pNMR
Mariapfarr 2014

Introduction to NMR relaxation

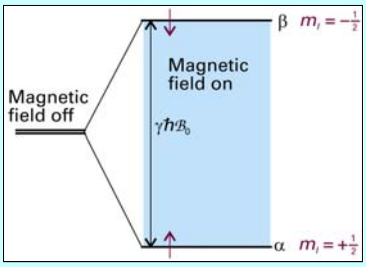
Jozef Kowalewski
Stockholm University

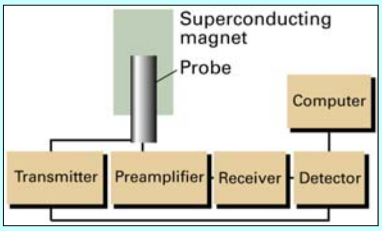
Outline

- What is NMR?
- Phenomenological Bloch equations
- Introductory example: spin-lattice relaxation
- Elements of statistics and theory of random processes
- Time-dependent perturbation theory
- A simple model and its predictions
- Dipole-dipole relaxation

What is NMR?

- Features:
  - ➢ Splitting controlled by the experimenter (B_0 field)
  - ➢ Many species possible to study ($I \neq 0$, γ_I), most common is ^1H
  - ➢ Very small energy splitting & population difference with the available magnets

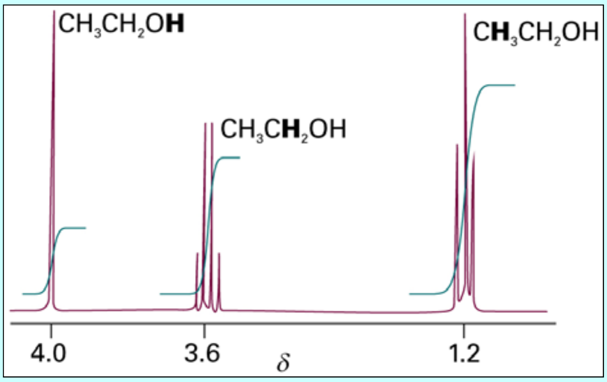




Atkins *et al*. "*Quanta, Matter and Change*"

^{1}H NMR of ethanol

- What NMR measures in solution:
  - ✓ Line positions (chemical shifts)
  - ✓ Splittings (*J*-couplings)
  - ✓ Integrals
  - ✓ Relaxation



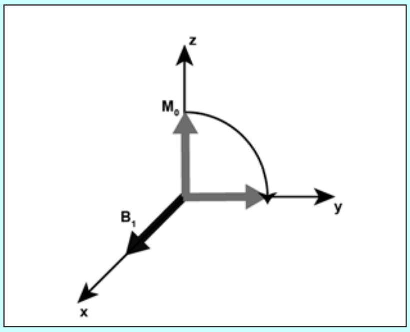
- Relaxation means return to equilibrium after a perturbation

Simple NMR: magnetization vector

- The equilibrium state of an ensemble of *N* (non-interacting) spins can be described by a *magnetization vector,* oriented along B_0 and with the length:

$$M_0 = \frac{N\gamma_I^2\hbar^2 I(I+1)B_0}{3k_BT}$$

- The magnetization vector is a classical quantity and can be described by classical physics
- Effect of radiofrequency pulses



Figures from: Kowalewski & Mäler, "*Nuclear Spin Relaxation in Liquids*", Taylor & Francis, 2006

