

Basic Principles of MRI - REVIEW

- Wait some time for spins to reach equilibrium in the magnetic field ($TR \geq 3 * T_1$):

$$M_z(t) = M_0(1 - e^{-t/T_1})$$

- Apply a pulse or series of pulses to bring magnetization into the x-y plane:

$$\theta = \omega_1 \tau = \gamma B_1 \tau$$

- Wait for spins to dephase (TE):

$$M_{xy}(t) = M_0 e^{-t/T_2^*}$$

- Turn on the receiver and observe the free induction decay (FID):

$$M_{xy}(t) = M_0 e^{-t/T_2^*} (\cos \omega_0 t)$$

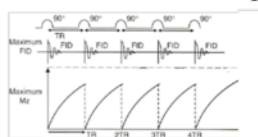
- Apply processing filters and Fourier transform FID to observe spectrum/image:

$$C(\omega) = \int_{-\infty}^{\infty} g(t) e^{-i\omega t} dt$$

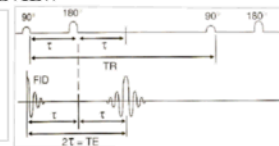
Define: TR - **repetition time**
TE - **echo time**

Basic Principles of MRI - T₁ contrast

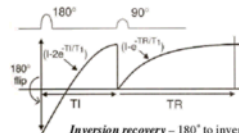
REVIEW



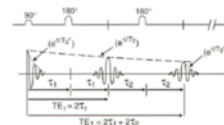
A **pulse sequence** consists of a pulse or series of pulses followed by data acquisition. Interval between sequences is the repetition time TR.



Spin echo - 2 pulses separated by TE/2 refocus magnetization at TE, the echo time



Inversion recovery - 180° to invert magnetization



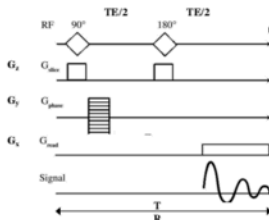
Multi spin echo allows multiple refocusing of magnetization, echo decays with T₂*

MRI - Image Construction - REVIEW

A **sequence timing diagram** is a graphical notation of the **pulses and gradients** applied during an MR pulse sequence.

One line for RF and for gradients in 3-orthogonal directions, one line for detected signal.

Gradient A gradient is an applied magnetic field that changes from point to point - usually in a **linear** fashion.



Spin echo is the most basic and commonly used pulse sequence for MRI

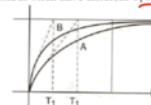
Contrast is generated for different tissues by altering TE and TR.

Three types of commonly applied contrast: T₁, T₂ and proton density.

Construct image

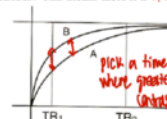
Basic Principles of MRI - T₁ contrast

T₁ Tissue Contrast Tissues often have different T₁ relaxation times



Tissue A has a **longer T₁ relaxation time** than Tissue B.

Thus, at short TR times there is a substantial difference in the detected RF signal intensity coming from the two tissues. This means there is a **T₁ contrast**.



Choose maximal contrast

Pick a time where greatest diff. for max contrast

Of course at time close to zero, there is no signal.

At long TR times (TR2) there is a reduced "T₁ effect".

For maximal contrast the TR time would be similar to the T₁ relaxation time of the tissue under study.

Sequence timing diagram for a standard spin echo pulse sequence.

Basic Principles of MRI

T₁ Characteristics: The T₁ characteristics of tissue have to do with the way protons are able to give off their energy to the surrounding lattice or absorb energy from the lattice.

The most efficient energy transfer, and thus the shortest T₁, occurs when the natural motional frequencies (i.e. translation, vibration, and rotation) of the protons are at the Larmor frequency.

$$\omega_0 = \gamma B_0 \quad \gamma = 42.6 \text{ MHz/Tesla for hydrogen}$$

Although the precessional frequency of a hydrogen proton is 42.6 MHz in a 1 Tesla magnetic field, the "natural motional frequency" of protons depends on the physical states of the tissue (i.e. the atoms to which they are attached or close to).

H₂O: The natural motional frequency of water protons is usually faster than the Larmor frequency

$$\omega(H_2O) \gg \omega_0$$

Solids: The natural motional frequency of protons in solids is usually slower than the Larmor frequency

$$\omega(\text{Solids}) < \omega_0$$

Fat and Proteinaceous Material: Protons in fat and protein have natural motional frequencies that are almost equal to the Larmor frequencies used in MRI

$$\omega(\text{Fat}) \approx \omega_0$$

Based on these statements, we would predict that fat and protein have the shortest T₁.

