SUPPORTING INFORMATION

Modeling Dissipative Magnetization Exchange Dynamics in Magnetic Resonance

I. DEFINITION OF ANISOTROPIC COEFFICIENTS IN MAS EXPERIMENTS

The CSA interaction is defined by the following Hamiltonian:

$$H_{CSA}(t) = \sum_{i=1}^{2} \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \omega_i^{(m)} e^{im\omega_r t} I_{iz}. \tag{S1}$$

The term $\omega_i^{(m)}$[1–4] denotes the component of the CSA interaction (associated with a particular spin, i=1 or 2) and is expressed in terms of spatial tensors $\left(R_{PAS,\lambda}^{(2)q_1}\right)$ defined in the principal axis system (PAS) as:

$$\omega_\lambda^{(m)} = \sum_{q_1,q_2=-2}^{2} R_{PAS,\lambda}^{(2)q_1}\, D_{q_1q_2}(\Omega_{PM})\, D_{q_2m}(\Omega_{MR})\, d_{m,0}(\beta_{RL}). \tag{S2}$$

where, λ=1, 2.

The non-zero components of the spatial tensor in the PAS have the following definitions: $R_{PAS,\lambda}^{(2)0} = \delta_{\lambda,CSA}$, $R_{PAS,\lambda}^{(2)\pm 2} = -\frac{1}{\sqrt{6}}\delta_{\lambda,CSA}\eta_\lambda$ with $\delta_{\lambda,CSA}$ and η_λ representing the CSA and asymmetry parameter, respectively.

The dipolar interactions between a pair of spins is represented by the two-spin Hamiltonian given below:

$$H_D(t) = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \omega_{12}^{(m)} e^{im\omega_r t} \left(2I_{1z}I_{2z} + \left(-\frac{1}{2}\right)\left(I_1^+I_2^- + I_1^-I_2^+\right)\right). \tag{S3}$$

with $\omega_{12}^{(m)}$ denoting anisotropic component of the dipolar interactions.

$$\omega_{12}^{(m)} = \sum_{q_1,q_2=-2}^{2} R_{PAS,dip}^{(2)q_1}\, D_{q_1q_2}(\Omega_{PM})\, D_{q_2m}(\Omega_{MR})\, d_{m,0}(\beta_{RL}). \tag{S4}$$

Analogous to the CSA interactions, the dipolar interactions are represented in terms of the spatial tensor operators, $R_{PAS,dip}^{(2)q}$ and are defined in its own PAS with $R_{PAS,dip}^{(2)0} = \sqrt{6}\, b_{IS}$ $\left(b_{IS} = \frac{\mu_0\gamma_I\gamma_S\hbar}{4\pi r^3}\right)$ being the only non-zero component. The notation $D_{m_1m_2}(\Omega)$ represents the Wigner-rotation matrix[5] and describes the transformation from the PAS to the lab axis system. A detailed description of this procedure is well-documented in the literature[4].

II. DERIVATION OF CORRECTIONS BASED ON MAGNUS FORMULA

Employing the prescription outlined by the Magnus expansion scheme[6], effective Hamiltonians incorporating the contributions from time-dependent terms in the Hamiltonian are derived. To second-order, the expansion coefficients in the Magnus formula are given by the following equations:

$$\bar{H} = \bar{H}^{(1)} + \bar{H}^{(2)}. \tag{S5}$$

$$\bar{H}^{(1)} = \frac{1}{T_c} \int_0^{T_c} H(t)\, dt. \tag{S6}$$

$$\bar{H}^{(2)} = \frac{-i}{2T_c} \int_0^{T_c} dt \int_0^{t} \left[H(t), H\left(t'\right) \right] dt'. \tag{S7}$$

To facilitate analytic description, correction terms are evaluated by employing the Fourier components of the time-dependent Hamiltonian. Accordingly, the above correction terms are evaluated through the Fourier components of the spin Hamiltonian.

$$H^{(1)} = H_0. \tag{S8}$$

$$H^{(2)} = \sum_{k \neq 0} \left(\frac{1}{2k\omega} \right) . \left[H_k, H_{-k} \right] + \sum_{k \neq 0} \left(\frac{1}{k\omega} \right) . \left[H_0, H_k \right]. \tag{S9}$$

In the case of R^2 experiments (corresponding to the N=2 resonance condition discussed in the main section), the Fourier components have the following definitions:

$$H_0 = \left(\omega_1^{(0)} - \omega_r \right) I_{1z} + \left(\omega_2^{(0)} + \omega_r \right) I_{2z} + \left(-\frac{1}{2} \right) \left[\omega_{12}^{(-2)} . \left(I_1^+ I_2^- \right) + \omega_{12}^{(2)} . \left(I_1^- I_2^+ \right) \right]. \tag{S10}$$

and,

$$H_k = \sum_{i=1}^{2} \sum_{\substack{k=-2, \\ k \neq 0}}^{2} \omega_i^{(k)} I_{iz} + \sum_{\substack{k=-2, \\ k \neq 0}}^{2} 2\omega_{12}^{(m)} \left(I_{1z} I_{2z} \right) + \sum_{k=1,3,4} \omega_{12}^{(m)} \left(I_1^+ I_2^- \right) + \sum_{k=-1,-3,-4} \omega_{12}^{(m)} \left(I_1^- I_2^+ \right). \tag{S11}$$

III. DESCRIPTION OF THE CSA INTERACTION FRAME USING BESSEL FUNCTIONS

In the standard Hilbert space, the transformation into the CSA interaction frame is effected using the unitary transformation, U_2 $(U_2 = exp(-iH_{CSA}(t)))$.

