Australia

Many estimates for the magnetic relaxation time of magnetic nanoparticle systems neglect the effect of the applied field strength. This is despite many applications involving relaxation dynamics under the influence of applied fields.

Here, an analytic approximation for the field-dependent Brownian relaxation time of single-domain, spherical magnetic nanoparticles in an external applied field is developed mathematically. Brownian relaxation involves physical particle rotations in a fluid. The derived expression is validated by comparison with existing empirically-derived expressions and by comparison to our particle-level simulations that allow particle rotations. Our approximation works particularly well for larger particles.

We then use the developed Brownian expression to analytically calculate the **total** magnetic relaxation time when both Brownian and Néel relaxation mechanisms are at play (solid lines in Figure). The Néel relaxation time is based on our previous work of internal magnetization dynamics.[1] Again, we show that the analytic expression matches the results found using our particle-level simulations (dots in Figure), this time with both particle rotations and internal magnetization dynamics considered.[2]

However, for some particle parameters and for large field strengths, our simulations reveal that the Brownian and Néel relaxation mechanisms are decoupled and it is not appropriate to combine these to calculate a total relaxation time.

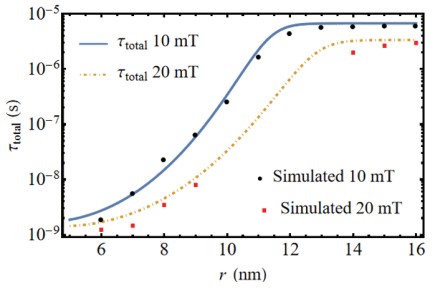

Figure: Total relaxation time τ_{total} for an ensemble of randomly aligned magnetic nanoparticles placed in an applied field of 10 mT (100 Oe) and 20 mT (200 Oe), as a function of particle radius r. The lines are results of our analytic expression, while dots are results of particle-level simulations.

[1] A.R. Chalifour, J.C. Davidson, N.R. Anderson, T.M. Crawford, and K.L. Livesey, Phys. Rev. B **104**, 094433 (2021).
[2] J.C. Davidson, N.R. Anderson and K.L. Livesey, *submitted* (2024).

Actuation of Magnetic Nanoparticles inside a cochlea phantom

Ankit Malhotra[1*], Justin Ackers[1], Matthias Graeser[1,3], Thorsten Buzug[1,3*], Verena Scheper[2], Anna C. Bakenecker[1]

[1] Fraunhofer IMTE, Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering, Lübeck, Germany
[2] Medizinische Hochschule Hannover, Klinik für Hals-Nasen-Ohrenheilkunde, Hannover, Germany
[3] Institute of Medical Engineering, University of Lübeck, Lübeck, Germany
Email: ankit.malhotra@imte.fraunhofer.de

Magnetic Nanoparticles (MNPs) are widely used in medical diagnostics and therapy due to their unique magnetic and electrical properties. In the past MNPs have been applied for drug delivery, magnetic manipulation, imaging, and hyperthermia. In this research the focus is on actuation of the MNPs through a cochlea phantom using rotating magnetic fields. The phantom used is a modified version of the Scala-Tympani phantom developed by Leon et al. [1]. The modifications include the extraction of the cochlea canal and surface modifications for improving the transparency of the phantom for observation under a microscope. The modified phantom was 3D printed (Agilista 3200 W, Keyence Deutschland GmbH, Germany) using AR-M2 as the resin material. The required magnetic field for the actuation of the MNPs was generated by using an MFG-100 (Magnebotix AG, Switzerland) device consisting of eight asymmetrically arranged electromagnets superimposed to form a spherical workspace with a diameter of approx. 10 mm. The device can produce varying and rotating fields up with an amplitude up to 20 mT for manipulation of the MNPs. For this research an 8 µl sample of dextran coated Fe_3O_4 MNPs (nanomag®-D, Micromod Partikeltechnologie, Germany) with diameter of 500 nm are used. The MNP sample is injected at the tip of the cochlea phantom prefilled with distilled water with a help of a syringe. Figure 1 shows the cochlea phantom with the MNPs with different time stamps showing the actuation of the MNPs inside the cochlea phantom at different positions. For actuating the MNPs inside the phantom, a homogeneous magnetic field of 15 mT was rotated with a frequency of 5 Hz. Due to the curved structure of the cochlear, the rotation axis was changed manually during the experiment to actuate the MNPs inside the cochlea's canal from the injection point at the round window towards the apex. This demonstrates the actuation of MNPs inside the cochlea which may enable localized drug delivery with MNPs as vehicles.

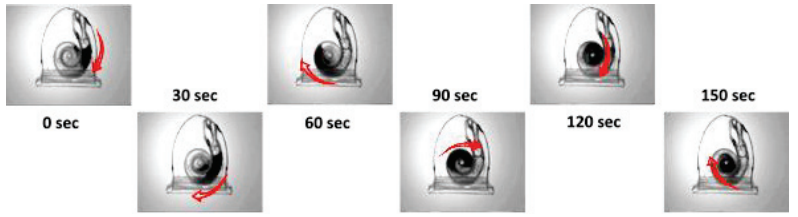

Figure 1 shows the actuation of the MNPs inside the cochlea phantom. The red arrows points to the direction of the MNPs inside the canals.

Reference: [1] Leon et al. Scala-Tympani Phantom With Cochleostomy and Round-Window Openings for Cochlear-Implant Insertion Experiments *J. Med. Devices*. Dec 2014, 8(4): 041010, https://doi.org/10.1115/1.4027617

Enhancing Protein Corona Formation on Bacterial Magnetosomes by Genetic Engineering

Simon Markert[1], Cornelia Jörke[2], Joachim H. Clement[2], Frank Mickoleit[1], Dirk Schüler[1]
[1]Dept. Microbiology, University of Bayreuth, D-95447 Bayreuth, Germany
[2]Dept. Hematology and Medical Oncology, Jena University Hospital, D-07747 Jena, Germany

Magnetic nanoparticles are of increasing importance for many applications in the (bio)medical field, for instance as agents for magnetic hyperthermia or imaging techniques [1]. A promising alternative to chemically synthesized nanoparticles are magnetosomes biomineralized by magnetotactic bacteria. In the alphaproteobacterium *Magnetospirillum gryphiswaldense* they consist of a monocrystalline magnetite core enveloped by a biological membrane consisting of phospholipids and a set of magnetosome-specific proteins. Due to their strictly genetically regulated biosynthesis, magnetosomes exhibit characteristics that can hardly be achieved by chemical synthesis, and are accessible to genetic engineering techniques that enable surface functionalization [2].

Utilizing abundant magnetosome proteins as anchors, we explored the display of artificial peptides on the magnetosome membrane to increase the particles' biocompatibility and to shield potentially toxic bacterial components. For this purpose, multiple arrays of the tripeptides GSA and PAS and a Protein G - derived domain capable of binding Albumin were expressed as fusions to the magnetosome membrane protein MamC. Upon incubation with serum proteins, protein corona formation was observed, which was up to ten-fold higher compared to the wildtype as determined by ELISA and electron microscopy. The genetic introduction of a TEV protease cleavage site enabled the controlled removal of both the proteins expressed on the magnetosome surface as well as the adsorbed corona. The peptide array decorated magnetosomes were shown to be biocompatible when incubated with mammalian cells. Moreover, cell viability was kept stable upon prolonged incubation when enveloped by a protein corona, and the particles' endotoxicity could be sufficiently shielded.

Thus, genetic engineering might not only provide a powerful tool to modify the magnetosome surface properties, but also to improve the biocompatibility for future *in vivo* applications.

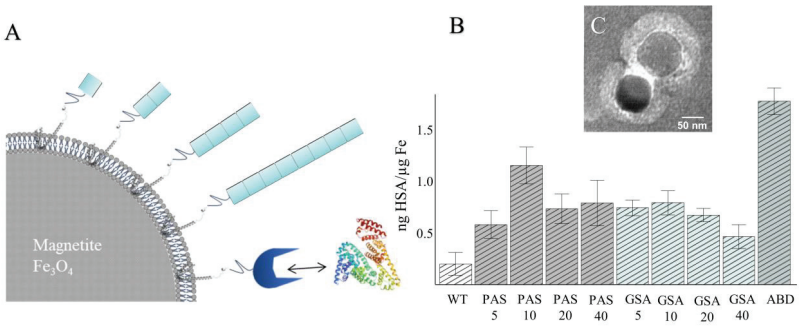

Figure - (A) Display of 5-40 modules of the tripeptide PAS/GSA and an Albumin-binding domain (ABD). (B) ELISA to determine the amount of HSA adsorbed to the modified magnetosomes. (C) TEM micrograph of magnetosomes with an assembled HSA protein corona

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Heating efficiency study of amino acid coated iron oxide nanoparticles

Martina Kubovčíková[1*], Ilona Smolková[2], Iryna Antal[1], Alena Juríková[1], Iryna Khmara[1], Natalia Kazantseva[2,3], Martina Koneracká[1], Jarmila Vilčáková[2,3] and Vlasta Závišová[1]

[1] Institute of experimental Physics Slovak Academy of Sciences, Watsonova 47, Kosice, Slovakia
[2] Centre of Polymer Systems, University Institute, Tomas Bata University in Zlín, Zlín, Czech Republic
[3] Faculty of technology, Tomas Bata University in Zlín, Zlín, Czech Republic
*Email: kubovcikova@saske.sk

Magnetic nanoparticles possess a variety of interesting physical and chemical properties, which offer opportunities for their use in different applications. Iron oxide magnetic nanoparticles (IONPs) are widely studied for their potential use in biological or medical application. Among them, magnetic fluid hyperthermia seems to be a perspective and advantageous way for cancer treatment. Magnetic fluid hyperthermia is using the ability of IONPs to generate heat under the applied alternating magnetic field. The efficiency of the hyperthermic treatment is affected among others by the surface chemistry of nanoparticles and their heating properties.

In this study, electrostatically stabilized iron oxide nanoparticles (MNPs) were synthetized and subsequently modified by amino acids cysteine (Cys) and proline (Pro) and by a poly amino acid poly-L-lysine (PLL) to enhance their biocompatibility. The prepared samples were labelled as Cys-MNPs, Pro-MNPs and PLL-MNPs and were characterized in terms of size distribution, zeta potential and magnetic properties. The hydrodynamic diameter determined by Dynamic Light Scattering method was 32, 67, 35 and 46 nm for MNPs, Cys-, Pro- and PLL-MNPs, respectively. All of the studied nanoparticles samples are positively charged with the zeta potential values ranging from 30 mV for unmodified MNPs to 48 mV for PLL-MNPs. Then the heating efficiencies of the nanoparticles suspensions in water and agarose gel were measured at 1049 kHz, 7.4 mT and from the heating rates the specific loss power values (SLP) were evaluated. The obtained SLP values (presented in Table below) are encouraging for further study and potential use in hyperthermia.

Sample	Heating rate (°C/min)	SLP (W/g)
MNPs	87.5 ± 0.3	308.1 ± 1.1
Cys-MNPs	7.1 ± 0.3	183.6 ± 6.8
Pro-MNPs	16.0 ± 0.3	281.6 ± 5.4
PLL-MNPs	14.2 ± 0.9	242.5 ± 14.2

This work was supported by the Slovak Research and Development Agency under the contract no. APVV-DS-FR-22-0037; Slovak Grant Agency VEGA 02/0049/23; the Operational Program Integrated Infrastructure funded by the ERDF ITMS2014+: ITMS 313011T533 (DIAGNAD). This work was also supported by the Ministry of Education, Youth and Sports of the Czech Republic (MSMT No. 8X23084) and DKRVO-(RP/CPS/2023/005).

Traffic light-based point-of-care test for the rapid stratification of fever syndromes

M. Mesas[3,4], A. del Valle[3,4], M. Martí[4], A. Pallarès-Rusiñol[2], J. Ferrer-Dalmau[2], B. Baró[1], Q. Bassat[1], M.I. Pividori[3,4*]

[1]ISGlobal, Barcelona Institute for Global Health, Hospital Clínic, Universitat de Barcelona
[2] BioEclosion SL, Avda. Can Domènech, Edifici Eureka, Campus de la Universitat Autònoma de Barcelona
[3]Grup de Sensors i Biosensors, Departament de Química, Universitat Autònoma de Barcelona, Bellaterra, 08193, Spain
[4]Biosensing and Bioanalysis Group, Institute of Biotechnology and Biomedicine, Universitat Autònoma de Barcelona, Bellaterra, 08193, Spain
[*]Email: isabel.pividori@uab.cat

Recent evidence highlights the significance of sTREM-1 and Ang-2 as quantitative novel biomarkers for assessing disease severity, treatment response, and outcomes in various conditions, including malaria, pneumonia, COVID-19, among others fever syndromes. Elevated sTREM-1 levels have shown strong correlations with disease severity, multiple organ dysfunction, and mortality. To aid in risk stratification, patients in this study were classified into three groups based on their sTREM-1 levels using the WHO-proposed traffic light color system.

A threshold value of 239 pg/mL represented the "green light," indicating low risk, while levels exceeding 629 pg/mL were designated as "red light," signifying an urgent need for admission. An intermediate "yellow light" indicated further monitoring. In this work, we present a rapid test integrating magnetic separation and electrochemical biosensing on a portable device operated by batteries. The laboratory prototype comprises two components: (1) a disposable cartridge containing magnetic particles conjugated with antibodies specific to the biomarker of interest, and (2) a digital reader equipped with an interface for quantitative electrochemical readout. The cartridge's microfluidic system facilitates magnetic actuation, while excess sample and reagents are removed. Within less than one minute, the digital reader provides quantitative readout of the biomarker levels in pg/mL, which is then displayed on the device's screen and transmitted to the accompanying App via Bluetooth.

The device's performance in classifying sTREM-1 levels is presented, demonstrating excellent readout results with a short 15-minute incubation step and a swift 2-minute readout process. This innovative point-of-care test holds great promise for aiding clinicians in rapid risk stratification and timely decision-making, potentially enhancing child survival outcomes and improving patient management in a variety of fever syndromes and specific diseases.

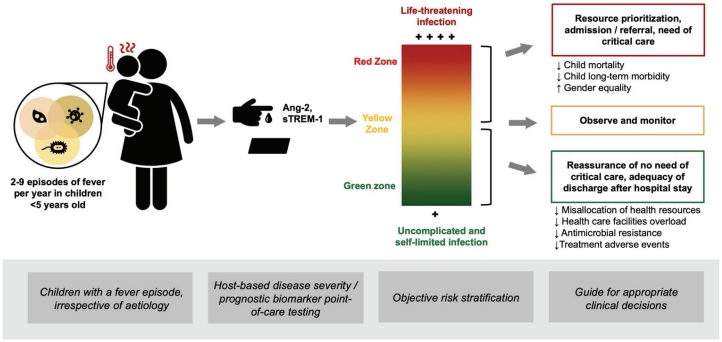

Figure 1: Conceptual framework for a Rapid Triage Test based on the point of care device for sTREM1 to risk-stratify fever.

Long-term-stability and biocompatibility of bacterial magnetosomes from *Magnetospirillum gryphiswaldense*

Frank Mickoleit[1]*, Cornelia Jörke[2], Reinhard Richter[3], Sabine Rosenfeldt[4,5], Simon Markert[1], Jula Tropschug[2], Anna Schenk[4,6], Dirk Schüler[1], and Joachim H. Clement[2]

[1]Dept. Microbiology, University of Bayreuth, D-95447 Bayreuth, Germany
[2]Dept. Hematology and Medical Oncology, Jena University Hospital, D-07747 Jena, Germany
[3]Dept. Experimental Physics V, University of Bayreuth, D-95447 Bayreuth, Germany
[4]Bavarian Polymer Institute (BPI), University of Bayreuth, D-95447 Bayreuth, Germany
[5]Physical Chemistry I, University of Bayreuth, D-95447 Bayreuth, Germany
[6]Physical Chemistry IV, University of Bayreuth, D-95447 Bayreuth, Germany

Email: frank.mickoleit@uni-bayreuth.de

Introduction Bacterial magnetosomes are promising tools for biomedical applications in diagnostics and therapy. In the model organism *Magnetospirillum gryphiswaldense*, they consist of a cuboctahedral magnetite core surrounded by a biological membrane. An important quality parameter for future applications is biocompatibility and long-term stability.
Objective We investigated the colloidal stability of isolated particles, their magnetic properties, the integrity of the magnetosome membrane, as well as potential cytotoxic effects when applied to human cell lines.
Methods Magnetosomes were isolated from bacteria by magnetic separation techniques. The particles were resuspended in 10 mM HEPES with 1 mM EDTA, pH 7.2, and stored under a nitrogen atmosphere at 4°C. The iron concentration was determined by atomic absorption spectroscopy. Physico-chemical characterization was performed by dynamic light scattering, vibrating sample magnetometry and transmission electron microscopy. Biocompatibility of magnetosomes was evaluated on the cell lines FaDu (hypopharynx carcinoma) and HCC78 (lung adenocarcinoma) using the PrestoBlue cell viability assay and the SYTOX assay.
Results Aliquots of purified magnetosomes were analyzed monthly over a period of one year. The size distribution, morphology and colloidal stability remained constant (overall particle diameter: month 1: 40.2 ± 5.7 nm; month 12: 39.6 ± 5.1 nm; zeta-potential: month 1: -35.8 ± 3.4 mV; month 12: -35.7 ± 3.7 mV). The saturation magnetization dropped to one-third of its initial value, which might be due to oxidation effects; however, the particles could still be efficiently attracted by magnetic fields. Magnetosomes exhibited a concentration-dependent effect on cell viability. For the FaDu and HCC78 cell lines average viability values of 73 (67-91; month 12: 67)% (FaDu) and 73 (36-90; month 12: 58)% (HCC78) were determined for 50 µg Fe cm^{-2} and 48 h of incubation.
Conclusion Our investigations demonstrate that magnetosomes can be safely stored for at least one year as an aqueous suspension without significant quality deficits.

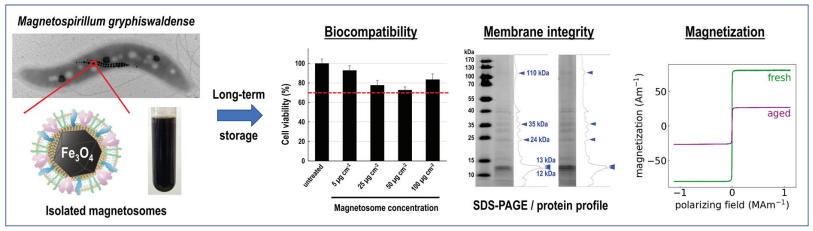

Figure - The stability of isolated magnetosomes upon long-term storage is examined with regard to their biocompatibility, as well as different physico-chemical parameters such as membrane integrity and saturation magnetization.

New protocol for observing adherence of magnetic particles and nanowires on cell surfaces using scanning electron microscopy imaging

Anca Emanuela Minuti[1*], Cristina Stavila[1,2], Horia Chiriac[1], Nicoleta Lupu[1]

1. Magnetic Materials and Devices, National Institute of Research and Development for Technical Physics, Iasi, Romania.
2. Faculty of Physics, "Alexandru Ioan Cuza" University, Iasi, Romania.
Email: aminuti@phys-iasi.ro

When studying the interaction between cells and nanomaterials, it is essential to image the effects of the material on the cell membrane. High Resolution Scanning Electron Microscopy (HR-SEM) is an effective method for evaluating the results of this interaction process as opposed to just imaging them using a conventional inverted microscope. When using magnetic particles (MNP) or nanowires (NWs) for cancer targeting, it is crucial to assess the presence and distribution of the magnetic material in relation to the targeted cells. Magnetic particle-mediated cancer treatment can be achieved through magnetic hyperthermia or magneto-mechanical actuation [1, 2]. However, to ensure the success of these methods, we need to obtain reliable images of the cell-nanoparticle interaction to determine if a sufficient quantity adhered to the cell surface as well as their distribution on the cell membrane.

