

## Pulsed NMR

Pulsed NMR is widely used for chemical analysis, in Magnetic Resonance Imaging (MRI), and a number of other applications of magnetic resonance. In this lab you will set up a pulsed NMR experiment and measure the time constants  $T_1$  and  $T_2^*$ . These measurements are made with protons in various samples with a frequency near 15 MHz and  $B_0 \approx 0.35 T$ . A separate write-up provides a necessary introduction to NMR and many of the phenomena and terms discussed here.

### The Apparatus

**NOTICE: BEFORE TURNING ON ANYTHING, READ THROUGH THIS ENTIRE PROCEDURE. MAKE SURE ALL CABLES ARE PROPERLY CONNECTED. IT IS POSSIBLE TO DAMAGE THE RF ELECTRONICS. RF electronics. DO NOT OPERATE THE RF SOURCE IF THE BNC CABLE IS NOT ATTACHED TO THE  $B_1$  COIL. DO NOT OPERATE WITH A PULSE DUTY FACTOR (PULSE DURATION/REPETITION TIME) GREATER THAN 1%. If overheating occurs, the unit should shut down. This can be reset after the problem is eliminated and the AC power cycled (turned OFF and then ON again.)** NOTE: In NMR, the term RF (Radio Frequency) refers to any signal or source operating in the range of frequencies roughly from hundreds of kilohertz through hundreds of megahertz, important in broadcasting, radar, AND most NMR applications. Special electronics techniques have been developed (RF transistors, RF connectors, etc.). Thus when we refer to RF, we could mean the oscillator, the amplifiers and mixers, or the receivers and signal chain elements.

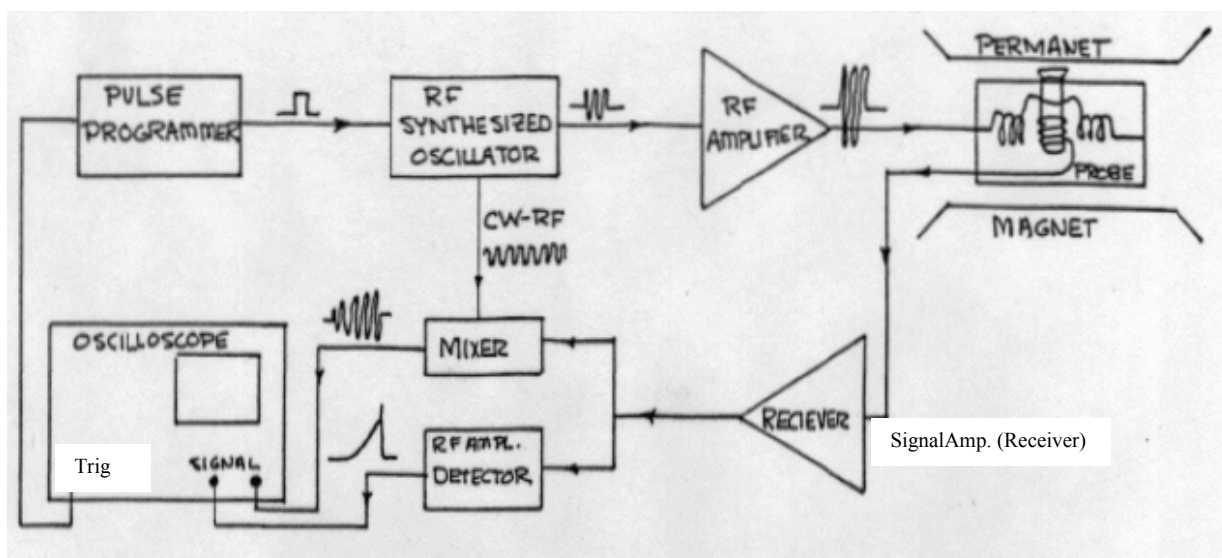


Figure 1– Schematic diagram of the major components of the pulsed NMR apparatus.

The apparatus is made by TeachSpin. More information is available on the TeachSpin website [www.teachspin.com/instruments/pulsed\\_NMR/specifications.shtml](http://www.teachspin.com/instruments/pulsed_NMR/specifications.shtml). TeachSpin

provides a nice tutorial that is a good compliment to the information presented here. A schematic of the apparatus is shown in Fig. 1. The magnetic field is provided by a permanent magnet consisting of two parallel pole tips connected by a soft-iron flux return. The direction of this field defines the  $\mathbf{z}$ -axis, and the quantization axis in the quantum-mechanical picture.

