Hybrid plasmonic nanoparticles for photothermal therapy: uniform and aggregated distributions

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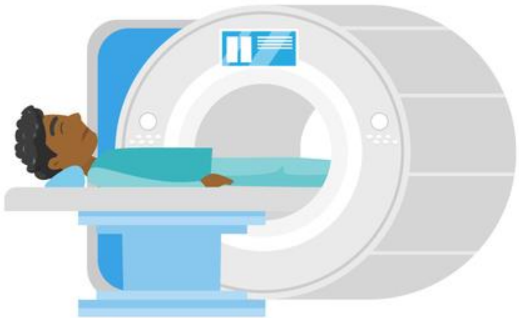
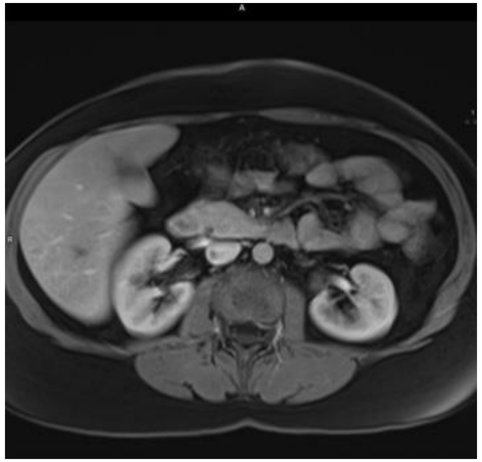
What is the research context?

Diagnostic phase: Magnetic Resonance Imaging (MRI)

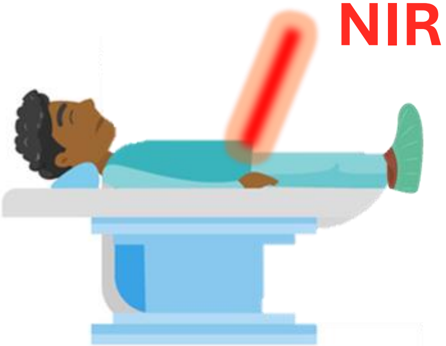
Contrast agents

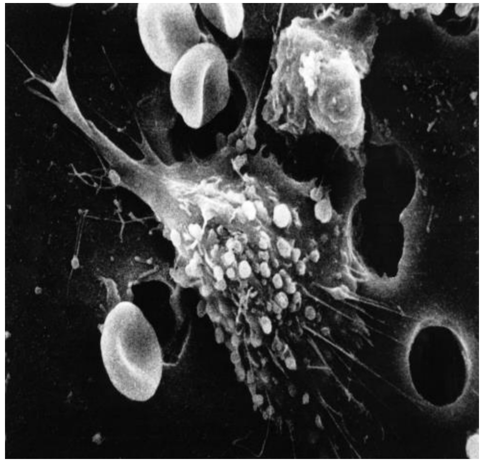




Treatment phase: Phototermal therapy (PTT)

Photothermal agents

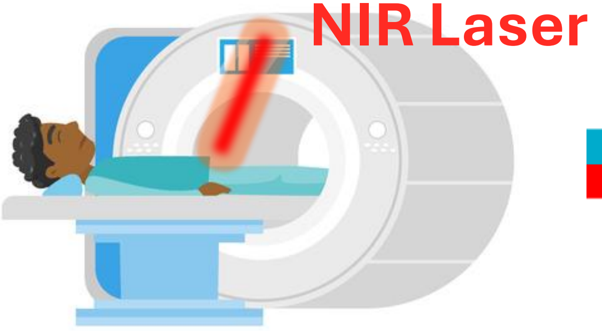


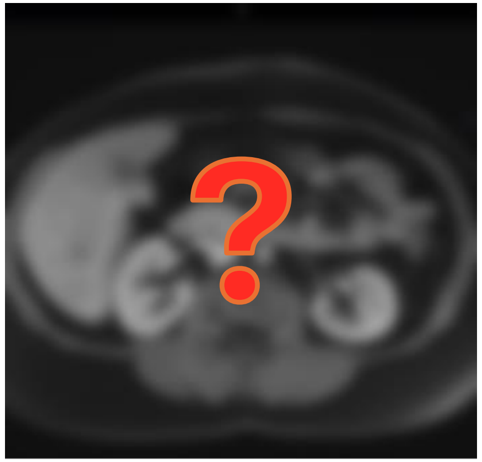


What is the research context?

Theranostic approach: MRI + PTT

Contrast/Photothermal agents





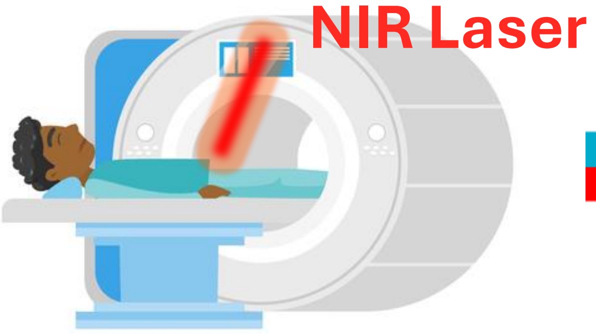
Underlying question:

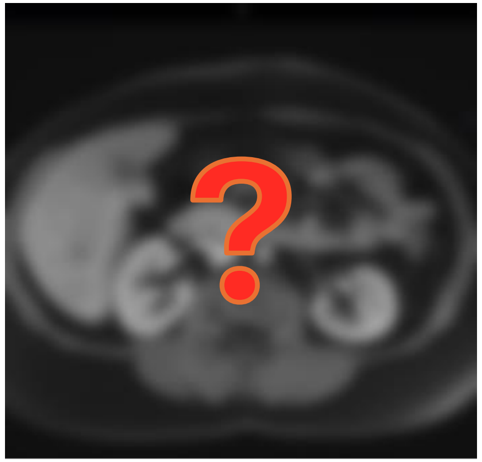
“How will the use of phototherapy modify MRI images?”

What is the research context?

Theranostic approach: MRI + PTT

Contrast/Photothermal agents





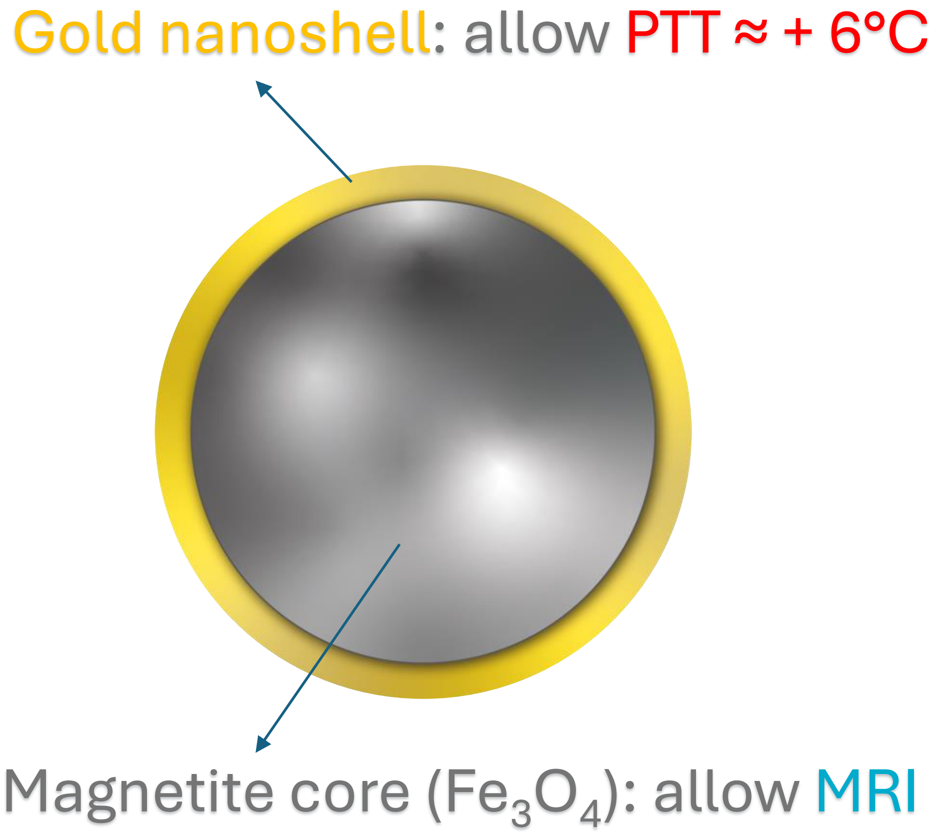
Underlying question:

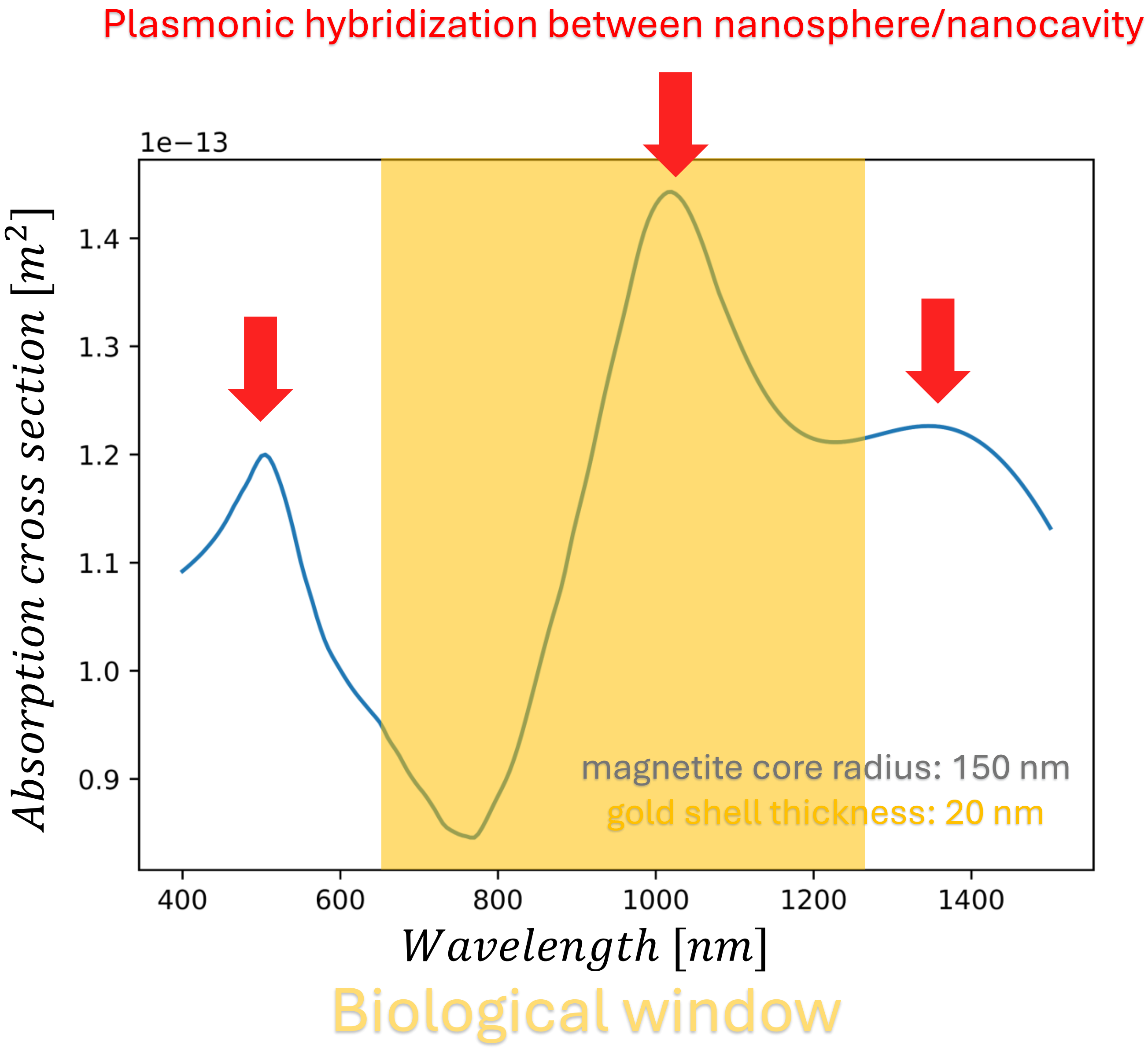
"How will the use of phototherapy modify MRI images?"

More precise question:

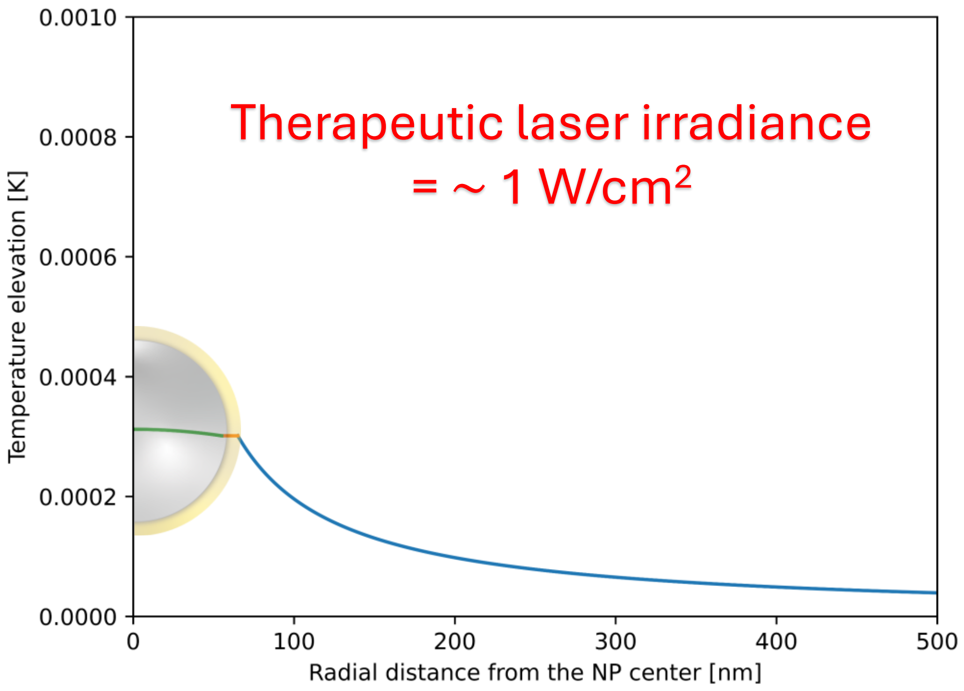
"How does laser illumination of a solution modify its transverse relaxation rate (R_2)? "

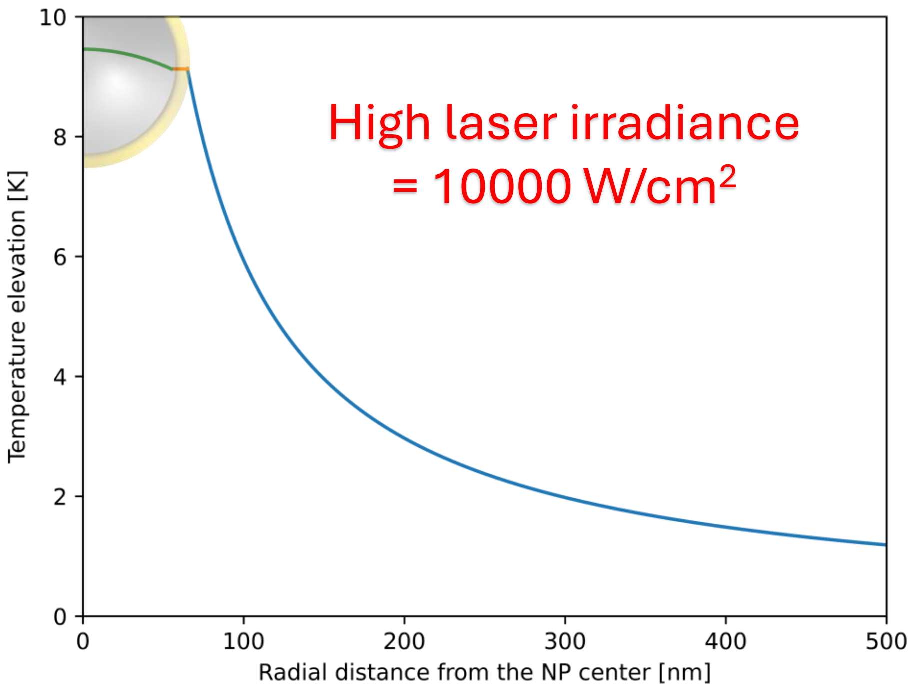
Hybrid nanoshell platforms are effective tunable Contrast/Photothermal agents





Is the therapeutic irradiance not enough for phototherapy?

