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Nuclear Magnetic Resonance

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Abstract

An overview of the significant historical events in the development of Nuclear Magnetic Resonance is presented. The underlying physics of NMR are discussed, including the quantum mechanical and semi-classical views of spin and the statistical properties of bulk spin moments. Methods of detection and pulse sequences are examined

1. INTRODUCTION

Nuclear Magnetic Resonance is a physical phenomenon. Under certain conditions, a particle with spin can absorb energy from a surrounding magnetic field. When this absorption happens, the particle in precession is said to be "in resonance" with the surrounding field.

There have been a number of Nobel Prizes awarded for work in NMR. Felix Bloch and Edgar Mills Purcell shared the Nobel Prize for physics in 1952 for their discovery of NMR. In 1991, Richard Ernst earned a Nobel in Chemistry for the development of the methodology of high resolution nuclear magnetic resonance spectroscopy. The 2002 Nobel Prize for chemistry went to Kurt Wüthrich for development of NMR spectroscopy. Paul Lauterbur and Peter Mansfield shared a Nobel Prize in Medicine in 2003 for demonstrating that gradient fields and Fourier transforms could be used to create two-dimensional pictures.

2. THE UNDERLYING PHYSICS

NMR is essentially a two-step process that works because we are able to observe the way large numbers of protons respond to magnetic fields. In the first step, we manipulate the spin orientations of the protons; and in the second step, we measure changes in those orientations with a detector. Although the magnetic field of each proton is tiny, and only a small fraction of the protons turn out to be detectable due to their alignment properties, there are many Avogadro numbers of them in the body, and we can measure the sum of all of those fields.

2.1 SPIN

In classical mechanics, an object can undergo two types of angular momentum: The first type, orbital angular momentum, is associated with motion of the center of mass of the object around some point – like the Earth orbiting around the sun. The second type, spin angular momentum, is associated with the rotation of an object – like the Earth spinning on its axis.

In quantum mechanics, elementary particles carry an intrinsic angular momentum (S). This has nothing to do with motion in space, but is somewhat analogous to classical spin and so the same term is used. Every kind of particle has a specific value of spin which never changes. For example, electrons, neutrons and protons have spin ½, while photons have spin 1. We will be interested in spin ½ in this instance, and particularly how particles with spin react to magnetic fields.

The Schrödinger equation, models this quantum mechanical behavior:

$$i\hbar \frac{\partial \Psi}{\partial t} = H\Psi \ .$$

It can be solved by separation of variables. The solution constructs simultaneous eigenfunctions of three commuting operators, H, L^2 and L_z. The algebraic theory of spin is exactly the same as that of orbital angular momentum, so one can write,

$$H\Psi = E\Psi, \quad S^2\Psi = \hbar^2 s(s+1)\Psi, \quad S_z\Psi = \hbar m\Psi .$$

This is usually written in Dirac notation

$$H\left|s\ m\right\rangle = E\left|s\ m\right\rangle, \quad S^2\left|s\ m\right\rangle = \hbar^2 s(s+1)\left|s\ m\right\rangle, \quad S_z\left|s\ m\right\rangle = \hbar m\left|s\ m\right\rangle,$$

where s is the spin (½) and m is either (+½ or –½). Thus the orientation takes on two values, which we interpret as parallel to an axis or antiparallel. For spin ½ particles, there are then two eigenstates,

$\left|\frac{1}{2}\ \left(+\frac{1}{2}\right)\right\rangle$, which we call spin up, and

$\left|\frac{1}{2}\ \left(-\frac{1}{2}\right)\right\rangle$, which we call spin down.

