Relaxation and Dynamic Nuclear Polarization Transfer DNP

Nuclear Overhauser Effect

Rotating Frame Nuclear Overhauser Effect

- The NMR signal intensity is proportional to $\gamma^{5/2} = (\gamma \cdot \gamma^{3/2})$
- γ concerns excitation, determining the population difference
- $\gamma^{3/2}$ concerns detection, determining the intensity of the nuclear magnetic moment. Furthermore, the detector sensitivity is proportional to frequency (directly proportional to γ), but the noise that increases with $\gamma^{1/2}$ must be accounted for.

- An artificial increase of intensity can be obtained by means of polarization transfer from a more sensitive nucleus
- NOE and ROE: transfer through space. The "insensitive" nucleus must relax mainly by the dipolar coupling with proton

Wiener Process

A continuous-time stochastic process $W(t)$ for $t>=0$ with $W(0)=0$ and such that the increment $W(t)-W(s)$ is Gaussian with mean 0 and variance $t-s$ for any $0<=s<t$, and increments for not overlapping time intervals are independent. **Brownian motion** (i.e., **random walk with random step sizes**) is the most common example of a Wiener process.

Weisstein, Eric W. "Wiener Process." From MathWorld--A Wolfram Web Resource.
http://mathworld.wolfram.com/WienerProcess.html

T_1 for a I= ½ nucleus

$N_{\beta 0}$

$N_{\alpha 0}$ e $N_{\beta 0}$ are the Boltzmann equilibrium populations

$N_{\alpha 0}$

$\Delta_0 = N_{\alpha 0} - N_{\beta 0}$ population difference at equilibrium

The populations of the two levels can be varied by employing a suited r.f.

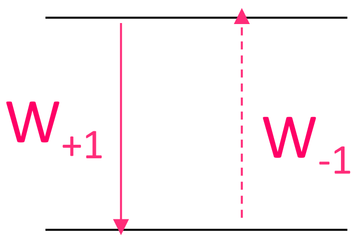
n_α and n_β out of equilibrium populations

$n_\beta = N_{\beta 0} + a$

$\Delta = n_\alpha - n_\beta$ population difference out of equilibrium

$n_\alpha = N_{\alpha 0} - a$

- After the perturbation the systems is reverting to equilibrium
- Considering the systems under a microscopic view:



$n_\beta = N_{\beta 0} + a$

$n_\alpha = N_{\alpha 0} - a$

$$\frac{W_{+1}}{W_{-1}} = \frac{N_{\alpha 0}}{N_{\beta 0}}$$

in order to attain the Boltzmann distributon

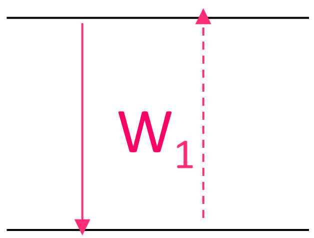
W: transition probability per unit time and per nucleus

the subscripts +1 e -1 indicate that the transition are single quantum

Since the populations' ratio is very close to 1, usually for simplicity sake, it is considered:

$$W_{-1} \approx W_{+1}$$

Therefore the deviation a is required to account for that at equilibrium the Boltman distribution is attained



$n_\beta = N_{\beta 0} + a$

$n_\alpha = N_{\alpha 0} - a$

We write the *gain-loss equations*. The first is the gain term.

$$\frac{dn_\beta}{dt} = W_1(-a) - W_1 a = -2aW_1$$

$$\frac{dn_\alpha}{dt} = W_1 a - W_1(-a) = 2aW_1$$

$$\boxed{\frac{d(n_\alpha - n_\beta)}{dt} = 4aW_1}$$

The population difference n_α-n_β is proportional to M_z

$$M_z(t) = N_0\left(n_\alpha \mu_{z\alpha} + n_\beta \mu_{z\beta}\right) = \frac{1}{2} N_0 \gamma \hbar \left(n_\alpha - n_\beta\right)$$

$$M_0 = \frac{1}{2} N_0 \gamma \hbar \left(N_{\alpha 0} - N_{\beta 0}\right)$$ therefore

$$M_z(t) - M_0 = \frac{1}{2} N_0 \gamma \hbar \left[(n_\alpha - n_\beta) - \left(N_{\alpha 0} - N_{\beta 0}\right)\right] = \frac{1}{2} N_0 \gamma \hbar (-2a)$$

recalling

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

$$2W_1 = \frac{1}{T_1}$$

Relaxation Mechanisms

The motion of the spins is decoupled from that of the molecules :

they are like the needles of compasses on ships in the storm

Bounty Rounds Cape Horn

http://cleangreengems.com/bounty/studycenter.htm

molecular collisions do not change spin orientation

Spontaneous Emission

- In re-establishing Boltzmann populations
- spontaneous emission does not play any role because the resonance frequencies of both electronic and nuclear spins are too low
- it is proportional to ν^3 and it is negligible for frequencies < 1 THz.

