"Biomedical applications based on magnetic nanoparticles"

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Constanta 2005

OUTLINE OF THE TALK

-Introduction to nanoscale materials

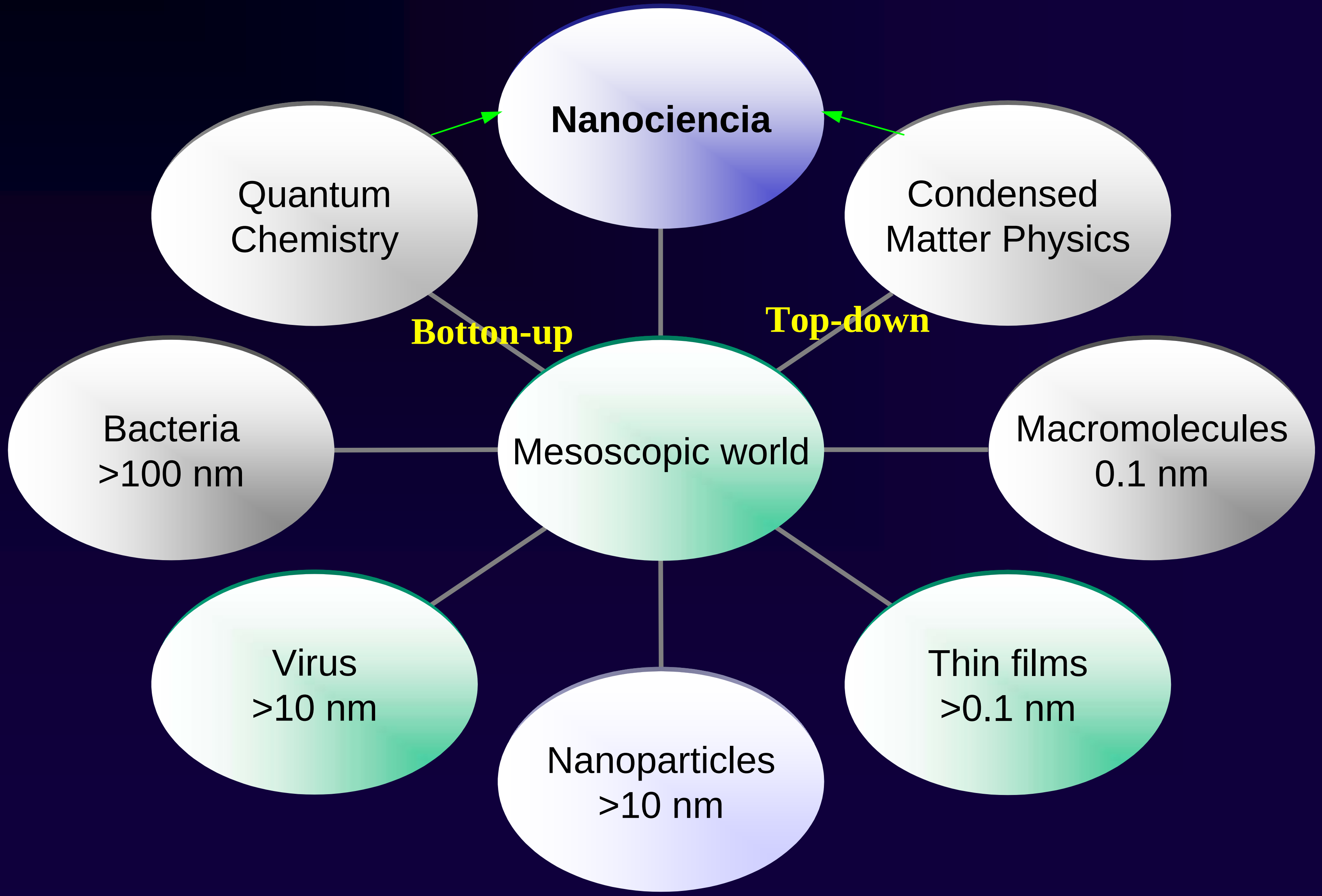
-Small magnetic particles

-Encapsulated nanoparticles:preparation and charaterization

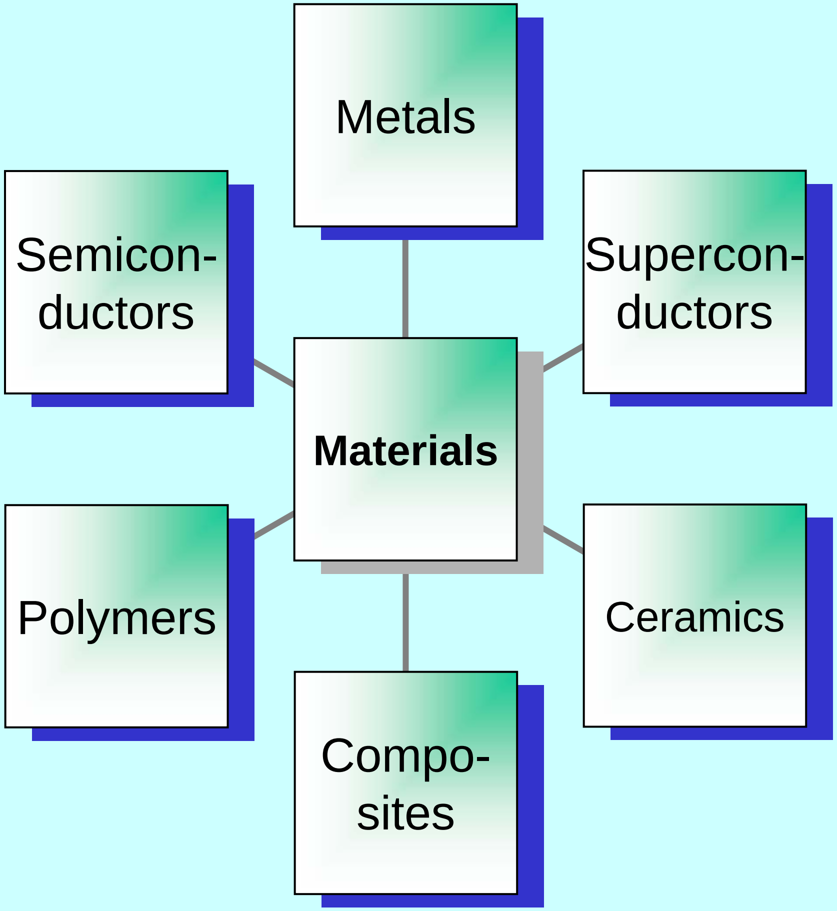
-Bioferrofluids for local drug delivery

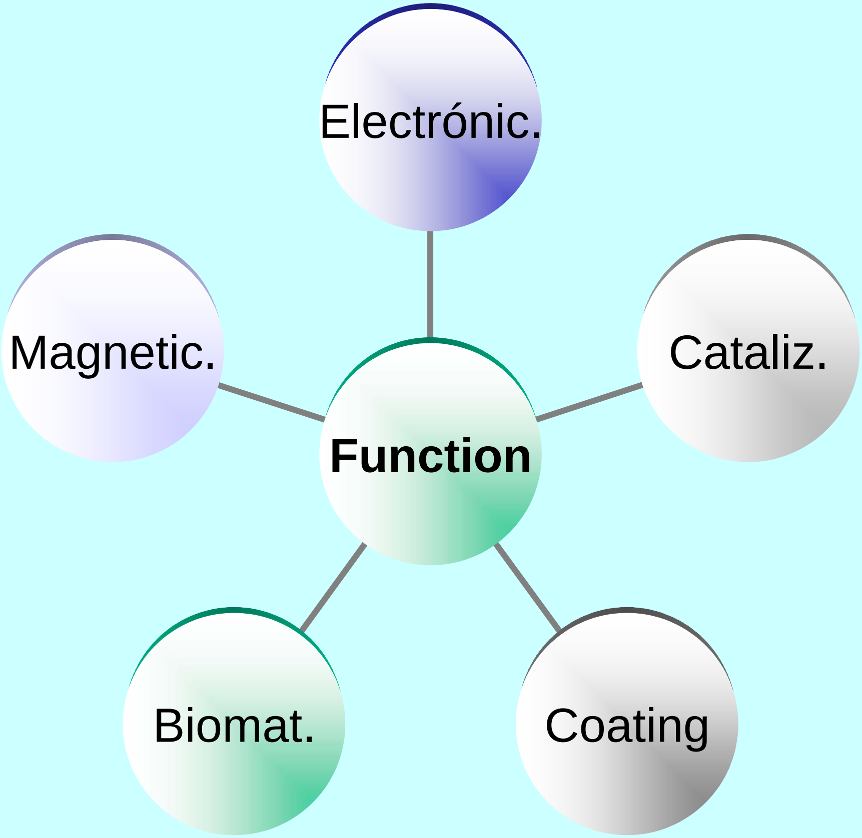
-Summary

Nanoscale is the meeting point between the molecular chemistry and condensed matter



The macroscopic world offer materials with a determine functionality wich can be modify 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

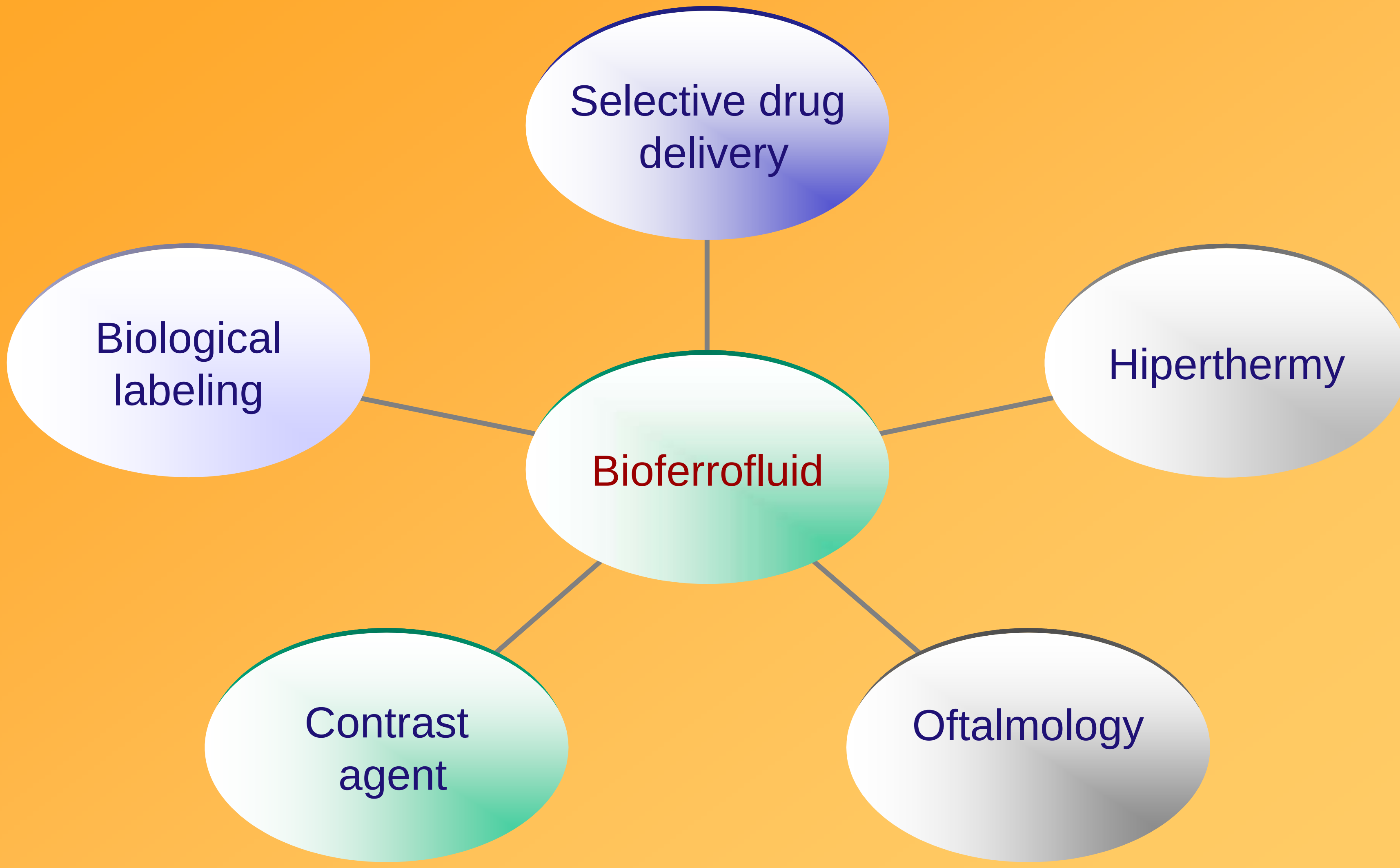
-Harder metals

-Catalysts

-Sensors based in nanoporous membranes

-Improved batteries ....

Medical application of magnetic nanoparticles



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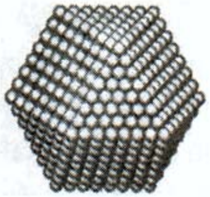
How small?

