Magnetic nanoparticles: synthesis, properties and biomedical applications

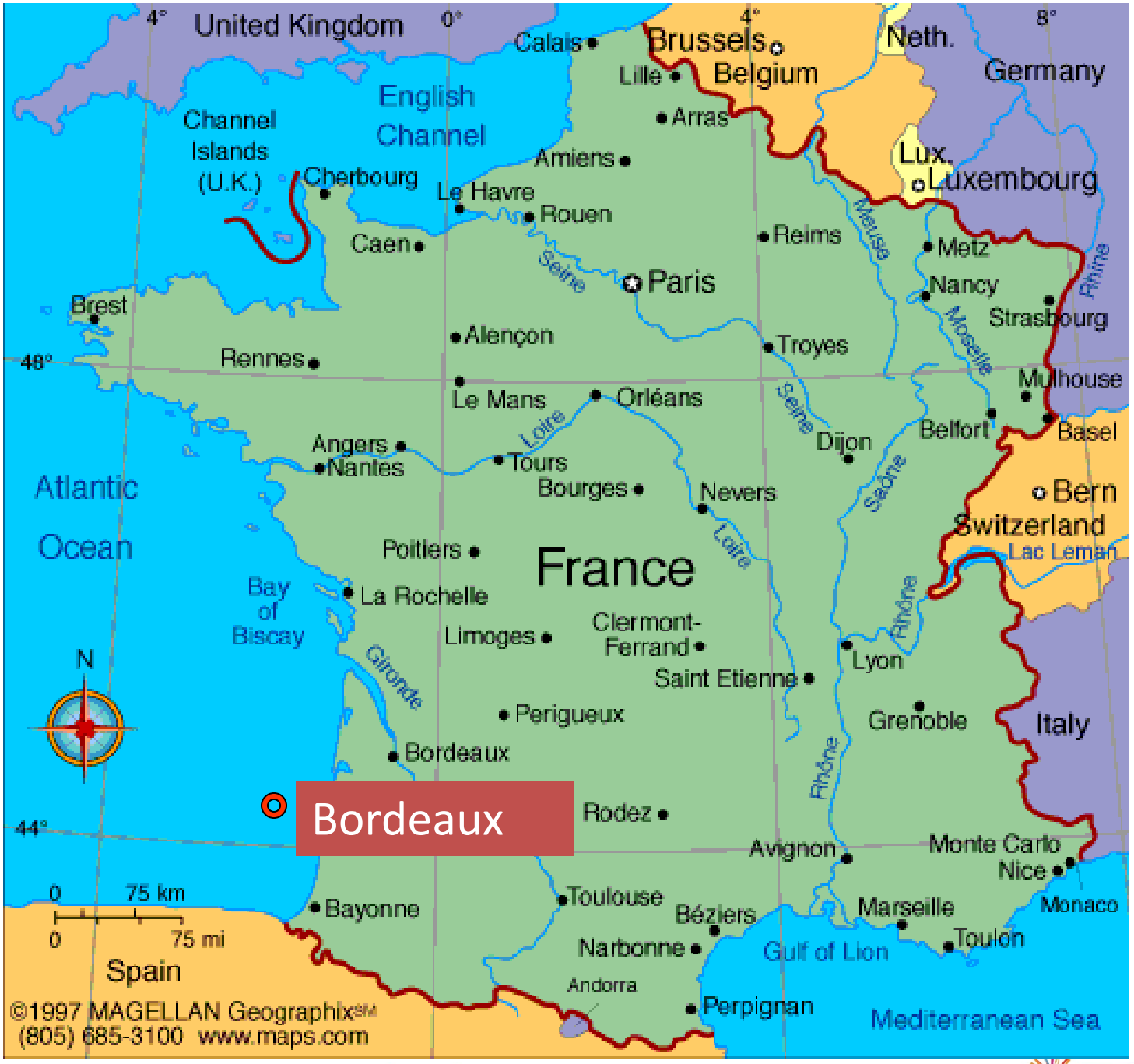
Olivier Sandre

olivier.sandre@u-bordeaux.fr
@olive_free

MAGNETIC NANOPARTICLES: SYNTHESIS, PROPERTIES AND BIOMEDICAL APPLICATIONS

Olivier Sandre, senior CNRS researcher at Univ. Bordeaux, France

LCPO
Laboratoire de Chimie des Polymères Organiques



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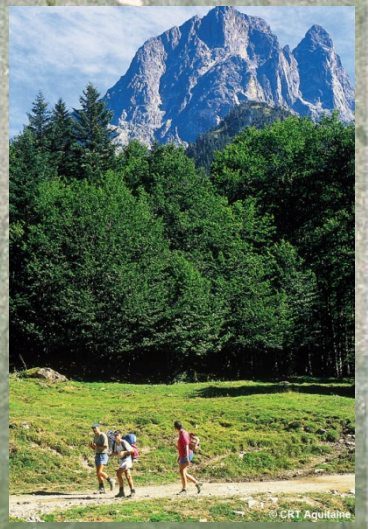
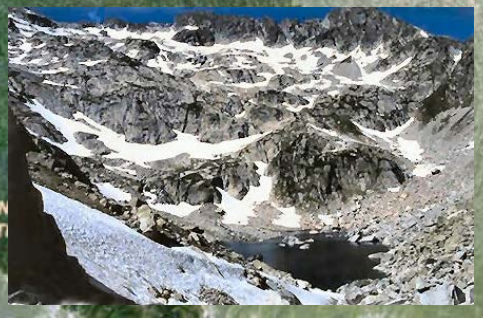




Magnetic nanoparticles (MNPs) Part 1: Synthesis and physical properties

• Part 1A: Chemistry of iron oxides and oxo-hydroxides:
Diversity of methods to prepare colloidal nanoparticles, either in non aqueous solvents: hydrothermal synthesis, polyol synthesis, thermal decomposition…
or in water: alkaline co-precipitation of iron salts (also in EG, DEG…)

• Part 1B: Magnetic behavior (ferro- /ferri- /antiferro- /superpara– magnetism…) and optical properties of MNPs (UV-vis absorption, magnetic birefringence)

• Part 1C: MNPs as contrast agents in Magnetic Resonance Imaging
Universal law for relaxometry (T_1/T_2 of water H spins near MNPs)

All properties are highly sensitive on MNP's size and shape (poly)dispersity!

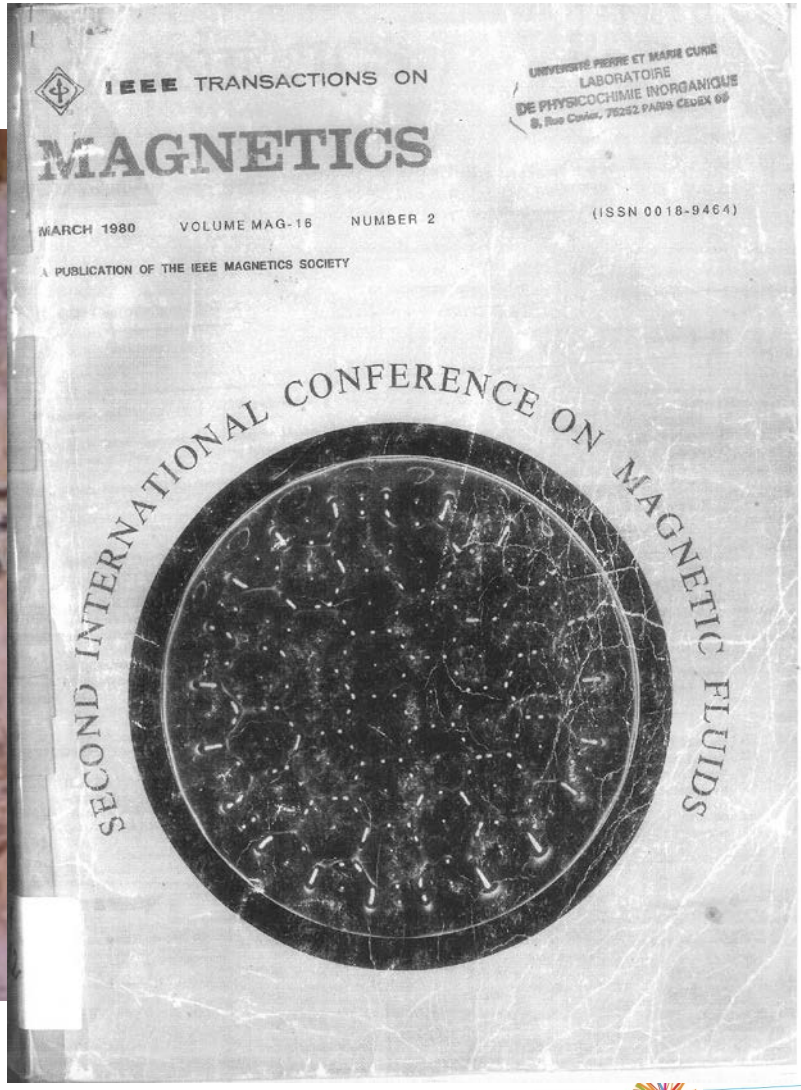
• Part 2A Magnetic Hyperthermia ('Tumor catabolism')

• Part 2B Nanomedicines – Magnetic carrier – Magnetic Guiding ('Tumor homing')

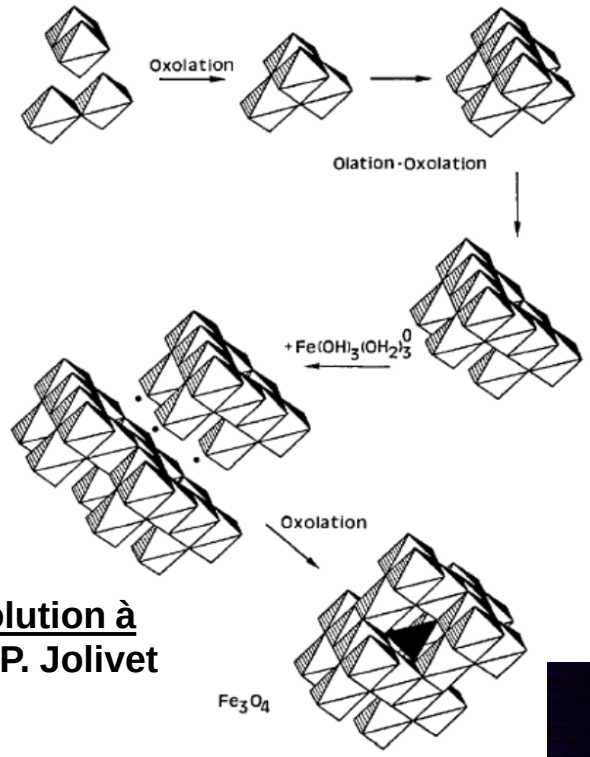
• Part 2C Drug Delivery Systems (DDS) based on Magnetic Core@Polymer Shells, Magnetic Polymer Shells, Magnetic Micelles, or Vesicles ('Polymersomes')

Diversity of iron oxides and oxo-hydroxides

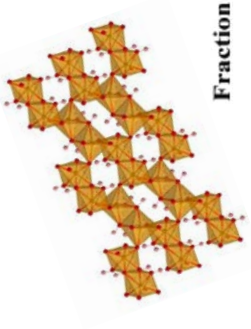
The Iron Oxides (Rochelle M. Cornell, Udo Schwertmann)

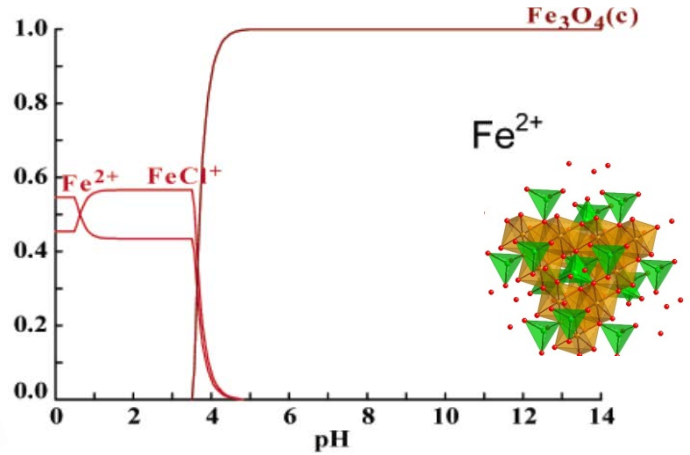


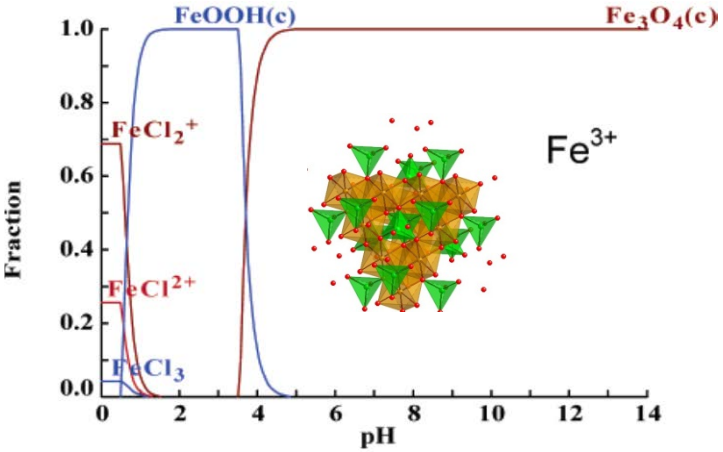
From solution of Fe^{2+} et Fe^{3+} salts towards solid phase



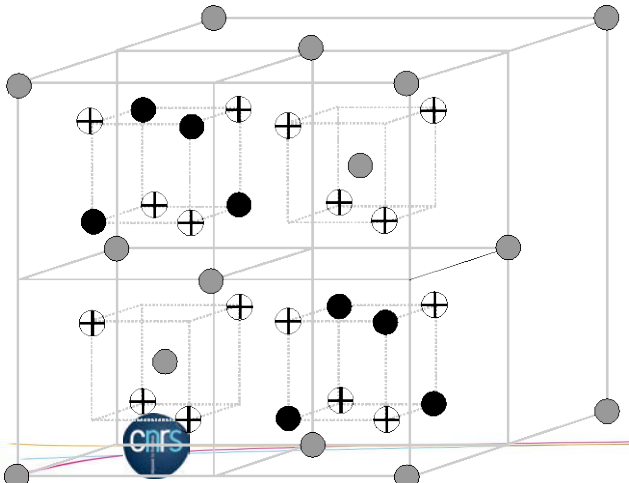
in De la solution à l'oxyde, J.-P. Jolivet

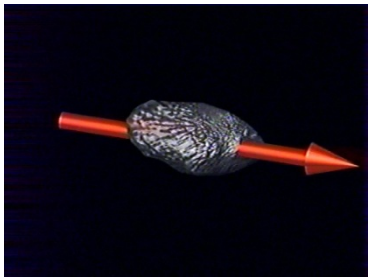






D.K. Kim et al.,
Chem. Mater. 2003, 15, 1617-1627





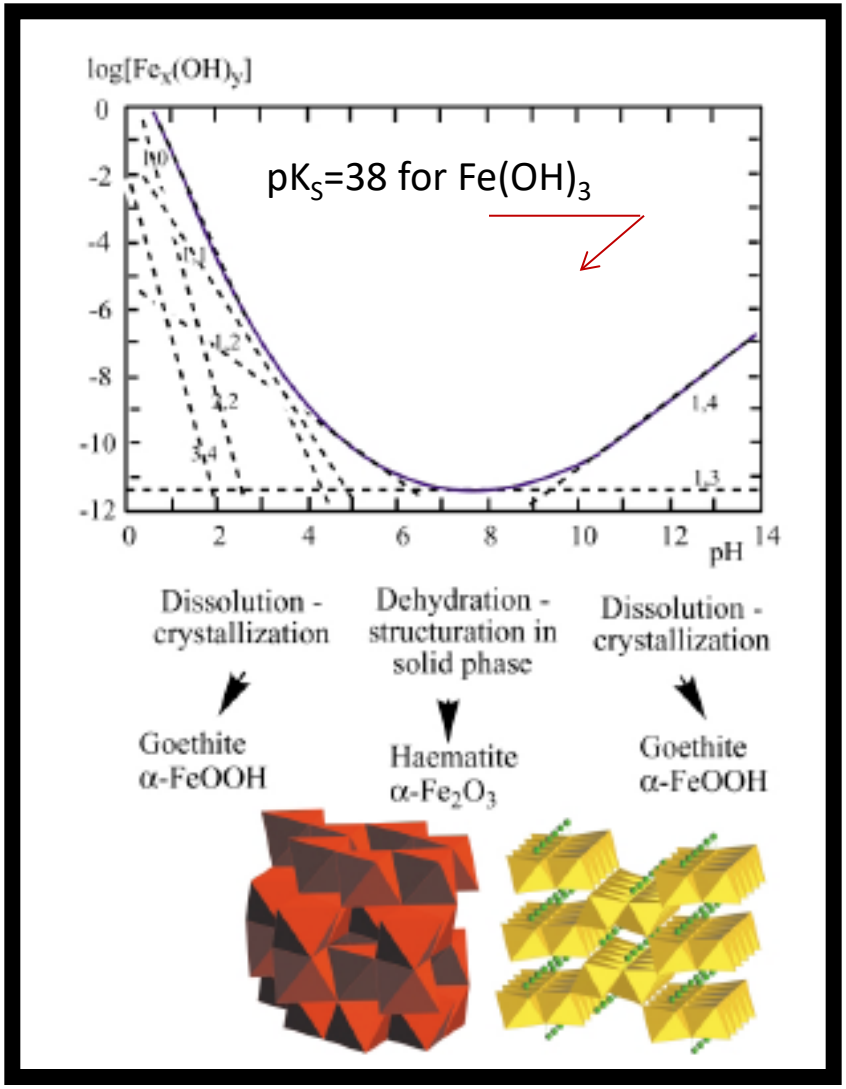
O^{2-}

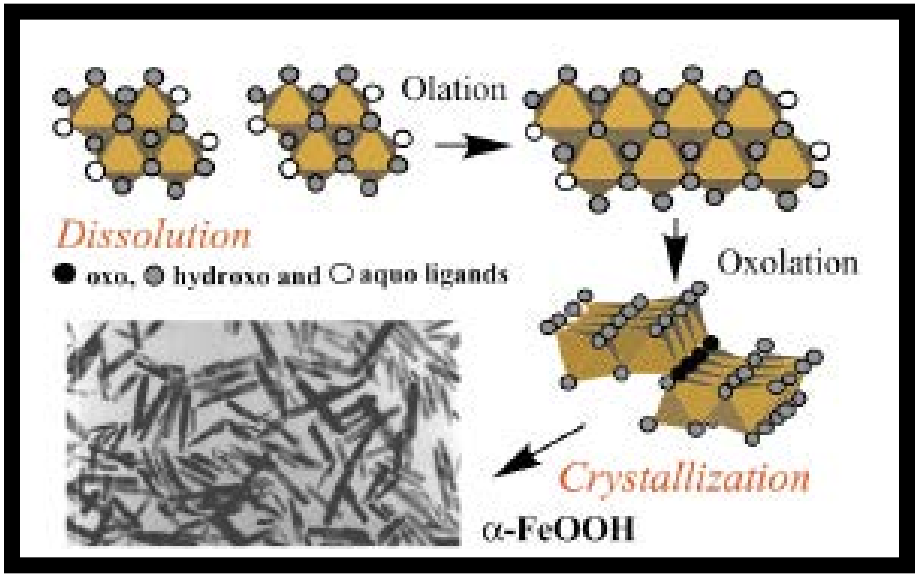
Fe^{3+} tetrahedral site

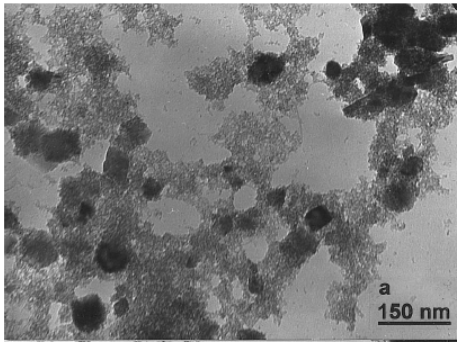
Fe^{2+}/Fe^{3+} octahedral site

Spinelle structure

Very narrow pH stability of $Fe^{3+}(H_2O)_6$ soluble ion

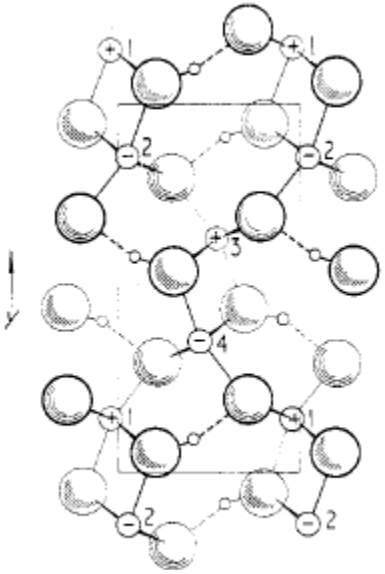


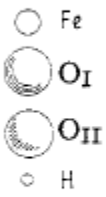


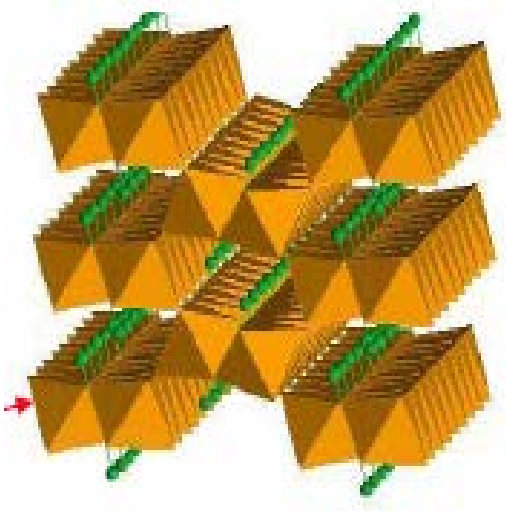


Jean-Pierre Jolivet, *Chem. Commun.*, 2004, 481-487

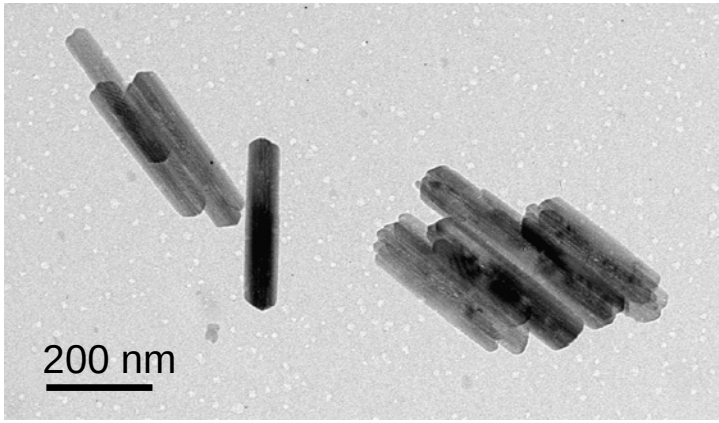
Antiferromagnetic clays made of iron^{+III} oxo-hydroxides



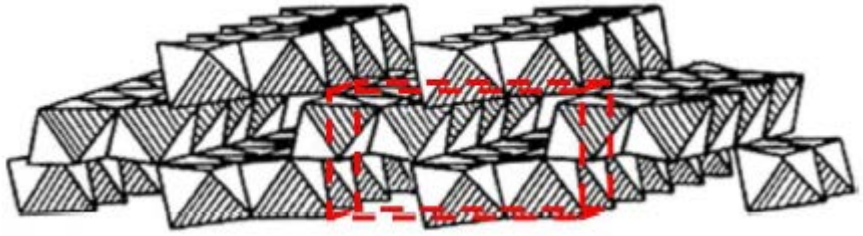




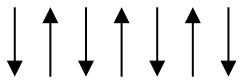
Orthorombic structure of γ–FeOOH
(Fe^{3+} in octahedral sites)



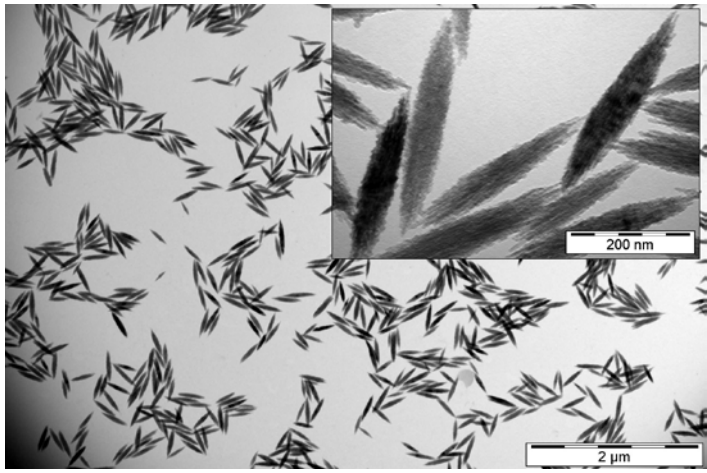
Goethite nanolaths γ–FeOOH
(rod-like)



Goethite is antiferromagnetic



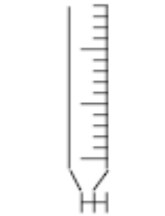
= 0 Resulting magnetization



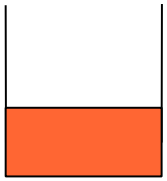
Accicular Haematite α–Fe_2O_3
(spindle-like)

Synthesis of antiferromagnetic goethite nanorods

1/ ferrihydrite alkaline precipitation



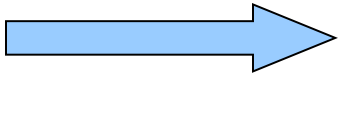
NaOH
1M



0.1M $Fe(NO_3)_3$

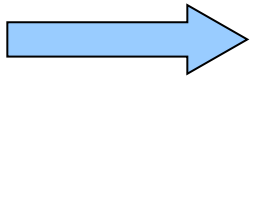
$Ni(NO_3)_2$ ou $Co(NO_3)_2$

2/ Slow dissolution X days at pH>11
→ goethite formation (ochre)



$\alpha - FeOOH$

3/ Washings H_2O
(5000 rpm)

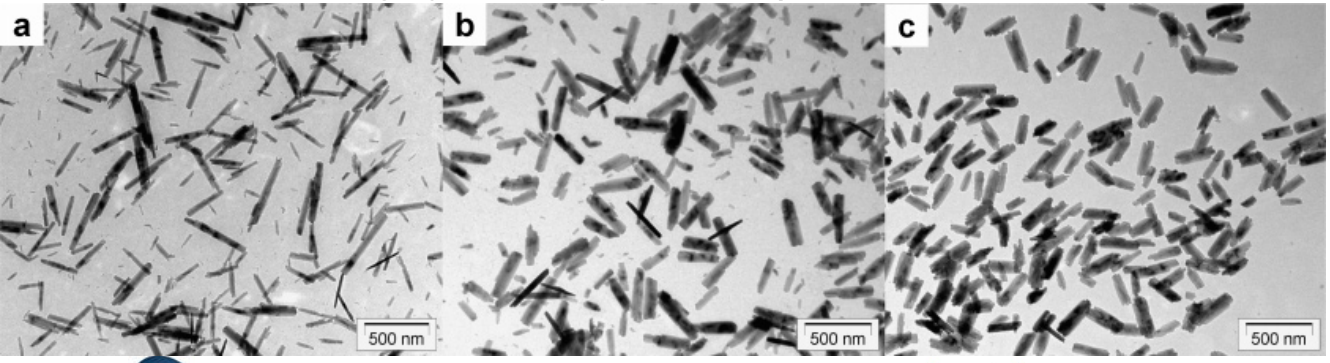


Dispersion in HNO_3 at pH=3

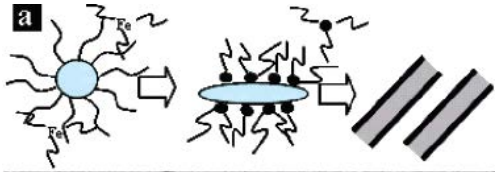
- PhD thesis J. Hernandez (UPMC 1998):
  10 days ageing at T=25C & pH13

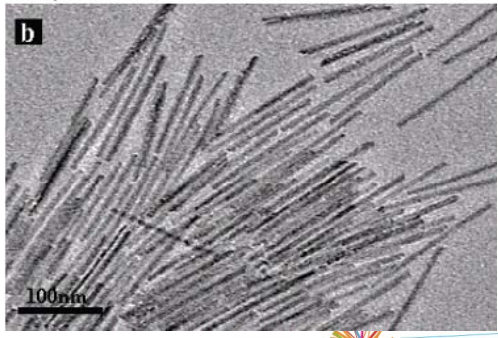
- S. Krehula et al. (Mat. Lett. 2002): hydrophobic base (TMAOH)
  Ageing during 1 – 21 days + "forced hydrolysis" (T=60 – 160C)

- D. Thies-Weesie et al. (Chem. Mater. 2007)
  Size-sorting by centrifugation steps



- Thermal decomposition Fe^{III}-oleate
  Taekyung Yu et al. (JACS 2007)





Doping of goethite nanorods with M^{n+} cations

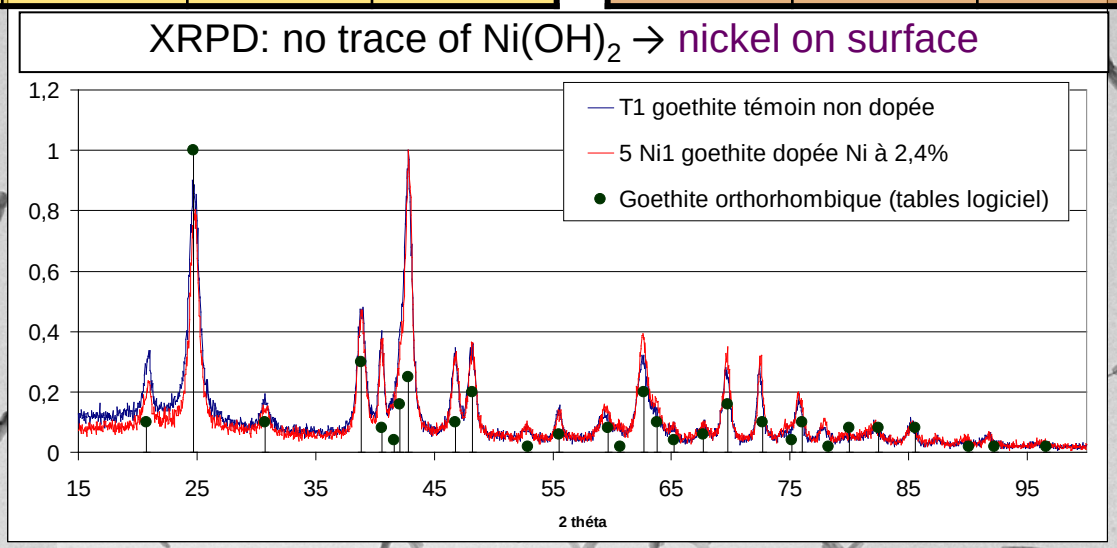
- U. Schwertmann & R.M. Cornell, Iron Oxides in the Laboratory (1991)
- B. Sing et al., Clay Minerals 2002 → Cr^{3+}, Mn^{3+}, Ni^{2+}
- M. Mohapatra et al., Hydromelallurgy 2002 → Cu^{2+}, Ni^{2+}, Co^{2+}, Mat. Chem. Phys. 2005 → Ce^{4+}

Ageing conditions: 24h in oven at 70° C - pH=11-12

Sample	pH_{ageing}	Ni/Fe	Φ v/v	D_{hyd} nm
T	11.1	0	0.21%	205
1Ni	11	0.6%	0.19%	198
5Ni	11.9	2.4%	0.17%	142
10Ni	12	2.8%	0.10%	168

Sample	pH_{ageing}	Co/Fe	Φ v/v	D_{hyd} nm
T	11.1	0	0.21%	205
1Co	12	1.0%	0.25%	284
5Co	12.2	2.6%	0.15%	169
10Co	12.2	9.6%	0.02%	238

XRPD: no trace of $Ni(OH)_2$ → nickel on surface



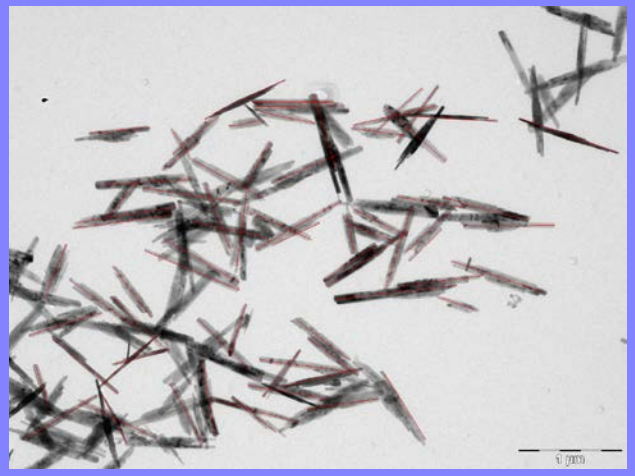
α–FeOOH: orthorombic mesh a=9.95Å b=3.01Å c=4.62Å

1 µm

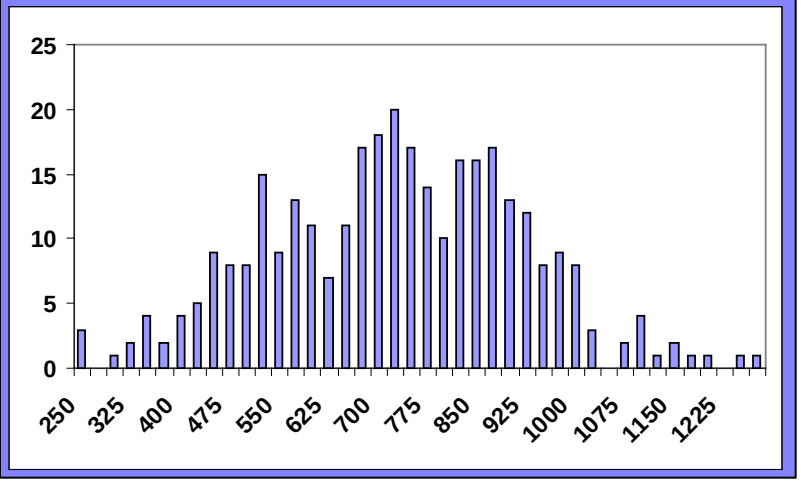
1 µm

Goethite nanorods doped with Co^{2+}

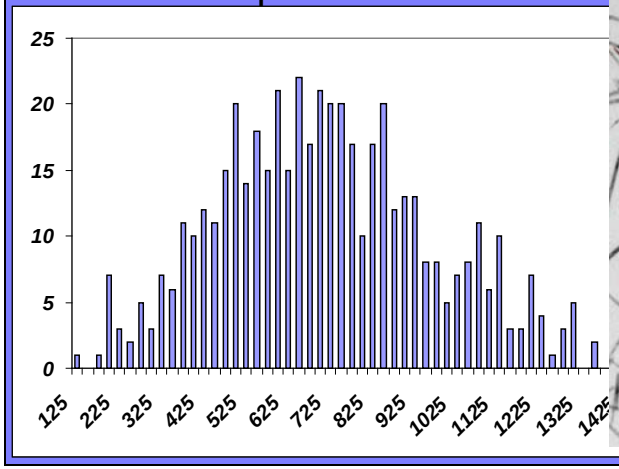
Goethite doped at 1%Co

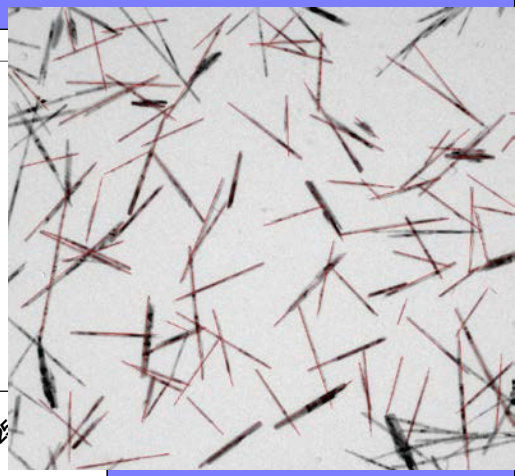


Hydrodynamic diameter = 284 nm
Mean length by TEM = 715 nm

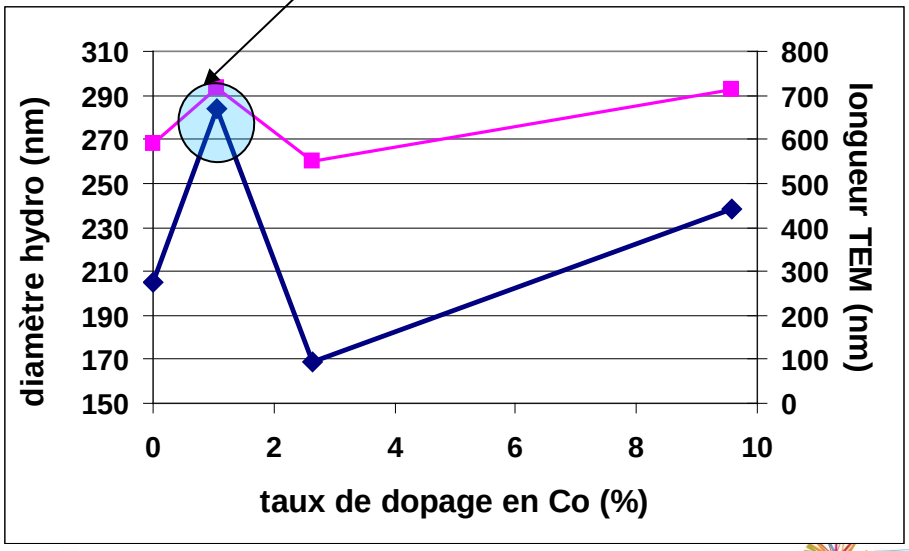


Goethite doped at 10%Co



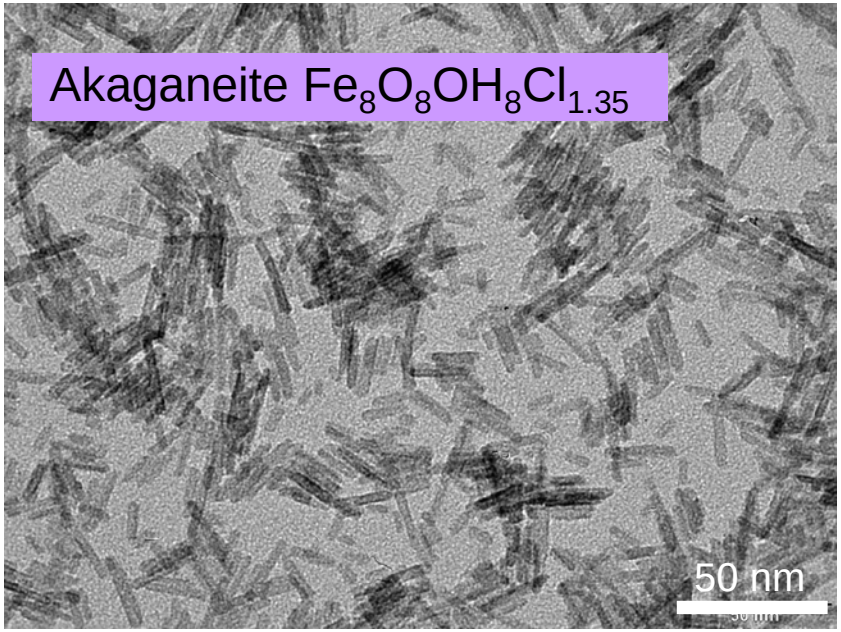


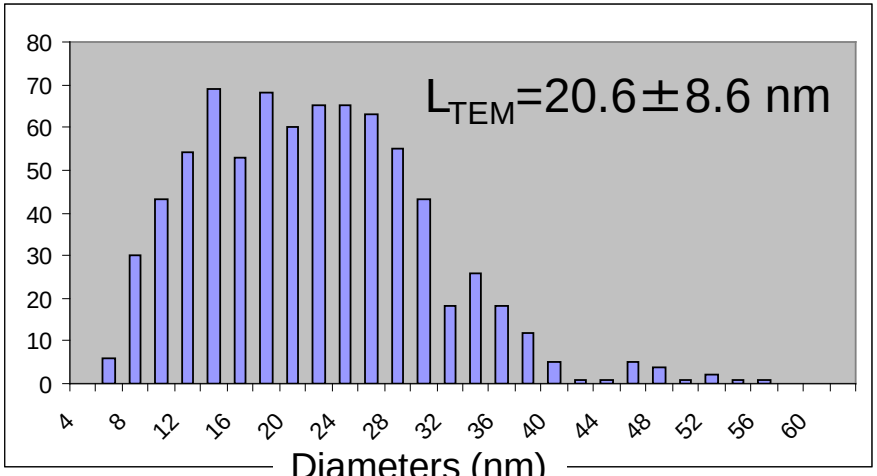
Large size associated with interesting magnetic properties (1Co1 sample)

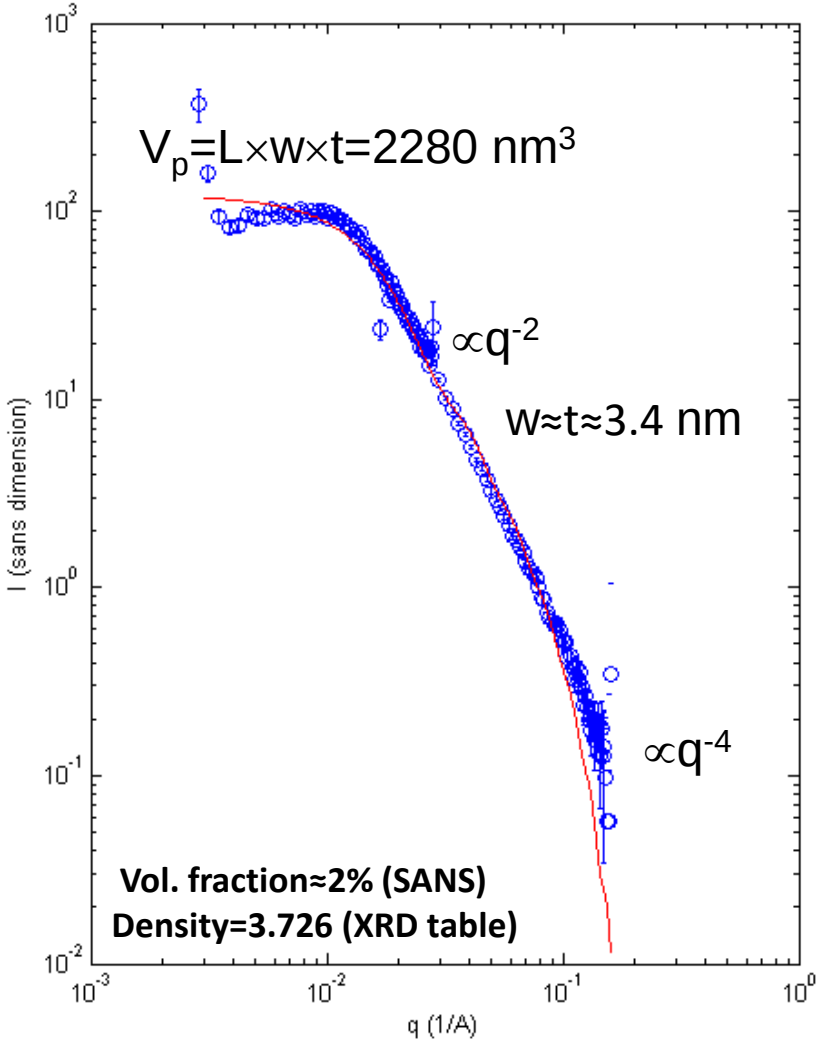


Non monotonous effect of Co doping on rods' size:

Antiferromagnetic nanorods of even smaller sizes



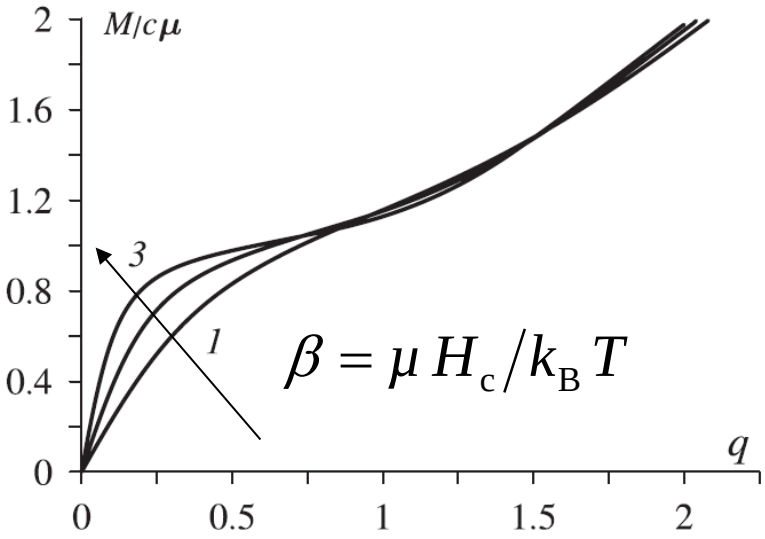




SANS on PAXY LLB-Saclay (oct. 2008)

Magneto-orientational behavior of a suspension of anti-ferromagnetic nanoparticles (NAF)

J. Phys.: Condens. Matter **20** (2008) 204120 Yu L Raikher, V. I. Stepanov (Perm, Russia) :

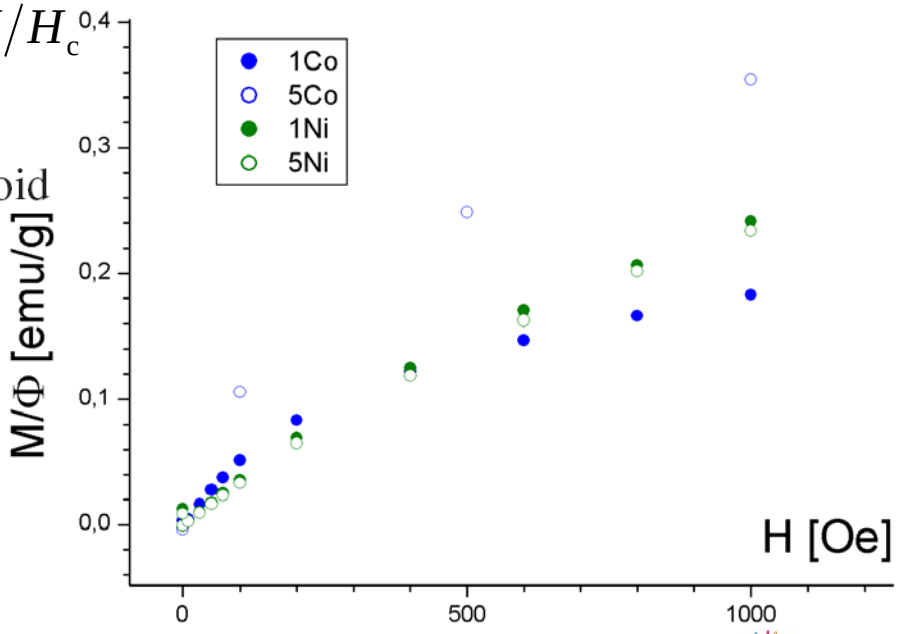


$$U = -\mu\,(\vec{e}.\vec{H}) + \tfrac{1}{2}\chi_A V(\vec{e}.\vec{H})^2$$

Figure 1. Reduced static magnetization of a NAF colloid

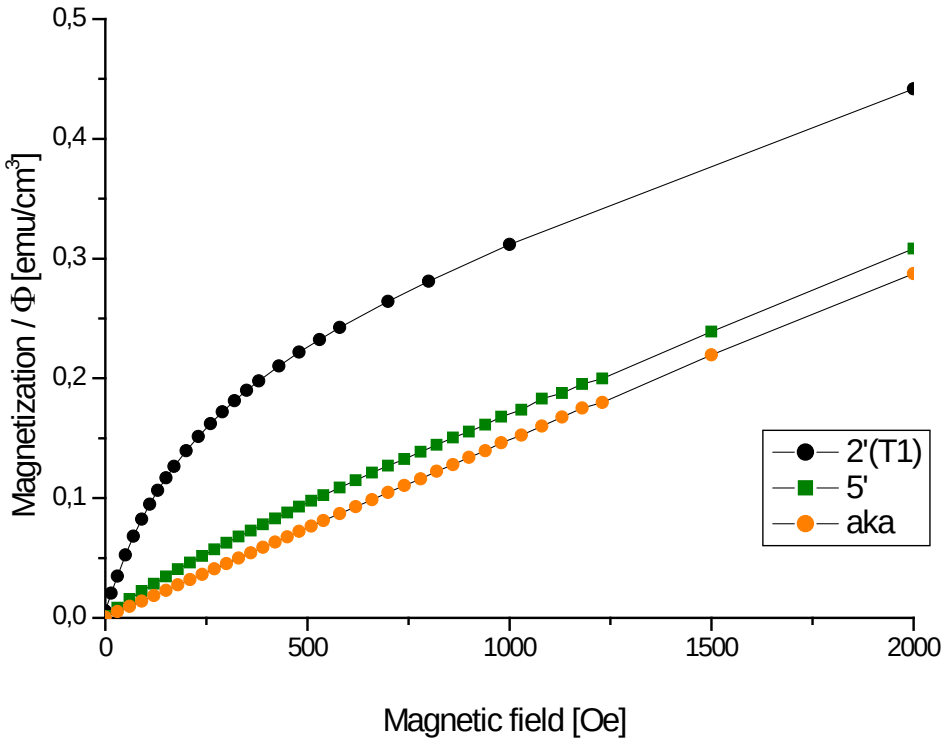
$$H_c = \mu/\chi_A V$$

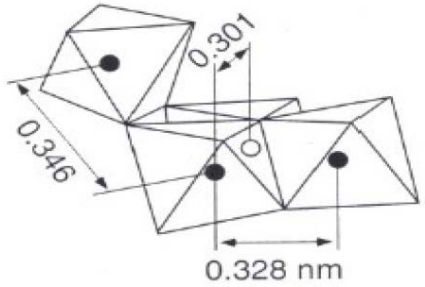
$\chi_A = \chi_{||} - \chi_{\perp}$



Magnetic behavior of antiferromagnetic nanorods

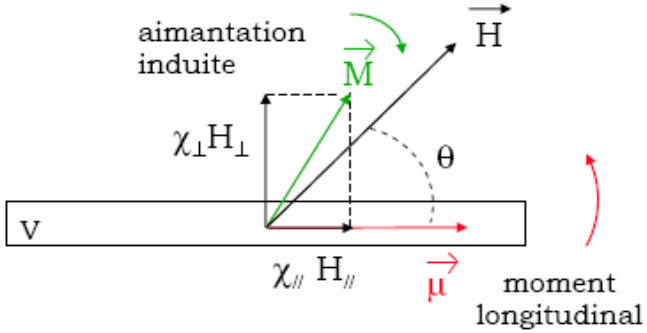
SQUID magnetometry at ambient temperature*





$\mu_{Fe+III}=5\ \mu_B$

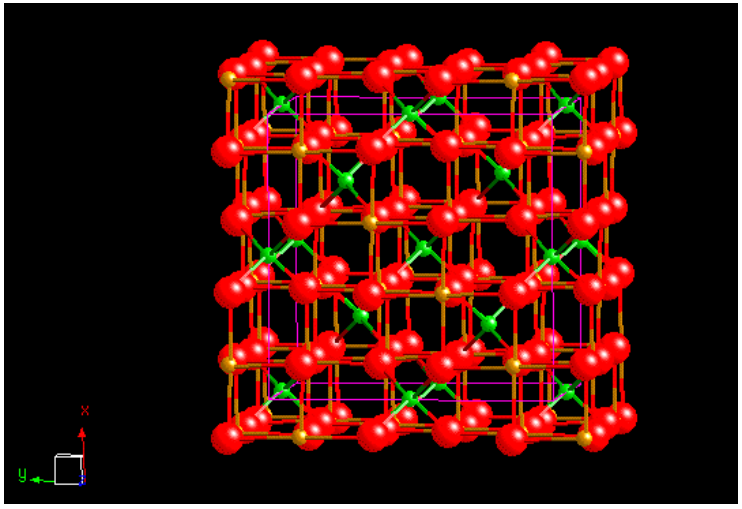
$\mu \approx 10000\ \mu_B \approx (N_{Fe})_{surf}^{1/2}\ \mu_{Fe}$

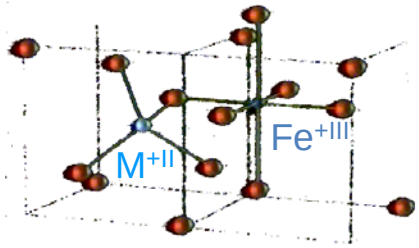


B. Lemaire, P. Davidson (LPS Orsay)

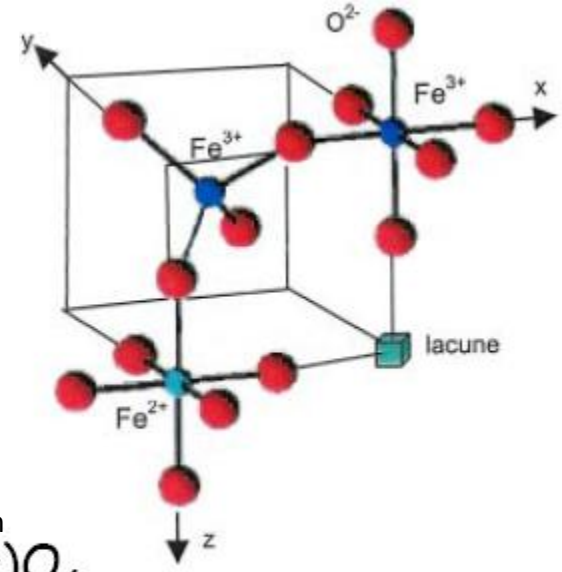
*measurement at INSP lab. (UPMC)

Magnetite: Crystalline Structure





$MO.Fe_2O_3$



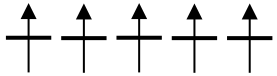
Spinelle structure:
direct or inverse

[4]=T_d [6]=O_h

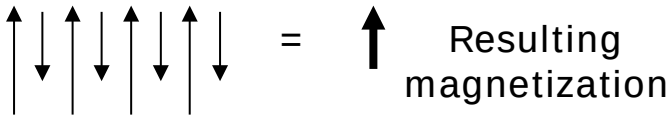
$(Fe^{3+})(Fe^{3+}\ Fe^{2+})O_4$

Fe^{2+} (d^6)=4 μ_B

Fe^{3+} (d^5)=5 μ_B



Magnetite is ferrimagnetic



<u>Exercise:</u> 1/calculate specific volume ($cm^3 \cdot mol^{-1}$) and mesh size a

<u>Data:</u> one unit cell is cubic and contains 8 Fe_3O_4 molecules

Mass density $\rho = 5.18 \times 10^3$ $kg \cdot m^{-3}$, Molar mass M=231.535 $g \cdot mol^{-1}$

1 Bohr magneton $\mu_B = 9.274 \times 10^{-24}$ $A \cdot m^2$

2/calculate the specific magnetization M_S of bulk Fe_3O_4 in $A \cdot m^{-1}$

<u>Answers:</u>

v=45 $cm^3 \cdot mol^{-1}$

a=8.396 Å

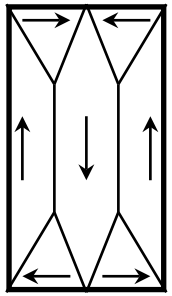
$M_S = 5 \times 10^5$ $A \cdot m^{-1}$

Magnetic domains and Bloch boundaries (walls)

Macroscopic magnets (bulk materials) are multi-domains

Size of mono-domain: ~ 30-50 nm for iron oxides

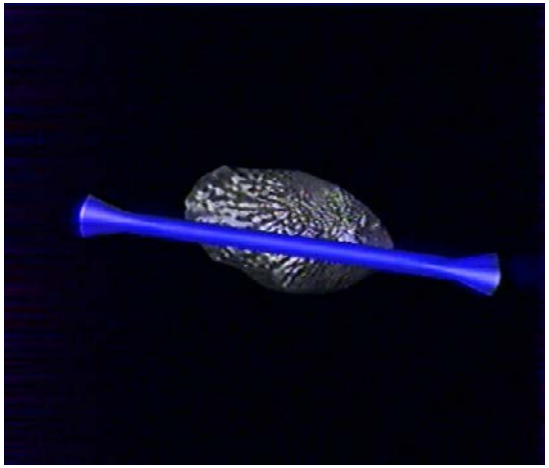
Curie-Weiss domains



Bloch walls

Rosensweig 1965, Néel 1955, Kittel 1946, Elmore 1938

One ~10 nm nanoparticle is a magnetic single domain



Exercise:

1:calculate magnetic moment (in nb of μ_B/MNP) for diameters: d=4 / 8 / 16 nm

2: calculate total nb of Fe ions per MNP for all d's

3: calculate nb of Fe ions on surface per MNP for all d's

Data:

1 Bohr magneton $\mu_B = 9.274 \times 10^{-24}$ A·m^2

For nano-crystalline Fe_3O_4, $M_S = 4 \times 10^5$ A·m^{-1}

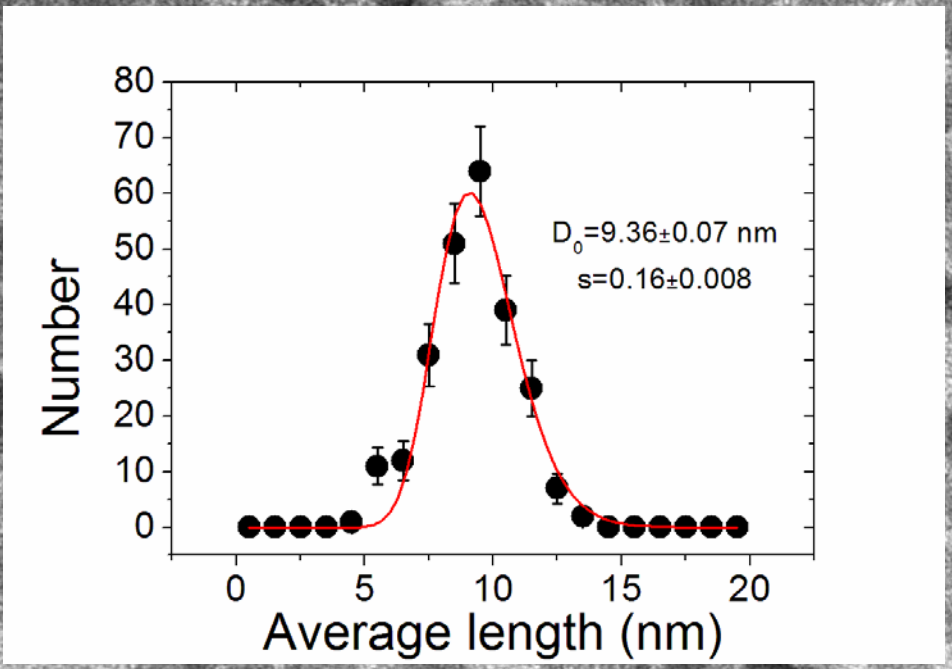
Answer:

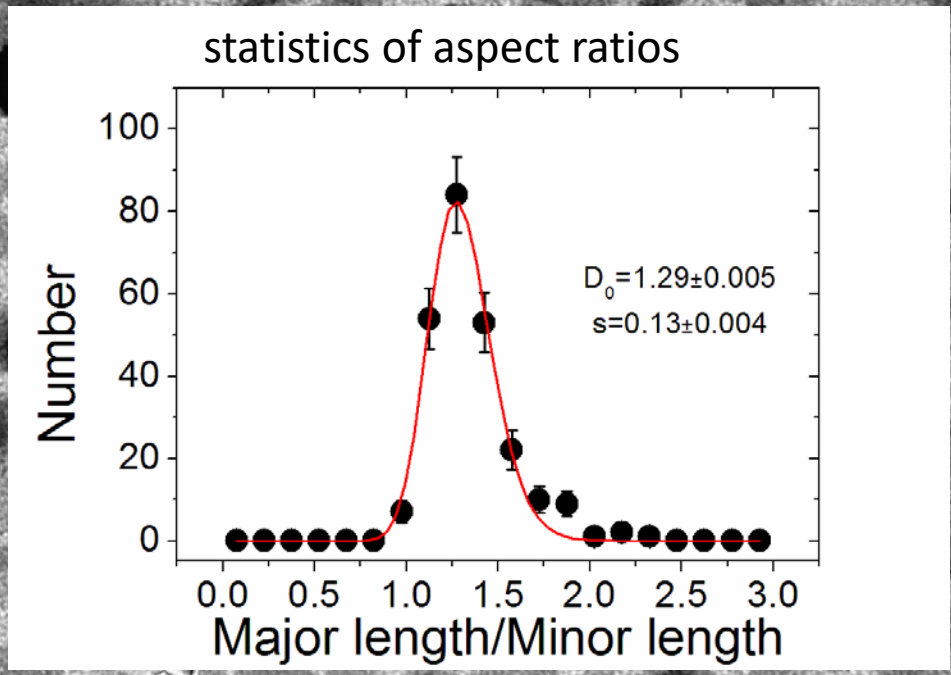
1: 1500 / 11000 / 90000 2: 1400 / 10700 / 87000

3: 290 (20%) / 1100 (10%) / 4500 (5%)

Shape anisotropy contribution to birefringence

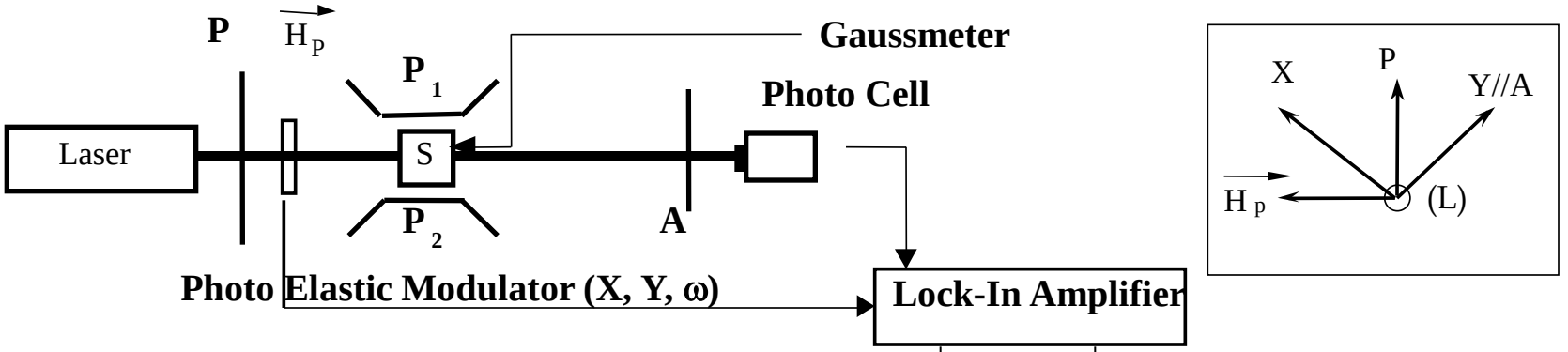
"Rock-like" particles: S1C fraction, coated with PAA_{2k}





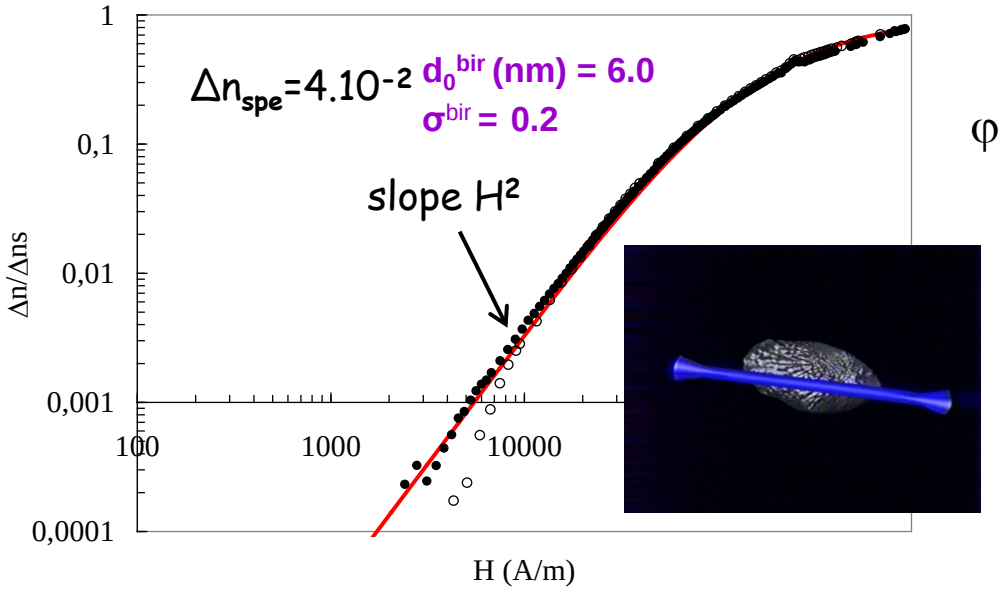
50 nm

Birefringence measurement under H field



E. Hasmonay et al. EPJB 1998

$I_1(\omega) \propto |\sin(\varphi)|$ $I_2(2\omega) \propto (t_{\parallel} - t_{\perp})$ dichroism



