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# *Monte Carlo Simulations of the $T_2$ Relaxation induced by Cubic Shaped Superparamagnetic NanoParticles*

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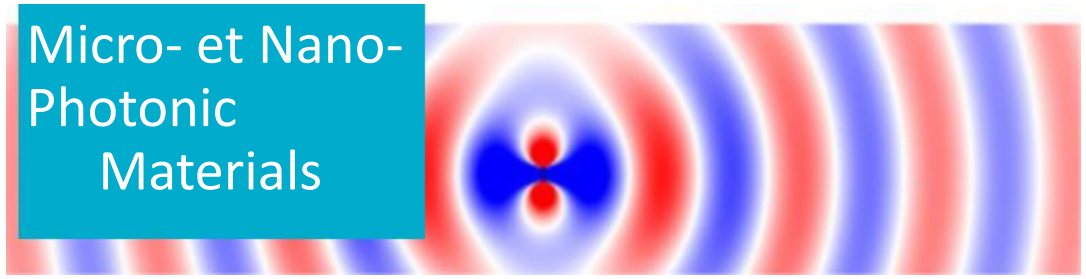
BIOPHYS

Micro- et Nano-Photonic Materials



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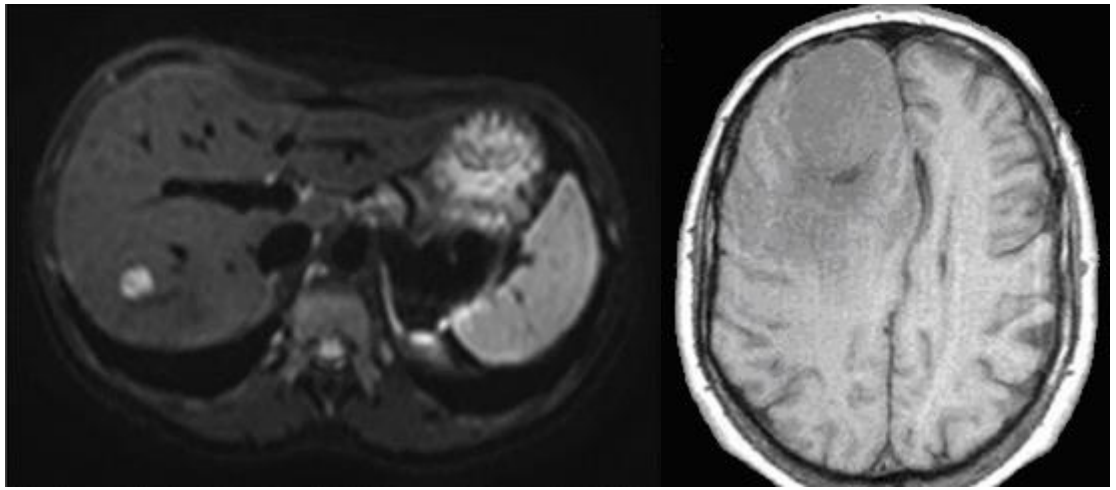
# MRI: Magnetic Resonance Imaging

- Physics behind the MRI: NMR
  - Static magnetic field: $B_0 \sim 5T$
  - Oscillating magnetic field: $B_1 \ll 1T$
    - Excitation of nuclear spins: $^1H$
    - Return to equilibrium: $T_1, T_2$
- Each tissue reacts differently
  - Natural contrast
  - Tumor detection

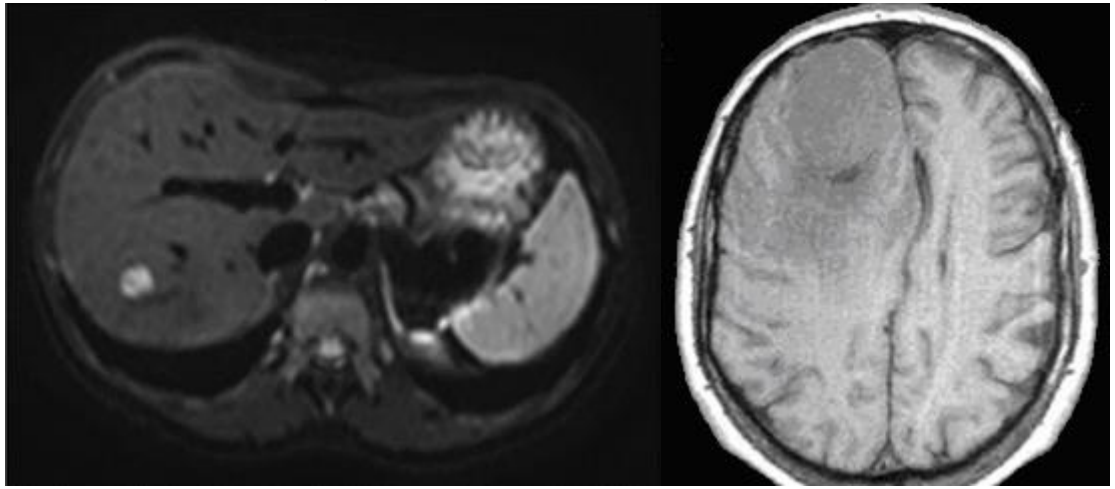


Liver & brain MRI Scans

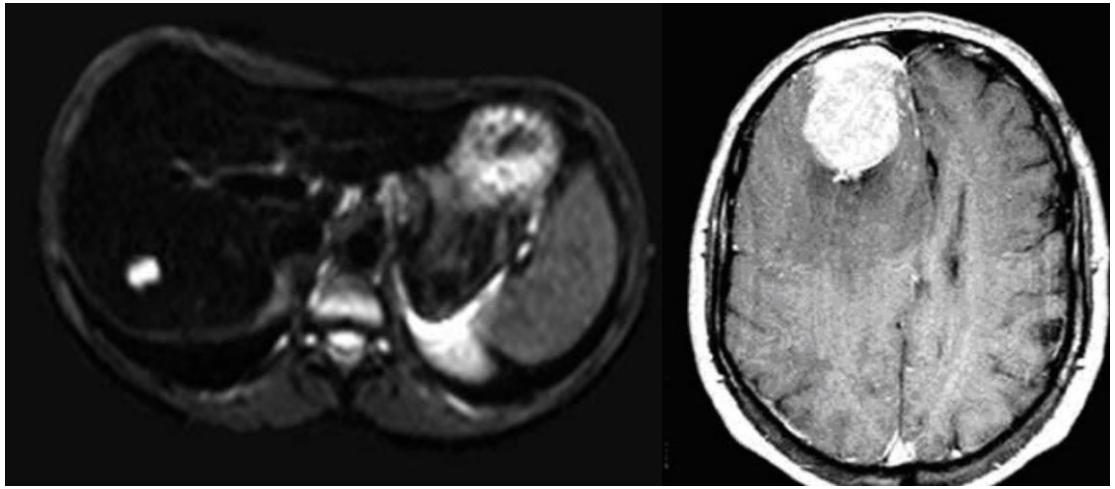
# CA's: Contrast Agents

- Accumulation in tissues
  - Shorten $T_1$ or $T_2$
  - Modify signal intensity
- Magnetic compounds
  - Magnetite / Maghemite
    - Signal « Killers »
  - Gadolinium complexes
    - Signal « Amplifiers »