Basic Principles of MRI

T₂ Characteristics The T₂ characteristics of tissue are determined by how fast the proton spins in the tissue dephase.

H₂O: Because of the structure of the water molecule and because of the sparsity of these molecules, spin-spin interaction among the protons is minimal.

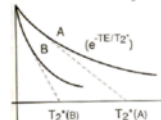
- The effect of one proton on another is relatively small
- Distance between protons in water is relatively large

Therefore, dephasing occurs at a much slower rate than other tissues and the T₂ relaxation time is long.

Solids: Solids (e.g. bone) are very compactly structured tissue, with additional dipolar interactions between protons. Thus, the T₂ for solids is short.

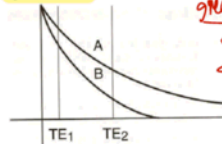
Fat and Proteinaceous Material: The dephasing or the T₂ for fat and proteinaceous material is between solids and H₂O.

T₂* Tissue Contrast Tissues often have different T₂* relaxation times



how fast dephase

At short TE times there is a smaller difference in the detected RF signal intensity coming from the two tissues than at longer TE times.



greatest contrast at short T₂

At very short TE times there is a reduced "T₂* effect".

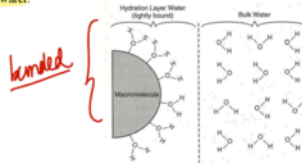
At long TE times there is an enhanced contrast or "T₂* effect", but the signal-to-noise is lower (because the signal has decayed).

SN ↓ decayed

Basic Principles of MRI

Proteinaceous Solutions Most of the water in the body is not free but is bound to a hydrophilic macromolecule such as a protein.

Such water molecules form hydration layers around the macromolecule and are called hydration layer water.



hindered

Bound H₂O molecules lose some of the freedom in their motion, and their natural motional frequencies get closer to the Larmor frequency yielding more efficient energy transfer and a shorter T₁ relaxation.

Shorter T₁ relaxation times lead to brighter pixels on T₁-weighted images.

If the protein content is high enough, hydration layer water can cause some T₂ shortening.

Shorter T₂ relaxation times lead to darker pixels on T₂-weighted images.

hindered water

Effects of Field Strength on T_1 and T_2

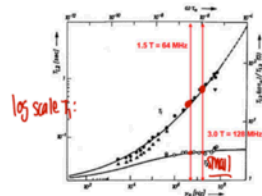
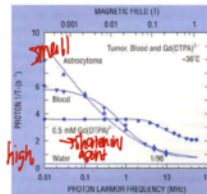


FIG. 2.5. Proton spin-lattice (T_1) and spin-spin (T_2) relaxation times in frog muscle as a function of frequency. (a) *Rana lessonae*. (●) T_1 at 25°C; (▲) T_1 at 30°C; (□) T_1 at 25°C; (△) T_1 at 30°C. (b) *Rana pipiens*. (●) T_1 at 25°C; (▲) T_1 at 30°C; (□) T_2 at 25°C; (△) T_2 at 30°C. (c) Curves are differentiated for $\omega_1 = 100$ kHz. (Ch-Ch) of Reference 40 with $\omega_1 = 1.1 \times 10^{12}$ sec $^{-1}$, $\alpha = 0.03$, and $T_{10} = T_{20} = 1.8 \times 10^{-2}$ sec. (From G. Held, F. Sauer, V. Polak, and S. Meibum, Z. Naturforsch. 36a, 59 (1977).)

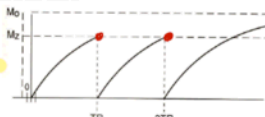
<https://www.chem.wisc.edu/areas/teich/chem438-tech-01-relax.htm>
adapted from Bloembergen, E.M. Purcell, R.V. Pound "Relaxation Effects in Nuclear Magnetic Resonance Absorption" *Physical Review* 1948, 73, 670-746.

Left: $1/T_1$ decreases with field strength.

