Nuclear Singlet Relaxation by Scalar Relaxation of the Second Kind in the Slow-Fluctuation Regime


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The singlet state of nuclear spin-1/2 pairs is protected against many common relaxation mechanisms. Singlet order, which is defined as the population difference between the nuclear singlet and triplet states, usually decays more slowly than the nuclear magnetization. Nevertheless, some decay mechanisms for nuclear singlet order persist. One such mechanism is called scalar relaxation of the second kind (SR2K), and involves the relaxation of additional nuclei (“third spins”) which have scalar couplings to the spin-1/2 pair. This mechanism requires a difference between the couplings of at least one third spin with the two members of the spin-1/2 pair, and depends on the longitudinal relaxation time of the third spin. The SR2K mechanism of nuclear singlet relaxation has previously been examined in the case where the relaxation rate of the additional spins is on the timescale of the nuclear Larmor frequency. In this paper we consider a different regime, in which the longitudinal relaxation of the third spins is on a similar timescale to the J-coupling between the members of the spin pair. This regime is often encountered when the spin-1/2 pair has scalar couplings to nearby deuterium nuclei. We show that the SR2K mechanism may be suppressed in this regime by applying a radiofrequency field which is resonant either with the members of the spin pair, or with the third spins. These phenomena are analyzed theoretically and by numerical simulations, and demonstrated experimentally on a diester of [13C2,2H2]-labelled fumarate in solution.

I. INTRODUCTION

Clusters of spin-1/2 nuclei may form magnetically “silent” configurations which are sheltered from NMR relaxation and decay with extended lifetimes. These long-lived states (LLS) may have decay rate constants which greatly exceed that of longitudinal magnetization. A long-lived state lifetime has surpassed the relaxation time constant $T_1$ by a factor of 50 in one case, and a lifetime exceeding 1 hour was observed for a naphthalene derivative in solution. Experiments have been performed in which LLS phenomena are combined with hyperpolarization methodology in order to generate nuclear spin systems which are far from equilibrium, and to maintain the non-equilibrium state for extended time intervals. There are potential applications to molecular imaging.

In the case of spin-1/2 pairs, the LLS is called singlet order and is defined as the population imbalance between the spin-0 singlet state and the spin-1 triplet states. The nuclear singlet state is antisymmetric with respect to particle exchange, while the three nuclear triplet states are exchange-symmetric. Small differences in chemical shift between the participating spins, or differential scalar couplings to spins outside the pair, allow experimental access to the nuclear singlet order using suitable radiofrequency pulse sequences. The decay time constant of singlet order is denoted $T_S$.

In solution, the dominant relaxation mechanism for the nuclear magnetization of spin-1/2 pairs is often the stochastic modulation of the dipole-dipole coupling between the two nuclei by the molecular tumbling (the “in pair DD mechanism”). This can be a strong mechanism for the decay of nuclear magnetization, but does not lead to a decay of nuclear singlet order. As a result, $T_S$ may exceed $T_1$ by a large factor.

Several mechanisms contribute to the rate constant $T_S^{-1}$ for the decay of singlet order. These include: motional modulation of dipole-dipole couplings to nuclear or electronic spins outside the pair, either in the same molecule or other molecules; chemical shift anisotropy, involving both the symmetric and the antisymmetric parts of the chemical shift tensors; spin-rotation interactions, involving the coupling of the nuclei to the angular momentum of the whole molecule or mobile parts of the molecule; and coherent “leakage”, which involves the mixing of the singlet and triplet states by symmetry-breaking coherent interactions.

Scalar relaxation of the second kind (SR2K) is well established as a mechanism of $T_S$ relaxation. This mechanism occurs when nuclei of interest have scalar couplings to additional nuclei which themselves relax rapidly. In many important cases the additional nuclei have spins $>1/2$ and their relaxation is dominated by motional modulation of the electric quadrupole coupling to local electric field gradients (“quadrupolar relaxation”). For clarity, we denote the spins whose relaxation is of primary interest by the symbol $S$, and the “additional nuclei” which are coupled to the spins $S$ by the symbol $I$. In many cases, $I$ and $S$ belong to different isotopic species, but this is not necessarily the case. The relaxation of the $I$-spins may induce appreciable $T_S$ relaxation of the $S$-spins when the $I$-spin relaxation is on the timescale of the $S$-spin Larmor precession, i.e.:

$$|\alpha S^I| T_S^I \sim 1$$

In this paper, the regime defined by Equation 1 is called the...
“fast fluctuation regime”, where “fluctuation” refers here to the stochastic transitions between the spin states of the S-spins, induced by spin-lattice couplings.

In the high-field NMR of diamagnetic materials, the fast-fluctuation regime of Equation 1 is only encountered when the I-spin relaxation is very rapid, which normally requires a quadrupolar relaxation mechanism for the I-spins. The cases of $^{13}$C nuclei which are scalar-coupled to $^{79}$Br, $^{81}$Br and $^{14}$N nuclei have been studied in detail [50–54]. SR2K also relaxes the singlet order of S-spin pairs, in the case that the S-spin pair has scalar couplings to relaxing I-spins. Singlet relaxation by SR2K (S-SR2K) has been studied theoretically in the fast-fluctuation regime of Equation 1 [55]. In this paper we discuss a second regime in which S-SR2K is active. This is the “slow fluctuation regime” of S-SR2K, which is defined as follows:

$$|2\pi J_{SS} T_1| \sim 1$$  \hspace{1cm} (2)

Here $J_{SS}$ is the scalar coupling between the members of the S-spin pair which support the nuclear singlet order. This regime is encountered when the spin-lattice relaxation of the I-spins is on the timescale of the scalar coupling between the S-spins. Since this scalar coupling is typically at least 6 orders of magnitude smaller than the nuclear Larmor frequency, the regime in Equation 2 is encountered for much slower I-spin relaxation than for Equation 1. Indeed, the regime in Equation 2 is frequently encountered when there are finite J-couplings to nuclei with moderately short relaxation times, such as is typical for deuterium. Even spin-1/2 species such as protons may relax fast enough to satisfy Equation 2. Since deuterium substitution is often used to engineer molecules in which the spin pair has a degree of magnetic isolation from its surroundings, this is a common situation in the field of singlet NMR. The slow-fluctuation regime in Equation 2 is therefore of much practical importance.

We present a theoretical analysis of the S-SR2K mechanism in the slow-fluctuation regime for the case of spin-1/2 pairs coupled to one or more third spins. We show that in some cases the singlet-SR2K mechanism leads to strongly biexponential decay of the nuclear singlet order. Theoretical rate expressions are also presented for the case of spin-1/2 pairs coupled to single spin-1/2 nuclei exhibiting an intrinsic relaxation mechanism of their own. We show that radio-frequency (rf) irradiation which is resonant with either of the two spin species (“spin locking”) can lead to a significantly reduced singlet relaxation contribution from S-SR2K and returns the decay of nuclear singlet order to a single exponential form.

We report the experimental observation of S-SR2K for $^{13}$C$_2$ singlet order in a solution of a $^{[13]}$C$_2$-$^2$H$_2$-labelled fumarate diester. The differential scalar couplings allow coherent access to the $^{13}$C singlet order, by the SLIC (Spin-Lock Induced Crossing) radiofrequency irradiation method [18]. The singlet relaxation is found to be biexponential, as expected. The singlet relaxation time constant $T_2$ increases with increasing $^{13}$C and $^2$H spin-locking rf field amplitudes as the S-SR2K mechanism is progressively quenched. The longest observed value of $T_2$ approaches 30 seconds. The experimental data are compared against theoretical rate expressions.

II. THEORY

A. Model spin system

Consider an ensemble of isolated spin systems, each consisting of three coupled spins-1/2. Each ensemble member contains a spin-1/2 pair, denoted $S_1$ and $S_2$, coupled to a single additional nucleus $I_3$, here assumed also to be spin-1/2 (see Figure 1). The couplings are assumed to be scalar (appropriate for isotropic solution) and are denoted $J_{13}$ between each spin pair, and $J_{23}$ for the out-of-pair couplings. For simplicity, the chemical shifts of spins $S_1$ and $S_2$ are assumed to be equal, and other relaxation mechanisms acting on the S-spins are ignored. The third spins $I_3$ have relaxation mechanisms of their own, which leads to the decay rate constants $R_{13}^f = (T_{13}^f)^{-1}$ and $R_{23}^f = (T_{23}^f)^{-1}$ for $I$-spin longitudinal and transverse magnetization, respectively.

B. Liouvillian

The quantum state of the spin ensemble is described by the spin density operator $\rho$. Its equation of motion is the Liouville-von Neumann equation:

$$\frac{d}{dt} \rho(t) = \hat{L}(t) \rho(t)$$  \hspace{1cm} (3)

where the Liouvillian superoperator $\hat{L}$ incorporates the coherent and incoherent influences on the spin system, and is given by:

$$\hat{L} = -i\hat{H}_{\text{coh}} + \Gamma$$  \hspace{1cm} (4)

where $\hat{H}_{\text{coh}}$ is the commutation superoperator of the coherent Hamiltonian $H_{\text{coh}}$, and $\Gamma$ is the relaxation superoperator. Equation 3 assumes the “homogeneous” form of the master equation, but ignoring thermal corrections [56–59].

In general, the Liouvillian superoperator $\hat{L}$ has a set of $N_L = N_H^2$ eigenoperators, denoted $Q_q$, with $q \in \{0, 1 \ldots N_L - 1\}$, where $N_H$ is the dimension of the Hilbert space, i.e. the number of spin states. For the ensemble of 3-spin-1/2 systems,
\(N_H = 8\) and \(N_L = 64\). Each Liouvillian eigenoperator has a characteristic eigenvalue, denoted \(\lambda_q\), such that:

\[
\hat{L}Q_q = \lambda_q Q_q
\]  

(5)

where in general:

\[
\lambda_q = -\lambda_q + i\omega_q
\]  

(6)

with \(\lambda_q\) and \(\omega_q\) both being real. All eigenoperators with \(\omega_q \neq 0\) correspond to coherences which decay with a rate constant \(\lambda_q\) and oscillate at a frequency \(\omega_q\). All eigenoperators with real eigenvalues, i.e. eigenvalues for which \(\omega_q = 0\), correspond to particular configurations of spin state populations which decay with a rate constant \(\lambda_q\).