↓ Natural Tissue Contrast



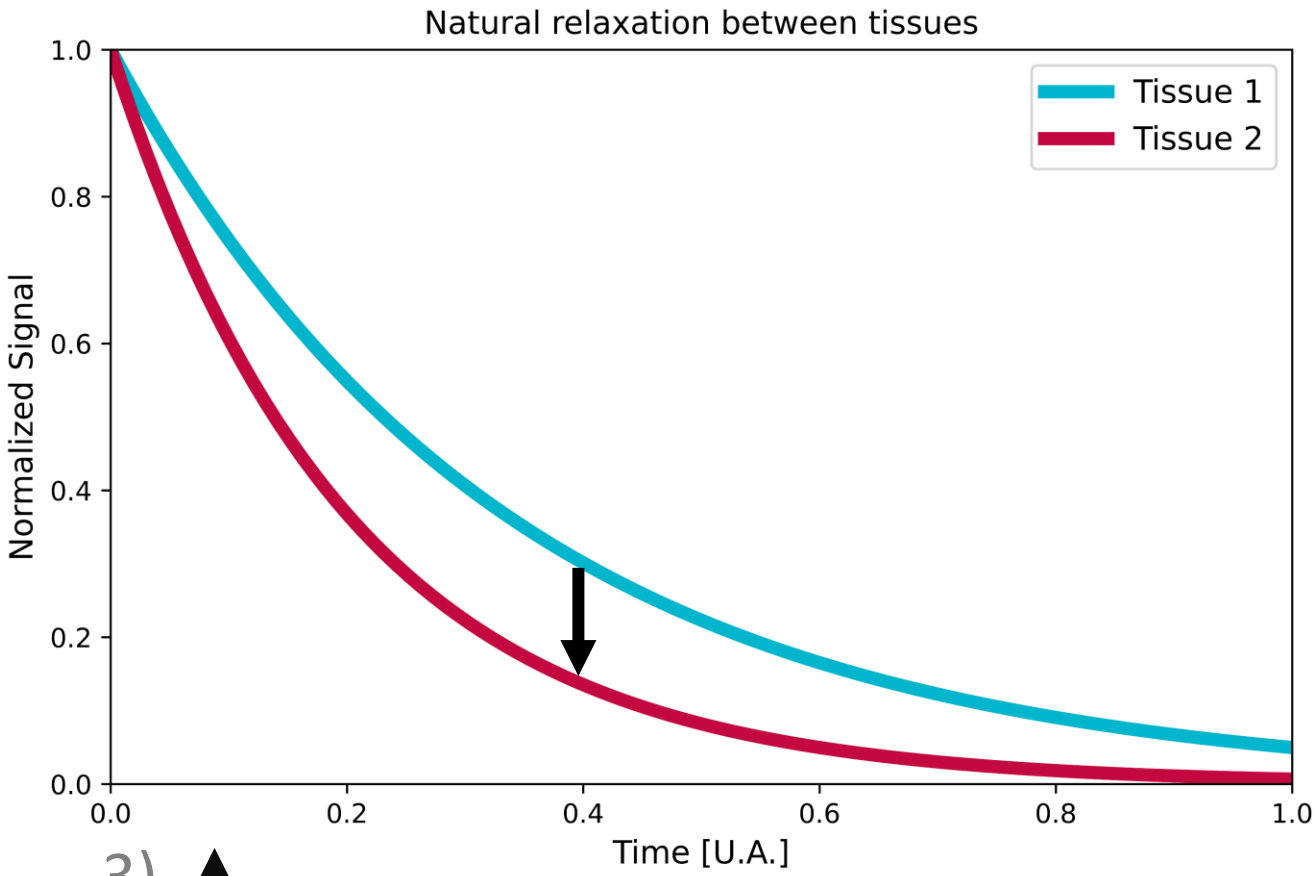
↓ CA's: Magnetite & Gadolinium Complex

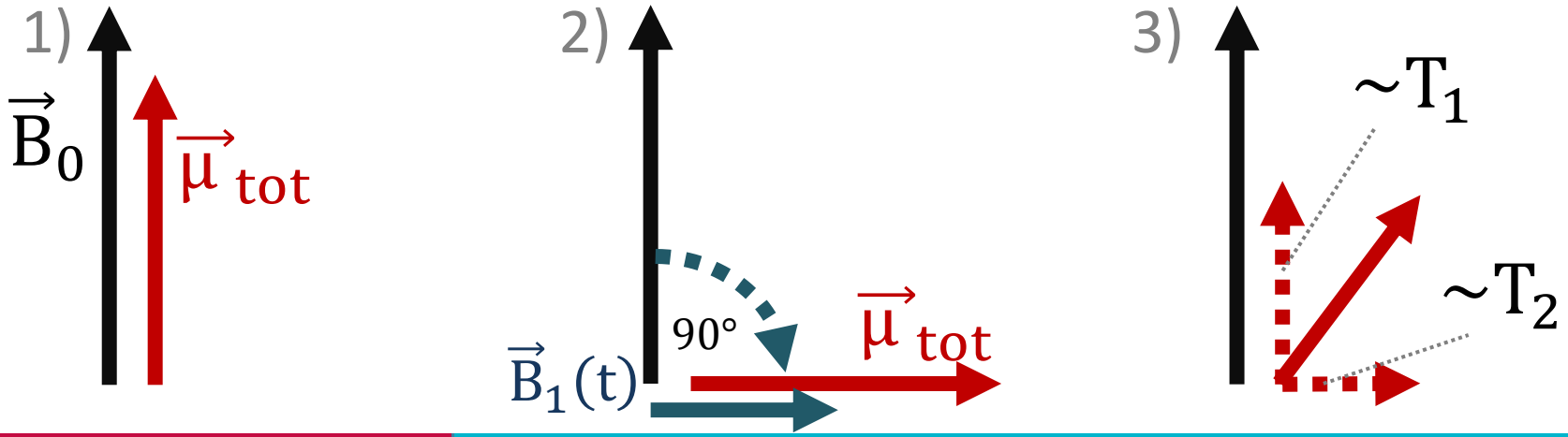


Liver & brain MRI Scans

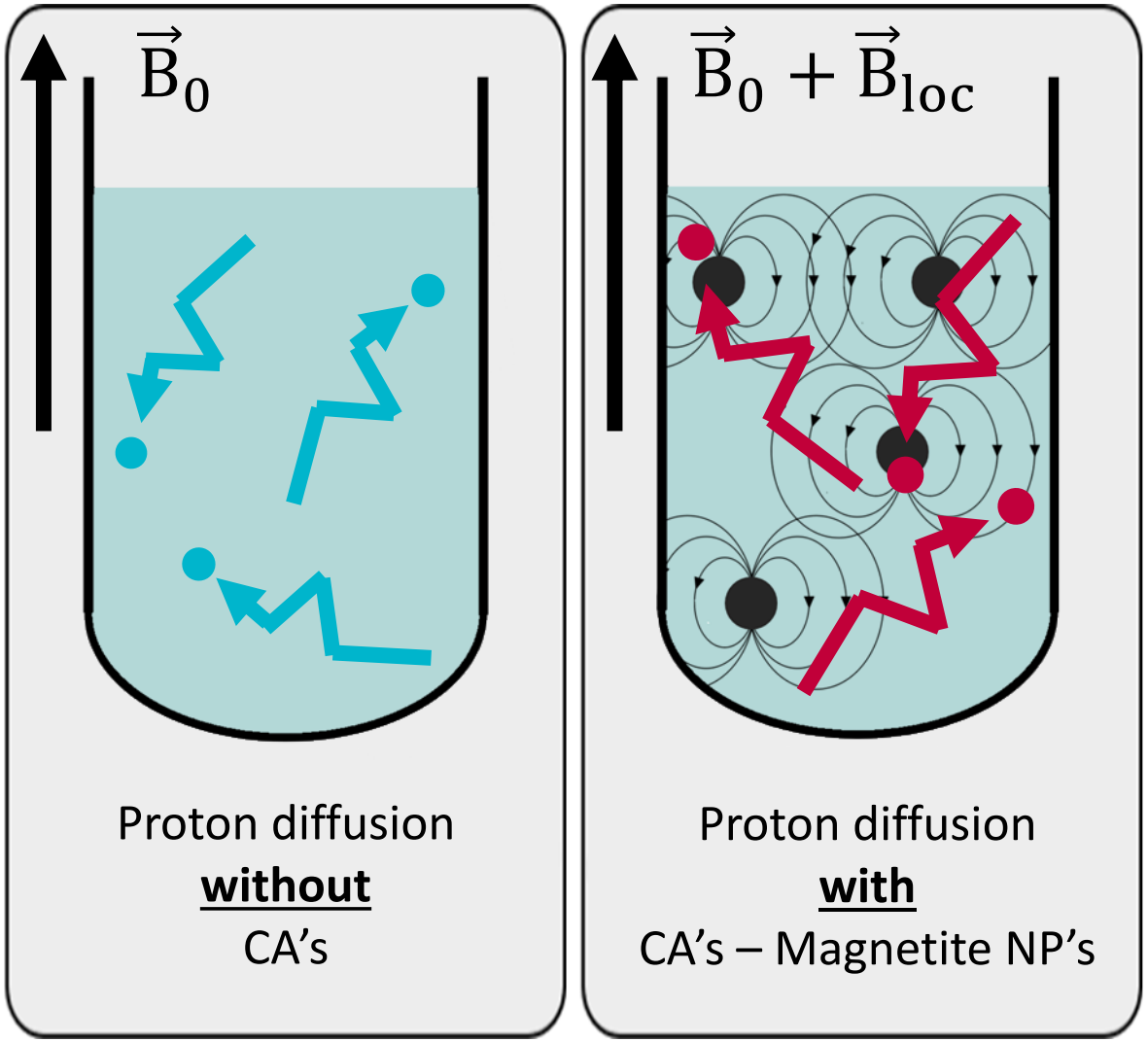
# Signal Acquisition

1) System at Equilibrium
2) Radio-Frequency Pulse
3) Return to Equilibrium
   - Characterised by $T_1, T_2$
   - Signal acquisition at $t$

