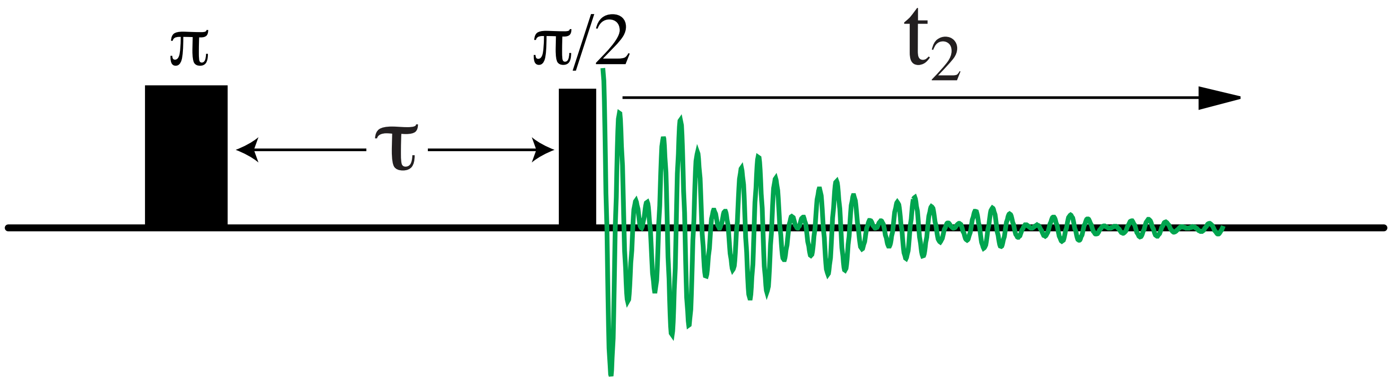
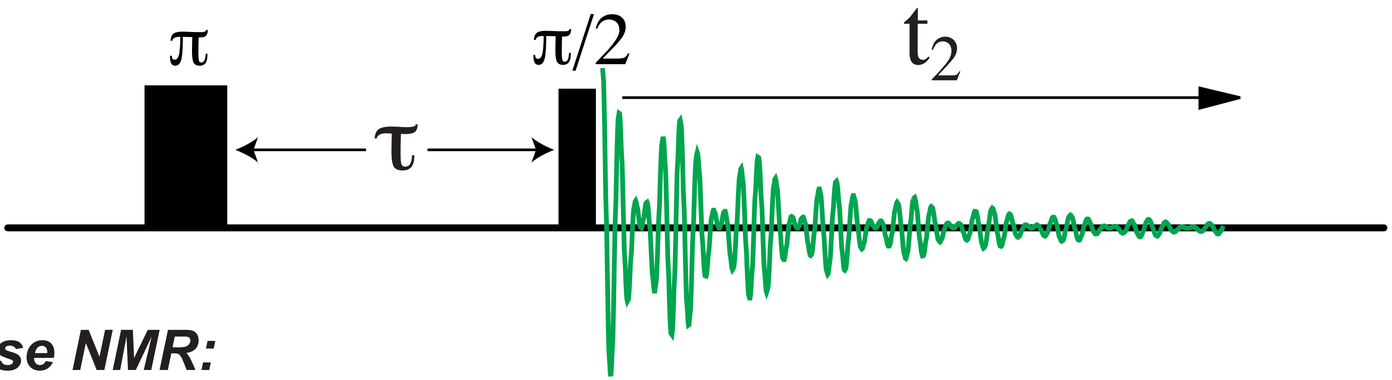
Advanced NMR & Imaging

Week 7: Spin Echoes, Diffusion, & Coherence Transfer

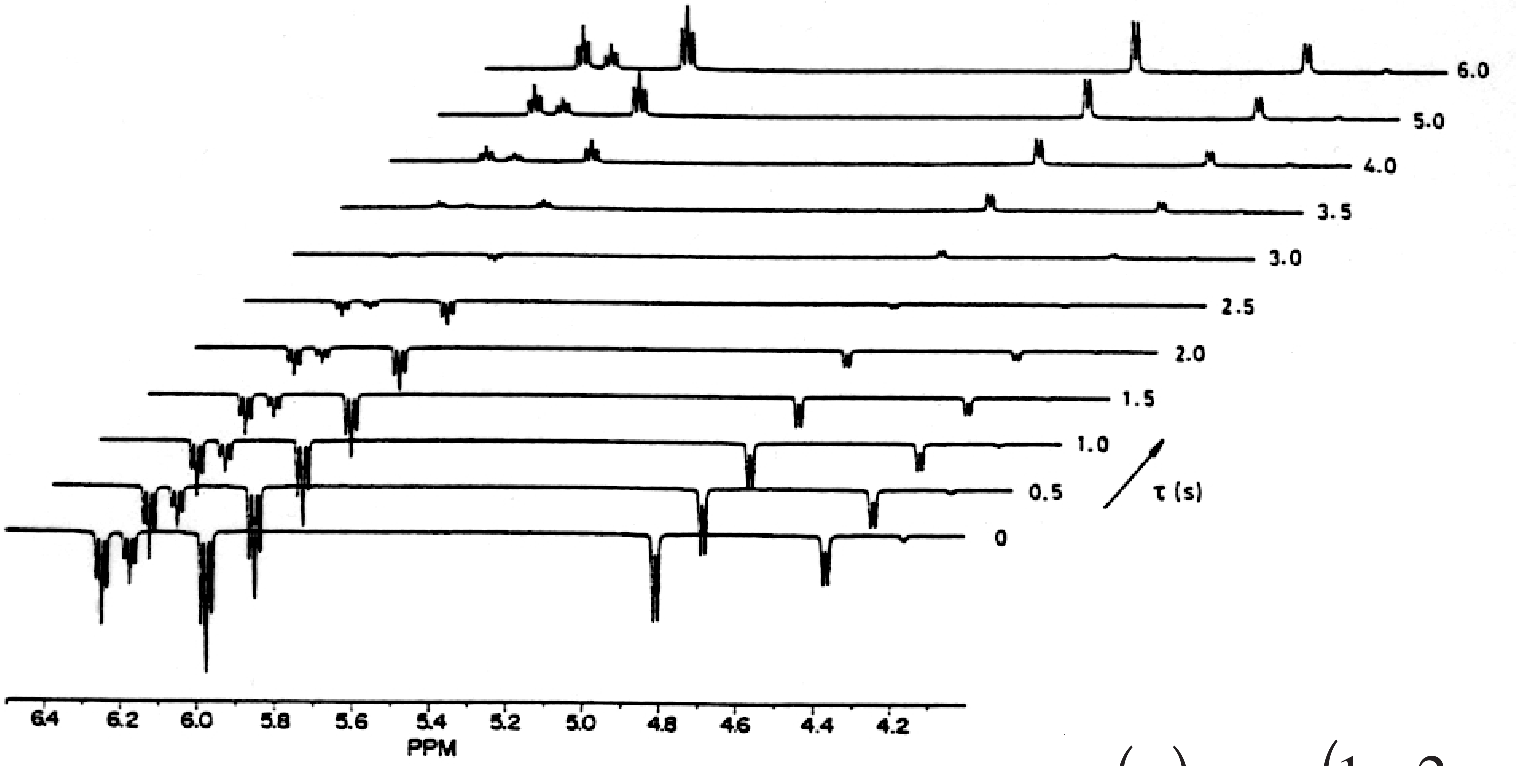
Dances with Spins: Multiple-Pulse NMR



Dances with Spins: Inversion-Recovery



Multiple-Pulse NMR:
Measurement of Longitudinal Relaxation Rates (T_1)



$$\alpha(\tau) = \alpha_0\left(1 - 2\exp(\tau/T_1)\right)$$

Objectives

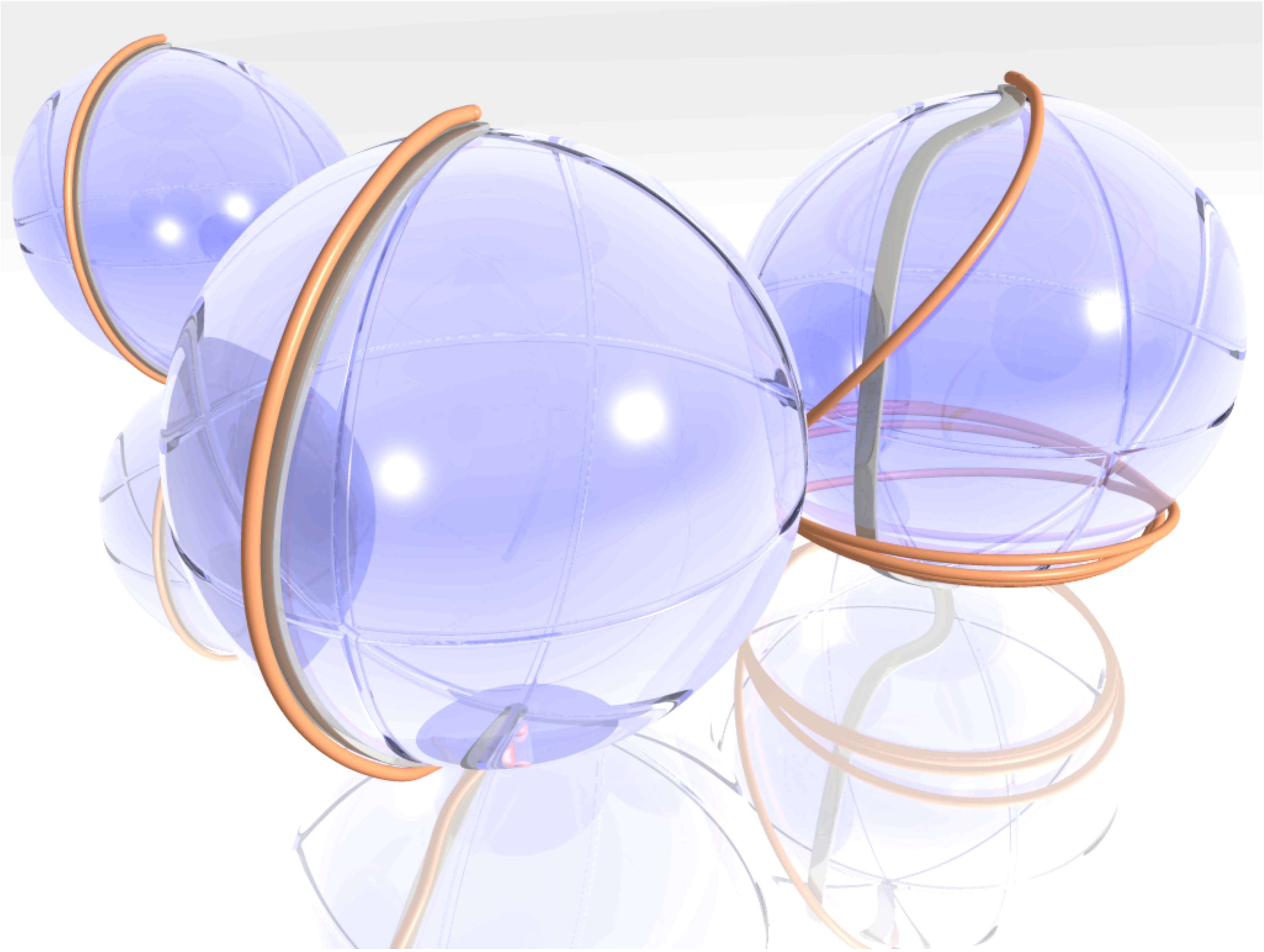
- Use the quantum-mechanical based vector description of NMR to develop and understand multiple pulse NMR spectroscopy

