On pulses, phases and gradients:
Phase cycling and Quadrature detection
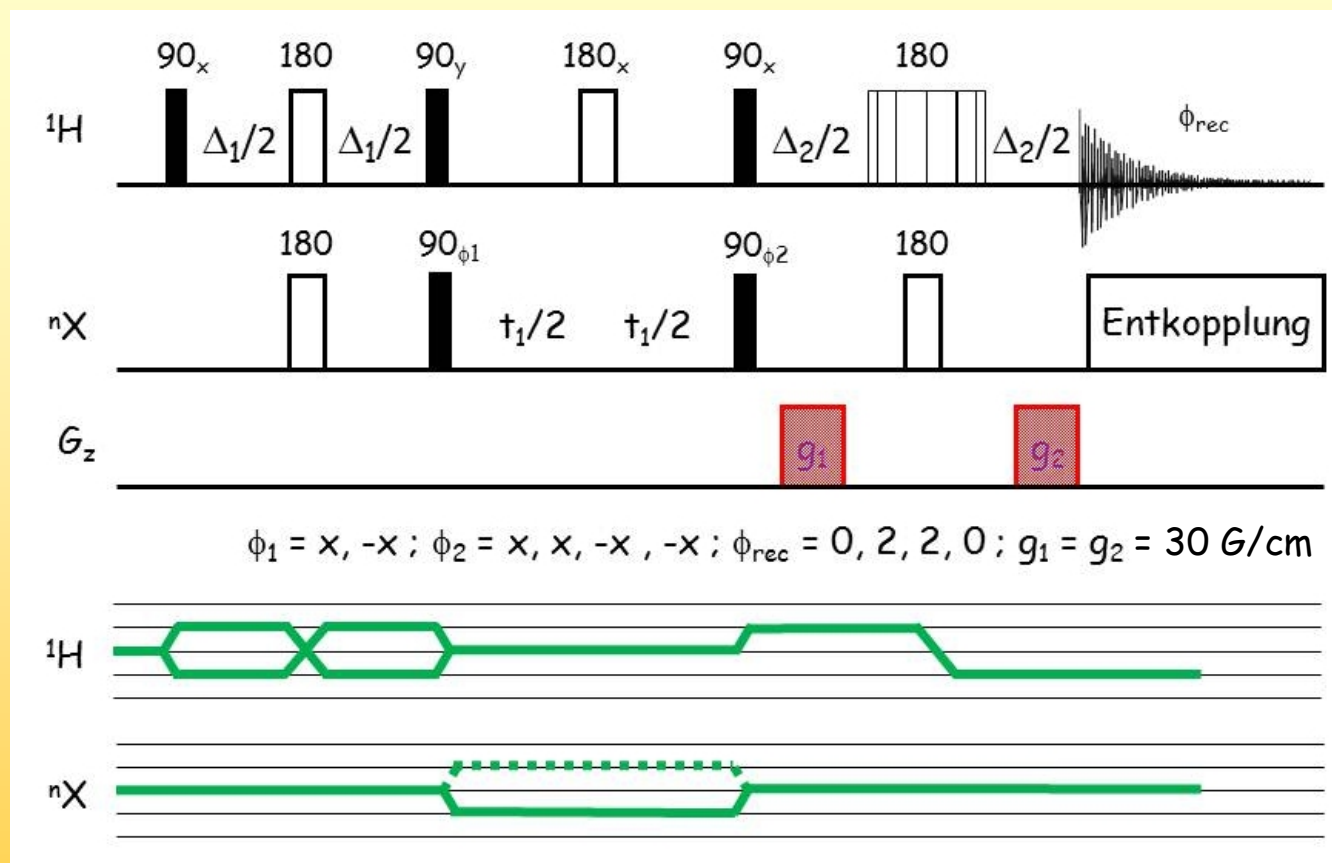
G-NMR-School 2020

MPI für Biophysikalische Chemie, Göttingen

17.2. – 21.2.2020

Description of pulse sequences

$\phi_1 = x, -x \; ; \; \phi_2 = x, x, -x, -x \; ; \; \phi_{rec} = 0, 2, 2, 0 \; ; \; g_1 = g_2 = 30 \text{ G/cm}$

"… 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.

Delays, z-rotations and coherence order

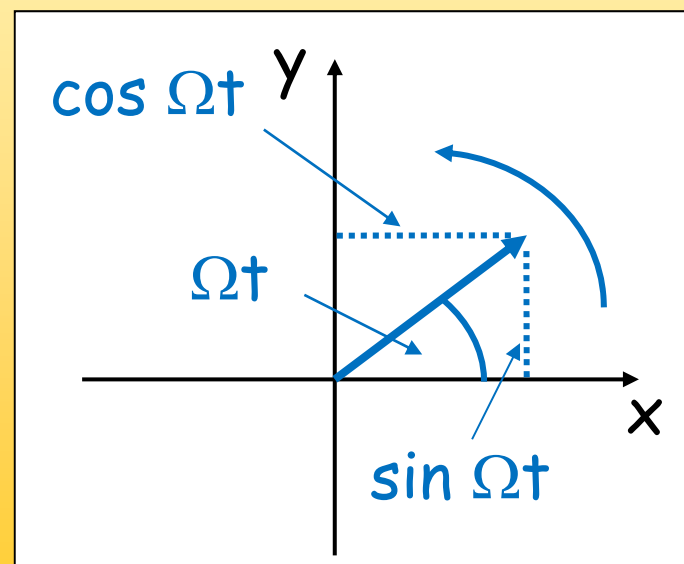# Delays, z-rotation and coherence order

During delays several interactions between spins and the magnetic field as well as other spins are active. One of the most important "delays" is the acquisition time that occurs in even the simplest 1D experiment. One example for an interaction with the external field is the evolution of chemical shift, a first example for z-rotation.

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

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

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

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

Delays, z-rotation and coherence order

In Cartesian coordinates this is a rotation in the x,y-plane. Since the phases of pulses are usually defined using Cartesian coordinates their use as product operator basis can be quite useful.

The rotation can also be viewed as a rotation in a complex plane, where it is a change of phase over time. This is sometimes called the "spherical representation" and might seem abstract at first but will help us later when dealing with gradients, pulse phases, coherence and coherence order.

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

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

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

Delays, z-rotation and coherence order

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

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

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

$$= \underbrace{1/2\,(I_+ + I_-)\cos\Omega\tau}_{I_x} - \underbrace{i/2\,(I_+ - I_-)\sin\Omega\tau}_{I_y} \qquad 1/i = -i$$

$$i/i = 1 \qquad \underbrace{+ 1/2\,(I_+ - I_-)\cos\Omega\tau}_{iI_y} - \underbrace{i/2\,(I_+ + I_-)\sin\Omega\tau}_{iI_x}$$

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

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

Delays, z-rotation and coherence order

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

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

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

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

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

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

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

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) !

Delays, z-rotation and coherence order

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

$$I_{1+}I_{2-} \xrightarrow{I_z\Omega\tau} I_{1+}exp(-i\Omega_1\tau)I_{2-}exp(+i\Omega_2\tau) = I_{1+}I_{2-}exp(-i[\Omega_1-\Omega_2]\tau) \Big\}$$

$$I_{1-}I_{2+} \xrightarrow{I_z\Omega\tau} I_{1-}exp(+i\Omega_1\tau)I_{2+}exp(-i\Omega_2\tau) = I_{1-}I_{2+}exp(+i[\Omega_1-\Omega_2]\tau) \Big\} ZQC$$

$$I_{1+}I_{2+} \xrightarrow{I_z\Omega\tau} I_{1+}exp(-i\Omega_1\tau)I_{2+}exp(-i\Omega_2\tau) = I_{1+}I_{2+}exp(-i[\Omega_1+\Omega_2]\tau) \Big\}$$

$$I_{1-}I_{2-} \xrightarrow{I_z\Omega\tau} I_{1-}exp(+i\Omega_1\tau)I_{2-}exp(+i\Omega_2\tau) = I_{1-}I_{2-}exp(+i[\Omega_1+\Omega_2]\tau) \Big\} DQC$$

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!!

Delays, z-rotation and coherence order

The spherical representation is connected to the concept of coherences and coherence order. 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 a spherical representation then using Cartesian coordinates.

The order p of a coherence C is defined according to its behavior under a z-rotation:

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

Delays, z-rotation and coherence order

We can now calculate the coherence order in the spherical as well as

the Cartesian representation

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

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

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

Cartesian operators represent mixtures of coherence order

$$I_x = I_+ + I_- \ \Rightarrow \text{ coherence order } p = -1 \text{ and } p = +1$$

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

$$\Rightarrow \text{ coherence order } p = \qquad +2 \qquad 0 \qquad 0 \qquad -2$$

It is easy to see that the maximum coherence order will depend on

the number of interaction spins

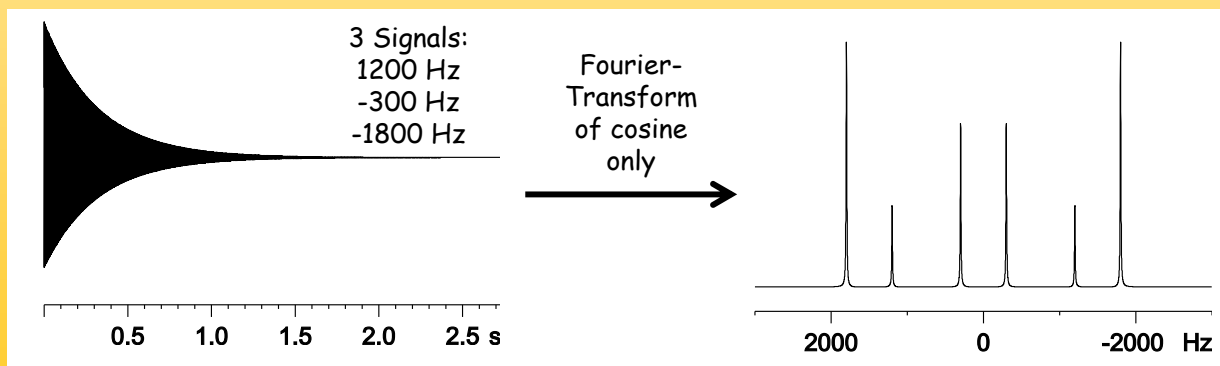# Quadrature detection in 1D

Quadrature Detection in 1D
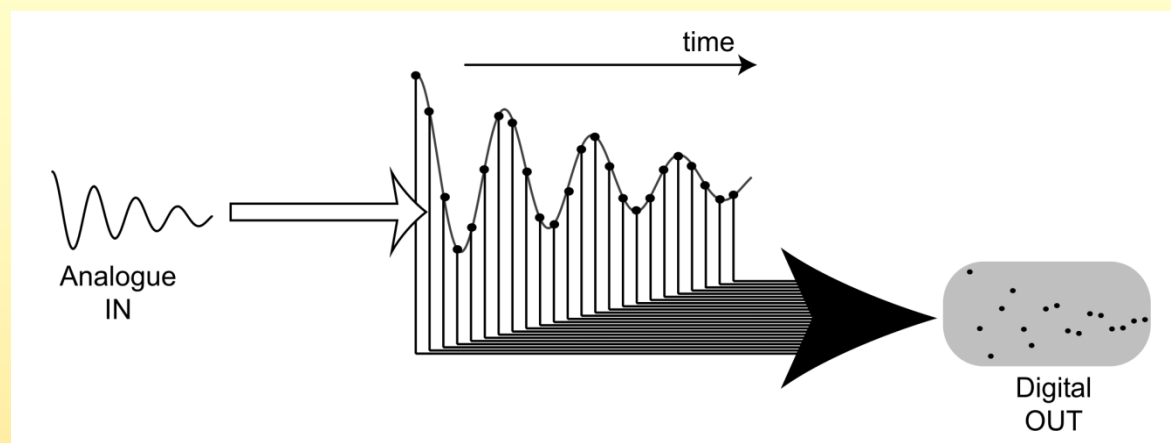
The proton signal on a spectrometer operating at 600.13 MHz has a typical frequency range from 600.1305 to 600.1295 MHz (± 5000 Hz). In order for the signal to be processed on a computer it needs to be digitized using an Analog-Digital-Converter (ADC).

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.
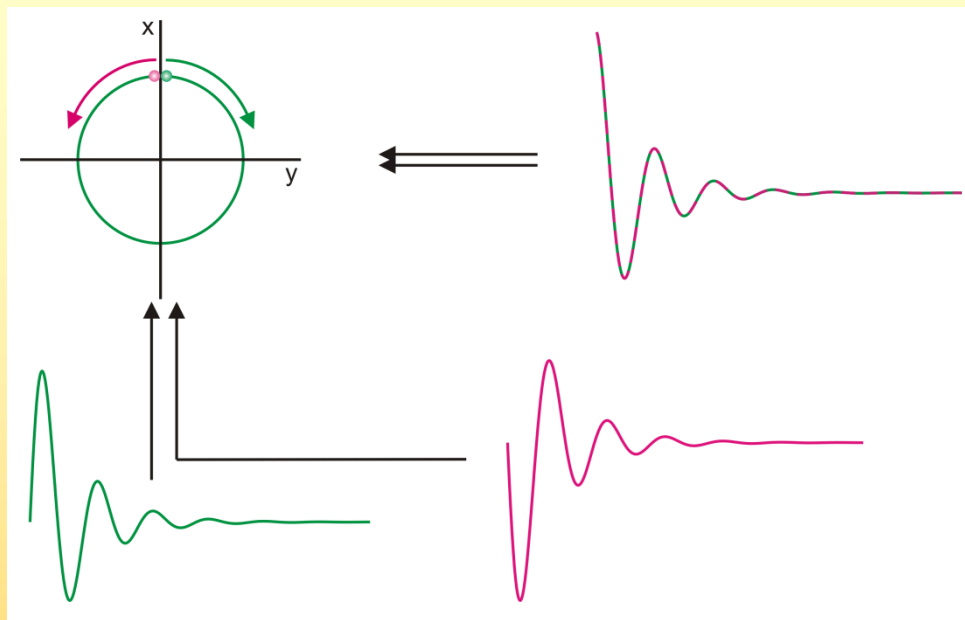
Quadrature Detection in 1D
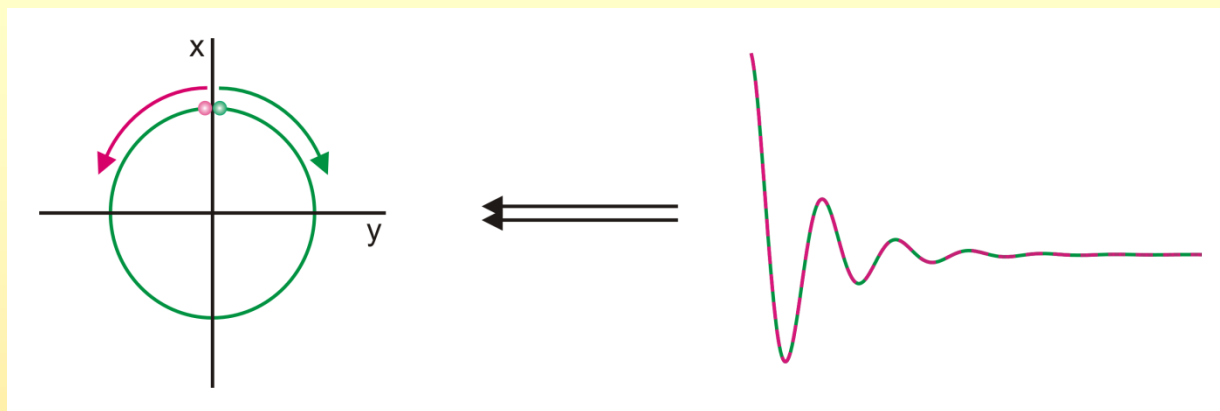
This leads to the problem that one has to deal with positive and
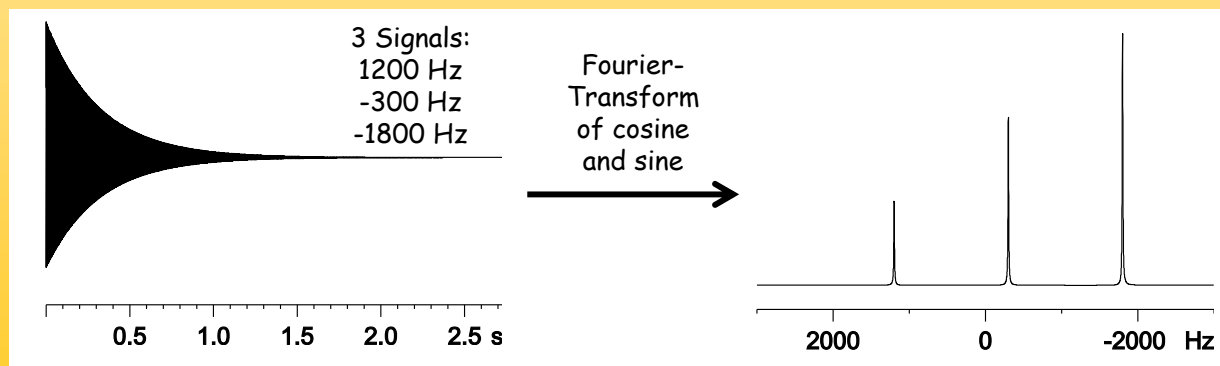
negative frequencies that are not easily distinguished:

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

3 Signals:
1200 Hz
-300 Hz
-1800 Hz

Fourier-
Transform
of cosine
only

0.5   1.0   1.5   2.0   2.5 s

2000   0   -2000 Hz
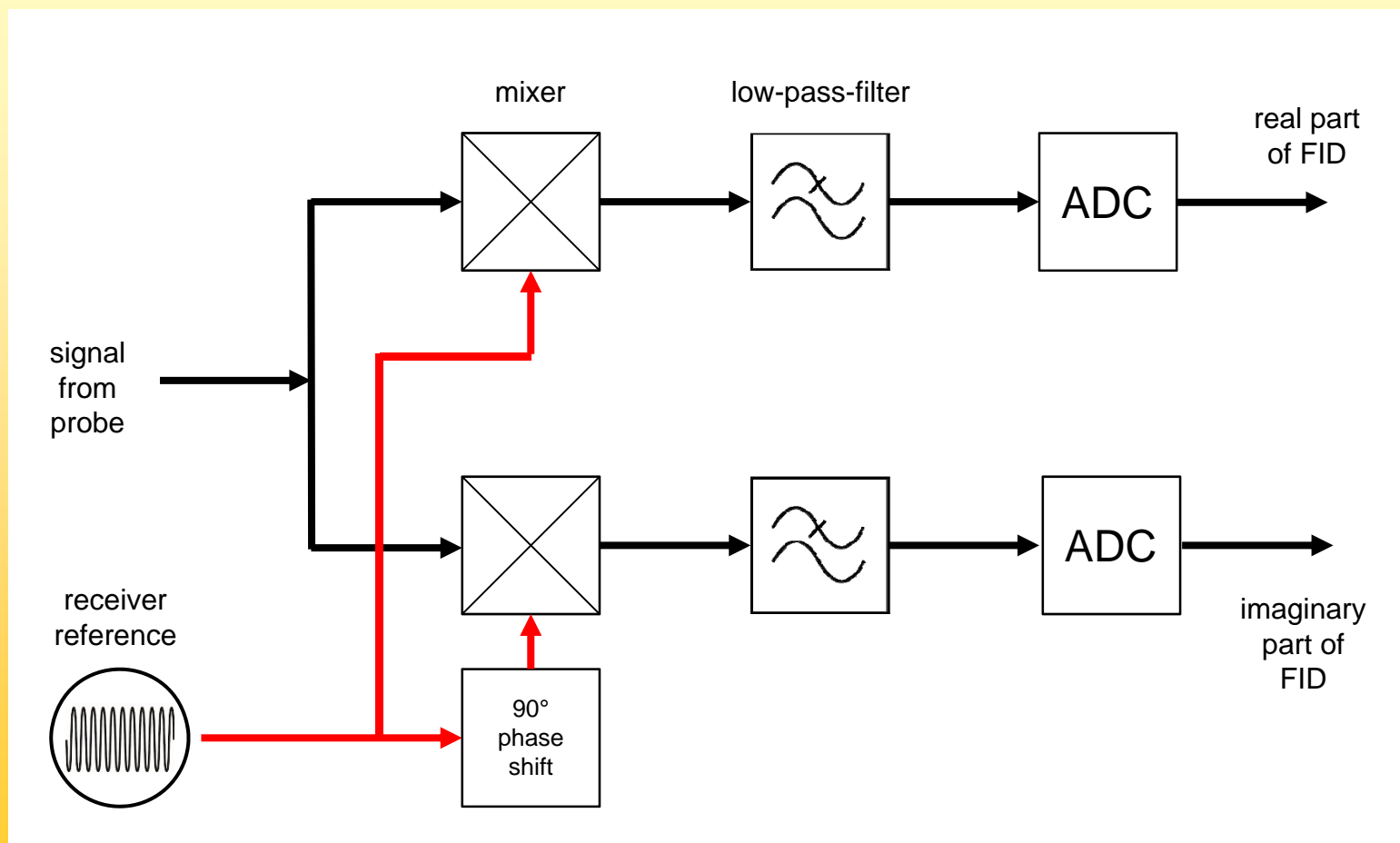
Quadrature Detection in 1D

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

3 Signals:
1200 Hz
-300 Hz
-1800 Hz

Fourier-Transform of cosine and sine

0.5   1.0   1.5   2.0   2.5 s

2000   0   -2000 Hz

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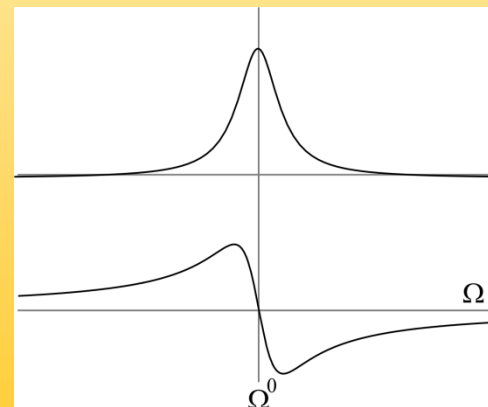
$$s(t) = [s_C(t) + i * s_S(t)] * \exp(-t/T_2) = \exp(i\Omega_0 t) \exp(-t/T_2)$$

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

$$S(\Omega) = \int_0^\infty s(t) \exp(-i\Omega t) \, dt = \frac{1}{(1/T_2) + i(\Omega - \Omega_0)} = A(\Omega) + i \, D(\Omega)$$
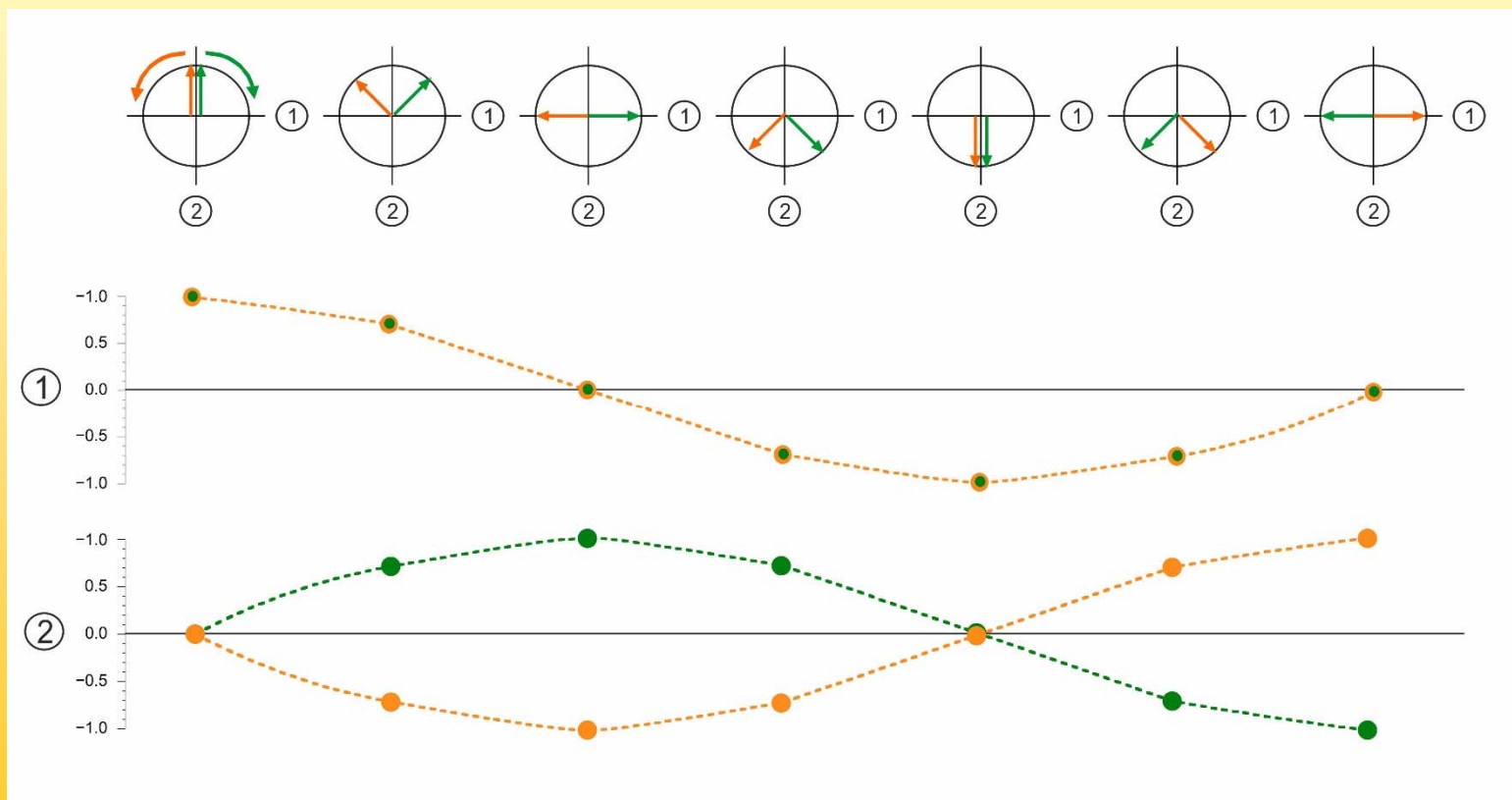
$$A(\Omega) = \frac{(1/T_2)}{(1/T_2)^2 + (\Omega - \Omega_0)^2}$$

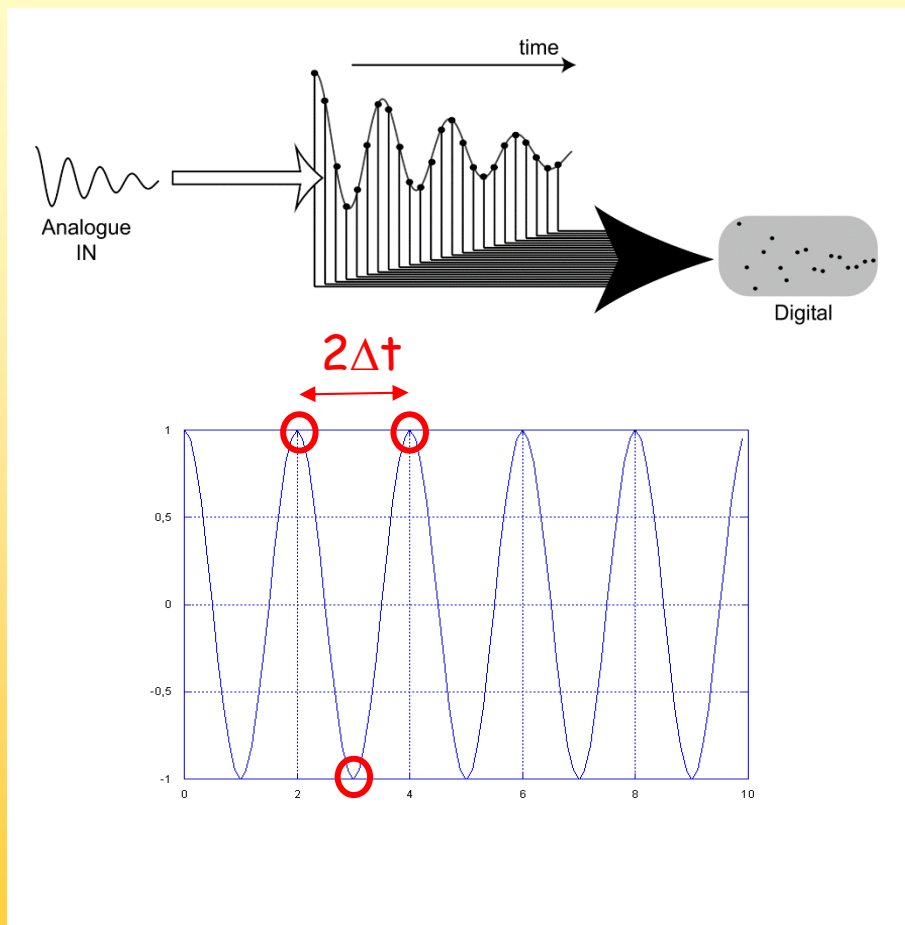$$D(\Omega) = -\frac{(\Omega - \Omega_0)}{(1/T_2)^2 + (\Omega - \Omega_0)^2}$$