Simple relaxation: Bloch equations

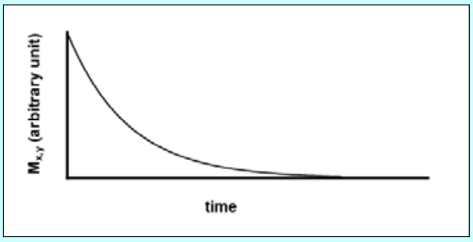
- Phenomenological description of the magnetization vector after a pulse (in rotating frame):

$$\frac{dM_x}{dt} = M_y\omega_{off} - \frac{M_x}{T_2}$$

$$\frac{dM_y}{dt} = -M_x\omega_{off} - \frac{M_y}{T_2}$$

$$\frac{dM_z}{dt} = \frac{M_0 - M_z}{T_1}$$

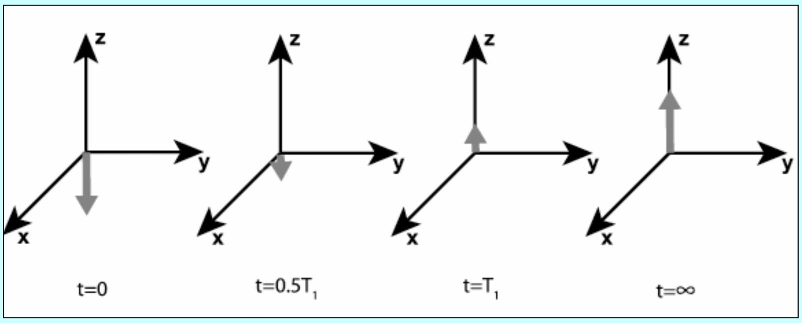
- Free induction decay (FID) on resonance decays exponentially with T_2, transverse relaxation time



$$M_{x,y} = M_0 \exp(-t/T_2)$$

Spin-lattice relaxation

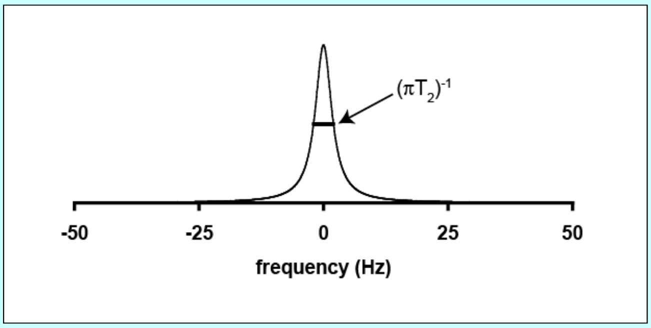
- Consider a sequence of two RF-pulses: (180º-t-90º-FID), called inversion-recovery experiment:



$$M_z(t) = M_0(1-2\exp(-t/T_1))$$

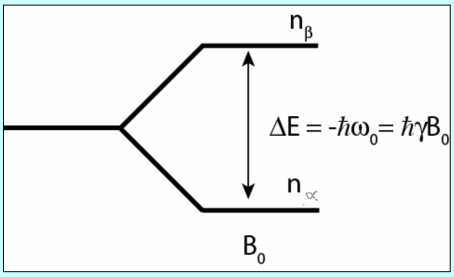
Meaning of T_1 and T_2

- Longitudinal relaxation (T_1): energy exchange with other degrees of freedom (the lattice)
- Transverse relaxation (T_2): loss of phase coherence, gives decay of FID and the line-broadening:



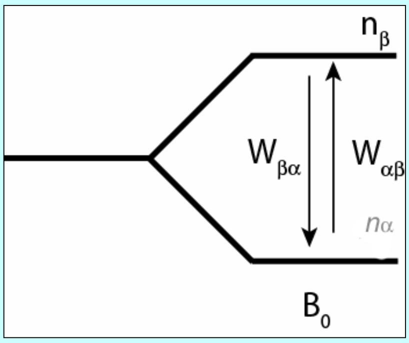
Simple theory – spin-lattice relaxation 1.

- Consider a system of I=1/2 spins
- Energy splitting proportional to B_0, ω_0=Larmor frequency
- Populations: n_α, n_β
- At equilibrium, Boltzmann distributed: n_α^{eq}, n_β^{eq}
- A non-equilibrium situation can be created by changing the magnetic field or by RF-pulses



Simple theory – spin-lattice relaxation 2.

