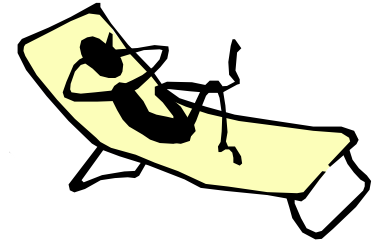


Lecture #3

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

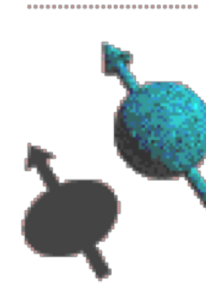
- Relaxation is the process by which the phase coherence among spins returns to its equilibrium value (as given by the Boltzmann distribution).
- Restoration of longitudinal magnetization, $M_z = \gamma\hbar\overline{\langle\hat{I}_z\rangle}$, is characterized by a time constant, T_1 .
- Disappearance of transverse magnetization, $M_{xy} = \gamma\hbar\left(\overline{\langle\hat{I}_x\rangle} + i\overline{\langle\hat{I}_y\rangle}\right)$, is characterized by a time constant, T_2 .

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



- We'll first look at some simple relaxation models to build intuition.

Nuclear Spins



Precession
frequency
 $\omega = \gamma B$

- 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 w/ 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



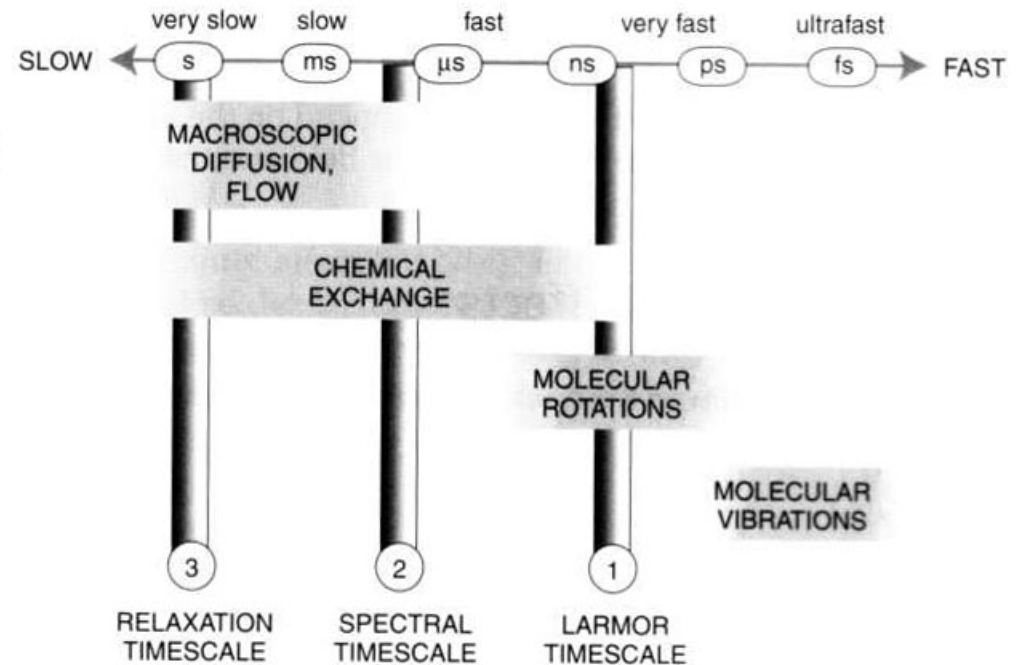
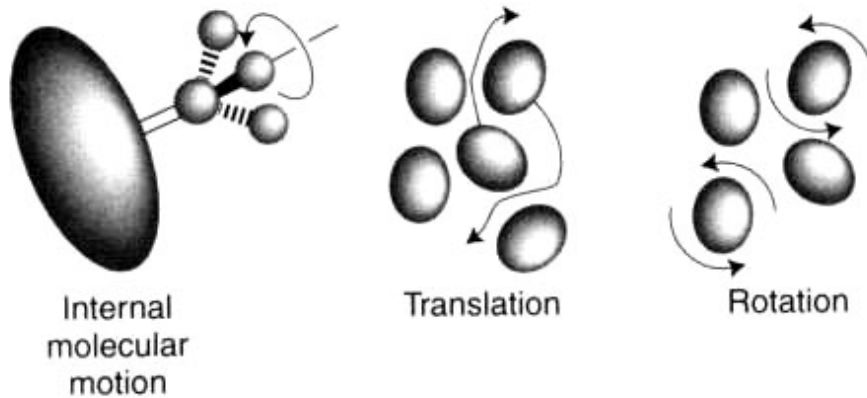
$$\text{Hamiltonian: } \hat{H} = -\hat{\mu} \cdot \vec{B} \quad \text{Magnetic moment: } \hat{\mu} = \gamma \hbar \hat{I}$$

