Vol 14 No 3, March 2005
1009-1963/2005/14(03)/0516-08

Chinese Physics

© 2005 Chin. Phys. Soc.
and IOP Publishing Ltd

Multiplet patterns due to co-existing intermolecular dipolar and intramolecular scalar couplings in liquid nuclear magnetic resonance*

Zhu Xiao-Qin(朱小钦)[a], Cai Cong-Bo(蔡聪波)[a],
Chen Zhong(陈 忠)[a,b,†], and Zhong Jian-Hui(钟健晖)[b]

[a] *Department of Physics, State Key Laboratory for Physical Chemistry of Solid Surface, Xiamen University, Xiamen 361005, China*

[b] *Departments of Radiology and Physics and Astronomy, University of Rochester, Rochester, NY 14642, USA*

(Received 24 August 2004; revised manuscript received 20 October 2004)

When both intermolecular dipolar couplings (D couplings) and intramolecular scalar couplings (J couplings) exist in a highly polarized multiple-spin liquid, some forbidden nuclear magnetic resonance signals originating from intermolecular multiple-quantum coherences may become observable. Moreover, their multiplet patterns are quite different from what are observed in a multiple-spin system with J couplings only. In this paper, these forbidden resonance peaks and unique multiplet patterns are studied theoretically and experimentally. For comparison and verification, an $I_2S_3 + X$ spin system is chosen as an example to present five types of signal patterns from the interactions of D and J couplings with either selective or non-selective radio-frequency pulse sequences for double-quantum coherences. The multiplet pattern rules for a more general $I_pS_q + X_k$ (p,q,$k = 1, 2, 3, \ldots$) spin system are derived as well. It is demonstrated that some unusual multiplet amplitude patterns such as (1:0:–1) may "magnify" J splittings, allowing more accurate measurement of J coupling in the case of small J coupling constants and/or in inhomogeneous fields. It is shown that the theoretical predictions, computer simulations, and experimental observations are all in agreement with one another very well.

Keywords: nuclear magnetic resonance, intermolecular multiple-quantum coherences, dipolar and scalar couplings, multiplet patterns

PACC: 3325, 3240, 7660

1. Introduction

The observation of intermolecular multiple-quantum coherences (MQCs) in water and other highly polarized spin systems has attracted tremendous attention in the nuclear magnetic resonance (NMR) community for the past ten years.[1–10] When a Cosy Revamped by Asymmetric Z-gradient Echo Detection (CRAZED) sequence ($(\pi/2) - t_1 -$ {gradient, length T}$-(\pi/2)-$ {gradient, length nT}$-$ t_2) is applied to a highly polarized spin system, intermolecular n-order MQCs can be observed. For example, if n is –2 or 2, signals originating from intermolecular double-quantum coherences (DQCs) will be detected. Although residual intermolecular dipolar interactions (D couplings) are usually cancelled in the liquid sample with isotropically oriented molecules, they come into play when the spherical symmetry of the magnetization distribution for the sample is broken in the presence of magnetic field gradients. The D couplings between distant nuclei in different molecules have been shown experimentally to generate intermolecular cross-peaks in a wide variety of two-dimensional (2D) NMR experiments in solutions.[1–3,11,12] On the other hand, scalar couplings (J couplings) are another kind of interaction between spins mediated through electrons of the chemical bonds. A conventional NMR spectrum is mainly characterized by chemical shifts and J couplings, which provide information about molecular

*Project supported by the National Natural Science Foundation of China (Grant Nos 10234070 and 10375049) and National Institutes of Health (Grant No NS41048).

†E-mail: chenz@jingxian.xmu.edu.cn

compositions and bond structures in a variety of samples including proteins.[13] In 2D NMR spectra, both D and J couplings may induce cross-peaks. Therefore, they both can be used to observe forbidden transitions indirectly in solution NMR. J couplings of spins in a molecule may result in intramolecular MQCs while D couplings of spins in different molecules may induce intermolecular MQCs in solution NMR. In most previous works, these two kinds of couplings were studied separately. It is worth exploring their effects when both couplings are significant in a highly polarized spin system. In 1998, Warren and co-workers studied the competitive effects between these two types of couplings with 2D NMR spectroscopy. They showed that co-existence of these two types of couplings introduces additional cross-peaks which are absent in spin systems with D couplings alone, and the multiplet patterns of the cross-peaks are quite different from the conventional ones.[14] However, a CRAZED pulse sequence with two non-selective $\pi/2$ pulses resulted in a very complex spectrum in their work. In addition, several peaks may overlap in one-dimensional (1D) or 2D spectra when the J coupling constant is small. This hinders quantitative studies of how the D and J couplings interact and what results from their co-existence. To the best of our knowledge, important issues such as how to characterize the multiplet pattern have not been resolved yet in works published to date. Complete theoretical expressions, confirmatory computer simulations, and quantitative experimental characterizations are of fundamental importance for our understanding of the underlying physical mechanisms in these coupled spin systems. Selective radio-frequency (RF) pulses have become more popular in NMR study in recent years. In our previous works, they were employed for investigating properties of intermolecular MQCs and high-resolution NMR spectra in inhomogeneous fields.[15−18] Selective pulses may simplify NMR spectra, and thus facilitate analysis of multiplet patterns.

