

Nuclear Magnetic Resonance (NMR)

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1 Introduction

Nuclear magnetic resonance (NMR) is a physical phenomenon in which nuclei in a magnetic field absorb and re-emit electromagnetic radiation. It is a widely used method in material and food science, just as in spectroscopy, chemistry, biology etc. It has a history of more than 70 years. NMR is also routinely used in advanced medical imaging techniques, such as in magnetic resonance imaging (MRI).

2 Theoretical background

There are two possible ways to introduce the fundamentals of NMR: 1) phenomenological, in which we consider the magnetization vector, as a classical physical variable, 2) quantum mechanistic description in which we consider the individual nuclear magnetism as the eigenvalues of the Zeeman–Hamilton operator and keep track of the time evolution of it. One can show that the above two descriptions are equivalent, but technically the former approach is easier and more expressive, thus we will discuss NMR in that classical way.

A magnetic moment inserted into a magnetic field interacts with that field in such a way that the magnetic moment experiences a torque due to the field. A consequence of the torque is that the magnetic moment starts to precess around the magnetic field. This is called the *Larmor-precession* that has an angular frequency of $\omega = \gamma \cdot B_0$, where B_0 is the magnetic field strength, and γ is the so-called *gyromagnetic ratio* unique to the nucleus. E.g. for proton $\gamma(^1\text{H}) = 2\pi \cdot 42.576 \text{ MHz/T}$.

The macroscopic magnetization vector (\mathbf{M}) is the magnetic moment in unit volume. The time evolution of \mathbf{M} is described by the *Bloch-equations* (1). These equations describe two different kind of interaction. One is due to the vector product $\mathbf{M} \times \mathbf{B}$ leading to precession and the other is the exponential relaxation to the equilibrium value. We consider the z axis pointing along the static B_0 field. M_0 is the equilibrium value of the magnetization vector. It is parallel with the static magnetic field thus has no x and y component.

T_1 and T_2 are the relaxation times. The magnetization vector decays in the x - y plane according to T_2 , and relaxes to the equilibrium value according to T_1 . Due to historical reasons T_1 and T_2 are called *spin-lattice* and *spin-spin* relaxation times, respectively. One can also call them *longitudinal* and *transverse* relaxation times, respectively.

$$\begin{aligned}\frac{dM_z(t)}{dt} &= \gamma \cdot (\mathbf{M}(t) \times \mathbf{B}(t))_z - \frac{M_z(t) - M_0}{T_1} \\ \frac{dM_x(t)}{dt} &= \gamma \cdot (\mathbf{M}(t) \times \mathbf{B}(t))_x - \frac{M_x(t)}{T_2} \\ \frac{dM_y(t)}{dt} &= \gamma \cdot (\mathbf{M}(t) \times \mathbf{B}(t))_y - \frac{M_y(t)}{T_2}\end{aligned}\tag{1}$$

In an NMR experiment a macroscopic sample is inserted into a homogeneous static field of several Tesla. Then a macroscopic magnetization parallel with the field will be induced. Then we apply a much smaller magnetic field (B_1 , with amplitude of several mT) that rotates about the z axis at the Larmor-frequency. B_1 creates a torque on the magnetization vector though it is much weaker than that from B_0 . Since B_1 rotates at the same frequency as the magnetization this will cause the magnetization to flip. It is much easier to visualize this effect when we use the rotating frame representation. Let us designate the laboratory Cartesian axes as x, y, z and the rotating frame axes as x', y', z' . We might also use the notations X, Y and Z designating the rotating frame. This frame rotates at the Larmor-frequency thus B_1 (which is perpendicular to B_0) seems to stay along let's say X . Accordingly the magnetization vector rotates around B_1 at an angular frequency $\omega_R = \gamma \cdot B_1$. This is called the *Rabi-precession*. Apply this small field for a time τ . This will cause the magnetization to flip by an angle of $\omega_R \cdot \tau$. We describe the given pulses by this angle.