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)
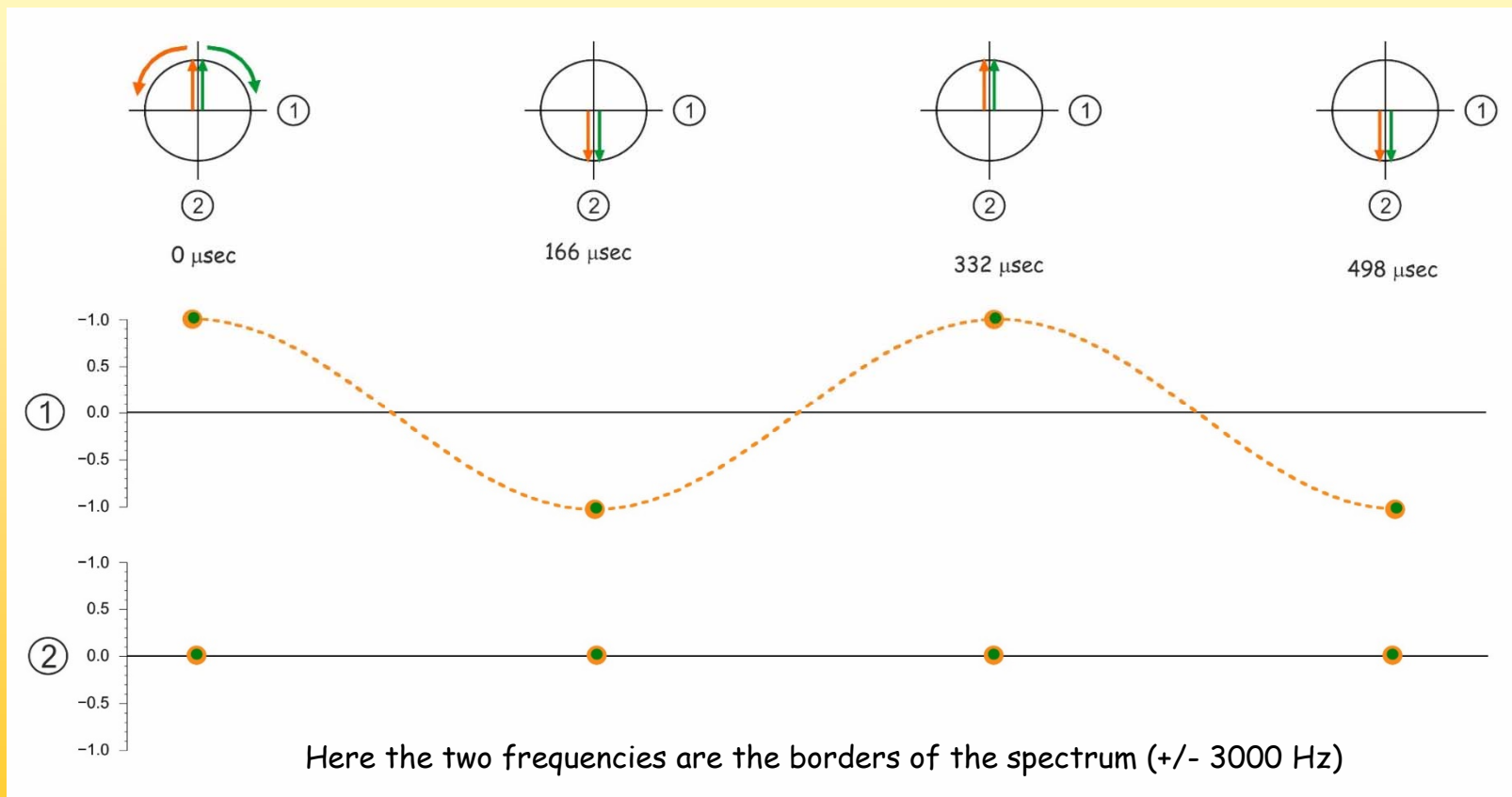
Quadrature Detection in 1D

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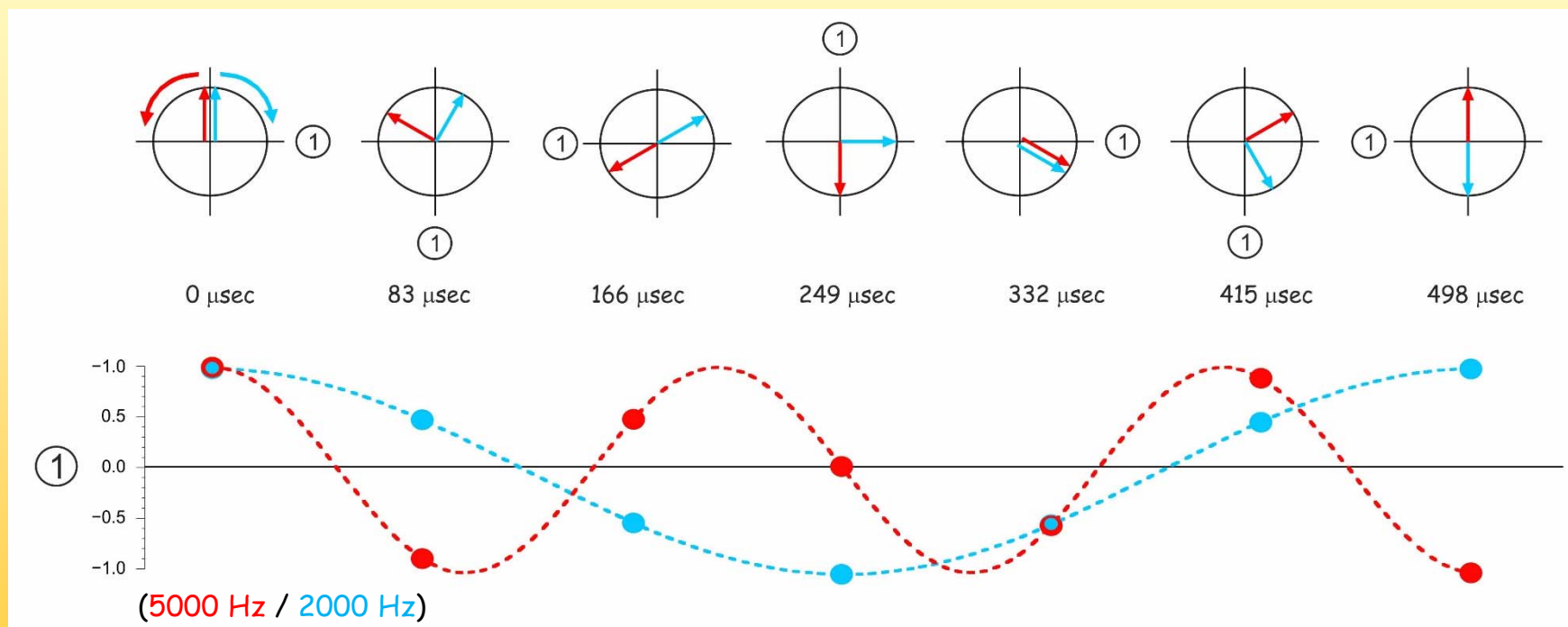

(2000 Hz / -1000 Hz)
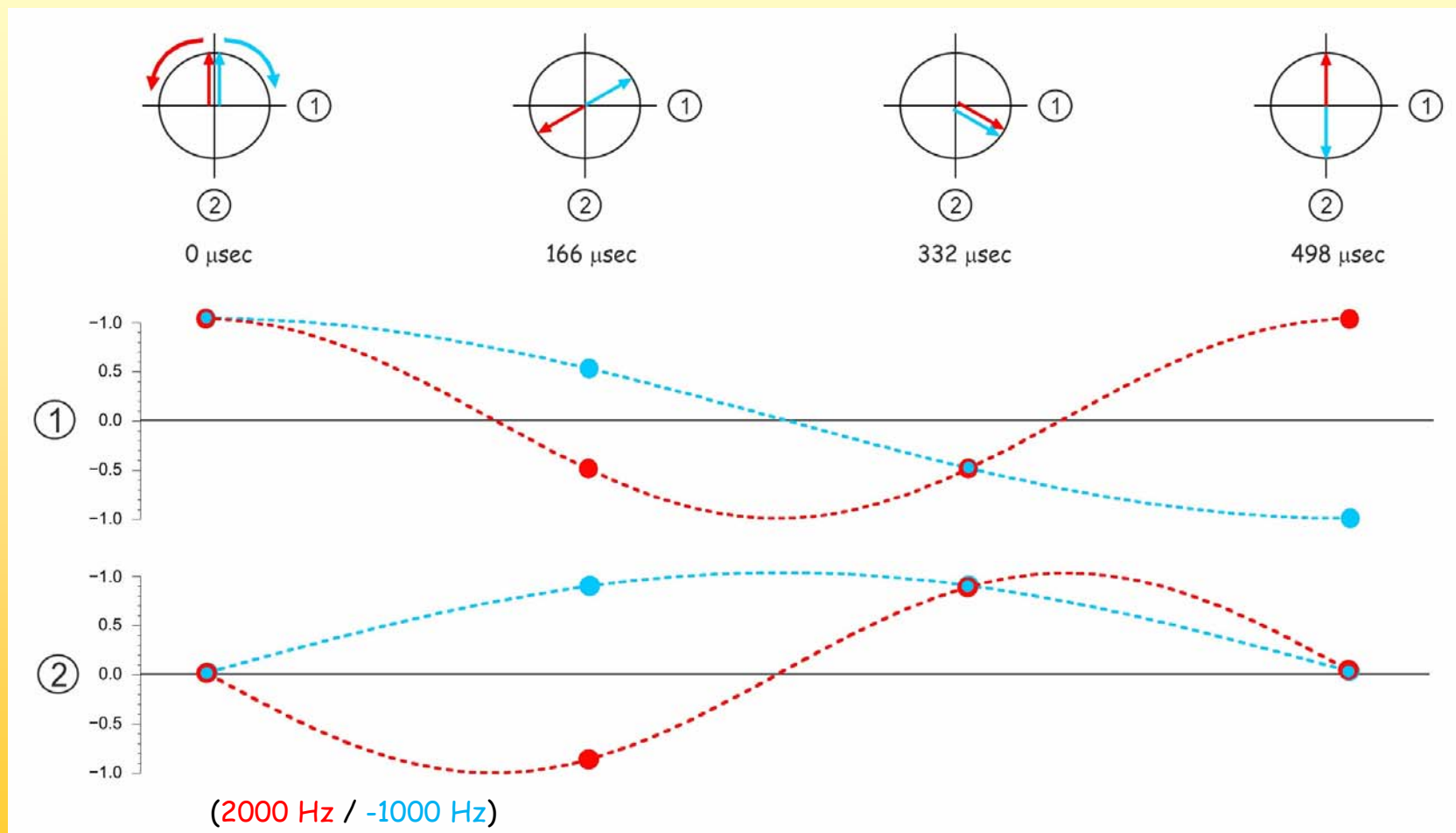
Quadrature Detection in 1D

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

0 µsec   83 µsec   166 µsec   249 µsec   332 µsec   415 µsec   498 µsec
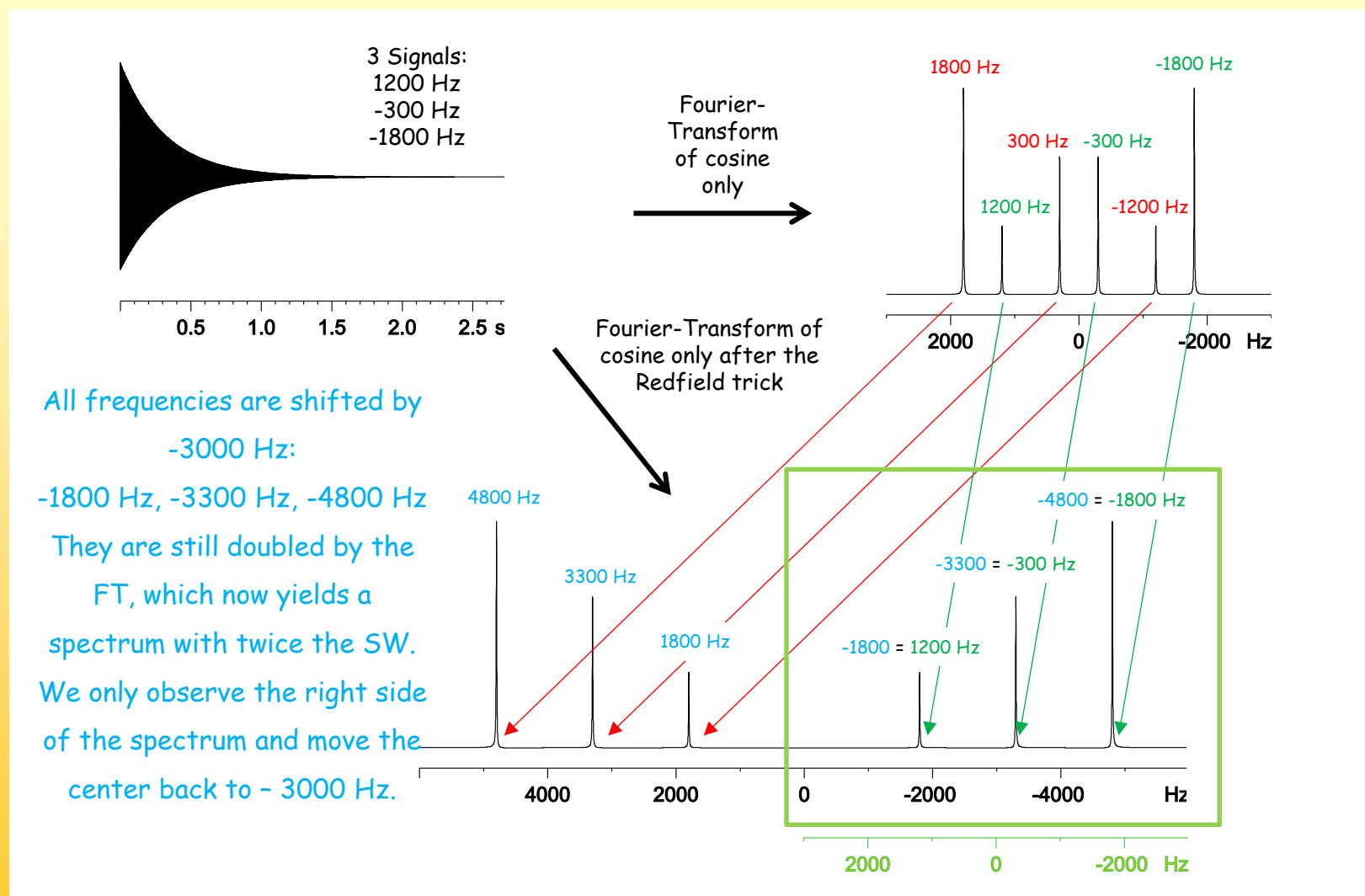
(6000 Hz / 0 Hz)
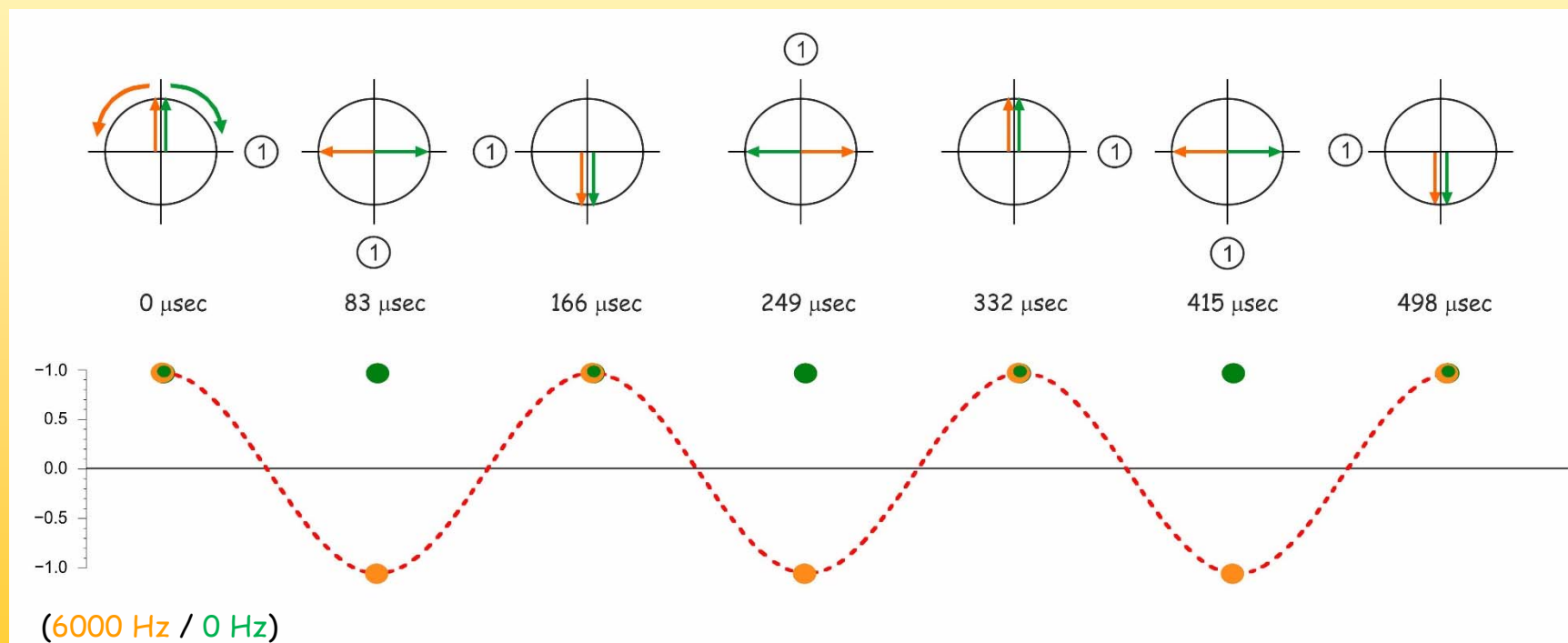
Quadrature Detection in 1D

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.

0 μsec 83 μsec 166 μsec 249 μsec 332 μsec 415 μsec 498 μsec

(5000 Hz / 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

3 Signals:
1200 Hz
-300 Hz
-1800 Hz

0.5   1.0   1.5   2.0   2.5 s

Fourier-
Transform
of cosine
only

1800 Hz   -1800 Hz

300 Hz   -300 Hz

1200 Hz   -1200 Hz

2000   0   -2000 Hz

Fourier-Transform of
cosine only after the
Redfield trick

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.

4800 Hz

3300 Hz

1800 Hz

-4800 = -1800 Hz

-3300 = -300 Hz

-1800 = 1200 Hz

4000   2000   0   -2000   -4000   Hz

2000   0   -2000 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

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

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

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

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

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

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

The low-pass filter leaves only two terms

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

---

Quadrature Detection in 1D

The shifted reference results in slightly modified terms

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

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

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

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

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

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

The low-pass filter again leaves only two terms

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

Quadrature Detection in 1D
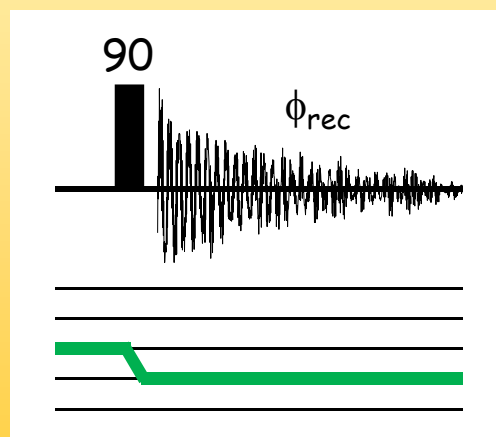
Both channels are combined to form a complex number

$$S = Re + i * Im$$

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

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

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

which corresponds to coherence order (-1) !

90

ϕ_{rec}

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?

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

Both are again multiplied in the mixer

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

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

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

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

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

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

The low-pass filter leaves only two terms

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

Quadrature Detection in 1D

The shifted reference results in slightly modified terms

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

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

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

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

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

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

The low-pass filter again leaves only two terms

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

---

Quadrature Detection in 1D

Both channels are again combined to form a complex number

$$S = Re + i * Im$$

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

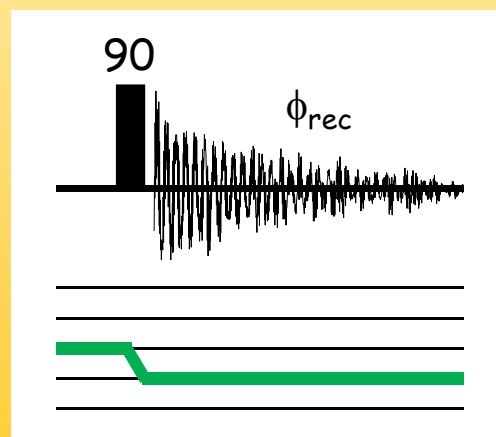$$+ i/2 * [I^+ \exp(-i\Omega t) + I^- \exp(+i\Omega t)]$$

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

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

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

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

90

ϕ_{rec}

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

$S = Re + i * Im =$

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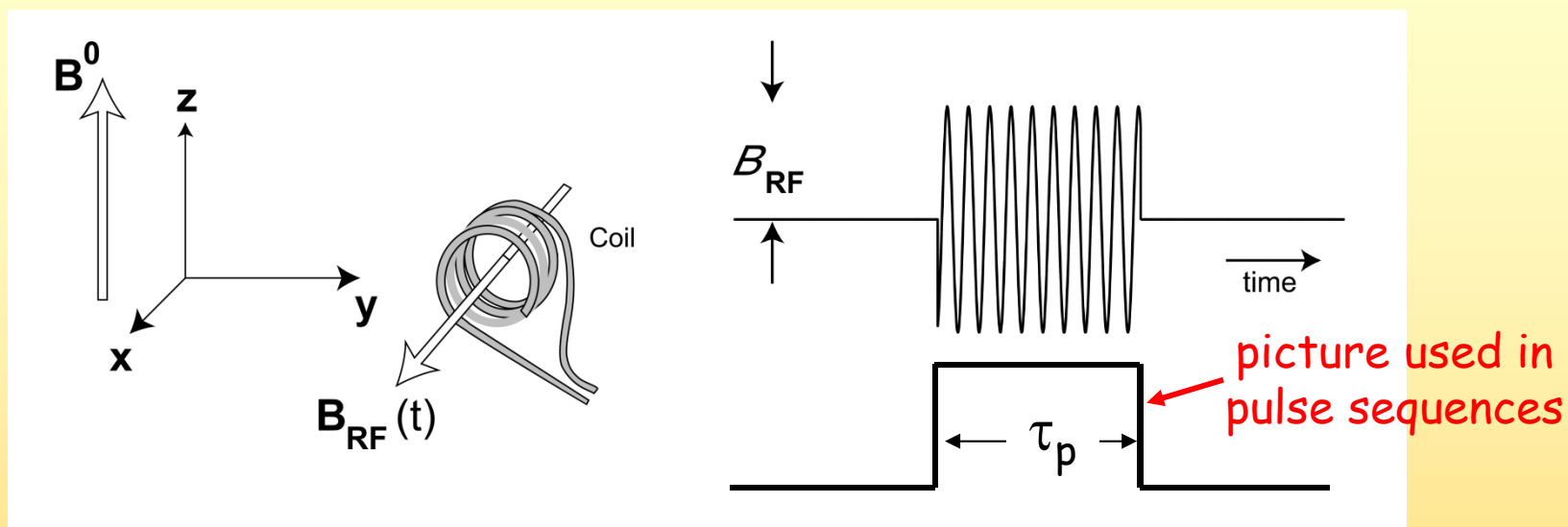
$= I^- \exp(+i(\Omega+\pi/2)t)$

we have

$S = -i * Re + Im =$

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

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

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

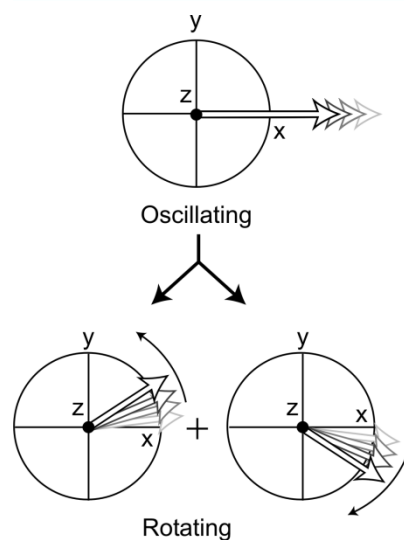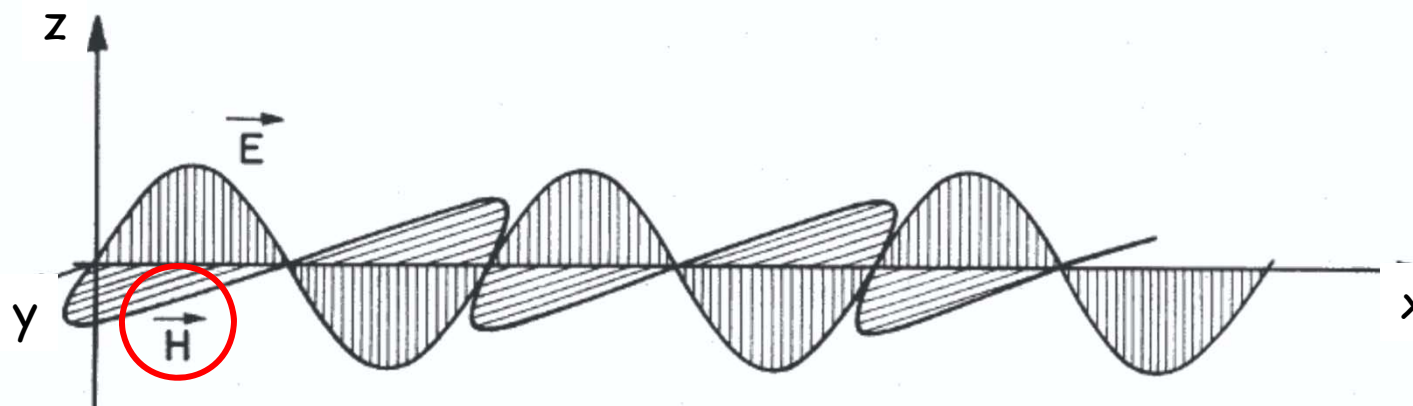# Pulses and coherence levels

Pulses and coherence levels

B^0

z

Coil

y

x

B$_{RF}$ (t)

