Relaxation I

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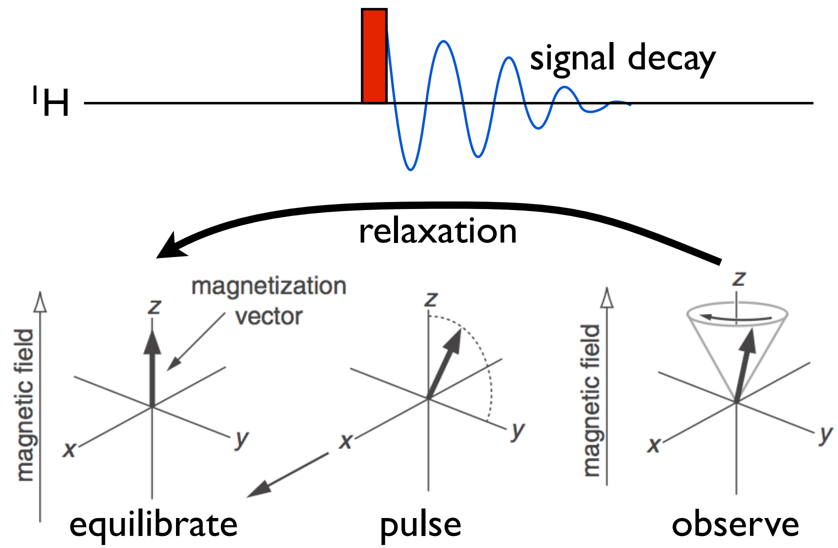
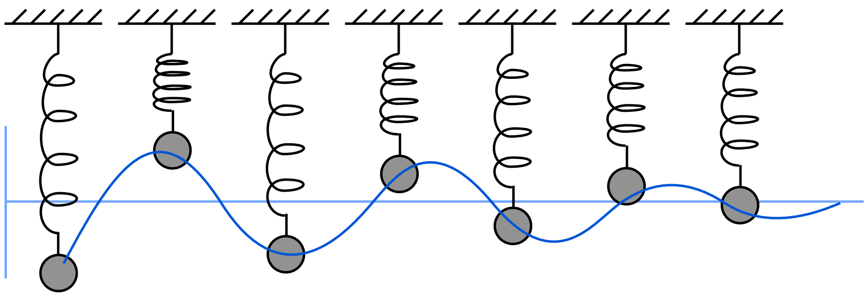
Revision: T1 and T2 relaxation

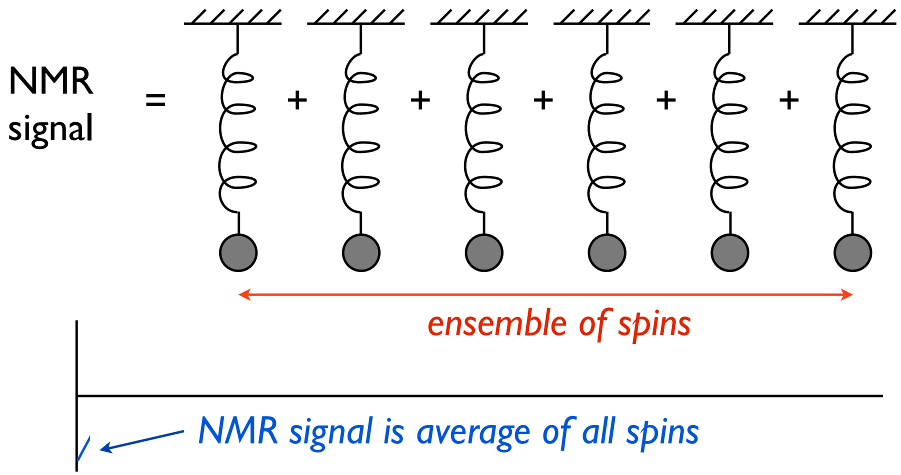


T_1 (longitudinal) relaxation



T_1 relaxation = return to rest position (energy lost to surroundings)

