A Rigorous Framework to Interpret Water Relaxivity. The Case Study of a Gd(III) Complex with an α-Cyclodextrin Derivative

Célia S. Bonnet,[a,c] Pascal H. Fries[a], Andrée Gadelle,[a] Serge Gambarelli,[b] and Pascale Delangle[a]**

[a] Laboratoire de Reconnaissance Ionique et de Chimie de Coordination, INAC/SCIB (UMR_E 3 CEA-UJF), CEA-Grenoble, 17 rue des Martyrs, F-38054 Grenoble Cedex 9, France

[b] Laboratoire de Résonance Magnétique, INAC/SCIB (UMR_E 3 CEA-UJF), CEA-Grenoble, 17 rue des Martyrs, F-38054 Grenoble Cedex 9, France

[c] Present address: School of Chemistry, Centre for Synthesis and Chemical Biology, Trinity College Dublin, Dublin 2, Ireland.

Dr Pascale DELANGLE, tel. +33438789822, fax. +33438785090, pascale.delangle@cea.fr

Dr Pascal H. FRIES, tel. +33438783107, fax. +33438785090, pascal-h.fries@cea.fr

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Appendix A. Electronic Spin Relaxation and Inner-Sphere Relaxivity

The quantum nature of the relaxation of an electronic spin and the expression of the standard component $B_{S,-1j}(t)$ of the dipolar magnetic field are briefly discussed. Details are given about the derivation of the ZFS Hamiltonian at the origin of this relaxation in the case of a Gd^{3+} complex. The mathematical analysis of the failure of the decomposition approximation at the basis of the SBM theory of inner-sphere relaxivity is presented.

Nature of Electronic Spin Relaxation

Electronic spin relaxation occurs because of the random time-variation of the ZFS Hamiltonian acting on the electronic spin S of a realization j of the Gd^{3+} complex. More precisely, it stems from the random differences among the operators $U_{ej}(t)$, which give the evolution of the quantum states of the spins S of the realizations j and are the solutions of the time-dependent Schrödinger equations[1] (A1) for the Hamiltonians $H_{e,j}^{(L)}(t)$

$$i\frac{d}{dt}U_{ej}(t) = H_{e,j}^{(L)}(t)U_{ej}(t) \tag{A1}$$

with the initial condition $U_{ej}(0) = \mathbf{1}$. Let $U_{ej}(t)^{\dagger}$ be the adjoint operator of $U_{ej}(t)$. Generally speaking, the relaxation of a physical property of the complex represented by an operator A is the incoherent time-evolution of an average of the time-dependent operator $U_{ej}(t)AU_{ej}(t)^{\dagger}$ over the realizations j. For the purpose of relaxivity theory, it is convenient to introduce the time-dependent components of the electronic spin S, which enter the expression of the dipolar magnetic field and are operators defined in eq (A2)

$$S_{zj}(t) \equiv U_{ej}(t)S_z U_{ej}(t)^{\dagger}, \; S_{\pm j}(t) \equiv U_{ej}(t)S_{\pm} U_{ej}(t)^{\dagger} \tag{A2}$$

The Standard Component $B_{S,-1j}(t)$ of the Dipolar Magnetic Field

In the (L) frame, let $\left(r_{jt},\theta_{jt},\phi_{jt}\right)$ be the spherical coordinates of the interspin I - S vector $\mathbf{r}_{jt}$ in the complex j. Introduce the orientation $\hat{r}_{jt} \equiv \left(\theta_{jt},\phi_{jt}\right)$ of $\mathbf{r}_{jt}$ and the spherical harmonics $Y_{2q}(\hat{r}_{jt})$ that depend on this orientation. In classical physics, the instantaneous dipolar field is a linear combination of products of the random functions $Y_{2q}(\hat{r}_{jt})\big/r_{jt}^3$ times components of the electronic magnetic moment. In quantum physics, these components are time-dependent operators $\gamma_S\hbar S_{d}(t)$ (direction d = z, $\pm$) that are proportional to the spin components $S_{d}(t)$ and follow their random dynamics given by the evolution law of the quantum states. The standard component $B_{S,-1j}(t)$, the TCF $k_{-1}^{IS}(t)$ of which gives the intramolecular relaxation rate $1/T_{1M}$ in eq (7), depends on the classical random motion of the interspin I - S vector $\mathbf{r}_{jt}$ through the functions $Y_{2q}(\hat{r}_{jt})\big/r_{jt}^3$ and on the quantum random dynamics of the electronic spin states through the time-dependent operators $S_{d}(t)$ (direction d = z, $\pm$). It reads[2]

$$B_{S,-1j}(t) = \sqrt{\frac{12\pi}{5}} g_S \mu_B \left[\frac{Y_{2,-2}(\hat{r}_{jt})}{r_{jt}^3} S_{+j}(t) + \frac{Y_{2,-1}(\hat{r}_{jt})}{r_{jt}^3} S_{zj}(t) - \frac{\sqrt{6}}{6} \frac{Y_{2,0}(\hat{r}_{jt})}{r_{jt}^3} S_{-j}(t) \right] \tag{A3}$$

Derivation of the Expression of the Fluctuating ZFS Hamiltonian in the Laboratory Frame

The expressions (9) and (10) of the static and transient ZFS Hamiltonians are rewritten in tensorial forms[1] that are convenient to express their time-evolution due to the actual and pseudo Brownian rotations of the complex. First, consider the static ZFS Hamiltonian defined by eq (9). In its principal molecular frame (P_S), introduce the components $S_q^{(2)}(P_S)$ of the usual spherical tensor operator[1] of rank 2 derived from S as $S_0^{(2)}(P_S) \equiv \sqrt{3/2}\left[S_{z_S}^2 - S(S+1)/3\right]$, $S_{\pm 1}^{(2)}(P_S) \equiv \mp(1/2)\left(S_{z_S}S_{\pm_S} + S_{\pm_S}S_{z_S}\right)$, $S_{\pm 2}^{(2)}(P_S) \equiv S_{\pm_S}^2/2$. In the $S_q^{(2)}(P_S)$ operator basis, the coefficients C_{Sq} of $H_{ZFS,S}^{(P_S)}$ are $C_{S0} = \sqrt{2/3}D_S$, $C_{S\pm 1} = 0$, $C_{S\pm 2} = E_S$ and $H_{ZFS,S}^{(P_S)}$ can be rewritten in the form of eq , which is convenient to express the evolution of this Hamiltonian due to the Brownian rotation of the complex of correlation time τ_R.

$$H_{ZFS,S}^{(P_S)} = \sum_{q=-2,0,2} C_{Sq} S_q^{(2)}(P_S) \tag{A4}$$

In the course of the Brownian rotational motion of the realization j, let $R_{jt}^{(P_S)}$ be the 3D rotation transforming the (L) frame into the (P_S) frame at time t. Denote the elements of the Wigner matrix[1] $D^{(2)}\left(R_{jt}^{(P_S)}\right)$ associated with the rotation $R_{jt}^{(P_S)}$ by $D_{qq'}^{(2)}\left(R_{jt}^{(P_S)}\right)$. In the (L) frame, the components $S_q^{(2)}(L)$ of the spherical tensor operator[1] of rank 2 derived from S are defined in terms of S_x, S_y, S_z in a way similar to that of $S_q^{(2)}(P_S)$ in terms of S_{x_S}, S_{y_S}, S_{z_S}. The "static" ZFS Hamiltonian $H_{ZFS,Sj}^{(L)}(t)$ of rank 2 generated by $H_{ZFS,S}^{(P_S)}$ is given by eq (A5).

$$H_{ZFS,Sj}^{(L)}(t) = \sum_{q=-2}^{2} \sum_{q'=-2,0,2} D_{qq'}^{(2)}\left(R_{jt}^{(P_S)}\right) C_{Sq'} S_q^{(2)}(L) \tag{A5}$$

