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Stochastic Liouville equation treatment of the electron paramagnetic resonance line shape of an S-state ion in solution

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Abstract

The current approaches used for the analysis of electron paramagnetic resonance (EPR) spectra of Gd^{3+} complexes suffer from a number of drawbacks. Even the elaborate model of Rast et al., where the electron spin relaxation is explained by the modulation of the zero field splitting (ZFS), by molecular tumbling (the so called *static* contribution) and deformations (*transient* contribution) is only readily applicable within the validity range of the Redfield theory, that is, when the ZFS is small compared to the Zeeman energy and the rotational and vibrational modulations are fast compared to the relaxation time. Spin labels (nitroxides, transition metal complexes) have been studied for years in systems that violate these conditions. The theoretical framework commonly used in such studies is the stochastic Liouville equation (SLE). We shall show how the physical model of Rast can be cast into the SLE formalism, paying special attention to the specific problems introduced by the Ornstein-Uhlenbeck process used to model the transient ZFS. The resulting equations are very general and valid for arbitrary correlation times, magnetic field strength, electron spin S or symmetry. We demonstrate the equivalence of the SLE approach with the Redfield approximation for two well-known Gd^{3+} complexes.

1. Introduction

Paramagnetic Gd^{3+} complexes are widely used as contrast agents in medical magnetic resonance imaging (MRI) because of the enhancement of the relaxation rate of the neighboring protons that they induce.¹ This enhancement, called *relaxivity*, is a consequence of the dipolar coupling between the proton nuclear spin and the electronic spin of the metal ion. Among other factors, relaxivity is determined by (1) the rotational correlation time of the complex τ_R , (2) the water residence time τ_m in the first coordination shell, and (3) the electronic spin relaxation, often described by the longitudinal and transverse relaxation times T_{1e} and T_{2e} . While the molecular factors influencing (1) and (2) are rather

well understood, the electronic spin relaxation of Gd^{3+} complexes relevant for MRI remains the subject of much discussion.^{2,3} The influence of the electronic spin relaxation on the relaxivity is essentially governed by the decay of the electronic spin magnetization in the direction parallel to the external field. This decay is described by the longitudinal electronic relaxation time T_{1e} . For Gd^{3+} complexes, it is generally too short to be measurable by commonly available techniques. Only recently direct measurement by Longitudinally Detected EPR (LODEPR) has been achieved on aqueous solutions of these complexes.⁴ Nevertheless, standard electron paramagnetic resonance allows the investigation of the decay of the electronic spin magnetization perpendicular to the external field, usually characterized by a transverse electronic relaxation time T_{2e} . The analysis of the transverse relaxation data allows the subsequent estimation of T_{1e} within the framework of a given model of the electronic relaxation. For a reasonable prediction of T_{1e} , one needs a model that correctly describes the underlying physics. Extensive experimental data are also required to determine accurately the underlying parameters. Consequently, the last few years have witnessed a considerable interest for new studies, both experimental and theoretical, on this particular subject.

The $^8S_{7/2}$ ion Gd^{3+} is well known to undergo zero-field splitting in the solid state.⁵ Proposed thirty years ago by Hudson and Lewis,⁶ the basic theory of the EPR line shape of Gd^{3+} complexes in solution uses a transient zero-field splitting (modulated by rotation or molecular distortions) as the main relaxation mechanism. This basic assumption leads to the calculation of a 7x7 (transverse) or 8x8 (longitudinal) relaxation matrix following Redfield.⁷ More recently, Rast et al.⁸⁻¹⁰ developed a refined model of the electronic relaxation of the S states of metal ion complexes in solutions. This refined treatment now includes the contribution of the static crystal field surrounding the Gd^{3+} ion as it is modulated by the rotation of the whole complex. It has also a part due to the usual transient crystal zero-field splitting (ZFS) caused by vibration, intramolecular rearrangement, and collision with surrounding solvent

molecules, described by an Ornstein-Uhlenbeck process.^{11,12} A good agreement with the measured peak-to-peak distances was obtained for $[\text{Gd}(\text{H}_2\text{O})_8]^{3+}$, $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$, and $[\text{Gd}(\text{DTPA-BMA})(\text{H}_2\text{O})]$ complexes in a new analysis of the experimental data measured by Powell.^{2,8,9} The final refinement of this theory, with a rigorous calculation of the EPR line shape, including dynamic frequency shifts and instrumental factors such as spectrum phasing, was successfully applied to the analysis of multiple frequency and temperature spectra of $[\text{Gd}(\text{H}_2\text{O})_8]^{3+}$ and $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^-$.¹⁰ Furthermore it was found that the combination of the static and transient crystal field effects was able to correctly predict the longitudinal relaxation times observed using the new LODEPR method.¹³ Independantly, Westlund and coworkers also recognized the necessity for two ZFS contributions but assumed a pseudo-rotational dynamic model for the transient part.¹⁴

However, these new models, as well as most of the previous approaches of this problem, were developed in the framework of the Redfield relaxation theory^{7,15} describing the time dependence of the correlation functions of the spin system components. This theory has essentially two limitations. Denoting by ω_0 the unperturbed Zeeman angular frequency and by H_I the time dependent perturbing Hamiltonian inducing electronic transitions between the Zeeman levels, one must have $|H_I|\tau_c \ll 1$ and $|H_I|^2\tau_c \ll \omega_0$, where τ_c is the correlation time of the fluctuating term H_I . The first condition can be violated when we consider large complexes. When the relevant time τ_c is the rotational correlation time of the complex, its inverse (i.e. the rotational diffusion constant D_R) can reach values of the same order as H_I , especially in the low temperature region where D_R decreases. The second condition corresponds to the secular approximation¹⁵ and may be violated when experiments are performed at low fields, mainly for large complexes and at temperatures just above 0 °C.

To overcome these problems, a new approach using Monte-Carlo (MC) simulations of the electronic relaxation processes was presented by Rast et al.¹⁶ A MC procedure for the reorientation of the Gd^{3+}

complexes, combined with an Ornstein-Uhlenbeck process^{11,12} was used to model the transient zero-field splitting, was applied to the electronic relaxation theory beyond the Redfield limit where there is no analytical solution. The slow molecular tumbling at low temperature was found to be of no consequence for the relatively small complexes studied ($[\text{Gd}(\text{H}_2\text{O})_8]^{3+}$ and $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^{2-}$) in the range of conventional EPR (0.34 T and above), but the extrapolation of the Redfield theory down to low fields (0.1 T and below) led to significant discrepancies. This was an important finding since such low magnetic fields are routinely used in NMRD experiments on Gd^{3+} complexes.

The Monte-Carlo approach offers a convenient way to test the Redfield theory near the limit of its validity region by a direct calculation of the transverse and longitudinal correlation functions. However, it currently leads to very long calculations when the two correlation times (one for rotation and one for the molecular deformations) differ by several orders of magnitude. In particular, the interesting case of slowly tumbling macromolecules, where an increased relaxivity is obtained thanks to the long rotation correlation time τ_R ,¹⁷ is difficult to treat in this fashion. They require the simulation of time ranges long enough to account for Brownian rotation (> 1 ns in this case) with a shorter resolution than the typical correlation time for the vibrations (< 1 ps). Furthermore, although the method can be used to simulate spectra in the frequency domain by a simple Fourier transform of the calculated transverse correlation function, it is less suitable for the simulation of continuous wave EPR spectra in the field domain. It is therefore worthwhile to consider alternative theoretical approaches that could bring more efficient tools for the understanding of such systems.