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

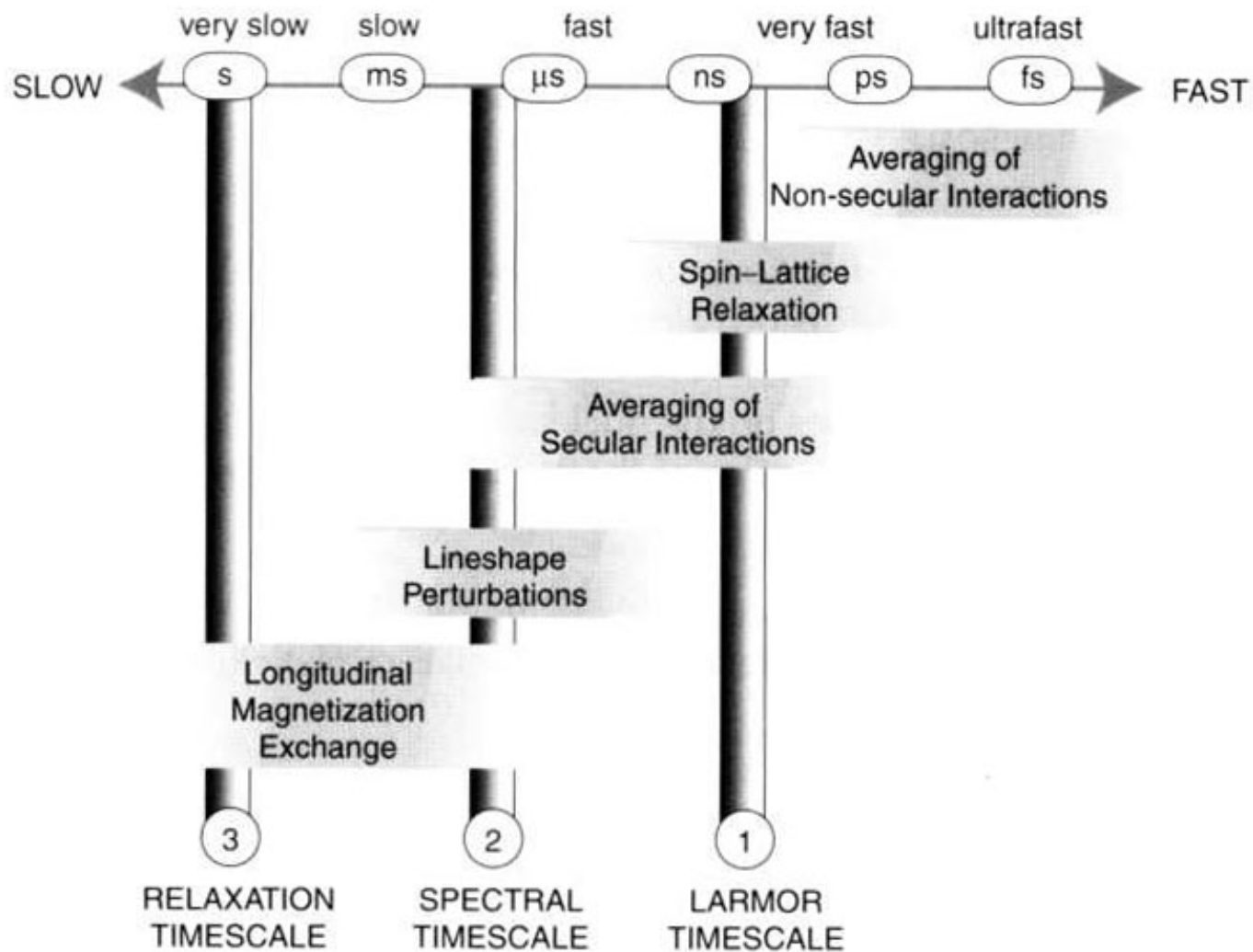
Molecular Motion

- 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

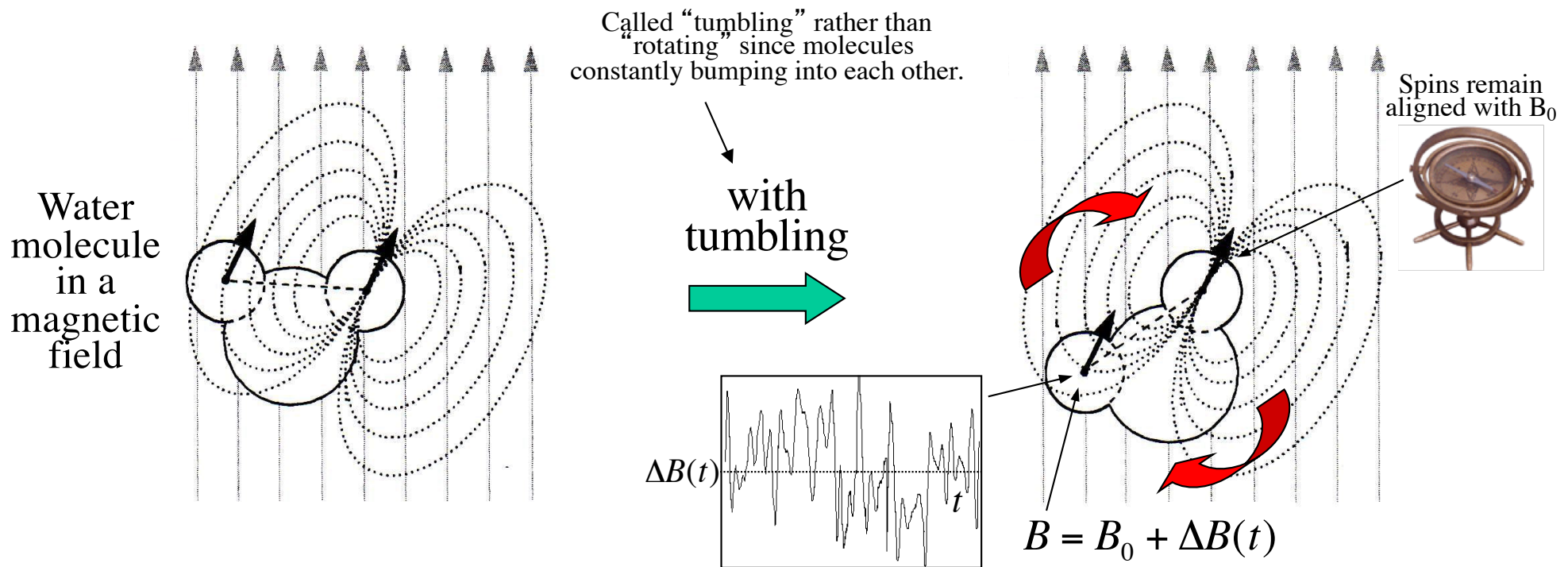


NMR Effects of Molecular Motion



In Vivo Magnetic Fields

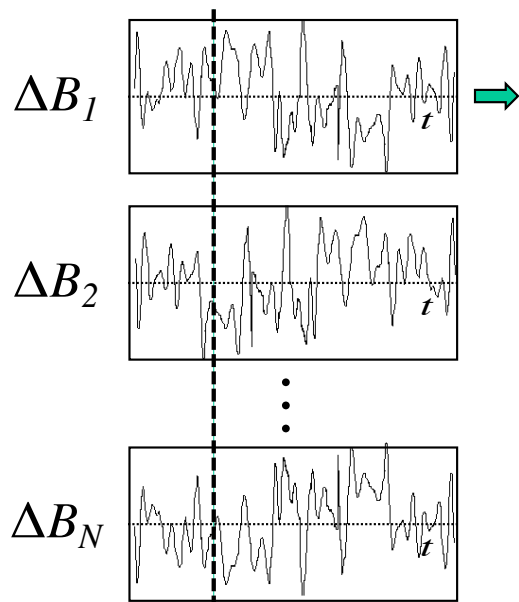
- One source of magnetic field variations is due to dipolar coupling and molecular tumbling.



