Monte Carlo simulations of transverse relaxation induced by superparamagnetic iron oxide nanoparticles with a semipermeable coating

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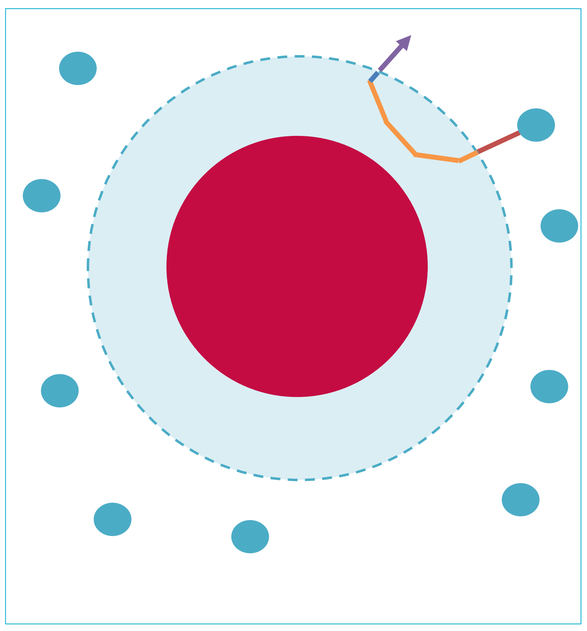
The slowed diffusion of water protons in the coating of superparamagnetic iron oxide nanoparticles is modeled through a random walk Monte Carlo algorithm. Nanoparticles are modeled as impermeable spheres, producing a dipolar magnetic field, surrounded by a semipermeable region. Entry and exit of a proton in the semipermeable coating is conditioned by coating permeability. The proton diffusion coefficient inside the coating is lower than in the solvent. The impact of coating size and diffusion coefficient on T_2 relaxation times is evaluated.

I. Contextualisation of the research

- Iron oxide nanoparticles can be used as negative T_2 contrast agents in nuclear magnetic resonance imaging.[1] For stability or functionalization reasons, they are usually coated with sugars, silica or polymers, which are semi-permeable to water.
- Transverse relaxation is caused by diffusion of water protons in magnetic field inhomogeneities created by the dipolar field from the nanoparticles. Therefore, the reduced diffusion in the semipermeable coating is expected to impact transverse relaxation times.
- An impact of coating thickness on transverse relaxation times was observed experimentally.[2,3]
- The present work aims at quantifying the effect of the coating diffusion coefficient and size on transverse relaxation times, via Monte Carlo simulations.

II. Methods – the algorithm

II. a. The modeled system



	Coating of a nanoparticle. Characterized by: • A diffusion coefficient D_C different to that of the solvent • A certain permeability to water P.
	Magnetic particle iron oxide core ; impermeable to water.
	Diffusing water proton spins.

II. b. The algorithm

1. The simulation space is generated. Its volume is $V = \frac{V_m}{f}$, with V_m the total volume of magnetic cores and f the user defined magnetic volume fraction.
   - The particle positions are set at random. They are copied 27 times periodically.
   - The space is divided in N^3 nodes.
   - A list of neighbouring particles (which are those within a cutoff radius R_C) is associated to each node.
2. Each proton diffuses.
   - The proton moves by $\sqrt{6D\tau}$ in a randomly chosen direction, where τ is the time step.
   - The closest node to that new position is found, and its list of neighbours is recuperated.
   - The exact total dipolar magnetic field B resulting from them at the position of the proton is computed.
   - The resulting proton dephasing is $\Delta\varphi = \gamma B\tau$, where γ is the proton gyromagnetic ratio.
   - At echo times τ_{IE}, the phase is inverted (= 180° pulse).
3. The total transverse magnetisation is computed. It is given at time t by:

$$M_{xy}(t) = \sqrt{M_x^2(t) + M_y^2(t)}$$

$$M_x(t) = \sum_i \cos(\varphi_i(t))$$

$$M_y(t) = \sum_i \sin(\varphi_i(t))$$

the sum being carried over all protons in the simulation.

