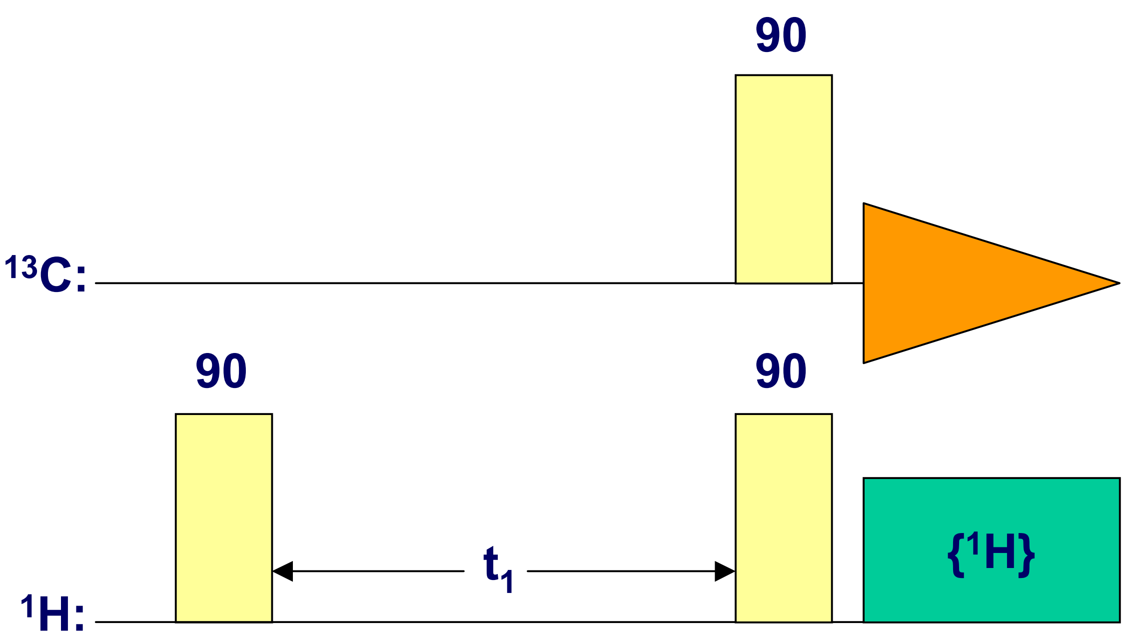
Heteronuclear correlation - HETCOR

- Last time we saw how the second dimension comes to be, and we analyzed how the ***COSY*** experiment (homonuclear correlation) works.

