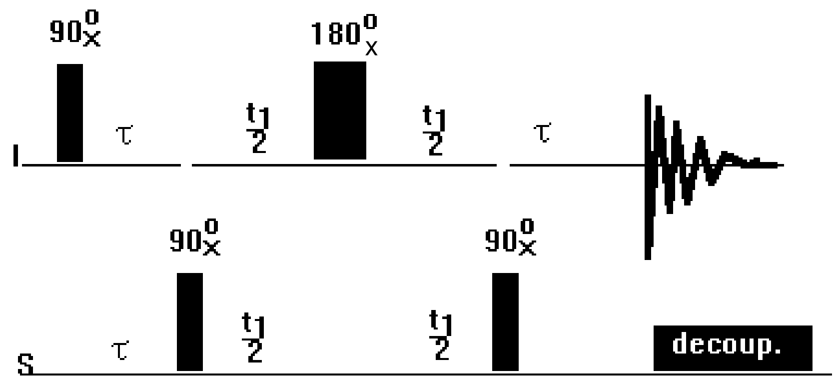
HMQC = Heteronuclear Multiple-Quantum Coherence

The pulse sequence:

(e.g.^{1}H) I: $90°_x$ ---τ---- -------$1/2t_1$ ------ $180°_x$ ------$1/2t_1$ ---- ------τ------ t_2

(e.g.^{13}C,^{15}N) S: $90°_x$ $90°_x$

Consider: Ω_I, Ω_S and J_{IS}



σ[eq.] $\mathbf{I}_z$

$\hat{H} = \pi/2\ (\hat{I}_x)$ $\downarrow 90°_x$

σ[0] $-\mathbf{I}_y$

$\hat{H} = \hat{I}_z(\Omega_I\tau)$ $\downarrow$

$$-\mathbf{I}_y \cos(\Omega_I\tau) + \mathbf{I}_x \sin(\Omega_I\tau)$$

$\hat{H} = 2\hat{I}_z\check{S}_z(J_{IS}\pi\tau)$

$$-\mathbf{I}_y \cos(\Omega_I\tau)\cos(\pi J_{IS}\tau)$$
$$+2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)$$
$$+\mathbf{I}_x \sin(\Omega_I\tau)\cos(\pi J_{IS}\tau)$$
$$+2\mathbf{I}_y\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)$$

$$-\mathbf{I}_y \cos(\Omega_I\tau)\cos(\pi J_{IS}\tau) + 2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)$$
$$+\mathbf{I}_x \sin(\Omega_I\tau)\cos(\pi J_{IS}\tau) + 2\mathbf{I}_y\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)$$

τ is set to to maximize the coherence transfer during the forthcoming steps:

- what is on $-\mathbf{I}_y$ and $+\mathbf{I}_x$ is the residual part (this **should be minimized**)
- what is on $\mathbf{I}_x\mathbf{S}_z$ and $\mathbf{I}_y\mathbf{S}_z$ will be transferred (this part **should be maximized**):

Thus, if $\tau = 1/(2J_{IS})$, then $\sin(\pi J_{IS}\tau) = 1$ and $\cos(\pi J_{IS}\tau) = 0$!

$$+2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau) \; +2\mathbf{I}_y\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)$$

$\hat{H} = \pi/2 \; (S_x)$ $\quad\downarrow 90°_x$

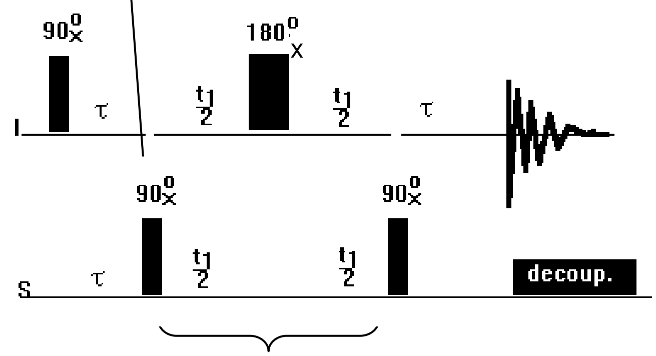
$$-2\mathbf{I}_x\mathbf{S}_y \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau) \; -2\mathbf{I}_y\mathbf{S}_y \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)$$

Both $-2\mathbf{I}_x\mathbf{S}_y$ and $-2\mathbf{I}_y\mathbf{S}_y$ are mixtures of heteronuclear zero- and double-quantum coherences. (Unlike for DQF-COSY and NOESY, here we use both terms.)

