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Cross Correlations in the Longitudinal Relaxation of Strongly Coupled Spins

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A generalized set of magnetization modes for quantifying cross-correlation contributions to longitudinal relaxation in strongly coupled spin systems is described in this paper. Such a set of modes (called longitudinal multiple-quantum modes) is used to unravel cross-correlation information in strongly coupled systems, where the strength of the *J* coupling tends to obscure such effects. The applicability of such methods is demonstrated for a small molecule which exhibits some strong coupling effects even at high magnetic field strengths. The contribution of "remote" cross correlations to the longitudinal relaxation of strongly coupled spins is detailed. © 2000 Academic Press

Key Words: **strong coupling; cross correlations; single-transition operators; longitudinal multiple-quantum modes; remote cross correlations.**

I. INTRODUCTION

The Redfield–Bloch semiclassical density operator theory is widely used to quantify spin relaxation (*1, 2*). Although the form of the Redfield equation is mathematically elegant, computing individual matrix elements for different spin systems is tedious and often provides little insight into multispin relaxation. A transformation to the basis of "modes," many of which can be directly related to physical observables, proves more useful (*3–6*). For longitudinal relaxation, these modes (known as "magnetization modes") are essentially various linear combinations of the populations of different energy levels, and have been used with great success to gain tangible structural and dynamic information in weakly coupled spin systems (*7, 8*). Signatures of cross-correlation processes in weakly coupled spin systems are immediately recognizable as an unequal recovery of different transitions of a spin multiplet—the "multiplet effect." It is not as evident when second-order effects are present, and most previous work on relaxation in strongly coupled systems has remained within the framework of the Redfield relaxation matrix (*9–14*). It has been noted that there are additional pathways (apart from those of cross correlations) for the creation of longitudinal spin order in such systems, due to the fact that strong coupling factors contribute unequally to the relaxation rates of various transitions of a spin (*15–17*). At first sight, it appears as if it is no longer possible to define a simple basis set of magnetization modes for strongly coupled spins and that the emergence of longitudinal spin order during the course of a relaxation experiment is no longer an exclusive signature of cross-correlation processes. Nevertheless, as will be shown, an attempt to retain the idea of magnetization modes does lead to a conceptual simplification in the treatment of relaxation in such systems.

We define a complete orthonormal set of magnetization modes corresponding to the expectation values of various zero-quantum and double-quantum single-transition operators, calculated in the eigenbasis. We call our set of modes so defined "longitudinal multiple-quantum modes (LMQM), as opposed to the usual single-spin or multispin modes, which refer to longitudinal spin order. These modes are valid for any spin system, regardless of the coupling information encoded in it. For systems with an inherent molecular symmetry (for example, magnetically equivalent spins), this symmetry can be exploited to define a set of symmetrized modes (*21–23*). Similarly, for systems of nonequivalent (weakly coupled) spins, a set of multispin order modes can be defined, each mode having a well-defined parity under spin inversion (*24, 25*). Such symmetrized and/or multispin modes can always be constructed as subsets of the more general LMQM modes. For systems with strong coupling and no inherent molecular symmetry, defining a simplified set of magnetization modes is no longer possible and one has to remain within the matrix of the complete LMQM modes (Fig. 1).

Recent experiments designed to measure cross correlations in transverse spin relaxation have generated much interest (*26–28*). An interesting feature of these experiments is the measurement of "remote" cross correlations, terms which have no explicit distance dependence from the spin of interest. Several workers (*29–32*) have pointed out the existence of such terms in the transverse relaxation of weakly coupled spin systems. We note in this paper that such remote cross corre-

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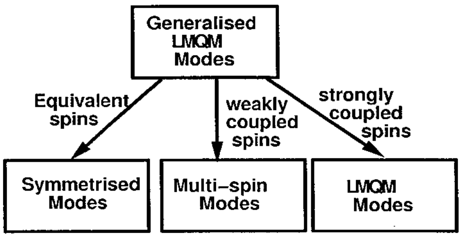

FIG. 1. The classification of magnetization mode sets for different spin systems.

lations affect the longitudinal relaxation as well of strongly coupled spins.

II. LONGITUDINAL MULTIPLE-QUANTUM MAGNETIZATION MODES

This paper concentrates on two relaxation mechanisms dominant at high magnetic fields, namely the intramolecular dipole–dipole (DD) interaction and the chemical shift anisotropy (CSA) of spin $\frac{1}{2}$ nuclei. The evolution equation of the orthonormalized modes $\{\nu_i\}$ has the same structure as the Redfield equation,

$$\frac{d}{dt}\,\nu_i(t) = \sum_{j=1}^{2^n} \Gamma_{ij}\nu_j(t), \qquad [1]$$

where Γ_{ij} is a $2^n \times 2^n$ symmetric matrix. The density operator can be expanded in terms of a complete set of orthogonal base operators $\{B_s\}$ with many possibilities for such basis sets. We prefer to express magnetization modes as combinations of single-transition operators (*18–20*). A single-transition operator is associated with the transition between two arbitrary energy levels $|r\rangle$ and $|s\rangle$, which may represent a zero-, single-, or multiple-quantum transition and can be treated as a virtual two-level system. The operators can be characterized thus:

$$\begin{aligned}
\langle i|I_0^{rs}|j\rangle &= (\delta_{ir}\delta_{jr} + \delta_{is}\delta_{js})\\
\langle i|I_x^{rs}|j\rangle &= (\delta_{ir}\delta_{js} + \delta_{is}\delta_{jr})/2\\
\langle i|I_y^{rs}|j\rangle &= i\,(-\delta_{ir}\delta_{js} + \delta_{is}\delta_{jr})/2\\
\langle i|I_z^{rs}|j\rangle &= (\delta_{ir}\delta_{jr} - \delta_{is}\delta_{js})/2.
\end{aligned} \qquad [2]$$

These operators are defined in the eigenbase of the Hamiltonian which makes them a suitable choice for describing strongly coupled spins.

A. LMQM Modes for an AB System

The LMQM modes and their operator representation in different bases (single transition and product operator) as well as the population combinations corresponding to these modes for a two-spin strongly coupled system (AB) are represented in Table 1.

