magnetic nanoparticles – biomedical applications

G3M

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Argentina

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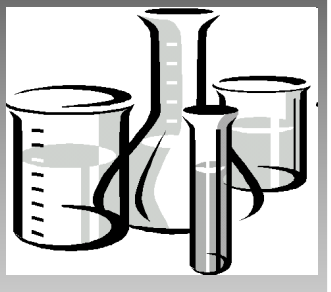
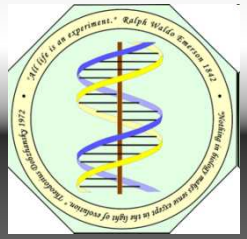
Vera Alvarez





Francisco H. Sánchez

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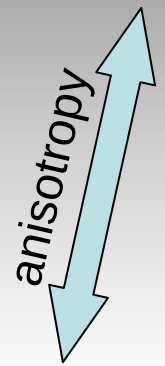
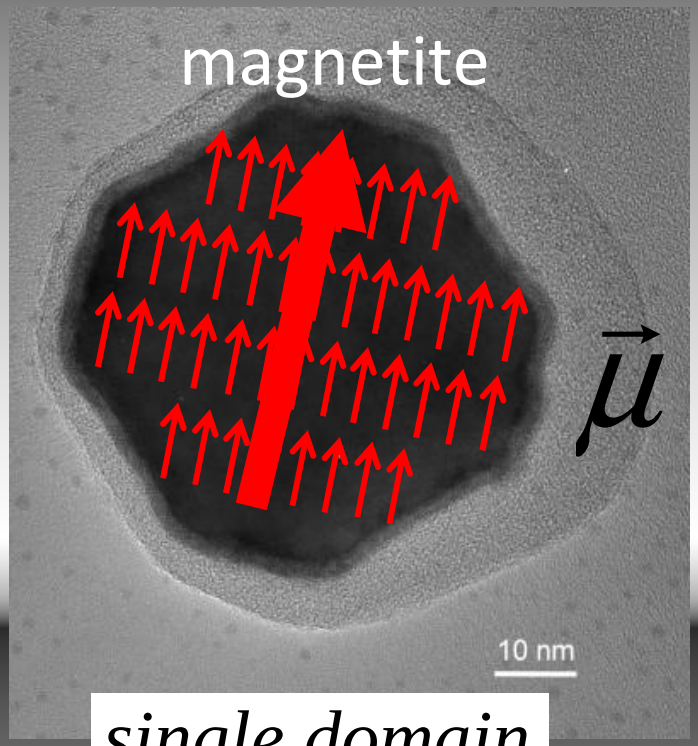
Eulanest

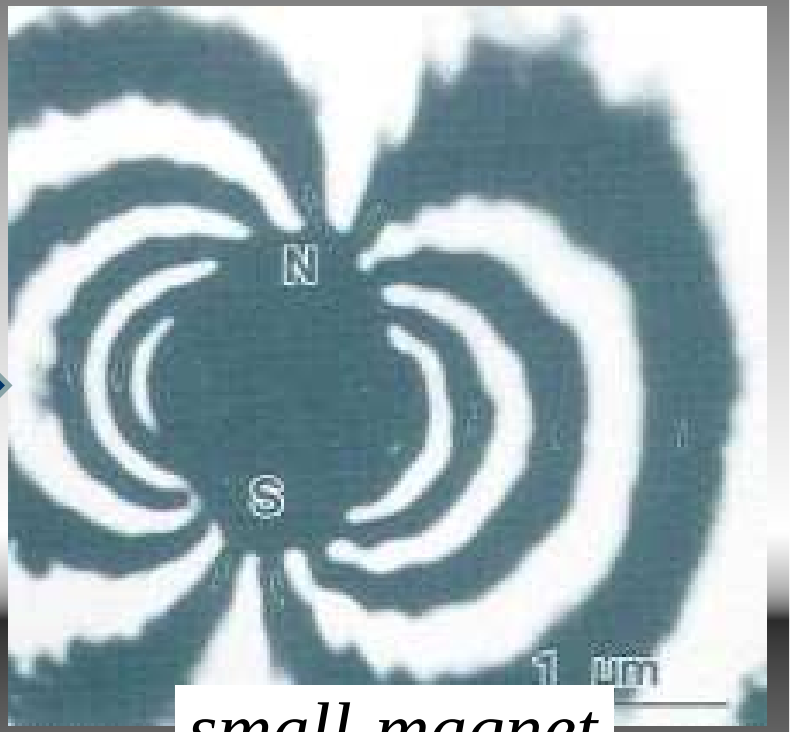
Magnetic nanoparticles





$\vec{\mu}$

single domain



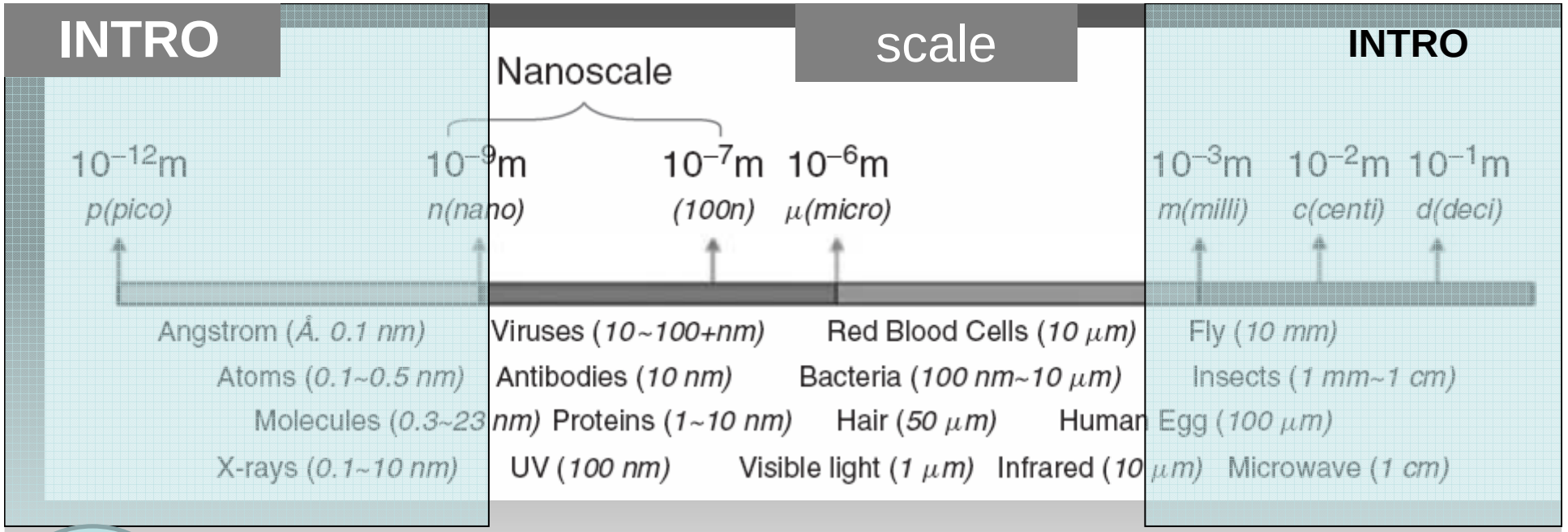
small magnet

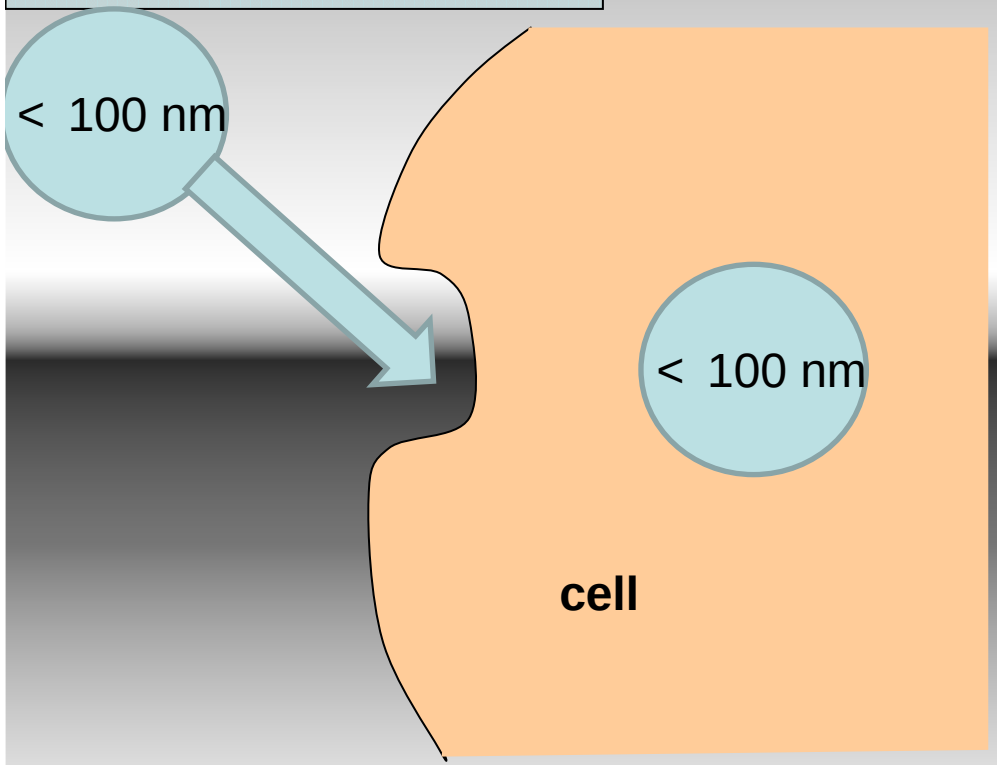
Eulanest

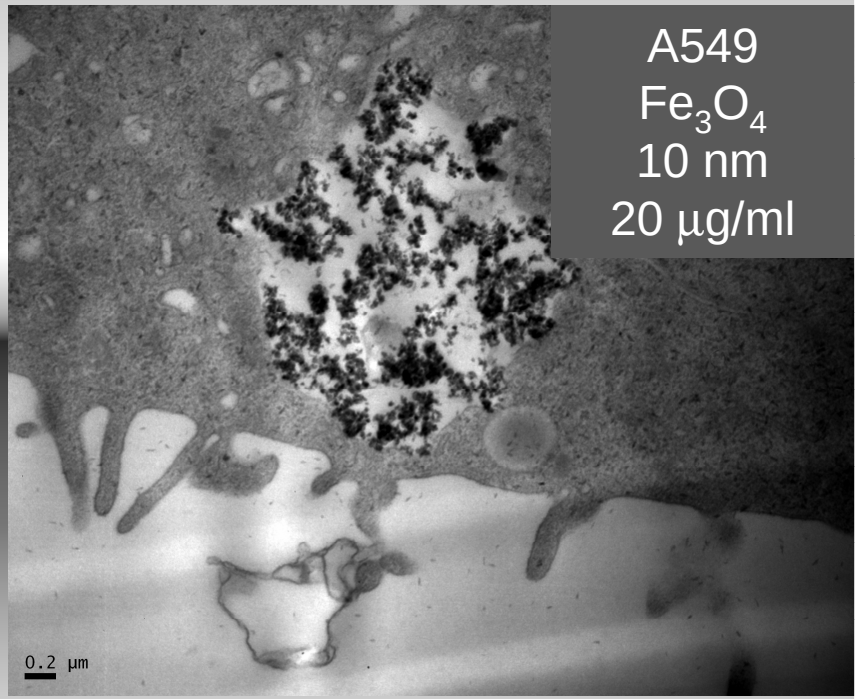
INTRO

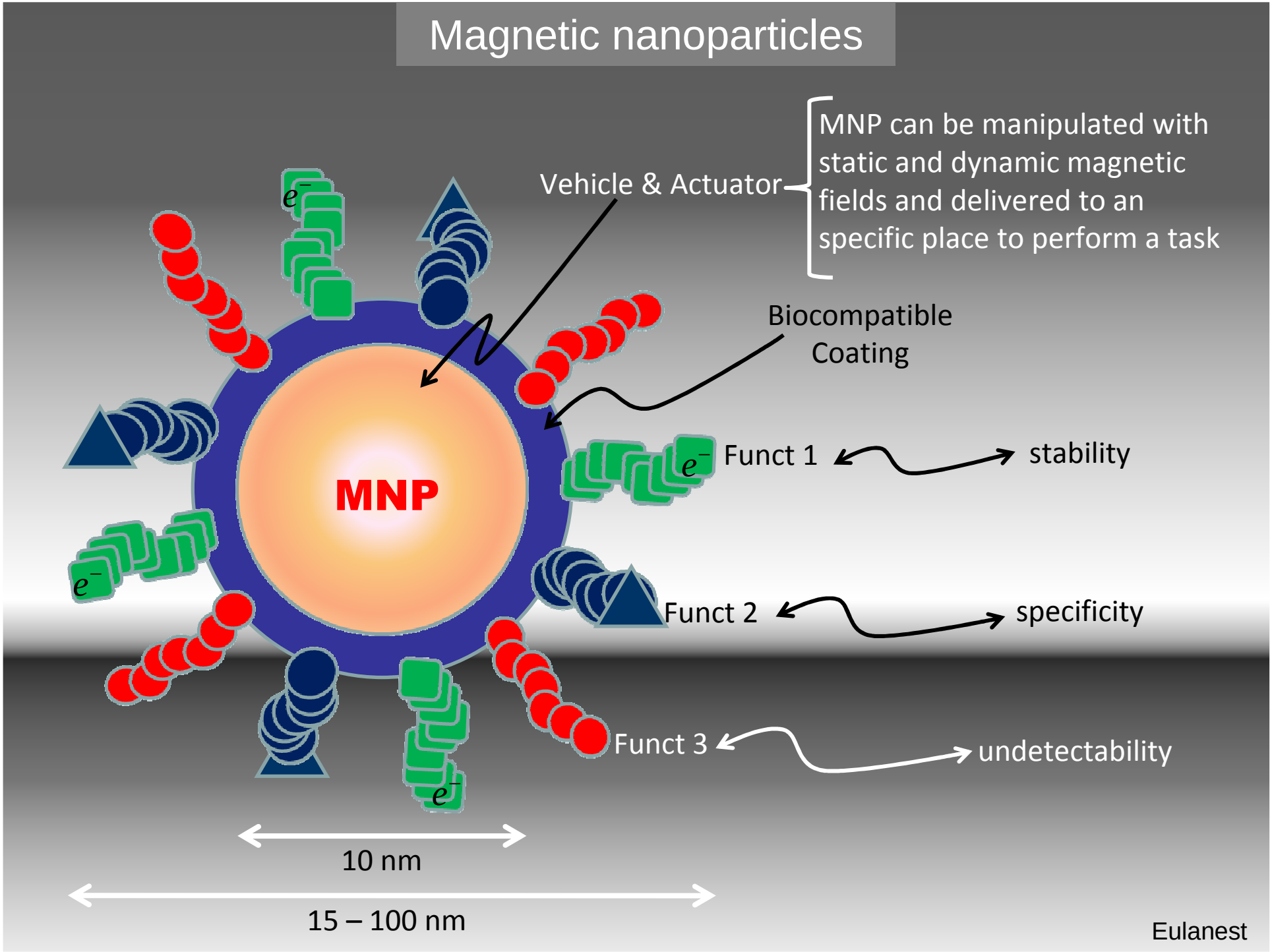
scale

INTRO



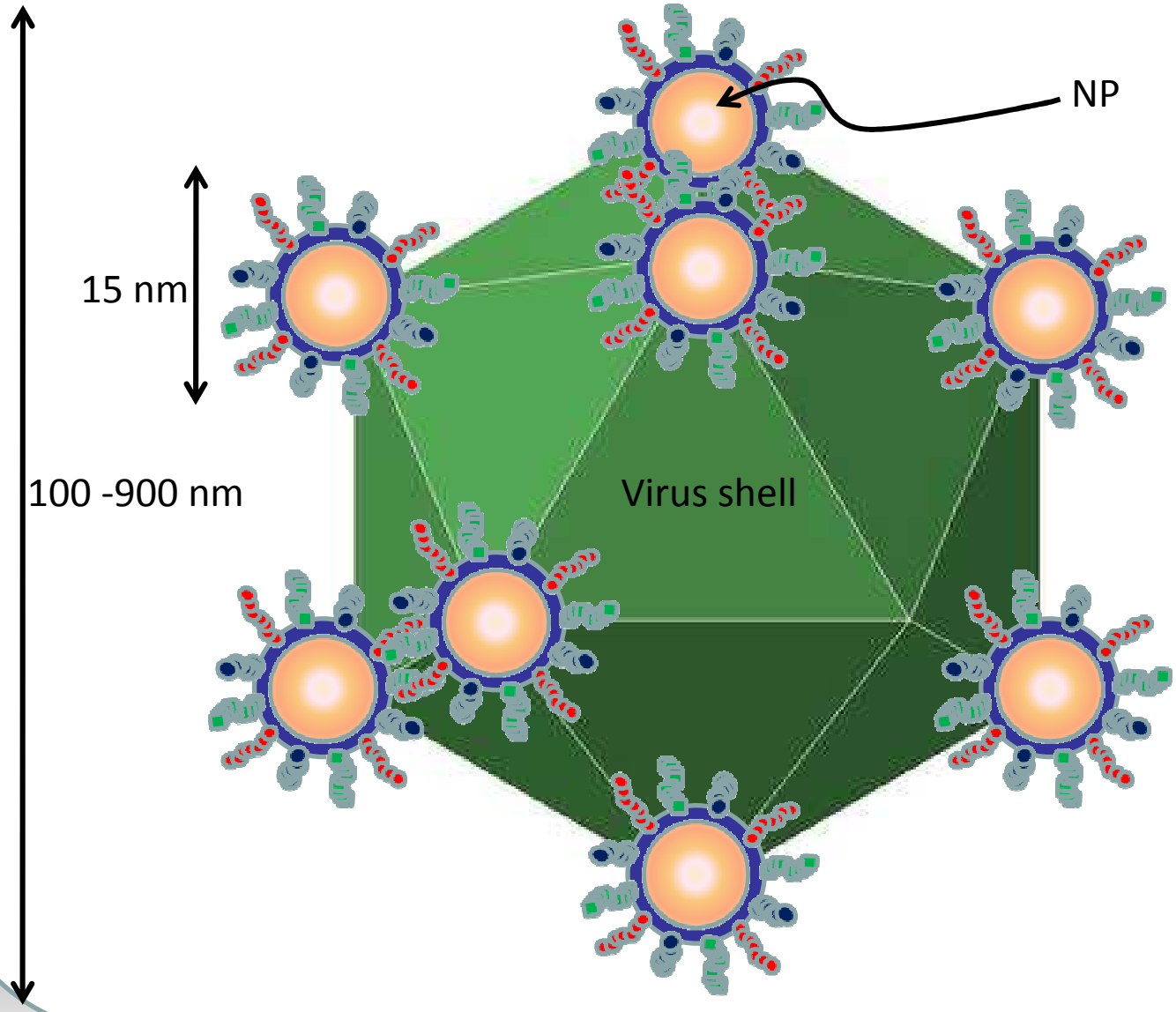





Magnetic nanoparticles
MNP can be manipulated with static and dynamic magnetic fields and delivered to an specific place to perform a task
Vehicle & Actuator
Biocompatible Coating
MNP
Funct 1
stability
Funct 2
specificity
Funct 3
undetectability
10 nm
15 – 100 nm
Eulanest

