Magnetic alignment and quadrupolar/paramagnetic cross-correlation in complexes of Na with LnDOTP\(^5\)

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**ABSTRACT**

The observation of a double-quantum filtered signal of quadrupolar nuclei (e.g. \(^{23}\)Na) in solution has been traditionally interpreted as a sign for anisotropic reorientational motion. Ling and Jerschow (2007)\(^{23}\) have found that a \(^{23}\)Na double-quantum signal is observed also in solutions of TmDOTP\(^5\). Interference effects between the quadrupolar and the paramagnetic interactions have been reported to lead to the appearance of double-quantum coherences even in the absence of a residual quadrupolar interaction. In addition, such processes lead to differential linebroadening effects between the satellite transitions, akin to effects that are well known for dipolar-CSA cross-correlation. Here, we report experiments on sodium in the presence of LnDOTP compounds, where it is shown that these cross-correlation effects correlate well with the pseudo-contact shift. In addition, anisotropic g-values of the lanthanide compounds in question, can also lead to alignment within the magnetic field, and consequently to the appearance of line splitting and double-quantum coherences. The two competing effects are demonstrated and it is concluded that both cross-correlated relaxation and alignment in the magnetic field must be at work in the systems described here.

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### 1. Introduction

Sodium is abundant in vivo and its relatively favorable NMR properties combined with its important physiological functions make it a particularly attractive nucleus to study in tissues and in vivo. The sodium gradient across cell membranes and walls has been a subject of interest due to its diagnostic value in assessing the functioning of cells\(^1–5\).

Sodium NMR experiments in the presence of lanthanide-containing chemical shift agents have become common for distinguishing between the signals from intra- and extracellular sodium compartments. Typically, a lanthanide ion in a chelating complex with an anisotropic g-tensor, such as Tm or Dy complexed with DOTA (1,4,7,10-tetraazacyclododecane-[1,4,7,10]-tetraacetic acid), DTPA (diethylenetriaminepentaacetic acid), DOTP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetra(methylene phosphonate)) or similar chelates, are used\(^6–10\). Cations, and sodium in particular, bind strongly to such agents, and a sizable pseudocontact shift in the sodium resonances can be observed\(^11,12\). The agent is thought to stay outside of the cell, and therefore the appearance of a significantly shifted sodium resonance is assigned to the extracellular compartment\(^2,5\), with typically a much smaller resonance seen for the intracellular sodium. Several in vivo studies have also been conducted based on such premises\(^8,13,14\).

Double- and triple-quantum filter experiments (DQF and TQF) are useful methods for determining the ions' motional or orientational properties\(^15–17\). DQF signals, if acquired with the necessary precautions can be made to respond solely to sodium ions that experience a residual quadrupolar interaction. TQF signals can arise from both a residual quadrupolar coupling and relaxation effects in the slow-motion regime\(^15–18\). It is the latter quality that is made use of when attempting to select intracellular sodium signals with a TQF experiment, because the tumbling rates are much slower in that compartment than in the extracellular one. Some other methods, based on jump-and-return\(^19\) and optimal control methodology\(^19–22\) have been developed to provide additional selectivity and specificity for residual quadrupolar couplings and slow motion regimes.

In addition, recent reports have combined multiple-quantum filters with the use of shift agents for answering certain questions about cell viability in vivo\(^8\). Recently, however, a new cross-correlated relaxation mechanism was reported, which would predict the appearance of DQF signals, even in the absence of a residual quadrupolar coupling\(^23\), thereby undermining long-held assumptions. This mechanism is based on the correlation between the paramagnetic pseudo-contact interaction with the nuclear spin and the quadrupolar interaction. This process then may lead to the appearance of DQF signals or to differential line broadening\(^23\).
In this work, we present a more systematic study of the NMR properties of sodium ions in the presence of different Lanthanide complexes, where sample conditions such as pH, sodium concentration, and temperature are examined as modifying the underlying mechanisms. Both a residual quadrupolar splitting and differential line broadenings are observed, as well as, DQF signals. These findings suggest that both a partial alignment of the complexes in the magnetic field, as well as, the above-mentioned cross-correlated relaxation mechanism occur in these complexes.