$\hat{H} = \hat{I}_z(\Omega_I[1/2t_1])$ and $S_z(\Omega_S[1/2t_1])$
$\hat{H} = 2\hat{I}_z\check{S}_z(J_{IS}\pi[1/2t_1])$

$\hat{H} = \pi\hat{I}_x$

$\hat{H} = \hat{I}_z(\Omega_I[1/2t_1])$ and $S_z(\Omega_S[1/2t_1])$
$\hat{H} = 2\hat{I}_z\check{S}_z(J_{IS}\pi[1/2t_1])$



„hetero" echo

The latter Hemiltonians are of a refocusing module; " ----1/2t_1 ---- 180° $_x$ ----1/2t_1 ---- „.
During a „heteronuclear echo” the heteronuclear coupling (JS) doesn't evolve and chemical shift doesn't evolve.

Furthermore, $S_z(\Omega_S[1/2t_1])$ followed by $S_z(\Omega_S[1/2t_1])$ is equal to $S_z(\Omega_S t_1)$.

Thus, the simplify Hem is composed of 2 terms only:

- $\hat{H} = \pi\hat{I}_x$ and
- $\hat{H} = S_z(\Omega_S t_1)$ applied consecutively.

$$\hat{H} = \pi\hat{I}_x \qquad -2\mathbf{I}_x\mathbf{S}_y \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau) \qquad -2\mathbf{I}_y\mathbf{S}_y \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)$$

$$\downarrow 180°_x$$

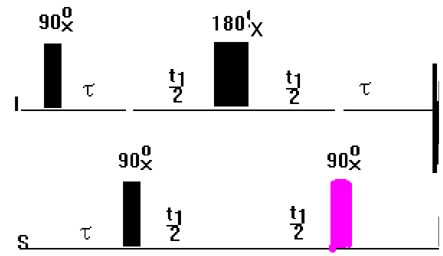
$$\hat{H} = S_z(\Omega_S t_1) \qquad -2\mathbf{I}_x\mathbf{S}_y \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau) \qquad +2\mathbf{I}_y\mathbf{S}_y \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)$$

$$\downarrow$$

$$-2\mathbf{I}_x\mathbf{S}_y \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1) +2\mathbf{I}_x\mathbf{S}_x \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\sin(\Omega_S t_1)$$
$$+2\mathbf{I}_y\mathbf{S}_y \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1) -2\mathbf{I}_y\mathbf{S}_x \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\sin(\Omega_S t_1)$$

memo: These 4 terms are all **h**eteronuclear **m**ultiple **q**uantum **c**oherences (HMQC)

$$-2\mathbf{I}_x\mathbf{S}_y \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1) + 2\mathbf{I}_x\mathbf{S}_x \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\sin(\Omega_S t_1)$$
$$+2\mathbf{I}_y\mathbf{S}_y \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1) - 2\mathbf{I}_y\mathbf{S}_x \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\sin(\Omega_S t_1)$$



$\hat{H} = \pi/2 \ (S_x)$ $\downarrow 90°_x$

$$-2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1) + 2\mathbf{I}_x\mathbf{S}_x \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\sin(\Omega_S t_1)$$
$$+2\mathbf{I}_y\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1) - 2\mathbf{I}_y\mathbf{S}_x \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\sin(\Omega_S t_1)$$

memo 1: $+2\mathbf{I}_x\mathbf{S}_x \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\sin(\Omega_S t_1)$ and $-2\mathbf{I}_y\mathbf{S}_x \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\sin(\Omega_S t_1)$ terms will not be observable at the end.

memo 2: $-2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)$ and $+2\mathbf{I}_y\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)$ are single quantum coherences on spin I. (both observables)

$$-2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1) \qquad +2\mathbf{I}_y\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)$$

