10. Phase Cycling and Pulsed Field Gradients

10.1 Introduction to Phase Cycling - Quadrature images

The selection of coherence transfer pathways (CTP) by phase cycling or PFGs is the tool that allows the observation of coherence that has traversed desired pathway. Once a pulse sequence is devised to generate a desired coherence, it remains to actively select the desired pathway through manipulation of the phase of the coherences; this is the realm of phase cycling and PFG.

Coherence selection procedures play an integral role in 2D and ND experiments. The signals that are desired are usually "contaminated" by signals arising from unwanted coherences, imperfections in the RF pulses, errors in the phase of the receiver reference frequency, and other sources of artifacts. The selection of the desired coherence and the suppression of artifacts arising from instrumental problems is accomplished by using the dependence of coherence orders on the phase of RF pulses.

As an introduction to phase cycling, let us consider the removal of some imperfections caused by instrumental problems, specifically quadrature images. The nuclear spins generate an oscillating signal in the RF coil that can be described as

$$M(e^{i\Omega t} + e^{-i\Omega t}) = 2M\cos(\Omega t) \qquad (10.1.1)$$

where M is the magnitude and Ω is the radio frequency (RF). The signal is demodulated by mixing it with the carrier RF, Ω_0. The process of demodulation subtracts the RF carrier signal from the received signal, producing the audio frequencies, which carry the information from the nuclear spins. The NMR detector is mathematically equivalent to $e^{-i\Omega t}$, a circularly polarized RF signal. Detection can be thought of as the product of the NMR signal with the detector:

$$M(e^{i\Omega t} + e^{-i\Omega t}) * e^{-i\Omega t} \qquad (10.1.2)$$

or

$$Me^{i(\Omega-\Omega)t} + Me^{-i(\Omega+\Omega)t} \qquad (10.1.3)$$

In Equation 10.1.3, $(\Omega+\Omega_{\circ})$ is the sum of two RF signals which is another RF signal; this signal is unwanted and is filtered out electronically. The difference term, $(\Omega-\Omega_{\circ})$, is the audio frequency that contains the information of the spin system.

The NMR detector is not ideal and pure circularly polarized radiation is not achievable. In the real world, the detector is contaminated with some amount of the oppositely rotating component, $e^{i\Omega t}$. This is the effect from the quadrature reference signals not having a relative phase shift of 90°. A real detector can be represented by:

$$e^{-i\Omega t} + \lambda e^{i\Omega t} \qquad (10.1.4)$$

Using this detector, we obtain from the demodulation of the NMR signal:

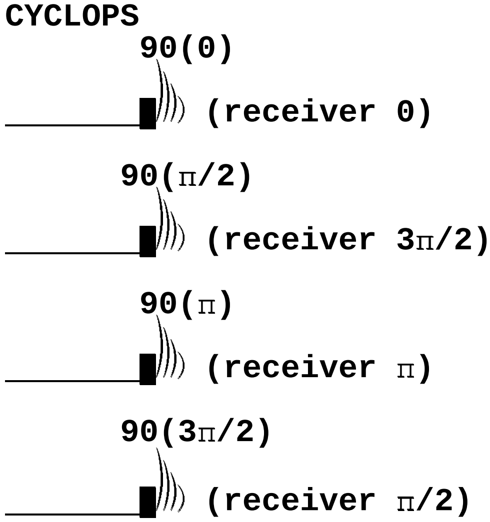
$$M(e^{i\Omega t} + e^{-i\Omega t}) * (e^{-i\Omega t} + \lambda e^{i\Omega t}), \qquad (10.1.5)$$

which can be expanded to:

$$Me^{i(\Omega-\Omega)t} + \lambda Me^{i(\Omega+\Omega)t} + Me^{-i(\Omega+\Omega)t} + \lambda Me^{-i(\Omega-\Omega)t}. \qquad (10.1.6)$$

As before the terms containing $\Omega+\Omega_o$ are RF frequencies that are eliminated by filters, but the audio frequency component, $\Omega-\Omega_o$, contains two terms at $\pm(\Omega-\Omega_o)$. Fourier transform of these signals will produce two peaks: the correct peak with magnitude M will appear at $-(\Omega-\Omega_o)$, but another peak with amplitude λM will appear at the symmetric position about the carrier frequency, $(\Omega-\Omega_o)$. This false signal is a quadrature image and is clearly undesirable. A phase cycle known as CYCLOPS is used to suppress these artifacts. The sequence consists of collecting and combining in a prescribed manner, the signals from 4 individual experiments. The phases of the excitation pulse and receiver are incremented by 90° in each experiment.

CYCLOPS



(10.1.7)

The sequences in 10.1.7 are a schematic of the CYCLOPS phase cycle procedure. In the following sections, we will analyze this procedure in detail, but we first must discuss an implementation of the product operators that is convenient for the discussion of phase cycling.