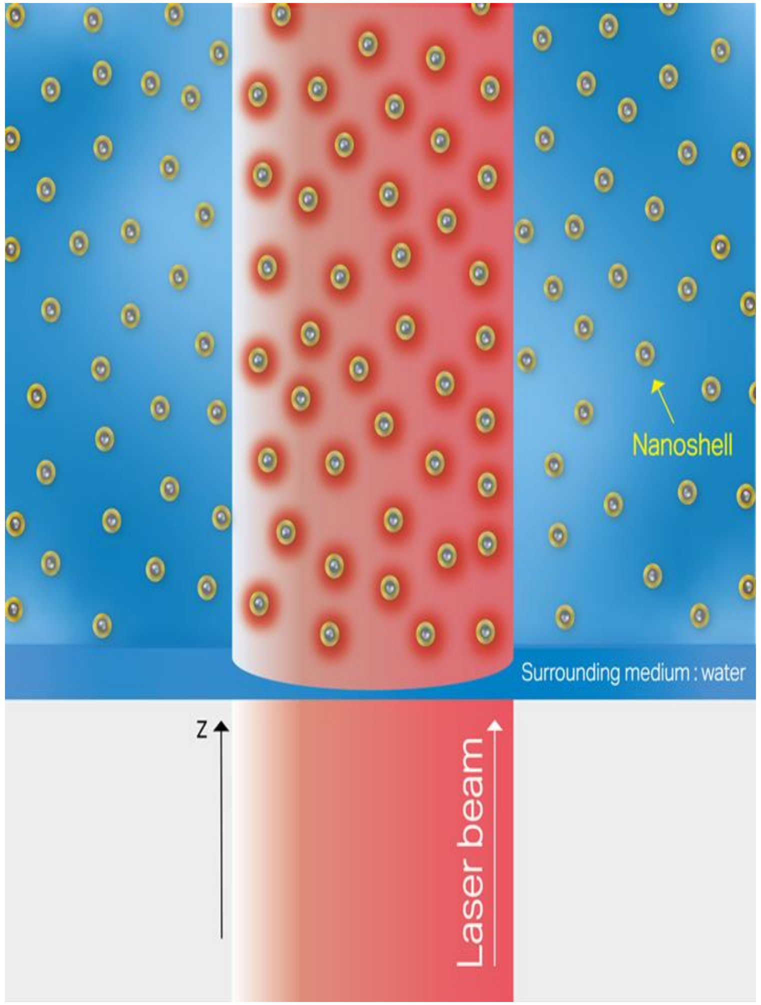




magnetite core radius: 55 nm

gold shell thickness: 10 nm

Collective thermal effects lead to a significant increase in temperature



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

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

NPs concentration

Extinction cross section

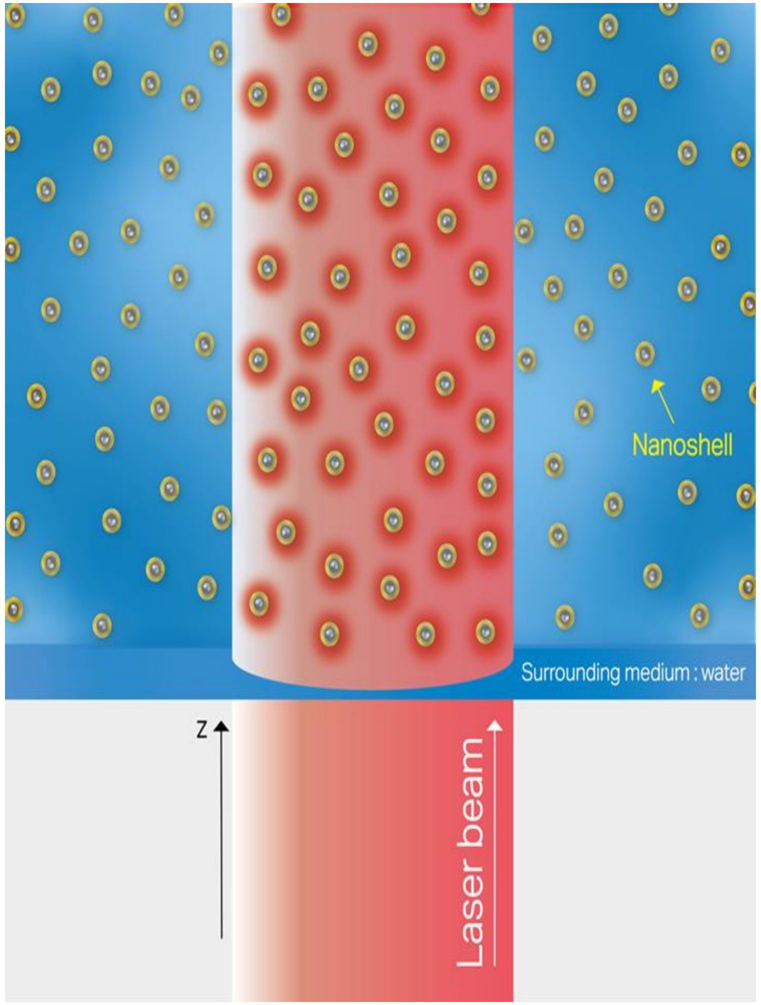
$$q\left(\vec{r'}\right) = I_0\,(N\,\sigma_{abs} + A_{water})\,e^{-(\sigma_{ext}\,N + A_{water})\,z}$$

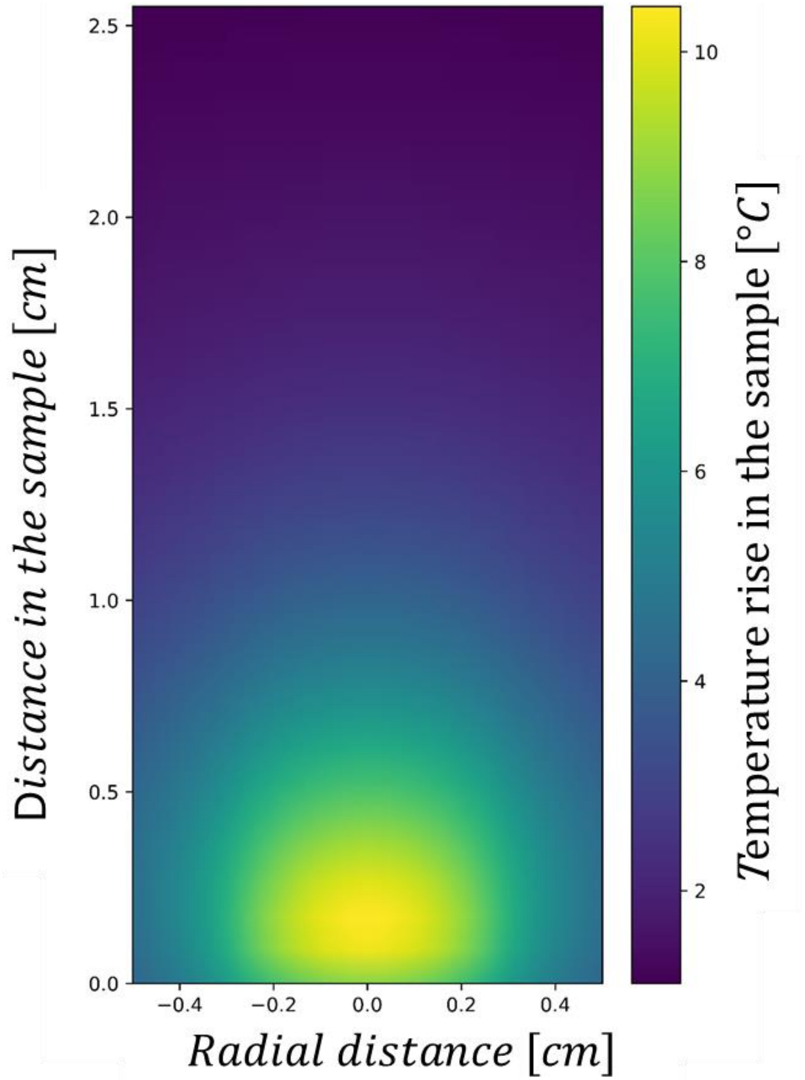
Absorption cross section

Distance in sample

Water absorption coefficient

Collective thermal effects lead to a significant increase in temperature

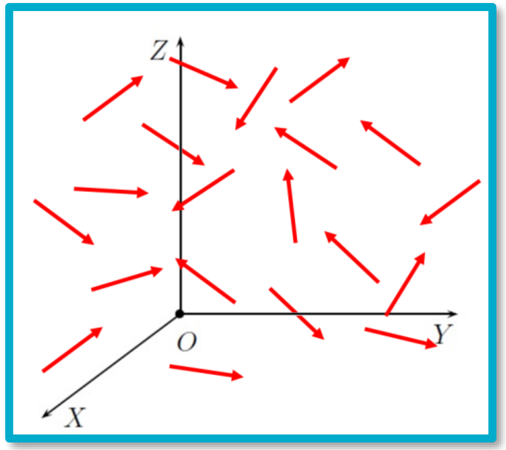




Sufficient temperature elevation for photothermal therapy

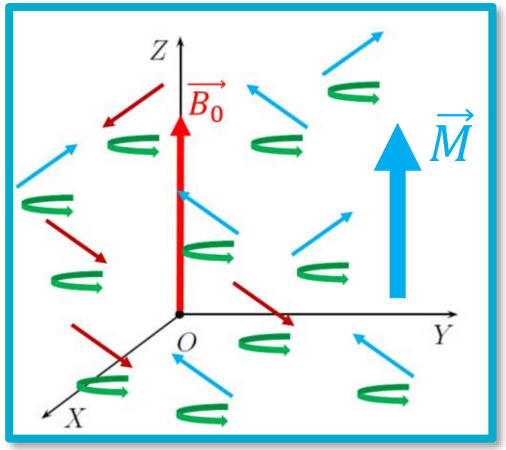
Nuclear magnetic resonance in 4 steps

Sample without magnetic field



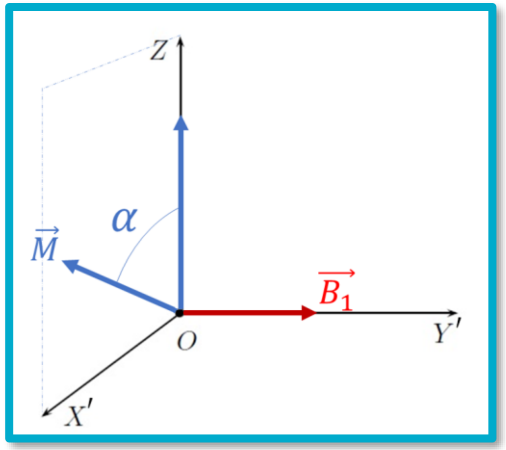
Randomized magnetic moments

Constant magnetic field $\overrightarrow{B_0}$



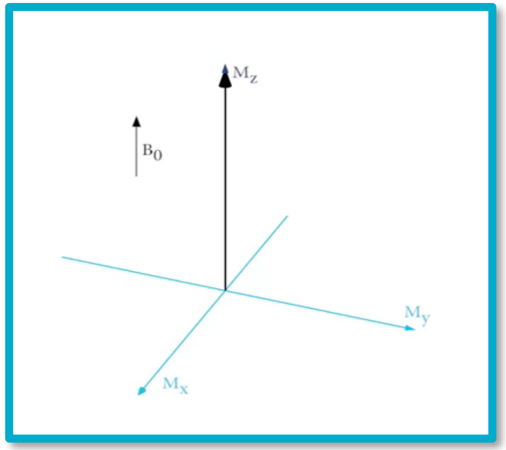
Resulting magnetization $\overrightarrow{M}$