This protocol outlines a simplified and effective method for preparing cell-based biological samples to observe nanomaterial surface adherence using SEM. For this new protocol we used silicon wafers as a substrate to grow cells, followed by the addition of the evaluated nanomaterial to the cell culture media for at least 24 hours of incubation. Next, the samples were washed to remove any non-adhered nanomaterials, and then fixed with glutaraldehyde and osmium tetroxide. The silicon wafers were dehydrated using increasing concentrations of alcohol and air-dried in the biological safety hood and vacuum, followed by a coat with a 5 nm gold sputtered film. Finally, the samples were imaged using a scanning electron microscope. For this purpose, we used different types of cells, i.e. normal dermal fibroblasts (NHDF), human osteosarcoma cells (HOS) and adipose-derived mesenchymal stem cells (ADSC) loaded with magnetite nanoparticles or Co-Fe nanowires. One of the advantages of using this new method is the replacement of difficult steps such as critical point drying of the samples to make the method quicker and easier to perform. Using SEM imaging obtained by this protocol, we can estimate nanomaterial interaction with the cell surface. For example, in Fig. 1 (a, b, e, f) MNPs are concentrated on the ADSC cell membrane, but avoiding the area with the nucleus while for Fig. 1 (c, d) the MNP are equally dispersed. For the observation of NWs, using HR-SEM, we can observe that for some samples (Fig 1, g, h), the NWs can spear the cell membrane, phenomenon not visible on the inverted microscope, while for others, the NWs just adhere to the cell membrane surface (Fig. 1, i-l) without affecting them in any way.

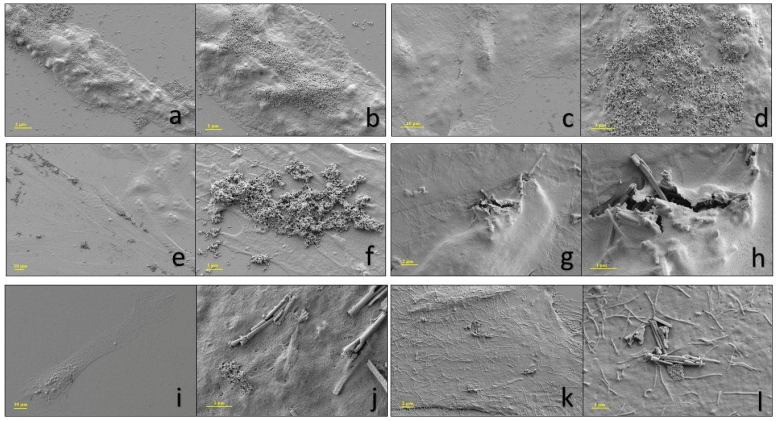

Figure. HR-SEM images of cells with nanomaterials. (a, b) ADSC with MNP on the surface, (c, d) ADSC with NWs, (e, f) NHDF with MNP, (g, h) NHDF with NWs, (i, j) ADSC with NWs, (k, l) HOS with NWs. Scale bar = 1 µm (b, d, f, h, j, l); Scale bar = 2 µm (a, g, k); Scale bar = 10 µm (c, e, i).

Financial support from the MCID Nucleu (PN 23 11 01 01) and PFE (Contract No. 5PFE/2022) Programs is highly acknowledged.

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Design, Fabrication, and Biological Evaluation of Polyphenol Loaded Smart Magnetic Nanocarriers for Targeted Breast Cancer Therapy

Mohammed Sahinsha Mohammed Mustafa, Krishnanand Nagarajan, Selvamani Palanisamy*, Latha Subbiah

Department of Pharmaceutical Technology and Centre for Excellence in Nanobio Translational Research, University College of Engineering, Bharathidasan Institute of Technology Campus, Anna University, Tiruchirappalli – 620 024, Tamil Nadu, India
***Email:** selvamani@aubit.edu.in **Mobile:** +91 98424 78785

In recent years, the utilization of nanoliposomes (NLPs) has revolutionized targeted drug delivery systems for cancer treatment. This study focuses into the synthesis and characterization of rutin-loaded CA-Fe_3O_4 magnetic liposomes, alongside their counterparts: blank liposomes (S1), CA-Fe_3O_4 nanoparticles (S2), and rutin loaded CA-Fe_3O_4 nanoliposomes (S3). Extensive characterization employing UV-Visible, FT-IR spectroscopy, zeta potential, EDAX, and electron microscopy (FE-SEM and HR-TEM) was conducted to elucidate their structural properties. Biological activity was further assessed through MTT assay, apoptosis via FACS analysis, scratch assay, and antiangiogenic activity through an *In-Ovo* CAM assay.

UV spectroscopic analysis revealed surface plasma resonance of the nanoparticles within the 200-800 nm range, while FT-IR analysis demonstrated the bonding of rutin molecules onto the nanoparticles. Zeta potential and size analyses indicated electric behaviour indicators, with S1 exhibiting -27.1 mV, S2 at -2.56 mV, and S3 at -30.2 mV, accompanied by corresponding size values of S1=209.2 nm, S2=89.59nm, and S3=209.2nm. Additionally, EDAX analysis detected Fe, C, H, O, P, and N presence in S1, S2, and S3, further supported by FE-SEM and HR-TEM, confirming the surface morphology and size of the magnetic liposomes. The saturation magnetization of the S3 nanoliposomes was estimated as 0.3 emu/g through VSM analysis.

The MTT assay demonstrated significant antitumor activity against the human breast cancer MCF-7 cell line, with IC_{50} values of 125 µM, 62.5 µM, and 15.625 µM for S1, S2, and S3, respectively. Fluorescent staining and flow cytometry elucidated cell viability and apoptosis, particularly noting S3's late apoptosis rate of 63.96%. Moreover, wound healing assays indicated accelerated restoration in the S3 group, while the chorioallantoic membrane assay (CAM) highlighted the potential impairments in angiogenesis after prolonged exposure to S3.

These comprehensive findings shed light on the composition, stability, and biological interactions of the formulated nanoparticles, emphasizing their potential biomedical applications. Moreover, the precise modulation of structural properties in S3 indicates promising prospects for targeted therapy and diagnostics, highlighting the significance of this research for future advancements in biomedicine. Leveraging liposome-based nanoparticle approaches has emerged as a leading strategy to achieve improved solubility, bioavailability, stability, and controlled delivery of therapeutic agents like rutin. The demonstrated antitumor efficacy of our formulated rutin-loaded CA- Fe_3O_4 magnetic liposomes underscores their potential as a promising carrier system for future cancer therapy applications.

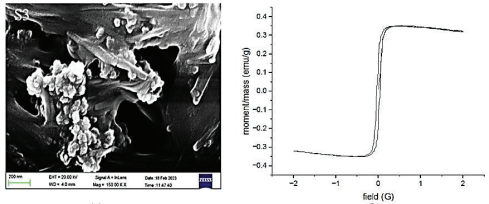


Figure : (a) FE-SEM analysis of S3 magnetic liposome; (b) VSM graph illustrating the S3 formulation data

Simultaneous therapeutic and diagnostic applications of magnetic PLGA nanoparticles loaded with doxorubicin in rabbit

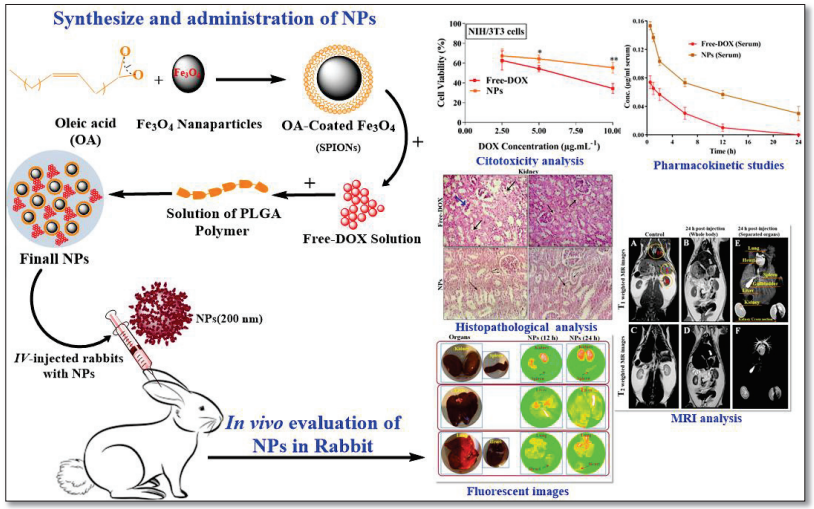
Jafar Mosafer[1]*, Hossein kamali[2], Frarhad Eisvand[2]

[1] Research Center of Advanced Technologies in Medicine, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

[2] Department of Pharmaceutics, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

*E-mail addresses: Mosafrj901@gmail.com (J. Mosafer).

In this study, doxorubicin (DOX) and superparamagnetic iron oxide nanocrystals (SPIONs) were encapsulated into the poly (lactide-co-glycolide)-b-poly(ethylene glycol) (PLGA-PEG) nanoparticles for theranostic purposes. The final prepared formulation which is called nanoparticles (NPs) exhibited a particle size with a mean diameter of ~209 nm and a sufficient saturation magnetization value of 1.65 emu/g. The NPs showed faster DOX release at pH 5.5 compared to pH 7.4. Also, the cytotoxicity effect of NPs increased compared to Free-DOX alone in C6 glioma cancer cells. For *in vivo* investigations, the 2.2 Kg rabbits were injected with NPs formulations via a central articular anterior vein in their ears. Furthermore, the images of rabbit organs were depicted via magnetic resonance (MR) and fluorescent imaging techniques. A negative contrast (dark signal) was observed in T_2 weighted MR images of intravenously *(IV)* -injected rabbits with NPs compared to the control ones. The organ's florescent images of NPs-injected rabbits showed a high density of red color related to the accumulation of DOX in liver and kidney organs. These data showed that the NPs have no cytotoxicity effect on the heart. Also, the results of histopathological tests of different organs showed that the groups receiving NPs and Free-DOX were almost similar and no significant difference was seen, except for the cardiac tissue in which the pathological effects of NPs were significantly less than the Free-DOX. Additionally, pharmacokinetic studies were also conducted at the sera and whole bloods of *IV*-injected rabbits with NPs and Free-DOX. The pharmacokinetic parameters showed that NPs could enhance the DOX retention in the serum compared to the Free-DOX. Altogether, we aimed to produce a powerful delivery nanosystem for its potential in dual therapeutic and diagnostic applications which are called theranostic agents.



OPTIMIZING MAGNETIC NANOPARTICLE HEATING IN TUMOR PHANTOMS USING ROTATING MAGNETIC FIELDS

Jakub Musiał[1]*, Artur Jędrzak[2] Rafał Bielas[1], Andrzej Skumiel[1]

[1]Chair of Acoustics, Faculty of Physics, Adam Mickiewicz University in Poznań
Uniwersytetu Poznańskiego 2, 61-614 Poznań, Poland
[2]NanoBioMedical Centre, Adam Mickiewicz University in Poznań,
Wszechnicy Piastowskiej 3, 61-614 Poznań, Poland
*e-mail: jakub.musial@amu.edu.pl

Despite the well-known potential of magnetic hyperthermia as a cancer treatment adjunct, inconsistent data on nanoparticle heating behavior has impeded its widespread clinical adoption. For instance, theoretical studies propose that rotating magnetic fields (RMFs) offer enhanced thermal effects compared to traditional alternating magnetic fields (AMFs) [1].

In this work, iron oxide nanoparticles, both uncoated and coated (with polydopamine), were synthesized in water at maximum stable concentrations. These nanoparticles, with sizes ranging from 8 to 10 nm, were employed to explore the monodomain regime, where Néel relaxation dominates over Brownian relaxation. Agar-based hydrogel phantoms, prepared using the magnetic fluids, served as tissue-mimicking tumor models. Dynamic viscosities of magnetic suspensions were measured to predict theoretical relaxation times as nanoparticle heating mechanisms are influenced by medium viscosity.

Heating efficiency was assessed using a patented two-phase RMF system (1-6 kA/m, 50-200 kHz), with AMF mode serving as a comparative benchmark [2,3]. Relaxational and hysteretic heat losses were analytically evaluated. Alignment of the RMF frequency with magnetic nanoparticle relaxation times according to the Raikher model, enabled optimizing the specific absorption rate (SAR) [1].

This could contribute to our understanding of tunable magnetic nanoparticle heating, with implications for optimizing clinical magnetic hyperthermia.

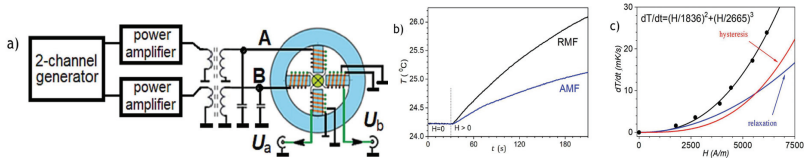


Fig. 1 (a) Schematic diagram of the RMF generator using a 2-phase system powered by sinusoidal signals.
(b) Comparison of the heating efficiency of RMF vs AMF in a ferrogel sample.
(c) Contribution of relaxation and hysteresis to thermal energy release with magnetic field variations.

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Real-Time Image-Guided Magnetic Theranostic System for Targeted Cancer Therapy via 5-Fluorouracil-Loaded Nanoliposomes

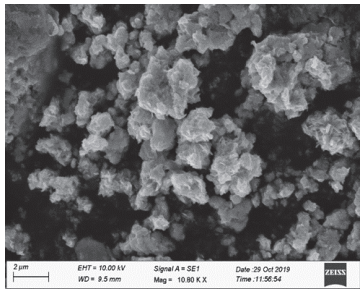
Krishnanand Nagarajan, Latha Subbiah, Madhumethra Ramasamy Govindaraj and Selvamani Palanisamy*

Department of Pharmaceutical Technology and Centre for Excellence in Nanobio Translational Research, University College of Engineering, Bharathidasan Institute of Technology Campus, Anna University, Tiruchirappalli – 620024, Tamil Nadu, India

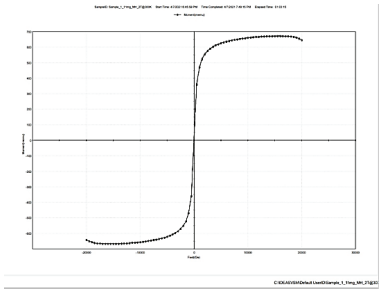
*Email: selvamani@aubit.edu.in Mobile: +91-98424 78785

Theranostics is an emerging field harnessing efficient therapeutics delivered precisely to target sites through multimodal imaging. Nano-sized drug delivery systems, particularly magnetic nanoparticles, offers promising approach for cancer theranostics, allowing for diagnostic and therapeutic capabilities simultaneously. In the present research, 5-fluorouracil (5-FU) and Indocyanine green were loaded into magnetic liposomes with the addition of iRGD peptide, a cyclic cell-penetrating peptide that enhances tumor targeting. Indocyanine green, with its near-infrared properties, serves as a clinically utilized MRI-contrast agent, while superparamagnetic iron oxide nanoparticles offer control over drug release and therapeutic efficacy through external magnetic fields. The developed nano liposomal formulation underwent comprehensive physicochemical and biological characterization, including in-vitro drug release studies, analysis of magnetic behavior, and cytotoxicity assessments.

Nanoliposomes ranging from 10 nm to 100 nm were formulated, demonstrating good stability and physicochemical properties suitable for drug delivery. In-vitro studies confirmed the sustained release of 5-FU from nanoliposomes, following zero-order release kinetics. Cytotoxicity assays on A549 lung cancer cells and Vero cells, exhibited significant growth inhibition, with IC_{50} values of 130 µg/mL-1 and 123 µg/mL-1 respectively. Furthermore, both free 5-FU and iRGD-ICG-5-FU-MNLs was found to induce apoptosis in A549 cells, suggesting their potential as targeted anticancer agents. Overall, this study underscores the potential of magnetic nanoparticle-based theranostics for precise cancer treatment, integrating imaging, targeted therapy, and controlled drug delivery within a single nanoplatform.



(a)



(b)

Figure: (a) The morphology of the iRGD-ICG-5-FU-MNLs was examined using a Scanning Electron Microscope. (b) The saturation magnetization of the magnetic nanoparticles was found to be 700 emu/g.

In vitro Evaluation of F127@magnetite on Glioblastoma Cell Lines

Mirela Nistor[1,2], Paula Alexandra Postu[1], Aurel Pui[2], Vera Balan[1,3], Rares-Ionut Stiufiuc[1,4] Brindusa Dragoi[1,2*]

[1]*Nanotechnology Laboratory, TRANSCEND Research Center, Regional Institute of Oncology, 2-4 General Henri Mathias Berthelot Street, 700483 Iași, Romania*
[2]*Faculty of Chemistry, Alexandru Ioan Cuza University of Iași, 11 Carol I Boulevard, 700506 Iași, Romania*
[3] *Biomedical Sciences Department, Faculty of Medical Bioengineering, Grigore T. Popa University of Medicine and Pharmacy of Iasi, 9-13 Kogalniceanu Street, 700454 Iasi, Romania*
[4]*Department of Nanobiophysics, MedFuture Research Center for Advanced Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy, 4-6 Pasteur Street, 400337 Cluj-Napoca, Romania*
*Email: brindusa.dragoi@yahoo.com

Glioblastoma (GBM) represents a heterogeneous group of central nervous system tumors associated with high morbidity and mortality[1]. The current standard protocol involving maximal resection followed by radiotherapy and/or chemotherapy has low efficiency with 90% recurrence within two years of the initial diagnosis[2]. In this unfavourable context, magnetic nanoparticles (MNPs) hold promises for therapy and imaging of such aggressive cancer. Due to their unique physico-chemical properties, biocompatibility and susceptibly to be manipulated by external magnetic fields, MNPs became popular among the studied drug carriers in recent years. Herein, the safety profile of drug-free magnetite coated with Pluronic F127, an FDA-approved biocompatible block copolymer, has been investigated in several GBM cell lines. The selection of the surfactant was justified by the ability to bypass the blood-brain barrier, as well[3].

Fe_3O_4 MNPs were successfully synthesized via the coprecipitation method using Pluronic F127 as dispersant and $FeCl_2$ and $FeCl_3$ (2:1, molar ratio) as metal precursors. Since the biological effect is intimately related to the physico-chemical properties of the MNPs, the sample was deeply characterized through different techniques, as follows. XRD results showed the formation of cubic spinel structure (Fd-3m space group type) with crystallite size of 9.89 nm. FT-IR and Raman spectroscopies provided molecular information about the structure and composition of F127@Fe_3O_4 based on the typical bonds' vibrations. TEM images displayed quasi-spherical particles of 25 nm, a good dispersion and negatively charged according to Zeta potential measurements (-24 mV). The VSM measurements confirmed the superparamagnetic proprieties of the MNPs (58 emu/g).

The cytotoxic profile of F127@Fe_3O_4 has been assessed on three GBM cell lines (A172, U118 and T98G), which exhibit different genetic alterations and morphologies. A172 and U118 cells were grown in DMEM media, while T98G cells were grown in Advanced MEM medium, all supplemented with 10% FBS and 1% PS. The cells were allowed to attach for 24 h and they were further exposed to F127@Fe_3O_4 (3 and 90 µg/ml) for different intervals of times (24 → 72 h). The growth rate of GBM cells has been monitored using CellTiter blue™ assay. The synthesized F127@Fe_3O_4 determined only minor variations of the growth rate of GBM cells in the range of 10 – 30 µg/mL MNPs evaluated in this study. Therefore, F127@Fe_3O_4 could be safely used for diagnosis and therapy of several types of resistant GBM tumors.

Acknowledgments: H2020–ERA-Chair, no 952390 and PN-III-P3-3.6-H2020-2020-0105/35/2021 (UEFISCDI).

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Role of Depletant in Binary Mixtures of Shape-Anisotropic Magnetic Particles

Margaret Rosenberg[1], Ekaterina Novak[2*], Elena Pyanzina[2], and Sofia Kantorovich[1]

[1] Faculty of Physics, University of Vienna, Bolzmanngasse 5, Vienna 1090, Austria.
[2] Institute of Natural Sciences and Mathematics, Ural Federal University, Ekaterinburg, 620000, Russia.
*Email: ekaterina.novak@urfu.ru.

Binary colloidal mixtures exhibit characteristic structural and phase behaviour, particularly when the components vary in size or interact selectively. The addition of a second component can elicit behaviour that is not inherent to the individual components, rendering mixing a potent tool for finely adjusting colloid properties.