One such approach is the stochastic Liouville equation (SLE).^{18,19} It is widely used in the analysis of EPR spectra of $S = 1/2$ molecules such as nitroxides and vanadyl chelates.²⁰ Kowalewski, Bertini and coworkers also demonstrated its usefulness in the study of nuclear magnetic relaxation of paramagnetic systems,²¹ including systems with more than one unpaired electron. Recently, Zhou and Westlund

applied this approach to the simulation of Gd^{3+} EPR spectra in solution using their pseudo-rotational transient ZFS model.²² In this paper, we show how Rast's model can be treated using the SLE formalism. We first apply the method to the simpler case of a rigid chelate, following the original development of Freed¹⁹ where the SLE solution is approximated by a combination of eigenfunctions of the stochastic operator responsible for relaxation, namely the rotational diffusion operator. The combination of rotation and deformations in the form of the Ornstein-Uhlenbeck process instead of pseudo-rotational diffusion adds a new level of complexity, since the well-known Wigner matrices are no longer sufficient to solve the problem. Numerical methods where an approximate solution is obtained by discretization of the stochastic parameter offer very general approaches to solving the SLE. However, they are often computationally expensive, especially if a high-resolution point grid is used to describe the discrete stochastic parameter. Zientara et al.²³ used an interesting alternative to the conceptually simple but fairly expensive finite-difference (FD) method²⁴ in their study of chemically induced dynamic electron and nuclear polarization (CIDEP/CIDNP).²⁵ The stochastic Liouville equation was solved by the variational Galerkin-finite elements (GFE) method (see for example Chung²⁶). The simple example of an axially symmetric g -tensor was presented²⁷ and the resulting calculations showed faster convergence for the GFE method than for the FD. Nevertheless, the finite elements method still requires solving very large linear equations system, so it is always useful to search for a more appropriate approach to the problem. In this paper, we show that the ZFS modulation by an Ornstein-Uhlenbeck process is readily treated using an expansion on a basis set of Hermite polynomials. The transient ZFS Hamiltonian takes a quite simple form, leading to a manageable system of equations for the SLE.

II. Theoretical section

II.1. Eigenfunctions expansion for a rigid ZFS with Brownian rotation

First we treat the case of a rigid S -state complex, where rotation is the only active modulation process.

Let λ be a line in the spectrum with D degenerate transitions contributing to the line. The absorbed power at frequency ω by molecules with orientation Ω is given by

$$p_\lambda(\Omega) = \Pi \hbar \omega \sum_{j=1}^D \gamma_e B_1 \langle \alpha_j | S_- | \beta_j \rangle Z_{\lambda_j}^{(1)\prime\prime}(\Omega) \quad (1)$$

with

$$Z_{\lambda_j}^{(n)} = Z_{\lambda_j}^{(n)\prime} + i Z_{\lambda_j}^{(n)\prime\prime} \quad (2)$$

$$\chi_{\lambda_j} = \langle \alpha_j | \rho | \beta_j \rangle - \langle \alpha_j | \rho_0 | \beta_j \rangle = \sum_{n=-\infty}^{+\infty} e^{in\omega t} Z_{\lambda_j}^{(n)} \quad (3)$$

where α and β are the spin states connected by transition λ_j .

In the high temperature approximation, the equilibrium density matrix may be written as:

$$\rho_0(\Omega) = \frac{\exp\left(\frac{-H(\Omega)}{k_B T}\right)}{\text{Tr}\left\{\exp\left(\frac{-H(\Omega)}{k_B T}\right)\right\}} \cong P_0(\Omega) \left\{ I - \frac{H(\Omega)}{k_B T} + \dots \right\} \quad (4)$$

P_0 is the probability density for the orientation, equal to $1/4\pi$ in an isotropic medium. Averaging over Ω

and assuming an orientation-independent transition probability, we obtain

$$\bar{Z}_{\lambda_j}^{(n)} = \int Z_{\lambda_j}^{(n)}(\Omega) P_0(\Omega) d\Omega \quad (5)$$

$$p_\lambda = \Pi \hbar \omega \sum_{j=1}^D \gamma_e B_1 \langle \alpha_j | S_- | \beta_j \rangle \bar{Z}_{\lambda_j}^{(1)\prime\prime} \quad (6)$$

We define the following time-dependent Hamiltonian

$$\hat{H} = \hat{H}_0 + \hat{H}_1(\Omega) + \hat{\varepsilon}(t) \quad (7)$$

$$\hat{H}_0 = \frac{\gamma_e B_0}{\hbar} \hat{S}_z$$

$$\hat{H}_1(\Omega) = \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \hat{T}_p^k D_{pq}^k(\Omega) \quad (8)$$

$$\hat{\varepsilon}(t) = \frac{1}{2} \gamma_e B_1 (\hat{S}_+ e^{-i\omega t} + \hat{S}_- e^{i\omega t}) \quad (9)$$

The summation over k is required depending on the maximum angular moment in the system: 2 for $S = 3/2$, 4 for $S = 5/2$, 6 for $S = 7/2$...

The density matrix evolution is governed by the stochastic Liouville equation of motion

$$\frac{\partial \hat{\rho}(\Omega, t)}{\partial t} = -i[\hat{H}(\Omega), \hat{\rho}(\Omega, t)] - \Gamma_\Omega \hat{\rho}(\Omega, t) \quad (10)$$

where Γ is a Markovian operator, in our case the rotational diffusion operator.

The equilibrium density matrix ρ_0 is time-independent, so its time derivative is zero. Looking at the Fourier transform of the matrix elements for our transition λ_j in the basis that diagonalizes \hat{H}_0 , and assuming that $\hat{\varepsilon} \ll \hat{H}_0, \hat{H}_1$, so that the equilibrium density matrix (eq. (4)) commutes with $\hat{H}_0 + \hat{H}_1$, one obtains the following steady-state equation for the Z matrix elements.²⁸

$$\begin{aligned} & (\omega - \omega_\lambda) Z_{ij}^{(1)} + \\ & \langle \alpha_j | [\hat{H}_1(\Omega), \hat{Z}^{(1)}(\Omega)] | \beta_j \rangle - \\ & i \langle \alpha_j | [\Gamma_\Omega \hat{Z}^{(1)}(\Omega)] | \beta_j \rangle + \\ & \frac{1}{2} \gamma_e B_1 \langle \alpha_j | \hat{S}_- | \beta_j \rangle (\chi_{\lambda_{j,+}}^{(0)} - \chi_{\lambda_{j,-}}^{(0)}) = \\ & - \langle \alpha_j | [\hat{S}_+, \hat{\rho}_0(\Omega)] | \beta_j \rangle = \\ & P(\Omega) \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\ & P(\Omega) \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \langle \alpha_j | [\hat{S}_+, \hat{H}_1(\Omega)] | \beta_j \rangle \end{aligned} \quad (11)$$

from which the equation for \bar{Z} becomes:

$$\begin{aligned}
& (\omega - \omega_\lambda) \bar{Z}_{\hat{j}}^{(1)} + \\
& \int P_0(\Omega) \langle \alpha_j | [\hat{H}_1(\Omega), \hat{Z}^{(1)}(\Omega)] | \beta_j \rangle d\Omega + \\
& \int P_0(\Omega) \langle \alpha_j | [\hat{\epsilon}, \hat{\rho}_0(\Omega)] | \beta_j \rangle d\Omega - \\
& i \int P_0(\Omega) \langle \alpha_j | \Gamma_\Omega \hat{Z}^{(1)}(\Omega) | \beta_j \rangle d\Omega + \\
& \frac{1}{2} \gamma_e B_1 \langle \alpha_j | \hat{S}_- | \beta_j \rangle (\bar{\chi}_{\lambda j,+}^{(0)} - \bar{\chi}_{\lambda j,-}^{(0)}) = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \int P(\Omega) \langle \alpha_j | [\hat{S}_+, \hat{H}_1(\Omega)] | \beta_j \rangle d\Omega
\end{aligned} \tag{12}$$

We can expand the matrix elements of Z in a complete set of orthogonal eigenfunctions G_m with eigenvalues E_m of the stochastic operator Γ . In the isotropic rotational diffusion case these become the Wigner matrices $D_{qq'}^k$ with eigenvalues $E(k, q, q') = D_R k(k+1)$. We see that any given m is actually a combination of (k, q, q') with $|q|, |q'| \leq k$. Axial anisotropic diffusion can also be treated using the following expression:

$$\Gamma_\Omega D_{qq'}^k = \{D_{R\perp} k(k+1) + (D_{R\parallel} - D_{R\perp})(q')^2\} \tag{13}$$

We can thus rewrite the matrix elements of $Z(\Omega)$ as follows:

$$Z_{\hat{j}}^{(n)}(\Omega) = \sum_m \langle \alpha_j | \hat{C}_m^{(n)}(\omega) | \beta_j \rangle G_m(\Omega) \tag{14}$$

Calculating the matrix elements of the frequency-dependent but orientation-independent operators in spin space \hat{C} is the key to solving the SLE. By applying Freed's development¹⁹ to our time-dependent Hamiltonian (8), we obtain the following final equation for the matrix elements of \hat{C} (see Appendix I for more details):

$$\begin{aligned}
& \frac{8\pi^2}{2L+1}(\omega - \omega_\lambda - iE_{m'}) \langle \alpha_j | \hat{C}_{L,R,R'}^{(n)}(\omega) | \beta_j \rangle + \\
& \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sum_{K=0}^{\infty} \sum_{Q,Q'=-K}^{+K} 8\pi^2 \langle \alpha_j | [\hat{T}_p^k, \hat{C}_{K,Q,Q'}^{(1)}] | \beta_j \rangle (-1)^{R-R'} \begin{pmatrix} L & K & k \\ -R & Q & p \end{pmatrix} \begin{pmatrix} L & K & k \\ -R' & Q & q \end{pmatrix} - \\
& \frac{N_{m'}}{2} \gamma_e B_1 \langle \alpha_j | \hat{S}_- | \beta_j \rangle (\hat{C}_{m'\lambda_{j,+}}^{(1)} - \hat{C}_{m'\lambda_{j,-}}^{(1)}) = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \delta_{0,m'} \frac{N_{m'}}{2} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{\pi}{2k+1} \gamma_e B_1 \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sqrt{(k-p)(k+p+1)} \langle \alpha_j | \hat{T}_{p+1}^k | \beta_j \rangle \delta_{m'(k,p,q)}
\end{aligned} \tag{15}$$

Eq. (15) defines an infinite set of linear equations for each matrix element of the \hat{C} operators. Solving this system for a finite basis defined by a maximum angular momentum L_{cut} , we can obtain numerical approximations of the relevant matrix elements $\langle \alpha_j | \hat{C}_m^{(n)}(\omega) | \beta_j \rangle$. This leads to the calculation of the absorption line shape through equation (6). The order of the required matrix is then $(2S+1)^2 \times M$, where M is the number of operators in the finite basis set.

II.2. ZFS with Brownian rotation and Gaussian deformations

The development presented above is only possible when the eigenfunctions G_m of the Markovian operator Γ have the convenient properties of orthogonality and ‘‘triple-integrability’’ (see eq. (31)). In the electron spin relaxation model of Rast et al.,^{8-10,16} two simultaneous Markov processes are considered. The first is Brownian rotation, which we treated above. The second is the modulation of the ZFS around its average value. An Ornstein-Uhlenbeck process, with a Gaussian probability distribution, describes this modulation. It is helpful to see this process as a dynamical equivalent to the phenomenon of *strain*,²⁹ often used in the analysis of disordered solid-state EPR spectra to describe a distribution of the spin Hamiltonian parameters, for example due to differences in the hydrogen bonding pattern around the spins. The concept is more often applied to the g -factor³⁰ (g -strain) and hyperfine coupling³¹ (A -strain), but several studies used it for ZFS as well³² (D , E -strain).

In order to solve the SLE, we must then find a convenient set of eigenfunctions based on the properties of both Markovian operators. This is achieved through the use of the eigenfunctions $Q_n(x)$ and eigenvalues E_n of the O-U operator, namely the Hermite polynomials of a stochastic variable x (see Appendix II):³³

$$Q_n = \frac{1}{\sqrt{2^n n!}} H_n \left(x \sqrt{\frac{1}{2\Delta^2}} \right) \quad (16)$$

$$\lambda_n = n\gamma$$

We must then consider the dependance of the spin Hamiltonian H_1 on the stochastic variable x . The full (i.e. static + transient) ZFS Hamiltonian can be written in the laboratory frame as follows:⁸⁻¹⁰

$$\hat{H}_1(\Omega, x) = \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \hat{T}_p^k D_{pq}^k(\Omega) + \sum_{\eta} B^{2\eta T}(x) \sum_{p,q=-2}^{+2} b_q^{2\eta T} \hat{T}_p^2 D_{pq}^2(\Omega) \quad (17)$$

The spin Hamiltonian is divided into two contributions, the so-called static part (the average ZFS acting on the electron spins, described by the constant magnitude coefficients $B^{k\eta}$ and modulated by molecular tumbling) and the transient part (described by the variable magnitude coefficients $B^{2\eta T}$).