The NMR “probe” consists of a pair of coils oriented with perpendicular axes that are perpendicular to  $\vec{B}_0$ . One coil, the transmitter coil, produces the oscillating field  $\vec{B}_1$  along the  $\mathbf{x}$ -axis. The transmitter coil is connected to the output of an amplified RF source that provides the radiofrequency (RF). The frequency of the oscillator is digitally controlled, and its amplitude is controlled by the pulse programmer. The most important feature of this is that the RF  $\vec{B}_1$  field can be turned on in pulses at pre-programmed times and with pre-programmed pulse duration. This is achieved with an electronic on-off switch that is controlled by logic signals from the pulse programmer. The pulses are “top hat” shaped and can be varied in duration, number of pulses, and repetition time. For example, the spin echo sequence requires an initial “ $\pi/2$ ” pulse followed by a  $\pi$  pulse at some later time. Special pulse sequences used to set  $T_2$  from  $T_2^*$  require an initial  $\pi/2$  pulse followed by a series of  $\pi$  pulses.

The second coil, oriented along the  $\mathbf{y}$ -axis is a pick-up coil that is connected to a preamplifier/receiver. The raw NMR signal is proportional to the projection of the magnetization along this  $\mathbf{y}$ -axis, i.e.  $S(\phi) \sim \sin(\phi)$ .

In most applications where high frequency signals are measured, we do not directly monitor at RF frequencies; rather we use a form of detector that generates a low frequency beat by MIXING the signal with a reference or carrier signal of nearly the same frequency. In the pulsed NMR apparatus, a single tunable signal generator is used to generate  $\vec{B}_1(t)$  and the reference signal. In a second circuit called the RF AMPLITUDE DETECTOR, the RF signal is rectified and converted to a slowly varying measure of the signal amplitude. The PS1-A apparatus has both a mixer that produces a low frequency beat signal, and an RF detector that produces a DC signal proportional to signal amplitude.

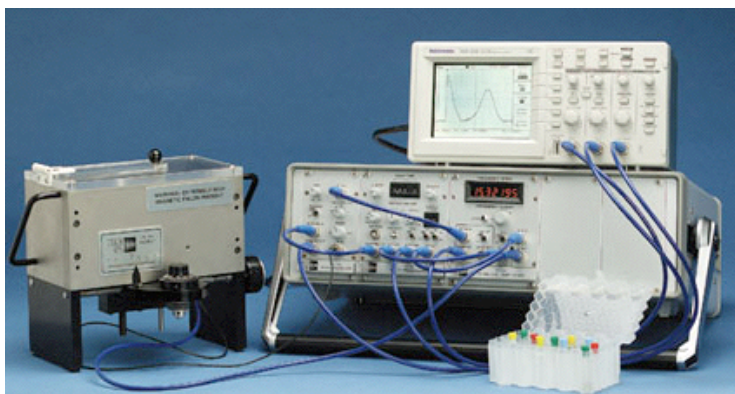


Figure 2 – The TeachSpin apparatus. The magnet is on the left.

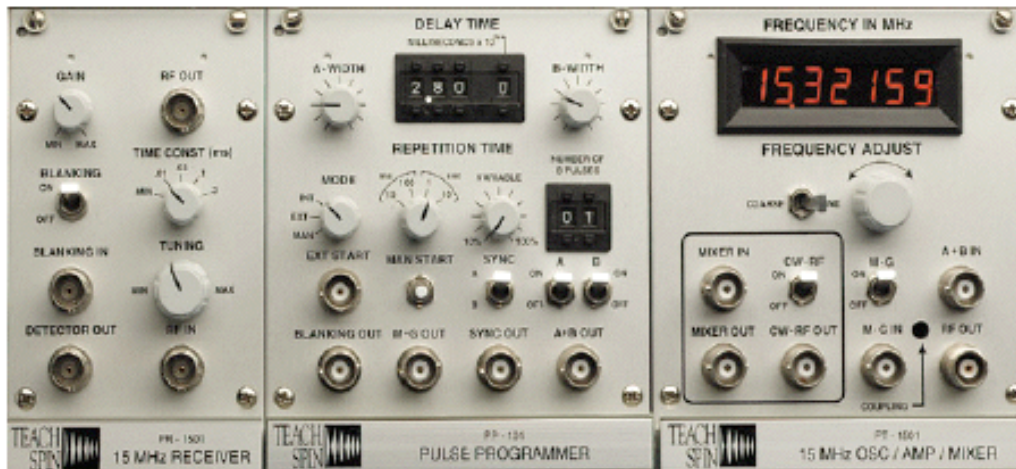


Figure 3 – The front panel of the electronics modules. The Left Module is the Signal Amplifier and Signal Amplitude Detector. The Central Module is the Pulse Programmer; and the Right Module is the RF Oscillator/Amplifier combination AND the Signal Mixer.

