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INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
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COLLEGE ON MEDICAL PHYSICS

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EDUCATIONAL NMR EXPERIMENTS

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Educational NMR Experiments

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Basic and advanced experiments for medical students and physicians to increase understanding of basic principles of NMR phenomena, relaxometry and MR tomography.

Course: September 1990, Trieste, Italy

"To study and understand physics without doing the experiments is the same as studying music without playing an instrument." (Physikpraktikum für Mediziner, A.F. Fercher)

This statement suits also very well for the basics of NMR spectroscopy and tomography.

So we would like to offer you some practical exercises on a mini NMR spectrometer and imager designed for eductional purposes. According to our experience these will be helpful also in understanding of the sophisticated theoretical background of NMR.

The excercises shall be split into four different stages:

1. basic NMR principles:
   - resonance frequency, gyromagnetic ratio
   - free induction decay (FID) experiment
   - spin echo (SE) experiment
   - repetition time (TR)

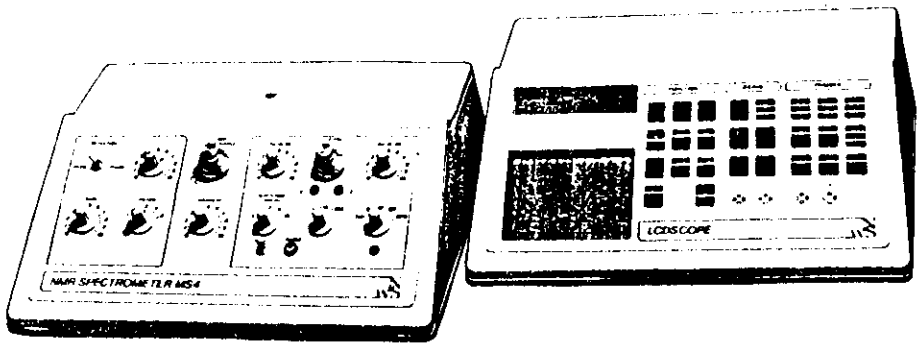
2. intermediate level:
   - SE sequence (dependence on TE, TR, T_1, T_2, q)
   - basics of contrast manipulation in MRI
   - estimation of T_2 (two point method)
   - IR sequence (dependence on T_1, T_1)
   - estimation of T_1 (null method)
   - CP (multiecho sequence)

3. NMR relaxometry:
   - SE (T_2 determination - multipoint method)
   - Carr-Purcell-Meiboom-Gill (CPMG) experiment
   - magnetic field inhomogeneity effect (T_2^*)
   - IR (T_1 determination - multipoint method)

4. MR imaging (tomography):
   - fast Fourier transformation (FFT)
   - gradient encoding
   - image reconstruction

Basic description of the Mini NMR Spectrometer/Imager MS4:

The MS4 consists of two separate units: NMR-spectrometer and digital data aquisition & processing system.



1. NMR-spectrometer:

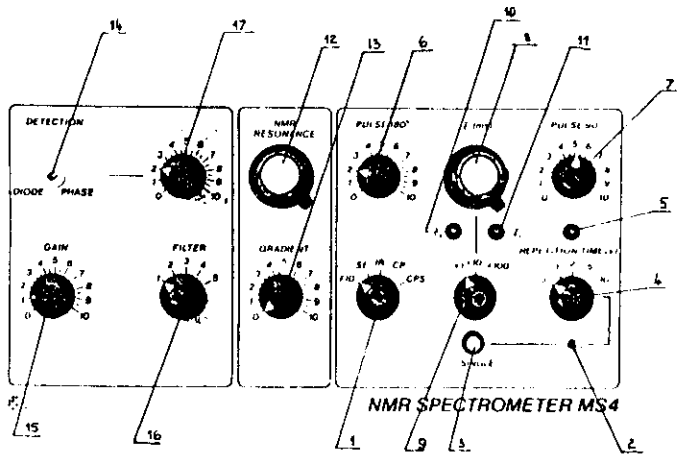
a) Magnet - the magnetic field is produced by a permanent magnet (B=0,2T). The sample will be positioned through the hole on the top of the spectrometer into the center of the magnet. The resonance frequency (about 9 MHz) can be set by a potentiometer(12).

b) RF transmitter, pulsprogrammer - the pulse sequences (RF pulses) will be programmed and sent into the sample.