A spinning charged particle acts like a magnetic dipole. The particle's magnetic dipole moment ($\vec{\mu}$) is proportional to its spin angular momentum,

$$\vec{\mu} = \gamma\vec{S} ,$$

and the proportionality constant (γ) is called the gyromagnetic ratio. If one considers a proton in a uniform magnetic field $\vec{B}_0 = B_0\hat{z}$ along the z-axis, the matrix representation of the Hamiltonian would be

$$\mathcal{H} = -\gamma B_0 S_z = -\gamma B_0 \frac{\hbar}{2}\begin{bmatrix} 1 & 0 \\ 0 & -1 \end{bmatrix}.$$

The Hamiltonian is time-independent, so the general solution to the time-dependent Schrödinger equation is,

$$i\hbar\frac{d}{dt}\chi = \mathcal{H}\chi .$$

Solution can be expressed in terms of "stationary states,"

$$\chi\ t\ = a\chi_+ e^{-i\frac{E_+ t}{\hbar}} + b\chi_- e^{-i\frac{E_- t}{\hbar}} .$$

Since $\mathcal{H}\left|s\ m\right\rangle = E\left|s\ m\right\rangle$,

$-\gamma B_0 \frac{\hbar}{2}\begin{bmatrix}1 & 0\\ 0 & -1\end{bmatrix}\begin{bmatrix}1\\ 0\end{bmatrix} = -\gamma B_0 \frac{\hbar}{2}\begin{bmatrix}1\\ 0\end{bmatrix}$ implies that for χ_+ the energy $E_+ = -\gamma B_0 \frac{\hbar}{2}$, and

$-\gamma B_0 \frac{\hbar}{2}\begin{bmatrix}1 & 0\\ 0 & -1\end{bmatrix}\begin{bmatrix}0\\ 1\end{bmatrix} = +\gamma B_0 \frac{\hbar}{2}\begin{bmatrix}0\\ 1\end{bmatrix}$ implies that for χ_- the energy $E_- = +\gamma B_0 \frac{\hbar}{2}$.

Putting this together,

$\chi\ t\ = a\chi_+ e^{-i\frac{-\gamma B_0 \frac{\hbar}{2} t}{\hbar}} + b\chi_+ e^{-i\frac{+\gamma B_0 \frac{\hbar}{2} t}{\hbar}}$, which can be written as $\chi\ t\ = \begin{pmatrix} ae^{\frac{i\gamma B_0 t}{2}} \\ be^{\frac{-i\gamma B_0 t}{2}} \end{pmatrix}$.

With a little foreknowledge, one can write $a = \cos(\frac{\alpha}{2}),\quad b = \sin(\frac{\alpha}{2}),$ and calculate the expectation values of S_x, S_y, and S_z.

$$\left\langle S_z \right\rangle = \begin{bmatrix} \cos(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} & \sin(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} \end{bmatrix} \frac{\hbar}{2}\begin{bmatrix}1 & 0\\ 0 & -1\end{bmatrix}\begin{bmatrix} \cos(\frac{\alpha}{2})e^{\frac{i\gamma B_0 t}{2}} \\ \sin(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} \end{bmatrix} = \frac{\hbar}{2}\sin\ \alpha\ \cos\ \gamma B_0 t$$

$$\left\langle S_y \right\rangle = \begin{bmatrix} \cos(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} & \sin(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} \end{bmatrix} \frac{\hbar}{2}\begin{bmatrix}0 & -i\\ i & 0\end{bmatrix}\begin{bmatrix} \cos(\frac{\alpha}{2})e^{\frac{i\gamma B_0 t}{2}} \\ \sin(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} \end{bmatrix} = -\frac{\hbar}{2}\sin\ \alpha\ \sin\ \gamma B_0 t$$

$$\left\langle S_z \right\rangle = \begin{bmatrix} \cos(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} & \sin(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} \end{bmatrix} \frac{\hbar}{2}\begin{bmatrix}1 & 0\\ 0 & -1\end{bmatrix}\begin{bmatrix} \cos(\frac{\alpha}{2})e^{\frac{i\gamma B_0 t}{2}} \\ \sin(\frac{\alpha}{2})e^{\frac{-i\gamma B_0 t}{2}} \end{bmatrix} = \frac{\hbar}{2}\cos\ \alpha$$

From the expression $\left\langle S_z \right\rangle = \frac{\hbar}{2}\cos\ \alpha$ one can infer that $\left\langle S \right\rangle$ is tilted away from the z-axis at a constant angle α. From the expressions for $\left\langle S_z \right\rangle$ and $\left\langle S_z \right\rangle$ one can infer that the spin vector precesses around the z-axis at a frequency $\omega = \gamma B_0$. This frequency is called the Larmor frequency and it is dependent on the gyromagnetic ratio of the particle and on the magnetic field.

