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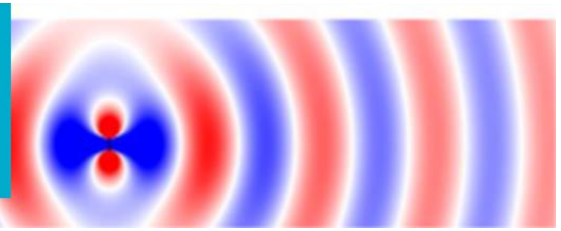
Effect of photothermal therapy on nuclear magnetic resonance imaging during concurrent use

C. Rousseau[1] , Q.L. Vuong[2], Y. Gossuin[2], B. Maes[1] and G. Rosolen[1]

1 Micro- and Nanophotonic Materials Group, Research Institute for Materials Science and Engineering, University of Mons

2 Biomedical Physics Unit, University of Mons

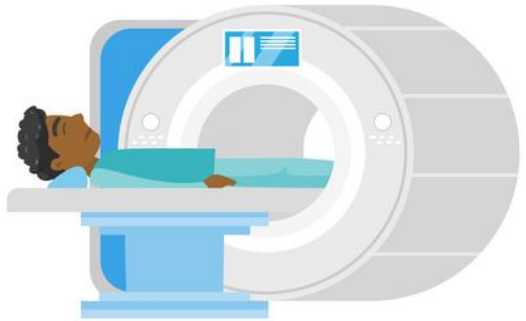
Matériaux Micro- et Nano-photoniques

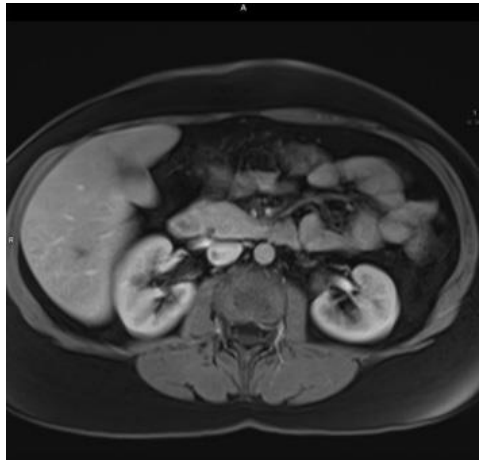


Introduction

Diagnostic phase: Magnetic Resonance Imaging (MRI)

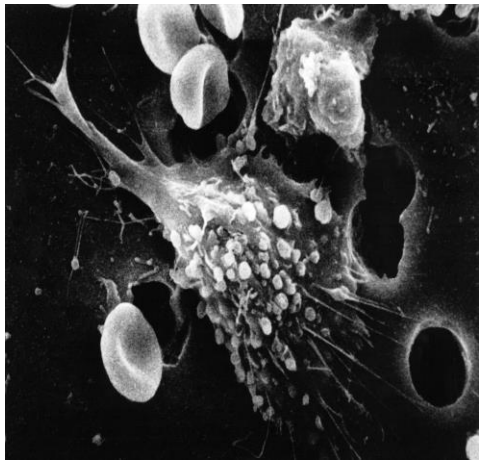
Contrast agents





Treatment phase: Phototermal therapy (PTT)

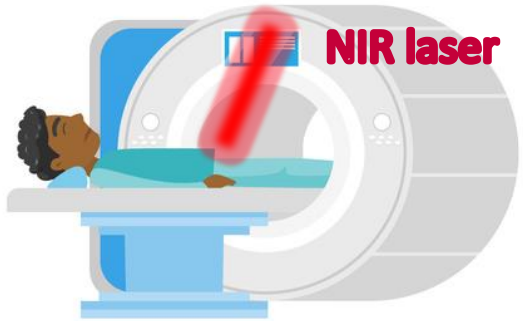
Photothermal agents

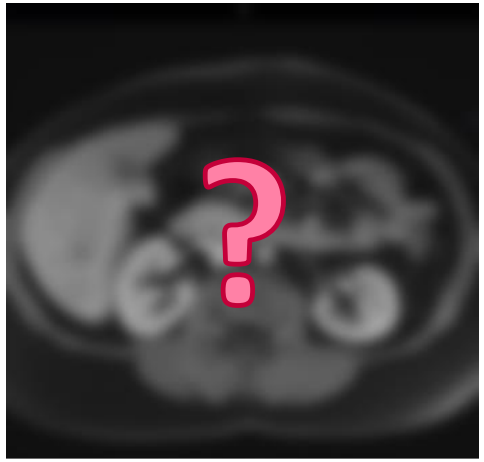


Introduction

Theranostic approach: MRI + PTT

Contrast/Photothermal agents





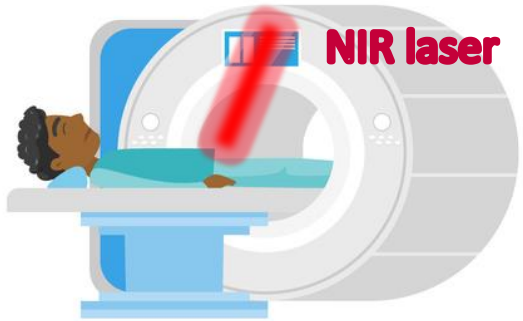
Underlying question:

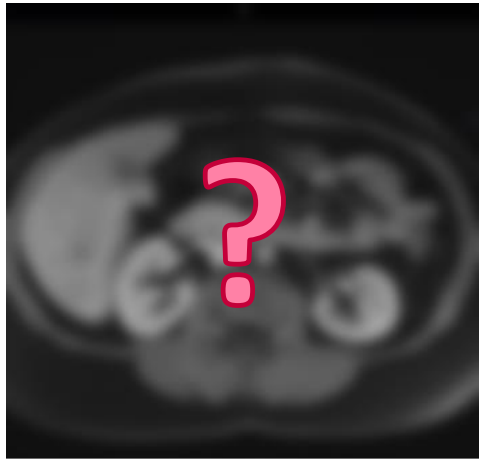
"How will the use of phototherapy modify MRI images?"

Introduction

Theranostic approach: MRI + PTT

Contrast/Photothermal agents





Underlying question:

"How will the use of phototherapy modify MRI images?"

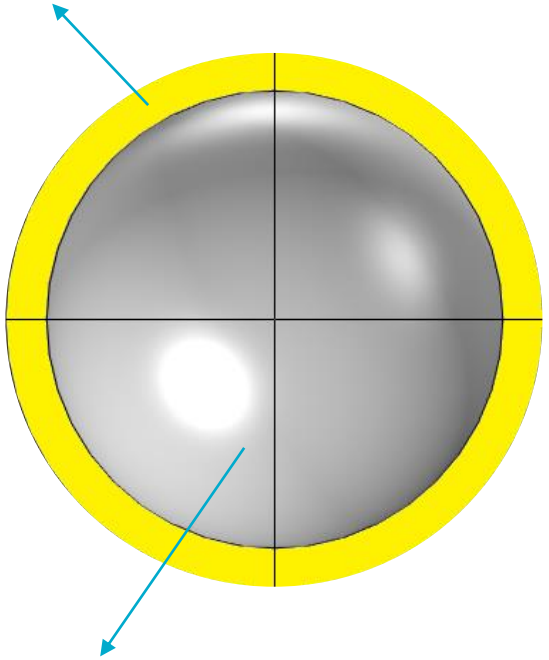
More precise question:

"How does laser illumination of a solution modify its transverse relaxation rate (R2)?"

