Magnetic Particles: Synthesis and Functionalisation

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Organisation

Magnetic Core Synthesis

Stabilisation and Functionalisation

Flow Chemistry and Characterisation

Talk 1

Talk 2

Talk 3

Part 1: Magnetic Core Synthesis

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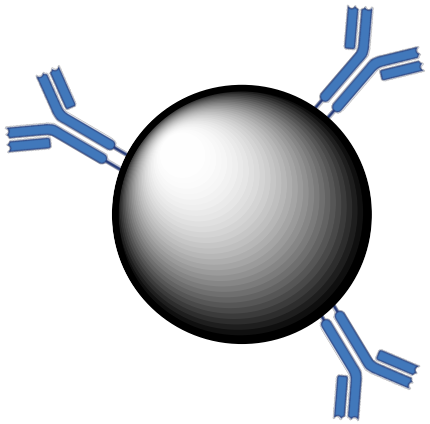
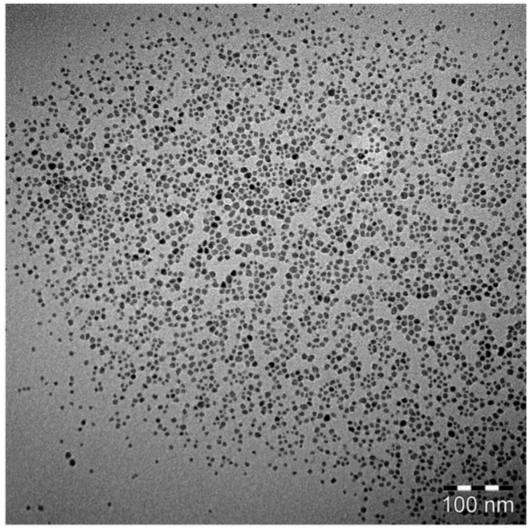
Magnetic Nanocarriers

Nanoparticles able to be guided and/or activated by a magnetic field used to transport substances to specific cells or tissues in the body.

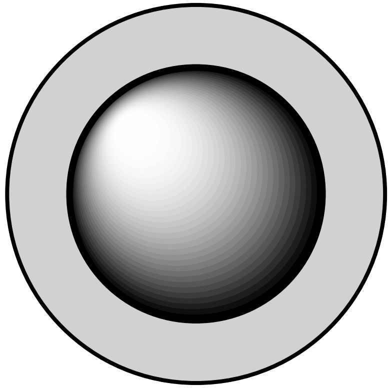
Functionalised

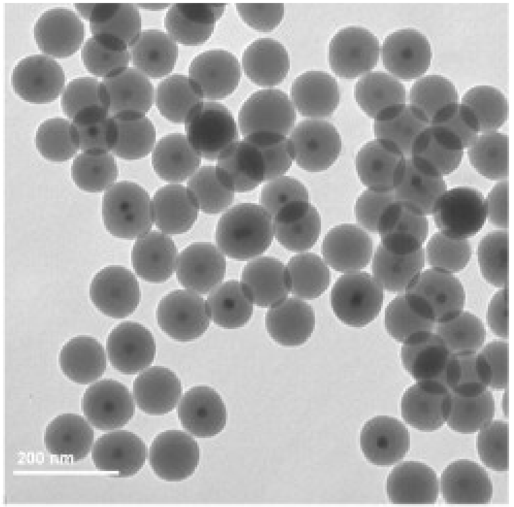




Stanicki *et al.* 2021
Journal of Material Chemistry B

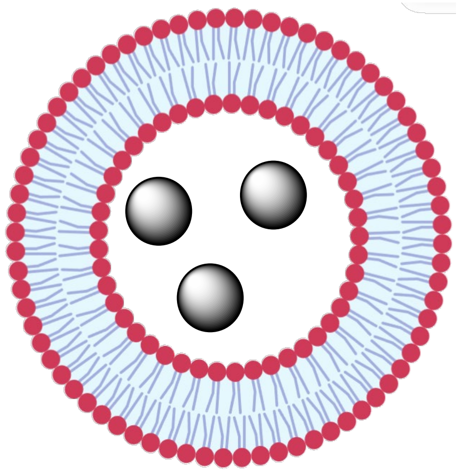
Core-shell

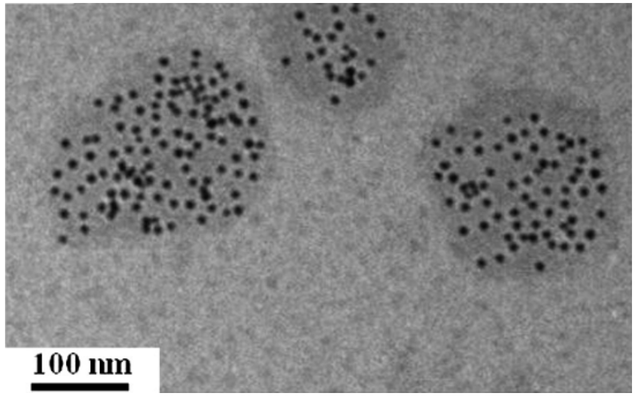




Jiang *et al.* 2012, Journal of Alloys and Compounds

Encapsulated

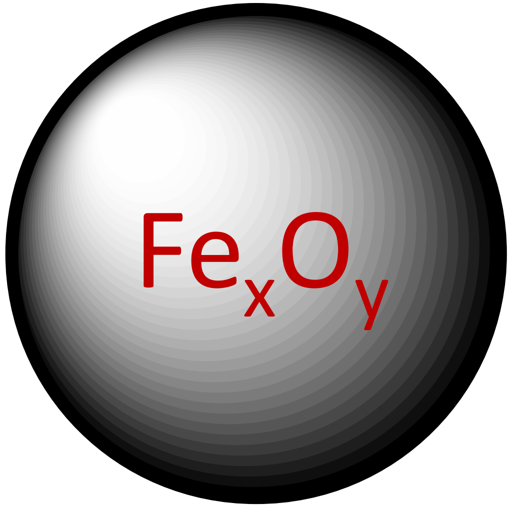




Won *et al.* 2012
Journal of Controlled Release

Iron Oxide Nanoparticles (IONPs)

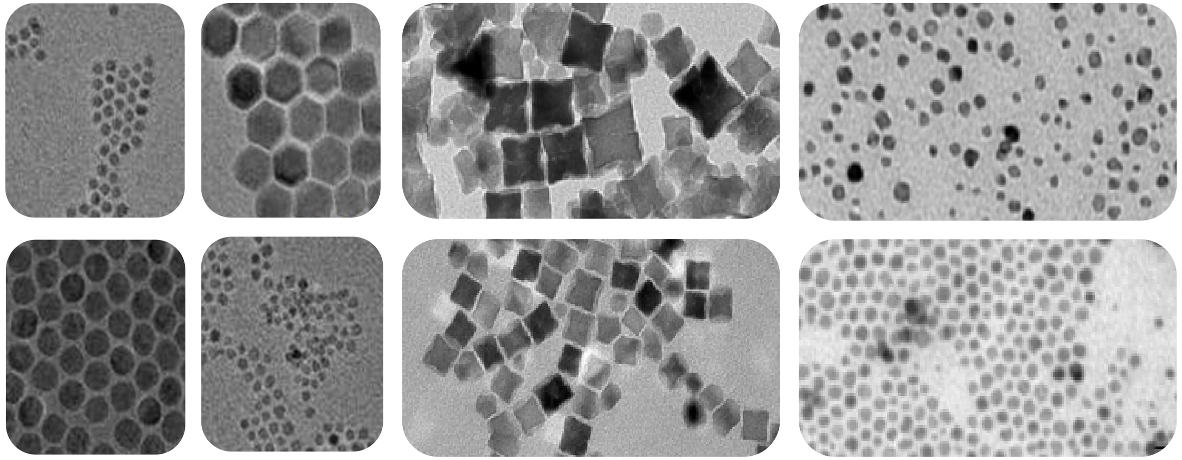
- Nanoparticles: 1 – 100 nm
- Biocompatible



- Magnetic properties:
  ferri-, ferro-, antiferro-magnetism

IONPs are superparamagnetic

- Variety of shapes:



Baaziz *et al*. 2015
J. Phys. Chem C

Guardia *et al*. 2010
Langmuir

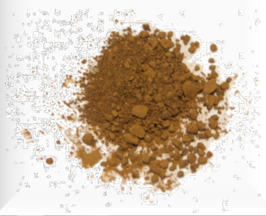
Belaïd *et al*. 2018
Nanotechnology

- Phases: 16 pure phases

Most common and stable phases

Hematite
(α-Fe_2O_3)

Maghemite
(γ-Fe_2O_3)



Magnetite
(Fe_3O_4)

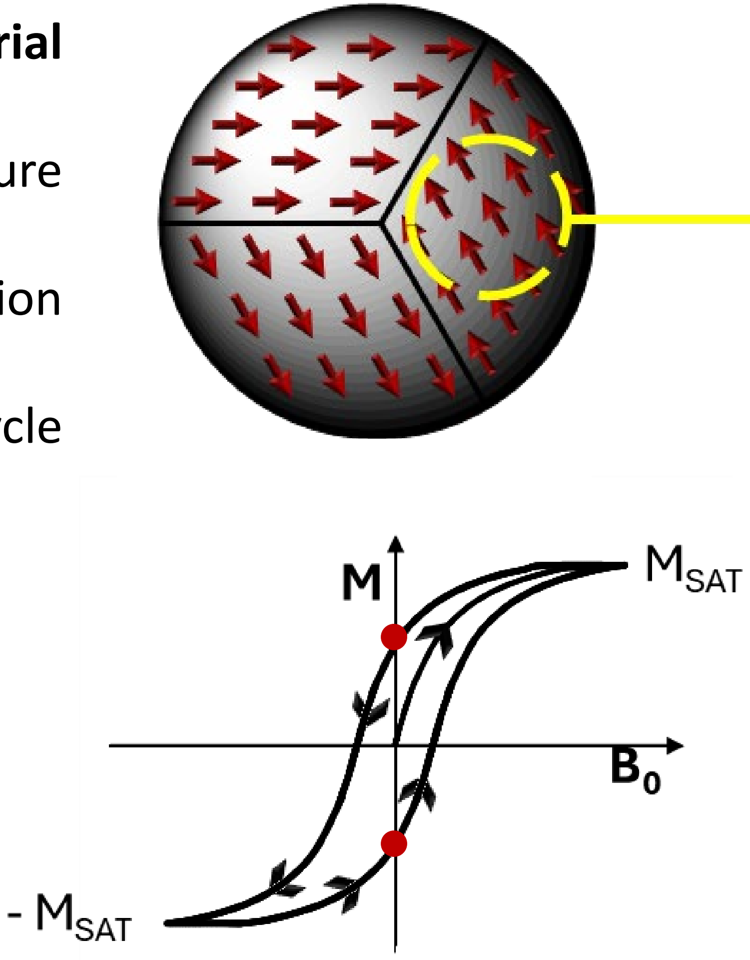
Superparamagnetism

Bulk material

Multiple domains structure

Remanent magnetisation

Hysteresis cycle

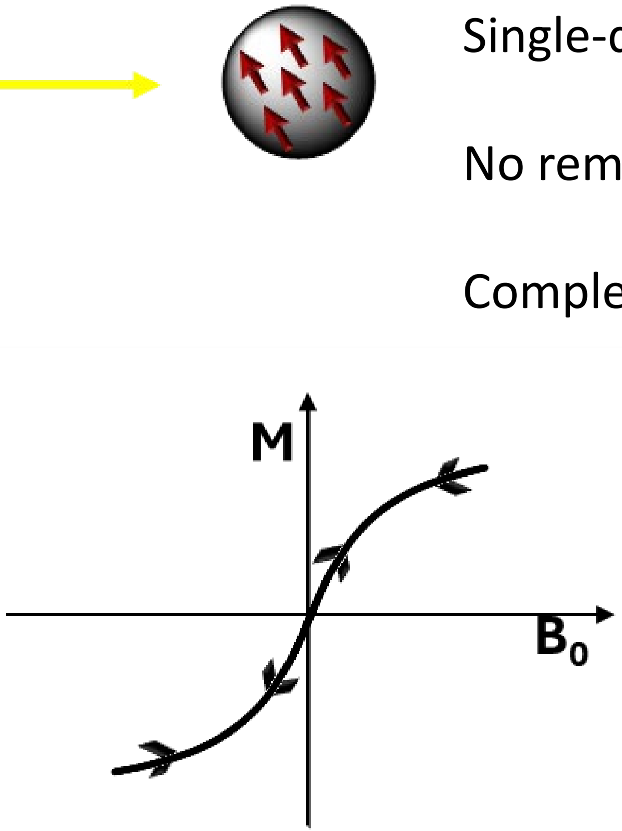


IONPs

Single-domain structure

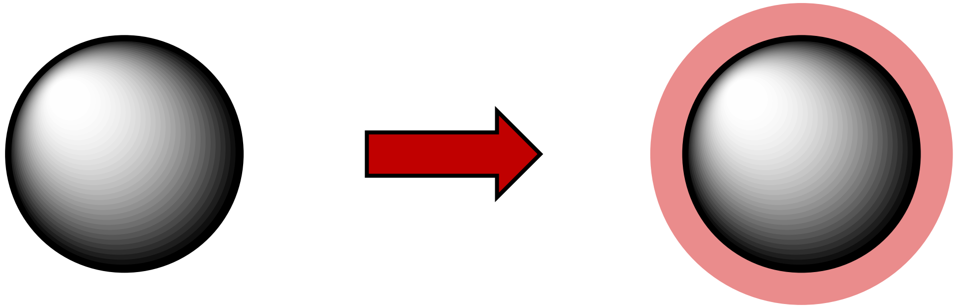
No remanent magnetisation

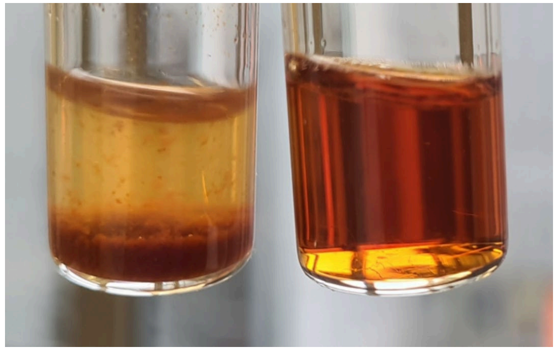
Completely reversible



Vangijzegem *et al.* 2023, Pharmaceutics

Surface Modification





Stabilisation

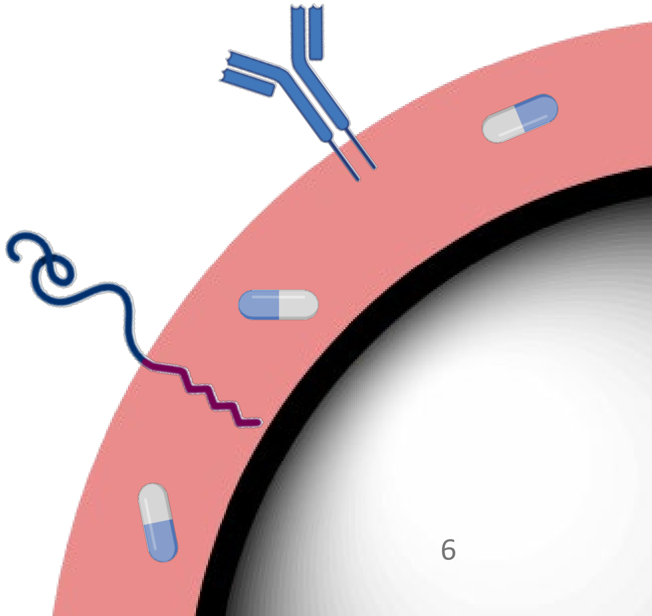
- Prevent aggregation
- Diminish oxidation

Stealth

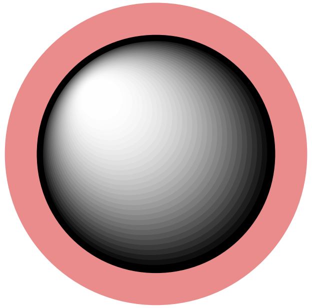
- Limited opsonisation
- Impeded immune system recognition
- Increased half-life time

Functionalisation / Vectorisation

- Specific targeting:
  - Peptides
  - Nanobodies
- Drug loading



Applications

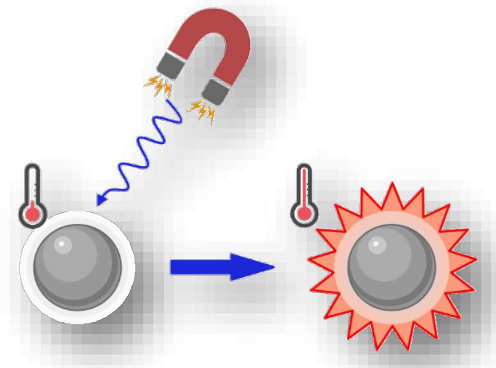


Therapy

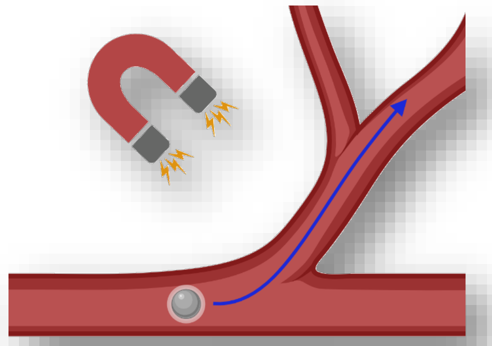
Diagnostic

Theranostic

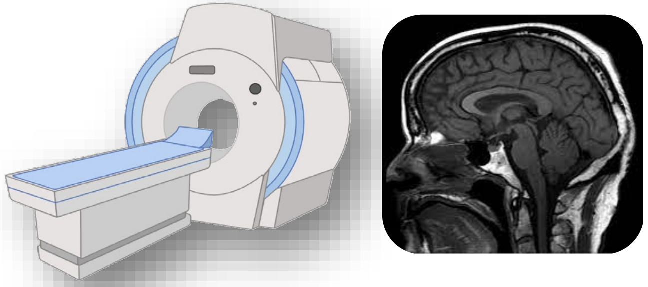
Magnetic Hyperthermia



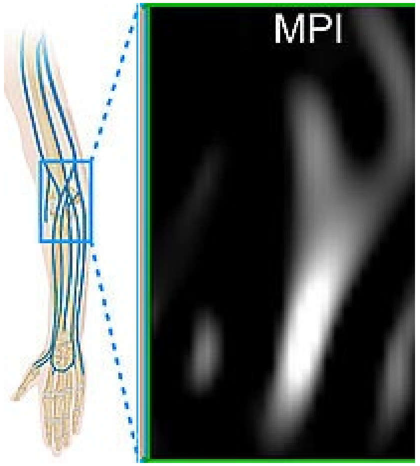
Magnetic Guided Delivery



Magnetic Resonance Imaging (MRI)

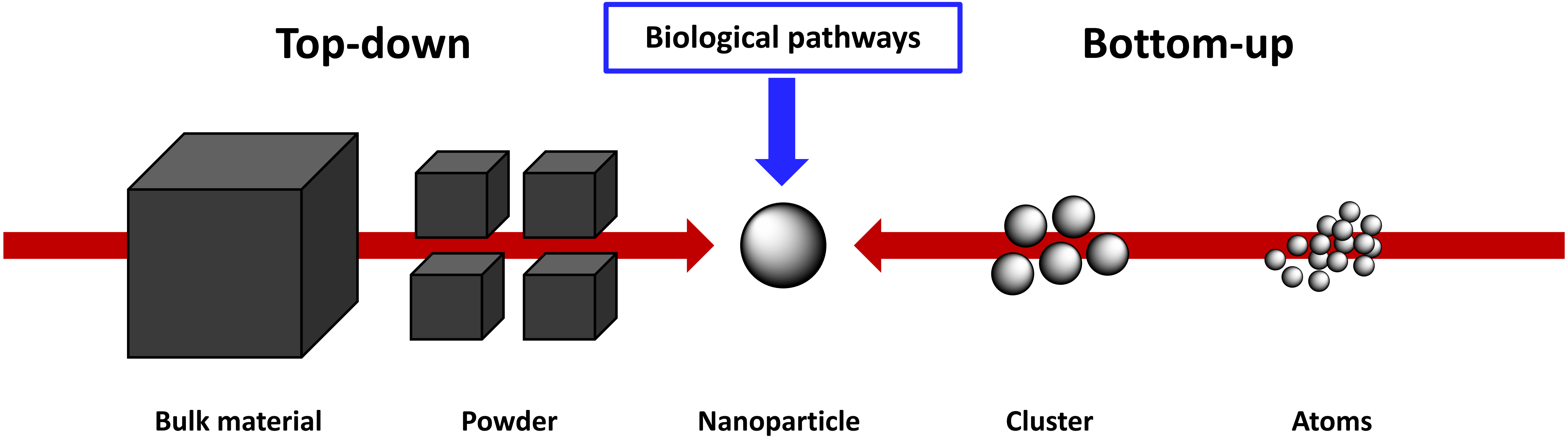


Magnetic Particle Imaging



Vogel et al. 2026

Magnetic Cores Synthesis



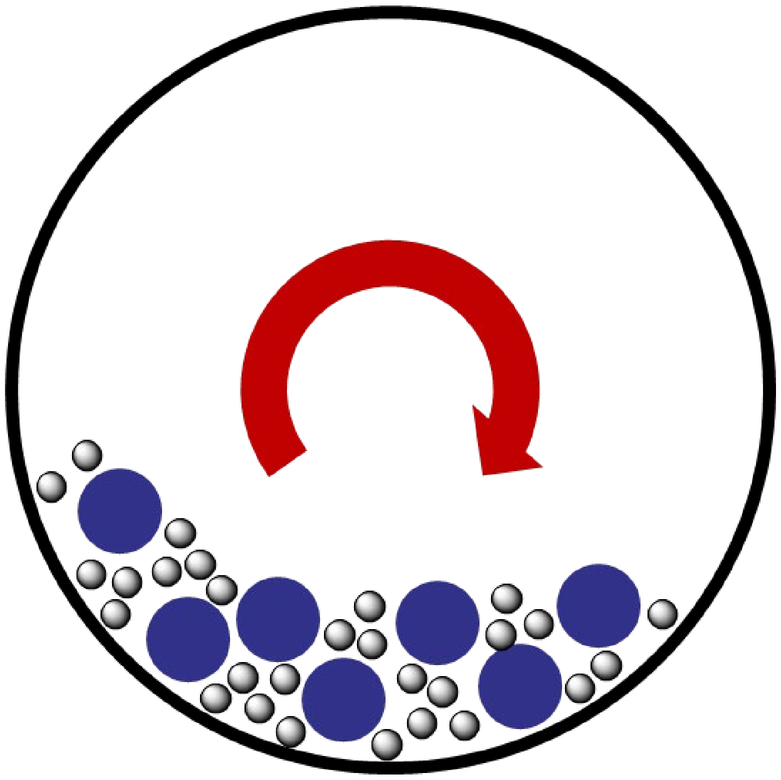
Ball milling

Laser ablation

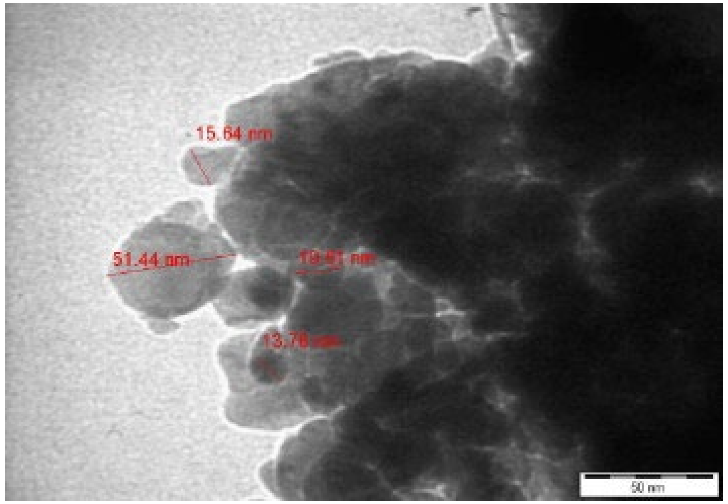
. . .

Co-precipitation
Micro-emulsion
Thermal decomposition
. . .

Ball Milling



IONPs in powder mainly for material industry

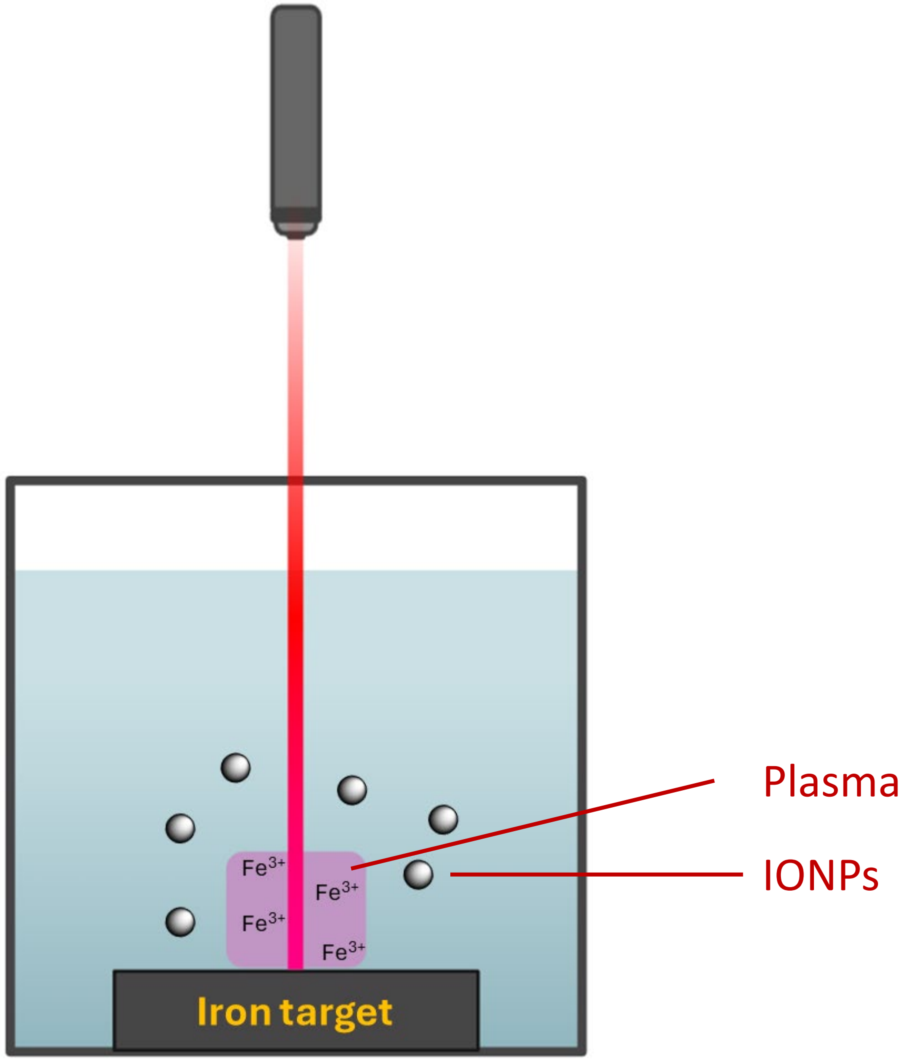


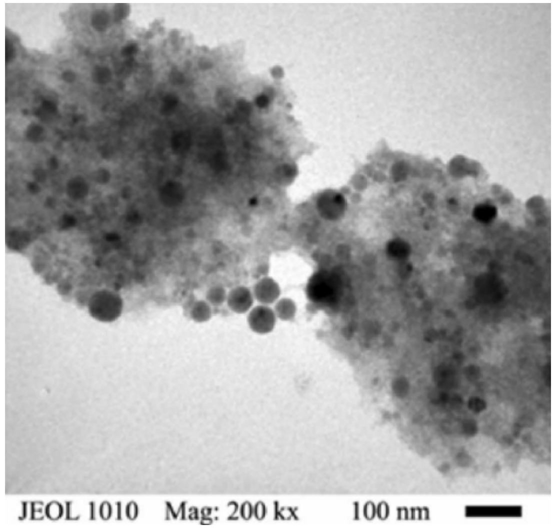
Arbain *et al.* 2011, Minerals Engineering

