On pulses, phases and gradients:

Productoperatorformalism - a practical approach

Greater Bay Area Magnetic Resonance Workshop

24.04.2024

Einem jeden Vorwitze nachzuhängen, und der Erkenntnissucht keine andre Grenzen zu verstatten, als das Unvermögen, ist ein Eifer, welcher der *Gelehrsamkeit* nicht übel ansteht. Allein unter unzähligen Aufgaben, die sich selbst darbieten, diejenige auswählen, deren Auflösung dem Menschen angelegen ist, ist das Verdienst der *Weisheit.*

To indulge in every pretense, and to allow the craving for knowledge no other limit than inability, is a zeal which is not ill-suited to scholarship. But to choose from the innumerable tasks that present themselves, the one whose resolution is incumbent on man, is the merit of wisdom

Immanuel Kant,
Träume eines Geistersehers,
erläutert durch Träume der Metaphysik

PROF – a practical approach

The PROF is a quantum mechanical concept that can be derived from the density matrix formalism.

BUT

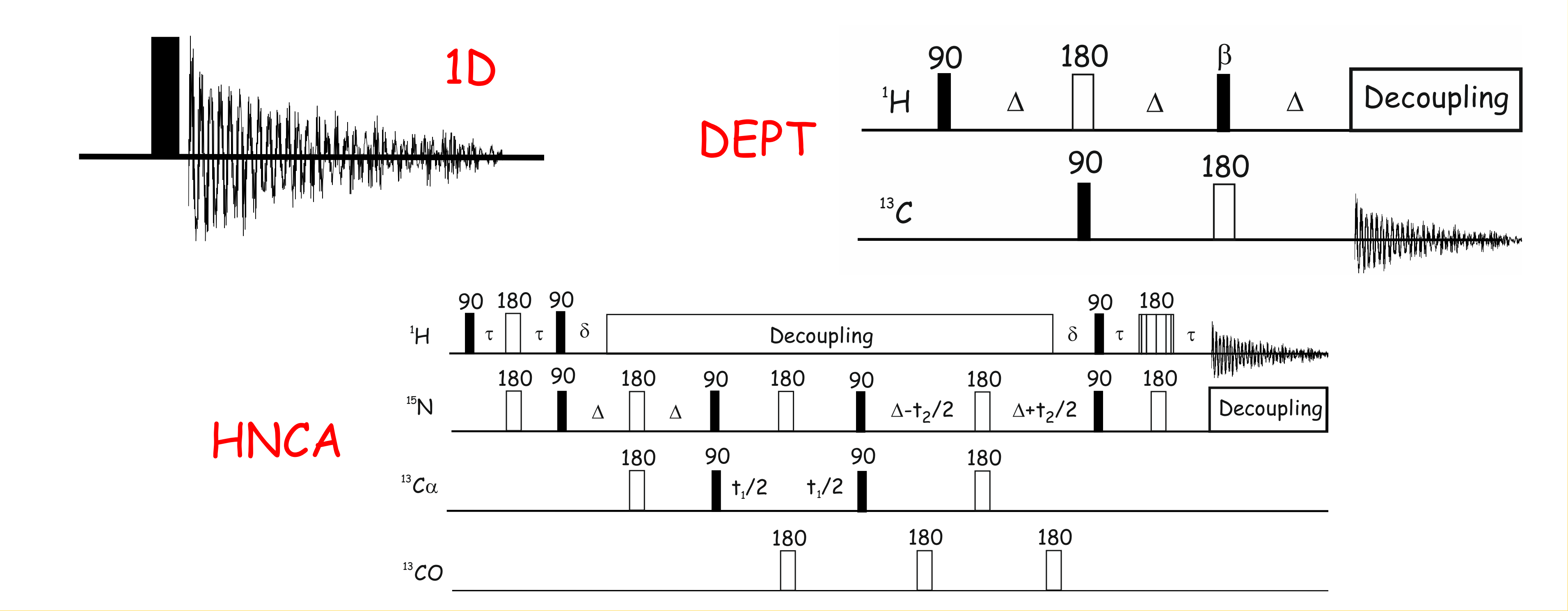
We do not need to do that, we can introduce it in an axiomatic fashion and use the rules given.

Then the PROF can be used by applying the rules, using only basic arithmetic and some trigonometrical rules.

O.W. Sørensen et al. *Prog. NMR. Spectrosc.* **16**, 163-192 (1983)

PROF – a practical approach

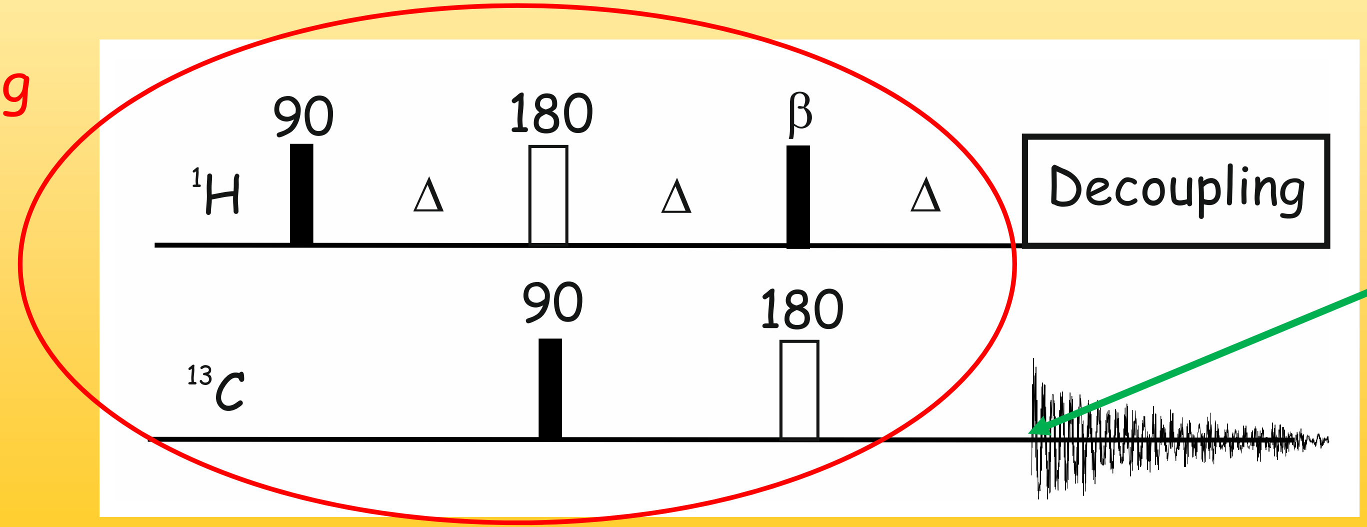
Our goal here is a theoretical description of NMR pulse-sequences, which can be of varying complexity



PROF – a practical approach

In a simple 1D and during the acquisition of more complex experiments, the usual selection rules apply. To understand more complex experiments we need to be able to calculate what is going on during the pulse sequence and to predict which detectable magnetization is present at the beginning of the acquisition

What is going on here ?

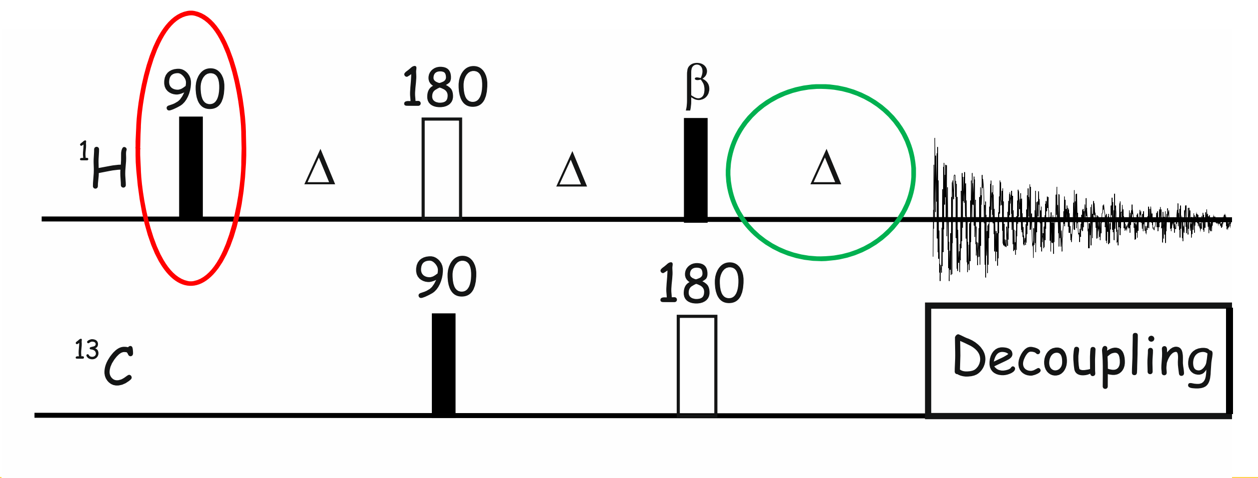


What is present here ?

PROF – a practical approach

Our means of manipulating magnetization during a pulse-sequence are threefold: we can use pulses and we can allow for chemical shift evolution and evolution of scalar coupling during delays. We can also apply gradients, which will need a slightly different type of product operators (for the discussion here we ignore the NOE-effect and relaxation)

Pulses are short, during their duration chemical shift an scalar coupling can be ignored



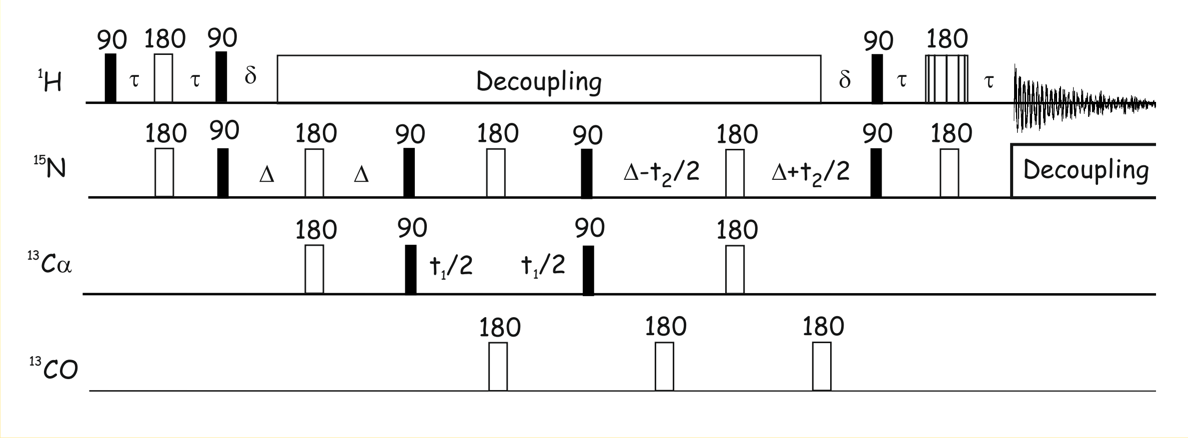
During delays evolution of chemical shift and scalar coupling takes place

PROF – a practical approach

That is how we want to do that:

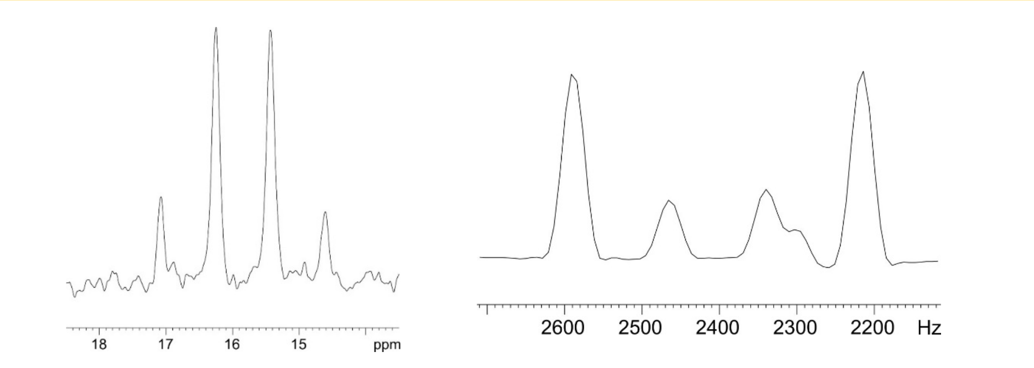
- How do the operator we use look like and how are they called
- What are the rules to describe pulses, chemical shift and scalar coupling
- Application to simple sequences, what is detectable, does the calculated spectrum correspond to the real one
- Calculation of pulse sequence building blocks and a look at a triple resonance experiment
- *Calculation of BIRD and TANGO pulses*
- *Understanding coupling pattern in an undecoupled HSQC*

PROF – a practical approach



How does an HNCA work and which parameters do we have to adjust ?