The superscript (1, 4) refers to the double quantum and (2, 3) to the zero quantum of the AB spin system (with the eigenstates labeled as $|1\rangle = |\alpha\alpha\rangle$, $|2\rangle = \cos\theta|\alpha\beta\rangle + \sin\theta|\beta\alpha\rangle$, $|3\rangle = -\sin\theta|\alpha\beta\rangle + \cos\theta|\beta\alpha\rangle$, and $|4\rangle = |\beta\beta\rangle$, where $\tan\theta = J/\delta_{AB}$, J being the coupling constant and δ_{AB} the difference in chemical shifts of the spins). A valid basis set of magnetization modes for this strongly coupled two-spin system (Table 1) is one that remains within the zero-quantum–double-quantum subspace of the single-transition operators (*18–20*). In the weak coupling limit ($\theta \to 0$), the operator definitions in Table 1 reduce to that for an AX spin system. Since single-spin magnetizations A_Z and B_Z are well-defined quantities for weakly coupled systems (AX), one can construct the multispin modes (commonly used in most experiments) as linear combinations of these LMQM modes. The evolution of the LMQM modes for the AB system is obtained as:

$$-\frac{d}{dt}\begin{bmatrix} \frac{1}{2}\langle I_0^{1,4} + I_0^{2,3}\rangle \\ \sqrt{2}\,\langle I_Z^{1,4}\rangle \\ \sqrt{2}\,\langle I_Z^{2,3}\rangle \\ \frac{1}{2}\langle I_0^{1,4} - I_0^{2,3}\rangle \end{bmatrix}
= \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & \rho_{1,4}(\mathbf{A}) & \sigma_{2,3}^{1,4}(\mathbf{A}+\mathbf{C}) & \delta_{1,4-2,3}^{1,4}(\mathbf{C}) \\ 0 & \sigma_{2,3}^{1,4}(\mathbf{A}+\mathbf{C}) & \rho_{2,3}(\mathbf{A}+\mathbf{C}) & \delta_{1,4-2,3}^{2,3}(\mathbf{A}+\mathbf{C}) \\ 0 & \delta_{1,4-2,3}^{1,4}(\mathbf{C}) & \delta_{1,4-2,3}^{2,3}(\mathbf{A}+\mathbf{C}) & \rho_{1,4-2,3}(\mathbf{A}) \end{bmatrix}
\times \begin{bmatrix} \frac{1}{2}\langle I_0^{1,4} + I_0^{2,3}\rangle \\ \sqrt{2}\langle\Delta(I_Z^{1,4})\rangle \\ \sqrt{2}\langle\Delta(I_Z^{2,3})\rangle \\ \frac{1}{2}\langle\Delta(I_0^{1,4} - I_0^{2,3})\rangle \end{bmatrix}. \qquad [3]$$

TABLE 1
The LMQM Modes for the AB System, Defined in the Eigenbasis of the Static Hamiltonian

LMQM modes in eigenbasis	Product operator modes	Population combinations
$\frac{1}{2}\langle I_0^{1,4} + I_0^{2,3}\rangle$	$\langle\frac{1}{2}1\rangle$	$\frac{1}{2}(P_1 + P_2 + P_3 + P_4)$
$\sqrt{2}\langle I_Z^{1,4}\rangle$	$\frac{1}{\sqrt{2}}\langle A_Z + B_Z\rangle$	$\frac{1}{\sqrt{2}}(P_1 - P_4)$
$\sqrt{2}\langle I_Z^{2,3}\rangle$	$\frac{1}{\sqrt{2}}\{\cos 2\theta\langle A_Z - B_Z\rangle - \sin 2\theta\langle A^+B^- + A^-B^+\rangle\}$	$\frac{1}{\sqrt{2}}(P_2 - P_3)$
$\frac{1}{2}\langle I_0^{1,4} - I_0^{2,3}\rangle$	$\langle 2A_ZB_Z\rangle$	$\frac{1}{2}(P_1 - P_2 - P_3 + P_4)$

Note. The product operator definitions and corresponding population combinations are also shown.

The ρ_μ terms in the real symmetric Γ matrix for the AB system defined above denote the self-relaxation of a LMQM mode μ while the σ_ν^μ $(=\sigma_\mu^\nu)$ and δ_ν^μ $(=\delta_\mu^\nu)$ terms refer to the cross relaxation between LMQM modes μ and ν. The **A** signifies the presence of autocorrelation terms in the element of the relaxation matrix and the **C** denotes cross-correlation terms. The Δ in $\langle \Delta m \rangle$ denotes the deviation of mode m from its thermal equilibrium value. The factorization of the matrix Γ into two blocks corresponding to symmetric and antisymmetric modes (which do not couple unless CSA–DD cross correlations are present), valid for weakly coupled spins, is now no longer possible, as the concept of spin inversion symmetry is not meaningful for strongly coupled spins.

The various elements of the AB relaxation matrix are obtained in terms of spectral densities as

$$
\begin{aligned}
\rho_{1,4} &= -2J_{AA}(\omega) - 2J_{BB}(\omega) - J_{ABAB}(\omega) - 4J_{ABAB}(\omega) \\
\sigma_{1,4}^{2,3} &= -2\cos 2\theta J_{AA}(\omega) + 2\cos 2\theta J_{BB}(\omega) \\
&\quad -2\sin 2\theta J_{AB}^{A}(\omega) - 2\sin 2\theta J_{AB}^{B}(\omega) \\
\delta_{1,4-2,3}^{1,4} &= 2\sqrt{2}[J_{AB}^{A}(\omega) + J_{AB}^{B}(\omega)] \\
\rho_{2,3} &= -\tfrac{4}{3}(1-\cos 4\theta)(J_{AA}(0) + J_{BB}(0)) - 2J_{AA}(\omega) \\
&\quad - 2J_{BB}(\omega) + \tfrac{8}{3}(1-\cos 4\theta)J_{AB}(0) \\
&\quad - \tfrac{1}{3}(1+\cos 4\theta)J_{ABAB}(0) - J_{ABAB}(\omega) \\
&\quad + \tfrac{4}{3}\sin 4\theta J_{AB}^{A}(0) - \tfrac{4}{3}\sin 4\theta J_{AB}^{B}(0) \\
\delta_{1,4-2,3}^{2,3} &= 2\sqrt{2}\cos 2\theta J_{AB}^{A}(\omega) - 2\sqrt{2}\cos 2\theta J_{AB}^{B}(\omega) \\
&\quad + 4\sqrt{2}\sin 2\theta J_{AB}(\omega) + 2\sqrt{2}\sin 2\theta J_{ABAB}(\omega) \\
\rho_{1,4-2,3} &= -4J_{AA}(\omega) - 4J_{BB}(\omega) - 2J_{ABAB}(\omega).
\end{aligned}
\qquad [4]
$$