In the CSA interaction frame, the static part of the dipolar Hamiltonian (say $H_{D,S}$) has both a (scaled) static as well as time-dependent terms. In a similar vein, the time-dependent part of the dipolar interactions in the interaction frame has additional time-dependent factors due to the CSA interactions. A detailed description of the transformed dipolar Hamiltonians is summarized by the equations given below:

$$\tilde{\tilde{H}}_{D,S}(t) = U_2 \tilde{H}_{D,S} U_2^{-1}. \tag{S12}$$

$$\begin{aligned}\tilde{H}_{SD}(t) &= U_2 H_{SD} U_2^{-1} \\ &= \left(-\frac{1}{2}\right)\left[\omega_{12}^{(-2)} e^{i(\phi_1(t)-\phi_2(t))} e^{-i(\phi_1(0)-\phi_2(0))} I_1^+ I_2^- + \omega_{12}^{(2)} e^{-i(\phi_1(t)-\phi_2(t))} e^{i(\phi_1(0)-\phi_2(0))} I_1^- I_2^+\right].\end{aligned} \tag{S13}$$

For the sake of compactness, the time-dependent phase factors in the above equation can be expressed as follows:

$$\exp\left(i\left[\phi_1(t)\right]\right) = \exp\left(i\left[\sum_{m=1,2}\left\{A_m \cos\left(m\omega_r t\right) + B_m \sin\left(m\omega_r t\right)\right\}\right]\right). \tag{S14}$$

with the A_m and B_m coefficients having the following definitions:
$A_m = 2\mathrm{Im}\left[\omega_1^{(m)}\right]$; $B_m = 2\mathrm{Re}\left[\omega_1^{(m)}\right]$.

Employing Bessel functions $(J_n(A))$, the time-dependent terms in the exponential are further simplified as given below:

$$\begin{aligned}\exp\left(i\left[\phi_1(t)\right]\right) = &\sum_{n_1=-\infty}^{\infty}(i)^{n_1} J_{n_1}(A_1)\exp\left(in_1\omega_r t\right) \times \sum_{n_2=-\infty}^{\infty}(i)^{n_2} J_{n_2}(A_2)\exp\left(in_2 2\omega_r t\right) \times \\ &\sum_{n_3=-\infty}^{\infty} J_{n_3}(B_1)\exp\left(in_3\omega_r t\right) \times \sum_{n_2=-\infty}^{\infty} J_{n_4}(B_2)\exp\left(in_4 2\omega_r t\right) \\ = &\sum_{k_1=-\infty}^{\infty} b_{k_1}\exp\left(ik_1\omega_r t\right).\end{aligned} \tag{S15}$$

In a similar vein, the CSA contribution from the second spin (manifested in the term $\exp\left(i\left[\phi\left(t\right)\right]\right)$ can also be expressed in terms of Bessel functions. The time-independent phase factor in the above equation has the following definition, $\phi_n(0) = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \frac{\omega_n^{(m)}}{im\omega_r}$.

The final form of the static dipolar Hamiltonian in the CSA interaction frame is represented by,

$$\begin{aligned}\tilde{H}_{SD}(t) &= U_2 H_{SD} U_2^{-1} \\ &= \left(-\frac{1}{2}\right) \sum_{k_1=-\infty}^{\infty} b_{k_1} \exp(ik_1\omega_r t) \sum_{k_2=-\infty}^{\infty} b_{k_2} \exp(ik_2\omega_r t) \begin{bmatrix} \omega_{12}^{(-2)} e^{-i(\phi_1(0)-\phi_2(0))} I_1^+ I_2^- \\ +\omega_{12}^{(2)} e^{i(\phi_1(0)-\phi_2(0))} I_1^- I_2^+ \end{bmatrix}.\end{aligned} \tag{S16}$$

Subsequently, the time-independent term from the above equation is derived by evaluating all possible combinations that result in a time-independent exponential factor (i.e. $k_1 + k_2 = 0$). The final form of the time-independent term is given below:

$$\tilde{H}_{SD} = \left(-\frac{1}{2}\right) \left[\omega_{12}^{(-2)} \exp(-i[\phi_1(0) - \phi_2(0)]) I_1^+ I_2^- + \omega_{12}^{(2)} \exp(i[\phi_1(0) - \phi_2(0)]) I_1^- I_2^+\right]. \tag{S17}$$

IV. DESCRIPTION OF THE CSA INTERACTION FRAME IN THE EXTENDED HILBERT SPACE

To describe the transformations in the extended Hilbert space, the time-dependent Hamiltonian in the interaction frame (refer to [Eq.(6)] in main section) is transformed into a time-independent Floquet Hamiltonian.

$$H_F = \omega_r I_F + H_{iso,F} + H_{CSA,F} + H_{SD,F} + H_{TD,F}. \tag{S18}$$

In the Floquet representation[7], the time-independent terms (of [Eq.(6)]) are represented through Floquet spin operators, diagonal in the extended space, while, the time-dependent terms are represented through Floquet operators off-diagonal in the extended space. A detailed description of this procedure is well-documented in the literature.

$$H_{iso,F} = \left(\omega_1^{(0)} - \omega_r\right) [I_{1z}]_0 + (\omega_2^{(0)} + \omega_r)[I_{2z}]_0. \tag{S19}$$

$$H_{CSA,F} = \sum_{m\neq 0} G_1^{(m)} [I_{1z}]_m + \sum_{m\neq 0} G_2^{(m)} [I_{2z}]_m. \tag{S20}$$

$$H_{SD,F} = \left(-\frac{1}{2}\omega_{12}^{(-2)}\right) [I_1^+ I_2^-]_0 + \left(-\frac{1}{2}\omega_{12}^{(2)}\right) [I_1^- I_2^+]_0. \tag{S21}$$

$$H_{TD,F} = \sum_{m\neq 0} G_{zz}^{(m)} [I_{1z} I_{2z}]_m + \sum_{m\neq 0,-2} G_{PM}^{(m)} \left[I_1^+ I_2^-\right]_m + \sum_{m\neq 0,2} G_{MP}^{(m)} \left[I_1^- I_2^+\right]_m . \tag{S22}$$

The 'G' coefficients described in the Floquet Hamiltonian are derived from the coefficients of the Hamiltonian in the interaction frame and are summarised in **Table-I** (refer to main section) .