B_{RF}

time

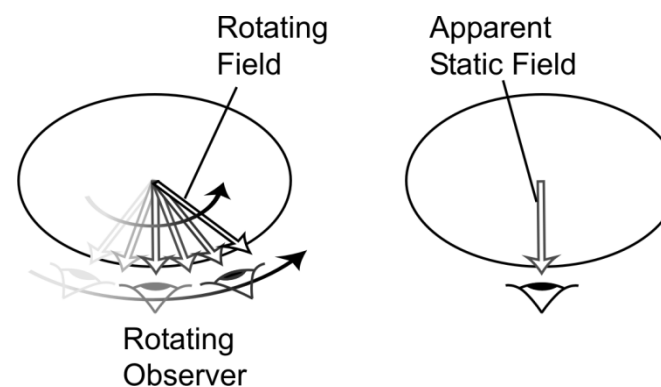picture used in pulse sequences

τ_p

An equally important tool of pulse sequences as delays are

obviously the pulses, i.e. irradiation of radio waves with a certain
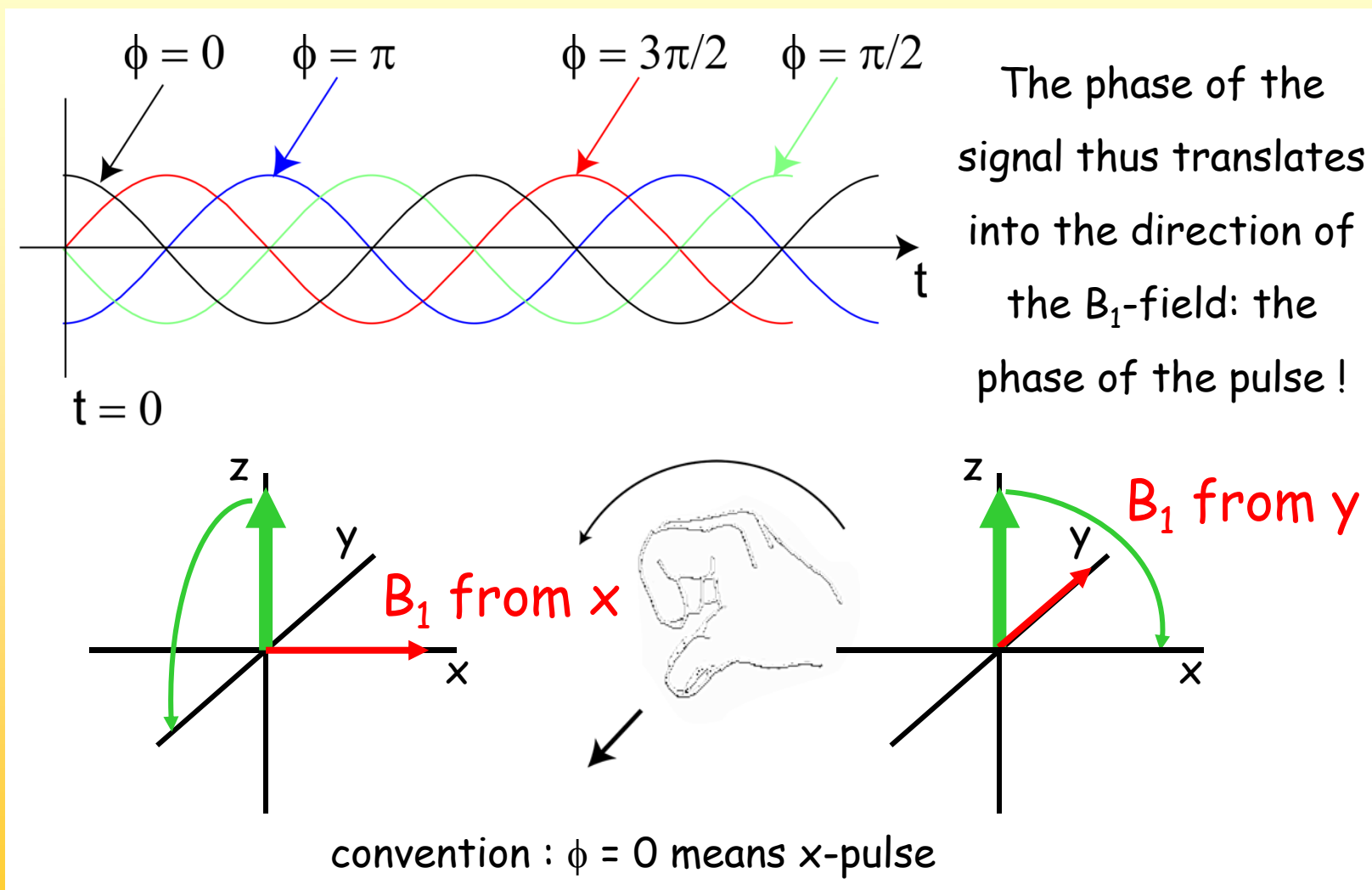
frequency, power and phase

Pulses and coherence levels

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

Pulses and coherence levels

$\phi = 0 \qquad \phi = \pi \qquad\qquad \phi = 3\pi/2 \qquad \phi = \pi/2$

t

t = 0

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

z

y

B_1 from x

x

z

B_1 from y

y

x

convention : $\phi = 0$ means x-pulse

Pulses and coherence levels

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

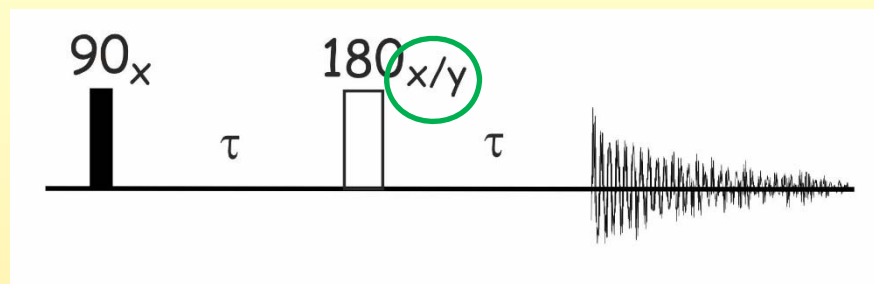$$I_z \xrightarrow{\ 90° \ I_x \ } -I_y \qquad\qquad I_z \xrightarrow{\ 90° \ I_y \ } I_x$$

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

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

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

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

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

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

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

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

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

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

The switching between the representations can complicate calculations !!

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

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

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

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

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

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

Pulses and coherence levels

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

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

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

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

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

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 !
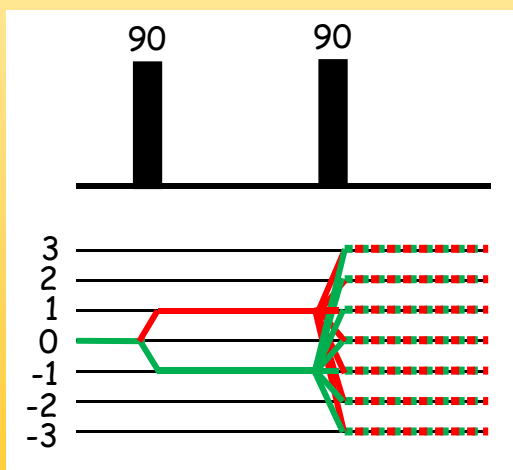
Pulses and coherence levels

To depict what is going on coherence transfer pathway diagrams are used
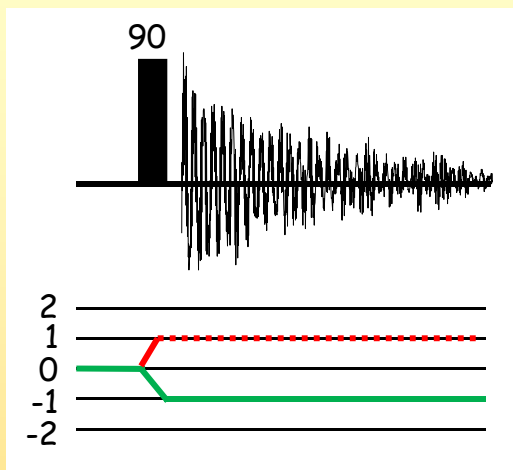
$$I_z \xrightarrow{\ 90_{-y}\ } I_x = 1/2\ (I_+ + I_-)$$

← — 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
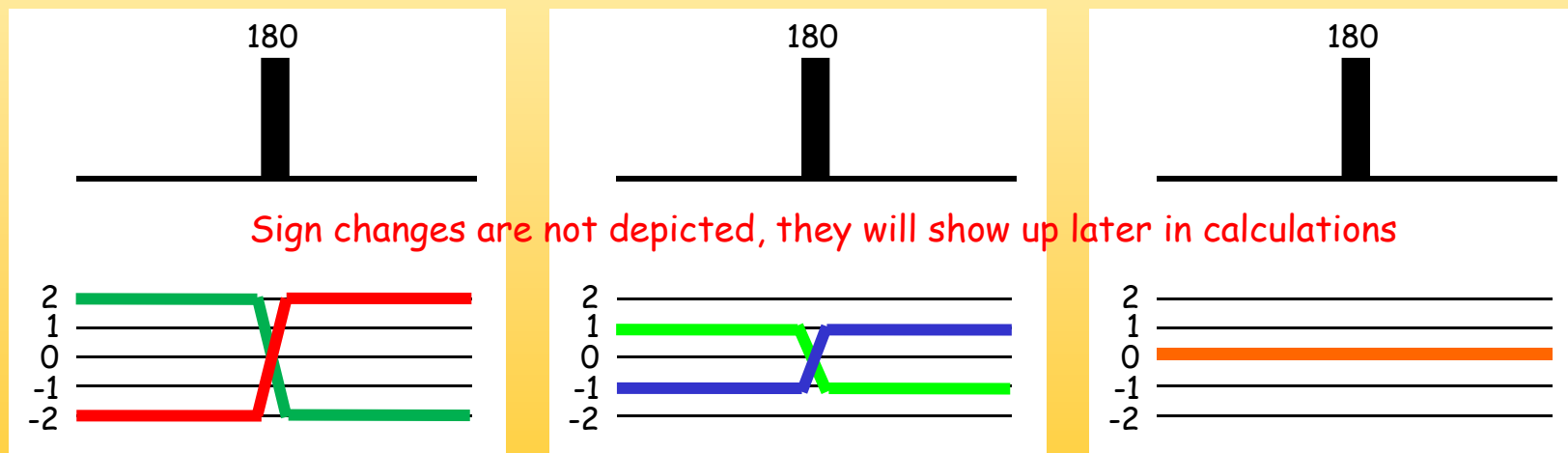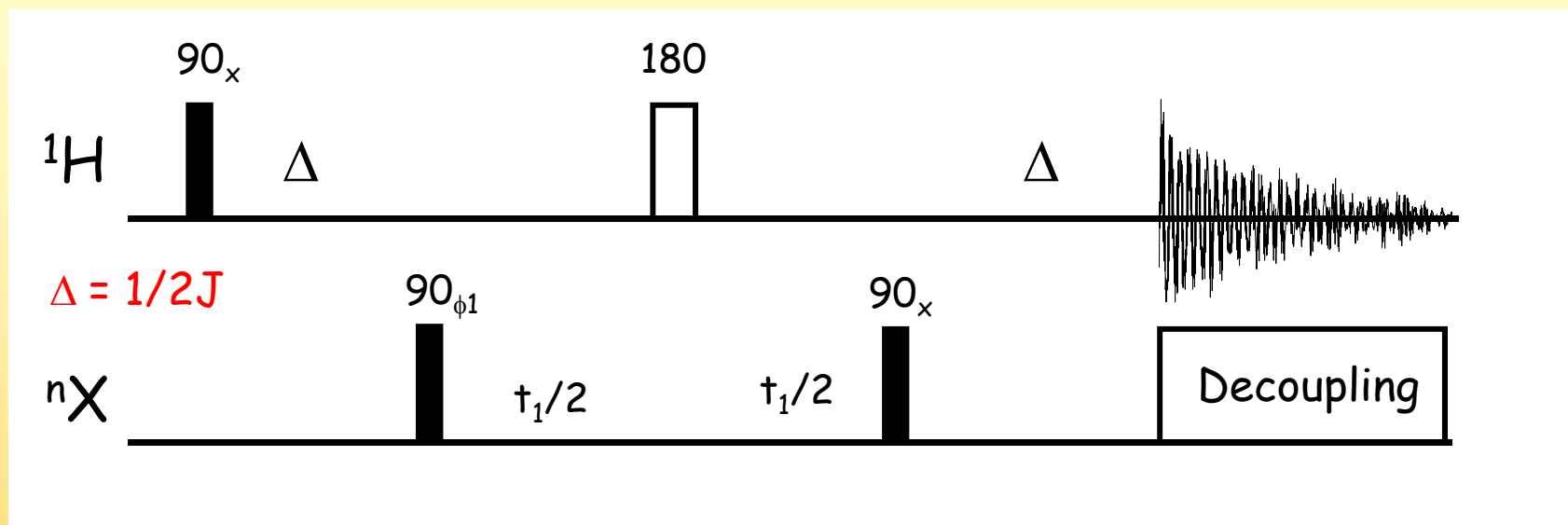
Phase cycling

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.
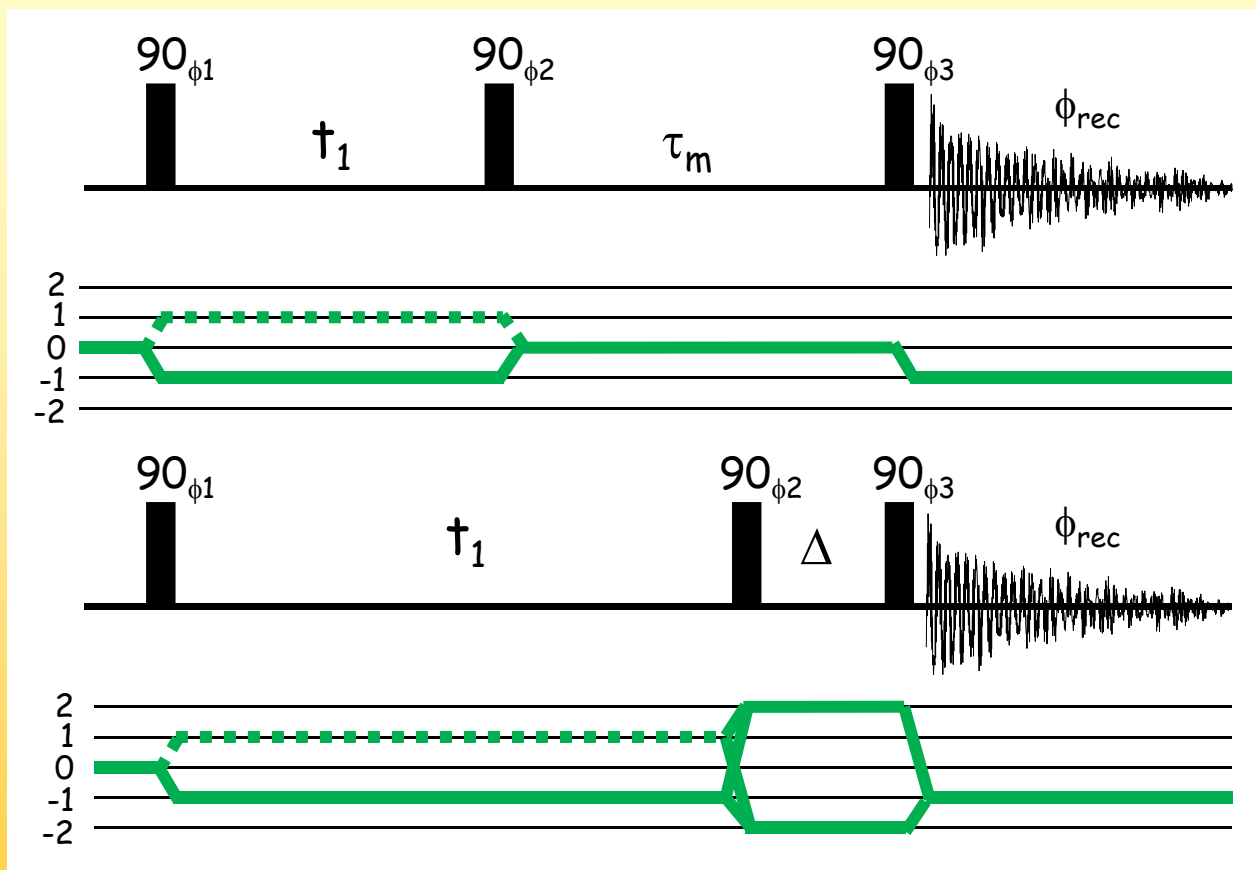
Phase Cycling

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.
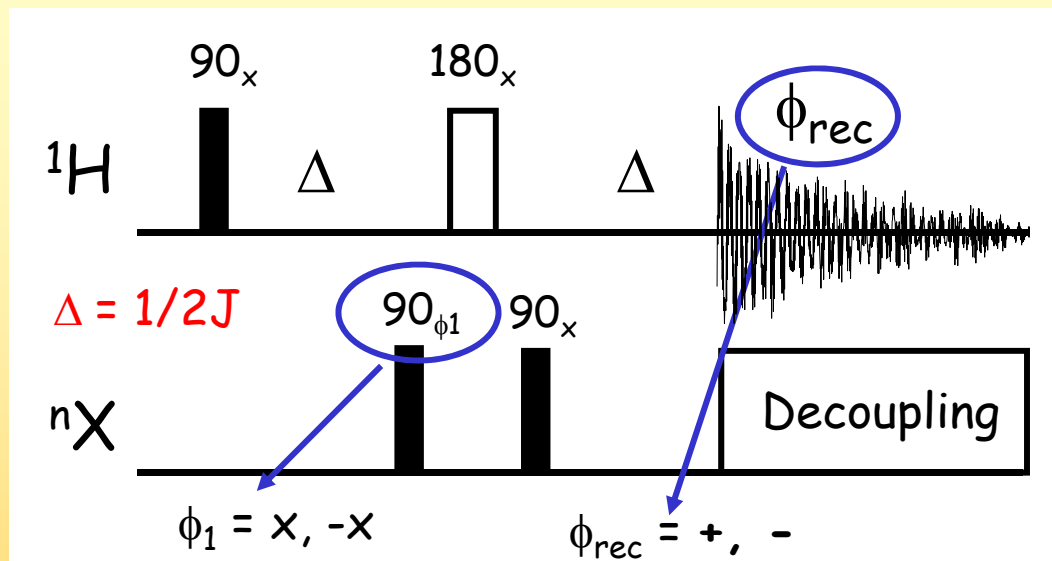
M. Levitt, "Spin Dynamics", Appendix 17.10

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
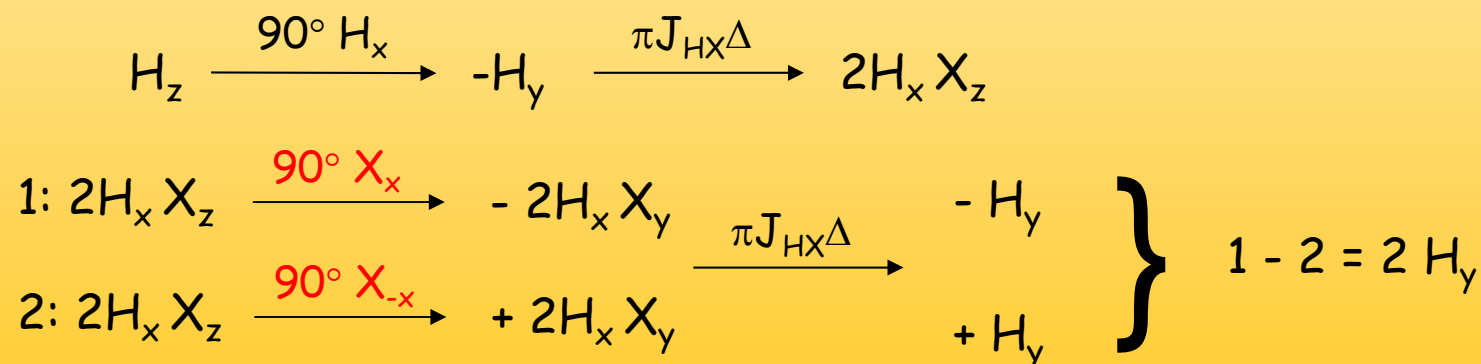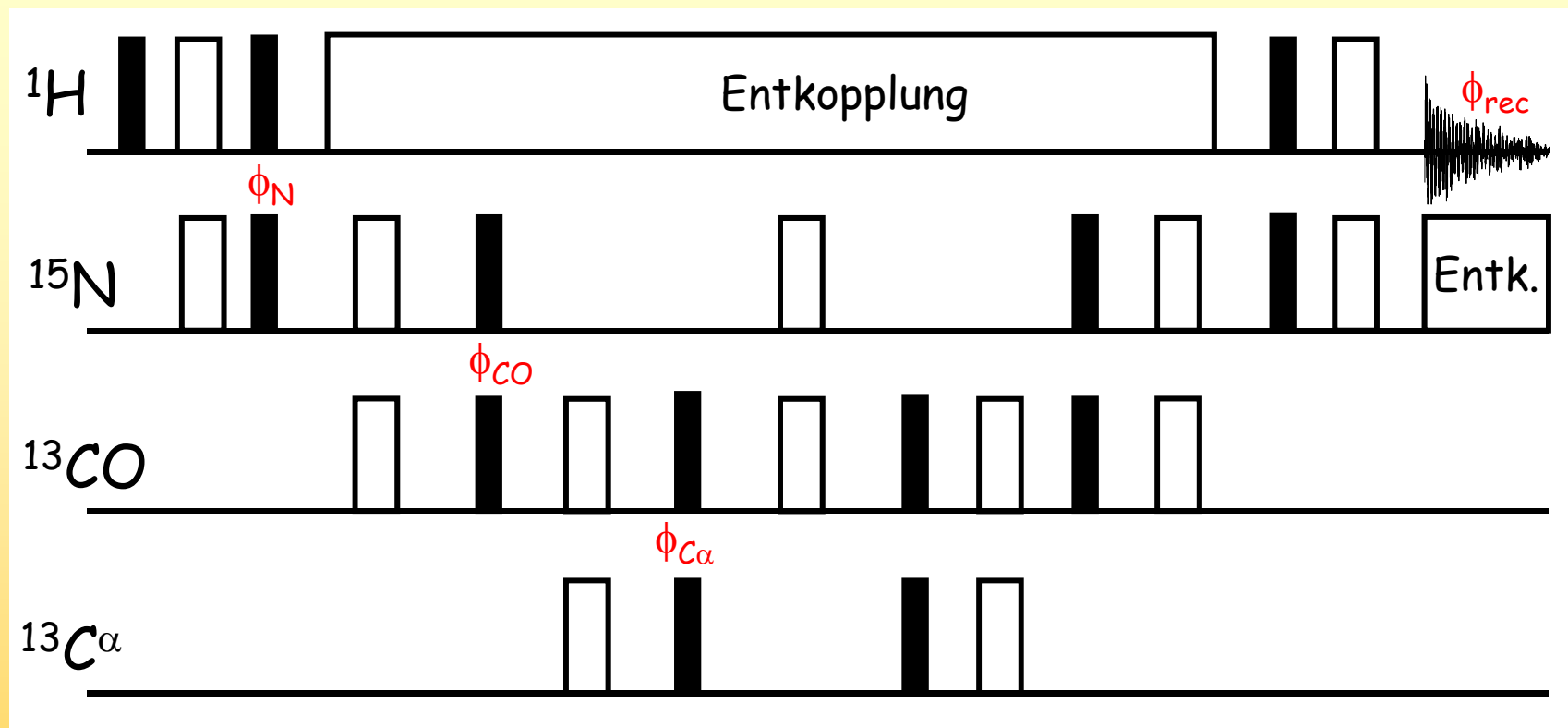
^{1}H 90$_x$ Δ 180$_x$ Δ ϕ_{rec}

$\Delta = 1/2J$ 90$_{\phi 1}$ 90$_x$

^{n}X   Decoupling

$\phi_1 = x, -x$ $\phi_{rec} = +, -$

protons not bound to X:

1: $\phi_1 = x \longrightarrow H_y$

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

$$1 - 2 = 0$$

$$H_z \xrightarrow{90° H_x} -H_y \xrightarrow{\pi J_{HX}\Delta} 2H_x X_z$$

$$1: 2H_x X_z \xrightarrow{90° X_x} -2H_x X_y \xrightarrow{\pi J_{HX}\Delta} -H_y$$

$$2: 2H_x X_z \xrightarrow{90° X_{-x}} +2H_x X_y \xrightarrow{\phantom{\pi J_{HX}\Delta}} +H_y$$

$$\left.\right\} 1 - 2 = 2H_y$$

Phase Cycling


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

ϕ_N = x, -x
ϕ_{CO} = x, x, -x, -x   } ϕ_{rec} = x, -x, -x, x, -x, x, x, -x
$\phi_{C\alpha}$ = 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:
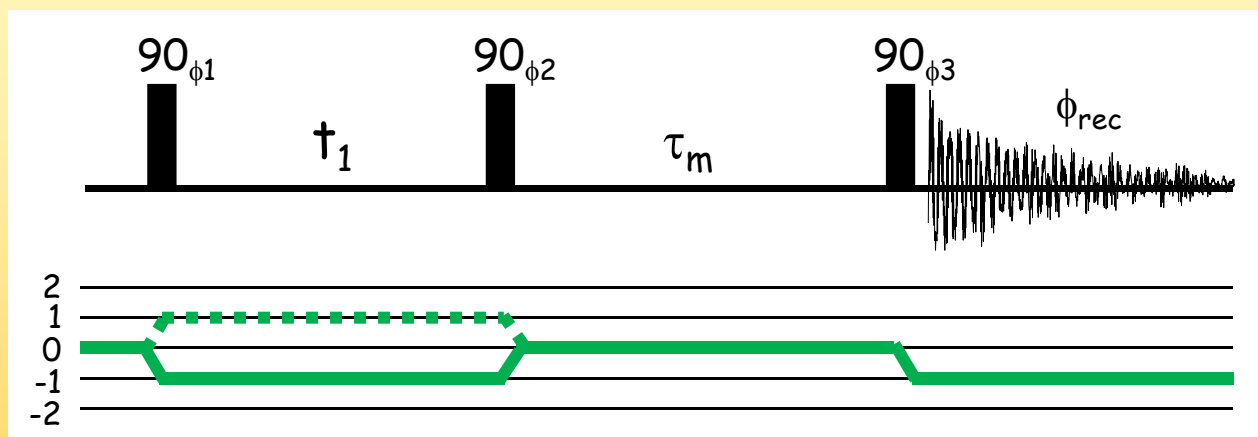
Remeber:
we detect
coherence order
(-1)

$\Delta p = +1$ $\Delta p = -1$ $\Delta p = -1$

0 → +1 →

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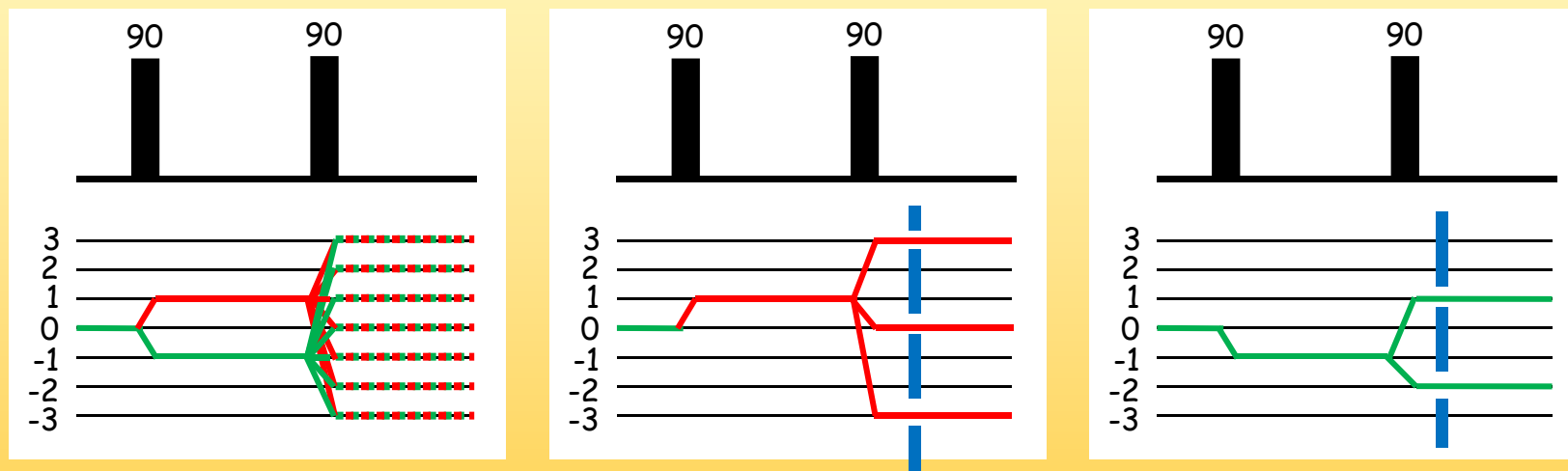
Note that instead of 1 to 3,0 and -3 a jump to 2, -1 and -4 would also be possible but would require another receiver phase (see below). Only the difference between the resulting levels is determined by the phase change.