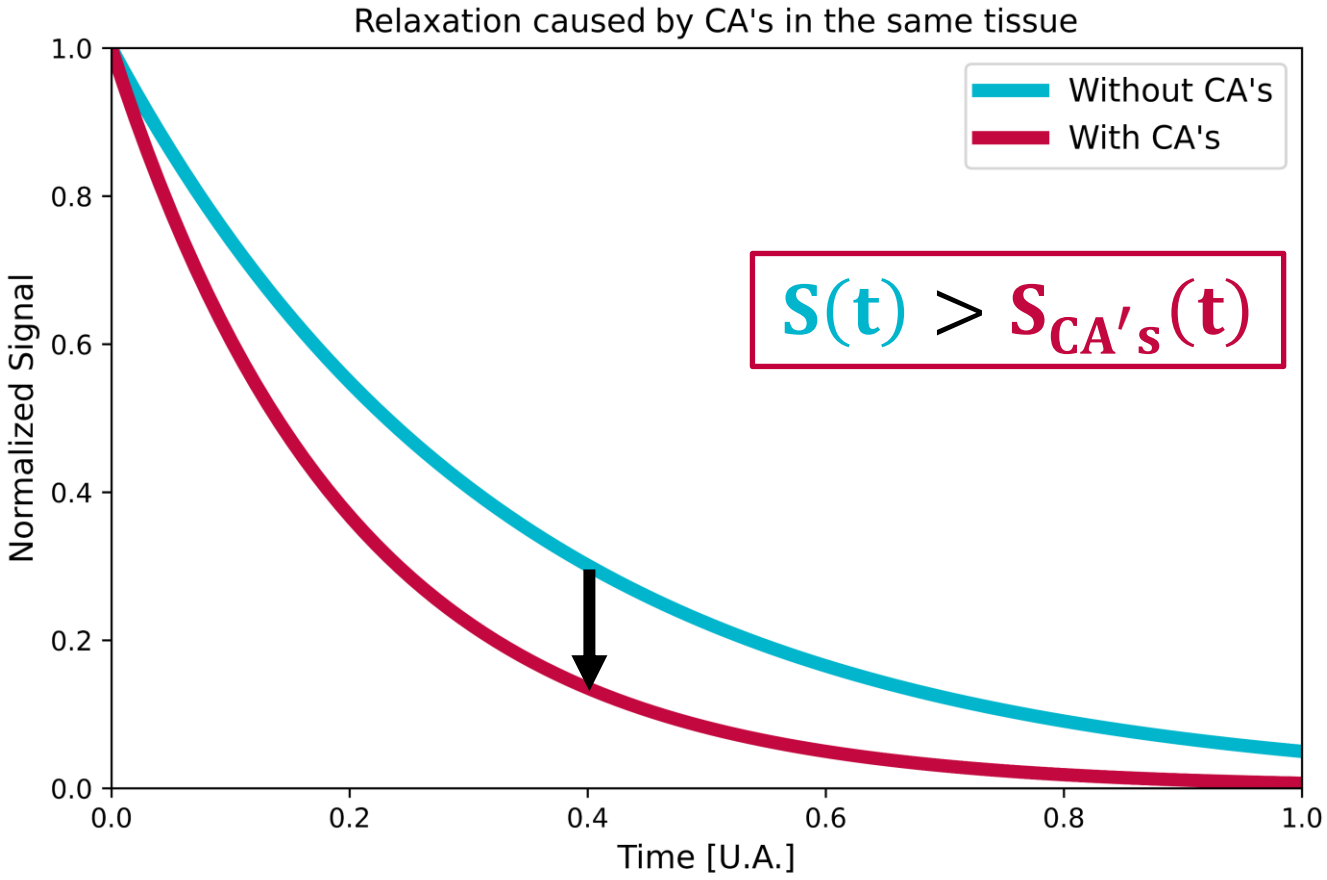


# NanoParticles as Contrast Agents

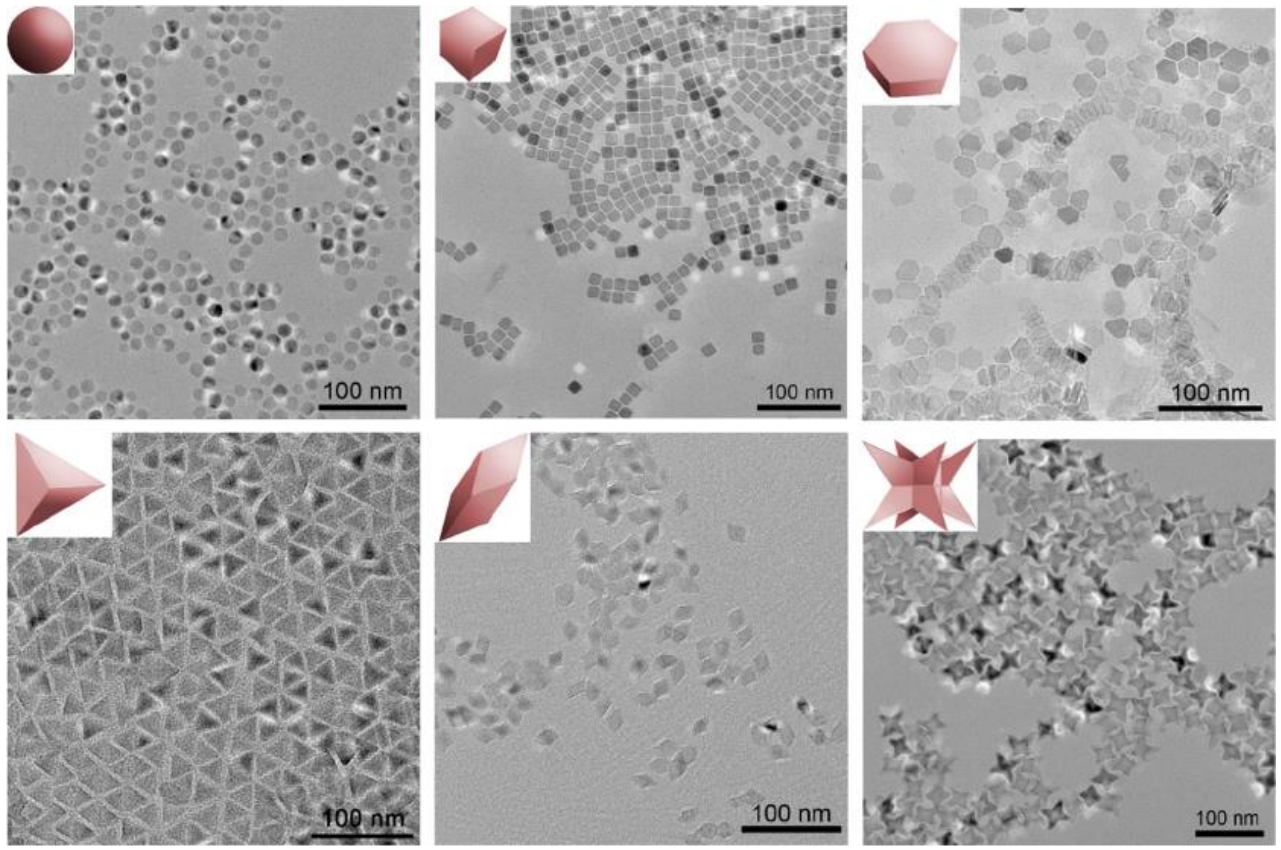



$$S(t) = I_0 e^{-t/T_2}$$



# Exotic NanoParticles

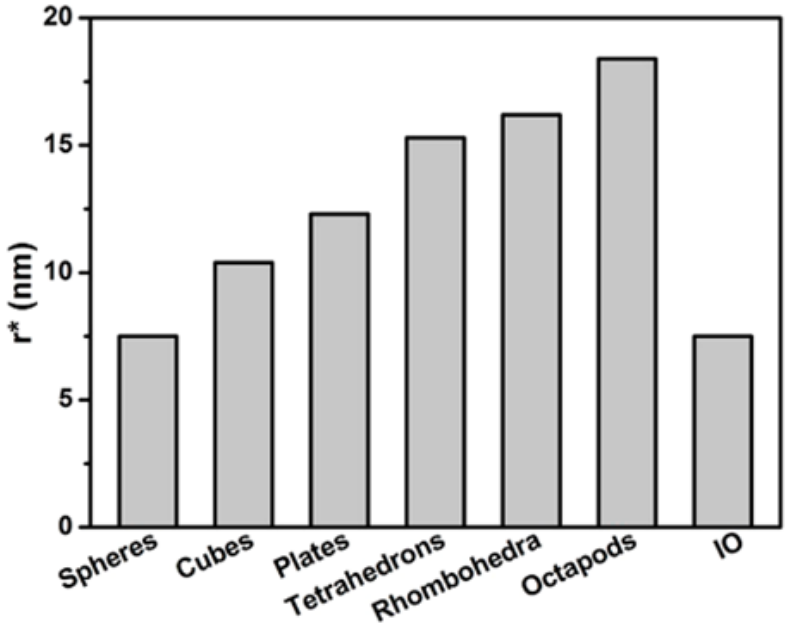
- Lots of synthetised shapes
  - Cubes, Cylinders, Stars, Flowers, Rods …
  - Experimental data
- $T_2$ Characterisation
  - Differences with spheres
  - No theoretical model



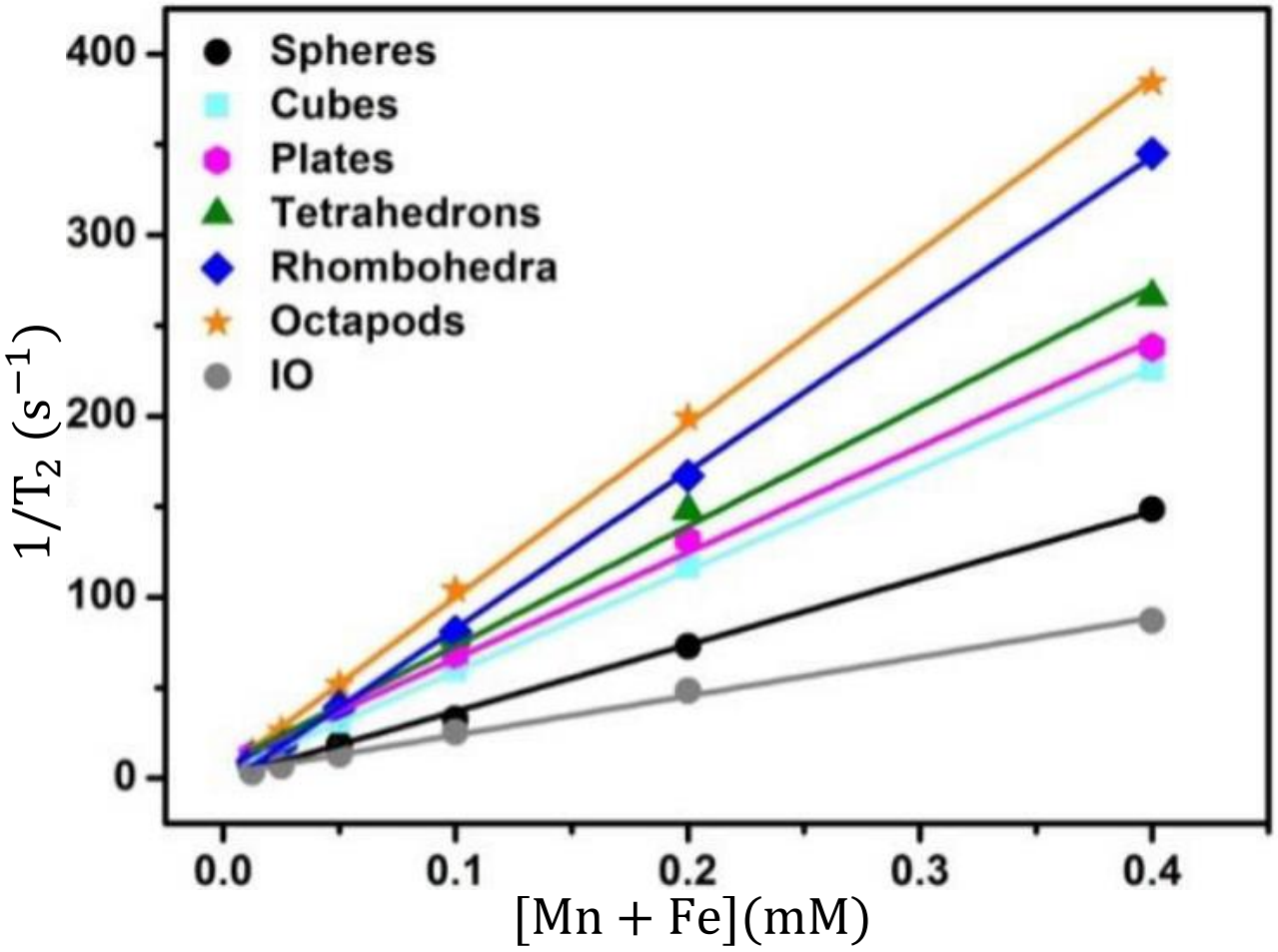

Yang, L., & Wang, Z. et al. (2018). The Roles of Morphology on the Relaxation Rates of Magnetic Nanoparticles. *ACS Nano*, *12*(5), 4605–4614.

# Results in litterature

- Relaxation Rates ($B_0 = 7T$)
  - Increase in $1/T_2$




Relaxation Rate over Magnetic ion concentration




Yang, L., & Wang, Z. et al. (2018). The Roles of Morphology on the Relaxation Rates of Magnetic Nanoparticles. *ACS Nano*, *12*(5), 4605–4614.

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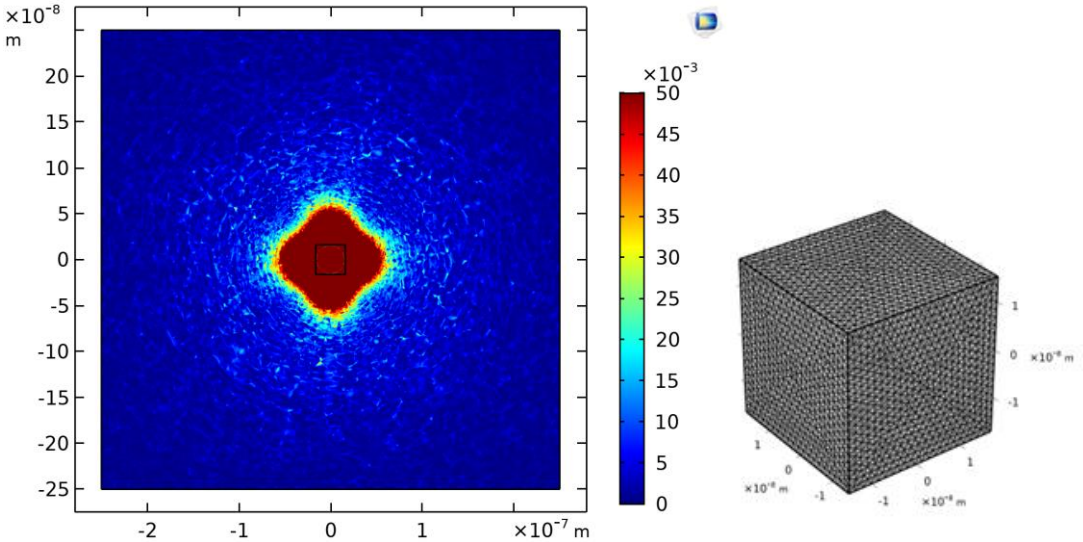
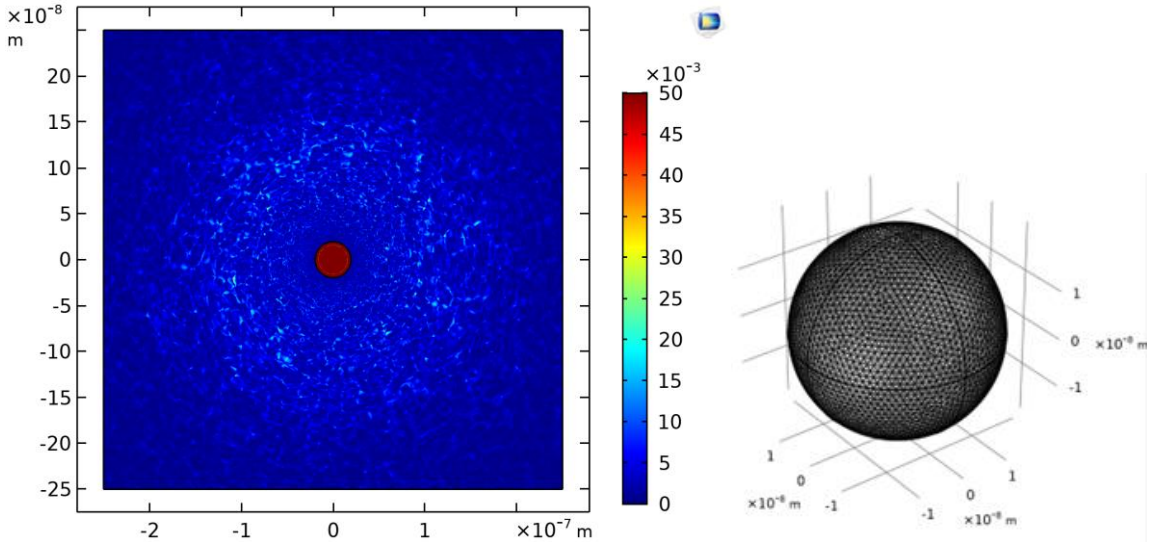
# Magnetic Field of Exotic Shapes

- Numerical resolution of Maxwell equations
  - Study of differences in field gradient
  - Comparizon cube/ sphere with analytical dipole



