^{1}H-NMR relaxation study of a magnetic ionic liquid as a potential contrast agent

Carla I. Daniel,[*,†] Fabián Vaca Chávez,[‡] Carla A. M. Portugal,[¶] João G. Crespo,[¶] and Pedro J. Sebastião[§]

†*REQUIMTE/LAQV, Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa*

‡*Condensed Matter Physics Centre, University of Lisbon, Lisbon, Portugal.*

¶*REQUIMTE/CQFB, Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa*

§*Instituto Superior Técnico, Universidade de Lisboa, Lisbon, Portugal; Centro de Física e Engenharia de Materias Avançados, Universidade de Lisboa, Lisbon, Portugal*

E-mail: cid17734@campus.fct.unl.pt

Theoretical models

Translational self-diffusion

In the case of isotropic liquids or isotropic phases of liquid crystal compounds the contribution of translational self-diffusion (SD) to the relaxation can be expressed by the Torrey's model[1] with a

$$\left(\frac{1}{T_1}\right)_{\mathrm{SD}} = C_d \frac{n\tau_D}{d^3}\left[\mathcal{T}(\omega\tau_D) + 4\mathcal{T}(2\omega\tau_D)\right], \tag{1}$$

where $\omega = 2\pi\nu_L$, $C_d = (1/2)(3\mu_0\gamma^2\hbar/(8\pi))^2$ is the strength of the dipolar interaction and $\mathcal{T}(\omega\tau_D)$ is a dimensionless analytical function that depends on the average time between diffusion jumps τ_D, the mean-square jump distance $\langle r^2 \rangle$, and the molecular width d. τ_D is related with the self-diffusion constant D by the relation $\langle r^2 \rangle = 6\tau_D D$. n is the density of ^{1}H spins.

Rotations/reorientations

Molecular rotations/reorientations (Rot) may be characterized by one or more correlation times according to the number of independent rotational axis considered to describe this motion. Usually, rotations along the molecular long axis and rotations/reorientations along a molecular transverse axis have different correlations times and the most simple model used to describe this relaxation process is given a Rot$_1$+Rot$_2$ where Rot$_i$ is given by the Bloemberger, Purcel and Pound (BPP) model:

$$\left(\frac{1}{T_1}\right)_{\mathrm{Rot}_i} = A_{\mathrm{Rot}_i}\left[\frac{\tau_{Rot_i}}{1+\omega^2\tau_{Rot_i}^2} + \frac{4\tau_{Rot_i}}{1+4\omega^2\tau_{Rot_i}^2}\right] \tag{2}$$

with $A_{\mathrm{Rot}_i} = 9\mu_0^2\gamma^4\hbar^2/(128\pi^2 r_{i_{eff}}^6)$ where $r_{i_{eff}}$ is an effective inter-spin distance.[2]

Cross-relaxation

^{35}Cl has nuclear spin 3/2 and cross-relaxation (CR) between the proton spins and ^{35}Cl nuclear spins can occur. Cross-relaxation has indeed been observed between proton spins and nitrogen and also between proton spins and ^{35}Cl spins.[3–5] Cross-relaxation may become significant when the proton's Larmor frequency is close to each one of the quadrupole frequencies of the other nucleus. The relaxation rate can be expressed by[3]

$$\left(\frac{1}{T_1}\right)_{\mathrm{CRi}} = A_{\mathrm{CRi}}\frac{\tau_{\mathrm{CRi}}}{1+(\omega-\omega_i)^2\,\tau_{\mathrm{CRi}}^2} \tag{3}$$

where ω_i, with $i = 1, 2, ...$, are the frequencies that correspond to the ^{35}Cl spin energy levels and A_{CRi} are parameters related with the strength of the interaction.