1. Theory

1.1. Mechanism of quadrupolar/paramagnetic cross-correlation

The treatment of the quadrupolar/paramagnetic cross-correlation mechanism presented here is similar to the more common paramagnetic/dipolar coupling cross-correlated mechanism, which has enabled the determination of geometrical constraints for structure determination in molecules [24–29].

The electron–nuclear interaction can occur either via the Fermi-contact interaction, which is a result of a non-vanishing probability for finding the electron at the site of the nucleus, or via a nuclear-electron spin dipolar interaction [30]. The Fermi-contact interaction can be neglected in the systems discussed here (Na–LnDOTP complexes), because the delocalization of the electron spins between the sodium nuclei and the coordinating ligand molecules is minimal. In the case of the nuclear-electron dipolar interaction, one may further distinguish the case of an isotropic susceptibility [31], or a susceptibility mechanism (Curie mechanism) [30,32,33]. In the former, the nuclear interacts directly with the electron spin, in the latter, the nucleus interacts with a time-averaged magnetic field produced by the rapidly relaxing electron spin. For Ln(III) except Gd(III), the electron spin relaxation time $T_2$ is much shorter than the rotational correlation time $\tau_\text{r}$, and the Solomon mechanism can be neglected [33]. In the special case of isotropic susceptibility the averaged magnetic moments are

$$\langle \mu_z \rangle = \frac{g_e \mu_B B_0}{3kT} S(S+1) \quad \text{and} \quad \langle S_z \rangle = 0,$$

where $g_e$ is the electron g-factor, $\mu_B$ is the Bohr magneton. For rare earth elements, one may replace the spin angular momentum by the total angular momentum, thus, the spin angular momentum $S$ should be substituted by the total angular momentum $J$, and the electronic g-factor, $g_e$, by the Landé factor $g_J$ [32].

The paramagnetic center may be anisotropic, in which case one may consider a thermally averaged anisotropic susceptibility tensor $\chi$ [34]. We now follow the treatment of Vega and Fiat [35] and describe the nucleus-electron dipolar interaction as

$$H_F = \gamma \mathbf{I} \cdot \mathbf{T} \cdot \mathbf{Iz} \cdot \mathbf{B}_0,$$

where the components of the tensor $T$ are given by

$$T_{ij} = \frac{1}{4\pi} \frac{1}{r_i r_j - \delta_{ij} r^2},$$

with $i,j$ being spatial indices, and $r_1, r_2, r_3$ are the coordinates x, y, z, respectively.

In the frame where $\chi$ is diagonal, one obtains

$$T \cdot \chi = \frac{1}{4\pi} \begin{pmatrix}
(3x^2 - r^2)\chi_x r^{-5} & 3xy\chi_y r^{-5} & 3xz\chi_z r^{-5} \\
3yx\chi_y r^{-5} & (3y^2 - r^2)\chi_y r^{-5} & 3yz\chi_z r^{-5} \\
3zx\chi_z r^{-5} & 3zy\chi_y r^{-5} & (3z^2 - r^2)\chi_z r^{-5}
\end{pmatrix},$$

where, $\chi_x$, $\chi_y$, and $\chi_z$ are the principal components of the susceptibility tensor, and $r$ is the distance between the nucleus and the paramagnetic center.