$\varphi = 2\pi \Delta n\, e / \lambda$ → $\Delta n = (n_{\parallel} - n_{\perp})$ birefringence

Plateau: $\Delta n_{sat} = \Delta n_{spe}\, \Phi$

Ferrofluid sample (maghemite γ-Fe_2O_3)

Starting materials : "True" ferrofluid

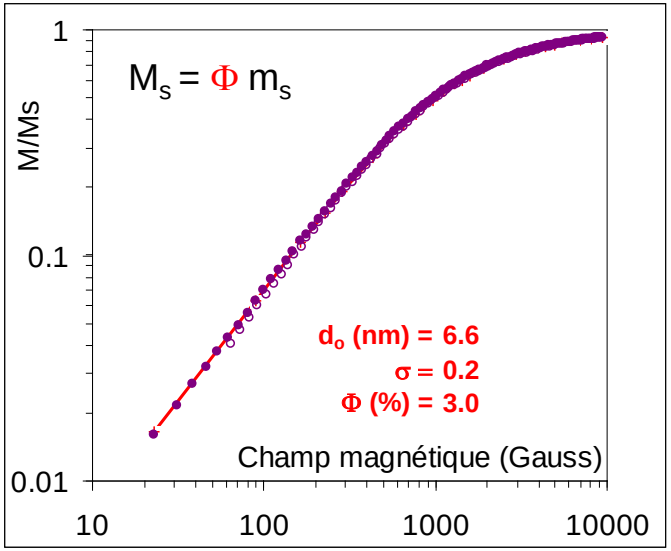
Ferrofluid = colloidal suspension of magnetic nanoparticles
which remains <u>stable whatever the intensity of applied magnetic field</u>

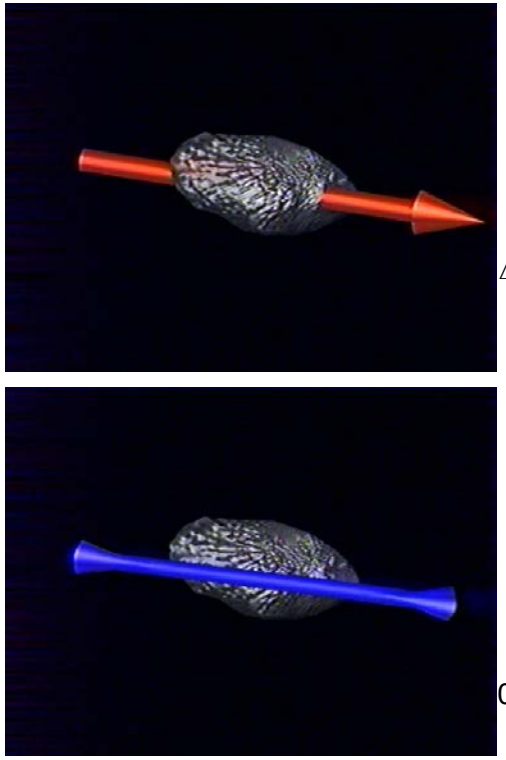
- no attraction of nanoparticles under B field gradient nor chaining by dipolar interaction

- but progressive orientation of dipoles according to Langevin's laws:

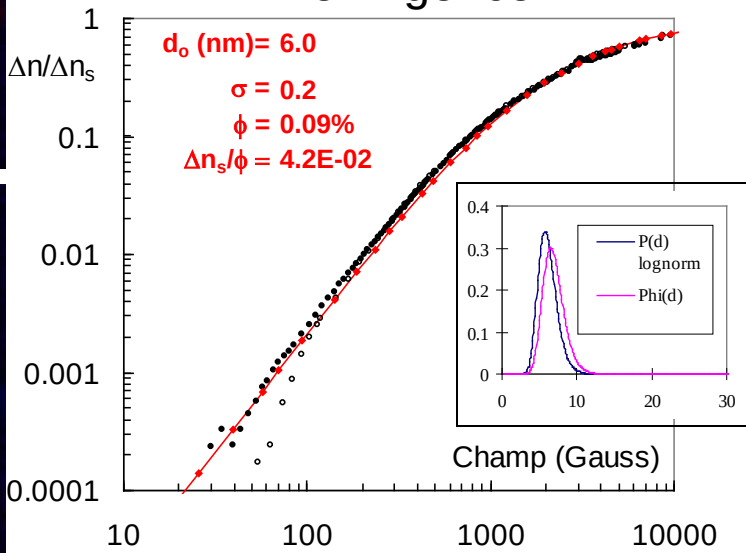
Magnetization

$m_s = 3{,}1.10^5$ A/m (SI) $m_s / 4\pi = 300$ G (CGS)

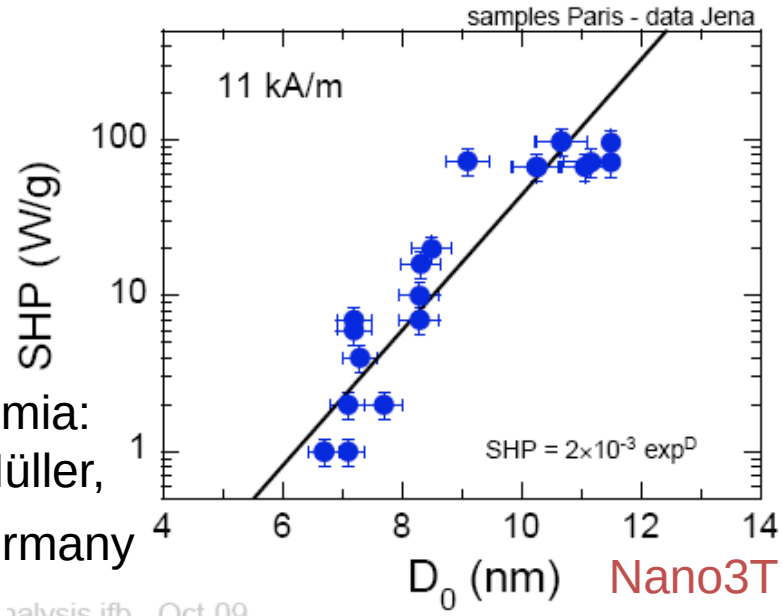


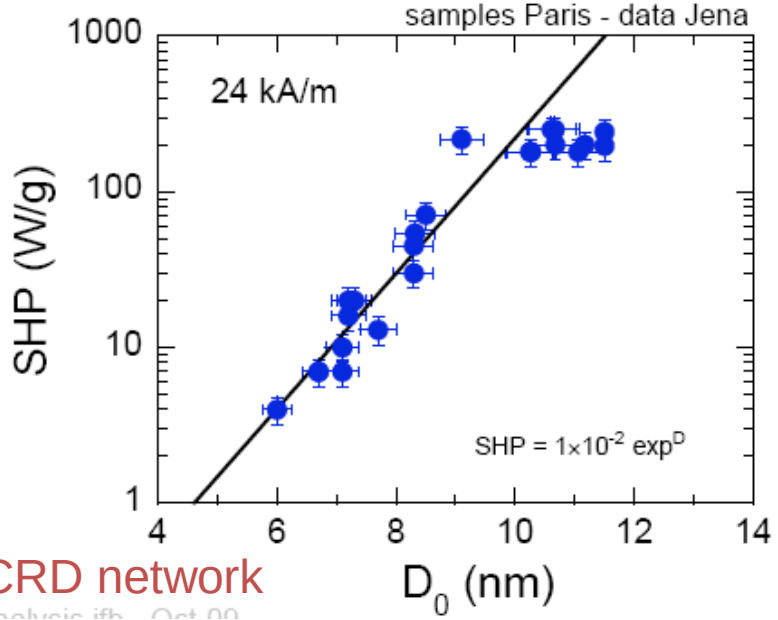


Birefringence



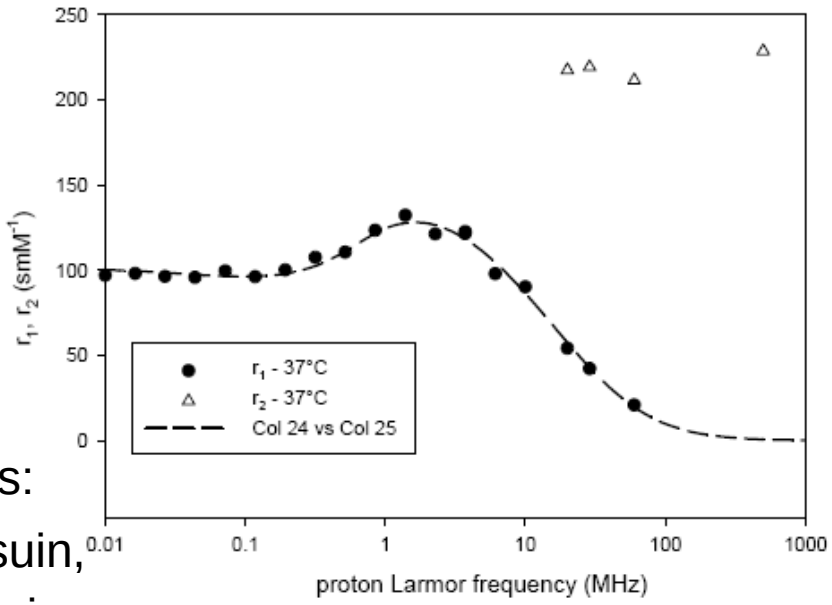
Improved properties of the larger magnetic NPs



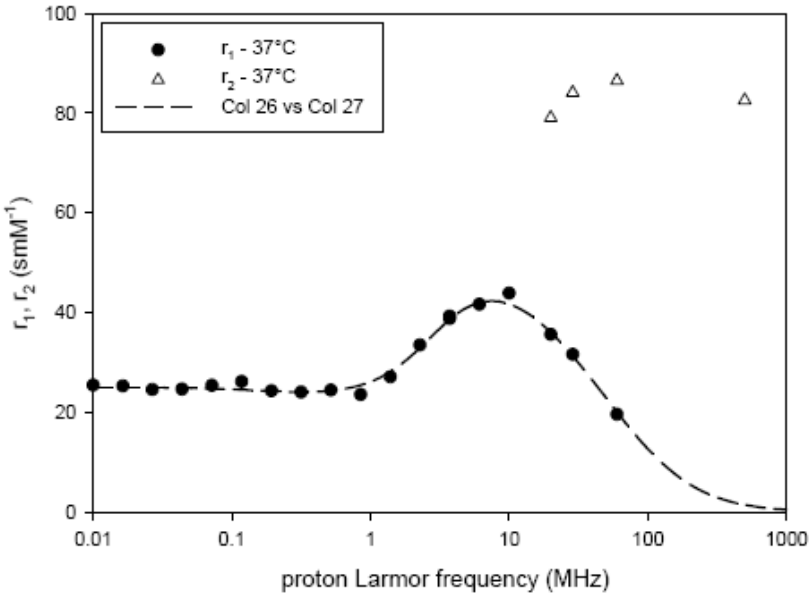


Hypethermia:
Robert Müller,
Jena, Germany

Nano3T 7th PCRD network



C1C2C3C4S5-PAA5K

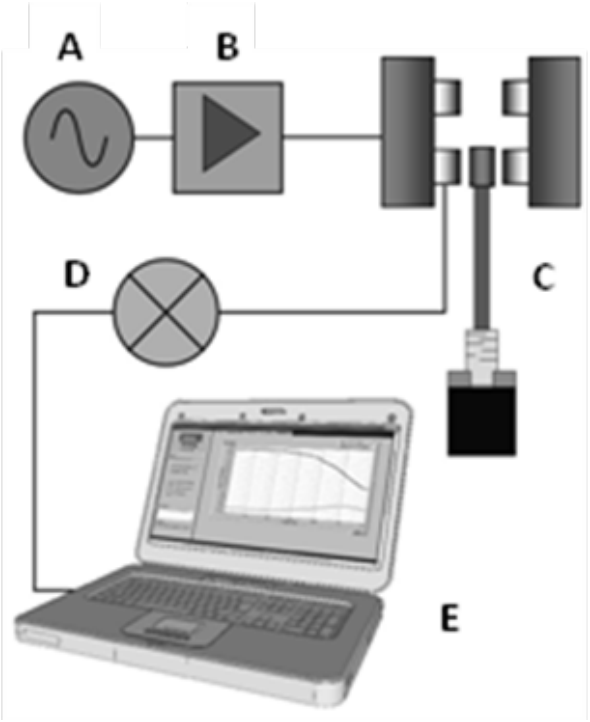


S2C14

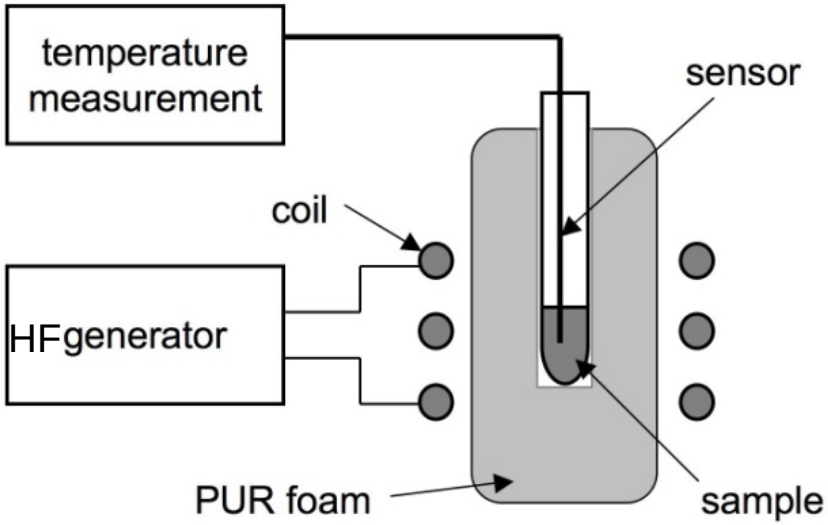
Relaxivities:
Yves Gossuin,
Mons, Belgium

High Frequency Magnetic Susceptometry / Hyperthermia

Astalan, A.; Ahrentorp, F.; Jonasson, C.; Blomgren, J.; Yan, M.; Courtois, J.; Berret, J.-F.; Fresnais, J.; Sandre, O.; Müller, R.; Dutz, S.; Johansson, C., AIP Conf. Proc. Series 2010

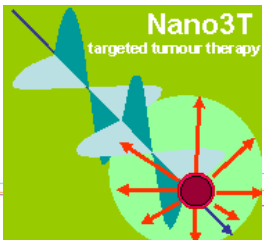


High frequency AC susceptometer built at the IMEGO company (Sweden)
AC signal source (A), current amplifier (B), coil system and mechanics (C), lock-in amplifier (D) and user interface software (E)



Hyperthermia set-up built by R. Müller, Jena (Germany)

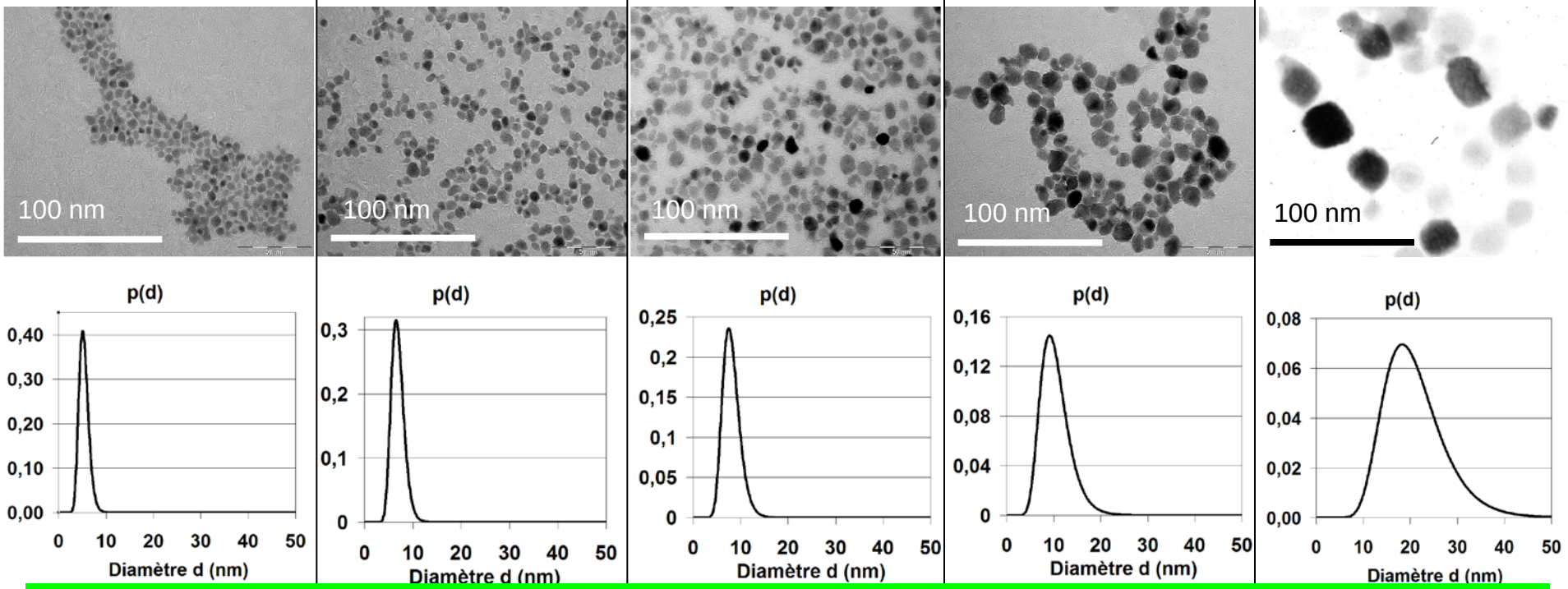
$$SHP = \pi \mu_0 \chi'' f_{RF} H_0^2 V_S$$



Role of the sizes' (mono)dispersity on the SHP effect

G. Glöckl, R. Hergt, J. Phys.: Condens. Matter 18 (2006) S2935–S2949: resonance effect

5,3nm / 0,19	6,8nm / 0,20	8,0nm / 0,21	10,2nm / 0,28	≈ 20nm / 0,3



SHP (at f =700 kHz, H_0=24.8 kAm^{-1}) =

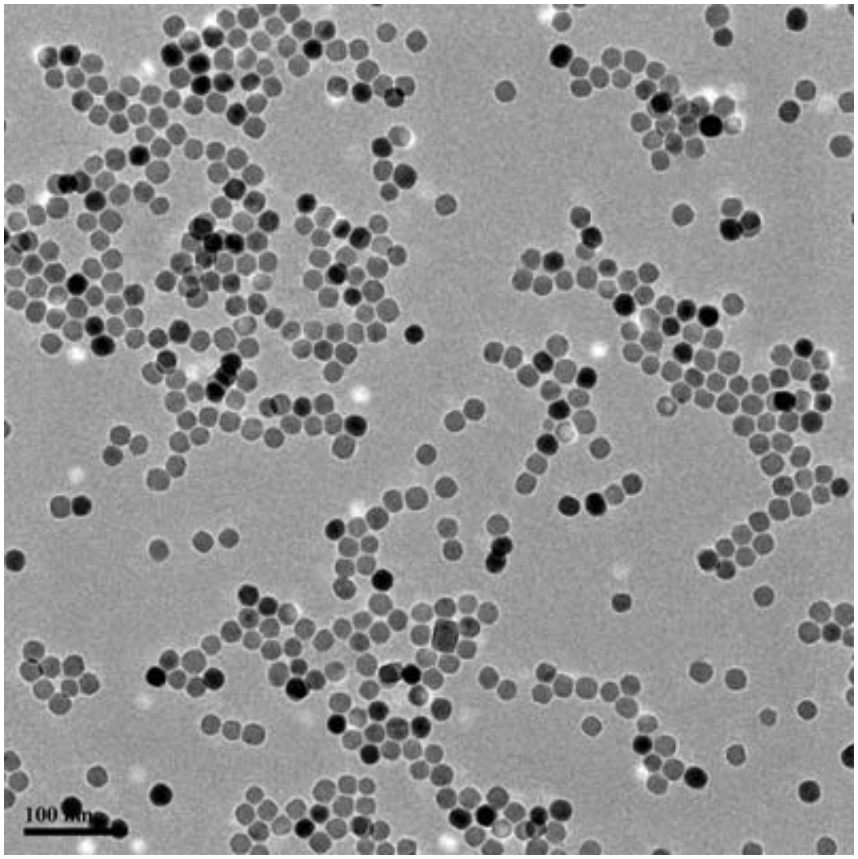
4 W/g 14 W/g 37 W/g 275 W/g 1650 W/g

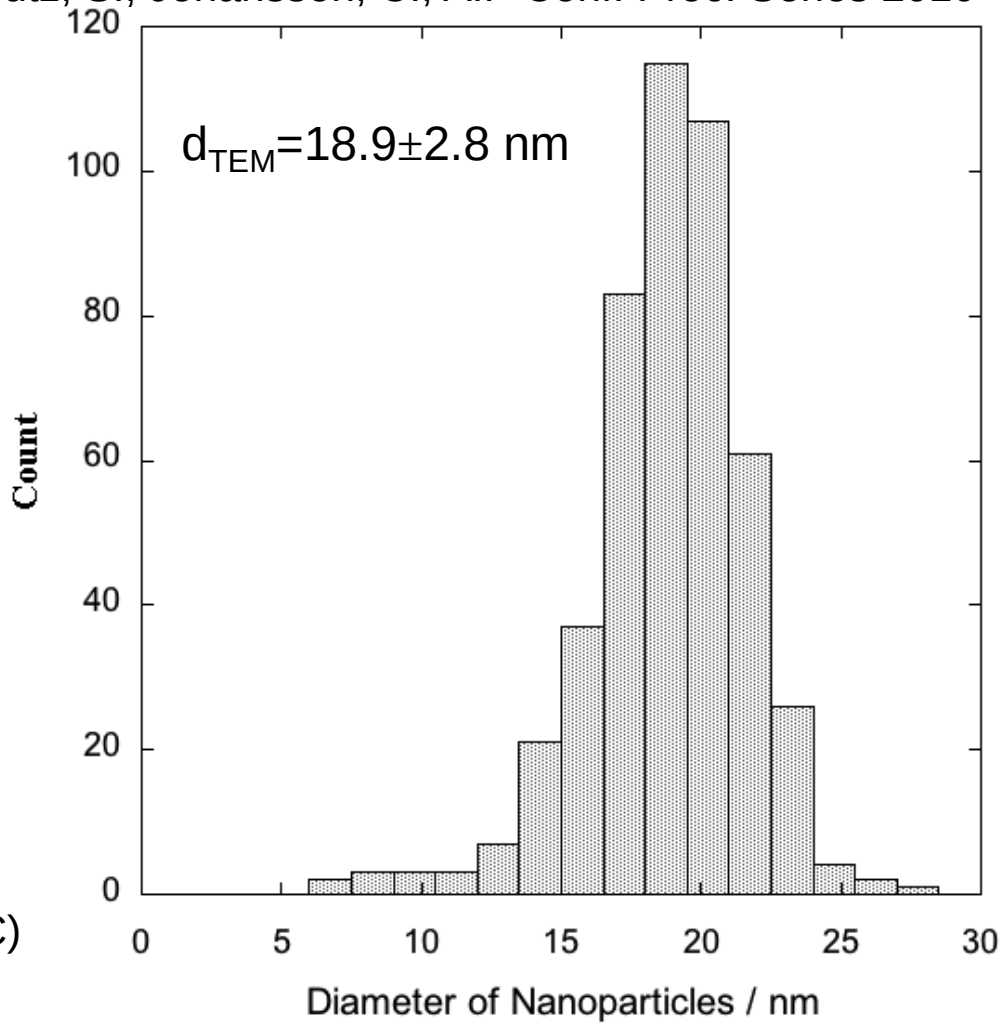
J-P. Fortin, C. Wihelm, J. Servais, C. Ménager, J-C. Bacri, F. Gazeau, J. Am. Chem. Soc. 129 2628 (2007)

M. Lévy, C. Wilhelm, J-M. Siaugue, O. Horner, J-C. Bacri, F. Gazeau, J. Phys. Cond. Mat. 20 204133 (2008)

Calibration sample: monodisperse Fe_3O_4 nano-spheres

Astalan, A.; Ahrentorp, F.; Jonasson, C.; Blomgren, J.; Yan, M.; Courtois, J.; Berret, J.-F.; Fresnais, J.; Sandre, O.; Müller, R.; Dutz, S.; Johansson, C., AIP Conf. Proc. Series 2010

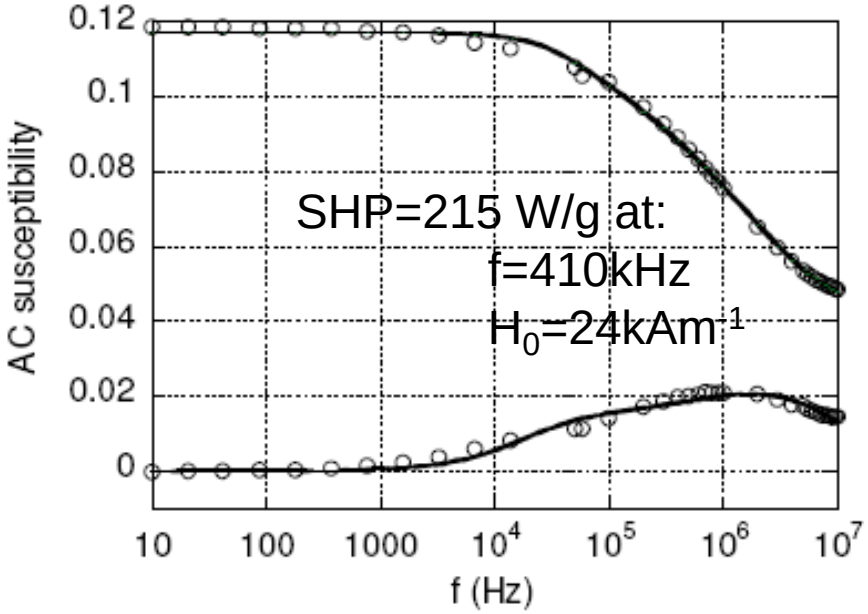




Fe-oleate decomposition in n-hexane (4h 70°C)
Q. Bin, O. T. Mefford (Clemson Univ, USA)
according to Park et al, Angew. Ch. 2005)

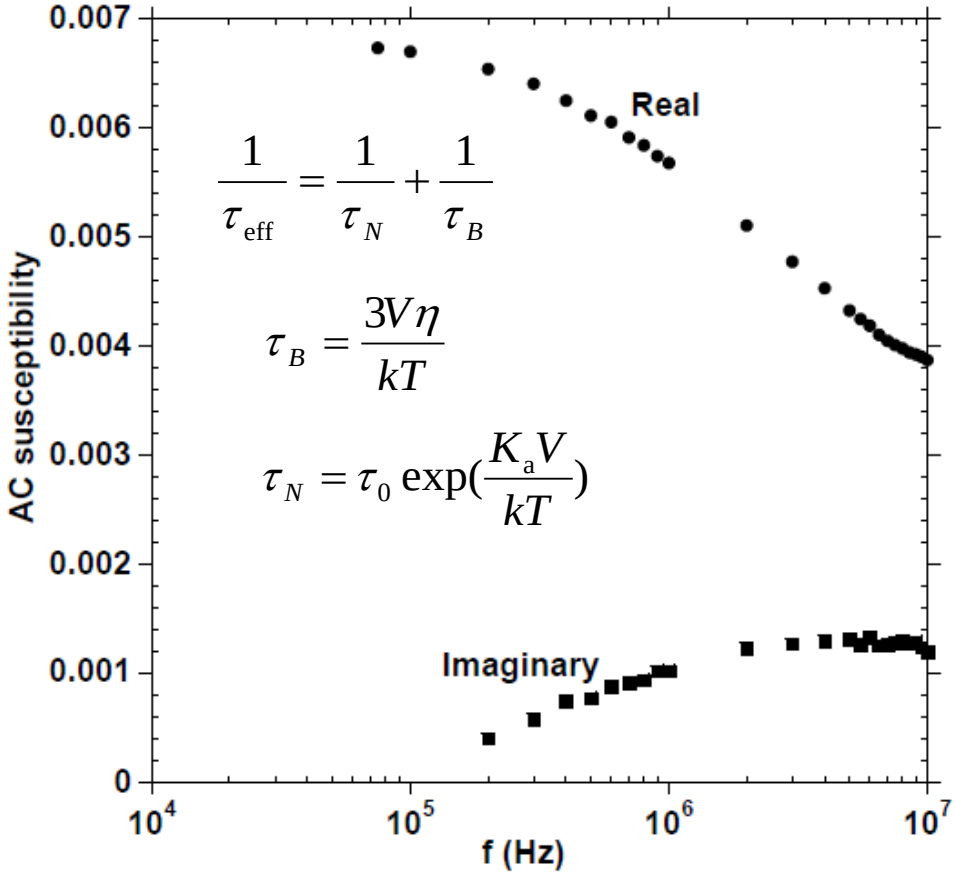
Role of MNP shape on the magnetic anisotropy K_a

Astalan, A.; Ahrentorp, F.; Jonasson, C.; Blomgren, J.; Yan, M.; Courtois, J.; Berret, J.-F.; Fresnais, J.; Sandre, O.; Müller, R.; Dutz, S.; Johansson, C., AIP Conf. Proc. Series 2010



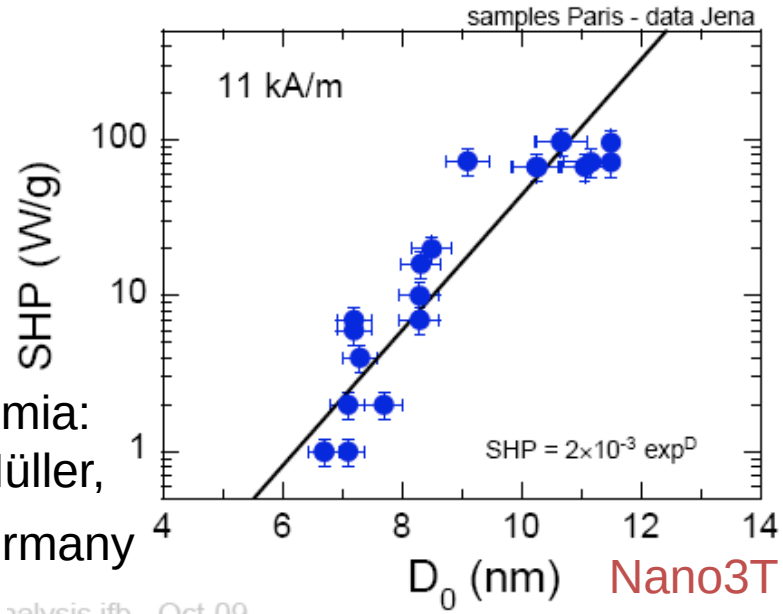
rock-like particles Ø16nm :
large χ'', Néel's band ~ 2MHz