- High production rate
- Simple
- Green
- Material easy to obtain

- Little control over shape
- Particle aggregation
- Amorphisation

Laser Ablation





Ramirez *et al.* 2025, Scientific Reports

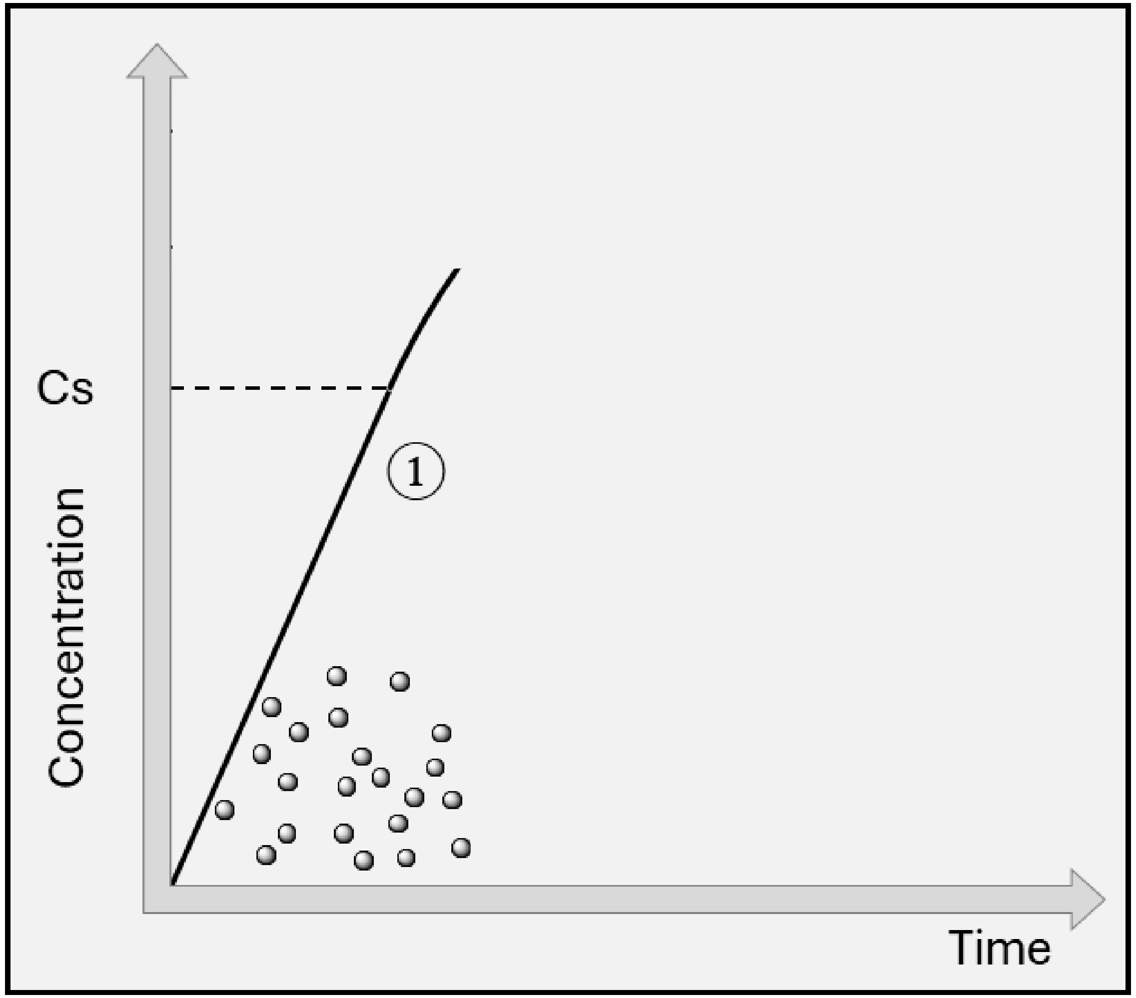
Spherical particles

Diameter: 30 - 40 nm

- Great purity
- No ligand or salt
- Control over phase and size

- Sensible to little variation
- Short synthesis
- Not scalable

Bottom-up Syntheses: LaMer's Model

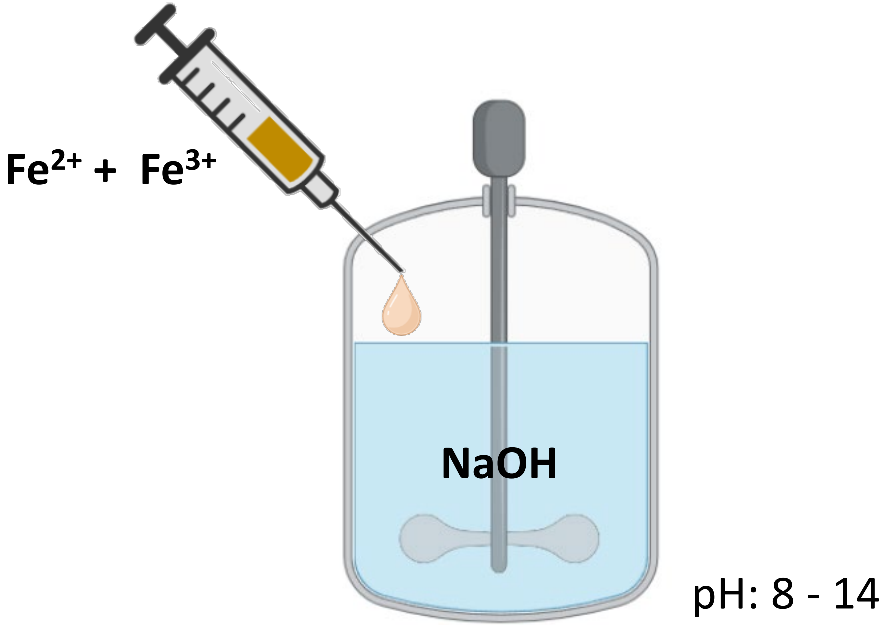


Vangijzegem *et al.* 2023, Pharmaceutics

1. **Monomers in solution**
2. **Burst nucleation**
3. **Growth**

Coprecipitation (Massart Process)

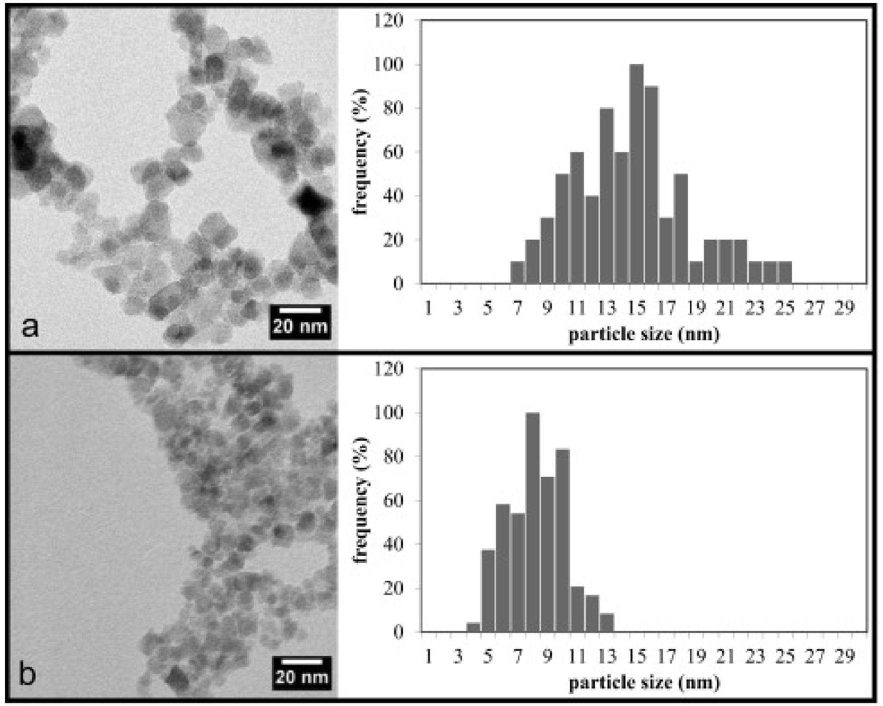
$$Fe^{2+} + 2\,Fe^{3+} + 8\,OH^- \rightarrow Fe_3O_4 + 4\,H_2O$$



- Easy to implement
- High yields
- Scalable
- Low temperature

Commercialised particles:

Sinerem® and Endorem®



Roth *et al.* 2014, Journal of Magnetism and Magnetic Materials

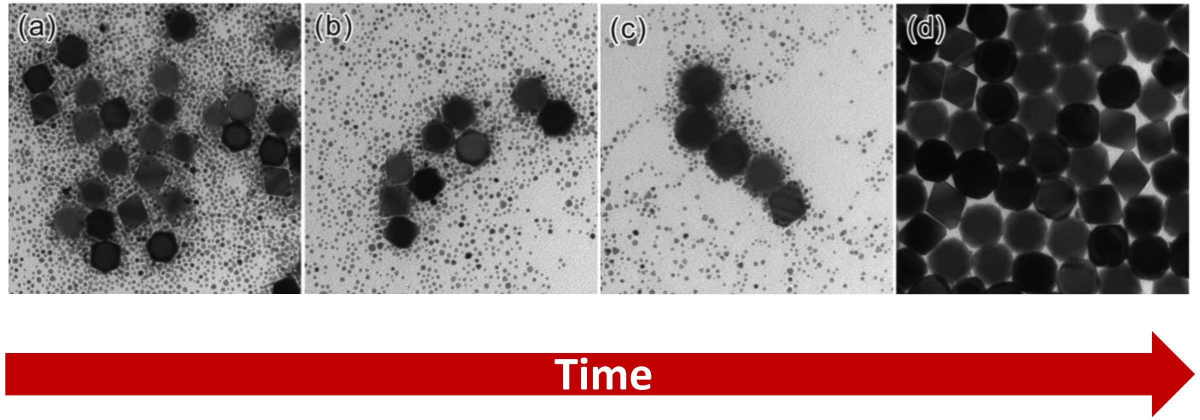
- Diameter: 3 - 30 nm
- High polydispersity
- Low crystallinity

Massart *et al.* 1981, IEEE Transactions on Magnetics

Coprecipitation

- Precursor concentration ↗ → Size ↗
- $[OH^-] / [Fe]$ → 1.4:1 Optimal magnetisation
- $[Fe^{3+}] / [Fe^{2+}]$ ↘ → Magnetisation ↗
- T° ↗ → Crystallinity and size ↗

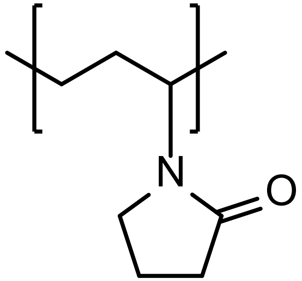
Ostwald Ripening



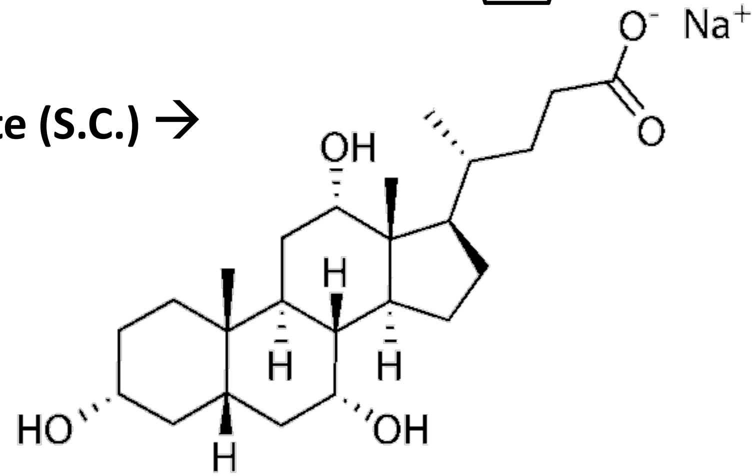
Maria Filippousi *et al.* (2014)

Surfactant effect on magnetic properties

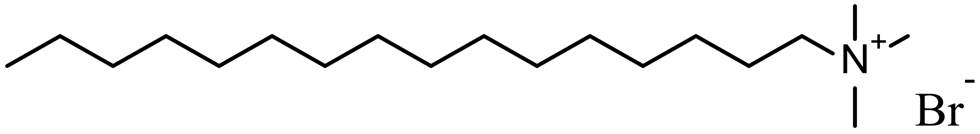
- **Polyvinylpyrrolidone (PVP)** → Non-ionic



- **Sodium cholate (S.C.)** → Anionic

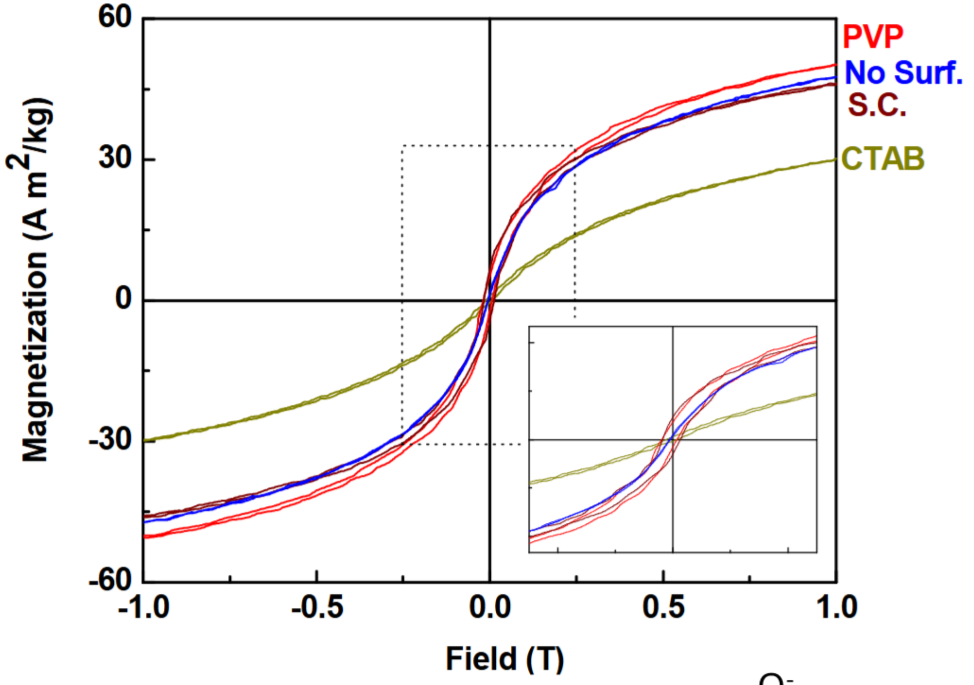


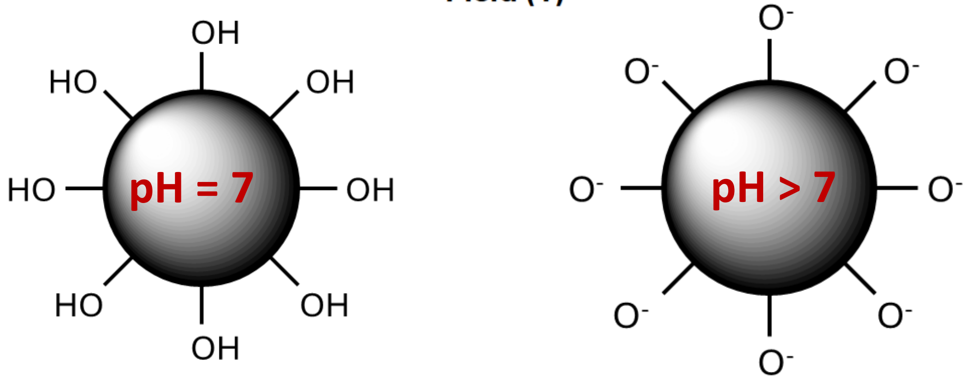
- **Cetrimonium bromide (CTAB)** → Cationic

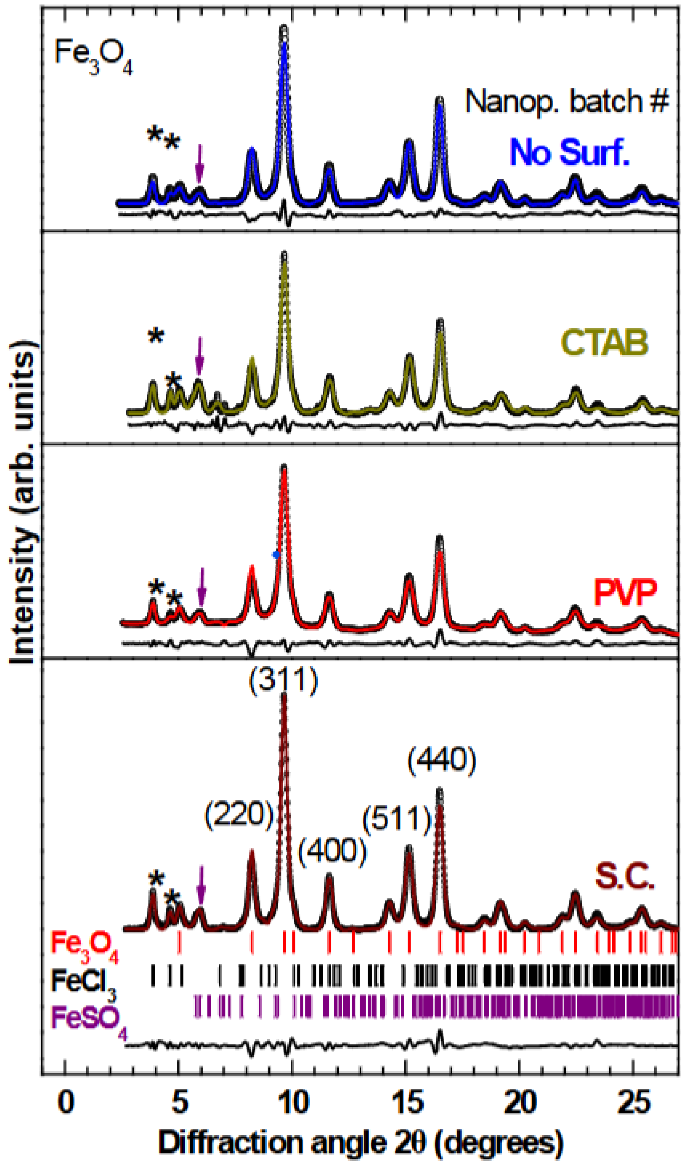


Roth *et al.* 2015, Journal of Magnetism and Magnetic Materials

Coprecipitation



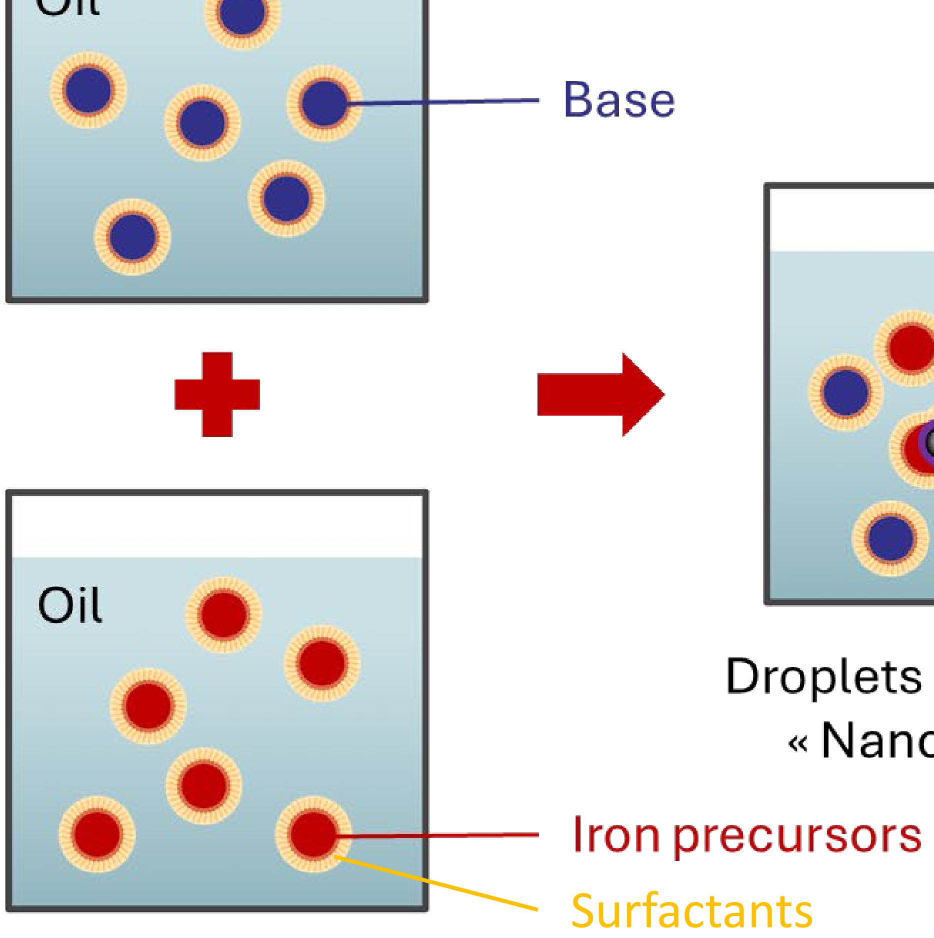


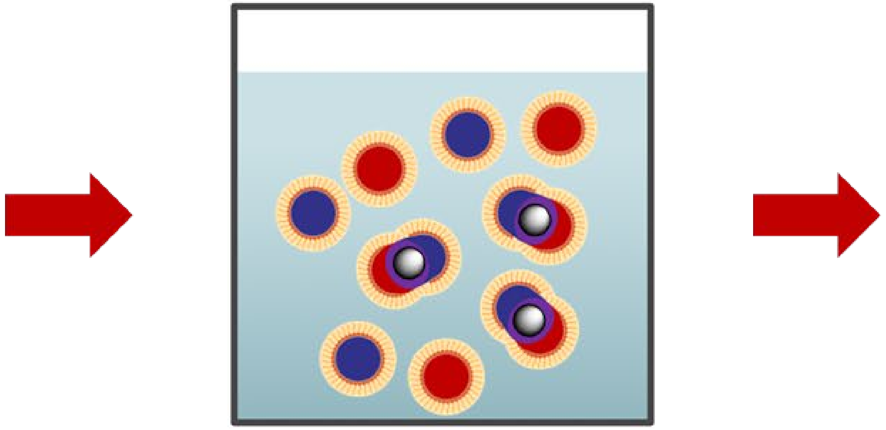


Filippousi *et al.* 2014, The Journal of Physical Chemistry

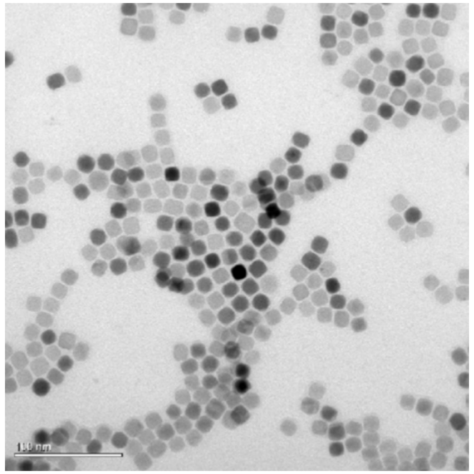
Microemulsion

$$Fe^{2+} + 2\,Fe^{3+} + 8\,OH^{-} \rightarrow Fe_3O_4 + 4\,H_2O$$



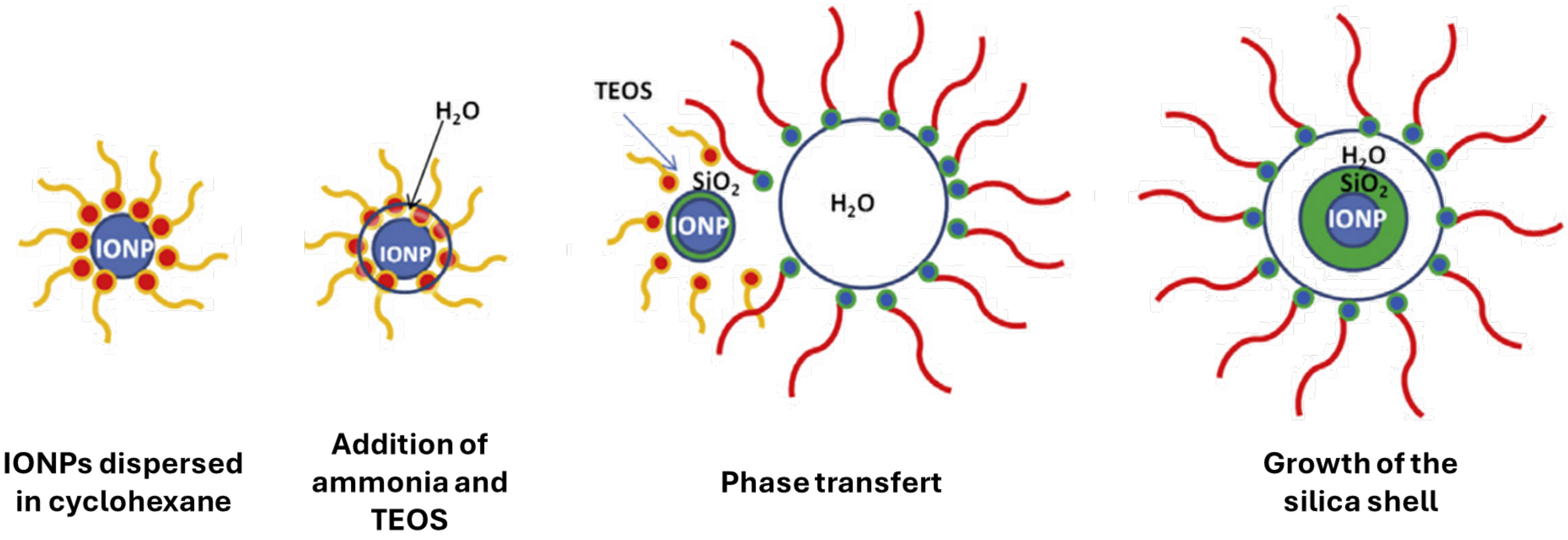


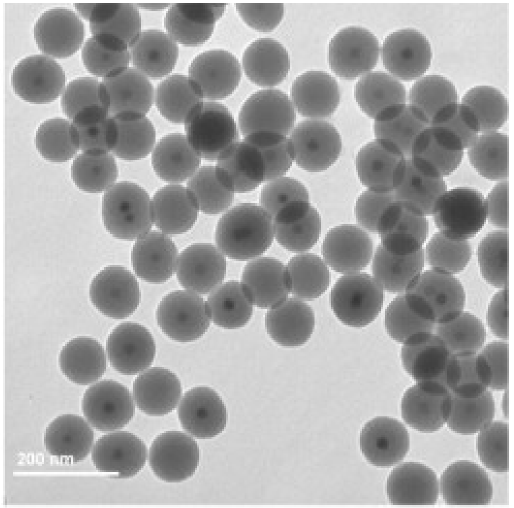
Droplets coalescence
« Nanoreactors »



Formation of IONPs

Microemulsion



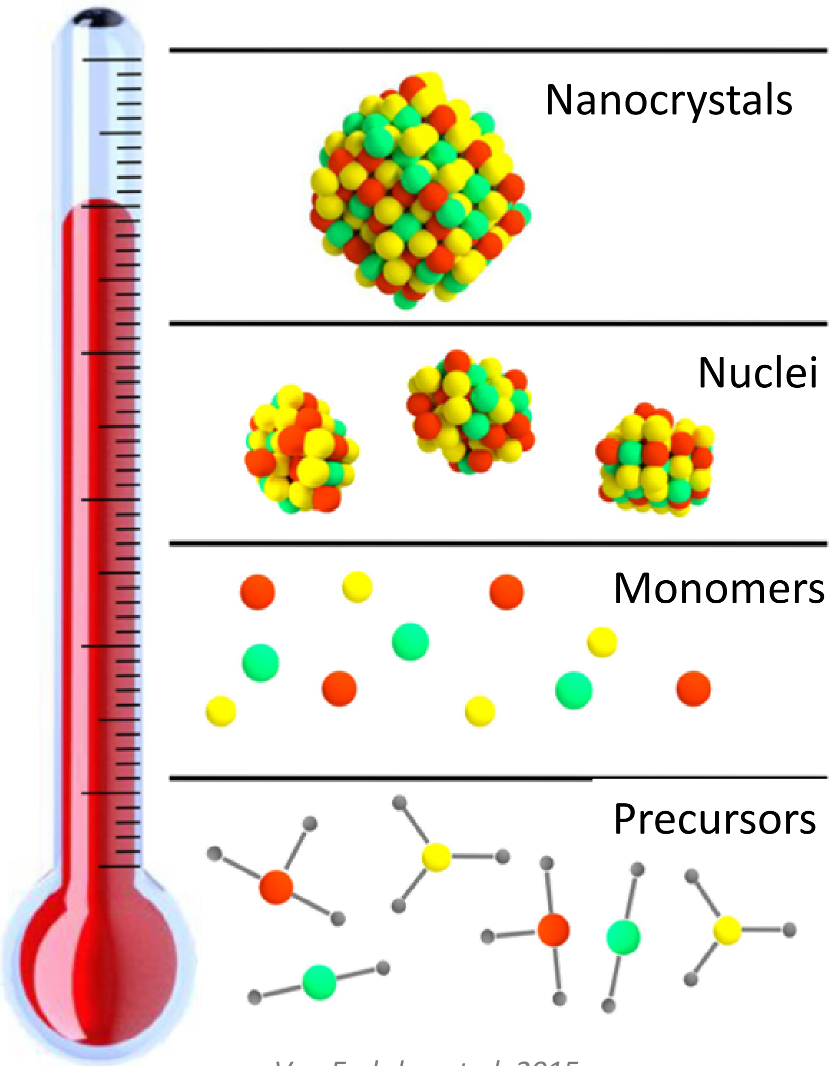


- Precise size control
- Narrow distribution
- Core-shell structure achievable

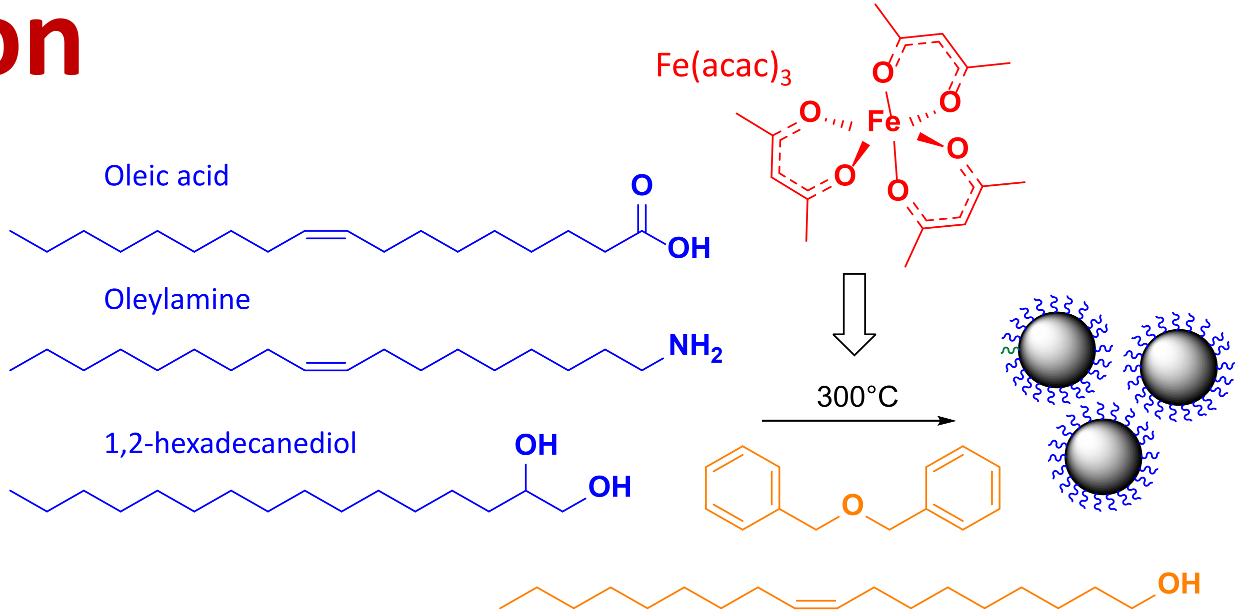
- High quantity of organic solvent
- Difficult to purify
- Reduced yield
- Not scalable

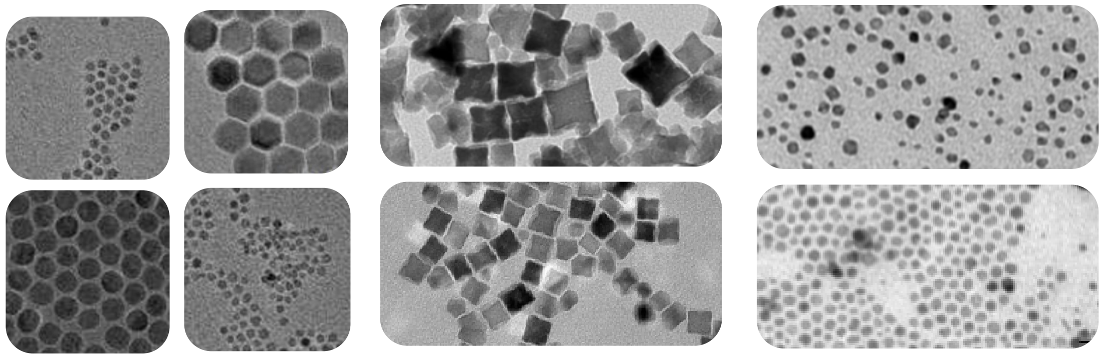
Jiang *et al.* 2012, Journal of Alloys and Compounds