- 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 $i=1, \dots, N$. Let $\Delta B_i(t)$ be the time varying field seen by the i^{th} spin.



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

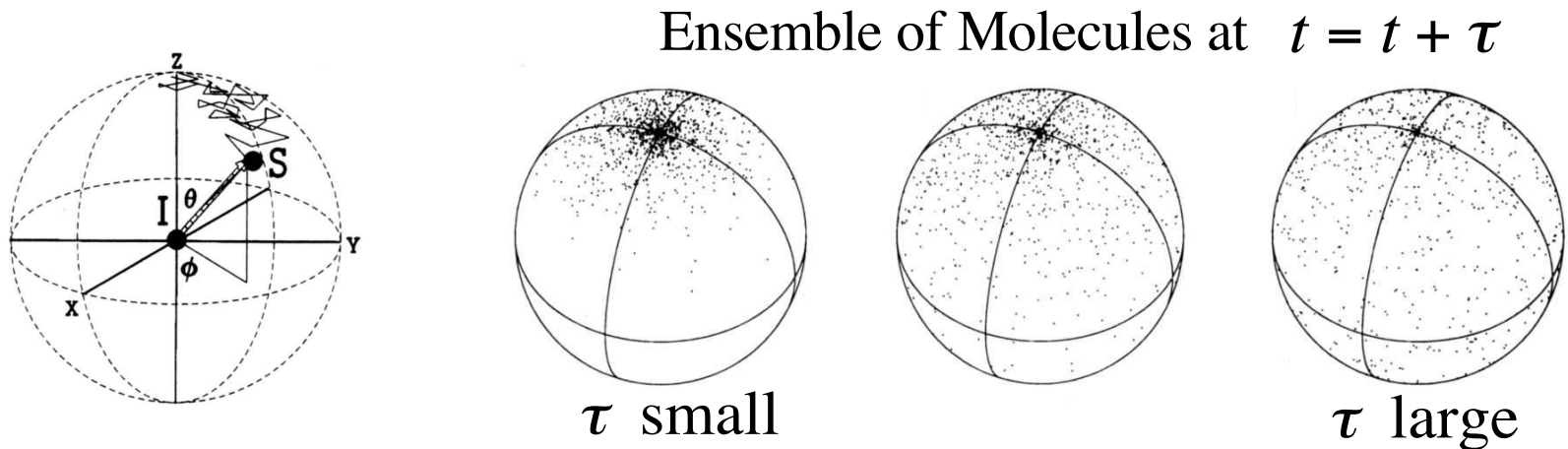
$$S(\omega) = \int_{-\infty}^{\infty} G(\tau) e^{-i\omega\tau} d\tau \quad \text{Wiener-Khinchin Theorem}$$

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 .