30 nm → 5 % atoms at the surface

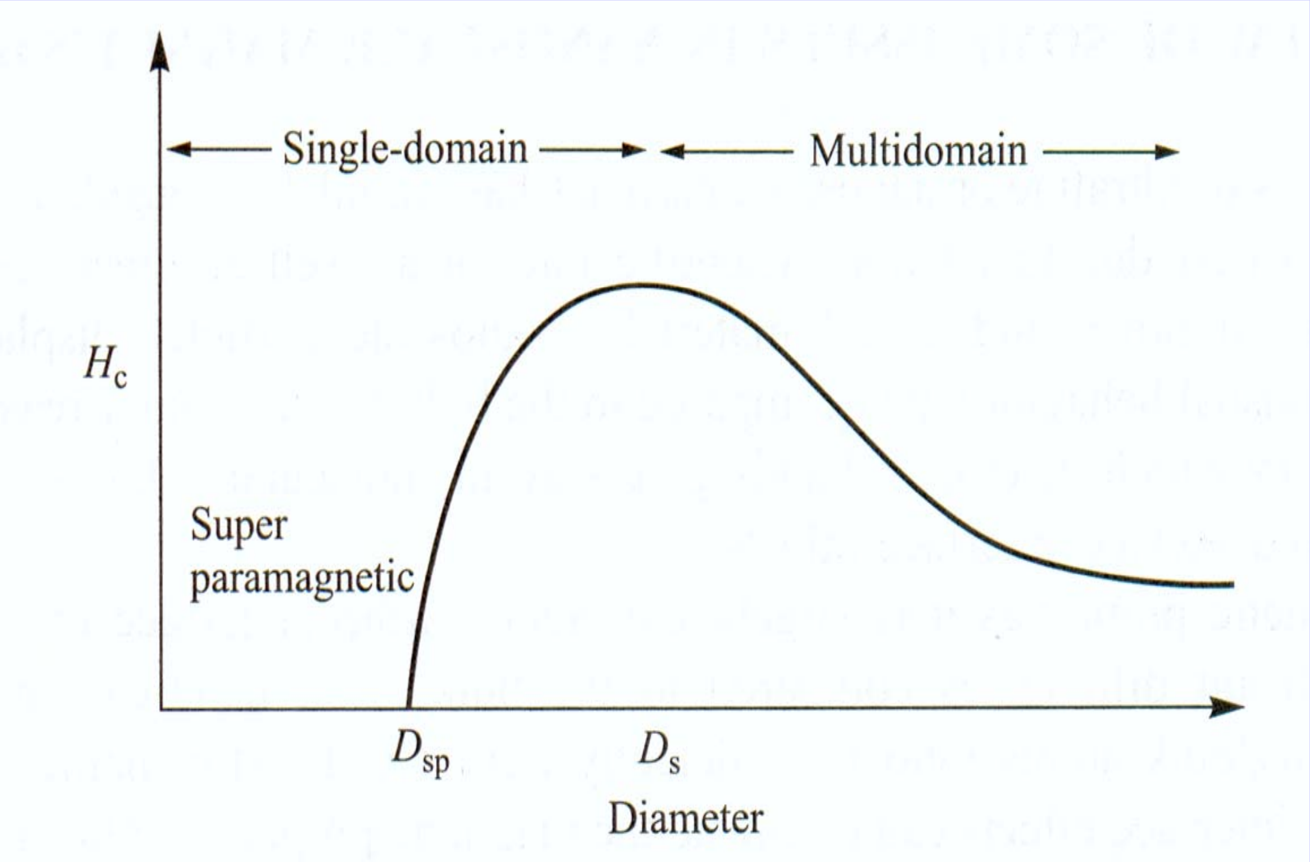
10 nm → 20 % atoms at the surface

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

Full-shell Clusters		Total Number of Atoms	Surface Atoms (%)
1 Shell		13	92
2 Shells		55	76
3 Shells		147	63
4 Shells		309	52
5 Shells		561	45
7 Shells		1415	35

Crítical size for single-domain particle

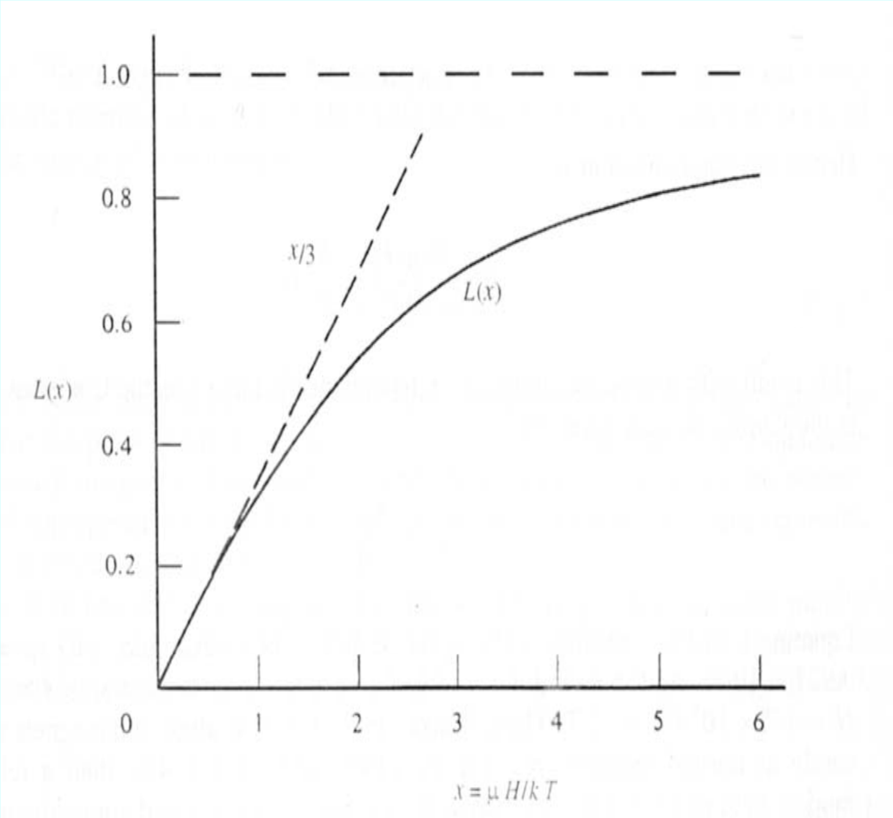


-Under size reduction the coercive field increases and the the particle becomes single-domain

-When E_K=KV as V → 0 then E_K → 0 **superparamagnetic limit** → **$KV = k_BT$**

-At this situation the particle magnetic moment will fluctuate independently of the particle

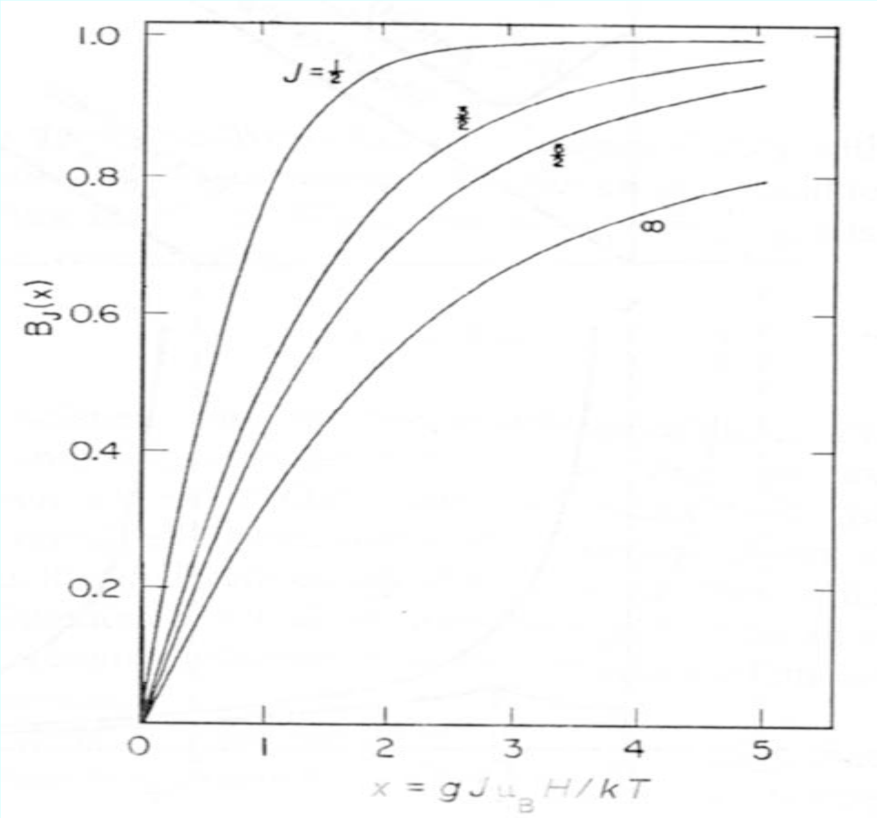
Classic paramagnet



If K → 0

The supermoment follows the Langevin law

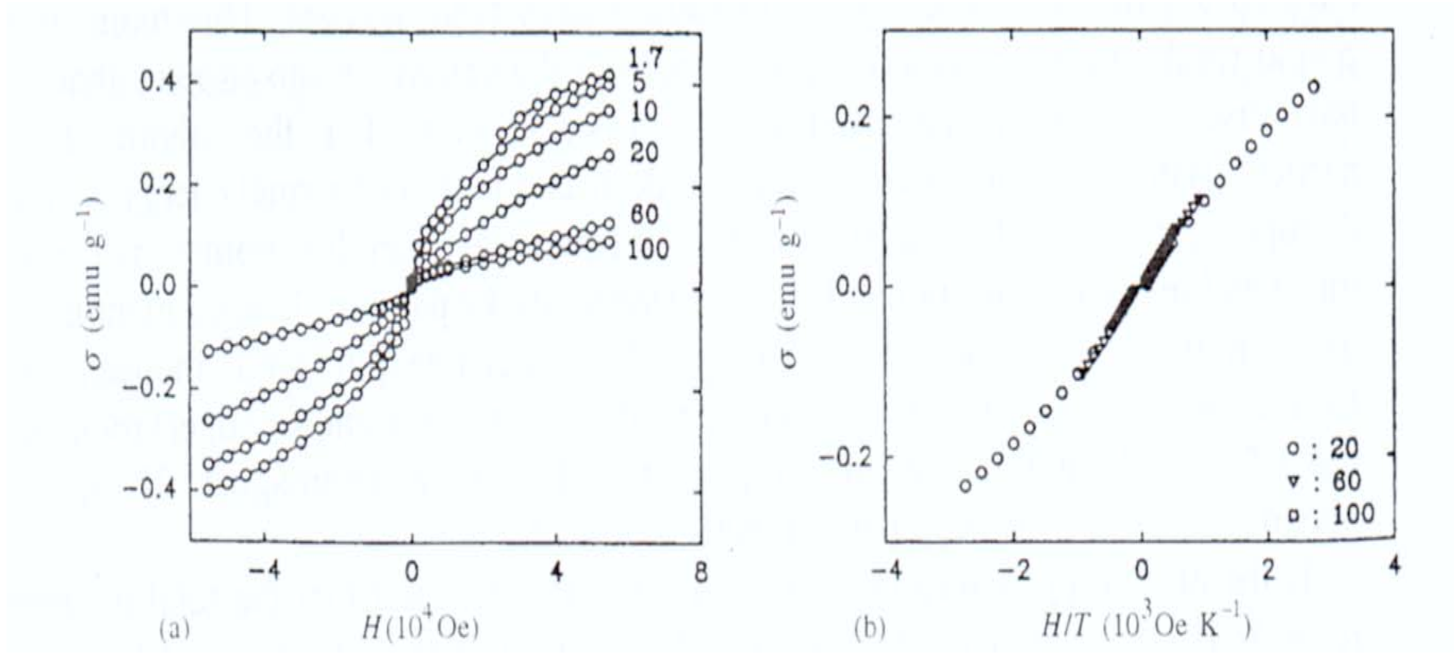
Quantum paramagnet



If K>>>

The supermoment follows the Brillouin J=1/2 law

Real superparamagnetic system



-No hystheresis

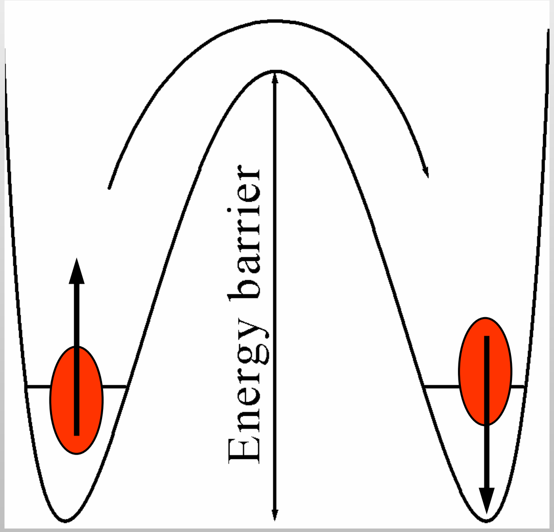
-The isotherm presents a universal H/T behaviour

Time effects:relaxation

Due to the stocastic nature of the thermal energy the superparamagnetism is a time dependent effect

$$\tau = \tau_0 \exp(-KV/k_BT)$$

τ time for magnetization reversal (depend on the anisotropy)



Si $\tau < \tau_{measure}$ superparamagnetism

τ_0 tipically 10^{-9} s

Critical volume to detect superparamagnetism:

$V_{sp}=25(k_BT/K)$ $\tau_{measure}=100$ s $T_B=KV_{sp}/25k_B$

$V_{sp}=4.5(k_BT/K)$ $\tau_{measure}=10^{-7}$s $T_B=KV_{sp}/4.5k_B$

T_B Mösbauer = 5.5 T_B magnetometry (FC y ZFC)

Fe y Co at 300K V_{sp}=16 y 7.6 nm

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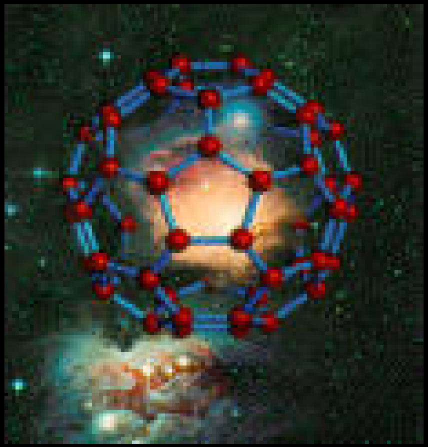
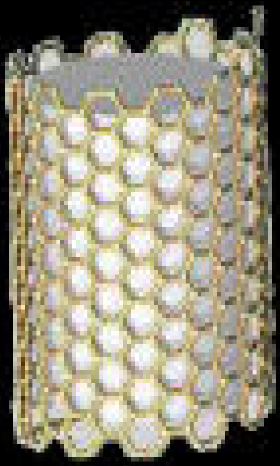
Particles coating: Carbon and Silica nanocages