Adding non-magnetic particles to a dispersion of magnetic soft (or hard) spheres is known to stimulate the phase separation of the system. Our aim is to investigate whether a similar effect occurs in binary mixtures of magnetic shape-anisotropic particles. In this work, we specifically undertake a theoretical and computational investigation of systems containing either ellipsoids [1-3] or platelets [4-6]. We consider platelets and ellipsoids as the two simplest deviations from a spherical shape, with the magnetic moment oriented along the short axis for platelets and along the long axis for ellipsoids. Our investigation goes beyond merely examining the influence of the nonmagnetic phase on self-assembly. It also delves into the impact of colloidal shape on system behaviour. We examine the microstructure to determine whether the inclusion of depletants results in quantitative or qualitative alterations in the radial distribution functions, structure factors, orientational correlations, bond order parameters, and static magnetic susceptibility. Our findings reveal a nuanced interplay between particle shape, the ratio of magnetic to nonmagnetic phases, and self-assembly scenarios. Analytical theory is employed to clarify how colloidal shape influences both the bonding volume and entropy gain of the depletant through the clustering of the magnetic component. This comprehensive investigation provides insights into the intricate behaviour of binary nanocolloidal systems and their potential for controlled tuning of colloidal properties.

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Scalable formulation of magnetic particle imaging tracers via flash nanoprecipitation

Aniela Nozka[1], Eric D. Imhoff[1], Ambar Velasquez-Albino[1], Andrii Melnyk[1], Carlos M. Rinaldi-Ramos[1,2*]

[1]Department of Chemical Engineering, University of Florida, Gainesville, FL, United States
[2]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, U.S.
*email: carlos.rinaldi@ufl.edu

Magnetic particle imaging (MPI) is a novel imaging modality through which an applied alternating magnetic field can sweep the subject and detect the presence of magnetic particles. The output of this imaging modality is a gradient map correlating to the spatial distribution of the concentration of the magnetic particles. Using magnetic particle tracers *in vivo* allows for tracking of drug delivery, anti-cancer vaccines, blood profusion imaging, and more with no signal attenuation due to tissue and without the use of ionizing radiation. On their own, iron oxide nanoparticles (IONPs) are not colloidally stable in aqueous phases, therefore, the addition of a hydrophilic shell is needed to transfer them to aqueous phase or biological media. Current methods focus on ligand exchange, however they are typically timely and not easily scalable. Flash nanoprecipitation (FNP) prepares magnetic composite nanocarriers (MCNCs) that kinetically trap hydrophobic components inside a block copolymer shell that is stable in the aqueous phase. Size is controlled through several formulation parameters. Drugs, particles, and other hydrophobic constituents can be stabilized in the core. Minimal work has been done to utilize FNP for the coating of hydrophobic IONPs. Previous work prepared FNP formulations with the inclusion of inorganic nanoparticles, however, little attention was given to the potential of these for MPI tracers, as very little MPI characterization was reported. Others studied FNP formulation parameters' effect on size and polydispersity of particles without the inclusion of inorganic nanoparticles, focusing on changing the percent core of the formulations and the total solids concentration. Herein, we demonstrate the formulation of magnetic composite nanocarriers characterized for use as MPI tracers. Size was recorded via dynamic light scattering and MPI characterization was done in both RELAX and 2D scan modes. Size was controlled between 100-300 nm by varying FNP conditions. MPI RELAX scan measurements indicate that maximum signals of about 77 $mgFe^{-1}$ can be obtained, with FWHM of 12 mT, indicating that MCNCs formulated using FNP are suitable for use as MPI tracers.

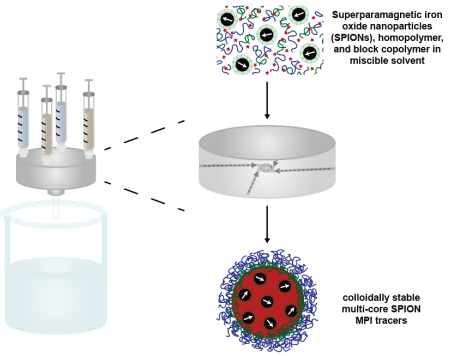

Figure 1. Formulation of MCNCs through flash nanoprecipitation using a multi-inlet vortex mixer (MIVM) allows for coating of multi core particles.

Unveiling the impact of the chemical composition of ternary ferrites on specific loss power

Miloš Ognjanović[1*], Marija Mirković[1], Magdalena Radović[1], Sanja Vranješ-Đurić[1] and Bratislav Antić[1]

[1]University of Belgrade, VINČA Institute of Nuclear Sciences-National Institute of the Republic of Serbia, Belgrade, Serbia,
*Email: miloso@vin.bg.ac.rs Mobile:381-63-855-9886

Magnetic nanoparticles (MNPs) have been intensively investigated for their application in the therapy and diagnosis primarily of malignant diseases. In the last decade, significant research has been conducted to investigate the effectiveness of combined therapy (CT) for malignant diseases using MNPs. Our research focuses on designing a nanoplatform for combined magnetic hyperthermia and radio-nuclide therapy. We used a polyol technique to prepare binary and ternary ferrite samples. The starting components are mixed in an appropriate stoichiometric ratio to obtain samples with a nominal composition of $(Zn_xMn_{1-x})Fe_2O_4$, (x = 0-1). ICP-OES analysis reveals a significant deviation from the nominal composition, indicating the potential formation of samples with polyvalent ions, $Mn^{2+/3+}$ and $Fe^{2+/3+}$, as well as a possible deviation from stoichiometry with the presence of vacancies. Using the polyol synthesis method, multicore nanoflower-like nanoparticles were obtained (*Figure 1a*). The flower-like morphology is preserved by changing the chemical composition of the particles, so the specific properties of nanoparticles in the series mostly depend on the type and arrangement of ions at cationic sites in the crystal lattice but not on the agglomeration of crystallites in the form of nanoflowers. Nanoparticles with multicore structures resembling a flower range from 47 nm to 63 nm and crystallite sizes between 9 nm and 11 nm. It was found that iron ions within magnetite (Fe_3O_4) were partially substituted, with up to 27 at. % by zinc or manganese individually, and up to 22 at. % by both zinc and manganese. The samples are superparamagnetic at room temperature, with a saturation magnetization value ranging from 59 emu/g to 73 emu/g.

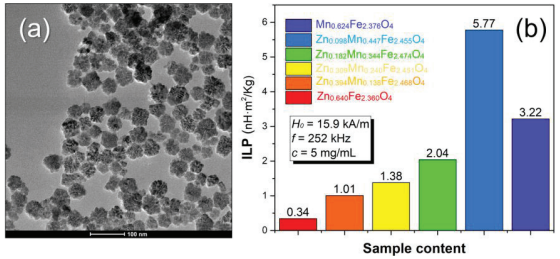

Figure 1. (a) TEM micrograph of the $Zn_{0.098}Mn_{0.447}Fe_{2.455}O_4$; (b) Intrinsic loss power of $Zn_xMn_yFe_{3-x+y}O_4$.

The highest heating efficiency had a sample with composition $Zn_{0.098}Mn_{0.447}Fe_{2.455}O_4$ (*ILP* was 5.77 nHm²/kg), *Figure 1b*. Using synchrotron-based high-energy X-ray powder diffraction data and PDF analysis, there are indications of local distortion at octahedral sites in the spinel crystal structure that increases with the concentration of manganese ions. Detailed structural and microstructural analysis of synthesized nanoparticles is underway. The obtained results show that it is possible to alter the physical, chemical, and colloidal properties by changing the chemical composition. This enables adjusting the efficiency of heat generation by nanoparticles when used as heat generators in magnetic hyperthermia and as carriers of radionuclides in cancer radio-nuclide therapy. Radiolabeling of the samples is our work in progress.

Acknowledgment

The research was financially supported by the Science Fund of the Republic of Serbia, Program PRISMA, Grant No. 4961, *Design of radioactive magnetic nanoconstructs for tumour therapy by synergy of nanobrachytherapy and magnetic hyperthermia* - RADIOMAG. We thank Dr. Emil Bozin for conducting synchrotron measurements at Argonne National Laboratory.

Evaluation of in vivo magnetization dynamics of magnetic nanoparticles in living tumor

Satoshi Ota [1,*], Hiroki Kosaka [2], Keita Honda [2], Kota Hoshino [2], Haruki Goto [3], Masato Futagawa [1], Yasushi Takemura [4], and Kosuke Shimizu [5]

[1] Department of Electrical and Electronic Engineering, Shizuoka University, Hamamatsu, Japan
[2] Electrical and Electronic Engineering Course, Graduate School of Integrated Science and Technology, Shizuoka University, Hamamatsu, Japan
[3] Department of Optoelectronics and Nanostructure Science, Graduate School of Science and Technology, Shizuoka University, Hamamatsu, Japan
[4] Department of Electrical and Computer Engineering, Yokohama National University, Yokohama, Japan
[5] Division of Innovative Diagnostic and Therapeutic Research Institute of Photonics Medicine Hamamatsu University School of Medicine, Hamamatsu, Japan
*E-Mail: ota.s@shizuoka.ac.jp

The magnetic relaxation time of magnetic nanoparticles (MNPs) is influenced by particle structure, the conditions of applied magnetic field, and the properties of surrounding environment such as viscosity of medium, which is important property to develop the biomedical applications using MNPs. In this study, we investigated the magnetization dynamics in living tumor implanted in the mouse body. The intratumor structure was analyzed by the estimated magnetic relaxation time in biological and non-biological systems.

Iron oxide MNPs, Resovist® (PDR pharma Co. Ltd, Tokyo, Japan), were measured. MNPs were dispersed in viscous liquids in the viscosity η= 0.87–45 mPa·s, which was adjusted by mixing diluted water with glycerol. In addition, MNPs were solidified using epoxy resin. The concentration of MNPs was 2.75 mg-Fe/mL in the fluid and solid samples. Human fibrosarcoma HT1080 or pancreas adenosarcoma BxPC3 cells were cultured and implanted subcutaneously into the right hip of BALB/c nu/nu male mice purchased from Japan SLC (Shizuoka, Japan). In the in vivo measurement, MNPs were injected into the tumors, which was covered by a coil set including an excitation, detection, and cancel coils. The pulsed magnetic field was applied to measure the magnetic relaxation process [1]. The magnetic relaxation time distribution of was estimated from the measured magnetic relaxation process.

Figure 1 shows the magnetic relaxation process and magnetic relaxation time distribution in fluid, solid, and intratumor samples. The magnetization in fluid was larger than that in solid owing to the particle physical rotation [2]. In the intratumor environment, the magnetic relaxation process was different from those in fluid and solid, which indicates that the magnetization dynamics in the intratumor environment was illustrated by mixing the complex conditions of non-biological samples. Additionally, based on the estimated magnetic relaxation time, the intratumor structure was represented by the distributions of viscous fluid and solid, which was discriminated in HT1080 and BxPC3 tumors.

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This work was partially supported by JSPS KAKENHI grant numbers 20H02163 and 20H05652, and 23H01419, JST ACT-X grant number JPMJAX21A5, Takahashi Industrial and Economic Research Foundation, and Terumo Life Science Foundation.

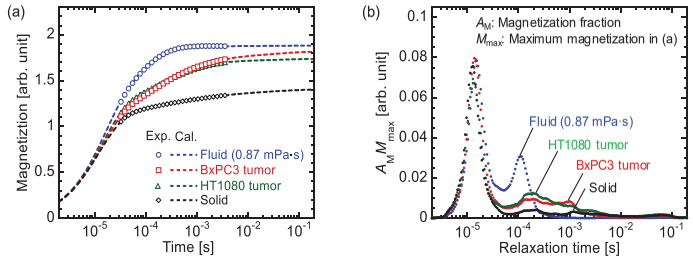


Fig. 1. (a) Measured magnetic relaxation process and (b) estimated magnetic relaxation time distribution.

Influence of anisotropy on the evolution of chains formed by magnetic nanoparticles under an applied magnetic field.

Amira Páez[1*], Sergiu Ruta[2], Lucia Gutierrez[1], Akira Satoh[3], David Serantes[4], Roy W. Chantrell[5],

[1]Inst. de Nanociencia y Materiales de Aragón (INMA, CSIC/UNIZAR) and CIBER-BBN, Zaragoza, Spain
[2] College of Business, Technology and Engineering, Sheffield Hallam University, United Kingdom.
[3]Akita Prefectural University, Japan
[4] Appl. Phys. Dept. and iMATUS, Universidade de Santiago de Compostela, Santiago de Compostela, Spain.
[5] Department of Physics, University of York, United Kingdom
*Email: ami@unizar.es

A huge amount of work has been made in the past two decades exploring the heating properties of magnetic nanoparticles (MNPs) when exposed to alternating magnetic fields. Such properties are crucial for a variety of applications ranging from magnetic hyperthermia to catalysis. One factor that has been poorly studied is the possibility that the magnetic colloid is dynamically evolving over time because of the exposure to the AC field, which may promote, for example, the organization of the particles into elongated assemblies or chains. A related question is what happens to these chains when the field is removed.

To study this, we performed theoretical simulations on the chain formation of magnetic nanoparticles. Systems of MNPs with same size and different anisotropy were simulated by including within a Brownian Dynamics (BD) code, the decoupling of the magnetisation from the lattice in terms of a standard Monte-Carlo (MC) model for uniaxial anisotropy particles. We simulated the initial configuration, under no field, then exposed the magnetic colloid to a strong DC magnetic field (chaining), and finally observed the system evolution when the field is switched off (unchaining). For computational efficiency, we used a DC field to simulate the starting assembly structure of elongated aggregates. The computational model proved well on the thermodynamic limit (see Figure).

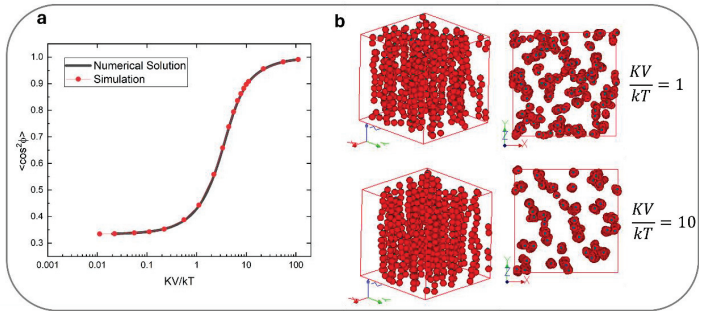


Figure. **(a)** Test in the thermodynamic limits for the relative orientation between particle direction (anisotropy axis) and moment orientation (the applied field direction). **(b)** Spatial disposition of the simulated particle systems under the DC field for two different anisotropies. For each value, two views are shown: oblique -left-, and top -right- with respect to the field direction.

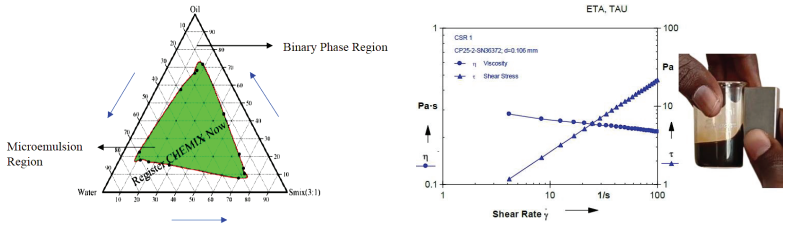
Fabrication of Magnetic Nanoemulsion Loaded with Letrozole for Targeted Oncotherapy

Selvamani Palanisamy, Krishnanand Nagarajan, Keerthivasan Ganesan and Latha Subbiah*

Department of Pharmaceutical Technology and Centre for Excellence in Nanobio Translational Research, University College of Engineering, Bharathidasan Institute of Technology Campus, Anna University, Tiruchirappalli – 620024, Tamil Nadu, India

*Email: lathasuba@aubit.edu.in Mobile: +91-98425 98097

Emulsions serve as effective delivery systems for hydrophobic drug molecules compared to hydrophilic ones, comprising two immiscible liquids in a biphasic liquid preparation. Nanoemulsions, a subset of dispersed particles, have garnered significant attention in therapeutics due to the prevalence of hydrophobic new chemical entities. These nanoemulsions hold promise across pharmaceuticals, cosmetics, diagnostics, drug therapies, and biotechnologies. To realize targeted drug delivery and minimize side effects, we developed a magnetic nanoemulsion using both high- and low-energy techniques. This involved processes like microfluidization, ultrasonication, high-pressure homogenization, phase inversion emulsification, and self-nanoemulsification. Furthermore, we employed the self-nanoemulsification technique to formulate LMNEs. An optimal excipient concentration was determined using a pseudo-ternary phase diagram. Stability studies confirmed the integrity of the formulation even under the influence of magnetic fields. *In vitro* characterization revealed an average globule size of 49.63 nm for LMNEs, with a charge of 26.9 eV and a polydispersity index of 0.428. FT-IR analysis confirmed successful stabilization of magnetic nanoparticles by citric acid and validated interaction between the drug and liposomes. Rheological properties of LMNEs were also assessed and the data confirms that the LMNE exhibits desired fluid and rheological properties, with homogeneous particle distribution evidenced by the observed increase in shear rate alongside shear stress. Evaluation of nanoemulsion formulation parameters indicated results within acceptable ranges. *In vitro* assessments showcased the potential of the developed magnetic nanoemulsion, promising improved pharmaceutical and therapeutic attributes. The letrozole-loaded magnetic nanoemulsion emerged as a viable candidate for controlled and targeted drug delivery against breast cancer. Ongoing work includes *in vitro* cell line studies and pre-clinical investigations to deepen our understanding of its efficacy and safety profile.



(a) (b)

Figure: (a) Pseudo-ternary phase diagram of quaternary system IPM/water at different Smix ratios; (b) Rheological properties of LMNEs.

Temperature Effects on Magnetorelaxometry Parameters of Immobilized Magnetic Nanoparticles

Kerstin Pansegrau[1*], Aaron Jaufenthaler[1], Frank Wiekhorst[2] and Daniel Baumgarten[1]

[1] Institute of Electrical and Biomedical Engineering, UMIT TIROL - Private University For Health Sciences and Health Technology, Hall in Tirol, Austria
[2] Physikalisch-Technische Bundesanstalt, Berlin, Germany
[*] Email: kerstin.pansegrau@umit-tirol.at

One future application of magnetic nanoparticles (MNPs) is magnetic hyperthermia. In order to ensure patient safety and therapy outcome, this application requires monitoring regarding the spatial concentration of MNPs. A promising monitoring tool is magnetorelaxometry (MRX), in which the magnetic moments of MNPs are aligned via an external excitation field and the relaxation of the MNP's net magnetic moment is measured after this field is switched off. The reconstruction of the MNP concentration is typically based on two relaxation signal parameters: relaxation amplitude ΔB, defined as the difference of the measured flux density for two time points, and relaxation time $t_{1/e}$, that indicates the time in which the relaxation signal has dropped to $1/e$ of its initial amplitude. Since magnetic hyperthermia is performed with different MNP systems and relaxation signals are evaluated for different temperatures, we investigate the temperature effect on the two relaxation parameters for commercial particle systems.

Two commercially available MNP samples (Perimag®, micromod, Germany and RCL-01, Resonant Circuits Limited, UK) with the same iron amount were immobilized in gypsum. Each sample was placed between an excitation coil and an optical magnetic gradiometer (Twinleaf, USA). A background magnetic field of $B \approx 20\,\mu T$ was applied for operating the sensor. All setup components were placed inside a magnetically shielded room. For both MNP samples, a measurement procedure consisting of six sets was performed. For subsequent sets, the orientation of the background magnetic field was alternated between parallel and antiparallel with respect to the orientation of the excitation magnetic field. Within each set, seven different excitation flux densities were applied and the respective relaxation behavior was measured. The first two sets were obtained at room temperature (22 °C). Subsequently, the MNPs were heated to 37.5 °C and two sets were recorded (set 3 and 4). After a cooling phase, the measurement at 22 °C was repeated (set 5 and 6).

Both MNP systems show a clear temperature dependence of the relaxation amplitudes and relaxation times for all investigated excitation flux densities and both background field orientations. Figure 1 exemplary shows the results for the RCL-01 sample. For an increased MNP temperature, the relaxation amplitude as well as the relaxation time clearly decreases. Since both relaxation parameters are similar for the two sets before heating and the two sets after cooling, the temperature effect seems to be reversible. The results for the Perimag® particle system indicate qualitatively the same behavior. For this reason, it is recommended to consider the temperature effects when reconstructing MNP concentration distributions as part of magnetic hyperthermia monitoring.