- Understand the principles of spin echoes

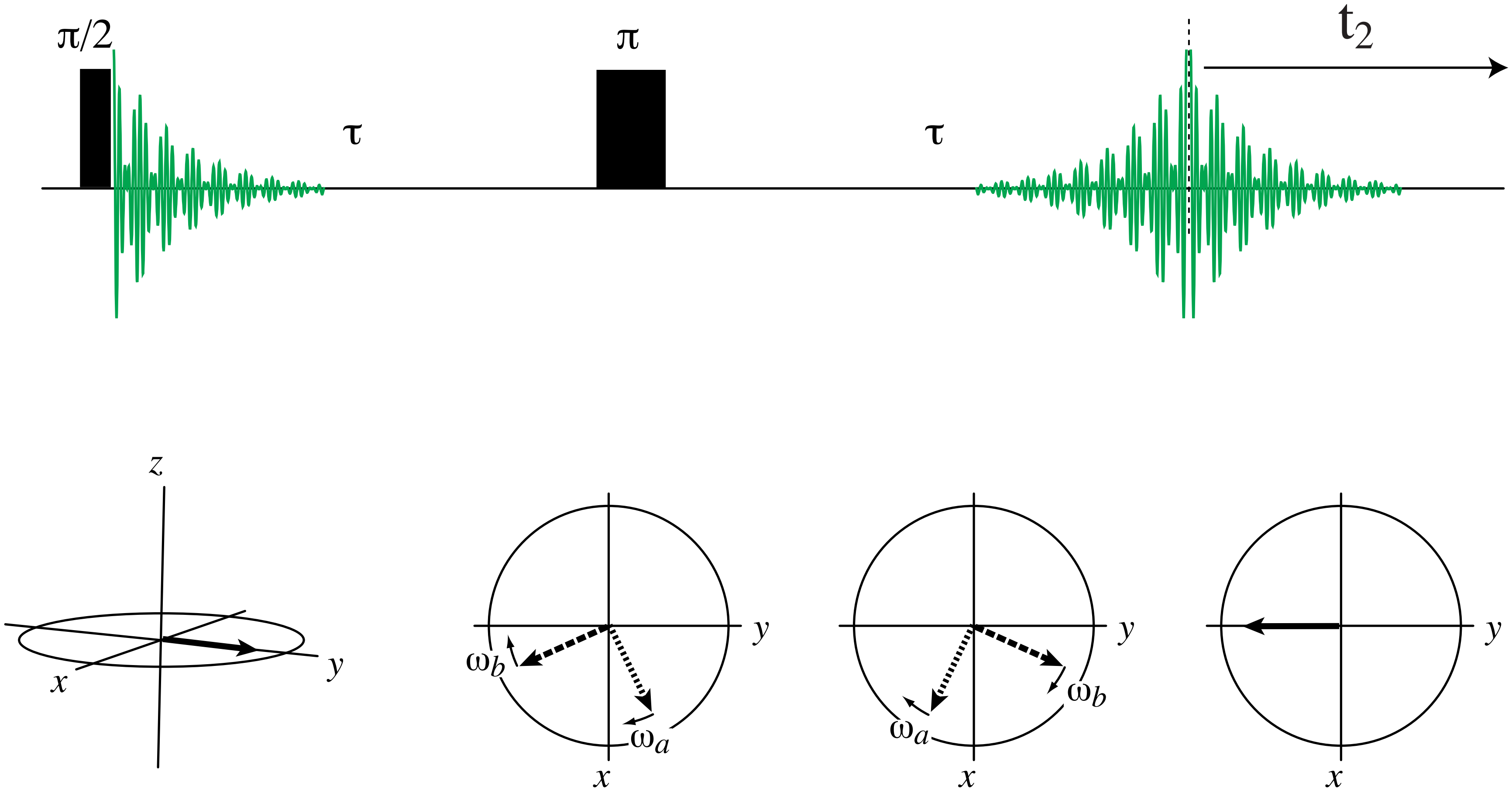
- Be able to use the product operator formalism to describe coherence transfer in coupled two-spin systems

- Understand the INPET experiment

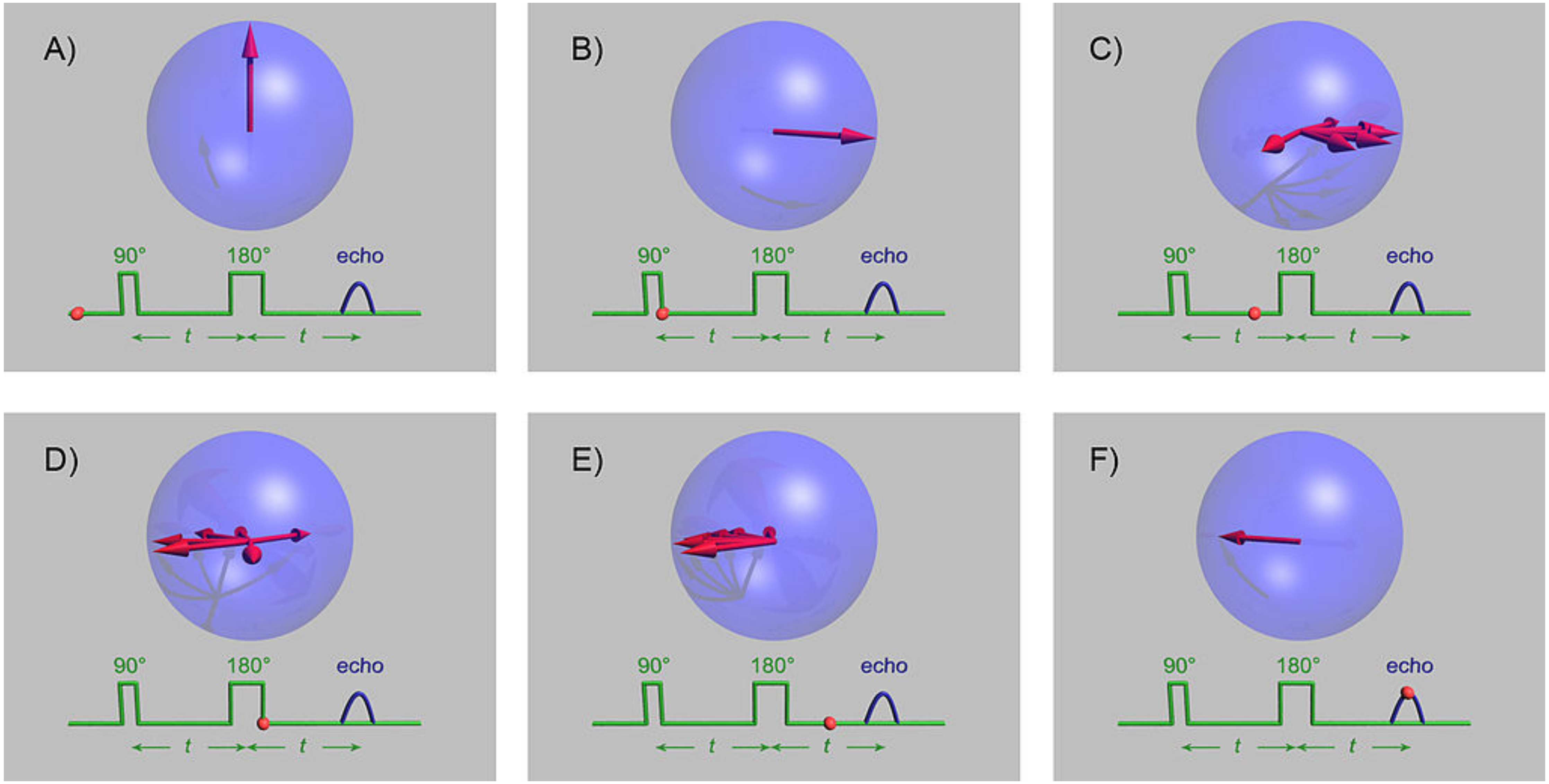
Dances with Spins



Dances with Spins: The Spin Echo

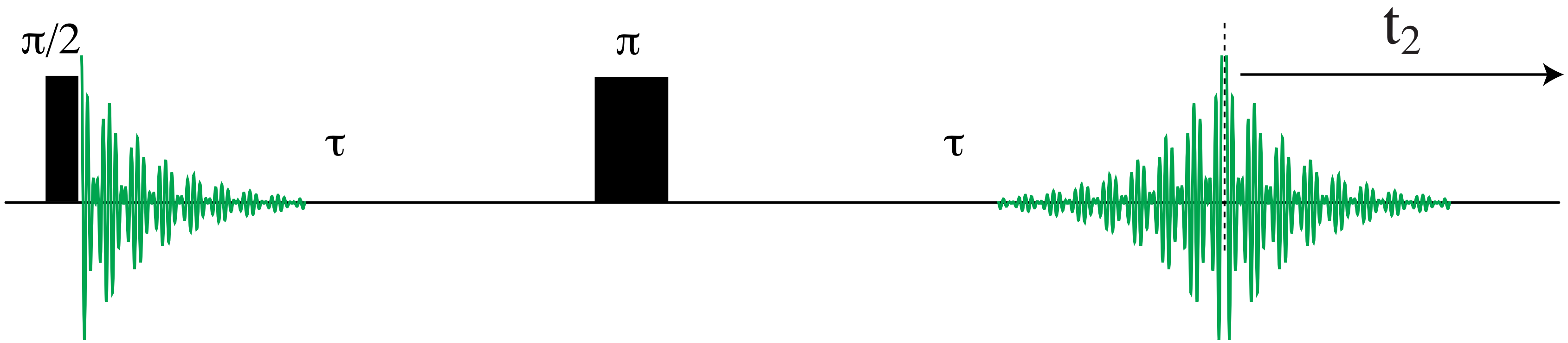


The Hahn Echo



https://en.wikipedia.org/wiki/Spin_echo

Dances with Spins: The Spin Echo



Multiple-Pulse NMR:
Measurement of Transverse Relaxation Rates (T_2)

