

Quantum Treatment of Intermolecular Multiple-Quantum Coherences with Intramolecular J Coupling in Solution NMR

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A recently introduced density matrix picture for dipolar effects in solution NMR (1996, *J. Chem. Phys.* 105, 874) gave complete solutions for intermolecular multiple-quantum coherences for single-component samples without scalar couplings. This paper, for the first time, shows that this quantum picture can lead to explicit signal expressions for multicomponent samples of molecules with internal scalar couplings (here assumed to generate a first-order spectrum) and long-range dipolar couplings. Experimental observation of a triplet in the indirectly detected dimension for a heteronuclear CRAZED sequence (¹³CHCl₃ sample, ZQ or 2Q coherences) gives clear evidence that the coupling is due to the intermolecular dipolar coupling. We also make comparisons with classical pictures which introduce the dipolar demagnetization field in multicomponent spin systems. © 1997 Academic Press

I. INTRODUCTION

Nonlinear effects in solution NMR spectra have attracted considerable interest recently (1–20). These effects are commonly interpreted using two superficially quite different pictures. The first explanation (2) invoked the dipolar demagnetizing field, which was originally added to the Bloch equations to explain multiple echoes in a continuous gradient (21–27) and recently corrected (12). The dipolar demagnetizing field arises because of intermolecular dipole–dipole interactions—the dipolar demagnetizing field at a certain position is the overall sum of the local fields generated by all the spins in the sample. If the spin distribution around is isotropic and spherically symmetric, this field is negligible; if the isotropy of the spin distribution is broken (by applying a field gradient or by a nonspherical sample), the demagnetizing field becomes significant. The dynamics which are calculated using modified Bloch equations that include the dipolar demagnetizing field are inherently nonlinear in terms of the magnetization, making the dynamics nonlinear and highly nonintuitive.

Alternatively, it is possible to write a density matrix treatment which explicitly shows the origin of the cross peaks in intermolecular multiple-quantum coherences (iMQCs). This “quantum picture” (3, 11) discards two main assumptions of NMR theory—the high-temperature approximation and the neglect of intermolecular dipole–dipole interactions. The original paper (3) examines the second-order term in the expansion of the equilibrium density matrix and showed that iMQCs could be converted into observable signals if some conditions were met. This quantum picture was later greatly extended to give a complete solution, completely omitting the high-temperature approximation (11), although only uncoupled spins were explicitly considered.

This paper, for the first time, shows that the quantum picture can lead to explicit signal expressions for molecules with internal scalar couplings (here assumed to generate a first-order spectrum) and long-range dipolar couplings. Here the specific application is to the HETERO-CRAZED sequence (Fig. 1) first demonstrated in Ref. (17), which detected ¹³C–¹H intermolecular two-spin operators ($I_{zi}S_{zj}$) present in the equilibrium density matrix. The quantum picture is very intuitive for understanding this sequence. Two-spin operators are rotated by a single 90° pulse into coherences $I_{xi}S_{xj} = (I_i^+S_j^+ + I_i^+S_j^- + I_i^-S_j^+ + I_i^-S_j^-)/4$ which evolve at the sum of the resonance frequencies (about 5/4 of the proton resonance frequency, since $\gamma_C \approx \gamma_H/4$) or the difference of the resonance frequencies (about 3/4 of the proton resonance frequency) during t_1 . They are transferred by another 90° pulse into two-spin, one-quantum coherences such as $I_{yi}S_{zj}$, which are converted by the dipolar coupling into observable magnetization I_{xi} during t_2 . The sum-frequency term can be retained by a 4:5 gradient echo; the difference-frequency term is retained by a 4:3 gradient echo. A classical calculation for this case would be quite involved, since scalar couplings cannot be correctly treated by the Bloch equations, and is far less intuitive: nothing evolves during t_1 at 5/4 or 3/4 of the proton resonant frequency, yet the nonlinearity makes a signal

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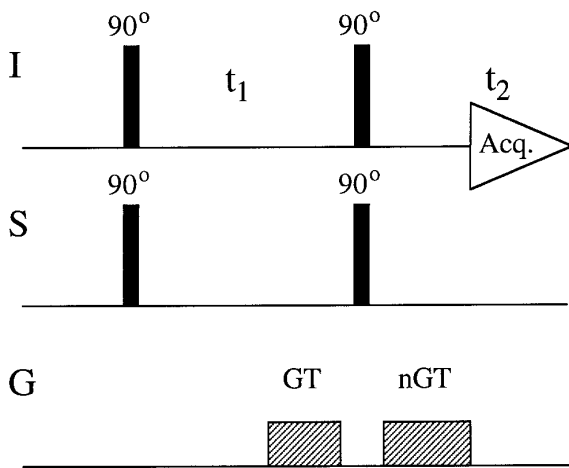


FIG. 1. The heteronuclear CRAZED pulse sequence, used to observe intermolecular heteronuclear multiple-quantum coherences in solution. A 90° pulse simultaneously given to both spins is followed by a free evolution time t_1 and a gradient pulse of strength G and length T . Immediately afterward, a second 90° pulse is given to both spins at once, followed by a second gradient pulse of area nGT . Detection of one spin occurs in t_2 . In real experiments, a portion of the first gradient pulse is applied at the beginning of the t_1 period to prevent radiation damping from rotating the concentrated I spin. For intermolecular ^{13}C - ^1H multiple-quantum coherences, a ratio of $\pm 3/4$ selects zero-quantum terms and a ratio of $\pm 5/4$ selects double-quantum terms.

emerge during t_2 . As we show below, internal scalar couplings increase the number of pathways for generating multiple-spin operators, but still permit analytical solution for the time evolution.

II. THEORY

The principles of a density matrix treatment for intermolecular multiple-quantum coherences for a single-component sample with uncoupled spins (e.g., the double-quantum coherence in H_2O after a double-quantum CRAZED sequence) are described in detail in the paper by Lee, Richter, Vathyam, and Warren (11), which we will call LRVW in what follows. We will extend the procedures to calculate the signal from the intermolecular heteronuclear multiple-quantum coherences in the presence of J coupling. The pulse sequence for the heteronuclear CRAZED experiment is shown in Fig. 1. For simplicity in notation, we will consider the simplest case of a $^{13}\text{CHCl}_3$ sample, where ^{13}C and H spins are J coupled. I and S denote two different kinds of spins ($I = \text{H}$, $S = ^{13}\text{C}$), and we will assume that the proton signal is detected in the detection period t_2 .

The secular part of the Hamiltonian for this spin system can be represented as

$$\begin{aligned}
 H/\hbar = & \sum_i^N (\Delta\omega_I I_{zi} + \Delta\omega_S S_{zi} + 2\pi J_{zi} S_{zi}) \\
 & + \sum_i^N \sum_j^N (3D_{ij}^{II} I_{zi} I_{zj} + 3D_{ij}^{SS} S_{zi} S_{zj}) \\
 & + \sum_i^N \sum_j^N 2D_{ij}^{IS} I_{zi} S_{zj}.
 \end{aligned} \quad [1]$$

The first part is the contribution from the Zeeman effects and the J coupling. The second and third parts account for the contributions from homonuclear and heteronuclear dipolar couplings, respectively, where the dipolar coupling constants are defined by

$$\begin{aligned}
 D_{ij}^{IS} &= \frac{\mu_0}{4\pi} \frac{\gamma_I \gamma_S \hbar}{4} \frac{1 - 3 \cos^2 \theta_{ij}}{r_{ij}^3}; \\
 D_{ij}^{II} &= \frac{\mu_0}{4\pi} \frac{\gamma_I^2 \hbar}{4} \frac{1 - 3 \cos^2 \theta_{ij}}{r_{ij}^3}.
 \end{aligned} \quad [2]$$

r_{ij} is the separation between spins i and j , θ_{ij} is the angle between the internuclear vector and the main magnetic field, and μ_0 is the vacuum permeability. Note that the homonuclear part of the dipolar Hamiltonian excludes terms like $\mathbf{I}_i \cdot \mathbf{I}_j$ for the same reason as explained in LRVW.

The explicit expression for the equilibrium density matrix without the high-temperature approximation can be written as (11)

$$\rho_{\text{eq}} = 2^{-(N+M)} \left[\prod_i (\mathbf{1} - \mathfrak{F}_I I_{zi}) \times \prod_k (\mathbf{1} - \mathfrak{F}_S S_{zk}) \right], \quad [3]$$

where $\mathfrak{F}_I = 2 \tanh(\hbar\omega_I/2kT)$, $\mathfrak{F}_S = 2 \tanh(\hbar\omega_S/2kT)$, and ω_I and ω_S are the Larmor frequencies of the I and S spins, respectively. The indices i and k run up to the number of I and S spins in the sample. Applying the first $(\pi/2)_y$ pulses, each z magnetization is rotated into x magnetization, giving

$$\begin{aligned}
 \rho(t_1 = 0) &= 2^{-(N+M)} \left[\prod_i (\mathbf{1} - \mathfrak{F}_I I_{xi}) \right. \\
 &\quad \times \left. \prod_k (\mathbf{1} - \mathfrak{F}_S S_{xk}) \right] \\
 &= 2^{-(N+M)} \sum_{n=0}^N \sum_{m=0}^M (-1)^{n+m} \\
 &\quad \times \underbrace{\mathfrak{F}_I^n \mathfrak{F}_S^m}_{n} I_{x1} I_{xj} \cdots \underbrace{S_{xk} S_{xl} \cdots}_{m}.
 \end{aligned} \quad [4]$$

The terms proportional to $\mathfrak{F}_I^n \mathfrak{F}_S^m$ are $(n+m)$ -spin operators of the form

$$\overbrace{I_{xi}I_{xj} \cdots}^n \cdots \overbrace{S_{zk}S_{xl} \cdots}^m,$$

which contain the intermolecular multiple-quantum coherences. For example, the operator $I_{+i}S_{+k}$ connects states separated by both a proton and a carbon spin flip, and evolves at the sum of the proton and carbon frequencies. For a $^{13}\text{CHCl}_3$ sample in a 600-MHz NMR spectrometer ($\gamma_S \approx \gamma_I/4$), this term will evolve at approximately (600 + 150) MHz in the laboratory frame during the t_1 period, generating terms like $I_{yi}S_{zk}$.

Multiple-quantum coherences in Eq. [4] can be converted into the observable signal in the following way. For the heteronuclear 2Q coherence $I_{+i}S_{+k}$, the second $(\pi/2)_y$ pulse converts this multiple-quantum coherence into the single-quantum coherence of I spin ($I_{yi}S_{zk}$). The dipolar couplings during the t_2 period can strip off the S_{zk} operator, giving observable 1-spin 1Q coherence. The precession frequency during the t_2 period will be close to 600 MHz. The gradient pulses before and after the second $(\pi/2)_y$ pulses should be set to 600:750 = 4:5 to select the coherence transfer pathway described above. In general, two gradient pulses function as a multiple-quantum filter. A coherence evolving with the

frequency of n times of the detection spin frequency during the t_1 period can be transformed into an observable, if we apply two gradient pulses in the ratio of 1 : n . In the rotating frame, when we detect the I spin at the t_2 period, all multiple-quantum coherences that had frequencies $\{(n - k(\gamma_S/\gamma_I))\Delta\omega_I + k\Delta\omega_S\}$ at the t_1 period could be rendered an observable single-quantum term by the intermolecular dipolar interaction. We will closely follow the procedures in LRVW (which handled only the single-spin case), and extend it to the heteronuclear case including J coupling. A derivation for the homonuclear case in the first-order spectrum approximation would be identical.