Contrast/Photothermal study

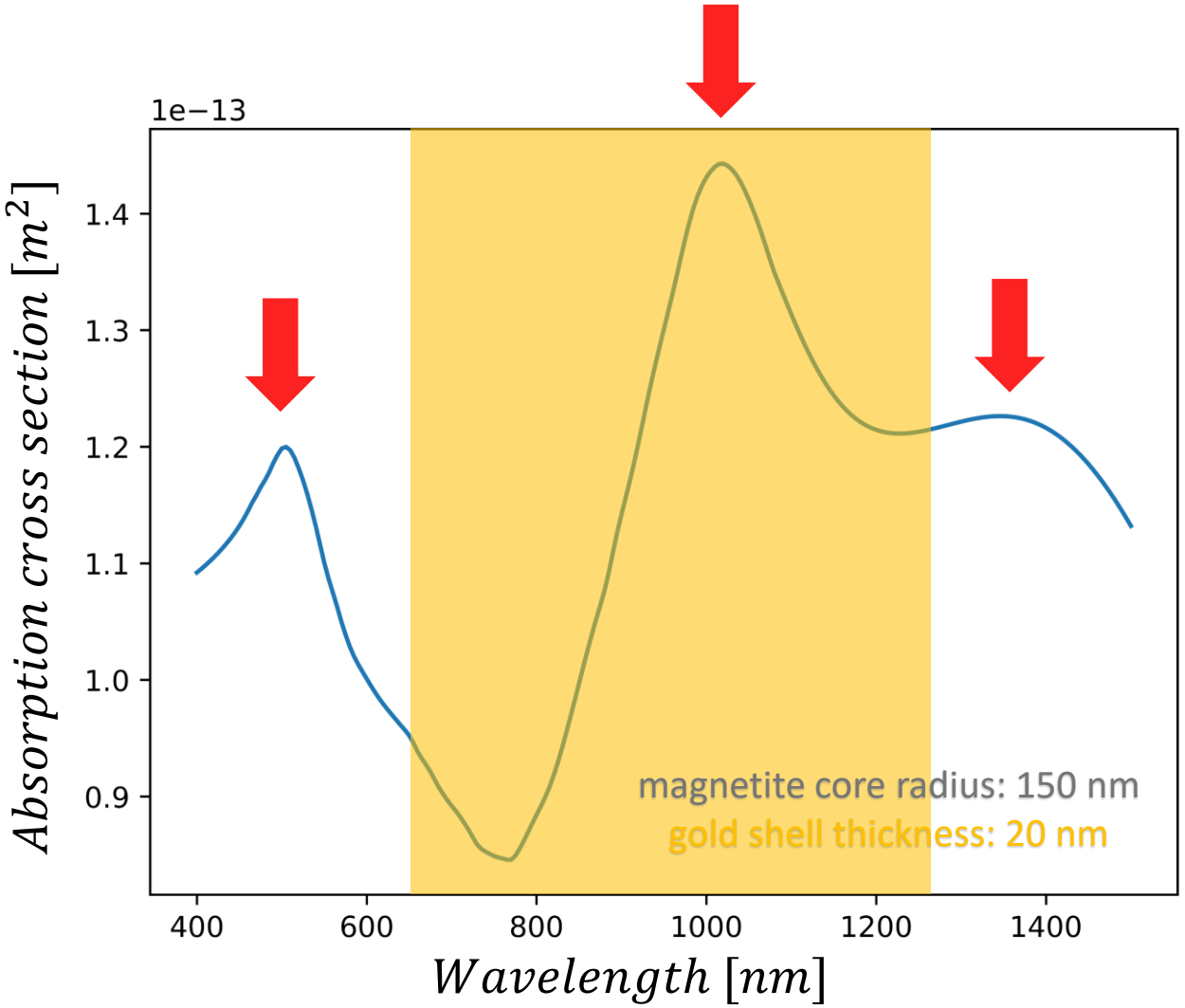
- Hybrid nanoshell platforms:

Gold nanoshell: allow PTT ≈ + 8°C



Magnetite core (Fe_3O_4) allow MRI

Plasmonic hybridization between nanosphere/nanocavity



Biological window

Temperature rise around nanoshell vs laser irradiance

- Steady-state heat transfer differential equation

$$T_{ext}(r) = \frac{Q_{core} + Q_{shell}}{4\,\pi\,r\,\kappa_{env}} + T_{\infty}$$

Temperature rise around nanoshell vs laser irradiance

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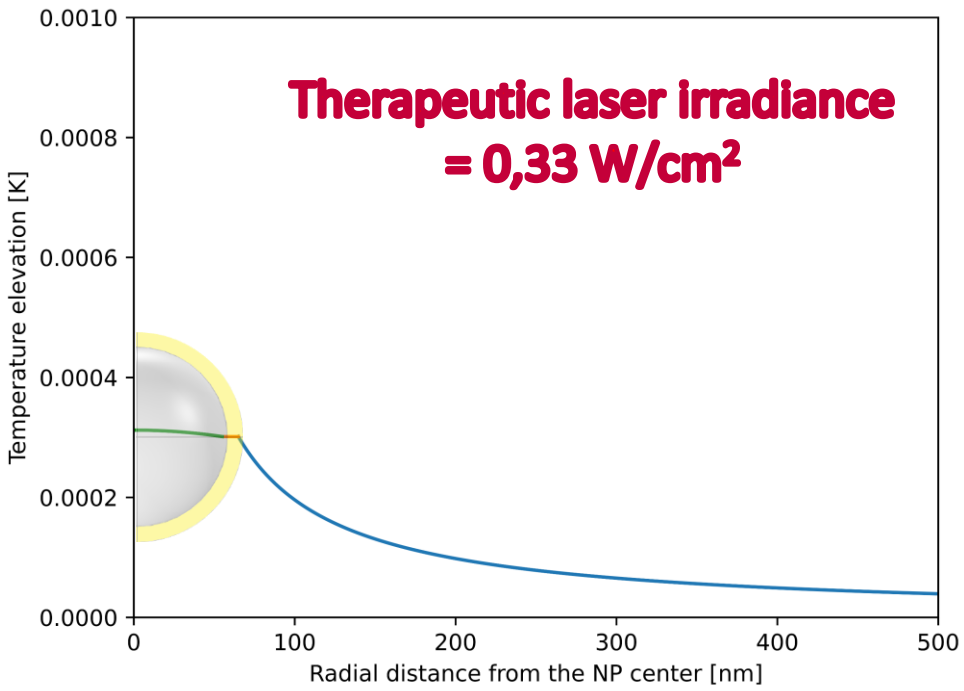
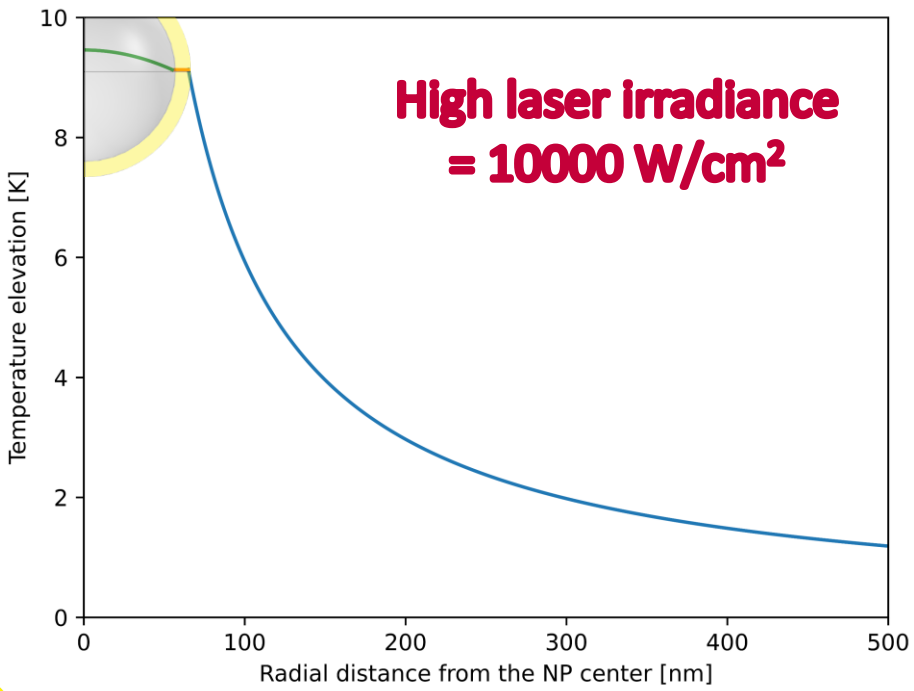
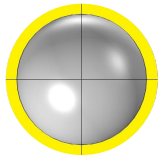






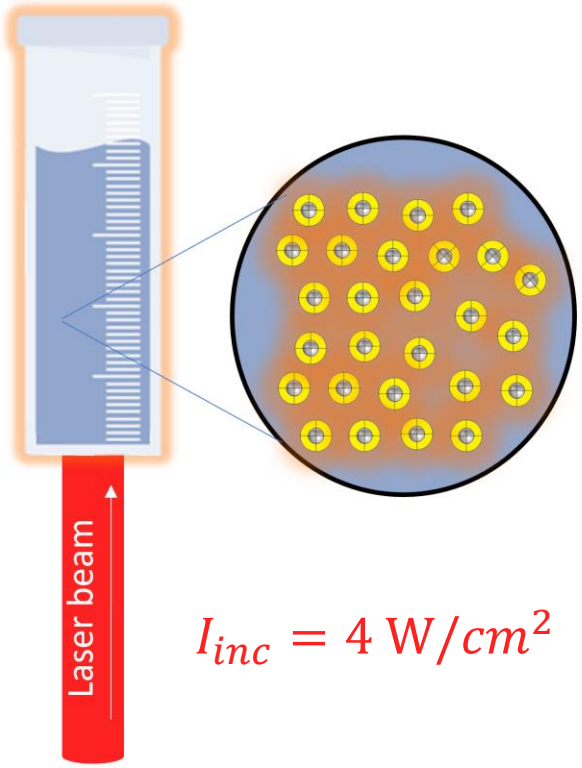
magnetite core radius: 55 nm

gold shell thickness: 10 nm

Contradiction with the experience?