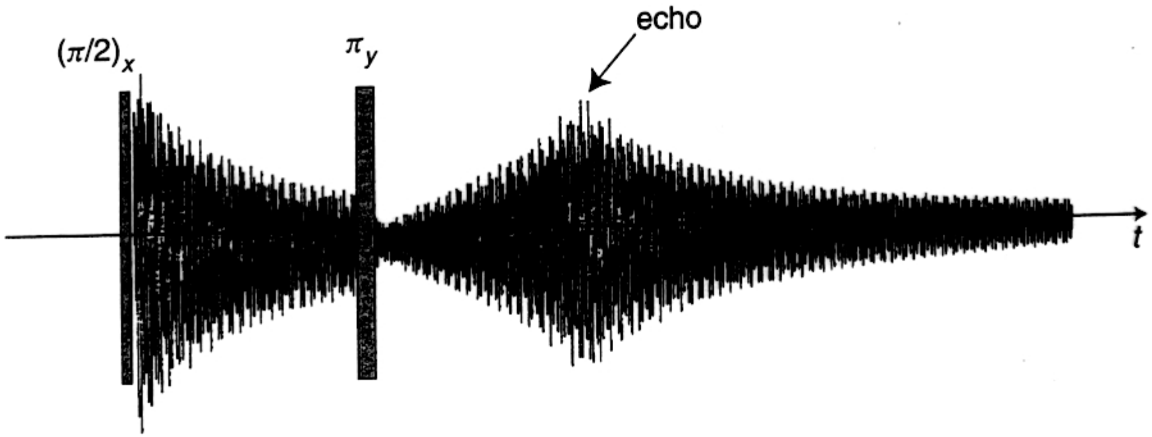
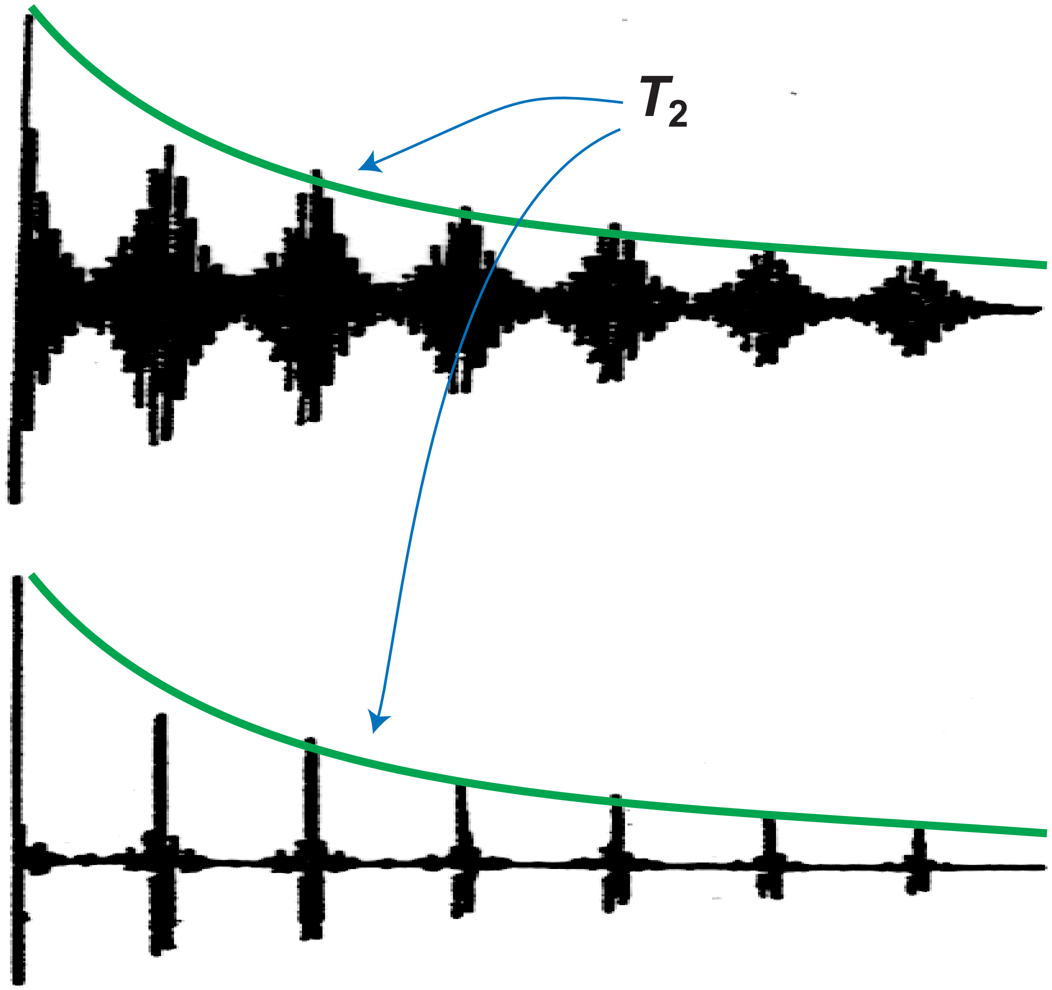


Figure 11.19 Experimental echo signal. Adapted from A. E. Derome, *Modern NMR Techniques for Chemistry Research*, Pergamon Press, Oxford, 1987, p. 91. (Reproduced by permission of Elsevier Science).

Dances with Spins: The Spin Echo

Multiple-Pulse NMR:
Measurement of Transverse Relaxation Rates (T_2)



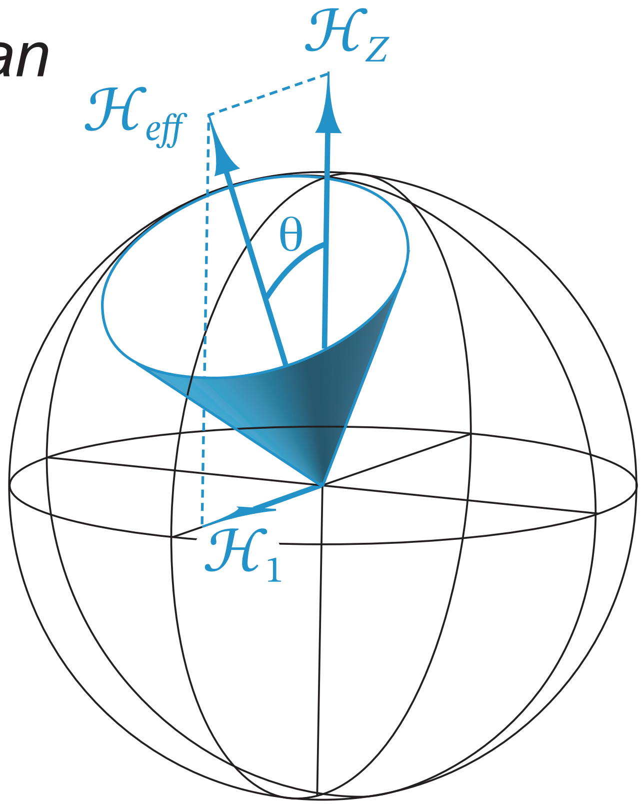
Spin Dynamics

$$\sigma(t) = \exp(-i\mathcal{H}t)\,\sigma(0)\exp(+i\mathcal{H}t)$$

the state at
a given time

the system Hamiltonian

the initial state



The motion of the ensemble magnetic moment (bulk magnetization, polarisation, a rotation around an axis defined by the Hamiltonian.

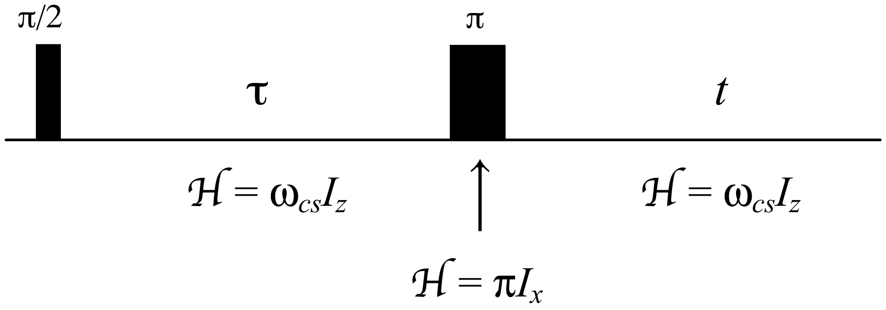
In the following we will often talk about the unitary evolution operator
$U = \exp(-iHt)$

Dances with Spins: The Spin Echo

We see from a very simple classical analysis that we expect the sequence to "refocus" the chemical shift interaction. Can we obtain this result analytically?

For a spin whose resonance frequency in the rotating frame is ω_{cs},

$$\mathcal{H} = \omega_{cs} I_z$$



(if we consider the pulse to be short compared to the chemical shift frequencies, then we can neglect chemical shift evolution during the pulse (the delta pulse approximation))

at time τ we have the operator for evolution

$$U = \exp(-i\omega_{cs}\tau I_z)$$

Immediately after the second pulse we have

$$U(\tau_+) = \exp(-i\pi I_x)\exp(-i\omega_{cs}\tau I_z),$$

and at a time t later this becomes

$$U(t+\tau) = \exp(-i\omega_{cs} t I_z)\exp(-i\pi I_x)\exp(-i\omega_{cs}\tau I_z)$$

which can be written under the form

$$U(t+\tau) = \exp(-i\omega_{cs}(t-\tau)I_z)\exp(-i\omega_{cs}\tau I_z)\exp(-i\pi I_x)\exp(-i\omega_{cs}\tau I_z). \tag{1.105}$$

Dances with Spins: The Spin Echo

$$U(t+\tau) = \exp(-i\omega_{cs}(t-\tau)I_z)\exp(-i\omega_{cs}\tau I_z)\exp(-i\pi I_x)\exp(-i\omega_{cs}\tau I_z). \qquad (1.105)$$

Considering the last three operators on the right hand side of eq. (1.105)

$$R = \exp(-i\omega_{cs}\tau I_z)\exp(-i\pi I_x)\exp(-i\omega_{cs}\tau I_z). \qquad (1.106)$$

It can be shown that if U is a unitary operator, $U\exp(A)U^{-1} = \exp\left(UAU^{-1}\right)$, and going back to equation (1.106) we can write

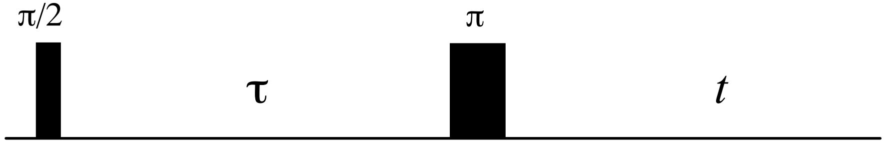
$$R = \exp(-i\omega_{cs}\tau I_z)\exp(-i\pi I_x)\exp(-i\omega_{cs}\tau I_z)\exp(i\pi I_x)\exp(-i\pi I_x)$$

where $\exp(-i\pi I_x)\exp(-i\omega_{cs}\tau I_z)\exp(i\pi I_x) = \exp(i\omega_{cs}\tau I_z)$ and equation (1.106) yields

$$R = \exp(-i\omega_{cs}\tau I_z)\exp(i\omega_{cs}\tau I_z)\exp(-i\pi I_x) = \exp(-i\pi I_x).$$