The correlation function of the stochastic variable in a Gaussian Markovian process (such as the Ornstein-Uhlenbeck process) is given by $\langle x(0)x(t) \rangle = \Delta^2 \exp\{-\gamma|t|\}$,³⁴ which we can compare with the proposed correlation function for the transient ZFS magnitude parameters

$\overline{B^{2\eta T}(t)B^{2\eta T}(t-\tau)} = (B^{2\eta T}(0))^2 e^{-|\tau|/\tau_v}$.^{9,16} At this point, we easily identify $\gamma = 1/\tau_v$. As discussed earlier, the correlation functions of the magnitude parameters are similar to that of x . This means that for each parameter, we must have $B^{2\eta T}(t) = 2^{1/2}x(t)B_{\eta T}$ so that $(B^{2\eta T}(0))^2 = (B_{\eta T})^2$ with our previous choice of $\Delta^2 = 1/2$. We rewrite eq. (41) as:

$$\begin{aligned}
& N_{m'} \sqrt{\pi} (\omega - \omega_\lambda - iE_{m'} - iE_{n'}) \langle \alpha_j | \hat{C}_{m',n'}^{(1)}(\omega) | \beta_j \rangle + \\
& \sum_n \sum_m \int \int_{x \Omega} G_m^*(\Omega) Q_n(x) e^{-x^2} G_m(\Omega) Q_n(x) \langle \alpha_j | [\hat{H}_1(\Omega, x), \hat{C}_{mm}^{(1)}(\omega, x)] | \beta_j \rangle d\Omega dx = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \delta_{0,m'} \frac{N_{m'}}{2} \delta_{0,n'} \sqrt{\pi} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \int \int_{x \Omega} G_m^*(\Omega) Q_n(x) P_0(\Omega) P_0(x) \langle \alpha_j | [\hat{S}_+, \hat{H}_1(\Omega)] | \beta_j \rangle d\Omega dx = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \delta_{0,m'} \frac{N_{m'}}{2} \frac{1}{\sqrt{2}} \delta_{0,n'} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \frac{2\pi}{2k+1} \gamma_e B_1 \sum_{k=2,4,6}^{2k+1} \sum_{\eta=1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sqrt{(k-p)(k+p+1)} \langle \alpha_j | \hat{T}_{p+1}^k | \beta_j \rangle \delta_{m',(k,p,q)} \int Q_n(x) P_0(x) e^{-x^2} dx + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \frac{2\pi}{5} \gamma_e B_1 \sum_{\eta=1}^5 \sqrt{2} B_{\eta T} \sum_{p,q=-2}^{+2} b_q^{2\eta} \sqrt{(2-p)(2+p+1)} \langle \alpha_j | \hat{T}_{p+1}^2 | \beta_j \rangle \delta_{m',(2,p,q)} \int x Q_n(x) P_0(x) e^{-x^2} dx
\end{aligned} \tag{18}$$

The transient ZFS contribution is then linear in the stochastic variable x , proportional to the 1st degree

Hermite polynomial $H_1(x) = 2x$ associated with the Ornstein-Uhlenbeck eigenvalue $E_1 = 1 \times \gamma = 1/\tau_v$.

$$\begin{aligned}
& N_{m'} \sqrt{\pi} (\omega - \omega_\lambda - iE_{m'} - iE_{n'}) \langle \alpha_j | \hat{C}_{m',n'}^{(1)}(\omega) | \beta_j \rangle + \\
& \sum_n \sum_m \int \int_{x \Omega} G_m^*(\Omega) Q_n(x) G_m(\Omega) Q_n(x) \langle \alpha_j | [\hat{H}_1(\Omega, x), \hat{C}_{mm}^{(1)}(\omega)] | \beta_j \rangle d\Omega dx = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{N_{m'}}{2} \frac{1}{\sqrt{2}} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle \delta_{0,m'} \delta_{n',0} + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{\pi}{2k+1} \frac{1}{\sqrt{2}} \gamma_e B_1 \sum_{k=2,4,6}^{2k+1} \sum_{\eta=1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sqrt{(k-p)(k+p+1)} \langle \alpha_j | \hat{T}_{p+1}^k | \beta_j \rangle \delta_{m',(k,p,q)} \delta_{n',0} + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{\pi}{5} \gamma_e B_1 \sum_{\eta=1}^5 \sqrt{2} B_{\eta T} \sum_{p,q=-2}^{+2} b_q^{2\eta} \sqrt{(2-p)(2+p+1)} \langle \alpha_j | \hat{T}_{p+1}^2 | \beta_j \rangle \delta_{m',(2,p,q)} \int x Q_n(x) P_0(x) e^{-x^2} dx
\end{aligned} \tag{19}$$

$$\begin{aligned}
& N_{m'} \sqrt{\pi} (\omega - \omega_\lambda - iE_{m'} - iE_{n'}) \langle \alpha_j | \hat{C}_{m',n}^{(1)}(\omega) | \beta_j \rangle + \\
& \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sum_{K=0}^{\infty} \sum_{Q,Q'=-K}^{+K} 8\pi^2 \langle \alpha_j | [\hat{T}_p^k, \hat{C}_{K,Q,Q',n}^{(1)}] | \beta_j \rangle (-1)^{R-R'} \begin{pmatrix} L & K & k \\ -R & Q & p \end{pmatrix} \begin{pmatrix} L & K & k \\ -R' & Q & q \end{pmatrix} \sqrt{\pi} \delta_{n',n} + \\
& \sum_{\eta} \sqrt{2} B_{\eta T} \sum_{p,q=-2}^{+2} b_q^{2\eta T} \sum_{K=0}^{\infty} \sum_{Q,Q'=-K}^{+K} 8\pi^2 \langle \alpha_j | [\hat{T}_p^2, C_{K,Q,Q',n}^{(1)}] | \beta_j \rangle (-1)^{R-R'} \begin{pmatrix} L & K & k \\ -R & Q & p \end{pmatrix} \begin{pmatrix} L & K & k \\ -R' & Q & q \end{pmatrix} \int x Q_n(x) Q_{n'}(x) e^{-x^2} dx = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \delta_{0,m'} \frac{N_{m'}}{2} \delta_{0,n'} \sqrt{\pi} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \frac{2\pi}{2k+1} \sqrt{\pi} \gamma_e B_1 \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sqrt{(k-p)(k+p+1)} \langle \alpha_j | \hat{T}_{p+1}^k | \beta_j \rangle \delta_{m',(k,p,q)} \delta_{n',0} + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \frac{2\pi}{5} \gamma_e B_1 \sum_{\eta=1}^5 \sqrt{2} B_{\eta T} \sum_{p,q=-2}^{+2} b_q^{2\eta} \sqrt{(2-p)(2+p+1)} \langle \alpha_j | \hat{T}_{p+1}^2 | \beta_j \rangle \delta_{m',(2,p,q)} \int x Q_n(x) P_0(x) e^{-x^2} dx
\end{aligned} \tag{20}$$

In order to evaluate the remaining integrals, we use the Hermite polynomials recurrence property:³⁵

$$H_{n+1}(x) = 2xH_n(x) - 2nH_{n-1}(x) \tag{21}$$

so that:

$$\int x H_{n'}(x) H_n(x) e^{-x^2} dx = 2^n (n+1)! \sqrt{\pi} \delta_{n',n+1} + 2^{n-1} n! \sqrt{\pi} \delta_{n',n-1} \tag{22}$$

