Topics in SSNMR and Dynamics of Proteins: Consequences of Intermediate Exchange

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Effects on NMR Spectra: Local, Angular Dynamics on Timescales from sec to ps


Krushelnitsky & Reichert Prog NMR 2005

# Notional Regimes for Motion

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<td>Fast</td>
<td>$\tau_c &lt;&lt; 1/\Delta\omega$</td>
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| Intermediate      | $\tau_c \approx 1/\Delta\omega$  
$\tau_c > T_2$ (or $T_1, T_2^{2Q}$ etc.) | $\mu$s  
$10^7$–$10^9$ s$^{-1}$ | Lineshape, short coherence times                   |
| Slow              | $T_1 > \tau_c > 1/\Delta\omega$ | ms–sec    | Population exchange                               |
| Ultraslow         | $\tau_c > T_1$              | min–days  | Time Dep Expts                                    |

**Rate and Amplitude controlled by Temp, Pressure and Hydration**
Chemical Exchange
Intermediate Exchange Timescale

\[ C_1 \underset{k_{21}}{\overset{k_{12}}{\leftrightarrow}} C_2 \]

\[ K_{eq} = \frac{[C_2]}{[C_1]} = \frac{k_{12}}{k_{21}} \]
Differential Equation Describing Precession, Chemical Exchange, and Relaxation

\[
\begin{pmatrix}
\frac{\partial M_1}{\partial t} \\
\frac{\partial M_2}{\partial t}
\end{pmatrix} =
\begin{pmatrix}
-i\Omega_1 - k_{12} - R_2 & k_{21} \\
k_{12} & -i\Omega_2 - k_{21} - R_2
\end{pmatrix}
\begin{pmatrix}
M_1 \\
M_2
\end{pmatrix}
\]
Effect of Precession and Relaxation on Magnetization

\[
\begin{pmatrix}
\frac{\partial M_1}{\partial t} \\
\frac{\partial M_2}{\partial t}
\end{pmatrix} =
\begin{pmatrix}
-i\Omega_1 - R_2 & 0 \\
0 & -i\Omega_2 - R_2
\end{pmatrix}
\begin{pmatrix}
M_1 \\
M_2
\end{pmatrix}
\]

\[M_i \equiv M^x_i + iM^y_i\]

\[
\frac{\partial M_1}{\partial t} = -(i\Omega_1 + R_2)M_1
\]

\[M_i(t) = M_i(0)e^{-(i\Omega_1 + R_2)t}\]

\[M(t) = \sum_i M_i(t)\]

Matrix is diagonal, two separable, solvable equations.
Effects of Chemical Exchange on Magnetization

\[
\begin{pmatrix}
\frac{\partial M_1}{\partial t} \\
\frac{\partial M_2}{\partial t}
\end{pmatrix}
= 
\begin{pmatrix}
-k_{12} & k_{21} \\
k_{12} & -k_{21}
\end{pmatrix}
\begin{pmatrix}
M_1 \\
M_2
\end{pmatrix}
\]
Effects of Exchange on Chemical Concentrations

\[ C_1 \overset{k_{12}}{\leftrightarrow} k_{21} C_2 \]

\[
\begin{align*}
\frac{\partial C_1}{\partial t} &= -k_{12} C_1 + k_{21} C_2 \\
\frac{\partial C_2}{\partial t} &= +k_{12} C_1 - k_{21} C_2
\end{align*}
\]

\[
\left( \begin{array}{c}
\frac{\partial C_1}{\partial t} \\
\frac{\partial C_2}{\partial t}
\end{array} \right) =
\left( \begin{array}{cc}
-k_{12} & k_{21} \\
k_{12} & -k_{21}
\end{array} \right)
\left( \begin{array}{c}
C_1 \\
C_2
\end{array} \right)
\]
Solving for Concentration over Time by Matrix Methods

\[ \frac{\partial \mathbf{c}}{\partial t} = -K \mathbf{c} \]

\[ \mathbf{c} = \begin{pmatrix} C_1 \\ C_2 \end{pmatrix} ; K = \begin{pmatrix} k_{12} & -k_{21} \\ -k_{12} & k_{21} \end{pmatrix} ; \]

\[ \mathbf{c}(t) = e^{-Kt} \mathbf{c}(0) \]

\[ D = U^{-1} K U \]

\[ K = U D U^{-1} \]

\[ e^{Kt} = U e^{-Dt} U^{-1} \]

\[ \mathbf{c}(t) = U e^{-Dt} U^{-1} \mathbf{c}(0) \]
\[ \mathbf{Ku}_i = \lambda_i \mathbf{u}_i ; \mathbf{u}_i = \begin{pmatrix} u_{i1} \\ u_{i2} \end{pmatrix} \]