Thus, equation (1.105) becomes

$$U(t+\tau) = \exp(-i\omega_{cs}(t-\tau)I_z)\exp(-i\pi I_x) \qquad (1.112)$$



Dances with Spins: The Spin Echo

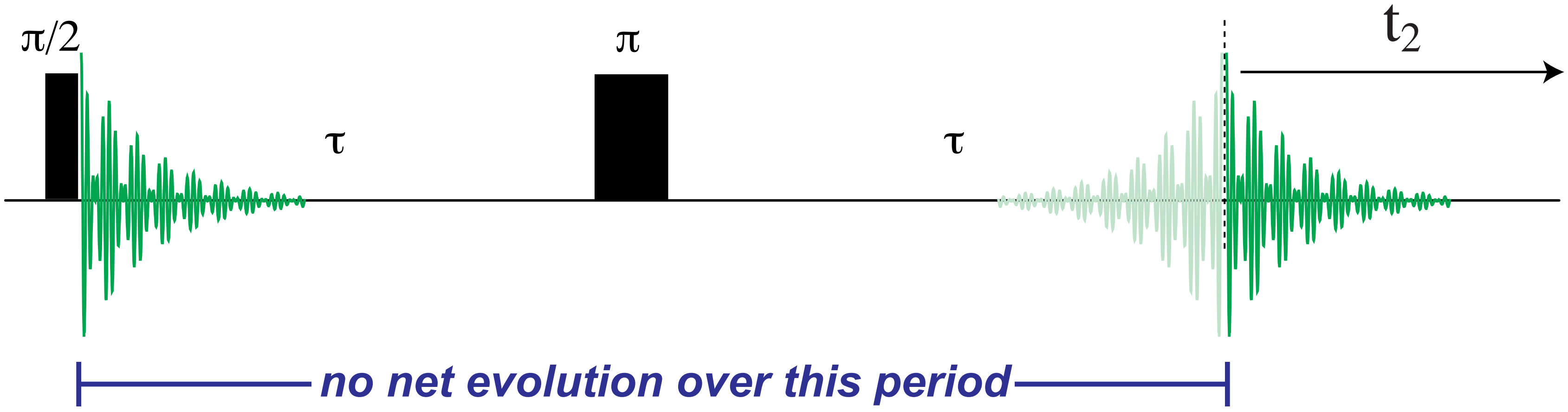
Average Hamiltonians

$$U(t+\tau) = \exp\left(-i\omega_{cs}(t-\tau)I_z\right)\exp\left(-i\pi I_x\right) \qquad (1.112)$$

Note that we have manipulated the evolution operator, which is a very common trick in NMR, and not the density matrix. Thus the result is valid for any initial state of the system represented by σ. We note that the total evolution operator consists of (i) an initial pulse of angle π about x, (ii) precession about z by an angle $\phi = \omega_{cs}(t-\tau)$. Note especially that for $\tau = t$,

$$\boxed{U(2\tau) = \exp\left(-i\pi I_x\right)} \qquad (1.113)$$

and the evolution is independent of chemical shift. This corresponds to the formation of a *spin echo*, as was predicted by the vector description.



Dances with Spins: The Spin Echo

Average Hamiltonians

no net evolution over this period
due to the chemical shift

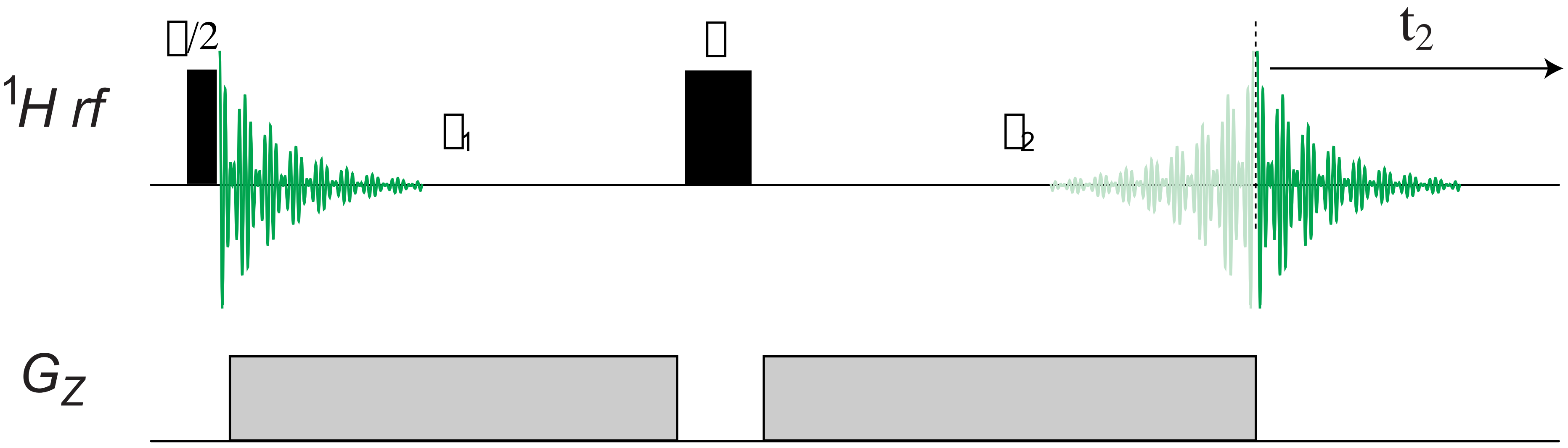
the intensity of the echo at time 2τ could be modulated by

transverse relaxation
molecular translational diffusion....

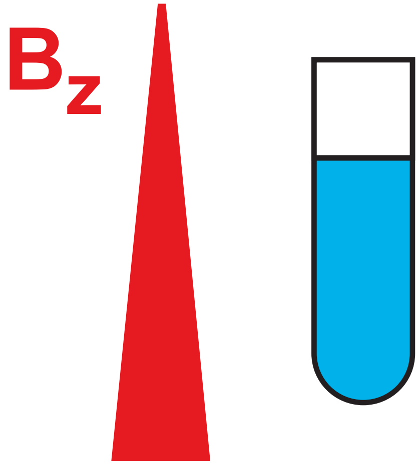
couplings to other spins.

NMR Measurement of Translational Diffusion

Pulsed Gradient Spin Echo (PGSE)



if a magnetic field gradient is generated across the sample, the spins will only be refocussed if their frequency is the same in τ_1 and τ_2.
This only happens if they do not move.

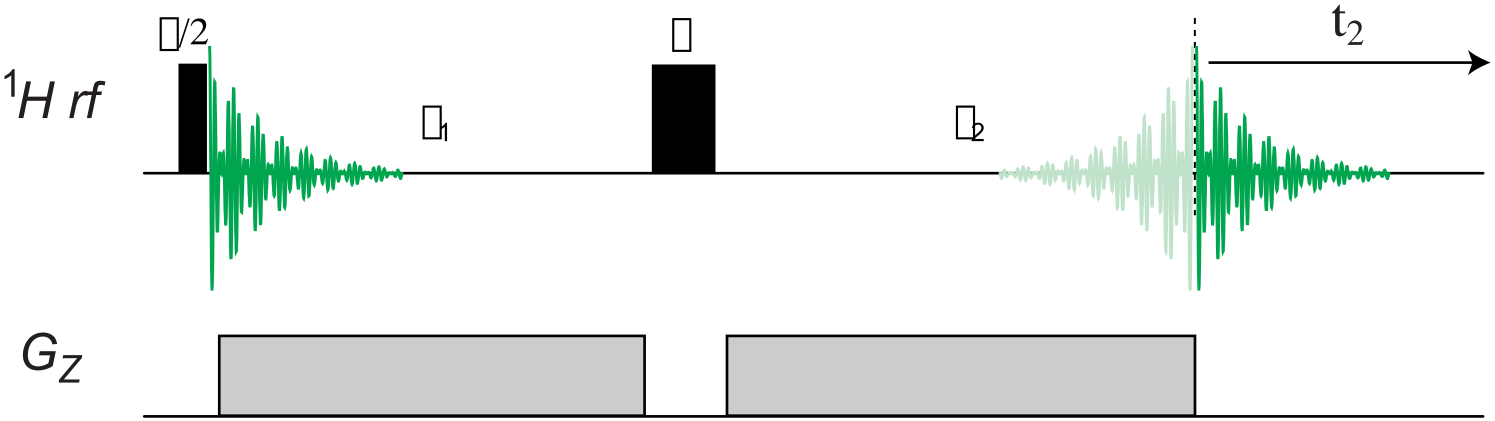


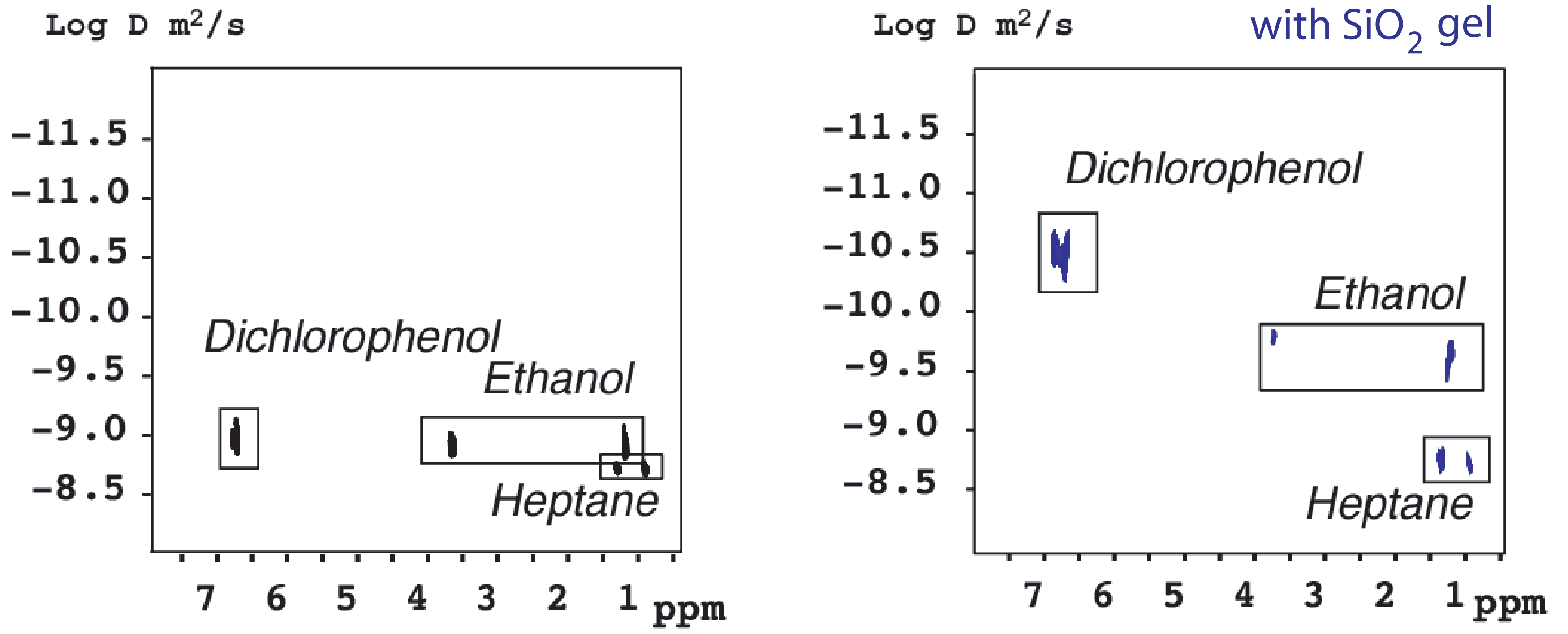
For Brownian translational diffusion, the echo intensity is given by:

$$I(2\tau) = I_0 \exp\left(-\frac{(2\tau)}{T_2}\right)\exp\left(-D(\gamma G_Z)^2 \frac{2\tau^3}{3}\right)$$

