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ELECTRONIC SUPPLEMENTARY INFORMATION

Multiscale modelling of nuclear magnetisation dynamics: Spin relaxation, polarisation transfer and chemical exchange in ^{129}Xe@cryptophane(*aq*) structures

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1 Cross-correlated dipole-dipole relaxation

Here, we give a brief justification of why cross-correlated dipole-dipole (DD) relaxation does not couple the time evolution of single-spin operators, which correspond to magnetisation observables, with other single-spin operators. Instead, the first possible couplings exist between single-spin and three-spin operators.

Let $\hat{S}_i$ be a single-spin operator acting on spin i, and $\hat{Q}$ an arbitrary operator of the Liouville space of the spin system. $\hat{Q}$ can be of any spin order up to N, where N is the total number of spins in the system. Coupling between the two operators caused by cross-correlated DD relaxation is determined by the corresponding matrix elements in the relaxation superoperator, which include factors of the following type [1]:

$$\left\langle \hat{S}_i \middle| \hat{\hat{S}}_a \hat{\hat{S}}_b \hat{\hat{S}}_{a'} \hat{\hat{S}}_{b'} \middle| \hat{Q} \right\rangle = \mathrm{Tr}\left\{ \hat{S}_i^{\dagger} \hat{\hat{S}}_a \hat{\hat{S}}_b \hat{\hat{S}}_{a'} \hat{\hat{S}}_{b'} \hat{Q} \right\}.$$

Here, the $\hat{\hat{S}}_a$ are commutation superoperators involving a single-spin operator $\hat{S}_a$. The DD coupling is a bilinear interaction that does not couple a spin with itself, meaning that a (a') and b (b') always refer to two different spins: $a \neq b$ and $a' \neq b'$. The action of the commutation superoperator product to the right yields

$$\hat{\hat{S}}_a \hat{\hat{S}}_b \hat{\hat{S}}_{a'} \hat{\hat{S}}_{b'} \hat{Q} = \hat{Q}_{a,b,a',b',\ldots},$$

where $\hat{Q}_{a,b,a',b',\ldots}$ is a product operator that includes single-spin operators of spins a, b, a', b'. Otherwise the operators would act on different spins and, hence, commute, yielding zero. The remaining matrix element

$$\left\langle \hat{S}_i \middle| \hat{Q}_{a,b,a',b',\ldots} \right\rangle$$

can only be non-zero if $\hat{Q}_{a,b,a',b',\ldots} = \hat{Q}_{a,b,a',i,\ldots}$, *i.e.*, when at least one of the indices of the ket operator coincides with that of the bra-operator. The operator with the smallest spin order that satisfies this condition and obeys $a \neq b$ and $a' \neq i$, is $\hat{Q}_{a,i,a',i}$, which is of spin order 3.

2 Equation of motion for chemically equivalent spin groups

To derive Eq. (18) in the main text, we simply compute the time derivative of $M_{z,I}(t)$ using the present definitions of the group quantities:

$$\begin{aligned}
\frac{d}{dt}M_{z,I}(t) &= \frac{d}{dt}\sum_{i\in I} S_{z,i}(t) = N_I \frac{d}{dt} S_{z,i\in I}(t) \\
&= -N_I \Bigg[\sum_{j\neq i} R_{z,ij}\Delta S_{z,i}(t) + \sum_{j\neq i} r_{z,ij}\Delta S_{z,j}(t)\Bigg]_{i\in I} \\
&= -N_I \Bigg[\sum_{J}\sum_{(j\neq i)\in J} R_{z,ij}\Delta S_{z,i}(t) + \sum_{J}\sum_{(j\neq i)\in J} r_{z,ij}\Delta S_{z,j}(t)\Bigg]_{i\in I}.
\end{aligned}$$