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

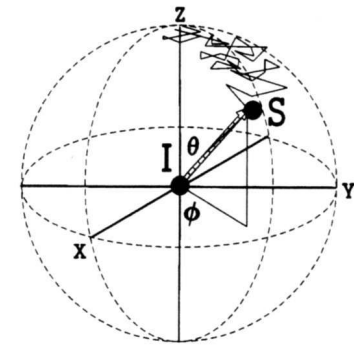
Molecular Tumbling

- 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.



- $\tau_c = \text{rotational correlation time} = \text{average time for a molecule to rotate over one radian, a measure of rotational coherence.}$
- 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.

$G(\tau)$ for a simple case



- Are exponential correlation functions a good fit for in vivo NMR?

$$G(\tau) = \langle \Delta B(t) \Delta B(t + \tau) \rangle \stackrel{?}{=} G(0) e^{-|\tau|/\tau_c}$$

Let's find out...

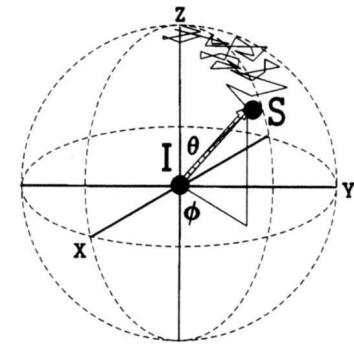
- For the case of a (nearly) spherical molecule undergoing isotropic tumbling, let $\Delta B(t) = F(\Omega)$, where for convenience Ω is a single angle variable representing $(\theta(t), \phi(t))$.

$$G(\tau) = \langle F(t) F^*(t + \tau) \rangle = \frac{1}{4\pi} \int_{\Omega} \int_{\Omega_0} F(\Omega_0) F^*(\Omega) P(\Omega_0 | \Omega, \tau) d\Omega_0 d\Omega$$

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

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

Fick's law of diffusion



- Fick's second law

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

Diffusion constant
Laplacian

- 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

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

Rotational diffusion constant
Fick's law for rotational diffusion.
Legendre operator (Laplacian with fixed r)

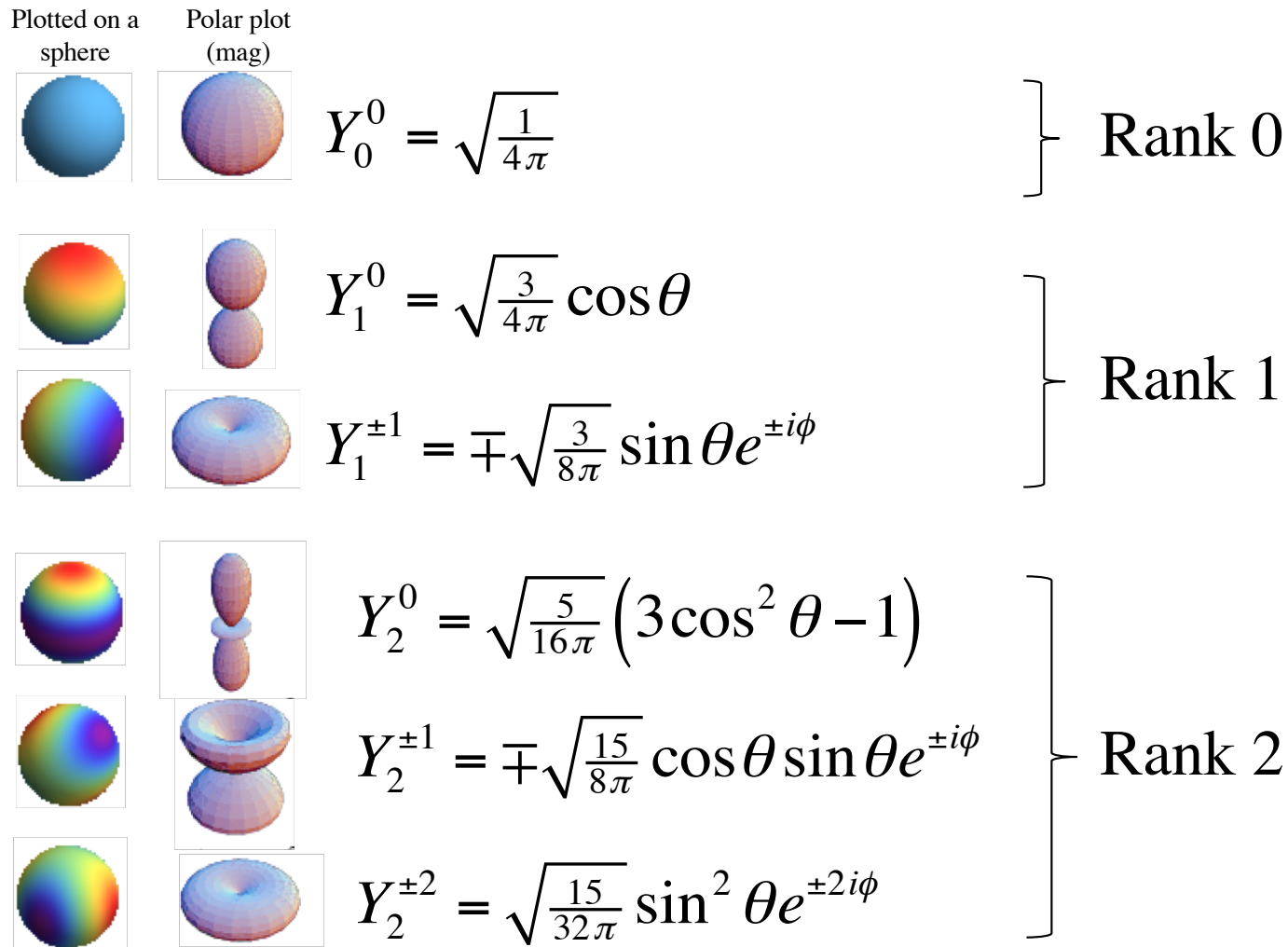
$G(\tau)$ for a simple case (cont.)