The Liouvillian always has at least one trivial eigenvalue equal to zero (\(\lambda_0 = 0\)) which represents the sum of populations for all states and is an invariant in a closed system. Eigenoperators with small values of the decay rate constant \(\lambda_q \ll (T_1^S)^{-1}\) are called long-lived states. In the cases considered here, there is only one long-lived state, with an eigenoperator given approximately by the \(S\)-spin singlet order:

\[Q_{LLS} \approx Q_{SO} = N_{SO} \mathbf{S}_1 \cdot \mathbf{S}_2\]  

(7)

where \(N_{SO} = -\frac{1}{2}\) is a normalization factor. This operator obeys the eigenequation:

\[
\hat{L}Q_{LLS} = \lambda_{LLS} Q_{LLS}
\]  

(8)

with:

\[
\lambda_{LLS} = -\lambda_{LLS}
\]  

(9)

and \(\lambda_{LLS} \ll (T_1^S)^{-1}\) is the decay rate constant for the long-lived state.

A set of \(N_L\) basis operators \(\mathbb{B} = \{B_0, B_1 \ldots B_{N_L-1}\}\) is said to be orthonormal if:

\[
(B_b|B_c) = \delta_{bc}
\]  

(10)

where \(\delta_{bc}\) is the Kronecker-delta, and the Liouville bracket of two operators is defined:

\[
[A|B] = \text{Tr}(A^\dagger B).
\]  

(11)

A \((N_L \times N_L)\)-dimensional matrix representation of the Liouvillian superoperator \(\hat{L}\) in the operator basis \(\mathbb{B}\) may be constructed by compiling the matrix elements:

\[
[\hat{L}]^{\mathbb{B}}_{bc} = (B_b|\hat{L}|B_c) = \text{Tr}(B_b^\dagger \hat{L}B_c).
\]  

(12)

Diagonalization of the matrix representation \([\hat{L}]^{\mathbb{B}}\) yields the eigenoperators and eigenvalues of the Liouvillian \(\hat{L}\).

1. Coherent Hamiltonian

The coherent Hamiltonian \(H_{\text{coh}}\) of the three-spin-1/2 system is conveniently written in the rotating reference frame as follows:

\[H_{\text{coh}} = H_S + H_I + H_{SS} + H_{SI}\]  

(13)

Here the \(S\)-spin Hamiltonians are given by:

\[
H_S = \omega_{\text{mut}}^S (S_z \cos \phi_S + S_x \sin \phi_S) + \Omega_1^S S_z + \Omega_2^S S_z
\]  

(14)

\[H_{SS} = \omega_S \mathbf{S}_1 \cdot \mathbf{S}_2\]

where the in pair J-coupling is written \(\omega_J = 2\pi J_{12}, \; \Omega_1^S\) and \(\Omega_2^S\) are the chemically shifted resonance offsets of the two \(S\)-spins, relative to the \(S\)-spin reference frequency, and \(\omega_{\text{mut}}^S\) represents the amplitude of the \(S\)-spin radiofrequency field, expressed as a nutation frequency. An implied sum is used for the \(S\)-spin operators, i.e. \(S_z = S_{1z} + S_{2z}\). The phase of the \(S\)-spin rf field is denoted \(\phi_S\). Similarly, the \(I\)-spin Hamiltonian is given by:

\[H_I = \omega_{\text{mut}}^I (I_z \cos \phi_I + I_x \sin \phi_I) + \Omega_3 I_{3z}\]  

(15)

The coherent Hamiltonian for the out of pair scalar couplings given by:

\[H_{SI} = 2\pi J_{13} S_{1z} I_{3z} + 2\pi J_{23} S_{2z} I_{3z}\]  

(16)

\[= \frac{1}{2} (\omega_S + \omega_I) S_z I_{3z} + \frac{1}{2} (\omega_S - \omega_I) S_{1z} I_{3z}\]

where the sum and difference of the out of pair couplings are denoted as follows:

\[\omega_\Sigma = 2\pi (J_{13} + J_{23})\]

(17)

\[\omega_\Delta = 2\pi (J_{13} - J_{23})\]

These expressions assume that the \(S\)-spins and \(I\)-spins are of different isotopic type.

2. \(S\)-spin relaxation superoperator

For simplicity, we assume that the relaxation of the \(S\)-spin system is caused by motional modulation of the dipole-dipole (DD) coupling between the two \(S\)-spins through the random tumbling of the molecules in solution. We assume the case of isotropic rotational diffusion in the extreme-narrowing limit, defined by a correlation time \(\tau_c\), which is short compared to the nuclear Larmor diffusion, i.e. \(|\omega_S^0|\tau_c < 1\) where \(\omega_S^0 = -\gamma_0 B_0^0\), \(\gamma_0\) is the magnetogyric ratio of the \(S\)-spins, and \(B_0^0\) is the static magnetic field. This condition is often well-satisfied for small molecules in isotropic solution. In these circumstances the relaxation superoperator for \(S\)-spin relaxation is given by:

\[
\hat{\Gamma}_S^{DD} \approx -\frac{6}{3} b_{12}^2 \tau_c \sum_{\mu = -2}^{+2} (-1)^\mu \hat{T}^{12}_\mu \hat{T}^{12}_{-\mu}\]  

(18)

where the dipole-dipole coupling constant between spins \(S_1\) and \(S_2\) is given by:

\[b_{12} = -\frac{\mu_0}{4\pi} \gamma_0^2 \hbar r_{12}^3\]  

(19)

where \(r_{12}\) is the distance between spins \(S_1\) and \(S_2\) (assume to remain fixed as the molecule tumbles in solution). The symbol \(\hat{T}^{12}_\mu\) denotes a commutation superoperator for the second-rank
spherical tensor operator component \( T_{2}^{12} \). There are five such operator components, given by:

\[
T_{2+2}^{12} = \frac{1}{2} S_{1}^{+} S_{2}^{+} \\
T_{2+1}^{12} = -\frac{1}{2} (S_{1}^{+} S_{2}^{-} + S_{1}^{-} S_{2}^{+}) \\
T_{20}^{12} = \frac{1}{\sqrt{6}} (3 S_{1}^{-} S_{2}^{+} - S_{1}^{+} S_{2}^{-}) \\
T_{2-1}^{12} = \frac{1}{2} (S_{1}^{+} S_{2}^{-} + S_{1}^{-} S_{2}^{+}) \\
T_{2-2}^{12} = \frac{1}{2} S_{1}^{+} S_{2}^{-}. \tag{24}
\]

The contribution of the dipole-dipole relaxation mechanism to the spin-lattice relaxation rate constant \( R_{1}^{S} = (T_{1}^{S})^{-1} \) of the \( S \)-spins is given by:

\[
(R_{1}^{S})_{DD} = -\frac{(S_{1}^{+} I_{1}^{DD} | S_{2}^{+})}{(S_{1}^{+} S_{2}^{+})} \tag{25}
\]

where the Liouville brackets are defined by Equation 11. This evaluates to:

\[
(R_{1}^{S})_{DD} = \frac{3}{2} \beta^{2}_{12} \tau_{c} \tag{26}
\]

in the extreme-narrowing limit.

In general, many mechanisms contribute to the \( S \)-spin relaxation, including dipole-dipole relaxation involving interactions with the \( I \)-spin, as well as chemical-shift anisotropy and spin-rotation mechanisms. For simplicity, all \( S \)-spin relaxation mechanisms other than the intra-pair dipole-dipole mechanism are ignored for now.

An important feature of the within pair DD relaxation mechanism is that it does not cause relaxation of the \( S \)-spin singlet order, when considered in isolation. This property may be expressed by the following equation:

\[
(R_{S})_{DD} = -\frac{(S_{1} \cdot S_{2} | I_{1}^{DD} | S_{1} \cdot S_{2})}{(S_{1} \cdot S_{2} | S_{1} \cdot S_{2})} = 0 \tag{27}
\]

where \( R_{S} \) is the rate constant for the decay of \( S \)-spin singlet order, \( R_{S} = (T_{S}^{S})^{-1} \), and \( T_{S} \) is the singlet relaxation time constant. Nuclear singlet order, expressed by the operator \( S_{1} \cdot S_{2} \), is therefore a long-lived state which is protected from intra-pair dipole-dipole relaxation.

In practice, the DD relaxation mechanism may induce some decay of nuclear singlet order, even when other mechanisms are absent. This is because the symmetry-breaking coherent terms in the spin Hamiltonian, namely the difference in chemical shifts \( \Omega_{\alpha} \), and the difference in J-couplings to additional spins \( \omega_{\alpha} \), induce a mixing between the singlet and triplet states of the \( S \)-spin pair. This state mixing allows singlet order to relax through “coherent leakage” into the rapidly relaxing triplet manifold\(^{166} \). In the case where there is no chemical shift difference \( \Omega_{\alpha} = 0 \), and the out of pair J-coupling difference is small compared to the in pair J-coupling \( |\omega_{\alpha}| < |\omega_{f}| \), the singlet leakage rate is given by:

\[
\langle R_{S} \rangle_{DD}^{\text{leakage}} \approx \frac{\beta^{2}}{3 b_{12} \tau_{c}^{2} + 12 \omega_{f}^{2}} \tag{28}
\]

\[
R_{S}^{\text{DD}} \approx \frac{\omega_{S}^{2}}{2 (R_{1}^{I})^{2} + 18 \omega_{f}^{2}}. \tag{29}
\]

In cases where \( \Omega_{\alpha} \neq 0 \), Equation 29 becomes:

\[
\langle R_{S} \rangle_{DD}^{\text{leakage}} \approx \frac{R_{S}^{I} (\omega_{S}^{2} + \Omega_{\alpha}^{2})}{2 (R_{1}^{I})^{2} + 18 \omega_{f}^{2}}. \tag{30}
\]

Equation 29 assumes that the \( S \)-spin spin-lattice relaxation rate constant \( R_{S}^{1} \) is dominated by the intra-pair dipole-dipole mechanism.