In this paper, a modified CRAZED pulse sequence with selective RF pulses is designed for studying multiplet patterns resulting from combined effects of D and J couplings. A homonuclear $I_2S_3 + X$ spin system is chosen as an example for the basic theoretical description, and five types of pattern expressions related to the splitting factors ($\cos(\pi Jt)$ and $\sin(\pi Jt)$) are presented. The rules of multiplet patterns are then extended to a more general $I_pS_q + X_k$ spin system (p, q, $k = 1, 2, 3, \ldots$). In order to verify the theoretical predictions, computer simulations and experimental observations are presented. All results are consistent with one another very well. A particular kind of multiplet patterns such as (1:0:−1) is further analysed and discussed since it has potential applications in measuring J coupling more accurately in the case of small J coupling constants and/or in inhomogeneous fields.

2. Theoretical description

A modified CRAZED pulse sequence depicted in Fig.1 with $n = -2$ can be applied to measure signals from intermolecular DQCs in a spin system with both significant D and J couplings. The two $\pi/2$ RF pulses in Fig.1 applied along the y axis (written as $(\pi/2)_y$) may be either selective or non-selective. A pair of linear gradient pulses is applied along the z axis with an area ratio of 1:−2 in order to select intermolecular DQCs. Since there are only two $\pi/2$ RF pulses in the pulse sequence, no signal from usual intramolecular DQCs can be detected.[19,20]

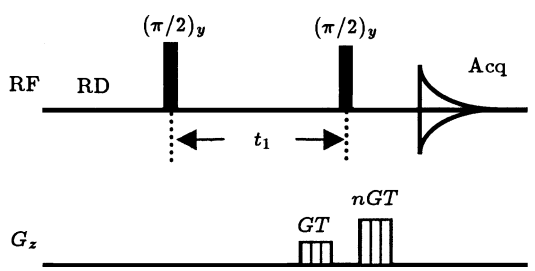


Fig.1. Modified CRAZED pulse sequence. A pair of linear gradient pulses is applied along the z axis with an area ratio of 1:−2 to select intermolecular DQCs, with G and T being the amplitude and duration of the first gradient, respectively.

A homonuclear $I_2S_3 + X$ spin system is chosen for deriving a theoretical expression for intermolecular DQCs in the presence of J couplings, where the I and S spins are scalar coupled to each other and the X spins are isolated. If the first $(\pi/2)_y$ pulse is selective for I spins and the second one excites all I, S, and X spins, the pulse sequence is represented as "I–ISX". Similar representation will be used in the following context. A combination of quantum and classical treatments is employed to treat the intramolecular J couplings and intermolecular D couplings simultaneously.[14,21] For simplicity, effects of radiation damping, relaxation, and diffusion are disregarded in the following discussion. For the $I_2S_3 + X$ spin system, its spin density matrix at thermal equi-

librium is given by[3,14]

$$\begin{aligned}\rho_{\rm eq} =&2^{-(N_I+N_S+N_X)}\prod_{i,\alpha}(1-\Im I_{iz,\alpha})\\ &\times\prod_{j,\beta}(1-\Im S_{jz,\beta})\\ &\times\prod_{k}(1-\Im X_{kz}),\end{aligned}\tag{1}$$

where $\Im = 2\tanh(\hbar\omega_0/2kT)$; N_I, N_S, and N_X represent the numbers of I, S, and X spins, respectively; the indices i and j run over each molecule of the sample, and k runs over each of the isolated X spins; the indices α and β count for multiple spins in the same molecule, in which α=1, 2 and β= 1, 2, and 3 for the I_2S_3 spin system, respectively. The first $(\pi/2)_y$ pulse, which is selective for I spins, converts z magnetization of I spins only into x magnetization. During the evolution period t_1, only coherences of I spins evolve under the first-order J couplings (proportional to $2I_{iz}S_{iz}$), chemical shift ($\omega_I t_1$), and the gradient pulse (γGTz). The density matrix just before the second RF pulse can therefore be given as

$$\begin{aligned}\rho(t_1) =&2^{-(N_I+N_S+N_X)}\prod_{i,\alpha}\{1-\Im c(t_1)^3[I_{ix,\alpha}\cos(\omega_I t_1+\gamma GTz)+I_{iy,\alpha}\sin(\omega_I t_1+\gamma GTz)]\\ &-2\Im c(t_1)^2 s(t_1)(S_{iz,1}+S_{iz,2}+S_{iz,3})[I_{iy,\alpha}\cos(\omega_I t_1+\gamma GTz)\\ &-I_{ix,\alpha}\sin(\omega_I t_1+\gamma GTz)]+4\Im c(t_1)s(t_1)^2(S_{iz,1}S_{iz,2}+S_{iz,1}S_{iz,3}+S_{iz,2}S_{iz,3})\\ &\times[I_{ix,\alpha}\cos(\omega_I t_1+\gamma GTz)+I_{iy,\alpha}\sin(\omega_I t_1+\gamma GTz)]\\ &+8\Im s(t_1)^3 S_{iz,1}S_{iz,2}S_{iz,3}[I_{iy,\alpha}\cos(\omega_I t_1+\gamma GTz)-I_{ix,\alpha}\sin(\omega_I t_1+\gamma GTz)]\}\\ &\times\prod_{j,\beta}(1-\Im S_{jz,\beta})\times\prod_{k}(1-\Im X_{kz}),\end{aligned}\tag{2}$$

where $c(t_1)=\cos(\pi J t_1)$ and $s(t_1)=\sin(\pi J t_1)$; ω_I represents the resonance offset of I spins in rotating frame; γGTz is the dephasing angle at the position z attributed to the gradient pulse with magnitude G and duration T, and γ is the gyromagnetic ratio. The second RF pulse interchanges the x and z magnetizations of both I and S spins. Since there are no further RF pulses after the second one, only terms of single-quantum coherences (SQCs) need to be kept.