The energies of the quantum state with S_z parallel to the magnetic field are

$$E_+ = -\gamma B_0 \frac{\hbar}{2},\ E_- = +\gamma B_0 \frac{\hbar}{2}.$$

This is an example of the Zeeman effect. Whenever an atom is placed in a uniform external magnetic field, the energy levels are shifted. The difference between the energies in this case is $\gamma B_0 \hbar$. This is equal to $\omega\hbar$ since $\omega = \gamma B_0$. In the same way that an atom can absorb or emit a photon and change energy state, a particular proton can be induced to change its magnetic field alignment if it receives an amount of energy equivalent to $\omega\hbar$ where ω is the Larmor frequency. This is the essence of nuclear magnetic resonance.

2.2 MACROSCOPIC SPIN

When making the transition from the quantum world to the macroscopic world, one begins to look at the average orientations of the spins of Avogadro numbers of protons.

There is a trade-off between the tendency of a spin system to remain aligned with the magnetic field, and the ability of the system to gain energy. Some fraction of the protons in a sample will gain energy from thermal contact with their surroundings and change to the higher energy state – that with the spin aligned antiparallel to the magnetic field as seen above. The total number of protons that align is related to the Boltzmann factor, which is the probability that a given system will be found at a particular energy. This factor is,

$$P(E) = e^{-\frac{E}{kT}}.$$

Using the factors derived above, it can be seen that the ratio of probabilities that a sample of protons will be in a particular state is,

$$\frac{P(E_+)}{P(E_-)} = \frac{e^{\frac{\gamma h B_0}{2kT}}}{e^{-\frac{\gamma h B_0}{2kT}}}.$$

Using $\gamma = 42.58 MHz/T$ (hydrogen), $B_0 = 1.5T$ (a real value for the magnetic field in the Philips Achieva MRI machine), and T=295K (room temperature – 72º F) we find

$$\frac{P(E_+)}{P(E_-)} \approx 1.00001$$

There is an almost vanishingly small preference of protons to be in the aligned state. The vast majority of protons cancel each others magnetic moments. The ratio above may be

barely above unity, but Avogadro's number is big. There will still be on the order of 10^{18} protons per gram of hydrogen sample that align with the static field. This is called the spin excess and provides a macroscopic magnetization that can be detected.

2.3 ROTATING MAGNETIC FIELDS

Quantum mechanically, the MRI system needs to be able to add energy to the protons under measurement in units of $\omega\hbar$. This implies a rotating a magnetic field at a frequency $\omega = \gamma B_0$

This rotating field is actually created using a single RF coil. The simplest way to visualize how this happens is shown in Figure 1. Recall that a current passing through an RF coil will create a magnetic field parallel or antiparallel to its axis depending on the current direction. If this current is varied sinusoidally, the resulting magnetic field vector will oscillate from positive to negative and back again as shown in Figure 1 (top).

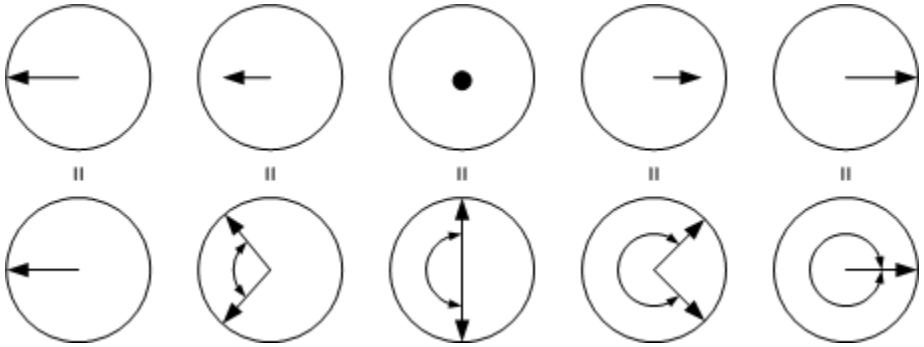

Figure 1: The RF field can be viewed as a sinusoidally varying signal in a single direction (top) as well as the sum of counter-rotating vectors (bottom).

