SSNMR -- Intermediate Exchange
Conformational Dynamics of Biopolymers:
“A few of my favorite things”: Chemical Exchange by: Bloch-McConnell, Stochastic Liouville and Redfield theory

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

Fluctuations in the Local Field Driven by Reorientation and Changes in Environment

Fig. 2 Typical CSA tensor principal directions for peptides. The least-shielded component is denoted as $\sigma_{11}$, and the most-shielded component is $\sigma_{33}$. For each tensor, one of the components points in a direction very nearly perpendicular to the peptide plane.

$\omega = A(1-3\cos^2\theta)$
Combined Effects of Relaxation, Coherent Evolution, and Chemical Exchange: The Bloch–McConnell Equations

\[
\frac{\partial M_1}{\partial t} = \left( i\Omega_1 + k + R_2 \right) M_1 - k M_2
\]

\[
\frac{\partial M_2}{\partial t} = \left( -i\Omega + k + R_2 \right) M_1 - k M_2
\]

\[
\tilde{m}(t) = U e^{-D_t} U^{-1} \tilde{m}(0)
\]
Effect of Evolution and Relaxation on Magnetization

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

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

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

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

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

Matrix is diagonal, two separable, solvable equations.
Chemical Exchange
Intermediate Exchange Timescale

\[
C_1 \leftrightarrow C_2
\]

\[
K_{eq} = \frac{[C_2]}{[C_1]} = \frac{k_{12}}{k_{21}}
\]
Effects of Exchange on Chemical Concentrations

\[ C_1 \leftrightarrow C_2 \]

\[
\frac{\partial C_1}{\partial t} = -k_{12} C_1 + k_{21} C_2 \\
\frac{\partial C_2}{\partial t} = +k_{12} C_1 - k_{21} C_2
\]

\[
\left( \begin{array}{c}
\frac{\partial C_1}{\partial t} \\
\frac{\partial C_2}{\partial t}
\end{array} \right) = 
\begin{pmatrix}
-k_{12} & k_{21} \\
k_{12} & -k_{21}
\end{pmatrix}
\left( \begin{array}{c}
C_1 \\
C_2
\end{array} \right)
\]
Effects of Chemical Exchange on Magnetization

\[
\begin{pmatrix}
\frac{\partial M_1}{\partial t} \\
\frac{\partial M_2}{\partial t}
\end{pmatrix} =
\begin{pmatrix}
-k_{12} & k_{21} \\
k_{12} & -k_{21}
\end{pmatrix}
\begin{pmatrix}
M_1 \\
M_2
\end{pmatrix}
\]
Solving for Concentration over Time by Matrix Methods – Chemical Exchange Only

\[
\begin{align*}
\frac{\partial \mathbf{c}}{\partial t} &= -K \mathbf{c} \\
\mathbf{c}(t) &= e^{-Kt} \mathbf{c}(0) \\
K &= \begin{pmatrix} k_{12} & -k_{21} \\ -k_{12} & k_{21} \end{pmatrix} \\
D &= U^{-1} K U \\
K &= U D U^{-1} \\
e^{Kt} &= U e^{-Dt} U^{-1} \\
\mathbf{c}(t) &= U e^{-Dt} U^{-1} \mathbf{c}(0)
\end{align*}
\]
\[ \mathbf{Ku}_i = \lambda_i \mathbf{u}_i \; ; \mathbf{u}_i = \begin{pmatrix} u_{i1} \\ u_{i2} \end{pmatrix} \]

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

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

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

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

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

**Eigenvalue Approach to Diagonalization**

**A: 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 Nonphysical Example

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

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

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

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

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

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

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

$$
\bar{K}_{ij} = \lambda_i \bar{u}_i
$$

$$
\begin{pmatrix}
  k & -k \\
  -k & k
\end{pmatrix}
\bar{u}_1 = 2k\bar{u}_1
$$

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

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

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

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

$$
U = \begin{pmatrix} a & b \\ c & d \end{pmatrix}; U^{-1} = \frac{1}{|U|} \begin{pmatrix} d & -b \\ -c & a \end{pmatrix}; U^{-1} = \frac{1}{2} \begin{pmatrix} 1 & -1 \\ 1 & 1 \end{pmatrix}
$$
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

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

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

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

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

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

See Bernasconi 1976 “Relaxation Kinetics” Academic Press
Note that $K$ is not symmetric; is it always diagonalizable for larger kinetic schemes (3-component or N-component kinetic system)?