Following the same procedure as for the static ZFS Hamiltonian, the transient ZFS Hamiltonian defined by eq (10) is rewritten in tensorial form in its principal molecular frame (P_T). Then, for the realization j of GdL, if $R_{jt}^{(P_T)}$ denotes the pseudo-rotation (ps) that results from the Brownian rotational diffusion of correlation time τ_v and transforms (L) into (P_T) at time t, $H_{ZFS,Tj}^{(L)}(t)$ is given by eq (A6).

$$H_{ZFS,Tj}^{(L)}(t) = \Delta_T \sum_{q=-2}^{2} D_{q0}^{(2)}\left(R_{jt}^{(P_T)}\right) S_q^{(2)}(L) \tag{A6}$$

To sum up, according to eqs (A5) and (A6), the total ZFS Hamiltonian $H_{ZFS,Sj}^{(L)}(t)$ of the realization j in the (L) frame, at the origin of the electron spin relaxation, is

$$H_{ZFS,Tj}^{(L)}(t) = \sum_{q=-2}^{2} \sum_{q'=-2,0,2} D_{qq'}^{(2)}\left(R_{jt}^{(P_S)}\right) C_{Sq'} S_q^{(2)}(L) + \Delta_T \sum_{q=-2}^{2} D_{q0}^{(2)}\left(R_{jt}^{(P_T)}\right) S_q^{(2)}(L) \tag{A7}$$

The Failure of the Decomposition Approximation.

We are in a position to explain easily why the decomposition approximation at the basis of the popular SBM theory fails, when the ZFS Hamiltonian incorporates a static contribution. The component $B_{S,-1j}(t)$ of the dipolar local field given by eq (A3) is a sum of products of spherical harmonics $Y_{2q}(\hat{r}_{jt})$ times spin operators $S_{jz}(t)$, $S_{j\pm}(t)$. The functions $Y_{2q}(\hat{r}_{jt})$ depend on the rotation $R_{jt}^{(P_S)}$ through the orientation $\hat{r}_{jt}$ of the interspin *I - S* vector. The spin operators depend on the same rotation via the evolution operator $U_{ej}(t)$ governed by the total electronic spin Hamiltonian $H_{e,j}^{(L)}(t)$, which includes the static ZFS contribution $H_{ZFS,Sj}^{(L)}(t)$ modulated by $R_{jt}^{(P_S)}$. Clearly, the fluctuations of a function $Y_{2q}(\hat{r}_{jt})$ and of an operator $S_{jz}(t)$ or $S_{j\pm}(t)$, which stem from $R_{jt}^{(P_S)}$, are correlated. This complicated correlation depends on the direction $\hat{u}(\overrightarrow{GdH}) \equiv \overrightarrow{GdH}/\|\overrightarrow{GdH}\|$ of the interspin *I - S* vector $\overrightarrow{GdH}$ in the (P_S) frame. At low field, for a given distance $\|\overrightarrow{GdH}\|$, this correlation gives rise to a strong dependence of $1/T_{1M}\left[\hat{u}(\overrightarrow{GdH})\right]$ on $\hat{u}(\overrightarrow{GdH})$, which is beyond the scope of the SBM approximation[2-4] and demonstrates the inadequacy of this formalism.

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Appendix B. Approximation of the Longitudinal Outer-Sphere Relaxivity r_1^{OS}

The OS-TCF $k_{-1}^{OS}(t)$ giving rise to the OS relaxivity r_1^{OS} is proportional to the sum of the TCFs of the components $B_{S,-1j}(t)$ of the local dipolar fields due to Gd^{3+} in the various pairs M_I/GdL. The operators $B_{S,-1j}(t)$ have the same formal expression of eq (A3) for both the IS and OS dynamics. The OS-TCF is given by eq 19

$$k_{-1}^{OS}(t) = N_{GdL} \frac{1}{N_{pair}} \sum_{j=1}^{N_{pair}} \frac{1}{2S+1} Tr_S \left\{ \left[B_{S,-1j}(t) \right]^{\dagger} B_{S,-1j}(0) \right\} \tag{19}$$

Now, the rotational Brownian motion of the complex and its relative translational diffusion with respect to M_I are correlated only when M_I and the complex collide and if the geometry of the latter is significantly anisotropic. To first approximation, the two motions can be assumed to be stochastically independent. Since the random motion of the *I* - *S* interspin vector $\mathbf{r}_{jt}$ is governed by the relative translational diffusion of the complex with respect to M_I, if the small spin eccentricity effects are neglected,[1] the motion of $\mathbf{r}_{jt}$ and the rotation of the complex are also uncorrelated. This justifies the absence of correlation between the fluctuations of a function $Y_{2,q}(\hat{r}_{jt})/r_{jt}^3$ and of an operator $S_{jz}(t)$ or $S_{j\pm}(t)$ entering the expression of $B_{S,-1j}(t)$. Thus, the initial configurations of the M_I/GdL pairs can be obtained by selecting (i) N_{I,O_S} random orientations of M_I and random positions O_S of Gd generating g_{IS} and (ii) for each of these random orientations of M_I and random positions O_S of Gd, the same random initial orientations (or) of (P_S) and vibrational (vib) orientations of (P_T) of GdL. Then, since the motions of M_I and O_S are independent of the rotational and vibrational motions of GdL, the TCFs $\left\langle \left[Y_{2,q'}(\hat{r}_{jt})^* / r_{jt}^3 \right] S_{d'j}(t)^{\dagger} \left[Y_{2,q}(\hat{r}_{j0}) / r_{j0}^3 \right] S_{dj}(0) \right\rangle$ (directions d, d' = z, ±) in eq 19 factor out into the independent dipolar TCFs $g_{2,q'q}(t) = \left\langle \left[Y_{2,q'}(\hat{r}_{jt})^* / r_{jt}^3 \right] \left[Y_{2,q}(\hat{r}_{j0}) / r_{j0}^3 \right] \right\rangle$ of eq 20 and the TCFS of the electronic spin components $\left\langle S_{d'j}(t)^{\dagger} S_{dj}(0) \right\rangle = \left\langle S_{d'j}(t)^{\dagger} S_{dj} \right\rangle$ defined in eqs (11) and (12), and more generally in eq (B1).

$$\left\langle S_{d'j}(t)^{\dagger} S_{dj} \right\rangle \equiv \frac{1}{N_{or-vib}} \sum_{j=1}^{N_{or-vib}} \frac{1}{2S+1} Tr_S \left[S_{d'j}(t)^{\dagger} S_{dj} \right] \tag{B1}$$

Because of the rotational invariance of the liquid solution, $g_{2,q'q}(t)$ and $\left\langle S_{d'j}(t)^{\dagger} S_{dj} \right\rangle$ simplify to $g_{2,q'q}(t) = \delta_{q'q} g_2(t)$ and $\left\langle S_{d'j}(t)^{\dagger} S_{dj} \right\rangle = \delta_{d'd}$, so that the expression of $k_{-1}^{OS}(t)$ in eq (19) reduces to eq (B2).

$$k_{-1}^{OS}(t) = \frac{12\pi}{5} g_S^2 \mu_B^2 g_2(t) \left[\left\langle S_{+j}(t)^{\dagger} S_{+j} \right\rangle + \left\langle S_{zj}(t)^{\dagger} S_{zj} \right\rangle + \frac{1}{6} \left\langle S_{-j}(t)^{\dagger} S_{-j} \right\rangle \right] \tag{B2}$$

Now, the longitudinal OS relaxivity r_1^{OS} has the same formal expression in terms of $k_{-1}^{OS}(t)$ as r_1^{IS} in terms of $k_{-1}^{IS}(t)$. It is given by eq (B3).

$$r_1^{OS} = 2\gamma_I^2 \, \text{Re} \int_0^\infty k_{-1}^{OS}(t) \exp(-i\omega_I t)\, dt \tag{B3}$$

In eq (B3), the factor $\exp(-i\omega_I t)$ multiplying the TCFs $\left\langle S_{\pm j}(t)^\dagger S_{\pm j} \right\rangle$ can be dropped since it hardly affects the values of the integrals involving these functions, since they approximately oscillate[2] at the much more rapid angular frequency $\mp\omega_S$. Besides, the equalities $\left\langle S_{-j}(t)^\dagger S_{-j} \right\rangle = \left\langle S_{+j}(t)^\dagger S_{+j} \right\rangle^* = \left\langle S_{+j}(t) S_{-j} \right\rangle$ hold. Thus, the expression (B3) of r_1^{OS} simplifies to eq (21).

