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

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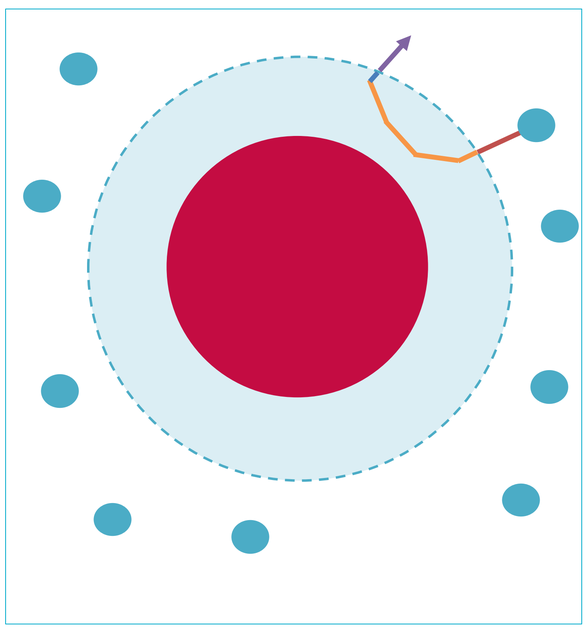
The altered diffusion of water protons in the coating of superparamagnetic iron oxide nanoparticles is studied through a random walk Monte Carlo algorithm. Nanoparticles are modeled as impermeable spheres, producing a dipolar magnetic field, surrounded by a semipermeable region. Entry and exit of a proton in the semipermeable coating is conditioned by coating permeability. Diffusion coefficient changes in the coating lead to significant variations in the NMR transverse relaxation rate induced by such nanoparticles, indicating R2 relaxation could be optimized through an appropriate choice of the coating properties.

I. Context 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 changes in the diffusion coefficient 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 thickness on transverse relaxation times, via Monte Carlo simulations.

II. Methods – the algorithm

II. a. The modeled system



	Coating of a nanoparticle. Characterized by: • its diffusion coefficient D_C different from that of the solvent; • its permeability to water P; • its thickness.
	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. Particles are copied 27 times periodically.
   - A Verlet list of particles is established.
   - The initial spin of all protons is at 90° of the z-axis, as it would following a pulse.
2. Each proton diffuses.
   - Its displacement follows a random walk.
   - The exact total dipolar magnetic field B resulting from the closest particles at its position is computed.
   - The resulting proton spin 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:

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

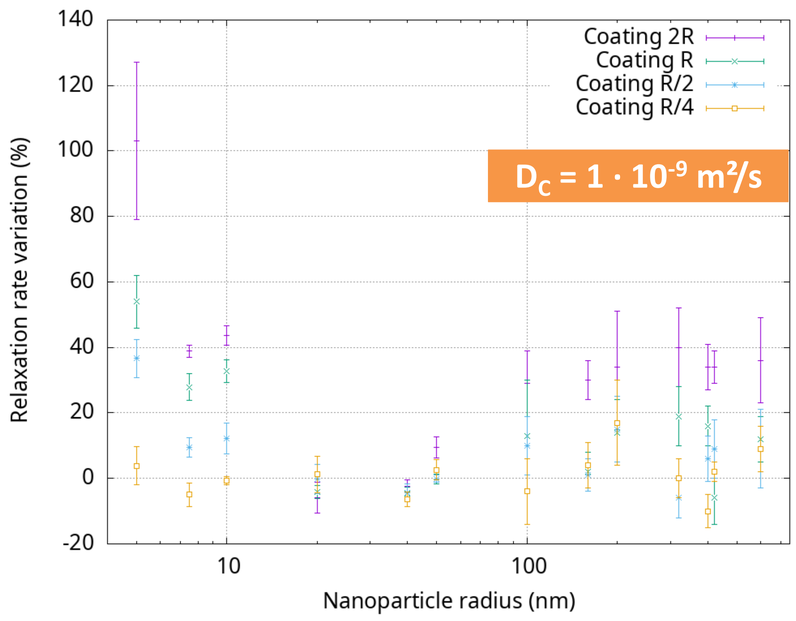
$$M_x(t) = \sum_i \cos(\varphi_i(t))$$

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

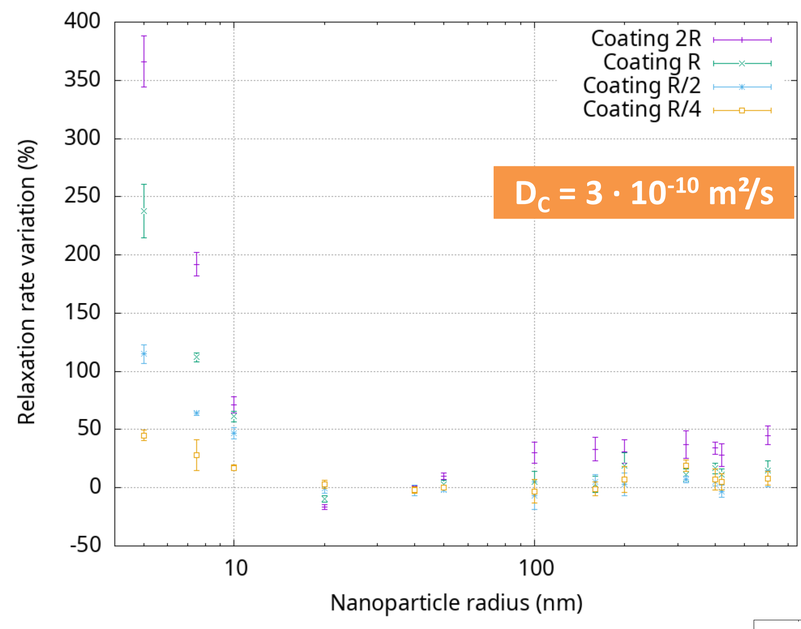
the sum being carried over all protons in the simulation.

4. The curve of magnetisation as a function of time is fitted to obtain the transverse relaxation rate R_2 (s^{-1}).

III. First results – impact of the coating thickness on R_2 rate



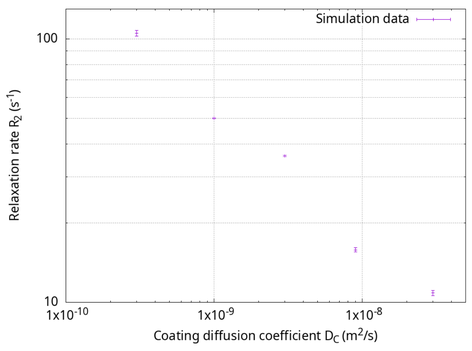
The variation of R_2 (with respect to the R_2 obtained without coating) increases (dramatically) for small particles and thick coatings.



This effect is amplified when the coating diffusion coefficient decreases.

In all simulations the solvent is water, with a diffusion coefficient $D_s = 3 \cdot 10^{-9}$ m²/s.

For a fixed radius (R = 7,5nm) and a fixed coating layer thickness (15nm), varying D_C, including the (less realistic, but theoretically interesting) case of coatings with *faster* diffusion than water, shows a nonlinear relationship between D_c and R_2.



Our results indicate that thick coatings with slow water diffusion lead to higher relaxation rates in small particles. This is in qualitative agreement with experimental data[2,3], and is a useful guideline for particle synthesis and coating choice.

Future goals are, to solidify those results

- To add data points with more extreme diffusion coefficients (notably very slow diffusion, up to $3 \cdot 10^{-11}$ m²/s)
- To add data points with more coating sizes for 5 and 7,5nm particles with $D_c = 3 \cdot 10^{-10}$ m²/s (most realistic case for polymer coatings).
- To quantitatively compare to experimental data.

[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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