Supporting Information

General expressions for Carr-Purcell-Meiboom-Gill relaxation dispersion for *N*-site chemical exchange

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S1. Kinetic matrices for N-site schemes

3-site linear BAC

$$K = \begin{bmatrix} -k_{12} - k_{13} & k_{21} & k_{31} \\ k_{12} & -k_{21} & 0 \\ k_{13} & 0 & -k_{31} \end{bmatrix} \quad \text{(S1)}$$

3-site linear ABC

$$K = \begin{bmatrix} -k_{12} & k_{21} & 0 \\ k_{12} & -k_{21} - k_{23} & k_{32} \\ 0 & k_{23} & -k_{31} \end{bmatrix} \quad \text{(S2)}$$

3-site triangular

$$K = \begin{bmatrix} -k_{12} - k_{13} & k_{21} & k_{31} \\ k_{12} & -k_{21} - k_{23} & k_{32} \\ k_{13} & k_{23} & -k_{31} - k_{32} \end{bmatrix} \tag{S3}$$

4-site linear

$$K = \begin{bmatrix} -k_{12} - k_{13} & k_{21} & k_{31} & 0 \\ k_{12} & -k_{21} & 0 & 0 \\ k_{13} & 0 & -k_{31} - k_{34} & k_{43} \\ 0 & 0 & k_{34} & -k_{43} \end{bmatrix} \tag{S4}$$

4-site kite

$$K = \begin{bmatrix} -k_{12} - k_{13} - k_{14} & k_{21} & k_{31} & k_{41} \\ k_{12} & -k_{21} & 0 & 0 \\ k_{13} & 0 & -k_{31} - k_{34} & k_{43} \\ k_{14} & 0 & k_{34} & -k_{43} - k_{41} \end{bmatrix} \tag{S5}$$

4-site star

$$K = \begin{bmatrix} -k_{12} - k_{13} - k_{14} & k_{21} & k_{31} & k_{41} \\ k_{12} & -k_{21} & 0 & 0 \\ k_{13} & 0 & -k_{31} & 0 \\ k_{14} & 0 & 0 & -k_{41} \end{bmatrix} \tag{S6}$$

4-site quadratic

$$K = \begin{bmatrix} -k_{12} - k_{13} & k_{21} & k_{31} & 0 \\ k_{12} & -k_{21} - k_{24} & 0 & k_{42} \\ k_{13} & 0 & -k_{31} - k_{34} & k_{43} \\ 0 & k_{24} & k_{34} & -k_{42} - k_{43} \end{bmatrix} \tag{S7}$$

S2. Average Magnetization

For completeness, the exact evolution of the average magnetization is obtained as:

$$\bar{M}(T) = e^{-R_{21}T}\sum_{n=1}^{N}\Lambda_n^m\left\langle \mathbf{p}\middle| e^{\hat{\mathbf{L}}\tau_{cp}}\middle|\mathbf{v}_n\right\rangle\left\langle \mathbf{v}_n\middle| e^{-\hat{\mathbf{L}}\tau_{cp}}\middle|\mathbf{p}\right\rangle \tag{S8}$$

in which the elements of $|\mathbf{d}\rangle$ are $\delta_{i,1}p_i^{1/2}$ and of $|\mathbf{p}\rangle$ are $p_i^{1/2}$ for $i = 1,\ldots, N$ and Λ_n and $\mathbf{v}_n$ are the eigenvectors and eigenvalues of $\mathbf{Z}(\tau_{cp})$.[16] The CPMG relaxation rate constant is defined as:

$$R_{cpmg}\left(\tau_{cp}\right) = \frac{-1}{4\tau_{cp}}\log\left\{\frac{\bar{M}(T+4\tau_{cp})}{\bar{M}(T)}\right\} \tag{S9}$$

for site 1 with a similar expression for the average magnetization. If $\Lambda_1 >> \Lambda_n$ for $n > 1$, then Eq. 18 is identical to Eq. 16.

S3. Cayley-Hamilton Theorem

Efficient accurate numerical methods allow calculation of $\exp\left\{2\hat{\mathbf{L}}\tau_{cp}\right\}$ (and its complex conjugate) needed to obtain $\mathbf{Z}(\tau_{cp})$ without initial calculation of the eigenvalues and eigenvectors of $\hat{\mathbf{L}}$. The Cayley-Hamilton theorem expresses the matrix exponential as:

$$\exp\left\{\hat{\mathbf{L}}2\tau_{cp}\right\} = \sum_{n=0}^{N-1}a_n(\tau_{cp})\hat{\mathbf{L}}^n \tag{S10}$$

in which

$$\begin{bmatrix} a_0(\tau_{cp}) \\ \vdots \\ a_{N-1}(\tau_{cp}) \end{bmatrix} = \begin{bmatrix} 1 & \lambda_1 & \cdots & \lambda_1^{N-1} \\ \vdots & \vdots & \ddots & \vdots \\ 1 & \lambda_N & \cdots & \lambda_N^{N-1} \end{bmatrix}^{-1}\begin{bmatrix} e^{\lambda_1 2\tau_{cp}} \\ \vdots \\ e^{\lambda_N 2\tau_{cp}} \end{bmatrix} \tag{S11}$$

the $N \times N$ matrix to be inverted is the Vandermonde matrix and λ_n is the n^{th} eigenvalue of $\hat{\mathbf{L}}$. Using this result,

$$\begin{aligned}\hat{\mathbf{H}}(\tau_{cp}) &= \log\left[\mathbf{Z}(\tau_{cp})\right] \\ &= \log\left(\left|a_0(\tau_{cp})\right|^2\right) + \log\left[\mathbf{E} + \left(\mathbf{Z}(\tau_{cp})/\left|a_0(\tau_{cp})\right|^2 - \mathbf{E}\right)\right] \\ &\approx \log\left(\left|a_0(\tau_{cp})\right|^2\right)\mathbf{E} + \left(\mathbf{Z}(\tau_{cp})/\left|a_0(\tau_{cp})\right|^2 - \mathbf{E}\right)\end{aligned} \tag{S12}$$

in which the lowest order approximation to the logarithm of the matrix exponential has been used in the last line and $\mathbf{Z}(\tau_{cp})$ is calculated using Eq. 20. Applying the lowest order approximation for the largest eigenvalue to the second term in Eq. 22 and using Eq. 16 gives:

$$R_{cpmg}\left(\tau_{cp}\right) = -\log\left(\left|a_0(\tau_{cp})\right|^2\right) - 1/Tr\left\{\left(\mathbf{Z}(\tau_{cp})/\left|a_0(\tau_{cp})\right|^2 - \mathbf{E}\right)^{-1}\right\} + R_{21} \tag{S13}$$

This expression yields accurate approximations at the cost of calculating the eigenvalues of $\hat{\hat{\mathbf{L}}}$ to obtain a_0.

S.4 Approximations for the Least Negative Eigenvalue

The main text uses the Newton-Raphson algorithm for approximating the desired eigenvalue. This method converges quadratically. Other methods include Laguerre's and Halley's methods, respectively:

$$\begin{aligned}\lambda_j &= \lambda_{j-1} - \frac{f(\lambda_{j-1})}{f'(\lambda_{j-1})}\left(\frac{1}{N} + \frac{N-1}{N}\sqrt{1 - \frac{N}{N-1}\frac{f(\lambda_{j-1})f''(\lambda_{j-1})}{f'(\lambda_{j-1})^2}}\right)^{-1} \\ \lambda_j &= \lambda_{j-1} - \frac{f(\lambda_{j-1})}{f'(\lambda_{j-1})}\left(1 - \frac{f(\lambda_{j-1})f''(\lambda_{j-1})}{2f'(\lambda_{j-1})^2}\right)^{-1}\end{aligned} \tag{S14}$$

Halley's method converges cubically and almost as rapidly as Laguerre's method, while avoiding radicals (Halley's method is a linearization of Laguerre's method).

