Memorial Sloan Kettering
Cancer Center

Magnetic Resonance

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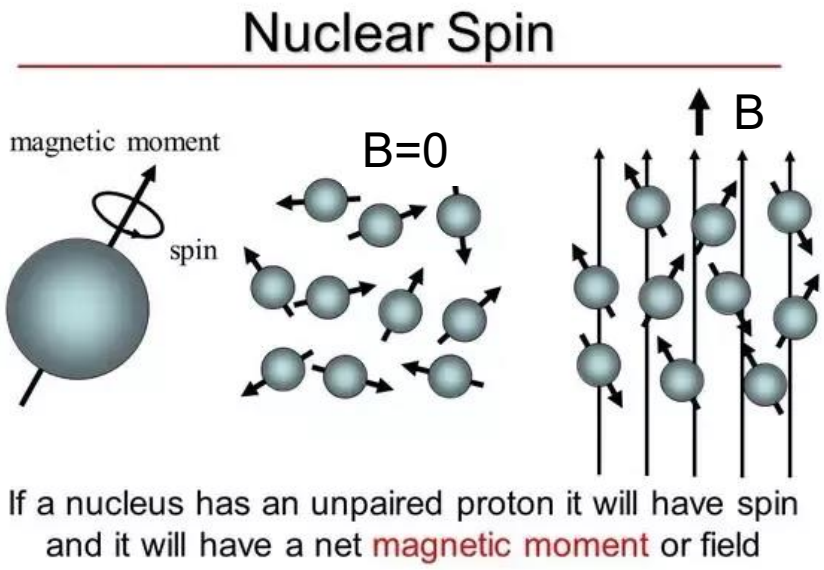
Source of signal: nuclear magnetic moment



https://www.quora.com/How-are-atomic-nucleii-and-magnets-similar

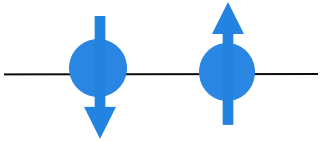
- Nuclei have a quantum property called spin.
- When the total nuclear spin is non-zero, it can be used for detection with magnetic resonance
- Some of the most common nuclei that are "visible" with magnetic resonance (MR) are ^{1}H, ^{13}C, ^{19}F and ^{31}P. Their spins are non-zero
- ^{12}C, ^{4}He have a net nuclear spin of 0 and are therefore not active in terms of magnetic resonance.

➢ Quantum mechanically many observable properties that we experience as continuous are actually discrete, like energy and momentum. Nuclei also have angular momentum as well which is also quantized. Spin is an aspect of quantized angular momentum

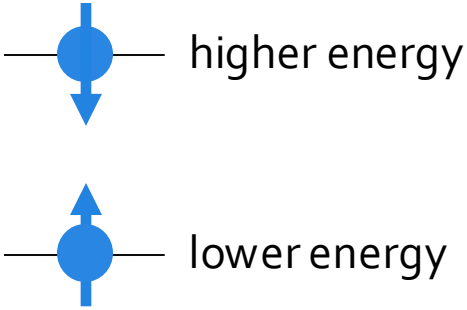
Source of signal: nuclear magnetic moment

- Protons have a spin of ½, which means they can align parallel or antiparallel to B

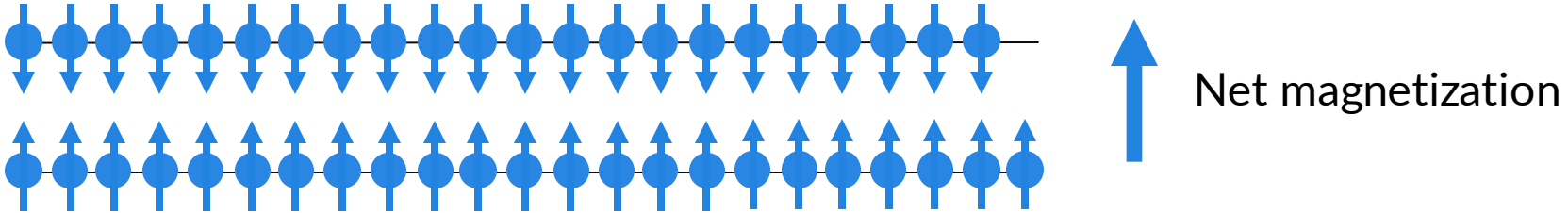
B = 0 energy



B ≠ 0

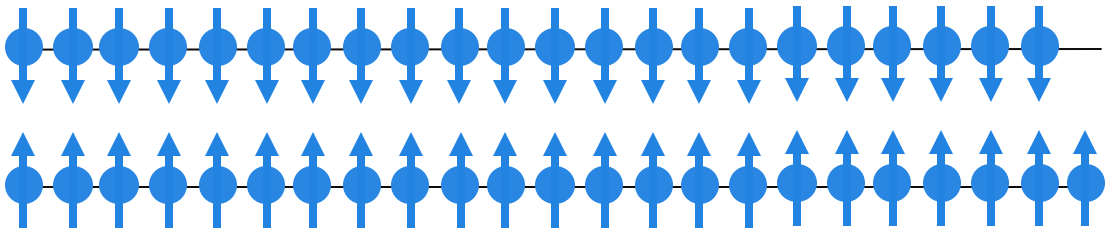


- At room temperature and at "reasonable" magnetic fields, the fraction of spins that are parallel and anti-parallel to the field are almost the same



- At room temperature and typical magnetic field of an MRI machine (3 Tesla), the mismatch of proton spin orientations is ~ 0.01%

Source of signal: nuclear magnetic moment

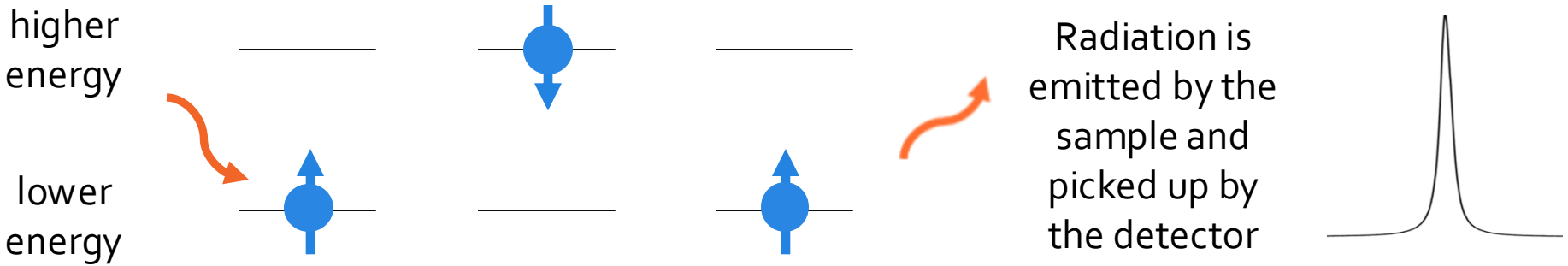


Net magnetization

- This small net magnetization of the nuclei in our body is what we detect with magnetic resonance.
- The higher the **magnetization** (i.e. mismatch of spin alignment, or **polarization**), the more signal we can get
- This magnetization can be "turned on" with a magnetic field and "turned off" when the magnetic field is gone

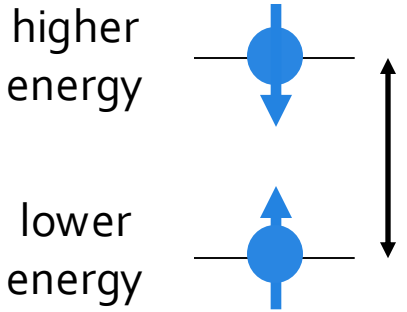
How do we detect this net magnetization (quantum first)

- In thermal equilibrium, we have some excess spins in the lower energy state



- The radiation used to excite spins to the higher energy, anti-parallel, state is called an **RF pulse** (radiofrequency pulse)
- The frequency of the RF pulse has to match the energy difference between the spin up and the spin down states $E = h f$
- The emitted energy is also at the RF frequency
- RF pulse puts spins in resonance and thus we detect **n**uclear **m**agnetic **r**esonance (NMR)

What does this energy gap between spin states depend on?



$\Delta E = h\gamma B$

h = Plank's constant
B = magnetic field, measured in Tesla [T]
γ = gyromagnetic ratio in Hz/T

- Gyromagnetic ratio is a property of each type of nucleus. It is different for ^{1}H, ^{13}C etc. Does not change with magnetic field

- Larger magnetic field results in larger energy gap
- Larger γ and same B-field results in larger energy gap

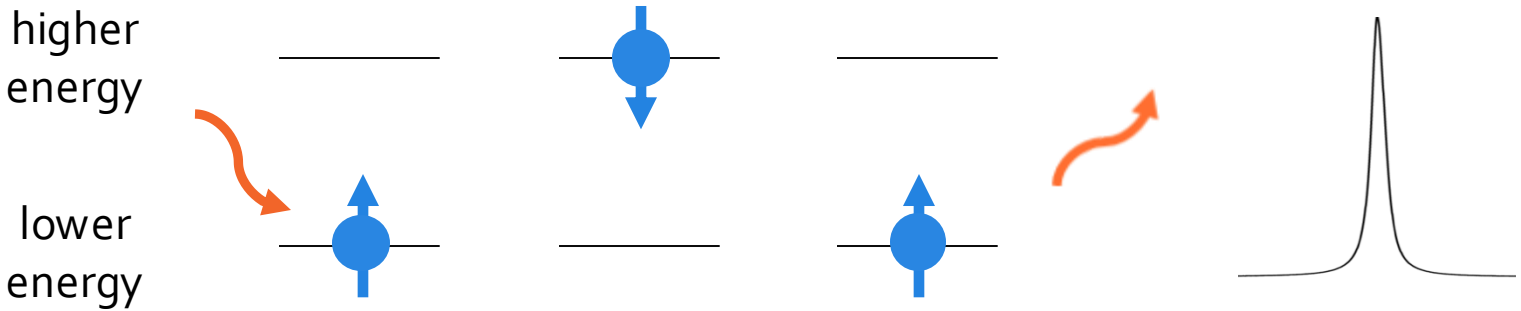
- As in fluorescence, to induce a transition between the two states we impart electromagnetic radiation.
- In fluorescence it was (often) visible light, but here it is in the radiofrequency range

$\Delta E = h\gamma B \quad \Delta E = hf \longrightarrow h\gamma B = h f \longrightarrow \boxed{f = \gamma B}$

Larmor frequency

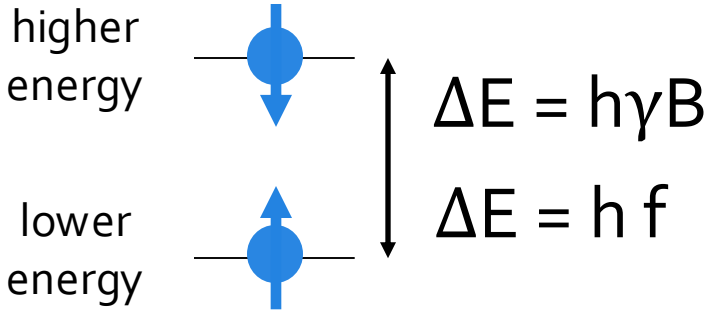
Larmor frequency

Larmor frequency $f = \gamma B$



- We induce the transition to the excited state by irradiating with energy at the Larmor frequency (called an RF pule).
- The emitted energy is again at the Larmor frequency of the spins at whatever field they are in.

Are there any ramifications of this energy gap?



- Of course, the larger the energy gap, the larger is the Larmor frequency.
- Practically need to excite at that frequency and receive the response at that

Additionally, the **polarization of the sample depends on how big the energy gap is**

$$\frac{N_-}{N_+} = e^{h\gamma B/kT}$$

$$\frac{N_- - N_+}{N_- + N_+} \sim \frac{h\gamma B}{2kT} = \text{polarization}$$

- Polarization depends on:
  - Gyromagnetic ratio (γ)
  - Magnetic field (B)
  - Temperature, T

Gyromagnetic ratios and abundances

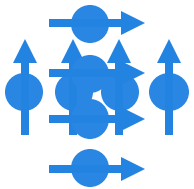
Particle	Spin	Gyromagnetic ratio (γ)	Natural abundance %	Abundance in human body %
Proton (^{1}H)	1/2	42.5781	99.985	63
Deuteron	1	6.5357	0.015	0.01
^{23}Na	3/2	11.2618	100	0.041
^{14}N	1	3.08	99.63	1.5
^{15}N	1/2	4.316	0.37	0.006
^{13}C	1/2	10.71	1.108	0.104

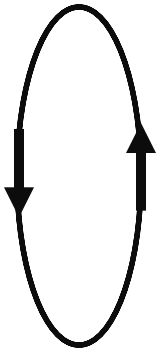
Proton wins because

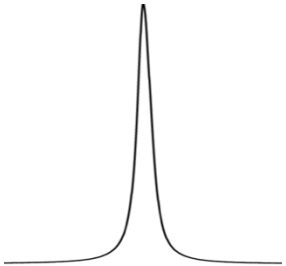
- Greater abundance → more nuclei to detect → better signal
- Larger γ and same B-field results in greater polarization → better signal

Bye bye quantum (for now): transitioning to the classical picture

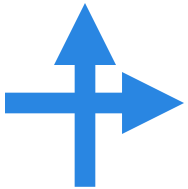
RF pulse

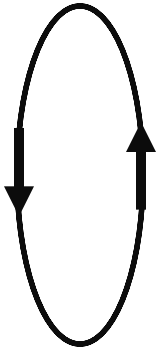


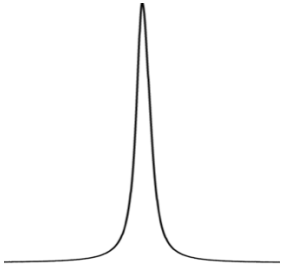




RF pulse

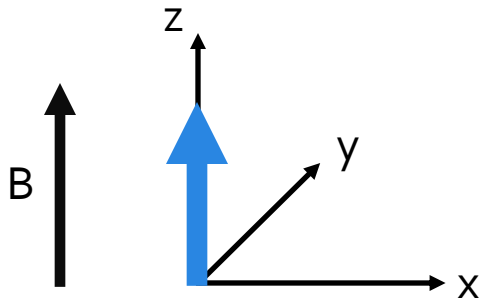






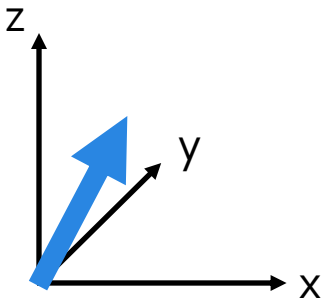
- Induce an oscillating signal in the coil.
- What is the frequency of that oscillating signal?
- Instead of thinking about extra spins, we think about the net magnetization vector they create

Flipping the net magnetization vector



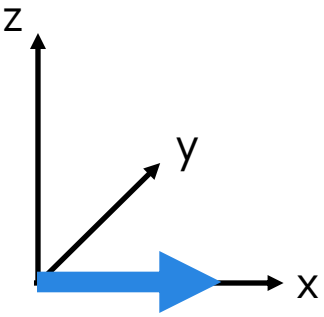
In **thermal equilibrium,** Magnetization is all along the z-axis (if B is also). M_z is maximum

No signal

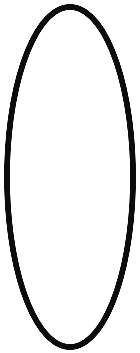


With a little bit of energy (still at Larmor frequency), flip the magnetization a bit into the x-y plane

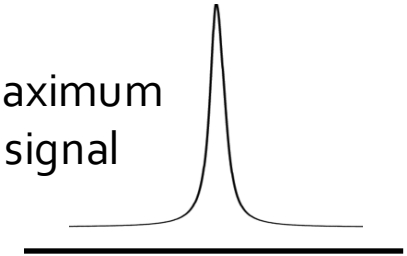
small signal



With more energy (still at Larmor frequency), flip the magnetization more into the x-y plane

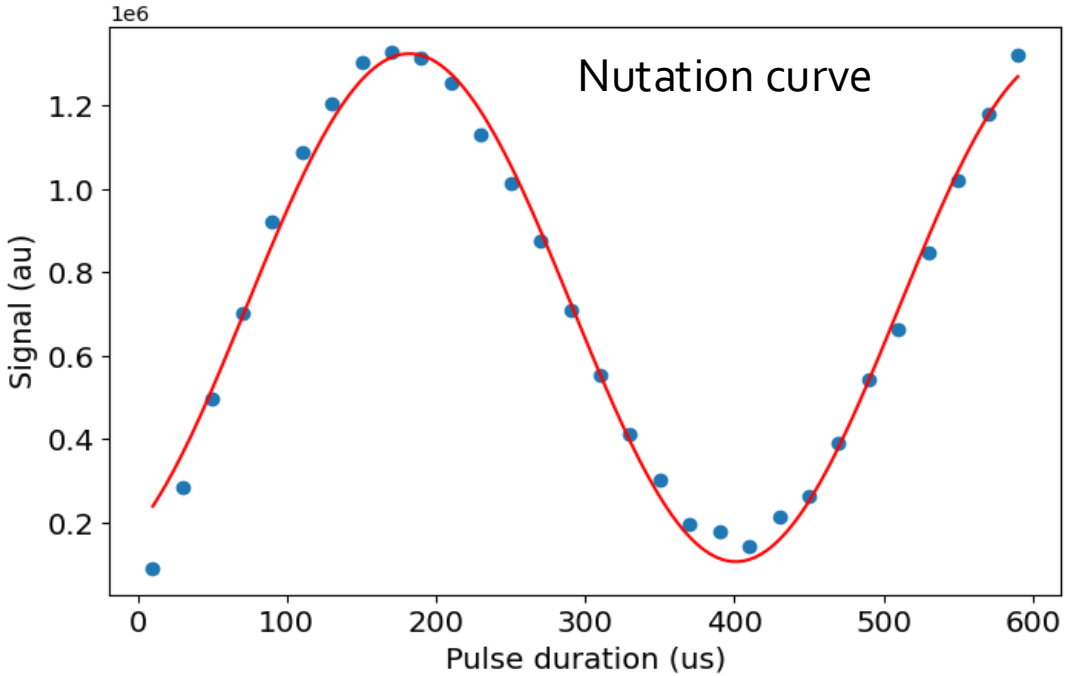


maximum signal



Flipping the net magnetization vector

If you plot the signal induced in the coil as a function of how much of the RF pulse you sent in you get a sine curve.

