

Communication

Long-lived states in solution NMR: Selection rules for intramolecular dipolar relaxation in low magnetic fields

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Received 2 February 2007; revised 21 May 2007
Available online 3 June 2007

Abstract

Recent work has shown that singlet states of two-spin systems in low magnetic fields can have lifetimes up to an order of magnitude longer than the usual spin–lattice relaxation time. This result may enable new applications of NMR, and in particular hyperpolarized NMR via parahydrogen-induced polarization, to the study of slow processes that take place over previously inaccessible timescales. At present it is unclear whether similar results apply to multi-spin systems, or if these long lifetimes are a peculiarity of the two-spin case. Moderately long-lived states have been observed in systems containing more than two spins, although the mechanisms that prolong their lifetimes are not well understood. Here we present formalism for the study of relaxation in multi-spin systems in low magnetic fields. This approach is used to derive a family of quantum-mechanical selection rules governing intramolecular dipolar relaxation at low field that may account for the extended lifetimes observed in multi-spin systems.

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Keywords: Extended lifetimes; Low field; Relaxation; Singlet state

1. Introduction

Many applications of nuclear magnetic resonance in chemistry and biomedicine are limited by the very small degree of nuclear spin polarization, and correspondingly weak signal strength, that can be obtained in conventional spectrometers. This challenge can be overcome, at least in part, by techniques such as dynamic nuclear polarization (DNP) [1] and parahydrogen-induced polarization (PHIP) [2] that can enhance the nuclear polarization by several orders of magnitude. The signal enhancements achieved by these techniques are, however, relatively short-lived owing to the spin–lattice (T_1) decay of the magnetization. Even with the use of long- T_1 nuclei such as ^{13}C , the useful lifetimes of hyperpolarized states are generally on the order

of a few minutes. Because many biomedical applications involve processes that take place over significantly longer timescales, methods for extending the lifetime of hyperpolarized signals could open up a range of new applications for NMR.

A step in this direction has been presented in Refs. [3–5], where it has been shown that the lifetimes of spin-singlet states in two-spin systems can be up to an order of magnitude longer than the spin–lattice relaxation times of the constituent spins. Extended lifetimes are observed only when chemical shift differences are negligible, as for instance in a low magnetic field [3] or under the influence of continuous radiofrequency irradiation [4,6]. In the absence of chemical shift effects the singlet is long-lived for two reasons: first, it is an eigenstate of the Hamiltonian, and, second, it cannot be converted into other states by intramolecular dipolar interactions [5]. As a result, the singlet state is preserved under coherent time evolution,

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and, moreover, it is immune to intramolecular dipolar interactions, which are often the dominant source of spin–lattice relaxation. This immunity is the consequence of a simple quantum-mechanical symmetry of the two-spin singlet state, namely that it changes sign under exchange of the two constituent spins. By contrast, the triplet states do not change sign under exchange. Because intramolecular dipolar interactions cannot modify the exchange parity of the wavefunction, they cannot mediate transitions between singlet and triplet states [3].

The situation is more complicated in systems containing more than two spins. In this case exchange parity does not forbid intramolecular dipolar relaxation. Just the same, however, long-lived states have been observed in multi-spin systems [7,8]. Pileio et al. [8] studied four-spin systems consisting of two distant, weakly coupled pairs that were prepared in a state where each pair was initially in a singlet state. Under radiofrequency irradiation, the lifetimes observed in these systems were a factor 4–8 longer as compared with standard T_1 relaxation. Jonischkeit et al. [7] employed PHIP techniques: hydrogen gas in a singlet state (parahydrogen) was added to organic compounds by hydrogenation, thereby creating a state in which two spins (out of many) were initially in a singlet state. In this study the molecules observed were rather general, with no particular specifications regarding molecular geometry or scalar couplings. Lifetime prolongation by a factor of 2–3 was achieved by keeping the product compounds at low field prior to measurement. It has been noted by Pileio et al. that the mechanism of prolongation is not yet fully understood. Indeed, scalar couplings lead to rapid mixing among the states of the multi-spin system, erasing any initial ‘singlet’ order and preventing the mechanism described by Caravetta et al. [3] from stabilizing the system.