Imagine that this magnetic field vector is actually the sum of two counter-rotating vectors as shown in Figure 6 (bottom). The vector direction of the sum of the two vectors in the bottom row will be the same as that of the vectors in the top row. Now if the rotational frequency of the vectors in the bottom row is chosen to rotate with a particle's Larmor frequency, and the direction of rotation is also chosen to match the direction of precession, the chosen rotating vector will have the characteristics required of the rotating magnetic field.

In a real MRI machine one defines a laboratory frame with the z-axis running down the bore of the superconducting magnet. This is the direction of the static magnetic field $\vec{B}_0$. The RF coil is typically placed around the subject along the x-axis. Figure 2 shows how this lab frame would look.

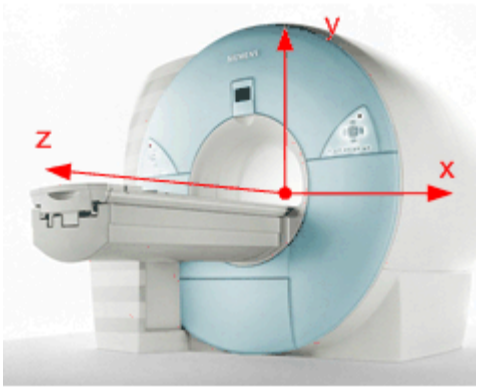

Figure 2: The laboratory coordinate system of an MRI machine.

2.4 ROTATING REFERENCE FRAMES

If one takes a semiclassical view of a subject immersed in the large static magnetic field of an MRI machine, one sees a macroscopic magnetic dipole moment $\vec{u} = \gamma \vec{J}$ which is a result of the sum of all of the quantum mechanical magnetic dipole moments $\vec{u} = \gamma \vec{S}$ of the subject. This macroscopic magnetic dipole moment will precess around the z-axis of the laboratory frame at a frequency $\omega = \gamma B_0$. The second rotating magnetic field designated B_1 will rotate around the z-axis in the x-y plane at the same frequency, as illustrated in Figure 3. Consider what this situation would look like in a frame of reference where the x-y plane is also rotating at $\omega = \gamma B_0$. Both B_0 and B_1 would be rotating at the same rate and would appear *static* in this reference frame.

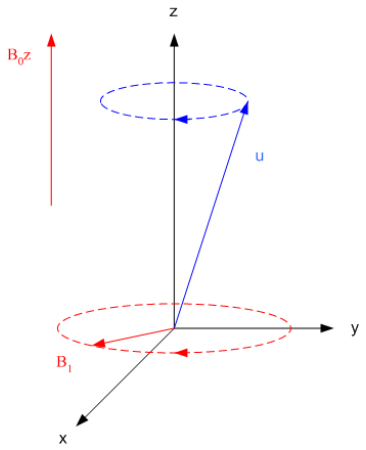

Figure 3: The Magnetic Fields and the Dipole Moment.