(1)- sequence selection
(4)- repetition time selection
(6)- 90° pulse adjustment
(7)- 180° pulse adjustment
(8)- adjustment of the delay between 90° and 180° pulse
(9)- delay multiplier

c) Receiver - the NMR-signal will be received, amplified and detected.

(14)- diode/phase sensitive selection switch
(15)- receiver gain adjustment



2. Digital data aquisition & processing system:

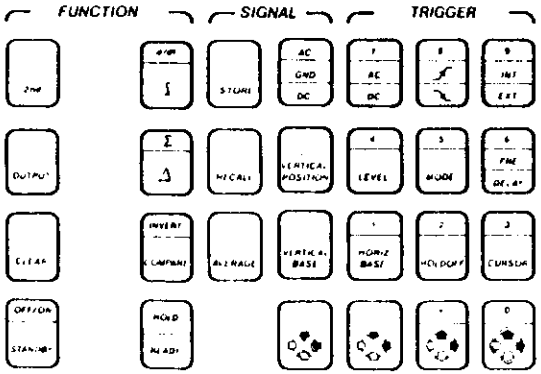
is a microcomputer controlled instrument. The NMR signal detected will be stored and displayed on a LCD display. The stored signal can also be postprocessed.

HOLD/READY- in "READY" mode the current signal is displayed. In "STORE" mode the last incoming signal is stored and displayed.

VERTICAL BASE- the vertical sensitivity selection, afterwards the ⇕ must be pressed.

HORIZONTAL BASE- the horizontal sensitivity selection, afterwards the ⇔ must be pressed.

RESET push-button- restores the starting parameters and is located on the rear panel (red button).

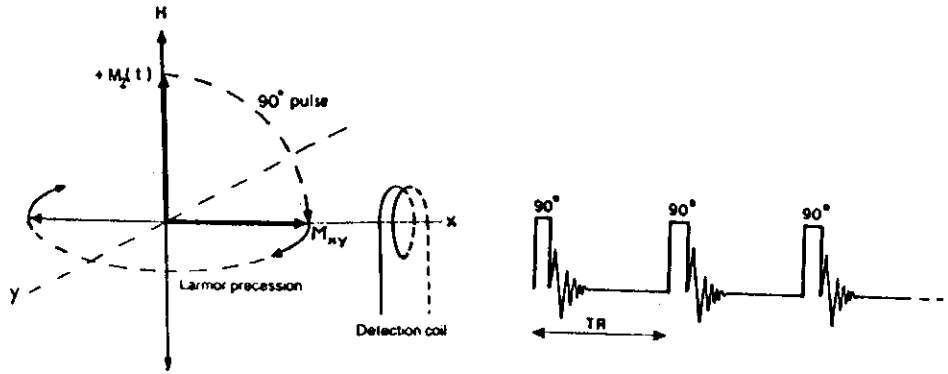


LCDSCOPE

1. Basic NMR principles

- FID (free induction decay), 90° HF puls
- resonance frequency, gyromagnetic ratio
- SE (spin echo), 180° HF puls
- repetition time (TR)

Free induction decay (FID) is a signal displayed on the LCD display after a sequence was applied consisting of only one single 90° RF excitation pulse. The signal amplitude is maximum when the pulse is exactely 90°. Only in this case the magnetisation M_z is rotated completly into the transversal (XY) plane, inducing maximum voltage in the coil.



Insert the probe into the magnet via the hole on the top of the spectrometer.

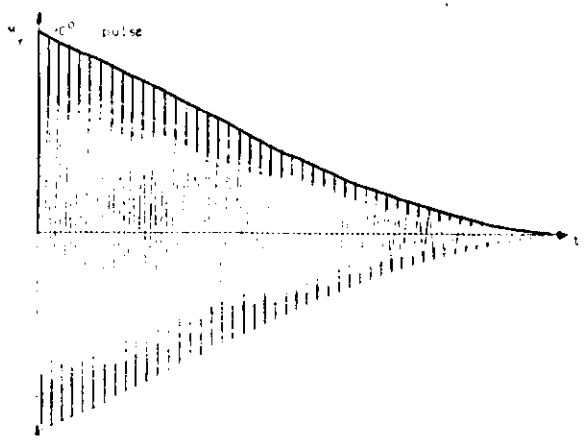
Now select the pulse sequence (only one pulse): FID (switch 1)
The sequence should be repeated each second: 1 (selector 4)
The 90° pulse (pulse width) adjustment: signal max. (button 6)

Set detection mode: diode mode (switch 14)
Adjust receiver gain so that the FID signal is approx. 4-6 volts. Pay attention on the Y sensitivity: (button 16)

[Note: a commercial MR tomograph usually sets the pulse width and receiver gain automatically each time after loading a pulse sequence (messages adjust transmitter and adjust receiver are displayed on the monitor).]

