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H4.SMR/638-23

College on Medical Physics:
Imaging and Radiation Protection

31 August - 18 September 1992

Educational NMR Experiments

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

Course: ICTP College on Medical Physics
September 1992, Trieste, Italy

INTRODUCTION

'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 educational purposes. According to our experience these will be helpful also in understanding of the sophisticated theoretical background of NMR.

The exercises shall be split into two different sections:

1. basic NMR principles:

- resonance frequency, gyromagnetic ratio
- free induction decay (FID) experiment
- spin echo (SE) experiment
- repetition time (TR)
- 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 (multiple pulse sequence)

2. 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 (MS4)
- digital data acquisition & processing system (LCDSCOPE)

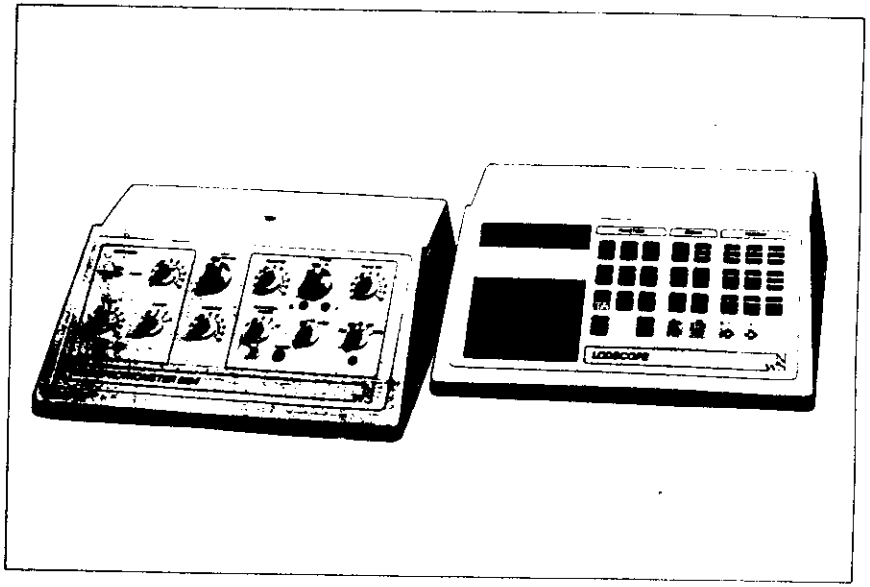

Fig.: Small MR Imager & NMR Spectrometer

1. NMR-spectrometer:

a) Magnet - the magnetic field is produced by a permanent magnet (B=0,3T). The sample will be positioned through the hole on the top of the spectrometer into the center of the magnet. The resonance frequency (about 12 MHz) can be set by a potentiometer (12).

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

(1) - sequence selection
(4) - repetition time selection
(6) - 90^{O} pulse adjustment
(7) - 180^{O} pulse adjustment
(8) - adjustment of the delay between 90^{O} and 180^{O} 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