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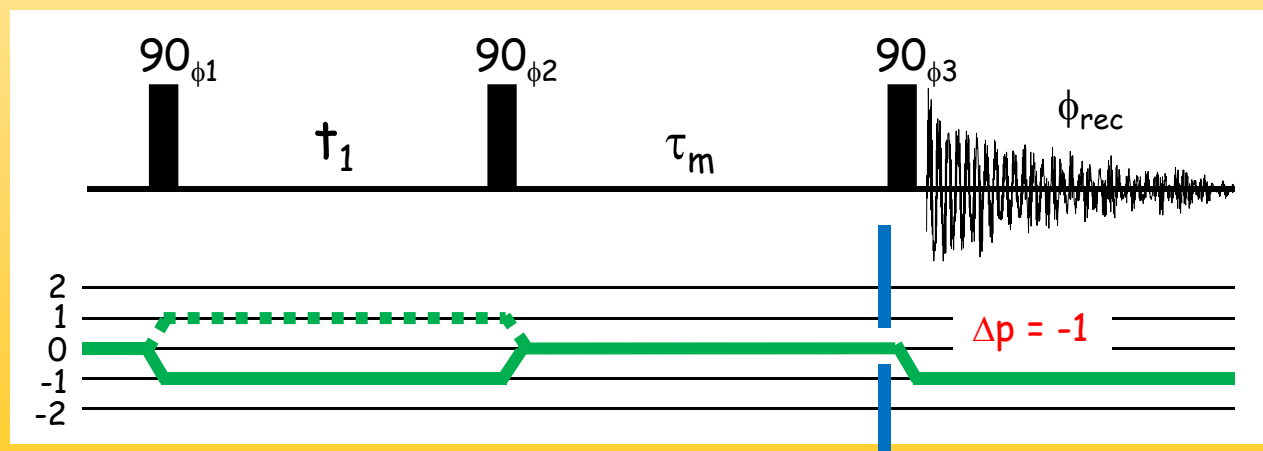
$$\phi_{rec} = -\sum_i \Delta p_i * \Delta\phi_i$$

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 ?
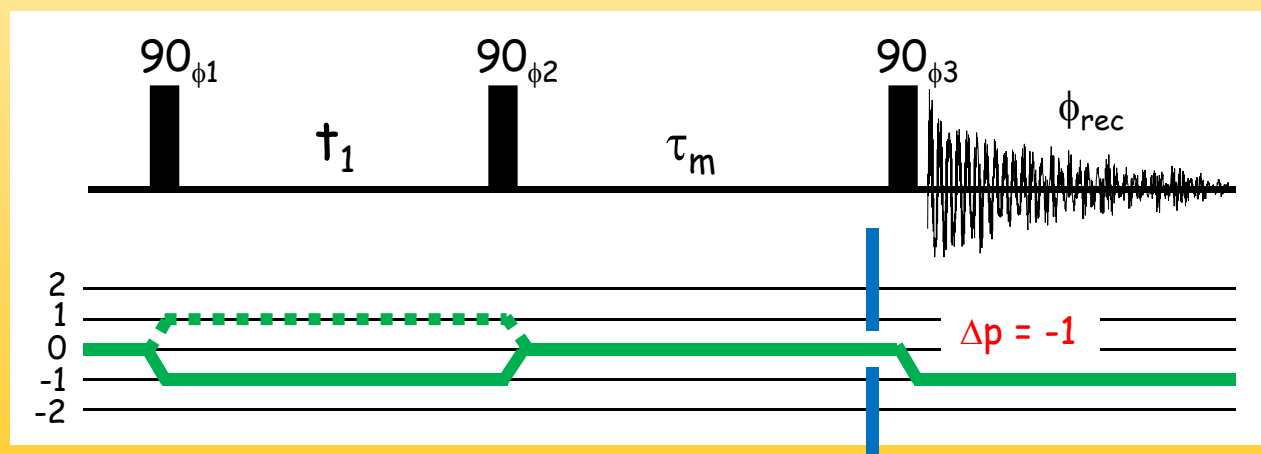
Phase Cycling

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

$\phi_{rec} = -\sum\limits_{i} \Delta p_i * \Delta\phi_i$

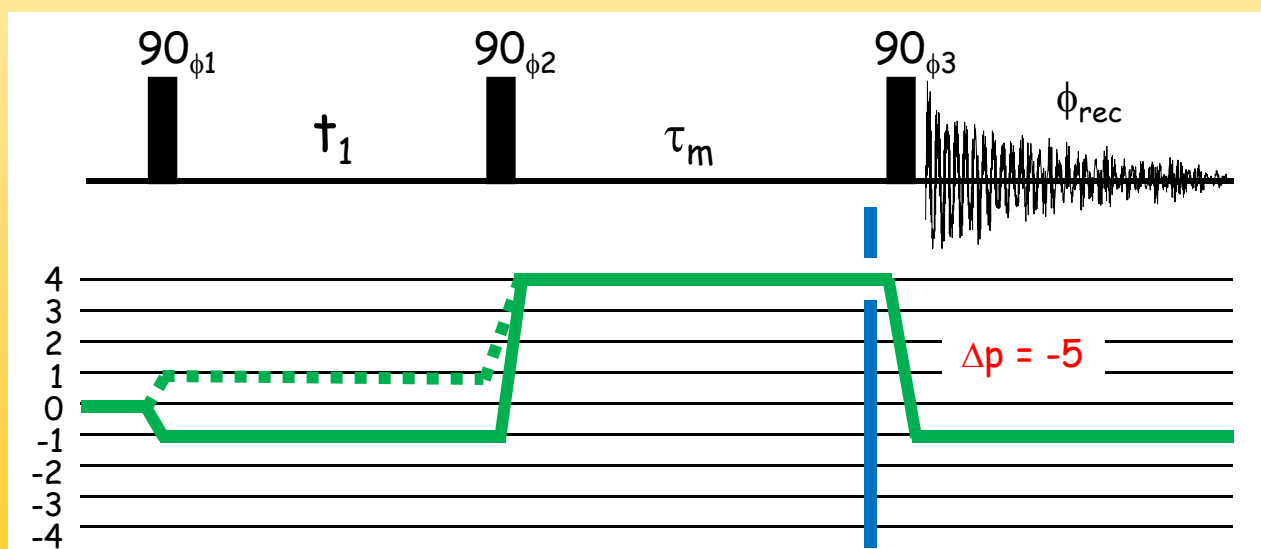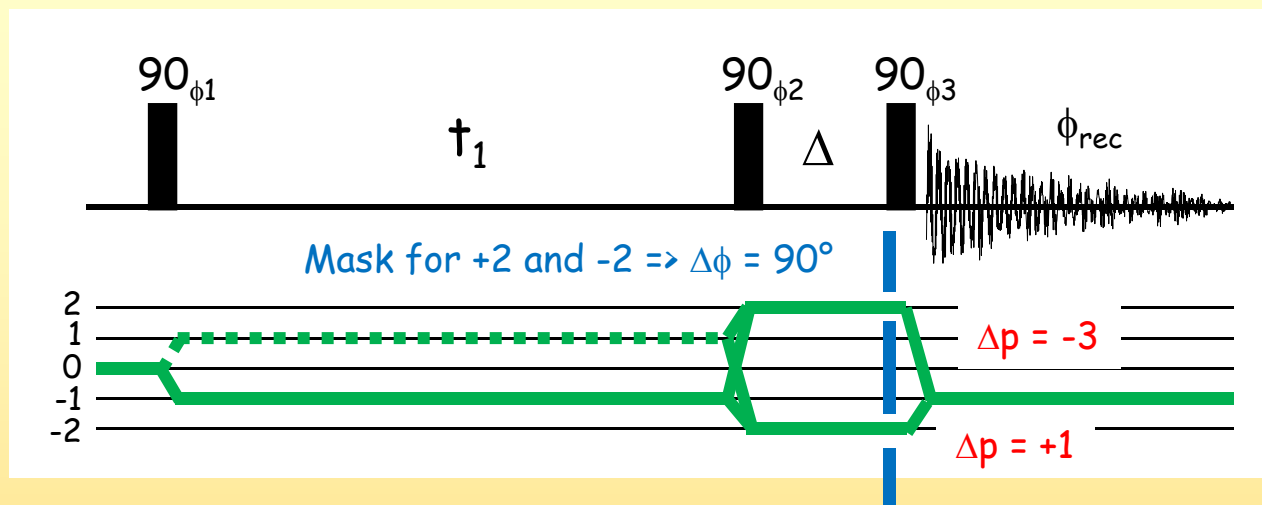|	$\Delta\phi_1$	$\Delta\phi_2$	$\Delta\phi_3$	$\sum \Delta p_i * \Delta\phi_i$	ϕ_{rec}
1	0	0	0	0	0
2	0	0	1	-1	1
3	0	0	2	-2	2
4	0	0	3	-3	3

Phase Cycling

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

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

	$\Delta\phi_1$	$\Delta\phi_2$	$\Delta\phi_3$	$\sum \Delta p_i * \Delta\phi_i$	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

$90_{\phi1}$ $90_{\phi2}$ $90_{\phi3}$

ϕ_{rec}

t_1 τ_m

4
3
2
1
0
-1
-2
-3
-4

Δp = -5

Phase Cycling

DQF-COSY

$90_{\phi 1}$ t_1 $90_{\phi 2}$ Δ $90_{\phi 3}$ ϕ_{rec}

Mask for +2 and -2 => $\Delta\phi$ = 90°

$\Delta p = -3$

$\Delta p = +1$

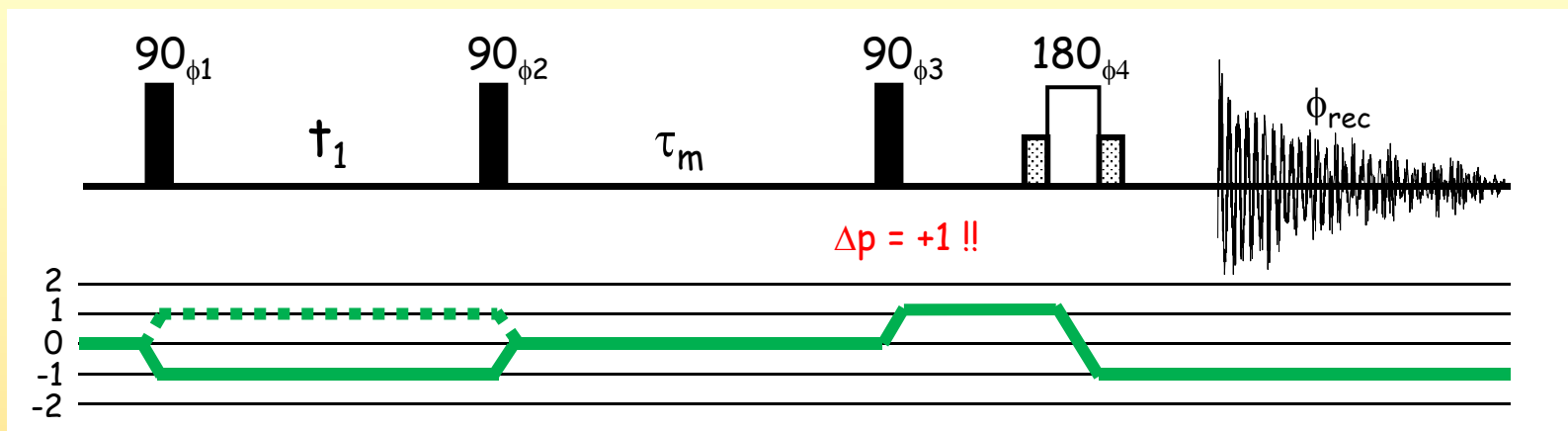$\Delta\phi_3$ = 0, 1, 2, 3

Δp = -3 and +1

	$\Delta\phi_1$	$\Delta\phi_2$	$\Delta\phi_3$	$\Sigma \Delta p_i * \Delta\phi_i$ $\Delta p = +1$	$\Sigma \Delta p_i * \Delta\phi_i$ $\Delta p = -3$	„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
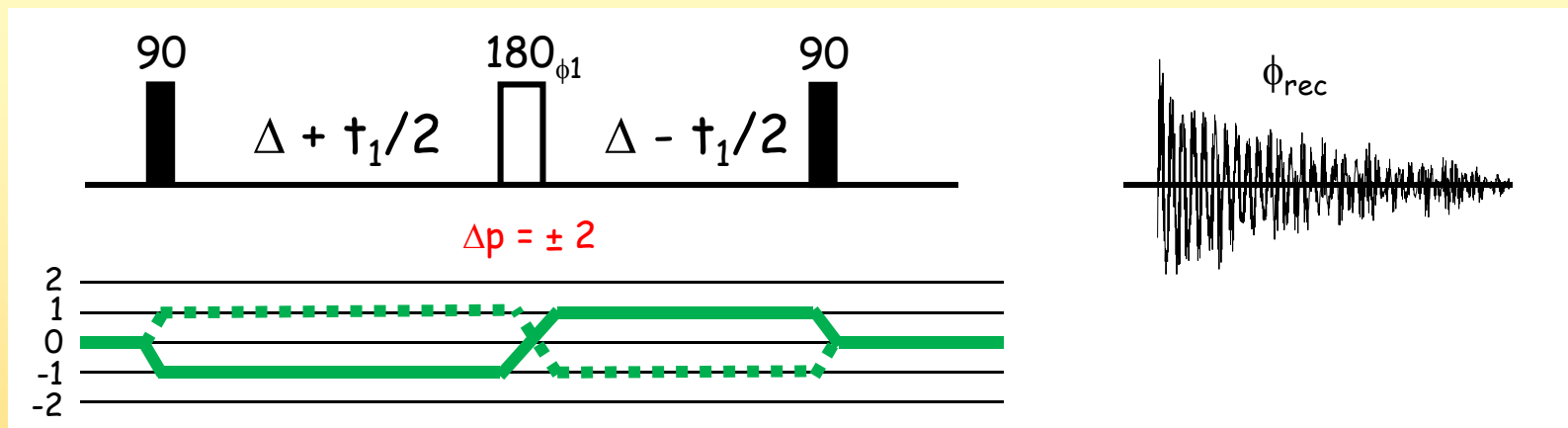
What if we add a WATERGATE water supression to the NOESY ?

$90_{\phi1}$ $90_{\phi2}$ $90_{\phi3}$ $180_{\phi4}$

t_1 τ_m ϕ_{rec}

$\Delta p = +1 !!$

2
1
0
-1
-2

	$\Delta\phi_1$	$\Delta\phi_2$	$\Delta\phi_3$	$\Delta\phi_4$	$\Sigma \Delta p_i * \Delta\phi_i$	„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.
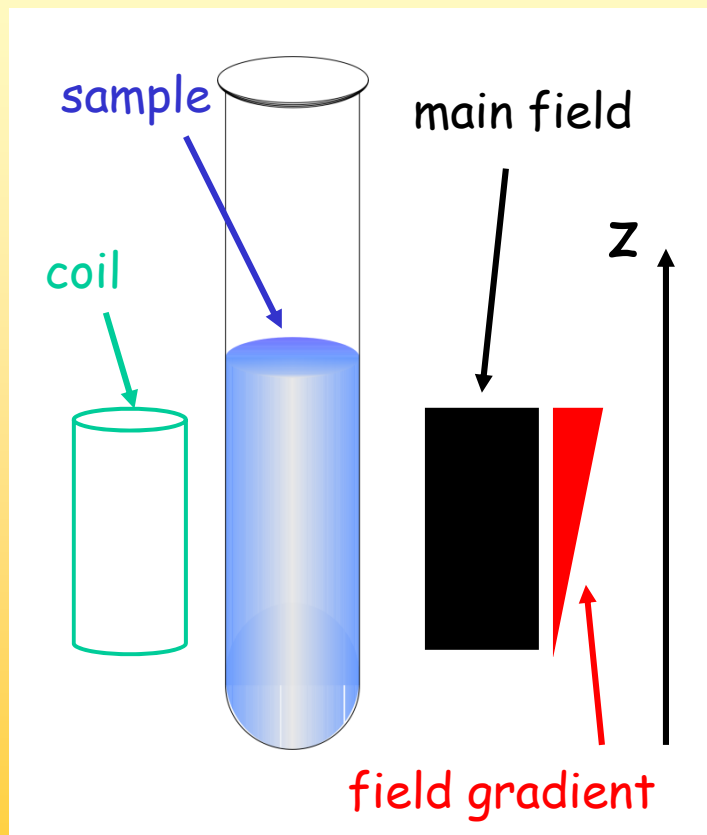

	$\Delta\phi_1$	$\Sigma\ \Delta p_i \ast \Delta\phi_i$ $\Delta p = +2$	$\Sigma\ \Delta p_i \ast \Delta\phi_i$ $\Delta p = -2$	„ϕ_{rec}" $\Delta p = +2$	„ϕ_{rec}" $\Delta p = -2$	ϕ_{rec}
1	0	0	0	0	0	0
2	1	2	-2	-2	2	2
3	2	4	-4	-4	4	0
4	3	6	-6	-6	6	2

Gradients and coherence levels

Gradients and coherence levels

Another powerful tool for NMR experiments are field gradients

sample

coil

main field

z

field gradient

While usually the homogeneity is kept as good and constant as possible, gradients are a way to change the magnetic field in a geometrically controlled manner. The Lamour frequency is then not the same for all molecules in the sample but spatially dependent:
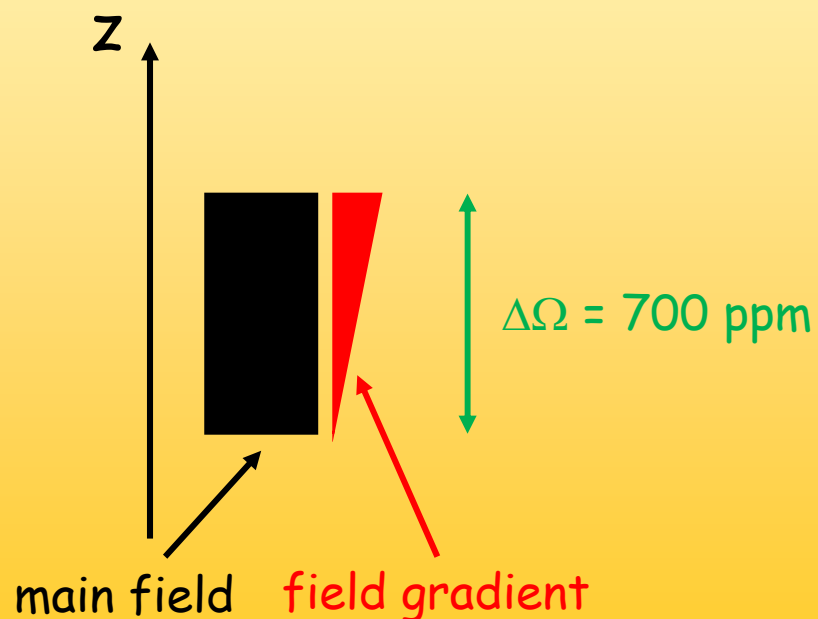
$$B = (1 + z) B_0$$
$$\omega = - \gamma B = - \gamma (1 + z) B_0$$

Gradients and coherence levels

Assuming a length of the coil of 2 cm and a typical gradient of 50 Gs/cm then we have a difference of ΔB = 10 mT (1 Gs = 0.1 mT) between the upper and lower end of the sample.

The gyromagnetic ratio for the protons (^{1}H) is γ =26.75*10^7 rad/sT.

Z

$\Delta\Omega$ = 700 ppm

main field   field gradient
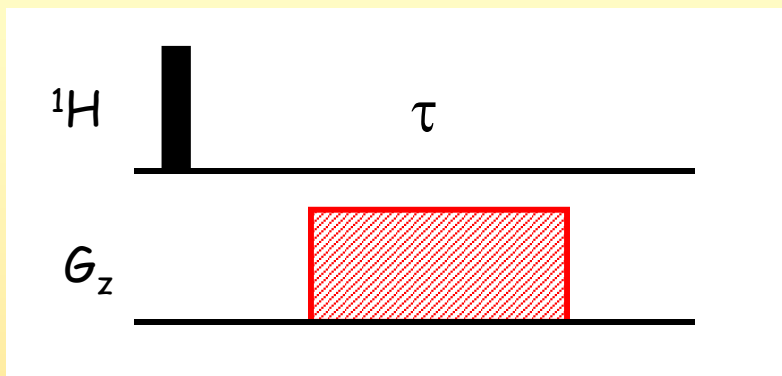
At a magnetic field of 14.1 T we thus obtain a frequency of

ν = $\omega/2\pi$ = $\gamma B/2\pi$ = 600 MHz

For a ΔB = 10 mT we thus obtain a

$\Delta\nu$ = 425 kHz, which corresponds

to ~700 ppm

(the minus is left out for clarity)

Gradients and coherence levels

Despite the spacial differences field gradients are in essence only delays

But the chemical shift is

dependent on the z-coordinate

$$B_z = B_0 + G_z$$

(G_z is the gradient field)

And since $\Omega_z = \gamma B_z = \gamma(B_0 + G_z) = \gamma B_0 + \gamma G_z = \Omega_0 + \Omega(z)$

If we apply that to what we already know we obtain

$$I_x = \tfrac{1}{2}\,(I^+ + I^-) \xrightarrow{\;I_z\Omega_z\tau\;} \tfrac{1}{2}\,[I^+ \exp(-i\Omega_z\tau) + I^- \exp(+i\Omega_z\tau)]$$

$$= \tfrac{1}{2}\,[I^+ \exp(-i(\Omega_0 + \Omega(z))\tau) + I^- \exp(+ i(\Omega_0 + \Omega(z))\,\tau)]$$

Gradients and coherence levels

That can be separated in a spatially dependent and an independent part

$$= \tfrac{1}{2} I^+ \exp(-i\Omega_0\tau) \; \mathit{exp\,(-\,i\Omega(z)\tau)}$$

$$+ \tfrac{1}{2} I^- \exp(+i\Omega_0\tau) \; \mathit{exp\,(+\,i\Omega(z)\tau)}$$

The additional phase created by the gradient has opposite sign for I^+ and I^-, and since $\Omega(z) = \gamma G_z$ it does not only depend on the gradient strength but also on the gyromagnetic ratio of the nuclei, the shift will depend on the type of nucleus.

We have seen that a gradient of 50 Gs/cm creates a difference of 425 kHz for ^{1}H spins, consequently the difference will be only 107 kHz for ^{13}C nuclei

Gradients and coherence levels

The additional shift will be twice as large for DQC then for SQC,

ZQC will not be affected at all, they are insensitive to gradients.

$$I_{1+}I_{2+} \xrightarrow{\ I_z\Omega_z\tau\ }$$

$$I_{1+}\exp(-i\Omega_z\tau)\,I_{2+}\exp(-i\Omega_z\tau) = I_{1+}I_{2+}\exp(-i(\Omega_1 +\Omega(z))\,\tau)\exp(-i(\Omega_2 +\Omega(z))\,\tau)$$

$$= I_{1+}I_{2+}\exp(-i[\Omega_1+\Omega_2]\tau)\ \textit{exp}\,(-\,\textit{i2}\Omega\textit{(z)}\tau)$$

This is the coherence order p !!

$$I_{1+}I_{2-} \xrightarrow{\ I_z\Omega_z\tau\ }$$

$$I_{1+}\exp(-i\Omega_z\tau)\,I_{2-}\exp(+i\Omega_z\tau) = I_{1+}I_{2-}\exp(-i(\Omega_1 +\Omega(z))\,\tau)\exp(+i(\Omega_2 +\Omega(z))\,\tau)$$

$$= I_{1+}I_{2-}\exp(-i[\Omega_1-\Omega_2]\tau)$$

$$\exp\,(-i[\Omega(z)-\Omega(z)]\tau) = 1$$

Here is the coherence order p = 0 !