- Assume simple kinetics for changing the populations of the two states:



$$\frac{dn_\alpha}{dt} = \left(n_\beta - n_\beta^{eq}\right)W_{\beta\alpha} - \left(n_\alpha - n_\alpha^{eq}\right)W_{\alpha\beta} =$$

$$= W_I\left(n_\beta - n_\beta^{eq} - n_\alpha + n_\alpha^{eq}\right)$$

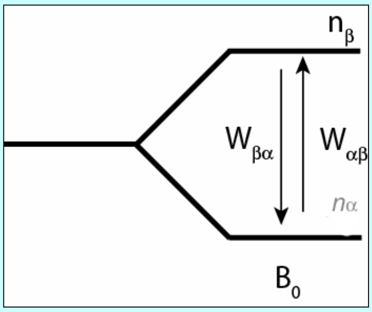
$$\frac{dn_\beta}{dt} = W_I\left(n_\alpha - n_\alpha^{eq} - n_\beta + n_\beta^{eq}\right)$$

Simple theory – spin-lattice relaxation 3.

- Instead of discussing changes in populations, we introduce the sum (N) and difference (n) in populations

$$\frac{dN}{dt} = 0$$

$$\frac{dn}{dt} = -2W_I\left(n - n^{eq}\right)$$



Simple theory – spin-lattice relaxation 4.

The simple result shows that the change in the difference in population (return to equilibrium or relaxation) occurs through an exponential process.

If we assume that the difference in population is proportional to the longitudinal component of the magnetization vector, $M_z(t)$, we can identify from the Bloch equations:

$$1/T_1 = 2W_I$$

$$\frac{dN}{dt} = 0$$

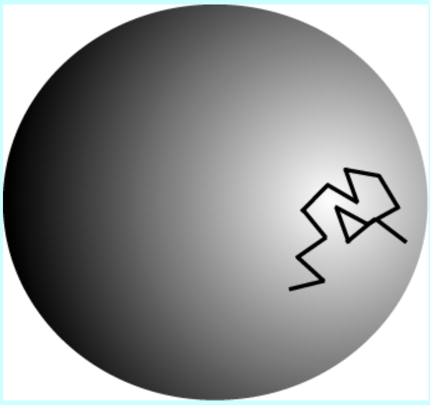
$$\frac{dn}{dt} = -2W_I\left(n - n^{eq}\right)$$

Transition probabilities

- The relaxation rate is proportional to the transition probability
- Transitions giving rise to NMR relaxation are non-radiative, they do not arise through emission or absorption of radiation from radiofrequency field
- They occur as a result of weak magnetic interactions within the sample, if those oscillate in time with frequency components at the Larmor frequency
- Weak interaction → slow relaxation

Where do the transitions come from?

- Weak magnetic interactions often anisotropic
- Time-dependence through molecular motions
- The reorientation of molecules (or molecule-fixed axes) can be pictured as a random walk on a sherical surface
- The combination of the motion and anisotropic interactions leads to:
- Hamiltonians varying randomly with time: ***stochastic interaction***

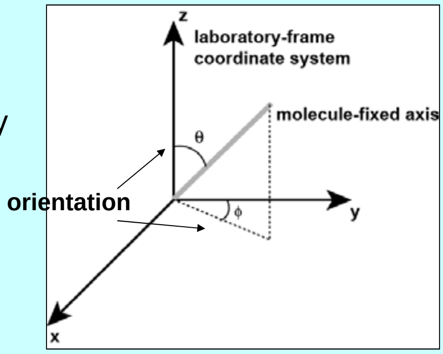


Stochastic variables 1.

- The orientation of a molecule-fixed axis can be described in terms of stochastic variables, characterized by probability density

$$p(x;y)dxdy =$$
$$= P(x \le X \le x+dx; y \le Y \le y+dy)$$

- Means: the probability that *X* and *Y* take on values in the indicated ranges



Stochastic variables 2.

