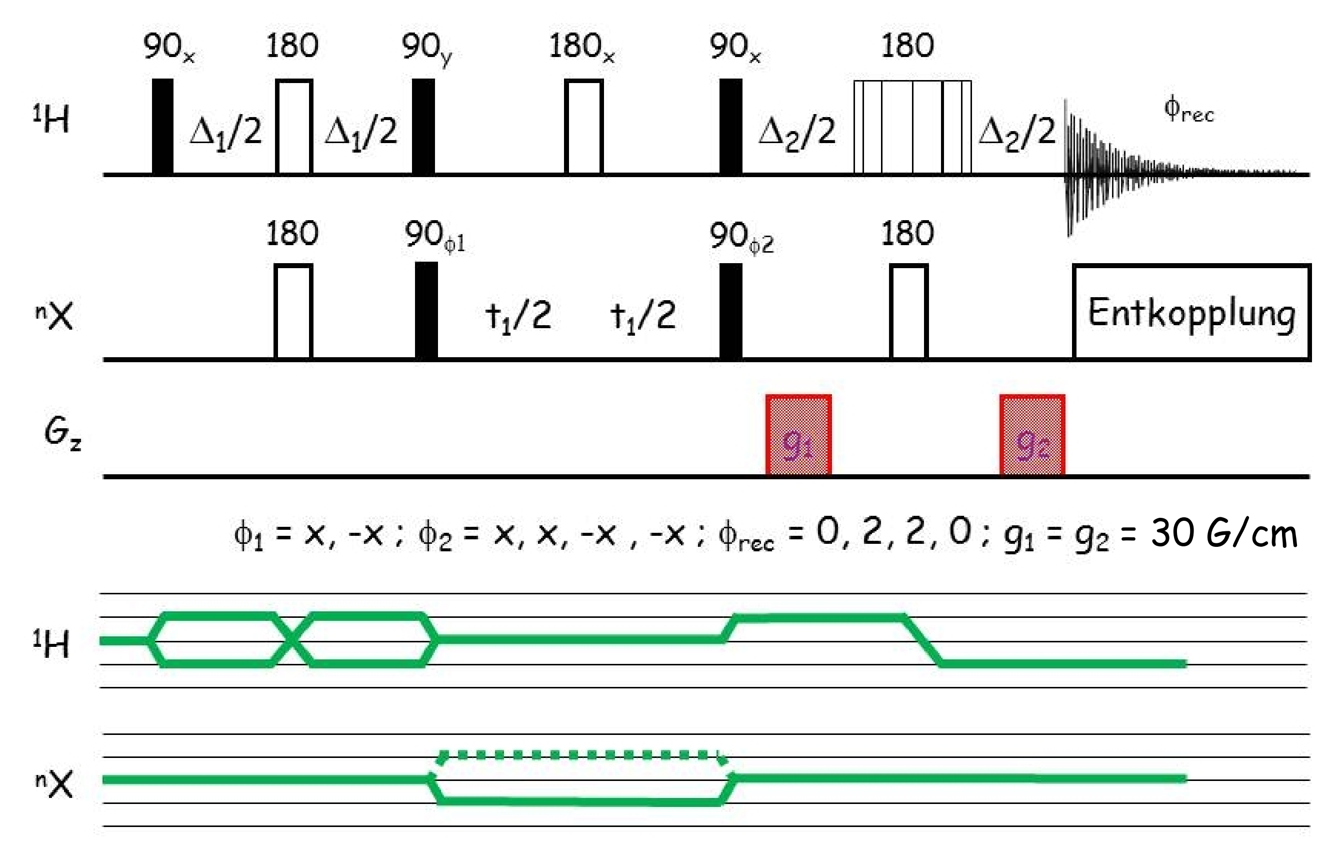
On pulses, phases and gradients:
Phase cycling and Quadrature detection
Part I

Greater Bay Area Magnetic Resonance Workshop

24.04.2024

Description of pulse sequences



ϕ_1 = x, -x ; ϕ_2 = x, x, -x , -x ; ϕ_{rec} = 0, 2, 2, 0 ; $g_1 = g_2$ = 30 G/cm

"… quadrature detection in F1 is achieved by States-TPPI incrementation of phase ϕ_1"

Description of pulse sequences

A full description of a pulse sequence does not only include pulses, gradients and delays, but also the phases, the *phase cycle*, the gradient strength and sometimes also the *coherence transfer pathways*.

The phase cycle - often combined with the action of gradients - makes sure that we do not only get the signals that we want with highest possible intensity but that we also suppress all other types of magnetization. And *quadrature detection* makes sure that we can obtain optimal resolution in the indirect dimensions.

To fully understand how a pulse sequence works we thus have to understand how phase cycling works, what effect gradients have and how we can place the center of the spectrum in the middle of the signals with out confusing higher and lower frequencies.

Coherence and

coherence order

Coherence and coherence order

To understand the effect of gradients and phase cycling we need to use the concept of coherence. The problem with coherence is that it is difficult to find an appropriate physical picture for it. So let us say it is connected with transverse magnetization.

This magnetization is manipulated in NMR experiments using gradients and pulse phases and it turns out that the effects of those are much easier to calculate using the spherical representation then using Cartesian coordinates. To do that we need to know what the order of a coherence is.

The order p of a coherence C is defined according to its behavior under a z-operator (e.g. chemical shift):

$$\boxed{C_p \xrightarrow{I_z \varphi\tau} C_p \exp(-ip\varphi\tau)}$$

Coherence and coherence order

Using that definition we can calculate the coherence order in the spherical as well as the Cartesian representation

$I_- \xrightarrow{I_z\Omega\tau} I_- \ \exp(+i\Omega\tau)$ => coherence order p = -1

$I_-I_+ \xrightarrow{I_z\Omega\tau} I_+I_-$ => coherence order p = 0

$I_+I_+ \xrightarrow{I_z\Omega\tau} I_+I_+ \exp(-i2\Omega\tau)$ => coherence order p = +2

Cartesian operators represent mixtures of coherence order

$I_x = I_+ + I_-$ => coherence order p = -1 and p = +1

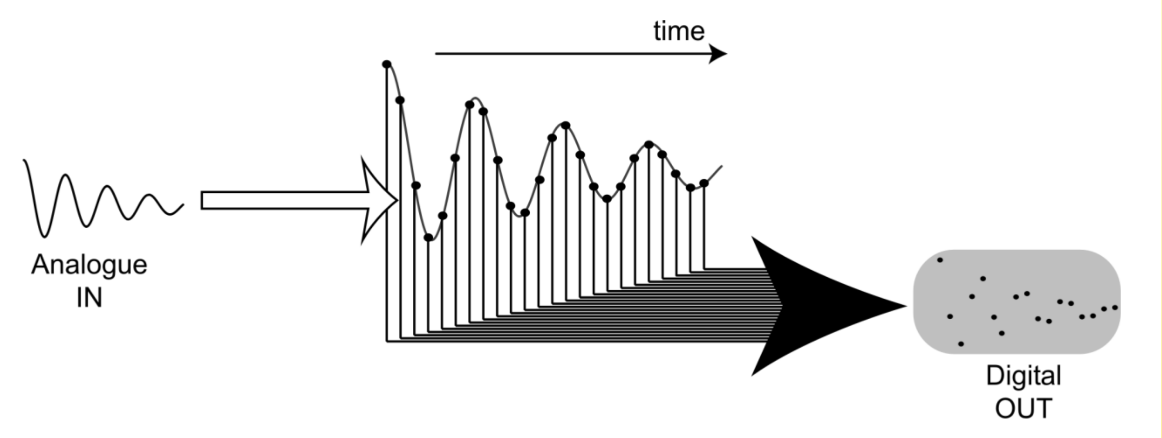
$$I_{1x}I_{2x} = \tfrac{1}{2}(I_{1+} + I_{1-}) * \tfrac{1}{2}(I_{2+} + I_{2-}) = \tfrac{1}{4}[I_{1+}I_{2+} + I_{1+}I_{2-} + I_{1-}I_{2+} + I_{1-}I_{2-}]$$

=> coherence order p = +2 0 0 -2

It is easy to see that the maximum coherence order will depend on the number of interacting spins

Quadrature detection in 1D

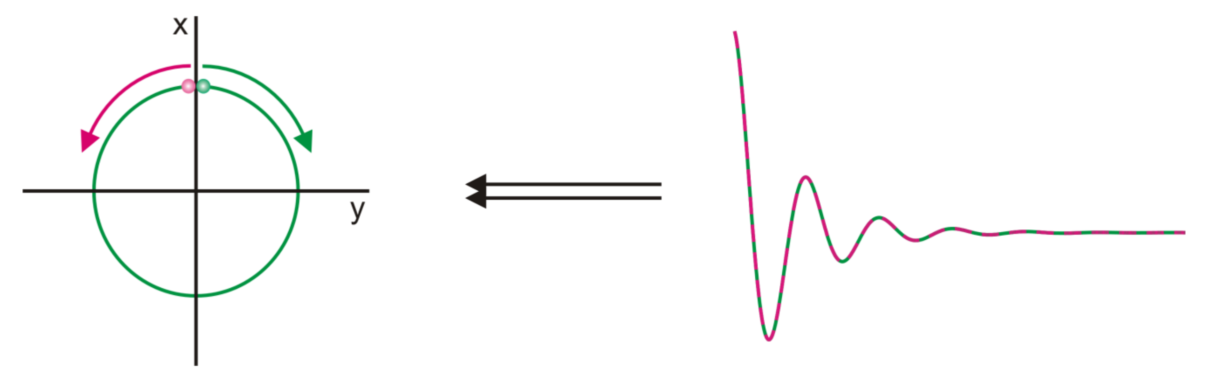
Quadrature Detection in 1D



The proton signal on a spectrometer operating at 600.13 MHz has a typical frequency range from 600.1305 to 600.1295 MHz (± 5000 Hz). In order for the signal to be processed on a computer it needs to be digitized using an Analog-Digital-Converter (ADC).

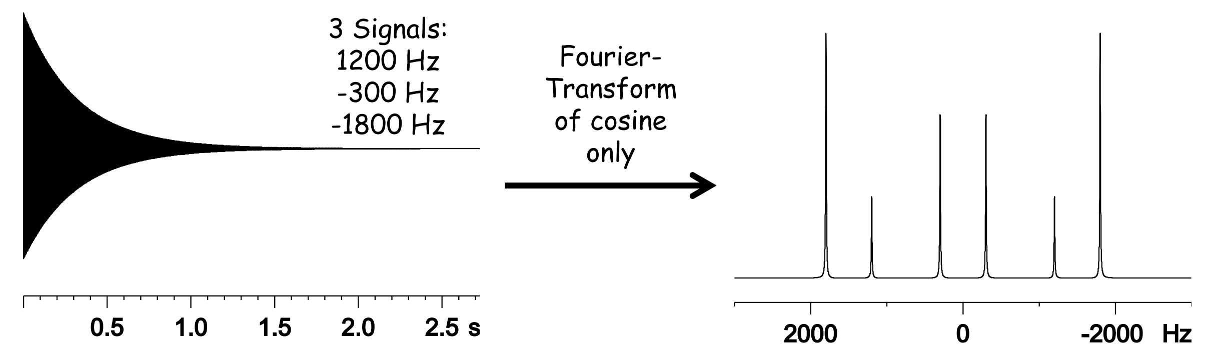
These frequencies are too high even for modern ADCs and therefore the reference frequency of 600.13 MHz is subtracted, to keep the frequency range as small as possible this is the center of the range.

Quadrature Detection in 1D

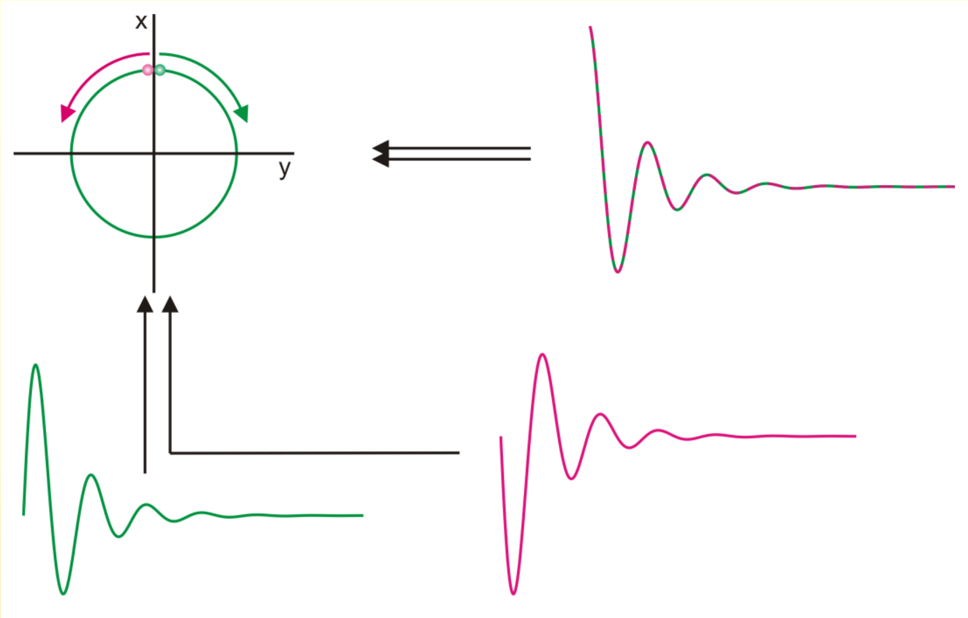


This leads to the problem that one has to deal with positive and negative frequencies that are not easily distinguished:

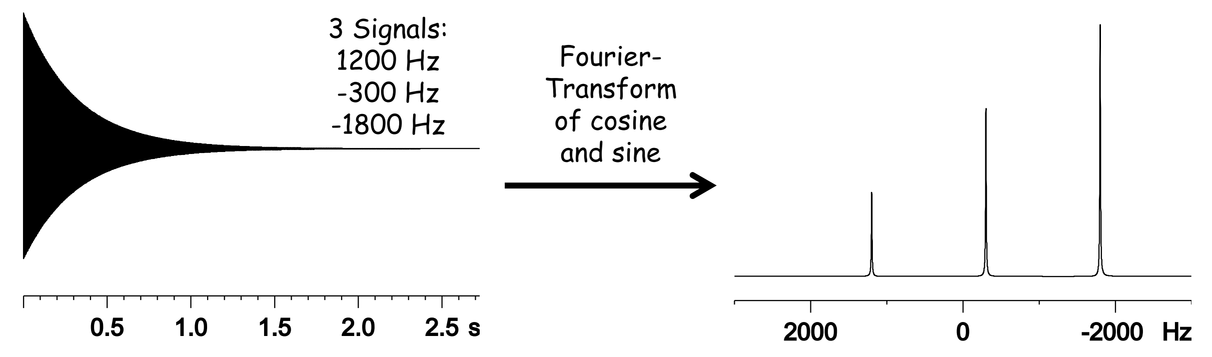
e.g. cos (x) = cos (-x)