NMR Measurement of Translational Diffusion

*Pulsed Gradient Spin Echo (PGSE) / **DOSY***





Caldarelli and coworkers, *Proc. Natl. Acad. Sci. USA*, 2003

Conclusions: Part I

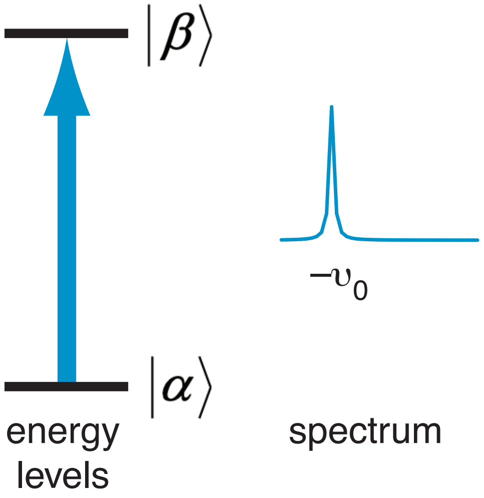
- The sequence τ - π - τ refocuses chemical shifts
- It leads to formation a “spin echo” at time 2τ, and allows measurement of T_2
- The average chemical shift Hamiltonian (or average propagator) for the sequence evaluated at times 2τ is zero.
- In the presence of a magnetic field gradient across the sample, the τ - π - τ sequence can be used to quantitatively measure translational diffusion in the sample. (The PGSE & DOSY experiments.)

Dances with Spins

What happens with more than one spin?

always better than “dancing with myself” (Billy Idol)
or “dancing on my own” (Robyn)??

Spin Operators & Basis Sets



So far we have been using the spin operators I_x, I_y *and* I_z to describe the state of a single spin. That is because, together with the identity matrix, **1**, they form a complete basis set.

For instance, the set of numbers

$$A_{ij} = \langle i|A|j\rangle$$

constitute the elements of the matrix representation of the operator A.

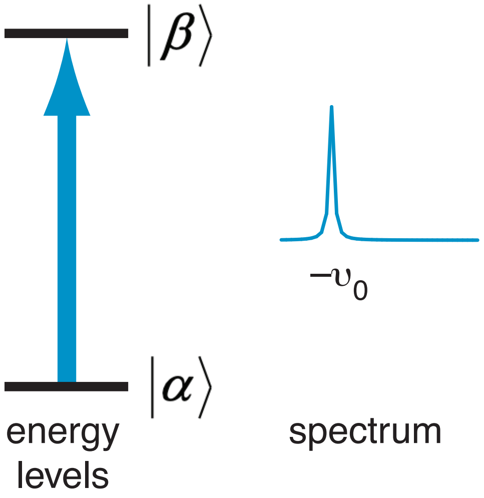
For a two-level, one spin $I = 1/2$ system, using the identity $1 = |1\rangle\langle 1| + |2\rangle\langle 2|$ to the left and right of an operator A, we obtain $A = A_{11}|1\rangle\langle 1| + A_{12}|1\rangle\langle 2| + A_{21}|2\rangle\langle 1| + A_{22}|2\rangle\langle 2|$ which yields a complete set of four orthogonal basis operators, with $1 = \alpha$ and $2 = \beta$,

$$|\alpha\rangle\langle\alpha| = I^{a} = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix} \qquad |\alpha\rangle\langle\beta| = I^{+} = \begin{pmatrix} 0 & 1 \\ 0 & 0 \end{pmatrix}$$

$$|\beta\rangle\langle\beta| = I^{\beta} = \begin{pmatrix} 0 & 0 \\ 0 & 1 \end{pmatrix} \qquad |\beta\rangle\langle\alpha| = I^{-} = \begin{pmatrix} 0 & 0 \\ 1 & 0 \end{pmatrix}$$

The operators I^{α} and I^{β} are called polarisatin operators and I^{+} and I^{-} are called shift operators.

Spin Operators & Basis Sets



$$|\alpha\rangle\langle\alpha| = I^{a} = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix} \qquad |\alpha\rangle\langle\beta| = I^{+} = \begin{pmatrix} 0 & 1 \\ 0 & 0 \end{pmatrix}$$

$$|\beta\rangle\langle\beta| = I^{\beta} = \begin{pmatrix} 0 & 0 \\ 0 & 1 \end{pmatrix} \qquad |\beta\rangle\langle\alpha| = I^{-} = \begin{pmatrix} 0 & 0 \\ 1 & 0 \end{pmatrix}$$

Basis sets are chosen for mathematical convenience, and a more often used basis set is obtained by taking the linear combinations:

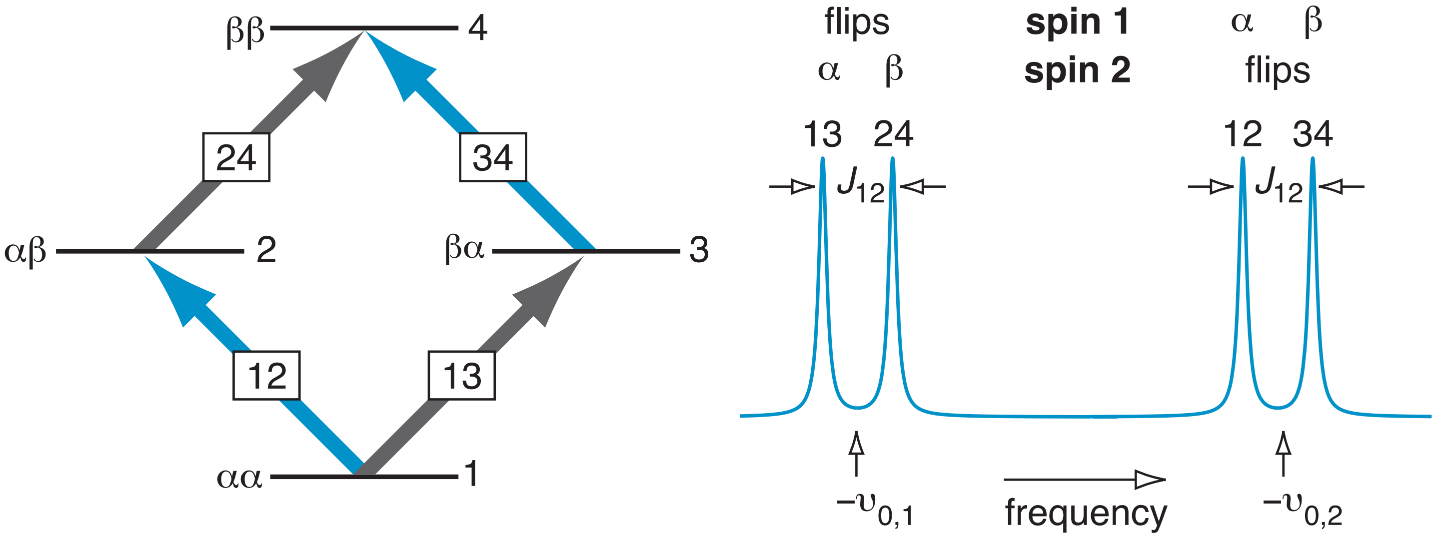
$$\tfrac{1}{2}\big(|1\rangle\langle 2| + |2\rangle\langle 1|\big) = I_x = \tfrac{1}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix} \qquad \tfrac{1}{2}\big(|1\rangle\langle 1| - |2\rangle\langle 2|\big) = I_z = \tfrac{1}{2}\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$$

$$-\tfrac{i}{2}\big(|1\rangle\langle 2| - |2\rangle\langle 1|\big) = I_y = \tfrac{i}{2}\begin{pmatrix} 0 & -1 \\ 1 & 0 \end{pmatrix} \qquad \tfrac{1}{2}\big(|1\rangle\langle 1| + |2\rangle\langle 2|\big) = \tfrac{1}{2}1 = \tfrac{1}{2}\begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix},$$

which are known as the Pauli matrices. Note that the fourth component is invariant to unitary transformation (rotation), such that the space is completely defined by I_x, I_y, and I_z.

(The three-dimensional space defined by the basis operators is called Liouville space (the space of operators) as opposed to the complex two-dimensional Hilbert space (the state space).)