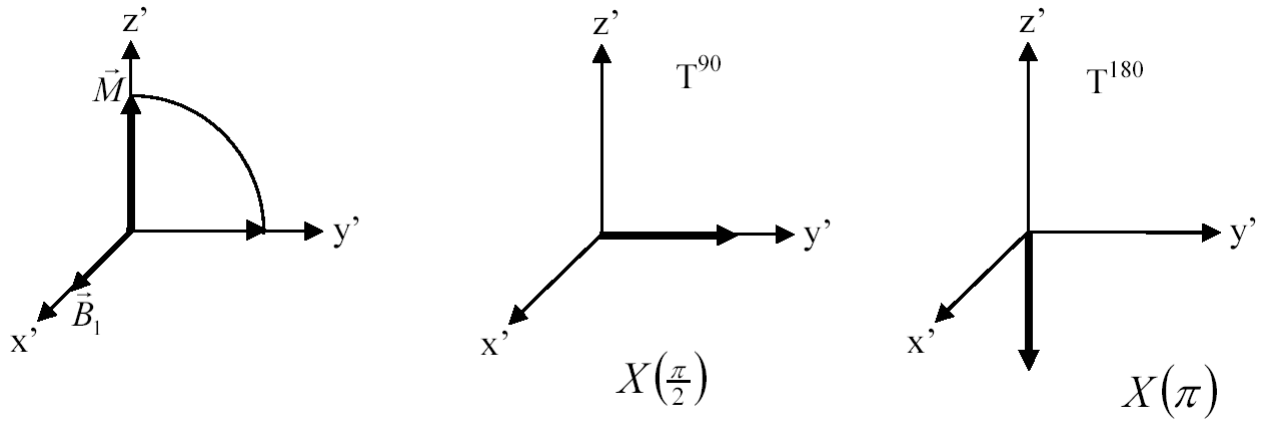


Figure 1: The basic process of pulse NMR. With a pulse one can flip the magnetization vector by an arbitrary angle just as 90° or 180° .

2.1 NMR signal

B_1 is created by the transmitter coil that surrounds the sample. The rf magnetic field generated in the coil is perpendicular to the static field. After the rf field B_1 is turned off, the magnetization will precess freely. In a coil (that can be the same one that was used to generate the B_1 field or it could be a separate receiver coil) with its axis perpendicular to the static field, this precessing magnetization will induce an rf current at the Larmor-frequency. This is the signal that we can detect. But what is the magnitude of the signal? Assume that the sample fills the volume of the receiver coil. The voltage induced in the coil is:

$$U = \mu_0 M A N \omega_L,$$

where μ_0 is the vacuum permeability, M is the magnetization of the sample, A is the area of cross-section of the coil, N is the number of turns and ω_L is the Larmor angular frequency.

What is the magnetization of the sample? According to Curie's law it can be written:

$$M = \frac{\rho_0 \gamma^2 \hbar^2 I(I+1)}{3k_B T} B,$$

where $\rho_0 = \frac{N_{\text{spin}}}{V_{\text{sample}}} = \frac{1}{V_{\text{cell}}}$ is the spin density, I is the spin (which is $1/2$ in the case of proton), k_B is the Boltzmann-constant and T is the temperature in Kelvin. It is easy to see that the Curie-susceptibility is

$$\chi_{\text{Curie}} = \frac{\mu_0 \gamma^2 \hbar^2 I(I+1)}{3k_B T \cdot V_{\text{cell}}}.$$

It is a very small susceptibility. Consider an example! Let's calculate the magnetization of $100 \mu\text{l}$ water inserted into a static field of $B = 7 \text{ T}$. First calculate the spin density! That is, the number of protons (hydrogen nuclei) in unit volume. The density of water and its molar mass is known ($\rho_w = 1000 \frac{\text{kg}}{\text{m}^3}$, $M_w = 18 \frac{\text{g}}{\text{mol}}$) and we know that every water molecule contains two hydrogen atoms. The spin density is:

$$\rho_0 = \frac{2N}{V} = \frac{2N_A \cdot \frac{m}{M_w}}{V} = \frac{2N_A \cdot \rho_w}{M_w} = \frac{2 \cdot 6 \cdot 10^{23} \frac{1}{\text{mol}} \cdot 1000 \frac{\text{kg}}{\text{m}^3}}{0,018 \frac{\text{kg}}{\text{mol}}} = 6,7 \cdot 10^{28} \frac{1}{\text{m}^3}.$$

Assume the temperature is 300 K thus the magnetization:

$$M = \frac{6,67 \cdot 10^{28} \frac{1}{\text{m}^3} \cdot (2\pi \cdot 42,58 \frac{\text{MHz}}{\text{T}})^2 \cdot (1,05 \cdot 10^{-34} \text{ Js})^2 \cdot \frac{1}{2} \cdot (\frac{1}{2} + 1)}{3 \cdot 1,38 \cdot 10^{-23} \frac{\text{J}}{\text{K}} \cdot 300 \text{ K}} \cdot 7 \text{ T} = 0,022 \frac{\text{A}}{\text{m}},$$

The magnetic moment of this sample is $\mu_v = M \cdot V = 0,022 \frac{\text{A}}{\text{m}} \cdot 10^{-7} \text{ m}^3 = 2,2 \cdot 10^{-9} \text{ Am}^2$. What amount of iron corresponds this magnetic moment? Since iron is ferromagnetic the magnetic moment in a unit cell is $g\mu_B$. To have the same magnetic moment, the number of iron atoms:

$$N_{\text{Fe}} = \frac{\mu_w}{g\mu_B} = \frac{2,2 \cdot 10^{-9} \text{ Am}^2}{1,855 \cdot 10^{-23} \text{ Am}^2} = 1,186 \cdot 10^{14}$$