A FID signal should be obtained on the LCD display. However, you

can observe only the enveloppe of a free induction signal because of the high frequency of the induced FID signal (9 MHz).



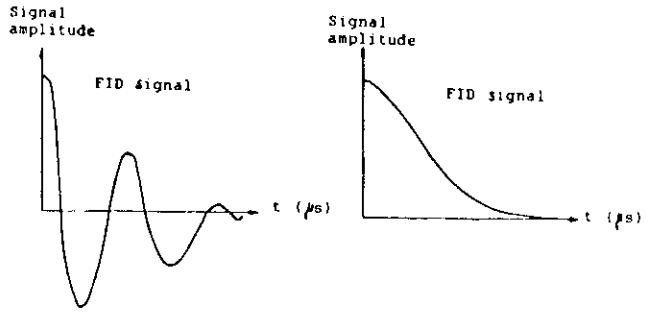
By changing the 90° pulse width (length of excitation) you can tip the magnetisation out of the XY plane. What happens if the pulse duration is longer or shorter? Why?

However, the RF frequency of the RF pulses has not been optimised yet. According to the theory the resonance frequency is equal to:

[Eq.1] $\nu = 1/2\pi \times \gamma \times B$

ν...resonance frequency (MHz)
γ...gyromagnetic ratio (MHz/T)
B...magnetic field strength (T)

Experimentally, we set the resonance frequency by watching the FID signal in phase detection mode: the positive signal amplitude should decay as slow as possible (see graph below).



Change detection mode : phase sensitive (switch 14)
Adjust the resonance frequency: (potentiometer 12)

Please note the potentiometer setting at resonance (potentiometer 12). The actual resonance frequency can be determined by using the following formula:

[Eq.2] $\nu = k \times P + C$

k,C...constants, given on the spectrometer
P...potentiometer setting

The gyromagnetic ratio can be calculated from Eq. 1 by using the resonance frequency calculated by Eq. 2. It is a specific constant for a certain nucleus. Thus it can be determined what kind of nucleus we are dealing with in our experiments (see tabel below).

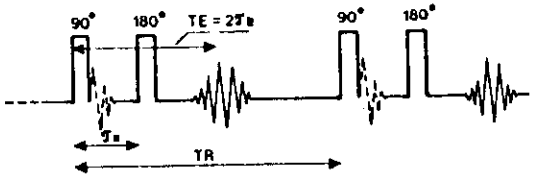
nucleus	gyromagnetic ratio (MHz/T)
^{1}H	267.5
^{13}C	67.3
^{23}Na	70.7
^{31}P	108.3

[Note: a MR tomograph adjusts the resonance frequency automatically each time after loading the sequence (a message adjust frequency is displayed on the monitor).]

Insert sample 2 into the probe!
Verify the resonance frequency.

Are we dealing with the same nucleus as in sample 1? Why?

A spin-echo (SE) signal occurs after the sample has been excited by a sequence composed of two RF pulses: a 90° and 180° pulse. The 90° pulse tips the magnetisation M_z into XY plane. The signal (FID) decays too fast because of magnetic field inhomogeneities. A 180° puls, applied afterwards, refocusses the magnetisation and a signal called spin-echo occurs (see graph below).



Setting the delay time between the 90° and 180° pulse (τ_1), we determine the time where the spin echo occurs (echo time $TE = 2 \times \tau_1$). The signal intensity of the echo is "corrected" for magnetic field inhomogenieties.

[Note: the SE sequence is one of the most commonly used sequences in MR tomography.]