- If *p*(*x*;*y*)=*p*(*x*)*p*(*y*) we say that the two variables are *statistically independent*
- We can also write: *p*(*x*;*y*)=*p*(*x*)*p*(*x*|*y*), the latter meaning the probability that *Y* takes on the value *y provided* that *X* takes on value *x* → *conditional probability*
- Average value (mean): $m_1 = \langle X \rangle = \int_{-\infty}^{\infty} xp(x)dx$
- The second moment around the mean (variance):

$$\mu_2 = \left\langle (X-m_1)^2 \right\rangle = \left\langle X^2 \right\rangle - m_1^2 = \sigma^2$$

Product of two variables: $m_{11} = \langle XY \rangle$

If the two variables are statistically independent: $m_{11} = \langle XY \rangle = \langle X \rangle \langle Y \rangle$

Stochastic variables 3.

- The mixed second moment:

$$\mu_{11} = \langle (X - m_{10}) \rangle \langle (Y - m_{01}) \rangle = \langle XY \rangle - m_{10} m_{01}$$

- Correlation coefficient:

$$\rho = \frac{\mu_{11}}{\sigma_X \sigma_Y}$$

- Vanishes if *X* and *Y* statistically independent

Stochastic functions of time

The time-dependence of anisotropic interactions can be described in terms of stochastic functions of time (stochastic processes) due to the random motions

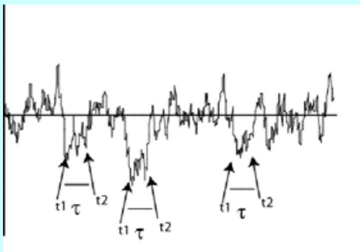
Average value: $$\langle Y(t) \rangle = \int_{-\infty}^{\infty} yp(y,t)\,dy$$

The properties of a stochastic function are in general dependent on *t*.

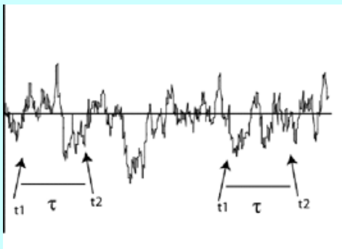
What is the correlation between $Y(t)$ at two time-points, t_1 and t_2?

What is the correlation between $Y(t)$ at two time-points, t_1 and t_2?

"t_1-t_2 small"



"t_1-t_2 large"



- Correlation vanishes for large time separations
- The same is true for an ensemble average over many spins

Stationary stochastic process

If t_1 and t_2 are close (defined by the time-scale of the random oscillation of $Y(t)$) a correlation is probable

Useful formulation with the conditional probability density for $Y(t)$ acquiring the value y_2 at t_2 provided that it takes on y_1 at t_1:

$$p(y_1,t_1;y_2,t_2) = p(y_1,t_1)p(y_1,t_1 \mid y_2,t_2)$$

If the probability $p(y_1,t_1)$ density does NOT vary with time, the process is called *stationary*. In such a case:

$$p(y_1,t_1 \mid y_2,t_2) = p(y_1,0 \mid y_2,t_2 - t_1) = p(y_1 \mid y_2,\tau)$$

Time-correlation functions

The average value of a product of a stationary process, $Y(t)$ at two different times can be defined. Because this quantity is only dependent on the time difference, $t=t_2-t_1$, we can define:

$$\langle Y(t_1)Y(t_2)\rangle = G(t_2 - t_1) = G(\tau)$$

Time-correlation function (TCF)

Autocorrelation function:

The same function correlated with itself at different time points. Acts as a correlation coefficient between the same stochastic variable at different points in time.

Cross-correlation function:

Different functions at different points in time are correlated

Properties of time-correlation functions

The autocorrelation function of Y at t=0 becomes the variance of Y:

$$G(0) = \langle Y(t)Y^*(t)\rangle = \left\langle |Y(t)|^2 \right\rangle = \sigma^2$$

The average of $Y(t)$ can often be assumed to be zero.

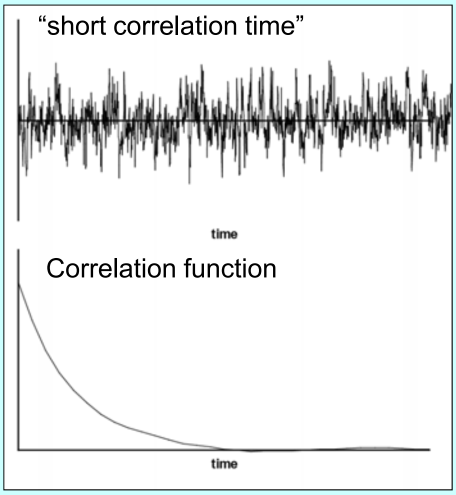
Reasonable to assume that correlation vanishes for long τ.

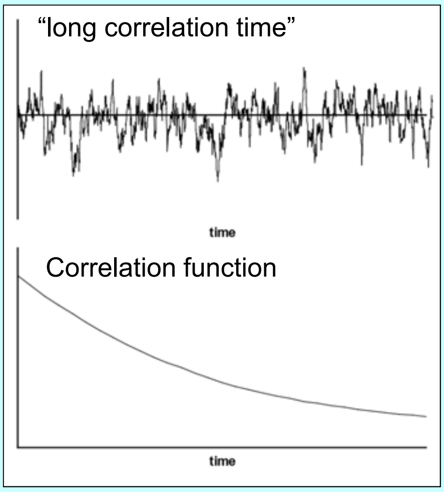
$$\lim_{\tau\to\infty} G(\tau) = 0$$

The following TCF works (and can be derived within a simple model): $G(\tau) = G(0)\exp(-|\tau|/\tau_c)$

The correlation time, τ_c, can be interpreted as a measure of persistence of the correlation of the values $Y(t)$ at different points in time.

Illustration of correlations on different time-scales





Size and temperature dependence of correlation time

One can use hydrodynamic arguments to derive the **Stokes-Einstein-Debye** relationship for a sphere:

$$\tau_c = \frac{4\pi\eta a^3}{3k_BT} = \frac{V\eta}{k_BT}$$

a = radius
η = viscosity

This relation is valid for a rank-2 spherical harmonics

- Correlation time increases with molecular size
- Correlation time increases with viscosity
- Correlation time decreases with temperature

The temperature dependence is often modeled by an Arrhenius-type expression:

$$\tau_c = \tau_0 \exp(E_a / k_BT)$$

Spectral density functions

Spectral density functions are Fourier transforms of the time-correlation functions.

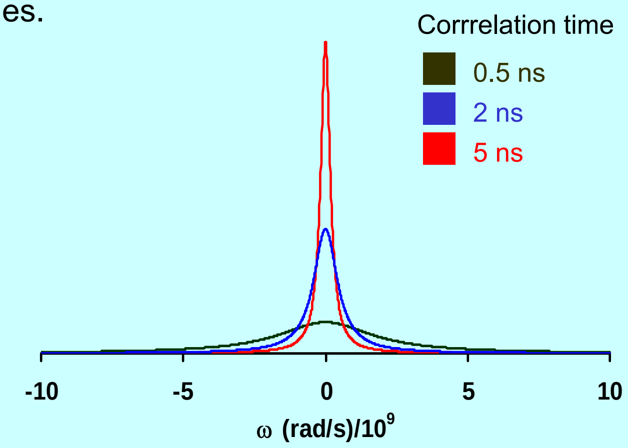
$$J(\omega) = 2\int_0^{\infty} G(\tau)\exp(-i\omega\tau)d\tau$$

From the exponentially decaying time-correlation function we get a *Lorentzian* spectral density

$$J(\omega) = G(0)\frac{2\tau_c}{1+\omega^2\tau_c^2}$$

Spectral density functions

The spectral density function as a function of frequency calculated with different correlation times.