10.2 Raising and Lowering Operators

In order to understand phase cycling, it is useful to use an alternate description of the product operators. The raising, $\mathbf{I}^{+}$, and lowering, $\mathbf{I}^{-}$, operators are well known in spectroscopy. Whereas the $\mathbf{I}_x$ and $\mathbf{I}_y$ operators involve both up and down transitions between energy levels, $\mathbf{I}^{+}$ and $\mathbf{I}^{-}$ only allow transitions in one direction. $\mathbf{I}^{+}$ is the transition up and $\mathbf{I}^{-}$ is the transition down.
These operators are defined as:

$$\mathbf{I}^{+} \equiv (\mathbf{I}_x + i\mathbf{I}_y)$$
$$\mathbf{I}^{-} \equiv (\mathbf{I}_x - iI_y). \qquad (10.2.1)$$

Combining and rearranging Equations 10.2.1, one obtains

$$\mathbf{I}_x = 1/2(\mathbf{I}^{+} + \mathbf{I}^{-})$$
$$\mathbf{I}_y = 1/(2i)(\mathbf{I}^{+} - \mathbf{I}^{-}) = -i/2(\mathbf{I}^{+} - \mathbf{I}^{-}). \qquad (10.2.2\ )$$

These operators have useful properties for the description of the evolution of a spin system subjected to phase shifts. For example, consider the effect of a phase shift, $=\phi\hat{\mathbf{I}}_z=>$, on the $\mathbf{I}^{+}$ and $\mathbf{I}^{-}$ operators,

$$\mathbf{I}^{+} \ =\phi\hat{\mathbf{I}}_z=> \ ? \qquad (10.2.3)$$

This can easily be calculated by using the known rotations of the Cartesian product operators

$$(\ \mathbf{I}_x + i\mathbf{I}_y\ ) \ =\phi\hat{\mathbf{I}}_z=> \mathbf{I}_x \cos\phi + \mathbf{I}_y \sin\phi + i\mathbf{I}_y \cos\phi - i\mathbf{I}_x \sin\phi. \qquad (10.2.4)$$

This can be simplified to

$$\mathbf{I}_x (\cos\phi - i^*\sin\phi) + i\mathbf{I}_y (\cos\phi - i^*\sin\phi) = \mathbf{I}_x\, e^{-i\phi} + i\mathbf{I}_y\, e^{-i\phi} \qquad (10.2.5)$$

or further to

$$(\mathbf{I}_x + i\mathbf{I}_y)\, e^{-i\phi} = \mathbf{I}^{+}\, e^{-i\phi}. \qquad (10.2.6)$$

In summary, Equation 10.2.3 becomes

$$\mathbf{I}^{+} =\phi\hat{\mathbf{I}}_z=> \mathbf{I}^{+}\, e^{-i\phi}. \qquad (10.2.7)$$

Likewise, the transformation for the $\mathbf{I}^{-}$ operator is

$$\mathbf{I}^{-} =\phi\hat{\mathbf{I}}_z=> \mathbf{I}^{-}\, e^{i\phi}. \qquad (10.2.8)$$

A phase shift, $=\phi\hat{\mathbf{I}}_z=>$, is equivalent to the chemical shift operator, $=\Omega_I t\hat{\mathbf{I}}_z=>$, and therefore, the evolution of $\mathbf{I}^+$ and $\mathbf{I}^-$ under chemical shift can be described as:

$\mathbf{I}^+$ $=\Omega_I t\hat{\mathbf{I}}_z\Rightarrow$ $\mathbf{I}^+ e^{-i\Omega t}$
and

$\mathbf{I}^-$ $=\Omega_I t\hat{\mathbf{I}}_z\Rightarrow$ $\mathbf{I}^- e^{i\Omega t}$.

The useful property of the raising and lowering operators is that they do not mix with a Z rotation. It is the behavior of these operators under Z rotations (phase shift and chemical shift) that makes them convenient for describing the behavior of spins in a phase cycled experiment.

10.3 Phase shifted RF pulses

Phase shifted RF pulses can be thought of as a composite pulse of an X axis pulse followed by a Z axis "pulse."

$$\mathbf{I}_z \ =\pi/2\hat{\mathbf{I}}_x\Rightarrow -\mathbf{I}_y \qquad (10.3.1)$$

This is the same as a 90°_x followed by a 0°_Z pulse,

$$\mathbf{I}_z =\pi/2\hat{\mathbf{I}}_x\Rightarrow -\mathbf{I}_y =0\hat{\mathbf{I}}_z\Rightarrow -\mathbf{I}_y = i/2(\mathbf{I}^+ - \mathbf{I}^-). \qquad (10.3.2)$$

The equivalent state using the raising and lowering operators is given to show the effects of the phase shift.

With a $\pi/2$ phase shift of a $\hat{\mathbf{I}}_x$ pulse, we obtain a $\hat{\mathbf{I}}_y$ pulse. This can be simulated as an X pulse followed by a 90° Z rotation,

$$\mathbf{I}_z =\pi/2\hat{\mathbf{I}}_y\Rightarrow \mathbf{I}_x = \mathbf{I}_z =\pi/2\hat{\mathbf{I}}_x\Rightarrow =\pi/2\hat{\mathbf{I}}_z\Rightarrow \mathbf{I}_x = 1/2(\mathbf{I}^+ + \mathbf{I}^-). \qquad (10.3.3)$$

For a 90° phase shift, the $\mathbf{I}^+$ component is multiplied by -i and the $\mathbf{I}^-$ component is multiplied by i.

