LECTURE 8

UNDERSTANDING T_1, T_2 AND T_2^*

Lecture Notes by Assaf Tal

T_1, T_2 AND T_2^* IN PATHOLOGY

How Pathology Changes T_1 and T_2

The main usefulness of T_1, T_2 and T_2^* in MRI comes not from their meaning – since they are not directly related to any physiological parameter – but from their sensitivity to microscopic pathological changes in tissue. This is a very interesting and important point:

> T_1, T_2 and T_2^* can reveal microscopic pathologies on a much smaller scale than the voxel size (although these pathologies must permeate a macroscopic region on the order of the voxel size to be detected, due to MRI's low sensitivity).

Pathologies can appear as either **hypointense** (dark) or **hyperintense** (bright) on T_1 or T_2 (or T_2^*) weighted images. Pathologies which are **isointense** (same as surroundings) are invisible, although a pathology might be isointense on a T_1 weighted image but hyper/hypo intense on a T_2 weighted image!

The following tables summarize some typical pathologies and their associated appearances:

Hypointense (Longer) T_1	Hyperintense (Shorter) T_1
Edema	Fat
Tumor	Subacute hemorrhage
Infarction	Melanin
Inflammation	Protein-rich fluid
Hyperacute hemorrhage	Slowly-flowing blood
Chronic hemorrhage	Paramagnetic substances (gadolinium, manganese, copper, etc)
Low proton density	Calcification
Calcification	Laminar necrosis of cerebral infarction
Flow void	
Tissue loss	

Hypointense (Shorter) T_2	Hyperintense (Longer) T_2
Low proton density	Edema
calcification	Tumor
fibrous tissue	Infarction
protein-rich fluid	Inflammation
flow void	Hyperacute hemorrhage
paramagnetic substances (iron, ferritin, melanin, deoxyhemoglobin, etc)	Chronic hemorrhage
	Extracellular methemoglobin subacute hemorrhage

The above are just rules of thumb and should never be used to make any sort of conclusive diagnosis. Leave those to the trained radiologists! We are not in the business of medical diagnosis, but rather in the business of understanding the reason for T_1 and T_2 contrast.

T_1 Hyperintensity Usually Means A Shorter T_1. T_2 Hyperintensity Usually Means A Longer T_2.

CSF, which has a long T_1, appears dark on T_1-weighted images. This is not a "law of nature" but has to do with the way T_1 contrast is usually created in MRI images, via rapid pulsing or inversion recovery. For both, high T_1 values appear darker, as discussed in the lecture dealing with creating T_1 and T_2 contrast.

On the other hand, T_2-weighted sequences often rely on some form of spin-echo, which has a signal dependence of the form

$$s \propto e^{-TE/T_2}.$$

As T_2 is increased, the signal decays more slowly, which results in hyperintensity (compared to normal, non-increased T_2). This means that hyperintensity corresponds to longer T_2s. It's very important not to automatically assume that hyperintensity means there is "more" of something. It all depends on the signal equation and type of contrast!

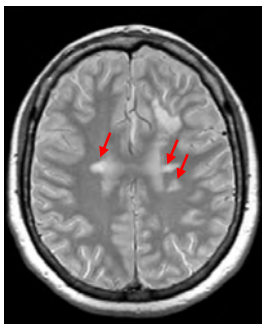
A Brief Example: Multiple Sclerosis

Multiple Sclerosis (MS) is an inflammatory disease of the central nervous system which affects about 2 million people worldwide. In MS, prologed inflammation leads to **demyelination** of neuronal

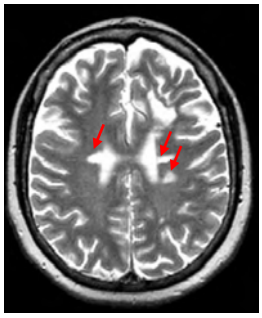
axons[1], resulting in symptoms ranging from impaired vision and fatigue to depression and musculoskeletal weakness. There are two major theories for why inflammation occurs: either via an autoimmune response, or via failure of myelin producing cells. There is no cure for MS, but drugs can delay its onset and effects[2].

The diagnosis of MS is often done by combining clinical evaluation with MRI imaging. The hallmark of MS is the appearance of **lesions** on the MRI scans. These are small round/oval structures that result from the underlying damage to brain tissue through the inflammatory processes. Most lesions appear hyperintense on T_2-weighted images and hypointense on T_1-weighted images. It is fairly common to see hyper-T_2/hypo-T_1 pathologies in MRI, and we will explain why in a bit. This means that the T_1 and T_2 images sometimes contain the same information

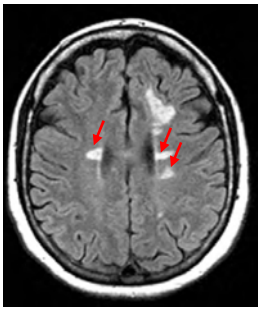
The problem with T_2 images is that hyperintense lesions are hard to tell apart from the cerebrospinal fluid (CSF). A sequence known as **FLAIR (FLuid Attenuated Inversion Recovery)** precedes the T_2-weighting imaging with an inversion recovery designed to null the CSF signal based on its long T_1.