J_{ij} here refers to the cross-correlation spectral density between the CSAs of spins i and j, J_{ii} denotes the autocorrelation spectral density of the CSA of spin i, J_{ij}^{k} denotes the cross-correlation spectral density of the CSA of spin k with the dipole of i and j, and J_{ijkl} refers to the dipolar interaction between the pairs of dipoles ij and kl. The expressions for these spectral densities are contained in (*33*). It is to be noted that the $\delta_{1,4-2,3}^{1,4}$ term of the Γ relaxation matrix, which couples the modes $\langle I_z^{1,4}\rangle$ and $\langle I_z^{1,4} - I_z^{2,3}\rangle$, is free from strong coupling and has contributions solely from CSA–DD cross correlations. The measurement of this relaxation rate (in the initial rate approximation) is hence a direct measure of such cross correlations. The $\frac{1}{2}\langle I_0^{1,4} + I_0^{2,3}\rangle$ mode is the sum of all the level populations and hence does not evolve in time. The $\frac{1}{2}\langle I_0^{1,4} - I_0^{2,3}\rangle$ signifies longitudinal two-spin order and can be created from the $\sqrt{2}\langle I_Z^{1,4}\rangle$ mode via cross correlations alone and from the $\sqrt{2}\langle I_Z^{2,3}\rangle$ mode from a combination of auto- and cross-correlation terms with strong coupling factors.

The picture simplifies in the weak coupling limit as now both the $\sqrt{2}\langle I_Z^{1,4}\rangle$ and the $\sqrt{2}\langle I_Z^{2,3}\rangle$ modes evolve into longitudinal two-spin order solely through CSA–DD cross correlations and all modes self-relax solely through autocorrelation terms.

B. LMQM Modes for an ABX System

An orthonormalized set of LMQM modes for a three-spin ABX system (with two of the spins A and B strongly coupled to each other and weakly coupled to spin X), is defined in Table 2.

The superscripts (1, 7) and (2, 8) refer to the two double quanta of the A and the B spins while (3, 4) and (5, 6) refer to the zero quanta of these spins (where $|1\rangle = \alpha\alpha\alpha$, $|2\rangle = \alpha\alpha\beta$, $|3\rangle = \cos\theta_+\alpha\beta\alpha + \sin\theta_+\beta\alpha\alpha$, $|4\rangle = -\sin\theta_+\alpha\beta\alpha + \cos\theta_+\beta\alpha\alpha$, $|5\rangle = \cos\theta_-\alpha\beta\beta + \sin\theta_-\beta\alpha\beta$, $|6\rangle = -\sin\theta_-\alpha\beta\beta + \cos\theta_-\beta\alpha\beta$, $|7\rangle = \beta\beta\alpha$, and $|8\rangle = \beta\beta\beta$, with the usual definitions of $\theta_\pm$ (*34*)). The labels (1, 2), (3, 5), (4, 6), and (7, 8) refer to the single-quantum transitions of the X spin. Here, the single-transition operator basis for the LMQM modes encompasses the double-quantum–zero-quantum subspace of the two strongly coupled spins and the single-quantum subspace of the weakly coupled spin.

Although the overall structure of the Γ matrix for the ABX system is rather complex, it is interesting to note the existence of some off-diagonal relaxation terms that arise purely from cross correlations and are free from any strong coupling effects. These Γ (relaxation) matrix elements in terms of spectral densities are

$$
\begin{aligned}
\Gamma^{2,5} &= 2\sqrt{2}[J_{AB}^{A}(\omega) + J_{AB}^{B}(\omega)] \\
\Gamma^{2,6} &= 2[J_{AX}^{A}(\omega) + J_{BX}^{B}(\omega)] \\
\Gamma^{2,8} &= -\sqrt{2}[J_{ABAX}(\omega) + J_{ABBX}(\omega)] \\
\Gamma^{4,6} &= 2\sqrt{2}[J_{AX}^{X}(\omega) + J_{BX}^{X}(\omega)] \\
\Gamma^{4,8} &= -2J_{AXBX}(\omega).
\end{aligned}
\qquad [5]
$$

The modes $\langle m_2\rangle$ and $\langle m_5\rangle$ are coupled through a sum of the CSA–DD cross-correlation rates $J_{AB}^{A}(\omega)$ and $J_{AB}^{B}(\omega)$. The sum of the two CSA–DD rates $J_{AX}^{A}(\omega)$ and $J_{BX}^{B}(\omega)$ can be estimated from the evolution of mode $\langle m_6\rangle$ from the mode $\langle m_2\rangle$ or vice versa. The modes $\langle m_2\rangle$ and $\langle m_8\rangle$ are coupled through a sum of the DD–DD cross-correlation rates $J_{ABAX}(\omega)$ and $J_{ABBX}(\omega)$. The mode $\langle m_4\rangle$ is relaxation coupled to the mode $\langle m_6\rangle$ through the CSA–DD rates $J_{AX}^{X}(\omega)$ and $J_{BX}^{X}(\omega)$. This mode also couples to the mode $\langle m_8\rangle$ solely through the dipolar cross-correlation spectral density $J_{AXBX}(\omega)$.