Thermal Decomposition



Van Embden et al. 2015
Chemistry of Materials

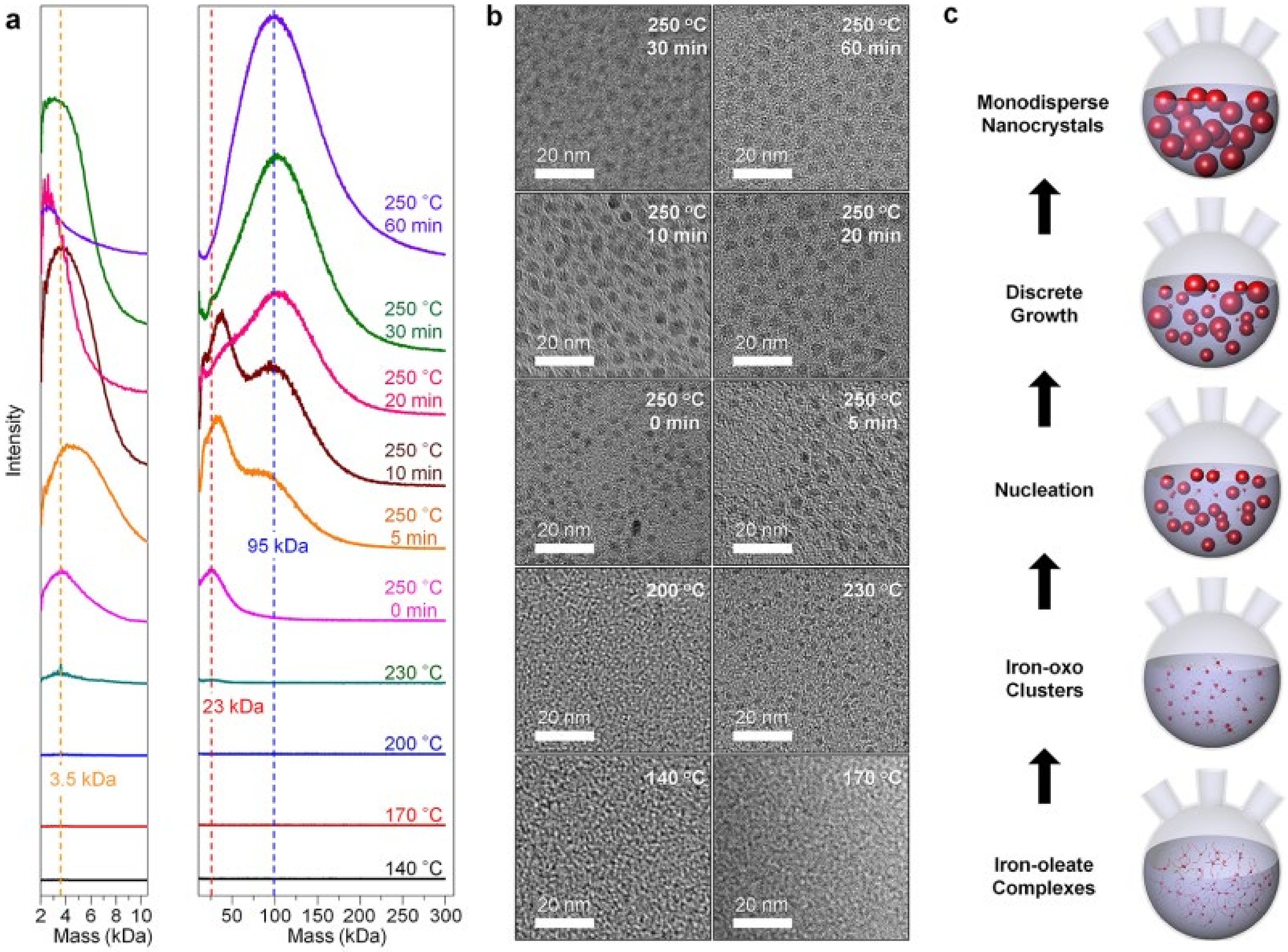


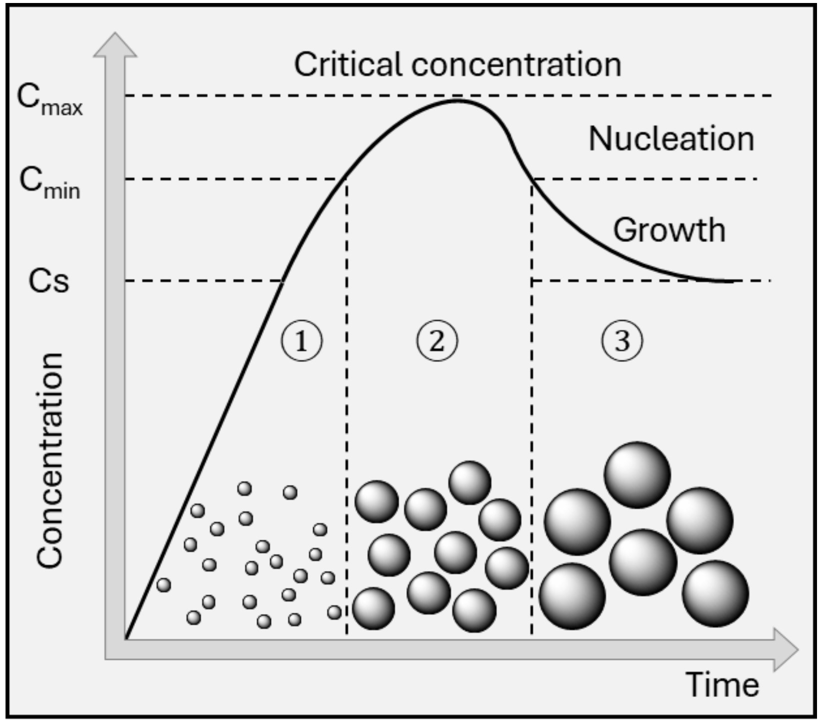


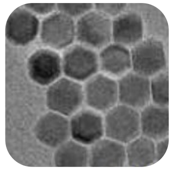
Baaziz et al. 2015
J. Phys. Chem C

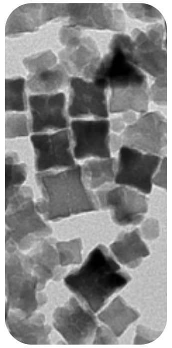
Guardia et al. 2010
Langmuir

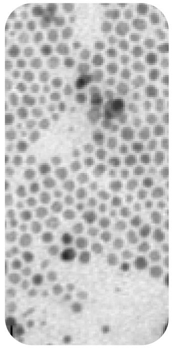
Belaïd et al. 2018
Nanotechnology


a
Intensity
250 °C 60 min
250 °C 30 min
250 °C 20 min
250 °C 10 min
250 °C 5 min
250 °C 0 min
230 °C
200 °C
170 °C
140 °C
95 kDa
23 kDa
3.5 kDa
2 4 6 8 10
Mass (kDa)
50 100 150 200 250 300
Mass (kDa)
b
250 °C 30 min
250 °C 60 min
250 °C 10 min
250 °C 20 min
250 °C 0 min
250 °C 5 min
200 °C
230 °C
140 °C
170 °C
20 nm
c
Monodisperse Nanocrystals
Discrete Growth
Nucleation
Iron-oxo Clusters
Iron-oleate Complexes


Critical concentration
C_{max}
C_{min}
Cs
Nucleation
Growth
① ② ③
Concentration
Time

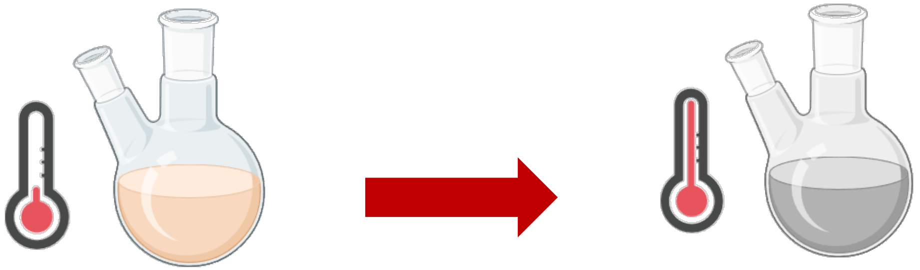






Thermal decomposition in polyol medium
→ Talk 3

Heat-up vs Hot Injection

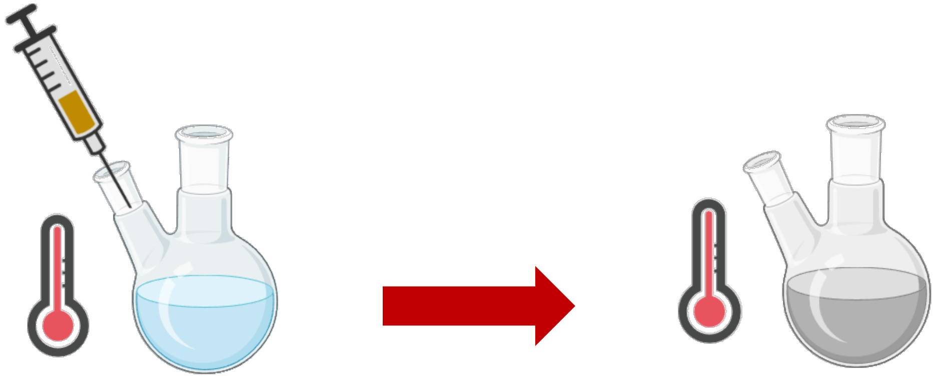


Slow Heating

Easy and safe to implement

Reproducible

Versatility



Rapid injection

Nucleation and growth separated

Greater control over size

Monodisperse particles

- Size and shape control
- Low size distribution
- High crystallinity and magnetisation
- Mixed ferrites

- High temperature → Risks
- Hydrophobic particles
- More purifications steps
- More solvent

Comparison

Method	Advantages	Disadvantages
Co-precipitation	• High quantity • Easy set-up	• Low crystallinity • High polydispersity
Microemulsion	• Specific small size • Core/shell structure	• Small yields • Large amount of solvents
Thermal decomposition	• High crystallinity • Variety of particles	• High temperature → Risks • Hydrophobic particles

Other methods

- Sol-gel
- Sonolysis
- Electrochemistry
- Vapor
- . . .

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Magnetic Particles: Synthesis and Functionalisation

Part 2: Stabilisation and Functionalisation

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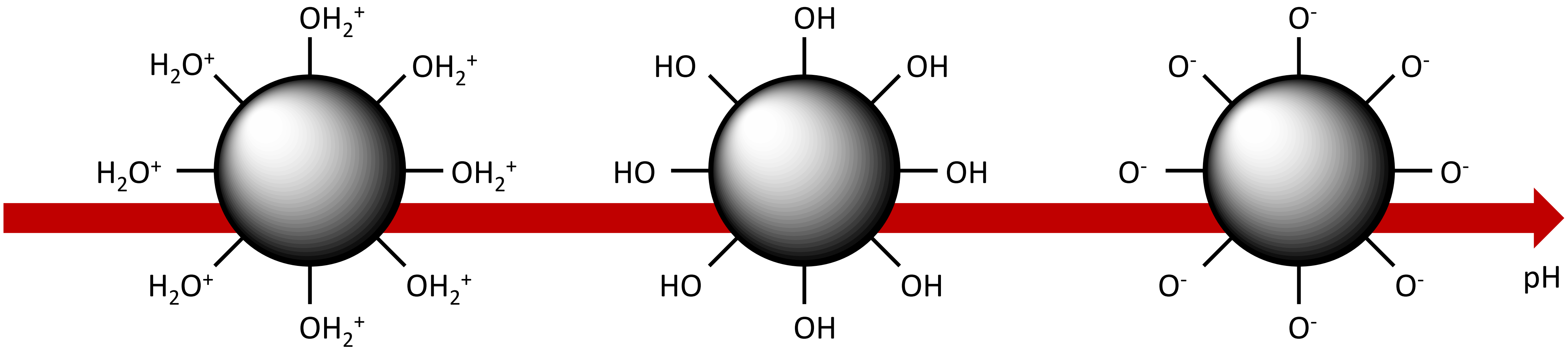
Particle Stability

IONPs are innately instable

- High surface to volume ratio
- Van Der Waals forces
- Magnetic dipole interaction

➥ Aggregation and precipitation → **Depends on pH and ionic strength**



Particle Stabilisation

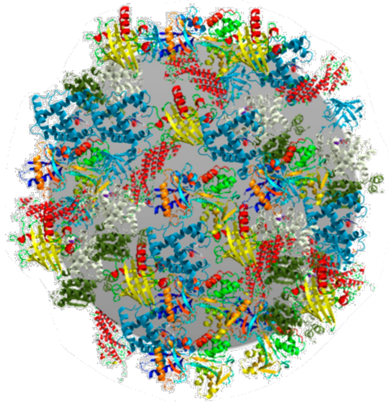
Prevent aggregation

Reduce oxidation

➥ Preservation of the magnetic properties

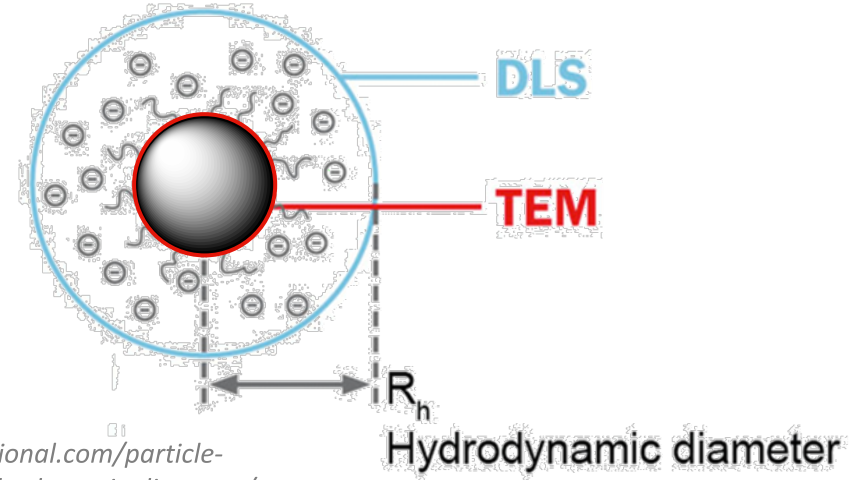
Stealth

➥ Prevent opsonisation and immune system recognition



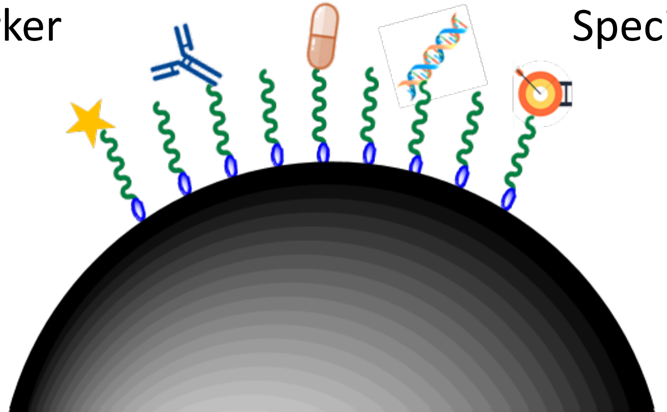
Control of the hydrodynamic diameter

➥ Diameter perceived by cells



https://www.fritsch-international.com/particle-sizing/fritsch-knowledge/hydrodynamic-diameter/

Basis for functionalisation

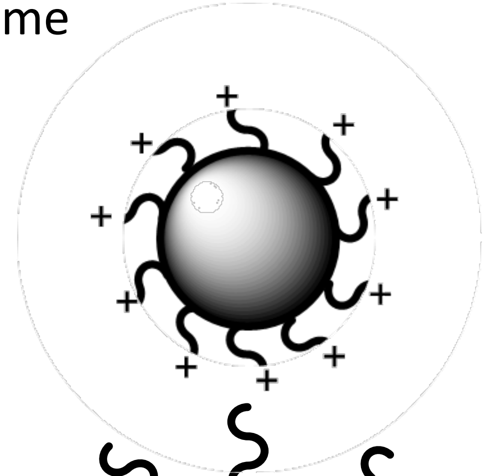


Stabilisation Methods

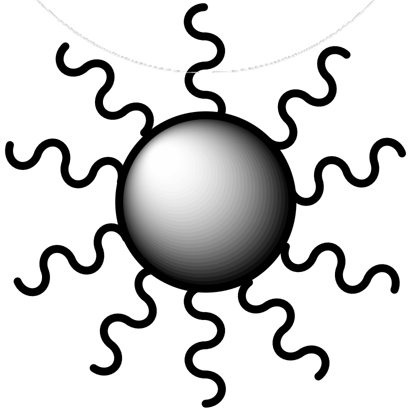
Ligand Addition

- Easy to implement
- Increase circulation time

Electrostatic repulsion

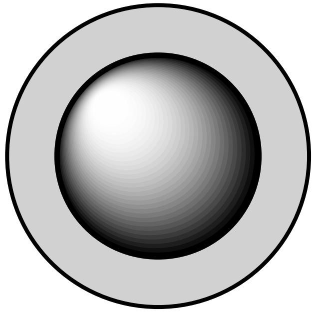


Steric repulsion



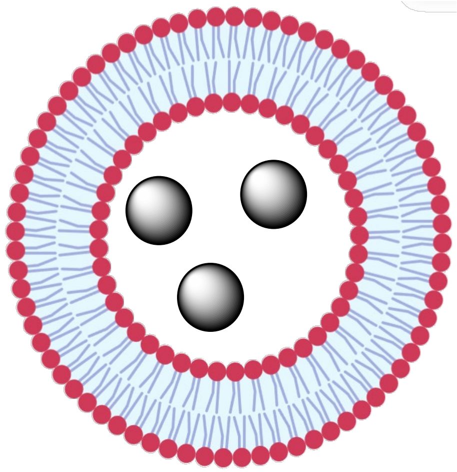
Inorganic coating

- Protect iron oxide core
- Gold or silica



Encapsulation

- Liposomes or micelles
- Complex nanocarriers
- High drug loading potential

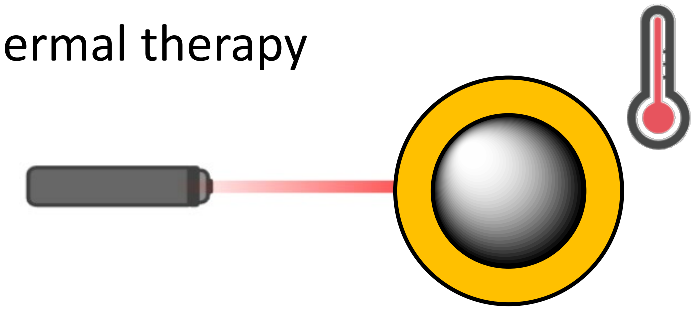


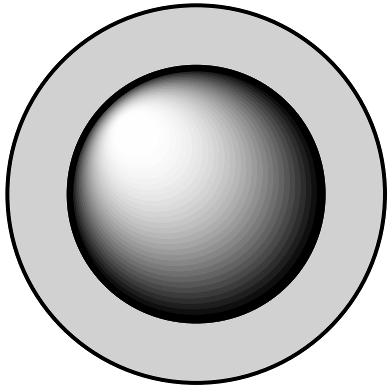
Core-Shell Structure

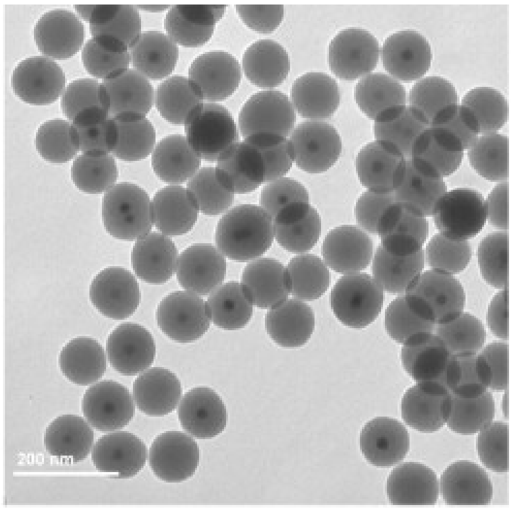
- Protective layer for the iron oxide core
- Surface easy to modify
- Obtained by microemulsion
- Hinder water acess

Gold (Fe_3O_4@Au)

- ROS formation → reduced toxicity
- Plasmonic resonance
- Photothermal therapy







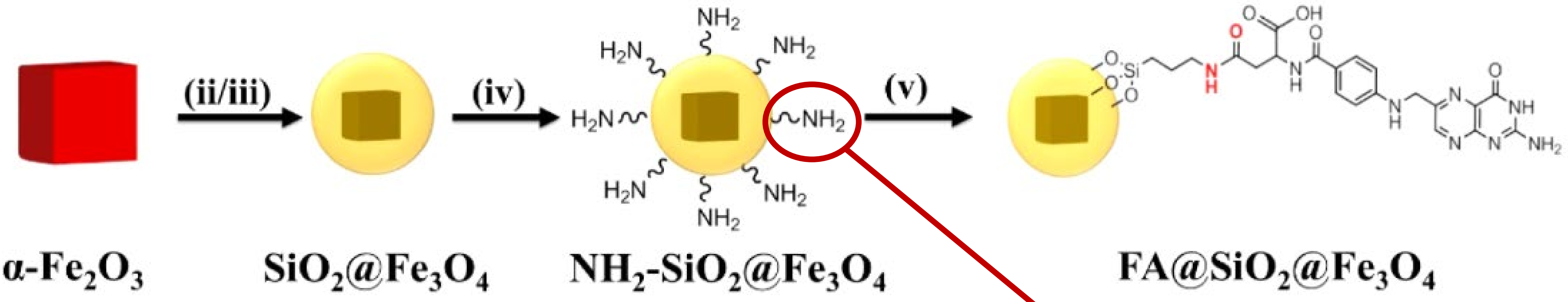
Jiang et al. 2012
Journal of Alloys and Compounds

Silica (Fe_3O_4@SiO_2)

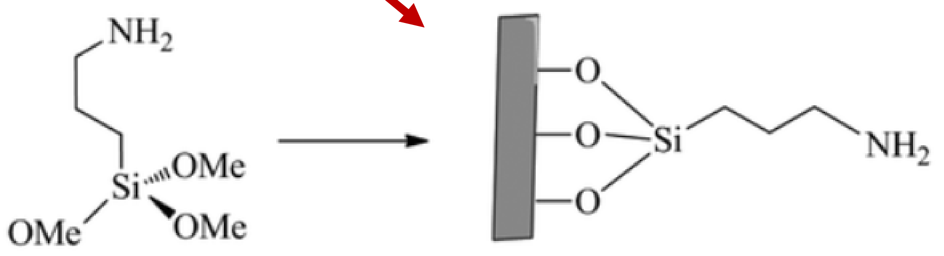
- Mostly inert in the body
- Possibility to design complex nanocarriers
- **Ferumoxsil®**: Oral administration of MRI contrast agent for bowel imaging.

Core-shell Structure

- Grafting of folic acid (FA) as a targeting agent for cancer cells



- Iron oxide as MRI contrast agent
- Silica shell:
  - Prevent aggregation
  - Increase colloidal stability
  - Tunable surface



(3-aminopropyl)trimethoxysilane (APTMS)

Wortmann *et al.* 2014, ACS Applied Materials and Interface

Taghavi *et al.* 2016, New Journal of Chemistry

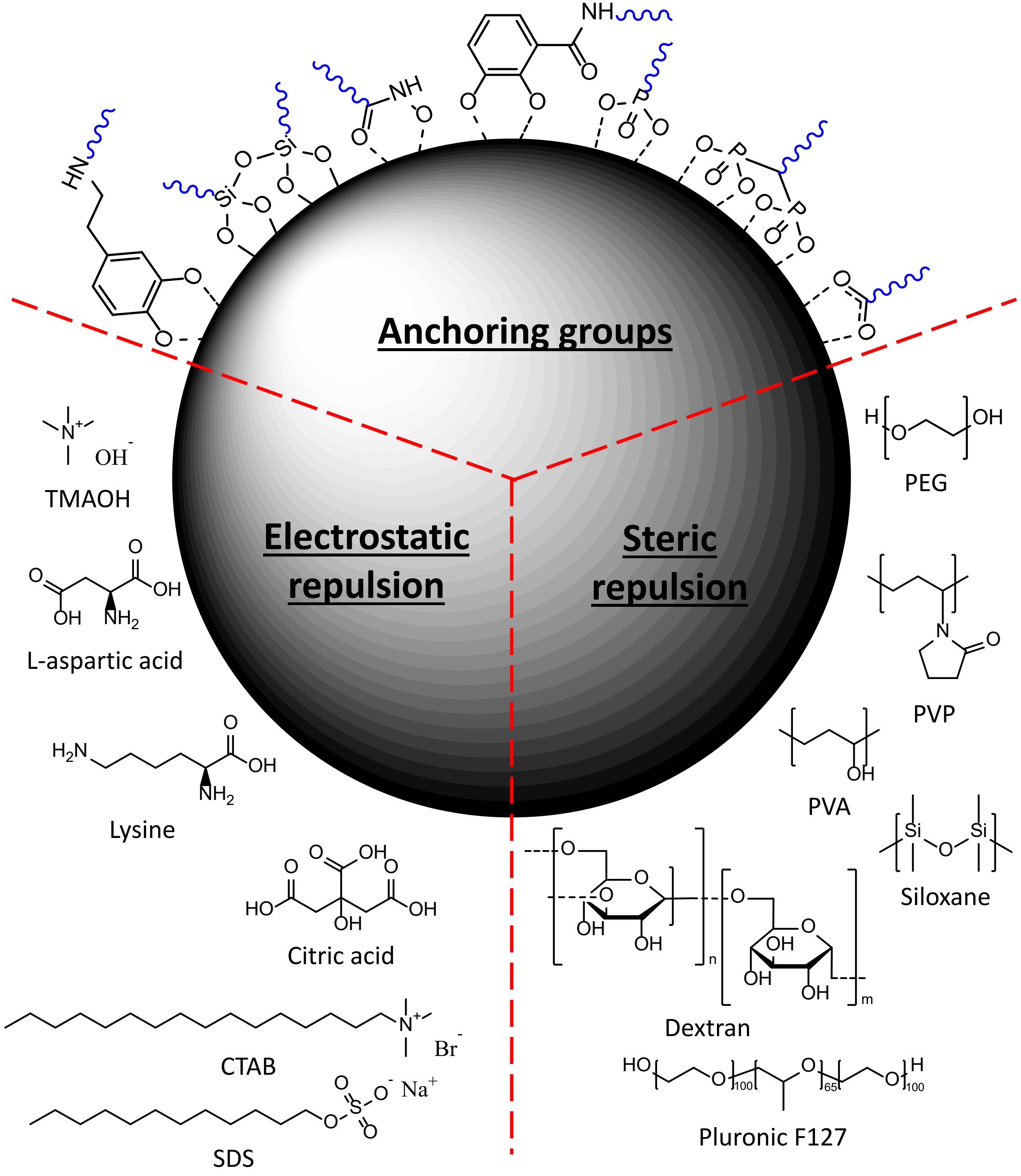
Ligand Addition

Anchoring group
- High affinity for the surface

Electrostatic
- Small charged molecules
- Simple to graft
- Surface still accessible
- Sensitive to pH and ionic media

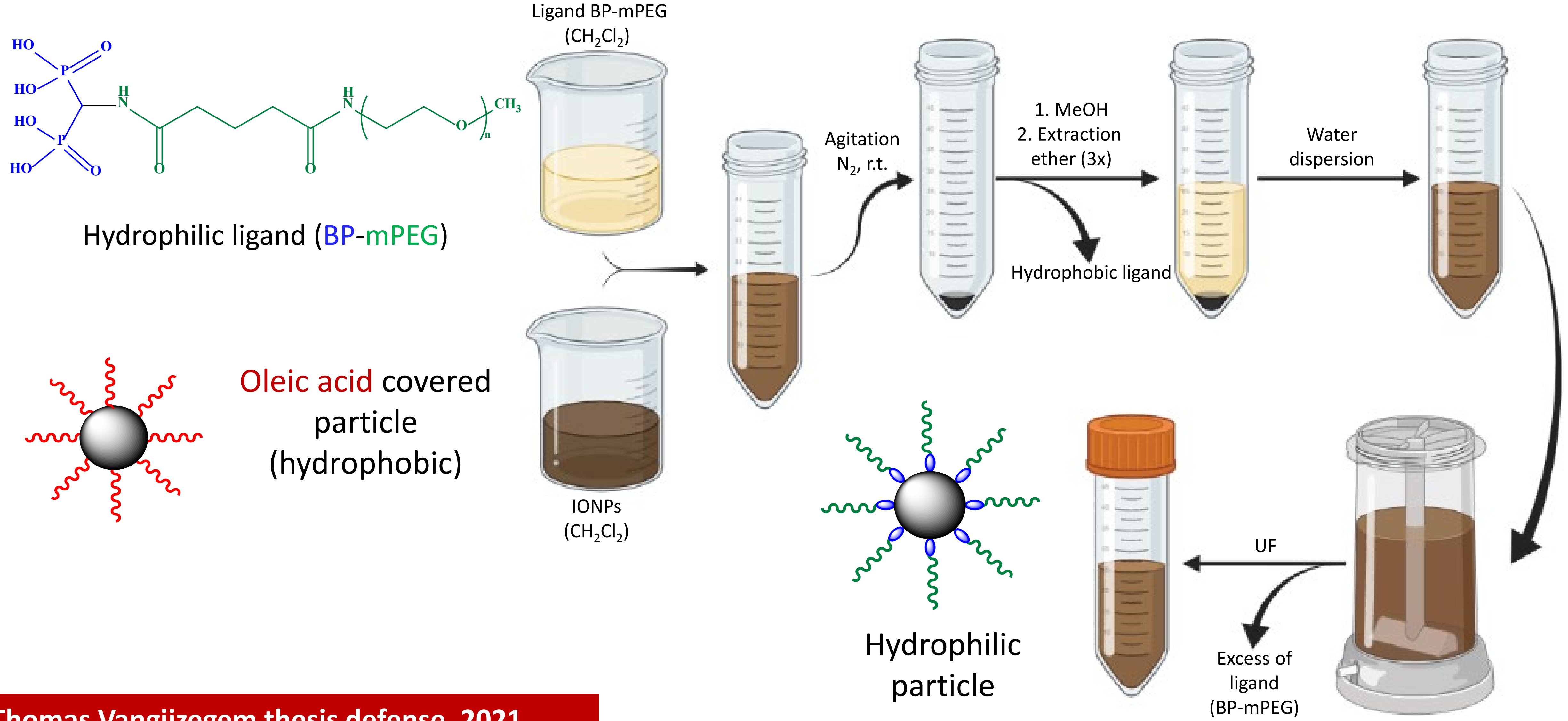
Steric
- Long polymers
- Increase particle stealth
- Not sensible to ionic strength