Spin Operators & Basis Sets



To calculate effects on spectra of two coupled spins we must first determine a suitable new basis set. The Hilbert space is now sixteen dimensional and we obtain a product basis spanned by 16 basis operators of the two spins I and S:

$\mathbf{1}, I_x, I_y, I_z, S_x, S_y, S_z,$
$I_xS_x, I_xS_y, I_xS_z, I_yS_x, I_yS_y, I_yS_z, I_zS_x, I_zS_y, I_zS_z,$

Spin Operators & Basis Sets

The matrix representation of these operators is in terms of 4 x 4 matrices obtained from the Pauli matrices for spin I = 1/2 using the direct product as follows:

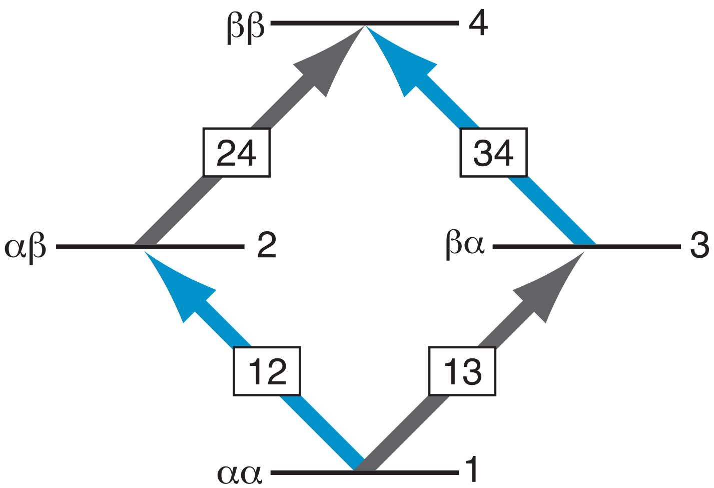
$$S_x = \mathbf{1} \otimes S_x = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \otimes \frac{1}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix} = \frac{1}{2}\begin{pmatrix} 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 \end{pmatrix}$$

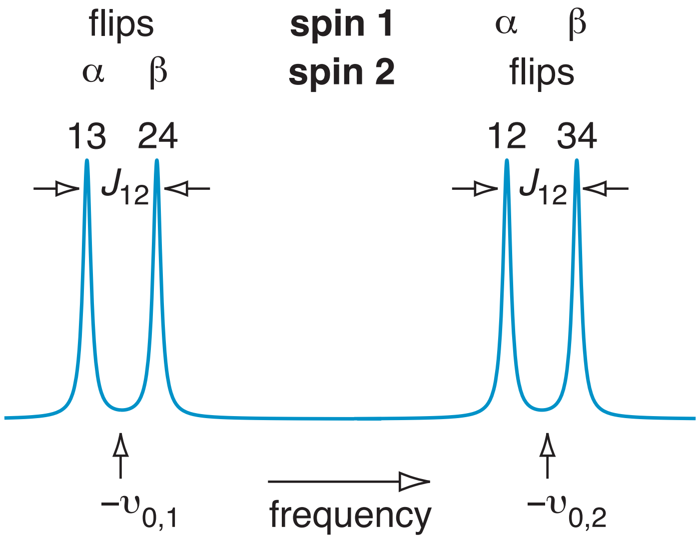
$$I_x = I_x \otimes \mathbf{1} = \frac{1}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix} \otimes \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} = \frac{1}{2}\begin{pmatrix} 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \end{pmatrix}$$

$$I_z S_z = I_z \otimes S_z = \frac{1}{2}\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} \otimes \frac{1}{2}\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} = \frac{1}{4}\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \quad \text{etc...}$$

Afterwards the calculation proceeds as before.

Hamiltonian in the 2 Spin System



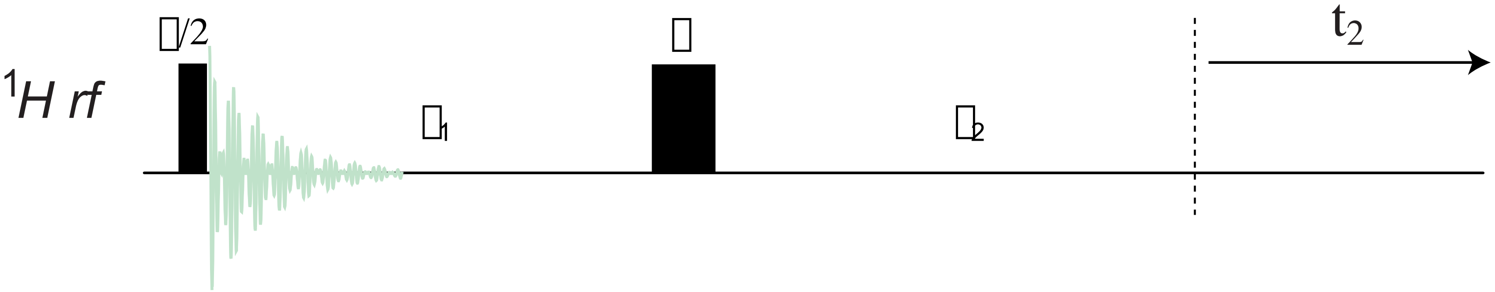


The full Hamiltonian can have up to 13 interactions. Fortunately most are usually zero or are unobservable. To describe the spectrum of a homonuclear 2 spin system in an isotropic liquid, the Hamiltonian now consists of three terms:

$$\mathcal{H} = \omega_1 I_{1z} + \omega_2 I_{2x} + \pi J 2 I_{1z} I_{2z}$$

(and where here we assume that $|\omega_1 - \omega_2| > J$, the so-called “weak coupling” approximation.)

Coupled Spins



$$\rho_+(0) = I_{1x} + I_{2x} \xrightarrow[\omega_\sigma = -\gamma B_0(1-\sigma_\sigma)]{\mathcal{H} = \omega_1 I_{1z} + \omega_2 I_{2x} + \pi J 2 I_{1z} I_{2z}} ?$$

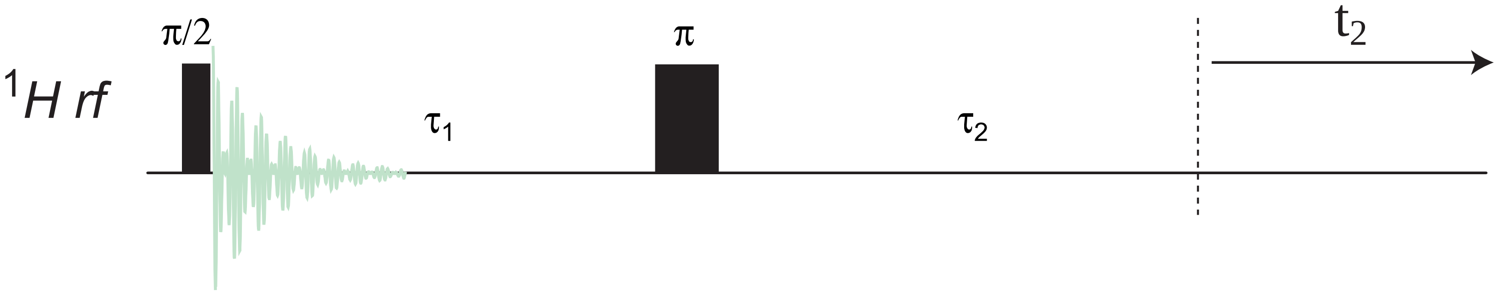
What is the effective Hamiltonian for the sequence?
We already know that the chemical shift terms are zero on average.
What happens to the J coupling term?

$$U^{tot} = \exp\{-i\pi J 2 I_{1z} I_{2z} \tau\} \exp\{-i\pi I_x\} \exp\{-i\pi 2 J I_{1z} I_{2z} \tau\}$$

$$U^{tot} = \exp\{-i\pi J 2 I_{1z} I_{2z} 2\tau\}$$

The J coulping term is not refocused by a π pulse applied to both spins.

Coupled Spins



Pure J evolution during the spin echo sequence for two coupled spins.

$$\sigma_+(0) = I_{1x} + I_{2x} \xrightarrow{\mathcal{H} = \pi J 2 I_{1z} I_{2z}} I_{1x}\cos(2\tau\pi J) + 2I_{1y}I_{2z}\sin(2\tau\pi J)$$

For $\tau = 1/4J$, $\sigma(2\tau) = 2I_{1y}I_{2z}$

This is called an anti-phase coherence

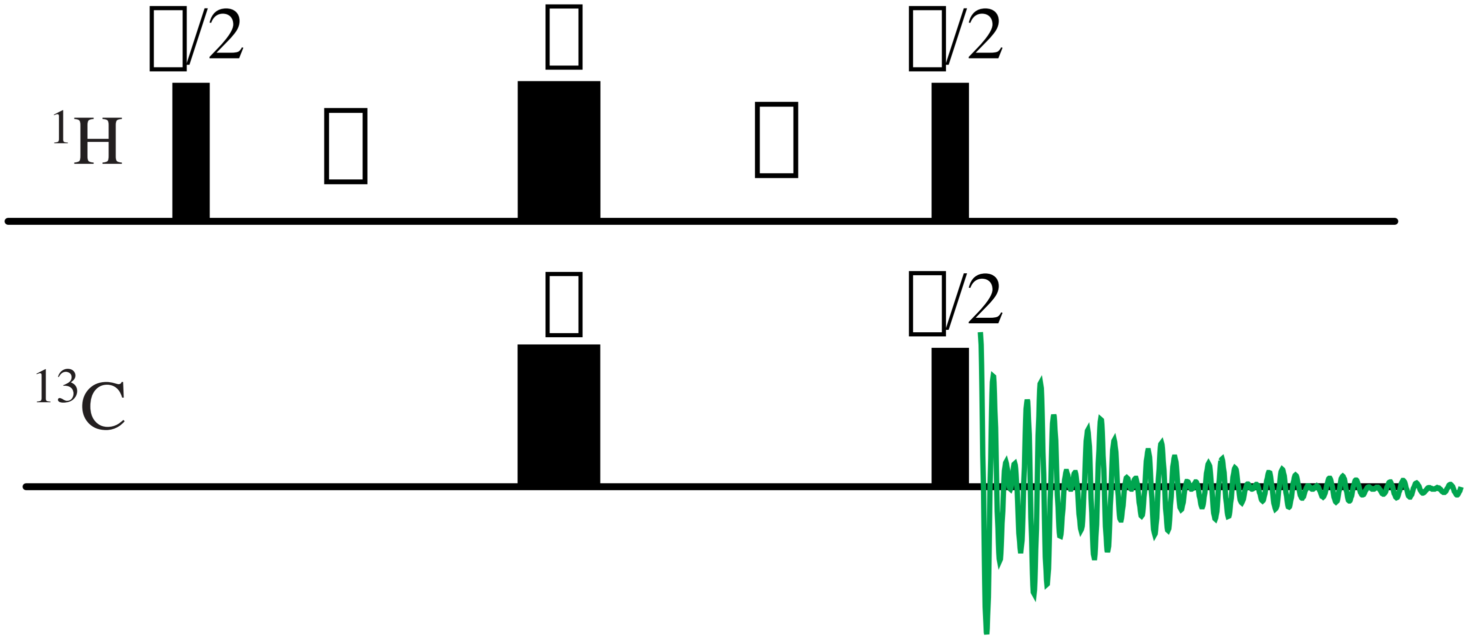
If we now apply a π/2 pulse along x we obtain

$$\sigma = -2I_{1z}I_{2y}$$

The coherence has been transferred from spin I_1 *to spin* I_2.