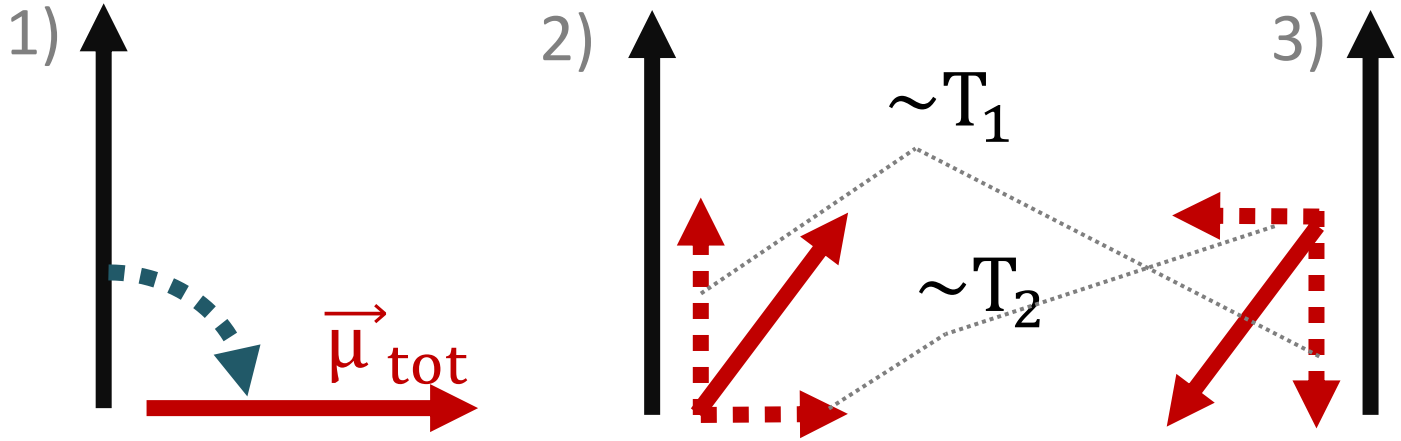

Relative difference cube - dipolar

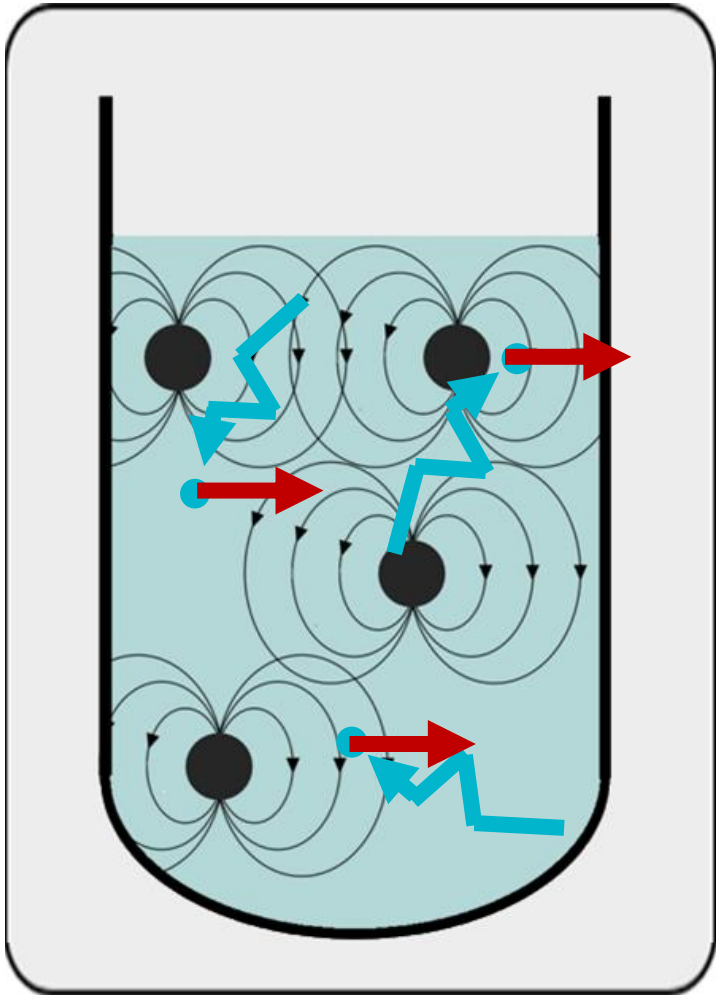



Relative difference sphere - dipolar

# Simulation of a CPMG Sequence

1. Starts at Excitation Pulse
2. Proton diffusion & Spin relaxation
   - Random Walk
   - Spin Dephasing ∝ Local Magnetic Field
3. Reverse magnetic Pulse



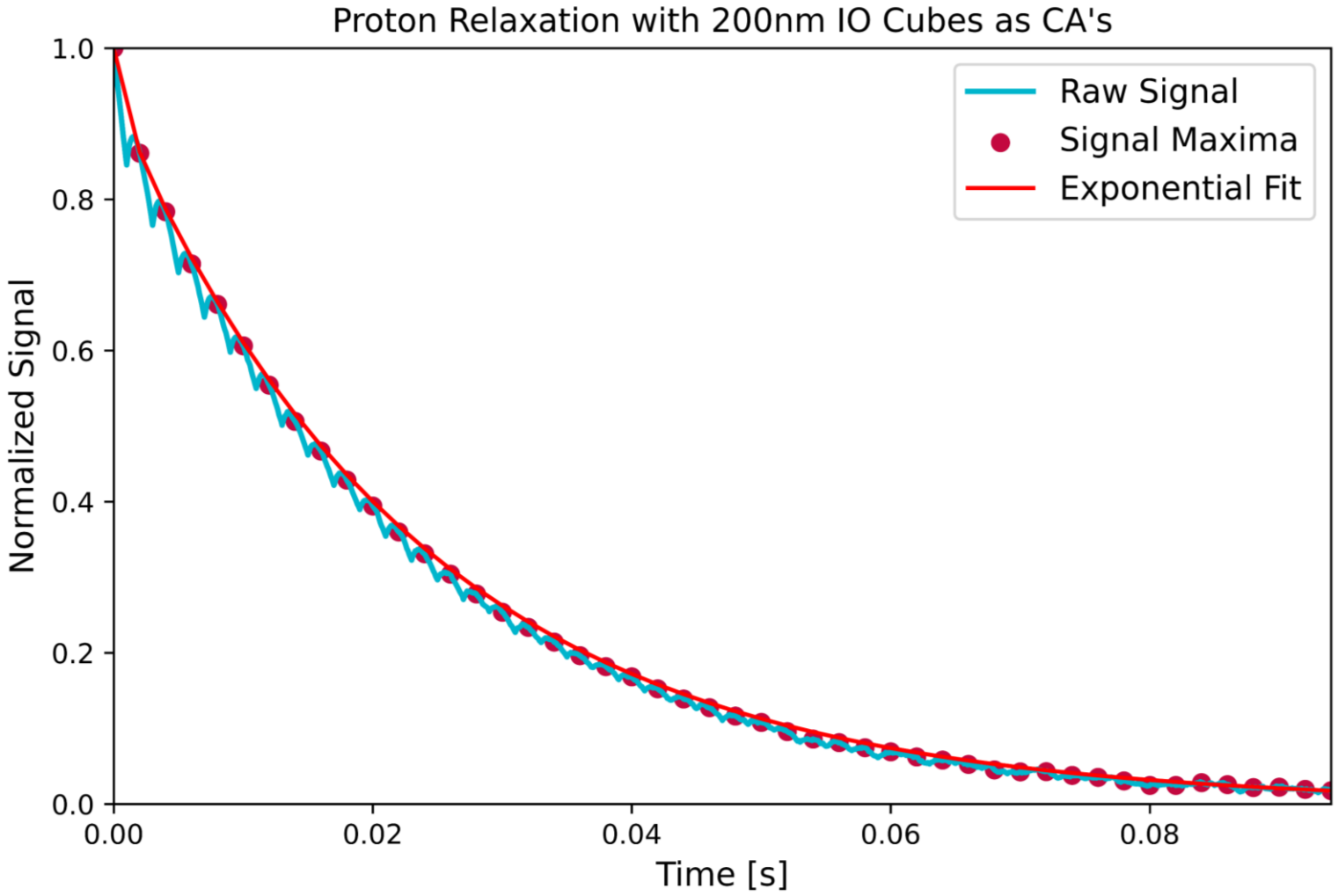
Proton relaxing in a water dispersant with CA's

# Signal Acquisition

- Small Signal increase
  - CPMG sequence
- Exponential Decay
  - Fit over maxima

