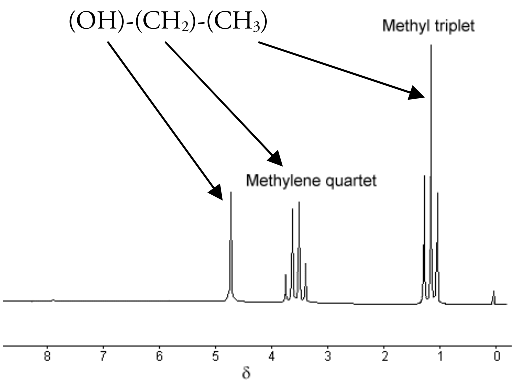
V

J-Coupling

Lecture notes by Assaf Tal

1. Origins of J-Coupling

In the previous lecture we've explained how and why ethanol should yield a spectrum having three peaks:

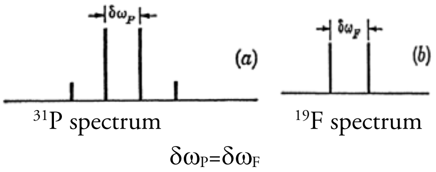


Today's high resolution NMR spectrometers, however, reveal fine structure, known as J-splittings. We will explain its origins and show how it can be used to our advantage.

1.1 Physical Origins

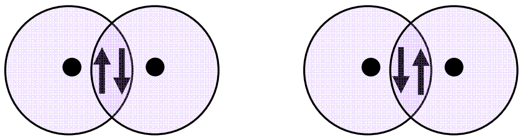
J-coupling, also known as **scalar coupling**, arises from nuclear magnetic moments in the same molecule affecting each other through the electron cloud, which is shared among atoms due to the molecular bonds in the molecule. This is **not** a direct interaction of the two nuclear magnetic dipole moments, but one which is **mediated through the chemical bond**.

Since this effect is observed in liquids, in which molecules tumble very fast and most interactions are averaged out, one would suspect this is some interaction which does not depend on the orientation of the molecule (since it doesn't get averaged out by the motion). The splitting's "size" – that is, sizes of the split peaks and their distances from each other - is also found to be independent of temperature and static field B_0. A third fact is that it is symmetric: for example, if we look at a phosphorous triflouride (PF_3) molecule, in which all nuclei have a spin-1/2, then we will measure a splitting in both the P and the F spectra:



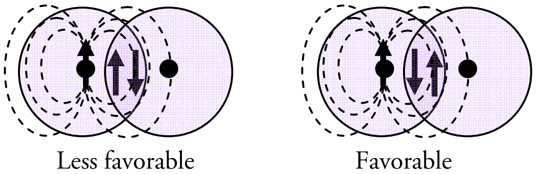
The first explanations for this was that the nuclear magnetic moment of nucleus A induces currents in the electronic cloud (shared between two nuclei A, B), which in turn create an induced moment which interacts with the nuclear moment of nucleus B. The calculated effect turned out to be too small.

The next explanation proposed, which is the accepted one today, relies on the Pauli exclusion principle. In the absence of a nuclear magnetic moment, the electronic spins in a chemical bond will be anti-parallel: either ↑↓ or ↓↑. In fact, the state of the system will be made up of an equal mixture of both. This is a quantum mixture (i.e. a linear superposition), not a statistical one.



In the absence of a nuclear spin,
the electronic state will be made up
of a mixture of both of these electronic
spin states.

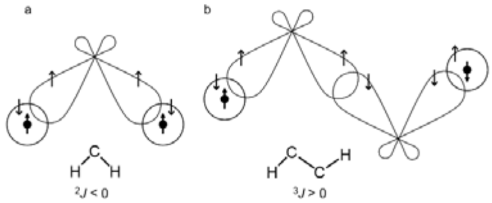
If we put a nuclear magnetic moment in atom A (the left one) then it will be more favorable for the electronic spin of atom A to point **down** (due to magnetic energy), and as a result for the electronic spin of atom B to point **up** (due to Pauli), and therefore for the nuclear magnetic moment at B to point **down** (again due to magnetic energy):



Less favorable

Favorable

This creates an **effective nuclear coupling** known as scalar or J-coupling, mediated via the chemical bond – that is, via the electronic cloud. The idea can be extended via several bonds and different nuclei:



The J-coupling causes a shift in the energy of two spins of the form

$$H_J = \frac{2\pi J}{\hbar}\hat{\mathbf{S}}_1 \cdot \hat{\mathbf{S}}_2 \,.$$

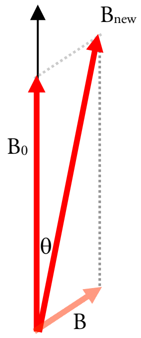
When the two nuclear spins are parallel (up-up or down-down) the energy is unfavorable, and when they are anti-parallel (up-down or down-up) the energy is more favorable.

1.2 NOMENCLATURE

All J-couplings derive from the same physical mechanism, but people sometimes make a distinction between them. First, a superscript preceding J refers to the number of bonds between the two nuclei, so ^2J means two bonds, such as in a H-C-H. Two such "twin" protons are sometimes called geminal in chemistry, so ^2J constants are sometimes called **geminal**. Subscripts following J indicate which nuclei are coupled, so coupling between two protons in H-C-H will be denoted $^2J_{HH}$. Three-bond couplings ^3J are called **vicinal**. More bonds are just termed "long-range", with J-couplings rarely exceeding 5 bonds (^5J). Proton-proton couplings also tend to decrease with the number of bonds (although not always!), and are on the order of 1-10 Hz.

1.3 THE SECULAR APPROXIMATION

The general hamiltonian for many NMR systems is very complicated. Fortunately, we can often simplify it using the secular approximation. Remember that we always have a constant, strong magnetic field B_0 point along the z-axis. What would the effect of adding another small, constant field? To a 0th approximation, it would be nothing: the added field is just too small. To the next approximation, let's assume without loss of generality the new field is in the xz plane and decompose the new field along the x and z axes:



Now, the x-component of the new merely tilts it very very very slightly away from the z-axis. How slightly?

$$\theta \le \theta_{\max} \approx \frac{B}{B_0} << 1$$

since the maximal angle θ_{max} is obtained when B is perpendicular to B_0, and then $\sin(\theta_{\max}) \approx \theta_{\max}$ because θ_{max} is so small. This tilt is so small it can be neglected for all practical purposes.