The 180° (Eqn. 10.3.4) and 270° (Eqn. 10.3.5) phase shifts can be described similarly:

$$\mathbf{I}_z \ =\pi/2\hat{\mathbf{I}}_{-x}\Rightarrow \mathbf{I}_y = \mathbf{I}_z =\pi/2\hat{\mathbf{I}}_x\Rightarrow =\pi\hat{\mathbf{I}}_z\Rightarrow \mathbf{I}_y = -i/2(\mathbf{I}^+ - \mathbf{I}^-) \qquad (10.3.4)$$

$$\mathbf{I}_z \ =\pi/2\hat{\mathbf{I}}_{-y}\Rightarrow \mathbf{I}_{-x} = \mathbf{I}_z =\pi/2\hat{\mathbf{I}}_x\Rightarrow =3\pi/2\hat{\mathbf{I}}_z\Rightarrow \mathbf{I}_{-x} = -1/2(\mathbf{I}^+ + \mathbf{I}^-). \qquad (10.3.5)$$

10.4 Elimination of Quadrature Images

As discussed in Section 10.1, if the signal is detected by a contaminated carrier signal then we obtain quadrature images. The signal for a X axis pulse given by

$$\lambda M e^{-i(\Omega-\Omega)t} + M e^{i(\Omega-\Omega)t}. \qquad (10.4.1)$$

Based on the phase shift behavior, we equate the NMR signal Eqn. 10.1.1, $Me^{i\Omega t}$ with M $\mathbf{I}^-$ and $e^{-i\Omega t}$ with M $\mathbf{I}^+$. With a 90° phase shift in the RF pulse, the $\mathbf{I}^+$ component or its equivalent $e^{-i(\Omega-\Omega)t}$ is multiplied by -i and the $\mathbf{I}^-$ component, $e^{i(\Omega-\Omega)t}$, is multiplied by i (Eqn. 10.3.3). Multiplication of the appropriate terms in Eqn. 10.4.1 with -i and i results in

$$-i\lambda M e^{-i(\Omega-\Omega)t} + iM e^{i(\Omega-\Omega)t} \qquad (10.4.2)$$

With a 180° phase shift in the RF we obtain

$$-\lambda M e^{-i(\Omega-\Omega)t} - M e^{i(\Omega-\Omega)t} \qquad (10.4.3)$$

and for a 270° phase shift:

$$i\lambda M e^{-i(\Omega-\Omega)t} - iM e^{i(\Omega-\Omega)t} \qquad (10.4.4)$$

The signals are acquired separately and combined in computer memory. However, we can not directly add these results since half are real and the other half are imaginary. Equations 10.4.1 and 10.4.3 and equations 10.4.2 and 10.4.4 are negatives of one another and need to be subtracted to retain the desired signal $Me^{i(\Omega-\Omega)t}$. In order to add the Eqns. 10.4.1 and 10.4.3 to equations 10.4.2 and 10.4.4, we need to multiply the even numbered equations by i to convert them to pure real. This operation is equivalent to phase shifting the receiver. Recalling Euler's formula of

$$e^{\pm iA} = \cos A \mp i \sin A, \qquad (10.4.5)$$

we obtain

$$\begin{aligned} e^{i0} &= 1, & e^{i3\pi/2} &= -i, \\ e^{i\pi} &= -1, \text{ and} & e^{i\pi/2} &= i, \end{aligned} \qquad (10.4.6)$$

which correspond to shifting the receiver phase by 0, 3π/2, π, and π/2, multiplication of equations 10.4.1 and 10.4.3 by 1 and -1, and multiplication of equations 10.4.2 and 10.4.4 by -i and i, respectively, we obtain

$$\lambda M e^{-i(\Omega-\Omega)t} + M e^{i(\Omega-\Omega)t}$$
$$-\lambda M e^{-i(\Omega-\Omega)t} + M e^{i(\Omega-\Omega)t}$$

$\lambda Me^{-i(\Omega-\Omega)t} + Me^{i(\Omega-\Omega)t}$
$-\lambda Me^{-i(\Omega-\Omega)t} + Me^{i(\Omega-\Omega)t}$. (10.4.7)

Adding equations 10.4.7, we are left with

$4^*Me^{i(\Omega-\Omega)t}$ (10.4.8)

The contaminating component, $\lambda Me^{-i(\Omega-\Omega)t}$, is eliminated along with the associated quadrature image in the spectrum. The desired component $Me^{i(\Omega-\Omega)t}$ is retained and has sum of the amplitudes from all experiments.