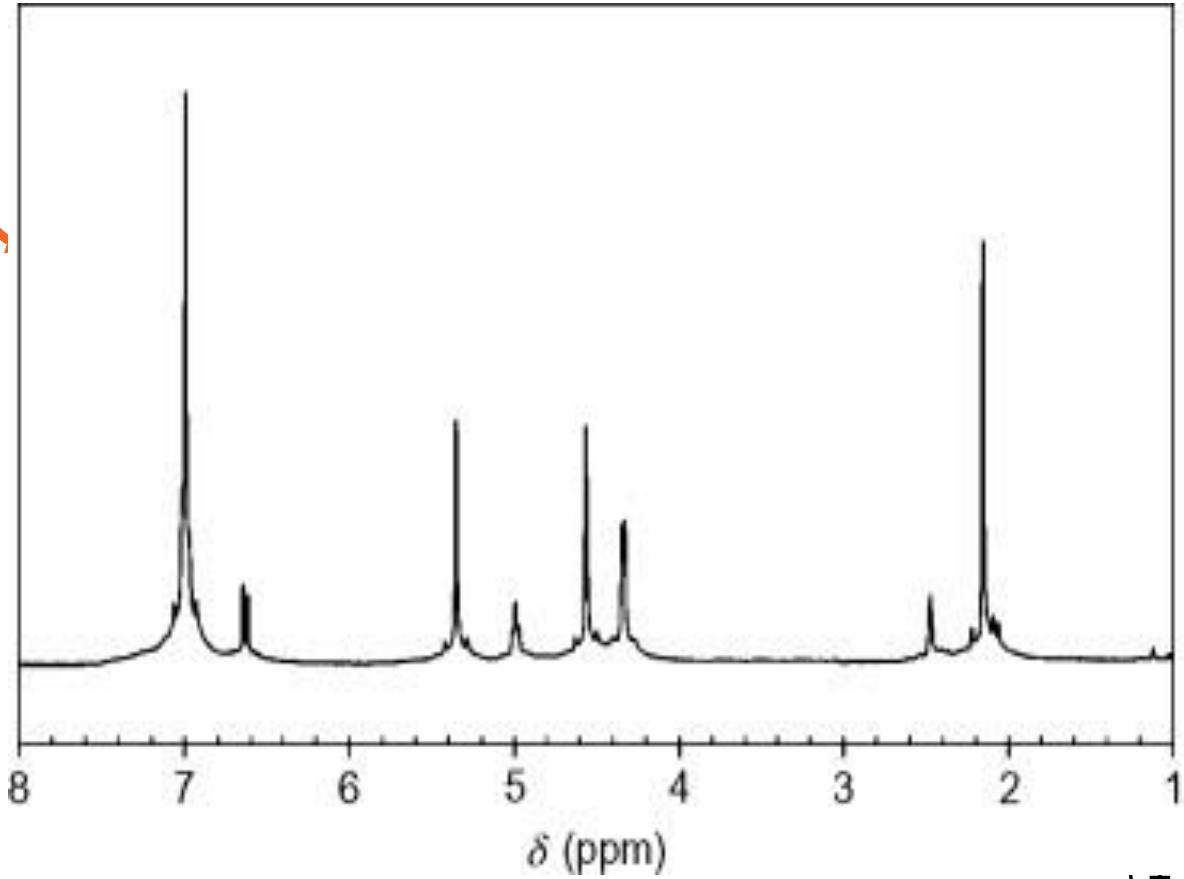


- In practice, you send an excitation pulse (at the Larmor frequency)
- The duration of the pulse corresponds to how much energy you imparted
- The first maximum in the signal corresponds to a 90° pulse, i.e. a 90° flip angle.

How does sending in RF and receiving RF give us info?

higher energy

lower energy



Larmor freq.

What is this ppm scale?

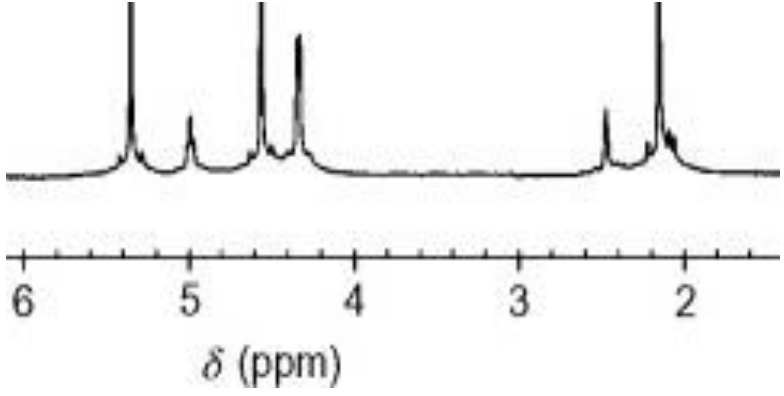
- For reasons we'll discuss shortly, not all protons feel the same magnetic field around them
- There is a local environment with a slightly modified B-field
- A slightly modified local B-field results in a slightly modified Larmor frequency $f = \gamma B$
- We have a reference frequency for what became a reference compound (often tetramethyl silanase, TMS)
- So we have f_{ref}, f_{loc}

$$\delta = \frac{f_{loc} - f_{ref}}{f_{ref}} \times 10^6$$

Chemical shift: how much the Larmor freq. changes
Measured in parts per million [ppm]

<u>Why is this better?</u>

- Where a certain species appears in ppm is independent of the magnetic field (as opposed to the frequency)
- More convenient scale

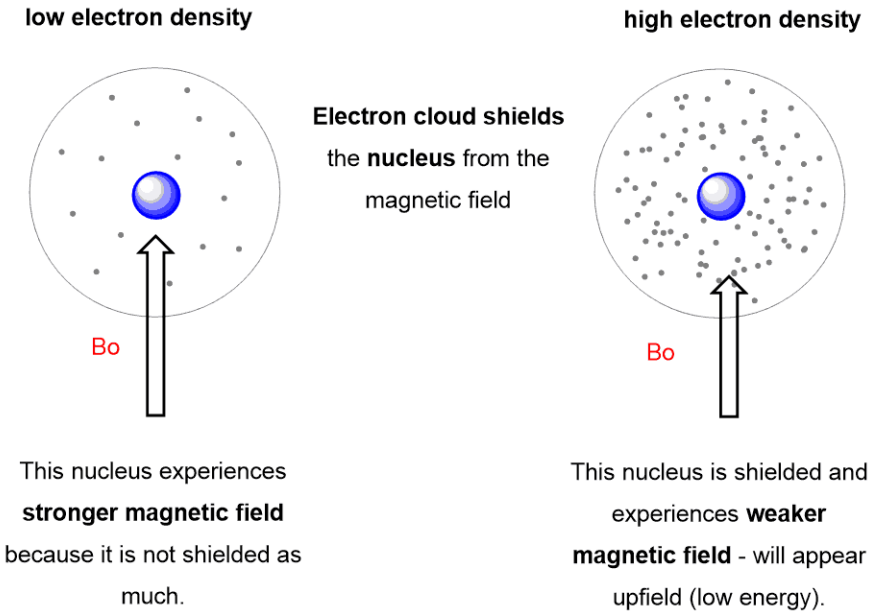


Why many peaks?

In short, even though there is one main magnetic field, each type of nucleus can feel a slightly different **local magnetic environment.**

Nuclear shielding:

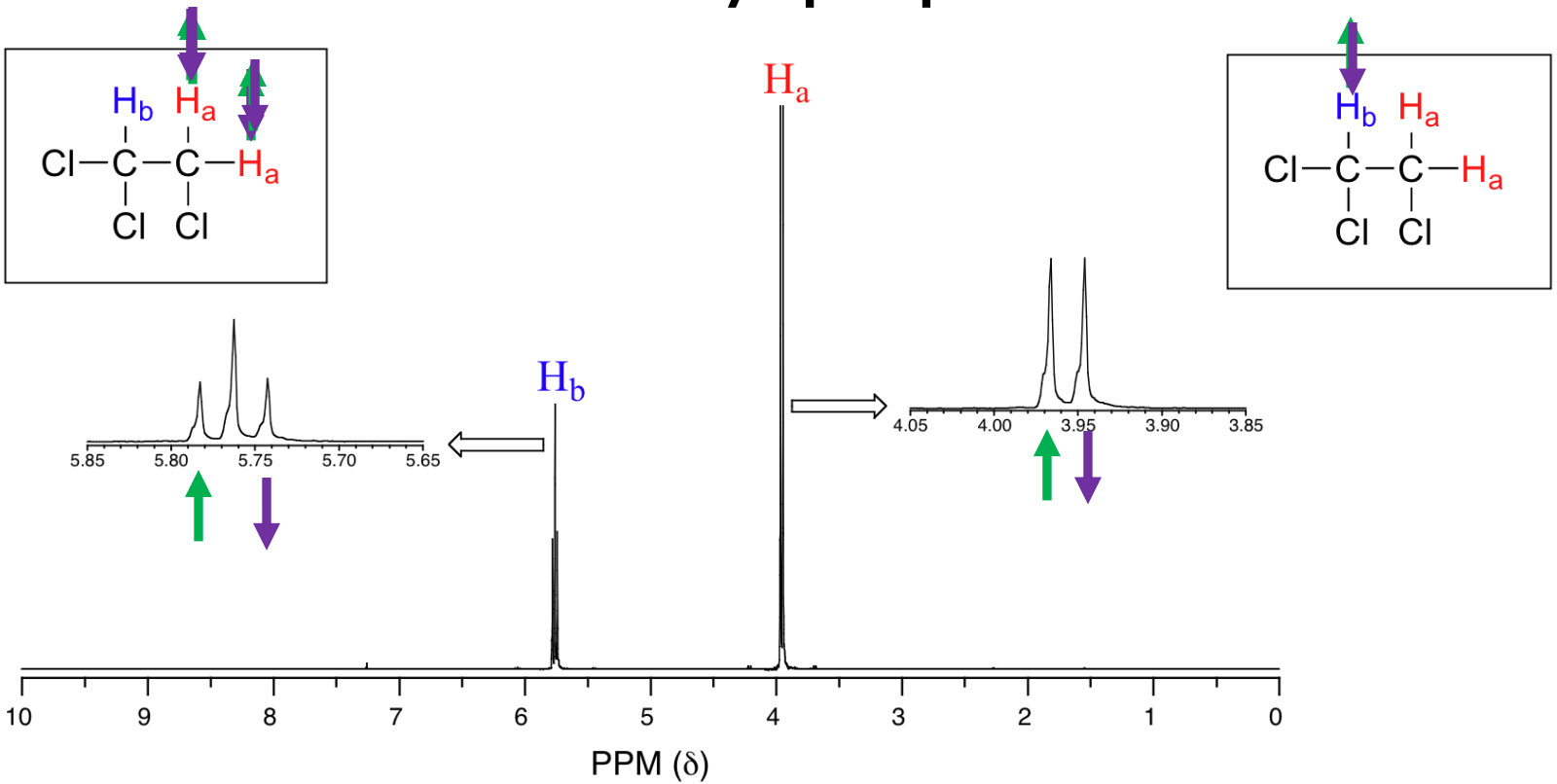
- Electrons orbit the nucleus and shield it from the bias field to different extents
- The effective B-field sensed by the nucleus is different those nuclei
- Since the effective B-field is different the Larmor frequency is slightly different
- Altered Larmor frequency is detected in emission



https://www.chemistrysteps.com/nmr-chemical-shift/

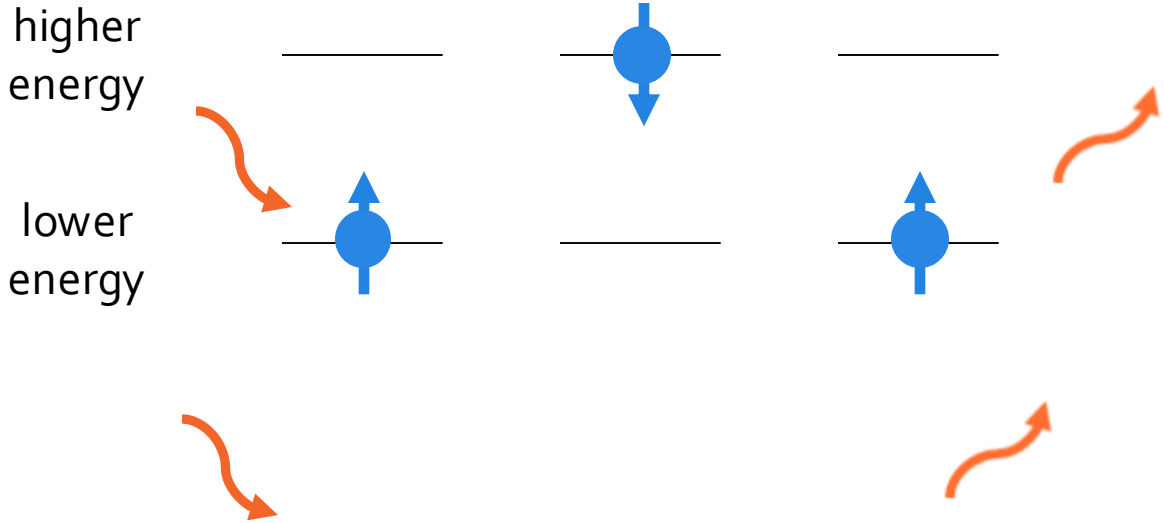
methyl chloroform

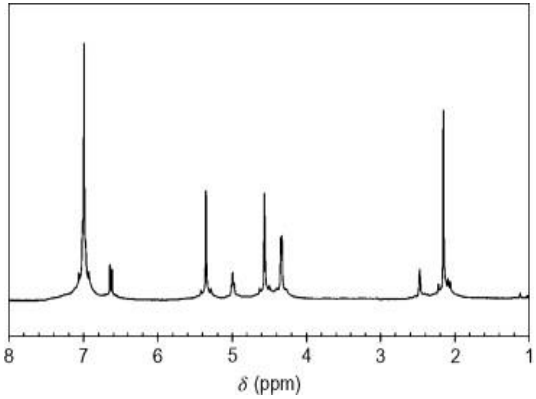
Why split peaks?



- This interaction of nearby spins that causes splitting is called **J-coupling**

We excite with one broad energy band but each species emit at their specific frequency





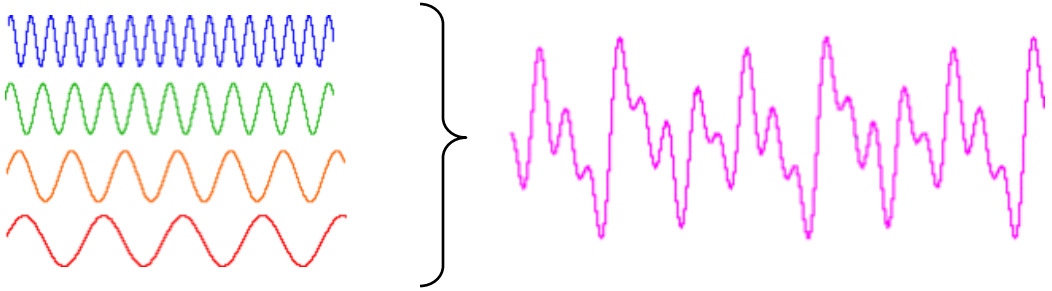
Excite with a band of frequency around the Larmor frequency

Emission comes out as a set of very close but distinct frequencies

Emitted frequencies usually reported on a ppm (chemical shift) scale

How do we detect and distinguish the different frequencies?