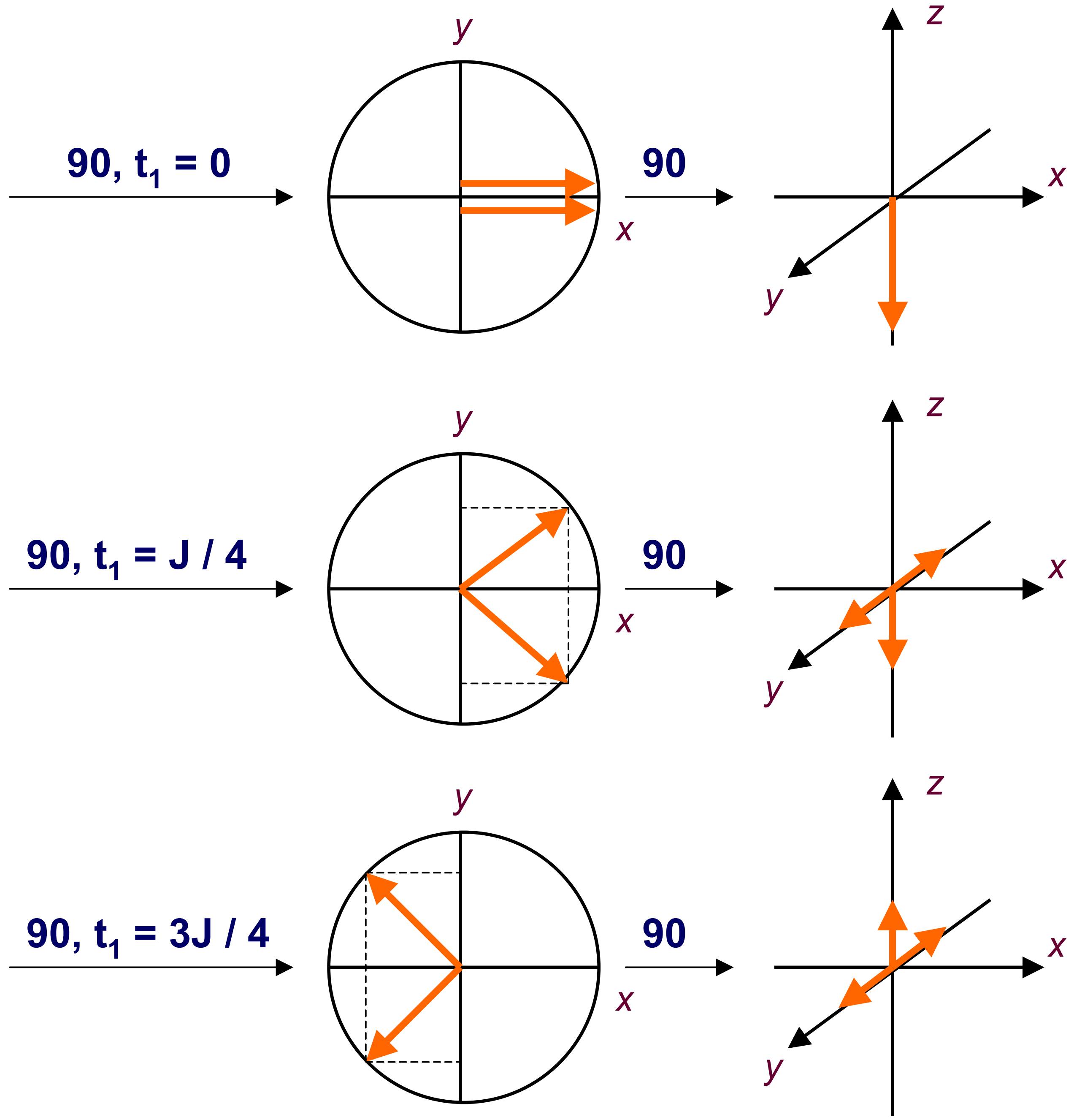
- In a similar fashion we can perform a 2D experiment in which we analyze heteronuclear connectivity, that is, which ^{1}H is connected to which ^{13}C. This is called ***HETCOR***, for ***HETero-nuclear CORrelation spectroscopy***.

- The pulse sequence in this case involves both ^{13}C and ^{1}H, because we have to somehow label the intensities of the ^{13}C with what we do to the populations of ^{1}H. The basic sequence is as follows:



HETCOR (continued)

- We first analyze what happens to the ^{1}H proton (that is, we'll see how the ^{1}H populations are affected), and then see how the ^{13}C signal is affected. For different $\mathbf{t_1}$ values we have:

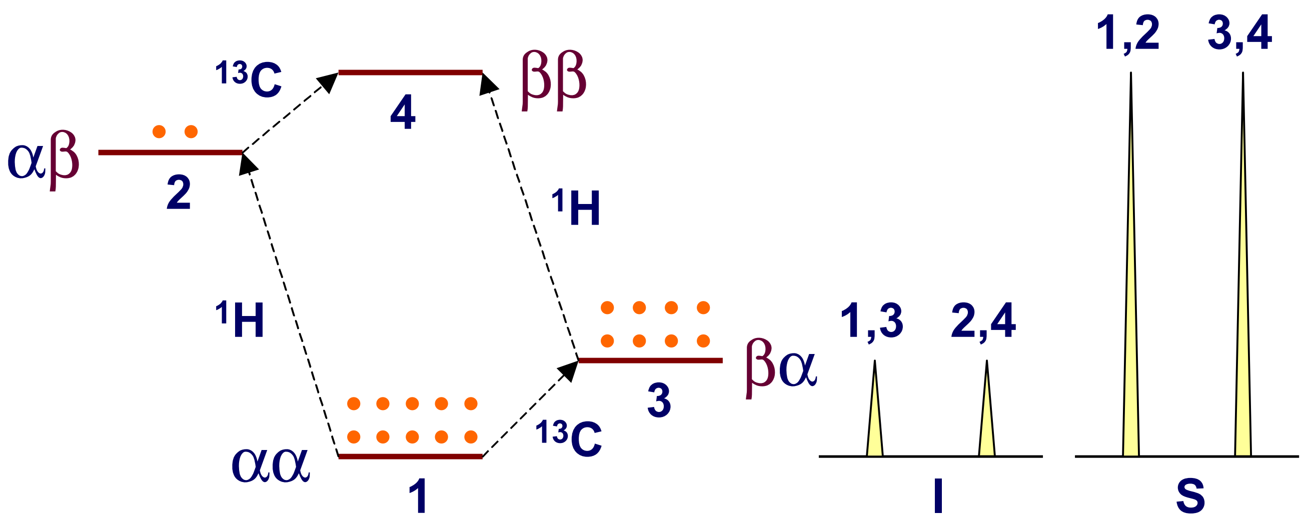


HETCOR (…)

- As was the case for COSY, we see that depending on the $\mathbf{t_1}$ time we use, we have a variation of the population inversion of the proton. We can clearly see that the amount of inversion depends on the $\mathbf{J_{CH}}$ coupling.

- Although we did it on-resonance for simplicity, we can easily show that it will also depend on the ^{1}H frequency (δ).

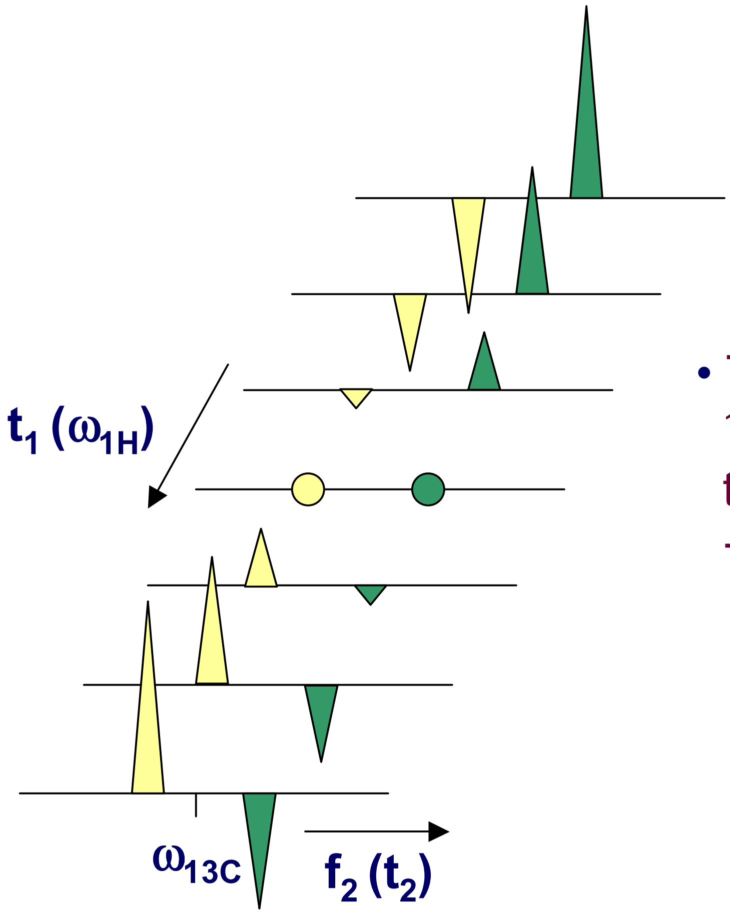
- From what we know from SPI and INEPT, we can tell that the periodic variation on the ^{1}H population inversion will have the same periodic effect on the polarization transfer to the ^{13}C. In this case, the two-spin energy diagram is ^{1}H-^{13}C:



- Now, since the intensity of the ^{13}C signal that we detect on $\mathbf{t_2}$ is modulated by the frequency of the proton coupled to it, the ^{13}C FID will have information on the ^{13}C ***and*** ^{1}H frequencies.