Stimolated Emission

- Magnetic fields fluctuating at the Larmor frequency are needed
- In the case of solids the lattice vibrations (phonons) are responsible for the exchange of energy between spins and lattice. Hence the name spin-lattice for the longitudinal relaxation
- In solution fluctuating magnetic fields are provided by the fluctuations, due to the molecular motions, with respect to the magnetic field of the anisotropic part of the tensors of the magnetic and electric interactions

Relaxation is faster:

- the greater the fluctuating magnetic fields
- in EPR much larger than in NMR also because of the much stronger magnetic moment
- the more relevant the components of molecular motions with suited frequency
- the frequencies relevant to EPR are at least 100 times higher than for NMR
- the T_1 in EPR are much smaller than in NMR

Dipolar mechanism

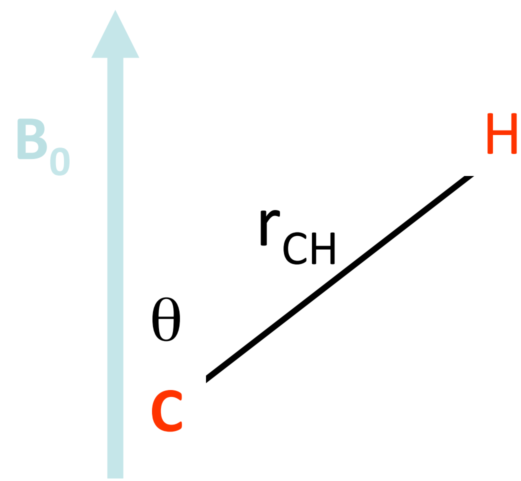
- For ^{13}C nuclei of atoms directly bound to hydrogen, is the main relaxation mechanism
- In the case of fast motions the relaxation rate of a ^{13}C close to a ^{1}H is:

$$\frac{1}{T_{1dip}} = \left(\frac{\mu_0}{4\pi}\right)^2 \hbar^2 \gamma_C^2 \gamma_H^2 \frac{1}{r_{C-H}^6} \tau_C$$

A quantitation of the relevance of the dipolar mechanism is obtained through NOE measurements

Nuclear Overhauser Effect for a heteronuclear $^{1}H^{13}C$ system

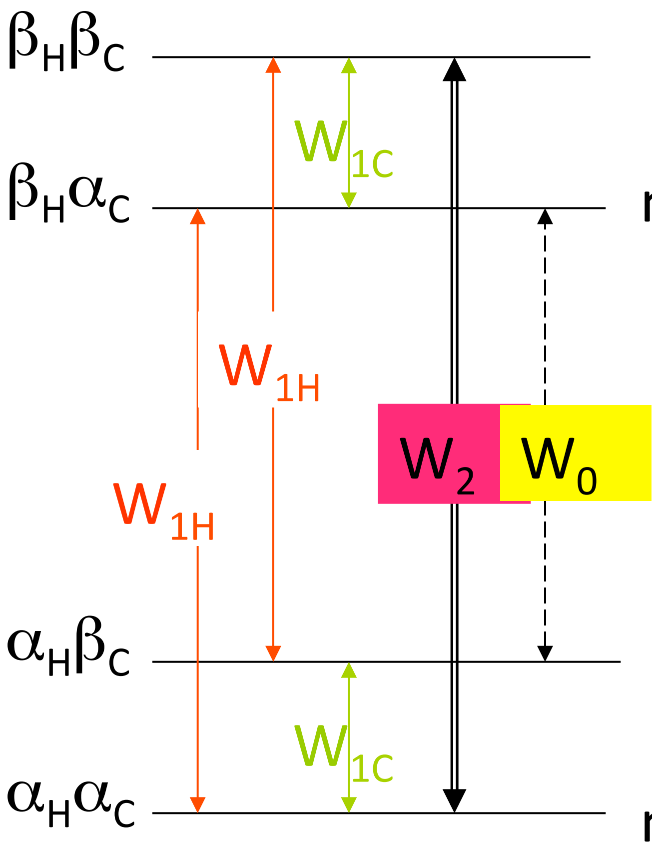
The nuclei are close in space and exclusively the through space dipolar interaction is considered



The H nuclear dipole generates magnetic field on the C and viceversa. Due to molecular motind θ (and r provided the C-H distance is not fixed) vary in time.

These magnetic fields, fluctuating in the laboratory axis systems, cause the mutual relaxation of the two nuclei.

Energy Levels and Populations for the System CH



$n_{\beta\beta} = N_{\beta H0} + b + N_{\beta C0} + a$

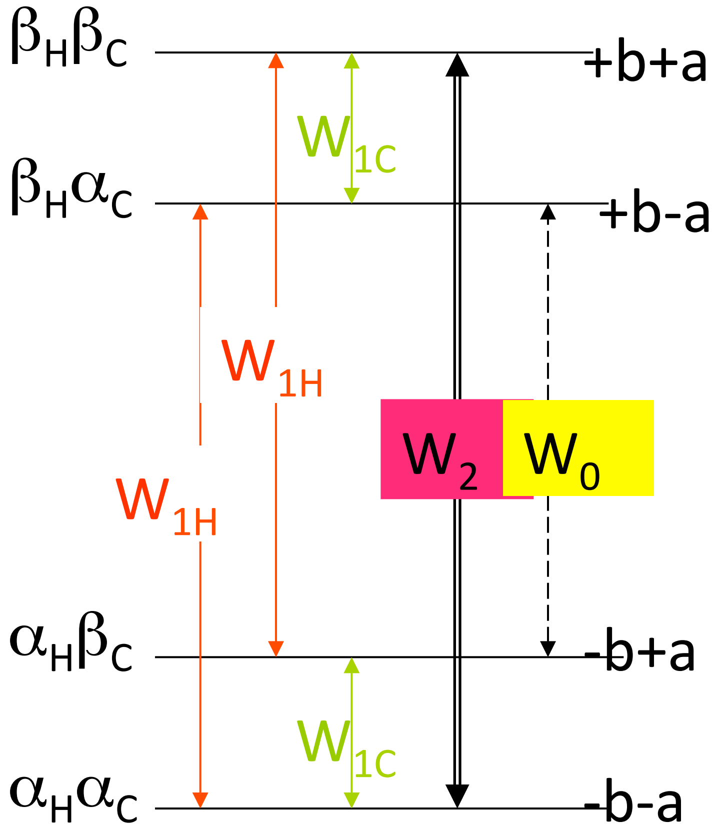
$n\beta\alpha = N_{\beta H0} + b + N_{\alpha C0} - a$