The Hamiltonian in Eq. (2) will depend on the set of Euler angles $\Omega$ that connect the orientation of $T \chi$ with the laboratory frame. One can then expand $H_F$ according to the rotational properties as

$$H_F(\Omega) = \sum_{m=-I}^{I} (-1)^m F_{2m}^0 Q_{2m} D_{2m}^m(\Omega),$$

where $D_{2m}^m$ are the Wigner rotation elements. Then the electronic/spatial components can be written as

$$F_{2m}^{0,0} = \frac{1}{4\pi} \left( \begin{array}{l}
\langle 1/3 \rangle \gamma B_0 r^{-5} \left[ (3x^2 - r^2)\chi_x + (3y^2 - r^2)\chi_y + (3z^2 - r^2)\chi_z \right],
\end{array} \right.$$

$$= \frac{1}{4\pi} \left( \begin{array}{l}
(3/y^2)\gamma B_0 r^{-5} \left[ 3x^2 - r^2 \right] - 3xy\gamma B_0 r^{-5} \left[ 3y^2 - r^2 \right] + 3yz\gamma B_0 r^{-5} \left[ 3z^2 - r^2 \right].
\end{array} \right.$$

$$F_{2m}^{1,0} = -\frac{1}{4\pi} \left( \begin{array}{l}
(3/2) \gamma B_0 r^{-5} \left[ (3x^2 - r^2)\chi_x + (3y^2 - r^2)\chi_y + (3z^2 - r^2)\chi_z \right],
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\end{array} \right.$$

$$F_{2m}^{1,1} = -\frac{1}{4\pi} \left( \begin{array}{l}
(3/2) \gamma B_0 r^{-5} \left[ (3x^2 - r^2)\chi_x + (3y^2 - r^2)\chi_y + (3z^2 - r^2)\chi_z \right],
\end{array} \right.$$

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\end{array} \right.$$

$$H_Q = \sum_{m=-2}^{2} (-1)^m F_{2m}^0 Q_{2m} T_{2m}^0.$$
Application of Redfield theory then yields the expressions of the conversion rates between different spherical tensor operators (see previous article, Table 1) in terms of the auto- and cross-correlated spectral density functions $f^{\mathcal{O}_0}, f^{\mathcal{O}_p}, f^{\mathcal{O}_q}$.

Both rotational motion and exchange can be the primary mechanisms for the fluctuations underlying the spectral density functions. Exchange would modulate the electric field gradient, thus leading to fluctuations in $\omega_Q$ directly. There is evidence for very strong binding of sodium to LnDOTP compounds [11], hence it is reasonable to assume that the rotational motion is the primary mechanism of the fluctuating relaxation mechanisms with $\omega_Q$ being constant. Assuming $\theta$ being the azimuthal angle between the principal components of the paramagnetic and quadrupolar interactions, a rotational correlation time $\tau_r$ and Larmor frequency $\omega$, one can write the cross-correlated spectral density function $f^{\mathcal{O}_p}$ as

$$f^{\mathcal{O}_p}(\omega) = \frac{\sqrt{6}}{8} f^{\mathcal{O}_p} \frac{\omega_0 \tau_r}{\omega_0^2} \frac{\tau_r}{1 + (\omega \tau_r)^2},$$  \hspace{1cm} (17)

in analogy with the dipolar/CSA cross-correlation [38] or dipolar/paramagnetic cross-correlation mechanisms [27]. Using the expressions of Eq. (9) for $f^{\mathcal{O}_p}$ and Eq. (6) of the pseudo-contact shift $\Delta \omega_{\text{PCS}} = f^{\mathcal{O}_0}$, one can rewrite Eq. (17) to reflect directly the contribution of the pseudo-contact shift to the cross-correlated spectral density function via

$$f^{\mathcal{O}_p}(\omega) = \frac{\sqrt{3}}{4 \pi} B_0 \gamma \left[ \frac{1}{8} \rho_0 \left( 3 \tau_r^2 - \tau_r^4 \right) \chi_2 - \Delta \omega_{\text{PCS}} \right].$$  \hspace{1cm} (18)

In order to set up an equation of motion, it is convenient to expand the density matrix in terms of spherical tensor operators,

$$\rho(t) = \sum_{lm} \rho_{lm}(t) T_{lm}.$$  \hspace{1cm} (19)