In this Proton Density (PD) image, as little T_1 and T_2 contrast is created (e.g. by taking long TRs and short TEs). "Typical" MS lesions appear hyperintense.



In this T_2-weighted image, the same lesions also appear hyperintense. However, they are difficult to identify due to the bright CSF. This is why FLAIR is used (next).



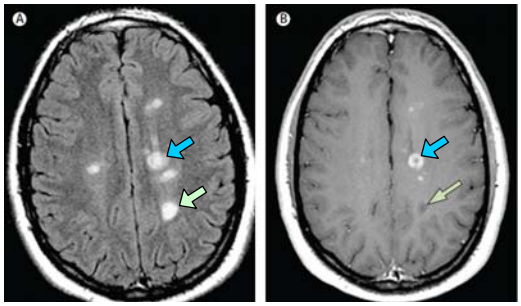
The FLAIR image is T_2-weighted, but it uses the long T_1 value of the CSF to null its signal with a special pulse sequence. This makes identifying the T_2-hyperintense lesions much easier.

Images taken from Sahraian and Eshaghi, Clin. Neurol. Neurosurg. 112:609-615 (2010)

Another image type often used is a T_1-image after the injection of a contrast agent such as **gadolinium** (Gd-DTPA, or Gd for short). The effect of Gd is to shorten T_1 substantially. As we have seen, rapid pulsing tends to saturate long T_1, which is why CSF appears dark on T_1 weighted images. Gd therefore causes hyperintensity wherever it reaches in the brain. Not all hyperintense T_2 lesions are also hyperintense on T_1 weighted contrast enhanced scans, but not always!

[1] This means the myelin sheeth that surrounds the neurons is somehow damaged or completely stripped. This, in turn, for leaves the neuron vulnerable to damage, as well as impairs its ability to conduct electrical impulses.

[2] Weizmann holds the patent rights for Copaxone, one of the most influential drugs on the market for treating MS.

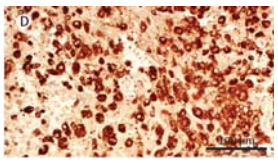


FLAIR Contrast Enhanced T_1

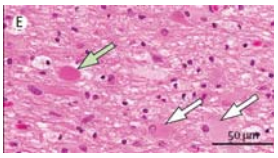
Most MS lesions are hyperintense on both image types (blue arrow). Some are hypointense, and are also known as **black holes**; those are usually older lesions in which inflammatory activity has somewhat declined. (image from Filippi et. al., Lancet Neurol 11:349-60 (2011))

The brain is special in having a **blood brain barrier** (BBB) which prevents contrast from entering the brain under normal circumstances. Lesions tend to "light up" whenever there is a breakdown of this barrier due to the inflammatory processes and the immune response at the site.

From a histopathological point of view, active lesions are a site of myelin breakdown. They are filled with macrophages, lymphocytes, and other cells, as well as myelin debris (taken up by the macrophages). Chronic (T_1-hypointense) inactive lesions have reduced cellular density, reduced inflammation and no active demyelination.



"Sea of macrophages" in an active MS lesion, obtained by staining for myelin proteolipid protein within macrophages (hyperintense on T_1-Gd).



Axonal swelling (green arrow) and reactive astrocytes (white arrow) in active MS lesion.

From: Filippi et. al., Lancet Neurol 11:349-60 (2011))

The above is by no means an exhaustive or even completely accurate treatment of MS in MRI, but was provided just to give the reader a feeling for how T_1 and T_2 might vary in a real-life pathology.

T_2* Requires Extra Care

We will defer discussion of T_2* to a later point in this lecture, for the simple reason that it is a very tricky parameter to measure. A large part of it comes from hardware imperfections which are obviously uninteresting and patient-independent. However, some T_2* decay is intrinsic to the tissue and is interesting. T_2* is created by field inhomogeneities, and these are induced on a microscopic scale whenever one magnetic material interfaces with another having a different magnetic susceptbility. The greatest inhomogeneity is created at air-tissue interfaces. These so-called **susceptibility artifacts** can be on either a macroscopic scale – as is near the air filled sinuses – in which case they are uninteresting and lead mainly to image artifacts; or they can be on a mesoscopic scale, much smaller than the voxel size, as can be at the interface between microscopic tissue in the brain. Such **mesoscopic susceptibility artifacts** can generate interesting and viable tissue contrast which is also sensitive to many changes. Extra care is needed to isolate the mesoscopic susceptibility effects from field imperfections and macroscopic susceptibility artifacts, since they all lead to a distortion in B_0.

