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NMR Relaxation in Multipolar AX Systems under Spin Locking Conditions

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A relaxation matrix has been calculated for a multipolar AX spin system under the on-resonance spin-locking condition. Auto- and cross-correlation terms between dipolar, quadrupolar, and CSA interactions are considered. It is shown that the spin-lock leads to many relaxation pathways being blocked, resulting in a considerably simplified relaxation network. The presence of spectral densities at zero frequency, associated with locked nuclei, allows efficient relaxation also in the absence of fast molecular motions. © 1999 Academic Press

INTRODUCTION

Nuclear magnetic relaxation experiments are often used in probing the dynamics of molecules (*1, 2*). The relaxation experiments that are most common are measurements of the longitudinal magnetization, either for low-natural abundance, low magnetogyric ratio nuclear species (such as carbon-13 or nitrogen-15 T_1 experiments (*3*)), or proton networks (the nuclear Overhauser enhancement, NOE, experiments (*4*)). The longitudinal relaxation of heteronuclei mainly carries information on relatively fast motions. The slow reorientation, such as in macromolecular species in solution, gives rise to the homonuclear cross-relaxation or the NOE effect. The NOE measurements are, however, in general more effective as a tool for structure determination than for dynamics (*4*). The dynamic information on slow molecular motions can be characterized more efficiently by applying RF field. Experiments of this type, suggested originally by Redfield (*5*), are usually called rotating-frame relaxation experiments. General aspects of the relaxation in the presence of radiofrequency fields in liquids have been dealt with by numerous authors (*6–12*). Two types of rotating-frame relaxation experiments on liquids are common. One category comprises the CAMELSPIN (*13*) or ROESY (for rotating-frame Overhauser enhancement spectroscopy) (*14*), the rotating frame counterparts of the homonuclear NOE spectroscopy. The other category is $T_{1\rho}$ measurements for heteronuclei with spin $\frac{1}{2}$ (*15–18*) and with higher spin quantum number (*6, 19–21*). This technique allows one to sample spectral densities at frequencies of the order of RF field strength, thus making slow processes effective. Several techniques allowing for sampling spectral densities at intermediate frequencies, utilizing the radiofrequency field positioned off-resonance (rather than at resonance frequency for one of the nuclear species), have also been proposed (*22–25*) and found to be important.

A special category of relaxation phenomena which has attracted much attention are the processes involving transfers between different types of spin order. These phenomena are most commonly observed in systems of scalar-coupled spins and require the presence of two or more correlated interactions involving nuclear spins and their environment. Also, these cross-correlation or interference phenomena are influenced by the presence of radiofrequency fields, which again introduce spectral densities (here, the cross-correlation spectral densities) at low frequencies (*7, 16, 26–30*). Moreover, the presence of the radiofrequency fields blocks certain unwanted magnetization transfer pathways (*26, 27, 30, 31*). All work on cross-correlation effects in systems of coupled spins in the presence of RF fields has been concerned with systems of nuclei with spin quantum number of $\frac{1}{2}$, where the relevant relaxation mechanisms are dipolar and chemical shielding anisotropy (CSA) interactions. In this paper, we perform a similar analysis for spin systems containing a spin $\frac{1}{2}$ (dipolar) nucleus coupled to a higher spin (multipolar) nucleus, where the quadrupolar interaction is also present.

Werbelow *et al.* (*32, 33*) have developed a theory for longitudinal relaxation in multipolar AX spin systems, where A has spin $\frac{1}{2}$ and X is a quadrupolar nucleus. It was shown that dipolar, quadrupolar autocorrelation terms and dipolar, quadrupolar cross-correlation terms may change spin order by ± 2 or not at all, while quadrupolar-CSA and dipolar-CSA cross-correlation terms may change spin order by ± 1. Other related work has been concerned with differential line broadening in the dipolar–multipolar spin systems (*34–37*), with unusual multiplet structure effects caused by the interference of dipolar and quadrupolar interactions (*38–40*) and with a careful treatment (*41*) of the phenomenon called by Abragam (*42*) the "scalar relaxation of the second kind." In this paper, we investigate AX systems under spin-locking conditions, when a strong RF field is applied selectively on one of the nuclei or simultaneously on both. A slightly different case of weak RF fields has recently been considered by Skrynnikov *et al.* (*43*);

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however, in that work attention was mainly paid to scalar relaxation.