$$S(t) = I_0 e^{-t/T_2}$$

- $1/T_2 = 43.22\ s^{-1}$



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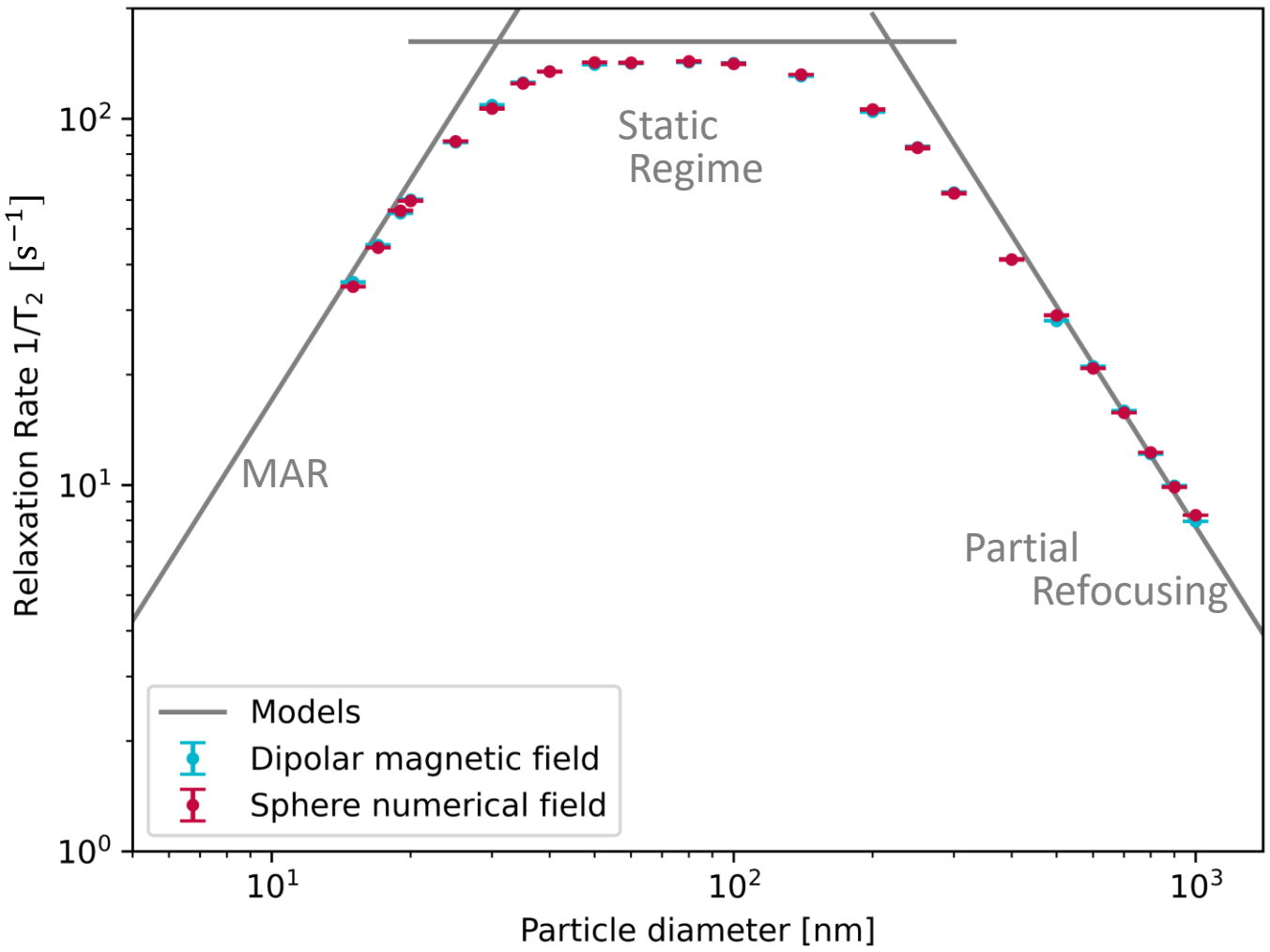
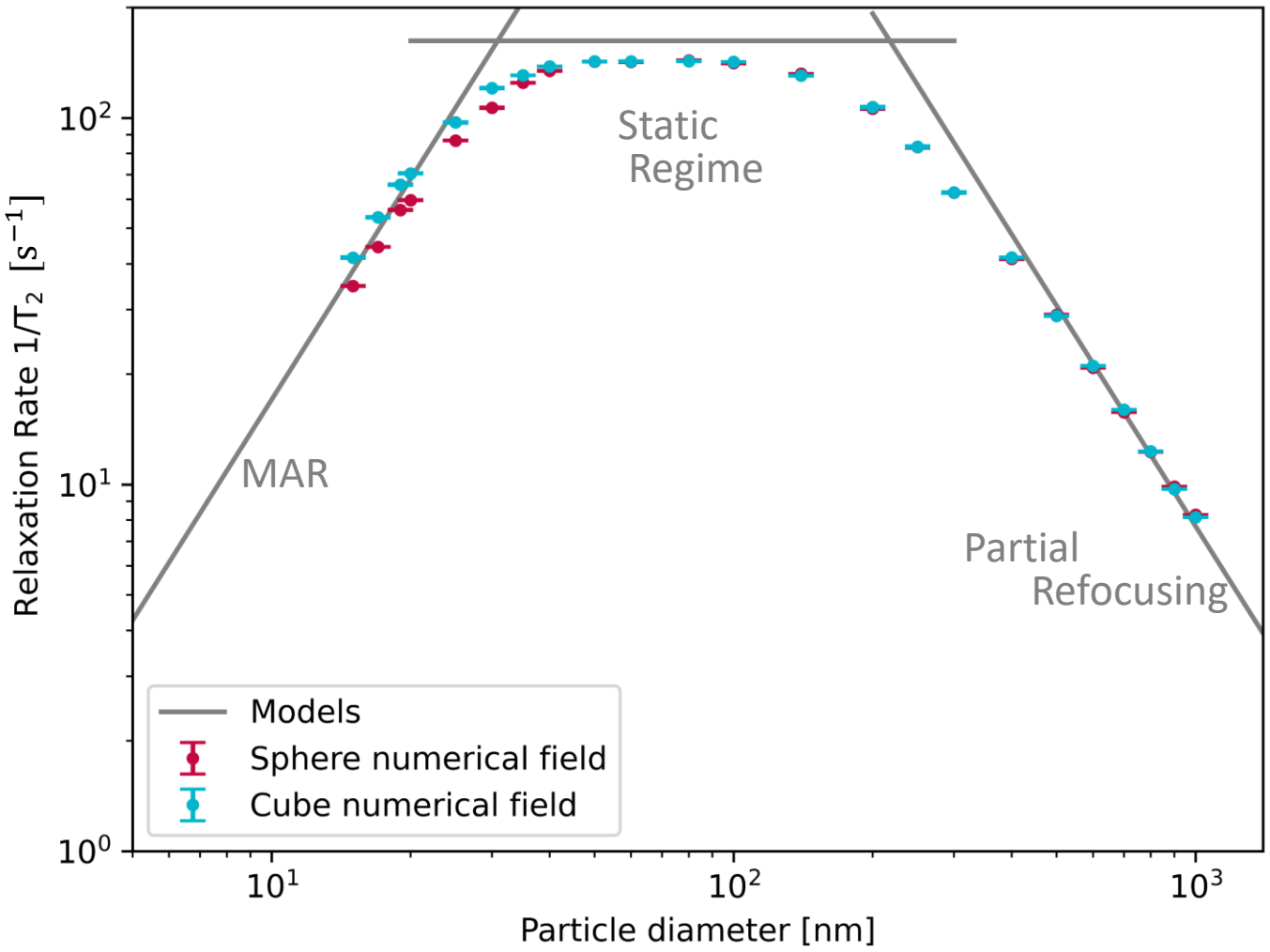
# Simulation Validation: Sphere - Dipolar




| Diameter [nm] | $1/T_2[s]$ Sphere | $1/T_2[s]$ Dipolar | Relative Difference |
|---|---|---|---|
| 15 | 34.80 | 35.81 | < 3 % |
| 20 | 59.64 | 60.06 | < 1 % |
| 30 | 106.58 | 108.83 | < 2 % |
| 40 | 134,44 | 134,58 | < 1% |
| > 40 | | | < 1 % |

- Magnetic Field:
  - Dipolar ⇔ Sphere
- Fit NMR Models
- Comparizon with existing data
  - Vuong, Q. L., Gillis, P., & Gossuin, Y. (2011). Monte Carlo simulation and theory of proton NMR transverse relaxation induced by aggregation of magnetic particles used as MRI contrast agents. In Journal of Magnetic Resonance (Vol. 212, Issue 1, pp. 139–148). Elsevier BV.

# Cubic-shaped CA's Induced Relaxation

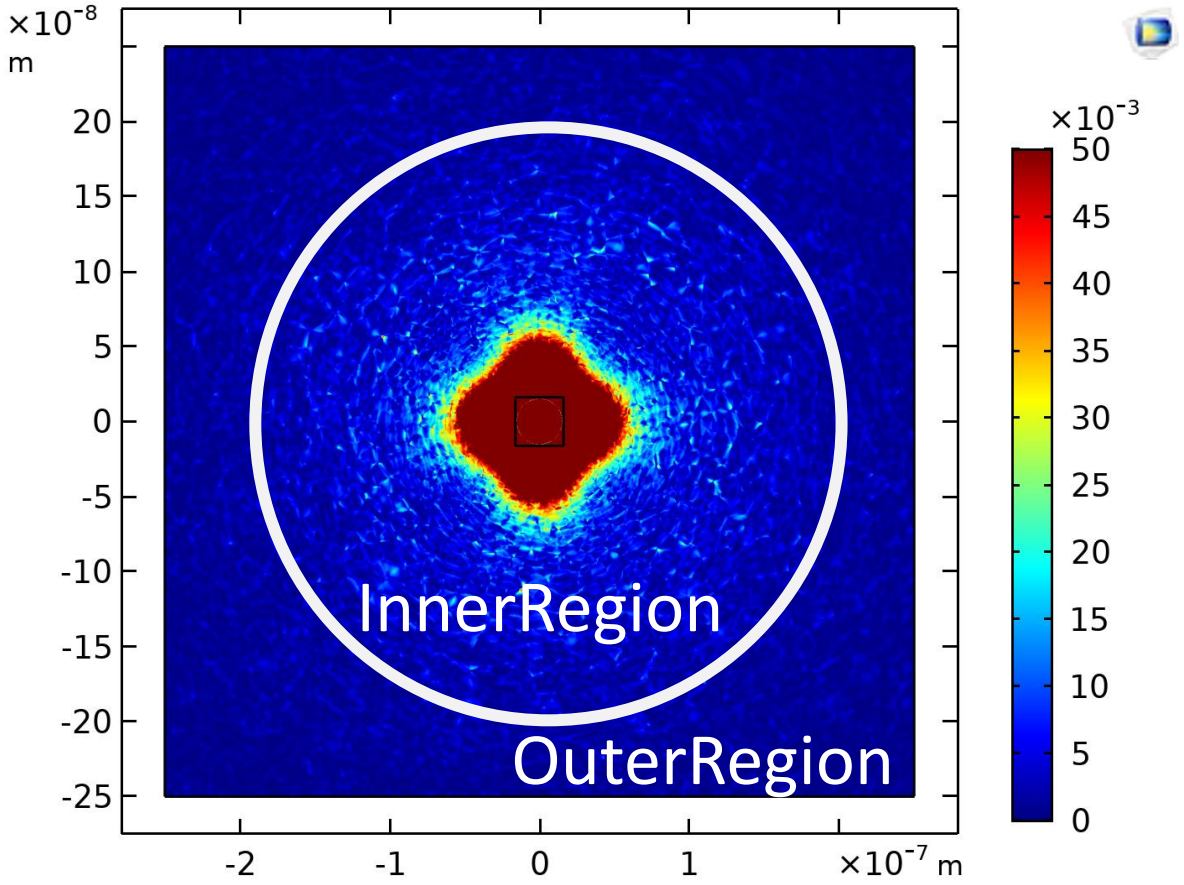



| Diameter [nm] | $1/T_2[s]$ Sphere | $1/T_2[s]$ Cube | Relative difference |
|---|---|---|---|
| 15 | 34.80 | 41.60 | 20% |
| 20 | 59.64 | 70.57 | 18% |
| 30 | 106.58 | 120.58 | 13% |
| 40 | 134,44 | 138,12 | < 3% |
| > 40 | | | < 1 % |

- NP's over 40 nm
  - **No** effect on $T_2$
- NP's under 40 nm
  - **Significant** in MAR (> 10%)
  - The smaller the size, the stronger the differences

# Interpretation: Inner/Outer-Region

- Proton: Close Relaxation – Far Relaxation
- High radius CA:
  - Protons diffusion: Static
  - Shape's impact reduced
- Low radius CA:
  - Protons diffusion: ~~Static~~
  - Shape's impact increased



# Conclusion

- Relaxation induced by Shaped Nanoparticles
  - Magnetic field differences maximized in InnerRegion
  - 20% increase in relaxation rates at 20 nm

# Perspectives

- Simulations needed for agglomerates
- New shapes options: Stars, Cylinders, Flowers, Octapods, …
- Shape Optimisation for contrast maximisation

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# Thank you for your attention

*Monte Carlo Simulations of the $T_2$ Relaxation induced by Cubic Shaped Superparamagnetic NanoParticles*