- The spherical harmonics, Y_l^m , are eigenfunctions of Δ_r , and form a complete orthonormal basis set, and the solution for Fick's law of rotational diffusion can be written as:

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

- Spherical harmonics: $Y_l^m(\theta, \phi)$
 - orthonormal over the surface of a sphere.
 - arise in multiple physical applications, e.g. atomic orbitals

The first few spherical harmonics



$G(\tau)$ for a simple case (cont.)

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

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

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

$$Y_l^m \text{ s are orthonormal: } \langle Y_l^m | Y_{l'}^{m'} \rangle = \begin{cases} 1 & \text{for } l = l' \text{ and } m = m' \\ 0 & \text{for } l \neq l' \text{ or } m \neq m' \end{cases}$$

$G(\tau)$ for a simple case (cont.)

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

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

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

A simple decaying exponential!

↓

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

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, η = viscosity

The Spectral Density Function

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

$$G(\tau) = \langle \Delta B(t) \Delta B(t + \tau) \rangle = G(0) e^{-\tau/\tau_c} \quad \leftarrow \text{stationary with exponential decay}$$

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

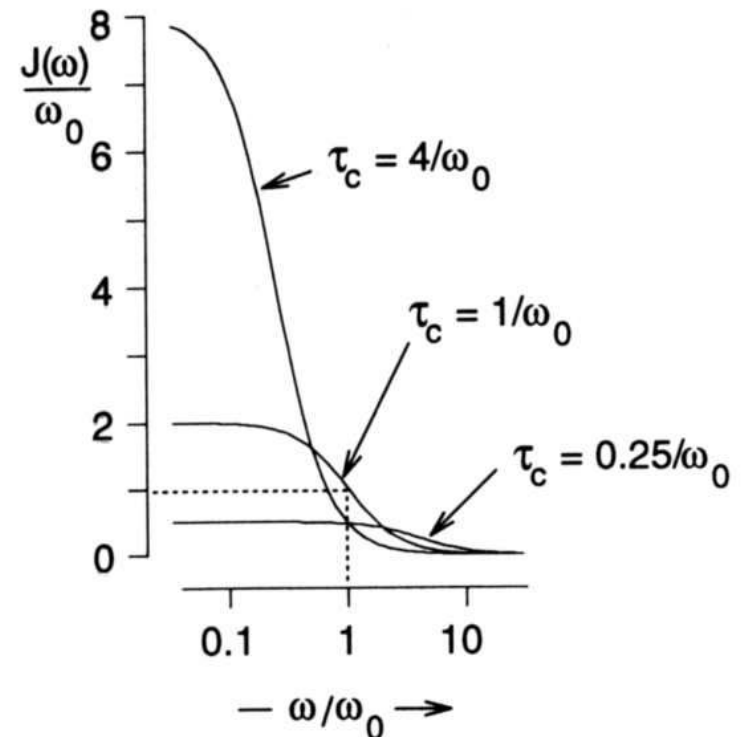
- The corresponding power spectrum is:

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

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.