THEORY

The theory presented here is based on two assumptions. First, the product of the correlation time of the corresponding interactions, τ_c, and RF nutation frequency, ω_1, is much smaller than unity; the condition $\omega_1\tau_c \ll 1$ means that the RF field does not interfere with relaxation processes (*42, 44*). This assumption amounts to replacing the spectral densities at frequency ω_1 by spectral densities at zero frequency. Second, the RF field is applied exactly on resonance and strong enough, so that all multiplet transitions are effected by the same RF field and ideal spin lock is achieved. These two assumptions also correspond to the case, when the dependence of the relaxation behavior on the strength and frequency of the RF field is quenched (*43, 45*).

Evolution of the density operator, σ, under relaxation follows

$$\frac{d\sigma}{dt} = -i[H, \sigma] + R(\sigma - \sigma^{eq}), \qquad [1]$$

where H is static Hamiltonian, σ^{eq} is the equilibrium density operator, and R is the relaxation superoperator. If the secular approximation and system without degenerate transitions is considered, then the relaxation matrix has a block diagonal form. Populations appear to be decoupled from coherences. The relaxation matrix can be calculated according to

$$R_{mn} = \sum_{q,\mu,\nu} (-1)^q J^{\mu,\nu}(\omega_q) tr\{B_m[T^{\mu}_{p,-q}, [T^{\nu}_{p,q}, B_n]]\}. \qquad [2]$$

B_m and B_n are magnetization modes; they will be introduced later for the AX system. $J^{\mu,\nu}(\omega_q)$ is the spectral density and $T^{\mu}_{p,-q}$ and $T^{\nu}_{p,q}$ are tensor operators representing interactions responsible for relaxation (*33*), p is the rank of the operators, and q is the order. μ and ν correspond to quadrupolar, dipolar, and CSA interactions. We assume that scalar relaxation of the second kind (*41, 42*) is not efficient. It is normally so, if spin locking fields on heteronuclei do not satisfy the Hartman–Hahn condition, $\omega_{1A} \neq \omega_{1X}$ (*43*) or if quadrupolar relaxation is not very fast, as can be the case for deuterons. Scalar relaxation of the first kind and random field interactions were not taken into account, since these mechanisms are rarely important. The latter mechanism is represented by rank one tensors and, consequently, cannot give any interference with rank two tensors.

Magnetization modes for the multipolar AX spin system can be constructed as a direct product of isolated spin modes (*32, 33*), which in turn are produced from irreducible tensor operators (*46*) of zeroth order. For the AX system, where nucleus A has spin $I = \frac{1}{2}$ and X has spin $S = 1$, normalized magnetization modes are

$$\begin{aligned}
\nu_{1(I)} &= \Delta\left\langle \sqrt{\frac{2}{3}}\, I_z \right\rangle, \\
\nu_{1(S)} &= \Delta\left\langle \frac{1}{2}\, S_z \right\rangle, \\
\nu_{3(IS)} &= \left\langle \sqrt{\frac{1}{3}}\, I_z(3S_z^2 - S^2) \right\rangle, \\
\nu_{2(IS)} &= \langle I_z S_z \rangle, \\
\nu_{2(S)} &= \left\langle \frac{1}{2} \sqrt{\frac{1}{3}}\, (3S_z^2 - S^2) \right\rangle, \qquad [3]
\end{aligned}$$

where the index i in ν_i corresponds to spin order. These magnetization modes are associated with combinations of the line intensities in A and X multiplets (*32*). Under ideal spin locking conditions, the quantization axis is directed along the B_1 field (*7*) and, therefore, z in Eq. [3] should be changed to x, if nuclei are locked along the x axis. The results for spin $S > 1$ are similar and are not presented here.

RESULTS AND DISCUSSIONS

The relaxation matrices below have been obtained using the C++ NMR library GAMMA (*47*). When no RF field is applied and only dipolar and quadrupolar interactions are taken into account, the relaxation of magnetization modes is described by Eq. [4a]. The result is essentially the same as one found by Werbelow *et al.* (*32*), except for common coefficients in front of spectral densities. This is because we used normalized magnetization modes in this work. The relaxation matrix has block diagonal form, which reflects the fact that dipolar and quadrupolar interactions may change spin order either by +2, −2, or not at all.