$n\alpha\beta = N_{\alpha H0} - b + N_{\beta C0} + a$

$n\alpha\alpha = N_{\alpha H0} - b + N_{\alpha C0} - a$

In the presence of dipolar coupling *cross-relaxation* occurs

Variation on Time of Populations



$$\frac{dn_{\alpha\beta}}{dt} = W_{1H}b + W_{1c}(-a) + W_0(b-a)$$
$$-W_{1H}(-b) - W_{1C}a - W_0(-b+a) =$$
$$= 2bW_{1H} - 2aW_{1C} + 2(b-a)W_0$$

$$\frac{dn_{\beta\beta}}{dt} = W_{1H}(-b) + W_{1c}(-a) + W_2(-b-a)$$
$$-W_{1H}b - W_{1C}a - W_2(a+b) =$$
$$= -2bW_{1H} - 2aW_{1C} - 2(a+b)W_2$$

$$\frac{dn_{\beta\alpha}}{dt} = W_{1H}(-b) + W_{1C}a + W_0(-b+a) - W_{1H}b - W_{1C}(-a) - W_0(b-a)$$

$$\frac{dn_{\beta\beta}}{dt} = -2bW_{1H} - 2aW_{1C} - 2(a+b)W_2$$

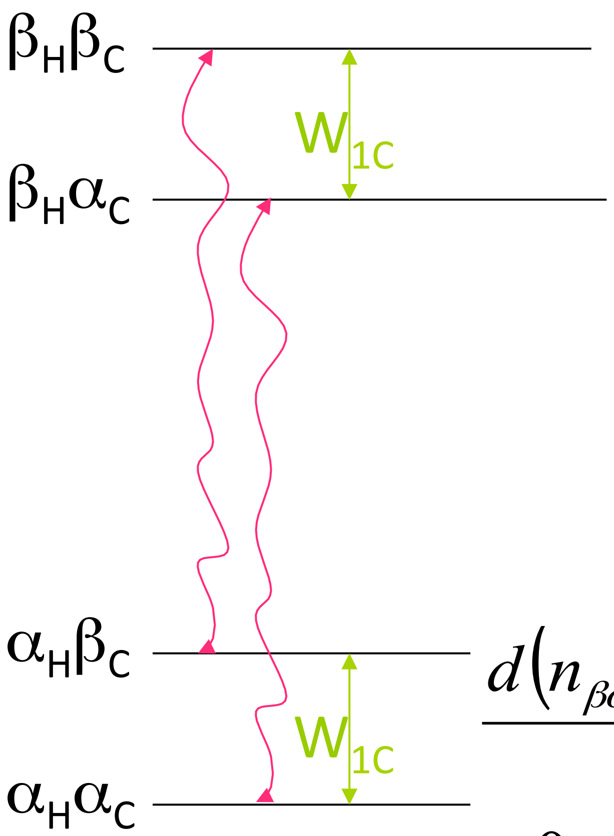
$$\frac{dn_{\beta\alpha}}{dt} = -2W_{1H}b + 2W_{1C}a - 2W_0(b-a)$$

for one ^{13}C transition:

$$\frac{d\left(n_{\beta\alpha} - n_{\beta\beta}\right)}{dt} = 4aW_{1C} - 2W_0\left(b-a\right) + 2(a+b)W_2$$

$$= 2a(2W_{1C} + W_2 + W_0) + 2b(W_2 - W_0)$$

Steady-state NOE



The experiment implies the continuos irradiation of proton transitions

ΔH= 0

At the steady state:

$$\frac{d\left(n_{\beta\alpha} - n_{\beta\beta}\right)}{dt} = 2a(2W_{1C} + W_2 + W_0) + 2b(W_2 - W_0)$$

$$= 0$$

concerns one ^{13}C transition

$$2a(2W_{1C} + W_2 + W_0) + 2b(W_2 - W_0) = 0$$

$$\frac{2a}{2b} = -\frac{W_2 - W_0}{2W_{1C} + W_2 + W_0} = \frac{\Delta C - \Delta C_0}{\Delta H - \Delta H_0}$$

ΔC is the ^{13}C population difference

ΔC_0 is the equilibrium ^{13}C population difference

analogously for ^{1}H

During the steady state experiment ΔH= 0

$$\frac{\Delta C - \Delta C_0}{-\Delta H_0} = -\frac{W_2 - W_0}{2W_{1C} + W_2 + W_0}$$

$$\frac{\Delta C - \Delta C_0}{\Delta H_0} = \frac{W_2 - W_0}{2W_{1C} + W_2 + W_0}$$

$$\frac{\Delta H_0}{\Delta C_0} = \frac{\gamma_H}{\gamma_C}$$

Where:

S_0 the intensity of the C signal for the unperturbed system

S_s that in the presence of steady state NOE

$$\frac{S_s - S_0}{S_0 \frac{\gamma_H}{\gamma_C}} = \frac{W_2 - W_0}{2W_{1C} + W_2 + W_0}$$

$$\boxed{\frac{S_s - S_0}{S_0} = \frac{\gamma_H}{\gamma_C} \frac{W_2 - W_0}{2W_{1C} + W_2 + W_0} = \eta}$$

η: Nuclear Overhauser enhancement factor

$$\frac{S_S}{S_0} = 1 + \eta$$

S_s/S_0 is the ratio of the intensities of the carbon signal in the presence of steady state NOE and in the absence of proton irradiation

In the case of exclusive **dipolar relaxation** and **extreme narrowing** hold: $W_2 : W_{1C} : W_0$ 12: 3 : 2

which leads to:

$$1 + \eta = 1 + \frac{1}{2}\frac{\gamma_H}{\gamma_C}$$

Since $\gamma_H/\gamma_C \approx 4$, the C signals with NOE have intensity 1+ η= 1+2

NB the effect magnitude **does not depend** on the number of close protons

Internuclear Distances by means of NOE

- When the dipolar interaction between the two nuclei is only one of the mechanisms that cause relaxation the observed NOE is not full
- The other transition probabilities, $W_{1C}*$, acting as leakage pathways, decrease the NOE

$$\eta = \frac{\gamma_H}{\gamma_C} \frac{W_2 - W_0}{2W_{1C} + W_2 + W_0 + 2W_{1C}*}$$

In the homonulcear case for overwhelming W*

$$\frac{1}{\eta} = 2 + \frac{2W*}{W_2 - W_0}$$

In the case of extreme narrowing:

$$W_1 \propto \frac{3\tau_c}{r^6} \qquad W_0 \propto \frac{2\tau_c}{r^6} \qquad W_2 \propto \frac{12\tau_c}{r^6}$$

e

$$W_2 - W_0 \propto \frac{10\tau_c}{r^6}$$

$$\frac{1}{\eta} \propto 2 + 2\rho * \frac{r^6}{\tau_c}$$

For analogous molecules it can be expected that ρ^*/τ_c are the same, so that the measured NOEs are proportional to r^{-6}.

In this way infomation on distances is obtained

Steady State NOE η: Dependence on the Motional Regime

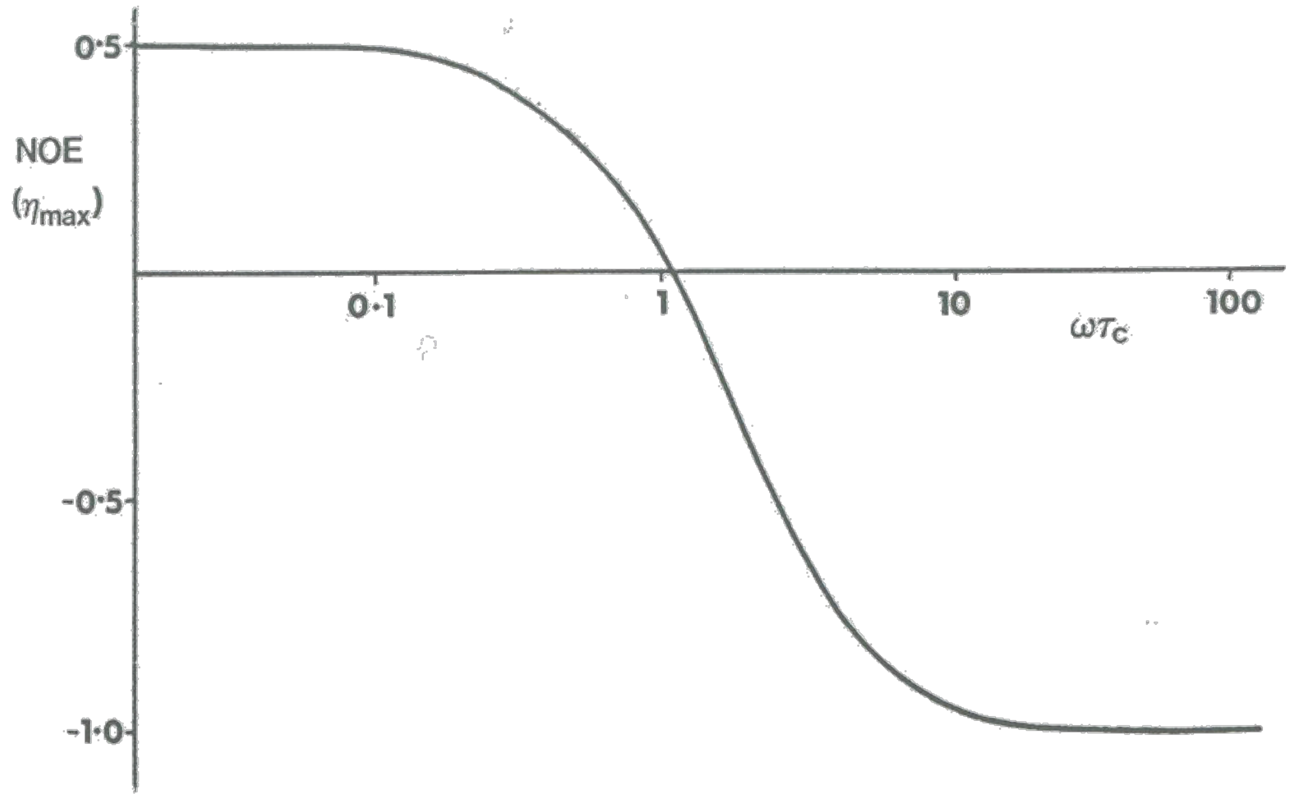
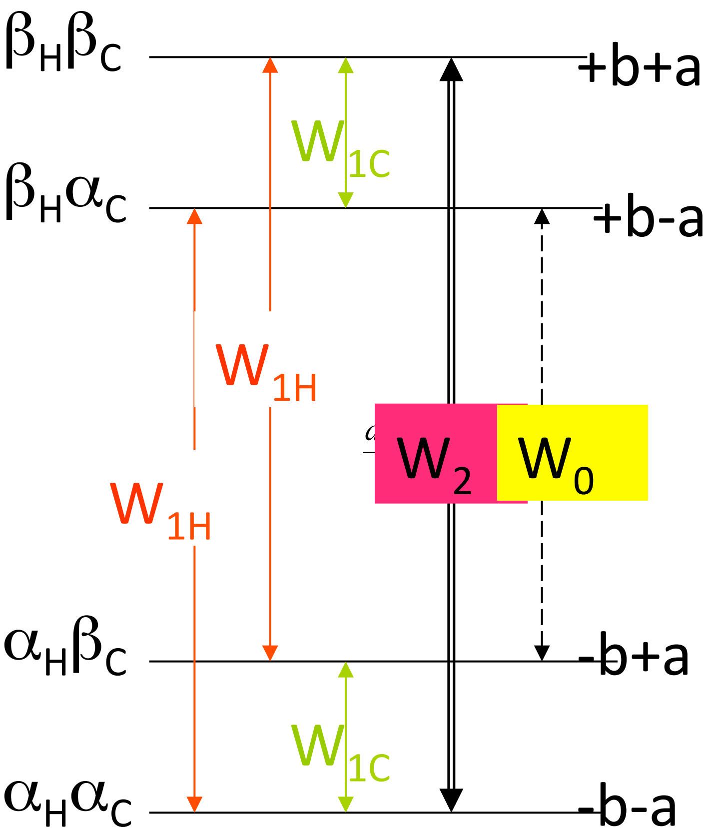