Quadrature Detection in 1D

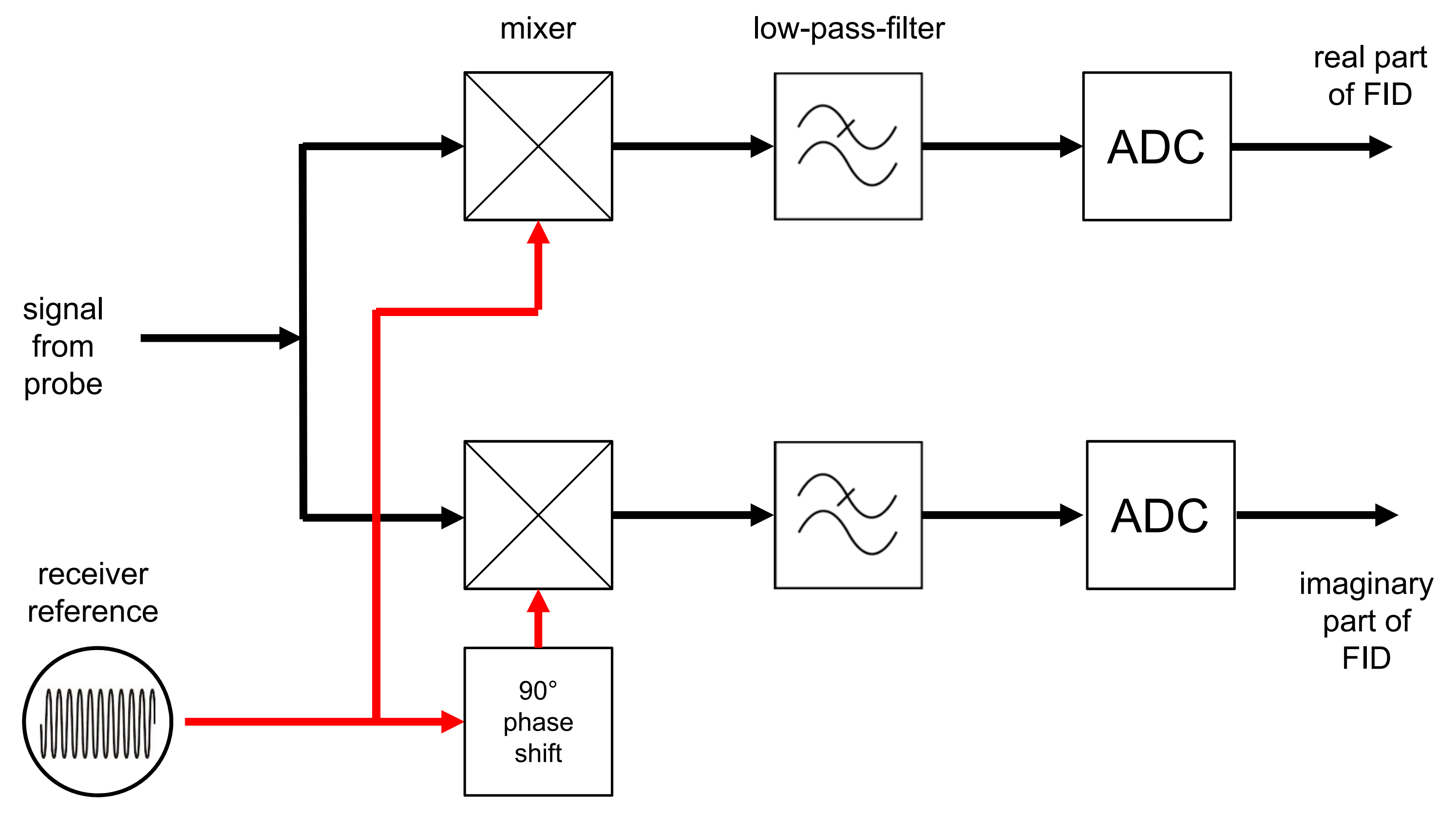


The solution is to obtain a second signal at an angel of 90° to distinguish the sense of rotation, i.e. the sign.
To do this with a second coil, however, is impractical



Quadrature Detection in 1D

It is therefore done by phase-shifting the reference signal



Quadrature Detection in 1D

To calculate how that works lets assume we have a cosine modulated signal, the receiver reference is a cosine as well, the two are multiplied in the mixer (☒)

$$s_C(t) = A \cos\omega t \cos\omega_{ref} t = A\,[\cos(\omega + \omega_{ref})t + \cos(\omega - \omega_{ref})t]$$

That means that after the low pass filter (≈) the following signal is digitized: $A \cos\Omega_0 t$ with $\Omega_0 = (\omega - \omega_{ref})$

The shifted receiver signal is a sine: $\cos(\varphi + \pi/2) = -\sin\varphi$

$$s_S(t) = A \cos\omega t \; {-\sin}\omega_{ref} t = A\,[-\sin(\omega + \omega_{ref})t + \sin(\omega - \omega_{ref})t]$$

That means that after the low pass filter (≈) the following signal is digitized: $A \sin\Omega_0 t$ with $\Omega_0 = (\omega - \omega_{ref})$

The sign of the frequency Ω_0 depends on wether $\omega > \omega_{ref}$ or $\omega < \omega_{ref}$

Quadrature Detection in 1D

The two components are combined to give of a complex number, in addition we have to keep in mind the decay of the signal:

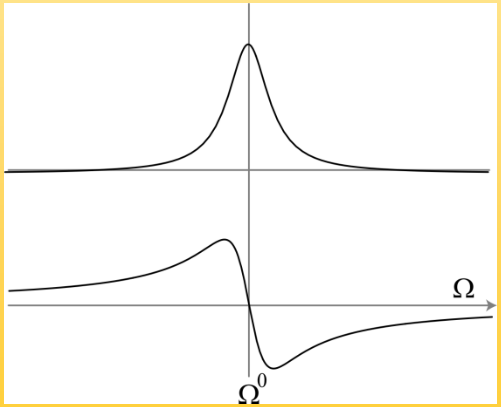
$$s(t) = [s_C(t) + i * s_S(t)] * \exp(-t/T_2) = \exp(i\Omega_0 t) \exp(-t/T_2)$$

Then we do an FT and obtain the frequency domain, the result consists also of complex numbers

$$S(\Omega) = \int_0^\infty s(t) \exp(-i\Omega t)\, dt = \frac{1}{(1/T_2) + i(\Omega - \Omega_0)} = A(\Omega) + i\, D(\Omega)$$

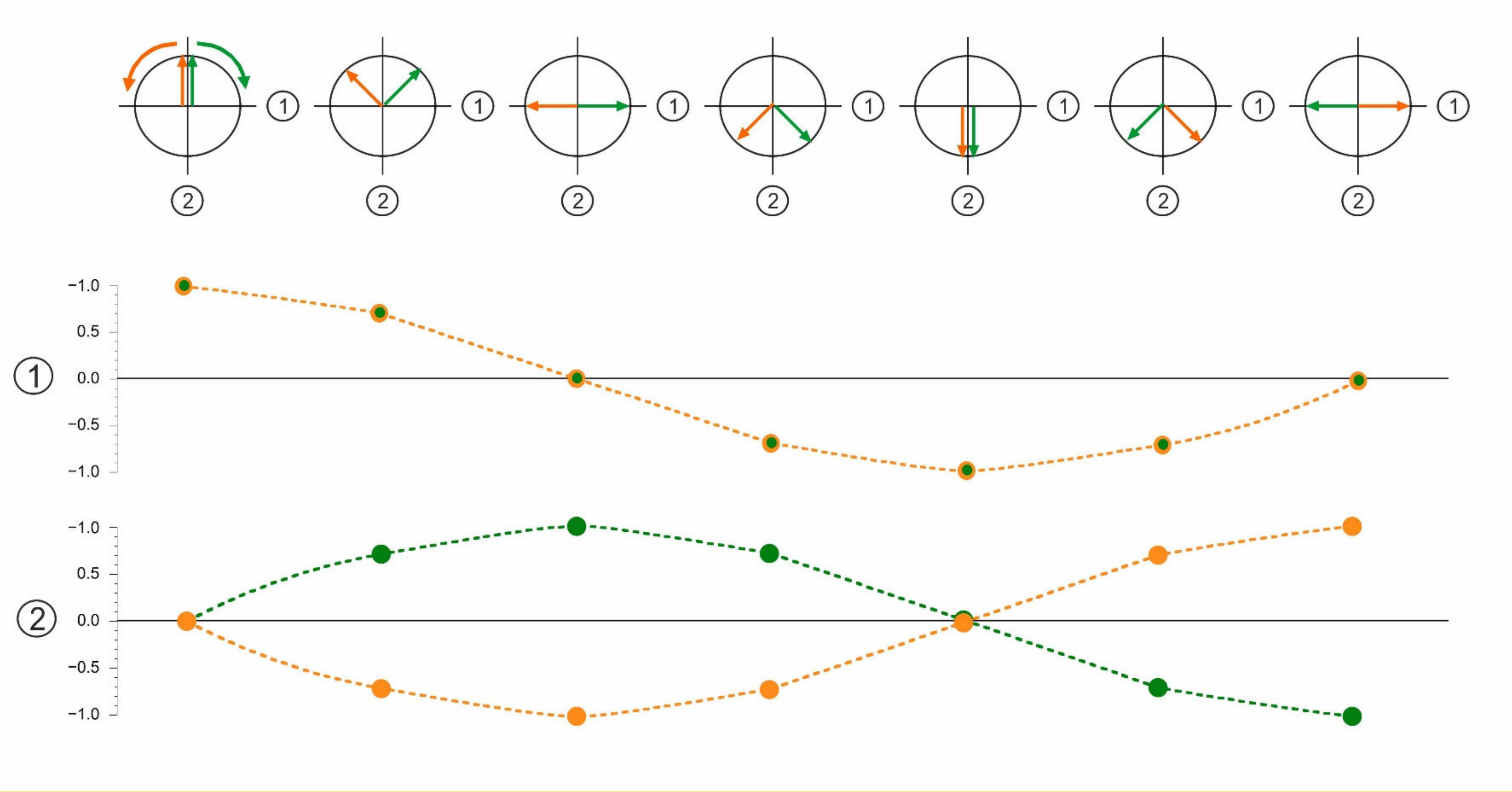
$$A(\Omega) = \frac{(1/T_2)}{(1/T_2)^2 + (\Omega - \Omega_0)^2}$$

$$D(\Omega) = - \frac{(\Omega - \Omega_0)}{(1/T_2)^2 + (\Omega - \Omega_0)^2}$$

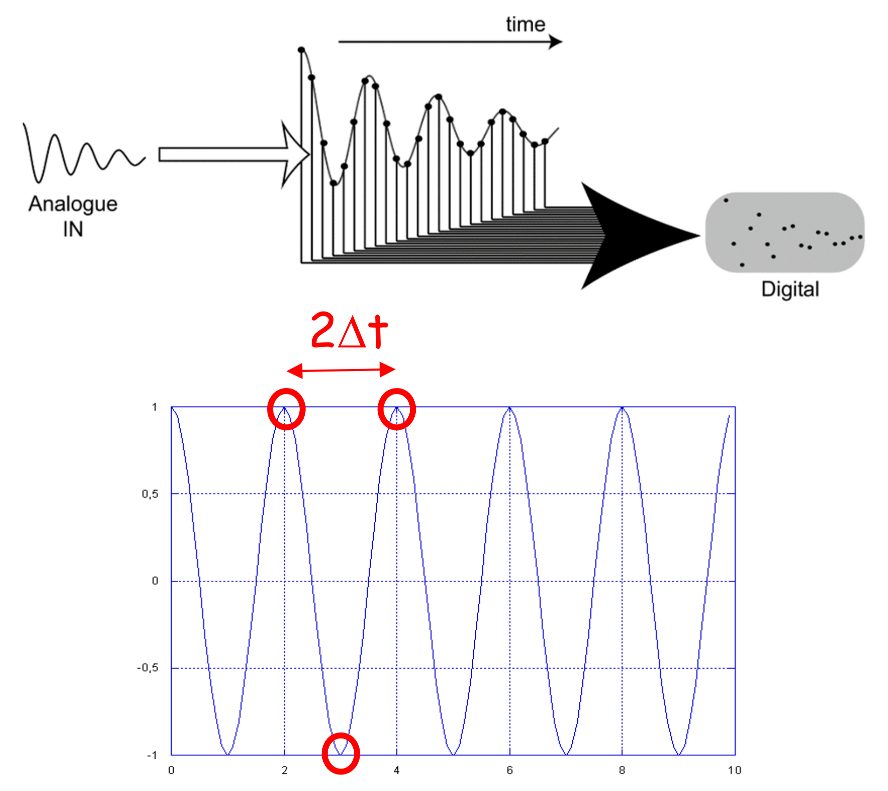


Quadrature Detection in 1D

Here is the graphical representation again, it shows the same idea: while two rotations in opposite directions can not be distinguish using one channel, using two perpendicular channels they can



Quadrature Detection in 1D



The digitization before processing imposes some restraints:

The digital FT (DFT) requires equidistant points.