The z-component of B gets added to B_0. Can we neglect it? **No**! Because the shifts induced by B_0 can be on the order of the chemical shifts we observe in the sample: $\gamma B_{new,z}=\gamma B_0+\gamma B_z$. Even if γB_0 is 500 MHz and γB_z is 20 Hz, it still has a very real effect on the order of other shifts we see.

This same reasoning can be extended to non-constant small B's, with one exception: if the extra fields have a temporal component that matches the resonance of the main field, it will induce a resonant transition. This is the entire principle on which NMR is built! Luckily, most additional interactions do not have this sort of resonant component, and we can retain their component parallel to the main field. This approximation is so prevalent in NMR that it merits its own textbox:

The secular approximation: If you have a large main field B_0, then a small, non-resonant additional interaction can be approximated to first order by retaining only its component along B_0.

1.4 Weak Coupling

Suppose we have two J-coupled spins. Their hamiltonian is:

$$H = \omega_1 \hat{S}_{1z} + \omega_2 \hat{S}_{2z} + \frac{2\pi J}{\hbar} \hat{\mathbf{S}}_1 \cdot \hat{\mathbf{S}}_2 .$$

Can we apply a secular approximation here? There are two fields so it's unclear what to compare the J-interaction to. This is resolved if we transform to a frame that rotates with an angular frequency ω_1, such that

$$H = \left(\omega_2 - \omega_1\right) \hat{\mathbf{S}}_2 + \frac{2\pi J}{\hbar} \hat{\mathbf{S}}_1 \cdot \hat{\mathbf{S}}_2 .$$

Now it becomes clear that for us to apply the secular approximation, we must have

$$\frac{J}{\Delta \nu} << 1 .$$

This is the weak coupling approximation, under which

$$\begin{aligned} H_J &= \frac{2\pi J}{\hbar}\left(\hat{S}_{1x}\hat{S}_{2x} + \hat{S}_{1y}\hat{S}_{2y} + \hat{S}_{1z}\hat{S}_{2z}\right) \\ &\approx \frac{2\pi J}{\hbar} \hat{S}_{1z}\hat{S}_{2z} \end{aligned}$$

Then:

$$H = \omega_1 \hat{S}_{1z} + \omega_2 \hat{S}_{2z} + \frac{2\pi J}{\hbar} \hat{S}_{1z}\hat{S}_{2z}$$

Unless otherwise noted, we will assume henceforth the weak coupling approximation, which holds for a surprising number of cases in NMR.

1.5 $\hbar = 1$

In NMR we many times set $\hbar = 1$ and talk in terms of frequency instead of energy. For example, the J-coupling hamiltonian will be

$$H = \omega_1 \hat{S}_{1z} + \omega_2 \hat{S}_{2z} + 2\pi J \hat{S}_{1z}\hat{S}_{2z} ,$$

where now the spin operators don't have any $\hbar$ in them:

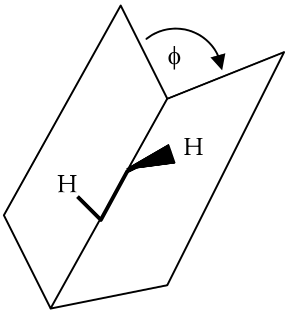
$$\hat{S}_x = \frac{1}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}, \; \hat{S}_y = \frac{1}{2}\begin{pmatrix} 0 & -i \\ i & 0 \end{pmatrix}, \; \hat{S}_z = \frac{1}{2}\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$$

We're going to adopt the same convention from this point onward unless otherwise stated.

3.4 J-Coupling Yields Important Structural Information

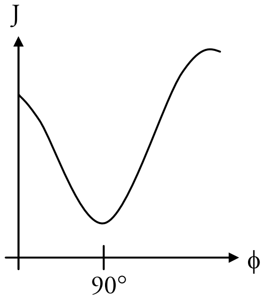
J is not just an annoying constant that splits lines, but can actually convey useful information and assist in analysis and peak assignment. For lactate, J-coupling assisted us in assigning peaks to chemical groups, since we knew the CH should yield four lines (split three times by CH_3) while CH_3 should yield two lines (split once by CH). This helped us assign the resonances in the spectrum without even knowing anything about their chemical shift a-priori.

The value of the J-coupling constant can yield structural information about a molecule. A scientist by the name of Martin Karplus found an empirical relation between the magnitude of vicinal (3-bond) $^3J_{HH}$ couplings and the dihedral angle ϕ of the bonds:



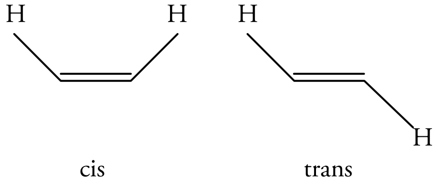
$$^3J(\phi) = A\cos^2(\phi) + B\cos(\phi) + C$$

Basically, each plane is defined by the C-C bond and the corresponding C-H bond, and ϕ is the angle between the two planes. The Karplus curve usually looks something like:

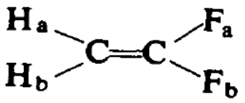


The idea is that the overlap between molecular orbitals – and hence the strength of the exchange interaction – varies when the angle ϕ changes. The overlap is minimal when the wavefunctions are orthogonal, so ^{3}J tends to be smallest when ϕ=90°.

The **Karplus equation** (above) is a major tool in structural chemistry. For example, the vicinal coupling changes between cis and trans configurations of double-bond alkenes:



This difference is seen for example in 1,1-difluoroethylene:



The ^{3}J coupling constant of H_a to F_b (trans) is different from the coupling of H_b to F_b (cis).

Incidentally, Karplus's original JACS paper from 1963 remains one of the journal's most cited papers of all time, and Karplus himself is a notable theoretical chemist who won the 2013 nobel prize (although not for his NMR work, but for his theoretical chemical modeling work).