Physical observables, LMQM modes, and experiments on a strongly coupled system. In general, sets of LMQM modes are designed to be directly relatable to experimental line intensities, thus preserving their intuitive physical interpretation. The density matrix during the relaxation period remains diagonal (for experiments designed to measure longitudinal relax-

TABLE 2
The LMQM Modes Defined for an ABX Spin System

Mode label	LMQM modes in eigenbasis	Product operator modes	Population combinations
$\langle m_1\rangle$	$\frac{1}{2\sqrt{2}}\langle I_0^{1,7} + I_0^{2,8} + I_0^{3,4} + I_0^{5,6}\rangle$	$\langle\frac{1}{2\sqrt{2}}1\rangle$	$\frac{1}{2\sqrt{2}}(P_1 + P_2 + P_3 + P_4 + P_5 + P_6 + P_7 + P_8)$
$\langle m_2\rangle$	$\langle I_Z^{1,7} + I_Z^{2,8}\rangle$	$\langle A_Z + B_Z\rangle$	$\frac{1}{2}(P_1 + P_2 - P_7 - P_8)$
$\langle m_3\rangle$	$\langle I_Z^{3,4} + I_Z^{5,6}\rangle$	$[\frac{1}{2}\{(\cos 2\theta_+ + \cos 2\theta_-)\langle A_Z - B_Z\rangle + (\sin 2\theta_+ + \sin 2\theta_-)\langle A^+B^- + A^-B^+\rangle\} + \{(\cos 2\theta_+ - \cos 2\theta_-)\langle A_Z - B_Z\rangle + (\sin 2\theta_- - \sin 2\theta_+)\langle A^+B^- + A^-B^+\rangle\}X_Z]$	$\frac{1}{2}(P_3 - P_4 + P_5 - P_6)$
$\langle m_4\rangle$	$\frac{1}{\sqrt{2}}\langle I_Z^{1,2} + I_Z^{3,5} + I_Z^{4,6} + I_Z^{7,8}\rangle$	$\frac{1}{\sqrt{2}}\langle X_Z\rangle$	$\frac{1}{2\sqrt{2}}(P_1 - P_2 + P_3 + P_4 - P_5 - P_6 + P_7 - P_8)$
$\langle m_5\rangle$	$\frac{1}{2\sqrt{2}}\langle I_0^{1,7} + I_0^{2,8} - I_0^{3,4} - I_0^{5,6}\rangle$	$\frac{1}{\sqrt{2}}\langle 2A_ZB_Z\rangle$	$\frac{1}{2\sqrt{2}}(P_1 + P_2 - P_3 - P_4 - P_5 - P_6 + P_7 + P_8)$
$\langle m_6\rangle$	$\langle I_Z^{1,7} - I_Z^{2,8}\rangle$	$\langle 2(A_Z + B_Z)X_Z\rangle$	$\frac{1}{2}(P_1 - P_2 - P_7 + P_8)$
$\langle m_7\rangle$	$\langle I_Z^{3,4} - I_Z^{5,6}\rangle$	$[\frac{1}{2}\{(\cos 2\theta_+ - \cos 2\theta_-)\langle A_Z - B_Z\rangle + (\sin 2\theta_- - \sin 2\theta_+)\langle A^+B^- + A^-B^+\rangle\} + \{(\cos 2\theta_+ + \cos 2\theta_-)\langle A_Z - B_Z\rangle + (\sin 2\theta_+ + \sin 2\theta_-)\langle A^+B^- + A^-B^+\rangle\}X_Z]$	$\frac{1}{2}(P_3 - P_4 - P_5 + P_6)$
$\langle m_8\rangle$	$\frac{1}{\sqrt{2}}\langle I_Z^{1,2} - I_Z^{3,5} - I_Z^{4,6} + I_Z^{7,8}\rangle$	$\frac{1}{\sqrt{2}}\langle 4A_ZB_ZX_Z\rangle$	$\frac{1}{2\sqrt{2}}(P_1 - P_2 - P_3 - P_4 + P_5 + P_6 + P_7 - P_8)$

ation). Hence a read pulse is required at the end of the evolution interval to convert magnetization modes into observable magnetization. The various LMQM modes are linear combinations of standard line intensities (SLIs (*35*)), where SLIs are experimental line intensities obtained by a small angle detection pulse.

The AB spin system. In terms of standard line intensities the modes are given by (*36*)

$$\sqrt{2}I_Z^{1,4}\rangle = \frac{1}{\sqrt{2}}\left[\frac{L_{13}}{(1-\sin 2\theta)} + \frac{L_{24}}{(1+\sin 2\theta)} + \frac{L_{12}}{(1+\sin 2\theta)} + \frac{L_{34}}{(1-\sin 2\theta)}\right]$$

$$\sqrt{2}\langle I_Z^{2,3}\rangle = \frac{1}{\sqrt{2}}\left[\frac{L_{13}}{(1-\sin 2\theta)} + \frac{L_{24}}{(1+\sin 2\theta)} - \frac{L_{12}}{(1+\sin 2\theta)} - \frac{L_{34}}{(1-\sin 2\theta)}\right]$$

$$\frac{1}{2}\langle I_0^{1,4} - I_0^{2,3}\rangle = \left[\frac{L_{13}}{(1-\sin 2\theta)} - \frac{L_{24}}{(1+\sin 2\theta)}\right] = \left[\frac{L_{12}}{(1+\sin 2\theta)} - \frac{L_{34}}{(1-\sin 2\theta)}\right]. \quad [6]$$

The ABX spin system. The modes of interest to us (since they directly encode cross-correlation information) are given in terms of SLIs by

$$\langle m_2\rangle = \frac{1}{2}\left[\frac{L_{14}}{1-\sin 2\theta_+} + \frac{L_{26}}{1-\sin 2\theta_-} + \frac{L_{37}}{1+\sin 2\theta_+} + \frac{L_{58}}{1+\sin 2\theta_-} + \frac{L_{13}}{1+\sin 2\theta_+} + \frac{L_{25}}{1-\sin 2\theta_-} + \frac{L_{47}}{1-\sin 2\theta_+} + \frac{L_{68}}{1-\sin 2\theta_-}\right]$$

$$\langle m_4\rangle = \left[L_{12} + L_{78} + \frac{1}{2}\left\{\frac{L_{35}}{\cos^2(\theta_+-\theta_-)} + \frac{L_{46}}{\cos^2(\theta_+-\theta_-)} + \frac{L_{45}}{\sin^2(\theta_+-\theta_-)} + \frac{L_{36}}{\sin^2(\theta_+-\theta_-)}\right\}\right]$$