Can we understand the pattern in undecopled 1Ds *and HSQCs*



PROF – a practical approach

What we will not cover today:

- Gradients can be handled with the PROF, but we will need a different set of operators, which we will introduce at the end but only use in later seminars
- Relaxation is completely ignored by the PROF
- Strong coupling can not be covered, the PROF assumes that chemical shift and scalar coupling are independent

The rules

The rules

The operators we will use can be single operators or products thereof

H_xC_z

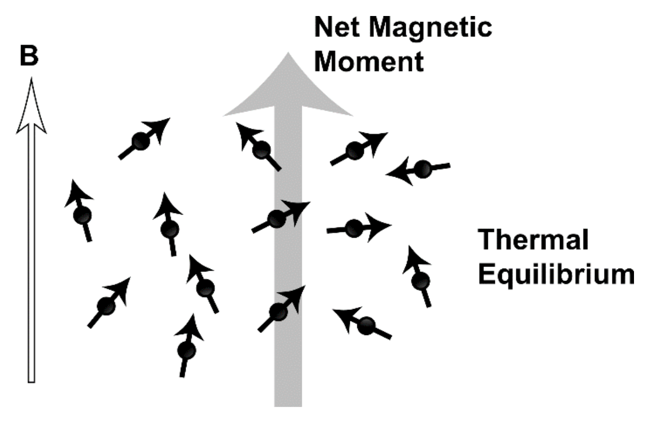
Type of nucleus
(here hydrogen, generally I and S is used)

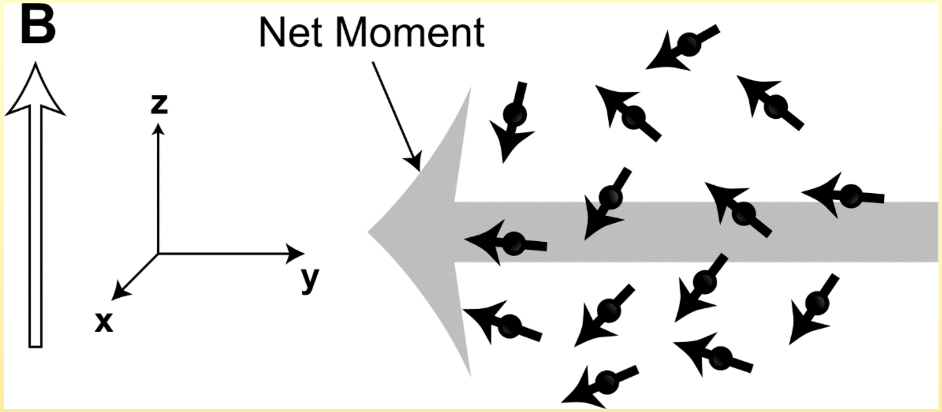
spacial orientation
(cartesian coordinates are good for pulse sequences)

$$A \xrightarrow{\beta B} C\cos\beta + D\sin\beta$$

All rules then look like this, where A,B,C and D are operators and β is the size of the interaction B (pulse angle, chemical shift, scalar coupling)

The rules





Some simple operators correspond to pictures we all know and use

Longitudinal magnetization H_z

Transvers in-phase magnetization H_x, H_y

H_z is the starting point of NMR experiments,

H_x, H_y are the only operators that correspond to detectable magnetization !

The rules

In addition, there are those types of magnetization that give the name to the PROF, are created by using more than one pulse and can not be easily visualized:

Transvers anti-phase magnetization $I_{1x}I_{2z}$

and

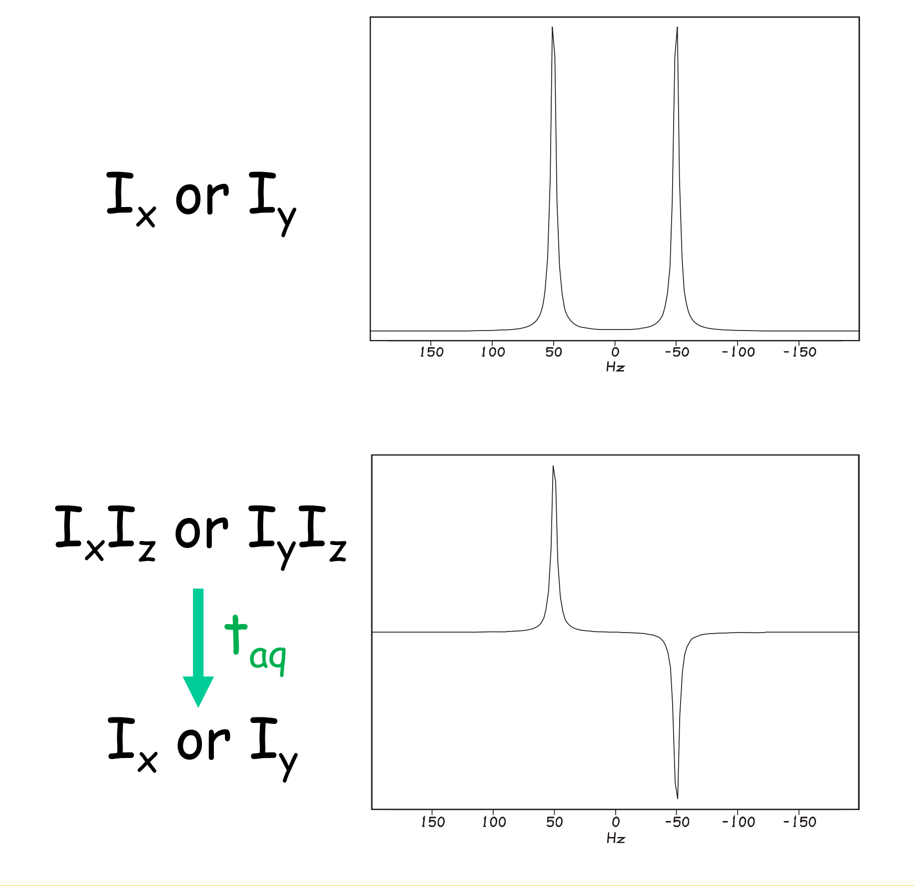
Multiple quantum magnetization $I_{1x}I_{2y}$

All these operators can be manipulated and converted into each other using pulses, chemical shift evolution and evolution of scalar coupling, but they can only be detected indirectly ("forbidden fruits from the tree of knowledge")

The rules

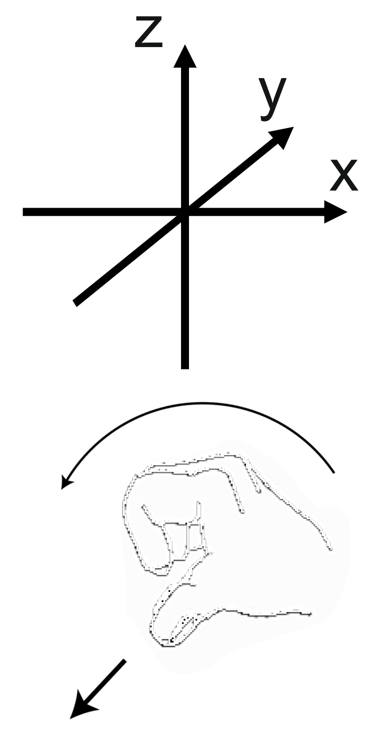
What is detectable ?

Detectable during an acquisition is either in-phase magnetization (I_x and I_y and combinations thereof) or anti-phase magnetization (I_xI_z or I_yI_z and combinations thereof), that yields in-phase magnetization during the acquisition



The rules

We will use a right-handed coordinate system



And we will utilize trigonometrical rules like those

$$\cos^2\alpha + \sin^2\alpha = 1$$

$$\sin^2\alpha = 2\ \sin\alpha\ \cos\alpha$$

$$\cos^2\alpha = \cos2\alpha - \sin2\alpha$$

$$\sin^2\alpha = \tfrac{1}{2}\ (1 - \cos\ 2\alpha)$$

$$\cos^2\alpha = \tfrac{1}{2}\ (1 + \cos\ 2\alpha)$$

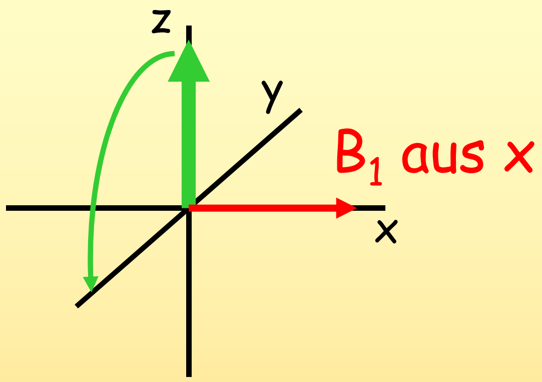
$$\sin(\alpha+\beta) = \sin\alpha\ \cos\beta + \cos\alpha\ \sin\beta$$

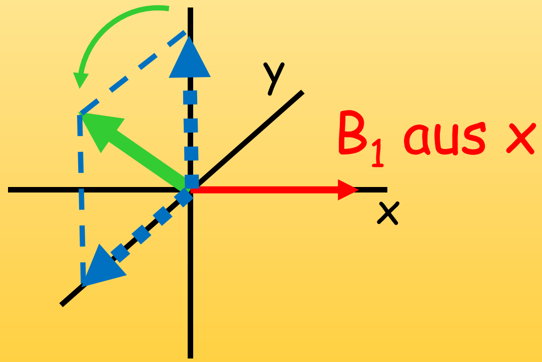
$$\sin(\alpha-\beta) = \sin\alpha\ \cos\beta - \cos\alpha\ \sin\beta$$

$$\cos(\alpha+\beta) = \cos\alpha\ \cos\beta - \sin\alpha\ \sin\beta$$

$$\cos(\alpha-\beta) = \cos\alpha\ \cos\beta + \sin\alpha\ \sin\beta$$

The rules





The rule for an x-pulse looks like that

x-pulse of angle β

$$I_z \xrightarrow{\beta I_x} I_z \cos\beta - I_y \sin\beta$$

$\beta = 90°$: $\cos\beta = 0$, $\sin\beta = 1$, the result is $-I_y$

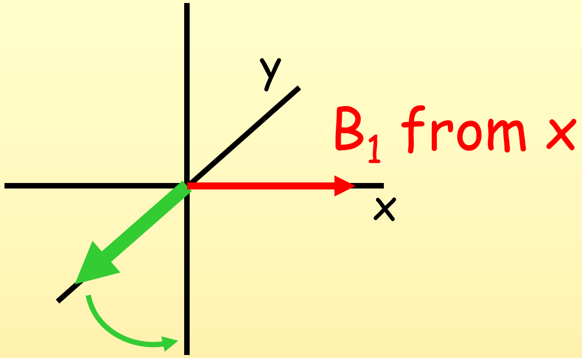
$\beta = 180°$: $\cos\beta = -1$, $\sin\beta = 0$ the result is $-I_z$

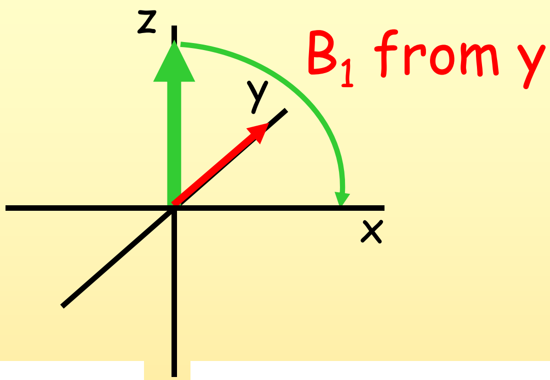
$\beta = 45°$: $\cos\beta = \frac{1}{2}\sqrt{2}$, $\sin\beta = \frac{1}{2}\sqrt{2}$,