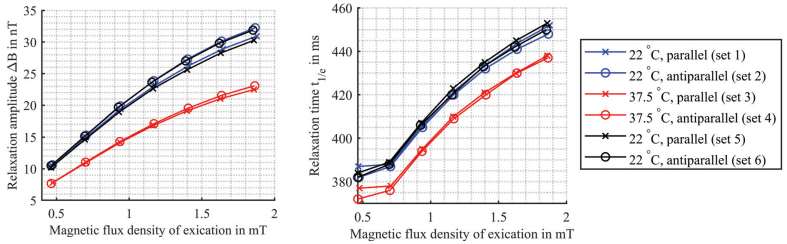


Figure 1. Left: Relaxation amplitudes of RCL-01 MNPs in dependence on the excitation flux density, the MNP temperature and the orientation of the background magnetic field with respect to the orientation of the excitation field. **Right:** Same as left, but for the relaxation times.

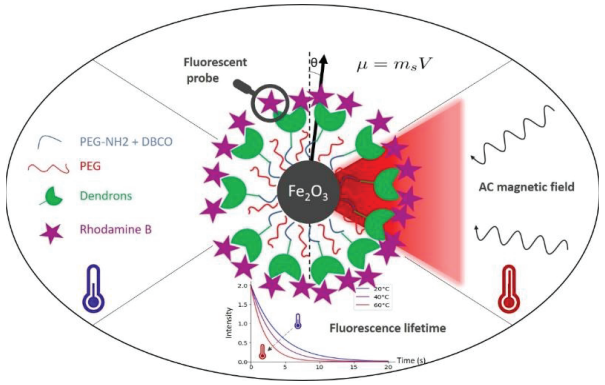
Acknowledgements
Financial support by the Austrian Science Fund (FWF, grant I 4357-B) and the German Research Foundation (grant WI 4230/4-1) is gratefully acknowledged.

Local temperature around iron oxide nanoparticles during hyperthermia

Ployart Olifie, Gélébart Frédéric, Dupuis Vincent, Secret Emilie, Abramson Sébastien, Siaugue Jean-Michel, Fresnais Jérôme

PHysicochimie des Electrolytes et Nanosystèmes InterfaciauX (PHENIX), Sorbonne Université, CNRS, F-75005 PARIS, FRANCE
Email: olifie.ployart@sorbonne-universite.fr

Iron oxide nanoparticles are widely used in the biomedical field thanks especially to their contrast properties in Magnetic Resonance Imaging (diagnostic[1]) and their heating properties (hyperthermia therapies[2]). In the second case, the heating of the nanoparticles under an alternative magnetic field (AMF) can directly be applied for cancer therapy or used in drug delivery treatments. These applications may require a precise control of the local temperature in the nanoparticle surroundings. A detailed understanding of the heat generation and exchange processes at the nanoparticle's scale is necessary but is still lacking, even though some studies have evidenced indirectly these local effects[3,4]. Our main objective is to progress towards this understanding by quantifying the heat transfers between a nanoparticle and its surrounding when an AMF is applied. To this end, a system consisting of a fluorescent probe covalently grafted to iron oxide nanoparticles was developed. The relative position of the probe from the nanoparticle's surface was controlled using dendrons of various thicknesses. This probe has a fluorescence lifetime that depends on the temperature[5]. Finally, a system that allows lifetime measurement of this probe in the presence of the AMF was developed. These measurements allow the assessment of the local temperature gradients around the nanoparticle surface in the 2-7 nm range. Lifetimes measurements are quick (few seconds) and highlight the variation of temperature obtained corresponding to the thermal energy transfer from the nanoparticles to the probe's environment in a stationary regime. Depending on the distance of the probe from the particle's surface, we were able to evidence the loss of thermal transfer at "long" distance (highest dendron's generation).



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Portable medical device based on magneto immunosensor for the diagnosis of celiac disorder.

J.C. Porras[1,3], A. Pallarès-Rusiñol[3], K. Alemany López[1], J. Ferrer-Dalmau[3], M.I. Pividori[1,2,3*]

[1]*Grup de Sensors i Biosensors, Departament de Química, Universitat Autònoma de Barcelona, Bellaterra, 08193, Spain.*

[2]*Biosensing and Bioanalysis Group, Institute of Biotechnology and Biomedicine, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain*

[3]*BioEclosion S.L, Parc de Recerca, Universitat Autònoma de Barcelona, Bellaterra, 08193, Spain.*

**Corresponding author: Isabel.Pividori@uab.cat*

Celiac disease (CD) is a chronic autoimmune disorder that affects individuals regardless of gender, age, or ethnicity, primarily arising from gluten intolerance in genetically predisposed individuals [1,2]. Although its prevalence impacts 1-2% of the global population, there has been a noticeable rise in reported cases over recent decades. The disparity between diagnosed and undiagnosed cases varies by country, with ratios ranging from 1 to 2 in Finland to 1 to 10 in the USA, Argentina, and Germany, suggesting a substantial percentages of cases remain undetected [3]. The main contributor to underdiagnosis is the variability of symptoms, which can mimic those of other diseases, ranging from small intestinal inflammation to diarrhea and other digestive disorders[1]. Current diagnostic methods, conducted in specialized laboratories, include serology, genotyping, and histology. Serology is considered the gold standard among these, despite its lower sensitivity, requiring further invasive tests for confirmation[4]. With the increase in cases, there is a critical need for rapid and accurate diagnostics, especially ones that simplify testing for community and primary care settings. To address this challenge, this work focuses on the study of novel biomarkers for CD based on synthetic deamidated-related peptides, enhancing the sensitivity of existing methods and integrating them into a novel magneto immunosensor. Derived from specific amino acid sequences of generic gliadin, these peptides exhibit a promising predictive value for CD detection. Therefore, when immobilized on magnetic particles, they can serve as distinctive biomarkers for the isolation of gliadin antibodies (figure 1), and the detection can then be accomplished by amperometry using an enzyme-labeled antibody. The deaminated peptides are integrated on a device platform composed by two main components (Figure 1): A) Disposable cartridge, including i) the sample holder containing reagents (including magnetic particles modified with peptide and the labelled-antibody which binds specifically the patient antibodies in 15 minutes), and ii) the cartridge containing the microfluidic and the electrode in which the magnetic actuation is performed, while the excess of sample and reagents are removed. B) Digital reader which allows the electrochemical readout in less than one minute. The output of the device is a quantitative response. This test demonstrates significant potential due to its affordability, speed, sensitivity, minimal handling requirements, and suitability for ambulatory CD screening in primary care. The approach consolidates the competitive advantages of existing diagnostic tests, offering point-of-care convenience, rapidity, user-friendliness, quantifiability, and high predictive power.

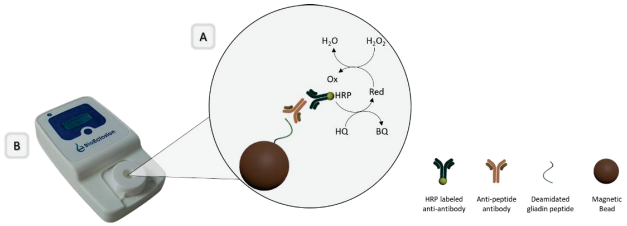

Figure 1. Schematic representation of the magneto electrochemical immunoassay.

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Development of high-throughput magnetic tweezers platform with three poles

Ali Mohammad Pourshahidi[1*] and Hans-Joachim Krause[1, 3*]

[1]Institute of Biological Information Processing, Bioelectronics (IBI-3), Forschungszentrum Jülich, Germany,
[3]Institute of Nano- and Biotechnologies (INB), FH Aachen University of Applied Sciences, 52428 Jülich, Germany,
e-mail: a.pourshahidi@fz-juelich.de, h.-j.krause@fz-juelich.de

Keywords: Magnetic nanoparticles, Magnetic tweezers, single-molecule force spectroscopy, magnetic particle actuation

Magnetic tweezers (MT) have become essential tools in biophysical research for probing the mechanical properties of cells and manipulating single molecules [1]. We report the development of a 3-pole magnetic tweezer platform, advancing from the original design in [2]. This platform enhances the application of translational forces on magnetic nanoparticles (MNPs), facilitating the establishment of a 'mechanical handle' for the exertion of predetermined forces. The platform is designed with upright sample dish for integration with an inverted microscope. A strong magnetic field gradient is generated utilizing electromagnets wound around a high-permeability yoke with sharp tips at their ends. The MNPs are pulled toward the location of the strongest magnetic field, which is at the very end of the sharp tip, attached to the magnetized yoke finger. Two-dimensional translational actuation is made possible by arranging three magnetizable yoke fingers with tips around the workspace. Maneuverability can be achieved by control of the coil currents at the magnetic poles, with optical detection of the MNP position and optional feedback. Figure 1 illustrates the 3D assembly of our design. The MT will be used for controlled mechanical stimulation of visually identified synapses in mouse primary neurons in vitro.

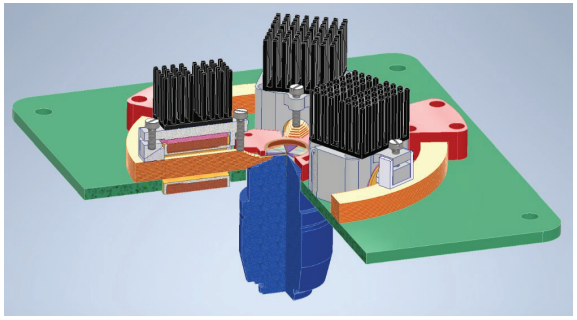

Figure 1. 3D model of the MT platform assembly. The yoke layers are tightly held together using the specific holders (red), and the electromagnets are covered by heat sinks (black) to reduce the heat generated by the electromagnets underneath. Below the assembly is the objective of the inverted microscope (blue).

Acknowledgements:
This work was funded by HORIZON-EIC-2022-Pathfinderopen-01-01, Project 101099579 “SynMech”.

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Improvement of magneto-microfluidic separation of nanoparticles by molecular adsorption

J. Queiros Campos[1*], G. Godeau[1] and P. Kuzhir[1]

[1] Université Côte d'Azur, CNRS UMR 7010, Institute of Physics of Nice, 17, rue Julien Lauprêtre, Nice 06200 France
*Email: Jordy.queiros-campos@univ-cotedazur.fr

The microfluidic manipulation of magnetic nanoparticles is a smart tool for different environmental and biomedical applications. In most of these applications, magnetic nanoparticles carry adsorbed molecules on their surface (micropollutants or biomolecules) which must be either delivered to a specific site (controlled drug delivery, gene transfection), either extracted from the solvent (immunological tests, protein purification, purifying water). Unfortunately, these techniques have a strong limitation related to a low efficiency of magnetic manipulation of the nanoparticles due to their Brownian motion and the low efficiency of their separation from the suspending fluid (magnetic separation) under flow in microfluidic circuits. However, the molecules adsorbed on the surface of the nanoparticles can reduce the repulsive colloidal interactions between nanoparticles and cause a low aggregation of nanoparticles. Such aggregation in the absence of an applied magnetic field leads to an
increase in the effective size of nanoparticles (or rather primary aggregates). Once the magnetic field is applied, the magnetic force exerted on the primary aggregates will be greatly amplified compared to the case of individual non-aggregated nanoparticles. In this case, the adsorbed molecules not only perform their function in the target applications but also ensure a significant improvement of the remote control of nanoparticles by magnetic fields, thus broadening their field of application.

In this work, we studied the effect of the quantity of adsorbed molecules on the efficiency of magnetic manipulation and separation of iron oxide nanoparticles (IONPs). Three distinct systems will be considered: (i) adsorption of a cationic dye (methylene blue (MB)) on the surface of IONPs coated with citrate ions; (ii) adsorption of curcumin (CUR) on the surface of IONPs coated with *β*-cyclodextrin (*β*-CD*)* for the controlled delivery of drugs; (iii) capture of antigens (AG) on the surface of IONPs functionalized by antibodies (AB) (application to immunoassays). We notice striking similarities between the behaviours of the three physicochemical systems in the magnetic fields [1,2,3].

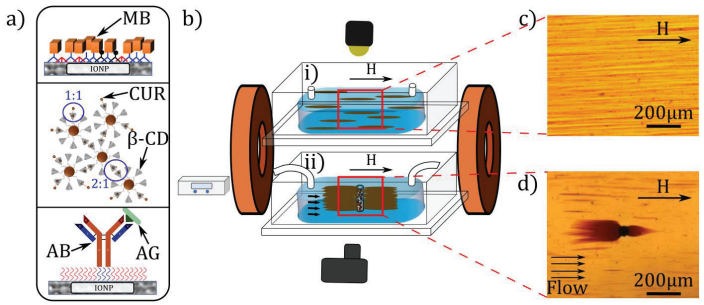

Figure. a) Physicochemical systems in which molecular binding to the functionalized IONP surface is used to promote primary aggregation in view of potential target applications. b) Experimental setups for secondary (field-induced) aggregation (i), magnetic separation (ii); c) Snapshot of the secondary aggregation; d) Snapshot of the magnetic separation of IONPs on the magnetized micropillar.

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Magnetic Micro Vortex for Molecule Convective Transport: Towards a Biomedical Application

M. Raboisson-Michel[1*], J. Campos-Queiros[1] and P. Kuzhir[1]

[1]Université Côte d'Azur, CNRS UMR 7010, Institute of Physics of Nice, 17, rue Julien Lauprêtre, Nice 06200 France
*Email: maxime.raboisson-michel@univ-cotedazur.fr.Cellular:+33-6-75-83-20-92

Ischemic stroke is the first disabling disease in France and accounts for 87% of all strokes. An ischemic stroke occurs when a thrombus, a fatty deposit lining the vessel walls, detaches and obstructs a blood vessel, blocking the blood flow and preventing the neighbouring tissues' oxygen supply, resulting in necrosis. The intravenous injection of tissue plasminogen activator, a serine protease that dissolves clots, during the first 3-4,5 hours following an event is crucial for the success of therapeutic treatment. However, such a method does not allow the efficient diffusion (more than 60 min) of the drug to the clot due to the stagnation of blood in the clogged vessel. Using magnetic iron oxide nanoparticles (IONP) can be very efficient in accelerating the transport of the drug in the occluded vessel(Sherman and Swan 2016; Liu *et al*, 2018). The idea is to rotate the elongated aggregates of the IONP by an oscillating magnetic field applied via the electric coils placed outside.
We are exploring the application and relevance of magnetic colloids in the biomedical field to help us understand the physical interactions of the particles with the magnetic field and the clot. This work allowed us to design an experimental setup that facilitated the characterization and manipulation of aqueous dispersions of synthesized magnetic IONPs in a closed in-vitro environment rudimentary simulating a blood vessel. Most of the work was done on the analysis of the experimental data and their compliance to the elaborated theoretical models: the self-assembly of IONP into elongated aggregates under the action of a rotating magnetic field; collective rotation of these aggregates, as well as the creation of a recirculating flow in a closed channel, mimicking a blocked blood vessel (Raboisson *et al*, 2020; Campos *et al*, 2024).

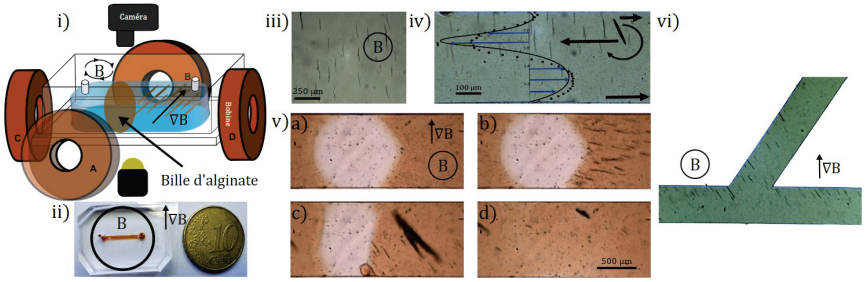

Figure 1: Experimental system comprising 4 Helmholtz coils (i) and a microfluidic channel (ii); image of the slender aggregates formed in 1 min by self-assembly of NPMs in a rotating magnetic field (iii); snapshot of a microfluidic channel with aggregates rolling to the left along the top wall and experimental and theoretical velocity profile (iv); photographs showing the kinetics of dissolution of a proxy clot (calcium alginate bead) following the convective flow of a dissolving agent (sodium citrate) over 0,3,7 and 13 mins (v); channel in Y form to begin the study of deviation of movement of aggregates (vi)

We finally tested the system based on polymer calcium alginate beads, used as a simple proxy for the physical model of blood clot dissolution and proof of concept of the proposed thrombolysis technique. Quantitatively, we manage to create the IONP rotating aggregates (of an average length of about 50 µm) in a very short time-lapse (about 1 min) elapsed from the moment when a rotating magnetic field of an amplitude 6 kA/m and frequency 5 Hz is applied; these aggregates are capable of generating the flows in a closed channel at a typical speed of 5-10 µm/s; these flows have been proved to enhance the mass transport of a dissolution reagent (trisodium citrate) towards a polymeric calcium alginate bead, such that its dissolution time decreases at least by order of magnitude with respect to that in the absence of the magnetic field when the dissolution agent is delivered to the bead through diffusion through a quiescent liquid medium.

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THE INFLUENCE OF ADMINISTRATION OF MAGNETIC CARRIERS ON HEATING EFFICIENCY IN TISSUE-MIMICKING PHANTOMS

Filip Ratajczak*, Rafał Bielas and Arkadiusz Józefczak

Faculty of Physics, Adam Mickiewicz University in Poznań
Uniwersytetu Poznańskiego 2, 61-614 Poznań, Poland
*E-mail: filip.ratajczak@amu.edu.pl

Magnetic carriers, such as magnetic Pickering emulsions and suspensions of colloidal capsules derived from these emulsions hold large potential for biomedical applications. In both of those systems substance of the dispersed phase is stored inside the core and protected by the particle shell [1]. They can be used as carriers in theranostics - the incorporation of magnetic nanoparticles within the structure of those systems enables them to be utilized as “micro-heaters” for magnetic heating applications and contrast agents in ultrasound imaging [2].

In our work, we inject magnetic particle suspension, magnetic Pickering emulsion, and suspension of colloidal capsules into tissue-mimicking agar phantoms. They were administered at varying flow rates to investigate their influence on magnetic carriers and heat distribution within the phantom during magnetic and ultrasound heating. The injection was performed using a microfluidic system and controlled via optical microscopy (**Fig. 1a**). Temperature distribution was observed using an infrared camera (**Fig. 1b**). The results of our work show the possibility of utilizing different injection methods for the optimization of hyperthermic effect.

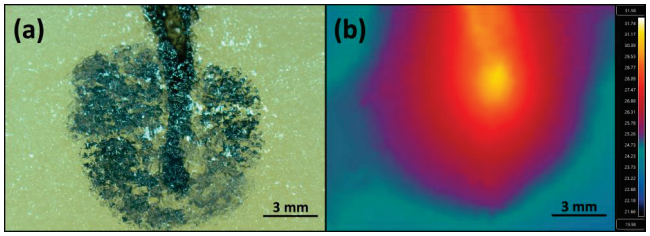

Fig. 1 (a) Microscopic image of a phantom after injection of magnetic suspension.
(b) Infrared image of temperature distribution in phantom after injection after 6 minutes of magnetic heating.

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Viability monitoring of cells using magnetic particle imaging

Amani Remmo[1*], Lena Kampen[2], Olaf Kosch[1], Antje Ludwig[2], Frank Wiekhorst[1], Norbert Löwa[1]

[1] Physikalisch-Technische Bundesanstalt, Abbestr. 2-12, 10587 Berlin, Germany
[2] Charité-Universitätsmedizin Berlin, Hessische Str. 3-4, 10115 Berlin, Germany
*Corresponding author: Amani Remmo, amani.remnmo@ptb.de

Current methods for cell population tracking often lack the necessary temporal resolution for studying cell behavior and face limitations in penetration depth, radiation exposure, resolution, and quantification accuracy. Furthermore, variations in cell viability may result in incomplete or inaccurate outcomes. In this study, we investigated the capability of magnetic particle imaging (MPI) for viability monitoring during tracking of cells labeled with magnetic nanoparticles (MNP).