2. A QUANTUM MECHANICAL TREATMENT

2.1 THE HAMILTONIAN AND SYSTEM

The J-coupling interaction is one which does not get averaged by the molecules' motion. It is of the form

$$H_J = 2\pi J \hat{I}_{1z}\hat{I}_{2z} = \frac{\pi J}{2}\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

This means that the full Hamiltonian of the system is

$$\begin{aligned} H &= -\omega_0^{(1)}\hat{I}_{1z} - \omega_0^{(2)}\hat{I}_{2z} + 2\pi J \hat{I}_{1z}\hat{I}_{2z} \\ &= \begin{pmatrix} -\omega_{\text{avg}} + \frac{\pi J}{2} & 0 & 0 & 0 \\ 0 & \frac{\Delta\omega - \pi J}{2} & 0 & 0 \\ 0 & 0 & \frac{-\Delta\omega - \pi J}{2} & 0 \\ 0 & 0 & 0 & \omega_{\text{avg}} + \frac{\pi J}{2} \end{pmatrix} \end{aligned}$$

where $\omega_{\text{avg}} = \frac{\omega_0^{(1)} + \omega_0^{(2)}}{2}$ and $\Delta\omega = \omega_0^{(2)} - \omega_0^{(1)}$. Now, we are very lucky that the hamiltonian is still diagonal. This means we still get to keep our old eigenfunctions of the hamiltonian without the J-coupling, which now have energies:

$$\begin{aligned} H\left|++\right\rangle &= \left(-\omega_{\text{avg}} + \tfrac{\pi J}{2}\right)\left|++\right\rangle \\ H\left|+-\right\rangle &= \left(\Delta\omega - \tfrac{\pi J}{2}\right)\left|+-\right\rangle \\ H\left|-+\right\rangle &= \left(-\Delta\omega - \tfrac{\pi J}{2}\right)\left|-+\right\rangle \\ H\left|--\right\rangle &= \left(-\omega_{\text{avg}} + \tfrac{\pi J}{2}\right)\left|--\right\rangle \end{aligned}$$

as you should verify explicitly (just do the matrix multiplication).

2.2 THE PROPAGATOR

The fact that H is diagonal makes it easy for us to calculate the propagator in matrix form:

$$U\left(t\right)=e^{-iHt/\hbar}=\begin{pmatrix} e^{i\left(\omega_{\text{avg}}-\frac{\pi J}{2}\right)t} & 0 & 0 & 0 \\ 0 & e^{i\left(-\frac{\Delta\omega}{2}+\frac{\pi J}{2}\right)t} & 0 & 0 \\ 0 & 0 & e^{i\left(\frac{\Delta\omega}{2}+\pi J\right)t} & 0 \\ 0 & 0 & 0 & e^{-i\left(\omega_{\text{avg}}+\frac{\pi J}{2}\right)t} \end{pmatrix}$$

The hamiltonian can be written as $H = H_1 + H_2 + H_J$, where $H_1 = -\omega_0^{(1)}\hat{I}_{1z}$, $H_2 = -\omega_0^{(2)}\hat{I}_{2z}$ and $H_J = 2\pi J\hat{I}_{1z}\hat{I}_{2z}$. A very important property of these three hamiltonians is that they all commute:

$$\left[H_1,H_2\right]=\left[H_1,H_J\right]=\left[H_2,H_J\right]=0\,.$$

This means we can decompose the propagator into each of its parts:

$$\begin{aligned} U\left(t\right) &= e^{-i\left(H_1+H_2+H_J\right)t/\hbar} \\ &= e^{-iH_1t/\hbar}e^{-iH_2t/\hbar}e^{-iH_Jt/\hbar} \\ &= U_1\left(t\right)U_2\left(t\right)U_J\left(t\right) \end{aligned}$$

Not only that: we can change the order of the terms (e.g. $U_1U_2U_J = U_1U_JU_2$). This means that when we propagate the density matrix, we can choose the order in which we calculate the effects of the different terms. For example, we could calculate the effect of the J-coupling first, then the Zeeman term for the second spin, then for the first:

$$U\rho U^\dagger = U_1\underbrace{U_2\overbrace{U_J\rho U_J^\dagger}^{\text{J-coupling}}U_2^\dagger}_{\text{Zeeman for 2nd spin}}U_1^\dagger$$

or we could first deal with the effects of the Zeeman interaction and chemical shifts, and only then calculate the effect of J-coupling:

$$U\rho U^\dagger = \overbrace{U_J\underbrace{U_2U_1\rho U_1^\dagger U_2^\dagger}_{\text{Zeeman}}U_J^\dagger}^{\text{J-coupling}}$$

and so forth. To sum up:

For weak J-coupling we can apply each interaction in turn, and we can choose the order in which the interactions will play out (the result will be the same).

2.3 THE ZEEMAN EVOLUTION

We've already seen how the Zeeman interaction evolves.

2.3 THE J-COUPLING EVOLUTION

We now come to the "meat" of the chapter: how does the weak J-coupling term affect the spins' evolution? To do that, we need to calculate its effects on the different density operator terms such as I_{ij} (i=1,2, j=x,y,z), and pairs such as $I_{ij}I_{mn}$ (i,m=1,2, j,n = x,y,z). This is a pain to do and I won't derive all of them, but I'll show you how to go about it and then just list the results.

Let's look at how I_{1x} evolves in time:

$$U_J\left(t\right)I_{1x}U_J^\dagger\left(t\right)\rightarrow ?$$

One way we could go about doing this is simply writing out everything explicitly:

$$U_J\left(t\right)=e^{-2\pi iJI_{1z}I_{2z}t}=\begin{pmatrix} e^{-\frac{i\pi Jt}{2}} & 0 & 0 & 0 \\ 0 & e^{\frac{i\pi Jt}{2}} & 0 & 0 \\ 0 & 0 & e^{\frac{i\pi Jt}{2}} & 0 \\ 0 & 0 & 0 & e^{-\frac{i\pi Jt}{2}} \end{pmatrix}$$

$$I_{1x} = I_x \otimes I = \frac{1}{2}\begin{pmatrix} 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \end{pmatrix}$$

and carry out the matrix multiplication by brute force, and finally take the trace of the resulting matrix with all possible combinations operators ($I_{ij}I_{mn}$, I_{ij}) and decompose it into a sum. A *slightly* easier approach uses the fact that

$$U_J\left(t\right)=e^{-2\pi iJI_{1z}I_{2z}/\hbar}=\cos\left(\tfrac{\pi Jt}{2}\right)I-i4I_{1z}I_{2z}\sin\left(\tfrac{\pi Jt}{2}\right)$$

This can be easily deduced from the matrix form above. Now we can compute, for any state ρ:

$$\begin{aligned} &U_J \rho U_J^\dagger \\ &= \left[\cos\left(\tfrac{\pi Jt}{2}\right) I - 4i I_{1z} I_{2z} \sin\left(\tfrac{\pi Jt}{2}\right)\right] \\ &\qquad \cdot\rho\cdot\left[\cos\left(\tfrac{\pi Jt}{2}\right) I + 4i I_{1z} I_{2z} \sin\left(\tfrac{\pi Jt}{2}\right)\right] \\ &= \cos^2\left(\tfrac{\pi Jt}{2}\right)\rho + 4i\cos\left(\tfrac{\pi Jt}{2}\right)\sin\left(\tfrac{\pi Jt}{2}\right)\left[\rho, I_{1z}I_{2z}\right] \\ &\qquad +16\sin^2\left(\tfrac{\pi Jt}{2}\right) I_{1z}I_{2z}\rho I_{1z}I_{2z} \end{aligned}$$

