1. Nuclear Magnetism

1.1 Magnetism

Before talking about magnetic resonance, we need to recount a few basic facts about magnetism.

Electrodynamics is the field of study that deals with magnetic (\(B\)) and electric (\(E\)) fields, and their interactions with matter. The basic entity that creates electric fields is the electric charge. For example, the electron has a charge and it creates an electric field about it. There is, however, no magnetic charge. The “elementary unit of magnetism” is the magnetic moment. It is more complicated than charge because it is a vector, meaning it has both magnitude and direction.

The magnitude of the generated magnetic field \(B\) is proportional to the size of the magnetic charge. The direction of the magnetic moment determines the direction of the field lines.

If you take a compass, which is nothing more than a magnetized iron needle, having a magnetic moment itself, it will align itself along the earth’s magnetic field. This illustrates another point of interest which we’ll make use of: magnetic moments tend to align themselves along the magnetic field they are in. The phrase “tend to” is quite sloppy, since, as we’ll see, it’s the things they do until they align themselves that constitute the heart of MRI.

Magnetic moments are measured in units of Joule/Tesla.
1.2 The Elementary Particles

Matter is made out of molecules, which are made out of atoms, which are made out of electrons orbiting a nucleus (made out of protons and neutrons). It is possible to further subdivide matter, but we shall stop at this level and treat the electron, proton and neutron as elementary point particles.

Water
Molecule

The elementary particles have intrinsic properties: mass and charge. We can visualize each as a tiny, charged sphere. As it turns out, quantum mechanics tells us this visualization isn’t correct, but it gives intuition and pretty good results, so we’ll keep it.

The spin of the nucleus is quantized, meaning it can only assume values in quanta of a basic unit, \( \hbar \), or its half-integer multiples: \( \frac{1}{2}\hbar, \frac{3}{2}\hbar, 2\hbar, \ldots \). Different atomic nuclei have different spin values; some examples are presented in the table below.

Nuclear spins greater than about \( \hbar \) are uncommon.

Rotating charge creates an effective magnetic moment. In other words, the nucleus creates a magnetic field about it as if it had an intrinsic magnetic moment. The magnetic moment is proportional to the spinning speed of the nucleus, hence it is also quantized.

The magnetic moment’s size is proportional to the spin. The constant of proportionality is called the gyromagnetic ratio and denoted \( \gamma \). It depends on the nucleus in question.

\[
|m| = \frac{1}{2} \gamma \hbar, \gamma \hbar, \frac{3}{2} \gamma \hbar, \ldots
\]

The following table lists the spin, gyromagnetic ratios and natural abundance of different nuclei that are often encountered in MR:

<table>
<thead>
<tr>
<th>Spin</th>
<th>( \gamma ) (MHz/T)</th>
<th>Nat. Abund.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^1\text{H})</td>
<td>( \frac{1}{2} )</td>
<td>42.6</td>
</tr>
<tr>
<td>(^2\text{H})</td>
<td>1</td>
<td>0.15( \gamma \hbar )</td>
</tr>
<tr>
<td>(^{12}\text{C})</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>(^{13}\text{C})</td>
<td>( \frac{1}{2} )</td>
<td>0.25( \gamma \hbar )</td>
</tr>
<tr>
<td>(^{31}\text{P})</td>
<td>( \frac{1}{2} )</td>
<td>0.4( \gamma \hbar )</td>
</tr>
<tr>
<td>(^{16}\text{O})</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>(^{17}\text{O})</td>
<td>( \frac{5}{2} )</td>
<td>0.14( \gamma \hbar )</td>
</tr>
</tbody>
</table>

(Spin is specified in units of \( \hbar \) )
1.4 **Molecules and Their Spins**

Molecules are made out of atoms, connected between them by chemical bonds. The most important molecule in MRI is without a doubt water:

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H -- O -- H
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A “typical” water molecule is actually:

```
\[ 16O \quad ^1H \quad ^1H \]
```

Oxygen-16 has no spin (its 8 protons pair up destructively, as do its 8 neutrons), and \(^1\text{H}\) has spin \(\frac{1}{2}\). Because of symmetry, the two hydrogen atoms are equivalent, in the sense that they behave as one spin-1/2 entity with double the magnetic moment.

There are variations on this basic water molecule in terms of isotopes. For example, a glass of water will contain water molecules such as:

```
\[ ^17O \quad ^2H \quad ^1H \]
```

which has markedly different NMR properties (\(^{17}\text{O}\) has spin 5/2, and Deuterium has spin 1), but deviations from the “regular” \(^2\text{H}_2\text{O}\) are so rare, that their contribution to any experiment are negligible.