The mass of this amount of iron:

$$m_{\text{Fe}} = M_{\text{Fe}} \cdot \frac{N_{\text{Fe}}}{N_A} = 55,85 \frac{\text{g}}{\text{mol}} \cdot \frac{1,186 \cdot 10^{14}}{6 \cdot 10^{23}} = 11 \text{ ng}$$

It is an immensely small amount of iron! You can see now how small magnetizations can we detect! Let the number of turns be $N = 10$, and the diameter of the cross-section of the coil is 5 mm, the Larmor-frequency is 300 MHz. The induced voltage is:

$$U = \mu_0 M A N \omega_L = 4\pi \cdot 10^{-7} \frac{\text{Vs}}{\text{Am}} \cdot 0,022 \frac{\text{A}}{\text{m}} \cdot (2,5 \cdot 10^{-3} \text{ m})^2 \pi \cdot 10 \cdot 2\pi \cdot 300 \cdot 10^6 \frac{1}{\text{s}} = 10 \text{ mV}$$

2.2 FID

A B_1 field of the correct amplitude and duration to produce a rotation of 90° is called a 90° (or a $\pi/2$) pulse. Consider now this pulse. Immediately following it, the magnetization lies along the rotating y' axis, and relaxes due to several mechanisms. This is called a FID (Free Induction Decay). Now the measured voltage decays exponentially only if the frequency of the transmitter was exactly the same as the Larmor-frequency of the irradiated spins. In general we see an oscillating signal that has an exponential envelope. On the other hand the time constant of the exponential decay of the envelope is not T_2 from the Bloch-equations since the magnetic field B_0 is not perfectly homogenous. Thus, some nuclei precess faster than others and the magnetization dephases in the $x'-y'$ plane. The decay of the signal will be exponential with a time constant of T_2^* , called the reversible relaxation time. (The T_2 is also called as irreversible relaxation time.) Between experiments one should wait at least $10 \cdot T_1$ in order to let the magnetization to relax to the equilibrium value. There are cases when they intentionally wait less then $10 \cdot T_1$, e.g. in MRI experiments to produce image with T_1 contrast.

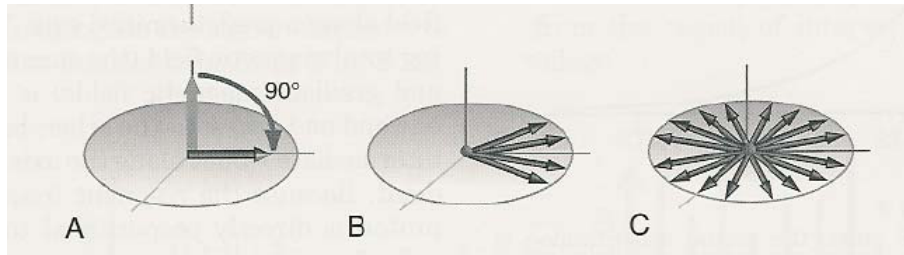


Figure 2: The scheme of FID. After a $\pi/2$ pulse the frequency of the detected signal is $(\omega_L - \omega)/2\pi$ (where $\omega/2\pi$ is the frequency of the transmitter). The signal decays exponentially with a time constant of T_2^* due to field inhomogeneity.

2.3 FT-NMR

In NMR technique the measured signal is the function of time. Thus the Fourier transform of the signal gives the spectrum in the frequency-domain. It is important to understand the concept of complex Fourier transformation (or double-channel Fourier transform).

The definition of the Fourier-transform:

$$\hat{x}(\omega) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} x(t) \cdot e^{-i\omega t} dt$$

(where $\hat{x}(\omega)$) is the Fourier transform of the signal $x(t)$. Even if $x(t)$ is a real signal the transformed one is complex in general. Thus we have two functions, the real and the complex part of the transformed signal. We will see later that the frequency of the measured signal can be negative. Strictly speaking, it is important to detect a signed frequency which is signed according to the Larmor-frequency (if it is less than the Larmor-frequency, it will be negative). If the original signal is real, then the real part of the transformed signal is even and the imaginary part of that is odd. So we can write that $\hat{x}(-\omega) = \hat{x}(\omega)^*$, where * denotes the complex conjugate. This shows that if we had only one real X channel then the sign of the frequency can not be determined¹.

One can solve this problem by using the double-channel Fourier transform. The measured signal is not only one time-dependent signal. It contains another one shifted by 90° in a given frequency of $\omega_{LO}/2\pi$. You can think of it as a vector that has two components. You have to measure both components in order to get the vector. We consider the two time-dependent signals as the real and imaginary parts of the complex signal $x(t)$. After the Fourier transform the sign of the frequency is unambiguous.