Paramagnetic relaxation induced by superparamagnetic particles

Proton spin-lattice relaxation can be affected by the presence of magnetic ions in two ways: i) the so-called *inner-sphere* relaxation, which occurs when relaxing protons bind temporarily to ions or ion complexes, and the ii) *outer-sphere* applies to protons that do not bind but move or diffuse close to magnetic ions or particles.[6] In a recent study of molecular dynamics in magnetic ionic liquid systems by proton spin-lattice relaxometry,[7] it was shown that the paramagnetic relaxation observed was better described considering an effective superparamagnetic outer-sphere contribution given by equation:

$$\begin{gathered}\left(\frac{1}{T_1}\right)_{PM} = 6\tau_d c\left\{S_c^2\, j_1(\omega,\tau_d,\tau_s\rightarrow\infty)+\right.\\ \left.\left[S(S+1)-S_c\,\mathrm{cotg}\frac{x}{2S}-S_c^2\right] j_1(\omega,\tau_d,\tau_s)\right\}\end{gathered} \tag{4}$$

where S is the electronic spin along the applied magnetic field, c is a quantity proportional to the molar concentration of magnetized particles, [M]. r is the distance of closest approach between the anion and the protonated cation, $\tau_d = \langle r^2\rangle/D$, D is the diffusion time constant, τ_s is the longitudinal electronic relaxation time and ω is the proton Larmor frequency. S_c is given by

$$S_c = \frac{2S+1}{2}\tanh^{-1}\left((2S+1)\frac{\omega}{\omega_r}\right) - \frac{1}{2}\tanh^{-1}\left(\frac{\omega}{\omega_r}\right) \tag{5}$$

where $\omega_r = 2\gamma kT/(\hbar\gamma_S)$ and γ_S is the electron's gyromagnetic ratio. The corresponding spectral density for outer-sphere relaxation is[6]

$$j_1(\omega,\tau_d,\tau_s) = \mathrm{Re}\left\{\frac{1+\Omega^{1/2}/4}{1+\Omega^{1/2}+4\Omega/9+\Omega^{3/2}/9}\right\} \tag{6}$$

where $\Omega = (i\omega + 1/\tau_s)\tau_d$.

Relaxivity Dispersion

In the case of the magnetic ionic liquid/DMSO solutions presented in this work we considered the inner-sphere relaxivity contribution expressed by:[8]

$$r_1^{is} \approx \frac{1}{1000}\frac{q^{st}}{14.04}\frac{1}{T_{1m}^H} \tag{7}$$

being q^{st} the number of DMSO molecules temporarily bind to the iron particles and $T_{1m}^H \gg \tau_m$ where τ_m is the DMSO residence binding time to the $FeCl_4^-$ (or $FeCl_3$).

$$\frac{1}{T_{1m}^H} = \frac{2}{15}(\frac{\mu}{4\pi})^2\frac{\hbar^2\gamma_I^2\gamma_S^2}{r_{Fe}^6}S_p(S_p+1)[3J(\omega_I,\tau_{d1})+7J(\omega_S,\tau_{d2})] \tag{8}$$

$$J(\omega,\tau_{\mathrm{di}}) = \frac{S^2\tau_{\mathrm{dig}}}{1+\omega^2\tau_{dig}^2} + \frac{(1-S^2)\tau_{di}}{1+\omega^2\tau_{di}^2} \tag{9}$$

$$\tau_{di} = \frac{1}{\tau_{mH}} + \frac{1}{T_{iS}} \tag{10}$$

$$\tau_{dig} = \frac{1}{\tau_{mg}} + \frac{1}{T_{iS}} \tag{11}$$

$$\frac{1}{T_1 s} = 2C[\frac{1}{1+\omega_s^2\tau_v^2} + \frac{4}{1+4\omega_s^2\tau_v^2}] \tag{12}$$

$$\frac{1}{T_2 s} = C[\frac{5}{1+\omega_s^2\tau_v^2} + \frac{2}{1+4\omega_s^2\tau_v^2} + 3] \tag{13}$$

with

$$C = \frac{1}{50}\Delta^2\tau_v[4S_p(S_p+1)-3] \tag{14}$$

The outer-sphere relaxivity contribution is given by:

$$r_1^{os} = \frac{32N_A\pi}{405}(\frac{\mu}{4\pi})^2\frac{\hbar^2\gamma_I^2\gamma_S^2}{RD}S_p(S_p+1)[3J^{os}(\omega_I,\tau_d),T_{1S}+7J^{os}(\omega_S,\tau_d),T_{2S}] \tag{15}$$

with $\tau_d = R^2/D$

$$J^{os} = \mathrm{Re}\left\{\frac{1+\frac{z}{4}}{1+z+\frac{4}{9}z^2+\frac{1}{9}z^3}\right\} \tag{16}$$

being, $z = i\omega\tau_d + \frac{\tau_d}{T_jS}$ is a complex and $j = 1, 2$

DMSO/$FeCl_3$ and DMSO/[P_{66614}][$FeCl_4$]

It is presented the relaxivity results and fitting curves obtained for DMSO/hexahydrated $FeCl_3$ for comparison with the DMSO/[P_{66614}][$FeCl_4$] solution.

References

(1) Torrey, H. C. Nuclear Spin Relaxation by Translational Diffusion. *Phys. Rev.* **1953**, *92*, 962–969.

(2) Bloembergen, N.; Purcell, E. M.; Pound, R. V. Relaxation Effects in Nuclear Magnetic Resonance Absorption. *Phys. Rev.* **1948**, *73*, 679–712.

(3) Kimmich, R.; Winter, F.; Nusser, W.; Spohn, K. H. Interactions and Fluctuations Deduced From Proton Field-cycling Relaxation Spectroscopy of Polypeptides, Dna, Muscles, and Algae. *J. Magn. Reson.* **1986**, *68*, 263–282.

(4) Pusiol, D. J.; Humpfer, R.; Noack, F. Nitrogen Nuclear-quadrupole Resonance Dips in The Proton Spin Relaxation Dispersion of Nematic and Smectic Thermotropic Liquid-crystals. *Z. Naturforsch., A: Phys. Sci.* **1992**, *47*, 1105–1114.

(5) Anoardo, E.; Pusiol, D. J., D. J.; Aguilera, C. NMR-Study of the T_1 Relaxation Disper-

sion In the Smectic Mesophase of 4-chlorophenyl 4-undecyloxybenzoate. *Phys. Rev. B: Condens. Matter* **1994**, *49*, 8600–8607.

(6) Gillis, P.; Roch, A.; Brooks, R. A. Corrected Equations for Susceptibility-induced T_2-shortening. *J. Magn. Reson.* **1999**, *137*, 402–407.

(7) Daniel, C. I.; Vaca Chávez, F.; Feio, G.; Portugal, C. A. M.; Crespo, J. G.; Sebastião, P. J. ^{1}H NMR Relaxometry, Viscometry, and PFG NMR Studies of Magnetic and Nonmagnetic Ionic Liquids. *J. Phys. Chem. B* **2013**, *117*, 11877–11884.

(8) Merbach, A., Helm, L., Toth, E., Eds. *The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging*, 2nd ed.; Wiley, 2013.

fitteia Report

(internet based fitter service)

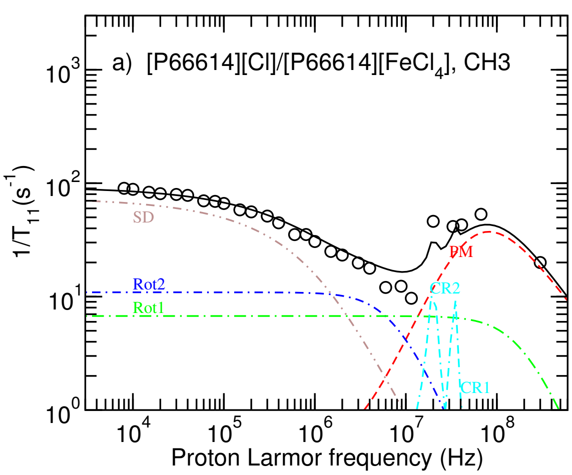
The Art of Model Fitting to Experimental Results[1]