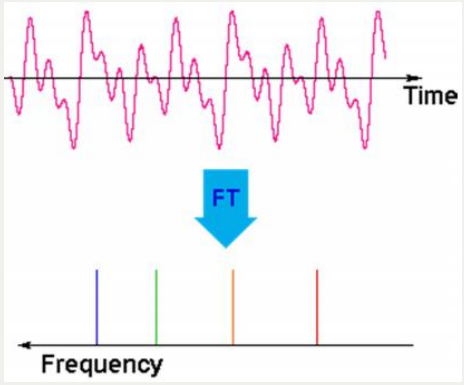
Nuclei re-emit RF radiation at their respective resonance frequencies

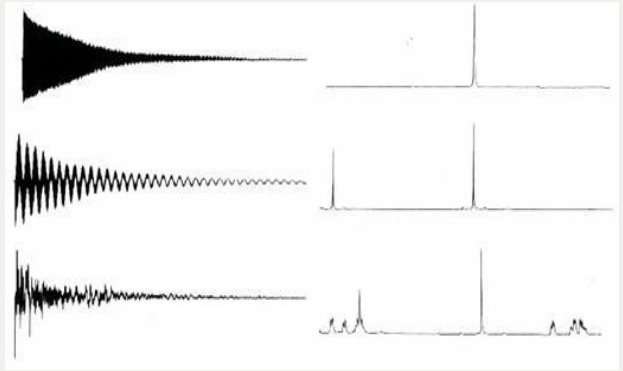


FID

Fourier Transform

NMR spectrum

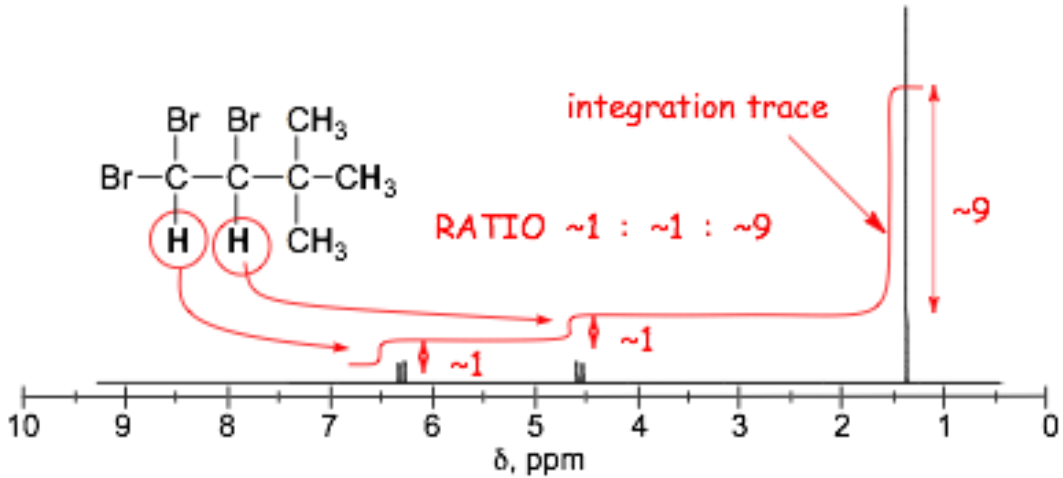




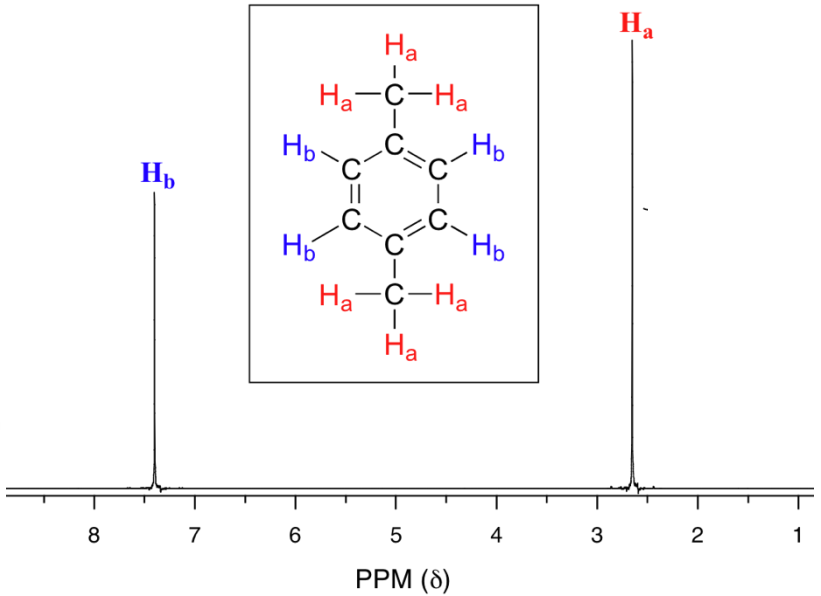
The radiation that we detect is called the **free induction decay (FID)**. It's a complicated mix of different sinusoidal functions attenuated in time

- Fourier transform converts time to frequency

A huge benefit of magnetic resonance is that it can be quantitative



1,1,1-Tribromohexane

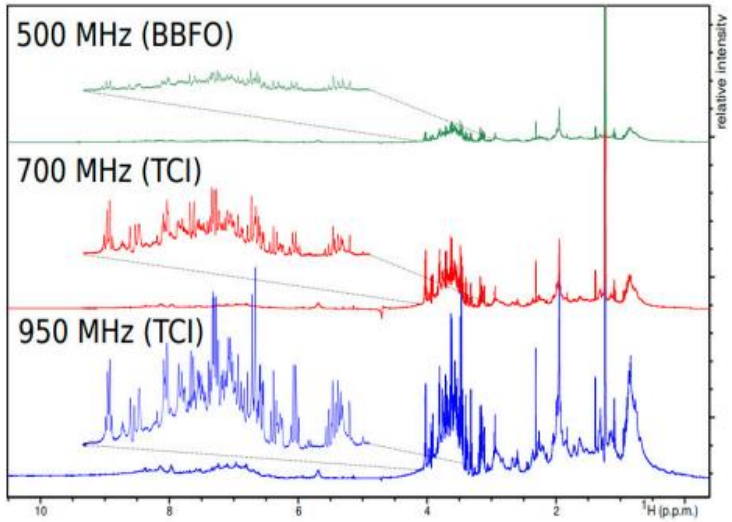


Xylene

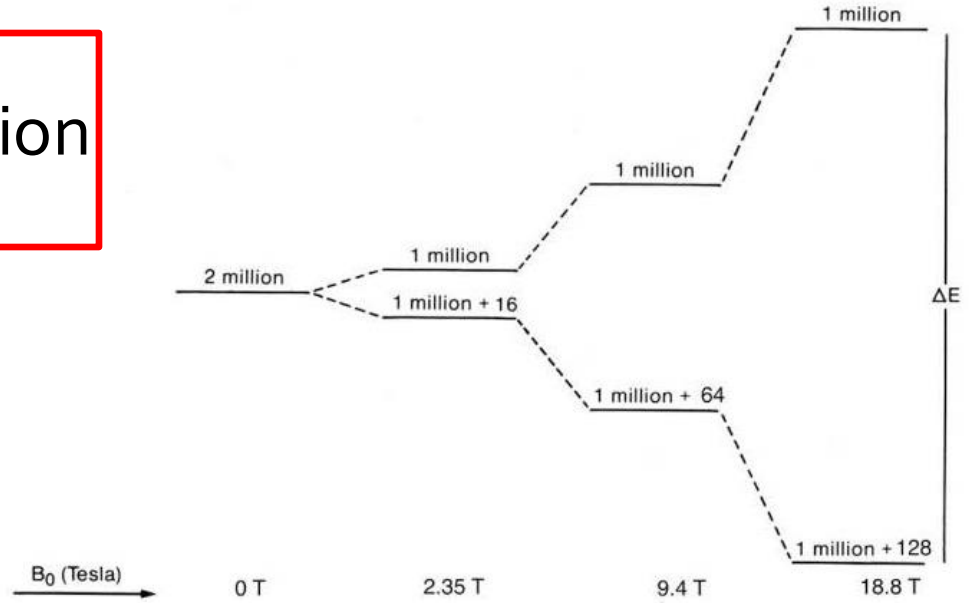
- One big drawback, however, is limited sensitivity
- The signal is low since polarization under thermal conditions is small

One straightforward way to increase sensitivity is with higher magnetic field

$$\frac{N_- - N_+}{N_- + N_+} \sim \frac{h\gamma B}{2kT} = \text{polarization}$$



Abdul-Hamid Emwas et al. 2019, NMR Spectroscopy for Metabolomics Research



- In NMR we often label the strength of the magnet by the Larmor frequency of protons at that field

MR broadly applied in two technologies: NMR and MRI

NMR: nuclear magnetic resonance

MR used to analyze the contents of a sample

- Analytical chemistry, elucidation of structures
- Metabolomics – analyze metabolite profiles of cells and tissues under various conditions
- Tracing experiments to look at flux through specific pathways

- **Most of analysis is identifying peaks and figuring out what they correspond do**
- **Resolution is largely defined as how well peaks can be resolved**

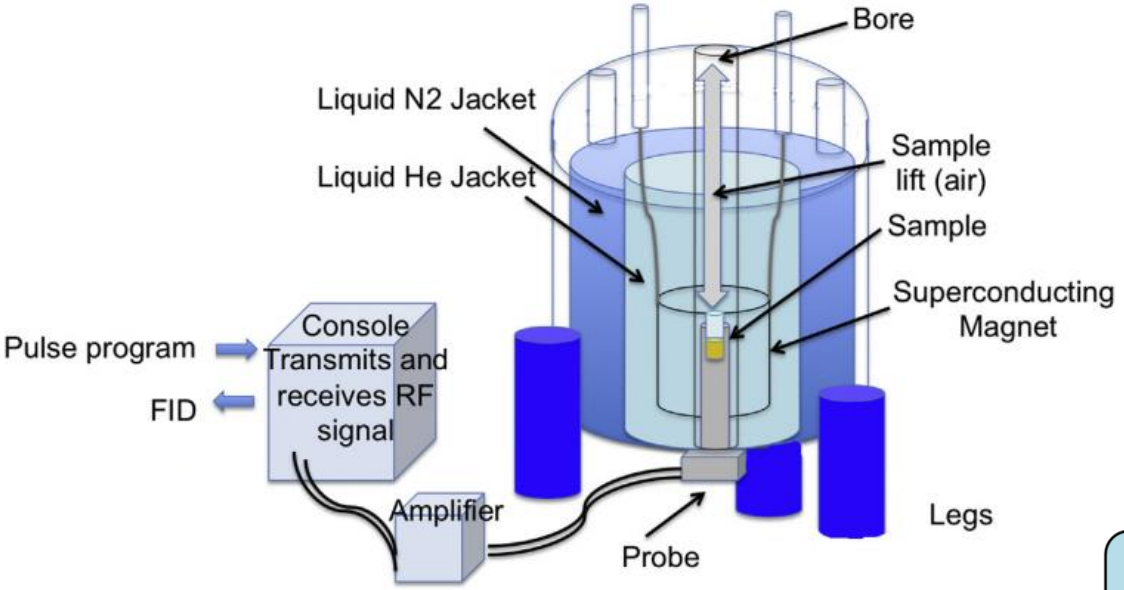
MRI: magnetic resonance imaging

MR used to image tissues in the body

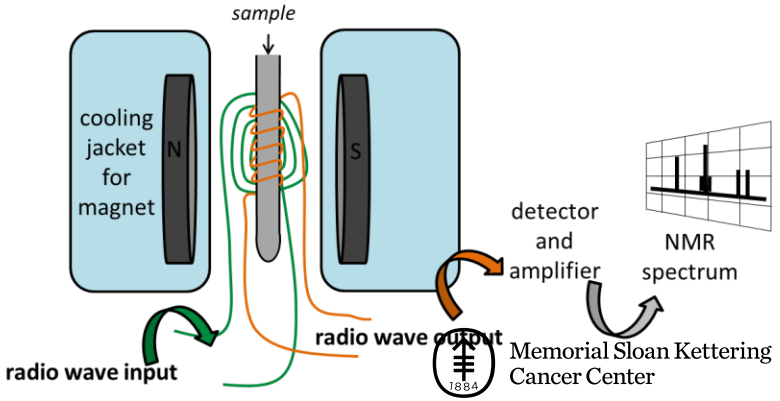
- Detect structural deviations indicative of different pathologies
- Can do magnetic resonance spectroscopy sometimes as well
- Can do molecular imaging in the body with more advanced techniques

- **Pulse sequences aim to best understand tissue composition and function**
- **Resolution is largely defined as how well neighboring voxels (volume elements) can be resolved**

A quick look at NMR hardware



- NMR instruments are referred to by the frequency of the RF radiation used for proton resonance (e.g. 400 / 500 / 600 MHz)

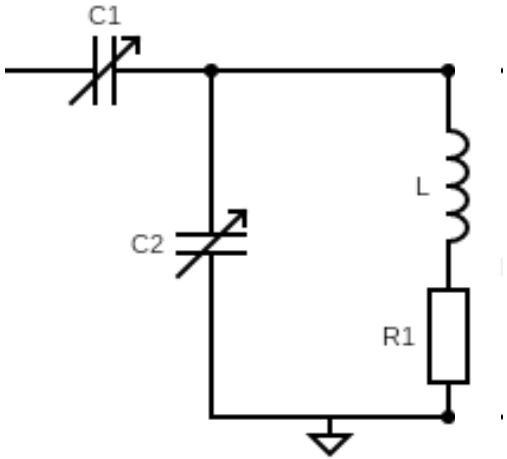


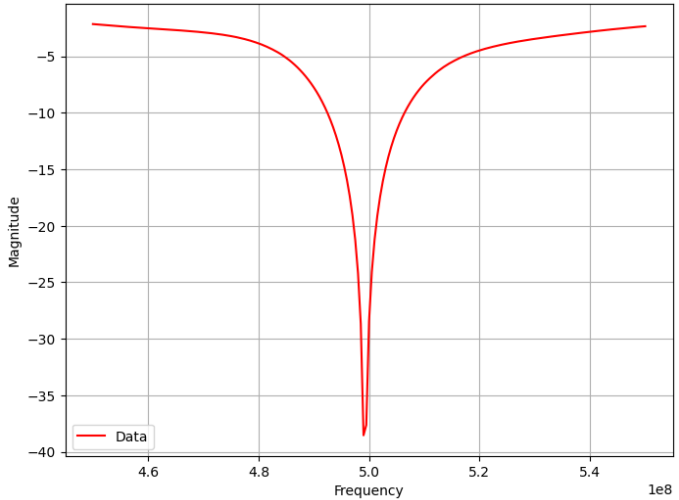
Shimming , Tuning and Matching

- One of the most important things for a clean, clear, well-resolvable signal is a uniform magnetic field. A non-uniformity will broaden width peaks (called **linewidth**) and reduce SNR
- We put in additional coils to add magnetic fields to make the space where the center is more uniform in magnetic field. That process is called **shimming**.

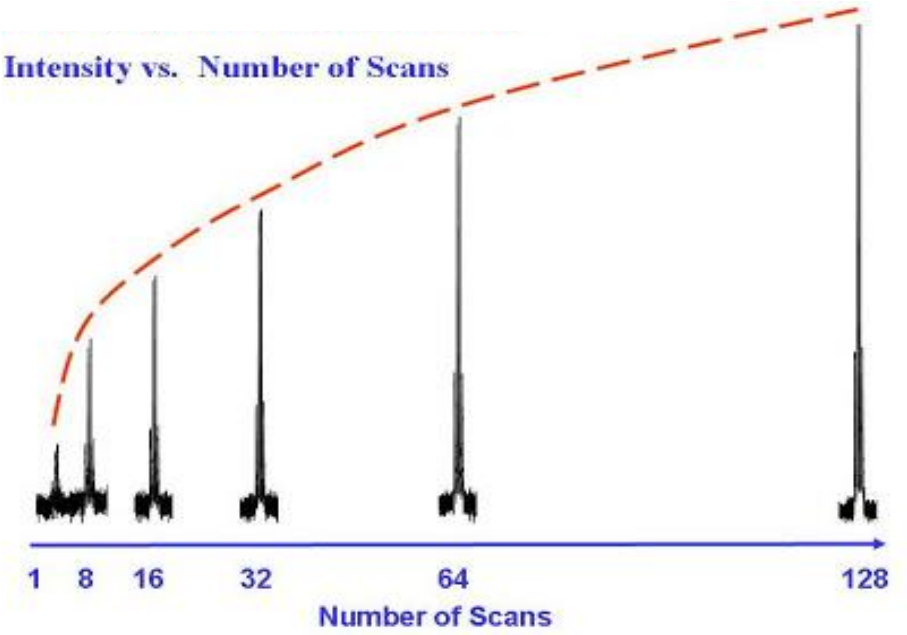
- The coils we use to detect magnetic resonance are usually built to be particularly sensitive at the Larmor frequency of the nuclear we want to detect

  - Coils modeled as an LC circuit.
  - Tuning two capacitors to maximize and the dip and minimize the width





SNR and scaling with number of scans



In order to double the signal-to-noise ratio in a particular spectrum: need to collect 4 times as many scans as were collected in the original spectrum.

Going from NMR to MRI: what's missing?

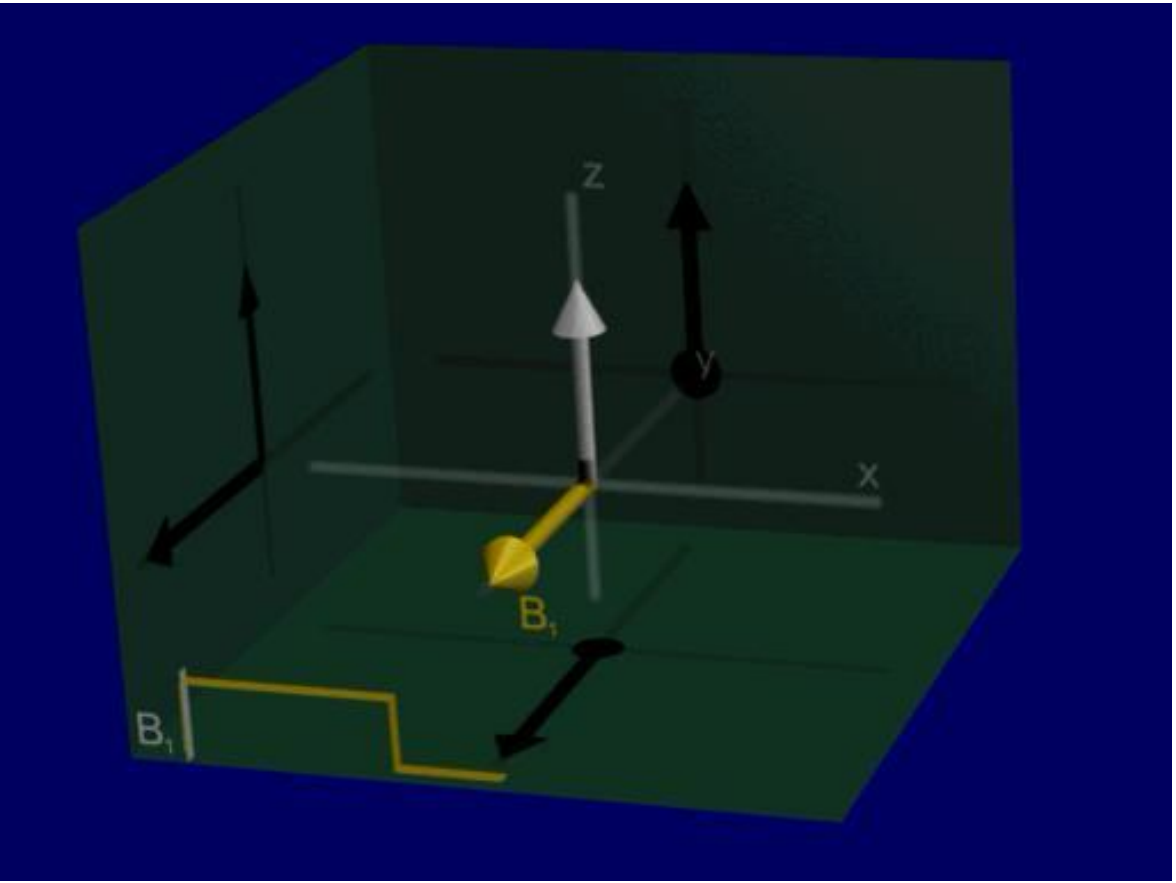
- Getting enough contrast in ppm between tissues of interest can take many scans and a large magnetic field (need a well-resolved spectrum for each voxel)
- We need another mechanism of distinguishing tissues. We need something else that can give us contrast

- We need a way of getting spatial information.
- Need to know what signal is coming from what region in the body