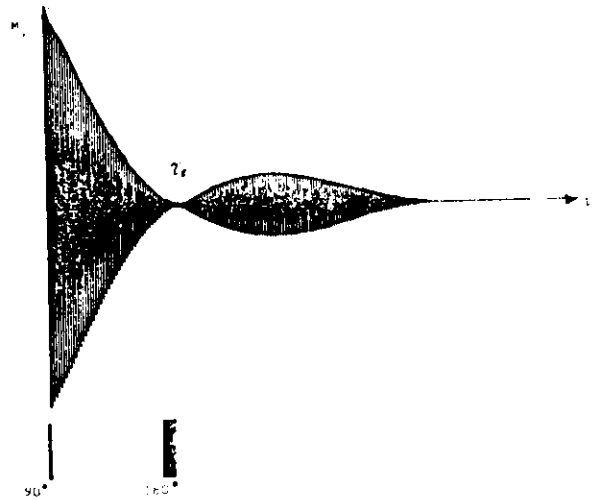
Insert again sample 1 into the magnet.

Resonance frequency should not be changed.

Now select the pulse sequence(90° - 180° pulse): SE (switch 1)
The sequence should be repeated every 2 sec: 2 (button 4)
The delay between 90° and 180° pulse (τ) min: 000 (potentiometer 8) and delay multiplier (9) 1.
The 90° pulse (pulse width) adjustment: FID max. (button 6)
The 180° pulse (pulse width) adjustment: SE max. (button 6)

Set detection mode: diode mode (switch 14)
Adjust receiver gain so that the FID signal is approx. 4-6 volts. Pay attention on the Y sensitivity: (button 16)

A FID and a SE signal should be displayed on the LCD screen, exactly between 90° pulse and the echo maximum you can observe the 180° pulse. As you already know, only the envelope of a FID and SE is shown because of the high frequency of the induced signals (9 MHz).



Vary the 90° pulse width! What happens to FID and SE signals? Why?

What happens if you change the 180° puls width? Why?

Change the delay time between 90° and 180° pulses. Estimate T_E and TE on the LCD display (pay attention to the sensitivity of the time axis!). If the SE disappears from the display, change the horizontal sensitivity of the oscilloscope.

2. Intermediate level

- SE sequence (dependence on TE, TR, T_1, T_2, q)
- basics of contrast manipulation in MRI
- estimation of T_2 (two point method)
- IR sequence (dependence on T_1, T_2)
- estimation of T_1 (null method)
- CP (multiecho sequence)

The signal amplitude in a spin echo experiment is following the equation:

[Eq. 3] $$S = q \times (1 - e^{-RD/T_1}) \times e^{-TE/T_2}$$

q... spin density
RD.. repetition time
TE.. echo time
T_1.. spin-lattice relaxatin time
T_2.. spin-spin relaxation time

The repetition time (RD) and echo time (TE) are pulse sequence parameters and can be set by the operator. Therefore we have the opportunity to manipulate the spin echo amplitude in various ways.

There are three major possibilities:

1. Setting repetition time (RD) long ($RD >> 5.T_1$) and TE short ($TE << T_2$):

$$(1 - e^{-RD/T_1}) \approx 1$$
$$e^{-TE/T_2} \approx 1$$

and $S \propto q$

In this case we get a "spin density weighted image" in MRI.

2. Setting repetition time (RD) short ($RD < 5.T_1$) and TE short ($TE << T_2$):

$$e^{-TE/T_2} \approx 1$$

and $S \propto q \times (1 - e^{-RD/T_1})$

This experiment results in a "T_1 weighted image" in MRI.

3. Setting repetition time (RD) long (RD>>5.T_1) and TE long (TE>T_2):

$$(1-e^{-RD/T_1}) \approx 1$$

$$\text{and } S \propto q \times e^{-TE/T_2}$$

Running this measurement we obtain a "T_2 weighted image" in MRI.

Estimate the amplitudes of a q, T_1 and T_2 weighted spin echo signal.

Hold all the settings from previous experiment unchanged. Change only repetition time (RD) and the time delay between the 90° and 180° pulse (τ_E):

1. *q density weighted: RD= 5s (button 4)*
   τ_E = 1ms (potentiometer 8)

2. *T_1 weighted: RD= 0,3s (button 4)*
   τ_E = 1ms (potentiometer 8)

3. *T_2 weighted: RD= 5s (button 4)*
   τ_E = 9ms (potentiometer 8)

Compare the SE amplitudes of q, T_1 and T_2 weighted signals.

Repeat all 3 measurements with sample 2.

Compare the spin echo amplitudes of sample 1 and 2 at the same instrumental settings.