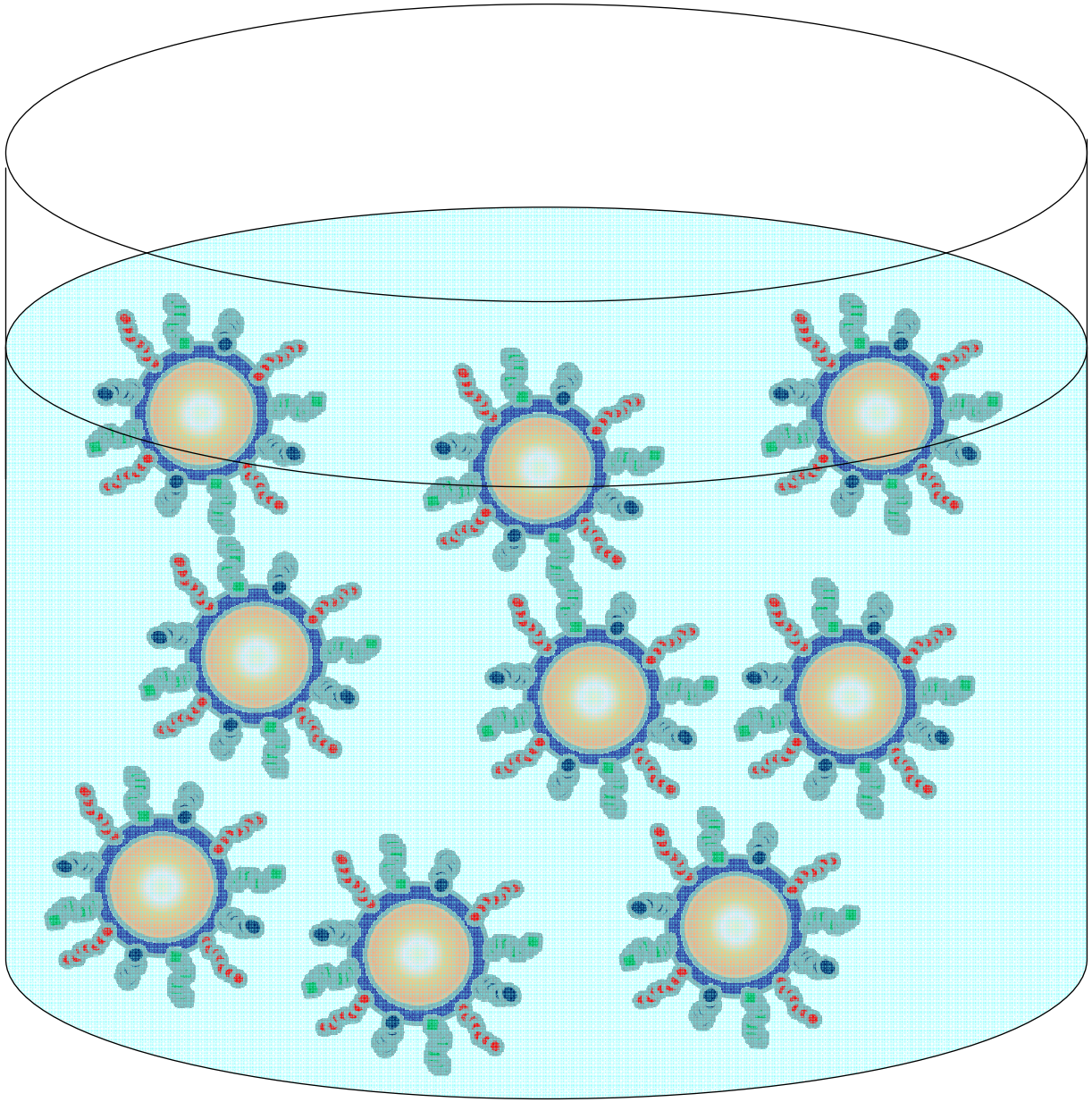
Complexes

MNP can be combined with other nanoscale entities to accomplish more complicated tasks



requirement

Ferrofluids



Eulanest

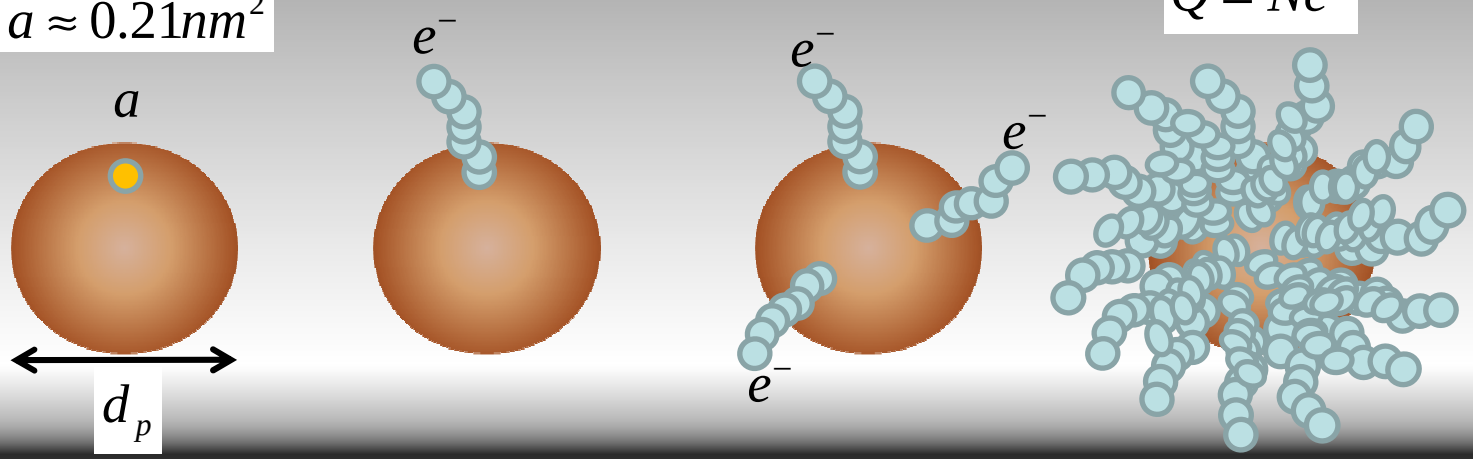
Electric charge

Ferrofluids stability

Binding of charged surfactant chains

a = area of surfactant “head”

$a \approx 0.21 nm^2$



Ideal max number of chains

$$N_{ideal} = \frac{area_{MNP}}{a} = \frac{\pi d_{MNP}^2}{a} \approx 1000\,(10\,nm)$$

Eulanest

Electric charge

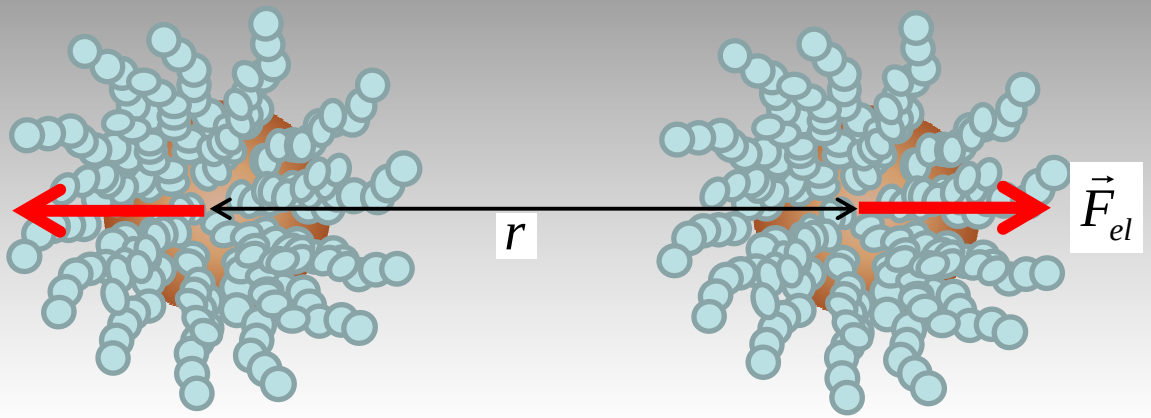
Ferrofluids stability

Binding of charged surfactant chains

$$Q = Ne^-$$

$$Q = Ne^-$$

$$F_{el} \approx \frac{N_{\max}^2 e^2}{4\pi\varepsilon_0 K r^2}$$



assuming

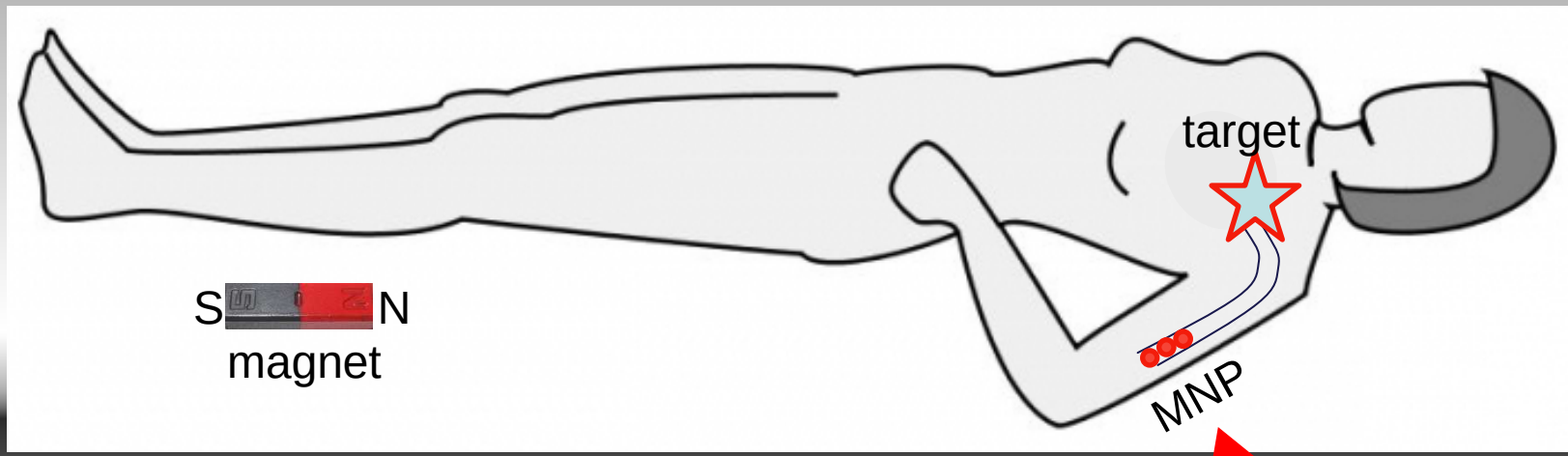
$$N_{\max} \approx 0.1 N_{ideal}$$

$$for\ r = d_{MNP} = 10nm$$

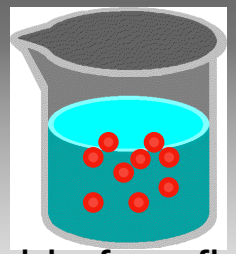
$$F_{el} \approx 0.6nN$$

Eulanest

Manipulation of MNP

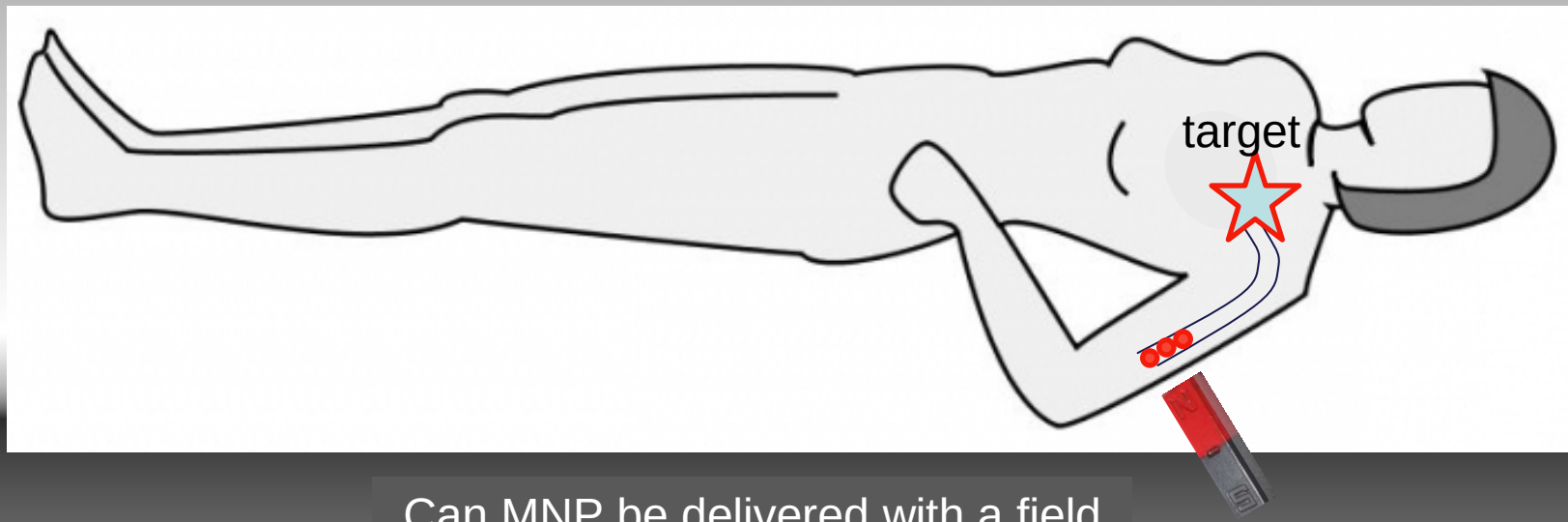


Can MNP be delivered with a field at a distance?



Stable ferrofluid

Manipulation of MNP



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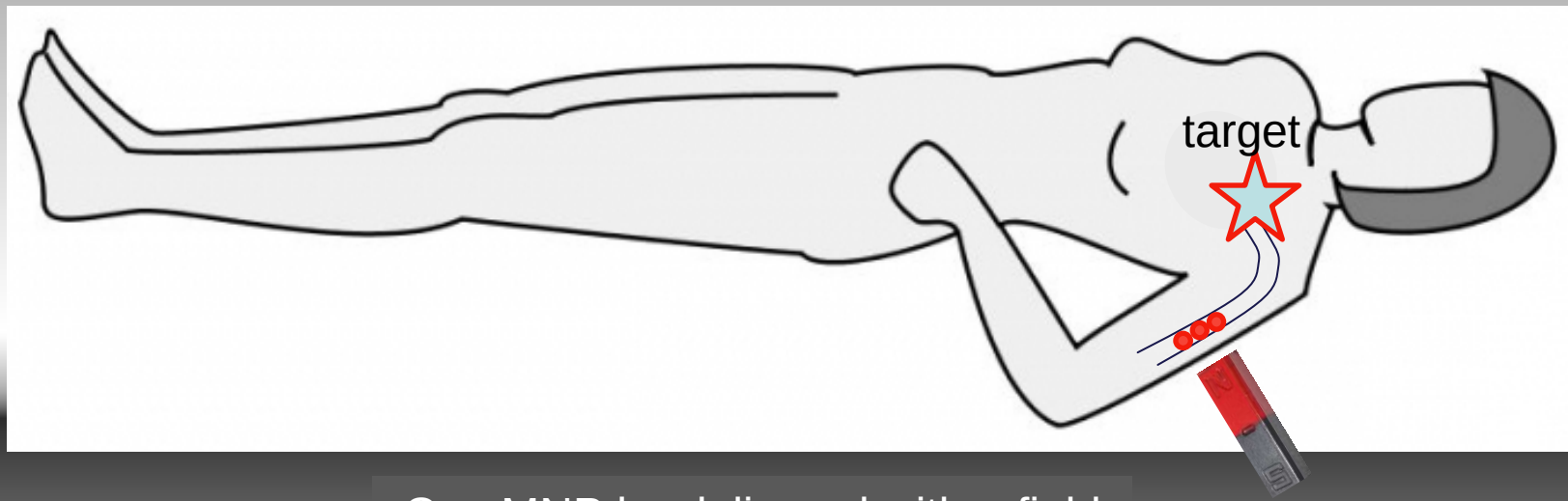

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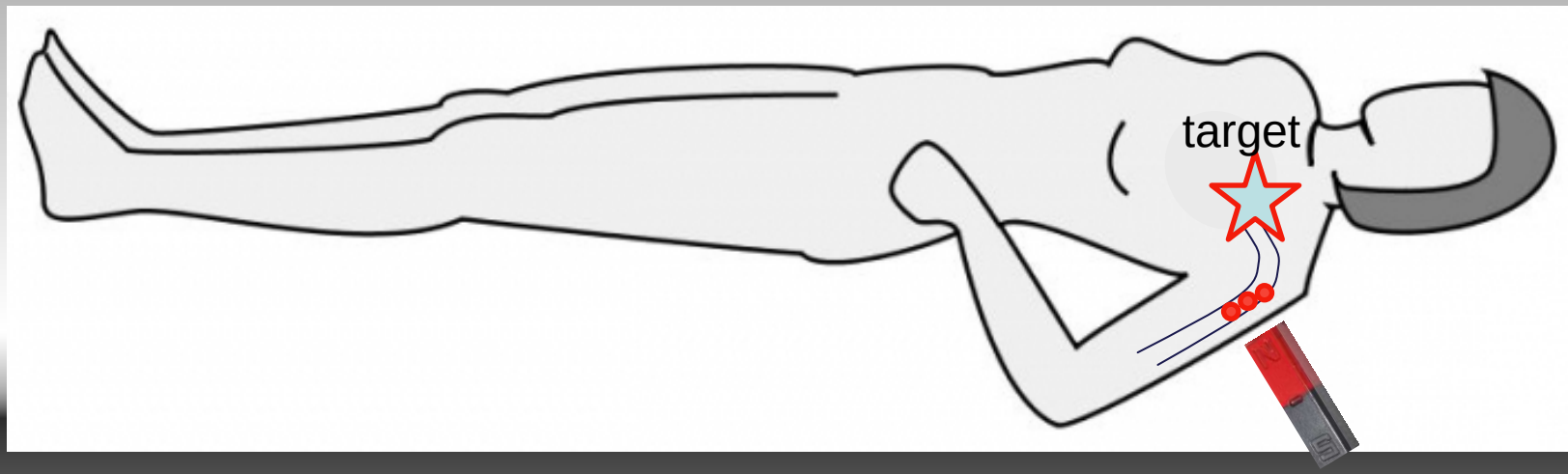

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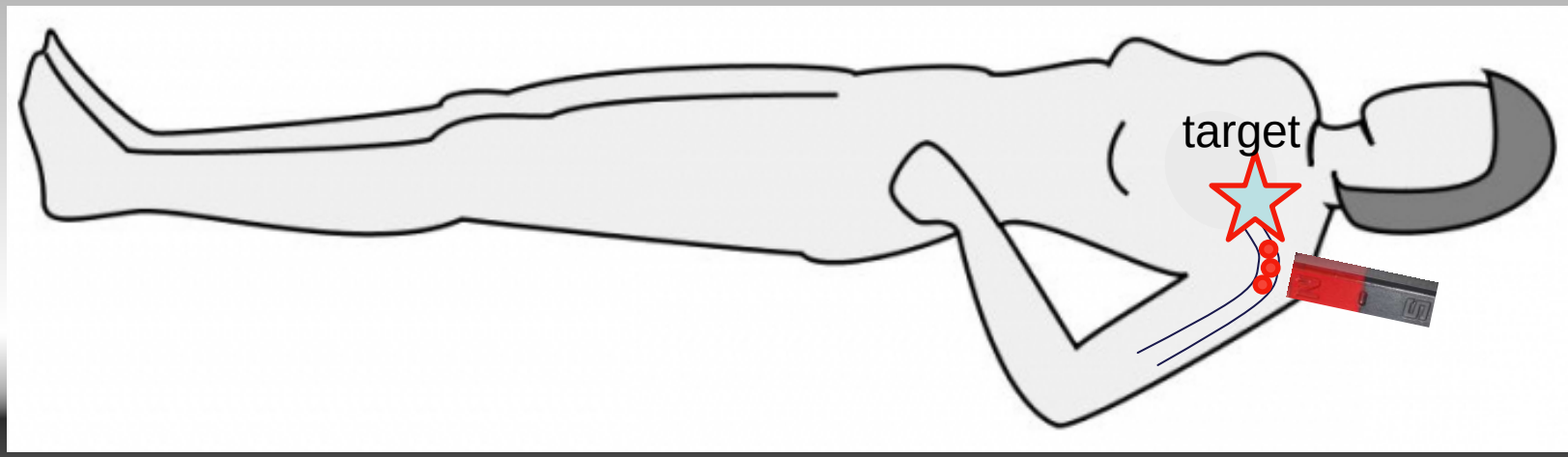