Time-dependent perturbation theory

$$\hat{H}(t) = \hat{H}_0 + \hat{V}(t)$$

- Hamiltonian acting on system is composed of two parts:
- Time-independent Hamiltonian with known solutions
- Time-dependent small *perturbation, stochastic function of time*
- Consider a two-level system
- The transition probability between the levels *a* and *b*:

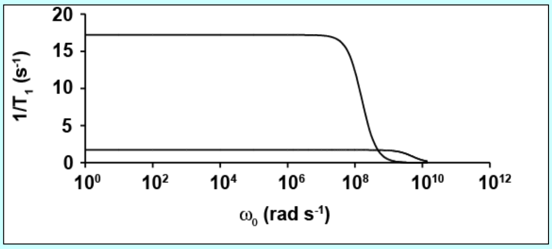
$$W_{ab} = 2\int_0^\infty G_{ba}(\tau)e^{-i\omega_{ab}\tau}d\tau = J_{ba}(\omega_{ab})$$

- Wiener- Khinchin theorem: the spectral density function is a measure of the distribution of fluctuations in $Y(t)$ among different frequencies

Simple two-level system

$$1/T_1 = 2W = 2G(0)\frac{2\tau_c}{1+\omega_0^2\tau_c^2}$$

ω_0 = Larmor frequency, (resonance frequency).

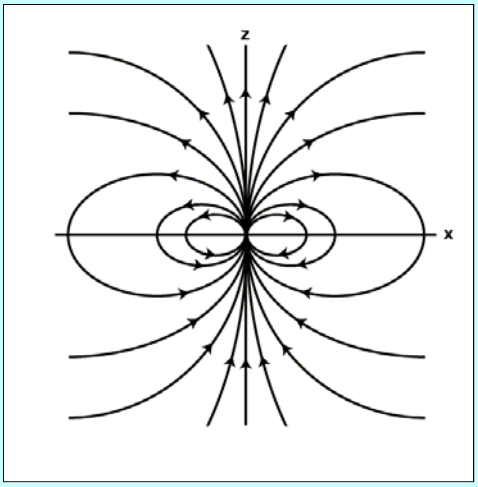


Relaxation interactions in real systems

- Dipole-dipole interaction
- Chemical shift anisotropy
- Quadrupolar interaction (I≥1)
- Spin-rotation
- Scalar
- Paramagnetic

The dipole-dipole (DD) interaction

- Every nuclear spin (*I*>0) acts as a magnetic dipole, generating a local magnetic field
- This magnetic field interacts with the magnetic moments of other nuclei nearby



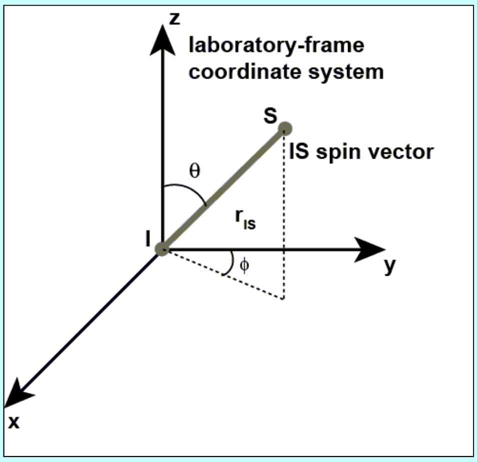
The dipole-dipole interaction 2

- The DD interaction energy:

$$H_{DD}(\Omega) \propto r_{IS}^{-3}(3\cos^2\theta - 1)\hat{I}_z\hat{S}_z$$

Ω (solid angle) stands for (θ, ϕ)

- The reorientation of the IS-axis – by molecular motion – affects the DD interaction



How to derive the exponential tcf?