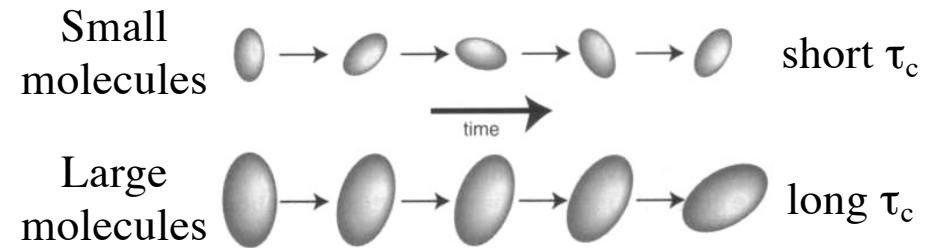


Typical Correlation Times

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

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

solvent viscosity
molecular radius



liquids: $\tau_c \approx 10^{-12} - 10^{-10}$ s

solids: $\tau_c \approx 10^{-8} - 10^{-6}$ s

Tissue or compound	Rotational Correlation time
Water: cerebral spinal fluid (CSF)	$\sim 10^{-11}$ s
Water: muscle	$\sim 10^{-9}$ s
Water: bone	$\sim 10^{-7}$ s
Albumin (representative protein)	$\sim 3 \times 10^{-8}$ s
Gd-DTPA	$\sim 6 \times 10^{-11}$ s
Water: ice at -2° C	$\sim 10^{-6}$ s

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 ω .

T_1 : Spin-Lattice Relaxation

- Assume an isotropic randomly fluctuating magnetic field given by

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

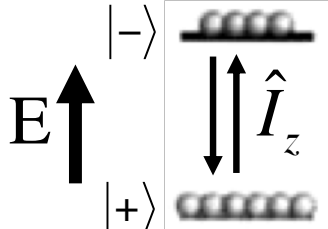
$$\text{where } \langle B_x^2 \rangle = \langle B_y^2 \rangle = \langle B_z^2 \rangle = \langle B^2 \rangle$$

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

$$\frac{1}{T_1} = \underbrace{\gamma^2 \left(\langle B_x^2 \rangle + \langle B_y^2 \rangle \right)}_{\text{power of the interaction}} \underbrace{J(\omega_0)}_{\text{fraction of the energy at } \omega=\omega_0} = 2\gamma^2 \langle B^2 \rangle \frac{\tau_c}{1 + \omega_0^2 \tau_c^2}$$

- 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

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


The diagram shows two energy levels, $|+\rangle$ (lower) and $|-\rangle$ (higher). An upward arrow labeled E indicates the energy difference between the states. A vertical double-headed arrow labeled \hat{I}_z indicates the spin operator along the z-axis.

- 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 ω_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

T_2 : Spin-Spin Relaxation

- The referring to T_2 as the “spin-spin relaxation time” is somewhat misleading as relaxation can actually occur without any spin-spin interactions.
- T_2 relaxation concerns loss of transverse coherences: $\overline{\langle \hat{I}_x \rangle}$ and $\overline{\langle \hat{I}_y \rangle}$
- Changes in $\overline{\langle \hat{I}_x \rangle}$ and $\overline{\langle \hat{I}_y \rangle}$ do not require energy transfer
- Fields in the z direction cause dephasing, and the slower the fluctuations, the more efficient this relaxation mechanism.

$$\frac{1}{T_2'} = \gamma^2 \langle B_z^2 \rangle J(0)$$

T₂: Spin-Spin Relaxation

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

$$\frac{1}{T_2} = \frac{1}{2T_1} + \frac{1}{T_2'} \quad \rightarrow \quad \text{Note, technically } 2T_1 > T_2, \text{ rather than the usually quoted } T_1 > T_2$$