$$\langle m_5\rangle = \sqrt{2}\left[\frac{L_{14}}{1-\sin 2\theta_+} + \frac{L_{26}}{1-\sin 2\theta_-} - \frac{L_{37}}{1+\sin 2\theta_+} - \frac{L_{58}}{1+\sin 2\theta_-}\right]$$

or equivalently,

$$\langle m_5 \rangle = \sqrt{2}\left[\frac{L_{13}}{1+\sin 2\theta_+} + \frac{L_{25}}{1+\sin 2\theta_-} - \frac{L_{47}}{1-\sin 2\theta_+} - \frac{L_{68}}{1-\sin 2\theta_-}\right]$$

$$\langle m_6 \rangle = \sqrt{2}[L_{12} - L_{78}]$$

or equivalently,

$$\langle m_6 \rangle = \frac{1}{\sqrt{2}}\left[\frac{L_{14}}{1-\sin 2\theta_+} - \frac{L_{26}}{1-\sin 2\theta_-} + \frac{L_{37}}{1+\sin 2\theta_+} - \frac{L_{58}}{1+\sin 2\theta_-} + \frac{L_{13}}{1+\sin 2\theta_+} - \frac{L_{25}}{1+\sin 2\theta_-} + \frac{L_{47}}{1-\sin 2\theta_+} - \frac{L_{68}}{1-\sin 2\theta_-}\right]$$

$$\langle m_8 \rangle = \sqrt{2}\left[\frac{L_{14}}{1-\sin 2\theta_+} - \frac{L_{26}}{1-\sin 2\theta_-} - \frac{L_{37}}{1+\sin 2\theta_+} + \frac{L_{58}}{1+\sin 2\theta_-}\right]$$

or equivalently,

$$\langle m_8 \rangle = \sqrt{2}\left[\frac{L_{13}}{1+\sin 2\theta_+} - \frac{L_{25}}{1+\sin 2\theta_-} - \frac{L_{47}}{1-\sin 2\theta_+} + \frac{L_{68}}{1-\sin 2\theta_-}\right]. \quad [7]$$

In order to experimentally measure cross correlations in strongly coupled spin systems using the above modes picture, we have carried out inversion recovery experiments on 2,5-dibromonitrobenzene (dissolved in deuterated benzene). The experiments have been performed on a Bruker AMX 400-MHz spectrometer at room temperature. The chemical shifts and coupling constants in this three-spin system are obtained as $\delta_A = 6.743$ ppm, $\delta_B = 6.71$ ppm, $\delta_X = 7.375$ ppm, $J_{AB} = 8.53$ Hz, and $J_{BX} = 2.1$ Hz. The splitting due to the para-coupling J_{AX} is too small to be observed in this system. Equilibrium values are zero for all modes except $\langle m_2 \rangle$ and $\langle m_4 \rangle$.

Nonselective inversion recovery experiments were performed to invert the modes $\langle m_2 \rangle$ and $\langle m_4 \rangle$ and monitor their relaxation (solely through cross-correlation mechanisms) to the LMQM modes $\langle m_5 \rangle$, $\langle m_6 \rangle$, and $\langle m_8 \rangle$. The spectra and the evolution of the various LMQM modes are plotted in Figs. 2 and 3. A small flip angle (10^0) pulse has been used to measure the population differences under the linear approximation (*14*). An imperfect π pulse accounts for the creation of some multispin order even at the beginning of the relaxation interval. Since some of the peaks in the AB part of the spectrum show a significant overlap, this part of the spectrum was fitted with six Lorentzians in order to evaluate the integrated line intensity of each component. The curves obtained for the LMQM modes containing cross-correlation information were fitted to biexponentials and the cross-correlation rate $\Gamma^{2,5}$ calculated in the initial rate approximation is 0.017 s^{-1}. The amount of magnetization transferred via CSA–DD cross correlation in the present case is rather small (≈1.0% of equilibrium $\langle m_2 \rangle$ magnetization), and it has been possible to extract the same using LMQM modes in a straightforward manner. The buildup of the modes $\langle m_6 \rangle$ and $\langle m_8 \rangle$ was not observable due to weak dipolar interactions involving the spatially distant X spin.

From the various sets of operator definitions of magnetization modes for different spin systems, it is clear that the single-transition operator definitions in the eigenbasis of the static Hamiltonian are conceptually simple and physically meaningful, making them a natural choice for any spin system.

III. REMOTE CROSS CORRELATIONS IN LONGITUDINAL RELAXATION

Cross correlations which do not explicitly depend on the distance of other spins from the spin(s) being considered are termed “remote” and contribute to the transverse relaxation of weakly coupled spin systems (*29–32*). It has been noted (*32*) that such correlations in weakly coupled spin systems affect the transverse relaxation of single- and multiple-quantum coherences and contribute to differential line broadening in the presence of J couplings and/or direct cross correlations. Such remote cross correlations also crop up in rotating frame relaxation experiments (for example, ROESY and its variants) as the spin locking causes the relaxation to become a mixture of longitudinal and transverse relaxation (*37*).

We note here that such “remote” terms affect longitudinal relaxation as well. In a strongly coupled two spin (AB) system, the cross correlation between the CSA of spin A and that of spin B affects the relaxation of the populations with contributions from the spectral density at zero and ω frequencies. In an ABX spin system, remote terms like the CSA–CSA cross correlations between spins A and B and the correlations between the CSA of spin A and the dipolar interaction between spins B and X and similarly between the CSA of spin B and the dipolar interaction between spins A and X at frequencies zero and ω contribute to longitudinal relaxation. In the limit that $\theta \rightarrow 0$ these remote cross correlations disappear, as is to be expected for weakly coupled spin systems.