To accomplish this, THP-1 cells, (human acute monocytic leukemia cell line), were incubated with citrate-coated Synomag® MNP, proven effective for cellular imaging by MPI[1]. We induced cell damage with hydrogen peroxide treatment for different time points and compared them to untreated MNP-loaded cells. Flow cytometry assessed the proportion of living and damaged cells in each sample. Simultaneously, we determined the loading status and MPI performance of the MNP-loaded cells with magnetic particle spectroscopy (MPS). Next, we explored their distinct behaviors in a real-time bolus experiment utilizing a preclinical MPI scanner. We found that the Synomag® MNP were fully internalized by THP-1 monocytes and generated a high MPI signal. The MPI signal depicts a fingerprint of a specific MNP state, which facilitates an improved analysis of subtle changes in the magnetic behavior of the MNP. Surprisingly, these signal changes could also be observed in damaged MNP-loaded cells. With the bolus experiment, we demonstrated the potential of MPI to perform quantitative real-time imaging of cells combined with determining the proportion of living and damaged cells. We showcased the combination of cell tracking and viability assessment through MPI (see Fig. 1), which will significantly enhance our ability to monitor cellular processes. Next, MPI tracking of inflammatory cells shall be used for the detection of pathological processes.

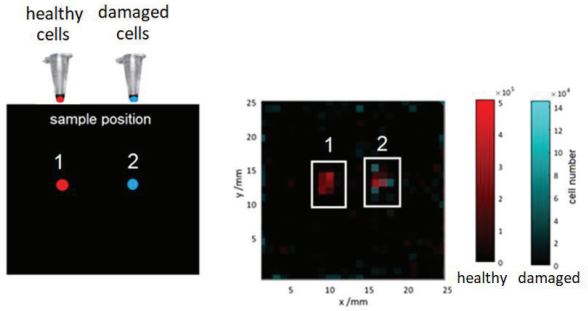

Figure 1 | MPI image of two samples containing healthy cells (left) and damaged cells (right) measured at the same time. Using the MPI signal fingerprint of each MNP state (healthy cells, damaged cells), color differentiation is possible by image reconstruction.

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Novel permalloys nanoparticles for CO_2 capture and conversion by magnetic hyperthermia

A. Santana-Otero *, A. Gallo-Cordova, María del Puerto Morales

Institute of Materials Science of Madrid (ICMM-CSIC), Sor Juana Inés de la Cruz 3, 28049 Madrid, Spain

**Email: antonio.santana@icmm.csic.es*

Recent advances have provided new insights into the capture and conversion of CO_2 into valuable molecules by applying the principles of green chemistry. Magnetic hyperthermia has emerged as a promising catalyst in this field. Magnetic heating offers clear advantages in terms of activation speed, considerably accelerating reactions compared to conventional heating methods. Thanks to the efficiency of magnetic hyperthermia, reactions that previously took hours to complete can now be achieved in a matter of minutes. Materials with high magnetic permeability, such as permalloys, stand out as effective nanoreactors due to their unique properties. Permalloys, composed primarily of iron and nickel ($FeNi_3$), exhibit some of the highest magnetic permeabilities in nature.[1–3] However, CO_2 capture requires the incorporation of these nanoparticles in organic frameworks to improve the efficiency of CO_2 capture and desorption, and facilitating its subsequent conversion into valuable molecules.[4] In the RENERG2CHEM project, we exploit the combination of novel high magnetic permeability permalloy-based nanoparticles and metal-organic frameworks to create nanocomposites that enhance CO_2 capture and its conversion into valuable molecules.

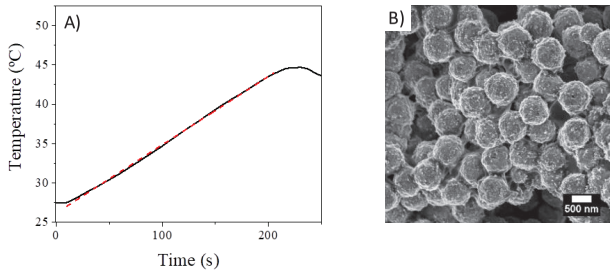

Figure 1. A) Heating ramp of FeNi3 nanoparticles in a solution of ethylene glycol (20 mg/mL) under 100 kHz and 60 mT. B) SEM image of agglomerates of FeNi3 nanoparticles prepared by a microwave assisted method in water.

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Synthesis of Fe@C core-shell nanoparticles for dual magnetic hyperthermia and photothermal cancer treatment

Sergio Santander[1,2], Ye Enyi[1] and Nguyen TK Thanh [2*]

*[1]Institute of Materials Research and Engineering (IMRE), Agency for Science, Technology and Research (A*STAR), Singapore; [2]Biophysics Group, Department of Physics & Astronomy University College London, Gower Street, London WC1E 6BT, UK and UCL Healthcare Biomagnetics and Nanomaterials Laboratories, 21 Albemarle Street, London W1S 4BS.*
**ntk.thanh@ucl.ac.uk, http://www.ntk-thanh.co.uk*

In recent years, the field of inorganic nanomaterials has witnessed a surge in the exploration of multifunctional nanoparticles for diverse biomedical applications. This study focuses on the synthesis of Fe@C core-shell nanoparticles for synergistic magneto-photothermal cancer treatments. The core-shell nanocomposite combines the unique magnetic moment of iron nanoparticles with the excellent photothermal characteristics of a carbon shell, offering a promising platform for targeted therapeutics.

The proposed synthesis process involves a one-pot synthetic method via thermal decomposition to establish core-shell nanoparticles. With the use of the same iron precursor (cyclopentadienyl dicarbonyl iron (II)) but with different reaction conditions can we obtain various iron-carbon nanoparticle variations. The cubic nature of the as-synthesised iron-carbon nanoparticles is confirmed by TEM, along with the FFT showing the nanoparticle cores to adopt a bcc crystal system (Fig. 1A). Furthermore, XRD also confirms the iron nature, followed by a mixture of carbon nitride compositions. The as synthesised nanoparticles is a good Fenton catalyst in showing the decrease in Rhodamine B absorbance in the presence of hydroxyl radicals when exposed to hydrogen peroxide (Fig. 1B). Nanoparticles exhibit a maximum temperature of 44ºC (within the mild temperature photothermal window)[1] when exposed to an 808 am laser for a time period of 5 min (Fig. 1C). Note that the container the sample is in measures a lower temperature (green and blue) than the sample itself (indicated by the red cross where the highest temperature was recorded). We have performed similar analyses to other iron-carbon nanoparticle species that have been synthesised via different synthetic routes in the presence of the same iron precursor, with the goal to determine structural, magnetic, photothermal and Fenton catalytic tunability for its potential usage in cancer treatment.

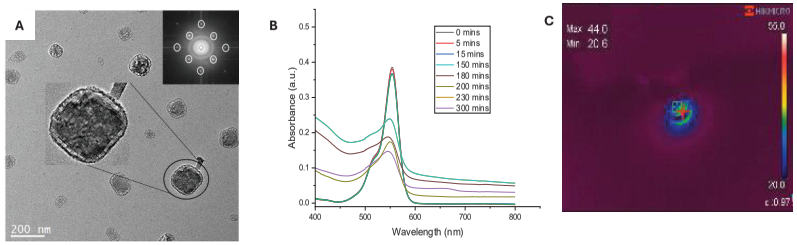

*Figure. **(A)** TEM image of as-synthesised nanoparticles with FFT (inset) via a synthetic pathway of 1.5:2 mole ratio HDTAC/HDA for 6 hr in oleylamine solvent. **(B)** Analysis of the degradation of Rhodamine B over a time period. **(C)** Analysis of photothermal properties of iron nanoparticles synthesised as in 1A. The bar colour indicates the temperature change in °C.*

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Iron oxide nanoparticles for biotechnological applications

Solange M. Selzer[1], Maria. L. Bonnet[2], Mauricio Galiano[2], Raquel. V. Vico[3], Nancy. F. Ferreyra[1]

[1]Departamento de Fisicoquímica,[2]Departamento de Química Biológica,[3]Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Argentina. Instituto de Investigaciones en Fisicoquímica de Córdoba (INFIQC-UNC-CONICET),
solange.selzer@unc.edu.ar; nfferreyra@unc.edu.ar; raquel.vico@unc.edu.ar

Iron oxide nanoparticles (IONPs) are extensively researched in the field of nanobiotechnology applications, especially for biotechnological purposes. Their exceptional physicochemical properties make them efficient for applications such as contrast agents for diagnostic imaging, biosensing, and protein separation, among others. The primary approach for attaining desired properties in IONPs for specific applications involves surface functionalization. Chemical functionalization not only can enhance colloidal stability by preventing agglomeration but also can facilitate the use of the IONPs as platforms for immobilizing biomolecules and enable the regulation or modulation of their internalization and intracellular fate.
In this context, we synthesized IONPs using the coprecipitation method and functionalized them with aryl carboxylic acid (IONP-Ar-COOH) or aryl amine groups (IONP-Ar-NH_2), with the aim of employing them in biomedical applications. Taking into account the medium to which the nanoparticles will be exposed, we evaluated their colloidal stability across a culture media with or without protein addition. These results were correlated with the cellular uptake of these nanoparticles and their effects on cell viability. Although differences were observed between the internalization of the nanoparticles, none of them were cytotoxic; they were used for different applications: IONP-Ar-COOH was used as a platform for immobilizing the lectin Concanavalin A (ConA) for biosensing glycan-lectin interactions, and IONP-Ar-NH_2 was used for the obtention of glyconanoparticles (Figure 1).

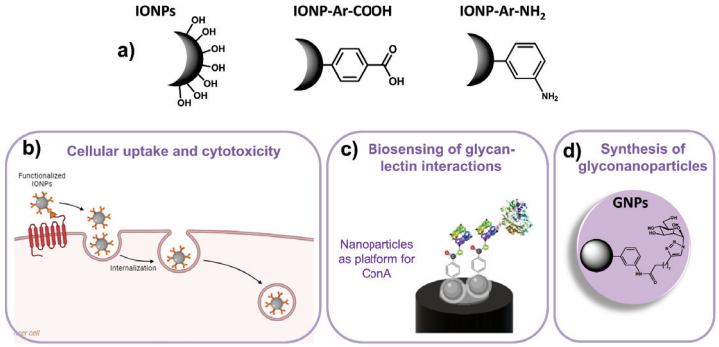

Figure 1. a) Schemes of the different IONPs synthesized, b) Representation of cellular internalization in ovarian cancer cells, c) IONP-Ar-COOH as platform for immobilization of ConA over glassy carbon electrodes and d) Representation of glyconanoparticles obtained from IONP-Ar-NH_2. The representations are not to scale.

Our results indicate that improved colloidal stability is crucial for achieving controlled entry into cells. These approaches demonstrate the versatility of functionalized IONPs for diverse types of devices, including therapeutic, preventive, and diagnostic ones.

Preparation and Colloidal Stability of Magnetic Drug Delivery Nanoassemblies for Cancer Treatment

Anna Hlukhaniuk[1,2,3*], Malgorzata Świętek[1], Lénaïc Lartigue[3], Jean-Michel Bouler[3], Daniel Horák[1]

[1] Institute of Macromolecular Chemistry CAS, Prague, Czech Republic
[2] Charles University, Prague, Czech Republic
[3] Nantes University, CEISAM UMR-CNRS 6230, Nantes, France
*Email: hlukhaniuk@imc.cas.cz

Smart drug delivery systems (DDS) open a window for novel medical treatments with controllable drug transportation and release at the target site, both critical for reducing the systemic toxicity of therapies and enhancing their efficacy. Magnetically responsive DDS are particularly perspective in terms of therapeutic and diagnostic agents' codelivery, as well as for multimodal cancer therapies combining, e.g., chemotherapy and magnetic hyperthermia.

Nanoassemblies (NA) of various compositions are often used in DDS. Encapsulation of magnetic nanoparticles (MNP) with gossypol (GS), an anticancer drug that selectively induces oxidative stress in cancer cells and promotes their apoptosis, allows achieving multifunctional DDS. Introducing polymeric material into NA aims to improve the system stability in aquatic media. Chitosan (CS) is one of the most exploited natural biopolymers in biomedical applications, including DDS.
Modifying the NA with GS-grafted CS increases the GS payload in the system and prolongs the GS release profile, firstly releasing GS grafted on CS, followed by release from the core due to CS degradation induced by low pH of tumour microenvironment and heat produced by magnetic hyperthermia. Furthermore, CS modification with a hydrophobic GS can increase its amphiphilicity, an important factor for stabilization of the system. Expecting temperature-induced structural changes, it is important to investigate the stability of aqueous NA suspensions under different temperature conditions and predict the behaviour of the NAs during magnetic hyperthermia therapy.

First, the spherical MNP (D_n=10 nm) were synthesized by thermal decomposition; separately, a series of CS-GS derivatives with an increasing load of GS (0, 1, 2.5, 7.5 and 10 mg of GS per 100 mg of CS) was prepared by free-radical grafting method. GS-based NA were flash precipitated in the presence of CS and CS-GS. The stability of NA was evaluated by dynamic light scattering using two approaches; in the first one, NA were incubated for 24 h at 50, 60 and 70 ° C, and in the second approach, NA were subjected to 5 successive heating-cooling cycles in the range between 20 and 70 ° C. The stability of NA was assessed from the changes in hydrodynamic diameter (D_h), polydispersity index and ζ-potential.

During all the tests, the samples remained colloidally stable at all temperatures; D_h changed only around ±20 nm. During the heating-cooling cycles, the NA containing CS-GS remained stable throughout all experiments, with a slight increase in the D_h, followed by a minor decrease of ζ-potential. In contrast, NA with non-modified CS lost the stability after the 3rd cycle.

The results indicate that NA stabilization with CS modified with anticancer GS not only allow to increase the GS loading, but also improves the stability of the NA at increased temperatures, compared to the stabilization with neat CS. It may also indicate the formation of strong interactions between CS, GS and MNP that are important for the DDS applications.

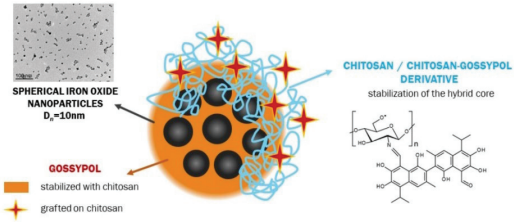

Figure. Scheme of NA stabilized with GS-grafted CS.

Biocompatible Fe_3O_4@CeO_2 Nanocomposites Synthesized via "Layer-by-Layer" Deposition

Yuliia Shlapa[1*], Katarina Siposova[2], Valentin-Adrian Maraloiu[3], Andrey Musatov[2], Anatolii Belous[1]

[1]V. I Vernadsky Institute of General & Inorganic Chemistry of the NAS of Ukraine, 32/34 Palladina ave., Kyiv 03142, Ukraine
[2]Institute of Experimental Physics SAS, Watsonova 47, Kosice, 040 01, Kosice, Slovakia
[3]National Institute of Materials Physics, 405A Atomistilor St, 077125, Magurele, Romania
*e-mail: yuliashlapa@ukr.net. Mobile: +38 099 327 18 63

Magnetic Fe_3O_4 nanoparticles (NPs) are of interest due to their biocompatibility and bio-functionality expressed as antimicrobial, antiviral, or antioxidant activities, as well as their additional ability to heat up under the exposure of an alternating magnetic field. At the same time, Fe_3O_4 NPs possess weak chemical stability and tend to oxidation in the air [1]. Development of complex magnetic nanocomposites based on Fe_3O_4, for example, with the "core@shell" structure, is relevant due to the following: i) covering the magnetic NPs with another bioactive inorganic nanomaterial (such as CeO_2 NPs) can promote the achieving some synergy in bio-functionality when compared to the individual (NPs), and ii) the appearance of the "shell" on Fe_3O_4 NPs may protect them against oxidation. The main objective of this research was to synthesize Fe_3O_4@CeO_2 nanocomposites (NCPs) with uniform shell coating, their physicochemical examination, and bioactivity assessment.

Fe_3O_4@CeO_2 "core@shell" NCPs with the 3-, 5-, and 7- layers of "CeO_2-shell" were synthesized using the "layer-by-layer" deposition of CeO_2 NPs on the surface of the pre-synthesized Fe_3O_4 NPs. XRD and XPS data revealed the formation of Fe_3O_4@CeO_2 composites, where the portion of CeO_2 growth with the increase in the expected number of "shell"-layers. HR TEM validated these results and demonstrated the formation of composite particles, in which ultrafine CeO_2 NPs were uniformly anchored on the surface of Fe_3O_4 NPs, forming "hedgehog"-like "core@shell" NCPs (Fig. 1a, b). It is worth noting that synthesis via "layer-by-layer" deposition provides obtaining Fe_3O_4@CeO_2 NCPs, whose morphology differs from the NCPs investigated and published recently in [2]. The calculated average size of these particles grew with the increase in the number of "shell layers" in the range from 20 to 35 nm (Fig. 1c). The magnetic measurements data demonstrated the expected decrease in magnetization values for NCPs caused by the increase in the non-magnetic CeO_2 percentage in the sample. At the same time, Fe_3O_4@CeO_2 NCPs saved the ability to heat up effectively in an alternating magnetic field (AMF). The magnetic fluids prepared based on the Fe_3O_4@CeO_2 NCPs possessed the high stability determined by their high positive zeta potential (ζ ≥ +30 mV).

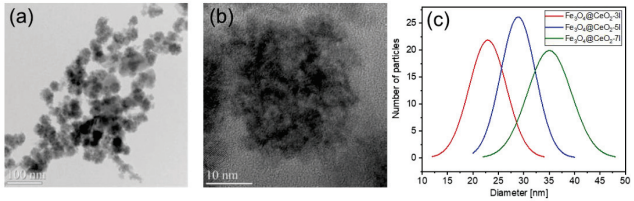

Figure 1. Representative TEM images for Fe_3O_4@CeO_2 NCPs with 5-layers of shell (a, b) and size distributions curves for a set of Fe_3O_4@CeO_2 NCPs

The prepared Fe_3O_4@CeO_2 NCPs possessed pronounced bio-activity (antioxidant and anti-amyloid activities). It is expected that the ability of these composites to heat up effectively will enhance their bioactivity potential when compared with individual Fe_3O_4 and CeO_2 NPs.

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Acknowledgement: This work was partially supported by grants No 0124U002212 in the framework of the Target Program of Scientific Researches of the NAS of Ukraine "Grants of the NAS of Ukraine to research laboratories/groups of young scientists of the NAS of Ukraine" (2024–2025), APVV 19-324 and MVTS SK-TW Azcai.

Magnetic Cubic Nanoparticles Based on Iron Oxide Doped by Metal Ions for Enhancing Magnetic Performance

Zuzana Šiška[1,2], Pavla Roupcová[1,2], Lubomír Havlíček[1,2], Roman Gröger[1,2], and Naděžda Pizúrová[1]

[1]Institute of Physics of Materials & CEITEC IPM, Czech Academy of Sciences, Žižková 22, 616 00 Brno, Czech Republic, siska.zuzana@ipm.cz

[2]Central European Institute of Technology, Brno University of Technology (CEITEC), Purkyňova 123, 612 00 Brno, Czech Republic, Zuzana.Kavciakova@ceitec.vutbr.cz

Nanoparticles based on the principle of magnetic activity applicable to biomedical applications have been getting the attention of many scientists owing to their magnetic properties and excellent biocompatibility. Currently, one of the most promising approaches involves using iron oxide and doped ferrite magnetic nanoparticles (MNPs). MNPs emerge as an auspicious new material for magnetic resonance imaging (MRI) and magnetic particle imaging (MPI) tracers. The challenge that still remains is the use of MNPs for magnetic hyperthermia (MH) focused on cancer cell therapy. The heating efficiency of MNPs induces raising temperature of cancer cells to a level that damages or kills them. This makes them a potentially attractive heating medium for MH.

To improve the magnetic performance of MNPs, we prepared a series of mixed transition metal (TM) ferrite nanoparticles using a thermal decomposition method. The main objective of the study was to carry out structural and magnetic characterization concerning the size, shape, composition, and magnetic properties. A key point in tuning the size and shape of the nanoparticles was to appropriately choose the synthesis parameters, such as the heating ramp, time and temperature of degassing, nucleation, and reflux. The concentration of nickel (Ni^{2+}) cobalt (Co^{2+}) dopants in ferrite MNPs was adjusted to obtain with size <20 nm (single-domain) preventing them from aggregating due to the absence of remanent magnetization at zero field. The cubic shape of the MNPs was achieved using the squalene/solvent ratio and the concentration of surfactant, which affected not only the shape but also the resulting size of MNPs. All MNPs samples subjected to TEM, EDS, and XRD analysis confirmed the phase composition of dopants in ferrite MNPs. The chemical and structural nature of nickel-cobalt ferrite MNPs compared to nickel-and-cobalt ferrite MNPs was correlated to their magnetic properties. Especially, the evaluation of M-H loops, ZFC/FC curves, M_S, and coercivity that were measured using PPMS. The detailed analysis of the mechanism of the doping effect in ferrite MNPs clarifies the influence of TM ions on its magnetic properties which could open new perspectives in designing biomedical nanomaterials with tailored properties by choosing suitable cation substitution.