The matrix form of Laguerre's method is:

$$\lambda_{j,Lag} = \lambda_{j-1} + \frac{1}{Tr\left\{\left(\mathbf{H}(\tau_{cp}) - \lambda_{j-1}\mathbf{E}\right)^{-1}\right\}} \times \left[\frac{1}{N} + \frac{N-1}{N}\left(1 - \frac{N}{N-1}\frac{Tr\left\{\left(\mathbf{H}(\tau_{cp}) - \lambda_{j-1}\mathbf{E}\right)^{-1}\right\}^2 - Tr\left\{\left(\mathbf{H}(\tau_{cp}) - \lambda_{j-1}\mathbf{E}\right)^{-2}\right\}}{Tr\left\{\left(\mathbf{H}(\tau_{cp}) - \lambda_{j-1}\mathbf{E}\right)^{-1}\right\}^2}\right)^{1/2}\right]^{-1} \quad \text{(S15)}$$

The matrix form of Halley's method is:

$$\lambda_j = \lambda_{j-1} + \frac{2Tr\left\{\left(\mathbf{H}(\tau_{cp}) - \lambda_{j-1}\mathbf{E}\right)^{-1}\right\}}{Tr\left\{\left(\mathbf{H}(\tau_{cp}) - \lambda_{j-1}\mathbf{E}\right)^{-1}\right\}^2 + Tr\left\{\left(\mathbf{H}(\tau_{cp}) - \lambda_{j-1}\mathbf{E}\right)^{-2}\right\}} \quad \text{(S16)}$$

S5 Characteristic Polynomials

S5.1 Expanded description of the general equation, exemplified for the triangular scheme

The full characteristic polynomial reads (as Eq. 27, with additional definition for ϕ)

$$f(\lambda)=\sum_{u=0}^{N}\lambda^{u}\sum_{s=0}^{N-u}\left(\left(\delta_{s,0}+\sum_{\substack{h_v,j_v=1\\0<v\le s\\h_0=0,j_0=0\\h_{v-1}<h_v\\h_v\neq j_v}}^{N}(-1)^{\phi}\prod_{g=1}^{s}\left(\sqrt{k_{h_g j_g}k_{j_g h_g}}\,\mathrm{sinc}\left\{\Delta\omega_{h_g j_g}\tau_{cp}\right\}\sum_{b=1}^{s}\delta_{h_g,j_b}\right)\right)\left(\delta_{u+s,N}+\sum_{\substack{l_r,m_r=1\\1<r\le N-u-s\\l_0=0,m_0=0\\l_{r-1}<l_r\neq m_r\\l_r\notin\{h_1\ldots h_s\}\\l_r\notin\{j_1\ldots j_s\}}}^{N}\prod_{g=1}^{N-u-s}k_{l_g m_g}\right)\right)$$

$$=\sum_{u=0}^{N}\lambda^{u}\sum_{s=0}^{N-u}\left(\left(\delta_{s,0}+\sum_{h_1=1}^{N}\sum_{\substack{j_1=1\\h_1\neq j_1}}^{N}\sum_{h_2=h_1+1}^{N}\sum_{\substack{j_2=1\\j_2\neq h_2}}^{N}\cdots\sum_{h_s=h_{s-1}+1}^{N}\sum_{\substack{j_s=1\\h_s\neq j_s}}^{N}(-1)^{\phi}\prod_{g=1}^{s}\left(\sqrt{k_{h_g j_g}k_{j_g h_g}}\,\mathrm{sinc}\left\{\Delta\omega_{h_g j_g}\tau_{cp}\right\}\sum_{b=1}^{s}\delta_{h_g,j_b}\right)\right)\left(\delta_{u+s,N}+\sum_{\substack{l_1=1\\l_1\notin\{h_1\ldots h_s\}\\l_1\notin\{j_1\ldots j_s\}}}^{N}\sum_{\substack{m_1=1\\m_1\neq l_1\\m_1\notin\{h_1\ldots h_s\}\\m_1\notin\{j_1\ldots j_s\}}}^{N}\sum_{\substack{l_2=l_1+1\\l_2\notin\{h_1\ldots h_s\}\\l_2\notin\{j_1\ldots j_s\}}}^{N}\sum_{\substack{m_2=1\\m_2\neq l_2\\m_2\notin\{h_1\ldots h_s\}\\m_2\notin\{j_1\ldots j_s\}}}^{N}\cdots\sum_{\substack{l_{N-u-s}=l_{N-u-s-1}+1\\l_{N-u-s}\notin\{h_1\ldots h_s\}\\l_{N-u-s}\notin\{j_1\ldots j_s\}}}^{N}\sum_{\substack{m_{N-u-s}=1\\m_{N-u-s}\neq l_{N-u-s}\\m_{N-u-s}\notin\{h_1\ldots h_s\}\\m_{N-u-s}\notin\{j_1\ldots j_s\}}}^{N}\prod_{g=1}^{N-u-s}k_{l_g m_g}\right)\right)$$

with $k_{0x},k_{x0}=0$ and $\phi=\sum_{c,d=1}^{s}\frac{1}{c}\delta(o_c,h_d)$ and $o_f=\sum_{\substack{w=f\\h_w\notin\{o_1\ldots o_{w-1}\}\\o_0=h_d}}^{c}\delta(o_{f-1},j_w)h_w$

(S17)

We demonstrate how to obtain a compact expression for the characteristic polynomial in the triangular case, by evaluating this equation (for calculation of ϕ, see below).

1. First sum (u=0 to N=3) – set u=0

returns $k_{12}k_{21}k_{31} + k_{12}k_{21}k_{32} + k_{12}k_{23}k_{31} + k_{12}k_{23}k_{32} + k_{13}k_{21}k_{31} + k_{13}k_{21}k_{32} + k_{13}k_{23}k_{31} + k_{13}k_{23}k_{32} - k_{12}k_{21}\mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp}) - k_{13}k_{31}\mathrm{sinc}^2(\Delta\omega_{13}\tau_c) - k_{23}k_{32}\mathrm{sinc}^2(\Delta\omega_{23}\tau_c) - \mathrm{sqrt}(k_{12}k_{21}k_{13}k_{31}k_{23}k_{32})\mathrm{sinc}(\Delta\omega_{12}\tau_{cp})\mathrm{sinc}(\Delta\omega_{13}\tau_c)\mathrm{sinc}(\Delta\omega_{23}\tau_c)$

1.1. Second sum (u=0 N-u=3) – set s=0, returns $k_{12}k_{21}k_{31} + k_{12}k_{21}k_{32} + k_{12}k_{23}k_{31} + k_{12}k_{23}k_{32} + k_{13}k_{21}k_{31} + k_{13}k_{21}k_{32} + k_{13}k_{23}k_{31} + k_{13}k_{23}k_{32}$

1.1.a. First factor in brackets returns 1

$\delta_{s,0}$ returns 1, and the h_v/j_v sum returns nothing (no h_v, j_v are set). Therefore, the first factor in brackets is 1.