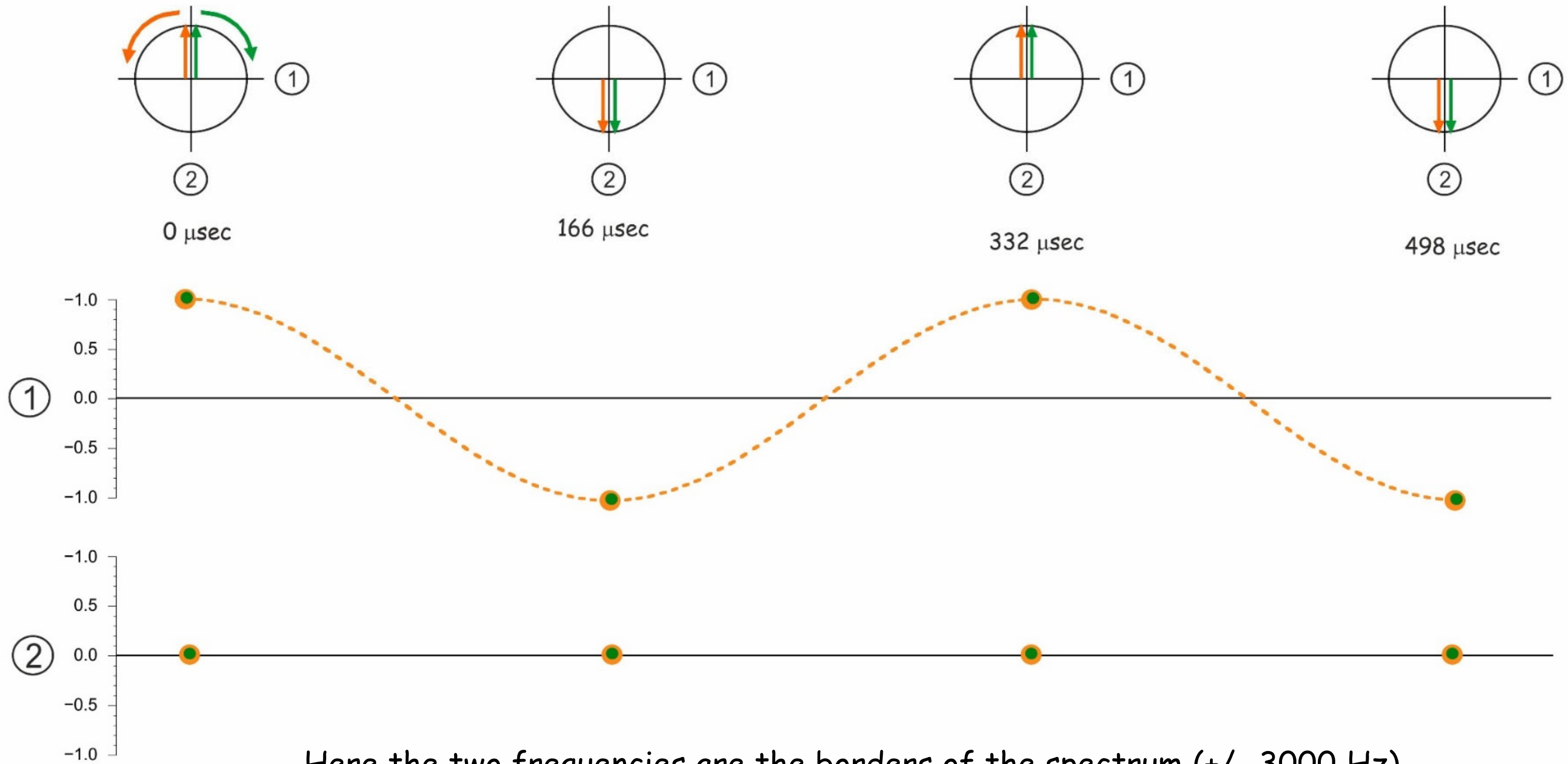
The Nyquist theorem demands that we have three time points per period, thus the highest frequency we can detect is

$$f_n = 1/(2\Delta t)$$

Quadrature Detection in 1D

Since we can distinguish the signs of the signals, the spectral width can be twice that: if we have sw = 6000 Hz, the sampling rate is Δt = 166.66 usec.

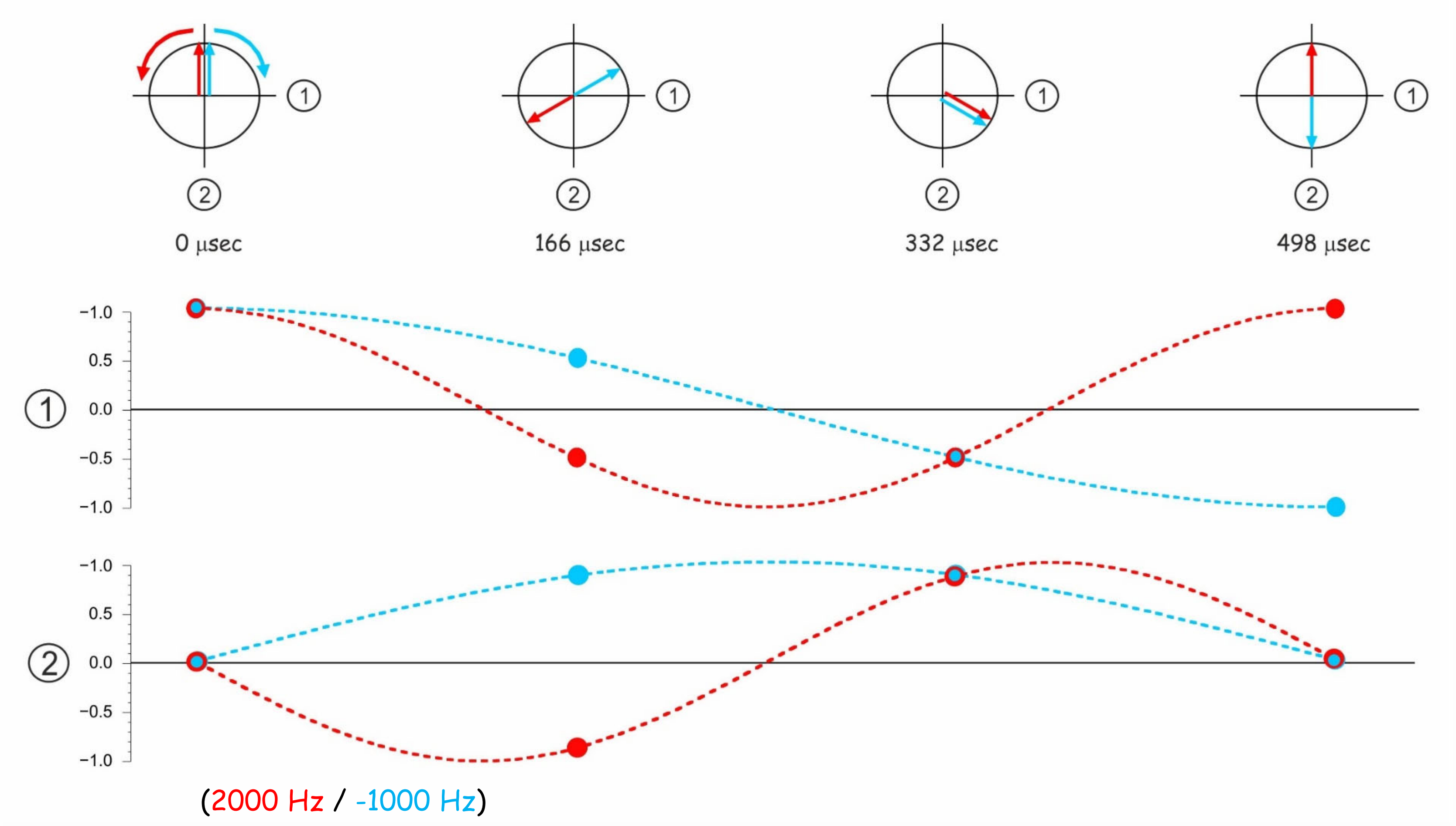
In the direct acquisition of a 1D higher frequencies will be removed by filters.



Here the two frequencies are the borders of the spectrum (+/- 3000 Hz)

Quadrature Detection in 1D

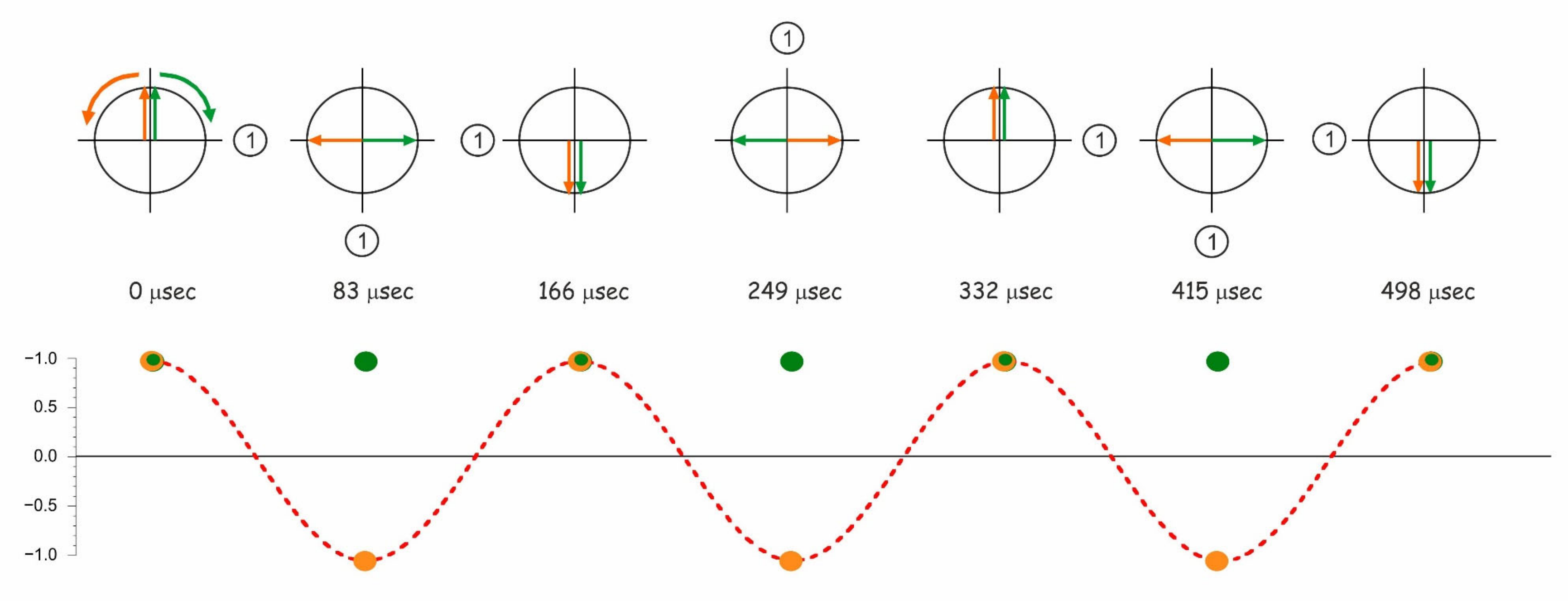
Frequencies that are not at the border of the spectral width look more normal



(2000 Hz / -1000 Hz)

Quadrature Detection in 1D

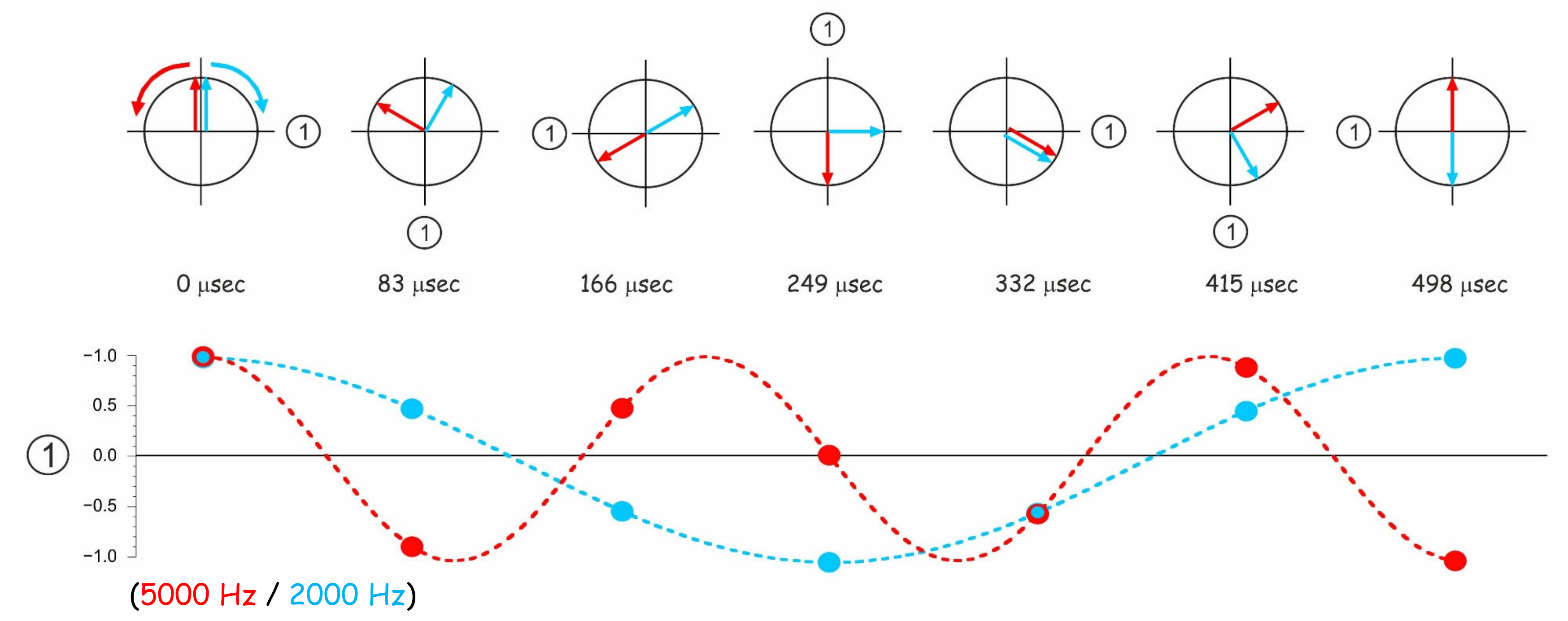
The solution presented so far made two ADCs necessary. A "cheaper" solution is the so called "Redfield-trick". Here the sampling rate is doubled and a single channel receiver is shifted proportional to the time. Thereby one sense of rotation is slowed down, the other sped up and the signals can be distinguished



(6000 Hz / 0 Hz)

Quadrature Detection in 1D

The sense of rotation is now the same for all resonances. The receiver is moving by 360° in 332 msec, which adds a frequency of 3000 Hz to every frequency. 2000 Hz become 5000 Hz and -1000 Hz become 2000 Hz.