During the t_1 evolution time, each spin operator evolves under the Zeeman interaction and the J coupling, using the standard transformation rules for evolution under scalar couplings in NMR (28):

$$\begin{aligned} e^{-iJ_{ij}I_{zi}I_{zj}t}I_{xi}e^{iJ_{ij}I_{zi}I_{zj}t} &= I_{xi}\cos(J_{ij}t/2) + 2I_{yi}I_{zj}\sin(J_{ij}t/2) \\ e^{-iJ_{ij}I_{zi}I_{zj}t}2I_{xi}I_{zj}e^{iJ_{ij}I_{zi}I_{zj}t} &= 2I_{xi}I_{zj}\cos(J_{ij}t/2) + I_{yi}\sin(J_{ij}t/2) \\ e^{-iJ_{ij}I_{zi}I_{zj}t}I_{yi}e^{iJ_{ij}I_{zi}I_{zj}t} &= I_{yi}\cos(J_{ij}t/2) - 2I_{xi}I_{zj}\sin(J_{ij}t/2) \\ e^{-iJ_{ij}I_{zi}I_{zj}t}2I_{yi}I_{zj}e^{iJ_{ij}I_{zi}I_{zj}t} &= 2I_{yi}I_{zj}\cos(J_{ij}t/2) - I_{xi}\sin(J_{ij}t/2). \end{aligned} \quad [5]$$

The resulting density matrix can be written as

$$\begin{aligned} \rho(t_1) &= 2^{-(N+M)} \\ &\times \prod_i \left[\mathbf{1} - \mathfrak{F}_I I_{xi} \cos(\pi J t_1) \cos(\Delta\omega_I t_1 + \gamma_I G T s_i) - \mathfrak{F}_I 2 I_{yi} S_{zi} \sin(\pi J t_1) \cos(\Delta\omega_I t_1 + \gamma_I G T s_i) \right. \\ &\quad \left. - \mathfrak{F}_I I_{yi} \cos(\pi J t_1) \sin(\Delta\omega_I t_1 + \gamma_I G T s_i) + \mathfrak{F}_I 2 I_{zi} S_{xi} \sin(\pi J t_1) \sin(\Delta\omega_I t_1 + \gamma_I G T s_i) \right] \\ &\times \prod_k \left[\mathbf{1} - \mathfrak{F}_S S_{zk} \cos(\pi J t_1) \cos(\Delta\omega_S t_1 + \gamma_S G T s_k) - \mathfrak{F}_S 2 S_{yk} I_{zk} \sin(\pi J t_1) \cos(\Delta\omega_S t_1 + \gamma_S G T s_k) \right. \\ &\quad \left. - \mathfrak{F}_S S_{yk} \cos(\pi J t_1) \sin(\Delta\omega_S t_1 + \gamma_S G T s_k) + \mathfrak{F}_S 2 S_{xk} I_{zk} \sin(\pi J t_1) \sin(\Delta\omega_S t_1 + \gamma_S G T s_k) \right], \end{aligned} \quad [6]$$

where $\Delta\omega_I$ and $\Delta\omega_S$ represent the offset resonance frequencies of the I spin and S spin in the corresponding doubly rotating frame of reference. s_i and s_k represent the positions of the i th I spin and the k th S spin along the direction of the field gradient applied during T with the strength of G , respectively. Note that S_{zi} is the S spin operator J coupled to the I_i spin and that I_{zk} is the I spin operator J coupled to the S_k spin.

Applying the second $(\pi/2)_y$ pulses, we get

$$\begin{aligned} \rho(t_1, t_2 = 0) &= 2^{-(N+M)} \\ &\times \prod_i \left[\mathbf{1} + \mathfrak{F}_I I_{zi} \cos(\pi J t_1) \cos(\Delta\omega_I t_1 + \gamma_I G T s_i) - \mathfrak{F}_I 2 I_{yi} S_{xi} \sin(\pi J t_1) \cos(\Delta\omega_I t_1 + \gamma_I G T s_i) \right. \\ &\quad \left. - \mathfrak{F}_I I_{yi} \cos(\pi J t_1) \sin(\Delta\omega_I t_1 + \gamma_I G T s_i) - \mathfrak{F}_I 2 I_{zi} S_{xi} \sin(\pi J t_1) \sin(\Delta\omega_I t_1 + \gamma_I G T s_i) \right] \\ &\times \prod_k \left[\mathbf{1} + \mathfrak{F}_S S_{zk} \cos(\pi J t_1) \cos(\Delta\omega_S t_1 + \gamma_S G T s_k) - \mathfrak{F}_S 2 S_{yk} I_{xk} \sin(\pi J t_1) \cos(\Delta\omega_S t_1 + \gamma_S G T s_k) \right. \\ &\quad \left. - \mathfrak{F}_S S_{yk} \cos(\pi J t_1) \sin(\Delta\omega_S t_1 + \gamma_S G T s_k) - \mathfrak{F}_S 2 S_{zk} I_{xk} \sin(\pi J t_1) \sin(\Delta\omega_S t_1 + \gamma_S G T s_k) \right]. \end{aligned} \quad [7]$$

Since there are no further RF pulses following in the sequence, the $(2 + 0)$ -quantum operators $I_{yi}S_{xi}$ and $S_{yk}I_{xk}$ cannot

give an observable signal and will be ignored for brevity. Applying the second gradient pulse of intensity G with duration of nT (i.e., gradient ratio = 1: n),

$$\rho(t_1, t_2 = nT) = 2^{-(N+M)}$$

$$\begin{aligned} & \times \prod_i \left\{ \begin{aligned} & \mathbf{1} + \mathfrak{F}_I I_{zi} c(t_1) \cos(\Delta\omega_i t_1 + \gamma_I G T s_i) \\ & + \frac{1}{2} \mathfrak{F}_I I_{xi} c(t_1) [\cos\{\Delta\omega_i t_1 + (1-n)\gamma_I G T s_i\} - \cos\{\Delta\omega_i t_1 + (1+n)\gamma_I G T s_i\}] \\ & - \frac{1}{2} \mathfrak{F}_I I_{yi} c(t_1) [\sin\{\Delta\omega_i t_1 + (1-n)\gamma_I G T s_i\} + \sin\{\Delta\omega_i t_1 + (1+n)\gamma_I G T s_i\}] \\ & - \mathfrak{F}_I I_{zi} S_{yi} s(t_1) \left[\cos\left\{\Delta\omega_i t_1 + \left(1 - n \frac{\gamma_S}{\gamma_I}\right) \gamma_I G T s_i\right\} - \cos\left\{\Delta\omega_i t_1 + \left(1 + n \frac{\gamma_S}{\gamma_I}\right) \gamma_I G T s_i\right\} \right] \\ & - \mathfrak{F}_I I_{zi} S_{xi} s(t_1) \left[\sin\left\{\Delta\omega_i t_1 + \left(1 - n \frac{\gamma_S}{\gamma_I}\right) \gamma_I G T s_i\right\} + \sin\left\{\Delta\omega_i t_1 + \left(1 + n \frac{\gamma_S}{\gamma_I}\right) \gamma_I G T s_i\right\} \right] \end{aligned} \right\} \\ & \times \prod_k \left\{ \begin{aligned} & \mathbf{1} + \mathfrak{F}_S S_{zk} c(t_1) \cos(\Delta\omega_s t_1 + \gamma_S G T s_k) \\ & + \frac{1}{2} \mathfrak{F}_S S_{xk} c(t_1) [\cos\{\Delta\omega_s t_1 + (1-n)\gamma_S G T s_k\} - \cos\{\Delta\omega_s t_1 + (1+n)\gamma_S G T s_k\}] \\ & - \frac{1}{2} \mathfrak{F}_S S_{yk} c(t_1) [\sin\{\Delta\omega_s t_1 + (1-n)\gamma_S G T s_k\} + \sin\{\Delta\omega_s t_1 + (1+n)\gamma_S G T s_k\}] \\ & - \mathfrak{F}_S S_{zk} I_{yk} s(t_1) \left[\cos\left\{\Delta\omega_s t_1 + \left(1 - n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} - \cos\left\{\Delta\omega_s t_1 + \left(1 + n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} \right] \\ & - \mathfrak{F}_S S_{zk} I_{xk} s(t_1) \left[\sin\left\{\Delta\omega_s t_1 + \left(1 - n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} + \sin\left\{\Delta\omega_s t_1 + \left(1 + n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} \right] \end{aligned} \right\}, \end{aligned} \quad [8]$$

where $c(t_1) \equiv \cos(\pi J t_1)$ and $s(t_1) \equiv \sin(\pi J t_1)$.

During the t_2 period we must consider the scalar couplings, the dipolar interactions, and the Zeeman interaction. The chemical shift evolution under the Zeeman interaction does not change the order of coherences and the number of spin operators. The J coupling and the dipolar coupling do not change the order of coherences either, but can strip off the spin operators to produce an observable signal (1-spin 1-quantum operators). The J coupling produces an observable signal from the operators of the type

$$S_{zk} I_{yk} s(t_1) \xrightarrow{J \text{ coupling}} -I_{xk} s(t_1) s(t_2).$$

The intermolecular dipolar couplings can give an observable signal in the following way:

$$\begin{aligned} I_{xi} I_{zj} & \xrightarrow{I-I \text{ dipolar coupling}} I_{yi}; \\ I_{xi} S_{zk} & \xrightarrow{I-S \text{ dipolar coupling}} I_{yi}. \end{aligned} \quad [9]$$

The J coupling can produce 1Q operators of the type $I_{yi} S_{zi}$ as well:

$$I_{xi} \xrightarrow{J \text{ coupling}} I_{xi} c(t_2) + I_{yi} S_{zi} s(t_2). \quad [10]$$

The operator S_{zi} in Eq. [10] cannot be later stripped off by the dipolar interactions because the I_i spin and S_i spin are in the same molecule if they are J coupled. Intramolecular dipolar interactions are assumed here to be averaged away by the rapid rotational motion of the molecule.