Right: T_1 increases with field strength, T_2 is relatively constant with field. Red lines represent clinically relevant field strengths. From: <http://mriquestions.com/bo-effect-on-t1-t2.html>

Basic Principles of MRI

Recall: If more than one 90° pulse is administered (at intervals of $t = TR$), then the maximum magnetization vector in the z-direction at this time is

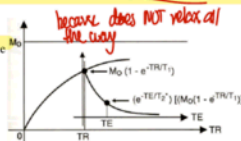


This means that when the magnetization vector flips into the x-y plane it has a maximum value of

$$M_{xy}(TE=0) = M_0(1 - e^{-TR/T_1})$$

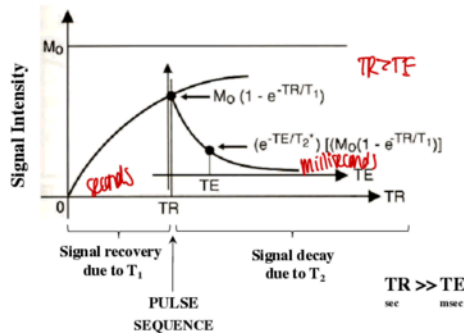
Thus the magnitude of the magnetization vector at time TE will be

$$M_{xy} = M_0(1 - e^{-TR/T_1})e^{-TE/T_2}$$



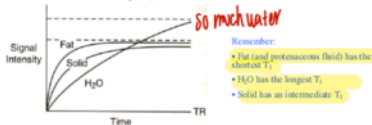
Due to this relationship between T_1 recovery at time TR and T_2 decay, these curves can be plotted on the same graph.

Recovery and Decay Curves



Basic Principles of MRI

T₁ and T₂ Curves The relative recovery (T₁) curves of fat, water, and solid tissue are shown below.

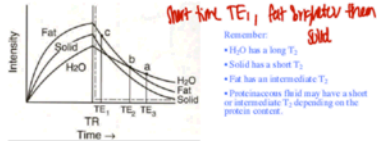


The overall signal intensity correlates with the proton density N(H).

$$I \propto N(H)(1 - e^{-TR/T_1})e^{-TE/T_2}$$

N(H) is the proton density of hydrogen

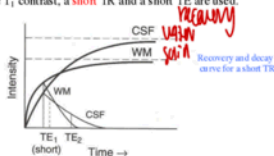
At time TR, if we transmit another RF pulse, the superimposed T₂ decay curve and T₁ curve is shown below



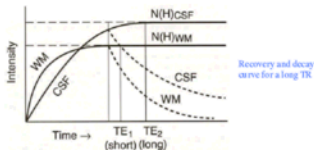
The contrast between tissues and the signal intensities depend on the TE and TR.

Basic Principles of MRI

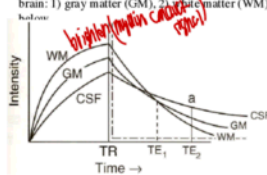
T₁-Weighted Image To maximize T₁ contrast, a short TR and a short TE are used.



T₂-Weighted Image To maximize T₂ contrast, an intermediate/long TR and a long TE are used.



T₁ and T₂ Curves The relative recovery (T₁) and decay (T₂) curves of different tissues in the brain: 1) gray matter (GM), 2) white matter (WM), 3) Cerebral Spinal Fluid (CSF) are shown below



Type of Tissue	T ₁ (msec)	T ₂ (msec)	N(H)
White Matter	510	67	0.61
Gray Matter	760	77	0.61
Edema	900	126	0.86
CSF	2650	180	1.00

Handwritten note: "water" under CSF.

If TE is really short we get an image with the following characteristics:

- White matter is **bright**
 - Gray matter is intermediate
 - Cerebral spinal fluid is **dark**
- Handwritten note: "faster no"

If TE is long we get an image with the following characteristics:

- Cerebral spinal fluid is **bright**
- Gray matter is intermediate
- White matter is **dark**

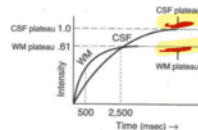
Handwritten notes: "long T₁ → long to recover", "short T₁ → short to recover"

Handwritten notes: "decay", "liquid - decay slower", "solid - first decay"

Basic Principles of MRI

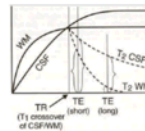
Proton Density The plateau of the recovery (T₁) curve of a tissue is determined by the proton density of that tissue N(H).

White matter has a lower proton density than cerebral spinal fluid but its T₁ is shorter. Therefore, there is a cross-over point where white matter and CSF have the same intensity.