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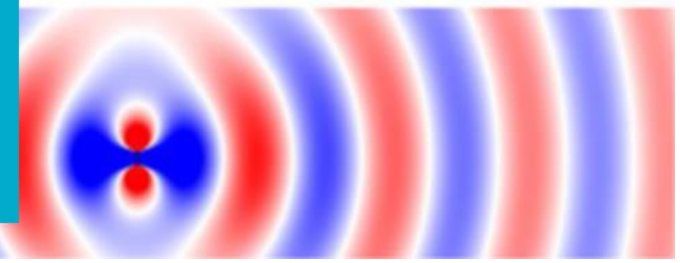
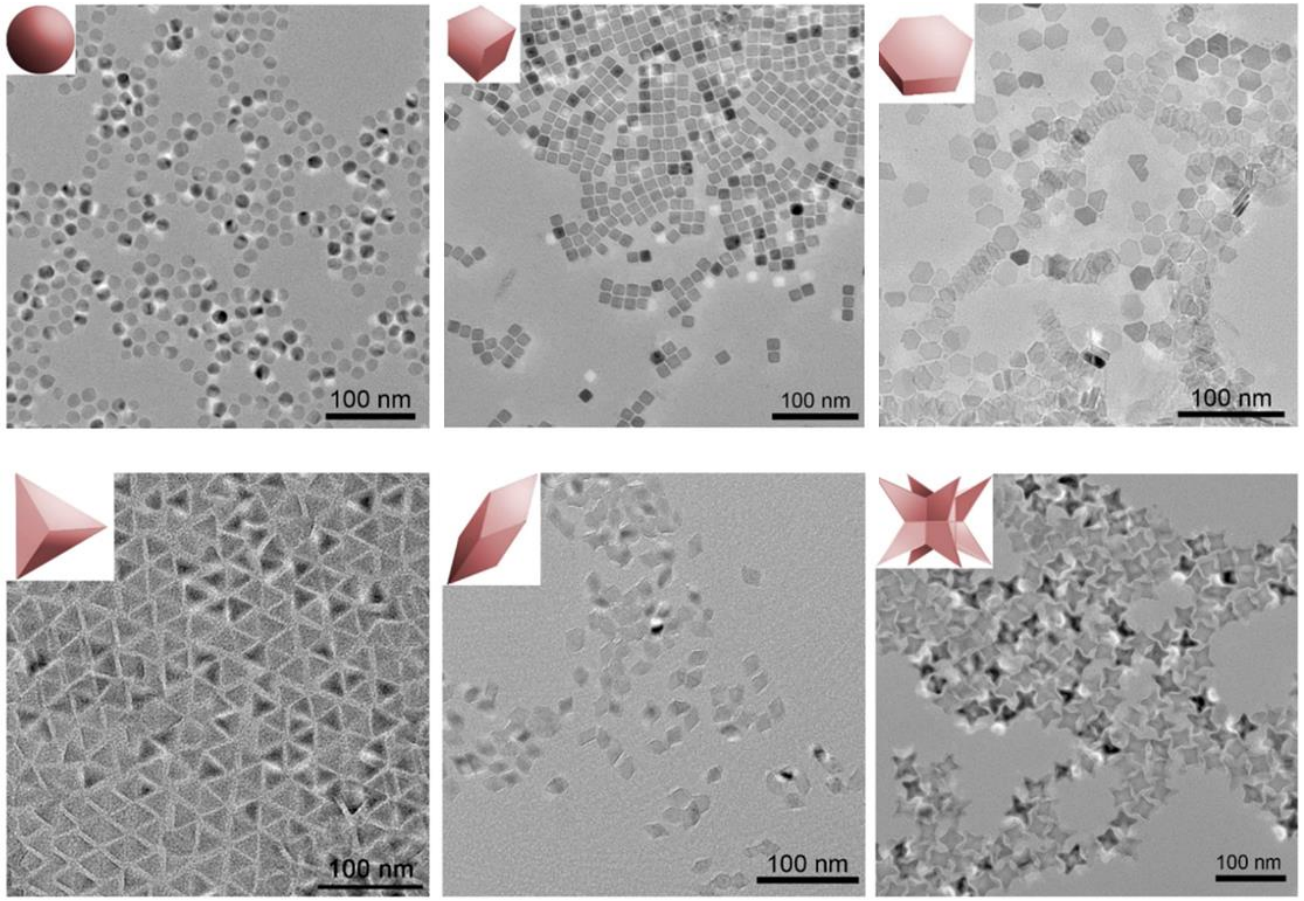


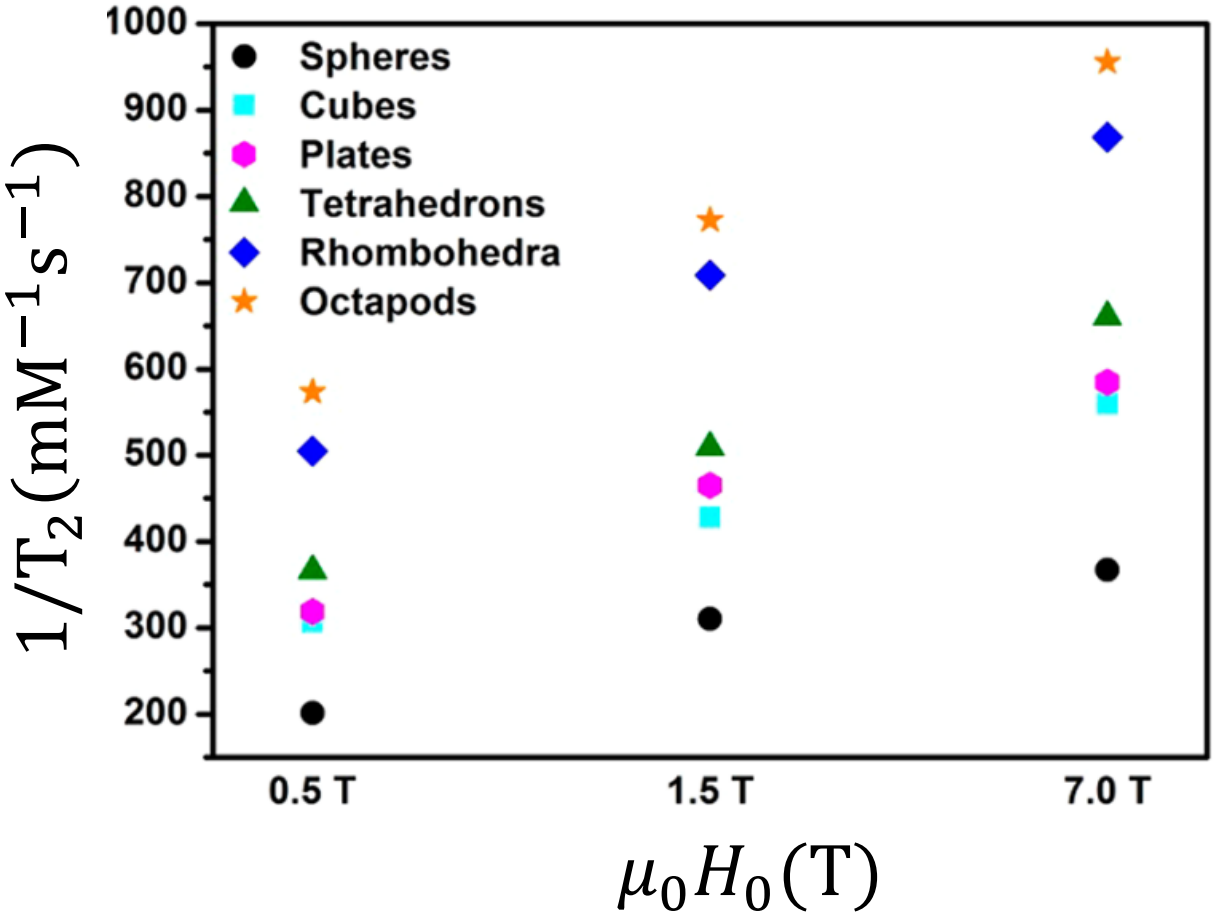
# Contenu du Backup

- NMRD
- Variations expérimentales de T2
- Calcul du champ magnétique
- Rayon sphérique effectif
- Agent de contraste T1 – T2
- Déphasage du spin des protons

# Variations expérimentales de $T_2$



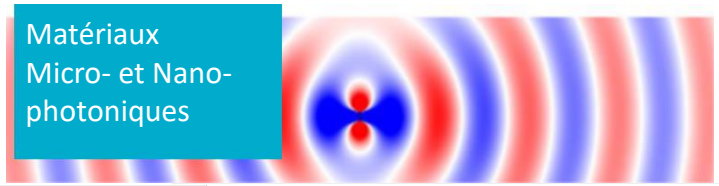

Images TEM de MnIO (Mn/Fe ≈ 1/6)




3. *L. Yang et al., 'The Roles of Morphology on the Relaxation Rates of Magnetic Nanoparticles', ACS Nano*