➡ Suitable for biomedical applications



Vangijzegem *et al.* 2023, Pharmaceutics

Ligand Exchange Protocol

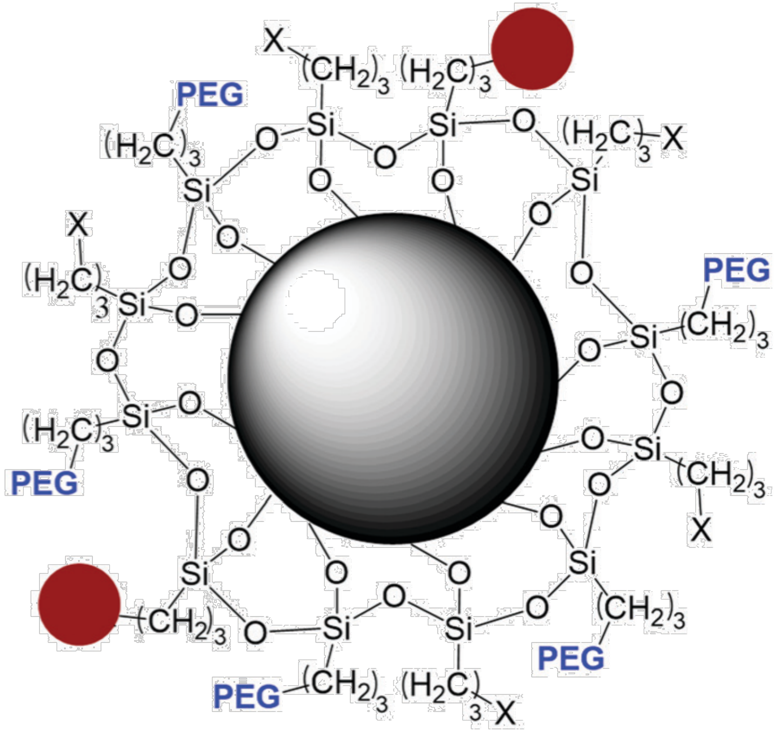


Thomas Vangijzegem thesis defense, 2021

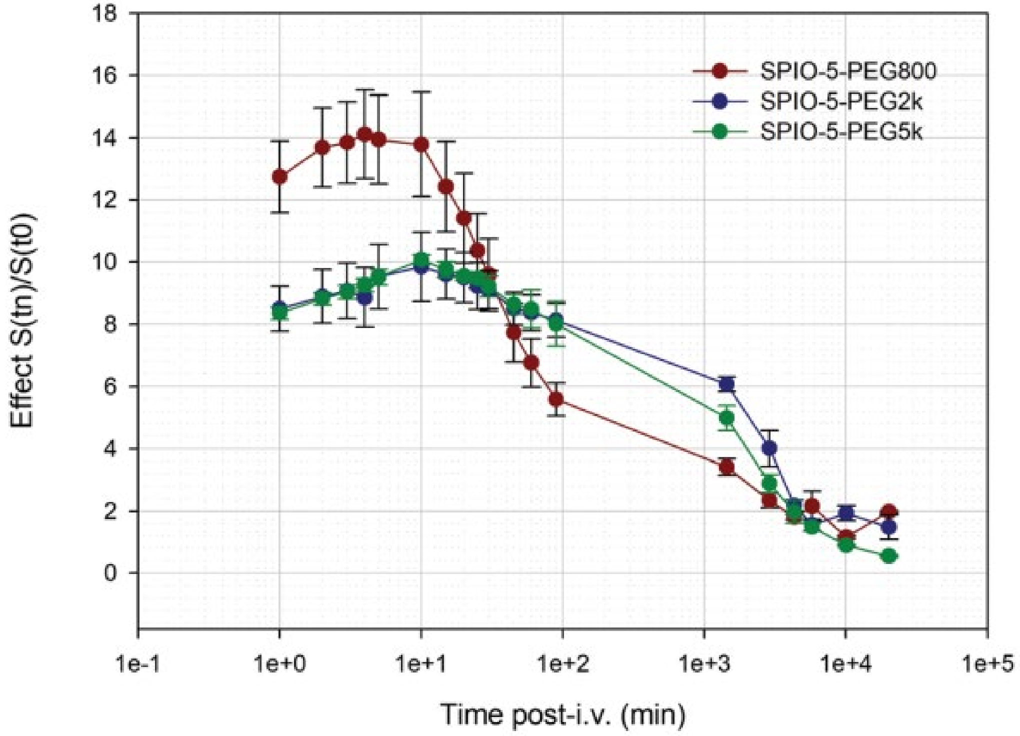
PEG Coating

Circulation time is a key parameter

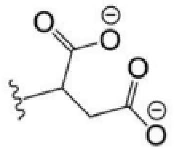
➥ Influenced by the length of the PEG chain



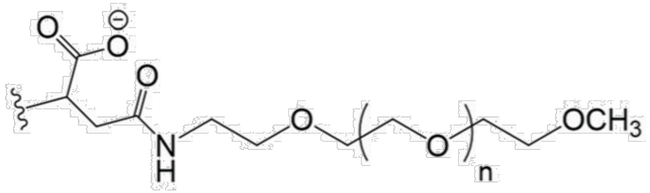
Bimodal IONPs: MRI and fluorescence imaging



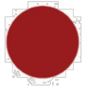
X =



PEG =



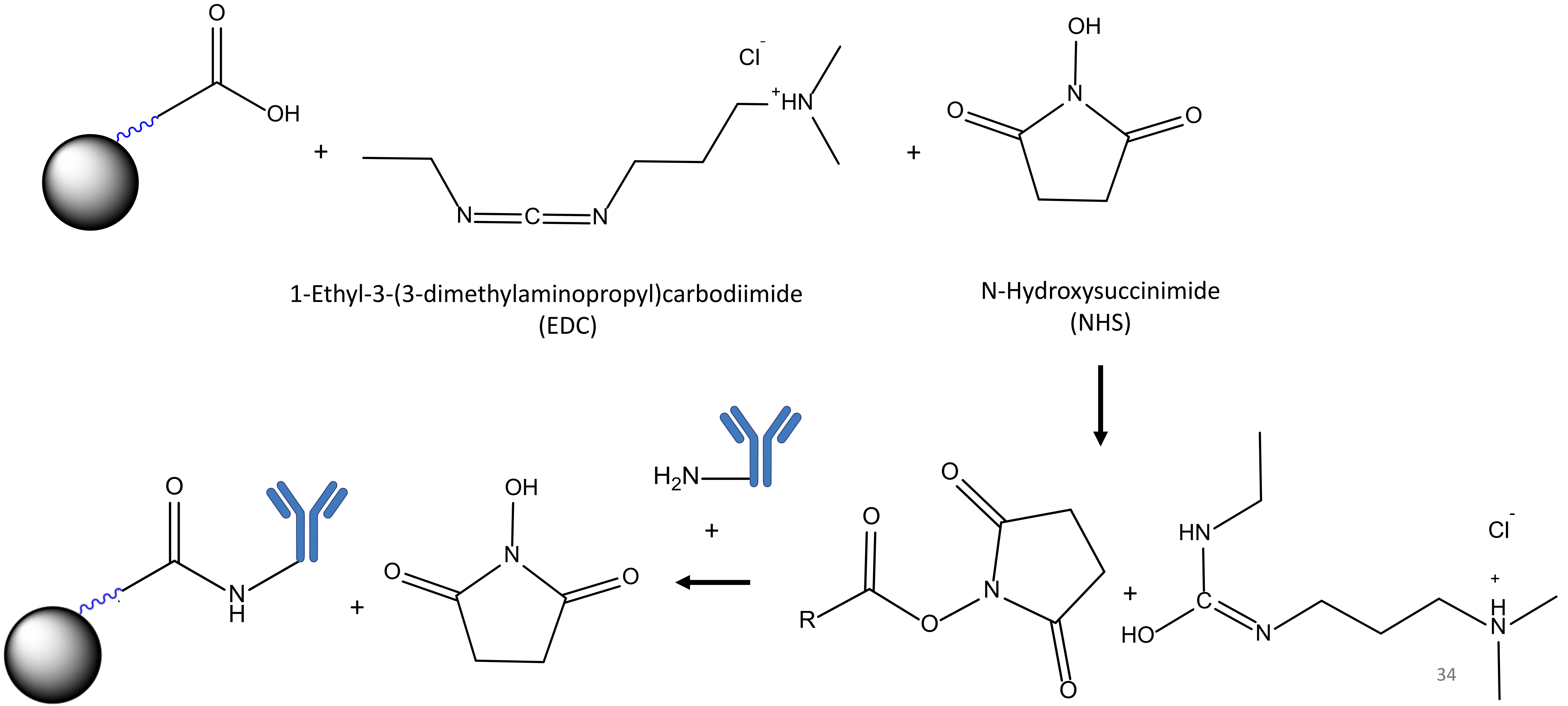
With n ~ 18, 45 or 113



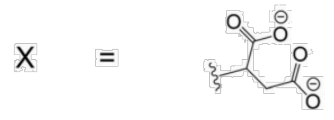
= ZW800 (near infra-red emitting dye)

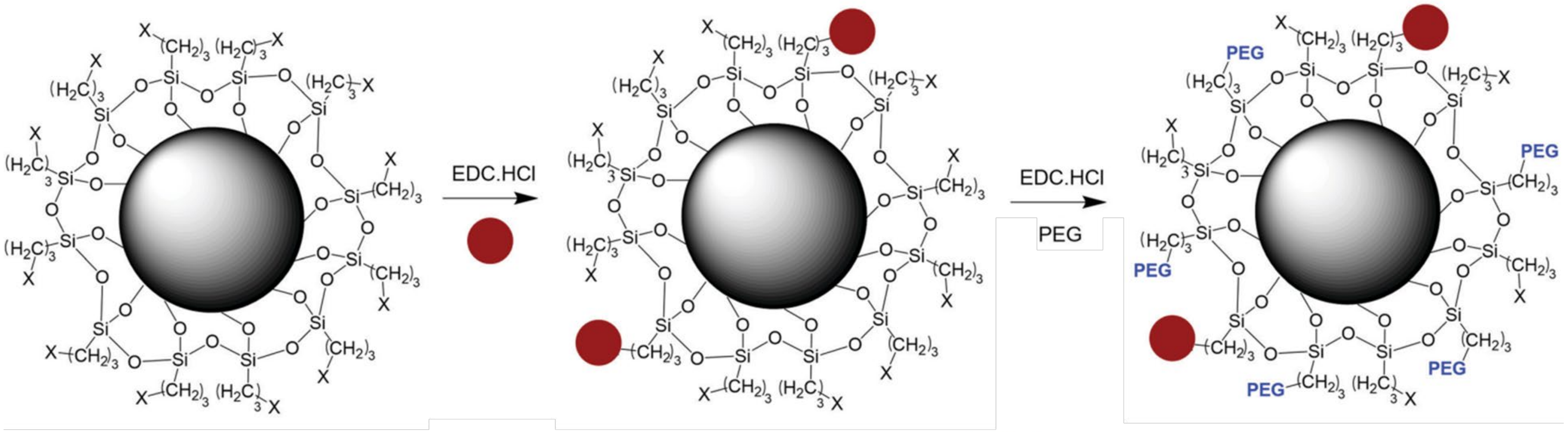
Stanicki *et al.* 2021, Journal of Material Chemistry B

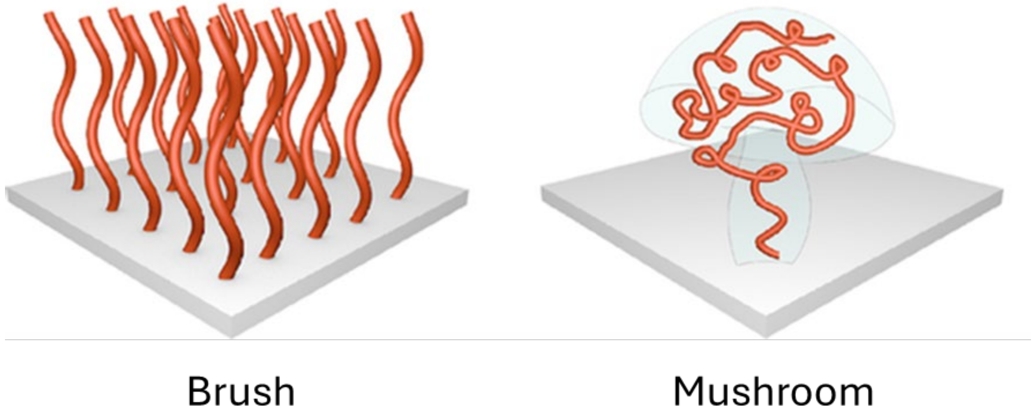
EDC/NHS Coupling



EDC/NHS Coupling







EDC/NHS Coupling

- Easy to implement
- Work on almost every primary amine
- Poor selectivity → Potential side reaction
- Need of carboxylic acid groups

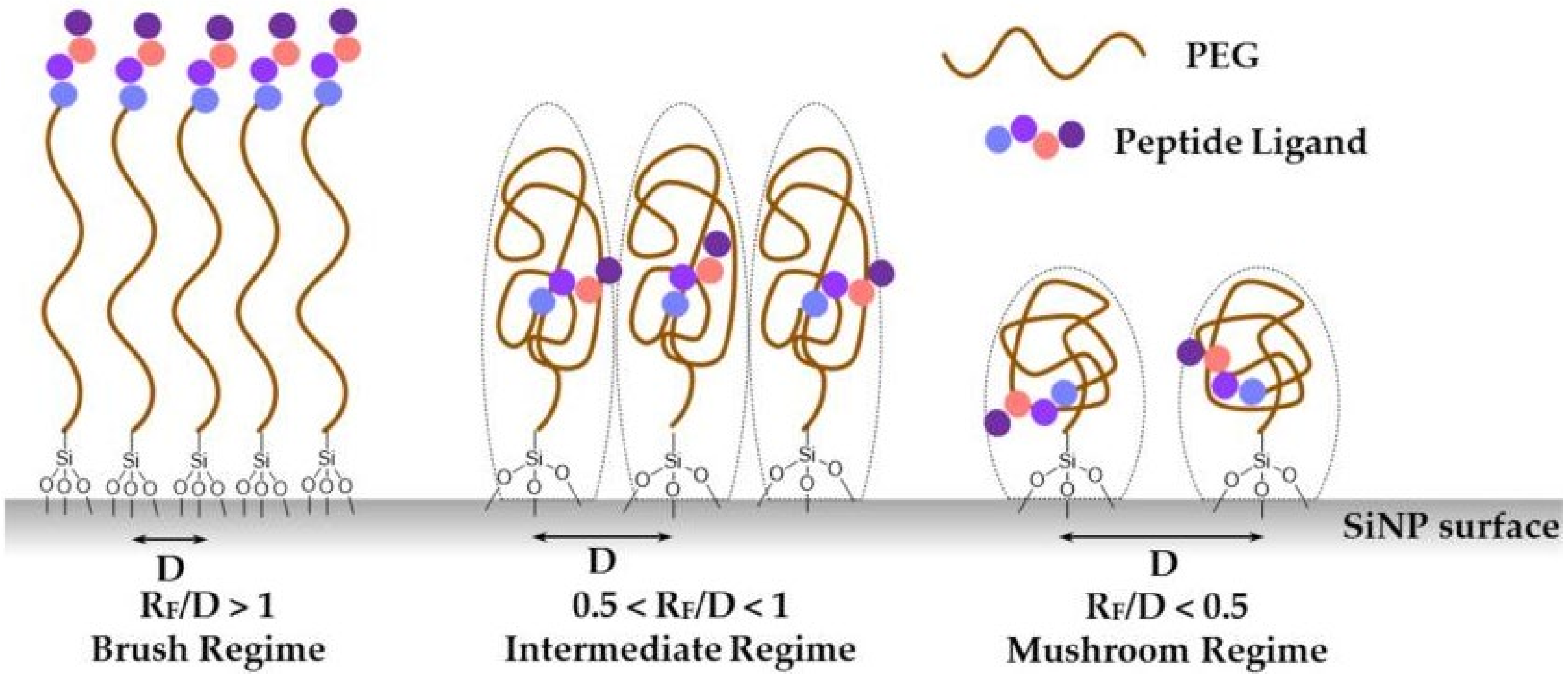
Wang *et al.* 2023, Angewandte Chemie

Vector Location

Conformational regime

- Density of grating → Distance between anchoring point (D)
- Length of the polymer → Length of the monomer (α) × degree of polymerization (N)

➥Flory radius : Rf = $\alpha \times N^{3/5}$



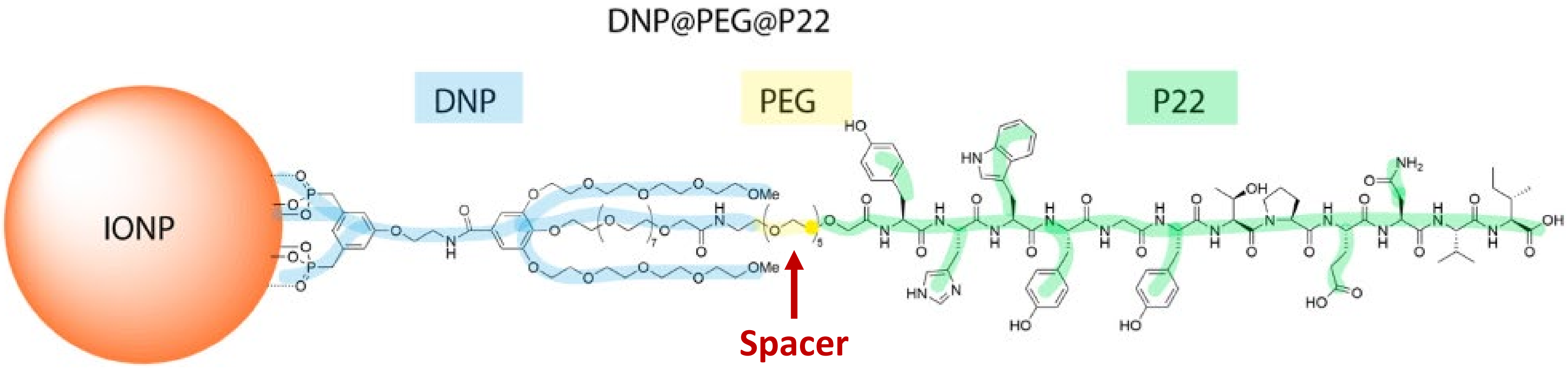
Vector can be burried into the polymer layer

⬇

Reduction of availability

Maurel *et al.* 2021, Nanomaterial

Addition of Spacers



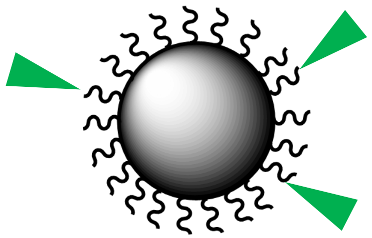
Nano-object for photothermal therapy of breast cancer

Without spacer: internalisation ~ 5% - 7%

Addition of spacer: prevention of peptide burying
➥ Increase of the internalisation

Coupled by EDC/NHS

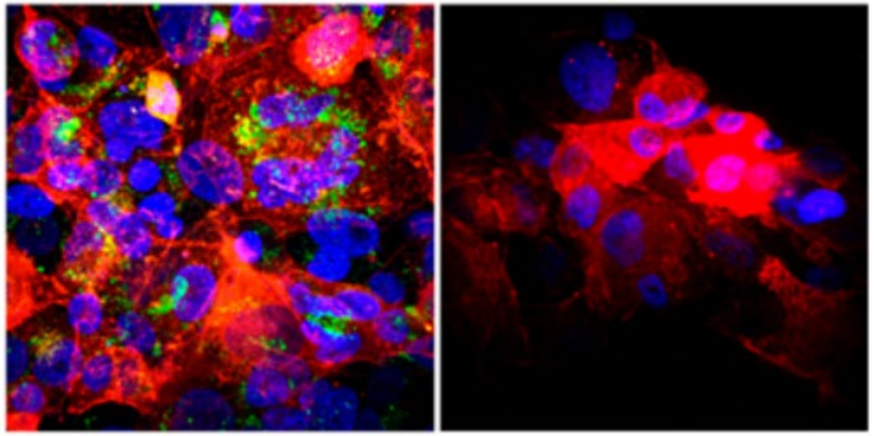
DNP-COOH + NH_2-PEG(6)-P22



Ramirez *et al.* 2025, Nanoscale

Addition of Spacers

Confocal microscopy

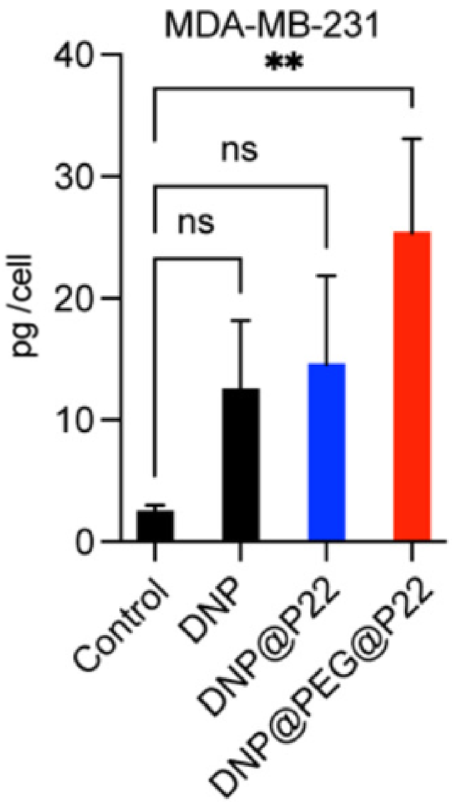


DNP@PEG@P22 DNP

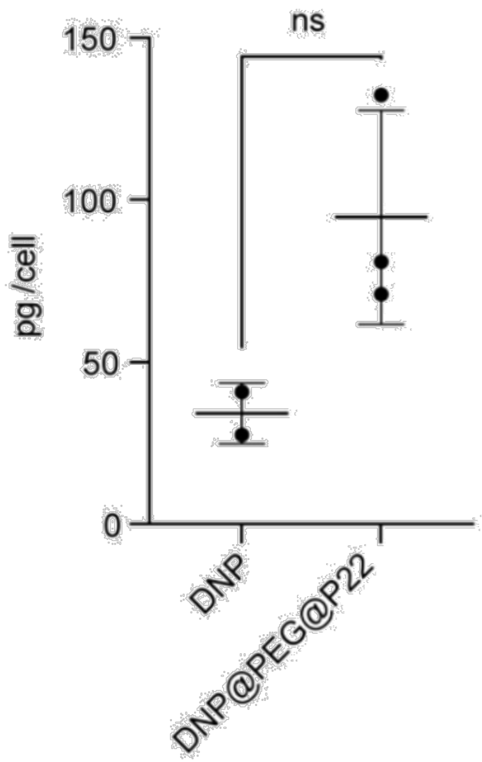
- Dapi: Nuclei
- Alexa Fluor™ 532 Phalloidin: Actin
- Alexa488: DNPs

Iron uptake

Prussian blue staining



ICP-MS



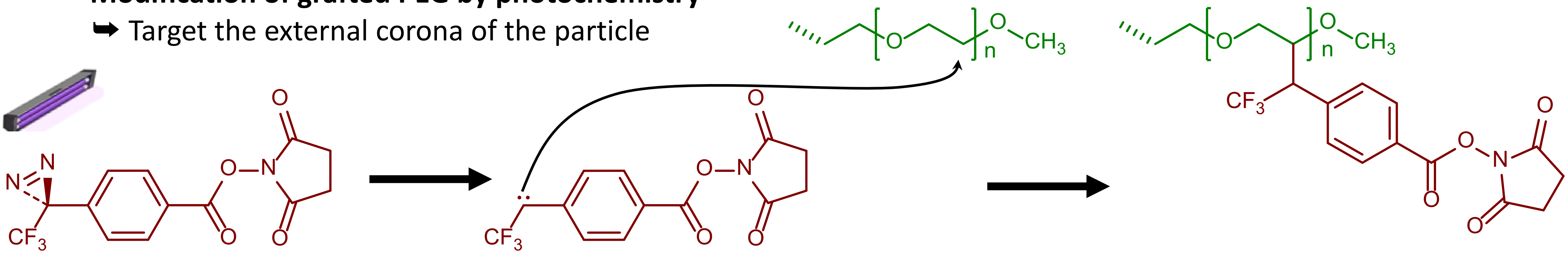
- **Iron uptake increased significantly**
- **IC50 dropped from 16 µg/mL to 6 µg/mL**

Ramirez *et al.* 2025, Nanoscale

Photochemistry

Modification of grafted PEG by photochemistry

➥ Target the external corona of the particle



Clip-TPD-NHS

Method

IONP (H_2O) [Fe] ≈ 50 mM

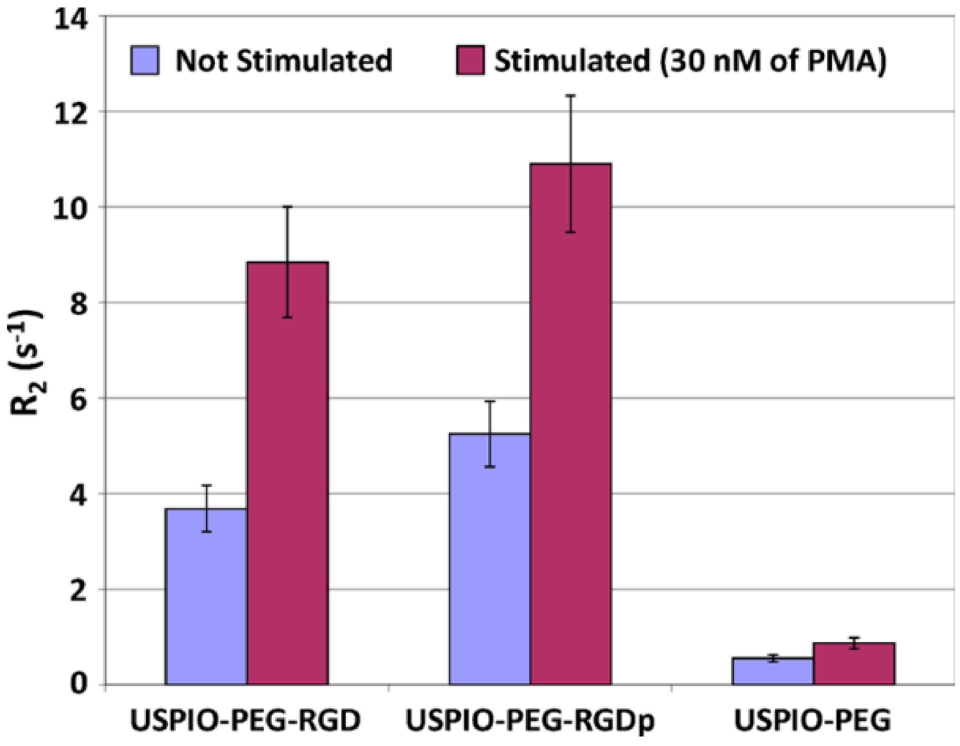
Clip (MeCN) [clip] ≈ 20 mM

r.t.; 30 min

Pourcelles *et al.* 2015, Bioconjugate Chemistry

Clip Grafting by Photochemistry

Transverse relaxation time (R_2) in Jurkat cells

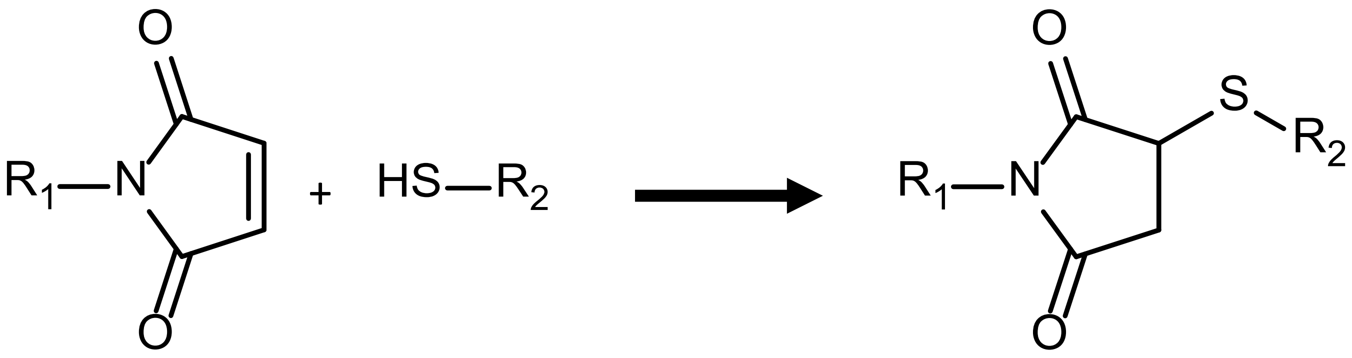


- Easy set up
- Grafting of a targeting peptide on external corona
- Particles properties are preserved
- Increased cellular internalisation
- Versatile technique: Different reactive groups can be added
- Suitable for different applications