Proton Density-Weighted Image

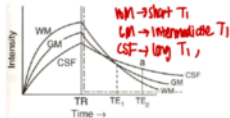
To maximize proton density differences, a long TR and a short TE are used.



Handwritten note: "Recovery and decay curve for a TR at the CSF/WM cross point"

T₁ and T₂-weighted MRI

The relative recovery (T_1) and decay (T_2) curves differs for different tissues in the brain: gray matter (GM), white matter (WM) and Cerebral Spinal Fluid (CSF).

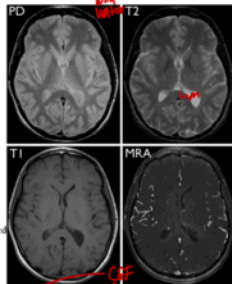


T ₁ , T ₂ , and Proton Density of Brain Tissues			
Type of Tissue	T1 (msec)	T2 (msec)	N(H)
White Matter	510	67	0.61
Gray Matter	760	77	0.69
Edema	900	126	0.86
CSF	2650	180	1.00

Contrast	TR	TE	WM	GM	CSF
PD	long	short	dark*	intermed	intermed
T ₁	short	short	bright	intermed	dark
T ₂	med/long	long	dark	intermed	bright

* WM has a lower proton density than CSF but its T_2 is shorter. Therefore, there is a cross-over point where WM and CSF have the same intensity.

<http://bit.ly/google.com/kbwin-ct-mr/ff>
Chris Howe MD PhD, UCSF



MRI – Gradients

Gradients introduce a spatial variation on $B_0 = B_{\text{in}}$, such that:

$$B_i(x,y,z) = B_0 + \Delta B_i(x,y,z)$$

As a result protons in different locations will precess at different frequencies.

The change in position is related to the strength of the gradient in each dimension:

$$\Delta B_i(x) = G_x \cdot x$$

The application of a gradient affects the precession frequency of the spins as a function of location:

Spins at γ B_0 precess at the Larmor frequency.

Spins at $\gamma B_0 - \gamma G_x$, χ precess slower.

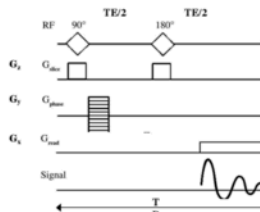
Spins at $\gamma B_0 + \gamma G_z \cdot x$ precess faster.

Gradients have units of field strength / distance: T/m or G/cm

MRI - Image Construction

Gradient A gradient is an applied magnetic field that changes from point to point - usually in a linear fashion.

For MR imaging, a linear gradient is created along all three axes to obtain information about position.



One line each for RF and for
gradients in 3-orthogonal
directions, one line for
detected signal

Need gradients in 3-directions
to generate a 3-D image.

Referred to as **slice**, **read** and **phase encode** directions.

By convention, these are defined as z , x and y respectively.

Sequence timing diagram for a standard spin echo pulse sequence.

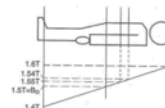
MRI – Slice Selection

Slice Selection Suppose a patient is on a table in the presence of an external magnetic field B_0 which is oriented along the z-axis. If we transmit an RF pulse and get an FID or an echo back, the received signal would be from the entire patient (i.e. there is no spatial discrimination).



Remember: The RF pulse be at the Larmor frequency ($\omega_0 = \gamma B_0$) in order to excite any protons in the patient.

If we make a magnetic field that varies from point to point, then each position will have its own Larmor frequency. This effect is achieved using a gradient coil.



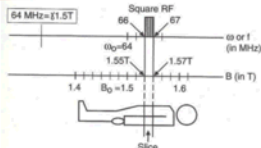
If we now transmit an RF pulse of a single frequency into the patient, we will receive signals corresponding to a slice in the patient.

The slice thickness depends on the **slope** of the gradient.

MRI – Slice Selection

Bandwidth If a single frequency RF pulse is transmitted into a patient under a gradient, we will receive signals from an infinitely thin line.

Therefore, an RF pulse with a range of frequencies is generally transmitted (i.e. a bandwidth of frequencies).



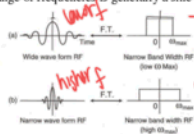
Remember: For ^1H ,
 $\gamma = 42.6 \text{ MHz/Tesla}$

In a 1.5 T field:
 $\omega_0 = \gamma B_0 \sim 64 \text{ MHz}$

In a 1.55 T, 1.57 T field:
 $\omega_0 \sim 66 - 67 \text{ MHz}$

The bandwidth that is selected determines the slice thickness.