Testing The Efficacy Of Magnetic Hyperthermia Using Non-Harmonic Electromagnetic Fields In Combination With Chemotherapeutic Drugs (5-Fluorouracil) : An In Vitro Study On Melanoma And Glioblastoma Multiforme Cell Lines

Lilia Souiade[1,*], Miguel-Ramón Rodríguez-García[1], Javier Domingo-Diez[1], Josefa Quiroz-Troncoso[4], Milagros Ramos[2,3,4] and José-Javier Serrano-Olmedo[1,2,3]

[1] Laboratory of Bioinstrumentation and Nanomedicine, Center for Biomedical Technology, Universidad Politécnica de Madrid, Campus de Montegancedo s/n, Pozuelo de Alarcón, 28223 Madrid, Spain;

[2] Centro de Investigación Biomédica en Red para Bioingeniería, Biomateriales y Nanomedicina, Instituto de Salud Carlos III, 28029 Madrid, Spain

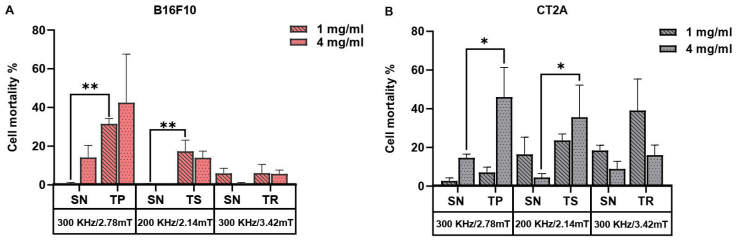
[3] Departamento de Tecnología Fotónica y Bioingeniería, ETSI Telecomunicaciones, Universidad Politécnica de Madrid, 28040 Madrid, Spain

[4] Experimental Neurology Unit, Center for Biomedical Technology, Universidad Politécnica de Madrid, Campus de Montegancedo s/n, Pozuelo de Alarcón, 28223 Madrid, Spain

*Email: lilia.souiade@ctb.upm.es

It has been previously shown that the use of trapezoidal pulsed alternating magnetic fields (TPAMF) on superparamagnetic nanoparticles enhance the efficiency of heating in magnetic hyperthermia and improve better the killing effect against cancer cells compared to the sinusoidal one. After some preliminary results presented previously, a systematic study is being carried out, both in cell cultures and with modal animals (mice), of the effective superior efficacy of the new treatment with non-harmonic fields with the aim of determining the optimal application conditions for tumour removal, as well as acquiring a better understanding of the physical-biological mechanisms behind this phenomenon. This conference contribution presents the results obtained so far, which are partially included in a paper under revision and partially new ones. Alternating symmetric pulsed magnetic fields of frequency ranging from 100kHz to 1MHz with trapezoidal waveforms have been essayed with several slopes from triangular to almost square (namely: TR (triangular), TP (trapezoidal with 50% flat) and TS (nearly square with 75% flat), as well as the sinusoidal waveform for comparison. Superparamagnetic particles at several concentrations have been used, ensuring the biocompatibility of the doses used, as well as the combination of thermal therapy and chemotherapy. The average temperature measured in cell culture does not exceed 1°C over the background temperature. An efficiency in the destruction of tumour cells is observed using non-harmonic fields, that becomes as higher as 30% compared to the use of harmonic magnetic fields, all the rest of variables equal but the type of pulse used. Differences are also observed between cell lines (See figure). The combination of mild hyperthermia and chemotherapy holds great promise for cancer treatment by inducing immunogenic cell death. The process of immunogenic cell death involves the release of danger signals from dying cancer cells, which in turn activates the immune system to target and destroy remaining cancer cells. The process of immunogenic cell death involves the release of danger signals from dying cancer cells, which in turn activates the immune system to target and destroy remaining cancer cells. Herein, we explored local mild magnetic hyperthermia in combination with chemotherapeutic drugs to boost the killing effects of our treatment plan and to induce immunogenic cell death (ICD). Although much more work is needed to fully understand the complex phenomena underpinning this extra mortality, our results reinforce the hypothesis that magnetic hyperthermia could really become an alternative technology for new improved anticancer therapies.

Figure: Cell mortality rates obtained by quantification using Image J software based on Calcein /PI test on B16F10 and CT2A cells subjected to two different treatment conditions. B16f10 cells exposed to different AMFs signals (TP/SN, TR/SN, TS/SN) for 30 min at 1 mg/ml and 4 mg/ml of APS-SPION (A). CT2A cells exposed to different AMFs signals (TP/SN, TR/SN, TS/SN) for 30 min at 1 mg/ml and 4 mg/ml of APS-SPION (B)



A novel method for improving sensitivity of MPI based on modulation of offset field and even harmonic signal

Zhongwei Bian[1,2], Ziwei Chen[1,2], Yu An[1, 2*],Jie Tian[1,2 *]

[1]School of Biological Science and Medical Engineering, Beihang University, Beijing, China
2 key Laboratory of Big Data-Based Precision Medicine (Beihang University), Ministry of Industry and Information Technology of the People's Republic of China, Beijing, 100191, China
*Email: tian@ieee.org

Magnetic particle imaging (MPI) relies on the nonlinearity of the magnetization curves of ferromagnetic material at high magnetic field strength, and it holds promise for high spatial resolution and sensitive detection of tracers in biomedicine. In MPI, nonlinear harmonic interference caused by electronic components is a typical problem, which to some extent distorts or affects the accuracy of the quantification of superparamagnetic iron oxide nanoparticles (SPIONs) and affects the sensitivity limits of measurement.

We propose a single-even harmonic imaging mode based on orthogonal scanning to suppress nonlinear harmonic interference. In this scanning mode, the excitation magnetic field is applied perpendicular to the imaging plane, and the entire 2D plane is traversed through point-by-point scanning. Each scan point contains both positive and negative states by modulating offset field, and the even harmonic signal is preserved by taking the difference between the signals of these two states.

We enhance the signal strength of even harmonics based on modulation of the offset field, which is an effective means to improve sensitivity. In the simulation results, the signal strength of the fundamental frequency is the highest. However, considering the actual measurement process, the fundamental frequency is usually filtered out due to interference from Excitation Feed-Through. Therefore, to ensure the stability of the measurement process, it is more reasonable to use harmonic signals from other frequency bands. The second harmonic has a stronger signal strength than the third harmonic, which favors sensitivity enhancement. In terms of suppressing harmonic interference, conventional background reduction techniques require the sample to be removed from the scanner to achieve a null background measurement. Our approach involves the use of the modulation of offset field, eliminating the need for frequent sample movement, which also ensures system stability for a long-duration signal acquisition.

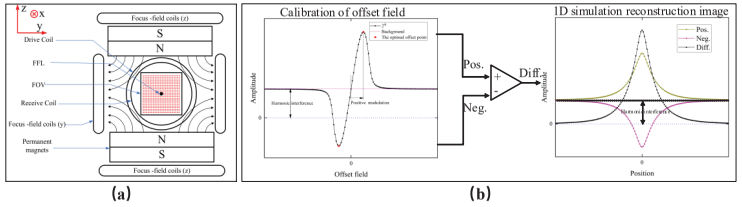


Figure. (a) Structure concept of scanner. The excitation field is applied along the Field-Free-Line (FFL) whose direction is orthogonal to the 2D plane. (b) Image reconstruction process of second harmonic based on modulated of offset field.

Fe-Cr-Nb-B magnetic particles for targeted chemotherapy

Cristina Stavila[1,2*], Anca Emanuela Minuti[1], Horia Chiriac[1], Nicoleta Lupu[1]

[1] Magnetic Materials and Devices, National Institute of Research and Development for Technical Physics, Iasi, Romania.
[2] Faculty of Physics, "Alexandru Ioan Cuza" University, Iasi, Romania.
Email: cstavila@phys-iasi.ro

The use of magnetic nanoparticles in cancer therapy offers promising opportunities for enhanced treatment outcomes. This study focuses on investigating the potential of Fe-Cr-Nb-B magnetic particles (MPs) for targeted chemotherapy applications. These MPs, characterized by their unique shape anisotropy, high saturation magnetization and low Curie temperature, exhibit promising capabilities for magnetic hyperthermia [1] and magneto-mechanical actuation (MMA) [2] in cancer treatment.

This study investigates the loading capacity of Fe-Cr-Nb-B MPs with clinical-grade chemotherapeutic agents and their potential use in targeted chemotherapy through magneto-mechanical actuation for cancer cell destruction. In the experimental setup, Fe-Cr-Nb-B nanoparticles were obtained by wet milling in oleic acid surfactant of amorphous ribbons. The nanoparticles were loaded with either Mitoxantrone (MTX) or Doxorubicin (DOX), whose quantity can be adjusted up to maximum drug loading. Drug-release tests were carried out using dialysis-bag method over 72h time. After a 30 min session of MMA, Adipose-Derived Mesenchymal Stem Cells (ADSC- healthy cells) and HOS (cancer cells) co-incubated with drug-loaded Fe-Cr-Nb-B MPs containing 1 % m/m of chemotherapeutic, were assessed using MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) cell viability test.

Results showed that $Fe_{68.2}Cr_{11.5}Nb_{0.3}B_{20}$ MPs can be efficiently loaded with MTX or DOX at considerable levels of up to 7.45% m/m for MTX and 7.02% m/m for DOX, as maximum drug loading and 21-24% cumulative drug release over 72 hours. This amount of chemotherapeutic is considered high for this type of particles, compared to other uncoated nanoparticles. Cell viability results after drug-loaded Fe-Cr-Nb-B MPs co-incubation and magneto-mechanical actuation on both ADSC and HOS, demonstrate selective toxicity towards cancer cells. MTT test also reveals efficient dual therapy consisting of both chemical and magnetic mechanisms. This research underscores the potential of Fe-Cr-Nb-B MPs as a feasible platform for targeted chemotherapy, offering improved therapeutic efficacy and reduced side effects in cancer treatment.

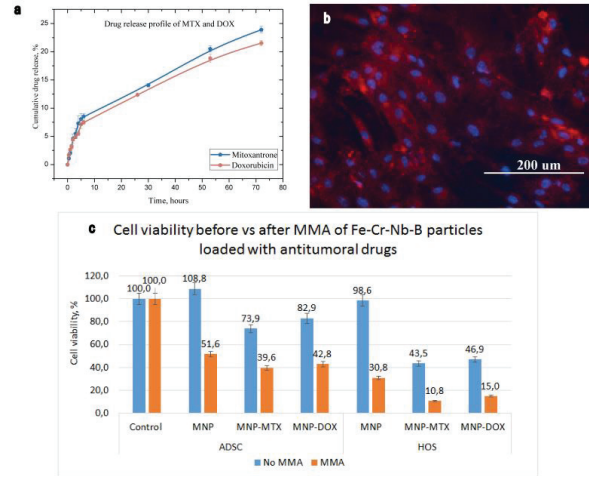


Figure 1. Fe-Cr-Nb-B magnetic particles loaded with Mitoxantrone or Doxorubicin. a) Drug release profiles of MTX or DOX; b) DOX-loaded MPs distribution in cell culture (blue color-DAPI stained cell nuclei, red color- DOX-loaded nanoparticles), images taken in GFP and RFP fluorescence filters, EVOS microscope; c) Cell viability after 24 hours of co-incubation with drug-loaded Fe-Cr-Nb-B MPs with 1 %m/m of chemotherapeutic, before and after MMA.

Financial support from the MCID Nucleu (PN 23 11 01 01) and PFE (Contract No. 5PFE/2022) Programmes is highly acknowledged.

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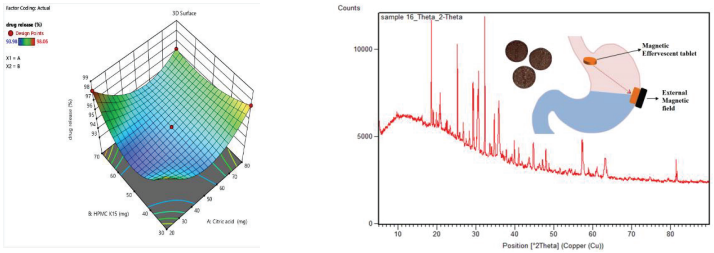
Formulation Optimization, Evaluation of Magnetically Targeted Pantoprazole Effervescent Tablets for Enhanced Anti-Ulcer Therapy

Latha Subbiah*, Krishnanand Nagarajan, Yogeshwaran Murugan and Selvamani Palanisamy

Department of Pharmaceutical Technology and Centre for Excellence in Nanobio Translational Research, University College of Engineering, Bharathidasan Institute of Technology Campus, Anna University, Tiruchirappalli – 620024, Tamil Nadu, India

*Email: lathasuba@aubit.edu.in Mobile: +91-98425 98097

Ulcers, a prevalent gastrointestinal disorder, arise when the lining of the alimentary tract becomes inflamed or damaged. Conventional treatment often poses several challenges and inefficiency due to insufficient drug targeting and systemic side effects associated with conventional oral medications. To address these issues, the present study was aimed to enhance the therapeutic effectiveness of pantoprazole, a widely used proton pump inhibitor, through the development of magnetically targeted effervescent tablets. These tablets, comprising pantoprazole sodium, effervescent excipients, and a magnetizable carrier material, underwent meticulous optimization using a Design of Experiments (DoE) approach to achieve desirable quality parameters such as disintegration time, effervescent time, and drug release profile. Several key studies were conducted to assess the formulation and performance of the tablets. Pre-formulation studies provided insights into ingredient compatibility, while pre-compression studies evaluated critical physicochemical parameters, all of which met the standards outlined by the Indian Pharmacopeia (I.P.). Optimization using Response Surface Methodology (RSM) with Central Composite Design (CCD) resulted in the identification of optimal parameters for effervescent time, disintegration time, and drug release percentage. Post-compression investigations confirmed the quality of tablets, demonstrating satisfactory attributes such as hardness, appearance, thickness, friability, drug content uniformity, and disintegration time. *In-vitro* dissolution studies revealed varying drug release percentages among different (F1, F2, F3 & F4) formulations, with formulation F2 displaying the most optimal release profile. The best drug release pattern was described by the first-order kinetic model, indicating a concentration-dependent reaction. Analysis through Fourier-transform infrared (FTIR) spectroscopy validated the presence of characteristic chemical bonds and functional groups in the pantoprazole formulation. X-ray diffraction (XRD) analysis confirmed the amorphous nature of the final formulation and detected diffraction peaks indicative of Fe_3O_4, suggestive of magnetic nanoparticles. These nanoparticles exhibited superparamagnetic behaviour, losing magnetism upon removal of the externally applied magnetic field, with a saturation magnetization of 3.9 emu/g. The results of the *in vivo* evaluation of the anti-ulcer capabilities shown that formulation F2 exhibited significant inhibition of ulcer formation in animal model subjected to externally applied magnetic field, surpassing the performance of traditional models. In conclusion, the results affirm the efficacy and quality of the developed effervescent granules, highlighting their potential for therapeutic applications, particularly in targeted drug delivery for ulcer treatment.



(a) (b)

Figure: (a) Drug content interaction effects; (b) XRD Analysis showing Pantoprazole Sodium and Iron Oxide Nanoparticles in final formulation.

Graphite oxide/nickel ferrite nanocomposites for magnetic hyperthermia

Anna Vas[1], Erzsébet Illés[2*]

[1] Department of Physical Chemistry and Materials Science, University of Szeged, Szeged, Hungary
[2] Department of Food Engineering, University of Szeged, Szeged, Hungary
E-mail: erzsebet.illes@mk.u-szeged.hu

Magnetic iron oxide nanoparticles (MNPs) are well-known for their great potential for biomedical use (for example drug-delivery, MRI contrast enhancement and hyperthermia), hence their possible diagnostic and therapeutic application has been the centre of many studies in the recent years. Beside magnetite, nickel-ferrite nanoparticles also seem to have promising magnetic properties for utilization in magnetic hypertermia. However, they require biocompatibilization with the application of a highly hydrophilic coating. Graphite oxide (GO) is a hydrophilic material, with high surface area and tuneable pH-dependent surface charge properties. By synthesizing GO/ MNP nanocomposites, it is possible to further enhance the heat production caused by an alternating magnetic field during hyperthermia sessions.

To study the effect of the nickel content and the various polymers used as protective layers on the surface of magnetic nanoparticles, nanocomposites were prepared with 1/5 and 1/10 GO/MNP mass ratios. The nickel content was 0%, 10% and 20%, while two different polymers (PAM and PEGMA-AA) were used to fully coat the nanomagnets. The dynamic light scattering (DLS) data on the coagulation kinetics of the various nanocomposite samples showed that there are notable differences in their colloidal stability. The critical coagulation concentrations were higher when PAM polymer was used and the nickel ratio also influenced the tolerance of the nanocomposites towards higher NaCl concentrations. Exposure for alternating magnetic field for 5 minutes showed that increasing the frequency (at the same magnetic field strength) results in a higher heat production. We are also planning to test hemocompatibility to evaluate the effects of the nanocomposites on blood components.

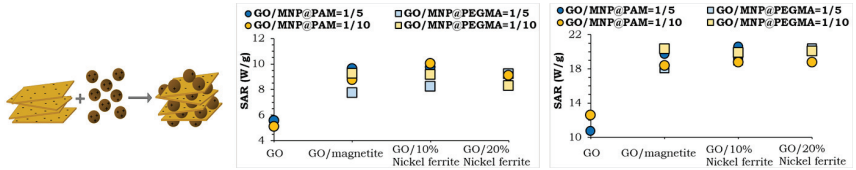


Figure 1. Schematic figure of formation (left) and AC magnetic hyperthermia of coated GO/ferrite composites at 109 kHz (centre) and 329 kHz (right)

Acknowledgments: This research was supported by the Hungarian National Research Development and Innovation Office (NRDIH) through the FK131739 project and by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.

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Studies of the magnetophoresis of magnetic labelled cells using a constant gradient separation device

Julia Martinez-Ramirez[1], Juan Víctor Caz[1], Lluis M Martinez[2], Maria Concepción Serrano[1] and Sabino Veintemillas-Verdaguer[1]

[1]Instituto de Ciencia de Materiales de Madrid, ICMM/CSIC, 28049 Madrid, Spain

[2] Sepmag Systems, Parc Tecnològic del Valles, E-08290 Barcelona, Spain

The ability to measure the mean iron content and its distribution in cells cultured in the presence of magnetic nanoparticles using their magnetophoretic motion has the potential to provide immediate feedback about a given labeling process and facilitate its optimization. Monitoring the separation process was carried out by optically detecting the transparency of a cell suspension subjected to a constant radial magnetic field gradient of 24T/m in a commercial device. A well stablished theory [1] had been developed for this process that permit the calculation of the magnetophoretic velocities that the cells attain during the separation process. This communication describes the protocol of the measurement, the approximations made in the determination of the magnetophoretic coefficient and the distribution of iron content among the cells. These procedures were applied to the labelling of L929 mouse fibroblasts loaded with chitosan coated magnetic nanoparticles and assessed by chemical analysis using standard procedures.

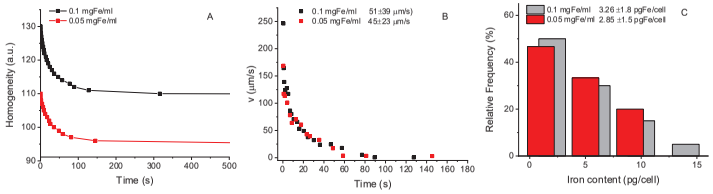

Figure 1. Comparison of two magnetophoretic experiments using L929 fibroblast cultured in presence two concentrations of chitosan coated magnetic nanoparticles of 8 nm. (A) raw data, (B) calculated magnetophoretic velocities and (C) Average iron contend and iron distribution among the cells. The analytical iron content per cell was 2.47 pgFe/cell for 0.1mg Fe/ml and 1.45 pgFe/cell for 0.05 mg Fe/ml.

[1] Andreu, Jordi S. et al. "Simple analytical model for the magnetophoretic separation of superparamagnetic dispersions in a uniform magnetic gradient." *Physical review. E, Statistical, nonlinear, and soft matter physics* 84 2 Pt 1 (2011): 021402.