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \end{bmatrix} =
\begin{bmatrix}
\begin{array}{l} \frac{8}{9}J^D(\omega_I-\omega_S) \\ +\frac{8}{3}J^D(\omega_I) \\ +\frac{16}{3}J^D(\omega_I+\omega_S) \end{array} &
\begin{array}{l} -\frac{2}{3}\sqrt{\frac{2}{3}}J^D(\omega_I-\omega_S) \\ +4\sqrt{\frac{2}{3}}J^D(\omega_I+\omega_S) \end{array} &
\begin{array}{l} -\frac{2}{9}\sqrt{2}J^D(\omega_I-\omega_S) \\ +\frac{4}{3}\sqrt{2}J^D(\omega_I) \\ -\frac{4}{3}\sqrt{2}J^D(\omega_I+\omega_S) \end{array} \\
\begin{array}{l} -\frac{2}{3}\sqrt{\frac{2}{3}}J^D(\omega_I-\omega_S) \\ +4\sqrt{\frac{2}{3}}J^D(\omega_I+\omega_S) \end{array} &
\begin{array}{l} \frac{1}{3}J^D(\omega_I-\omega_S) \\ +J^D(\omega_S) \\ +2J^D(\omega_I+\omega_S) \\ +4J^Q(\omega_S) \\ +16J^Q(2\omega_S) \end{array} &
\begin{array}{l} \frac{1}{3}\sqrt{\frac{1}{3}}J^D(\omega_I-\omega_S) \\ -2\sqrt{\frac{1}{3}}J^D(\omega_I+\omega_S) \\ -12\sqrt{\frac{1}{3}}K^{D-Q}(\omega_S) \end{array} \\
\begin{array}{l} -\frac{2}{9}\sqrt{2}J^D(\omega_I-\omega_S) \\ +\frac{4}{3}\sqrt{2}J^D(\omega_I) \\ -\frac{4}{3}\sqrt{2}J^D(\omega_I+\omega_S) \end{array} &
\begin{array}{l} \frac{1}{3}\sqrt{\frac{1}{3}}J^D(\omega_I-\omega_S) \\ -2\sqrt{\frac{1}{3}}J^D(\omega_I+\omega_S) \\ -12\sqrt{\frac{1}{3}}K^{D-Q}(\omega_S) \end{array} &
\begin{array}{l} \frac{1}{9}J^D(\omega_I-\omega_S) \\ +\frac{4}{3}J^D(\omega_I) \\ +3J^D(\omega_S) \\ +\frac{2}{3}J^D(\omega_I+\omega_S) \\ +12J^Q(\omega_S) \end{array}
\end{bmatrix}
\times \begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \end{bmatrix}
$$

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix} =
\begin{bmatrix}
\begin{array}{l} \frac{1}{3}J^D(\omega_I-\omega_S) \\ +4J^D(\omega_I) \\ +J^D(\omega_S) \\ +2J^D(\omega_I+\omega_S) \\ +4J^Q(\omega_S) \\ +16J^Q(2\omega_S) \end{array} &
\begin{array}{l} -\sqrt{\frac{1}{3}}J^D(\omega_I-\omega_S) \\ +6\sqrt{\frac{1}{3}}J^D(\omega_I+\omega_S) \\ -12\sqrt{\frac{1}{3}}K^{D-Q}(\omega_S) \end{array} \\
\begin{array}{l} -\sqrt{\frac{1}{3}}J^D(\omega_I-\omega_S) \\ +6\sqrt{\frac{1}{3}}J^D(\omega_I+\omega_S) \\ -12\sqrt{\frac{1}{3}}K^{D-Q}(\omega_S) \end{array} &
\begin{array}{l} J^D(\omega_I-\omega_S) \\ +3J^D(\omega_S) \\ +6J^D(\omega_I+\omega_S) \\ +12J^Q(\omega_S) \end{array}
\end{bmatrix}
\times \begin{bmatrix} \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix} \tag{4a}
$$

Autocorrelation of the quadrupolar interaction, in the form of spectral densities J^{Q}, contributes only to the diagonal terms, since it acts on X nuclei and pure spin S rank three order does not exists for $S = 1$.