To gain familiarity with the apparatus, use an oscilloscope to understand each of the following functions:

- pulse sequencing
- detection,
- signal mixing to low frequency
- RF amplitude detection.

First observe the CW-RF generator output using the CW-RF out BNC. (Make sure the RF OUT is hooked up to the NMR coil.) You should measure a sinusoidal signal of frequency about 15 MHz. The Frequency Adjust changes this by only a few percent because the RF electronics are narrowly tuned. The tuning knob on the Signal Amplifier module can be used to optimize

Next, hook up the scope to the pulse programmer output (labeled A+B OUT). The pulse programmer can produce a single pulse excitation pulse (*A* Pulse) and one or more subsequent pulses (*B* Pulses) with variable repetition rate. The pulse widths of *A* and *B* can be set independently. Set  $N=1$  and observe the programming pulse as you select pulse *A*, pulse *B*, or both. Vary the pulse widths and repetition time. Next, set  $N$  to some number greater than 2 and observe what happens when you vary the repetition time and pulse parameters. The pulse parameter output (*A+B* OUT) will be connected to the oscillator (*A+B* IN) to modulate the RF output i.e., the  $\approx 15\text{MHz}$  sinusoid is multiplied by the pulse programmer output. (When the programmer output is TTL-LOW (0 V), the RF output is ZERO.) The SYNC signal will be used to trigger the oscilloscope. This SYNC signal can be triggered from *A* and/or *B*. BLANKING is a logical signal used to turn off the preamplifier input during the pulse in order to prevent bad effects from the huge RF signal input to the preamp.

## Finding the Pulsed NMR Signal

Place a sample in the probe: H<sub>2</sub>O with CuSO<sub>4</sub> is a good choice because T<sub>1</sub>, the time constant for recovery of the equilibrium nuclear magnetization, is shortened to a few milliseconds by the paramagnetic Cu<sup>+</sup> ions. In pure H<sub>2</sub>O, T<sub>1</sub> ≈ 2.3 seconds so that the time between measurements must be several times this, which would be quite inconvenient. Hook up the outputs of both the MIXER (OUT) and RF Detector (OUT) to the inputs of the 54642A oscilloscope. Connect the Sync Out to the External Trigger input of the scope. The following set of values is a good starting point:

Frequency 15.32 MHz

CWRF ON

A ON, B OFF

REPETITION 0.1 sec

SYNC A

BLANKING ON

TIME CONST 0.01 ms

Oscilloscope: 500 mV/cm for Detector and 5 V/cm for Mixer.

Set sweep speed to 1 ms/cm scale.

Set Edge/Trigger to Ext, rising edge. Check that scope is triggering externally.

Observe the signals. You will generally find the DETECTOR output more useful, except when it is desirable to measure the beat frequency directly. To understand this, vary the RF frequency and watch the beat frequency change. Find  $\nu_0$  by varying the oscillator frequency to find zero beat frequency. Since the permanent magnet is somewhat temperature dependent so is  $\nu_0$ . Now vary the position of the sample horizontally using the knob to maximize the width of the pulse. The frequency may have to be readjusted as you do this. Do the same with the vertical position.

Vary the pulse width  $\tau$ . Find values of  $\tau$  that give  $\pi$ ,  $\pi/2$  etc. tip-angle. For example, as the pulse width is increased from the minimum value, the first maximum of signal amplitude (observed with either the detector or mixer signal) corresponds to a  $\pi/2$  pulse, and the subsequent minimum to a  $\pi$  pulse. Vary the RF frequency and find

With  $\tau$  set for a  $\pi/2$  pulse, vary the RF frequency and observe the mixer and detector outputs. You should also use these signals to familiarize yourself with the preamplifier (15 MHz Receiver). The preamp is frequency tunable for maximum matching to the signal frequency. An output for the amplified signal from the pick-up coil is provided, and the preamp gain is variable. Observe the effects of turning blanking on and off.