The figure below shows two examples. If the FID is an exponential decay in the real channel and zero in the imaginary channel then the Fourier transform of the FID is a Lorentzian signal centered to the zero frequency.² This is the case when the NMR transmitter frequency ($\omega_{LO}/2\pi$) exactly matches the Larmor frequency of the nuclei ($\omega_L/2\pi$). In general we see a signal that has an exponentially decaying envelope shown in the second figure below. The phase shift between the two channels is exactly 90°. The frequency of the oscillation is the difference between the NMR frequency and the Larmor frequency, $(\omega_L - \omega_{LO})/2\pi$. The Fourier transform of this lineshape is also a Lorentzian, centered to the frequency $(\omega_L - \omega_{LO})/2\pi$. As you can see, the center of the Fourier transform lineshape is the Larmor frequency of the nuclei. A common practice is to consider the Larmor frequency as the zero frequency and to measure the shift in ppm.³

¹Similar to this is when you see the projection of an orbiting object. You can not determine whether it rotates clockwise or anticlockwise unless you see both the x and y projections.

²This is the reason why the Lorentzian function is special.

³That is, the frequency shift in Hz divided by the Larmor frequency in MHz. ppm stands for *parts per million*, ie, 10^{-6} .

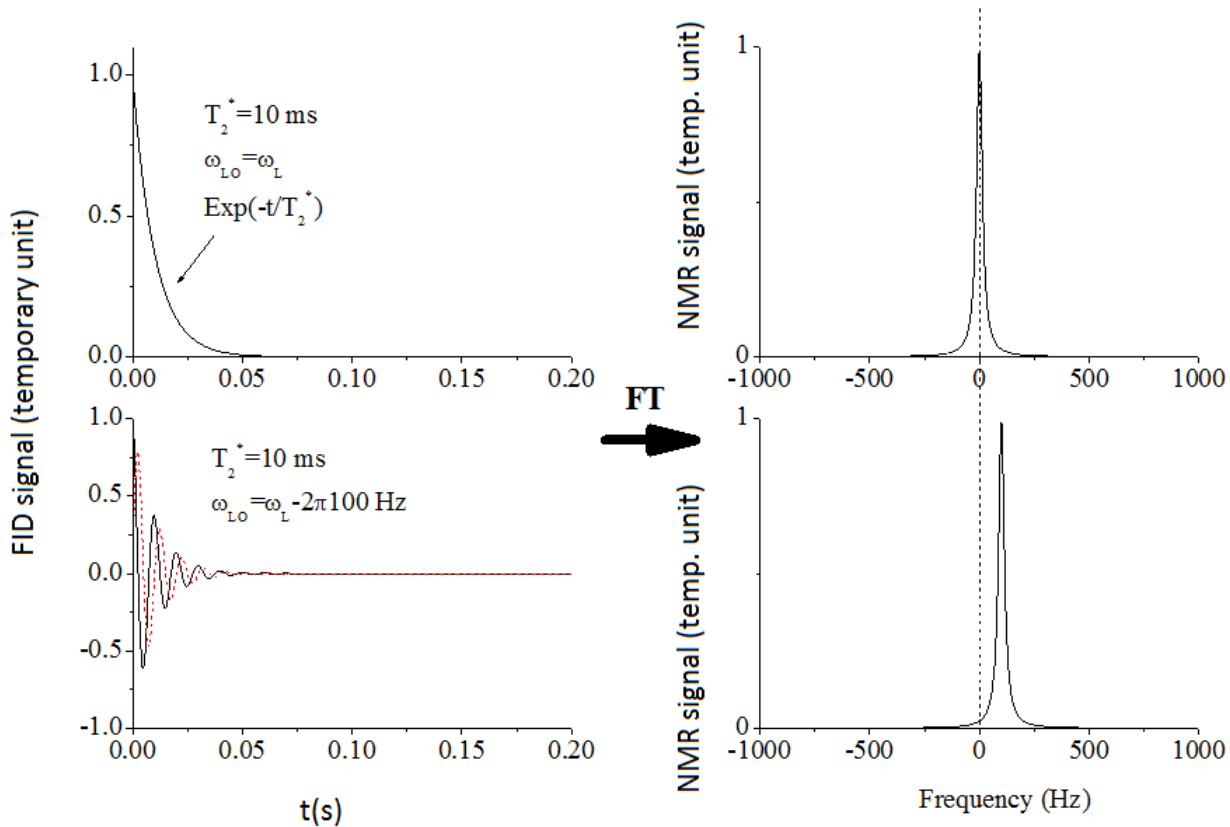


Figure 3: Fourier transforms of two different FID signals. The left side shows the time domain and the right side shows the frequency domain. The solid black and dashed red lines show the detected signals shifted by 90° with respect to each other.