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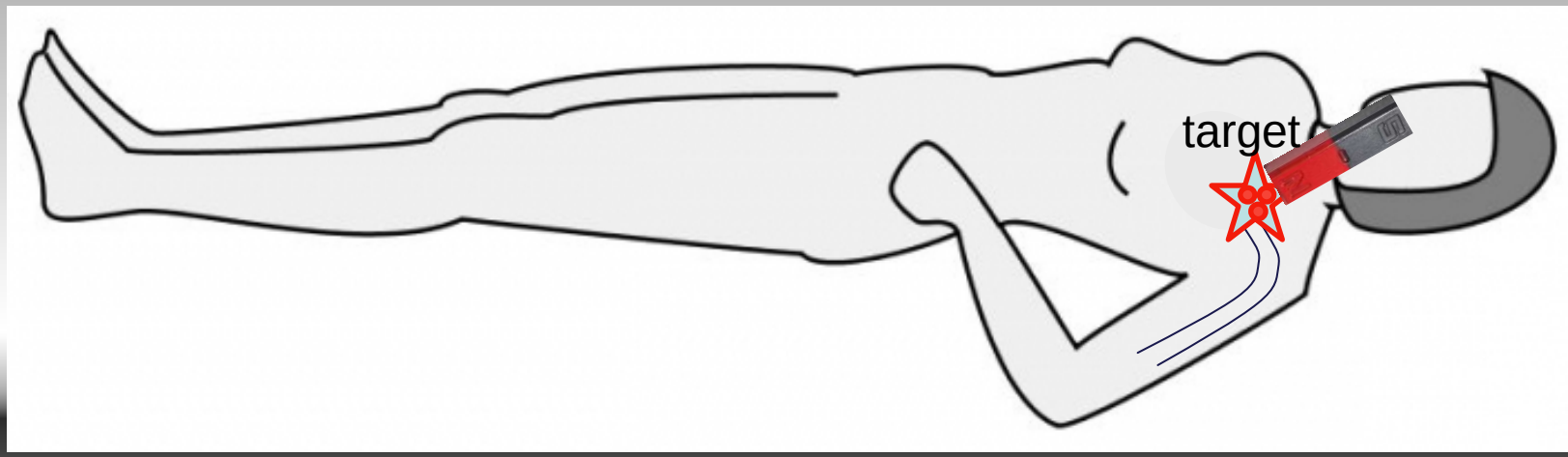
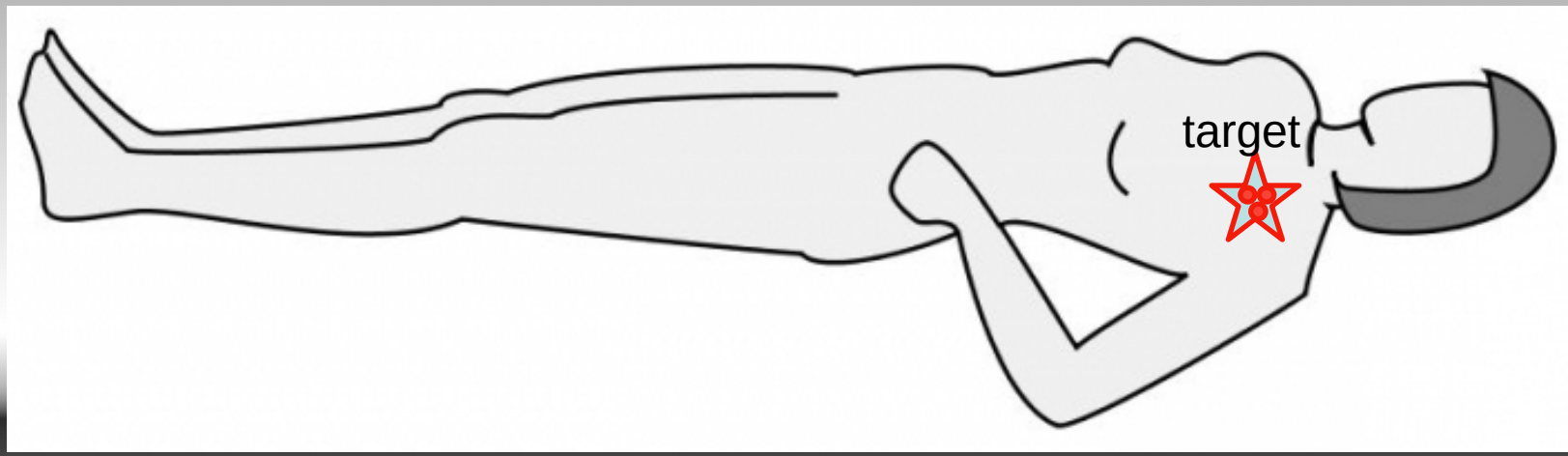
Manipulation of MNP



Can MNP be delivered with a field at a distance?

Manipulation of MNP

Transfection Drug release MR Imaging hyperthermia



Magnetic field

Manipulation of MNP

$$U_{\vec{B}} = -\vec{m} \cdot \vec{B} \Rightarrow \vec{F}_{\vec{B}} = \vec{\nabla}\left(\vec{m} \cdot \vec{B}\right)$$

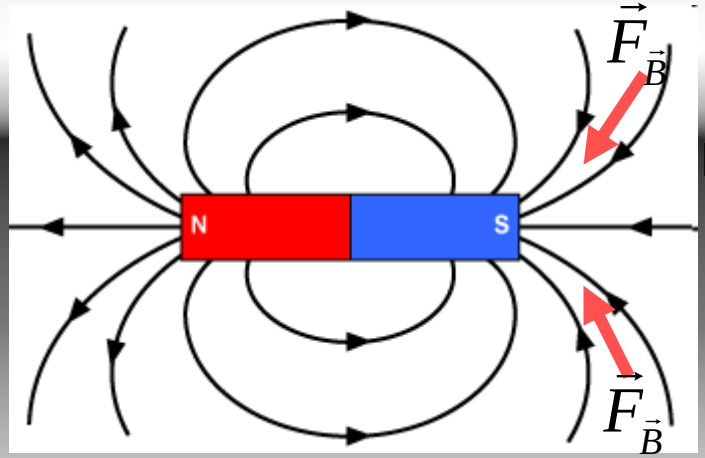
$$\vec{F}_{\vec{B}} = V_p \left(B \frac{dM}{dB} + M(B) \right) \vec{\nabla} B$$

Magnetic field

Manipulation of MNP

$$\vec{F}_{\vec{B}} = V_p\left(B\frac{dM}{dB} + M(B)\right)\vec{\nabla}B \approx \begin{cases} \mu_0^{-1}V_p\chi\vec{\nabla}B^2 & si\ B << B_S \\ m\vec{\nabla}B & si\ B \approx B_S \end{cases}$$

Problem: field intensity B decreases fast away from magnet pole



B lines

And B^2 decreases even faster!!

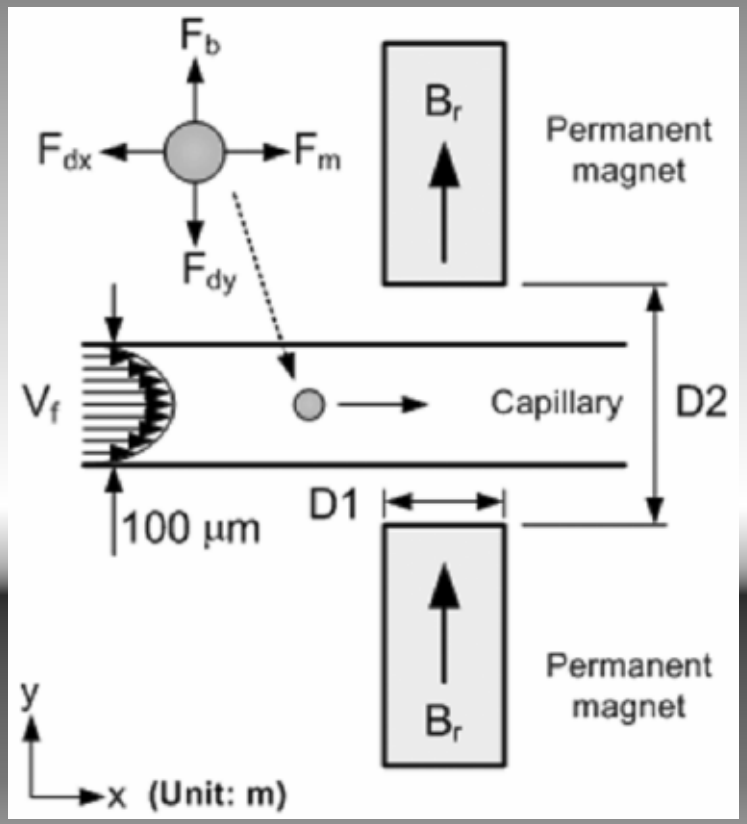
Eulanest

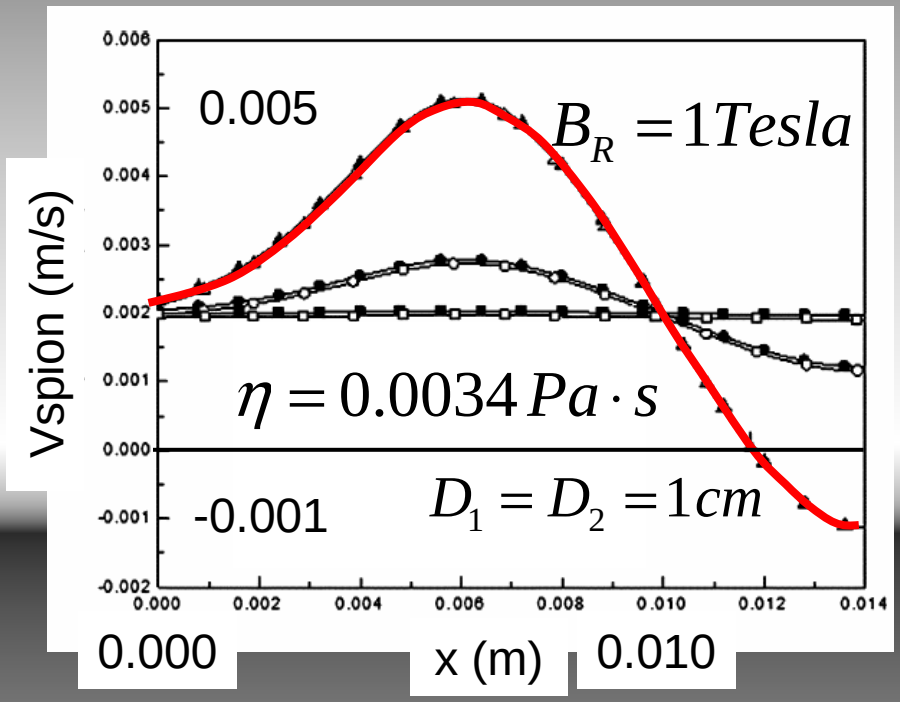
Magnetic field

Manipulation of MNP

KIM *et al.* | IEEE TRANSACTIONS ON MAGNETICS, VOL. 42, NO. 4, APRIL 2006 | 979

Motion in capillars, v ~ 2mm/s

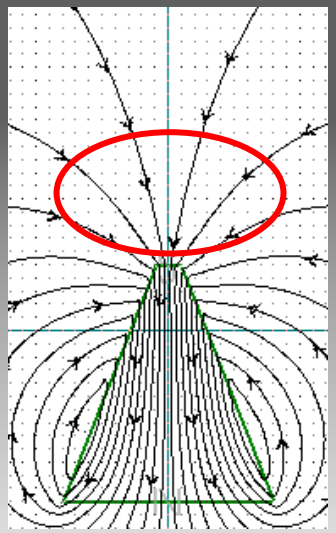




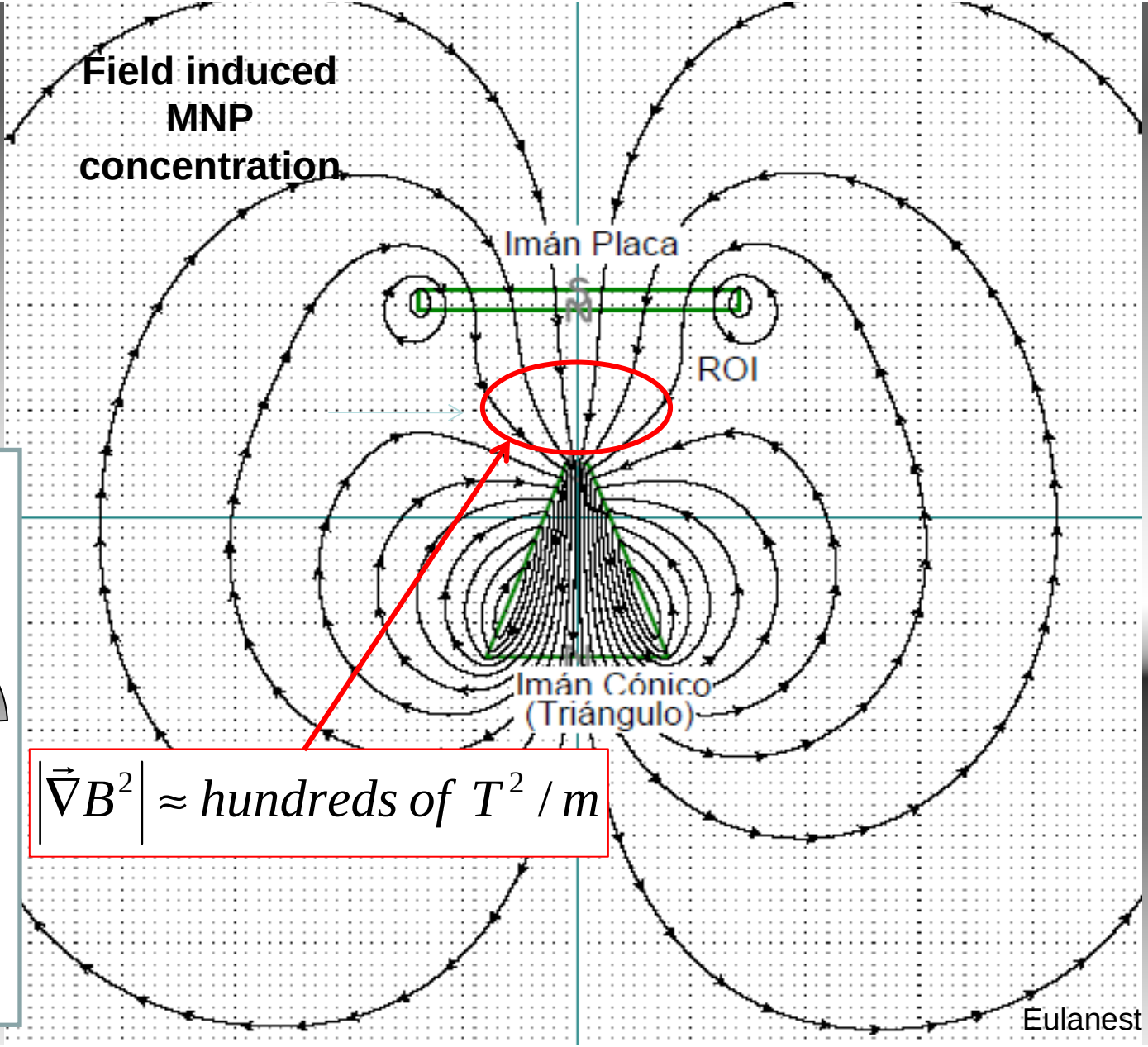
Magnetic field

Manipulation of MNP

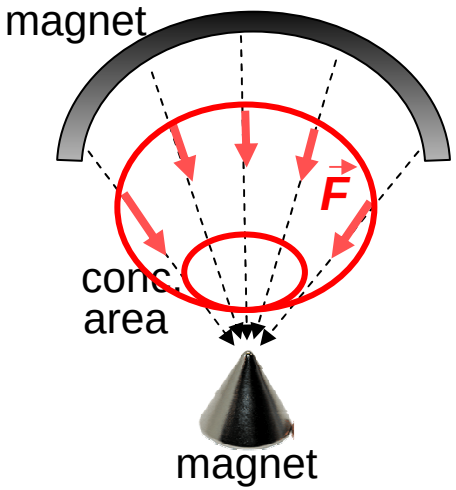
Vizimag bidimensional simulation: “plate” + “cone” magnets