Connected with assumption of microscopic reversibility, a similarity transformation $U$, below, can be used to symmetrize $K$ (to form $K'$), assuring us that it is always diagonalizable.

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

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

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

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

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

\[
\tilde{m}(t) = U e^{-D t} U^{-1} \tilde{m}(0)
\]
\[ \mathbf{K} + \mathbf{R} + i\mathbf{L} = \begin{pmatrix} i\Omega + R_2 + k & -k \\ -k & -i\Omega + R_2 + k \end{pmatrix} \]

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

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

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

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

\[ c = d = k \]

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

Question: what is the meaning of Eigenvalues, the Imaginary vs. Real part
General Questions

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

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

Meaning of lambda values? Real part? Imaginary part? Meaning of the coefficients in front of the exponent?

Analogy with Single Spin, no Exchange

\[ M_i(t) = M_i(0) e^{-(i\Omega_i + R_2)t} \]
Questions about Fast Limit

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

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

What is the frequency when \( k >> \Omega \)?
What is/re the number of lines when \( k >> \Omega \)?
What is/are the linewidths when \( k >> \Omega \)?

\[ \lambda \sim R_2; \]
\[ \lambda \sim R_2 + 2k \]
Questions about Slow Limit

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

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

What is the number of lines when \( k << \Omega \)?
What is/are the frequencies when \( k << \Omega \)?
What is/are the linewidths when \( k << \Omega \)?

\[ \lambda \sim (R_2 + k) + i\Omega; \]
\[ \lambda \sim (R_2 + k) - i\Omega \]
Differential Equation Describing Precession, Chemical Exchange, and Relaxation

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

\[ K_{eq} = \frac{[C_2]}{[C_1]} = \frac{k_{12}}{k_{21}} \]

\[ \begin{pmatrix} \frac{\partial M_1}{\partial t} \\ \frac{\partial M_2}{\partial t} \end{pmatrix} = \begin{pmatrix} -i\Omega_1 - k_{12} - R_2 & k_{21} \\ k_{12} & -i\Omega_2 - k_{21} - R_2 \end{pmatrix} \begin{pmatrix} M_1 \\ M_2 \end{pmatrix} \]

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

\[ S_{slow}(\omega) = \frac{k + R_2}{(R_2 + k)^2 + (\Omega - \omega)^2} + \frac{k + R_2}{(R_2 + k)^2 + (\Omega + \omega)^2} \]
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: \( k \gg \Omega \)

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

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

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

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

\[
c = d = k
\]

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

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

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

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

\( k >> \Omega \)

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

\( x << 1; \sqrt{1+x} \approx 1 + \frac{x}{2} + ... \)

\[ \lambda \approx (R_2 + 2k), (R_2 + \frac{\Omega^2}{2k}) \]
Exchange Broadening
Interference of Conformational Exchange with Shift Evolution

- Slow Limit scales with $k$ or $1/\tau_c$
- Fast Limit scales with $1/k$ or $\tau_c$
- Coalescence $k \sim \Delta \omega_{iso} / \sqrt{2}$
- The ability to probe this broadening allows one to document rare events (poorly populated species) and study the rates of processes. In contrast to $R_1$ measurements, its sensitive to timescales from high nanosecond to mid-millisecond, and therefore to important functional events in binding recognition folding and catalysis.
Triosephosphate Isomerase: Lid Opening ~ Turnover

Sharon Rozovsky et al, JMB 2001
General Solution:
Numerical Simulations of SLE

\[ \frac{\partial \tilde{m}}{\partial t} = -(iL + R + K)\tilde{m} \]
\[ \frac{\partial \tilde{\rho}}{\partial t} = -(iL + R + K)\tilde{\rho} \]
\[ L = [H, \rho] \]
\[ \tilde{\rho}(t_0 + t) = e^{-iL(t) + R + K} \tilde{\rho}(t_0) \]

Numerical integration of the (linearized, Taylors expansion) equations, evaluation of derivatives

Spinevolution (Vershtort and Griffin JMR 2006)
…Asymmetric N site hop model subsequently added.

SPINACH (Kuprov)
Orientation Dependence of Frequency

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

CSA
Dipolar
Quadrupolar
J

e.g. Deuterium Powder Relaxation, Exchange: Wittebort Olejniczak and Griffin 1987,
CSA Tensor Orientation Change

Analysis according to above 2 site hop theory— but in place of two environments/isotropic shifts, the two alternative “sites” correspond to two angles of the truncated CSA, keeping time averaged terms that commute with $B_0$.