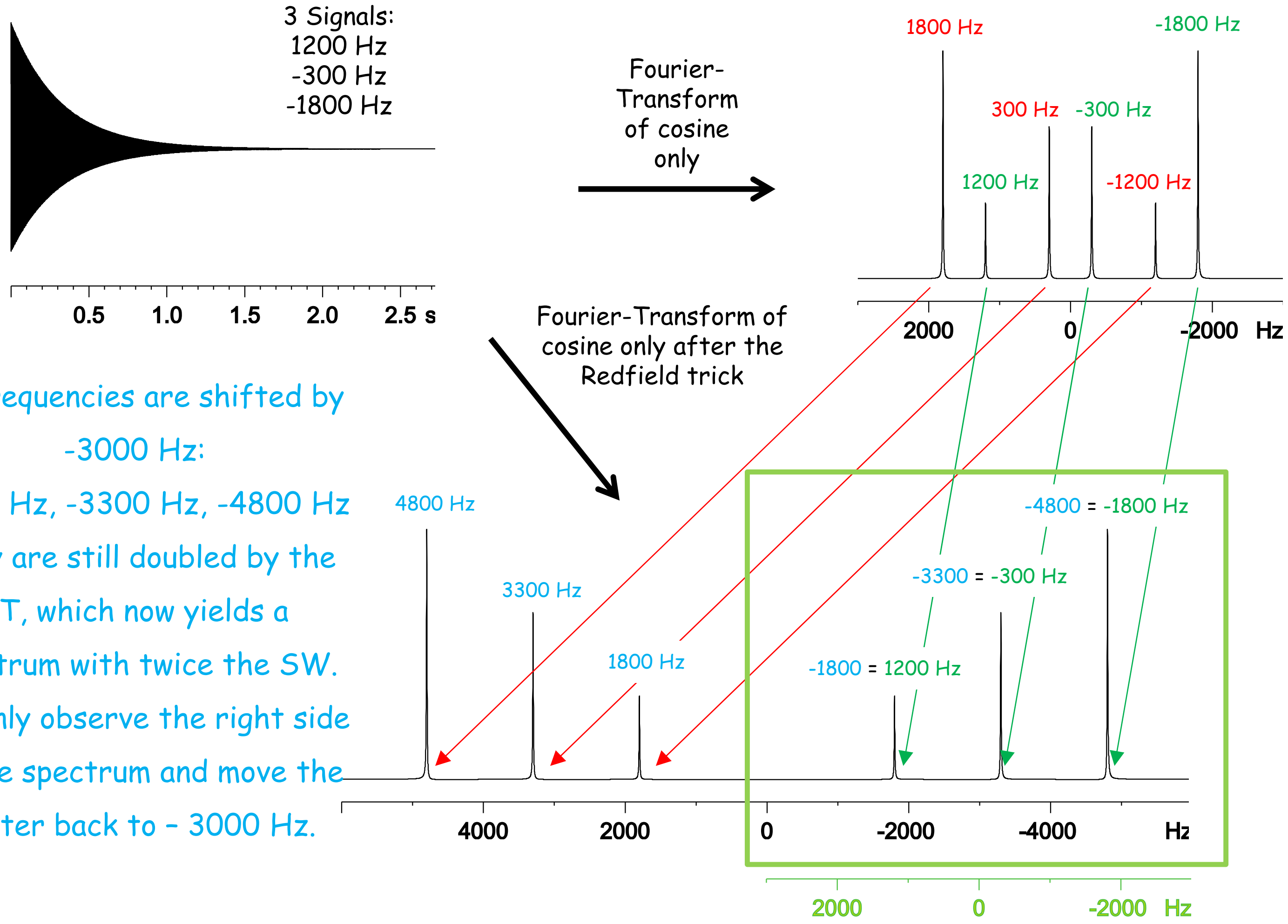
We could also move the receiver counter-clockwise and would get -1000 Hz from 2000 Hz and -4000 Hz from -1000 Hz !!

Quadrature Detection in 1D

We could also move the receiver counter-clockwise. Then we would add -3000 Hz to every frequency and would get -1000 Hz from 2000 Hz and -4000 Hz from -1000 Hz.

The important point is that all frequencies have *the same sign* in the end so that they are virtually all on the same side of the center frequency. If we then apply the Fourier transform, we get a spectrum of twice the spectral width (since we doubled the sampling rate) in which all peaks appear twice, symmetric about the center.
One half of the spectrum then corresponds to the “normal” spectrum with an SW of 3000 Hz and the correct number of sognals in the correct positions.

Quadrature Detection in 1D



All frequencies are shifted by -3000 Hz:

-1800 Hz, -3300 Hz, -4800 Hz

They are still doubled by the FT, which now yields a spectrum with twice the SW. We only observe the right side of the spectrum and move the center back to - 3000 Hz.

Quadrature Detection in 1D

Now we have seen that we can distinguish two counter-rotating components, what does that mean in terms of coherences ?

Another calculation shows that the sign discrimination we just saw is equivalent to the selection of one coherence order by the receiver. We replace the linearly polarized magnetization by two counter-rotating signals:

$$I_x \longrightarrow \tfrac{1}{2}[I^+ \exp(-i\omega t) + I^- \exp(i\omega t)]$$

The same applies to the receiver reference signals:

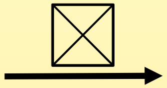
$$\cos(\omega_{ref}t) = \exp(i\omega_{ref}t) + \exp(-i\omega_{ref}t)$$

$$\cos(\omega_{ref}t + \pi/2) = i\exp(i\omega_{ref}t) - i\exp(-i\omega_{ref}t)$$

Quadrature Detection in 1D

Signal and reference are multiplied in the mixer to yield the real part of our complex signal

$$\cos(\omega_{ref}t) = \exp(i\omega_{ref}t) + \exp(-i\omega_{ref}t)$$



$$\tfrac{1}{2}[\,I^{+}\exp(-i\omega t) + I^{-}\exp(i\omega t)] * [\exp(i\omega_{ref}t) + \exp(-i\omega_{ref}t)]$$

$$= \tfrac{1}{2}\{I^{+}[\exp(-i\omega t)\exp(i\omega_{ref}t) + \exp(-i\omega t)\exp(-i\omega_{ref}t)]$$
$$+ I^{-}[\exp(i\omega t)\exp(i\omega_{ref}t) + \exp(i\omega t)\exp(-i\omega_{ref}t)]\}$$

$$= \tfrac{1}{2}\{I^{+}[\exp(-i(\omega-\omega_{ref})t) + \exp(-i(\omega+\omega_{ref})t)]$$
$$+ I^{-}[\exp(+i(\omega+\omega_{ref})t) + \exp(+i(\omega-\omega_{ref})t)]\}$$

The low-pass filter leaves only two terms

$$\tfrac{1}{2}\{I^{+}\exp(-i\Omega t) + I^{-}\exp(+i\Omega t)\} = \mathrm{Re}$$

Quadrature Detection in 1D

The shifted reference results in slightly modified terms

$$\cos(\omega_{ref}t + \pi/2) = i\exp(i\omega_{ref}t) - i\exp(-i\omega_{ref}t)$$

$$\xrightarrow{\boxtimes} \tfrac{1}{2}[I^{+}\exp(-i\omega t) + I^{-}\exp(i\omega t)] * i * [\exp(i\omega_{ref}t) - \exp(-i\omega_{ref}t)]$$

$$= \tfrac{1}{2}i * \{I^{+}[\exp(-i\omega t)\exp(i\omega_{ref}t) + \exp(-i\omega t)\exp(-i\omega_{ref}t)]$$
$$- \quad I^{-}[\exp(i\omega t)\exp(i\omega_{ref}t) - \exp(i\omega t)\exp(-i\omega_{ref}t)]\}$$

$$= \tfrac{1}{2}i * \{I^{+}[\exp(-i(\omega-\omega_{ref})t) + \exp(-i(\omega+\omega_{ref})t)]$$
$$- \quad I^{-}[\exp(+i(\omega+\omega_{ref})t) + \exp(+i(\omega-\omega_{ref})t)]\}$$

The low-pass filter again leaves only two terms

$$\xrightarrow{\approx} \tfrac{1}{2}\, i * \{I^{+}\exp(-i\Omega t) - I^{-}\exp(+i\Omega t)\} = \mathrm{Im}$$

Quadrature Detection in 1D

Both channels are combined to form a complex number

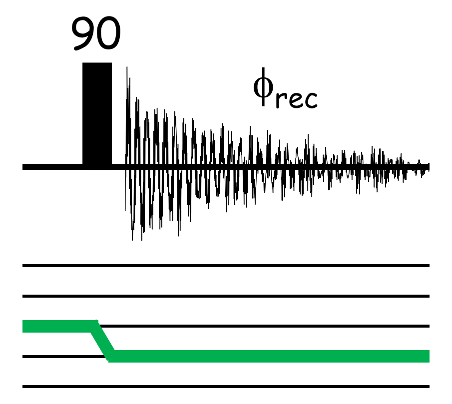
$$S = Re + i * Im$$

$$\tfrac{1}{2}[I^{+} \exp(-i\Omega t) + I^{-} \exp(+i\Omega t)]$$

$$+ i * i * \tfrac{1}{2}[I^{+} \exp(-i\Omega t) - I^{-} \exp(+i\Omega t)]$$

$$= I^{-} \exp(+i\Omega t)$$

which corresponds to coherence order (-1) !



we detect

coherence order

(-1)

Note: If we would choose $S = Re - i * Im$ we would detect I^{+} !!

Quadrature Detection in 1D

What happens if we create I_y magnetization first?

$$I_y \longrightarrow -i/2 \ast [I^+ \exp(-i\omega t) - I^- \exp(i\omega t)]$$

Both are again multiplied in the mixer

$$\boxtimes \longrightarrow -i/2 \ast [I^+ \exp(-i\omega t) - I^- \exp(i\omega t)] \ast [\exp (i\omega_{ref} t) + \exp (-i\omega_{ref} t)]$$

$$\cos (\omega_{ref} t) = \exp (i\omega_{ref} t) + \exp (-i\omega_{ref} t)$$

$$= -i/2 \ast \{I^+ [\exp(-i\omega t) \exp (i\omega_{ref} t) + \exp(-i\omega t) \exp (-i\omega_{ref} t)]$$
$$- \quad I^- [\exp(i\omega t) \exp (i\omega_{ref} t) + \exp(i\omega t) \exp (-i\omega_{ref} t)]\}$$

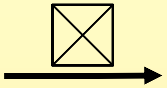
$$= -i/2 \ast \{I^+ [\exp(-i(\omega-\omega_{ref})t) + \exp(-i(\omega+\omega_{ref})t)]$$
$$- I^- [\exp(+i(\omega+\omega_{ref})t) + \exp(+i(\omega-\omega_{ref})t)]\}$$

The low-pass filter leaves only two terms

$$\longrightarrow \quad -i/2 \ast \{I^+ \exp(-i\Omega t) - I^- \exp(+i\Omega t)\} = \text{Re}$$

Quadrature Detection in 1D

The shifted reference results in slightly modified terms



$$-i/2 \ast [I^+ \exp(-i\omega t) - I^- \exp(i\omega t)] \ast i \ast [\exp(i\omega_{ref} t) - \exp(-i\omega_{ref} t)]$$

$$\cos(\omega_{ref} t + \pi/2) = i \exp(i\omega_{ref} t) - i \exp(-i\omega_{ref} t)$$

$$= \tfrac{1}{2} \ast \{I^+ [\exp(-i\omega t) \exp(i\omega_{ref} t) - \exp(-i\omega t) \exp(-i\omega_{ref} t)]$$

$$- \quad I^- [\exp(i\omega t) \exp(i\omega_{ref} t) - \exp(i\omega t) \exp(-i\omega_{ref} t)]\}$$

$$= \tfrac{1}{2} \ast \{I^+ [\exp(-i(\omega-\omega_{ref})t) - \exp(-i(\omega+\omega_{ref})t)]$$

$$- \quad I^- [\exp(+i(\omega+\omega_{ref})t) - \exp(+i(\omega-\omega_{ref})t)]\}$$

The low-pass filter again leaves only two terms

$$\tfrac{1}{2} \ast \{I^+ \exp(-i\Omega t) + I^- \exp(+i\Omega t)\} = \mathrm{Im}$$

Quadrature Detection in 1D

Both channels are again combined to form a complex number

$$S = Re + i * Im$$

$$-i/2 * [I^{+} \exp(-i\Omega t) - I^{-} \exp(+i\Omega t)]$$

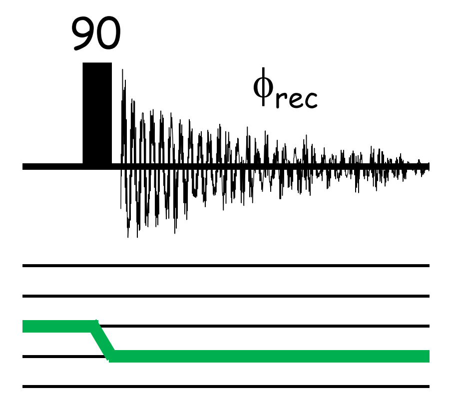
$$+ i/2 * [I^{+} \exp(-i\Omega t) + I^{-} \exp(+i\Omega t)]$$

$$= i * I^{-} \exp(+i\Omega t)$$

$$= I^{-} \exp(+i(\Omega+\pi/2)t)$$

$i \exp(i\Omega t) = \exp(+i(\Omega+\pi/2)t$

We have a phase shift by 90°, but again this corresponds to coherence order (-1)



we detect coherence order (-1)

Quadrature Detection in 1D

$$I_x \longrightarrow I^- \exp(+i(\Omega)t)$$

$$I_y \longrightarrow I^- \exp(+i(\Omega+\pi/2)t)$$

We have seen that by shifting the phase of the original signal (e.g. by shifting the pulse by that phase) we get a phase shift in the resulting signal.

But they were obtained via the two phase shifted reference signals which were combined to a complex signal.

Those can then by easily manipulated by simple data processing operations and we will do one of those now that we will need later when we think about echo/anti-echo processing.