Gradients and coherence levels

The calculation is a bit more involved for mixed MQC:

heteronuclear ZQC are not insensitive to gradients !

$$H_+C_+ \xrightarrow{\;I_z\Omega_z\tau\;}$$

$H_+\exp(-i\Omega_{Hz}\tau)\,C_+\exp(-i\Omega_{Cz}\tau) = H_+C_+\exp(-i(\Omega_H + \Omega_H(z))\,\tau)\exp(-i(\Omega_C + \Omega_C(z))\,\tau)$

$= H_+C_+\exp(-i[\Omega_H + \Omega_C]\tau)\;\mathit{exp\,(-\,i[\Omega_H(z) + \Omega_C(z)]\tau)}$

$= H_+C_+\exp(-i[\Omega_H + \Omega_C]\tau)\;\mathit{exp\,(-\,i[\gamma_H G + \gamma_C G]\tau)}$

$= H_+C_+\exp(-i[\Omega_H + \Omega_C]\tau)\;\mathit{exp\,(-\,i[\gamma_H + \gamma_C]\,G\tau)}$

$$H_+C_- \xrightarrow{\;I_z\Omega_z\tau\;}$$

$H_+\exp(-i\Omega_z\tau)\,C_-\exp(+i\Omega_z\tau) = H_+C_-\exp(-i(\Omega_H + \Omega_H(z))\,\tau)\exp(+i(\Omega_C + \Omega_C(z))\,\tau)$

$= H_+C_-\exp(-i[\Omega_H - \Omega_C]\tau)\;\mathit{exp\,(-\,i[\Omega_H(z) - \Omega_C(z)]\tau)}$

$= H_+C_-\exp(-i[\Omega_H - \Omega_C]\tau)\;\mathit{exp\,(-\,i[\gamma_H - \gamma_C]\,G\tau)}$
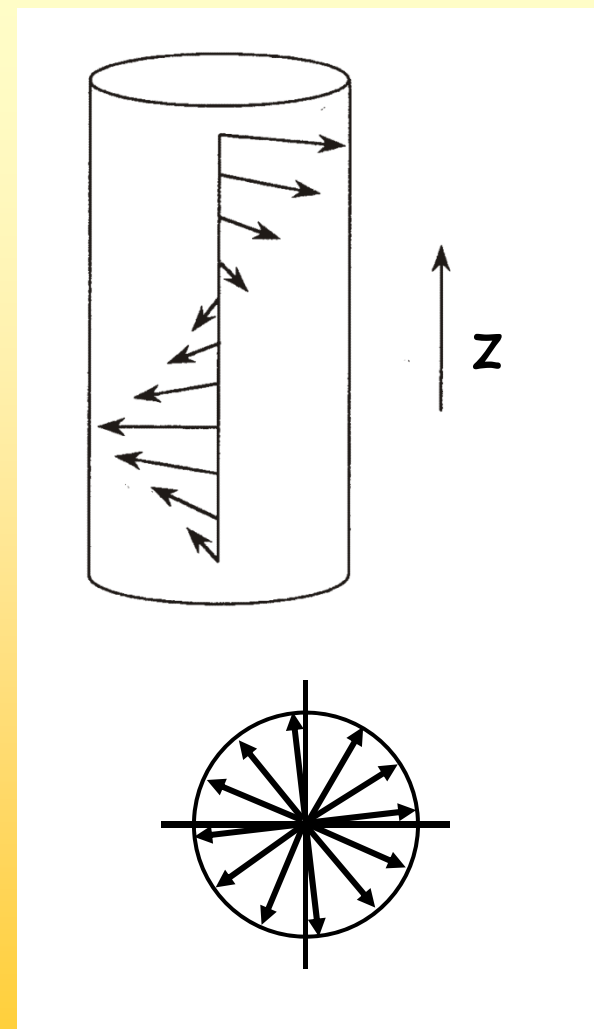
Gradients and coherence levels

Since the chemical shift evolution during the delay is spatially dependent, a single gradient will destroy magnetization. However, the changes in the magnetic field are not random, the sign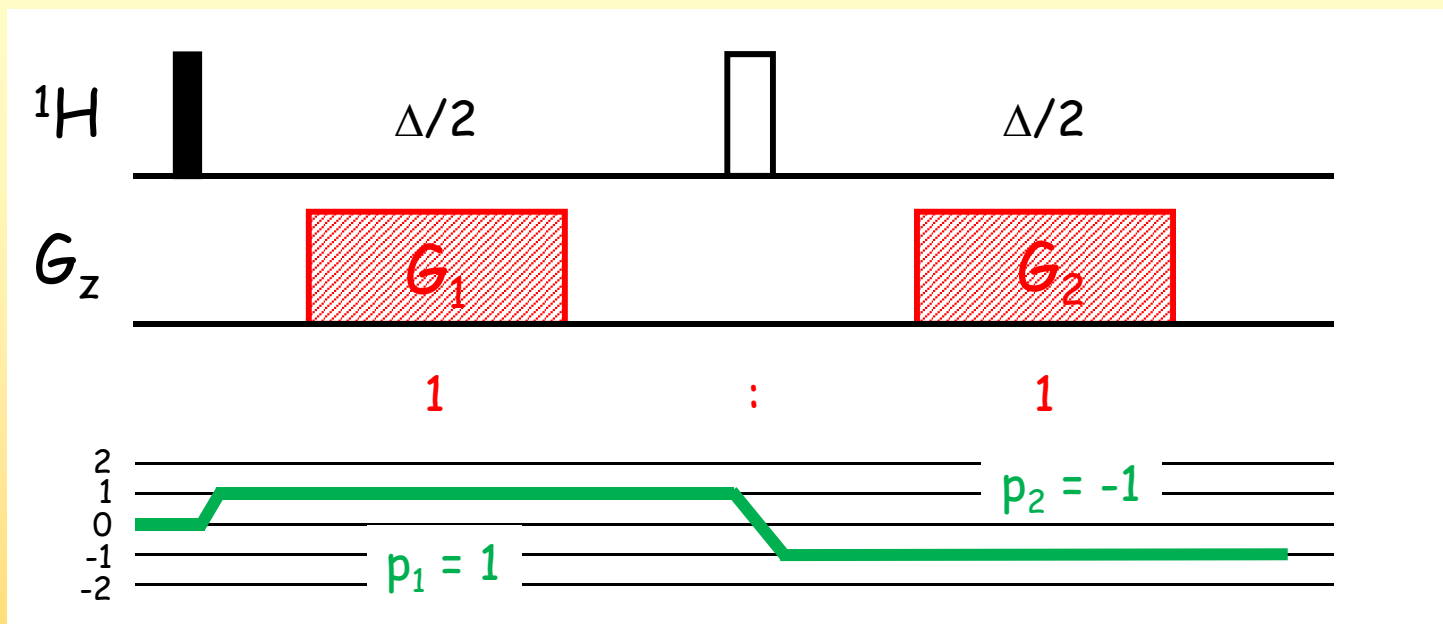al can thus be recovered by appropriate other gradients. Gradients can be applied in both +z and –z, i.e. in both directions of the magnetic field. (Given the proper equipment one can also apply x and y gradients, but those are rarely used in high resolution NMR these days)

Gradients and coherence levels

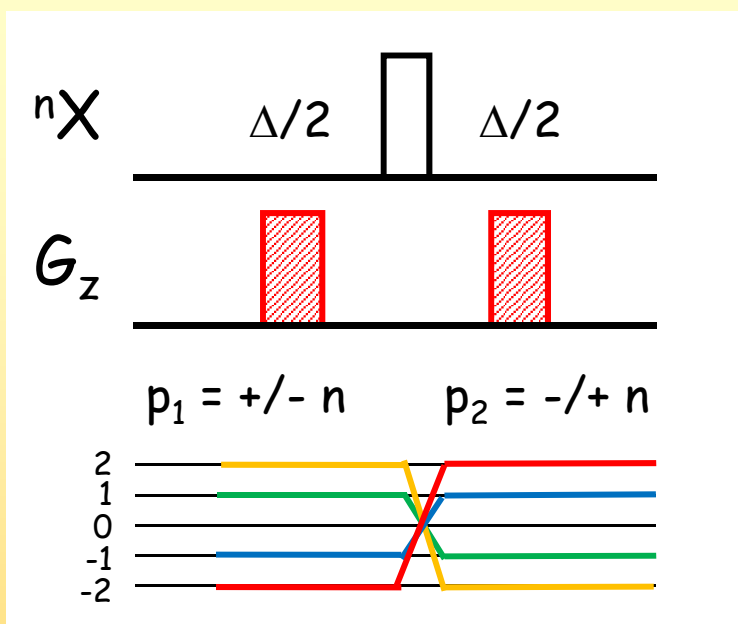To revers the effect of a gradient there are several ways

180° pulses reverse the effect of chemical shift and thus also that of gradients.

Another way of looking at it: the products of coherence order and gradient

strength for all gradients have to add up to 0 !

$p_1 * G_1 + p_2 * G_2 = 1 * 1 + -1 * 1 = 0$ (if $G_1 = G_2$)

Gradients and coherence levels

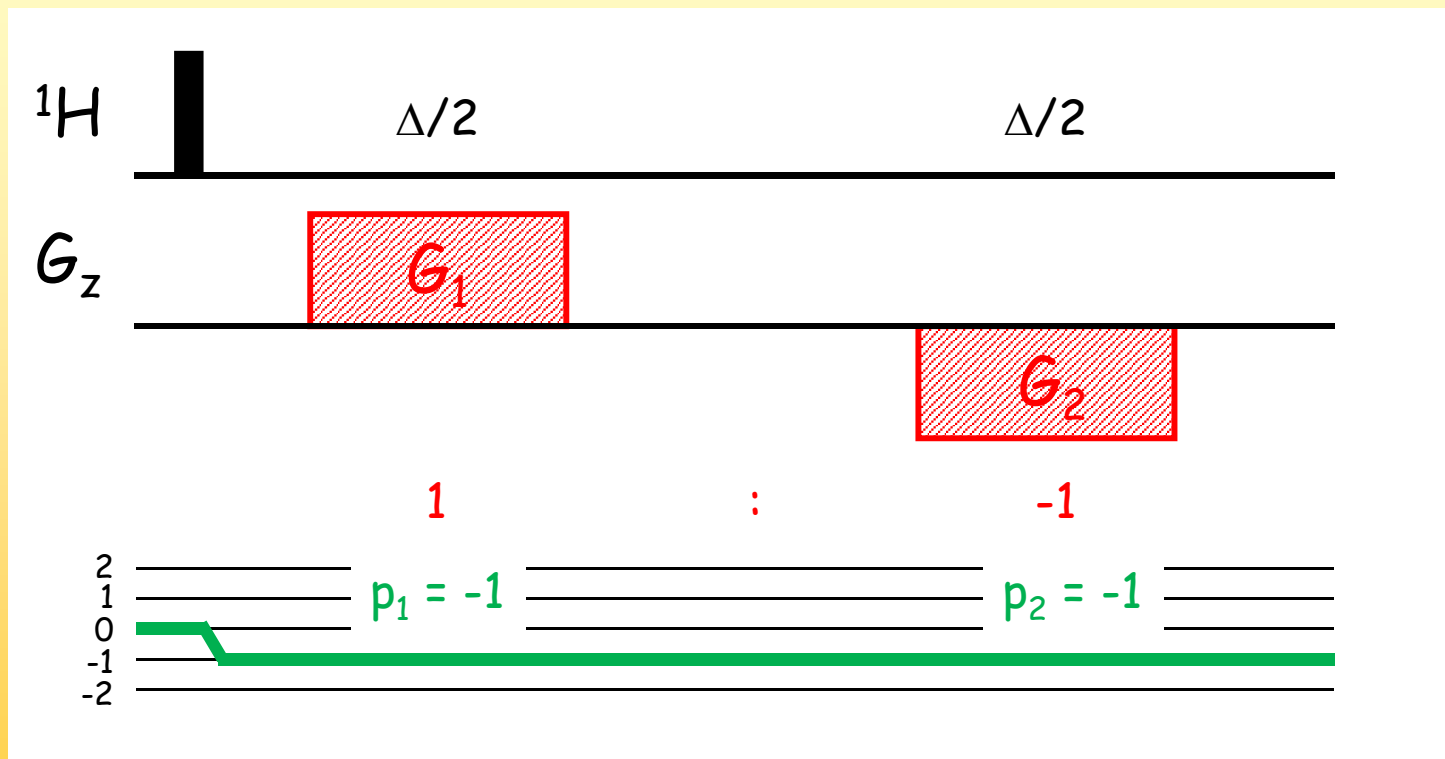^{n}X $\Delta/2$ $\Delta/2$

G_z

$p_1 = +/- n$ $p_2 = -/+ n$

2
1
0
-1
-2

That is why two gradients "clean up" a 180° pulse and why WATERRGATE works so well for suppression of water signals
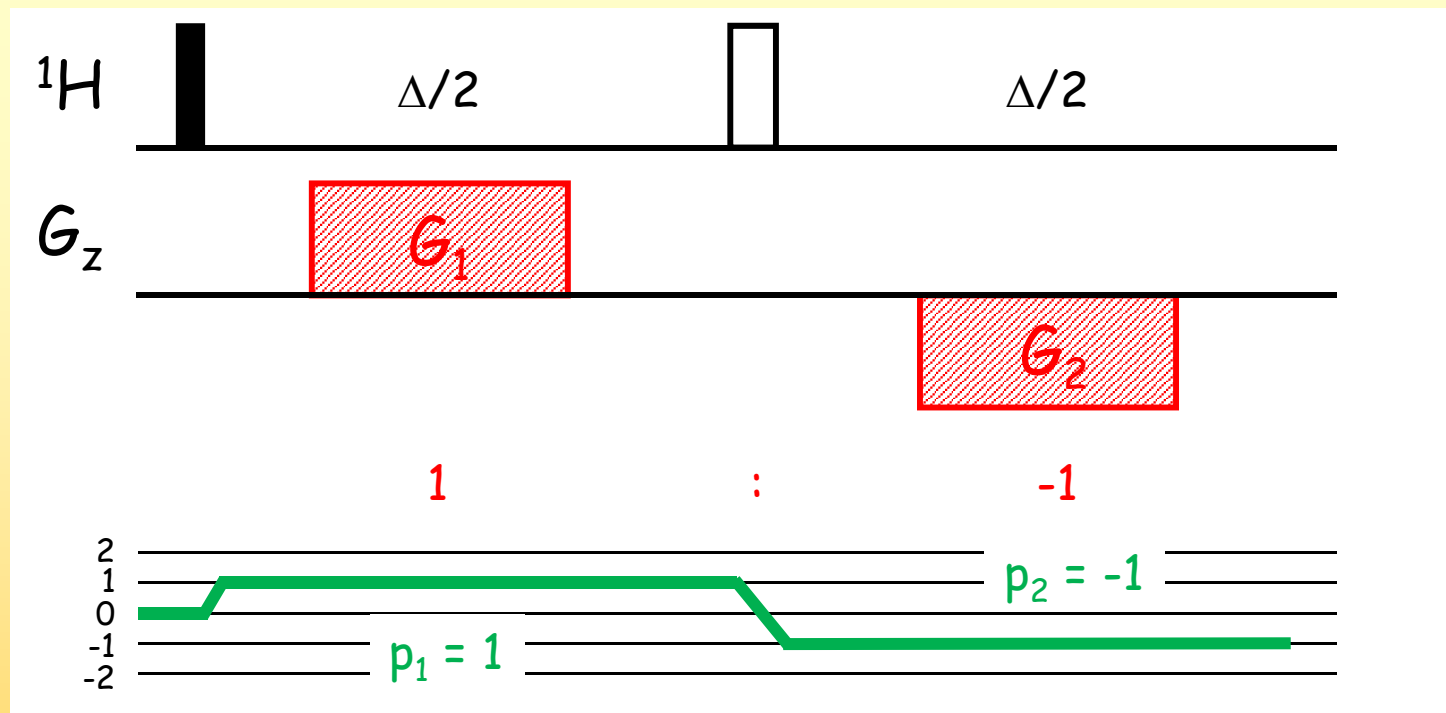
^{1}H 90 180 90_{H_2O} Δ 90_{H_2O} Δ

G_z
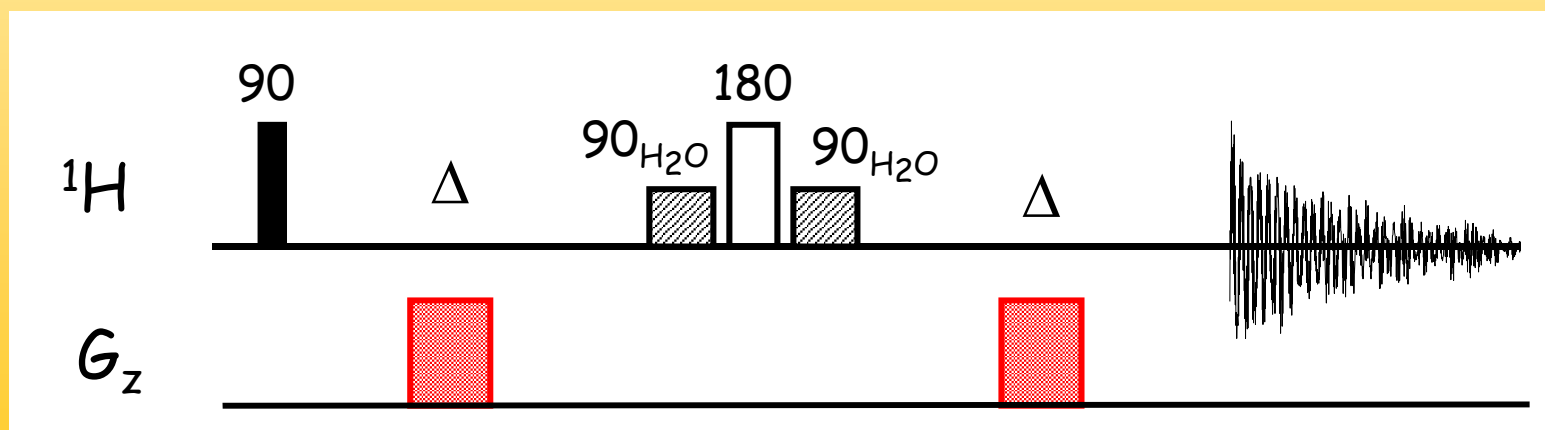
Gradients and coherence levels

Instead of changing the sign of the coherence order we can change that of the gradient

^1H

$\Delta/2$ $\Delta/2$

G_z

G_1

G_2

1 : -1

2
1
0
-1
-2

$p_1 = -1$ $p_2 = -1$

$$p_1 * G_1 + p_2 * G_2 = -1 * 1 + -1 * -1 = 0$$
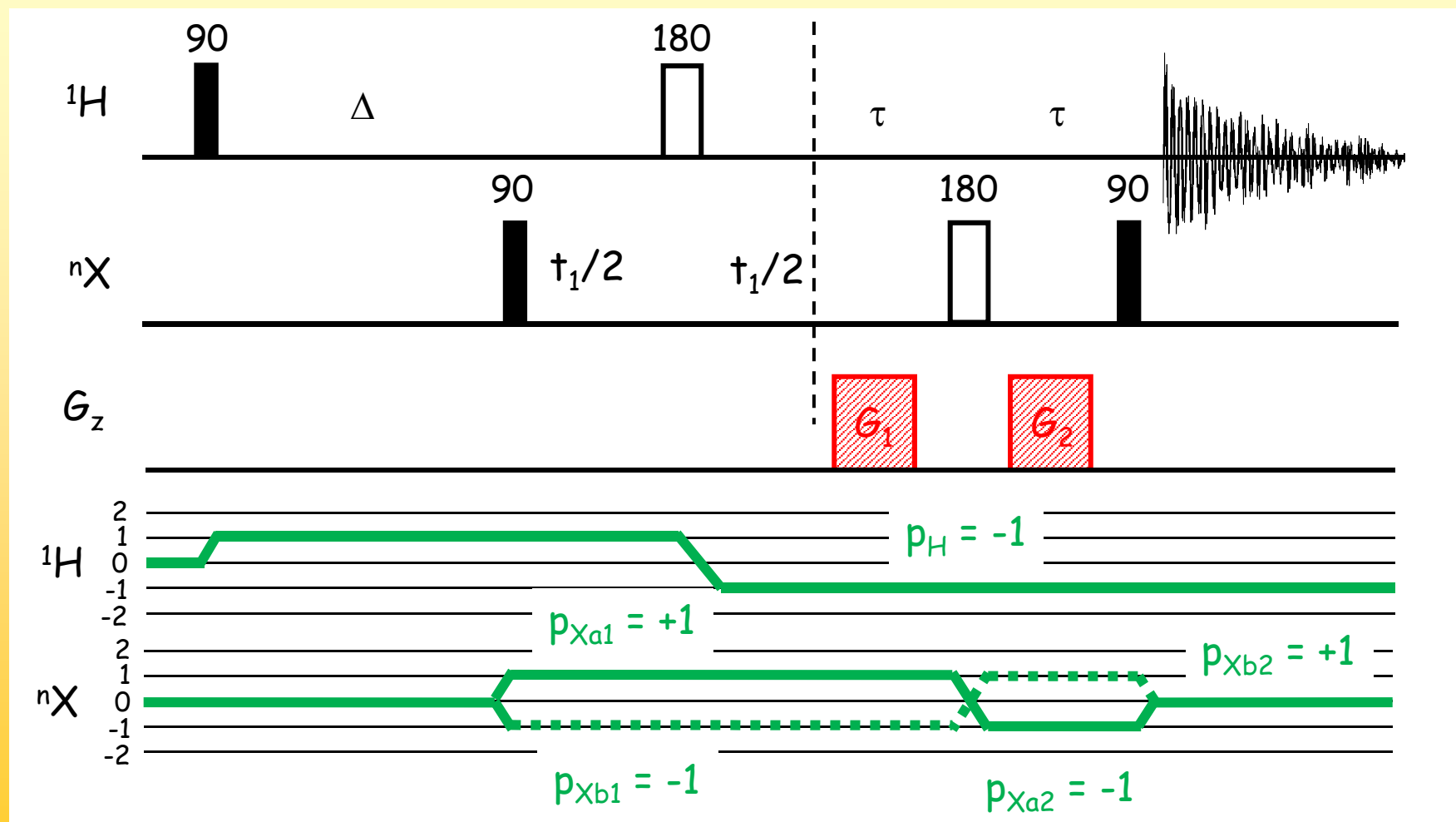
Gradients and coherence levels

Here we use two opposite gradients to reduce the effect on the overall stability

of the setup, but use the 180° pulse to still create a strong gradient

$p_1 * G_1 + p_2 * G_2 = 1 * 1 + -1 * -1 = 2$ (if $G_1 = -G_2$)

These bipolar gradients are used e.g. in DOSY experiments
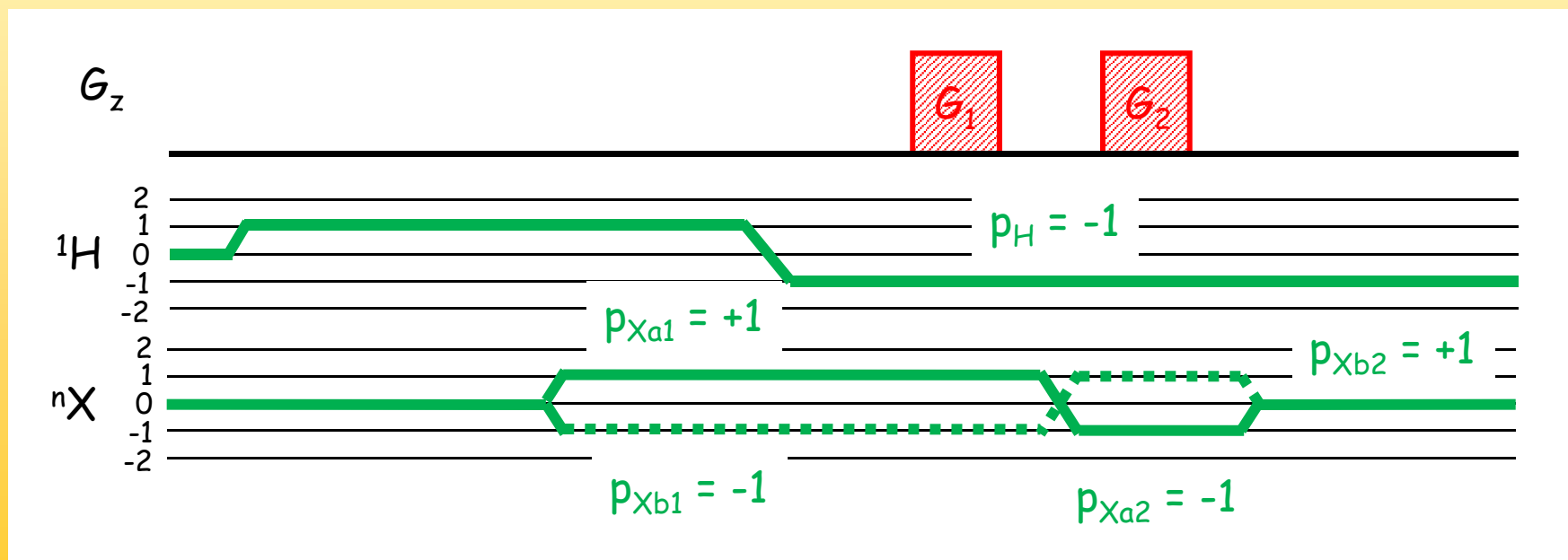
Gradients and coherence levels

Now lets look at a "real" experiment: an HMBC with gradient selection

Gradients and coherence levels

Gradients, coherence levels and gyromagnetic ratio still have to add up to 0. There are two pathways for the X-nucleus (we will learn later why), since gradients are sensitive to the sign of the coherence level we will not be able to select them simultaneously.

Gradients and coherence levels

G_z

G_1 G_2

^1H

2
1
0
-1
-2

$p_H = -1$

$p_{Xa1} = +1$

^nX

2
1
0
-1
-2

$p_{Xb2} = +1$

$p_{Xb1} = -1$ $p_{Xa2} = -1$
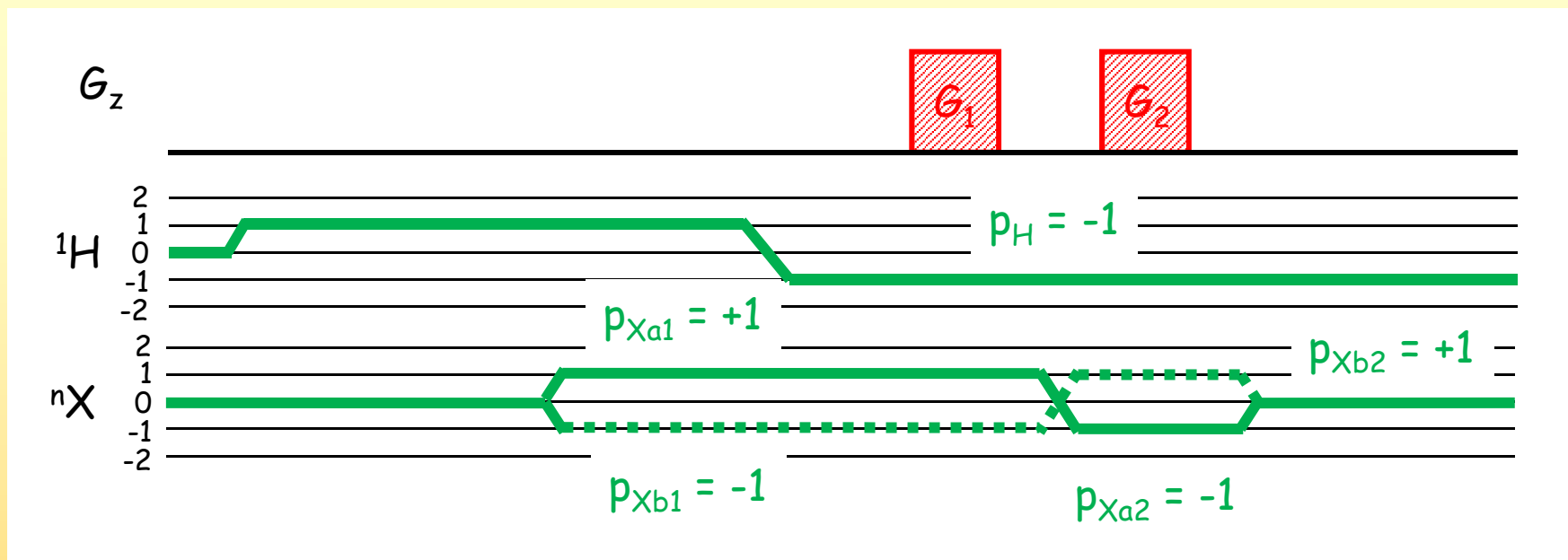
Pathway a:

$(p_H * \gamma_H + p_{Xa1} * \gamma_X) * G_1 + (p_H * \gamma_H + p_{Xa2} * \gamma_X) * G_2 = 0$

$(-\gamma_H + \gamma_X) * G_1 + (-\gamma_H - \gamma_X) * G_2 = 0$
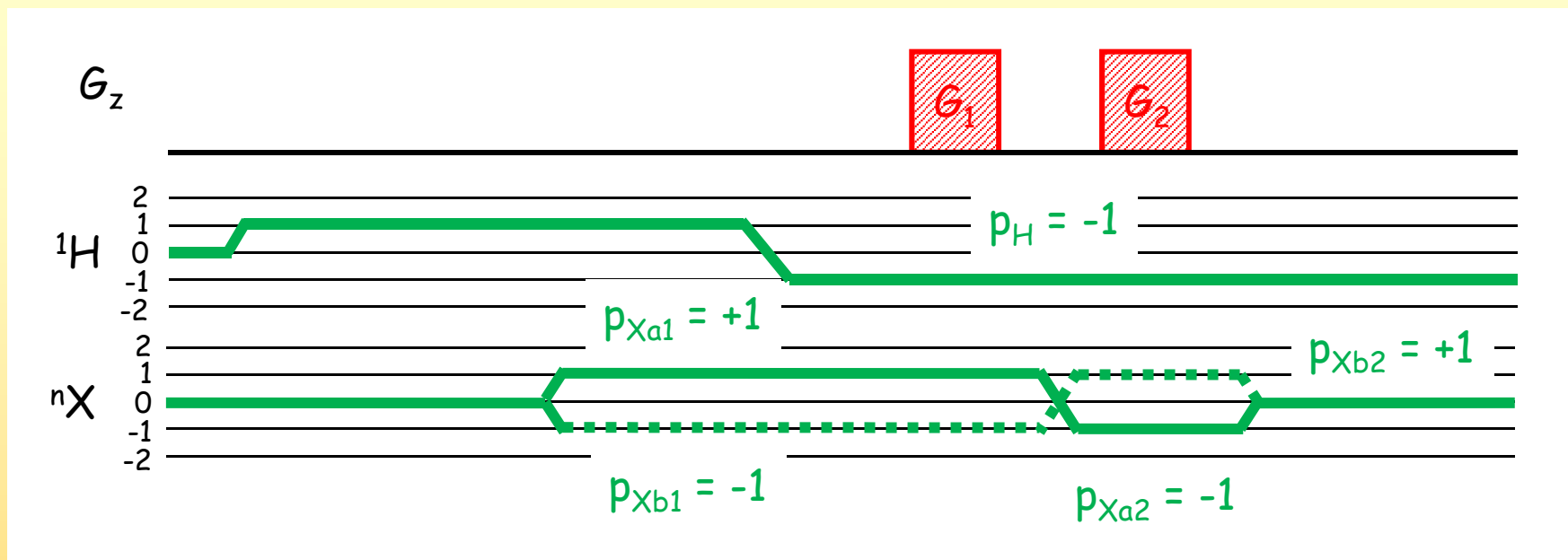
$n = \gamma_X / \gamma_H$

$(-\gamma_H + \gamma_X) * G_1 = (\gamma_H + \gamma_X) * G_2$

$$G_2 = \frac{(-\gamma_H + \gamma_X)}{(\gamma_H + \gamma_X)} * G_1 = \frac{(-\gamma_H + n * \gamma_H)}{(\gamma_H + n * \gamma_H)} * G_1 = -\frac{(1 - n)}{(1 + n)} * G_1$$

Gradients and coherence levels

G_z

^1H

$p_H = -1$

$p_{Xa1} = +1$

$p_{Xb2} = +1$

^nX

$p_{Xb1} = -1$

$p_{Xa2} = -1$

Pathway b:

$n = \gamma_X / \gamma_H$

$- \dfrac{(1 - n)}{(1 + n)} * G_1$

$(p_H * \gamma_H + p_{Xb1} * \gamma_X) * G_1 + (p_H * \gamma_H + p_{Xb2} * \gamma_X) * G_2 = 0$

$(-\gamma_H - \gamma_X) * G_1 + (-\gamma_H + \gamma_X) * G_2 = 0$

a vs. b

$(-\gamma_H - \gamma_X) * G_1 = (\gamma_H - \gamma_X) * G_2$

$$G_2 = \frac{(-\gamma_H - \gamma_X)}{(\gamma_H - \gamma_X)} * G_1 = \frac{(-\gamma_H - n * \gamma_H)}{(\gamma_H - n * \gamma_H)} * G_1 = - \frac{(1 + n)}{(1 - n)} * G_1$$

Gradients and coherence levels

This is exactly what you will find in pulse programs, only

written a little different.

```
"cnst30=(1-sfo2/sfo1)/(1+sfo2/sfo1)"

define list<gradient> EA1 = { 1.000 -cnst30}
define list<gradient> EA2 = { -cnst30 1.000}

(p3 ph4):f2
  d0
  (p2 ph2)
  d0
  p16:gp1*EA1
  d16
  (p24:sp7 ph5):f2
  DELTA4
  p16:gp1*EA2
  d16 pl2:f2
  (p3 ph5):f2
  d20
  (p14:sp3 ph1):f2
  d20
  4u BLKGRAD
  go=2 ph31
```

$n = \gamma_X / \gamma_H = sfo2/sfo1$

$$a: G_2 = - G_1 \frac{(1 - n)}{(1 + n)}$$

$$b: G_2 = - G_1 \frac{(1 + n)}{(1 - n)}$$

$$G_1 = - G_2 \frac{(1 - n)}{(1 + n)}$$

Gradients and coherence levels

Two more things:

An advantage of gradients compared to phase cycling is that the selection is accomplished with a single scan, no addition or subtraction of signals is necessary. So there are no subtraction artefacts and the receiver gain can be adjusted to the desired signal and does not have to accommodate signals that disappear later.