For example, if $\rho = I_{1x}$, then

$$\left[I_{1x}, I_{1z}I_{2z}\right] = \left[I_{1x}, I_{1z}\right] I_{2z} = -iI_{1y}I_{2z}$$

and

$$I_{1z}I_{2z}I_{1x}I_{1z}I_{2z} = \overbrace{I_{1z}I_{1x}I_{1z}}^{-\frac{1}{4}I_{1x}}\overbrace{I_{2z}^2}^{\frac{1}{4}I} = -\frac{1}{16}I_{1x}$$

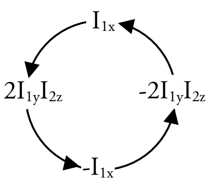
so

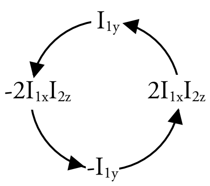
$$\begin{aligned} &U_J I_{1x} U_J^\dagger \\ &= \left[\cos^2\left(\tfrac{\pi Jt}{2}\right) - \sin^2\left(\tfrac{\pi Jt}{2}\right)\right] I_{1x} + 4\cos\left(\tfrac{\pi Jt}{2}\right)\sin\left(\tfrac{\pi Jt}{2}\right) I_{1y}I_{2z} \\ &= \cos\left(\pi Jt\right) I_{1x} + \sin\left(\pi Jt\right) 2I_{1y}I_{2z} \end{aligned}$$

We can repeat this for all possible combinations. I will not do the explicit math here and merely quote the results. The following operators are *unaffected* by the J-coupling Hamiltonian:

$$\begin{aligned} &I \\ &I_{1z} \\ &I_{2z} \\ &I_{1z}I_{2z} \\ &I_{1x}I_{2x} \\ &I_{1x}I_{2y} \\ &I_{1y}I_{2x} \\ &I_{1y}I_{2y} \end{aligned}$$

The remaining ones perform a right-handed "rotation" as indicated by the following diagram:





Two similar circles exist for I_{2x} and I_{2y} (just swap 1↔2 in the above diagrams). The "angular momentum" of these rotations is

$$\omega_J = \pi J \ .$$

Example: Suppose $\rho = I_{2y}$. How does it evolve under the weak J-coupling Hamiltonian?
Answer:

$$I_{2y} \xrightarrow{\text{weak J-coupling}} I_{2y}\cos\left(\pi Jt\right) - 2I_{1z}I_{2x}\sin\left(\pi Jt\right)$$

2.4 RF PULSES

As with the case of no J-coupling, "hard" RF pulses are assumed so strong and short that no chemical shift or J coupling occur while they are applied. Is this a good approximation? Hard pulses often take tens of milliseconds to apply on a spectrometer, while J coupling values are on the order of 10-100 Hz, so very negligible evolution takes place during the pulse's application. The approximation is very good.

Some pulses out there are not "hard" and take a long amount of time to apply. During such pulses one cannot neglect the J-coupling or chemical shift evolution. We won't deal with such advanced pulses in this course.

3. PULSE-ACQUIRE REVISITED

3.1 DERIVING J-SPLITTINGS

Let's look at two spins with weak J-coupling between them. Starting from thermal equilibrium, the state of the system is (neglecting the constant identity matrix term):

$$\rho = \frac{\gamma_1 B_0}{2kT} I_{1z} + \frac{\gamma_2 B_0}{2kT} I_{2z} \equiv a_1 I_{1z} + a_2 I_{2z}$$

This could be any pair of nuclei, e.g. C-H, so we're not assuming the same γ's. Furthermore, we've omitted the identity part since it does not evolve in time and therefore does not contribute to the measured signal.

A "hard" π/2 pulse will tilt the product operators to the xy-plane

$$\rho = a_1 I_{1x} + a_2 I_{2x}.$$

Let's now let the system evolve. We're free to choose whether to apply the Zeeman or J-coupling evolution first. I'll go with the Zeeman (chemical shift) Hamiltonian first:

$$\begin{aligned}\rho \to\, & a_1\left[I_{1x}\cos(\omega_1 t) - I_{1y}\sin(\omega_1 t)\right]\\ & + a_2\left[I_{2x}\cos(\omega_2 t) - I_{2y}\sin(\omega_2 t)\right]\end{aligned}$$

Next, let's apply the J-coupling hamiltonian:

$$\begin{aligned}\rho \to\, & a_1\cos(\omega_1 t)\left[I_{1x}\cos(\pi Jt) + 2I_{1y}I_{2z}\sin(\pi Jt)\right]\\ & - a_1\sin(\omega_1 t)\left[I_{1y}\cos(\pi Jt) - 2I_{1x}I_{2z}\sin(\pi Jt)\right]\\ & + a_2\cos(\omega_2 t)\left[I_{2x}\cos(\pi Jt) + 2I_{1z}I_{2y}\sin(\pi Jt)\right]\\ & - a_2\sin(\omega_2 t)\left[I_{2y}\cos(\pi Jt) - 2I_{1z}I_{2y}\sin(\pi Jt)\right]\end{aligned}$$

As you can see, things can get ugly real fast. But fear not! Let's assume these are heteronuclear spins and acquire a signal from spin 1:

$$s(t) \sim \mathrm{tr}\left(\left(\hat{S}_{1x} + i\hat{S}_{1y}\right)\rho\right)$$

Only I_{1x} and I_{1y} will contribute to the signal so we can safely disregard all other terms and obtain:

$$s(t) \sim a_1\cos(\pi Jt)e^{i\omega_1 t}$$

We have neglected relaxation. We see that our FID is now modulated by the J-coupling evolution. Remembering that

$$\cos(x) = \tfrac{1}{2}\left(e^{ix} + e^{-ix}\right)$$

we rewrite s(t) as

$$s(t) \sim \tfrac{a_1}{2}\left[e^{i2\pi\left(\nu_1 + \frac{J}{2}\right)t} + e^{i2\pi\left(\nu_1 - \frac{J}{2}\right)t}\right].$$

where $\omega_1 \equiv 2\pi\nu_1$. We observe two effects:

1. The J-coupling amplitude modulation cos(πJt) has led to two observable peaks, at $\nu_1 \pm \frac{J}{2}$. **This is the splitting we've seen in the spectrum of ethanol (and other molecules).**
2. The amplitude of each peak has been halved compared to the original, unsplit peak. **We've lost half of our SNR**, although the total integrated area hasn't changed.