$$r_1^{OS} = A \, \text{Re} \int_0^\infty g_2(t) \left[G_{//}^{nor}(t) \exp(-i\omega_I t) + \frac{7}{3} G_\perp^{nor}(t) \right] dt \tag{21}$$

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Appendix C. Theoretical Expression of the EPR Spectrum

The EPR absorption function is the energy of the oscillating field $\mathbf{B}_1$ absorbed per second by the GdL complexes[1]. It is proportional to the imaginary part $\chi''(\omega, \omega_S)$ of their susceptibility up to a multiplicative factor depending on the sample, but irrelevant in an EPR experiment which yields a signal of arbitrary intensity. To simplify the notation, the EPR absorption function is still denoted by $\chi''(\omega, \omega_S)$, which can be written as

$$\chi''(\omega, \omega_S) = \xi_{S_x} \int_0^\infty \cos \omega t \left\langle S_x(t) S_x \right\rangle dt \tag{C1}$$

where ξ_{S_x} is an arbitrary multiplicative factor. Since the TCF $\left\langle A(t) B \right\rangle$ of two Hermitian operators A and B, such as S_x, S_y, is a real function, substituting the definitions $S_+(t) = S_x(t) + i S_y(t)$ and $S_- = S_x - i S_y$ for $S_+(t)$ and S_- in the TCF $\left\langle S_+(t) S_- \right\rangle$, it is easily seen that $\left\langle S_x(t) S_x \right\rangle$ can be rewritten in the form of eq (C2).

$$\left\langle S_x(t) S_x \right\rangle = \frac{1}{2} \mathrm{Re} \left\langle S_+(t) S_- \right\rangle \tag{C2}$$

Define the associated TCF $G_\perp^{\mathrm{nor,slow}}(t, B_0) \equiv G_\perp^{\mathrm{nor}}(t, B_0) \exp(-i \omega_S t)$, where the argument B_0 of $G_\perp^{\mathrm{nor,slow}}(t, B_0)$ indicates that this TCF is calculated for the external field value B_0. Within the Redfield limit[2-4] of the electronic relaxation and beyond, it can be shown that $G_\perp^{\mathrm{nor,slow}}(t, B_0)$ does not display any rapid oscillations,[5,6] so that the oscillatory behavior of $G_\perp^{\mathrm{nor}}$ is that of $\exp(i \omega_S t)$. Replacing $\left\langle S_x(t) S_x \right\rangle$ by its expression (C2) in eq (C1) and using the definition eq 26 of $G_\perp^{\mathrm{nor}}(t, B_0)$, $\chi''(\omega, \omega_S)$ can be rewritten as

$$\chi''(\omega, \omega_S) = \xi_a \int_0^\infty \mathrm{Re} \left\{ G_\perp^{\mathrm{nor,slow}}(t, B_0) \exp(i \omega_S t) \left[\exp(i \omega t) + \exp(-i \omega t) \right] \right\} dt \tag{C3}$$

If the oscillating frequency ω is high enough, the integral of the rapidly oscillating term $\exp\left[i(\omega_S + \omega) t \right]$ is negligible near resonance, i.e., for $\omega \cong \omega_S = |\gamma_S| B_0$, and can be dropped. The susceptibility $\chi''(\omega, \omega_S)$ reduces to the form of eq (C4).

$$\chi''(\omega, \omega_S) = \chi''\left(\omega, |\gamma_S| B_0 \right) = \xi_a \mathrm{Re} \int_0^\infty G_\perp^{\mathrm{nor,slow}}(t, B_0) \exp\left[i(|\gamma_S| B_0 - \omega) t \right] dt \tag{C4}$$

Let T_{2e}^{eff} be the characteristic decay time of $G_\perp^{\mathrm{nor,slow}}$, so that the half width of the absorption line is $1/\left(2 T_{2e}^{\mathrm{eff}} \right)$. If this width is significantly smaller than the oscillating frequency ω, the relative variation of B_0 with respect to the central field $B_c \equiv \omega / |\gamma_S|$ is small in the B_0 domain around B_c, where $\chi''\left(\omega, |\gamma_S| B_0 \right)$ has appreciable values. Thus, $G_\perp^{\mathrm{nor,slow}}(t, B_0)$ can be approximated by $G_\perp^{\mathrm{nor,slow}}(t, B_c)$ and $\chi''(\omega, \omega_S)$ simplifies to the expressions in eqs (C5) and (26)

$$\chi''(\omega,\omega_S) \cong \xi_a \, \text{Re} \int_0^\infty G_\perp^{\text{nor,slow}}(t,B_c) \exp\left[i(\omega_S - \omega)t\right] dt$$

$$= \xi_a \, \text{Re} \int_0^\infty G_\perp^{\text{nor}}(t,B_c) \exp(-i\omega t) \exp\left[i(\omega_S - \omega)t\right] dt \tag{C5}$$

Redfield Limit

In an external field $\mathbf{B}_0$, the transverse electronic (e) TCF $G_\perp(t)$ can be conveniently written in terms of the operator $S_+(t) \equiv U_e(t)^\dagger S_+ U_e(t)$ as

$$G_\perp(t) = \frac{1}{2S+1} \text{tr}\left[\overline{S_+(t)S_-}\right] \tag{C6}$$

where the bar represents the ensemble average over the various realizations of the complex.[5, 7] In order to express $G_\perp(t)$ as the product $G_\perp(t) \equiv G_\perp^{\text{slow}}(t) \exp(i\omega_S t)$ of a slowly varying term $G_\perp^{\text{slow}}(t)$ times a fast oscillating function $\exp(i\omega_S t)$, introduce the slowly varying time-dependent operator[5, 7]

$$\tilde{S}_+(t) \equiv \exp\left(-i\omega_S S_z t\right) S_+(t) \exp\left(i\omega_S S_z t\right) \tag{C7}$$

The matrix $\left(\overline{\tilde{S}_+(t)}_{MM'}\right)$ of the average value of $\tilde{S}_+(t)$ in the standard basis $|SM\rangle \equiv |M\rangle$ $(-S \le M \le S)$ of the eigenstates of $\mathbf{S}^2$ and S_z is the solution of the Redfield relaxation equation[1, 4, 5, 7]

$$\frac{d}{dt}\overline{\tilde{S}_+(t)}_{MM'} = \sum_{M_1,M_1'}' R_{MM',M_1M_1'}(-\omega_S)\overline{\tilde{S}_+(t)}_{M_1M_1'} \tag{C8}$$

where the symbol $\sum'$ means that the summation is restricted by the condition $M - M' = M_1 - M_1'$ and $\left(R_{MM',M_1M_1'}(-\omega_S)\right)$ is the Redfield relaxation super-matrix. The elements $R_{MM',M_1M_1'}(-\omega_S)$ are linear combinations [ref [7], eq 8] of complex spectral densities $j_{mm',m_1m_1'}(-\omega_S)$, which are associated with the modulation of the static and transient ZFS Hamiltonians by Brownian actual rotations and pseudo-rotations, respectively. Thus, according to ref [7], eqs 24, 29, these spectral densities are given by

$$j_{mm',m_1m_1'}(\omega) = j_{mm',m_1m_1'}^{\text{ZFS}}(\omega,\Delta_S,\tau_R) + j_{mm',m_1m_1'}^{\text{ZFS}}(\omega,\Delta_T,\tau_v) \tag{C9}$$

with

$$j_{mm',m_1m_1'}^{\text{ZFS}}(\omega,\Delta,\tau) = \frac{1}{20}\frac{(2S+3)!}{(2S-2)!}\Delta^2\frac{\tau}{1+\omega^2\tau^2}(1+i\omega\tau)\times$$

$$\times(-1)^{2S-m-m_1}\begin{pmatrix} S & 2 & S \\ -m & m-m' & m' \end{pmatrix}\begin{pmatrix} S & 2 & S \\ -m_1 & m-m' & m_1' \end{pmatrix} \tag{C10}$$