Each crystal orientation analyzed separately and then powder pattern constructed.

See Solum Zilm Michl Grant 1983
Intermediate Exchange Powder Lineshapes

\[ P(t)dt = \frac{1}{k} dt \]
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.
Exchange during MAS: 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.

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

Suwelack Rothwell and Waugh '80

1/9/18
Chemical Exchange, Tensor Reorientation Interferes with MAS

See Frydman et al 1990 and Schmidt et al 1986
MAS Lineshapes: Sensitivity to Near Intermediate Exchange Conditions
Characterizing the Exchange Linewidth

Sometimes Rex can be extracted from the spectrum..... but more practically, with other contributions to linewidths, and irregular lineshapes, Rex can be obtained from the decay of echo-refocused magnetization. Either an echo (single pi pulse), a CPMG train, or a spin lock refocuses the chemical shift, to allow an accurate measurement of relaxation, and provides experimentally controllable variables, such as a field strength, frequency. Exchange processes will cause failure to refocus, decay of the echo with increasing delay (in addition to $R_2^\circ$).
$R_{1\rho}$ : Relaxation During Spinlock

near resonant, in phase, spin lock, variable strength and length

Intensity

Freq. (kHz)

Time (ms)

8000
Measurements Reflect Sum of $R_{2^o}$ and $R_{ex}$

If $R_2$ is known or predicted, $R_{ex}$ can be extracted and analyzed. They are of comparable order of magnitude in many cases.

$$R_{1\rho} = R_1 \cos^2 \theta + R_2 \sin^2 \theta + R_{ex} \sin^2 \theta$$

$R_{ex}$: Chemical Exchange modulates an interaction (e.g. Isotropic Shift)

$\theta$: Effective Field Angle

$R_1, R_2^o$: in the absence of exchange
Separating $R_2$ from $R_{ex}$

Refocusing time (field strength for T1rho, interpulse pulse frequency for CPMG) can be a tool to discern the rate constant, if they are of comparable magnitude to the rate constant!

For example, if $\tau_c \sim 1$ ms, and the echo delay is 10 ms, magnetization will fail to recover. With a 100us delay echo (done 100 times) the magnetization will largely recover (Carr Purcell Meiboom Gill sequence Rev. Sci. Instrum. 29, 688 (1958);) will succeed.

A rare chemical event would causes dephasing only during the 100us echo element it occurs in, but would not accumulate over the whole 10 ms period.
Lab Frame vs. Rotating Frame Exchange Relaxation
Fast Limit (Redfield) of Asymmetric 2 Site Hop

\[ R_{ex} = p_1 p_2 \tau_c \Omega^2 \]

Free Procession

\[ R_{ex} = p_1 p_2 \Delta \Omega^2 \frac{\tau_c}{\left(1 + \omega_e^2 \tau_c^2\right)} \]

During Spin Lock (T1rho)

High applied field asymptote of Rex is zero, obtaining a \( R_{2^o} \) estimate.
Relaxation Due to Rapid Angular Fluctuations

\[ \mathcal{H} = \mathcal{H}_0 + \mathcal{H}_1 \]

\( \mathcal{H}_0 \) is the average (constant). \( \mathcal{H}_1 \) fluctuates and averages to 0.

\[ \frac{\partial \sigma}{\partial t} = -i [\mathcal{H}, \sigma] \]

Move to a frame where the action of \( \mathcal{H}_0 \) is the invisible (overbar).

How do the \( \mathcal{H}_1 \) fluctuations, which averages to 0, affect the observables?

\[ \tilde{A} = e^{i \mathcal{H}_0 t} A e^{-i \mathcal{H}_0 t} \]

\[ \frac{\partial \sigma}{\partial t} = -i [\tilde{\mathcal{H}}_1, \sigma] \]
Generating Second Order Expressions

\[
\frac{\partial \sigma}{\partial t} = -i [\mathcal{H}_1, \sigma]
\]

\[
\sigma(t) = \sigma(0) - i \int_0^t [\mathcal{H}_1(t'), \sigma(t')] dt'
\]

\[
\frac{\partial \sigma}{\partial t} = -\int_0^t [\mathcal{H}_1(t), \mathcal{H}_1(t'), (\sigma(t') - \sigma_{eq})] dt'
\]
Lab Frame vs. Rotating Frame Exchange Relaxation
Redfield of Asymmetric 2 Site Hop Intermediate

\[ R_{ex} = p_1 p_2 \tau_c \Omega^2 \]  