1.1.b. Second factor in brackets returns $k_{12}k_{21}k_{31} + k_{12}k_{21}k_{32} + k_{12}k_{23}k_{31} + k_{12}k_{23}k_{32} + k_{13}k_{21}k_{31} + k_{13}k_{21}k_{32} + k_{13}k_{23}k_{31} + k_{13}k_{23}k_{32}$

1.1.b.1 $\delta_{u+s,N}$ returns 0.

1.1.b.2 l_r, m_r sum term returns $k_{12}k_{21}k_{31} + k_{12}k_{21}k_{32} + k_{12}k_{23}k_{31} + k_{12}k_{23}k_{32} + k_{13}k_{21}k_{31} + k_{13}k_{21}k_{32} + k_{13}k_{23}k_{31} + k_{13}k_{23}k_{32}$

$1 < r < 3$; this means that there are a total of 6 index variables, generating combinations $\{l_1,m_1,l_2,m_2,l_3,m_3\}$. Each of the variables cycles, in principle from 1-3, generating 3^6=729 terms.

However, most combinations are ruled out because of the statements under the sum sign.

Examples. The following combinations $\{l_1; m_1; l_2; m_2; l_3; m_3\}$ are fine: {1;2;2;1;3;1}; {1;3;2;1;3;1}

In this particular case, l_1,… l_3 are restrained because $l_r-1 < l_r$, but also $1<l_r<3$, effectively setting l_1, … l_3 to 1 … 3.

m_r can be equal to m_{r-1}, but not to l_r.

$\{1, ... h_v, ... h_s\}$ and $\{1, ... j_v, ... j_s\}$ are empty. Therefore, {1;2;2;1;3;2} is fine, but {1;3;2;2;3;2} is not allowed because $h_2 = j_2$.

For the l_r,m_r sum, all valid combinations are:

{1,2,2,1,3,1};{1,2,2,1,3,2};{1,2,2,3,3,1};{1,2,2,3,3,2};{1,3,2,1,3,1};{1,3,2,1,3,2};{1,3,2,3,3,1};{1,3,2,3,3,2}.

1.1.b.2.1 Product within each l_r,m_r sum

The product for each l_r,m_r combinations is formed by cycling through g=1...3. For the first combination {1,2,2,1,3,1}, the resulting product is $k_{12}k_{21}k_{31}$.

1.2. Second sum (u=0 N-u=3) – set s=1, returns 0

1.2.a. First factor in brackets returns 0

1.2.a.a $\delta_{s,0}$ returns 0

1.2.a.b h_v/j_v sum, returns 0

The following combinations for the indices $\{h_1,j_1\}$ are returned: {1,2},{1,3},{2,1},{2,3},{3,1},{3,2}.

1.2.a.b.a (-1) term - irrelevant

1.2.a.b.b.1 product in h_v/j_v sum: example for {1,2}

exemplified for {1,2}, set g=1 selects h_1=1, j_1=2, returns 0

1.2.a.b.b.1.a $\delta_{hg,jb}$ sum

This sum ensures that in the 1.2.a.a.1 product, there are only k factors which yield a "closed kinetic structure". This means that for a in each k_{ab} there is another k_{cd} in the product with d=a. This is, for example, true for $k_{12}k_{21}$ and for $k_{12}k_{23}k_{31}$, but not for $k_{12}k_{31}$ because there is no "matching" number for 3 in k_{31}.

For the combination {1,2}, and for g=1 (h_1=1, j_1=2), we obtain: $\delta_{1,2} = 0$

1.2.a.b.b.1.b square root/sinc term

exemplified for {1,2}, set g=1 selects h_1=1, j_1=2, returns $\mathrm{sqrt}(k_{12}k_{21})\mathrm{sinc}(\Delta\omega_{12}\tau_{cp})$

1.2.b. Second factor in bracket is irrelvant because first factor is 0

1.3. Second sum (u=0 N-u=3) – set s=2

returns $-k_{12}k_{21}(k_{32}+k_{31})\mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp}) - k_{13}k_{31}(k_{21}+k_{23})\mathrm{sinc}^2(\Delta\omega_{13}\tau_c) - k_{23}k_{32}(k_{12}+k_{13})\mathrm{sinc}^2(\Delta\omega_{23}\tau_c)$

1.3.a. First product in brackets returns $-k_{12}k_{21}\mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp}) - k_{13}k_{31}\mathrm{sinc}^2(\Delta\omega_{13}\tau_c) - k_{23}k_{32}\mathrm{sinc}^2(\Delta\omega_{23}\tau_c)$

1.3.a.a $\delta_{s,0}$ returns 0

1.3.a.b h_v/j_v sum, returns $-k_{12}k_{21}\mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp}) - k_{13}k_{31}\mathrm{sinc}^2(\Delta\omega_{13}\tau_c) - k_{23}k_{32}\mathrm{sinc}^2(\Delta\omega_{23}\tau_c)$

The following combinations for the indices $\{h_1,j_1,h_2,j_2\}$ are returned:

{1,2,2,1},{1,2,2,3},{1,2,3,1},{1,2,3,2},{1,3,2,1},{1,3,2,3},{1,3,3,1},{1,3,3,2},{2,1,3,1},{2,1,3,2},{2,3,3,1},{2,3,3,2}

1.3.a.b.a (-1) term - in the example for {1,2,2,1}, this term becomes -1 because φ=1 (see separate explanation below)

1.3.a.b.b.1 product in h_v/j_v sum: example for {1,2,2,1}

exemplified for {1,2,2,1}, set g=1 selects h_1=1, j_1=2, returns $\mathrm{sqrt}(k_{12}k_{21})\mathrm{sinc}(\Delta\omega_{12}\tau_{cp})$

exemplified for {1,2,2,1}, set g=2 selects h_2=2, j_2=1, returns $\mathrm{sqrt}(k_{21}k_{12})\mathrm{sinc}(\Delta\omega_{12}\tau_{cp})$

1.3.a.b.b.1.a $\delta_{hg,jb}$ sum

For the combination {1,2,2,1}, and for g=1 (h_1=1, j_1=2), we obtain: $\delta_{1,2} + \delta_{1,2} = 1$

For the combination {1,2,2,1}, and for g=2 (h_2=2, j_2=1), we obtain: $\delta_{2,1} + \delta_{2,2} = 1$

1.3.a.b.b.1.b square root/sinc term

exemplified for {1,2,2,1}, set g=1 selects h_1=1, j_1=2, returns $\mathrm{sqrt}(k_{12}k_{21})\mathrm{sinc}(\Delta\omega_{12}\tau_{cp})$

exemplified for {1,2,2,1}, set g=2 selects h_2=2, j_2=1, returns $\mathrm{sqrt}(k_{21}k_{12})\mathrm{sinc}(\Delta\omega_{12}\tau_{cp})$

1.3.a.b.b.2 product in h_v/j_v sum: example for {1,2,3,1}; returns 0 because one of the factors is 0.

1.3.a.b.b.2.a $\delta_{hg,jb}$ sum.

For the combination {1,2,3,1}, and for g=1 (h_1=1, j_1=2), we obtain: $\delta_{1,3} + \delta_{1,1} = 1$

For the combination {1,2,3,1}, and for g=2 (h_2=3, j_2=1), we obtain: $\delta_{3,2} + \delta_{3,1} = 0$ (product becomes 0 because of this)

1.3.a.b.b.2.b square root/sinc term -irrelevant

1.3.b. Second factor in brackets depends on the product in the first bracket. For h_1,j_1,h_2,j_2={1,2,2,1}, the second factor in brackets returns $k_{32}+k_{31}$ because combinations of indices for $\{l_1,m_1\}$ are {3,1},{3,2}. l_1 cannot be equal to h_1 or h_2, as indicated as a condition on the sum sign.