HETCOR (…)

- Again, the intensity of the ^{13}C lines will depend on the ^1H population inversion, thus on ω_{1H}. If we use a stacked plot for different t_1 times, we get:



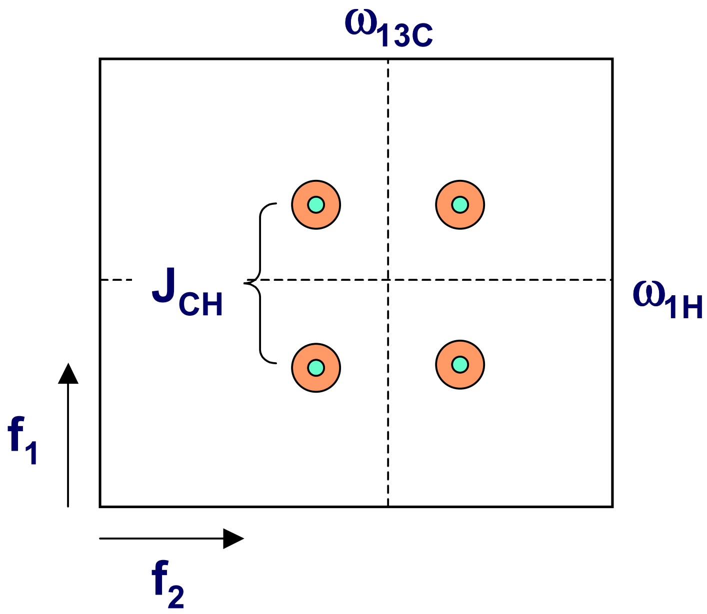
- The intensity of the two ^{13}C lines will vary with the ω_{1H} and J_{CH} between +5 and -3 as it did in the INEPT sequence.

- Mathematically, the intensity of one of the ^{13}C lines from the multiplet will be an equation that depends on ω_{13C} on t_2 and ω_{1H} on t_1, as well as J_{CH} on both time domains:

$$A_{13C}(t_1, t_2) \propto \text{trig}(\omega_{1H}t_1) * \text{trig}(\omega_{13C}t_2) * \text{trig}(J_{CH}t_1) * \text{trig}(J_{CH}t_2)$$

HETCOR (…)

- Again, Fourier transformation on both time domains gives us the 2D correlation spectrum, in this case as a contour plot:



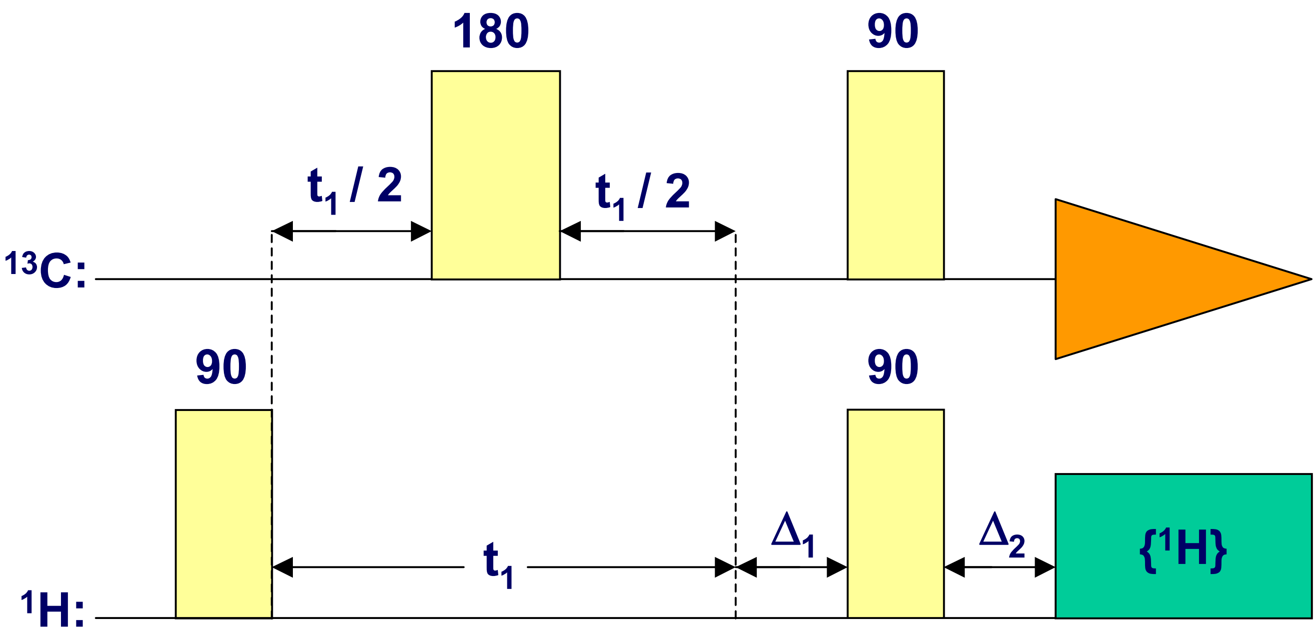
- The main difference in this case is that the 2D spectrum is not symmetrical, because one axis has ^{13}C frequencies and the other ^{1}H frequencies.