Furthermore, due to eq. (38), we can write:

$$\begin{aligned}
\int x Q_n(x) P_0(x) e^{-x^2} dx &= \frac{1}{\sqrt{\pi}} \int x Q_n(x) e^{-2x^2} dx = \\
\frac{1}{\sqrt{\pi}} \frac{1}{2} \int H_1(x) H_n(x) e^{-2x^2} dx &= \frac{1}{\sqrt{\pi}} \frac{1}{2} \frac{2\sqrt{\pi}}{\sqrt{2}} \delta_{n',1} = \frac{\delta_{n',1}}{\sqrt{2}}
\end{aligned} \tag{23}$$

$$\begin{aligned}
& \frac{8\pi^2}{2L+1} \sqrt{\pi} (\omega - \omega_\lambda - iL(L+1)D_R - \frac{in'}{\tau_v}) \langle \alpha_j | \hat{C}_{m',n'}^{(1)}(\omega) | \beta_j \rangle + \\
& \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sum_{K=0}^{\infty} \sum_{Q,Q'=-K}^{+K} 8\pi^2 \langle \alpha_j | [\hat{T}_p^k, \hat{C}_{K,Q,Q',n}^{(1)}] | \beta_j \rangle (-1)^{R-R'} \begin{pmatrix} L & K & k \\ -R & Q & p \end{pmatrix} \begin{pmatrix} L & K & k \\ -R' & Q & q \end{pmatrix} \sqrt{\pi} \delta_{n',n} + \\
& \sum_{\eta} B_{\eta T} \sum_{p,q=-2}^{+2} b_q^{2\eta T} \sum_{K=0}^{\infty} \sum_{Q,Q'=-K}^{+K} 8\pi^2 \langle \alpha_j | [\hat{T}_p^2, \hat{C}_{K,Q,Q',n}^{(1)}] | \beta_j \rangle (-1)^{R-R'} \begin{pmatrix} L & K & k \\ -R & Q & p \end{pmatrix} \begin{pmatrix} L & K & k \\ -R' & Q & q \end{pmatrix} \left\{ \sqrt{(n+1)\pi} \delta_{n',n+1} + \sqrt{\frac{\pi}{n}} \delta_{n',n-1} \right\} = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{8\pi^2}{(2L+1)} \frac{1}{\sqrt{2}} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle \delta_{0,m'} \delta_{0,n'} + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{\pi}{2k+1} \frac{1}{\sqrt{2}} \gamma_e B_1 \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sqrt{(k-p)(k+p+1)} \langle \alpha_j | \hat{T}_{p+1}^k | \beta_j \rangle \delta_{m',(k,p,q)} \delta_{n',0} + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{\pi}{5} \gamma_e B_1 \sum_{\eta=1}^5 B_{\eta T} \sum_{p,q=-2}^{+2} b_q^{2\eta} \sqrt{(2-p)(2+p+1)} \langle \alpha_j | \hat{T}_{p+1}^2 | \beta_j \rangle \delta_{m',(2,p,q)} \delta_{n',1}
\end{aligned} \tag{24}$$

III. Computation details and results

A program implementing the system of equations defined by eq. (24) was developed.³⁶ The program iteratively solves the large (typically 10^4 - 10^5 matrix elements) but relatively sparse system for a series of magnetic field and EPR frequency values. In general, solving such large matrix problems is made feasible by computational methods that do not require the storage (in memory or on disk) of the original matrix or modified copies of it. The same matrix, whose elements are recalculated when needed, is used repeatedly to multiply one or several vectors that eventually converge toward the solution. Since the system of equations is neither real nor symmetric, the usual Lanczos/conjugate gradient method³⁷ are not applicable in our case. Instead, we use the more general but slower biconjugate gradient (BiCG) algorithm.³⁸ Performance is improved by using a good approximation of the solution vector as an initial guess. This is trivially achieved in a spectrum simulation by assuming that each calculated point is a reasonable approximation for the next one, provided of course that the magnetic field or frequency difference between the points is not too large. Unfortunately, since the matrix elements between all possible spin states are involved (not just those linked by a single quantum EPR transition), the transition frequency ω_λ is not unique and it is not possible to take the spectral step variable $\omega - \omega_\lambda$ out of

the equations (as proposed by Freed³⁹). Therefore we cannot transform our problem of multiple linear systems into one single eigenvalue problem followed by several continuous fractions calculations to simulate continuous wave EPR spectra in the field domain. It is necessary to solve one linear system for each spectral point. However, we note that such a transformation would be possible in the frequency domain.

We want to establish the equivalence of the approach presented in the theoretical section with the Redfield approximation derived by Rast. Using the published electron spin parameters (ZFS magnitude coefficients, g -factor) and correlation times (isotropic rotation, transient ZFS modulation) obtained through a Redfield analysis of experimental EPR spectra, we applied the program to simulate the room temperature X-band (9.5 GHz) cw EPR spectra of two well-known complexes in aqueous solution, namely $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$ ⁹ and $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^-$ ¹⁰. Rast et al. did not consider the dynamic frequency shifts in their theoretical linewidth analysis of $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$. This was simply not possible, as they used the original experimental data of Powell,⁴⁰ which do not include the central resonance field of the line. Consequently, the natural g -factor has not been determined within the framework of the Rast model and we simply assumed the same value as for $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^-$. This hypothesis should not have any effect other than a small shift of the spectrum. The higher (4th and 6th) order ZFS terms were found to play little or no role at all for both these chelates, so our Hamiltonian was limited to 2nd order. For the sake of simplicity, we assumed that the reduced ZFS magnitude parameters a_2 and a_{2T} can be used as spin Hamiltonian parameters with an axial symmetry (i.e. $B^2 = a_2$, $B^{2T} = a_{2T}$). This is of course not true for the low-symmetry complex $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$. However, since the Redfield relaxation matrix does not depend on the actual symmetry, except for the existence or not of the ZFS, this approximation should be acceptable as long as the Redfield theory is valid. The line shapes were simulated using a minimal basis set ($L_{\text{cut}} = 2$) and a larger one ($L_{\text{cut}} = 4$). In the absence of

transient ZFS contribution, the Hermite polynomial expansion is of course unnecessary, so we set $n_{\text{cut}} = 0$. The correlation time τ_v is very short (~ 1 ps) compared to $1/\omega_0$ at X-band, so we can take advantage of the argument of Freed et al.⁴¹ regarding the basis set size versus correlation time and \hat{H}_1 magnitude. We assume that a fairly small n_{cut} will be sufficient to account for a non-zero transient ZFS modulation and choose $n_{\text{cut}} = 2$ (i.e. 3 degrees of Hermite polynomials: 0, 1, 2) in that case. Figures 1 and 2 show the SLE-simulated ($L_{\text{cut}} = 2$ and 4) spectra of both compounds when the full (static + transient) ZFS Hamiltonian modulation is accounted for. The effect of the basis set size is not immediately apparent for $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^-$, but the $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$ lineshape clearly changes when L_{cut} is raised from 2 to 4. In all cases, we note that the spectrum is not a perfect Lorentzian derivative as there is some asymmetry between the low field and high field part of the spectrum. This is of course expected, since the Zeeman Hamiltonian changes significantly along the field-swept spectrum. The $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$ spectrum is broader, so the effect is more pronounced than for $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^-$.

