Comment

Comment on "Nuclear spin relaxation and non-ergodic quasi-equilibria"

N.R. Skrynnikov, R. Brüschweiler

Laboratorium für Physikalische Chemie, ETH Zentrum, CH-8092 Zurich, Switzerland

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Abstract

Spin relaxation is described for a system of three accidentally degenerate nuclear spins that can be individually monitored, e.g., via heteronuclear scalar coupling partners. The exact treatment based on Bloch–Wangsness–Redfield theory is shown to be consistent with the stochastic Liouville equation correcting and extending earlier findings (Brüschweiler, Chem. Phys. Lett. 270 (1997) 217). The transition to the Solomon regime is discussed when degeneracy is removed. © 1997 Elsevier Science B.V.

Nuclear spin cross relaxation, known as the nuclear Overhauser effect (NOE), has emerged since the pioneering work of Solomon [1] as a powerful method for the elucidation of molecular structure and dynamics in the liquid state. For biomolecules in particular, $^1H-^1H$ NOE information on intramolecular distances measured using multidimensional NOESY experiments [2,3] is indispensible for determining their three-dimensional molecular structures [4–6]. Since in the standard 2-D NOESY experiment cross relaxation of single-spin order $I_{iz} \rightarrow I_{jz}$ is monitored via cross peaks, the involved spins must be non-degenerate. In ^{15}N or ^{13}C labeled systems, on the other hand, 3-D or 4-D NOESY experiments [6] can be applied that include as additional dimensions the chemical shifts of ^{15}N or ^{13}C spins that are scalar J coupled to the cross-relaxing protons. This allows cross relaxation to be measured between degenerate protons, provided that their ^{15}N or ^{13}C coupling partners are non-degenerate (Fig. 1). This situation is termed here accidental degeneracy among the proton spins. In contrast, cross-relaxation processes of the type $I_{iz} \rightarrow I_{jz}$ between equivalent spins with symmetry-induced degeneracy, such as between two protons in a rapidly rotating methyl group, cannot be easily monitored. In the past, auto- and cross-relaxation processes in the A_3 spin system and similar systems with symmetry-induced degeneracy were addressed [8–11] using Bloch–Wangsness–Redfield (BWR) relaxation theory [12–15]. For dipolar relaxation mechanisms that preserve the symmetry most treatments use symmetry-adapted bases to simplify the computations.

In a recent Letter [16], longitudinal cross relaxation was investigated in an accidentally degenerate three-spin system undergoing slow rotational tumbling. The occurrence of a non-ergodic quasi-equilibrium, as predicted by the stochastic Liouville equation (SLE), was rationalized in terms of constants of the motion of the underlying Liouville–von Neumann equation. It was also shown that the more specialized Solomon equations, which in the
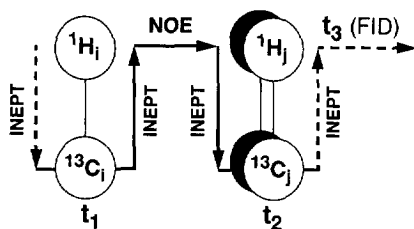
Fig. 1. Schematic heteronuclear 3-D NMR NOESY experiment allowing the detection of cross relaxation between accidentally degenerate protons that are scalar coupled to non-degenerate ^{13}C nuclei. Polarization is transferred between protons and carbons using INEPT [7]. 3-D cross peaks appear at the positions $\{\omega_1, \omega_2, \omega_3\} = \{\omega(C_i), \omega(C_j), \omega(H_j)\}$ with $i, j = 1,2,3$.

spin-diffusion regime ($\omega_0 \tau_c \gg 1$) involve only single-spin order terms I_{jz}, are inconsistent with the SLE. This inconsistency was incorrectly attributed to a failure of BWR theory. Instead, general BWR theory gives within its validity range the same result as the SLE treatment. In the following we present the general BWR treatment of an accidentally degenerate three-spin 1/2 system and discuss the transition to the Solomon equations when the degeneracy is alleviated.