We have seen already that gradients do NOT
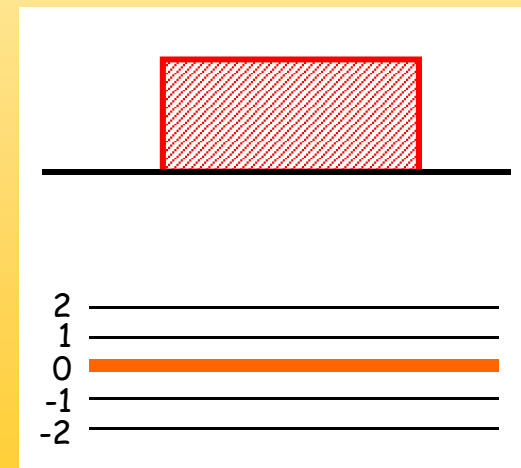
affect coherence order 0:

$p * G = 0$ for $p = 0$ independent of G !!

Since ZQC and z-magnetization both have

coherence order 0, they can not be

separated or suppressed by gradients

(nor separated by phase cycling).

Quadrature detection in 2D

Quadrature Detection in 2D

The problem of sign discrimination when putting the carrier in the center of the spectrum occurs in every dimension of an nD-spectrum.

In case of 1D-NMR we have seen that we can solve the problem by obtaining a complex signal i.e. by selecting only one coherence level.

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

$$S(\Omega) = A(\Omega) + i\, D(\Omega)$$

$90_{\phi 1}$ $90_{\phi 2}$ ϕ_{rec} t_1

$\phi_2 = 0, 1, 2, 3$
$\phi_{rec} = 0, 2, 0, 2$
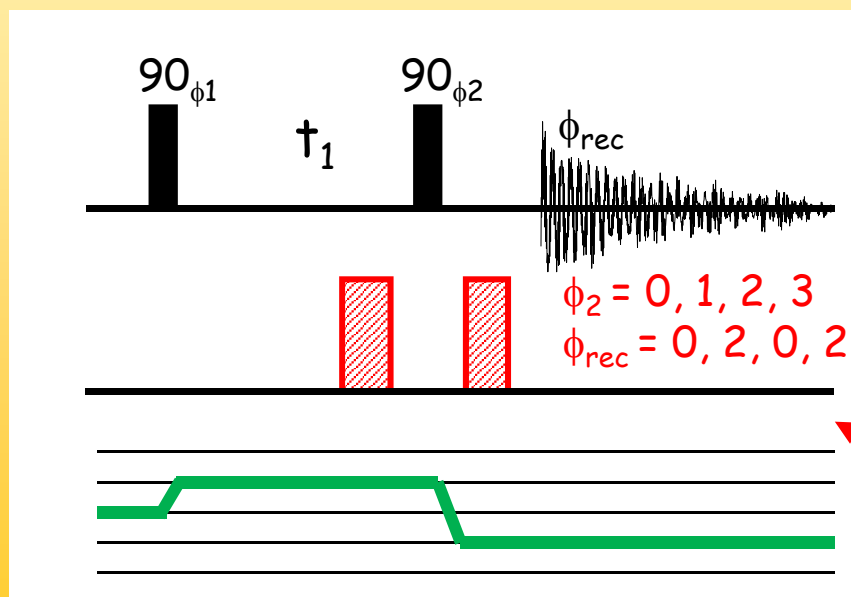
We have seen now that we can select one coherence level in the indirect dimension of an nD using either gradients or a phase cycle, so it should be easy to obtain a complex signal.

"Service-COSY"

Phase cycling, Gradients and Quadrature-Detection
G-NMR-School 2020

Peter Schmieder
FMP

Quadrature Detection in 2D

The signal we obtain is then:

$$s(t_1,t_2) = \exp(i\Omega_A t_1) \exp(-t_1/T_2) \exp(i\Omega_B t_2) \exp(-t_2/T_2)$$

After the first FT we get:

$$S(t_1,\Omega_2) = \exp(i\Omega_A t_1) \exp(-t_1/T_2) [A(\Omega_2) + i\, D(\Omega_2)]$$

And the second FT yields:

$$S(\Omega_1,\Omega_2) = [A(\Omega_1) + i\, D(\Omega_1)] [A(\Omega_2) + i\, D(\Omega_2)]$$

$$S(\Omega_1,\Omega_2) = [A(\Omega_1)\, A(\Omega_2) - D(\Omega_1)\, D(\Omega_2)] + i\, [A(\Omega_1)\, D(\Omega_2) + D(\Omega_1)\, A(\Omega_2)]$$

We will only look at the real part of the spectrum and as it turns out the frequency discrimination worked but we have dispersive components in the signal ! We need a magnitude calculation and loose resolution.

Quadrature Detection in 2D

The solution is to record and store the real and imaginary part in the indirect dimension separately as cosine and sine component. After the first FT we get:

$$S_C(t_1, \Omega_2) = \cos(\Omega_A t_1) \exp(-t_1/T_2) [A(\Omega_2) + i\, D(\Omega_2)]$$

$$S_S(t_1, \Omega_2) = \sin(\Omega_A t_1) \exp(-t_1/T_2) [A(\Omega_2) + i\, D(\Omega_2)]$$

If we now take only the real part and combine both to yield a complex dataset we get what we want:

$$S(t_1, \Omega_2) = [\cos(\Omega_A t_1) + i\, \sin(\Omega_A t_1)] \exp(-t_1/T_2)\, A(\Omega_2)$$
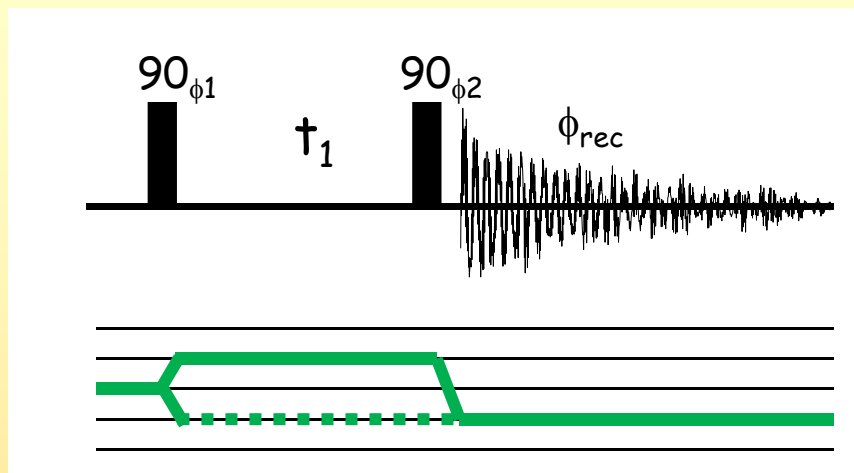
$$S(t_1, \Omega_2) = \exp(i\Omega_A t_1) \exp(-t_1/T_2)\, A(\Omega_2)$$

$$S(\Omega_1, \Omega_2) = [A(\Omega_1) + i\, D(\Omega_1)]\, A(\Omega_2)$$

$$S(\Omega_1, \Omega_2) = \boxed{A(\Omega_1)\, A(\Omega_2)} + i\, D(\Omega_1)\, A(\Omega_2)$$

Now the real part has pure absorption phase, this is Ruben-States-Haberkorn

Quadrature Detection in 2D

This means that we allow two coherence levels (ϕ_2 needs to be set properly).

In addition, we have to manipulate ϕ_1, to obtain a cosine and a sine signal:

$\phi_1 = x, \phi_2 = x$

$$I_z \xrightarrow{\ 90° I_x\ } -I_y \xrightarrow{\ I_z\Omega\tau\ } -I_y\cos\Omega t + I_x\sin\Omega t \xrightarrow{\ 90° I_x\ } -I_z\cos\Omega t + I_x\sin\Omega t$$

$\phi_1 = y, \phi_2 = x$

$$I_z \xrightarrow{\ 90° I_y\ } I_x \xrightarrow{\ I_z\Omega\tau\ } I_x\cos\Omega t + I_y\sin\Omega t \xrightarrow{\ 90° I_x\ } I_x\cos\Omega t + I_z\sin\Omega t$$

Quadrature Detection in 2D

There are several established ways to do it, TPPI is the 2D-variant of the Redfield-trick.

They all achieve the same goal but they differ in the way the affect axial peaks and the position of peaks outside the frequency range given by the Nyquist theorem.

"States"   "States-TPPI"   "TPPI"

"Ruben-States-Haberkorn"

ϕ_1	t_1	ϕ_{rec}	ϕ_1	t_1	ϕ_{rec}	ϕ_1	t_1	ϕ_{rec}
x	0	x	x	0	x	x	0	x
y	0	x	y	0	x	y	$\Delta t/2$	x
x	Δt	x	-x	Δt	-x	-x	Δt	x
y	Δt	x	-y	Δt	-x	-y	$3\Delta t/2$	x

Quadrature Detection in 2D

By collecting a sine in first FID and cosine in the second, the other

part does not contribute to the signal and is "wasted".

$\phi_1 = x, \phi_2 = x$

$$I_z \xrightarrow{90° I_x} -I_y \xrightarrow{I_z\Omega\tau} -I_y\cos\Omega t + I_x\sin\Omega t \xrightarrow{90° I_x} \cancel{-I_z\cos\Omega t} + I_x\sin\Omega t$$

$\phi_1 = y, \phi_2 = x$

$$I_z \xrightarrow{90° I_y} I_x \xrightarrow{I_z\Omega\tau} I_x\cos\Omega t + I_y\sin\Omega t \xrightarrow{90° I_x} I_x\cos\Omega t + \cancel{I_z\sin\Omega t}$$

To recover that loss a scheme was designed that obtained the name

"sensitivity enhancement", even so the length of the sequence prevents

an actual enhancement in case of faster relaxing molecules. One part

of the signal is stored and the other recovered during the sequence.

Quadrature Detection in 2D

^{1}H 90_x Δ_1 Δ_1 90_y $t_1/2$ $t_1/2$ 90_x Δ_2 Δ_2 90_y Δ_1 Δ_1 90_x

^{n}X 90_x $90_{x/-x}$ 90_y Decoupling
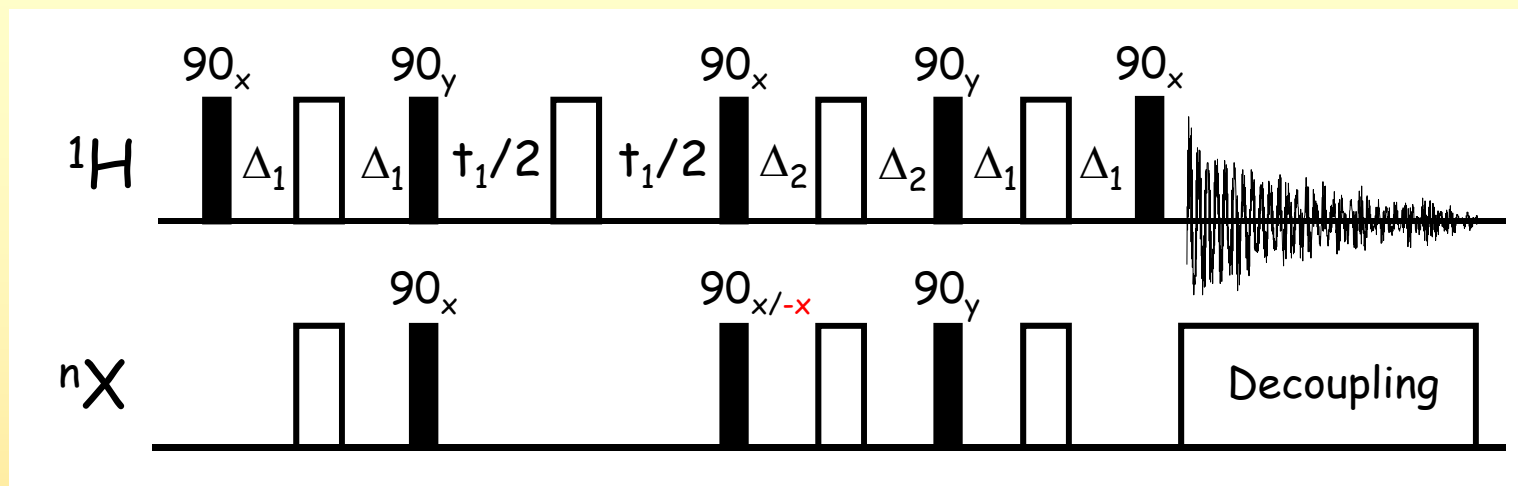
The idea is to collect two FIDs with a slightly modified phase cycle that will allow both components to reach the receiver, albeit with different sign, and store them seperately for further manipulation

$$- N_yH_z \cos\Omega t_1 + N_xH_z \sin\Omega t_1 \longrightarrow \pm N_zH_y \cos\Omega t_1 + N_xH_y \sin\Omega t_1 \longrightarrow$$

$$\pm H_x \cos\Omega t_1 + N_xH_y \sin\Omega t_1 \longrightarrow \pm H_z \cos\Omega t_1 - N_zH_y \sin\Omega t_1 \longrightarrow$$

$$\pm H_z \cos\Omega t_1 + H_x \sin\Omega t_1 \longrightarrow \pm H_y \cos\Omega t_1 + H_x \sin\Omega t_1$$

Quadrature Detection in 2D

Now we take the sum and the difference of the both FIDs we have collected

$$\pm H_y \cos\Omega t_1 + H_x \sin\Omega t_1$$

sum $\longrightarrow$ $2\ H_x \sin\Omega t_1$

difference $\longrightarrow$ $2\ H_y \cos\Omega t_1$

We have calculated before that we can convert H_y into H_x by taking the FID resulting from that magnetization and switching real and imaginary part and changing the sign of the real part.

We thus obtain the two signals:

$2\ H_x \cos\Omega t_1$ $2\ H_x \sin\Omega t_1$

Which is exactly the same as if we would have done States, except we have a factor of 2 in there, which will lead to the enhancement.

Quadrature Detection in 2D

A related situation occurs when using gradients for coherence selection. We have seen that we can only select one pathway but that we need two. The solution has already been presented in the previous section we can use different signs for the gradients and collect both pathways. Since they are called echo and anti-echo so is the quadrature procedure.
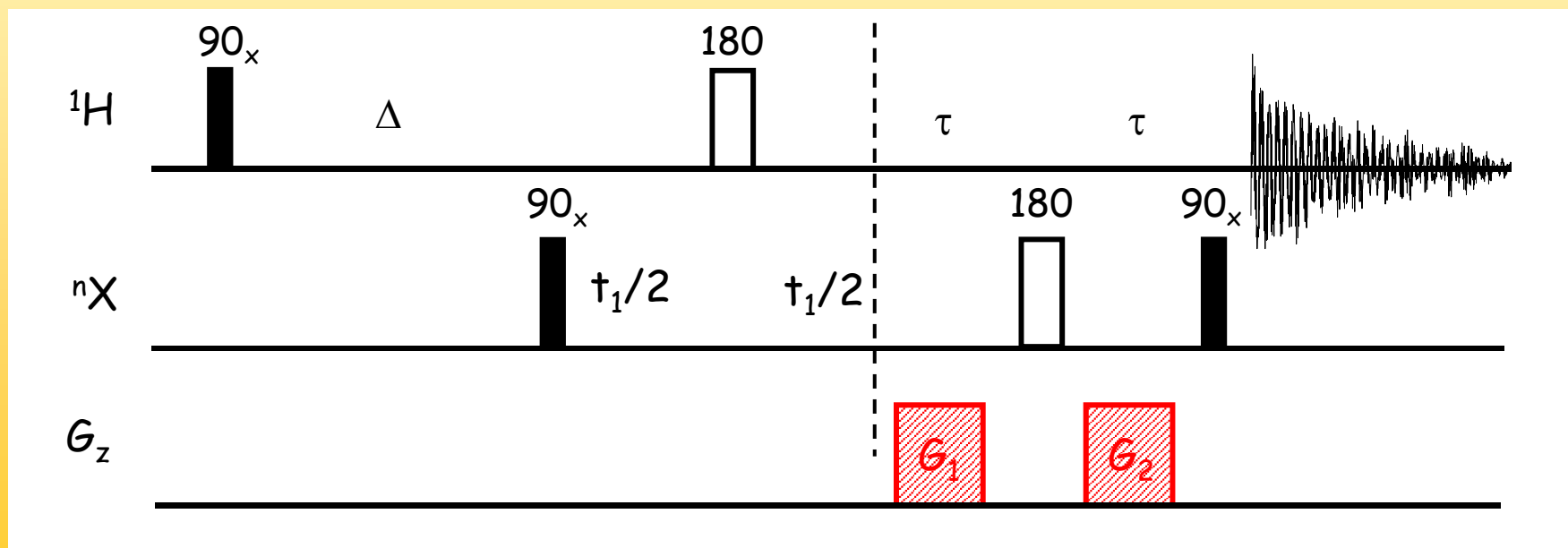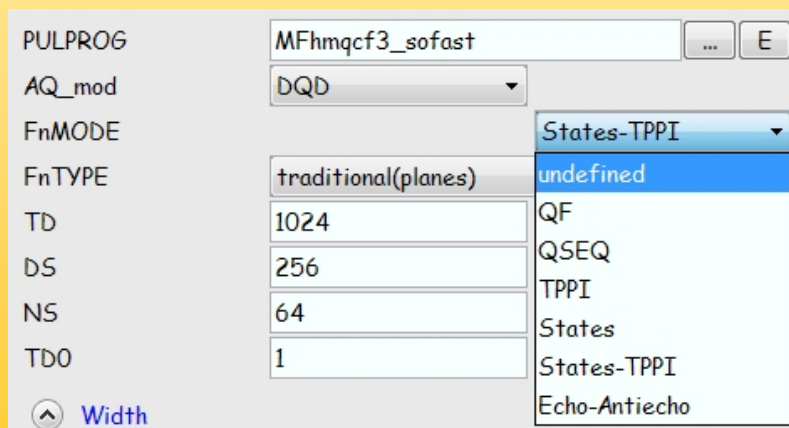
Quadrature Detection in 2D

In echo/anti-echo we collect both X_+ and X_-. Since these contain $[X_x + X_y]$ as well as $[X_x - X_y]$ and since $\exp(\pm\,\Omega_x t)$ contains a sine and a cosine, manipulation of the magnetization is possible to yield the same situation as with sensitivity enhancement:

$$H_x \cos(\Omega_X t_1) \; \pm \; H_y \sin(\Omega_x t_1)$$

Again forming the sum and the difference and manipulating the real and imaginary part somewhat yields data to be processed like States.

PULPROG	MFhmqcf3_sofast	...	E
AQ_mod	DQD		
FnMODE		States-TPPI	
FnTYPE	traditional(planes)	undefined	
TD	1024	QF	
DS	256	QSEQ	
		TPPI	
NS	64	States	
TD0	1	States-TPPI	
⌄ Width		Echo-Antiecho	

On Bruker spectrometers you actually choose the type of quadrature detection and the software will do it for you

Quadrature Detection in 2D

We heard already that the different schemes for quadrature detection differ in the way they handle axial peaks.

Axial peaks arise from magnetization that does not experience the phase shifts prior to the evolution time. These signals are treated differently by the various quadrature detection schemes. They do not "feel" changes in ϕ_1 and thus only experience the receiver phase.

ϕ_1	t_1	ϕ_{rec}
x	0	x
y	0	x
x	Δt	x
y	Δt	x

If we use States the axial peaks will be detected as what they are: peaks at zero frequency which is the center of the spectrum

Quadrature Detection in 2D

ϕ_1	t_1	ϕ_{rec}
x	0	x
y	0	x
-x	Δt	-x
-y	Δt	-x

ϕ_1	t_1	ϕ_{rec}
x	0	x
y	$\Delta t/2$	x
-x	Δt	x
-y	$3\Delta t/2$	x

In case of States-TPPI, the sign of the receiver is changed from point to point. Since the same is done for $\phi 1$, the real signals do not differ from States. But the axial peaks a shifted by half the sweep width to the edge of the spectrum.

In case of TPPI, the sign of the receiver is not changed so the axial peaks stay in the center. But the real peaks are shifted and the processing moves the spectrum by half the sweep width so the axial peaks are again at the edge.

Quadrature Detection in 2D

time

Analogue
IN

Digital
OUT
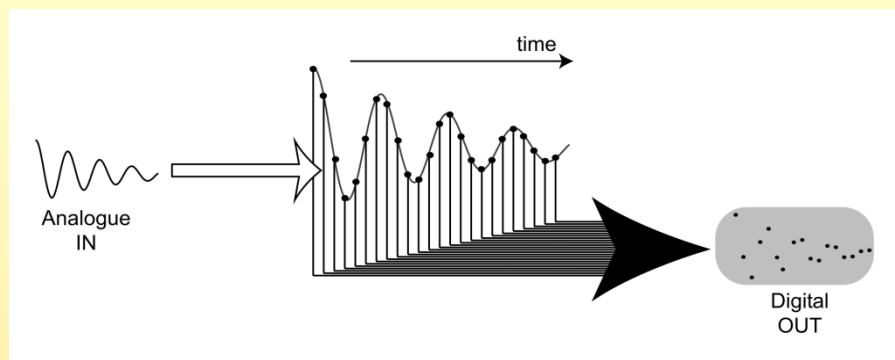
The effects that are observed regarding peaks outside the chosen spectral range result from the digitization of the signal prior to processing.

$2\Delta t$
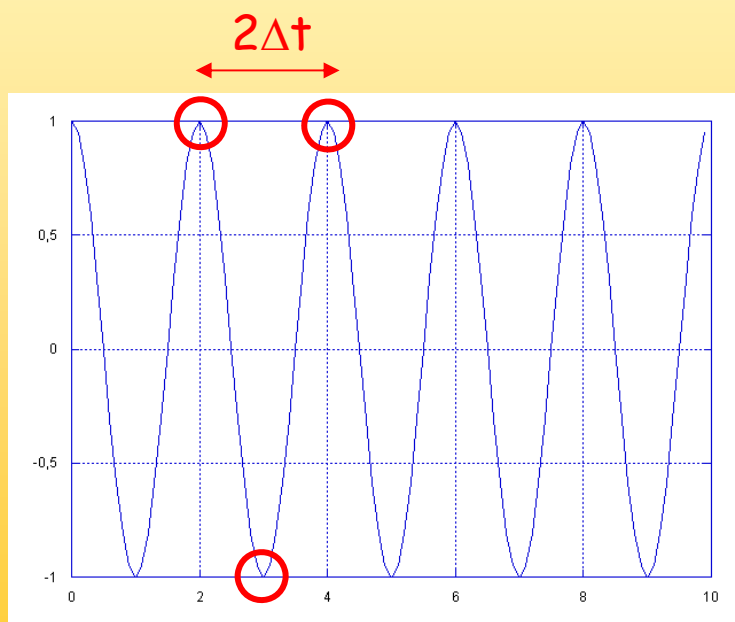
The Nyquist-theorem states that the highest frequency detectable with a sampling rate of Δt is

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

which means that we have to have three datapoints per period. Since we can distinguish the sign we have a spectral width

$$SW = 2 * f_n = 1/\Delta t$$

Quadrature Detection in 2D

If a frequency is higher than the Nyquist-Frequency it simply appears as if the frequency were lower since the digitizer can simply not distinguish the higher frequency from a lower one within the "Nyquist range".