A bit of MRI nomenclature

- The main static magnetic field is called B_0
- Magnets are referred to by their magnetic field (not RF). E.g. 3T magnet
- The RF pulse is sometimes called B1 – an electromagnetic pulse of an oscillating E-B field at the RF frequency.
- The main, static field, B_0, is oriented in the z-direction by convention

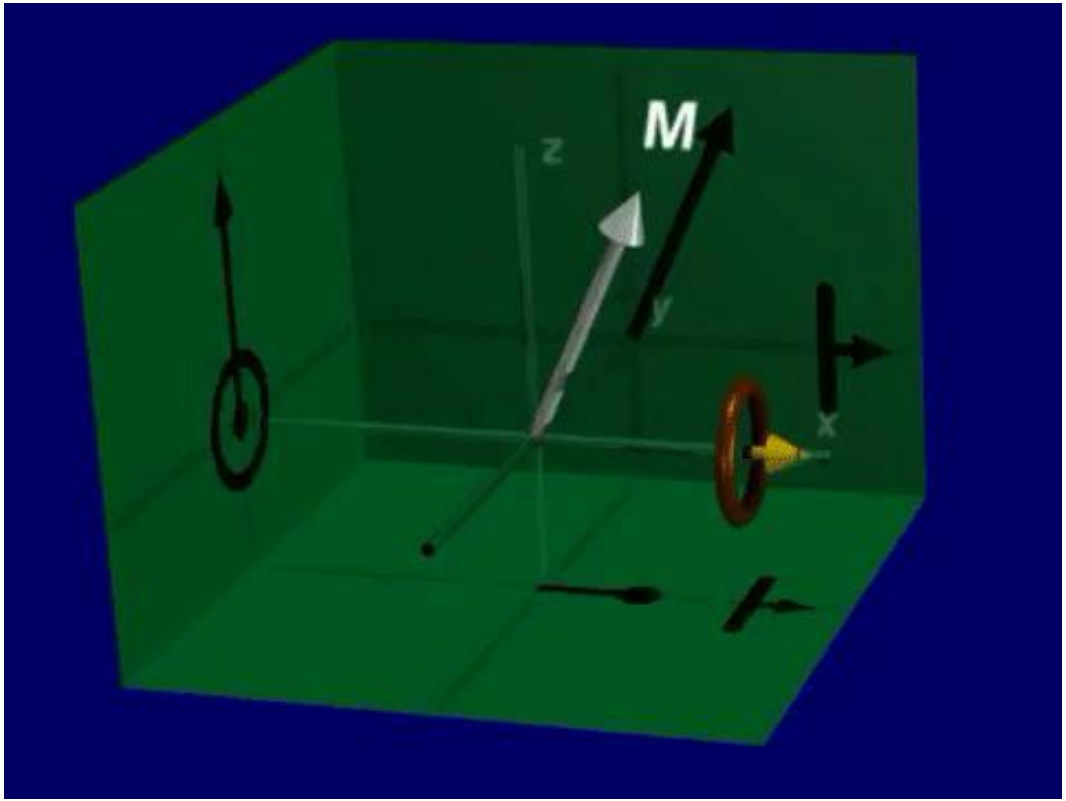
Visualizing precession



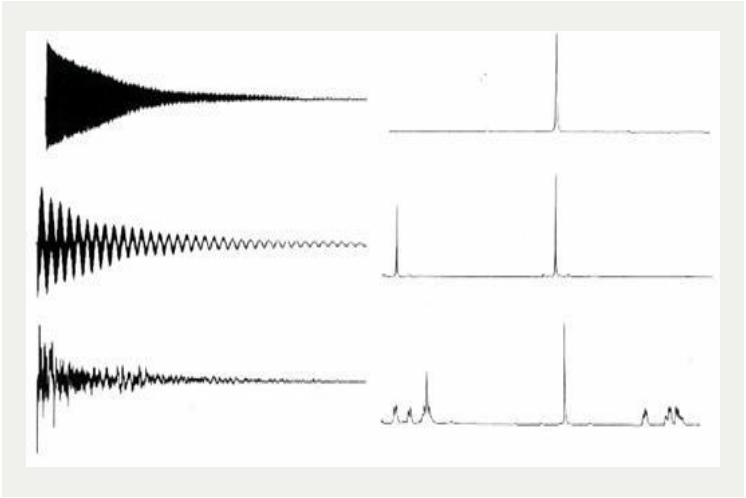
- Net magnetization starts in the z-direction
- RF pulse (B1) in a perpendicular direction
- As RF pulse persists, the magnetization tilts more and more (larger flip angle) towards the xy-axis
- Net magnetization also rotates at RF

Peder Larson simulation

Visualizing precession



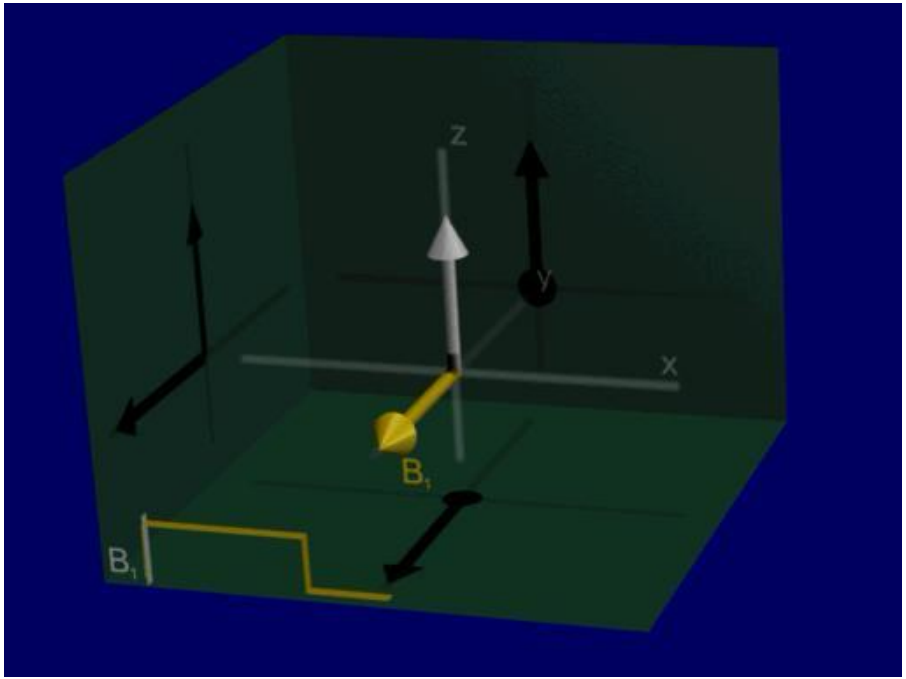
- What we measure is the projection of M into the xy-plane, i.e. M_{xy}



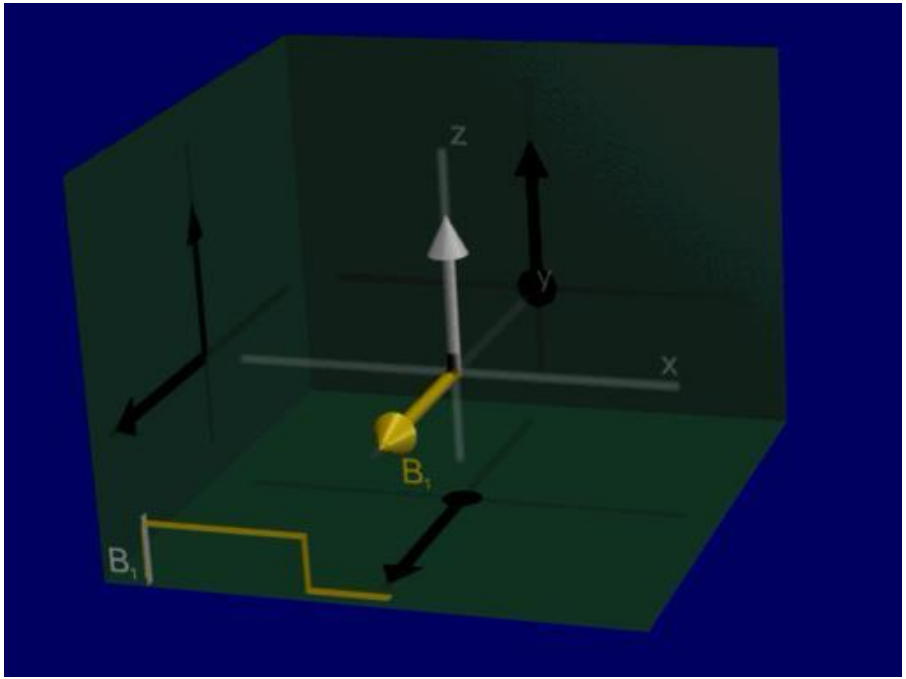
Peder Larson simulation

Lab frame vs. Rotating frame

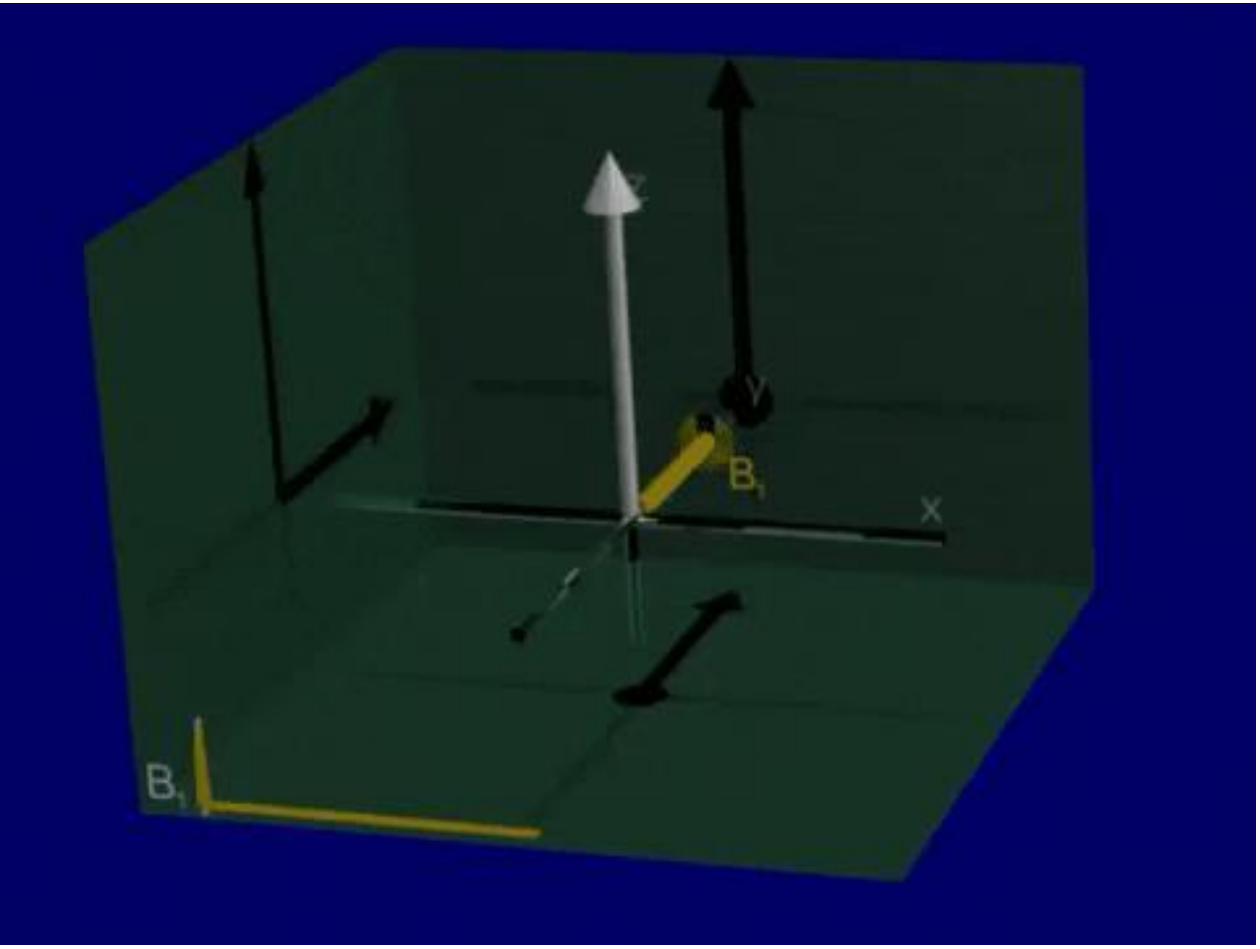
Lab frame



Rotating frame



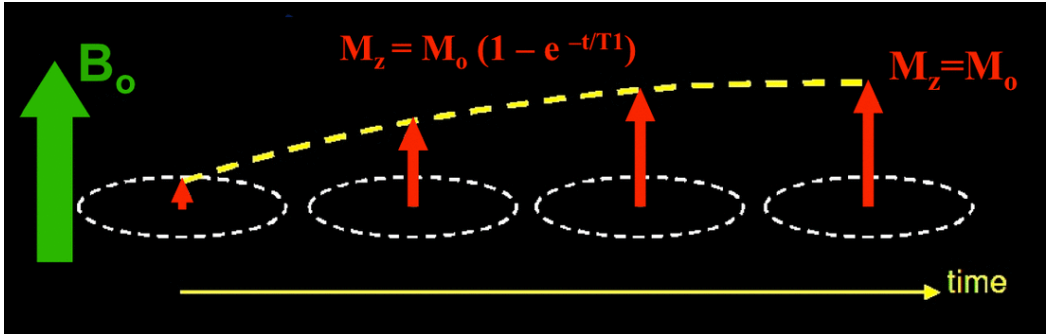
What happens after an RF pulse now with decay



- The B1 / RF pulse adds energy to the system and takes the system out of equilibrium
- Two modes of dissipating that energy take the system back to equilibrium
- One is called **spin-lattice relaxation** and it acts on a time scale called **T1**
- The other is called **spin-spin relaxation** and its time scale is **T2**

What is T1

- **Spin lattice relaxation** (or thermal relaxation or longitudinal relaxation) is one dissipation of the imparted energy (from the RF pulse). It dissipates into the lattice or the environment (through vibrations etc).
- As a result, the net magnetization goes back to its thermal equilibrium magnitude and orientation (along the z-direction)



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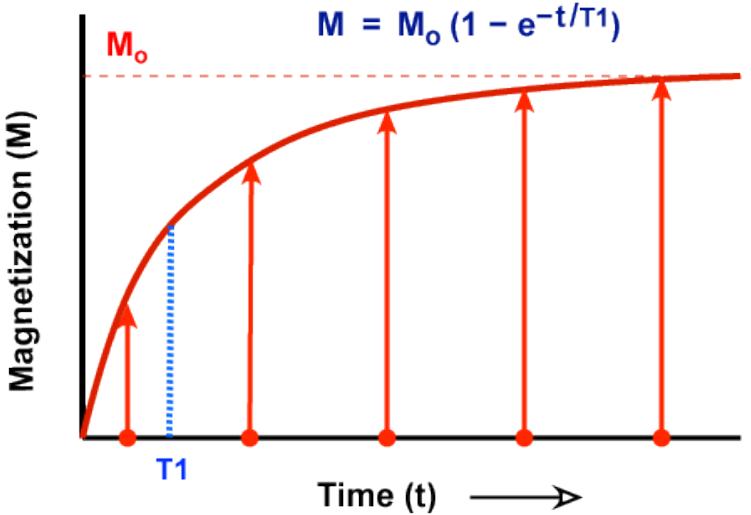
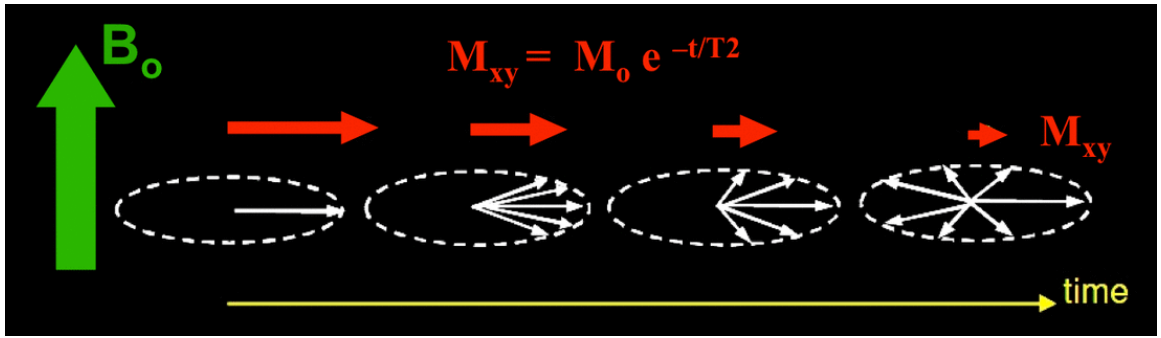


- T1 is measured in seconds
- T1 of water at room temperature and B~1T is a few seconds

Memorial Sloan Kettering Cancer Center

What is T2

- **Spin-spin relaxation** (or transverse relaxation) is the dephasing of spins through interaction with each other.
- Although we may think of the magnetization vector in the x-y plane as one vector, but it's really made up of many small vectors initially pointing in the same direction.
- Over time, however, the directions of the small vectors change such that eventually they combine to a net zero transverse magnetization
- As a result, the transverse magnetization disappears over a time-scale T2.
- Dephasing due to T2 is *not recoverable*



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- T2 also measured in seconds
- T2 < T1

What is T2*

- The apparent dephasing of the transverse magnetization is faster than just the spin-spin interactions would suggest
- The reason is that magnetic field inhomogeneities can cause a faster deterioration of M_{xy}
- B_0 field inhomogeneities cause some spins to precess faster and some slower which results in loss of coherence.
- This faster decay time scale is called T2*
- $T2^* < T2$
- Since this dephasing is due to steady field inhomogeneities, it is recoverable by a 180° pulse

Block equation

$$\frac{d\vec{M}(\vec{r},t)}{dt} = \gamma\vec{M}(\vec{r},t) \times \vec{B}(\vec{r},t) + \begin{bmatrix} -1/T_2(\vec{r}) & 0 & 0 \\ 0 & -1/T_2(\vec{r}) & 0 \\ 0 & 0 & -1/T_1(\vec{r}) \end{bmatrix} \vec{M}(\vec{r},t) + \begin{bmatrix} 0 \\ 0 \\ M_0(\vec{r})/T_1(\vec{r}) \end{bmatrix}$$

$$M_x(t) = M_o\, e^{-t/T2} \sin \omega t$$

$$M_y(t) = M_o\, e^{-t/T2} \cos \omega t$$

$$M_z(t) = M_o\, (1 - e^{-t/T1})$$

T1 and T2 in biological tissues

	T_1(ms)			T_2(ms)		
Tissue	0.5 T	1.5 T	3.0 T	0.5 T	1.5 T	3.0 T
White matter	520[f]	560[a]	832[i]	107[b]	82[c]	110[i]
Grey matter	780[f]	1100[a]	1331[i]	110[b]	92[c]	80[i]
CSF	–	2060[e]	3700	–	–	–
Muscle	560[g]	1075[d]	898[h]	34[g]	33[g]	29[h]
Fat	192[b]	200[b]	382[h]	108[b]	–	68[h]
Liver	395[b]	570[e]	809[h]	96[b]	–	34[h]
Spleen	760[b]	1025[e]	1328[h]	140[b]	–	61[h]

Peder Larson lectrures

- Can also try to distinguish T1 and T2 of tumors vs. healthy tissue.
- T1 and T2 of water at those fields is on the order of a few seconds.

How can we measure these relaxation times? Spin echo

- Many different sequences that manipulate the orientation of the magnetization vector to get the needed parameters.

- We will take a look at one or two of those simplest sequences to get a basic familiarity with how they work

Measuring T1

Let's work it out on the white board

TR = repetition time
TR is the time between consecutive 90° RF pulses

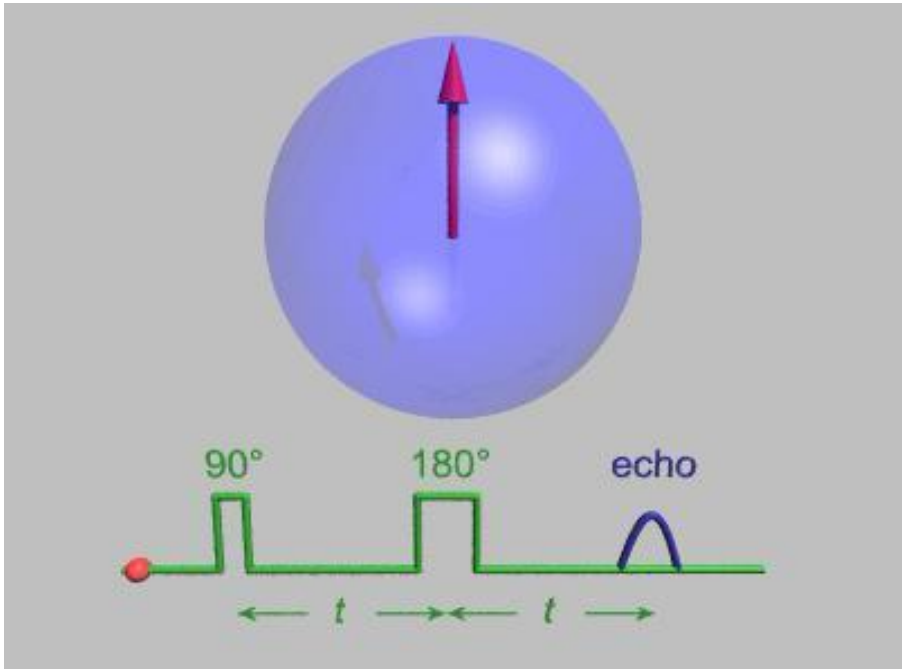
$$S = M_0(1 - e^{-\frac{TR}{T1}})$$

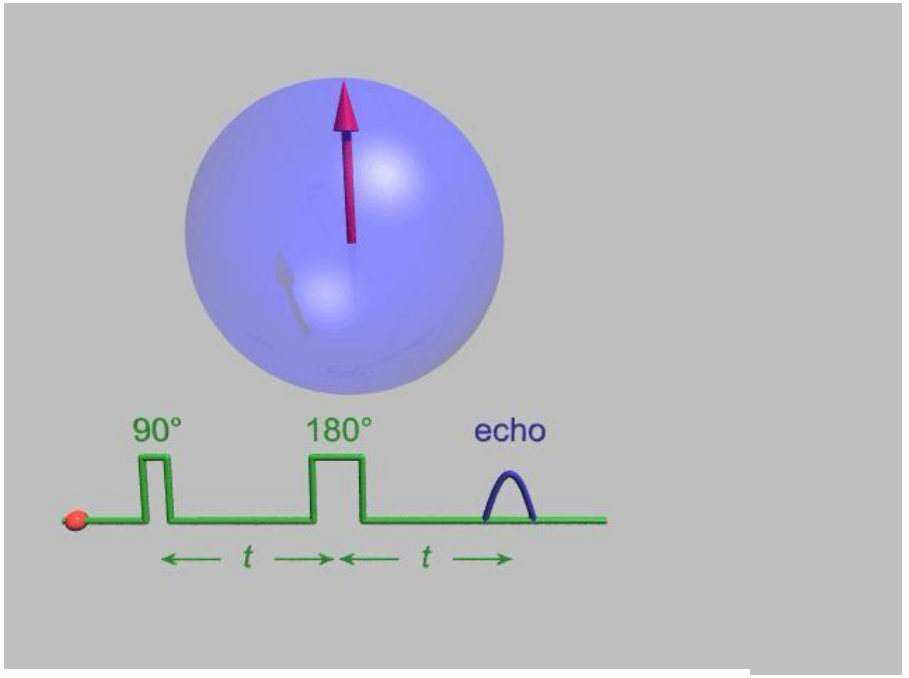
- The return of M_z over time is called a recovery.

Measuring T2

Let's work it out on the white board

We use something called **spin echo** or a **Hahn echo**





Wikipedia

TE is the echo time and is twice time interval between the 90° and the 180° pulses

ettering

T1 contrast example

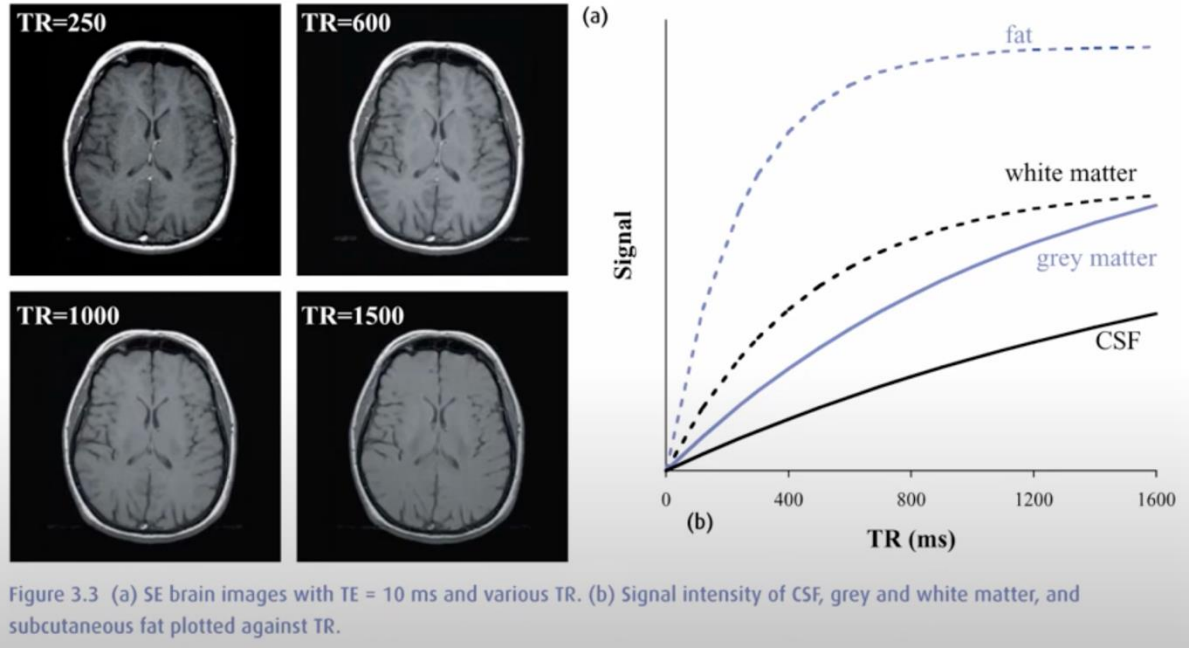
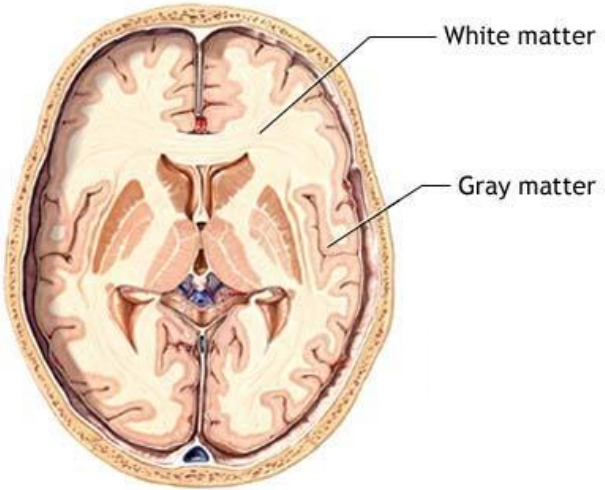


Figure 3.3 (a) SE brain images with TE = 10 ms and various TR. (b) Signal intensity of CSF, grey and white matter, and subcutaneous fat plotted against TR.



Which has a longer T1: gray matter or white matter?

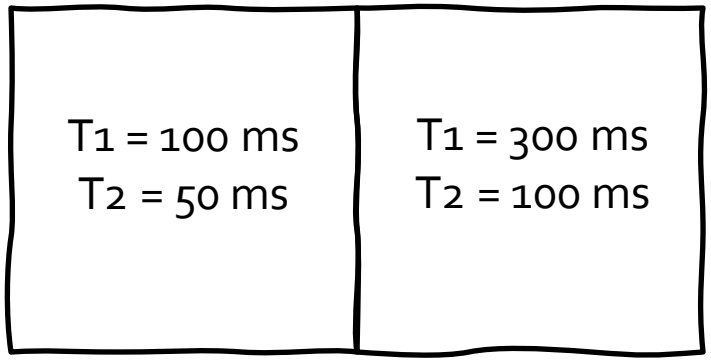
- With T1 contrast, short T1 looks bright and long T1 looks dark

In liquid samples we sometimes add gadolinium (Gd) to reduce T1.

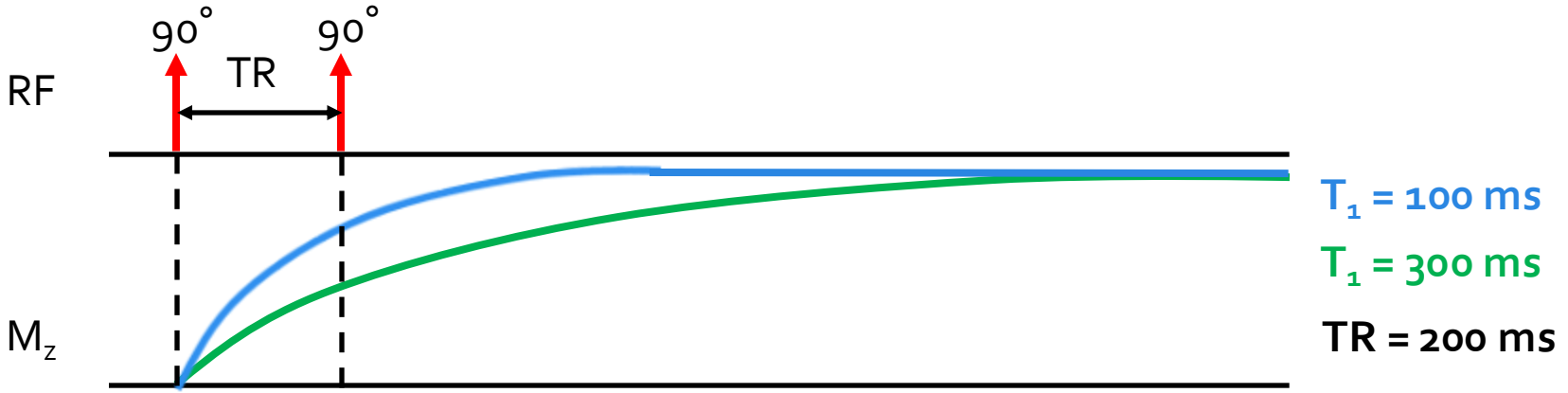
Spin echo exercise

- Break up into groups of 2 or 3

- Design a spin echo sequence (choose TR and TE) to get:
  (a) A T1 contrast image
  (b) A T2 contrast image
  (c) In each case say which part of the sample looks dark and which looks bright



Getting T1 contrast



Choose a short TR such that it is in-between the T1's of the two tissues

Blue tissue looks bright

Green tissue looks dark

- With T1 contrast, short T1 looks bright and long T1 looks dark
- The return of M_z over time is called a recovery.

Getting T2 contrast

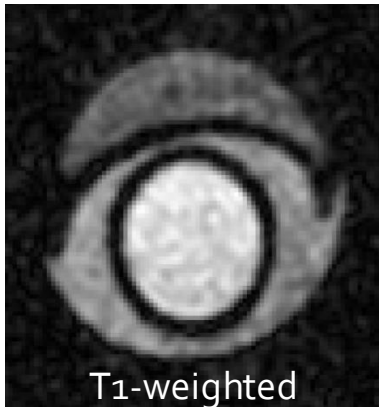
Suppose there is a blue tissue with **T2 = 100ms** and a green **T2 = 300ms**

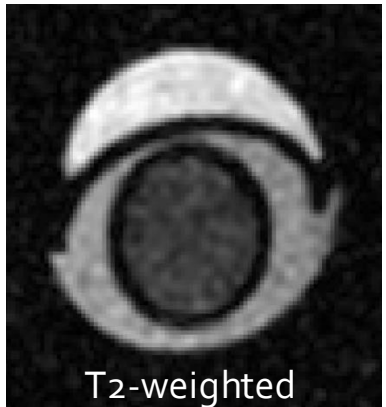
Let's choose **TE = 200ms**

By the time the 180° pulse came 200ms later, the blue tissue xy-magnetization decayed since it's T2 was only 100ms. Its echo is minimal and it is dark.

By the time the 180° pulse came 200ms later, the the green tissue still has some xy-magnetization since it's T2 is 300ms and the echo is significant and it is bright.

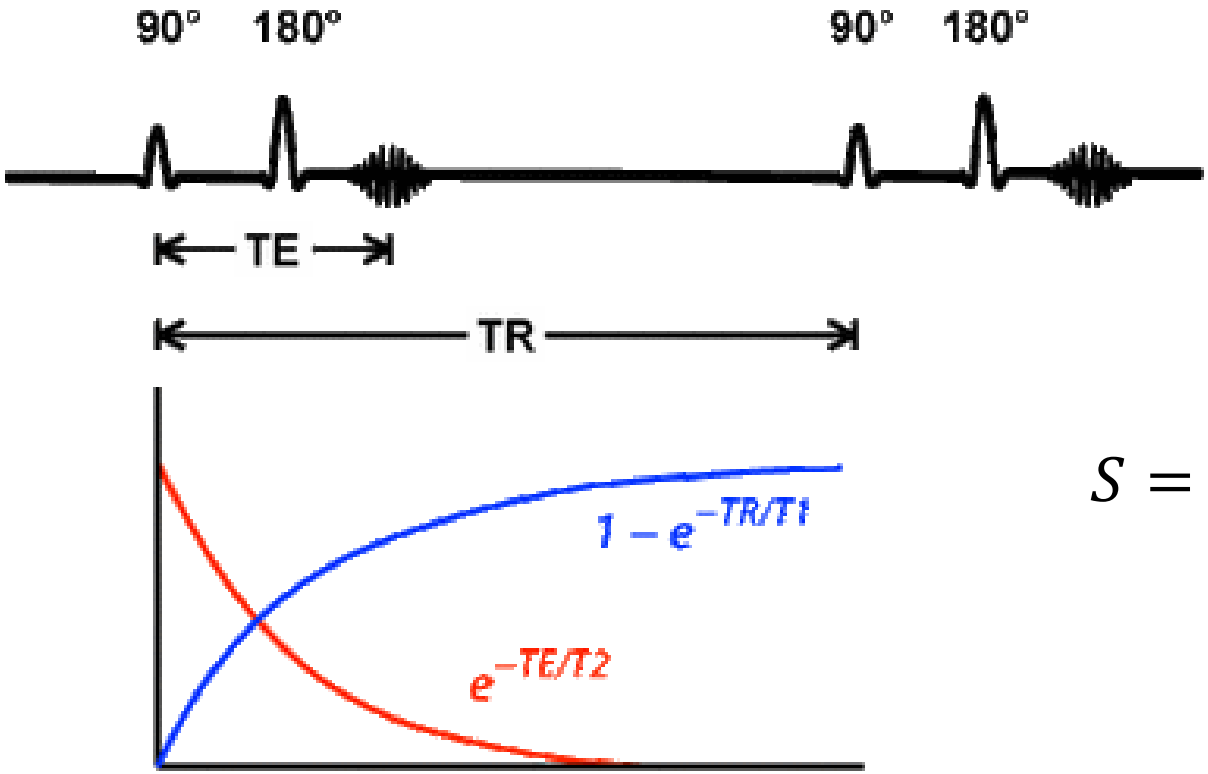
- With T2 contrast, short T2 looks dark and long T2 looks bright
- With T1 contrast, short T1 looks bright and long T1 looks dark





Combining TR and TE

Let's work it out on the white board



$$S = M_0(1 - e^{-\frac{TR}{T1}})e^{-\frac{TE}{T2}}$$

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Generating contrast: proton density, T1, T2, T2*

Sequence type	TR	TE	Contrast

How do relaxation properties of tumors differ from normal tissue?

ordering of intracellular water in malignant tissue.

Hazlewood *et al.* (6) have measured the relaxation times and diffusion coefficient of water protons in normal and tumor tissue. They attributed the increase in the relaxation times for tumor tissue to a change in the interaction of water molecules with macromolecular structures of the cell. In another study, Hazlewood *et al.* (7) asserted that the genotype of the host influences the relaxation times.