Free Procession

\[ R_{ex} = p_1 p_2 \Delta \Omega^2 \frac{\tau_c}{\left(1 + \omega_e^2 \tau_c^2\right)} \]  

During Spin Lock T1rho

At high applied field it tends (slowly) to zero
→ obtain R2 “control”
Caveat– strong fields needed, heating
Determining $k_{\text{ex}}$ from $R_{\text{ex}}$

**In lab frame**

$$R_{\text{ex}} = p_1 p_2 \Delta \Omega^2 \tau_c$$

**In rotating frame**

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

- A unique solution for $\Delta \Omega$ $p_1$ $p_2$ and $k_{\text{ex}} = k_f + k_r$ based on $R_{\text{ex}}$ – if $\Delta \Omega$ and $p_1$ $p_2$ are available from from other data, and assume a simple kinetic model.

- In addition, variation of the spin lock strength $\omega_e$ is potentially useful (dispersion curves). When its weak, the full effect is expected. If it is high enough, the exchange contribution is removed.

$$\omega_e \gg 1/\tau_c^2$$
Dispersion Curves: A Constraint for Identifying the rates

\[ R_{2}(\omega^2) \text{s}^{-1} \]

Rates, s\(^{-1}\)
- 500
- 1500
- 3000
- 7500
- 12500

“Frame Transformation” of Spectral Density Centered on “CS” Conditions $\omega_1 = n\omega_r$

Random Fluctuation Model - Approximate Initial Relaxation due to CSA during a Spinlock and MAS for Fast Limit

Farès, Qian, and Davis, *J Chem Phys* 2005

\[
\left\langle \frac{1}{\tau_{1\rho}} \right\rangle = \frac{1}{240} \gamma^2 \delta^2 B_0^2 \sin^2(\beta_{L_d}) \sum_{m=-2}^{2} (6A_{|m|} + \eta^2 B_{|m|})
\times [j(\omega_e + 2\omega_R) + j(\omega_e - 2\omega_R) + 2j(\omega_e + \omega_R)
+ 2j(\omega_e - \omega_R)]. \tag{A26}
\]

Experimental Analysis Involving Dipolar Mechanisms:
Methyl Rotors: Akasaka Ganapathy MacDowell Naito *J Chem Phys* 1983
Experimental DMS: Krushelnitsky et al *SSNMR* 2002
Redfield and Model Free expressions for $R_1\rho$
During MAS: $1/\tau_c >> \omega_r, \omega_1 > \delta$

$$R_{1\rho}^{CSA} = \frac{(\delta_{CSA}\omega_N)^2}{4} \left( \frac{1}{3}J(\omega_1 - 2\omega_r) + \frac{2}{3}J(\omega_1 - \omega_r) 
+ \frac{2}{3}J(\omega_1 + \omega_r) + \frac{1}{3}J(\omega_1 + 2\omega_r) \right)$$

$$R_{1\rho}^{NH} = \frac{\delta_{NH}^2}{4} \left( 3J(\omega_H) + \frac{1}{3}J(\omega_1 - 2\omega_r) + \frac{2}{3}J(\omega_1 - \omega_r) 
+ \frac{2}{3}J(\omega_1 + \omega_r) + \frac{1}{3}J(\omega_1 + 2\omega_r) \right)$$

Here, $\omega_1$ is the spinlock field amplitude expressed in rad/s (small off-resonance effects are neglected), $\omega_r/2\pi$ is the spinning frequency, and $\omega_H$ and $\omega_N$ are the Larmor frequencies of $^1$H and $^{15}$N, respectively; $\delta_{CSA}$ is the reduced chemical shift.

$$J(\omega) = \frac{2}{5}(1 - S_{NH}^2) \frac{\tau_{c,eff}}{1 + \omega^2\tau_{c,eff}^2}$$
R₂ expressions: Range of Validity

\[ R_{1\rho} = R_1 \cos^2 \theta + R_2^\circ \sin^2 \theta + R_{ex} \sin^2 \theta \]

\( R_{ex} \): Due to chemical exchange
\( \theta \): Effective Field Angle
\( R_2^\circ \): in the absence of exchange- knowledge needed to extract Rex

I mentioned that the fluctuation is more effective for R₂ and R₁ρ when its slower.
But \( R_2 \sim \Delta \omega^2 (\tau_c) \) blows up when the correlation time is too long.
Unphysical!