We consider an idealized accidentally degenerate three-spin 1/2 system in isotropic solution, where scalar J couplings between the three spins are assumed to be absent and dipolar relaxation by other nuclei as well as CSA and other relaxation mechanisms are neglected. Longitudinal dipolar relaxation of this system follows the master equation [3]

$$\frac{d\sigma}{dt} = -\hat{\Gamma}(\sigma - \sigma_{eq}).\qquad(1)$$

Starting out from single-spin order $\sigma(0) = I_{jz}$ $\sigma(t)$ evolves then in a 7-dimensional Liouville subspace spanned by the orthogonal operators containing an odd number of single-spin operators

$$B_1 = I_{1z}, \quad B_2 = I_{2z}, \quad B_3 = I_{3z},$$

$$B_4 = 4I_{1z}I_{2z}I_{3z},$$

$$B_5 = \sqrt{2}(I_{1z}I_{2+}I_{3-} + I_{1z}I_{2-}I_{3+}),$$

$$B_6 = \sqrt{2}(I_{1-}I_{2z}I_{3+} + I_{1+}I_{2z}I_{3-}),$$

$$B_7 = \sqrt{2}(I_{1+}I_{2-}I_{3z} + I_{1-}I_{2+}I_{3z}).\qquad(2)$$

Spin operators containing an even number of single-spin operators, such as $2I_{1z}I_{2z}$ or $2^{-1/2}I_{1+}I_{2-}$, relax

in a Liouville subspace that is disconnected from the one of Eq. (2) [17,18]. In Eq. (1) unitary evolution caused by the Zeeman part $-i\hat{H}_Z = -i\omega_0[I_{1z} + I_{2z} + I_{3z}, \ldots]$ was dropped, since $-i\hat{H}_Z B_j = 0$ ($j = 1, \ldots, 7$) and $\hat{H}_Z$ commutes with $\hat{\Gamma}$. The three Hermitian operators

$$B_8 = \sqrt{2}\,i(I_{1z}I_{2+}I_{3-} - I_{1z}I_{2-}I_{3+}),$$

$$B_9 = \sqrt{2}\,i(I_{1-}I_{2z}I_{3+} - I_{1+}I_{2z}I_{3-}),$$

$$B_{10} = \sqrt{2}\,i(I_{1+}I_{2-}I_{3z} - I_{1-}I_{2+}I_{3z}),\qquad(3)$$

which are anti-symmetric with respect to permutation of the spin indices of the two shift operators, are not excited by dipolar relaxation due to their different symmetry properties [17,18]. They are however coupled to the zero-quantum terms B_5, B_6 and B_7 by chemical shift evolution, which becomes important when degeneracy is removed (vide infra). The Redfield matrix elements Γ_{mn} can be expressed as a function of the power spectral density

$$J_{ij,kl}(\omega) = \int_{-\infty}^{\infty} C_{ij,kl}(t)\cos(\omega t)\,dt,\qquad(4)$$

where

$$C_{ij,kl}(t) = \langle r_{ij}^{-3}(0)\,r_{kl}^{-3}(t)\,Y_{20}(\theta_{ij}(0),\varphi_{ij}(0))$$
$$\times Y_{20}(\theta_{kl}(t),\varphi_{kl}(t))\rangle\qquad(5)$$

$J_{ij,kl}(\omega)$ is sampled at frequency zero, at the Larmor frequency $\omega_0 = -\gamma B_0$, and at $2\omega_0$. $Y_{20}(\Omega)$ is a spherical harmonic, and r_{ij}, $\theta_{ij}(t)$ and $\varphi_{ij}(t)$ are the polar coordinates of the internuclear vector r_{ij} between spins i and j in the laboratory frame. ζ defines the prefactor

$$\zeta = \frac{4\pi}{10}\gamma^4\left(\frac{h}{2\pi}\right)^2\left(\frac{\mu_0}{4\pi}\right)^2$$

that will be used below, where γ is the gyromagnetic ratio, h is Planck's constant, and μ_0 is the permeability of free space. Thus, for a spherical top molecule tumbling with a correlation time $\tau_c = 1/(6D)$, where D is the rotational diffusion constant [5],

$$J_{ij,kl}(\omega) = \frac{1}{4\pi}P_2(\cos\chi_{ij,kl})\frac{2\tau_c}{1 + \omega^2\tau_c^2}.\qquad(6)$$

$P_2(x) = (3x^2 - 1)/2$ and $\chi_{ij,kl}$ is the angle between the internuclear vectors r_{ij} and r_{kl}. The Redfield matrix elements Γ_{mn} are symmetric ($\Gamma_{mn} = \Gamma_{nm}$) and given by

$$\Gamma_{11} = \tfrac{1}{2}\zeta\{J_{12,12}(0) + 3J_{12,12}(\omega_0)$$
$$+ 6J_{12,12}(2\omega_0) + J_{13,13}(0) + 3J_{13,13}(\omega_0)$$
$$+ 6J_{13,13}(2\omega_0)\},$$

$$\Gamma_{44} = 3\zeta\{J_{12,12}(\omega_0) + J_{13,13}(\omega_0) + J_{23,23}(\omega_0)\},$$