Pourcelles *et al.* 2015, Bioconjugate Chemistry

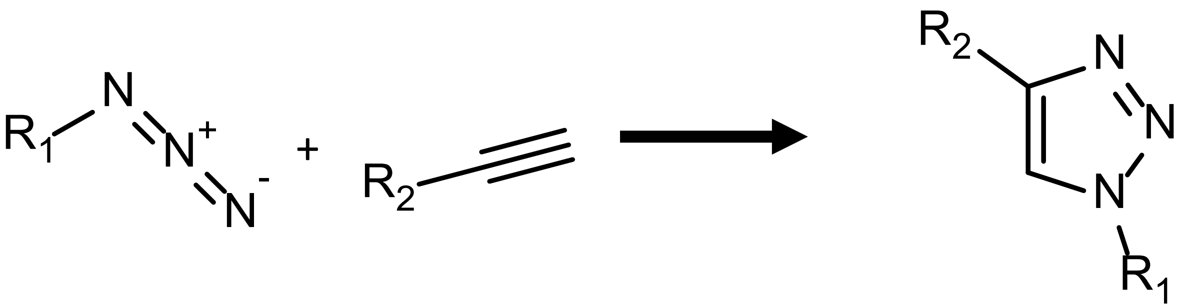
Other Coupling

Maleimide/Thiols



- Specificity
- Proteins containing cysteine
- PEG-maleimide

Click Chemistry

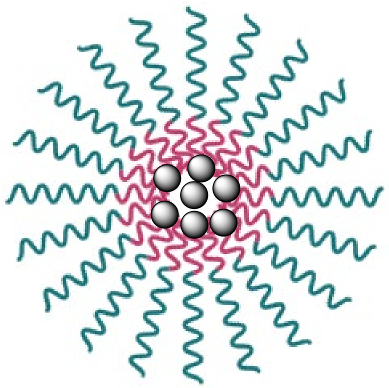


- More specificity
- Modified proteins
- PEG-Azide

Encapsulation

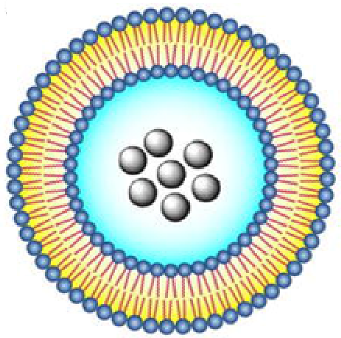
- Work with hydrophilic or hydrophobic particles
- Stealth and prolonged circulation
- Liposomes: Double loading
  ➥ Particles and drug
- Magnetically controlled delivery
- Same vectorisation methods can be applied

Micelles

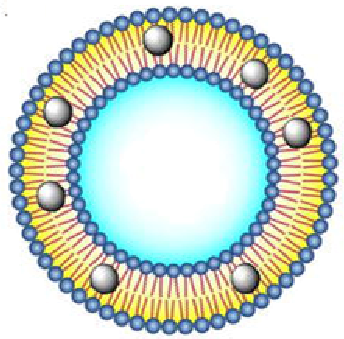


Liposomes / Polymersomes

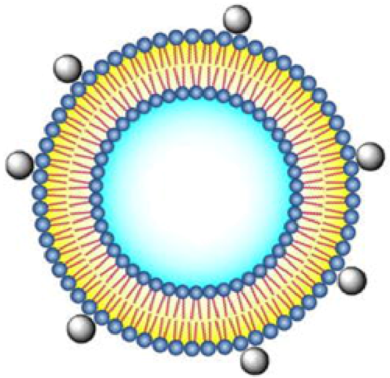
Hydrophilic IONPs
in aqueous core



Hydrophobic IONPs
in the organic layer



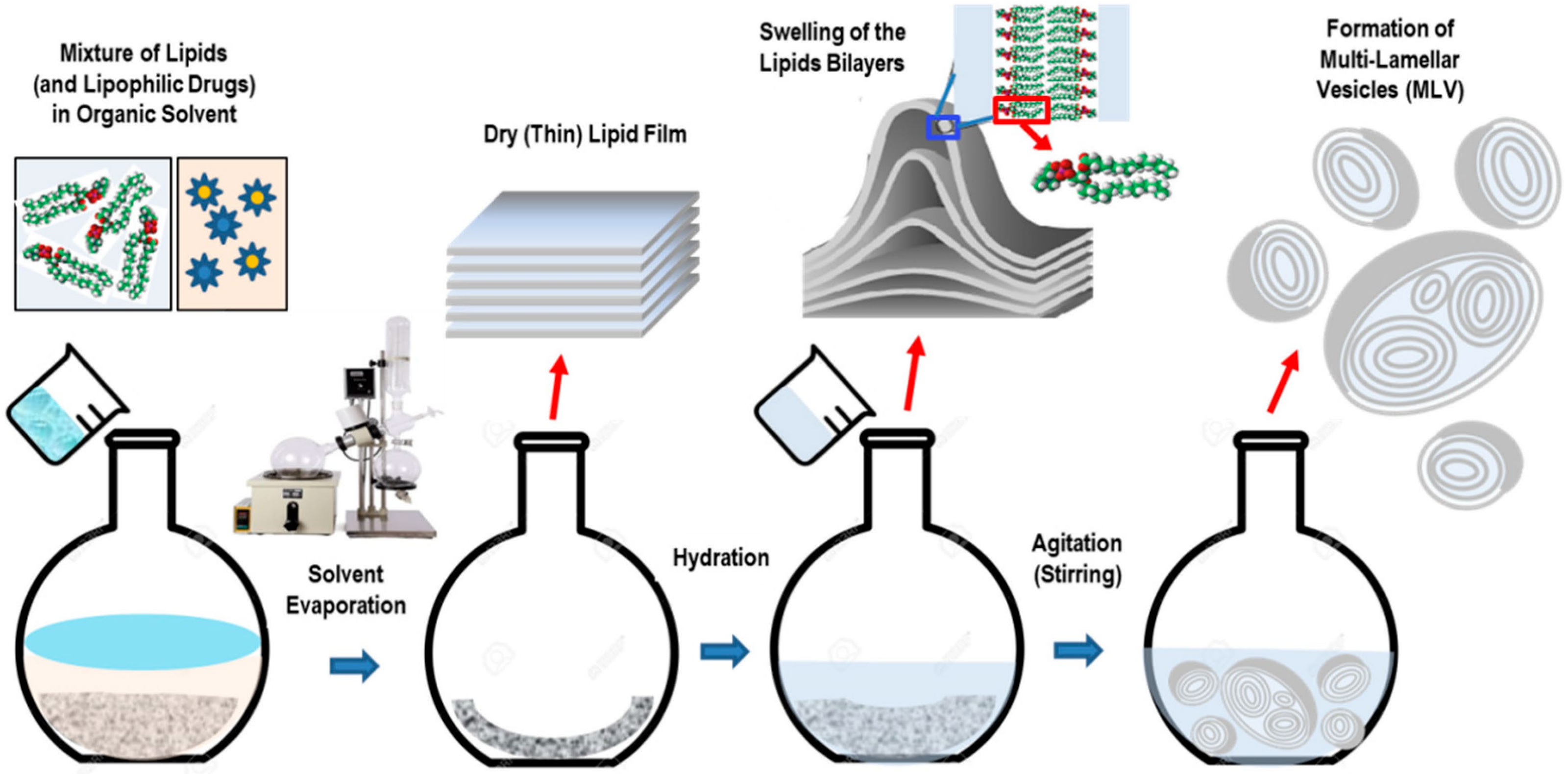
Bonding of IONPs
on the surface



Maroń *et al.* 2022, IntechOpen

Preparation Methods

- **Thin film hydration (Bangham method)**



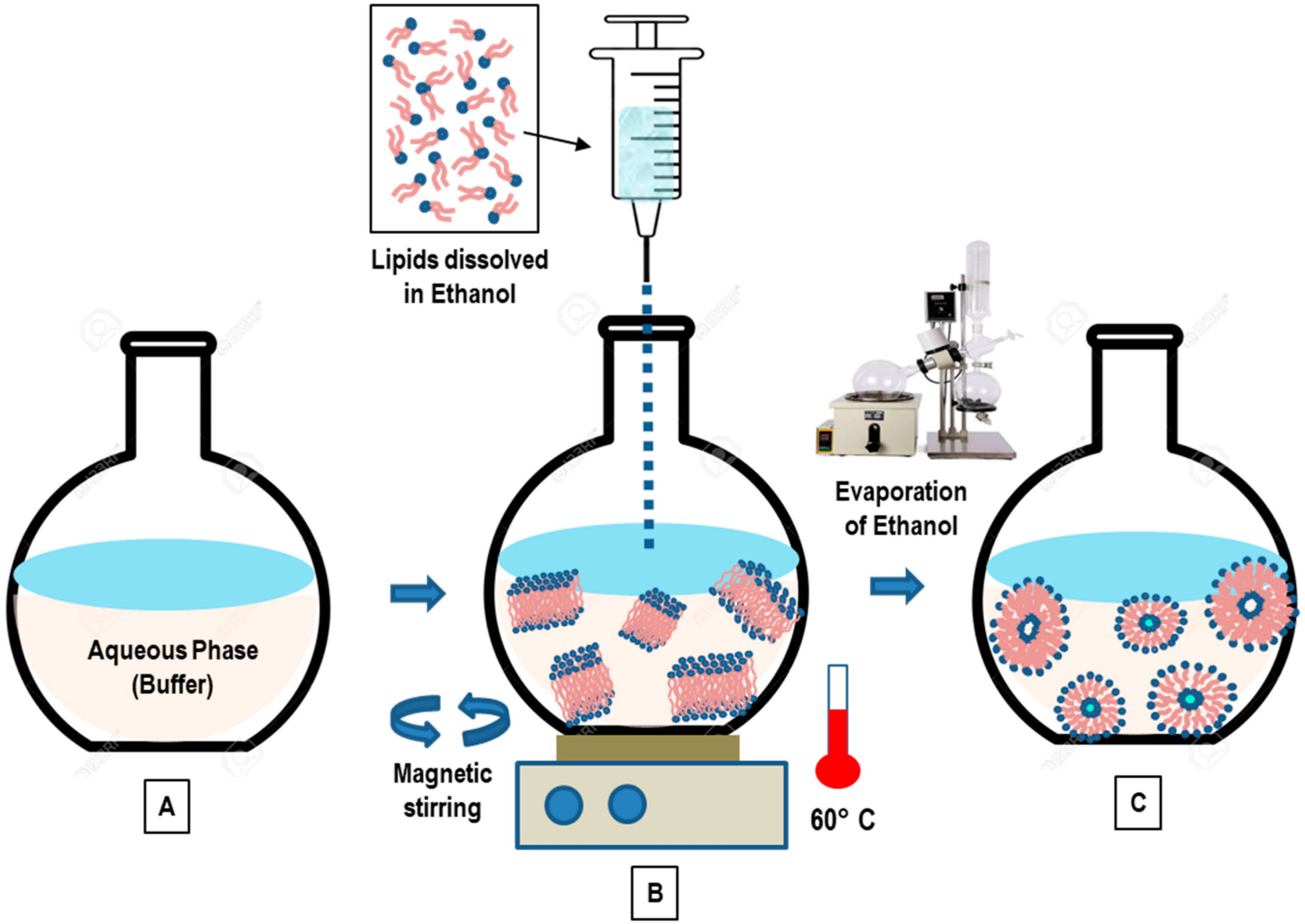
- Simplicity
- Versatility; wide range of compounds
- Suitable for hydrophilic and hydrophobic substances

- Traces of organic solvent
- Low productivity → not scalable
- High polydispersity
- Less efficient for hydrophilic compound encapsulation

Lombardo *et al.* 2022, Pharmaceutics

Preparation Methods

- **Ethanol injection**

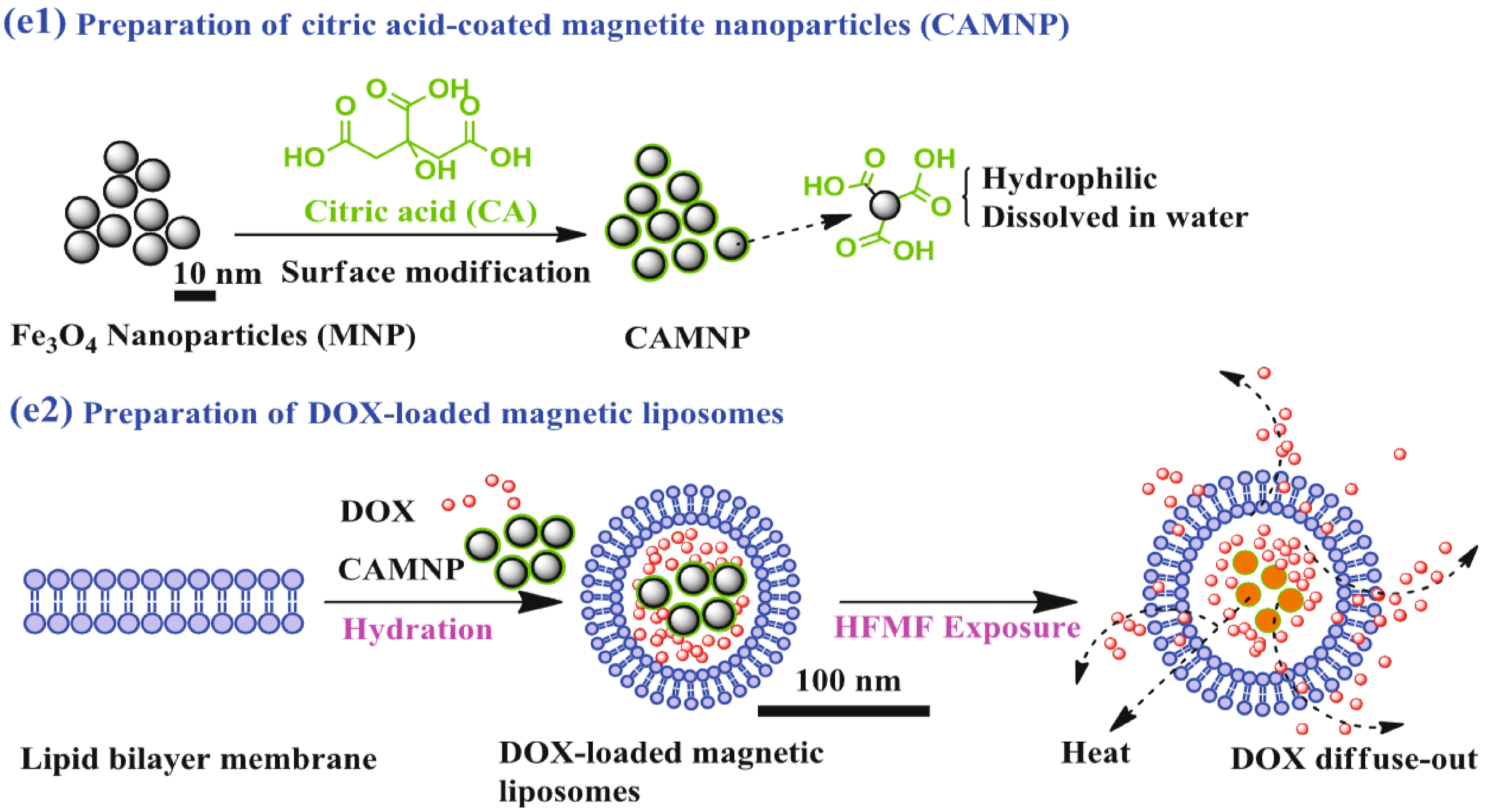


- Fast and reproducible
- Mild solvent
- Scalability
- Unilamellar vesicles

- Traces of ethanol
- Low liposome concentration
- Risk of denaturation for proteins
- Strict parameter control

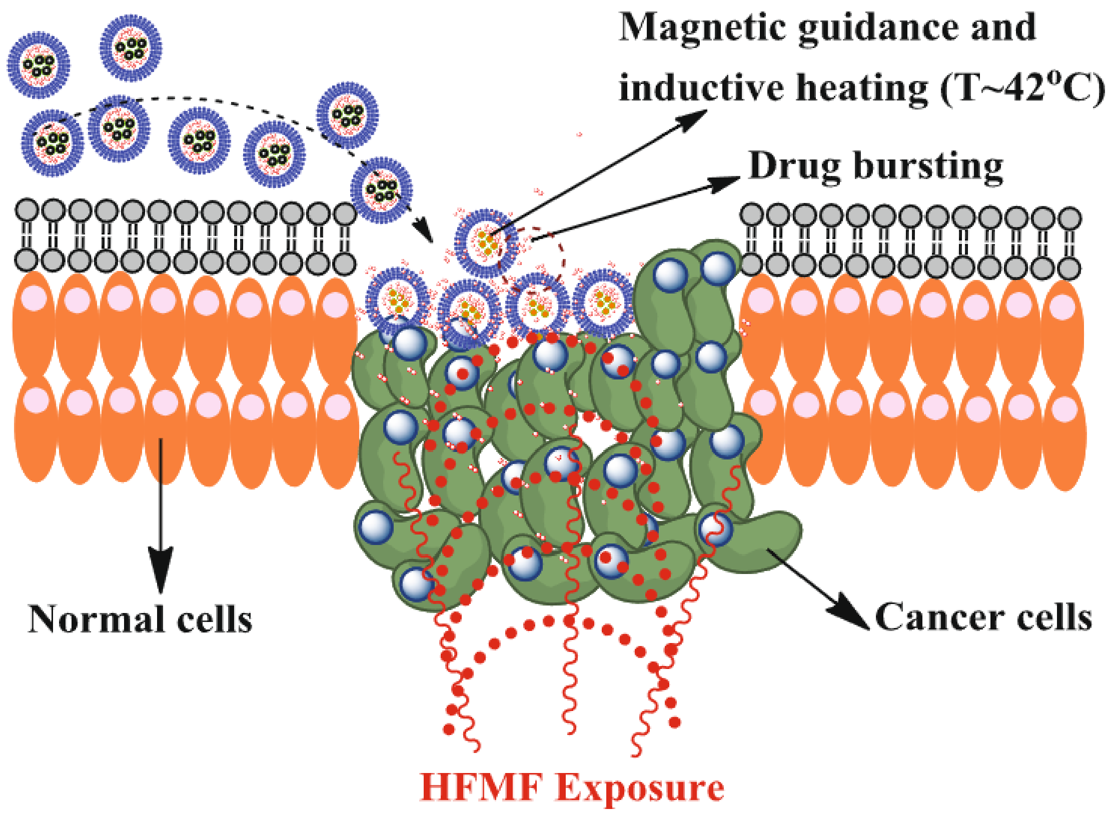
Lombardo *et al.* 2022, Pharmaceutics

Magnetoliposomes Application



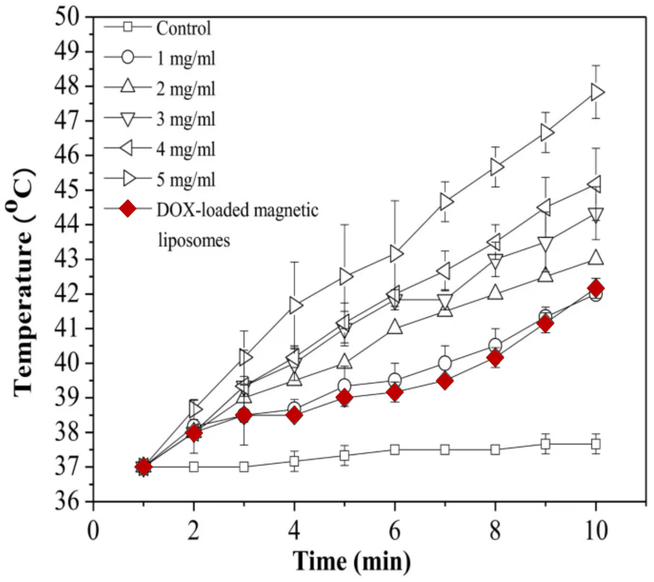
Hardiansyah *et al.* 2014, Nanoscale Research Letters

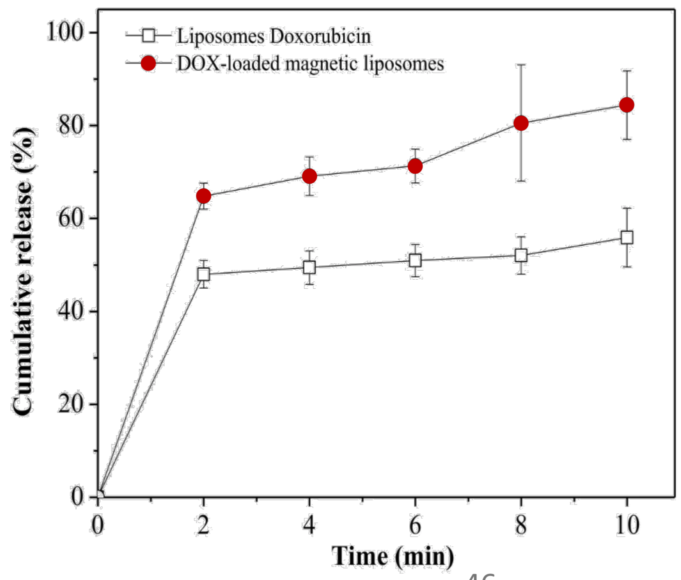
Magnetoliposomes Application



DOX-loaded magnetoliposomes

- Magnetically guided drug carrier
- Enhanced controlled release
- Photothermic effect

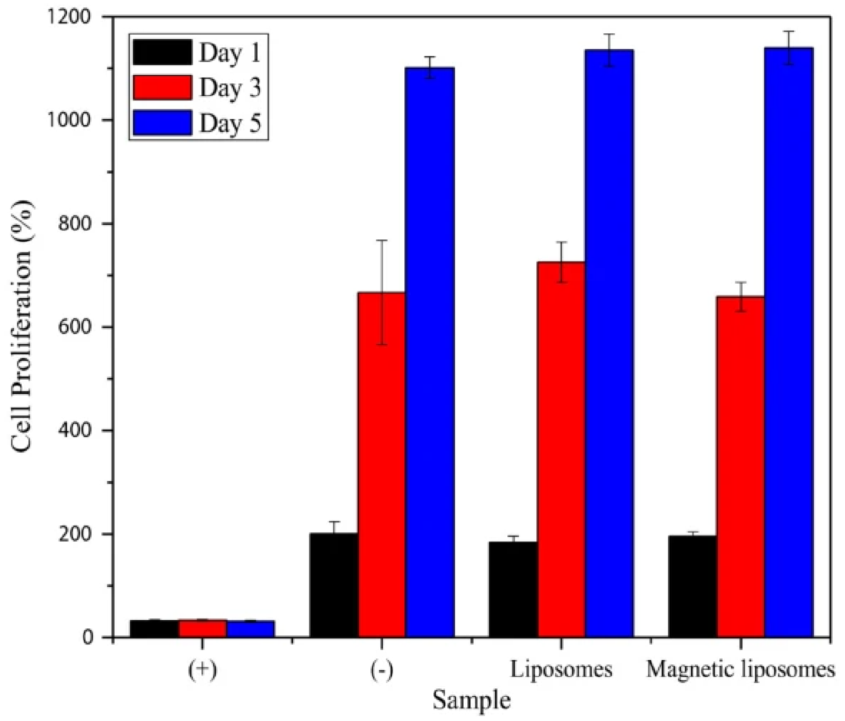




Hardiansyah *et al.* 2014, Nanoscale Research Letters

Magnetoliposomes Application

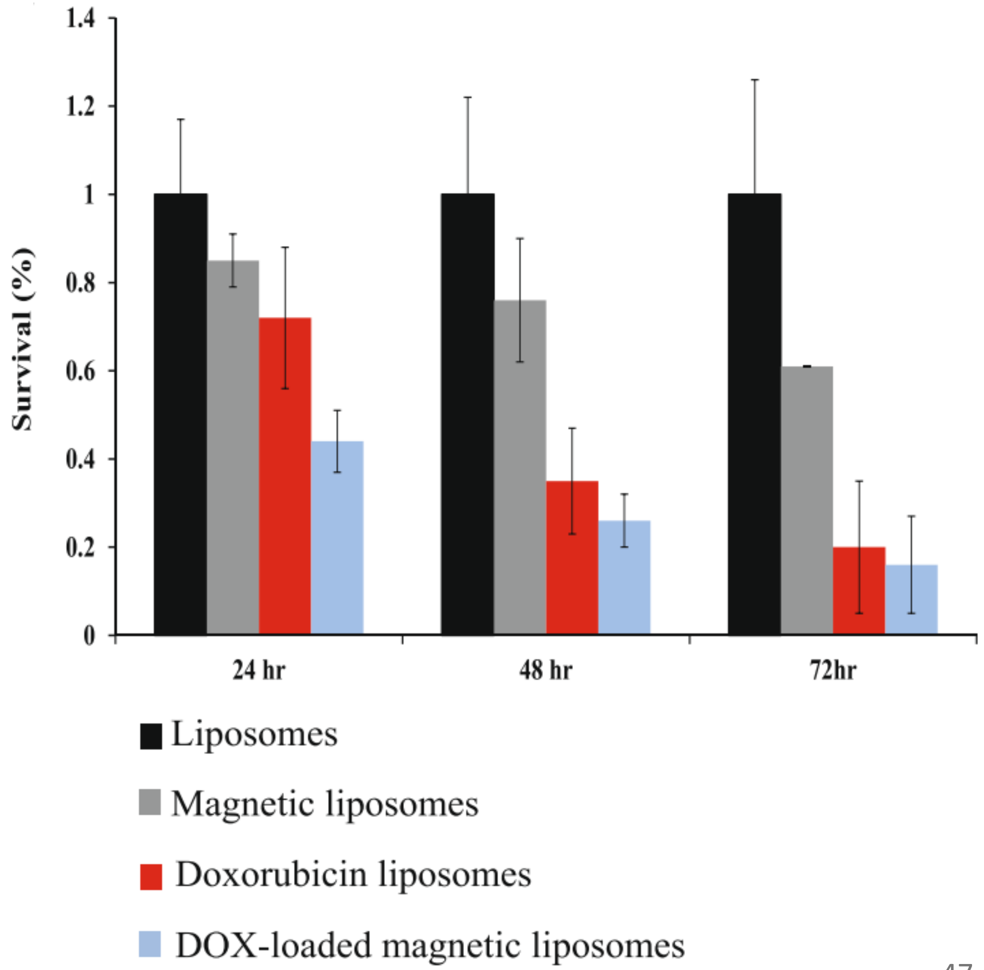
MTT assays on murine fibroblast healthy cells (L-929)



(+) Cells treated with DMSO

(-) Cells treated with medium only

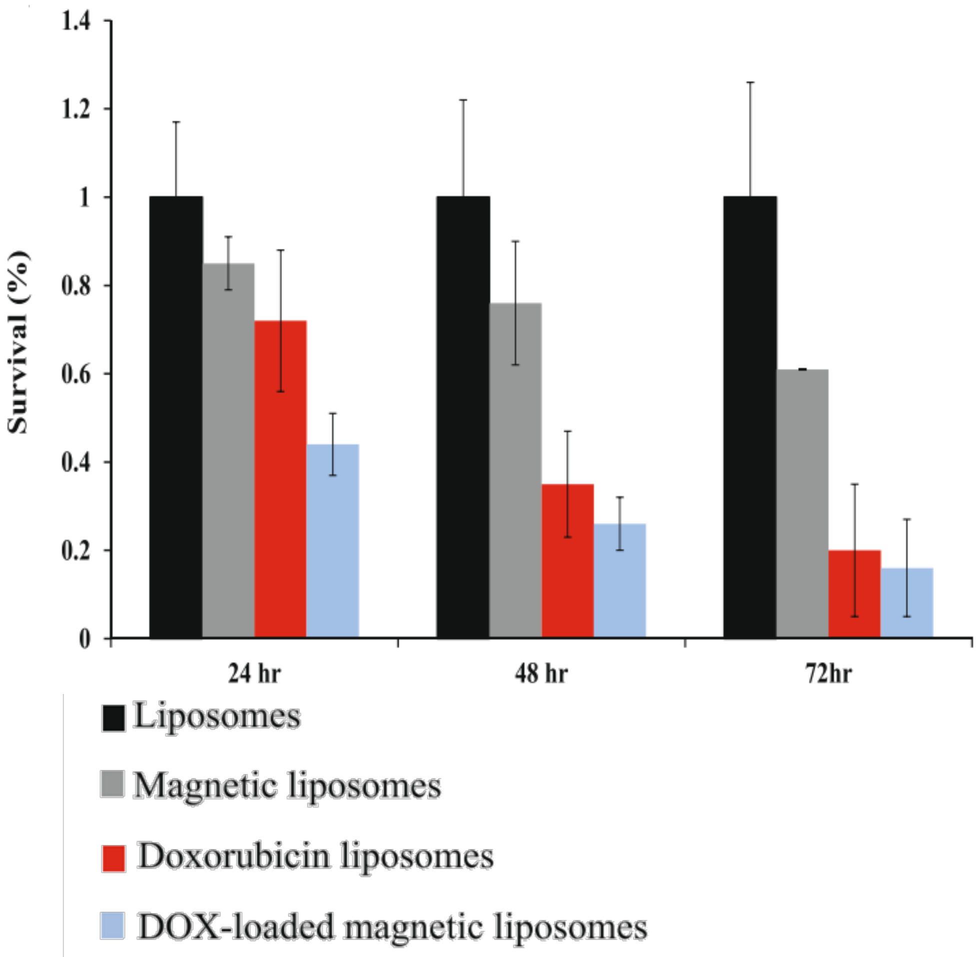
MTT assay on murine colon carcinoma cells (CT-26)



Hardiansyah *et al.* 2014, Nanoscale Research Letters

Magnetoliposomes Application

MTT assay on murine colon carcinoma cells (CT-26)



DOX-loaded magnetoliposomes

- Great biocompatibility
- Controlled burst release: 40% → 80%
- Heating capacity: 42°C in 10 min
- Cell killing efficiency: 56% in 24h
- Synergetic treatment:

  Hyperthermia: 15% killing

  Chemotherapy: 38% killing

Heat from hyperthermia increases blood flow

➥ Increase DOX uptake

Hardiansyah *et al.* 2014, Nanoscale Research Letters

Conclusions

Stabilisation

Inorganic Coating

- Protect magnetic core
- Combination of material properties

Ligand Addition

- Versatility of ligand
- Structure modulation

Encapsulation

- Drug targeted delivery
- Great bicompatibility

Vectorisation

- EDC/NHS coupling
- Photochemistry

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Magnetic Particles: Synthesis and Functionalisation

Part 3: Flow Chemistry and Characterisations

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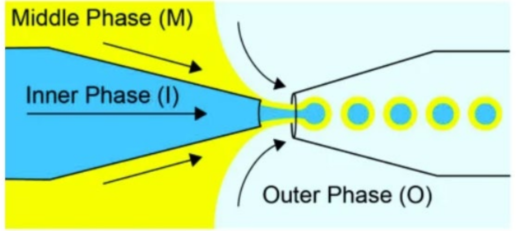
Flow Chemistry

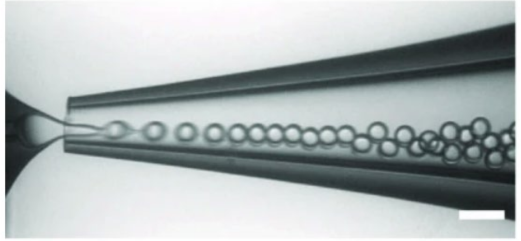
Flow chemistry refers to an automated chemical process that operates continuously, using a constant flow of reactants or solvents.

Developed in 1876 for the industrial synthesis of sulfuric acid.

