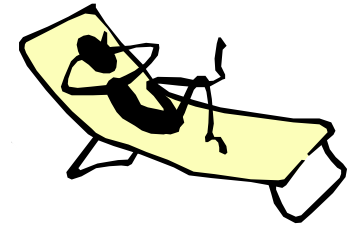# Lecture #4
Basics of Relaxation

- 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, $M_z = \gamma \hbar \overline{\left\langle \hat{I}_z \right\rangle}$, is characterized by a time constant, T_1.

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

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

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

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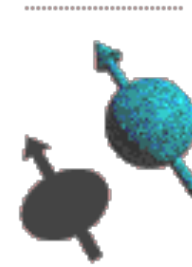
- A spin in a magnetic field simply undergoes Larmor precession.

- 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 ½ nuclei. (spins > ½ 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
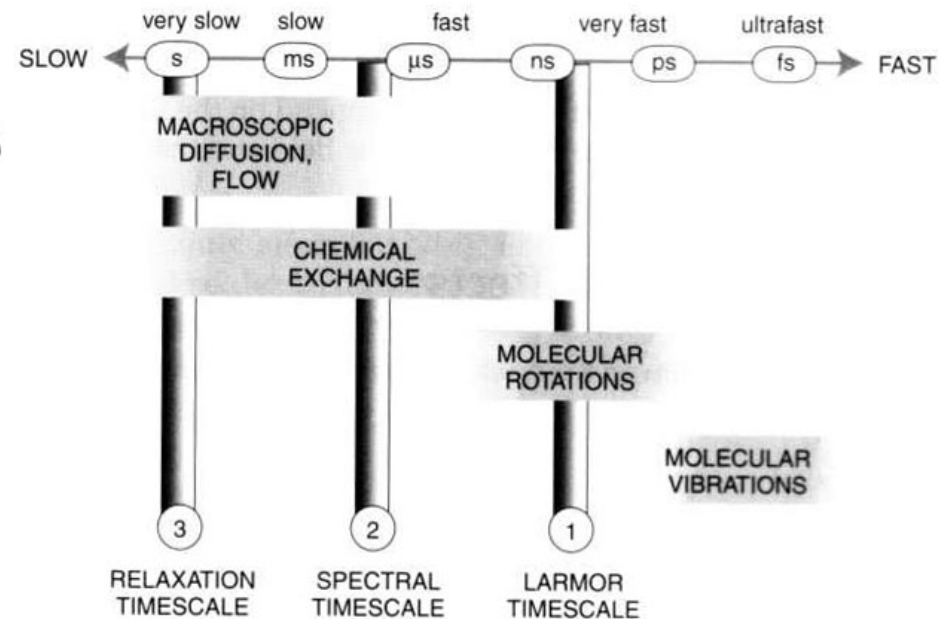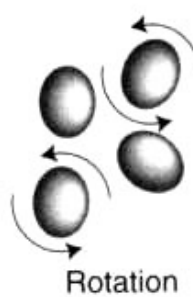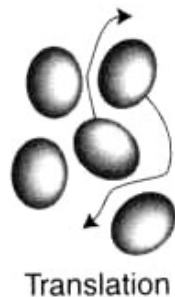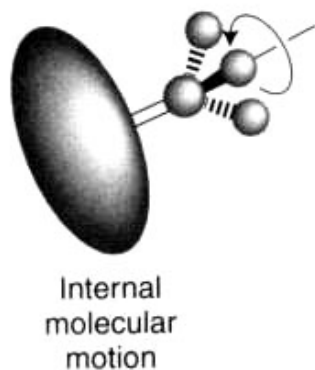
Hamiltonian: $\hat{H} = -\hat{\vec{\mu}} \cdot \vec{B}$ Magnetic moment: $\hat{\mu} = \gamma \hbar \hat{I}$