Field induced MNP concentration



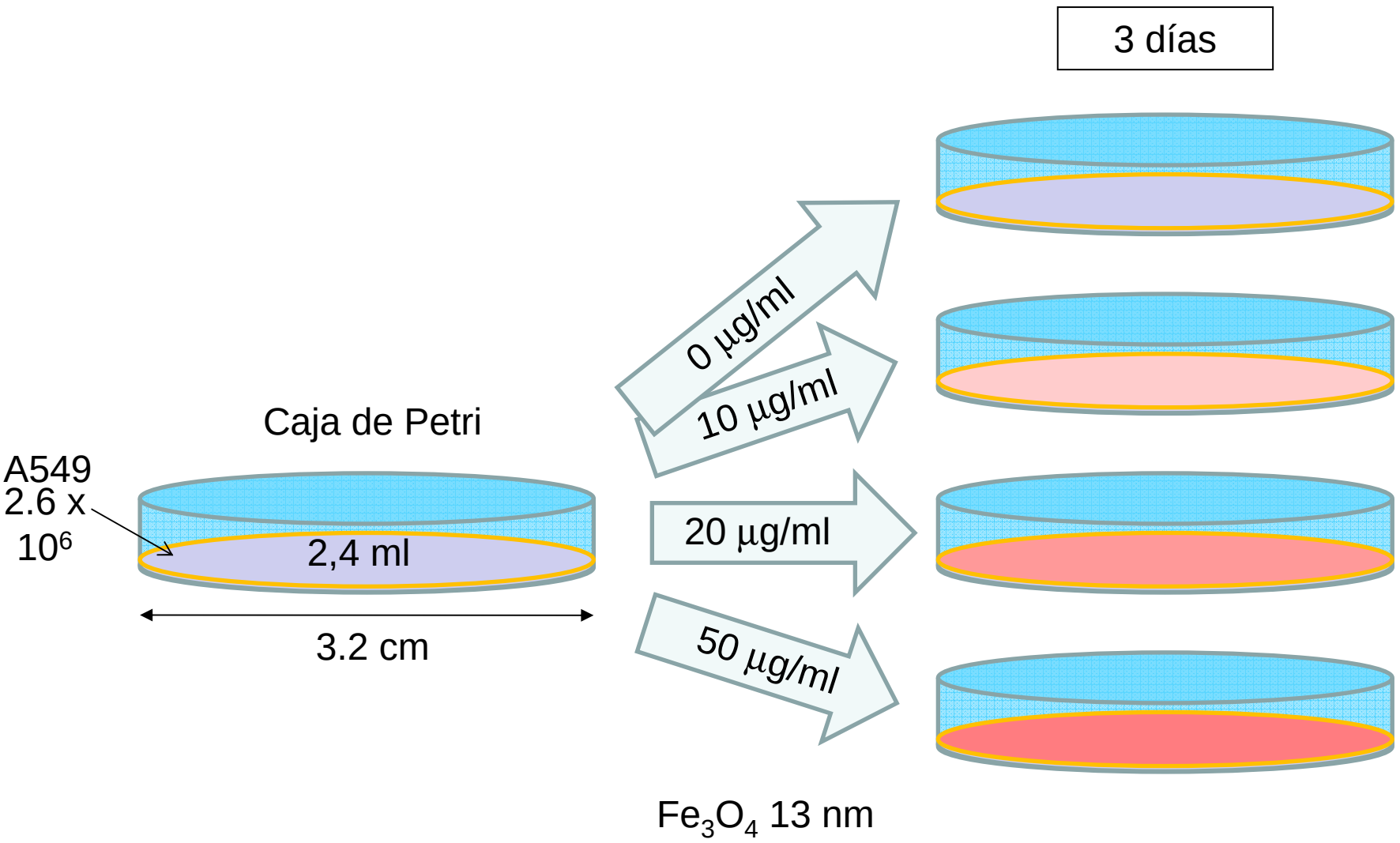
possible configuration



$$\left|\vec{\nabla}B^2\right| \approx hundreds\ of\ T^2/m$$

Eulanest

Citotoxicidad

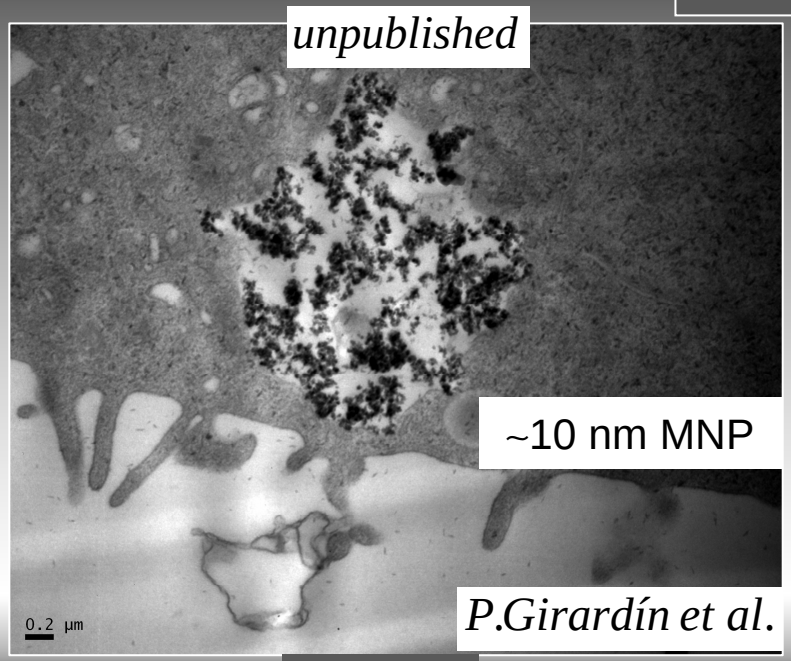


Magnetic field

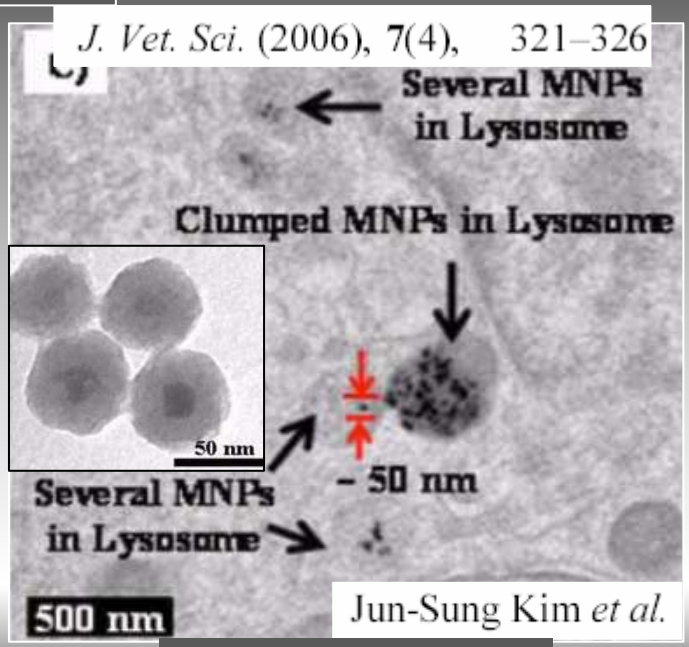
Manipulation of MNP

What would the mechanical effects of F_B on cells?

A549 cells



Fe_3O_4



$CoFe_2O_4@SiO_2$

Effective elastic constants in cells

$$k \approx 4\times10^{-5}\ N/m - 4\times10^{-4}\ N/m$$

F. Jülicher

C. R. Acad. Sci. Paris, t. 2, Série IV, p. 849–860, 2001

Wanichapichart, P., *et al.*

Vol. 24 (Suppl.) 2002 : Membrane Sci. &Tech.

Manipulation of MNP

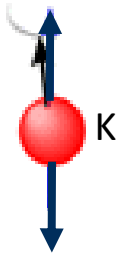
What else MNP do?

Relaxation Mechanisms

For $\mu B_{app} << k_B T$:

fixed particle

Néel: *moment oscillation*



$$\tau_N = \tau_0 \exp\left(\frac{KV}{kT}\right)$$

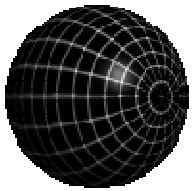
anisotropy constant

particle volume

viscous media

(*ferrofluid*)

Brown: (*particle rotation*)

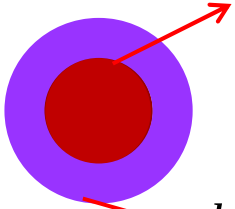


$$\tau_B = \frac{3\eta V}{kT}$$

viscosity

particle volume

volume?



magnetic volume
Néel

hydrodinamic volume
Brown

$$\frac{1}{\tau} = \frac{1}{\tau_B} + \frac{1}{\tau_N}$$

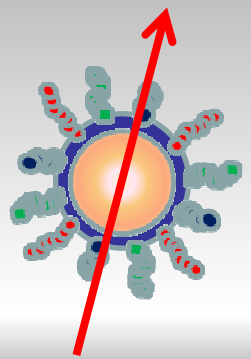
T fluctuations

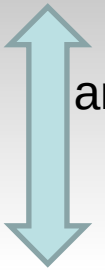
Manipulation of MNP

Thermal energy

kT

Makes magnetic moment fluctuate





anisotropy axis

Free particle

Eulanest

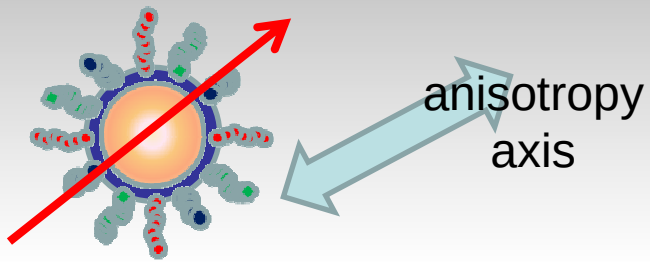
T fluctuations

Manipulation of MNP

Thermal energy

kT

Makes magnetic moment fluctuate



Free
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Manipulation of MNP

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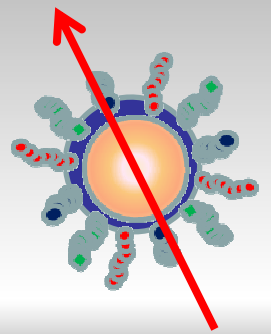
Makes magnetic moment fluctuate



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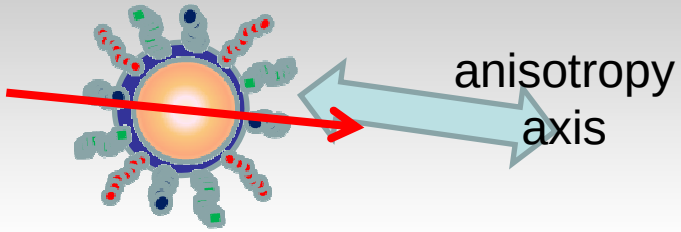

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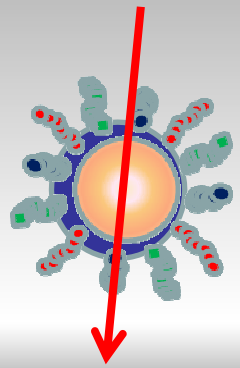
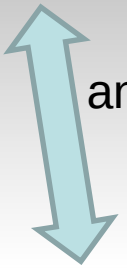




anisotropy Axis K

Free particle

Brown relaxation

$$\tau_B = \frac{3\eta V_H}{kT}$$

Eulanest

T fluctuations

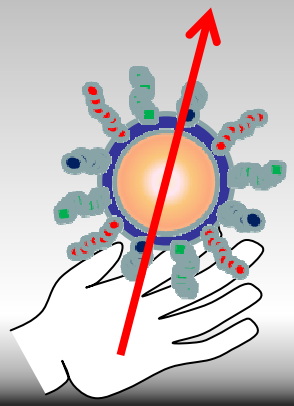
Manipulation of MNP

Thermal energy

kT

Makes magnetic moment fluctuate

anisotropy
Axis K



Fixed
particle

T fluctuations

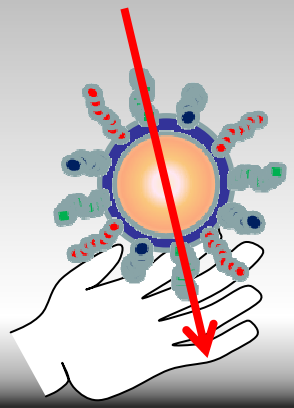
Manipulation of MNP

Thermal energy

kT

Makes magnetic moment fluctuate

anisotropy
Axis K



Fixed
particle

T fluctuations

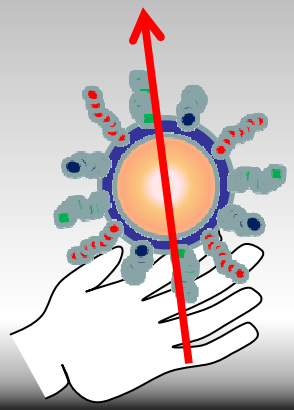
Manipulation of MNP

Thermal energy

kT

Makes magnetic moment fluctuate

anisotropy
Axis K



Fixed particle

T fluctuations

Manipulation of MNP

Thermal energy

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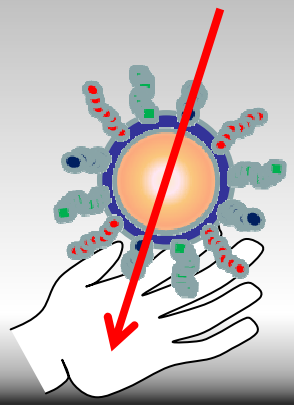
Makes magnetic moment fluctuate

anisotropy
Axis K



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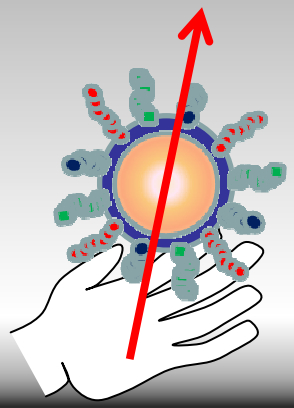


Fixed particle

$$\tau_N = \tau_0 e^{KV_M / kT}$$

Neel relaxation

Eulanest

T fluctuations

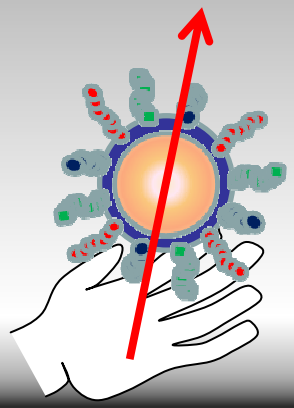
Manipulation of MNP

Thermal energy

kT

Makes magnetic moment fluctuate

anisotropy
Axis K



Fixed particle

$$\tau_N = \tau_0 e^{KV_M / kT}$$

Neel relaxation

Eulanest

RF Field

Manipulation of MNP

a magnetic field produces a Torque on the particle moment

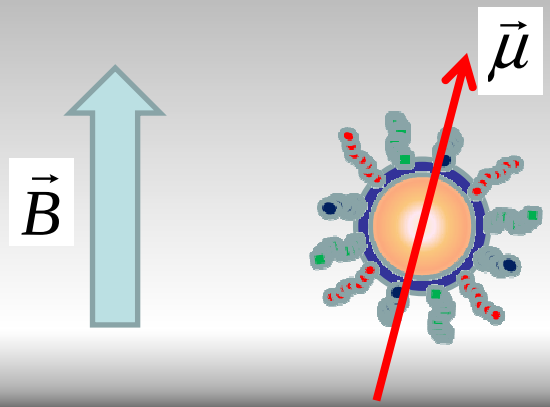
$$\vec{\tau} = \vec{\mu} \times \vec{B}$$

Particle moment tends to align with field

Thermal energy

$$kT$$

Prevents complete alignement



RF Field

Manipulation of MNP

a magnetic field produces a Torque on the particle moment

$$\vec{\tau} = \vec{\mu} \times \vec{B}$$

Particle moment tends to align with field

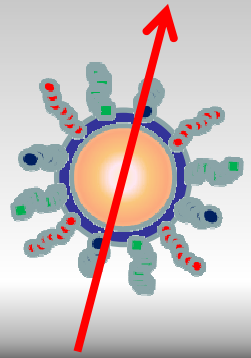
Thermal energy

$$kT$$

Prevents complete alignement

Field inversion

$\vec{B}$



MNP absorb power from the field and release it to the surrounding medium (SAR)

Eulanest

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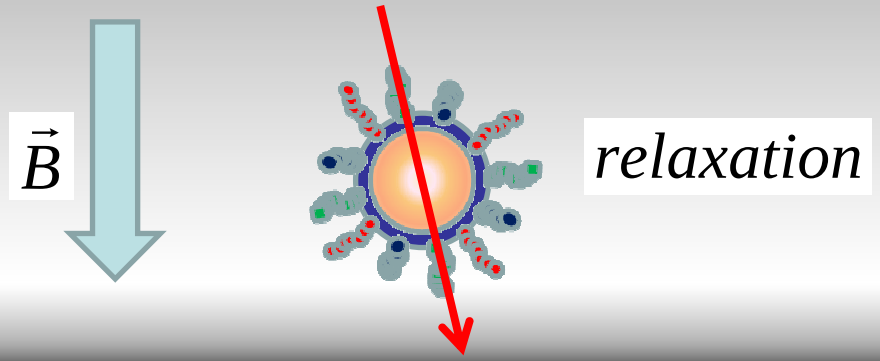

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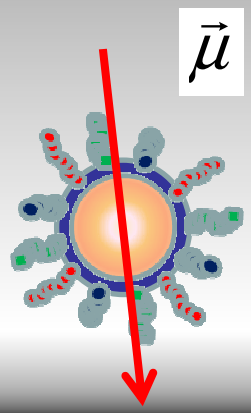

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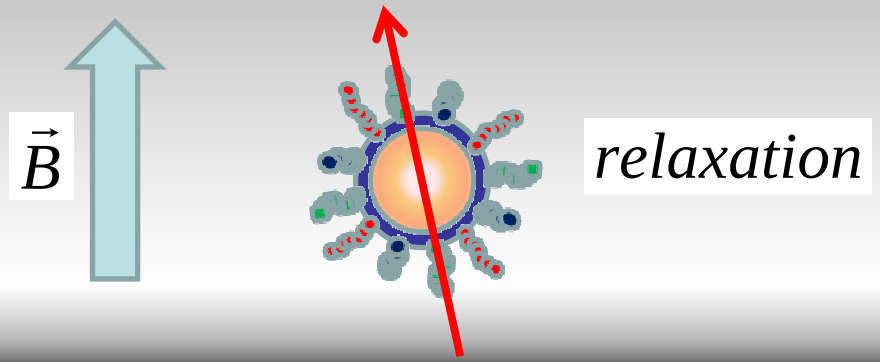


MNP absorb power from the field and release it to the surrounding medium (SAR)

Absorption is largest when time τ equals the inverse of field frequency ω

Eulanest

RF Field

Manipulation of MNP

hyperthermia

Basic Principle

cancer cells **<u>are more temperature sensitive</u>** than normal ones. They undergo apoptosis at temperatures of 42 – 43 °C, while normal ones do it at 46 – 47 °C

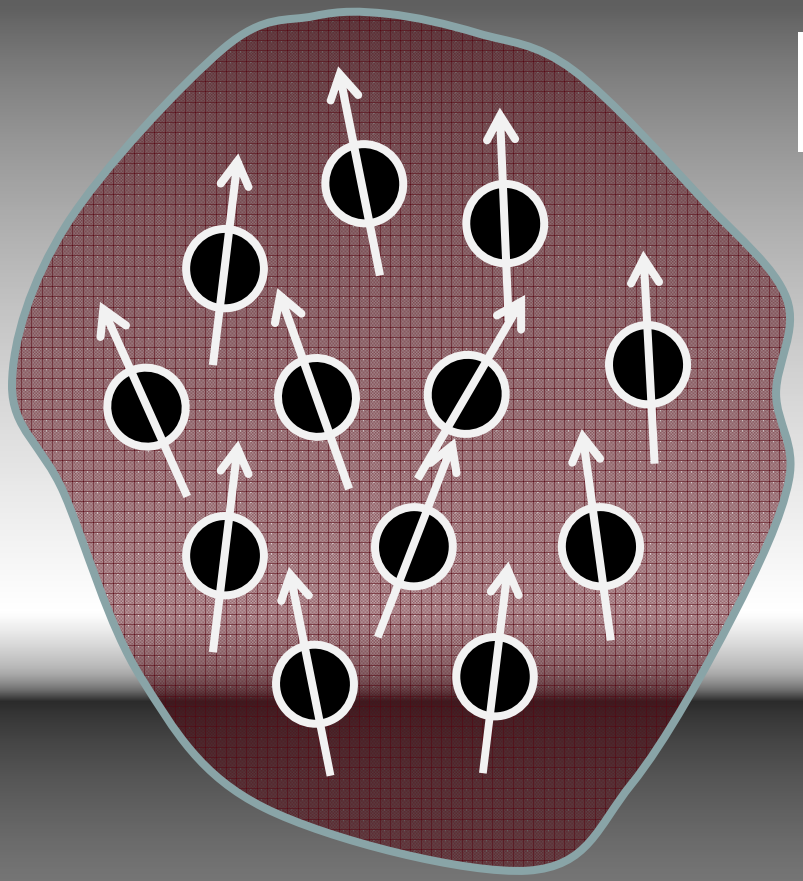
R.K. Gilchrist et al., Ann. Surg. **146**, 596, 1957

Andreas Jordan Hospital Charitè, Berlín. 100 kHz, 15 kA/m

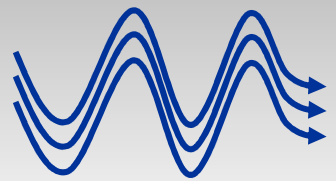
Ingrid Hilger, Institute of Diagnostic and Interventional Radiology, Jena

Manipulation of MNP

energy absorption from a RF field (SAR)



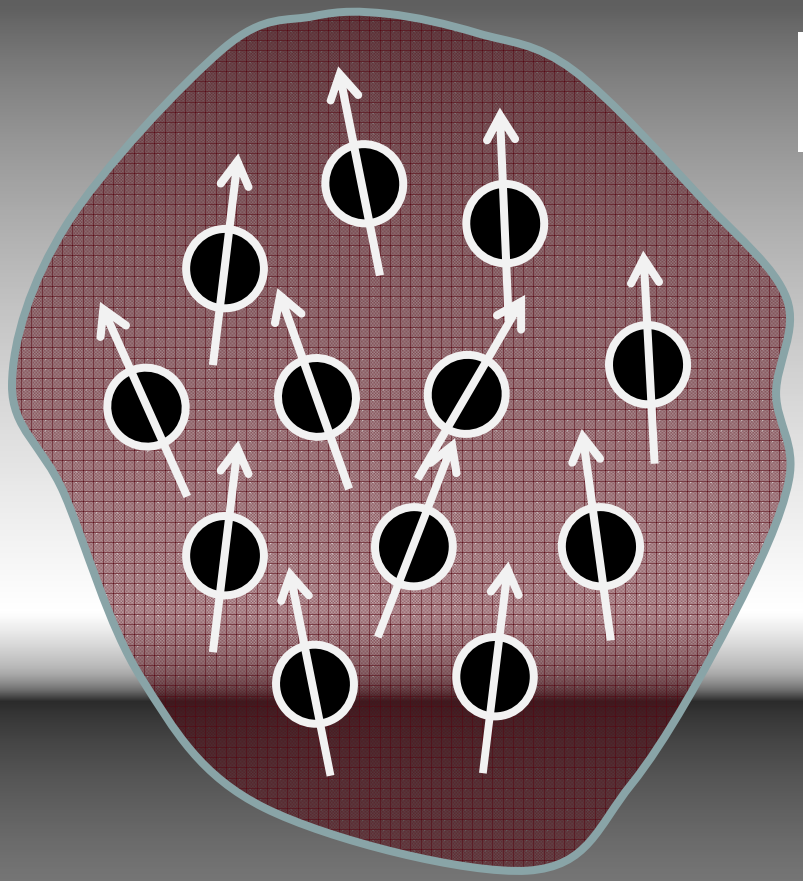
$$\tau \approx 1/\omega$$



T

Manipulation of MNP

energy absorption from a RF field (SAR)