Here we point out that a family of quantum-mechanical selection rules for transitions mediated by intramolecular dipolar interactions may be at least partially responsible for the extended lifetimes observed in multi-spin systems in low fields. These selection rules are a consequence of rotational symmetries that are well known in other contexts; however, their significance for NMR relaxation in low magnetic fields has not, to our knowledge, been noted in the literature. In addition to these selection rules, there exist certain spin systems for which the allowed transitions are suppressed, resulting in extended lifetimes. In the following, we will use the phrase ‘low field’ to refer generically to any situation where chemical shifts are negligible. This could be a low external magnetic field, application of a suitable RF irradiation [4,6] or a simple absence of chemical shift differences.

2. Theory

In low magnetic fields, the motionally averaged Hamiltonian for a system of coupled spins consists only of scalar couplings:

$$H_0 = \sum_{k < l} 2\pi J_{kl} \vec{I}_k \cdot \vec{I}_l.$$

This approximation is applicable in fields where $|\omega_k - \omega_l| \ll |2\pi J_{mn}|$, i.e., where the chemical shift differences are smaller than the scalar couplings. For protons, this corresponds to a field less than roughly 10 mT in typical systems. In this low field limit, the Hamiltonian is rotationally invariant and therefore commutes with the total spin $\vec{I} = \sum_k \vec{I}_k$. As a result, the Hamiltonian and the total spin can be diagonalized with the same choice of basis, so that the energy eigenstates are also eigenstates of the total spin angular momentum $\vec{I}^2 = (\sum_k \vec{I}_k)^2$ and its z -component $I_z = \sum_k I_z^k$. This is in contrast to the high field case, where the Zeeman interaction dominates and the energy eigenstates are (approximate) eigenstates of I_z but not of \vec{I}^2 . The low field energy eigenstates can be denoted by, where j is the total spin angular momentum, m is the magnetic quantum number $m = -j, \dots, +j$, and λ is a non-angular quantum number that distinguishes multiplets that have the same value of j but distinct energies (except in cases of accidental degeneracy). For instance, the three-spin system, discussed in the more detail in the ensuing, has a degenerate quadruplet of eigenstates with $j = 3/2$ and two degenerate doublets with $j = 1/2$, each doublet characterized by an individual energy value (Fig. 1).

Intramolecular dipolar relaxation is mediated by the Hamiltonian [9]

$$H_{DD} = - \sum_{k < l} b_{kl} \left(\frac{(\vec{r}_{kl} \cdot \vec{I}_k)(\vec{r}_{kl} \cdot \vec{I}_l)}{r_{kl}^2} - \frac{1}{3} \vec{I}_k \cdot \vec{I}_l \right), \quad (1)$$

where $b_{kl} = 3\mu_0\gamma^2\hbar/4\pi r_{kl}^3$ and \vec{r}_{kl} is the (time-dependent) vector connecting spins k and l . For studies at low field, it is natural to express this Hamiltonian in terms of operators having definite angular momentum quantum numbers. The dipolar Hamiltonian may be re-written as

$$H_{DD} = -\sqrt{\frac{8\pi}{15}} \sum_{k < l} \sum_{M=-2}^2 b_{kl} Y_{2,-M}(\hat{r}_{kl}) T_{2,M}^{kl}, \quad (2)$$

where $Y_{2,M}$ are rank-2 spherical harmonics and $T_{2,M}$ are a set of second rank spin operators that have spin 2 with respect to the total spin \vec{I} . Explicitly, in terms of $I_{\pm} = (I_x \pm iI_y)/\sqrt{2}$, we have

$$T_{20}^{kl} = \frac{1}{\sqrt{6}} \{2I_z^k I_z^l - (I_+^k I_-^l + I_-^k I_+^l)\},$$

$$T_{2\pm 1}^{kl} = \pm \frac{1}{\sqrt{2}} \{I_z^k I_{\pm}^l + I_{\pm}^k I_z^l\}, \quad T_{2\pm 2}^{kl} = I_{\pm}^k I_{\pm}^l.$$

The fact that the spin-dependent portion of the dipolar Hamiltonian contains only spin 2 operators implies a selection rule. For any given low field eigenstate $|jm\lambda\rangle$ and each pair of spins kl the Wigner–Eckart theorem states that [10]

$$\langle j' m' \lambda' | T_{L,M}^{kl} | j m \lambda \rangle = C(jLj'; mMm') \langle j' \lambda' | T_L^{kl} | j \lambda \rangle \Delta(jLj') \delta_{m'm+M} \quad (3)$$

in terms of the reduced matrix elements $\langle j' \lambda' | T_L^{kl} | j \lambda \rangle$, the Clebsch–Gordan coefficients $C(jLj', mMm')$, and ‘triangular