In order to get a numerical descriptor of the line shape, we measured the peak to peak widths of the calculated spectra (field difference between the highest and lowest point of the derivative). We compare the predicted peak-to-peak widths under the Redfield theory and the stochastic Liouville equation (both with and without transient ZFS) with the experimental measurements in Table I. Considering that the parameters are obviously biased towards the Redfield theory, there is a fairly good agreement between the SLE predictions and the experimental results. As noted by Freed et al.⁴¹ the size of the required basis set for convergence of the line shape (expressed by the angular momentum cutoff value L_{cut}) appears to increase with the time-dependent Hamiltonian (ZFS in our case) magnitude ($a_2 = 0.35 \times 10^{10} \text{ s}^{-1}$ for $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^-$, $0.92 \times 10^{10} \text{ s}^{-1}$ for $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$). In the static + transient ZFS case, the linewidth change going from $L_{\text{cut}} = 2$ to 4 is just 10% (less than 10 G) for $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^-$, whereas it is about 15% (over 100 G) for $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$. We also checked that increasing L_{cut} above 4

caused no further line width change. With $L_{\text{cut}} = 6$, the $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$ line shape is indistinguishable from the $L_{\text{cut}} = 4$ simulation. The choice of $n_{\text{cut}} = 2$ is *a posteriori* justified by the good agreement of the static + transient ZFS peak-to-peak widths calculated under the Redfield and Liouville theories. Furthermore, this low cutoff value remains sufficient even when the O-U correlation time τ_v is not much shorter than the 2nd order rotational $\tau_2 = 1/(6D_R)$. In a simulation using modified $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$ parameter set, with τ_v set to 25 ps (a typical value obtained from NMR measurements taking into account only a transient ZFS contribution to the electron spin relaxation¹), changing n_{cut} from 2 to 4 yielded no noticeable change in the X-band lineshape with a peak-to-peak width of 888 G (Redfield: 647 G). When lineshape convergence is achieved, i.e. with a high enough L_{cut} , the agreement between the Redfield theoretical results is quite good provided that the peak-to-peak width remains small compared to the central field (~ 0.34 T at X-band). Thus we can say that our equations and computer program are indeed the Liouville equivalent to the Redfield theory of Rast. Testing the accuracy of the SLE predictions out of the Redfield validity range is a more difficult but obviously very important question. As a first test of the lineshape convergence beyond the perturbation regime, we ran simulations for the case where the static ZFS is not negligible compared to the Zeeman Hamiltonian by setting $a_2 = \omega_0 = 9.5$ GHz. In this case, the system is not expected to have an experimentally observable EPR spectrum. Yet for $L_{\text{cut}} = n_{\text{cut}} = 2$, a significant absorption signal was calculated for the low-field part of the selected spectral window ($B_0 = 0.25$ T). This signal vanished for $L_{\text{cut}} = 4$, replaced by a very broad background (non-zero absorption) all over the spectral window. Only very small changes were observed by setting $n_{\text{cut}} = 4$. A small but noticeable change in the calculated spectrum was obtained for $L_{\text{cut}} = 6$, but still without any distinct resonance line shape.

The sample calculations presented here can be used as benchmarks of the current program performance. The simulation time on a PC (1-2 GHz CPU frequency) is between 1 hour ($L_{\text{cut}} = 2$, slowly varying

spectrum, i.e. broad lines as in the case of $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$ and several days (sharp line, $L_{\text{cut}} = 4$ or large ZFS) for 100-200 spectral points. This is obviously not suitable for the analysis of real-life spectra. Better performance may be obtained in the future through more efficient algorithms or clever approximations.

IV. Conclusion

A general method for the calculation of the solution cw EPR line shape of an S -state ion with arbitrary zero field splitting (ZFS), such as Cr^{3+} , Mn^{2+} , Eu^{2+} or Gd^{3+} is presented. It combines the physical relaxation model of Rast et al. with the stochastic Liouville equation (SLE) to obtain expressions valid even in the slow-motion regime of particular interest for macromolecular MRI contrast agents, and at the low magnetic fields commonly used in nuclear magnetic relaxation dispersion (NMRD) experiments. We show how the eigenfunction method of Freed can be used to solve the SLE in the case of the combined static (modulated by rotation) and transient (modulated by an Ornstein-Uhlenbeck process, i.e. diffusion along a Gaussian distribution curve) ZFS contribution. The method is demonstrated with a computer program in order to validate it and estimate its computational cost. We observe that within the validity domain of the approach of Rast (weak ZFS, rapid tumbling), the SLE predictions confirm the results obtained using the Redfield approximation.

V. Acknowledgement

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A1. Appendix I

Assuming that the orientation dependence of the Hamiltonian eigenvalues can be neglected, we can then write

$$\begin{aligned}
& (\omega - \omega_\lambda) \bar{Z}_{\dot{j}}^{(1)} + \sum_m \int P_0(\Omega) G_m(\Omega) \langle \alpha_j | [\hat{H}_1(\Omega), \hat{C}_m^{(1)}(\omega)] | \beta_j \rangle d\Omega + \\
& \int P_0(\Omega) \langle \alpha_j | [\hat{\varepsilon}, \hat{\rho}_0(\Omega)] | \beta_j \rangle d\Omega + \\
& \frac{1}{2} \gamma_e B_1 \langle \alpha_j | \hat{S}_- | \beta_j \rangle (\bar{\chi}_{\lambda j,+}^{(0)} - \bar{\chi}_{\lambda j,-}^{(0)}) = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \int P(\Omega) \langle \alpha_j | [\hat{S}_+, \hat{H}_1(\Omega)] | \beta_j \rangle d\Omega
\end{aligned} \tag{25}$$

The second and third integrals vanish for $m = 0$ due to the $E_0 = 0$ eigenvalue associated with $D_{qq'}^0 = 1$ and for all the other m values since for an isotropic distribution $P_0(\Omega)$ is a constant, proportional to G_0 (see also eq. (3) from Freed et al.⁴¹) and thus orthogonal to any other G_m . Moreover, due to the definition of \bar{Z} (eq. (14)):

$$\hat{Z}_{\dot{j}}^{(n)} = \sum_m \langle \alpha_j | \hat{C}_m^{(n)}(\omega) | \beta_j \rangle \tag{26}$$

The only n of interest is $n = 1$ from the main equation for the absorbed power (eq. (6)). Nevertheless, we still need to calculate the other C_m matrix elements because of the commutator with H_1 . We multiply the Z steady-state equation (11) by G_m^* and then integrate over Ω :

$$\begin{aligned}
& N_{m'} (\omega - \omega_\lambda - iE_{m'}) \langle \alpha_j | \hat{C}_{m'}^{(1)}(\omega) | \beta_j \rangle + \\
& \sum_m \int G_m^*(\Omega) G_m(\Omega) \langle \alpha_j | [\hat{H}_1(\Omega), \hat{C}_m^{(1)}(\omega)] | \beta_j \rangle d\Omega + \\
& \frac{N_{m'}}{2} \gamma_e B_1 \langle \alpha_j | \hat{S}_- | \beta_j \rangle (\hat{C}_{m'\lambda j,+}^{(1)} - \hat{C}_{m'\lambda j,-}^{(1)}) = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \delta_{0,m'} \frac{N_{m'}}{2} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \int P(\Omega) G_m^*(\Omega) \langle \alpha_j | [\hat{S}_+, \hat{H}_1(\Omega)] | \beta_j \rangle d\Omega
\end{aligned} \tag{27}$$

The third term on the left hand side represents the deviation from spin equilibrium in the upper (+) and lower (-) spin states connected by transition λ_j . It can be neglected when no saturation occurs.