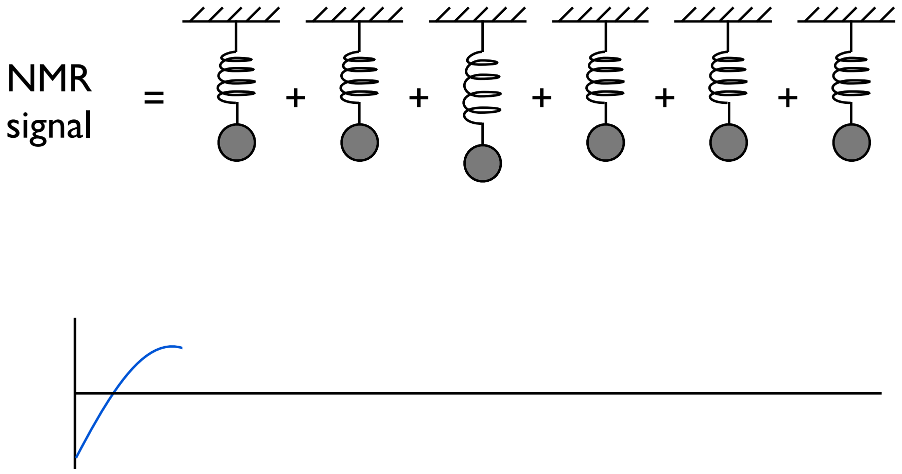
T_2 (transverse) relaxation



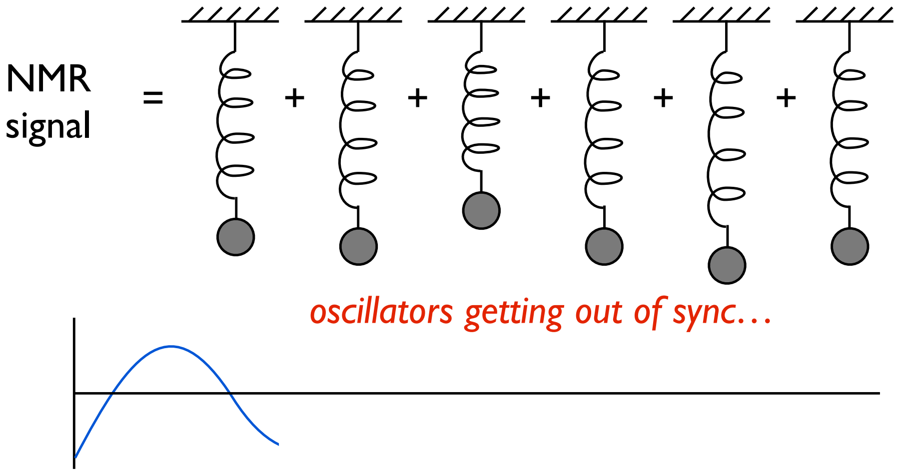
ensemble of spins

NMR signal is average of all spins

T_2 (transverse) relaxation

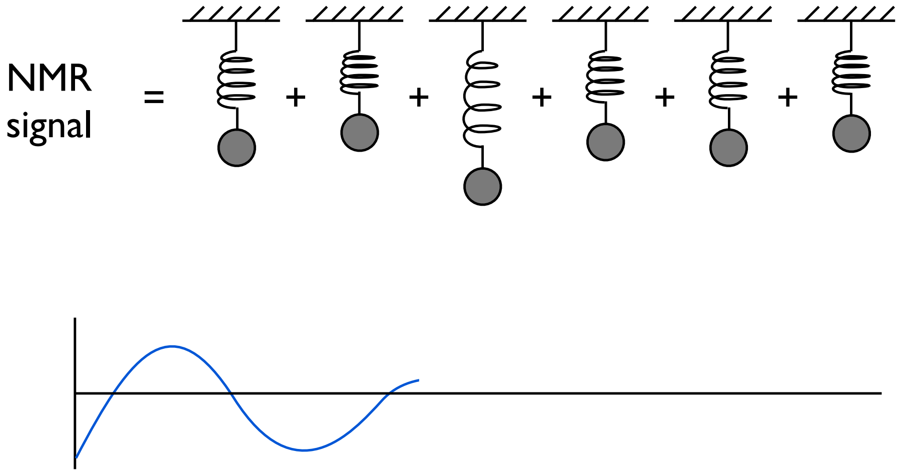


T_2 (transverse) relaxation

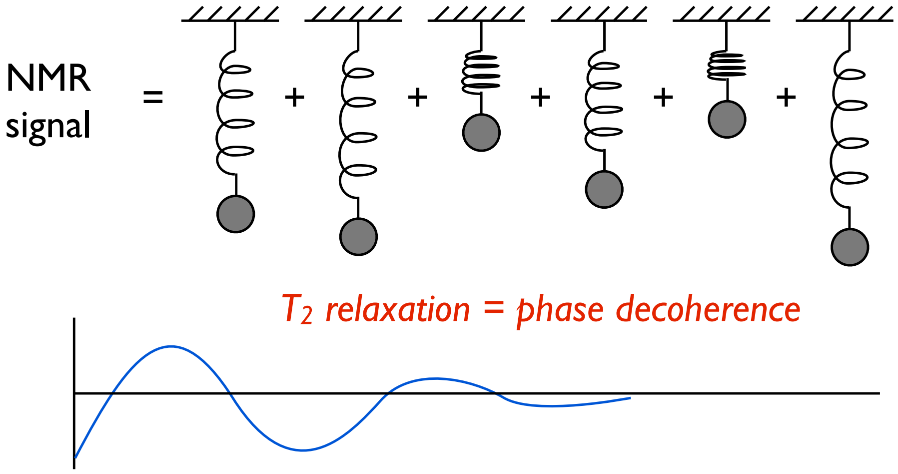


oscillators getting out of sync…

T_2 (transverse) relaxation



T_2 (transverse) relaxation

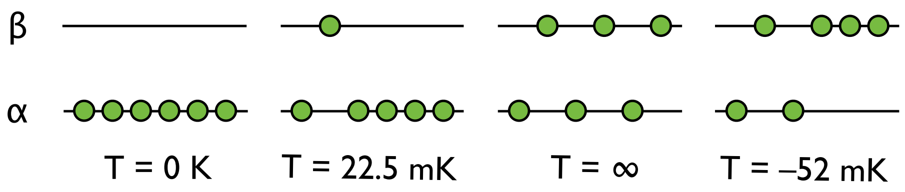


T_2 relaxation = phase decoherence

NMR energies and timescales

- Energy of optical transition (green light, 500 nm)
  = hc / λ = 4 x 10^{-19} J = 60 kcal mol^{-1}
- Energy of NMR transition (700 MHz)
  = hν = 5 x 10^{-25} J = 7 x 10^{-5} kcal mol^{-1}
- Thermal energy at room temperature
  = k_BT = 4 x 10^{-21} J = 0.6 kcal mol^{-1}
- Timescale of spontaneous emission at optical frequencies
  ~ 10^{-15} seconds
- Timescale of spontaneous emission at NMR frequencies
  = $3\pi c^3/(2h\gamma^2\omega^3)$ = 10^{20} seconds
- Age of universe = 13.7 billion years ~ 10^{17} seconds!
- Spontaneous (or stimulated) emission is completely negligible for NMR. Instead, relaxation occurs through decoherence (T_2) or exchange of energy with the environment – the *lattice* (T_1)