As a representative case, the relevant equation for the single-quan

$$\frac{d}{dt} \begin{pmatrix} v_{11} \\ v_{21} \\ v_{12} \end{pmatrix} = -\left( \mathbf{R} + i \mathbf{\Omega} \right) \begin{pmatrix} v_{11} \\ v_{21} \\ v_{12} \end{pmatrix},$$  \hspace{1cm} (20)

where the non-zero elements of the 3 by 3 matrix $\mathbf{R}$ can be determined from the corresponding Redfield expression [23,39] as

$$R_{11} = \frac{1}{2} f^{\mathcal{O}_p}(0) + \frac{3}{8} f^{\mathcal{O}_p}(\omega) + \frac{9}{8} f^{\mathcal{O}_q}(0) + \frac{3}{8} f^{\mathcal{O}_q}(\omega) + \frac{6}{5} f^{\mathcal{O}_q}(2\omega),$$  \hspace{1cm} (21)

$$R_{12} = \frac{3 \sqrt{3}}{5} \left[ 2 f^{\mathcal{O}_p}(0) + f^{\mathcal{O}_q}(\omega) \right],$$  \hspace{1cm} (22)

$$R_{13} = \frac{9}{5} \left[ \frac{3}{5} f^{\mathcal{O}_q}(0) - f^{\mathcal{O}_q}(2\omega) \right],$$  \hspace{1cm} (23)

$$R_{21} = \frac{\sqrt{3}}{2} \left[ 2 f^{\mathcal{O}_p}(0) + f^{\mathcal{O}_p}(\omega) \right],$$  \hspace{1cm} (24)

$$R_{22} = \frac{1}{2} f^{\mathcal{O}_p}(0) + \frac{15}{8} f^{\mathcal{O}_p}(\omega) + \frac{3}{8} f^{\mathcal{O}_q}(0) + \frac{3}{8} f^{\mathcal{O}_q}(\omega) + \frac{6}{5} f^{\mathcal{O}_q}(2\omega),$$  \hspace{1cm} (25)

$$R_{23} = \frac{3}{\sqrt{3}} \left[ f^{\mathcal{O}_p}(0) + 3 f^{\mathcal{O}_q}(\omega) \right],$$  \hspace{1cm} (26)

$$R_{31} = 2 \left[ \frac{3}{5} f^{\mathcal{O}_q}(0) - f^{\mathcal{O}_q}(2\omega) \right],$$  \hspace{1cm} (27)

$$R_{32} = \frac{4}{\sqrt{3}} \left[ f^{\mathcal{O}_p}(0) + 3 f^{\mathcal{O}_q}(\omega) \right],$$  \hspace{1cm} (28)

$$R_{33} = \frac{1}{2} f^{\mathcal{O}_p}(0) + \frac{33}{8} f^{\mathcal{O}_p}(\omega) + \frac{6}{5} f^{\mathcal{O}_q}(0) + \frac{3}{8} f^{\mathcal{O}_q}(\omega) + \frac{9}{5} f^{\mathcal{O}_q}(2\omega).$$  \hspace{1cm} (29)

Corresponding expressions can be derived for the singly negative cross-correlations

$$\frac{9}{8} f^{\mathcal{O}_q}(\omega) \pm \frac{3 \sqrt{3}}{2} f^{\mathcal{O}_p}(0) + 3 f^{\mathcal{O}_q}(\omega),$$  \hspace{1cm} (30)

where one transition shows constructive while the other shows destructive interference with the cross-correlation effect, thus clearly pointing to a difference in linewidths between the two. It will be shown below, that such differential linebroadening effects can indeed be seen in the spectra of the complexes under investigation.

In addition, the appearance of a differential dynamic frequency shift (DFS) of all three resonances is expected [18,39,42], which would resemble a residual quadrupolar coupling interaction [18]. Under most practical circumstances, however, it may be overshadowed by the large resonance broadening due to paramagnetic relaxation.