$N_{m'}$ is the normalization factor defined as

$$N_{m'} = \int G_{m'}^*(\Omega) G_{m'}(\Omega) d\Omega \quad (28)$$

More explicitly, using the Wigner matrices orthogonality relation

$$N_k^{qq'} = \frac{8\pi^2}{2k+1} \quad (29)$$

The $[\hat{H}_0, \hat{C}_m]$ and $[\hat{\varepsilon}, \hat{H}_1]$ commutator integrals in eq. (27) can be evaluated by use of the Hamiltonian \hat{H}_1 defined in eq. (8).

$$\begin{aligned} & \int G_{m'}^*(\Omega) G_m(\Omega) \left\langle \alpha_j \left[\hat{H}_1(\Omega), \hat{C}_m^{(1)} \right] \beta_j \right\rangle d\Omega = \\ & \int G_{m'}^*(\Omega) G_m(\Omega) \left\langle \alpha_j \left[\sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \hat{T}_p^k D_{pq}^k(\Omega), \hat{C}_m^{(1)} \right] \beta_j \right\rangle d\Omega = \quad (30) \\ & \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \left\langle \alpha_j \left[\hat{T}_p^k, \hat{C}_m^{(1)} \right] \beta_j \right\rangle \int G_m^*(\Omega) G_m(\Omega) D_{pq}^k(\Omega) d\Omega \end{aligned}$$

The $\int G_m^*(\Omega) G_m(\Omega) D_{pq}^k(\Omega) d\Omega$ integral can be calculated by use of 3j symbols

$$\int D_{p_1 q_1}^{k_1}(\Omega) D_{p_2 q_2}^{k_2}(\Omega) D_{p_3 q_3}^{k_3}(\Omega) d\Omega = 8\pi^2 \begin{pmatrix} k_1 & k_2 & k_3 \\ p_1 & p_2 & p_3 \end{pmatrix} \begin{pmatrix} k_1 & k_2 & k_3 \\ q_1 & q_2 & q_3 \end{pmatrix} \quad (31)$$

Similarly we have for the other commutator:

$$\begin{aligned} & \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \int P(\Omega) G_{m'}^*(\Omega) \left\langle \alpha_j \left[\hat{S}_+, \hat{H}_1(\Omega) \right] \beta_j \right\rangle d\Omega = \\ & \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \frac{1}{4\pi} \gamma_e B_1 \int G_{m'}^*(\Omega) \left\langle \alpha_j \left[\hat{S}_+, \hat{H}_1(\Omega) \right] \beta_j \right\rangle d\Omega = \\ & \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \frac{1}{4\pi} \gamma_e B_1 \int G_{m'}^*(\Omega) D_{pq}^k(\Omega) \left\langle \alpha_j \left[\hat{S}_+, \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \hat{T}_p^k \right] \beta_j \right\rangle d\Omega = \quad (32) \\ & \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \frac{1}{4\pi} \frac{8\pi^2}{2k+1} \gamma_e B_1 \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \left\langle \alpha_j \left[\hat{S}_+, \hat{T}_p^k \right] \beta_j \right\rangle \delta_{m', \ell(k,p,q)} \end{aligned}$$

The $[\hat{S}_+, \hat{T}_p^k]$ commutator is readily evaluated with the aid of Racah's rules:⁴²

$$\begin{aligned} & \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \frac{2\pi}{2k+1} \gamma_e B_1 \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \langle \alpha_j | [\hat{S}_+, \hat{T}_p^k] | \beta_j \rangle \delta_{m'(k,p,q)} = \\ & \frac{\hbar}{k_B T} \frac{1}{N} \frac{\pi}{2k+1} \gamma_e B_1 \sum_{k=2,4,6} \sum_{\eta=1}^{2k+1} B^{k\eta} \sum_{p,q=-k}^{+k} b_q^{k\eta} \sqrt{(k-p)(k+p+1)} \langle \alpha_j | \hat{T}_{p+1}^k | \beta_j \rangle \delta_{m'(k,p,q)} \end{aligned} \quad (33)$$

A2. Appendix II

Let x be the stochastic variable describing the Gaussian process of molecular distortions. Eq. (11) takes the following form:

$$\begin{aligned} & (\omega - \omega_\lambda) \hat{Z}_{\tilde{\lambda}}^{(1)}(\Omega, x) + \\ & \langle \alpha_j | [H_1(\Omega, x), \hat{Z}^{(1)}(\Omega, x)] | \beta_j \rangle - \\ & i \langle \alpha_j | [\Gamma_\Omega + \Gamma_x) \hat{Z}^{(1)}(\Omega, x)] | \beta_j \rangle + \\ & \frac{1}{2} \gamma_e B_1 \langle \alpha_j | \hat{S}_- | \beta_j \rangle (\chi_{\lambda j,+}^{(0)} - \chi_{\lambda j,-}^{(0)}) = \\ & P(\Omega) P(x) \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle + \\ & P(\Omega) P(x) \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \langle \alpha_j | [\hat{S}_+, \hat{H}_1(\Omega)] | \beta_j \rangle \end{aligned} \quad (34)$$

Let us now examine the properties of the Markovian operator associated with the Ornstein-Uhlenbeck process:^{12,34}

$$\Gamma_x = \gamma \frac{\partial}{\partial x} \left(\Delta^2 \frac{\partial}{\partial x} + x \right) = \gamma \left(\Delta^2 \frac{\partial^2}{\partial x^2} + x \frac{\partial}{\partial x} + 1 \right) \quad (35)$$

A suitable set of eigenfunctions $Q_n(x)$ and eigenvalues E_n of the O-U operator can be obtained using Hermite polynomials:³³

$$\begin{aligned} Q_n &= \frac{1}{\sqrt{2^n n!}} H_n \left(x \sqrt{\frac{1}{2\Delta^2}} \right) \\ \lambda_n &= n\gamma \end{aligned} \quad (36)$$

At this point, it is useful to set $\Delta^2 = 1/2$. With these definitions, we can write the following orthogonality relationship:

$$\int_{-\infty}^{+\infty} Q_n(x) Q_{n'}(x) \exp\{-x^2\} dx = \sqrt{\pi} \delta_{nn'} \quad (37)$$

We note that $\bar{Z}_{ij}^{(n)} = \int_{-\infty}^{+\infty} \sum_m \langle \alpha_j | C_{m,n}^{(n)}(\omega) | \beta_j \rangle P_0(x) dx$, where $P_0(x)$ is the Gaussian probability distribution of x .

$$P_x = \frac{1}{\sqrt{2\Delta^2\pi}} \exp\left\{-\frac{x^2}{2\Delta^2}\right\} = \frac{1}{\sqrt{\pi}} \exp\{-x^2\} \quad (38)$$

Eigenfunctions of the combined operator $(\Gamma_\Omega + \Gamma_x)$ are trivially obtained by the product of the respective eigenfunctions of each individual operator, and the associated eigenvalue is of course given by:

$$\{\Gamma_\Omega + \Gamma_x\} G_m(\Omega) Q_n(x) = (E_m + E_n) G_m(\Omega) Q_n(x) \quad (39)$$

Assuming independent diffusion processes for the rotation and deformation, we express the angular and Gaussian dependences of the Z matrix elements using the complete set of the Wigner matrices and Hermite polynomials.