- Pretty cool. Now, we still have the $\mathbf{J_{CH}}$ coupling splitting all the signals of the 2D spectrum in little squares. The $\mathbf{J_{CH}}$ are in the 50 - 250 Hz range, so we can start having overlap of cross-peaks from different **CH** spin systems.

- We'll see how we can get rid of them without decoupling (if we decouple we won't see ^{1}H to ^{13}C polarization transfer…).

HETCOR with no J_{CH} coupling

- The idea behind it is pretty much the same stuff we did with the refocused INEPT experiment.

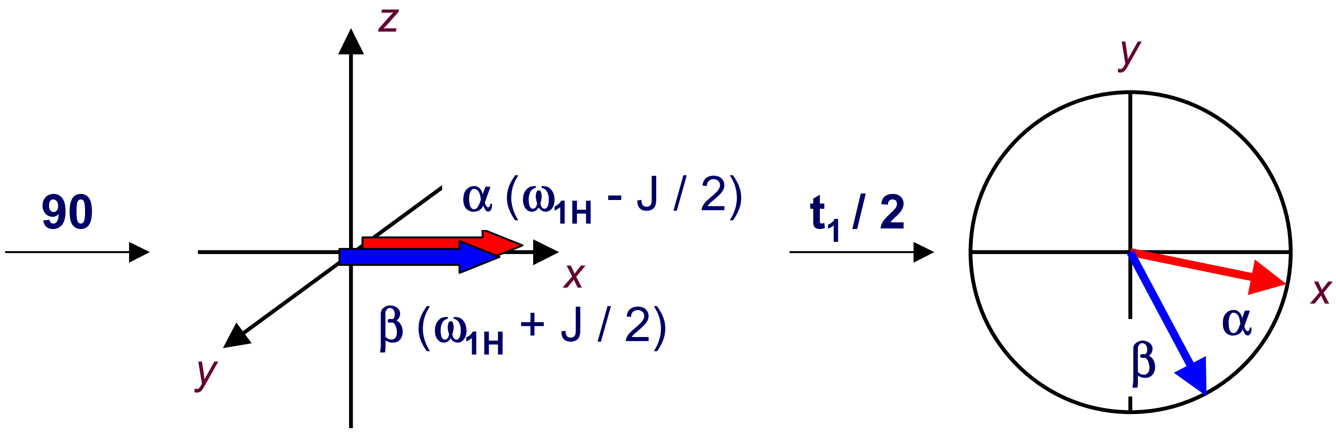