Eigenvalue Approach to Diagonalization

\[ \mathbf{D} = \begin{pmatrix} \lambda_1 & 0 \\ 0 & \lambda_2 \end{pmatrix} \]

\[ \mathbf{U} = \begin{pmatrix} \langle u_{11} \rangle & \langle u_{21} \rangle \\ \langle u_{12} \rangle & \langle u_{22} \rangle \end{pmatrix} \]

\[ \mathbf{K} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \]

\[ |\mathbf{K} - \lambda \mathbf{I}| = \begin{vmatrix} a - \lambda & b \\ c & d - \lambda \end{vmatrix} = (a - \lambda)(d - \lambda) - bc = 0 \]

\[ \lambda = \frac{a + d}{2} \pm \frac{\sqrt{(a + d)^2 - 4(ad - bc)}}{2} \]

\[ \mathbf{A}: \text{Meaning of } \lambda \]
Let’s Look at Three Cases

\[ \lambda = \frac{a + d}{2} \pm \frac{\sqrt{(a + d)^2 - 4(ad - bc)}}{2} \]

\[ X = \begin{pmatrix} a & b \\ c & d \end{pmatrix} = \begin{pmatrix} 0 & 1 \\ -1 & 0 \end{pmatrix} \]

\[ K' = \begin{pmatrix} a & b \\ c & d \end{pmatrix} = \begin{pmatrix} k & -k \\ -k & k \end{pmatrix} \]

\[ K = \begin{pmatrix} a & b \\ c & d \end{pmatrix} = \begin{pmatrix} k_{12} & -k_{21} \\ -k_{12} & k_{21} \end{pmatrix} \]
Try to Solve a Meaningless Example

\[ \lambda = \frac{a + d}{2} \pm \frac{\sqrt{(a + d)^2 - 4(ad - bc)}}{2} \]

\[ X = \begin{pmatrix} a & b \\ c & d \end{pmatrix} = \begin{pmatrix} 0 & 1 \\ -1 & 0 \end{pmatrix} \]

\[ \lambda = 0 \pm \frac{\sqrt{(0)^2 - 4(0 + 1)}}{2} = \sqrt{-1} \]
Solve the Eigenvalue Problem for Symmetric Two Site Exchange

\[ \lambda = \frac{a + d}{2} \pm \sqrt{\frac{(a + d)^2 - 4(ad - bc)}{2}} \]

\[ K' \begin{pmatrix} a & b \\ c & d \end{pmatrix} = \begin{pmatrix} k & -k \\ -k & k \end{pmatrix} \]

\[ \lambda = \frac{2k}{2} \pm \sqrt{\frac{(2k)^2 - 4(k^2 - k^2)}{2}} = k \pm k \]

\[ D = \begin{pmatrix} 2k & 0 \\ 0 & 0 \end{pmatrix} \]
Solve for the Transformation Matrices $U$ and $U^{-1}$

$$K\tilde{u}_i = \lambda_i \tilde{u}_i$$

$$
\begin{pmatrix}
  k & -k \\
  -k & k \\
\end{pmatrix}
\begin{pmatrix}
  u_1 \\
  u_2 \\
\end{pmatrix}
= 2k\tilde{u}_1
$$

$$ku_{11} - ku_{12} = 2ku_{11}; -ku_{11} + ku_{12} = 2ku_{12}; u_{11} = -u_{12}$$

$$
\begin{pmatrix}
  k & -k \\
  -k & k \\
\end{pmatrix}
\begin{pmatrix}
  u_2 \\
  u_2 \\
\end{pmatrix}
= 0k\tilde{u}_2
$$

$$ku_{21} - ku_{22} = 0ku_{21}; -ku_{21} + ku_{22} = 0ku_{22}; u_{21} = u_{22}$$

$$U = \begin{pmatrix}
  \langle u_{11} \rangle & \langle u_{21} \rangle \\
  \langle u_{12} \rangle & \langle u_{22} \rangle \\
\end{pmatrix} = \begin{pmatrix}
  1 & 1 \\
  -1 & 1 \\
\end{pmatrix}$$

