Nuclear spin relaxation in paramagnetic systems ($S \geqslant 1$) under fast rotation conditions

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Abstract

A new theoretical model for nuclear spin relaxation in paramagnetic systems in solution has been developed. Fast rotational motion is included in the model, both as a source of modulation of the static zero-field splitting, which provides a mechanism for electron spin relaxation, and as an origin of the stochastic variation of the electron spin–nuclear spin dipole–dipole interaction leading to nuclear spin relaxation. At the limit of low magnetic field, the model is essentially identical to the earlier formulations from our laboratory, but new closed-form expressions are given for the inner- and outer-sphere relaxation at the high-field limit. Numerical comparisons with a general theory are reported for the inner-sphere case. In addition, some nuclear magnetic relaxation dispersion (NMRD) profiles from the literature are considered for systems where experiments have been done with both low-molecular weight paramagnetic complexes and their adducts with proteins. Previously developed theories are used to interpret data for the slowly rotating protein adducts, and good fits of the fast-rotating counterparts are obtained by further adjustment of one or two additional parameters.
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1. Introduction

NMR resonance frequencies and relaxation properties of nuclear spins residing in paramagnetic transition metal complexes in solution are strongly influenced by the presence of unpaired electron spin [1]. In particular, the nuclear spin relaxation rates in paramagnetic solutions are very much higher than in the diamagnetic counterparts. In the context of nuclear spin–lattice relaxation, one commonly speaks about the paramagnetic relaxation enhancement, PRE. Strong PRE effects can also be seen for nuclear spins belonging to the solvent or to ligands that spend only a small portion of the time in the coordination sphere of the paramagnetic metal ion. The PRE effect, especially when studied as a function of the magnetic field (the nuclear magnetic relaxation dispersion, NMRD, experiment) can be an important source of information on structural as well as dynamic properties of a system, provided that an adequate theoretical model is available. The NMRD profiles are an important and commonly used tool in the characterisation of paramagnetic complexes, such as Gd(III) chelates, considered for possible applications as contrast agents for magnetic resonance imaging, MRI [2,3].

The theory of PRE has developed along two lines. First, the "classical" theory of the PRE for a nuclear spin in a paramagnetic molecule, T_{1I}^{-1}, is known as the Solomon–Bloembergen–Morgan (SBM) approach [1,4–7]. The SBM theory was developed in the high-field limit and for highly symmetric complexes. It assumes that the PRE arises through simple stochastic modulation of the hyperfine interaction between the nuclear and electron spins by molecular tumbling, electron spin relaxation and, possibly, chemical exchange. The hyperfine interaction consists of a dipolar part and a scalar term (the latter is not modulated by rotation). The dipolar part, usually considered dominant for proton relaxation, is assumed to have a constant strength corresponding to a certain nuclear spin–electron spin distance. The electron spin relaxation is assumed to originate from the collisional modulation of the zero-field splitting (ZFS) [7], with zero average, and is described by a second-order perturbation Redfield-type theory [8]. Luz and Meiboom

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[9] formulated a simple expression for the measured enhancement of the nuclear spin–lattice relaxation rate, T_{1P}^{-1}, in a situation when the nuclear spin exchanges, with lifetime τ_{M}, between an in-complex site with the spin-lattice relaxation rate T_{1I}^{-1} and the bulk

$$T_{1P}^{-1} = \frac{P_{\mathrm{M}} q}{T_{1I} + \tau_{\mathrm{M}}}, \tag{1}$$

where P_{M} is the molar ratio of the concentrations of paramagnetic species to the ligand (or solvent) protons and q is the number of ligands in the bound position. This contribution to the PRE is called inner-sphere relaxation. The ligand or solvent molecules can also experience PRE without ever entering the inner coordination sphere of the paramagnetic species. This second mechanism, referred to as outer-sphere (OS) relaxation, is usually less important and more difficult to describe, as it allows for stochastic variation of the nuclear spin–electron spin distance. The outer-sphere contribution to the PRE, $T_{1,\mathrm{OS}}^{-1}$, can be added to Eq. (1) as a second term. An important theoretical model for the outer-sphere relaxation was given by Hwang and Freed [10] and was modified by Freed [11]. Both the SBM approach and the Hwang–Freed formulation are based on a very simple description of the electron spin relaxation. An improved description of electron relaxation, but still valid only in the high-field limit and in the perturbation regime (the Redfield limit), was proposed by Rubinstein et al. [12].

For systems with an electron spin quantum number $S \geqslant 1$, the high-field limit assumption may often be violated by the presence of a strong ZFS interaction. Depending on the strength of the ZFS and the motional conditions, the ZFS can act as the principal origin of the electron spin energy level structure, as the source of electron spin relaxation or as both. A large ZFS in combination with slow motions can, in addition, bring the electron spin relaxation outside the Redfield limit. The complicated nature of electron spin relaxation and its effects on nuclear spin relaxation can be described, under rather general conditions, using a theory formulated by Benetis et al. [13–16] and extended by Kowalewski and co-workers [17–19]. This theory is commonly called the general slow-motion theory. Briefly, the nuclear spin couples via the hyperfine interaction with a generalised lattice described by a Liouville superoperator containing quantum mechanical interactions (Zeeman interaction, ZFS) as well as classical degrees of freedom (reorientation, distortion). The nuclear spin relaxation is within the Redfield limit, but the electron spin relaxation does not need to be. The inner-sphere PRE is computed by setting up and inverting a very large matrix. This approach has been demonstrated to be useful as a predictive tool [18,19] and as a way to perform least-squares fits to experimental NMRD data [17,20]. The computational effort required is however very large.

Besides this general approach, or as an alternative to it, several simpler models for the inner-sphere PRE have been proposed. The static ZFS was allowed to influence the electron spin energy levels by Sharp and co-workers [21,22] and by Bertini et al. [1,23]. Westlund [24] developed a low-field theory for electron spin relaxation and the PRE for $S = 1$, generalised subsequently by Nilsson and Kowalewski [25] to higher S quantum numbers. Bertini et al. [26] and Kruk et al. [27] formulated a similar theoretical model, valid for arbitrary relation between the electron Zeeman interaction and the static ZFS. All these approaches [21–27] assume that the electron spin relaxation and reorientational motion are uncorrelated (the decomposition approximation); in the more recent work [26,27] it is explicitly required that the reorientation has to be so slow that it only contributes through powder-averaging of the orientation-specific nuclear spin relaxation in the paramagnetic complexes.

Among other related developments, one should also mention the improvements of high-field electron spin relaxation theory by Rast et al. [28], which has also been incorporated in an SBM-like approach to the PRE by Borel et al. [29], and recent work by Sharp and Lohr [30,31], offering an alternative view of the role of electron spin relaxation processes in the PRE. Abernathy and Sharp [32] also proposed the "spin dynamics" method, designed to deal with intermediate rate reorientation processes. The outer-sphere PRE has also received some attention. Developments relevant to the present work were proposed some time ago by Sharp and co-workers [33,32] and, more recently, by Kruk et al. [27,34,35].

In the present article, we turn our attention to the case where the tumbling of the complex is fast. The theory is presented in Section 2. The basic assumptions are as follows:

- the unperturbed Hamiltonian is the Zeeman interaction at high field and static (quadratic), axially symmetric ZFS at low field;
- the electron relaxation is in the perturbation (Redfield) regime;
- the dipole–dipole and the static ZFS principal axis systems coincide (this assumption can easily be omitted);
- for the outer-sphere case, the translational diffusion is assumed uncorrelated with reorientation and with electron spin relaxation.