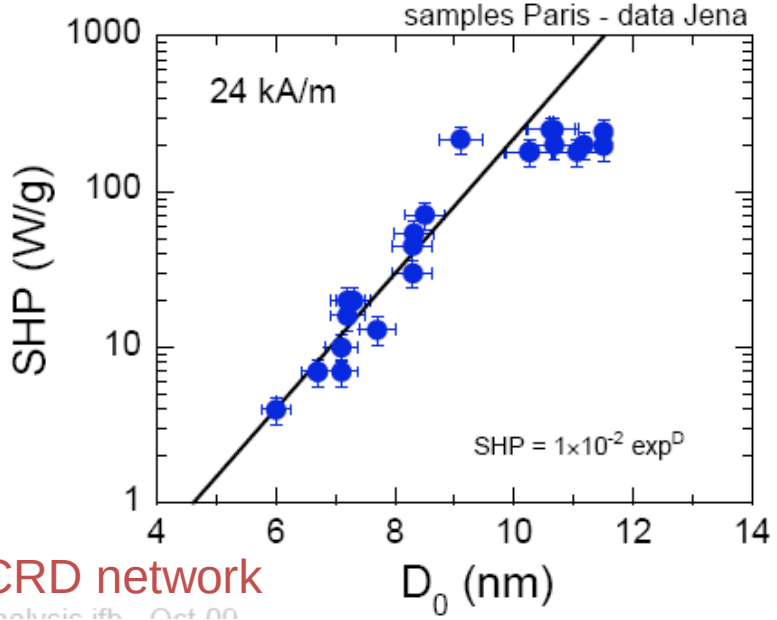
$$\chi(\omega) = C \int \frac{r_C^6}{\left(1 + j\omega\tau_{eff}(r_H)\right)} f(r_H) dr_H + \chi_{high}$$



spheres Ø19nm: weak χ'', Néel's band ~ 5MHz

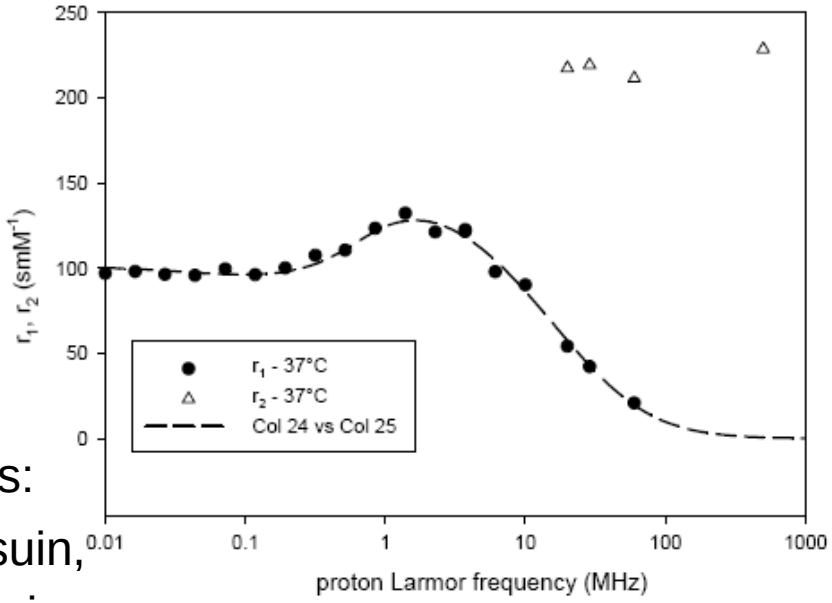
Improved properties of the larger magnetic NPs



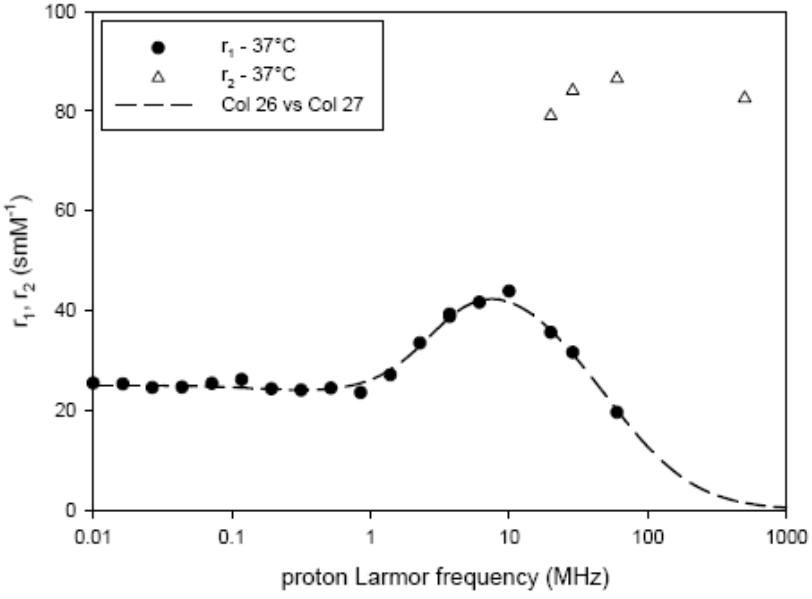


Hypethermia:
Robert Müller,
Jena, Germany

Nano3T 7th PCRD network



C1C2C3C4S5-PAA5K



S2C14

Relaxivities:
Yves Gossuin,
Mons, Belgium

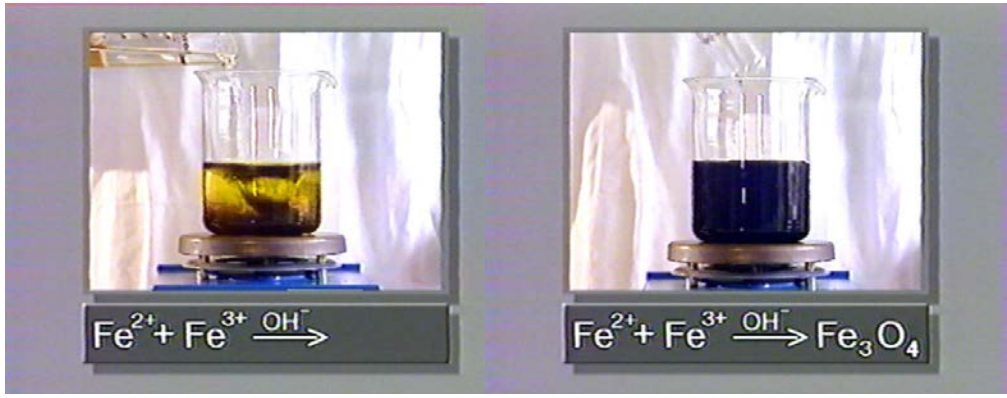
Ionic Ferrofluids: the coprecipitation synthesis

- Massart's process:

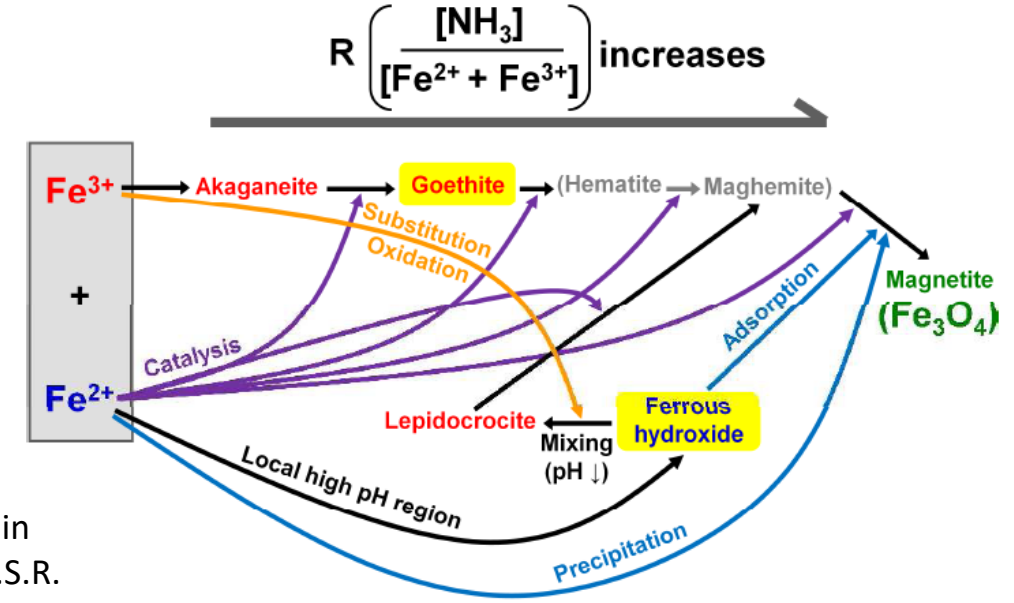
Alkaline coprecipitation of $FeCl_2$ & $FeCl_3$
→ magnetite Fe_3O_4 nanoparticles

$$Fe^{2+}_{(aq)} + 2Fe^{3+}_{(aq)} + 8OH^-_{(aq)} \rightarrow Fe_3O_{4(s)} + 4H_2O_{(l)}$$

R. Massart *IEEE Trans. Magn.* **17** 1247 (1981)



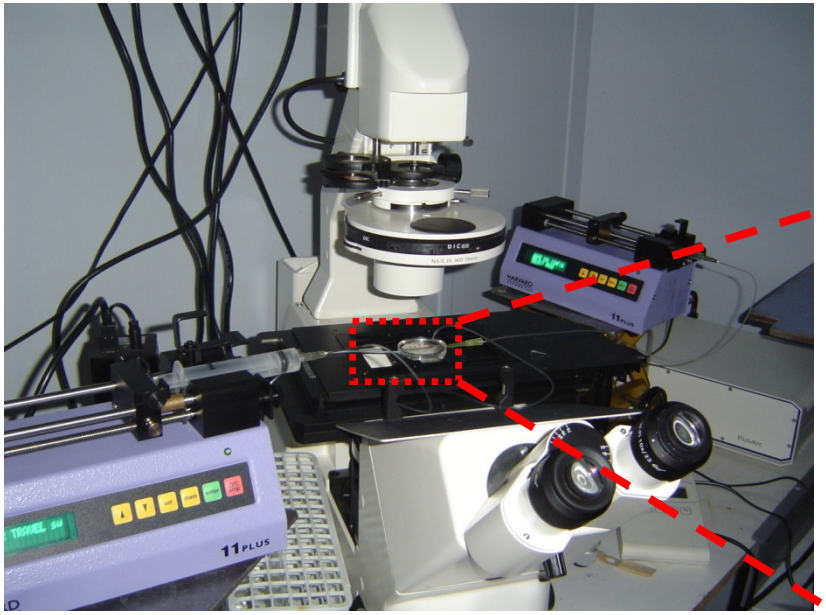
Oxidation by $Fe(NO_3)_3$
→ maghemite γ-Fe_2O_3 nanoparticles
in acidic medium (HNO3): stabilized by electrostatic surface charges (PZC≈7)



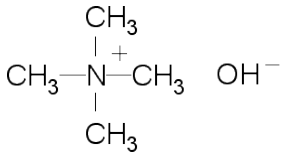
A. Abou-Hassan, O. Sandre, and V. Cabuil, *Chapter 9: Microfluidics for the synthesis of iron oxide nanoparticles*, in Microfluidic Devices in Nanotechnology: Applications, C.S.S.R. Kumar, Editor. **2010**, John Wiley & Sons, Inc: Hoboken, NJ, USA. p. 323-360

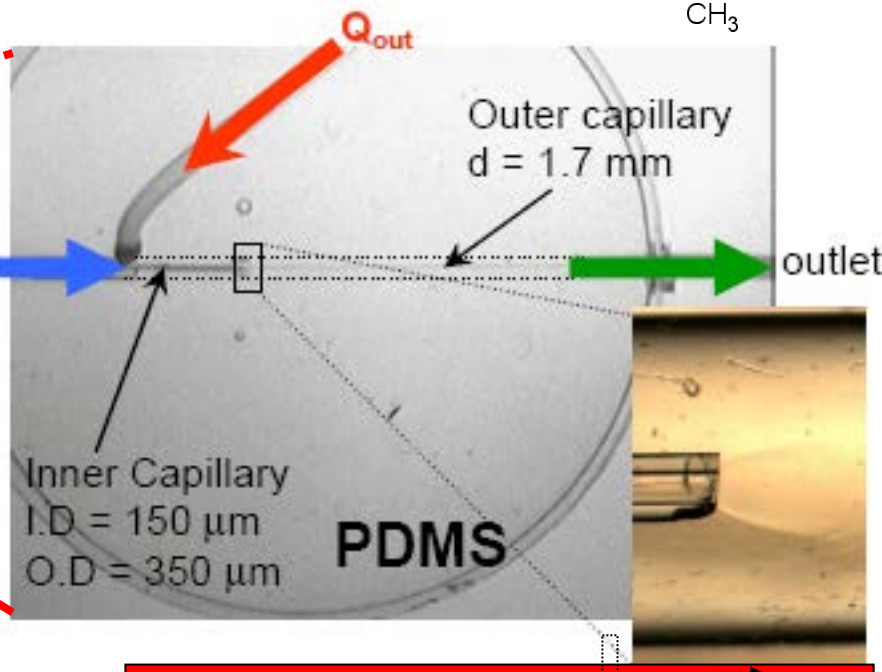
T. Ahm at al. *J. Phys. Chem.* (2012) pre-print

Microfluidics as a tool to get an insight of the kinetics of the coprecipitation reaction



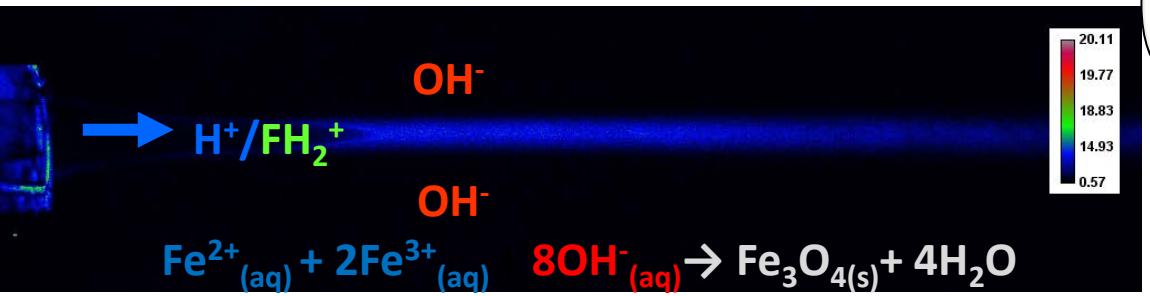
Answer to clogging issue: 3D geometry and non flocculating counterion of base TMA⁺

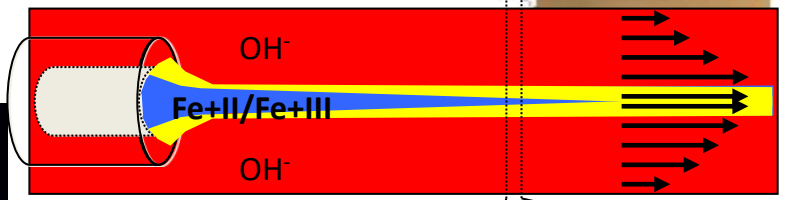




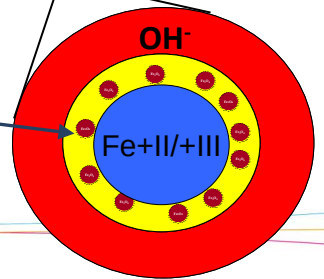
PhD thesis Ali Abou Hassan (2 oct 2009)

A. Abou Hassan, O. Sandre, V. Cabuil, P. Tabeling, *Chem. Commun.* 2008, 1783



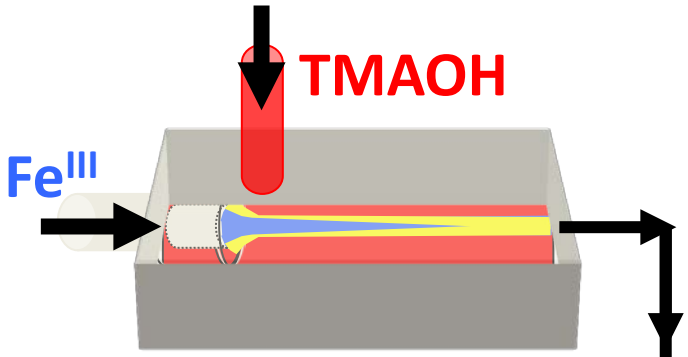


Nanoparticles at the interface

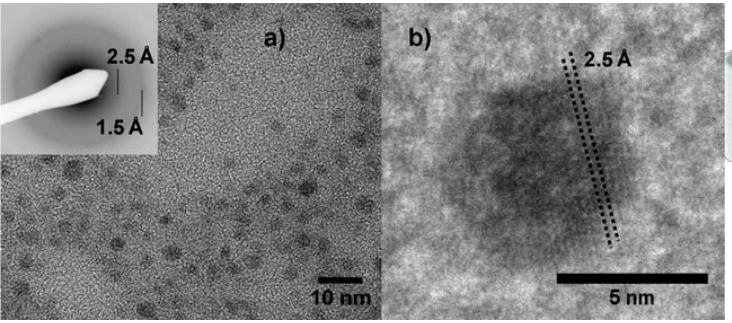


Microfluidics as a tool to get an insight of the mechanism of goethite formation

Two micro-reactors in-line

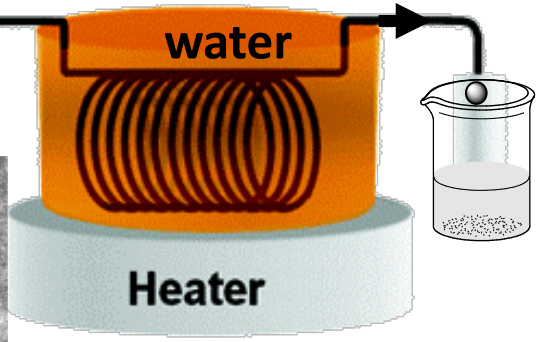


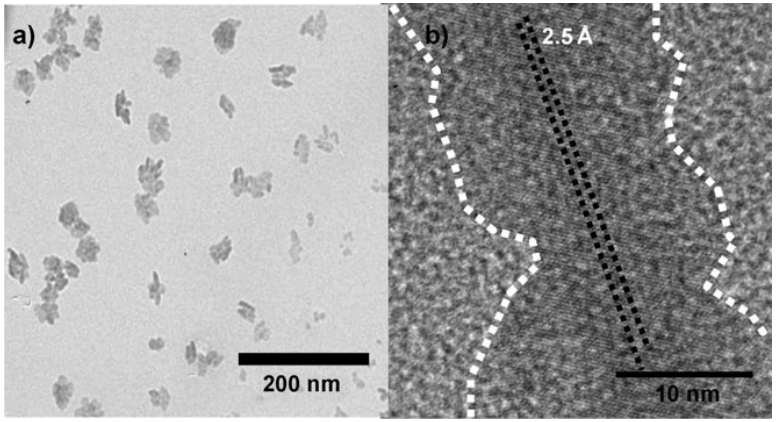
µR1: nucleation (seeds)



“2-lines ferrihydrite” nanodots ∅ = 4±1 nm

µR2: growth T=60°C

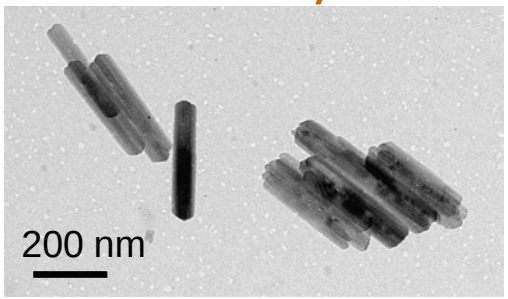




15 min / 60°C: Goethite nanorods

L=30±17 nm and w=7±4 nm

Final state as in macro synthesis



→ check “oriented aggregation” mechanism

J. F. Banfield et al. *Science* 2000, 289, 751

A. Abou-Hassan, O. Sandre, S. Neveu, V. Cabuil, *Angew. Ch.* **48** 1-5 (2009)

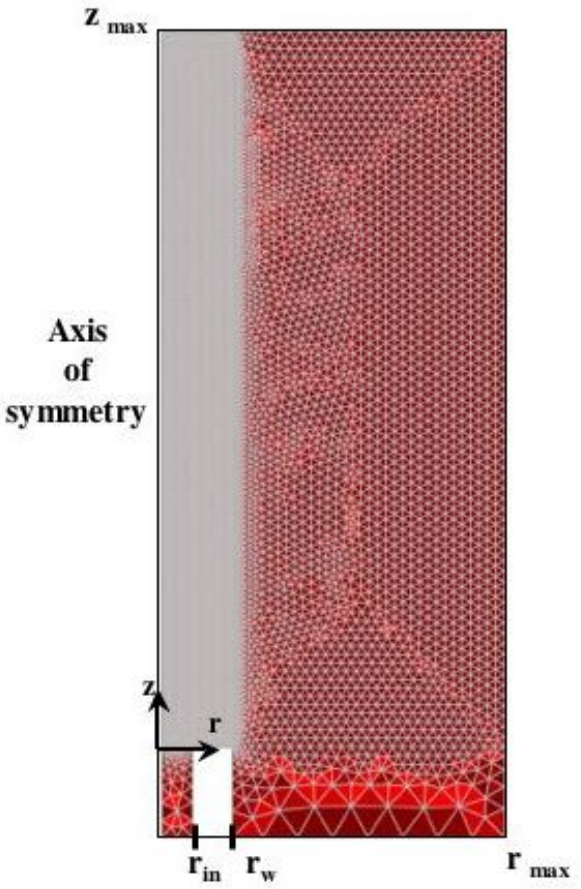
Microfluidics as a tool to get an insight of the mechanism of goethite formation

- **FEM lab simulations**

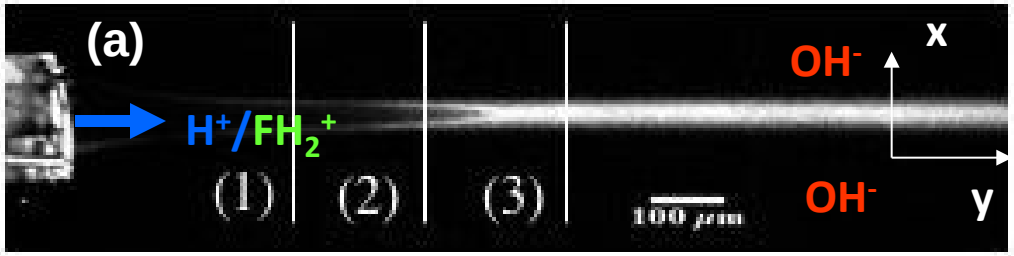
$$\frac{\partial C_i}{\partial t} + \mathrm{div}(C_i \mathbf{u} + \mathbf{j}_i) = \sigma_i$$

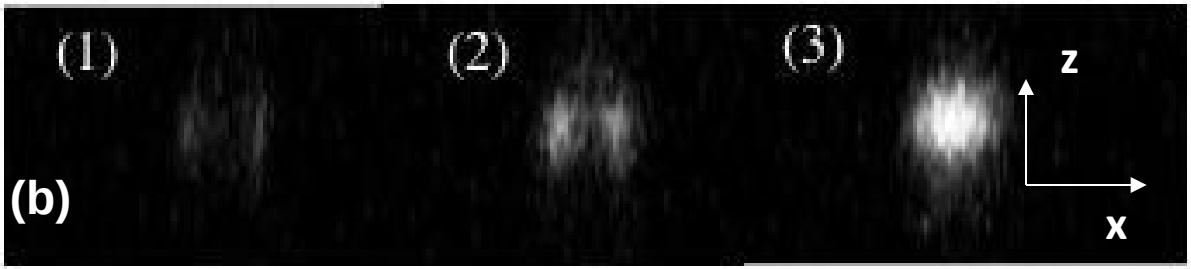
$$\mathbf{j}_i = -D_i \,\mathrm{grad} C_i + \frac{D_i}{k_B T} C_i Z_i e \mathbf{E}$$

(Nernst-Planck)



- **Confocal Laser Scanning Microscopy: Fluorescein as pH reporter dye**

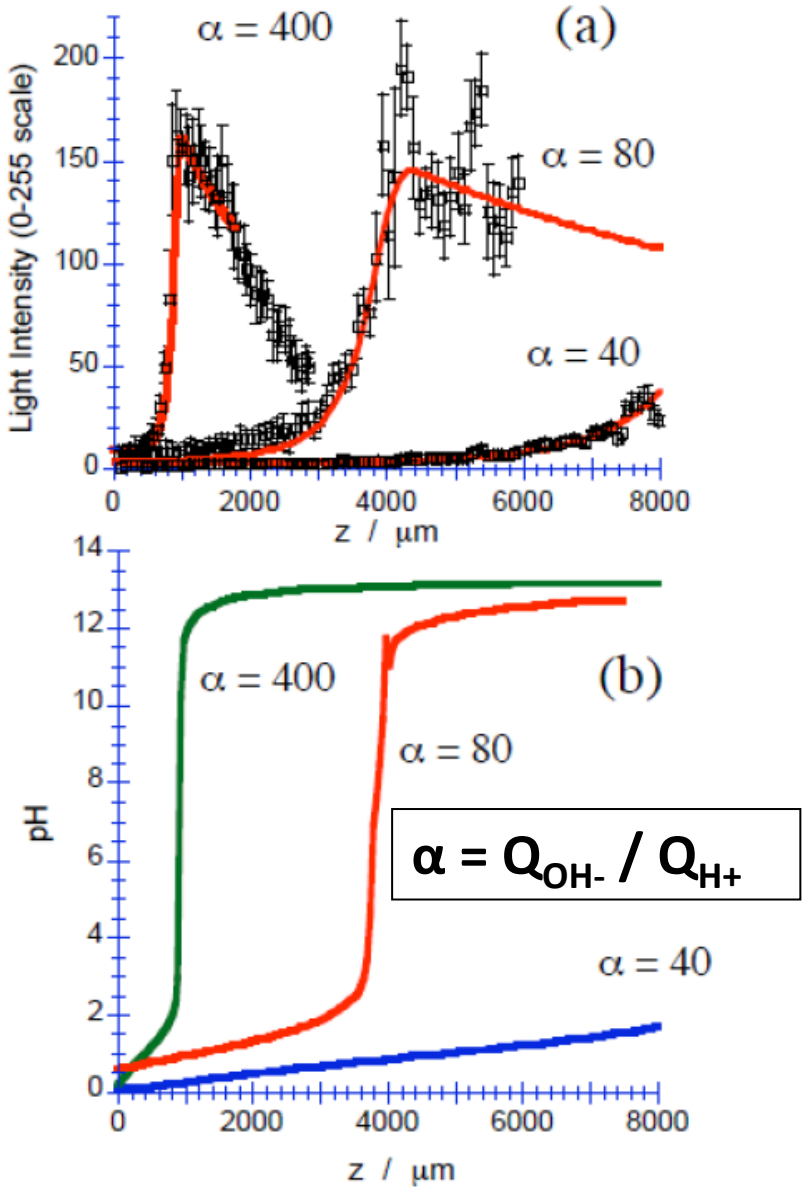




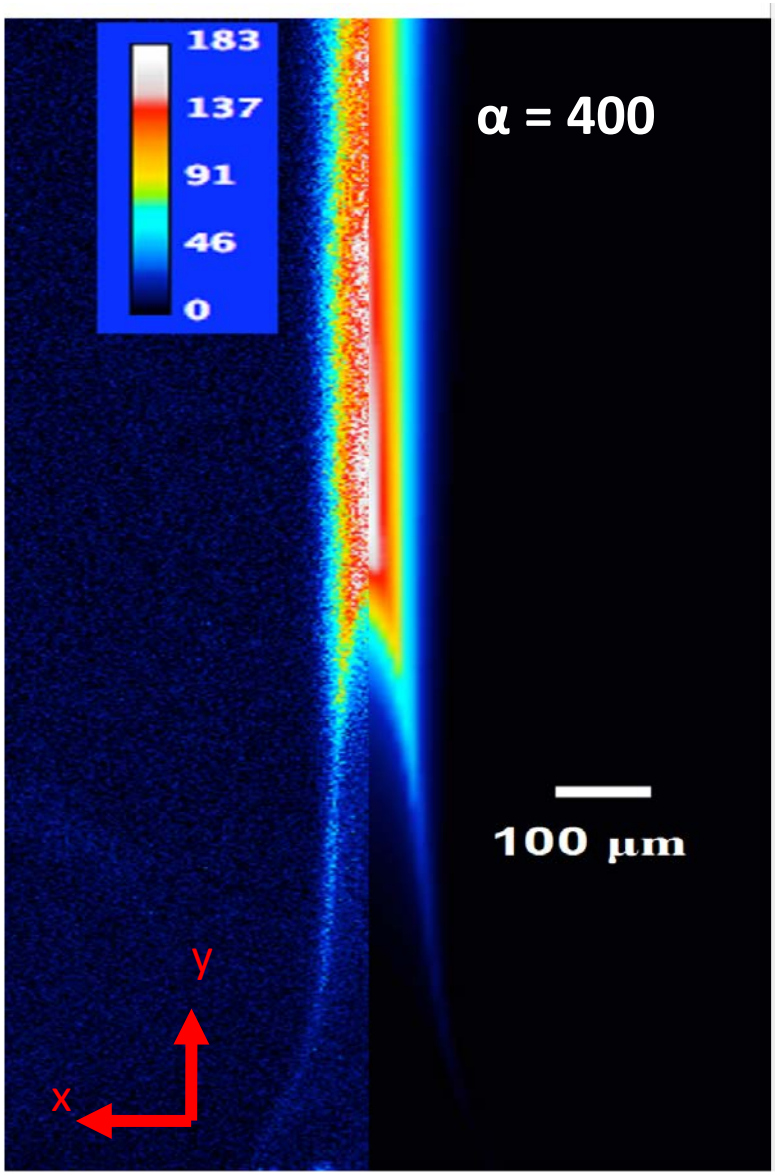
pH = f(α) with α = Q_{OH^-} / Q_{H^+}

A. Abou-Hassan, J-F. Dufrêche, O. Sandre, G. Mériguet, O. Bernard, V. Cabuil, *J. Chem. Phys.* C 2009

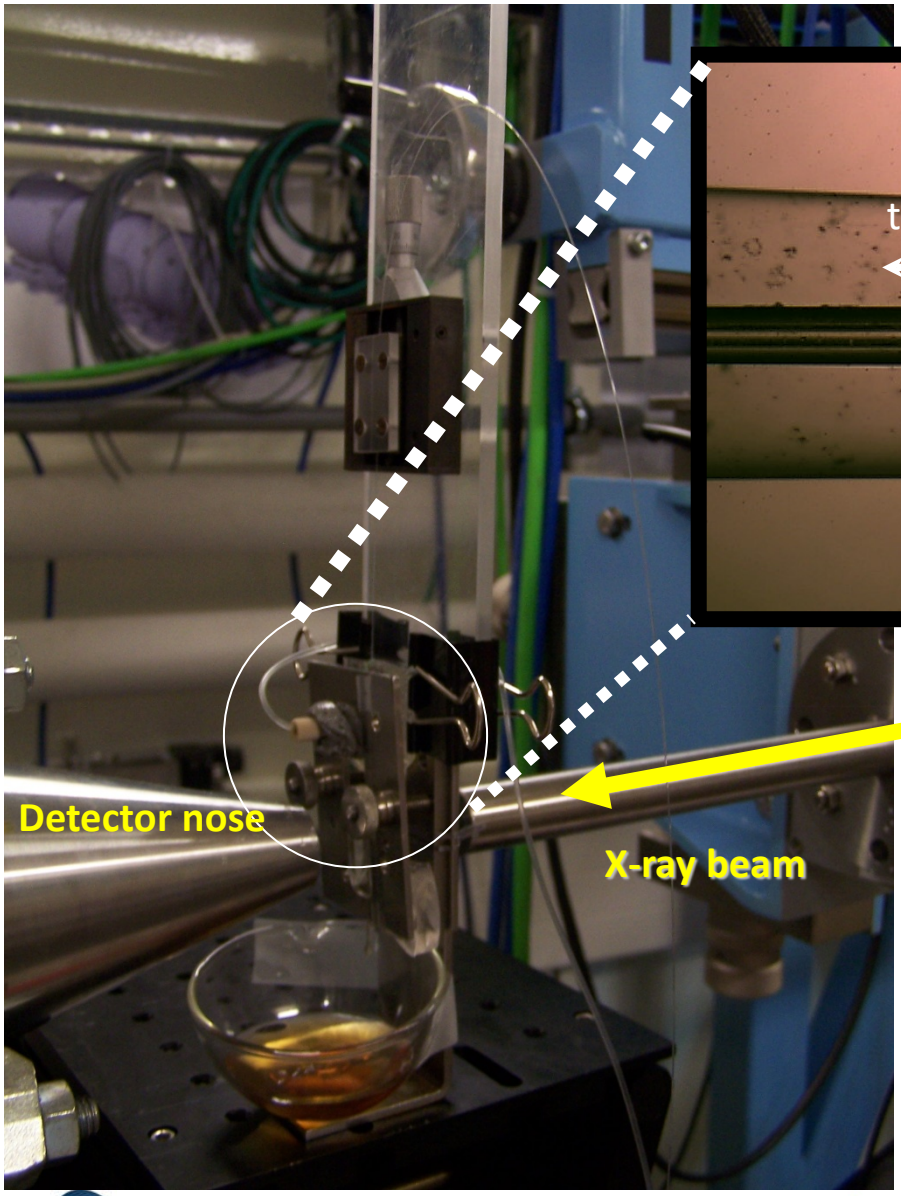
Microfluidics as a tool to get an insight of the mechanism of goethite formation