Outline Of Relaxation Theory

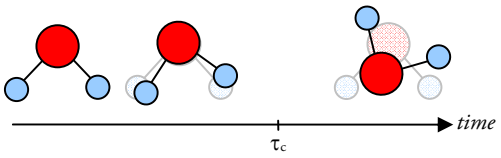
Spins Are Subjected To Microscopic Fluctuating Magnetic Fields Due To Their Thermal Motion

We've already remarked that spins are subjected to fluctuating fields due to their rotational thermal motion (see "Spin Dynamics" lecture). It is these fluctuating fields that lead to relaxation. The fluctuating fields $\mathbf{B}_D$ felt by a spin can be composed into components transverse & longitudinal to the main B_0 field:

$$\mathbf{B}_D(t) = \mathbf{B}_{D,\perp}(t) + \mathbf{B}_{D,\parallel}(t) .$$

It is instructive to assign some orders of magnitude to these fluctuations. We define the **rotational correlation time**, τ_c, in an informal manner as follows: imagine opening your eyes at t=0, then shutting your eyes and re-opening them at some time t>0. If we open the eyes "fast enough", you

can predict that the orientation of the molecule will remain close to its orientation at t=0. However, after a certain amount of time, you will not be able to predict the orientation of the molecule at all. The time-scale at which this happens is the rotational correlation time.

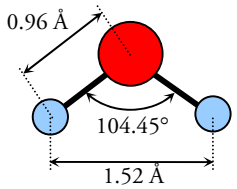


The correlation time of a molecule will depend on the temperature, its environment and its size. For a spherical molecule of hydrodynamic radius r in a liquid with viscosity η, Stoke derived an expression for the rotational correlation time:

$$\tau_c = \frac{4\pi\eta r^3}{3kT}.$$

Number time. For water (≈18 Da) at room temperature it is about one picosecond = 10^{-12} seconds. For ubiquitin (≈9 kDa) in water, τ_c is a few nanoseconds.

How about the size of the fluctuations? In a water molecule the sources of fluctuations are dipolar and can be divided into intra- and inter-molecular. Because the dipolar field goes as r^{-3}, the intermolecular contributions are only a second order effect, and we are left with the intramolecular ones, exerted by one hydrogen in H_2O on the other. First, we must examine the geometry of the water molecule:



The dipolar field created by one spin at the position of the other is:

$$\mathbf{B} = \frac{\mu_0}{4\pi}\frac{3\hat{\mathbf{r}}(\mathbf{m}\cdot\hat{\mathbf{r}})-\mathbf{m}}{r^3}$$

where **r** is the vector connecting both hydrogen atoms. We see that the maximal and minimal values of **B** occur when **m** and **r** are either parallel or antiparallel, leading to the values:

$$|\mathbf{B}_{\max}| = \frac{\mu_0 m}{2\pi r^3}$$

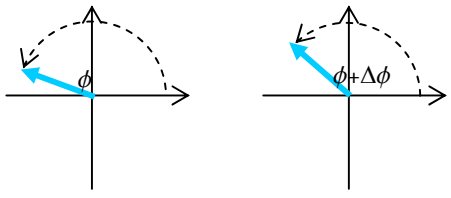
Hence the magnitude of the fluctuations vary between $\pm|\mathbf{B}_{\max}|$. Fixing $|\mathbf{r}|$=1.52Å and $|\mathbf{m}| = 1.4\times10^{-26}\frac{J}{T}$ (^{1}H magnetic moment), this amounts to

$$|\mathbf{B}_{\max}| \approx 8\times10^{-4}\ T = 8\ \text{Gauss}.$$

To a first approximation, as we will argue next, the longitudinal fluctuating field causes transverse relaxation and the transverse fluctuating field causes the longitudinal relaxation.