The RF pulse for a range of frequencies is generally a sine wave ($\sin x / x$).



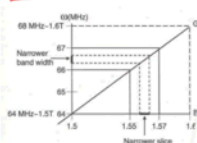
The wider the waveform in the time domain the narrower it is in the frequency domain.

$$\Delta \omega_z = \gamma G_z \cdot \Delta z$$

The narrower the waveform in the time domain the wider it is in the frequency domain.

Slice Thickness There are two ways to change slice thickness:

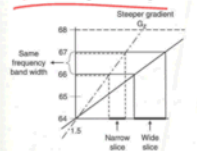
1) Change the frequency bandwidth of the RF pulse



Slice thickness can be decreased by using a narrower bandwidth

There is an electronic limitation to how much we can decrease the bandwidth.

2) Change the slope of the magnetic field gradient



Slice thickness can be decreased by increasing the slope of the magnetic field gradient.

The change in the magnetic field along the z-axis is called the z-gradient (G_z) or slice select gradient.

There is a machine limitation to how much we can increase the gradient.

This is the more common method.

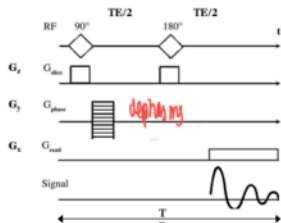
The echo signal we get back from the slice is from the entire slice

MRI – Spatial Encoding

Spatial Encoding Thus far, we have discussed how to get information from an entire slice, but we do not have spatial information within the slice.

To create an image, we need to know how much signal comes from each pixel (2-D) or more accurately, each voxel (volume element). This process is called spatial encoding.

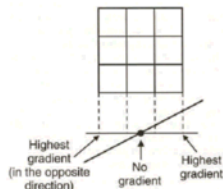
There are two parts to spatial encoding: frequency encoding and phase encoding.



MRI – Frequency Encoding

Frequency Encoding Gradient (Read Gradient) To get spatial information in the x-direction of the slice we apply the frequency encoding gradient, G_x in the x-direction.

To help understand, we are going to employ a 3x3 grid representing 9 voxels in a single slice and examine the effects of gradients.



The G_x gradient is applied during the time the echo is received, i.e., during read out.

MRI – Frequency Encoding

Frequency Encoding Gradient

For purposes of illustration and simplicity, suppose the number of protons in each pixel corresponds to a integer value.

When we transmit an RF pulse with frequencies appropriate for a particular slice, all the protons will start to precess in phase at the Larmor frequency (ω_0).

0	1	1
1	2	0
-2	0	1

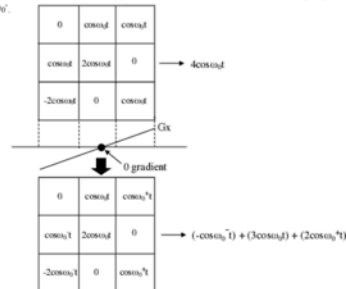
RF

0	$\cos\omega_0 t$	$\cos\omega_0 t$
$\cos\omega_0 t$	$2\cos\omega_0 t$	0
$-2\cos\omega_0 t$	0	$\cos\omega_0 t$

The signal we record will be the sum of all the signals from each pixel (i.e. $4 \cos \omega_0 t$), but there is no spatial information.

If a frequency encoding gradient in the x-direction is applied, then each column will have slightly different frequencies; $\omega_0, \omega_0 + \omega_x, \omega_0 - \omega_x$.

0	1	1
1	2	0
-2	0	1



The signal we record will still be the sum of all the individual signals; however, now each **column** of pixels has a different frequency.

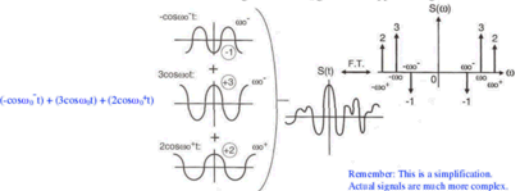
MRI - Image Construction

Frequency Encoding Gradient

If we look at the Fourier transform of the signal without a G_x gradient we get



If we look at the Fourier transform of the signal after a G_x gradient is applied we get

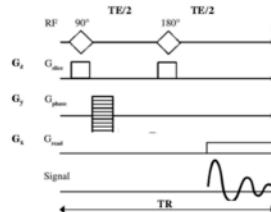


Remember: This is a simplification.
Actual signals are much more complex.