> 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

Internal molecular motion

Translation

Rotation

very slow   slow   fast   very fast   ultrafast

SLOW ← s   ms   µs   ns   ps   fs → FAST

MACROSCOPIC DIFFUSION, FLOW

CHEMICAL EXCHANGE

MOLECULAR ROTATIONS

MOLECULAR VIBRATIONS

3 RELAXATION TIMESCALE

2 SPECTRAL TIMESCALE

1 LARMOR TIMESCALE

NMR Effects of Molecular Motion
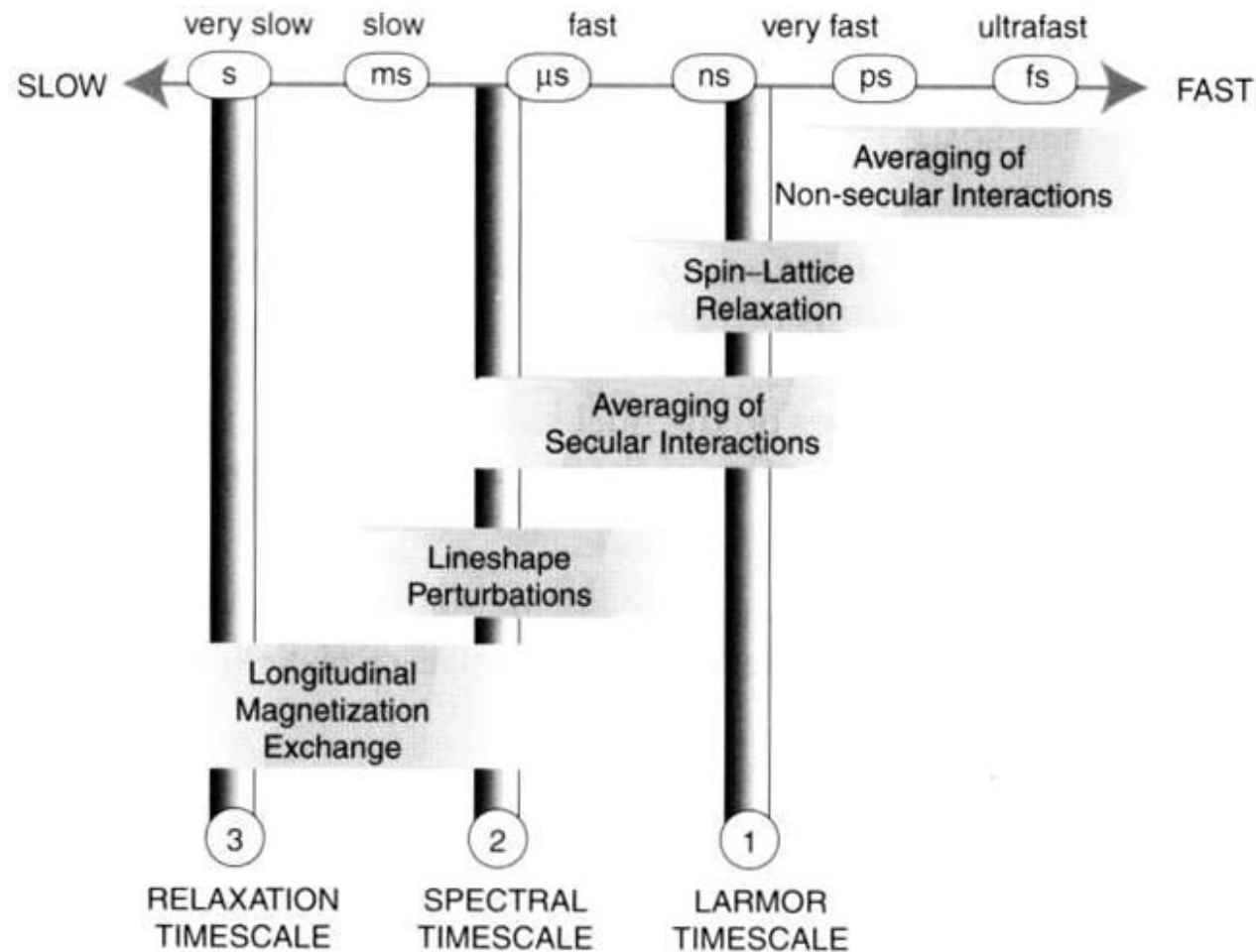
In Vivo Magnetic Fields

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

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

Water molecule in a magnetic field

with tumbling

Spins remain aligned with B_0

$\Delta B(t)$

t

$B = B_0 + \Delta B(t)$
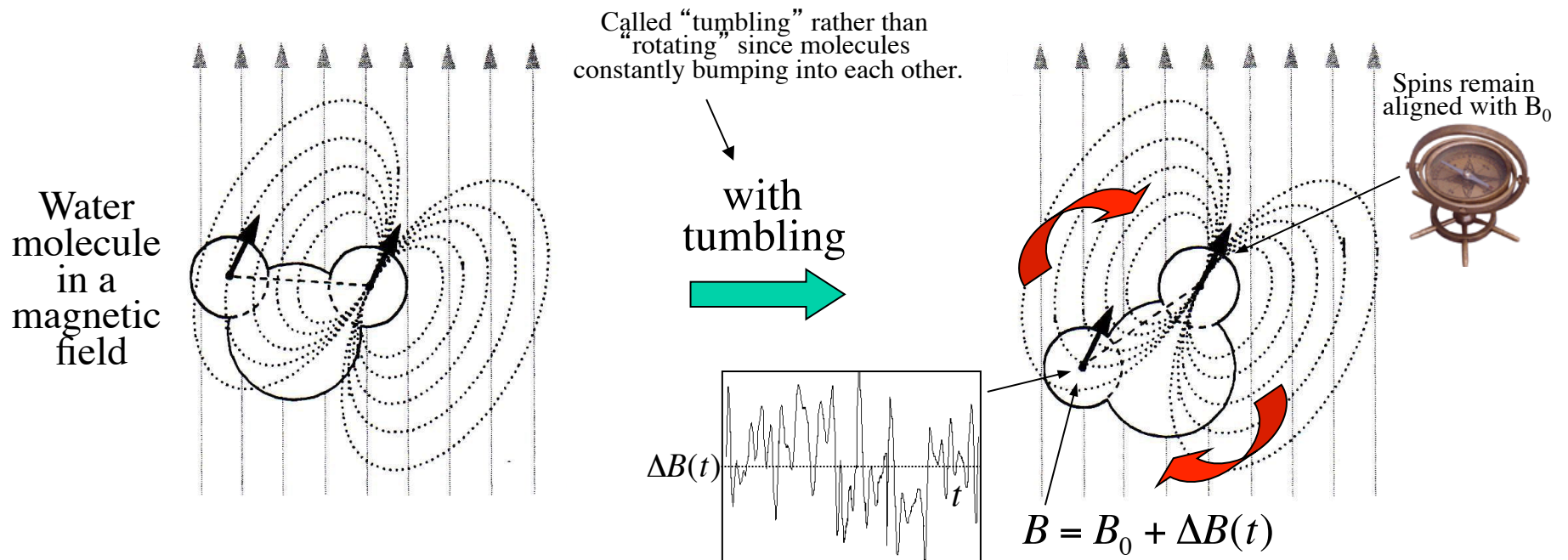
- While $\langle \Delta B(t) \rangle = 0$, the instantaneous effect is *not* negligible.