Introducing the J coupling and keeping possible observable terms only gives

$$\rho(t_1, t_2) = 2^{-(N+M)}$$

$$\times \prod_i \left\{ \begin{aligned} & \mathbf{1} + \mathfrak{F}_I I_{zi} c(t_1) \cos(\Delta\omega_I t_1 + \gamma_I G T s_i) \\ & + \frac{1}{2} \mathfrak{F}_I I_{xi} c(t_1) c(t_2) [\cos\{\Delta\omega_I t_1 + (1-n)\gamma_I G T s_i\} - \cos\{\Delta\omega_I t_1 + (1+n)\gamma_I G T s_i\}] \\ & - \frac{1}{2} \mathfrak{F}_I I_{yi} c(t_1) c(t_2) [\sin\{\Delta\omega_I t_1 + (1-n)\gamma_I G T s_i\} + \sin\{\Delta\omega_I t_1 + (1+n)\gamma_I G T s_i\}] \\ & + \frac{1}{2} \mathfrak{F}_I S_{xi} s(t_1) s(t_2) \left[\cos\left\{\Delta\omega_I t_1 + \left(1 - n \frac{\gamma_S}{\gamma_I}\right) \gamma_I G T s_i\right\} - \cos\left\{\Delta\omega_I t_1 + \left(1 + n \frac{\gamma_S}{\gamma_I}\right) \gamma_I G T s_i\right\} \right] \\ & - \frac{1}{2} \mathfrak{F}_I S_{yi} s(t_1) s(t_2) \left[\sin\left\{\Delta\omega_I t_1 + \left(1 - n \frac{\gamma_S}{\gamma_I}\right) \gamma_I G T s_i\right\} + \sin\left\{\Delta\omega_I t_1 + \left(1 + n \frac{\gamma_S}{\gamma_I}\right) \gamma_I G T s_i\right\} \right] \\ & + \text{unobservable terms} \end{aligned} \right.$$

$$\times \prod_k \left\{ \begin{aligned} & \mathbf{1} + \mathfrak{F}_S S_{zk} c(t_1) \cos(\Delta\omega_S t_1 + \gamma_S G T s_k) \\ & + \frac{1}{2} \mathfrak{F}_S S_{xk} c(t_1) c(t_2) [\cos\{\Delta\omega_S t_1 + (1-n)\gamma_S G T s_k\} - \cos\{\Delta\omega_S t_1 + (1+n)\gamma_S G T s_k\}] \\ & - \frac{1}{2} \mathfrak{F}_S S_{yk} c(t_1) c(t_2) [\sin\{\Delta\omega_S t_1 + (1-n)\gamma_S G T s_k\} + \sin\{\Delta\omega_S t_1 + (1+n)\gamma_S G T s_k\}] \\ & + \frac{1}{2} \mathfrak{F}_S I_{xk} s(t_1) s(t_2) \left[\cos\left\{\Delta\omega_S t_1 + \left(1 - n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} - \cos\left\{\Delta\omega_S t_1 + \left(1 + n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} \right] \\ & - \frac{1}{2} \mathfrak{F}_S I_{yk} s(t_1) s(t_2) \left[\sin\left\{\Delta\omega_S t_1 + \left(1 - n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} + \sin\left\{\Delta\omega_S t_1 + \left(1 + n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} \right] \\ & + \text{unobservable terms} \end{aligned} \right. \quad [11]$$

In the heteronuclear case where only the I spin is detected, Eq. [11] can be effectively reduced into

$$\rho(t_1, t_2) = 2^{-(N+M)}$$

$$\times \prod_i \left\{ \begin{aligned} & \mathbf{1} + \mathfrak{F}_I I_{zi} c(t_1) \cos(\Delta\omega_I t_1 + \gamma_I G T s_i) \\ & + \frac{1}{2} \mathfrak{F}_I I_{xi} c(t_1) c(t_2) [\cos\{\Delta\omega_I t_1 + (1-n)\gamma_I G T s_i\} - \cos\{\Delta\omega_I t_1 + (1+n)\gamma_I G T s_i\}] \\ & - \frac{1}{2} \mathfrak{F}_I I_{yi} c(t_1) c(t_2) [\sin\{\Delta\omega_I t_1 + (1-n)\gamma_I G T s_i\} + \sin\{\Delta\omega_I t_1 + (1+n)\gamma_I G T s_i\}] \end{aligned} \right.$$

$$\times \prod_k \left\{ \begin{aligned} & \mathbf{1} + \mathfrak{F}_S S_{zk} c(t_1) \cos(\Delta\omega_S t_1 + \gamma_S G T s_k) \\ & + \frac{1}{2} \mathfrak{F}_S I_{xk} s(t_1) s(t_2) \left[\cos\left\{\Delta\omega_S t_1 + \left(1 - n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} - \cos\left\{\Delta\omega_S t_1 + \left(1 + n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} \right] \\ & - \frac{1}{2} \mathfrak{F}_S I_{yk} s(t_1) s(t_2) \left[\sin\left\{\Delta\omega_S t_1 + \left(1 - n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} + \sin\left\{\Delta\omega_S t_1 + \left(1 + n \frac{\gamma_I}{\gamma_S}\right) \gamma_S G T s_k\right\} \right] \end{aligned} \right. \quad [12]$$

The terms multiplied by $s(t_1)s(t_2)$ come from the coherence transfer from the S spin to I spin as in a hetero-COSY sequence, i.e.,

$$\begin{array}{c}
 S_z \xrightarrow{(\pi/2)_y} S_x \xrightarrow{J \text{ coupling}} \xrightarrow{\text{Zeeman}} \\
 -2S_x I_z s(t_1) \xrightarrow{(\pi/2)_y} 2S_z I_y s(t_1) \\
 \xrightarrow{J \text{ coupling}} \xrightarrow{\text{Zeeman}} I_x s(t_1) s(t_2). \quad [13]
 \end{array}$$

These terms cannot give any observable by themselves (without dipolar couplings) after spatial averaging except when $n = \pm\gamma_S/\gamma_I$. With intermolecular dipolar couplings, the situation is different: 1Q operators of the form

$$\overbrace{I_{x1} I_{zj} I_{zk} \cdots}^p \overbrace{S_{z1} S_{z2} \cdots}^q,$$

after $(p + q)$ commutations with the dipolar Hamiltonian, can produce an observable signal.

Expansion of Eq. [12] produces this type of operator in two distinct ways. The terms multiplied by $\mathfrak{S}_I \mathfrak{S}_I^p \mathfrak{S}_I^q c(t_1)c(t_2)$ involve no coherence transfer between S and I spins due to J coupling, and are analogous to the terms retained in the coupling-free calculation. The others have a factor of $\mathfrak{S}_S \mathfrak{S}_I^p \mathfrak{S}_I^q s(t_1)s(t_2)$, and these terms appear due to the coherence transfer from S spins to I spins as explained earlier. We will denote each contribution as ρ_D and ρ_J . The spatial modulations of these two types are different, and we will treat each case separately.

A. Terms without Coherence Transfer Due to J Coupling

The terms with $\mathfrak{S}_I \mathfrak{S}_I^p \mathfrak{S}_I^q$ (I_{xi} component) can be written as

$$\begin{aligned}
 & \frac{1}{2} I_{xi} c(t_1) c(t_2) \overbrace{I_{zj1} I_{zj2} \cdots}^p \overbrace{S_{z11} S_{z12} \cdots}^q \\
 & \times \{ c(t_1) \}^{p+q} [\cos \{ \Delta\omega_I t_1 - (n-1) \gamma_I G T s_i \} \\
 & \quad - \cos \{ \Delta\omega_I t_1 + (n+1) \gamma_I G T s_i \}] \\
 & \times \overbrace{[\cos(\Delta\omega_I t_1 + \gamma_I G T s_{j1}) \cos(\Delta\omega_I t_1 + \gamma_I G T s_{j2}) \cdots]}^p \\
 & \times \overbrace{[\cos(\Delta\omega_S t_1 + \gamma_S G T s_{11}) \cos(\Delta\omega_S t_1 + \gamma_S G T s_{12}) \cdots]}^q. \quad [14]
 \end{aligned}$$

Note that we change the indices

$$\overbrace{I_{zj} I_{zk} \cdots}^p \overbrace{S_{z1} S_{z2} \cdots}^q \rightarrow \overbrace{I_{zj1} I_{zj2} \cdots}^p \overbrace{S_{z11} S_{z12} \cdots}^q$$

to avoid confusion. The product of cosine functions must be converted into a sum of cosines to evaluate the effect of the spatial modulation. The

$$\overbrace{\cos(\Delta\omega_I t_1 + \gamma_I G T s_{j1}) \cos(\Delta\omega_I t_1 + \gamma_I G T s_{j2}) \cdots}^p$$

factor will lead to terms of the type $\cos\{m\Delta\omega_I t_1 + \gamma_I G T s_j(m)\}$. This term evolves at a frequency of $m\Delta\omega_I$ during the t_1 period, and represents m -quantum coherence in the I spin. For compactness, we define $s_j(m)$ as one of the combinations of terms with the difference between positive and negative signs of s_j being m ; for example, $s_j(1)$ for the $p = 3$ case can be one of $(s_{j1} + s_{j2} - s_{j3})$, $(s_{j1} - s_{j2} + s_{j3})$, and $(-s_{j1} + s_{j2} + s_{j3})$. Then the first part of Eq. [14] would have terms like

$$\begin{aligned}
 & \cos \{ \Delta\omega_I t_1 + (1-n) \gamma_I G T s_i \} \times \overbrace{\cos(\Delta\omega_I t_1 + \gamma_I G T s_{j1}) \cdots}^p \overbrace{\cos(\Delta\omega_S t_1 + \gamma_S G T s_{11}) \cdots}^q \\
 & \Rightarrow \cos \{ \Delta\omega_I t_1 + (1-n) \gamma_I G T s_i \} \cos \{ m \Delta\omega_I t_1 + \gamma_I G T s_j(m) \} \cos \{ k \Delta\omega_S t_1 + \gamma_S G T s_l(k) \} \\
 & = \frac{1}{4} \left[\begin{array}{l} \cos \{ (m+1) \Delta\omega_I t_1 + k \Delta\omega_S t_1 + (1-n) \gamma_I G T s_i + \gamma_I G T s_j(m) + \gamma_S G T s_l(k) \} \\ + \cos \{ (m+1) \Delta\omega_I t_1 - k \Delta\omega_S t_1 + (1-n) \gamma_I G T s_i + \gamma_I G T s_j(m) - \gamma_S G T s_l(k) \} \\ + \cos \{ (m-1) \Delta\omega_I t_1 - k \Delta\omega_S t_1 - (1-n) \gamma_I G T s_i + \gamma_I G T s_j(m) - \gamma_S G T s_l(k) \} \\ + \cos \{ (m-1) \Delta\omega_I t_1 + k \Delta\omega_S t_1 - (1-n) \gamma_I G T s_i + \gamma_I G T s_j(m) + \gamma_S G T s_l(k) \} \end{array} \right] \\
 & = (A + B + C + D)/4. \quad [15]
 \end{aligned}$$

The coherence transfer pathway that passes the gradient filter is selected by adjusting n . The terms that survive after spatial averaging due to the gradient pulses should not depend on the absolute position of the spins (II). For the A term in Eq. [15], a nonvanishing signal is obtained when $\gamma_I(1 - n + m) + \gamma_S k = 0$, i.e., $m + 1 = n - (\gamma_S/\gamma_I)k$. Similarly the B , C , and D terms do not vanish when $m + 1 = n + (\gamma_S/\gamma_I)k$, $m - 1 = -n + (\gamma_S/\gamma_I)k$, and $m - 1 = -n - (\gamma_S/\gamma_I)k$. The resulting spatial part becomes $\cos\{\gamma_I GT(s_{j1} - s_i)\} \cdots \cos\{\gamma_S GT(s_{i1} - s_i)\} \cdots$, which depends only on the relative position of the spins (II). Then we can rewrite Eq. [15] as

$$\frac{1}{4} \begin{bmatrix} \cos\{(n - k')\Delta\omega_I t_1 + k\Delta\omega_S t_1\} \delta_{m+1, n-k'} \\ + \cos\{(n + k')\Delta\omega_I t_1 - k\Delta\omega_S t_1\} \delta_{m+1, n+k'} \\ + \cos\{(n - k')\Delta\omega_I t_1 + k\Delta\omega_S t_1\} \delta_{m-1, -n+k'} \\ + \cos\{(n + k')\Delta\omega_I t_1 - k\Delta\omega_S t_1\} \delta_{m-1, -n-k'} \end{bmatrix} \times \cos\{\gamma_I GT(s_{j1} - s_i)\} \cdots \cos\{\gamma_S GT(s_{i1} - s_i)\} \cdots, \quad [16]$$

where $k' = (\gamma_S/\gamma_I)k$.