Oscillating magnetic field $\overrightarrow{B_1}$

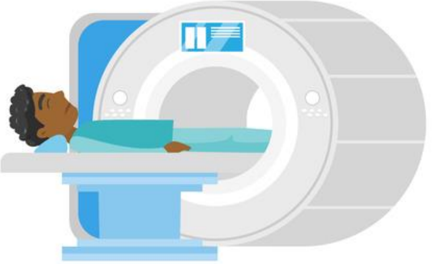


System out of equilibrium

Relaxation



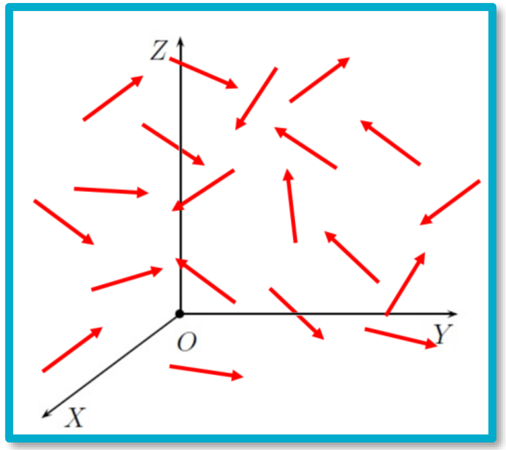
Return to magnetization equilibrium



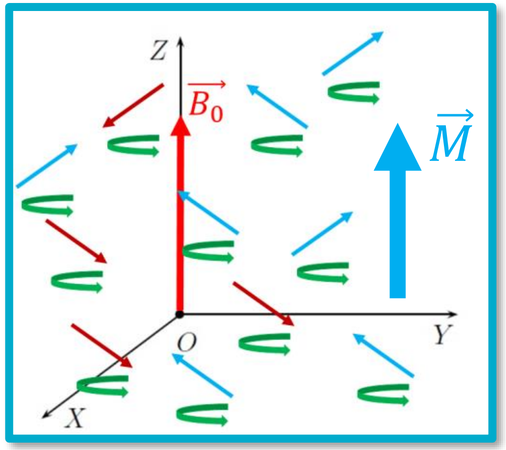
MRI imaging based on the relaxation times

Nuclear magnetic resonance in 4 steps

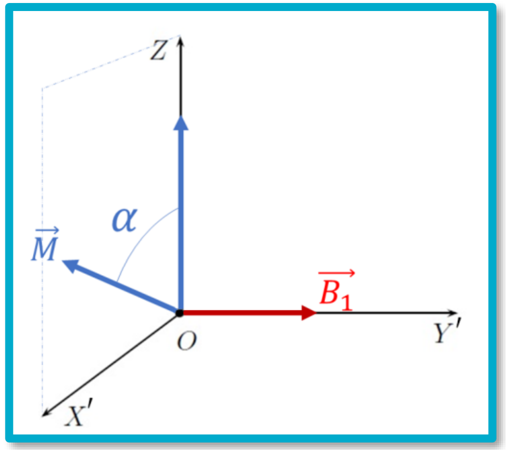
Sample without magnetic field	Constant magnetic field $\overrightarrow{B_0}$	Oscillating magnetic field $\overrightarrow{B_1}$	Relaxation



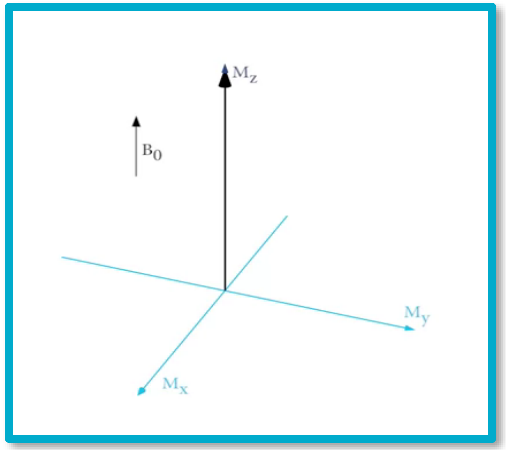
Randomized magnetic moment



Resulting magnetization $\overrightarrow{M}$



System out of equilibrium

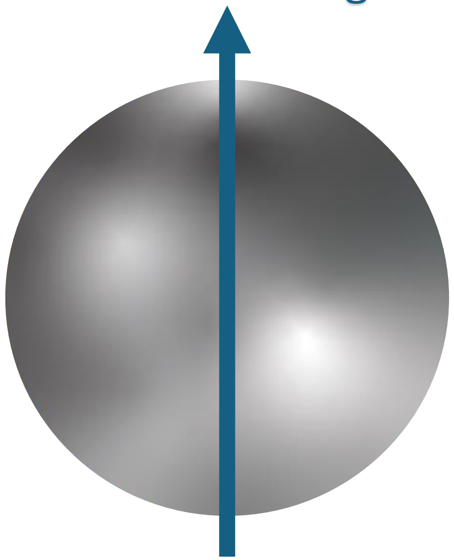


Return to magnetization equilibrium

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

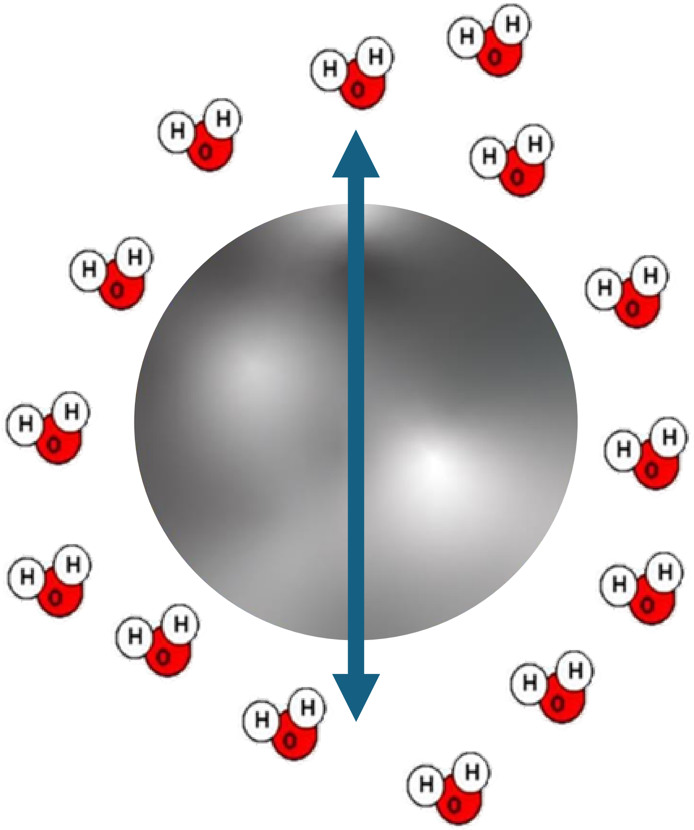
→ describe by the transverse relaxation rate R_2 [s^{-1}]

Impact of the contrast agent on relaxation



Magnetite nanoparticle
(core of our nanoshells)

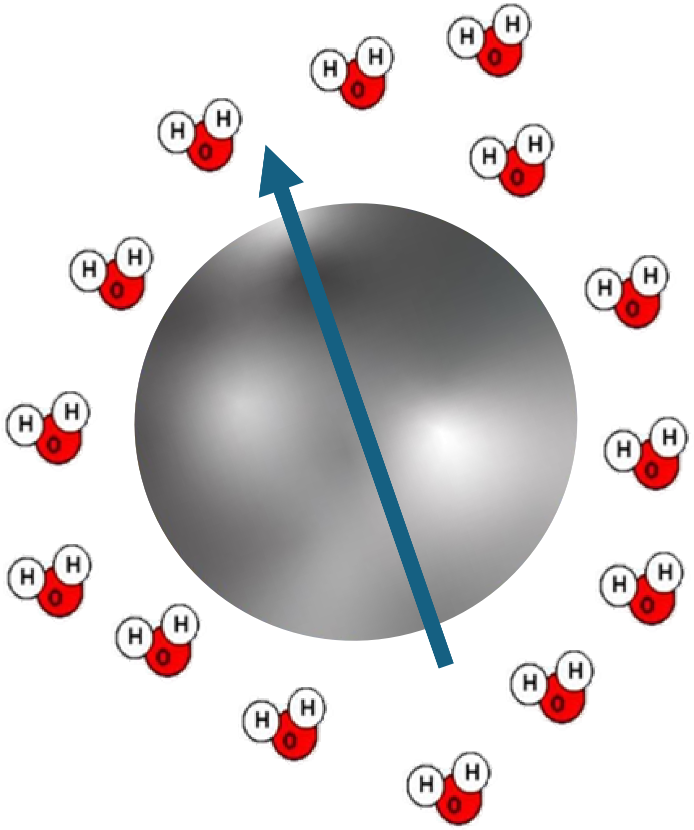
Impact of the contrast agent on relaxation