The Longitudinal Fluctuating Field Leads to T_2 Relaxation

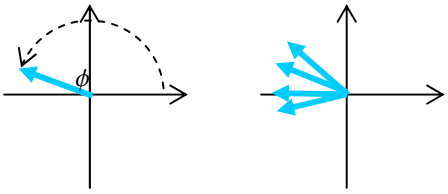
We start by showing how a fluctuating longitudinal field leads to transverse T_2 decay. Imagine exciting a spin onto the xy plane. Without the fluctuating field, it would just execute precession and make a phase $\phi=\gamma B_0 t$ after precessing for a time t. With the fluctuating field along z the precessing frequency fluctuates as well, with the end result being a slightly different precessing frequency at the end, $\phi+\Delta\phi$, where $\Delta\phi$ depends on the exact nature of the fluctuations (imagine turning a wheel with a shaking hand):



No fluctuations
("Firm hand")

With fluctuations
("Shaky hand")
Note here $\Delta\phi<0$

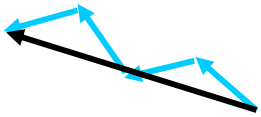
Now imagine a number of spins. In the absence of fluctuations they would all make the same angle. In the presence of fluctuations, they would fan out (remember, each spin feels a different fluctuation):



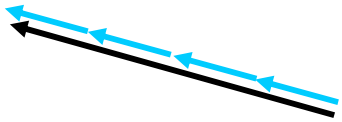
Many spins,
no fluctuations.
(microscopic view)

Many spins,
fluctuations.
(microscopic view)

This is what happens microscopically. Now, the **macroscopic** magnetization is the (vector) sum of the microscopic magnetization. What happens when you sum vectors that don't point in the same direction? They (partially) cancel out. Example:



Adding up slightly "out-of-phase" magnetization vectors leads to signal loss (smaller vector sum).



When all vectors are in-phase there is no signal loss.

You can now see why the magnetization in the plane decays:

> The fluctuating z-field causes the spins to spread out (**dephase**), and hence add up destructively, leading to a decay of the macroscopic magnetization vector, **M**.

How fast does **M** decay – what determines T_2? Quite simply: the rate of fluctuations. Fast fluctuations will result in lesser dephasing and hence slower decay.

An analogy from physics might help you see this: think of diffusion. An ink is injected into two cups containing two fluids, one denser than the other. In which cup will the ink spread further? In the *less dense* fluid. The idea is that the additional collisions it undergoes per unit time in the dense fluid slow the ink down and minimize the distance it can diffuse to at a given amount of time. A similar process occurs when discussing T_2: you can think of the spin's phase as "diffusing" under the action of the fluctuating field – slower fluctuations mean "fewer collisions" and hence a "less dense" environment, leading to greater "diffusion" (dephasing, in our case).

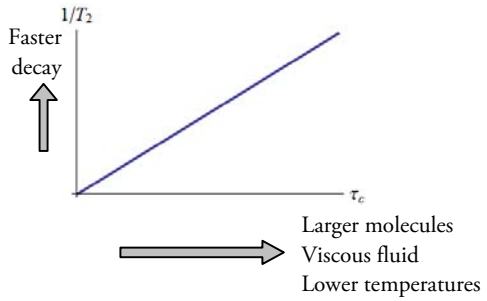
This directly relates to molecule sizes, because:

Large molecules
- → Tumble slowly
- → Slow fluctuations
- → Short T_2 (fast decay)

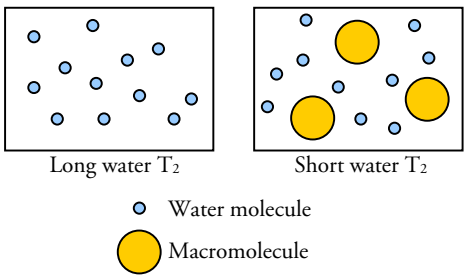
Small molecules
- → Tumble fast
- → Fast fluctuations
- → Long T_2 (slow decay)

Hence, large molecules such as proteins have short T_2s, and as a result suffer from both broad linewidths (leading to a lack of spectral resolution) and smaller signal intensities (leading to lesser SNR). This is one of the reasons why the study of large proteins can be very challenging.

We can draw this graph:



In tissue, water can be free (A) or in the vicinity of large macromolecules (B), which slow it down and lengthens its T_2:



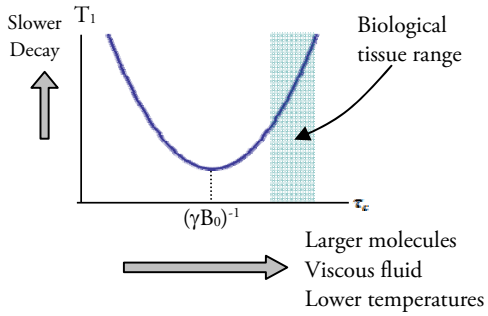
In solids, where motion is greatly reduced, T_2 can be extremely short.

The Transverse Fluctuating Field Leads to T_1 Relaxation

Remember one of our earliest questions when discussing relaxation: how can it be that a tiny RF component compared to B_0 can excite the spins? The answer we found is that the RF field can excite the spins if it is on resonance. We can reverse the reasoning and state the a transverse fluctuation will appreciately affect to z-component of the spins if it is resonant.