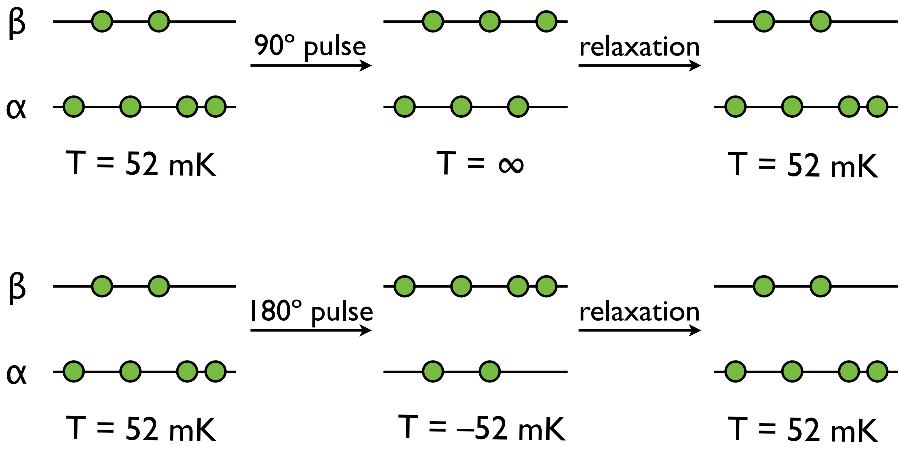
Spin temperature



Boltzmann: $$\frac{n_\beta}{n_\alpha} = \exp\left(\frac{E_\alpha - E_\beta}{k_B T}\right)$$ **ΔE = 700 MHz**

- Useful to define 'spin temperature' based on populations
- 6 spins in above picture don't give accurate representation of real NMR samples:
  $n_\alpha/n_\beta \approx 1.0001$ for ^{1}H at room temperature, 700 MHz
- Spin temperature always equals bulk temperature at equilibrium, but applying pulses can add energy to the system – spins subsequently 'cool' towards equilibrium
- Negative temperatures are well-defined and are hotter than positive temperatures!

Effect of pulses on spin temperature



Pulses add energy to the system!

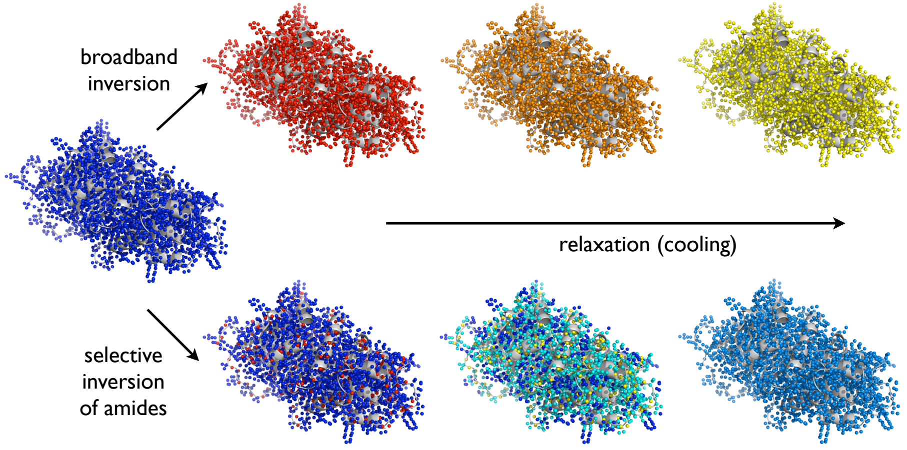
How much energy do pulses contribute?

- H_2O has 110 M concentration of ^{1}H spins
- Population difference between spin states:
  $\Delta E/k_BT \approx 0.000125$ molecule^{-1}
- Total spins flipped:
  N = (0.000125 molecule^{-1}) x (6 x 10^{23} molecule mol^{-1}) x (110 mol L^{-1})
  = 8 x 1021 L-1
- 180° pulse, entire population is inverted: spin temperature becomes negative!
  Energy absorbed is:
  Q = N ΔE = 0.004 J L^{-1}
- Volumetric heat capacity of water is 4180 J K^{-1} L^{-1}, so:
  ΔT = 1 μK
- Completely negligible! BUT total rf energy absorbed can still be significant, particularly for salty samples (dielectric heating).

Longitudinal relaxation changes the *energy* of spins

- We have seen that pulsing increases the energy contained within the spin system, increasing the spin temperature.
- Longitudinal relaxation is the process by which the spins re-equilibrate with the (cooler) environment – a process resulting in the transfer of energy to the surrounding lattice (environment).
- This can only occur through specific microscopic mechanisms…

A thermal description of cross-relaxation



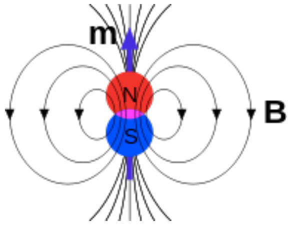
- Cross-relaxation: the effect of neighbouring spins on relaxation processes e.g. faster relaxation of isolated hot spins in a bath of cooler spins
- Cross-relaxation processes must have a microscopic mechanism!