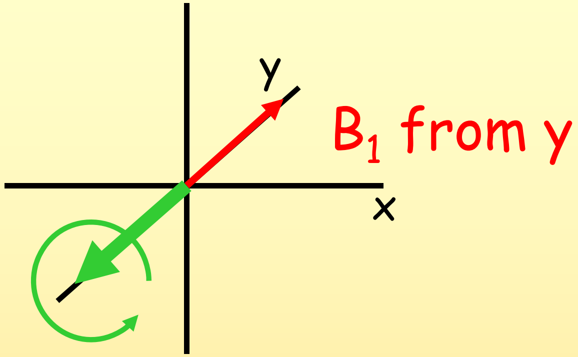
the result is

$\frac{1}{2}\sqrt{2}\, I_z - \frac{1}{2}\sqrt{2}\, I_y$

The rules







$$I_z \xrightarrow{\beta I_x} I_z \cos\beta - I_y \sin\beta$$

$$I_z \xrightarrow{\beta I_y} I_z \cos\beta + I_x \sin\beta$$

$$I_z \xrightarrow{\beta I_{-x}} I_z \cos\beta + I_y \sin\beta$$

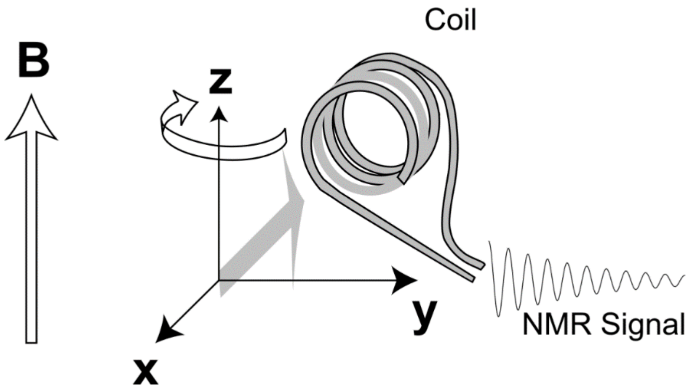
$$I_z \xrightarrow{\beta I_{-y}} I_z \cos\beta - I_x \sin\beta$$

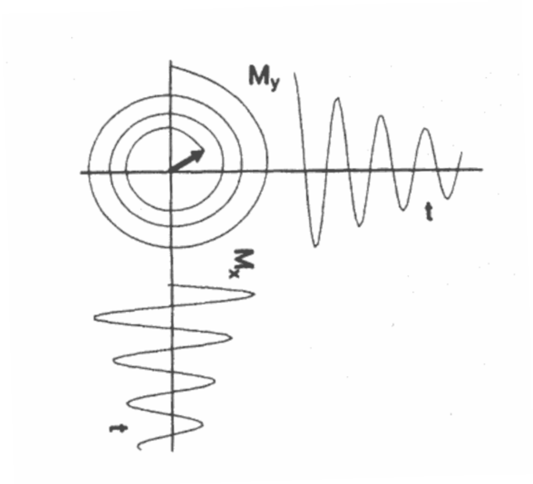
$$I_x \xrightarrow{\beta I_y} I_x \cos\beta - I_z \sin\beta$$

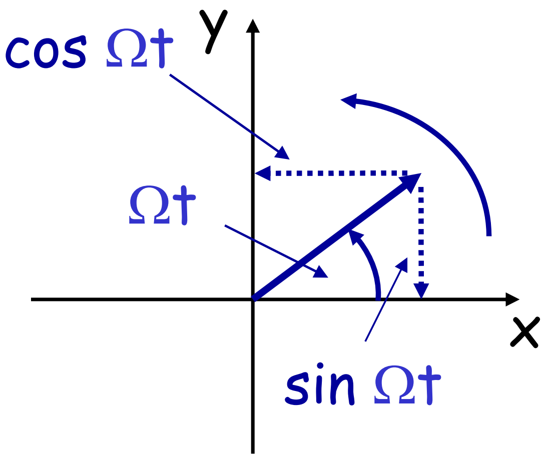
$$I_y \xrightarrow{\beta I_x} I_y \cos\beta + I_z \sin\beta$$

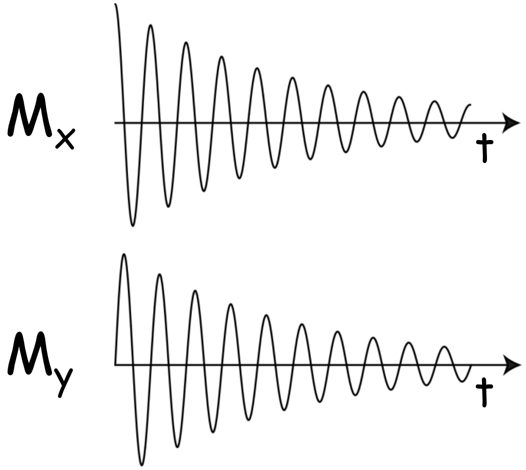
$$\left.\begin{array}{l} I_x \xrightarrow{\beta I_x} I_x \\ I_y \xrightarrow{\beta I_y} I_y \end{array}\right\} \text{no effect !!}$$

The rules



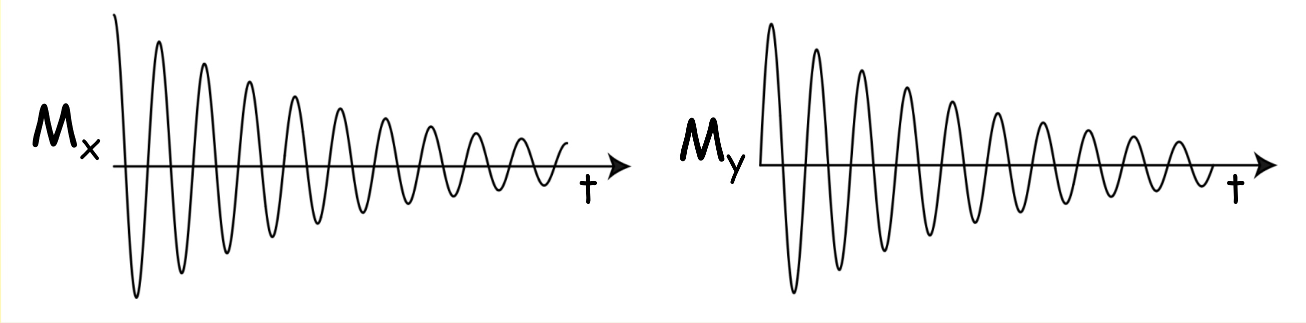






The rules for chemical shift can also be understood using trusted pictures. We consider quadrature detection, i.e. we obtain a complex signal (see next seminar)

The rules



$$M_x = \cos \Omega_0 t \, \exp(-t/T_2) \qquad M_y = \sin \Omega_0 t \, \exp(-t/T_2)$$

$$M = M_x + i\,M_y = [\cos \Omega_0 t + i \sin \Omega_0 t\,]\exp(-t/T_2)$$

$$M = \exp(i\Omega_0 t)\exp(-t/T_2)$$

This we will ignore !

using Eulers relation:

$$\exp(i\alpha) = \cos\alpha + i\sin\alpha \text{ and } \exp(-i\alpha) = \cos\alpha - i\sin\alpha$$

The rules

The rules for chemical shift look like that

The chemical shift Ω_0 acts for a time τ

$$I_x \xrightarrow{I_z\Omega_0\tau} I_x \cos \Omega_0\tau + I_y \sin \Omega_0\tau = I_x \cos 2\pi\delta\tau + I_y \sin 2\pi\delta\tau$$

angular frequency Ω_0

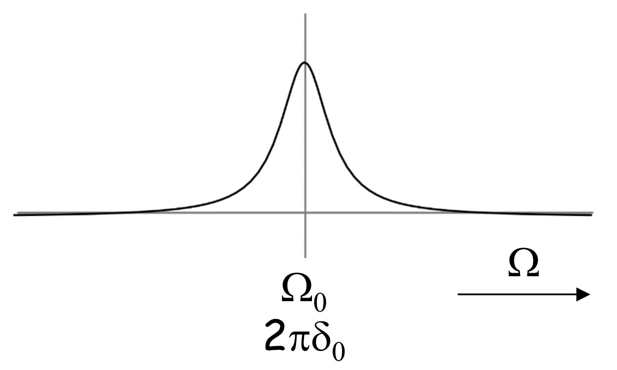
„normal“ frequency δ (in Hertz)

We assume that we do quadrature detection

If we apply an FT we obtain an absorbtive signal at the position of Ω_0 or $2\pi\delta$

$$I_x \cos \Omega_0\tau \longrightarrow I \exp (i\Omega_0\tau)$$

$$I_x \cos 2\pi\delta\tau \longrightarrow I \exp (i2\pi\delta_0\tau)$$



The rules

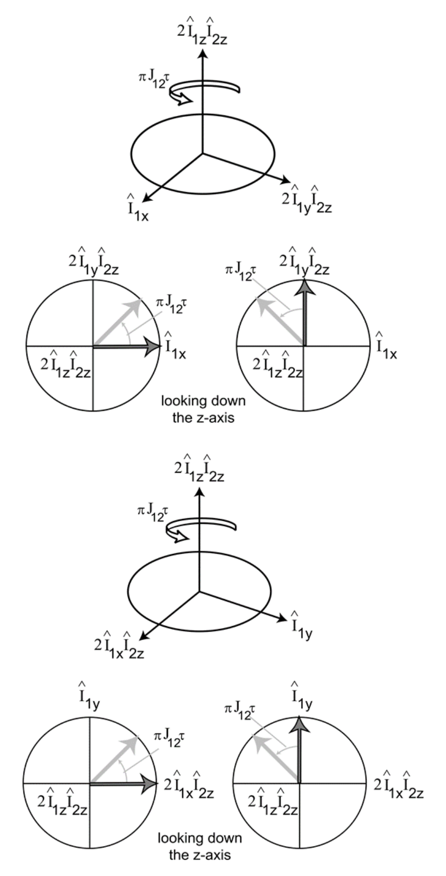
Now we consider scalar coupling, here we have two rules

Starting from in-phase coupling creates anti-phase

$$I_{1x} \xrightarrow{I_{1z}I_{2z}\pi J_{12}\tau} I_{1x}\cos\pi J_{12}\tau + 2I_{1y}I_{2z}\sin\pi J_{12}\tau$$

Starting from anti-phase we return to in-phase

$$I_{1x}I_{2z} \xrightarrow{I_{1z}I_{2z}\pi J_{12}\tau} I_{1x}I_{2z}\cos\pi J_{12}\tau + I_{1y}\sin\pi J_{12}\tau$$



Calculating 1D spectra

Calculating 1D spectra

To calculate 1D spectra we will use chemical shift and scalar coupling, they can be applied sequentially. We start with in-phase magnetization.

$$I_{1x} \xrightarrow{I_z\Omega_1 t_{aq}} I_{1x} \cos \Omega_1 t_{aq} + I_{1y} \sin \Omega_1 t_{aq}$$

If we do quadrature detection we get: $I_1 \exp(i\Omega_1 t_{aq})$

$$I_1 \exp(i\Omega_1 t_{aq}) \xrightarrow{I_{1z}I_{2z}\pi J_{12} t_{aq}} I_1 \exp(i\Omega_1 t_{aq}) \cos\pi J_{12} t_{aq} + 2I_1 I_{2z} \exp(i\Omega_1 t_{aq}) \sin\pi J_{12} t_{aq}$$

Only the first term is relevant, since only in-phase yields signal

$$I_1 \exp(i\Omega_1 t_{aq}) \cos\pi J_{12} t_{aq} = \tfrac{1}{2} I_1 \exp(i2\pi\delta_1 t_{aq}) [\exp(i\pi J_{12} t_{aq}) + \exp(-i\pi J_{12} t_{aq})]$$

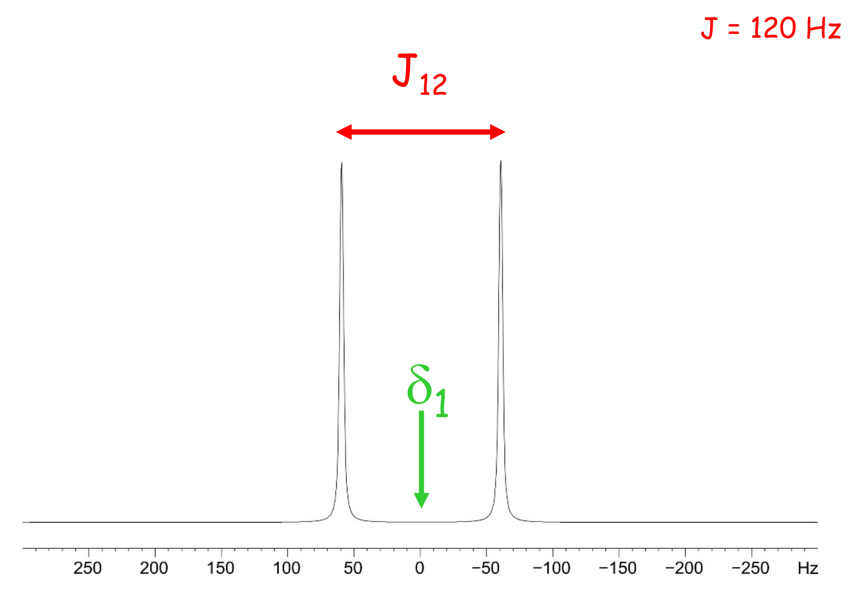
Calculating 1D spectra

$\cos \alpha = \frac{1}{2}\,[\exp(+i\alpha) + \exp(-i\alpha)]$

$$I_1 \exp(i\Omega_1 t_{aq}) \cos \pi J_{12} t_{aq} = \frac{1}{2} I_1 \exp(i2\pi\delta_1 t_{aq})\,[\exp(i\pi J_{12} t_{aq}) + \exp(-i\pi J_{12} t_{aq})]$$

$$= \frac{1}{2} I_1\,[\exp(i2\pi(\delta_1 + J_{12}/2)t_{aq}) + \exp(i2\pi(\delta_1 - J_{12}/2)t_{aq})]$$