1.1.2. Mechanism of alignment

Alignment of small molecules in strong magnetic fields as a result of anisotropic magnetic susceptibility has been observed for diamagnetic organic molecules. It was demonstrated by $^2$H line splittings as a result of residual quadrupolar interactions [43]. Since then, paramagnetically-induced alignment in the magnetic field has been used for aligning proteins and lipids [34].

Since the degree of preferential alignment is relatively small, one may neglect the non-secular terms of the quadrupolar coupling, and the residual quadrupolar interaction may be written as

$$H_Q = \frac{\sqrt{3}}{2} \left[ \frac{\omega_0}{2} T^{\mathcal{O}_q} - \frac{\omega_0}{2} (\mathbf{I}_1 - \mathbf{I}_2), \right]$$  \hspace{1cm} (31)

where

$$\omega_0^{\text{res}} = \omega_Q \left( P_2 (\cos \theta) + \frac{\eta}{2} \cos 2\phi \sin^2 \theta \right),$$  \hspace{1cm} (32)

with $P_2$ the second order Legendre polynomial, and $\theta$ and $\phi$ the angles describing the rotation from the quadrupolar principal axis system to the orientation of the magnetic field ($z$) in the laboratory frame, and the rest as above. The angled brackets describe time averaging of the parameters. The parameter $\omega_0$ is included within the angled brackets to indicate that the electric field gradient itself may fluctuate. A common case where the electric field gradient
would fluctuate independently from the rotational motion would be realized when the field gradient is determined by the interaction with the sodium ion's hydration shell.

If the time scales of the two processes are sufficiently far apart, the orientational averaging and the intrinsic field gradient averaging could be considered separately. In this case, and assuming for simplicity averaging could be considered separately. In this case, and assuming for simplicity \( \eta = 0 \), one can rewrite the residual quadrupolar coupling constant as

\[
\alpha_{\text{res}}^Q = (\alpha_{\text{Q}})(2 \cos^2 \theta - 1) \left( 3 \cos^2 x - 1 \right) \left( \frac{Z_2 Z_3}{2} \right) + \frac{3}{2} \frac{\sin^2 \theta \cos 2\phi (Z_2 - Z_3)}{2}.
\]

where as before, \( \chi_\alpha \), \( \chi_\beta \), and \( \chi_\gamma \) are the principal components of the susceptibility tensor, \( \alpha \) and \( \beta \) are the azimuthal and elevation angles, respectively, between the principal components of the (averaged) quadrupolar coupling tensor and the susceptibility tensor \( \chi \). [34]. This expression can be derived based on averaging over the Boltzmann probabilities of the orientationally-dependent energy levels [30,34,43].

Eqs. (31)–(33) predict a line splitting akin to a first order quadrupolar splitting, albeit with a motionally reduced coupling constant.

For the experimental results of Fig. 5, solutions contained 25.5 mM LnDOTP(TEA)_5 and 8.6 mM NaCl, pH 7.4. For the experimental results of Fig. 6, the spectra were generated using an exponential window function with a line broadening factor of 25 Hz.

Two types of samples were prepared: LnDOTP-Na5 and LnDOTP(TEA)5 (TEA is tetraethylammonium). The compounds were prepared by mixing LnCl3 solutions with a slight excess of DOTP solution and titrating the solutions by either NaOH or TEA hydroxide to pH level of 7.5, to obtain the sodium or TEA salts, respectively. For variable pH experiments the pH was adjusted by either NaOH, or HCl. The DQF-MA data were obtained via the integrals of the magnitude spectra for the values of the delay \( \tau \) that gave the maximum intensity.

For the results presented in Fig. 2, the solutions were prepared from samples of LnDOTP-Na5 at pH 7.4 at concentrations in the range of 6–14 mM. The data in the graph were normalized to the same concentration (10 mM) simply by multiplying by the relative concentration factor.