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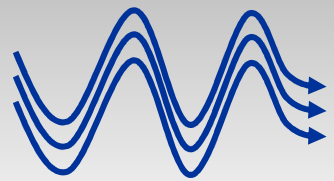
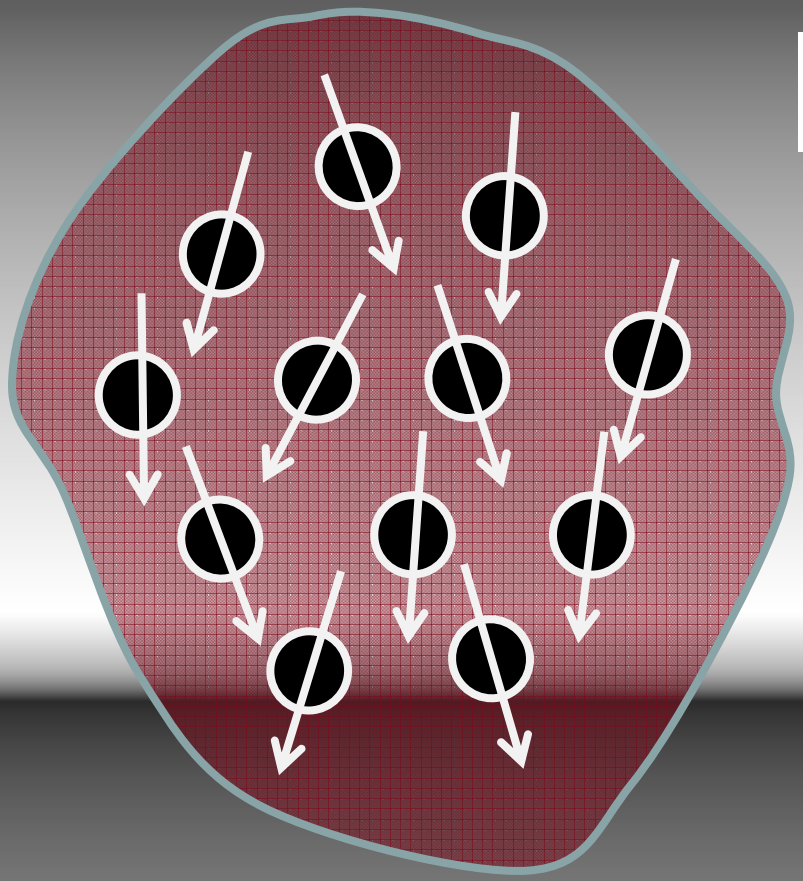


T

Manipulation of MNP

energy absorption from a RF field (SAR)



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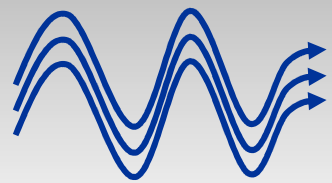
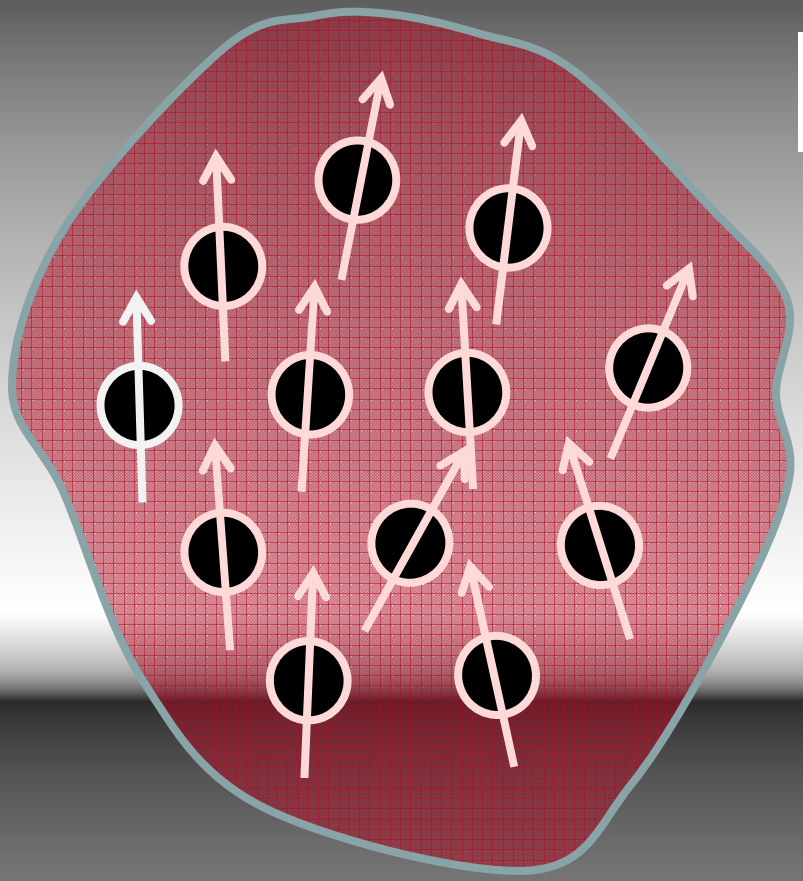


T

Manipulation of MNP

energy absorption from a RF field (SAR)



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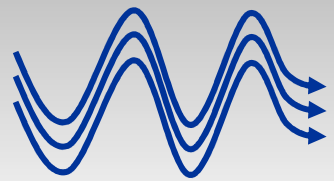

T

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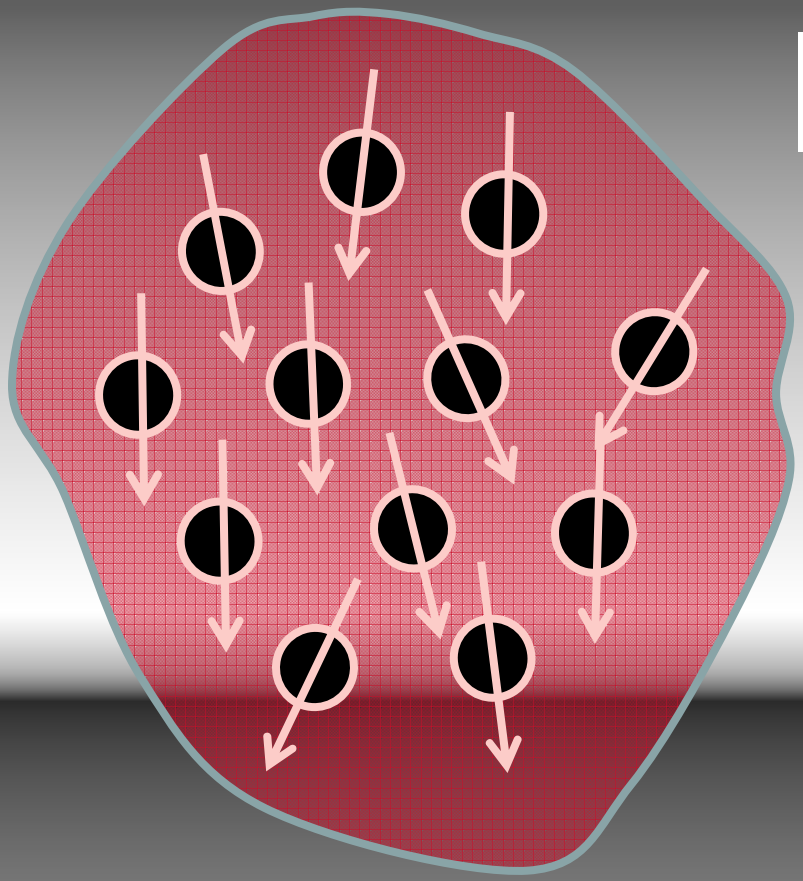

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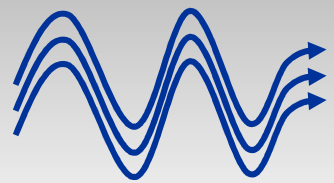
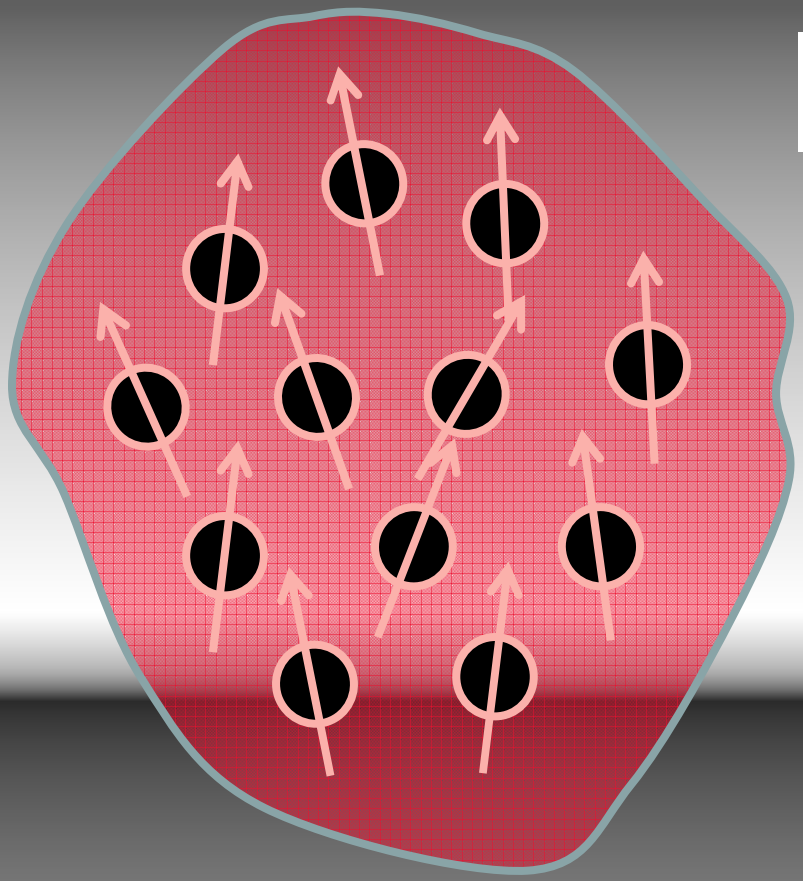


T

Manipulation of MNP

energy absorption from a RF field (SAR)



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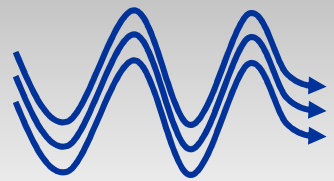
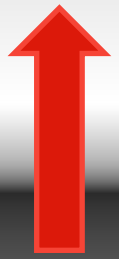


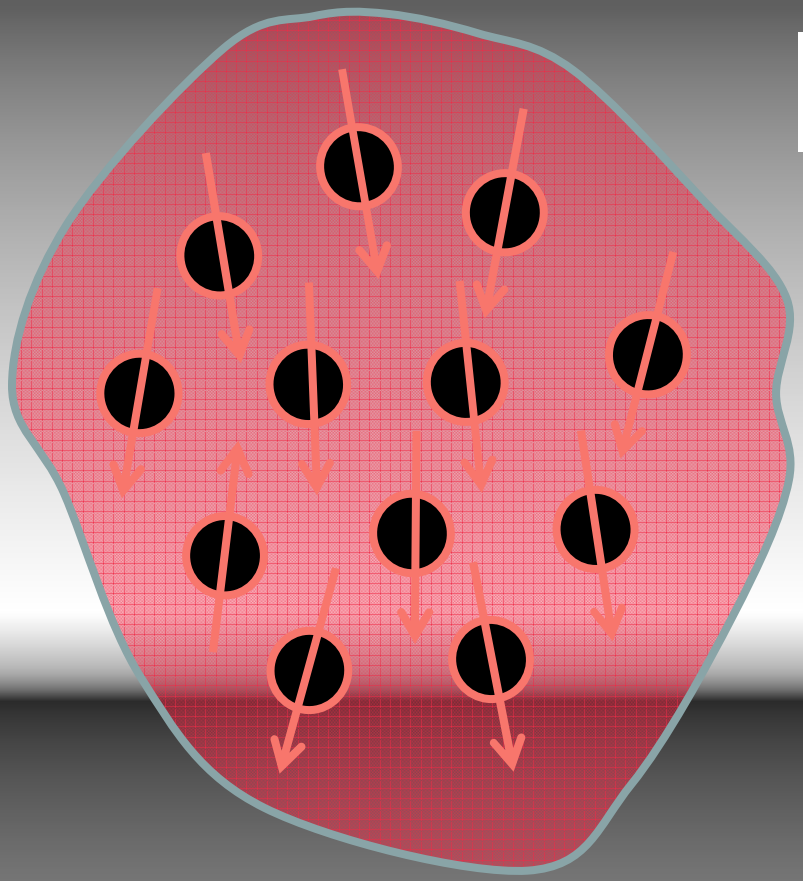
T



Eulanest

Manipulation of MNP

energy absorption from a RF field (SAR)



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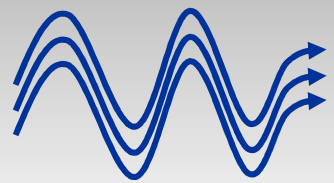
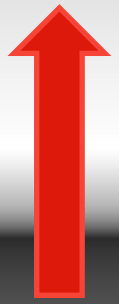


T



Eulanest

Manipulation of MNP

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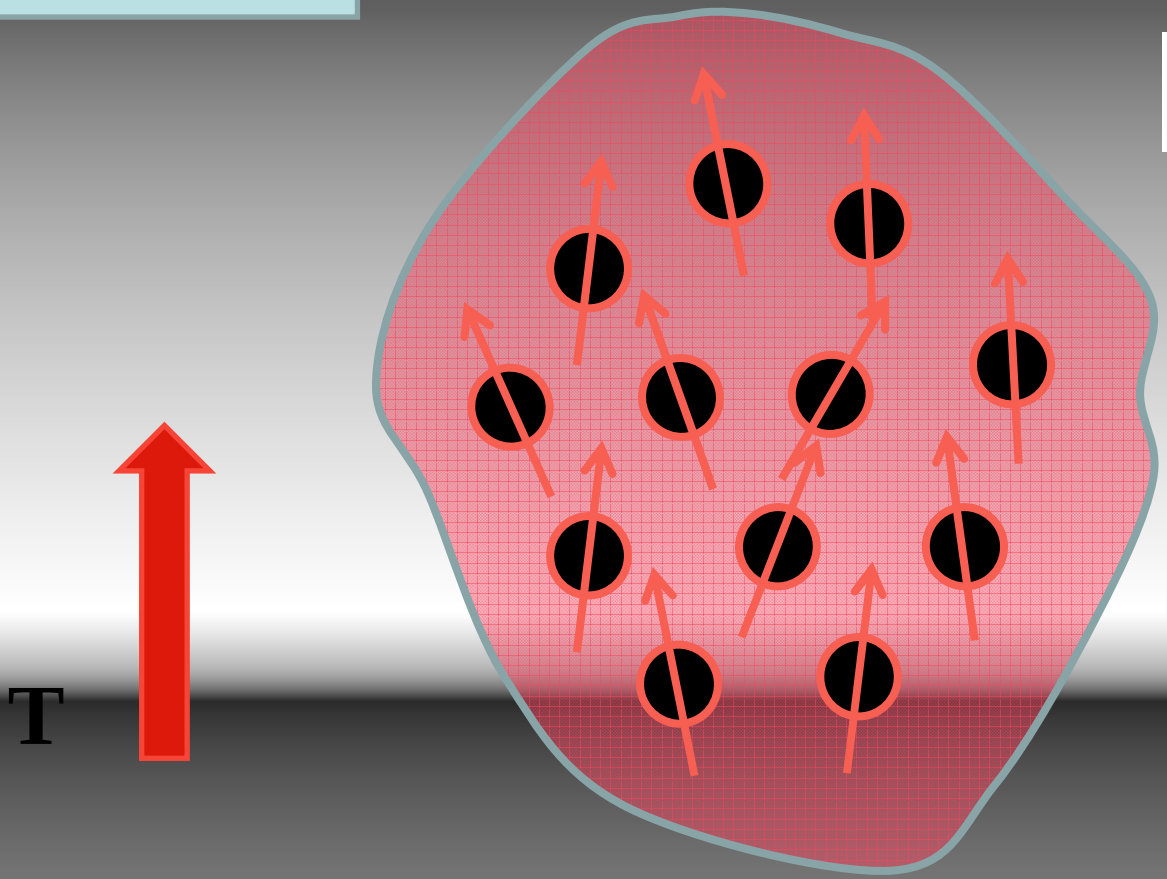

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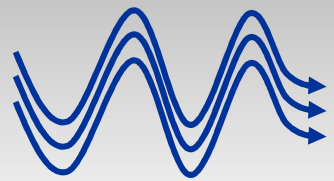

T

Eulanest

Manipulation of MNP

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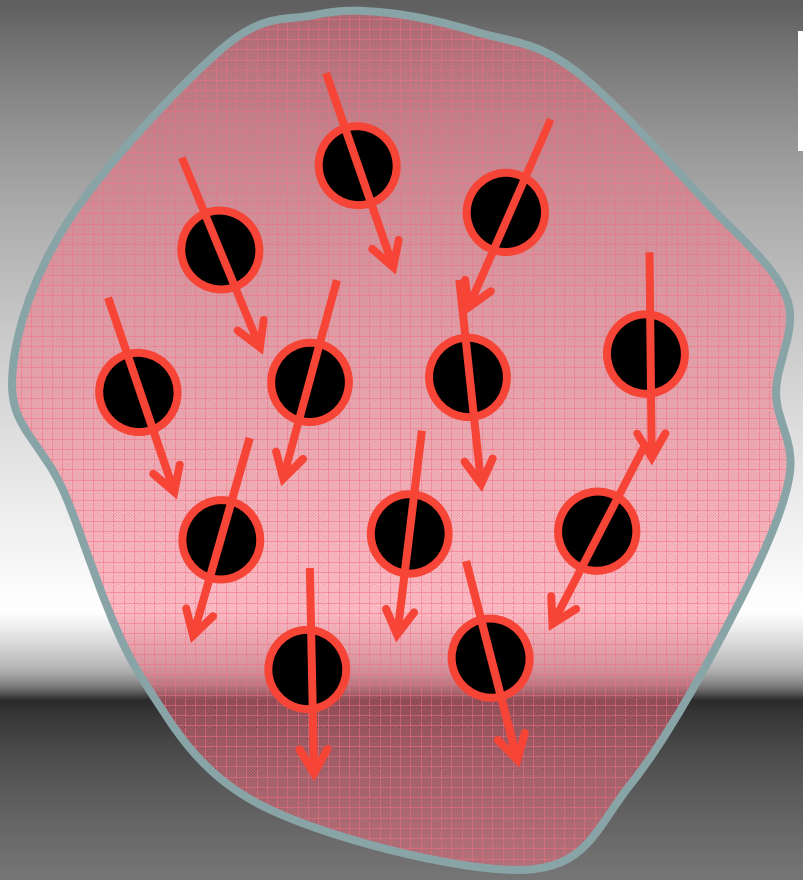