1.4. Second sum (u=0 N-u=3) – set s=3

returns -sqrt($k_{12}k_{21}k_{13}k_{31}k_{23}k_{32}$)sinc($\Delta\omega_{12}\tau_{cp}$)sinc($\Delta\omega_{13}\tau_c$)sinc($\Delta\omega_{23}\tau_c$)

1.4.a. First factor in brackets returns -sqrt($k_{12}k_{21}k_{13}k_{31}k_{23}k_{32}$)sinc($\Delta\omega_{12}\tau_{cp}$)sinc($\Delta\omega_{13}\tau_c$)sinc($\Delta\omega_{23}\tau_c$)

1.4.a.a $\delta_{s,0}$ returns 0

1.4.a.b h_v/j_v sum, returns -sqrt($k_{12}k_{21}k_{13}k_{31}k_{23}k_{32}$)sinc($\Delta\omega_{12}\tau_{cp}$)sinc($\Delta\omega_{13}\tau_c$)sinc($\Delta\omega_{23}\tau_c$)

The following combinations for the indices $\{h_1,j_1,h_2,j_2\}$ are returned:

{1,2,2,1,3,1};{1,2,2,1,3,2};{1,2,2,3,3,1};{1,2,2,3,3,2};{1,3,2,1,3,1};{1,3,2,1,3,2};{1,3,2,3,3,1};{1,3,2,3,3,2}.

1.4.a.b.a (-1) term - in the example for {1,2,2,3,3,1}, this term becomes -1 because φ=1 (see separate explanation below)

1.4.a.b.b.1 product in h_v/j_v sum: example for {1,2,2,3,3,1}:

sqrt($k_{12}k_{21}k_{13}k_{31}k_{23}k_{32}$)sinc($\Delta\omega_{12}\tau_{cp}$)sinc($\Delta\omega_{13}\tau_c$)sinc($\Delta\omega_{23}\tau_c$)

exemplified for {1,2,2,3,3,1}, set g=1 selects h_1=1, j_1=2, returns sqrt($k_{12}k_{21}$)sinc($\Delta\omega_{12}\tau_{cp}$)

exemplified for {1,2,2,3,3,1}, set g=2 selects h_2=2, j_2=3, returns sqrt($k_{23}k_{32}$)sinc($\Delta\omega_{32}\tau_{cp}$)

exemplified for {1,2,2,3,3,1}, set g=3 selects h_3=3, j_3=1, returns sqrt($k_{13}k_{31}$)sinc($\Delta\omega_{31}\tau_{cp}$)

1.4.a.b.b.1.a $\delta_{hg,jb}$ sum

For the combination {1,2,2,3,3,1}, and for g=1 (h_1=1, j_1=2), we obtain: $\delta_{1,2} + \delta_{1,3} + \delta_{1,1} = 1$

For g=2 and g=3, the sum is also 1.

1.4.a.b.b.1.b square root/sinc term

exemplified for {1,2,2,3,3,1}, set g=1 selects h_1=1, j_1=2, returns sqrt($k_{12}k_{21}$)sinc($\Delta\omega_{12}\tau_{cp}$)

1.4.a.b.b.2 product in h_v/j_v sum: example for {1,2,2,3,3,2}: returns 0

exemplified for {1,2,2,3,3,2}, set g=1 selects h_1=1, j_1=2, returns 0 (see below why that is)

terms for g=2 or g=3 are irrelevant because the term for g=1 is 0

1.4.a.b.b.2.a $\delta_{hg,jb}$ sum

For the combination {1,2,2,3,3,2}, and for g=1 (h_1=1, j_1=2), we obtain: $\delta_{1,2} + \delta_{1,3} + \delta_{1,2} = 0$

For the combination {1,2,2,3,3,2}, and for g=2 (h_2=2, j_2=3), we obtain: $\delta_{2,2} + \delta_{2,3} + \delta_{2,2} = 2$

For the combination {1,2,2,3,3,2}, and for g=3 (h_3=3, j_3=2), we obtain: $\delta_{3,2} + \delta_{3,3} + \delta_{3,2} = 1$

1.4.a.b.b.2.b squre root/sinc term - irrelevant

2. First sum (u=0 to N=3) – set u=1

returns $\lambda[k_{12}k_{21} + k_{12}k_{23} + k_{13}k_{21} + k_{13}k_{23} + k_{21}k_{31} + k_{21}k_{32} + k_{23}k_{31} + k_{23}k_{32} - k_{12}k_{21}\text{sinc}^2(\Delta\omega_{12}\tau_{cp}) - k_{13}k_{31}\text{sinc}^2(\Delta\omega_{13}\tau_c) - k_{23}k_{32}\text{sinc}^2(\Delta\omega_{23}\tau_c)]$

3. First sum (u=0 to N=3) – set u=2: returns $\lambda^2(k_{12} + k_{21} + k_{13} + k_{31} + k_{23} + k_{32})$

4. First sum (u=0 to N=3) – set u=3: returns λ^3

As a result, the characteristic polynomial for the triangualar model reads:

$$f(\lambda) = \lambda^3 + \lambda^2(k_{12} + k_{21} + k_{13} + k_{31} + k_{23} + k_{32}) + \lambda[k_{12}k_{21} + k_{12}k_{23} + k_{13}k_{21} + k_{13}k_{23} + k_{21}k_{31} + k_{21}k_{32} + k_{23}k_{31} + k_{23}k_{32} - k_{12}k_{21}\text{sinc}^2(\Delta\omega_{12}\tau_{cp}) - k_{13}k_{31}\text{sinc}^2(\Delta\omega_{13}\tau_c) - k_{23}k_{32}\text{sinc}^2(\Delta\omega_{23}\tau_c)] +$$

$k_{12}k_{21}k_{31} + k_{12}k_{21}k_{32} + k_{12}k_{23}k_{31} + k_{12}k_{23}k_{32} + k_{13}k_{21}k_{31} + k_{13}k_{21}k_{32} + k_{13}k_{23}k_{31} + k_{13}k_{23}k_{32} -$
$k_{12}k_{21}\mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp}) - k_{13}k_{31}\mathrm{sinc}^2(\Delta\omega_{13}\tau_c) - k_{23}k_{32}\mathrm{sinc}^2(\Delta\omega_{23}\tau_c) -$
$\mathrm{sqrt}(k_{12}k_{21}k_{13}k_{31}k_{23}k_{32})\mathrm{sinc}(\Delta\omega_{12}\tau_{cp})\mathrm{sinc}(\Delta\omega_{13}\tau_c)\mathrm{sinc}(\Delta\omega_{23}\tau_c)$ (S18)

S5.2 Calculation of ϕ

The sinc term product are only unequal 0 when they represent "closed kinetic structures". For given a combination of rate constants, each site would be connected by two rate constants of that combination (for example: $\{k_{12}, k_{21}\}$ or $\{k_{12}, k_{23}, k_{31}\}$). For n < 4, there can only be found one closed kinetic structure per combination. For that reason, ϕ is 1.

In the linear 4-site scheme, one interesting subset of combinations:

$\{h_1, j_1, h_2, j_2, h_3, j_3, h_4, j_4\} = \{k_{12}, k_{21}, k_{34}, k_{43}\}$

In this case, two independent closed kinetic structure are present (ϕ = 2): k_{12}-k_{21} and k_{34}-k_{43}; there is no connection between site 2 and 3 in this case.