This can be simplified by considering the relation (29)

$$\cos^n \theta = \frac{1}{2^n} \sum_{m=-n}^n {}_n\mathbf{C}_{(n-|m|)/2} \cos(m\theta), \quad [17]$$

where ${}_n\mathbf{C}_{\text{half integer}} \equiv 0$ and ${}_n\mathbf{C}_k \equiv n!/k!(n-k)!$. Then the first part of Eq. [14] can be written as

$$\frac{1}{2} I_{xi} c(t_1) c(t_2) \overbrace{I_{zj1} I_{zj2} \cdots}^p \overbrace{S_{z11} S_{z12} \cdots}^q \{c(t_1)\}^{p+q} \times \frac{1}{2^{p+q}} \cos\{\Delta\omega_I t_1 + (1-n)\gamma_I GT s_i\} \times \sum_{m=-p}^p {}_p\mathbf{C}_{(p-|m|)/2} \cos\{m\Delta\omega_I t_1 + s_j(m)\gamma_I GT\} \times \sum_{k=-q}^q {}_q\mathbf{C}_{(q-|k|)/2} \cos\{k\Delta\omega_S t_1 + s_i(k)\gamma_S GT\},$$

which leads to

$$\frac{1}{2} I_{xi} c(t_1) c(t_2) \overbrace{I_{zj1} I_{zj2} \cdots}^p \overbrace{S_{z11} S_{z12} \cdots}^q \{c(t_1)\}^{p+q} \times \frac{1}{2^{p+q+2}} \sum_{m=-p}^p {}_p\mathbf{C}_{(p-|m|)/2} \sum_{k=-q}^q {}_q\mathbf{C}_{(q-|k|)/2} \times \begin{bmatrix} \cos\{(n - k')\Delta\omega_I t_1 + k\Delta\omega_S t_1\} \delta_{m+1, n-k'} \\ + \cos\{(n + k')\Delta\omega_I t_1 - k\Delta\omega_S t_1\} \delta_{m+1, n+k'} \\ + \cos\{(n - k')\Delta\omega_I t_1 + k\Delta\omega_S t_1\} \delta_{m-1, -n+k'} \\ + \cos\{(n + k')\Delta\omega_I t_1 - k\Delta\omega_S t_1\} \delta_{m-1, -n-k'} \end{bmatrix} \times \cos\{\gamma_I GT(s_{j1} - s_i)\} \cdots \cos\{\gamma_S GT(s_{i1} - s_i)\} \cdots = A' + B' + C' + D'. \quad [18]$$

The first and third terms in the brackets of Eq. [18], which we label A' and C' , are the same, and so are B' and D' . A' and B' differ only in the sign of k , as do B' and D' . Therefore we can choose A' as a representative term, and we obtain

$$\frac{1}{2} I_{xi} c(t_1) c(t_2) \overbrace{I_{zj1} I_{zj2} \cdots}^p \overbrace{S_{z11} S_{z12} \cdots}^q \{c(t_1)\}^{p+q} \times \frac{1}{2^{p+q+2}} \sum_{k=-q}^q {}_q\mathbf{C}_{(q-|k|)/2} {}_p\mathbf{C}_{(p-|n-k'-1|)/2} \times \cos\{(n - k')\Delta\omega_I t_1 + k\Delta\omega_S t_1\} \times \cos\{\gamma_I GT(s_{j1} - s_i)\} \cdots \cos\{\gamma_S GT(s_{i1} - s_i)\} \cdots. \quad [19]$$

The second part of Eq. [14] can be obtained by changing the sign of n . Again all four terms as in Eq. [18] are equivalent, and D gives the same expression as in Eq. [19]. The multiplying factor becomes ${}_p\mathbf{C}_{(p-|m|)/2} = {}_p\mathbf{C}_{(p-|n-k'+1|)/2}$. The I_{yi} component from Eq. [12] is obtained analogously. Collecting all pieces together, we get

$$\rho_D^{p+q} = \mathfrak{F}_I^{p+1} \mathfrak{F}_S^{q2} \mathfrak{F}_2^{-(N+M)} \{c(t_1)\}^{p+q+1} c(t_2) \frac{1}{2^{p+q+1}} \frac{1}{p!q!} \times {}_q\mathbf{C}_{(q-|k|)/2} ({}_p\mathbf{C}_{(p-|n-k'-1|)/2} - {}_p\mathbf{C}_{(p-|n-k'+1|)/2}) \times \sum_{i \neq j} \sum_{j1 \neq} \cdots \sum_{\neq l1 \neq} \cdots \left[\begin{array}{l} \left(\overbrace{I_{xi} I_{zj1} I_{zj2} \cdots}^p \overbrace{S_{z11} S_{z12} \cdots}^q \cos\left\{ \left(n - k \frac{\gamma_S}{\gamma_I} \right) \Delta\omega_I t_1 + k\Delta\omega_S t_1 \right\} \right) \\ - \overbrace{I_{yi} I_{zj1} I_{zj2} \cdots}^p \overbrace{S_{z11} S_{z12} \cdots}^q \sin\left\{ \left(n - k \frac{\gamma_S}{\gamma_I} \right) \Delta\omega_I t_1 + k\Delta\omega_S t_1 \right\} \right) \\ \times [\cos\{\gamma_I GT(s_{j1} - s_i)\} \cdots \cos\{\gamma_S GT(s_{i1} - s_i)\} \cdots] \end{array} \right]. \quad [20]$$

Note that $1/p!q!$ is necessary to convert the ordered sum ($j_1 < j_2 < j_3 < \dots$) into the orderless sum ($j_1 \neq j_2 \neq j_3 \neq \dots$) [cf. Eq. [28] in Ref. (11)]. The coefficient term can be written as

$$\begin{aligned} & \frac{1}{p!q!} {}_q\mathbf{C}_{(q-|k|)/2}({}_p\mathbf{C}_{\{p-|n-k'-1|/2\}} - {}_p\mathbf{C}_{\{p-|n-k'+1|/2\}}) \\ &= \frac{1}{\left(\frac{q}{2} + \frac{k}{2}\right)! \left(\frac{q}{2} - \frac{k}{2}\right)!} \\ & \times \left[\frac{n-k'}{\left(\frac{p+1}{2} + \frac{n-k'}{2}\right)! \left(\frac{p+1}{2} - \frac{n-k'}{2}\right)!} \right] \\ & \xrightarrow{(p, q) \rightarrow (p', q')} \\ & \times \frac{1}{q'!(q'+k)} \frac{n-k'}{p'!(p'+n-k')!}, \quad [21] \end{aligned}$$

where $p' = (p - n + k' + 1)/2$ and $q' = (q - k)/2$ (i.e., $p = 2p' + n - k' - 1$ and $q = 2q' + k$).

The heteronuclear and homonuclear dipolar Hamiltonians convert the multispin operators into the observable single-spin operator [cf. Eq. [67] in Ref. (11)], and Eq. [20] can be written as

$$\begin{aligned} & \rho_D^{p+q} \\ &= 2^{-(N+M+1)} \mathfrak{S}_I^{p+1} \mathfrak{S}_S^q \{c(t_1)\}^{p+q+1} \\ & \times c(t_2) t_2^{p+q} \sum_{i=1}^N (-1)^{(p+q-1)/2} \\ & \times \sum_{k=-q}^q [I_{xi} \sin\{(n-k')\Delta\omega t_1 + k\Delta\omega_s t_1\} \\ & + I_{yj} \cos\{(n-k')\Delta\omega t_1 + k\Delta\omega_s t_1\}] \\ & \times \frac{(n-k')}{p'!(p'+n-k')!} \\ & \times \left(\sum_{j=1}^N \frac{3}{4} D_{ij}^H \cos\{\gamma_I GT(s_j - s_i)\} \right)^{2p'+n-k'-1} \\ & \times \frac{1}{q'!(q'+k)!} \\ & \times \left(\sum_{l=1}^M \frac{1}{2} D_{il}^{IS} \cos\{\gamma_S GT(s_l - s_i)\} \right)^{2q'+k}. \quad [22] \end{aligned}$$

Summing up all observable terms, we get

$$\begin{aligned} & \rho_D(t_1, t_2) \\ &= 2^{-(N+M+1)} \mathfrak{S}_I c(t_1) c(t_2) \sum_{i=1}^N \sum_{k=-q}^q (-1)^{(n-2+k-k')/2} \\ & \times [I_{xi} \sin\{(n-k')\Delta\omega t_1 + k\Delta\omega_s t_1\} \\ & + I_{yj} \cos\{(n-k')\Delta\omega t_1 + k\Delta\omega_s t_1\}] \\ & \times (\Lambda_i^H)^{-1} (n-k') \\ & \times \sum_{p'=0}^{(N-n+k')/2} \frac{(-1)^{p'}}{p'!(p'+n-k')!} (\Lambda_i^H)^{2p'+n-k'} \\ & \times \sum_{q'=0}^{(M-k)/2} \frac{(-1)^{q'}}{q'!(q'+k)!} (\Lambda_i^{IS})^{2q'+k}, \quad [23] \end{aligned}$$

where

$$\begin{aligned} \Lambda_i^H &\equiv \mathfrak{S}_I c(t_1) t_2 \sum_{j=1}^N \frac{3}{4} D_{ij}^H \cos\{\gamma_I GT(s_j - s_i)\} \\ \Lambda_i^{IS} &\equiv \mathfrak{S}_S c(t_1) t_2 \sum_{l=1}^M \frac{1}{2} D_{il}^{IS} \cos\{\gamma_S GT(s_l - s_i)\}. \end{aligned}$$