$$U = \begin{pmatrix}
  a & b \\
  c & d \\
\end{pmatrix}; U^{-1} = \frac{1}{|U|}\begin{pmatrix}
  d & -b \\
  -c & a \\
\end{pmatrix}; U^{-1} = \frac{1}{2}\begin{pmatrix}
  1 & -1 \\
  1 & 1 \\
\end{pmatrix}$$
Homework: Confirm that this expression yields the inverse generally

\[ U = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \]

\[ U^{-1} = \frac{1}{|U|} \begin{pmatrix} d & -b \\ -c & a \end{pmatrix} \]

Homework: Confirm in this specific case that this is the correct transformation matrix

\[ K = \begin{pmatrix} k & -k \\ -k & k \end{pmatrix} \]

\[ U = \begin{pmatrix} 1 & 1 \\ -1 & 1 \end{pmatrix} \]

Homework: Write equations for the concentration over time and check their validity
Arbitrary Two-Site Exchange Can Also be Solved

\[ \lambda = \frac{a + d}{2} \pm \frac{\sqrt{(a + d)^2 - 4(ad - bc)}}{2} \]

\[ K = \begin{pmatrix} a & b \\ c & d \end{pmatrix} = \begin{pmatrix} -k_{12} & k_{21} \\ k_{12} & -k_{21} \end{pmatrix} \]

\[ \lambda = \frac{-k_{12} - k_{21}}{2} \pm \frac{\sqrt{(-k_{12} - k_{21})^2 - 4(k_{12}k_{21} - k_{12}k_{21})}}{2} \]

\[ \lambda = -k \pm k \]

\[ k \equiv k_{12} + k_{21} \]

See Bernasconi 1976 “Relaxation Kinetics” Academic Press
Note that $K$ is not symmetric; is it always diagonalizable for any dimension?

Connected with microscopic reversibility, a similarity transformation ($U$) symmetrizes $K$ (to form $K'$), assuring us that it is always diagonalizable.

**HOMEWORK:** Show that if $U$ is defined as below, it renders the matrix of rate constants symmetric. A real symmetric matrix is always diagonalizable.

\[
C_n k_{nm} = C_m k_{mn}
\]

\[
U_{ij} = \sqrt{P_i} \delta_{ij}
\]

\[
K'_{ij} = \sqrt{K_{ij} K_{ji}} = \sqrt{\frac{P_j}{P_i}} K_{ij}
\]
Combined Effects of Precession, Chemical Exchange, and Relaxation

\[
\begin{pmatrix}
\frac{\partial M_1}{\partial t} \\
\frac{\partial M_2}{\partial t}
\end{pmatrix} = -\begin{pmatrix}
i\Omega_1 + k + R_2 \\
-k
\end{pmatrix} \begin{pmatrix} M_1 \\ M_2 \end{pmatrix}
\]

\[
\bar{m}(t) = U e^{-Dt} U^{-1} \bar{m}(0)
\]
\[
K + R + iL = \begin{pmatrix}
     i\Omega + R_2 + k & -k \\
     -k & -i\Omega + R_2 + k
\end{pmatrix}
\]

\[
\lambda = (R_2 + k) \pm \sqrt{k^2 - \Omega^2}
\]

\[
U = \begin{pmatrix}
     a & b \\
     c & d
\end{pmatrix};
U^{-1}_{ij} = \frac{1}{ad - bc} \begin{pmatrix}
     d & -b \\
     -c & a
\end{pmatrix}
\]

\[
a = i(\Omega + \sqrt{\Omega^2 - k^2})
\]

\[
b = i(\Omega - \sqrt{\Omega^2 - k^2})
\]

\[
c = d = k
\]

\[
M(t) = M_1(t) + M_2(t) = \frac{(a + c)(d - b)}{ad - bc} e^{-\lambda_1 t} + \frac{(b + d)(a - c)}{ad - bc} e^{-\lambda_2 t}
\]
Amplitudes in More Detail: Slow Exchange: $k \ll \Omega$