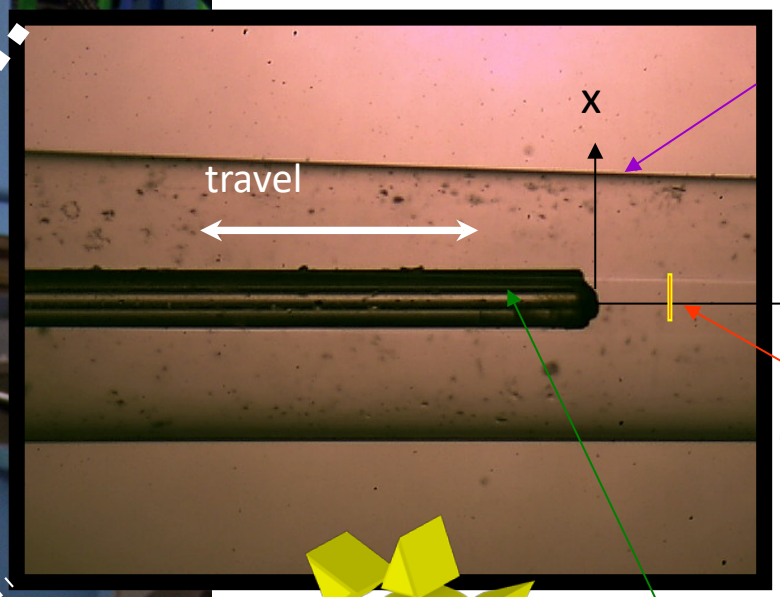


$\alpha = Q_{OH^-} / Q_{H^+}$



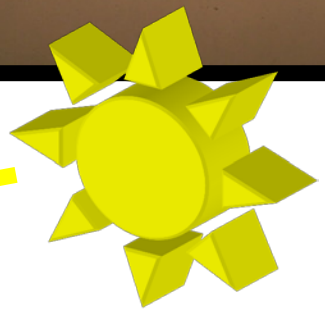
Detection of first seeds using SAXS in microfluidics





Lindemann glass capillary
∅ = 1,6 mm
(wall thickness = 10 µm)

beam 300 x 100 µm cross-section at fixed position

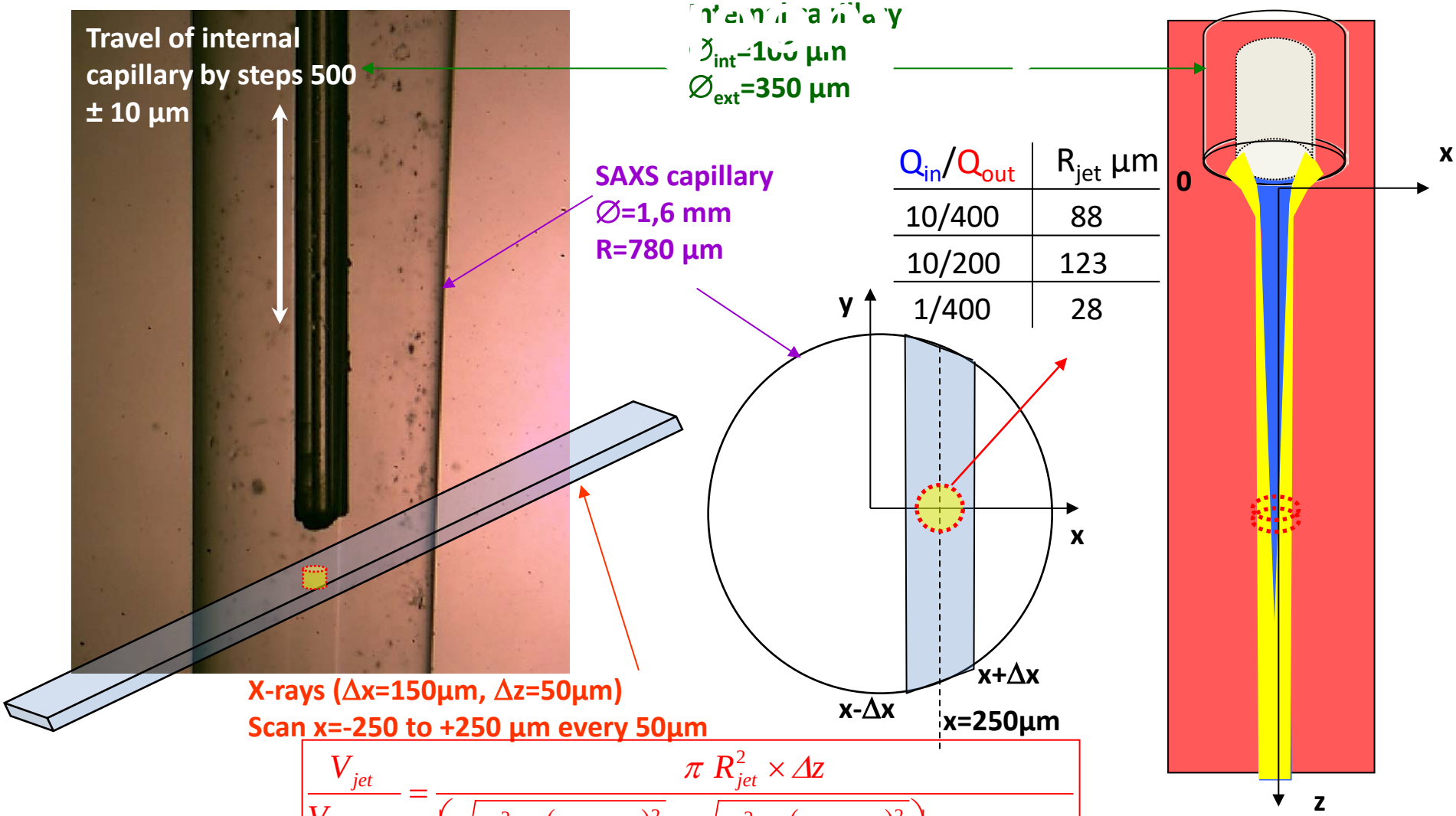


Internal capillary
$\varnothing_{int}$ = 100 µm
$\varnothing_{ext}$ = 350 µm

SAXS measurements on SWING line at SOLEIL synchrotron (July 2009)

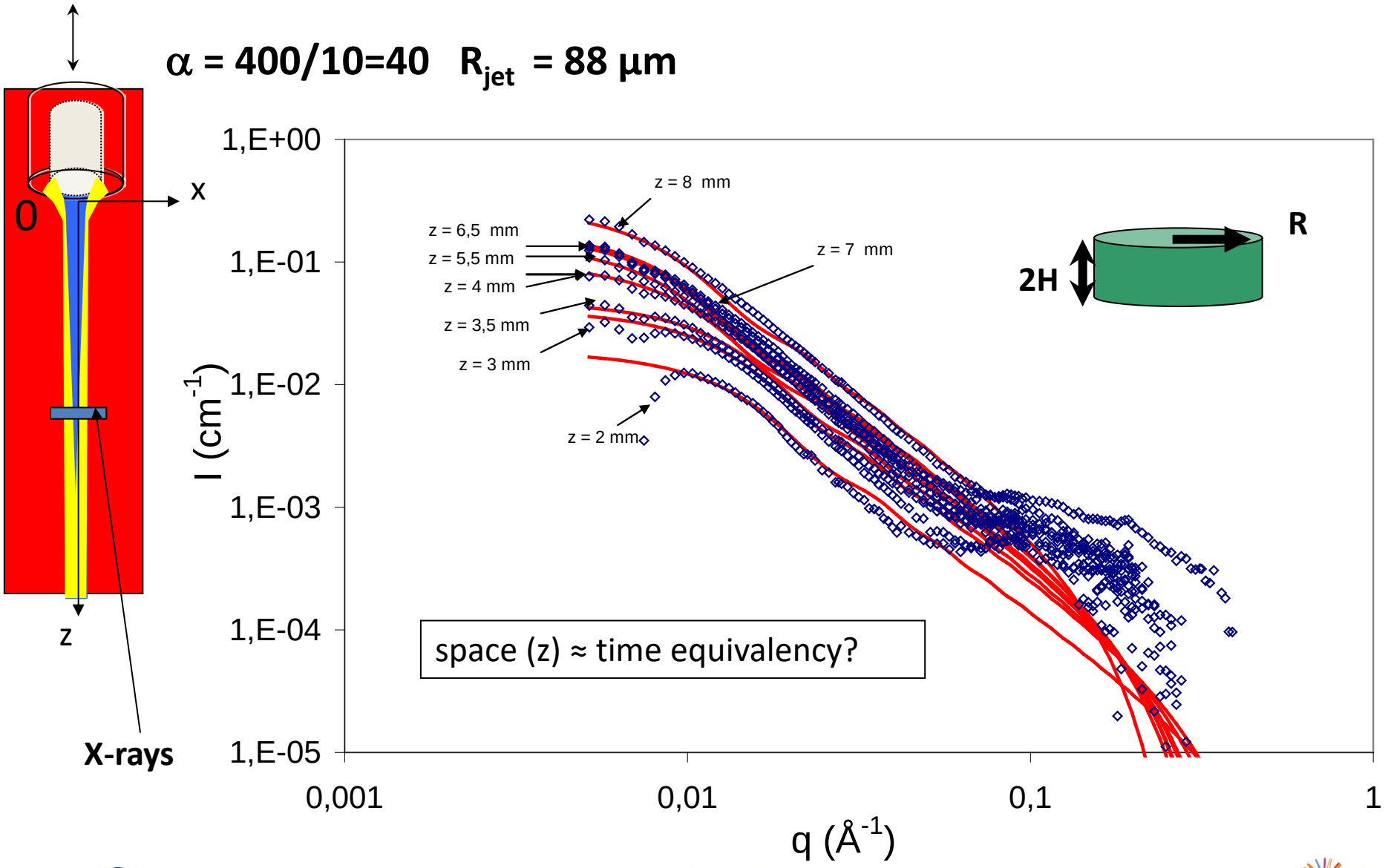
Abou Hassan, O. Sandre,
V. Dupuis, Olivier Spalla

Detection of first seeds using SAXS in microfluidics

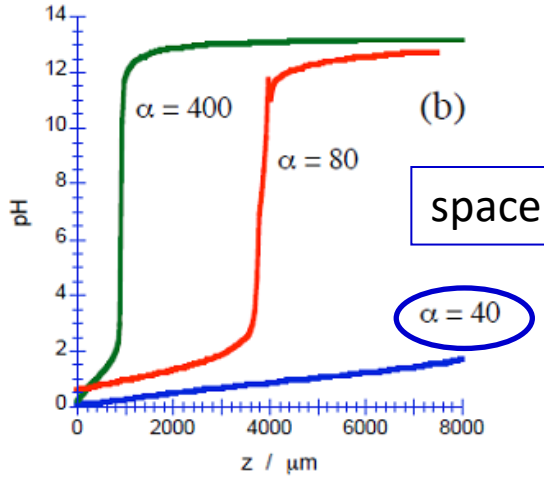


$$\frac{V_{jet}}{V_{diffusant}} = \frac{\pi R_{jet}^2 \times \Delta z}{\left(\sqrt{R^2-(x-\Delta x)^2}+\sqrt{R^2-(x+\Delta x)^2}\right)\times 2\Delta x \times \Delta z}$$

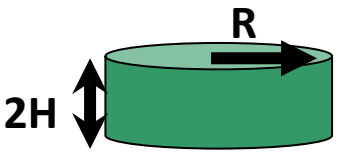
Preliminary SAXS results: intensity curves along z



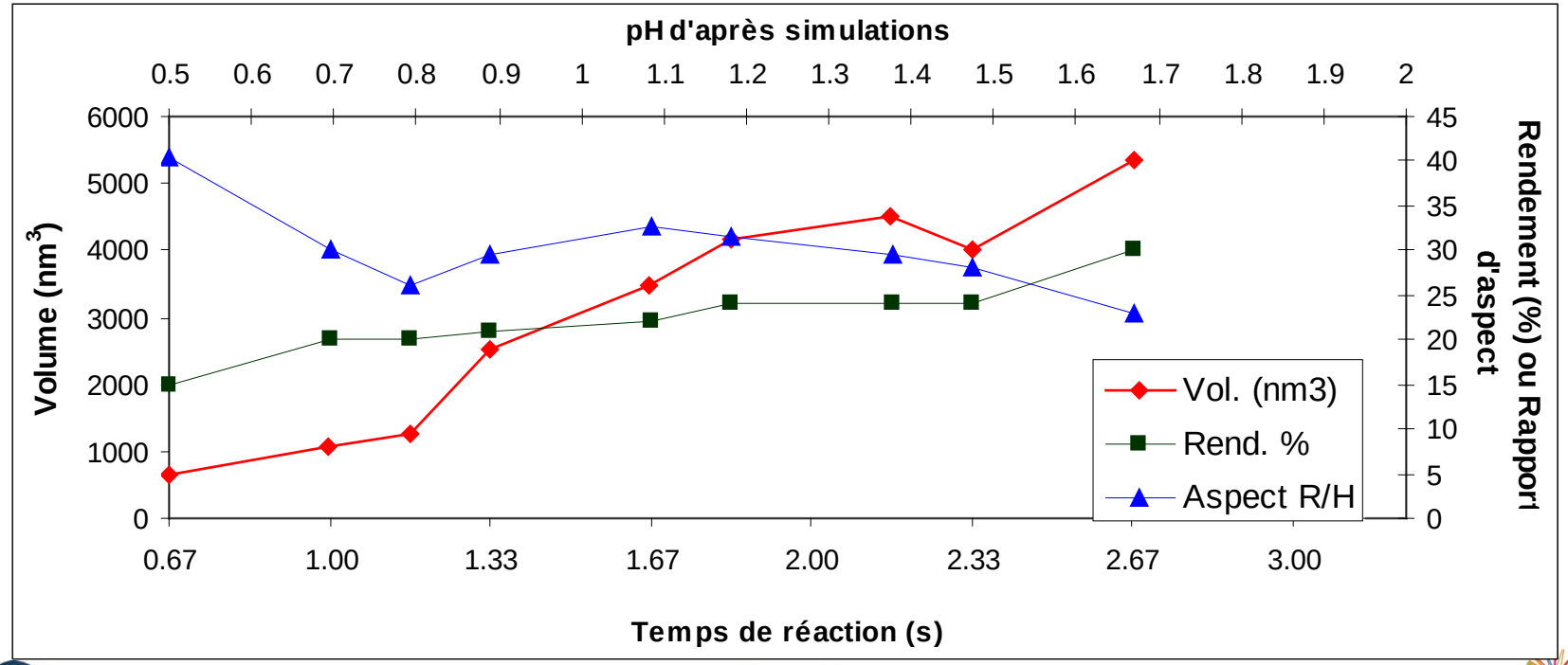
Preliminary SAXS results: fits as disk form factor



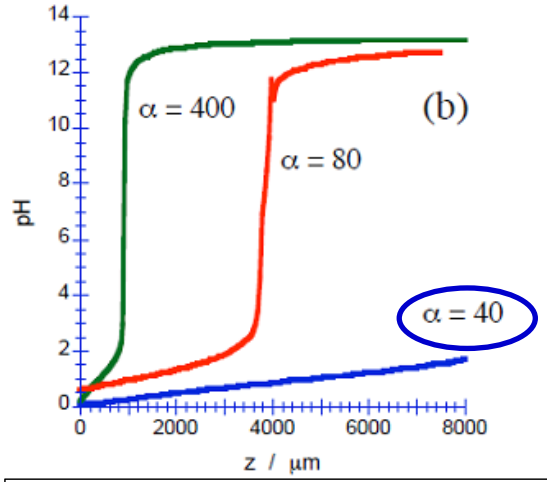
space (z) ≈ pH equivalency

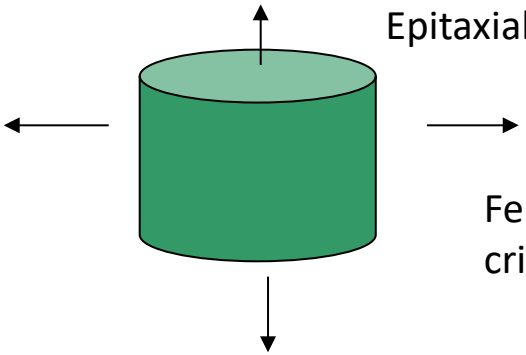


Anisotropy R/H ↘



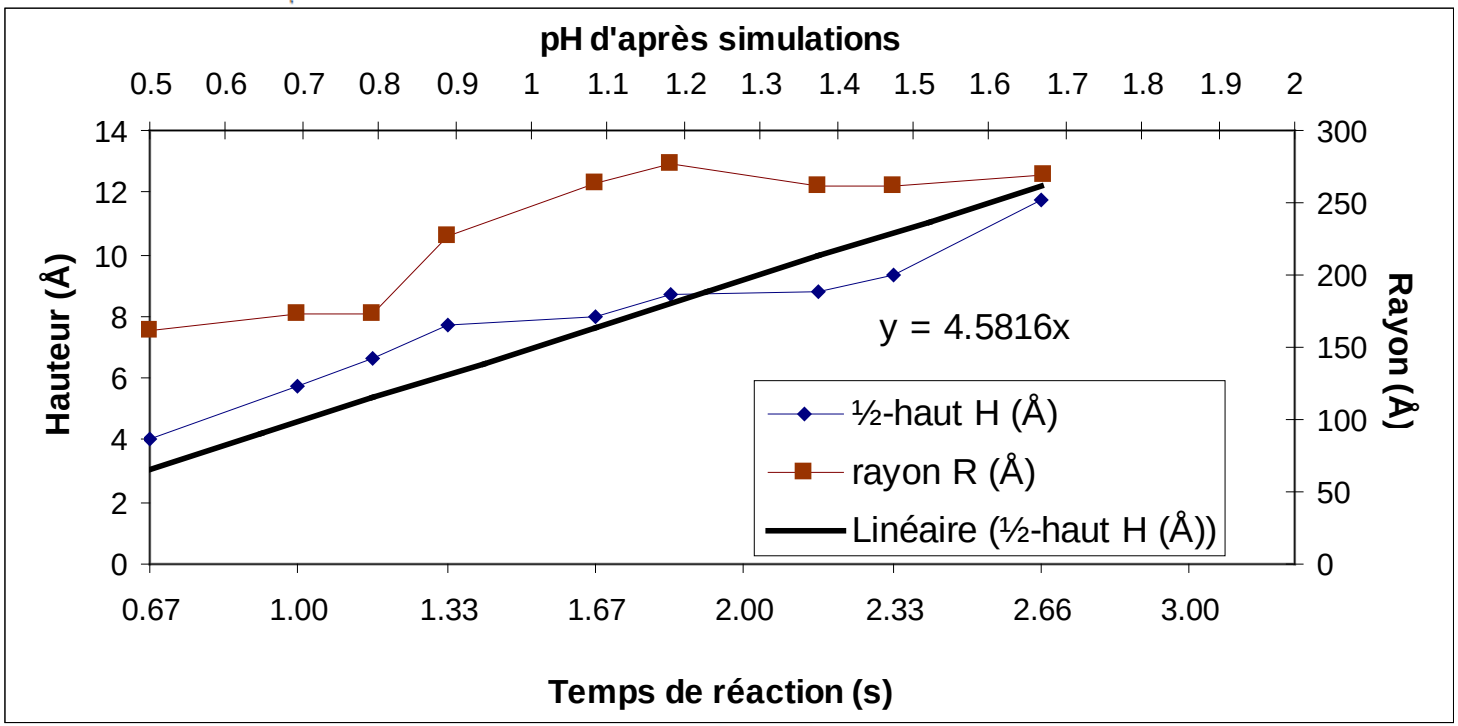
Preliminary SAXS results: fits as disk form factor





Epitaxial growth rate ≈ 9Å/s

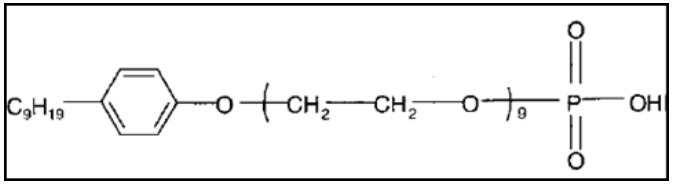
$Fe(OH)_3$ as fractal gel or cristallyne structure Bernalite



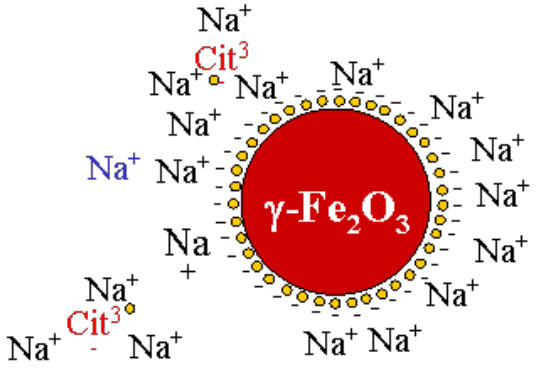
Coatings of iron oxide and oxo-hydroxide NPs for their dispersion in various media

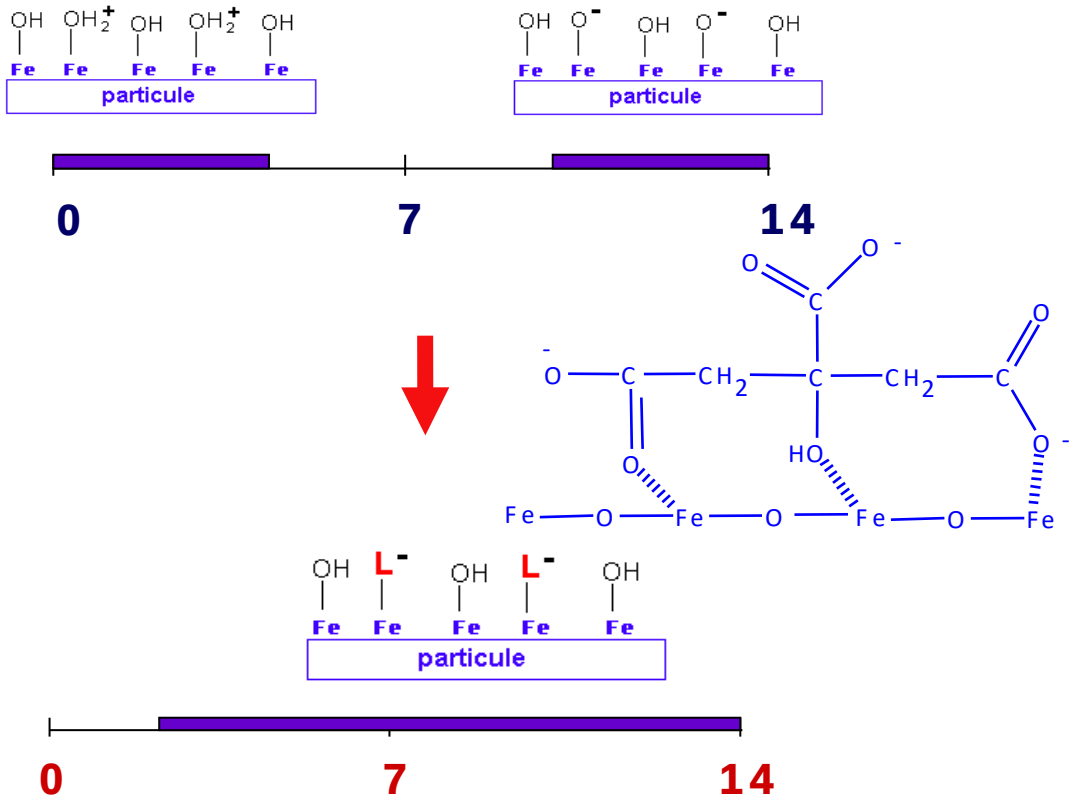
Different coatings to insure colloidal stability :

- surfactants (oleic acid, phosporic di-ester ,…) for organic solvents (alkanes, chlorinated,…)



- sodium citrate in aqueous neutral medium (pH=7.2) or sodium polyacrylate (2000 or 5000 g/moL)



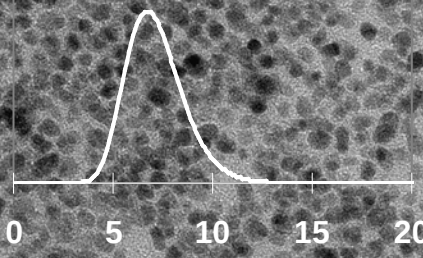


20 mol%/Fe addition precipitation-redispersion

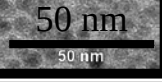
J. A. Galicia, O. Sandre, F. Cousin, D. Guemghar, C. Ménager, V. Cabuil, *J. Phys.-Cond. Mat.* **2003**. 15 S1379.

Ionic Ferrofluids: demixtion & size sorting

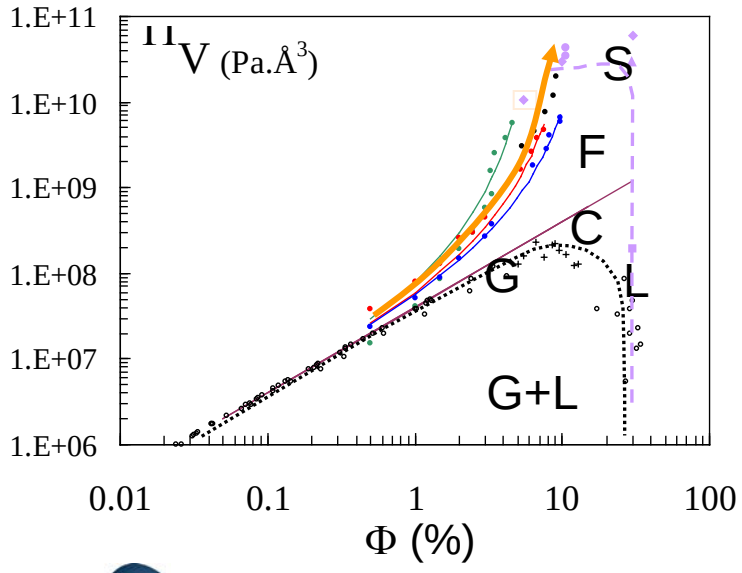
- Size Polydispersity: P(d, nm)



- Fractionated separations



R. Massart, E. Dubois, V. Cabuil, E. Hasmonay, J. Magn. Magn. Mater. 149 1 (1995)



835mL ferrofluide acide DE1,
Φ=2.5% d_0=7nm σ=0.39

HNO3 en excès

C1
250mL Φ=6.4%
d_0=8.6nm σ=0.35

S1

HNO_3

HNO_3

C1C

C1S
200mL Φ=3.5%
d_0=7.6nm σ=0.30

S1C
65mL Φ=4.2%
d_0=7.4nm σ=0.25

S1S-HNO3
85mL Φ=1.8%
d_0=6.6nm σ=0.21

1) Na_3Cit 2) dialyse

S1S-Na3Cit
20mL Φ=3.2%
d_0=6.6nm σ=0.21
$[Na_3Cit]$ =1.4x10^{-2} M

HNO_3

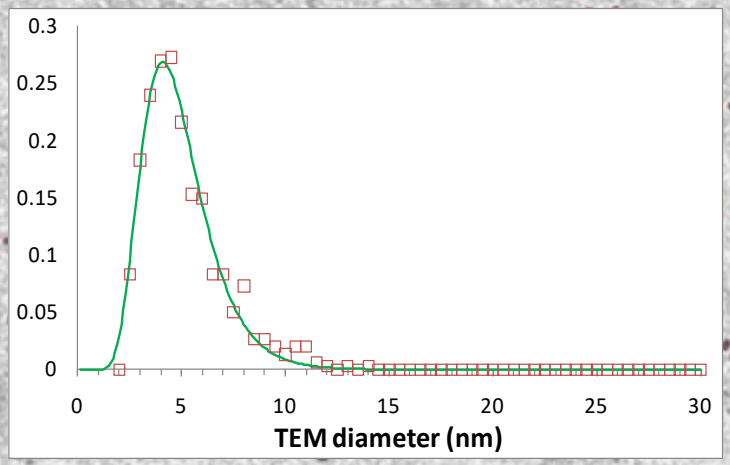
C2
140mL Φ=2.8%
d_0=8.5nm σ=0.29

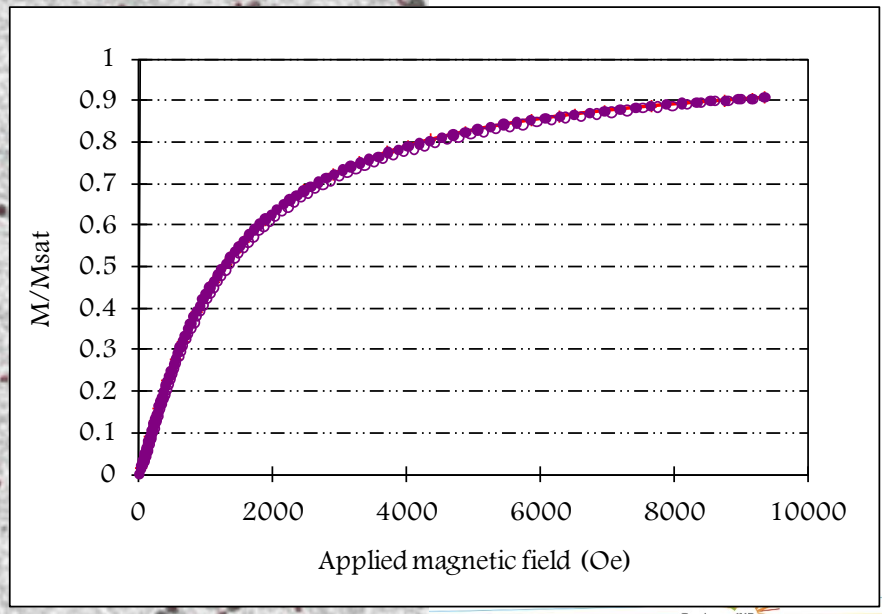
S2-HNO3
160mL Φ=1.2%
d_0=7.1nm σ=0.26

S2-CH_2Cl_2
25mL Φ=1.2%
d_0=6.8nm σ=0.24

Size-sorted "ionic ferrofluid" as elementary bricks

USPIO fraction	Given name in this work	D_H of bare MNPs in HNO_3 nm / PDI	Average diameters by TEM	Average diameters by VSM	Saturation magnetization emu/g A/m	r_2 (4.7T) $s^{-1}mM^{-1}_{Fe}$	SLP at f=800 kHz, H_0=11 kA/m W/g
S1S2S3	6-7 nm	11 / 0.12	d_n=4.9 nm, d_w=6.9 nm (N=600)	d_n=6.5 nm, d_w=7.5 nm	55±1 2.8×10^5	70	2±1





Size-sorted "ionic ferrofluid" as elementary bricks

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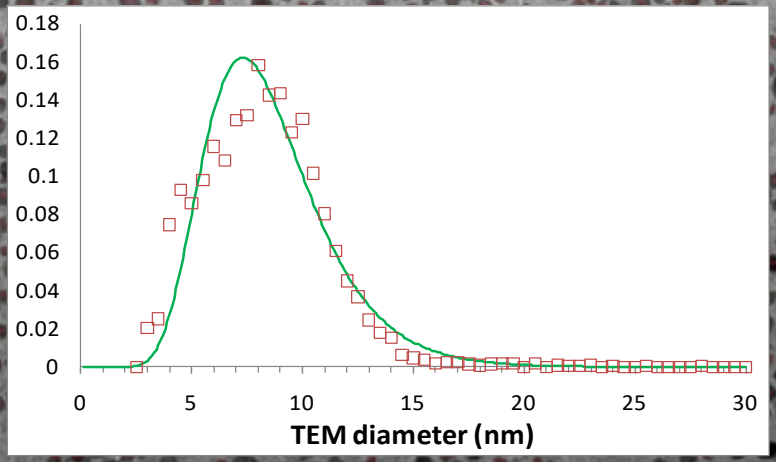
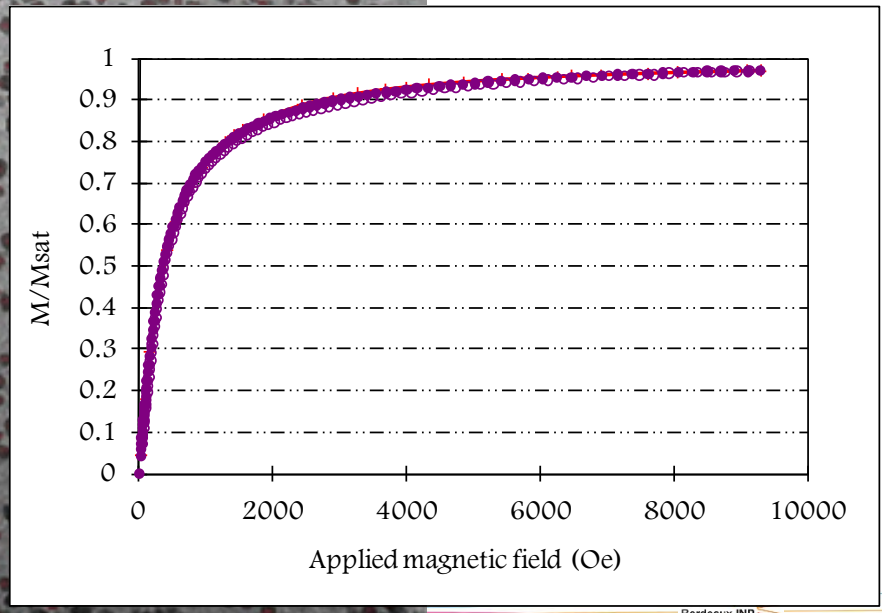
S1S2S3	6-7 nm	11 / 0.12	d_n=4.9 nm, d_w=6.9 nm (N=600)	d_n=6.5 nm, d_w=7.5 nm	55±1 2.8×10^5	70	2±1
S1C2	8-10 nm	23 / 0.16	d_n=8.5 nm, d_w=11.6 nm (N=3800)	d_n=8.2 nm, d_w=10.0 nm	60 3.0×10^5	104	9±1