We can express Λ_i in terms of the dipolar demagnetizing time, $\tau_{dl} \equiv (\gamma_I \mu_0 M_0^I)^{-1}$ and $\tau_{dS} \equiv (\gamma_S \mu_0 M_0^S)^{-1}$ [cf. Eq. [78] in Ref. (11)], as follows:

$$\begin{aligned} \Lambda_i^H &= -\frac{1}{2} \frac{t_2}{\tau_{dl}} \cos(\pi J t_1), \\ \Lambda_i^{IS} &= -\frac{1}{3} \frac{\gamma_I t_2}{\gamma_S \tau_{dS}} \cos(\pi J t_1). \quad [24] \end{aligned}$$

From the series expansion of the Bessel function

$$J_\nu(x) = \sum_{k=0}^{\infty} \frac{(-1)^k}{k!(k+\nu)!} \left(\frac{x}{2}\right)^{2k+\nu}, \quad [25]$$

Eq. [23] can be simplified to

$$\begin{aligned} & \rho_D(t_1, t_2) \\ &= 2^{-(N+M+1)} \mathfrak{S}_I \cos(\pi J t_1) \cos(\pi J t_2) \sum_{i=1}^N \sum_k i^{n-2+k-k'} \\ & \times [I_{xi} \sin\{(n-k')\Delta\omega t_1 + k\Delta\omega_s t_1\} \\ & + I_{yj} \cos\{(n-k')\Delta\omega t_1 + k\Delta\omega_s t_1\}] \\ & \times (\Lambda_i^H)^{-1} (n-k') J_{n-k'}(2\Lambda_i^H) J_k(2\Lambda_i^{IS}). \quad [26] \end{aligned}$$

Finally, we put the t_2 evolution under the chemical shift,

$$\begin{aligned} \rho_D^{\text{obs}}(t_1, t_2) &= 2^{-(N+M+1)} \mathfrak{S}_I \cos(\pi J t_1) \cos(\pi J t_2) \sum_{i=1}^N \sum_k i^{n-2+k-k'} \\ &\times (\Lambda_i^H)^{-1} (n-k') J_{n-k'} (2\Lambda_i^H) J_k (2\Lambda_i^S) \\ &\times \left[\begin{array}{l} I_{xi} \{ \cos(\Delta\omega_i t_2) \sin[(n-k') \Delta\omega_i t_1 \\ + k\Delta\omega_s t_1] - \sin(\Delta\omega_i t_2) \\ \times \cos[(n-k') \Delta\omega_i t_1 + k\Delta\omega_s t_1] \} \\ + I_{yi} \{ \cos(\Delta\omega_i t_2) \cos[(n-k') \Delta\omega_i t_1 \\ + k\Delta\omega_s t_1] + \sin(\Delta\omega_i t_2) \\ \times \sin[(n-k') \Delta\omega_i t_1 + k\Delta\omega_s t_1] \} \end{array} \right]. \end{aligned} \quad [27]$$

The signal from the density matrix in Eq. [27] is [cf. Eqs. [78] and [81] in Ref. (11)]

$$\begin{aligned} M_D^{I+}(t_1, t_2) &= \text{Tr} \{ \rho(t_1, t_2) \gamma \hbar (I_x + iI_y) \} \\ &= M_0^I \exp \left\{ -i \left[\left(n - k \frac{\gamma_S}{\gamma_I} \right) \Delta\omega_I + k\Delta\omega_S \right] t_1 \right\} \\ &\times \sum_k i^{n-1+k(1-\gamma_S/\gamma_I)} \exp(i\Delta\omega_i t_2) \cos(\pi J t_1) \\ &\times \cos(\pi J t_2) \times \left(n - k \frac{\gamma_S}{\gamma_I} \right) \left(\frac{\tau_{dl}}{t_2 \cos(\pi J t_1)} \right) \end{aligned}$$

$$\begin{aligned} &\times J_{n-k(\gamma_S/\gamma_I)} \left(-\frac{t_2 \cos(\pi J t_1)}{\tau_{dl}} \right) \\ &\times J_k \left(-\frac{2}{3} \frac{\gamma_I}{\gamma_S} \frac{t_2 \cos(\pi J t_1)}{\tau_{dS}} \right). \end{aligned} \quad [28]$$

This is the signal that arises without coherence transfer from the S spins to the I spins due to the J coupling. If the two spins are not J coupled, substituting $J = 0$ in Eq. [28] gives the signal from the intermolecular heteronuclear coherences due to the dipolar interactions:

$$\begin{aligned} M^{I+} &= M_0^I \exp \left\{ -i \left[\left(n - k \frac{\gamma_S}{\gamma_I} \right) \Delta\omega_I + k\Delta\omega_S \right] t_1 \right\} \\ &\times \exp(i\Delta\omega_i t_2) \times \sum_k i^{n-1+k(1-\gamma_S/\gamma_I)} \left(n - k \frac{\gamma_S}{\gamma_I} \right) \\ &\times \left(\frac{\tau_{dl}}{t_2} \right) J_{n-k(\gamma_S/\gamma_I)} \left(-\frac{t_2}{\tau_{dl}} \right) J_k \left(-\frac{2}{3} \frac{\gamma_I}{\gamma_S} \frac{t_2}{\tau_{dS}} \right). \end{aligned} \quad [29]$$

This result is compared with a simple classical calculation in the Appendix; as we discuss in Section III, the classical calculation is simple only if the J couplings are ignored.

B. Terms with Coherence Transfer Due to J Coupling

The procedure is completely equivalent to the previous case. The terms with $\mathfrak{S}_S \mathfrak{S}_I^p \mathfrak{S}_S^q$ are of the type

$$\begin{aligned} &\frac{1}{2} I_{xi} s(t_1) s(t_2) \overbrace{I_{xj1} I_{xj2} \cdots}^p \overbrace{S_{zj1} S_{zj2} \cdots}^q \{ c(t_1) \}^{p+q} \\ &\times \left[\cos \left\{ \Delta\omega_s t_1 + \left(1 - n \frac{\gamma_I}{\gamma_S} \right) \gamma_S G T s_i \right\} - \cos \left\{ \Delta\omega_s t_1 + \left(1 + n \frac{\gamma_I}{\gamma_S} \right) \gamma_S G T s_i \right\} \right] \\ &\times \underbrace{\left[\cos(\Delta\omega_i t_1 + \gamma_I G T s_{j1}) \cos(\Delta\omega_i t_1 + \gamma_I G T s_{j2}) \cdots \right]}_p \underbrace{\left[\cos(\Delta\omega_s t_1 + \gamma_S G T s_{i1}) \cos(\Delta\omega_s t_1 + \gamma_S G T s_{i2}) \cdots \right]}_q. \end{aligned} \quad [30]$$

When we convert the product of cosines into a sum of cosines, we obtain

$$\begin{aligned} &\cos \{ \Delta\omega_s t_1 + (\gamma_S - n\gamma_I) G T s_i \} \times \overbrace{\cos(\Delta\omega_i t_1 + \gamma_I G T s_{j1}) \cdots}^p \overbrace{\cos(\Delta\omega_s t_1 + \gamma_S G T s_{i1}) \cdots}^q \\ &\Rightarrow \cos \{ \Delta\omega_s t_1 + (\gamma_S - n\gamma_I) G T s_i \} \cos \{ m\Delta\omega_i t_1 + \gamma_I G T s_j(m) \} \cos \{ k\Delta\omega_s t_1 + \gamma_S G T s_i(k) \} \\ &= \frac{1}{4} \left[\begin{array}{l} \cos \{ m\Delta\omega_i t_1 + (k+1)\Delta\omega_s t_1 + \gamma_I G T (s_j(m) - ns_i) + \gamma_S G T (s_i(k) + s_i) \} \\ + \cos \{ m\Delta\omega_i t_1 + (k-1)\Delta\omega_s t_1 + \gamma_I G T (s_j(m) + ns_i) + \gamma_S G T (s_i(k) - s_i) \} \\ + \cos \{ m\Delta\omega_i t_1 - (k+1)\Delta\omega_s t_1 + \gamma_I G T (s_j(m) + ns_i) + \gamma_S G T (s_i(k) + s_i) \} \\ + \cos \{ m\Delta\omega_i t_1 - (k-1)\Delta\omega_s t_1 + \gamma_I G T (s_j(m) - ns_i) + \gamma_S G T (s_i(k) - s_i) \} \end{array} \right]. \end{aligned} \quad [31]$$

For the first term to pass the gradient filter, we need $m = n - (\gamma_s/\gamma_I)(k + 1)$. The order of coherence of S spins is $(k + 1)$. The resulting signal will be $\cos\{(n - (k + 1)')\Delta\omega_I t_1 + (k + 1)\Delta\omega_S t_1\}$, where $(k + 1)' \equiv (k + 1)(\gamma_s/\gamma_I)$ as before. Then the term multiplied by $\cos\{\Delta\omega_S t_1 + (1 - n(\gamma_I/\gamma_S))\gamma_S G T s_i\}$ in Eq. [30] is

$$\begin{aligned} & \frac{1}{2} I_{xi} s(t_1) s(t_2) \overbrace{I_{zj1} I_{zj2} \cdots S_{z11} S_{z12} \cdots}^p \overbrace{\cdots}^q \{c(t_1)\}^{p+q} \frac{1}{2^{p+q+2}} \sum_{m=-p}^p {}_p\mathbf{C}_{(p-|m|)/2} \sum_{k=-q}^q {}_q\mathbf{C}_{(q-|k|)/2} \\ & \times \begin{bmatrix} \cos\{(n - (k + 1)')\Delta\omega_I t_1 + (k + 1)\Delta\omega_S t_1\} \delta_{m, n-(k+1)'} \\ + \cos\{(n + (k - 1)')\Delta\omega_I t_1 - (k - 1)\Delta\omega_S t_1\} \delta_{m, -(n-(k+1)')} \\ + \cos\{(n - (k + 1)')\Delta\omega_I t_1 + (k + 1)\Delta\omega_S t_1\} \delta_{m, -n+(k+1)'} \\ + \cos\{(n + (k - 1)')\Delta\omega_I t_1 - (k - 1)\Delta\omega_S t_1\} \delta_{m, n-(k-1)'} \end{bmatrix} \\ & \times \cos\{\gamma_I G T (s_{j1} - s_i)\} \cdots \cos\{\gamma_S G T (s_{11} - s_i)\} \cdots \end{aligned} \quad [32]$$

Again, these four terms contribute in the same way, and we can rewrite Eq. [32] as

$$\begin{aligned} & \frac{1}{2} I_{xi} s(t_1) s(t_2) \overbrace{I_{zj1} I_{zj2} \cdots S_{z11} S_{z12} \cdots}^p \overbrace{\cdots}^q \\ & \times \{c(t_1)\}^{p+q} \frac{1}{2^{p+q}} \sum_{k=-q}^q {}_q\mathbf{C}_{(q-|k|)/2} {}_p\mathbf{C}_{(p-|n-(k+1)'|)/2} \\ & \times \cos\{(n - (k + 1)')\Delta\omega_I t_1 + (k + 1)\Delta\omega_S t_1\} \\ & \times \cos\{\gamma_I G T (s_{j1} - s_i)\} \cdots \\ & \times \cos\{\gamma_S G T (s_{11} - s_i)\} \cdots \\ = & \frac{1}{2} I_{xi} s(t_1) s(t_2) \overbrace{I_{zj1} I_{zj2} \cdots S_{z11} S_{z12} \cdots}^p \overbrace{\cdots}^q \\ & \times \{c(t_1)\}^{p+q} \frac{1}{2^{p+q}} \sum_{k=-q+1}^{q+1} {}_q\mathbf{C}_{(q-|k-1|)/2} {}_p\mathbf{C}_{(p-|n-k'|)/2} \\ & \times \cos\{(n - k')\Delta\omega_I t_1 + k\Delta\omega_S t_1\} \\ & \times \cos\{\gamma_I G T (s_{j1} - s_i)\} \cdots \\ & \times \cos\{\gamma_S G T (s_{11} - s_i)\} \cdots \end{aligned} \quad [33]$$