The discovery of graphitic nanostructures as fullerenes and nanotubes offers the possibility to fill nanoscale cavities with transition metals





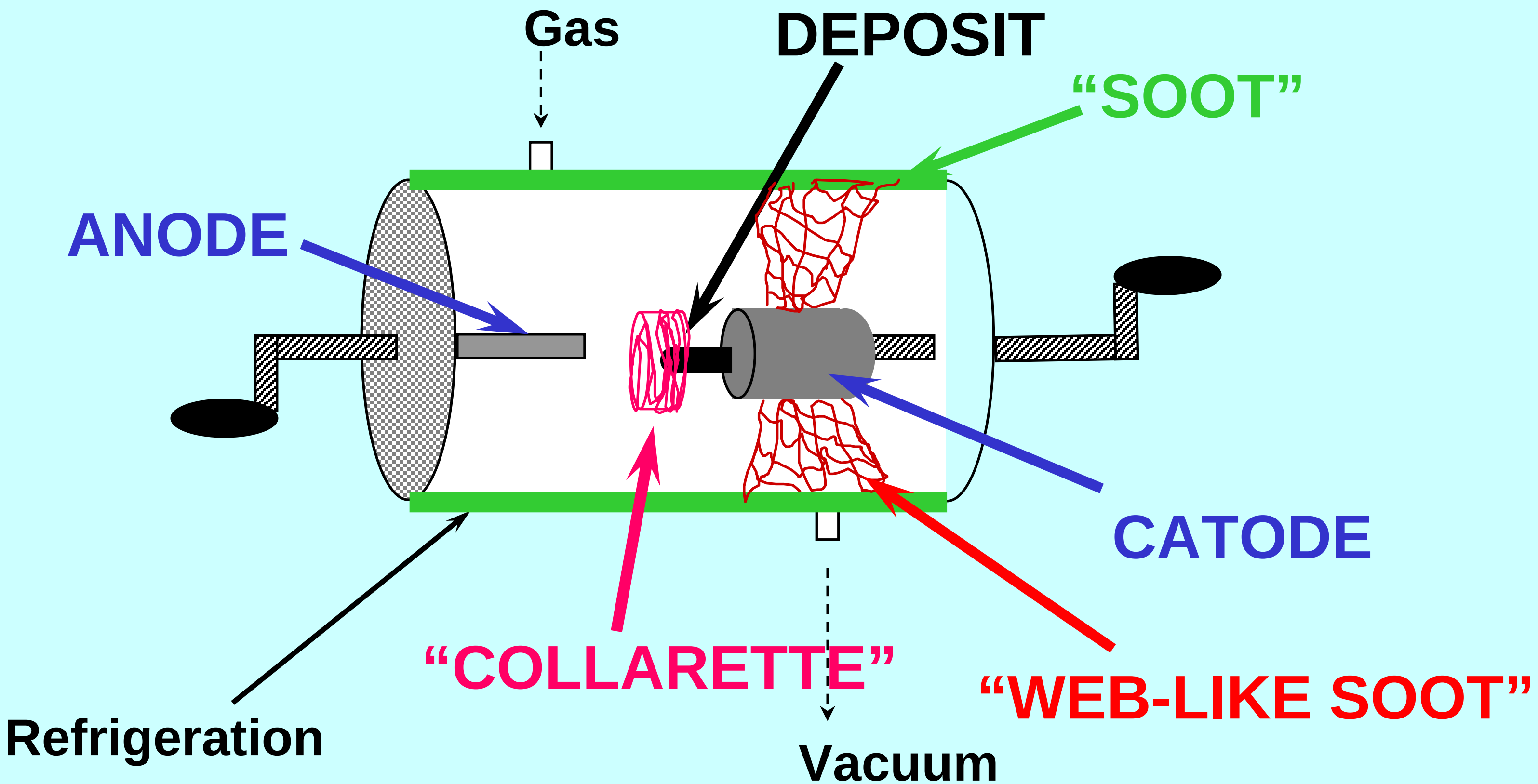
The confinenement of this small amount of material promises:

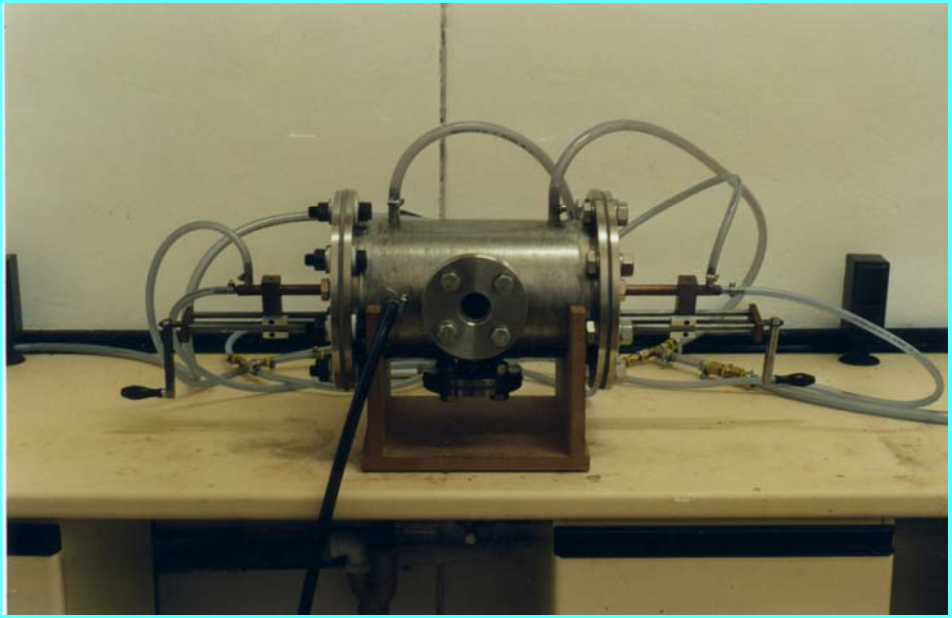
-Novel physical properties

-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

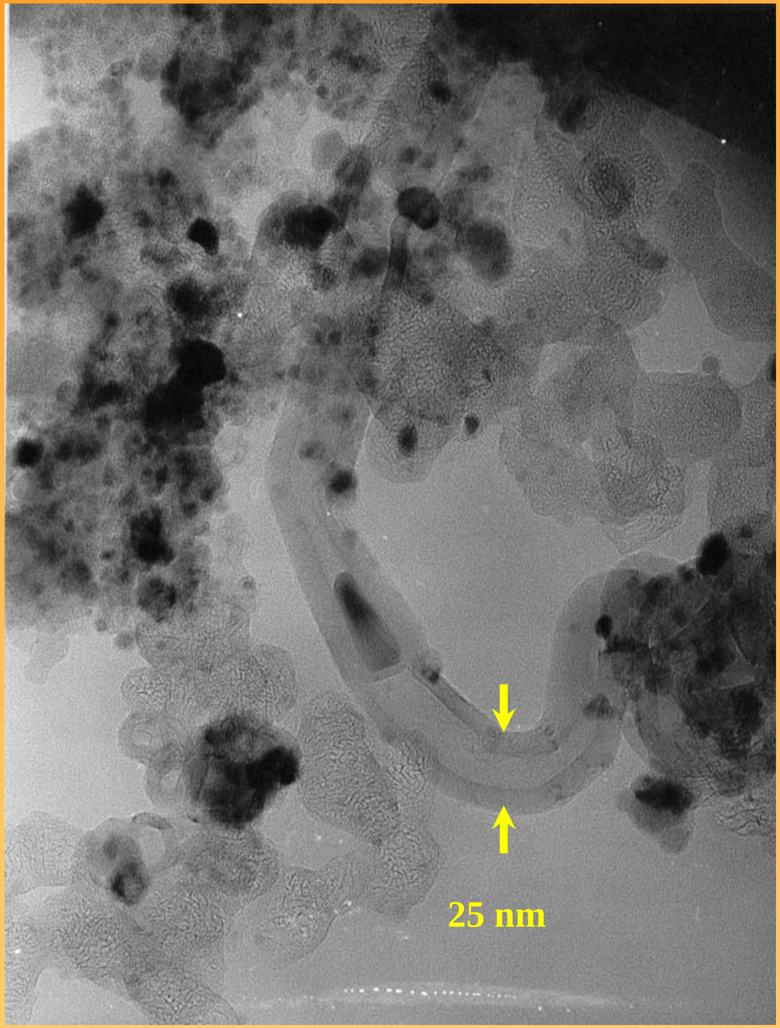
Products showing the web-like soot on the collarette