Dynamic Monitoring of Magnetic Nanoparticle Translocation into Monkey Brain via Intranasal Administration Using MRI

Masaomi Washino[1*], Kota Nomura[1,3], Akiko Tanaka[2], Toshiyasu Sakane[2], Satoshi Seino[3], Takashi Nakagawa[3], Yuki Hori[4], and Naruhiko Sahara[4]

[1] Advanced Technology R&D Center, Mitsubishi Electric Corp., Hyogo, Japan.
[2] Department of Pharmaceutical Technology, Kobe Pharmaceutical University, Kobe, Japan.
[3] Graduate School of Engineering, Osaka University, Osaka, Japan
[4] Department of Functional Brain Imaging, National Institutes for Quantum and Radiological Science and Technology, Chiba, Japan
*Email: Washino.Masaomi@ap.MitsubishiElectric.co.jp Mobile: +81-6-6497-3470

Magnetic Particle Imaging (MPI) involves injecting magnetic nanoparticles (MNPs) into the body as tracers for disease detection. We are developing functional MNPs that bind to specific targets, particularly for neurodegenerative diseases like Alzheimer's [1-2]. The blood-brain barrier (BBB) poses challenges for intravenous MNPs delivery to the brain, prompting us to explore intranasal administration as an alternative route. Recent advancements in intranasal drug delivery to the brain have primarily involved studies with monkeys [3], whereas research on intranasal delivery of MNPs has focused on mice [4]. We conducted intranasal administration in monkeys and monitored brain entry using MRI in vivo imaging.

We used two cynomolgus monkeys from New Drug Research Center, Inc. and administered functional MNPs (10.6 mg Fe/mL, 0.5 mL in each nasal cavity) via spray inhalation 72 and 24 hours before MRI scans. A custom spray device was employed, and MRI was performed with a human MRI machine (Signa HDxt 3.0T, GE Yokogawa Medical Systems) at 24 and 72 hours post-administration initially. Subsequently, the same monkey from the 72-hour group received another MNP dose via the same method, and MRI scans were conducted 30 minutes, 1 hour, 3 hours, and 4 hours later. This study was approved by the Animal Care Council at New Drug Research Center, Inc.

The MRI images of the monkey head are shown in Fig. 1. Imaging from 30 minutes to 4 hours post-administration shows black areas in the nasal mucosa and near the olfactory bulbs. In contrast, brain tissue imaging is visible at 24 hours and 72 hours post-administration. This suggests that the administered functional MNPs reached the nasal mucosa and near the olfactory bulbs, remained there from 30 minutes to 4 hours post-administration, and disappeared by 24 hours and 72 hours post-administration.

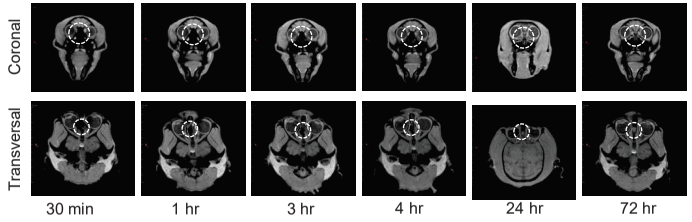

Figure. 1 MRI images of the monkey head after intranasal administration (circled areas indicate the location of the olfactory bulbs). The top row depicts coronal sections, and the bottom row shows transversal sections. Images at 24 hours post-administration are from a different individual, while the rest are from the same individual.

Acknowledgements
We would like to express our gratitude to New Drug Research Center Inc. and Hamamatsu University School of Medicine for their assistance in refining this research. This work was supported by AMED under grant numbers JP20hm0102073, JP21hm0102073, and JP22hm0102073.

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[1] K. Nomura et al.: *IEEE Magn. Lett.*, 14, 8100105 (2023).
[2] S. Seino et al.: *Journal of Controlled Release*., 367, 515-521 (2024).
[3] T. Sakane et al.: *Pharmaceutics*., 12, 1227 (2020).
[4] D Kou et al.: *Nano Lett.*, 23, 11, 5381–5390 (2023).

Molecular Dynamics Simulation of Interacting Magnetic Nanoparticles using a Hybrid Approach of Langevin dynamics and Monte Carlo Simulations

***M. Wolfschwenger*[1*], *A. Jaufenthaler*[1], *F. Hanser*[1], *D. Baumgarten*[1]**

[1] Institute of Electrical and Biomedical Engineering, UMIT TIROL – Private University for Health Sciences and Health Technology, Hall in Tirol, Austria
* manuel.wolfschwenger@umit-tirol.at

Magnetic nanoparticles (MNPs) are of interest for a variety of biomedical applications, e.g. for cancer treatment. A very promising therapy is magnetic drug targeting, where precise prediction of the local particle accumulation is required. This is a very challenging task due to several complex flow phenomena. Computational models can provide support to improve the scientific knowledge of those phenomena and act as planning tools. For this purpose, a variety of macroscopic fluid-flow models describing the particle transport have been developed. They can be applied to macroscopic systems but are limited in simulating realistic particle ensembles with all interactions due to the vast number of particles involved. Therefore, microscopic models are needed. Studying ferrofluid dynamics on microscopic scales, however, is quite challenging due the huge difference in timescales between magnetic motion and physical movement of the particles. Therefore, we aim at developing and validating a model that handles the huge difference in timescales efficiently. Slow mechanical degrees of freedom are handled by Langevin dynamics (LD), whereas the Monte Carlo (MC) method is used for equilibrating the magnetic subsystem.

For our model, we assume all MNPs to be spherical, uniformly magnetized and to have uniaxial anisotropy. Each particle consists of a magnetic core surrounded by a stabilizing surfactant layer. The cores can be considered as single domain particles with a total magnetic moment. The solvent is considered as thermally equilibrated at the timescale of the MNP's motion. Thus, the random collisions of the solvent molecules with the MNPs are modelled as fast fluctuating terms.

The particles in colloidal systems interact with each other through several repulsive and attractive forces. We implemented the attractive van der Waals forces, the magnetic dipole-dipole interactions and the repulsions from the electrostatic double layer and steric interactions. To compute the interactions between the particles, we use the Ewald summation method, with an error control algorithm. Periodic boundary conditions are employed to study the properties of bulk material. Adaptive timestep solvers with an embedded solution are used to perform the numerical integration of the differential equations.

We successfully validated our model with known analytical results and investigated several cases of structure formation with and without external applied magnetic fields.

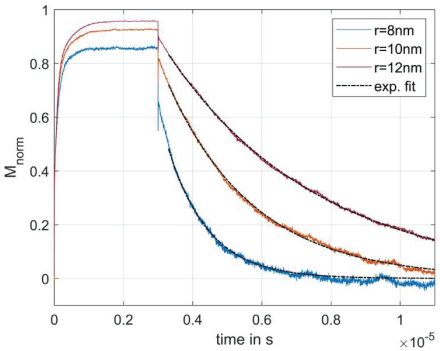

Figure 1: Magnetization and relaxation of non-interacting particles of different size.

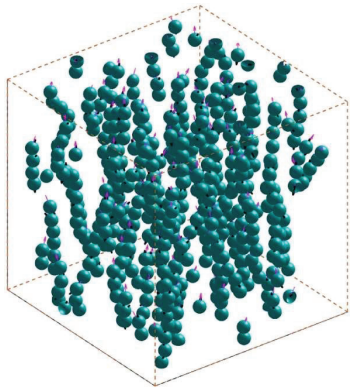

Figure 2: Simulated particle ensemble yielding chain structures.

Biocompatibility and Cytotoxic Evaluation of Cobalt-Doped Magnetite (Co-Fe_3O_4) Nanoparticles on Breast Cancer Cells

Camelia-Mihaela Zara-Danceanu[1,2], Mirela Nistor[1,3], Aurel Pui[3], Vera Balan[1,4], Rares-Ionut Stiufiuc[1,5], Brindusa Dragoi[1,3*]

[1]*Nanotechnology Laboratory, TRANSCEND Research Center, Regional Institute of Oncology, 2-4 General Henri Mathias Berthelot Street, 700483 Iași, Romania*
[2]*National Institute of Research and Development for Technical Physics, 700050, Iasi, Romania*
[3]*Faculty of Chemistry, Alexandru Ioan Cuza University of Iași, 11 Carol I Boulevard, 700506 Iași, Romania*
[4]*Biomedical Sciences Department, Faculty of Medical Bioengineering, Grigore T. Popa University of Medicine and Pharmacy of Iasi, 9-13 Kogalniceanu Street, 700454 Iasi, Romania*
[5]*Department of Nanobiophysics, MedFuture Research Center for Advanced Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy, 4-6 Pasteur Street, 400337 Cluj-Napoca, Romania*
*Email: brindusa.dragoi@yahoo.com" brindusa.dragoi@yahoo.com

According to the World Health Organization, breast cancer is the second leading cause of death for women in the world. Globally, this disease causes over 650.000 deaths annually. Various conventional treatments such as radiotherapy, chemotherapy and surgery have been used for several decades to treat breast cancer; however, many of these treatments are associated with serious side effects, including death. The development of reliable and well-tolerated cancer nanomedicines is one of the key objectives of modern approaches for cancer therapy, such as targeted therapy, magnetic hyperthermia, and ferroptosis-based therapy. The use of magnetic nanoparticles (MNPs) for breast cancer diagnosis and therapy has become more common because of their controllable properties, such as size, shape, surface chemistry and thermochemical stability, along with their biocompatibility.

Magnetite doped with varying concentrations of cobalt (1%, 5%, 10%) and cobalt ferrite NPs were synthesized employing a wet chemical approach, specifically through the coprecipitation of metal chloride solutions (2:1, molar ratio), conducted within a basic medium and facilitated by the presence of a surfactant, Pluronic F127.

We investigate in detail the intrinsic physiochemical and magnetic properties of Co-doped Fe_3O_4 and cobalt ferrite NPs, as well as their biocompatibility and cytotoxicity. The main properties, that is, crystallinity and magnetic behavior, were evaluated by means of powder X-ray diffraction (XRD) and Vibrating Sample Magnetometry (VSM), respectively. XRD analysis confirmed the formation of the cubic spinel structure with crystallite sizes around 10 nm. The as-synthesized Co-doped Fe_3O_4 magnetic nanoparticles exhibit superparamagnetic behavior (55-58 emu/g). Other chemical, structural, and morphological properties were assessed by DLS, Zeta Potential, FTIR, and TEM.

Biocompatibility of the as-synthesized Co-doped Fe_3O_4 of various concentrations (3, 10, 30, 90 and 270 µg/ml) at different time intervals (24, 48 and 72 h) against human breast cancer (MDA-MB-231, HCC, MCF-7) cell lines and normal human breast cells (MCF-10A) has been evaluated. Compared to control samples, synthesized MNPs showed low cytotoxicity in all cell types, making them suitable candidates for biomedical applications, such as cancer diagnosis, molecular imaging, hyperthermia, and drug delivery. Morphological analysis confirms the findings of the MTT test; cells incubated with various concentrations of Co-doped Fe_3O_4 exhibit normal morphology with the particles distributed on the surface of the cells.

Acknowledgments: H2020–ERA-Chair, no 952390 and PN-III-P3-3.6-H2020-2020-0105/35/2021 (UEFISCDI).

Is it Possible to Explain SAR in Nanoparticle-Mediated Magnetic Hyperthermia As The Linear Sum Of Harmonic Contributions When Using Pulsed Alternating Magnetic Fields?

Moisés Gilberto Zaragoza Medina[1]*, Isidoro Martínez Ramírez [2,3], Lorena Marrodán-Bretón[2,3], Jaime Santoyo Salazar[1] and José Javier Serrano-Olmedo[2,3]**

[1] Center for Research and Advanced Studies of the National Polytechnic Institute, 07360 Ciudad de México, México;
[2] Laboratory for Bioinstrumentation and Nanomedicine, Center for Biomedical Technology (CTB), Universidad Politécnica de Madrid (UPM), 28040 Madrid, Spain;
[3] Networking Center for Biomedical Research: Bioengineering, Biomaterials and Nanomedicine, Instituto de Salud Carlos III, 28029 Madrid, Spain;
Emails: *moises.zarzoza@cinvestav.mx, **josejavier.serrano@upm.es

Magnetic nanoparticles (MNPs) have the ability to absorb energy when they are subjected to an external magnetic field. In an alternating magnetic field, the supplied energy increases as multiple cycles of magnetization are completed per unit of time. Consequently, if all the energy absorbed by the MNPs is converted into heat, it becomes an ideal method for hyperthermia treatment.

It has been observed that these treatments improve when high frequencies are utilized (100 kHz - 1 MHz), resulting in increased heat production using low concentrations of MNPs. However, there are clinical and equipment limitations which may lead to a loss of control over the treatment's effects. New approaches would contribute to solve these problems.

Physical models for a mono-frequency signal (sinusoidal pulses) have been proposed and experimentally validated. Therefore, if this model is extended to encompass all frequencies present in a non-sinusoidal signal, it should match the data for any signal shape. In this contribution, we compare the simplest model with experimental data for five different signal shapes: sinusoidal (Sin), triangular (TR), triangular trapezoidal (TT), trapezoidal (TP), and Square Trapezoidal (TS) signals in a magnetic hyperthermia experiment at various magnetic field amplitudes, frequencies of 100, 200 and 500 kHz and concentrations of 38.6 and 75 mg/ml. Maghemite MNPs with a diameter of 10 nm are dissolved in water and isolated from the environment within a calorimeter composed of two shells: one shell consists of water maintained at a constant temperature (37°C), and an inner shell that creates a void between the water and the recipient with MNPs.

The needed parameters, which are the magnetic anisotropy K (J/m^3), τ_N (s), which characterizes the Neel relaxation time at 310 K, the Curie temperature T_c (K), which characterizes the magnonic effect that reduces magnetization as a function of temperature, and the initial temperature T_0 (K), are obtained by fitting into sinusoidal data and projected into the rest of the wave forms. This projection can be seen in the figure 1.

The result was for those shapes where the contribution of high frequencies are low, then the supposition of superposition of the power for all the harmonics present in the signal is accurate. However, for the signal TS, where is needed high frequencies, suggest that the model fails for large frequencies, questioning the most common model used in the literature.

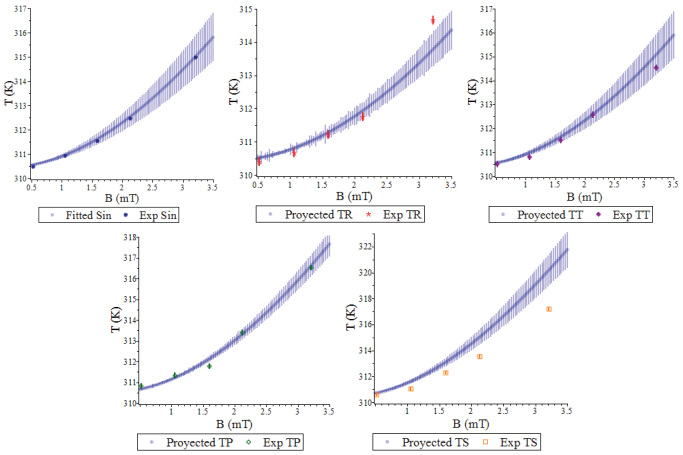

Figure 1: Experimental and projected data of magnetic hyperthermia were collected. The reported temperatures were measured at 100 kHz for various values of magnetic field amplitude after 15 minutes of exposure, starting from an initial temperature of 37 °C. Magnetic nanoparticles (MNPs) were dissolved in water at a concentration of 75 mg/ml.

Stability studies of ultrasmall iron oxide nanoparticles for MRI T_1 contrast agent

Mingyi Zheng[1], Liudmyla Storozhuk[1], Graeme Stasiuk[2] and Nguyen TK Thanh[1]*

*ntk.thanh@ucl.ac.uk, http://www.ntk-thanh.co.uk

[1]Biophysics Group, Department of Physics & Astronomy University College London, Gower Street, London WC1E 6BT, UK and UCL Healthcare Biomagnetics and Nanomaterials Laboratories, 21 Albemarle Street, London W1S 4BS

[2]Imaging Chemistry and Biology, School of Biomedical Engineering and Imaging Sciences, King's College London,,St. Thomas' Hospital. Westminster Bridge Road, London, SE1 7EH

Currently, ultra-small superparamagnetic iron oxide nanoparticles (USPIONs) have emerged as promising T_1 contrast agents for MRI due to their good biocompatibility compared to gadolinium-based contrast agents that have been approved for clinical use, as well as their high r_1 relaxation rate and adjustable pharmacokinetics.[1] It is crucial to understand the biocompatibility properties of nanoparticles and how they effects on the body.

Previously in our group we synthesised different core sizes (1.7 ± 0.3 nm (F-50), 2.7 ± 0.5 nm (F-5), 5.4 ± 0.5 nm (F-0)) nanoparticles.[2] Dynamic light scattering (DLS) results show that F-50 is the most stable, and its hydrodynamic diameters (d_h) remained unchanged up to 0.9 M, only slight increase and statistiscally different at 1.1 M NaCl (Figure 1a). However, F-5 showed aggregation with a significant increase in particle size at 1.1 M NaCl (Figure 1a). F-50 and F-5 are also most stable for a wide range of pH 4-9, while F-0 became unstable for at all pH (Figure 1b).

According to these results, F-50 is a suitable candidates for exploring their potential applications in biomedicine using different tests such as CCK-8 assay, prussian blue staining, assessment of ROS generation, fluorescence microscopy.

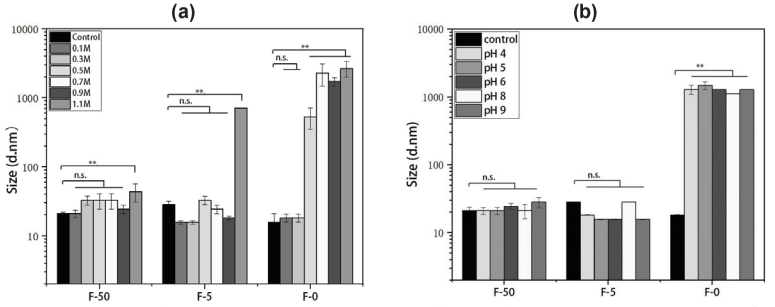

Figure 1. Variation of d_h for three USPIONs under different **a**) ionic strengths conditions **b)** pHs measured by DLS. The results are presented as mean ± s.d., n=3. Statistical analysis was performed using Student's t-test and the significance is displayed as * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Reference:

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2. Nanoscale, 2021, 13, 8795.

Quantification Results of Targeted Magnetic Particles In vivo and In vitro Human Tissues Based on Self-developed FFL-MPI

Siao Lei[1,2], Chao Li[3], Yuan Feng[1,2], Jie He[1,2], Jian Zhou[3*], Yu An[1, 2*], and Jie Tian[1,2*]

[1] School of Engineering Medicine and School of Biological Science and Medical Engineering, Beihang University, Beijing, China

[2] CAS Key Laboratory of Molecular Imaging, the Beijing Key Laboratory of Molecular Imaging, Institute of Automation, Chinese Academy of Sciences, Beijing, China

[3] Department of Thoracic Surgery, Peking University People's Hospital, No.11 Xizhimen South Street, Xicheng District, Beijing, China

*Email: zhoujian@bjmu.edu.cn, yuan1989@buaa.edu.cn, tian@ieee.org

Magnetic Particle Imaging (MPI) is an innovative molecular imaging technique that enables the quantification of magnetic particle concentrations. The MPI device, based on the field-free line (FFL), has attracted considerable attention due to its superior signal-to-noise ratio, along with its open structure offering enhanced operational versatility. Our self-developed FFL-based open MPI device has exhibited outstanding performance in terms of resolution and low power consumption.

To ascertain the suitability of this device for in vivo applications and its compatibility with human tissue, we conducted experiments using a subcutaneous lung cancer tumor mouse model and human lung cancer tissue, respectively. The results revealed that following the intravenous injection of Perimag particles targeting the epidermal growth factor receptor into the subcutaneous lung cancer tumor mouse model, the MPI signals in the liver and tumor gradually increased over time, with the liver exhibiting significantly stronger signal intensity compared to the tumor. Furthermore, when scanning human lung cancer tissue incubated with these particles using our self-developed device, MPI devices effectively quantified the concentration of magnetic particles in human tissue. These findings underscore the applicability of our self-developed MPI device in both in vivo and human tissue settings.