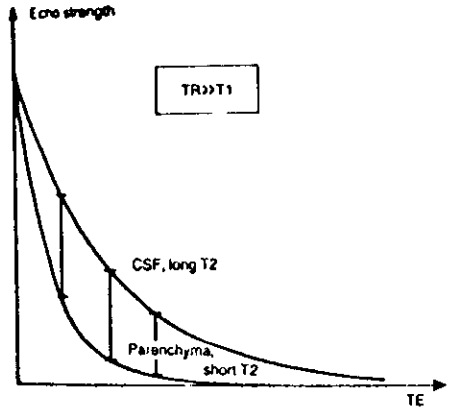
Suppose, that normal tissue has a q, T_1 and T_2 similar to sample 1 and the pathologically altered tissue like sample 2. Which parameters for the SE sequence would you choose in order to achieve better contrast between the normal and pathological tissue?

Note: In order to reconstruct an image, the MR tomograph divides the whole slice into volume elements (voxels). Signals from each such voxel are detected (for exampel SE amplitudes). According to these amplitudes a grey value is assigned to corresponding pixel on the image of this slice.

So, if the normal and pathological tissue show almost the same SE amplitudes, the same grey scale value will be assigned to corresponding pixels and there will be no contrast in the image. Therefore, we suggest to select the sequence parameters so that the differences in SE amplitudes between normal and pathological tissue will be as large as possible.

Measure the SE amplitudes for different TE, holding constant RD=2sec.

Why is the SE amplitude decreasing with increasing TE? Discuss the differences between both samples?



What TE value would you choose at a repetition time of 2sec in order to get a better contrast between normal (sample 1) and pathological (sample 2) tissue?

We are now able also to estimate the T_2 relaxation time for both samples!

According to Eq.3, if q and repetition time RD are unchanged, we get:

$$S_1 / S_2 = e^{-TE_1 / T_2} / e^{-TE_2 / T_2}$$

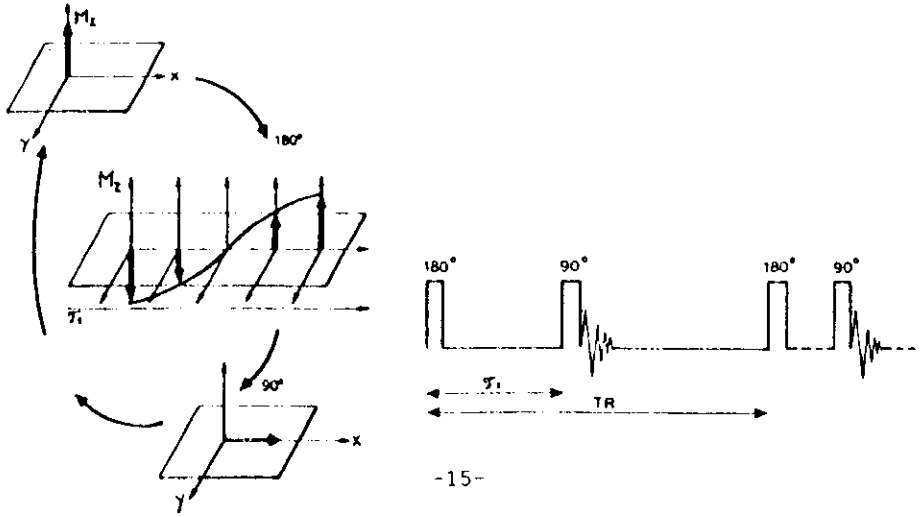
S_1, S_2 ... spin echo amplitudes
TE_1, TE_2 ... spin echo times

resolving this equation, we get:

[Eq.4] $$T_2 = (TE_2 - TE_1) / \ln (S_1 / S_2)$$

Calculate the T_2 relaxation time for both samples.

Inversion recovery (IR) sequence is composed of a 180° pulse and after a time delay τ_1 a 90° pulse. The 180° pulse tips the M_z magnetisation into the -Z axis, the system is allowed for a time τ_1 to relax. The following 90° puls tips the magnetisation into the XY plane where we are able to detect a signal (see picture below).



Insert again sample 1 in the magnet.

Resonance frequency should not be changed.

