Supporting information for
Protein Dynamics from Nuclear Magnetic Relaxation

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1 Correlation function and spectral density function

We chose a model-free approach to describe motions in liquid and solid phases.

1.1 Correlation function and spectral density function found in liquid

The correlation function used for the global tumbling $\mathcal{C}_0(t)$ is classically taken as:

$$\mathcal{C}_0(t) = e^{-\frac{t}{\tau_c}} \tag{S. 1}$$

The correlation function, for the model-free (MF) and the extended model-free (EMF) approaches, has been taken as:

$$\mathcal{C}_{liq}^{MF}(t) = \mathcal{C}_0(t)\mathcal{C}_f(t) \tag{S. 2}$$

$$\mathcal{C}_{liq}^{EMF}(t) = \mathcal{C}_0(t)\mathcal{C}_f(t)\mathcal{C}_s(t) \tag{S. 3}$$

with:

$$\mathcal{C}_i(t) = S_i^2 + (1-S_i^2)e^{-\frac{t}{\tau_i}} \tag{S. 4}$$

where i stands for f (fast motions) or s (slow motions). The corresponding spectral density function for the MF and EMF approaches are:

$$J_{liq}^{MF}(\omega) = \frac{2}{5}\left((1-S_f^2)\frac{\tau_{fe}}{1+(\omega\tau_{fe})^2} + S_f^2\frac{\tau_c}{1+(\omega\tau_c)^2}\right) \tag{S. 5}$$

$$J_{liq}^{EMF}(\omega) = \frac{2}{5}\left(S^2\frac{\tau_c}{1+(\omega\tau_c)^2} + (1-S_f^2)\frac{\tau_{fe}}{1+(\omega\tau_{fe})^2} + (S_f^2-S^2)\frac{\tau_{se}}{1+(\omega\tau_{se})^2}\right) \tag{S. 6}$$

with $\tau_{ie}^{-1} = \tau_i^{-1} + \tau_c^{-1}$, the effective correlation time for the motion, with the order of parameter S_i^2 and

$$S^2 = S_f^2 S_s^2 \tag{S. 7}$$

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1.2 Correlation function and spectral density function found in solids

Correlations functions in solids are characterized by the absence of global tumbling

$$C^{MF}_{solid}(t) = C_f(t) \tag{S. 8}$$

$$C^{EMF}_{solid}(t) = C_f(t)C_s(t) \tag{S. 9}$$

Only the fluctuating part of the interaction contributes to relaxation (the non-fluctuating part corresponds to a coherent interaction). The spectral density function is defined as the Fourier transform of the decaying part of the correlation function.

$$J^{MF}_{solid}(\omega) = \frac{2}{5}\left((1-S_f^2)\frac{\tau_f}{1+(\omega\tau_f)^2}\right) \tag{S. 10}$$

$$J^{EMF}_{solid}(\omega) = \frac{2}{5}\left((S_s^2-S^2)\frac{\tau_f}{1+(\omega\tau_f)^2}+(S_f^2-S^2)\frac{\tau_s}{1+(\omega\tau_s)^2}(1-S_f^2-S_s^2+S^2)\frac{\tau_p}{1+(\omega\tau_p)^2}\right) \tag{S. 11}$$

in which S^2 is defined as Eq. S. 7 and,

$$\tau_p^{-1} = \tau_s^{-1} + \tau_f^{-1} \tag{S. 12}$$

In the case of methyl groups, we used a two correlation times model with angular constraint already present in the literature [1]:

$$J^{MF}_{Met}(\omega,\theta_{i,j}) = \frac{1}{5}\left((1-\alpha S_f^2)\frac{\tau_{fe}}{1+(\omega\tau_{fe})^2}+\alpha S_f^2\frac{\tau_c}{1+(\omega\tau_c)^2}\right) \tag{S. 13}$$

where α depends on the angle $\theta_{i,j}$ between the rotation axis of the methyl group and the principal axis of the interaction as:

$$\alpha = \left(\frac{3\cos^2[\theta_{i,j}]-1}{2}\right)^2 \tag{S. 14}$$

2 Relaxation rates for a selection of spin systems

2.1 Amplitudes of the interactions

We first define the dipolar constant δ_{ij}, the chemical shift anisotropy (CSA) constant Δ_i and the quadrupolar constant Ξ by:

$$\delta_{ij} = \frac{\mu_0\hbar\gamma_i\gamma_j}{4\pi r_{i,j}^3} \tag{S. 15a}$$

$$\Delta_i = \frac{\Delta\sigma_i\gamma_i B_0}{3} \tag{S. 15b}$$

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[1] Kay, JACS Vol 124 NO 22, 2002

$$\Xi = \frac{e^2 qQ}{\hbar} \tag{S. 15c}$$

where μ_0 is the permeability of free space, $\hbar$ is the reduced Planck constant, γ_i is the gyromagnetic ratio of the nucleus i, $r_{i,j}$ is the distance between the two nucleis i and j, B_0 is the magnetic field, $\Delta\sigma$ the chemical shift anisotropy (we assume a axially symmetrical tensor), eQ is the nuclear quadrupole moment, and eq the electric field gradient along its principal axis.

2.2 Nitrogen-15 relaxation rates in an ^{15}N^{1}H group

The longitudinal relaxation rate of nitrogen-15 in a NH group is:

$$\mathcal{R}_1(\omega) = \frac{1}{4}\delta_{NH}^2\left(3J[\omega_N] + J[\omega_N - \omega_H] + 6J[\omega_N + \omega_H]\right) + \Delta_N^2 J[\omega_N] \tag{S. 16}$$

The transverse relaxation rate is:

$$\begin{aligned}\mathcal{R}_2(\omega) =& \frac{1}{8}\delta_{NH}^2\left(4J[0] + 3J[\omega_N] + J[\omega_N - \omega_H] + 6J[\omega_H] + 6J[\omega_N + \omega_H]\right) \\ &+ \frac{1}{2}\Delta_N^2(3J[0] + 2J[\omega_N])\end{aligned} \tag{S. 17}$$

In our simulation we took $J(\omega) = J_{liq}^{MF}(\omega)$ (See Eq. S. 5) andthe other parameters are given in Table 1.

σ_N	$r_{N,H}$	τ_c	S	τ_f
175 ppm	1.02 Å	5 or 10 ns	0.8	100 ps

Table 1 : Parameters used to calculate nitrogen-15 for relaxation rates in ^{15}N^{1}H group.

2.3 Carbon-13 relaxation rates in a ^{13}C^{1}H$_3$ group:

To calculate the relaxation rates of ^{13}C in a ^{13}C^{1}H$_3$ group, four interactions have been considered: dipolar interactions with all three protons and the CSA of the carbon-13 nucleus. The angle ϕ lies between the rotation axis of the methyl group and each CH bond. The longitudinal relaxation rate is:

$$\mathcal{R}_1(\omega) = \frac{3}{4}\delta_{CH}^2\left(3J[\omega_C,\phi] + J[\omega_C - \omega_H,\phi] + 6J[\omega_C + \omega_H,\phi]\right) + \Delta_N^2 J[\omega_C, 0] \tag{S. 18}$$

The transverse relaxation rate is:

$$\begin{aligned}\mathcal{R}_2(\omega) =& \frac{3}{24}\delta_{CH}^2(4J[0,\phi] + 3J[\omega_C,\phi] + J[\omega_C - \omega_H,\phi] + 6J[\omega_H,\phi] + 6J[\omega_C + \omega_H,\phi]) \\ &+ \frac{1}{4}\Delta_N^2(4J[0,0] + 3J[\omega_C, 0])\end{aligned} \tag{S. 19}$$

In this equation, the spectral density function is J_{Met}^{MF} (see Eq S. 13). We considered an ideal geometry for the methyl group, and we oriented the CSA vector along the CC axis.

τ_c	S_f^2	τ_f	σ_C	$r_{C,H}$	ϕ
5 or 10 ns	0.6	50 ns	25 ppm	1.115 Å	109.47°

Table 2 : Parameters used to calculate carbon-13 relaxation rates in a $^{13}C^1H_3$ group

2.4 Deuterium relaxation rates in a $^{13}C^2H^1H_1$ group

Three dipolar interactions and one quadrupolar interaction (CSA negligeable) contribute to the relaxation rate of deuterium in $^{13}C^1H_2{}^2H$ group. The longitudinal relaxation rate is:

$$\begin{aligned}\mathcal{R}_1(\omega) = & \frac{1}{4}(\delta_{DC}^2(3J[\omega_D,\theta_{C,D}]+J[\omega_C-\omega_D,\theta_{C,D}]+6J[\omega_C+\omega_D,\theta_{C,D}]) \\ & +2\delta_{DH}^2(3J[\omega_D,\theta_{H,D}]+J[\omega_H-\omega_D,\theta_{H,D}]+6J[\omega_H+\omega_D,\theta_{H,D}])) \\ & +\frac{1}{40}\Xi^2(12J[\omega_D,\theta_{Quad}])+3J[\omega_D,\theta_{Quad}])\end{aligned} \tag{S. 20}$$

The transverse relaxation rate is:

$$\begin{aligned}\mathcal{R}_2(\omega) = & \frac{2}{8}\delta_{CD}^2(4J[0,\theta_{C,D}]+3J[\omega_D,\theta_{C,D}]+J[\omega_C-\omega_D,\theta_{C,D}]+6J[\omega_C,\theta_{C,D}]+6J[\omega_C+\omega_D,\theta_{C,D}]) \\ & +\frac{1}{8}\delta_{HD}^2(4J[0,\theta_{H,D}]+3J[\omega_D,\theta_{H,D}]+J[\omega_D-\omega_H,\theta_{H,D}]+6J[\omega_H,\theta_{H,D}]+6J[\omega_D+\omega_H,\theta_{H,D}]) \\ & +\frac{1}{80}\Xi(9J[0,\theta_{Quad}]+15J[\omega_D,\theta_{Quad}]+6J[2\omega_D,\theta_{Quad}])\end{aligned} \tag{S. 21}$$

$J(\omega,\theta_{i,j})$ is depending between the angle between the principal axis of the interaction and the rotation axis of the methyl group (see Eq. S. 13) . The principal axis of the quadrupolar interaction is considered aligned with the CC bond.

τ_c	S_f^2	τ_f	σ_C	$\Xi/2\pi$	$r_{C,D}$	$r_{D,H}$	θ_{Quad}	$\theta_{H,D}$	$\theta_{C,D}$
5 or 10 ns	0.6	100 ps	25 ppm	2167.10^3 Hz	1.110 Å	1.115 Å	0°	90°	109.47°

Table 3 : Parameters used to calculate deuterium relaxation rates in a $^{13}C^2H^1H_1$ group

2.5 Carbonyl carbon-13 relaxation rates:

We considered only the CSA of the carbonyl and the dipolar interactions with $^{13}C_\alpha$, $^1H_\alpha$, ^{15}N and the $^1H^N$ nuclei.

The longitudinal relaxation rate is:

$$\begin{aligned}\mathcal{R}_1(\omega) =& \frac{\delta_{CC}}{4}(J[0]+3J[\omega_C]+6J[2\omega_C]) \\ &+\frac{\delta_{CH_\alpha}}{4}(J[\omega_C-\omega_H]+3J[\omega_C]+6J[\omega_H-\omega_C]) \\ &+\frac{\delta_{CN}}{4}(J[\omega_C-\omega_N]+3J[\omega_C]+6J[\omega_N-\omega_C]) \\ &+\frac{\delta_{CH^N}}{4}(J[\omega_C-\omega_H]+3J[\omega_C]+6J[\omega_H-\omega_C]) \\ &+\Delta_C J[\omega_C]\end{aligned} \tag{S. 22}$$

The transverse relaxation rate is:

$$\begin{aligned}\mathcal{R}_2(\omega) =& \frac{\delta_{CC}}{8}(5J[0]+9J[\omega_C]+6J[2\omega_C]) \\ &+\frac{\delta_{CH_\alpha}}{8}(4J[0]+J[\omega_C-\omega_H]+3J[\omega_C]+3J[\omega_H]+6J[\omega_H-\omega_C]) \\ &+\frac{\delta_{CN}}{8}(4J[0]+J[\omega_C-\omega_N]+3J[\omega_C]+3J[\omega_N]+6J[\omega_N-\omega_C]) \\ &+\frac{\delta_{CH^N}}{8}(4J[0]+J[\omega_C-\omega_H]+3J[\omega_C]+3J[\omega_H]+6J[\omega_H-\omega_C]) \\ &+\frac{\Delta_C}{6}(4J[0]+3J[\omega_C])\end{aligned} \tag{S. 23}$$

A model-free spectral density function has been chosen, without angular constraint and the following parameters have been used to give evaluate this relaxation rate.

τ_c	S_f^2	τ_f	$\Delta\sigma_C$	$r_{C,N}$	r_{C,H_N}	r_{C,C_α}	r_{C,H_α}
5 or 10 ns	0.85	50 ps	140 ppm	1.33 Å	2.0 Å	1.52 Å	2.1 Å

Table 4 : Parameters used to calculate carbonyl carbon-13 relaxation rates

3 Chemical exchange simulations

Spectra in the presence of chemical exchange (Figure 7.d-m) were simulated with a simple integration of Bloch-McConnell equations. Chemical exchange saturation transfer (CEST) and dark-state exchange saturation transfer (DEST) saturation profiles (Figure 8.d-f) were obtained using an integration of Bloch-McConnell equations in the presence of a weak radio-frequency field. The exchange constant was k_{ex} = 200 s^{-1}; with $p_B = 2\%$ (Figure 8-d) or $p_B = 10\%$ (Figure 8-f) and a static magnetic field strength of 18.7 T. CEST Profiles were simulated with an amplitude of radiofrequency fields ν_1 = 25 Hz (d-e) while DEST profiles were simulated with three different radiofrequency fields.

A classical model-free spectral density function was used (see Equ. 5) to describe intrinsic relaxation rates. Simulations of CEST profiles (Figure 8.d-e) were carried out with an overall correlation time τ_c = 7 ns for both ground and excited states, an internal correlation time τ_f = 100 ps and an order parameter S_f^2 = 0.9. DEST profiles were simulated with τ_c = 7 ns for the ground state, τ_c = 10 μs in the excited state, parameters of internal dynamics were τ_f = 100 ps and S^2 = 0.9 in both states. Proton decoupling in simulations was achieved with an on-resonance continuous wave radiofrequency irradiation with an amplitude νH = 1 kHz.

4 Further readings

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