We deal with the inner- and outer-sphere case separately. The fast-rotating systems can be treated relatively easily at high field, at least under certain conditions. The low-field case is more difficult, and we can only handle the limiting case of zero magnetic field discussed by and large in our earlier work [25,27]. In Section 3, we present some illustrative simulated NMRD profiles and use the present methods to interpret some experimental NMRD datasets.

2. Theory

2.1. General framework

In general, one assumes the nuclear spin system to be weakly coupled to the lattice, which permits us to use the Redfield theory to describe nuclear relaxation processes. Under this assumption, the nuclear spin–lattice relaxation rate of ligand nuclei bound to the paramagnetic site is given as the real part of the complex spectral density, taken at the nuclear spin Larmor frequency [13–19,25,27,34]:

$$T_{1I}^{-1} = 2\,\mathrm{Re}\Big(K_{1,1}^{\mathrm{DD}}(-\omega_I)\Big). \tag{2}$$

The dipole–dipole interaction between the nuclear spins of the first coordination shell and the unpaired electron spin is modulated by the rotational motion of the complex and by the electron spin dynamics. The spectral density $K_{1,1}^{\mathrm{DD}}(-\omega_I)$ in this case is given by [25,27]

$$
\begin{aligned}
K_{1,1}^{\mathrm{DD}}t(-\omega_I) = {} & 30(C^{\mathrm{DD}})^2 \sum_{q\in(-1,0,1)} \\
& \times \sum_{p\in(-1,0,1)} \begin{pmatrix} 2 & 1 & 1 \\ 1-q & q & -1 \end{pmatrix} \begin{pmatrix} 2 & 1 & 1 \\ 1-p & p & -1 \end{pmatrix} \\
& \times \int_0^\infty Tr_{\mathrm{L}}\Big\{ S_q^{1(L)^+} D_{0,1-q}^{2^*}[\Omega_{ML}(t)] \\
& \times \exp\Big(-\mathrm{i}\hat{L}_{\mathrm{L}}t\Big) S_p^{1(L)} D_{0,1-p}^2[\Omega_{ML}(0)] \rho_{\mathrm{L}}^{\mathrm{eq}} \Big\} \\
& \times \exp(-\mathrm{i}\omega_I t)\,\mathrm{d}t.
\end{aligned}
\tag{3}
$$

The dipole–dipole constant C^{DD} is given by: $C^{\mathrm{DD}} = \mu_0 \hbar \gamma_I \gamma_{\mathrm{S}} / 4\pi r_{IS}^3$, where r_{IS} is the distance between the interacting spins I and S. The q-component of the first-order irreducible spherical tensor operator for the electron spin, $S_q^{1(L)}$, is written in the laboratory frame (L), while the Wigner rotation matrix $D_{0,1-q}^2(\Omega_{ML})$ describes the transformation from the molecule-fixed dipole–dipole frame (M) to the (L) frame through the set of Euler angles Ω_{ML}. Invoking the decomposition approximation [16,25,27], the lattice density operator $\rho_{\mathrm{L}}^{\mathrm{eq}}$ is the direct product of the reorientational density operator, $\rho_{\mathrm{R}}^{\mathrm{eq}}$, and the electron spin density operator $\rho_{\mathrm{S}}^{\mathrm{eq}}(\rho_{\mathrm{L}}^{\mathrm{eq}} = \rho_{\mathrm{R}}^{\mathrm{eq}} \otimes \rho_{\mathrm{S}}^{\mathrm{eq}})$ and it is assumed to be in thermal equilibrium. The decomposition approximation has been shown to be valid for slowly rotating systems [18,19,25,27]. In this study, we investigate the applicability and limitations of the decomposition approximation in systems that rotate fast. The correlation function in Eq. (3) contains the lattice Liouville superoperator, $\hat{L}_{\mathrm{L}}$, that determines the time evolution of the system. The lattice Liouville superoperator is given as a sum of a Markov operators, $\hat{L}_{\mathrm{R}}$ and $\hat{L}_{\mathrm{D}}$, describing classically the rotational diffusion and the distortion of the complex, respectively, and the electron spin Liouvillian $\hat{L}_{\mathrm{S}}$

$$\hat{L}_{\mathrm{L}} = \hat{L}_{\mathrm{R}} + \hat{L}_{\mathrm{D}} + \hat{L}_{\mathrm{S}}. \tag{4}$$

The electron spin Liouvillian, $\hat{L}_{\mathrm{S}}$, is in turn defined as the sum of the Liouvillian, $\hat{L}_{\mathrm{Zeeman}}$, generated by the electron spin Zeeman Hamiltonian, H_{Zeeman}, and the Liouvillians, $\hat{L}_{\mathrm{ZFS}}^{\mathrm{S}}$ and $\hat{L}_{\mathrm{ZFS}}^{\mathrm{T}}$, corresponding to the static and transient parts ($H_{\mathrm{ZFS}}^{\mathrm{S}}$ and $H_{\mathrm{ZFS}}^{\mathrm{T}}$) of the ZFS, respectively

$$\hat{L}_{\mathrm{S}}(t) = \hat{L}_{\mathrm{Zeeman}}(t) + \hat{L}_{\mathrm{ZFS}}^{\mathrm{S}}(t) + \hat{L}_{\mathrm{ZFS}}^{\mathrm{T}}(t). \tag{5}$$

The static part of the ZFS can be thought of as an average over rapid oscillations, caused by complex vibrations and collisions with the surrounding solvent. The transient ZFS corresponds to instantaneous deviations from the average. The stochastic modulation of the two terms is connected with random rotations and distortions. If the Zeeman coupling is much larger than the ZFS interaction ($H_{\mathrm{Zeeman}} \gg H_{\mathrm{ZFS}}^{\mathrm{S}}$, the high-field limit), the electron spin precesses around the external laboratory magnetic field. In this case, the Zeeman interaction is considered as a time-independent Hamiltonian describing the energy level structure. Stochastic time dependencies of the ZFS interactions ($H_{\mathrm{ZFS}}^{\mathrm{S}}(t)$ and $H_{\mathrm{ZFS}}^{\mathrm{T}}(t)$) provide a physical mechanism of electron spin relaxation, recently described by Rast et al. [28]. At low magnetic field, the electron spin precession occurs around the principal axis system of the static ZFS tensor (P_{S}) and the energy-level structure is determined by the static ZFS interaction. In this regime, the transient component of the ZFS interactions, $H_{\mathrm{ZFS}}^{\mathrm{T}}(t)$, is responsible for electron spin relaxation processes. With the static ZFS as the main Hamiltonian, one might consider the Zeeman coupling, $H_{\mathrm{Zeeman}}(t)$, as a perturbation contributing to the electron spin relaxation. However, the Redfield description requires the relaxation Hamiltonian to be characterised by a zero average, a condition not fulfilled by Zeeman interaction. In slowly rotating systems, this can be handled in a formally correct way by always including the Zeeman interaction in the unperturbed Hamiltonian [26,27]. In rapidly rotating systems, this procedure cannot be applied and we will therefore work at the "strict" low-field limit, where the effect of the Zeeman interaction can be neglected altogether.