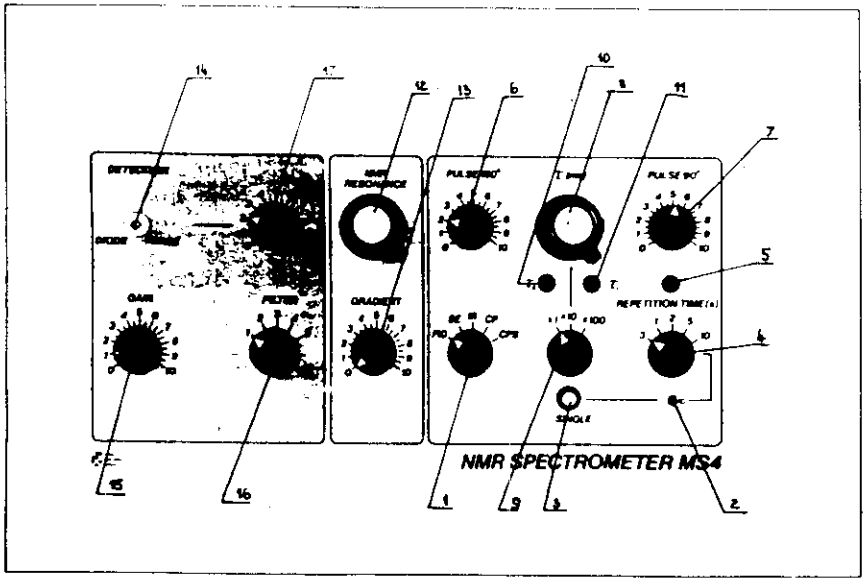

Fig.: NMR Spectrometer MS4 front panel controls

2. Digital data acquisition & 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).

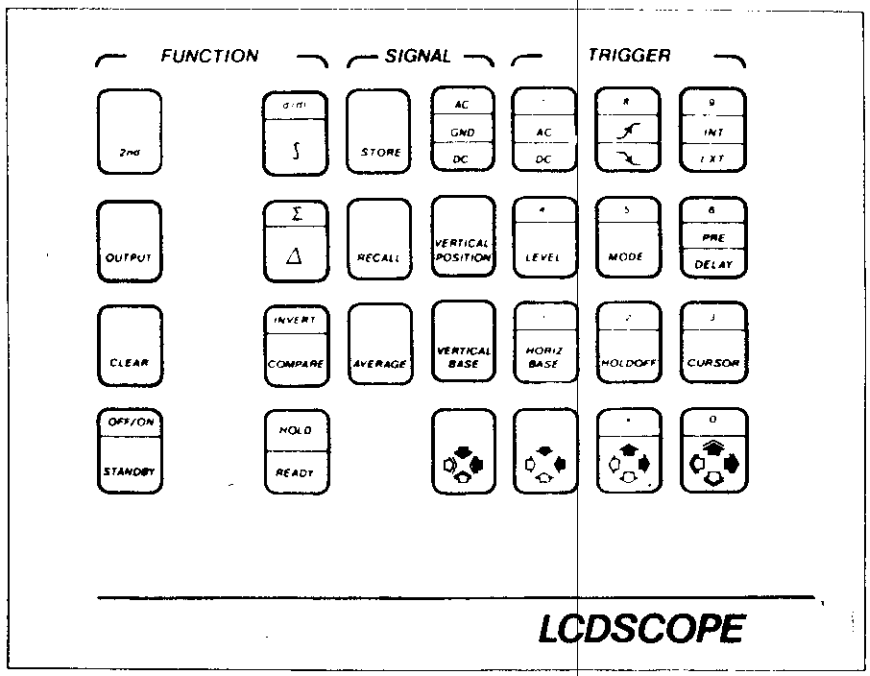

Fig.: LCDSCOPE keyboard layout

1. Basic NMR principles

- FID (free induction decay), 90° RF pulse
- resonance frequency, gyromagnetic ratio
- SE (spin echo), 180° RF pulse
- repetition time (TR)
- 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, TI)
- estimation of T_1 (null method)
- CP (multiple pulse sequence)

Free Induction Decay (FID)

Free induction decay is a signal displayed on the LCD display after a radio frequency (R.F.) pulse sequence was applied consisting of only one single 90° R.F. excitation pulse. The signal amplitude is maximum when the pulse is exactly 90°. Only in this case the magnetization M_Z is rotated completely into the transversal (XY) plane, inducing maximum voltage in the coil.

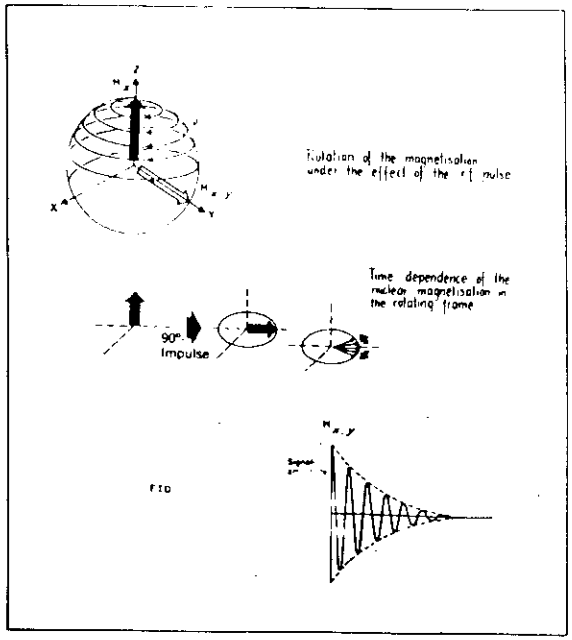

Fig.: Free Precession Decay (FID) signal

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

Select the R.F. 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 ≈ 4-6 volts. Pay attention to the Y sensitivity: (button 16)

A FID signal should be obtained on the LCD display. However, you can observe only the envelope of a free induction signal because of the high frequency of the induced FID signal (MS4 spectrometer - 12 MHz).