We suggested (12) and then demonstrated (11, 14) that

tetraploid ascites carcinoma and Ehrlich
were used.

All mice and rats were killed by cer
The samples were placed unwashed in
tubes with an outside diameter of 8 mm fo
The NMR measurements were obtained
tissue re

Water
ples by v

of each tissue is shown in Table 1 and
and 2.

relaxation mechanism that could ex-
relaxation times T_1 and T_2 in tumor
with normal ones has been published
Another parameter that could influence
T_2 is the tissue pH; this possibility has
ously (13, 15, 16). In this paper we dis-
ence of water content in tumors on the
and T_2.

have shown that the results for sys-
arge proportion of water can be con-
xchange between free and bound water.
change between free and bound water
observed (obs) relaxation time should
ge of the relaxation rates of the free

$$(a/T_{\text{bound}}) + [(1 - a)/T_{\text{free}}] \qquad \text{(A)}$$

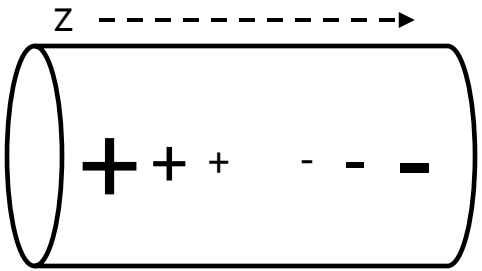
of bound water; (*b*) in samples with lo
(0 to 36%), relaxation time T_2 is mo
modification of the bound water fracti
does not "feel" changes of the water cont

Equation B explains the dependenc
water content. The increase of free wate
relation with the observed relaxation
water. The obtained values for the relax
mature brain and heart have the same r
of malignant tumors tissues. This fact
observed differences between the relaxa
T_2 of the malignant and normal tissues
increase in the freedom of tissue water r
a lesser degree, of water structure in ma
in normal tissue (19).

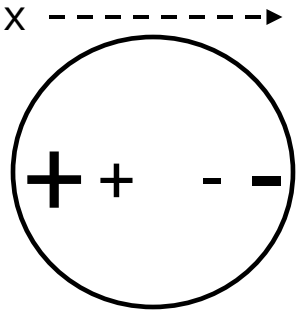
There is a good correlation between the
T_2 and the increase of water content in
sues (liver, heart, and brain). The relax
T_2 decreased as the tissues matured. Th
T_2 in immature brain decreased from 1

In our discussion of MRI, we have still ignored the "I"

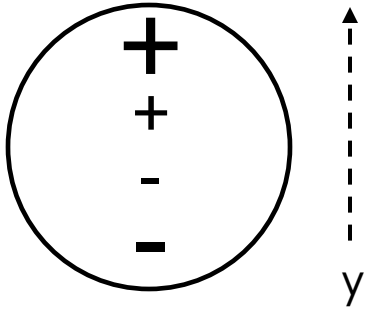
- How can you distinguish which part of the body the signal came from?
- In MRI this is called **spatial encoding** or **signal localization**
- Fundamental idea is that we put in 3 extra coils to create 3 possible magnetic field gradients.
- We can add a small additional magnetic field that varies in the z-axis (along the main magnetic field. This is a z-gradient, G_z
- We can add a small magnetic field gradient along the x-direction, G_x
- We can add a small magnetic field gradient along the y-direction, G_y



$$B(z) = B_0 + G_z \cdot z$$
$$\omega(z) = \gamma(B_0 + G_z \cdot z)$$



$$B(x) = B_0 + G_x \cdot x$$
$$\omega(x) = \gamma(B_0 + G_x \cdot x)$$



$$B(y) = B_0 + G_y \cdot y$$
$$\omega(y) = \gamma(B_0 + G_y \cdot y)$$

How do we use gradients to select a voxel in a tissue?

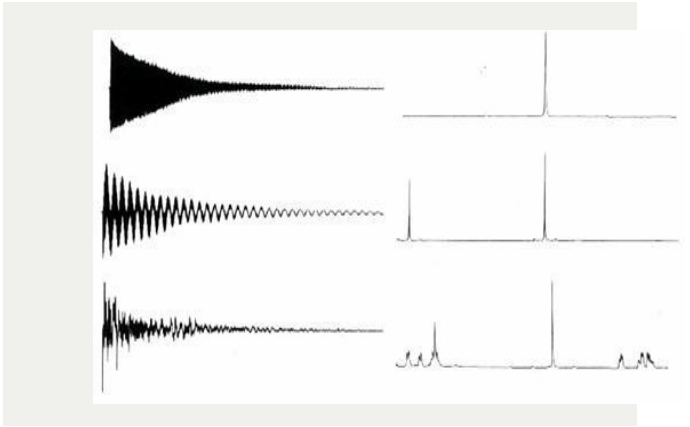
- First if you apply a gradient in z, G_z, slices in z will each feel a slightly different magnetic field and hence have a slightly different Larmor frequency
- Then when you apply an RF pulse, that pulse will only affect the one slice in z that is rotating at the Larmor frequency
- ➢ This is often called **slice selection**

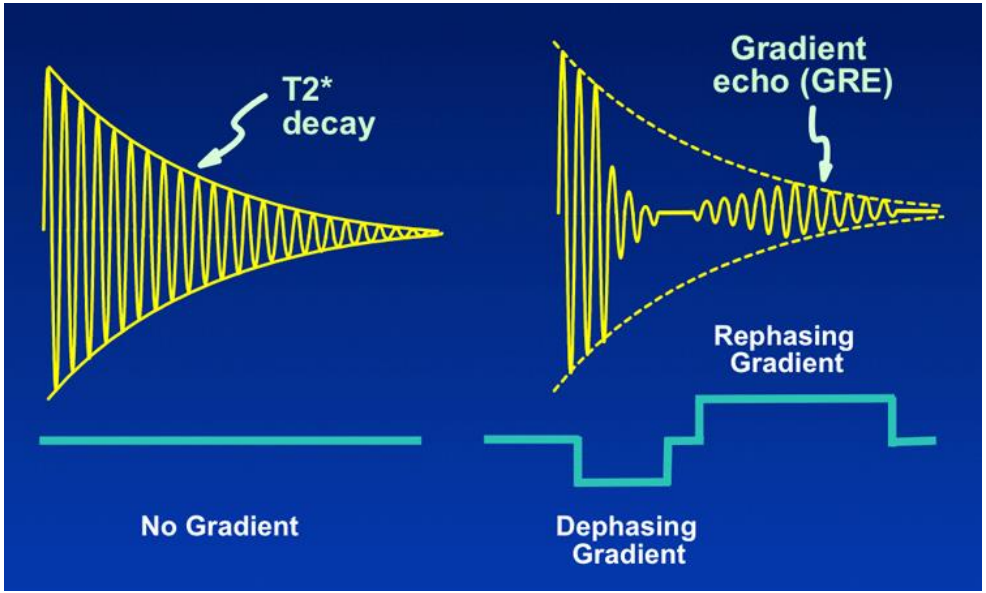
- During acquisition, the x-gradient, G_x, is turned on .
- With this gradient, each slice in x will have a slightly different Larmor frequency.
- When detecting signal, you can tell which position the signal came from based on the Larmor frequency detected. This is called **frequency-encoding**

- Just before recording the signal, the gradient in y, G_y, is briefly turned on and then off.
- When the gradient is turned on, the frequency of the spins changes.
- When the gradient is turned off, the spins return to their original frequencies but they will have attained an extra phase. Location in y can be identified based on this extra phase
- This is called **phase-encoding**

Measuring T2*

How can we measure T_2^* ?
Why not just measure how quickly the FID decays?
The problem is that we have frequency encoding
→ The frequency encoding is acting like an inhomogeneity
→ Need to recover the dephasing we caused by G_x





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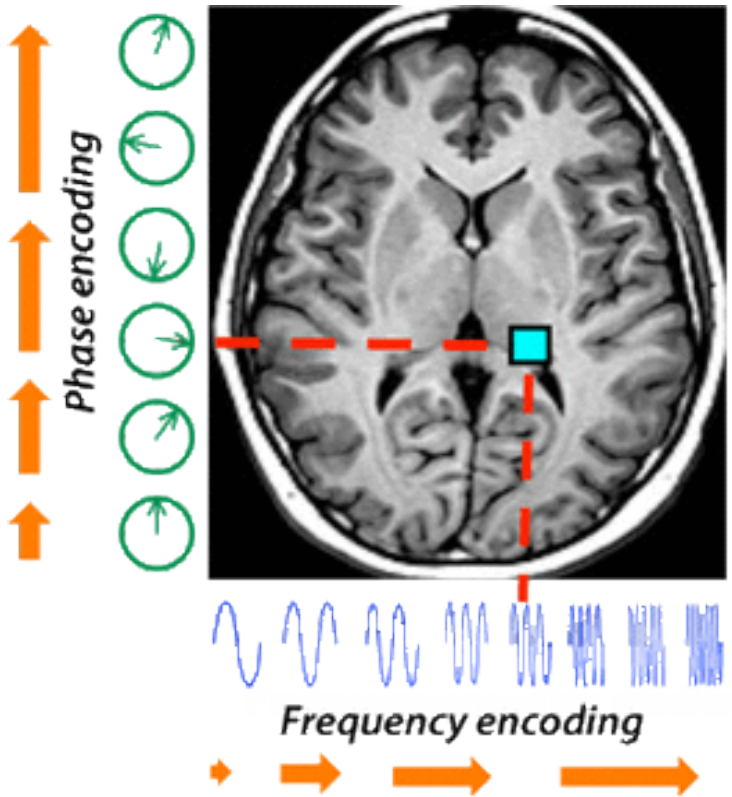
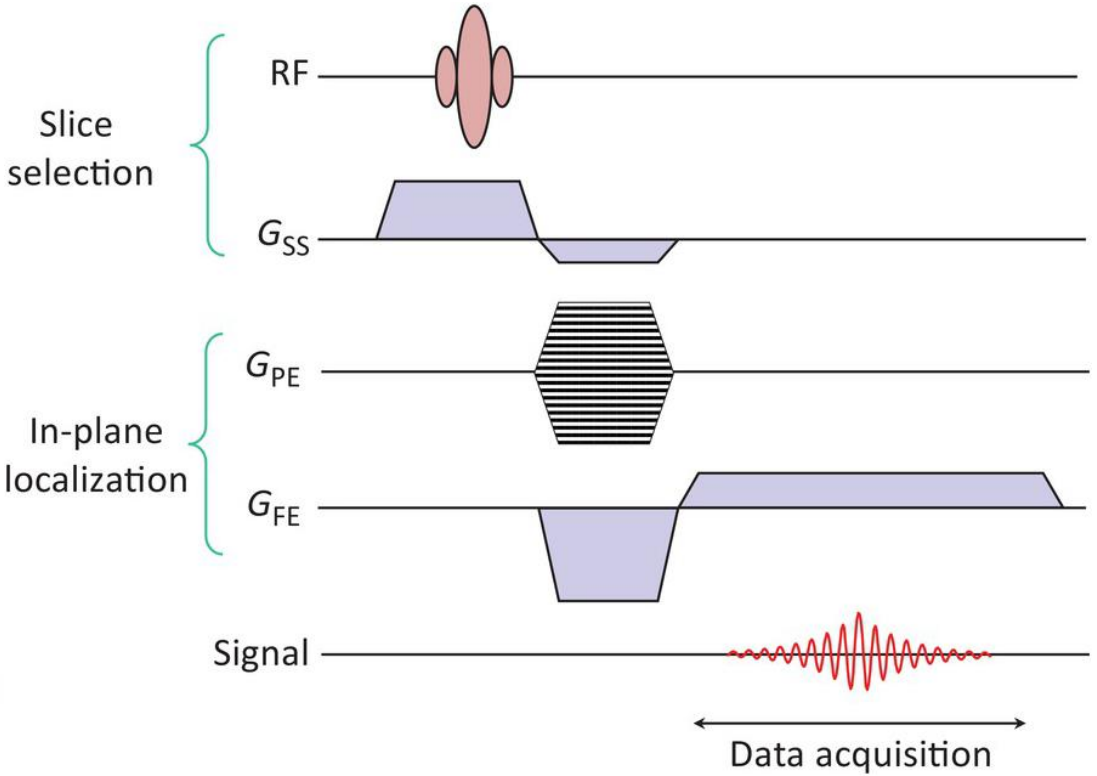
Gradient echo:
We apply a reverse gradient to undo the dephasing we caused. Get an echo at a characteristic time.
It's like a spin echo but instead of a 180° flip in RF, we apply an extra gradient

How do we use gradients to select a voxel in a tissue?





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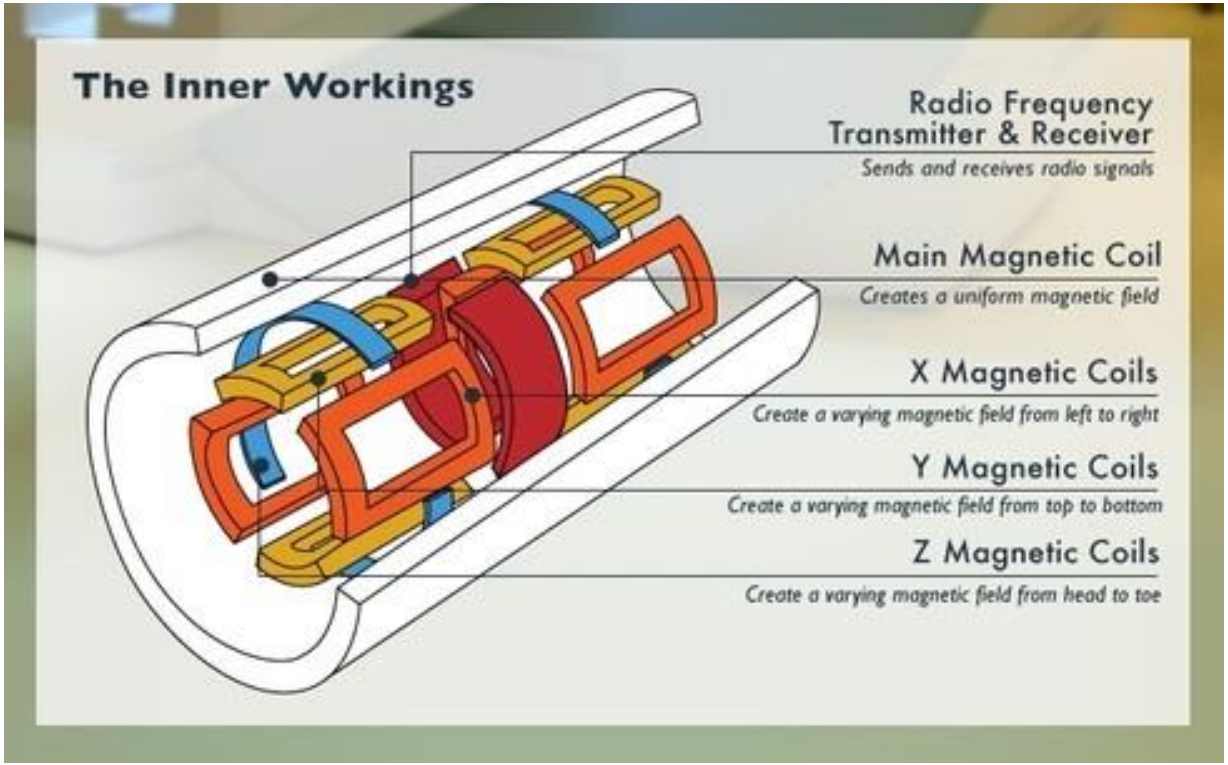
What does the inside of a magnet looks like?

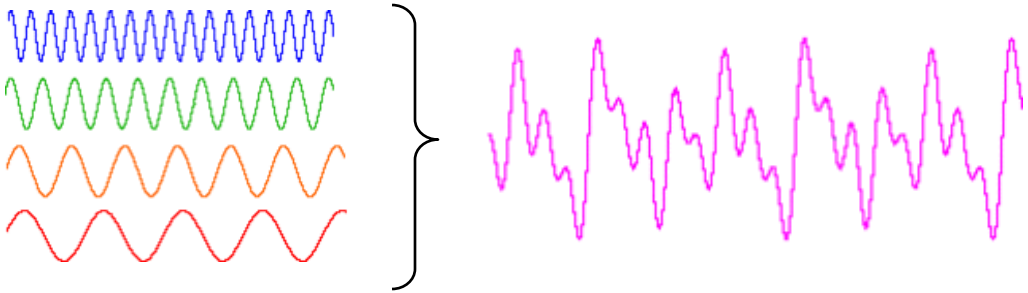


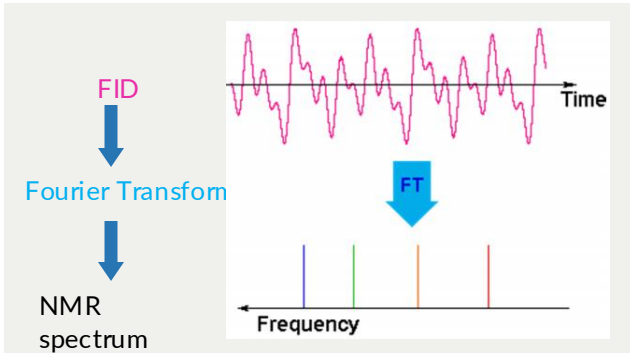
- The main field is often a super conducting electromagnet but in principle doesn't have to be
- Can have shim coils as well to make the field more uniform

Introducing k-space

- **Slice selection**: with RF you select out and excite only one slice in z.
- **Frequency encoding**: By putting a gradient in x, different locations in x will have different Larmor frequencies
- **Phase encoding**: By putting a gradient in y for a short time (and then turning it off), each position in y has a different phase