Subject	Plots-Paper-P66614, CH3_final
Date	Wednesday 5th November, 2014, 18:11
Affiliation	carla.daniel@dq.fct.unl.pt 194.210.232.202
Abstract	Fit report produced with the fit results of function: y=((T<2) ? iT1ISpara(f, 300.0, taud1/(1 + pow(2*pi*f*tauv, p)), taus, M, r, S) : 1e-9) + BPP(f, Arot, tau) + BPP(f, Arot1, tau1) + (T<2) ? CROSSRELAX(f, adip, tdip, fdip) : 1e-10 + (T<2) ? CROSSRELAX(f, adip1, tdip1, fdip1) : 1e-10 + (T<2) ? Torrey1(f, d, r*1e10, n, taud/(6.0*(1 + pow(2*pi*f*tauv, p)))) : Torrey1(f, d, r*1e10, n, tauD) to the 55 experimental points, considering 10 free parameters.

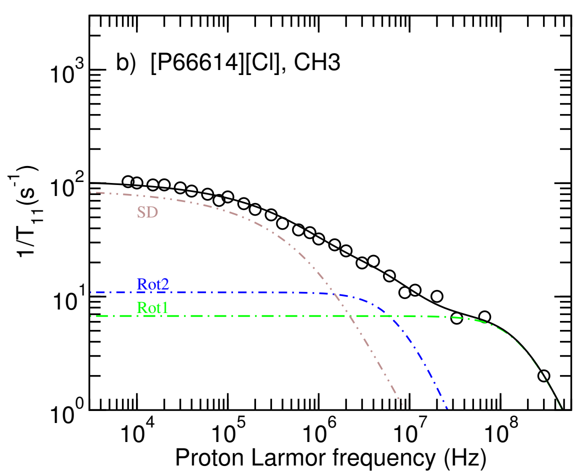
$taud1 = 6.3465 \times 10^{-09} \pm 5.9527 \times 10^{-10}$	$n = 7 \times 10^{+22}$ (fixed)
$taus = 1 \times 10^{-11} \pm 6.431 \times 10^{-13}$	$tauD = 1.4574 \times 10^{-08} \pm 6.9147 \times 10^{-10}$
$taud = 7.3387 \times 10^{-08} \pm 3.4833 \times 10^{-09}$	$adip = 2.5352 \times 10^{+07} \pm 1.108 \times 10^{+07}$
$Arot = 1.85 \times 10^{+08}$ (fixed)	$tdip = 5 \times 10^{-07} \pm 3.2912 \times 10^{-07}$
$tau = 1.18 \times 10^{-08}$ (fixed)	$fdip = 3.4 \times 10^{+07}$ (fixed)
$Arot1 = 2.81 \times 10^{+09}$ (fixed)	$tauv = 3.85 \times 10^{-10}$ (fixed)
$tau1 = 4.8 \times 10^{-10}$ (fixed)	$p = 1.1303$ (fixed)
$M = 0.014$ (fixed)	$adip1 = 2.518 \times 10^{+07} \pm 9.2404 \times 10^{+06}$
$r = 2.5314 \times 10^{-10} \pm 1.3679 \times 10^{-12}$	$tdip1 = 5 \times 10^{-07}$ (fixed)
$S = 400$ (fixed)	$fdip1 = 2 \times 10^{+07} \pm 3.1437 \times 10^{+05}$
$d = 8 \pm 0.017602$	

$\chi^2[2] = 13.727 \qquad \chi^2[1] = 132.281$

$\chi^2_t = 146.008$



recta-1.pdf



recta-2.pdf

[1]"The Art of Model Fitting to Experimental Results", P.J. Sebastião, *Eur. J. Phys.* **35** (2014) 015017

fitteia Report

(internet based fitter service)