$$\hat{Z}_{ij}^{(l)}(\Omega, x) = \sum_n \sum_m \langle \alpha_j | \hat{C}_{m,n}^{(l)}(\omega) | \beta_j \rangle G_m(\Omega) Q_n(x) \quad (40)$$

Similar to eq. (27), we multiply by $G_m^* \times Q_n^* \times \exp(-x^2)$ and integrate over x and Ω . We obtain a new set of coupled linear equations that depend both on the angular momentum index m and the Hermite index n . The Hermite polynomials are real so $Q_n^* = Q_n$.

$$\begin{aligned}
& N_{m'} \sqrt{\pi} (\omega - \omega_\lambda - iE_{m'} - iE_{n'}) \langle \alpha_j | \hat{C}_{m',n'}^{(1)}(\omega) | \beta_j \rangle + \\
& \sum_n \sum_m \int_x \int_\Omega G_{m'}^*(\Omega) Q_{n'}(x) G_m(\Omega) Q_n(x) \langle \alpha_j | [\hat{H}_1(\Omega, x), \hat{C}_{mn}^{(1)}(\omega)] | \beta_j \rangle d\Omega dx = \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{N_{m'}}{2} \delta_{0,n'} \gamma_e B_e \gamma_e B_0 \langle \alpha_j | \hat{S}_- | \beta_j \rangle \int Q_{n'}(x) P_0(x) e^{-x^2} dx + \\
& \frac{\hbar}{k_B T} \frac{1}{N} \frac{1}{2} \gamma_e B_1 \int_x \int_\Omega G_{m'}^*(\Omega) Q_{n'}(x) P_0(\Omega) P_0(x) e^{-x^2} \langle \alpha_j | [\hat{S}_+, \hat{H}_1(\Omega)] | \beta_j \rangle d\Omega dx
\end{aligned} \tag{41}$$

The integral over x of $Q_n \times P_0(x)$ is simply $2^{-1/2}$ for $n' = 0$, and 0 otherwise. Notice that since the index n' is directly related to the Hermite polynomial degree, the size of the system increases linearly with the cutoff value n_{cut} .

VI. References

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Table I. Experimental and simulated room T X-band peak-to-peak widths for [Gd(DOTA)(H₂O)]⁻ and [Gd(DTPA)(H₂O)]²⁻

Complex	SLE (L_{cut} = 2)	SLE (L_{cut} = 4)	Redfield	Experiment
DOTA static	48 G	56 G	46.5 G	-
DOTA static + transient	80 G	88 G	83.4 G	89 G
DTPA static	396 G	576 G	417.9 G	-
DTPA static + transient	444 G	690 G	509.4 G	637 G

Figure captions

Figure 1: SLE-simulated X-band derivative spectrum of $[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^-$ with static + transient ZFS;

$L_{\text{cut}} = 2$ (left), 4 (right).

Figure 2: SLE-simulated X-band derivative spectrum of $[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$ with static + transient ZFS;

$L_{\text{cut}} = 2$ (left), 4 (right).

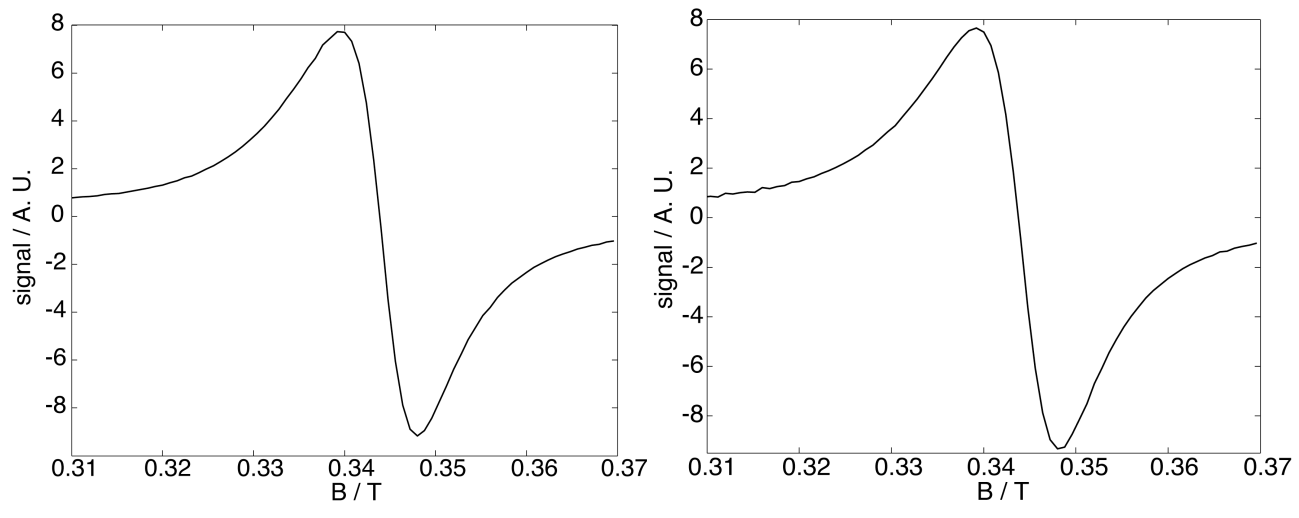


Figure 1

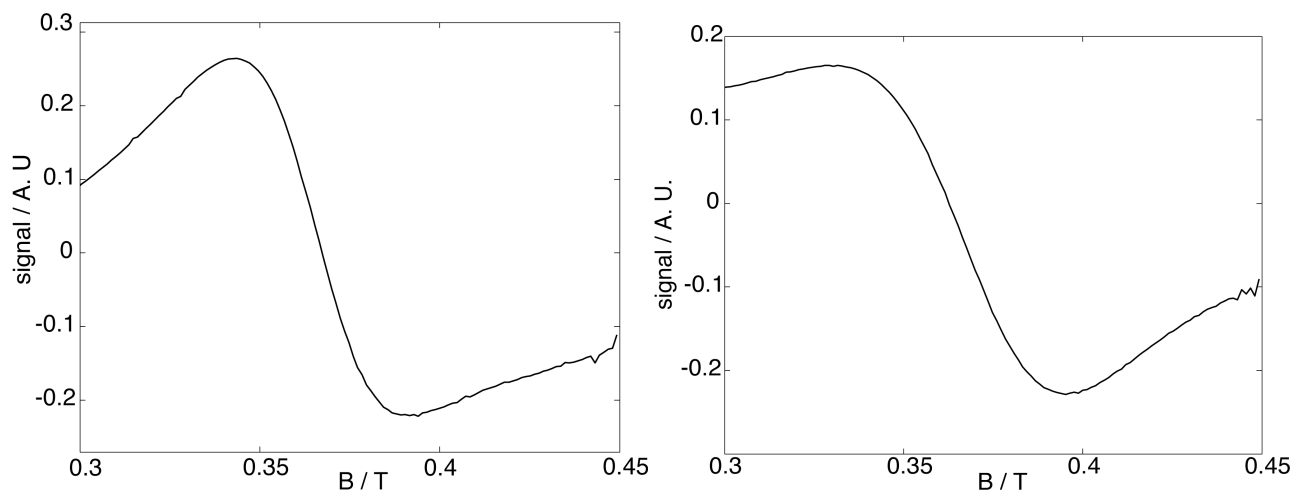


Figure 2