Because $\left\langle M \left| S_+ \right| M' \right\rangle = \sqrt{S(S+1) - M'(M'+1)}\, \delta_{M,M'+1}$ and the initial value of $\overline{\tilde{S}_+(t)}$ is $\overline{\tilde{S}_+(0)} = S_+$, the only non-vanishing coefficients $\overline{\tilde{S}_+(t)}_{MM'}$ form the band $\overline{\tilde{S}_+(t)}_{M,M-1}$ ($-S+1 \le M \le S$). Introduce the column matrix $X(t) \equiv \left(X_M(t) \right)$ with the $2S$ components $X_M(t) \equiv \overline{\tilde{S}_+(t)}_{M,M-1}$ and the Redfield relaxation sub-matrix $R^{(X)} \equiv \left(R^{(X)}_{MM_1} \right)$ of coefficients $R^{(X)}_{MM_1} \equiv R_{MM-1,M_1M_1-1}(-\omega_S)$, the evolution eq (C8) simplifies to

$$\frac{\mathrm{d}}{\mathrm{d}t} X_M(t) = \sum_{-S+1 \le M_1 \le S} R^{(X)}_{MM_1} X_{M_1}(t) \tag{C11}$$

The complex matrix $R^{(X)}$ is symmetric with respect to its diagonal and its anti-diagonal. To be complete for the present model of fluctuating ZFS Hamiltonian, the detailed expression of the matrix $R^{(X)}$ of a Gd^{3+} complex of spin $S = 7/2$ is given now. Define the dimensionless spectral density $\overline{j}(\omega,\tau)$ as

$$\overline{j}(\omega,\tau) \equiv \frac{1}{1 + \omega^2 \tau^2} \tag{C12}$$

The 7×7 matrix $R^{(X)}$ is the sum of static and transient contributions

$$R^{(X)} = R^{(X)\mathrm{ZFS}}\left(\omega, \Delta_\mathrm{S}, \tau_\mathrm{R}\right) + R^{(X)\mathrm{ZFS}}\left(\omega, \Delta_\mathrm{T}, \tau_\mathrm{v}\right) \tag{C13}$$

of the form

$$R^{(X)\mathrm{ZFS}}\left(\omega, \Delta, \tau\right) = \Delta^2 \tau \begin{pmatrix} R_{11} & R_{12} & R_{13} & 0 & 0 & 0 & 0 \\ R_{12} & R_{22} & R_{23} & R_{24} & 0 & 0 & 0 \\ R_{13} & R_{23} & R_{33} & 0 & R_{35} & 0 & 0 \\ 0 & R_{24} & 0 & R_{44} & 0 & R_{24} & 0 \\ 0 & 0 & R_{35} & 0 & R_{33} & R_{23} & R_{13} \\ 0 & 0 & 0 & R_{24} & R_{23} & R_{22} & R_{12} \\ 0 & 0 & 0 & 0 & R_{13} & R_{12} & R_{11} \end{pmatrix} \tag{C14}$$

where the coefficients $R_{\lambda\mu}$ are functions of (ω,τ) given by

$$R_{11}(\omega,\tau) = -\frac{6}{5}\left[9 + (29 + 13i\omega\tau)\,\overline{j}(\omega,\tau) + (11 - 8i\omega\tau)\,\overline{j}(2\omega,\tau)\right],$$

$$R_{12}(\omega,\tau) = \frac{24\sqrt{21}}{5}\,\overline{j}(\omega,\tau),\ \ R_{13}(\omega,\tau) = 6\sqrt{\frac{21}{5}}\,\overline{j}(2\omega,\tau),$$

$$R_{22}(\omega,\tau) = -\frac{6}{5}\left[4 + (29 + 3i\omega\tau)\,\overline{j}(\omega,\tau) + (21 + 2i\omega\tau)\,\overline{j}(2\omega,\tau)\right] \tag{C15}$$

$$R_{23}(\omega,\tau) = \frac{24}{\sqrt{5}}\,\overline{j}(\omega,\tau),\ \ R_{24}(\omega,\tau) = 12\sqrt{3}\,\overline{j}(2\omega,\tau),$$

$$R_{33}(\omega,\tau) = -\frac{6}{5}\left[1 + (13 - 3i\omega\tau)\,\overline{j}(\omega,\tau) + (31 + 8i\omega\tau)\,\overline{j}(2\omega,\tau)\right],\ \ R_{35}(\omega,\tau) = 24\,\overline{j}(2\omega,\tau),$$

$$R_{44}(\omega,\tau) = -6\left[(1 - i\omega\tau)\,\overline{j}(\omega,\tau) + (7 + 2i\omega\tau)\,\overline{j}(2\omega,\tau)\right]$$

The solution of the linear system (C11) of differential equations is obtained by diagonalizing the matrix $R^{(X)}$. Because $R^{(X)}$ is symmetric with respect to its diagonal and its anti-diagonal, its similarity transformation $T^{-1}R^{(X)}T$ by the symmetric matrix T

$$T_{MM_1} \equiv \frac{1}{\sqrt{2}}\left[\delta_{-M,M_1-1} - \text{sign}(M)\delta_{M,M_1} + \sqrt{2}\delta_{M,M_1}\delta_{-M,M_1-1} \right] \quad (-S+1 \leq M, M_1 \leq S) \quad (C16)$$

with $\text{sign}(M) = -1$ for $M \leq 0$, $\text{sign}(M) = 1$ for $M > 0$, has the block diagonal form

$$T^{-1}R^{(X)}T = \begin{pmatrix} R_a^{(X)} & \mathbf{0} \\ \mathbf{0} & R_b^{(X)} \end{pmatrix} \quad (C17)$$

Note that $T^{-1} = T$. The order n_e of the square matrix $R_a^{(X)}$ is $n_e = S$ for S integer and $n_e = S + 1/2$ for S half-integer. Furthermore, since the transformation $T^{-1}X(0)$ of the initial value $X(0)$ is of the form

$$T^{-1}X(0) = \begin{pmatrix} X_a(0) \\ \mathbf{0} \end{pmatrix} \quad (C18)$$

with $X_a(0)$ of dimension n_e, the transformation $T^{-1}X(t)$ of the solution $X(t)$ of eq (C11) reduces to

$$T^{-1}X(t) = T^{-1}\exp\left[R^{(X)}t \right]X(0) = T^{-1}\exp\left[R^{(X)}t \right]TT^{-1}X(0)$$

$$= \exp\left[T^{-1}R^{(X)}Tt \right]T^{-1}X(0) = \exp\left[\begin{pmatrix} R_a^{(X)}t & \mathbf{0} \\ \mathbf{0} & R_b^{(X)}t \end{pmatrix} \right]\begin{pmatrix} X_a(0) \\ \mathbf{0} \end{pmatrix} \quad (C19)$$

$$= \begin{pmatrix} \exp\left[R_a^{(X)}t \right]X_a(0) & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{pmatrix} = \begin{pmatrix} X_a(t) & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{pmatrix}$$

Thus, the Redfield limit $G_\perp^{\text{Redfield}}(t)$ of the transverse electronic TCF $G_\perp(t)$ is given by

$$G_\perp^{\text{Redfield}}(t) = \frac{1}{2S+1}\text{tr}\left[\exp(i\omega_s S_z t)\overline{\tilde{S}_+(t)}\exp(-i\omega_s S_z t)S_- \right]$$

$$= \exp(i\omega_s t)\frac{1}{2S+1}\text{tr}\left[\overline{\tilde{S}_+(t)}S_- \right] = \exp(i\omega_s t)\frac{1}{2S+1}\text{tr}\left[S_+^\dagger \overline{\tilde{S}_+(t)} \right] \quad (C20)$$

$$= \exp(i\omega_s t)\frac{1}{2S+1}X(0)^\dagger.X(t) = \exp(i\omega_s t)\frac{1}{2S+1}X_a(0)^\dagger.X_a(t)$$