FIGURE 2.6
Dependence of maximum homonuclear NOE enhancement on $\omega\tau_c$. Note the log scale of $\omega\tau_c$.

TOE (Transient NOE)



Starting condition: π pulse on ^{1}H

$\Delta H_{180} = -\Delta H_0$ $2b = 2\Delta H_0$

$\Delta C = \Delta C_0$ $2a = 0$

since ΔH_0 and ΔC_0 are constants

$$\frac{d(\Delta H - \Delta H_0)}{dt} = \frac{d\Delta H}{dt}$$

$$\frac{d(\Delta C - \Delta C_0)}{dt} = \frac{d\Delta C}{dt}$$

$$\frac{dn_{\beta\beta}}{dt} = -2bW_{1H} - 2aW_{1C} - 2(a+b)W_2$$

$$\frac{dn_{\beta\alpha}}{dt} = -2W_{1H}b + 2W_{1C}a - 2W_0(b-a)$$

$$\frac{dn_{\alpha\beta}}{dt} = 2W_{1H}b - 2W_{1C}a + 2W_0(b-a)$$

2 a= -(ΔC-ΔC_0)

2 b= -(ΔH-ΔH_0)

$$\frac{d\Delta C}{dt} = \frac{d\left(n_{\beta\alpha} - n_{\beta\beta}\right)}{dt} = 2a(2W_{1C} + W_2 + W_0) + 2b(W_2 - W_0)$$

$$\frac{d\Delta H}{dt} = \frac{d\left(n_{\alpha\beta} - n_{\beta\beta}\right)}{dt} = 2b(2W_{1H} + W_2 + W_0) + 2a(W_2 - W_0)$$

$$\frac{d\left(\Delta C-\Delta C_0\right)}{dt}=-\left(\Delta C-\Delta C_0\right)\left(2W_{1C}+W_2+W_0\right)-\left(\Delta H-\Delta H_0\right)\left(W_2-W_0\right)$$

$$\frac{d\left(\Delta H-\Delta H_0\right)}{dt}=-\left(\Delta H-\Delta H_0\right)\left(2W_{1H}+W_2+W_0\right)-\left(\Delta C-\Delta C_0\right)\left(W_2-W_0\right)$$

Performing the following substitutions:

$x=(\Delta H-\Delta H_0)$ $\quad$ $y=(\Delta C-\Delta C_0)$

$R_H= 2W_{1H}+W_2+W_0$ $\quad$ $R_C=2W_{1C}+W_2+W_0$ $\quad$ $\sigma_{HC}=W_2-W_0$

one recognizes two coupled first order differential equations

Solomon Equations

$$\frac{dx}{dt}=-R_H x-\sigma_{HC} y$$

$$\frac{dy}{dt}=-R_C y-\sigma_{HC} x$$

Solution for the homonuclear case

The solution is simple for $R_H = R_C$ (homonuclear case)

$$y(\tau) = 1/2\exp(-R\tau)\left[\exp(\sigma\tau) - \exp(-\sigma\tau)\right] = \exp(-R\tau)\sinh(\sigma\tau)$$