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 relaxation.
- Transverse relaxation is caused by fluctuations at any frequency

Sources of fluctuating magnetic fields: dipole-dipole interactions

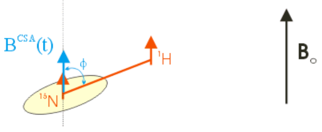
- All nuclei (I≠0) have a magnetic dipole that creates a local magnetic field
- Field strength is proportional to gyromagnetic ratio – strongest for ^{1}H, weak for ^{2}H, ^{15}N
- Field is spatially dependent – effect of neighbouring nuclei depends on relative orientation
- e.g. average ^{1}H dipolar field experienced by ^{15}N nucleus in amide (r = 1.06 Å) is 2.4 mT
  – just 0.015% of static field (150 ppm)



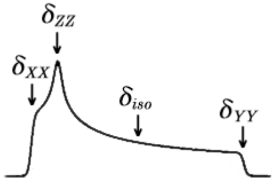
$$\mathbf{B}(\mathbf{r}) = \nabla \times \mathbf{A} = \frac{\mu_0}{4\pi}\left(\frac{3\mathbf{r}(\mathbf{m}\cdot\mathbf{r})}{r^5} - \frac{\mathbf{m}}{r^3}\right).$$

Sources of fluctuating magnetic fields: chemical shift anisotropy

- Electron distribution is not perfectly symmetric about a nucleus
- The extent of shielding depends on the orientation of nearby bonds relative to the static field – i.e. on the orientation of the molecule
- The 'chemical shift' is not really a number – it's a tensor! What we think of as the chemical shift is the average over all orientations (isotropic tumbling)
- CSA approx. equal to chemical shift range of nucleus, e.g. 170 ppm for ^{15}N
- Fluctuations in local field proportional to B_0 – becomes significant at high fields



$B^{CSA}(t) \propto \gamma_N B_0 \Delta\sigma_N [3\cos^2\phi(t)-1]$



Sources of fluctuating magnetic fields: chemical exchange

- Chemical exchange = chemical reaction converting molecule into a different chemical species, e.g.
  - folding / unfolding
  - ligand binding
  - cis / trans isomerisation
  - aromatic ring flips
- If the chemical shift is different in the new state, the nucleus experiences a shift in the local magnetic field

free $\rightleftharpoons$ bound

$\Delta\delta \sim 1$ ppm

$B_{loc} \sim B_0 \, \Delta\delta$

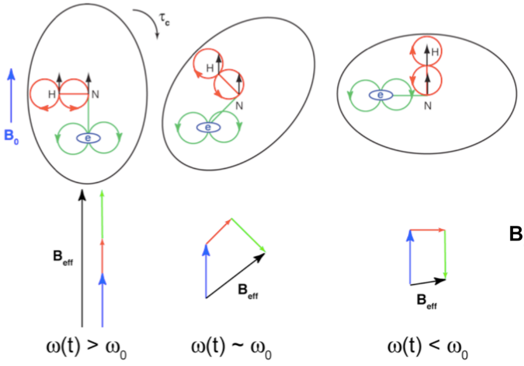
Summary of local field sources

- dipolar: $B_{loc} \propto \gamma_H/r^3 \approx 2.4$ mT (150 ppm) independent of B_0
- CSA: $B_{loc} \propto B_0 \cdot \Delta\sigma$ (170 ppm) proportional to B_0
- chemical exchange: $B_{loc} \sim B_0 \cdot \Delta\delta \sim 1$ ppm proportional to B_0
- Paramagnetism, quadrupolar interactions (^2H), scalar couplings…

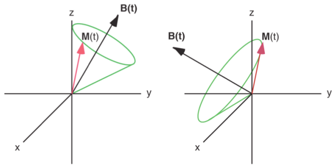
- All fluctuations are much weaker than the static field, B_0
- Sensitivity of spins to these local field fluctuations depends on their gyromagnetic ratio – ^1H most sensitive, ^{15}N least sensitive