- 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 $i=1,\ldots N$. Let $\Delta B_i(t)$ be the time varying field seen by the ith spin.

ΔB_1

ΔB_2

$\vdots$

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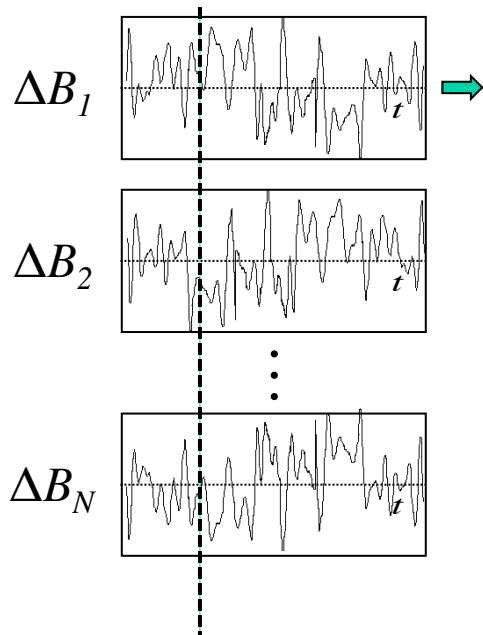
- $\Delta B_i(t)$ is a random function of time. Process is *ergodic* if time averages equal averages of i: e.g. $\left\langle \Delta B_i^2(t_0) \right\rangle_i = \left\langle \Delta B_i^2(t) \right\rangle_t = \left\langle B^2 \right\rangle$

- One function we care about is the *statistical correlation* between $\Delta B_i(t)$ and $\Delta B_i(t+\tau)$, $G_i(t,\tau) = \left\langle \Delta B_i(t)\Delta B_i(t+\tau) \right\rangle$. 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 $G(\tau)$.

$$S(\omega) = \int_0^{\infty} G(\tau)e^{-i\omega\tau}\,d\tau = \lim_{T\to\infty}\frac{1}{T}\int_0^{T} G(\tau)e^{-i\omega\tau}\,d\tau$$

Wiener-Khinchin Theorem

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

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

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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.

Ensemble of Molecules at $t = t + \tau$

τ small τ large
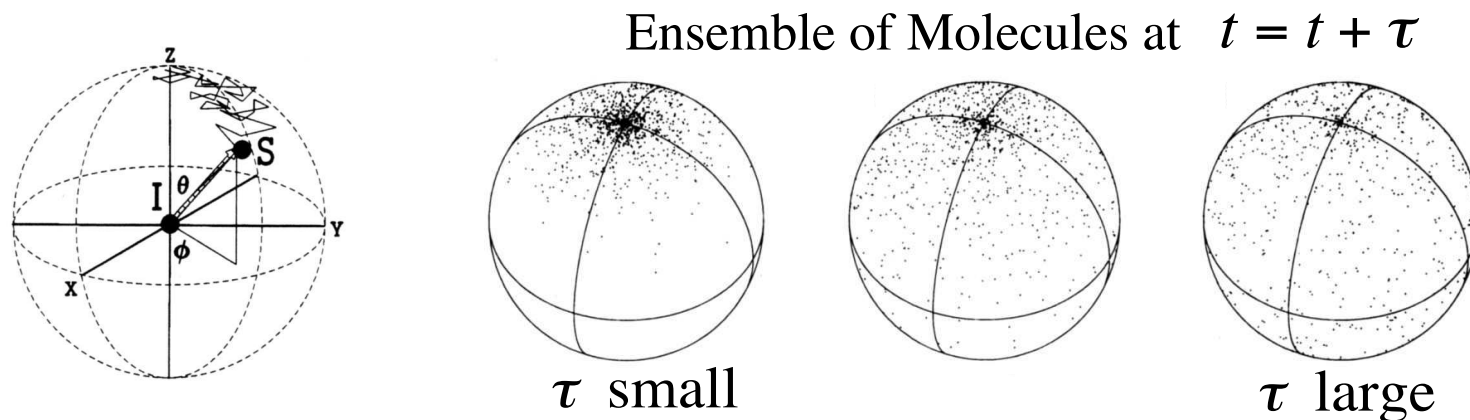
- τ_c = *rotational correlation time* = average time for a molecule to rotate over one radian, a measure of rotational coherence.