Quadrature Detection in 1D

We switch the real and the imaginary part and change the sign of the real part

Re $= -i/2 * \{I^{+} \exp(-i\Omega t) - I^{-} \exp(+i\Omega t)\}$ Im $= \frac{1}{2} * \{I^{+} \exp(-i\Omega t) + I^{-} \exp(+i\Omega t)\}$

We take the result of the I_y magnetization and use that

Instead of

$$S = Re + i * Im =$$

$$-i/2 * [I^{+} \exp(-i\Omega t) - I^{-} \exp(+i\Omega t)] + i/2 * [I^{+} \exp(-i\Omega t) + I^{-} \exp(+i\Omega t)]$$

$$= I^{-} \exp(+i(\Omega+\pi/2)t)$$

we have

$$S = -i * Re + Im =$$

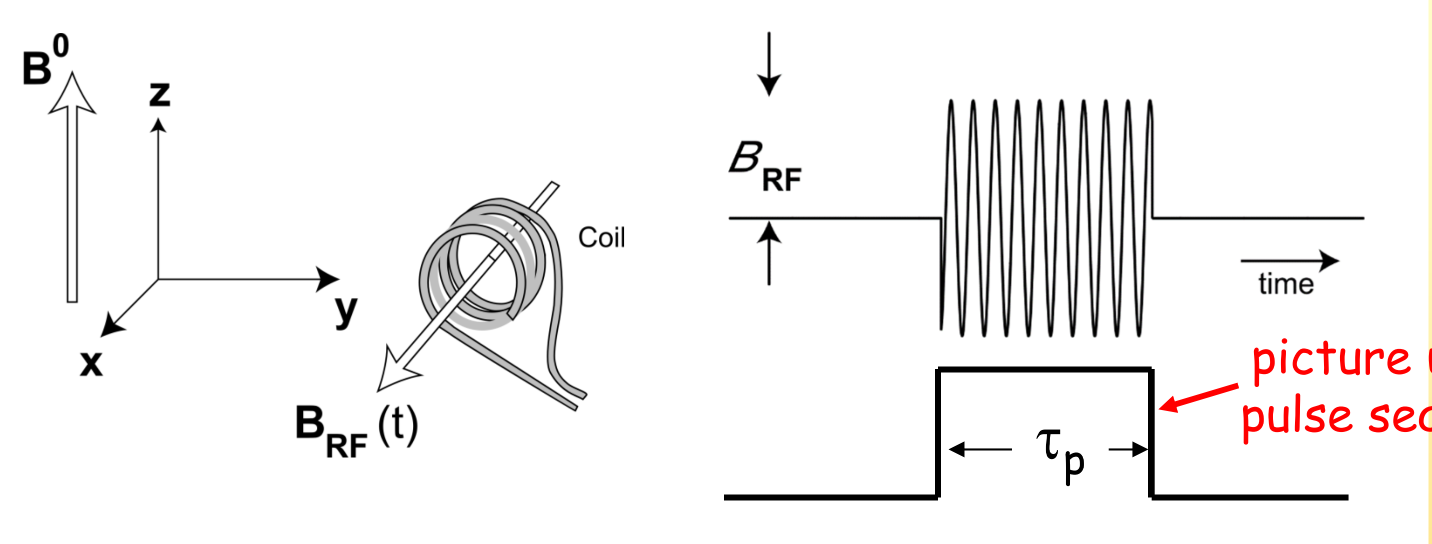
$$-\tfrac{1}{2} * [I^{+} \exp(-i\Omega t) - I^{-} \exp(+i\Omega t)] + \tfrac{1}{2} * [I^{+} \exp(-i\Omega t) + I^{-} \exp(+i\Omega t)]$$

$$= I^{-} \exp(+i\Omega t)$$

This data manipulation results in the same signal as the one resulting from I_x !!

Pulses and coherence levels

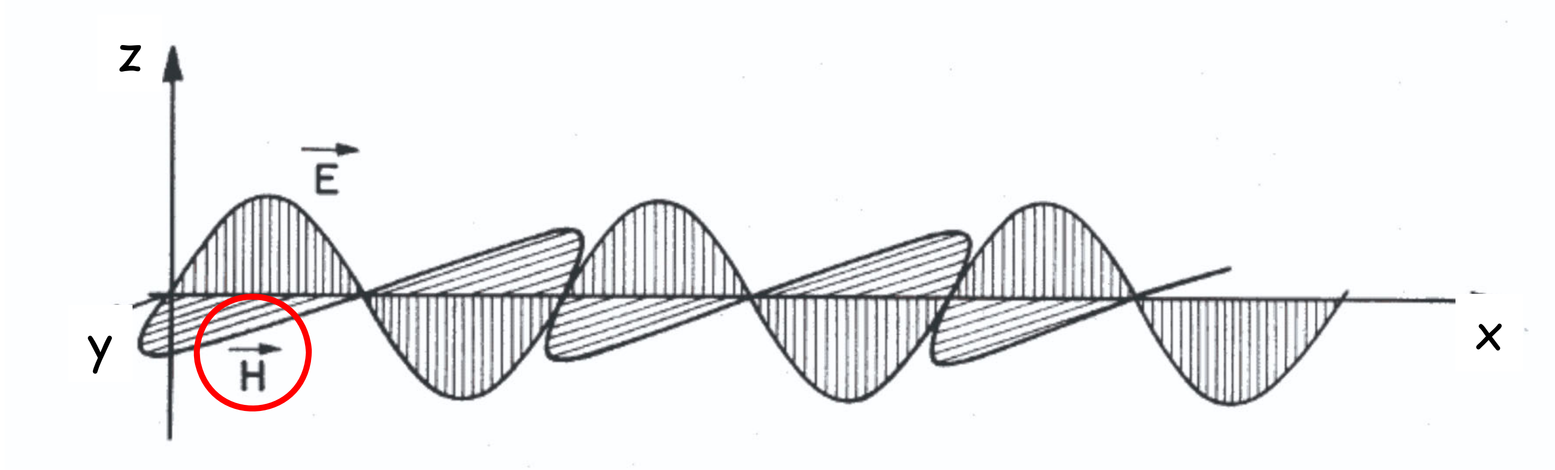
Pulses and coherence levels

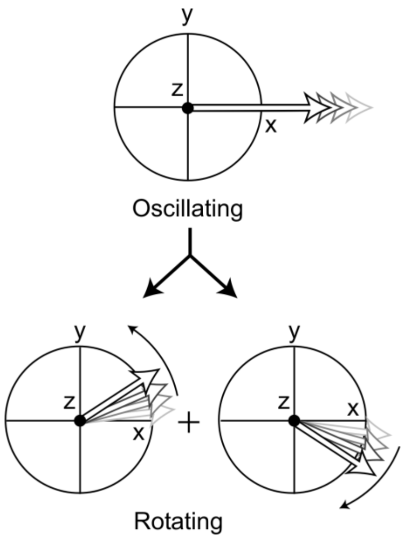


picture used in pulse sequences

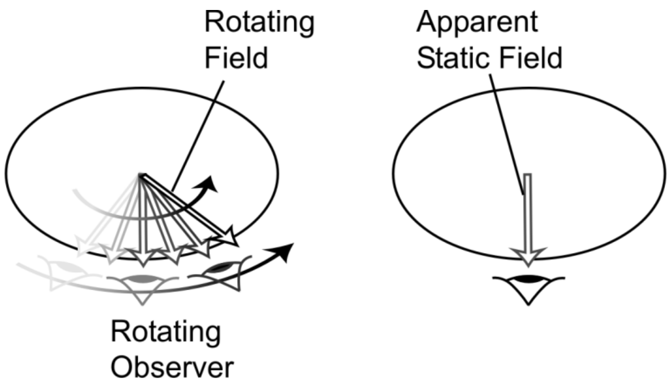
An equally important tool of pulse sequences as delays are obviously the pulses, i.e. irradiation of radio waves with a certain frequency, power and phase

Pulses and coherence levels

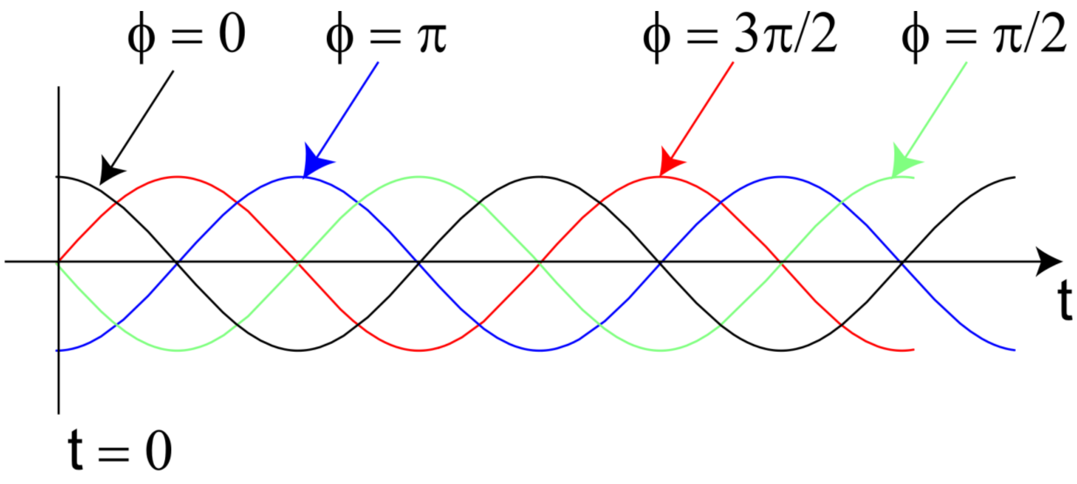




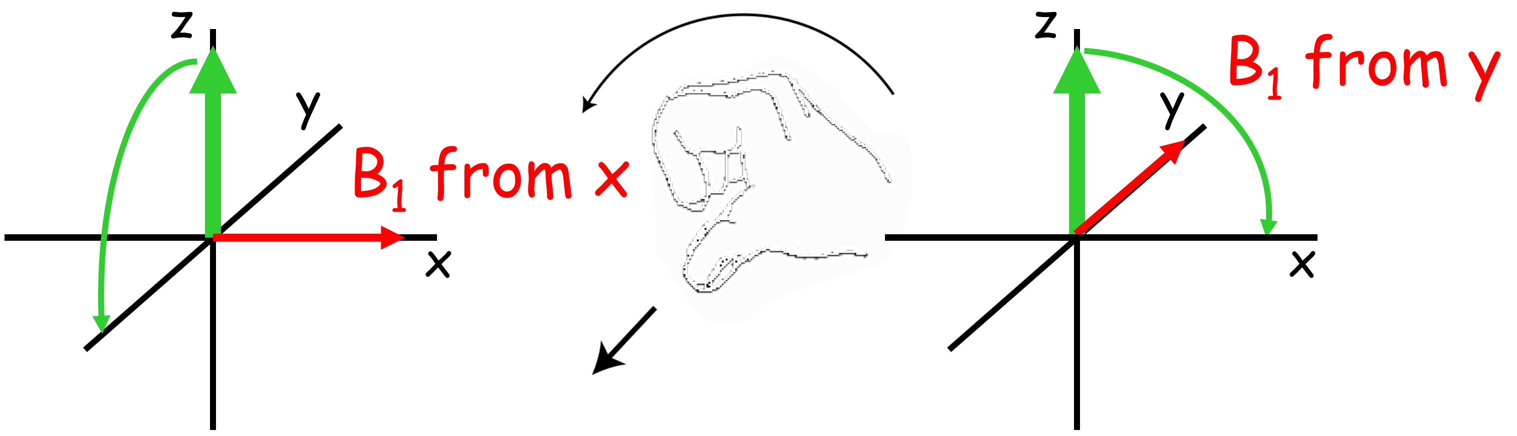
In the rotating frame commonly used in NMR the oscillation translates into a static field



Pulses and coherence levels



The phase of the signal thus translates into the direction of the B_1-field: the phase of the pulse !



convention : ϕ = 0 means x-pulse

Pulses and coherence levels

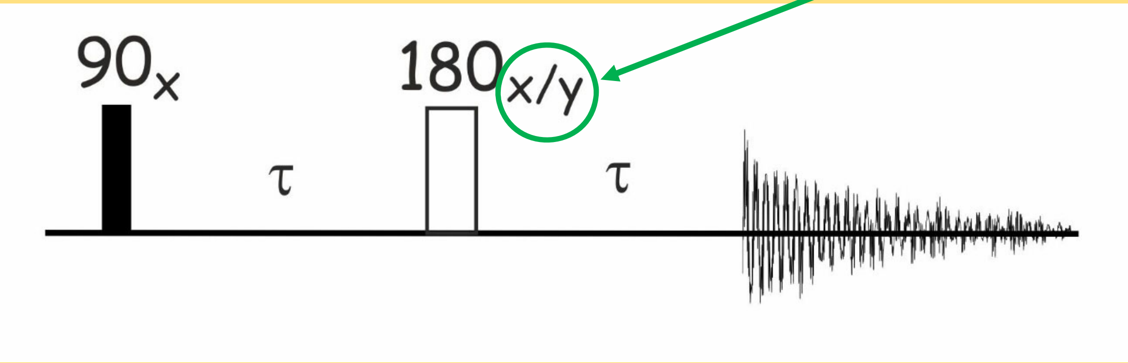
Some simple calculations can show the effect of the phase of pulses.

$$I_z \xrightarrow{90° \, I_x} -I_y \qquad\qquad I_z \xrightarrow{90° \, I_y} I_x$$

more general: changing the pulse phase is a rotation around the z-axis !

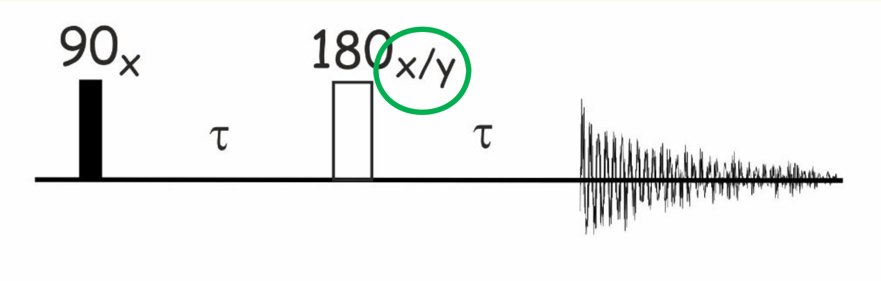
$$I_z \xrightarrow{90° \, I_\varphi} I_x \sin\varphi - I_y \cos\varphi$$

Now lets see the effect of a phase shift in a simple spin echo



The phase of this 180° pulse is changed by 90°

Pulses and coherence levels



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

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

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

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

a 90° phase shift in a 180°-pulse changes the sign of refocussed magnetization !!