Calculations have been performed on homonuclear strongly coupled two-spin (AB) and three-spin (ABX) systems to analyze the effects of remote cross correlations. Explicit calcula-

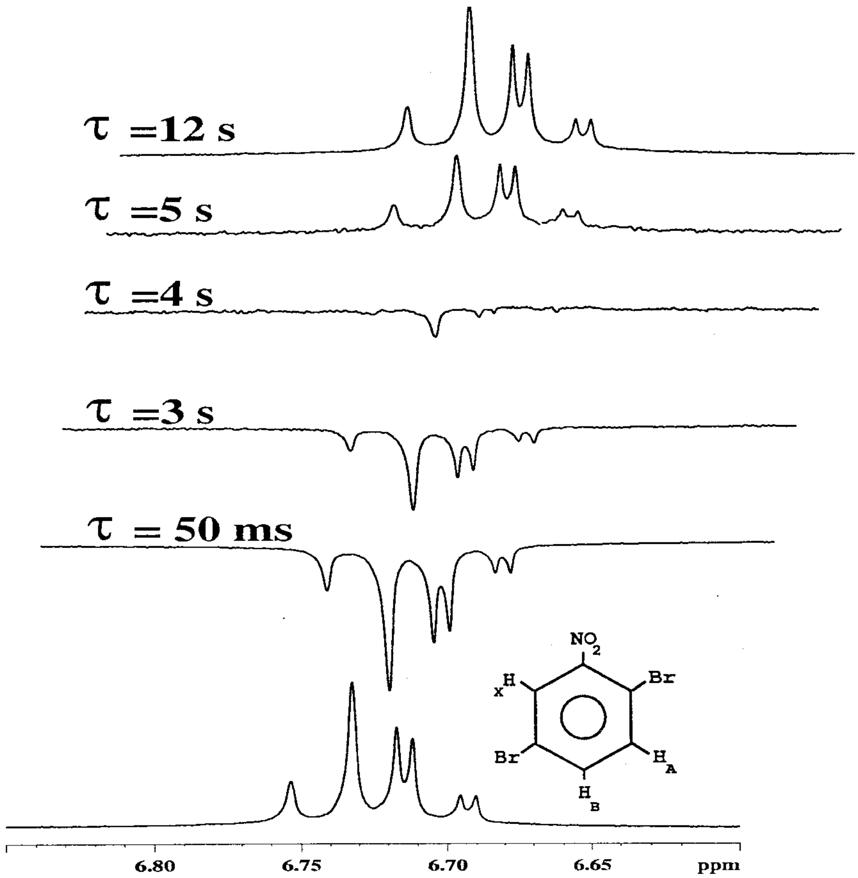

FIG. 2. The ^{1}H inversion recovery spectra of 2,5-dibromonitrobenzene, plotted as a function of the relaxation time. A nonselective inversion of all the three spins has been performed and only the AB part of the total spectrum is shown here. A small flip angle (10°) detection pulse has been used.

tions of all elements of the relaxation matrix have been verified using the software package "Mathematica." The transition probabilities $W_{\alpha\beta}$ have been clubbed into a column vector **W** and expanded (matrix-fashion) in terms of auto- and cross-correlation spectral densities, in order to achieve a "pictorial" depiction of the dependence of various W's on different spectral densities (*38*).

A. The AB Spin System

The contributions of different spectral densities to longitudinal relaxation of the strongly coupled AB spin system can be expressed as

$$\mathbf{W}_{\mathrm{AB}}^{\mathrm{SQ/MQ}} = -\sum_{n=0}^{2} A(n\omega)^{\mathrm{SQ/MQ}} \mathbf{J}_{\mathrm{auto}}(n\omega) + C(n\omega)^{\mathrm{SQ/MQ}} \mathbf{J}_{\mathrm{cross}}(n\omega), \quad [8]$$

where

$$\mathbf{W}_{\mathrm{AB}}^{\mathrm{SQ}} = \begin{bmatrix} W_{13} \\ W_{24} \\ W_{12} \\ W_{34} \end{bmatrix}; \quad \mathbf{W}_{\mathrm{AB}}^{\mathrm{MQ}} = \begin{bmatrix} W_{14} \\ W_{23} \end{bmatrix} \quad [9]$$

with the $W_{\alpha\beta}$ referring to various single-quantum (or multiple-quantum) transition probabilities, and the auto- and cross-correlation spectral density vectors being defined as

$$\mathbf{J}_{\mathrm{auto}}(n\omega) = \begin{bmatrix} J_{\mathrm{AA}}(n\omega) \\ J_{\mathrm{BB}}(n\omega) \\ J_{\mathrm{ABAB}}(n\omega) \end{bmatrix}; \quad \mathbf{J}_{\mathrm{cross}}(n\omega) = \begin{bmatrix} J_{\mathrm{AB}}^{\mathrm{A}}(n\omega) \\ J_{\mathrm{AB}}^{\mathrm{B}}(n\omega) \\ J_{\mathrm{AB}}(n\omega) \end{bmatrix}. \quad [10]$$

The auto- and cross-correlation coefficient matrices $A^{\mathrm{SQ/MQ}}(n\omega)$ and $C^{\mathrm{SQ/MQ}}(n\omega)$, respectively, have been computed in the

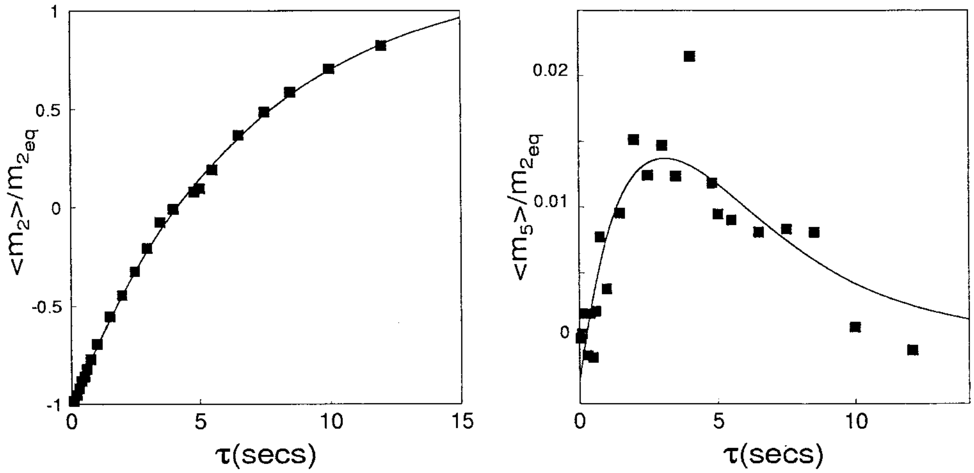

FIG. 3. The evolution of the LMQM modes $\langle m_2 \rangle$ and $\langle m_5 \rangle$ plotted as a function of the recovery time τ. The emergence of the $\langle m_5 \rangle$ mode is due solely to CSA–DD cross correlations.