- 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 of exponentially.

$G(\tau)$ for a simple case
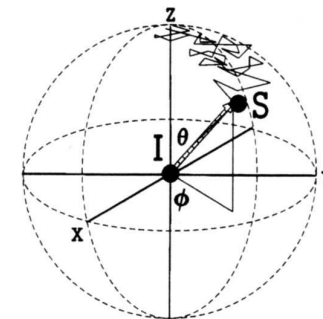
- Are exponential correlation functions a good fit for in vivo NMR?

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

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 $(\theta(t),\phi(t))$.

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

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.

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Fick's law of diffusion
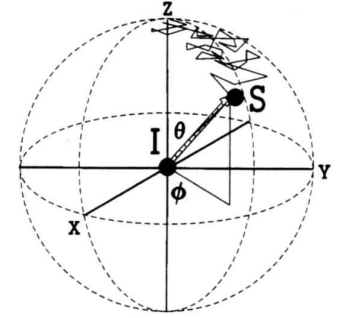
- Fick's second law

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

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

Rotational diffusion constant

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

Fick's law for rotational diffusion.

Legendre operator (Laplacian with fixed r)

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$G(\tau)$ 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:

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

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

The first few spherical harmonics

Plotted on a sphere   Polar plot (mag)

$$Y_0^0 = \sqrt{\tfrac{1}{4\pi}}$$

Rank 0

$$Y_1^0 = \sqrt{\tfrac{3}{4\pi}} \cos\theta$$

$$Y_1^{\pm 1} = \mp\sqrt{\tfrac{3}{8\pi}} \sin\theta\, e^{\pm i\phi}$$

Rank 1

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

$$Y_2^{\pm 1} = \mp\sqrt{\tfrac{15}{8\pi}} \cos\theta \sin\theta\, e^{\pm i\phi}$$

$$Y_2^{\pm 2} = \sqrt{\tfrac{15}{32\pi}} \sin^2\theta\, e^{\pm 2 i\phi}$$

Rank 2
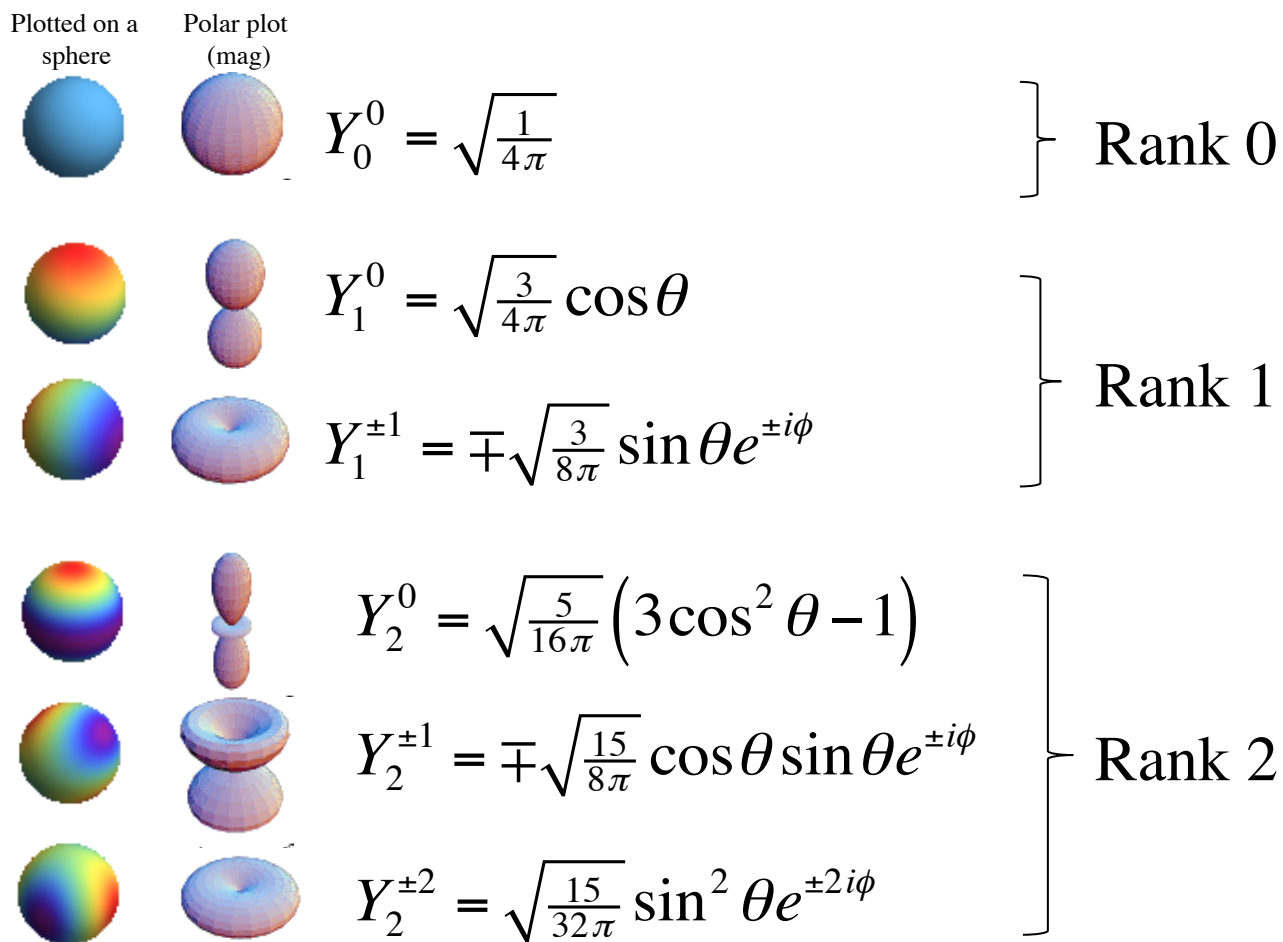
$G(\tau)$ for a simple case (cont.)