To describe the transformation into the CSA interaction frame, the Hamiltonian is initially expressed as a sum of zero order (H_0) and perturbing terms (H_1). The perturbing Hamiltonian, H_1 is further expressed as a sum of diagonal, $H_{1,d}$ and off-diagonal terms, $H_{1,od}$ as illustrated below:

$$H_0 = \omega_r I_F . \tag{S23}$$

$$H_{1,d} = H_{iso,F} + H_{SD,F} + H_{TD,F} . \tag{S24}$$

$$H_{1,od} = H_{CSA,F} . \tag{S25}$$

This is then followed by a unitary transformation of the Floquet Hamiltonian as given below:

$$H_{eff} = e^{i\lambda S_1} H_F e^{-i\lambda S_1} . \tag{S26}$$

The transformation function, S_1 is expressed as:

$$S_1 = -i \left[\sum_{m\neq 0} C_1^{(m)} [I_{1z}]_m + \sum_{m\neq 0} C_2^{(m)} [I_{2z}]_m \right] .$$

S_1 is chosen such that the off-diagonal contributions resulting from $H_{1,od}$ are compensated at least to first order. The coefficients in the transformation function are chosen based on the equation given below.

$$H_1^{(1)} = H_{1,d} + H_{1,od} + i \left[S_1, H_0\right] . \tag{S27}$$

To first order, the coefficients in S_1 are chosen such that, $H_{1,od} = -i\left[S_1, H_0\right]$ and are given by, $C_1^{(m)} = \frac{\omega_1^{(m)}}{m\omega_r}$ and $C_2^{(m)} = \frac{\omega_2^{(m)}}{m\omega_r}$.

Subsequently, employing the transformation function, S_1, the various terms in $H_{1,d}$ are transformed as given below:

$$\tilde{H}_{iso,F} = e^{i\lambda S_1} H_{iso,F} e^{-i\lambda S_1} = H_{iso,F} . \tag{S28}$$

As illustrated above, the isotropic part of the chemical shift interaction remains invariant in the CSA interaction frame. This is analogous to the description in the standard Hilbert space (refer to

[Eq.(S23)]). In a similar vein, the static part of the dipolar interaction in the CSA interaction frame does get transformed into diagonal and off-diagonal terms. For illustrative purposes, we confine our discussion only to the diagonal part of the Hamiltonian in the extended space. Accordingly, the static part of the dipolar interaction in the CSA interaction frame is represented by the following equation:

$$\tilde{H}_{SD,F} = e^{i\lambda S_1} H_{SD,F} e^{-i\lambda S_1} = \left(-\frac{1}{2}\omega_{12,e}^{(-2)}\right)\left[I_1^+ I_2^-\right]_0 + \left(-\frac{1}{2}\omega_{12,e}^{(2)}\right)\left[I_1^- I_2^+\right]_0. \tag{S29}$$

The coefficients in the above equation have the following definitions:
$\omega_{12,e}^{(-2)} = \omega_{12}^{(-2)}\cos(q)$ and $\omega_{12,e}^{(2)} = \omega_{12}^{(2)}\cos(q)$, where $q = \sqrt{2\sum\limits_{m=1,2} \frac{\left(\omega_1^{(m)} - \omega_2^{(m)}\right)\left(\omega_1^{(-m)} - \omega_2^{(-m)}\right)}{(m\omega_r)^2}}$
As a first level of approximation, all other off-diagonal contributions emerging from the $H_{SD,F}$ and $H_{TD,F}$ are completely ignored and the effective Floquet Hamiltonian in the CSA interaction reduces to the form given below:

$$H_{eff} = (\omega_1^{(0)} - \omega_r)I_{1z} + (\omega_2^{(0)} + \omega_r)I_{2z} + \left(-\frac{1}{2}\right)\left(\omega_{12,e}^{(-2)} I_1^+ I_2^- + \omega_{12,e}^{(2)} I_1^- I_2^+\right). \tag{S30}$$

While the form of the Hamiltonian is similar to the one derived in [Eq.(S17)], the coefficients associated with them are significantly different.

V. DESCRIPTION OF R^2 IN $I_1 - I_2 - S_N$ SYSTEM

To describe the effects of depolarization of the S-spins, we begin with a model system, $I_1 - I_2 - S_N$. In the rotating frame, the Hamiltonian of the system is represented by,

$$H(t) = H_I(t) + H_S(t) + H_{IS}(t) + H_{RF}. \tag{S31}$$

In [Eq.(S31)], $H_I(t)$ represents Hamiltonian for a homonuclear dipolar coupled carbon-spin pair including chemical shift (both isotropic and anisotropic) and dipolar interaction terms as shown below:

$$\begin{aligned} H_I(t) = &\sum_{i=1}^{2} \omega_i^{(0)} I_{iz} + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{i=1}^{2} \omega_i^{(m)} e^{im\omega_r t} I_{iz} \\ &+ \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \omega_{12}^{(m)} e^{im\omega_r t}\left[2I_{1z}I_{2z} + \left(-\frac{1}{2}\right)\cdot\left(I_1^+ I_2^- + I_1^- I_2^+\right)\right] \end{aligned} \tag{S32}$$

$H_S\,(t)$ represents Hamiltonian for neighboring proton-spins including chemical shift (both isotropic and anisotropic) and dipolar interaction terms as shown below:

$$\begin{aligned} H_S\,(t) = & \sum_{j=1}^{N} \omega_j^{(0)} S_{jz} + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{j=1}^{N} \omega_j^{(m)} e^{im\omega_r t} S_{jz} \\ & + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{j<k=1}^{N} \omega_{jk}^{(m)} e^{im\omega_r t} \left[\, 2S_{jz}S_{kz} + \left(-\tfrac{1}{2}\right) \cdot \left(S_j^+ S_k^- + S_j^- S_k^+\right) \right] \end{aligned} \qquad \text{(S33)}$$