Relaxation increases by the magnetic fluctuations experienced by each proton

- Néel relaxation

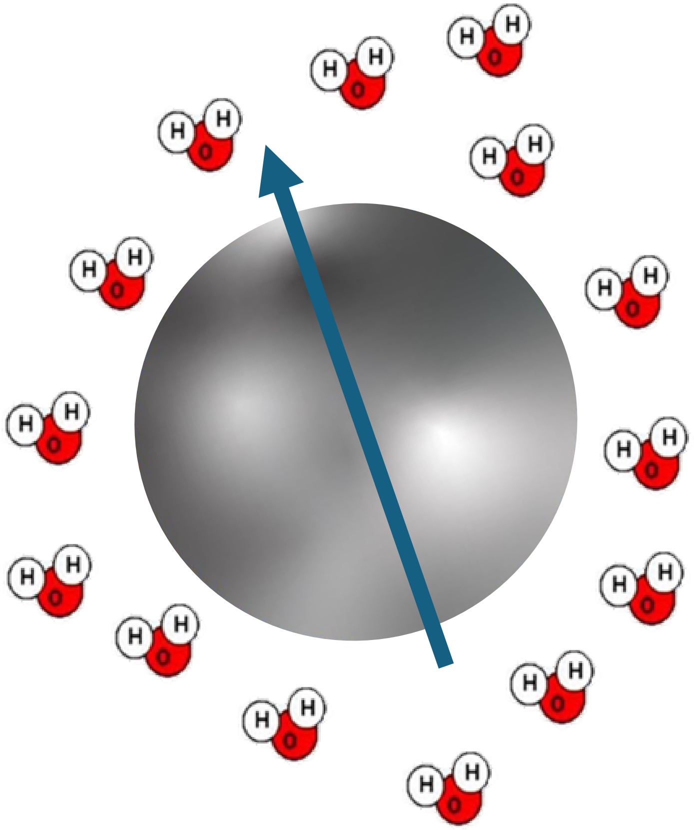
Impact of the contrast agent on relaxation



Relaxation increases by the magnetic fluctuations experienced by each proton

- Néel relaxation
- Brownian relaxation

Impact of the contrast agent on relaxation



Relaxation increases by the magnetic fluctuations experienced by each proton

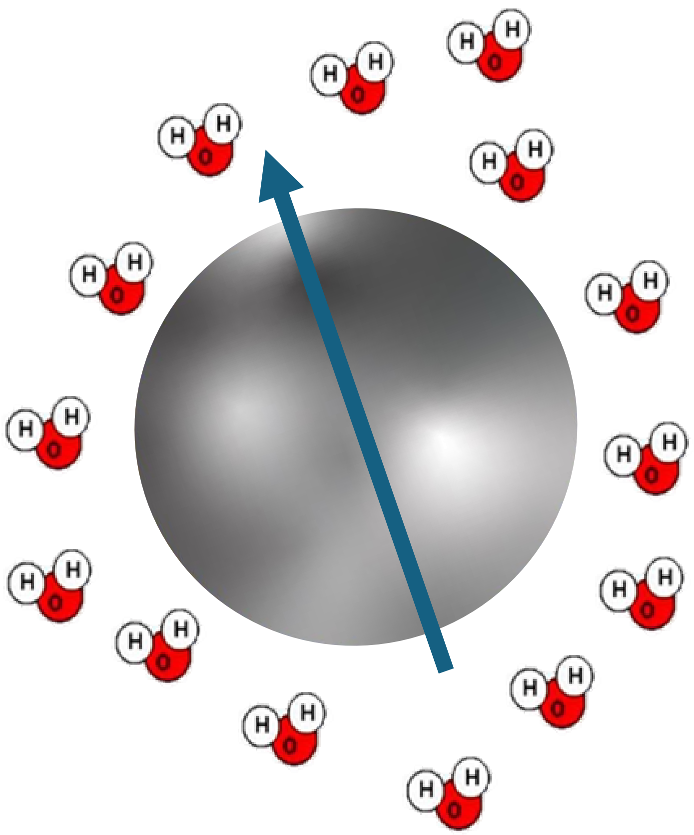
- Néel relaxation
- Brownian relaxation

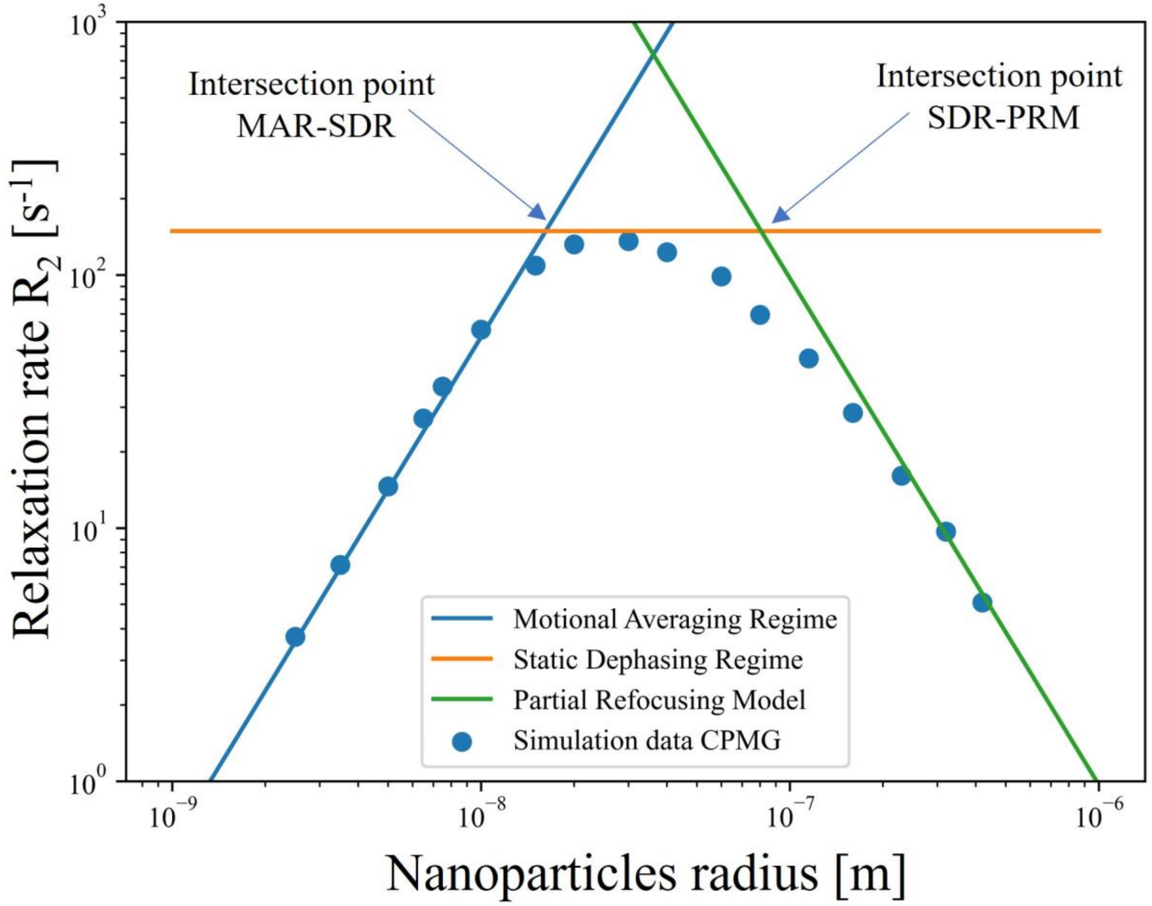
Temperature influences both processes

↓

Relaxation depends on temperature

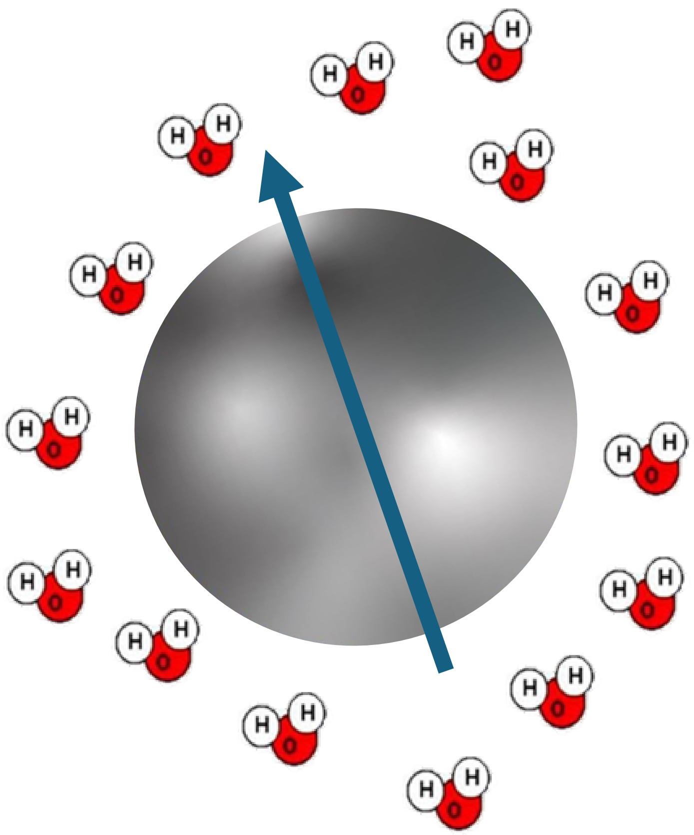
Impact of the contrast agent on relaxation