In the quadratic case, the combinations

{1,2,2,4,3,1,4,3} or {1,3,2,1,3,4,4,2}

correspond to k_{12}, k_{24}, k_{43} and k_{31} and the other way around. Structurally, the kinetic structure for both of these combinations resembles one square (ϕ = 1).

In the quadratic case, we also find the combination {1,2,2,1,3,4,4,3} and {2,4,4,2,1,3,3,1}, with two closed kinetic structures (ϕ = 2).

The number of closed kinetic structures in a given combination is determined by the following expression.

$$\phi = \sum_{c,d=1}^{s} \frac{1}{c}\delta(o_c, h_d) \text{ and } o_f = \sum_{\substack{w=f \\ h_w \notin \{o_1 \ldots o_{w-1}\} \\ o_0 = h_d}}^{c} \delta(o_{f-1}, j_w) h_w \quad \text{(S19)}$$

The expression for ϕ returns the number of closed kinetic structures for a given combination of rate constant indices. The order of rate constant indices $h_1, j_1, h_2, j_2, h_3, j_3, ..., h_n, j_n$ is not important, each set of h_v, j_v corresponds to a rate constant. For each constant, the number of members of the kinetic structure to which it belongs is determined. The Kronecker Delta on the right screens for the next (connected) rate constant of the kinetic structure. The product will only be 1 if rate constant index h_d, essentially referring to a site, is part of a c-membered ring (c can be 2). h_d is defined by the encapsulating sum in the encapsulating function (see above) and runs from 1 to s, corresponding to the number of rates in the analyzed combination.

Example. We look at the following combination with s=2.

$h_1=1$; $j_1=2$; $h_2=2$; $j_2=3$; $h_3=3$; $j_3=1$

For d=2, and testing for a closed triangle by setting c to 3, we have to find o_3 which is defined recursively.

o_f is:

$o_1 = \delta(o_0,j_1)h_1 + \delta(o_0,j_2)h_2 + \delta(o_0,j_3)h_3 = \delta(2,2)1 + \delta(2,3)2 + \delta(2,1)3 = 1$

$o_2 = \delta(o_1,j_2)h_2 + \delta(o_1,j_3)h_3 = \delta(1,3)2 + \delta(1,1)3 = 3$

$o_3 = \delta(o_1,j_2)h_2 = \delta(3,3)2 = 2$

Because $o_3=h_2$, $\delta(o_c,h_d) = 1$, and the sum over all d becomes 1 (each summand is 1/3).

Another example. s=2 and c=3.

$h_1=1$; $j_1=2$; $h_2=2$; $j_2=1$; $h_3=3$; $j_3=4$

$o_0=2$

$o_1 = \delta(o_0,j_1)h_1 + \delta(o_0,j_2)h_2 + \delta(o_0,j_3)h_3 = \delta(2,2)1 + \delta(2,1)2 + \delta(2,4)3 = 1$

$o_2 = \delta(o_1,j_2)h_2 + \delta(o_1,j_3)h3 = \delta(1,1)2 + \delta(1,4)3 = 2$

$o_3 = \delta(o_1,j_3)h_3 = \delta(2,4)h_3 = 0$

The resulting sum for c=3 is 0.

Another example. We look at the following (triangle) combination with s=2.

h_1=1; j_1=2; h_2=2; j_2=3; h_3=3; j_3=1

We are testing for a closed two-site kinetic structure by setting c to 2.

$o_1 = \delta(o_0,j_1)h_1 + \delta(o_0,j_2)h_2 + \delta(o_0,j_3)h_3 = \delta(2,2)1 + \delta(2,3)2 + \delta(2,1)3 = 1$

$o_2 = \delta(o_1,j_2)h_2 + \delta(o_1,j_3)h3 = \delta(1,3)2 + \delta(1,1)3 = 3$

$\delta(o_c,h_d) = \delta(3,2) = 0$

Another example. We look at the following special quadratic combination with s=2.

h_1=1; j_1=2; h_2=2; j_2=1; h_3=3; j_3=4; h_4=4; j_4=3

We are testing for a closed two-site kinetic structure by setting c to 2.

$o_1 = \delta(o_0,j_1)h_1 + \delta(o_0,j_2)h_2 + \delta(o_0,j_3)h_3 + \delta(o_0,j_3)h_4 = \delta(2,2)1 + \delta(2,1)2 + \delta(2,4)3 + \delta(2,3)3 = 1$

$o_2 = \delta(o_0,j_1)h_1 + \delta(o_0,j_2)h_2 + \delta(o_0,j_3)h_3 + \delta(o_0,j_3)h_4 = \delta(1,1)2 + \delta(1,4)3 + \delta(1,3)3 = 2$

$\delta(o_c,h_d) = \delta(2,2) = 1$

The resulting summands (1/c) $\delta(o_c,h_d)$ for all 4 sites are 1/2 + 1/2 + 1/2 + 1/2, giving the result ϕ = 2.

S5.3 Additional examples for approximations and characteristic polynomials

The characteristic polynomial for the 2-site kinetic model reads:

$$f(\lambda) = \lambda^2 + \lambda(k_{12}+k_{21}) + k_{12}k_{21}\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\} \quad \text{(S20)}$$

From this polynomial and Eq. 20, compact forms of the Newton-Raphson approximation can be obtained. $\mathrm{Exp_1Log_0\lambda_1}$ is shown in Eq. 29. $\mathrm{Exp_1Log_0\lambda_{2,NR}}$ reads:

$$R_{cpmg}(\tau_{cp}) = R_{21} + k_{ex}p_a p_b\left[1-\mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\right]\left[\frac{1-p_a p_b\left[1-\mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\right]}{1-2p_a p_b\left[1-\mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\right]}\right] \quad \text{(S21)}$$

The characteristic polynomial for the 4-site linear scheme (BACD), obtained from Eq. 27 and S4, reads:

$$\begin{aligned}
f(\lambda) &= \lambda^4 \\
&+ \lambda^3(k_{12} + k_{21} + k_{13} + k_{31} + k_{34} + k_{43}) \\
&+ \lambda^2[k_{12}k_{21}\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\} + k_{13}k_{31}\{1 - \mathrm{sinc}^2(\Delta\omega_{13}\tau_{cp})\} + k_{34}k_{43}\{1 - \mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})\} \\
&\quad + k_{12}(k_{31} + k_{34} + k_{43}) + k_{13}(k_{21} + k_{34} + k_{43}) + k_{21}(k_{31} + k_{34} + k_{43}) + k_{31}k_{43}] \\
&+ \lambda[k_{12}k_{21}(k_{31} + k_{34} + k_{43})\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\} + k_{13}k_{31}(k_{21} + k_{43})\{1 - \mathrm{sinc}^2(\Delta\omega_{13}\tau_{cp})\} \\
&\quad + k_{34}k_{43}(k_{12} + k_{13} + k_{21})\{1 - \mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})\} + k_{12}k_{31}k_{43} + k_{13}k_{21}k_{34} + k_{13}k_{21}k_{43}] \\
&+ [k_{12}k_{21}k_{31}k_{43}\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\} + k_{13}k_{31}k_{21}k_{43}\{1 - \mathrm{sinc}^2(\Delta\omega_{13}\tau_{cp})\} + k_{34}k_{43}k_{13}k_{21}\{1 - \mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})\} \\
&\quad + k_{12}k_{21}k_{34}k_{43}\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp}) - \{1 - \mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})\} + \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\,\mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})] \\
&\quad \text{(S22)}
\end{aligned}$$