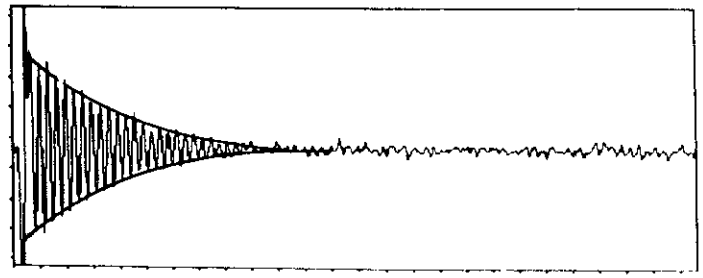

Fig.: FID signal is an envelope of resonance frequency

By changing the 90° pulse width (length of excitation) you can tip the magnetization 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 optimized yet. According to the theory the resonance frequency is proportional to magnetic field density. to:

Eq.1 $$\nu = \frac{\pi}{2} \cdot \gamma \cdot B$$

- 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 sensitive detection mode: the positive signal amplitude should decay as slow as possible (see figure below).

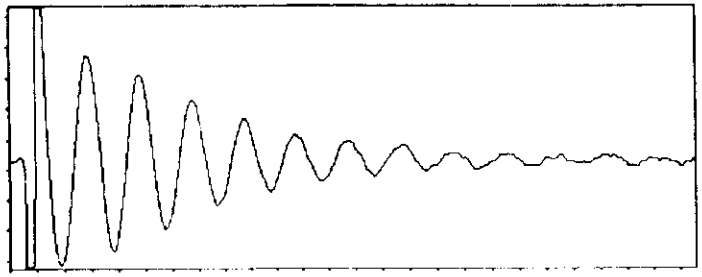

Fig.: FID signal off resonance

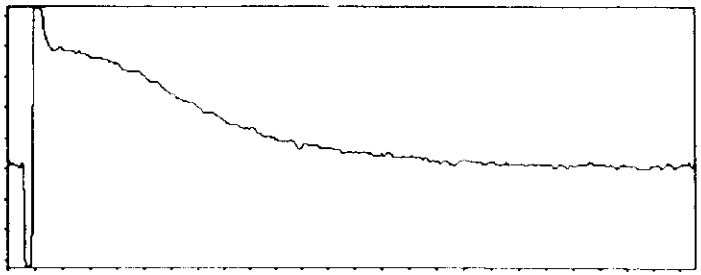

Fig.: FID signal in resonance

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

Gyromagnetic ratio

The gyromagnetic ratio (γ) can be calculated from Eq. 1 by using the resonance frequency of the spectrometer (12 MHz) and the known value of the magnetic field density (B). It is a specific constant for certain nucleus.

Table 1.: Properties of nuclei important for NMR tomography:

nucleus	relative natural abundance in %	relative sensitivity in comparison with ^1H at constant field B_0	relative sensitivit biological sistems according to biological abundance	resonance frequency at 1 Tesla in MHz
^1H	99.98	1	1	42.58
^2H	0.016	9.7×10^{-3}	6.2×10^{-5}	6.56
^{13}C	1.11	1.6×10^{-2}	2.5×10^{-4}	10.69
^{19}F	100	8.3×10^{-1}	6.3×10^{-5}	40.07
^{23}Na	100	9.3×10^{-2}	1.0×10^{-3}	11.28
^{31}P	100	6.6×10^{-3}	1.4×10^{-3}	17.24

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

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

Since the duration of the 90° R.F. pulse was adjusted before the magnet was adjusted to the resonant value, the duration of 90° R.F. pulse is not optimal. So after the resonance conditions are met, the final adjustments of the 90° R.F. pulse duration is necessary. The adjustment is done exactly the same way as before. The pulse width is varied until the signal following it, reaches its maximum value.