$\hat{H} = \hat{I}_z(\Omega_I\tau)$ $\downarrow$

$$-2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\cos(\Omega_I\tau)$$
$$-2\mathbf{I}_y\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\sin(\Omega_I\tau)$$
$$+2\mathbf{I}_y\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\cos(\Omega_I\tau)$$
$$-2\mathbf{I}_x\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\sin(\Omega_I\tau)$$

memo 1:

$$-2\mathbf{I}_y\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\sin(\Omega_I\tau) \ +2\mathbf{I}_y\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\cos(\Omega_I\tau) = 0$$

memo 2:

$$-2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\cos(\Omega_I\tau) - 2\mathbf{I}_x\mathbf{S}_z \sin(\Omega_I\tau)\sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\sin(\Omega_I\tau) =$$
$$-2\mathbf{I}_x\mathbf{S}_z \sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)[\cos^2(\Omega_I\tau) + \sin^2(\Omega_I\tau)] = -2\mathbf{I}_x\mathbf{S}_z \sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)$$

Finally, the remaining signal term is:

$$-2\mathbf{I}_x\mathbf{S}_z \sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)$$

$$\hat{H} = 2\hat{I}_z\check{S}_z(J_{IS}\pi\tau) \qquad \downarrow$$

$$-2\mathbf{I}_x\mathbf{S}_z \sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\cos(\pi J_{IS}\tau) \qquad \mathbf{-I}_y \sin(\pi J_{IS}\tau)\cos(\Omega_S t_1)\sin(\pi J_{IS}\tau)$$

as mentioned previously if $\tau = 1/(2J_{IS})$ then $\sin(\pi J_{IS}\tau) = 1$ and $\cos(\pi JIS\tau) = 0$
Therefore before ACQ the only term is that of $\mathbf{-I}_y \cos(\Omega_S t_1)$

$$\hat{H} = \hat{I}_z(\Omega_I[t_2]) \text{ and } S_z(\Omega_S[t_2]) \qquad \downarrow$$

$$\hat{H} = 2\hat{I}_z\check{S}_z(J_{IS}\pi[t_2])$$

$$\mathbf{-I}_y \cos(\Omega_S t_1)\cos(\Omega_I t_2)\cos(\pi J_{IS} t_2)$$
$$+2\mathbf{I}_x\mathbf{S}_z \cos(\Omega_S t_1)\cos(\Omega_I t_2)\sin(\pi J_{IS} t_2)$$
$$+\mathbf{I}_x \cos(\Omega_S t_1)\sin(\Omega_I t_2)\cos(\pi J_{IS} t_2)$$
$$+2\mathbf{I}_y\mathbf{S}_z \cos(\Omega_S t_1)\sin(\Omega_I t_2)\sin(\pi J_{IS} t_2)$$

memo 1: put the receiver on x

therefore only the single x term remains : $+\mathbf{I}_x \cos(\Omega_S t_1)\sin(\Omega_I t_2)\cos(\pi J_{IS} t_2)$

memo 2: $\sin(A)\cos(B) = 1/2[\sin(A+B)+\sin(A-B)]$

therefore

$$-1/2\mathbf{I}_x \cos(\Omega_S t_1)\ [+\sin\{(\Omega_I+\pi J_{IS})t_2\}+ \sin\{(\Omega_I-\pi J_{IS})t_2\}]$$