The PRE of nuclei residing in solvent molecules outside of the first coordination shell is caused by modulation of the intermolecular dipolar interaction by translational diffusion. This contribution to nuclear spin relaxation is denoted outer-sphere (in a recent contribution from our laboratory [35] we coined the concept "diffuse second sphere" (DSS), to be used when the interaction between the paramagnetic species and the solvent is described by a radial distribution function, rdf. Here, we use the notation "outer-sphere" both for the DSS situation and for the so-called force-free case, where the rdf is uniform from the distance of closest approach and outward). In the same manner as for the bound ligand nuclei, the outer-sphere nuclear spin–lattice

relaxation rate is given by the real part of the corresponding spectral density [34]

$$T_{1,\text{OS}}^{-1} = 2\,\text{Re}\left(K_{1,1}^{\text{OS}}(-\omega_I)\right). \tag{6}$$

The spectral density $K_{1,1}^{\text{OS}}(-\omega_I)$ for the outer-sphere PRE is the Fourier-Laplace transform of the time correlation function, which describes three types of motion: translational diffusion, electron spin dynamics, and reorientation [27,34]

$$K_{1,1}^{\text{OS}}(-\omega_I) = 30(C^{\text{OS}})^2 \sum_{q\in(-1,0,1)} \sum_{p\in(-1,0,1)}$$
$$\times \begin{pmatrix} 2 & 1 & 1 \\ 1-q & q & -1 \end{pmatrix} \begin{pmatrix} 2 & 1 & 1 \\ 1-p & p & -1 \end{pmatrix}$$
$$\times \int_0^\infty Tr_{\text{L}} \left\{ S_q^{1(L)+} \frac{D_{0,1-q}^{2*}[\Omega_{IS}(t)]}{r_{IS}^3(t)} \right.$$
$$\times \exp\left(-i\hat{L}_{\text{L}}t\right) S_p^{1(L)} \frac{D_{0,1-p}^{2}[\Omega_{IS}(0)]}{r_{IS}^3(0)} \rho_{\text{L}}^{\text{eq}} \right\}$$
$$\times \exp(-i\omega_I t)\,\mathrm{d}t. \tag{7}$$

The outer-sphere constant is defined as $C^{\text{OS}} = \mu_0 \hbar \gamma_I \gamma_S / 4\pi$. The vector $\vec{r}_{IS}$ is defined as $\vec{r}_{IS} = \vec{r}_I - \vec{r}_S$, where $\vec{r}_I$ and $\vec{r}_S$ describe the positions in the L frame of the spins S and I, respectively, and Ω_{IS} represents the angles specifying the direction of $\vec{r}_{IS}$. The additional Liouville superoperator $\hat{L}_{\text{T}}$ describing the stochastic translational motion is now included into the lattice Liouvillian $\hat{L}_{\text{L}}$:

$$\hat{L}_{\text{L}} = \hat{L}_{\text{R}} + \hat{L}_{\text{D}} + \hat{L}_{\text{T}} + \hat{L}_{\text{S}}, \tag{8}$$

where the electron spin Liouville operator $\hat{L}_{\text{S}}$ is defined by Eq. (5). Generalising the decomposition approximation, the equilibrium lattice density operator is expressed as a direct product of the corresponding equilibrium density operators for the subsystems: $\rho_{\text{L}}^{\text{eq}} = \rho_{\text{S}}^{\text{eq}} \otimes \rho_{\text{R}}^{\text{eq}} \otimes \rho_{\text{T}}^{\text{eq}}$.

In order to proceed, we investigate separately three cases of interest: (a) high-field limit, inner-sphere PRE, (b) high-field limit, outer-sphere PRE, (c) low-field limit, inner- and outer-sphere PRE. For each of these cases, we concentrate on the effects of fast rotation and on the validity of the decomposition approximation.

2.2. The high-field limit, inner-sphere relaxation

In the high-field region, the electron spin is quantised in the laboratory (L) frame. The Zeeman interaction acts as the unperturbed Hamiltonian determining the electron spin energy level structure. The time-dependent part of the electron spin Hamiltonian, which causes transitions between the energy levels, is given by the sum of the static and transient ZFS: $H(t) = H_{\text{ZFS}}^{\text{S}(L)}(t) + H_{\text{ZFS}}^{\text{T}(L)}(t)$. The static ZFS tensor is defined in its own principal axis system P_{S}, which is fixed in the molecule.

The transformation of the second-rank irreducible spherical electron spin tensor operators from the P_{S} to the L frame [25] gives the following representation of the static ZFS Hamiltonian in the L frame:

$$H_{\text{ZFS}}^{\text{S}(L)}(t) = \sum_{n=0,\pm1,\pm2} (-1)^n A_n^{(L)}(t) S_{-n}^2, \tag{9}$$

where

$$A_n^{(L)}(t) = \left[\left(\frac{2}{3}\right)^{1/2} D_{\text{S}} D_{0,n}^2(\Omega_{P_{\text{S}}L}(t)) \right.$$
$$\left. + E_{\text{S}}\left(D_{2,n}^2(\Omega_{P_{\text{S}}L}(t)) + D_{-2,n}^2(\Omega_{P_{\text{S}}L}(t))\right) \right]. \tag{10}$$

The Wigner rotation matrices in the above equation describe the orientation of the static ZFS tensor with respect to the external magnetic field. The time dependence of the static ZFS defined in the L frame originates from isotropic rotational diffusion of the complex (the $\hat{L}_{\text{R}}$ term in the lattice Liouvillian of Eq. (4)). The relaxation effects of the static ZFS can be described by its magnitude $\Delta_{\text{S}}^2 = (2/3)D_{\text{S}}^2 + 2E_{\text{S}}^2$ (the D_{S} and E_{S} terms correspond to the axial and rhombic part of the static ZFS tensor in its principal frame) and a rotational correlation time τ_{R} for rank-two spherical harmonics.

The time modulation of the transient ZFS is caused by distortions of the complex that originate from vibrations and collisions with solvent molecules. In the same manner as the static ZFS Hamiltonian, the transient ZFS tensor is defined in its own principal frame, P_{T}. In this paper, we assume that the pseudorotational model [12,16,17,36] describes the time modulations of the transient ZFS (the $\hat{L}_{\text{D}}$ term in the lattice Liouvillian of Eq. (4)) in the L frame. According to this model, the principal direction of the transient ZFS changes with time, following the rotational diffusion equation. The assumption leads to the following form of the transient ZFS Hamiltonian in the L frame

$$H_{\text{ZFS}}^{\text{T}(L)}(t) = \sum_{n=0,\pm1,\pm2} (-1)^n V_n^{(L)}(t) S_{-n}^2, \tag{11}$$

where

$$V_n^{(L)}(t) = \left[\left(\frac{2}{3}\right)^{1/2} D_{\text{T}} D_{0,n}^2(\Omega_{P_{\text{T}}L}(t)) \right.$$
$$\left. + E_{\text{T}}\left(D_{2,n}^2(\Omega_{P_{\text{T}}L}(t)) + D_{-2,n}^2(\Omega_{P_{\text{T}}L}(t))\right) \right]. \tag{12}$$

In full analogy to the above description of the static ZFS Hamiltonian, the relaxation effect of the transient ZFS is described by its magnitude, $\Delta_{\text{T}}^2 = (2/3)D_{\text{T}}^2 + 2E_{\text{T}}^2$, where the D_{T} and E_{T} terms correspond to the axial and rhombic part of the transient ZFS tensor, respectively, and a distortional correlation time, τ_{D}, for second-rank spherical harmonics. We assume that the transient ZFS

is independent of rotation and that the angles $\Omega_{P_TL}(t)$ and $\Omega_{P_SL}(t)$ are statistically uncorrelated.