We should mention here how the NMR spectrum parameters depend on the digitizing parameters. The receiver unit of the NMR spectrometer resembles of a custom oscilloscope. It measures with a given digitizing rate, f_0 , and gets N data points. The spectrum thus has frequency values from $-f_0/2$ to $f_0/2$. The spectral resolution is f_0/N .

2.4 Spin-echo

The so-called *spin-echo* technique was developed to remove the effect of the applied field inhomogeneity. Suppose that a 90° pulse is applied along x' at time 0 to a spin system for which magnetic field inhomogeneity is the major contribution to T_2^* . Shortly thereafter, the spin isochromats will have dephased in the $x'-y'$ plane, although the individual spin isochromats have not yet dephased. Suppose at a time τ later, a 180° pulse is applied along the x' axis. Any magnetization along the z direction would simply be inverted to the $-z$ direction and be of no consequence. Of the magnetization remaining in the $x'-y'$ plane each one of the spin isochromats would be rotated 180° about the x' axis. As a consequence, those spin isochromats which had gotten ahead of the average spin isochromats by a certain angle are now behind the average of the pack of spin isochromats by the same amount. Those spin isochromats which were going slower than average and had gotten behind the rotating y' axis are now ahead of the rotating y' axis by the equivalent amount. Therefore, following the 180° pulse, the spin isochromats begin to rephase to form a net magnetization as the rapid isochromats catch up with the slow ones. The result is that the magnetization becomes refocussed along the $-y'$ axis at time 2τ and it will cause an inverted spin echo, as shown in the sketch below. It is also possible to get spin echoes by applying the 180° pulse along the y' axis in the rotating frame. The refocussing will then take place along the y' axis so the echo will have the same sign as the FID. You can see a nice simulation here: http://en.wikipedia.org/wiki/Spin_echo

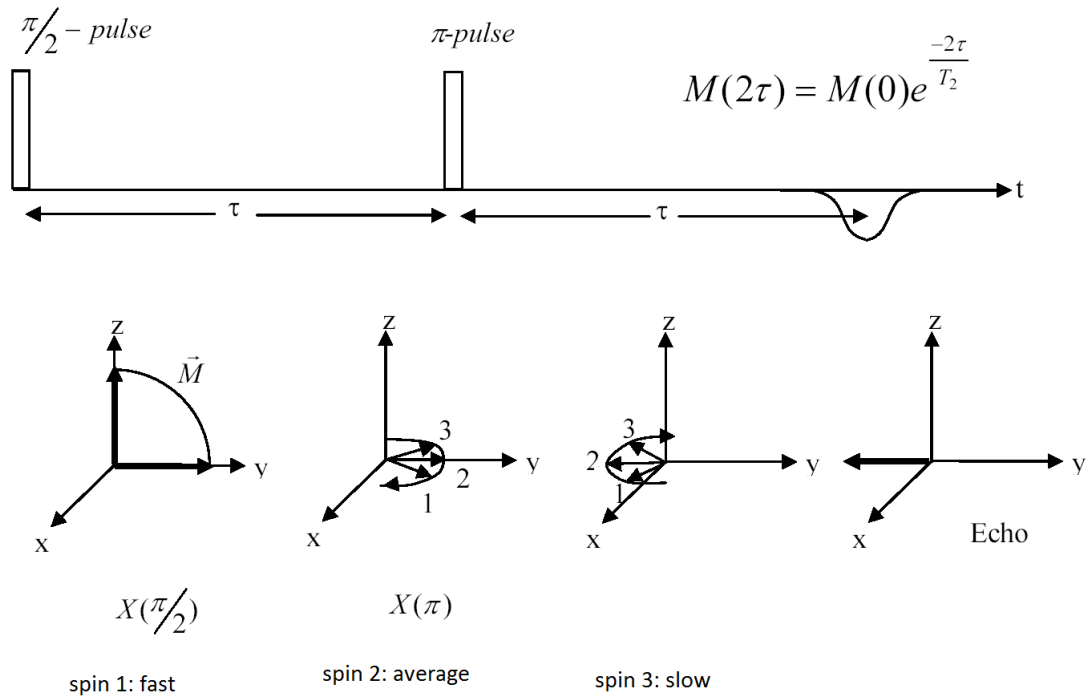


Figure 4: The spin-echo. After a $\pi/2$ pulse applied along the x' axis we get an FID along the y' axis. After a time delay of τ a π pulse is applied which will cause the spins to rephase.

The gradient echo is a common method in MRI. A magnetic field gradient is created inside the magnet (the magnetic field points to the z direction but the magnitude is space-dependent). Thus the Larmor frequency is space-dependent and we see a much faster dephasing of the spins. After a short delay the gradient is inverted and a gradient echo is formed analogue to the spin echo.