This rotating reference frame turns out to be very useful for understanding what is happening in MRI systems. The equation of motion for the dipole moment in the laboratory frame is,

$$\frac{d\vec{u}}{dt} = \vec{u} \times \gamma \left[\vec{B}_0 + \vec{B}_1 \ \ t \ \right].$$

If H_1 is taken along the x-axis, and a transform is made into the rotating frame, the equation of motion becomes,

$$\frac{\delta \vec{u}}{\delta t} = \vec{u} \times \gamma \left[\left(B_0 - \frac{\omega}{\gamma} \right) \hat{z} + B_1 \hat{x}' \right].$$

An effective magnetic field can then be defined in this frame,

$$B_{eff} = \left(B_0 - \frac{\omega}{\gamma} \right) \hat{z} + B_1 \hat{x}',$$

The cosine of the angle between the z-axis and the effective field is then

$$\cos \ \theta \ = \frac{B_0 - \dfrac{\omega}{\gamma}}{B_{eff}}.$$

The angle θ in the macroscopic rotating frame view corresponds to the angle α in the quantum mechanical treatment developed previously. If $\omega = \gamma B_0$, the term in parentheses in B_{eff} above drops out and the magnetic moment sees a torque of,

$$\vec{u} \times \gamma \vec{B}_1 .$$

A magnetic moment that is initially parallel to the static field (in the z-axis) will be caused to rotate in the z-y plane at a frequency of $\omega = \gamma B_1$ as illustrated in Figure 4. (N.B. the orientation of the axes in the figure, with the z-axis vertical).

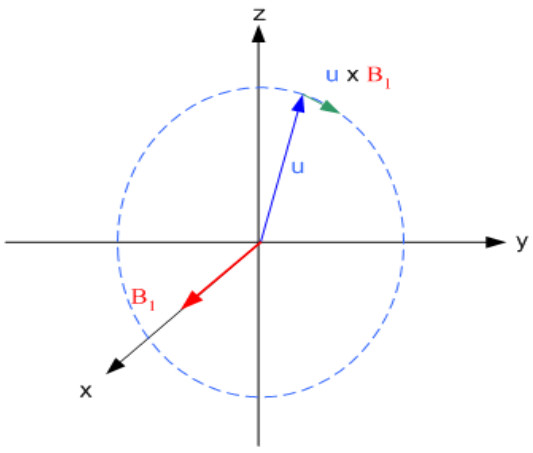

Figure 4: The magnetic dipole moment rotated by the torque of the RF field.

In the jargon of NMR systems, if the rotating magnetic field is turned on for a time corresponding to a rotation of $\vec{u}$ around a quarter of the circle in Figure 4 and then turned off, it is called a $\pi/2$ pulse. This is because $\vec{u}$ will rotate $\pi/2$ radians in that time. Figure 5 shows the effect of a pulse of this type on the macroscopic magnetic dipole moment as viewed in the lab frame. Think of the tip of the vector as initially precessing tightly around the z-axis under the influence of the strong static magnetic field B_0.

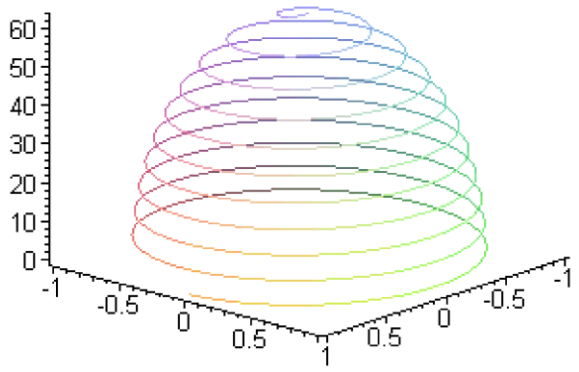

Figure 5: Effect of a $\pi/2$ pulse in the lab frame.

When the rotating magnetic field is turned on, a torque is applied to $\vec{u}$ which tends to rotate its precession into the x-z plane. Since $\vec{u}$ is precessing, it *spirals* down to the x-z plane.

2.5 RELAXATION

Once a proton spin is manipulated to cause it to precess around the z-axis in the x-y plane, as a result of a $\pi/2$ pulse for example, it does not remain in that state. The proton spins want to return to their equilibrium value. This process returns a sample back to the initial state with a spin excess number of protons aligned with the static magnetic field as predicted by the ratio of Boltzmann factors.

