Characterization of superparamagnetic particles with MR relaxometry: good and bad news

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***Superparamagnetic particles** are used as contrast agents in cellular and molecular **Magnetic Resonance Imaging (MRI).** Their efficiency can be predicted by a suited theoretical model. Moreover the fitting of **Nuclear Magnetic Resonance (NMR)** relaxation data by this theory provides the size and saturation magnetization of the particles. It is therefore **crucial to validate the theory** in different experimental conditions.*

1. Relaxation induced by superparamagnetic particles

- Superparamagnetic nanoparticles = contrast agents for T_2-weighted MRI.
- Relaxation = dynamics of the proton NMR signal
  - in the direction of B_0 (longitudinal relaxation, time T_1)
  - in the plane ⊥ to B_0 (transverse relaxation, time T_2)
- Superparamagnetic relaxation ≺ dipolar interaction between the huge particle magnetic moment and those of (water) protons + time modulation by the diffusion of (water) protons.

⇒drastic decrease of T_2 and slighter decrease of T_1 : faster relaxation!

⇒Relaxation model developed by Roch et al (1) in the *Motional Averaging Regime (MAR).*

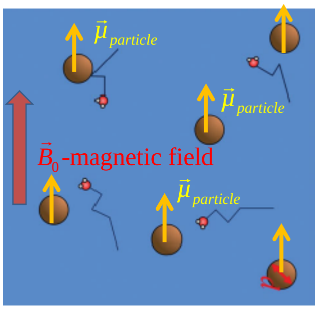

***Figure 1:** sketch of NMR relaxation of water protons induced by magnetic particles*

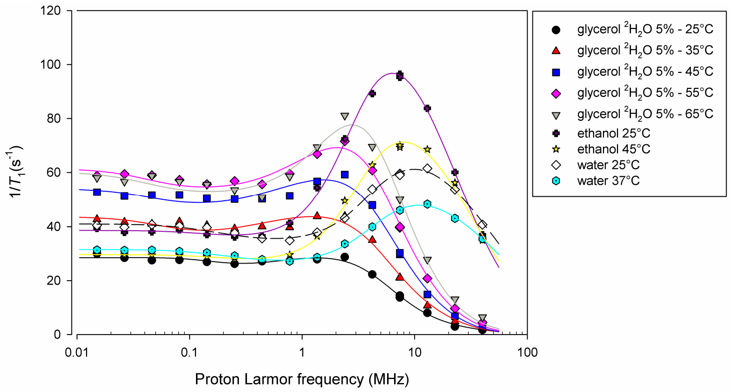

***Figure 2:** T_1 NMRD profiles of different suspensions of USPIO particles, [Fe] = 1.49 mM. The lines are fittings by the relaxation model of Roch [1].*

- Theoretical validity of the Roch model depends on:

-the radius R and magnetization Mv of the particles,

-the diffusion properties of protons in the particles suspension,

⇒2 relevant parameters:

1. the proton diffusion time $\tau_D = R^2/D$ where D is the diffusion coefficient of protons.
2. the Larmor frequency shift at the equator of the particle, $\Delta\omega = \gamma\mu_0 M_v/3$.

- *MAR* is applicable when $\Delta\omega\tau_D<1$ → Roch model is valid when $\Delta\omega\tau_D<1$.

2. Questions

- Is the theory valid outside the MAR? Change R, Mv (2) or ***Diffusion coefficient***

⇒change the temperature, solvent or both (Fig. 2)

- Is the theory valid for T_1 and T_2 simultaneously?

⇒Simultaneous fitting of T_1 and T_2 data (Fig. 3)

- Is the theory valid for another nucleus (^2H)?

⇒Measurement and fitting for a suspension of particles in heavy water (Fig. 4.)

- Samples = Suspensions of Ultra Small Particles of Iron Oxide (USPIOs): R = 3.76 nm (σ=0.2) and Mv = 330000 A/m.
- Experimental data = values of T_1 and T_2 at different magnetic fields = Nuclear Magnetic Relaxation Dispersion (NMRD) curve.

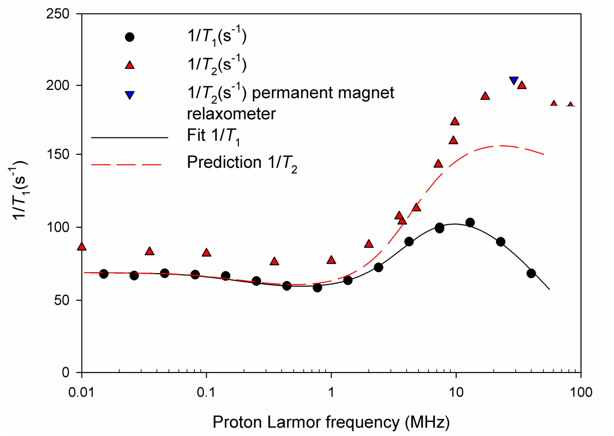

***Figure 3:** T_1 and T_2 NMRD profiles of an aqueous suspension of USPIO particles at 25°C, [Fe] = 2.5 mM. The plain line is a fitting of the T_1 data while the dashed line is the prediction of T_2 using the parameters obtained from the T_1 fitting.*

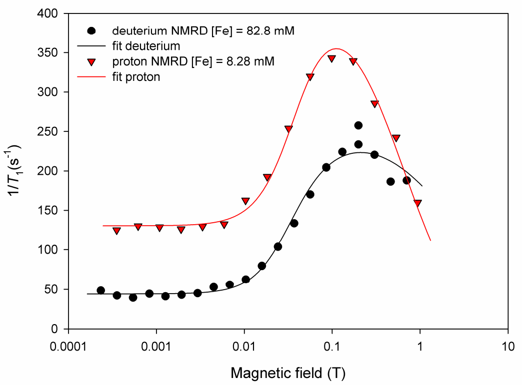

***Figure 4:** ^2H and ^1H T_1 NMRD profiles of 20 nm clusters of USPIO particles at 37°C. Line are fittings by the Roch model.*

2. Answers

Good news ☺

- The **Roch** model allowed to **fit the T_1 data** even **outside** the **MAR** (up to $\Delta\omega\tau_D$ = 187).
- R values obtained from the fittings (from 4 to 6nm) consistent with the actual radius value.

⇒determination of **radius still valid** even **outside** the **MAR.**

- Mv values always smaller, when outside the MAR, than the actual magnetization value.

⇒The ***Mv*** values are **not reliable outside** the **MAR.**

- **^{2}H NMRD** can be fitted by the Roch theory : **dipolar relaxation** instead of quadrupolar relaxation because of the enormous magnetic moment of the particle.

Bad news ☹

- **Impossible** to **fit simultaneously** the **T_1 and T_2** NMRD profile (while in the MAR condition).

4. References

1. Roch et al. Journal of Chemical Physics 110, 11, (1999). 2. Vuong et al. Advanced Healthcare Materials 1, 4 (2012). 3. Gossuin et al. Nanotechnology 27, 155706 (2016).