the following term can be found $- \mathbf{I}_x$ [+ .. + ..] at Ω_I , Ω_S

if one sets the phase that *cos is absorptive (a) in* t_1

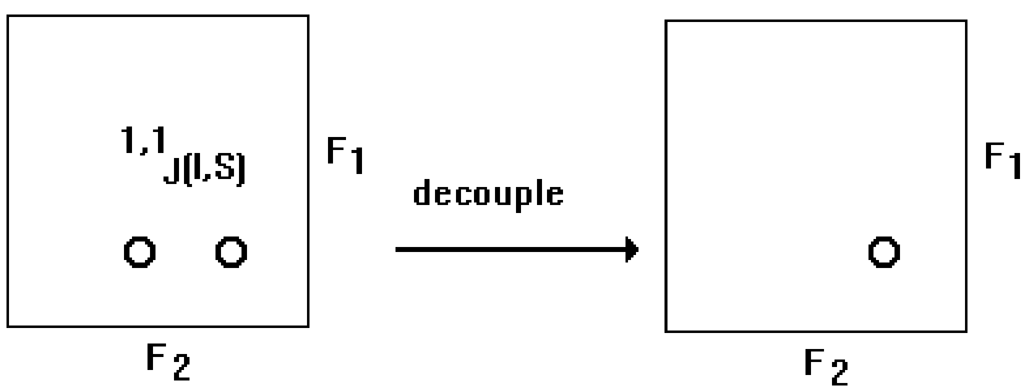
sin is absorptive (d) in t_2

$\mathbf{I}_x$ [+a .. +a ..] at Ω_I , Ω_S

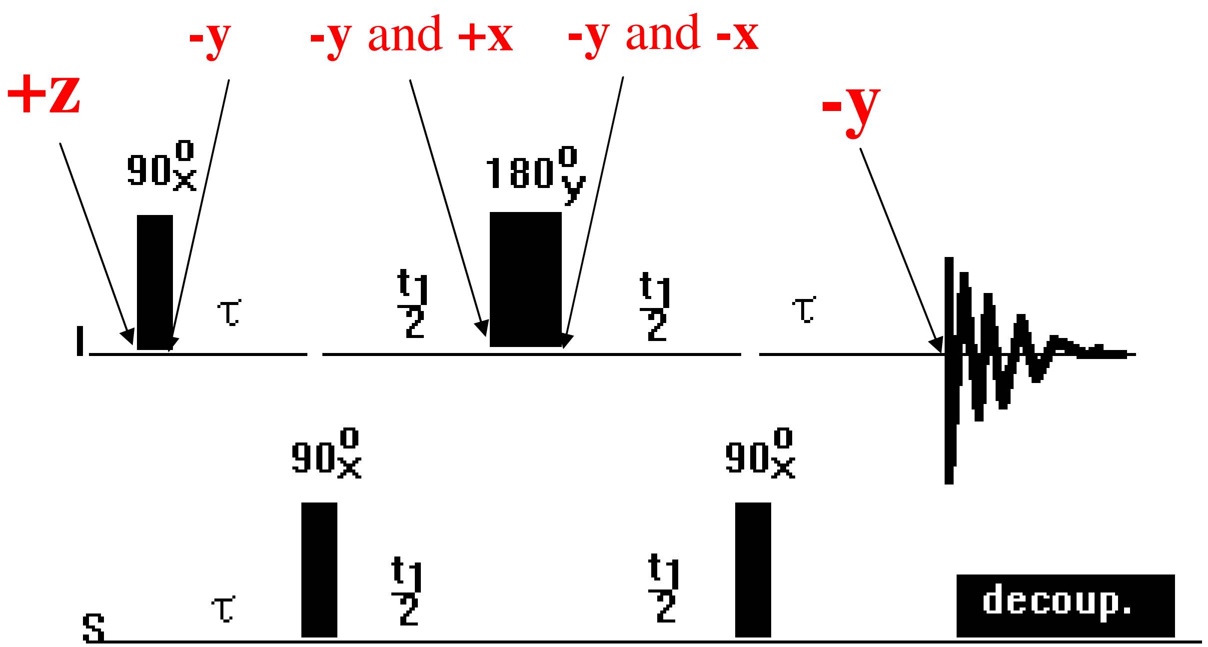
Singulet in F1 and the in phased doublet in F2. ($^{1,1}J[H,N] \cong 90$ Hz, $^{1,1}J[H,C] \cong 150$ Hz)

if we decouple during t_2 ($\hat{H} = 2\hat{I}_z\check{S}_z(J_{IS}\pi[t_2])$ is not active) then the spectrum is

$\mathbf{I}_x$ [+a] at Ω_I , Ω_S



Monitoring balk H_2O along the sequence:



What is happaning with the balk water during the HSQC pulses? If $\tau + t_1/2 = \Delta$, then

$$+H_z \text{—}(90^\circ{}_x)\rightarrow -H_y$$

$$\text{—}(H_z(\Omega_H \Delta)\rightarrow -H_y\cos(\Omega_H \Delta) + H_x\sin(\Omega_H \Delta)$$

$$\text{—}(180^\circ{}_y)\rightarrow -H_y\cos(\Omega_H \Delta) - H_x\sin(\Omega_H \Delta)$$

$$\text{—}(H_z(\Omega_H \Delta)\rightarrow -H_y\cos(\Omega_H \Delta) + H_x\sin(\Omega_H \Delta) - H_x\sin(\Omega_H \Delta) - H_y\cos(\Omega_H \Delta) = -H_y$$

Water before acquisition is aligned along -y. Thus, most of the water is detected during t_2. This is a dreadful news.