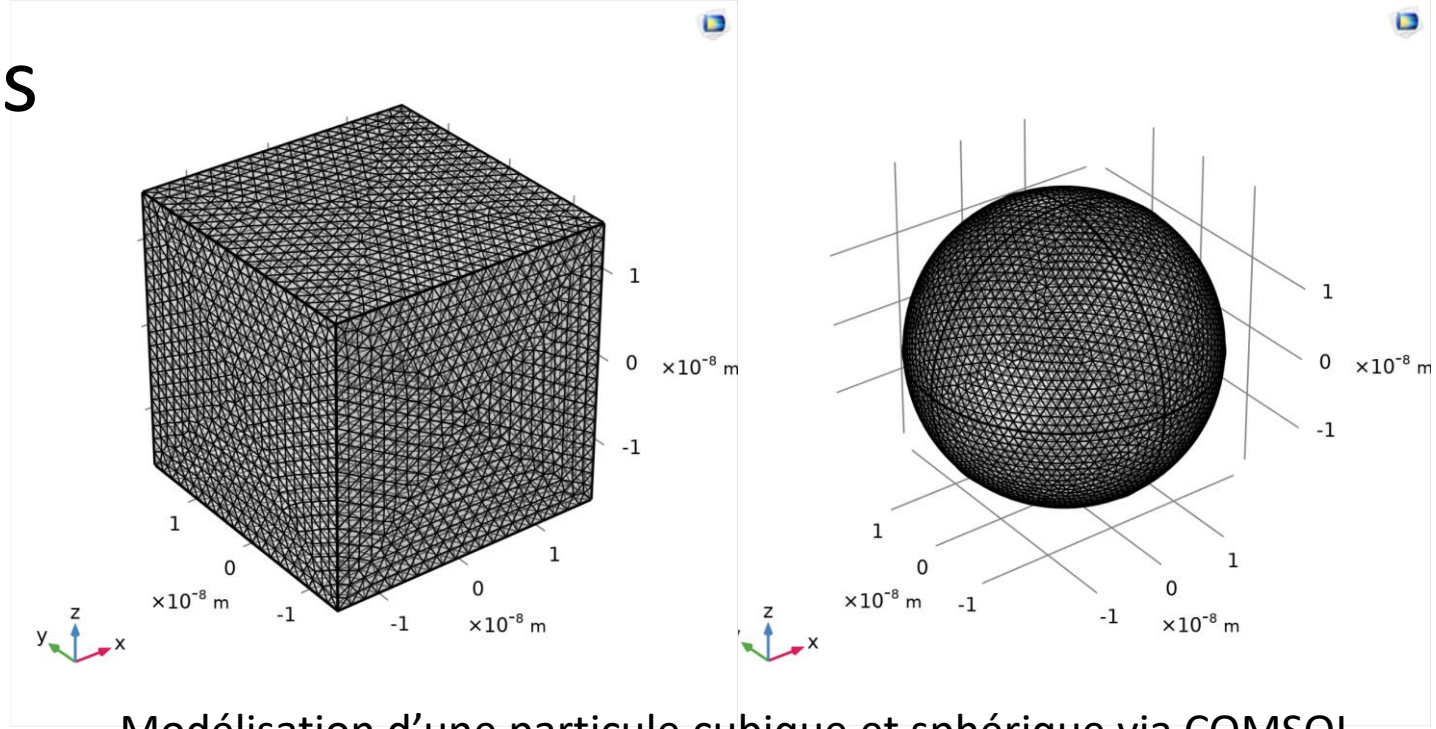
# Calcul du Champ Magnétique

- Méthode des éléments finis (FEM)
  - COMSOL (logiciel commercial) →




- Complexité des formes
  - Optimisation requise
  - Paramétrisation

des formes




Modélisation d'une particule cubique et sphérique via COMSOL

# Rayon sphérique effectif

- Pour comparer au cas sphérique
  - $V_{forme} = V_{S,\,eff}$

- Pour le cube :
  - $(2R_C)^3 = 4\pi R_{S,\,eff}^3/3$

$\Leftrightarrow \; R_C = \sqrt[3]{\pi/6}\, R_{S,\,eff}$

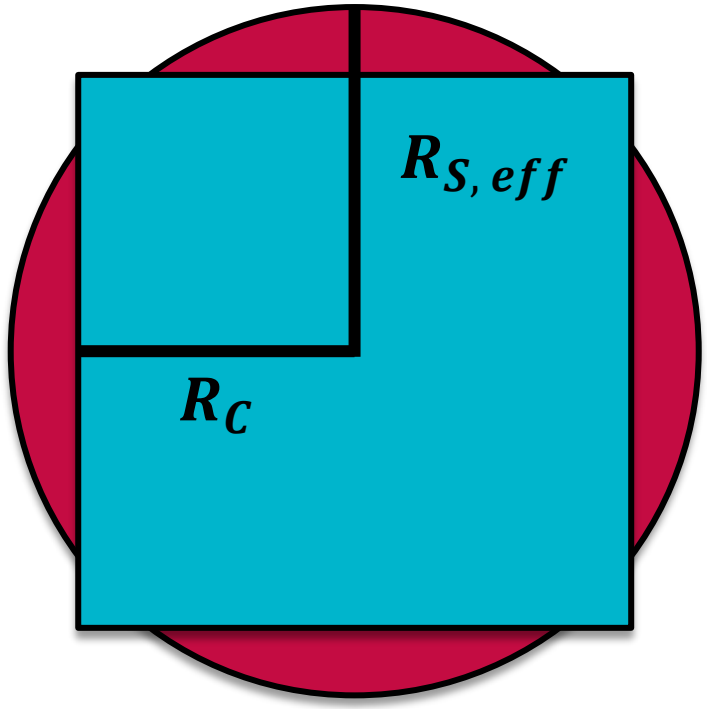
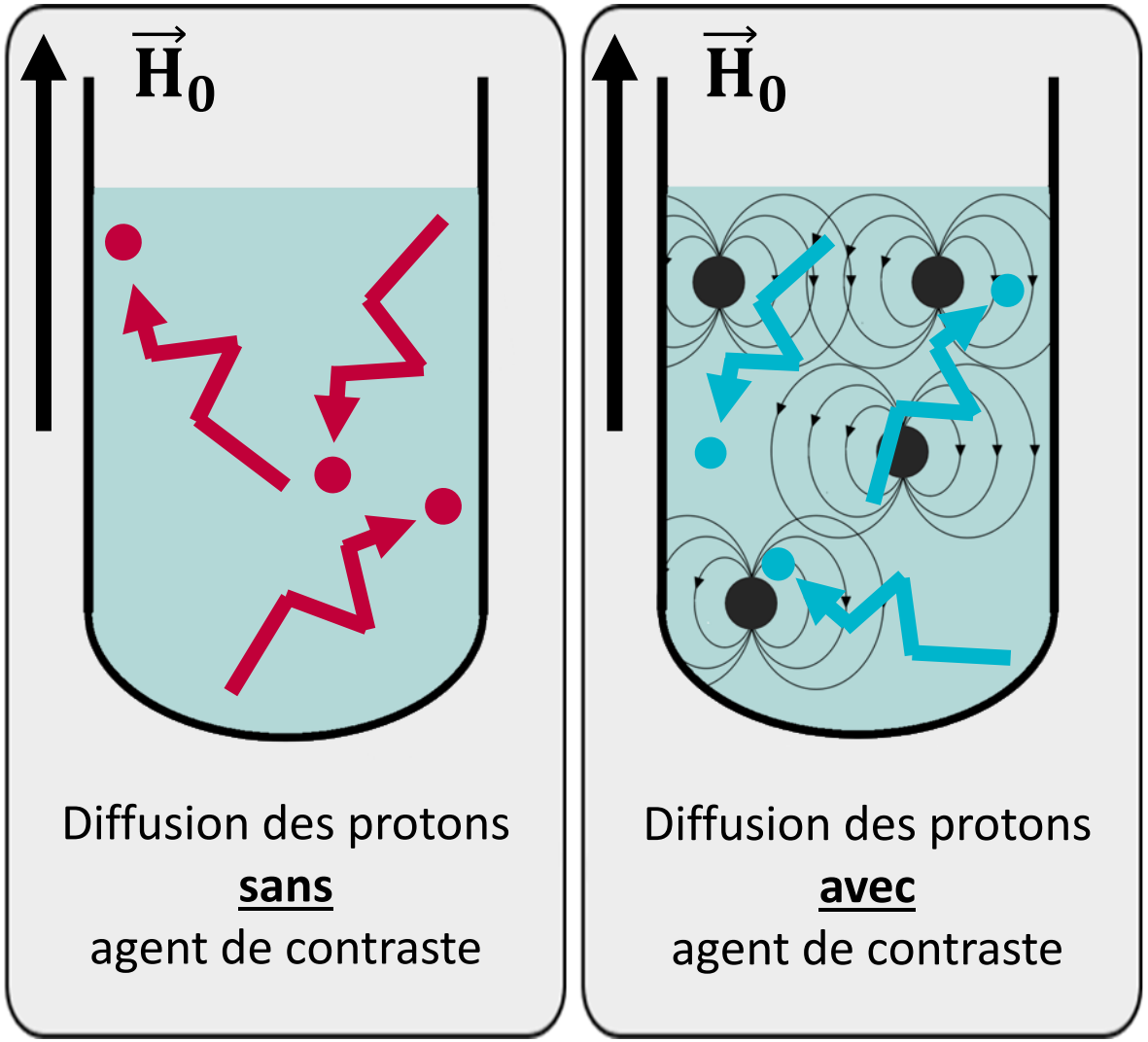



Schéma 2D de l'équivalence $V_C = V_S$

# Agent de contraste $T_2$




Diffusion des protons **sans** agent de contraste

Diffusion des protons **avec** agent de contraste

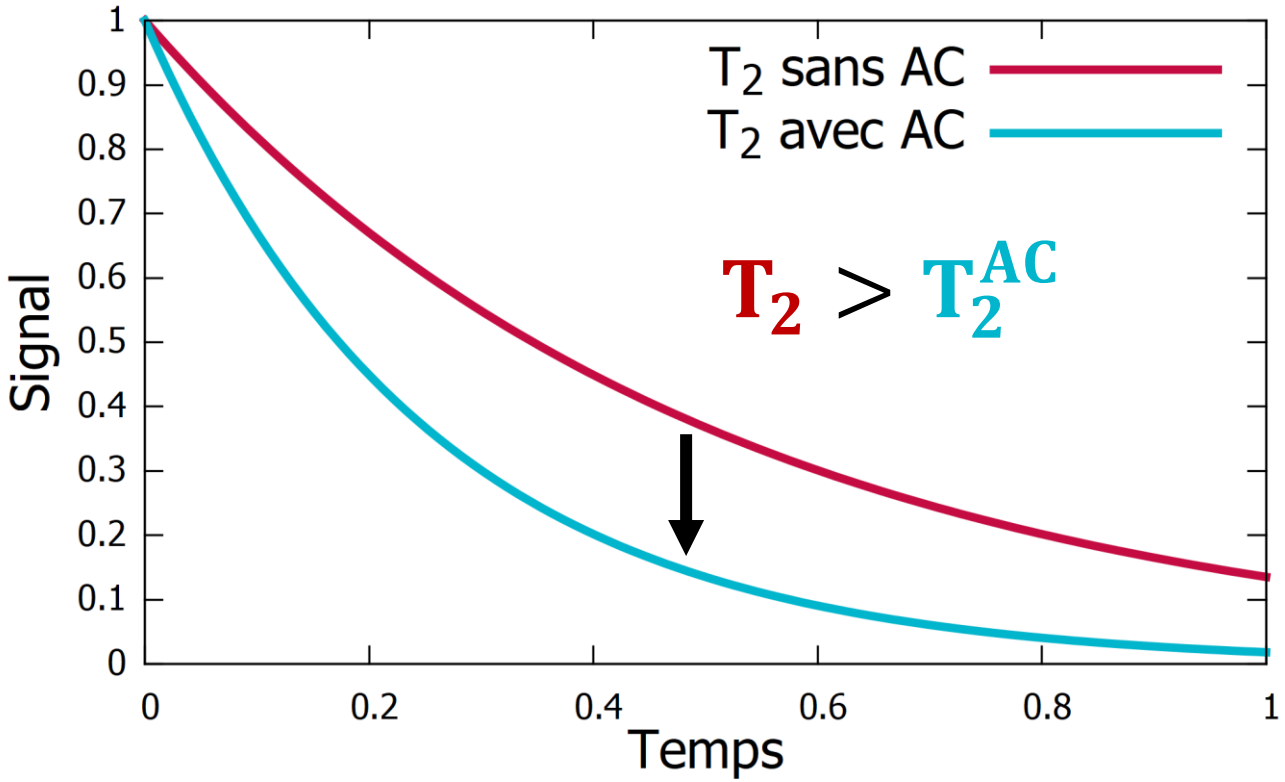
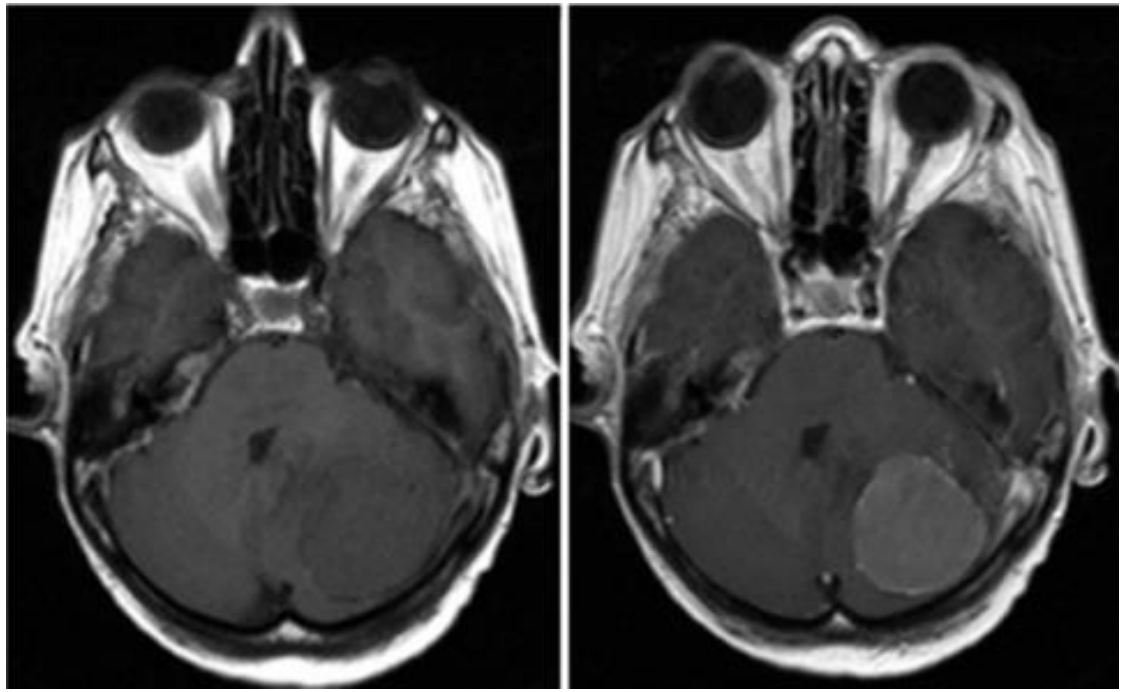



Schéma de relaxation pour deux $T_2$ différents.