-Fullerenes

-Amorphous carbon

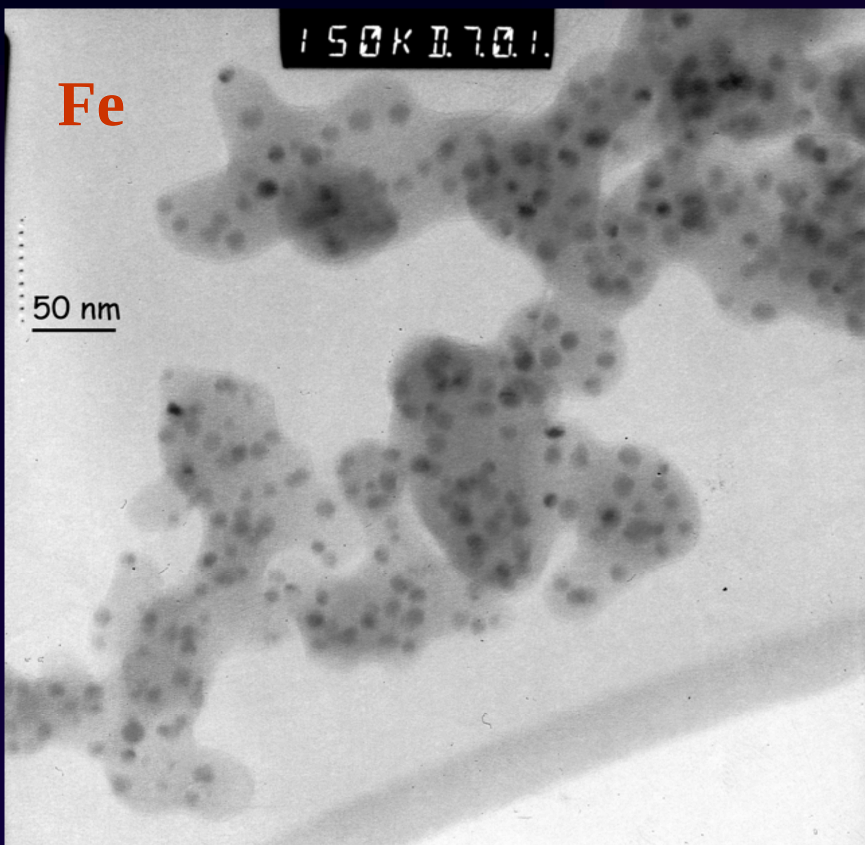
-Graphitic structures

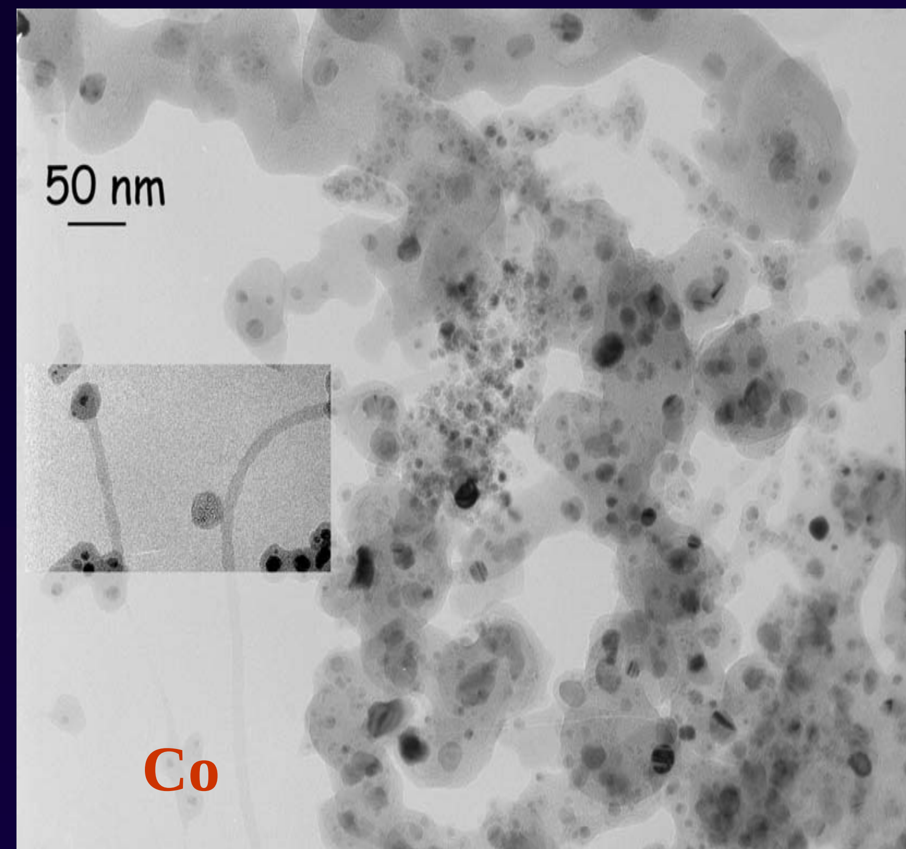
Manganese encapsulated nano particles



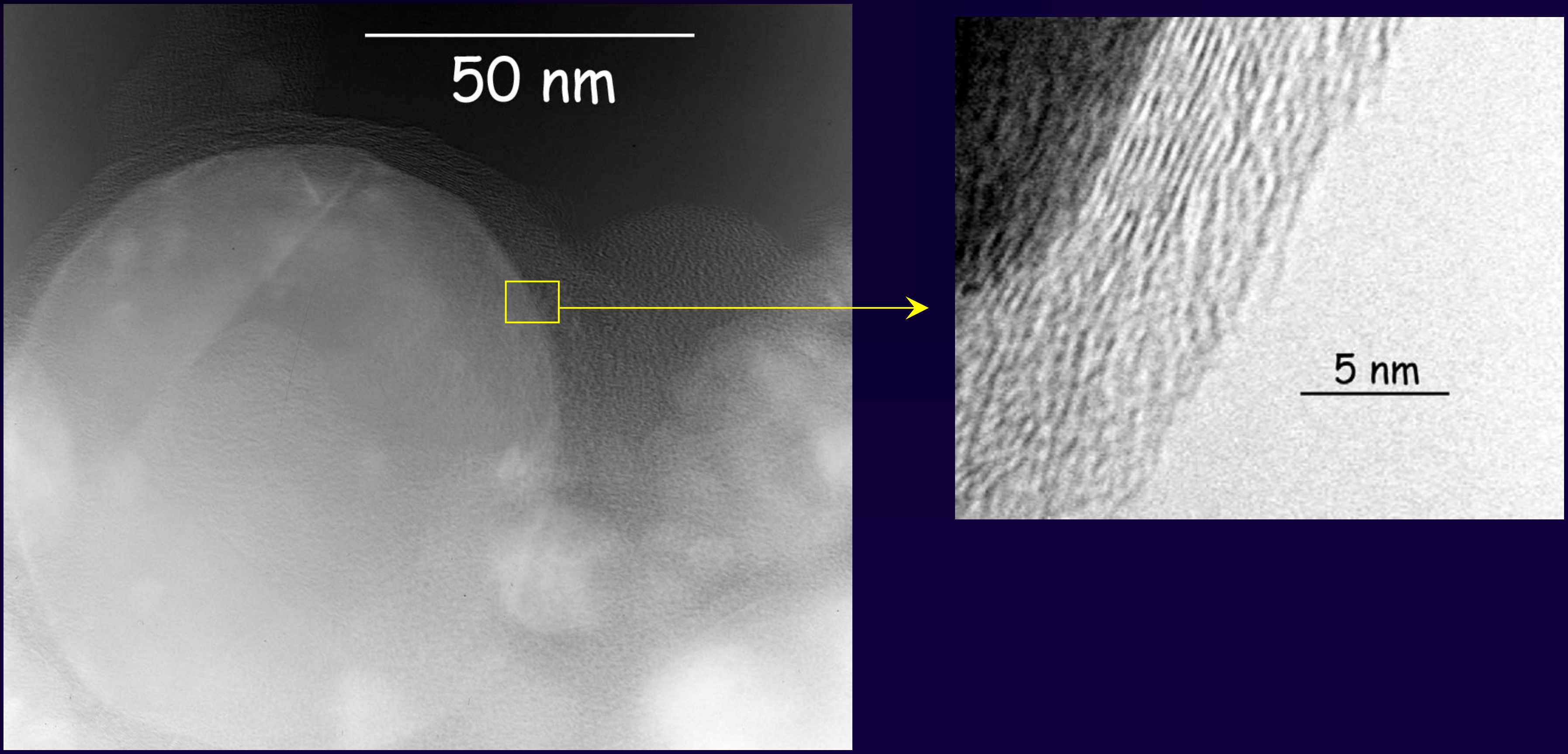
-Graphitic multiwall nanotubes
-Catalytic particles forming large single wall nanotubes
-Small particles sourronded by polygonal layers: Onions
-Metallic inclusions in nanotubes
-Nanoparticles encapsulated in graphitic layers and glassy carbon

TEM images of Fe & Co encapsulated nanoparticles





Fe coated by graphitic layers

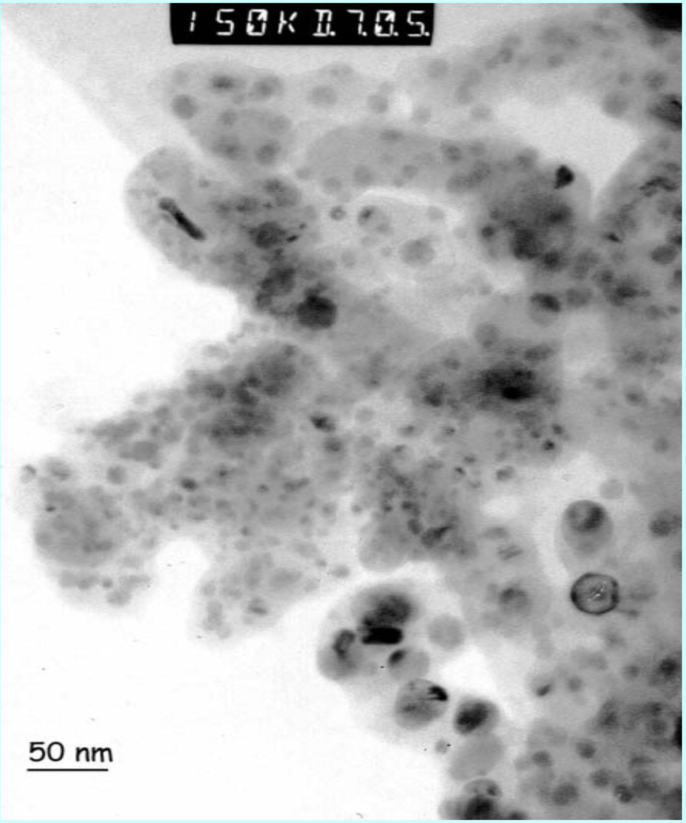


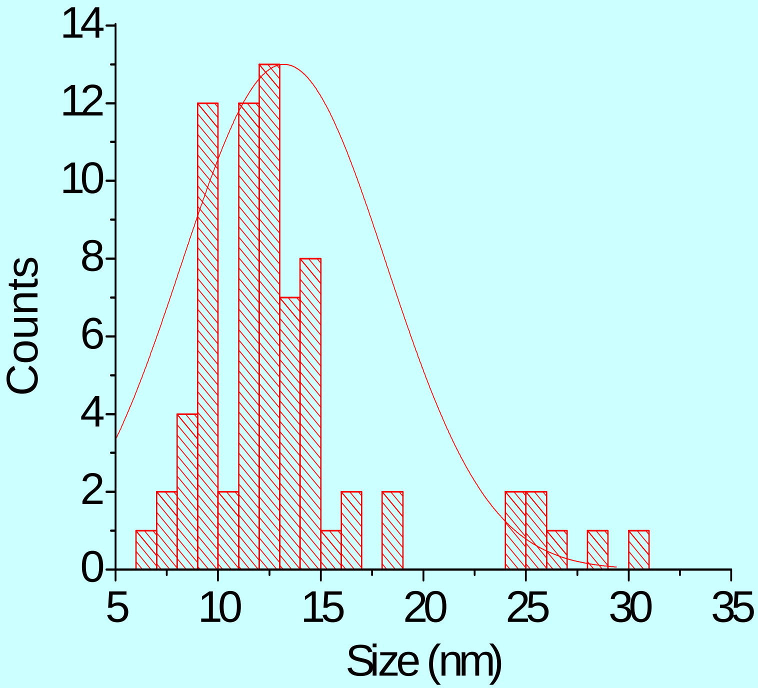
Sample treatment an average size

-Samples are sonicated in a dilution of surfactant (SDS and distilled water (5g/l))

-Magnetic separation is acheived 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

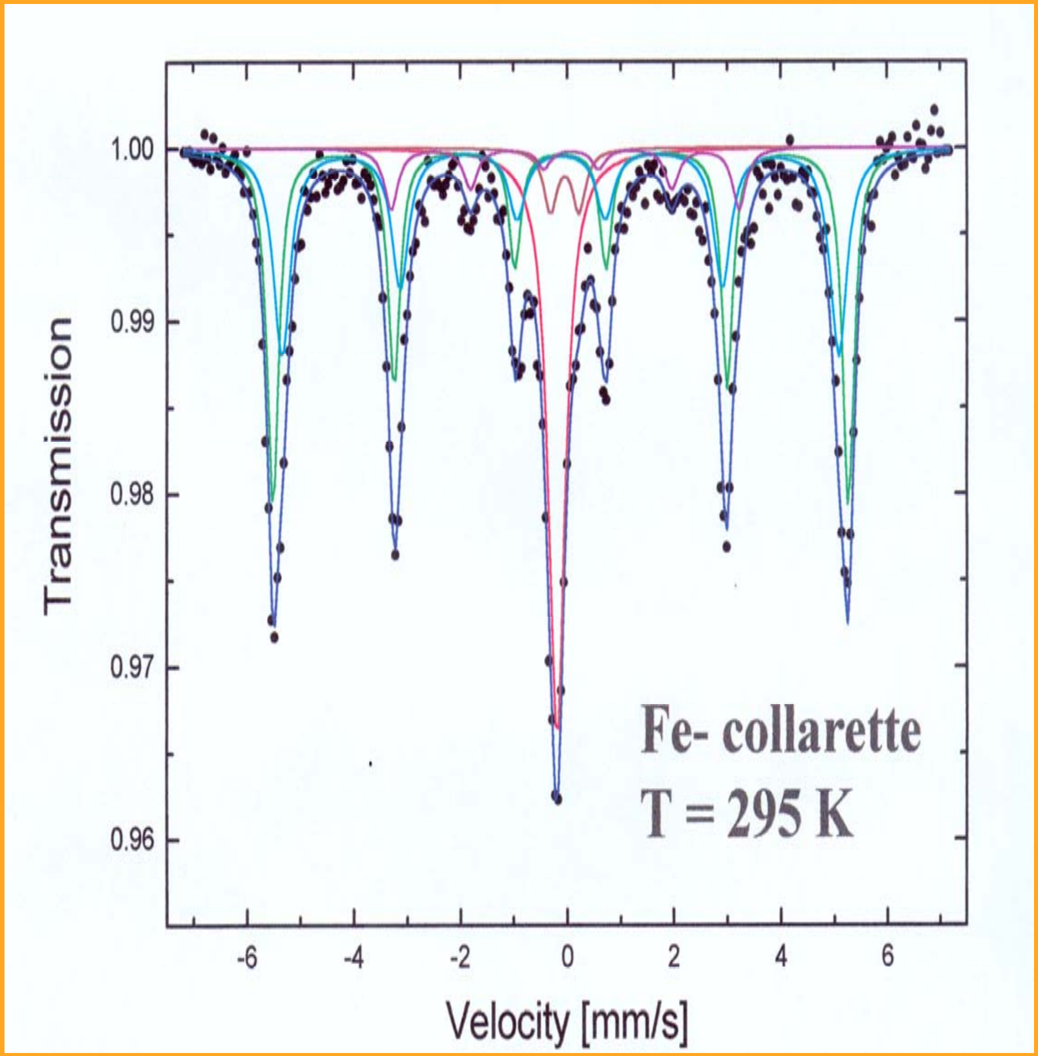
Si $\tau < \tau_{medida}$ superparamagnetism

Critical volume to detect superparamagnetism:

$V_{sp}=25(k_B T/K)$ $\tau_{static}=100$ s $T_B=KV_{sp}/25k_B$

$V_{sp}=4.5(k_B T/K)$ $\tau_{mössbauer}=10^{-7}$s $T_B=KV_{sp}/4.5k_B$

Móssbauer spectroscopy



No indication of SP relaxation at room temperature

Estimated particle size 13-9 nm (interparticle interaction)

α–Fe

Two sextets (34T and 31T)

Fe_3C

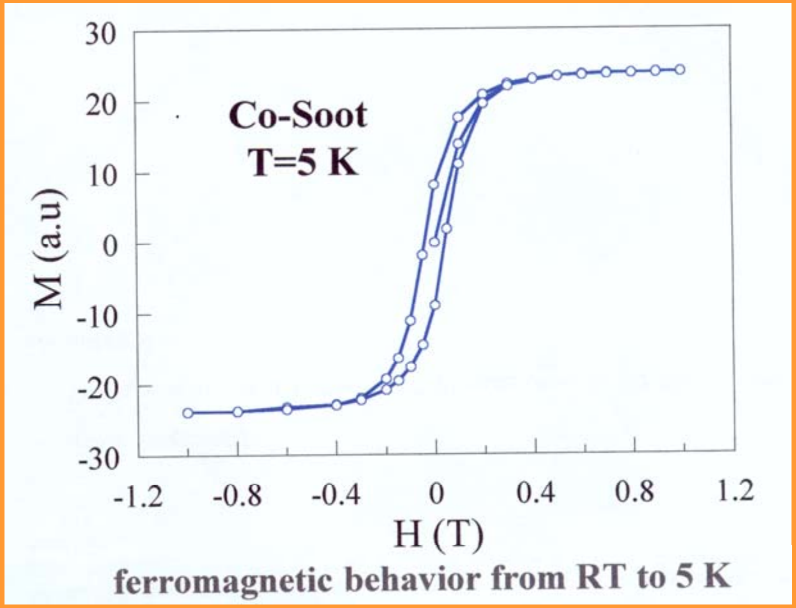
A sextet (25.1 T)