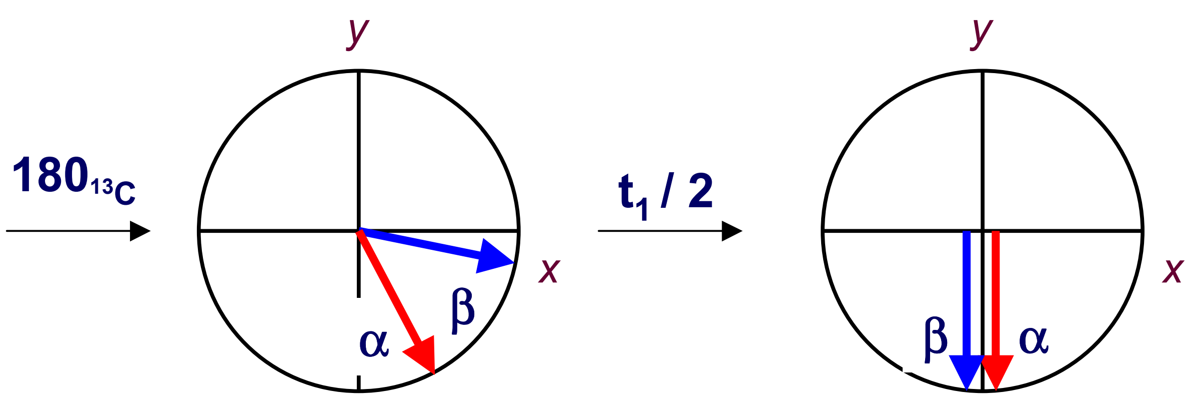
- We use a ^{13}C π pulse to refocus ^1H magnetization, and two delays to to maximize polarization transfer from ^1H to ^{13}C and to get refocusing of ^{13}C vectors before decoupling. As in INEPT, the effectiveness of the transfer will depend on the delay Δ and the carbon type. We use an average value.

- We'll analyze the case of a methine (CH) carbon...

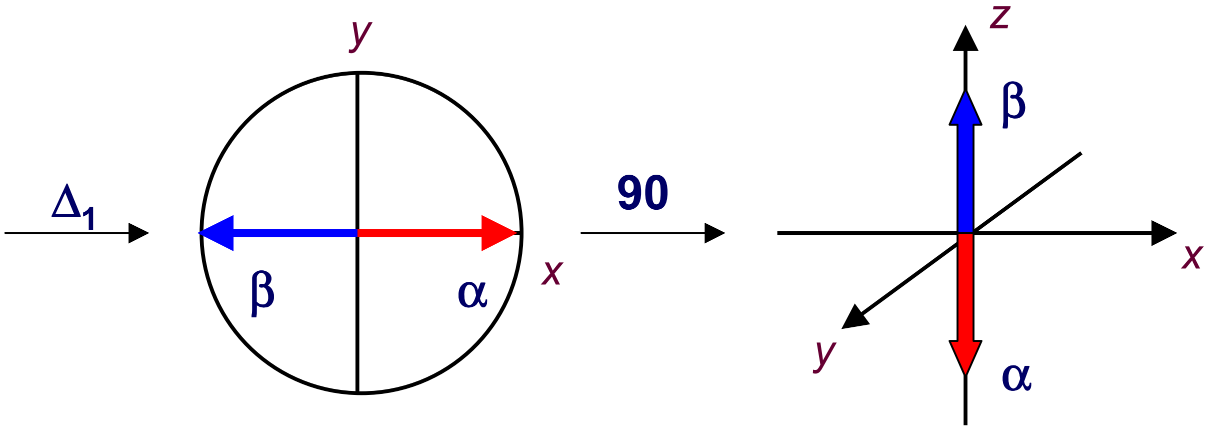
HETCOR with no J_{CH} coupling (continued)

- For a certain **t_1** value, the ^{1}H magnetization behavior is:



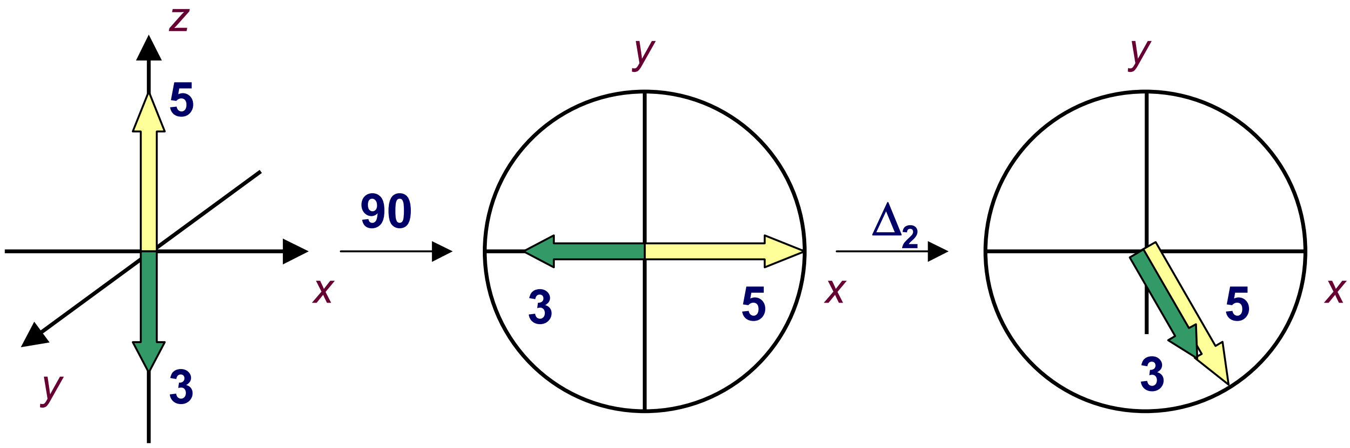


- Now, if we set Δ_1 to **1 / 2J** both ^{1}H vectors will dephase by by exactly 180 degrees in this period. This is when we have maximum population inversion for this particular **t_1**, and no **J_{CH}** effects:

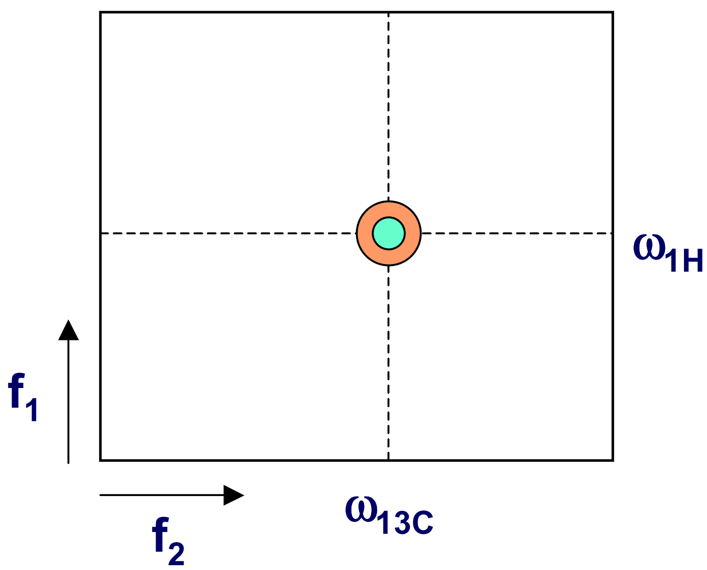


HETCOR with no J_{CH} coupling (…)

- Now we look at the ^{13}C magnetization. After the proton **π / 2** we will have the two ^{13}C vectors separated in a 5/3 ratio on the **<z>** axis. After the second delay Δ_2 (set to **1 / 2J**) they will refocus and come together:



- We can now decouple ^{1}H because the ^{13}C magnetization is refocused. The 2D spectrum now has no **J_{CH}** couplings (but it still has the chemical shift information), and we just see a single cross-peak where formed by the two chemical shifts:



Summary

- The HETCOR sequence reports on which carbon is attached to what proton and shows them both - Great for natural products stuff.

- The way this is done is by inverting ^{1}H population and varying the transfer of ^{1}H polarization to 13C during the variable t1.

- We can obtain a decoupled version by simply lumping in an refocusing echo in the middle.

Next time

- HOMO2DJ spectroscopy.

- Coherence transfer and multiple quantum spectroscopy.

HAVE A COOL (AND SAFE) BREAK!!!

(and work on the take-home…)