Summary of local field sources

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



$$\frac{d\mathbf{M}(t)}{dt} = \mathbf{M}(t) \times \gamma \mathbf{B}(t)$$



$$\begin{aligned}\mathbf{B}_{eff}(t) &= \mathbf{B}_{isotropic} + \mathbf{B}_{anisotropic}(t) \\ &= \mathbf{B}_{isotropic} + \mathbf{B}_{longitudinal}(t) + \mathbf{B}_{transverse}(t) \\ &= \left[B_0 + B_z(t)\right]\hat{\mathbf{k}} + B_x(t)\hat{\mathbf{i}} + B_y(t)\hat{\mathbf{j}}\end{aligned}$$

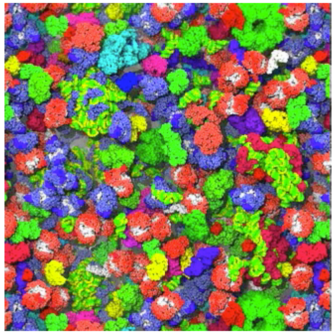
Quantifying fluctuations

- Rotational diffusion is a stochastic process – molecules rotate in small, random jumps
- Field fluctuations can be characterised by a correlation function:

$$G(\tau) = \overline{B_{\text{loc}}(0)B_{\text{loc}}(\tau)}$$

- Simple rotational diffusion can be described by an exponential correlation function with correlation time τ_c:

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



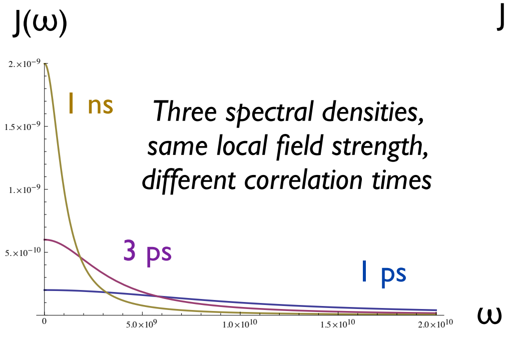
- Correlation time proportional to molecular weight – big molecules tumble slowly

Spectral densities

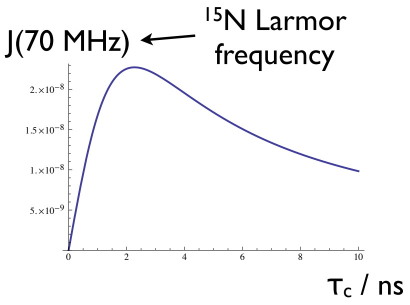
- The correlation time τ_c describes a rough 'frequency', $1/\tau_c$, where the fluctuations are strong
- More precise calculations need to know exactly 'how much fluctuation' there is at a given frequency
- To determine this we take the Fourier transform of the correlation function – the spectral density function $J(\omega)$:

$$G(\tau) = \overline{B_{\text{loc}}^2}e^{-\tau/\tau_c} \qquad J(\omega) = \overline{B_{\text{loc}}^2}\left(\frac{2\tau_c}{1+\omega^2\tau_c^2}\right)$$

Spectral densities



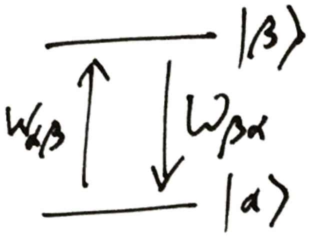
Three spectral densities, same local field strength, different correlation times



$$G(\tau) = \overline{B_{\text{loc}}^2}e^{-\tau/\tau_c} \qquad J(\omega) = \overline{B_{\text{loc}}^2}\left(\frac{2\tau_c}{1+\omega^2\tau_c^2}\right)$$

Calculating relaxation rates

1-spin system:



Transition rates $W_{\alpha\beta} \approx W_{\beta\alpha}$

- Slightly different because of ΔE (must reproduce Boltzmann dist.)
- This needs a much more sophisticated treatment with quantum description of environment (lattice)