➢ **The different frequencies and phases are all acquired at once**



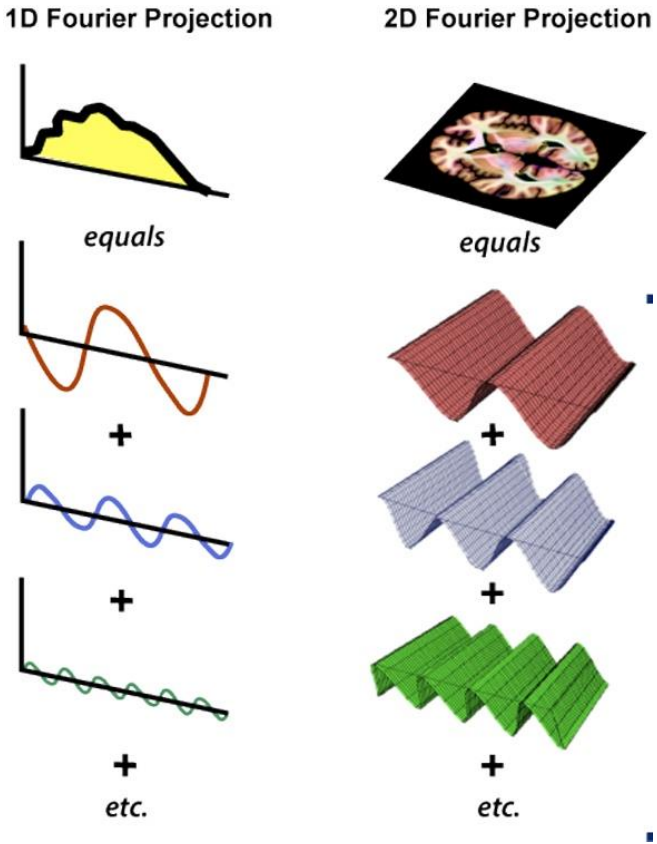


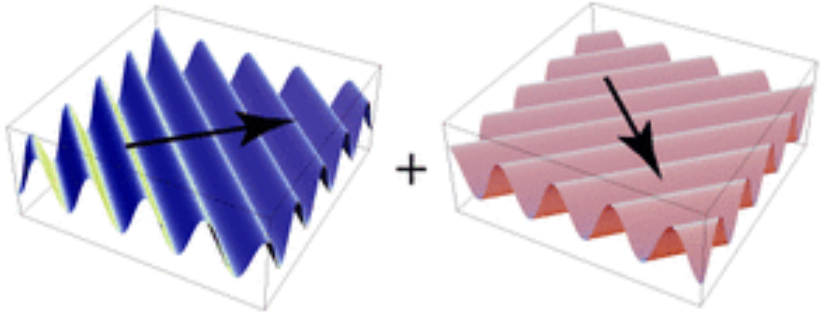
➢ **But now the different frequencies represent positions/space**

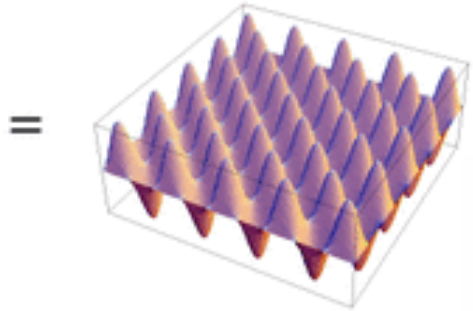
Introducing k-space

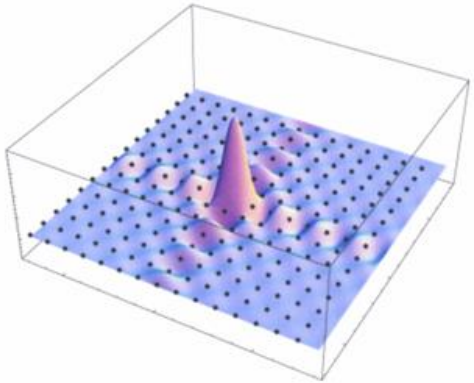
Introducing k-space

- A bit of 2D intuition









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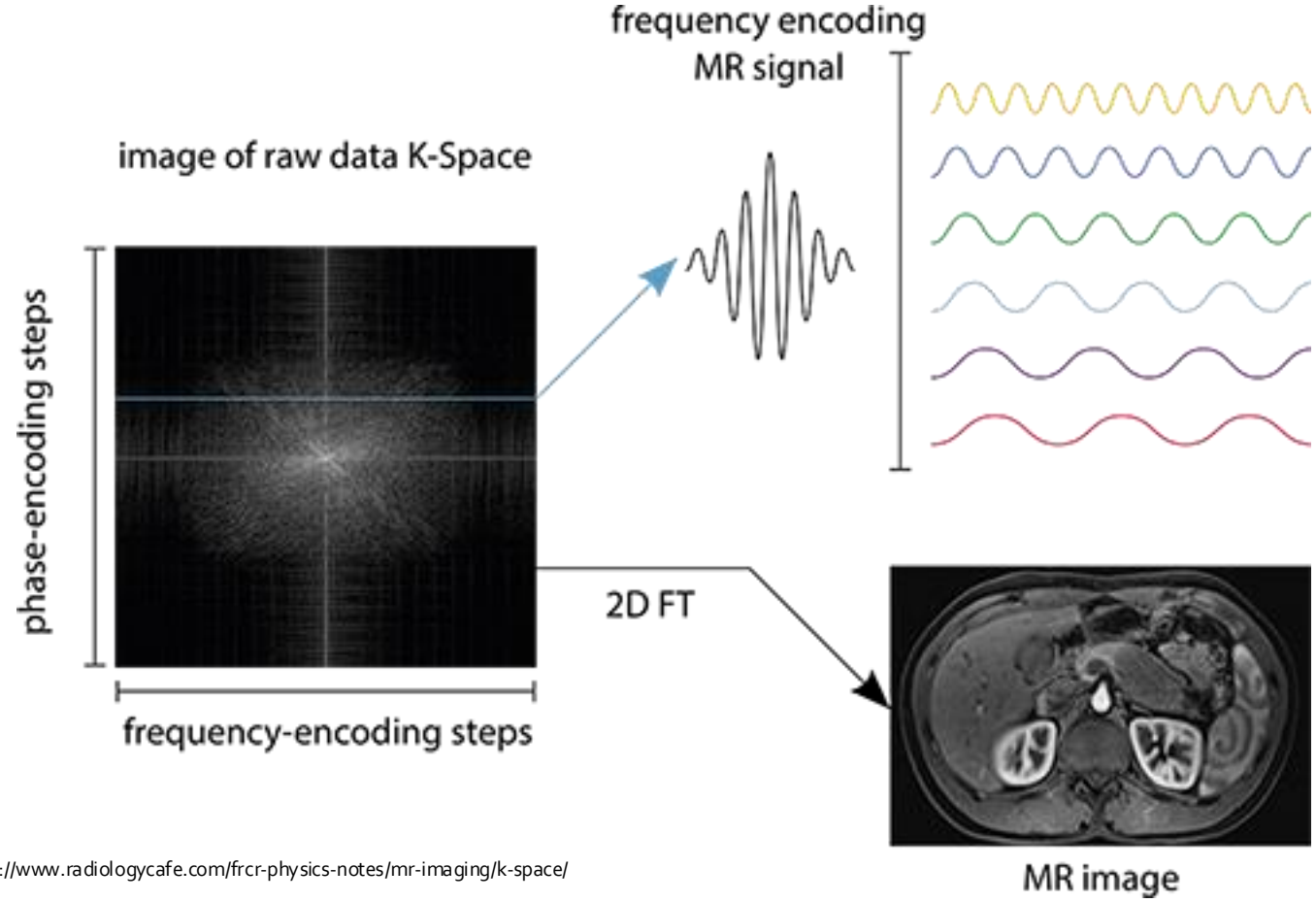
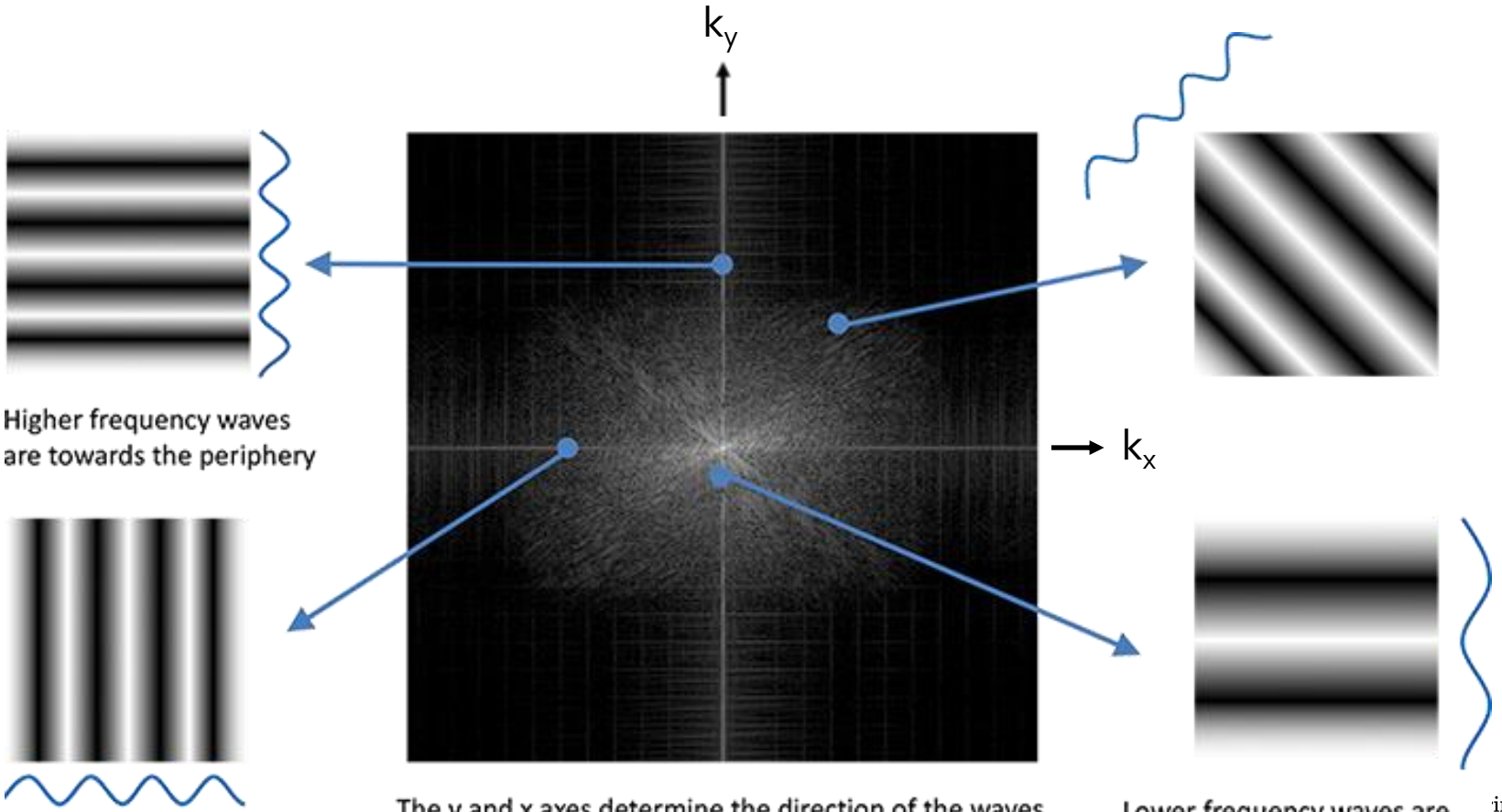
Introducing k-space



https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/k-space/

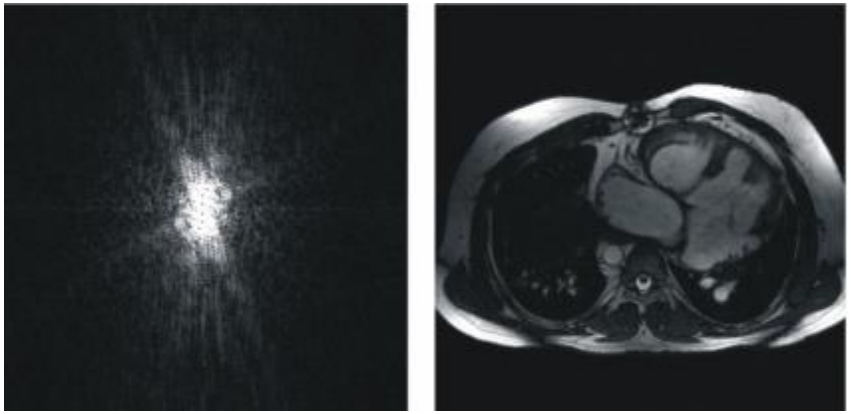
Introducing k-space



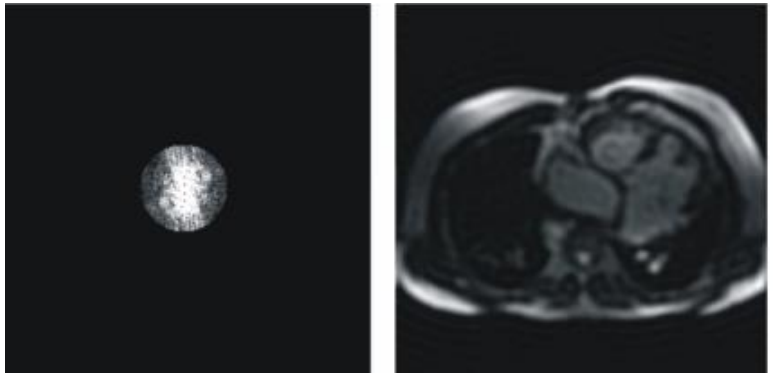
https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/k-space/

Introducing k-space

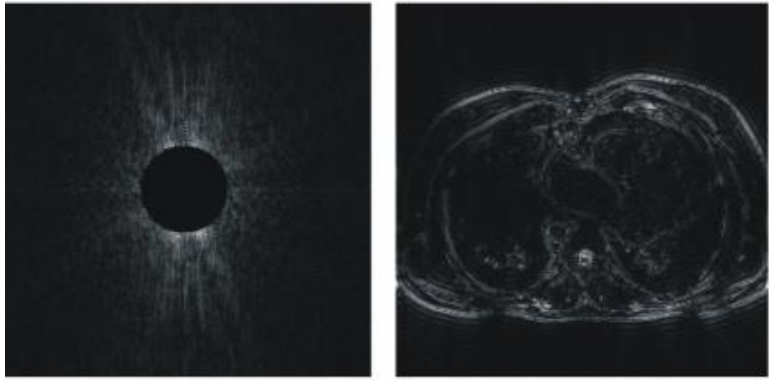
Utilize all of k-space



Cut off large k (low-pass filter)



Cut off small k (high-pass filter)



- Through the gradients in x and in y (the frequency encoding and phase encoding) we traverse k space
- The more of this k-space we acquire the better we can reconstruct the image

We have now discussed a number of contrast mechanisms in magnetic resonance

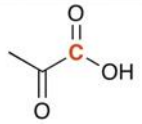
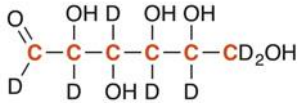
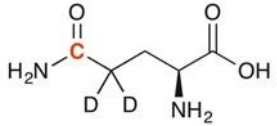
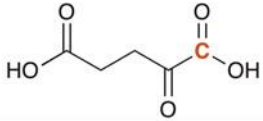
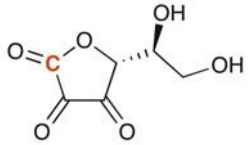
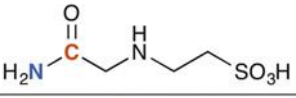
- Proton density
- T1-weighted
- T2-weighted

- In all of these, is the contrast coming from a material property or a biological function?

- Can we modify our experiment to imagine a biological function with MR
  - Molecular imaging

Detecting other nuclei in NMR / MRI: ^{13}C

- What is the challenge in imaging ^{13}C?
  - Low abundance of ^{13}C
  - Low polarization
- What is the benefit in imaging ^{13}C?
  - Low abundance means possibility to trace injected, enriched substrate
  - Study metabolomic changes
  - Simpler spectra
- We can overcome these challenges by
  - Enriching a substance with ^{13}C
  - Hyperpolarizing

Name	Structure
1-^{13}C-Pyruvate	
$^{13}C_6$,1,2,3,4,5,6,6-$^{2}H_7$-Glucose	
4-$^{2}H_2$,5-^{13}C-Glutamine	
1-^{13}C-α-Ketoglutarate	
1-^{13}C-Dehydroascorbate	
N-(2-^{13}C,2-^{15}N-2-Acetamido)-2-Aminoethanesulfonic Acid	

Carbon-13 Nitrogen-15

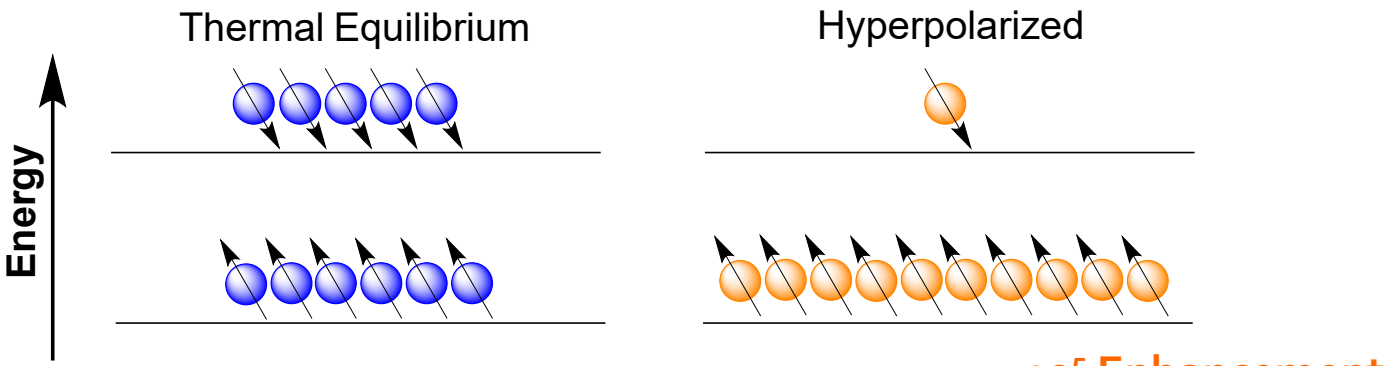
Noninvasive Interrogation of Cancer Metabolism with Hyperpolarized ^{13}C MRI

Andrew Cho[1], Justin Y.C. Lau[2,3], Benjamin J. Geraghty[2,3], Charles H. Cunningham[2,3], and Kayvan R. Keshari[1,4,5]

Hyperpolarization

- We have a number of techniques to transfer polarization to a nucleus of interest (such as ^{13}C) and temporarily enhance its signal.