- for τ > 0 y(τ) is the product of an increasing function and one decraseaing
- it must possess a maximum

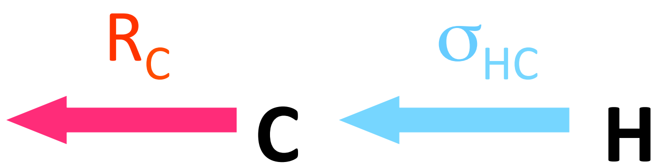
$$\tau_{Max} = \frac{1}{2\sigma}\ln\frac{R+\sigma}{R-\sigma}$$

The value of the maximum increment for the homonuclear transient NOE is::

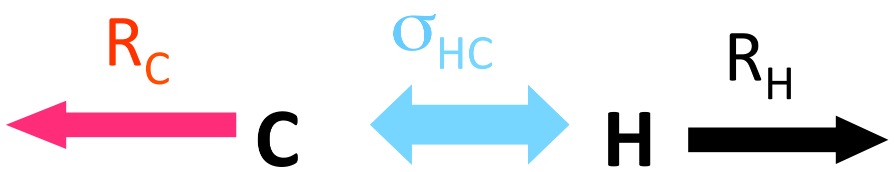
$$\eta_{Max}^{transiente} = \left(\frac{R+\sigma}{R-\sigma}\right)^{-\left[\frac{R-\sigma}{2\sigma}\right]} - \left(\frac{R+\sigma}{R-\sigma}\right)^{-\left[\frac{R+\sigma}{2\sigma}\right]}$$

Steady State **NOE** and **TOE:** Comparison

steady state NOE: asymmetric



transient NOE: symmetric



R refers to self-relaxation, σ to mutual relaxation

Depencence of TOE η on the Motional Regime

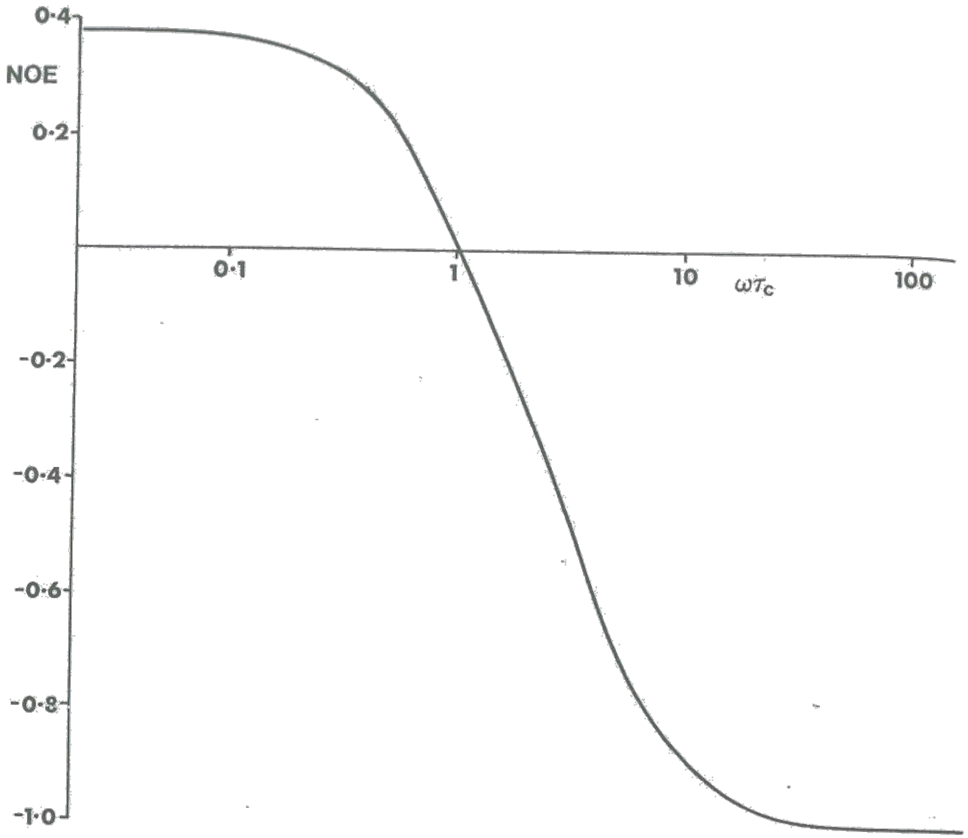
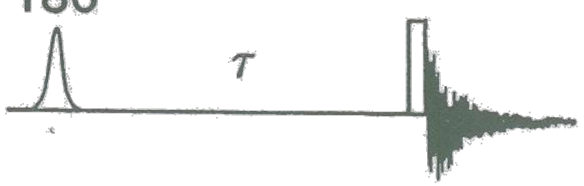


FIGURE 4.16
Plot of $\eta_{max}^{transient}$ (the maximum enhancement attainable in a two-spin homonuclear system, using a transient NOE experiment) against $\omega\tau_c$. Note the similarity to the curve for steady-state enhancements vs. $\omega\tau_c$ (Figure 2.6).