Semi-classical approximation : $W_{\alpha\beta} = W_{\beta\alpha}$

but instead of discussing populations we use the difference from equilibrium, ie. $n_\alpha \longrightarrow n_\alpha - n_\alpha^0$

$n_\beta \longrightarrow n_\beta - n_\beta^0$

Define Hamiltonian and wavefunction:

TDSE: $\dfrac{\partial \Psi(t)}{\partial t} = -i \mathcal{H} \Psi(t)$

$\mathcal{H}_0 = \omega_0 I_z$

$\mathcal{H}_0 |\alpha\rangle = -\frac{1}{2}\omega_0 |\alpha\rangle$

①

$\mathcal{H}_0 |\beta\rangle = +\frac{1}{2}\omega_0 |\beta\rangle$

Initial wavefunction: $\Psi(0) = c_\alpha(0)|\alpha\rangle + c_\beta(0)|\beta\rangle$

Applying TDSE $\Rightarrow \Psi(t) = c_\alpha(0)e^{-\frac{1}{2}i\omega_0 t}|\alpha\rangle + c_\beta(0)e^{\frac{1}{2}i\omega_0 t}|\beta\rangle$

If we redefine $\Psi(t) = c_\alpha(t)e^{-\frac{1}{2}i\omega_0 t}|\alpha\rangle + c_\beta(t)e^{\frac{1}{2}i\omega_0 t}|\beta\rangle$ ①

then clearly $c_\alpha(t) = c_\alpha(0)$ and $c_\beta(t) = c_\beta(0)$

do not vary under $\mathcal{H}_0$.

Approach for calculation of $W_{\beta\to\alpha}$:

1. Start with $\Psi(0) = |\beta\rangle$
2. Calculate time evolution under $\mathcal{H}_1$ = random field:

   $\Psi(t) = c_\alpha(t)\,|\alpha\rangle + c_\beta(t)\,|\beta\rangle$
3. As spin started in $|\beta\rangle$, $W_{\beta\alpha} = \dfrac{d(c_\alpha^* c_\alpha)}{dt}$

TDSE: $\dfrac{\partial\Psi}{\partial t} = -i\left[\mathcal{H}_0 + \mathcal{H}_1(t)\right]\Psi$

$$\text{LHS (using ②)} = \frac{dc_\alpha}{dt} e^{-\frac{1}{2}i\omega_0 t}|\alpha\rangle - \frac{1}{2}i\omega_0\, c_\alpha e^{-\frac{1}{2}i\omega_0 t}|\alpha\rangle + \frac{dc_\beta}{dt} e^{\frac{1}{2}i\omega_0 t}|\beta\rangle + \frac{1}{2}i\omega_0\, c_\beta e^{\frac{1}{2}i\omega_0 t}|\beta\rangle$$

$$\text{RHS} = -i(\mathcal{H}_0 + \mathcal{H}_1)\left(c_\alpha e^{-\frac{1}{2}i\omega_0 t}|\alpha\rangle + c_\beta e^{\frac{1}{2}i\omega_0 t}|\beta\rangle\right)$$

(using ②)

$$= -ic_\alpha e^{-\frac{1}{2}i\omega_0 t}\mathcal{H}_1|\alpha\rangle \cancel{+} - ic_\beta e^{\frac{1}{2}i\omega_0 t}\mathcal{H}_1|\beta\rangle - \frac{1}{2}i\omega_0\, c_\alpha e^{-\frac{1}{2}i\omega_0 t}|\alpha\rangle + \frac{1}{2}i\omega_0\, c_\beta e^{\frac{1}{2}i\omega_0 t}|\beta\rangle \quad \text{(using ①)}$$

