“Biomedical applications based on magnetic nanoparticles”

R. Fernández-Pacheco¹, C. Marquina², D. Serrate² and J.G Valdivia¹
M. Gutierrez¹ and M.R. Ibarra¹,²

¹Instituto de Nanociencia de Aragón, Edificio Interfacultades II, Zaragoza (Spain)
²Instituto de Ciencia de Materiales de Aragón (CSIC/Universidad de Zaragoza), Facultad de Ciencias, Zaragoza (Spain)

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OUTLINE OF THE TALK

- **Introduction to nanoscale materials**
- Small magnetic particles
- Encapsulated nanoparticles: preparation and characterization
- Bioferrofluids for local drug delivery
- Summary
Nanoscale is the meeting point between the molecular chemistry and condensed matter.
The macroscopic world offers materials with a determined functionality which can be modified by size reduction.
Applications of Nanoscience

Scale reduction at nanoscopic level open new views for science and applications

- Therapeutic drugs
- Tagging of DNA and DNA chips
- Information storage
- Magnetic refrigeration

- Harder metals
- Catalysts
- Sensors based in nanoporous membranes
- Improved batteries .......
Medical application of magnetic nanoparticles

- Selective drug delivery
- Biological labeling
- Hiperthermy
- Contrast agent
- Oftalmology

Bioferrofluid
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How small?

- 30 nm → 5% atoms at the surface
- 10 nm → 20% atoms at the surface
- 3 nm → 50% atoms at the surface

**TABLE 2.1** The relation between the total number of atoms in full shell clusters and the percentage of surface atoms

<table>
<thead>
<tr>
<th>Full-shell Clusters</th>
<th>Total Number of Atoms</th>
<th>Surface Atoms (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Shell</td>
<td>13</td>
<td>92</td>
</tr>
<tr>
<td>2 Shells</td>
<td>55</td>
<td>76</td>
</tr>
<tr>
<td>3 Shells</td>
<td>147</td>
<td>63</td>
</tr>
<tr>
<td>4 Shells</td>
<td>309</td>
<td>52</td>
</tr>
<tr>
<td>5 Shells</td>
<td>561</td>
<td>45</td>
</tr>
<tr>
<td>7 Shells</td>
<td>1415</td>
<td>35</td>
</tr>
</tbody>
</table>
- Under size reduction the coercive field increases and the particle becomes single-domain.

- When $E_k = KV$ as $V \to 0$ then $E_k \to 0$ **superparamagnetic limit** $KV = k_B T$.

- At this situation the particle magnetic moment will fluctuate independently of the particle.
If $K \to 0$

The supermoment follows the Langevin law

If $K \gg>$

The supermoment follows the Brillouin $J=1/2$ law
Real superparamagnetic system

- No hysteresis
- The isotherm presents a universal H/T behaviour
Due to the stochastic nature of the thermal energy the superparamagnetism is a time dependent effect.

\[ \tau = \tau_0 \exp(-KV/k_B T) \]

\( \tau \) time for magnetization reversal (depend on the anisotropy)

\[ V_{sp} = 25(k_B T/K) \quad \tau_{measure} = 100 \text{ s} \quad T_B = KV_{sp}/25k_B \]

\[ V_{sp} = 4.5(k_B T/K) \quad \tau_{measure} = 10^{-7} \text{ s} \quad T_B = KV_{sp}/4.5k_B \]

\( T_B \) Mösbauer = 5.5 \( T_B \) magnetometry (FC y ZFC)

Fe y Co at 300K \( V_{sp} = 16 \text{ y } 7.6 \text{ nm} \)
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The discovery of graphitic nanostructures as fullerenes and nanotubes offers the possibility to fill nanoscale cavities with transition metals.