For the results presented in Fig. 3, the integrals of the magnitude DQF-MA spectra are represented vs. the 25Na chemical shifts of a solution of 15 mM TmDOTP(TEA)_5 + 10 mM NaCl in H2O.

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For the experimental results of Fig. 5, solutions contained 25.5 mM LnDOTP(TEA)_5 and 8.6 mM NaCl, pH 7.4, where Ln = Tm or Dy.

3. Results and discussion

The results of the samples containing 10 mM of the LnDOTP5− compounds and 50 mM of [Na+] are shown in Figs. 2 and 3. A spectrum acquired after a single 90° pulse shows a single symmetric peak, indicative of a superposition of lines having the same shape. As previously reported for TmDOTP5− [23], DQF-MA signals can be observed even in isotropic solution. The maximum DQF-MA integrals were determined for a range of \( \tau \) values for any given LnDOTP5− sample, and plotted vs. the size of the observed pseudo-contact shift (Fig. 2). A good correlation between the two is observed, and is consistent with the prediction of Eqs. (17) and (18).

The chemical shifts in the plot are represented as absolute values for conformity and for the ease of correlating the absolute shift value with the DQF-MA intensity. The shifts were positive for Er, Yb and negative for Pr, Nd, Sm and Dy. In order to further explore the influence of the asymmetric g-factor and consequently the susceptibility on the sodium ions, an investigation was performed where the pH was varied. It is known that at lower pH, the negatively charged moieties of the LnDOTP5− complexes are saturated to a larger extent by H+, and therefore, lower binding affinity is found for sodium. Indeed, this effect is realized in Fig. 3, where a plot of the maximum DQF-MA integrals vs. pseudo-contact shift is
A good correlation is seen between DQF-MA integrals and shift, as in Fig. 2, but most importantly, the correlation is equally good with pH. It is seen that at low pH, less sodium binding affinity is found, as evidenced by smaller DQF intensity and consequently smaller pseudo-contact shift. At large pH, larger binding affinity is seen, as indicated by a larger DQF-MA integrals and a larger pseudo-contact shift.

This above-seen behavior would, in principle be consistent with the observation of alignment in the magnetic field as a result of anisotropic susceptibility tensors, as well, and evidence for both mechanisms will be explored further below. Such alignment should lead to splitting of the $^{23}Na$ spectrum due to non-vanishing quadrupole interaction. Such a splitting is indeed observed at low sodium concentrations. Fig. 4 shows representative 1D NMR spectra of samples containing 25.5 mM of TmDOTP(TEA)$_5$ and DyDOTP(TEA)$_5$. A significant line broadening of up to 400 and 250 Hz, respectively, is observed in these spectra, which upon closer inspection hints at an asymmetric underlying line splitting. This splitting can be interpreted as arising from a residual quadrupolar coupling due to anisotropic susceptibility, and the asymmetry appears such that the right side in the resonance of the TmDOTP$^5$ sample shows lower intensity than the left side. The reverse pattern is observed for DyDOTP$^5$. The two samples have opposite signs of the pseudo-contact shift (see Fig. 4). Although this effect could be a coincidence, it served as a first indication that an asymmetry in the $g$-factors had an influence on the observed interactions and the appearance of the spectra here. At the high sodium concentrations described in Figs. 2 and 3, and in the previously published work [23], such an indication of a line splitting was not observed, presumably and consequently much larger sodium concentrations had been used, because bulk sodium only bound weakly to the complex [11]. For the low sodium concentration, the sodium ions are likely to bind only to the single 4-fold symmetry site of the complex.

The observed asymmetry in the lineshape can be explained as follows: The satellite transitions appear asymmetric because of a differential line broadening, brought about by the cross-correlated relaxation mechanism, as described in Eq. (30). It is also seen that this differential line broadening effect is reversed as the sign of the pseudo-contact shift (and the anisotropy in the $g$-value) is reversed.