Now select the pulse sequence(180° -τ-90° pulse): IR (switch 1)
The sequence should be repeated every 2 sec: 2 (button 4)
The delay between 180° and 90° pulse (τ_1) min: 000 potentiometer 8) and delay multiplier (9) 1.
The 180° pulse (pulse width) adjustment: FID=0 (button 6)
The 90° pulse (pulse width) adjustment: FID max. (button 6)

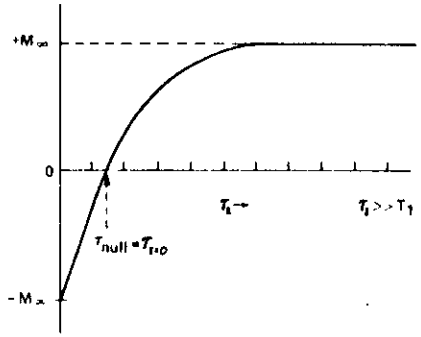
Set detection mode: diode mode (switch 14)
Adjust receiver gain so that the FID signal is approx. 4-6 volts. Pay attention on the Y sensitivity: (button 16)

Now you should be able to detect FID signal immedeately after 90° pulse.

What happens if you vary the delay time between the pulses?

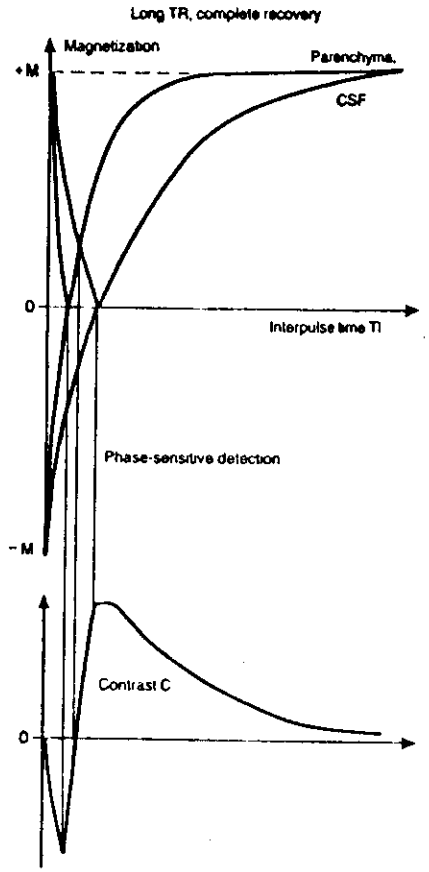
Change τ_1 and observe the FID signal - it shows you the recovery of the magnetisation M_z in the Z axis (see graph below).
Pay attention: in diode detection mode you can only observe the absolute value of the signal.

Change the delay multiplier (9) to 10x and turn the potentiometer again. (The FID signal will disapear out of the display or it will be to short, thus change the trigger switch in position 2 on the rear panel . Now you will observe (trigger) only the (second) 90° pulse without the 180° pulse.)



Do it for both samples!

You can now choose the IR sequence parameters for both samples in order to obtain optimal image contrast.



Find the time delay T_{I_0} where the FID signal equals zero.

The time delay of zero Z-magnetisation (FID signal=0) depends on the T_1 relaxation time. Therefore we are able to calculate T_1 according to the following equation:

[Eq. 6] $T_1 = T_{I_0} / \ln 2$ T_{I_0} ... inversion time

The time delay in ms (T_{I_0}) can be calculated according to formula:

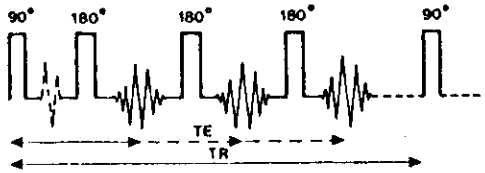
[Eq.5] $T_{I_0} = 10 + pot \times 0.42$

pot...potentiometer setting

Estimate the T_1 relaxation time for both samples.

Carr-Purcell (CP) multiecho sequence:

This sequence starts by applying one 90° pulse and after a delay TE/2 a train of 180° pulse, at time delay TE apart. The first 90° puls tips the magnetisation M_z into XY plane. The following pulses refocuss the decaying signal and we obtain a train of spin echo signals.



Insert sample 1 into the magnet.

Alter instrumental parameters according to previous SE sequence optimisation. Then, change the sequence selection button to CP.

Change the settings for 90° and 180° pulses. What happens? Vary also the time delay between them.

3. NMR relaxometry

T_2 determination by multipoint SE:

In order to determine T_2 relaxation times accurately, one has to measure the magnetisation curve for different TE times (not only 2).