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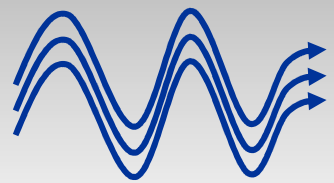

Manipulation of MNP

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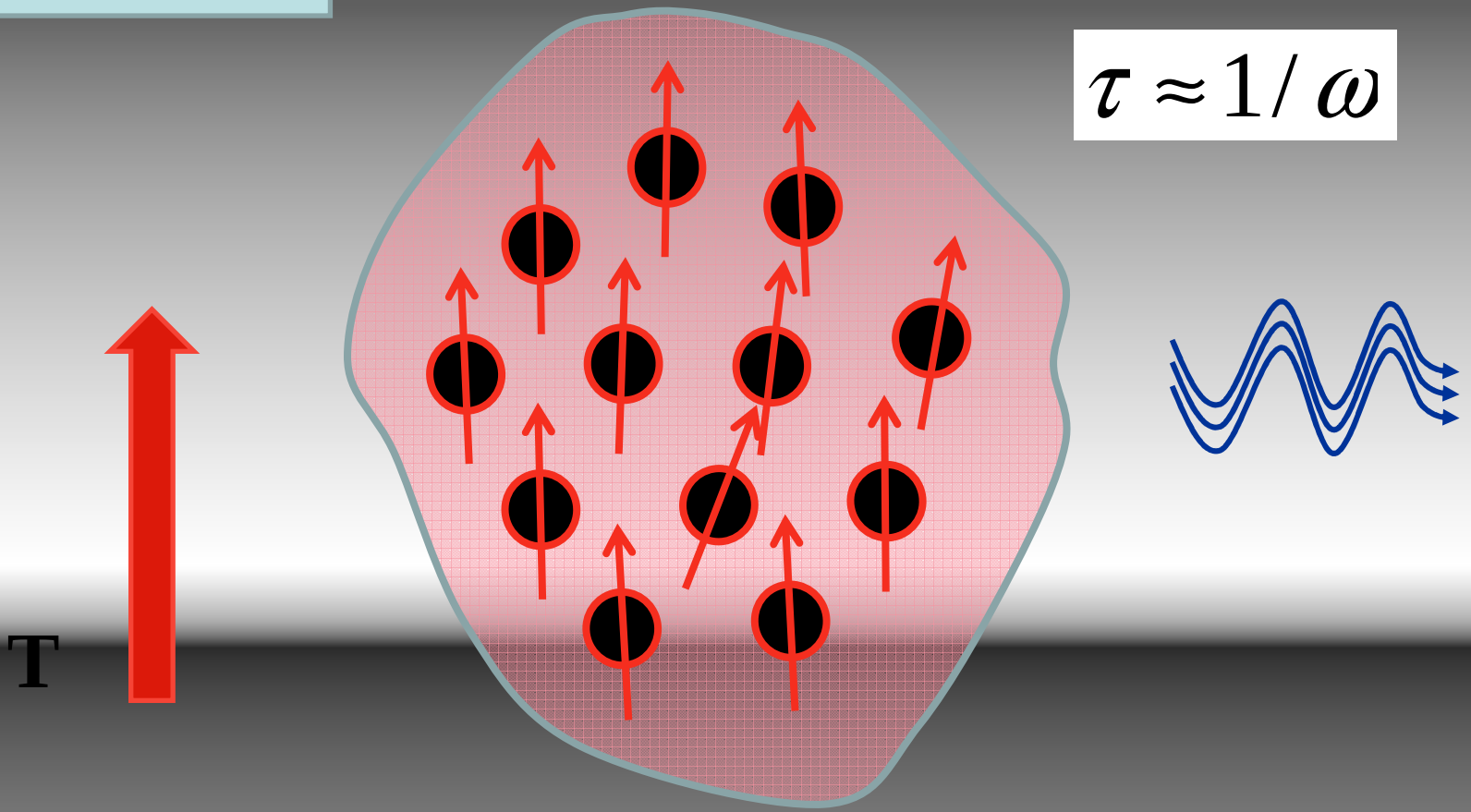

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Manipulation of MNP

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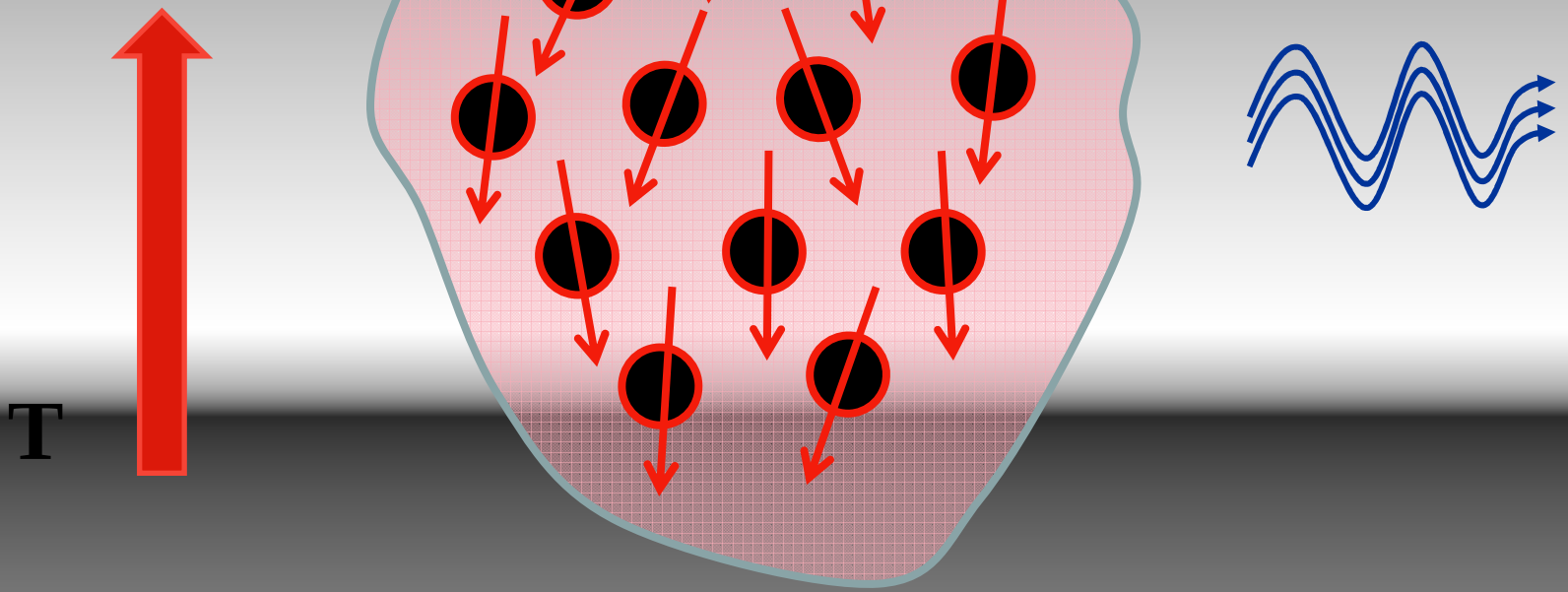
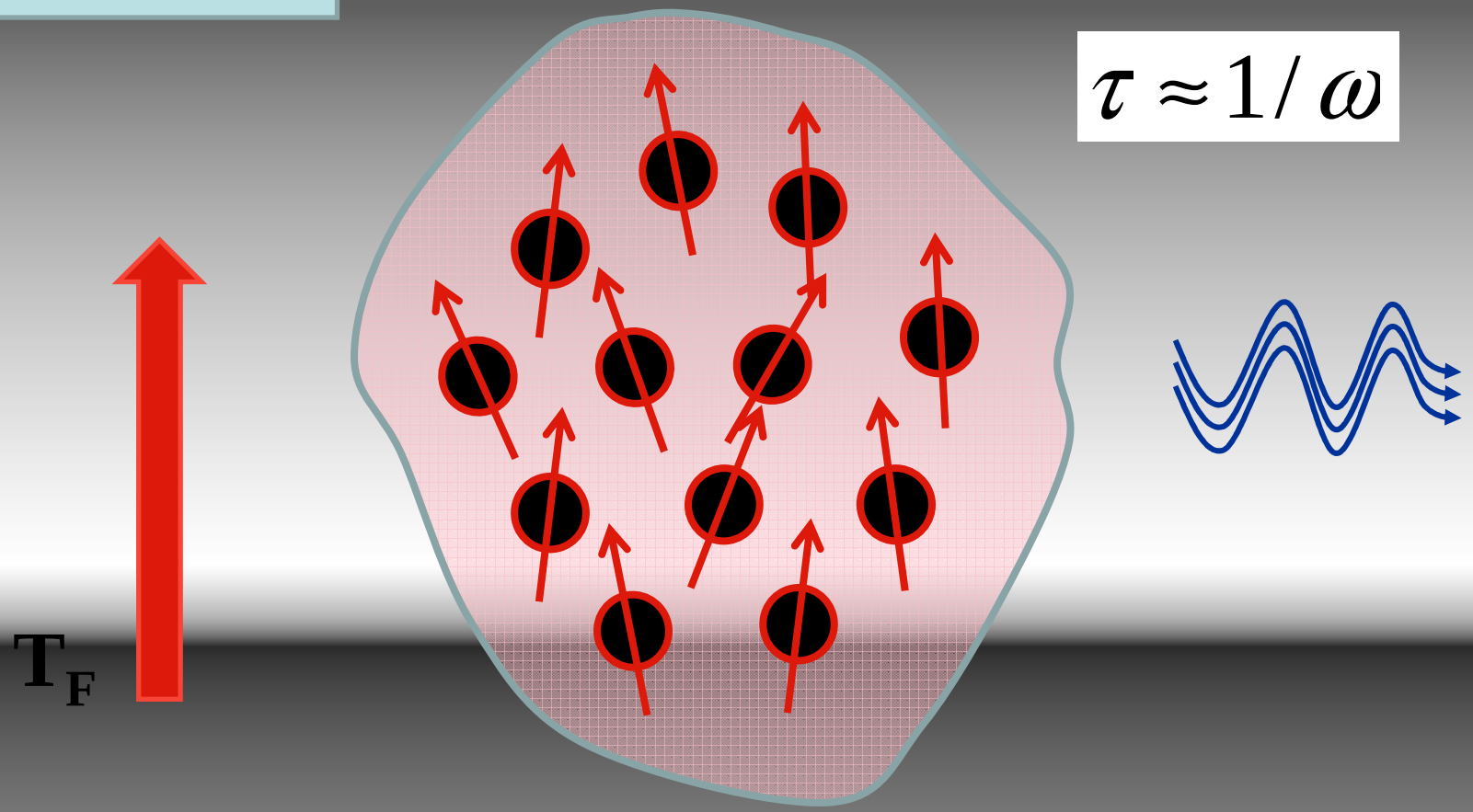


$$\tau \approx 1/\omega$$

Manipulation of MNP

energy absorption from a RF field (SAR)



$$\tau \approx 1/\omega$$

$$SAR \approx f\left(M_S, V_{MNP}, H_0, \omega, T\right)\frac{\omega\tau}{1+(\omega\tau)^2}; \quad need \ \ for\ 1kW/g$$

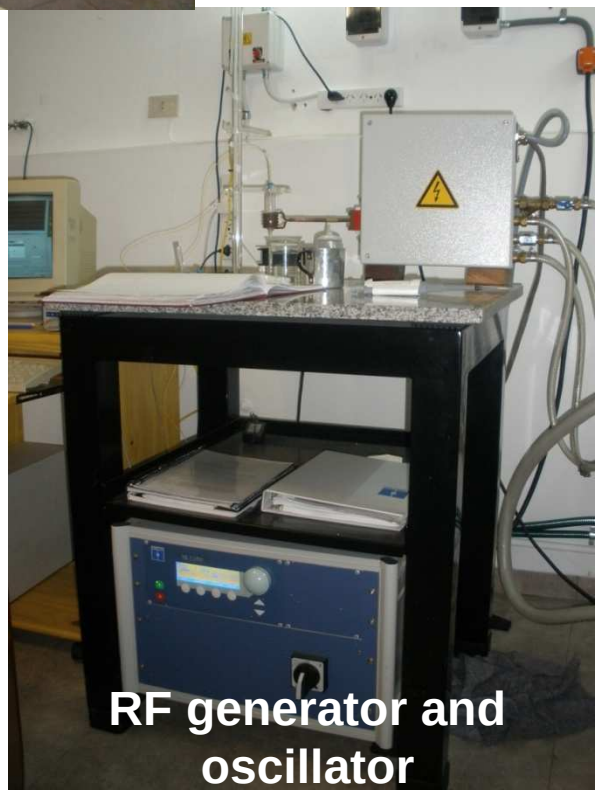
Eulanest

SAR

$$0 \leq H \leq 700\ Oe$$

$$f \leq 300\ kHz$$

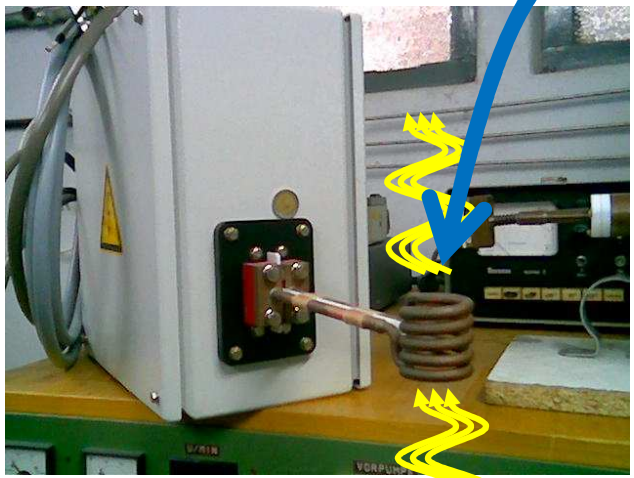
Experimental



SAR

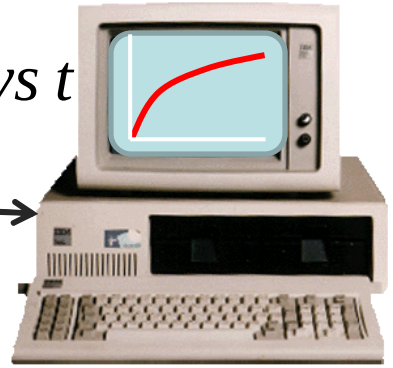
Ferrofluid (FF)