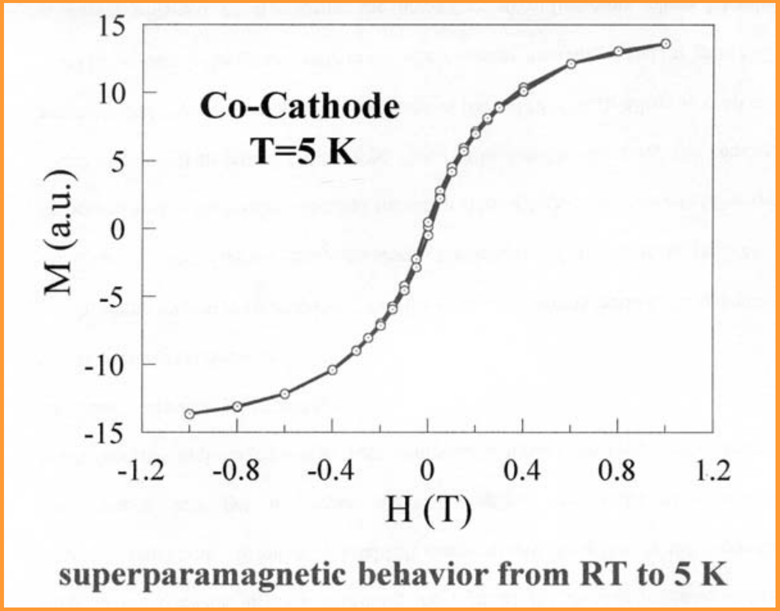
γ-Fe

Singlet and doublet

H.R. Rechenberg et al. J. Magn. Magn. Mat 226-230 (2001) 1930

Magnetization measurements





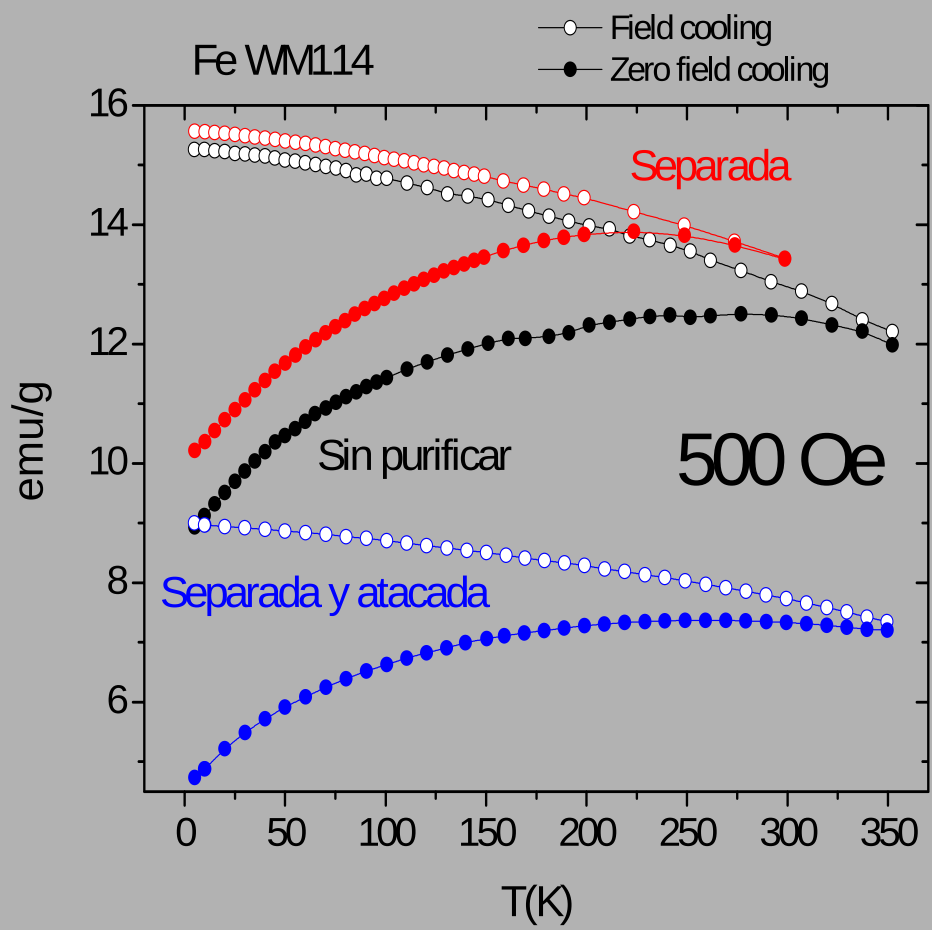
Blocked particles

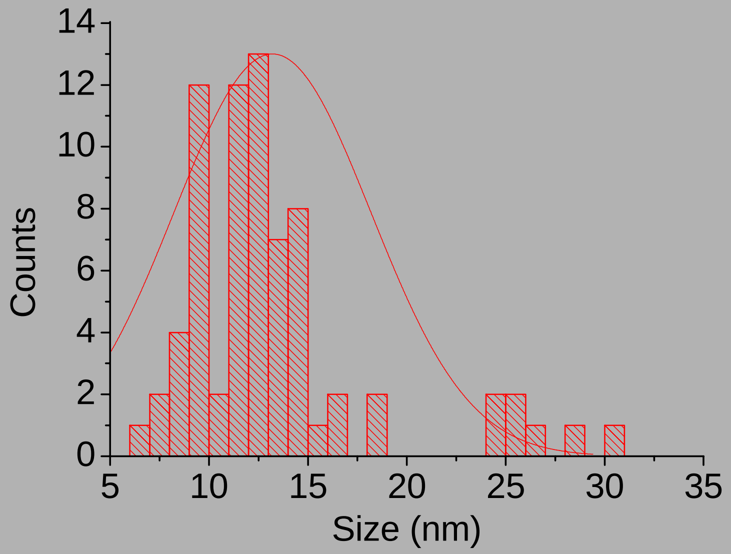
Large/correlated particles

Superparamagnetic particles

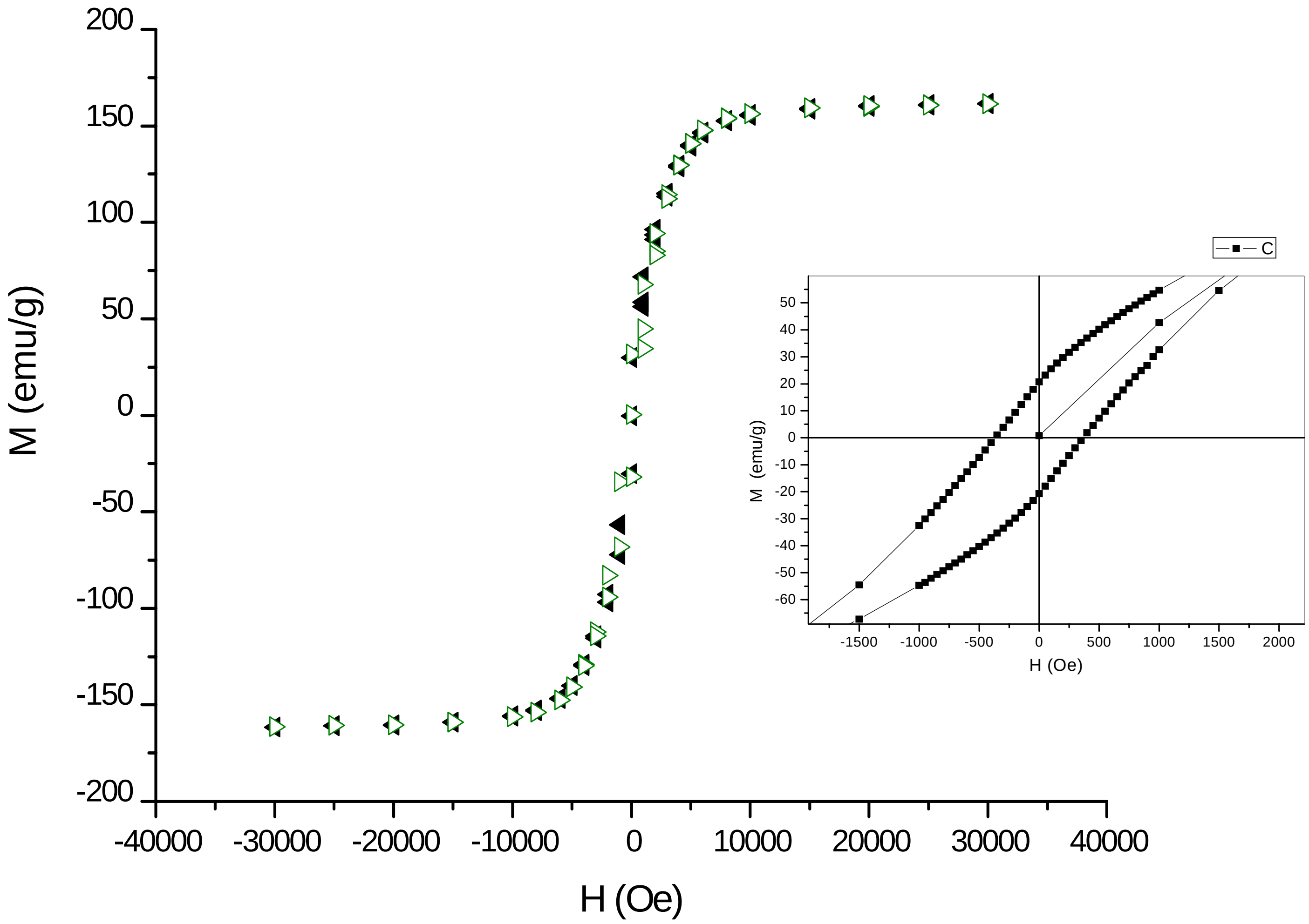
Small particles

Blocking temperature is determinaed from FC and ZFC

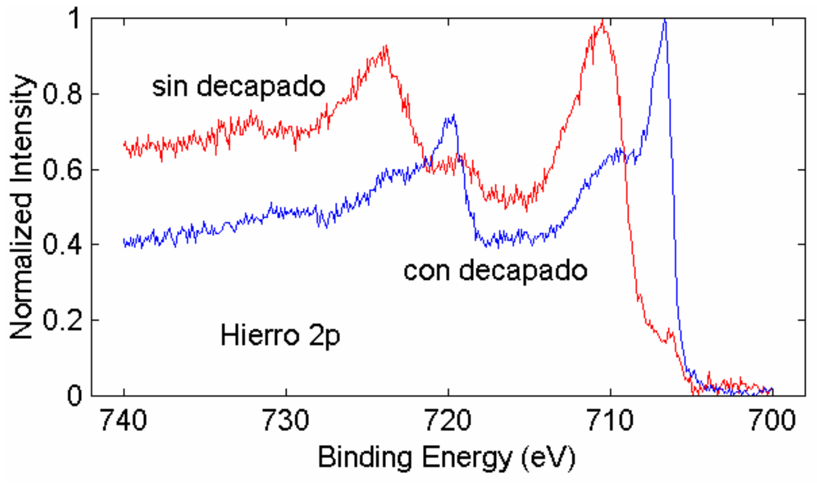


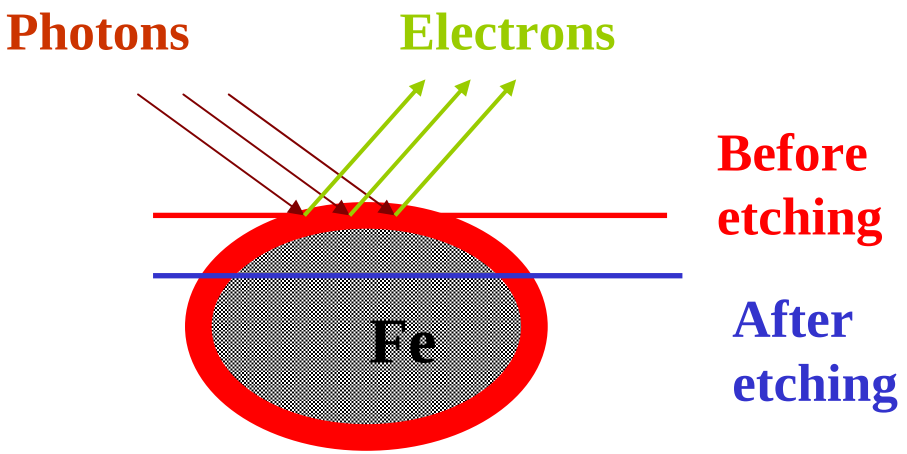


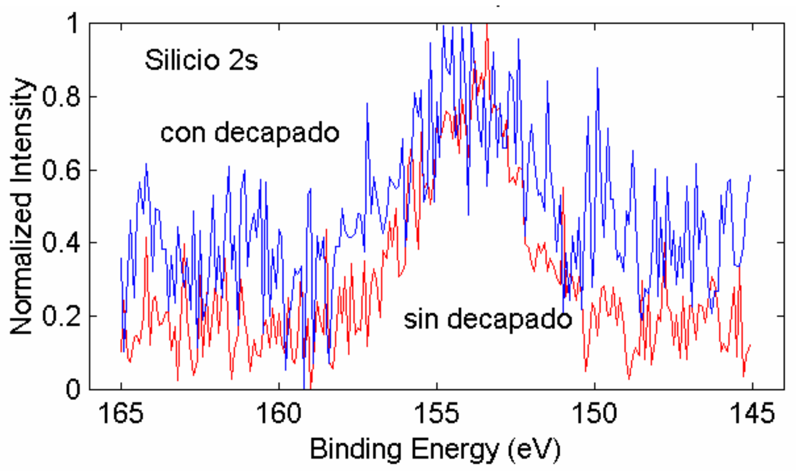
Silica encapsulated Fe nanoparticles

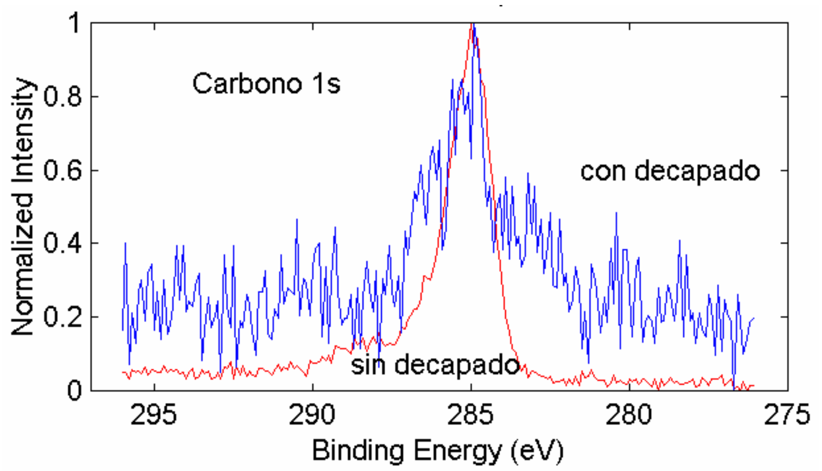


Fe encapsulated in Silica X-Ray Photoelectron Spectroscopy

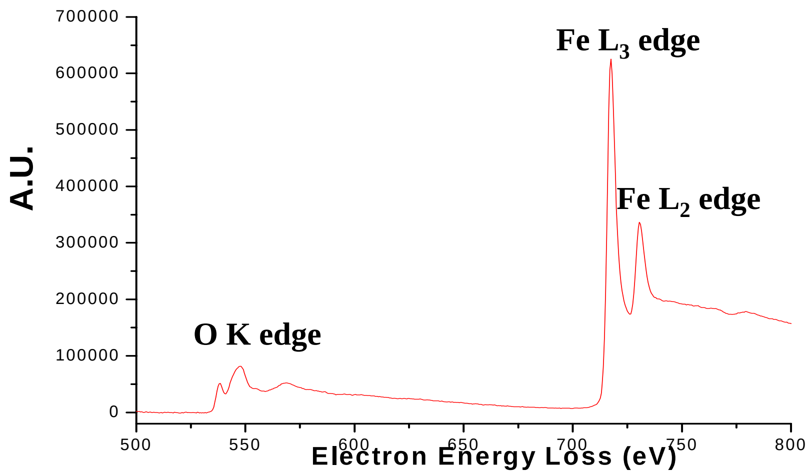


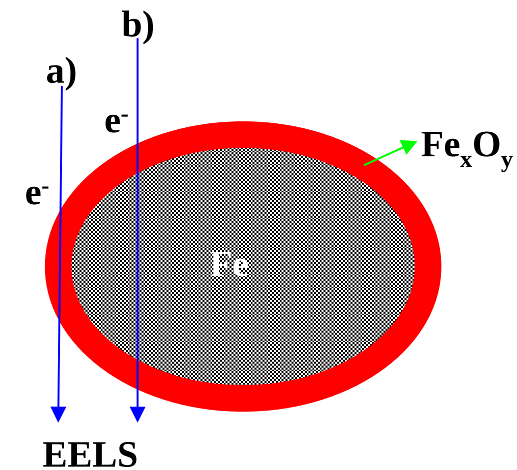