$f_n + \Delta f$ f_n

$f_n + \Delta f$ f_n $f_n - \Delta f$
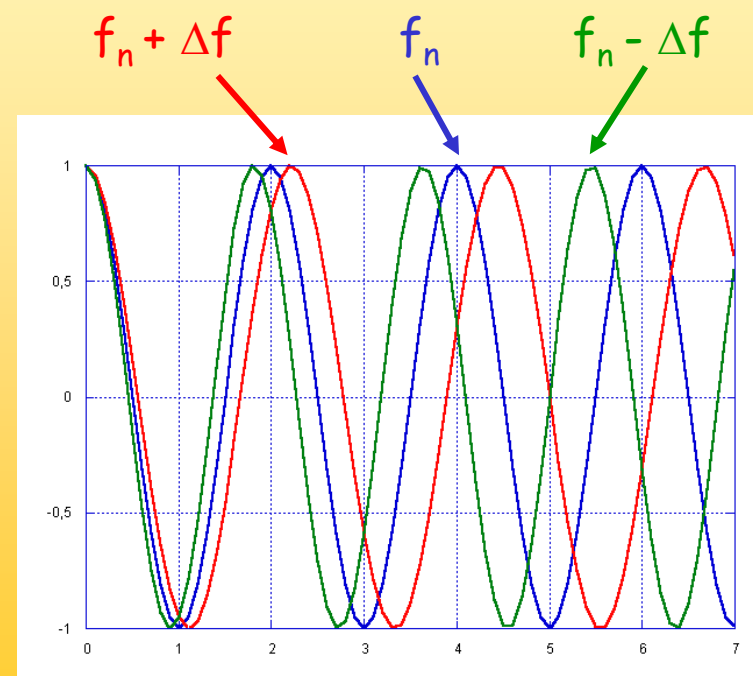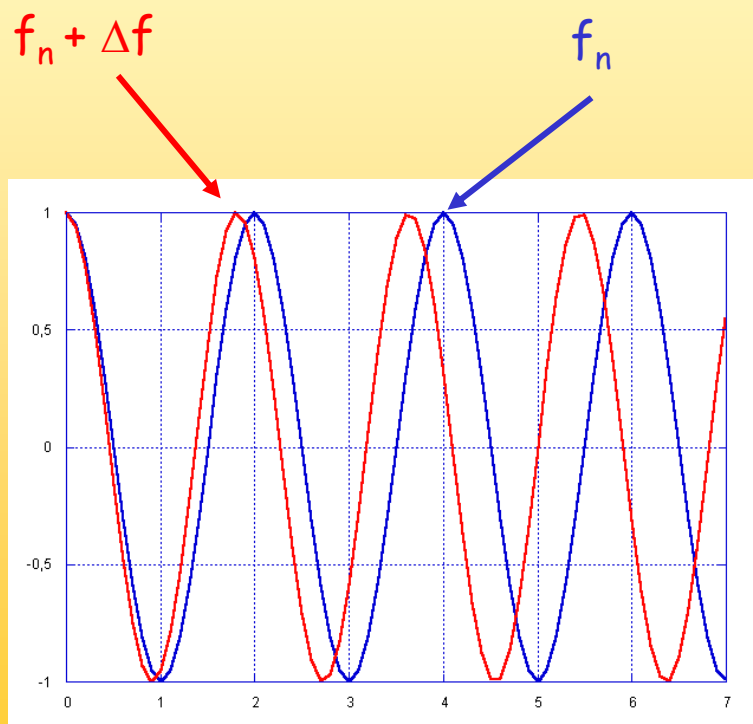
Quadrature Detection in 2D

The sign of a frequency outside the Nyquist range is dependent on the type of sampling. If only a cosine signal is collected (TPPI, Redfield) then a signal is "folded", i.e. F+ΔF is replaced by F-ΔF. If a complex signal is collected (States, States-TPPI, echo/antiecho), then the signal is "aliased", i.e. F+ΔF is replaced by (-(F-ΔF))
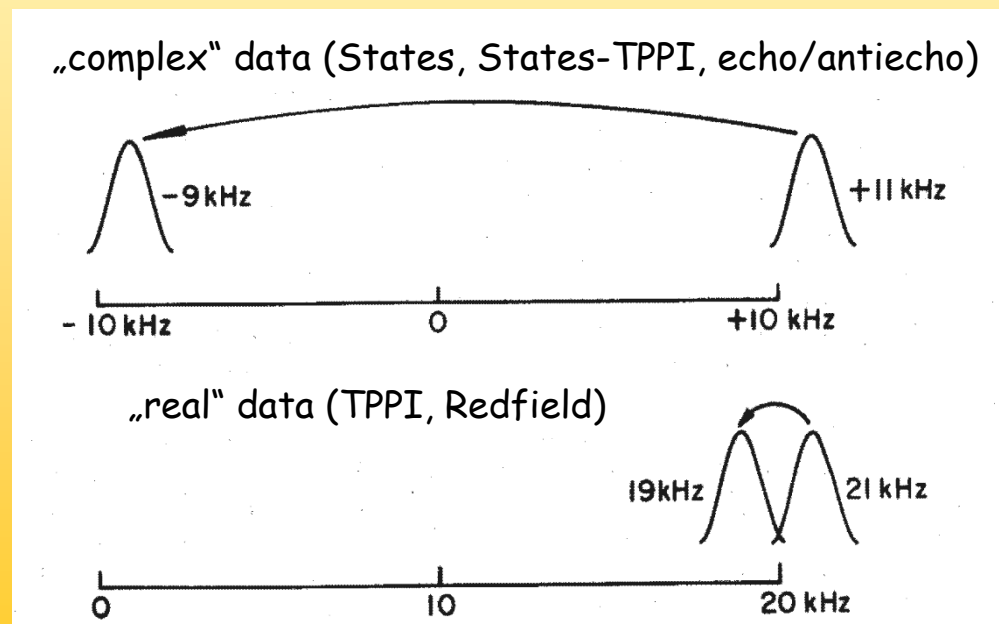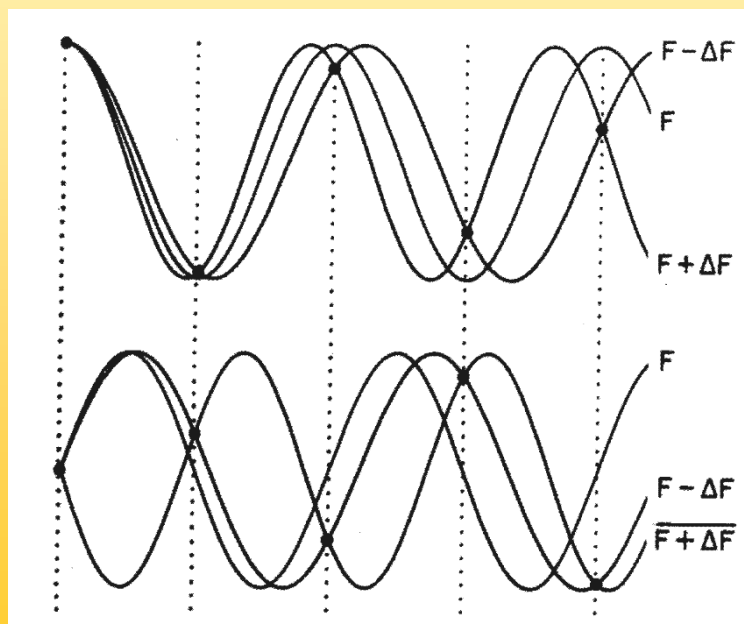
Quadrature Detection in 2D

In summary all schemes yield in principle identical results, they differ, however, with respect to axial peak suppression and in the way peaks outside the spectral range are folded or aliased.
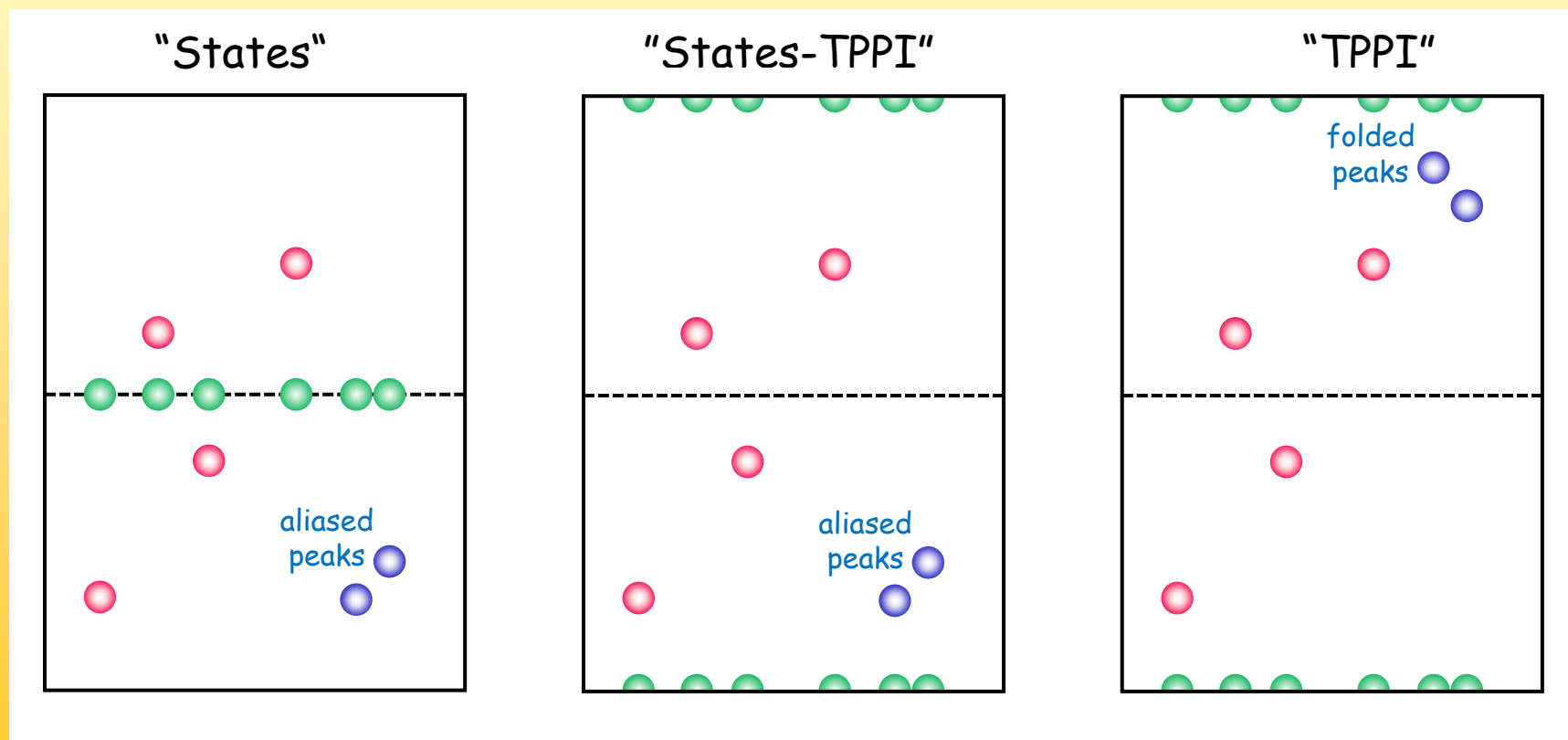
Z-Filter (ZQ-Suppression)

Z-Filter (ZQ-Suppression)

We have already discussed that neither a gradient nor phase-cycling is capable of separating z-magnetization from ZQC and thus suppressing one of them. This is a problem in several types of spectra the most prominent one is the NOESY of small molecules.

^1H 90_x t_1 90_x τ_m 90_x ϕ_{rec}

G_z *This gradient helps but does not suppress ZQC !!*
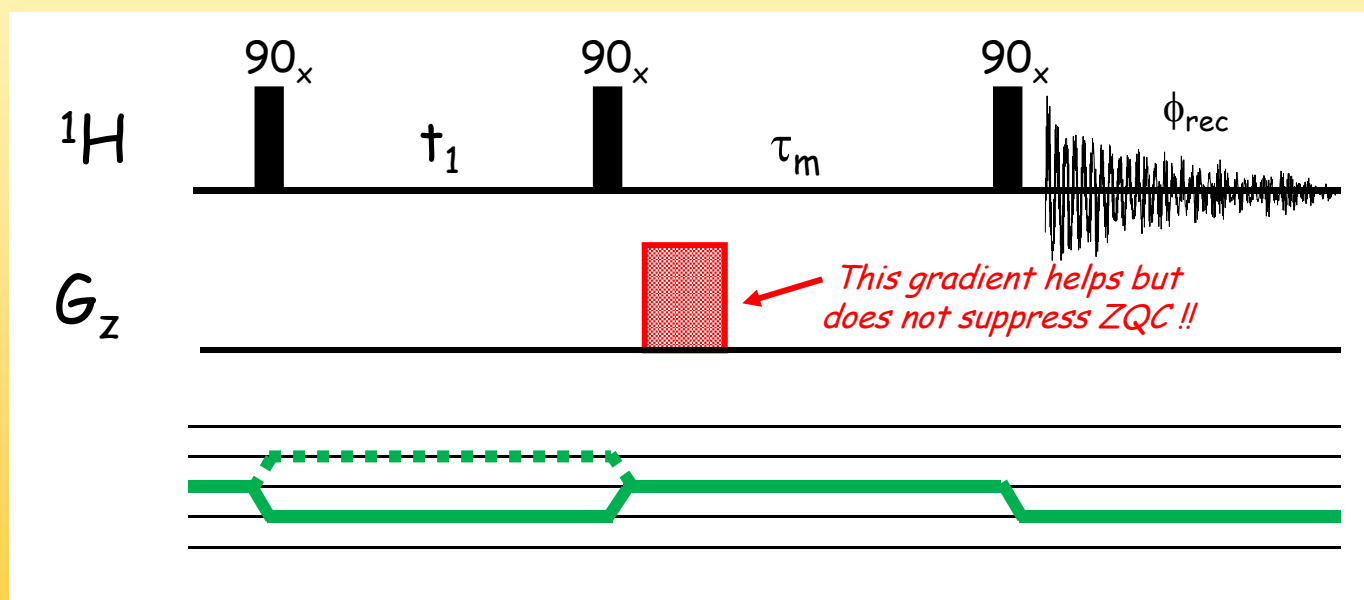
For larger molecules ZQC relax quite fast and vanish on their own

Z-Filter (ZQ-Suppression)

Why is that a problem ?

$$H_{1z} \xrightarrow{\quad 90^\circ\ H_x \quad} -H_{1y} \xrightarrow{\quad 2\pi\delta_H t_1 \quad} -H_{1y} \cos 2\pi\delta_{H1} t_1 + H_{1x} \sin 2\pi\delta_{H1} t_1$$

$$\xrightarrow{\quad \pi J_{HH} t_1 \quad} -H_{1y} \cos 2\pi\delta_{H1} t_1 \cos \pi J_{HH} t_1 + 2H_{1x} H_{2z} \cos 2\pi\delta_{H1} t_1 \sin \pi J_{HH} t_1$$

$$+ H_{1x} \sin 2\pi\delta_{H1} t_1 \cos \pi J_{HH} t_1 + 2H_{1y} H_{2z} \sin 2\pi\delta_{H1} t_1 \sin \pi J_{HH} t_1$$

$$\xrightarrow{\quad 90^\circ\ H_x \quad} \boxed{-H_{1z} \cos 2\pi\delta_{H1} t_1 \cos \pi J_{HH} t_1} - \boxed{2H_{1x} H_{2y} \cos 2\pi\delta_{H1} t_1 \sin \pi J_{HH} t_1}$$

$$+ H_{1x} \sin 2\pi\delta_{H1} t_1 \cos \pi J_{HH} t_1 - 2H_{1z} H_{2y} \sin 2\pi\delta_{H1} t_1 \sin \pi J_{HH} t_1$$

This will yield the NOESY peaks   But this contains ZQCs !!

$$\xrightarrow{\quad \tau_m\ ,\ 90^\circ\ H_x \quad} H_{1y} \cos 2\pi\delta_{H1} t_1 \cos \pi J_{HH} t_1 + H_{2y} \cos 2\pi\delta_{H1} t_1 \cos \pi J_{HH} t_1$$

$$\xrightarrow{\quad t_2 \quad} H_{1y} \cos 2\pi\delta_{H1} t_1 \cos \pi J_{HH} t_1 \cos 2\pi\delta_{H1} t_2 \cos \pi J_{HH} t_2 \quad \text{diagonal peak}$$

$$H_{2y} \cos 2\pi\delta_{H1} t_1 \cos \pi J_{HH} t_1 \cos 2\pi\delta_{H2} t_2 \cos \pi J_{HH} t_2 \quad \text{cross peak}$$

Z-Filter (ZQ-Suppression)

$2H_{1x}H_{2y} = 2\,(\tfrac{1}{2}(H_{1+} + H_{1-})\,\tfrac{1}{2i}(H_{2+} - H_{2-}) = \tfrac{1}{2i}\,[H_{1+}H_{2+} \boxed{+\ H_{1-}H_{2+}\ -\ H_{1+}H_{2-}} -\ H_{1-}H_{2-}]$

ZQC

$= \tfrac{1}{2i}\,[H_{1-}H_{2+} - H_{1+}H_{2-}] = \tfrac{1}{2i}\,[(H_{1x} - i\,H_{1y})(H_{2x} + i\,H_{2y}) - (H_{1x} + i\,H_{1y})(H_{2x} - i\,H_{2y})]$

$= \tfrac{1}{2i}\,[H_{1x}H_{2x} - i\,H_{1y}H_{2x} + i\,H_{1x}H_{2y} + H_{1y}H_{2y} - H_{1x}H_{2x} - i\,H_{1y}H_{2x} + i\,H_{1x}H_{2y} - H_{1y}H_{2y}]$

$= H_{1x}H_{2y} - H_{1y}H_{2x}$

$\xrightarrow{\ 90°\ H_x\ }$

$H_{1x}H_{2z}\cos 2\pi\delta_{H1}t_1 \sin\pi J_{HH}t_1 - H_{1z}H_{2x}\cos 2\pi\delta_{H1}t_1 \sin\pi J_{HH}t_1$

$\xrightarrow{\ t_2\ }$

$H_{1y}\cos 2\pi\delta_{H1}t_1 \sin\pi J_{HH}t_1 \cos 2\pi\delta_{H1}t_2 \sin\pi J_{HH}t_2$ diagonal peak

$-\ H_{2y}\cos 2\pi\delta_{H1}t_1 \sin\pi J_{HH}t_1 \cos 2\pi\delta_{H2}t_2 \sin\pi J_{HH}t_2$ cross peak

The position of the peaks are the same but the phase

is different and they are antiphase peaks

Z-Filter (ZQ-Suppression)

That leads to heavy distortions in the peaks (left spectrum) and prevents

a reliable integration and thus distance determination, that would be
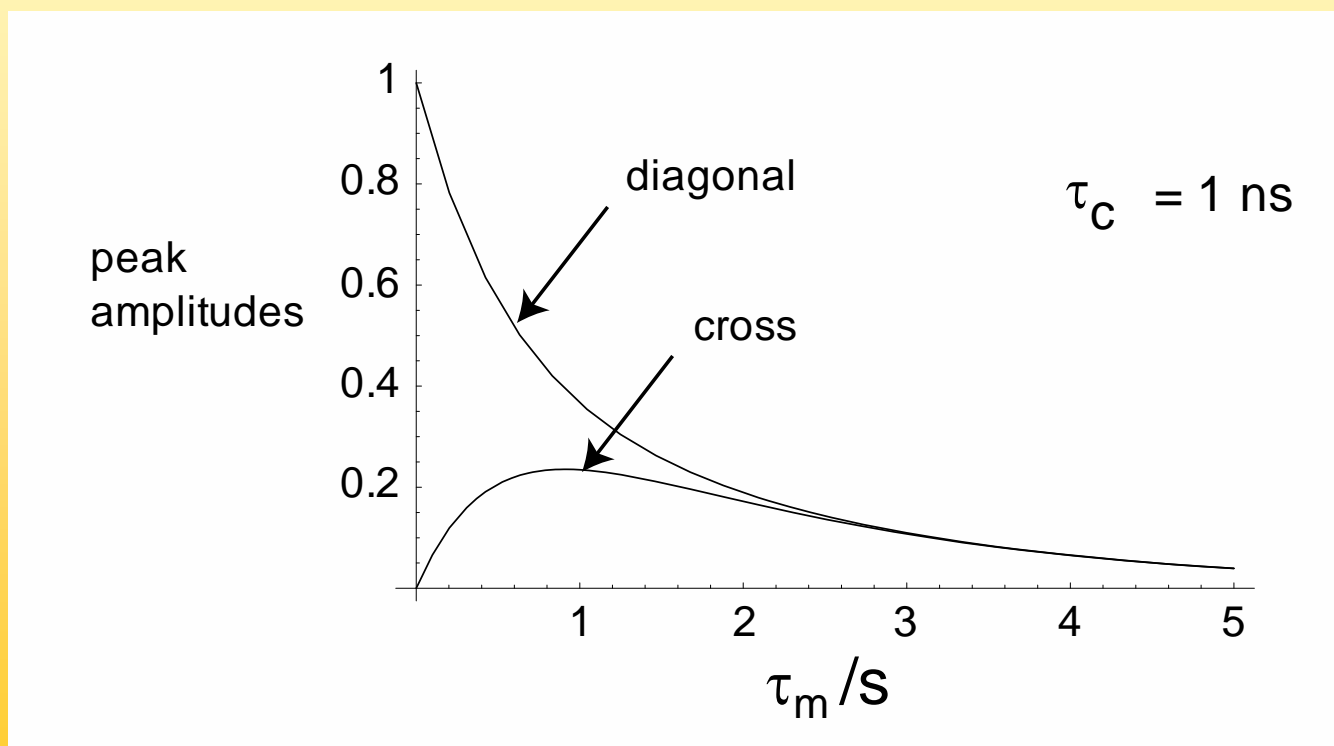
possible with the spectrum on the right
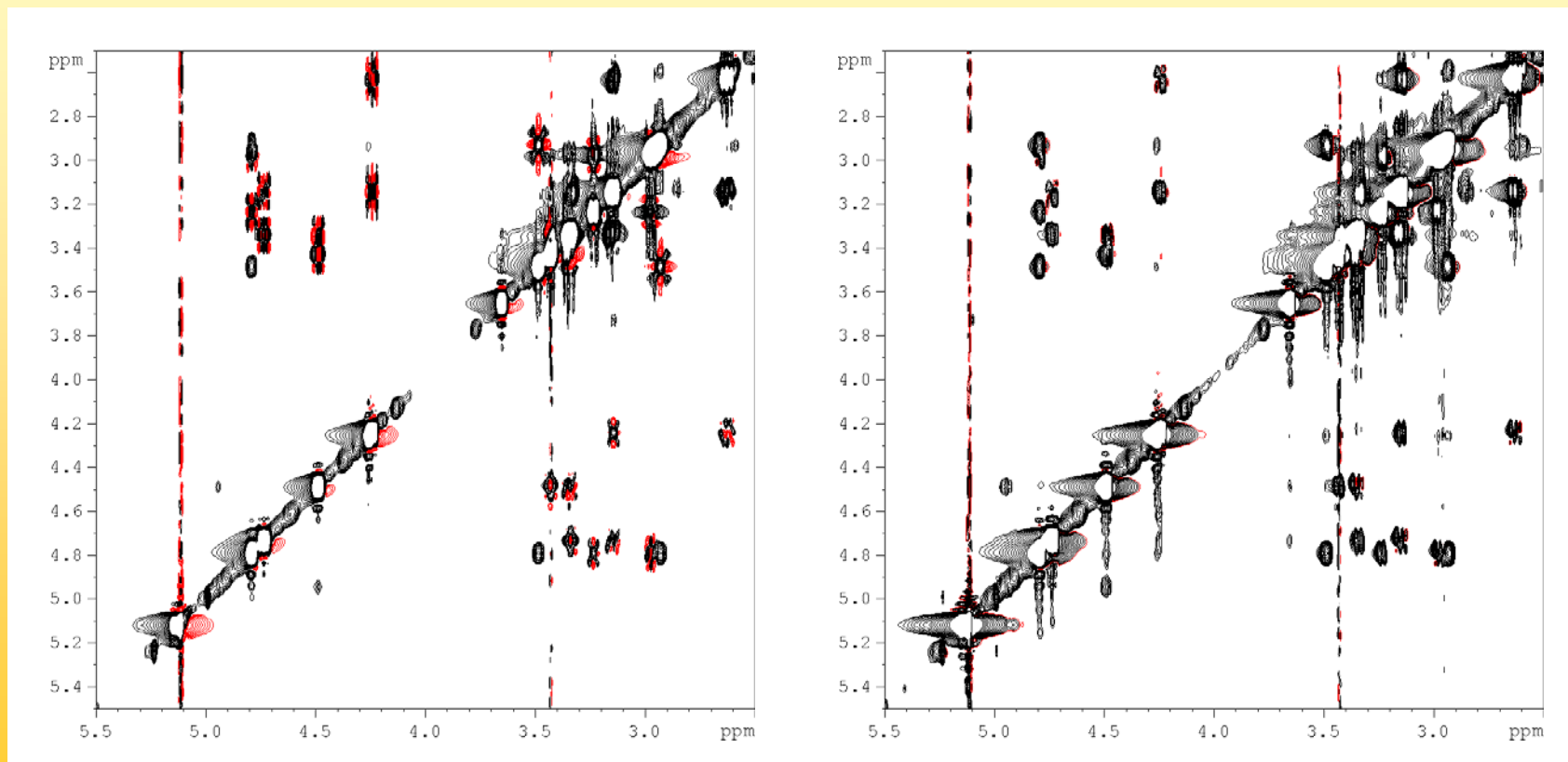
Z-Filter (ZQ-Suppression)

But there is a difference that we can exploit:

$$H_{1z} \xrightarrow{\tau_m} H_{1z} [\{1+\exp(-2\sigma\tau_m)\} \exp(-(\rho-\sigma)\tau_m)] + H_{2z} [\{1-\exp(-2\sigma\tau_m)\} \exp(-(\rho-\sigma)\tau_m)]$$

This is dependent on τ_m but not as an oscillation !

peak amplitudes

diagonal

cross

$\tau_c = 1$ ns

τ_m / s

Z-Filter (ZQ-Suppression)

$$H_{1-}H_{2+} - H_{1+}H_{2-} \xrightarrow{\tau_m} H_{1-}H_{2+} \exp(-i[\Omega_2-\Omega_1]\,\tau_m) - H_{1+}H_{2-} \exp(-i[\Omega_1-\Omega_2]\,\tau_m)$$

Whereas this oscillates with τ_m! That means that we can achieve a cancelation of the signals from ZQCs if we vary the evolution of ZQCs and add up the result. There are two ways of doing that:

Random variation of τ_m systematic movement of an 180° pulse
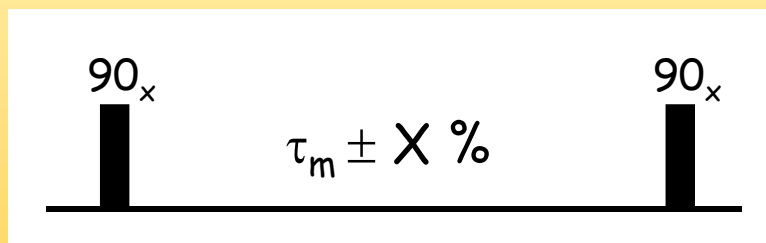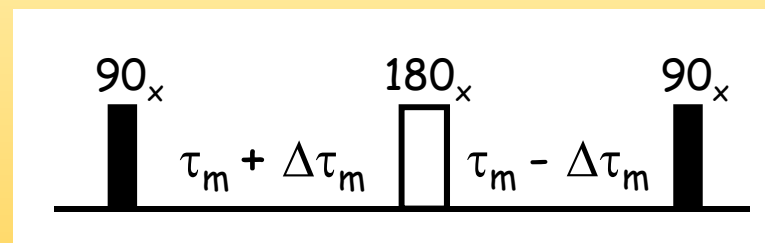
If you want to be accurate with your mixing time then the second solution is for you

---

Z-Filter (ZQ-Suppression)