Size-sorted "ionic ferrofluid" as elementary bricks

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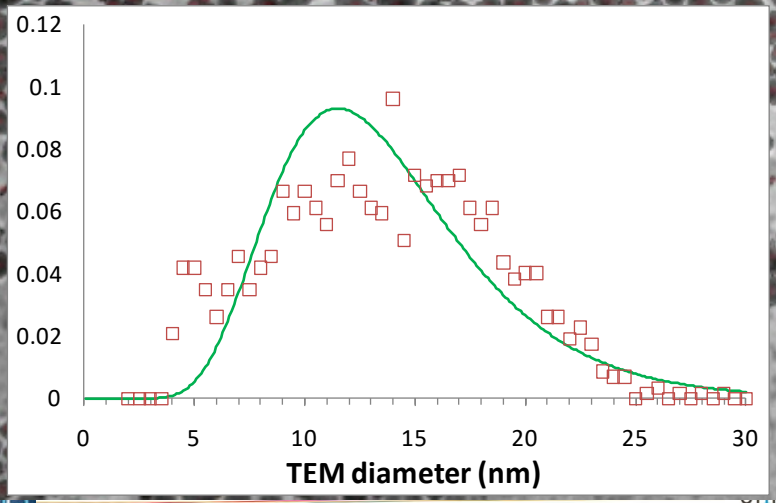
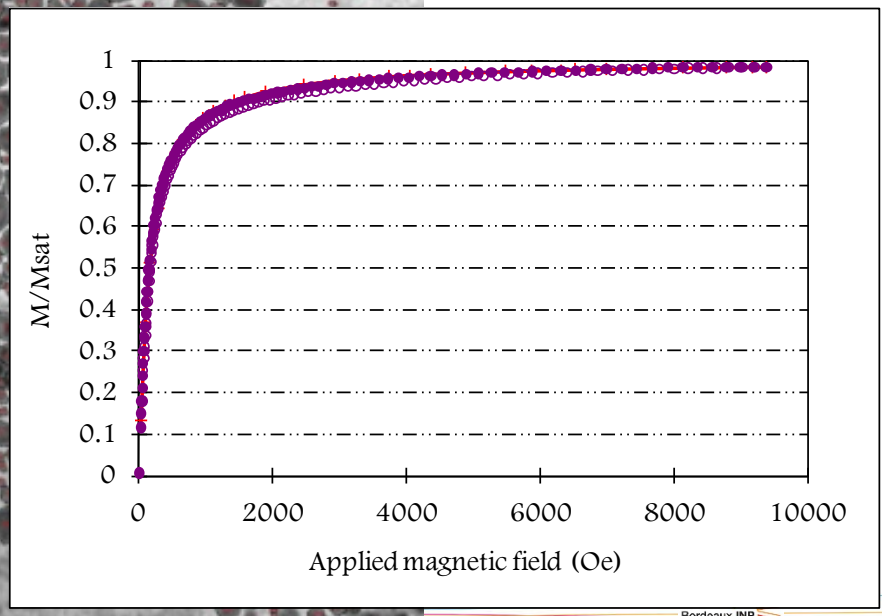
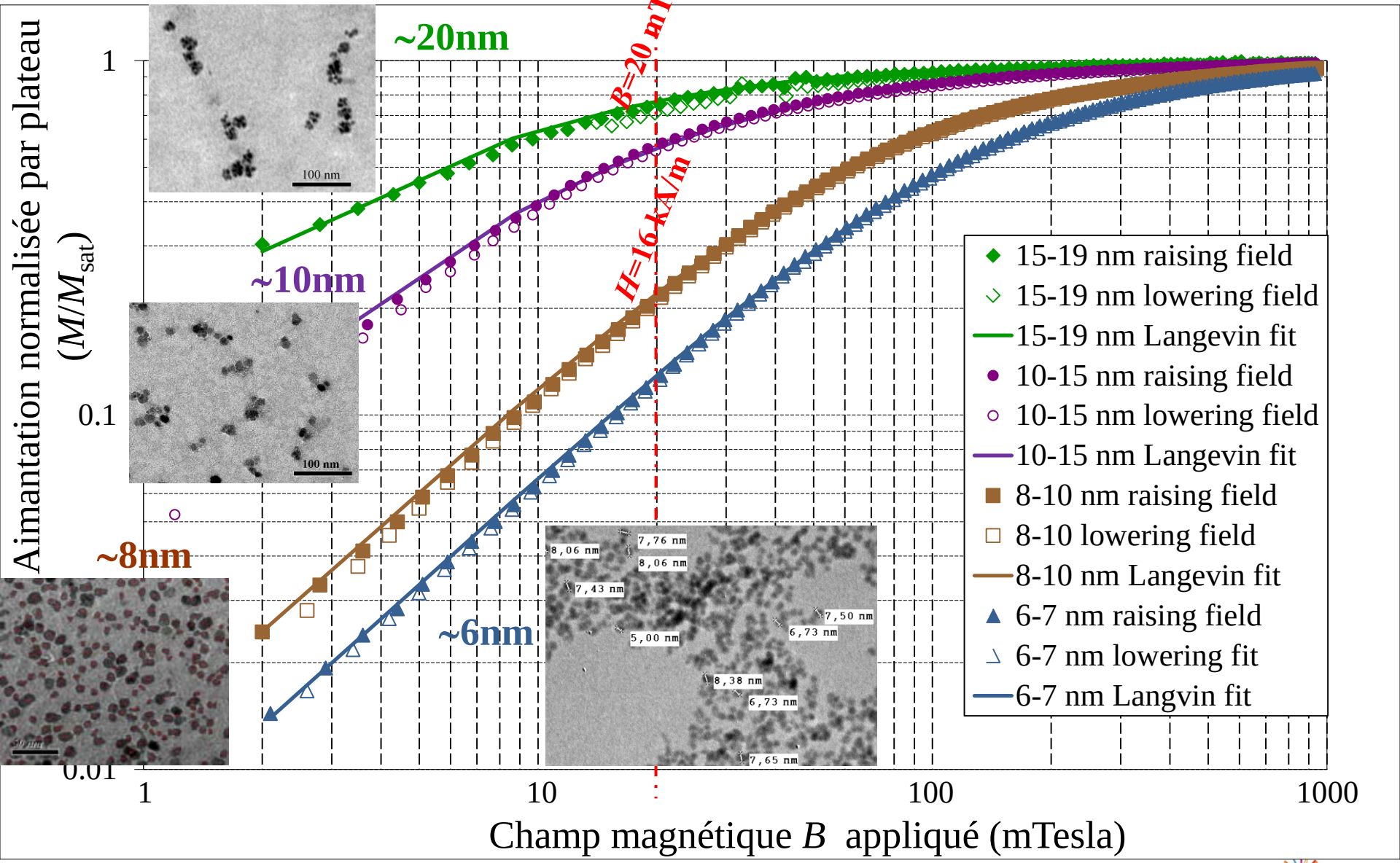
S1S2S3	6-7 nm	11 / 0.12	d_n=4.9 nm, d_w=6.9 nm (N=600)	d_n=6.5 nm, d_w=7.5 nm	55±1 2.8×10^5	70	2±1
S1C2	8-10 nm	23 / 0.16	d_n=8.5 nm, d_w=11.6 nm (N=3800)	d_n=8.2 nm, d_w=10.0 nm	60 3.0×10^5	104	9±1
C1C2S3S4	10-15 nm	38 / 0.26	d_n=13.8 nm, d_w=20 nm (N=1140)	d_n=10.4 nm, d_w=14.8 nm	70±1 3.5×10^5	293	80±5





Magnetization curves along the size-grading process

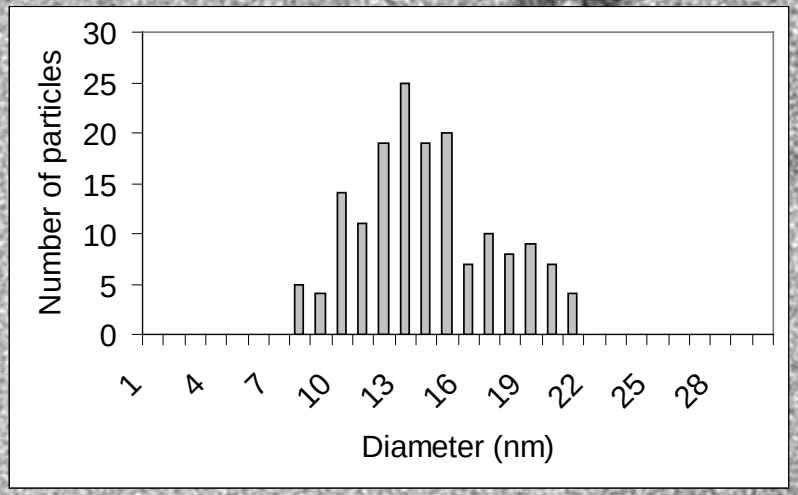


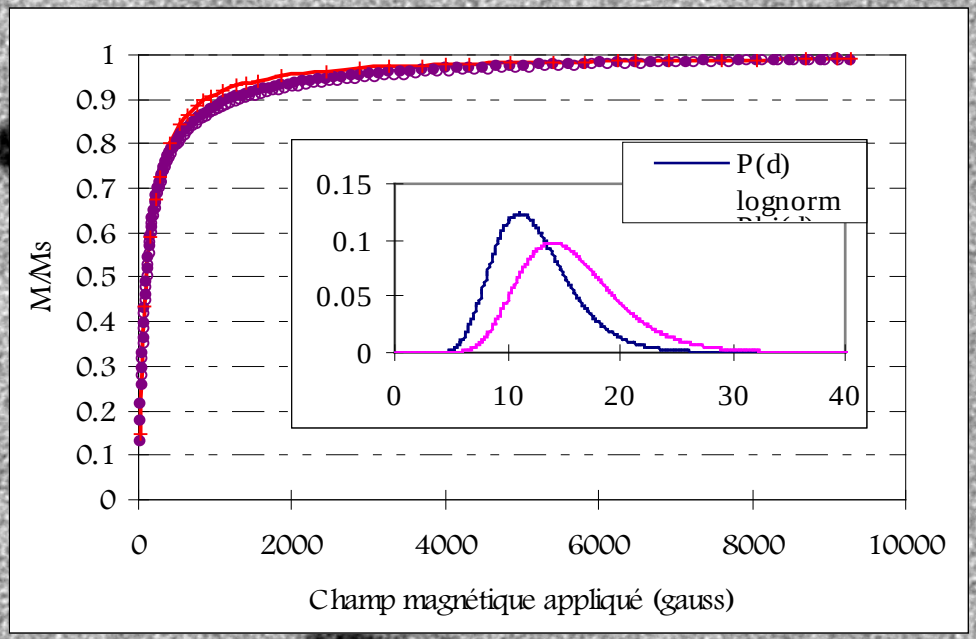
Larger nanoparticles for larger physical effects?

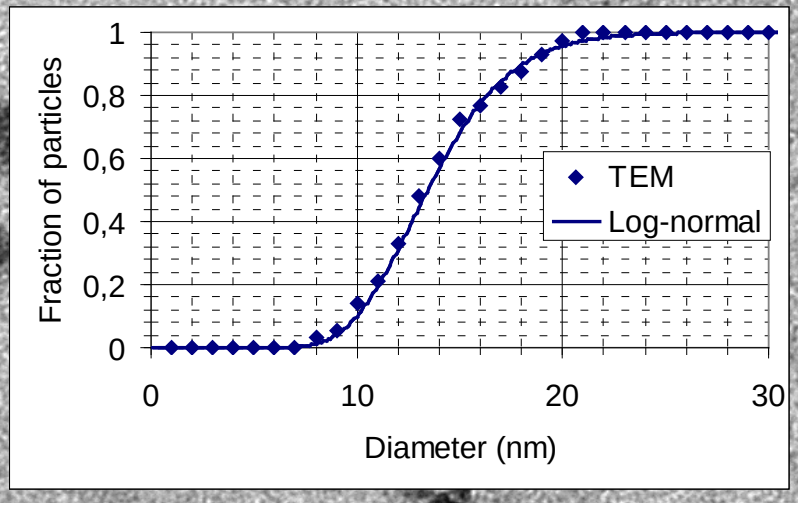
Obtained by multiple phase separation (C1C2C3C4)

$\langle d \rangle_{TEM}$ = 13.9 nm

$\langle d \rangle_{VSM}$ = 11.8 nm







$d_w = \langle d^4 \rangle / \langle d^3 \rangle_{VSM \text{ or } TEM} \approx 16$ nm

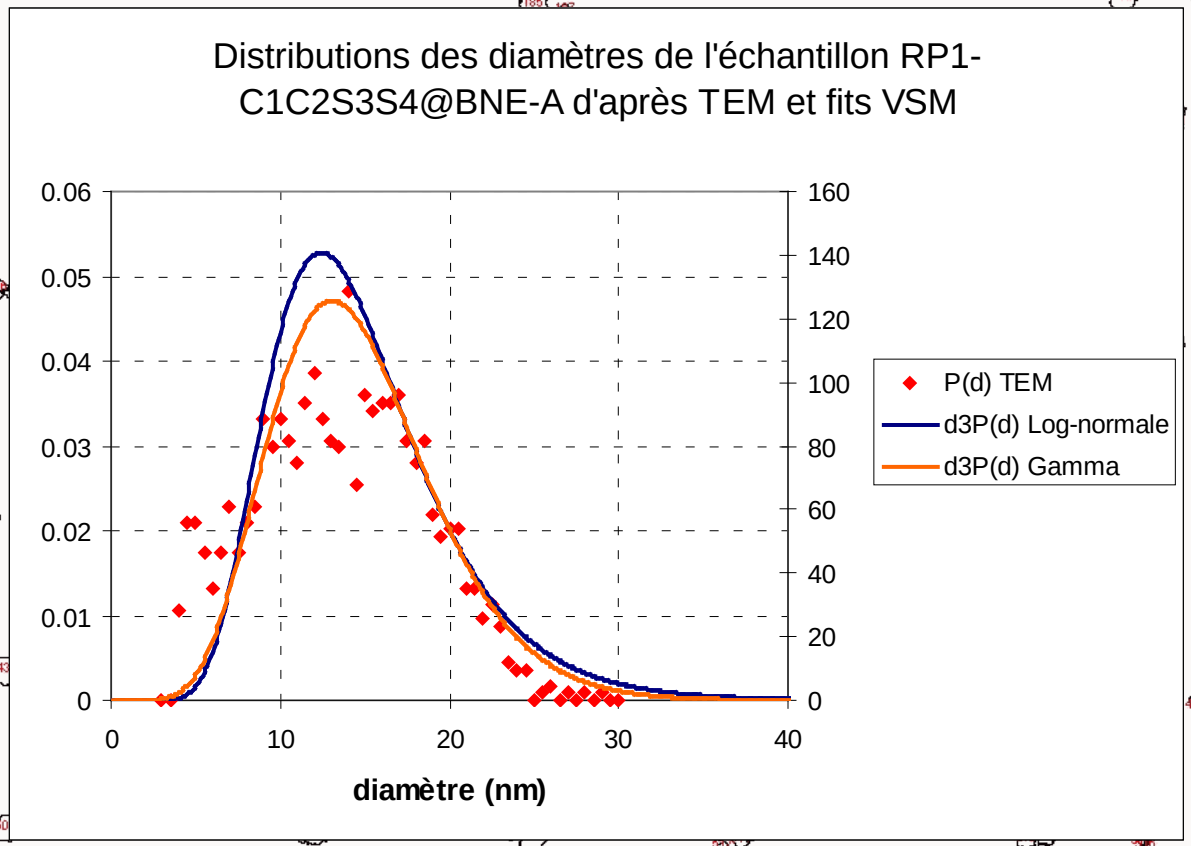
100 nm

$\langle d^n \rangle = d_0^n \exp(n\sigma^2/2) \rightarrow d_w = \langle d^4 \rangle / \langle d^3 \rangle = d_0 \exp(3.5\sigma^2)$

Size-sorted fraction: C1C2S3S4

$\langle d \rangle_{TEM}$ = 13.3 nm

$d_w = \langle d^4 \rangle / \langle d^3 \rangle_{VSM}$ = 14.8 nm



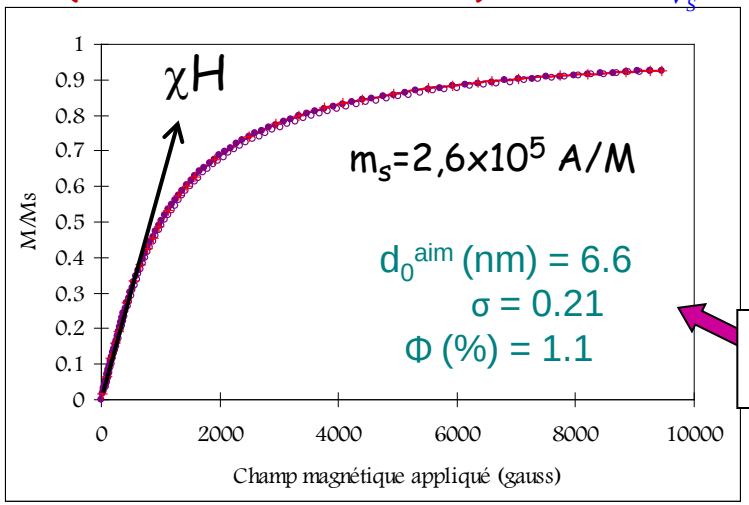
Magnetic/magneto-optical properties of size-sorted MNPs

Vibrating sample magnetometry

$$M = \frac{1}{V_S}\int M_S \frac{\pi}{6} D^3 L\left(\frac{\mu_0 M_S \pi D^3 H}{6kT}\right) f_{LN}(D)\,dD$$

Smaller NPs (S1S fraction d=6nm)

a.

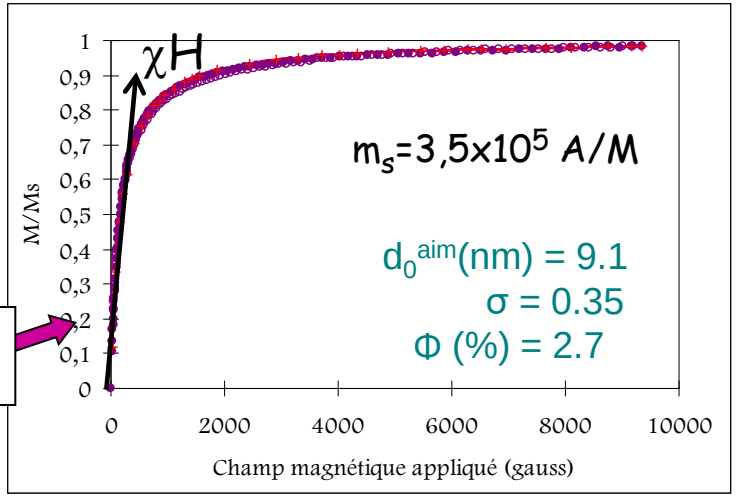


$M_{sat} = m_s \Phi$

1st order Langevin's curve

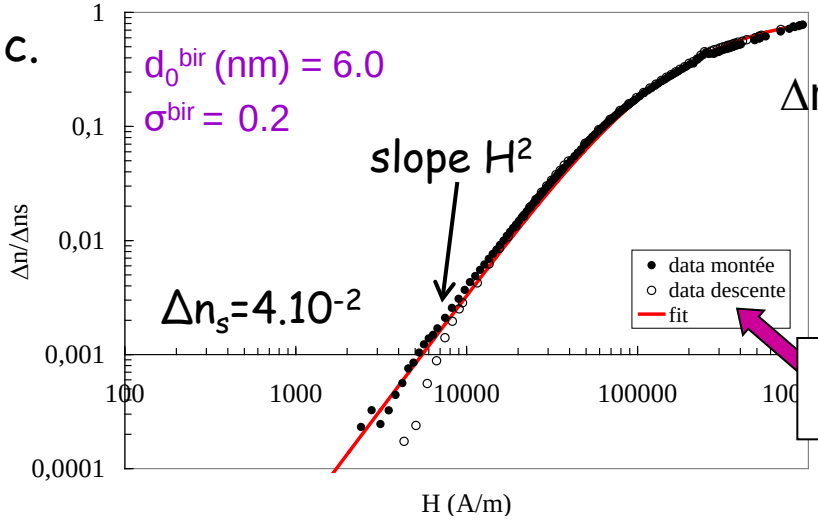
Larger NPs (C1C fraction d=9nm)

b.



Static Magneto-birefringence

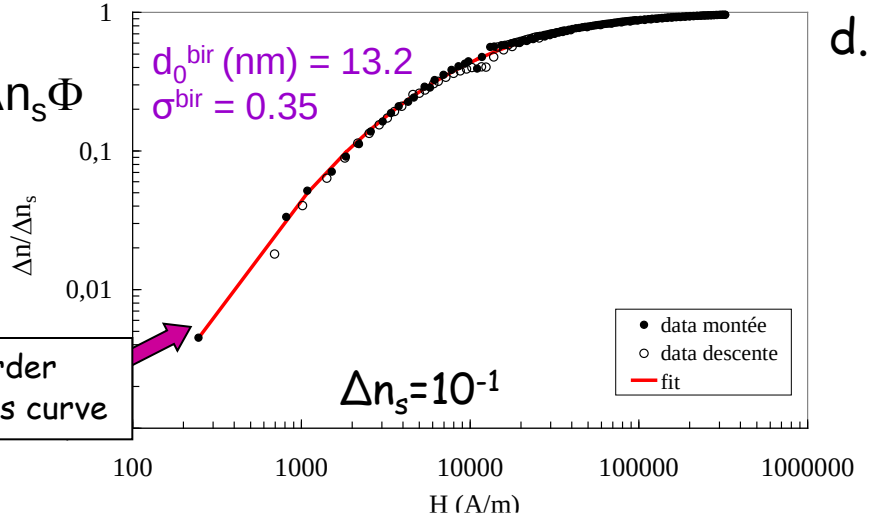
c.



$\Delta n_{sat} = \Delta n_s \Phi$

2nd order Langevin's curve

d.



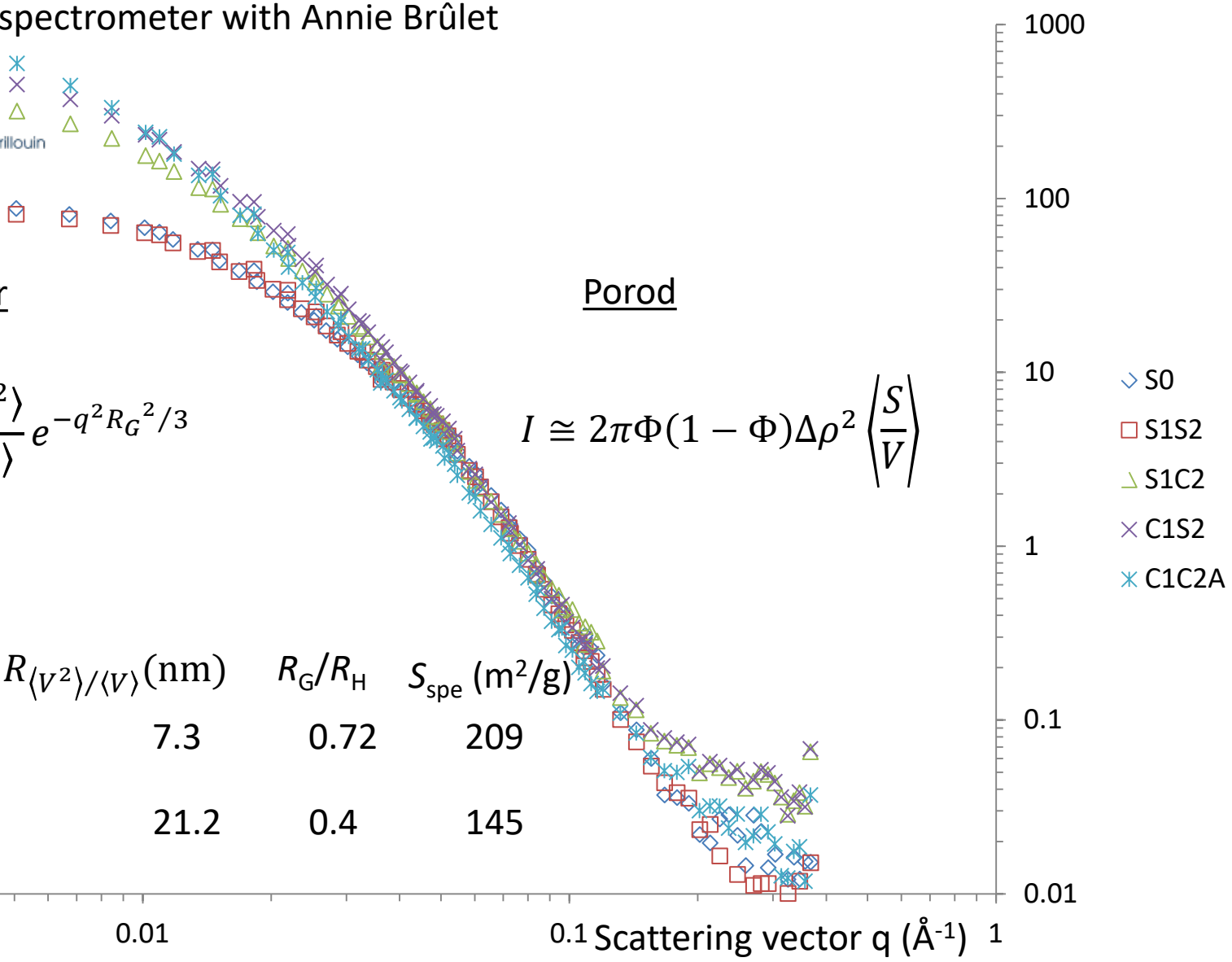
→ more monodisperse and superparamagnetic

→ larger, ferrimagnetic and more anisotropic

Particle form factors by small angle neutron scattering

SANS Intensity normalized by volume fraction Φ (cm^{-1})

PACE spectrometer with Annie Brûlet



Guinier

$$I \cong \Phi \Delta\rho^2 \frac{\langle V^2 \rangle}{\langle V \rangle} e^{-q^2 {R_G}^2/3}$$

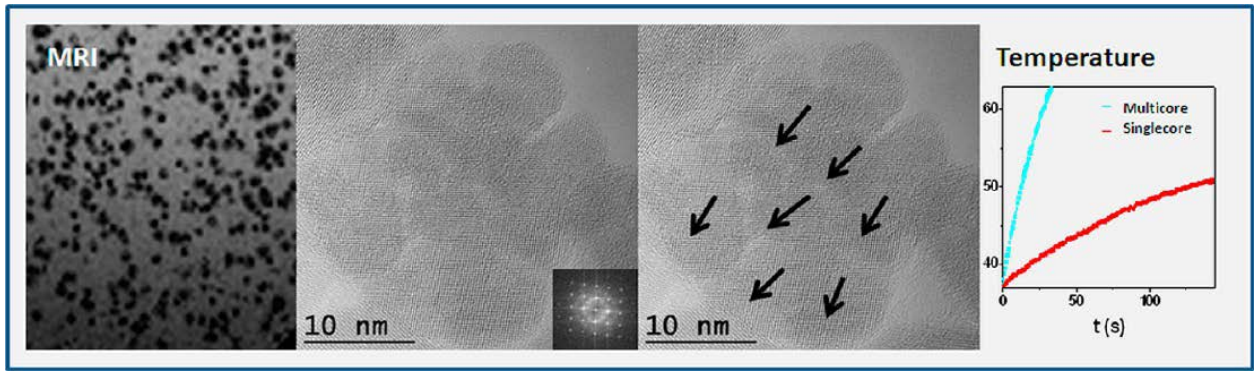
Porod

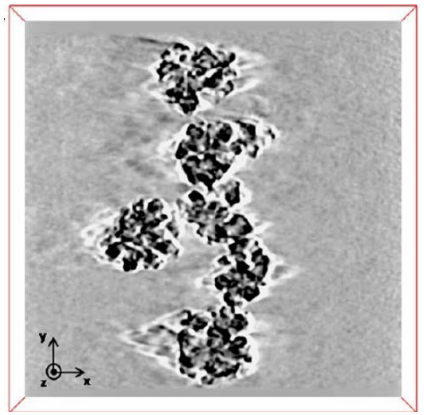
$$I \cong 2\pi\Phi(1-\Phi)\Delta\rho^2 \left\langle \frac{S}{V} \right\rangle$$

	R_G (nm)	$R_{\langle V^2 \rangle / \langle V \rangle}$ (nm)	R_G/R_H	S_{spe} (m^2/g)
S_0:	9.2	7.3	0.72	209
C_1C_2A:	16.7	21.2	0.4	145

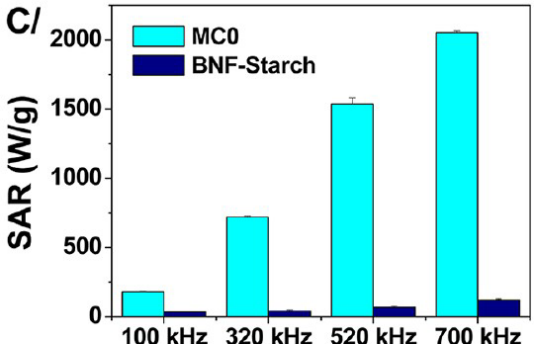
Synthesis & properties of multi-core "nanoflowers"

L. Lartigue, P. Hugounenq, D. Alloyeau, S. P. Clarke, M. Lévy, J-C. Bacri, R. Bazzi, D. F. Brougham, C. Wilhelm, F. Gazeau, ACS Nano 6, 10935–10949 (2012)

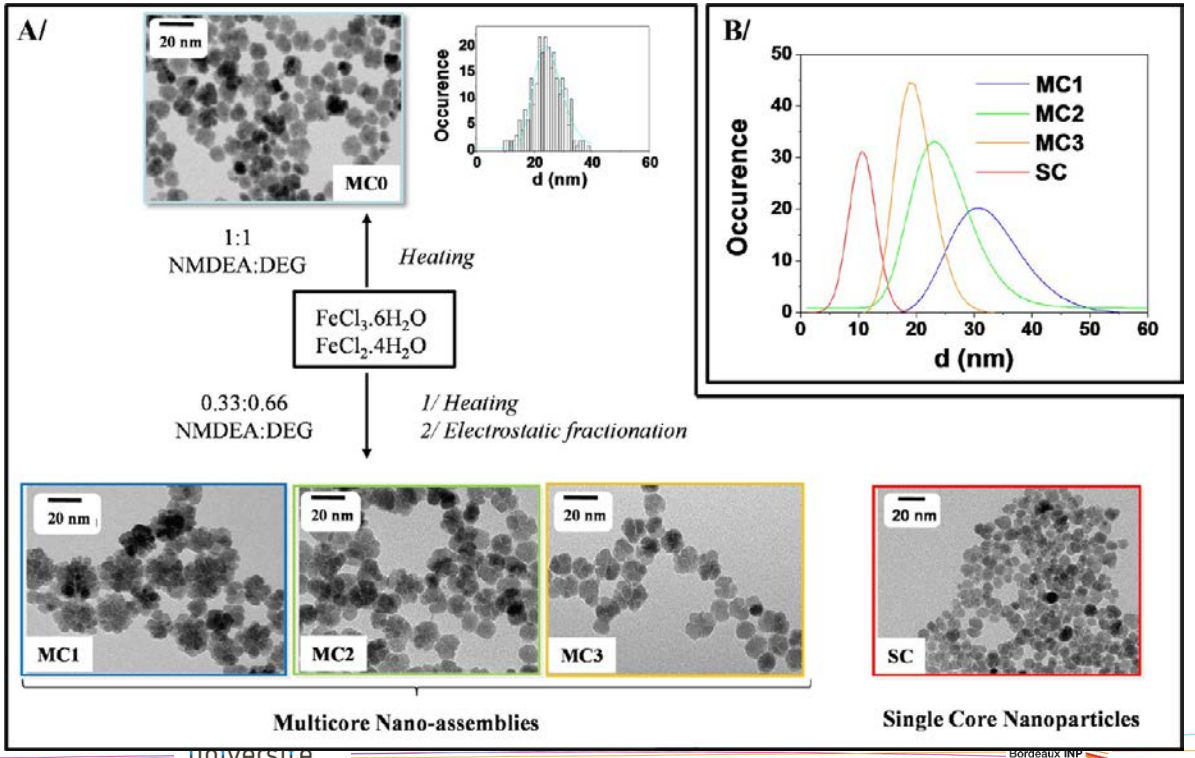




→ superior heating properties (here values at H_{max}=29 kA/m)