MRI – Phase Encoding

Phase Encoding In addition to using the G_z gradient for slice selection and the G_x gradient for encoding in the x-direction, we add another gradient G_y in the y-direction. This is called the **phase-encoding gradient**.

The G_y gradient is turned on before the G_x gradient, but after the RF pulse.

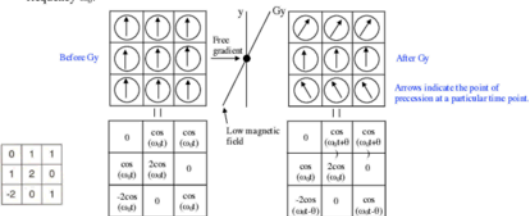


Since the G_y gradient is applied during TE, it affects the precession of the spins and thus affects the **phase** of the signal.

The laddering in the G_y gradient indicates that it is incremented in successive acquisitions.

MRI – Phase Encoding

After a 90° RF pulse (before G_x or G_y), all the protons in the selected slice precess at the same frequency ω_0 .



Upon exposing the slice to a G_y gradient – a magnetic field gradient in the y-direction, protons exposed to a stronger magnetic field will precess faster than protons exposed to a weaker field.

Once the G_y gradient is turned off, all the protons will again be in the same magnetic field, and will again precess at the same frequency; however, each row will be **out of phase** with the other rows

MRI - Image Construction

Phase Encoding

A separate phase encoding step is performed for each row of pixels that is to be discriminated in the slice.

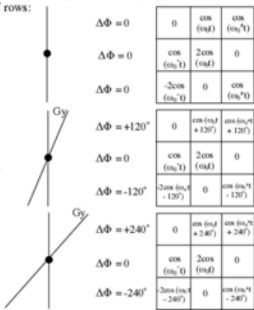
For example, if we have 3 rows of pixels we would perform 3 phase-encoding steps. To figure out the phase shifts, we divide 360° by the number of rows:

$$\Delta\theta = \frac{360^\circ}{\# \text{ of rows}}$$

For three rows the phase shift is 120° , so the three phase encoding steps are at gradients of 0° , 120° , and 240° .

Each phase encoding step takes a time TR . If we wanted to discriminate 256 rows then imaging would take time $256 \times TR$ to be completed.

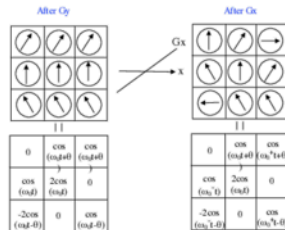
Each signal has information in it about the entire picture, but when performing image reconstruction a single phase-encoding gradient does not provide enough information to fully differentiate each pixel.



MRI – Image Construction

Following the removal of the G_y gradient there is a difference in the rows of pixels based on phase (θ).

To read the signal, we turn on the G_x gradient, which introduces frequency encoding in the x direction.

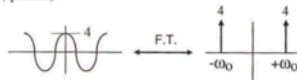


Thus, the protons in each pixel have a distinct **frequency** and a distinct **phase**, which are unique and encode for the x and y coordinates for that pixel.

The shades of gray in an MR image are determined by the magnitude or amplitude of the signal at each pixel.

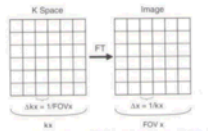
MRI - k space

Recall: Fourier Transformation is used to convert a time domain signal (FID) to a frequency domain signal (spectrum):



This is adequate for NMR Spectroscopy. In MRI imaging however, we need to convert a time domain signal (FID) to a spatially resolved signal (image).

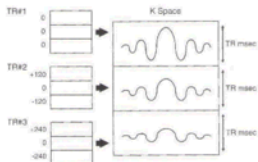
Define: k-space as the Fourier transform of the MR image.



k space is referred to as a **"spatial frequency"** domain. k-space and the image are **Fourier pairs**.

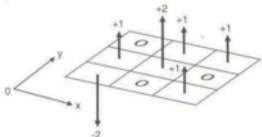
MRI - k space

During data acquisition: Each FID acquired is digitized and placed into memory. Each row in k-space contains the received signal corresponding to 1 PE gradient.