If we think of the transverse fluctuating field in terms of its frequency components, we might imagine that when $\tau_c \sim 1/(\gamma B_0)$ – that is, when the fluctuations are on resonance – the longitudinal relaxation will be most effective, leading to the shortest possible T_1. Conversely, as τ_c becomes slower or faster than $1/(\gamma B_0)$, we can predict that it will be less effective at inducing longitudinal relaxation, leading to longer T_1s.

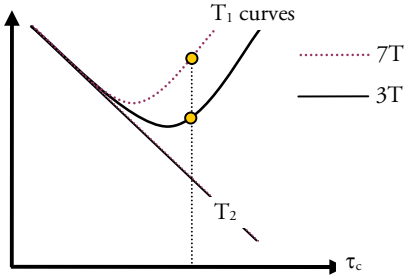
This general analysis turns out to be quite true, and we can draw a general curve relating the correlation time and T_1:



An important question now arises: on which "side" of this curve are we in biological tissue? A typical MRI magnet is ~ 3T and has a frequency of ~127 MHz for protons. The correlation time for free water is ~ 1 picosecond, so $1/\tau_c \sim$ THz=10^{12} Hz, and we are well to the right of the "dip".

T_1 Increases With Increasing B_0; T_2 Is Largely Unaffected by B_0

Our T_1 curve also shows us that T_1 is expected to increase with B_0. Since we are to the right of the dip, we see that increasing B_0 will "push" the curve to the right and decrease $1/T_1$, or increase T_1. This is indeed consistent with what we see in actual experiments. This is illustrated in the following schematic graph:

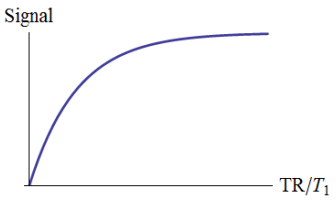


T_2 tends to slightly decrease with increasing field strength. This seems not to be indicated by our diagram, which does not depend on B_0. However, our theory was incomplete and omits more complicated effects (e.g. the transverse field can also contribute to T_2 relaxation by transferring magnetization from longitudinal to transverse states). These corrections tend to be small to negligble in fluid tissue. In semi-fluid/solid tissue such as bone and cartilage this approximation is somewhat less valid. We will not treat these more complicated cases here.

The increases in T_1 are usually sub-linear and lead to better T_1 contrast. To see why this is so, consider the steady state signal in a spoiled GRE sequence:

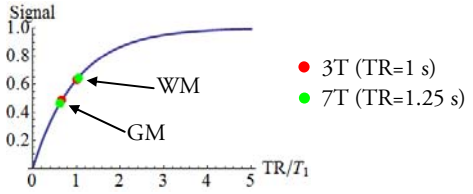
$$S \propto \frac{1-e^{-TR/T_1}}{1-\cos(\alpha)e^{-TR/T_1}}\sin(\alpha)\cdot$$

Plotting this as a function of TR/T_1 for, say, α=90°, we get:



For a fixed TR, the signal from two tissue types having two T_1 values would be represented by two points on that graph. For concereteness, let's take TR=1 sec, $T_1^{GM} = 1.5$ sec, $T_1^{WM} = 1.0$ sec. The

two signal intensities correspond to the two red points on this graph:



When we climb to 7T both increase. Taking values from the Table in Lecture 3, we have $T_1^{WM} = 1.2$ sec, $T_1^{GM} = 2.0$ sec. Adjusting the TR to 1.25 we get the two green points on the graph, which are farther apart, implying increased contrast at 7T. Numerically,

$$S_{WM}^{3T} = 0.632 \qquad S_{WM}^{7T} = 0.632$$
$$S_{GM}^{3T} = 0.487 \qquad S_{WM}^{7T} = 0.632$$
$$\underbrace{\Delta S^{3T} = 0.145}_{TR=1.0\text{ sec}} \qquad \underbrace{\Delta S^{7T} = 0.182}_{TR=1.25\text{ sec}}$$

The signal difference is about 25% larger at 7T. This is only half the story, thought, because SNR also improves at higher fields approximately linearly with B_0, effectively[3] leading to lower noise levels and therefore even greater CNR.

Had we kept the same TR=1.0 sec in the above example we would have obtained

$$S_{WM}^{7T} = 0.565$$
$$S_{WM}^{7T} = 0.393$$
$$\underbrace{\Delta S^{7T} = 0.172}_{TR=1.0\text{ sec}}$$

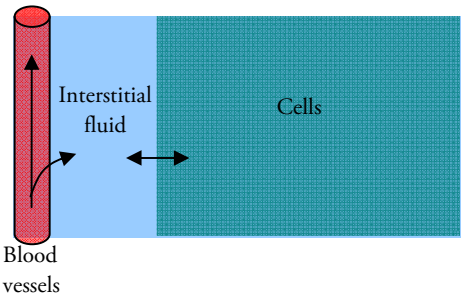
This is still an increase in contrast, but a milder one. It is also interesting to note the signals themselves have diminished because of the longer T_1s (which imply that, for the same TR, we saturate our magnetization more).