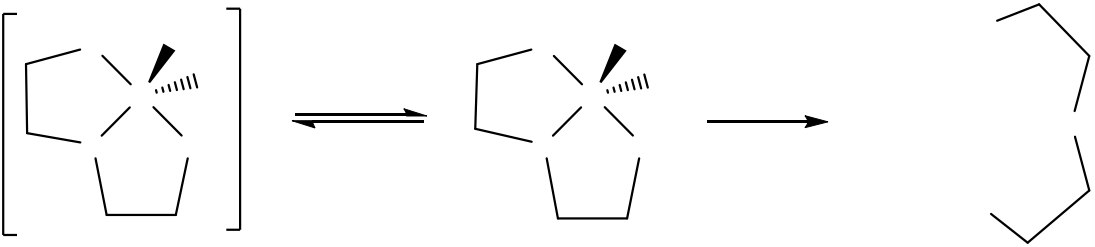


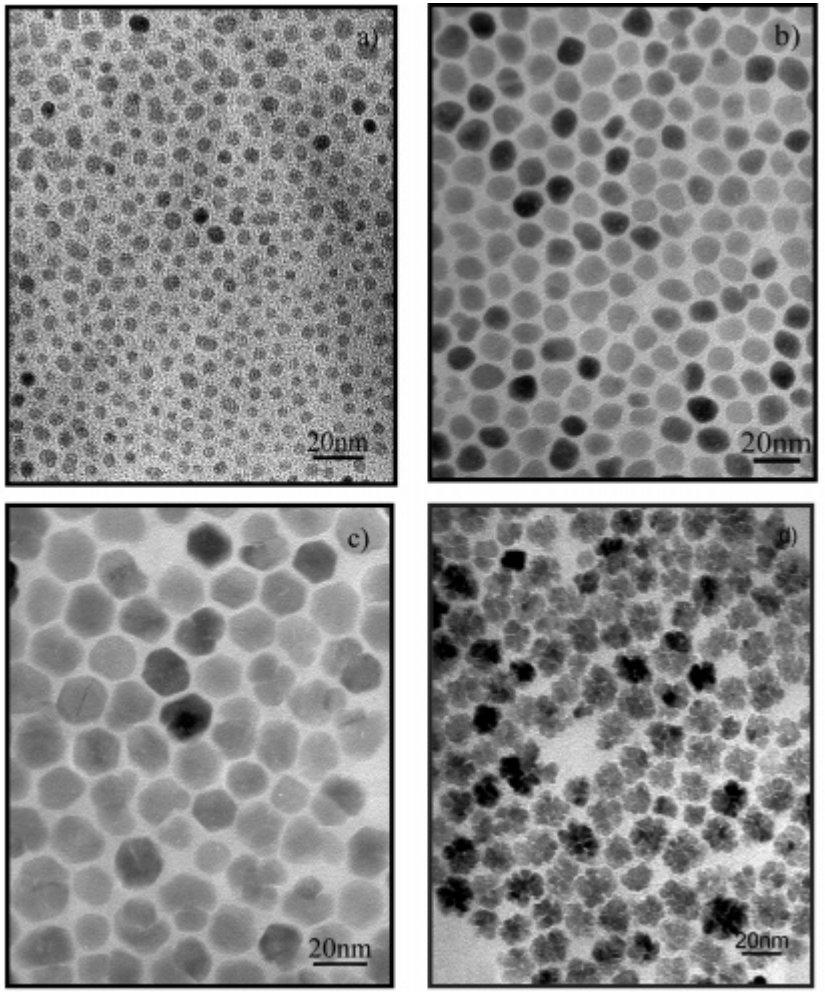
→ also high transverse relaxivity: r_2=365 $s^{-1}mM_{Fe}^{-1}$ at 9.25MHz (0.22T/37°C)



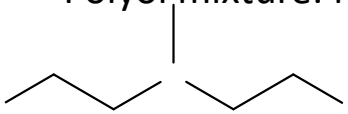
Nanoflower synthesis: the New Orleans method

D. Caruntu, G. Caruntu, Y. Chen, C. J. O'Connor, G. Goloverda, V. L. Kolesnichenko, *Chem. Mater.* **2004,** *16,* 5527-5534

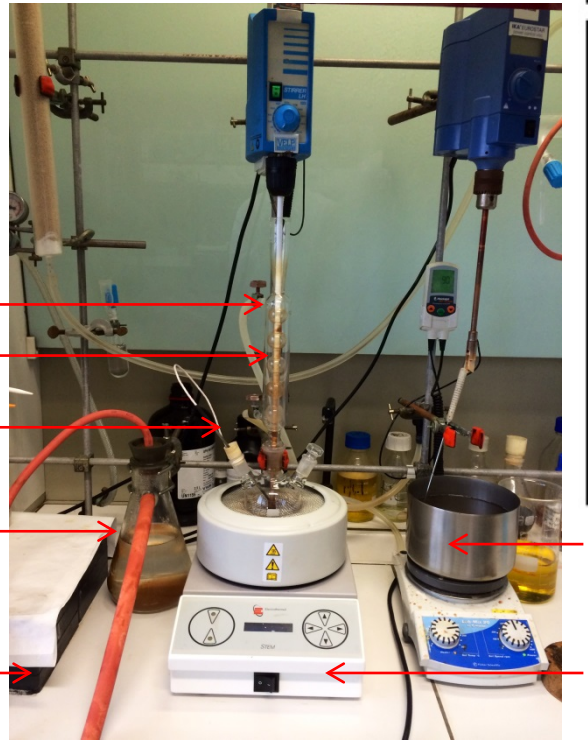




Polyol mixture: N-methyl diethanolamine / DEG (1:1)

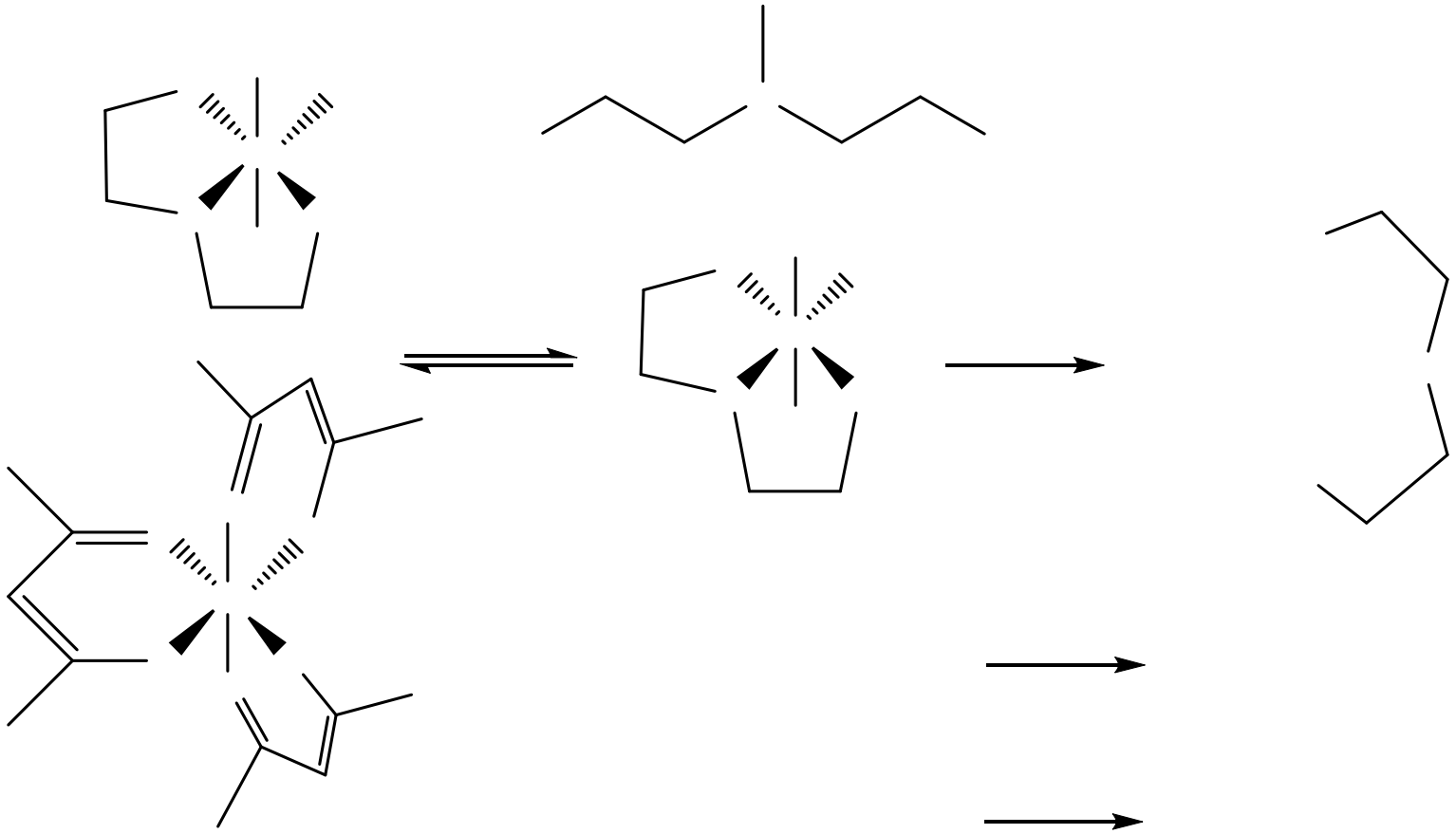


- 2 mmol $FeCl_2$
- 4 mmol $FeCl_3$
- 16 mmol NaOH
- 40 g DEG
- 40 g NMEDA
- 220°C 5h



- Precursor
- Polyol composition
- Temp/Duration
- Water content

Forced hydrolysis mechanistic pathway (Caruntu)



1) D. Caruntu, G. Caruntu, Y. Chen, C. J. O'Connor, G. Goloverda, V. L. Kolesnichenko, *Chem. Mater.* **2004,** *16,* 5527-5534;
2) S. Sun and H. Zeng et al, *J. A. C. S.*, **2002**, *124*, 8204-8205 and **2004**, *126*, 273-279
3) F.A. Tourinho, R. Franck, R. Massart, *J. Materials Science* **1990**, *25*, 3249-3254

Large library of sample batches

Batch name	Nomenclature
15ff	$DN1000_{HU}$-5h
17ff	$D5000_{HI}$-20m
25ff	$DN500_{HU}$-4h
30ff	$DN1000_{HU}$-5h
31ff	$DN500_{HU}$-1h
32ff	$DN500_{HU}$-5h
34ff	$DN100_{HU}$-5h*
35ff	$DN100_{HU}$-5h
36ff	$DN100_{HU}$-5h

Batch name	Nomenclature
28AA	$DN100_{HU}$-220-5h-Cl
29AA	$DN200_{HU}$-220-5h-Cl
02MA	$DN300_{HU}$-220-5h-Cl
09MA	$DN400_{HU}$-220-5h-Cl
10MA	$DN500_{HU}$-220-5h-Cl
11MA	$DN50_{HU}$-220-5h-Cl
27MA	DN0-220-5h-Acac
12MA	DN100-220-5h-Acac
17MA	DN200-220-5h-Acac
18MA	DN300-220-5h-Acac
19MA	DN400-220-5h-Acac
20MA	DN500-220-5h-Acac
15JA	DD100-250-5h-Cl
10JA	TD100-250-5h-Cl

Vary µL water in 120 g polyol mixture:

EG: Ethylene Glycol
DEG: Diethylene Glycol
TEG: Triethylene Glycol
DEA: Diethanolamine
NMDEA: N-methyldiethanolamine
TEA: Triethanolamine
DIA: N-ethyl Diisopropylamine

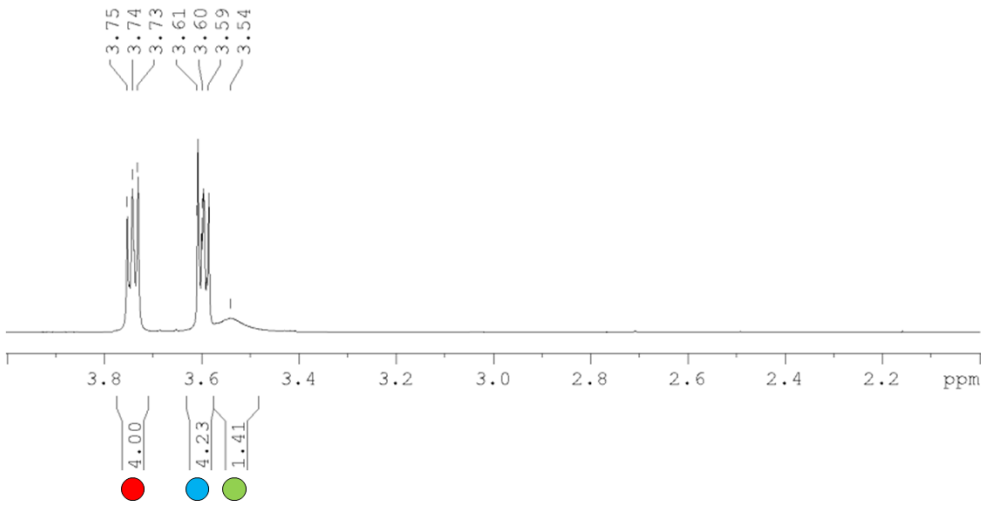
D=pure DEG
DN=DEG/NMDEA (1:1)
DD=DEG/DEA (1:1)
TD=TEG/DEA (1:1)

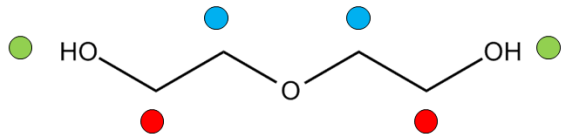
HU=heating up
HI=hot injection
* no stirring

Cl=2 mmol $FeCl_2$, 4 mmol$FeCl_3$,16 mmol NaOH
Acac=6 mmol $Fe(acac)_3$,16 mmol NaOH

Study of polyol route: fate of solvent molecules

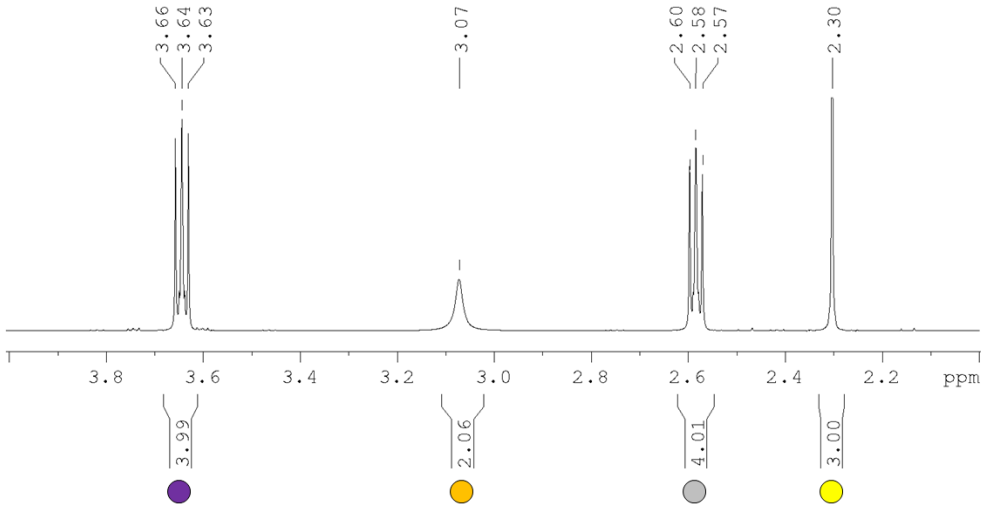
a)

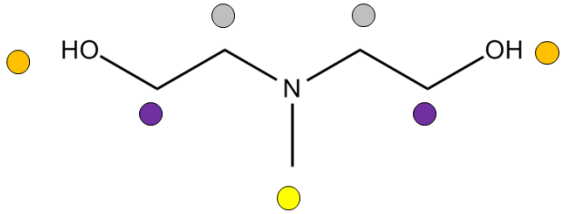




Diethylene glycol (DEG)

b)

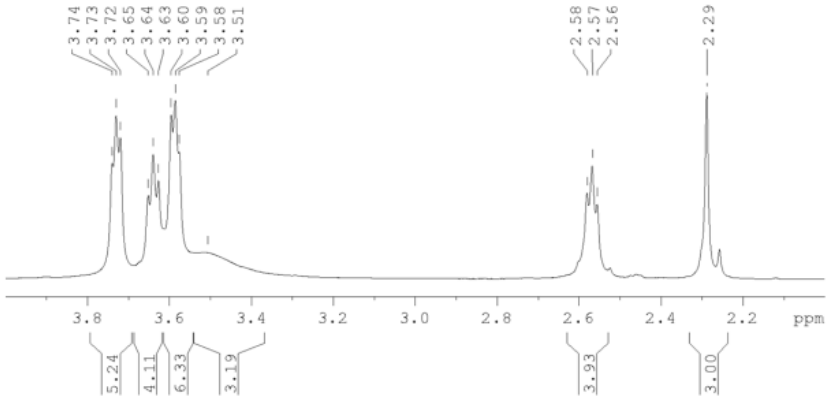




N-methyldiethanolamine (NMDEA)

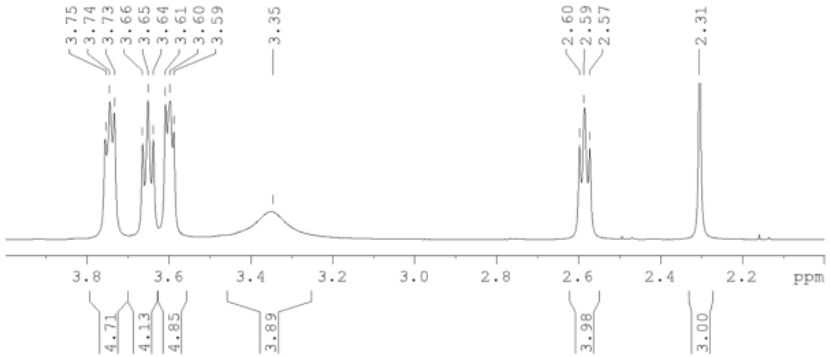
Study of polyol route: fate of solvent molecules

c)



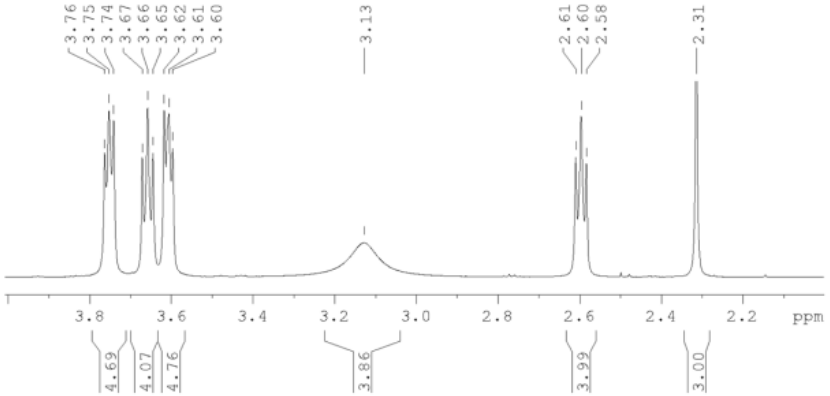
DEG, NMDEA, NaOH, $FeCl_2$, $FeCl_3$

d)



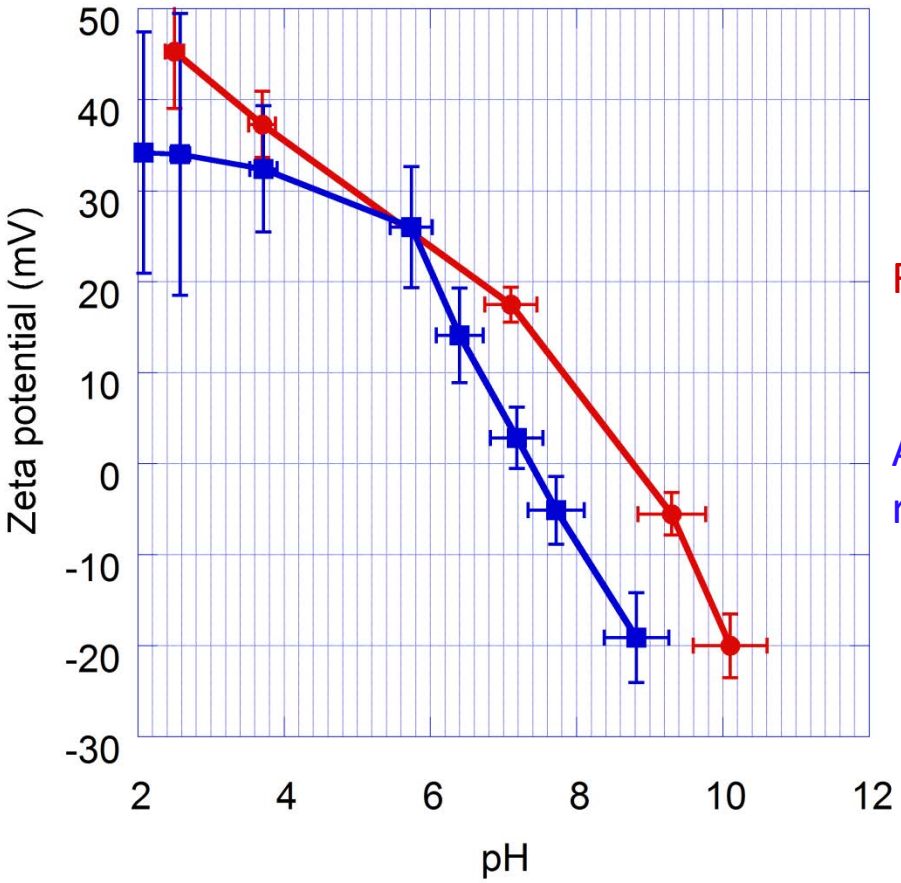
DEG, NMDEA, NaOH, $FeCl_2$, $FeCl_3$, H_2O
Before reaction

e)



DEG, NMDEA, NaOH, $FeCl_2$, $FeCl_3$, H_2O
After reaction

Study of polyol route: fate of solvent molecules



Right after synthesis

→ PZC = pKa of NMDEA

After washings (precipitation-redispersion cycles at alkaline pH)

- Can be oxidized in boiling $Fe(NO_3)_3$: $Fe_3O_4 \rightarrow \gamma\text{–}Fe_2O_3$
- Washed and stabilized in water at pH~7 with citrate ligand or PEG-phosphonate

Hydrodynamic size by DLS

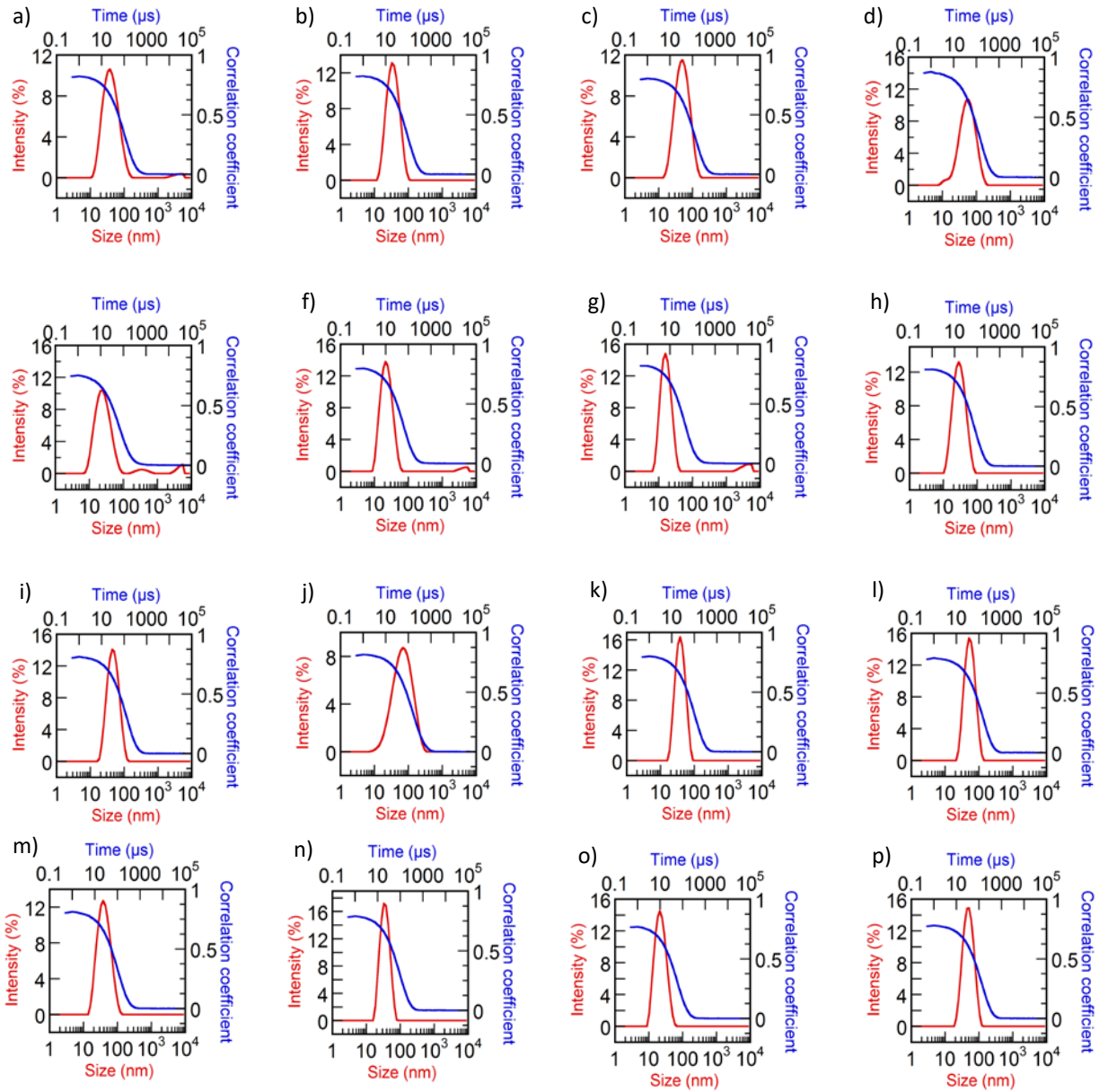
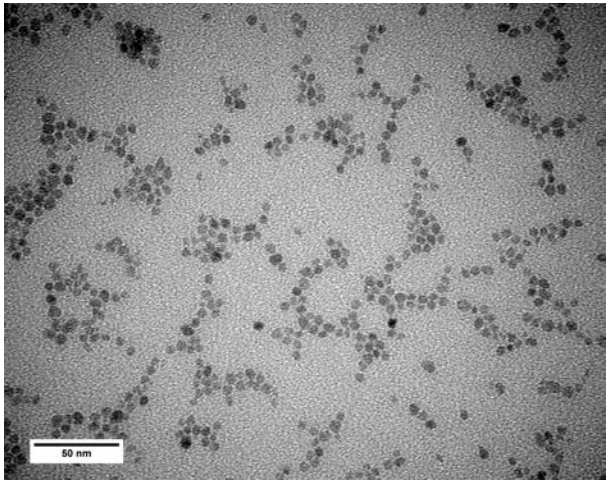


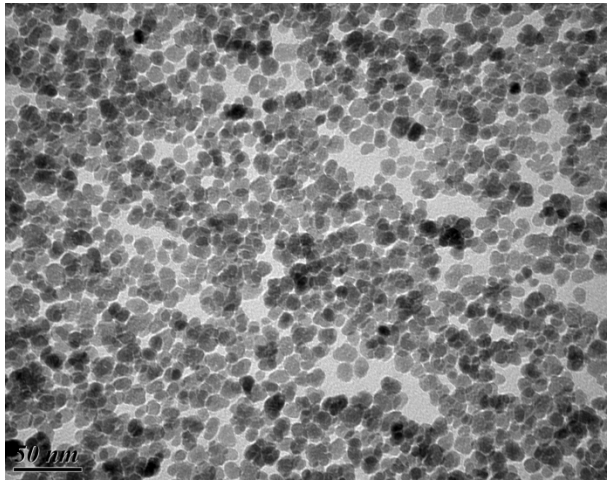
Figure	Batch	D_h (nm)	PDI
a	5ff	36	0.22
b	7ff	32	0.14
c	12ff	44	0.18
d	15ff	46	0.23
e	17ff	24	0.32
f	19ff	22	0.18
g	20ff	16	0.21
h	21ff	27	0.14
i	22ff	43	0.14
j	25ff	55	0.26
k	26ff	36	0.10
l	27ff	50	0.11
m	29ff	37	0.16
n	31ff	33	0.08
o	32ff	21	0.13
p	33ff	45	0.12
q	34ff	30	0.19
r	35ff	36	0.13

Variety of Fe_3O_4 NP batches synthesized in DEG:NMDEA

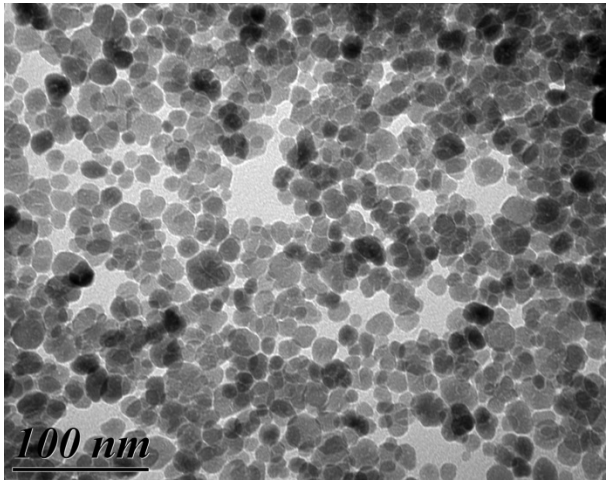
$$\langle d \rangle = d_0 e^{\sigma^2/2} \qquad var(d) = {d_0}^2 \left(e^{\sigma^2/2} - 1\right)$$