10.5 Phase shifts by data routing

The actual "phase shifting" of the receiver usually is not accomplished by RF phase shifts, but by specific data routing in the computer memory. As an example, consider the signal:

$e^{i\omega t} = \cos \omega t + i^*\sin \omega t$ (10.5.1)

where the cosine and sine functions represent the digitized output of two orthogonal receiver channels X (real) and Y (imaginary), respectively. A 90° phase shift is represented as $e^{i\pi/2} = i$. Multiplying the signal 10.5.1 with i yields

$i * e^{i\omega t} = i * (\cos \omega t + i^*\sin \omega t) = i * \cos \omega t - \sin \omega t$. (10.5.2)

The X channel, represented by the cosine function, is now the imaginary part of the signal and the Y channel, represented by the sine function, is the negative of the real part of the signal. A 90° phase shift in the receiver is equivalent to swapping the real and imaginary channels combined with the negation of one of them. For CYCLOPS the X and Y channels are routed to two separate memory locations in the computer representing the real and imaginary parts of the complex pair as follows:

ϕ	A	B
0°	X	Y
90°	-Y	X
180°	-X	-Y
270°	Y	-X

where the negative signs mean that the signal is subtracted from memory. This method is a perfect 90° phase shift and can not introduce errors that would occur if implemented in hardware. By taking other linear combinations of the X and Y channels, arbitrary "receiver" phase shifts can be generated in computer memory.

10.6 The Rules of Phase Cycling[22]

Specific rules are available for the construction of phase cycling regimens. By following these rules, the phase cycle for the selection of a given coherence transfer pathway can be constructed for any pulse sequence. In summary, the rules are:

1) Write down all possible changes in coherence, Δm, due to the pulse.
2) Mark the desired coherence change and place a bracket next to it.
3) Place a closing bracket after the last undesired coherence change.
4) Count the number of terms N inside the brackets.
5) Calculate the proper phase shifts using Eqn 10.6.1.

$$\phi_i = 2\pi k/N \quad k= 0,1,...,N-1 \qquad (10.6.1)$$

6) Repeat steps 1) through 5) for all other pulses in the sequence.
7) The receiver phase, ψ, is calculated for each phase cycle step i by Eqn. 10.6.2.

$$\psi = -\Sigma\, \Delta m_i\, \phi_i \qquad (10.6.2)$$

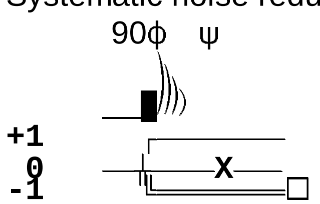
where Δm_i is the coherence order change at the ith pulse and ϕ_i is the phase of that pulse.

Several common phase cycles will now be developed using these rules.

10.7 Automatic Baseline Compensation or Systematic noise reduction.

A common problem is data that is biased by a constant signal. This type of signal can arise from DC offset in amplifiers or other systematic noise. The elimination of this type of artifact relies on the constant nature of the signal.

Systematic noise reduction



(10.7.1)

The diagram in 10.7.1 has the pulse sequence on top and below is the coherence transfer pathway (CTP).[22] The double lines in 10.7.1 mark the desired coherence transfer pathway. Single lines are coherence orders that may occur but are undesired. The x marks the pathway that is to be blocked. Magnetization at thermal equilibrium has coherence order 0 (level 0). Pulses cause transitions between levels while chemical shift and coupling evolution do not change the coherence order. By convention, we detect coherence order -1 as indicated by the box at level -1. With a perfect detector, only -1 coherence is observed.

Following the procedure of 10.6:

1) Possible changes in coherence due to the pulse

   $\Delta m = +1$
   $\Delta m = 0$
   $\Delta m = -1$.

   At thermal equilibrium the coherence order is 0. Only ±1 coherence can be excited from thermal equilibrium.

2) Mark the desired coherence change and place a bracket next it. Here the desired change is set in boldface.

   +1, 0, **-1**)

3) Place a closing bracket after last undesired coherence change, here we want to suppress 0 order coherence. A change of +1 can be ignored since with a perfect detector only the -1 coherence is detected.

   +1,(0, **-1**)

4) Count the number of terms, N, inside the brackets:

$N=2$

5) Calculate RF phase shifts for this pulse using Eqn. 10.6.1.

$\phi_i = 2\pi k/N$ k= 0,1,...,N-1

For N=2, k has values of 0 and 1.

$\phi_1 = 2\pi*0/2 = 0$

$\phi_2 = 2\pi*1/2 = \pi$

6) The receiver phase is calculated from Eqn. 10.6.2.

$$\psi = -\Sigma\, \Delta m_i\, \phi_i$$

In this case,

$$\psi_1 = -(-1)*0$$

$$\psi_2 = -(-1)*\pi$$

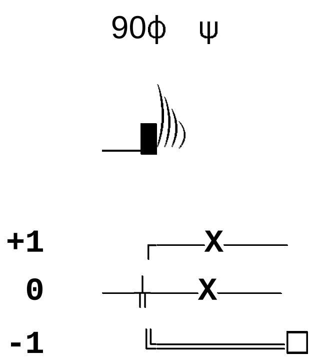
The complete phase cycling is given by the following table.

ϕ:	0	π
ψ:	0	π

Two experiments are collected. The phase of the pulse ϕ is changed from 0 to π with a corresponding change in the receiver phase of 0 to π. The phase shift in the receiver is accomplished simply by subtracting the signals arising from the two pulses.

10.8 Elimination of quadrature images and DC offset.

We now return to the elimination of quadrature images and the development of the CYCLOPS procedure (Section 10.4).