Pre-multiply both sides by $\langle\alpha|$ and use orthonormality:

$$\frac{dc_\alpha}{dt} e^{-\frac{1}{2}i\omega_0 t} \cancel{-\frac{1}{2}i\omega_0 c_\alpha e^{-\frac{1}{2}i\omega_0 t}} = -ic_\alpha e^{-\frac{1}{2}i\omega_0 t}\langle\alpha|\mathcal{H}_1|\alpha\rangle - ic_\beta e^{\frac{1}{2}i\omega_0 t}\langle\alpha|\mathcal{H}_1|\beta\rangle \cancel{-\frac{1}{2}i\omega_0 c_\alpha e^{-\frac{1}{2}i\omega_0 t}}$$

$$\Rightarrow \frac{dc_\alpha}{dt} = -ic_\alpha H_{\alpha\alpha} \underline{-ic_\beta e^{i\omega_0 t} H_{\alpha\beta}} \qquad ③$$

* Transfer from c_β to c_α *

eg. $\mathcal{H}_1 = I_z \Rightarrow H_{\alpha\beta} = \langle\alpha|I_z|\beta\rangle = 0$

$\mathcal{H}_1 = I_x \Rightarrow H_{\alpha\beta} = \langle\alpha|I_x|\beta\rangle = \langle\alpha|\left(\frac{1}{2}|\alpha\rangle + \frac{1}{2}|\beta\rangle\right) = \frac{1}{2}$

$\Rightarrow$ Transverse fields are essential !

$$=0, \quad c_\beta = 1, \quad c_\alpha = 0$$

$$\Rightarrow \left.\frac{dc_\alpha}{dt}\right|_{t=0} = -i e^{i\omega_0 t} H_{\alpha\beta}(t) \qquad \textcircled{4}$$

$$\Rightarrow c_\alpha(t) = -i \int_0^t e^{i\omega_0 t'} H_{\alpha\beta}(t')\, dt' \qquad \textcircled{5}$$

Transition rate $W_{\alpha\beta} = \frac{dP_\alpha}{dt} = \frac{d(c_\alpha^* c_\alpha)}{dt} = c_\alpha \frac{dc_\alpha^*}{dt} + c_\alpha^* \frac{dc_\alpha}{dt}$

Using ④ and ⑤:

$$\Rightarrow W_{\alpha\beta} = -i\left[\int_0^t e^{i\omega_0 t'} H_{\alpha\beta}(t')\, dt'\right] \cdot i e^{-i\omega_0 t} H_{\alpha\beta}^*(t)$$
$$+ i\left[\int_0^t e^{-i\omega_0 t'} H_{\alpha\beta}^*(t')\, dt'\right] \cdot (-i) e^{i\omega_0 t} H_{\alpha\beta}(t)$$

$$= \int_0^t e^{i\omega_0 (t'-t)} H_{\alpha\beta}(t') H_{\alpha\beta}^*(t)\, dt$$
$$+ \int_0^t e^{-i\omega_0 (t'-t)} H_{\alpha\beta}^*(t') H_{\alpha\beta}(t)\, dt$$

Let $\tau = t - t'$:

$$W_{\alpha\beta} = \int_0^t e^{-i\omega_0 \tau} H_{\alpha\beta}(t-\tau) H_{\alpha\beta}^*(t)\, d\tau + \int_0^t e^{i\omega_0 \tau} H_{\alpha\beta}^*(t-\tau) H_{\alpha\beta}(t)\, d\tau$$

Using stationary property of H_1 fluctuations, shift time by $(\tau - t)$ and take ensemble average:

$$W_{\alpha\beta} = \int_0^t e^{-i\omega_0 \tau}\, \overline{H_{\alpha\beta}(\tau) H_{\alpha\beta}^*(0)}\, d\tau + \int_0^t e^{i\omega_0 \tau}\, \underbrace{\overline{H_{\alpha\beta}(\tau) H_{\alpha\beta}^*(0)}}_{=\text{autocorrelation function } G(\tau)}\, d\tau$$

$$= \int_0^\infty \left(e^{-i\omega_0 \tau} + e^{i\omega_0 \tau}\right) G(\tau)\, d\tau = 2\int_0^\infty \cos(\omega_0 \tau)\, G(\tau)\, d\tau$$

(change integral limits assuming $G(t) \to 0$
ie. theory valid for times $t \gg \tau_c$)

$$= 2\, J(\omega_0).$$