\[ M(t) = M_1(t) + M_2(t) = \frac{(a + c)(d - b)}{ad - bc} e^{-\lambda_1 t} + \frac{(b + d)(a - c)}{ad - bc} e^{-\lambda_2 t} \]

\[ \lambda_{1,2} = (R_2 + k) \pm \sqrt{k^2 - \Omega^2} \approx R_2 + k \pm i\Omega \]

\[ a = i(\Omega + \sqrt{\Omega^2 - k^2}) \approx 2i\Omega \]

\[ b = i(\Omega - \sqrt{\Omega^2 - k^2}) \approx 0 \]

\[ c = d = k \]

\[ M(t) = M_1(t) + M_2(t) = e^{-\lambda_1 t} + e^{-\lambda_2 t} = e^{-i\Omega t} e^{-(R_2 + k)t} + e^{i\Omega t} e^{-(R_2 + k)t} \]

\[ S(\omega) = \frac{k + R_2}{(R_2 + k)^2 + (\Omega - \omega)^2} + \frac{k + R_2}{(R_2 + k)^2 + (\Omega + \omega)^2} \]

A: Meaning of Ampl Re vs Im
Amplitudes in More Detail: Fast Limit: \( k \gg \nu \)

\[
M(t) = M_1(t) + M_2(t) = \frac{(a + c)(d - b)}{ad - bc} e^{-\lambda_1 t} + \frac{(b + d)(a - c)}{ad - bc} e^{-\lambda_2 t}
\]

\[
\lambda_{1,2} = (R_2 + k) \pm \sqrt{k^2} = (R_2 + 2k), R_2
\]

\[
a = i(\Omega + \sqrt{\Omega^2 - k^2}) \approx -k
\]

\[
b = i(\Omega - \sqrt{\Omega^2 - k^2}) \approx k
\]

\[
c = d = k
\]

\[
M(t) = M_1(t) + M_2(t) \approx 0e^{-\lambda_1 t} + 2e^{-\lambda_2 t} \approx 2e^{-R_2 t}
\]

\[
S(\omega) \approx \frac{2R_2}{R_2^2 + (\omega)^2}
\]
Reaction Time 100-1000 $\mu$s

$k \approx \delta$

\[
S_{fast}(\omega) \approx \frac{2R_2}{R_2^2 + (\omega)^2}
\]

\[
S_{slow}(\omega) = \frac{k + R_2}{(R_2 + k)^2 + (\Omega - \omega)^2} + \frac{k + R_2}{(R_2 + k)^2 + (\Omega + \omega)^2}
\]
Triosephosphate Isomerase: Lid Opening~Turnover

\[ ^{19}\text{F} \text{ 400 MHz Loop Tryptophan} \]

Unligated

G3P at \( K_m \) 1.2 mM

G3P Saturation 10 mM

\( ^{19}\text{F} \text{ Chemical Shift, ppm} \)

Positions catalytic residues and enhances \( k_{\text{cat}} \): CLOSING
Suppress side reaction: FREEZE
Allow rapid \( k_{\text{off}} \): OPEN

Davenport et al. (1991) Biochemistry, 30, 5821-5826

Sharon Rozovsky et al, JMB 2001
Slow Exchange Limit Contributions to Linewidth

\[ K + R + iL = \begin{pmatrix} i\Omega + R_2 + k & -k \\ -k & -i\Omega + R_2 + k \end{pmatrix} \]

\[ \lambda = (R_2 + k) \pm \sqrt{k^2 - \Omega^2} \]

\[ k \ll \Omega \]

\[ \lambda \approx R_2 + k \pm i\Omega \]
Fast Limit Contributions to Linewidth

\[ \mathbf{K} + \mathbf{R} + i\mathbf{L} = \begin{pmatrix} i\Omega + R_2 + k & -k \\ -k & -i\Omega + R_2 + k \end{pmatrix} \]

\[ \lambda = (R_2 + k) \pm \sqrt{k^2 - \Omega^2} \]

\[ k \gg \Omega \]

\[ \lambda \approx (R_2 + 2k), (R_2) \]

\[ x \ll 1; \sqrt{1 + x} \approx 1 + \frac{x}{2} + \ldots \]

\[ \lambda \approx (R_2 + 2k), \left( R_2 + \frac{\Omega^2}{2k} \right) \]
Exchange Broadening
Interference with Isotropic Chemical Shift Evolution