2.5 The CP pulse sequence

On exact resonance in an inhomogeneous field, the 90° pulse yields an FID with a time constant T_2^* . At a time τ later, a 180° pulse is applied and the echo maximum occurs at time 2τ , since the time required for rephasing the spin isochromats equals the time it took for dephasing. Because the spin echo arises from magnetization that has regrouped along the $-y'$ axis, the echo will be inverted compared to the FID. Another 180° pulse at time 3τ will result in another echo at time 4τ and this will be right side up. One can continue to apply 180° pulses with a spacing of 2τ with echoes occurring between each of the pulses. This spin echo train is called a Carr–Purcell (CP) spin echo train (Carr and Purcell, 1954). The echo amplitude maxima should decay with the time constant T_2 , the intrinsic spin-spin relaxation time, which is the time it takes for the magnetization to decay in the x - y plane in the absence of any external field inhomogeneity.

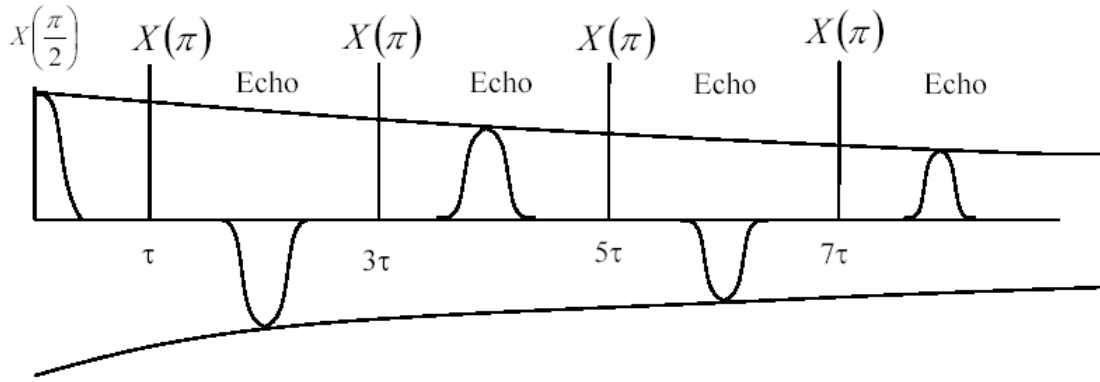


Figure 5: The Carr-Purcell echo train. π pulses are applied with a spacing of 2τ . The echo amplitude decays with time constant T_2

2.6 The CPMG pulse sequence

In practice, Carr-Purcell echo trains usually result in measured T_2 's that are too short because of cumulative errors of each pulses not being exactly 180° pulses and of B_1 inhomogeneity which spreads out the magnetization in a plane containing B_0 and B_1 . One way to compensate for these errors is to alternate the phase of each 180° pulse by 180° phase shifts as shown below. The first 90° pulse occurs with the rotating B_1 field along the rotating x' axis. The first 180° pulse, however, would have its rotating B_1 field along the Y axis. The second 180° pulse would have the rotating B_1 field along the rotating $-Y$ axis and so on. In this way, any pulse length errors are cancelled on alternate echoes.

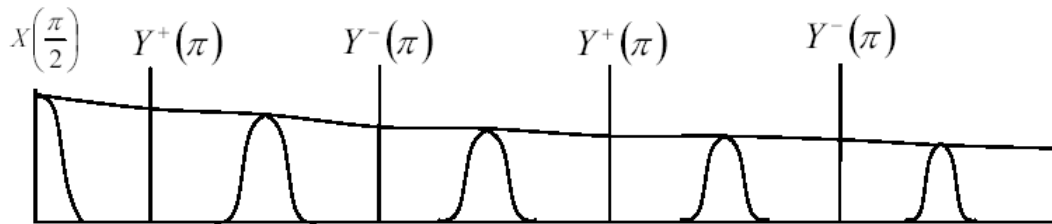


Figure 6: The CPMG echo train. All the echoes have the same sign since the echoes are always formed along the same direction in the rotating frame. This is a slight inconvenience compared to the bipolar CP echoes which have no baseline ambiguity.

2.7 Inversion recovery

In order to measure the spin-lattice relaxation time T_1 the nuclear spins have to be prepared in some non-equilibrium configuration and then, after some waiting period during which the spins are allowed to relax, a pulse monitors the state of the spins. The recovery of the nuclear spin population is monitored as a function of the waiting time.