$$\Gamma_{55} = \tfrac{1}{4}\zeta\{5J_{12,12}(0) + 3J_{12,12}(\omega_0)$$
$$+ 6J_{12,12}(2\omega_0) + 5J_{13,13}(0)$$
$$+ 3J_{13,13}(\omega_0) + 6J_{13,13}(2\omega_0)$$
$$+ 6J_{23,23}(\omega_0) - 8J_{12,13}(0)\},$$

$$\Gamma_{12} = \tfrac{1}{2}\zeta\{-J_{12,12}(0) + 6J_{12,12}(2\omega_0)\},$$

$$\Gamma_{14} = 3\zeta J_{12,13}(\omega_0),$$

$$\Gamma_{15} = \frac{1}{\sqrt{2}}\zeta\{J_{12,13}(0) + 6J_{12,13}(2\omega_0)\},$$

$$\Gamma_{16} = \frac{1}{\sqrt{8}}\zeta\{2J_{12,13}(0) - 3J_{12,13}(\omega_0) - J_{12,23}(0)$$
$$+ 6J_{12,23}(2\omega_0) - 2J_{13,23}(0) - 3J_{13,23}(\omega_0)\},$$

$$\Gamma_{45} = -\frac{3}{\sqrt{2}}\zeta\{J_{23,23}(\omega_0) + J_{12,13}(\omega_0)\},$$

$$\Gamma_{56} = \tfrac{1}{4}\zeta\{4J_{12,12}(0) - 2J_{12,13}(0) + 3J_{12,13}(\omega_0)$$
$$- 2J_{12,23}(0) + 3J_{12,23}(\omega_0) - J_{13,23}(0)$$
$$+ 6J_{13,23}(2\omega_0)\}. \tag{7}$$

The Redfield elements that are not given explicitly in Eq. (7) can be easily derived from the ones listed above by permutation of the spin labels, which enter $J_{ij,kl}(\omega)$ as indices. For example, element Γ_{46} is obtained from Γ_{45} by exchanging spin 1 with spin 2:

$$\Gamma_{46} = -\frac{3}{\sqrt{2}}\zeta\{J_{13,13}(\omega_0) + J_{12,23}(\omega_0)\}.$$

In case of different chemical shifts Ω_1, Ω_2 and Ω_3 Eq. (1) is modified according to

$$\frac{d\sigma}{dt} = -i\hat{\hat{H}}_Z \sigma - \hat{\hat{\Gamma}}(\sigma - \sigma_{eq}), \tag{8}$$

where

$$\hat{\hat{H}}_Z = [\,\Omega_1 I_{1z} + \Omega_2 I_{2z} + \Omega_3 I_{3z}, \dots\,]$$

and the zero-quantum subspace must be extended by the three operators B_8, B_9 and B_{10} defined in Eq. (3). They show a slightly different auto- and cross-relaxation behavior than their symmetric counterparts B_5, B_6 and B_7:

$$\Gamma_{88} = \tfrac{1}{4}\zeta\{5J_{12,12}(0) + 3J_{12,12}(\omega_0)$$
$$+ 6J_{12,12}(2\omega_0) + 5J_{13,13}(0) + 3J_{13,13}(\omega_0)$$
$$+ 6J_{13,13}(2\omega_0) + 4J_{23,23}(0) + 6J_{23,23}(\omega_0)$$
$$- 8J_{12,13}(0)\},$$

$$\Gamma_{89} = \tfrac{1}{4}\zeta\{-4J_{12,12}(0) + 2J_{12,13}(0)$$
$$- 3J_{12,13}(\omega_0) + 2J_{12,23}(0) - 3J_{12,23}(\omega_0)$$
$$- 3J_{13,23}(0) - 6J_{13,23}(2\omega_0)\}. \tag{9}$$

The commutator superoperator part of Eq. (8) has the elements:

$$-i\Big[\hat{\hat{H}}_Z\Big]_{58} = i\Big[\hat{\hat{H}}_Z\Big]_{85} = \Omega_2 - \Omega_3,$$

$$-i\Big[\hat{\hat{H}}_Z\Big]_{69} = i\Big[\hat{\hat{H}}_Z\Big]_{96} = \Omega_3 - \Omega_1,$$

$$-i\Big[\hat{\hat{H}}_Z\Big]_{7,10} = i\Big[\hat{\hat{H}}_Z\Big]_{10,7} = \Omega_1 - \Omega_2.$$

Thus, the differential chemical shifts induce oscillations in the two-dimensional subspaces $\{B_5, B_8\}$, $\{B_6, B_9\}$ and $\{B_7, B_{10}\}$. If sufficiently large, these oscillations suppress certain relaxation pathways by rendering certain terms of matrix Γ in Eq. (8) non-secular. Note that auto-correlated dipolar dynamic frequency shifts lead to the same type of oscillatory behavior, which however is usually rather small [19].