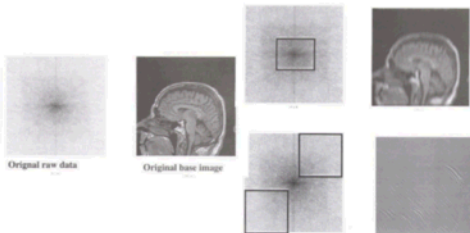
This creates a 2D time domain data space that can be Fourier transformed to yield the final image.

0	1	1
1	2	0
-2	0	1



MRI - k space

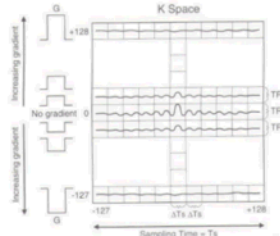
So if the center of k-space contains the maximum signal, then why not just make an image with the central high signal intensity data?



We can do this but the edges of the structure will be very coarse. The center of k-space contains the **majority** of the signal, but the periphery of k-space contains all the **fine detail** of the image.

MRI - k space

In a real-life imaging situation, there would be many more PE steps (usually 32-256) and thus many more lines in k-space.

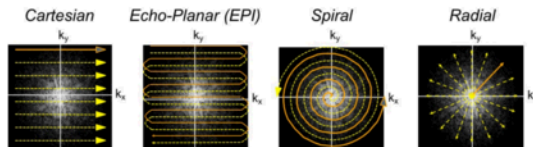


Note that the center of k-space contains the **maximum signal**. This occurs for 2 reasons:

1. the center line contains the data set with no applied phase encode gradient. (application of a PE gradient causes dephasing and reduces the echo signal)
2. The peak of the acquired spin (or gradient) echo is centered in the sampling time window.

MRI - k space

There is no obligation to fill k-space consecutively or linearly.

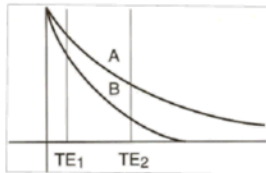
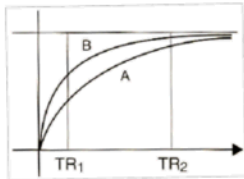


- Common methods of filling k-space are Cartesian, zig zag (Echo-Planar), radially and zigzag.
- This can be achieved adjusting the strength and duration of G_x and G_y in successive PE acquisitions.
- Allows rapid acquisition, over or under sampling, removal of motion artifacts.

MRI Image Characteristics

Signal-to-Noise Ratio Several factors that affect image signal-to-noise ratio (SNR) are:

- 1) Magnetic Field Strength, B_0 : The higher the value of B_0 , the higher the nuclear polarization and the larger the voltage induced in the coil by the precessing protons, thus higher SNR.
- 2) TE and TR times: Signal intensity and thus SNR depends on the TR and TE times selected.



- 3) RF Coil: There is a noise contribution from the RF coil due to random fluctuations in the copper conductor. There is also noise from the patient since humans are conducting.
- 4) Repetition: Acquiring and adding multiple images with the same parameters will increase signal-to-noise because the MRI signal is coherent and noise is incoherent.
- 5) Number of Phase and Frequency-Encoding Steps: If the number of phase and frequency-encoding steps is increased (i.e. smaller pixels) the SNR per pixel decreases proportionally.
- 6) An increase in the slice thickness gives a proportional increase in the image SNR.

MRI Image Characteristics

Spatial Resolution Several factors that affect image spatial resolution are:

- 1) Slice thickness
- 2) Number of phase encoding steps
- 3) Number of frequency encoded data points collected

Contrast-to-Noise Ratio Several factors that affect image contrast-to-noise are:

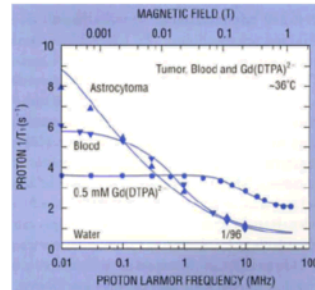
- 1) Magnetic Field Strength, B_0 : The intrinsic T_1 contrast between tissues is greater at **lower** magnetic field strengths.

In general, however, a higher magnetic field strength is preferred because:

- Shorter echo times
- Higher signal-to-noise ratio
- Effect of T_1 -shortening contrast agents is more dramatic
- Increased spectral separation in Magnetic Resonance Spectroscopy.