(10.8.1)

In sequence 10.8.1, a single 90° pulse excites Z magnetization at coherence order 0 to orders ±1. To eliminate quadrature images +1 coherence must be blocked. Removal of systematic noise is accomplished by blocking 0 order coherence.

Following the procedure of 10.6:

1) List the possible coherence changes.

   +1, 0, -1

2) Mark the desired coherence change and place a bracket next to it.

   +1, 0, **-1**)

3) Place closing bracket after last undesired coherence change.

(+1, 0, **-1**)

Note: +1 must be eliminated with an imperfect detector.

4) Count the number of terms inside the brackets.

N=10.

5) The RF phase shifts for this pulse are

$\phi_1 = 2\pi*0/3 = 0$
$\phi_2 = 2\pi*1/3 = 2\pi/3$
$\phi_3 = 2\pi*2/3 = 4\pi/3$.

6) Calculate the receiver phases,
$\psi_1 = -(-1)*0 = 0$
$\psi_2 = -(-1)*2\pi/3 = 2\pi/3$
$\psi_3 = -(-1)*4\pi/3 = 4\pi/3$

The phase cycle for the CTP in sequence 10.8.1 is

ϕ: 0 $2\pi/3$ $4\pi/3$
ψ: 0 $2\pi/3$ $4\pi/3$.

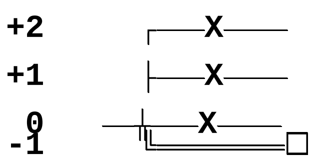
This 3-step sequence is not the normal 4-step CYCLOPS sequence (Section 10.4), which is

ϕ: 0 $\pi/2$ π $3\pi/2$
ψ: 0 $\pi/2$ π $3\pi/2$.

The main reason that the 4-step phase cycling routine arises is that 90° phase shifts are much easier to implement in hardware than are sub-90° phase shifts. The CYCLOPS procedure was invented long before sub-90° phase shifts were commonly available on spectrometers.

10.9 CYCLOPS

To arrive at the normal CYCLOPS phase cycle, consider a fictitious level at coherence order +2 that is to be eliminated. This level of coherence cannot be generated from equilibrium magnetization and therefore, need not be eliminated. However, there is nothing preventing us from removing nonexistent things. The CTP of 10.7.1 is modified by the addition of a +2 coherence order level producing the CTP in 10.9.1.



(10.9.1)

1)	List the possible coherence changes

+2, +1, 0, -1.

2)	Mark the desired coherence change

+2, +1, 0, **-1**).

3)	Place a closing bracket after last undesired coherence change

(+2, +1, 0, **-1**).

4) Count the number of terms inside the brackets

N=4.

5) The RF phase shifts for this pulse are

$\phi_1 = 2\pi*0/4 = 0$

$\phi_2 = 2\pi*1/4 = \pi/2$

$\phi_3 = 2\pi*2/4 = \pi$

$\phi_4 = 2\pi*3/4 = 3\pi/2$.

6) The receiver phases are

$\psi_1 = -(-1)*0 = 0$

$\psi_2 = -(-1)*\pi/2 = \pi/2$

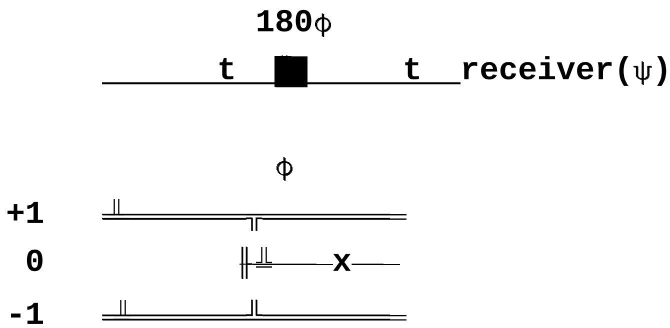
$\psi_3 = -(-1)*\pi = \pi$

$\psi_4 = -(-1)*3\pi/2 = 3\pi/2$.

This is the normal CYCLOPS routine that is commonly used in spectrometers to reduce quadrature images. As discussed in Section 10.5, the receiver phase shifts are normally implemented through data routing.

10.10 EXORCYCLE

EXORCYCLE is a phase cycling routine designed to remove imperfections in a 180° rotation of transverse magnetization. A 180° pulse on transverse coherence is equivalent to interchange of $\mathbf{I}^+$ to $\mathbf{I}^-$. Coherence transfers of 0 and ±1 need to be eliminated.



(10.10.1)

1) The desired coherence changes at the 180° pulse are

$\Delta m = \pm 2$.

2) Writing all possible changes and labeling as above

(**+2** +1 0 -1) -2.

3) This gives N = 4 terms inside the bracket, leading to phase shifts for ϕ of

$\phi_1 = 0, \pi/2, \pi, 3\pi/2$.

4) The receiver phase cycle is now calculated,

$\psi_1 = -(2) * 0 = 0$
$\psi_2 = -(2) * \pi/2 = \pi$
$\psi_1 = -(2) * \pi = 2\pi = 0$
$\psi_2 = -(2) * 3\pi/2 = 3\pi = \pi$.