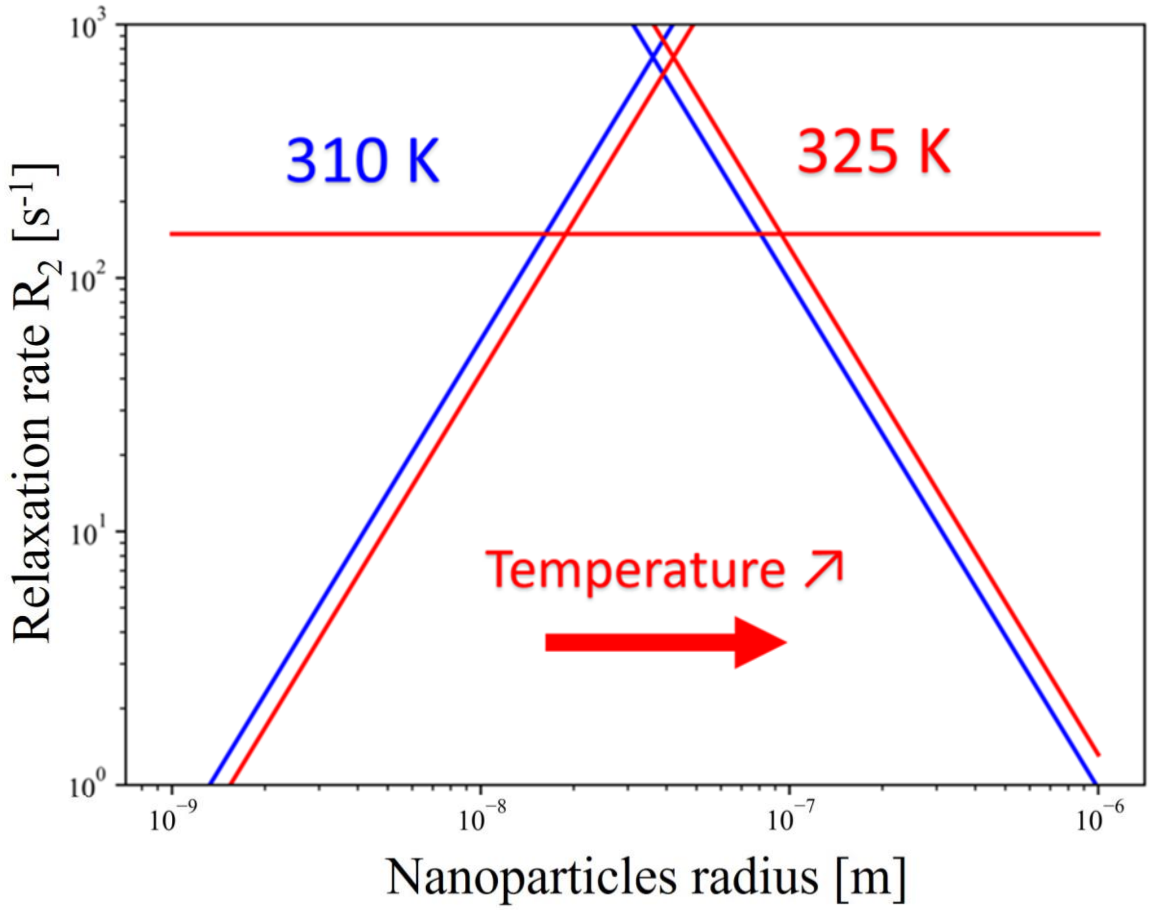




The relaxation also depends on the size of the nanoparticles

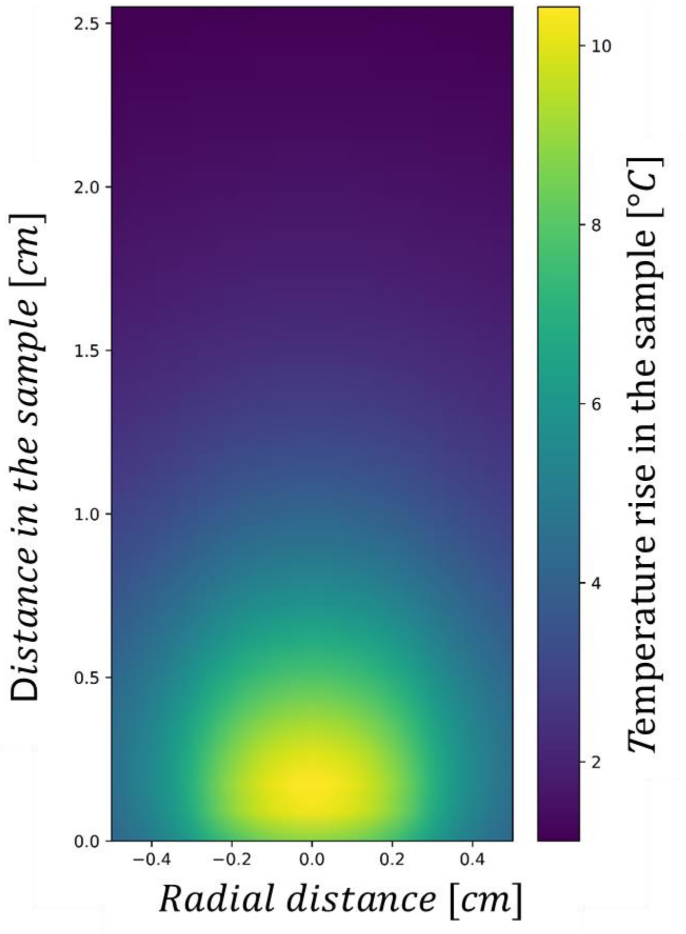
Impact of the contrast agent on relaxation



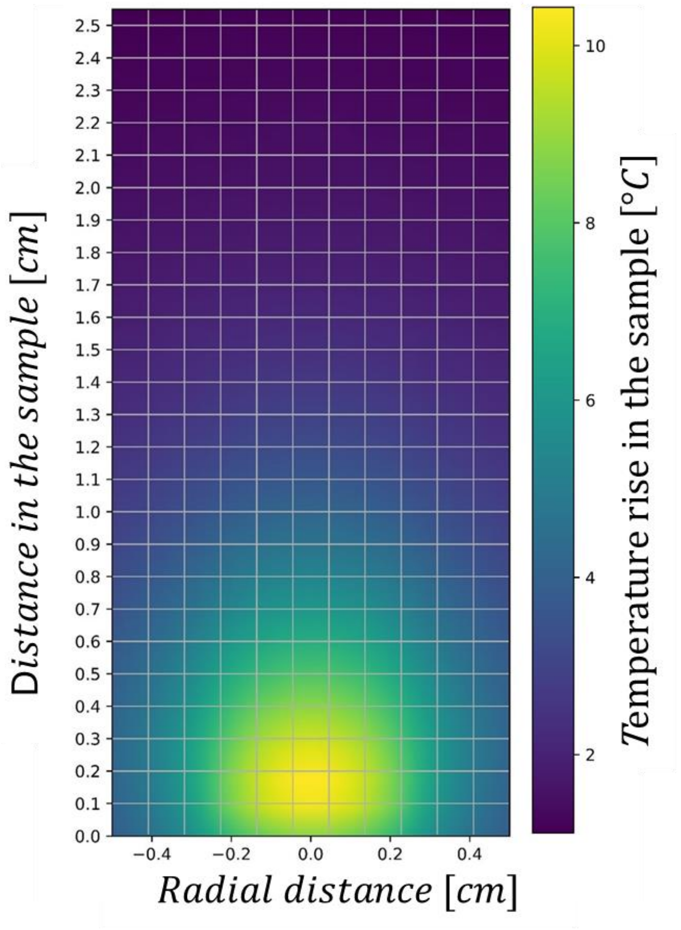


Shift due to the increase in temperature

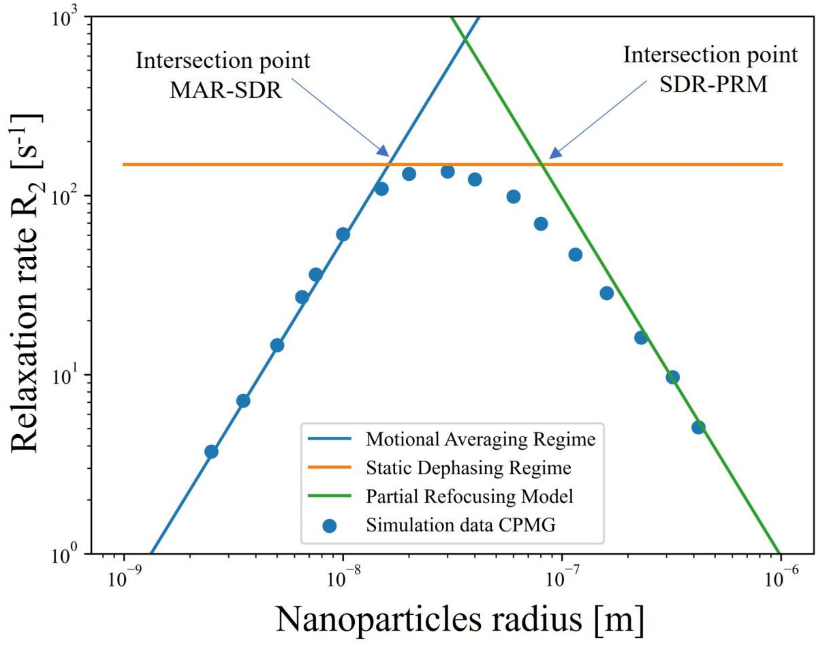
Calculation procedure of the relaxation maps