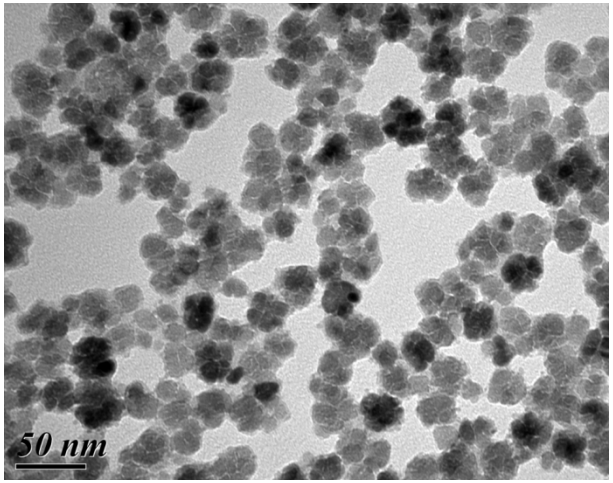
4FF: *d*=6.2±1.0 nm



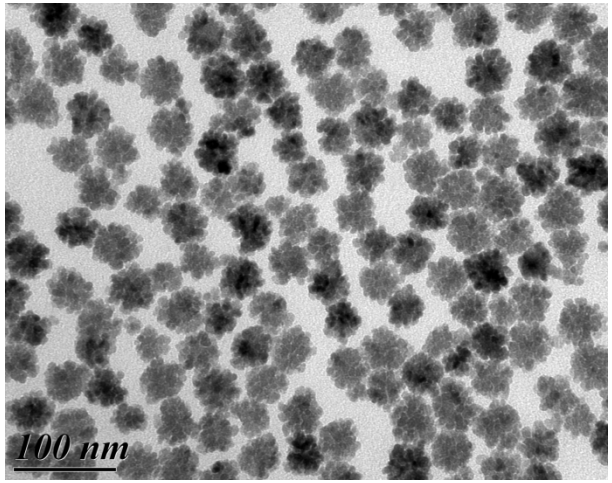
23FF: *d*=10.5±1.9 nm



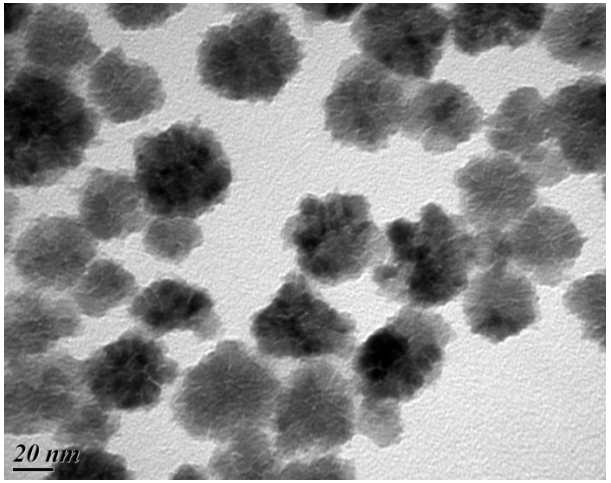
25FF: *d*=14.2±3.2 nm



29FF: d_{out}=26.6±4.2 nm



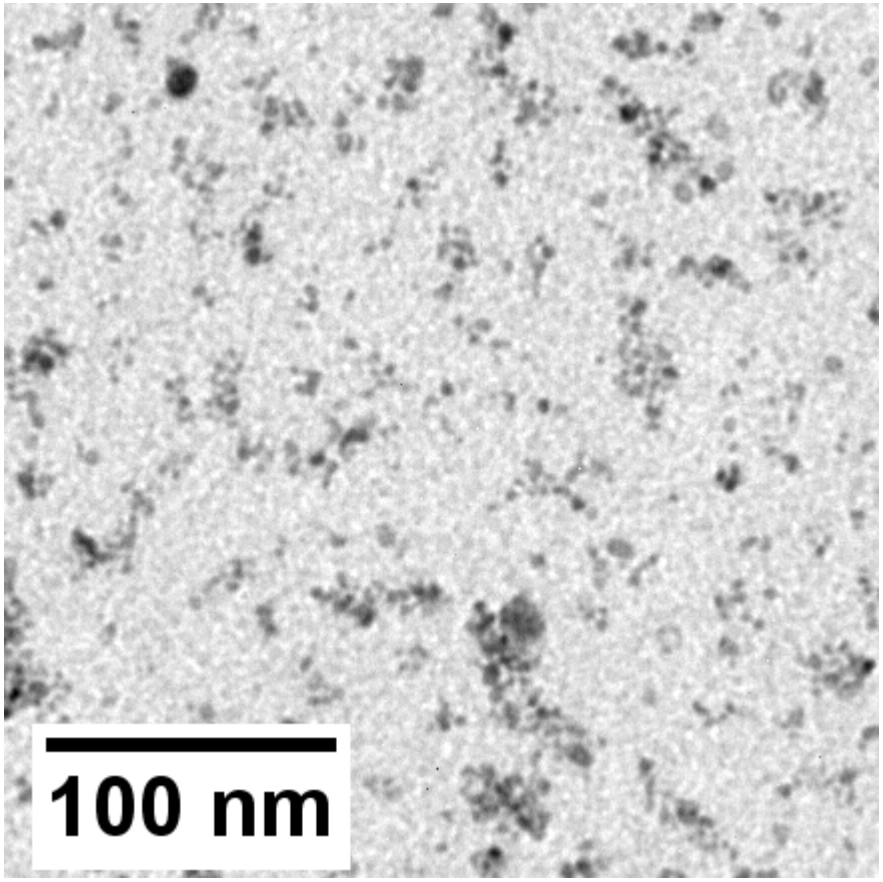
15FF: d_{out}=36.3±4.8 nm

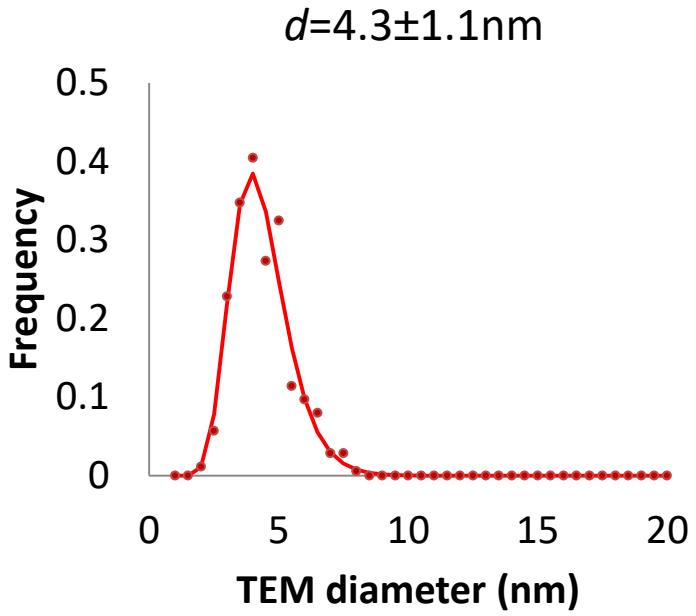


30FF: d_{out}=41.1±8.6 nm

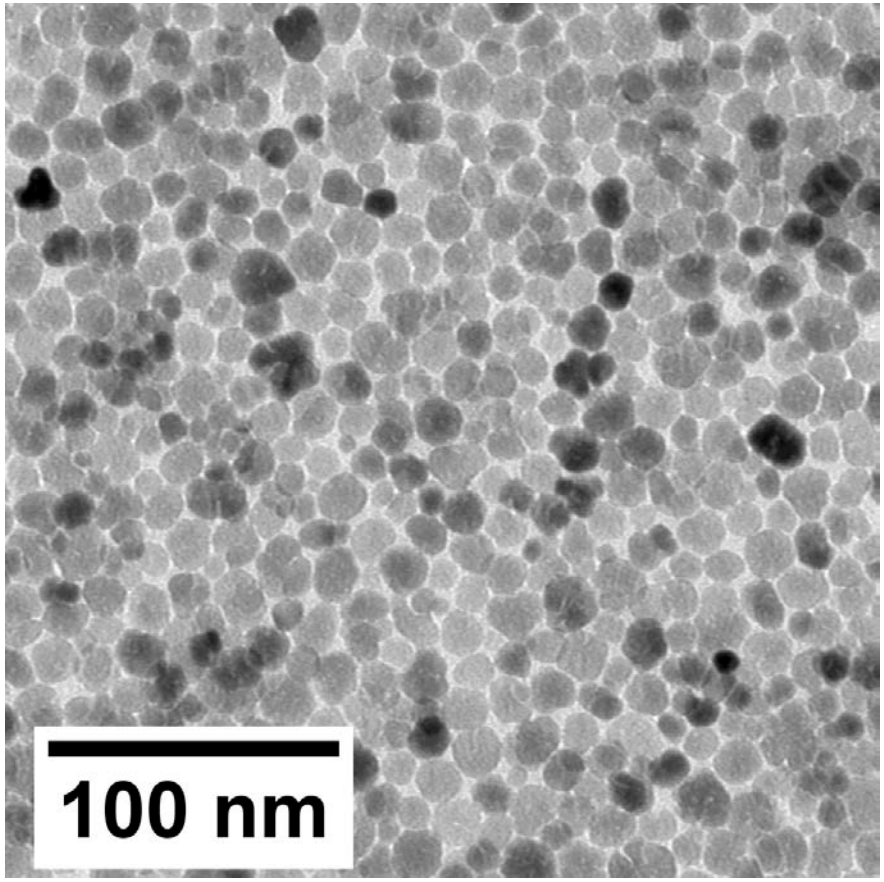
G. Hemery, A. C. Keyes Jr., E. Garaio, I. Rodrigo, J. A. Garcia, F. Pazaola, E. Garanger, O. Sandre, arXiv preprint: 1701.05858

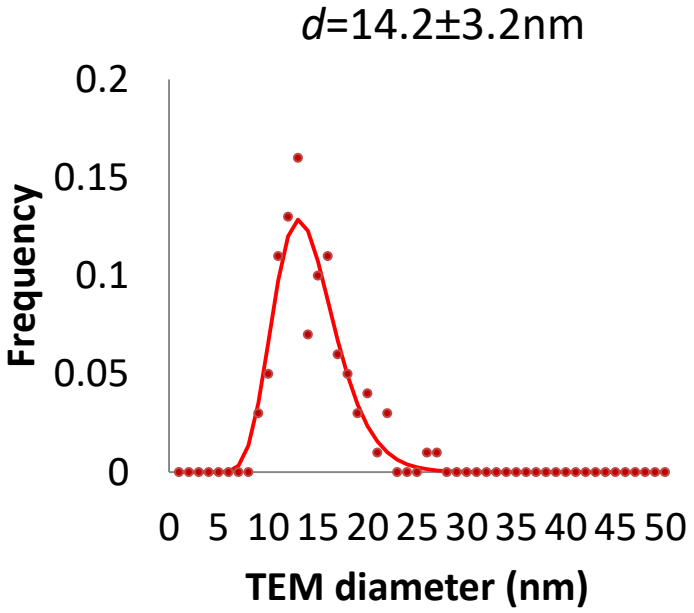
Example of ultra-small nanosphere sample: 17FF



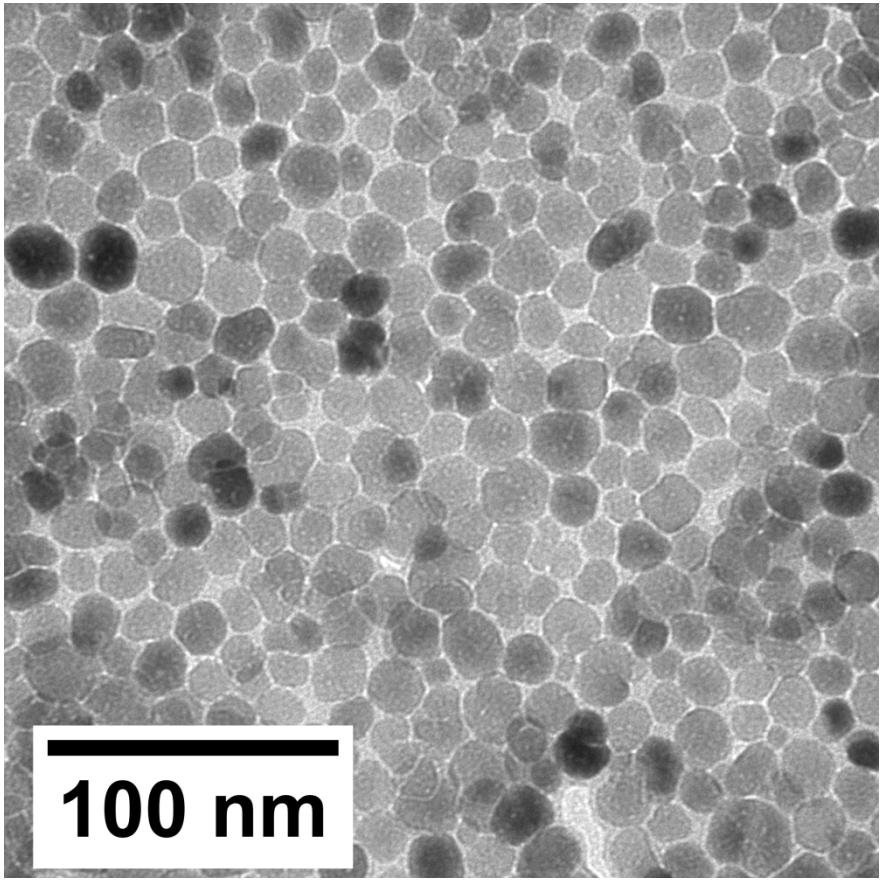


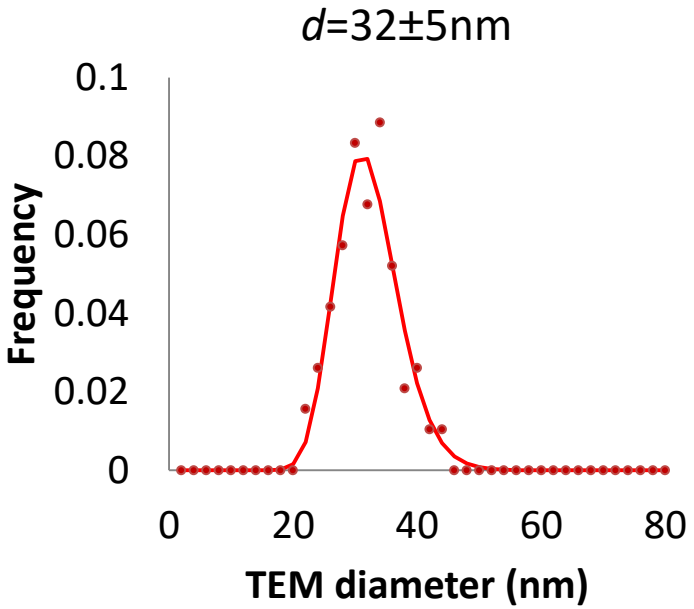
Example of medium size nanosphere sample: 25FF



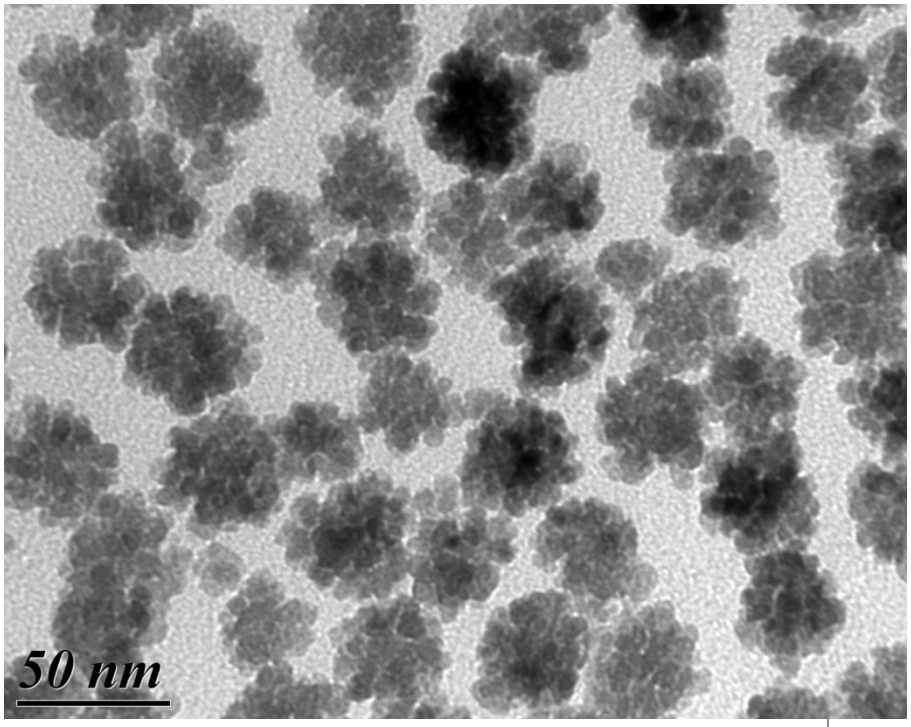


Example of very large size nanosphere sample: 34FF

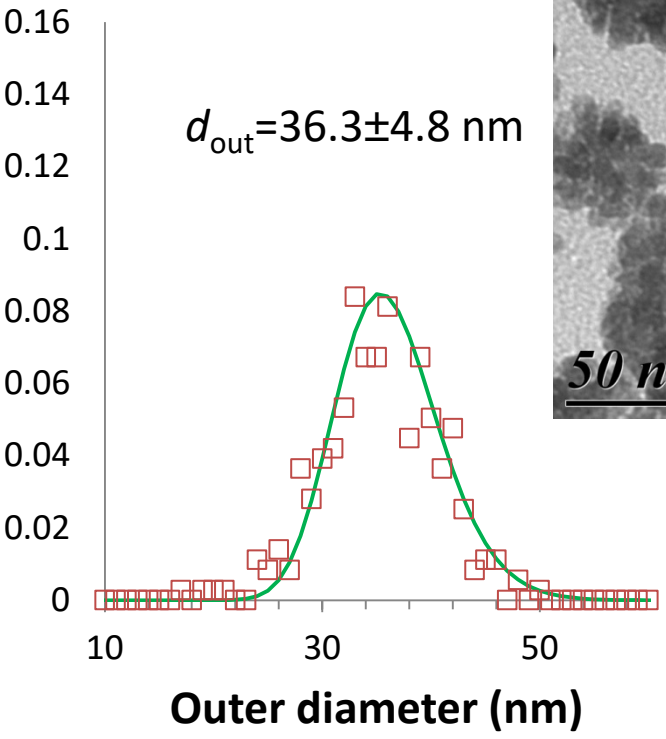




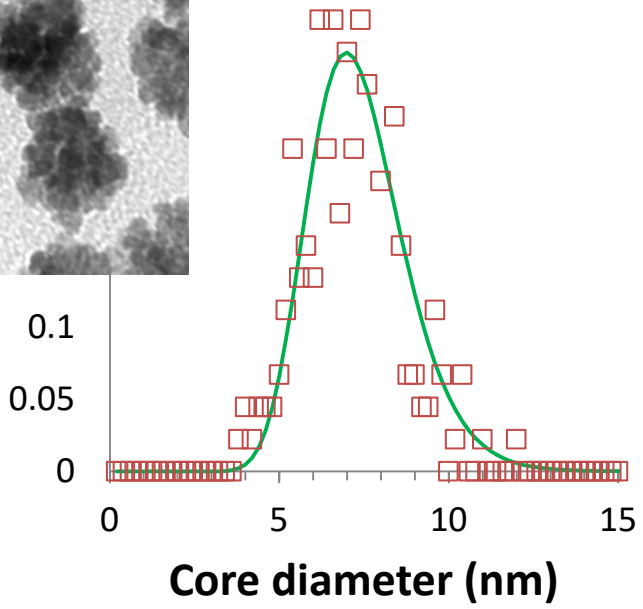
Example of nanoflower sample: 15FF



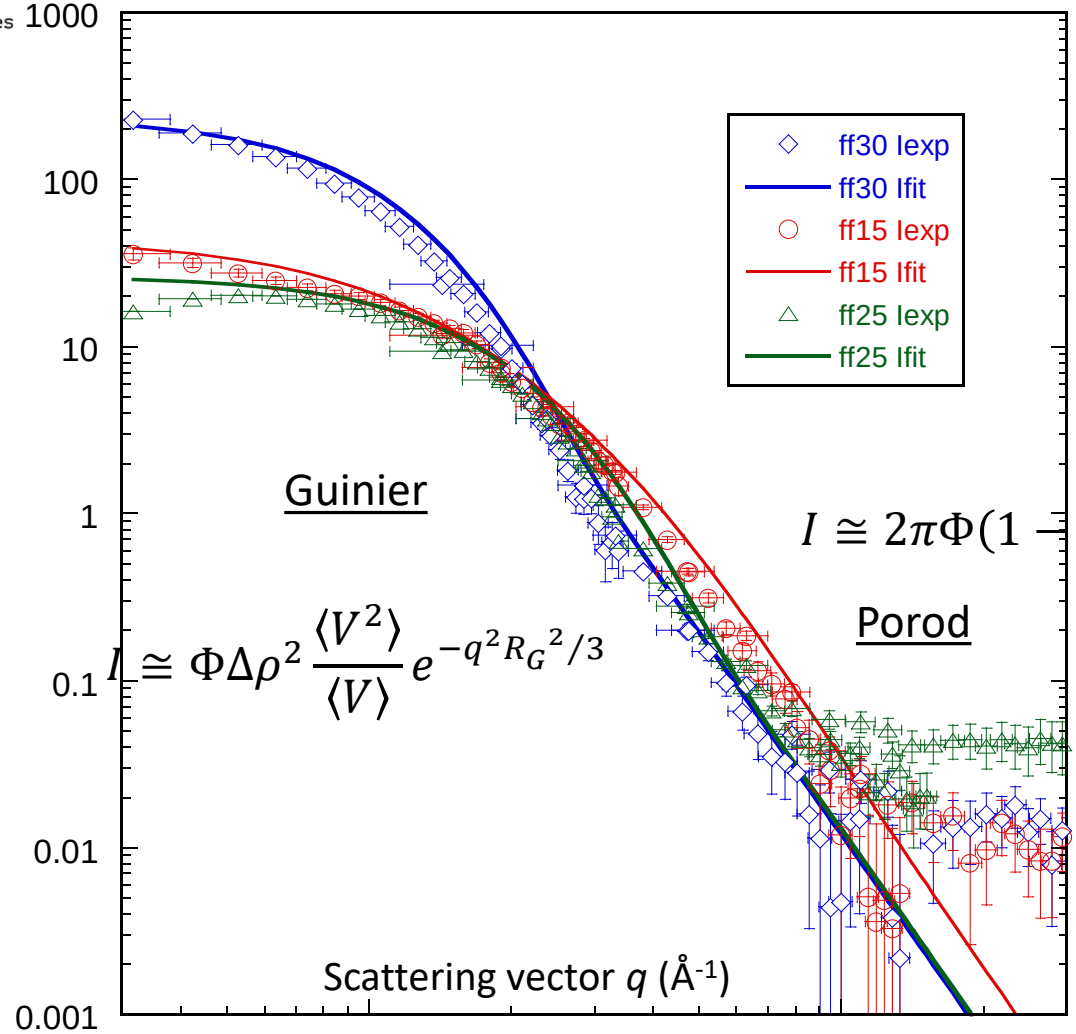
d_{out}=36.3±4.8 nm



d_{core}=7.4±1.4 nm



Particle form factors by small angle neutron scattering



PACE spectrometer
with Annie Brûlet

Orphée
Laboratoire Léon Brillouin

Guinier

$$I \cong \Phi\Delta\rho^2 \frac{\langle V^2 \rangle}{\langle V \rangle} e^{-q^2 {R_G}^2/3}$$

Porod

$$I \cong 2\pi\Phi(1-\Phi)\Delta\rho^2 \left\langle \frac{S}{V} \right\rangle$$

$$\left\langle \frac{S}{V} \right\rangle^{\text{the}} = 3 \Big/ \left(R_{\langle V^2 \rangle / \langle V \rangle} \right)$$

	R_G (nm)	$R_{\langle V^2 \rangle / \langle V \rangle}$(nm)	R_{TEM}(nm)	S_{spe} (m²/g)	S_{spe}^{the}
30ff:	18.9	18.1±3.9	23.5 ± 4.2	31.7	33.1
25ff:	10.5	10.4±2.3	7.1 ± 1.6	52.6	57.7
15ff:	19	10.6±3.9	17.5 ± 2.4	89.9	56.6

Necessity to measure precisely iron oxide concentration

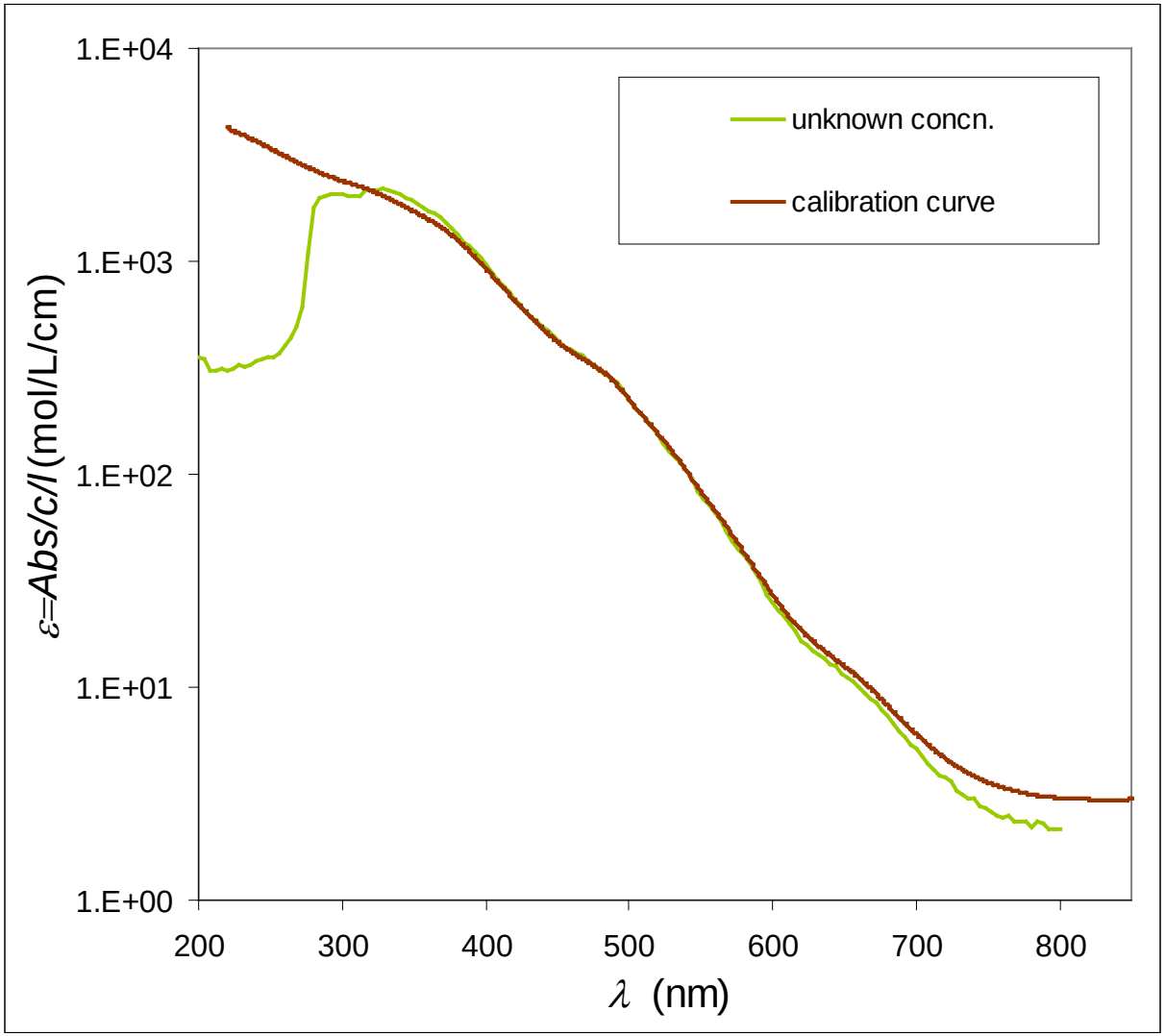
Experimental measurement of all properties (m_S, Δn_S, SHP, P(q), r_1, r_2…) require the total iron concentration.

Available methods are:

• Atomic Absorption Spectroscopy (or ICP): sensitive (10^{-5}M) but ±5%

• Redox titration (Charlot) by $K_2Cr_2O_7/SnCl_2$: precise (±1%) but not sensitive (10^{-1}M)

• Whole UV-Vis curve: precise (±1%) and sensitive (10^{-4}M)

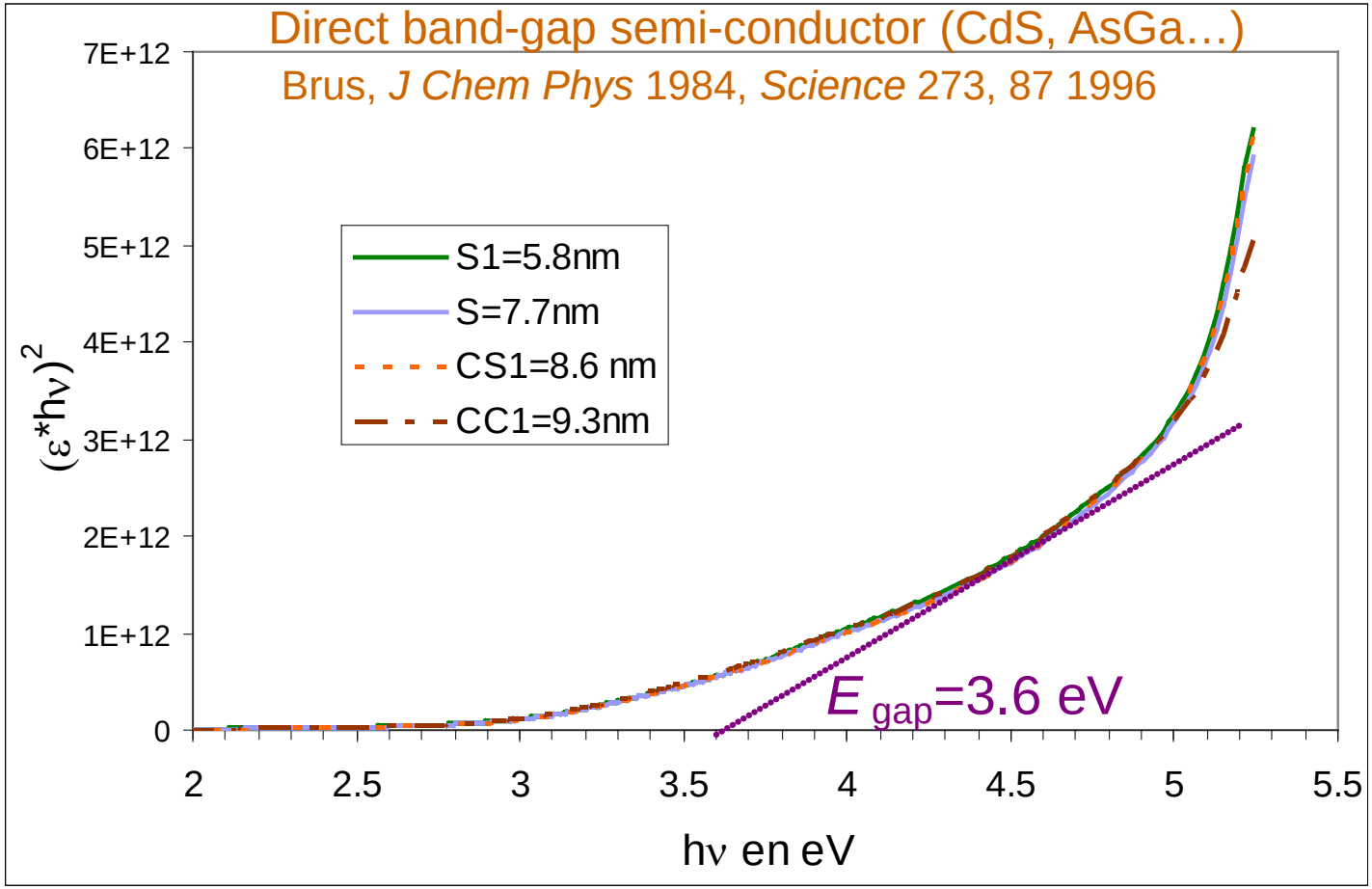


• "Ferrozine assay": highly sensitive (10^{-7}M) from OD_{562nm} according to *Small* 5 (2009) 256

UV-Vis extinction is independent on MNP size distribution

Constant → $c(h\nu - E_g^{bulk})^{1/2}$ ← 3,6 eV for Fe_2O_3 Shannon, *J. Phys. Chem. Ref. Data* 2002

UV-Vis molar extinction coefficient → $\varepsilon = \dfrac{c(h\nu - E_g^{bulk})^{1/2}}{h\nu}$



A. Abou-Hassan UPMC thesis 2009 2010 Best thesis prize in physical chemistry (SFP/SCF)
→ no size-dependent gap in the case of γ-Fe_2O_3
(the exciton diffusion length is presumably much smaller than the size of the USPIOs, thus no confinment)

Conclusion on Part 1 (Synthesis & Properties of MNPs)

- Since 30 years, the aqueous route (alkaline coprecipitation) leads to a quantitative production (~100g dry γ–Fe_2O_3) of magnetic nanoparticles that can be further functionalized (organic solvent, polymer matrix, biological coatings...). Today the up-scalable method is polyol route.

- Samples have inherent size / shape polydispersity, which can be a drawback for long-range ordering (*e.g.* colloidal or liquid crystals) but, according to Curie's principle, this is a great advantage to get large physical properties!

- The outlooks for biological applications (MRI contrast agents and magnetic hyperthermia) might be to play on the anisotropy constant K_a (shape anisotropy or other "irregularity") rather than on the size only, because of the difficulty to stabilize large MNPs (*e.g.* Ø>20nm) in biological media (ionic strength and flocculent proteins).