Next, we include also the CSA interaction. In Eq. [4b], we collect the additional terms that this interaction gives rise to. Dipolar-CSA and quadrupolar-CSA cross-correlation terms couple magnetizations differing in spin order by unity and the block diagonal form of the relaxation matrix is destroyed. This results in a much more complicated relaxation network, and the problem arises to separate contribution from different relaxation pathways.

$$-\frac{d}{dt}\begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \\ \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix}$$

$$= \begin{bmatrix} 4J^{C(I)}(\omega_I) & 0 & 0 & -8\sqrt{\frac{2}{3}}K^{D-C(I)}(\omega_I) & 0 \\ 0 & 4J^{C(S)}(\omega_S) & 0 & -4K^{D-C(S)}(\omega_S) & 24\sqrt{\frac{1}{3}}K^{Q-C(S)}(\omega_S) \\ 0 & 0 & \begin{array}{c} 4J^{C(I)}(\omega_I) \\ +12J^{C(S)}(\omega_S) \end{array} & \begin{array}{c} -8\sqrt{\frac{1}{3}}K^{D-C(I)}(\omega_I) \\ +24\sqrt{\frac{1}{3}}K^{Q-C(S)}(\omega_S) \end{array} & -12K^{D-C(S)}(\omega_S) \\ -8\sqrt{\frac{2}{3}}K^{D-C(I)}(\omega_I) & -4K^{D-C(S)}(\omega_S) & \begin{array}{c} -8\sqrt{\frac{1}{3}}K^{D-C(I)}(\omega_I) \\ +24\sqrt{\frac{1}{3}}K^{Q-C(S)}(\omega_S) \end{array} & \begin{array}{c} 4J^{C(I)}(\omega_I) \\ +4J^{C(S)}(\omega_S) \end{array} & 0 \\ 0 & 24\sqrt{\frac{1}{3}}K^{Q-C(S)}(\omega_S) & -12K^{D-C(S)}(\omega_S) & 0 & 12J^{C(S)}(\omega_S) \end{bmatrix} \times \begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \\ \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix}. \quad [4b]$$

It is also worth noting that the cross-correlation spectral densities, $K(\omega)$, in both Eqs. [4a] and [4b] are taken at the frequencies common to the two interfering interactions.

A disadvantage of the experiment in the laboratory frame is the absence of $J(0)$ or $K(0)$. Different correlation functions for Brownian motion, reviewed by Woessner (*48*), have the general form

$$J(\omega) = \sum_k \frac{A^k \tau_c^k}{1 + (\omega \tau_c^k)^2}.$$

In the absence of fast motions, when the regime $(\omega\tau_c^k)^2 \gg 1$ is reached for all k, correlation function tends to vanish at $\omega \neq 0$. Thus, relaxation becomes in principle *infinitely* long for large rigid biomolecules or in the case of viscous media.

One way to overcome these problems is to measure relaxation in the presence of RF field. Equations [5] and [6] provide relaxation matrices when one of the nuclei, A or X, respectively, is spin-locked. In analogy with Eq. [4], Eqs. [5a] and [6a] contain the terms arising from the dipolar and quadrupolar interactions and their interference. Equations [5b] and [6b] give additional terms associated with CSA and interference terms involving that interaction.