If we subject this to a Fourier transform we will obtain two lines, centered around δ_1 with a distance of J_{12}: a doublet



Calculating 1D spectra

If we have two coupling partners we need to apply the coupling twice

$$I_{1x} \xrightarrow{I_z\Omega_1 t_{aq}} I_{1x} \cos \Omega_1 t_{aq} + I_{1y} \sin \Omega_1 t_{aq}$$

$$I_1 \exp (i\Omega_1 t_{aq}) \xrightarrow{I_{1z}I_{2z}\pi J_{12}\tau} \xrightarrow{I_{1z}I_{3z}\pi J_{13}\tau}$$

As before only the in-phase part is relevant

$$\cos \alpha \cos \beta = \tfrac{1}{2} [\cos(\alpha + \beta) + \cos(\alpha - \beta)]$$

$$I_1 \exp (i\Omega_1 t_{aq}) \cos\pi J_{12} t_{aq} \cos\pi J_{13} t_{aq}$$

$$= \tfrac{1}{2} I_1 \exp (i2\pi\delta_1 t_{aq})[\cos\pi(J_{12}+J_{13})\, t_{aq} + \cos\pi(J_{12}-J_{13})\, t_{aq}]$$

If we use Euler again we will end up with four lines

Calculating 1D spectra

$$I_1 \exp\,(i\Omega_1 t_{aq})\; \cos\pi J_{12} t_{aq}\; \cos\pi J_{13} t_{aq}$$

$$\cos\alpha \cos\beta = \tfrac{1}{2}\,[\cos(\alpha + \beta) + \cos(\alpha - \beta)]$$

$$= \tfrac{1}{2}\, I_1 \exp\,(i2\pi\delta_1 t_{aq})[\cos\pi(J_{12}{+}J_{13})t_{aq} + \cos\pi(J_{12}{-}J_{13})t_{aq}]$$

$$= \tfrac{1}{4}\, I_1 \exp\,(i2\pi\delta_1 t_{aq})\; [\exp(i\pi(J_{12}{+}J_{13})t_{aq} + \exp(i\pi(-J_{12}{-}J_{13})t_{aq}$$

$$+ \exp(i\pi(J_{12}{-}J_{13})\;{}_{aq} + \exp(i\pi(-J_{12}{+}J_{13})t_{aq}]$$

$$\cos\alpha = \tfrac{1}{2}\,[\exp\,(+i\alpha) + \exp\,(-i\alpha)]$$

$$= \tfrac{1}{4}\, I_1 \exp\,(i2\pi(\delta_1 + J_{12}/2 + J_{13}/2)t_{aq})$$

$$+\tfrac{1}{4}\, I_1 \exp\,(i2\pi(\delta_1 - J_{12}/2 - J_{13}/2)t_{aq})$$

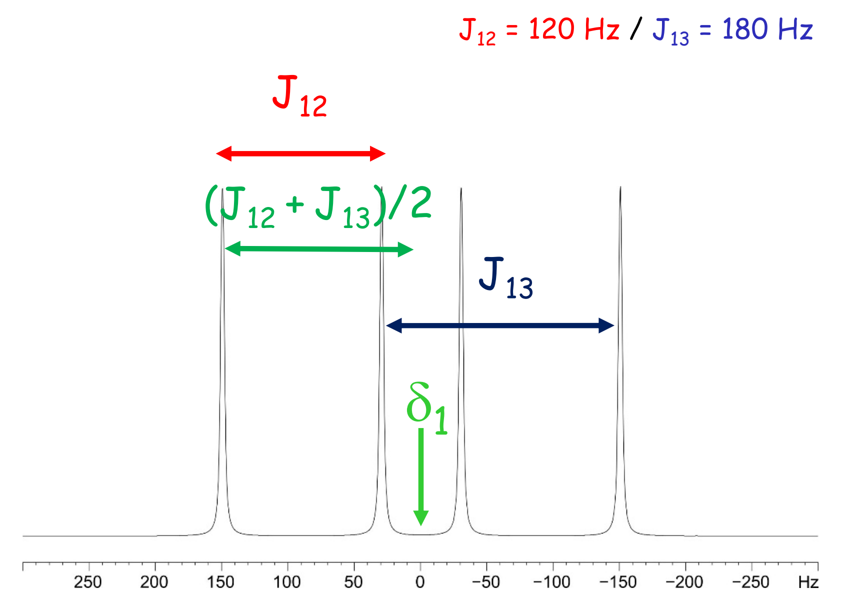
$$+\tfrac{1}{4}\, I_1 \exp\,(i2\pi(\delta_1 + J_{12}/2 - J_{13}/2)t_{aq})$$

$$+\tfrac{1}{4}\, I_1 \exp\,(i2\pi(\delta_1 - J_{12}/2 + J_{13}/2)t_{aq})$$

Calculating 1D spectra

The lines have equal intensity.

This case is common for homonuclear J-couplings, but not possible for heteronuclear one-bond couplings



Calculating 1D spectra

If the two coupling constant are identical (XH_2) we get something different. $J = J_{12} = J_{13}$

$I_1 \exp(i\Omega_1 t_{aq})(\cos\pi J t_{aq})^2$

$\cos^2\alpha = \frac{1}{2}(1 + \cos 2\alpha)$

$= \frac{1}{2} I_1 \exp(i2\pi\delta_1 t_{aq})(1 + \cos\pi(2J)t_{aq})$

$\cos\alpha = \frac{1}{2}[\exp(+i\alpha) + \exp(-i\alpha)]$

$= \frac{1}{2} I_1 \exp(i2\pi\delta_1 t_{aq}) +$

$\frac{1}{4} \exp(i2\pi\delta_1 t_{aq})[\exp(i\pi(2J)t_{aq} + \exp(i\pi(-2J)t_{aq}]$

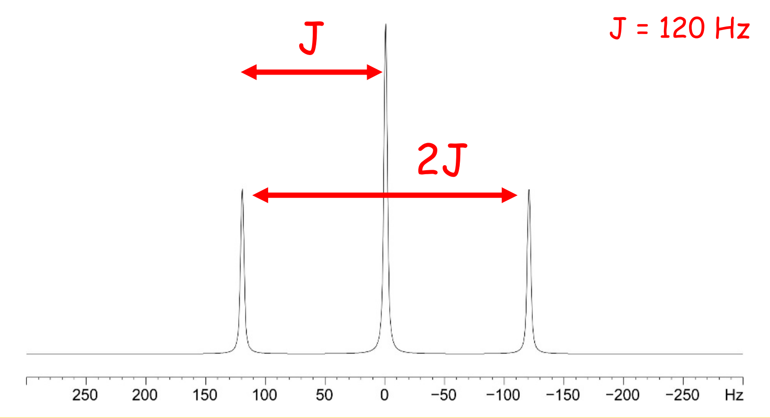
$= \frac{1}{2} I_1 \exp(i2\pi\delta_1 t_{aq})$

$+ \frac{1}{4} \exp(i2\pi(\delta_1 + J)t_{aq})$

$+ \frac{1}{4} \exp(i2\pi(\delta_1 - J)t_{aq})$

Calculating 1D spectra

That means only three lines, the center one is twice as intense as the other two: a triplet (1:2:1)



Calculating 1D spectra

What if we have three coupling constants of equal size ?

$$(\cos\pi Jt_{aq})^3 = \tfrac{1}{2}\,(1 + \cos\pi(2J)t_{aq})\,(\cos\pi Jt_{aq})$$

$\cos^2\alpha = \tfrac{1}{2}\,(1 + \cos 2\alpha)$

$$= \tfrac{1}{2}\cos\pi Jt_{aq} + \tfrac{1}{2}\cos\pi(2J)t_{aq}\,\cos\pi Jt_{aq}$$

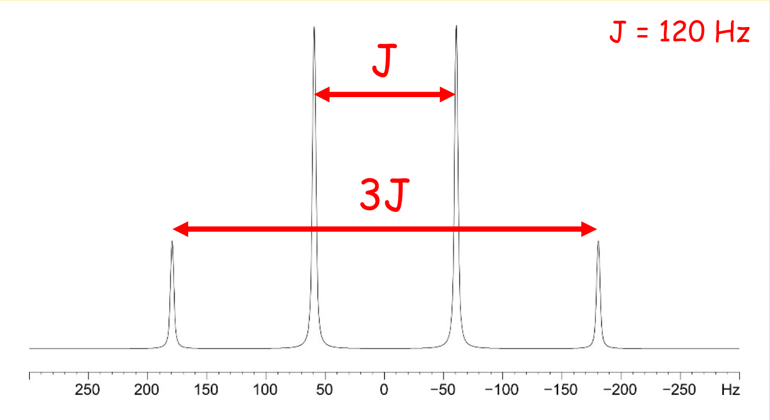
$$= \tfrac{1}{2}\cos\pi Jt_{aq} + \tfrac{1}{4}\cos\pi(3J)t_{aq} + \tfrac{1}{4}\cos\pi Jt_{aq}$$

$$= \tfrac{3}{4}\cos\pi Jt_{aq} + \tfrac{1}{4}\cos\pi(3J)t_{aq}$$

$\cos\alpha\,\cos\beta = \tfrac{1}{2}\,[\cos(\alpha + \beta) + \cos(\alpha - \beta)]$

This will yield a quartet

(1:3:3:1)