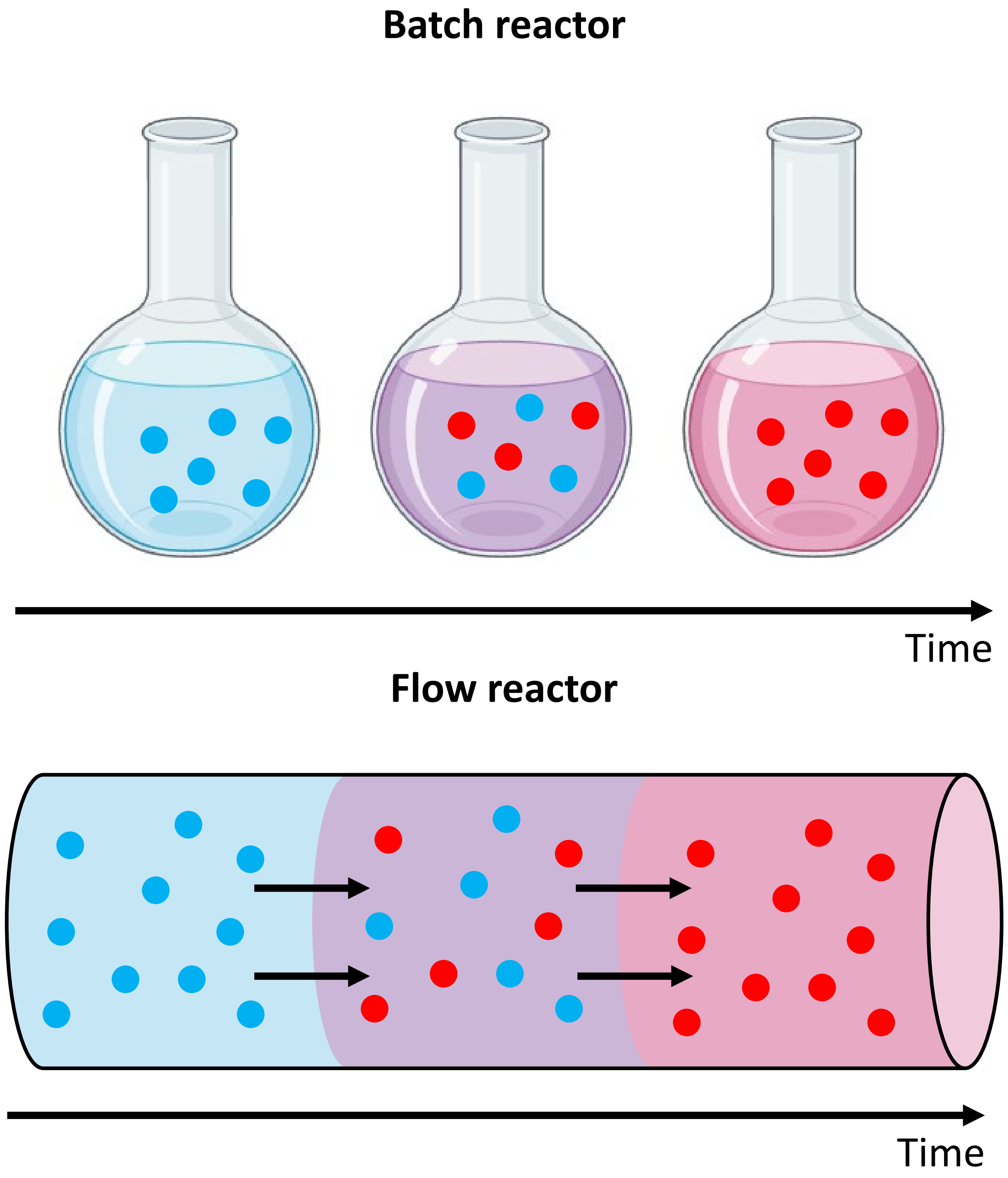
Mainly used for organic synthesis

- Particle synthesis
- Particle functionalisation → Photochemistry
- Liposome/polymersome formation





O’Callaghan *et al.* 2024, The European Physical Journal E

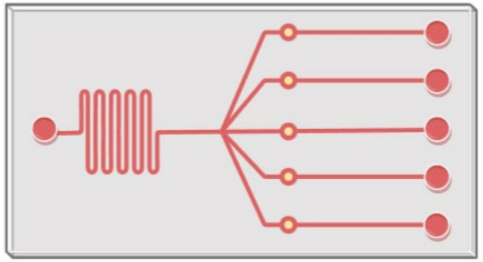


Flow Chemistry

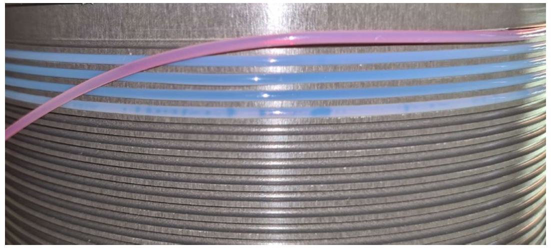
Basic principles of flow chemistry

- Pumps and reagent feeding
- Mixing
- Heat transfer
- Pressure control

Microfluidic Reactor



Millifluidic Reactor



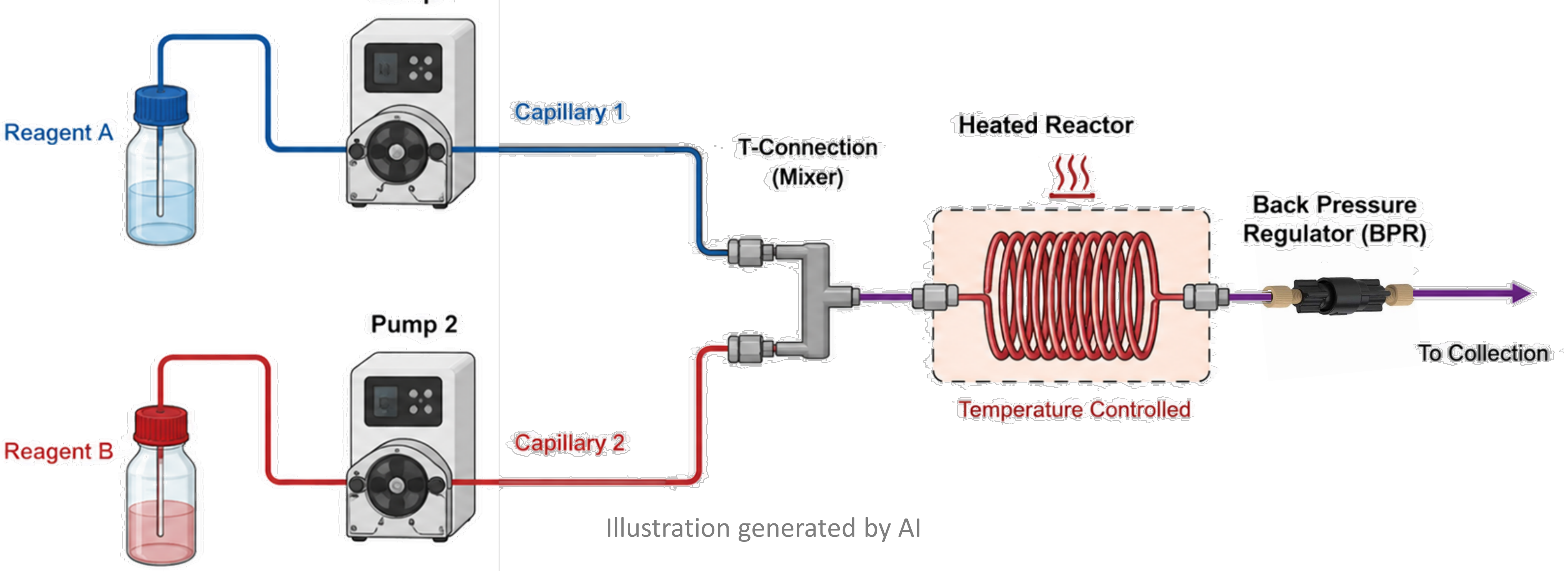


Illustration generated by AI

Flow Chemistry

Basic principles of flow chemistry

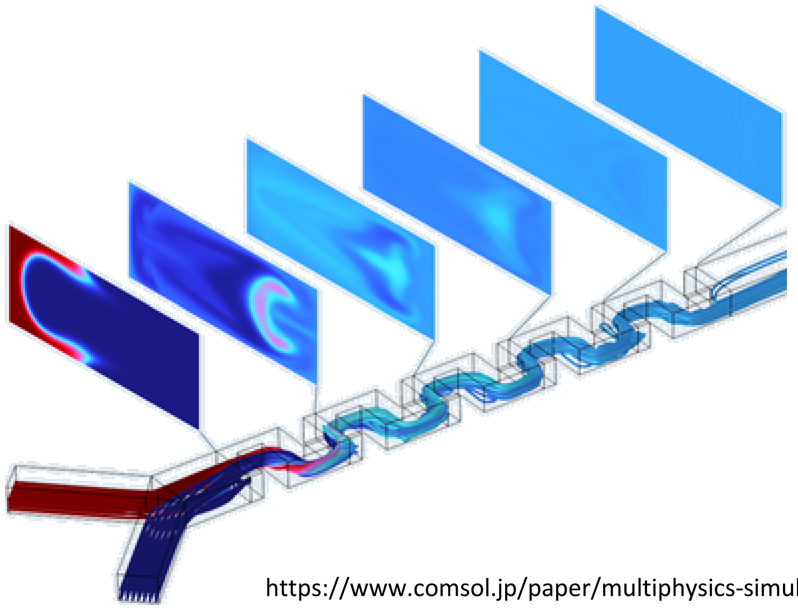
- Pumps and reagent feeding
- Mixing
- Heat transfer
- Pressure control

Residence time: $\tau = \frac{V}{Q}$

Where:

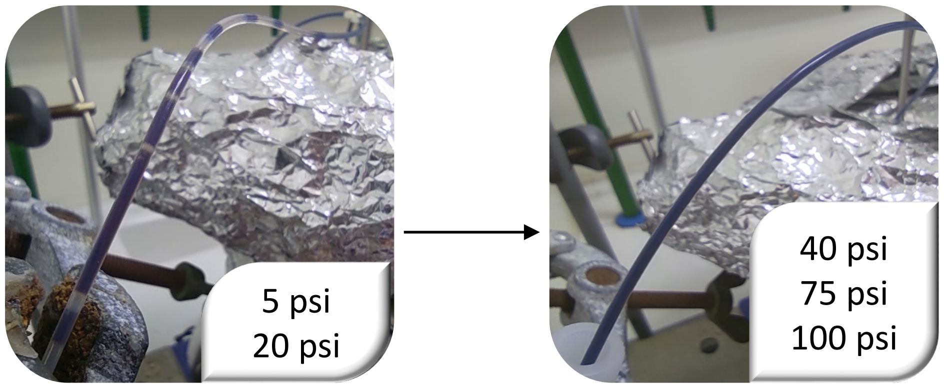
- τ = residence time
- V = reactor volume
- Q = volumetric flow rate

Mixing



https://www.comsol.jp/paper/multiphysics-simulation-of-chaotic-mixing-in-microfluidic-devices-136052

Pressure regulation



Advantages of Flow Chemistry

Smaller reactor size

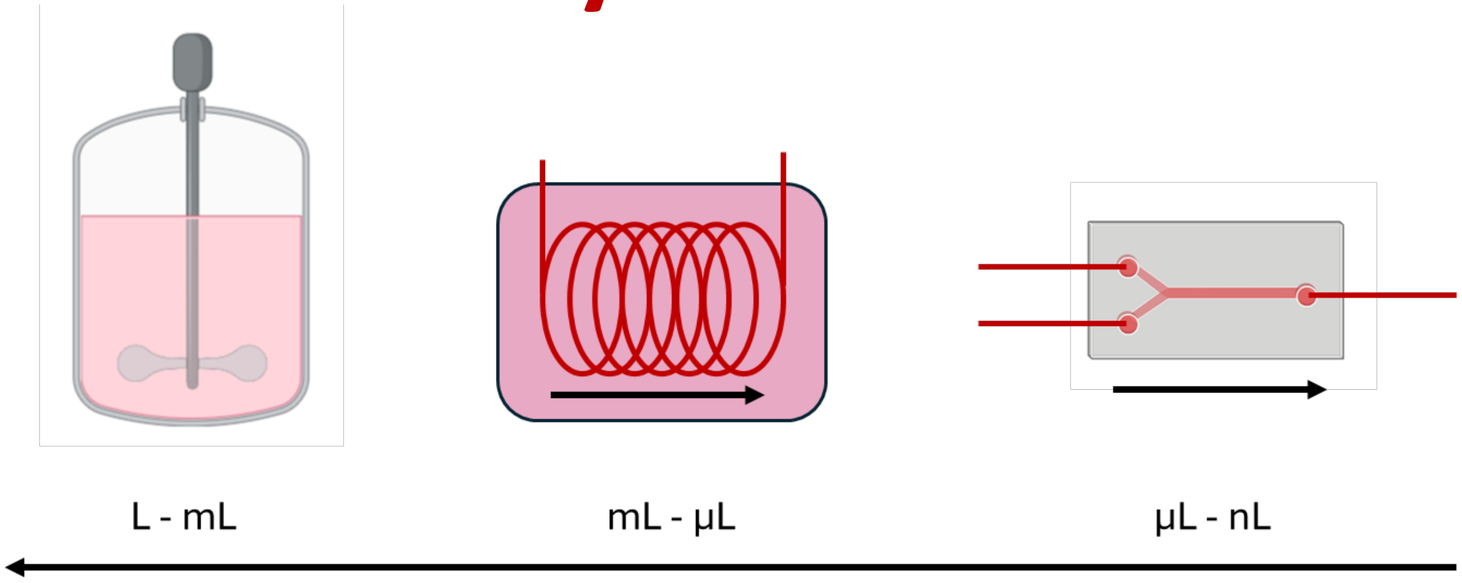
➥ **Higher surface to volume ratio**

Improved safety
- Smaller reaction volumes
- Better control of hazardous reactions

Better heat transfer
- Efficient temperature control
- Reduced hot spots
- Faster mixing

Higher reproducibility
- Precise control of reaction conditions
- Consistent product quality

Process intensification
- Faster reactions
- Higher yields/selectivity
- Easier automation

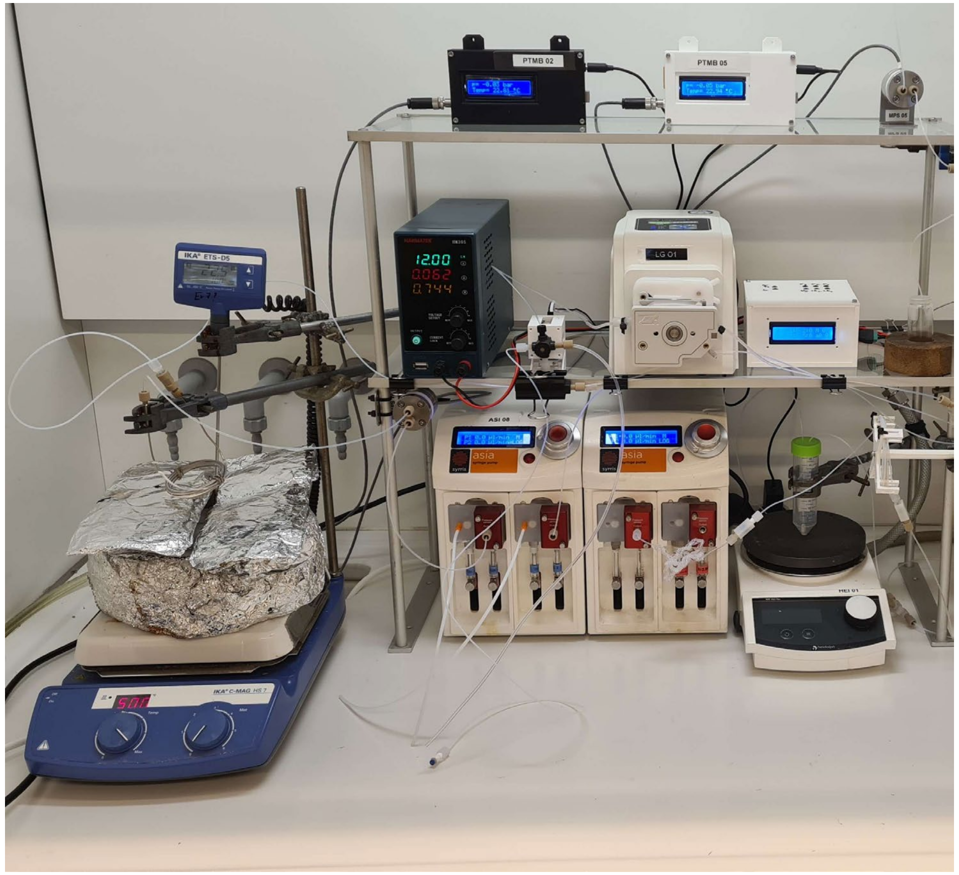


Scalability
- Scale-up through “numbering-up”
- Easier industrial production

Green chemistry
- Reduced solvent consumption
- Lower energy demand

Disadvantages and Limitations

Convoluted set-up
➥ Many things can go wrong



High initial cost
- Specialized equipment
- Pumps, pressure regulators, microreactors

Risk of clogging
- Solid formation can block channels
- Problematic for heterogeneous reactions

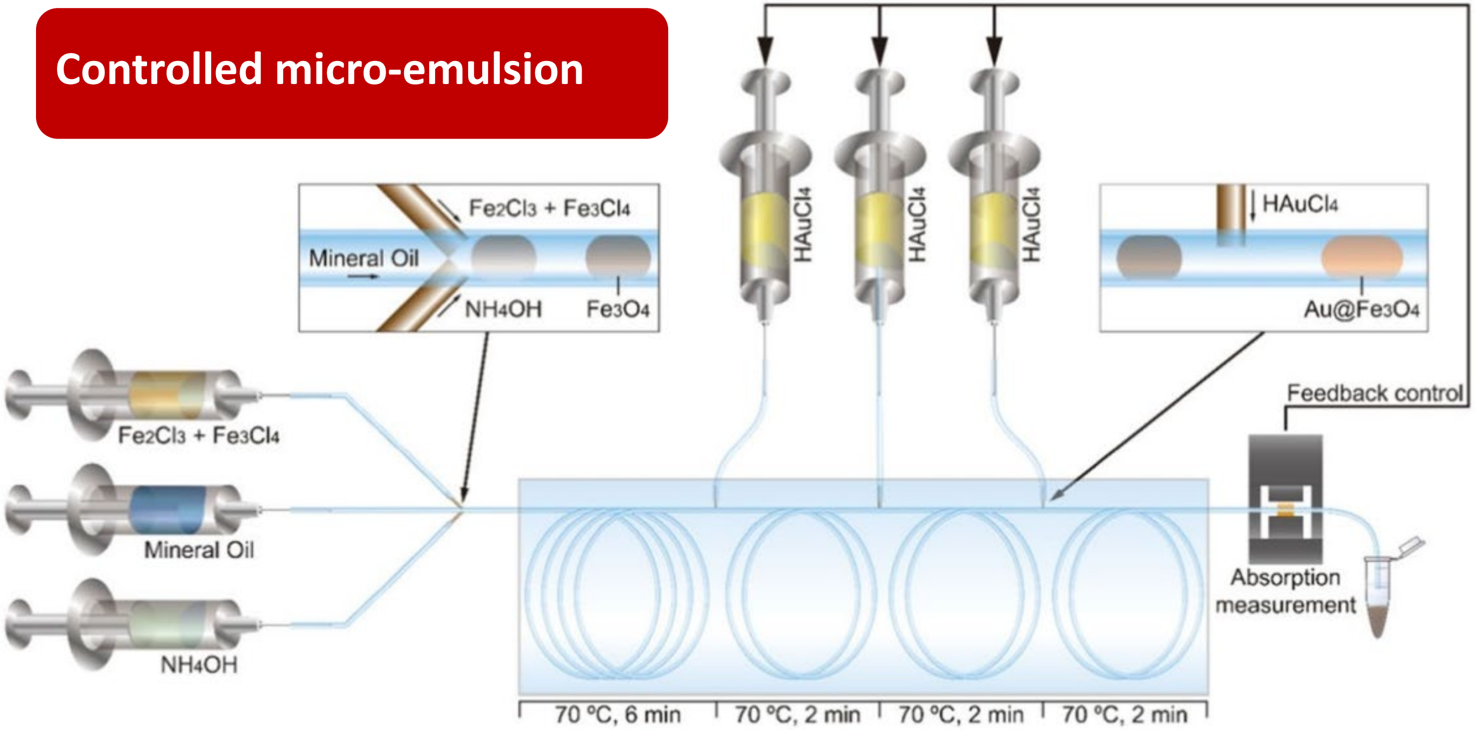
Complex system
- Requires engineering knowledge
- More difficult optimization

Limited reaction types
- Some reactions are easier in batch
- Difficulties with highly viscous mixtures

Cleaning and maintenance
- Fouling
- Reactor cleaning challenges

Applications: Core-shell Particles

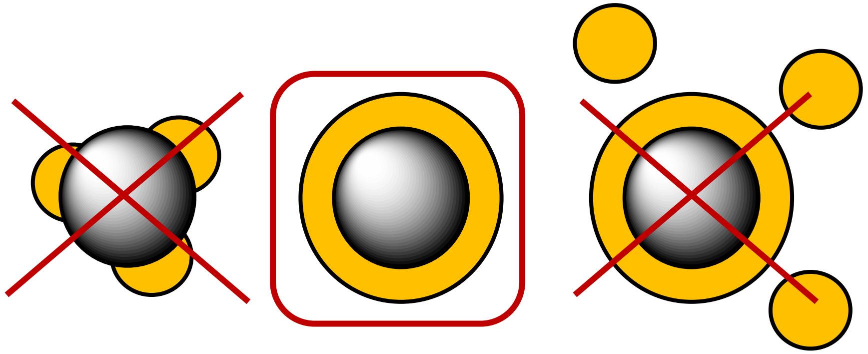
Controlled micro-emulsion

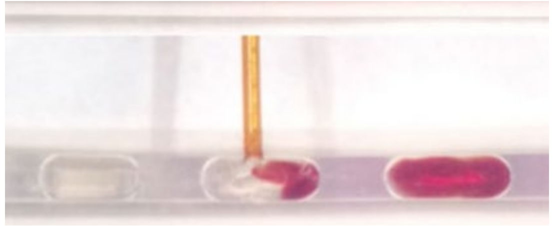


Theranostic application

- MRI contrast agent
- Photothermal therapy

Use of the « Simplex » algorithm to find the optimal flow rates



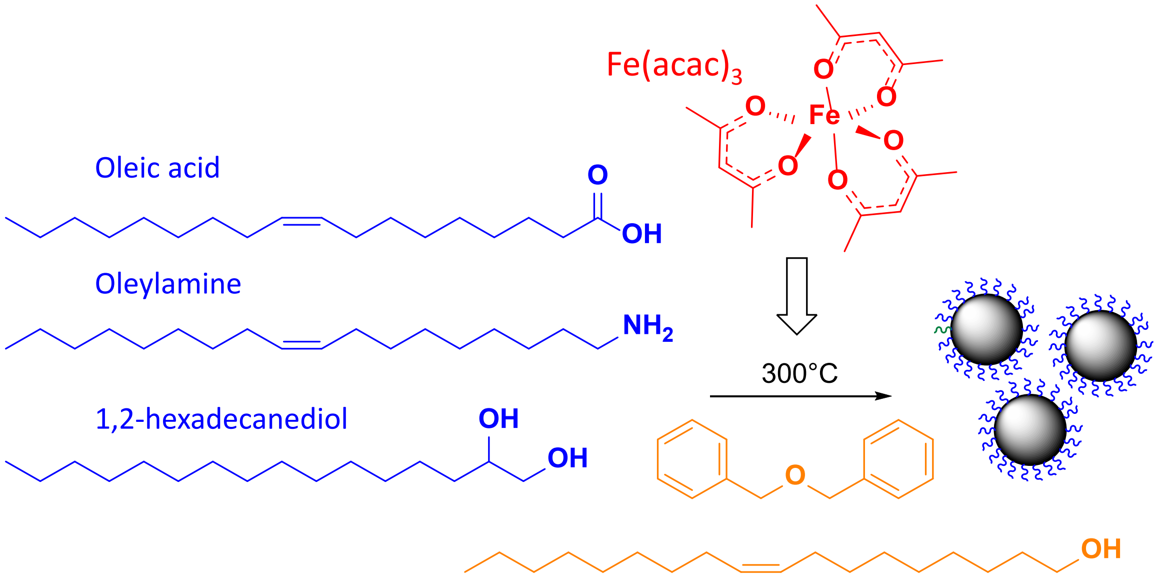


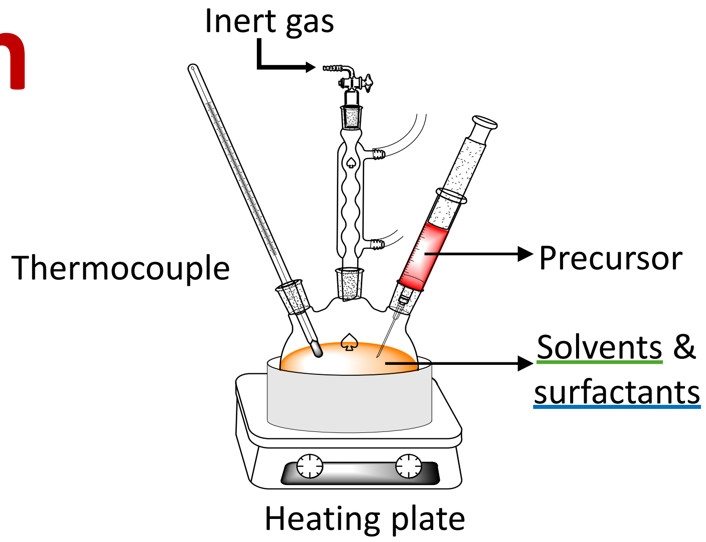
Formation of a gold shell

- **Optimal condition reached in 30 min**
- **Simple set-up**
- **Great replicability**
- **Iron core 5.8 nm – Gold shell 3.5 nm**

Ahrberg *et al.* 2020, Scientific Reports

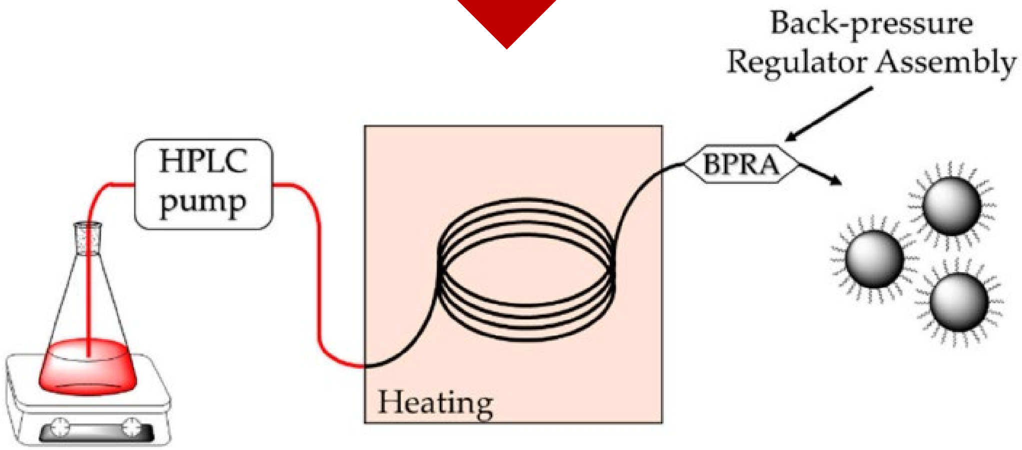
Flow Thermal Decomposition





Issues

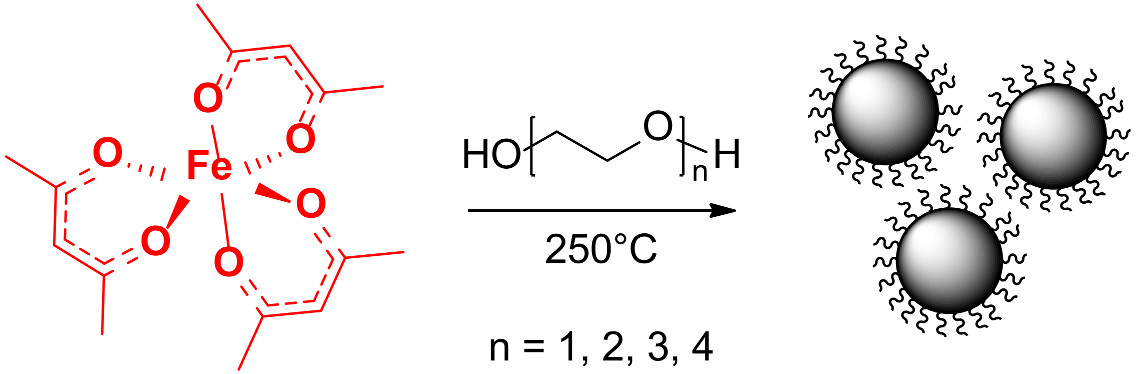
- ~~Low safety~~
- ~~Low scalability potential~~
- Hydrophobic coating



Vangijzegem *et al.* 2020, Nanomaterials

Thermal Decomposition in Polyol Medium

Polyol Medium



The solvent plays three roles:

- High boiling point solvent
- Reducing agent
- Stabiliser

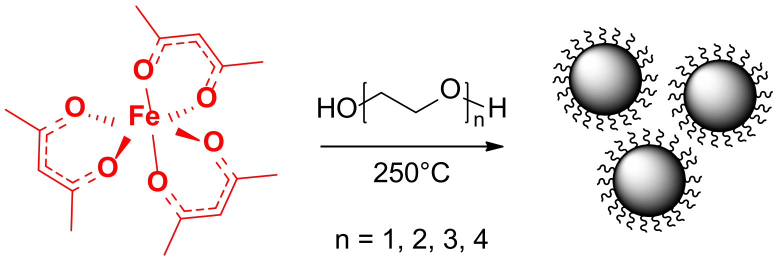
Hydrophilic particles

➡ Less solvent for purification

Greener process

Still needs stabilisation post synthesis

Thesis Project

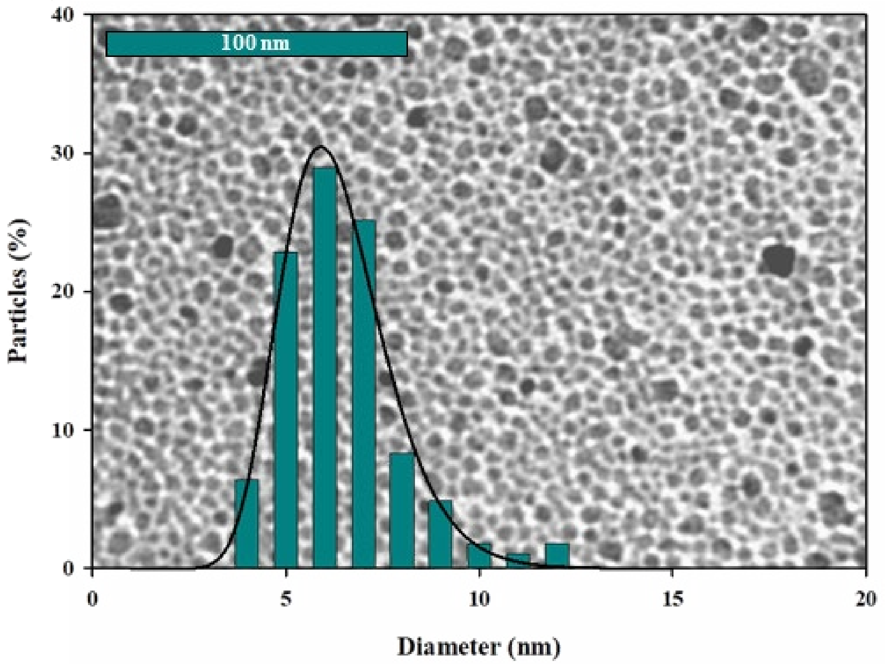


(+ Stabilisers)