According to equation [Eq.3], holding repetition time constant, we obtain:

$$M(t) = M_0 \times e^{-t/T_2}$$

hence:

[Eq.7] $$\ln M(t)/M_0 = - t/T_2$$

Plotting $M(t)/M_0$ vs. t on a semilogarithmic graph, we get a straight line and its slope determines the relaxation time T_2.

This method is not very accurate for long TE, because molecular diffusion causes deviations.

Insert sample 1 into the magnet.

Follow the instruction for the SE experiment; repetition time should be at least 2s (RD >5.T_1)
If the spin echo is not observed, change the time scale on the oscilloscope, subsequently switch the trigger in position T_2 (echo)!

Measure SE amplitudes for both samples at different TE's, plot amplitude values on a graph M(t) vs. time. Draw also a graph ln $M(t)/M_0$ vs. t and determine the T_2 relaxation time out of it.

Carr-Purcell (CP) sequence:

This sequence has the advantage compared to the multiecho experiment, that the diffusion effect is corrected. However, make sure that all pulses are optimised.

Taking into account also diffusion effects, the signal amplitude in a SE experiment equals:

[Eq.8] $S(t)=S_0 \cdot e^{-(t/T_2 + \gamma \cdot G \cdot D \cdot \tau \cdot t/3)}$

γ...gyromagnetic ratio
G...gradient (magnetic field inhomogeneity)
D...diffusion koeficient
τ...time between 180° pulses

Setting the delay time between the 180° pulses short, equation [Eq.8] reduces to:

$$S(t)=S_0 \times e^{-t/T_2}$$

and the evaluation of T_2 is analogous to the previous experiments (multiecho experiment).

Determine the T_2 relaxation time for both samples!

Insert sample 1 into the magnet.

Alter instrumental parameters according to previous SE sequence optimisation. Then, change the sequence selection button to CP.

Time delay between the pulses should be as short as possible. The repetition time should be at least $5T_1$.

In order to obtain the envelope of SE maxima easier, switch sequence selector to CPS.

Adjust the time axis of the oszilloscope.

Measure at least 8 SE maxima at different times on the curve and draw a graph S vs. time. Determination of T_2 follows as previously.

Inversion recovery:

We have already estimated T_1 by the "null method". However, more reliable T_1 relaxation time determinations should be carried out more accurately. Via an IR experiment it is possible to detect the magnetisation recovery accurately.

The M_z recovery in an IR experiment is described by the following equation:

$$M_z(t)=M_{\infty} \times (1-2 \times e^{-t/T_1})$$

hence:

$$\ln (1/2) \times (1-M(t)/M_{\infty}) = -t/T_1$$

Measuring the magnetisation recovery (FID signal) at different time delays between 90° and 180° pulses and plotting $\ln (1/2) \times (1-M_z(t)/M_{\infty})$ vs. time, allows to determine T_1.

The experiment should be performed as earlier described. Repetition time should be longer than $10 \times T_1$ (2-5 s for our samples). The time delays between 90° and 180° puls (τ) should be increased in steps of $\tau_{1/2}/5$ till about 2 x $\tau_{1/2}$, afterwards in steps of 2 x $\tau_{1/2}$.

Measure the whole recovery curve and plot the signal amplitudes in a graph $M_z(t)$ vs. time. Draw also a graph $\ln(1/2) \times (1-M_z(t)/M_{\infty})$ vs. time and determine T_1 out of the this graph.

Determine T_1 for both samples.

Magnetic field inhomogeneity effect:

The decrease of FID signal amplitude is described by a time constant T_2^*. It is always shorter than the actual T_2 relaxation time, because of the inhomogeneity of the magnetic field. T_2^* of a FID can be determined by measuring the time at which the FID decreases to 1/2 of the initial value:

$$T_2^* = t_{1/2}/\ln 2$$

The inhomogeneity of the magnetic field can be also increased by superimposing an additional gradient onto the static magnetic field.

Measure FID signal of sample 1.

Apply additional gradient : 0, 4, 8 (gradient button)

Measure $t_{1/2}$ (full width at half maximum)for different magnetic field inhomogeneities and determine T_2^*.

Compare T_2^* and T_2 relaxation times of the same sample determined by SE experiments.

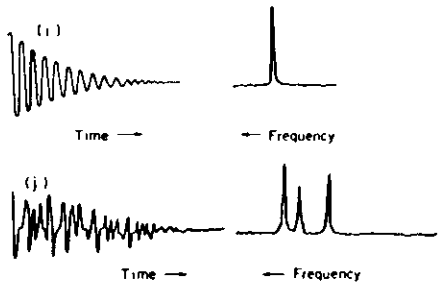
4. Imaging

The main problem in MR tomography is how to measure the NMR signals only from a certain volume of the sample (patient) without loosing the spatial information.