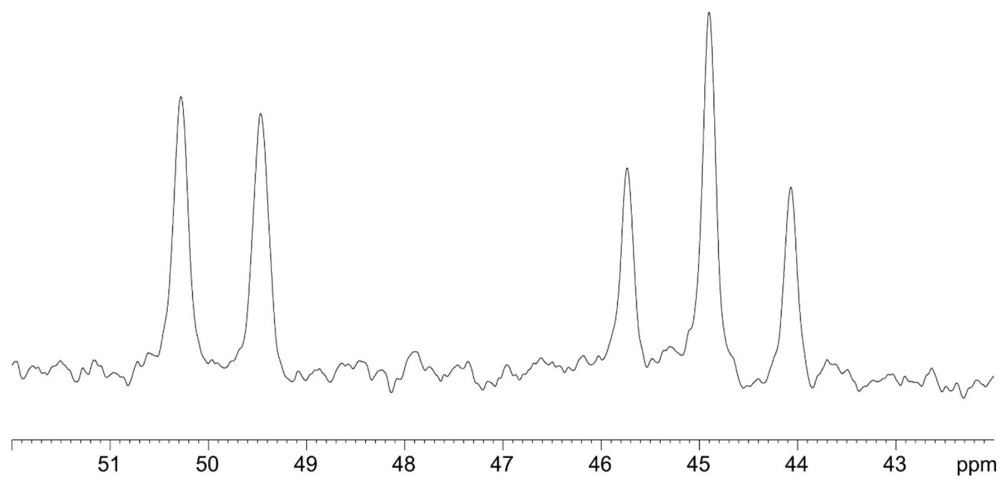


Calculating 1D spectra

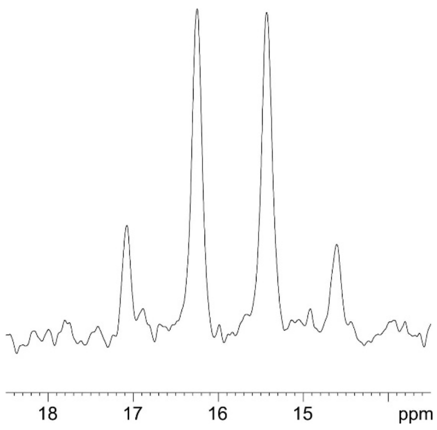
These are the well known pattern

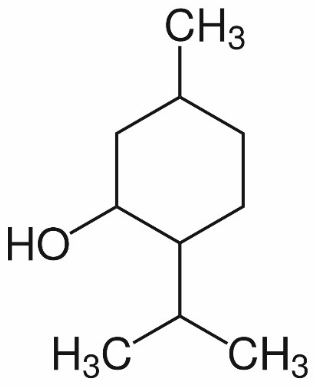
^{13}C of Menthol-CH

^{13}C of Menthol-CH_2



^{13}C of Menthol-CH_3





Calculating 1D spectra

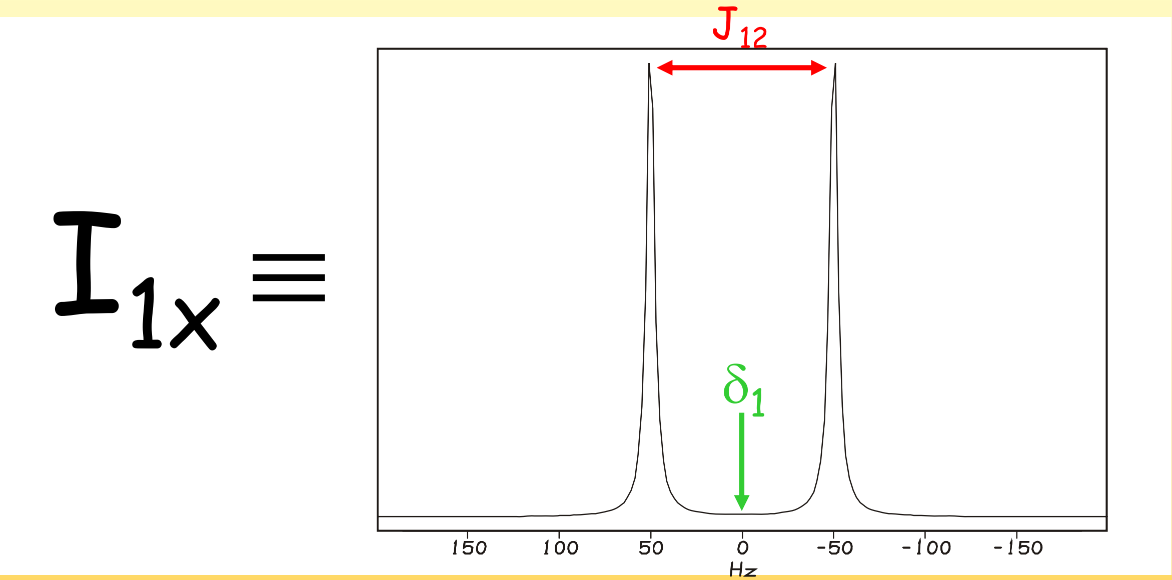
One more thing: what about anti-phase magnetization ?

We calculated in-phase already:

$$I_{1x} \xrightarrow{I_z\Omega_1 t_{aq}} I_1 \exp\,(i\Omega_1 t_{aq})$$

$$I_1 \exp\,(i\Omega_1 t_{aq}) \xrightarrow{I_{1z}I_{2z}\pi J_{12} t_{aq}}$$

$$I_{1x} \equiv$$



$$\tfrac{1}{2}\, I_1\,[\exp\,(i2\pi(\delta_1 + J_{12}/2)t_{aq}) + \exp\,(i2\pi(\delta_1 - J_{12}/2)t_{aq})]$$

Calculating 1D spectra

The calculation is very similar starting from anti-phase magnetization

$$I_{1x} I_{2z} \xrightarrow{I_z \Omega_1 t_{aq}} I_{1x} I_{2z} \cos \Omega_1 t_{aq} + I_{1y} I_{2z} \sin \Omega_1 t_{aq}$$

If we do quadrature detection we get: $I_1 I_{2z} \exp (i\Omega_1 t_{aq})$

$$I_1 I_{2z} \exp (i\Omega_1 t_{aq})$$

$$\xrightarrow{I_{1z} I_{2z} \pi J_{12} t_{aq}} I_1 I_{2z} \exp (i\Omega_1 t_{aq}) \cos\pi J_{12} t_{aq} + I_1 \exp (i\Omega_1 t_{aq}) \sin\pi J_{12} t_{aq}$$

Only the second term is relevant, since only in-phase yields signal

$\sin \alpha = \frac{1}{2} [\exp (+i\alpha) - \exp (-i\alpha)]$

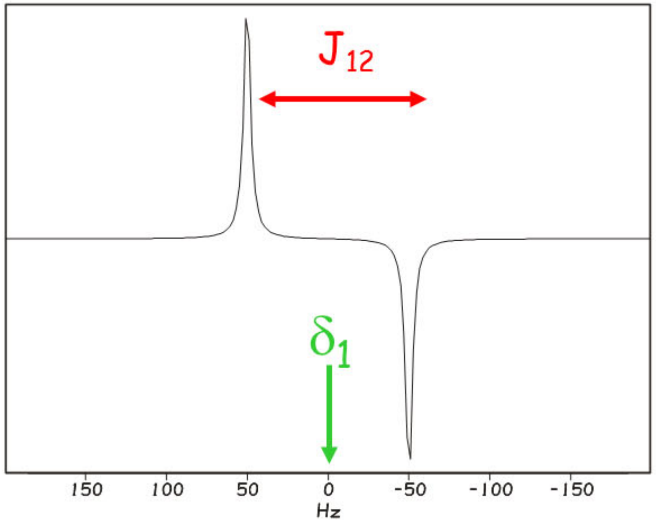
$$I_1 \exp (i\Omega_1 t_{aq}) \sin\pi J_{12} t_{aq} = \frac{1}{2} I_1 \exp (i2\pi\delta_1 t_{aq}) [\exp (i\pi J_{12} t_{aq}) - \exp (-i\pi J_{12} t_{aq})]$$

Calculating 1D spectra

$$I_1 \exp(i\Omega_1 t_{aq}) \sin\pi J_{12}\tau = \tfrac{1}{2} I_1 \exp(i2\pi\delta_1 t_{aq}) [\exp(i\pi J_{12} t_{aq}) - \exp(-i\pi J_{12} t_{aq})]$$

$$= \tfrac{1}{2} I_1 [\exp(i2\pi(\delta_1 + J_{12}/2)t_{aq}) - \exp(i2\pi(\delta_1 - J_{12}/2)t_{aq})]$$

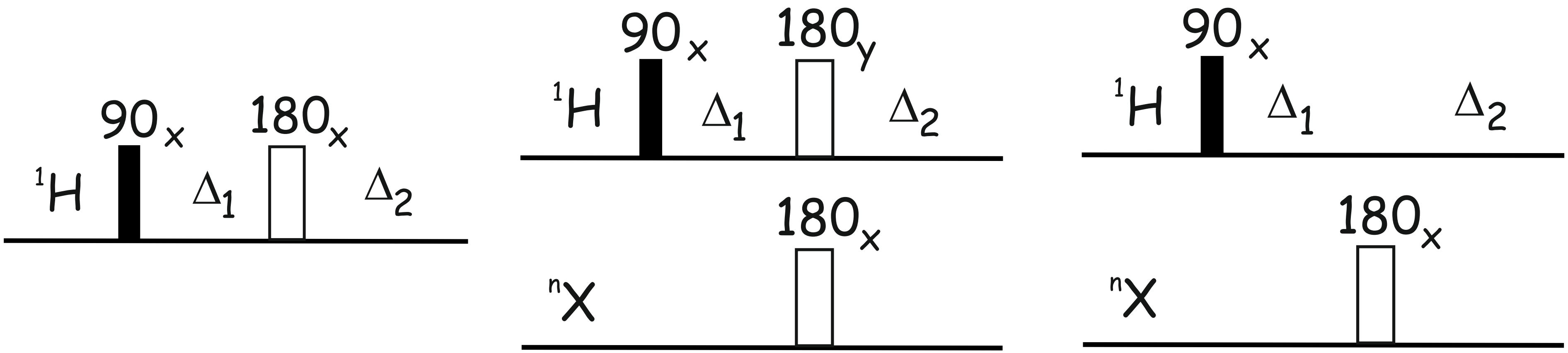
$$2I_{1x}I_{2z} \equiv$$



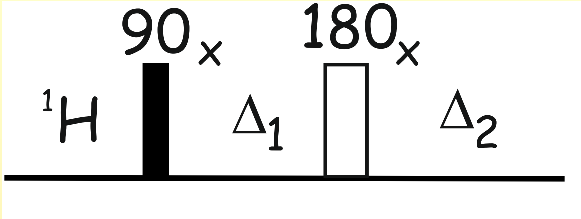
Building blocks

Building blocks

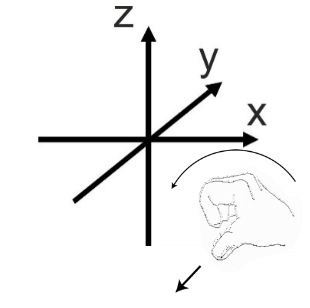
After we have seen that the result of PROF calculation correspond to reality, we calculate the building blocks of the most common pulse sequences



Building blocks



This is a simple echo, we start with chemical shift



$$H_z \xrightarrow{90^\circ\, H_x} -H_y \xrightarrow{\Omega_H\Delta_1} -H_y \cos \Omega_H\Delta_1 + H_x \sin \Omega_H\Delta_1$$

$$I_z \xrightarrow{\beta I_x} I_z \cos \beta - I_y \sin \beta$$

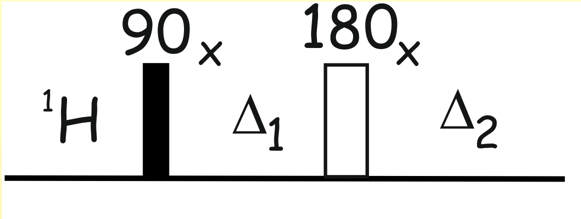
$$\xrightarrow{180^\circ\, H_x} H_y \cos \Omega_H\Delta_1 + H_x \sin \Omega_H\Delta_1$$

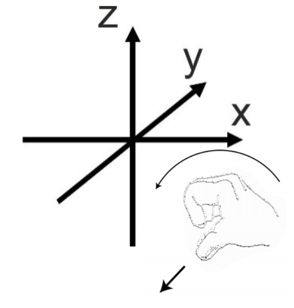
$$I_y \xrightarrow{I_z\, \Omega\tau} I_y \cos \Omega\tau - I_x \sin \Omega\tau$$

$$\xrightarrow{\Omega_H\Delta_2} H_y \cos \Omega_H\Delta_1 \cos \Omega_H\Delta_2 - H_x \cos \Omega_H\Delta_1 \sin \Omega_H\Delta_2$$

$$H_x \sin \Omega_H\Delta_1 \cos \Omega_H\Delta_2 + H_y \sin \Omega_H\Delta_1 \sin \Omega_H\Delta_2$$

Building blocks





$$H_y \cos \Omega_H \Delta_1 \cos \Omega_H \Delta_2 - H_x \cos \Omega_H \Delta_1 \sin \Omega_H \Delta_2$$

$$H_x \sin \Omega_H \Delta_1 \cos \Omega_H \Delta_2 + H_y \sin \Omega_H \Delta_1 \sin \Omega_H \Delta_2$$

$$= H_y \cos \Omega_H (\Delta_1 - \Delta_2) + H_x \sin \Omega_H (\Delta_1 - \Delta_2)$$

if $\Delta_1 = \Delta_2 = \Delta$

$$= H_y$$

$\sin(\alpha + \beta) = \sin \alpha \cos \beta + \cos \alpha \sin \beta$

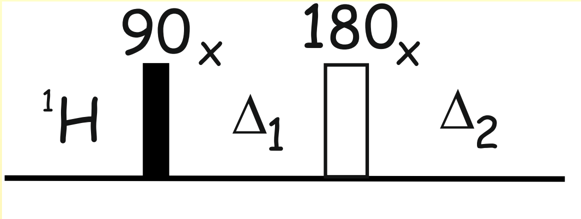
$\sin(\alpha - \beta) = \sin \alpha \cos \beta - \cos \alpha \sin \beta$

$\cos(\alpha + \beta) = \cos \alpha \cos \beta - \sin \alpha \sin \beta$

$\cos(\alpha - \beta) = \cos \alpha \cos \beta + \sin \alpha \sin \beta$

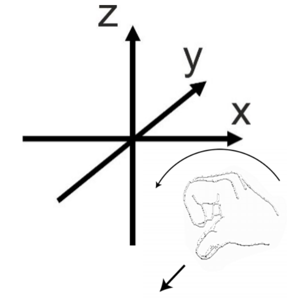
That means: if we have two equal delays chemical shift is refocussed !