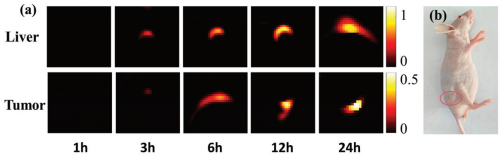

Figure 1. **(a)** MPI images of the liver and HCC 827 tumor model in a mouse at different time points after intravenous injection of particles through the tail vein. We tested a total of six mice. **(b)** Mouse tumor model. 100 µl of Perimag particles with a iron concentration of 5 mg/ml were intravenously injected, targeting the epidermal growth factor receptor.

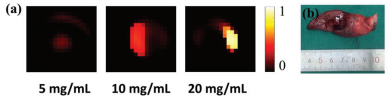

Figure 2. **(a)** MPI images of human lung cancer tissue after incubation with particles of different iron concentrations followed by PBS washing. **(b)** Image of human lung cancer tissue.

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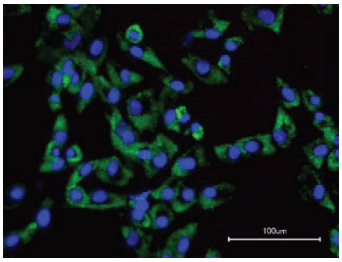

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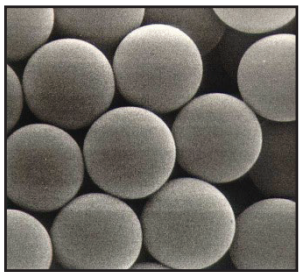

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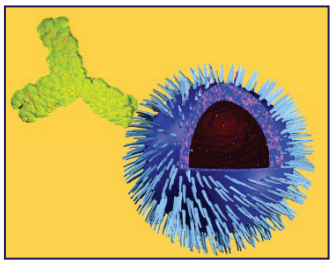
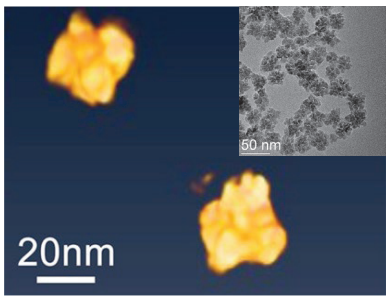
- **components in diagnostic kits and biosensors[2]**



synomag®-D

- **for MRI and MPI research**
- **for hyperthermia applications[3]**



- **Do you require particle design and modification in compliance with ISO 13485?**

Get in contact with us: info@micromod.de or www.micromod.de

References:

[1] Labeling of hMSC with fluorescent perimag® (nucleus: blue; perimag® in cytoplasm: green) , T. Kilian *et al. Nanomedicine* **2016**, 11 (*15*) 1957-1970.
[2] Viability assessment of Salmonella cells with nanomag®-D particles, E. Fernandez *et al. Biosensors and Bioelectronics* **2014**, (*52*) 239-246.
[3] TEM tomography image of synomag®-D, L.J. Zeng, Chalmers University of Technology, Göteborg.

Catalan Institute of Nanoscience and Nanotechnology (ICN2)

ABOUT US

ICN2 is a non-profit international research institute located close to Barcelona (Catalonia, Spain) devoted to the generation of knowledge, materials and devices in the broad fields of ICT, health, energy and the environment.

The expertise of the **ICN2** lies at the nanoscale, where new properties, interactions and ways to exploit them in everyday life are being discovered. Among its goals is to bring together scientists from diverse backgrounds in the pursuit of better science, better training and better outreach to society, while also seeking out new ways to engage with local and global industry.

MISSION

To open and explore new frontiers of knowledge at the nanoscale, and bring value to society in the form of new understanding, capabilities and innovation, while inspiring and providing broad training to the next generations of researchers.

VISION

ICN2 aims to be influential in the scientific community for its ground-breaking research, and in society for its ultimate impact in innovative, transformative and sustainable solutions to tackle societal challenges.

VALUES

COMMITMENT
COLLABORATION
TRANSFORMATION

ICN2 IN FIGURES

- Around 300 people
- 19 research groups
- >40 nationalities
- 14M€ of annual budget
- 12 ERC grants
- Around 200 publications per year
- Nearly 60% competitive funding
- 8 EIC grants
- >80,000 citations

ICN2
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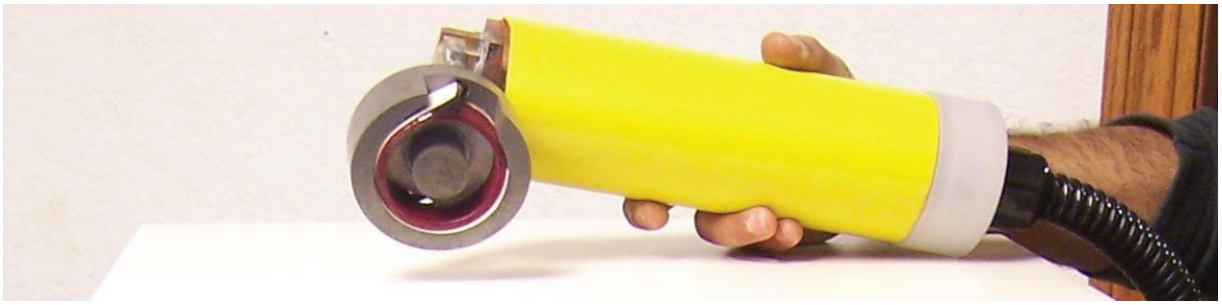
Breakthrough in Magnetic Hyperthermia Treatment

(Treating Gioblastoma: An aggressive and fatal cancer)

Hand Portable Heating Device: Cancer research has used magnetic hyperthermia to enhance the effectiveness of chemotherapy. Conventional treatments to treat brain tumors have used over-sized round magnetic heating coils to encompass the entire skull. This fails because the magnetic field is too weak. The use on a light weight portable hand unit with a flat planar coil can be targeted at the tumor's location or scan a wider area. Heating is controlled in a 30-70 mm diameter pattern and penetrates 30-50 mm into brain tissue.



Brain Tumors can be treated with radiation and surgery. But to remove all cancerous lesions is difficult. Employing nanoparticles and magnetic hyperthermia offers a method to control the spread of the tumor when other treatments have failed.

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About us

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NTSOL focuses its commercial activities on the development and manufacturing of instrumentation for AC/DC magnetic field generation, or Magnetometry. These Systems are used for characterising the magnetic properties of nanomaterials and for its applications in different areas.

A tight interaction with customers to satisfy their requirements is our major fingerprint as manufacturer.

We are committed with magnetic nanomaterial's users to provide the best to benefit their research and/or industrial activities. NTSOL offers commercial alternatives to suit customer requirements and purchase capabilities: Sales or renting ?

For achieving this goal, "flexibility" guides our actions concerning the design, development, manufacturing and commercialization of NTSOL advanced instrumentation.

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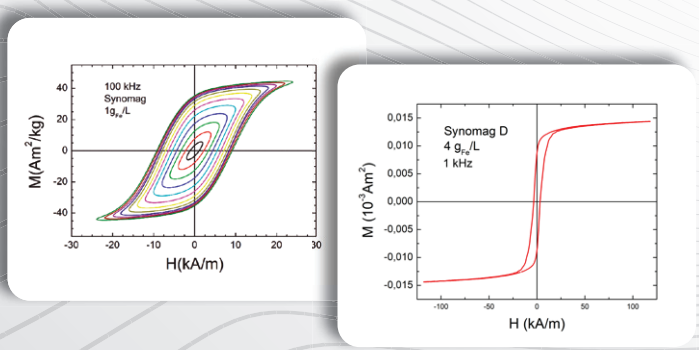
- **ADVANCE AC Hyster** is an inductive magnetometer working in a field frequency range between 25 and 350 kHz up to 24 kA/m.



Nanotech Solutions

Headquarters:
C\Miguel Unamuno, 2 3°B
40150 Villacastín, Spain

Commercial office:
C\Tomás Bretón, 50-52 4°
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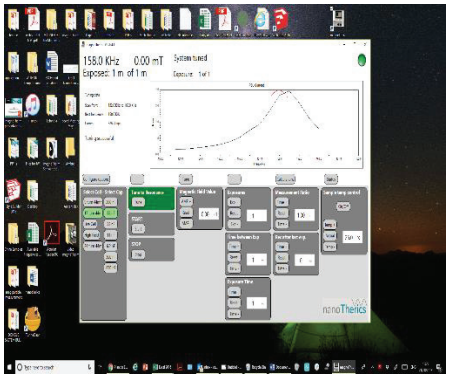

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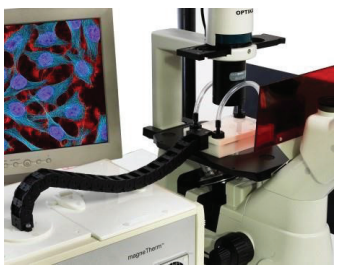

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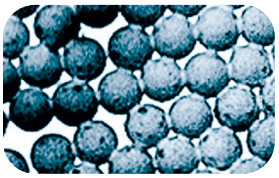

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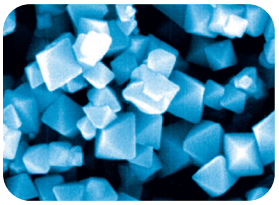

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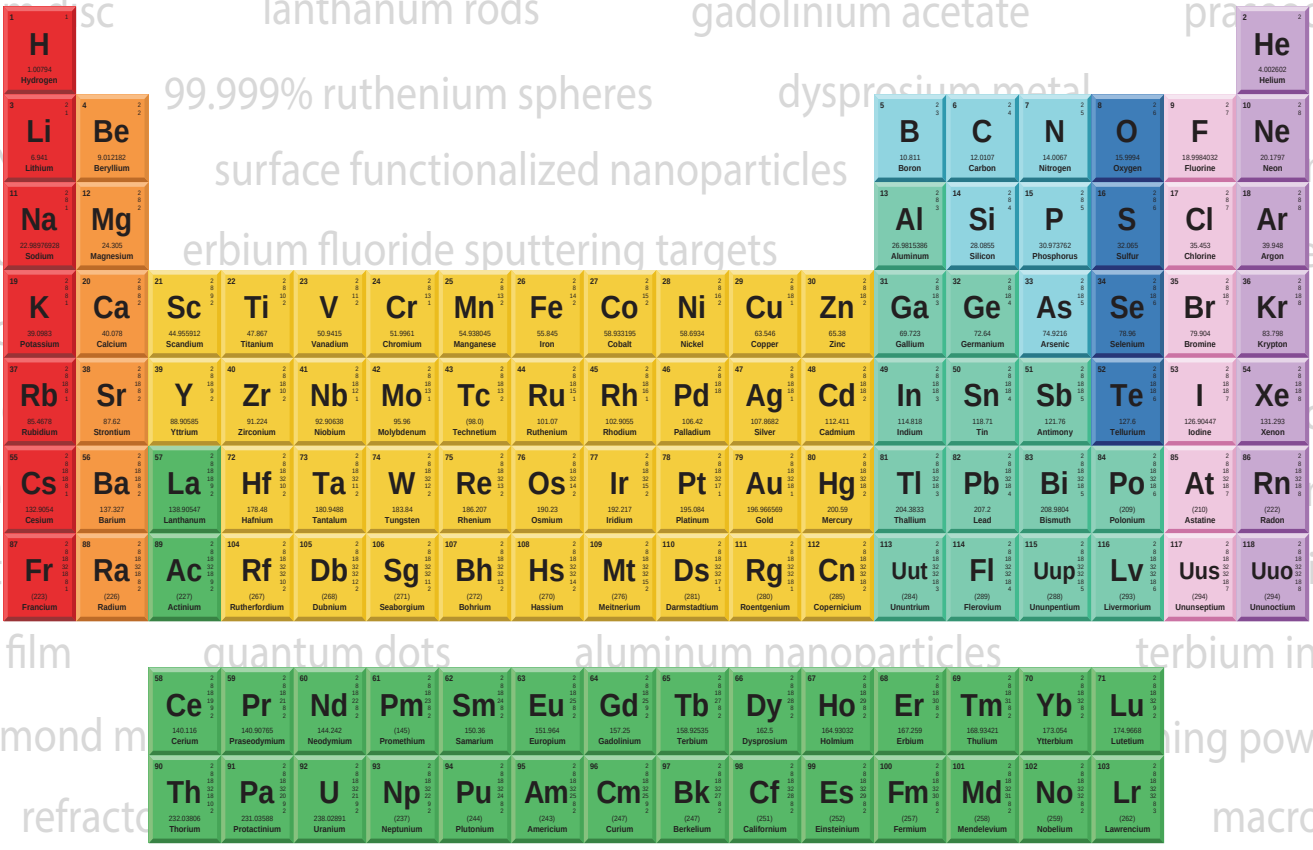

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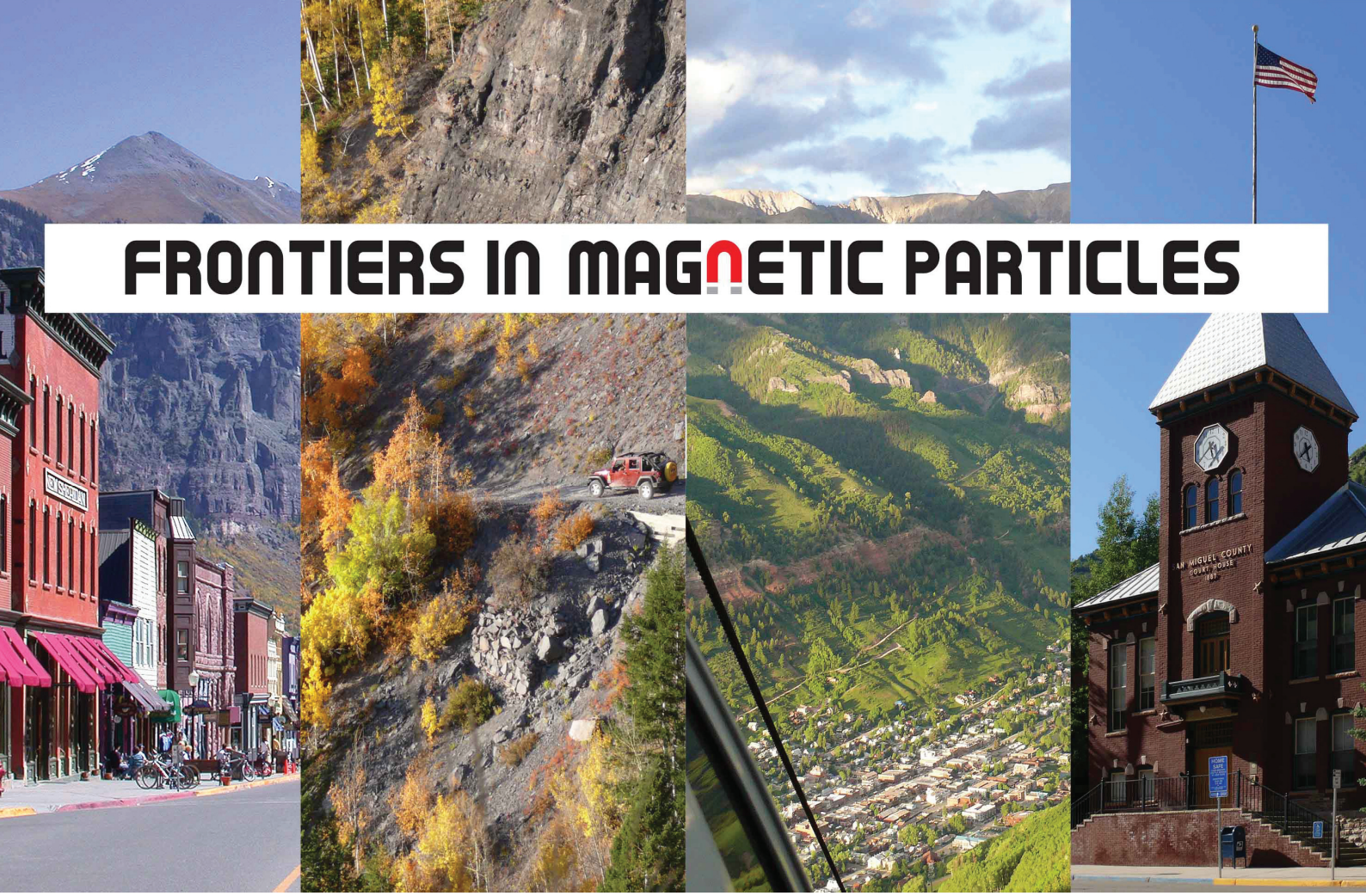

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2025

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Organizers: O. Thompson Mefford (Clemson U.) and Jennifer Andrew (U. Florida)

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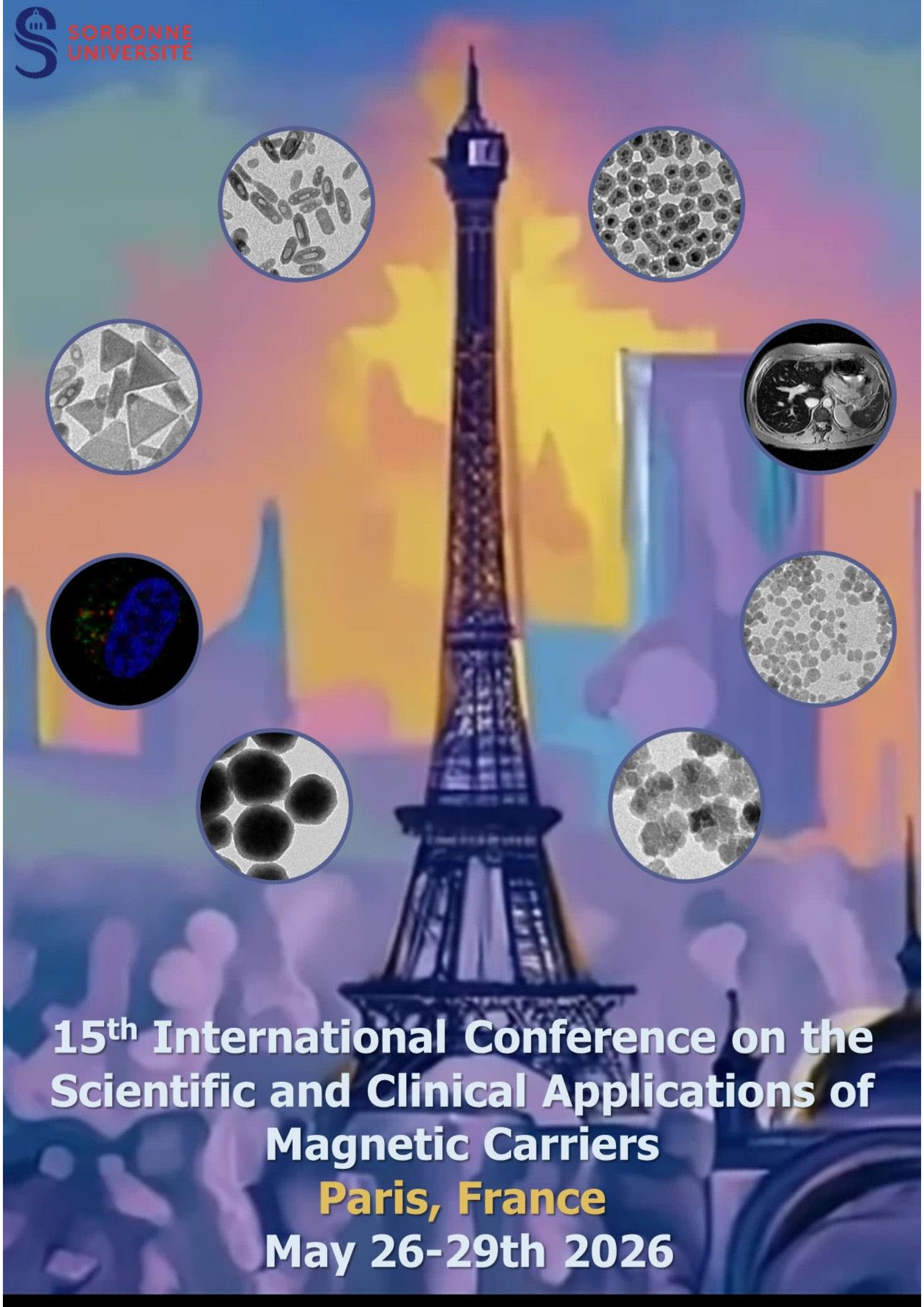
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