The solution

$$\sigma(t) = \exp\Big\{\Big(-i\hat{\hat{H}}_Z - \hat{\hat{\Gamma}}\Big)t\Big\}(\sigma(0) - \sigma_{eq}) + \sigma_{eq}$$

of the inhomogeneous master equation Eq. (8) was evaluated numerically by the diagonalization method with initial condition $\sigma(0) = 2I_{1z}$. Results are shown in Fig. 2 for the three-spin system, which was previously discussed by the SLE [16], undergoing isotropic tumbling in the high-field limit $\omega_0\tau_c \gg 1$, where dynamic frequency shifts vanish [19]. In case of full degeneracy $\Omega_1 = \Omega_2 = \Omega_3$ (Fig. 2), the results obtained from the stochastic Liouville equation are
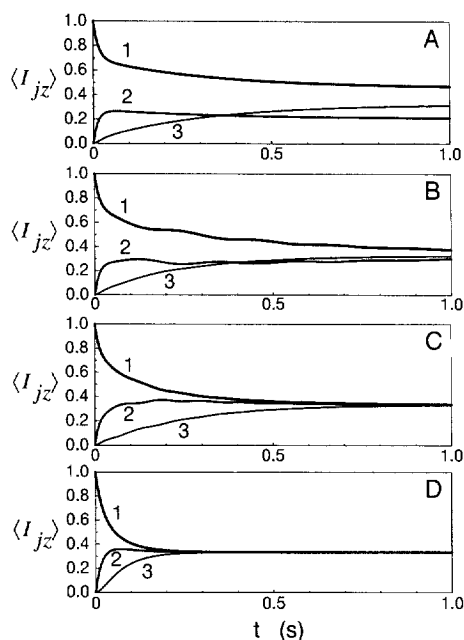
Fig. 2. Effect of longitudinal intramolecular relaxation on Zeeman polarizations $\langle I_{jz} \rangle$ ($j = 1,2,3$) in a three-proton system tumbling isotropically in the high-field limit with $\tau_c = 25$ ns and $\omega_0 \tau_c \gg 1$. The geometric arrangement of the three spins is linear with distances $r_{12} = 2.0\,\text{Å}$, $r_{23} = 2.2\,\text{Å}$ and initial condition is $\sigma(0) = 2I_{1z}$. Panels A to D show the cross-relaxation behavior for different chemical shifts Ω_1, Ω_2 and Ω_3: (A) $\Omega_1 = \Omega_2 = \Omega_3 = 0$, (B) $\Omega_1 = 0$, $\Omega_2 = 0$, $\Omega_3/(2\pi) = 5$ Hz, (C) $\Omega_1 = 0$, $\Omega_2/(2\pi) = 5$, $\Omega_3/(2\pi) = 10$ Hz, (D) $\Omega_1 = 0$, $\Omega_2/(2\pi) = 1000$, $\Omega_3/(2\pi) = 2000$ Hz.

exactly recovered (fig. 3 in Ref. [16]). For small chemical shift differences the chemical shift evolution in the zero-quantum subspace manifests itself in small-amplitude oscillations (Fig. 2B and C). If the chemical shift differences are sufficiently large (Fig. 2D) the oscillations disappear and the relaxation behavior converges towards the solution of the generalized Solomon equations that include only the basis operators B_1, B_2 and B_3 (fig. 2 of Ref. [16]). Cross relaxation to three-spin order B_4 is negligible since $\omega_0 \tau_c \gg 1$ [16].

Strong J coupling effects can lead to oscillatory TOCSY-like modulations in longitudinal cross-relaxation experiments [3] and J couplings can lead to an oscillatory behavior in transverse cross relaxation experiments [20]. In the present context, small ampli-

tude oscillations (Fig. 2B and C) arise for longitudinal cross relaxation in the absence of scalar J couplings solely because of small chemical shift differences. In this regime, where the secular approximation of BWR theory is not valid, longitudinal cross relaxation of the three-spin $1/2$ system involves a 10-dimensional Liouville subspace. While the transition to the accidentally degenerate case allows a reduction to a 7-dimensional space, an increase of the chemical shift differences which moves the system away from degeneracy gradually leads to the 4-dimensional longitudinal subspace $\{B_1, \ldots, B_4\}$, since symmetric and anti-symmetric zero-quantum operators $\{B_5, B_8\}$, $\{B_6, B_9\}$, $\{B_7, B_{10}\}$ exhibit oscillations that efficiently 'decouple' them from the rest. In this regime the secular approximation of BWR theory applies. If in addition $\omega_0 \tau_c \gg 1$, the widely used generalized Solomon equations become valid.

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