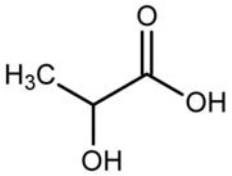
Thus, we can summarize the effect of J-coupling on the spectrum of a spin pair:

> If a resonance A is coupled via weak J-coupling to reosnance B, do the following:
> 1. Halve the amplitude, and:
> 2. Replace the resonance at ν with two resonances at $\nu \pm \frac{J}{2}$

J-splittings can be a boon or a curse. They let us sometimes identify which peak corresponds to which part of the molecule. On the other hand, they reduce the SNR and complicate the spectrum, and it is therefore sometimes desirable to make them go away. This is called **decoupling** and we'll show how to do this in a bit.

3.2 Multiple Couplings

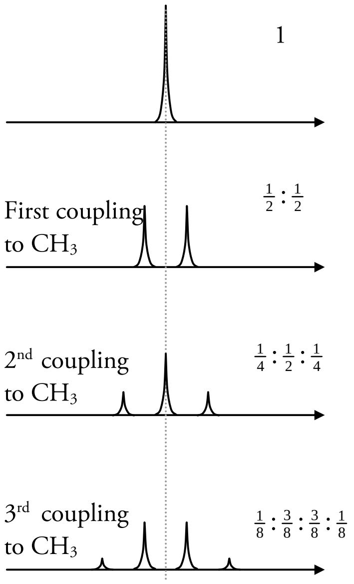
The above calculation was carried out for a weakly coupled pair of spins. What happens in more realistic situations? For example, in lactatic acid,



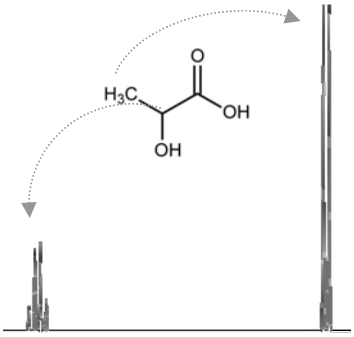
the hydrogens in the CH_3 and CH groups are J-coupled. This means the H in CH is coupled to **three** hydrogens in CH_3, and gets split three times. On the other hand, the CH_3 resonance gets split only **once** by the H in CH.

Multiple J-splittings are dealt with (in the weak regime!) by applying the splitting rule multiple times. Thus:

CH spectrum for Lactate



Here's a simulated spectrum of lactate in water:



This spectrum illustrates the boon/curse duality. On the one hand, it is more complicated than the original spectrum which should've had only two peaks. On the other hand, we immediately know which peak corresponds to which group in the molecule: the single split peak is from the CH_3 group, while the group of four peaks at a $\frac{1}{8}:\frac{3}{8}:\frac{3}{8}:\frac{1}{8}$ ratio is from the triply-split CH.

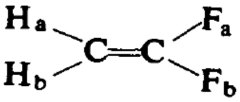
3.3 Strong Coupling

The analysis of strong coupling is not an impossible feat for two spins, since all you need to do is diagonalize the hamiltonian, find the energy levels and calculate the density matrix's time evolution. We're not going to delve on that in this course, but we will mention what happens to the spectral pattern for strong J coupling. For two spins, as $\Delta\nu$ becomes smaller, you get a "roofing" effect, where the outermost peaks become smaller until they reduce to nothing:

3.4 Magnetic & Chemical Equivalence

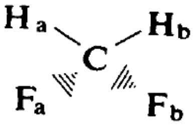
Two nuclei are **chemically equivalent** if they have the same chemical shift, i.e. are in the same chemical environment. The nuclei are **magnetically equivalent** if they are chemically equivalent **and** have the same J-coupling to all other nuclei in the molecule.

An example of chemical equivalence without magnetic equivalence is given by 1,1-difluoroethylene:



AA' system

H_a and H_b are chemically equivalent, but the J-coupling between H_a and F_b is different from that between H_b and F_b (trans vs cis). The fact that H_a is coupled to F_a the same way H_b is coupled to F_b is irrelevant. On the other hand, difluoromethane is both chemically and magnetically equivalent:



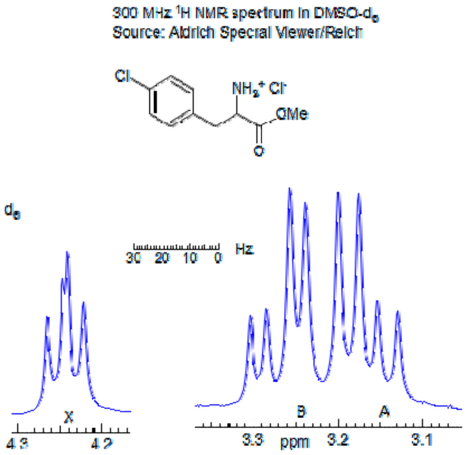
A_2 system

The NMR literature uses the following notation: capital latin letters are used to denote chemical shift, with letters “far away” in the alphabet denoting spins which have a chemical shift separation much larger than their J-coupling different, e.g. AX. If the letters are close, the J-coupling is considered strong, e.g. AB or ABC. “Medium” coupling between three spins might be denoted by AMX. Another example: ABX is a system with 3 spins, where A and B are “close” compared to their J-coupling constants and X is “far away”.

If two spins have the same chemical shift and different J-couplings to a third spin (i.e. are not magnetically equivalent), they will be denoted AA’. Magnetically equivalent spins will be denoted A_2 (or A_3, or A_n, depending on how many spins there are). Not all systems can be expressed with the alphabet notation, but many can and it is a useful and widely used notation.

3.5 More Complex Couplings

The coupling patterns of many other systems can be studied, but complexity is exponential in the number of spins. For example, the simple ABX proton system is not simple at all:

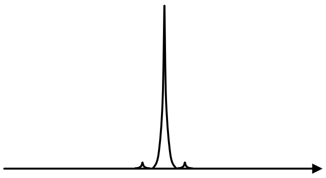


300 MHz ^1H NMR spectrum in DMSO-d_6
Source: Aldrich Spectral Viewer/Reich

NMR chemists who specialize in assigning peaks and studying small molecules become adept with time in many of these patterns, but their study is quite specialized and we will not pursue it further in this course.