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \end{bmatrix} = \begin{bmatrix}
\begin{array}{l} \frac{16}{9}J^D(0) \\ +\frac{4}{9}J^D(\omega_I-\omega_S) \\ +\frac{4}{3}J^D(\omega_I) \\ +\frac{8}{3}J^D(\omega_S) \\ +\frac{8}{3}J^D(\omega_I+\omega_S) \end{array} & 0 & \begin{array}{l} \frac{8}{9}\sqrt{2}J^D(0) \\ -\frac{1}{9}\sqrt{2}J^D(\omega_I-\omega_S) \\ +\frac{2}{3}\sqrt{2}J^D(\omega_I) \\ -\frac{2}{3}\sqrt{2}J^D(\omega_S) \\ -\frac{2}{3}\sqrt{2}J^D(\omega_I+\omega_S) \end{array} \\
0 & \begin{array}{l} \frac{1}{3}J^D(\omega_I-\omega_S) \\ +J^D(\omega_S) \\ +2J^D(\omega_I+\omega_S) \\ +4J^Q(\omega_S) \\ +16J^Q(2\omega_S) \end{array} & 0 \\
\begin{array}{l} \frac{8}{9}\sqrt{2}J^D(0) \\ -\frac{1}{9}\sqrt{2}J^D(\omega_I-\omega_S) \\ +\frac{2}{3}\sqrt{2}J^D(\omega_I) \\ -\frac{2}{3}\sqrt{2}J^D(\omega_S) \\ -\frac{2}{3}\sqrt{2}J^D(\omega_I+\omega_S) \end{array} & 0 & \begin{array}{l} \frac{8}{9}J^D(\omega_I) \\ +\frac{5}{9}J^D(\omega_I-\omega_S) \\ +\frac{2}{3}J^D(\omega_I) \\ +\frac{1}{3}J^D(\omega_S) \\ +\frac{10}{3}J^D(\omega_I+\omega_S) \\ +12J^Q(\omega_S) \end{array}
\end{bmatrix} \times \begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \end{bmatrix} \tag{5a}
$$

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix} = \begin{bmatrix}
\begin{array}{l} \frac{8}{3}J^D(0) \\ +\frac{1}{3}J^D(\omega_I-\omega_S) \\ +2J^D(\omega_I) \\ +J^D(\omega_S) \\ +2J^D(\omega_I+\omega_S) \\ +4J^Q(\omega_S) \\ +16J^Q(2\omega_S) \end{array} & 0 \\
0 & \begin{array}{l} J^D(\omega_I-\omega_S) \\ +3J^D(\omega_S) \\ +6J^D(\omega_I+\omega_S) \\ +12J^Q(\omega_S) \end{array}
\end{bmatrix} \times \begin{bmatrix} \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix}
$$

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \\ \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix}
= \begin{bmatrix}
\begin{array}{l} \frac{8}{3}J^{C(I)}(0) \\ +2J^{C(I)}(\omega_I) \end{array} & 0 & 0 & \begin{array}{l} -\frac{16}{3}\sqrt{\frac{2}{3}}K^{D-C(I)}(0) \\ -4\sqrt{\frac{2}{3}}K^{D-C(I)}(\omega_I) \end{array} & 0 \\
0 & 4J^{C(S)}(\omega_S) & 0 & 0 & 24\sqrt{\frac{1}{3}}K^{Q-C(S)}(\omega_S) \\
0 & 0 & \begin{array}{l} \frac{8}{3}J^{C(I)}(0) \\ +2J^{C(I)}(\omega_I) \\ +12J^{C(S)}(\omega_S) \end{array} & \begin{array}{l} -\frac{16}{3}\sqrt{\frac{1}{3}}K^{D-C(I)}(0) \\ -4\sqrt{\frac{1}{3}}K^{D-C(I)}(\omega_I) \\ +24\sqrt{\frac{1}{3}}K^{Q-C(S)}(\omega_S) \end{array} & 0 \\
\begin{array}{l} -\frac{16}{3}\sqrt{\frac{2}{3}}K^{D-C(I)}(0) \\ -4\sqrt{\frac{2}{3}}K^{D-C(I)}(\omega_I) \end{array} & 0 & \begin{array}{l} -\frac{16}{3}\sqrt{\frac{1}{3}}K^{D-C(I)}(0) \\ -4\sqrt{\frac{1}{3}}K^{D-C(I)}(\omega_I) \\ +24\sqrt{\frac{1}{3}}K^{Q-C(S)}(\omega_S) \end{array} & \begin{array}{l} \frac{8}{3}J^{C(I)}(0) \\ +2J^{C(I)}(\omega_I) \\ +4J^{C(S)}(\omega_S) \end{array} & 0 \\
0 & 24\sqrt{\frac{1}{3}}K^{Q-C(S)}(\omega_S) & 0 & 0 & 12J^{C(S)}(\omega_S)
\end{bmatrix} \times \begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \\ \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix} \tag{5b}
$$