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

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

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

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

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

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

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

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

A simple decaying exponential!

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

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:

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

  – a molecule's "memory" of its orientation decays exponentially in time.

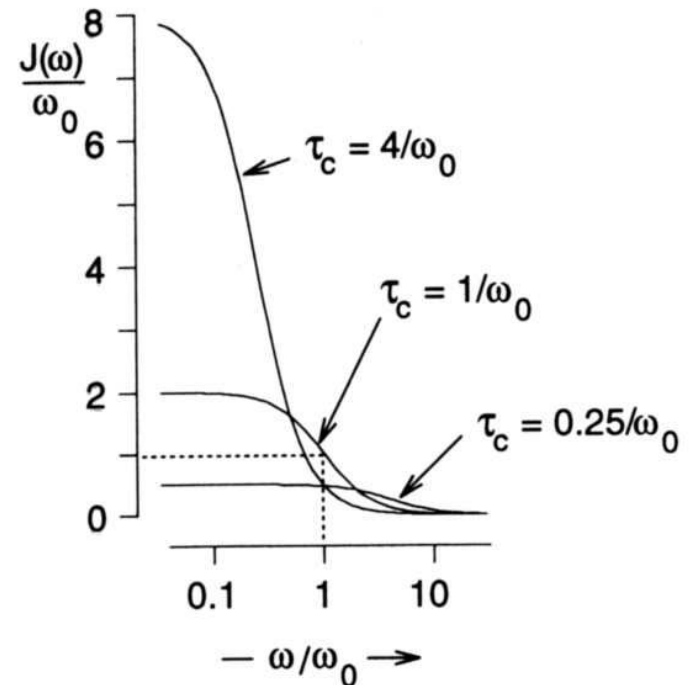 – virtually all correlation functions in NMR are exponential.

- The corresponding power spectrum is:

$$S(\omega) = \int_0^\infty G(\tau)e^{-i\omega\tau}\, d\tau$$

  From which we'll define the spectral density function:

$$J(\omega) \equiv \tfrac{1}{2}\int_{-\infty}^\infty e^{-|\tau|/\tau_c}e^{-i\omega\tau}\, d\tau = \frac{\tau_c}{1+\omega^2\tau_c^2}$$
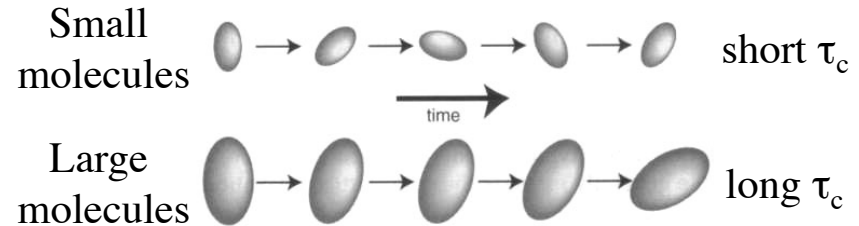
  Note, we'll address the $G(0)$ term later.