The second term in Eq. [30] which is multiplied by $\cos\{\Delta\omega_S t_1 + (1 - n(\gamma_I/\gamma_S))\gamma_S G T s_i\}$ is obtained by changing the sign of n , which can be written as

$$\begin{aligned} & \frac{1}{2} I_{xi} s(t_1) s(t_2) \overbrace{I_{zj1} I_{zj2} \cdots S_{z11} S_{z12} \cdots}^p \overbrace{\cdots}^q \\ & \times \{c(t_1)\}^{p+q} \frac{1}{2^{p+q}} \sum_{k=-q}^q {}_q\mathbf{C}_{(q-|k|)/2} {}_p\mathbf{C}_{(p-|n-(k+1)'|)/2} \\ & \times \cos\{(n - (k - 1)')\Delta\omega_I t_1 + (k - 1)\Delta\omega_S t_1\} \\ & \times \cos\{\gamma_I G T (s_{j1} - s_i)\} \cdots \\ & \times \cos\{\gamma_S G T (s_{11} - s_i)\} \cdots \\ = & \frac{1}{2} I_{xi} s(t_1) s(t_2) \overbrace{I_{zj1} I_{zj2} \cdots S_{z11} S_{z12} \cdots}^p \overbrace{\cdots}^q \\ & \times \{c(t_1)\}^{p+q} \frac{1}{2^{p+q}} \sum_{k=-q-1}^{q-1} {}_q\mathbf{C}_{(q-|k+1|)/2} {}_p\mathbf{C}_{(p-|n-k'|)/2} \\ & \times \cos\{(n - k')\Delta\omega_I t_1 + k\Delta\omega_S t_1\} \\ & \times \cos\{\gamma_I G T (s_{j1} - s_i)\} \cdots \\ & \times \cos\{\gamma_S G T (s_{11} - s_i)\} \cdots \end{aligned} \quad [34]$$

Then the net signal is

$$\begin{aligned} \rho_J^{(p+q)} = & \mathfrak{S}_I^p \mathfrak{S}_S^{q+1} 2^{-(N+M)} s(t_1) s(t_2) \{c(t_1)\}^{p+q} \frac{1}{2^{p+q+1}} \frac{1}{p!q!} \times \sum_k {}_p\mathbf{C}_{\{p-|n-k'|\}/2} ({}_q\mathbf{C}_{(q-|k-1|)/2} - {}_q\mathbf{C}_{(q-|k+1|)/2}) \\ & \times \sum_{i \neq j} \sum_{j1 \neq} \cdots \sum_{\neq l1 \neq} \cdots \left[\begin{aligned} & \left(\overbrace{I_{xi} I_{zj1} I_{zj2} \cdots S_{z11} S_{z12} \cdots}^p \overbrace{\cdots}^q \cos\left\{\left(n - k \frac{\gamma_S}{\gamma_I}\right)\Delta\omega_I t_1 + k\Delta\omega_S t_1\right\} \right. \\ & \left. - \overbrace{I_{yi} I_{zj1} I_{zj2} \cdots S_{z11} S_{z12} \cdots}^p \overbrace{\cdots}^q \sin\left\{\left(n - k \frac{\gamma_S}{\gamma_I}\right)\Delta\omega_I t_1 + k\Delta\omega_S t_1\right\} \right) \\ & \times \left[\overbrace{\cos\{\gamma_I G T (s_{j1} - s_i)\} \cdots}^p \overbrace{\cos\{\gamma_S G T (s_{11} - s_i)\} \cdots}^q \right] \end{aligned} \right] \end{aligned} \quad [35]$$

The coefficient term can be simplified as

$$\begin{aligned}
& \frac{1}{p!q!} {}_p\mathbf{C}_{(p-|n-k'|)/2} ({}_q\mathbf{C}_{(q-|k-1|)/2} - {}_q\mathbf{C}_{(q-|k+1|)/2}) \\
&= \frac{k}{\left(\frac{q-k+1}{2}\right)! \left(\frac{q+k+1}{2}\right)!} \\
&\quad \times \frac{1}{\left(\frac{p-n+k'}{2}\right)! \left(\frac{p+n-k'}{2}\right)!} \\
&\quad \xrightarrow{(p, q) \rightarrow (p', q')} \\
&\quad \frac{k}{q!(q'+k)!} \frac{1}{p'!(p'+n-k')!}, \quad [36]
\end{aligned}$$

where $p' \equiv (p - n + k')/2$ and $q' \equiv (q - k + 1)/2$ (i.e., $p = 2p' + n - k'$ and $q = 2q' + k - 1$). Note the difference in the definition of (p', q') from the previous case (see Eq. [21]).

Following the same procedure from Eq. [20] to Eq. [27], we obtain the expression for the final density matrix

$$\begin{aligned}
& \rho_J^{\text{obs}} \\
&= 2^{-(N+M+1)} \sum_S \sin(\pi J t_1) \sin(\pi J t_2) \sum_{i=1}^N \sum_k i^{n+k-k'} k \\
&\quad \times (\Lambda_i^{\text{IS}})^{-1} J_{n-k'} (2\Lambda_i^{\text{II}}) J_k (2\Lambda_i^{\text{IS}}) \\
&\quad \times \begin{bmatrix} I_{xi} \{ \cos(\Delta\omega_j t_2) \sin[(n-k')\Delta\omega_j t_1 \\ + k\Delta\omega_{st1}] - \sin(\Delta\omega_j t_2) \\ \times \cos[(n-k')\Delta\omega_j t_1 + k\Delta\omega_{st1}] \} \\ + I_{yi} \{ \cos(\Delta\omega_j t_2) \cos[(n-k')\Delta\omega_j t_1 \\ + k\Delta\omega_{st1}] + \sin(\Delta\omega_j t_2) \\ \times \sin[(n-k')\Delta\omega_j t_1 + k\Delta\omega_{st1}] \} \end{bmatrix}. \quad [37]
\end{aligned}$$

Therefore the signal induced by the coherence transfer from S to I due to J coupling is

$$\begin{aligned}
& M_J^{I+}(t_1, t_2) \\
&= \text{Tr} \{ \rho(t_1, t_2) \gamma_I \hbar (I_x + iI_y) \} \\
&= \frac{\gamma_I}{\gamma_S} M_0^S \exp(i\Delta\omega_j t_2) \sin(\pi J t_1) \sin(\pi J t_2) \\
&\quad \times \sum_k i^{n+1+k(1-\gamma_S'/\gamma_I)}
\end{aligned}$$

$$\begin{aligned}
& \times \exp \left\{ -i \left[\left(n - k \frac{\gamma_S}{\gamma_I} \right) \Delta\omega_I + k\Delta\omega_S \right] t_1 \right\} \\
& \times k \left(\frac{3}{2} \frac{\gamma_S}{\gamma_I} \frac{\tau_{ds}}{t_2 \cos(\pi J t_1)} \right) J_{n-k(\gamma_S/\gamma_I)} \left(-\frac{t_2 \cos(\pi J t_1)}{\tau_{dl}} \right) \\
& \times J_k \left(-\frac{2}{3} \frac{\gamma_I}{\gamma_S} \frac{t_2 \cos(\pi J t_1)}{\tau_{ds}} \right). \quad [38]
\end{aligned}$$

Note that the signal intensity is proportional to the equilibrium magnetization of the S spin, scaled by the ratio of the magnetogyric ratios of the two nuclei. This arises from the fact that the source of the signal is the S spins as indicated in Eq. [12].

C. Heteronuclear CRAZED Signal

The total signal is the sum of the two contributions with and without the coherence transfer due to J coupling. Adding Eqs. [28] and [38], we obtain

$$\begin{aligned}
& M_{\text{total}}^{I+}(t_1, t_2) \\
&= M_0^I \sum_k i^{n-1+k(1-\gamma_S'/\gamma_I)} \exp \left\{ -i \left(n - k \frac{\gamma_S}{\gamma_I} \right) \Delta\omega_{I1} \right\} \\
&\quad \times \exp(-ik\Delta\omega_{st1}) \exp(i\Delta\omega_{I2}) \\
&\quad \times J_{n-k(\gamma_S/\gamma_I)} \left(-\frac{t_2 \cos(\pi J t_1)}{\tau_{dl}} \right) J_k \left(-\frac{2}{3} \frac{\gamma_I}{\gamma_S} \frac{t_2 \cos(\pi J t_1)}{\tau_{ds}} \right) \\
&\quad \times \left[\cos(\pi J t_1) \cos(\pi J t_2) \left(n - k \frac{\gamma_S}{\gamma_I} \right) \right. \\
&\quad \times \left. \left(\frac{\tau_{dl}}{t_2 \cos(\pi J t_1)} \right) - \sin(\pi J t_1) \sin(\pi J t_2) \right. \\
&\quad \times \left. \left. \frac{\gamma_S}{\gamma_I} k \left(\frac{3}{2} \frac{\gamma_S}{\gamma_I} \frac{\tau_{ds}}{t_2 \cos(\pi J t_1)} \right) \right] \right]. \quad [39]
\end{aligned}$$

This explicitly shows that two-dimensional Fourier transformation will give multiple peaks located at $F_1 = (n - k(\gamma_S/\gamma_I))\Delta\omega_I + k\Delta\omega_S$ and $F_2 = \Delta\omega_I$, where $(n - k(\gamma_S/\gamma_I))$ and k represent the order of coherences of the I and S spins during the t_1 period, respectively. The order of coherences should of course be integers; this is also clear in Eqs. [18] and [32], which were obtained from the condition to pass the gradient filter. Note that the k -quantum coherence in the S spins is combined with $(n - k(\gamma_S/\gamma_I))$ -quantum coherence in the I spins; that is, k is scaled by the ratio of the gyromagnetic ratios. The total order of coherence may be regarded as n quantum as in the homonuclear case for 1:n gradient pulses. Note that the signal intensity is proportional

to the product of the two Bessel functions whose orders represent the order of coherences of the two spins.

Equation [39] is quite general, and can be applied to both homonuclear ($\gamma_I = \gamma_S$) and heteronuclear ($\gamma_I \neq \gamma_S$) cases. However, care must be taken for the homonuclear case. Equation [39] is valid if the resonance frequencies of the I and S spins differ by much more than the reciprocal of the dipolar demagnetizing time τ_d (~ 3 Hz for pure water), and by much more than the reciprocal of the J coupling. If instead the resonance frequency difference is much smaller than the reciprocal of the demagnetizing time, the factor of $2/3$ should be removed in Eq. [39]; if the resonance frequency difference is much smaller than the J coupling, the spins are magnetically fully equivalent, and $J = 0$ should be substituted into Eq. [39].