In most cases, the leakage contribution to singlet relaxation, as treated by Equation 29, is very weak. However, this expression assumes that the \( I \)-spins, to which the \( S \)-spin pair is coupled, do not themselves relax. As shown below, the \( I \)-spin relaxation can greatly increase the leakage contribution beyond that predicted by Equation 29.

### 3. \( I \)-spin relaxation superoperator

Consider the case where the \( I \)-spin, to which the \( S \)-spin pair is coupled, also undergoes relaxation. The \( I \)-spin relaxation may be treated by including a suitable relaxation superoperator \( \hat{I}_{r} \) in the Liouvillian. For simplicity, we use here a phenomenological relaxation superoperator, which endows the \( I \)-spin system with a relaxation rate constant \( R_{I}^{I} = (T_{I}^{I})^{-1} \) for \( I \)-spin operators which are parallel to the external magnetic field, and a relaxation rate constant \( R_{I}^{b} = (T_{I}^{I})^{-1} \) for \( I \)-spin operators which are perpendicular to the external magnetic field. The detailed microscopic mechanisms of the \( I \)-spin relaxation are not considered at this point.

A relaxation superoperator of appropriate form is given by:

\[
\hat{I}_{r} = -\sum_{\mu} \left( R_{I}^{I} | S_{\mu} I_{x} \rangle \langle S_{\mu} I_{x} | + R_{I}^{b} | S_{\mu} I_{x} \rangle \langle S_{\mu} I_{x} | + R_{I}^{b} | S_{\mu} I_{x} \rangle \langle S_{\mu} I_{y} | \right) \tag{31}
\]

where the sum is taken over a complete set of orthogonal \( S \)-spin operators.

The complete Liouvillian superoperator, within this simplified model of the spin system and its relaxation, is given by:

\[
\hat{L} = -i \hat{H}_{\text{coh}} + \hat{I}_{r}^{DD} + \hat{I}_{r}^{\text{then}}. \tag{32}
\]

### C. Case of no applied rf fields

Consider the case without the application of resonant rf fields \( \omega_{\text{rf}} = \omega_{S}^{1} = 0 \). A convenient operator basis, consisting of 64 orthonormal operators, may be defined such that the first four operators are given by:

\[
\mathcal{B} = \left\{ \sqrt{2} T_{10}^{12}, -\sqrt{2} T_{20}^{12}, (T_{10}^{1} - T_{10}^{2}) T_{10}^{3}, 2\sqrt{2} T_{10}^{10}, \ldots \right\}. \tag{33}
\]
The spherical tensor operator components are given by:

\[
\begin{align*}
T_{10}^j &= I_j^c \\
T_{10}^{12} &= -3^{-1/2} \mathbf{S}_1 \cdot \mathbf{S}_2 \\
T_{10}^{12} &= -8^{-1/2} (\mathbf{S}_1^2 \mathbf{S}_2^2 - \mathbf{S}_1^2 \mathbf{S}_2^2) \\
T_{12}^{12} &= 6^{-1/2} (3\mathbf{S}_1 \mathbf{S}_2 - \mathbf{S}_1 \mathbf{S}_2).
\end{align*}
\]

(34)

In the absence of rf fields, the superoperator matrix representation of \( \hat{L} \) is block diagonal in the basis \( \mathbb{B} \), with the 4 \(
\times \) 4 block defined by the first four operators of \( \mathbb{B} \) not connected by finite matrix elements to any other operators. This block is given by:

\[
\begin{bmatrix}
0 & -\frac{\omega_S}{\pi} b_1^2 \tau_c & 0 & -i\omega_A / \sqrt{6} \\
0 & -\frac{\omega_S}{\pi} b_2^2 \tau_c & 0 & -i\omega_A / 2\sqrt{3} \\
-\omega_A / \sqrt{6} & i\omega_S / 2\sqrt{3} & -\omega_S^2 \tau_c & -i\omega_A \\
-\omega_A / \sqrt{6} & i\omega_S / 2\sqrt{3} & -i\omega_A & -\omega_S^2 \tau_c
\end{bmatrix}
\]

Assuming that the S-spin relaxation is dominated by the intra-pair dipole-dipole mechanism, this may be written as:

\[
\begin{bmatrix}
0 & -\frac{\omega_S}{\pi} R_1^S \tau_c & 0 & -i\omega_A / \sqrt{6} \\
0 & 0 & 0 & -i\omega_A / 2\sqrt{3} \\
-\omega_A / \sqrt{6} & i\omega_S / 2\sqrt{3} & -\omega_S^2 \tau_c & -i\omega_A \\
-\omega_A / \sqrt{6} & i\omega_S / 2\sqrt{3} & -i\omega_A & -\omega_S^2 \tau_c
\end{bmatrix}
\]

(36)

This matrix has four complex eigenvalues. The decay rate constant of the long-lived state is given by minus the smallest negative eigenvalue (see equation 9). The rate constants \( \lambda_q \) for the decay of eigenoperators \( \hat{Q}_q \), with \( q \in \{0 \ldots 63 \} \), may be derived from the matrix representation of \( \hat{L} \) in the basis \( \mathbb{B} \), as described in equations 5 to 6. These rate constants are plotted against the I-spin relaxation rate constant \( R_1^I \) for a typical set of parameters in Figure 2. Numerical simulations were performed by using the Mathematica-based NMR software package SpinDynamica\textsuperscript{60}. The colouring of the different eigenvalue curves is arbitrary. Apart from the trivial eigenvalue \( \lambda_0 = 0 \) (horizontal dashed line), which belongs to the unity eigenoperator and which represents the conserved sum of all state populations, the smallest rate constant (bold line) corresponds to the decay rate constant \( R_{LLS} \) for the long-lived mode of S-spin singlet order.

It has not proved possible to obtain a compact exact form for this rate constant. However, an approximate analytical result may be obtained by deploying Pramas-van Vleck perturbation theory\textsuperscript{61-65}. The method is described in the Appendix, and leads to the following expression:

\[
R_{LLS} \approx \frac{3 R_1^S}{10} + \frac{R_1^I \omega_2^2}{8 \rho^2} - \frac{1}{40} \sqrt{144(R_1^I)^2 - 40R_1^I \omega_2^2 \omega_A^2 + \frac{25(R_1^I)^2 \omega_A^4}{\rho^4}}
\]

(37)

where:

\[
\rho^2 = (R_1^I)^2 + \omega_2^2
\]

(38)

For the typical parameters, this expression yields values which are indistinguishable from the numerical results (Figure 3). Equation 37 shows that a finite relaxation rate constant \( R_1^I \) for the I-spin augments the relaxation rate constant \( R_{LLS} \) for the long-lived state by mixing in a dependence on the S-spin relaxation rate \( R_1^S \). In other words, the leakage mechanism for long-lived state decay is augmented by the relaxation of the I-spin. This is the essence of the S-SR2K mechanism.
A plot of the relaxation rate constant $R_{\text{LLS}}$ against the $I$-spin relaxation rate constant $R_1^I$ is shown for typical parameters in Figure 3. When $R_1^I = 0$ the long-lived relaxation rate $R_{\text{LLS}}$ is very small and given by the coherent leakage term (see Equation 29). However, the long-lived relaxation rate rapidly increases as $R_1^I$ increases. A maximum in $R_{\text{LLS}}$ is achieved when the $I$-spin relaxation rate constant matches the $J$-coupling between the $S$-spins, $R_1^S = \omega_J$ (indicated by the vertical grey line in Figure 3). The relaxation rate of the long-lived state decreases slowly as $R_1^I$ increases beyond $\omega_J$.

The behaviour has the following physical interpretation: The longitudinal relaxation processes of the $I$-spin cause fluctuations in the local magnetic field at the site of the $S$-spins, as transmitted by the heteronuclear $J$-couplings. If the $J$-couplings are different ($\omega_J \neq 0$), the local field fluctuations induce singlet-triplet transitions, allowing singlet order to leak into the more rapidly relaxing triplet manifold. Since the energy difference between the singlet and central triplet states of the $S$-spins corresponds to $\omega_J$ in frequency units, the effect is strongest when the $I$-spin relaxation rate $R_1^I$ matches the $J$-coupling $\omega_J$.

The maximum rate of long-lived state relaxation, induced by the SR2K mechanism, is given by evaluating Equation 37 at the condition $R_1^I = \omega_J$ which leads to the following expression:

$$R_{\text{LLS}}^{\text{max}} \simeq \frac{3R_1^S}{10} + \frac{\omega_0^2}{16\omega_J} - \frac{1}{40} \sqrt{144(R_1^S)^2 - \frac{20R_1^S \omega_0^2}{\omega_J} + \frac{25\omega_0^4}{4\omega_J^2}}.$$  \hspace{1cm} (39)

The value of $R_{\text{LLS}}^{\text{max}}$ is shown by the horizontal grey line in Figure 3. For the parameters shown, the “worst case” ratio of the long-lived state relaxation rate constant $R_{\text{LLS}}$ to the longitudinal relaxation rate constant $R_1^I$ is $\sim 0.32$, i.e. the long-lived state decays only about 3 times slower than the longitudinal magnetization.

Figure 4 shows a contour plot of the “worst case” ratio of the long-lived and longitudinal $S$-spin relaxation rate constants, $R_{\text{LLS}}^{\text{max}}/R_1^S$, as a function of the two coupling parameters $\omega_0$ and $\omega_J$, which are also expressed as ratios of $R_1^S$. The blue shading indicates the region of parameter space where the long-lived state is well-protected against the SR2K mechanism. This requires that the heteronuclear difference frequency $\omega_0$ is not too large (less than roughly twice the $S$-spin relaxation rate constant $R_1^S$), and the $S$-spin $J$-coupling $\omega_J$ is not too small (at least $R_1^S$). In this region, the maximum value of the long-lived state decay time constant $T_{\text{LLS}}$, taking into account the SR2K mechanism alone, is at least 20 times $T_1$. In the very worst case, on the other hand, where $\omega_0$ is large and $\omega_J$ is small, the SR2K mechanism induced by a single $I$-spin-1/2 may give rise to a long-lived-state relaxation rate constant $R_{\text{LLS}} = (2/5)R_1^S$, i.e. the ratio of $T_{\text{LLS}}$ to $T_1$ is not larger than 2.5.

Although Figure 4 represents the “worst case” scenario, in which the $I$-spin relaxation rate constant is always chosen to give the fastest possible leakage, this plot indicates that the SR2K mechanism of long-lived state relaxation is likely to be commonly encountered. It may be no coincidence that a time constant ratio of $T_{\text{LLS}}/T_1 \sim 3$ is frequently encountered in practice, unless special precautions are taken.

We now consider the nature of the long-lived state, i.e. the eigenoperator $\hat{Q}_{\text{LLS}}$ with eigenvalue $\lambda_{\text{LLS}} = -R_{\text{LLS}}$. In many regions of parameter space, this eigenoperator corresponds closely to the singlet order operator $T_{\text{sing}}^{\text{SO}}$ of Equation 34.
ever, this is not always the case. The coefficient of singlet order in the long-lived eigenoperator $Q_{LLS}$ is given by:

$$c_{SO} = (\sqrt{2}T_{00}^{12} | Q_{LLS} )$$  \hspace{1cm} (40)$$

with the Liouville bracket defined by Equation 11. A coefficient $c_{SO} > 1$ indicates that the long-lived state is pure singlet order; a coefficient $c_{SO} < 1$ indicates that the long-lived state consists of singlet order mixed with other operators. Figure 5 shows plots of the coefficient $c_{SO}$ for the long-lived eigenstate as a function of the relaxation rate constant $R_1$, for various values of the rate constant $R_2$, assuming pure dipole-dipole relaxation for the $S$-spins. These plots show that the long-lived state corresponds to nearly pure singlet order in the case of no $I$-spin relaxation ($R_1 = 0$) and relatively rapid $S$-spin relaxation. However, in other cases, the long-lived state consists of a mixture of singlet order with other operators. The admixture of other operators is maximal near the condition $R_1 = \omega_I$, where singlet-SR2K is most significant.

In the extreme case of $R_1 = 0$ (no $S$-spin relaxation), but finite $I$-spin relaxation, the long-lived state corresponds to the operator $\sqrt{2}S_1 S_2$, i.e. “zz-order”, rather than singlet order (blue line in Figure 5). In this case the singlet-order coefficient in the LLS is given by:

$$c_{SO} = (\sqrt{2}T_{00}^{12} | \sqrt{2}S_1 S_2 ) = \frac{1}{\sqrt{3}} = 0.578$$  \hspace{1cm} (41)$$

for all $R_1 > 0$. The physical interpretation of this is as follows: the singlet order operator may be expressed:

$$\sqrt{2}T_{00}^{12} = -\sqrt{\frac{2}{3}} S_1 S_2 - \frac{1}{\sqrt{6}} (S_1^2 S_2 + S_1 S_2^2 ).$$  \hspace{1cm} (42)$$

If the $I$-spin has significant relaxation, and there is no $S$-spin relaxation, the second term (the “flip-flop” term) dephases under the SR2K effects, while the first term (the “zz” term) remains invariant. However, the isolation of these two terms is disrupted if there is significant $S$-spin relaxation, in which case the singlet order takes over its usual role as the long-lived eigenoperator.

The relaxation of $S$-spin singlet order is non-monoeponential in the regime where the coefficient $c_{SO}$ is significantly less than 1. Figure 6 shows simulated trajectories of the decay of singlet order in the presence of SR2K effects for various values of the $S$-spin relaxation rate constant $R_2$. In the extreme case of $R_1 = 0$, the “zz” part of the singlet order does not decay at all (blue line). Note that increasingly large values of $R_2$ do not induce more rapid singlet relaxation: the main effect of increasing $R_2$ is merely to reduce the biexponentiality of the relaxation trajectory.

D. SR2K suppression by resonant rf fields

The effect of SR2K on the relaxation of the long-lived state is strongly influenced by the application of resonant radiofrequency fields. The resonant fields may be applied to either the $I$-spins or the $S$-spins.

1. $I$-spin rf fields

The effect of a resonant $I$-spin field may be explored by numerical simulations of the Liouvillian eigenvalues, including a finite value of $\omega_{\text{nut}}$ in Equation 15. The decay rate constants $\lambda_{SO}$ of the Liouvillian eigenoperators are plotted against the rf field amplitude on the $I$-spins, expressed as a nutation frequency $\omega_{\text{nut}}$. Figure 7 shows plots of the coefficient $c_{SO}$ for the long-lived eigenstate as a function of the relaxation rate constant $R_1$, for various values of $\omega_{\text{nut}}$. In the extreme case of $R_1 = 0$, the “zz” part of the singlet order does not decay at all (blue line). Strong $I$-spin rf fields suppress the SR2K decay mechanism.
line. The application of strong I-spin RF fields suppresses the SR2K-induced decay of the long-lived state.

The dependence of \( \lambda_{\text{LLS}} \) on the I-spin RF field amplitude is explored for a range of values of the rate constant \( R^I_1 \) in Figure 8. Two regimes may be identified: When the I-spin relaxation is slow \( (R^I_1 < |\omega_I|) \), a strong increase in the decay rate of the LLS is observed when the I-spin RF field amplitude matches the condition \( \omega_{\text{nut}}^I = |\omega_I| \). This is a variant of the spin-lock-induced-crossing (SLIC) condition \(^{18}\). When the I-spin relaxation is rapid \( (R^I_1 < |\omega_I|) \), the application of a small I-spin RF field has little effect. In all cases, an applied RF field with amplitude \( \omega_{\text{nut}}^I > |\omega_I| \) suppresses the SR2K-induced decay of the long-lived state. However, the effect is small when the I-spin has very rapid I-spin relaxation.

An approximate analytical expression for \( \lambda_{\text{LLS}} \) has been obtained in the near magnetic equivalence regime, \( |\omega_I| \gg |\omega_\Delta| \), and the limit of a strong I-spin RF field, \( |\omega_{\text{nut}}^I| \gg |\omega_\Delta| \), and assuming \( R^I_1 = R^2_1 \). The derivation is given in the appendix. This expression is as follows:

\[
R_{\text{LLS}}(\omega_{\text{nut}}^I) \approx \frac{3R^S_{\Delta}}{10} + \frac{A}{8D} - \frac{9}{20} \sqrt{\frac{4(R^S_1)^2}{9} - \frac{5}{324} \left(8R^S_1ABC - A\right)}
\]

(43)

where the following abbreviations have been used:

\[
A = R^I_1(\omega_{\text{nut}}^\Delta^2 + \omega_\Delta^2 + (R^I_1)^2)
\]

(44)

\[
B = (R^I_1)^2 + (\omega_{\text{nut}}^I - \omega_\Delta)^2
\]

(45)

\[
C = (R^I_1)^2 + (\omega_{\text{nut}}^I + \omega_\Delta)^2
\]

(46)

\[
D = (R^I_1)^4 + (\omega_{\text{nut}}^I - \omega_\Delta)^2 + 2R^I_1(\omega_{\text{nut}}^I + \omega_\Delta^2)
\]

(47)

The values of Equation 43 are shown by the dots in Figure 8 and agree well with the numerical results (except for a single point on the line with \( R^I_1 = 0.01 \text{ s}^{-1} \) at \( \omega_{\text{nut}}^I / 2\pi = 10 \text{ Hz} \).

2. S-spin RF fields

The SR2K mechanism of long-lived-state decay is also strongly influenced by radiofrequency fields resonant with the S-spin pair.

The decay rate constants of the Liouvillian eigenoperators are plotted against the RF field amplitude on the S-spins, expressed as a nutation frequency \( \omega_{\text{nut}}^S \), in Figure 9. In this simulation, the I-spin relaxation rate constant \( R^I_1 \) is matched to the S-spin J-coupling \( \omega_J \), which maximises the SR2K effect in the absence of RF fields. The decay rate constant of the long-lived state is shown by the bold line. The application of a very small S-spin RF field sharply increases the decay rate constant \( \lambda_{\text{LLS}} \). A further increase in the S-spin field amplitude first accelerates the decay rate of the long-lived state, until a maximum decay rate is reached at around \( \omega_{\text{nut}}^S \approx \omega_J \). Further increase of the RF field amplitude sharply decreases the relaxation rate constant, indicating the suppression of the SR2K mechanism.

The sharp increase in the rate constant \( \lambda_{\text{LLS}} \) at very small values of \( \omega_{\text{nut}}^S \) is remarkable. This regime is explored in more detail in Figure 10. This shows clearly the increase in the decay rate constant of the long-lived state when very small S-spin fields are applied, accompanied by complex branching and merging of the other Liouvillian eigenvalues.

This behaviour may be understood qualitatively as follows: In the case of significant I-spin relaxation, and no S-spin relaxation, the “zz” component of S-spin singlet order is longer lived than the “flip-flop” component, since the latter is dephased by the rapid I-spin relaxation (see Equation 42 and subsequent discussion). The long-lived eigenoperator in the absence of an S-spin RF field is therefore close to “zz” order for the S-spins (see Figure 5). This situation corresponds to
the left-hand edges of the plots in Figures 9 and 10. The application of a very weak $S$-spin rf field is enough to mix the slowly relaxing “zz” component of $S$-spin singlet order with the more rapidly relaxing “flip-flip” component. This leads to a significant increase in the relaxation rate constant of the long-lived state, as shown clearly by the bold lines in Figures 9 and 10. The relaxation rate constant of the long-lived state comes down again when the $S$-spin rf field becomes marginal when the $I$-spin relaxation rate constant $R^1_I$ is large.

E. The case of a quadrupolar $I$-spin

Consider the case where the additional nucleus $I_3$ is spin-1, such that the isolated three spin system in the ensemble consists of a spin-$1/2$ pair and a quadrupolar nucleus. The $I$-spin possesses a dominant quadrupolar relaxation mechanism due to the coupling interaction between the intrinsic electric quadrupole moment and the local electric field gradient (EFG) being motionally modulated by the random tumbling of the molecules in solution. We assume, for simplicity, that the relaxation mechanism of the $I$-spin is not cross-correlated with the in pair dipole-dipole relaxation mechanism of the $S$-spins.

For the case of isotropic tumbling in the extreme-narrowing limit, the quadrupolar relaxation superoperator for the $I$-spin is given by:

$$\hat{\Gamma}_I^Q \simeq -\frac{3}{10} \omega_Q^3 \sum_{\mu=-2}^{+2} (-1)^\mu \tilde{J}_2^3 \tilde{J}_{2-\mu}^3$$

where the quadrupolar coupling constant of the spin-1 nucleus $I_3$ is given by:

$$\omega_Q = \frac{e^2 Q}{2h}$$

where $Q$ is the electric quadrupolar moment of the quadrupolar nucleus, and $eq$ is the electrical field gradient at the quadrupolar nucleus. The five operator components $\tilde{J}_{2\mu}^3$ are given by:

$$T_{2+2}^3 = \frac{1}{2} (I_2^+)^2$$

$$T_{2+1}^3 = -\frac{1}{2} (I_2^+ I_3^- + I_3^- I_2^-)$$

$$T_{20}^3 = \frac{1}{\sqrt{6}} (3 I_2^2 - I_3^2)$$

$$T_{2-1}^3 = \frac{1}{2} (I_2^- I_3^- + I_3^- I_2^+)$$

$$T_{2-2}^3 = \frac{1}{2} (I_2^-)^2$$
The quadrupolar relaxation mechanism is the dominant decay process contributing to the longitudinal relaxation rate constant $R_1^I = (T_1^I)^{-1}$ of the $I$-spin, and is given by:

$$R_1^I = -\frac{(I_z|\hat{f}_Q^S|I_z)}{(I_z|I_z)} = \frac{3}{2} \omega_0^2 \tau_c.$$  

for the case that $I_3$ is spin-1. In this instance, the complete Liouvillian superoperator is given by:

$$L = -i\hat{H}_{\text{coh}} + \hat{f}_{S}^{DD} + \hat{f}_{Q}^{Q}.$$  

A numerical analysis of the Liouvillian eigenvalues $\lambda_q$, plotted against the quadrupolar relaxation rate constant $R_q^I$ of the spin $I_3 = 1$, is shown in Figure 12. All parameters are identical to those in section II C, with the exception that the $I$-spin relaxation uses the semi-classical quadrupolar relaxation superoperator in Equation 56. The maximum SR2K relaxation rate constant is found to be $\sim 15\%$ higher than the case of $I_3 = 1/2$. An analytical expression for the singlet rate constant in this case has not been found.

The grey region of Figure 12 denotes the typical range of quadrupolar spin-lattice relaxation rate constants for deuterium nuclei covalently attached to small organic molecules dissolved in solution. The shaded area coincides with the region of maximal singlet relaxation (bold line), demonstrating that deuterium nuclei can provide a significant relaxation source for the singlet order of the spin-1/2 pair.

For the case of a quadrupolar $I$-spin, the biexponential nature of the long-lived state and its behaviour under the application of on resonant $I$-spin and $S$-spin radiofrequency fields are detailed in the Supplementary Material (SM).

III. EXPERIMENTS

A. Experimental methods

It proved difficult to identify a test molecular system containing a three-spin system with appropriate properties. We therefore studied the perdeuterated ethyl/proplyl diester of 2,3-$^{13}$C$_2$-fumarate (1-(ethyl-$d_5$) 4-((propyl-$d_7$)-3)-but-2-enedioate-$^{13}$C$_2$-$d_2$).  

[FIG. 13. Molecular structure, labelling scheme and scalar coupling constant pattern of I. Black circles denote $^{13}$C nuclei, grey circles denote $^2$H nuclei. $R^1 = CD_2CD_3$ and $R^2 = CD_2CD_2CD_3$.]

The relevant portion of the experimental $^{13}$C NMR spectrum of I is shown in Figure 14. The chemical shift of the $^{13}$C$_2$ resonance was referenced with respect to the CDC$_3$ solvent peak at 77.2 ppm. The experimental $^{13}$C NMR spectrum of I was fitted using the MatLab-based NMR software package Spinach$^{67}$. The fitted scalar couplings and chemical shifts (including their differences) for I in CDC$_3$ solvent at 25°C are given in Table I.
FIG. 14. Relevant portion of the experimental $^{13}$C NMR spectrum of I dissolved in degassed CDCl$_3$ solution acquired at 11.75 T ($^{13}$C nuclear Larmor frequency = 125.8 MHz) and 25°C with 64 transients. Black curve: experimental $^{13}$C spectrum; blue curve: simulated $^{13}$C spectrum. Small signals from synthetic impurities are observed beyond 133.5 ppm.

The spin system is in the near-equivalence regime, since the difference in scalar couplings $|J_{12} - J_{13}|$ is less than half of $J_{23}$.

The $^{13}$C longitudinal relaxation time $T_1$($^{13}$C) was estimated experimentally by using the inversion-recovery pulse sequence. Under the same conditions, the resulting relaxation curve (see the Supplementary Material (SM)) shows a single exponential recovery with a longitudinal $^{13}$C relaxation time: $T_1$($^{13}$C) = 14.0 ± 0.5 s.

C. Deuterium NMR

The $^2$H spectrum of I is shown in the Supplementary Material (SM). The longitudinal $^2$H relaxation time $T_1$($^2$H) was estimated experimentally by using the inversion recovery pulse sequence. For the case of degassed CDCl$_3$ solution at 11.7 T and 25°C, the experimental relaxation curve (see the Supplementary Material (SM)) shows a single exponential recovery with a longitudinal $^2$H relaxation time: $T_1$($^2$H) = 168 ± 7 ms.

D. Singlet NMR

Symmetry-breaking interactions, such as small differences in chemical shift between the participating spins, or differential scalar couplings to other magnetic nuclei outside of the singlet pair are required for coherent access to the nuclear singlet order$^{14}$. In this case, the differential out-of-pair scalar couplings allow coherent access to the $^{13}$C nuclear singlet order of I, by using known radiofrequency pulse techniques which operate in the near-equivalence regime$^{10,13,18,22}$, as shown by Warren and coworkers$^{14,26,35}$. In the current study, the spin-lock induced crossing (SLIC) pulsed method$^{18}$ was used, as shown in Figure 15. Details of the SLIC pulse sequence, parameter optimization and the “T$_{00}$ filter” are found in the Supplementary Material (SM). The parameters of the SLIC pulse were chosen to maximise triplet-singlet population conversion: $\omega_{SLIC} / 2\pi = 71.5$ Hz and $\tau_{SLIC} = 27$ ms, i.e. the conversion was complete in a time: $\tau_{SLIC} \approx 2^{-1/2}|(J_{12} - J_{13})|^{-1}$. The maximum amplitude of the singlet-filtered $^{13}$C NMR signal, relative to that induced by a single 90° pulse, was found to be 0.067. The loss relative to the theoretical maximum of 1/3 (AA’XX’ spin systems) is not yet fully understood. The parameters used for this pulse sequence are such that the generation of $^{13}$C$_2$ singlet order takes place predominantly through the differential $^{13}$C-$^2$H couplings, with the small chemical shift difference between the $^{13}$C nuclei playing a negligible role.

IV. RESULTS

A. Singlet order decay in the absence of rf fields

A decay curve for the $^{13}$C signal intensity of I under the pulse sequence shown in Figure 15 is shown in Figure 16. The experimental decay (black data points) is well fitted with a biexponential decay function of the form: A exp{-t/T_A} + B exp{-t/T_B} (black curve). The fit parameters are: A = 0.772, $T_A = 240 ± 40$ ms, B = 0.504, $T_B = 3.6 ± 0.3$ s. Note that the decay is much faster than that of longitudinal $^{13}$C magnetization ($T_1$($^{13}$C) = 14.0 s). The rapid quenching of nuclear singlet order, and the biexponential decay, support a strong role for SR2K as a singlet relaxation mechanism in this system.

Numerical simulation of the long-lived state relaxation dynamics requires an estimate of the rotational correlation time $\tau_c$. This was estimated by analyzing the experimental relaxation time constant $R_1$ for the $^2$H nuclei adjacent to the $^{13}$C spin pair, using Equation 55 which applies for extreme-narrowing isotropic rotational tumbling$^{59}$. The following analysis refers to data obtained on 0.207 M I dissolved in degassed CDCl$_3$ solution acquired at 11.7 T ($^{13}$C nuclear Larmor frequency = 125.8 MHz) and 25°C. The deuteron quadrupole coupling constant $\omega_Q / 2\pi = 96.9$ kHz was estimated by using the quantum chemistry package Gaussian 09$^{98}$. NMR computations employed the GIAO-DFT/B3LYP/6-31G+(d,p) level of theory incorporating the use of the keyword “pick-
FIG. 15. Pulse sequence for preparing long-lived nuclear singlet order in I and monitoring its decay. The experiments used the following parameters: \( \omega_{\text{SLIC}}/2\pi = 71.5 \text{ Hz} \) and \( t_{\text{SLIC}}/2\pi = 27 \text{ ms} \). The "T00 filter" selects out signals that do not pass through nuclear singlet order\(^6\). "MA" denotes the "magic angle" (54.7°). The grey boxes denote optional "spin-locking" rf fields, with nutation frequencies \( \omega_{\text{SLIC}}^O \) and \( \omega_{\text{SLIC}}^S \), which are active during the singlet evolution delay \( t_{\text{EV}} \). The superscripts \( I \) and \( S \) denote the \( ^2\text{H} \) and \( ^{13}\text{C} \) spin-locking rf fields, respectively. An interval of 150 s was used between successive transients.

et\(^{69}\). Default CDCl\(_3\) solvent inclusion was chosen. Biaxiality of the quadrupole coupling tensor is small and is neglected. From comparing the experimental relaxation time \( T_1(^2\text{H}) = 168 \pm 7 \text{ ms} \) with Equation 55, which was derived for the case of a molecule undergoing isotropic rotational diffusion\(^48\), and assuming that the quadrupolar mechanism dominates the deuteron relaxation, we estimate a correlation time for the overall tumbling of the molecule in solution: \( \tau_C = 10.7 \pm 0.5 \text{ ps} \). The contribution of dipole-dipole interactions to \( ^2\text{H} \) longitudinal relaxation is found to be negligible and is ignored.

A numerical simulation of the the long-lived state decay is shown by the grey curve in Figure 16. The simulation considers a 4-spin system of the \( ^{13}\text{C}_2 \) spin pair and the two adjacent deuterons. The deuterons are modelled as spin-1 nuclei.

The numerical simulation propagates the spin density operator (nuclear singlet order) forward in time under the Liouville-von Neumann equation (Equation 3) with a Liouvillian consisting of coherent and incoherent interactions (Equation 4). In this case, the coherent Hamiltonian takes the following form:

\[
H_{\text{coh}} = \omega_l S^z + \frac{1}{2} (\omega_S + \omega_A)(S_1^z I_2^z + S_2^z I_2^z) \]

and includes the complete scalar coupling constant map shown in Figure 13 and the isotropic chemical shift difference between the \( ^{13}\text{C} \) labelling sites \( \Delta \Omega_{13} = 2\pi 7.75 \text{ rads}^{-1} \) (obtained from the fit of the experimental \( ^{13}\text{C} \) NMR spectrum of I).

The relaxation superoperator has the following composition:

\[
\hat{\Gamma} = \hat{\Gamma}_S^{DD} + \hat{\Gamma}_S^{SL} + \hat{\Gamma}_S^{CSA} + \hat{\Gamma}_I^Q
\]

FIG. 16. Experimental relaxation curve (black data points) showing the decay of \( ^{13}\text{C} \) signal intensity for 0.207 M I dissolved in degassed CDCl\(_3\) solvent acquired at 11.75 T (\( ^{13}\text{C} \) nuclear Larmor frequency = 125.8 MHz) and 25°C with 2 transients per data point, using the pulse sequence in Figure 15. All experimental signal amplitudes were normalized to the first data point. The decay curve was fitted with a biexponential decay function (black curve): 

\[
A \exp\{-t/T_A\} + B \exp\{-t/T_B\}
\]

where \( A = 0.772, T_A = 240 \pm 40 \text{ ms}, B = 0.504, T_B = 3.6 \pm 0.3 \text{ s} \). A simulated relaxation curve for the decay of \( ^{13}\text{C} \) nuclear singlet order is shown by the grey curve. The simulation includes dipole-dipole relaxation between the \( ^{13}\text{C} \) labels and the deuteron sites, \( ^{13}\text{C} \) CSA relaxation, quadrupolar relaxation for the two deuterons, and the J-coupling network presented in Table I. A simulation neglecting the \( ^{13}\text{C} \)–\(^2\text{H} \) scalar couplings is shown by the blue curve.

The singlet-triplet leakage relaxation mechanism emerges naturally from the simulation by the virtue of: (i) longitudinal relaxation for the S-spins; and (ii) scalar couplings between the carbon pair and the quadrupolar nuclei. The presence of the out of pair J-couplings and an efficient quadrupolar relaxation mechanism for the coupled spin-1 nuclei introduces the S-SR2K mechanism.

A simulation of the \( ^{13}\text{C} \) singlet order decay (Figure 16, grey curve) yields a biexponential relaxation curve, which is in respectable agreement with the experimental data, although a discrepancy remains. The discrepancy between experimental and estimated \( ^{13}\text{C} \) singlet order decay curves could be attributed to additional relaxation mechanisms including: dipole-dipole couplings to remote nuclei in I and with molecules in the solvent, and spin-rotation or spin-
FIG. 17. Experimental relaxation curves showing the decay of $^{13}$C nuclear singlet order for 0.207 M $I$ dissolved in degassed CDCl$_3$ solvent acquired at 11.75 T ($^{13}$C nuclear Larmor frequency = 125.8 MHz) and 25°C with 2 transients per data point. The decay of $^{13}$C nuclear singlet order was measured by using the pulse sequence described in Figure 15 in the presence of $^{2}$H spin-locking rf fields (nutation frequency $= \omega_{\text{nut}}/(2\pi)$) during the singlet evolution delay $\tau_{\text{EV}}$. Nutation frequencies: Black: $\omega_{\text{nut}}/(2\pi) = 200$ Hz; Grey: $\omega_{\text{nut}}/(2\pi) = 640$ Hz. The singlet relaxation time constants are: Black filled circles: $T_S = 5.3 \pm 0.4$ s; Grey open squares: $T_S = 11.7 \pm 0.4$ s. All the fitted curves have a single exponential form. All signal amplitudes were normalized to the first data point.

FIG. 18. Black data points: experimental dependence of the singlet lifetime $T_S^{-1}$ on $^{2}$H spin-locking rf field amplitudes (nutation frequency $= \omega_{\text{nut}}/(2\pi)$) for 0.207 M $I$ dissolved in degassed CDCl$_3$ solvent acquired at 11.75 T ($^{13}$C nuclear Larmor frequency = 125.8 MHz) and 25°C. Black curve: simulated dependence of $T_S^{-1}$ on $\omega_{\text{nut}}/(2\pi)$. Simulations include singlet relaxation from the SR2K mechanism only.

diation with $\omega_{\text{nut}}/(2\pi) = 640$ Hz nutation frequency. The singlet relaxation time constant is $T_S = 11.7 \pm 0.4$ s. In agreement with the theory presented in section II D, the application of a resonant rf field on the $^2$H nuclei ($I$-spins) suppresses the singlet-SR2K mechanism and extends the singlet lifetime $T_S$.

The experimental singlet relaxation rate constants $T_S^{-1}$ as a function of $^2$H spin-locking rf field amplitude, expressed as the nutation frequency $\omega_{\text{nut}}/(2\pi)$, are shown by the black data points in Figure 18. Numerically determined singlet relaxation rate constants are shown by the black curve. Simulations include singlet relaxation from the SR2K mechanism only.

The experimental singlet relaxation rate constants $T_S^{-1}$ increase dramatically, and reach a maximum, as $\omega_{\text{nut}}/(2\pi)$ approaches $J_{23} = 71.5$ Hz, corresponding to a match between the $^2$H nutation frequency and the $^{13}$C-$^2$H J-coupling, as predicted by the theory given above. The experimental and numerical curves are in excellent agreement. The experimental singlet relaxation rate constants $T_S^{-1}$ decrease with increasing $^2$H spin-locking rf field amplitude, beyond a nutation frequency of $\sim 150$ Hz. The $^{13}$C singlet relaxation time constant at the largest $^2$H nutation frequency of $\omega_{\text{nut}}/(2\pi) = 640$ Hz is given by $T_S = 11.7 \pm 0.4$ s, corresponding to a rate constant of $T_S^{-1} = (85 \pm 3) \times 10^{-3}$ s$^{-1}$. Further increases in $^2$H rf field amplitudes were precluded by instrumental limitations. Although the application of a strong $^2$H rf field greatly extended the lifetime of the $^{13}$C singlet state, the longest observed time constant $T_S$ was still shorter than the spin-lattice relaxation time constant $T_1(13)$ $C = 14.0 \pm 0.5$ s in the same system.

The singlet relaxation rate constant $T_S^{-1}$ can be predicted in the presence of an on resonant radiofrequency field applied continuously to the deuterium nuclei throughout the singlet evolution interval $\tau_{\text{EV}}$. By using Equation 43, which applies for extreme-narrowing isotropic rotational tumbling, the estimate of the longitudinal relaxation time for the $^2$H nucleus (which was consequently used for the estimate of the rota-

B. Application of a $^2$H rf field

Experimental relaxation curves showing the decay of $^{13}$C nuclear singlet order for $I$ in the presence of on resonant $^2$H spin-locking rf fields are presented in Figure 17.

The black curve in Figure 17 shows the decay of $^{13}$C nuclear singlet order with coherent continuous wave irradiation, $\omega_{\text{nut}}/(2\pi) = 200$ Hz nutation frequency, applied to the $^2$H spins. The decay is monoexponential and has a decay time constant: $T_S = 5.3 \pm 0.4$ s. The grey curve in Figure 17 displays the decay of $^{13}$C nuclear singlet order in the presence of $^2$H CW irra-

internal-motion couplings$^{33,39,70}$.

The good match of the simulation to the experimental data, including the prominent biexponentiality of the decay, strongly supports the hypothesis that the relaxation of nuclei which have J-couplings to the $^{13}$C$_2$ spin pair induce singlet relaxation by a S-SR2K mechanism.

The importance of the S-SR2K mechanism may be tested by considering a second simulation (blue curve) in which the quadrupolar relaxation of the two deuterons is disconnected to the constituent nuclei of the singlet state by setting the $^{13}$C-$^2$H scalar couplings to zero, while leaving all other interactions unchanged. In this case, the simulation returns a much slower monoexponential decay (blue curve) which is clearly inconsistent with the experimental data. We conclude that scalar-relaxation-of-the-second-kind is a dominant relaxation mechanism for $^{13}$C$_2$ singlet order in this system.

Experimental relaxation curves showing the decay of $^{13}$C nuclear singlet order for $I$ in the presence of on resonant $^2$H spin-locking rf fields are presented in Figure 17.

The black curve in Figure 17 shows the decay of $^{13}$C nuclear singlet order with coherent continuous wave irradiation, $\omega_{\text{nut}}/(2\pi) = 200$ Hz nutation frequency, applied to the $^2$H spins. The decay is monoexponential and has a decay time constant: $T_S = 5.3 \pm 0.4$ s. The grey curve in Figure 17 displays the decay of $^{13}$C nuclear singlet order in the presence of $^2$H CW irra-

internal-motion couplings$^{33,39,70}$.

The good match of the simulation to the experimental data, including the prominent biexponentiality of the decay, strongly supports the hypothesis that the relaxation of nuclei which have J-couplings to the $^{13}$C$_2$ spin pair induce singlet relaxation by a S-SR2K mechanism.

The importance of the S-SR2K mechanism may be tested by considering a second simulation (blue curve) in which the quadrupolar relaxation of the two deuterons is disconnected to the constituent nuclei of the singlet state by setting the $^{13}$C-$^2$H scalar couplings to zero, while leaving all other interactions unchanged. In this case, the simulation returns a much slower monoexponential decay (blue curve) which is clearly inconsistent with the experimental data. We conclude that scalar-relaxation-of-the-second-kind is a dominant relaxation mechanism for $^{13}$C$_2$ singlet order in this system.
tional correlation time $\tau_c$, the in pair $^{13}$C-$^{13}$C dipole-dipole coupling constant (see the Supplementary Material (SM)), and the spin system parameters obtained from fitting the experimental $^{13}$C NMR spectrum, the following prediction of the singlet relaxation rate constant in the presence of CW irradiation resonant with the deuteron spins with 640 Hz nutation frequency is obtained: $T_S^{-1}(\omega_{\text{nut}}^S/2\pi = 640\text{ Hz}) = (6.4 \pm 0.5) \times 10^{-3}\text{ s}^{-1}$. As shown in the Supplementary Material (SM), dipole-dipole couplings from the central $^{13}$C nuclei to the adjacent deuteron spins are expected to provide an additional contribution to the singlet relaxation rate constant: $T_S^{-1}(\text{DD}) = (25 \pm 1) \times 10^{-3}\text{ s}^{-1}$. These combined mechanisms predict a value of $T_S$ of $31.8 \pm 0.9\text{ s}$, which is considerably longer than that found experimentally. The discrepancy is provisionally attributed to other relaxation mechanisms such as: long-range intramolecular dipole-dipole couplings, intermolecular dipole-dipole couplings, paramagnetic relaxation associated with molecular oxygen dissolved in solution, and spin-rotation or spin-internal-motion$^{33,39,70}$. We have not investigated these issues further.

C. Application of a $^{13}$C rf field

Experimental relaxation curves showing the decay of $^{13}$C nuclear singlet order for I in the presence of on resonant $^{13}$C rf fields are presented in Figure 19.

The decays have a single exponential form in all cases, with the singlet decay time constant increasing from $T_S = 9.6 \pm 0.6\text{ s}$ for a $^{13}$C field with nutation frequency of 200 Hz, to a time constant of $T_S = 23 \pm 4\text{ s}$ with a $^{13}$C nutation frequency of 1 kHz. Further increases in $^{13}$C rf field amplitudes were precluded by instrumental limitations. Note that the singlet lifetime of $23\text{ s}$ exceeds the $^{13}$C spin-lattice relaxation time constant of $T_1(^{13}\text{C}) = 14.0 \pm 0.5\text{ s}$ in the same system.

The experimental singlet relaxation rate constants $T_S^{-1}$ as a function of $^{13}$C spin-locking rf field amplitude, expressed as the nutation frequency $\omega_{\text{nut}}^S/2\pi$, are shown by the black data points in Figure 20. The first data point corresponds to $\omega_{\text{nut}}^S/2\pi = 0\text{ Hz}$. Numerically determined singlet relaxation rate constants are shown by the black curve. Simulations include singlet relaxation from the SR2K mechanism only.

The numerical simulation shows dramatic increase in the singlet relaxation rate constants $T_S^{-1}$ with the application of only a weak rf field on the $S$-spins, in agreement with the simulations presented in section II D. A maximum experimental singlet relaxation rate constant is observed at approximately $\omega_{\text{nut}}^S/2\pi = 25\text{ Hz}$, in agreement with the numerical simulation. The profile of the experimental and numerical curves are in good agreement.

The singlet decay rate constants $T_S^{-1}$ decrease with increasing $^{13}$C rf field amplitude beyond a nutation frequency of $\omega_{\text{nut}}^S/2\pi \sim 100\text{ Hz}$. A discrepancy between experimental and numerical results is observed in this case, and is attributed to additional relaxation mechanisms, such as the $^{13}$C-$^2\text{H}$ dipole-dipole contribution.

D. Simultaneous rf fields on $^2\text{H}$ and $^{13}$C nuclei

A further extension in $^{13}$C singlet lifetime is achieved by applying simultaneous rf fields resonant with the $^{13}$C and $^2\text{H}$ nuclei (see Figure 21). In this case, the two fields have a cumulative effect on the suppression of the singlet-scalar relax-
Figure 15 in the presence of simultaneous singlet order was measured by using the pulse sequence described in Figure 21 in the presence of simultaneous singlet order was measured by using the pulse sequence described in and 2513 acquired at 11.75 T (see Figure 22). This compound displays an exceptionally long 13C singlet lifetime, which exceeds $T_S = 1$ hour for a degassed solution in low magnetic field. Could this long lifetime be limited by weak SR2K effects from the 28 remote deuterons?

The $^2$H $T_1$ has been estimated to be $(905 \pm 45) \times 10^{-3}$ s by an inversion-recovery experiment for II dissolved in degassed acetone-$d_6$ solvent acquired at 9.4 T (nuclear Larmor frequency = 61.4 MHz) and 25°C. The measured $^2$H longitudinal relaxation time is relatively long compared to typical deuteron relaxation times in solution, presumably reflecting the high mobility of the deuterated side chains.

The contribution of SR2K relaxation to the singlet lifetime of II is estimated by analysing the deuteron relaxation time $T_1(^2\text{H}) = (905 \pm 45) \times 10^{-3}$ s$^{-1}$ using Equation 37.

For simplicity, assume that the differential J-coupling $\omega_\Delta$ is the same for all 28 deuterons. The total contribution to the 13C singlet relaxation rate constant is given approximately by:

$$T_S^{-1}(\text{from}^{2}\text{H}) \simeq 28 \times \text{eqn} \; 37$$

using $R_S^\Delta = (3/2) b_{CC}^2 \tau_e$ and the following spin system parameters: $\omega_J/2\pi = 54.6 \, \text{Hz}$, $\tau_e = 20 \, \text{ps}$, and $b_{CC}/2\pi = -2.654 \, \text{kHz}$ (estimated from a 13C,13C internuclear separation of 142 pm).

Equation 59 is a strong function of the differential J-coupling $\omega_\Delta$. It is hard to obtain an experimental estimate of this parameter, since the $^2$H,13C couplings are too small to resolve. Quantum chemistry calculations may be feasible but would have to take into account the conformational flexibility and have not been attempted at this stage.

Nevertheless we note that the observed 13C singlet relaxation rate constant of $0.21 \pm 0.02 \times 10^{-3}$ s$^{-1}$ could be fully attributed to the SR2K mechanism if all 28 remote deuterons had a differential coupling of only $|\omega_\Delta/2\pi| = 0.35 \, \text{Hz}$ to the two 13C nuclei. This value is not wildly unreasonable. The issue could be settled by applying resonant $^1$H or 13C irradiation in an attempt to further extend the 13C singlet relaxation time by suppressing the SR2K mechanism. The resonant irradiation would have to be applied in low magnetic field. This experiment is planned.

VI. CONCLUSION

We conclude that the SR2K mechanism may be an important contribution to limiting long singlet lifetimes, and cannot
be neglected, even in the case of remote quadrupolar spins.

It should be noted that other interesting molecules may also exhibit S-SR2K. Systems comprising of H\textsubscript{2}C=CD-CO\textsubscript{2}R substructures, such as styrene-d\textsubscript{1}, are of suitable type. However, the S-SR2K mechanism may only be isolated through implementing field cycling experiments as the large proton chemical shift difference introduces relaxation contributions from singlet-triplet leakage. It is also not yet known whether the proton singlet state of H\textsubscript{2}C=CX-CO\textsubscript{2}R systems, where X is a quadrupolar nucleus relaxing on the timescale of the proton nuclear Larmor frequency, such as Br or Cl, display observable S-SR2K. Investigations into this effect are feasible on molecular systems such as bromoacrylates and bromothiophenes but would require detailed computational modelling or molecular dynamics, and also measurement of the quadrupolar X-atom T\textsubscript{1}.

**SUPPLEMENTARY MATERIAL**

See supplementary material for details regarding chemical synthesis, experimental methods, quantum chemistry, and numerical simulations.

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**APPENDIX: PERTURBATIVE TREATMENT**

A. Effective Hamiltonian via Primas-van Vleck perturbation theory

Consider the standard perturbation problem where the eigenstates and eigenvalues of the main Hamiltonian, H\textsubscript{0}, are perturbed by λV with λ ≪ 1:

\[ H = H_0 + \lambda V. \]  

(61)

In most cases, an approximate solution may be derived by Rayleigh-Schrödinger perturbation theory\textsuperscript{71}. In the case of degenerate or near-degenerate eigenvalues, the Rayleigh-Schrödinger approach becomes difficult. For the current problem, we prefer the Primas-van Vleck perturbation approach, also called the contact transformation, rather than the Rayleigh-Schrödinger approach\textsuperscript{61–65}.

The set of eigenvalues of H\textsubscript{0} is called the spectrum of H\textsubscript{0} and is denoted by:

\[ \sigma(H_0) = \{ \lambda_1, \lambda_2, \ldots, \lambda_N \} \]

\[ H_0|n_j\rangle = \lambda_j|n_j\rangle. \]  

(62)

A particular eigenvalue of H\textsubscript{0} may be degenerate so that more than one eigenvector may belong to the same eigenvalue. We denote the multiplicity of an eigenvalue by D\textsubscript{j} and distinguish the corresponding eigenvectors by introducing a second label \(|n_{jk}\rangle\). The degenerate eigenvectors fulfill the equation:

\[ H_0 \left( \sum_{k=1}^{D_j} c_{jk}|n_{jk}\rangle \right) = \lambda_j \left( \sum_{k=1}^{D_j} c_{jk}|n_{jk}\rangle \right) \]  

(63)

and span a D\textsubscript{j} dimensional eigenspace of \(\lambda_j\). The projection superoperator onto the eigenspace belonging to the eigenvalue \(\lambda_j\) is defined as:

\[ \hat{P}_j = \sum_{k=1}^{D_j} |n_{jk}\rangle \langle n_{jk}|. \]  

(64)

Consider the sum of all such projection superoperators:

\[ \hat{P}_0 = \sum_{j=1}^{N} \hat{P}_j. \]  

(65)

The superoperator \(\hat{P}_0\) may be used to decompose any operator into a parallel (commuting) and anti-parallel (non-commuting) part with respect to \(H_0\):

\[ Q_\parallel = \hat{P}_0 Q \quad Q_\perp = I - Q_\parallel \]

\[ \hat{P}_0 Q_\parallel = Q_\parallel \quad \hat{P}_0 Q_\perp = 0. \]  

(66)

Parallel and anti-parallel parts remain parallel and anti-parallel upon commutation with \(H_0\):

\[ [H_0, Q_\perp] = S_\perp \]  

(67)

with \(S_\perp\) being some anti-parallel operator.

With these considerations in place we slightly reformulate the perturbation problem. We are searching for a unitary transformation superoperator \(\hat{U}\) that block-diagonalizes \(H\). In general the action of the superoperator \(\hat{U}\) may be expressed as shown below:

\[ \hat{U} H = H_0 + W \]

\[ W = \hat{U} H - H_0. \]  

(68)

Here \(W\) is a block-diagonal operator, still to be determined. This approach amounts to removing off-diagonal elements between different eigenspaces of \(H_0\). The transformation superoperator \(\hat{U}\) is generally given by the exponential of an anti-hermitian generator \(\hat{G}\):

\[ \hat{U} = \exp(\hat{G}) \]

\[ \hat{G}^\dagger = -\hat{G}. \]  

(69)

The choice of \(\hat{G}\) is ill-defined at this point since any unitary equivalent form of \(\hat{G}\) would lead to an unitary equivalent representation. This issue is circumvented by imposing the following constraints:

\[ \hat{P}_0 G = 0 \quad \hat{P}_0 W = W. \]  

(70)
A perturbative solution to equation 68 is constructed by expanding $\hat{G}$ and $W$ in powers of $\lambda$:

$$
\hat{G} = \lambda \hat{G}_1 + \lambda^2 \hat{G}_2 + \ldots \\
W = \lambda W_1 + \lambda^2 W_2 + \ldots 
$$

(71)

Truncating $W$ at a certain point leads to an effective Hamiltonian within the eigenspaces of $H_0$. Substitution of the power series expansion into equation 68 leads to:

$$
\lambda W_1 + \lambda^2 W_2 + \ldots = \left( \sum_{n=0}^{\infty} \frac{1}{n!} \hat{G}_n^2 H \right) - H_0 \\
= \lambda V \\
+ (\lambda \hat{G}_1 + \lambda^2 \hat{G}_2 + \ldots) H \\
+ (\lambda \hat{G}_1 + \lambda^2 \hat{G}_2 + \ldots)^2 H \\
+ \ldots 
$$

(72)

Collecting terms of the same power in $\lambda$ leads to recursive commutator equations of the type:

$$
\hat{H}_0 G_1 = V - W_1 = A_1 - W_1 \\
\hat{H}_0 G_2 = \hat{G}_1 V + \frac{1}{2} \hat{G}_2^2 H_0 - W_2 = A_2 - W_2 \\
\ldots \\
\hat{H}_0 G_n = A_n - W_n. 
$$

(73)

We may solve for $W_n$ by making use of the properties in equation 67 and the constraints of equation 70:

$$
\hat{P}_0 (\hat{H}_0 G_n) = 0 \\
\hat{P}_0 A_n - \hat{P}_0 W_n = \hat{P}_0 A_n - W_n \\
\implies W_n = \hat{P}_0 A_n. 
$$

(74)

The result for $W_n$ may then be substituted back into equation 73. To solve for $G_n$ we calculate the pseudo-inverse of $\hat{H}_0$. The solution to the perturbative treatment is therefore given by:

$$
W_n = \hat{P}_0 A_n \\
G_n = \hat{H}_0^+ (A_n - W_n) = \hat{H}_0^+ (A_n - \hat{P}_0 A_n).
$$

(75)

B. Application of Primas-van Vleck perturbation theory

We applied Primas-van Vleck perturbation theory in section 2.3 to derive the analytic expressions for the various spin-lock cases. We illustrate the method for the simplest case of no applied rf fields. The other results may be obtained in a similar manner.

As explained in the main text, the dynamics of this case may be restricted to a $4 \times 4$ block of the full Liouvillian. The relevant block takes the form:

$$
\begin{pmatrix}
0 & 0 & 0 & -i\omega_3/\sqrt{6} \\
0 & -\frac{3}{2}R_1^2 & 0 & i\omega_3/2\sqrt{6} \\
0 & 0 & -R_1^3 - \frac{1}{3}R_1^3 & -i\omega_3 \\
-i\omega_3/\sqrt{6} & i\omega_3/2\sqrt{6} & -i\omega_3 & -R_1^3 - \frac{1}{3}R_1^3
\end{pmatrix}
$$

(76)

We attempt to find a perturbative solution by making the following assumption:

$$
L_0 + L_1 = 
\begin{pmatrix}
0 & 0 & 0 & 0 \\
0 & -\frac{3}{2}R_1^2 & 0 & 0 \\
0 & 0 & -R_1^3 - \frac{1}{3}R_1^3 & -i\omega_3 \\
0 & 0 & -i\omega_3 & -R_1^3 - \frac{1}{3}R_1^3
\end{pmatrix}
$$

(77)

To get reasonable results it is important to notice that the separation between the eigenvalues $0$ and $-\frac{3}{2}R_1^2$ is not big enough to ignore the state mixing of $|1\rangle$ and $|2\rangle$. As a result the set $\{|1\rangle, |2\rangle\}$ forms a quasi-degenerate manifold and the set $\{|3\rangle, |4\rangle\}$ forms a degenerate manifold. The projector $\hat{P}_0$ onto the subspace of $L_0$ is consequently given by:

$$
\hat{P}_0 Q = (|1\rangle\langle 1| + |2\rangle\langle 2|) Q (|1\rangle\langle 1| + |2\rangle\langle 2|) \\
+ (|3\rangle\langle 3| + |4\rangle\langle 4|) Q (|3\rangle\langle 3| + |4\rangle\langle 4|).
$$

(78)

Equation 73 shows that the anti-hermitian generator, $\hat{G}_1$, of the transformation is recursively determined from $H_0$ and $V$. For problems in Hilbert space $H$ and $V$ will be hermitian. For generators in Liouville space such as $L_0$ and $L_1$ to be hermitian, so that Primas-van Vleck perturbation theory remains valid. The effective Liouvillian to second order may then be written as:

$$
L_{eff} = L_0 + \lambda \hat{P}_0 A_1 + \lambda^2 \hat{P}_0 A_2.
$$

(79)

The first order term is given by:

$$
W_1 = 
\begin{pmatrix}
1 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0
\end{pmatrix}
- \begin{pmatrix}
0 & 0 & 0 & -i\omega_3/\sqrt{6} \\
0 & 0 & 0 & i\omega_3/2\sqrt{6} \\
0 & 0 & 0 & 0 \\
-i\omega_3/\sqrt{6} & i\omega_3/2\sqrt{6} & 0 & 0
\end{pmatrix}
$$

(80)

As a result the recursion for the generator to first order may be evaluated to give:

$$
G_1 = 
\begin{pmatrix}
0 & 0 & 0 & -3\sqrt{\frac{3}{2}} \frac{a_0}{(3R_1^2 + R_1^2)^2 + 9a_0^2} \\
0 & 0 & 0 & -75\sqrt{\frac{3}{2}} \frac{a_0}{(15R_1^2 - 4R_1^2)^2 + 225a_0^2} \\
i\sqrt{\frac{3}{2}} \frac{a_0}{(3R_1^2 + R_1^2)^2 + 9a_0^2} & 75\sqrt{\frac{3}{2}} \frac{a_0}{(15R_1^2 - 4R_1^2)^2 + 225a_0^2} & 0 \\
i\sqrt{\frac{3}{2}} \frac{a_0}{(3R_1^2 + R_1^2)^2 + 9a_0^2} & 75\sqrt{\frac{3}{2}} \frac{a_0}{(15R_1^2 - 4R_1^2)^2 + 225a_0^2} & 0
\end{pmatrix}
$$

(81)
Such that the second order correction amounts to:

$$W_2 = \left( \begin{array}{cc} \frac{3R_1^2 + R_2^2}{2(3R_1^2 + R_2^2 + 9\sigma_j^2)} & \frac{30R_1^2 + R_2^2}{4(3R_1^2 + R_2^2 + 9\sigma_j^2)} + 450\sigma_j^2 \\ \frac{3(30R_1^2 + R_2^2)}{4(3R_1^2 + R_2^2 + 9\sigma_j^2)} & \frac{(30R_1^2 + R_2^2)(15R_1^2 - 4R_2^2)(30R_1^2 + R_2^2)}{2(3R_1^2 + R_2^2 + 9\sigma_j^2)} \\ \end{array} \right)$$

The general structure of the effective Liouvillian is given by:

$$L_{eff} = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$