Calculation of the temperature elevation map

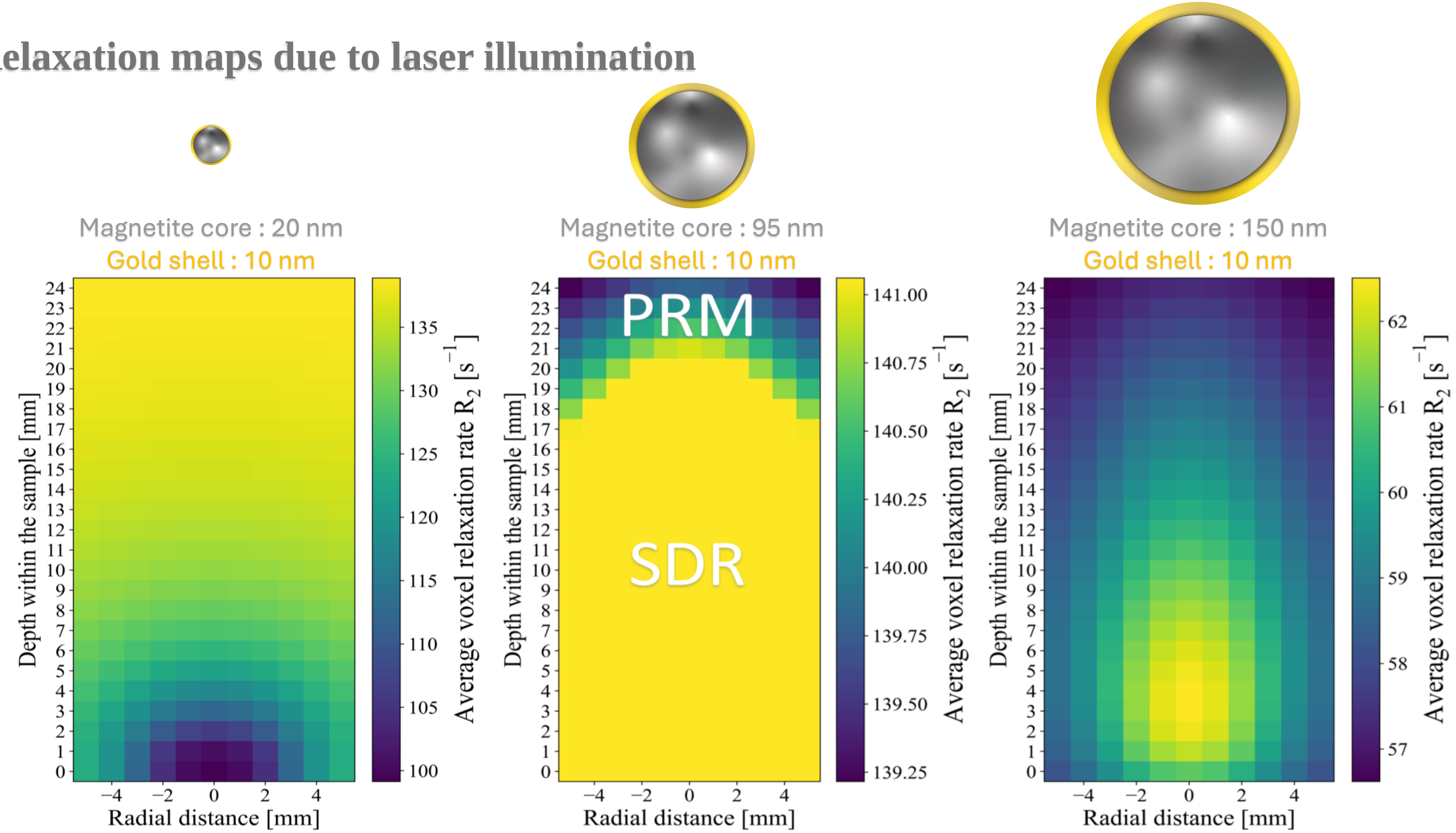


Voxel discretization procedure



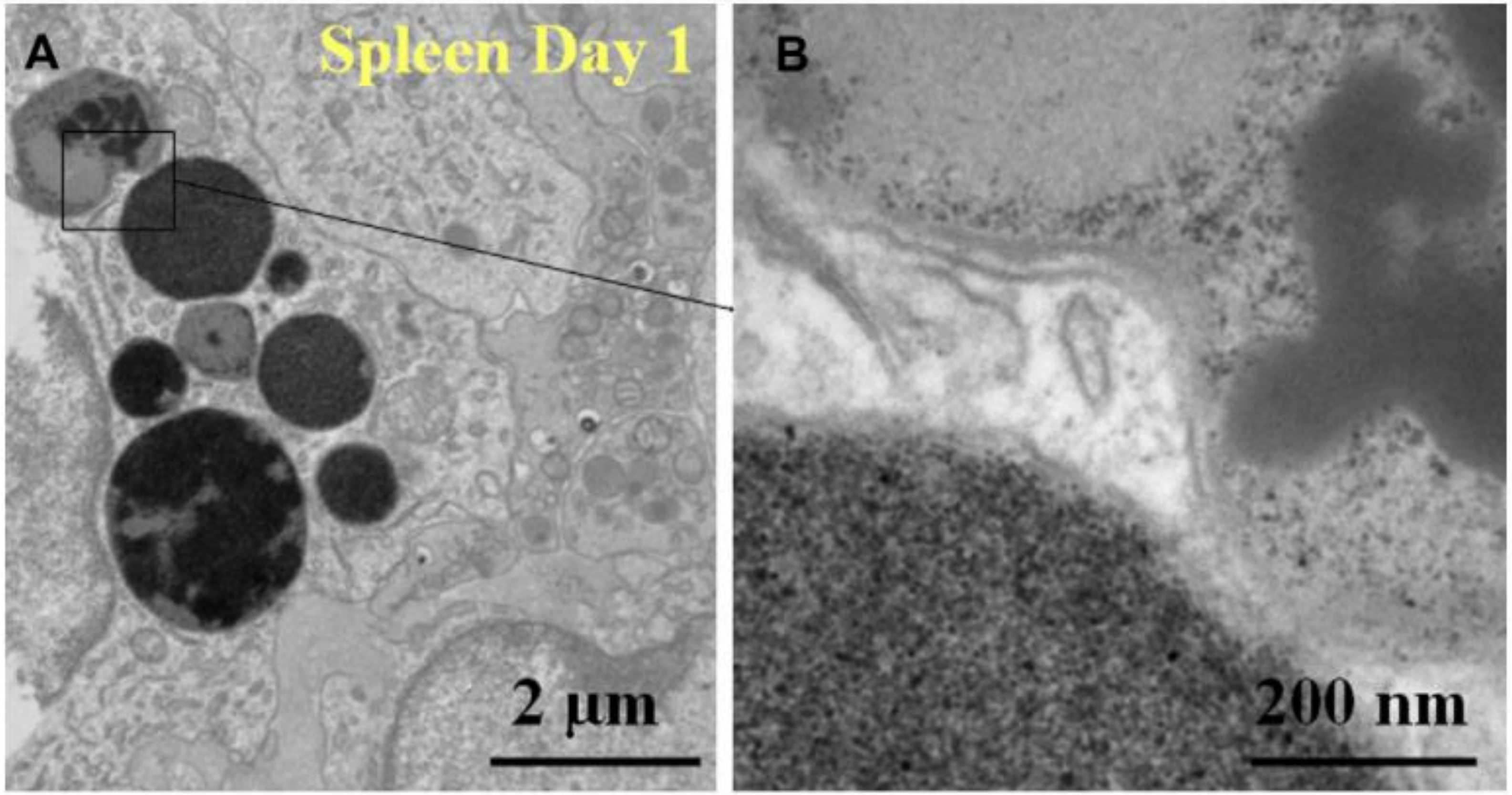
Choose of the relaxation model for each voxel

Relaxation maps due to laser illumination



Up to 30% modification for a core radius around 20-25 nm !