The characteristic polynomial for the 4-site quadratic scheme (-B-A-C-D-), obtained from Eq. 27 and S7, reads:

$$\begin{aligned}
f(\lambda) &= \lambda^4 \\
&+ \lambda^3(k_{12} + k_{21} + k_{13} + k_{31} + k_{24} + k_{42} + k_{34} + k_{43}) \\
&+ \lambda^2[k_{12}k_{21}\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\} + k_{13}k_{31}\{1 - \mathrm{sinc}^2(\Delta\omega_{13}\tau_{cp})\} + k_{34}k_{43}\{1 - \mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})\} + \\
&k_{24}k_{42}\{1 - \mathrm{sinc}^2(\Delta\omega_{24}\tau_{cp})\} + k_{12}(k_{31} + k_{34} + k_{42} + k_{43}) + k_{13}(k_{21} + k_{34} + k_{42} + k_{43}) + k_{21}(k_{31} + k_{34} +
\end{aligned}$$

$k_{42} + k_{43}) + k_{24}(k_{31} + k_{34} + k_{43}) + k_{31}(k_{42} + k_{43})] + \lambda[k_{12}k_{21}(k_{31} + k_{34} + k_{42} + k_{43})\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\} + k_{13}k_{31}(k_{21} + k_{24} + k_{42} + k_{43})\{1 - \mathrm{sinc}^2(\Delta\omega_{13}\tau_{cp})\} + k_{24}k_{42}(k_{12} + k_{13} + k_{31} + k_{34})\{1 - \mathrm{sinc}^2(\Delta\omega_{24}\tau_{cp})\} + k_{34}k_{43}(k_{12} + k_{13} + k_{21} + k_{24})\{1 - \mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})\} + k_{12}k_{31}(k_{42} + k_{43}) + k_{12}k_{24}(k_{31}+k_{34}+k_{43}) + k_{12}k_{34}k_{42} + k_{13}k_{21}(k_{34} + k_{42} + k_{43}) + k_{13}k_{24}(k_{34}+k_{42}) + k_{13}k_{34}k_{42} + k_{21}k_{31}(k_{42}+k_{43}) + k_{21}k_{34}k_{42} + k_{24}k_{31}k_{43}] + [k_{12}k_{21}(k_{31}k_{42} + k_{31}k_{43} + k_{34}k_{42})\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\} + k_{13}k_{31}(k_{21}k_{42} + k_{21}k_{43} + k_{24}k_{43})\{1 - \mathrm{sinc}^2(\Delta\omega_{13}\tau_{cp})\} + k_{34}k_{43}(k_{12}k_{24} + k_{13}k_{21} + k_{13}k_{24})\{1 - \mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})\} + k_{24}k_{42}(k_{12}k_{31} + k_{12}k_{34} + k_{13}k_{34})\{1 - \mathrm{sinc}^2(\Delta\omega_{24}\tau_{cp})\} + k_{13}k_{31}k_{24}k_{42}\{1 - \mathrm{sinc}^2(\Delta\omega_{24}\tau_{cp}) - \mathrm{sinc}^2(\Delta\omega_{13}\tau_{cp}) + \mathrm{sinc}^2(\Delta\omega_{13}\tau_{cp})\,\mathrm{sinc}^2(\Delta\omega_{24}\tau_{cp})\} + k_{12}k_{21}k_{34}k_{43}\{1 - \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp}) - \mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp}) + \mathrm{sinc}^2(\Delta\omega_{12}\tau_{cp})\,\mathrm{sinc}^2(\Delta\omega_{34}\tau_{cp})\} + 2\mathrm{sqrt}(k_{12}k_{21}k_{24}k_{42}k_{43}k_{34}k_{31}k_{13})\{1 - \mathrm{sinc}(\Delta\omega_{12}\tau_{cp})\,\mathrm{sinc}(\Delta\omega_{34}\tau_{cp})\,\mathrm{sinc}(\Delta\omega_{13}\tau_{cp})\,\mathrm{sinc}(\Delta\omega_{24}\tau_{cp})\}]$

(S23)

S5.4 Exact solution for eigenvalues from characteristic polynomial (three states)

For three states, the least negative exact eigenvalue for $\mathbf{H_{10}}$ can be calculated with

$$\lambda = -\frac{c_2}{3c_3} + 2\sqrt{-\frac{p}{3}}\cos[\frac{1}{3}\arccos(\frac{3q}{2p}\sqrt{-\frac{3}{p}})] \tag{S24}$$

and

$$p = \frac{3c_3c_1 - c_2 2}{3c_3^a}$$
$$q = \frac{2c_2^3 - 9c_3c_2c_1 + 27c_3^2c_0}{27c_3^3} \tag{S25}$$

and the coefficents c_0, ..., c_3 correspond to the coefficients for λ^0, ..., λ^3 in the characteristic polynomial (Eq. S18).

Supplemental Figures

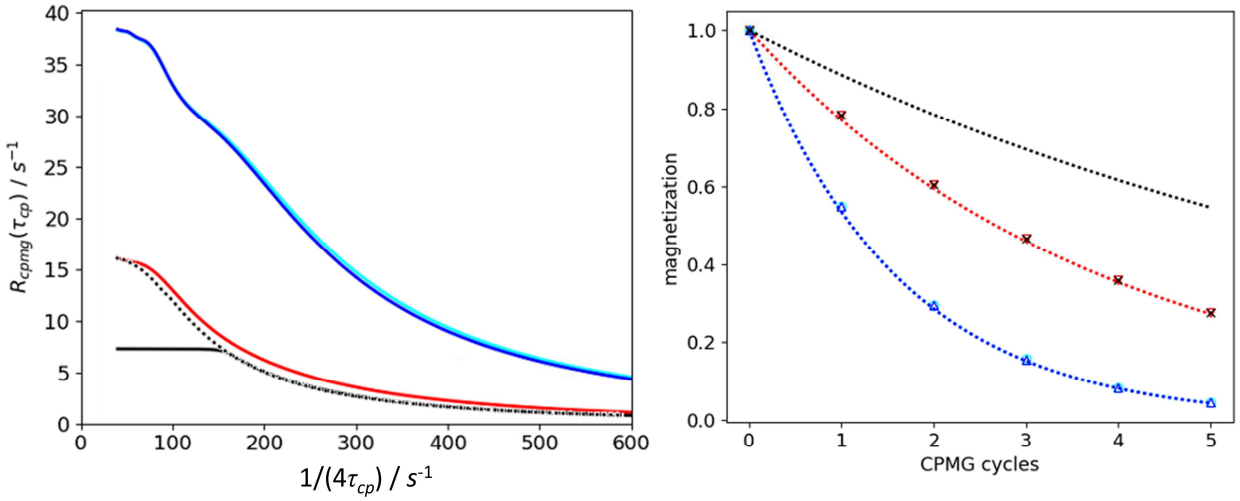

Fig. S1: Effect of a kinetically isolated minor site in the 4-site linear scheme on decay curves and exact solutions. Exact single-eigenvalue CPMG curves and for kite (cyan), star (blue), quadratic (red) and linear BACD (black) schemes and exact multi-eigenvalue curve for the linear scheme (black dotted). Right: Exponential decays at $1/(4\tau_{cp})$ = 60 s^{-1}. Color codes as in the left panel. Symbols represent calculated multi-exponential magnetization decay for site R_{cpmg}s are inaccurate for linear and star schemes at small $1/\tau_{cp}$ due to the "kinetically isolated" minor site D. This implies that the exact single-eigenvalue solution for linear scheme in the left panel are not accurate at small $1/\tau_{cp}$. Parameters: $k_{12} + k_{21}$ = 200 s^{-1}; $k_{13} + k_{31}$ = 200 s^{-1}; $k_{14} + k_{41}$ = 300 s^{-1}; $k_{24} + k_{42}$ = 50 s^{-1}; $k_{34} + k_{43}$ = 20 s^{-1}; $\Delta\omega_{AB}$ = 630 s^{-1}; $\Delta\omega_{AC}$ = -940 s^{-1}; $\Delta\omega_{AD}$ = 1900 s^{-1}; p_A = 0.85; p_B = 0.04; p_C = 0.04; p_D = 0.07.