In the last step, the spins were divided into the groups J, within which they are chemically equivalent. Each spin j can belong to the same chemically equivalent group as i ($J = I$), or to a different, chemically non-equivalent group ($J \neq I$). We treat these cases separately:

$$\begin{aligned}
\frac{d}{dt}M_{z,I}(t) &= -N_I \Bigg[\sum_{(j\neq i)\in I} R_{z,II}\Delta S_{z,i}(t) + \sum_{(j\neq i)\in I} r_{z,II}\Delta S_{z,j}(t)\Bigg]_{i\in I} \\
&\quad - N_I \Bigg[\sum_{J\neq I}\sum_{j\in J} R_{z,IJ}\Delta S_{z,i}(t) + \sum_{J\neq I}\sum_{j\in J} r_{z,IJ}\Delta S_{z,j}(t)\Bigg]_{i\in I} \\
&= -\Bigg[\sum_{(j\neq i)\in I} R_{z,II}\Delta M_{z,I}(t) + N_I r_{z,II}\sum_{(j\neq i)\in I}\Delta S_{z,j}(t) \\
&\quad + \sum_{J\neq I}\sum_{j\in J} R_{z,IJ}\Delta M_{z,I}(t) + N_I\sum_{J\neq I} r_{z,IJ}\Delta M_{z,J}(t)\Bigg].
\end{aligned}$$

Then, using Eq. (17) of the main text, which is based on the requirement that chemically equivalent spins have identical time evolution, we get

$$\begin{aligned}
\frac{d}{dt}M_{z,I}(t) &= -\Bigg[(N_I-1)R_{z,II}\Delta M_{z,I}(t) + N_I r_{z,II}(N_I-1)\Delta S_{z,j\in I}(t) \\
&\quad + \sum_{J\neq I} N_J R_{z,IJ}\Delta M_{z,I}(t) + N_I\sum_{J\neq I} r_{z,IJ}\Delta M_{z,J}(t)\Bigg] \\
&= -\Bigg[(N_I-1)(R_{z,II}+r_{z,II})\Delta M_{z,I}(t) \\
&\quad + \sum_{J\neq I} N_J R_{z,IJ}\Delta M_{z,I}(t) + N_I\sum_{J\neq I} r_{z,IJ}\Delta M_{z,J}(t)\Bigg] \\
&= -\Bigg[(R^{\mathrm{CE}}_{z,I} + R^{\mathrm{CnE}}_{z,I})\Delta M_{z,I}(t) + N_I\sum_{J\neq I} r_{z,IJ}\Delta M_{z,J}(t)\Bigg].
\end{aligned}$$

where $(N_I-1)(R_{z,II}+r_{z,II}) \equiv R^{\mathrm{CE}}_{z,I}$ and $\sum_{J\neq I} N_J R_{z,IJ} \equiv R^{\mathrm{CnE}}_{z,I}$.

3 Equation of motion for population-weighted magnetisation

The equation of motion for the population-weighted magnetisation, $\boldsymbol{O}(t) = \boldsymbol{P}(t) \odot \boldsymbol{M}(t)$, is obtained by using the product rule of differentiation:

$$\frac{d}{dt}\boldsymbol{O}(t) = \frac{d}{dt}\left[\boldsymbol{P}(t) \odot \boldsymbol{M}(t)\right] = \left[\frac{d}{dt}\boldsymbol{P}(t)\right] \odot \boldsymbol{M}(t) + \boldsymbol{P}(t) \odot \frac{d}{dt}\boldsymbol{M}(t).$$

In chemical equilibrium conditions we may now use Eq. (39) of the main article for the first term involving the site populations. In the second term we note that the time propagation of the magnetisation vector $\boldsymbol{M}(t)$ is driven by the propagator matrix $\boldsymbol{L}$ incorporating the coherent and incoherent Hamiltonians appropriate to the sites. This leads to

$$\frac{d}{dt}\boldsymbol{O}(t) = \boldsymbol{\nu}_{\mathrm{eq}}\boldsymbol{P}(t) \odot \boldsymbol{M}(t) + \boldsymbol{P}(t) \odot \boldsymbol{L}\boldsymbol{M}(t),$$

and employing the associativity of the Hadamard product $\odot$ one obtains

$$\begin{aligned}\frac{d}{dt}\boldsymbol{O}(t) &= \boldsymbol{\nu}_{\mathrm{eq}}\boldsymbol{P}(t) \odot \boldsymbol{M}(t) + \boldsymbol{L}\boldsymbol{P}(t) \odot \boldsymbol{M}(t) \\ &= \Big(\boldsymbol{\nu}_{\mathrm{eq}} + \boldsymbol{L}\Big)\boldsymbol{P}(t) \odot \boldsymbol{M}(t) \\ &= \Big(\boldsymbol{\nu}_{\mathrm{eq}} + \boldsymbol{L}\Big)\boldsymbol{O}(t).\end{aligned}$$

Here, $\boldsymbol{M}(t) = \boldsymbol{M}_z(t)$ and $\boldsymbol{L} = -\boldsymbol{R}_z$ in the longitudinal case, whereas $\boldsymbol{M}(t) = \boldsymbol{M}_+(t)$ and $\boldsymbol{L} = i\boldsymbol{\omega} - \boldsymbol{R}_+$ in the transverse case. Thermalisation of this equation is carried out exactly as in the absence of chemical exchange (see the main text).

4 Dipole-dipole time-correlation functions

The DD time-correlation functions (TCFs), $G_{IJ}^{D}(\tau)$, between each pair of spin groups IJ are shown in Figures S1, S2 and S3 for the Xe(aq), Xe@3AC(aq) and Xe@6AC(aq) systems, respectively.

Longer MD trajectories with larger number of molecules would provide better statistics for the TCFs and, hence, more reliable values for the fitted parameters. However, we believe that the present MD trajectories are sufficiently long for relatively reliable DD TCFs.

Different choices of the final time point of the TCFs to be included in the exponential fits result in slightly different values for the fitted parameters. In our case the values remained within roughly 20% of our ultimate choice, where we strived to include as much of the TCF as possible, before it became too noisy. Following this procedure, the final time points were chosen to be 1 ns less than the length of the full production period for the Xe@Cr(aq) systems, and 0.5 ns for the Xe(aq) system.

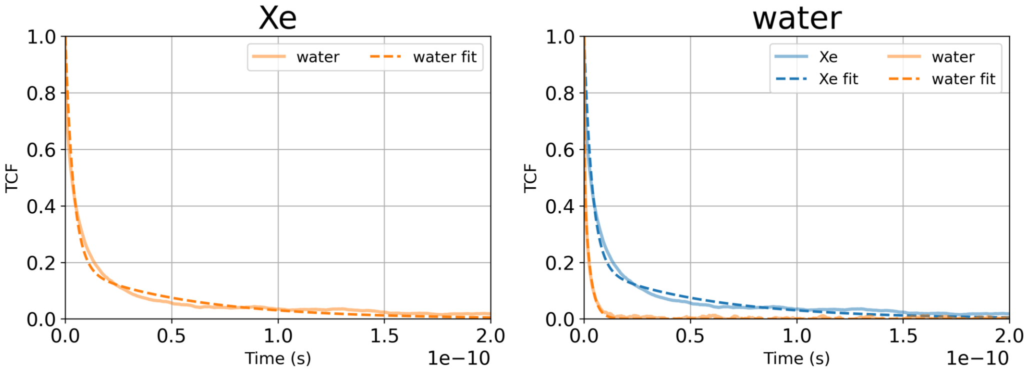

Figure S1: Dipole-dipole time-correlation functions for the Xe(aq) system. (a) $G_{IJ}^{D}(\tau)$ with $I = {}^{129}$Xe, $J = {}^{1}$H. (b) $G_{IJ}^{D}(\tau)$ with $I = {}^{1}$H, $J = {}^{129}$Xe (blue) and $G_{II}^{D}(\tau)$ with $I = {}^{1}$H (orange). Molecular dynamics data in full lines, Lipari-Szabo fit in dashed lines.

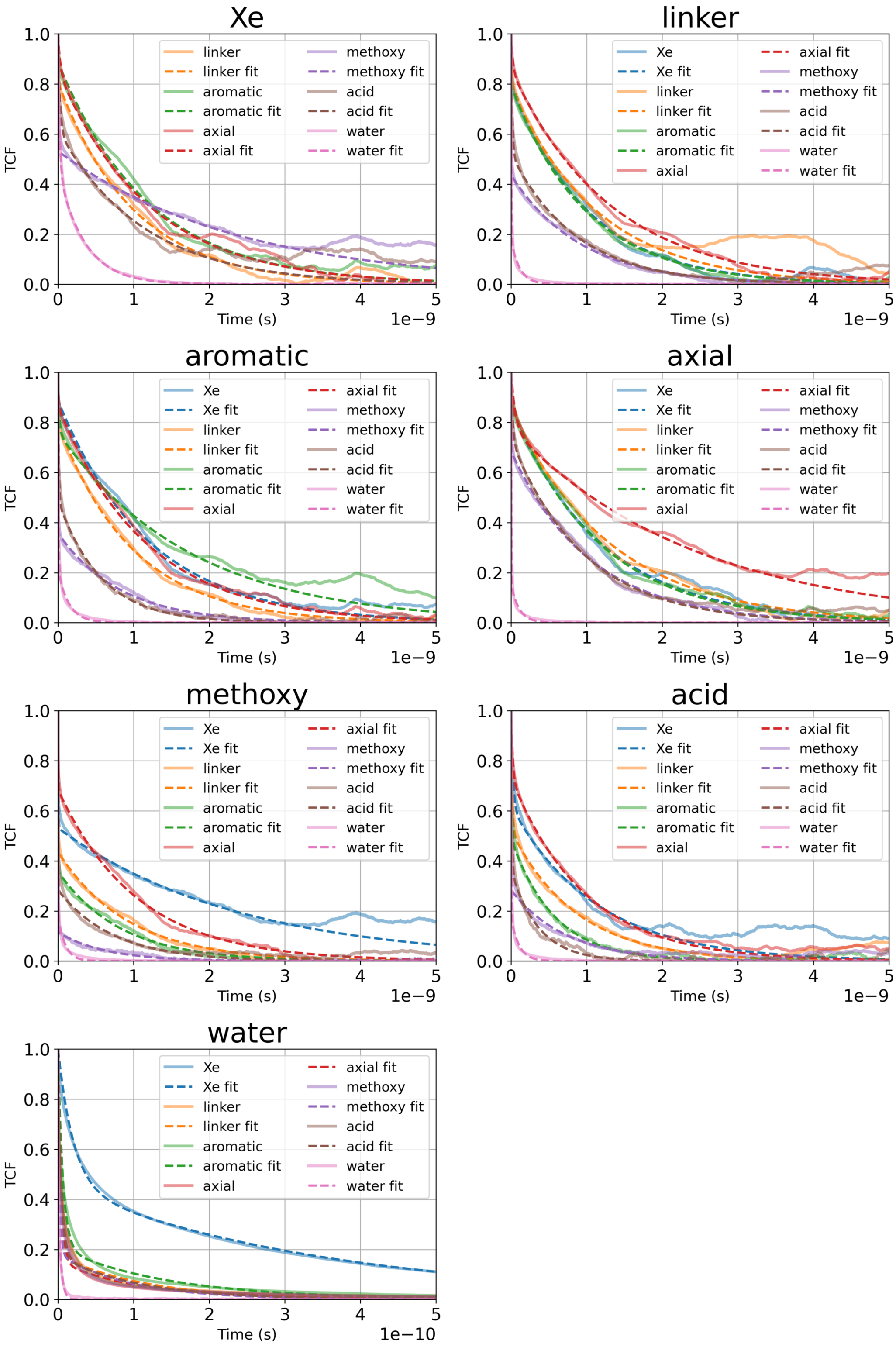

Figure S2: Dipole-dipole time-correlation functions $G_{IJ}^{D}(\tau)$ for the Xe@3AC(aq) system. In each panel, the spin group I is indicated by the panel title and the spin groups J are given in the legend. Molecular dynamics data in full lines, Lipari-Szabo fit in dashed lines.

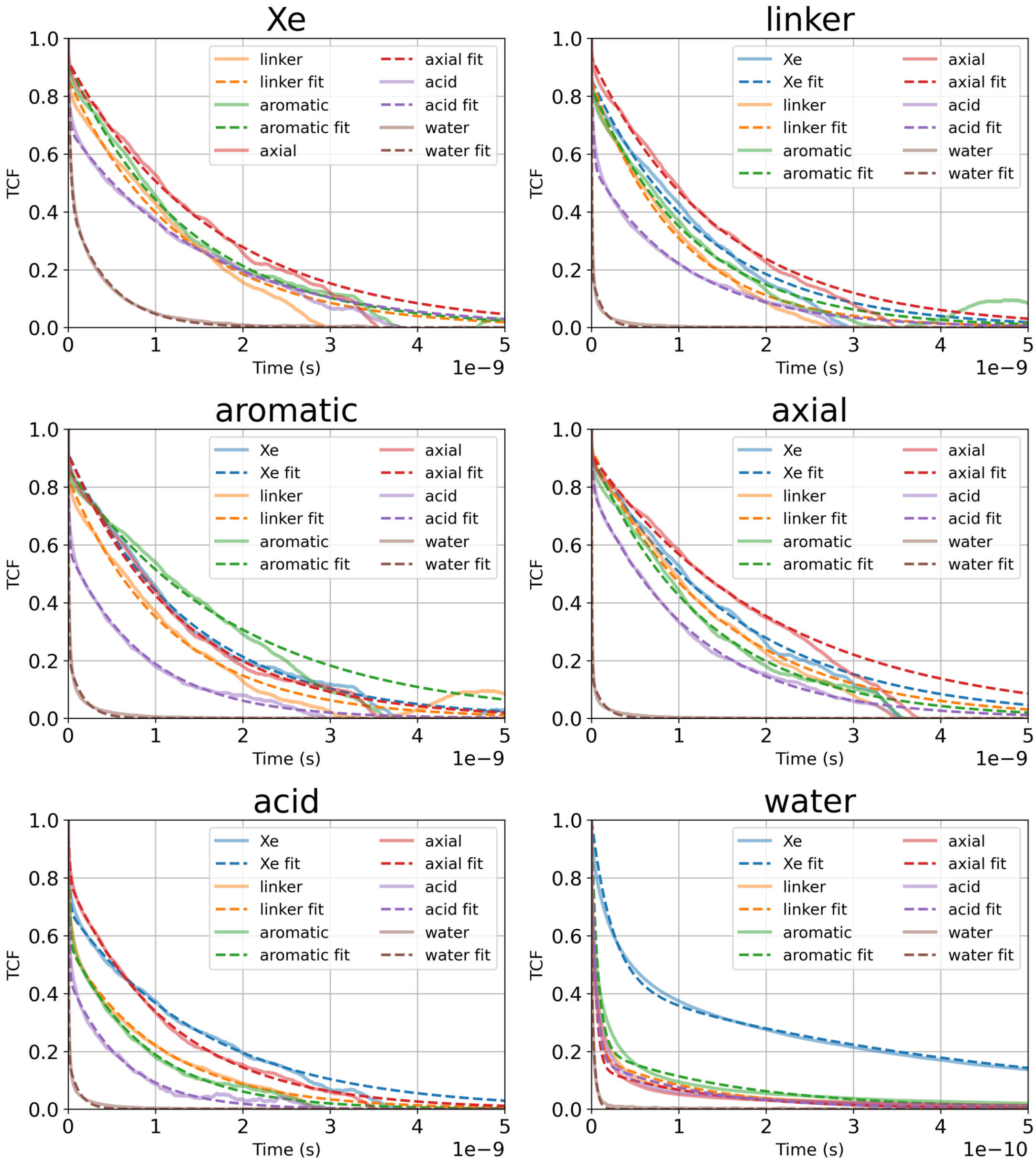

Figure S3: Dipole-dipole time-correlation functions $G_{IJ}^{D}(\tau)$ for the Xe@6AC(aq) system. In each panel, the spin group I is indicated by the panel title and the spin groups J are given in the legend. Molecular dynamics data in full lines, Lipari-Szabo fit in dashed lines.

5 Chemical exchange rates

Starting from Eq. (3) of the main text

$$K_a = \frac{[\mathrm{Xe@Cage}]_{\mathrm{eq}}}{[\mathrm{Xe}]_{\mathrm{eq}}[\mathrm{Cage}]_{\mathrm{eq}}}$$

and using the relations

$$[\mathrm{Xe}]_{\mathrm{eq}} = [\mathrm{Xe}]_{\mathrm{init}} - [\mathrm{Xe@Cage}]_{\mathrm{eq}}$$
$$[\mathrm{Cage}]_{\mathrm{eq}} = [\mathrm{Cage}]_{\mathrm{init}} - [\mathrm{Xe@Cage}]_{\mathrm{eq}},$$

we get

$$K_a = \frac{[\mathrm{Xe@Cage}]_{\mathrm{eq}}}{\Big([\mathrm{Xe}]_{\mathrm{init}} - [\mathrm{Xe@Cage}]_{\mathrm{eq}}\Big)\Big([\mathrm{Cage}]_{\mathrm{init}} - [\mathrm{Xe@Cage}]_{\mathrm{eq}}\Big)}.$$

This is equivalent to the quadratic polynomial equation for $[\mathrm{Xe@Cage}]_{\mathrm{eq}}$:

$$K_a[\mathrm{Xe@Cage}]_{\mathrm{eq}}^2 - \big(K_a[\mathrm{Xe}]_{\mathrm{init}} + K_a[\mathrm{Cage}]_{\mathrm{init}} + 1\big)[\mathrm{Xe@Cage}]_{\mathrm{eq}} + K_a[\mathrm{Xe}]_{\mathrm{init}}[\mathrm{Cage}]_{\mathrm{init}} = 0.$$

With given $[\mathrm{Xe}]_{\mathrm{init}}$ and $[\mathrm{Cage}]_{\mathrm{init}}$, the above equation can be solved to obtain $[\mathrm{Xe@Cage}]_{\mathrm{eq}}$, from which the equilibrium concentrations $[\mathrm{Xe}]_{\mathrm{eq}}$ and $[\mathrm{Cage}]_{\mathrm{eq}}$ follow.

6 ^{129}Xe-^{1}H dipole-dipole relaxation as a function of τ_c

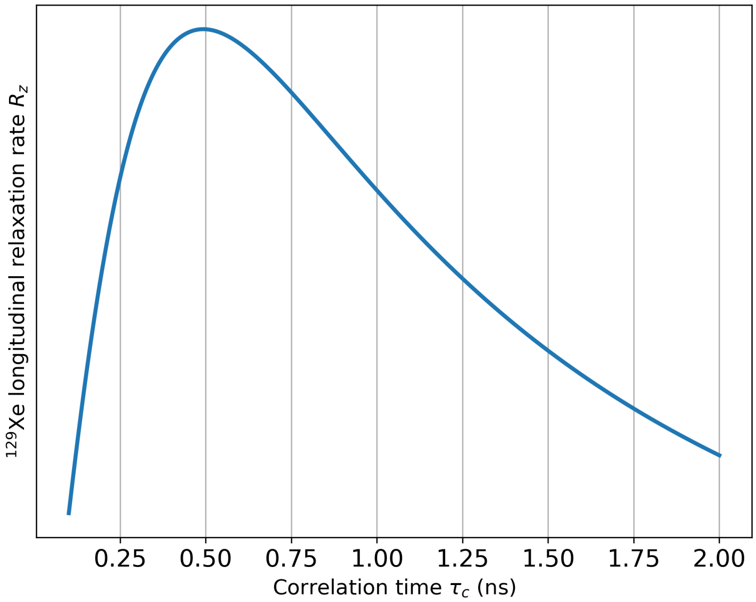

Figure S4: Longitudinal relaxation rate (in arbitrary units) of a ^{129}Xe nucleus caused by DD coupling to a proton as a function of the rotational correlation time τ_c.

Using Eq. (6) in the main text for the longitudinal auto-relaxation rate,

$$R_z = \frac{1}{24}\left[3J^D(\omega_{\mathrm{Xe}}) + J^D(\omega_{\mathrm{Xe}} - \omega_{\mathrm{H}}) + 6J^D(\omega_{\mathrm{Xe}} + \omega_{\mathrm{H}})\right],$$

and the spectral density functions appropriate for isotropic rotational tumbling (here omitting the $G(0)$ factor, see the main text),

$$J^D(\omega) = \frac{\tau_g}{1 + \omega^2\tau_g^2},$$

$R_z(\tau_c)$ can be plotted for a ^{129}Xe nucleus DD-coupled to a proton. Note that in the main text we interpret the Lipari-Szabo fit parameter τ_g to represent τ_c. The relaxation rate reaches a maximum at $\tau_c \approx 0.5$ ns, which is quite close to the rotational correlation time of 0.6 ns found for the Xe@0AC($C_2D_2Cl_4$) system [2]. The relaxation rate *decreases* when τ_c increases from this point onward, and precisely this is observed in the present simulations, where correlation times of 1.38 and 1.48 ns are found for Xe@3AC(aq) and Xe@6AC(aq), respectively.

References

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(2) M. Luhmer, B. M. Goodson, Y.-Q. Song, D. D. Laws, L. Kaiser, M. C. Cyrier and A. Pines, *J. Am. Chem. Soc.*, 1999, **121**, 3502–3512.