Spin-Echo (SE)

A spin echo 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 magnetization M_z into XY plane. The signal (FID) decays too fast because of magnetic field inhomogeneities. A 180° pulse, applied afterwards, refocuses the magnetization and a signal called spin-echo occurs (see graph below).

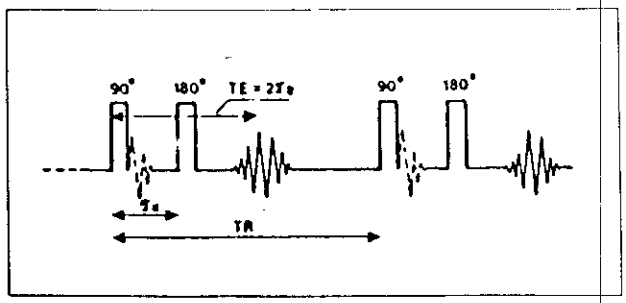

Fig.: Spin Echo (SE) R.F. pulse sequence

Setting the delay time between the 90° and 180° pulse (τ_E), we determine the time where the spin echo occurs (echo time $TE = 2 \cdot \tau_E$). 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 NMR tomography.

Insert again sample 1 into the magnet.
Resonance frequency should not be changed (on resonance!).

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_E) 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 ≈ 4-6 volts. Pay attention to the Y sensitivity: (button 16)

A FID and a SE signals 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 (12 MHz).

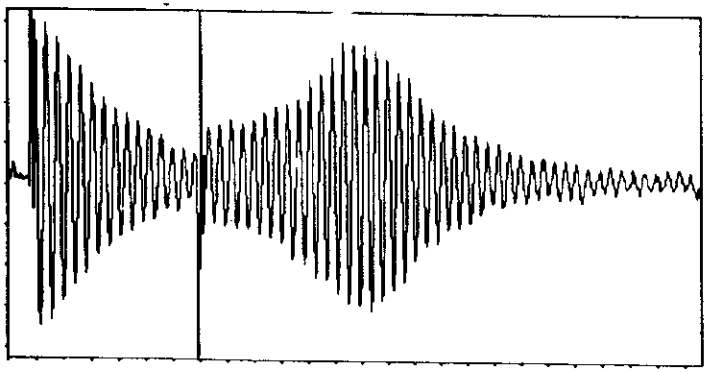

Fig.: Spin Echo (SE) signal

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

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

Change the delay time between 90° and 180° pulses. Estimate τ_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.

Influence of relaxation times on the NMR signal amplitude

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

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

q	- spin density
RD	- repetition time
TE	- echo time
T_1	- spin-lattice relaxation 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 ($RD \gg 5 \cdot T_1$) and TE short ($TE \ll T_2$) :

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

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

$$\text{and } S \propto q$$

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

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

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

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

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

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

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

and $$s \propto q \cdot e^{-TE/T_2}$$

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 90^0 and 180^0 pulse (τ_E):

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

2. *T_1 weighted: RD = 0.3s (button 4)*
   τ_E = 1 ms (potentiometer 8)

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

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

Repeat all 3 measurements with sample.

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 example SE amplitudes). According to these amplitudes a gray 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 gray 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 = 2 s.

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

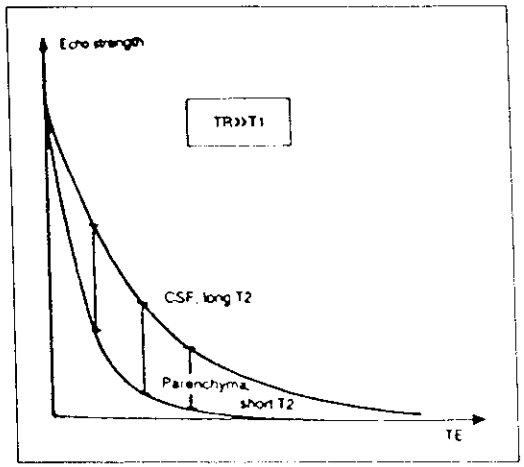

Fig.:

What TE value would you choose at a repetition time of 2 s in order to get a better contrast between nominal (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:

$$S_1/S_2 = \frac{e^{-TE_1/T_1}}{e^{-TE_2/T_2}}$$

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

resolving this equation, we get:

Eq.4 $$T_2 = \frac{(TE_2 - TE_1)}{\ln(S_1/S_2)}$$

Calculate the T_2 relaxation time for both samples.