The PRE of nuclei residing in the first coordination shell is caused by the dipolar interaction (we neglect here the scalar part of the hyperfine interaction) between the nuclear and electron spins, modulated by the electron spin relaxation and the rotational diffusion of the complex, cf. Eq. (3). If the reorientation is rapid, it is also an origin of the electron spin relaxation, as mentioned above. It means that, for a rapidly rotating system, the decomposition of the correlation function into a part describing the electron spin system and a part corresponding to the spatial variables requires a detailed analysis. We assume $\tau_R^2 \Delta_S^2 \ll 1$, i.e., that the contribution to the electron relaxation caused by rotational modulation of the static ZFS can be treated by the Redfield theory. According to second-order perturbation theory, the time evolution of the electron spin density operator, $\rho_S'(t)$, is described by the equation

$$\frac{d|\rho_S'(t)\rangle}{dt} = -\int_0^t \hat{\hat{L}}_1'(t)\hat{\hat{L}}_1'(t-\tau)|\rho_S'(t)\rangle d\tau, \qquad (13)$$

where the prime indicates that all the operators are considered in the interaction representation, i.e.,

$$|\rho_S'(t)\rangle = \exp(i\hat{\hat{L}}_0 t)|\rho_S(t)\rangle,$$

$$\hat{\hat{L}}_1'(t) = \exp(i\hat{\hat{L}}_0 t)\hat{\hat{L}}_1'(t)\exp(-i\hat{\hat{L}}_0 t),$$

and $\hat{\hat{L}}_1'(t)$ is a time-dependent Liouvillian. We must notice that the static ZFS coupling, expressed in the laboratory (L) frame, is a part of the time-dependent Liouville operator due to its modulation by the rotational diffusion. In general, after integration in the right-hand side of Eq. (13), one gets a quantity dependent on the upper integration limit, t, through the time dependence of spatial variables. If the static ZFS coupling is the perturbing Liouvillian, the dependence on the t parameter is manifested by the $\Omega_{P_SL}(t)$ value. Assuming the PS and M frames to coincide, we note that the same function $\Omega_{P_SL}(t)$ is present explicitly, modulating the dipole–dipole interactions, in the correlation function given by Eq. (3). For that reason, the correlation function $K_{1,1}^{DD}(-\omega_I)$ should be written in the form

$$K_{1,1}^{DD}(-\omega_I) = 30(C^{DD})^2 \sum_{q \in (-1,0,1)}$$
$$\times \sum_{p \in (-1,0,1)} \begin{pmatrix} 2 & 1 & 1 \\ 1-q & q & -1 \end{pmatrix} \begin{pmatrix} 2 & 1 & 1 \\ 1-p & p & -1 \end{pmatrix}$$
$$\times \int_0^\infty Tr_R \left\{ D_{0,1-q}^{2*}[\Omega_{ML}(t)] \right.$$
$$\times \left[Tr_S \left(S_q^{1(L)^+} \exp\left(-i(\hat{\hat{L}}_S + \hat{\hat{L}}_D)t\right) S_p^{1(L)} \right) \right]$$
$$\times D_{0,1-p}^2[\Omega_{ML}(0)] \rho_L^{eq} \right\} \exp(-i\omega_I t) dt. \qquad (14)$$

Thus, in the first step, the average with respect to spin variables (Tr_S) should be computed, giving a function depending on $\Omega_{ML}(t)$; in the next step, one can average the total expression with respect to spatial variables (Tr_R).

In the derivation of the Redfield theory it is assumed that t is such a long time that the integrand in Eq. (13) will have decayed to zero for times much shorter than t, and that no error will be introduced by extending the limit of integration to infinity. This assumption makes the right-hand side of Eq. (13) independent of t, which leads to the common definition of a Redfield relaxation superoperator [8,37]. As stated above, the electron spin system satisfies the Redfield condition; in other words, the rotational diffusion is so fast that the electron spin can see only average, time-independent effects of the molecular reorientation. This fact permits us to factorise the correlation function $K_{1,1}^{DD}(-\omega_I)$ into a product of the correlation function for the rotationally modulated $\Omega_{ML}(t)$ angle and the correlation function for the electron spins

$$K_{1,1}^{DD}(-\omega_I) = 30(C^{DD})^2 \sum_{q \in (-1,0,1)}$$
$$\times \sum_{p \in (-1,0,1)} \begin{pmatrix} 2 & 1 & 1 \\ 1-q & q & -1 \end{pmatrix} \begin{pmatrix} 2 & 1 & 1 \\ 1-p & p & -1 \end{pmatrix}$$
$$\times \int_0^\infty \langle D_{0,1-q}^{2*}[\Omega_{P_SL}(t)] D_{0,1-p}^2[\Omega_{P_SL}(0)] \rangle$$
$$\times Tr_S \left\{ S_q^{1(L)^+} \exp\left(-i(\hat{\hat{L}}_S + \hat{\hat{R}})t\right) S_p^{1(L)} \rho_L^{eq} \right\}$$
$$\times \exp(-i\omega_I t) dt \qquad (15)$$

with the electron spin relaxation superoperator $\hat{\hat{R}} = \hat{\hat{R}}_{ZFS}^S + \hat{\hat{R}}_{ZFS}^T$. The correlation function for the molecular reorientational motion takes the simple form

$$\langle D_{mk}^{2*}[\Omega_{P_SL}(t)] D_{mk}^2[\Omega_{P_SL}(0)] \rangle = \frac{1}{5}\exp\left(-\frac{t}{\tau_R}\right) \qquad (16)$$

where τ_R is the rotational correlation time for rank-two spherical harmonics.

The remaining problem now is the electron spin dynamics part of the correlation function or, indeed, the issue of electron spin relaxation. The time development of the matrix element $\sigma_{\alpha\alpha'}^S$ of the electron density operator is described by the Redfield theory and is given by the equation

$$\frac{d\sigma_{\alpha\alpha'}^S(t)}{dt} = -i\omega_{\alpha\alpha'}\sigma_{\alpha\alpha'}^S(t) + \sum_{\beta\beta'} R_{\alpha\alpha'\beta\beta'}\left(\sigma_{\beta\beta'}^S - \sigma_{\beta\beta'}^0\right). \qquad (17)$$

Application of the secular approximation restricts the summation to include only those terms where $\omega_{\alpha\alpha'} - \omega_{\beta\beta'} \ll R_{\alpha\alpha'\beta\beta'}$. The relaxation matrix elements $R_{\alpha\alpha'\beta\beta'}$ are linear combinations of spectral densities. The resulting electron spin relaxation rates of the Redfield theory are expressed in terms of spectral densities $J_{ZFS}^S(\omega)$ and $J_{ZFS}^T(\omega)$ of the static and transient ZFS, respectively:

$$J_{ZFS}^S(\omega) = \frac{1}{5}\Delta_S^2 \frac{\tau_R}{1+\omega^2\tau_R^2}, \tag{18}$$

$$J_{ZFS}^T(\omega) = \frac{1}{5}\Delta_D^2 \frac{\tau_D}{1+\omega^2\tau_D^2}. \tag{19}$$

The Redfield description of the electron spin relaxation in terms of spectral densities is valid as long as the conditions $\tau_R^2\Delta_S^2 \ll 1$ and $\tau_D^2\Delta_T^2 \ll 1$ are fulfilled. These results are identical to the conclusions of Rast et al. [28].