III. Validations of the simulation algorithm

1. Validations of the field computation:
   - Comparison of the field at various positions with and without cutoff.
   - Comparison of T_2 without diffusion to the static model prediction.
2. Validations of the diffusion:
   - Comparison of the magnetisation in a B gradient to its analytical expression.
   - Graphs of the probability density of proton positions as a function of time
3. Validation of both: for particles without coating, the bell curve of the relaxation rate R_2 as a function of the particle magnetic radius was obtained and compared to
   - The motional averaging model, dominating for small radii:

$$R_2 = \frac{16}{45} f\ \tau_D\ (\gamma B_{eq})^2$$

where $\tau_D = \frac{R^2}{D}$ and Beq is the particle equatorial field.

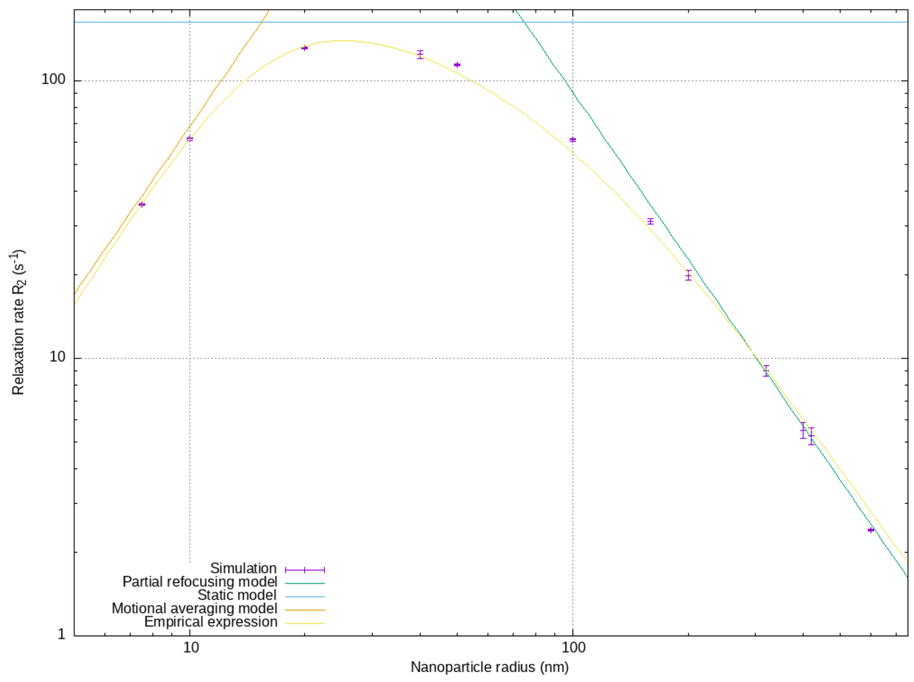
   - The static model, giving the maximum relaxation rate:

$$R_2 = \frac{2\pi}{3\sqrt{3}} \gamma f B_{eq}$$

   - The partial refocusing model, for bigger particles:

$$R_2 = 2{,}25\ f\ \frac{(1{,}34 + fc)^{5/3}}{\tau_D}\ \sqrt[3]{c} \text{ where } c = \sqrt{16/5}\ \gamma\ B_{eq}\tau_{IE}$$

   - The empirical equation of the relaxation rate as a function of the radius developed by Vuong for the same parameters [4].



Physical parameters: f = 3.14 · 10^{-6}, no coating, D = 3 · 10^{-9} m²/s, τ_{IE} = 0.5ms, B_{eq} = 0.16 T. Simulation parameters : 50 nanoparticles, N = 50, R_C = 4481nm, 10000 protons by simulation, 3 simulations per data point

This curve will be reproduced for nanoparticles with a coating.

The end goal of this research: to compare our simulations with experimental data [2,3].

[1] Vuong, Q.L., Gillis, P., Roch, A. and Gossuin, Y. *WIREs Nanomed Nanobiotechnol*. 2017, **9(6)**, e1468.
[2] Brero, F., Basini, M., Avolio, M., Orsini, F., Arosio, P., Sangregorio, C., Innocenti, C., Guerrini, A., Boucard, J., Ishow, E., Lecouvey, M., Fresnais, J., Lartigue, J. and Lascialfari, A. *Nanomaterials*. 2020, **10(9)**, 1660.
[3] La Conte, L.E.W., Nitin, N., Zurkiya, O., Caruntu, D., O'Connor, C.J., Hu, X. and Bao, G. Journal of Magnetic Resonance Imaging. 2007, **26(6)**, 1634-1641.
[4] Vuong, Q.L.. PhD Thesis. 2011.

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