The resulting EXORCYCLE phase cycle is

ϕ: 0 π/2 π 3π/2

ψ: 0 π 0 π.

To make the operation of this phase cycle a bit more transparent, let us use the product operators to show how this sequence works. Transverse magnetization is represented as:

$$-\mathbf{I}_y \cos \omega_I t + \mathbf{I}_x \sin \omega_I t \qquad (10.10.2)$$

If the 180° pulse is misset, i.e., the actual pulse angle <180° by some small angle β, here are the calculations for the four different RF phases on transverse magnetization.

$$=(\pi-\beta)\hat{\mathbf{I}}_x \Rightarrow (-\mathbf{I}_y \cos(\pi-\beta) - \mathbf{I}_z \sin(\pi-\beta)) \cos \omega_I t + \mathbf{I}_x \sin \omega_I t \qquad (10.10.3)$$

$$=(\pi-\beta)\hat{\mathbf{I}}_y \Rightarrow -\mathbf{I}_y \cos \omega_I t + (\mathbf{I}_x \cos(\pi-\beta) - \mathbf{I}_z \sin(\pi-\beta)) \sin \omega_I t \qquad (10.10.4)$$

$$=(\pi-\beta)\hat{\mathbf{I}}_{-x} \Rightarrow (-\mathbf{I}_y \cos(\pi-\beta) + \mathbf{I}_z \sin(\pi-\beta)) \cos \omega_I t + \mathbf{I}_x \sin \omega_I t \qquad (10.10.5)$$

$$=(\pi-\beta)\hat{\mathbf{I}}_{-y} \Rightarrow -\mathbf{I}_y \cos \omega_I t + (\mathbf{I}_x \cos(\pi-\beta) + \mathbf{I}_z \sin(\pi-\beta)) \sin \omega_I t \qquad (10.10.6)$$

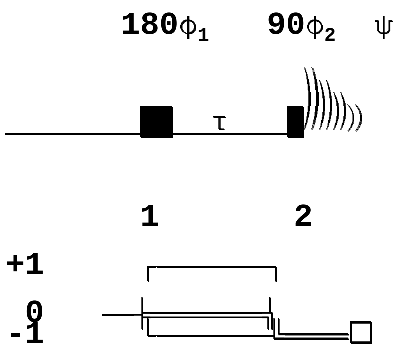
In sequences 10.10.3 and 10.10.5, and in sequences 10.10.4 and 10.10.6 the $\mathbf{I}_z$ terms are opposite in sign. Adding the acquired data from these pairs of sequences will eliminate the $\mathbf{I}_z$ component. These pairs are then subtracted to retain the desired transverse operators, $\mathbf{I}_x$ and $\mathbf{I}_y$. The elimination of the $\mathbf{I}_z$ term is not important if this sequence is followed by the acquisition period, since Z magnetization is not detected. If this sequence, however, is an element of a longer pulse sequence, other pulses can follow the spin echo segment. These pulses will rotate the undesired $\mathbf{I}_z$ into the transverse plane and cause artifacts to appear in the spectrum. This exercise shows that in any individual step of a phase cycle unwanted terms are retained, and only through combinations of phase shifted experiments, consisting of RF phase shifts and addition or subtraction in computer memory, do the desired terms co-add and the undesired terms cancel.

Another scenario that can give rise to artifacts arises if ,during the first evolution period in the spin echo sequence, some Z magnetization is generated from longitudinal relaxation. An imperfect 180° pulse then generates unwanted transverse coherence from the Z magnetization. The EXORCYCLE sequence eliminates ±1 coherence transfer; and, as can be shown with product operator analysis, the interfering transverse component is eliminated.

Phase cycling does not eliminate the undesired coherences in a single acquisition; but is only effective upon addition of the separate experiments in the computer memory. However, with respect to the interpretation of the pulse sequence, the EXORCYCLE phase cycle can be considered to eliminate the $\mathbf{I}_z$ component at this point in the sequence. No matter what occurs in the pulse sequence beyond this point, any signals that arise from the $\mathbf{I}_z$ terms will remain opposite in sign and be canceled in the computer memory.

10.11 Inversion of longitudinal magnetization

A major use for inversion of Z magnetization is to decouple (or recouple) the scalar coupling interaction between two spins (Section ####). If the inversion is not perfect, transverse magnetization is produced which can interfere with the desired coherences. The use of longitudinal inversion pulses is also important in the measurement of relaxation parameters. In the inversion recovery sequence, Sequence 10.11.1, longitudinal magnetization +Z is ideally inverted to pure -Z magnetization. Imperfections in the pulse may cause some transverse magnetization to appear. Phase cycling is used to eliminate this unwanted coherence. The desired change in coherence order is 0 in this case since both +Z and -Z are of order 0.



(10.11.1)

Proceeding as before:

ϕ_1:

$\Delta m = 0$

(+1 **0**) -1

N=2

The phases for the inversion 180° pulse are found.