Inversion Recovery (IR) - spin - lattice relaxation

Inversion recovery sequence is composed of a 180° pulse and after a time delay T_1 a 90° pulse. The 180° pulse tips the M_Z magnetization into the -Z axis, the system is allowed to relax for a time T_1. The following 90° pulse tips the magnetization into the XY plane where we are able to detect a signal (see picture below).

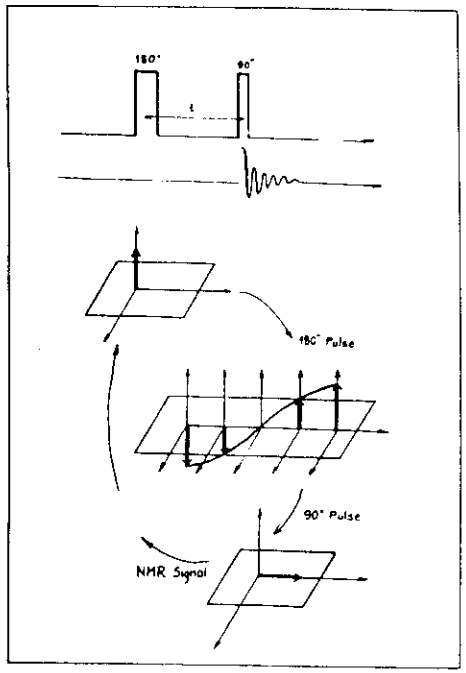

Fig.: Inversion Recovery (IR) pulse sequence and signal formation

Insert again sample 1 in the magnet.

Resonance frequency should not be changed (on resonance!).

Select the pulse sequence ($180^o - \tau_E - 90^o$ pulse): IR (switch 1) The sequence should be repeated every 2 sec: 2 (button 4). The delay between 180^0 and 90^o pulse (τ_E) min: 000 potentiometer (8) and delay multiplier (9) 1.
The 180^o pulse (pulse width) adjustment: FID=0 (button 6)The 90^o pulse (pulse width) adjustment: FID max. (button 6)

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

You should be able to detect FID signal immediately after 90° pulse.

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

Change T_1 and observe the FID signal - it shows you the recovery of the magnetization 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 disappear out of the display or it will be to short, thus change the trigger switch in position 2 on the rear panel. You will observe (trigger) only the (second) 90^o pulse without the 180^o pulse).

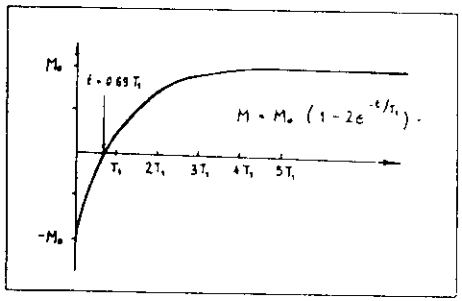

Fig.: Time dependence of the FID signal following the 90^o pulse

Do it for both samples!