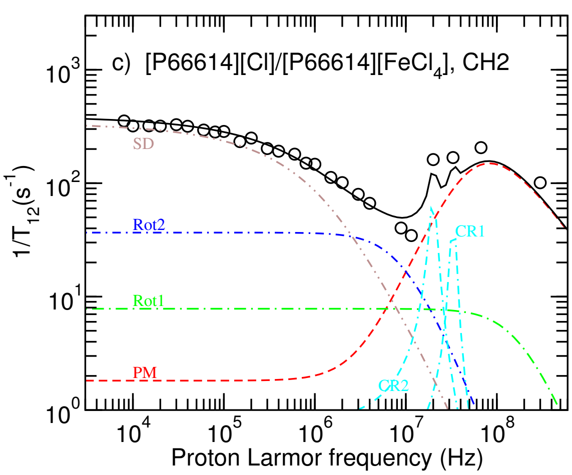
The Art of Model Fitting to Experimental Results[1]

Subject	Plots-Paper-P66614, CH2_final
Date	Wednesday 5th November, 2014, 18:12
Affiliation	carla.daniel@dq.fct.unl.pt 194.210.232.202
Abstract	Fit report produced with the fit results of function: y=((T<2) ? iT1ISpara(f, 300.0, taud1/(1 + pow(2*pi*f*tauv, p)), taus, M, r, S) : 1e-9) + BPP(f, Arot, tau) + BPP(f, Arot1, tau1) + (T<2) ? CROSSRELAX(f, adip, tdip, fdip) : 1e-10 + (T<2) ? CROSSRELAX(f, adip1, tdip1, fdip1) : 1e-10 + (T<2) ? Torrey1(f, d, r*1e10, n, taud/(6.0*(1 + pow(2*pi*f*tauv, p)))) : Torrey1(f, d, r*1e10, n, tauD) to the 53 experimental points, considering 10 free parameters.

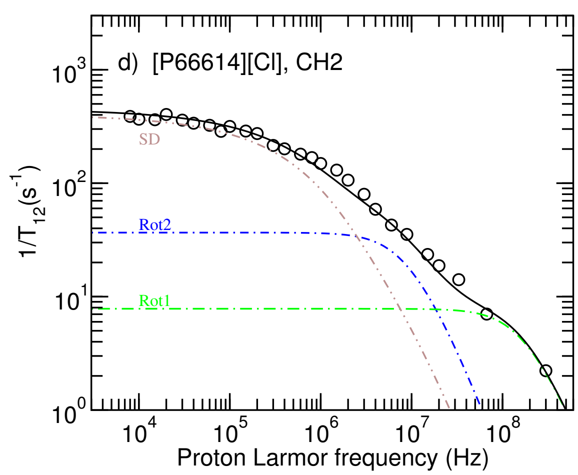
$taud1 = 6.0183 \times 10^{-09} \pm 7.3524 \times 10^{-10}$
$taus = 1 \times 10^{-11} \pm 1.7137 \times 10^{-12}$
$taud = 7.34 \times 10^{-08}$ (fixed)
$Arot = 7.33 \times 10^{+08}$ (fixed)
$tau = 1.0009 \times 10^{-08}$ (fixed)
$Arot1 = 3.03 \times 10^{+09}$ (fixed)
$tau1 = 5.16 \times 10^{-10}$ (fixed)
$M = 0.014$ (fixed)
$r = 1.5859 \times 10^{-10} \pm 2.6898 \times 10^{-12}$
$S = 400$ (fixed)
$d = 4.5148 \pm 0.068607$