To obtain the final expression for the inner-sphere nuclear spin relaxation rates in the Zeeman limit, we proceed in analogy with our earlier work [26–28,34]. It should be emphasised that this step has not been taken by Rast et al. [28]; Borel et al. [29] performed this step in a simplified, SBM-like manner. Here, we define the superoperator $\hat{\hat{M}}_{DD}^{Zeeman}$ for the inner-sphere relaxation

$$\hat{\hat{M}}_{DD}^{Zeeman} = -i\hat{\hat{L}}_{Zeeman} + \hat{\hat{R}}_{ZFS}^T + \hat{\hat{R}}_{ZFS}^S + \left(i\omega_I + \frac{1}{\tau_R}\right)\hat{\hat{1}}. \tag{20}$$

The matrix elements of the superoperator $\hat{\hat{M}}_{DD}^{Zeeman}$ are provided in Appendix A for $S = 3/2$ and in the Supplementary Material for the other electron spin quantum numbers (expressions for the most interesting $S = 7/2$ case are both numerous and lengthy). Using the $\hat{\hat{M}}_{DD}^{Zeeman}$ superoperator, the inner-sphere spectral density $K_{1,1}^{DD}(-\omega_I)$ can be written in the Zeeman limit as

$$K_{1,1}^{DD}(-\omega_I) = \frac{1}{5}(C^{DD})^2 \frac{1}{2S+1}$$
$$\times \sum_{m\in(-1,0,1)} \int_0^\infty Tr_S\left\{ S_m^{1(P)^+} \exp\left(-\hat{\hat{M}}_{DD}^{Zeeman}\tau\right) S_m^{1(P)} \right\} d\tau. \tag{21}$$

Thus, we can formulate the compact expression for the nuclear spin–lattice relaxation rate of the inner-sphere nuclei, which is the high-field counterpart of Eq. (13) of Nilsson and Kowalewski [25]

$$\left(T_{1,DD}^{Zeeman}\right)^{-1}(\omega_I) = (C^{DD})^2$$
$$\times \frac{2S(S+1)}{15}\text{Re}\Big\{ s_{-1,-1}^{DD,(Zeeman)}$$
$$+ s_{0,0}^{DD,(Zeeman)} + s_{1,1}^{DD,(Zeeman)} \Big\}. \tag{22}$$

The electron spectral densities, $s_{m,m}^{DD,(Zeeman)}$, of the inner-sphere relaxation in the Zeeman limit for rapidly rotating systems have the form

$$s_{m,m}^{DD,(Zeeman)} = \frac{3}{S(S+1)(2S+1)} c_m^* \left(\hat{\hat{M}}_{DD}^{Zeeman}\right)^{-1} c_m \tag{23}$$

where c_m is a projection vector for the electron spin tensor operator S_m^1 [18,25–27,34], appropriate for the high-field limit.

2.3. The high-field limit, outer-sphere relaxation

In this case, we begin with Eq. (7) rather than Eq. (3). For the outer-sphere PRE, the lattice dynamics is governed by translational diffusion and electron spin dynamics. The electron spin dynamics is the result of the modulation of the static and transient ZFS by the rotational and distortional motions, respectively. Following our earlier work [34], we consider the translational motion as statistically uncorrelated with the electron spin dynamics and assume that the solvent molecules move independently of the complex. Thus, the translational motion is also uncorrelated with the reorientational motion. Under these assumptions, the correlation function for the outer-sphere PRE, Eq. (7), can be separated into one function involving only the electron spin part and another including the correlation function for the translation diffusion

$$K_{1,1}^{OS}(-\omega_I) = 30(C^{OS})^2 \sum_{q\in(-1,0,1)} \sum_{p\in(-1,0,1)}$$
$$\times \begin{pmatrix} 2 & 1 & 1 \\ 1-q & q & -1 \end{pmatrix}\begin{pmatrix} 2 & 1 & 1 \\ 1-p & p & -1 \end{pmatrix}$$
$$\times \int_0^\infty \left\langle \frac{D_{0,1-q}^{2*}[\Omega_{IS}(\tau)]}{r_{IS}^3(t)}\frac{D_{0,1-p}^2[\Omega_{IS}(0)]}{r_{IS}^3(0)} \right\rangle$$
$$\times Tr_S\left\{ S_q^{1(L)^+}\exp\left(-i(\hat{\hat{L}}_S + \hat{\hat{R}})\tau\right) S_p^{1(L)}\rho_L^{eq} \right\}$$
$$\times \exp(-i\omega_I\tau)\,d\tau. \tag{24}$$

Eq. (24) is the outer-sphere counterpart of Eq. (1). A detailed description of the correlation function for translation diffusion, including the possibility of intermolecular interactions between the paramagnetic species and the solvent, described in terms of the potential of mean force or the radial distribution functions, $g(r)$, is presented in our earlier papers [34,35]. The only difference compared to these works is that the relaxation superoperator, $\hat{\hat{R}}$, contains a distortional as well as a rotational component.

2.4. The low-field limit

In the low-field regime, the static ZFS (if present) is the main Hamiltonian and the electron spin is quantised in the molecule-fixed static ZFS principal frame, P_S (the case of systems with vanishing static ZFS requires special treatment and will be the subject of a forthcoming paper). The Zeeman interaction is neglected. Independently of the rate of the reorientational motion of the complex, the electron spin relaxation is caused by distortional motion, modelled as pseudorotation. As far as the electron spin relaxation is concerned, the situation thus becomes identical to that described by Nilsson and Kowalewski [25]. The inner-sphere PRE also follows the results of that study. The corresponding case of the

outer-sphere PRE in the low-field limit has been treated by Kruk et al. [34] in the case of force-free diffusion. A generalisation to the diffuse second-sphere situation is straightforward [35].

For slowly rotating systems, we can also deal with the intermediate regime, when the Zeeman interaction is non-negligible and a static ZFS is present [26,27]. If the rotation is fast, we get into difficulties, however, because the two interactions that should be included in the main Hamiltonian have a stochastic time dependence with respect to each other. For this reason, one cannot now establish a simple physical picture of the electron spin subsystem in a similar manner as in the Zeeman and ZFS limits, by decomposing the electron spin Hamiltonian into a main and a perturbing part.

3. Results and discussion

This section is divided into two parts. In the first part, we discuss the inner-sphere and outer-sphere contributions to the PRE effect in the low-field as well as in the high-field regimes. We compare the calculations of the inner-sphere PRE based on the present theory with predictions of the general slow-motion theory. The validity of the present theory is determined in the low-field limit by the condition: $H_{ZFS}^{S} \gg H_{ZFS}^{T}$, while the validity condition in the high-field limit is: $H_{Zeeman} \gg H_{ZFS}^{T} + H_{ZFS}^{S}$. All the data are presented as the PRE of aqueous protons (110 M) in the presence of 1 mM paramagnetic species. The PRE under these conditions is also referred to as "relaxivity." The number of solvent molecules entering the first coordination sphere of the metal is assumed to be unity for the inner-sphere case and zero for the outer-sphere. All the calculated NMRD profiles presented in this section make use of a certain set of fixed parameters. Both the static and the transient ZFS are assumed to be axially symmetric, $E_S = E_T = 0$. Under these conditions, the ZFS amplitudes are simply related to the axial ZFS parameter, $\Delta_Q = \sqrt{2/3} D_Q$, where $Q = S$ or T. The principal axes of the static ZFS and the dipole–dipole interaction are assumed to coincide. For the inner-sphere case, the proton–electron spin distance is set to $r_{IS} = 300$ pm, while the outer-sphere contributions are obtained for the distance of closest approach $d = 400$ pm and the diffusion coefficient $D_{12} = 7 \times 10^{-10}$ m²/s. The amplitude of the transient ZFS, Δ_T, and the distortional correlation time, τ_D, are: $\Delta_T = 0.01$ cm⁻¹ and $\tau_D = 4$ ps. The corresponding parameters related to the static ZFS are $\Delta_S = 0.04$ cm⁻¹, $\tau_R = 30$ ps. The magnetogyric ratio of the proton is used for the nuclear spin, while γ_S for the electrons is set to 1.7588×10^{11} T⁻¹ s⁻¹, corresponding to $g_e = 2.0023$. In the second part, we employ the new theoretical tools to interpret experimental NMRD profiles for some gadolinium(III)-containing systems.