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

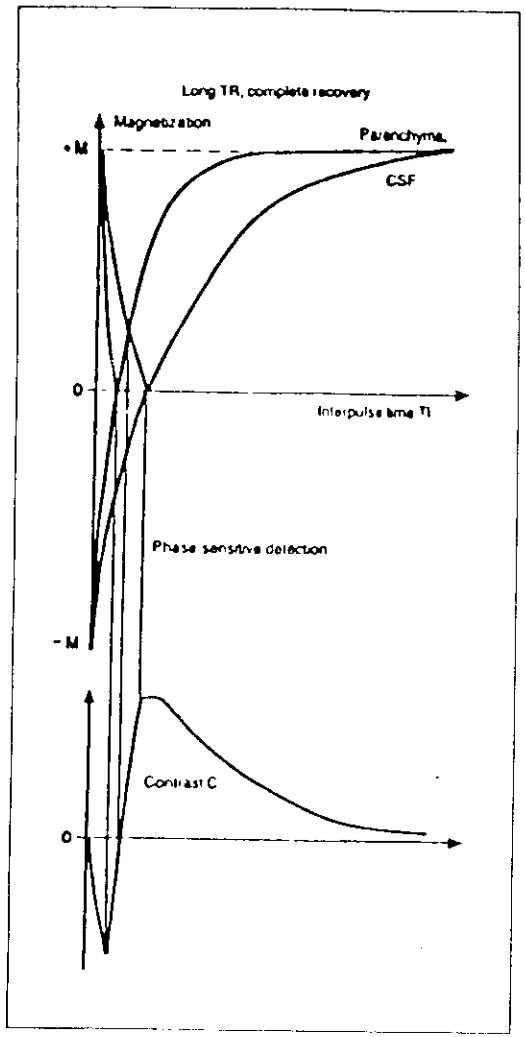

Fig.: Dependence of the contrast in the T_1 weighted image on the time between 180° and 90 ° pulses that the nuclei are allowed to relax

Find the time delay T_1, where the FID signal equals zero.

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

Eq. 6 $$T_1 = \frac{T_{1=0}}{\ln 2} \qquad T_{1=0} \text{ - inversion time}$$

The time delay in ms (τ_E) can be calculated according to formula:

Eq.5 $$\tau_E = 10 + pot \times 0.42 \qquad pot \text{ - potentiometer setting}$$

Estimate the T_1 relaxation time for both samples.

Carr-Purcell (CP) multiple pulse sequence

This sequence starts by applying one 90° pulse, followed by a train of 180° pulses, first pulse is separated by a delay of TE/2 and all the consecutive pulses by time delay TE. The first 90° pulse tips the magnetization M_Z into XY plane. The following pulses refocus the decaying signal and we obtain a train of spin echo signals.

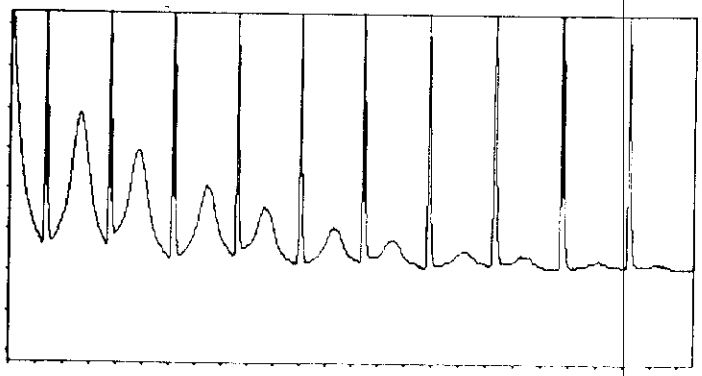

Fig.: Carr-Purcell (CP) multiple pulse sequence and its signal

Insert sample 1 into the magnet.
Alter instrumental parameters according to previous SE sequence optimization. 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.

2. 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 received signal (detected in the time domain, see below).

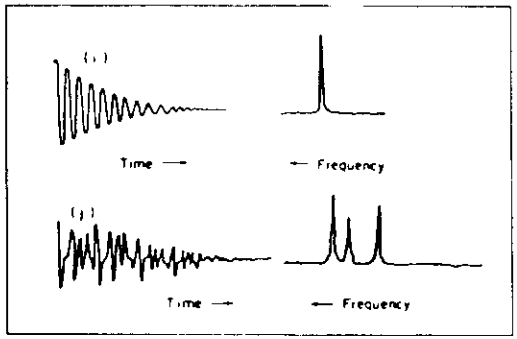

Fig.: Time and frequency domain presentation of NMR signals

Insert sample 1 into the spectrometer.
Measure the SE : (RD = 1s, TE = 2ms).