eigenbasis. Only spectral densities at the frequency ω contribute to the single-quantum transition probabilities whereas the multiple-quantum transition probabilities have contributions only from spectral densities at zero and 2ω frequencies. Explicit calculation of the various coefficient matrices for the AB spin system yields the transition probabilities for the single-quantum levels as

$$\mathbf{W}_{\mathrm{AB}}^{\mathrm{SQ}} = -\begin{bmatrix} (1+\cos 2\theta) & 2\sin^2\theta & (\frac{1}{2}-\sin 2\theta) \\ (1+\cos 2\theta) & 2\sin^2\theta & (\frac{1}{2}+\sin 2\theta) \\ 2\sin^2\theta & (1+\cos 2\theta) & (\frac{1}{2}+\sin 2\theta) \\ 2\sin^2\theta & (1+\cos 2\theta) & (\frac{1}{2}-\sin 2\theta) \end{bmatrix} \begin{bmatrix} J_{\mathrm{AA}}(\omega) \\ J_{\mathrm{BB}}(\omega) \\ J_{\mathrm{ABAB}}(\omega) \end{bmatrix} + \begin{bmatrix} (-\sin 2\theta+\cos 2\theta+1) & (-\sin 2\theta+2\sin^2\theta) & 2\sin 2\theta \\ (-\sin 2\theta-\cos 2\theta-1) & (-\sin 2\theta-2\sin^2\theta) & -2\sin 2\theta \\ (\sin 2\theta+2\sin^2\theta) & (\sin 2\theta+\cos 2\theta+1) & -2\sin 2\theta \\ (\sin 2\theta-2\sin^2\theta) & (\sin 2\theta-\cos 2\theta-1) & 2\sin 2\theta \end{bmatrix} \begin{bmatrix} J_{\mathrm{AB}}^{\mathrm{A}}(\omega) \\ J_{\mathrm{AB}}^{\mathrm{B}}(\omega) \\ J_{\mathrm{AB}}(\omega) \end{bmatrix}. \quad [11]$$

In the weak coupling limit, these two transition probabilities can be identified as belonging to the "A" spin and are equal in the absence of cross correlations. The presence of strong coupling and/or cross correlations (including the direct CSA–DD cross-correlation spectral densities $J_{\mathrm{AB}}^{\mathrm{A}}(\omega)$ and $J_{\mathrm{AB}}^{\mathrm{B}}(\omega)$ and the remote CSA–CSA cross-correlation spectral density $J_{\mathrm{AB}}(\omega)$) lifts this degeneracy. For equivalent spin systems ($\theta \rightarrow \pi/4$), where the sum mode (the total spin magnetization or the sum of all the single-quantum transition probabilities) is the only physical observable, the contribution of these remote terms to the longitudinal relaxation cancels out.

The difference in the single-quantum transition probabilities W_{13} and W_{24} is given by

$$W_{13} - W_{24} = \sin 2\theta J_{\mathrm{ABAB}}(\omega) + 2(1+\cos 2\theta) J_{\mathrm{AB}}^{\mathrm{A}}(\omega) + 4\sin^2\theta J_{\mathrm{AB}}^{\mathrm{B}}(\omega) + 4\sin 2\theta J_{\mathrm{AB}}(\omega). \quad [12]$$

The expression for the multiple-quantum (double and zero) level transition probabilities is obtained as

$$\mathbf{W}_{AB}^{MQ} = \begin{bmatrix} 0 & 0 & 0 \\ -\frac{4}{3}\sin^2 2\theta & -\frac{4}{3}\sin^2 2\theta & -\frac{1}{3}(1-\sin^2 2\theta) \end{bmatrix} \times \begin{bmatrix} J_{AA}(0) \\ J_{BB}(0) \\ J_{ABAB}(0) \end{bmatrix} + \begin{bmatrix} 0 & 0 & 0 \\ \frac{4}{3}\sin 2\theta\cos 2\theta & -\frac{4}{3}\sin 2\theta\cos 2\theta & \frac{8}{3}(1-\sin^2 2\theta) \end{bmatrix} \times \begin{bmatrix} J_{AB}^{A}(0) \\ J_{AB}^{B}(0) \\ J_{AB}(0) \end{bmatrix} + \begin{bmatrix} 0 & 0 & -2 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} J_{AA}(2\omega) \\ J_{BB}(2\omega) \\ J_{ABAB}(2\omega) \end{bmatrix}. \quad [13]$$

In the weak coupling limit, the zero-quantum transition probability W_{23} depends only on the dipolar autocorrelation spectral density at zero frequency, while in the presence of strong coupling, all auto- and cross-correlation spectral densities contribute. The double-quantum transition probability W_{14}, on the other hand, has a sole contribution from the dipolar autocorrelation spectral density at 2ω, regardless of the strength of the coupling and has no contribution from cross correlations.