Building blocks



Now we look what happens

with homonuclear coupling J_{HH}



$$H_{1z} \xrightarrow{90^\circ H_x} -H_{1y} \xrightarrow{\pi J_{HH}\Delta_1} -H_{1y}\cos \pi J_{HH}\Delta_1 + 2H_{1x}H_{2z}\sin \pi J_{HH}\Delta_1$$

$$\xrightarrow{180^\circ H_x} H_{1y}\cos \pi J_{HH}\Delta_1 - 2H_{1x}H_{2z}\sin \pi J_{HH}\Delta_1$$

$$\xrightarrow{\pi J_{HH}\Delta_2} H_{1y}\cos \pi J_{HH}\Delta_1 \cos \pi J_{HH}\Delta_2$$

$$- 2H_{1x}H_{2z}\cos \pi J_{HH}\Delta_1 \sin \pi J_{HH}\Delta_2$$

$$- 2H_{1x}H_{2z}\sin \pi J_{HH}\Delta_1 \cos \pi J_{HH}\Delta_2$$

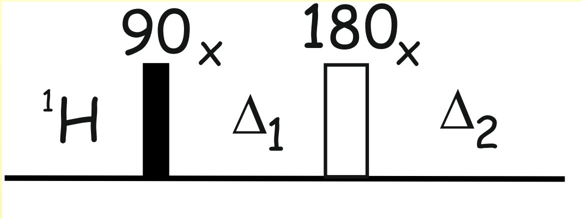
$$- H_{1y}\sin \pi J_{HH}\Delta_1 \sin \pi J_{HH}\Delta_2$$

$$I_{1z} \xrightarrow{\beta I_x} I_z\cos\beta - I_y\sin\beta$$

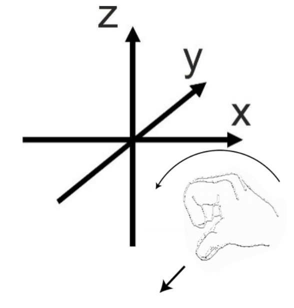
$$I_{1y} \xrightarrow{I_{1z}I_{2z}\pi J_{12}\tau} I_{1y}\cos \pi J_{12}\tau - 2I_{1x}I_{2z}\sin\pi J_{12}\tau$$

$$2I_{1x}I_{2z} \xrightarrow{I_{1z}I_{2z}\pi J_{12}\tau} 2I_{1x}I_{2z}\cos\pi J_{12}\tau + I_{1y}\sin\pi J_{12}\tau$$

Building blocks



$$\sin(\alpha + \beta) = \sin\alpha \cos\beta + \cos\alpha \sin\beta$$
$$\sin(\alpha - \beta) = \sin\alpha \cos\beta - \cos\alpha \sin\beta$$
$$\cos(\alpha + \beta) = \cos\alpha \cos\beta - \sin\alpha \sin\beta$$
$$\cos(\alpha - \beta) = \cos\alpha \cos\beta + \sin\alpha \sin\beta$$

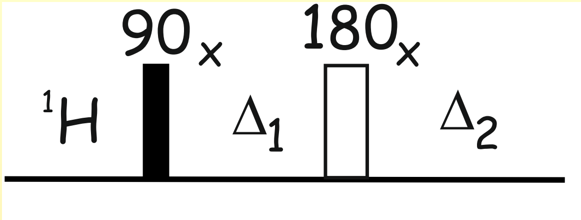


$$H_{1y} \cos \pi J_{HH}\Delta_1 \cos \pi J_{HH}\Delta_2 - 2H_{1x} H_{2z} \cos \pi J_{HH}\Delta_1 \sin \pi J_{HH}\Delta_2$$
$$-2H_{1x} H_{2z} \sin \pi J_{HH}\Delta_1 \cos \pi J_{HH}\Delta_2 - H_{1y} \sin \pi J_{HH}\Delta_1 \sin \pi J_{HH}\Delta_2$$
$$= H_{1y} \cos \pi J_{HH} (\Delta_1 + \Delta_2) - 2H_{1x} H_{2z} \sin \pi J_{HH} (\Delta_1 + \Delta_2)$$

if $\Delta_1 = \Delta_2 = \Delta$ $\quad H_{1y} \cos \pi J_{HH}\, 2\Delta - 2H_{1x} H_{2z} \sin \pi J_{HH}\, 2\Delta$

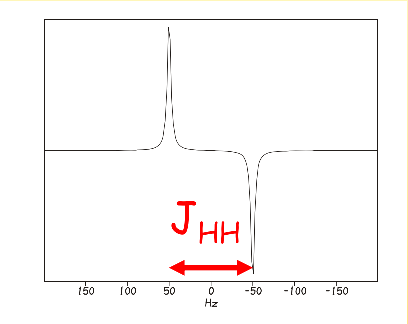
That means: even if we have two equal delays homonuclear coupling will evolve and is not refocussed

Building blocks



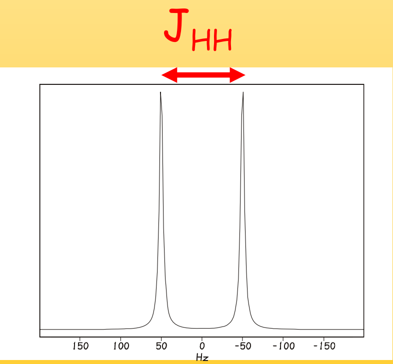
We can understand a couple of things from that

$$H_{1y} \cos \pi J_{HH} 2\Delta - 2H_{1x} H_{2z} \sin \pi J_{HH} 2\Delta$$



If we choose $\Delta = 1/4J_{HH}$ we get $2H_{1x} H_{2z}$,

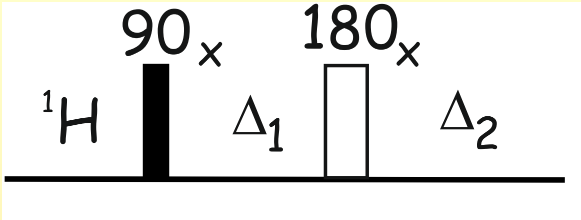
this will result in an anti-phase signal



If we choose $\Delta = 1/2J_{HH}$ we get H_{1y},

this will result in an in-phase signal

Building blocks



We can understand a couple of things from that

$$H_{1y} \cos \pi J_{HH} 2\Delta - 2H_{1x} H_{2z} \sin \pi J_{HH} 2\Delta$$

If we choose Δ short compared to 1/2J, the effect of the coupling will be small, in that case this type of coupling may be ignored

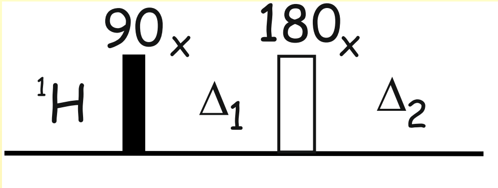
$J = 5$ Hz, $2\Delta = 7$ msec $\ll 1/2J = 100$ msec

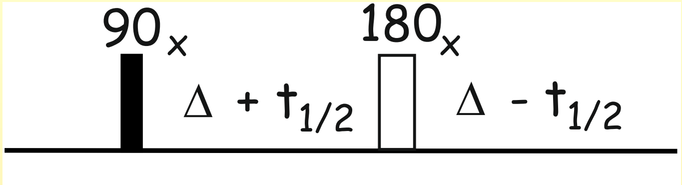
$\cos \pi J_{HH} 2\Delta = 0.99$

$\sin \pi J_{HH} 2\Delta = 0.08$

Which means coupling has barely evolved, that will be important in INEPT or HSQC

Building blocks





And we can understand how „constant-time“ works

$$\Delta_1 = \Delta + t_{1/2} \quad \Delta_2 = \Delta - t_{1/2}$$

$$H_y \cos \Omega_H (\Delta_1 - \Delta_2) + H_x \sin \Omega_H (\Delta_1 - \Delta_2) = H_y \cos \Omega_H t_1 + H_x \sin \Omega_H t_1$$

Chemical shift evolves as usual

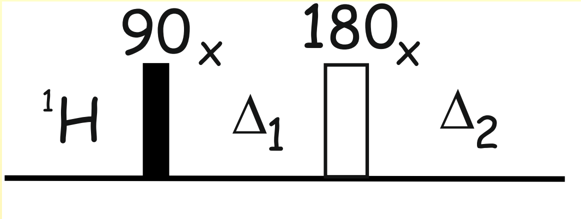
$$H_{1y} \cos \pi J_{HH} (\Delta_1 + \Delta_2) - 2H_{1x} H_{2z} \sin \pi J_{HH} (\Delta_1 + \Delta_2) =$$

$$H_{1y} \cos \pi J_{HH} 2\Delta - 2H_{1x} H_{2z} \sin \pi J_{HH} 2\Delta$$

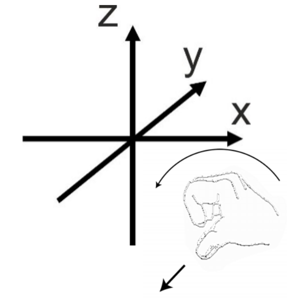
Scalar coupling evolves for a constant time,

if $\Delta = 1/4J$ we get anti-phase magnetization

Building blocks



Last but not least we look at heteronuclear coupling J_{HX}



$$H_z \xrightarrow{90^\circ H_x} -H_y \xrightarrow{\pi J_{HX}\Delta_1} -H_y \cos \pi J_{HX}\Delta_1 + 2H_x X_z \sin \pi J_{HX}\Delta_1$$

$$\xrightarrow{180^\circ H_x} H_y \cos \pi J_{HX}\Delta_1 + 2H_x X_z \sin \pi J_{HX}\Delta_1$$

$$\xrightarrow{\pi J_{HX}\Delta_2} H_y \cos \pi J_{HX}\Delta_1 \cos \pi J_{HX}\Delta_2$$

$$- 2H_x X_z \cos \pi J_{HX}\Delta_1 \sin \pi J_{HX}\Delta_2$$

$$+ 2H_x H_z \sin \pi J_{HX}\Delta_1 \cos \pi J_{HX}\Delta_2$$

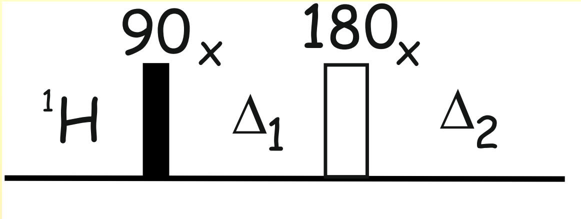
$$+ H_y \sin \pi J_{HX}\Delta_1 \sin \pi J_{HX}\Delta_2$$

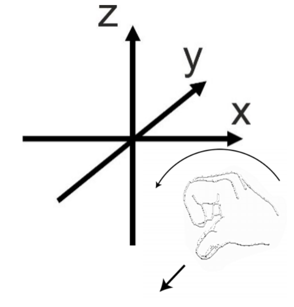
$$I_{1z} \xrightarrow{\beta I_x} I_z \cos \beta - I_y \sin \beta$$

$$I_{1y} \xrightarrow{I_{1z} I_{2z} \pi J_{12}\tau} I_{1y} \cos \pi J_{12}\tau - 2I_{1x} I_{2z} \sin \pi J_{12}\tau$$

$$2I_{1x} I_{2z} \xrightarrow{I_{1z} I_{2z} \pi J_{12}\tau} 2I_{1x} I_{2z} \cos \pi J_{12}\tau + I_{1y} \sin \pi J_{12}\tau$$

Building blocks





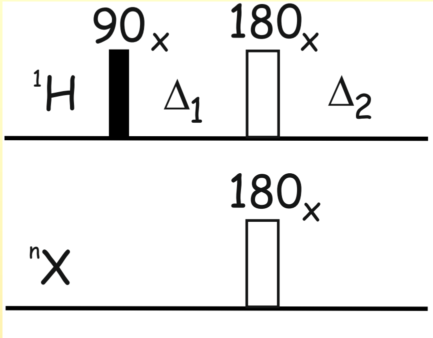
$$\sin(\alpha + \beta) = \sin\alpha \cos\beta + \cos\alpha \sin\beta$$
$$\sin(\alpha - \beta) = \sin\alpha \cos\beta - \cos\alpha \sin\beta$$
$$\cos(\alpha + \beta) = \cos\alpha \cos\beta - \sin\alpha \sin\beta$$
$$\cos(\alpha - \beta) = \cos\alpha \cos\beta + \sin\alpha \sin\beta$$

$$H_y \cos \pi J_{HX}\Delta_1 \cos \pi J_{HX}\Delta_2 - 2H_x X_z \cos \pi J_{HX}\Delta_1 \sin \pi J_{HX}\Delta_2$$
$$+ 2H_x H_z \sin \pi J_{HX}\Delta_1 \cos \pi J_{HX}\Delta_2 + H_y \sin \pi J_{HX}\Delta_1 \sin \pi J_{HX}\Delta_2$$
$$= H_y \cos \pi J_{HX}(\Delta_1 - \Delta_2) - 2H_x X_z \sin \pi J_{HX}(\Delta_1 - \Delta_2)$$

if $\Delta_1 = \Delta_2 = \Delta$ we get H_{1y}

That means: if we have two equal delays heteronuclear coupling will not evolve, it is refocussed

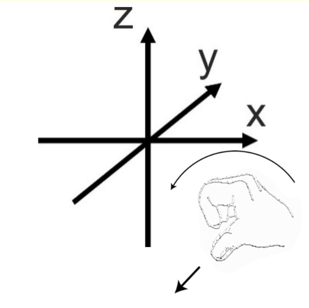
Building blocks



Now we add a 180°-X-pulse and again think about

Ω_H, J_{HH} and J_{HX}

Ω_H and J_{HH} we know from the previous calculation !