### $T_2^*$

The observed “ring down time”,  $T_2^*$ , is the combination of several contributions, most notably saturation recovery (measured by  $T_1$ ), dephasing in the presence of fluctuating magnetic fields due to the motion of spins in the lattice ( $T_2$ ), and inhomogeneous magnetic field broadening ( $T_2^B$ ). The combination of the rates is the inverse of  $T_2^*$ :

$$\frac{1}{T_2^*} = \frac{1}{2T_1} + \frac{1}{T_2} + \frac{1}{T_2^B}$$

Use the storage function of the oscilloscope to acquire a single pulse and measure  $T_2^*$ . You can also download the scope's memory to a PC for offline analysis. (See separate instructions.) The effects of magnetic field inhomogeneity on  $T_2^*$  can be demonstrated by changing the sample position. This changes the homogeneity of  $\mathbf{B}_0$  across the sample and thus changes  $T_2^B$ .

## Spin Echo

Spin echo is one of the elegant and most useful features of pulsed NMR and clearly shows that  $T_2^*$  has several contributions, in particular that due to magnetic field inhomogeneity. Consider a sample in which the atoms are fixed so that each atom is in a slightly different magnetic field. The NMR signal will be made up of magnetization with a spread of frequencies resulting from the differences in magnetic field at the position of each atom. Each atom has a different frequency; and the spectrum is broader as the inhomogeneity increases. This is called inhomogeneous broadening.

Consider two spins, spatially separated, that have frequencies  $\omega_1 = \omega_0 + \delta/2$  and  $\omega_2 = \omega_0 - \delta/2$ . After a  $\pi/2$  pulse, the two spins are parallel, pointing along the  $\hat{y}_R$  axis in the rotating frame. This produces the maximum NMR signal amplitude. After some time,  $t$ , the two spins are out of phase by  $\Delta\phi = \delta t$  radians. You should show that the NMR signal from the combination of the two spins is proportional to  $\cos(\Delta\phi/2)$ . Now a  $\pi$  pulse is a rotation of  $\pi$  radians of both spins about the  $\hat{x}_R$  axis so that the phase difference is reversed, that is spin 1, which was ahead of spin-2 is now behind, or  $\Delta\phi \Rightarrow \Delta\phi' = -\Delta\phi$ . After another interval  $t$ , the total phase difference is  $\Delta\phi + \Delta\phi' = 0$ . The spins are back in phase and the signal is again a maximum. In fact the spins move randomly in the sample and diffuse from their original positions, so the original signal is not completely recovered, but if diffusion is slow compared to  $1/T_2$ , it is fact possible to get a good measure of the intrinsic spin-spin interaction.

Observing this effect shows that name spin echo is quite appropriate. You will use both pulse  $A$  and pulse  $B$  for this measurement. Set up with the triggering (SYNC) from pulse  $A$ , Adjust the width of pulse  $A$  for  $\pi/2$ . Now switch to pulse  $B$  (pulse  $A$  off, SYNC from pulse  $B$ ,  $N=1$ ). Set the width of pulse  $B$  for  $\pi$ . Now switch both  $A$  and  $B$  on, with the scope triggered from  $A$ , and vary the repetition time. You should see the spin echo. Measure the dependence of the echo size on repetition time.

The pulse sequence is  $\pi/2 - t/2 - \pi - t - \pi \dots$  where  $t$  is the programmed repetition time, on the order of several to 10 milliseconds (or longer).

## $T_2$

We have seen that the dephasing of spins that leads to inhomogeneous broadening can be reversed using the spin echo sequence. The other contributions to  $T_2^*$  are homogeneous, the

same for all spins in the sample, and cannot be reversed. Thus, as the echo time is increased, the echo decreases due to the homogeneous broadening effects.

The spin echo sequence could be used with varying echo times to measure the homogeneous contributions  $T_1$  and  $T_2$ . Alternatively, a sequence with multiple echoes is often employed. To observe this, set up the spin echo experiment, and increase the number of  $B$  pulses. Plot the echo amplitudes as a function of  $B$  pulse number. The resulting exponential decay has a time constant  $\approx T_2$  as long as  $T_1 \ll T_2$ . You will measure  $T_1$  in the next section.

## $T_1$

The common method for measuring  $T_1$  is called saturation-recovery or inversion-recovery. This method relies on the fact that the spin system is initially perturbed by a  $\pi$  pulse so that the populations are not in equilibrium. The sample is then examined in time intervals following the removal of the perturbation.