Optimal flow parameters:

- Temperature: 250 °C
- PTFE Tubing: - Length : 1 m
  - Internal diameter: 1 mm
  - Volume: 0.48 mL
- Flowrate: 1 $mL.min^{-1}$

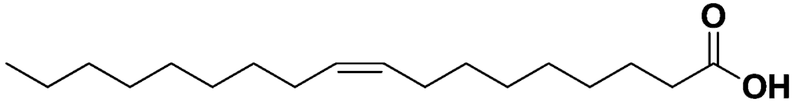
➡ **Residence time: 48 s**



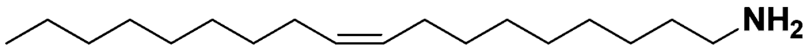
Stabilisers Influence on IONPs Properties

Classical thermal decomposition

Oleic acid

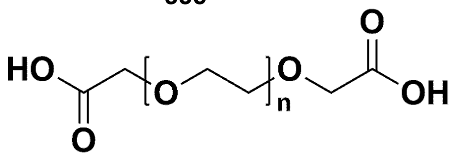


Oleylamine

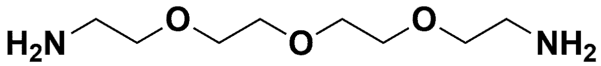


Polyol medium

PEG$_{600}$-diacid

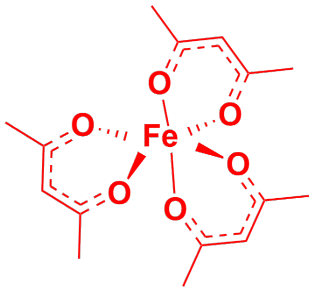


Diamino tetraethylene glycol (TREG-NH$_2$)



Unchanged parameters:

- Solvent: Tetraethylene glycol (TREG)
- Precursor: Fe(acac)$_3$ 50 mM



- T°: 250 °C
- Tubing: Length = 1 m
  Internal diameter = 1 mm
- Flowrate: 1 mL.min^{-1}

Residence time: 48 s

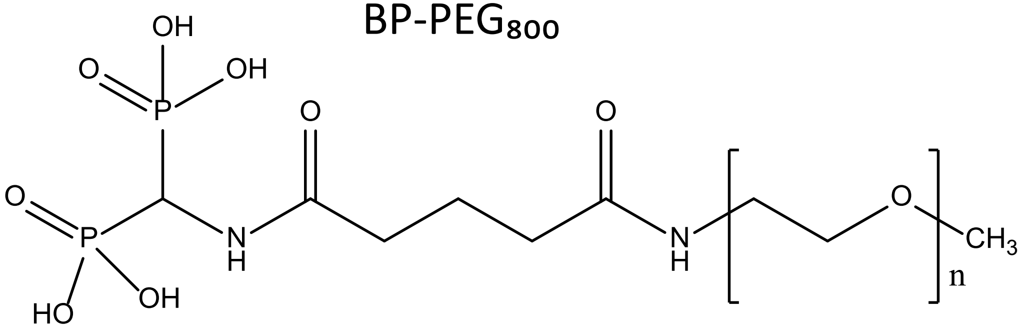
Modified parameters:

- Nature of stabiliser
- Iron to stabiliser molar ratio
  1:0, 1:1, 1:2, 1:3

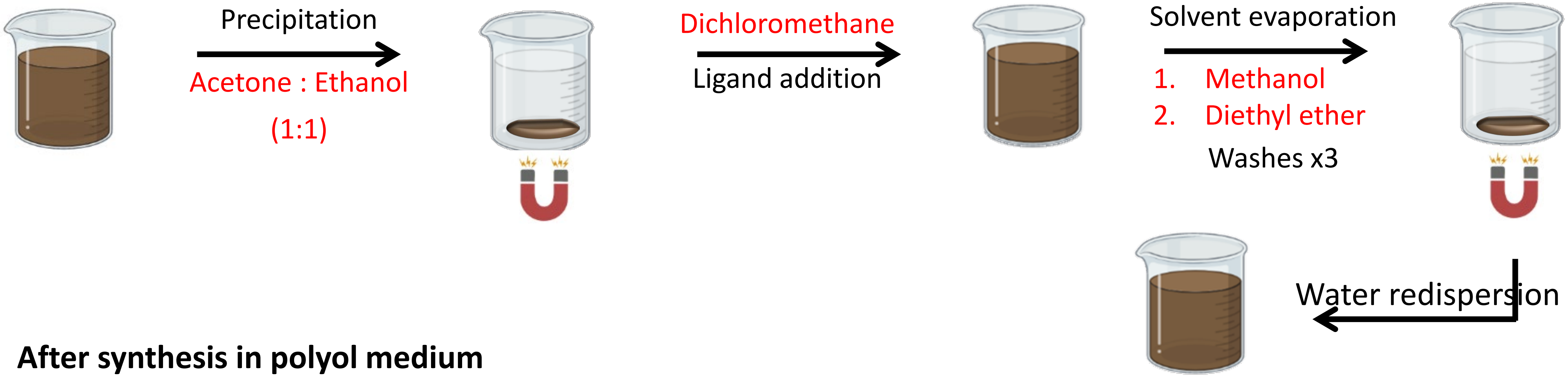
Particle stabilisation

Ligand Exchange

BP-PEG$_{800}$



After synthesis in classical medium



After synthesis in polyol medium

- Less steps

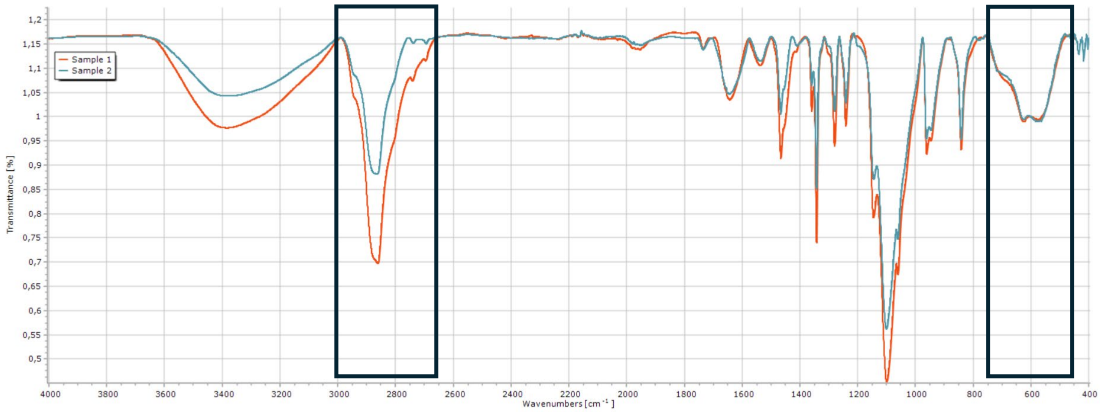
- Less organic solvents used

Surface Analyses

IONPs are magnetic and dark

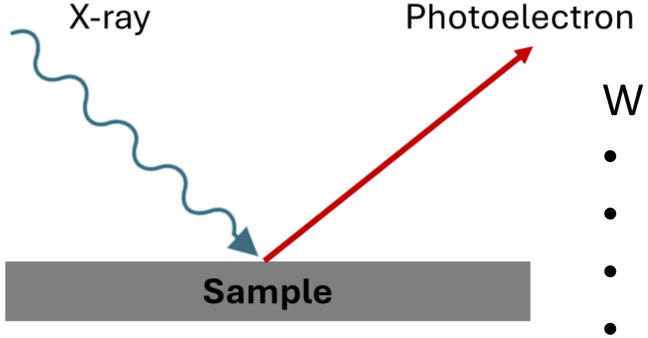
- No classical NMR measurement
- Light absorption → No UV-Vis measurement

Fourier-transform infrared (FTIR) spectroscopy



- Compound identification
- Semi-quantitative measurements

X-ray photoelectron spectroscopy (XPS)



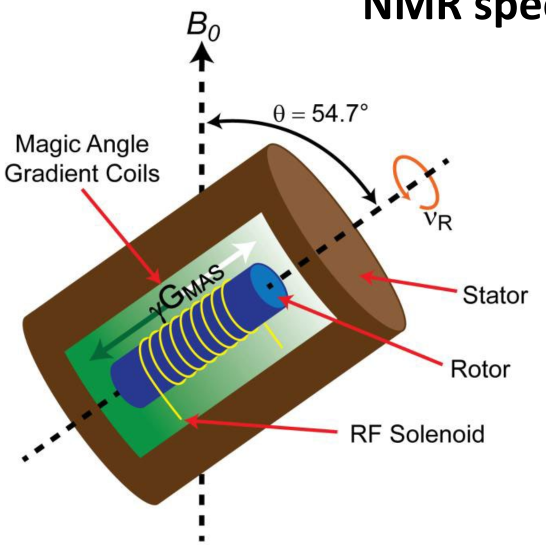
$$E_B = h\nu - E_K - \phi$$

Where:

- E_B: *binding energy,*
- $h\nu$: X-ray energy,
- E_K: kinetic energy,
- ϕ: work function

- Elemental composition
- Oxidation state

High resolution magic angle spinning (HR-MAS) NMR spectroscopy



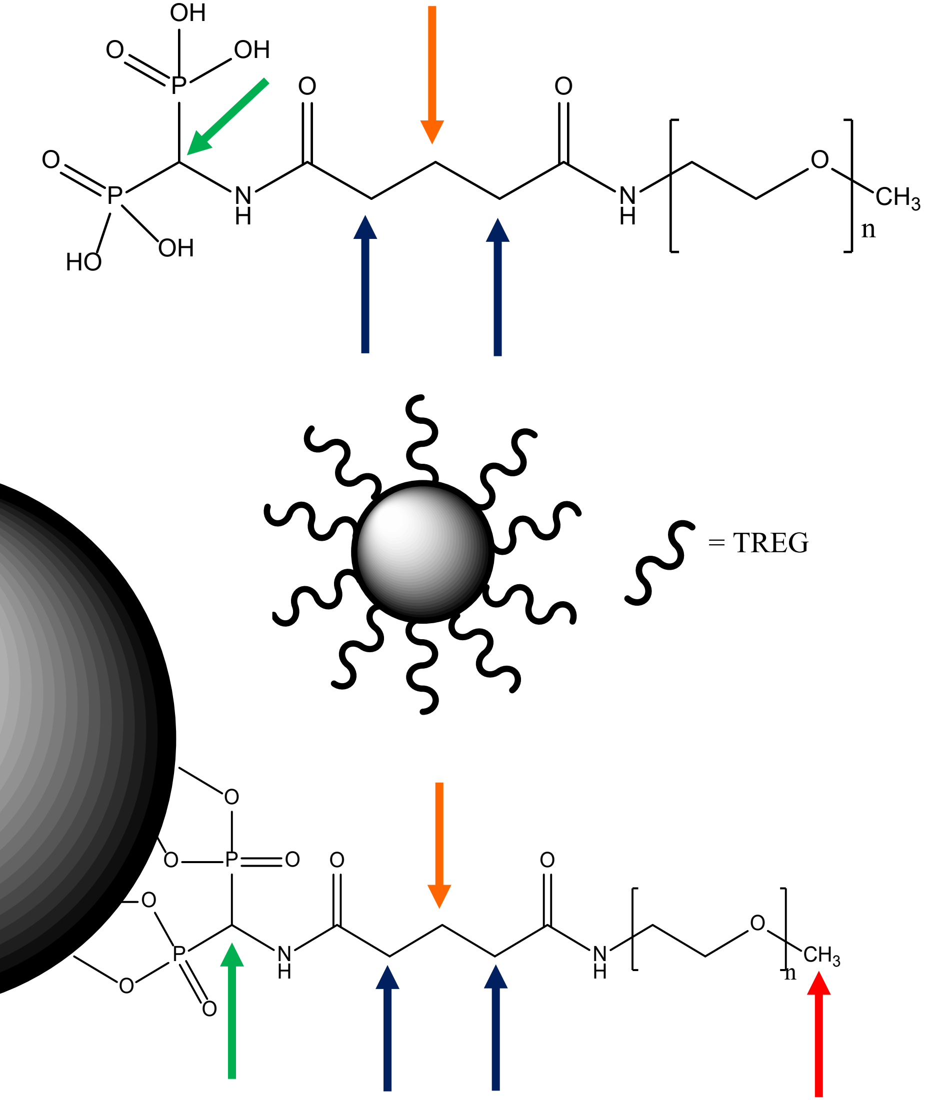
Magic angle: 54.7°
Angular dependence term

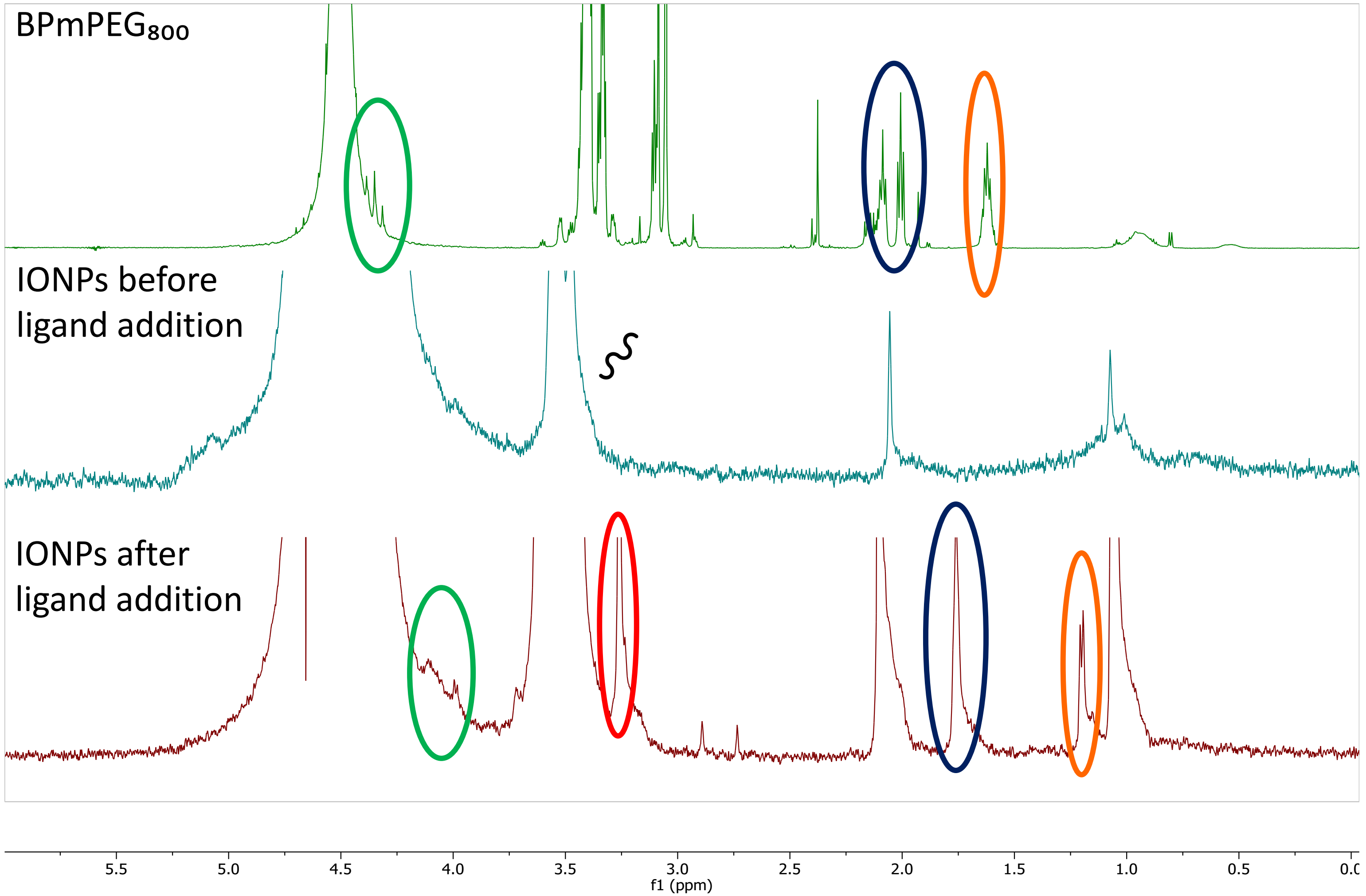
$$3\cos^2\theta - 1 = 0$$

Suppression of anisotropy due to magnetic susceptibility differences

Alam *et al.* 2012, Advanced Aspects of Spectroscopy

HR-MAS NMR Spectroscopy





Size and Shape Characterisations

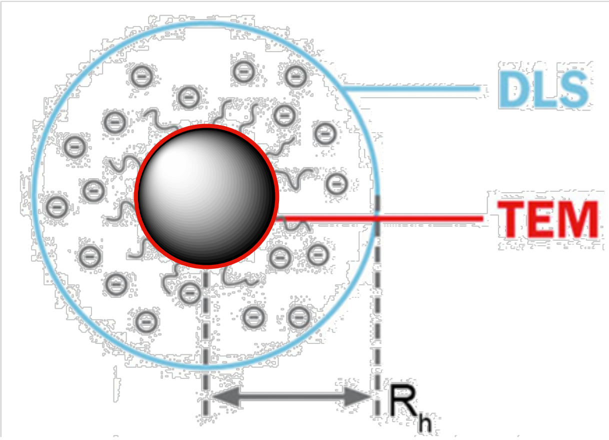
Dynamic light scattering (DLS)

- Based on Brownian motion
  - Large particles move slowly
  - Small particles move fast

$$D = \frac{k_B T}{6\pi\eta R_H}$$

Where :

- D: diffusion coefficient,
- R_H: hydrodynamic radius,
- η: viscosity,
- T: temperature.



- Hydrodynamic diameter
- Size distribution
- Polydispersity

Transmission electron microscopy

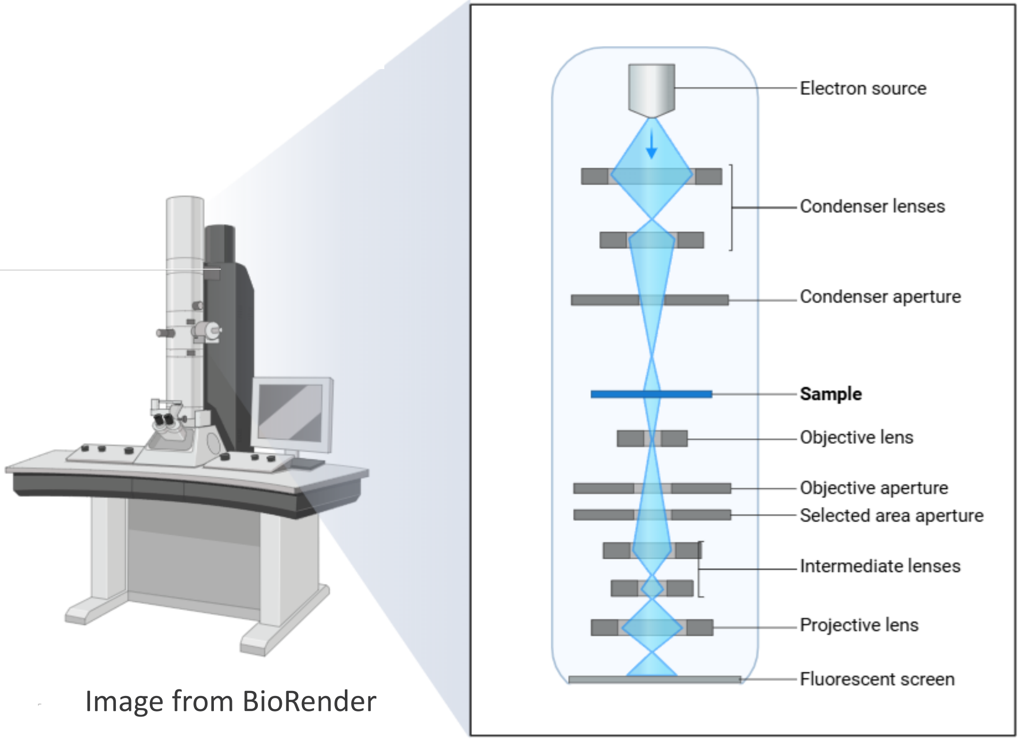
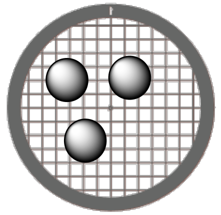
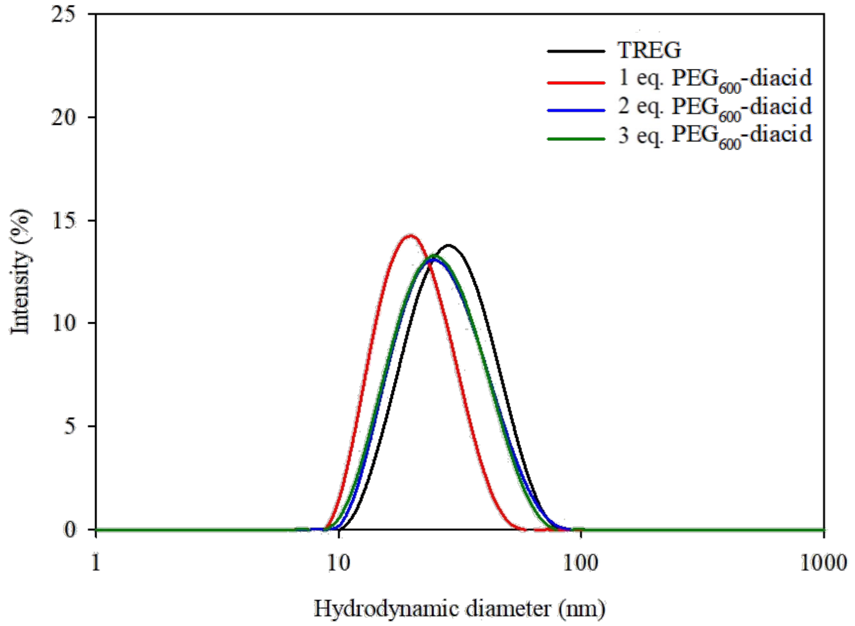


Image from BioRender

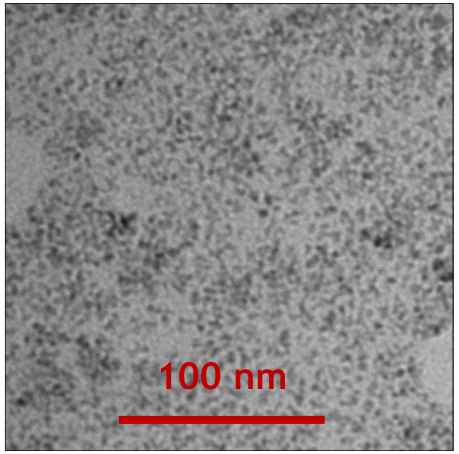


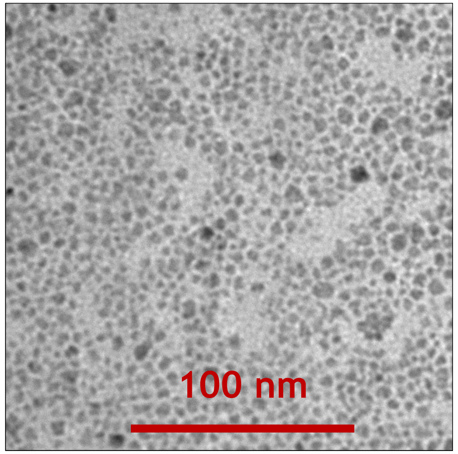
- 2D images of sample
- Great resolution (down to 1 Å)

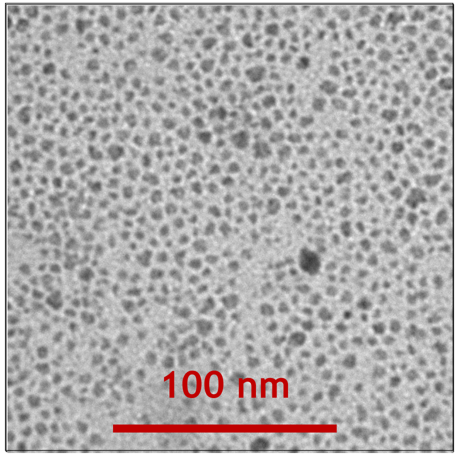
PEG_{600}-diacid: Morphology

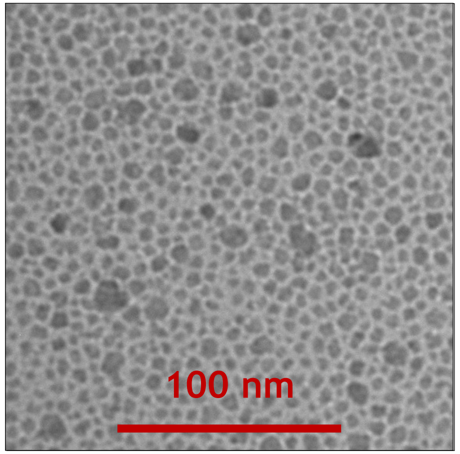


# Eq. PEG_{600}-diacid	D_{TEM} (nm)	PDI
0	4.4 ± 0.9	1.15
1	5.4 ± 1.3	1.18
2	6.0 ± 1.3	1.16
3	7.0 ± 1.6	1.16

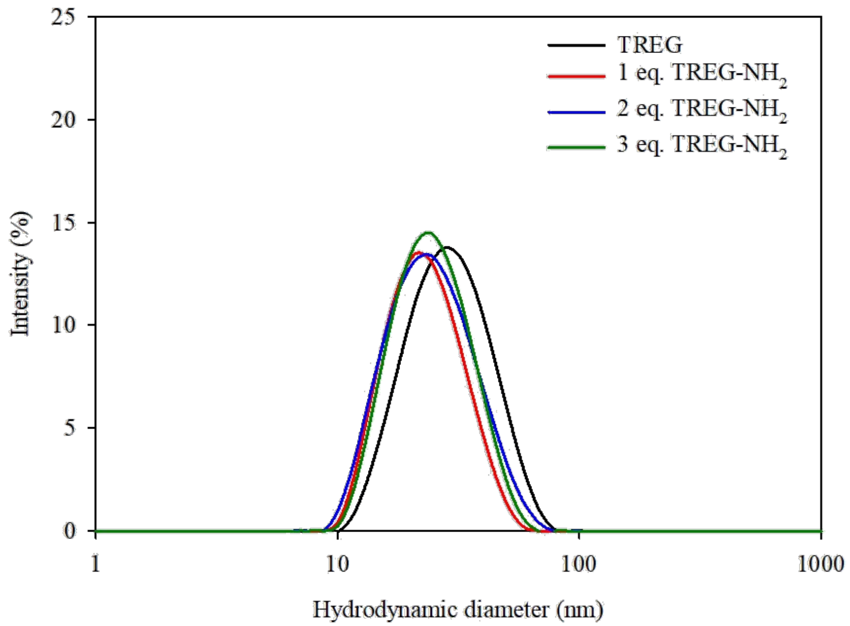




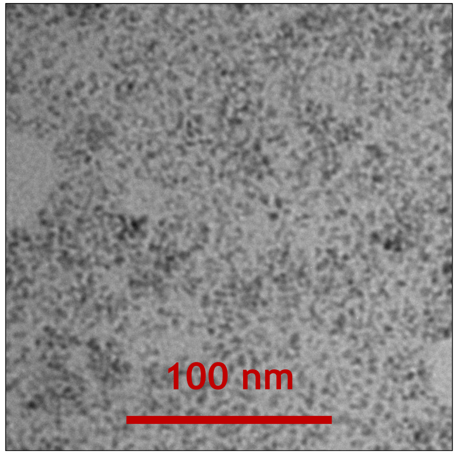


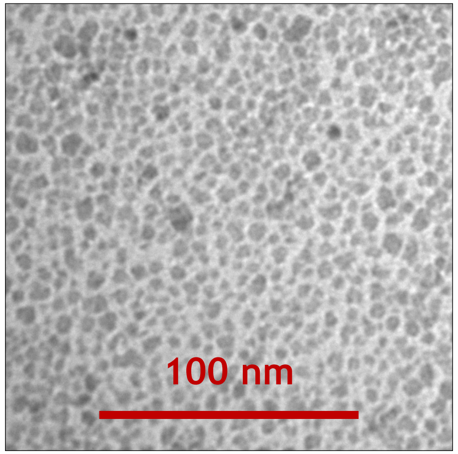


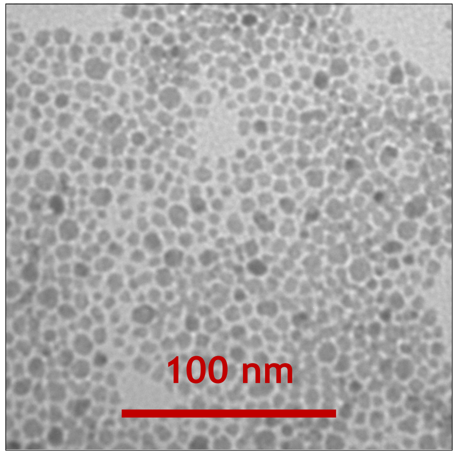
TREG-NH_2: Morphology

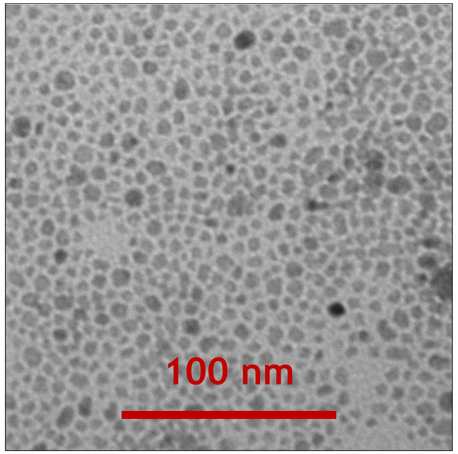


# Eq. TREG-NH_2	D_{TEM} (nm)	PDI
0	4.4 ± 0.9	1.15
1	5.3 ± 1.3	1.24
2	5.5 ± 1.2	1.15
3	5.6 ± 1.1	1.12



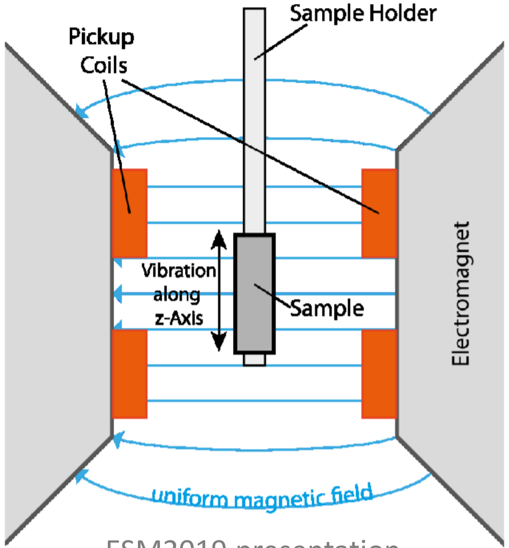






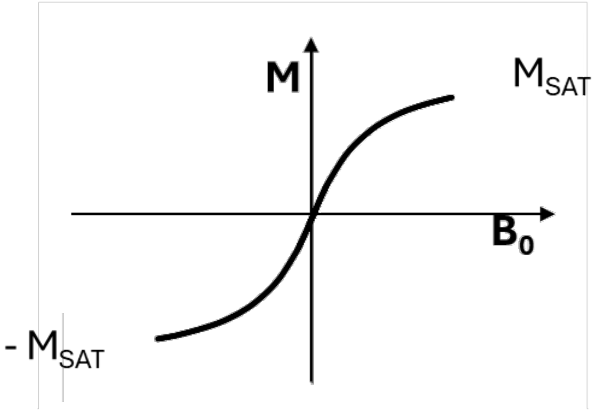
Magnetic Properties

Vibrating Sample Magnetometry (VSM)