- Consider a stationary process: $Y_{2,0}(t) = \sqrt{(5/16\pi)}(3\cos^2\theta(t) - 1)$
- The tcf is: $G_2(\tau) = \langle Y_{2,0}(t)Y_{2,0}^*(t+\tau)\rangle =$

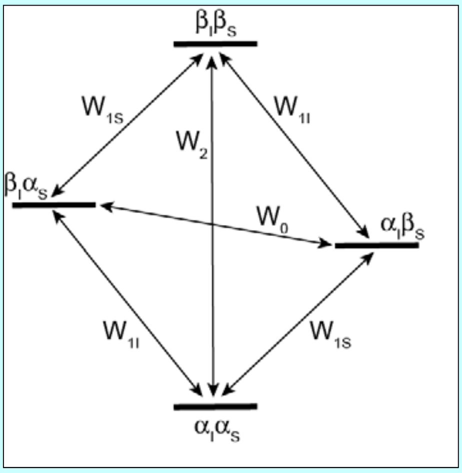
$$= \int\int Y_{2,0}(\Omega_0)Y_{2,0}^*(\Omega)P(\Omega_0)P(\Omega_0 \mid \Omega, \tau)d\Omega_0 d\Omega$$

- Isotropic liquid: $P(\Omega) = P(\Omega_0) = 1/4\pi$
- Conditional probability $P(\Omega_0 \mid \Omega, \tau)$ from Fick's law for rotational diffusion: $\frac{\partial}{\partial\tau} f(\Omega,\tau) = D_R\hat{\Delta}_R f(\Omega,\tau)$
- Boundary condition: $P(\Omega_0 \mid \Omega, 0) = \delta(\Omega - \Omega_0)$
- Leads to: $G_2(\tau) = \frac{1}{4\pi}\exp[-6D_R\tau]$
- Identical to the ”guessed” exponential function with: $\tau_c = 1/6D_R$

The dipole-dipole relaxation

- To understand the DD relaxation, we need to consider transition probabilities in a *four-level system*
- Transition probabilities originate from molecular motion by stochastic variation of the DD interaction,

$$W_{ab} \sim J(\omega_{ab})$$



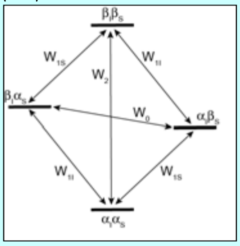
Spin-lattice relaxation: Solomon equations

$$\frac{d\langle \hat{I}_z\rangle}{dt} = -(W_0 + 2W_{1I} + W_2)(\langle \hat{I}_z\rangle - I_z^{eq}) - (W_2 - W_0)(\langle \hat{S}_z\rangle - S_z^{eq})$$

$$\frac{d\langle \hat{S}_z\rangle}{dt} = -(W_2 - W_0)(\langle \hat{I}_z\rangle - I_z^{eq}) - (W_0 + 2W_{1S} + W_2)(\langle \hat{S}_z\rangle - S_z^{eq})$$

or

$$\frac{d}{dt}\begin{pmatrix} \langle \hat{I}_z\rangle \\ \langle \hat{S}_z\rangle \end{pmatrix} = -\begin{pmatrix} \rho_I & \sigma_{IS} \\ \sigma_{IS} & \rho_S \end{pmatrix}\begin{pmatrix} \langle \hat{I}_z\rangle - I_z^{eq} \\ \langle \hat{S}_z\rangle - S_z^{eq} \end{pmatrix}$$



$$\left.\begin{aligned} \rho_I &= W_0 + 2W_{1I} + W_2 \\ \rho_S &= W_0 + 2W_{1S} + W_2 \end{aligned}\right\} \text{spin-lattice relaxation rates}$$