[3] By "effectively" I mean that both noise and signal change as the field increases, but when we normalize things back it appears as if the noise has decreased. For example, assume S=1.0, and n=0.1 is the noise SD at 3T, so SNR=S/n=1.0. At 7T we might get S=3.0, n=0.15, so SNR=2.0. Normalizing the 7T result by dividing by 3, we get S=1.0, n=0.05, yielding the same SNR=2.0. Thus a higher SNR is equivalent to effectively reducing the noise while keeping the signal constant.

Note. T_1 does not always become longer with increasing B_0. One notable exception is phosphorous (^{31}P) imaging, in which T_1 actually becomes shorter, leading to better SNR but worse CNR. This comes about because of additional, more complicated effects we have not discussed here, such as *chemical shift anisotropy*, which creates field fluctuations originating from the way electrons are distributed around the nucleus. For protons (^{1}H), however, the above discussion is fairly accurate.

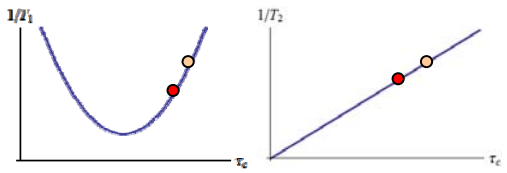
T_1 and T_2 Both Increase in Edema

Let's take the relatively simple case of edema[4]. In edema, water accumulates in the interstitium, which constitutes about 25% of the body's total fluids (cells contain another two thirds, and the remainder is allocated to blood vessels and cerebrospinal fluid).



We've remarked that T_1 appears hypointense and T_2 appears hyperintense. This actually means that both T_1 and T_2 tend to increase. When you think of edema, the additional water tends to reduce the viscosity in the interstitial space, leading to a shorter correlation time, which – looking at the graphs of T_1 and T_2 – leads to an increase in both:

[4] In Hebrew: בצקת.



Healthy tissue
Edema

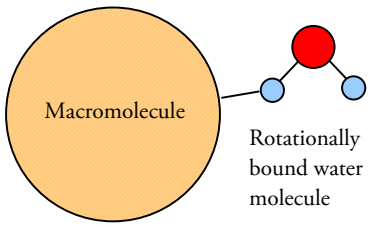
Multi-Compartment Relaxation Models

A more realistic look at relaxation in biological tissue must take into account their multi-compartmental nature. Water in tissue exists in **pools**, or **compartments**, which might exchange. For example, the intracellular and extracellular spaces have different viscosity and therefore different T_1, T_2 values.

Even within cells different pools may exist. For example, in neurons, water trapped within the myelin sheath have a shorter T_2 compared to water diffusing around inside the cell, because of their restricted motion (as remarked earlier, solid/semi-solid phases tend to have longer correlation times and therefore shorter T_2s).

Exchange effects, in which water crosses from one pool to another one, cause further complications. If a water molecule jumps from intra- to extra-cellular space very rapidly[5], it will average out their respective T_2s and T_1s and we will only observe an average tissue T_1 and T_2.

Different microscopic environments can also be considered as different compartments. For example, water can chemically bind and unbind with macromolecules in their environment. This can be a single-bond, meaning the water molecule is still free to rotate, or a double-bond, meaning the water is irrotationally bound:



[5] The definition of "rapid" is a fine point we will not tackle here. We will only remark at this point that exchange is *rapid*

These processes usually happen on fast timescales, meaning we only get to see an average of them. If we denote by f_f, f_{rb} and f_{irb} the fraction of free, rotationally bound and irrotationally bound water molecules, we get

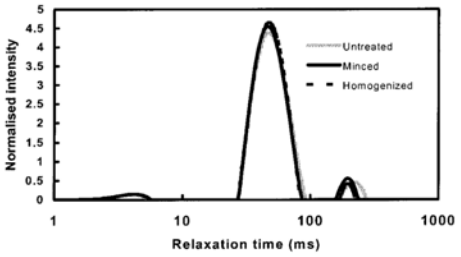
$$\frac{1}{T_1} = \frac{f_f}{T_{1,f}} + \frac{f_{rb}}{T_{1,rb}} + \frac{f_{irb}}{T_{1,irb}}.$$

Usually, $T_{1,f} >> T_{1,rb} > T_{1,irb}$. However, note that even small fractions can cause significant differences. For example, putting $T_{1,f}$=1 sec, $T_{1,rb}$=1 ms and $T_{1,irb}$=0.1 ms, and setting f_f=0.9, f_{rb}=0.09 and f_{irb}=0.01, we get

$$\left(\frac{1}{T_1}\right)_{ms} = \frac{0.9}{1000} + \frac{0.09}{1} + \frac{0.01}{0.1} \approx 10 \text{ ms}$$

which is a far cry from the 1000 ms of free water, even though 90% of the spins are in the free water phase!