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \end{bmatrix} =
\begin{bmatrix}
\begin{array}{l} \frac{8}{9} J^D(\omega_I - \omega_S) \\ + \frac{8}{3} J^D(\omega_I) \\ + \frac{16}{3} J^D(\omega_I + \omega_S) \end{array} & 0 & \begin{array}{l} \frac{1}{9}\sqrt{2} J^D(\omega_I - \omega_S) \\ - \frac{2}{3}\sqrt{2} J^D(\omega_I) \\ + \frac{2}{3}\sqrt{2} J^D(\omega_I + \omega_S) \end{array} \\
0 & \begin{array}{l} \frac{2}{3} J^D(0) \\ + \frac{1}{6} J^D(\omega_I - \omega_S) \\ + J^D(\omega_I) \\ + \frac{1}{2} J^D(\omega_S) \\ + J^D(\omega_I + \omega_S) \\ + 6 J^Q(0) \\ + 10 J^Q(\omega_S) \\ + 4 J^Q(2\omega_S) \end{array} & 0 \\
\begin{array}{l} \frac{1}{9}\sqrt{2} J^D(\omega_I - \omega_S) \\ - \frac{2}{3}\sqrt{2} J^D(\omega_I) \\ + \frac{2}{3}\sqrt{2} J^D(\omega_I + \omega_S) \end{array} & 0 & \begin{array}{l} 2 J^D(0) \\ + \frac{5}{18} J^D(\omega_I - \omega_S) \\ + \frac{1}{3} J^D(\omega_I) \\ + \frac{3}{2} J^D(\omega_S) \\ + \frac{5}{3} J^D(\omega_I + \omega_S) \\ + 6 J^Q(\omega_S) \\ + 6 J^Q(2\omega_S) \end{array}
\end{bmatrix}
\times \begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \end{bmatrix} \quad [6a]
$$

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix} =
\begin{bmatrix}
\begin{array}{l} \frac{2}{3} J^D(0) \\ + \frac{5}{6} J^D(\omega_I - \omega_S) \\ + J^D(\omega_I) \\ + \frac{1}{2} J^D(\omega_S) \\ + 5 J^D(\omega_I + \omega_S) \\ + 6 J^Q(0) \\ + 10 J^Q(\omega_S) \\ + 4 J^Q(2\omega_S) \end{array} & 0 \\
0 & \begin{array}{l} 2 J^D(0) \\ + \frac{1}{2} J^D(\omega_I - \omega_S) \\ + 3 J^D(\omega_I) \\ + \frac{3}{2} J^D(\omega_S) \\ + 3 J^D(\omega_I + \omega_S) \\ + 6 J^Q(\omega_S) \\ + 6 J^Q(2\omega_S) \end{array}
\end{bmatrix}
\times \begin{bmatrix} \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix}
$$

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \\ \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix} =
\begin{bmatrix}
4 J^{C(I)}(\omega_I) & 0 & 0 & 0 & 0 \\
0 & \begin{array}{l} \frac{8}{3} J^{C(S)}(0) \\ + 2 J^{C(S)}(\omega_S) \end{array} & 0 & \begin{array}{l} - \frac{8}{3} K^{D-C(S)}(0) \\ - 2 K^{D-C(S)}(\omega_S) \end{array} & 0 \\
0 & 0 & \begin{array}{l} 4 J^{C(I)}(\omega_I) \\ + 8 J^{C(S)}(0) \\ + 6 J^{C(S)}(\omega_S) \end{array} & 0 & \begin{array}{l} - 8 K^{D-C(S)}(0) \\ - 6 K^{D-C(S)}(\omega_S) \end{array} \\
0 & \begin{array}{l} - \frac{8}{3} K^{D-C(S)}(0) \\ - 2 K^{D-C(S)}(\omega_S) \end{array} & 0 & \begin{array}{l} 4 J^{C(I)}(\omega_I) \\ + \frac{8}{3} J^{C(S)}(0) \\ + 2 J^{C(S)}(\omega_S) \end{array} & 0 \\
0 & 0 & \begin{array}{l} - 8 K^{D-C(S)}(0) \\ - 6 K^{D-C(S)}(\omega_S) \end{array} & 0 & \begin{array}{l} 8 J^{C(S)}(0) \\ + 6 J^{C(S)}(\omega_S) \end{array}
\end{bmatrix}
\times \begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \\ \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix}. \quad [6b]
$$