A π pulse (just continue a $\pi/2$ pulse until the precession moves through the x-z plane, and past, until the magnetic dipole precesses around to the –z axis) will add enough energy to the protons in the body to change the quantum state of each one of the lower energy protons involved in the spin excess from E_+ (the lower energy spin ½ state) to E_- (the higher energy spin –½ state).

This energy is returned during relaxation. The relaxation is exponential and caused by several mechanisms. The time constant describing the relaxation due to the combined effects of the several mechanisms is called the *Combined Relaxation Time* and is designated T_2^*.

One of the mechanisms responsible for returning energy is related to the local environment of the protons. The local environment is called the "lattice" (since most of the early experimenters in Nuclear Magnetic Resonance were solid-state physicists). The

excess energy above the ground state that was acquired by each proton during the rotating field pulse is returned to its surroundings. This mechanism is called spin-lattice relaxation and the corresponding time constant (T_1) is called the spin-lattice relaxation time – the time it takes to reduce the *longitudinal* magnetization by a factor of e. Some typical values for various human tissues are shown in Table 1.

Another mechanism driving relaxation is the spin-spin relaxation. This mechanism is driven by *local* inhomogeneities in the magnetic field. Different values of the local magnetic field lead to different precession frequencies. For example, electrons can shield nuclei from the ambient magnetic field.[1] This difference in magnetic field leads to the individual spins gradually "dephasing" and resulting in a reduction in the total *transverse* magnetization vector to its equilibrium value of 0. Table 1 also shows typical values for T_2.

Tissue	T_1 (ms)	T_2 (ms)
Gray Matter	950	100
White Matter	600	80
Muscle	900	50
Cerebrospinal Fluid	4500	2200
Fat	250	60
Arterial Blood	1200	200
Venous Blood	1200	100

Table 1: Approximate values of relaxation parameters T_1 and T_2 at $B_0 = 1.5$T, T = 37º C

There is an additional dephasing of the spins due to *external* field inhomogeneities and is defined to be

$$T_2^{'} = \gamma \Delta B_0 .$$

The combined relaxation time is defined as

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

3.0 DETECTION

In the previous sections it has been shown how an NMR system manipulates the magnetic dipole moments of protons under examination. The result of this process is to cause the magnetic dipole moment to precess into certain orientations. Once the driving force is removed, the dipole moments continue to precess and produce their own

[1] This is, in fact, the basis for NMR Spectroscopy. The structure of nearby electrons affects the local environment of the protons allowing us to discern the 3-D structure of the surrounding elements.

changing magnetic fields. It is the change in those fields over time which allows us to observe the Nuclear Magnetic Resonance phenomenon and its decay.

Consider first a hypothetical macroscopic bar magnet spinning in the vicinity of a coil, as illustrated in Figure 6. This is simply an electric generator. Now imagine replacing the magnet with the precessing magnetization of the body caused by the actions of the external static field and the rotating field.

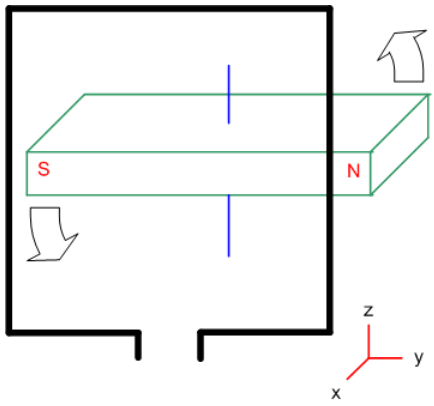

Figure 6: An electric generator.

This situation is illustrated in Figure 7. This illustration shows a red magnetic field vector, B(t), rotating in the x-y plane representing the precessing proton spins. A (thick black) coil is shown placed in the x-z plane with its center at the origin to detect the changing field.