Let’s look at another molecule type: fat. There are many types of fat molecules in the body, most are triglyceride molecules made out of glycerol and 3 fatty acids. Here is Glycerol:

```
\[
\text{H} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H}
\]
```

Glycerol

As before, natural abundance dictates that almost all (~99%) Carbon molecules will have no spin. Same goes for the oxygen molecules. So we’re really left with just the signal from the hydrogen nuclei, which are really just single protons. This leads to a general conclusion:

Due to natural abundance and a high \(\gamma\), the signal in MRI in tissue is dominated by the signal from the Hydrogen (\(^1\text{H}\))

Hence we can (to a good approximation) neglect all other nuclei. There is another reason for that, having to do with the MRI machine: the signals from the other nuclei are filtered out – this is possible because of their radically different \(\gamma\)’s. We’ll have more to say about this later on.
1.5 TISSUE

The body is made out of tissue: a bunch of (not necessarily identical) cells that perform the same function. For example, muscle tissue, nervous tissue, etc. Tissue is made out different things: cells, an extra-cellular matrix, blood vessels, etc – depending on its nature.

A single mm$^3$ of tissue contains $10^{19}$ hydrogen atoms, most in water molecules and fat. Those two give the main signals in MRI. Other molecules are significantly less prominent because they are not as plentiful as water/fat. For example, Glutamine can be observed in the brain, but its concentration is only ~ 10 millimolar. Compare that to, say, the concentration of pure water ($5.5 \times 10^4$ millimolar) and take into account tissue is made predominantly out of water.

Large macromolecules often don’t contribute to the signal because of another reason: Their complex structure means they relax very fast; that is, when we irradiate them, they decay back to their ground state before we can get a significant signal.

Distinction should be made between water that’s bound to macromolecules and water that is free. Bound water, just like the macromolecules it is part of, is also virtually undetectable due to fast relaxation.

We summary:

In MRI, the largest signal comes from water, then fat, and then (tailing far behind) from other molecules. Most large molecules are undetectable anyway.

1.6 BULK MAGNETIZATION

In an MRI machine one cannot study single spins or single molecules. A typical voxel is ~ mm$^3$, and it often contains many many spins. MRI therefore studies the properties of nuclear spins in bulk.

Suppose you have N molecules in a volume V, each having a magnetic moment $\mathbf{m}_i$. Recall that the moments are all vectors, so we can imaging a vector “attached” to each atom. In general, without the large external field of the MRI machine, they would all point in different directions:

The bulk magnetization $\mathbf{M}$ of the volume V is defined as the (vector!) sum over all elements in the volume:

$$\mathbf{M} = \sum_{i=1}^{N} \mathbf{m}_i$$

It is $\mathbf{M}$ that MRI studies. In the above example, $\mathbf{M}=0$ because the spins cancel out each other:

Upon the application of an external field, the spins tend to align along the field – although thermal motion will prevent them from doing so completely. A “snapshot” of the spins in the presence of an external field might look like this:
We will discuss how this thermal equilibrium is reached in subsequent lectures. For now it is merely important that you understand the concept of bulk magnetization.

In general, $M = M(r)$:

What volume $V$ should we use? On the one hand, we want enough spins in $V$ to make it statistically meaningful – that is, we want the variance to be small as possible. Put another way, we want $M$ to vary smoothly if we start shifting our volume of interest around.

<table>
<thead>
<tr>
<th>Volume of Water</th>
<th>Number of spins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liter $= 10^3$ cm$^3$</td>
<td>$10^{25}$</td>
</tr>
<tr>
<td>cm$^3$</td>
<td>$10^{22}$</td>
</tr>
<tr>
<td>mm$^3$</td>
<td>$10^{19}$</td>
</tr>
<tr>
<td>$\mu$m$^3$</td>
<td>$10^{16}$</td>
</tr>
<tr>
<td>(10 nm)$^3$</td>
<td>$10^4$</td>
</tr>
<tr>
<td>nm$^3$</td>
<td>10</td>
</tr>
</tbody>
</table>

So it seems smaller than a box with sides 10 nm is shaky.

On the other hand, is there an upper limit on $V$? A natural choice might be a voxel (~ mm$^3$), but there is a lot of variance inside a voxel. Sometimes to understand the signal originating from a single voxel we need to think in terms of what happens inside the voxel because there is a lot happening inside that mm$^3$. So, in general, we stick to the smallest $V$ we can take (say, (10 nm)$^3$).

From now on when we talk about the magnetization vector we will take it to mean the bulk (macroscopic) magnetization vector. At times I will remark how the macroscopic picture ties in with the microscopic one.
2. Spin Interactions

2.1 How a Magnetic Moment "Talks" with the Environment

Having established that our star molecule is water and our star atom \(^1\text{H}\), having spin \(\frac{1}{2}\) and a magnetic moment \(\mu = \frac{1}{2} \gamma h\) \((\gamma = 2\pi \times 42.57 \text{ MHz/Tesla})\), we need to ask ourselves how such spins behave. Physics teaches us that the nuclear magnetic moment interacts with its surroundings through magnetic fields alone:

1. It gives off a magnetic field.
2. It is affected by magnetic fields.

When trying to understand its behavior we need to ask ourselves two questions:

1. What is the effect of a magnetic field on the magnetic moment?
2. What creates the magnetic fields felt by the moment, and how can we calculate them?