The matrix containing the transition probabilities $W_{\alpha\beta}$ (both single and multiple quantum) as its elements is related to the Γ matrix (Eq. [3]) by the transformation $\Gamma = VWV^{-1}$. The transformation matrix V for the AB system is given by

$$V = \frac{1}{2}\begin{bmatrix} 1 & 1 & 1 & 1 \\ \sqrt{2} & 0 & 0 & -\sqrt{2} \\ 0 & \sqrt{2} & -\sqrt{2} & 0 \\ 1 & -1 & -1 & 1 \end{bmatrix}. \quad [14]$$

Hence, the various elements of the Γ matrix (which are the different self- and cross-relaxation rates of the LMQM modes) are given in terms of the transition probabilities as

$$\rho_{1,4} = \tfrac{1}{2}[W_{12} + W_{34} + W_{13} + W_{24} + 4W_{14}]$$

$$\sigma_{2,3}^{1,4} = \tfrac{1}{2}[W_{13} + W_{24} - W_{12} - W_{34}]$$

$$\delta_{1,4-2,3}^{1,4} = \frac{1}{\sqrt{2}}[W_{12} - W_{34} + W_{13} - W_{24}]$$

$$\rho_{2,3} = \tfrac{1}{2}[W_{12} + W_{34} + W_{13} + W_{24} + 4W_{23}]$$

$$\delta_{1,4-2,3}^{2,3} = \frac{1}{\sqrt{2}}[W_{13} - W_{24} - W_{12} + W_{34}]$$

$$\rho_{1,4-2,3} = [W_{12} + W_{34} + W_{13} + W_{24}]. \quad [15]$$

Similar expressions can be derived for the ABX system as well.

B. The ABX Spin System

The longitudinal relaxation of the ABX spin system has contributions from both remote CSA–CSA cross correlations and remote CSA–DD cross correlations. The various single-quantum and multiple-quantum transition probabilities $\mathbf{W}_{ABX}^{SQ/MQ}$ can be expressed in terms of column vectors as

$$\mathbf{W}_{(AB)}^{SQ} = \begin{bmatrix} W_{13} \\ W_{14} \\ W_{25} \\ W_{26} \\ W_{37} \\ W_{47} \\ W_{58} \\ W_{68} \end{bmatrix}; \quad \mathbf{W}_{(X)}^{SQ} = \begin{bmatrix} W_{12} \\ W_{35} \\ W_{46} \\ W_{78} \end{bmatrix}, \quad [16]$$

where the single transitions have been grouped as belonging to the AB multiplet or the X spin. The six double- and zero-quantum transition probabilities have been grouped into the column vectors

$$\mathbf{W}_{ABX}^{DQ} = \begin{bmatrix} W_{17} \\ W_{28} \\ W_{16} \\ W_{38} \\ W_{15} \\ W_{48} \end{bmatrix}; \quad \mathbf{W}_{ABX}^{ZQ} = \begin{bmatrix} W_{34} \\ W_{56} \\ W_{24} \\ W_{57} \\ W_{23} \\ W_{67} \end{bmatrix}. \quad [17]$$

The contribution of remote cross-correlation terms to longitudinal relaxation, for the various single- and multiple-quantum transition probabilities, is obtained as

$$(\mathbf{W}_{(AB)}^{SQ})_{remote} = \begin{bmatrix} \sin 2\theta_+ & \sin 2\theta_+ & -2\sin 2\theta_+ \\ \sin 2\theta_+ & \sin 2\theta_+ & -2\sin 2\theta_+ \\ \sin 2\theta_- & \sin 2\theta_- & 2\sin 2\theta_- \\ -\sin 2\theta_- & -\sin 2\theta_- & -2\sin 2\theta_- \\ \sin 2\theta_+ & \sin 2\theta_+ & -2\sin 2\theta_+ \\ \sin 2\theta_+ & \sin 2\theta_+ & -2\sin 2\theta_+ \\ \sin 2\theta_- & \sin 2\theta_- & 2\sin 2\theta_- \\ -\sin 2\theta_- & -\sin 2\theta_- & -2\sin 2\theta_- \end{bmatrix} \times \begin{bmatrix} J_{BX}^{A}(\omega) \\ J_{AX}^{B}(\omega) \\ J_{AB}(\omega) \end{bmatrix} \quad [18]$$

$$(\mathbf{W}^{\mathrm{ZQ}}_{\mathrm{ABX}})_{\mathrm{remote}} = \begin{bmatrix} \frac{2}{3}(1-\cos 4\theta_+) & \frac{2}{3}(1-\cos 4\theta_+) & -\frac{4}{3}(1-\cos 4\theta_+) \\ -\frac{2}{3}(1-\cos 4\theta_-) & -\frac{2}{3}(1-\cos 4\theta_-) & -\frac{4}{3}(1-\cos 4\theta_-) \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} J^{\mathrm{A}}_{\mathrm{BX}}(0) \\ J^{\mathrm{B}}_{\mathrm{AX}}(0) \\ J_{\mathrm{AB}}(0) \end{bmatrix}. \qquad [19]$$

The single-quantum transition probabilities that belong to the AB multiplet (it is no longer possible to distinguish transitions as belonging to a spin, as the spins are now strongly coupled) have contributions from the CSA–CSA remote term J_{AB} and the CSA–DD remote spectral densities $J^{\mathrm{A}}_{\mathrm{BX}}$ and $J^{\mathrm{B}}_{\mathrm{AX}}$, all at the frequency ω. These contributions vanish in the weak coupling limit and as is expected, the single-quantum transition probabilities belonging to the X spin ($\mathbf{W}^{\mathrm{SQ}}_{(\mathrm{X})}$) are not affected by such remote cross correlations. Only the zero-quantum transitions W_{34} and W_{56} have contributions from the CSA–CSA and CSA–DD remote cross correlations at zero frequency. These terms drop out in the weak coupling limit. The double-quantum transition probabilities have contributions from all the autocorrelation dipolar spectral densities at 2ω and a contribution (that depends on the coupling strength θ) from the DD–DD cross-correlation spectral density J_{AXBX} at the frequency 2ω. They do not have any contributions from remote cross correlations. All other remote cross correlations that involve the CSA of the X spin, namely J_{AX}, J_{BX}, and $J^{\mathrm{X}}_{\mathrm{AB}}$, do not contribute.

IV. CONCLUSIONS

We describe a method, based on a generalized set of magnetization modes, for quantifying cross correlations in strongly coupled systems. The applicability of this method has been experimentally demonstrated for a strongly coupled spin system. Since strong coupling reintroduces the contribution of CSA auto- and CSA–CSA cross-correlation spectral densities at zero frequency to longitudinal relaxation, this modes method is applicable to the study of large biomolecules having strongly coupled spins such as some carbohydrates, aliphatic carbons in protein side chains, and nucleic acids, where strong coupling effects persist in diastereotopic protons even at high field strengths (*39*, *40*).

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