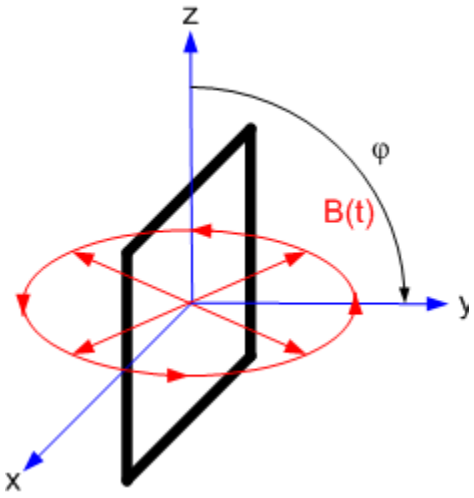

Figure 7: A stylized NMR detector.

The rotating magnetic field should look familiar; it is just like the field applied to manipulate the precession of the proton spins, but here it is due to the proton spins themselves.

The rotating magnetic field caused by the macroscopic moment could be described by,

$$\vec{B}\ t\ = B\ \cos\omega t\hat{x} + \sin\omega t\hat{y}\ \ .$$

Taking into account the angle φ (which corresponds to the angle of precession; through which the torque of the rotating RF field caused the spins to rotate; and also through which the change in energy due to relaxation will cause the spins to rotate the other way), it can be seen that,

$$\vec{B}\ t\ = B\sin\phi\ \cos\omega t\hat{x} + \sin\omega t\hat{y}\ \ .$$

The flux through the coil is found by the universal flux rule. If one imagines the field is constant over the coil at any particular time ($d\varphi/dt$ is constant – valid since the relaxation time is measured in hundreds of milliseconds, and the RF field is measured in megahertz) it can be shown that

$$\Phi = \int_{-L/2}^{L/2} dx \int_{-L/2}^{L/2} dz\ \ \hat{y}\bullet B\ \ t\ \ = L^2\ \ \hat{y}\bullet B\ \ t\ \ \ = L^2 B\sin\omega t\sin\phi\,.$$

Differentiating to find the induced emf:

$$\mathcal{E} = -\frac{d}{dt}L^2 B\sin\omega t\sin\phi = -L^2 B\omega\cos\omega t\sin\phi\,.$$

Figure 8 shows how a response (the induced EMF in the coil) to a π pulse might be seen.

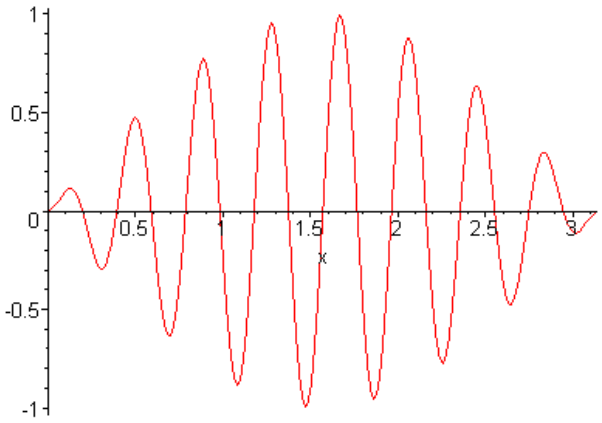

Figure 8: The response of a system after application of a pi pulse.

The signal grows from zero to a maximum when the magnetic field is rotating in the x-y plane. At this point, $\phi = \pi/2$ and a $\pi/2$ pulse has been applied. The signal then decreases until the spins are precessing in the –y axis at which point a π pulse has been applied.

If the driving rotating magnetic field were removed at the $\pi/2$ point, the relaxation process would begin and an exponential decay of the signal would be seen, with the time constant determined by T_2^*. Figure 9 shows what the response to a $\pi/2$ pulse, followed by a relaxation might look like. The decay portion of the signal envelope is known as the Free Induction Decay (FID).