Typical Correlation Times

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

solvent viscosity

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

molecular radius

Small molecules → → → → short τ_c

time

Large molecules → → → → long τ_c

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)	~ 10^{-11} s
Water: muscle	~ 10^{-9} s
Water: bone	~ 10^{-7} s
Albumin (representative protein)	~ 3×10^{-8} s
Gd-DTPA	~ 6×10^{-11} s
Water: ice at -2° C	~ 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, ΔB(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 ΔB(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

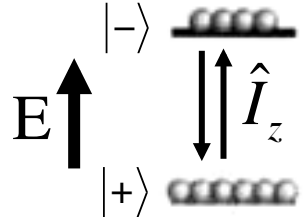$$\Delta \vec{B}(t) = B_x(t)\vec{x} + B_y(t)\vec{y} + B_z(t)\vec{z}$$

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

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

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

- 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

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

- 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.

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

T$_2$: Spin-Spin Relaxation

- Spin transitions also cause loss of transverse phase coherence and hence are a second factor in T$_2$ relaxation.

$$\frac{1}{T_2} = \frac{1}{2T_1} + \frac{1}{T_2'}$$

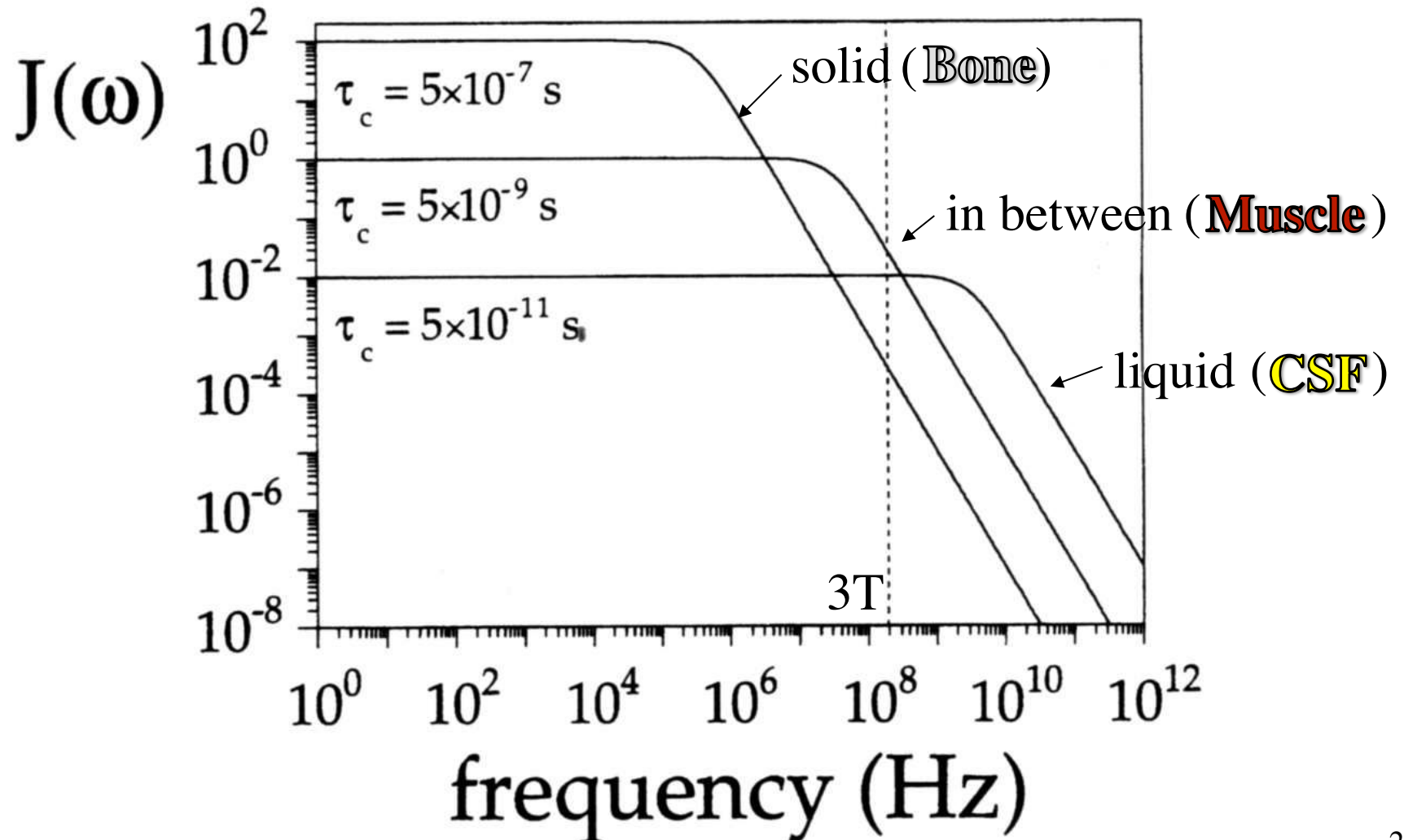➡ Note, technically 2T$_1$ > T$_2$, rather than the usually quoted T$_1$ > T$_2$