3.1. The inner-sphere and outer-sphere PRE

In Fig. 1, we present the NMRD profiles of protons residing in the first coordination sphere, in the low-field as well as in the high-field regimes for the spin quantum number $S = 1$. The product of the rotational correlation time and the static ZFS (in angular frequency units) is 0.4, a value chosen because it can be considered representative for experimentally relevant situations in systems with higher S quantum numbers. It is reasonably consistent with the assumed validity of the perturbation of Redfield regime. The NMRD profiles in the low- and high-field limits based on the present theory are extended outside the range of their validity in order to show their behaviour in the intermediate regime. We compare the obtained curves with the prediction of the general slow-motion theory. One can conclude that, for spin $S = 1$, the whole NMRD profile obtained by extension of the approaches valid in the low- and high-field limits is close to the general-theory predictions. For this particular spin quantum number, the results of the Solomon–Bloembergen–Morgan approach (SBM), with the transient ZFS as the only relaxation mechanism for the electron spin, also coincide (not shown) with general theory.

The situation becomes more complicated for higher electron spin quantum numbers. The results for $S = 5/2$ are shown in Fig. 2. This figure shows that extending the present theory outside the range of its validity does not reproduce proper values of PRE in the intermediate regime. The SBM approach, without the static ZFS contribution to the electron relaxation, works well at high field but breaks down at low field, as expected. The
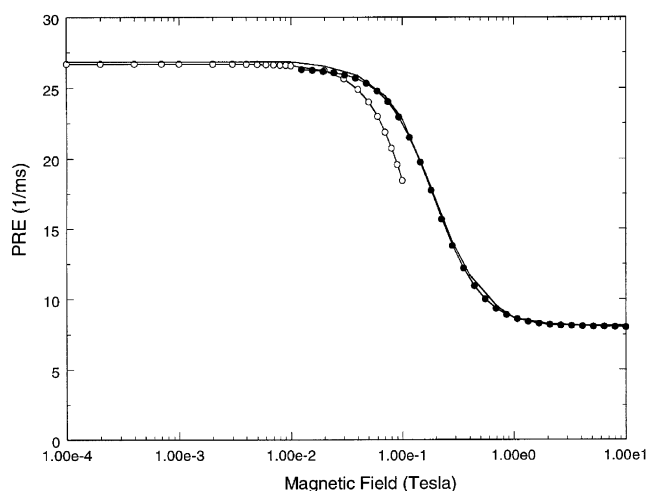

Fig. 1. Calculated inner-sphere NMRD profiles for the electron spin quantum number $S = 1$ in the low-field regime (solid line with empty circles) and in the high-field regime (solid line with solid circles). All the parameters are given in the text. The prediction of the slow-motion theory is shown as a solid line.
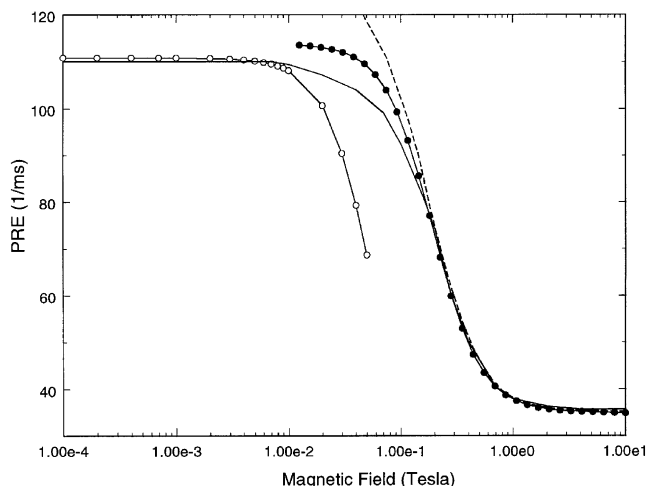
Fig. 2. Calculated inner-sphere NMRD profiles for the electron spin quantum number $S = 5/2$ in the low-field regime (solid line with empty circles) and in the high-field regime (solid line with solid circles). All the parameters are given in the text. The prediction of the slow-motion theory is shown as the solid line. The SBM results are shown as a dashed line.

data in Fig. 2 are representative for the inner-sphere NMRD profiles for $S > 1$ in general.

The outer-sphere NMRD profiles shown in Fig. 3 correspond to the inner-sphere PRE presented in the Fig. 1 ($S = 1$). A general description (corresponding to the slow-motion theory) of the outer-sphere PRE is not available. For this reason, we compare the predictions of the present theory with the calculations based on the Hwang and Freed theory [10] and the ZFS limit theory of Bayburt and Sharp [33]. Clearly, with the particular parameter set chosen here, the electron spin relaxation
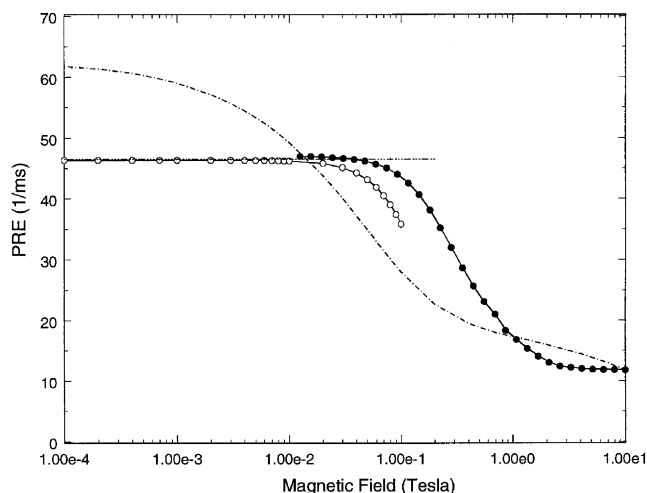
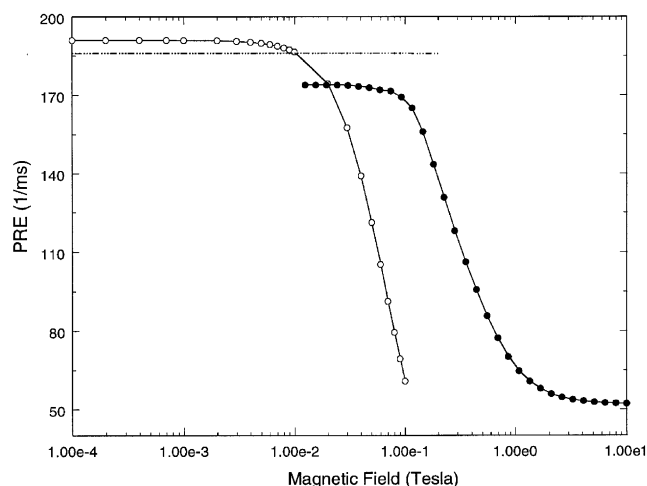

Fig. 3. Calculated outer-sphere NMRD profiles for the electron spin quantum number $S = 1$ in the low-field regime (solid line with empty circles) and in the high-field regime (solid line with solid circles). Comparison of the present approach with the Bayburt–Sharp theory (-·······-) and the Hwang–Freed theory (dashed-dotted line).

Fig. 4. Calculated outer-sphere NMRD profiles for the electron spin quantum number $S = 5/2$ in the low-field regime (solid line with empty circles) and in the high-field regime (solid line with solid circles): the present theory and the Bayburt–Sharp approach (-·······-).

effects are important at low field and the Hwang and Freed theory deviates from the present calculations. The present low-field theory corresponds to Bayburt and Sharp's results, as reported earlier [34]. The outer-sphere PRE calculations for the electron spin quantum number $S = 5/2$ are presented in Fig. 4. The chosen set of parameters is the same as in Fig. 3. The reason for the discrepancy of about 10% between the Bayburt and Sharp theory and our predictions in the low-field case for the electron spins $S > 1$ is the simple description of the electron relaxation (correct only for $S = 1$) used by Bayburt and Sharp. For higher values of the static ZFS, the discrepancies between the present approach and that of Bayburt and Sharp become even more pronounced (not shown).