Let $-R_{e,\lambda} + is_{e,\lambda}$ be the λ-th eigenvalue $(1 \leq \lambda \leq n_e)$ of the relaxation matrix $R_a^{(X)}$ and $U_\lambda \equiv (u_{\lambda'\lambda})_{1\leq\lambda'\leq n_e}$ its associated eigenvector column matrix. The quantities $R_{e,\lambda}$ with $R_{e,\lambda} \geq 0$ and $s_{e,\lambda}$ are the λ-th electronic relaxation rate and the λ-th dynamic frequency shift (s), respectively. The initial value $X_a(0)$ can be expanded in the basis U_λ of the eigenvectors of $R_a^{(X)}$ as

$$X_a(0) = \sum_{1 \leq \lambda \leq n_e} c_\lambda U_\lambda \tag{C21}$$

so that, according to eq (C19), $X_a(t)$ can be written as

$$X_a(t) = \sum_{1 \leq \lambda \leq n_e} c_\lambda \exp\left[\left(-R_{e,\lambda} + i s_{e,\lambda}\right)t\right]U_\lambda = \left(\sum_{1 \leq \lambda \leq n_e} c_\lambda \exp\left[\left(-R_{e,\lambda} + i s_{e,\lambda}\right)t\right]u_{\lambda'\lambda}\right)_{1 \leq \lambda' \leq n_e} \tag{C22}$$

Introducing the real components $x_{a\lambda'}$ of $X_a(0) \equiv (x_{a\lambda'})_{1 \leq \lambda' \leq n_e}$ and the complex components of $X_a(t)$ given by eq (C22), the expression (C20) of $G_\perp^{\text{Redfield}}(t)$ in the external field B_0 takes the analytical form

$$G_\perp^{\text{Redfield}}(B_0, t) = \exp(i\omega_S t) \sum_{1 \leq \lambda \leq n_e} w_\lambda \exp\left[\left[\left(-R_{e,\lambda} + i s_{e,\lambda}\right)t\right]\right] \text{ with } w_\lambda \equiv \frac{1}{2S+1} c_\lambda \sum_{1 \leq \lambda' \leq n_e} u_{\lambda'\lambda} x_{a\lambda'} \tag{C23}$$

It is the sum of n_e decaying complex exponentials of complex weights w_λ. The Redfield limit of the approximation (C5) or (26) of the absorption function $\chi''(\omega, \omega_S)$ is obtained from the expression of $G_\perp^{\text{Redfield,nor}}(B_0, t) \equiv G_\perp^{\text{Redfield}}(B_0, t) / G_\perp^{\text{Redfield}}(B_0, 0)$ calculated for the central field $B_0 = B_c$.

General Case

The TCF $G_\perp^{\text{nor}}(t, B_c)$, involved in the expression of $\chi''(\omega, \omega_S)$ in eqs (C5) and (26), is computed by MC simulation.[6, 8] In the time domain of the simulation, the statistical error on $G_\perp^{\text{nor}}(t, B_c)$ does not decrease in proportion to the modulus $\left|G_\perp^{\text{nor}}(t, B_c)\right|$ with increasing time t. For the numbers of GdL realizations used in the present simulations, the relative error on $G_\perp^{\text{nor}}(t, B_c)$ becomes significant with respect to $\left|G_\perp^{\text{nor}}(t, B_c)\right|$, when $\left|G_\perp^{\text{nor}}(t, B_c)\right| < 0.003$, i.e., for $t \geq t_{\text{cut-off}} \cong 1.6$ ns. In order to avoid that this statistical noise at long time induces small unphysical effects on the EPR spectrum, a direct solution would be to set $G_\perp^{\text{nor}}(t, B_c) = 0$ for $t \geq t_{\text{cut-off}}$. However, this zero padding (rectangular windowing) would create a discontinuity of $G_\perp^{\text{nor}}(t, B_c) = 0$ at $t = t_{\text{cut-off}}$, leading to Gibbs oscillations in the EPR spectrum. A convenient way to keep the actual features of $G_\perp^{\text{nor}}(t, B_c)$ as long as possible in the interval $0 \leq t < t_{\text{cut-off}}$ and to set $G_\perp^{\text{nor}}(t, B_c) \to 0$ continuously for $t \geq t_{\text{cut-off}}$ is to multiply $G_\perp^{\text{nor}}(t, B_c)$ by a decreasing positive window (w) function $f_w(t)$, which is 1, nearly up to $t = t_{\text{cut-off}}$, and then rapidly, but continuously, decreases to 0. A convenient choice of $f_w(t)$ using the hyperbolic tangent is

$$f_w(t) \equiv 1 - \tanh\left[\left(t/t_{\text{cut-off}}\right)^{n_w}\right] \tag{C24}$$

with an exponent $n_w \cong 10$, chosen to be $n_w = 12$ in this work.

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Experimental part

Chemicals

All the chemicals were purchased from Aldrich and used without further purification. All the solvents used were HPLC-grade solvents. Heavy water D_2O (99.9% in D) was obtained from Eurisotop. The water used was purified by passing through a Millipore Milli-Q reverse-osmosis cartridge system (resistivity 18 MΩ cm). The exact concentrations of the metal stock solutions were systematically determined by colorimetric titration using standardized H_2Na_2edta solution (Merck).

Synthesis of hexakis(2-*O*-carboxymethyl-3,6-anhydro)-α-cyclodextrin, hexasodium salt (ACXNa$_6$):

The per(3,6-anhydro)-α-cyclodextrin was prepared according to literature procedures.[1] A solution of per(3,6-anhydro)-α-cyclodextrin (1 g, 1.15 mmol) in dry DMSO (10 mL) was stirred for 3 hours with a solution of NaH in DMSO (2 N, 7 mL) at room temperature under an argon atmosphere. Sodium monochloroacetate (1.6 g, 14 mmol) was added and the mixture was maintained at 45 °C under an argon atmosphere for 15 hours. DMSO was removed under vacuum, the residue was dispersed in acetone for one day and then was centrifuged. The precipitate was dissolved in water (200 mL) and dialysed (3 days, 1.5 L water, Spectra/Port®CE Sterile DispoDialysers®-cellulose ester membrane-MWCO 500). The final solution was lyophilized and 1 g of product was obtained (54 %).

^{1}H NMR (400 MHz, D_2O, δ) : 3.82 (t, J = 3.0 Hz, 6H, H$_2$), 4.03 (dd, J = 11.0 and 2.5 Hz, 6H, H$_6$'), 4.09 (ABd, J = 15.9 Hz, 6H, H$_7$), 4.14 (ABd, J = 15.9 Hz, 6H, H$_7$'), 4.29 (d, J = 11.0 Hz, 6H, H$_6$) 4.34 (dd, J = 5.0 and 2.1 Hz, 6H, H$_4$), 4.65 (s, 6H, H$_5$), 4.77 (t, J = 5.0 Hz, 6H, H$_3$), 5.35 (d, J = 3.0 Hz, 6H, H$_1$)

^{13}C NMR (125 MHz, D2O, δ) : 70.9 (C$_6$), 72.8 (C$_3$), 73.1 (C$_7$), 76.3 (C$_5$), 77.6 (C$_2$), 80.7 (C$_4$), 101.0 (C$_1$), 179.7 (C$_8$)

Anal. Calculated for ACXNa$_6$, 14.5 H_2O : C, 35.90%, H, 5.21%, Na, 8.59%. Found C, 35.86%, H, 5.03%, Na, 8.53%.
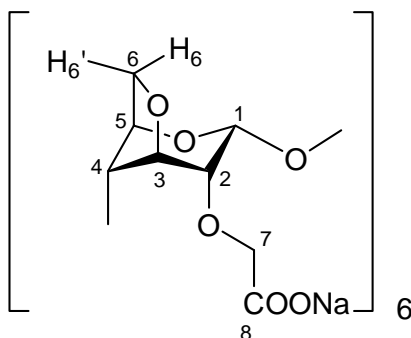
Scheme S1. Numbering scheme for NMR assignment

The synthesis carried out to obtain the deuterated product was the same but for the use of deuteriated sodium monochloroacetate.

