

Relaxation III

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Sources of fluctuating local fields

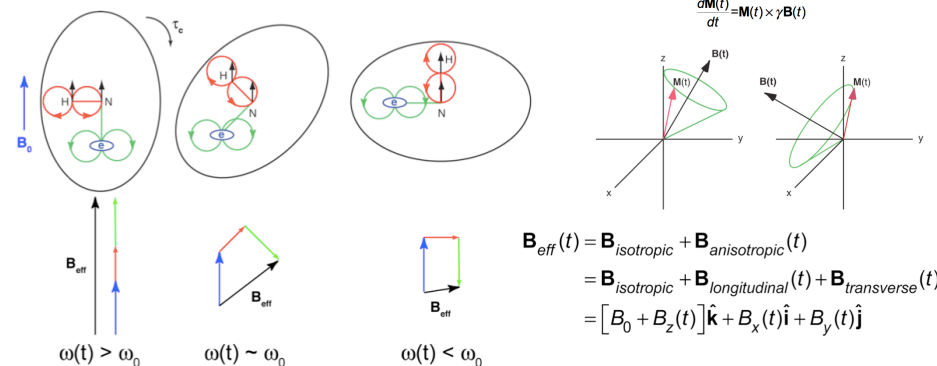
- Dipole-dipole (DD): $B_{loc} \propto \gamma_H/r^3 \approx 2.4 \text{ mT (150 ppm)}$
independent of B_0
- Chemical shift anisotropy (CSA): $B_{loc} \propto B_0 \cdot \Delta\sigma$ (170 ppm)
proportional to B_0
- chemical exchange (R_{ex}): $B_{loc} \sim B_0 \cdot \Delta\delta \sim 1 \text{ ppm}$
proportional to B_0
- Paramagnetism, quadrupolar interactions (^2H), scalar couplings...
- All fluctuations are much weaker than the static field, B_0
- Sensitivity of spins to these local field fluctuations depends on their gyromagnetic ratio – ^1H most sensitive, ^{15}N least sensitive

The microscopic mechanism of relaxation: fluctuating local magnetic fields

- Relaxation is caused by locally fluctuating magnetic fields
- These can have multiple origins – dipole-dipole interactions, chemical shift anisotropy, paramagnetism, chemical exchange...
- Effect on spin relaxation depends on timescale (frequency) of fluctuations
- Pulses – weak magnetic fields oscillating on-resonance at the Larmor frequency – cause transitions between energy levels. In an identical way, **random fluctuations in local fields at the Larmor frequency cause longitudinal and transverse relaxation.**
- Transverse relaxation is additionally caused by fluctuations **at any frequency**

Sources of fluctuating local fields

local field is vector sum of lots of interactions, and depends strongly on orientation of molecule



Quantifying fluctuations: Correlation functions and spectral densities

- The correlation function $G(\tau)$ describes how quickly fluctuations in the local field decay:

$$G(\tau) = \overline{B_{\text{loc}}^2} e^{-\tau/\tau_c}$$

- In simple cases this can be described by a single correlation time τ_c , which defines a rough 'frequency', $1/\tau_c$, where the fluctuations are strongest
- This can be made more precise by the idea of the spectral density function $J(\omega)$, the Fourier transform of the correlation function:

$$J(\omega) = \overline{B_{\text{loc}}^2} \left(\frac{2\tau_c}{1 + \omega^2\tau_c^2} \right)$$

- Special case: $J(0)$ is the integral of the correlation function

$$J(0) = 2\overline{B_{\text{loc}}^2}\tau_c$$

Longitudinal relaxation in the random field model

- Longitudinal relaxation changes the energy of the spin – a *non-adiabatic* process (*non-secular*, in Keeler's terminology)
- In direct analogy to rf pulses, only fluctuations at the Larmor frequency ω_0 are important
- Relaxation rate is proportional to the spectral density at this frequency, and the magnitude of the fluctuations:

$$R_z = \gamma^2 \overline{B_{\text{loc}}^2} j(\omega_0)$$

The random field model

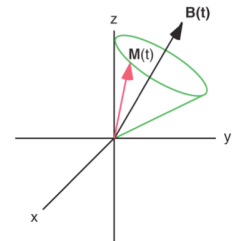
- Isolated spin (e.g. ^{129}Xe) with Larmor frequency ω_0
- Fluctuating local field B_{loc}
- Fluctuations are isotropic: $\overline{B_{\text{loc},x}^2} = \overline{B_{\text{loc},y}^2} = \overline{B_{\text{loc},z}^2}$
- Timescale of fluctuations described by correlation time τ_c and reduced spectral density function $j(\omega)$

Non-adiabatic (non-secular) contributions to transverse relaxation in the random field model

- Fluctuations at the Larmor frequency cause spins to rotate – this changes the x or y magnetisation as well as the z magnetisation
- Relaxation rate proportional to spectral density at this frequency, and the magnitude of the fluctuations:

$$R_{xy} = \frac{1}{2} \gamma^2 \overline{B_{\text{loc}}^2} j(\omega_0)$$

- Transverse relaxation rate only half as fast as longitudinal relaxation – only one of x and y magnetisations are affected



Adiabatic (secular) transverse relaxation in the random field model

- Fluctuations in the local field – on any timescale – cause the Larmor frequency to fluctuate
- Over an ensemble of many spins, this gradually results in coherences getting out of sync

$$\frac{dM^+(t)}{dt} = i\{\omega_0 + \omega_z(t)\}M^+(t)$$

Average over all sub-ensembles to give the bulk magnetization of the sample:

$$\langle M^+ \rangle(t) = e^{i\omega_0 t} \left\langle \exp \left[i \int_0^t \omega_z(t') dt' \right] \right\rangle \langle M^+ \rangle(0)$$

Total transverse relaxation in the random field model

- Adiabatic contribution to transverse relaxation proportional to spectral density at zero frequency:

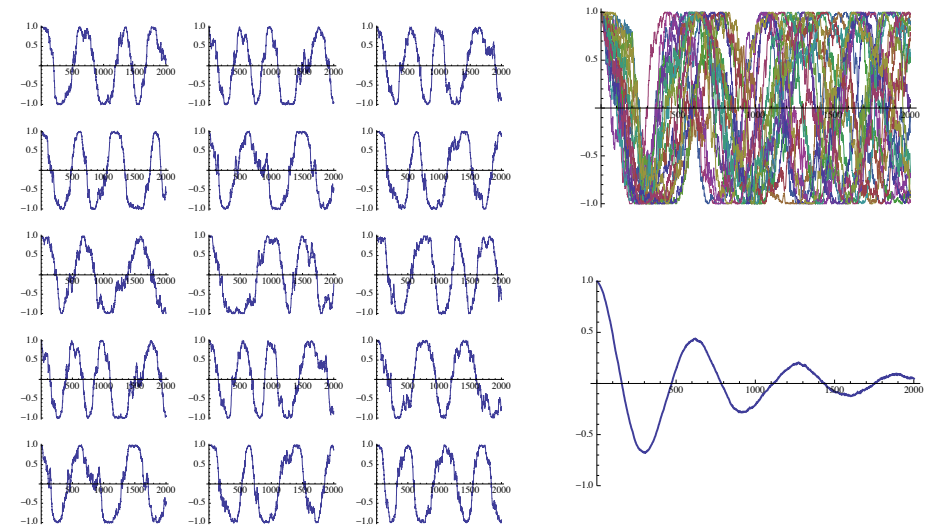
$$R_{xy} = \frac{1}{2} \gamma^2 \overline{B_{loc}^2} j(0)$$

- This is the total area under the correlation function – *in other words, slowly decaying fluctuations cause the most transverse relaxation*
- Total transverse relaxation rate is the sum of adiabatic and non-adiabatic contributions:

$$R_{xy} = \frac{1}{2} \gamma^2 \overline{B_{loc}^2} j(0) + \frac{1}{2} \gamma^2 \overline{B_{loc}^2} j(\omega_0)$$

- Macromolecular limit (slow motion): Only $j(0)$ term is significant

Simulation of adiabatic (secular) transverse relaxation in the random field model



Dipolar relaxation of two spins

$$\text{Dipolar coupling: } b = \frac{\mu_0 \gamma_1 \gamma_2 \hbar}{4\pi r_{IS}^3}$$

Longitudinal relaxation (from Solomon equations):

$$R_1^{(S)} = b^2 \left[\frac{3}{20} j(\omega_S) + \frac{3}{10} j(\omega_I + \omega_S) + \frac{1}{20} j(\omega_I - \omega_S) \right]$$

Transverse relaxation:

$$R_2^{(S)} = b^2 \left[\frac{1}{10} j(0) + \frac{3}{20} j(\omega_I) \right] \begin{matrix} \swarrow \text{secular} \\ \nwarrow \text{non-secular} \end{matrix} \\ + \frac{3}{40} j(\omega_S) + \frac{3}{20} j(\omega_I + \omega_S) + \frac{1}{40} j(\omega_I - \omega_S) \\ = b^2 \left[\frac{1}{10} j(0) + \frac{3}{20} j(\omega_I) \right] + \frac{1}{2} R_1^{(S)}$$

where does this term come from?

Dipolar relaxation of two spins

Dipolar coupling: $b = \frac{\mu_0 \gamma_1 \gamma_2 \hbar}{4\pi r_{IS}^3}$

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Transverse relaxation:

$$\begin{aligned} R_2^{(S)} &= b^2 \left[\frac{1}{10}j(0) + \frac{3}{20}j(\omega_I) \right. \\ &\quad \left. + \frac{3}{40}j(\omega_S) + \frac{3}{20}j(\omega_I + \omega_S) + \frac{1}{40}j(\omega_I - \omega_S) \right] \\ &= b^2 \left[\frac{1}{10}j(0) + \frac{3}{20}j(\omega_I) \right] + \frac{1}{2}R_1^{(S)} \end{aligned}$$

Cross-relaxation (NOE):

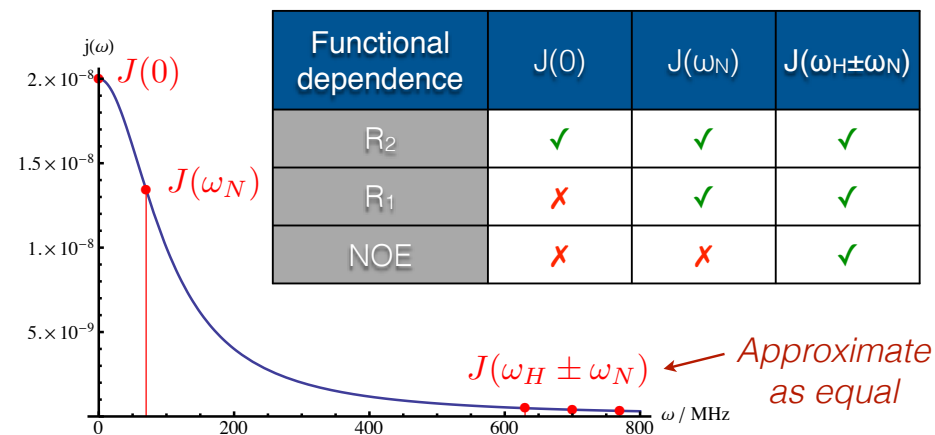
$$\sigma_{IS} = b^2 \left[\frac{3}{10}j(\omega_I + \omega_S) - \frac{1}{20}j(\omega_I - \omega_S) \right]$$

Deuteration

Dipolar coupling: $b = \frac{\mu_0 \gamma_1 \gamma_2 \hbar}{4\pi r_{IS}^3}$

- Fluctuations in local field $\sim \gamma^2$
- $\gamma_D/\gamma_H \approx 0.15$, and $(\gamma_D/\gamma_H)^2 \approx 0.02$
- Deuteration can dramatically decrease transverse relaxation rates by eliminating unwanted relaxation pathways

Reduced spectral density mapping



Combined measurement of R_1 , R_2 and NOE can disentangle contributions of $J(0)$, $J(\omega_N)$ and $J(\omega_H)$

Transverse cross-relaxation

- Longitudinal cross-relaxation is an important effect, responsible for the NOE, arising from the dipolar interaction of spins:

$$\sigma_{12} = b^2 \left[\frac{3}{10}j(\omega_{0,1} + \omega_{0,2}) - \frac{1}{20}j(\omega_{0,1} - \omega_{0,2}) \right]$$

- Is there an analogous relaxation process between transverse spins? Yes!

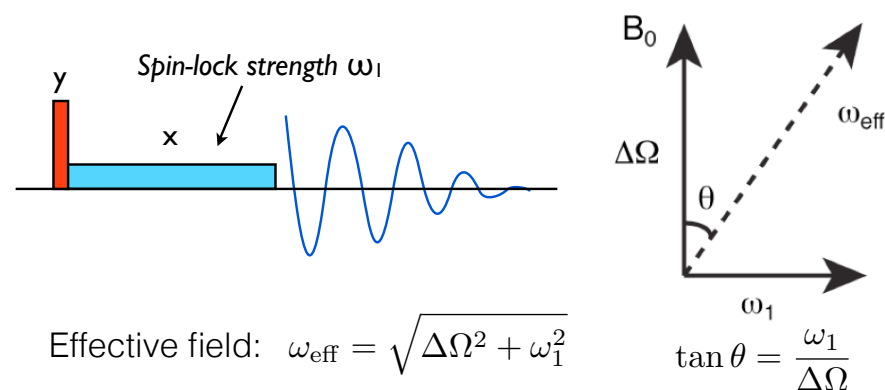
$$\eta_{12} = b^2 \left[\frac{1}{10}j(0) + \frac{3}{20}j(\omega_0) \right]$$

- Why don't we normally see it?

The secular approximation

- States with different eigenfrequencies do not cross-relax
- e.g. z magnetisation has zero frequency, so all spins can cross-relax
- Transverse magnetisation – coherences generally have different frequencies (different nuclei, different chemical shifts) and effects of cross-relaxation contributions rapidly cancel out
- 'Different' in this context means $\Delta\omega \gg$ linewidth

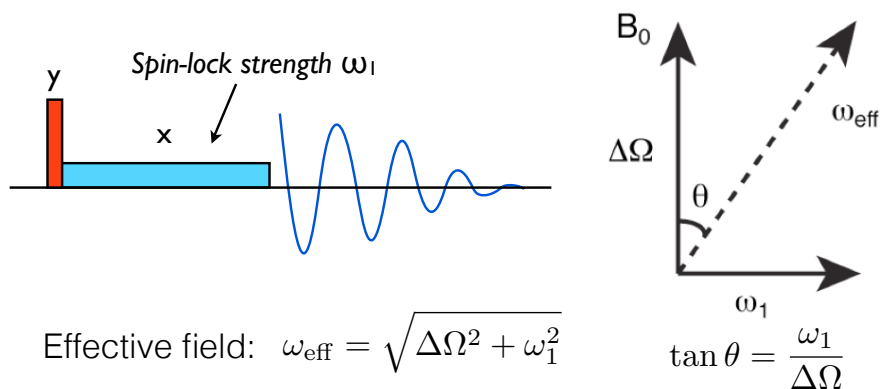
Spin-locking and $R_{1\rho}$ relaxation



$$\text{Effective field: } \omega_{\text{eff}} = \sqrt{\Delta\Omega^2 + \omega_1^2}$$

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

Spin-locking and transverse cross-relaxation (ROESY)

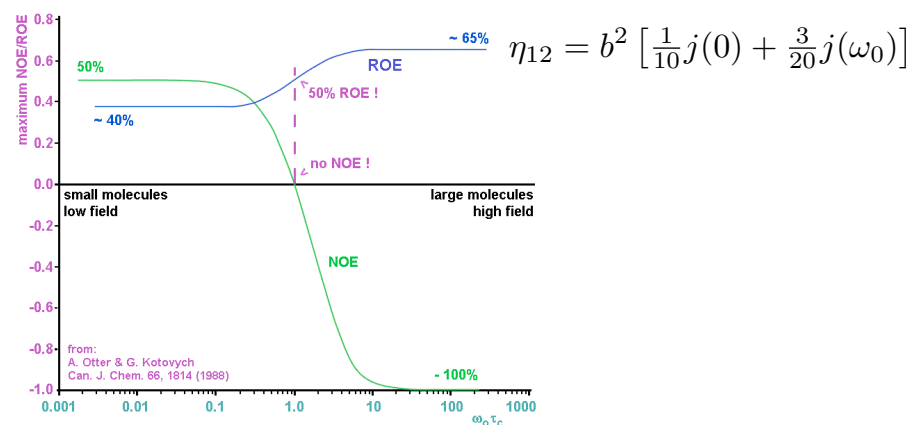


$$\text{Effective field: } \omega_{\text{eff}} = \sqrt{\Delta\Omega^2 + \omega_1^2}$$

$$\tan \theta = \frac{\omega_1}{\Delta\Omega}$$

- Provided $\omega_1 \gg \Delta\Omega$, spins are locked along x axis
- Now transverse cross-relaxation is coherent and can become significant
- Rate still depends on $\gamma_1^2 \gamma_2^2$ – much more important for ^1H than ^{15}N

NOESY vs ROESY



$$\sigma_{12} = b^2 \left[\frac{3}{10} j(\omega_{0,1} + \omega_{0,2}) - \frac{1}{20} j(\omega_{0,1} - \omega_{0,2}) \right]$$