$$\begin{aligned}\rho(t_1,t_2=0) =&2^{-(N_I+N_S+N_X)}\prod_{i,\alpha}[1+\Im c(t_1)^3 I_{iz,\alpha}\\ &\times\cos(\omega_I t_1+\gamma GTz)\\ &-\Im c(t_1)^3 I_{iy,\alpha}\sin(\omega_I t_1+\gamma GTz)\\ &-2\Im c(t_1)^2 s(t_1)\\ &\times(S_{ix,1}+S_{ix,2}+S_{ix,3})I_{iz,\alpha}\\ &\times\sin(\omega_I t_1+\gamma GTz)\\ &+\text{unobservable terms}]\\ &\times\prod_{j,\beta}(1-\Im S_{jx,\beta})\\ &\times\prod_{k}(1-\Im X_{kx}).\end{aligned}\tag{3}$$

Since the J coupling terms commute with the other secular parts of the Hamiltonian including the dipolar field, the evolution due to J couplings during the detection period t_2 can be written as

$$\begin{aligned}\rho(t_1,t_2) =&2^{-(N_I+N_S+N_X)}\prod_{i,\alpha}[1+\Im c(t_1)^3 I_{iz,\alpha}\\ &\times\cos(\omega_I t_1+\gamma GTz)\\ &-\Im c(t_1)^3 c(t_2)^3 I_{iy,\alpha}\sin(\omega_I t_1+\gamma GTz)\\ &-\Im c(t_1)^2 s(t_1)c(t_2)s(t_2)\\ &\times(S_{iy,1}+S_{iy,2}+S_{iy,3})\sin(\omega_I t_1+\gamma GTz)\\ &+\text{unobservable terms}]\\ &\times\prod_{j,\beta}[1-\Im S_{jx,\beta}c(t_2)^2\\ &+\text{unobservable terms}]\\ &\times\prod_{k}(1-\Im X_{kx}).\end{aligned}\tag{4}$$

When the intermolecular dipolar interactions are treated with the classical dipolar field, the longitudinal and transverse magnetizations can be respectively written as Eqs.(5) and (6) as follows:

$$M_z(t_1,t_2,z) = -2M_0^I c(t_1)^3\cos(\omega_I t_1+\gamma GTz),\tag{5}$$

$$\begin{aligned}M^+_{\rm total}(t_1,t_2,z) =&M_x^I+{\rm i}M_y^I+M_x^S\\ &+{\rm i}M_y^S+M_x^X+{\rm i}M_y^X\\ =&2{\rm i}M_0^I c(t_1)^3 c(t_2)^3\sin(\omega_I t_1+\gamma GTz)\\ &+M_0^X+3M_0^S[2{\rm i}c(t_1)^2 s(t_1)c(t_2)s(t_2)\\ &\times\sin(\omega_I t_1+\gamma GTz)+c(t_2)^2],\end{aligned}\tag{6}$$

where M_0^I, M_0^S, and M_0^X represent the equilibrium magnetizations per unit volume of I, S, and X spins,

respectively. The distant-dipolar field is given by[14,22]

$$B_{\rm d} = -[2t_2\Delta_{\rm s}c(t_1)^3/\tau_{\rm d}^I]\cos(\omega_I t_1 + \gamma GTz), \qquad (7)$$

where $\tau_{\rm d}^I = (\gamma\mu_0 M_0^I)^{-1}$ is the dipolar demagnetizing time of the I spins; $\Delta_{\rm s} = [3(\hat{\boldsymbol{s}}\cdot\hat{\boldsymbol{z}})^2 - 1]/2$, in which the unit $\hat{\boldsymbol{s}}$ defines the direction of coherence-selection gradients, and $\hat{\boldsymbol{z}}$ is the direction of the static magnetic field. Since the gradient field is oriented along the z direction, i.e. when $\hat{\boldsymbol{s}} = \hat{\boldsymbol{z}}$, we have $\Delta_{\rm s} = 1$. Finally, the transverse magnetizations of the I, S, and X spins after the evolution under the chemical shift (ωt_2), second gradient pulse ($-2\gamma GTz$), and distant dipolar field during the detection period are given as