- Slow Limit scales with $k$ or $1/\tau_c$
- Fast Limit scales with $1/k$ or $\tau_c$
- Maximal effect (coalescence, critical point) when $k \approx \Delta \omega_{iso} / \sqrt{2}$ to $k \approx \Delta \omega_{iso}$
- The ability to probe this broadening allows one to study rare events (poorly populated species)
Fast Limit Contributions to Linewidth

$T_1 \rho$, Related to Woessner 1961 J Chem Phys; fast limit

$$R_{ex} = p_1 p_2 \Delta \Omega^2 / k \frac{1}{\left(1 + \frac{\omega_e^2}{k^2}\right)^2}$$

CPMG: Allerhand and Gutowsky 1965 J Chem Phys; fast limit approx

$$R_{ex} = \frac{1}{2 \tau_{ex}} - \frac{1}{\tau_{CPMG} \xi} \sinh^{-1}\left[\frac{1}{\tau_{ex}} \sinh\left(\frac{\tau_{CPMG} \xi}{2}\right)\right]$$

$$\xi = \sqrt{k^2 - 4 p_1 p_2 (\Delta \Omega)^2}$$
Important Alternatives to “N-site” Hopping Models

Smoluchowski equation for continuous diffusion in a potential, $U$. Potentially more direct connection to molecular interpretation.

1D example below includes diffusion and convection

Finite difference numerical approaches used

See work of Robert Vold: applications to SSNMR

$$R(\phi) = D \left[ \frac{\partial^2}{\partial \phi^2} + \frac{1}{kT} U'(\phi) \frac{\partial}{\partial \phi} + \frac{1}{kT} U''(\phi) \right]$$
Distributed Dynamics

\[ P(t)dt = \frac{1}{2k\Gamma(1 + 1/\beta)} \exp(-|t \cdot k|^\beta) dt \]

- Kaplan and Garroway showed (JMR 1982) that homogeneous and inhomogeneous distributions or rates can be distinguished based on NMR lineshapes.
Orientation Dependence of Frequency

\[ \omega = A(1 - 3\cos^2\theta) \]
Intermediate Exchange Lineshapes

\[ P(t)dt = \frac{1}{k} dt \]
Triosephosphate Isomerase Lid Motion Rate ~ Turnover

Loop Opening/Closing Observed at Half Saturation Ligation

G3P, 30 °C

TIM Active site / DL G3P (% ligated)

Echo Delay

30 µs

100 µs

140 µs

Θ ~ 30 - 60°
k_{cat} ~ 5 \times 10^3 s^{-1}
P_{op}/P_{cl} ~ 3.0

Deuterium Frequency, kHz

Positions catalytic residues and enhances k_{cat}; CLOSING
Suppress side reaction; FREEZE
Allow rapid k_{off}; OPEN

1YPI
Davenport et al. (1991) Biochemistry, 30, 5821-5826
7TIM

Open

Closed
DNA Dynamics at a Methylation Site

[5’-(dGATAGCGCTATC)-3’] DNA dodecamer

Dynamics Apparent in SSNMR Lineshape

Not Seen in Solution NMR Relaxation

Miller, Drobny, Varani et al JACS 2006

Figure 1. (a) Deuterium quadrupolar echo pulse sequence line shapes (2.6 μs 90° pulse with 40 μs echo delay; changes in signal-to-noise are due to different concentrations in each sample); (b) Simulated decay of the $C_1$ component of the correlation function describing the motions of C/D/CH bonds embedded in a rigid-rodlike DNA molecule tumbling at 3.9 ns and subject to internal motion at the indicated frequencies. In the absence of internal diffusion (blue), the decay is monoexponential; for fast internal motions, the decay is strongly multieponential (red), reflecting the modulation of the correlation functions by multiple motional mechanisms. Slower internal motions become invisible in the correlation functions (purple). (c–e) Relaxation parameters for C-H2^"": (c) solution $T_1$, (d) solution $T_{1p}$, (e) solid-state $T_{1Z}$. Experimental procedures are given in the Supporting Information.
Chemical Exchange During MAS

\[ \omega(t) = \omega_{iso} + \delta \left[ C_1 \cos(\gamma + \omega_t) + C_2 \cos(2\gamma + 2\omega_t) + S_1 \sin(\gamma + \omega_t) + S_2 \cos(2\gamma + 2\omega_t) \right] \]

\[ C_1 = -\frac{\sqrt{2}}{2} \sin(2\beta) \left( 1 + \frac{\eta}{3} \cos(2\alpha) \right) \]

\[ C_2 = -\frac{1}{2} \left( \sin^2 \beta - \frac{\eta}{3} (1 + \cos^2 \beta) \cos(2\alpha) \right) \]

\[ S_1 = -\frac{\eta \sqrt{2}}{3} \sin(\beta) \sin(2\alpha) \]

\[ S_2 = -\frac{\eta}{3} \cos(\beta) \sin(2\alpha) \]