![Fig. 2.](image)

**Fig. 2.** (a) DQF-MA integrals vs. buildup time (b) DQF-MA maximum integral vs. $^{23}Na$ chemical shift for different LnDOTP Na$_5$ samples. The chemical shifts in the plot are represented as absolute values for conformity and for the ease of correlating the absolute shift value with the DQF-MA intensity. The shifts were positive for Er and Yb and negative for Pr, Nd, Sm and Dy. The dotted line represents a fitted line passing through the origin, indicating a good linear relationship.

![Fig. 3.](image)

**Fig. 3.** DQF shifts vs. DQF-MA peak integrals at different solution pH of 15 mM TmDOTP(TEA)$_5$ + 10 mM NaCl in H$_2$O. The pH was adjusted via addition of NaOH or HCl.

shown. A good correlation is seen between DQF-MA integrals and shift, as in Fig. 2, but most importantly, the correlation is equally good with pH. It is seen that at low pH, less sodium binding affinity is found, as evidenced by smaller DQF intensity and consequently smaller pseudo-contact shift. At large pH, larger binding affinity is seen, as indicated by a larger DQF-MA integrals and a larger pseudo-contact shift.

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**Fig. 4.** Representative 1D spectra of $^{23}Na^+$ in solutions of [NaCl] = 8.6 mM, [TmDOTP(TEA)$_5$] = 25.5 mM and [DyDOTP(TEA)$_5$] = 25.5 mM. pH = 7.5, measured at 333 K. The chemical shifts at the maximum intensities were 14,480 Hz (109.7 ppm) and −3450 Hz (−26.1 ppm) for the Tm and Dy complexes, respectively.

![Fig. 5.](image)

**Fig. 5.** Results of echo experiments (90°–$\tau$–180°–$\tau$–acquire) at different echo times $\tau$ for both TmDOTP(TEA)$_5$ and DyDOTP(TEA)$_5$. The samples consisted of 25.5 mM LnDOTP(TEA)$_5$ and 8.6 mM NaCl and were adjusted to pH 7.4. The measurements were performed at 60 °C.
when comparing the results from the Tm to the ones observed from the Dy complexes.

For a clearer demonstration of the presence of a quadrupolar splitting, a spin echo experiment was performed on both the TmDOTP(TEA)$_5$ and DyDOTP(TEA)$_5$ samples. As shown in Fig. 5, it was observed that at increasing echo times, the splitting became more and more apparent. This tendency may be interpreted in the following way: At short echo times, the dominant tensors contributing to the observed signal are $T_{1,±1}$ and thus the spectrum resembles that of a single pulse. As the echo time is increased, the processes $T_{1,±1} \rightarrow T_{2,±1}$ and $T_{1,±1} \rightarrow T_{3,±1}$ become more significant as a result of either the residual quadrupolar interaction or the cross-correlation relaxation mechanisms. These processes strengthen the appearance of the satellite transitions relative to the center band.

Fig. 5 also reveals a much clearer indication of an asymmetry between the satellite transitions than was seen before in Fig. 4. This differential line broadening effect is a clear indication of a cross-correlated mechanism occurring with a rate constant given in Eq. (30).

Spin-echo experiments were further investigated at two different magnetic fields, and the results are summarized in Table 1. Different echo times were necessary to reveal the splitting at the two fields, likely as a result of the differences in the residual quadrupolar interaction and relaxation effects. The ratio between the observed splittings at the two fields is $340 \text{Hz}/140 \text{Hz} = 2.43$. Following alignment theory [30,34,43], a dependence with the square of the magnetic field is expected according to Eq. (33).