# Agent de contraste $T_1$

- Intensifie le signal dans la zone tumorale
  - Contraste positif



Clichés IRM du cerveau pris à Erasme

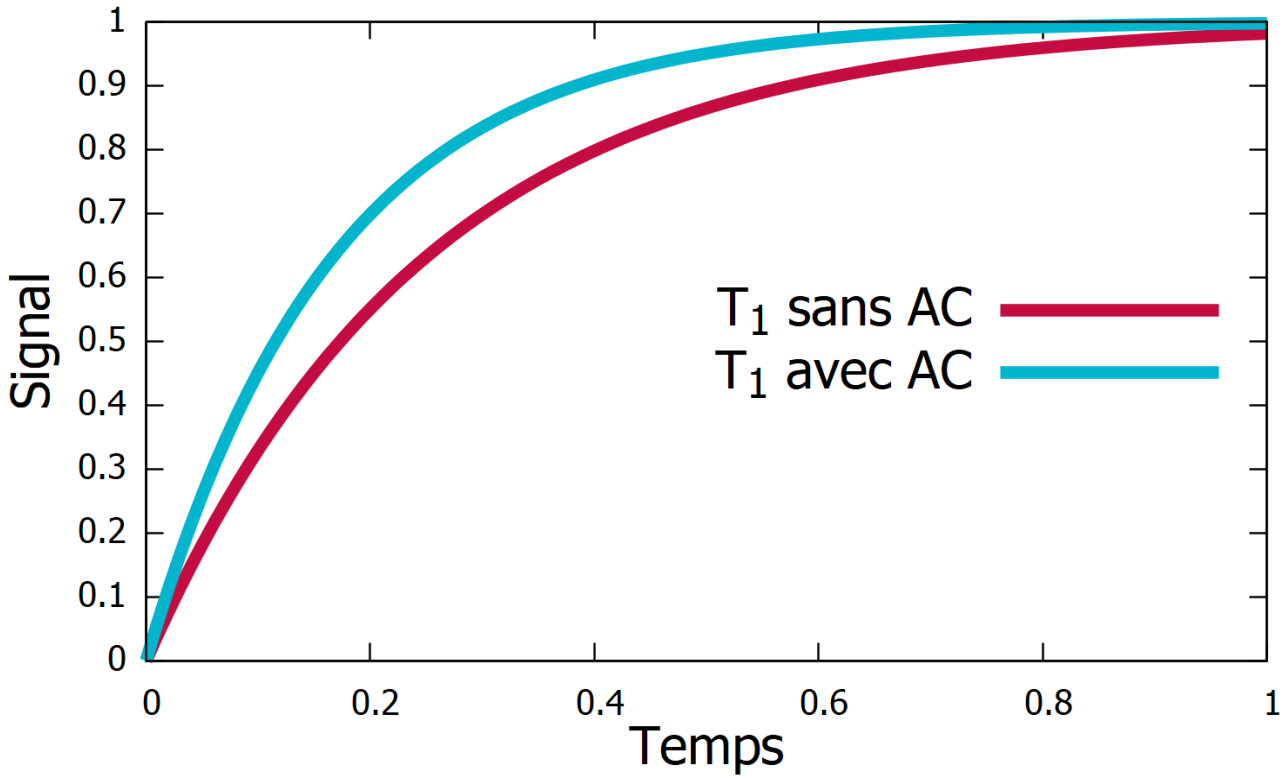


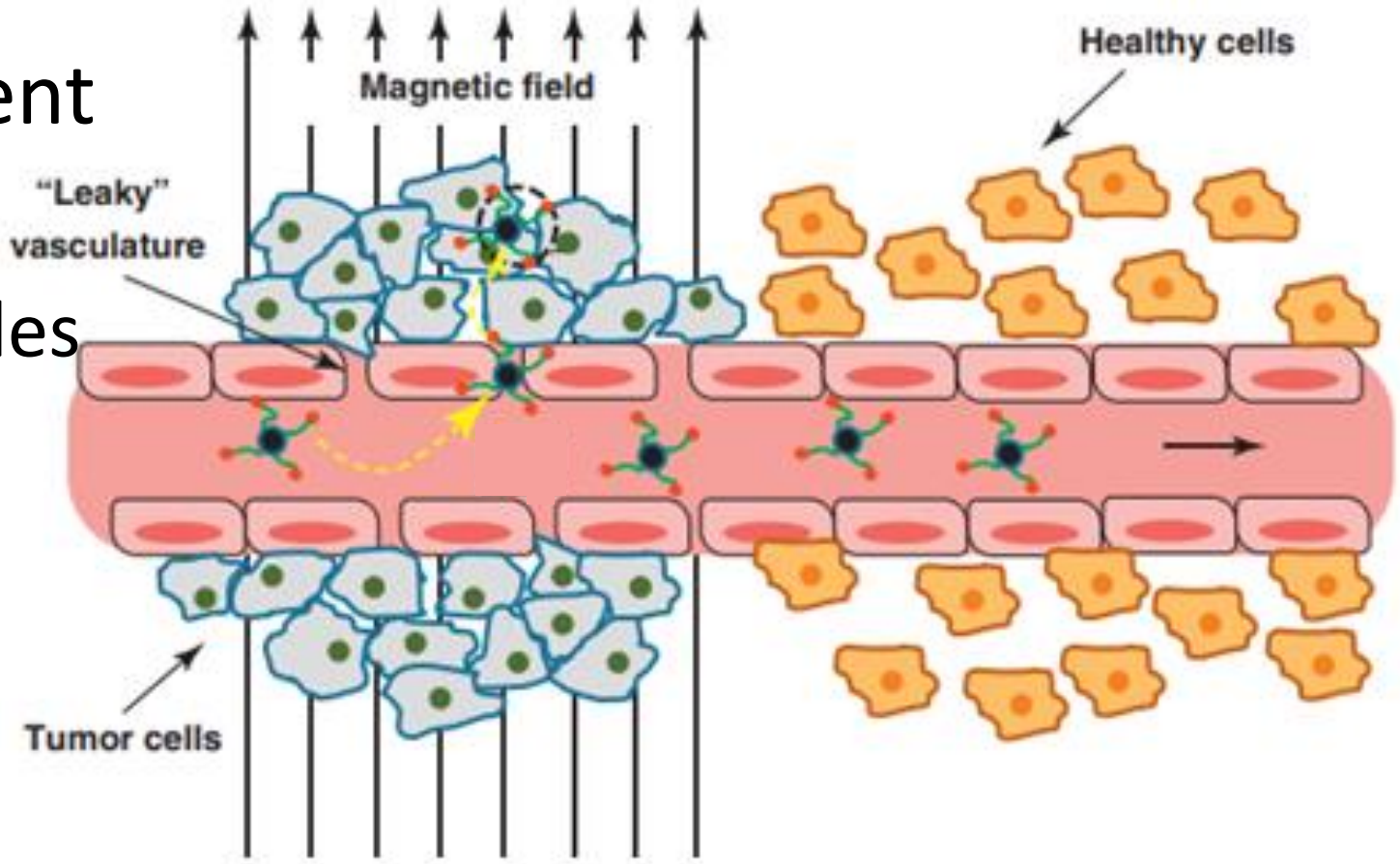

Schéma de relaxation pour deux $T_1$ différents.

# Ions accumulation in tumoral zone

- La zone tumorale a besoin d'un grand flux sanguin
  - Création d'un système vasculaire « difforme »
    - Cellules endothéliales mal alignées
- Enhanced  Permeability and Retention effect (EPR)
  - Les particules peuvent diffuser en dehors du circuit sanguin
  - Agrégation dans les zones tumorales
- Passive targeting

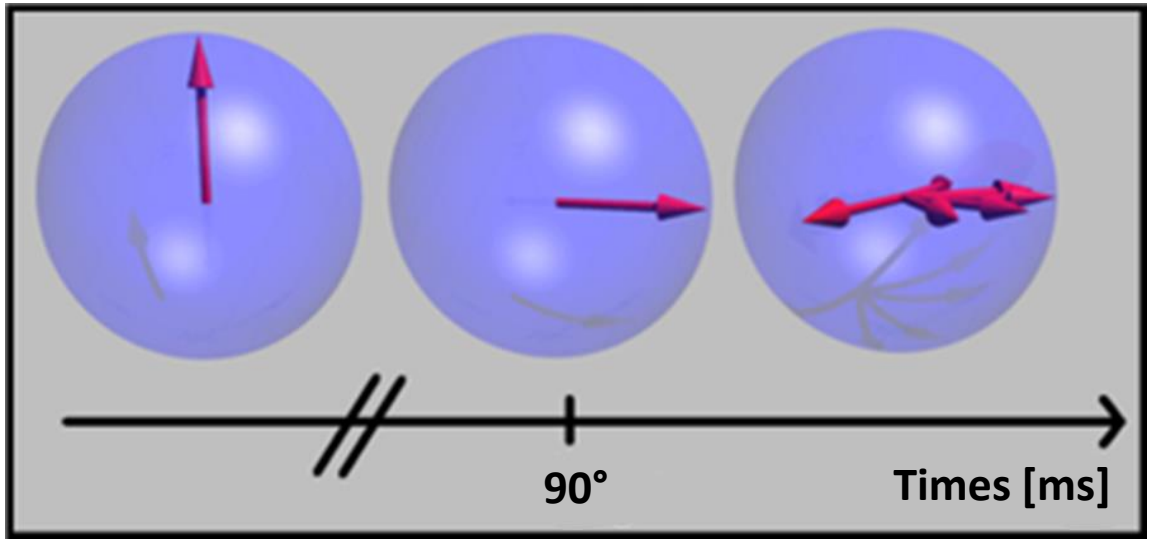
# Ions accumulation in tumoral zone

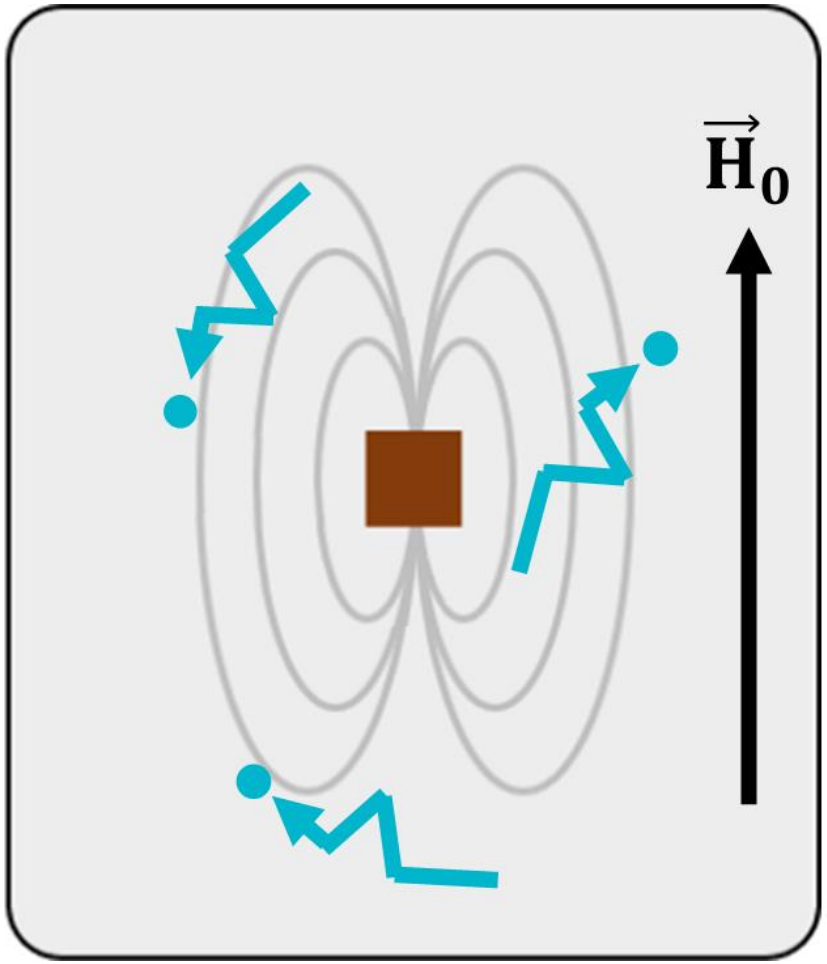
- Application d'un gradient de champ localisé
  - Force magnétique attire les NPs
  - Aide à la rétention
- Utilisation de ligands
- Active targeting



# Déphasage du spin des protons

➢ Les AC créent des inhomogénéités de champ magnétique




$$\Delta\phi_i(t) = \gamma\mu_0 H_z \Delta t$$