Rotating Frame Nuclear Overhauser Effect

~~transverse cross-relaxation~~

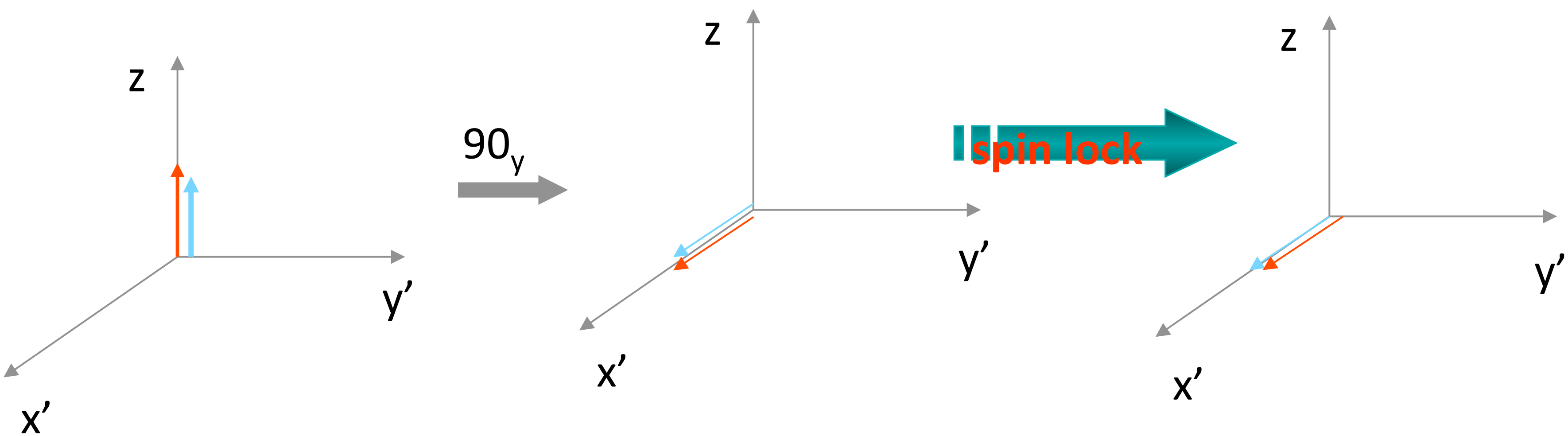
There is no polarization transfer between spin I and spin S transverse magnetizations

It happens exclusively when $\omega_I = \omega_S$, i.e. degenerate nuclei, or

when the two nuclei look degenerate, that is they have the same Lamor frequency

The former case is not interesting because it is impossible to detect the magnetization tranfer between two degenerate spins

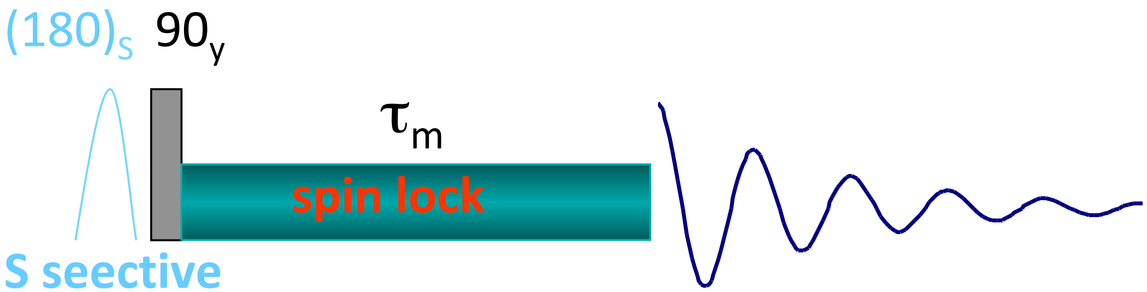
We can pretend that the two nuclei have the same Larmor frequency by the spin lock



they can cross talk because they are close

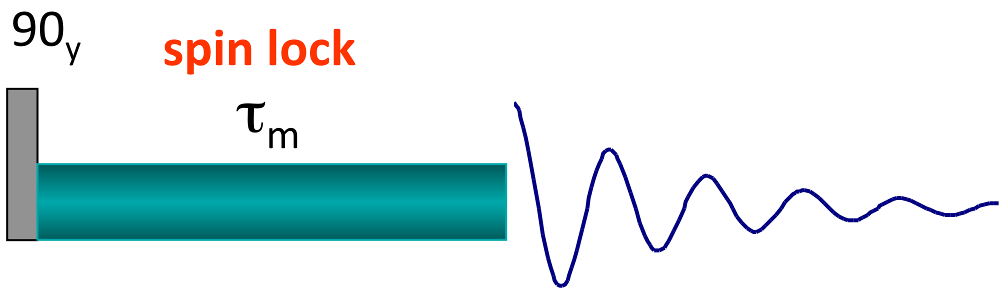
- ✓ The simplest spin lock consists of a r. f. magnetic field on x’
- ✓ The field must be strong enough so that the effective field is on the x’ axis for both spins, which have different off-sets
- ✓ In the rotating frame the transverse magnetizations of both spins appear static
- ✓the magnetization is called spin locked
- ✓since the two vectors, M_I and M_S, do not diverge during the application of the spin lock, they look to possess the same Larmor frequency
- ✓ under these conditions transverse cross-relaxation can take place
- ✓ the result can be detected by recording the usual FID after the removal of the spin lock