$\phi_1 = 2\pi k/2$ (k=0,1)

$\phi_1 = 0,2$

The receiver phase for all RF phases is then

$\psi_1 = -(0) * \phi_1 = 0.$

If the experiment is repeated too rapidly such that there are transverse coherences that have not completely relaxed to equilibrium between experiments, then we will have coherence order changes of ±2. If $\Delta m = +2$ is also to be eliminated then

ϕ_1:

(+2 +1 **0** -1)
N=4

and the rf pulse phases are

$\phi_1 = 0, \pi/2, \pi, 3\pi/2$

with all of the receiver phases being

$\psi_1 = -(0) * \phi_1 = 0.$

The 90° read pulse transfers the Z magnetization to the transverse plane for detection and so the desired coherence order change is -1. This pulse can be phased cycled with the CYCLOPS sequence to eliminate quadrature images (Section 10.9).

The phase cycles for complicated experiments with many pulses and many different orders of coherences are easily derived by following the above rules. The procedure in Section 10.6 will be used to develop phase cycling regimens for the two dimensional experiments described in this article.

10.12 Pulsed Field Gradients and Coherence Selection

Recently, an old technique has been introduced as a complement to phase cycling. Pulsed field gradients can be used to select (or deselect) coherence transfer pathways. Recent advances in the use of pulsed field gradients for multidimensional spectroscopy have spurred the manufacturers to supply high resolution probes fitted with gradient coils.

The principle on which this technique is based is the phase sensitivity of different coherence orders. A coherence when subjected to a phase shift has a resultant phase dependent upon the order of coherence. For example,

Coherence order 1:

$$\mathbf{I}^{+} \stackrel{\phi\hat{\mathbf{I}}_z}{=\!=\!>} \mathbf{I}^{+} e^{-i\phi} \quad (10.12.1)$$

Coherence order 2:

$$\mathbf{I}^{+}\mathbf{S}^{+} \stackrel{\phi\hat{\mathbf{I}}_z + \phi\hat{\mathbf{S}}_z}{=\!=\!>} \mathbf{I}^{+}\mathbf{S}^{+} e^{-i2\phi} \quad (10.12.2)$$

Coherence order 0:

$$\mathbf{I}^{-}\mathbf{S}^{+} \stackrel{\phi\hat{\mathbf{I}}_z + \phi\hat{\mathbf{S}}_z}{=\!=\!>} \mathbf{I}^{-}\mathbf{S}^{+} e^{0} \quad (10.12.3)$$

$$\mathbf{I}_z \stackrel{\phi\hat{\mathbf{I}}_z}{=\!=\!>} \mathbf{I}_z e^{0} \quad (10.12.4)$$

In general, a coherence with order ±p will experience a phase shift according to

$$I_1^{\pm}I_2^{\pm}I_3^{\pm}. . .I_p^{\pm} \stackrel{\phi\hat{\mathbf{I}}_z}{=\!=\!>} (I_1^{\pm}I_2^{\pm}I_3^{\pm}. . .I_p^{\pm})\, e^{\mp ip\phi}. \quad (10.12.5)$$

This sensitivity to phase shift is the property that is used in phase cycling. In phase cycling, however, the phase of the RF pulses is shifted to effect a phase shift in the coherence. The phase shift of the desired coherence is then followed by an appropriate shift in the receiver phase such that the signal arising from the desired coherence constructively interferes with signals from previous experiments. If a radiofrequency Z pulse were accessible, then the coherence itself could be phase shifted. A Z pulse could be accomplished by a transient change in the Larmor frequency. This could be implemented experimentally by changing the magnetic field strength for a specified time. A spin would experience a higher (or lower) magnetic field strength and would precess at a different frequency. If calibrated properly, an arbitrary phase shift, governed by Eqn. 10.12.5, could be obtained. A more practical use of changes in the magnetic field strength is to use a magnetic field gradient. If a spatially inhomogeneous magnetic field is applied to a sample, then the same spin on different molecules in different parts of the sample will feel different magnetic field strengths and process at different frequencies.

If a 90° pulse is applied to a spin system and then a pulsed magnetic field gradient (PFG) is applied, transverse coherences in different magnetic fields (different parts of the sample) are subjected to a phase shift dependent on the strength and duration of the PFG. After the PFG the transverse spin vectors throughout the sample are dephased and, since the detected signal comes from all parts of the sample, the integrated signal is zero. The dephasing, however, can be reversed by several methods, to be described below.

10.13 Gradient Recalled Echoes

```
     90
RF   █_________receiver(ψ)

PFG     -▀--▄ --                                        (10.13.1)
```

By reversing the direction of a dephasing gradient, the transverse coherences can be rephased and the signal recovered in a gradient recalled echo. For a transverse coherence $\mathbf{I}^{+}$ generated by the 90° pulse in Sequence 10.13.1, the first PFG dephases the coherence:

$$\mathbf{I}^{+} = \gamma G(r) t \hat{\mathbf{I}}_z \Rightarrow \mathbf{I}^{+} e^{-i\gamma G(r)t} \qquad (10.13.2)$$

where γ is the magnetogyric ratio of the nucleus and G(r) represents the magnitude and distribution of the gradient field. By applying an opposite and equal PFG the coherence is recovered:

$$\mathbf{I^+}\, e^{-i\gamma G(r)t} \;\; {=}{-}\gamma G(r)t\hat{\mathbf{I}}_z{\Rightarrow} \;\; \mathbf{I^+}\, e^{-i\gamma G(r)t} * e^{i\gamma G(r)t} = \mathbf{I^+} \tag{10.13.3}$$