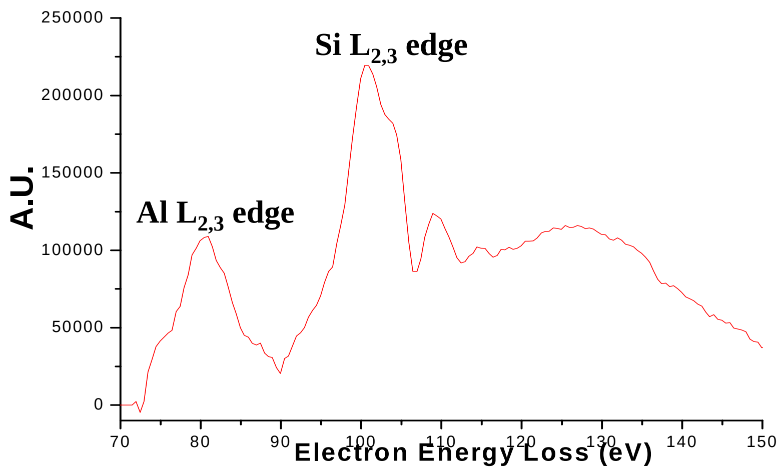


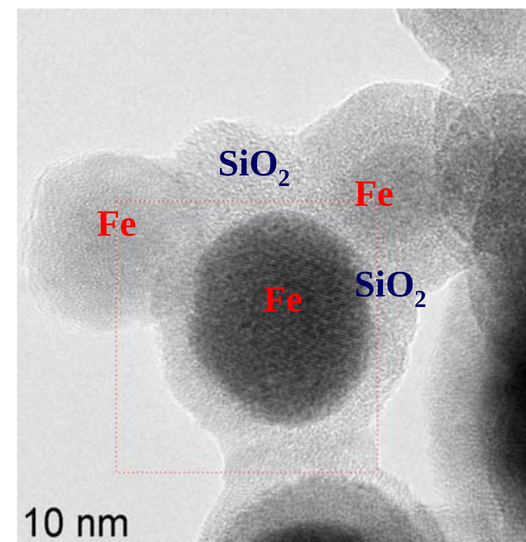
Fe encapsulated nanoparticles Electron Energy Loss Spectra (EELS) (in collaboration J. Arbiol)



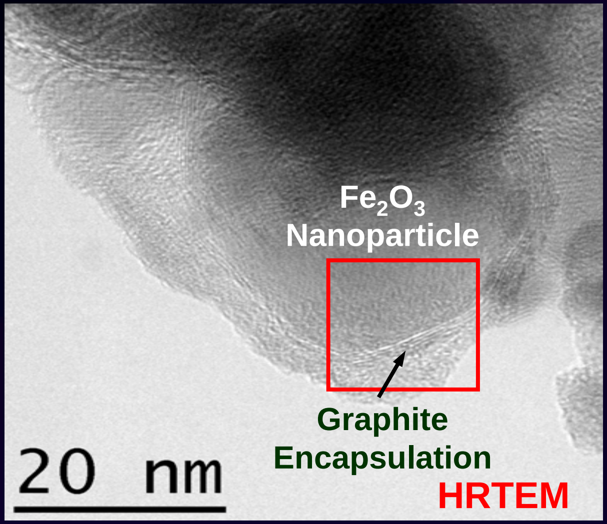


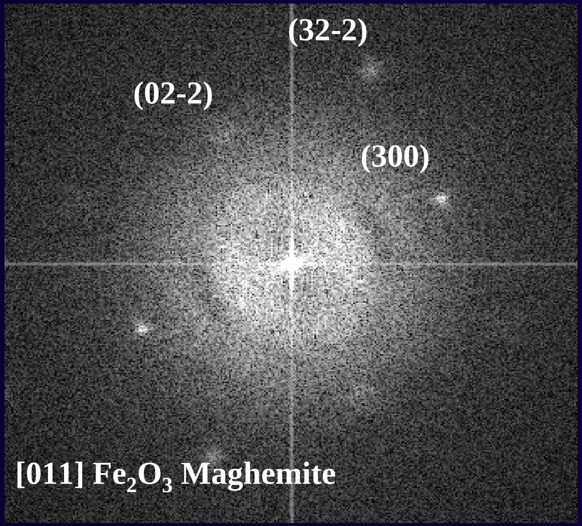
aSurface Spectrum
bInside Spectrum

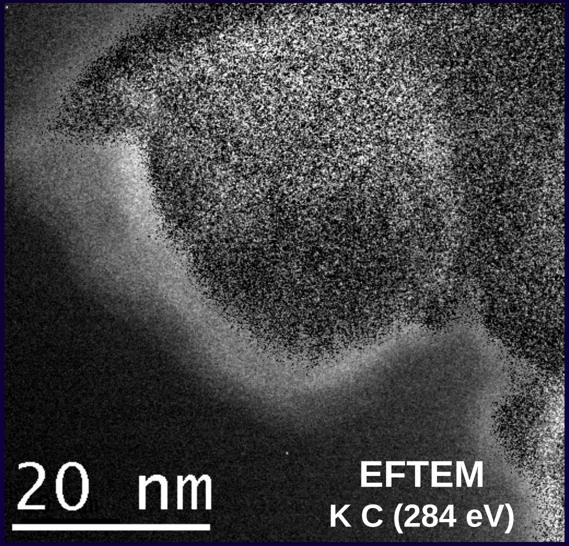


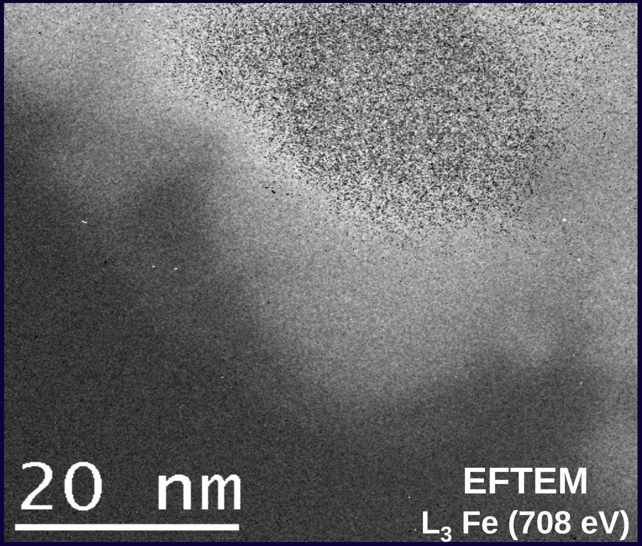


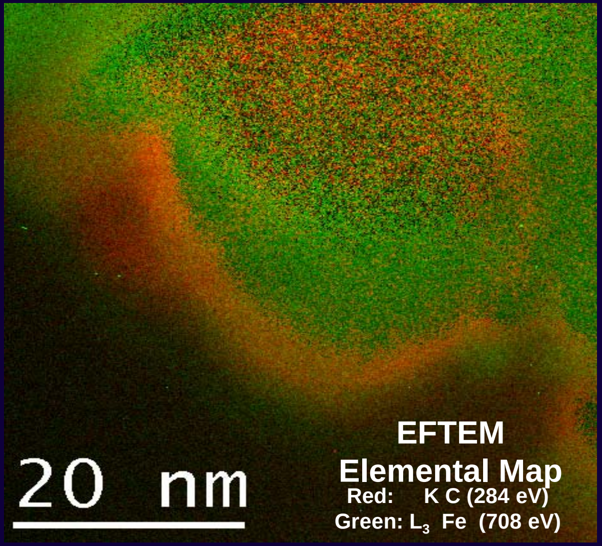
High Resolution Transmision Electron Microscopy of carbon encapsulated iron nanoparticles











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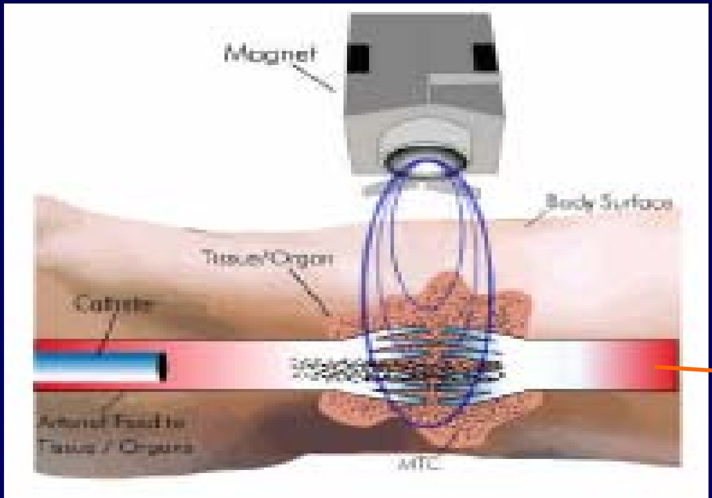
BIOFERROFLUIDS AS THERAPEUTIC CARRIERS

-They should be magnetic to by guided by applied magnetic fields

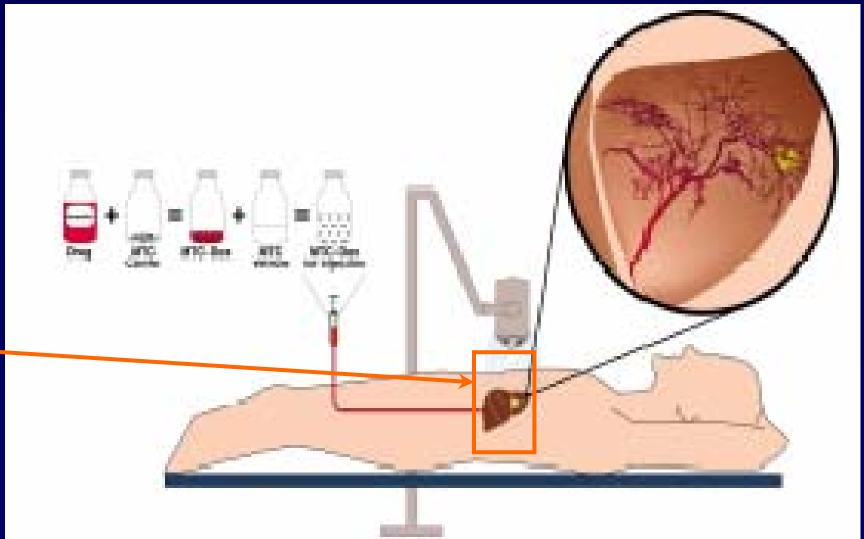
-The magnetic materials are not biocompatibles