Polarisation Transfer: INEPT

coherence transfer from protons to carbon-13

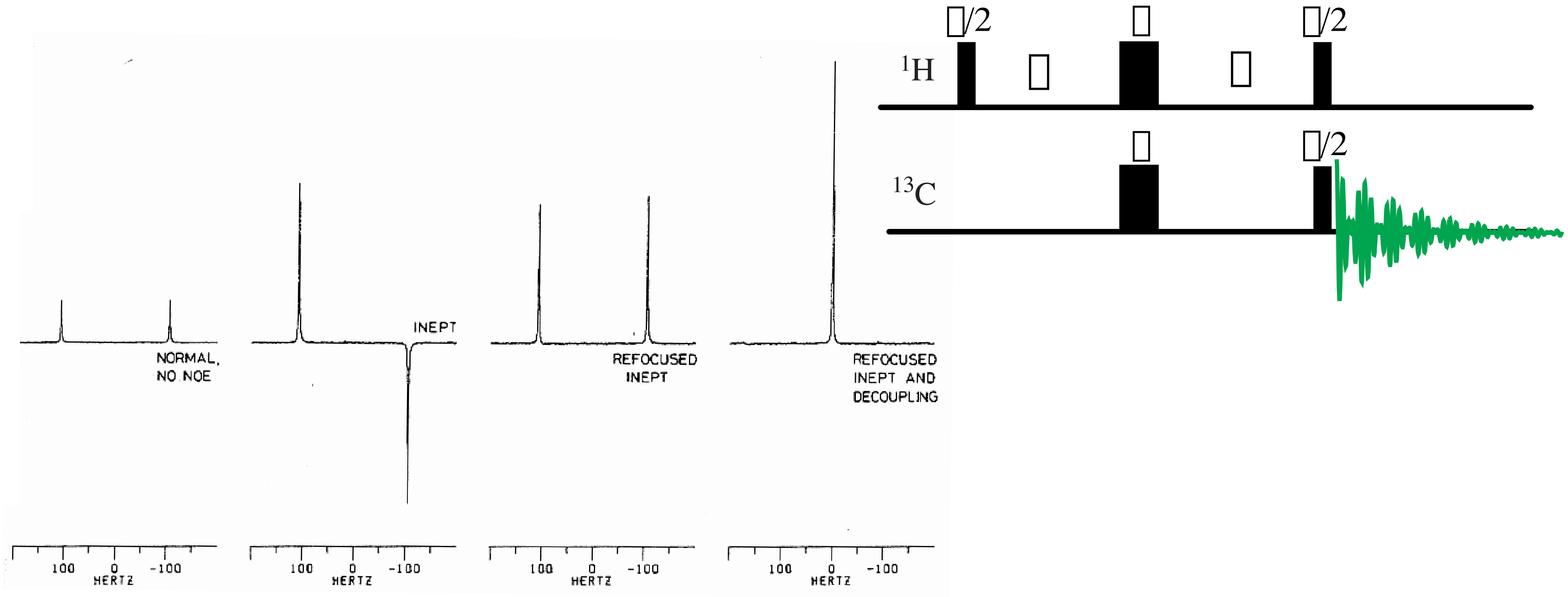


Coherence transfer by a heteronuclear spin echo sequence:

observation of a carbon-13 signal with the sensitivity of 1H.

Polarisation Transfer: INEPT

coherence transfer from protons to carbon-13



Coherence transfer by a heteronuclear spin echo sequence:

Observation of a carbon-13 signal with the sensitivity of 1H: for a CH group the intensity of the carbon-13 signal will be increased by the ratio $\gamma_H/\gamma_C = 4$.

Why is it called an Anti-Phase Coherence?

We have just seen that after a π/2 pulse applied along y, to generate $\sigma(0) = I_{1x}$, the evolution (not including the chemical shift) would be:

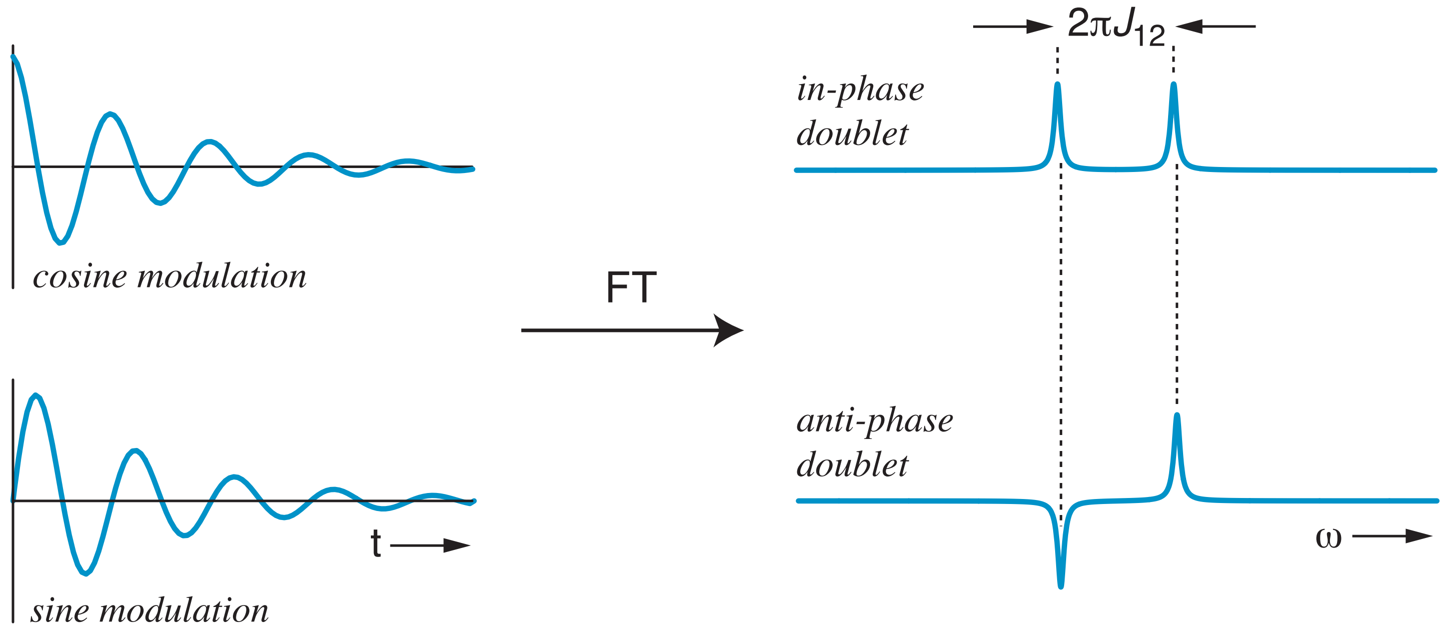
$$\sigma(t) = I_{1x}\cos(2\pi Jt) + 2I_{1y}I_{2z}\sin(2\pi Jt)$$

The I_{1x} term is observable, and the $I_{1y}I_{2z}$ term is not, and Fourier transform of a cosine function $\cos(a)$ yields an in-phase doublet with frequency separation a.

If, on the other hand $\sigma(0) = I_{1y}I_{2z}$ then

$$\sigma(t) = 2I_{1y}I_{2z}\cos(2\pi Jt) + I_{1x}\sin(2\pi Jt)$$

Again, the I_{1x} term is observable and Fourier transform of a sine function $\sin(a)$ yields an anti-phase doublet with frequency separation a.



Polarisation Transfer: INEPT

coherence transfer between heteronuclei

Sensitivity enhancement of rare nuclei by INEPT.

For an X-H group the the intensity of the X signal will be increased by the ratio γ_H/γ_X.

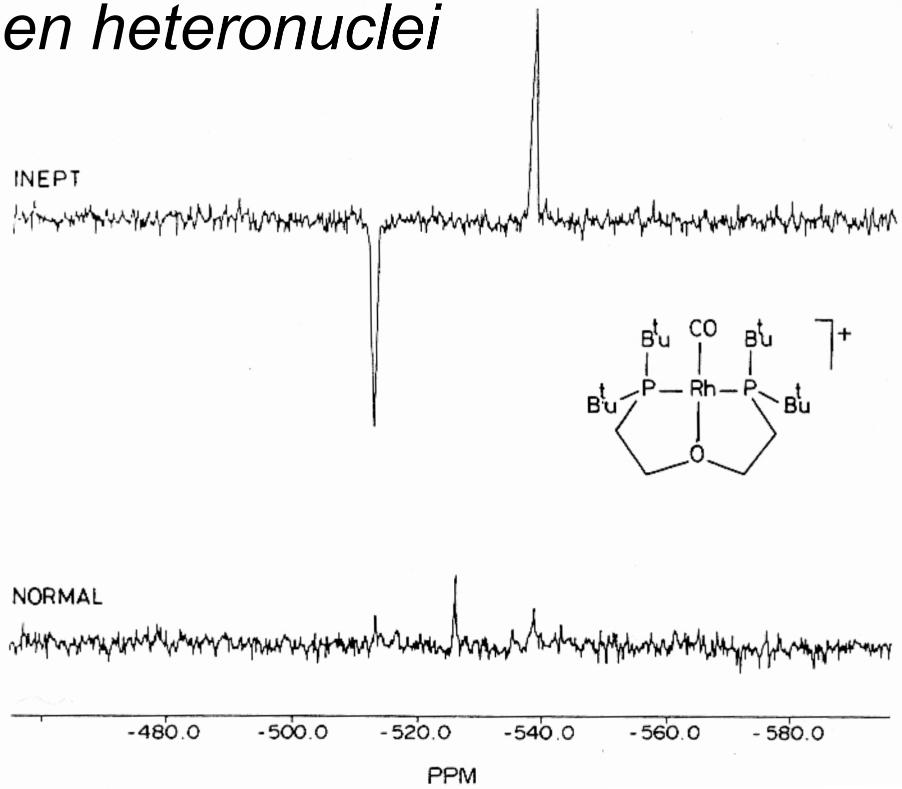


Figure 6.11 INEPT enhancement of ^{103}Rh by polarisation transfer from ^{31}P (courtesy of Dr. C. Brevard, Bruker Spectrospin, and Dr. D. H. M. W. Thewissen *et al.*, ITC-TNO, Utrecht, The Netherlands).