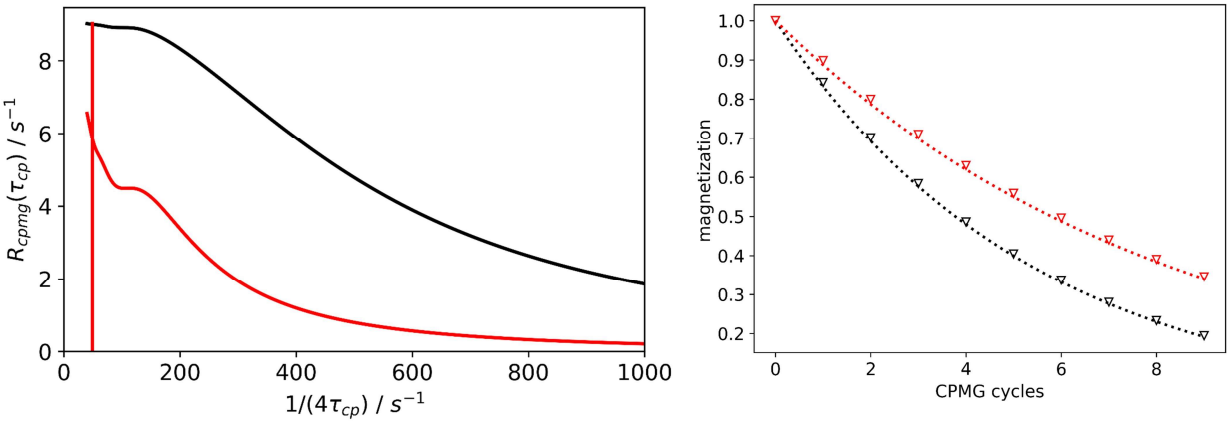

Fig. S2: Effect of relatively fast minor site exchange on the CPMG curves of 3-site schemes. Left: Exact CPMG curves are and for triangular (red) and linear BAC (black) schemes. In this particular case, R_{cpmg}s at small $1/\tau_{cp}$ differ between the two schemes, which is otherwise unusual. This can be explained with the combination of slow exchange between A and B, and a (relatively) fast exchange connection between B and C in the triangular case. Right: Exponential decays at $1/(4\tau_{cp})$ = 49 s^{-1}. Color codes as in the left panel. Exact single-eigenvalue exponential decays (dotted line) and multi-exponential magnetization decays (symbols) match, which means that the single-eigenvalue solutions in the left panel are accurate. Parameters: $k_{12} + k_{21} = 90$ s^{-1}, $k_{13} + k_{31} = 70$ s^{-1}, $k_{23} + k_{32} = 1000$ s^{-1}; $\Delta\omega_{AB} = 210$ s^{-1}; $\Delta\omega_{AC} = -1600$ s^{-1}; $p_A = 0.88$; $p_B = 0.06$; $p_C = 0.06$.

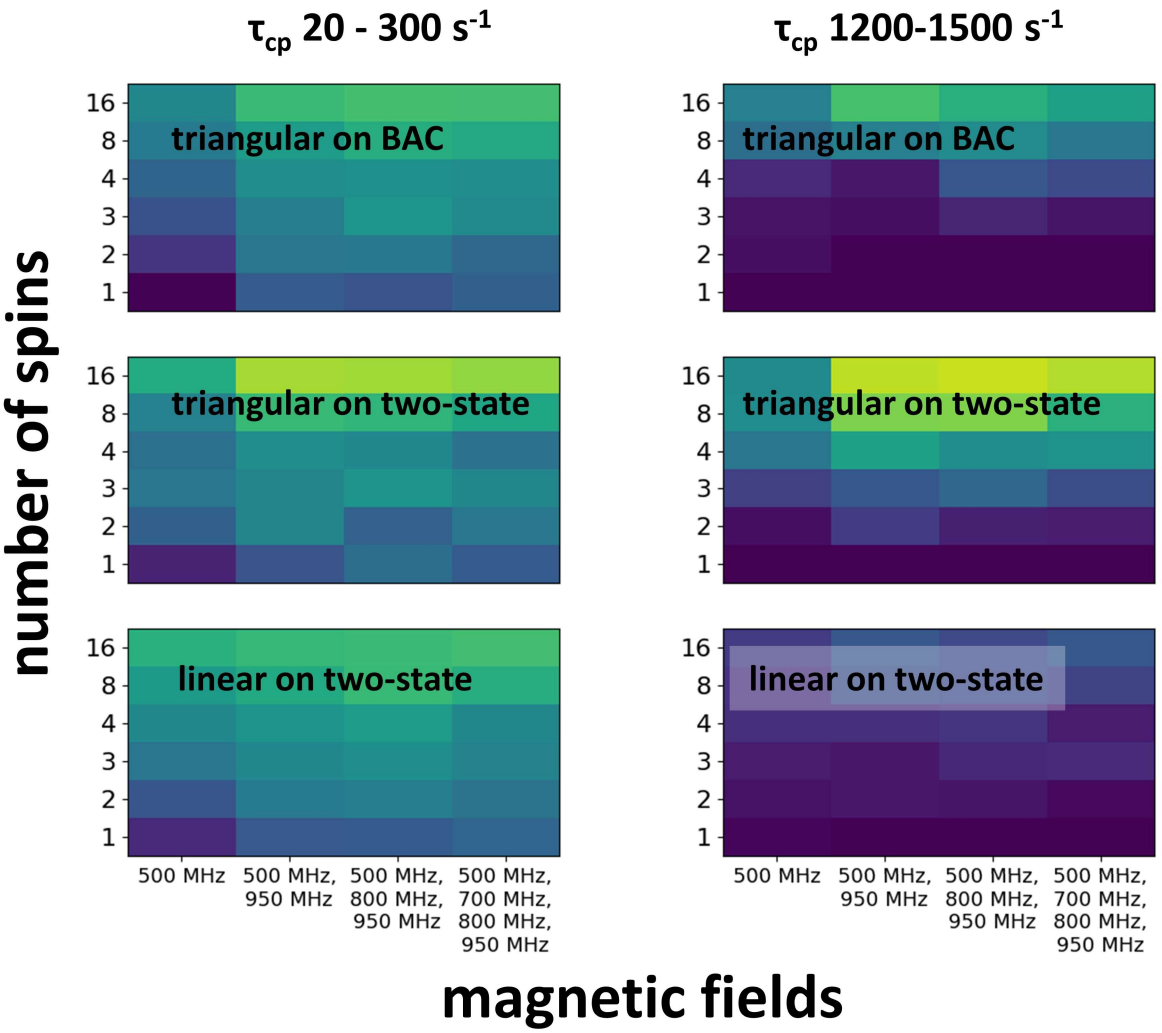

Fig. S3: Dependency of scheme distinguishability on magnetic field selection and spin number – lower boundary. In Extension of ***Figure 5***, we show what could be referred to as the lower distinguishability cutoff for randomly generated $\Delta\omega_{AB}$/ $\Delta\omega_{AC}$ sets; instead of the average (Fig 5) of the resulting RMS, we show here the average minus 2 standard deviations.