The experimentally observed factor is larger than the theoretically expected one of $(11.74 \text{T}/8.45 \text{T})^2 = 1.93$. This difference may be the result of experimental error due to signal-to-noise ratio differences between the two instruments or a result of possible field effects on the cross-correlated relaxation mechanism, which would affect the widths of the satellites transitions. Owing to extensive overlap among the peaks, such effects could lead to changes in the apparent peak positions. Although we have already mentioned that splittings due to the dynamic frequency shifts (DFSs) are expected to be weak in magnitude, the observed increase of the splitting with increased magnetic field further eliminates DFS as an additional mechanism, since the DFS is expected to change insignificantly, or even decrease with increasing magnetic field [18,42].

The signatures of quadrupolar coupling and cross-correlated relaxation are often difficult to distinguish from each other, especially in the absence of a clear line splitting. One test, however, that should allow one to differentiate more specifically between the two mechanisms is to compare the intensities of the DQF-MA and TQF signals. On the basis of previous calculations that considered only quadrupolar coupling [15,16,18], the DQF-MA/TQF ratio is expected to be smaller than one. It would even be significantly smaller than that in practice, due to the antiphase nature of the DQF-MA signal and the presence of considerable line broadening leading to partial DQF-MA signal cancellation.

The experimentally-observed ratios are given in Table 2 at different temperatures and sodium concentrations. The ratio is vastly larger under all conditions (factors of 2.5–6.5 are observed). We take this result as a clear indication that an additional mechanism (other than alignment alone) has to be invoked to explain such ratios. Therefore, the most likely candidate is the previously-described [23] and aforementioned mechanism of paramagnetic/quadrupolar cross-correlated relaxation, given that differential linebroadening was observed as well.

Other interesting facts seen in Table 2 are that the DQF-MA/TQF factor decreases with increasing temperature. This tendency is the result of reduced susceptibility that leads to reduced relaxation rates due to the cross-correlated relaxation mechanism, and makes the residual quadrupolar interaction a more significant source of the formation of high rank tensors. As discussed above, this latter mechanism yields similar intensities for DQF-MA and TQF signals. It was shown that increased temperature may cause a temperature dependence of $1/T_2$ or $1/T_2^*$ of the paramagnetic susceptibility $\gamma$ (as a result of the electronic relaxation mechanisms [44]) and thus the spectral densities $S_{ij}^{P}$ in Eqs. (21)–(30) will have a similar dependence, with $f^{PP}$ proportional to $1/T^2$ or $1/T^3$. On the other hand, the effect of the residual quadrupolar interaction will be proportional to $1/T^2$ or $1/T^3$ and thus increasing temperature will decrease the importance of the cross-correlated relaxation mechanism and hence decrease the DQF-MA/TQF ratio. The result that at room temperature the splitting at 8.45 T could not be resolved would be consistent with the stated temperature trends, since the $f^{PP}$ term would be more prominent at lower temperature and lead to larger broadening, thus masking the splitting effect.

4. Conclusions

In conclusion, we identify two mechanisms giving rise to the appearance of double-quantum filtered signals, line splittings, and differential linebroadening in samples of sodium solutions containing LnDOTP$^-$ complexes: molecular alignment in the magnetic field, leading to a residual quadrupolar interaction, and paramagnetic-quadrupolar cross-correlation. The evidence presented for the former is the appearance of quadrupolar splittings, which are much larger than splittings that could arise from dynamic frequency shifts, and which correlate with the $g$-anisotropy of the ions in question. The evidence for the cross-correlation mechanism are differential line broadening effects, and large ratios between the double-quantum and the triple-quantum filtered signals, which could not be explained by alignment effects.

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References


| Table 2 | DQF/TQF ratios observed at two temperatures for a sample containing [TmDOTP (TEA)$_5$] = 25.5 mM and [NaCl] = 8.6 mM. |
|-----------------|-----------------|-----------------|-----------------|
| $^{23}$Na concentration (mM) | 3.8 | 8.6 | 51.6 |
| Temperature (°C) | 22 | 60 | 22 | 50 | 22 | 60 |
| T21/T31 (experimental) | 6.5 | 2.5 | 6.5 | 3 | 4 | 4.1 |