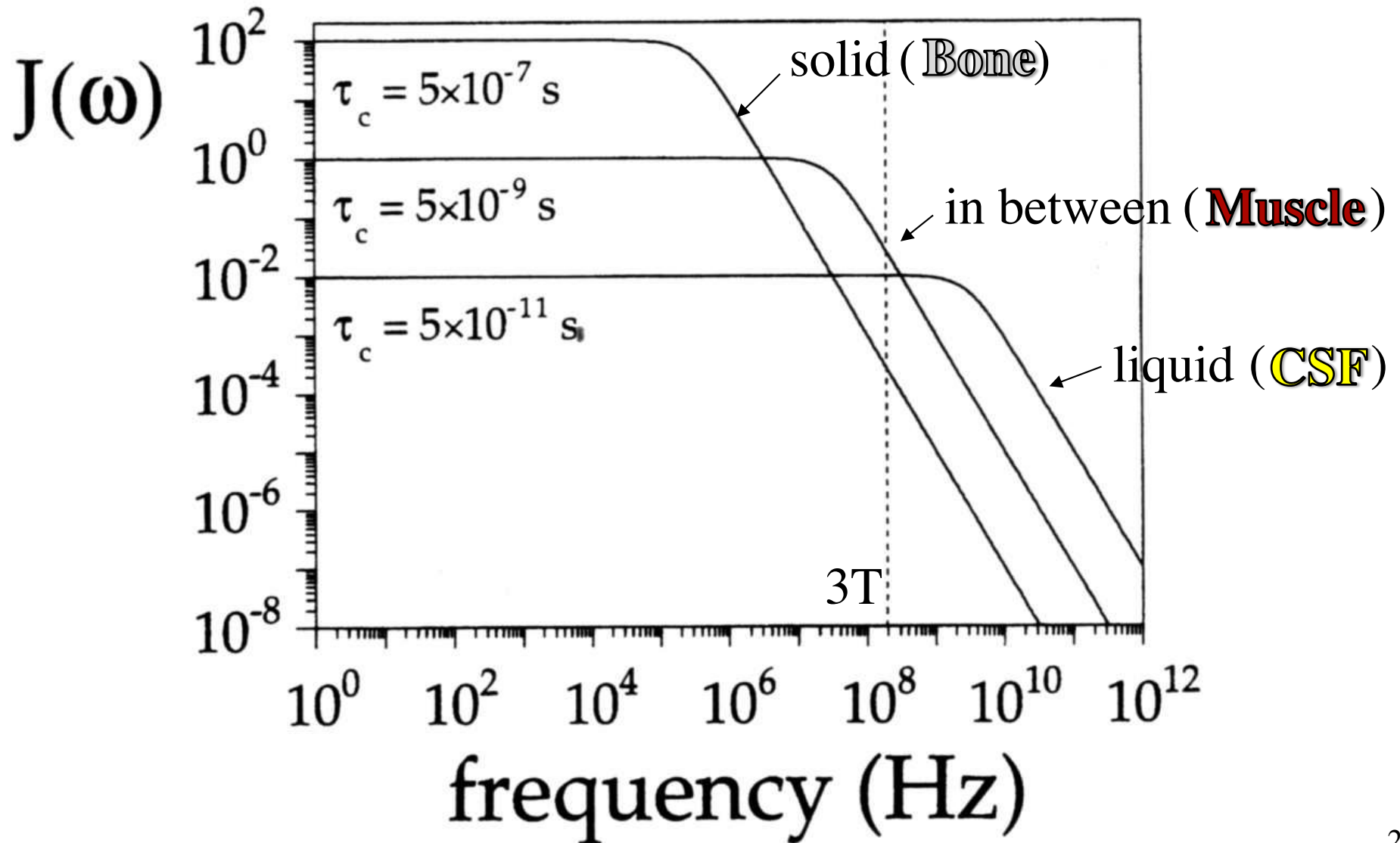
$$\frac{1}{T_2} = \gamma^2 \langle B_z^2 \rangle J(0) + \frac{\gamma^2}{2} \langle B_x^2 + B_y^2 \rangle J(\omega_0)$$

- Full expression...

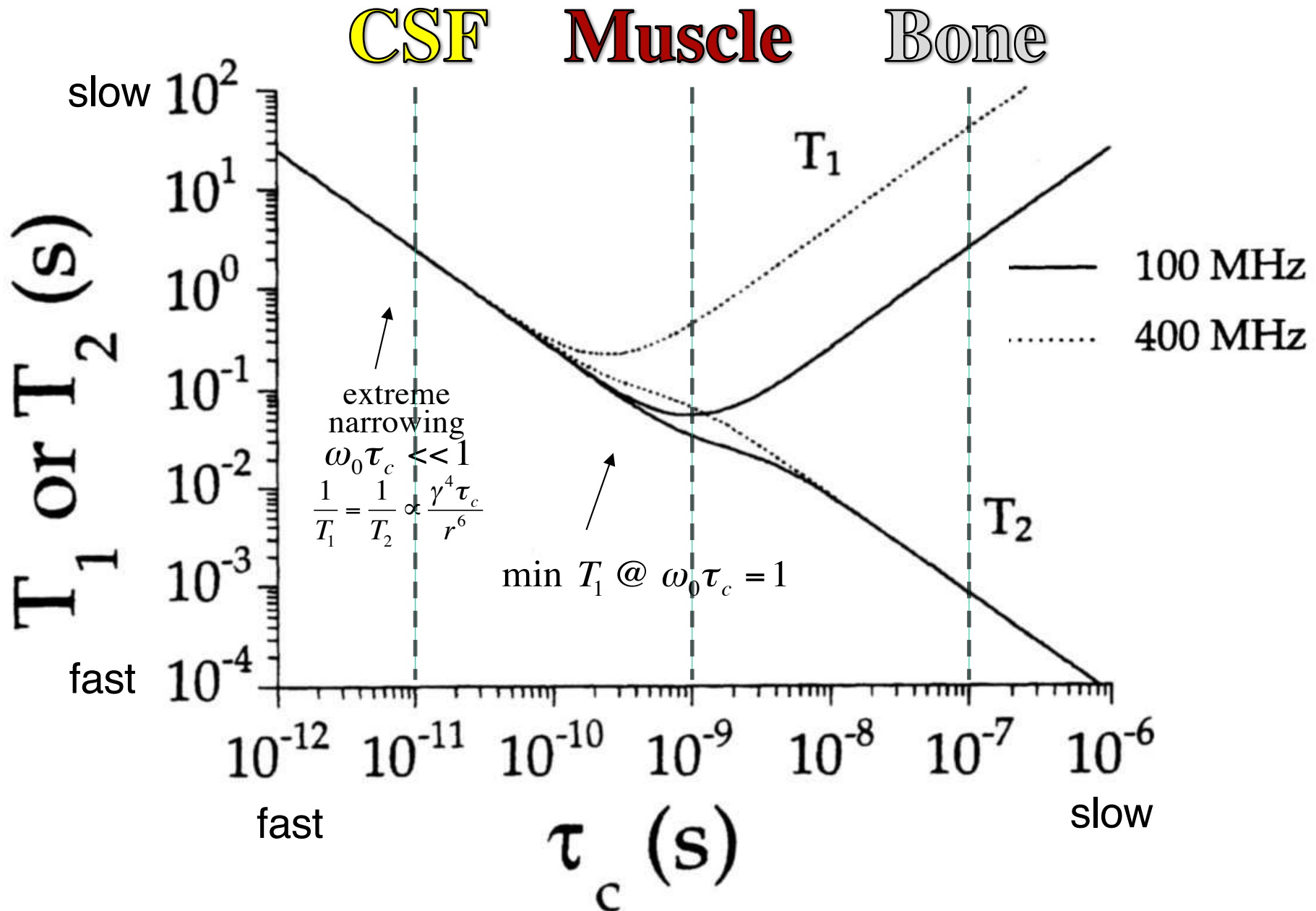
$$\frac{1}{T_2} = \gamma^2 \langle B^2 \rangle (J(0) + J(\omega_0)) = \gamma^2 \langle B^2 \rangle \left(\tau_c + \frac{\tau_c}{1 + \omega_0^2 \tau_c^2} \right)$$