Pulses and coherence levels

The result is obviously the same when we use the spherical operators

$$I_x = \tfrac{1}{2}\,(I_+ + I_-) \xrightarrow{I_z\Omega\tau} \tfrac{1}{2}\,[I_+ \exp(-i\Omega\tau) + I_- \exp(+i\Omega\tau)]$$

$$= \tfrac{1}{2}\,[(I_x + iI_y) \exp(-i\Omega\tau) + (I_x - iI_y) \exp(+i\Omega\tau)]$$

$$\xrightarrow{\pi I_x} \tfrac{1}{2}\,[(I_x - iI_y) \exp(-i\Omega\tau) + (I_x + iI_y) \exp(+i\Omega\tau)]$$

$$= \tfrac{1}{2}\,[I_- \exp(-i\Omega\tau) + I_+ \exp(+i\Omega\tau)]$$

$$\xrightarrow{I_z\Omega\tau} \tfrac{1}{2}\,[I_- \exp(-i\Omega\tau) \exp(+i\Omega\tau) + I_+ \exp(+i\Omega\tau) \exp(-i\Omega\tau)\,] = I_x$$

The switching between the representations can complicate calculations !!

$$\xrightarrow{\pi I_y} \tfrac{1}{2}\,[(-I_x + iI_y) \exp(-i\Omega\tau) + (-I_x - iI_y) \exp(+i\Omega\tau)]$$

$$= \tfrac{1}{2}\,[-I_- \exp(-i\Omega\tau) - I_+ \exp(+i\Omega\tau)]$$

$$\xrightarrow{I_z\Omega\tau} \tfrac{1}{2}\,[-I_- \exp(-i\Omega\tau) \exp(+i\Omega\tau) - I_+ \exp(+i\Omega\tau) \exp(-i\Omega\tau)\,] = -\,I_x$$

Pulses and coherence levels

Now lets look what 180° pulses do to coherences in the spherical representation

$I_+ = (I_x + iI_y) \xrightarrow{\pi I_x} (I_x - iI_y) = I_-$ $\quad$ $I_- = (I_x - iI_y) \xrightarrow{\pi I_x} (I_x + iI_y) = I_+$

$I_+ = (I_x + iI_y) \xrightarrow{\pi I_y} (-I_x + iI_y) = -I_-$ $\quad$ $I_- = (I_x - iI_y) \xrightarrow{\pi I_y} (-I_x - iI_y) = -I_+$

$$I_+ I_- = (I_x + iI_y)(I_x - iI_y) \xrightarrow{\pi I_x} (I_x - iI_y)(I_x + iI_y) = I_- I_+$$

$$I_+ I_- = (I_x + iI_y)(I_x - iI_y) \xrightarrow{\pi I_y} (-I_x + iI_y)(-I_x - iI_y) = I_- I_+$$

ZQC

$$I_+ I_+ = (I_x + iI_y)(I_x + iI_y) \xrightarrow{\pi I_x} (I_x - iI_y)(I_x - iI_y) = I_- I_-$$

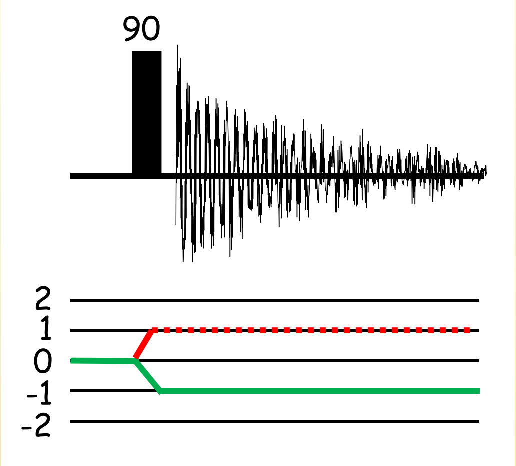
$$I_+ I_+ = (I_x + iI_y)(I_x + iI_y) \xrightarrow{\pi I_y} (-I_x + iI_y)(-I_x + iI_y) = I_- I_-$$

DQC

We see that a 180° pulse changes the sign of the coherence order, but a 90° phase shift of the pulse changes the sign of the coherence only for SQC. It seems obvious that this can be utilized to separate the coherences which is exactly what is done using a phase cycle !

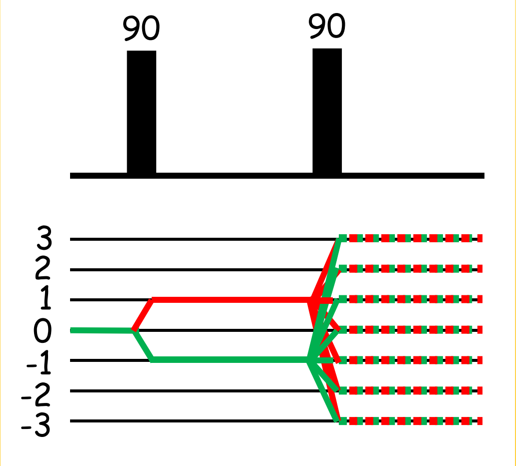
Pulses and coherence levels

To depict what is going on coherence transfer pathway diagrams are used



$$I_z \xrightarrow{90_{-y}} I_x = 1/2\,(I_+ + I_-)$$

Removed by quadrature detection

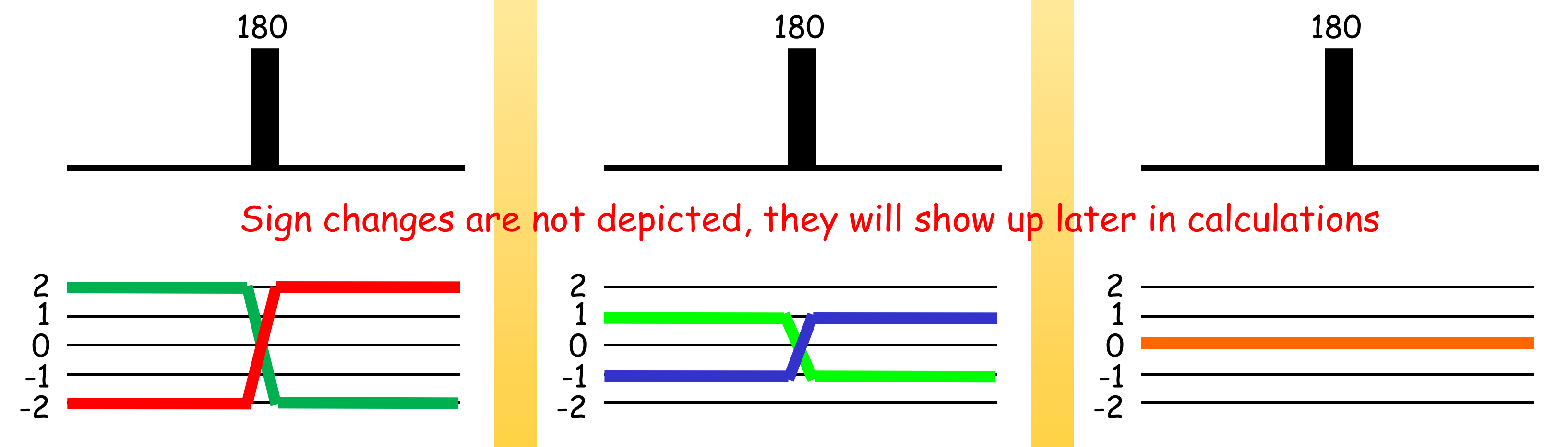


While the first 90° pulse can only create coherences of order 1 and -1 (in case of a β-pulse also 0 is left) all subsequent 90° pulses create all orders of coherence, the upper limit is the number of spins that couple with each other. That's one reason why we need phase cycling !!

Pulses and coherence levels

180° pulses are different in that respect, as we have seen they only invert the order of coherence.

This is only true, however, if they are perfect 180° pulses. Those are difficult to achieve and thus a lot of phase cycling or gradients are applied to 180° pulses.



Sign changes are not depicted, they will show up later in calculations

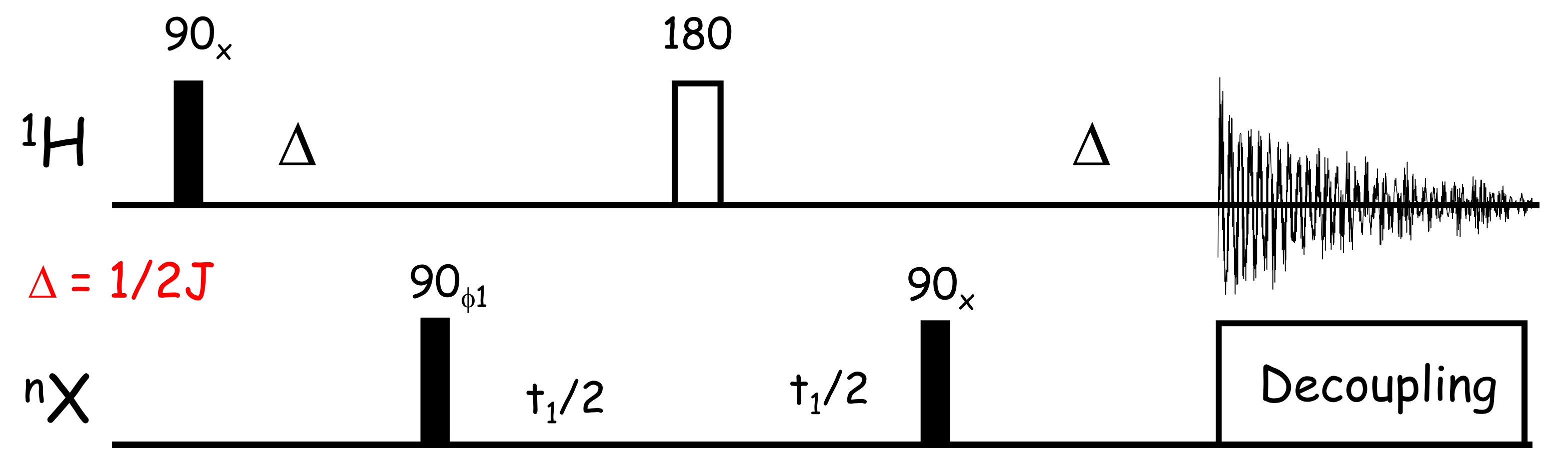
Phase cycling

Phase Cycling

In almost all NMR experiments the pulse sequence does not only create desirable types of magnetization but also various kinds of unwanted ones. To get the spectrum that we want we thus have to select the magnetization we want and suppress all other types. We will later learn that gradients are a good way to do that but one procedure that is used in all NMR pulse sequences is phase cycling. In most experiments it is necessary to record the FID several times to obtain a sufficient signal-to-noise ratio. Using a phase cycle means that we vary the phase of one or several pulses in a systematic manner to select the signals we want. This in turn then makes a certain number of repetitions necessary to complete a full phase cycle.

Phase Cycling

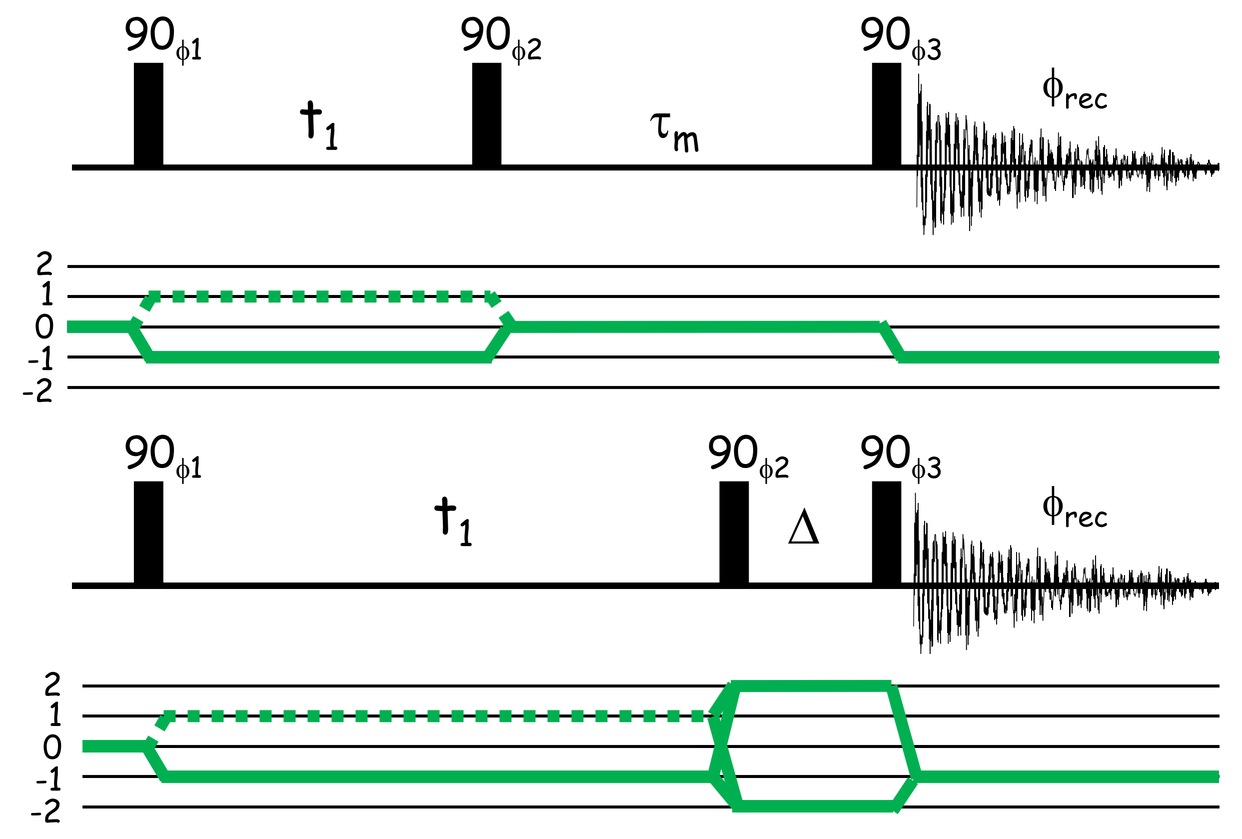
One example is the HMQC experiment



If this experiment is recorded using a sample with ^{13}C in natural abundance, 99% of the ^1H nuclei will create undesirable signals that are present as stripes parallel to F1 unless something is done to suppress them.

Phase Cycling

Another example is the difference between NOESY and DQF-COSY



The sequences are very similar but need to produce quite different results

Phase Cycling

All phase cycles work by adding up the desired signals and subtracting out the undesired ones. That means that they depend on the stability of the equipment used and will have more problems if strong, sharp signals need to be suppressed.

Many phase cycles, in particular in heteronuclear experiments and also triple resonance experiments are simple subtraction schemes.