$$H_z \xrightarrow{90^\circ H_x} -H_y \xrightarrow{\pi J_{HX}\Delta_1} -H_y \cos \pi J_{HX}\Delta_1 + 2H_x X_z \sin \pi J_{HX}\Delta_1$$

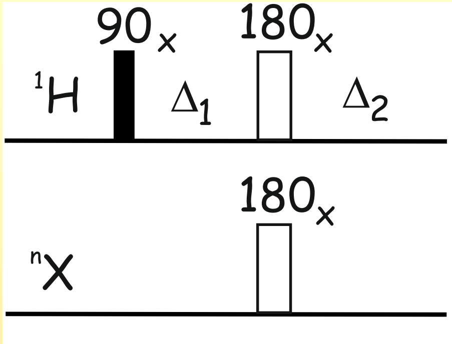
$$\xrightarrow[180^\circ X_x]{180^\circ H_x} H_y \cos \pi J_{HX}\Delta_1 - 2H_x X_z \sin \pi J_{HX}\Delta_1 \xrightarrow{\pi J_{HX}\Delta_2}$$

$$H_y \cos \pi J_{HX}\Delta_1 \cos \pi J_{HX}\Delta_2 - 2H_x X_z \cos \pi J_{HX}\Delta_1 \sin \pi J_{HX}\Delta_2$$

$$-2H_x H_z \sin \pi J_{HX}\Delta_1 \cos \pi J_{HX}\Delta_2 - H_y \sin \pi J_{HX}\Delta_1 \sin \pi J_{HX}\Delta_2$$

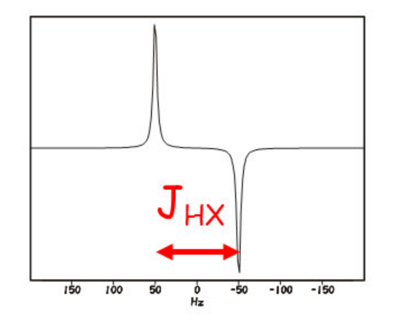
$$= H_y \cos \pi J_{HX} (\Delta_1 + \Delta_2) - 2H_x X_z \sin \pi J_{HX} (\Delta_1 + \Delta_2)$$

Building blocks



if $\Delta_1 = \Delta_2 = \Delta$: $H_y \cos \pi J_{HX} 2\Delta - 2H_x X_z \sin \pi J_{HX} 2\Delta$

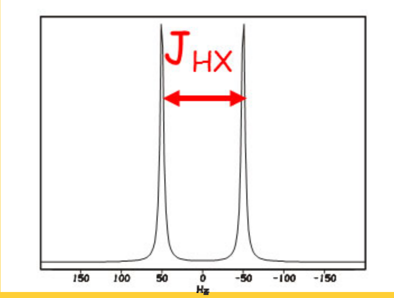
that means heteronuclear coupling will not be refoccused



If we choose $\Delta = 1/4J_{HH}$ we get $-2H_x X_z$,

this will result in an anti-phase signal

and is important in the HSQC

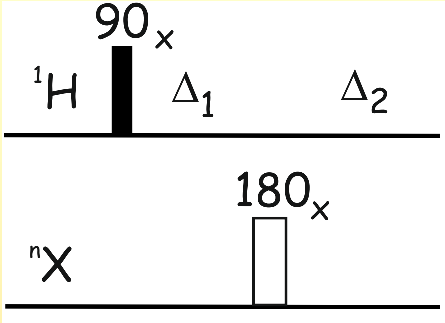


If we choose $\Delta = 1/2J_{HH}$ we get H_y,

this will result in an in-phase signal,

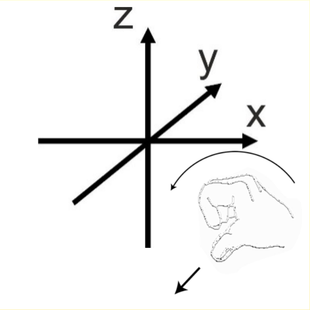
This often used for pulse determination

Building blocks



Now we leave out 180°-H-pulse and again think about Ω_H, J_{HH} and J_{HX}

Ω_H and J_{HH} will both evolve in this case, it is a simple delay



$$H_z \xrightarrow{\qquad} -H_y \xrightarrow{\qquad\qquad} -H_y \cos \pi J_{HX}\Delta_1 + 2H_x X_z \sin \pi J_{HX}\Delta_1$$

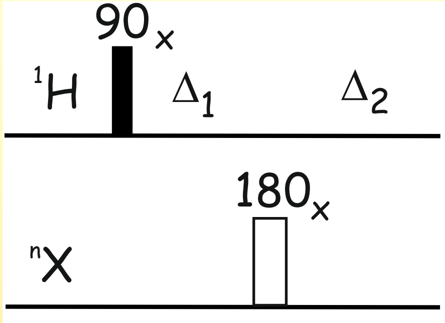
$$\xrightarrow{180^\circ\ X_x} -H_y \cos \pi J_{HX}\Delta_1 - 2H_x X_z \sin \pi J_{HX}\Delta_1 \xrightarrow{\pi J_{HX}\Delta_2}$$

$$-H_y \cos \pi J_{HX}\Delta_1 \cos \pi J_{HX}\Delta_2 + 2H_x X_z \cos \pi J_{HX}\Delta_1 \sin \pi J_{HX}\Delta_2$$

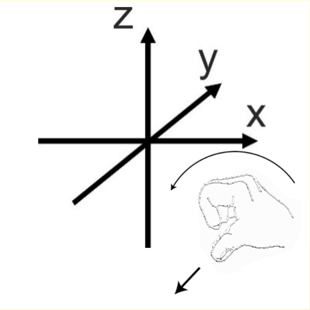
$$-2H_x H_z \sin \pi J_{HX}\Delta_1 \cos \pi J_{HX}\Delta_2 - H_y \sin \pi J_{HX}\Delta_1 \sin \pi J_{HX}\Delta_2$$

$$= -H_y \cos \pi J_{HX}(\Delta_1 - \Delta_2) - 2H_x X_z \sin \pi J_{HX}(\Delta_1 - \Delta_2)$$

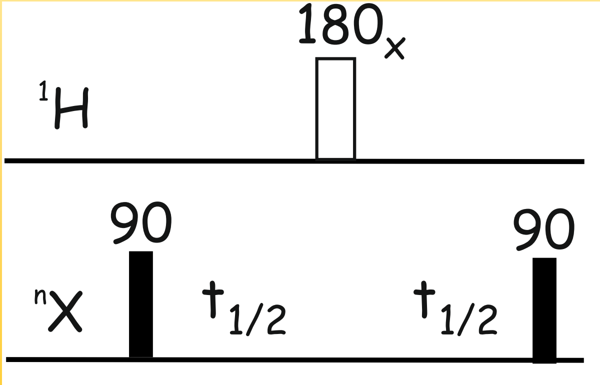
Building blocks



$$- H_y \cos \pi J_{HX} (\Delta_1 - \Delta_2) - 2H_x X_z \sin \pi J_{HX} (\Delta_1 - \Delta_2)$$



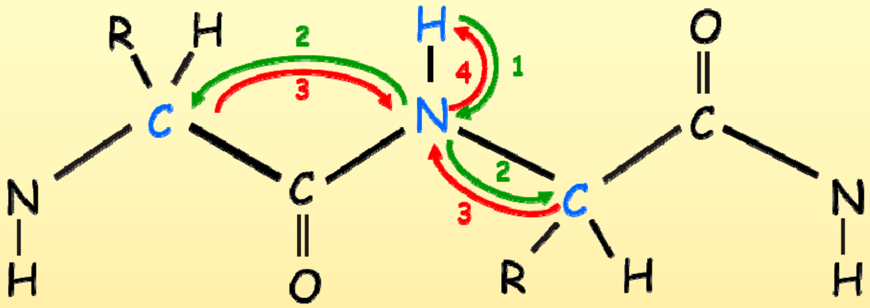
if $\Delta_1 = \Delta_2 = \Delta$: $- H_y$ that means heteronuclear coupling will be refocussed

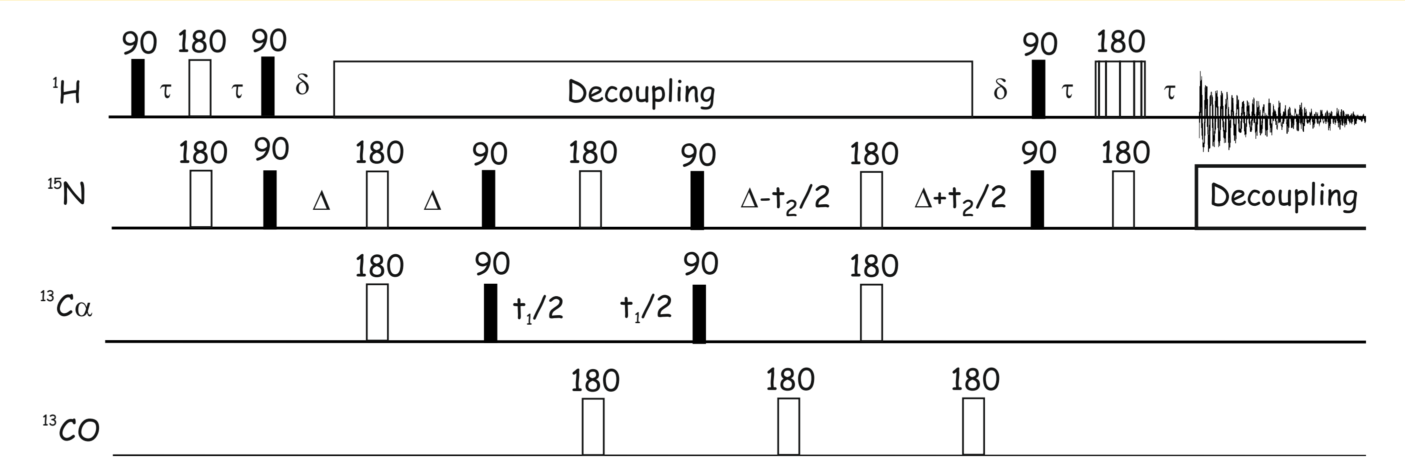


And that is the reason why heteronuclear decoupling can be achieved with a simple pulse in indirect dimensions of multidimensional spectra

Building blocks

Let us use the building blocks to rationalize the HNCA experiment



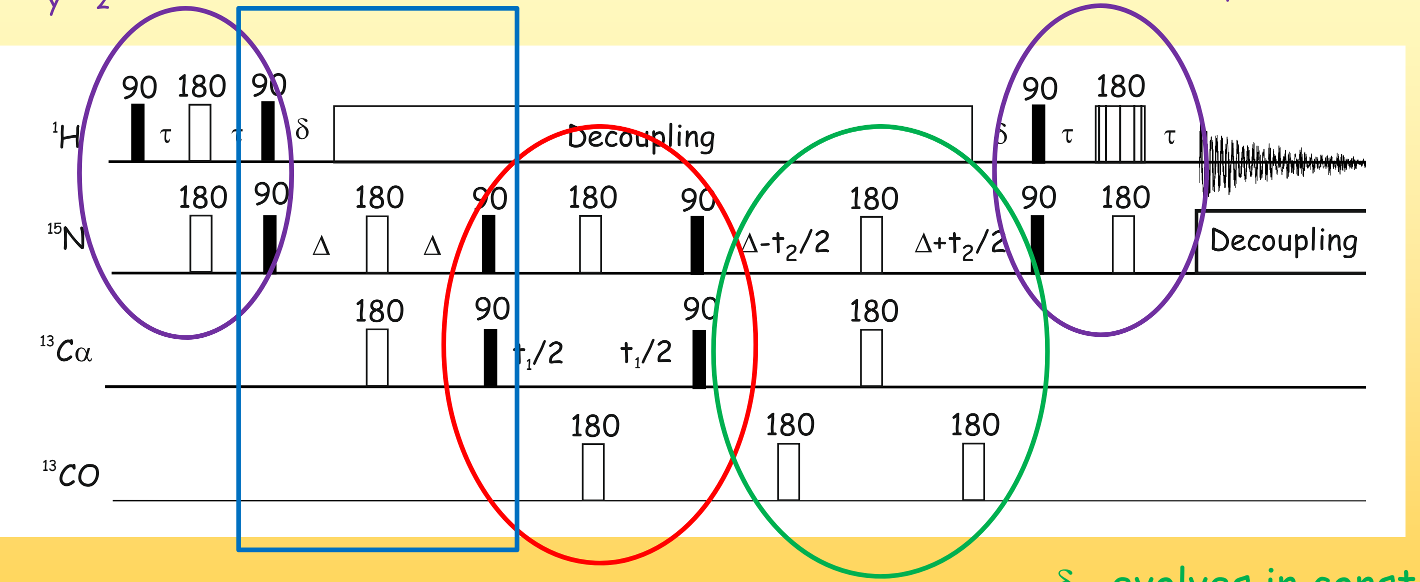


Building blocks

δ_H is refocussed
J_{HH} does not matter
$\tau = 1/4\ (^1J_{HN})$
$H_x \rightarrow H_yN_z$

$\delta = 1/2(^1J_{HN})$
$\Delta = 1/8\ (^1J_{C\alpha N})$
why 1/8 ? next slide !