\[ R_2 (\tau_c) = \Delta \omega^2 (\tau_c^2) \ll 1, \text{ so } \tau_c < \Delta \omega \]
Valid Application Range for R1ρ expressions

\[ \tau_c \ll T_{1ρ} \quad \text{and} \quad R_{1ρ} \tau_c = \Delta \omega^2 \left( \frac{\tau_c^2}{1+\omega^2 \tau_c^2} \right) \ll 1 \quad (\text{where} \quad \omega = \omega_1 +/- n\omega_ρ) \]

→ Fast processes

\[ \omega^2 \tau_c^2 \ll 1 \quad R_{1ρ} \tau_c \sim \Delta \omega^2 \left( \frac{\tau_c^2}{1+\omega^2 \tau_c^2} \right) \ll 1 \quad \text{so} \quad (\tau_c, \Delta \omega)^2 \ll 1 \quad \tau_c < 10^{-5} \]

→ Slower processes weak perturbing field

\[ \omega^2 \tau_c^2 \gg 1, \quad \Delta \omega^2 \left( \frac{\tau_c^2}{1+\omega^2 \tau_c^2} \right) \ll 1 \quad \text{so} \quad \Delta \omega^2 \left( \frac{\tau_c^2}{\omega^2 \tau_c^2} \right) \ll 1 \quad \Delta \omega^2 \ll \omega^2 \]

\[ \Delta \omega \sim 10^4 \quad \text{and} \quad \omega_1 +/- n\omega_ρ \sim 10^6 \]

Assuming \( \Delta \omega \sim 10^4-10^5 \) \( \omega_1 +/- n\omega_ρ \sim 10^4 - 10^6 \)
Redfield expressions Indicate Novel Features Compared to Solution

\[ R_{1p}^{CSA} = \frac{(\delta_{CSA\omega_N})^2}{4} \left( \frac{1}{3} J(\omega_1 - 2\omega_r) + \frac{2}{3} J(\omega_1 - \omega_r) \right) + \frac{2}{3} J(\omega_1 + \omega_r) + \frac{1}{3} J(\omega_1 + 2\omega_r) \]  
\[ R_{1p}^{NH} = \frac{\delta_{NH}^2}{4} \left( 3J(\omega_H) + \frac{1}{3} J(\omega_1 - 2\omega_r) + \frac{2}{3} J(\omega_1 - \omega_r) \right) + \frac{2}{3} J(\omega_1 + \omega_r) + \frac{1}{3} J(\omega_1 + 2\omega_r) \]

Here, \( \omega_1 \) is the spinlock field amplitude expressed in rad/s (small off-resonance effects are neglected), \( \omega_r/2\pi \) is the spinning frequency, and \( \omega_H \) and \( \omega_N \) are the Larmor frequencies of \(^1\text{H}\) and \(^{15}\text{N} \), respectively; \( \delta_{CSA} \) is the reduced chemical shift.

\[ J(\omega) = \frac{2}{5} (1 - S_{NH}^2) \frac{\tau_{c,\text{eff}}}{1 + \omega^2 \tau_{c,\text{eff}}^2} \]

The nuclear magnetic resonance relaxation data analysis in solids: General \( R_1/R_{1p} \) equations and the model-free approach

Rauf Kurbanov, Tatjana Zinkevich, and Alexey Krushelnitsky
MAS $R_{1\rho}$ Experiments

$$R_{1\rho} = R_1 \cos^2 \theta + R_2 \sin^2 \theta + R_{\text{ex}} \sin^2 \theta$$

$R_{\text{ex}}$ : Due to chemical exchange  
$\theta$ : Effective Field Angle  
$R_1, R_2$ : in the absence of exchange

$k= 1, 1000, \underline{30,000}, >10^{10} \text{ s}^{-1}$
Caution Regarding Interpretation

Vanderhart and Garroway J Chem Phys 1979
Global Analysis

\[
\begin{align*}
\kappa_{\text{ex}}(T, \omega_0, \omega_1, \omega_r) \\
R_2(T, \omega_0, \omega_1, \omega_r) \\
I(t, T, \omega_0, \omega_1, \omega_r)
\end{align*}
\]

Prior $^2\text{H}$ lineshape and relaxation Analysis: Brown Vold & Hoatson ’96
This Analysis by $^{13}\text{C}$ T1ρ (C. Quinn & McDermott ’09)
$T_2 \sim 10 - 60 \text{ s}^{-1}$