Potentiometry.

Carbonate-free 0.1 molL^{-1} KOH and 0.1 molL^{-1} HCl were prepared from Fisher Chemicals concentrates. Potentiometric titrations were performed in 0.1 molL^{-1} aqueous KCl or NaCl or Bu$_4$NCl (electrolyte solution) under an argon atmosphere, the temperature was controlled to ±0.1 °C with a circulating water bath. The p[H] (p[H] = -log[H$^+$], concentration in molarity) was measured in each titration with a combined pH glass electrode (Metrohm) filled with 3M KCl and the titrant addition was automated by use of a 751 GPD titrino (Metrohm). The electrode was calibrated in hydrogen ion concentration by titration of HCl with KOH in 0.1 molL^{-1} electrolyte solution.[2] A plot

of meter reading versus p[H] allows the determination of the electrode standard potential (E°) and the slope factor (f). Continuous potentiometric titrations with HCl and KOH 0.1 molL^{-1} were conducted on 20 mL of aqueous solutions containing 0.001 molL^{-1} of ACX in 0.1 molL^{-1} of electrolyte solution, with an interval of 2 minutes between 2 points. The titrations of the metal complexes were performed on 20 mL solutions of ACX (0.001 M) containing 0.5, 1 and 2 equivalents of metal cation, with with an interval of 5 to 30 minutes between 2 points. Back titrations with 0.1 molL^{-1} KOH were systematically performed after each experiment to check whether thermodynamic equilibrium had been achieved.

Experimental data were refined using the computer program Hyperquad 2000.[3, 4] All equilibrium constants are concentration quotients rather than activities and are defined as:

$\beta_{mlh} = \dfrac{[M_m L_l H_h]}{[M]^m [L]^l [H]^h}$. The ionic product of water at 25 °C and 0.1 molL^{-1} ionic strength is pK$_w$ =

13.77.[5] Fixed values were used for pK$_w$, ligand's acidity constants and total concentrations of metal, ligand and acid. All values and errors (one standard deviation) reported are at least the average of three independent experiments.

NMR spectroscopy

^{1}D spectra and assignment

NMR spectra were recorded either on a Bruker Avance-400 or a Varian Mercury-400 spectrometer at 298 K. ^{1}H NMR spectra were typically recorded with 10 ppm window and 32 k data points in the time domain. TOCSY experiments were performed using a MLEV-17[6] spin-lock sequence with a mixing time of 200 ms. t-ROESY experiments were recorded with a mixing time of 250 ms.[7, 8] For paramagnetic samples, the window was adjusted to 60 ppm (Eu) or 120 ppm (Yb).

Diffusion coefficient determination

Diffusion coefficient measurement were performed on a Bruker Avance-500 spectrometer equipped with a 5 mmm BBI probe with a triple axis gradient-field, using the bipolar stimulated spin echo sequence.[9] Diffusion coefficients were obtained using, I(δ, Δ, g)= I$_0$ exp[-$\gamma^2 g^2 \delta^2(\Delta-^\delta/_3)$D], where I($\delta$, Δ, g) and I$_0$ are the intensities in the presence of gradient pulses of strength g and in absence of gradient pulses respectively. The length of the gradient pulse is δ, Δ is the diffusion delay and γ is the gyromagnetic ratio (for protons, γ = 26.7520×10^7 rad.T^{-1}.s^{-1}). The values of Δ and δ used in the diffusion coefficient measurements were 96 ms and 2 ms respectively. In the experiments g was incremented from 0.59 to 47.79 G.cm^{-1}.

The samples were prepared in D$_2$O, with [ACX] = 0.2, 1, 10, 25 mM with or without KCl 0.1 M. The lutetium complex was prepared in situ by adding one equiv. of Lu(OTf)$_3$.

^{2}H NMR

^{2}H NMR spectra were acquired on a Varian Mercury-400 spectrometer (9.4 T, 61.42 MHz), equipped with a 5 mm AutoSwitchable probe, with 2000 Hz of spectral width. The longitudinal relaxation times T$_1$ were obtained with the inversion-recovery sequence.[10] The samples were prepared in H$_2$O with [ACX] = 2, 10, 25 mM with or without KCl 0.1 M. The lanthanum complex was prepared in situ by adding one equiv. of La(OTf)$_3$, pH = 6.

^{17}O NMR:

^{17}O NMR spectra were acquired on a Varian Mercury-400 spectrometer(9.4 T, 54.25 MHz), equipped with a 5 mm AutoSwitchable probe, with 10000 Hz of spectral width. Small aliquots of a concentrated solution of DyCl$_3$.6H$_2$O were added to a 30 mM ACX solution, so that [Dy] ranges from 0 to 90 mM. The chemical shifts of the ^{17}O peak are recorded versus the fraction of Dy added. The value of Δ/[H$_2$0] was previously determined by doing the same experiment with DyCl$_3$.6H$_2$O only. The number of water molecule q directly bound to the lanthanide is obtained using

$$\delta_{OLn}^{para} = q\Delta \frac{[Dy(ligand)_n(H_2O)_q]}{[H_2O]}$$, where δ_{OLn}^{para} is the paramagnetic chemical shift of ^{17}O, Δ is the

paramagnetic chemical shift of the ^{17}O bound to Dy.[11, 12]

EPR

The EPR spectra were recorded on a BRUKER continuous wave X band EMX spectrometer at room temperature, with a rectangular cavity ER 4116 DM. The Gd_2ACX complex solution was prepared in situ by mixing one equivalent of ligand with two equivalents of Gd in KCl 0.1 mol.L^{-1}, pH = 5. The $Gd_2ACX(OH)_2$ complex solution was prepared from the Gd_2ACX solution by adjusting the pH to 8 with KOH 0.1 M. The diamagnetic complex of Yttrium was prepared as described above and doped with 10% of gadolinium.

Luminescence

Terbium luminescence lifetimes were measured by recording the decay of the emission intensity at 545 nm after excitation at 368 nm (direct excitation of Tb, $\epsilon = 0.34$ L.mol^{-1}.cm^{-1}). Europium luminescence lifetimes were recorded the same way with the emission fixed at 616 nm and the excitation at 396 nm (direct excitation of Eu, $\epsilon = 2.77$ L.mol^{-1}.cm^{-1}). The signals were analyzed as single-exponential decays. The instrument settings were as follows : a gate time of 1 ms, a flash count of 1, excitation and emission slit widths of 10 nm, and a varied delay time.
The complexes are prepared in situ by mixing 0.9 equiv. of the metal solution with one equivalent of ligand and the concentration used were as follow : [MACX] = 0.1 ; 1 ;10 mmol.L^{-1} in Millipore water and D_2O with the desired electrolyte (KCl, NaCl, Bu$_4$NCl 0.1 mol.L^{-1}or no electrolyte).

Relaxivity measurements

The $R_1 = 1/T_1$ NMRD profiles were obtained at 298 K in the range $0.03 - 35$ MHz by using a Spinmaster FFC (fast field cycling) NMR relaxometer (Stelar, Italy).
Two samples were prepared in situ by mixing the appropriate amounts of ACX and $GdCl_3.6H_2O$:
    [ACX] = 1.11 mM, [Gd] = 0.89 mM and pH = 6
        [ACX] = 1.53 mM, [Gd] = 0.95 mM and pH = 6
These two samples gave the same NMRD profile.