3.6 Low Natural Abundance NMR-Visible Isotopes Minimize the Coupling Effect

J-couplings can exist between similar nuclei, possibly mediated via other nuclei (such as H-C-C-H), or can exist between different nuclei, such as C-H couplings. However, one rarely sees such heteronuclear coupling effects in most hydrogen spectra, because most other NMR active nuclei appear only at very low natural abundances in nature. For example, ^{13}C has a natural abundance of about 1%. Most carbon nuclei are ^{12}C, which has no nuclear spin and induces no splittings. For example, a typical hydrogen peak coupled to a neighboring carbon nucleus might look like this:

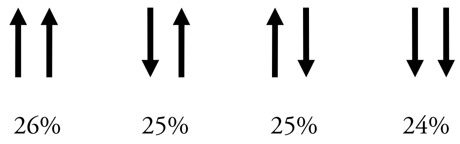


The large unsplit peak originates from the 99% of all hydrogen nuclei with ^{12}C neighbors. The tiny satellite peaks originate from the 1% of hydrogen nuclei with ^{13}C neighbors – those hydrogen nuclei got split.

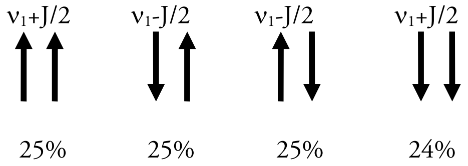
Incidentally, the low natural abundance of ^{13}C can be circumvented by labeling molecules with ^{13}C – that is, replacing ^{12}C nuclei with ^{13}C nuclei. This is possible by using ^{13}C as a substrate when synthesizing the molecules.

3.7 The “Meaning” of J-Coupling

The splitting effect of J-coupling is sometimes explained in the literature as follows: in our statistical ensemble of spins, say a hydrogen and a carbon, each can be at an up or down state. Due to the external B_0 magnetic field, the up state has a slight preference over the down state, so we might get the following configurations at thermal equilibrium, neglecting J-coupling which is much much smaller than the lab Zeeman interaction terms (percentages are exaggerated):



Since the J-coupling term looks like $\hat{S}_{1z}\hat{S}_{2z}$ - positive for parallel pairs, negative for anti-parallel pairs, we see that for some of the pairs the first spin will experience a slightly lower precession frequency and for some pairs a slightly higher, based on the state of the second spin:



This "explains" why we see two lines instead of one for spin 1: half of the spins of the first nucleus (26%+24%) have a precession frequency $\nu_1 + \frac{J}{2}$, while the other half have a precession frequency $\nu_1 - \frac{J}{2}$ and two lines appears.

This explanation is complete and utter nonsense because it relies on a classical statistical ensemble average. The splitting effect of J-coupling is observable in theory even with a single spin pair, i.e. a single molecule. It is a purely quantum mechanical manifestation which transfers polarization from, say, S_{1x} to $2S_{1y}S_{2z}$ and back again to S_{1x}. What is $2S_{1y}S_{2z}$? One is temped to think of it as a system in which one spin is in the S_{1y} state while the other is in the S_{2z} state, but this is not quite "right". For example, if we were to measure a signal, we would find that (calculate this!):

$$\begin{aligned}&\mathrm{Tr}\left(\hat{M}_{xy}\rho\right)\\&\quad=\mathrm{Tr}\left(\left(\gamma\left(S_{1x}+iS_{1y}\right)\otimes\gamma\left(S_{2x}+iS_{2y}\right)\right)\left(S_{1y}\otimes S_{2z}\right)\right)\\&\quad=0\end{aligned}$$

So why can't we see a signal? What we classically think of as "one spin is in the S_{1y} state while the other is in the S_{2z} state" is really $\rho = S_{1y} + S_{2z}$ and not $\rho = S_{1y}S_{2z}$. The state $\rho = S_{1y}S_{2z}$ has no classical analogue and, while some people have suggested pictorial representations, they all become too complicated or break down at one point. It is therefore to stick to a simpler view of the world: S_{1x}, S_{1y}, S_{1z}, S_{2x}, S_{2y}, S_{2z} are all classically comprehensible quantities, but $S_{1x}S_{2x}$, $S_{1x}S_{2y}$, $S_{1z}S_{2x}$, ... are all quantum mechanical entities with no classical analogue. We will therefore adopt the conservative but true approach stating that:

> J-coupling is a quatum mechanical phenomenon without a classical analogue, which transfers magnetization from observable states (say, S_{1x}) to non-observable states (say, $S_{1y}S_{2z}$) and back again at a rate given by ~ 1/J.

4. Decoupling

Sometimes J-coupling splittings are useful. For example, in the ethanol spectrum the number of splittings lets us "assign" multiplet groups to different parts of the molecule. However, splittings are often unwanted:

1. They crowd the spectrum.
2. They make you lose SNR.
3. In some pulse sequences the multiplet peaks can have different phases and interfere destructively with one another, leading to weird, often unintelligible spectral patterns.

We can make the splitting "go away" in heteronuclear systems using **decoupling**. To understand how, let's first look at the effect of π pulses on the NMR spectrum.

4.1 Spin Echoes (π-Pulses) Do Not Refocus J-Coupling Evolution in Homonuclear Spin Systems.

It is very important to realize that J-coupling evolution continues to evolve during a train of π pulses given on a homonuclear system, and is **not refocused** by them unless special circumstances occur (see below).

To see this, it's easier to switch to the Hamiltonian view. The effect of a π-pulse along, say, the x-axis can be viewed as the application of a propagator $U = e^{iI_x\pi}$. Furthermore, if we have weak J-coupling, our propagator during the system's evolution is $U(\tau)=e^{-iHt/\hbar}=e^{-i[\omega_1 I_z+\omega_2 S_z+2\pi J I_z S_z]}$ - let's assume for simplicity we have two coupled spins. The propagator describing a τ-180-τ block is:

$$\begin{aligned} U &= U(\tau)U_{180,x}U(\tau) \\ &= U_1 U_2 U_J U_{180,x}^{(1)} U_{180,x}^{(2)} U_1 U_2 U_J \end{aligned}$$

where U_i is the Zeeman propagator and U_J is the J-coupling propagator during τ. The U_i's and U_J all commute. Furthermore, $U_{180,x}^{(j)}=e^{i\pi I_{j,x}}$ commute among themselves because they act on different spins. All we have to figure out is what is the commutator of combinations such as $e^{i\pi I_{1x}}$ and U_1 or U_J. First, note that an I_z product operator evolves into $-I_z$ under a rotation:

$$U_{180,x}^{(1)} I_{1z} \left(U_{180,x}^{(1)}\right)^{\dagger} = -I_{1z}\,.$$

so:

$$U_{180,x}^{(1)} I_{1z} = -I_{1z} U_{180,x}^{(1)}\,.$$

We now prove this for any function of I_{1z}, i.e.:

$$e^{i\pi I_{1x}} f(I_{1z}) = f(-I_{1z}) e^{i\pi I_{1x}}\,.$$

To see this is true, just expand $f(I_{1z})$ in a Taylor series and start applying $e^{i\pi I_{1x}}$ to the terms. Terms having an even power of I_{1z} will remain unaffected while those with an odd number will get a minus sign:

$$\begin{aligned} e^{i\pi I_{1x}} f(I_{1z}) &= e^{i\pi I_{1x}} \sum_{n=0}^{\infty} \frac{f^{(n)}(0) I_{1z}^n}{n!} \\ &= \sum_{n=0}^{\infty} \frac{f^{(n)}(0)(-I_{1z})^n}{n!} e^{i\pi I_{1x}} \\ &= f(-I_{1z}) e^{i\pi I_{1x}} \end{aligned}$$