1D ROE Experiment



La combinazione dell'impulso selettivo di π e di quello (non selettivo) di 90 genera uno stato in cui M_I è lungo x' mentre M_S è lungo –x'

Durante lo spin-lock può avvenire la cross-relaxation trasversale



reference spectrum without cross-relaxation

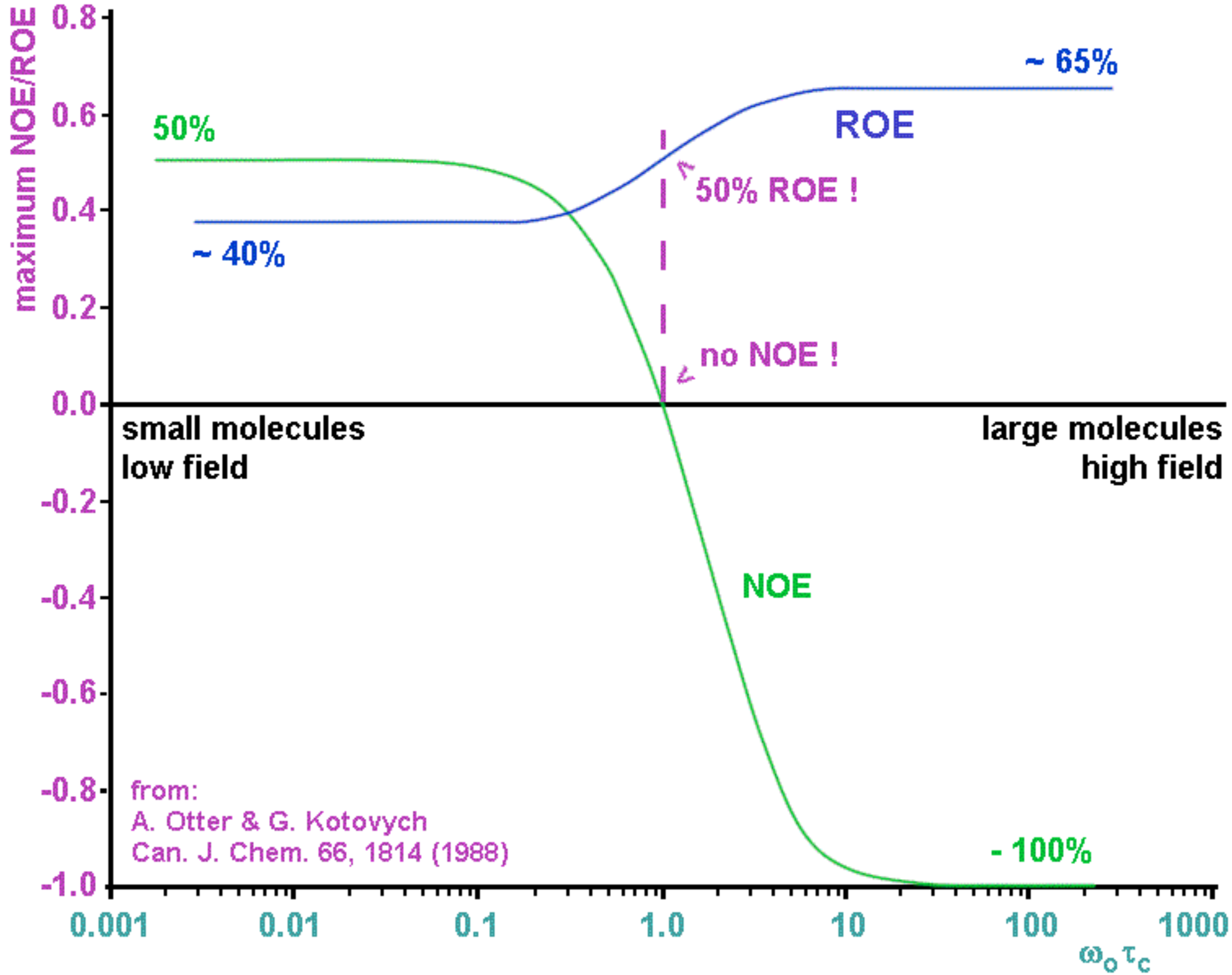
for DIFFROE

without the first selective 180 pulse

Dependence on the molecular tumbling frequency

- The NOE is positive for motions faster than the Larmor frequency
- is negative for slow motions
- it is zero for intermediate motional regimes
- The TOE displays an analogous dependence as NOE, its maximum value is slightly lower
- The ROE is always positive and it does not become zero because of the motional regime !!!

η Comparison for NOE and ROE



http://nmr.chem.ualberta.ca/nmr_news/98-08.htm

In the case of off-resonance ROE , that is the effective B is not lying on the transverse plane, there is a combination of ROE (for the transverse components) and of NOE per le componenti longitudinali

- The signal intensity is proprtional to $\gamma \cdot \gamma^{3/2}$
- By means of NOE an increase of intensity is obtained by an artificial increase of the Boltzmann factor (the population difference)
- It is needed that the weak nucleus is relaxed mainly by the dipolar coupling with protons. ^{15}N and ^{29}Si have $\gamma < 0$ and their increments are < 0 (-5 for ^{15}N)

Dynamic Nuclear Polarization Electron-Nucleus in Soluzione

- The term DNP is properly used to adress the polarization transfer from e- to nucleus
- It can be obtained both in solid and in liquid state
- The Overhauser Effect is the mechanism for the DNP in solution