Macroscopic
T° rise ≈ 18°C

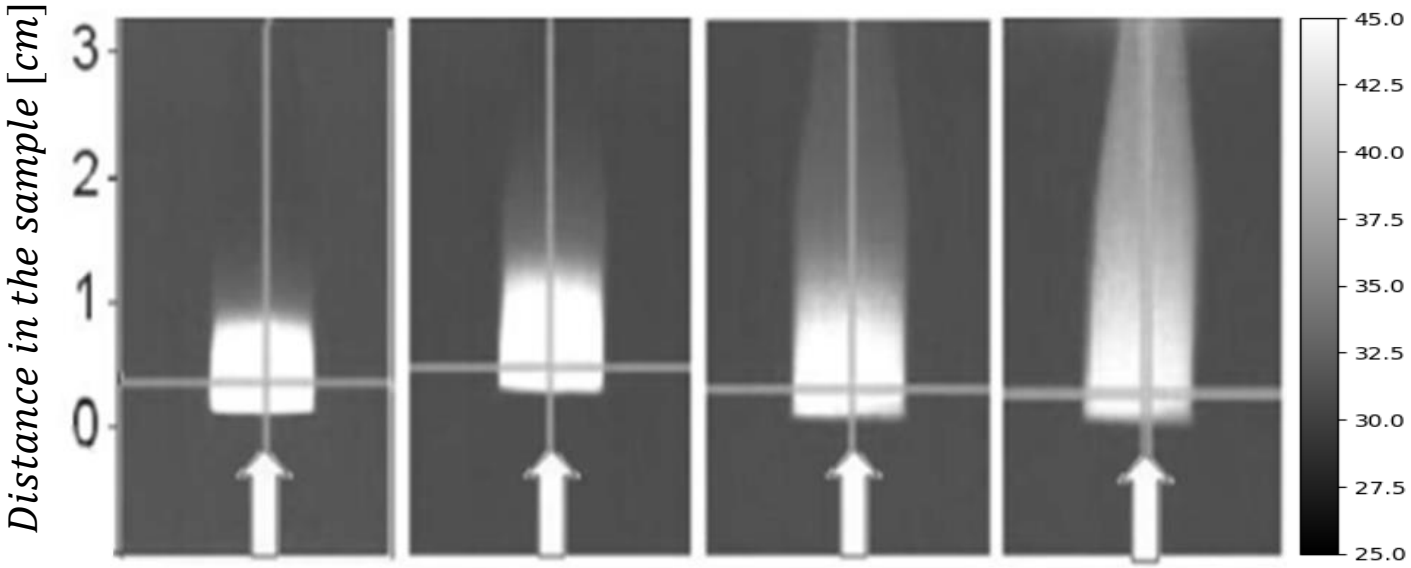
Experimental set-up



$I_{inc} = 4\ W/cm^2$

Experimental results

Nanoparticle concentration (N) $= 5 \times 10^9\ cm^{-3}$



N $N/4$ $N/8$ $N/16$ °C

T°$_{amb}$ = 28°C

[1] G. S. Terentyuk et al., J. Biomed. Opt., vol. 14, n° 2, 2009.

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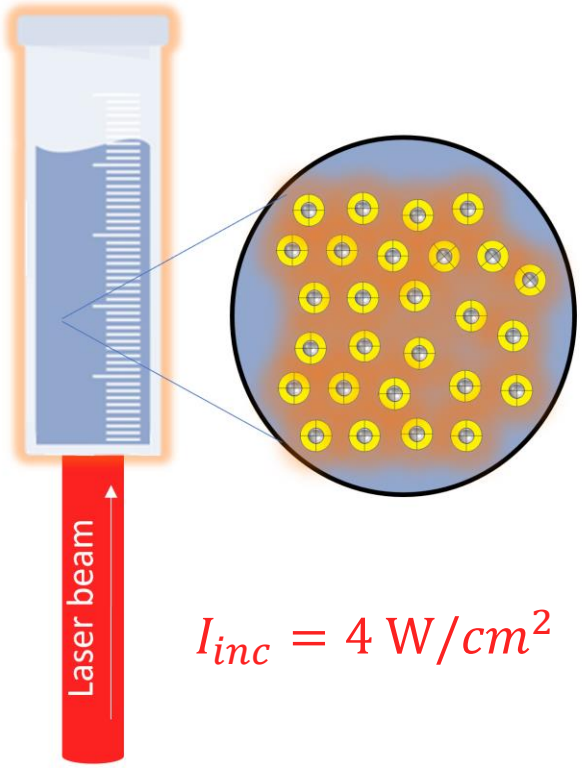

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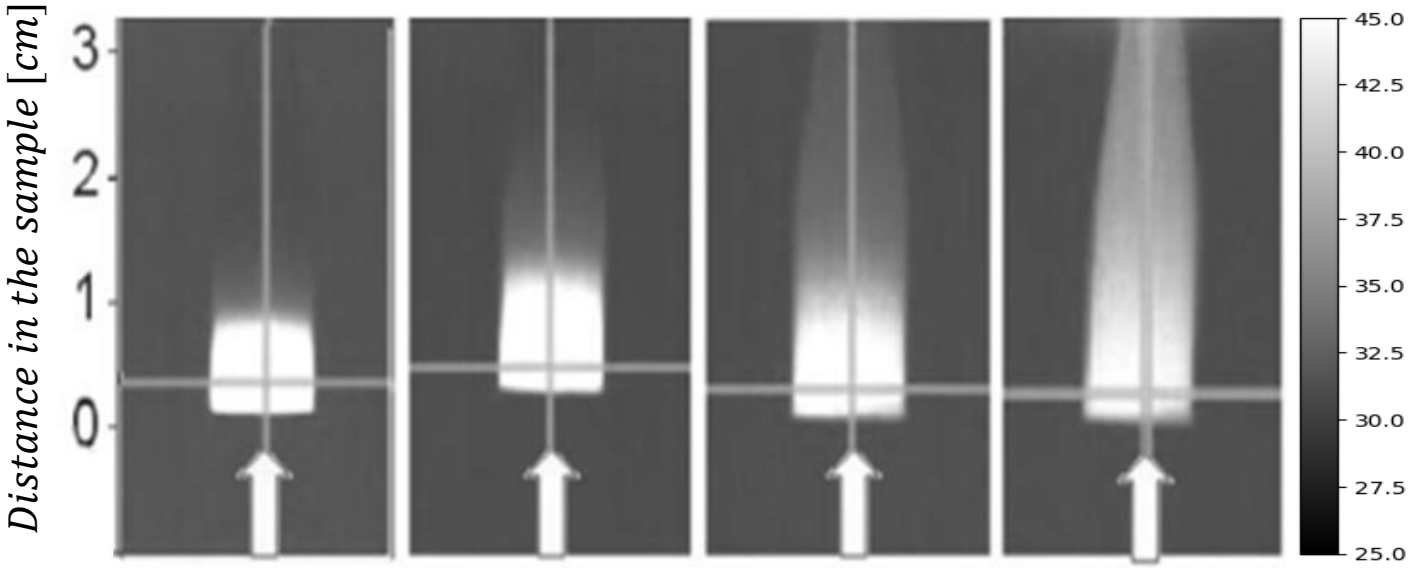


T°$_{amb}$ = 28°C

" How can nanosimulation be linked to macro experiments?"

Solution: collective thermal interactions of nanoparticles

- Sum contribution of all NPs in the sample:

$$T_{collective}(\vec{r}) = \sum_{k=1}^{N} \frac{q_k\left(\overrightarrow{r'}\right)}{4\pi\kappa_{env}|\overrightarrow{r_k} - \vec{r}|} + T_{amb}$$

Solution: collective thermal interactions of nanoparticles

- Sum contribution of all NPs in the sample: continuous approximation

$$T_{collective}(\vec{r}) = \iiint \frac{q\left(\vec{r'}\right)}{4\pi\kappa_{env}\left|\vec{r'} - \vec{r}\right|} dr' + T_{amb}$$