We notice that the relaxation now depends on contributions from zero-frequency auto- and cross-correlation spectral densities (adiabatic terms), which do not vanish in the case of large molecules or viscous solvents. These spectral densities exist for interactions associated with the nucleus under lock. Thus, for example, $J^D(0)$, $J^{C(I)}(0)$ and $K^{D-C(I)}(0)$, or $J^D(0)$, $J^Q(0)$, $J^{C(S)}(0)$ and $K^{D-C(I)}(0)$ are important when nuclei A or X are locked, respectively. In Eq. [6a], we can also see that for slowly reorienting molecules, the relaxation of $\nu_{1(S)}$ and $\nu_{3(IS)}$ modes becomes single exponential under spin-lock applied on quadrupolar nucleus. Another important difference between these equations and Eq. [4] is that dipolar–quadrupolar interference is absent under spin-lock. Therefore, in the absence of CSA, modes like $\nu_{1(S)}$, $\nu_{2(IS)}$, and $\nu_{2(S)}$ relax exponentially. Further, in the limit of extreme narrowing, where all the spectral densities become frequency independent and can thus be taken at zero frequency, it becomes immaterial which nucleus to lock. Equations [5a] and [6a] are then transformed into

$$-\frac{d}{dt}\begin{bmatrix}\nu_{1(I)}\\ \nu_{1(S)}\\ \nu_{3(IS)}\end{bmatrix}=\begin{bmatrix}\frac{80}{9}J^D(0) & 0 & \frac{1}{9}\sqrt{2}J^D(0)\\ 0 & \begin{array}{l}\frac{10}{3}J^D(0)\\ +20J^Q(0)\end{array} & 0\\ \frac{1}{9}\sqrt{2}J^D(0) & 0 & \begin{array}{l}\frac{52}{9}J^D(0)\\ +12J^Q(0)\end{array}\end{bmatrix}\times\begin{bmatrix}\nu_{1(I)}\\ \nu_{1(S)}\\ \nu_{3(IS)}\end{bmatrix}$$

$$-\frac{d}{dt}\begin{bmatrix}\nu_{2(IS)}\\ \nu_{2(S)}\end{bmatrix}=\begin{bmatrix}\begin{array}{l}8J^D(0)\\ +20J^Q(0)\end{array} & 0\\ 0 & \begin{array}{l}10J^D(0)\\ +12J^Q(0)\end{array}\end{bmatrix}\times\begin{bmatrix}\nu_{2(IS)}\\ \nu_{2(S)}\end{bmatrix}. \qquad [7]$$

Finally, let us consider the case when both A and X nuclei are spin-locked by the RF field. The results for this case are presented in Eqs. [8a] (the effects of dipolar and quadrupolar interactions) and [8b] (the effects of the CSA and its interference with dipolar and quadrupolar interactions).

$$-\frac{d}{dt}\begin{bmatrix}\nu_{1(I)}\\ \nu_{1(S)}\\ \nu_{3(IS)}\end{bmatrix}=\begin{bmatrix}\begin{array}{l}\frac{16}{9}J^D(0)\\ +\frac{4}{9}J^D(\omega_I-\omega_S)\\ +\frac{4}{3}J^D(\omega_I)\\ +\frac{8}{3}J^D(\omega_S)\\ +\frac{8}{3}J^D(\omega_I+\omega_S)\end{array} & 0 & \begin{array}{l}-\frac{4}{9}\sqrt{2}J^D(0)\\ +\frac{1}{18}\sqrt{2}J^D(\omega_I-\omega_S)\\ -\frac{1}{3}\sqrt{2}J^D(\omega_I)\\ +\frac{1}{3}\sqrt{2}J^D(\omega_S)\\ +\frac{1}{3}\sqrt{2}J^D(\omega_I+\omega_S)\end{array}\\ 0 & \begin{array}{l}\frac{2}{3}J^D(0)\\ +\frac{1}{6}J^D(\omega_I-\omega_S)\\ +J^D(\omega_I)\\ +\frac{1}{2}J^D(\omega_S)\\ +J^D(\omega_I+\omega_S)\\ +6J^Q(0)\\ +10J^Q(\omega_S)\\ +4J^Q(2\omega_S)\end{array} & 0\\ \begin{array}{l}-\frac{4}{9}\sqrt{2}J^D(0)\\ +\frac{1}{18}\sqrt{2}J^D(\omega_I-\omega_S)\\ -\frac{1}{3}\sqrt{2}J^D(\omega_I)\\ +\frac{1}{3}\sqrt{2}J^D(\omega_S)\\ +\frac{1}{3}\sqrt{2}J^D(\omega_I+\omega_S)\end{array} & 0 & \begin{array}{l}\frac{2}{9}J^D(0)\\ +\frac{7}{18}J^D(\omega_I-\omega_S)\\ +\frac{5}{3}J^D(\omega_I)\\ +\frac{5}{6}J^D(\omega_S)\\ +\frac{7}{3}J^D(\omega_I+\omega_S)\\ +6J^Q(\omega_S)\\ +6J^Q(2\omega_S)\end{array}\end{bmatrix}\times\begin{bmatrix}\nu_{1(I)}\\ \nu_{1(S)}\\ \nu_{3(IS)}\end{bmatrix} \qquad [8a]$$