\( \delta \) is the tensor width: \( \sigma_{zz} - \sigma_{iso} \)

\( \eta \) is the asymmetry: \( (\sigma_{xx} - \sigma_{yy}) / \delta \)

\( R_Z(\alpha)R_Y(\beta)R_Z(\gamma) \) transforms to the Rotor Fixed Frame at \( t=0 \) from the Laboratory Fixed Frame
Fast MAS vs. Liquid

\[ \omega(t) = \omega_{\text{iso}} + \delta \left[ C_1 \cos(\gamma + \omega, t) + C_2 \cos(2\gamma + 2\omega, t) + S_1 \sin(\gamma + \omega, t) + S_2 \cos(2\gamma + 2\omega, t) \right] \]

\[ \omega_r >> \delta \]

\[ \omega(t) \approx \omega_{\text{iso}} \]

Simulated using SPINEVOLUTION (Veshtort and Griffin) (Meier and Earl, 1985 JACS; Lyerla Yannoni Fyfe 1982 Acc Chem Res)
Tensor Orientation Change: Slow MAS

See Frydman et al 1990 and Schmidt et al 1986
Tensor Orientation Change : Static

Figure 3. The $^{13}$C methyl powder patterns for two-site exchange: (a) experimental spectra; (b) simulated spectra.
MAS Lineshapes: Sensitivity to Near Intermediate Exchange Conditions

Fig. 1. Calculated MAS (left column) and rotating sample (right column) 2H NMR powder spectra for a quadrupole coupling tensor whose principal axis system can assume two equally probable orientations $\Omega = [0, \tan^{-1}(2)], 0$ and $\Omega = [0, \tan^{-1}(\sqrt{2})], \phi$ relative to the crystalline-fixed axis system ($C_{4h} = 200$ kHz, $\omega_q = 0.09$, $\omega/2\pi = 5$ kHz, Gaussian line broadening of 250 Hz). The simulations employ rate constants $k_4$ (in both) of (a) $10^5$, (b) $10^6$, (c) $10^7$, (d) $10^8$, (e) $10^9$, (f) $10^6$, (g) $10^7$, and (h) $10^8$. 

1/23/08 Kristensen et al JMR
Exchange Linewidths $f(\omega_r)$

Figure 2
A Schmidt and S Vega
J Chem Phys 1987

Linewidths for a system
Undergoing 2 site flips:
Floquet Treatment vs.
Perturbation Approx.

$$R_{ex} \approx \frac{\delta^2}{15} \left(1 + \frac{\eta^2}{3} \right) \left[ \frac{\tau_c}{(1 + 4\omega_r^2 \tau_c^2)} + \frac{2\tau_c}{(1 + \omega_r^2 \tau_c^2)} \right]$$

Suwelack Rothwell and Waugh '80

1/23/08
Exchange Linewidths $f(\omega_r)$ for three crystallites

$$R_{ex} \approx \frac{\delta^2}{15} \left( 1 + \frac{\eta^2}{3} \right) \left[ \frac{\tau_c}{1 + 4 \omega_r^2 \tau_c^2} + \frac{2 \tau_c}{1 + \omega_r^2 \tau_c^2} \right]$$

$$R_{ex} \approx \frac{\delta^2}{15} (1 + 3\eta) \left[ \frac{9}{4 \omega_r^2 \tau_c} \right]$$
\( R_{ex} \) Linewith Contributions for Interference with Chemical Shift Evolution

- Slow Limit scales with \( k \) or \( 1/\tau_c \)
- Fast Limit scales with \( 1/k \) or \( \tau_c \)
- Maximal effect (coalescence, critical point) when \( k \approx \Delta \omega_{iso} / \sqrt{2} \) to \( k \approx \Delta \omega_{iso} \)
$R_{ex}$ Linewith Contributions
for Interference with Chemical Shift TENSOR Refocusing