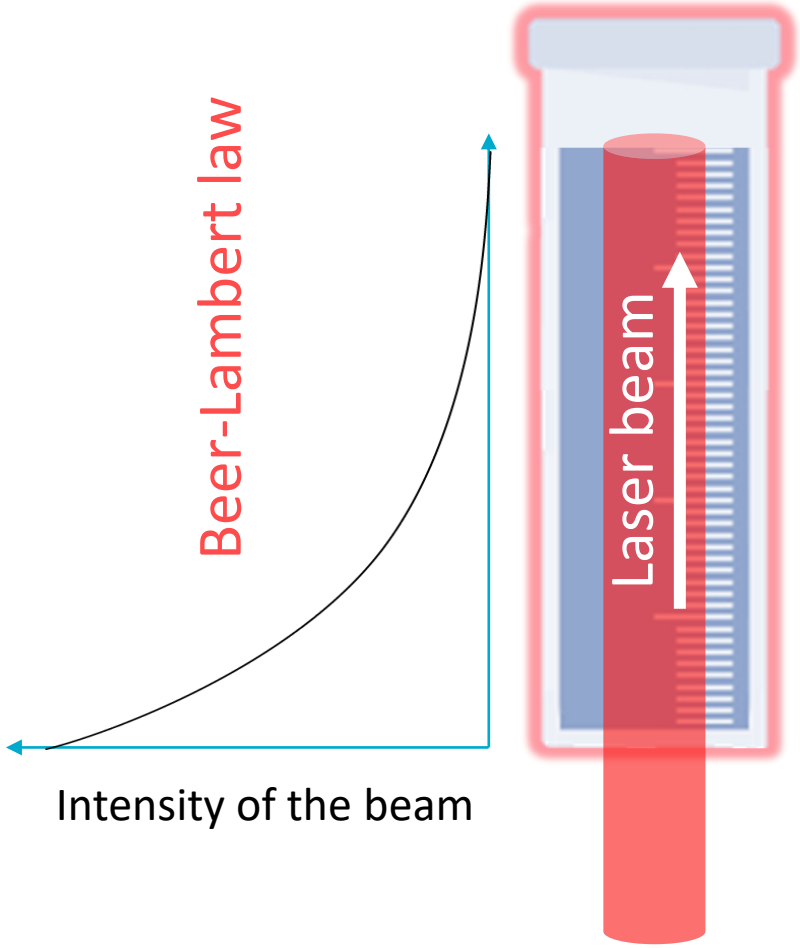
Laser beam

Extinction cross section

$$q\left(\vec{r'}\right) = I_0\, N\, \sigma_{abs}\, \boxed{e^{(-\sigma_{ext}\, N\, z)}}$$

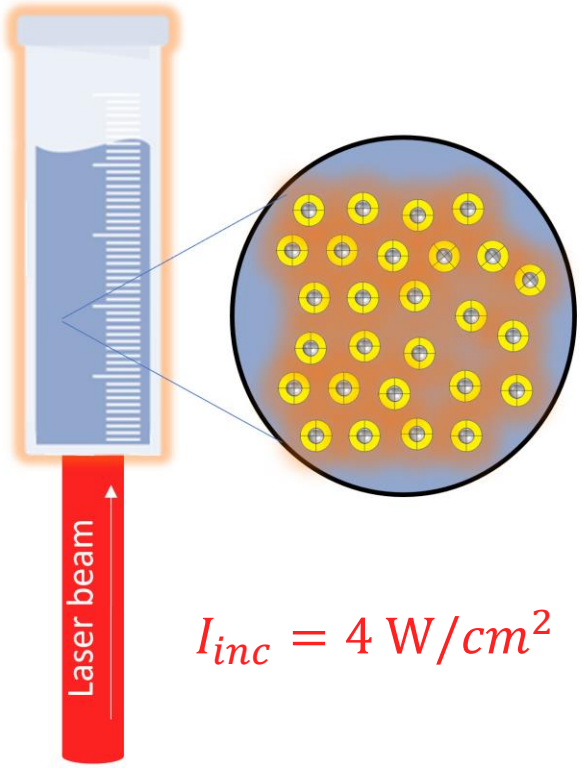
Absorption cross section

Distance in sample



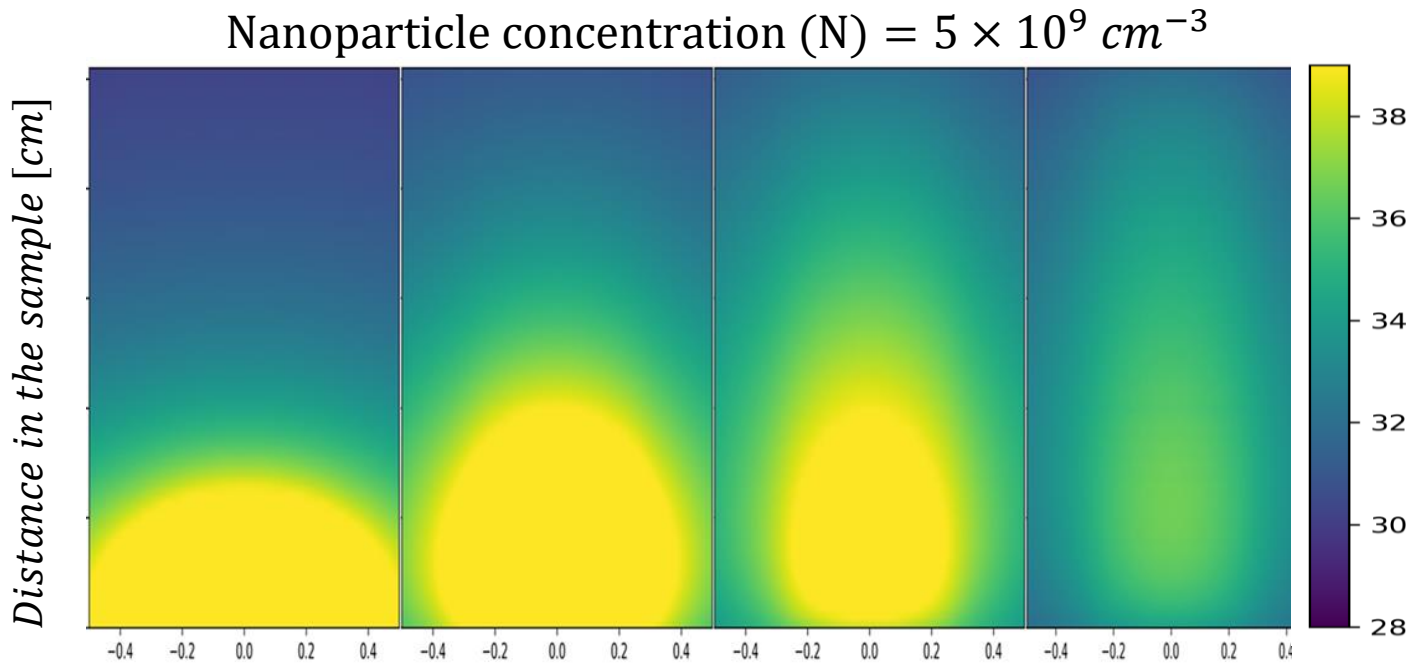
Good agreement between simulations and experiments

Simulation set-up



$I_{inc} = 4\ \mathrm{W}/cm^2$

Numerical results



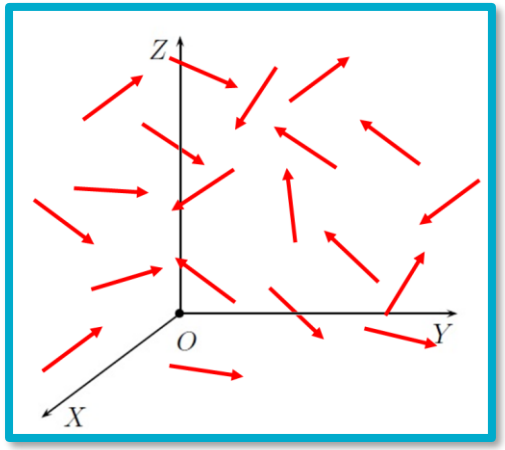
N $N/4$ $N/8$ $N/16$ °C

T°$_{amb}$ = 28°C

Elevation of solvant temperature ≈ 6°C

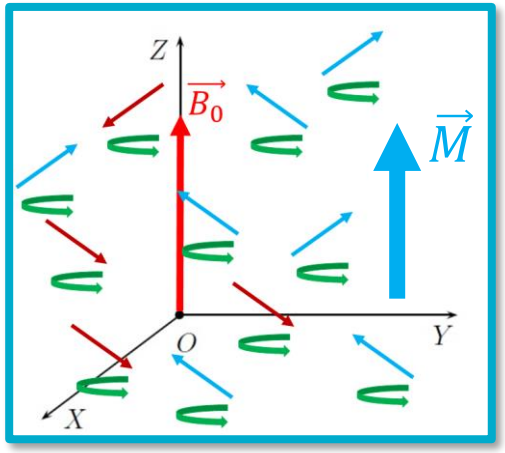
Nuclear Magnetic Resonance: R2, a parameter related to the signal in MRI

Sample without magnetic field



Randomized magnetic moment

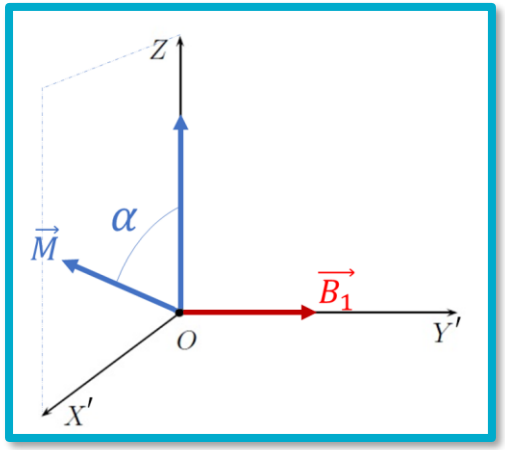
Constant magnetic field $\overrightarrow{B_0}$