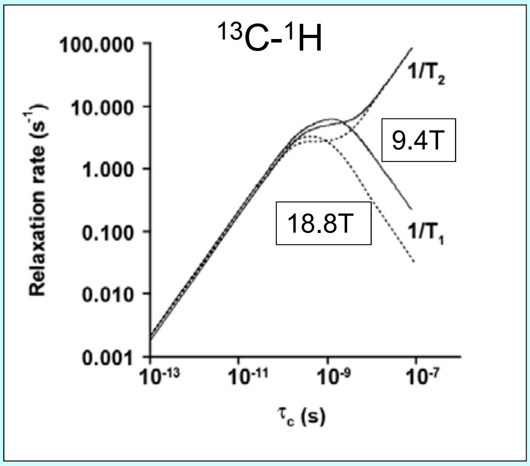
$$\sigma_{IS} = W_2 - W_0 \qquad \text{cross-relaxation rate}$$

Single exponential relaxation

- ... (well-defined T_1) occurs only in some limiting cases:
- ✓ I and S are identical (e.g. protons in water)
- ✓ One of the spins (say S) has another, faster relaxation mechanism (e.g. unpaired electron spin)
- ✓ One of the spins (say I) is saturated by rf irradiation (e.g. ^{13}C-{^{1}H} experiment)
- Otherwise, bi-exponential relaxation

^{13}C relaxation under proton decoupling

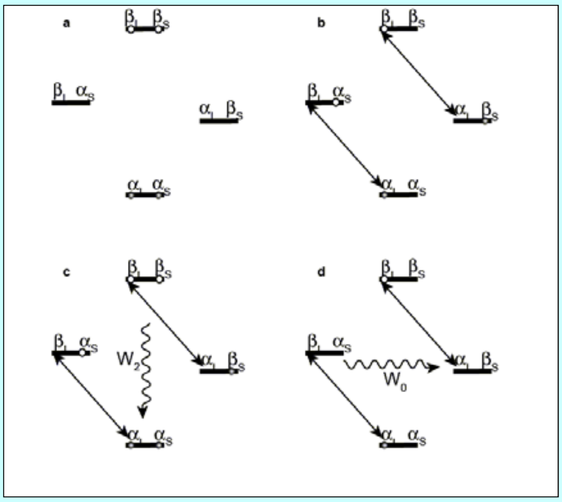
- Spin-tattice relaxation rate (T_1^{-1}) depends on the molecular size (τ_c) and the magnetic field
- For rapidly-moving systems (small molecules, extreme narrowing) $T_1^{-1}=T_2^{-1}$



The nuclear Overhauser effect

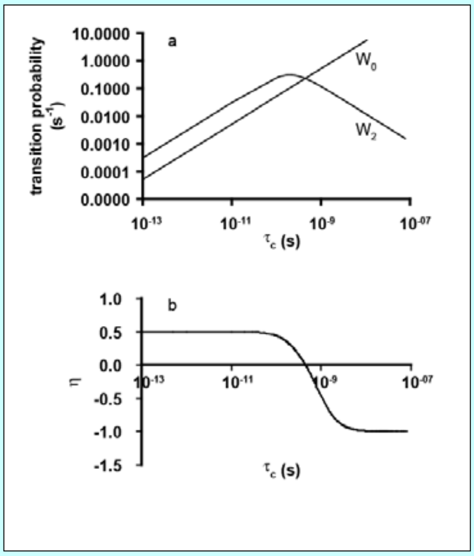
- Continuous irradiation of the I-spin creates non-equilibrium populations for the S-spin
- This multiplies the S-spin signal intensity by a factor 1+η (the NOE factor),

$$\eta = \frac{\gamma_I \sigma_{IS}}{\gamma_S \rho_S}$$



The Nuclear Overhauser effect 2.

- The transition probabilities W_0 and W_2 have different correlation time dependences
- Example: I & S are both protons, B_0=21 T



Summary

- Relaxation rates are related to transition probabilities
- Relaxation (transitions) occur through a combination of anisotropic interactions and random walk motion
- Fundamental quantities: time-correlation functions and spectral densities for the stochastic processes
- The relationship between transition probabilities and the random motions can be derived through time-dependent perturbation theory
- Important source of relaxation: the dipole-dipole interaction