3.2. Comparison with experimental data

The main purpose of the present work is to provide improved tools for analysis and interpretation of NMRD profiles for solvent protons in solutions of transition metal ions and their rapidly rotating complexes. A major problem in the NMRD profile analysis in general, shared by the present approach, is that the number of parameters to be varied is large. An advantage is obtained, however, if the NMRD profiles are collected for a rapidly rotating system as well as for an analogous slowly rotating system, obtained by binding the low-molecular weight complex to a protein. PRE data for the complex bound to a protein can be analysed using the theory presented in the earlier contribution from our laboratory [27]. Because of the assumption of slow rotation, the rotational correlation time does not enter this approach and the number of parameters is therefore reduced. It is reasonable to expect that the

parameters, other than the rotational correlation time, obtained for a slowly rotating system should not change much for the case of fast rotation. For the purpose of illustrating the use of our approach, we have chosen two pairs of Gd(III) systems in aqueous solution: the complex Gd–DTPA–SA (DTPA, diethylenetriaminepentaacetic acid; SA, sulfonamide), in the absence and in the presence of carbonic anhydrase (CA), and the Gd–EDTA^{-} (EDTA, ethylenediaminetetraacetic acid) complex, bound to the protein bovine serum albumin (BSA) and in the absence of the protein. The Gd–DTPA–SA experimental datasets have been published by Anelli et al. [38] and the authors provided us with the data in numerical form. We chose the following strategy to obtain a reasonable least-squares fit to this set of experimental NMRD profiles. In the first step, we analysed the experimental data for the slowly rotating, protein-containing system, using the theory described previously [27]. With this approach we concentrated our interest on four parameters. Three of them control the electron spin relaxation: the amplitudes of the transient and static components of the ZFS splitting (Δ_T and Δ_S) and the correlation time τ_D describing the time fluctuations of the transient ZFS. The inner-sphere contribution scales with the sixth power of the electron spin–nuclear spin distance, r_{IS}. This distance is our fourth parameter to be adjusted. The relative diffusion coefficient, D_{12}, the distance of closest approach, d, and the exchange lifetime, τ_M, were held fixed throughout the calculations at the values used by Anelli et al. [38], $d = 360$ pm and $\tau_M = 560$ ns, assuming that there is one water molecule in the first coordination sphere of the metal ion, i.e., $q = 1$. The exchange lifetime does not enter the theory for the relaxation rate of a nucleus in a paramagnetic complex (T_{1I}^{-1} above), but does influence in an important way the relation between the T_{1I}^{-1} and the measured PRE, according to Eq. (1). The four-parameter ($\Delta_T, \tau_D, \Delta_S, r_{IS}$) fit was performed for the (Gd–DTPA–SA)–CA complex and the results are listed in Table 1. An analogous fit neglecting the rather small outer-sphere contribution was also performed (second line in Table 1). The experimental NMRD profiles and the least-squares fits according to the first line in Table 1 are also presented in Fig. 5. Among parameters collected in Table 1, the proton–metal distance, r_{IS}, deserves a comment. The value obtained in the present model (with or without the outer-sphere contribution) is rather short, compared to 300–310 pm reported by Anelli et al. [38]. A probable explanation is that the fitted distance is correlated with the exchange lifetime and other r_{IS}, τ_M pairs produce a fit of very similar quality. For example, a fit with $\tau_M = 604$ ns (not shown) yields the $r_{IS} = 296$ pm. Thus, to get a reliable estimate of r_{IS}, one would need an independent and trustworthy measurement of τ_M.

To obtain the fit for the rapidly rotating system (in the absence of carbonic anhydrase), only the rotational

Table 1
Parameters obtained by least-squares fits of the inner-sphere and outer-sphere relaxation theories to the experimental data for Gd–DTPA–SA in aqueous solution, in the presence and absence of carbonic anhydrase (CA)

	$\Delta_T\ 10^{-2}$ cm^{-1}	τ_D ps	$\Delta_S\ 10^{-2}$ cm^{-1}	r_{IS} pm	τ_R ps	$D_{12}\ 10^{-9}$ m^2/s	d pm	τ_M ns	q	SD
(Gd–DTPA–SA)–CA[b]	1.8	17	2.3	270	—	2.6[a]	360	560[a]	1[a]	4.1%
(Gd–DTPA–SA)–CA[c]	1.9	15	2.2	269	—	—	—	560[a]	1[a]	4.7%
(Gd–DTPA–SA)–CA[d]	1.7	9.9	0[a]	266	12 000[a]	—	—	560[a]	1[a]	7.8%
Gd–DTPA–SA[b]	1.8	17	2.3	270	27	2.6[a]	360	560[a]	1[a]	4.2%

[a] The value kept constant in the fitting procedure.
[b] Fit using the present theory.
[c] Fit using the present theory, outer-sphere contribution excluded.
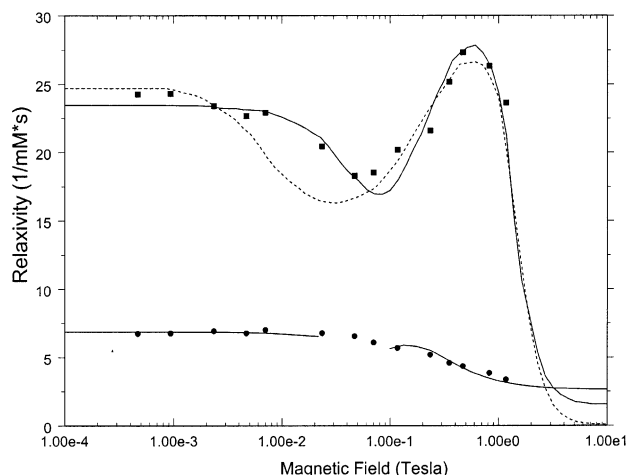[d] Fit using the SBM theory.

Fig. 5. Experimental and calculated (solid line) NMRD profiles for Gd–DTPA–SA in aqueous solution in the presence (solid squares) and absence (solid circles) of the carbonic anhydrase. The parameters used to obtain the solid lines are given in Table 1. The fit using the SBM theory for the (Gd–DTPA–SA)–CA system is shown as a dashed line.

Fig. 6. Experimental and calculated NMRD profiles for Gd–EDTA⁻ in aqueous solution in the presence (solid circles) and absence (solid squares) of the bovine serum albumin. The least-squares fits of the present theory (solid lines) and the prediction of the slow-motion theory (dashed line) in the intermediate regime for the rapidly rotating system. The parameters used to obtain the dashed line and the solid lines are given in Table 2.

correlation time τ_R was re-optimised. The fitting was performed simultaneously in the low- and high-field regions, neglecting experimental points in the intermediate regime. The results are shown in Table 1 and in Fig. 5. We note that the reoptimized rotational correlation time seems a little too short for the complex of this size.

For the sake comparison, we have also performed a three-parameter fit ($\Delta_T, \tau_D, r_{IS}, \Delta_S = 0, \tau_R = 12$ ns as estimated by Anelli et al. [38]) of the data for the (Gd–DTPA–SA)–CA complex using the Solomon–Bloembergen–Morgan approach [1,4–7] and including only the inner-sphere contribution. The results are also shown in Table 1 and Fig. 5. The low-field shape of the SBM profile is in disagreement with the experimental data, which conforms to our earlier experience [27,39] and is the result of neglecting the effect of the static ZFS. The SBM analysis of the data for the (Gd–DTPA–SA) complex can be found in the paper by Anelli et al. [38].