In order to get optimum results in FT NMR experiment, the following procedure is recommended for manual setup of MS4 spectrometer and LCD SCOPE:

- reset LCDSCOPE or press 2nd, 2 (NMR parameters)
- select spin echo pulse program
- select phase detection
- select trigger position 1 (back panel of MS4)
- adjust resonance, if the signal is far out of resonance, temporarily increase time base to 100 us/cm, so that aliasing effects are not misleading the adjustment.
- select diode detection
- adjust 90° and 180° R.F. pulse widths and signal gain

- select phase detection
- select trigger position E (back panel of MS4)
- press 2nd, 3 (imaging parameters)
- adjust off resonance so that you get one to two waves per division.
- press FFT-cont. (FFT representation of data)
- adjust resonance so that peak is in the middle of the screen
- adjust magnetic field gradient so that the FFT signal is approximately 6 divisions wide
- fine adjust the position so that the signal is as centered as possible

Hint: The gradient coils are producing some heat, which is warming the permanent magnet. Due to the temperature dependence of the magnet the magnetic field is therefore slightly shifting. The experience shows that after about one hour at certain level of gradient the equilibrium temperature is reached and magnetic field is stabilized. But in spite of this effect the rate of magnetic field shifting is so slow that it allows normal measurement (0.3 or 1 second repetition time and no averaging) and only occasional adjustment is necessary. If you intend to average signal or use long repetition times then it is recommended to wait for temperature stabilization. The best test for properly centered FFT signals is how well the two FFT signals (projections), which are 180° apart in measure image menu, are adjusted. It is important to adjust position so that the slopes of the signals are properly covered (blue and reed signal on the left side of the screen). The amplitude match is less important because amplitude depends on frequency and is slightly decreasing in high frequency region.

Measure the Fast Fourier Transform (FFT) of the SE signal.

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

What 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 of more frequencies: the FFT is broader (see graph below).

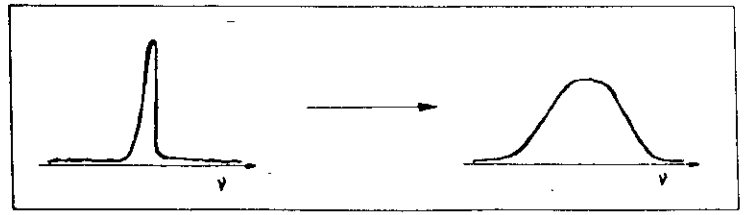

Fig.: The effect of magnetic field gradient on frequency domain FID signal width

2. Frequency encoding is the next step toward 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).

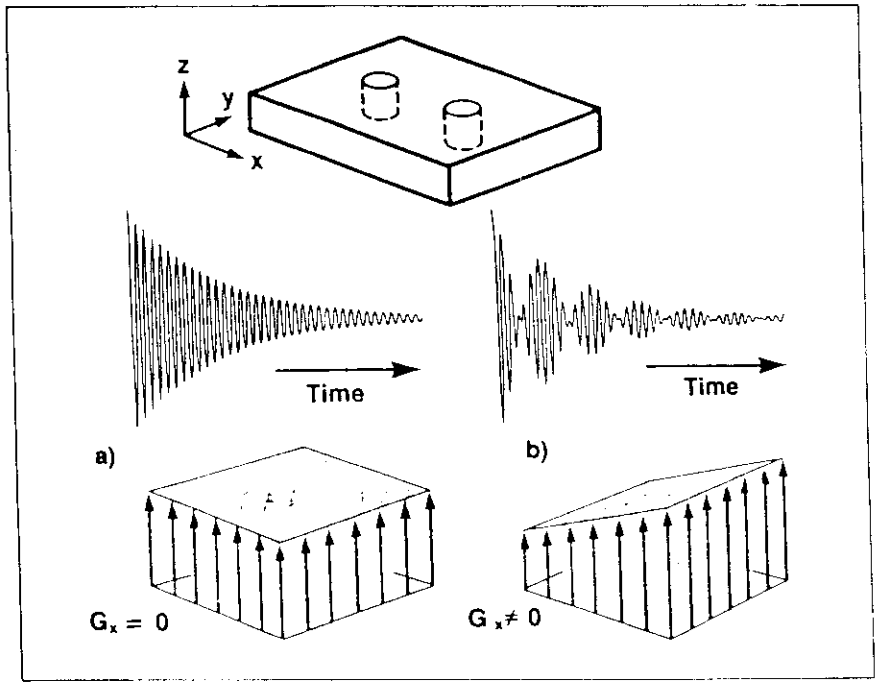

Fig.: Comparison of the FID signal without and with the magnetic field gradient

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 phantom sample 3 in the direction of the magnetic field gradient. Repeat the measurement and FFT.