There is no general rules as to whether T_2 contrast between tissues is increased/decreased as a function of magnetic field strength since T_2 is highly tissue specific.

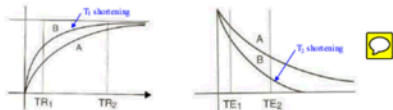
- 2) TR and TE times
- 3) The difference in relaxation times between tissues
- 4) Proton density



Contrast Altering Agents for MRI

MRI Contrast Agents T_1 and/or T_2 relaxation times can be shortened considerably in the presence of paramagnetic species.

T_1 Shortening leads to an increase in signal intensity. T_2 shortening produces a decrease in signal intensity.



Paramagnetic Species Paramagnetic species are species that have unpaired electrons.

The strength/effectiveness of paramagnetic species in shortening T_1/T_2 relaxation times depends on the number of unpaired electrons in the ion.

T_1 Relaxation Agents The mechanism of T_1 relaxation is generally through dipole-dipole interactions between paramagnetic species and water protons. The lanthanide ion Gd^{3+} is by far the most frequently chosen T_1 contrast agent.

Dipole-dipole interaction: Individual charges on a molecule (Gd^{3+}) interact with the individual charges of opposite sign on another molecule (water).

Contrast Agents for MRI: Gadolinium

Gadolinium Contrast Agents Gadolinium has seven unpaired electrons. When Gd^{3+} comes in close proximity with protons of water molecules it decreases their T_1 relaxation time.

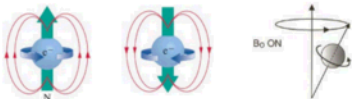
Unpaired electrons are generally not common since most stable molecules have a closed-shell configuration without a suitable unpaired spin.

Gadolinium ions, because of their magnetic moment, exert an influence on the local magnetic field causing rapid-spin dephasing and a decrease in the T_2 relaxation time.

Electron Spin Resonance The interaction of unpaired electron spins with an external magnetic field is called electron spin resonance.

The magnetic field of an electron is 657 times stronger than the magnetic field of a proton spin.

If the unpaired electron oscillates at or near the Larmor frequency, they will have a strong T_1 effect. This is the case for the unpaired electrons in Gd^{3+} .



Note: anything that produces an oscillating magnetic field at the Larmor frequency will increase T_1 effects.



Contrast Agents for MRI: Gadolinium

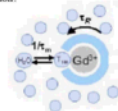
Gadolinium Contrast Mechanism Since the electron spin of Gadolinium matches the Larmor frequency, it induces electron-nuclear dipolar interactions, increasing the rate of transfer of energy to the lattice, which shortens the T_1 relaxation time.

The magnetic field of gadolinium's unpaired electrons does not extend very far, so the contrast agent must be in proximity to hydrogen (the source of our MRI signal).

Rapid water exchange and slow rotation of gadolinium agents are essential for high relaxivity MRI.

There are two mechanisms that result in enhanced relaxivity:

- Inner sphere relaxation: Water molecules can temporarily bind to $Gd-DTPA$ and will be relaxed very efficiently due to its proximity to the unpaired electrons on the metal ion.
- Outer sphere relaxation: Water molecules that diffuse close to the metal ion, but are not bound can also be relaxed, although this mechanism is not as efficient as inner sphere relaxation.

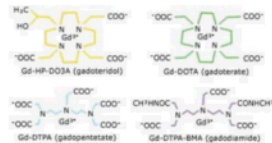


Slow rotation of gadolinium, such as when bound to a protein, relaxes the neighboring water molecules more effectively since this slow fluctuation is closer to the water's magnetic resonance.

During an imaging sequence, many thousands of water molecules are bound, relaxed, and released from the metal ion.

Contrast Agents for MRI: Gadolinium

Gadolinium Chelates Gadolinium is toxic, so for in vivo use it is wrapped in a non-toxic jacket, called a chelate (e.g. DTPA, DOTA, etc.)



Chelates pair up some of the gadolinium's unpaired electrons (some remain free). Chelates thus reduce the number of water molecules bound to gadolinium and the corresponding T_1 relaxation effect.

Chelating agents alone can have significant toxicity due to their ability to bind other metals in the body, such as calcium and magnesium. The use of a chelate is therefore mutually beneficial.

Fortunately, metal complexes are generally very stable.