The relaxation times at 400 MHz were determined on Varian Mercury-400 and Unity-400 spectrometers. The relaxivity values were obtained through eq (2) with the measured diamagnetic relaxation rate $R_{10} = R_{20} = 0.4$ s^{-1}.
The study of the variation of the PRE with [GdL] was carried out on a Varian Mercury-400 spectrometer. A capillary tube containing D_2O was inserted in the samples prepared in light water, for the lock. The T_1 values were measured by the saturation-recovery sequence using small detection angles to avoid ADC overflow and radiation damping.
The r_1, r_2 and $r_{1\rho}$ were measured on a Varian Unity-400 spectrometer, with a 29 dB attenuator placed on the receiver canal to avoid ADC overflow with these samples prepared in light water. A capillary tube containing the sample was inserted in a 5 mm NMR tube containing D_2O. The T_1 values measured by the standard inversion-recovery sequence and the saturation-recovery sequence with small detection angles gave the same values, demonstrating that there were no artifacts caused by radiation damping. The T_2 measured by the CPMG sequence and the $T_{1\rho}$ measured by classical spin-lock experiments gave the same values.[13]
Because the relaxivities follow the significant variation with temperature of the GdL/water molecular dynamics, they are best measured on the same spectrometer operating at a fixed displayed temperature. Indeed, denoting the solution viscosity by η, the PRE decrease with temperature is about 3 % per Kelvin, when assuming that it follows the variation in η/T of the diffusional correlation times stemming from Stokes-Einstein laws. Therefore, even small uncontrolled temperature differences, stemming from the use of different spectrometers, would lead

to spurious variations of the PRE that may be significant with respect to its departure, often modest, from a linear increase with $[GdL]$. A small temperature difference ($\sim$ 1 K) between the two spectrometers used in this study explains the difference of 2% in the measured r_1: $r_1 = 22.4$ mM^{-1}.s^{-1} (Mercury) and 22.9 mM^{-1}.s^{-1} (Unity).

The samples for the T_1 measurements of the protons of the outersphere probes at 400 MHz as a function of the concentration of Gd are prepared in KCl 0.1 mol.L^{-1} and D_2O, as follow : [ACX] = 2 mmol.L^{-1}, $[CH_3SO_3Na]$ = [tBuOH] = 2*[(CH$_3$)$_4$NCl] = 20 mmol.L^{-1} and [Gd] ranges from 0 to 6 mmol.L^{-1}. The same experiment has been performed without ACX. The relaxivities due to GdACX^{3-} and Gd(D$_2$O)$^{3+}$ were obtained as the slopes of the linear increases of the PREs R_{1p} *vs* [Gd^{3+}] for [Gd^{3+}] < [ACX] and in absence of ACX, respectively.

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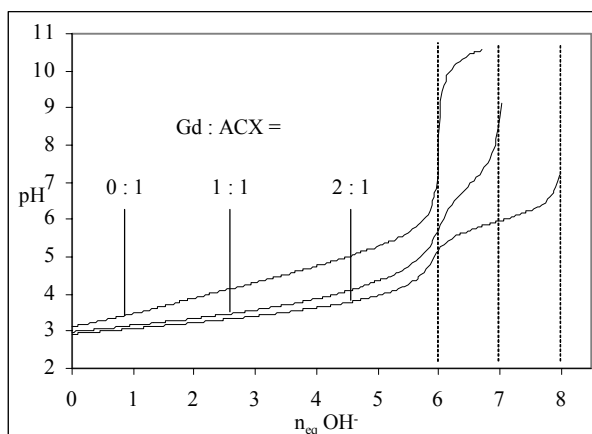(13) Canet, D.; Boubel, J. C.; Canet-Soulas, E., *La RMN: Concepts, Méthodes et Applications*. Dunod: Paris, 2002.

Figure S1. Alkalimetric titrations of solutions containing 10^{-3} mM $ACXH_6$ with 0, 1 and 2 equivalents of $GdCl_3$, in water KCl 0.1 M at 298 K.
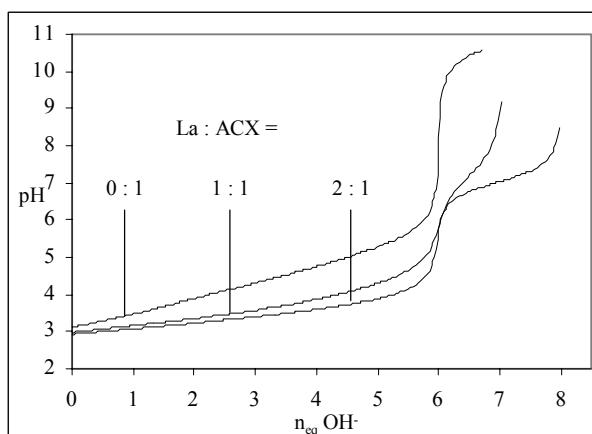

Figure S2. Alkalimetric titrations of solutions containing 10^{-3} mM $ACXH_6$ with 0, 1 and 2 equivalents of $LaCl_3$, in water KCl 0.1 M at 298 K.
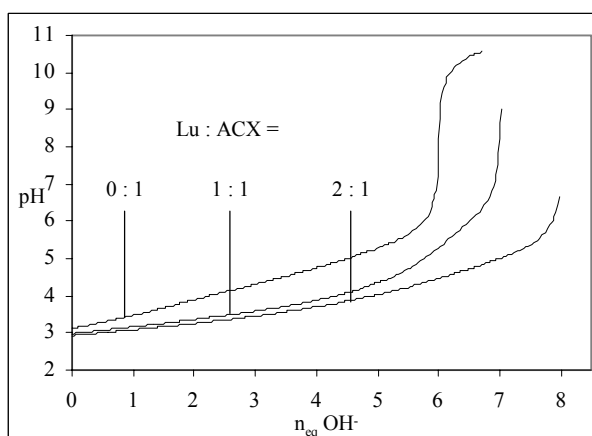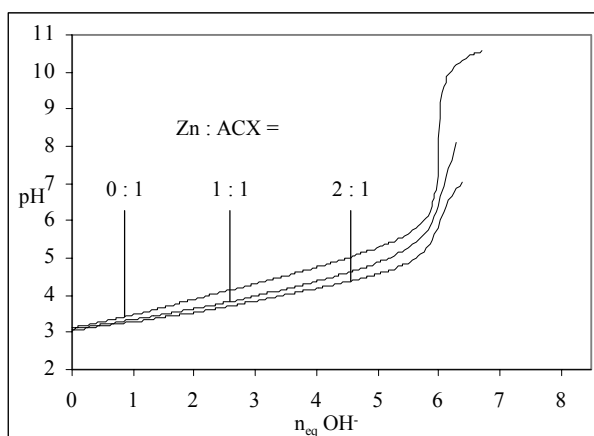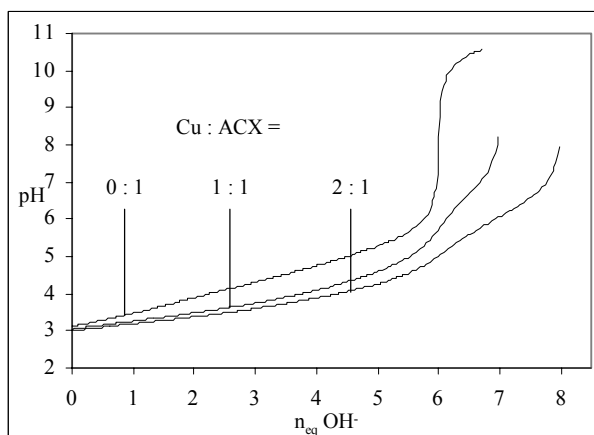

Figure S3. Alkalimetric titrations of solutions containing 10^{-3} mM $ACXH_6$ with 0, 1 and 2 equivalents of $LuCl_3$, in water KCl 0.1 M at 298 K.
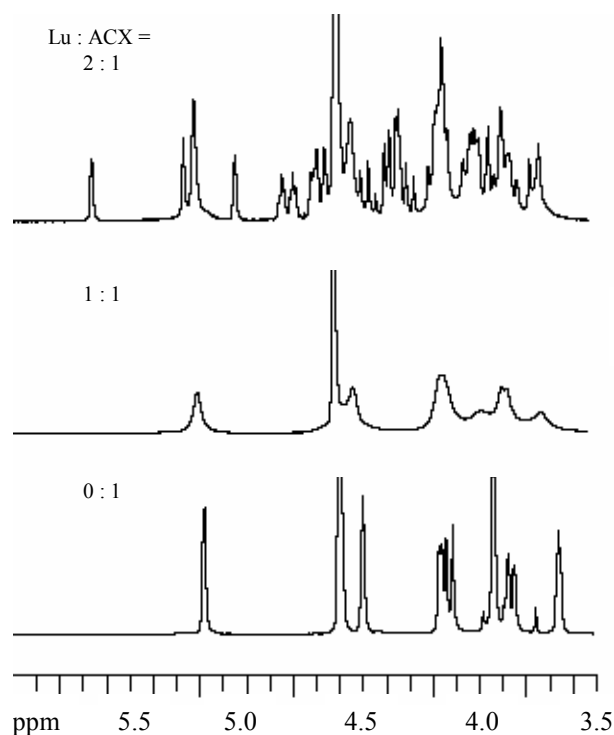
Figure S4. Alkalimetric titrations of solutions containing 10^{-3} mM $ACXH_6$ with 0, 1 and 2 equivalents of $ZnCl_2$, in water KCl 0.1 M at 298 K.