This means that

$$e^{i\pi I_{1x}} e^{i\alpha I_{1z}\tau} = e^{-i\alpha I_{1z}\tau} e^{i\pi I_{1x}}$$

for any constant α. In other words,

$$U_{180,x}^{(1)} U_1(\tau) = U_1(-\tau) U_{180,x}^{(1)}\,.$$

The second spin is of course unaffected with the pulse acting on the first spin, and commutes with it:

$$U_{180,x}^{(1)} U_2(\tau) = U_2(\tau) U_{180,x}^{(1)}$$

U_J, on the other hand, contains I_{1z} and its sign gets flipped (again, I_{2z} behaves as a "scalar" as far as $U_{180,x}^{(1)}$ is concerned):

$$U_{180,x}^{(1)} U_J(\tau) = U_J(-\tau) U_{180,x}^{(1)}\,.$$

Similarly, for the second pulse:

$$\begin{aligned} U_{180,x}^{(2)} U_1(\tau) &= U_1(\tau) U_{180,x}^{(2)} \\ U_{180,x}^{(2)} U_2(\tau) &= U_2(-\tau) U_{180,x}^{(2)} \\ U_{180,x}^{(2)} U_J(\tau) &= U_J(-\tau) U_{180,x}^{(2)} \end{aligned}$$

Using these identities, we can simplify the full propagator as follows:

$$\begin{aligned} U &= U_1(\tau) U_2(\tau) U_J(\tau) \\ &\quad \cdot U_{180,x}^{(1)} U_{180,x}^{(2)} U_1(\tau) U_2(\tau) U_J(\tau) \\ &= U_{180,x}^{(1)} U_{180,x}^{(2)} U_J(2\tau) \end{aligned}$$

What happened is that the $U_1(\tau)$ and $U_2(\tau)$ on the left got converted into $U_i(-\tau)$ by the two operators $U_{180,x}^{(1)} U_{180,x}^{(2)}$ when commuting with them (and then canceled out with $U_1(\tau)$ and $U_2(\tau)$ on the right of $U_{180,x}^{(1)} U_{180,x}^{(2)}$), while $U_J(\tau)$ remained unaffected, since each operator $U_{180,x}^{(j)}$ flipped its sign once, and both left it unchanged. We say that the 180s **refocused the chemical shift evolution but did not refocus the homonuclear J-coupling evolution**.

4.2 Spin Echoes (π-Pulses) **Do** Refocus J-Coupling Evolution in Heteronuclear Spin Systems.

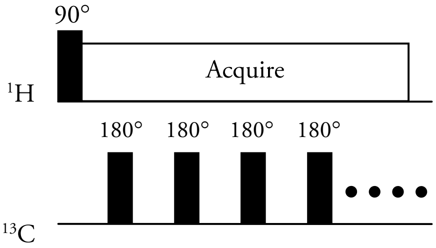
What happens with heteronuclear coupling? Here we have independent control of the transmitters for both the first and second nuclei, so we can choose to pulse on the first, the second or both; in other words, we can have any of these combinations:

$$U^{(1)}_{180,x}$$
$$U^{(2)}_{180,x}$$
$$U^{(1)}_{180,x}U^{(2)}_{180,x}$$

Each combination will have a different effect. For example: The first will refocus the J-coupling and chemical shift evolution of the 1st spin but leave the chemical shift evolution of the 2nd spin intact. Our conclusions, by the way, are **not true** for strong (J>>Δω) homonuclear J-coupling, since we can't decompose the propagator into commuting, independet parts ($U_1U_2U_J$) like we did for the weak coupling case.

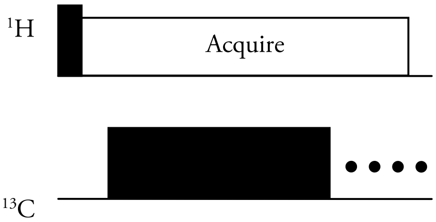
4.3 DECOUPLING

In heteronuclear systems is possible to remove splitting in nucleus A by transmitting on nucleus B. To see why this would happen, think about the following sequence for measuring the spectrum of a hydrogen nucleus while giving 180° pulses to the ^{13}C nucleus:



Each of the 180° pulses on the carbon will refocus the chemical shift evolution of the ^{13}C nuclei, while also refocusing the heteronuclear J-coupling without affecting the chemical shift evolution of the hydrogen nucleus.

One can think of a limiting process in which the 180 pulses become closely spaced, in which case the irradiation becomes continuous:

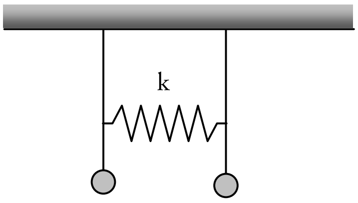


This is how most decoupling schemes are actually implemented. They have funny names like WALTZ-16. The exact details are outside the scope of this course, but the concept is straightforward as we've just discussed.

5. INEPT: COHERENT POLARIZATION TRANSFER

The coupling between spins can be used to transfer magnetization or "polarization" between them coherently. The most famous experiment or "module" for doing so is called INEPT: INsensitive nuclei Enhanced by Polarization Transfer. The idea here is that transfering polarization between a nucleus with large γ (that has "a lot" of polarization) to one with small γ (which usually has less polarization) allows one to enhance the SNR of the experiment considerably.