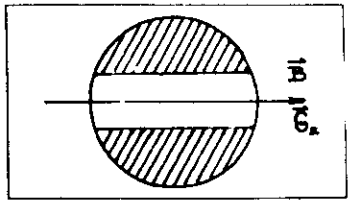

Fig.: Phantom sample oriented in the direction of magnetic field gradient

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

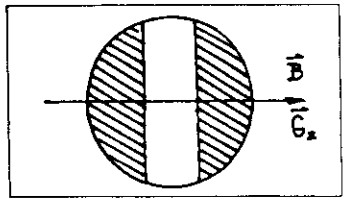

Fig.: Phantom sample turned for 90° in the direction perpendicular to the magnetic field gradient

Repeat the previous measurements and FFT with the gradient turned off.
Discuss the differences! In what 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.

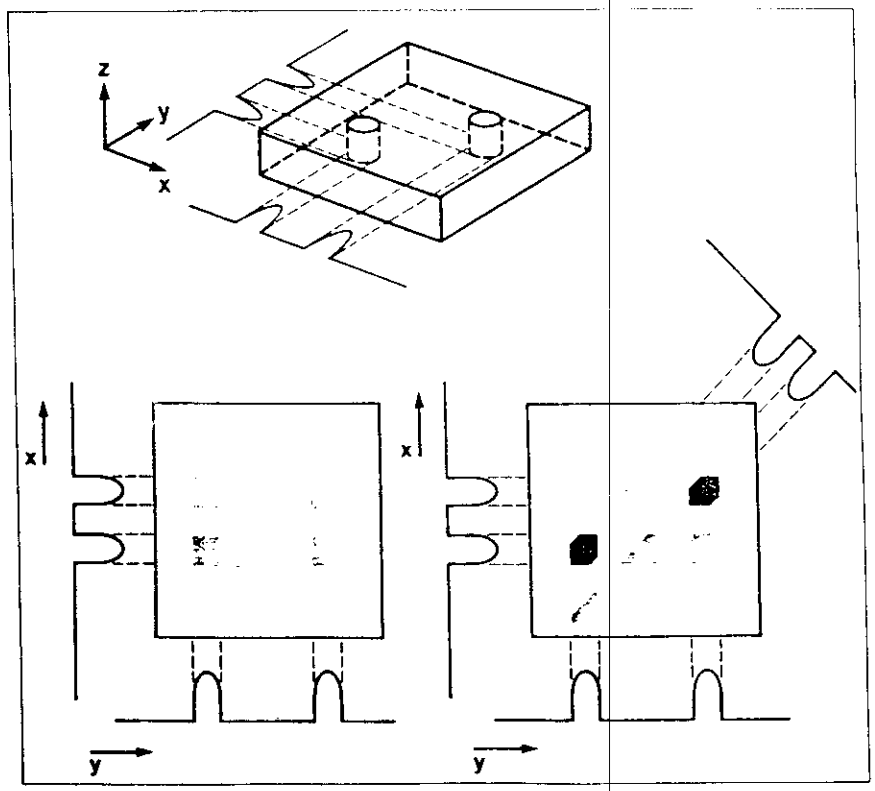

Fig.: The principle of back projection reconstruction method

The image will be reconstructed by backprojection reconstruction. The measured signals at different angles with respect to the encoding gradient are Fourier transformed and afterwards an image is reconstructed out of these projections. The reconstruction algorithm is made of simple additions of every projection to the reconstruction matrix at the angle it was measured.

Insert sample 5.

According to the instructions of the imaging software program set the parameters of the imager.

Take the image of the sample 4.

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

Turn the sample for 90^{o}. Repeat the experiment. Image should now be rotated by the same angle.

Repeat the imaging without the gradients turned on. Discuss the result.

Repeat MR imaging using Algebraic Reconstruction Technique (A.R.T.). Discuss the difference.