Figure S5. Alkalimetric titrations of solutions containing 10^{-3} mM $ACXH_6$ with 0, 1 and 2 equivalents of $CuCl_2$, in water KCl 0.1 M at 298 K.

Figure S6. 400 MHz proton NMR spectra during the titration of ACX with Lu(OTf)$_3$ in D$_2$O at 298 K.
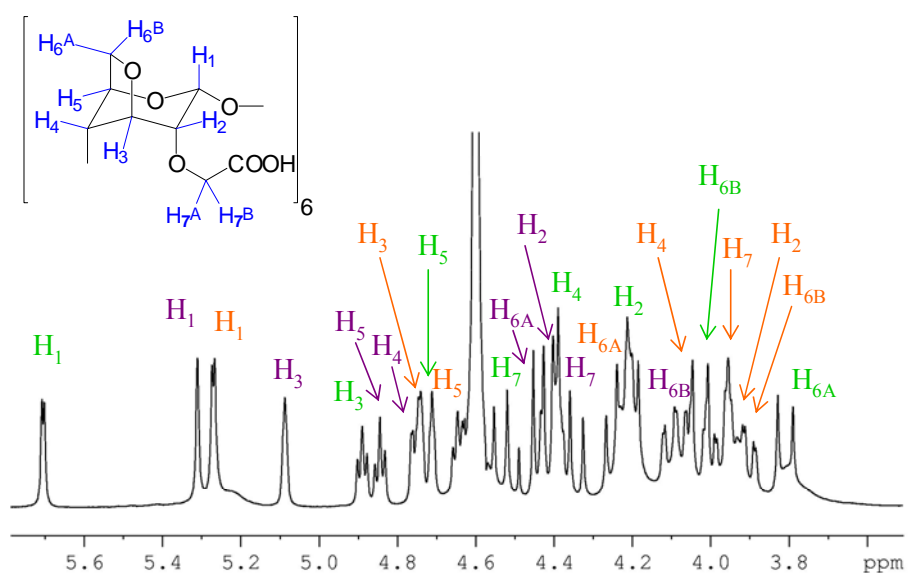

Figure S7. Assignment of the ^{1}H NMR spectrum of the Lu$_2$ACX complex at 400 MHz in D$_2$O at 25 °C (non equivalent spin systems are represented with different colors).
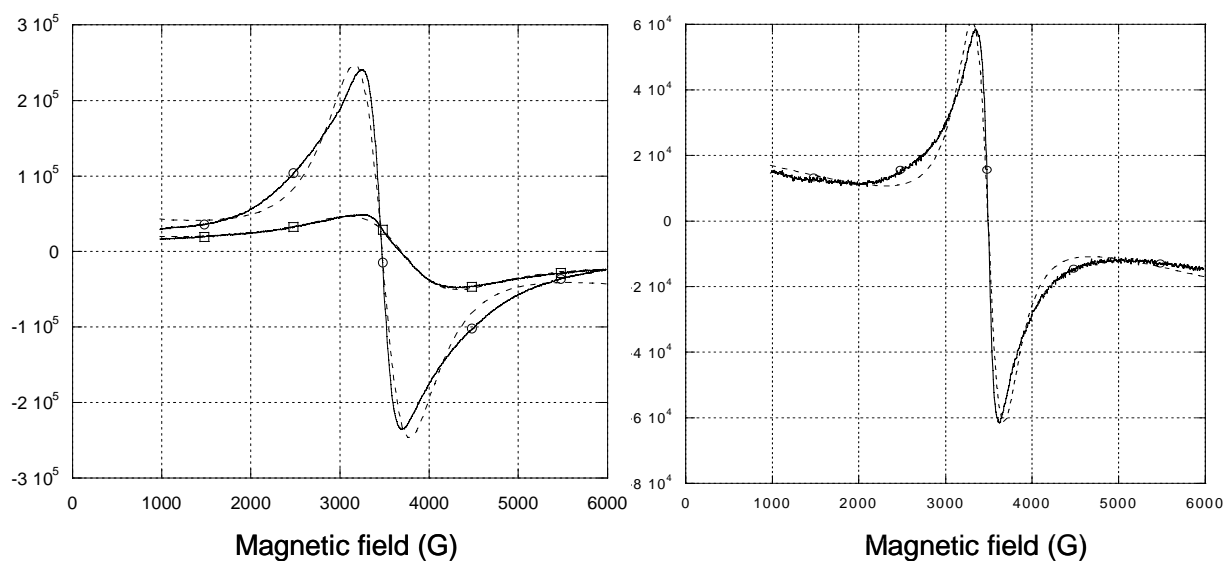
Figure S8. X-band EPR spectra of : **left** Gd_2ACX (○), $Gd_2ACX(OH)_2$ (□), **right** GdYACX (○) complexes. Dotted lines represent the fits to derivatives of lorentzian shapes including a linear baseline correction.

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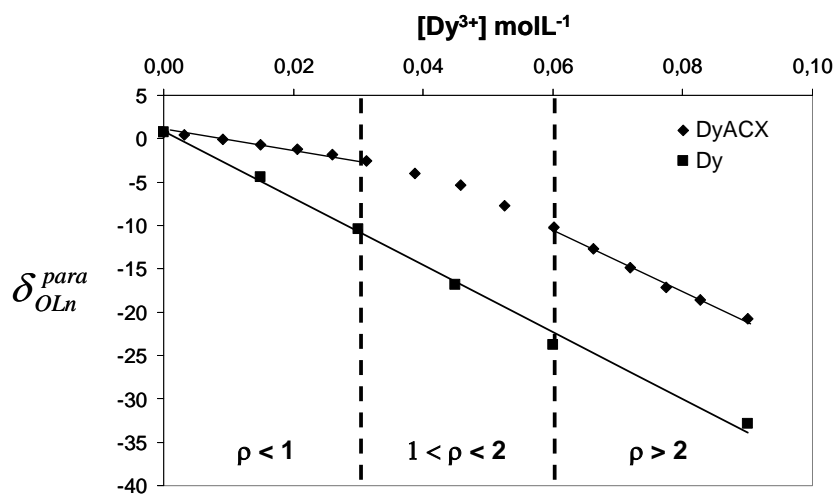**Figure S9.** ^{17}O NMR shifts at 54.25 MHz and 25 °C as a function of $[Dy^{3+}]$ in the presence of $[ACX] = 30$ mM and $[KCl] = 1$ M, $\rho = [Dy^{3+}]/[ACX]$.

Table S1. Relaxivity of water protons in H_2O KCl 0.1 M measured at 400 MHz and 298 K.

[GdACX] mM	r_1 $s^{-1}mM^{-1}$
0.19	22.4(2)
0.95	22.5(2)
1.9	22.2(2)

Table S2. Luminescence lifetimes in H_2O and D_2O and calculated hydration states in water KCl 0.1 M for the complexes EuACX and TbACX

	$\tau_{H2O}(ms)$	$\tau_{D2O}(ms)$	q_{Parker}	$q_{Horrocks}$
EuACX	0.21	1.95	4.8	4.5
TbACX	0.60	1.43	4.5	4.1