2.2 Effect of a Magnetic Field

When an MRI patient lies in an MRI scanner he/she is exposed to a high (> 1 Tesla), constant magnetic field. The MRI scanner uses coils to irradiate the patient with magnetic fields. The gradient coils that are used for imaging give off a magnetic field. It is therefore vital that we understand the effects of magnetic fields on a magnetic moment.

From a microscopic point of view, classical physics teaches us that the magnetic moment \(\text{precesses}\) about the magnetic field with an angular frequency \(\omega = \gamma |B|\). That is, \(\mathbf{m}\)’s component perpendicular to \(\mathbf{B}\) goes around it in a circle.

\[
\omega = \gamma |B|
\]

That’s all there is to it, really! \(\omega\) is called the Larmor frequency of the magnetic moment. How fast is this precession? This depends on \(B\) and on \(\gamma\). Different nuclei precess with different Larmor frequencies. In a 3T magnet:

<table>
<thead>
<tr>
<th>Nucleus</th>
<th>Precession freq. (in MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^1\text{H})</td>
<td>136</td>
</tr>
<tr>
<td>(^13\text{C})</td>
<td>32</td>
</tr>
<tr>
<td>(^31\text{P})</td>
<td>51.6</td>
</tr>
</tbody>
</table>

All this is true for a single, microscopic magnetic moment in vacuum.

What about the bulk magnetization? Well, it turns out it behaves the same way, with one caveat: one needs to add \textit{ad hoc} thermal relaxation effects – the spins “want” to return to their equilibrium position along \(B_0\), the main field. The source of this relaxation is tiny fluctuations in the local magnetic field and will be discussed in a subsequent lecture. So for bulk magnetization:

\[\text{Precession + Thermal relaxation}\]

The above description assumed \(B\) was constant and pointing in one direction. What if it’s changing (in either size or magnitude)? Then the instantaneous axis of precession and angular velocity change along with it.

2.3 Sources of Magnetic Field

Question 2 will be the next subject. Meanwhile we will focus on the first. We can think of several sources of magnetic fields at the moment’s position:

1. External: external (to the sample) fields.
   a. Main field, \(B_0\).
   b. Gradients.
   c. RF.
   d. Earth’s magnetic field.
2. Atomic:
   a. Created by the electrons’ orbit around the nucleus: moving charges create magnetic fields (Ampere’s Law)
   b. The electrons have a spin magnetic moment themselves, and these create a magnetic moment at the nucleus’ position.
3. Intra-Molecular:
   a. Magnetic fields created by spin magnetic moments of
neighboring atoms in a molecule.

4. Extra-Molecular: other molecules have

These fields can be classified into two categories:
1. “Internal” fields which originate from the “sample” (the test subject).
2. External fields created by the MRI machine (B₀, RF, gradient).

It turns out these two give rise to two completely different phenomena:
1. The internal fields can be treated as random fluctuations. These lead the spins to relax back to thermal equilibrium, which is along B₀, the main field.

2. The external fields are responsible for the spin precession, as described previously. For example, the M “wants” to precess about B₀:

The total effect of all fields is therefore both these effects: precession (external fields) + relaxation (internal fields).
2.4 **The Chemical Shift**

One other effect needs to be mentioned before moving on. When you take an atom and put it in an external field, the electrons around the nucleus will tend to “shield” the nucleus, forming a local magnetic field opposite the main field and proportional to it:

$$\mathbf{B}_0 \rightarrow \mathbf{B}_0 - \Delta \mathbf{B} = (1 - \chi) \mathbf{B}_0$$

Hence the local field felt by the nucleus will not be \( \mathbf{B}_0 \) but rather

$$\mathbf{B}_0 - \Delta \mathbf{B} = (1 - \chi) \mathbf{B}_0$$

This is usually a very small effect (~ 1-10^4 Hz for protons), much smaller than \( g \mathbf{B}_0 \). \( \chi \)’s value depends on the exact chemical configuration of the electrons – hence the name of this effect, *the chemical shift*. In MRI, this means that different molecules will precess with slightly different angular velocities. In particular,

$$\omega_{\text{water}} = \gamma B = \gamma(1 - \chi_{\text{water}}) \mathbf{B}_0$$

$$\omega_{\text{fat}} = \gamma B = \gamma(1 - \chi_{\text{fat}}) \mathbf{B}_0$$

It turns out (experimentally) that

$$\omega_{\text{water}} - \omega_{\text{fat}} = \gamma(\chi_{\text{fat}} - \chi_{\text{water}}) \mathbf{B}_0$$

This is equal to 450 Hz at 3T.

It is important to emphasize that this is a **small** effect compared to the main field. In its absence, e.g., all protons would precess with the same angular velocity \( \omega = \gamma \text{protons} \mathbf{B}_0 \) and same for all carbons, all phosphorus, etc. The chemical shift introduces a small “spread” in the frequencies, as similar nuclei in different molecules will have slightly different precession frequencies: