Lecture #3
Basics of Relaxation

• Topics
  – Molecular motion
  – Stochastic processes
  – A simple model of relaxation
  – $T_1$ and $T_2$

• Handouts and Reading assignments
  – Levitt, Chapters 19.1-3, 20.1-3,
  – Kowalewski, Chapter 2.
NMR Relaxation

• Relaxation is the process by which the phase coherence among spins returns to its equilibrium value (as given by the Boltzmann distribution).

• Restoration of longitudinal magnetization, \( M_z = γ\hbar\langle \hat{I}_z \rangle \), is characterized by a time constant, \( T_1 \).

• Disappearance of transverse magnetization, \( M_{xy} = γ\hbar\left(\langle \hat{I}_x \rangle + i\langle \hat{I}_y \rangle\right) \), is characterized by a time constant, \( T_2 \).

Do the other coherences, e.g. \( \langle 2\hat{I}_z\hat{S}_z \rangle, \langle 2\hat{I}_x\hat{S}_x \rangle, \langle 2\hat{I}_y\hat{S}_y \rangle \), ..., also relax?

• We’ll first look at some simple relaxation models to build intuition.
Nuclear Spins

- A spin in a magnetic field simply undergoes Larmor precession.

- Relaxation is all about phase coherence among groups of spins.

- Magnetic fields are the only way to interact with the magnetic moment of a spin $\frac{1}{2}$ nuclei. (spins $> \frac{1}{2}$ interact with E-field gradients)

- In general, any change in the magnetic field (magnitude and/or direction) seen by a nuclear spin will change its magnetic moment.

  Hamiltonian: $\hat{H} = -\hat{\mu} \cdot \vec{B}$

  Magnetic moment: $\hat{\mu} = \gamma \hbar \hat{I}$

Basic principle: spatial and temporal magnetic field variations are the primary source of NMR relaxation.
Molecular Motion

- In vivo, molecular motion is the key source of spatially and temporally varying magnetic fields.
- Time scales of these motions determine the corresponding physical effects.

Physical effects
NMR Effects of Molecular Motion

Diagram showing the effects of molecular motion on NMR spectra, categorized by time scales: very slow (s), slow (ms), fast (μs), very fast (ns), ultrafast (ps, fs), and fast. The diagram includes:

- Averaging of Non-secular Interactions
- Spin-Lattice Relaxation
- Averaging of Secular Interactions
- Lineshape Perturbations
- Longitudinal Magnetization Exchange

Time scales are divided into:

1. Larmor Timescale
2. Spectral Timescale
3. Relaxation Timescale
In Vivo Magnetic Fields

• One source of magnetic field variations is due to dipolar coupling and molecular tumbling.

\[ B = B_0 + \Delta B(t) \]

Called “tumbling” rather than rotating since molecules constantly bumping into each other.

• While \( \langle \Delta B(t) \rangle = 0 \), the instantaneous effect is not negligible.

• We need to take a close look at the properties of \( \Delta B(t) \).
Brief Review of Stochastic Processes

• The perturbing magnetic field, $\Delta B(t)$, is modeled as a stochastic process and represents a family of time functions.

• For example, consider a collection of nuclear spins, $I_i$, for $i=1,…N$. Let $\Delta B_i(t)$ be the time varying field seen by the $i^{th}$ spin.

$\Delta B_1$

$\Delta B_2$

$\Delta B_N$

At any time, $t_0$, $\Delta B(t_0)$ is a random variable with zero mean and variance $= \langle B^2 \rangle$. $\Delta B(t)$ is stationary if statistics independent of $t_0$.

- $\Delta B_i(t)$ is a random function of time. Process is ergodic if time averages equal averages over $i$: e.g. $\langle \Delta B_i^2(t_0) \rangle_i = \langle \Delta B_i^2(t) \rangle_i = \langle B^2 \rangle$

- One function we care about is the statistical correlation between $\Delta B_i(t)$ and $\Delta B_i(t+\tau)$, $G_i(t, \tau) = \langle \Delta B_i(t) \Delta B_i(t+\tau) \rangle$. Averaging over all spins yields $G(t, \tau)$.

- For a stationary process: $G(t, \tau) = G(\tau)$, i.e. independent of $t$.

- A second highly useful function is the Fourier transform of $G(\tau)$. 

$$S(\omega) = \int_{-\infty}^{\infty} G(\tau) e^{-i\omega \tau} d\tau \quad \text{Wiener-Khinchin Theorem}$$

$S(\omega)$ is called the power spectrum and represents the power available at each frequency. This function plays a fundamental role in NMR relaxation theory.
Molecular Tumbling

• Consider a water molecule undergoing isotropic tumbling (Brownian motion). For simplicity, we’ll arbitrarily place the $I$ spin at the origin and assume the inter-nuclear distance is fixed.

\[ t_c = \text{rotational correlation time} = \text{average time for a molecule to rotate over one radian, a measure of rotational coherence.} \]

• Almost all NMR relaxation processes are described by an exponential correlation function: $G(\tau) = G(0)e^{-|\tau|/\tau_c}$

• That is, the correlation between the position of a molecule at two points in time falls off exponentially.
G(τ) for a simple case

- Are exponential correlation functions a good fit for in vivo NMR?
  \[ G(τ) = \langle ΔB(t)ΔB(t + τ)\rangle \approx G(0)e^{-|τ|/τ_c} \]
  Let’s find out…

- For the case of a (nearly) spherical molecule undergoing isotropic tumbling, let \( ΔB(t) = F(Ω) \), where for convenience \( Ω \) is a single angle variable representing \((θ(t), φ(t))\).

\[
G(τ) = \left\langle F(t)F^*(t + τ)\right\rangle = \frac{1}{4π} \int \int F(Ω_0)F^*(Ω)P(Ω_0 | Ω, τ)\,dΩ_0\,dΩ
\]

probability of finding the molecule at \( Ω_0 \) starting at angle \( Ω \) after a time \( τ \)

- To derive an expression of \( G(τ) \), we’ll start with Fick’s law of diffusion.
Fick’s law of diffusion

• Fick’s second law

\[
\frac{\partial f(x,y,z)}{\partial t} = D \left( \frac{\partial^2 f(x,y,z)}{\partial x^2} + \frac{\partial^2 f(x,y,z)}{\partial y^2} + \frac{\partial^2 f(x,y,z)}{\partial z^2} \right) = D \Delta f(x,y,z)
\]

• In spherical coordinates, the Laplacian operator is:

\[
\Delta = \frac{1}{r^2} \frac{\partial}{\partial r} \left( r^2 \frac{\partial}{\partial r} \right) + \frac{1}{r^2 \sin \theta} \frac{\partial}{\partial \theta} \left( \sin \theta \frac{\partial}{\partial \theta} \right) + \frac{1}{r^2 \sin^2 \theta} \frac{\partial^2}{\partial \phi^2}
\]

• In our case, fixing the radius \( r \) and just considering the angular components, yields

\[
\frac{\partial P(\Omega_0 | \Omega, \tau)}{\partial t} = D_r \Delta_r P(\Omega_0 | \Omega, \tau)
\]

Legendre operator (Laplacian with fixed \( r \))

Fick’s law for rotational diffusion.
$G(\tau)$ for a simple case (cont.)

- The spherical harmonics, $Y^m_l$, are eigenfunctions of $\Delta_r$, and form a complete orthonormal basis set, and the solution for Fick’s law of rotational diffusion can be written as:

$$P(\Omega_0 | \Omega, \tau) = \sum_l \sum_m Y^m_l(\Omega_0) Y^m_l(\Omega) e^{-l(l+1)D_r \tau}$$

- Spherical harmonics: $Y^m_l(\theta, \phi)$
  - orthonormal over the surface of a sphere.
  - arise in multiple physical applications, e.g. atomic orbitals.
The first few spherical harmonics

\[ Y_0^0 = \sqrt{\frac{1}{4\pi}} \]

\[ Y_1^0 = \sqrt{\frac{3}{4\pi}} \cos \theta \]

\[ Y_1^\pm = \mp \sqrt{\frac{3}{8\pi}} \sin \theta e^{\pm i\phi} \]

\[ Y_2^0 = \sqrt{\frac{5}{16\pi}} \left( 3 \cos^2 \theta - 1 \right) \]

\[ Y_2^\pm = \mp \sqrt{\frac{15}{8\pi}} \cos \theta \sin \theta e^{\pm i\phi} \]

\[ Y_2^{\pm 2} = \sqrt{\frac{15}{32\pi}} \sin^2 \theta e^{\pm 2i\phi} \]
\(G(\tau)\) for a simple case (cont.)

- Substituting back into the equation for \(G(\tau)\)

\[
G(\tau) = \frac{1}{4\pi} \sum_l \sum_m e^{-l(l+1)D_r|\tau|} \int Y_l^m(\Omega_0) F(\Omega_0) d\Omega_0 \int F^*(\Omega) Y_l^m(\Omega) d\Omega
\]

- In general, solving can be difficult, except when the functions, \(F(\Omega)\), can be expressed as sums of spherical harmonics.

\(Y_l^m\)s are orthonormal: 
\[
\langle Y_l^m | Y_{l'}^{m'} \rangle = \begin{cases} 
1 & \text{for } l = l' \text{ and } m = m' \\
0 & \text{for } l \neq l' \text{ or } m \neq m' 
\end{cases}
\]
$G(\tau)$ for a simple case (cont.)

- Example: the secular approximation of the dipolar coupling Hamiltonian is:

$$H_D = F(\Omega) = \frac{\mu_0 \gamma^2 \hbar}{4\pi r^3} \sqrt{\frac{3}{2}} \left(3\cos^2 \theta(t) - 1 \right) = \frac{\mu_0 \gamma^2 \hbar}{4\pi r^3} \sqrt{\frac{24\pi}{5}} Y_2^0$$

- Because of the orthogonality of $Y_l^m$ s, all of the terms but one are zero:

$$G(\tau) = \frac{3\mu_0^2 \gamma^4 \hbar^2}{40\pi^2 r^6} e^{-6D_r \tau} \left| \langle Y_2^0^* | Y_2^0 \rangle \right|^2 = \frac{3\mu_0^2 \gamma^4 \hbar^2}{40\pi^2 r^6} e^{-\tau/\tau_c}$$

where $\tau_c = \frac{1}{6D_r}$ and $D_r = \frac{kT}{8\pi a^3 \eta}$ Stokes-Einstein equation for nearly spherical molecules:

- $a =$ radius, $\eta =$ viscosity

A simple decaying exponential!
The Spectral Density Function

• Hence, the correlation function is typically taken to be of the form:

\[ G(\tau) = \langle \Delta B(t) \Delta B(t + \tau) \rangle = G(0)e^{-\tau/\tau_c} \]

  - stationary with exponential decay
  - a molecule’s “memory” of its orientation decays exponentially in time.
  - virtually all correlation functions in NMR are exponential.

• The corresponding power spectrum is:

\[ S(\omega) = \int_{-\infty}^{\infty} G(\tau)e^{-i\omega\tau} \, d\tau \]

From which we’ll define the spectral density function:

\[ J(\omega) \equiv \frac{1}{2} \int_{-\infty}^{\infty} e^{-|\tau|/\tau_c} e^{-i\omega\tau} \, d\tau = \frac{\tau_c}{1 + \omega^2 \tau_c^2} \]

Note, we’ll address the \( G(0) \) term later.
Typical Correlation Times

- For nearly spherical molecules, the Stokes-Einstein relation yields...

\[ \tau_c = \frac{1}{6D_r} = \frac{4\pi \eta a^3}{3kT} \]

liquids: \( \tau_c \approx 10^{-12} - 10^{-10} \text{ s} \)

solids: \( \tau_c \approx 10^{-8} - 10^{-6} \text{ s} \)

<table>
<thead>
<tr>
<th>Tissue or compound</th>
<th>Rotational Correlation time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water: cerebral spinal fluid (CSF)</td>
<td>( \sim 10^{-11} \text{ s} )</td>
</tr>
<tr>
<td>Water: muscle</td>
<td>( \sim 10^{-9} \text{ s} )</td>
</tr>
<tr>
<td>Water: bone</td>
<td>( \sim 10^{-7} \text{ s} )</td>
</tr>
<tr>
<td>Albumin (representative protein)</td>
<td>( \sim 3 \times 10^{-8} \text{ s} )</td>
</tr>
<tr>
<td>Gd-DTPA</td>
<td>( \sim 6 \times 10^{-11} \text{ s} )</td>
</tr>
<tr>
<td>Water: ice at -2° C</td>
<td>( \sim 10^{-6} \text{ s} )</td>
</tr>
</tbody>
</table>
Random Fields

• While dipolar coupling is the most important source of in vivo relaxation, it is not the simplest to analyze.

• The random magnetic fields, $\Delta B(t)$, seen by two dipolar coupled nuclei are clearly not independent, but rather correlated.

• For now, we’ll ignore this complication (to be revisited next lecture) and assume each nuclei sees an independent, time-varying random field $\Delta B(t)$ with corresponding spectral density:

$$J(\omega) = \frac{\tau_c}{1 + \omega^2 \tau_c^2}$$

Indicates energy from the lattice at frequency $\omega$. 
T<sub>1</sub>: Spin-Lattice Relaxation

- Assume an isotropic randomly fluctuating magnetic field given by

\[
\Delta \vec{B}(t) = B_x(t)\hat{x} + B_y(t)\hat{y} + B_z(t)\hat{z}
\]

where \( \langle B_x^2 \rangle = \langle B_y^2 \rangle = \langle B_z^2 \rangle = \langle B^2 \rangle \)

- The relaxation of \( M_z \) can then be shown to be (we’ll derive later):

\[
\frac{1}{T_1} = \gamma^2 \left( \langle B_x^2 \rangle + \langle B_y^2 \rangle \right) J(\omega_0) = 2\gamma^2 \langle B^2 \rangle \frac{\tau_c}{1 + \omega_0^2 \tau_c^2}
\]

\[
\text{power of the interaction} \quad \text{fraction of the energy at } \omega = \omega_0
\]

- The word “lattice” is a solid-state term, short for “crystal lattice”. We still call \( T_1 \) the “spin-lattice relaxation time” even though in vivo there is no actual crystal.
Key Features of $T_1$ Relaxation

\[
\frac{1}{T_1} = \gamma^2 \left( \langle B_x^2 \rangle + \langle B_y^2 \rangle \right) J(\omega_0) = 2\gamma^2 \left\langle B^2 \right\rangle \frac{\tau_c}{1 + \omega_0^2 \tau_c^2}
\]

- Changes in $M_z$ induced by spin transitions between energy states
- Requires energy exchange between spin system and the lattice.
- As a resonant system, energy exchange occurs at $\hbar \omega_0$
- Hence, $T_1$ relaxation and Rf excitation are much the same process
  - Transverse magnetic fields at $\omega_0$ are needed to induce transitions
  - Rf excitation: we provide a coherent rotating $B_1$ field
  - $T_1$ relaxation: lattice provides the $B_1$ field
T₂: Spin-Spin Relaxation

- The referring to T₂ as the “spin-spin relaxation time” is somewhat misleading as relaxation can actually occur without any spin-spin interactions.

- T₂ relaxation concerns loss of transverse coherences: \( \langle \hat{I}_x \rangle \) and \( \langle \hat{I}_y \rangle \)

- Changes in \( \langle \hat{I}_x \rangle \) and \( \langle \hat{I}_y \rangle \) do not require energy transfer

- Fields in the z direction cause dephasing, and the slower the fluctuations, the more efficient this relaxation mechanism.

\[
\frac{1}{T'_2} = \gamma^2 \left\langle B_z^2 \right\rangle J(0)
\]
T₂: Spin-Spin Relaxation

- Spin transitions also cause loss of transverse phase coherence and hence are a second factor in T₂ relaxation.

\[
\frac{1}{T_2} = \frac{1}{2T_1} + \frac{1}{T'_2}
\]

Note, technically 2T₁ > T₂, rather than the usually quoted T₁ > T₂.

\[
\frac{1}{T_2} = \gamma^2 \langle B_z^2 \rangle J(0) + \frac{\gamma^2}{2} \langle B_x^2 + B_y^2 \rangle J(\omega_0)
\]

- Full expression…

\[
\frac{1}{T_2} = \gamma^2 \langle B^2 \rangle (J(0) + J(\omega_0)) = \gamma^2 \langle B^2 \rangle \left( \tau_c + \frac{\tau_c}{1 + \omega_0^2 \tau_c^2} \right)
\]

probes the spectral density at 0 and ω₀.
The Spectral Density Function

\[ J(\omega) = \begin{cases} 10^2 & \tau_c = 5 \times 10^{-7} \text{ s} \\ 10^0 & \tau_c = 5 \times 10^{-9} \text{ s} \\ 10^{-2} & \tau_c = 5 \times 10^{-11} \text{ s} \end{cases} \]

- solid (Bone)
- in between (Muscle)
- liquid (CSF)

frequency (Hz)

\[ 10^0 \quad 10^2 \quad 10^4 \quad 10^6 \quad 10^8 \quad 10^{10} \quad 10^{12} \]

\[ 3T \]
Relaxation Rates vs $\tau_c$

![Diagram showing relaxation rates vs $\tau_c$.](image)

- **CSF**, **Muscle**, and **Bone** regions are indicated.
- The graph compares $T_1$ and $T_2$ relaxation times as a function of $\tau_c$.
- The relationship between $T_1$, $T_2$, and $\tau_c$ is given by:
  \[
  \frac{1}{T_1} = \frac{1}{T_2} + \frac{4}{r^6} \tau_c
  \]
- For extreme narrowing, $\omega_0 \tau_c \ll 1$.
- The minima of $T_1$ occur when $\omega_0 \tau_c = 1$.
- The graph includes lines for 100 MHz and 400 MHz.
Relaxation Rates vs $B_0$

- $T_1$ (s)
- $T_2$ (s)

- $\tau_c=10^{-11}$ s → free water
- $\tau_c=10^{-9}$ s → viscous liquid
- $\tau_c=10^{-7}$ s → solid
Summary

- Lattice provides random time-varying magnetic fields.
  - x-y components cause transitions  \( \Rightarrow \) \( T_1 \) relaxation (also \( T_2 \))
  - z component causes dephasing  \( \Rightarrow \) \( T_2 \) relaxation

- From our simple model of uncorrelated, random \( \Delta B(t) \) ...
  \[
  \frac{1}{T_1} = 2\gamma^2 \langle B^2 \rangle J(\omega_0) \quad \frac{1}{T_2} = \gamma^2 \langle B^2 \rangle (J(0) + J(\omega_0))
  \]

- \( T_1 \) relaxation depends on transverse fields having energy at the Larmor frequency.

- \( T_2 \) relaxation depends on both \( J(0) \) and \( J(\omega_0) \).

- Helps explain relaxation rates versus \( B_0 \) and some observed tissues relaxation behavior.
Next Lecture: Relaxation through dipolar coupling