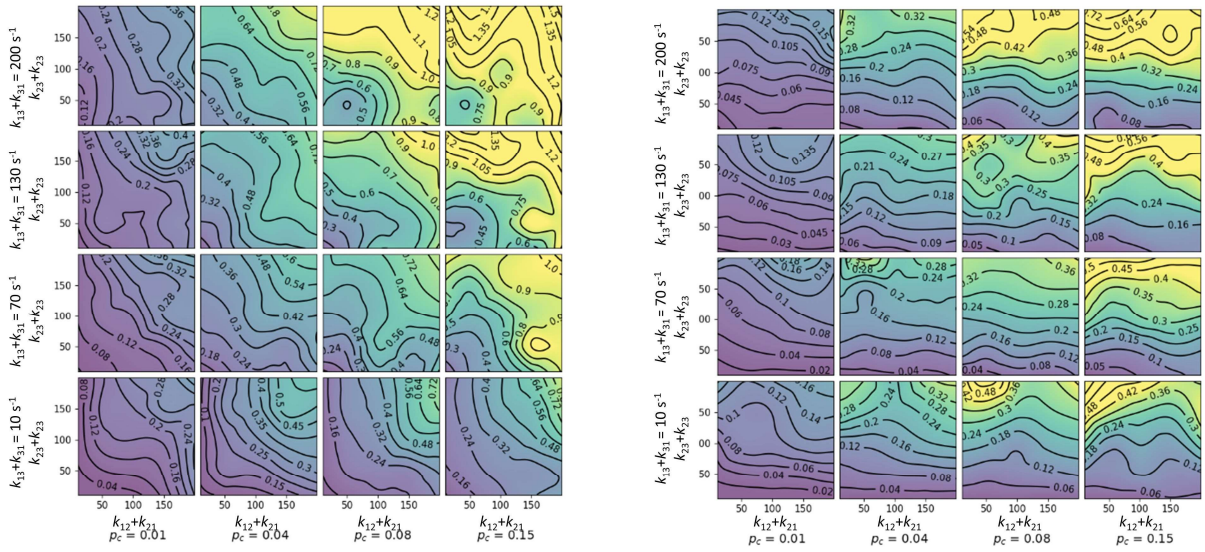

Fig. S4: Distinguishability of the triangular kinetic scheme from the two-state model. This Figure is equivalent to the bottom panels of Figure 5, but the data were fit against a two-state model as opposed to a three-state BAC model.

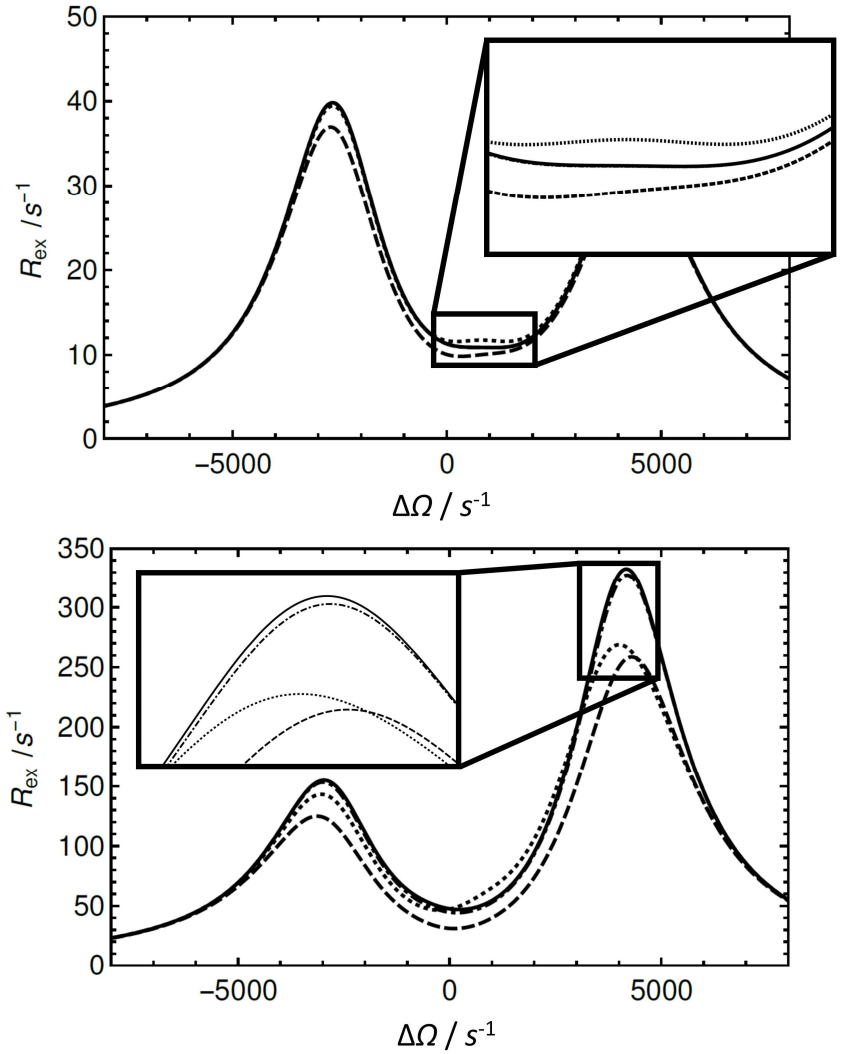

Fig S5: New second-order approximation (eigenvalue) approximation for the R_{ex} contribution to $R_{1\rho}$ for the kite-like 4-state chemical exchange scheme at different minor site populations. (Solid) Numerical calculation of $R_{ex}=-\lambda/\sin 2\theta$ from the least negative real eigenvalue of the 12×12 evolution matrix, (dashed) calculation from the first order approximation from Eq. 11 in Koss et al., 2017, (dotted) calculation from the Woodbury approximation from Eq. 50 in Koss et al., 2017, (dashed-dotted) calculation from the new second-order eigenvalue (Laguerre) approximation from Eq. 27 in this paper and Eq. 11 in Koss et al, 2017. The insets exemplify regions in which the results of the calculations differ (top figure: perfect overlap of dashed-dotted with solid). Parameters used for all calculations were used for all calculations were $\omega_1 = 1250\ s^{-1}$; $k_{12} + k_{21} = 140\ s^{-1}$, $k_{13} + k_{31} = 350\ s^{-1}$, $k_{34} + k_{43} = 700\ s^{-1}$ and $k_{14} + k_{41} = 350\ s^{-1}$, $\Omega_B - \Omega_A = -850\ s^{-1}$, $\Omega_C - \Omega_A = 2550\ s^{-1}$, and $\Omega_D - \Omega_A = -4250\ s^{-1}$.

Top and bottom figure differ in the choice of populations. Top (as in Koss et al., 2017): $p_A = 0.95$, $p_B = 0.05$, $p_C = 0.025$, $p_D = 0.005$. Bottom: $p_A = 0.79$, $p_B = 0.08$, $p_C = 0.06$, $p_D = 0.07$.