In inversion recovery the first pulse (π pulse) inverts the spin population (and thus the magnetization) and the recovery therefore goes from $-M_0$ to M_0 where M_0 is the thermal equilibrium magnetization attainable only after waiting for a time much longer than T_1 . The second pulse ($\pi/2$ pulse) measures the magnetization after the waiting period. Specifically, the magnetization after waiting for a time τ is given by

$$M(\tau) = M_0 \cdot (1 - \exp(-\tau/T_1))$$

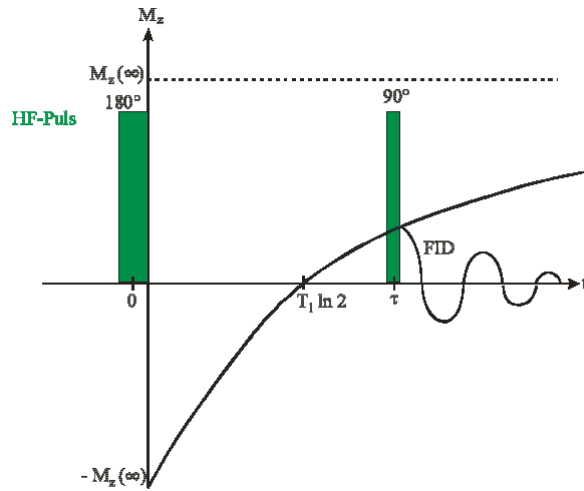


Figure 7: The inversion recovery sequence. The first $\pi/2$ pulse prepare the nuclear spins and then, after some waiting period during which the spins are allowed to relax, the second pulse monitors the state of the spins.

2.8 Phase cycling

There are several imperfections in the NMR circuit (Just as dead time, ringing, offset problems, etc.). To remove some of these effects the so-called phase cycling method is used. Consider a straightforward example. The digitizer circuit creates an offset after the pulse. This offset will distort the spectrum at the zero frequency. This component however can be removed by systematically varying the phase of pulses in a pulse sequence and that of the receiver coil. Consider a FID. If we measure it two times, with the first pulse points along x' at the first experiment and $-x'$ in the second, after subtracting the signals from each other there will be no offset as you can see in the figure below. In the programming language of the Bruker instrument one can write this as follows:

$$\Phi_1 = 0 \ 2$$

$$\Phi_{31} = 0 \ 2$$

Where Φ_1 is the phase of the first pulse, Φ_{31} is the phase of the receiver. 0, 1, 2, 3 denotes the coordinates X , Y , $-X$ and $-Y$, respectively.

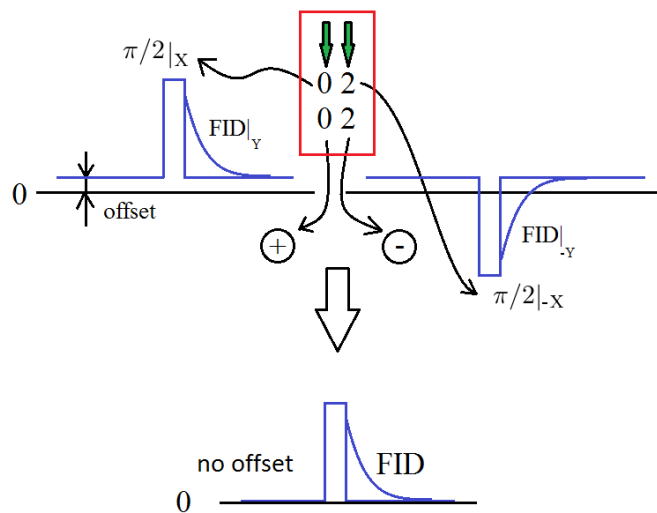


Figure 8: phase cycling in the case of a FID

In the following example we make a spin echo experiment. We want to remove the first FID. The syntax to do this is the following simple code:

$$\Phi_1 = 0 2$$

$$\Phi_2 = 0 1$$

$$\Phi_{31} = 0 0$$

Φ_2 is the direction of the π pulse. The disadvantage of this sequence is that although the FID was removed, the π pulse remained just as the offset.