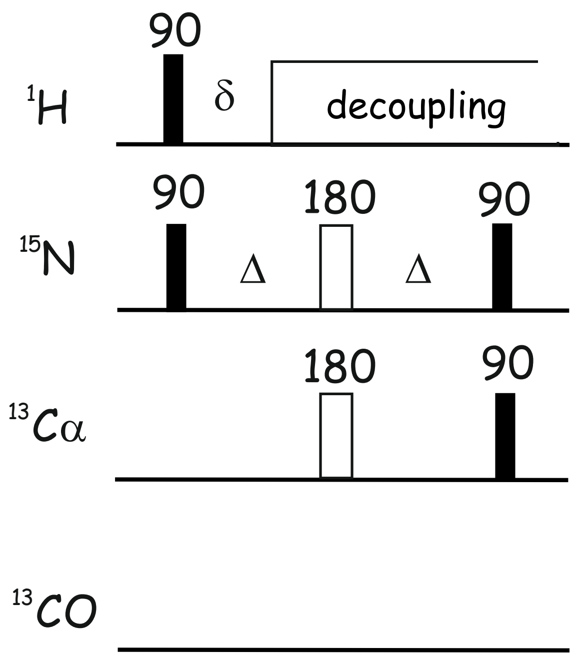
δ_H is refocussed
J_{HH} does not matter
$\tau = 1/4\ (^1J_{HN})$
$H_yN_z \rightarrow H_x$



$\delta_{C\alpha}$ evolves
$J_{C\alpha N}$ and $J_{C\alpha CO}$ are refocussed

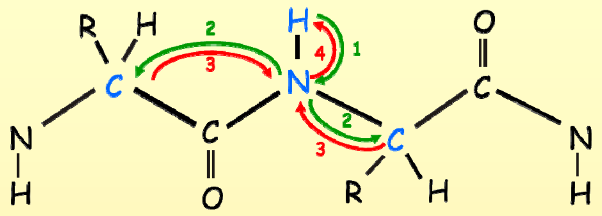
δ_N evolves in constant time
$J_{C\alpha N}$ evolves during 2Δ (which is $1/4\ (^1J_{C\alpha N})$)
and J_{NCO} is refocussed

Building blocks



δ_N and J_{NCO} are refocussed

$$H_zN_y \xrightarrow{H_zN_z\pi J_{HN}\delta} N_x$$



$$^1J_{NC1\alpha} \approx {}^2J_{NC2\alpha}$$

$$N_x \xrightarrow{N_zC_{1z}\pi^1J_{NC\alpha}2\Delta} N_x \cos \pi J_{NC1a}2\Delta - 2N_yC_{1z} \sin \pi J_{NC1a}2\Delta$$

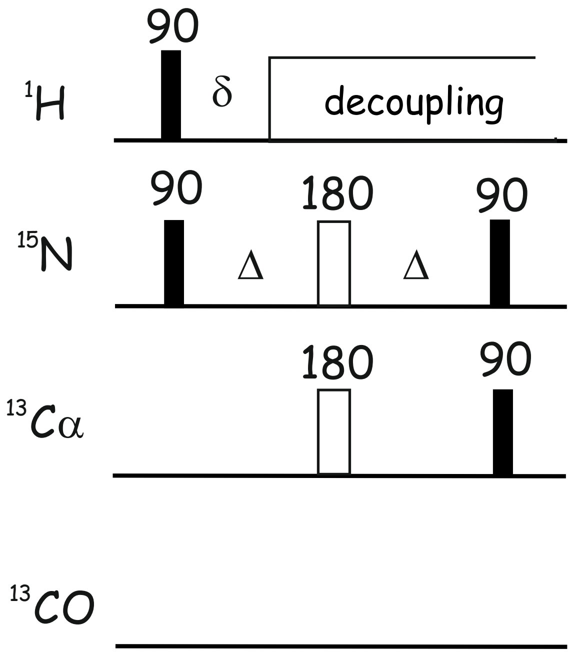
$$\xrightarrow{N_zC_{1z}\pi^2J_{NC\alpha}2\Delta} N_x \cos \pi J_{NC1a}2\Delta \ \cos \pi J_{NC2a}2\Delta$$

$$+ 2N_yC_{2z} \cos \pi J_{NC1a}2\Delta \ \sin \pi J_{NC2a}2\Delta$$

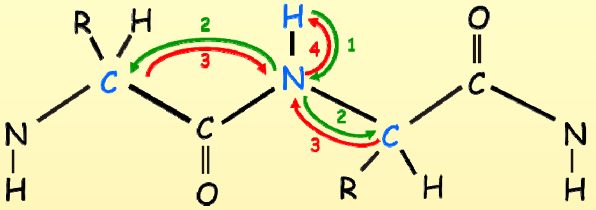
$$- 2N_yC_{1z} \sin \pi J_{NC1a}2\Delta \ \cos \pi J_{NC2a}2\Delta$$

$$+ 4N_xC_{1z}C_{2z} \sin \pi J_{NC1a}2\Delta \ \sin \pi J_{NC2a}2\Delta$$

Building blocks



δ_N and J_{NCO} are refocussed



$$N_x \cos \pi J_{NC1a}2\Delta \ \cos \pi J_{NC2a}2\Delta$$

$$+\ 2N_yC_{2z} \cos \pi J_{NC1a}2\Delta \ \sin \pi J_{NC2a}2\Delta$$

$$-\ 2N_yC_{1z} \sin \pi J_{NC1a}2\Delta \ \cos \pi J_{NC2a}2\Delta$$

$$+\ 4N_xC_{1z}C_{2z} \sin \pi J_{NC1a}2\Delta \ \sin \pi J_{NC2a}2\Delta$$

Those two will give the magnetization that will go through

If we choose $\Delta = 1/4J$ we will have nothing even though $\sin(\pi/2) = 1$ because $\cos(\pi/2) = 0$

So we use $\Delta = 1/8J$ we get $\sin(\pi/4) = \cos(\pi/4) = \frac{1}{2}\sqrt{2}$ and the product is 0.5 !

Spherical representation

Spherical representation

We have now seen that we can understand pulse sequences quite well using product operators based on Cartesian coordinates. We are, however, free in the choice of our coordinate system. As it turns out, rotating the coordinate system by 45° can be usefull:

$$I_x = 1/2\ (I_+ + I_-) \qquad I_+ = I_x + iI_y$$

$$I_y = 1/2i\ (I_+ - I_-) \qquad I_- = I_x - iI_y$$

The operators I^+ and I^- are also called “raising” and “lowering” operators.

As you can see, we derive those operators from our Cartesian operators by treating the x and y component as real and imaginary part in a complex plane

Spherical representation

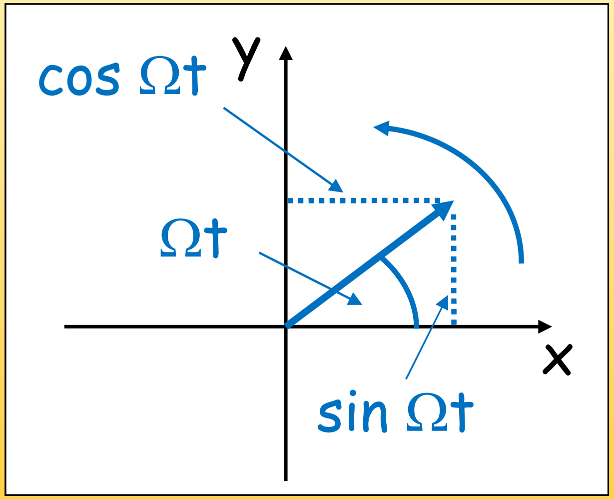
An evolution of chemical shift can thus be viewed as a rotation in a complex plane, where there is a change of phase over time. This will help us later when dealing with gradients, pulse phases, coherence and coherence order.

$$I_x \xrightarrow{I_z\Omega\tau} I_x \cos\Omega\tau + I_y \sin\Omega\tau$$

$$I_y \xrightarrow{I_z\Omega\tau} I_y \cos\Omega\tau - I_x \sin\Omega\tau$$

$$I_z \xrightarrow{I_z\Omega\tau} I_z$$

While z is unaffected, x is converted into y, y into –x and so forth.



Spherical representation

How do I_+ and I_- evolve under chemical shift ?

$I_+ = I_x + iI_y$ $\quad$ $I_- = I_x - iI_y$ $\quad$ $I_x = 1/2(I_+ + I_-)$ $\quad$ $I_y = 1/2i(I_+ - I_-)$

$$I_+ \xrightarrow{I_z\Omega\tau} \overset{I_x}{\boxed{I_x \cos \Omega\tau + I_y \sin \Omega\tau}} + \overset{iI_y}{\boxed{iI_y \cos \Omega\tau - iI_x \sin \Omega\tau}}$$

1/i = -i

$$= \overset{I_x}{\boxed{1/2\ (I_+ + I_-) \cos \Omega\tau}} - \overset{I_y}{\boxed{i/2\ (I_+ - I_-) \sin \Omega\tau}}$$

i/i = 1

$$\overset{iI_y}{\boxed{+\ 1/2\ (I_+ - I_-) \cos \Omega\tau}} - \overset{iI_x}{\boxed{i/2\ (I_+ + I_-) \sin \Omega\tau}}$$

$$= I_+ \cos \Omega\tau - i\ I_+ \sin \Omega\tau$$

$$= I_+ \exp\ (-i\Omega\tau)$$

Spherical representation

How do I_+ and I_- evolve under a z-rotation (like chemical shift) ?

$I_+ = I_x + iI_y$ $I_- = I_x - iI_y$ $I_x = 1/2(I_+ + I_-)$ $I_y = 1/2i(I_+ - I_-)$

$$I_- \xrightarrow{I_z\Omega\tau} I_x \cos \Omega\tau + I_y \sin \Omega\tau - iI_y \cos \Omega\tau + iI_x \sin \Omega\tau$$

$$= 1/2\ (I_+ + I_-) \cos \Omega\tau - i/2\ (I_+ - I_-) \sin \Omega\tau$$

$$- 1/2\ (I_+ - I_-) \cos \Omega\tau + i/2\ (I_+ + I_-) \sin \Omega\tau$$

$$= I_- \cos \Omega\tau + i\ I_- \sin \Omega\tau$$

$$= I_- \exp\ (+i\Omega\tau)$$

This is quite simple, the operators merely acquire a phase. They have opposite sense of rotation

I_+ and I_- as well as I_x and I_y are also called single quantum coherences (SQC) !

Spherical representation

Products of I^+ and I^- are, of course, also possible if several spins are involved

$$\left.\begin{aligned} I_{1+}I_{2-} &\xrightarrow{I_z\Omega\tau} I_{1+}\exp(-i\Omega_1\tau)\, I_{2-}\exp(+i\Omega_2\tau) = I_{1+}I_{2-}\exp(-i[\Omega_1-\Omega_2]\tau) \\ I_{1-}I_{2+} &\xrightarrow{I_z\Omega\tau} I_{1-}\exp(+i\Omega_1\tau)\, I_{2+}\exp(-i\Omega_2\tau) = I_{1-}I_{2+}\exp(+i[\Omega_1-\Omega_2]\tau) \end{aligned}\right\} \text{ZQC}$$

$$\left.\begin{aligned} I_{1+}I_{2+} &\xrightarrow{I_z\Omega\tau} I_{1+}\exp(-i\Omega_1\tau)\, I_{2+}\exp(-i\Omega_2\tau) = I_{1+}I_{2+}\exp(-i[\Omega_1+\Omega_2]\tau) \\ I_{1-}I_{2-} &\xrightarrow{I_z\Omega\tau} I_{1-}\exp(+i\Omega_1\tau)\, I_{2-}\exp(+i\Omega_2\tau) = I_{1-}I_{2-}\exp(+i[\Omega_1+\Omega_2]\tau) \end{aligned}\right\} \text{DQC}$$

We have also seen that I_x contains two counter-rotating components

$$I_x = I_+ + I_- \xrightarrow{I_z\Omega\tau} I_+ \exp(-i\Omega\tau) + I_- \exp(+i\Omega\tau)$$

To distinguish those two will be the task of quadrature detection!!

That's it

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