The second set of experimental data, i.e., the NMRD profiles for Gd–EDTA⁻ and (Gd–EDTA)–BSA has been presented in a review by Koenig and Brown [40]. The analysis was performed in a similar manner as described above for the Gd–DTPA–SA complex. The differences were as follows: the inner-sphere contribu-
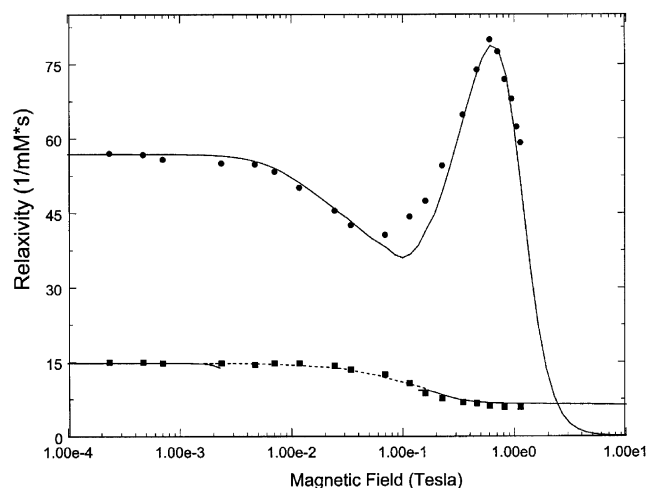
tion to the PRE was assumed to be dominant (the outer-sphere part was neglected) and the five parameters $\Delta_T, \tau_D, \Delta_S, r_{IS}$, and τ_M were all adjusted (assuming $q = 3$ [40]). The fit in the fast-rotation case was made by holding the four parameters, $\Delta_T, \tau_D, \Delta_S, r_{IS}$, constant at the values obtained for the protein complex and adjusting only the correlation time τ_R and the exchange lifetime τ_M. The small difference between the obtained exchange lifetimes in the slowly and rapidly rotating systems gives a certain improvement of the fit. The resulting parameters are reported in Table 2 and the best fits are presented in Fig. 6, together with the prediction of the general theory calculated for the same set of parameters in the absence of the protein. All the resulting parameters, Δ_T, τ_D and Δ_S, τ_R, satisfy the validity condition of the Redfield limit ($\Delta_S\tau_R \cong 0.3$–0.4 for both complexes). We have also fitted the (Gd–EDTA)–BSA dataset assuming only two water molecules in the first coordination sphere ($q = 2$, not shown). The resulting standard deviation is somewhat smaller than for $q = 3$. The *IS* distance is shorter for $q = 2$ and so is the exchange lifetime; the other parameters are very similar to those shown in Table 2.

Table 2
Parameters obtained by least-squares fits of the inner-sphere relaxation theory to the experimental data for Gd–EDTA⁻ in aqueous solution in the presence and absence of bovine serum albumin (BSA)

	$\Delta_T\ 10^{-2}\,cm^{-1}$	τ_D ps	$\Delta_S\ 10^{-2}\,cm^{-1}$	r_{IS} pm	τ_R ps	τ_M ns	q	SD
(Gd–EDTA)–BSA	1.9	15	2.6	305	—	491	3[a]	4.3%
Gd–EDTA⁻	1.9[a]	15[a]	2.6[a]	305[a]	65	460	3[a]	4.7%

[a] The value kept constant in the fitting procedure.

4. Concluding remarks

The effects of fast rotation of paramagnetic complexes on the inner- and outer-sphere paramagnetic relaxation enhancement have been investigated theoretically. Expressions for the PRE have been derived in the high-field limit and at very low magnetic field. The new theoretical model for the inner-sphere relaxation has been compared with the general slow-motion theory and has been found to perform well within the validity range of the Redfield theory for electron spin relaxation. The model has also been applied to the analysis of the experimental nuclear magnetic relaxation dispersion profiles of two low-molecular weight Gd(III) complexes for which data were also available in slowly rotating, protein-bound form. Reasonably good fits were possible to obtain by adjusting only one or two parameters for the small complexes. We hope that the theory presented here will be found useful in the work on new, efficient contrast agents for MRI as well as in other studies of paramagnetic complexes in solution.

Acknowledgments

Appendix A

We provide here the non-zero matrix elements of the superoperator $\hat{M}_{DD}^{Zeeman}$ of Eq. (20) for $S = 3/2$. The supermatrix elements refer to the electron spin eigenstates, labelled as follows:

$$|1\rangle = |S, S\rangle, \ldots |2S + 1\rangle = |S, -S\rangle. \tag{A.1}$$

The elements related to the longitudinal electron spin relaxation are given by

$$M_{1,1,1,1} = M_{2,2,2,2} = M_{3,3,3,3} = M_{4,4,4,4}$$
$$= i\omega_I + \frac{1}{\tau_R} + 6J^T(\omega_S) + 6J^T(2\omega_S)$$
$$+ 6J^S(\omega_S) + 6J^S(2\omega_S), \tag{A.2}$$

$$M_{1,1,2,2} = M_{2,2,1,1} = M_{3,3,4,4} = M_{4,4,3,3}$$
$$= -6J^T(\omega_S) - 6J^S(\omega_S), \tag{A.3}$$

$$M_{1,1,3,3} = M_{3,3,1,1} = M_{2,2,4,4} = M_{4,4,2,2}$$
$$= -6J^T(2\omega_S) - 6J^S(2\omega_S). \tag{A.4}$$

The elements related to the transverse electron spin relaxation are given by

$$M_{1,2,1,2} = M_{3,4,3,4}$$
$$= i(\omega_I - \omega_S) + \frac{1}{\tau_R} + 6J^T(0) + 6J^T(\omega_S)$$
$$+ 6J^T(2\omega_S) + 6J^S(0) + 6J^S(\omega_S)$$
$$+ 6J^S(2\omega_S), \tag{A.5}$$

$$M_{1,3,1,3} = i(\omega_I - 2\omega_S) + \frac{1}{\tau_R} + 6J^T(0) + 6J^T(\omega_S)$$
$$+ 6J^T(2\omega_S) + 6J^S(0) + 6J^S(\omega_S)$$
$$+ 6J^S(2\omega_S), \tag{A.6}$$

$$M_{1,4,1,4} = i(\omega_I - 3\omega_S) + \frac{1}{\tau_R} + 6J^T(\omega_S)$$
$$+ 6J^T(2\omega_S) + 6J^S(\omega_S) + 6J^S(2\omega_S), \tag{A.7}$$

$$M_{2,3,2,3} = i(\omega_I - \omega_S) + \frac{1}{\tau_R} + 6J^T(\omega_S) + 6J^T(2\omega_S)$$
$$+ 6J^S(\omega_S) + 6J^S(2\omega_S), \tag{A.8}$$

$$M_{2,4,2,4} = i(\omega_I - 2\omega_S) + \frac{1}{\tau_R} + 6J^T(\omega_S)$$
$$+ 6J^T(2\omega_S) + 6J^S(\omega_S) + 6J^S(2\omega_S), \tag{A.9}$$

$$M_{1,2,3,4} = M_{3,4,1,2} = M_{2,1,4,3} = M_{4,3,2,1}$$
$$= -6J^T(2\omega_S) - 6J^S(2\omega_S), \tag{A.10}$$

$$M_{1,3,2,4} = M_{2,4,1,3} = M_{3,1,4,2} = M_{4,2,3,1}$$
$$= 6J^T(\omega_S) + 6J^S(\omega_S). \tag{A.11}$$

The elements $M_{\beta,\alpha,\beta,\alpha}$ can be obtained from the elements $M_{\alpha,\beta,\alpha,\beta}$ by replacing the electron Larmor frequency ω_S with $-\omega_S$. The corresponding matrix elements for the outer-sphere case can be obtained as described in [34]. The expressions for other values of the S quantum number will be provided by the authors upon request.

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