Basic ideas to perform imaging experiments by NMR:

1. fast Fourier transformation (FFT)
2. frequency encoding

1. Fast Fourier transformation (FFT) is a mathematical tool which computes the frequency distribution of the recieved signal (detected in the time domain, see below).



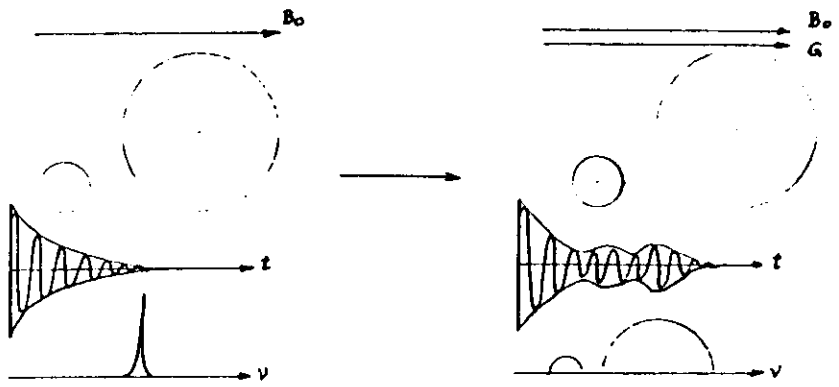
Insert sample 1 into the spectrometer.

Measure the SE : (RD=1s, TE=2ms).
Calculate the Fourier transform (FFT) of the SE signal.

Repeat the experiments with the gradient turned on : 4, 8 (gradient button)

Which changes do you observe in FT at different gradient strengths?
Notice, that by turning on the gradient (G), you change the magnetic field uniformity in the sample ($B_0 \pm G$ instead of B_0). According to Eq.1, the NMR signal will be composed by more frequencies: the FFT is broader (see graph below).

2. Frequency encoding is the next step towards imaging. The magnetic field in the sample is changed by a known linear magnetic gradient. The frequency distribution of the signal, depending on this gradient, can be correlated to the spatial coordinates of the selected volume (see below).



Insert sample 3 into the spectrometer.

Measure SE (RD=1s, TE=2ms)
Turn the gradient on (gradient position at 8).
Perform FFT of the SE.

Align the two tubes inside the sample 3 in the direction of the magnetic field gradient . Repeat the measurement and FFT.

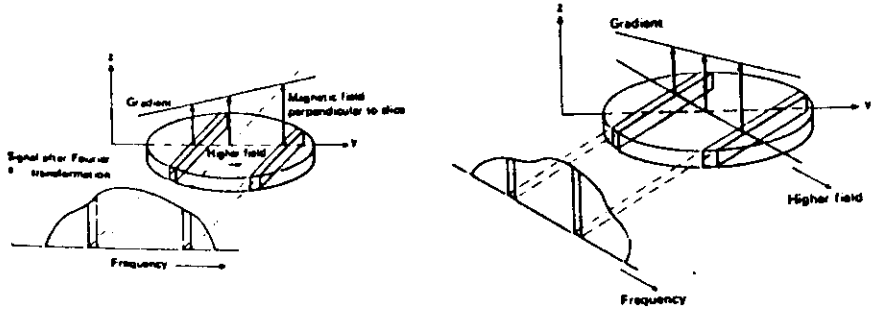
Turn the sample about 90° and repeat the measurement and FFT.

Repeat the previous measurements and FFT with the gradient turned off.

Discuss the differences! In which positions are the two tubes aligned with the direction of the gradient?

After introducing the basic principles of imaging, we can take an image of sample 4.

The image will be reconstructed by backprojection reconstruction. The measured signals at different angles in respect to the encoding gradient are transformed by a FFT and afterwards an image is reconstructed out of these projections.



Insert sample 5.

According to the instructions of the programm for imaging experiment set the parameters of the imager.

Take the image of the sample 4.

Analyse the picture. What is the result of filtering the image ?

Turn the sample for 90°. Repeat the experiment. Image should now be turned by the same angle.

Repeat the imaging without the gradients turned on.

Vary the sequence parameters (RD and TE) and discuss changes in contrast.