$$\frac{1}{T_2} = \gamma^2 \left\langle B_z^2 \right\rangle J(0) + \frac{\gamma^2}{2} \left\langle B_x^2 + B_y^2 \right\rangle J(\omega_0)$$
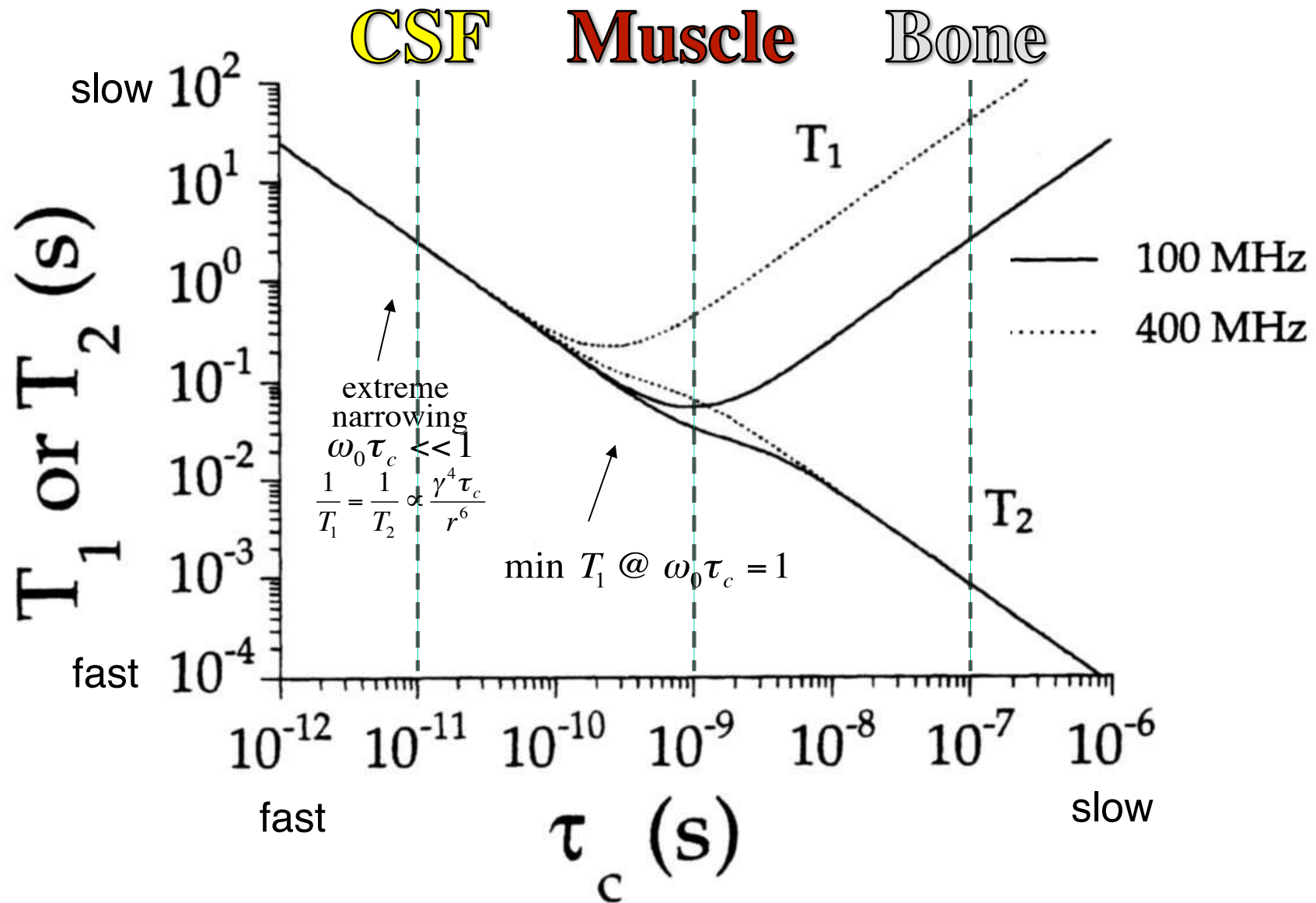
- Full expression…