We conclude with a concrete example. It is possible to separate the different compartments and prepare a histogram of T_1 and T_2 values in a given tissue, through methods we will not discuss here. This was done for excised pork muscle at low fields (0.47 T), giving a histogram of the form[6]:



The histogram showed little variation when the muscle was minced or homogenized, indicating the different T_2 pools did not originate from extra/intracellular compartments. Following further experiments, the authors show that the fastest component (~ few percent) originates from water bound to macromolecules; the largest peak corresponds to water located within organized protein structures; and the fastest peak (longest T_2)

[6] Taken from Bertman et. al., J. Agric. Food Chem. 49:3092-3100 (2001)

reflects extra-myofibrillar water (i.e. between the fibers of the muscle).

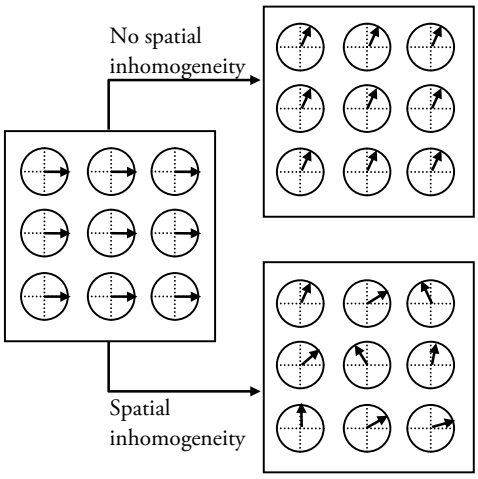
T_2^* Contrast

B_0-Inhomogeneity Leads to Both Signal Loss and Phase Shifts In Gradient Echo Images

We now forget about T_2^* for a moment and assume we only have microscopic T_2 effects and B_0 inhomogeneity. If our inhomogeneities are time-independent, $\Delta B(\mathbf{r})$, then spins at $\mathbf{r}$ will have an offset $\gamma\Delta B(\mathbf{r})$ and accumulate a phase $\phi(\mathbf{r},t)=\gamma\Delta B(\mathbf{r})t$ after a time t. Our transverse magnetization will behave as:

$$M_{xy}(\mathbf{r},t)=M_{xy}(\mathbf{r},0)e^{-i\gamma\Delta B(\mathbf{r})t}$$

This means that if all of our spins start out in-phase at time t=0, then end up dephasing at later times:



The acquired signal at point $\mathbf{r}$ will simply be the result of convolving M_{xy} with the PSF centered at that point:

$$\begin{aligned} s(\mathbf{r},t) &= \int PSF(\mathbf{r}'-\mathbf{r})M_{xy}(\mathbf{r}',t)d\mathbf{r}' \\ &= \int PSF(\mathbf{r}'-\mathbf{r})M_{xy}(\mathbf{r}',0)e^{-i\gamma\Delta B(\mathbf{r}')t}d\mathbf{r}' \end{aligned}$$

Let's suppose for simplicity the PSF is a cube (or rectangle) the size of the voxel, so

$$s(\mathbf{r},t)\approx\int_{\text{voxel}}M_{xy}(\mathbf{r}',0)e^{-i\gamma\Delta B(\mathbf{r}')t}d\mathbf{r}'$$

Without knowing the exact form of $\Delta B(\mathbf{r}')$ we cannot make any exact claims, but we can see that overall two effects will occur:

1. **Dephasing**: The spins will go out of phase, leading to a loss of signal.
2. **Net phase accumulation**: The spins might accumulate some average non-zero phase which would create a non-zero phase for the signal s(**r**,t).

