CIT Center for Information Technology
National Institutes of Health

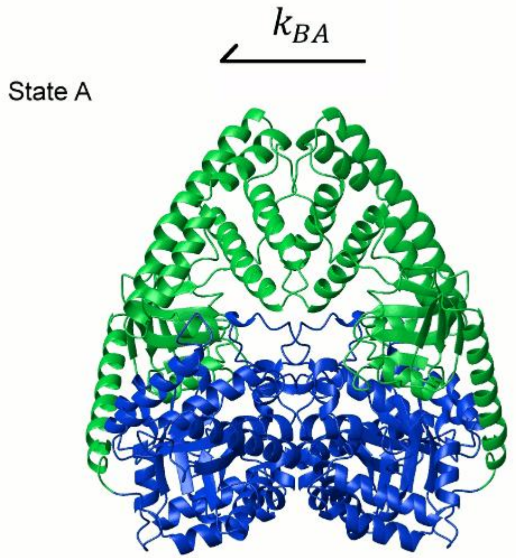
Model of Large Scale Conformational Mobility in Proteins

Yaroslav Ryabov

Outline

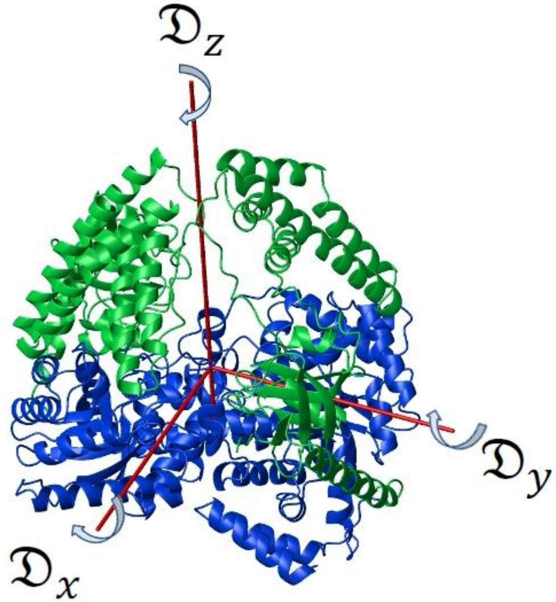
- Conformational transitions on different time scales
- Equation of rotational diffusion
- Eigenfunctions of free diffusion Liouville operator
- Conformational transitions and associated system of linear differential equations
- Eigen and non-Eigen decompositions
- Abel's impossibility and the way we trick it:
  Time domain vs. Frequency domain.
- What to expect: Illustrative calculations

Time scale of Conformational transitions

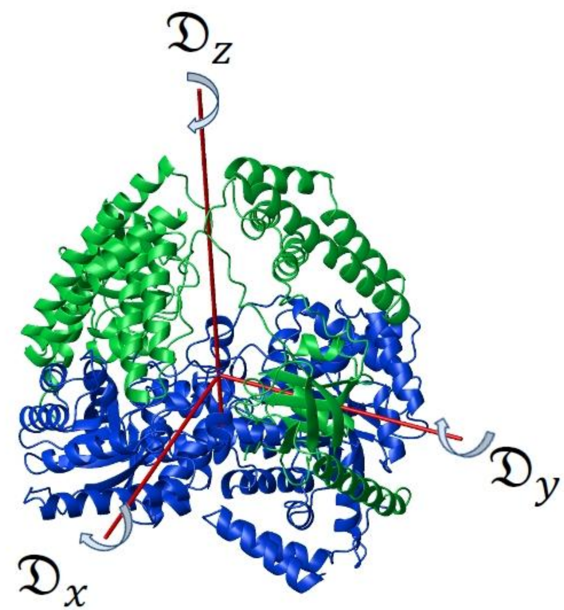


$$\tau_c = \frac{1}{k_{AB} + k_{BA}}$$

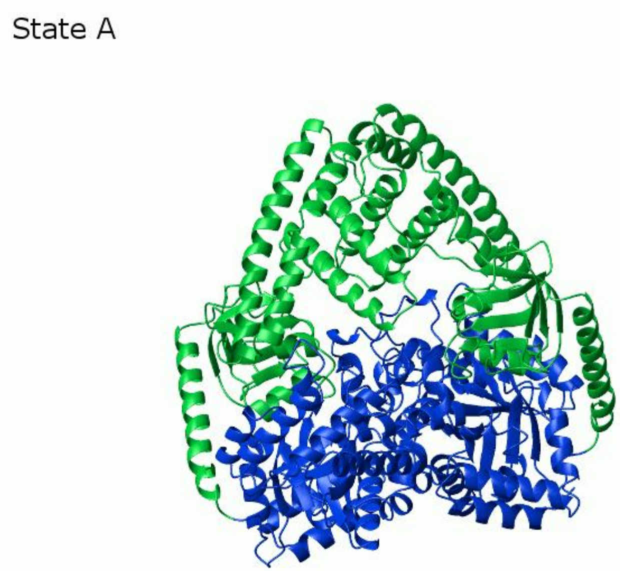
Time scale of Rotational diffusion



$$\tau_{\mathfrak{D}} = \frac{1}{2(\mathfrak{D}_x + \mathfrak{D}_y + \mathfrak{D}_z)}$$



Conformation transitions on different time scales



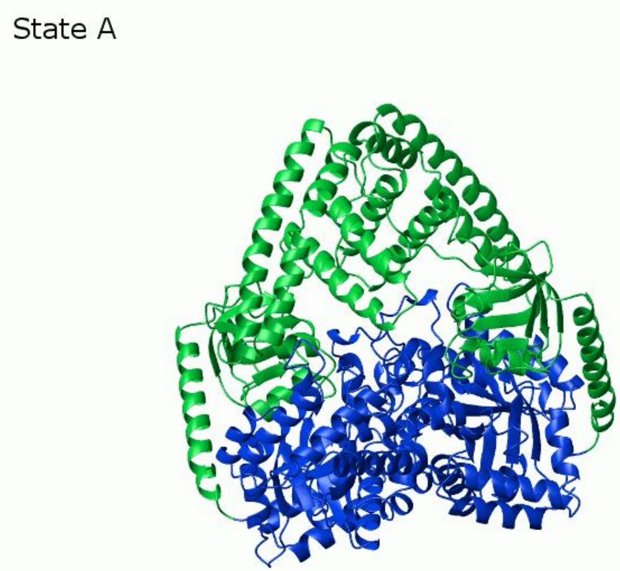
Slow Exchange

$$\tau_c \gg \tau_{\mathfrak{D}}$$

Approximation of **two species** with **two different structures** and **two diffusion tensors**

$\mathfrak{D}^A$ and $\mathfrak{D}^B$

Conformation transitions on different time scales



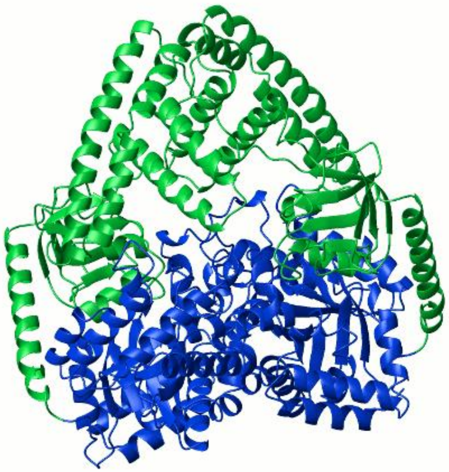
Fast Exchange

$$\tau_c \ll \tau_{\mathfrak{D}}$$

Approximation of **single conformer** with **one averaged structure** and **one averaged diffusion tensor**

$$\bar{\mathfrak{D}}$$

Conformation transitions on different time scales



Intermediate Exchange

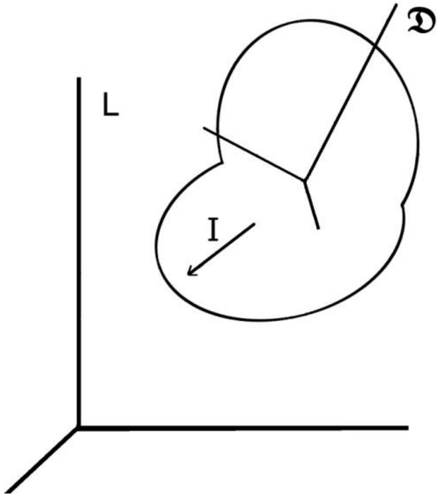
$$\tau_c \sim \tau_{\mathfrak{D}}$$

?

Rotational diffusion of Rigid molecule

Orientation correlation function

$$C_l(t) = \langle P_l[\boldsymbol{n}(t) \cdot \boldsymbol{n}(0)] \rangle$$



Spectral density

Fourier transform

$$J_l(\omega)$$

Linear Combination

Experimental observables: R1, R2 etc.

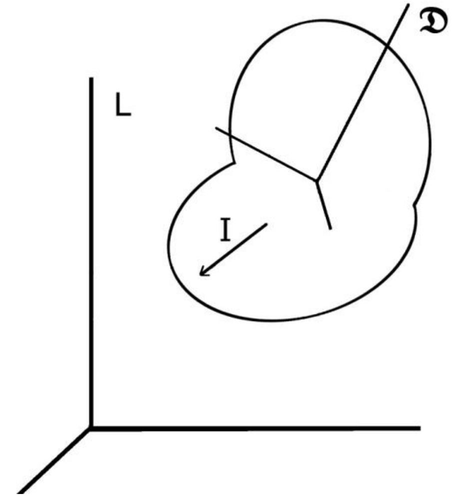
Rotational diffusion of Rigid molecule

Orientation correlation function

$$C_l(t) = \langle P_l[\boldsymbol{n}(t) \cdot \boldsymbol{n}(0)] \rangle$$

Spectral density

$$J_l(\omega)$$



Statistic averaging

$$\langle \ldots \rangle = \iint \ldots \underline{p(\Omega, t | \Omega^0)} p_{eq}(\Omega^0)\, d\Omega d\Omega^0$$

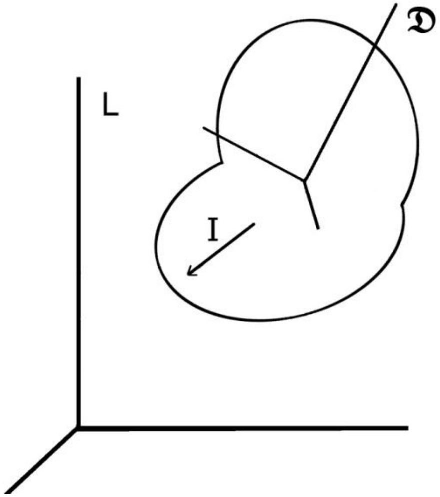
$$p_{eq}(\Omega^0) = \frac{1}{8\pi^2}$$

Isotropic environment

Rotational diffusion of Rigid molecule

Equation for Green's function

$$\frac{\partial p(\Omega, t|\Omega^0)}{\partial t} = -\hat{L}^{\mathrm{T}}\mathfrak{D}\hat{L}\, p(\Omega, t|\Omega^0)$$



Initial conditions

$$p(\Omega, t|\Omega^0)|_{t=+0} = \delta(\Omega - \Omega^0)$$

Operator of spatial rotations

$$\hat{L}^{\mathrm{T}} = \{L_x, L_y, L_z\}$$

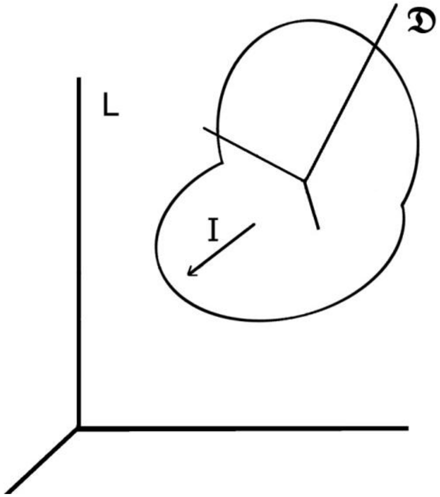
$$\hat{L} = i[\vec{r} \times \vec{\nabla}] \qquad \vec{\nabla} = \left\{\frac{\partial}{\partial x}, \frac{\partial}{\partial y}, \frac{\partial}{\partial z}\right\}$$

F. Perrin (1934, 1936); L.D. Favro (1960)

Rotational diffusion of Rigid molecule

Equation for Green's function

$$\frac{\partial p(\Omega, t|\Omega^0)}{\partial t} = -\hat{L}^{\mathrm{T}}\mathfrak{D}\hat{L}\, p(\Omega, t|\Omega^0)$$



Eigen functions $\Psi^l_{mn}(\Omega)$ of $\hat{L}^{\mathrm{T}}\mathfrak{D}\hat{L}$ operator

$$\hat{L}^{\mathrm{T}}\mathfrak{D}\hat{L}\,\Psi^l_{mn}(\Omega) = E^l_n \Psi^l_{mn}(\Omega)$$

Ansatz Solution

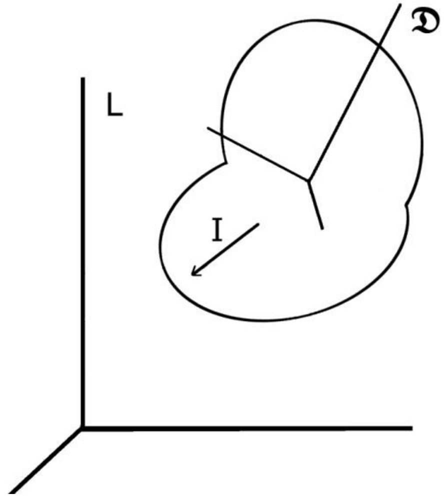
$$p(\Omega, t|\Omega^0) = \sum_{l=0}^{\infty} \sum_{m,n=-l}^{l} c^l_{mn}(\mathrm{t})\Psi^l_{mn}(\Omega)$$

L.D. Favro (1960)

Rotational diffusion of Rigid molecule

Equation for Green's function

$$\frac{\partial p(\Omega, t|\Omega^0)}{\partial t} = -\hat{L}^{\mathrm{T}}\mathfrak{D}\hat{L}\, p(\Omega, t|\Omega^0)$$



Eigen functions $\Psi^l_{mn}(\Omega)$ of $\hat{L}^{\mathrm{T}}\mathfrak{D}\hat{L}$ operator

$$\hat{L}^{\mathrm{T}}\mathfrak{D}\hat{L}\, \Psi^l_{mn}(\Omega) = E^l_n \Psi^l_{mn}(\Omega)$$

$$p(\Omega, t|\Omega^0) = \sum_{l=0}^{\infty} \sum_{m.n=-l}^{l} \Psi^{l*}_{mn}(\Omega^0)\Psi^l_{mn}(\Omega)e^{-E^l_n t}$$

Solution

$$\Psi^l_{mn}(\Omega) = \sum_{k=-l}^{l} A^l_{mk}(\mathfrak{D}_x, \mathfrak{D}_y, \mathfrak{D}_z)D^{(l)}_{kn}(\Omega)$$

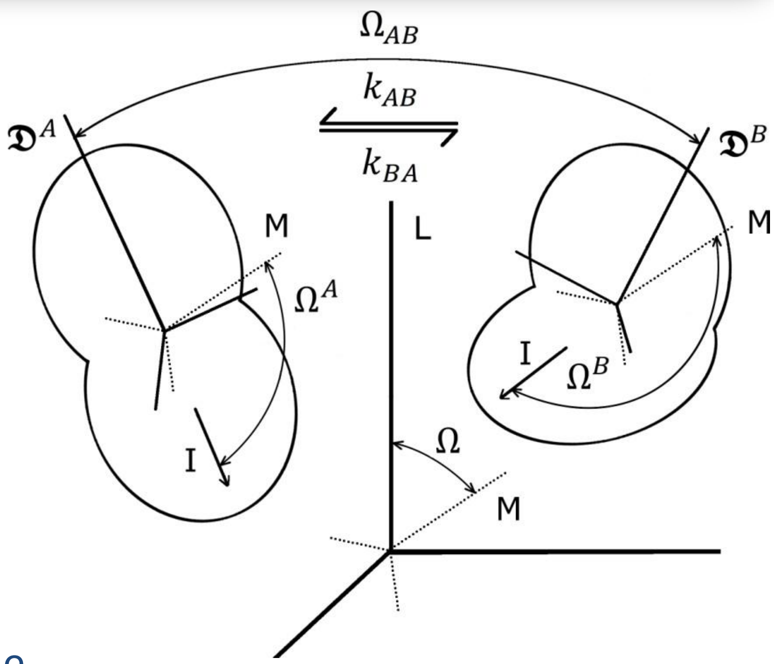
Wigner rotation matrix

L.D. Favro (1960)

Rotational diffusion of semi-Rigid molecule

Conformation transition between discrete set of states

- Molecule tumbles in isotropic solvent
- Molecule exchanges between discrete conformations $\varepsilon = A, B, \ldots$
- In each conformation state molecule is rigid and have diffusion tensor $\mathfrak{D}^{\varepsilon}$
- The transition time is much shorter than the time which molecule spends in any conformation

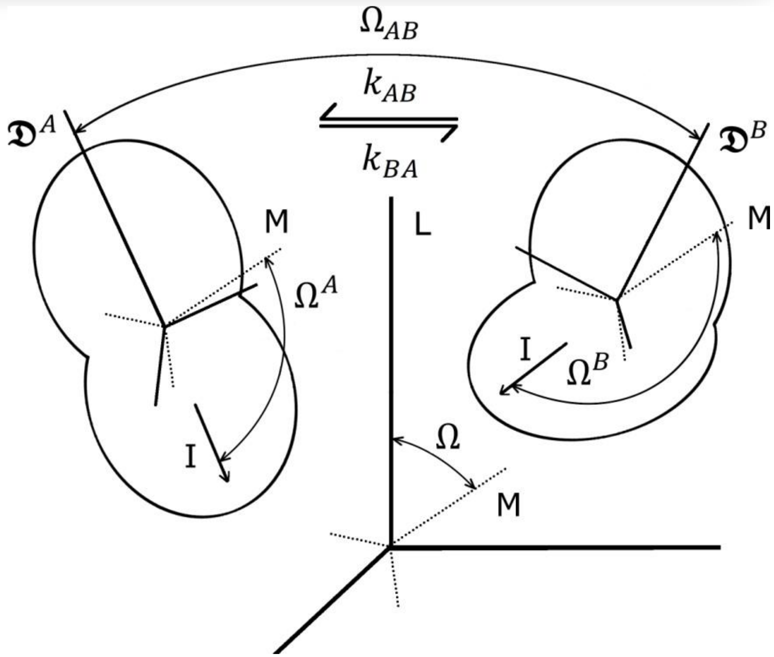


Berne, Pecora (1968); Wong, Case and Szabo (2009)

Rotational diffusion of semi-Rigid molecule

Equations for Green's functions

$$\frac{\partial p^{\varepsilon\eta}(\Omega, t|\Omega^0)}{\partial t} = -\hat{L}^{\mathrm{T}}\mathfrak{D}^{\varepsilon}\hat{L}\, p^{\varepsilon\eta}(\Omega, t|\Omega^0) \boxed{+ \sum_{\mu\neq\varepsilon} K_{\varepsilon\mu}\, p^{\mu\eta}(\Omega, t|\Omega^0)}$$



Conformation exchange

Initial conditions

$$p^{\varepsilon\eta}(\Omega, t|\Omega^0)|_{t=+0} = \delta_{\varepsilon\eta}\delta(\Omega - \Omega^0)$$

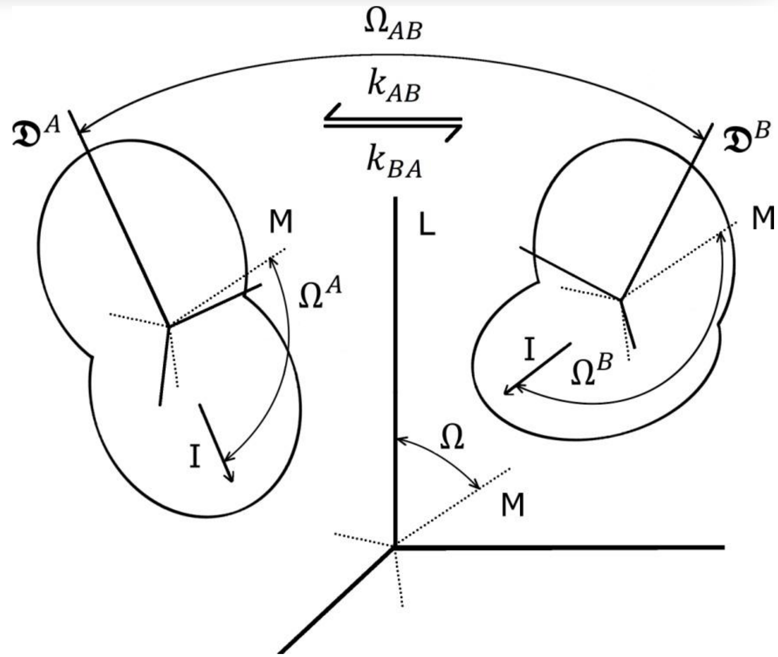
$$\boldsymbol{K} = \begin{pmatrix} -\sum_{\varepsilon\neq A} k_{\varepsilon A} & k_{AB} & \vdots \\ k_{BA} & -\sum_{\varepsilon\neq B} k_{\varepsilon B} & \vdots \\ \cdots & \cdots & \end{pmatrix}$$

Berne, Pecora (1968); Wong, Case and Szabo (2009)

Rotational diffusion of semi-Rigid molecule

Equations for Green's functions

$$\frac{\partial p^{\varepsilon\eta}(\Omega, t|\Omega^0)}{\partial t} = -\hat{L}^{\mathrm{T}}\mathfrak{D}^{\varepsilon}\hat{L}\, p^{\varepsilon\eta}(\Omega, t|\Omega^0) + \sum_{\mu\neq\varepsilon} K_{\varepsilon\mu}\, p^{\mu\eta}(\Omega, t|\Omega^0)$$



Eigenfunctions are not available

in closed forms

Rotational diffusion of semi-Rigid molecule

Equations for Green's functions

$$\frac{\partial p^{\varepsilon\eta}(\Omega, t|\Omega^0)}{\partial t} = -\hat{L}^{\mathrm{T}} \mathfrak{D}^{\varepsilon} \hat{L}\, p^{\varepsilon\eta}(\Omega, t|\Omega^0) + \sum_{\mu \neq \varepsilon} K_{\varepsilon\mu}\, p^{\mu\eta}(\Omega, t|\Omega^0)$$

Ansatz of non-eigen decomposition

$$p^{\varepsilon\eta}(\Omega, t|\Omega^0, 0) = \sum_{l=0}^{\infty} \sum_{g,q=-l}^{l} c_{l,gq}^{\varepsilon\eta}(t) \underline{D_{gq}^{(l)}(\Omega)}$$

$$\boxed{\Psi_{mn}^{\varepsilon,l}(\Omega) = \sum_{k,p=-l}^{l} A_{mp}^{\varepsilon,l} D_{pk}^{(l)}(\Omega_{\mathfrak{D}}^{\varepsilon}) \underline{D_{kn}^{(l)}(\Omega)}}$$

Wigner rotation matrix

Rotational diffusion of semi-Rigid molecule

Equations for Green's functions

$$\frac{\partial p^{\varepsilon\eta}(\Omega, t|\Omega^0)}{\partial t} = -\hat{L}^{\mathrm{T}}\mathfrak{D}^{\varepsilon}\hat{L}\, p^{\varepsilon\eta}(\Omega, t|\Omega^0) + \sum_{\mu\neq\varepsilon} K_{\varepsilon\mu}\, p^{\mu\eta}(\Omega, t|\Omega^0)$$

Ansatz of non-eigen decomposition

$$p^{\varepsilon\eta}(\Omega, t|\Omega^0, 0) = \sum_{l=0}^{\infty}\sum_{g,q=-l}^{l} c^{\varepsilon\eta}_{l,gq}(t) D^{(l)}_{gq}(\Omega)$$

$$U^{\varepsilon,l}_{pk} = \sum_{n=-l}^{l} D^{(l)*}_{np}(\Omega)\Psi^{\varepsilon,l}_{nk}(\Omega)$$

Unitary transformation between sets of $\Psi^{\varepsilon,l}_{nk}(\Omega)$ and $D^{(l)}_{kn}(\Omega)$

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients

$$\frac{\partial c_{l,mn}^{\varepsilon\eta}(t)}{\partial t} = -\sum_{s,q=-l}^{l} U_{ns}^{\varepsilon,l} E_{s}^{\varepsilon,l} U_{sq}^{\varepsilon,l\dagger} c_{l,mq}^{\varepsilon\eta}(t) + \sum_{\mu\neq\varepsilon} K_{\varepsilon\mu}\, c_{l,mn}^{\mu\eta}(t)$$

Initial conditions

$$c_{l,mn}^{\varepsilon\eta}(t)\Big|_{t=+0} = \frac{2l+1}{8\pi^2} D_{mn}^{(l)*}(\Omega^0)\delta_{\varepsilon\eta}$$

Formal Solution

$$p^{\varepsilon\eta}(\Omega, t|\Omega^0, 0) = \sum_{l=0}^{\infty} \sum_{g,q=-l}^{l} c_{l,gq}^{\varepsilon\eta}(t) D_{gq}^{(l)}(\Omega)$$

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients

$$\frac{\partial c_{l,mn}^{\varepsilon\eta}(t)}{\partial t} = -\sum_{s,q=-l}^{l} U_{ns}^{\varepsilon,l} E_{s}^{\varepsilon,l} U_{sq}^{\varepsilon,l\dagger} c_{l,mq}^{\varepsilon\eta}(t) + \sum_{\mu\neq\varepsilon} K_{\varepsilon\mu}\, c_{l,mn}^{\mu\eta}(t)$$

Ryabov, Clore, Schwieters (2012)

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients (no restrictions)

$$\frac{\partial c_{l,mn}^{\varepsilon\eta}(t)}{\partial t} = -\sum_{s,q=-l}^{l} U_{ns}^{\varepsilon,l} E_{s}^{\varepsilon,l} U_{sq}^{\varepsilon,l\dagger} c_{l,mq}^{\varepsilon\eta}(t) + \sum_{\mu\neq\varepsilon} K_{\varepsilon\mu}\, c_{l,mn}^{\mu\eta}(t)$$

Ryabov, Clore, Schwieters (2012)

Equations for decomposition coefficients (axial symmetry and co-linearity of the axes of symmetry)

$$\frac{\partial f_{l,m}^{\varepsilon\eta}(t)}{\partial t} = -\left[l(l+1)\mathfrak{D}_{\perp}^{\varepsilon} + m^2\left(\mathfrak{D}_{\parallel}^{\varepsilon} - \mathfrak{D}_{\perp}^{\varepsilon}\right)\right] f_{l,m}^{\varepsilon\eta}(t) + \sum_{\mu\neq\varepsilon} K_{\varepsilon\mu}\, f_{l,m}^{\mu\eta}(t)$$

Berne, Pecora (1968); Wong, Case and Szabo (2009)

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients

$$\frac{\partial \boldsymbol{c}^{\eta}_{l,m}(t)}{\partial t} = \mathbf{M}_l \boldsymbol{c}^{\eta}_{l,m}(t)$$

Matrix Form

$$k^{\varepsilon} = \sum_{\varepsilon \neq \eta} k_{\varepsilon\eta}$$

$$\mathbf{M}_l = \begin{pmatrix} \mathbf{U}^{A,l}\mathbf{E}^{A,l}\mathbf{U}^{A,l\dagger} - k^{A}\mathbf{I}_{2l+1} & k_{AB}\mathbf{I}_{2l+1} & \vdots \\ k_{BA}\mathbf{I}_{2l+1} & \mathbf{U}^{B,l}\mathbf{E}^{B,l}\mathbf{U}^{B,l\dagger} - k^{B}\mathbf{I}_{2l+1} & \vdots \\ \cdots & \cdots & \end{pmatrix}$$

$$\left[\boldsymbol{c}^{\eta}_{l,m}(t)\right]_{\varepsilon} = \begin{pmatrix} c^{\varepsilon\eta}_{l,ml}(t) \\ \vdots \\ c^{\varepsilon\eta}_{l,m-l}(t) \end{pmatrix}$$

$$\mathbf{E}^{\varepsilon,l} = \begin{pmatrix} E^{\varepsilon,l}_{l} & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & E^{\varepsilon,l}_{-l} \end{pmatrix}$$

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients

$$\frac{\partial \boldsymbol{c}_{l,m}^{\eta}(t)}{\partial t} = \mathbf{M}_l \boldsymbol{c}_{l,m}^{\eta}(t)$$

Block dimension $(2l+1)$

$$\mathbf{M}_l = \begin{pmatrix} \mathbf{U}^{A,l}\mathbf{E}^{A,l}\mathbf{U}^{A,l\dagger} - k^A \mathbf{I}_{2l+1} & k_{AB}\mathbf{I}_{2l+1} & \vdots \\ k_{BA}\mathbf{I}_{2l+1} & \mathbf{U}^{B,l}\mathbf{E}^{B,l}\mathbf{U}^{B,l\dagger} - k^B \mathbf{I}_{2l+1} & \vdots \\ \cdots & \cdots & \end{pmatrix}$$

N_{states}

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients

$$\frac{\partial \boldsymbol{c}_{l,m}^{\eta}(t)}{\partial t} = \mathbf{M}_l \boldsymbol{c}_{l,m}^{\eta}(t)$$

$\mathbf{M}_l$ dimension $N_{states}(2l+1)$

$l = 1$ Dielectric spectroscopy

$l = 2$ NMR, ligh scattering

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients

$$\frac{\partial \boldsymbol{c}_{l,m}^{\eta}(t)}{\partial t} = \mathbf{M}_l \boldsymbol{c}_{l,m}^{\eta}(t)$$

$\mathbf{M}_l$ dimension $N_{states}(2l+1)$

No solution in closed forms for $\boldsymbol{c}_{l,m}^{\eta}(t)$

Even for $l = 1$ and $N_{states} = 2$

due to **Abel impossibility theorem (1824)**

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients in frequency domain

$$\sigma\tilde{\boldsymbol{c}}^{\eta}_{l,m}(\sigma) - \boldsymbol{c}^{\eta}_{l,mn}(t)\big|_{t=+0} = \mathbf{M}_l \tilde{\boldsymbol{c}}^{\eta}_{l,m}(\sigma)$$

$$\sigma = \gamma + i\omega$$

Complex frequency

$$\tilde{\boldsymbol{c}}^{\eta}_{l,m}(\sigma) \coloneqq \mathcal{L}[\boldsymbol{c}^{\eta}_{l,m}(t)]$$

Laplace transform

Initial conditions

$$\left[\boldsymbol{c}^{\eta}_{l,mn}(t)\big|_{t=+0}\right]_{\varepsilon} = \delta_{\varepsilon\eta}\frac{2l+1}{8\pi^2}\begin{pmatrix} D^{(l)*}_{m,l}(\Omega^0) \\ \vdots \\ D^{(l)*}_{m,-l}(\Omega^0) \end{pmatrix}$$

Rotational diffusion of semi-Rigid molecule

Equations for decomposition coefficients in frequency domain

$$\tilde{\mathbf{c}}^{\eta}_{l,m}(\sigma) = \left(\sigma \mathbf{I}_{N_{states}(2l+1)} - \mathbf{M}_l\right)^{-1} \mathbf{c}^{\eta}_{l,mn}(t)\Big|_{t=+0}$$

$$\begin{pmatrix} \mathbf{U}^{A,l}\mathbf{Q}^{A,l}\mathbf{U}^{A,l\dagger} & k_{AB}\mathbf{I}_{2l+1} & \vdots \\ k_{BA}\mathbf{I}_{2l+1} & \mathbf{U}^{B,l}\mathbf{Q}^{B,l}\mathbf{U}^{B,l\dagger} & \vdots \\ \cdots & \cdots & \end{pmatrix}^{-1}$$

Matrix inversion does **NOT** depend on solving Eigen problem

No restrictions from Abel theorem

$$\mathbf{Q}^{\varepsilon,l} = \mathbf{E}^{\varepsilon,l} + \left(k^{\varepsilon} + \sigma\right)\mathbf{I}_{2l+1}$$

Rotational diffusion of semi-Rigid molecule

Green's functions in frequency domain

$$\tilde{p}^{\varepsilon\eta}(\Omega,\sigma|\Omega^0,0)=\sum_{l=0}^{\infty}\sum_{g,q=-l}^{l}\underline{\tilde{c}^{\varepsilon\eta}_{l,gq}(\sigma)}D^{(l)}_{gq}(\Omega)$$

Green's function in time domain

$$p^{\varepsilon\eta}(\Omega,t|\Omega^0,0)=\sum_{l=0}^{\infty}\sum_{g,q=-l}^{l}\underline{c^{\varepsilon\eta}_{l,gq}(t)}D^{(l)}_{gq}(\Omega)$$

Rotational diffusion of semi-Rigid molecule

Correlation function in frequency domain

$$\tilde{C}(\sigma) = \iint \underline{\tilde{p}(\Omega_{\mathrm{LM}}, \sigma | \Omega_{\mathrm{LM}}^0, 0)} p_{eq}(\Omega_{\mathrm{LM}}^0) \times$$

$$\times \sum_{m,k,k'=-l}^{l} D_{mk}^{l*}(\Omega_{\mathrm{LM}}) D_{mk'}^{l}(\Omega_{\mathrm{LM}}^0) D_{k0}^{l*}(\Omega_{\mathrm{MI}}) D_{k'0}^{l}(\Omega_{\mathrm{MI}})\, d\Omega_{\mathrm{LM}} d\Omega_{\mathrm{LM}}^0$$

Correlation function in time domain

$$C(t) = \iint \underline{p(\Omega_{\mathrm{LM}}, t | \Omega_{\mathrm{LM}}^0, 0)} p_{eq}(\Omega_{\mathrm{LM}}^0) \times$$

$$\times \sum_{m,k,k'=-l}^{l} D_{mk}^{l*}(\Omega_{\mathrm{LM}}) D_{mk'}^{l}(\Omega_{\mathrm{LM}}^0) D_{k0}^{l*}(\Omega_{\mathrm{MI}}) D_{k'0}^{l}(\Omega_{\mathrm{MI}})\, d\Omega_{\mathrm{LM}} d\Omega_{\mathrm{LM}}^0$$

Rotational diffusion of semi-Rigid molecule

Correlation function in frequency domain (no restrictions)

Ryabov, Clore, Schwieters (2012)

$$\tilde{C}_l(\sigma) = \frac{4\pi}{2l+1}\sum_{\varepsilon,\eta}\mathbf{Y}_l^T(\Omega_{\varepsilon \mathrm{I}})\mathbf{A}^{\varepsilon,l\dagger}\mathbf{R}^{\varepsilon\eta}(\sigma)\mathbf{A}^{\eta,l}\mathbf{Y}_l^*(\Omega_{\eta \mathrm{I}})P_{eq}^{\eta}$$

Correlation function in time domain (axial symmetry and co-linearity of the axes of symmetry)

$$C_l(t) = \frac{4\pi}{2l+1}\sum_{m=-l}^{l}\sum_{\varepsilon,\eta} f_{l,m}^{\varepsilon\eta}(t)Y_{l,m}(\Omega^{\varepsilon})Y_{l,m}^*(\Omega^{\eta})P_{eq}^{\eta}$$

Berne, Pecora (1968); Wong, Case and Szabo (2009)

Rotational diffusion of semi-Rigid molecule

Correlation function in frequency domain (no restrictions)

$$\tilde{C}_l(\sigma) = \frac{4\pi}{2l+1} \sum_{\varepsilon,\eta} \mathbf{Y}_l^T(\Omega_{\varepsilon \mathrm{I}}) \mathbf{A}^{\varepsilon,l\dagger} \mathbf{R}^{\varepsilon\eta}(\sigma) \mathbf{A}^{\eta,l} \mathbf{Y}_l^*(\Omega_{\eta \mathrm{I}}) P_{eq}^{\eta}$$

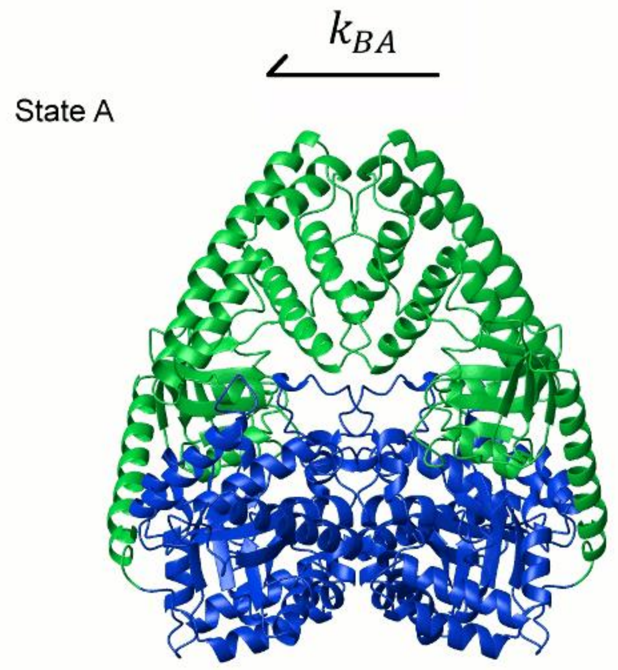
Spectral density

$$J_l(\omega) = Re\left\{ \tilde{C}_l(\sigma)\Big|_{\sigma \to i\omega} \right\}$$

Experimental observables: R1, R2 etc.

Illustrative calculations

EI dimer



Estimations of XplorNIH @ 300 K

$$\mathfrak{D}_x^A = 29.16 \times 10^7\ [s^{-1}] \qquad \tau_{\mathfrak{D}}^A = 53.73\ \ [ns]$$

$$\mathfrak{D}_y^A = 31.47 \times 10^7\ [s^{-1}]$$

$$\mathfrak{D}_z^A = 32.43 \times 10^7\ [s^{-1}]$$

$$\mathfrak{D}_x^B = 15.71 \times 10^7\ [s^{-1}] \qquad \tau_{\mathfrak{D}}^B = 79.99\ \ [ns]$$

$$\mathfrak{D}_y^B = 15.82 \times 10^7\ [s^{-1}]$$

$$\mathfrak{D}_z^B = 30.99 \times 10^7\ [s^{-1}]$$

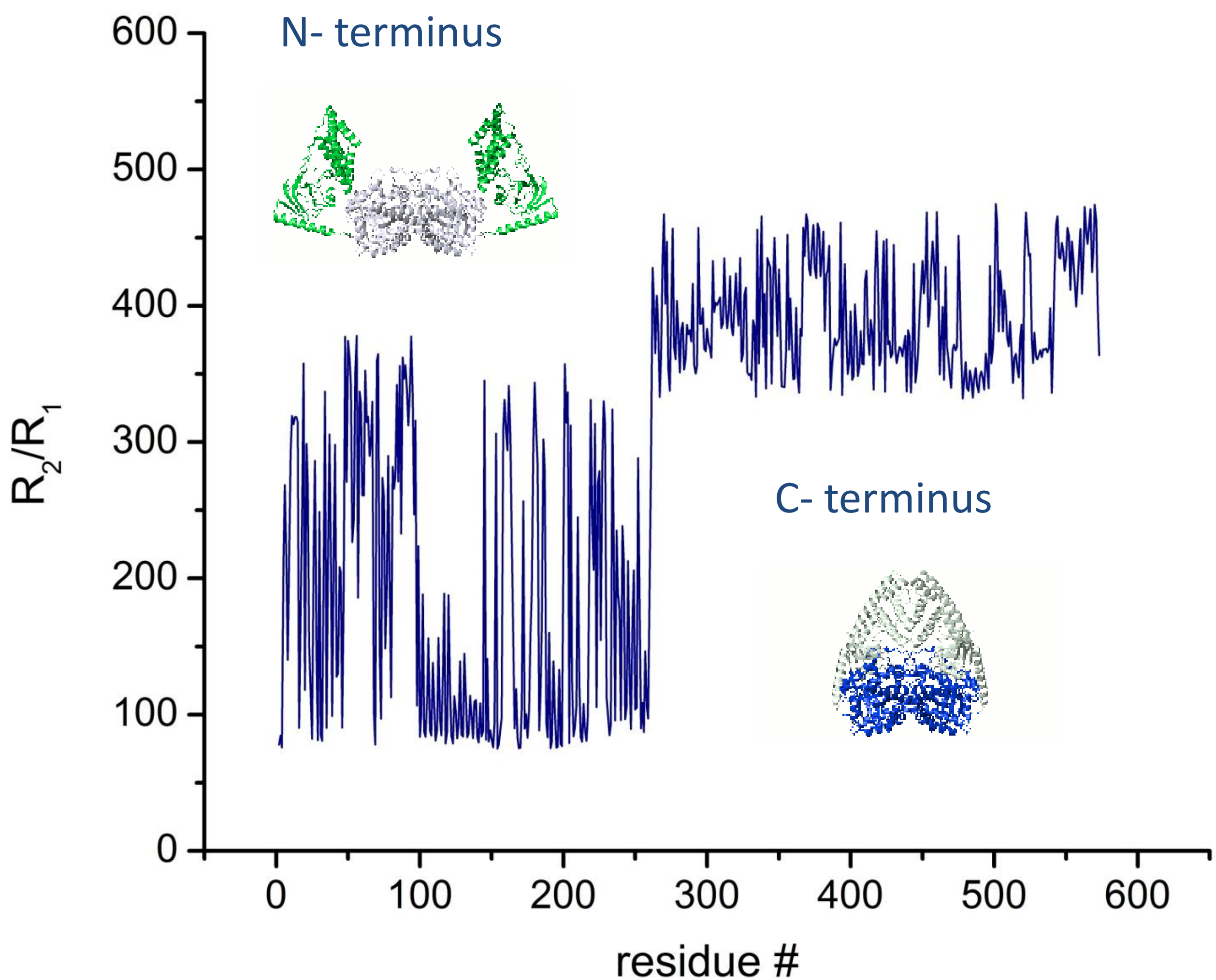
Assumptions

Symmetric motions $\Omega_{\mathrm{AB}}\!:\{\alpha_{\mathrm{AB}} = 0, \beta_{\mathrm{AB}} = 0, \gamma_{\mathrm{AB}} = 0\}$

Equal occupation $P_{eq}^A = P_{eq}^B = 1/2 \qquad k_{AB} = k_{BA}$

Illustrative calculations

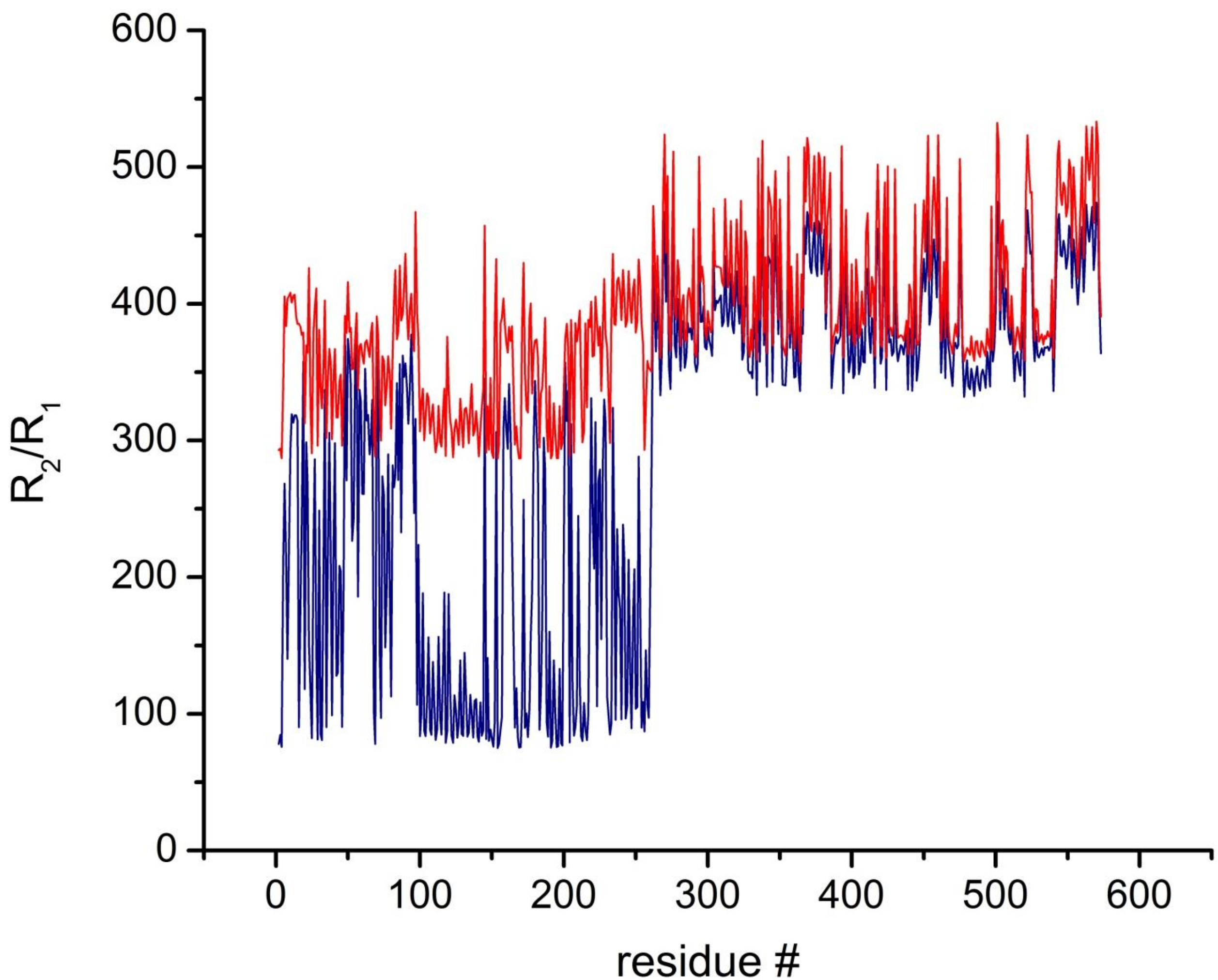
NMR relaxation rates for 600 MHz @ 300 K



$$k = \frac{2}{\tau_{\mathfrak{D}}^{A} + \tau_{\mathfrak{D}}^{B}} = 155.57 \;\; [ns^{-1}]$$

Illustrative calculations

NMR relaxation rates for 600 MHz @ 300 K

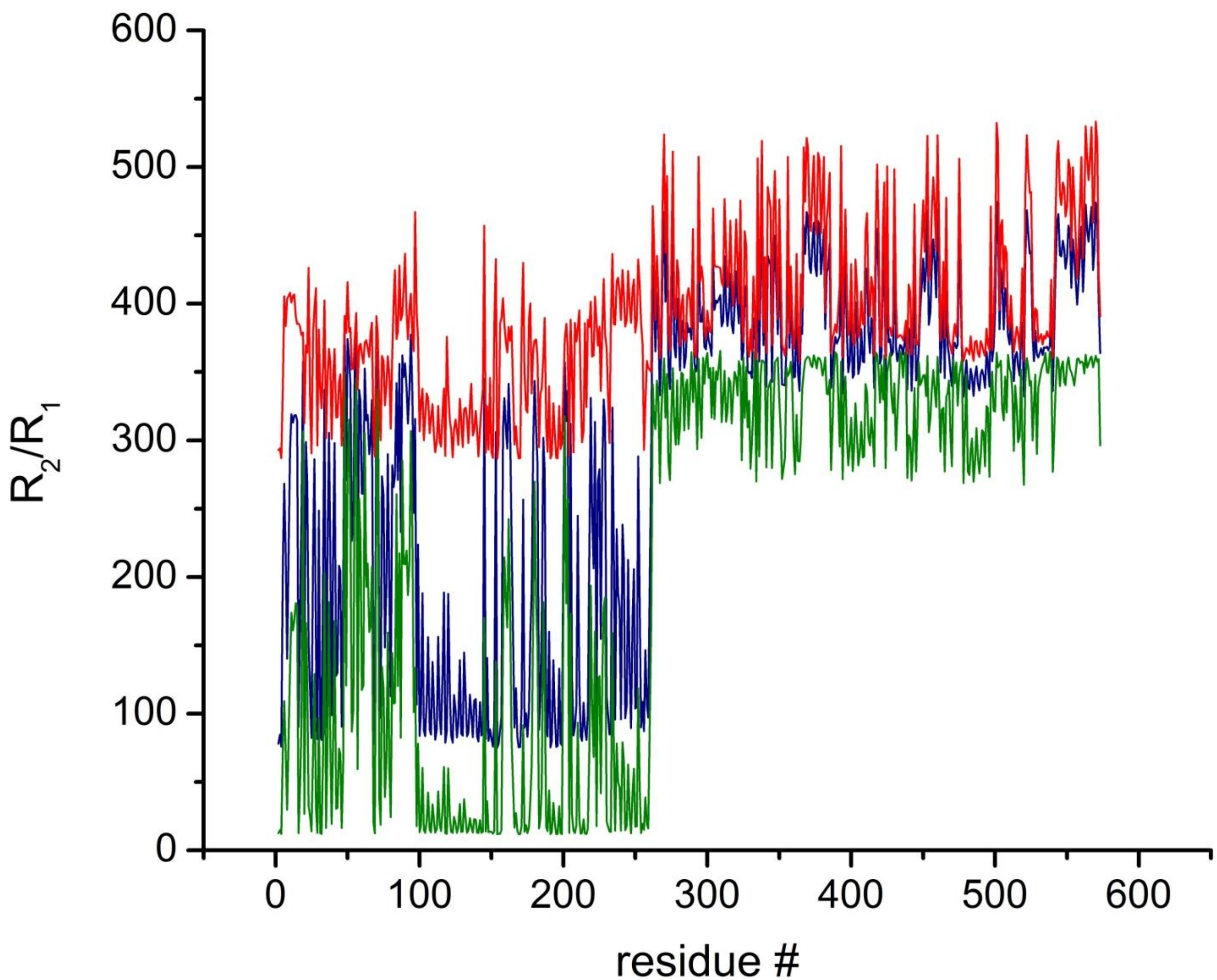


$$k_{slow} = 0.1 \times k$$

$$k = \frac{2}{\tau_{\mathfrak{D}}^{A} + \tau_{\mathfrak{D}}^{B}} = 155.57 \;\; [ns^{-1}]$$

Illustrative calculations

NMR relaxation rates for 600 MHz @ 300 K



$k_{slow} = 0.1 \times k$

$$k = \frac{2}{\tau_{\mathfrak{D}}^{A} + \tau_{\mathfrak{D}}^{B}} = 155.57 \ [ns^{-1}]$$

$k_{fast} = 10 \times k$

Concluding notes

Our Model

- Provides closed form solutions in frequency domain ready for evaluation of spectral density etc.
- Provides known limiting cases and is reproduced by Monte Carlo simulations
- Not universal: discusses only the transitions between discrete states
- However, accounts for arbitrary symmetry of diffusion tensors, arbitrary reorientation of molecules upon conformation transition, and coupling between diffusion tumbling and conformation exchange

Acknowledgments

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- G. Marius Clore

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