The most useful type of heteronuclear coherence would be double-quantum and zero-quantum coherences involving 1Q coherence in the I spin and 1Q coherence in the S spin. For the ^1H and ^{13}C heteronuclear case, we have $\gamma_S/\gamma_I = 1/4$. For the $n = \pm 5/4$ case, we get the double-quantum peaks located at $(F_1, F_2) = \{\mp(\Delta\omega_I + \Delta\omega_S), \Delta\omega_I\}$. The resulting signal can be written as

$$\begin{aligned}
 M_{2Q}^{I+}(t_1, t_2) &= iM_0^I \exp(i\Delta\omega_I t_2) \exp\{\mp i(\Delta\omega_I + \Delta\omega_S)t_1\} \\
 &\times J_1\left(-\frac{t_2 \cos(\pi J t_1)}{\tau_{dI}}\right) J_1\left(-\frac{2}{3} \frac{\gamma_I}{\gamma_S} \frac{t_2 \cos(\pi J t_1)}{\tau_{dS}}\right) \\
 &\times \left[\cos(\pi J t_1) \cos(\pi J t_2) \left(\frac{\tau_{dI}}{t_2 \cos(\pi J t_1)}\right) \right. \\
 &\quad \left. - \sin(\pi J t_1) \sin(\pi J t_2) \right. \\
 &\quad \left. \times \frac{\gamma_S}{\gamma_I} \left(\frac{3}{2} \frac{\gamma_S}{\gamma_I} \frac{\tau_{dS}}{t_2 \cos(\pi J t_1)}\right) \right]. \quad [40]
 \end{aligned}$$

The zero-quantum peaks obtained if $n = \pm 3/4$ are located at $(F_1, F_2) = \{\mp(\Delta\omega_I - \Delta\omega_S), \Delta\omega_I\}$, and the signal is

$$\begin{aligned}
 M_{ZQ}^{I+}(t_1, t_2) &= iM_0^I \exp(i\Delta\omega_I t_2) \exp\{\mp i(\Delta\omega_I - \Delta\omega_S)t_1\} \\
 &\times J_1\left(-\frac{t_2 \cos(\pi J t_1)}{\tau_{dI}}\right) J_1\left(-\frac{2}{3} \frac{\gamma_I}{\gamma_S} \frac{t_2 \cos(\pi J t_1)}{\tau_{dS}}\right) \\
 &\times \left[\cos(\pi J t_1) \cos(\pi J t_2) \left(\frac{\tau_{dI}}{t_2 \cos(\pi J t_1)}\right) \right. \\
 &\quad \left. + \sin(\pi J t_1) \sin(\pi J t_2) \right. \\
 &\quad \left. \times \frac{\gamma_S}{\gamma_I} \left(\frac{3}{2} \frac{\gamma_S}{\gamma_I} \frac{\tau_{dS}}{t_2 \cos(\pi J t_1)}\right) \right]. \quad [41]
 \end{aligned}$$

It is important to notice that the peaks observed in the indirectly detected dimension (see Fig. 2) are a triplet while a doublet was observed in the directly detected dimension. This is clear evidence that the coupling was due to the intermolecular dipolar couplings. If the coupling were due to the intramolecular J coupling, the 2Q and ZQ spectra in the indirectly detected dimension would have been singlets (28). For an intermolecular 2Q or ZQ transition (involving, for example, the proton on molecule 1 and the carbon on molecule 2), the remaining two spins (proton on molecule 2, carbon on molecule 1) can be $\alpha\alpha$ (adding $2J$ to the transition frequency), $\beta\beta$ (subtracting $2J$ from the transition frequency), or $\alpha\beta/\beta\alpha$ (leaving the transition frequency unaffected).

Also notice that the 2Q and ZQ signals are different in the sign of the second term. To verify the effect of J coupling in peak multiplicities we can take the Taylor series expansion $J_1(x) \approx x/2$ for the Bessel functions in Eqs. [40] and [41], which is valid for early times in t_2 . This gives

$$\begin{aligned}
 M^{I+}(\Delta\omega_I \pm \Delta\omega_S, \Delta\omega_I) &\propto A(1 + \cos(2\pi J t_1)/2) \\
 &\times \cos(\pi J t_2) \mp B \sin(2\pi J t_1) \sin(\pi J t_2), \quad [42]
 \end{aligned}$$

where $A = (1/6)(\gamma_I/\gamma_S)(t_2/\tau_{dS})$ and $B = (1/8)(\gamma_S/\gamma_I)(t_2/\tau_{dI})$. The upper sign is for the double-quantum case and the lower sign is the zero-quantum signal. Along the indirectly detected dimension, the A term gives in-phase peaks whose intensities are 1:2:1, and the B term produces antiphase peaks with relative intensities of 2:0:-2. The antiphase nature of the B term makes the two outer peaks asymmetric, which originates from the coherence transfer due to J coupling. For neat $^{13}\text{CHCl}_3$, $A:B = 1:3$. Therefore the relative intensities of a triplet peak along the indirectly detected dimension will be 7:2:-5 for the double-quantum signal while that of the zero-quantum signal will be -5:2:7. This explains why the peaks in the experimental spectra in Fig. 2 run in the opposite direction for DQ and ZQ sequences.

Figure 3 shows numerical simulations based on Eqs. [40] and [41]. They agree fairly well with Eq. [42] obtained by considering only the first-order term in the series expansion. The outer peaks appear larger than the middle peak, which is contradictory to the experimental result (Fig. 2). However, it is very difficult to predict the relative intensities quantitatively since we ignored all the other effects (e.g., relaxation, radiation damping, diffusion) except the dipolar and J coupling which can affect peak intensities.

In principle, we would expect higher-order intermolecular cross peaks. For the case of $n = 3/4$ and $k = 5$, multiple-quantum coherence evolving at $2\Delta\omega_I - 5\Delta\omega_S$ during the t_1 period will pass the gradient filter too. However, these peaks are not observed experimentally because their magnetization is modulated by the product of higher-order Bessel functions

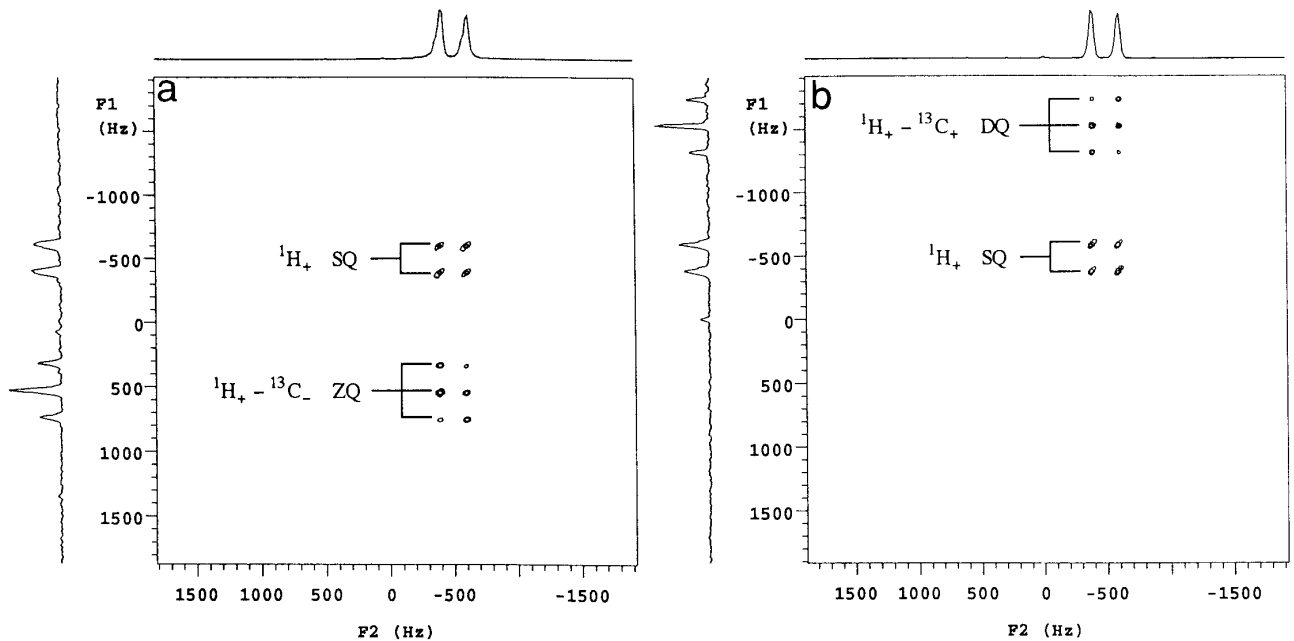


FIG. 2. Two-dimensional spectra ($256 \times 2K$ data points each) with detection of ^1H magnetization on a Varian 600-MHz Inova NMR spectrometer at 298 K. Carbon-13-enriched chloroform (99%) was purchased from Isotec Inc. and used without further purification. Neat $^{13}\text{CHCl}_3$ solution was used for our experiments. The sample was contained in a 5-mm-o.d. NMR tube and sealed. We used about $6.7 \times 10^{-3} M$ ferric acetylacacetate as a relaxation agent to reduce the T_1 of carbon from 22.0 to 9.5 s, thus shortening the experiments. Gradient strength G is 18 G/cm, and T is 4 ms. Proton and carbon resonance offsets are -500 and -1000 Hz, respectively, and the J coupling constant is 210 Hz. The pulse repetition delay is 60 s. (a) Ratio n is $-3/4$. Zero-quantum triplet cross peaks appear at $F_2 = -500$ Hz, $F_1 = 500$ Hz ($\Delta\omega_{\text{H}} - \Delta\omega_{\text{C}}$). (b) Ratio n is $-5/4$. Double-quantum triplet cross peaks appear at $F_2 = -500$ Hz, $F_1 = -1500$ Hz ($\Delta\omega_{\text{H}} + \Delta\omega_{\text{C}}$). The relative intensities of two outer peaks in a triplet (same position in F_2) are different between DQ and ZQ cases. A simple phase cycling (\pm) on the first carbon 90° pulse and receiver phase eliminates the residual proton SQ coherences (since the gradient ratio is closer to -1); however, we also lose some information about the J coupling effect on DQ and ZQ coherences (see Ref. (17)).

(i.e., $J_2 \times J_3$), whose intensities are much lower at the short times where relaxation processes have not yet begun to dominate. This effect is exacerbated in our case since τ_{dS} is 64 times longer than τ_{dI} , meaning that the maximum of higher-order Bessel function occurs at times much too long to escape relaxation.

III. DISCUSSION AND CONCLUSIONS

The quantum calculation is involved because many difference coherence transfer pathways, both intramolecular and intermolecular, must be considered. However, the calculation shows explicitly that the quantum mechanical picture, with its intuitive power, can still be used to visualize the effects of intermolecular dipolar couplings even when the spectrum is structured by internal couplings.