Larmor frequency

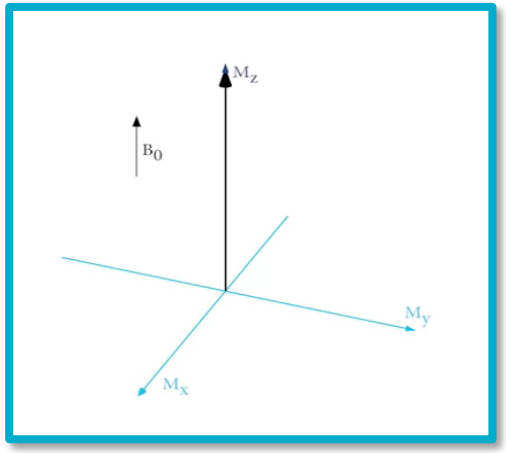
Resulting magnetization $\vec{M}$

Oscillating magnetic field $\overrightarrow{B_1}$



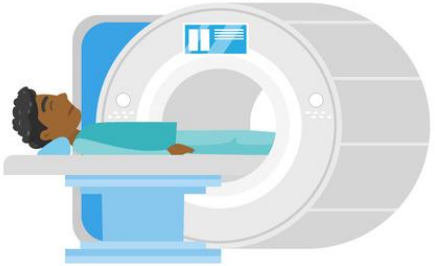
System out of equilibrium

Relaxation



Return to magnetization equilibrium

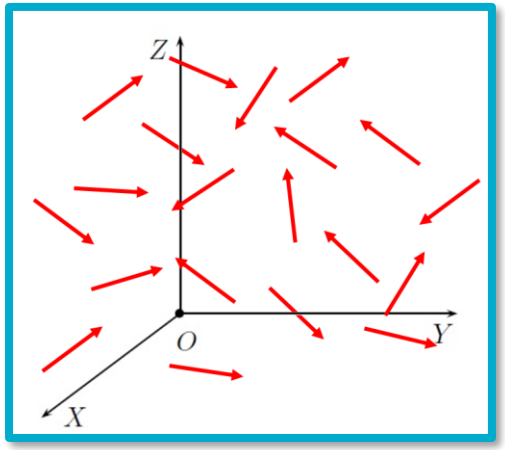
Relaxation times



MRI imaging based on the relaxation times

Nuclear Magnetic Resonance: R2, a parameter related to the signal in MRI

Sample without magnetic field



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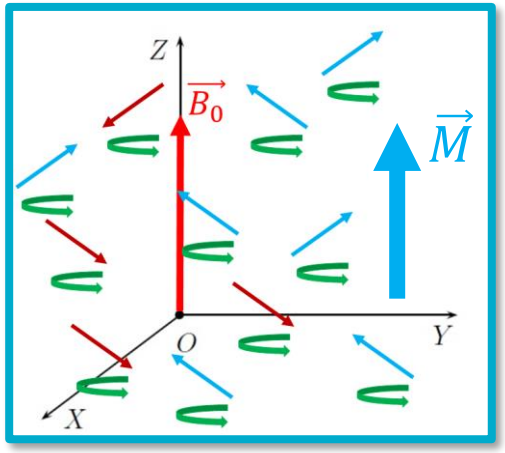

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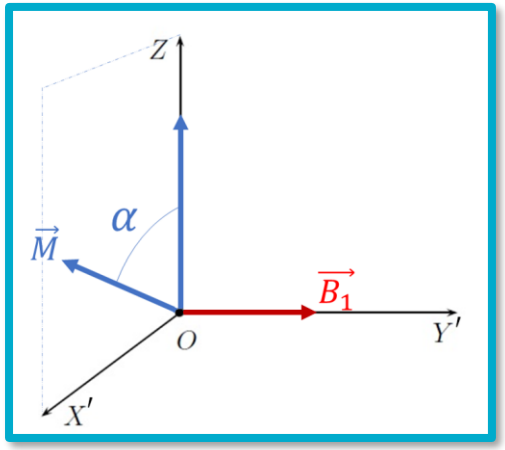

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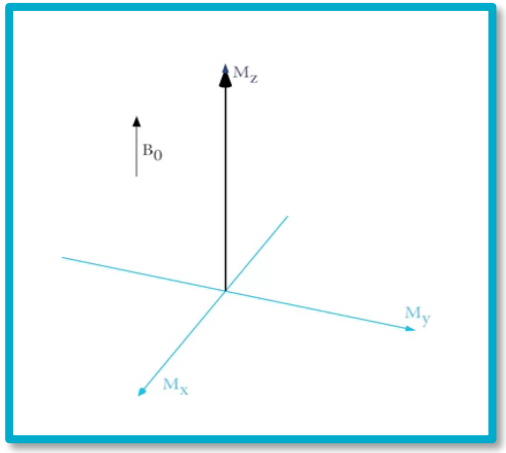


Return to magnetization equilibrium

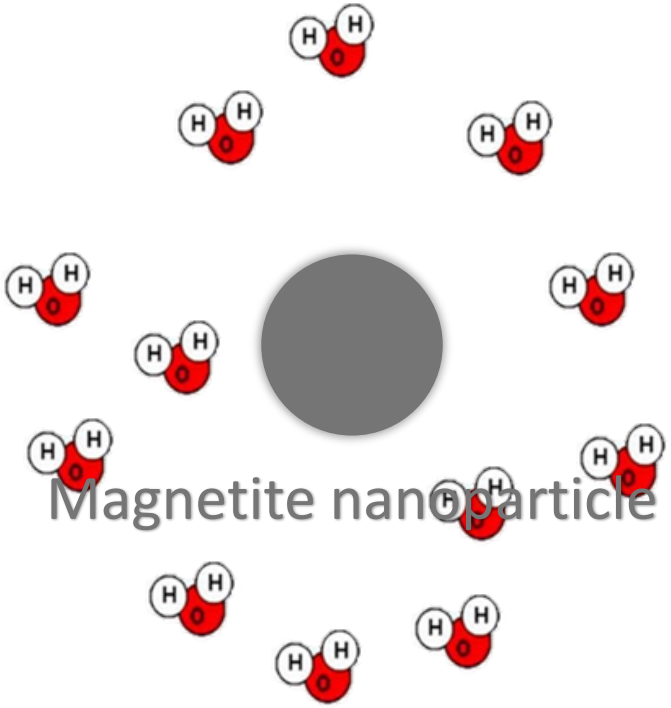
Transverse relaxation: return to equilibrium of the transverse component of $\vec{M}$

→ progressive dephasing of magnetic dipoles

→ describe by the transverse relaxation rate R_2 [s^{-1}]

Relaxation process and temperature influence

- Relaxation caused by the magnetic fluctuations experienced by each proton



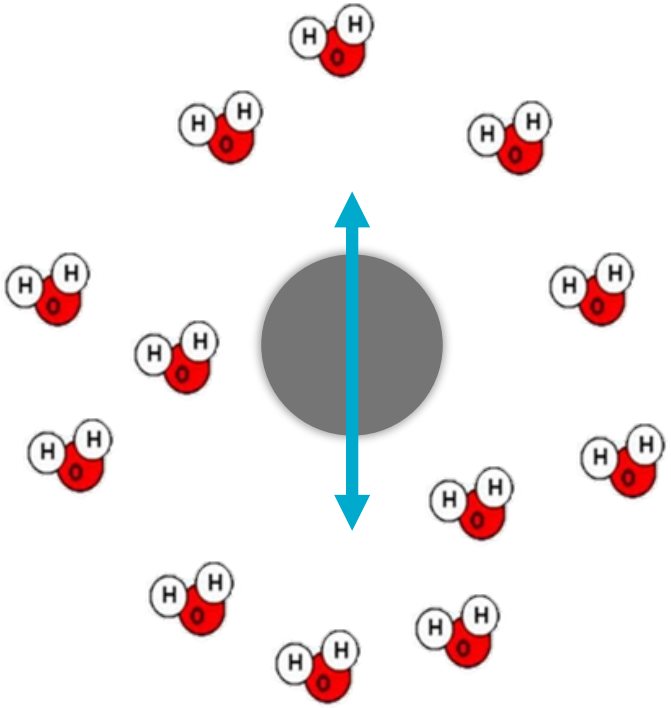
The contrast agents add magnetic fluctuations in the system