$H_{IS}\,(t)$ represents Hamiltonian for heteronuclear dipolar interactions representative of the coupling between ${}^{13}C$-spins and ${}^{1}H$-spins as shown below:

$$H_{IS}\,(t) = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{i=1}^{2} \sum_{j=1}^{N} \omega_{ij}^{(m)} e^{im\omega_r t} \left(2I_{iz}S_{jz}\right) \qquad \text{(S34)}$$

In Eqs.(S32)-(S34), ω_r represents the spinning frequency, while $\omega_{i/j}^{(0)}$ represents the isotropic chemical shifts of the respective spins. $\sum\limits_{\substack{m=-2,\\ m\neq 0}}^{2} \omega_\lambda^{(m)} e^{im\omega_r t}$ represents time-dependent anisotropic interactions i.e., CSA ($\lambda = i/j$) and dipolar coupling coefficient ($\lambda = 12/jk/ij$).
The time-independent components $\omega_\lambda^{(m)}$[1–4] are represented by

$$\omega_\lambda^{(m)} = \sum_{m_1=-2}^{2} R_{P,\lambda}^{(2)m_1} \sum_{m_2=-2}^{2} D_{m_1 m_2}(\Omega_{PM}) \sum_{\substack{m=-2,\\ m\neq 0}}^{2} D_{m_2 m}(\Omega_{MR}). \qquad \text{(S35)}$$

In [Eq.(S35)], the term $R_{P,\lambda}^{(2)m_1}$ denotes the component of the irreducible spatial tensor defined in the principal axis system (PAS) (λ =CSA or dipolar interaction) and $D_{m_1 m_2}(\Omega_{AB})$ denotes the Wigner rotation matrix[5]. In the PAS of the CSA interactions, $R_{P,\lambda}^{(2)0} = \delta_{aniso}$ and $R_{P,\lambda}^{(2)\pm 2} = -\frac{1}{\sqrt{6}}\delta_{aniso}\eta$ (δ_{aniso} and η represent the CSA and asymmetry parameter, respectively) components are non-zero in the PAS, while only non-zero term in the dipolar principal axis frame is $R_{P,IS}^{(2)0} = \sqrt{6} b_{IS}$ ($b_{IS} = \frac{\mu_0 \gamma_I \gamma_S \hbar}{4\pi r_{IS}^3}$ denotes the dipolar-coupling constant expressed in rad/s).
Radio-frequency (RF) field (also known as decoupling field) is applied along the proton (S) channel during mixing to - (i) minimize the heteronuclear dipolar interactions representative of the coupling between ${}^{13}C$-spins and ${}^{1}H$-spins, (ii) improve the efficiency of ${}^{13}C$-${}^{13}C$ magnetization exchange, and (iii) enhance the spectral resolution of ${}^{13}C$ nuclei.
In the rotating frame, the RF Hamiltonian become time-independent. Accordingly, RF Hamilto-

nian in the rotating frame[8] is described by

$$H_{RF} = \omega_{rf} \sum_{j=1}^{N} S_{jx} \,. \tag{S36}$$

Here, ω_{rf} represents the amplitude of the RF field applied along the proton channel.

To describe the interference effects in R^2 experiments, the Hamiltonian [Eq.(S31)] is transformed into an interaction frame defined by the transformation operator $U_1 = e^{in\omega_r t I_{1z}} e^{-in\omega_r t I_{2z}}$ as represented below:

$$\tilde{H}(t) = U_1 H(t) U_1^{-1} = \tilde{H}_I(t) + \tilde{H}_S(t) + \tilde{H}_{IS}(t) + \tilde{H}_{RF} \tag{S37}$$

where,

$$\begin{aligned}\tilde{H}_I(t) =& (\omega_1^{(0)} - n\omega_r) I_{1z} + (\omega_2^{(0)} + n\omega_r) I_{2z} + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{i=1}^{2} \omega_i^{(m)} e^{im\omega_r t} I_{iz} + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \omega_{12}^{(m)} e^{im\omega_r t} \left(2I_{1z}I_{2z}\right) \\ &+ \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \omega_{12}^{(m)} \left[\left(-\frac{1}{2}\right) \cdot \left(I_1^+ I_2^- e^{i(m+2n)\omega_r t} + I_1^- I_2^+ e^{i(m-2n)\omega_r t} \right) \right] .\end{aligned} \tag{S38}$$

Meanwhile; $H_S(t)$, $H_{IS}(t)$ and H_{RF} remain invariant under unitary transformation U_1 such that $\tilde{H}_S(t) = H_S(t)$, $\tilde{H}_{IS}(t) = H_{IS}(t)$ and $\tilde{H}_{RF} = H_{RF}$.

Depending on the matching condition ($m + 2n = 0$ or $m - 2n = 0$, $n = 0.5$ or 1), a part of the dipolar Hamiltonian [Eq.(S38)] becomes time-independent (also referred as **recoupled Hamiltonian**) and is responsible for the polarization transfer from spin I_1 to spin I_2. To further simplify the description, the Hamiltonian in the interaction frame is rotated such that the effective field experienced by the S-spin is quantized along the z-axis.

Subsequently, the interaction frame Hamiltonian [Eq.(S37)] is further transformed into an interaction frame of the effective field for the proton-spins defined by the transformation operator $U_2 = \exp\left(i \sum_{j=1}^{N} \theta_j S_{jy} \right)$,

$$\tilde{H}_T(t) = U_2 \tilde{H}(t) U_2^{-1} = \tilde{\tilde{H}}_I(t) + \tilde{\tilde{H}}_S(t) + \tilde{\tilde{H}}_{IS}(t) + \tilde{\tilde{H}}_{RF} \,. \tag{S39}$$

Based on the offset and RF field, an effective field for the proton spins (see Figure S1) is defined as -

$$\omega_{j,eff} = \sqrt{\left(\omega_j^{(0)}\right)^2 + \left(\omega_{rf}\right)^2} \tag{S40}$$

$$\text{here} \quad \sin\theta_j = \frac{\omega_{rf}}{\omega_{j,eff}},$$

$$\cos\theta_j = \frac{\omega_j^{(0)}}{\omega_{j,eff}},$$

$$\text{and} \quad \tan\theta_j = \frac{\omega_{rf}}{\omega_j^{(0)}}.$$

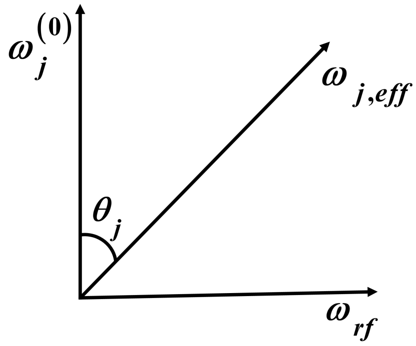

FIG. S1. Definition of θ_j employed in defining an effective field ($\omega_{j,eff}$) for the proton-spins based on the offset ($\omega_j^{(0)}$) and RF field (ω_{rf}).

In the tilted frame, the I-spin interactions remain invariant (i.e., $\tilde{\tilde{H}}_I(t) = U_2\tilde{H}_I(t)U_2^{-1} = \tilde{H}_I(t)$), while the S-spin Hamiltonian, RF Hamiltonian, and the coupling term, H_{IS} get modified.

Accordingly, $\tilde{\tilde{H}}_S(t) + \tilde{\tilde{H}}_{RF}$ is expressed as:

$$\tilde{\tilde{H}}_S(t) = \tilde{\tilde{H}}_{iso,S}(t) + \tilde{\tilde{H}}_{CSA,S}(t) + \tilde{\tilde{H}}_{D,S}(t) + \tilde{\tilde{H}}_{RF}. \tag{S41}$$

where,

$$\tilde{\tilde{H}}_{iso,S}(t) + \tilde{\tilde{H}}_{RF} = \sum_{j=1}^{N} \omega_{j,eff} S_{jz},$$

$$\tilde{\tilde{H}}_{CSA,S}(t) = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{j=1}^{N} \omega_j^{(m)} e^{im\omega_r t}\left[S_{jz}\cos\theta_j - S_{jx}\sin\theta_j\right],$$

$$\tilde{\tilde{H}}_{D,S}(t) = \tilde{\tilde{H}}_{ZQ,S}(t) + \tilde{\tilde{H}}_{SQ,S}(t) + \tilde{\tilde{H}}_{DQ,S}(t). \tag{S42}$$

Here $\tilde{\tilde{H}}_{ZQ,S}$, $\tilde{\tilde{H}}_{SQ,S}$ and $\tilde{\tilde{H}}_{DQ,S}$ stands for transformed zero-quantum, single-quantum and double-quantum Hamiltonians corresponding to the proton-spins, respectively.

$$\begin{aligned}\tilde{\tilde{H}}_{ZQ,S}(t) = &\sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{j<k=1}^{N} \omega_{jk}^{(m)} e^{im\omega_r t} A_{zz,jk} S_{jz} S_{kz} \\ &+ \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{j<k=1}^{N} \omega_{jk}^{(m)} e^{im\omega_r t}\left(\frac{1}{4}\left[A_{pm,jk}S_j^+ S_k^- + A_{mp,jk}S_j^- S_k^+\right]\right).\end{aligned} \tag{S42a}$$

$$\text{here} \quad A_{zz,jk} = \left(2\cos\theta_j\cos\theta_k - \sin\theta_j\sin\theta_k\right),$$

$$A_{pm,jk} = A_{mp,jk} = \left(2\sin\theta_j\sin\theta_k - \cos\theta_j\cos\theta_k - 1\right).$$

$$\tilde{\tilde{H}}_{SQ,S}(t) = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{j<k=1}^{N} \omega_{jk}^{(m)} e^{im\omega_r t} \left[\frac{1}{2} \begin{pmatrix} A_{zp,jk} S_{jz} S_k^{+} + A_{zm,jk} S_{jz} S_k^{-} \\ \\ +A_{pz,jk} S_j^{+} S_{kz} + A_{mz,jk} S_j^{-} S_{kz} \end{pmatrix} \right]. \tag{S42b}$$

$$\text{here } \; A_{zp,jk} = A_{zm,jk} = \left(-2\cos\theta_j \sin\theta_k - \sin\theta_j \cos\theta_k\right),$$

$$A_{pz,jk} = A_{mz,jk} = \left(-2\sin\theta_j \cos\theta_k - \cos\theta_j \sin\theta_k\right).$$

$$\tilde{\tilde{H}}_{DQ,S}(t) = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{j<k=1}^{N} \omega_{jk}^{(m)} e^{im\omega_r t} \left[\frac{1}{4} \left(A_{pp,jk} S_j^{+} S_k^{+} + A_{mm,jk} S_j^{-} S_k^{-} \right) \right] \tag{S42c}$$

$$\text{here } \; A_{pp,jk} = A_{mm,jk} = \left(2\sin\theta_j \sin\theta_k - \cos\theta_j \cos\theta_k + 1\right)$$

$$\tilde{\tilde{H}}_{IS}(t) = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{i=1}^{2} \sum_{j=1}^{N} \omega_{ij}^{(m)} e^{im\omega_r t} \left[(2I_{iz}) . \left(S_{jz} \cos\theta_j - S_{jx} \sin\theta_j \right) \right] \tag{S43}$$

To incorporate the corrections emerging from the time-dependent terms, the time-dependent Hamiltonian in the tilted rotating frame is transformed to a time-independent Floquet Hamiltonian, H_F.

$$H_F = \omega_r I_F + H_{F,I}^{(iso)} + H_{F,I}^{(CSA)} + H_{F,I}^{(D)} + H_{F,S}^{(eff)} + H_{F,S}^{(CSA)} + H_{F,S}^{(D)} + H_{F,IS}^{(D)} \tag{S44}$$

where

$$H_{F,I}^{(iso)} = (\omega_1^{(0)} - n\omega_r)[I_{1z}]_0 + (\omega_2^{(0)} + n\omega_r)[I_{2z}]_0 \,,$$

$$H_{F,I}^{(CSA)} = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} G_1^{(m)} [I_{1z}]_m + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} G_2^{(m)} [I_{2z}]_m \,,$$

$$\begin{aligned} H_{F,I}^{(D)} =& G_{PM}^{(0)} \left[I_1^{+} I_2^{-}\right]_0 + G_{MP}^{(0)} \left[I_1^{-} I_2^{+}\right]_0 + \sum_{m\neq 0} G_{zz}^{(m)} [I_{1z} I_{2z}]_m + \sum_{m\neq 0,-2} G_{PM}^{(m)} \left[I_1^{+} I_2^{-}\right]_m \\ &+ \sum_{m\neq 0,2} G_{MP}^{(m)} \left[I_1^{-} I_2^{+}\right]_m \,, \end{aligned}$$

$$H_{F,S}^{(eff)} = \sum_{j=1}^{N} \omega_{j,eff} \left[S_{jz}\right]_0 \,,$$

$$H_{F,S}^{(CSA)} = \sum_{j=1}^{N} \sum_{\substack{m=-2,\\ m\neq 0}}^{2} G_j^{(m)} \left(\left[S_{jz}\right]_m \cos\theta_j - \left[S_{jx}\right]_m \sin\theta_j \right) ,$$

$$H_{F,S}^{(D)} = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \sum_{j<k=1}^{N} \left(\begin{array}{l} G_{zz,jk}^{(m)} \left[S_{jz}S_{kz}\right]_m + G_{PM,jk}^{(m)} \left[S_j^+ S_k^-\right]_m + G_{MP,jk}^{(m)} \left[S_j^- S_k^+\right]_m \\ \\ +G_{ZP,jk}^{(m)} \left[S_{jz}S_k^+\right]_m + G_{ZM,jk}^{(m)} \left[S_{jz}S_k^-\right]_m + G_{PZ,jk}^{(m)} \left[S_j^+ S_{kz}\right]_m \\ \\ +G_{MZ,jk}^{(m)} \left[S_j^- S_{kz}\right]_m + G_{PP,jk}^{(m)} \left[S_j^+ S_k^+\right]_m + G_{MM,jk}^{(m)} \left[S_j^- S_k^-\right]_m \end{array} \right), \text{ and}$$

$$\begin{aligned} H_{F,IS}^{(D)} =& \sum_{j=1}^{N} \sum_{\substack{m=-2,\\ m\neq 0}}^{2} G_{I_1 S_j}^{(m)} \left[\left[I_{1z}S_{jz}\right]_m \cos\theta_j - \left[I_{1z}S_{jx}\right]_m \sin\theta_j \right] \\ &+ \sum_{j=1}^{N} \sum_{\substack{m=-2,\\ m\neq 0}}^{2} G_{I_2 S_j}^{(m)} \left[\left[I_{2z}S_{jz}\right]_m \cos\theta_j - \left[I_{2z}S_{jx}\right]_m \sin\theta_j \right] . \end{aligned}$$

A detailed description of the G-coefficients along with the operators involved in the Floquet Hamiltonian H_F [Eq.(S44)] is given in **Table** I.

To describe the effects of the CSA interactions of the I-spins; the Floquet Hamiltonian is expanded in the form of a convergent series in orders of the perturbation parameter λ, as shown below:

$$H_F = H_0 + \lambda H_1 + \lambda^2 H_2. \tag{S45}$$

Here, the parameter λ is used exclusively for ordering purposes, and H_0 represents the zero-order Hamiltonian, which is formulated as:

$$H_0 = \omega_r I_F + \sum_{j=1}^{N} \omega_{j,eff} S_{jz}.$$

Subsequently, H_1 and H_2 are expressed as:

$$H_1 = H_{1,d} + H_{1,od}.$$

$$H_2 = H_{F,S}^{(CSA)} + H_{F,S}^{(D)} + H_{F,IS}^{(D)}.$$

In the above representation, the I-spin interactions (excluding CSA) are retained along $H_{1,d}$, while, $H_{1,od}$ comprises the CSA interactions.

$$H_{1,d} = H_{F,I}^{(iso)} + H_{F,I}^{(D)}.$$

TABLE I. Description of the G-coefficients along with the operators involved in the Floquet Hamiltonian H_F derived for multi-spin ($I_1 - I_2 - S_N$) model system. The Fourier index "m" varies from -2 to 2 ($m \neq 0$). The indices involved have the following values: i = 1 to 2, j = 1 to N and $k > j$.

Operator	Coefficient	Operator	Coefficient
1. $H_{F,I}$			
$\left[I_1^+ I_2^-\right]_0$	$G_{PM,12}^{(0)} = -\frac{1}{2}\omega_{12}^{(-2)}$	$\left[I_1^- I_2^+\right]_0$	$G_{MP,12}^{(0)} = -\frac{1}{2}\omega_{12}^{(2)}$
$[I_{iz}]_m$	$G_i^{(m)} = \omega_i^{(m)}$	$[I_{1z} I_{2z}]_m$	$G_{zz}^{(m)} = 2\omega_{12}^{(m)}$
$\left[I_1^+ I_2^-\right]_m$	$G_{PM}^{(m)} = -\frac{1}{2}\omega_{12}^{(m)}$	$\left[I_1^- I_2^+\right]_m$	$G_{MP}^{(m)} = -\frac{1}{2}\omega_{12}^{(m)}$
2. $H_{F,S}^{(CSA)}$			
$[S_{jz}]_m$	$G_j^{(m)} = \omega_j^{(m)}$	$[S_{jx}]_m$	$G_j^{(m)} = \omega_j^{(m)}$
3. $H_{F,S}^{(D)}$			
$[S_{jz} S_{kz}]_m$	$G_{zz,jk}^{(m)} = \omega_{jk}^{(m)} A_{zz,jk}$	$\left[S_j^+ S_k^-\right]_m$	$G_{PM,jk}^{(m)} = \frac{1}{4}\omega_{jk}^{(m)} A_{pm,jk}$
$\left[S_j^- S_k^+\right]_m$	$G_{MP,jk}^{(m)} = \frac{1}{4}\omega_{jk}^{(m)} A_{mp,jk}$	$\left[S_{jz} S_k^+\right]_m$	$G_{ZP,jk}^{(m)} = \frac{1}{2}\omega_{jk}^{(m)} A_{zp,jk}$
$\left[S_{jz} S_k^-\right]_m$	$G_{ZM,jk}^{(m)} = \frac{1}{2}\omega_{jk}^{(m)} A_{zm,jk}$	$\left[S_j^+ S_{kz}\right]_m$	$G_{PZ,jk}^{(m)} = \frac{1}{2}\omega_{jk}^{(m)} A_{pz,jk}$
$\left[S_j^- S_{kz}\right]_m$	$G_{MZ,jk}^{(m)} = \frac{1}{2}\omega_{jk}^{(m)} A_{mz,jk}$	$\left[S_j^+ S_k^+\right]_m$	$G_{PP,jk}^{(m)} = \frac{1}{4}\omega_{jk}^{(m)} A_{pp,jk}$
$\left[S_j^- S_k^-\right]_m$	$G_{MM,jk}^{(m)} = \frac{1}{4}\omega_{jk}^{(m)} A_{mm,jk}$		
4. $H_{F,IS}^{(D)}$			
$[I_{iz} S_{jz}]_m$	$G_{I_i S_j}^{(m)} = 2\omega_{ij}^{(m)}$	$[I_{iz} S_{jx}]_m$	$G_{I_i S_j}^{(m)} = 2\omega_{ij}^{(m)}$

$$H_{1,od} = H_{F,I}^{(CSA)}.$$

To describe the effects of the CSA interactions of I-spins, the Hamiltonian is transformed employing the transformation function, S_1 $\left(i.e.,\ S_1 = -i\left[\sum_{m\neq 0} C_1^{(m)} [I_{1z}]_m + \sum_{m\neq 0} C_2^{(m)} [I_{2z}]_m \right] \right)$. Accordingly, the transformed Floquet Hamiltonian is represented as:

$$\tilde{H}_F = e^{-i\lambda S_1} H^F e^{i\lambda S_1} = H_0^{(1)} + H_1^{(1)} + H_2^{(1)} + ... \tag{S46}$$

Employing **BCH** (Baker-Campbell-Hausdorff) expansion and combining like terms, the various orders of corrections to the effective Hamiltonian are derived systematically as-

$$H_0^{(1)} = H_0\,, \tag{S46a}$$

$$H_1^{(1)} = H_{1,d} + H_{1,od} + i\left[S_1, H_0\right]\,, \tag{S46b}$$

$$H_2^{(1)} = H_2 + i\left[S_1, H_{1,d}\right]. \tag{S46c}$$

Based on the discussion for the isolated two-spin system (I_1-I_2), the Hamiltonian after the first transformation reduced to the form given below:

$$\tilde{H}_F = \omega_r I_F + \tilde{H}_{1,d} + H_2 + \sum_{j=1}^{N} \omega_{j,eff}^{(0)} \left[S_{jz}\right]_0 \tag{S47}$$

where $\tilde{H}_{1,d} = \left(-\frac{1}{2}\right)\left[\omega_{12,e}^{(-2)}.\left[I_1^+ I_2^-\right]_0 + \omega_{12,e}^{(2)}.\left[I_1^- I_2^+\right]_0\right]$

To describe the effects of the protons, the Hamiltonian is further transformed such that the off-diagonal contributions from H_2 are folded. Subsequently, effective Hamiltonian is expressed as-

$$H_{eff} = \omega_r I_F + \tilde{H}_{1,d} + \sum_{j=1}^{N} \omega_{j,eff}^{(0)} \left[S_{jz}\right]_0 + \frac{i}{2}\left[S_2, H_2\right]. \tag{S48}$$

In the above equation, the contributions from the protons result through cross-term between the CSA of S-spins and heteronuclear dipolar interactions i.e.,

$$e_1 = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \left[C_{1p}^{(m)} G_{I_1 S_1^-}^{(-m)} - C_{I_1 S_1^-}^{(m)} G_{1p}^{(-m)}\right] + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \left[C_{I_1 S_1^+}^{(m)} G_{1m}^{(-m)} - C_{1m}^{(m)} G_{I_1 S_1^+}^{(-m)}\right], \text{ and}$$

$$d_1 = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \left[C_{1p}^{(m)} G_{I_2 S_1^-}^{(-m)} - C_{I_2 S_1^-}^{(m)} G_{1p}^{(-m)}\right] + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \left[C_{I_2 S_1^+}^{(m)} G_{1m}^{(-m)} - C_{1m}^{(m)} G_{I_2 S_1^+}^{(-m)}\right].$$

Here, $C_{1p}^{(m)} = \frac{G_{1p}^{(m)}}{m\omega_r + \omega_{1,eff}^{(0)}}$, $C_{1m}^{(m)} = \frac{G_{1m}^{(m)}}{m\omega_r - \omega_{1,eff}^{(0)}}$, $C_{I_1 S_1^+}^{(m)} = \frac{G_{I_1 S_1^+}^{(m)}}{m\omega_r + \omega_{1,eff}^{(0)}}$, and $C_{I_1 S_1^-}^{(m)} = \frac{G_{I_1 S_1^-}^{(m)}}{m\omega_r - \omega_{1,eff}^{(0)}}$.

Extending the above discussion, the effective Hamiltonian is represented by the following equation,

$$\begin{aligned} H_{eff} =& \omega_r I_F + \sum_{j=1}^{N} \omega_{j,eff}^{(0)} \left[S_{jz}\right]_0 + \left(-\frac{1}{2}\right) \left[\omega_{12,e}^{(-2)} \cdot \left[I_1^+ I_2^-\right]_0 + \omega_{12,e}^{(2)} \cdot \left[I_1^- I_2^+\right]_0\right] + \sum_{j=1}^{N} e_j \left[I_{1z} S_{jz}\right]_0 \\ & + \sum_{j=1}^{N} d_j \left[I_{2z} S_{jz}\right]_0 . \end{aligned} \tag{S49}$$

where, $e_j = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \left[C_{S_j^+}^{(m)} G_{I_{1z}S_j^-}^{(-m)} - C_{I_{1z}S_j^-}^{(m)} G_{S_j^+}^{(-m)}\right] + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \left[C_{I_{1z}S_j^+}^{(m)} G_{S_j^-}^{(-m)} - C_{S_j^-}^{(m)} G_{I_{1z}S_j^+}^{(-m)}\right]$, and

$$d_j = \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \left[C_{S_j^+}^{(m)} G_{I_{2z}S_j^-}^{(-m)} - C_{I_{2z}S_j^-}^{(m)} G_{S_j^+}^{(-m)}\right] + \sum_{\substack{m=-2,\\ m\neq 0}}^{2} \left[C_{I_{2z}S_j^+}^{(m)} G_{S_j^-}^{(-m)} - C_{S_j^-}^{(m)} G_{I_{2z}S_j^+}^{(-m)}\right].$$

Here, $C_{S_j^+}^{(m)} = \frac{G_{S_j^+}^{(m)}}{m\omega_r + \omega_{j,eff}^{(0)}}$, $C_{S_j^-}^{(m)} = \frac{G_{S_j^-}^{(m)}}{m\omega_r - \omega_{j,eff}^{(0)}}$, $C_{I_{1z}S_j^+}^{(m)} = \frac{G_{I_{1z}S_j^+}^{(m)}}{m\omega_r + \omega_{j,eff}^{(0)}}$, $C_{I_{1z}S_j^-}^{(m)} = \frac{G_{I_{1z}S_j^-}^{(m)}}{m\omega_r - \omega_{j,eff}^{(0)}}$,

$C_{I_{2z}S_j^+}^{(m)} = \frac{G_{I_{2z}S_j^+}^{(m)}}{m\omega_r + \omega_{j,eff}^{(0)}}$, and $C_{I_{2z}S_j^-}^{(m)} = \frac{G_{I_{2z}S_j^-}^{(m)}}{m\omega_r - \omega_{j,eff}^{(0)}}$.

TABLE II. NMR parameters* employed in the multi-spin simulations.

Atom	δ_{iso} (ppm)	δ_{aniso} (ppm)	η	Ω_{PM} (deg)
V_{CO}	173.70	87.1	0.5	(-35.2,112.0,60.0)
$V_{C\gamma 1}$	18.50	20.8	0.4	(145.2,153.2,-132.6)
$L_{C\delta 2}$	20.10	28.6	0.6	(-161.2,131.1,-39.1)
L_{CO}	181.20	-84.0	0.8	(118.5,114.0,52.4)
$V_{C\beta}$	32.90	12.2	0.5	(44.5,130.1,50.0)
$V_{H\alpha}$	4.60	-3.1	0.4	(126.9,153.0,101.3)
$V_{H\beta}$	1.90	5.3	0.3	(31.9,102.8,172.1)
$V_{1H\gamma 1}$	1.066	5.1	0.1	(-58.7,48.8,-4.5)
$V_{1H\gamma 2}$	1.00	5.4	0.5	(141.4,92.3,-37.4)
$L_{H\alpha}$	3.80	2.7	0.6	(-111.2,35.2,-68.5)
$L_{H\beta 1}$	1.45	3.2	0.4	(-61.3,52.8,-64.6)
$L_{H\gamma}$	1.30	4.8	0.1	(-64.0,53.3,-61.6)
$L_{1H\delta 1}$	0.76	6.6	0.3	(141.8,100.0,43.8)
t_{mix} = 30 ms				
^1H frequency =	500 MHz			
CW decoupling	strength = 100 kHz			

*The crystal structure of N-Ac-VL[9] was optimized by density functional theory (DFT)-based quantum chemical calculations using the CASTEP module[10,11] of the Materials Studio 2019 software[12,13]. The optimization was performed using the generalized gradient approximation (GGA) and the Perdew-Burke-Ernzerhof (PBE) exchange correlation functional in an OTFG ultrasoft pseudopotential formalism. NMR calculations on the optimized structure of dipeptide N-Ac-VL were performed using the Gauge Including Projector Augmented Wave (GIPAW)[14,15] method with plane wave basis cut-off energy of 600 eV and k-point spacing of 0.05 Å^{-1}. The isotropic chemical shifts ($\delta_{iso} = \sigma_{ref} - \sigma_{iso}$) for the protons and carbons were calculated using reference values (σ_{ref}) of 30.7 ppm and 170.4 ppm, respectively.

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