To measure  $T_1$  using saturation recovery, apply a  $\pi/2$  pulse to the nuclear magnetization, immediately after the pulse is small, nearly 0, and it recovers to thermal equilibrium with the time constant  $T_1$ . Since the NMR signal size just after the pulse is a measure of  $M_0$  before the pulse, you can observe the recovery to thermal equilibrium with a second  $\pi/2$  pulse as you vary the time separating the two pulses. WARNING: if  $M_T$  is appreciable when the second  $\pi/2$  pulse is applied, the signal will not be proportional to  $M_0$ , rather it will be some combination that cannot be easily interpreted. Saturation absorption methods thus depend on the condition  $T_2^* \ll T_1$ . Fortunately you can affect and tune  $T_2^*$

To measure  $T_2$  using inversion recovery, apply a  $\pi$  pulse to obtain the population inversion and then sample the magnetization with a  $\pi/2$  pulse as you vary the time separating the two pulses. The magnetization will start at  $-M_0$  right after the first pulse and head toward  $+M_0$  with a time constant  $T_1$ . Note that the signal will pass through zero.

The pulse sequence is  $\pi - \mathbf{t}/2 - \pi/2 - \mathbf{t} - \pi/2 \dots$  where  $\mathbf{t}$  is the programmed repetition time, on the order of  $10^3$ 's of milliseconds (shorter for the  $\text{CuSO}_4$  doped water sample).

## Changing Samples

Now that you are adept at measuring the NMR parameters  $T_1, T_2, \text{etc.}$ , you can try other samples. In addition to  $\text{Cu}_2\text{SO}_4$ , you should do glycerine, mineral oil, Vaseline, and pure  $\text{H}_2\text{O}$ .

## Measuring the Chemical Shift

When the nucleus is imbedded in an atom the actual magnetic field is partially shielded by the magnetic field of the circulating electrons, so that the measured frequency  $\nu$  is

$$\nu = \nu_0(1 - \alpha)$$

where  $\nu_0$  is some reference frequency, which might be that for an isolated nucleus, and  $\alpha$  is

called the chemical shift, which is typically a few parts per million or ppm. Proton chemical shifts are typically of 10 ppm, and are very important in analytical NMR because they provide a means to distinguish protons in different chemical environments. Because they are so small chemical shifts cannot be practically measured with our apparatus, due to the inhomogeneous broadening, i.e. nonuniformity of magnetic field and the effects of temperature.

## Other pulse sequences

You can generate other pulse sequences including the MG sequence, which involves a change of phase of the applied RF. See the reading, in particular Slichter's book.

## Caveats

Permanent magnets are temperature sensitive. The approximate temperature coefficient for this

magnet is  $\frac{dB}{dt} \approx \frac{4G}{^{\circ}C}$ .

### Questions

- (1) Explain how NMR is related to MRI.
- (2) Look up chemical shifts for similar samples and compare with yours.
- (3) Explain how chemical shifts can be used to make MRI sensitive to hydrogen in chemical environments other than H<sub>2</sub>O.
- (4) Explain how NMR/MRI techniques can be used to distinguish normal tissue from tumors.
- (5) Which of the following nuclei are not of interest to MRI? Explain why not.  
 $^1\text{H}$ ,  $^2\text{H}$ ,  $^{12}\text{C}$ ,  $^{13}\text{C}$ ,  $^{23}\text{Na}$ ,  $^4\text{He}$ ,  $^{129}\text{Xe}$ ,  $^{31}\text{P}$
- (6) In one form of functional MRI, brain function is studied by imaging the phosphorous-containing compound ATP. Explain why this is possible.
- (7) Explain briefly what " $\pi/2$ " and " $\pi$ " pulses do.

### References

A good primer on NMR is at [www.cis.rit.edu/htbooks/nmr/inside.htm](http://www.cis.rit.edu/htbooks/nmr/inside.htm)

Haken and Wolf, Chapter 20.

Principles of Magnetic Resonance, C.P. Slichter, Springer Chapters 1-2.

### **APPENDIX – Using the Agilent 54600 Program to Capture the Scope Information**

Check that the data cable is connected to the back of the scope and to the data port on the computer. Start up the computer and log in. Click on the shortcut to agt5400.xls. Allow it to initialize Active X.

It will start up Excel with some extra controls for the scope in the upper right menu bar. Use Connect to Scope to start a connection. Open a new Excel spreadsheet. Then use the Get Waveform icon to capture the scope traces into the spreadsheet. Then you can manipulate or graph the data just as in any other Excel spreadsheet.