High accumulation of nanoparticles in the organs: spleen/liver

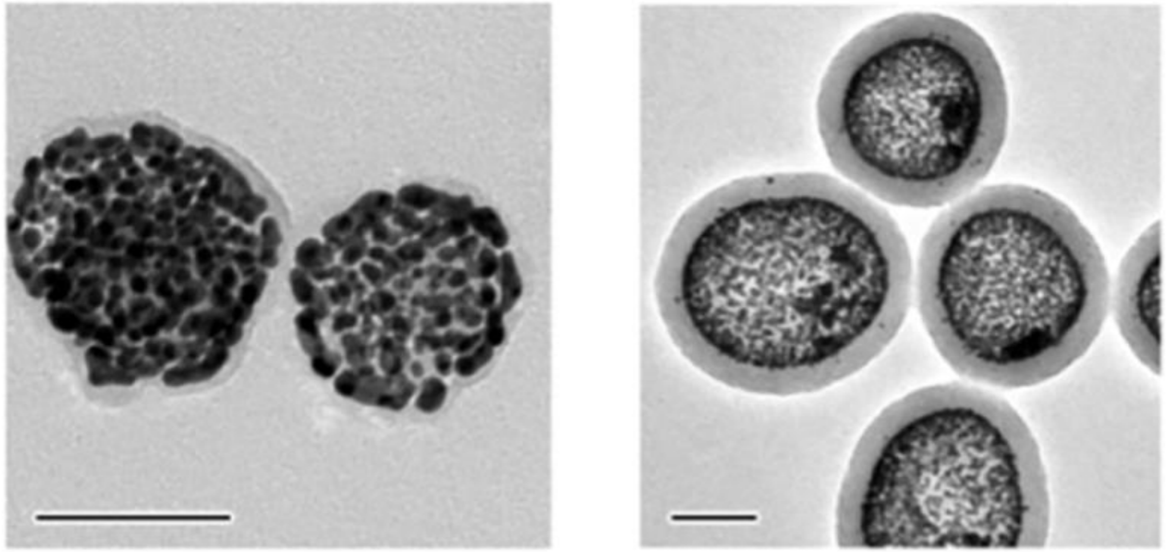


Michael Levy et al., Biomaterials **2011**

Aggregation leads to dependent scattering

Take a step back to jump better

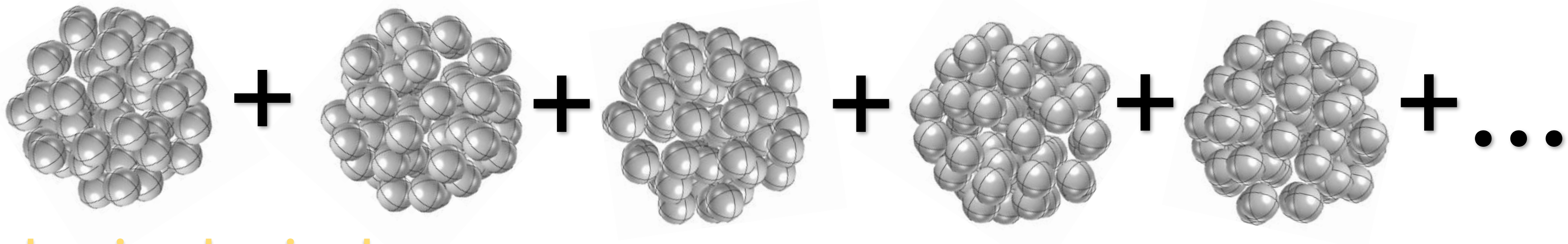
Cluster of gold nanoparticles coated with resorcinol formaldehyde



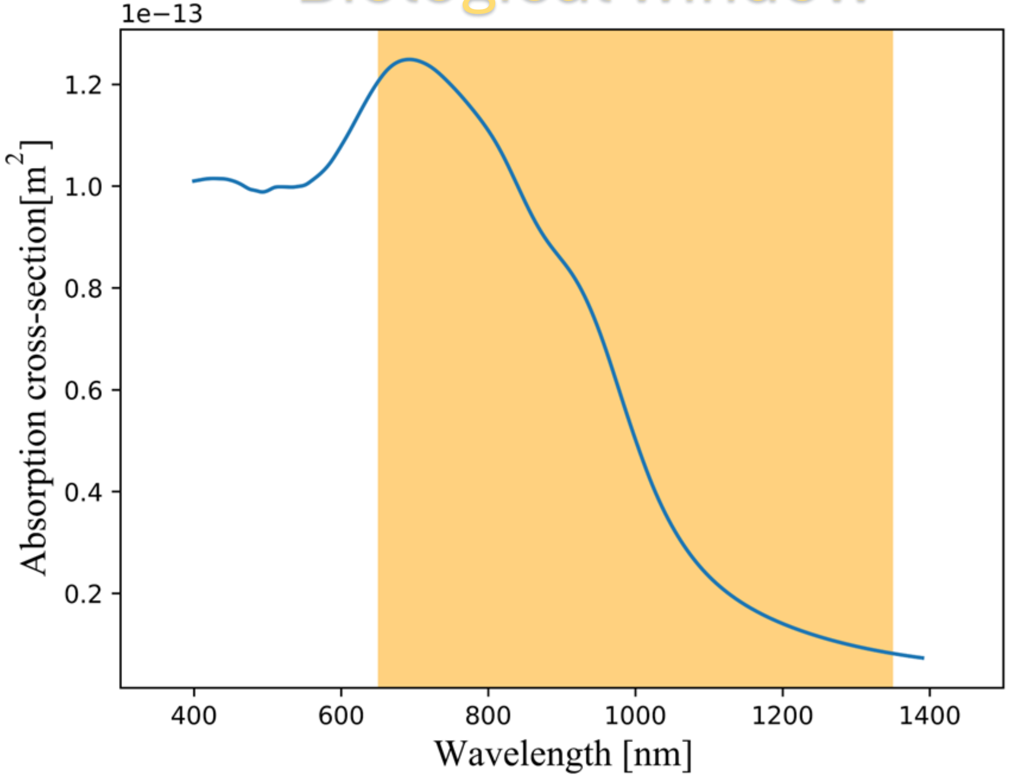
Jinxing Chen et al, *ACS Nano* **2022**

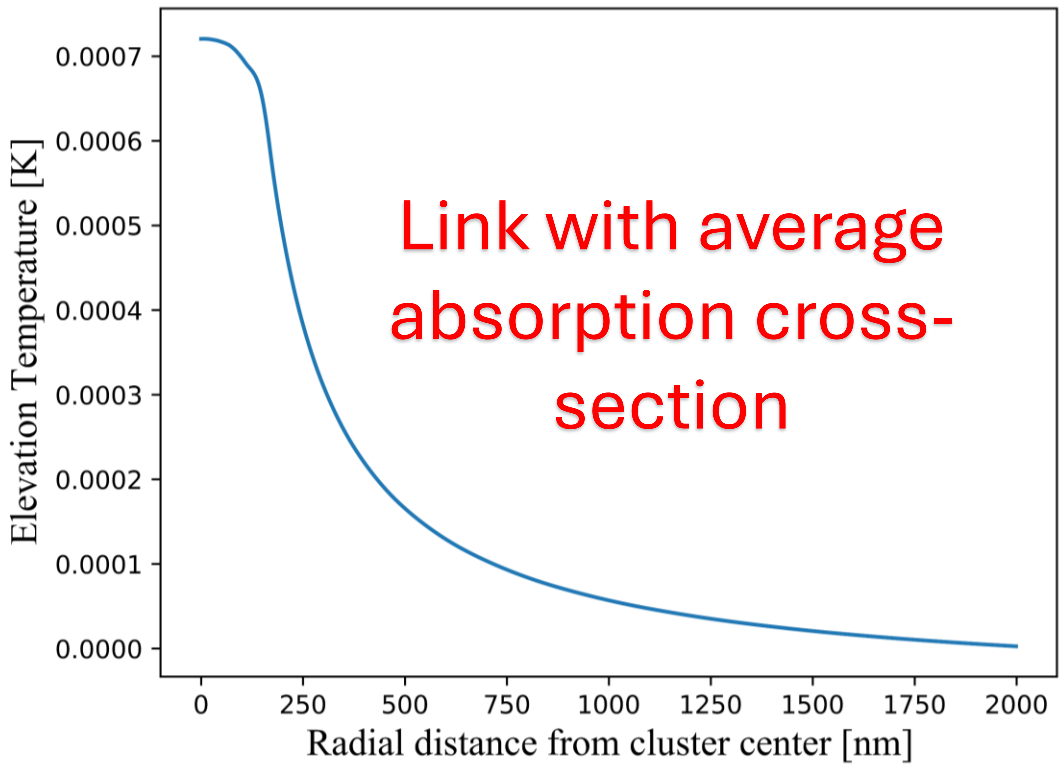
What is the average optical and thermal response of such clusters?

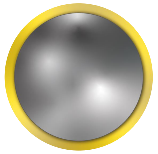
Nanoshell clusters maintain an absorption peak within the biological window



Biological window





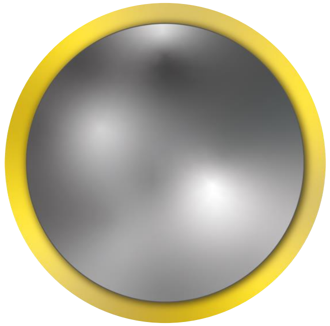
50 x 

Magnetite core : 20 nm

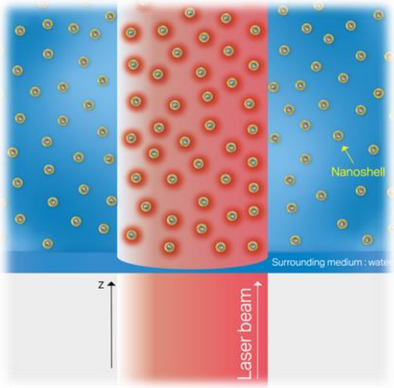
Gold shell : 10 nm

Conclusion

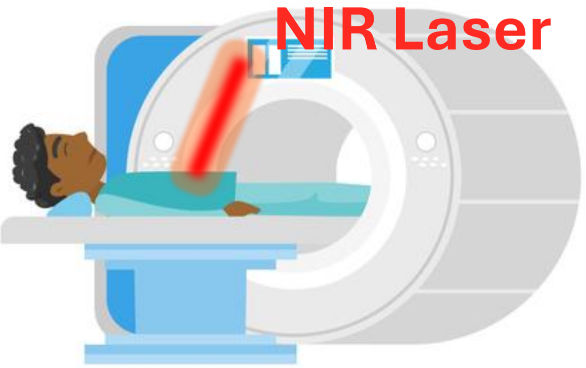
Framework for mapping changes in R_2 due to phototherapy with Ns



Nanoshell promising for real-time PTT monitoring by MRI



Optimal Ns geometry
20-25 nm radius core
10 nm thickness shell



Outlooks

- Adaptation of the framework for clusters
- Consider a biological medium with large aggregation