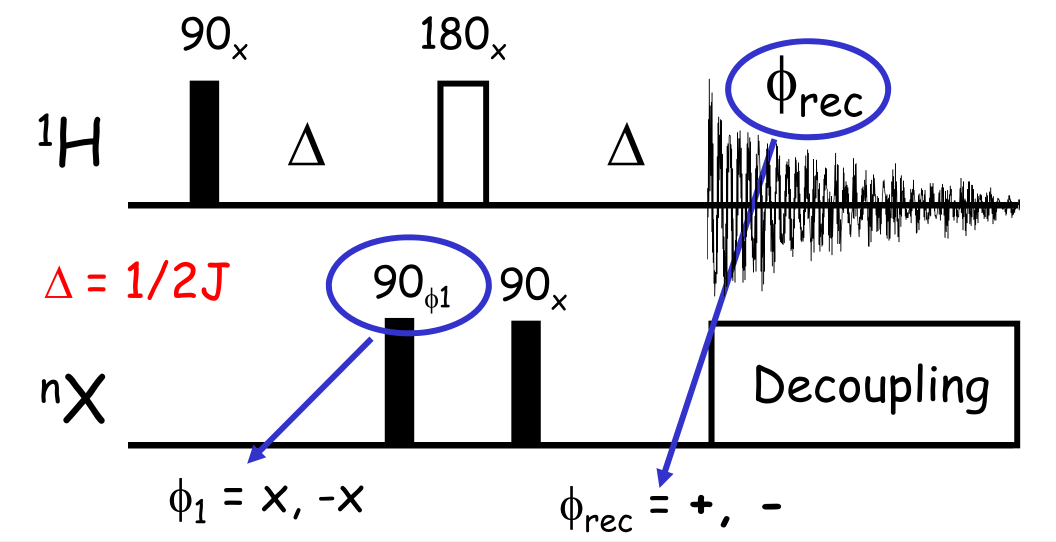
For more complex phase cycles one has to calculate the coherence order transfer efficiency for which some quite straightforward rules have been established. The optimal suppression of the undesired pathways is more complex.

M. Levitt, "Spin Dynamics", Appendix 17.10

L. Mitschang et al. J. Chem. Phys. 102, 3089-3098 (1995)

Phase Cycling

A first "real" phasecycle can be seen in a 1D-HMQC type experiment



protons not bound to X:

1: $\phi_1 = x \longrightarrow H_y$

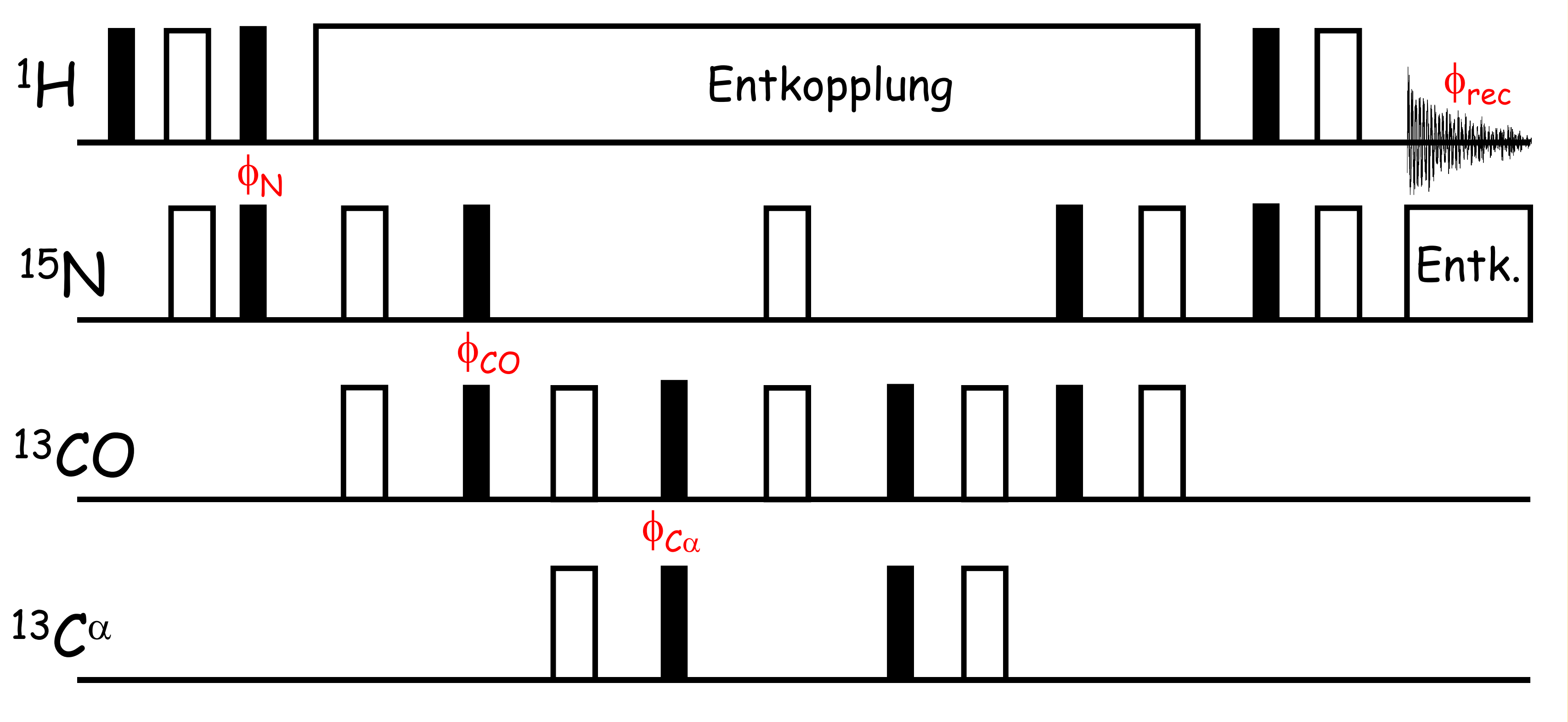
2: $\phi_1 = -x \longrightarrow H_y$

$1 - 2 = 0$

$$H_z \xrightarrow{90^\circ\, H_x} -H_y \xrightarrow{\pi J_{HX}\Delta} 2H_xX_z$$

$$\begin{array}{l} 1:\ 2H_xX_z \xrightarrow{90^\circ\, X_x} -\,2H_xX_y \\ 2:\ 2H_xX_z \xrightarrow{90^\circ\, X_{-x}} +\,2H_xX_y \end{array} \xrightarrow[\pi J_{HX}\Delta]{90^\circ\, C_x} \left.\begin{array}{l} -\,H_y \\ +\,H_y \end{array}\right\}\ 1 - 2 = 2\,H_y$$

Phase Cycling

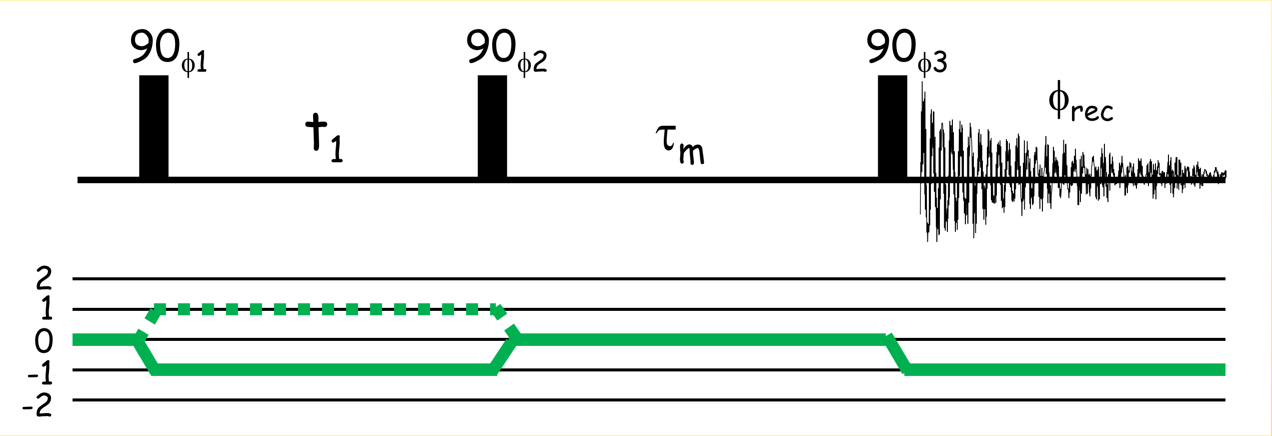


In more complex experiments like the HN(CO)CA the idea remains the same:

$$\left.\begin{array}{l}\phi_N = x, -x \\ \phi_{CO} = x, x, -x, -x \\ \phi_{C\alpha} = x, x, x, x, -x, -x, -x, -x\end{array}\right\} \phi_{rec} = x, -x, -x, x, -x, x, x, -x$$

Phase Cycling

If we want to go beyond simple subtractions we have to use some recipes. We have to choose the coherence order pathway that represents the desired signals, this will dictate the coherence order *changes* Δp that we need to accomplish. For a NOESY we thus need the following pathways:



Remeber:
we detect
coherence order
(-1)

$0 \xrightarrow{\Delta p = +1} +1 \xrightarrow{\Delta p = -1}$

$0 \xrightarrow{\Delta p = -1} -1 \xrightarrow{\Delta p = +1}$

$0 \xrightarrow{\Delta p = -1} -1$

It is important to note that we select *changes* in coherence order, not the coherence order itself !!

Phase Cycling

The variable we have is the phase increment we use for each of the pulses.

We have to go full circle, i.e. we divide 360° by the number of phase cycle steps we want to execute. If we want to do 4 steps then the phase cycle will be 0°, 90°, 180°, 270°. In a (Bruker) pulse program steps of 90° are pre-defined for simplicity, such a phase cycle would then be written as:

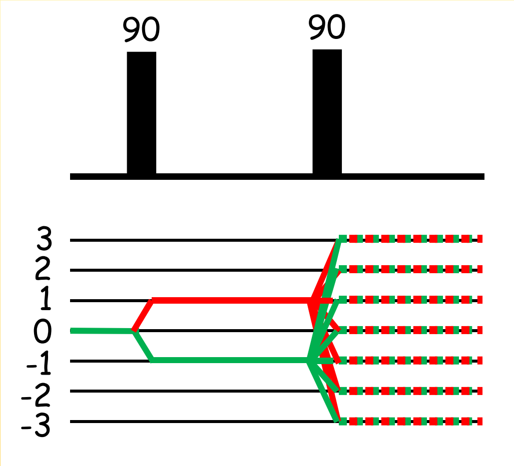
phx = 0 1 2 3

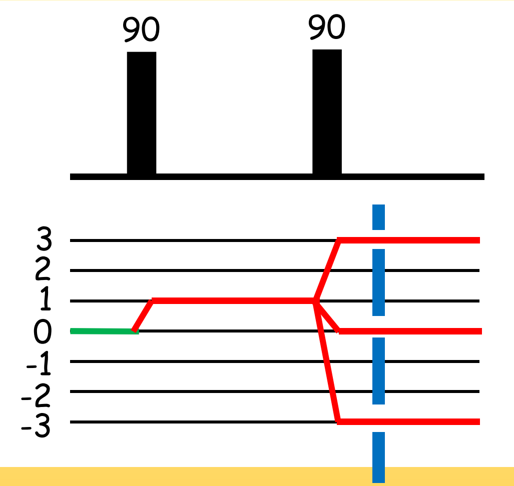
If we have 6 steps we end up with steps of 60° and this would be written as:

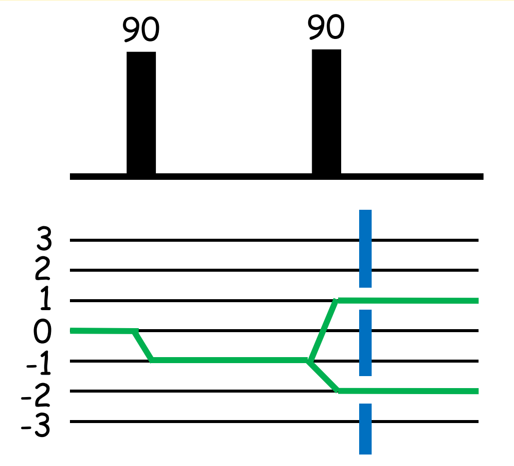
phx = (360) 0 60 120 180 240 300 or phx = (6) 0 1 2 3 4 5

Phase Cycling

The number of steps that we need to choose depends on the *difference* between coherence order changes that we want to select. This can be thought of as a mask that we use on the coherence order *changes*. If we cycle the second pulse in steps of 120° we select every third coherence order *change*.







Note that instead of 1 to 3,0 and -3 a jump to 2, -1 and -4 would also be possible but would require another receiver phase (see below). Only the difference between the resulting levels is determined by the phase change.

Phase Cycling

Which of the coherence order pathways finds its way to the receiver depends on the phase cycle not only of the various pulses in the pulse sequence but also on the receiver phase. Only if all phase changes combined with the desired coherence order changes add up signal will be obtained.

The formula to calculate the desired receiver phase is:

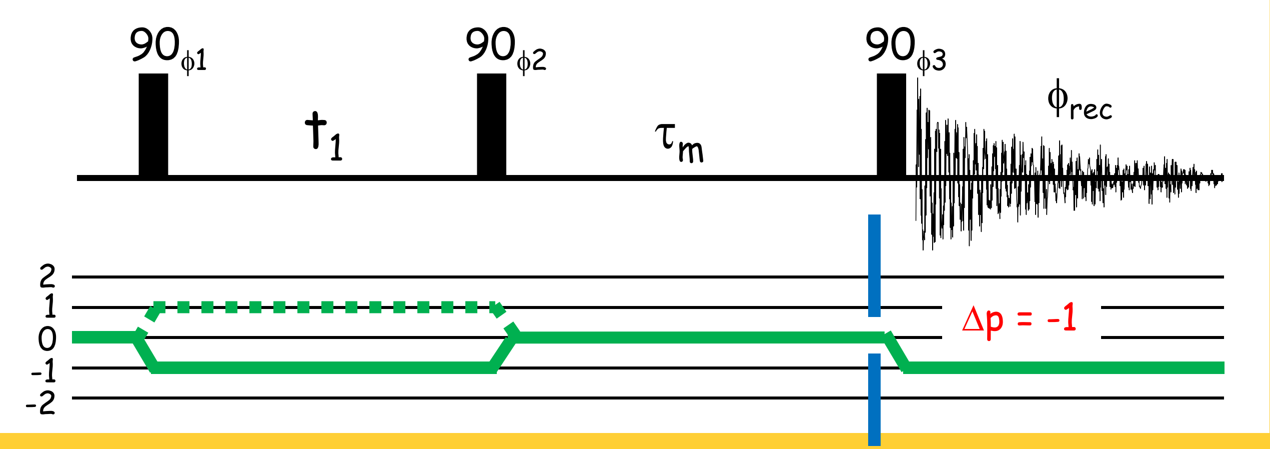
$$\phi_{rec} = -\sum_{i} \Delta p_i * \overset{!}{\Delta\phi_i}$$

Were i is the number of the phasecycle step.