For example, if the inhomogeneity only varies weakly in the voxel, we can use a Taylor expansion, keeping things in 1D and assuming the voxel's center coincides with x=0 for simplicity:

$$\Delta B(x)\approx\Delta B(0)+\left(\frac{d\Delta B}{dx}\right)_0 x$$

Substituting this into the signal, and assuming we have a homogeneous voxel (again, for simplicity):

$$\begin{aligned} s(\mathbf{r},t) &= \int_{-\Delta x/2}^{\Delta x/2} e^{-i\gamma\Delta B(x)t}dx \\ &= e^{-i\gamma\Delta B(0)t}\int_{-\Delta x/2}^{\Delta x/2} e^{-i\gamma\left(\frac{d\Delta B(x)}{dx}\right)_0 xt}dx \\ &= \underbrace{e^{-i\gamma\Delta B(0)t}}_{\substack{\text{overall}\\ \text{constant}\\ \text{phase}}}\underbrace{\Delta x\cdot\text{sinc}\left[\gamma\left(\frac{d\Delta B(x)}{dx}\right)_0\frac{\Delta x}{2}t\right]}_{\text{signal decay due to dephasing}} \end{aligned}$$

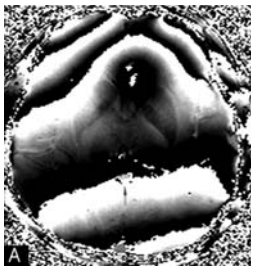
We see that for a linear inhomogeneity the signal does not decay exponentially with time but rather as a sinc function.

While a linear approximation over a voxel might be a good approximation for the macroscopic fields, that is not the case for the microscopic ones. In a macroscopic ~ 1 mm^3 voxel there is significant heterogeneity and the microscopic fields are very complicated. Their average effect is not a linear gradient over the voxel, but some statistical distribution of fields, leading to a statistical distribution of spin phases inside the voxel. This statistical distribution leads more naturally (although not always!) to a more exponential decay.

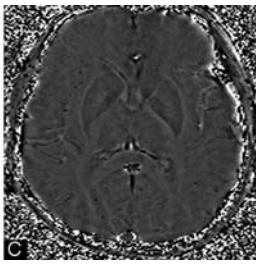
Phase Imaging Reveals Microstructure Due To Microscopic Susceptibility

As seen before, susceptibility artifacts can lead to the signal being a complex quantity. Instead of looking at **magnitude images**, we can try looking at **phase images**, that is plot the phase of the signal as each point. This might tell us something about the microstructure that created it.

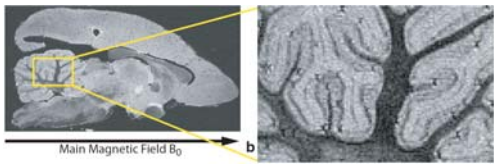
When acquiring phase images, one usually gets something that looks like this (images taken from Haacke et. al., AJNR 30:19-30 (2009)):



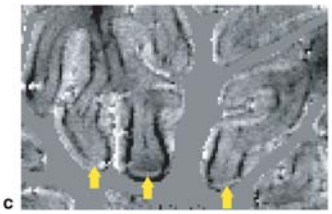
The gross variations are due to macroscopic inhomogeneity effects such as the main field's imperfections. They can be addressed by **unwrapping** the phase (canceling out its discontinuities). Once this is done, we assume that the slowly changing components of the inhomogeneity are caused by macroscopic fields, and we can get rid of them by applying a **high pass filter** which assures us we remain only with the fast changing – hopefully microscopic – parts of the phase:



We can indeed see some contrast here between the different tissue types and also some vessel-related contrast, as will be discussed below. Indeed, by multiplying the phase and magnitude images we can get what's known as a **susceptibility weighted image**. Such images usually show better contrast for some structures, such as blood vessels, or iron-containing structures, which are known to create microscopic susceptibility artifacts around them. For example, Shmueli et. al. have examined the cerebellum in a marmoset brain at 11.7 Tesla. In humans, the cerebellum appears almost as a separate structure attached to the base of the brain, which is involved in coordinating a great deal of our motor activity. Shmueli et. al. have been able to delineate the purkinje cell layers in the marmoset brain (Magn. Reson. Med., 62:1510-1522 (2009)):



Left: Simple gradient-echo MR image (magnitude). Right: zoomed in cerebellum.



The phase of the above image (following unwrapping and high pass filtering), clearly showing the purkinje cell layers with high contrast.

The contrast between the different cell layers in the cerebellum is highly correlated to their **iron content** (iron particles have a large electronic magnetic moment and induce significant field distortions on a microscopic scale).

From T_2^* To T_2

We've presented T_2 are stemming from microscopic temporal field fluctuations, and T_2' as stemming from static spatial inhomogeneities. What would happen if we created a static inhomogeneity but let a water molecule diffuse (translationally, not rotationally!) through it? The field the molecule would "see" would fluctuate as it would move around. If the molecule moves around fast enough, T_2' would "become" T_2!

This is not a hypothetical situation and it happens often in tissue. For example, water can diffuse around a blood vessel (venous blood has deoxygenated hemoglobin which is paramagnetic).

These effects play a big role in undersanding hemodynamic effects in functional imaging.

One way to think about T_2' vs T_2 is as follows: imagine running a spin-echo experiment. Whatever the spin-echo keeps is T_2, and whatever goes away is T_2'.