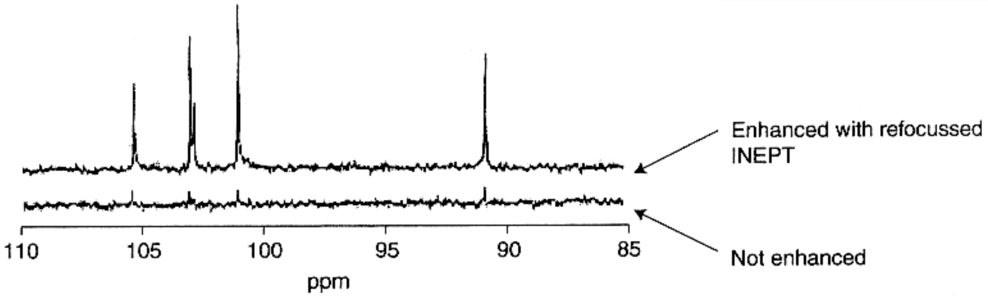
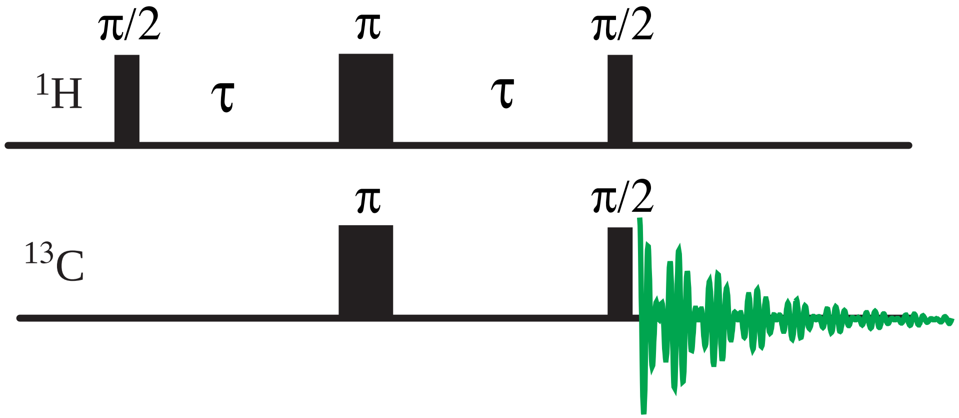


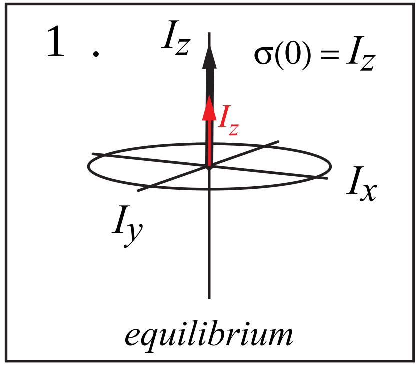
Figure 13.38 Experimental ^{15}N spectra of gramicydin in aqueous solution, using a single $\pi/2$ pulse to excite the ^{15}N spectrum (bottom) and using refocussed INEPT (top). Adapted from *'Encyclopedia of Nuclear Magnetic Resonance'*, D. M. Grant, and R. K. Harris (Eds), Wiley, Chichester Vol. 4, p. 2533. (Reproduced by permission of John Wiley & Sons, Inc.)

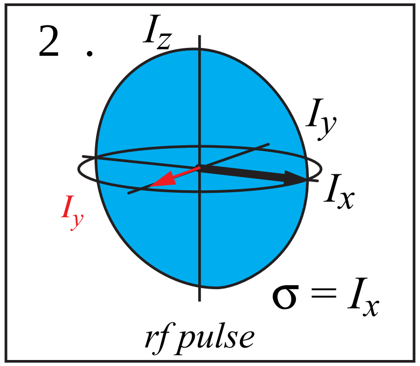
Polarisation Transfer: INEPT

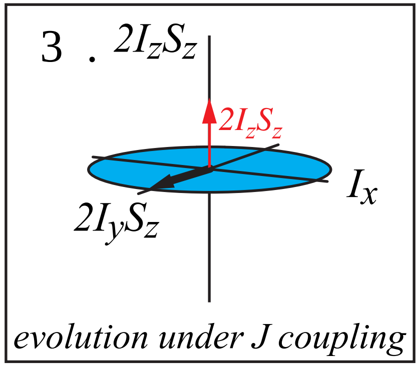
coherence transfer from protons to carbon-13

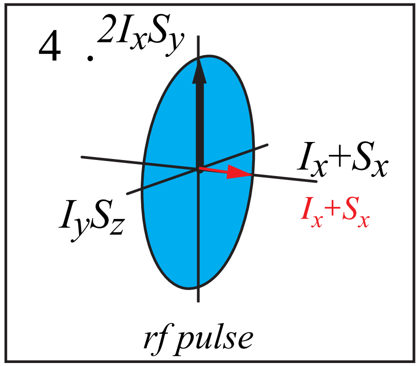


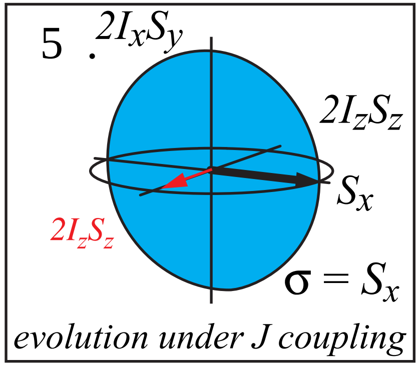
Evolution under different Hamiltonians is often confined to distinct three-dimensional subspaces.







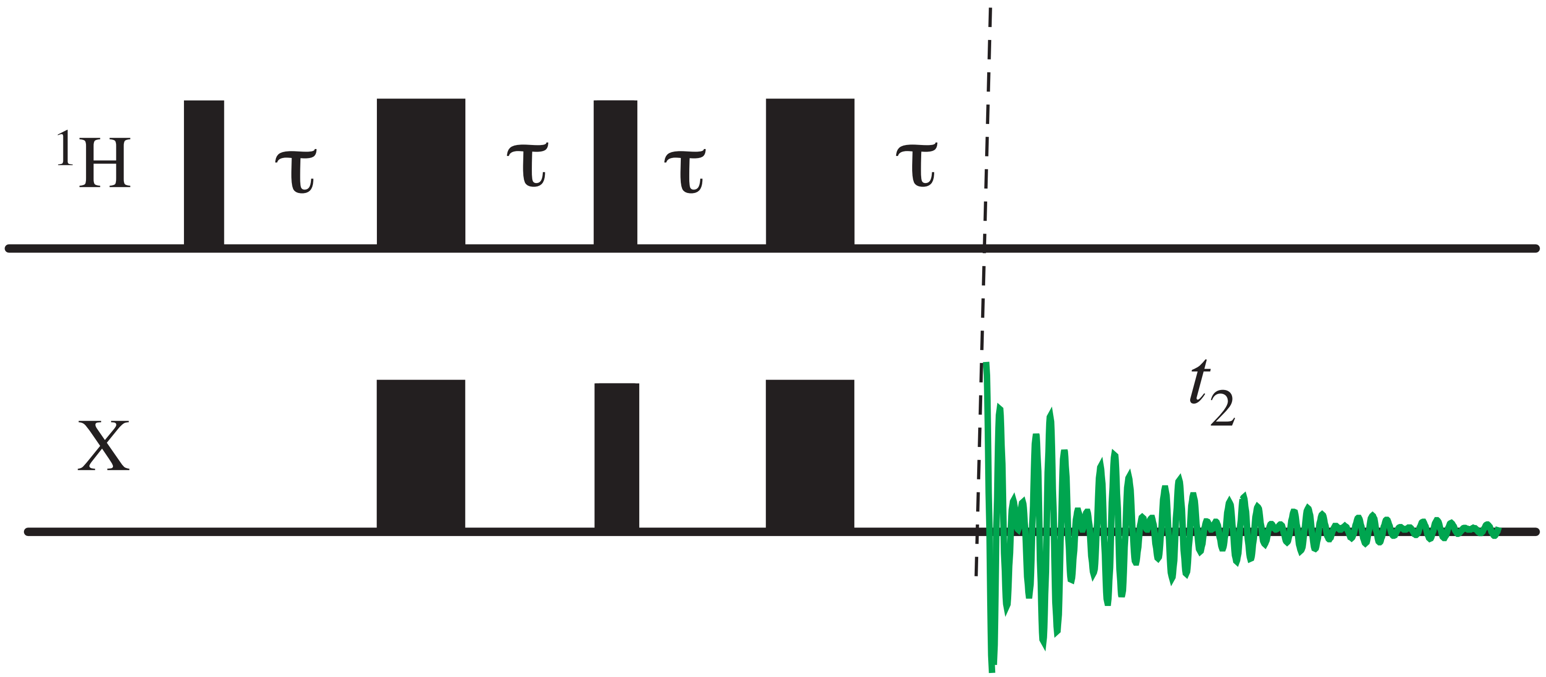




This description is referred to as the "product operator formalism."

Polarisation Transfer: refocused INEPT

coherence transfer from protons to attached X nuclei



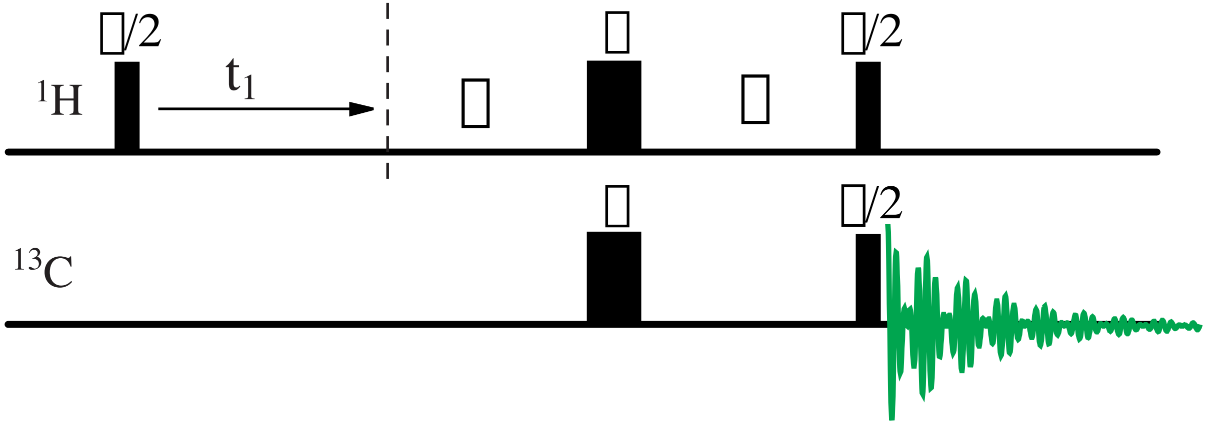
Use the product operator fomalism to determine the spectrum observed in t_2 with this pulse sequence.

Dances with Spins

Can we use coherence transfer
to make connections?

Proton-Carbon Correlation Spectroscopy?

multi-dimensional NMR



couldn't we add another acquisition time on protons to find out which proton is connected to which carbon?

Conclusions: Part II

- The sequence τ - π - τ refocuses chemical shifts, but it does when the π pulse is applied to both spins it does not refocus J couplings.

- The product operator formalism allows to easily visualise and determine transformations between operators in coupled spin systems, *without the need for calculations*.

- In a two-spin J coupled system, evolution under the effect of the *J* coupling generates anti-phase coherences of the type IxSz.

- A 90° pulse on an anti-phase coherence of one spin can transform it into anti-phase coherence of the other spin: *coherence transfer*.

- The INEPT experiment increases the sensitivity of low γ nuclei (e.g.^{13}C, ^{15}N, ^{31}P…) by transferring polarisation from high γ nuclei (e.g. ^{1}H)

Homework

Learn the course material.

for detailled derivations and steps of the QM description (for this week and last week) ***read QM4NMR*** *on Moodle.*

For the product operator formalism, ***read chapter 7 of Keeler***

Pay particular attention to understanding the ***spin echo*** *and* ***coherence transfer***