↓

Increase the relaxation

Relaxation process and temperature influence

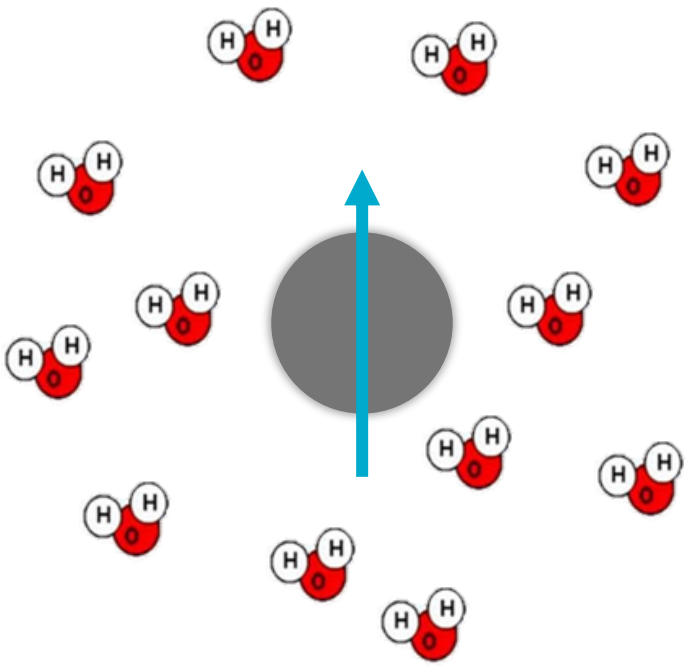
- Relaxation caused by the magnetic fluctuations experienced by each proton



- Néel relaxation

Relaxation process and temperature influence

- Relaxation caused by the magnetic fluctuations experienced by each proton



Temperature influences both processes

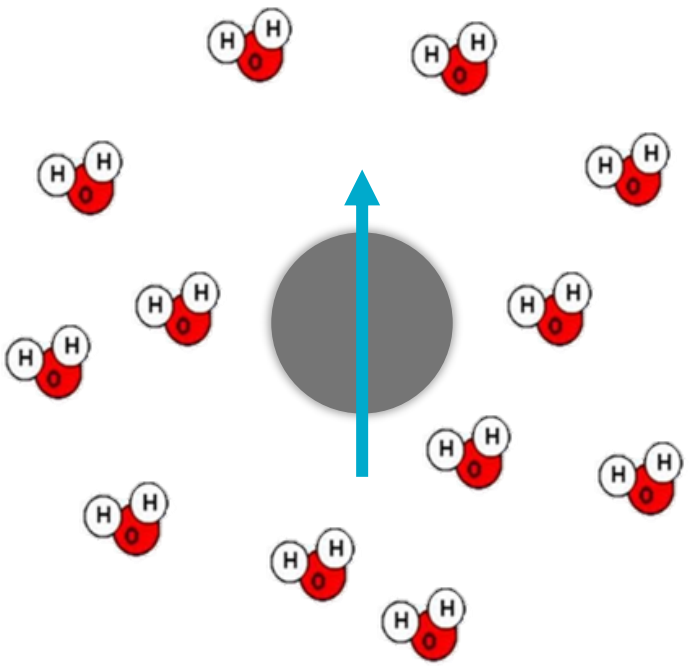
↓

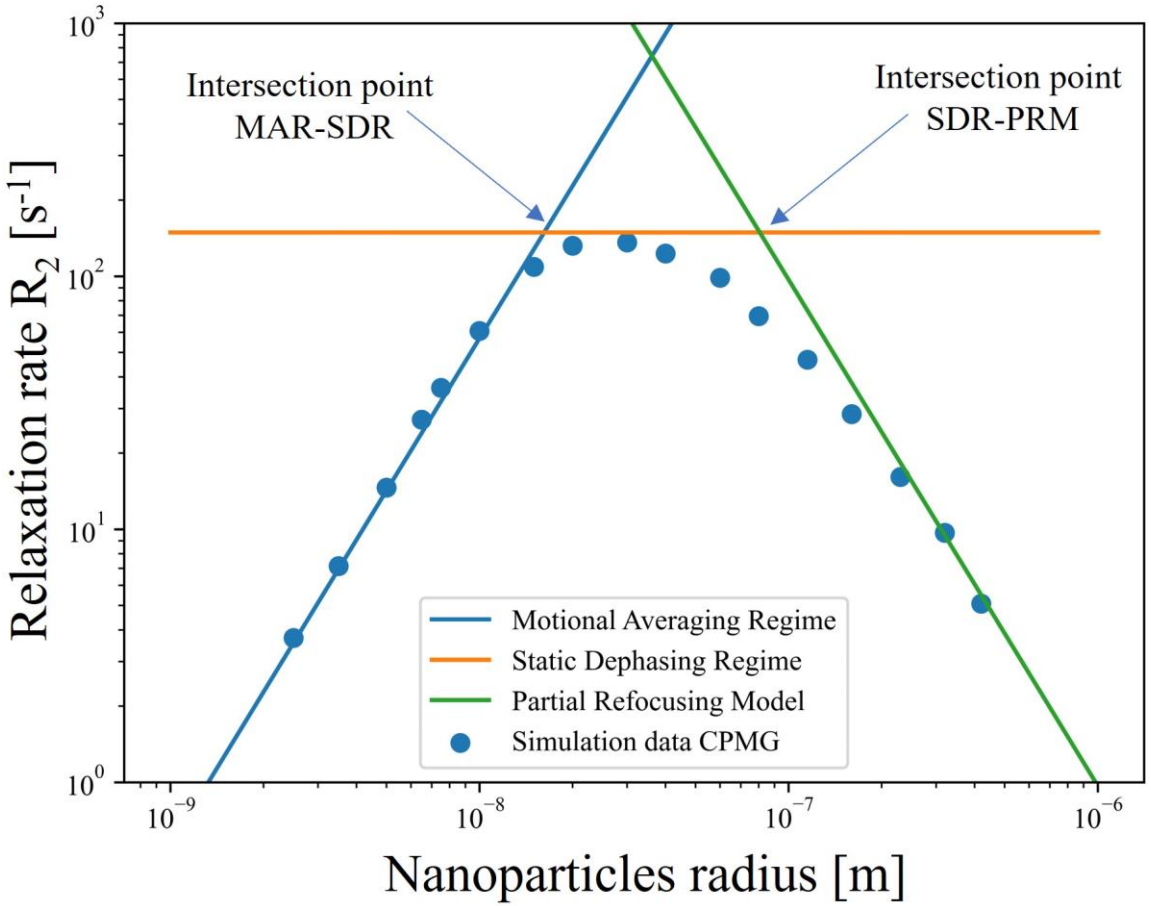
Relaxation depends on temperature

- Néel relaxation
- Brownian relaxation

Relaxation process and temperature influence

- Relaxation caused by the magnetic fluctuations experienced by each proton



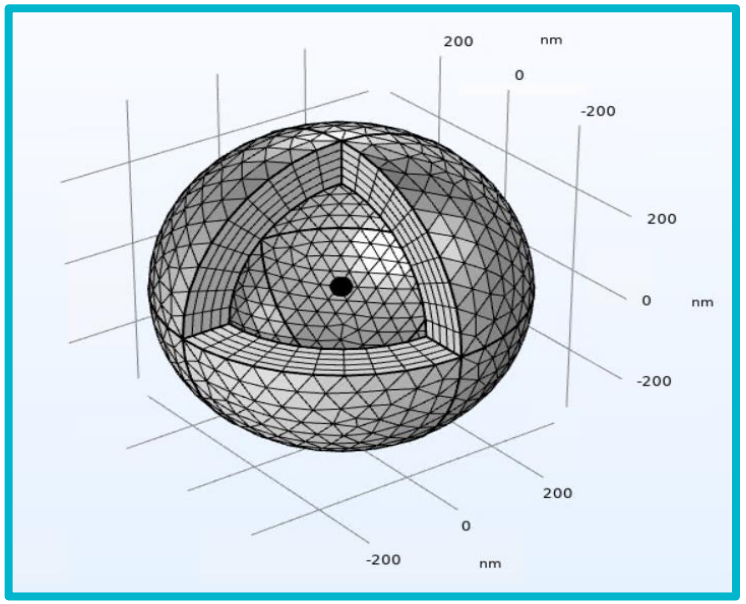


- Néel relaxation
- Brownian relaxation

The relaxation also depends on the size of the nanoparticles

Calculation procedure

1) COMSOL Multiphysics simulations → σ_{abs} and σ_{ext}



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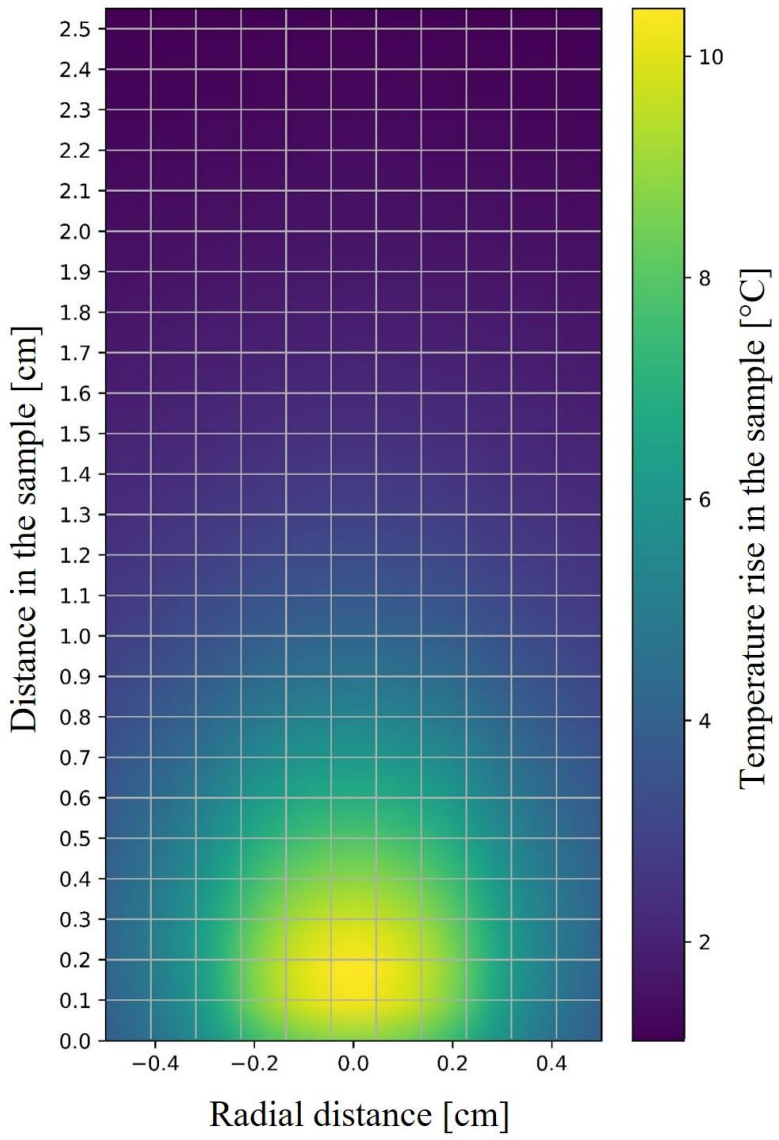
1) COMSOL Multiphyscis simulations → σ_{abs} and σ_{ext}

2) Calculate the map of the temperature rise with the collective model

3) Discretize the map in voxel + compute the mean value



Calculation procedure

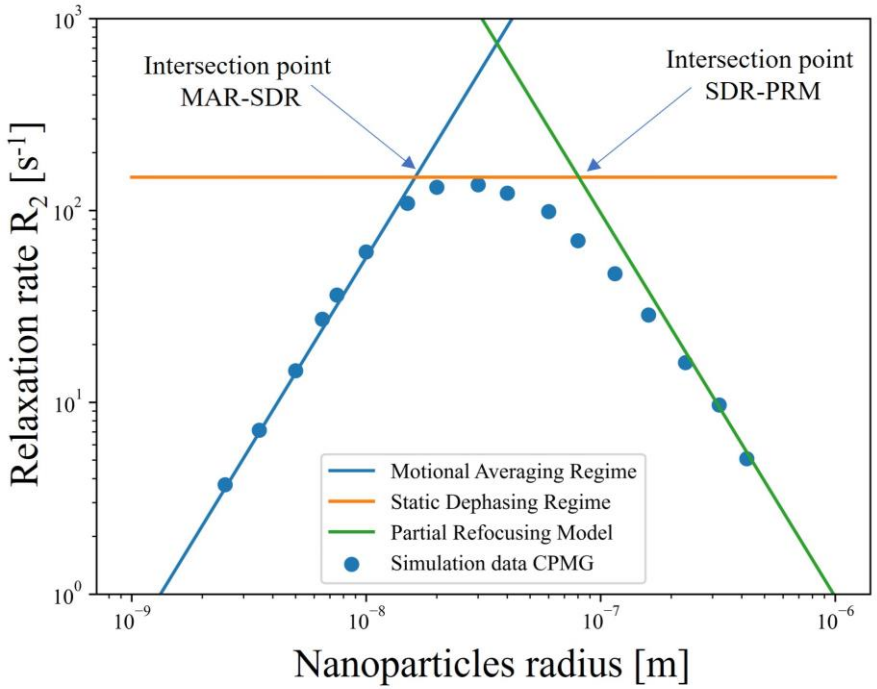
1) COMSOL Multiphyscis simulations → σ_{abs} and σ_{ext}

2) Calculate the map of the temperature rise with the collective model

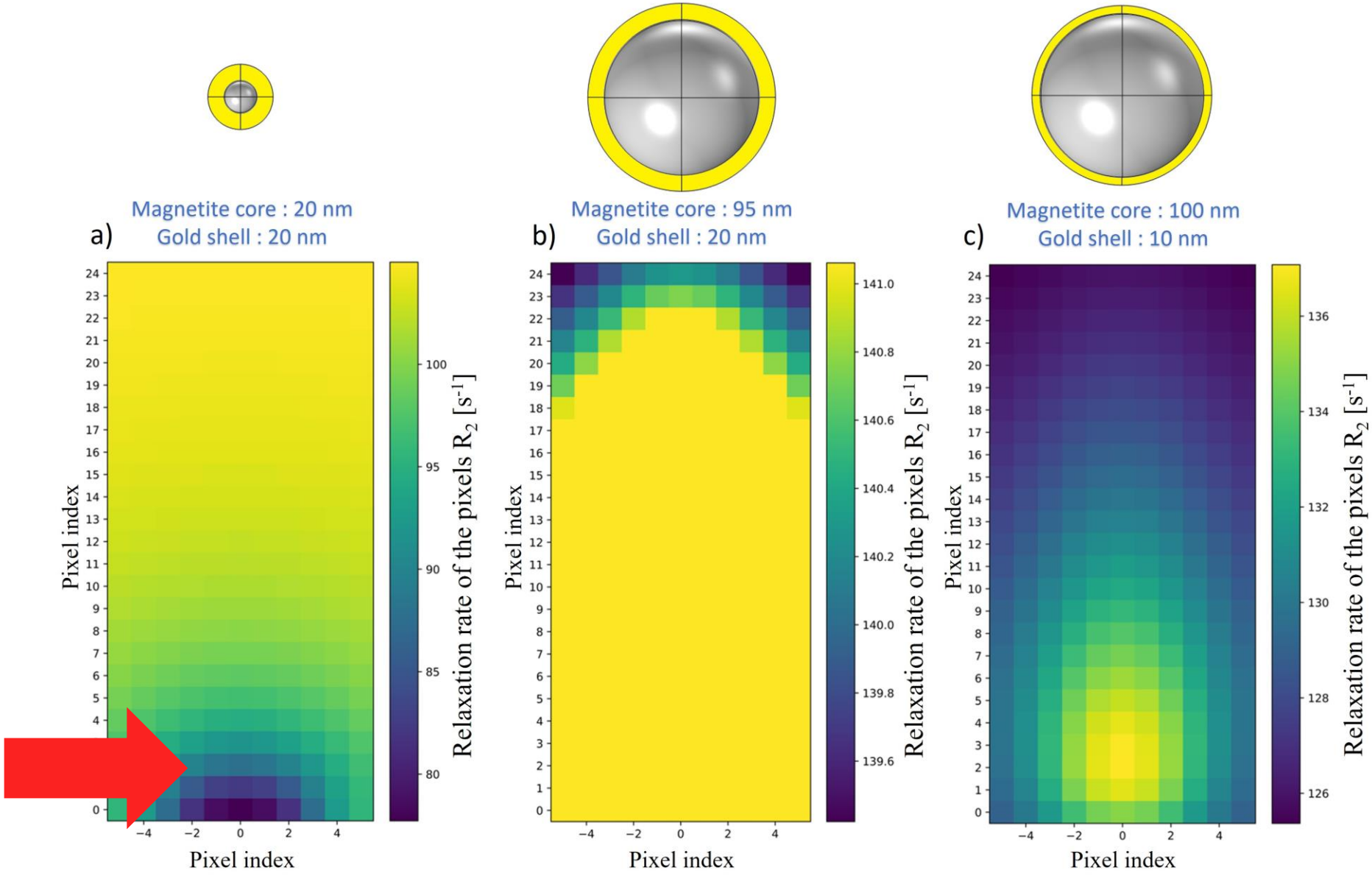
3) Discretize the map in voxel + compute the mean value

4) Choose of the relaxation model for each voxel

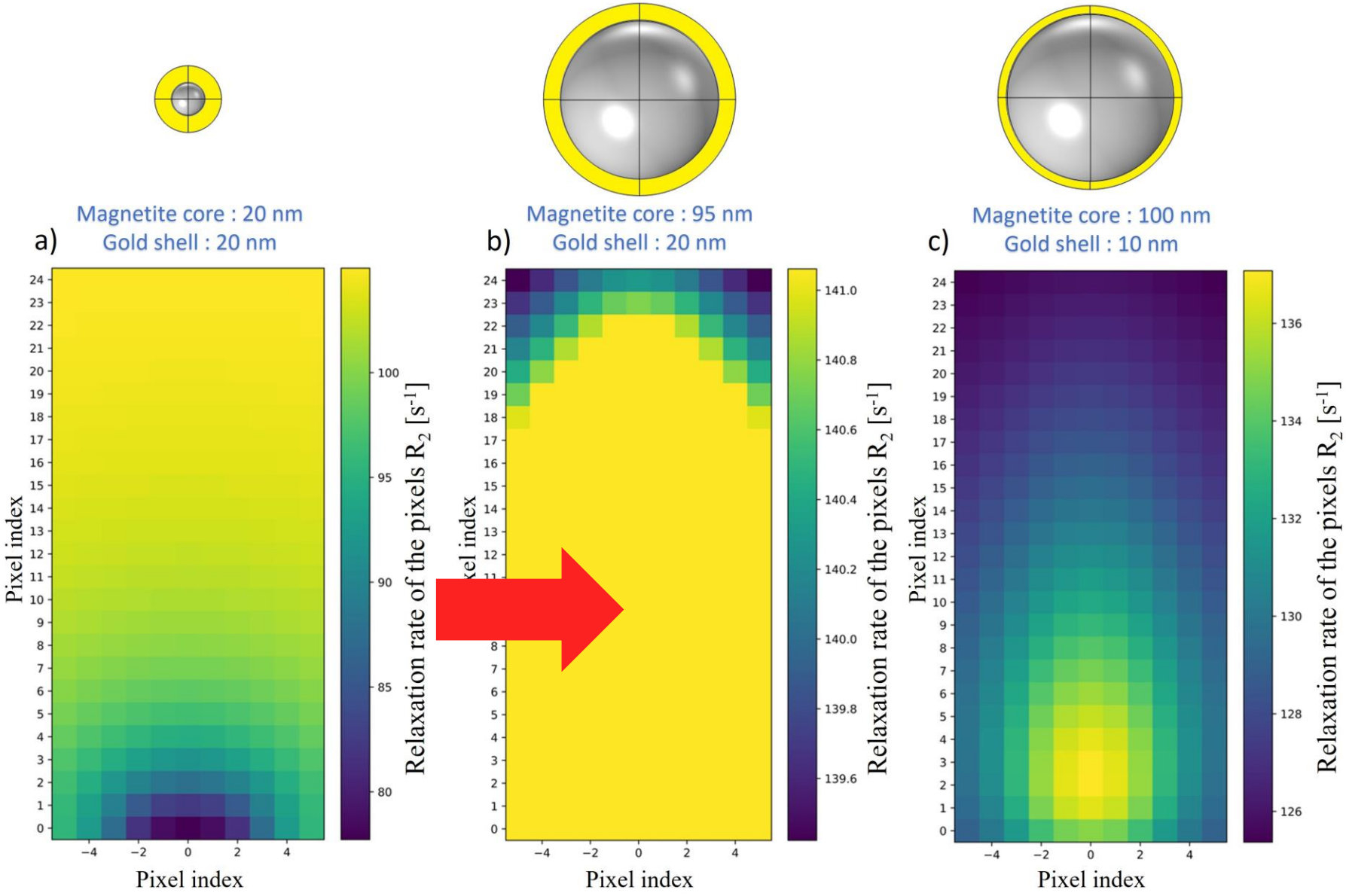
5) Plot the map of the modification of R_2 in the sample



Results


a)
Magnetite core : 20 nm
Gold shell : 20 nm
b)
Magnetite core : 95 nm
Gold shell : 20 nm
c)
Magnetite core : 100 nm
Gold shell : 10 nm
Pixel index
Relaxation rate of the pixels R_2 [s^{-1}]

Results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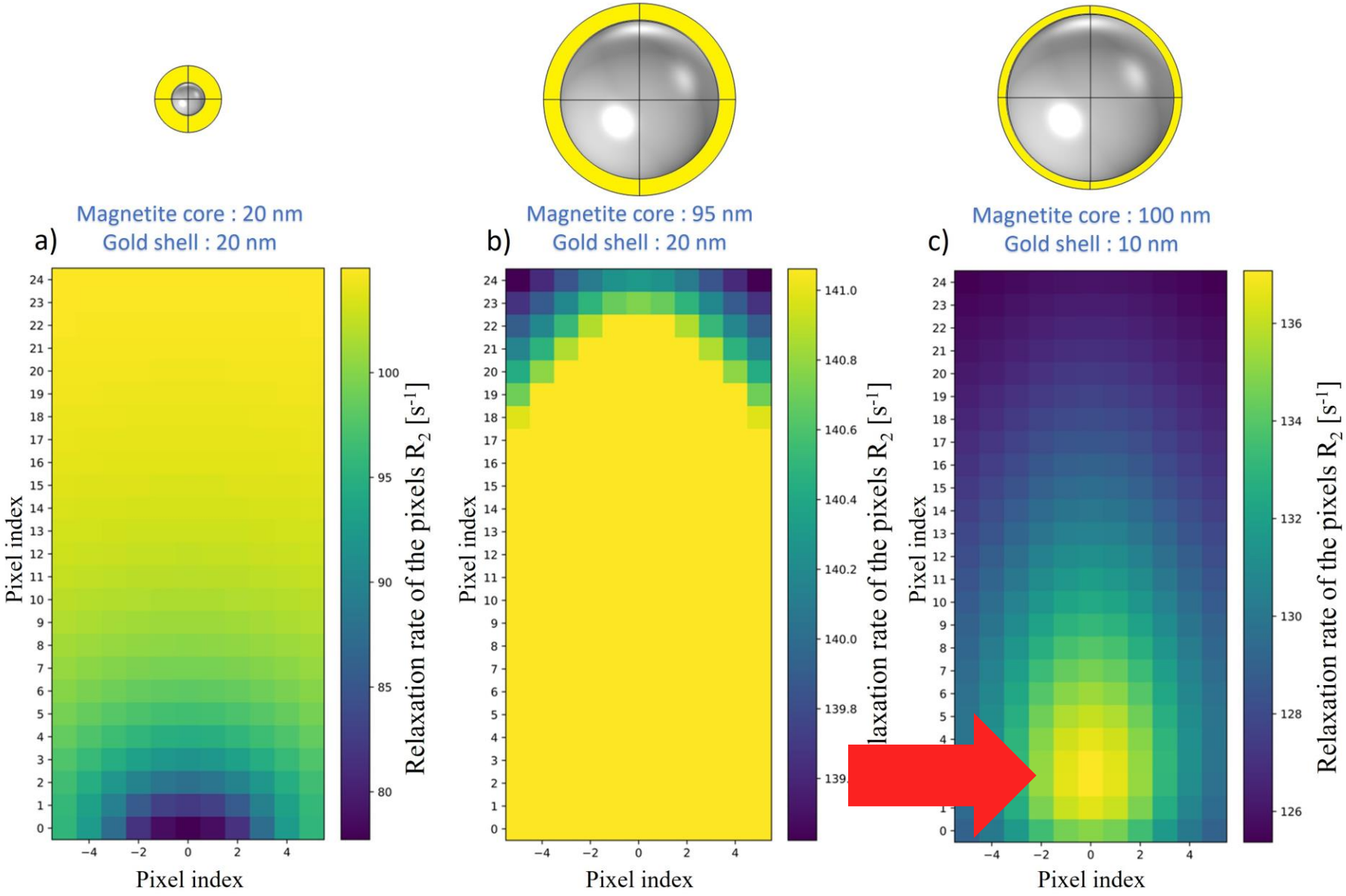
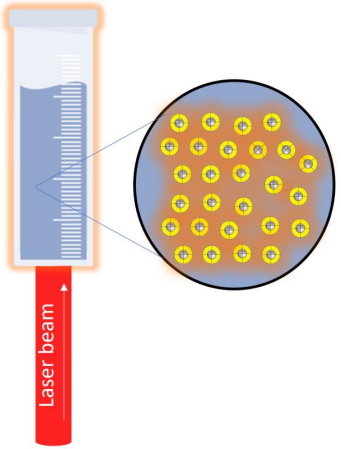


Particle geometry strongly influences R_2 response

Conclusion



- A procedure to evaluate the modification of R_2 in a solution subjected to laser illumination has been developed

→ based on the collective thermal effects between nanoparticles and relaxation theory

→ laser illumination can either increase or decrease the effect of the contrast agent on relaxation, depending on the nanoparticle size

Outlook:

→ Optimisation of the nanoshell parameters to attain desired effect on R_2

→ Consider the biological environment in modelisation