The confinement of this small amount of material promises:

- Novel physical properties
- Protection of the encapsulated metals from oxidation by resistant carbon cages
Kratschmer-Huffman Method

- The anode is a graphite-metal composite
- Several carbon and graphitic structures are obtained
Arc-discharge Furnace

Products showing the web-like soot on the collarette

- Fullerenes
- Amorphous carbon
- Graphitic structures
Manganese encapsulated nano particles

- Graphitic multiwall nanotubes
- Catalytic particles forming large single wall nanotubes
- Small particles surrounded by polygonal layers: Onions
- Metallic inclusions in nanotubes
- Nanoparticles encapsulated in graphitic layers and glassy carbon
TEM images of Fe & Co encapsulated nanoparticles
Fe coated by graphitic layers
Sample treatment an average size

- Samples are sonicated in a dilution of surfactant (SDS and distilled water (5g/l))
- Magnetic separation is achieved in a field gradient of 3 kOe/cm
- Chemical etching with aqua regia is made to remove the uncovered metallic particles
Magnetic characterization

-SQUID magnetometry

-Mössbauer spectroscopy

Si $\tau < \tau_{\text{medida}}$ superparamagnetism

Critical volume to detect superparamagnetism:

$V_{sp} = 25(k_B T/K)$ \hspace{1cm} $\tau_{\text{static}} = 100\ s$ \hspace{1cm} $T_B = k_B V_{sp}/25k_B$

$V_{sp} = 4.5(k_B T/K)$ \hspace{1cm} $\tau_{\text{mössbauer}} = 10^{-7}s$ \hspace{1cm} $T_B = k_B V_{sp}/4.5k_B$
Mössbauer spectroscopy

No indication of SP relaxation at room temperature

Estimated particle size 13-9 nm (interparticle interaction)

\( \alpha-\text{Fe} \)

Two sextets (34T and 31T)

\( \text{Fe}_3\text{C} \)

A sextet (25.1 T)

\( \gamma-\text{Fe} \)

Singlet and doublet

Magnetization measurements

**Blocked particles**
- Large/correlated particles

**Superparamagnetic particles**
- Small particles
Blocking temperature is determined from FC and ZFC.
Silica encapsulated Fe nanoparticles
Fe encapsulated in Silica X-Ray Photoelectron Spectroscopy

![Graphs showing normalized intensity vs. binding energy for different elements before and after etching.]

**Photons**
- Before etching
- After etching

**Electrons**
- Before etching
- After etching
Fe encapsulated nanoparticles Electron Energy Loss Spectra (EELS) (in collaboration J. Arbiol)

![Graphs showing EELS spectra with peaks at Fe L$_2$ edge, Fe L$_3$ edge, O K edge, Si L$_{2,3}$ edge, Al L$_{2,3}$ edge.]

- a) Surface Spectrum
- b) Inside Spectrum

10 nm
High Resolution Transmission Electron Microscopy of carbon encapsulated iron nanoparticles

$\text{Fe}_2\text{O}_3$ Nanoparticle

Graphite Encapsulation

HRTEM

[011] $\text{Fe}_2\text{O}_3$ Maghemite

EFTEM

$\text{K C (284 eV)}$

$\text{L}_3 \text{Fe (708 eV)}$

Elemental Map

Red: $\text{K C (284 eV)}$

Green: $\text{L}_3 \text{Fe (708 eV)}$
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BIOFERROFLUIDS AS THERAPEUTIC CARRIERS

- They should be magnetic to be guided by applied magnetic fields
- The magnetic materials are not biocompatibles
- The nanoparticles should be encapsulated
- The surrounded material should be able to adsorb and desorb the drug

J. Johnson et al., EC&M 3 (2002) 12
Local drug delivery by using magnetic carriers

New development at the INA
Laparoscopic implant of a permanent magnet

Solid tumor
Magnet implantation
External applied magnetic field
Intravenous administration of magnetic carriers
BIOFERROFLUIDS

- Biocompatibility
- Drug adsorption/desorption
- Proteins conjugation

Plasma Krästchmer-Hoffman

[Images showing HRTEM and plasma treatment]
Endoscope  
Trocar for magnet implantation  
Implant  

Bioferrofluid  
Intravenous administration  

In-Vivo localization of magnetic particles by systemic administration and using magnetic implants

In coll. Hospital Clínico Veterinario
Magnet implant in the left kidney

Localization of nanoparticles

Right kidney without magnetic implant

Lack of nanoparticles
Kidney with magnetic implant:
Moderate concentration of nanoparticles

Rabbit 22

Rabbit 23
Nanoparticles traveling in blood

Tested biocompatibility
Dynamic of the adsorption and release of Doxorubicine on carbon coated magnetic nanoparticles

Saturation after 20 minutes        Complete release after 100 hours
Matter manipulation at atomic level

Intelligent nanovectors

Targeting
Magnetic targeting future for cancer therapy?
THANKS VERY MUCH!