If the time between the application of the PFGs is long enough for something to happen to the spin such that it does not "see" a field of the same magnitude and opposite polarity, then the coherence remains dephased and does not contribute to the final detected signal. For example, if molecular diffusion occurs such that during the time between the PFGs the molecule moves from its initial position in the sample to a different position that experiences a significantly different magnetic field during the second PFG, then the rephasing gradient will not be completely effective in recovering the signal (Eqn 10.13.4).

$$\mathbf{I^+} = \gamma G(r)t\hat{\mathbf{I}}_z{\Rightarrow} \;\; \mathbf{I^+}\, e^{-i\gamma G(r)t} {=}{-}\gamma G'(r)t\hat{\mathbf{I}}_z{\Rightarrow} \;\; \mathbf{I^+}\, e^{-i\gamma G(r)t} * e^{i\gamma G'(r)t} = \mathbf{I^+} e^{i\gamma[G'(r) - G(r)]t} \tag{10.13.4}$$

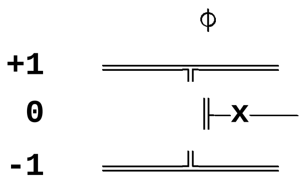
The phase introduced by the first PFG is not canceled by the second PFG and thus the signal is not completely refocused. This effect been used for solvent suppression, taking advantage of the rapid diffusion of water compared to macromolecules.

10.14 PFGs and the Spin Echo Sequence

Consider the spin echo sequence discussed in Section 10.10. The EXORCYCLE sequence requires four separate experiments to eliminate artifacts arising from imperfections in the 180° pulse. Elimination of the same artifacts can be accomplished in a single experiment by using PFGs.

180ϕ

```
    t  ██  t  receiver(ψ)
```



(10.14.1)

In this sequence, $\mathbf{I}^+$ coherence is transferred to $\mathbf{I}^-$ and vice versa by the 180° pulse. As described in Section 10.10, an imperfect pulse will transfer some $\mathbf{I}^+$ to $\mathbf{I}_z$, which may cause artifacts in the final spectrum. EXORCYCLE removes the $\mathbf{I}_z$ component by shifting the phase of the 180° pulse and thus the phase of the coherence.

The phase cycle can be easily replaced by using pulsed field gradients.

```
           180φ
RF      t  ██  t  receiver(ψ)

PFG   ---■-----■---
```

(10.14.2)

We will follow a $\mathbf{I}^+$ coherence through Sequence 10.14.2. The first PFG dephases the coherence as:

$$\mathbf{I}^+ = \gamma G(r) t \hat{\mathbf{I}}_z \Rightarrow \mathbf{I}^+ e^{-i\gamma G(r)t}. \quad (10.14.3)$$

The 180° pulse transforms $\mathbf{I}^+$ to $\mathbf{I}^-$,

$$\mathbf{I}^+ e^{-i\gamma G(r)t} \overset{\pi \hat{\mathbf{I}}_x}{\Longrightarrow} \mathbf{I}^- e^{-i\gamma G(r)t} \quad (10.14.4)$$

and finally the second PFG, which is identical to the first PFG, rephases the $\mathbf{I}^-$ coherence.

$$\mathbf{I}^- e^{-i\gamma G(r)t} \quad = -\gamma G(r)t\hat{I}_z \Rightarrow \; \mathbf{I}^- e^{-i\gamma G(r)t} * e^{i\gamma G(r)t} = \mathbf{I}^- \qquad (10.14.5)$$

The inverse sensitivity of the $\mathbf{I}^+$ and $\mathbf{I}^-$ coherences to the gradient induced phase shift causes the signal to refocus in the two identical PFGs. Any imperfection in the 180° pulse will produce $\mathbf{I}_z$ magnetization from gradient-dephased transverse magnetization present before the RF pulse (Sequence 10.14.3). The undesired $\mathbf{I}_z$ magnetization is labeled with the dephased transverse magnetization that occurred during the PFG.

$$\mathbf{I}^+ e^{-i\gamma G(r)t} \quad = \beta\hat{I}_x \Rightarrow \; \mathbf{I}_z \; e^{-i\gamma G(r)t} \sin(\beta) \qquad (10.14.6)$$

If there is another RF pulse later in the experiment, the transverse magnetization created from the Z magnetization of Eqn. 10.14.6 will retain the dephased information and, in the absence of a rephasing gradient, will not contribute to the final signal.

$$\mathbf{I}_z e^{-i\gamma G(r)t} \quad = \pi/2\hat{I}_x \Rightarrow -\mathbf{I}_y e^{-i\gamma G(r)t} \qquad (10.14.7)$$

For Z magnetization that is present before the imperfect 180° pulse, any generated transverse magnetization will be dephased by the second PFG.

Pulsed field gradients also can be used to remove the phase cycling necessary to select a given coherence. They can also be used to select either the +**I** or **-I** coherence for magnitude-mode quadrature detection. PFGs promise to be an extremely useful tool in NMR spectroscopy.