↑ probes the spectral density at 0 and ω_0

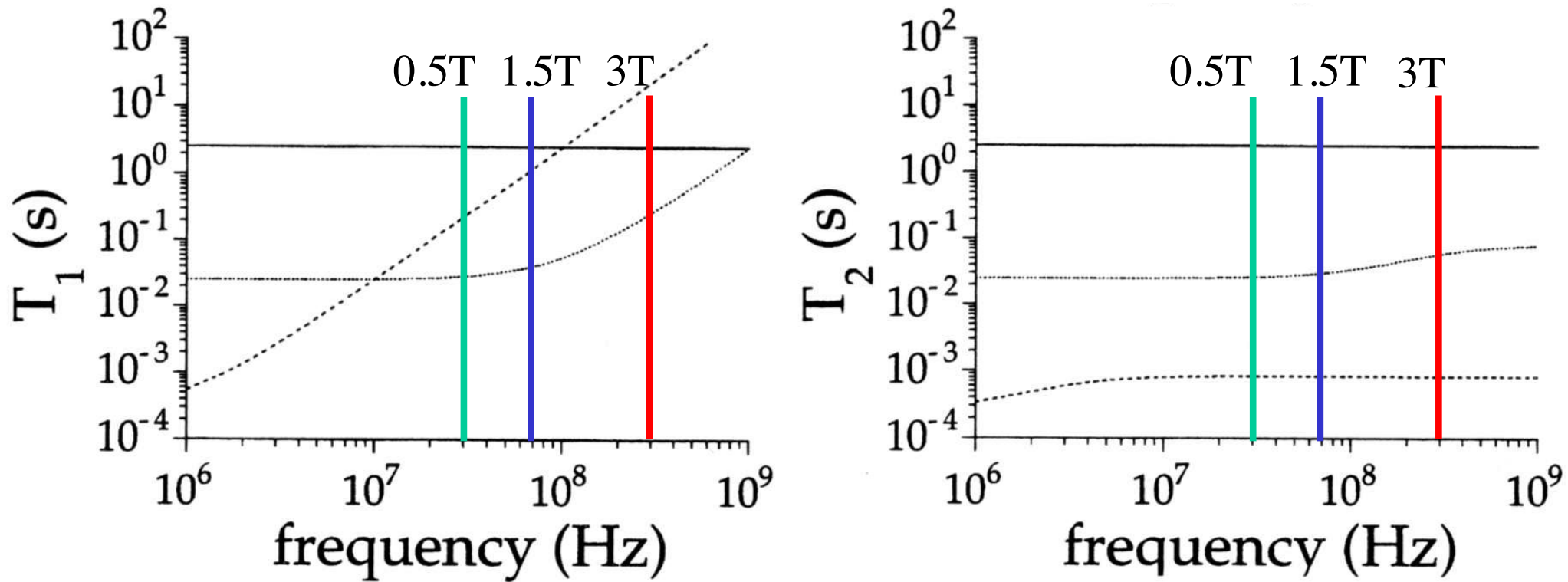
The Spectral Density Function



Relaxation Rates vs τ_c



Relaxation Rates vs B_0



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

Summary

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