$$\begin{aligned}
M^{I+} =& M_0^I c(t_1)^3 c(t_2)^3[\exp(\mathrm{i}\omega_I t_1 + \mathrm{i}\gamma GTz) - \exp(-\mathrm{i}\omega_I t_1 - \mathrm{i}\gamma GTz)] \\
&\times \exp(\mathrm{i}\omega_I t_2 - \mathrm{i}2\gamma GTz)\sum_m \mathrm{i}^m J_m[-2t_2 c(t_1)^3/\tau_{\rm d}^I]\exp(\mathrm{i}m\omega_I t_1 + \mathrm{i}m\gamma GTz), \qquad (8a)\\
M^{S+} =& 3M_0^S\{c(t_1)^2 s(t_1)c(t_2)s(t_2)[\exp(\mathrm{i}\omega_I t_1 + \mathrm{i}\gamma GTz) - \exp(-\mathrm{i}\omega_I t_1 - \mathrm{i}\gamma GTz)] \\
&+ c(t_2)^2\exp(\mathrm{i}\omega_S t_2 - \mathrm{i}2\gamma GTz)\} \\
&\times \sum_m \mathrm{i}^m J_m[-4t_2 c(t_1)^3/3\tau_{\rm d}^I]\exp(\mathrm{i}m\omega_I t_1 + \mathrm{i}m\gamma GTz), \qquad (8b)\\
M^{X+} =& M_0^X\exp(\mathrm{i}\omega_X t_2 - \mathrm{i}2\gamma GTz)\exp(\mathrm{i}m\omega_I t_1 + \mathrm{i}m\gamma GTz) \\
&\times \sum_m \mathrm{i}^m J_m[-4t_2 c(t_1)^3/3\tau_{\rm d}^I]. \qquad (8c)
\end{aligned}$$

The Bessel function expansion, $\exp(\mathrm{i}\xi\cos\alpha) = \sum_{m=-\infty}^{\infty}\mathrm{i}^m J_m(\xi)e^{\mathrm{i}m\alpha}$, is used for the distant dipolar field $B_{\rm d}$, where $J_m(\xi)$ is Bessel function of integer order m and $\xi = \gamma\mu_0 M_0^I t_2$ is the argument of the Bessel function. In order to evaluate the signal of the whole sample, average of the complex magnetization over all z positions is taken. If the size scale of a sample is much larger than the dipolar correlation distance of spatial modulation, spatial averaging across the sample retains only terms with $m = -n \pm 1$, which do not depend on the absolute position in the sample.[3,23] Therefore, the resulting transverse magnetizations can be written as

$$\begin{aligned}
M^{I+} \approx& -\mathrm{i}M_0^I\exp(\mathrm{i}\omega_I t_2) \\
&\times \exp(\mathrm{i}2\omega_I t_1)(t_2/\tau_{\rm d}^I)c(t_1)^6 c(t_2)^3, \qquad (9a)\\
M^{S+} \approx& -2\mathrm{i}M_0^S\exp(\mathrm{i}\omega_S t_2) \\
&\times \exp(\mathrm{i}2\omega_I t_1)(t_2/\tau_{\rm d}^I)c(t_1)^5 s(t_1)c(t_2)s(t_2), \qquad (9b)\\
M^{X+} \approx& 0. \qquad (9c)
\end{aligned}$$

Since most CRAZED experiments satisfy the condition of small dipolar field effects, i.e. $\xi \ll 1$, the Bessel functions can be approximated with the first term of its Tailor expansion $J_m(\xi) \cong (\xi/2)^m/m!$. Furthermore, since the value of Bessel function with more than one order is very small, only zero-order and first-order Bessel functions need to be kept.

Now we further analyse the expressions of signals from intermolecular DQCs for I, S, and X spins given by Eq.(9), resulting from a "I–ISX" pulse sequence. I spins are affected by the two $\pi/2$ pulses and gradient fields as shown in Fig.1. It results in a residual dipolar field, $B_{\rm d}$, related to M_0^I magnetization (see Eq.(7)), which affects all I, S, and X spins during t_2 period. Since I spins are coupled to S spins, the residual dipolar field is modulated by J couplings from the three S spins ($c(t_1)^3$) as shown in Eq.(7). Although only one $\pi/2$ pulse has been applied to the S spins, the J couplings between S and I spins result in the S signal originating from intermolecular DQCs. Its coherence transfer pathway can be represented as follows:

$$I^+ \xrightarrow{J_{IS}t_1} I^+ S_z c(t_1)^2 s(t_1) \xrightarrow{(\pi/2)_{IS}} I_z S^+ c(t_1)^2 s(t_1) \xrightarrow{J_{IS}t_2} S^+ c(t_1)^2 s(t_1)c(t_2)s(t_2).$$

On the other hand, since X spins are uncoupled to I spins, the signal of X spins approximates zero (see Eq.(9c)). The S signal shown in Eq.(9b) represents a new type of cross-peak in the presence of J couplings, which disappears in the absence of J couplings. Unique multiplet patterns of this type of cross-peak will be discussed in the next section. Since each cosine term stands for two in-phase peaks and each sine

term produces two anti-phase peaks, they are called "splitting factors". Equation (9b) predicts that the S signal in 2D spectrum appears a triplet with 1:0:−1 along F_2 axis and a septet with 1:4:5:0:−5:−4:−1 along the F_1 axis. Equation (9a) predicts that the I signal in 2D spectrum appears as a quartet with 1:3:3:1 along F_2 axis and a septet with 1:6:15:20:15:6:1 along the F_1 axis.

When an "ISX-I" pulse sequence is employed, similar to the above analysis, one can derive the following signals:

$$M^{I+} \approx -\mathrm{i}M_0^I \exp(\mathrm{i}\omega_I t_2) \exp(\mathrm{i}2\omega_I t_1)(t_2/\tau_\mathrm{d}^I)c(t_1)^3 c(t_1+t_2)^3, \quad (10a)$$

$$M^{S+} \approx -2\mathrm{i}M_0^S \exp(\mathrm{i}\omega_S t_2) \times \exp(\mathrm{i}\omega_I t_1 + \mathrm{i}\omega_S t_1)(t_2/\tau_\mathrm{d}^I)c(t_1)^5 c(t_2)^2, \quad (10b)$$

$$M^{X+} \approx -\frac{2}{3}\mathrm{i}M_0^X \exp(\mathrm{i}\omega_X t_2) \times \exp(\mathrm{i}\omega_I t_1 + \mathrm{i}\omega_X t_1)(t_2/\tau_\mathrm{d}^I)c(t_1)^3. \quad (10c)$$

The I spins are affected by the two $\pi/2$ pulses and gradient fields as shown in Fig.1, so it also results in a residual dipolar field, B_d, related to M_0^I magnetization (see Eq.(7)), which affects all I, S, and X spins during t_2 period. Since I spins are coupled to S spins, the residual dipolar field is modulated by J couplings from the three S spins ($c(t_1)^3$) as shown in Eq.(7). Due to D couplings modulated by J couplings and pure J couplings, Eq.(10a) shows that the I signal originating from intermolecular DQCs satisfies $M^{I+} \propto c(t_1)^3 c(t_1+t_2)^3$. It predicts that the I signal appears as a quartet with 1:3:3:1 along the F_1 axis and a quartet with 1:3:3:1 along the diagonal direction. Since there exists only one RF pulse applied to S and X spins, no dipolar field results from S and X spins, which would affect the I signal. In addition, since the RF pulse applied to S and X spins is the first one, there exists no additional effect on the evolution of I spins. Therefore, the I signal is the same as that using "I–I" pulse sequence. On the other hand, when "ISX–I" pulse sequence is employed, Eq.(10c) predicts that the X spin signal originating from intermolecular DQCs has a quartet with 1:3:3:1 along F_1 axis and no splitting along F_2 axis since X spins are uncoupled to I spins.

An "ISX–X" pulse sequence produces a residual dipolar field of X spins without modulation by J couplings. Therefore, the signals originating from intermolecular DQCs with both pure D and J couplings are described as

$$M^{I+} = -\frac{2}{3}\mathrm{i}M_0^I \exp(\mathrm{i}\omega_I t_2) \times \exp(\mathrm{i}\omega_I t_1 + \mathrm{i}\omega_X t_1)(t_2/\tau_\mathrm{d}^X)c(t_1+t_2)^3, \quad (11a)$$

$$M^{S+} \approx -\mathrm{i}M_0^S \exp(\mathrm{i}\omega_S t_2) \times \exp(\mathrm{i}\omega_S t_1 + \mathrm{i}\omega_X t_1)(t_2/\tau_\mathrm{d}^X)c(t_1+t_2)^2, \quad (11b)$$

$$M^{X+} \approx -\frac{1}{4}\mathrm{i}M_0^X \exp(\mathrm{i}\omega_X t_2) \times \exp(\mathrm{i}2\omega_X t_1)(t_2/\tau_\mathrm{d}^X). \quad (11c)$$

Equation (11a) predicts that the I signal appears as a quartet with 1:3:3:1 along the diagonal direction. Similarly, Eq.(11b) predicts that the S signal appears as a triplet with 1:2:1 along the diagonal direction. Equation (11c) predicts that the X signal appears as a singlet without splitting, which is the same as that when "X–X" pulse sequence is employed with D couplings alone.

When both D and J couplings are significant, multiplet patterns of the signals originating from intermolecular DQCs are quite different from those originating from intermolecular DQCs or intramolecular DQCs alone. The relations between the observed transverse magnetization M^+ and splitting factors under different pulse sequences for an I_2S_3+X spin system are listed in Table 1. Multiplet patterns for a general $I_pS_q+X_k$ spin system are also listed in the fourth column in Table 1.

Table 1. Relationship between M^+ and splitting factors for I_2S_3+X and $I_pS_q+X_k$ spin systems.

Sequence	Position of peak	M^+ for I_2S_3+X	M^+ for $I_pS_q+X_k$
"I–ISX"	$(2\omega_I, \omega_I)$	$M^{I+} \propto c(t_1)^6 c(t_2)^3$	$M^{I+} \propto c(t_1)^{2q} c(t_2)^q$
	$(2\omega_I, \omega_S)$	$M^{S+} \propto c(t_1)^5 s(t_1) c(t_2) s(t_2)$	$M^{S+} \propto c(t_1)^{2q-1} s(t_1) c(t_2)^{p-1} s(t_2)$
"ISX–I"	$(2\omega_I, \omega_I)$	$M^{I+} \propto c(t_1)^3 c(t_1+t_2)^3$	$M^{I+} \propto c(t_1)^q c(t_1+t_2)^q$
	$[(\omega_I+\omega_S), \omega_S]$	$M^{S+} \propto c(t_1)^5 c(t_2)^2$	$M^{S+} \propto c(t_1)^{p+q} c(t_2)^p$
	$[(\omega_I+\omega_X), \omega_X]$	$M^{X+} \propto c(t_1)^3$	$M^{X+} \propto c(t_1)^q$
"ISX–X"	$[(\omega_I+\omega_X), \omega_I]$	$M^{I+} \propto c(t_1+t_2)^3$	$M^{I+} \propto c(t_1+t_2)^q$
	$[(\omega_S+\omega_X), \omega_S]$	$M^{S+} \propto c(t_1+t_2)^2$	$M^{S+} \propto c(t_1+t_2)^p$
	$(2\omega_X, \omega_X)$	$M^{X+} \propto 1$(No Splitting)	$M^{X+} \propto 1$(No Splitting)