But there is a potential problem: the NOESY should be executed with a phase cycle of 4, even if supported by gradients, maybe even 8 for suppression of central signals. If we now repeat every FID with a decent number of increments for τ_m then we easily end up with 80 scans or more for every FID, which makes the experiment extremely lengthy
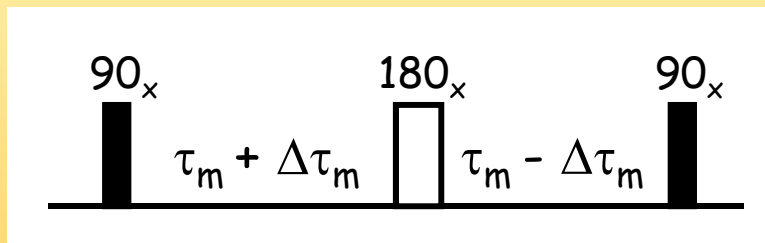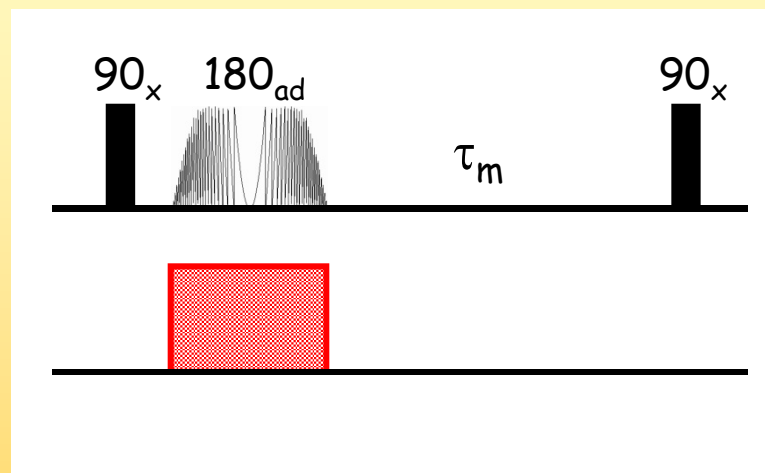

An impressive solution to that problem was designed in James Keelers group and can be found here:

Angewandte Chemie Int. Ed. **42**, 3938-3941 (2003)

Z-Filter (ZQ-Suppression)

They use a combination of an adiabatic 180° pulse and a gradient to

obtain a z-filter in one go:

To understand this we have to take a closer look at an adiabatic pulse,

that is performing an adiabatic fast passage

Z-Filter (ZQ-Suppression)

Here the offset of the pulse, i.e. the frequency with that it is executed, is changed over the length of the pulse, in a full adiabatic passage this is done from far off resonance at lower frequency to far off resonance at higher frequency (or vice versa). That influences the position of the effective field that is rotating the magnetization.
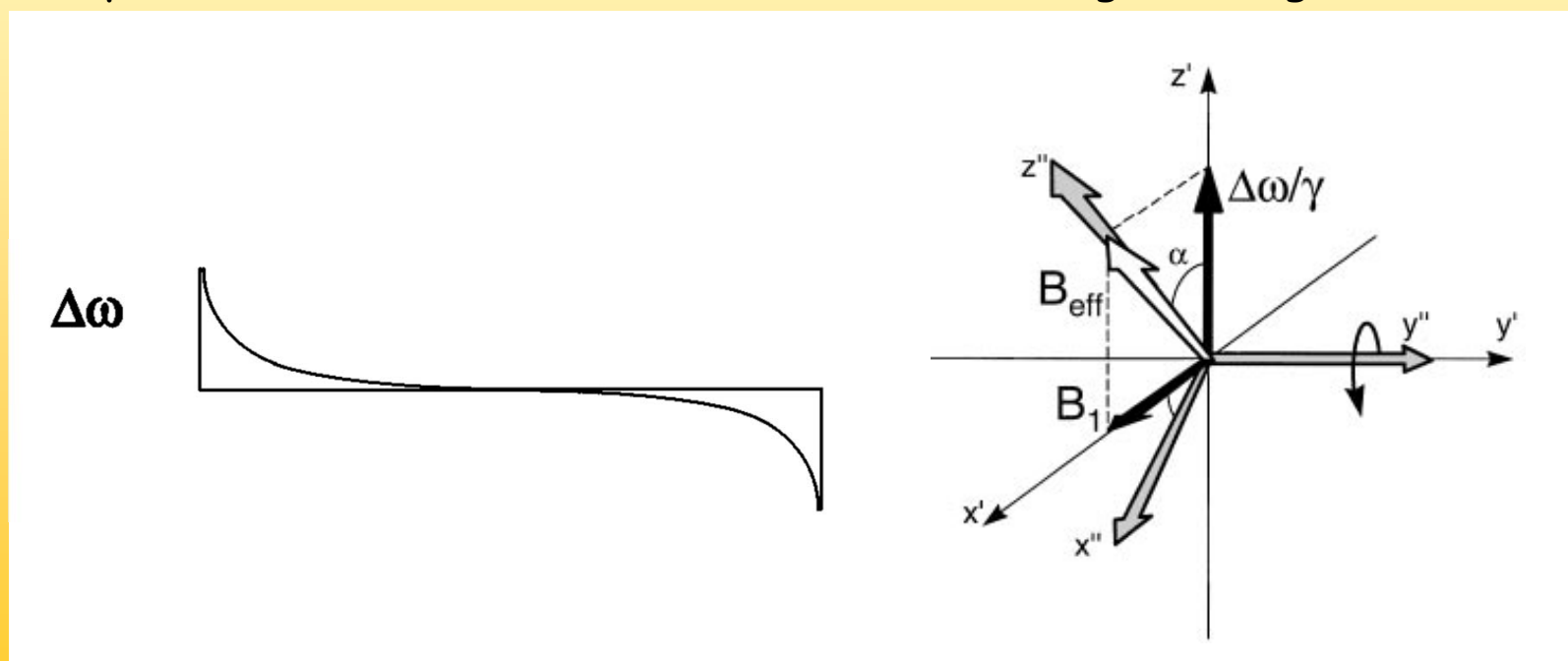
Z-Filter (ZQ-Suppression)
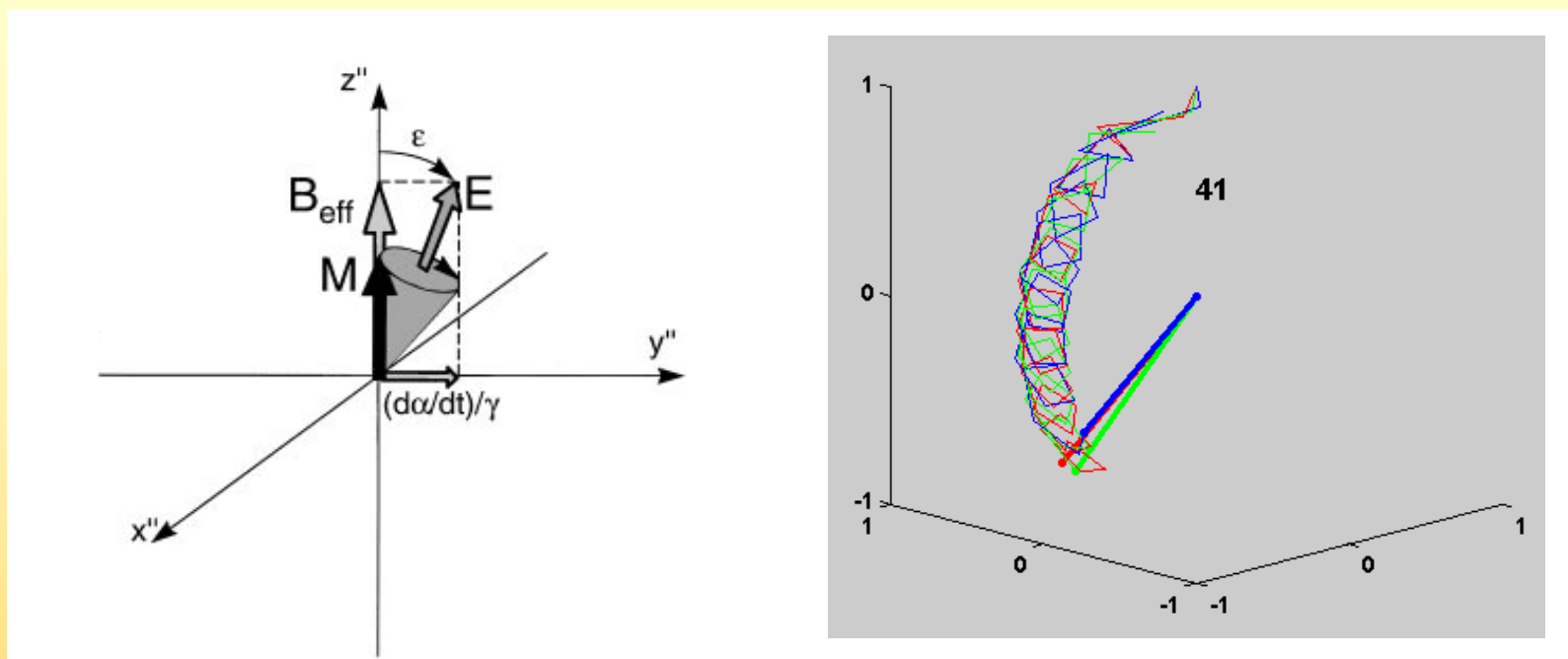
The effective field is moving from the z-axis ($\Delta\omega/\gamma$ is dominating) towards the x,y-plane (B_1 is dominating) and to the $-z$-axis in the end ($\Delta\omega/\gamma$ is dominating again) . If this is done slowly enough the "adiabatic condition" is fulfilled and the magnetization, that is rotating around the effective field, is following that path.

Z-Filter (ZQ-Suppression)

This has two consequences:

The pulse can invert magnetization over a wide range of frequencies, since it starts far off resonance from the spectral range anyway.
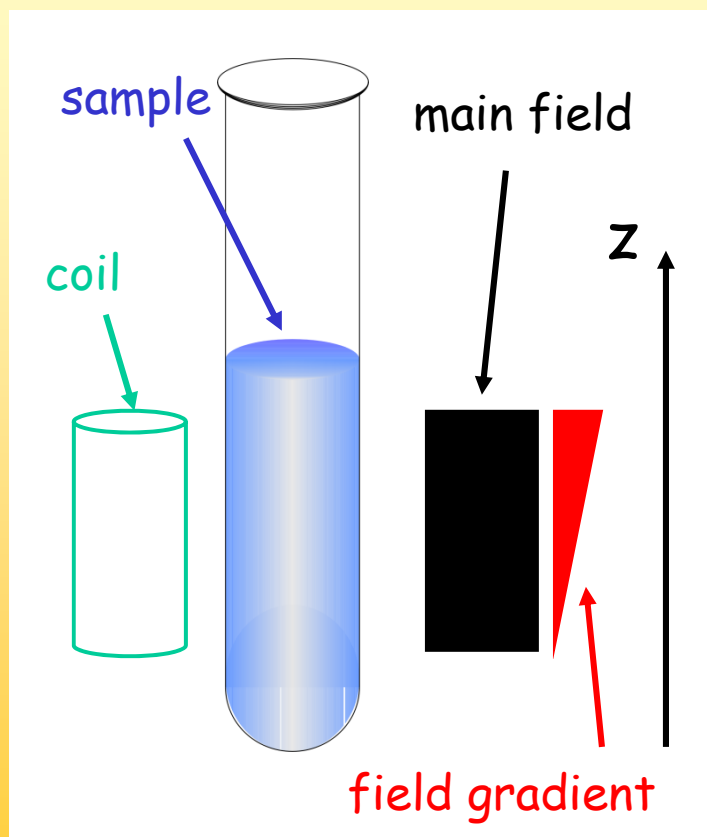
And it does not hit all magnetization vectors at the same time as a conventional pulse does.

That means a typical adiabatic pulse like a smoothed chirp can invert a range a 60 kHz but it inverts the magnetization vectors over that range "one at a time"

Gradients and coherence levels

sample

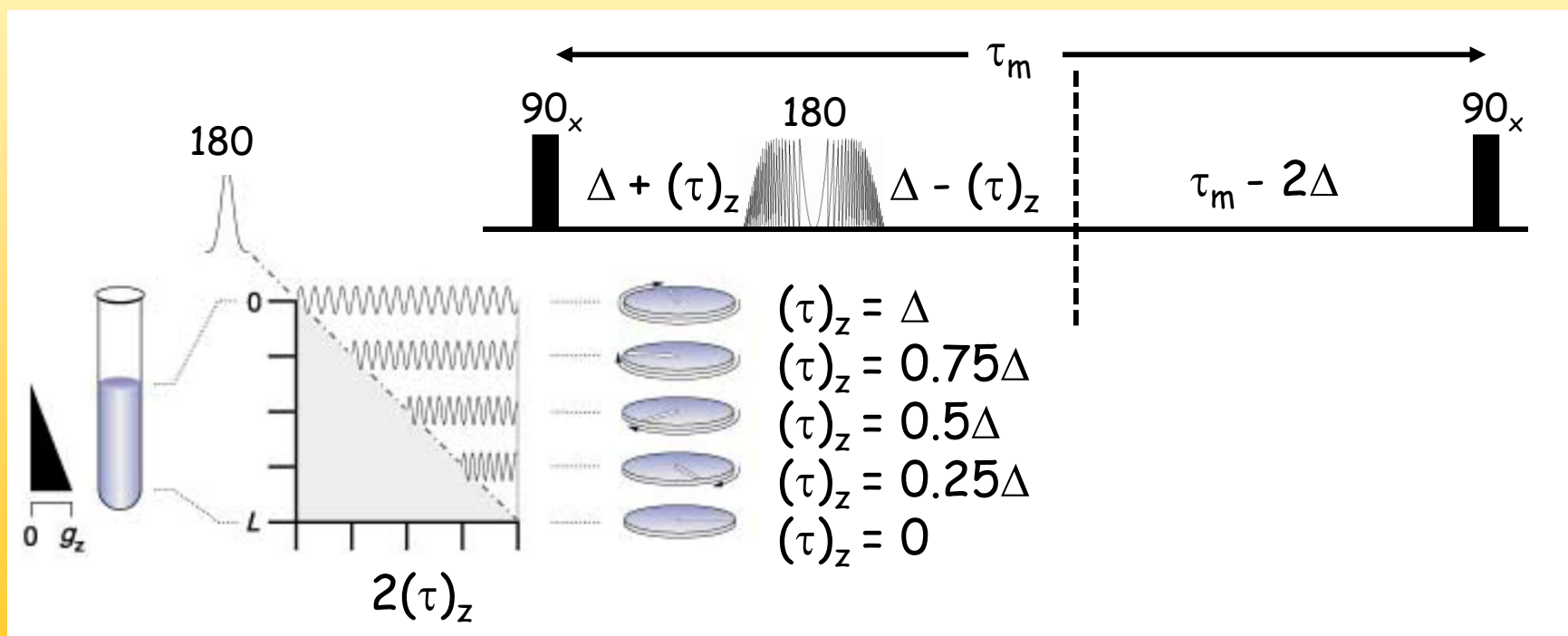main field

coil

z

field gradient
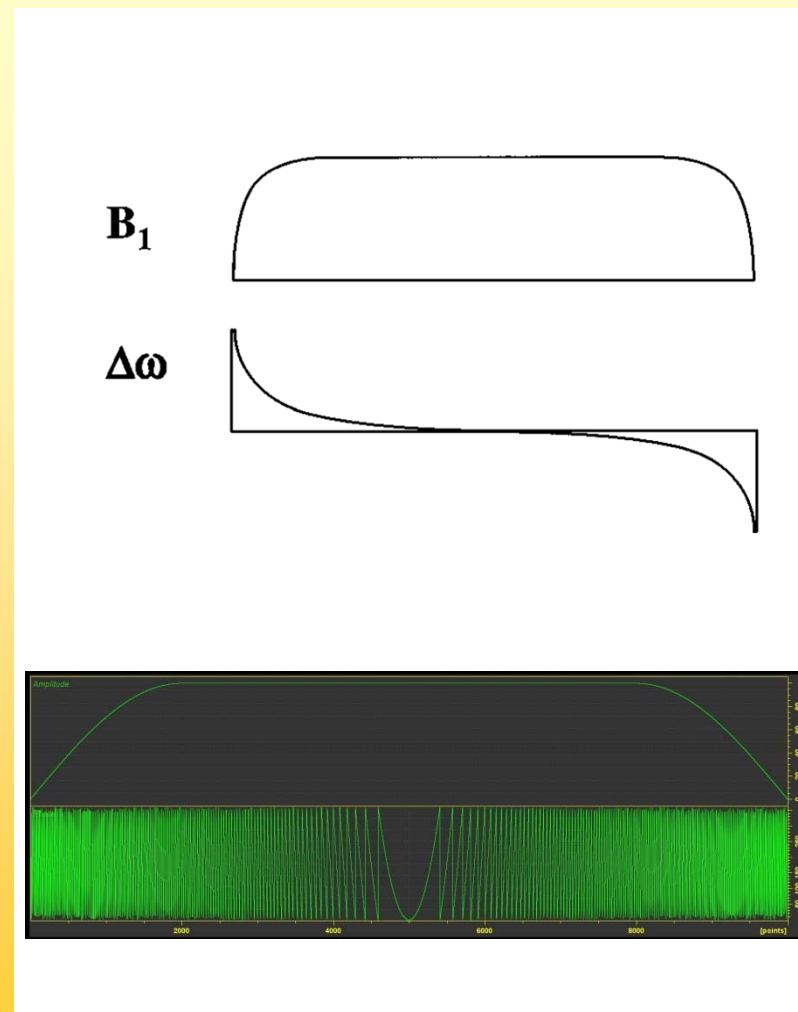
We have already calculated what a gradient does to the sample volume: We use a gradient of 5 G/cm, that means the frequencies at both ends of the sample differ by 40 kHz. If we apply an adiabatic 180° pulse during that gradient it will still invert all spins but not all at the same time, the moment of inversion will depend on the position in the sample.
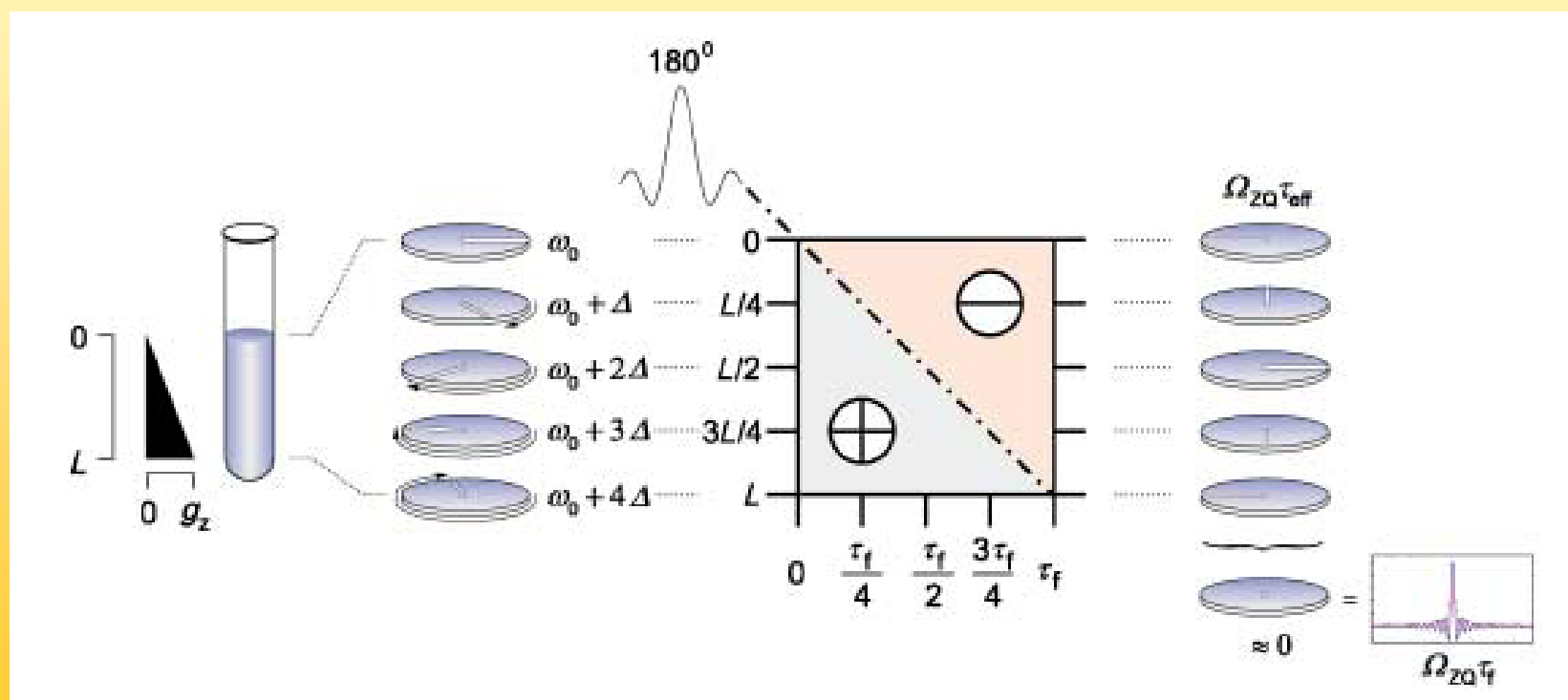
Z-Filter (ZQ-Suppression)

While the z-magnetization does not care about the inversion, the ZQCs do.
The sample is split up in infinitesimal small slices by the gradient and in
each the 180 pulse is doing its job at a different time. That means in each
slice the ZQCs are refocussed to a different degree

$$\tau_m$$

$$90_x \qquad 180 \qquad\qquad 90_x$$

$$180$$

$$\Delta + (\tau)_z \qquad \Delta - (\tau)_z \qquad \tau_m - 2\Delta$$

$$(\tau)_z = \Delta$$
$$(\tau)_z = 0.75\Delta$$
$$(\tau)_z = 0.5\Delta$$
$$(\tau)_z = 0.25\Delta$$
$$(\tau)_z = 0$$

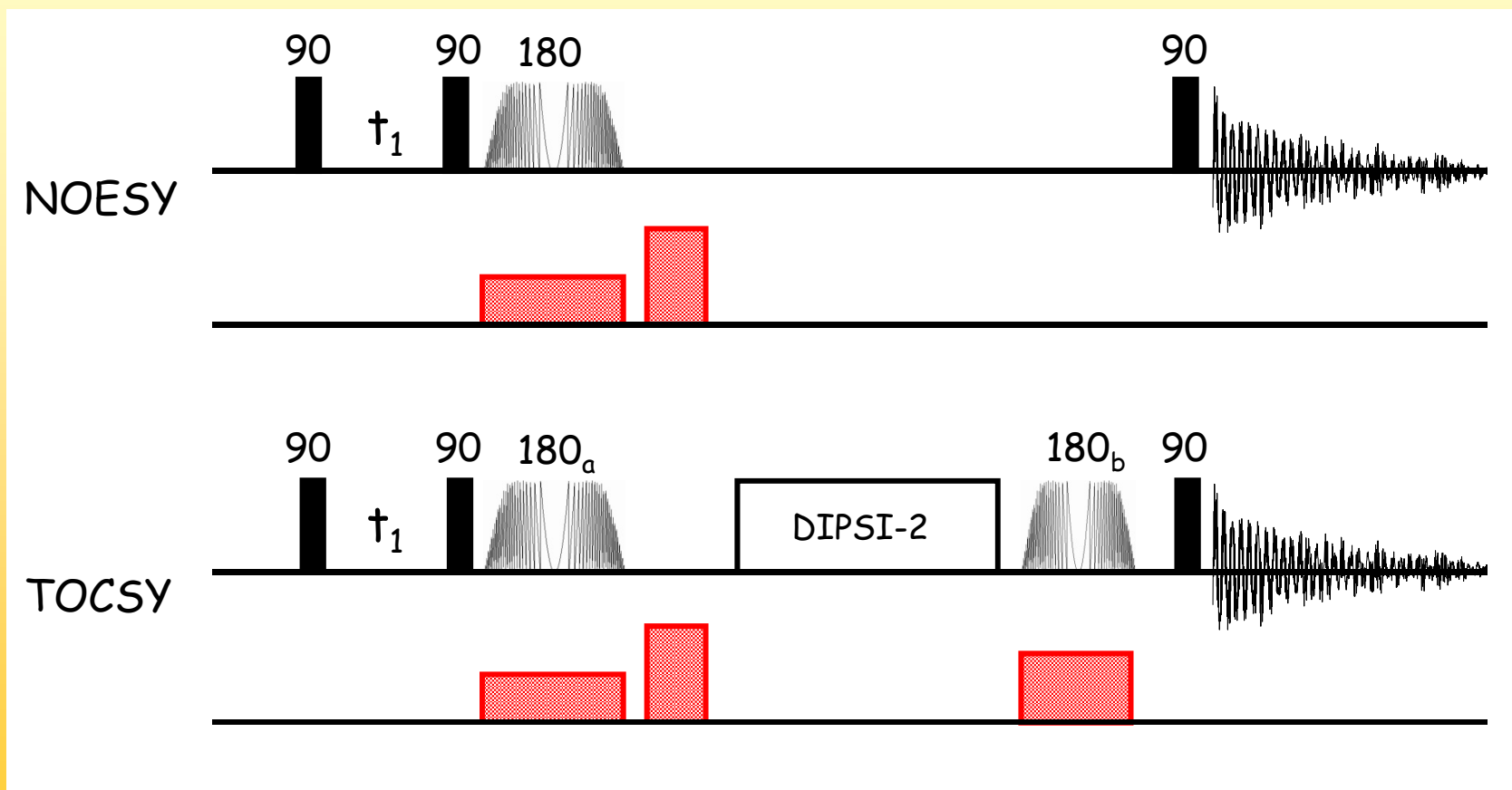$$0 \quad g_z$$

$$2(\tau)_z$$

Z-Filter (ZQ-Suppression)

And while the z-magnetization remains as if there was no 180° pulse, the sum of all ZQCs will be zero, the ZQCs are cancelled without a cumbersome repetition of the experiments beyond the requirements of signal-to-noise.
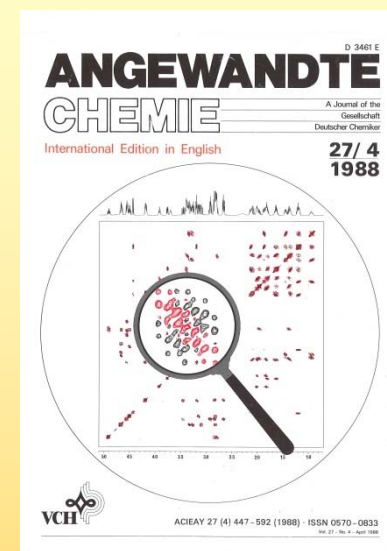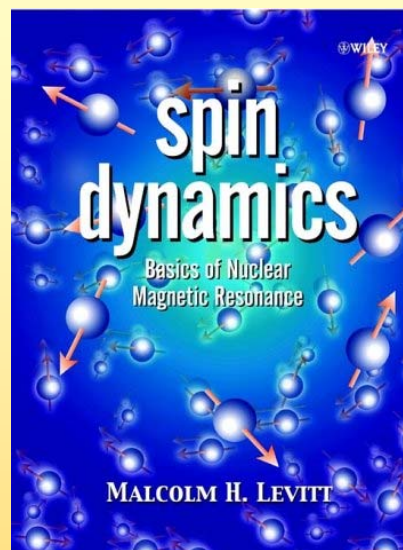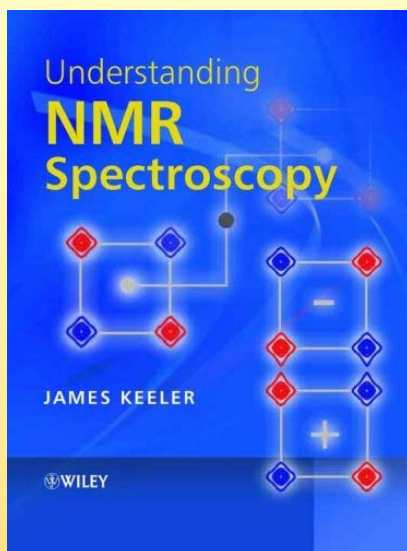
Z-Filter (ZQ-Suppression)

This can be used in a variety of experiments, for example:

„Further reading":

Questions: schmieder@fmp-berlin.de

Scripts: schmieder.fmp-berlin.info/teaching.htm

That's it