SAR / SLP in FF



$f \approx 50\,kHz - 1\,MHz$

$H_0 \leq 700\,Oe$



T *vs* t

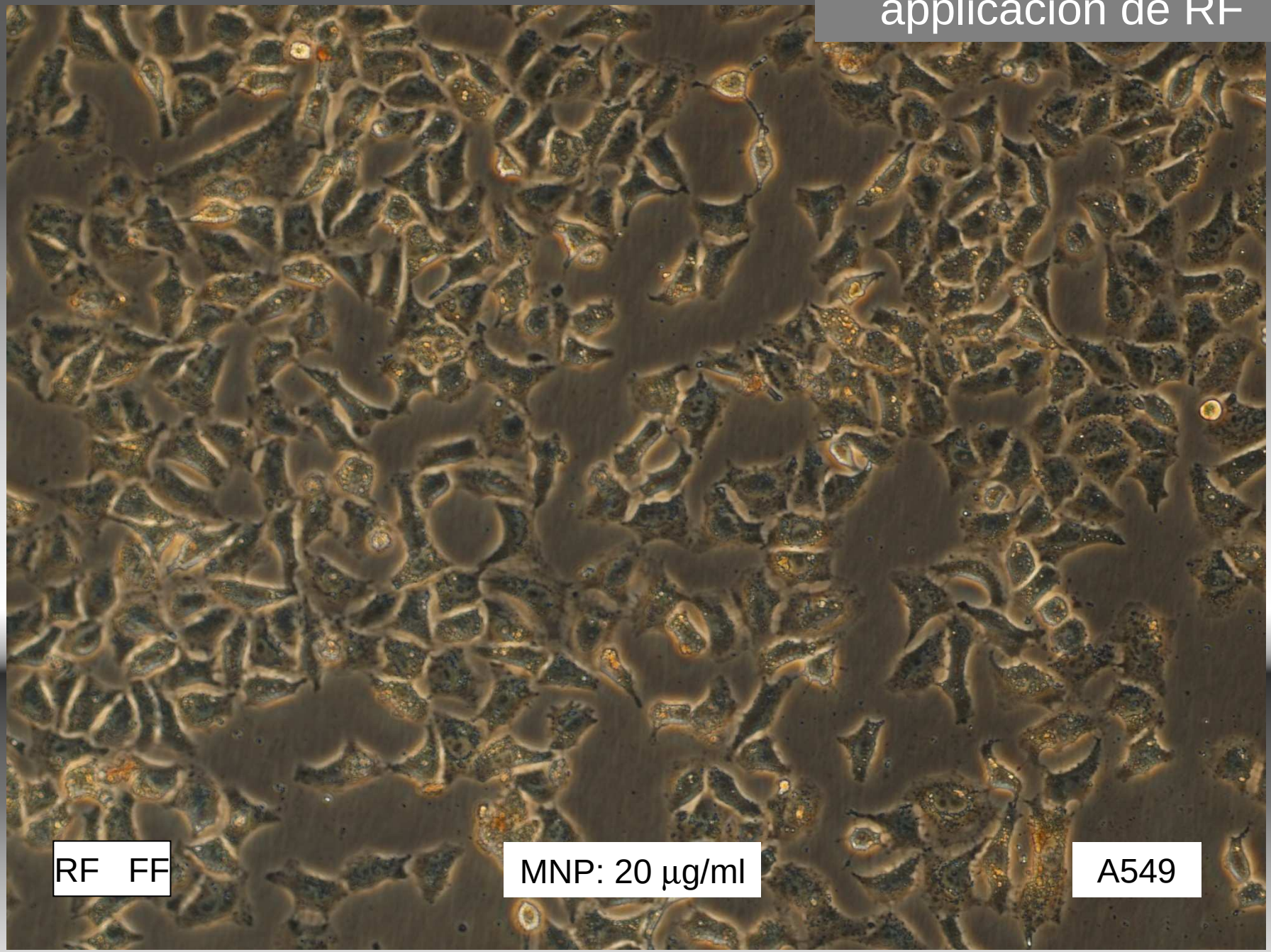
signal conditioner

optic fibers

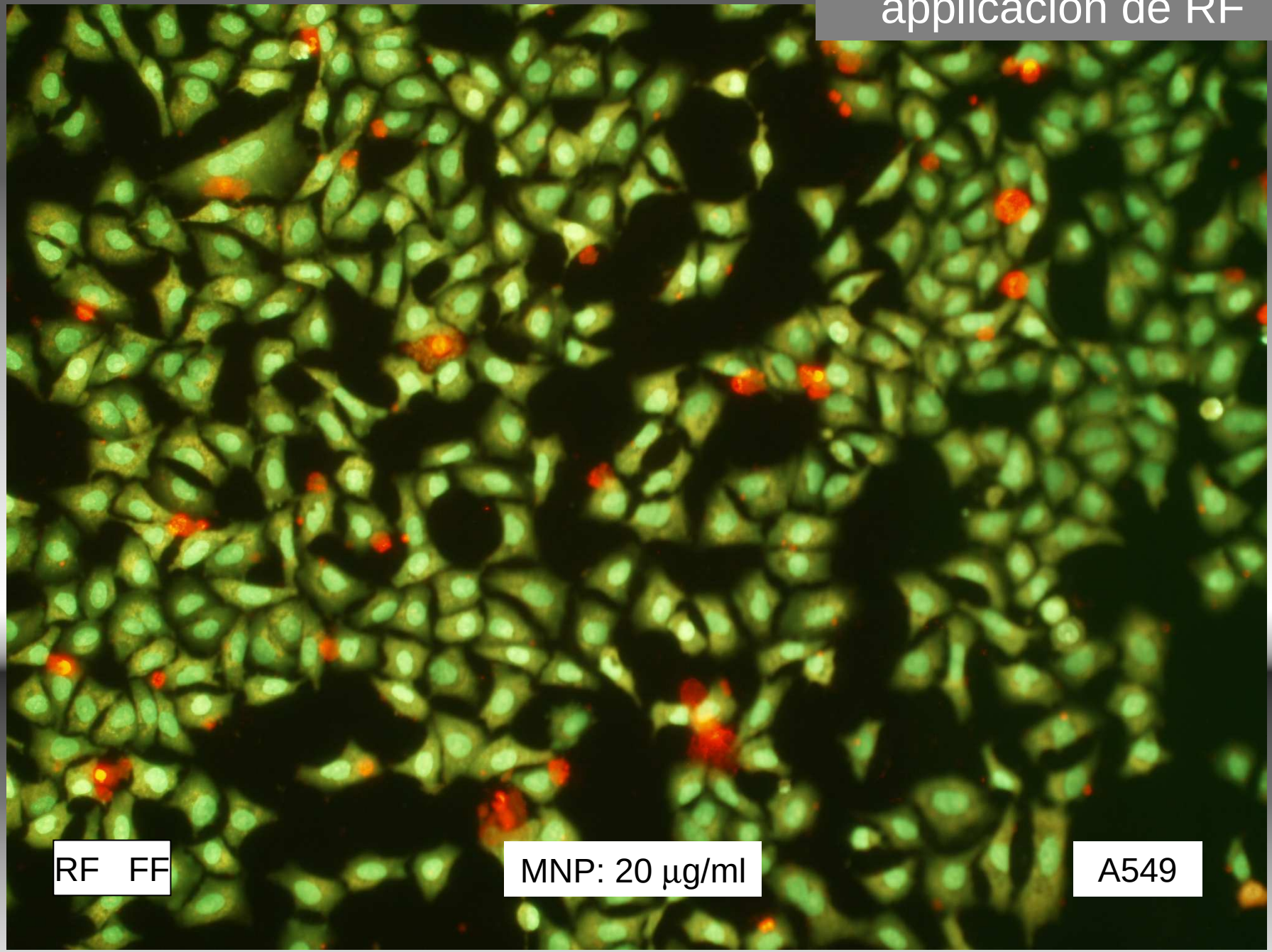
temperature measurement

ferrofluid

applicación de RF

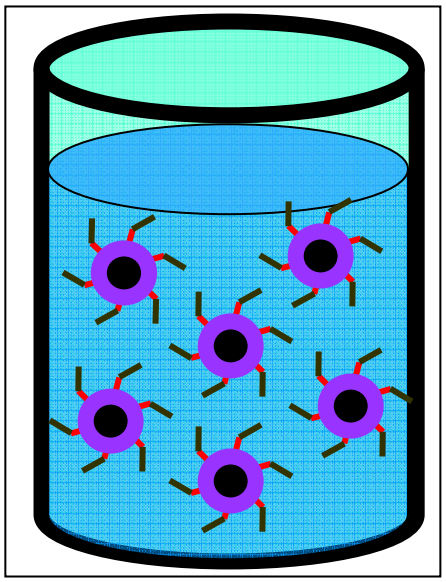


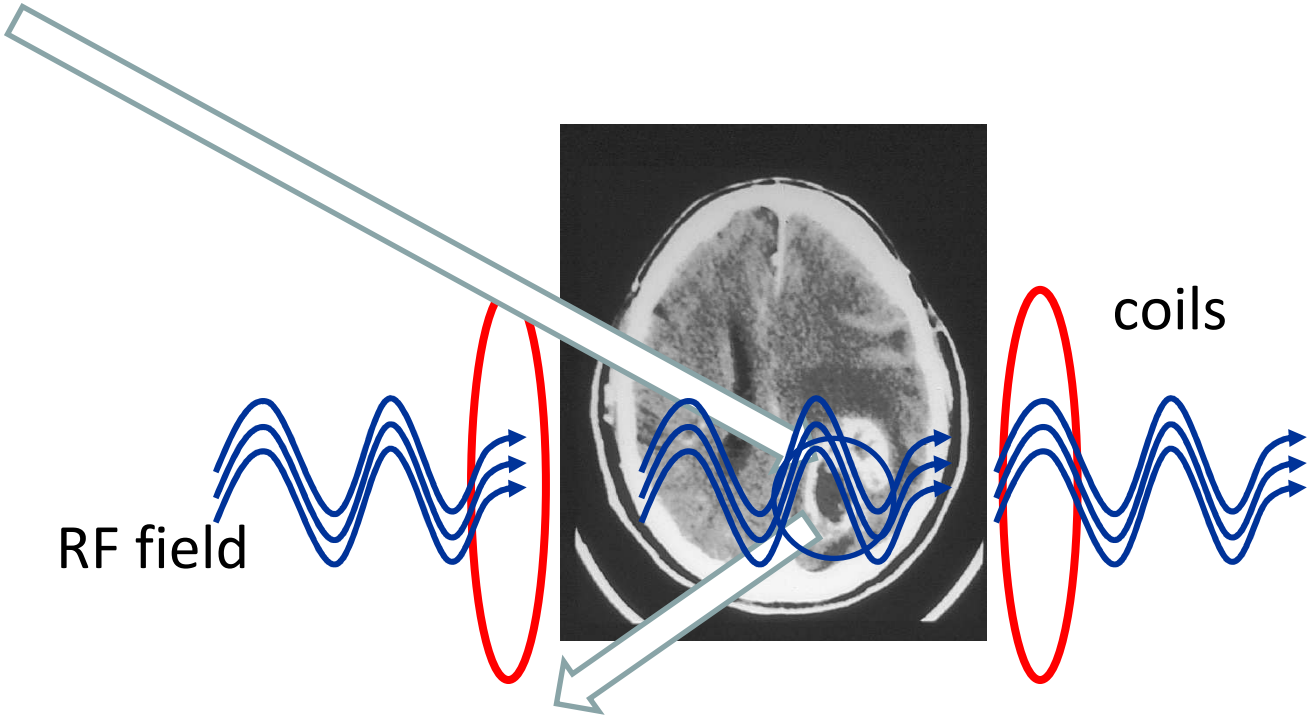
applicación de RF



Therapy by selective localized **hyperthermia**

Ferrofluid (Fe_3O_4 in aqueous solution)





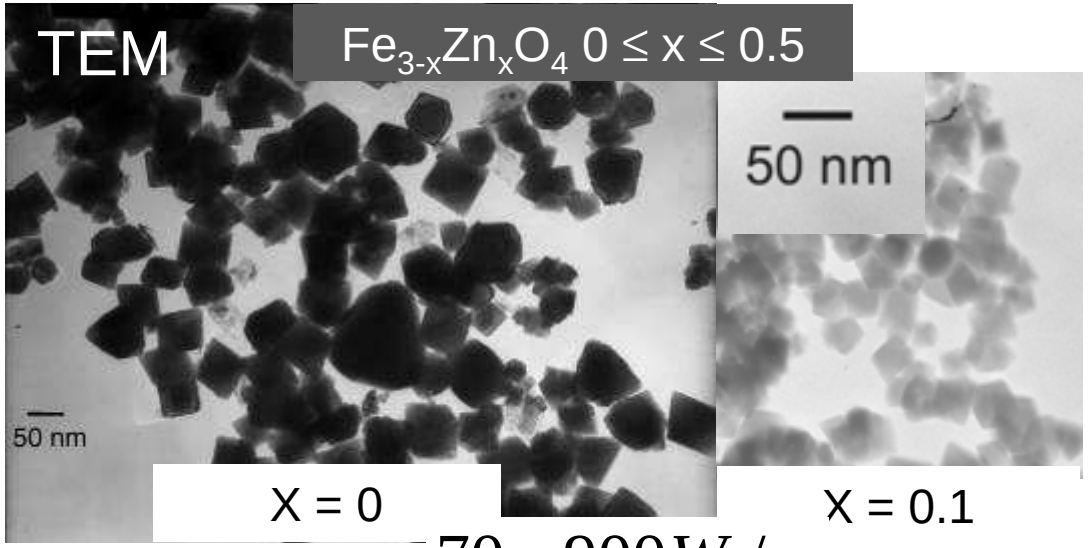
Dissipated Power-SAR
$\rightarrow T \approx$ 42-45 °C
(hyperthermia)

RF Field

MNP - SAR

TEM

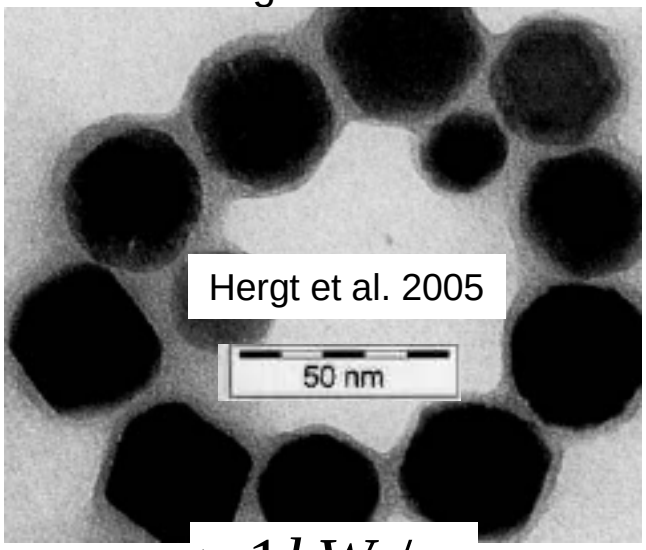
$Fe_{3-x}Zn_xO_4$ $0 \leq x \leq 0.5$



X = 0 X = 0.1

$$70 - 900 W / g$$

magnetosomes

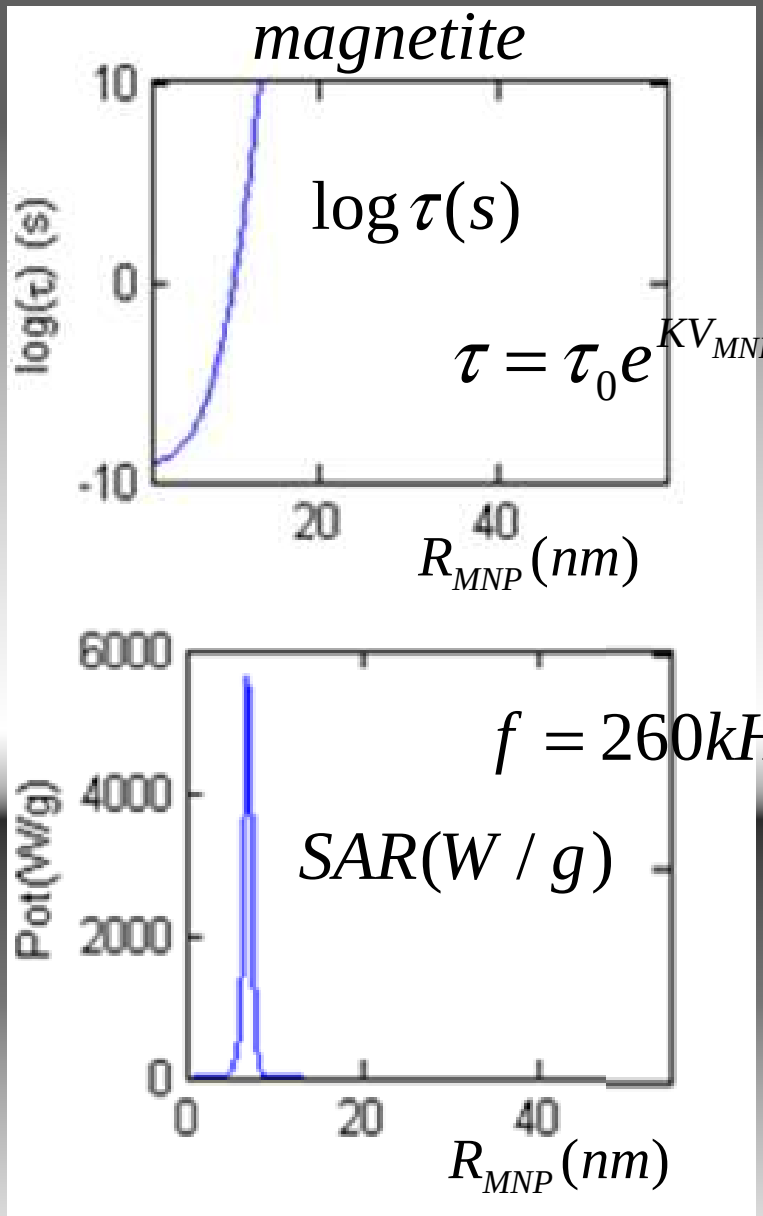


$$> 1 kW / g$$

RF Field

MNP - SAR

$$SAR \approx \frac{\mu_0 M_S^2 V f H_0^2}{3 k_B T \rho} \frac{\omega\tau}{1+(\omega\tau)^2}$$



Eulanest

RF Field

MNP - SAR

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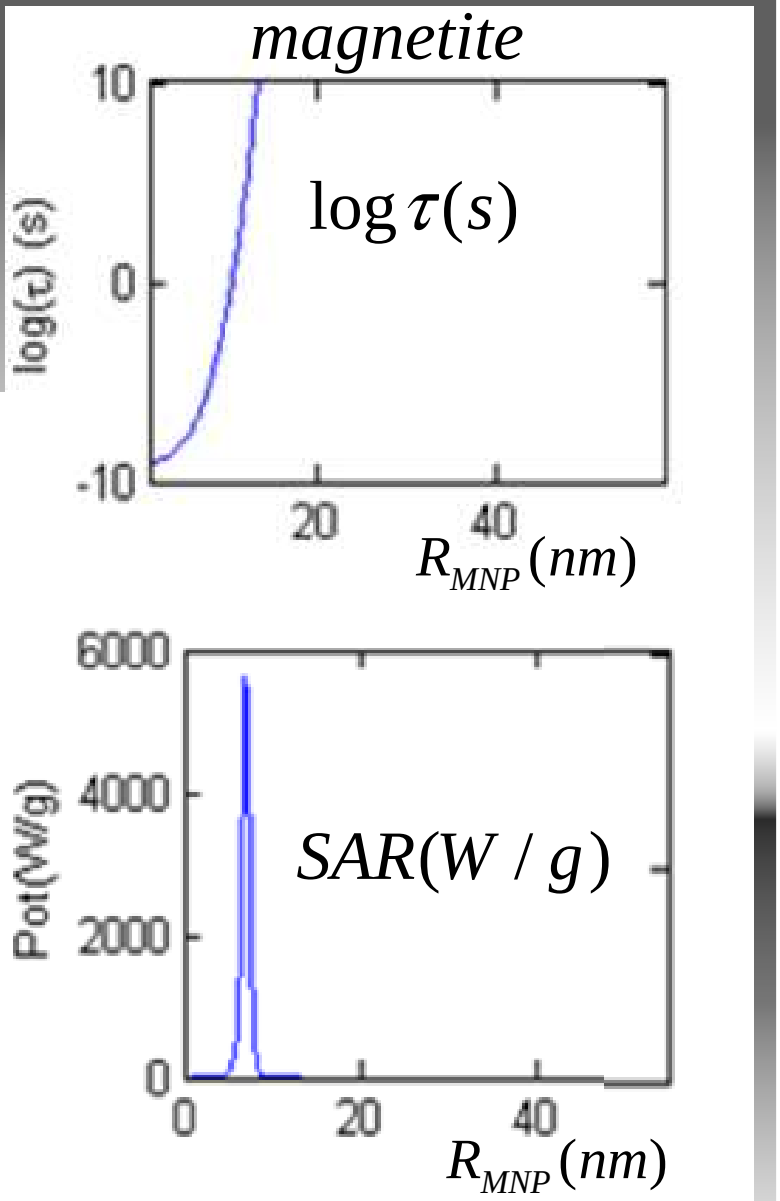
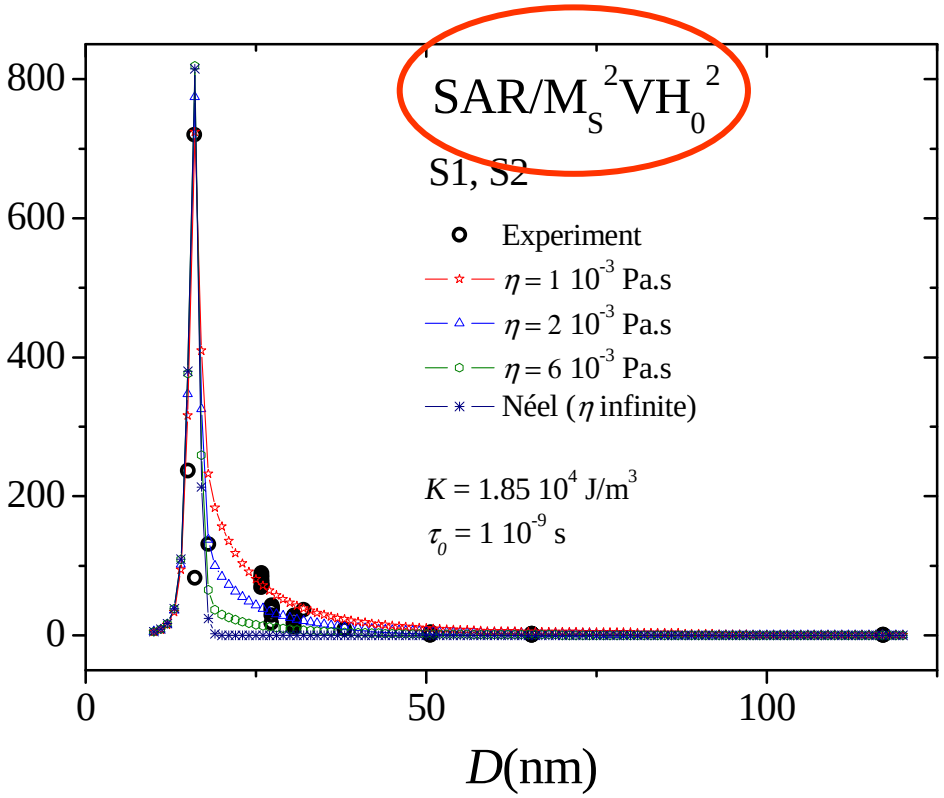




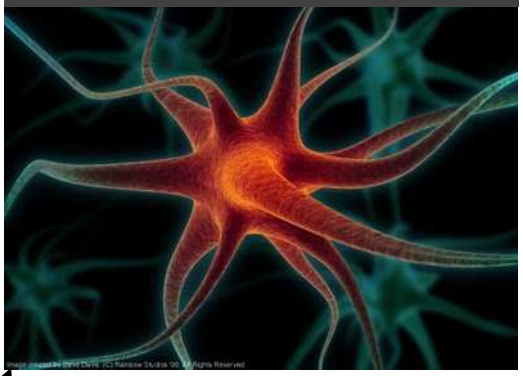
Magnetofección terapia génica c/invasividad mínima en cerebro envejecido

Projectos

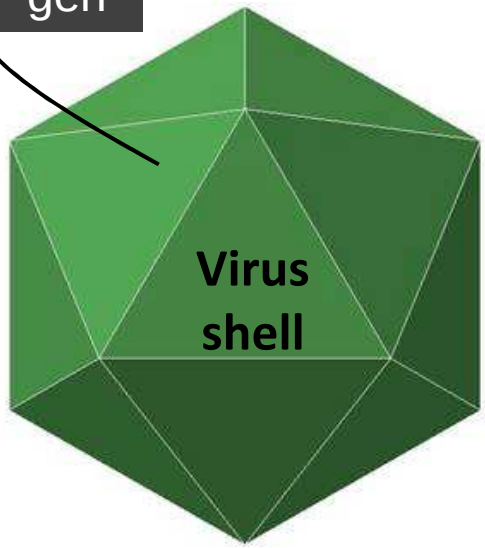
INIBIOLP
Instituto de Investigaciones Bioquímicas de La Plata