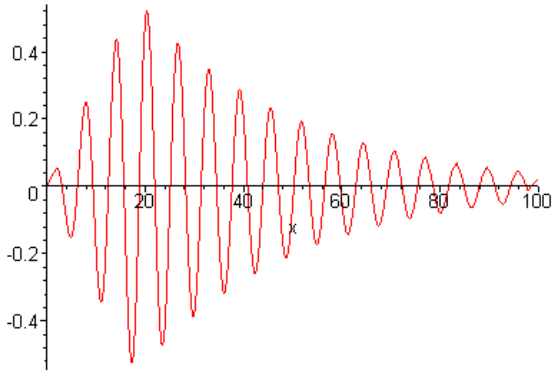

Figure 9: Free induction decay following a pi/2 pulse.

The signal shown in Figure 9 is typically demodulated (in the sense of rectifying and filtering) and displayed as an exponentially decaying curve from the point at which the driving field is removed. Figure 10 shows what a typical demodulated FID signal could look like. This is also how the FID signal would appear in the rotating reference frame, by the way.

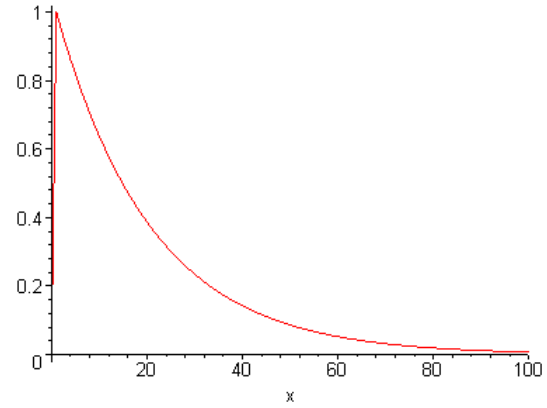

Figure 10: Demodulated free induction decay following a pi/2 pulse

3.1 PULSE SEQUENCES

An NMR experiment will consist of many measurements of the FID. The arrangement of stimuli (gradients, RF pulses – the rotating magnetic field) and measurements are

arranged in a *Sequence Diagram*. An example of the most basic sequence is shown in Figure 11.

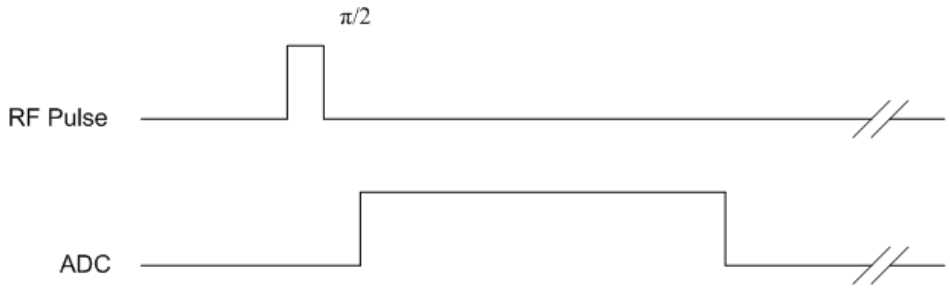

Figure 11: A basic NMR pulse sequence diagram

Here a $\pi/2$ pulse is applied, and the FID is measured by enabling an Analog to Digital Converter (ADC) which converts the FID signal into a numerical representation. It is assumed that the pulse sequence repeats a large number of times.

The subject of pulse sequence creation is itself very rich. Sequences of excitations and measurements can be combined to characterize various additional phenomena in the test subject. Although many pulse sequences have been developed, they will always be composed from variations on the theme of first manipulating the spins of a sample and then observing the relaxation.

4.0 SUMMARY

The field of Nuclear Magnetic Resonance is incredibly rich. From its humble beginnings in 1946, various applications of NMR have been taken to incredible lengths. Today, we can use NMR spectroscopy to understand the three-dimensional structure of chemicals. NMR microscopy, which is a high spatial resolution version of Magnetic Resonance Imaging, is allowing studies of chemical processes in single cells down to the scale of a micrometer. Nuclear Magnetic Resonance has applications in fields as diverse as biology, materials science, chemical physics, petrochemicals, food processing, polymers and, of course, medicine.

The physics of Nuclear Magnetic Resonance is deceptively simple, but the solutions to the related scientific and engineering problems are fiendishly clever.

Refereneces

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