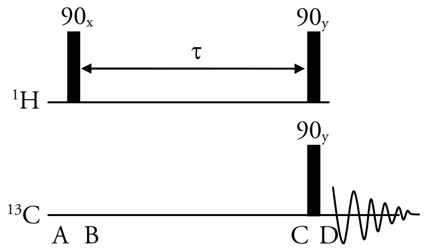
The best analogy is that of coupled pendula:



If we take out one pendulum from equilibrium and let it swing then, by a miracle, its amplitude will decay while the amplitude of the second pendulum will increase. This will then reverse, transferring motion back to pendulum 1, ad infinitum or until frictional losses kick in (this behavior happens if k is weak enough). The spring plays the role of J-coupling and determines the time to transfer. The mechanical analogy is not perfect but it should give you the rough idea.

5.1 INEPT

The basic INEPT pulse sequence is shown below for a simple 2-spin hydrogen-carbon system:



We're going to neglect the initial carbon polarization and focus on what happens to the hydrogen polarization, because that's the interesting part, so:

$$\rho_A = b_H H_z .$$

Following excitation (B):

$$\rho_B = b_H H_y .$$

If we now let our system evolve we must take into account both the chemical shift and J-coupling evolution (assumed weak), which we can play out in any order we choose:

$$\begin{aligned}\rho_B &\xrightarrow{\text{chem. shift}} b_H\left[H_y\cos(\omega_H t)+H_x\sin(\omega_H t)\right]\\ &\xrightarrow{\text{J-coupling}} b_H H_y\cos(\pi Jt)\cos(\omega_H t)\\ &\quad -b_H 2H_xC_z\sin(\pi Jt)\cos(\omega_H t)\\ &\quad +b_H H_x\sin(\omega_H t)\cos(\pi Jt)\\ &\quad +b_H 2H_yC_z\sin(\omega_H t)\sin(\pi Jt)\\ &= \rho_C\end{aligned}$$

If we now select $\tau = 1/2J$, then $\pi J\tau = \pi/2$ and

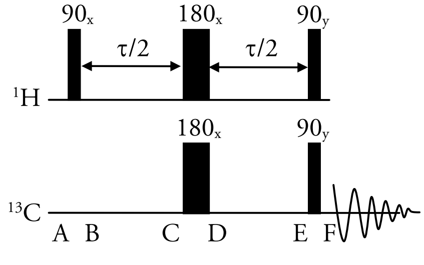
$$\begin{aligned}\rho_C = &-b_H 2H_xC_z\cos(\omega_H t)\\ &+b_H 2H_yC_z\sin(\omega_H t)\end{aligned}$$

The last pulse will then bring the system into the state:

$$\begin{aligned}\rho_D = &\,b_H 2H_zC_x\cos(\omega_H t)\\ &-b_H 2H_yC_x\sin(\omega_H t)\end{aligned}$$

1. The H_zC_x term will then evolve into C_y (and back into H_zC_x), meaning into a carbon signal. We have thus transferred the excited hydrogen signal to the carbon nucleus.
2. Here's the important part: the size of the transferred term is proportional to b_H, the Boltzmann factor of the hydrogen nucleus, and not b_C. This is big, because $b_H / b_C = \gamma_H / \gamma_C \approx 4$, meaning we've **amplified the signal four-fold!**
3. The H_yC_x term is "invisible" and is never seen. To convince yourself of that, recall that under free evolution both H_y and C_x rotate: H_y evolves into a combination of H_x and H_y, and C_x evolves into C_x and C_y. Now calculate $\mathrm{tr}\left(M_{xy}\left(H_x\otimes C_x\right)\right)$, $\mathrm{tr}\left(M_{xy}\left(H_x\otimes C_y\right)\right)$, $\mathrm{tr}\left(M_{xy}\left(H_y\otimes C_x\right)\right)$, $\mathrm{tr}\left(M_{xy}\left(H_y\otimes C_y\right)\right)$ and see they are all zero! Thus they do not contribute to the acquired signal.
4. We've set τ=1/2J. This means we need to know J beforehand. In reality J is guessed and then τ is fine-tuned at the spectrometer to maximize the signal enhancement.

The INEPT sequence can be further improved by removing the chemical shift evolution between the two 90° pulses using two π-pulses:



The calculation becomes even easier now. As before,

$$\rho_A = b_H H_z .$$
$$\rho_B = b_H H_y .$$

Now upon evolution from B to E we only need to take into account the J-coupling evolution:

$$\rho_C = b_H H_y \cos(\pi J \tau) - b_H 2H_x C_z \sin(\pi J \tau).$$

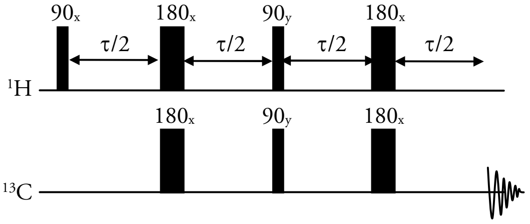
If we select $\tau = 1/2J$ as before,

$$\rho_C = -b_H 2H_x C_z \sin(\pi J \tau),$$

which after the final pulse turns into:

$$\rho_D = b_H 2H_z C_x.$$

We can turn $\rho_D = b_H 2H_z C_x$ back into $b_H C_y$ if we let J-coupling run its course while canceling out the chemical shift evolution:

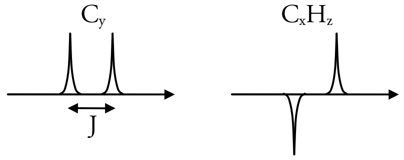


Why bother with this refocused version? Well, you can show that each will give rise to a slightly different FID expression, up to a constant overall phase and T_2 relaxation which we omit:

$$\begin{aligned} b_H 2H_z C_x &\to b_H \sin(\pi J t) e^{-i\omega_C t} \\ &\propto \tfrac{1}{2} b_H \left[e^{-i(\omega_C - \pi J)t} - e^{-i(\omega_C + \pi J)t} \right] \\ b_H C_y &\to b_H \cos(\pi J t) e^{-i\omega_C t} \\ &\propto \tfrac{i}{2} b_H \left[e^{-i(\omega_C - \pi J)t} + e^{-i(\omega_C + \pi J)t} \right] \end{aligned}$$

You can show this explicitly by calculating $\mathrm{Tr}\left(M_{xy} U(t) \rho U^\dagger(t)\right)$ (do it as an exercise!). Thus, the resulting split peaks acquired on the carbon nucleus will look slightly different for both cases: for the first the two peaks will point in opposite direction, i.e. will yield an *anti-phase* doublet, while for the second the two peaks will be *in-phase*:

Appearance of different product operator terms in the spectrum, up to a constant overall phase.



The second option is not very desirable because the two peaks can be wide and very close and might end up canceling each other out, leading to a loss of signal. There, in-phase terms are always more desirable.