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix} = \begin{bmatrix} \begin{array}{l} \frac{2}{3}J^D(0) \\ +\frac{1}{2}J^D(\omega_I-\omega_S) \\ +J^D(\omega_I) \\ +\frac{15}{6}J^D(\omega_S) \\ +3J^D(\omega_I+\omega_S) \\ +6J^Q(0) \\ +10J^Q(\omega_S) \\ +4J^Q(2\omega_S) \end{array} & 0 \\ 0 & \begin{array}{l} 2J^D(0) \\ +\frac{1}{2}J^D(\omega_I-\omega_S) \\ +3J^D(\omega_I) \\ +\frac{3}{2}J^D(\omega_S) \\ +3J^D(\omega_I+\omega_S) \\ +6J^Q(\omega_S) \\ +6J^Q(2\omega_S) \end{array} \end{bmatrix} \times \begin{bmatrix} \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix}
$$

$$
-\frac{d}{dt}\begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \\ \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix} = \begin{bmatrix} \begin{array}{l} \frac{8}{3}J^{C(I)}(0) \\ +2J^{C(I)}(\omega_I) \end{array} & 0 & 0 & 0 & 0 \\ 0 & \begin{array}{l} \frac{8}{3}J^{C(S)}(0) \\ +2J^{C(S)}(\omega_S) \end{array} & 0 & 0 & 0 \\ 0 & 0 & \begin{array}{l} \frac{8}{3}J^{C(I)}(0) \\ +2J^{C(I)}(\omega_I) \\ +8J^{C(S)}(0) \\ +6J^{C(S)}(\omega_S) \end{array} & 0 & 0 \\ 0 & 0 & 0 & \begin{array}{l} \frac{8}{3}J^{C(I)}(0) \\ +2J^{C(I)}(\omega_I) \\ +\frac{8}{3}J^{C(S)}(0) \\ +2J^{C(S)}(\omega_S) \end{array} & 0 \\ 0 & 0 & 0 & 0 & \begin{array}{l} 8J^{C(S)}(0) \\ +6J^{C(S)}(\omega_S) \end{array} \end{bmatrix} \times \begin{bmatrix} \nu_{1(I)} \\ \nu_{1(S)} \\ \nu_{3(IS)} \\ \nu_{2(IS)} \\ \nu_{2(S)} \end{bmatrix}. \qquad [8b]
$$

Again, one has nonvanishing contributions from $J^D(0)$, $J^Q(0)$, $J^{C(I)}(0)$, and $J^{C(S)}(0)$. It is also important to notice the absence of any interference terms in Eq. [8].

In summary, the present analysis shows that relaxation measurements on multipolar AX spin systems in the presence of an RF field allow one to sample spectral densities at zero frequency, which give nonvanishing contributions for systems with slow molecular motions. In addition, the application of spin-lock blocks certain relaxation pathways, considerably simplifying interpretation of the experiments. We believe that this type of experiment will turn out especially important for the dynamic studies of large biomolecules, where fractional ^{2}H enrichment is used.

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