Facultad de Ciencias Médicas

Neurona defectuosa



gen



virus ~ 80 nm

ADN viral + gen terapéutico

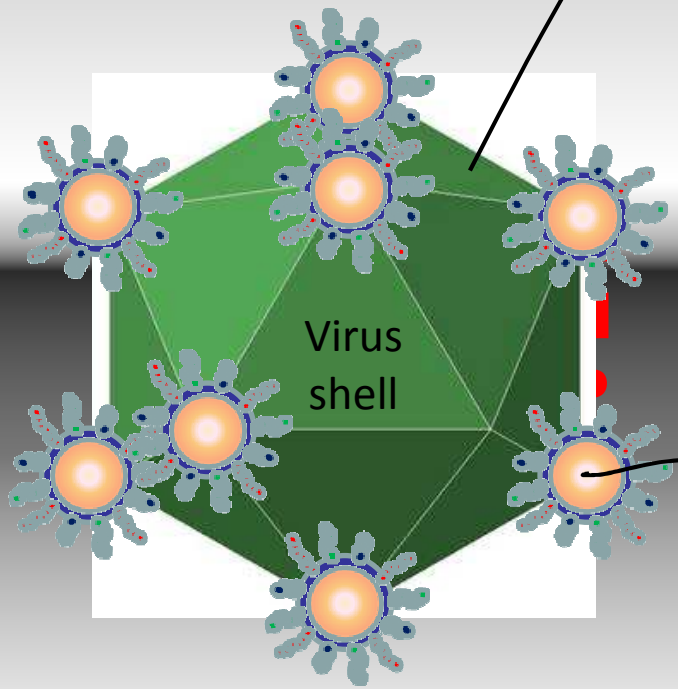
penetración ⇒ mecanismos biologicos

⇒ producción de proteina terapeutica

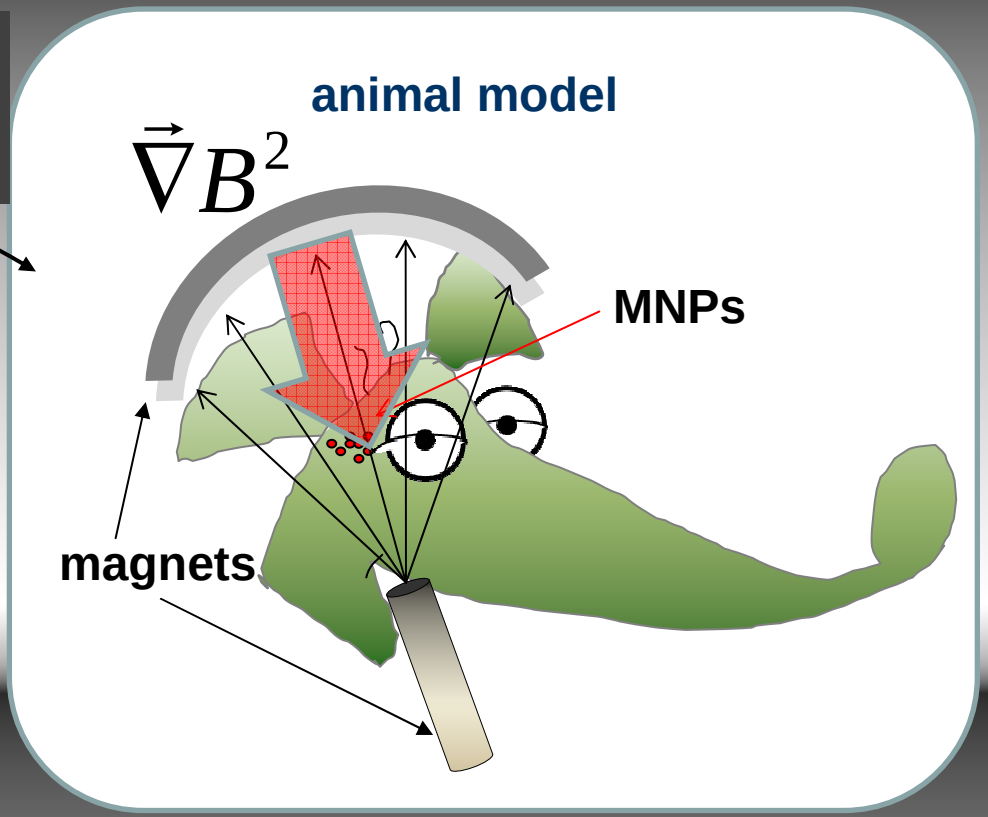
Rodolfo Goya

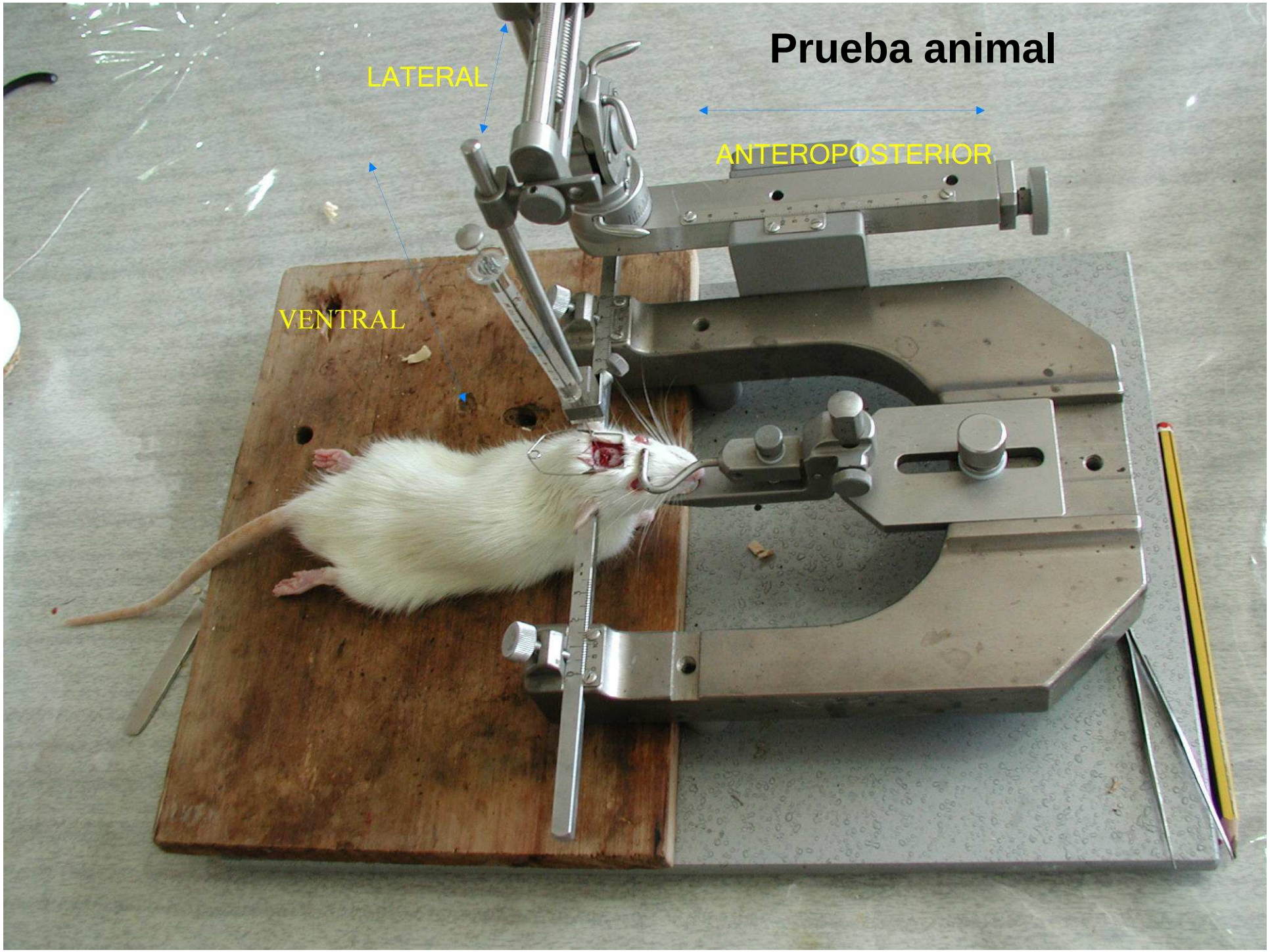
Projects

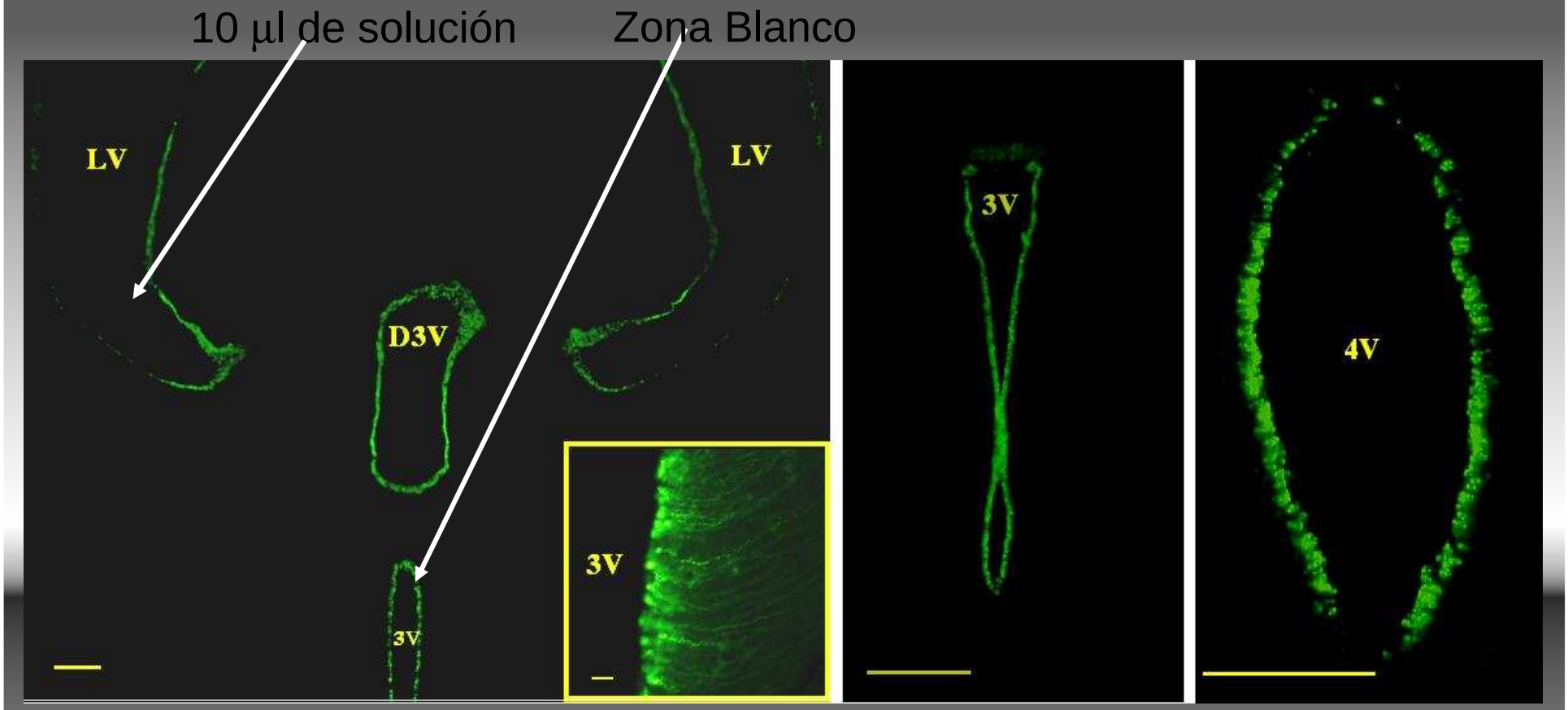
Magnetic assisted transfection

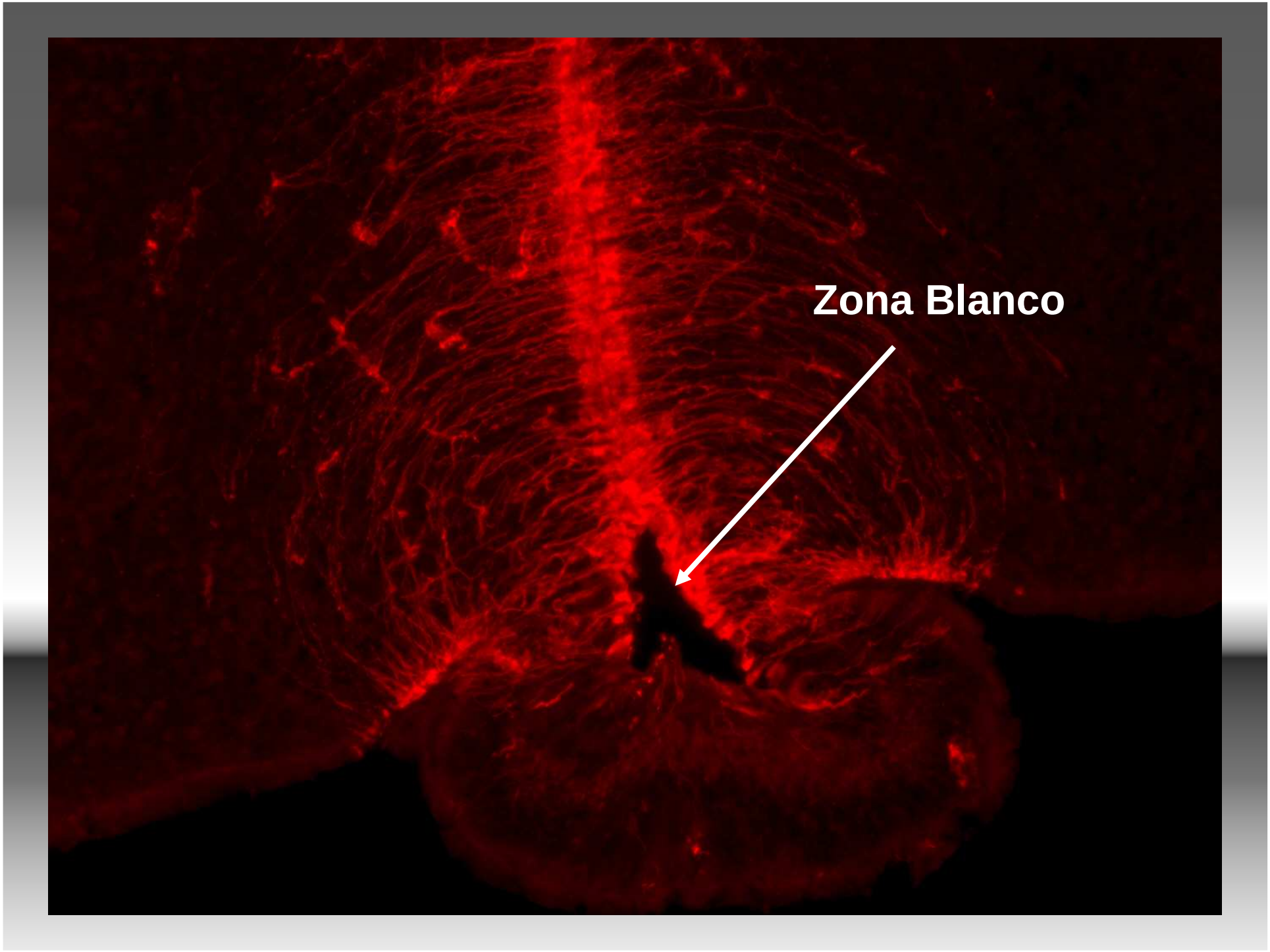


MNP




Prueba animal
LATERAL
ANTEROPOSTERIOR
VENTRAL


10 µl de solución
Zona Blanco
LV
LV
D3V
3V
3V
3V
4V


Zona Blanco

magnetofección

Projectos

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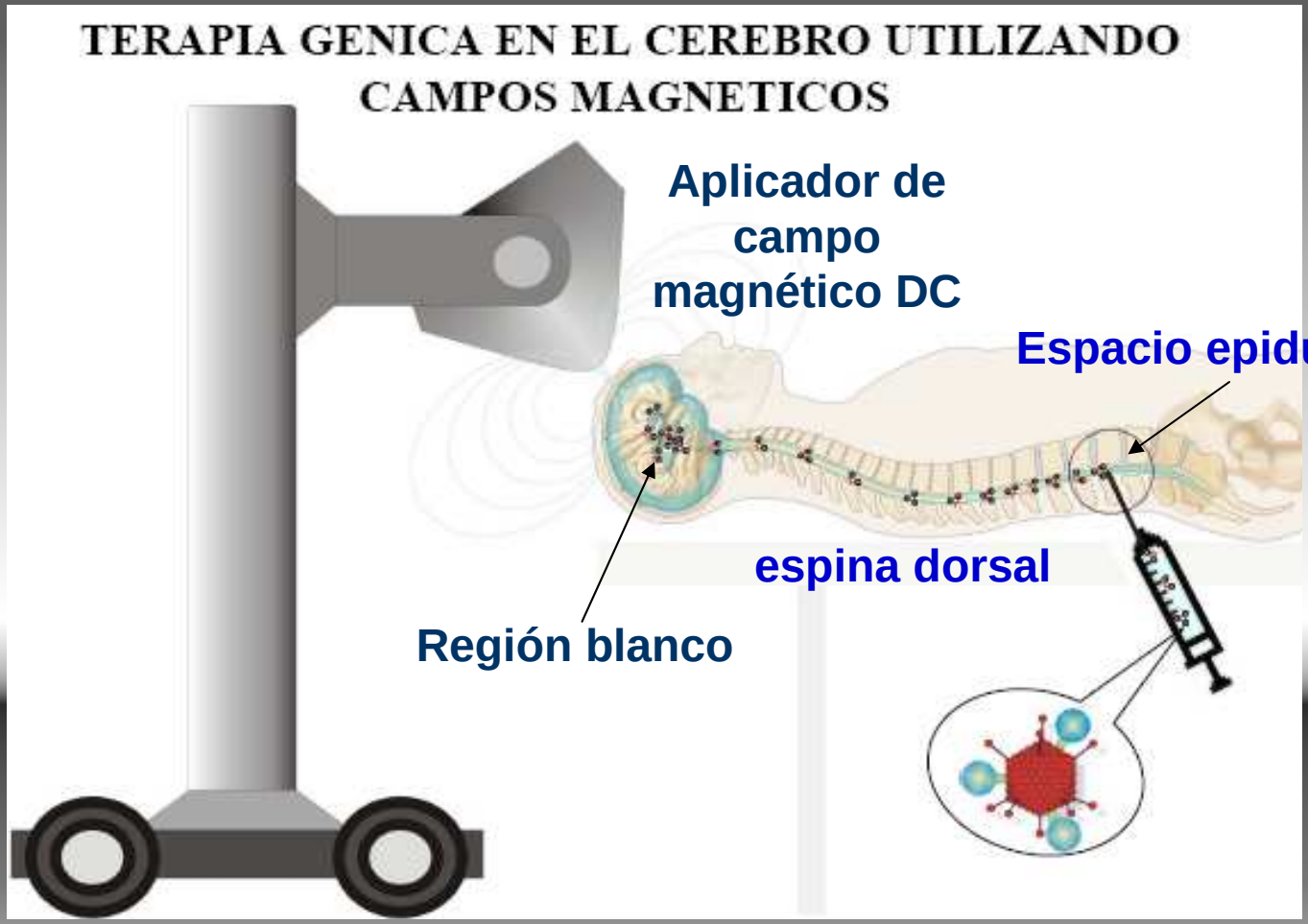
FACULTAD DE CIENCIAS MÉDICAS



TERAPIA GÉNICA MÍNIMAMENTE INVASIVA POR MAGNETOFECCIÓN PARA CEREBRO ENVEJECIDO

Many Thanks