$n = 7 \times 10^{+22}$ (fixed)
$tauD = 1.46 \times 10^{-08}$ (fixed)
$adip = 1.2856 \times 10^{+08} \pm 4.3852 \times 10^{+07}$
$tdip = 5 \times 10^{-07} \pm 3.2303 \times 10^{-07}$
$fdip = 3.3206 \times 10^{+07} \pm 1.6025 \times 10^{+06}$
$tauv = 3.85 \times 10^{-10}$ (fixed)
$p = 1.1303$ (fixed)
$adip1 = 1.479 \times 10^{+08} \pm 3.2848 \times 10^{+07}$
$tdip1 = 5 \times 10^{-07} \pm 1.9932 \times 10^{-08}$
$fdip1 = 2 \times 10^{+07} \pm 3.356 \times 10^{+05}$

$\chi^2[2] = 28.6349$ $\chi^2[1] = 69.7377$
$\chi^2_t = 98.3727$



recta-1.pdf



recta-2.pdf

[1]"The Art of Model Fitting to Experimental Results", P.J. Sebastião, *Eur. J. Phys.* **35** (2014) 015017

fitteia Report

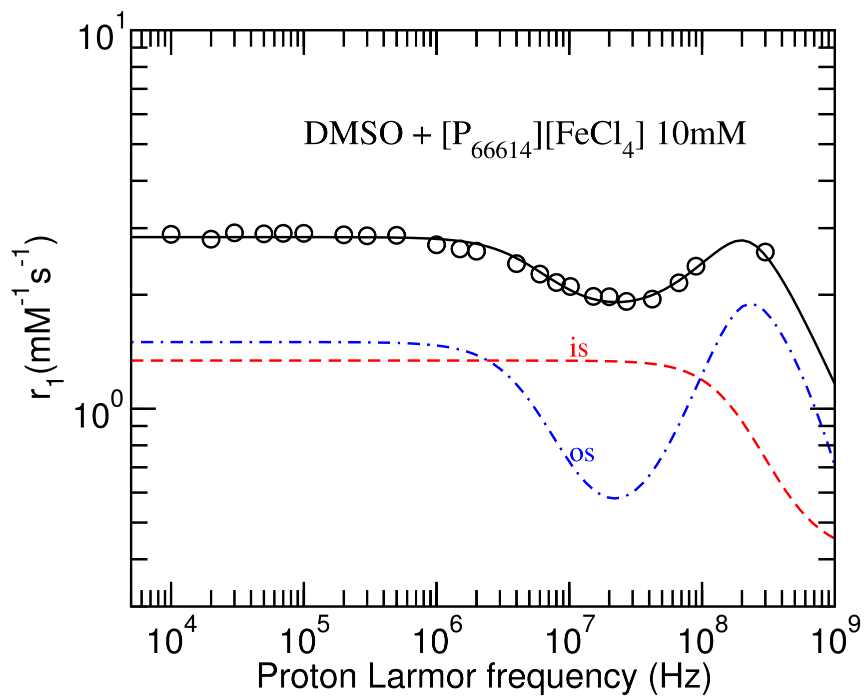
(internet based fitter service)

The Art of Model Fitting to Experimental Results[1]

Subject	P66614-FeCl4-DMSO, Fit-10mM-r1-final
Date	Friday 24th July, 2015, 15:02
Affiliation	carla.daniel@dq.fct.unl.pt 84.90.100.162
Abstract	Fit report produced with the fit results of function: y=x/14040*iT1innerSmallS(f, 295.0, tmg, tmH, tv, ZFS, r, S0*n, S) + iT1outerSmallS(f, 295.0, D, tv, ZFS, R, S0*n) to the 23 experimental points, considering 5 free parameters.

$tmg = 1$ (fixed)	$D = 7 \times 10^{-10}$ (fixed)
$tmH = 1.1197 \times 10^{-12} \pm 6.5915 \times 10^{-14}$	$tv = 2.5882 \times 10^{-12} \pm 2.5312 \times 10^{-13}$
$r = 3.5 \times 10^{-10} \pm 2.2172 \times 10^{-11}$	$ZFS = 2.8787 \times 10^{+10} \pm 2.1614 \times 10^{+09}$
$S0 = 3$ (fixed)	$R = 7.9588 \times 10^{-10} \pm 2.9725 \times 10^{-11}$
$n = 1.0001$ (fixed)	$x = 8$ (fixed)
$S = 0$ (fixed)	