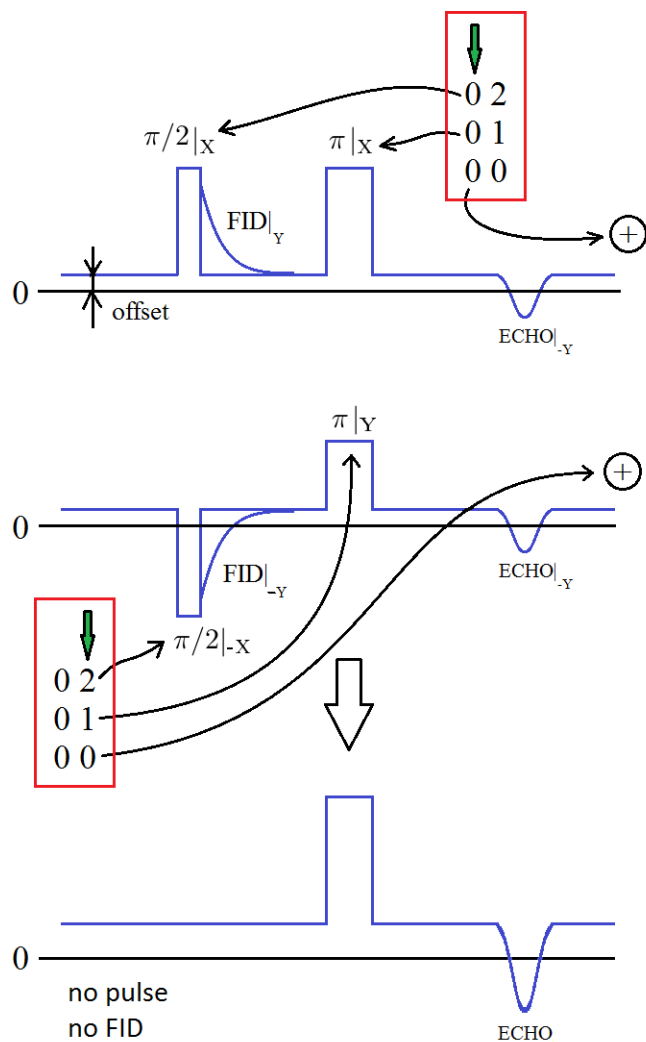


Figure 9: phase cycling in spin echo experiment.

An improved version of the upper experiment is the following. We take 4 measurements thus removing the FID, the pulses and the offset. What remains is only the echo signal.

$$\begin{aligned}\Phi_1 &= 0\ 0\ 0\ 0 \\ \Phi_2 &= 0\ 2\ 1\ 3 \\ \Phi_{31} &= 0\ 0\ 2\ 2\end{aligned}$$

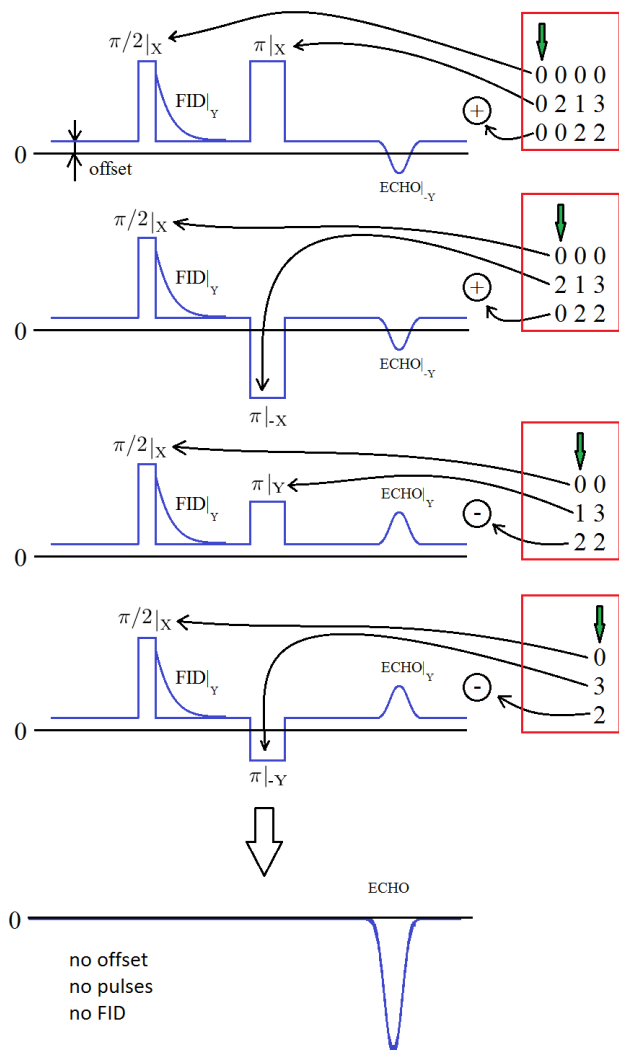


Figure 10: modified phase cycling for spin echo sequence.

One can show that it is worthy to permute the phases as shown below.

$$\begin{aligned}\Phi_1 &= 0\ 0\ 0\ 0\ 1\ 1\ 1\ 1\ 2\ 2\ 2\ 2\ 2\ 3\ 3\ 3\ 3 \\ \Phi_2 &= 0\ 2\ 1\ 3\ 1\ 3\ 2\ 0\ 2\ 0\ 2\ 0\ 3\ 1\ 3\ 1\ 0\ 2 \\ \Phi_{31} &= 0\ 0\ 2\ 2\ 1\ 1\ 3\ 3\ 2\ 2\ 0\ 0\ 3\ 3\ 1\ 1\end{aligned}$$