$$\frac{1}{T_2} = \gamma^2 \left\langle B^2 \right\rangle \left(J(0) + J(\omega_0) \right) = \gamma^2 \left\langle B^2 \right\rangle \left(\tau_c + \frac{\tau_c}{1 + \omega_0^2 \tau_c^2} \right)$$
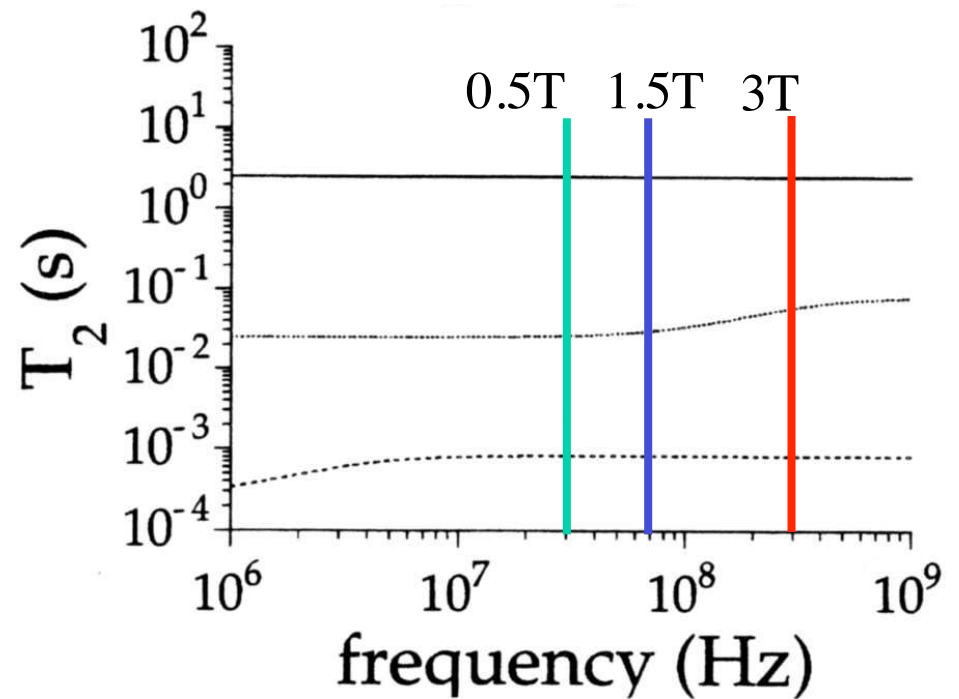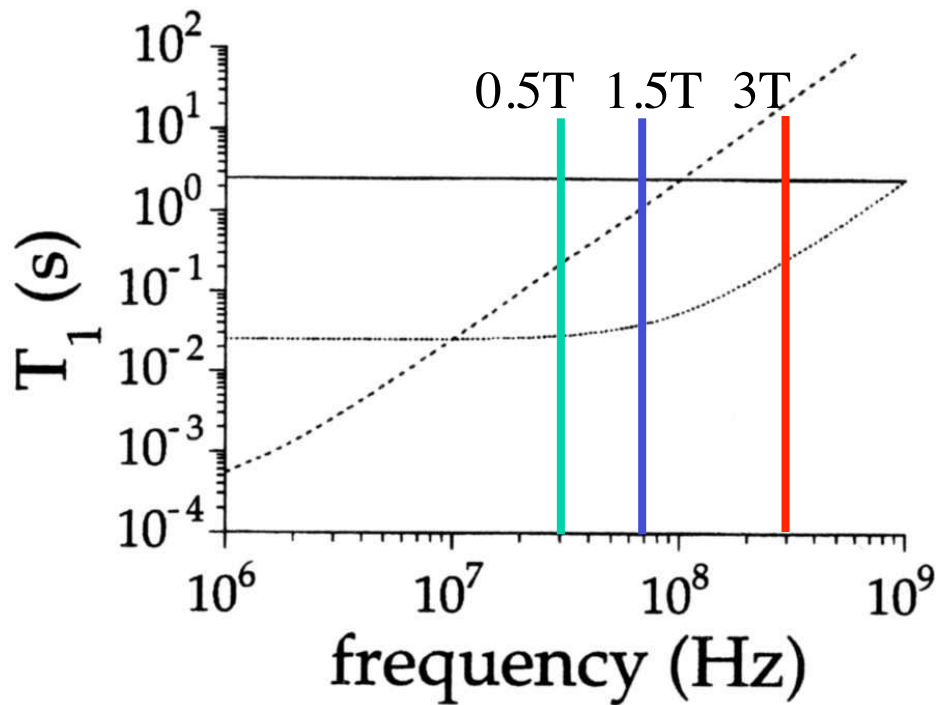
probes the spectral density at 0 and ω_0

The Spectral Density Function

Relaxation Rates vs τ_c

CSF　Muscle　Bone

slow

T_1 or T_2 (s)

10^2
10^1
10^0
10^{-1}
10^{-2}
10^{-3}
10^{-4}

fast

T_1

100 MHz

400 MHz

extreme
narrowing
$\omega_0 \tau_c \ll 1$

$$\frac{1}{T_1} = \frac{1}{T_2} \propto \frac{\gamma^4 \tau_c}{r^6}$$

min T_1 @ $\omega_0 \tau_c = 1$

T_2

10^{-12} 10^{-11} 10^{-10} 10^{-9} 10^{-8} 10^{-7} 10^{-6}

fast

slow

τ_c (s)

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Relaxation Rates vs B_0

Summary

- Lattice provides random time-varying magnetic fields.

    - x-y components cause transitions $\Longrightarrow$ T_1 relaxation (also T_2)
    - z component causes dephasing $\Longrightarrow$ T_2 relaxation

- From our simple model of uncorrelated, random $\Delta B(t)$ ...

$$\frac{1}{T_1} = 2\gamma^2 \left\langle B^2 \right\rangle J(\omega_0) \qquad \frac{1}{T_2} = \gamma^2 \left\langle B^2 \right\rangle \left(J(0) + J(\omega_0) \right)$$

- 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