$\chi^2[1] = 5.28254 \qquad \chi^2_t = 5.28254$



recta-1.pdf

[1]"The Art of Model Fitting to Experimental Results", P.J. Sebastião, *Eur. J. Phys.* **35** (2014) 015017

fitteia Report

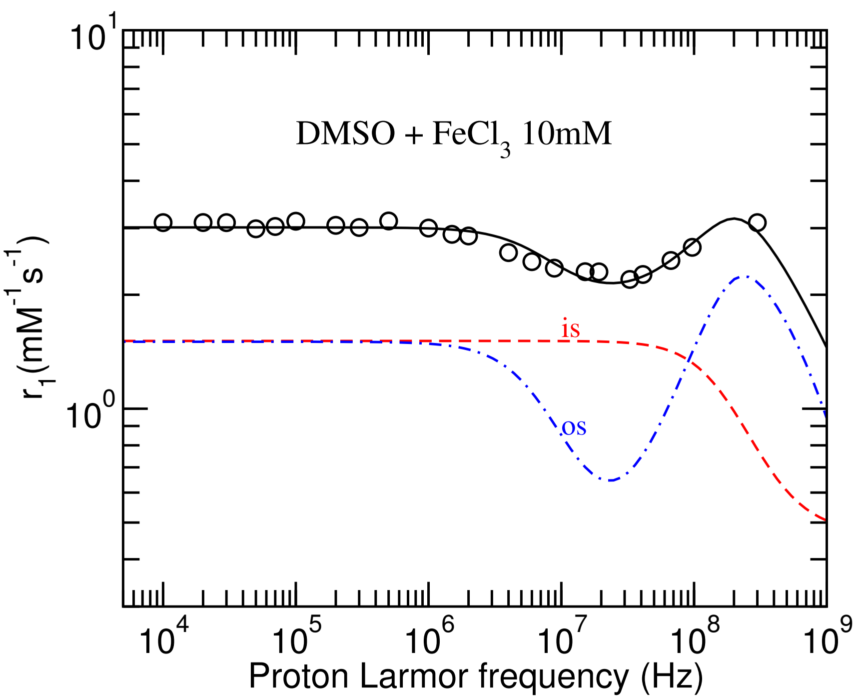
(internet based fitter service)

The Art of Model Fitting to Experimental Results[1]

Subject	FeCl3-DMSO, Fit-10mM-r1-final
Date	Friday 24th July, 2015, 15:03
Affiliation	carla.daniel@dq.fct.unl.pt 84.90.100.162
Abstract	Fit report produced with the fit results of function: y=x/14040*iT1innerSmallS(f, 295.0, tmg, tmH, tv, ZFS, r, S0*n, S) + iT1outerSmallS(f, 295.0, D, tv, ZFS, R, S0*n) to the 23 experimental points, considering 6 free parameters.

$tmg = 1$ (fixed)	$D = 7 \times 10^{-10}$ (fixed)
$tmH = 1.2759 \times 10^{-12} \pm 8.5858 \times 10^{-14}$	$tv = 3.0213 \times 10^{-12} \pm 2.6997 \times 10^{-13}$
$r = 3.5 \times 10^{-10} \pm 1.3408 \times 10^{-11}$	$ZFS = 3.0863 \times 10^{+10} \pm 2.5376 \times 10^{+09}$
$S0 = 3$ (fixed)	$R = 7.2522 \times 10^{-10} \pm 3.0103 \times 10^{-11}$
$n = 1.0001$ (fixed)	$x = 8 \pm 4.347$
$S = 0$ (fixed)	

$\chi^2[1] = 11.9318 \qquad \chi_t^2 = 11.9318$



recta-1.pdf

[1]"The Art of Model Fitting to Experimental Results", P.J. Sebastião, *Eur. J. Phys.* **35** (2014) 015017