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Theory of Stochastic Dipolar Recoupling in Solid State Nuclear Magnetic Resonance

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Abstract

Dipolar recoupling techniques in solid state nuclear magnetic resonance (NMR) consist of radio-frequency (rf) pulse sequences applied in synchrony with magic-angle spinning (MAS) that create non-zero average magnetic dipole-dipole couplings under MAS. Stochastic dipolar recoupling (SDR) is a variant in which randomly chosen rf carrier frequency offsets are introduced to cause random phase modulations of individual pairwise couplings in the dipolar spin Hamiltonian. Several aspects of SDR are investigated through analytical theory and numerical simulations: (1) An analytical expression for the evolution of nuclear spin polarization under SDR in a two-spin system is derived and verified through simulations, which show a continuous evolution from coherent, oscillatory polarization exchange to incoherent, exponential approach to equilibrium as the range of random carrier offsets (controlled by a parameter $f_{\max}$) increases; (2) In a many-spin system, polarization transfers under SDR are shown to be described accurately by a rate matrix in the limit of large $f_{\max}$, with pairwise transfer rates that are proportional to the inverse sixth power of pairwise internuclear distances; (3) Quantum mechanical interferences among non-commuting pairwise dipole-dipole couplings, which are a complicating factor in solid state NMR studies of molecular structures by traditional dipolar recoupling methods, are shown to be absent from SDR data in the limit of large $f_{\max}$, provided that coupled nuclei have distinct NMR chemical shifts.

Keywords

magic-angle spinning; molecular structure; Liouville operator; decoherence

Introduction

In nuclear magnetic resonance (NMR) studies of the molecular structures of solids¹⁻¹³, dipolar recoupling techniques are commonly employed as measurements of magnetic dipole-dipole couplings, and hence distances, between atomic nuclei under high-resolution spectroscopic conditions. Dipolar recoupling techniques¹⁴⁻¹⁷ consist of periodic and cyclic¹⁸ sequences of radio-frequency (rf) pulses that are applied in synchrony with magic-angle spinning (MAS), with the pulse sequence cycle time τ_c equal to a multiple of the sample rotation period τ_R . Under MAS and in an interaction representation with respect to the rf pulses, the nuclear spin dipole-dipole coupling Hamiltonian for a system of like spins has the time-dependent form^{19,20}

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$$\tilde{H}_D(t) = \sum_{i>j} \frac{\gamma^2 \hbar}{R_{ij}^3} (a_{ij} e^{i\omega_R t} + a_{ij}^* e^{-i\omega_R t} + b_{ij} e^{2i\omega_R t} + b_{ij}^* e^{-2i\omega_R t}) \times [c(t) I_{i+} I_{j+} + c(t)^* I_{i-} I_{j-} + d(t) (I_{i+} I_{zj} + I_{zi} I_{j+}) + d(t)^* (I_{i-} I_{zj} + I_{zi} I_{j-}) + e(t) (3I_{zi} I_{zj} -$$

(1)

where γ is the nuclear gyromagnetic ratio, R_{ij} is the distance between nuclei i and j , ω_R is the MAS frequency, I_i is the spin angular momentum vector operator for spin i , and $I_{\pm} = I_x \pm iI_y$. The complex coefficients a_{ij} and b_{ij} are functions of the internuclear direction relative to an axis system fixed in the MAS rotor^{19,21}. The coefficients c , d , and e (with $e = e^*$) depend on the details of the rf pulse sequence and are the same for all spin pairs (assuming perfectly homogeneous rf fields). In Eq. (1), $\tilde{H}_D(t)$ is expressed in angular frequency units, as are all other Hamiltonian operators below.

Without rf pulses, $c = d = 0$, $e = 1$, and the time average of $\tilde{H}_D(t)$ is zero (*i.e.*, the nuclei are *decoupled* by MAS). With pulses, in general $\tilde{H}_D^{(0)} \equiv \frac{1}{\tau_c} \int_0^{\tau_c} dt \tilde{H}_D(t) \neq 0$ (*i.e.*, the spins are

recoupled). If $\frac{\gamma^2 \hbar}{R_{ij}^3} \tau_c \ll 1$ for all spin pairs and if other types of spin interactions (*e.g.*, anisotropic or isotropic chemical shifts) are not recoupled or are negligibly small, to a good approximation the net evolution of the nuclear spin system during the recoupling sequence is equivalent to evolution under the average Hamiltonian $\tilde{H}_D^{(0)}$, which generally has the form

$$\tilde{H}_D^{(0)} = \sum_{i>j} \frac{\gamma^2 \hbar}{R_{ij}^3} A_{ij} \quad (2)$$

where the Hermitian operator A_{ij} is a linear combination of the five operator terms on the right-hand side of Eq. (1). In applications of dipolar recoupling to structural problems, one hopes to extract the internuclear distances R_{ij} from NMR signals that are determined by evolution under $\tilde{H}_D^{(0)}$. However, the couplings between spins with relatively large R_{ij} act as perturbations on the couplings between spins with relatively small R_{ij} . In general, $[A_{ij}, A_{ik}] \neq 0$. Therefore, couplings between spins with relatively large R_{ij} have relatively minor effects on the

eigenvalues and eigenstates of $\tilde{H}_D^{(0)}$, and hence relatively minor effects on the nuclear spin evolution and NMR signals. Unfortunately, the larger internuclear distances are often the most important distances in structural studies, while shorter distances (*e.g.*, one-bond and two-bond distances in a ^{13}C -labeled organic molecule) are already known from elementary principles of chemical bonding. In practice, the quantum mechanical suppression of weak dipole-dipole couplings by stronger couplings, arising from the non-commutivity of pairwise coupling terms in $\tilde{H}_D^{(0)}$ and sometimes called “dipolar truncation” in the solid state NMR literature²²⁻²⁵, commonly prevents quantitative measurements of structurally significant internuclear distances in multiply-labeled or uniformly-labeled samples²⁶.

I have recently introduced a variant of dipolar recoupling techniques, called “stochastic dipolar recoupling” (SDR), that is intended to eliminate quantum mechanical interferences among pairwise dipole-dipole couplings and thereby facilitate measurements of internuclear distances in solid state NMR²⁷. In this paper, I discuss several theoretical aspects of SDR. In particular, I derive an analytical expression for the evolution of nuclear spin polarization under SDR in a two-spin system, discuss the generalization of this expression to many-spin systems, and present the results of numerical simulations on three-spin systems that illustrate important properties of SDR.

General Properties of Stochastic Dipolar Recoupling

In an SDR measurement, one applies an rf pulse sequence that consists of alternating blocks of double-quantum (DQ) dipolar recoupling and free evolution under isotropic chemical shifts (CS), with durations $n\tau_R$ and $m\tau_R$, as shown in Fig. 1. By definition, the average nuclear spin Hamiltonian during DQ periods is

$$\tilde{H}_D^{(0)} = \sum_{i>j} \frac{\gamma^2 \hbar}{R_{ij}^3} (g_{ij} I_{+i} I_{+j} + g_{ij}^* I_{-i} I_{-j}) \quad (3)$$

During the k^{th} CS period, the average Hamiltonian is

$$\tilde{H}_{CS}^{(0)}(k) = \sum_i (\delta_i + f_k) I_{zi} \quad (4)$$

where δ_i is the chemical shift of spin i and f_k is an rf carrier frequency offset, generally different in each CS period. The net spin evolution operator after N DQ and CS periods can be written

$$U(N) = \prod_{k=1}^N \left\{ \exp \left[-im \tilde{H}_{CS}^{(0)}(k) \tau_R \right] \exp \left[-in \tilde{H}_D^{(0)} \tau_R \right] \right\} \quad (5a)$$

$$= \exp \left[-im \sum_{k=1}^N \tilde{H}_{CS}^{(0)}(k) \tau_R \right] \prod_{k=1}^N \exp \left[-in \tilde{H}_D^{(0)}(k) \tau_R \right] \quad (5b)$$

with $\tilde{H}_D^{(0)}(1) = \tilde{H}_D^{(0)}$ and

$$\tilde{H}_D^{(0)}(k) = \exp \left[im \sum_{q=1}^{k-1} \tilde{H}_{CS}^{(0)}(q) \tau_R \right] \tilde{H}_D^{(0)} \exp \left[-im \sum_{q=1}^{k-1} \tilde{H}_{CS}^{(0)}(q) \tau_R \right] \quad (6a)$$

$$= \sum_{i>j} \frac{\gamma^2 \hbar}{R_{ij}^3} \left[g_{ij} e^{i\Phi_{ij}(k)} I_{+i} I_{+j} + g_{ij}^* e^{-i\Phi_{ij}(k)} I_{-i} I_{-j} \right] \quad (6b)$$

for $k > 1$. Eqs. (5) and (6) describe a transformation of $\tilde{H}_D^{(0)}$ to a new interaction representation with respect to $\tilde{H}_{CS}^{(0)}(k)$. In this representation, the CS periods have the effect of introducing phase modulations of the pairwise couplings between spins i and j , determined by the chemical shifts and carrier frequency offsets according to

$$\Phi_{ij}(k) = \sum_{q=1}^{k-1} m (\delta_i + \delta_j + 2f_q) \tau_R \quad (7)$$

In general, $\Phi_{ij}(k)$ is different for each spin pair, provided the chemical shift sums $\delta_i + \delta_j$ are different.

In earlier work on frequency-selective dipolar recoupling²⁸, carrier frequency offsets were chosen specifically to make $\Phi_{ij}(k) = 0$ for one spin pair and $\Phi_{ij}(k) = (k-1)\Phi_{ij}(2) \neq 0$ for all other spin pairs. Then all pairwise couplings on the right-hand side of Eq. (6b) were averaged to zero in a coherent manner, except for the coupling between the selected spin pair.

In SDR, f_k values are chosen randomly from the interval $[-f_{\text{max}}, f_{\text{max}}]$, with different random choices in each repetition of a given measurement (*i.e.*, in each “scan”). When $m f_{\text{max}} \tau_R$ is large, the resulting random phase modulations in Eq. (6b) are expected to average all pairwise dipole-dipole couplings to zero in an incoherent manner that is loosely analogous to the manner in

which dipole-dipole couplings are averaged to zero by random molecular tumbling in liquid state NMR. If $\delta_i + \delta_j$ is different for each spin pair, the phase modulations of different pairwise couplings should tend to be uncorrelated. Nuclear spin evolution under SDR, when averaged over many scans, should then be analogous to the cross-relaxation processes (*i.e.*, nuclear Overhauser effects) among dipole-coupled spins that are commonly observed and exploited in NMR studies of liquids and solutions²⁹⁻³². Rather than evolving in a coherent, oscillatory fashion, nuclear spin polarizations should approach quasi-equilibrium values in an exponential-like fashion that can be described by polarization transfer rates that are proportional to R_{ij}^{-6} . Quantum mechanical interference among non-commuting pairwise couplings (*i.e.*, dipolar truncation) should be absent in the limit of large $mf_{\max}\tau_R$. It should be possible to control the progression from coherent to incoherent nuclear spin dynamics through the parameter $f_{\max}$.

In a previous report²⁷, these expectations regarding the behavior of NMR signals in an SDR measurement were verified experimentally. Fig. 2 shows additional experimental ^{13}C solid state NMR data that demonstrate the properties of SDR in two-spin systems. Experiments were performed on doubly- $^{13}\text{CH}_3$ -labeled sodium bisulfite adduct of acetone ($^{13}\text{C}_2$ -BSA) in powdered form, with 1:20 dilution of labeled molecules in unlabeled molecules to attenuate intermolecular dipole-dipole couplings. In this compound, the intramolecular ^{13}C - ^{13}C distance is $2.51 \text{ \AA}$ ^{15,33}. In the fully coherent limit ($f_{\max} = 0$) and with the rf carrier frequency fixed at a value such that $\delta_i + \delta_j = 0$, the NMR signals exhibit a damped oscillatory dependence on the recoupling period $N\tau_R$, with an oscillation period that is inversely proportional to the matrix element $|\langle ++ | \tilde{H}_D^{(0)} | -- \rangle|$, or proportional to R^3 . In the fully incoherent limit ($mf_{\max}\tau_R \gg 1$), the NMR signals decay monotonically with increasing $N\tau_R$, on a time scale that is inversely proportional to $|\langle ++ | \tilde{H}_D^{(0)} | -- \rangle|^2$, or proportional to R^6 .

In the intermediate case ($0 < mf_{\max}\tau_R < 1$), one might expect that no simple theory could describe the dependence of NMR signals on $N\tau_R$ and that numerical simulations would be necessary to analyze or reproduce experimental data. Surprisingly, for two-spin systems, an analytical expression that is valid for all values of $f_{\max}$ can be derived, as shown below.

Analytical Theory for Two-Spin Systems

In a two-spin system, $\tilde{H}_D^{(0)} = \frac{\gamma^2 \hbar}{R^3} (gI_{+1}I_{+2} + g^* I_{-1}I_{-2})$ and

$\tilde{H}_{CS}^{(0)}(k) = \frac{1}{2} (\delta_1 + \delta_2 + 2f_k) (I_{z1} + I_{z2}) + \frac{1}{2} (\delta_1 - \delta_2) (I_{z1} - I_{z2})$. With the definitions

$$J_{\Sigma} \equiv \frac{1}{2} (I_{z1} + I_{z2}) \quad (8a)$$

$$J_{\Delta} \equiv \frac{1}{2} (I_{z1} - I_{z2}) \quad (8b)$$

$$J_x \equiv \frac{1}{2} (I_{+1}I_{+2} + I_{-1}I_{-2}) \quad (8c)$$

$$J_y \equiv -\frac{i}{2} (I_{+1}I_{+2} - I_{-1}I_{-2}) \quad (8d)$$

and the assumption $\delta_1 + \delta_2 = 0$ (*i.e.*, the rf carrier frequency is at the average of the two NMR frequencies when $f_k = 0$), the evolution operator for SDR in Eq. (5a) becomes

$$U(N) = \exp \left[-iN m (\delta_1 - \delta_2) \tau_R J_{\Delta} \right] \prod_{k=1}^N \left\{ \exp(-i2mf_k \tau_R J_{\Sigma}) \exp \left[-i \text{ind}_{12} \tau_R (J_x \cos \alpha + J_y \sin \alpha) \right] \right\} \quad (9)$$

with $d_{12} \equiv \frac{2\gamma^2\hbar}{B^3}|g|$ and $g=|g|e^{i\alpha}$. As in earlier examples of “fictitious spin-1/2” operators in NMR^{28,34-36}, the operators J_x , J_y , and J_Σ satisfy the same commutation relations as the three components of an angular momentum vector operator, *e.g.*, $[J_x, J_y] = iJ_\Sigma$. Moreover, these three operators commute with J_Δ . Eq. 9 can then be rewritten as

$$U(N) = \exp[-iNm(\delta_1 - \delta_2)\tau_R J_\Delta] \exp(ij_\Sigma \alpha) \times \left\{ \prod_{k=1}^N \left\{ \exp(-i2mf_k \tau_R J_\Sigma) \exp(-ind_{12} \tau_R J_x) \right\} \right\} \exp(-iJ_\Sigma \alpha) \quad (10)$$

using the relation $\exp(iJ_\Sigma \alpha) J_x \exp(-iJ_\Sigma \alpha) = J_x \cos \alpha + J_y \sin \alpha$, which is a consequence of the commutation relations among J_x , J_y , and J_Σ .

We assume that the initial state of the two-spin system is described by longitudinal polarizations $p_1(0)$ and $p_2(0)$. This state corresponds to a density operator

$$\rho(0) = p_1(0) I_{z1} + p_2(0) I_{z2} \quad (11a)$$

$$= p_\Delta(0) J_\Delta + p_\Sigma(0) J_\Sigma \quad (11b)$$

with $p_\Delta(0) = p_1(0) - p_2(0)$ and $p_\Sigma(0) = p_1(0) + p_2(0)$. Subsequent evolution under $U(N)$ transforms the system to a state described by the density operator $\rho(N) = U(N)\rho(0)U(N)^{-1}$. Eqs. (10) and (11) and the commutation relations given above, according to which J_x , J_y , and J_Σ are generators of rotations in a three-dimensional space in analogy to the usual properties of angular momentum operators, imply that

$$\rho(N) = p_\Delta(0) J_\Delta + p_\Sigma(0) \left[u(N) J_x + v(N) J_y + w(N) J_\Sigma \right] \quad (12)$$

In other words, the J_Δ component of the density operator is conserved, and the J_Σ component of the density operator is transformed into a linear combination of J_x , J_y , and J_Σ . The coefficients $u(N)$, $v(N)$, and $w(N)$ form a three-dimensional “polarization” vector of unit length, which is derived from the initial polarization vector $(u(0), v(0), w(0)) = (0, 0, 1)$ by application of a series of rotations, alternating between a rotation about x by $\theta_x = -nd_{12}\tau_R$ and a rotation about J_Σ by $\theta_\Sigma(k) = -2mf_k\tau_R$ as is apparent in Eq. (10). The initial and final rotations about J_Σ by $-\alpha$ and α and the final transformation about J_Δ by $-Nm(\delta_1 - \delta_2)\tau_R$ in Eq. (10) do not affect longitudinal polarizations and hence do not affect the calculations below.

In an SDR experiment, one averages over many scans, with different random choices of f_k values in each scan²⁷. The measured NMR signals depend only on the final longitudinal polarizations at the end of the SDR period in Fig. 1, in other words the final J_Σ component of the density operator, or the value $w(N)$. In principle, the average value of this quantity can be calculated from the expression

$$\langle w(N) \rangle = \langle \text{Tr} \{ J_\Sigma U(N) J_\Sigma U(N)^{-1} \} \rangle \quad (13a)$$

$$= \text{Tr} \{ J_\Sigma \langle U(N) J_\Sigma U(N)^{-1} \rangle \} \quad (13b)$$

$$= \text{Tr} \left\{ J_\Sigma \left\langle \prod_{k=1}^N \left\{ \exp[i\theta_\Sigma(k) J_\Sigma] \exp(in\theta_x J_x) \right\} J_\Sigma \prod_{k'=1}^N \left\{ \exp[-i\theta_\Sigma(k') J_\Sigma] \exp(-in\theta_x J_x) \right\} \right\rangle \right\} \quad (13c)$$

where $\langle F \rangle$ symbolizes the average of a function F over the f_k values. However, each f_k appears twice in Eq. (13c), in both $U(N)$ and $U(N)^{-1}$, preventing a simple evaluation of the average even in the absence of correlations among f_k values, *i.e.*, even if $\langle f_k f_{k'} \rangle = \delta_{k,k'} \langle f_k^2 \rangle$. In contrast, the same quantity can also be calculated from the expression

$$\langle w(N) \rangle = \langle (0,0,1) \cdot \prod_{k=1}^N R_{\Sigma}(\theta_{\Sigma}(k)) R_x(\theta_x) \cdot \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix} \rangle \quad (14a)$$

$$= (0,0,1) \cdot \left\langle \prod_{k=1}^N R_{\Sigma}(\theta_{\Sigma}(k)) R_x(\theta_x) \right\rangle \cdot \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix} \quad (14b)$$

$$= (0,0,1) \cdot \prod_{k=1}^N \langle R_{\Sigma}(\theta_{\Sigma}(k)) \rangle R_x(\theta_x) \cdot \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix} \quad (14c)$$

where $R_{\Sigma}(\theta)$ and $R_x(\theta)$ are 3×3 matrices for rotations about J_{Σ} and J_x in the space spanned by J_x , J_y , and J_{Σ} . Eq. (14c) assumes that f_k values with different k are uncorrelated, as is true in SDR experiments. The rotation matrices are readily evaluated as

$$R_x(\theta_x) = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos \theta_x & -\sin \theta_x \\ 0 & \sin \theta_x & \cos \theta_x \end{pmatrix} \quad (15)$$

$$\langle R_{\Sigma}(\theta_{\Sigma}) \rangle = \begin{pmatrix} \langle \cos \theta_{\Sigma} \rangle & -\langle \sin \theta_{\Sigma} \rangle & 0 \\ \langle \sin \theta_{\Sigma} \rangle & \langle \cos \theta_{\Sigma} \rangle & 0 \\ 0 & 0 & 1 \end{pmatrix} \quad (16a)$$

$$= \begin{pmatrix} \frac{1}{\theta_{\max}} \sin \theta_{\max} & 0 & 0 \\ 0 & \frac{1}{\theta_{\max}} \sin \theta_{\max} & 0 \\ 0 & 0 & 1 \end{pmatrix} \quad (16b)$$

with $\theta_{\max}(k) = -2mf_{\max}\tau_R$. Eq. (16b) assumes that all f_k values are sampled uniformly from the same interval $[-f_{\max}, f_{\max}]$. Combining Eqs. (14-16),

$$\langle w(N) \rangle = (0,0,1) \cdot \begin{pmatrix} \frac{1}{\theta_{\max}} \sin \theta_{\max} & 0 & 0 \\ 0 & \frac{1}{\theta_{\max}} \sin \theta_{\max} \cos \theta_x & -\frac{1}{\theta_{\max}} \sin \theta_{\max} \sin \theta_x \\ 0 & \sin \theta_x & \cos \theta_x \end{pmatrix}^N \cdot \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix} \quad (17)$$

In the limit $\theta_{\max} \gg 1$ [which is a short correlation limit for the phase factors $e^{i\Phi_{ij}(k)}$ in Eq. (6b)],

$$\langle w(N) \rangle \approx (0,0,1) \cdot \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & \sin \theta_x & \cos \theta_x \end{pmatrix}^N \cdot \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix} \quad (18a)$$

$$= \cos^N \theta_x \quad (18b)$$

implying an exponential decay of the total NMR signal, proportional to $e^{-\lambda N}$ with

$$\lambda = -\ln(\cos \theta_x) = -\ln\left(\cos \frac{2n\gamma^2 \hbar |g| \tau_R}{R^3}\right). \text{ In the weak coupling limit } \theta_x \ll 1, \lambda \approx \frac{2\gamma^4 (n\hbar |g| \tau_R)^2}{R^6}.$$

For arbitrary parameters, $\langle w(N) \rangle$ can be evaluated by diagonalizing the lower right-hand 2×2 block of the 3×3 matrix in Eq. (17). In general, the two eigenvalues ε_+ and ε_- of the 2×2 block are complex numbers, and the two eigenvectors are not orthogonal. Nonetheless, the eigenvalues can be determined from a quadratic equation in the usual way, the vector $(0,0,1)$ can be represented as a linear combination of the two eigenvectors, and this linear combination

can be projected back onto the vector (0,0,1) after multiplying the two eigenvector components by ε_+^N and ε_-^N . The resulting general expression for $\langle w(N) \rangle$ is

$$\langle w(N) \rangle = \frac{\varepsilon_+^N (\cos\theta_x - \varepsilon_-) - \varepsilon_-^N (\cos\theta_x - \varepsilon_+)}{\varepsilon_+ - \varepsilon_-} \quad (19a)$$

$$\varepsilon_{\pm} = \frac{1}{2} \left(1 + \frac{\sin\theta_{\max}}{\theta_{\max}} \right) \cos\theta_x \pm \frac{1}{2} \sqrt{\left(1 + \frac{\sin\theta_{\max}}{\theta_{\max}} \right)^2 \cos^2\theta_x - 4 \frac{\sin\theta_{\max}}{\theta_{\max}}} \quad (19b)$$

In the limit of large $\theta_{\max}$, $\varepsilon_+ \approx \cos\theta_x$, $\varepsilon_- \approx 0$, and Eq. (18b) is recovered. Note that Eq. (19) and the preceding derivation are not restricted to spin-1/2 nuclei. In Eq. (19b), the quantity $\sin\theta_{\max}/\theta_{\max}$ results from evaluating $\langle \cos\theta_{\Sigma} \rangle$ with a uniform distribution of θ_{Σ} over the interval $[-\theta_{\max}, \theta_{\max}]$. For any other distribution that is symmetric about $\theta_{\Sigma} = 0$, Eqs. (17-19) are valid after substituting $\langle \cos\theta_{\Sigma} \rangle$ for $\sin\theta_{\max}/\theta_{\max}$.

Fig. 3 compares SDR data for a system of two ^{13}C nuclei calculated either from Eq. (19) or from full numerical simulations. The excellent agreement between the two calculations serves to verify Eq. (19). In Fig. 3a, both calculations assume $g = 1/2$ and the numerical simulations

assume an ideal double-quantum Hamiltonian $\tilde{H}_D^{(0)}$ during DQ periods. In Fig. 3b, the calculations assume that the POST-C7 sequence of Hohwy *et al.*¹⁴ is applied during DQ periods and that the sample is a powder with an isotropic distribution of molecular orientations in the MAS rotor. Values of g , and hence θ_x , are then orientation-dependent. For calculations with Eq. (19), values of g are extracted from the numerical calculation of the two-spin evolution

operator $U(2\tau_R)$ for one POST-C7 cycle, based on the relation $\tilde{H}_D^{(0)} = \frac{i}{2\tau_R} \ln U(2\tau_R)$.

In Fig. 3a, the SDR data are purely cosinusoidal when $f_{\max} = 0$, reflecting a coherent oscillation of the spin system between states of pure longitudinal polarization and pure double-quantum coherence. The data approach a purely exponential decay in the limit of large $f_{\max}$, reflecting incoherent evolution towards a state of zero net polarization when averaged over f_k values, with a decay constant λ that agrees well with the predictions above. In Fig. 3b, the orientation dependence of g produces a damping of oscillations when $f_{\max} = 0$. This damping is simply an effect of orientational averaging, not a deviation from coherent dynamics. In the limit of large $f_{\max}$, the orientation dependence of g causes the SDR data to follow a multi-exponential decay. Up to the value of N at which $\langle w(N) \rangle \approx 0.40$, the calculated SDR data can be approximated by a stretched exponential form $\langle w(N) \rangle = e^{-(\lambda N)^{\beta}}$ with $\beta \approx 0.80$. The precise value of β is expected to depend on the choice of recoupling sequence for the DQ periods, as different recoupling sequences produce different dependences of g on orientation.

Theory and Simulations for Many-Spin Systems

Formally, the evolution of longitudinal spin polarizations under SDR in a many-spin system can be described by the following equation, which is a generalization of Eq. (14):

$$p_{ij}(N) = \vec{v}_j \cdot \left[\langle \vec{U}_{CS} \rangle \cdot \langle \vec{U}_{DQ} \rangle \right]^N \cdot \vec{v}_i \quad (20)$$

$p_{ij}(N)$ is the amplitude for polarization transfer from spin i to spin j after N DQ and CS periods. If the density operator for the many-spin system contains L operator components, then $\vec{v}_i$ and $\vec{v}_j$ are L -dimensional vectors that represent states of longitudinal polarization on spins i and j , and $\vec{U}_{DQ}$ and $\vec{U}_{CS}$ are $L \times L$ matrices that represent transformations under H_{DQ} and H_{CS} in the L -dimensional Liouville space³⁷⁻³⁹.

Derivation of a general analytical expression analogous to Eq. (19) from Eq. (20) for a many-spin system is not a simple matter and will not be pursued here. However, in the limit $\theta_{\max} \gg$

$$1 \text{ and } \text{nd}_{ij}\tau_R \equiv \frac{2n\gamma^2\hbar}{R_{ij}^3}|g_{ij}|\tau_R \ll 1 \text{ (for all spin pairs simultaneously),}$$

$$p_{ij}(N) \approx [W^N]_{ij} \quad (21a)$$

where W is a polarization transfer “rate matrix”, with dimension $K \times K$ for a K -spin system, and with matrix elements

$$W_{qq'} = \begin{cases} -\sin^2 \frac{\text{nd}_{qq'}\tau_R}{2}, q \neq q' \\ 1 - \sum_{q'' \neq q} \sin^2 \frac{\text{nd}_{qq''}\tau_R}{2}, q = q' \end{cases} \quad (21b)$$

Eq. (21) follows from the observation that evolution for one DQ period transforms an initial density operator proportional to I_{zi} to a density operator proportional to

$$e^{-iH_{DQ}\tau_R} I_{zi} e^{iH_{DQ}\tau_R} \approx \left[\prod_{j \neq i} \left(1 - \sin^2 \frac{\text{nd}_{ij}\tau_R}{2} \right) \right] I_{zi} - \sum_{j \neq i} \sin^2 \frac{\text{nd}_{ij}\tau_R}{2} I_{zj} + C \quad (22)$$

where C is a sum of coherences (*i.e.*, operators that are entirely off-diagonal in a direct-product basis of eigenstates of I_{zi}). When $\theta_{\max} \gg 1$, all coherences acquire random phase modulations and are averaged to zero after a single SDR block (provided all spin pairs have distinct chemical shift sums, as discussed above and shown below).

Figs. 4-6 show numerical simulations of polarization transfers in a hypothetical three-spin system that illustrate several important features of SDR measurements on many-spin systems. In these simulations, the system consists of three ^{13}C nuclei at the vertices of a right triangle with 2.0 Å and 3.0 Å sides, as shown in Fig. 4. “Rate approximation” simulations, calculated from Eq. 21, are also shown.

Figs. 4a, 4b, and 4c show the dependence of polarization transfers on $N\text{nd}\tau_R$ for various values of $f_{\max}$, with $m = 1$, different chemical shifts for the three ^{13}C nuclei, and $g = 0.01$. When $f_{\max} = 0$, the SDR sequence becomes a frequency-selective recoupling sequence²⁸. Because $\delta_1 + \delta_2 = 0$, spins 1 and 2 are recoupled and exchange polarization in an oscillatory manner. Other polarization transfers are suppressed. As $f_{\max}$ increases, oscillatory polarization exchange between spins 1 and 2 becomes damped and other polarization transfers acquire significant amplitudes. In the limit of large $f_{\max}$, all polarization transfers calculated numerically agree well with rate approximation calculations.

Fig. 4d shows the dependence of polarization transfers on $N\text{nd}\tau_R$ when $m = 0$, *i.e.*, under a traditional coherent double-quantum dipolar recoupling sequence with no phase modulations of pairwise couplings. Interestingly, all polarization transfers exhibit nearly periodic behavior with a period determined by the strongest coupling, which is between spins 1 and 2. Transfers between spins 1 and 3 oscillate between negative and positive amplitudes, reflecting a competition between direct transfer from spin 1 (negative amplitude) and indirect transfer through spin 2 (positive amplitude). Transfers between spins 2 and 3 are primarily positive in amplitude, indicating that indirect transfer through spin 1 dominates. The periodic behavior of all polarization transfers in Fig. 4d is one manifestation of quantum mechanical interference among pairwise couplings in a many-spin system.

Fig. 5 shows the dependence of polarization transfers on $N\text{nd}\tau_R$ for various values of the ^{13}C chemical shifts, with large $f_{\max}$, $m = 1$, and $g = 0.01$. When chemical shift differences are small, the numerically simulated polarization transfer amplitudes deviate from the rate approximation

calculations. This is because phase modulations of individual pairwise couplings are not uncorrelated when the chemical shift differences are small. The rate approximation behavior is recovered when the chemical shift differences satisfy $m|\delta_i - \delta_j| \tau_R / 2\pi > 0.01$, which is not a stringent condition for typical ^{13}C NMR spectra.

Fig. 6 shows simulations identical to those in Fig. 4, except that the POST-C7 sequence¹⁴ is used in DQ periods, rather than assuming an ideal double-quantum Hamiltonian with $g = 0.01$. The value of g is therefore orientation-dependent in Fig. 6, as would be the case in experiments on unaligned polycrystalline or noncrystalline samples. Polarization transfers in Fig. 6 are qualitatively the same as in Fig. 4, but with distributions of oscillation periods or polarization transfer rates.

Discussion

The exact analytical expression in Eq. (19) for SDR measurements on a two-spin system is one of the major results of this paper. It is remarkable that Eq. (14) leads directly to the expression in Eq. (19) while Eq. (13) appears intractable, despite the fact that Eqs. (13) and (14) appear to be equivalent formulations of the quantity $\langle w(N) \rangle$. Eq. (13) is an expression for $\langle w(N) \rangle$ in a Schrodinger representation, where the dimensionality of the evolution operator $U(N)$ is the same as the dimensionality of the density operator, while Eq. (14) is an expression for $\langle w(N) \rangle$ in a Liouville (or superoperator) representation, where the dimensionality of the evolution operator is the square of the number of operators that form a basis for the density operator [*i.e.*, 3×3 when the relevant part of the density operator is a linear combination of three basis operators, as in Eq. (12)]. In the Liouville representation, the NMR signal depends linearly, rather than quadratically, on the evolution operator, thereby simplifying the evaluation of averages over the random variables f_k . This is but one example of the more general principle that stochastic processes have a simpler appearance in the Liouville representation than in the Schrodinger representation^{37,39-41}.

A second major result is the demonstration that polarization transfers under SDR in a general many-spin system are accurately described by the rate matrix defined in Eq. (21) in the limits $\theta_{\max} \gg 1$ and $nd_{ij}\tau_R \ll 1$, provided that each spin has a unique chemical shift. This means that SDR data from a system of K spin-1/2 nuclei can be analyzed or simulated using $K \times K$ matrices, rather than the $2^K \times 2^K$ matrices that are generally required in simulations of coherent dynamics of the same system. For $k \geq 6$, this is an important practical advantage of SDR.

The fact that polarization transfer rates under SDR depend only on pairwise dipolar coupling constants d_{ij} shows that dipolar truncation is absent. In previous studies of polarization transfer among ^{13}C nuclei in many-spin systems in biochemical solids^{22,24,42-44}, transfers among spins with relatively weak dipole-dipole couplings have been shown to be detectable, even in the presence of stronger couplings, when the polarization transfer occurs by ^{13}C - ^{13}C spin diffusion under MAS without proton decoupling. Although dipolar truncation may be considered to be absent in such experiments, in the restricted sense that the weaker ^{13}C - ^{13}C couplings are not entirely switched off by the stronger couplings, the polarization transfer rates may still be subject to quantum mechanical interferences among noncommuting pairwise couplings and are certainly dependent on the network of ^1H - ^{13}C and ^1H - ^1H couplings. Quantitative analysis of ^{13}C - ^{13}C spin diffusion data exclusively in terms of pairwise ^{13}C - ^{13}C couplings is not possible. Thus, although ^{13}C - ^{13}C spin diffusion data can provide important constraints on biomolecular structures^{24,42,43,45,46}, spin diffusion experiments are qualitatively different from SDR.

The comparative simplicity of nuclear spin dynamics under SDR suggests that SDR will become a useful tool in molecular structure determination by solid state NMR.

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Figure 1.

General form of a radio-frequency pulse sequence for stochastic dipolar recoupling (SDR) experiments in ^{13}C solid state NMR. Magic-angle spinning with a sample rotation period τ_R is assumed. Initially, ^1H - ^{13}C cross-polarization and a ^{13}C 90° pulse prepare longitudinal ^{13}C spin polarization. The subsequent SDR period consists of N blocks of alternating double-quantum recoupling (DQ) and chemical shift precession (CS), with durations $n\tau_R$ and $m\tau_R$. The ^{13}C carrier frequency is shifted from its nominal value by an offset f_k in the k^{th} CS period, where f_k is chosen randomly from the interval $[-f_{\text{max}}, f_{\text{max}}]$. To reduce effects of transverse spin relaxation and pulse imperfections in experiments, the SDR period is followed by a “zero dipolar recoupling” (ZDR) period with duration $N'(n + m)\tau_R$ before the application of a second ^{13}C 90° pulse and the detection of NMR signals. The ZDR period ideally produces no net evolution of longitudinal spin polarizations and is therefore omitted from the theoretical analysis and numerical simulations in this paper. In experiments, the quantity $N + N'$ (and hence the total pulse sequence duration and number of pulses) is kept constant as N is varied. Two possible realizations of the ZDR period are shown: (upper) the carrier frequency offset in CS periods is fixed at a value f_z that avoids all frequency-selective recoupling conditions^{27,28}; (lower) DQ periods occur as groups of two, with an overall 90° phase shift of all pulses in the second period of each group (symbolized by $\overline{\text{DQ}}$) to produce time-reversal⁴⁷.

Figure 2.

Experimental ^{13}C NMR data for $^{13}\text{C}_2$ -BSA powder obtained with the pulse sequence in Figure 1, using the lower ZDR realization. Data were acquired at 100.4 MHz ^{13}C NMR frequency and 7.45 kHz MAS frequency ($\tau_R = 134.23 \mu\text{s}$), with 130 kHz ^1H decoupling fields. The POST-C7 sequence of Hohwy *et al.*¹⁴ was used in DQ periods, with $n = 2$, $m = 1$, and $N + N' = 64$. ^{13}C NMR signal amplitudes are plotted as a function of the net recoupling period $Nn\tau_R$ for the indicated values of f_{max} . Oscillatory dependences, indicative of coherent nuclear spin dynamics in the two-spin, dipole-coupled system, are observed when $f_{\text{max}}\tau_R \ll 1$. Monotonic decay, indicative of incoherent dynamics, develops at larger values of f_{max} .

Figure 3.

Comparisons of numerical simulations (circles) and exact calculations (lines) of stochastic dipolar recoupling data for two-spin systems. Numerical simulations involve propagation of the 4×4 density matrix for a pair of spin-1/2 nuclei under the 4×4 Hamiltonian matrices in the DQ and CS periods of the SDR pulse sequence, evaluation of the final longitudinal spin polarizations, and averaging over f_k values, using NMR pulse sequence simulation programs written specifically for this purpose. Exact calculations use the analytical expression in Eq. (19). (a) ^{13}C spin pairs with a 3.0 Å internuclear distance, assuming an ideal double-quantum Hamiltonian in DQ periods with $g = 1/2$, $\tau_R = 125 \mu\text{s}$, $n = 2$, and $m = 1$. Numerical simulations are averaged over 1728 random choices of f_k values. (b) ^{13}C spin pairs with a 2.0 Å internuclear distance, using the POST-C7 recoupling sequence in DQ periods with $\tau_R = 125 \mu\text{s}$, $n = 2$, and

$m = 1$. Numerical simulations include the full time-dependences of rf fields and dipole-dipole couplings under MAS to determine the propagator for DQ periods, and are averaged over 1728 orientations in the MAS rotor, with different random choices of f_k values for each orientation. Exact calculations use orientation-dependent g values extracted from the numerically determined propagator for DQ periods.

Figure 4.

Numerical simulations of nuclear spin polarization transfers under stochastic dipolar recoupling in a system of three coupled ^{13}C nuclei with the indicated geometry, assuming an ideal double-quantum Hamiltonian in DQ periods with $g = 0.01$, $\tau_R = 125 \mu\text{s}$, and $n = 2$. Chemical shifts of spins 1, 2, and 3 are 2.0, -2.0, and 0.0 kHz, respectively. Simulations are averaged over 1728 random choices of f_k values. (a) Amplitude of polarization transfer between spins 1 and 2 for values of f_{max} indicated in panel c, with $m = 1$. Dashed lines are guides to the eye. Solid orange line is a rate approximation simulation (see text). (b) Amplitude of polarization transfer between spins 1 and 3. (c) Amplitude of polarization transfer between spins 2 and 3. (d) Polarization transfer amplitudes with $m = 0$, corresponding to a traditional dipolar recoupling experiment.

Figure 5.

Numerical simulations with the same conditions as in Figure 4, but with the indicated chemical shifts, $f_{\max} = 64.0$ kHz, and $m = 1$. Amplitudes of polarization transfer between spins 1 and 2 (a), spins 1 and 3 (b), and spins 2 and 3 (c) are shown. Solid purple lines are rate approximation simulations.

Figure 6.

Same as Figure 4, but assuming the POST-C7 sequence in DQ periods and averaging over 1728 orientations in the MAS rotor, with different random choices of f_k values for each orientation. Dashed lines are guides to the eye. Solid orange lines are rate approximation simulations.