It would be possible to also extend the nonlinear Bloch equations into nonlinear master equations which explicitly handle the spin operators within each molecule, and then use the mean field approximation to couple molecules. However, with two spins in each molecule, this means that in general 15 independent equations (all the products $I_\alpha S_\beta$ and all the

terms I_α or S_β , where α and β can be x , y , or z) must be considered. For the heteronuclear CRAZED sequence, all of the zero-quantum terms except for I_z and S_z (which give the demagnetizing field) and all of the two-quantum terms can be ignored in both t_1 and t_2 , since they do not lead to observable signal. Thus only 10 independent equations (I_x , I_y , I_z , $I_x S_z$, $I_y S_z$, S_x , S_y , S_z , $S_x I_z$, and $S_y I_z$) would have to be solved, but this is still substantially more complex than the uncoupled spin case. Such an approach is discussed formally in Ref. (15), although no explicit signal calculations are done there; our paper is the first calculation which produces an analytical result in the presence of couplings.

The classical and quantum results will give the same answer; the boundary between solid-like behavior, where quantum and classical pictures are expected to deviate, and liquid-like behavior has been treated in detail elsewhere (30). The classical picture may have some computational advantages, as it does in the absence of J couplings, because radiation damping and diffusion can be included. However, the most important use of the quantum picture, as in previous work, is to give an intuitive picture and to predict the effects of new pulse sequences, since the properties of multiple-

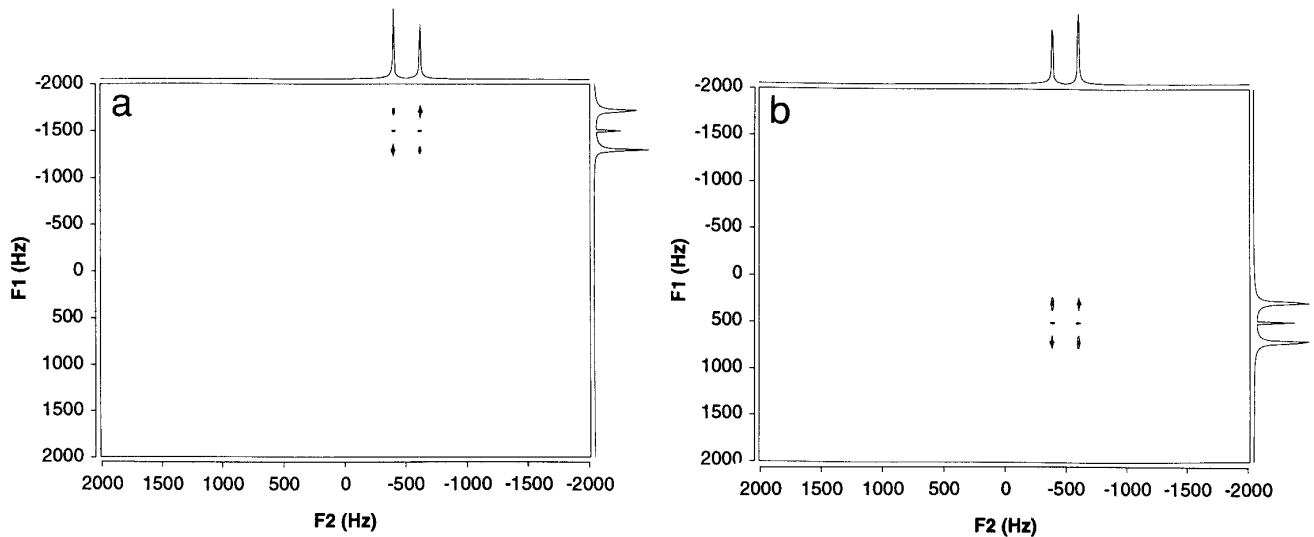


FIG. 3. Simulations of two-dimensional spectra based on (a) Eq. [40] (DQ coherence) and (b) Eq. [41] (ZQ coherence) with same resonance offsets and J coupling constant of the experiments in Fig. 2. The outer peaks in both simulations are larger than the middle peak (see text).

quantum coherences are well understood. Thus, inclusion of intramolecular couplings into the quantum picture gives a strong foundation for devising the next generation of experiments.

APPENDIX

Classical Calculation Based on Modified Bloch Equations for a Multicomponent System

For comparison, we present here the classical calculation based on nonlinear Bloch equations for the case where there are no scalar couplings. At equilibrium, the magnitude of the magnetization which is all on the z axis is given by

$$M_0 = \sum_j M_0^j \hat{z}. \quad [\text{A1}]$$

After the second 90° pulses followed by the chemical shift evolution during t_1 and the first gradient pulse, the longitudinal and transverse components of the magnetization are

$$M_z = - \sum_j \{ M_0^j \cos(\Delta\omega_j t_1 + \gamma_j G T z) \}$$

$$M^+ = i M_y = i \sum_j \{ M_0^j \sin(\Delta\omega_j t_1 + \gamma_j G T z) \}, \quad [\text{A2}]$$

where $\Delta\omega_j$ and γ_j are the resonance frequency in the rotating frame and the gyromagnetic ratio of the j spin, respectively. For simplicity in notation, we transform $t_1 + T$ into t_1 and $t_1 + nT$ into t_2 after the gradient pulses. After the second gradient pulse and precession during t_2 , we can have the following equation if the resonance frequency of each spin differs by much more than the reciprocal of the dipolar demagnetizing time,

$$M_z = - \sum_j \{ M_0^j \cos(\Delta\omega_j t_1 + \gamma_j G T z) \}$$

$$M^+ = i \sum_j \left[M_0^j \sin(\Delta\omega_j t_1 + \gamma_j G T z) \exp i \left\{ \Delta\omega_j t_2 + \gamma_j n G T z - \tau_{d_j}^{-1} t_2 \cos(\Delta\omega_j t_1 + \gamma_j G T z) \right\} - \sum_{k \neq j} \left[\frac{2}{3} \frac{\gamma_j}{\gamma_k} \tau_{d_k}^{-1} t_2 \cos(\Delta\omega_k t_1 + \gamma_k G T z) \right] \right], \quad [\text{A3}]$$

where τ_{d_j} is the dipolar demagnetizing time of the j spin. Using the identity

$$\exp(iz \cos \theta) = \sum_{m=-\infty}^{\infty} i^m J_m(z) \exp(im\theta), \quad [\text{A4}]$$

the observable single-quantum magnetization becomes

$$M^+ = i \sum_j \left[\begin{aligned} & M_0^j \frac{1}{2i} \{ \exp i(\Delta\omega_j t_1 + \gamma_j GTz) - \exp(-i(\Delta\omega_j t_1 + \gamma_j GTz)) \} \exp i(\Delta\omega_j t_2 + \gamma_j n GTz) \\ & \times \sum_{m_j=-\infty}^{\infty} i^{m_j} J_{m_j} \left(-\frac{t_2}{\tau_{dj}} \right) \exp i(m_j \Delta\omega_j t_1 + \gamma_j m_j GTz) \\ & \times \prod_{k \neq j} \left\{ \sum_{m_k=-\infty}^{\infty} i^{m_k} J_{m_k} \left(-\frac{2}{3} \frac{\gamma_j}{\gamma_k} \frac{t_2}{\tau_{dk}} \right) \exp i(m_k \Delta\omega_k t_1 + \gamma_k m_k GTz) \right\} \end{aligned} \right]. \quad [A5]$$

To find the effect of spatial modulation, we collect all the position-dependent terms as

$$\begin{aligned} & \{ \exp(i\gamma_j GTz) - \exp(-i\gamma_j GTz) \} \\ & \times \exp(i\gamma_j n GTz) \sum_{m_j} \exp(i\gamma_j m_j GTz) \\ & \times \prod_{k \neq j} [\sum_{m_k} \exp(i\gamma_k m_k GTz)] \\ & = \sum_{m_j} \sum_{m_k} \left[\exp i \left\{ \left(n + 1 + m_j + \sum_{k \neq j} m_k \left(\frac{\gamma_k}{\gamma_j} \right) \right) \gamma_j GTz \right\} \right. \\ & \quad \left. - \exp i \left\{ \left(n - 1 + m_j + \sum_{k \neq j} m_k \left(\frac{\gamma_k}{\gamma_j} \right) \right) \gamma_j GTz \right\} \right]. \end{aligned} \quad [A6]$$

In order for a magnetization to be nonzero after spatial averaging, one of the expressions in Eq. [47] must be constant with respect to position and thus must have a coefficient of zero for the z direction. Therefore, we require the following condition for there to be a signal:

$$m_j + \sum_{k \neq j} m_k \left(\frac{\gamma_k}{\gamma_j} \right) = -(n \pm 1).$$

Using the Bessel function relations $J_{-n}(x) = (-1)^n J_n(x)$ and $J_{n-1}(x) + J_{n+1}(x) = (2n/x)J_n(x)$ the resulting signal can be written as

$$\begin{aligned} & M^+ \\ & = i^{\{n-1+\sum_{k \neq j} m_k(1-\gamma_k/\gamma_j)\}} \sum_j M_0^j \exp(i\Delta\omega_j t_2) \\ & \quad \times \exp \left\{ -i \left(n - \sum_{k \neq j} m_k \left(\frac{\gamma_k}{\gamma_j} \right) \right) \Delta\omega_j t_1 \right\} \end{aligned}$$

$$\begin{aligned} & \times \left(n - \sum_{k \neq j} m_k \left(\frac{\gamma_k}{\gamma_j} \right) \right) \left(\frac{\tau_{dj}}{t_2} \right) J_{(n-\sum_{k \neq j} m_k(\gamma_k/\gamma_j))} \left(-\frac{t_2}{\tau_{dj}} \right) \\ & \times \prod_{k \neq j} \exp(-im_k \Delta\omega_k t_1) J_{m_k} \left(-\frac{2}{3} \frac{\gamma_j}{\gamma_k} \frac{t_2}{\tau_{dk}} \right). \end{aligned} \quad [A7]$$

In the case of a two-spin, I and S system, this equation becomes

$$\begin{aligned} & M^{I^+} \\ & = i^{n-1+k(1-\gamma_s/\gamma_I)} M_0^I \exp \left\{ -i \left(n - k \frac{\gamma_S}{\gamma_I} \right) \Delta\omega_I t_1 \right\} \\ & \quad \times \exp(-ik \Delta\omega_S t_1) \exp(i\Delta\omega_I t_2) \\ & \quad \times \left(n - k \frac{\gamma_S}{\gamma_I} \right) \left(\frac{\tau_{dI}}{t_2} \right) J_{n-k(\gamma_S/\gamma_I)} \left(-\frac{t_2}{\tau_{dI}} \right) \\ & \quad \times J_k \left(-\frac{2}{3} \frac{\gamma_I}{\gamma_S} \frac{t_2}{\tau_{dS}} \right), \end{aligned} \quad [A8]$$

which is exactly the same as the result from the density matrix calculation, Eq. [29].

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