That means for every pulse we multiply the desired change in coherence order with the (change in) phase and then all products are added up, multiplied by (-1) to yield the receiver phase.

Phase Cycling

In case of the NOESY we obtain the following phase cycle: We vary $\phi 3$ in steps of 90° which will give us coherence order 0, ± 4 , ± 8 … if we choose the receiver properly so that a change of coherence order by -1 is accomplished in the last step. We leave $\phi 1$ and $\phi 2$ at 0 since the creation of coherence orders of 4 or 8 (and changes by -5 or -7) is rather unlikely (see below). They thus can be ignored in the calculation since they always yield 0. So our phase cycle is $\phi 3$ = 0, 1, 2, 3, what is the receiver phase ?

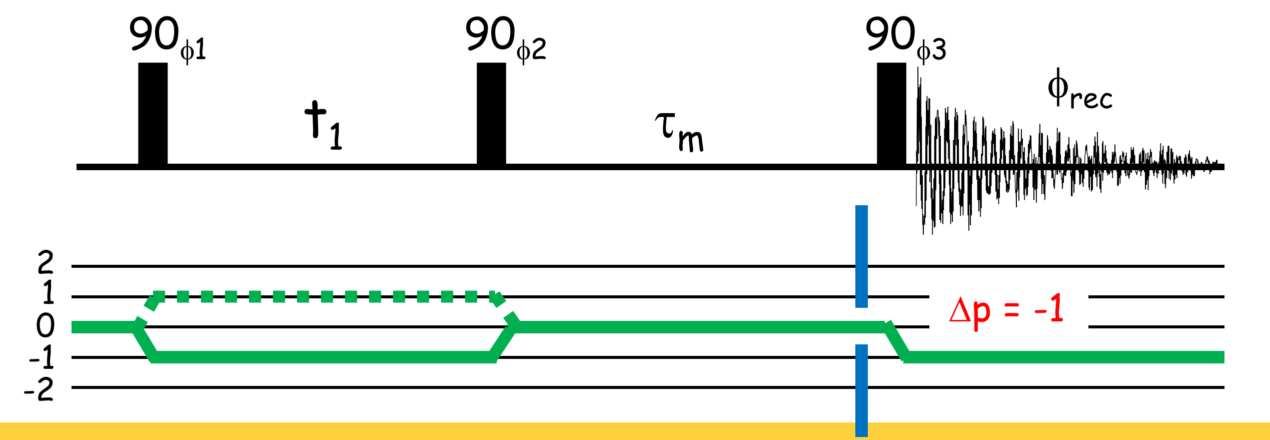


Phase Cycling

$\phi_3 = 0, 1, 2, 3$ and $\Delta p = -1$

$\phi_{rec} = -\sum_i \Delta p_i * \Delta\phi_i$

	ϕ_1	ϕ_2	ϕ_3	$\Sigma\, \Delta p_i * \Delta\phi_i$	ϕ_{rec}
1	0	0	0	0	0
2	0	0	1	-1	1
3	0	0	2	-2	2
4	0	0	3	-3	3

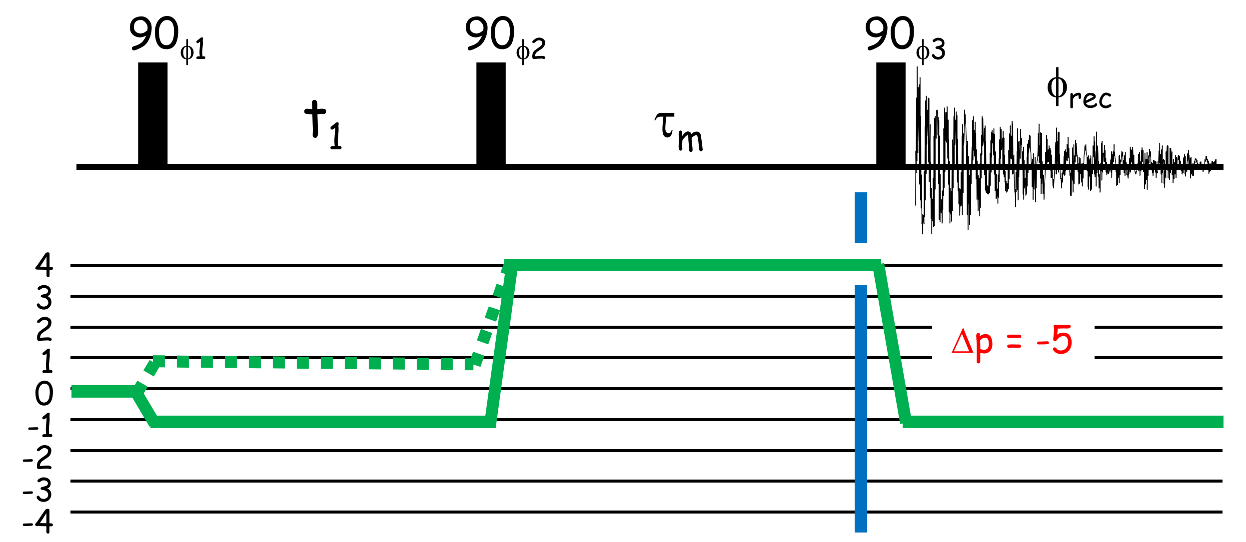


Phase Cycling

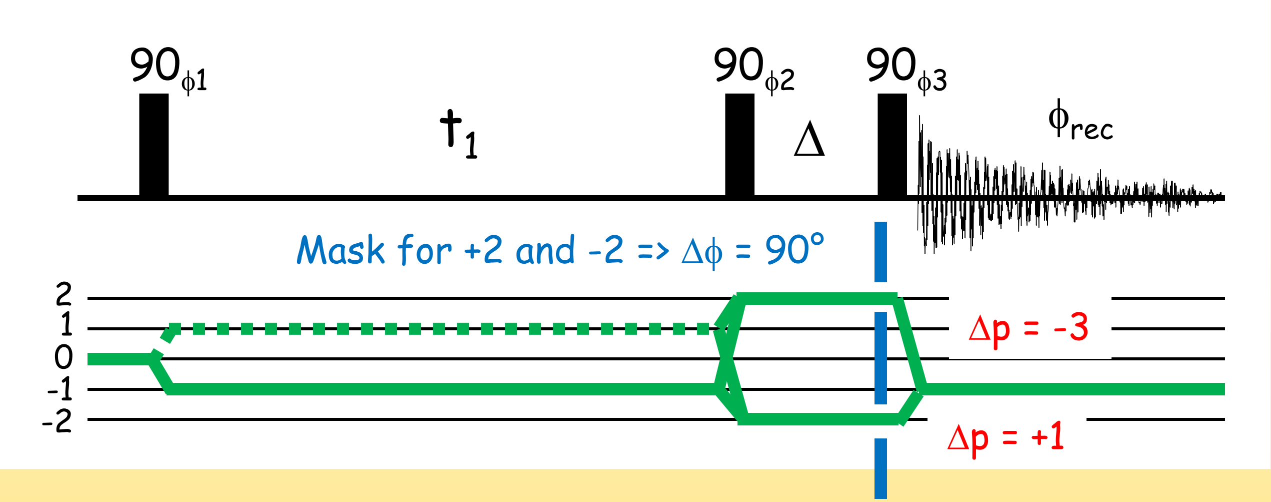
$\Delta\phi_3$ = 0, 1, 2, 3 and $\Delta p = -5$

$\phi_{rec} = -\sum_i \Delta p_i * \Delta\phi_i$

	ϕ_1	ϕ_2	ϕ_3	$\Sigma \Delta p_i * \Delta\phi_i$	ϕ_{rec}
1	0	0	0	0	0
2	0	0	1	-5	1
3	0	0	2	-10	2
4	0	0	3	-15	3



Phase Cycling



DQF-COSY

ϕ_3 = 0, 1, 2, 3

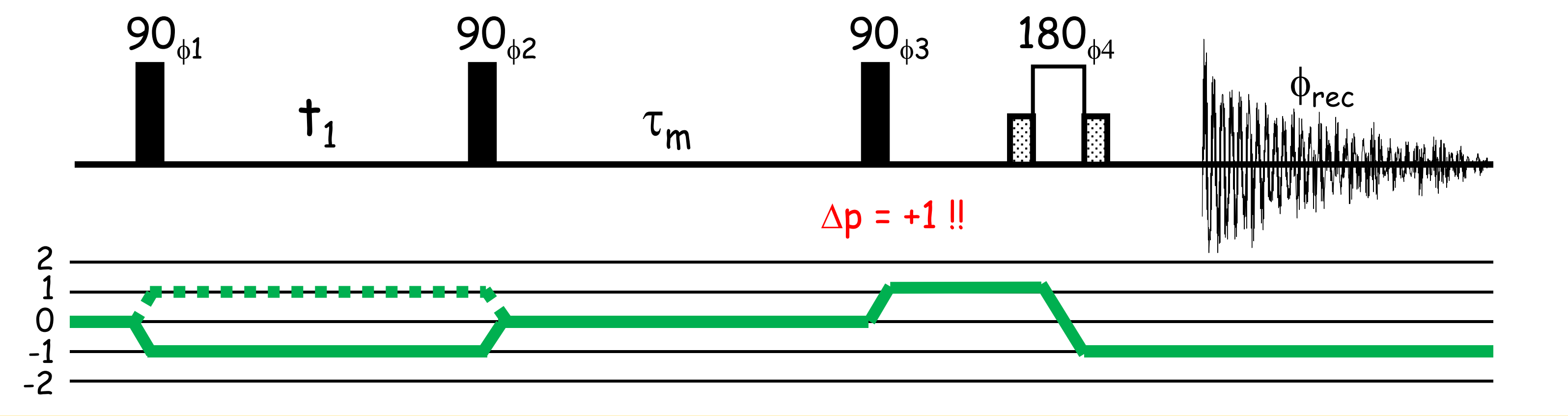
Δp = -3 and +1

	ϕ_1	ϕ_2	ϕ_3	$\Sigma\, \Delta p_i * \Delta\phi_i$ $\Delta p = +1$	$\Sigma\, \Delta p_i * \Delta\phi_i$ $\Delta p = -3$	„ϕ_{rec}“ $\Delta p = +1$	„ϕ_{rec}“ $\Delta p = -3$	ϕ_{rec}
1	0	0	0	0	0	0	0	0
2	0	0	1	1	-3	-1	3	3
3	0	0	2	2	-6	-2	6	2
4	0	0	3	3	-9	-3	9	1

Using „modulo 4“ we obtain identical phasecycles for both pathways

Phase Cycling

What if we add a WATERGATE water supression to the NOESY ?

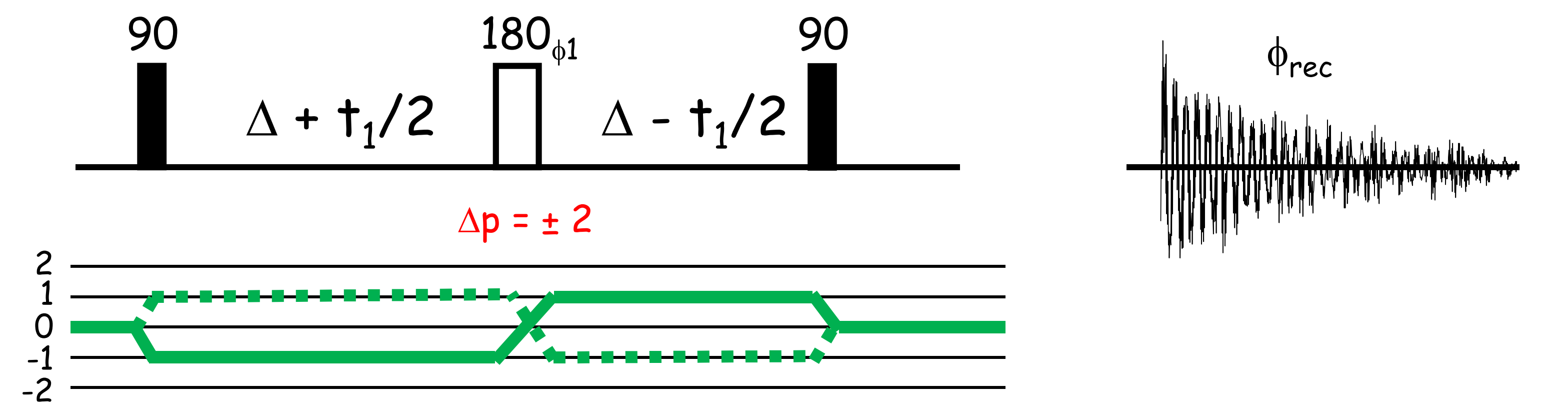


	ϕ_1	ϕ_2	ϕ_3	ϕ_4	$\Sigma \Delta p_i * \phi_i$	„ϕ_{rec}“	ϕ_{rec}
1	0	0	0	0	0	0	0
2	0	0	1	0	1	-1	3
3	0	0	2	0	2	-2	2
4	0	0	3	0	3	-3	1

Since all phases are relative angles ϕ_{rec} = 1, 0, 3, 2 will work as well !!

Phase Cycling

Another important phase cycle is the "Exorcycle" that is used to correct 180° pulses that are applied to transverse magnetization.



	ϕ_1	$\Sigma \Delta p_i * \Delta\phi_i$ $\Delta p = +2$	$\Sigma \Delta p_i * \Delta\phi_i$ $\Delta p = -2$	„ϕ_{rec}" $\Delta p = +2$	„ϕ_{rec}" $\Delta p = -2$	ϕ_{rec}
1	0	0	0	0	0	0
2	1	2	-2	-2	2	2
3	2	4	-4	-4	4	0
4	3	6	-6	-6	6	2

That's it

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