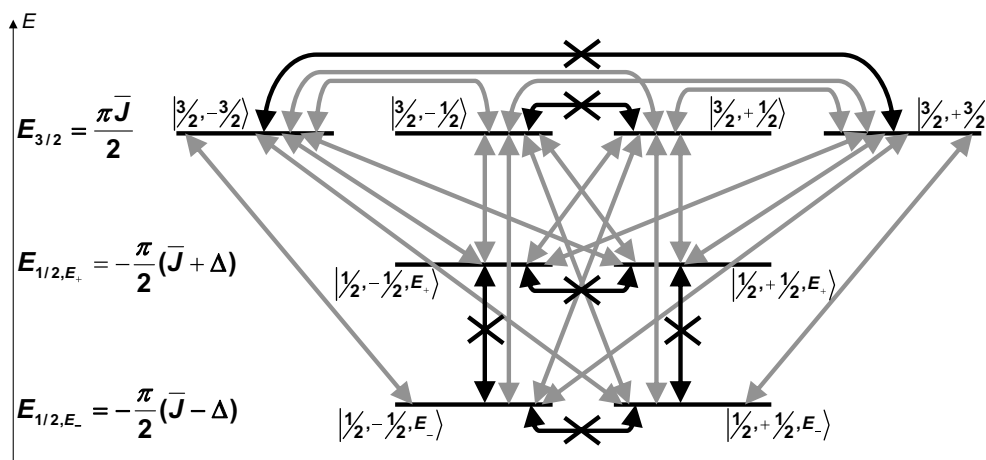


Fig. 1. Schematic energy level diagram of three-spin system in low ($|\omega_k - \omega_l| \ll J_{mn}$) magnetic fields. Light gray arrows mark allowed transitions, while black crossed arrows mark forbidden transitions.

relation' $\Delta(jLj')$, which vanishes unless $j' = |j - L|, |j - L| + 1, \dots, j + L$ [10]. As in the high field case, the matrix element in Eq. (3) vanishes if m' is not equal to $m + M$; at low field the matrix elements are subject to the additional constraints imposed by the triangular relation. Combining Eqs. (2) and (3) results in the following expression for the matrix elements of the dipolar Hamiltonian in the eigenbasis $|jm\lambda\rangle$:

$$\langle j'm'\lambda' | H_{DD} | jm\lambda \rangle = -\sqrt{\frac{8\pi}{15}} \sum_{k<1} \sum_{M=-2}^2 b_{kl} Y_{2-M}^{kl} C(j2j'; mMm') \times \langle j'\lambda' || T_2^{kl} || j\lambda \rangle \delta_{m', m+M} \Delta(jLj'). \quad (4)$$

Hence, the following selection rule is obtained:

$$\langle j'm'\lambda' | H_{DD} | jm\lambda \rangle = 0 \quad \text{if } j \neq |j' - 2|, \dots, j' + 2, \quad (5)$$

which holds at every instant of time and for all orientations of the molecule. Eq. (5) dictates that certain matrix elements of the dipolar Hamiltonian *must* vanish; however, depending on the specifics of the spin system, other matrix elements may 'accidentally' be small or even vanish.

As a consequence of Eq. (5), to first order in perturbation theory, intramolecular dipolar interactions cannot mediate transitions between states whose j values violate the selection rule in Eq. (5). As a result, many dipolar relaxation pathways that would be available to the system at high field are forbidden at low field because the corresponding matrix elements vanish [9]. Thus, equilibrium can only be achieved via higher order relaxation pathways.

3. Results and discussion

The selection rule (5) generalizes the results described by Caravetta et al. [3] to systems containing more than two spins, while reproducing the results described therein for the special case of two-spin systems. In the two-spin case, the singlet state has $j = 0$ while the triplet states have $j = 1$; because these values violate the inequality in Eq. (5),

singlets and triplets cannot mix via intramolecular dipolar interactions. On the other hand, relaxation within the three triplet states is allowed, in agreement with conclusions of Ref. [3].

In systems with more than two spins, the selection rule in Eq. (5) may provide a mechanism of stabilization for certain states, albeit a weaker one than in the case of two spins. As an example illustrating the features of the low field case, and to make the foregoing discussion more explicit, we now present a detailed description of the three-spin case, which is the simplest non-trivial example. To simplify the discussion, we will make two approximations: first, in all calculations we will assume that the applied magnetic field is negligible. This is a reasonable assumption, as it has been shown [5] that zero-field relaxation in two-spin singlets is not qualitatively modified by application of moderate magnetic fields. Second, we will work in the extreme narrowing limit [9], which assumes that the molecular tumbling rate is much faster than the characteristic frequency of the spin oscillations. This approximation is well justified at low field, where the latter frequencies are on the order of the scalar coupling of the system, which are typically tens of Hertz or less in homonuclear proton systems.

In the low field limit, the Hamiltonian for the three-spin system is

$$H = 2\pi(J_{12}\vec{I}_1 \cdot \vec{I}_2 + J_{13}\vec{I}_1 \cdot \vec{I}_3 + J_{23}\vec{I}_2 \cdot \vec{I}_3). \quad (6)$$

The eigenstates of this Hamiltonian can be found by first choosing a basis of eigenstates of \vec{I}^2 and I_z . The $j = 3/2$ states are given by

$$|3/2, m\rangle = \{ |\alpha\alpha\alpha\rangle, (|\alpha\alpha\beta\rangle + |\alpha\beta\alpha\rangle + |\beta\alpha\alpha\rangle)/\sqrt{3}, (|\alpha\beta\beta\rangle + |\beta\alpha\beta\rangle + |\beta\beta\alpha\rangle)/\sqrt{3}, |\beta\beta\beta\rangle \} \quad (7)$$

for $m = +3/2, \dots, -3/2$. These four states are eigenstates of \vec{I}^2 and of the Hamiltonian, Eq. (6). In addition, there are two pairs of states with spin $j = 1/2$, which we label by 'A' and 'B'. The choice of basis for these states is not

unique. For simplicity, we choose the ‘A’ pair to consist of those states where spins 2 and 3 are in a singlet state:

$$|1/2, m\rangle_A = \{(|\alpha\alpha\beta\rangle - |\alpha\beta\alpha\rangle)/\sqrt{2}, (|\beta\alpha\beta\rangle - |\beta\beta\alpha\rangle)/\sqrt{2}\} \quad (8)$$

for $m = +1/2, -1/2$. The second pair is then uniquely specified:

$$|1/2, m\rangle_B = \{(2|\beta\alpha\alpha\rangle - |\alpha\alpha\beta\rangle - |\alpha\beta\alpha\rangle)/\sqrt{6}, -(2|\alpha\beta\beta\rangle - |\beta\alpha\beta\rangle - |\beta\beta\alpha\rangle)/\sqrt{6}\}. \quad (9)$$

These states are the eigenstates of \vec{I}^2 , but not of the Hamiltonian. The matrix elements of the Hamiltonian in the basis $\{|3/2, 3/2\rangle, \dots, |3/2, -3/2\rangle, |1/2, 1/2\rangle_A, |1/2, 1/2\rangle_B, |1/2, -1/2\rangle_A, |1/2, -1/2\rangle_B\}$ are given by

$$H = \frac{\pi}{2} \begin{pmatrix} \bar{J} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \bar{J} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \bar{J} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \bar{J} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \hat{J} & K & 0 & 0 \\ 0 & 0 & 0 & 0 & K & J' & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \hat{J} & K \\ 0 & 0 & 0 & 0 & 0 & 0 & K & J' \end{pmatrix}, \quad (10)$$

where $\bar{J} = (J_{12} + J_{13} + J_{23})$, $\hat{J} = -3J_{23}$, $J' = J_{23} - 2J_{13} - 2J_{12}$, and $K = \sqrt{3}(J_{13} - J_{12})$. The $j = 3/2$ states are thus eigenstates of the Hamiltonian with energy $\pi\bar{J}/2$, while the remaining Hamiltonian eigenstates with $j = 1/2$ are determined by a two-by-two diagonalization. The energies are given by

$$E_{\pm} = \frac{\pi}{2} \left(-\bar{J} \pm 2\sqrt{J_{12}^2 + J_{13}^2 - J_{23}^2 - J_{12}J_{23} - J_{13}J_{23} - J_{12}J_{13}} \right) \equiv \frac{\pi}{2}(-\bar{J} \pm A). \quad (11)$$

The schematic energy level diagram is shown in Fig. 1. The corresponding eigenstates can be specified in terms of a single mixing angle:

$$\begin{aligned} |1/2, m, E_+\rangle &= \cos\psi|1/2, m\rangle_A + \sin\psi|1/2, m\rangle_B, \\ |1/2, m, E_-\rangle &= -\sin\psi|1/2, m\rangle_A + \cos\psi|1/2, m\rangle_B, \end{aligned} \quad (12)$$

where ψ is specified by

$$\tan\psi = \frac{-J_{12} - J_{13} + 2J_{23} + A}{\sqrt{3}(-J_{12} + J_{13})}. \quad (13)$$

The states $\{|1/2, 1/2, E_-\rangle, |1/2, -1/2, E_-\rangle, |1/2, 1/2, E_+\rangle, |1/2, -1/2, E_+\rangle\}$ are eigenstates of \vec{I}^2 and the Hamiltonian. Using the basis of Hamiltonian eigenstates, we can compute the transition rates between these states that result from intramolecular dipolar interactions. We begin from the standard expression for the transition rate between a pair of states $|a\rangle$ and $|b\rangle$ [9]:

$$\begin{aligned} W_{ab} &= \int_{-\infty}^{+\infty} \overline{\langle a|H_{DD}(t)|b\rangle\langle b|H_{DD}(t+\tau)|a\rangle} e^{-i(E_a-E_b)\tau} \\ &= \frac{8\pi}{15} \sum_{ij,kl,M,M'} b_{ij}b_{kl} \langle a|T_M^{ij}|b\rangle\langle b|T_{M'}^{kl}|a\rangle \\ &\quad \times \int_{-\infty}^{+\infty} \overline{Y_{2,-M}(\hat{r}_{ij}(t))Y_{2,-M'}(\hat{r}_{kl}(t+\tau))} e^{-i(E_a-E_b)\tau}. \end{aligned} \quad (14)$$

In the extreme narrowing limit and assuming isotropic reorientation the correlation function is given by [11]

$$\begin{aligned} &\int_{-\infty}^{+\infty} \overline{Y_{2M}(\hat{r}_{ij}(t))Y_{2M'}(\hat{r}_{kl}(t+\tau))} e^{-i(E_a-E_b)\tau} \\ &= \tau_c(-1)^M \delta_{M,-M'} P_2(\cos\theta_{ij,kl})/4\pi, \end{aligned} \quad (15)$$

where $\theta_{ij,kl}$ is the angle, in the frame of the molecule, between \hat{r}_{ij} and \hat{r}_{kl} , and τ_c is the correlation time for the molecular tumbling. P_2 is the second order Legendre polynomial. From this, we obtain

$$W_{ab} = \frac{2\tau_c}{15} \sum_{ij,kl,M} (-1)^M b_{ij}b_{kl} \langle a|T_M^{ij}|b\rangle\langle b|T_{-M}^{kl}|a\rangle P_2(\cos\theta_{ij,kl}). \quad (16)$$

In general, the rates in Eq. (16) will depend upon a large number of parameters that describe the spatial geometry of the spins and their couplings. However, in the case of the three-spin system just three parameters will suffice. These are (1) the ratio, κ , of r_{12} and r_{13} ; (2) the angle, θ , between \hat{r}_{12} and \hat{r}_{13} ; and (3) the mixing angle ψ , introduced above, that specifies the energy eigenstates according to the scalar couplings as in Eqs. (12) and (13). Using these three dimensionless parameters, together with the length of r_{12} , we can compute the rates in Eq. (16). With this specification the rates W_{ab} depend on r_{12} only as an overall factor. For purposes of relative comparisons, this overall factor can be ignored. The geometrical parameters κ and θ are illustrated in Fig. 2.

Evaluating the rate matrix, Eq. (16), in the basis of Hamiltonian eigenstates $\{|3/2, 3/2\rangle, \dots, |3/2, -3/2\rangle, |1/2, 1/2, E_-\rangle, |1/2, -1/2, E_-\rangle, |1/2, 1/2, E_+\rangle, |1/2, -1/2, E_+\rangle\}$, we find

$$W = \frac{3\mu_0^2\gamma^4\hbar^2\tau_c}{40\pi^2r_{12}^6} \begin{pmatrix} A & 2A & 2A & 0 & B & 4B & C & 4C \\ 2A & A & 0 & 2A & 2B & 3B & 2C & 3C \\ 2A & 0 & A & 2A & 3B & 2B & 3C & 2C \\ 0 & 2A & 2A & A & 4B & B & 4C & C \\ B & 2B & 3B & 4B & 0 & 0 & 0 & 0 \\ 4B & 3B & 2B & B & 0 & 0 & 0 & 0 \\ C & 2C & 3C & 4C & 0 & 0 & 0 & 0 \\ 4C & 3C & 2C & C & 0 & 0 & 0 & 0 \end{pmatrix}, \quad (17)$$

where A is a dimensionless function that determines the rate of transitions between the $j = 3/2$ states, and that depends on the geometrical parameters κ and θ . B and C are dimensionless functions dictating transition rates to

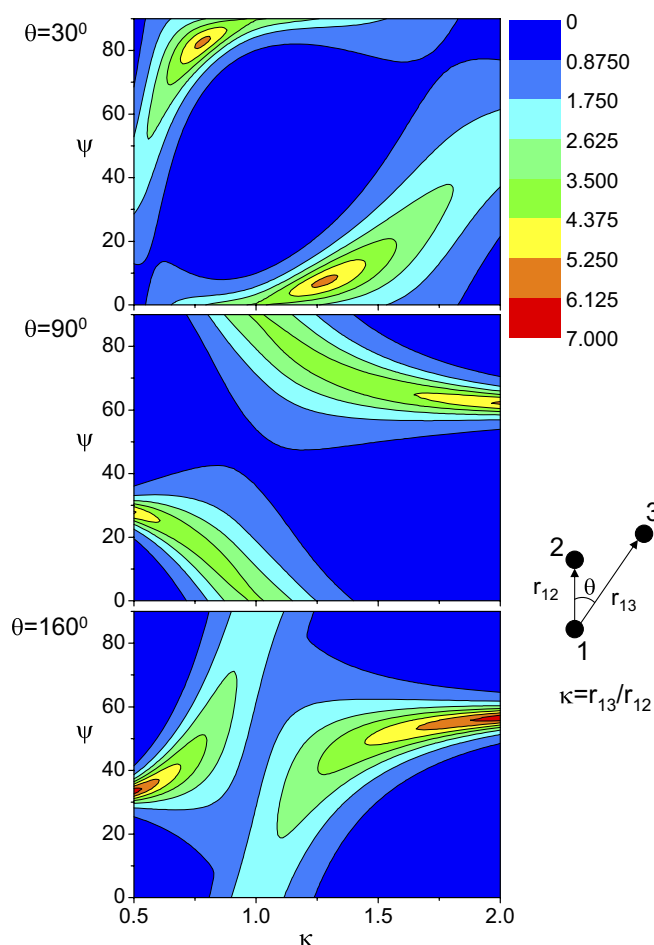


Fig. 2. The ratio R (Eq. (20)), which measures the relative lifetimes of the longest-lived population imbalances at high field and at low field. The ratio R is shown as a function of ψ and κ for several values of θ : 30° (top), 90° (middle), 160° (bottom). The insert illustrates the definition of geometrical factors κ and θ .

and from the $j = 1/2$ states, and that depend on the mixing angle ψ in addition to κ and θ . These functions are complicated in general, and have been included in the Appendix. As required by the selection rule (5), the rates for transitions between pairs of states with $j = 1/2$ (in the four lower right blocks of the matrix) vanish. Furthermore, the Wigner–Eckart theorem implies that all of the transitions between $j = 3/2$ states are proportional to a common reduced matrix element (which contains the dependence κ and θ) multiplied by combinations of Clebsch–Gordon coefficients that are independent of the molecular details of the molecule (function A). Similarly, transition rates between the $j = 3/2$ states and the $j = 1/2$ states with energy E_- are proportional to a common function of κ , θ , and ψ , as are the rates between the $j = 3/2$ states and the $j = 1/2$ states with energy E_+ (functions B and C , respectively). In Fig. 1, we display the low field energy levels for the three-spin system, together with the allowed and forbidden transitions.

The rate matrix Eq. (17) has particular relevance to the lifetimes of states of three-spin systems prepared using

PHIP [7]. In PHIP, parahydrogen in a nuclear spin-singlet state is added to another molecule by hydrogenation. Because the parahydrogen carries no net spin, the density matrix of the three-spin product molecule has zero population in the $j = 3/2$ states; the initial density matrix involves *only* the $j = 1/2$ states. Likewise, in molecules with larger numbers of spins, the state of highest spin is vacant following hydrogenation. In a typical PHIP experiment, the hydrogenation is carried out over a short period of time (several seconds), and even in very weak magnetic fields the off-diagonal coherences are averaged to zero [12]. To a very good approximation, then, the initial state is described by two populations in the $j = 1/2$, E_+ and E_- states. Typically, these populations will deviate significantly from thermal equilibrium. Two features of the rate matrix Eq. (17) can result in an extended lifetime of this non-equilibrium state. First, because of the selection rule in Eq. (5), the $j = 1/2$ states cannot come to equilibrium via direct transitions; rather, they must equilibrate by a two-stage process involving transitions to the $j = 3/2$ levels, followed by transitions back to the $j = 1/2$ levels. This in itself may lead to a modest prolongation of non-equilibrium conditions created by PHIP. In addition, however, further prolongation can result in those special cases where one or both of the functions B or C happens to be small. In this case, the smallness of the corresponding rates, in conjunction with the selection rule in Eq. (5), imposes a sort of ‘bottleneck’ on the equilibration process, thereby stabilizing the population in one or both of the $j = 1/2$ states.

To estimate the degree to which the lifetimes of the $j = 1/2$ states of the three-spin system are prolonged in relation to the corresponding lifetimes of states at high field, we re-evaluate the matrix Eq. (17) in a basis appropriate to the high field case. In the high field limit where the chemical shifts are well resolved, the eigenstates of the Hamiltonian, to a very good approximation, are given by Zeeman states. Evaluating W in the basis $\{|\alpha\alpha\alpha\rangle, |\alpha\alpha\beta\rangle, |\alpha\beta\alpha\rangle, |\beta\alpha\alpha\rangle, |\beta\beta\alpha\rangle, |\beta\alpha\beta\rangle, |\alpha\beta\beta\rangle, |\beta\beta\beta\rangle\}$, using the same formulas (14)–(16) and the same extreme narrowing approximation that led to Eq. (17), we can obtain the transition rates for the three-spin system at high field. The resulting expression for W is lengthy and has been discussed previously in the literature [11,13], and so will not be reproduced here. We can use the high field rate matrix to compute the ratio of the lifetimes of the longest-lived population imbalances at high field and at low field. When the populations are disturbed from equilibrium, they return to equilibrium according to a standard set of rate equations [9]:

$$\frac{d\rho_a}{dt} = \sum_b \left(W_{ab} - \delta_{ab} \sum_c W_{ac} \right) (\rho_b - \rho_b^{\text{Equilibrium}}). \quad (18)$$

The solution to these equations is multi-exponential decay, with the decay rates dictated by eigenvalues α_a of the matrix in parentheses in Eq. (18):

$$\left(\rho_b(t) - \rho_b^{\text{Equilibrium}}\right) = \sum_c d_{bc} e^{\lambda_c t}, \quad (19)$$

where the eigenvalues are, of course, negative, and d_{bc} are a set of constants determined by the initial conditions. The longest-lived population imbalance therefore decays away with a lifetime set by the eigenvalue of smallest non-zero magnitude (there is always at least one zero eigenvalue corresponding to the equilibrium state). We may therefore define a measure of lifetime enhancement through the ratio of the smallest non-zero eigenvalue, evaluated at high field and at low field:

$$R = \frac{\text{Smallest non-zero eigenvalue of } \left(W_{ab}^{\text{High}} - \delta_{ab} \sum_c W_{ac}^{\text{High}}\right)}{\text{Smallest non-zero eigenvalue of } \left(W_{ab}^{\text{Low}} - \delta_{ab} \sum_c W_{ac}^{\text{Low}}\right)}. \quad (20)$$

Although other metrics can be formulated, R serves to illustrate many of the important features of lifetime prolongation at low field.

Fig. 2 shows the ratio R , Eq. (20), as a function of κ and ψ for several values of θ . The ratio R is periodic in ψ with period $\pi/2$, and hence only one period is shown. In general, the lifetime prolongation observed experimentally will depend strongly on the geometric and coupling details of the specific molecule. In some favorable cases displayed in Fig. 2, the intramolecular dipolar decay lifetime of the longest-lived population imbalance at low field is roughly a factor of 7 longer than in the high field case. These large enhancements occur when one of the functions B or C in Eq. (16) are small, resulting in a slow decay rate for one of the $j = 1/2$ doublets. These ratios indicate that the physics described here may account for the enhanced lifetimes observed in multi-spin systems [7,8], which are of a similar magnitude.

In practice, the lifetime enhancement will be somewhat less than that indicated by Fig. 2 for two reasons: First, this estimate ignores the contribution of all relaxation mechanisms other than intramolecular dipolar interactions. In those cases where intramolecular dipolar relaxation is highly suppressed, the contributions of these other relaxation mechanisms will be appreciable. Second, the extreme narrowing limit used in Eq. (15) overestimates the autocorrelation functions, and hence the transition rates, at high field. However, for the systems and field strengths under consideration here, the errors introduced by extreme narrowing are not expected to qualitatively modify the conclusions.

4. Conclusions

The foregoing discussion highlights some of the differences between nuclear spin relaxation at high field and at low field. In low magnetic fields, transitions mediated by intramolecular dipolar interactions are subject to an additional selection rule that is absent at high field. In addition, the energy eigenstates at low field can exhibit

patterns of mixing that suppress certain transitions allowed, in principle, by the selection rule. Taken together, these factors can lead to moderate lifetime enhancements in systems with more than two spins, as illustrated above for the case of the three-spin system. These mechanisms may account for the extended lifetimes observed in Refs. [7,8]. If the mechanisms described here are responsible for the enhanced lifetimes observed in multi-spin systems [7,8], then PHIP-enhanced NMR spectra should show a predictable pattern of time evolution with respect to the duration of time between hydrogenation at low field and transport to high field. Moreover, the longest-lived component of the NMR spectrum may show certain predictable features that can be exploited for high field imaging and spectroscopy.

Acknowledgments

We thank Prof. R.E. Lenkinski for the stimulating discussions and suggestions during the work and Prof. S. Vega for comments on the manuscript.

Appendix A

The dimensionless functions A , B , and C referred to in the text are given by

$$\begin{aligned} A(\kappa, \theta) &= \frac{1}{48} \left\{ 2 + \frac{2}{\kappa^6} + \frac{2}{(1 + \kappa^2 - 2\kappa \cos \theta)^3} \right. \\ &\quad + \frac{1 + 3 \cos 2\theta}{\kappa^3} + \frac{1 + 4\kappa^2 - 8\kappa \cos \theta + 3 \cos 2\theta}{\kappa^3 (1 + \kappa^2 - 2\kappa \cos \theta)^{5/2}} \\ &\quad \left. + \frac{4 + \kappa^2 - 8\kappa \cos \theta + 3\kappa^2 \cos 2\theta}{(1 + \kappa^2 - 2\kappa \cos \theta)^{5/2}} \right\}, \\ B(\kappa, \theta, \psi) &= \frac{\sin^2 \psi}{64\kappa^6} \left\{ 2 - \kappa^3 + 2\kappa^6 - 3\kappa^3 \cos 2\theta \right\} \\ &\quad + \frac{\sin \psi \cos \psi}{32\sqrt{3}} \left\{ 2 - \frac{2}{\kappa^6} - \frac{1}{(1 + \kappa^2 - 2\kappa \cos \theta)^{5/2}} \right. \\ &\quad \times \left[\kappa^2 + 4 - \frac{4}{\kappa} - \frac{1}{\kappa^3} - \frac{8(\kappa^3 - 1) \cos \theta}{\kappa^2} \right. \\ &\quad \left. \left. + \frac{3(\kappa^5 - 1) \cos 2\theta}{\kappa^3} \right] \right\} \\ &\quad + \frac{\cos^2 \psi}{192} \left\{ 2 + \frac{3 \cos 2\theta + 1}{\kappa^3} + \frac{2}{\kappa^6} \right. \\ &\quad + \frac{8}{(1 + \kappa^2 - 2\kappa \cos \theta)^3} + \frac{1}{(1 + \kappa^2 - 2\kappa \cos \theta)^{5/2}} \\ &\quad \times \left[-8 + 4\kappa^2 - \frac{8}{\kappa} + \frac{4}{\kappa^3} + \frac{16(1 + \kappa^3) \cos \theta}{\kappa^2} \right. \\ &\quad \left. \left. - \frac{12(1 + \kappa^5) \cos^2 \theta}{\kappa^3} \right] \right\}, \end{aligned}$$

and

$$C(\kappa, \theta, \psi) = B\left(\kappa, \theta, \frac{\pi}{2} + \psi\right).$$

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