- Slow Limit scales with $k$ or $1/\tau_c$
- Fast Limit scales with $1/k$ or $\tau_c$
- Amplitude related to $\delta/\omega_r$
- Maximal effect when $k\sim\omega_r$
- Effect gone when $\omega_r > \delta$ (or if $k$ is moved out of kinetic regime by heating, cooling, drying etc.)
More Generally, This Approach Also Applies to the Density Matrix, With Couplings, etc.

\[
\frac{\partial \tilde{m}}{\partial t} = -(iL + R + K)\tilde{m}
\]

\[
\frac{\partial \tilde{\rho}}{\partial t} = -(iL + R + K)\tilde{\rho}
\]

\[
L = [H, \rho]
\]

\[
\tilde{\rho}(t_0 + t) = e^{-i(L(t)+R+K)} \tilde{\rho}(t_0)
\]
Interference With Decoupling; Amine Rotor

\[ R_{ex} \approx \frac{4\omega_d^2 I(I + 1)}{15} \left( \frac{\tau_c}{1 + \omega_1^2 \tau_c^2} \right) \]

\[ R_{ex} \approx \frac{4\omega_d^2 I(I + 1)}{15} \frac{1}{\omega_1^2 \tau_c} \]

Rothwell and Waugh 1981

Long et al JACS 1994
$R_{ex}$ Linewith Contributions
for Interference with Proton Decoupling

- Slow Limit scales with $k$ or $1/\tau_c$
- Fast Limit scales with $1/k$ or $\tau_c$
- Amplitude related to $\omega_D$
- Maximal effect when $k \sim \omega_1$
- Effect gone when $\omega_1 >>> \omega_D^{HH}$ (or if $k$ is moved out of kinetic regime by heating, cooling, drying etc.)
$R_{ex}$ -like Interference with Coherent Transfer

- Assume Coherent Transfer of Longitudinal Magnetization (eg $I_z$-$S_z$) involves Intermediary Coherence (eg ZQC)
- Conformational Exchange Causes Interference with Exchange Mechanism, either because of Failed Decoupling or Fluctuations in Time Dependent Chemical Shift
- Could be thought of as an exchange broadening on ZQC
\( R_{ex} \)-like Interference with Coherent Transfer

1) ZQ Coherence experiences fluctuations in dipolar couplings. Dephasing amplitude related to \( \omega_D \). Maximal effect when \( k \sim \omega_1 \)

2) ZQ Coherence experiences chemical shift fluctuations due to changes in orientation of CSA. Dephasing amplitude related to \( \delta \), and maximal effect when \( k \sim \omega_r \)
**R_{ex} Interference with Coherent Transfer**

- Specific Example which MV set up in SPINEVOLUTION: Two Carbons during RFDR Magnetization Exchange Period
- Begin with magnetization on one spin only and follow \( I_z \) and \( S_z \) over time.
- One of them is also in Chemical Exchange with both CSA (\( \delta = 10 \) kHz) and couplings to attached protons changing. \( \omega_r \) moderate (16 kHz).
Efficiency of Cross Peak Development in RFDR: Varying the Chemical Exchange Rates
Exchange Interference in MAS NMR: dynamics in MAS NMR modulates large anisotropic interactions

(1) CSA refocusing under MAS is defeated by large angle jumps if $k \sim \omega_r$ and $\delta \sim \omega_r$,

(2) Decoupling by proton irradiation is defeated by moderate or large angle jumps when $k \sim \omega_1$ and $\omega_D \sim \omega_1$

(3) The performance of coherent transfer sequences is degraded by large angle jumps over a similar range of conditions (provided transverse coherences are important in the spin evolution).

There may be useful analogies between these problems and the well-understood effect of exchange induced interference with the evolution of the isotropic shift, and the resultant signature broadening effects (which of course also occurs for MAS NMR).
REFERENCES

Simulate Tensor Orientation Change During MAS (DMS)

Conditions as for Schmidt et al., 108 degree hop, axial static tensor of width 4.6 kHz; Simulation with SPINEVOLUTION. Very broad interference condition.
Tensor Orientation Change: Slow MAS

See Frydman et al 1990 and Schmidt et al 1986