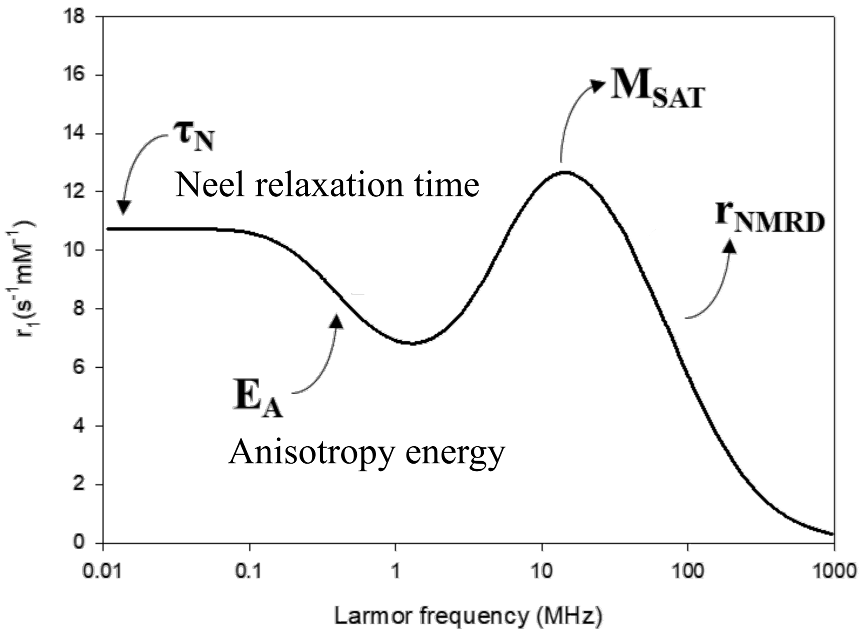
ESM2019 presentation

Based on Faraday's law:
Sample movement
➡ Induced electrical current
➡ Proportionnal to magnetisation



- Confirm superparamagnetic behaviour
- Saturation magnetisation

Nuclear magnetic relaxation dispersion profiles (NMRD profiles)
Longitudinal relaxivity at different fields

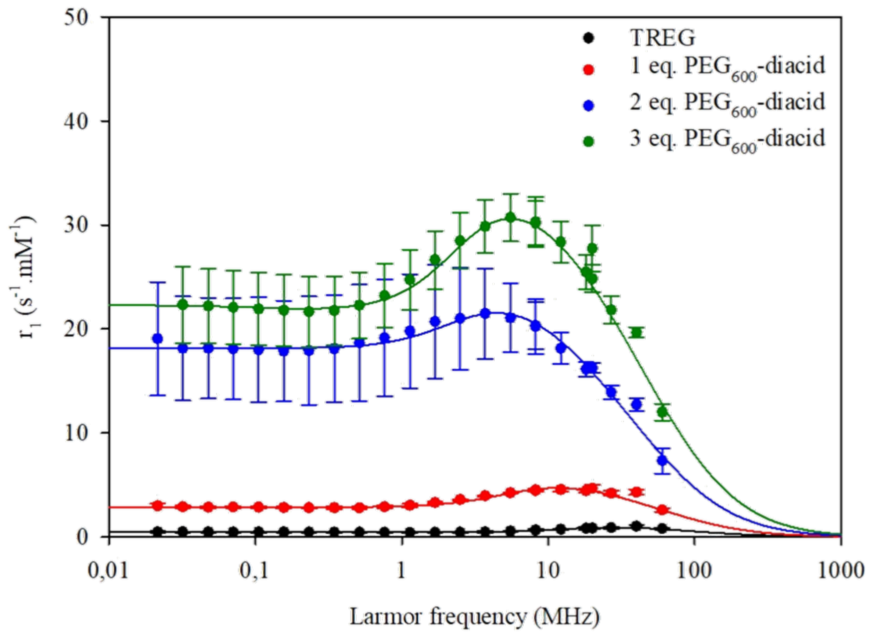


- Fitting gives access to multiple parameters
- Sensitive to particles propertie and aggregation

  ➡ Synthesis replicability

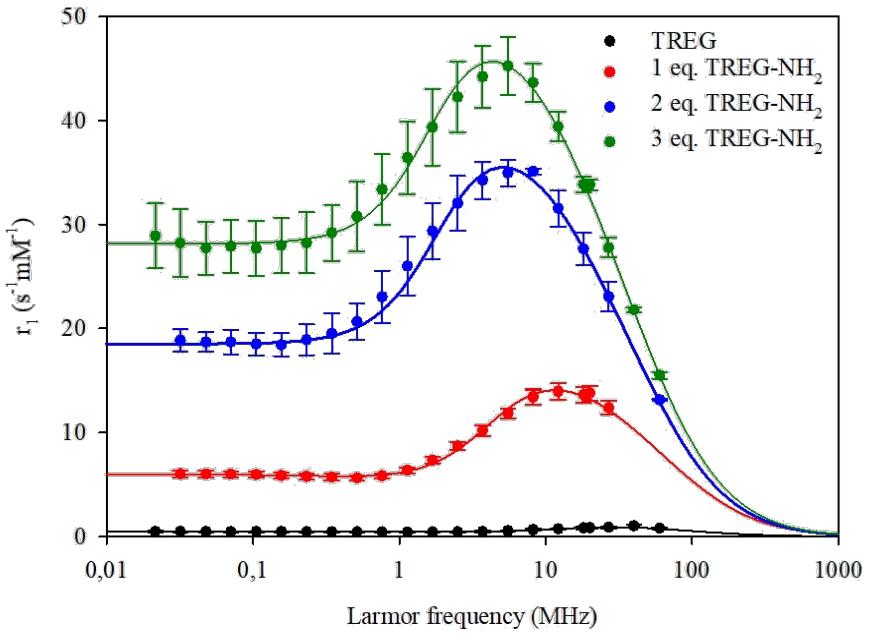
Relaxometry: NMRD Profiles

PEG-diacid



	M_S^{NMRD} ($A.m^2.kg^{-1}_{Fe}$)
TREG	12.5
1 eq. PEG_{600}-diacid	21.2
2 eq. PEG_{600}-diacid	36.3
3 eq. PEG_{600}-diacid	38.9

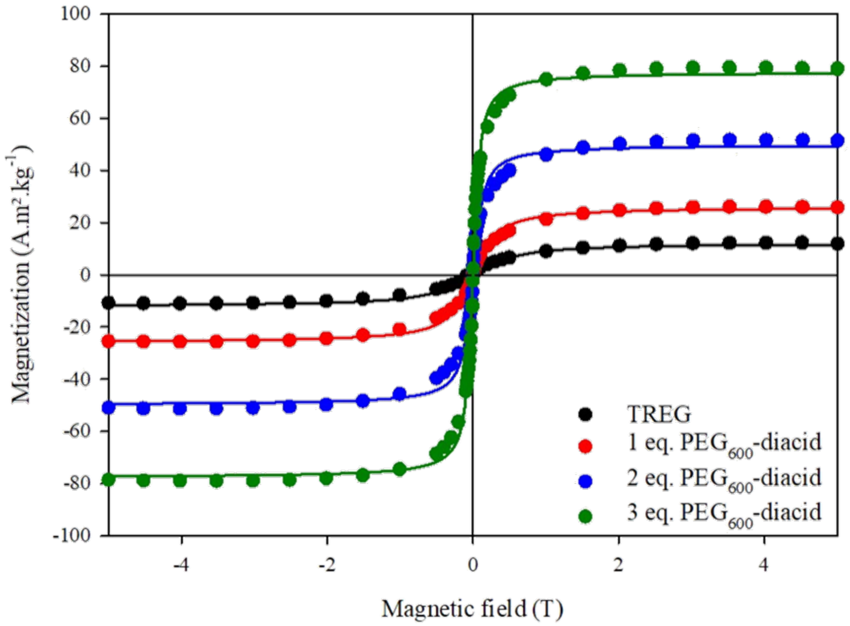
TREG-NH_2



	M_S^{NMRD} ($A.m^2.kg^{-1}_{Fe}$)
TREG	12.5
1 eq. TREG-NH_2	38.5
2 eq. TREG-NH_2	46.3
3 eq. TREG-NH_2	50.6

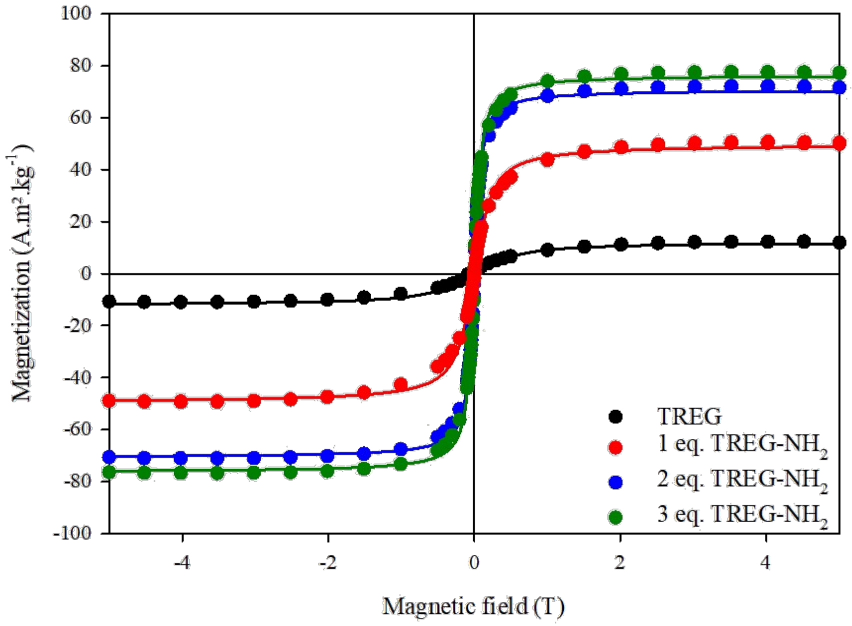
Vibrating Sample Magnetometry (VSM)

PEG-diacid



Steady increase	M_S^{VSM} ($A.m^2.kg^{-1}_{Fe}$)
TREG	12.2
1 eq. PEG_{600}-diacid	26.1
2 eq. PEG_{600}-diacid	50.0
3 eq. PEG_{600}-diacid	77.8

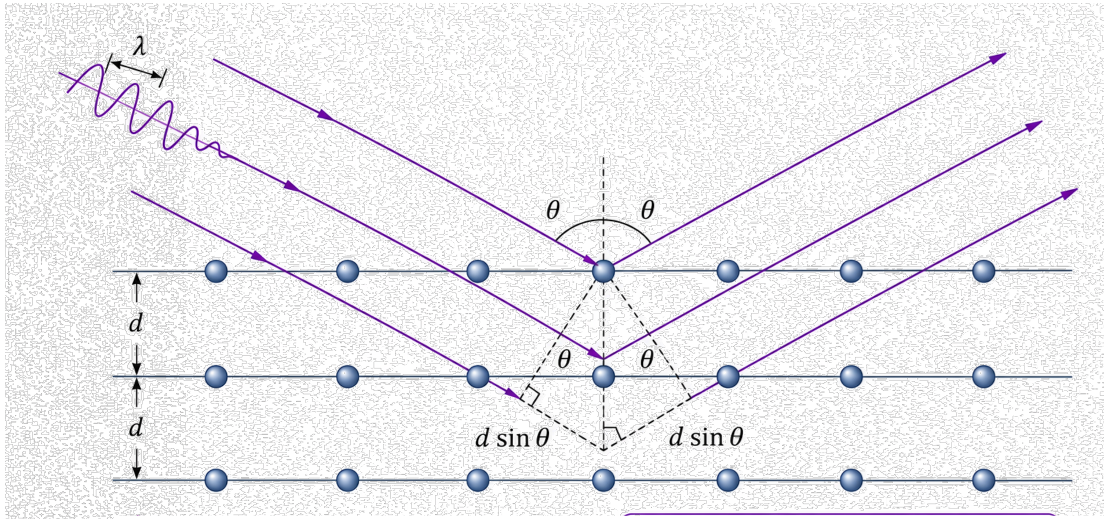
TREG-NH_2



Plateau	M_S^{VSM} ($A.m^2.kg^{-1}_{Fe}$)
TREG	12.2
1 eq. TREG-NH_2	49.8
2 eq. TREG-NH_2	79.7
3 eq. TREG-NH_2	82.5

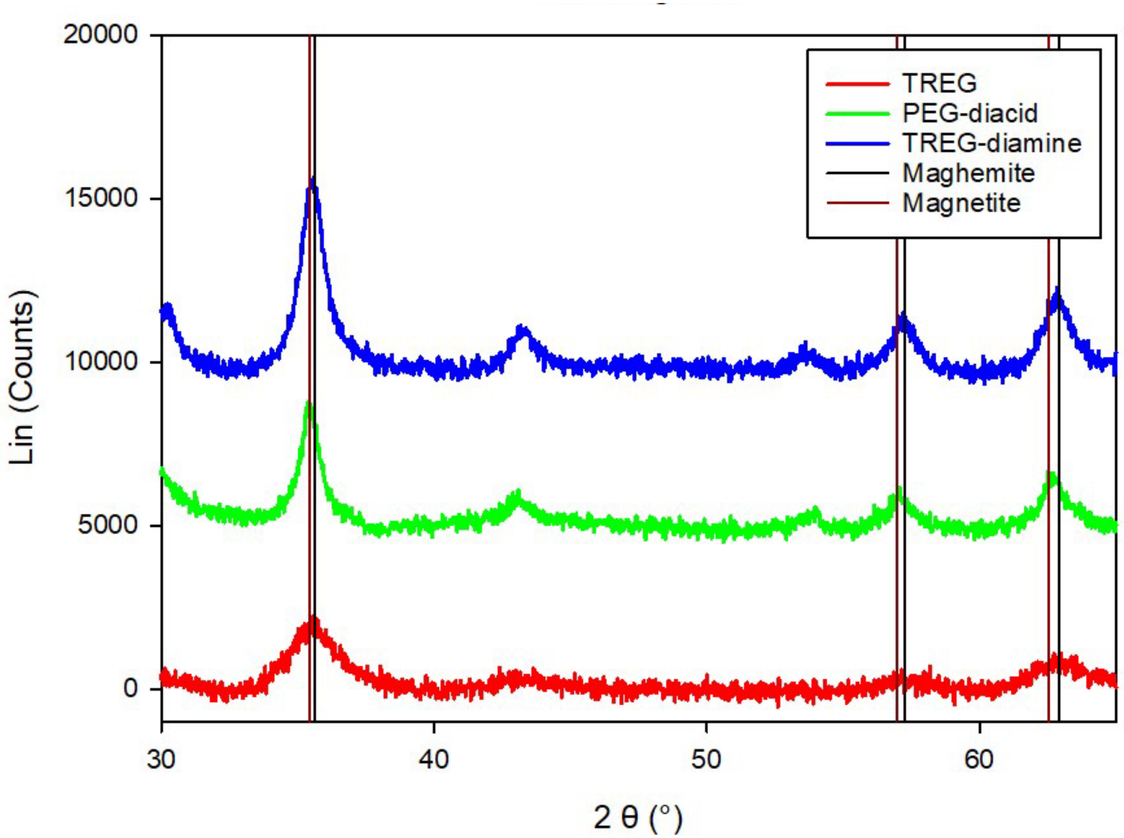
Crystalline Phase

X-ray diffraction



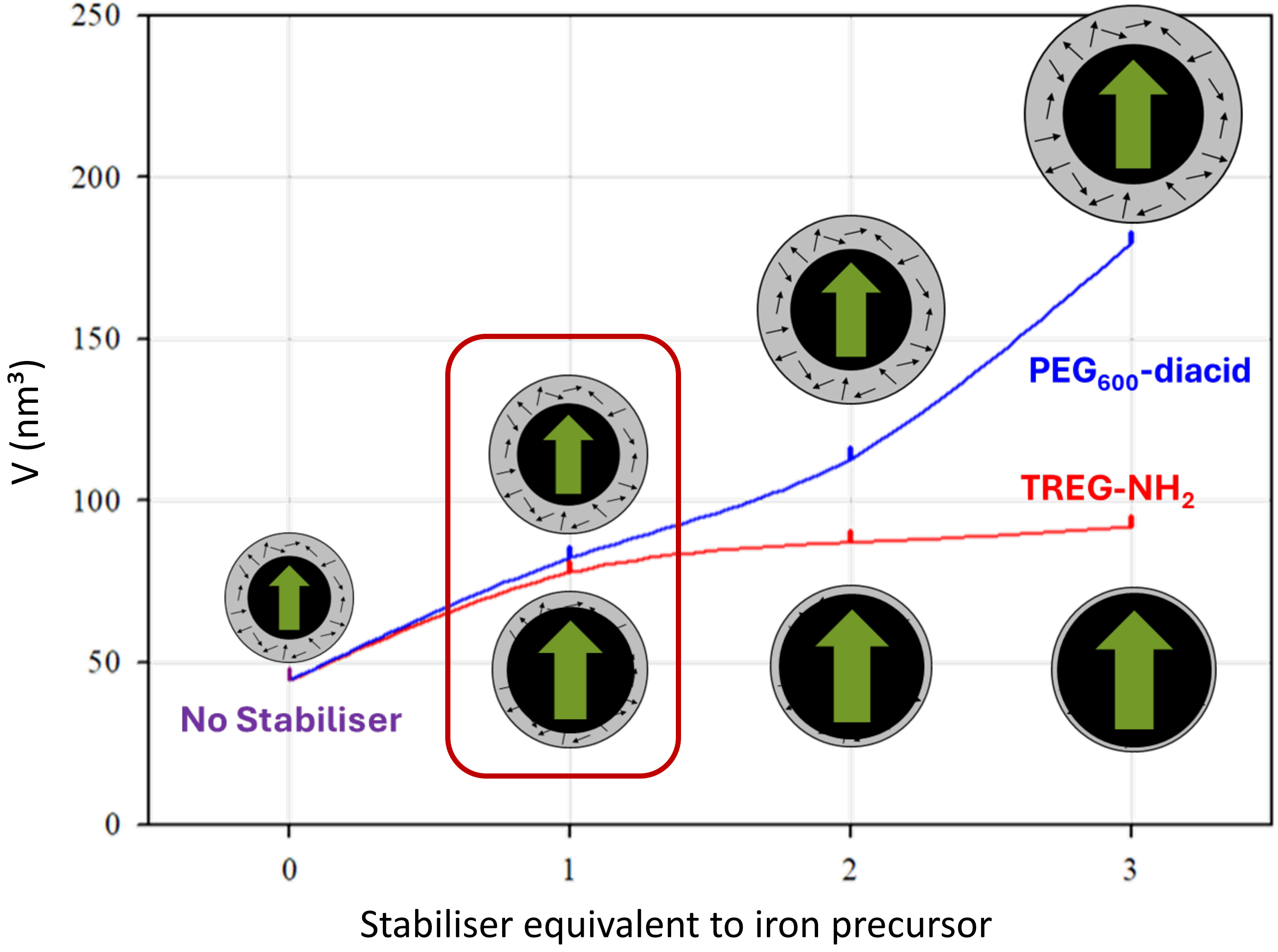
Bragg's law: $n\lambda = 2d\ sin\theta$

- Peaks position
  → Crystalline structure
- Full width at half maximum
  → Crystallite size



- PEG-diacid: Smaller crystallite
  Closer to magnetite
- $TREG-NH_2$: Larger crystallite
  Closer to maghemite

Influence on Particle Growth



At 1 eq

Same shape

Similar size

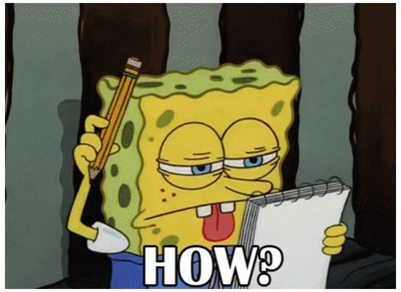
5.4 nm ≈ 5.3 nm

Different M_{sat}

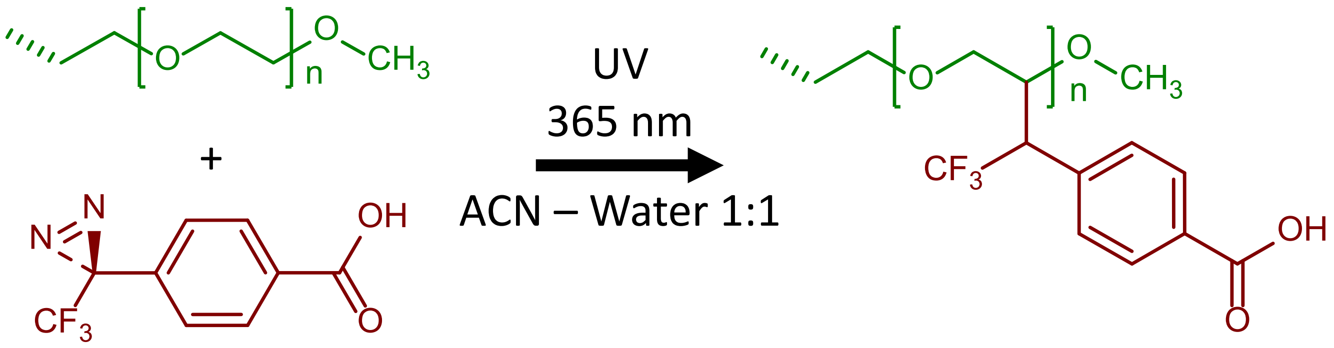
26.1 $A.m^2.kg^{-1}$ < 49.8 $A.m^2.kg^{-1}$

Nature of stabiliser influences:

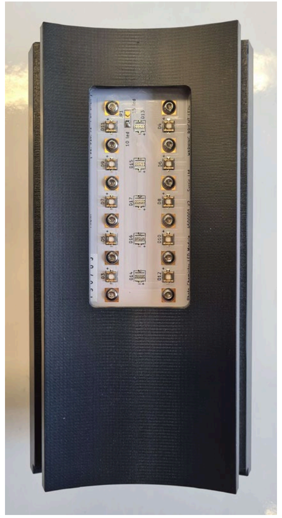
- Crystallinity
- Iron oxide phase



Flow Photochemistry



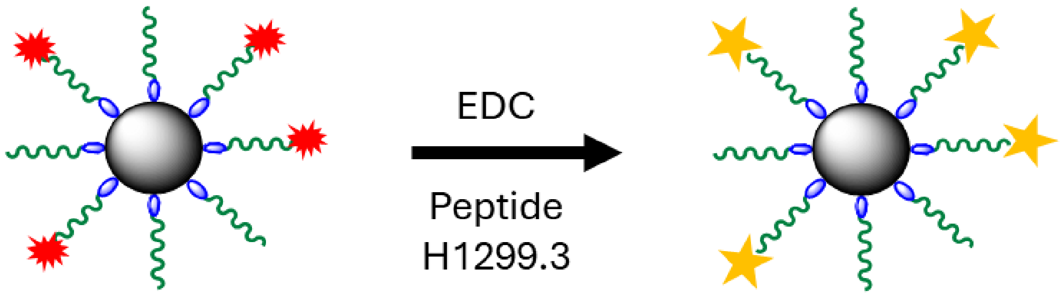
PFA Tubing



365 nm UV lamp

H1299.3 Peptide → **Increases internalisation in A549 cells (human lung cancer)**

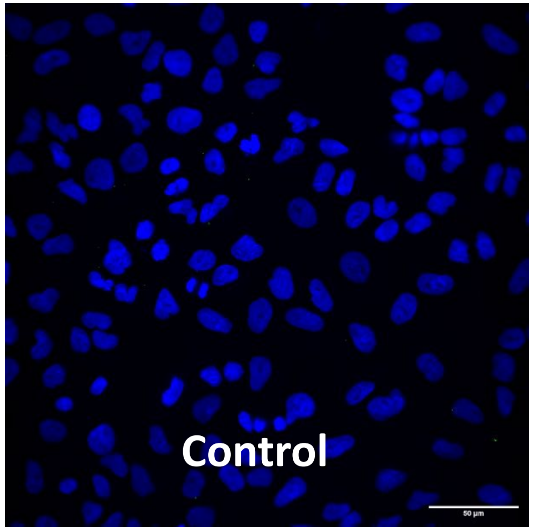
Sequence: LQWRRDDNVHNFGVWARYRL-{NH-PEG_4-NH_2}

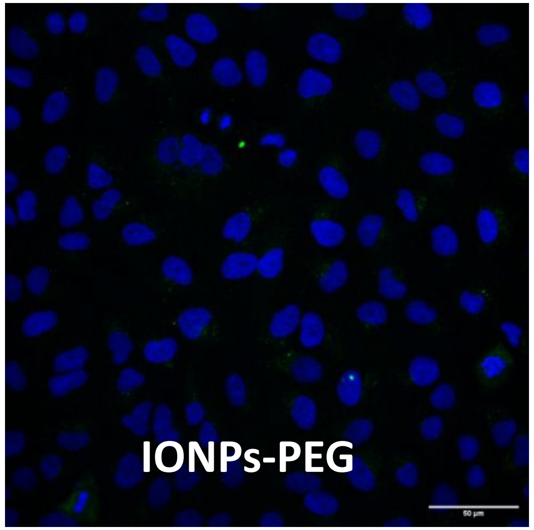


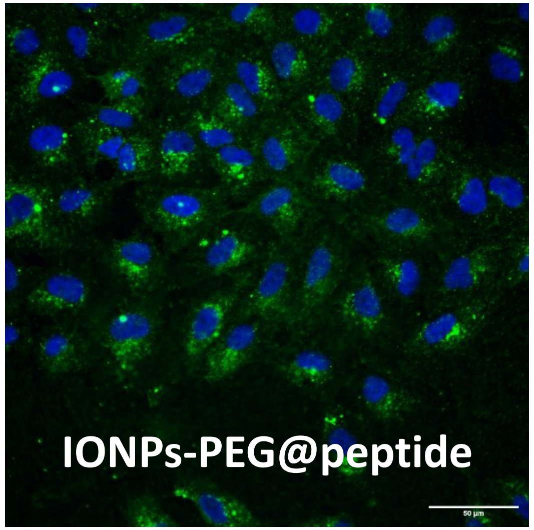
IONP **PEG-COOH**

IONP **PEG-H1299.3**

Internalisation Tests

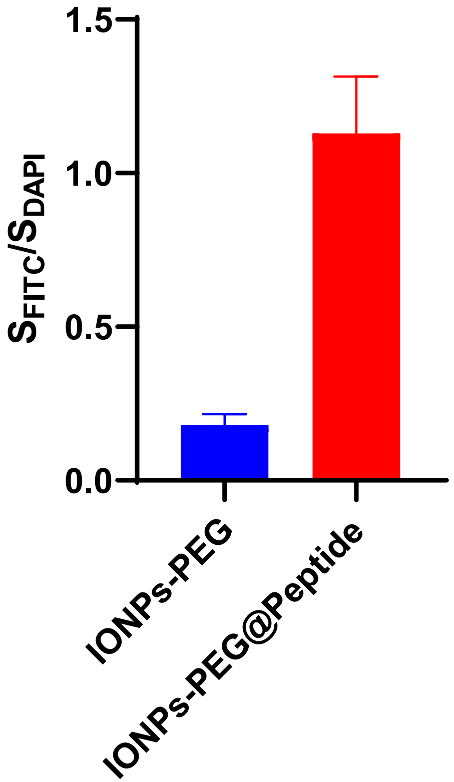


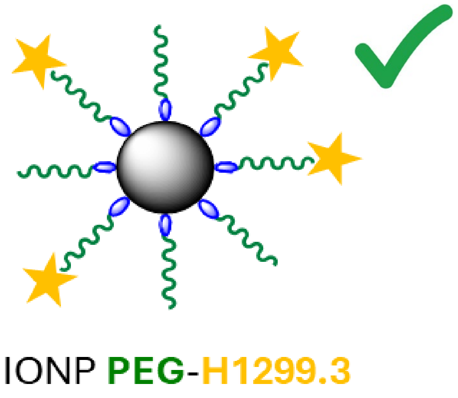




Markers

- Dapi: Nuclei
- FITC: IONPs





- **Increase of the internalisation**
- **Indirect proof of peptide grafting**

Conclusions

Flow Chemistry

- Finer parameter control
- Increased reproducibility
- Automatisation
- Greener process
- Wide range of application

- Complex set-up
- Set-up specific to a reaction
- Cleaning and maintenance

Characterisations

Morphology

- DLS: Hydrodynamic diameter
- TEM: Core diameter and shape

Crystalline phase

- XRD: IONPs phase and crystallite size

Magnetic properties

- VSM: Saturation magnetisation
- NMRD profile: Reproducibility

Surface analyses

- FTIR: Chemical functions
- XPS: Elemental composition
- HR-MAS: NMR at solid liquid interface

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