3. Experiment

All experiments were performed on a Varian Unity+500 spectrometer, equipped with self-shielded z-gradient coils and a 5mm HCN triple-resonance RF coil with 1.5cm effective length. A sample with methyl ethyl ketone solution (60% solution in acetone-d_6 solvent) was used. X spins represent the CH_3 protons in the methyl group. I and S spins represent the CH_2 and CH_3 protons in the ethyl group, respectively. The modified CRAZED sequence with two selective/nonselective RF pulses and two gradient pulses as shown in Fig.1 was used. Gradient strengths were calibrated with a gradient profile experiment. A typical set of experimental parameters was as follows: relaxation delay (RD) was 10s, to allow the spin system to return to its full equilibrium state and prevent any possible stimulated echoes; and the acquisition time was 1.0s. To suppress the effect of radiation damping, the pulse width of the $\pi/2$ non-selective pulse was extended to 39.1μs by deliberately detuning the probe. The pulse width of selective $\pi/2$ pulse was 20.7ms. Gradient amplitude $G \approx 0.1$T/m and gradient duration T=1.2 ms were used. The frequency offsets of I, S, and X were 390, –356, and 200Hz, respectively.

4. Results and discussion

Since each cosine term splits the peak into two in-phase peaks and each sine term produces two anti-phase peaks, the relative amplitude of splitting patterns can be predicted from the theoretical expressions with splitting factors. For example, the expression $M^{S+} \propto c(t_1)^5 s(t_1) c(t_2) s(t_2)$ (see Eq.(9b)) predicts a triplet with 1:0:–1 amplitude ratio along F_2 axis and a septet with 1:4:5:0:–5:–4:–1 along the F_1 axis. When the unimportant coefficients in Eq.(9b) are neglected, the relative amplitude of multiplet pattern can be represented by an intuitive matrix-like expression as $\begin{pmatrix} 1 & 0 & -1 \\ 4 & 0 & -4 \\ 5 & 0 & -5 \\ 0 & 0 & 0 \\ -5 & 0 & 5 \\ -4 & 0 & 4 \\ -1 & 0 & 1 \end{pmatrix}$. Similarly, the matrix-like expressions of other predicted multiplet patterns discussed in the last section are listed in column 1 of Fig.2.

Computer simulations based on a physical model can provide a powerful tool for verifying the theoretical predictions and experimental observations. Since the classical modified Bloch equation is much more efficient for numerical calculations, the modified Bloch equation, in which a non-linear term was introduced to represent the distant dipolar field, was used to simulate 2D intermolecular DQC spectra in the presence of J couplings. Since it is difficult to describe J couplings in the Bloch equation, we recently proposed the concept of coherence matrix to include the J couplings into the non-linear Bloch equation. The chemical shift, inhomogeneous background field, dipolar field, radiation damping, diffusion, relaxation, and J couplings can be described easily by the operation of the coherence matrix in the nonlinear Bloch equation. A simulation algorithm based on the coherence matrix was used to simulate NMR signals originating from intermolecular DQCs in the presence of Jcouplings. The detailed description of the coherence matrix and simulation algorithm will be reported in a separate paper. The parameter sets of computer simulation were chosen to be as close to the actual experiments as possible. The simulated results are listed in column 2 of Fig.2.

The multiplet patterns of the experimental spectra are shown in column 3 of Fig.2. Experimental results show that the multiplet pattern of S signal using "ISX–I" sequence is similar to that of I signal using "I–ISX" sequence. Moreover, I signals using "ISX–X" or "ISX–I" pulse sequence are similar to those of S signals using "ISX–X" sequence, whose multiplet patterns are oriented along diagonal axis. For clarification, all these similar signals have been omitted from Fig.2. Since both simulated and experimental signals are shown in absolute mode, cross-peaks of negative type are indistinguishable from the positive ones in the spectra. Some of the predicted cross-peaks are too small to be observed in 2D experimental spectra but are still visible in the projections given in (a), (b), and (c) in Fig.2. It demonstrates that the simulated and experimental results are in good agreement with the theoretical predictions. Since the multiplet pattern of the cross-peak shown in (c) of Fig.2 is along the diagonal direction and has low resolution, the middle peak in F_1 projection of the experimental spectrum is smaller than that of the simulated spectrum.

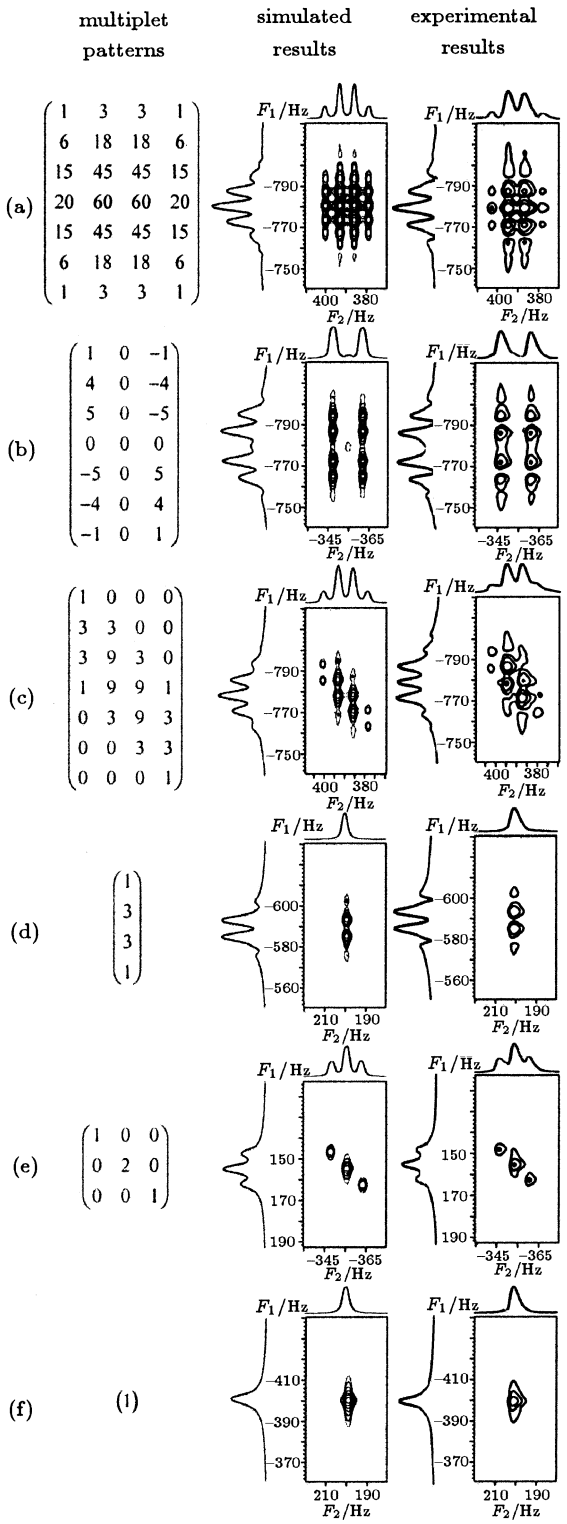


Fig.2. Theoretical predictions, computer simulations, and experimental results of multiplet patterns from intermolecular DQCs of an $I_2S_3 + X$ spin system. (a) I signal using "I–ISX" pulse sequence; (b) S signal using "I–ISX"; (c) I signal using "ISX–I"; (d) X signal using "ISX–I"; (e) S signal using "ISX–X"; and (f) X signal using "ISX–X".

It is worth paying some attention to the amplitude patterns of $\frac{1}{4}(1:0:-1)$ and $\frac{1}{16}\begin{pmatrix} 1 & 0 & -1 \\ 0 & 0 & 0 \\ -1 & 0 & 1 \end{pmatrix}$ in the multiplet patterns. For an $I_2S_3 + X$ spin system, when the "I–ISX" pulse sequence is employed, the expression of $M^{S+} \propto c(t_1)^5 s(t_1) c(t_2) s(t_2)$ can be deduced to a triplet with the intensity ratio of $\frac{1}{4}(1:0:-1)$ in the 1D spectrum. This is an apparent doublet since the central line has zero intensity due to the anti-phase effect of the sine term. This pattern "magnifies" the J splitting in the detection dimension two times. It may have potential applications in measuring J coupling in the case of small J coupling constants and/or in inhomogeneous magnetic fields.

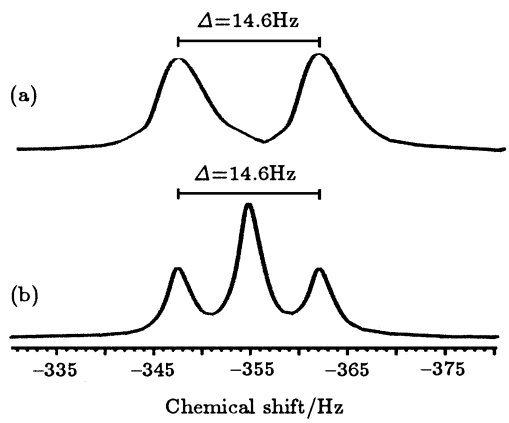


Fig.3. ^{1}H spectra of S spins from (a) intermolecular DQCs using "I-ISX", and (b) conventional SQC using single-pulse sequence. Δ is double the J splitting.

Figure 3 shows the 1D S signals with t_1=0.01 s from intermolecular DQCs using "I–ISX" sequence and conventional 1D spectrum using single-pulse sequence. Although each spectrum in Fig.3 shows that the J coupling constant is about 7.3 Hz, the splitting in Fig.3(a) is double that in Fig.3(b). Additionally, when "I-$IS(X)$" pulse sequence is employed, the multiplet pattern of S signals originating from intermolecular DQCs is $\frac{1}{16}\begin{pmatrix} 1 & 0 & -1 \\ 0 & 0 & 0 \\ -1 & 0 & 1 \end{pmatrix}$ in a 2D spectrum. It "magnifies" the splitting along the diagonal direction $2\sqrt{2}$ times, which can be compared to the case of $\frac{1}{16}\begin{pmatrix} 1 & 2 & 1 \\ 2 & 4 & 2 \\ 1 & 2 & 1 \end{pmatrix}$, whose peaks are prone to overlap. Therefore, the multiplet pattern of

$\frac{1}{16}\begin{pmatrix} 1 & 0 & -1 \\ 0 & 0 & 0 \\ -1 & 0 & 1 \end{pmatrix}$ may make it easy to analyse the parameters such as chemical shifts, J coupling constant, and relative peak area in a 2D spectrum. It may also find applications in inhomogeneous fields and magnetic resonance imaging (MRI).[24,25]

5. Conclusion

When both D and J couplings in a multiple-spin system are significant, the muliplet patterns of cross-peaks originating from the intermolecular DQCs in original CRAZED sequence are complex.[14] In this paper, A modified CRAZED pulse sequence with selective RF pulses has been utilized to simplify intermolecular cross-peaks. The multiplet patterns of cross-peaks originating from the intermolecular DQCs can therefore be analysed more directly and intuitively. It is demonstrated that the theoretical predictions of the multiplet patterns for an I_2S_3+X spin system are consistent with the simulated results and experimental observations. Furthermore, theoretical predictions of multiplet patterns are extended to a more general $I_pS_q+X_k$ (p,q,k=1, 2, 3,. . .) spin system. In addition, the multiplet amplitude patterns such as $\frac{1}{4}(1:0:-1)$ in 1D spectrum are shown to "magnify" the J splitting two times, which may be used to measure J coupling in the case of small J coupling constants and/or in inhomogeneous fields. A combined use of complete theoretical descriptions, computer simulation, and experimental observations provide a convenient way to understand the competitive mechanism between the intramolecular J couplings and intermolecular D couplings. The method proposed herein may prove useful in high-resolution NMR spectroscopy in inhomogeneous fields via intermolecular dipolar interactions.

References

[1] Warren W S, Richter W, Andreotti A H and Farmer II B T 1993 *Science* **262** 2005

[2] He Q, Richter W, Vathyam S and Warren W S 1993 *J. Chem. Phys.* **98** 6779

[3] Lee S, Richter W, Vathyam S and Warren W S 1996 *J. Chem. Phys.* **105** 874

[4] Levitt M H 1996 *Concepts Magn. Reson.* **8** 77

[5] Kimmich R and Ardelean I 1999 *J. Chem. Phys.* **110** 3708

[6] Jeener J 2000 *J. Chem. Phys.* **112** 5091

[7] Zhong J H, Chen Z, Zheng S K and Kennedy S D 2001 *Chem. Phys. Lett.* **350** 260

[8] Chen Z and Zhong J H 2001 *J. Chem. Phys.* **114** 5642

[9] Zheng S K, Chen Z, Chen Z W and Zhong J H 2001 *Chin. Phys.* **10** 558

[10] Wang H and Li G Y 2005 *Acta Phys. Sin.* **54** 1429 (in Chinese)

[11] Richter W and Warren W S 2000 *Concepts Magn. Reson.* **12** 396

[12] Chen Z, Chen Z W, Hwang D W, Zhong J H and Hwang L P 2004 *J. Magn. Reson.* **171** 244

[13] Enster R R, Bodenhausen G and Wokaum A 1987 *Principles of Nuclear Magnetic Resonance in One and Two Dimensions* (Oxford: Clarendon)

[14] Ahn S, Lee S and Warren W S 1998 *Mol. Phys.* **95** 769

[15] Chen Z, Chen Z W and Zhong J H 2001 *J. Chem. Phys.* **115** 10769

[16] Chen Z, Lin G X and Zhong J H 2001 *Chem. Phys. Lett.* **333** 96

[17] Chen Z, Chen Z W and Zhong J H 2002 *J. Chem. Phys.* **117** 8426

[18] Chen Z, Chen Z W and Zhong J H 2004 *J. Am. Chem. Soc.* **126** 446

[19] Freeman R 1998 *Concepts Magn. Reson.* **10** 63

[20] Ye C H, Miao X J and Liu M L 2002 *J. Mol. Struct.* **602** 335

[21] Kimmich R 1997 *NMR Tomography, Diffusometry, Relaxometry* (Berlin: Springer)

[22] Ardelean I and Kimmich R 2000 *J. Magn. Reson.* **143** 101

[23] Chen Z, Zheng S K and Zhong J H 2001 *Chem. Phys. Lett.* **347** 143

[24] Zu D L, Guo H, Song X Y and Bao S L 2002 *Chin. Phys.* **11** 1008

[25] Lu G, Liu M L, Li L Y and Ye C H 2002 *Chin. Phys. Lett.* **19** 1385