-The nanoparticles should be encapsulated

-The sourrounded material should be able to adsorb and desorb the drug

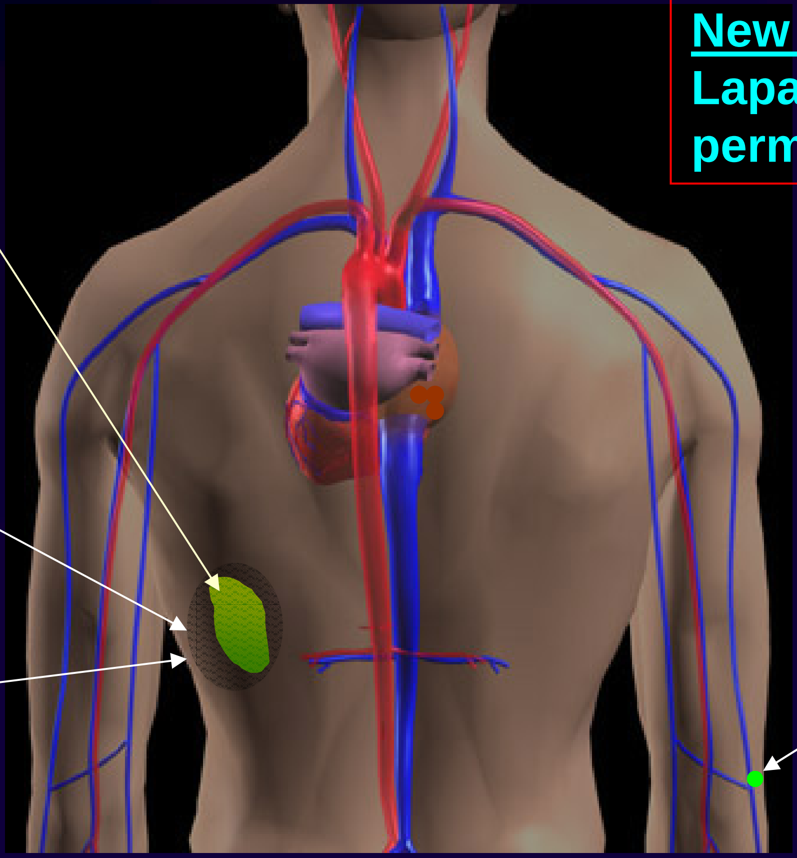


J.Johnson et al., EC&M 3 (2002) 12

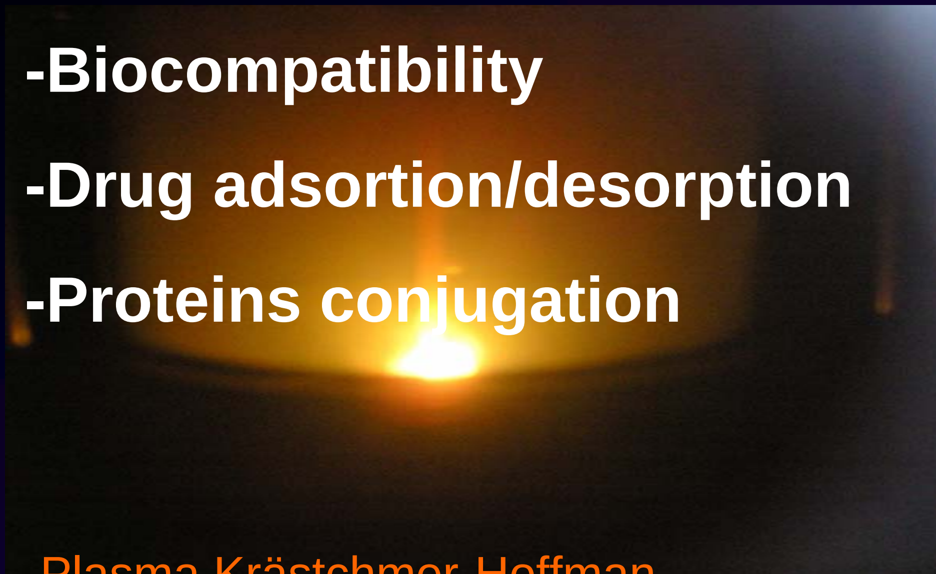


Local drug delivery by using magnetic carriers

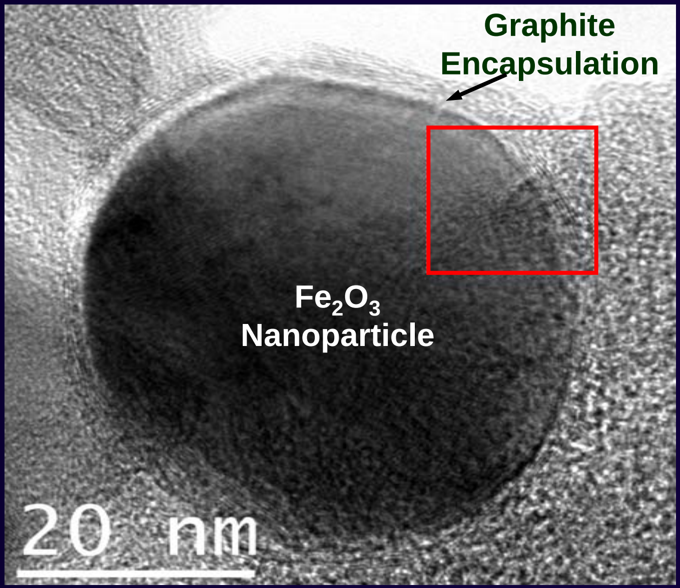
New development at the INA
Lapararoscopic implant of a permanent magnet

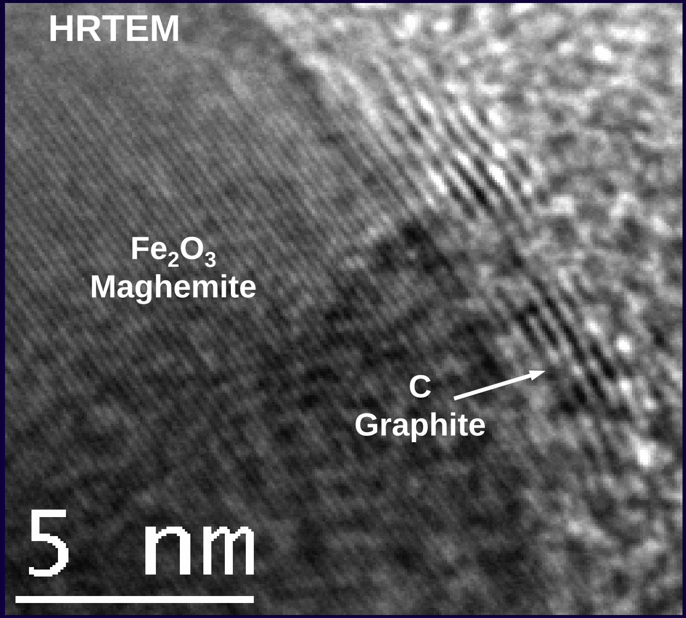


BIOFERROFLUIDS

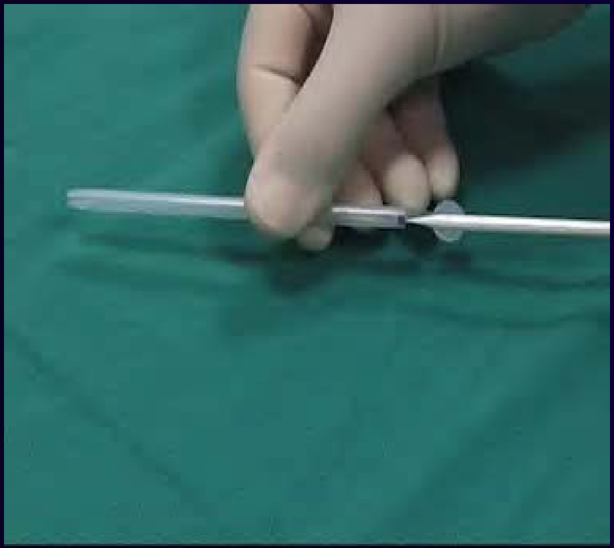


Plasma Krästchmer-Hoffman





Endoscope



Trocar for magnet implantation

Implant

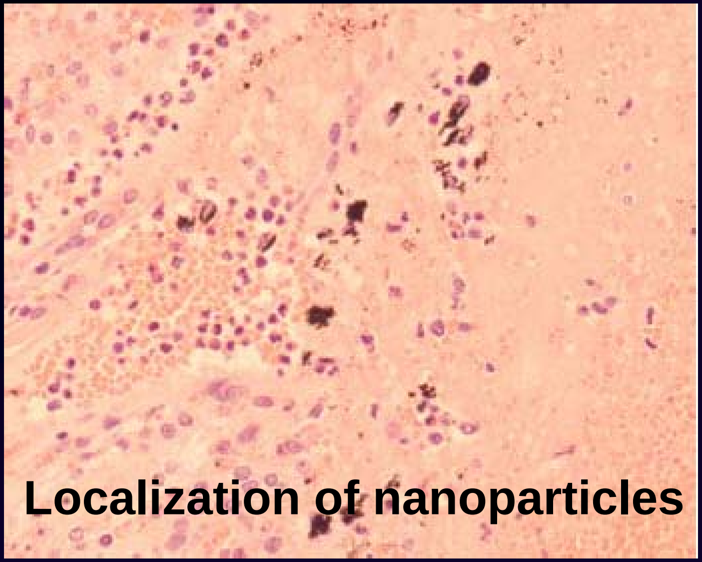
Bioferrofluid

Intravenous administration

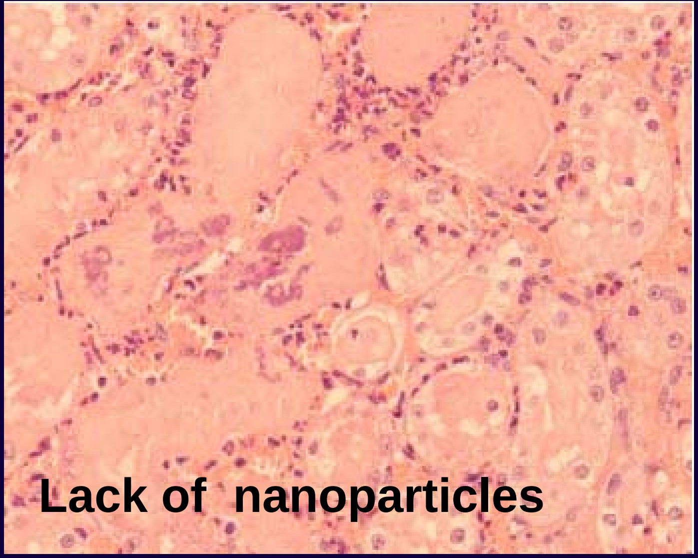
In-Vivo localization of magnetic particles by systemic administration and using magnetic implants

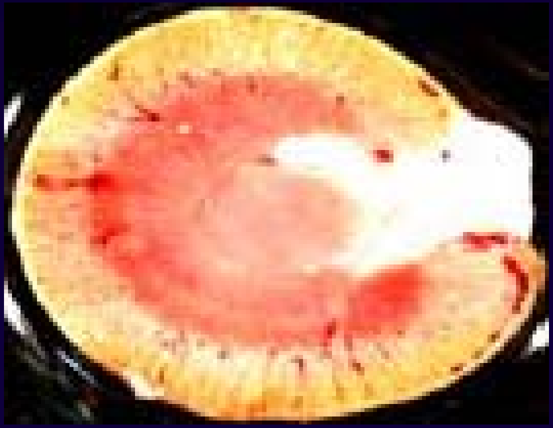
In coll. Hospital Clínico Veterinario

Magnet implant in the left kidney



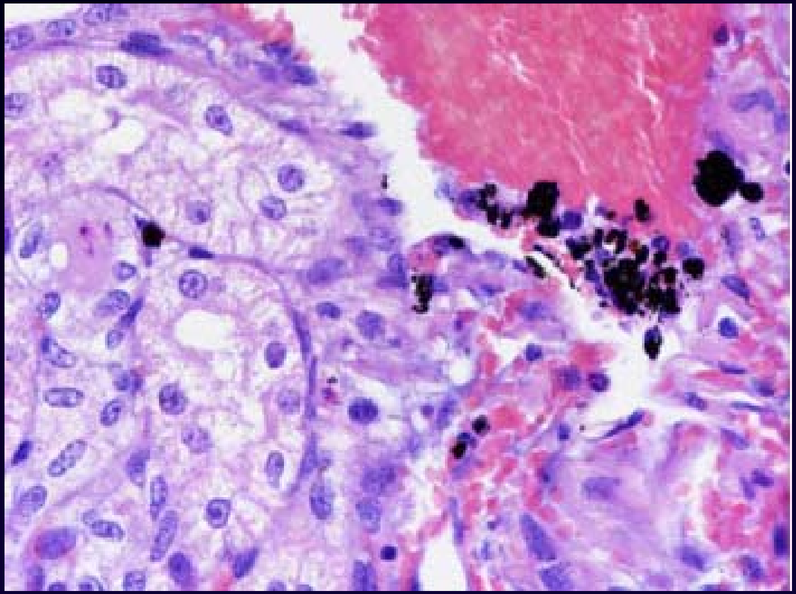
Right kydney witout magnetic implant



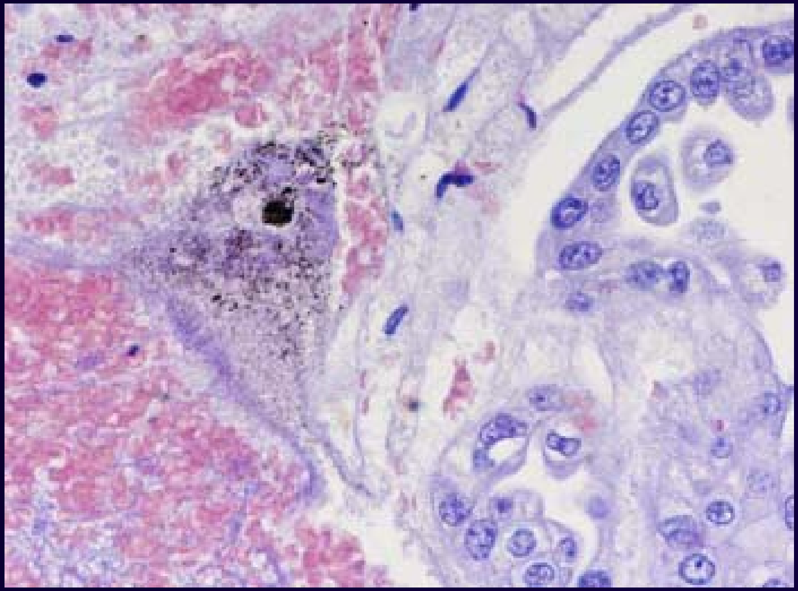


Kidney with magnetic implant:

Moderate concentration of nanoparticles



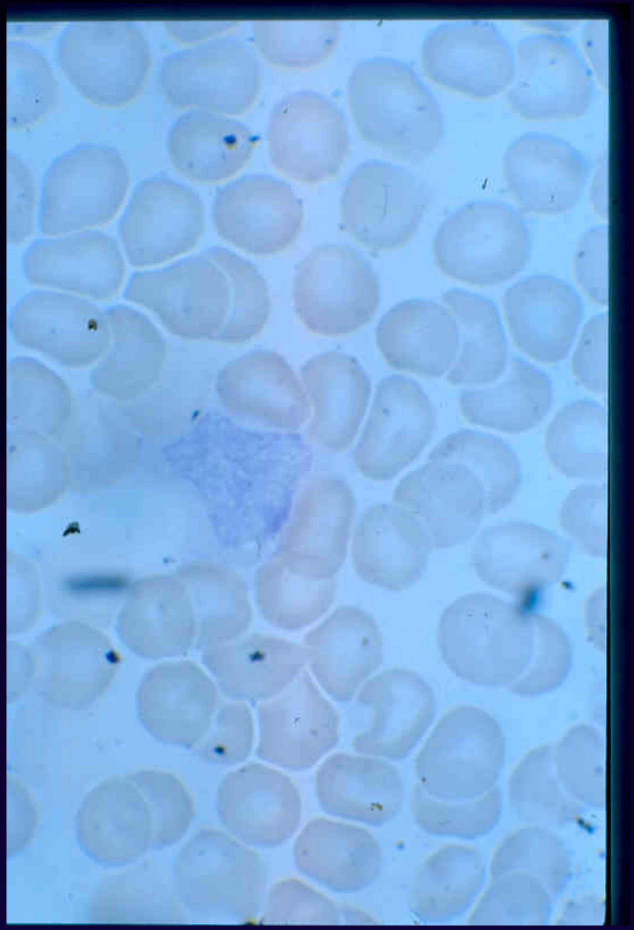
Rabbit 22

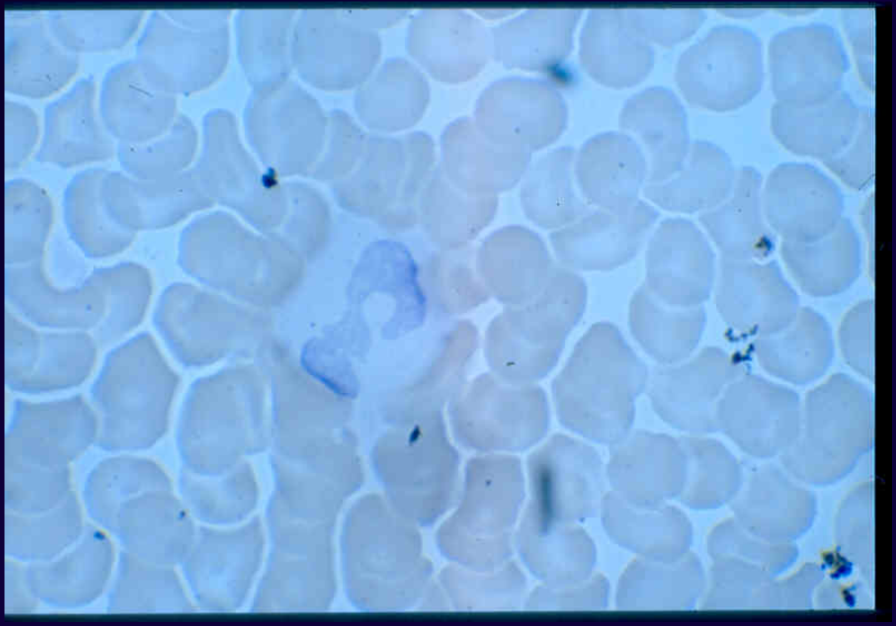


Rabbit 23

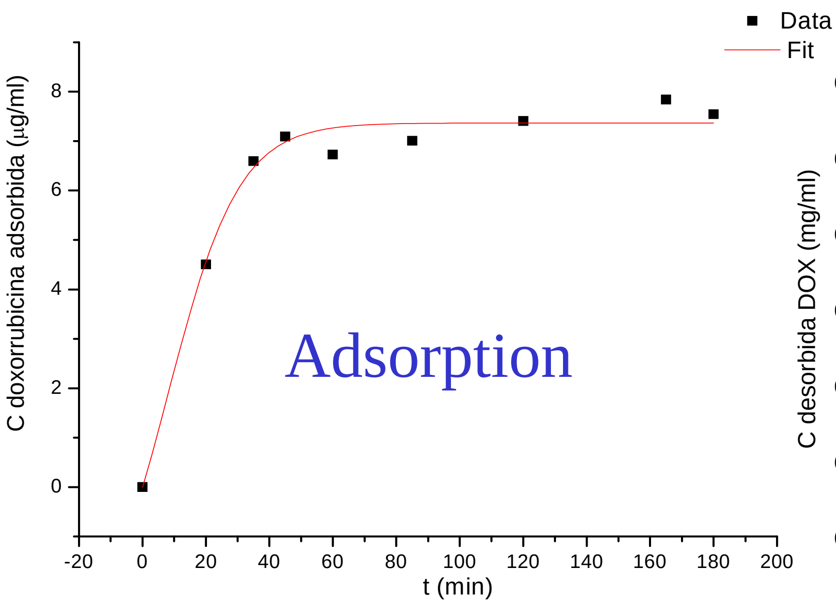
Nanoparticles traveling in blood

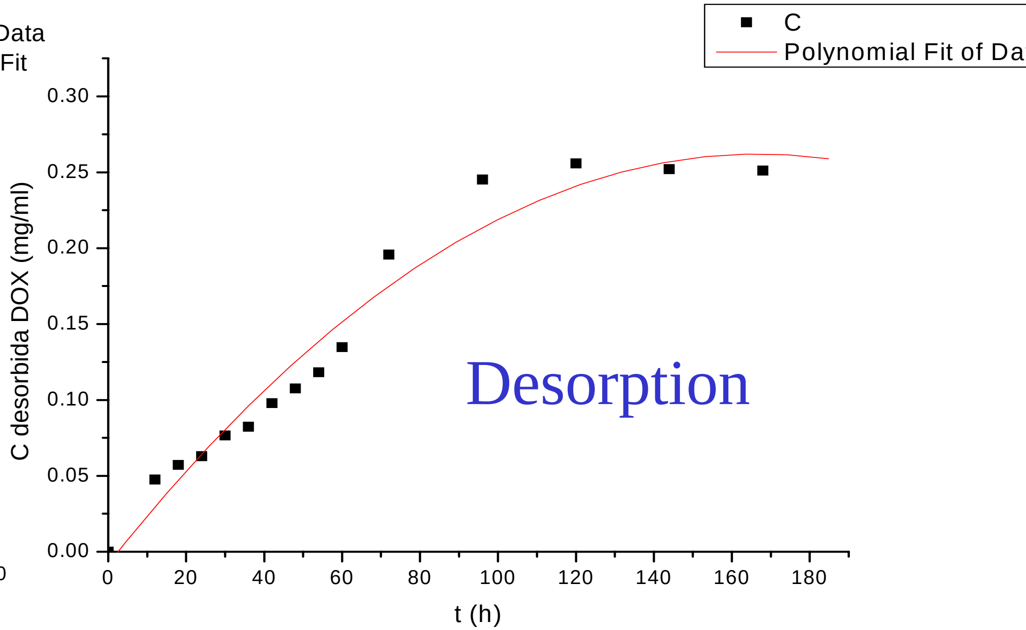
Tested biocompatibility





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

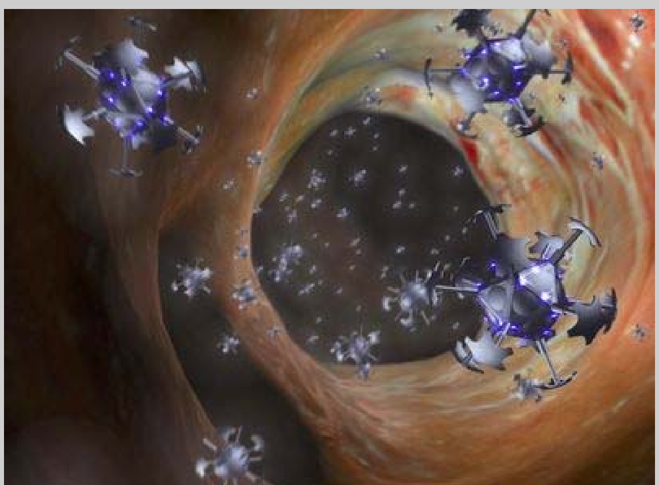




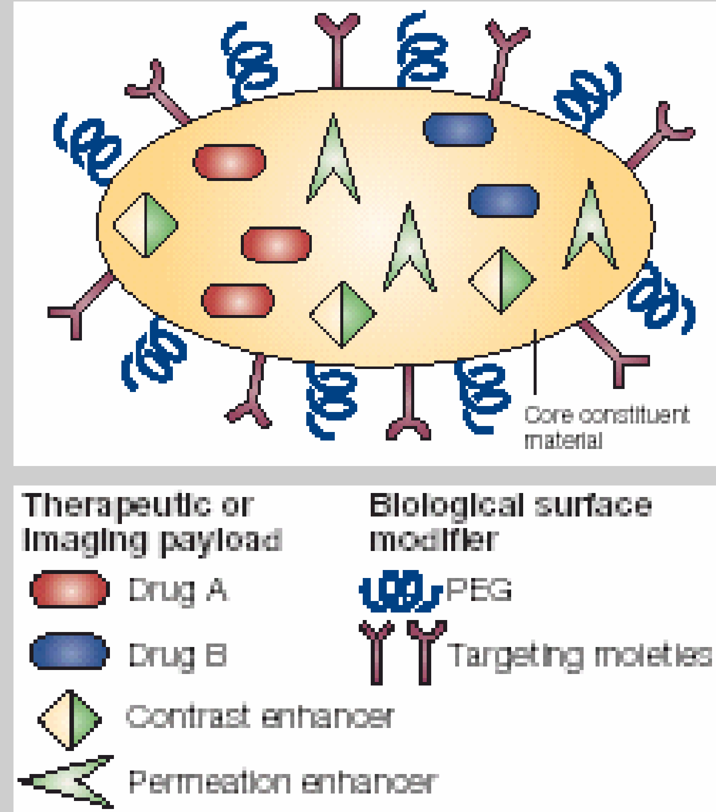
Saturation after 20 minutes

Complete release after 100 hours

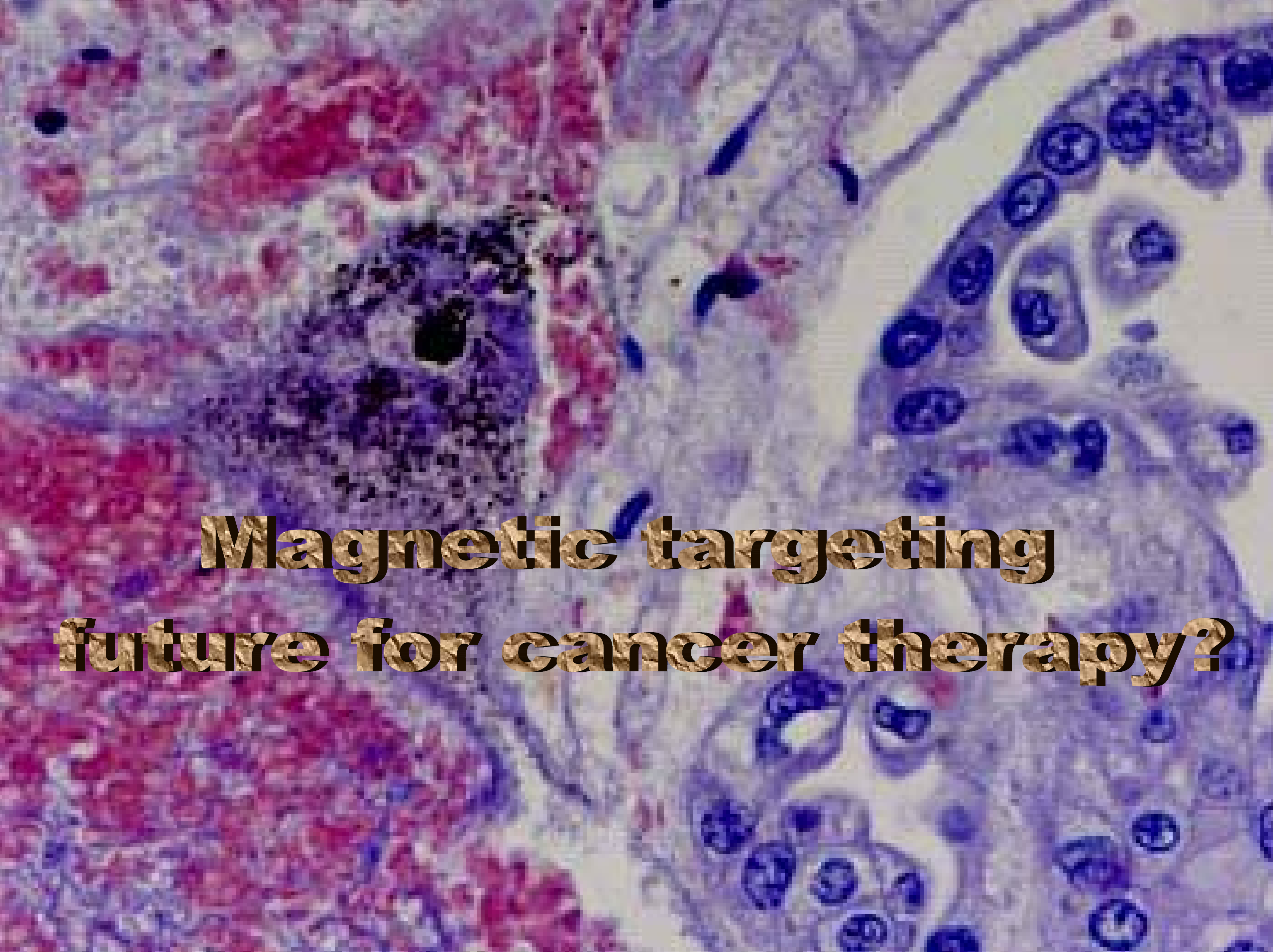
Matter manipulation at atomic level



Targeting



Inteligent nanovectors


Magnetic targeting
future for cancer therapy?


THANKS VERY MUCH!