- The polarization can go from ~0.0001% to 30%



= 10^5 Enhancement

- The polarized state is out of equilibrium so it only lasts for ~T1

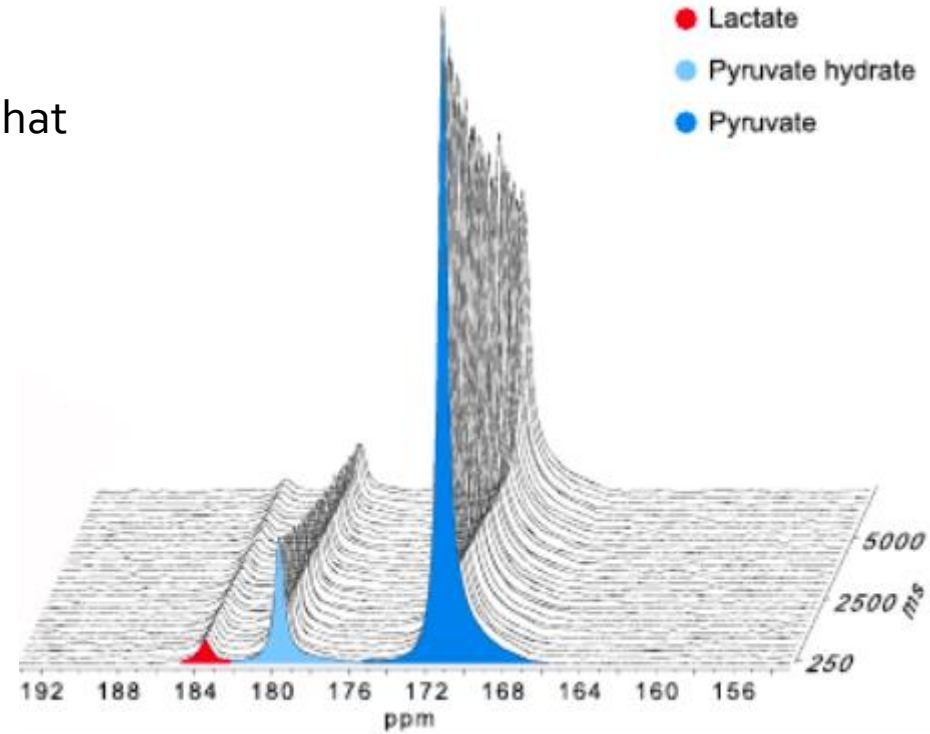
Can now image that molecule and do MRS

- MRS: magnetic resonance spectroscopy
- Use the gradients of an MRI to do spatial encoding AND get chemical shift information to distinguish different molecules

- Inject hyperpolarized pyruvate and see what it gets converted to

- In this case this was done with a small number of cells but can do it in human patients too.

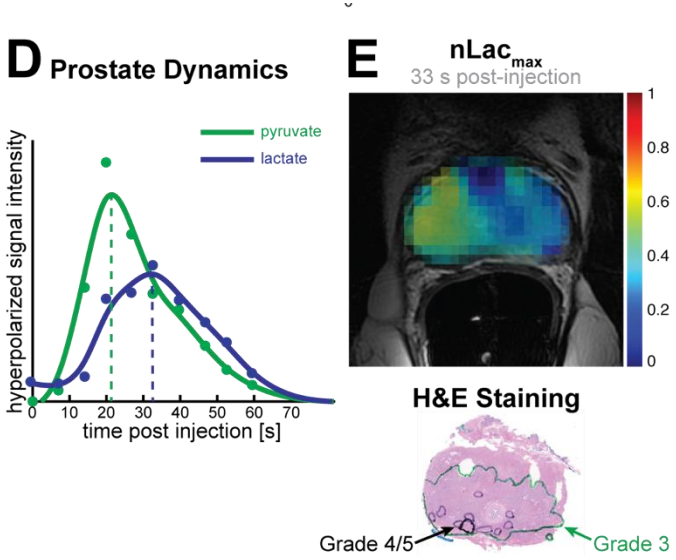
- Signal decays with T1
- Every time you pulse you kill signal and it never comes back

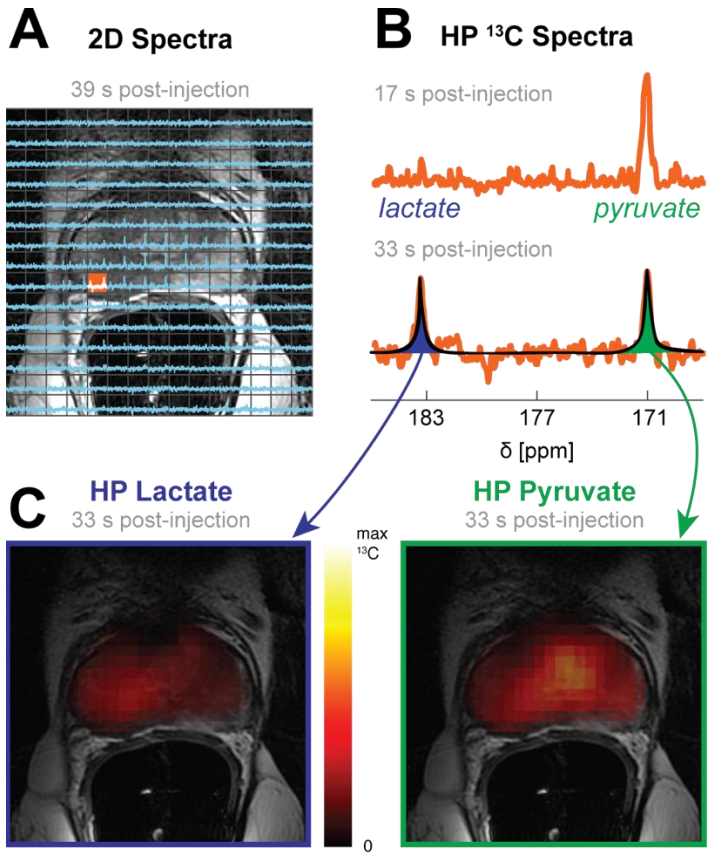


Lees et al 2020, Multi-sample measurement of hyperpolarized pyruvate-to-lactate flux in melanoma cells

Hyperpolarized MRS in humans

- Inject a cancer patient with HP pyruvate and look at it's conversion in the body
- Imaging pyruvate's conversion to lactate has the potential to annotate cancer grade





Granlund et al 2019, Hyperpolarized MRI of Human Prostate Cancer Reveals Increased Lactate with Tumor Grade Driven by Monocarboxylate Transporter 1

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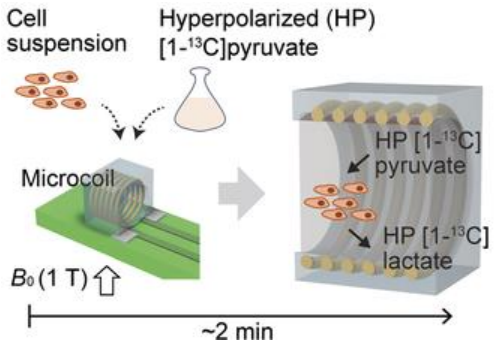
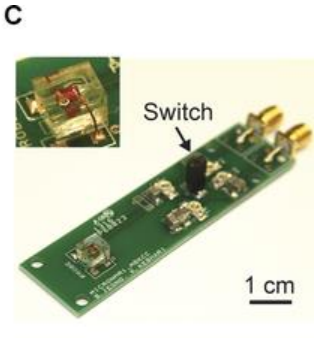
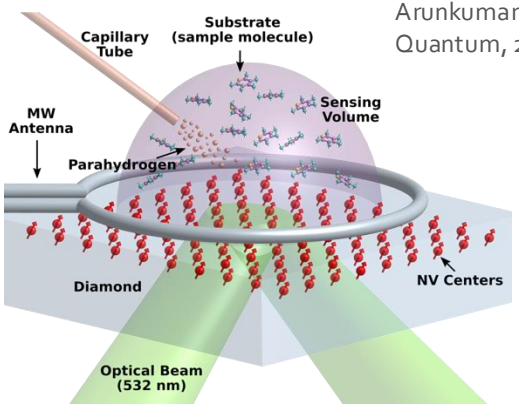
MR beyond standard coils

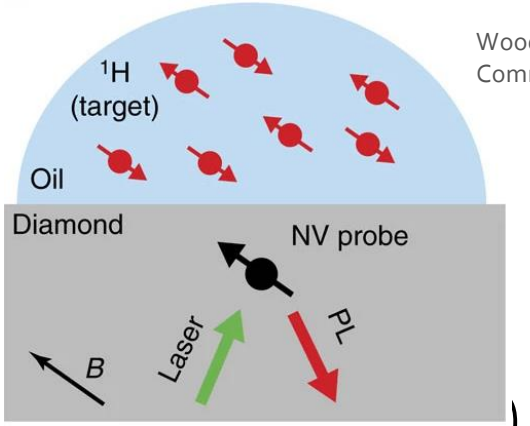


Jeong et al, Science Advances 2017





Arunkumar et al, PRX Quantum, 2021



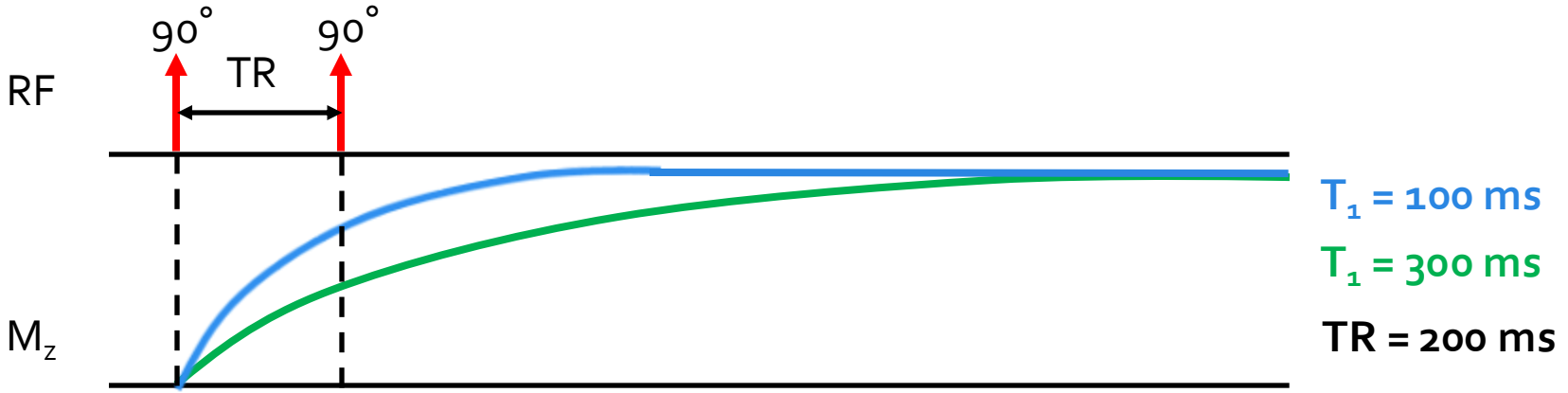
Wood et al, Nat Comm. 2017

Memorial Sloan Kettering Cancer Center

Possibilities are endless

Let’s keep learning!

Getting T1 contrast



Choose a short TR such that it is in-between the T1's of the two tissues

Blue tissue looks bright

Green tissue looks dark

- With T1 contrast, short T1 looks bright and long T1 looks dark
- The return of M_z over time is called a recovery.

Getting T2 contrast

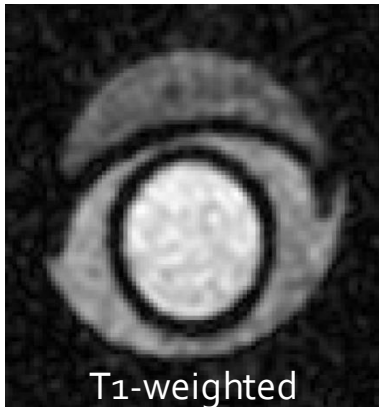
Suppose there is a blue tissue with **T2 = 100ms** and a green **T2 = 300ms**

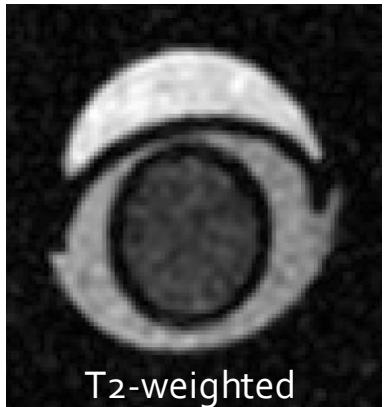
Let's choose **TE = 200ms**

By the time the 180° pulse came 200ms later, the blue tissue xy-magnetization decayed since it's T2 was only 100ms. Its echo is minimal and it is dark.

By the time the 180° pulse came 200ms later, the the green tissue still has some xy-magnetization since it's T2 is 300ms and the echo is significant and it is bright.

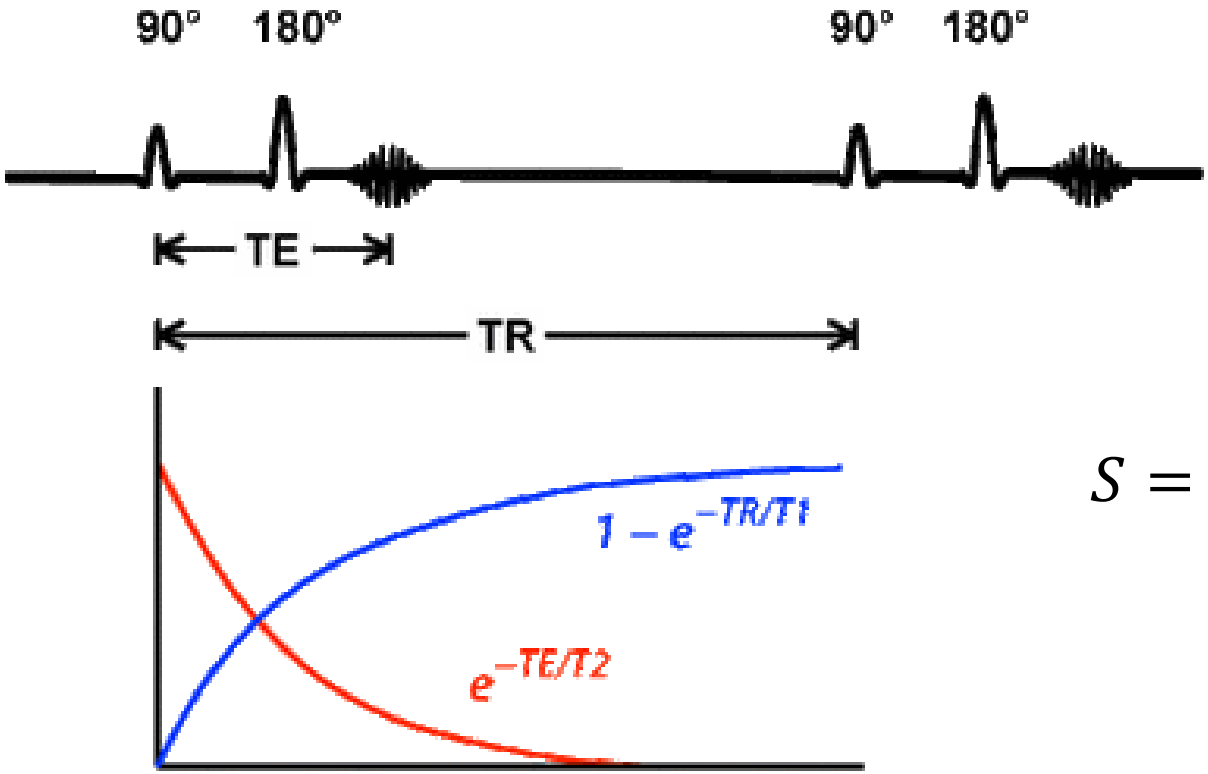
- With T2 contrast, short T2 looks dark and long T2 looks bright
- With T1 contrast, short T1 looks bright and long T1 looks dark





Combining TR and TE

Let's work it out on the white board



$$S = M_0(1 - e^{-\frac{TR}{T1}})e^{-\frac{TE}{T2}}$$

https://mriquestions.com/

Introducing k-space

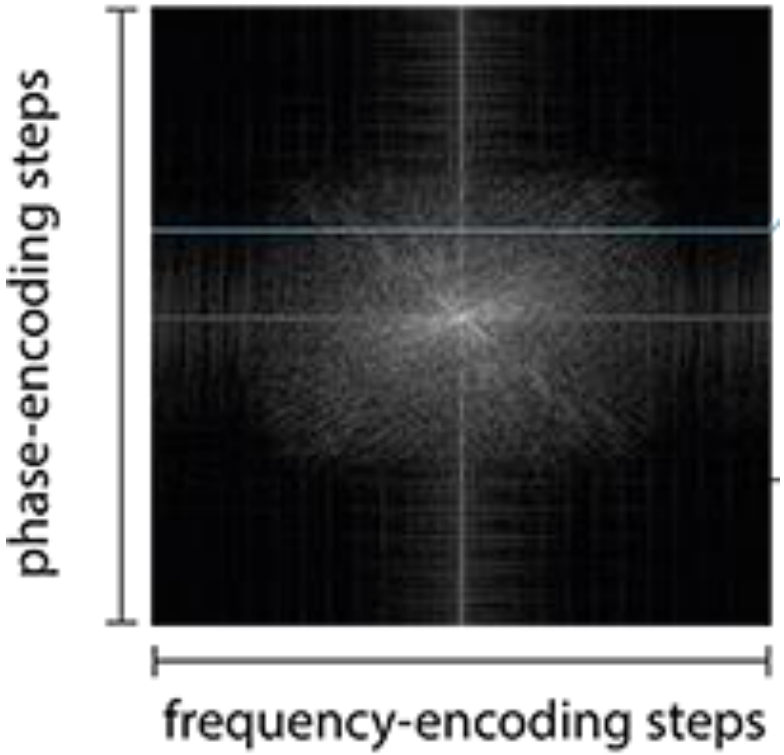
- A wave largely has 3 parameters (actually 4)

$$s(x,t) = A\sin(kx + \phi) + \mathrm{h}$$

$$s(x,t) = A\sin(kx + \phi)$$

k is a spatial frequency here: k ~ $\frac{1}{\lambda}$

- Small k (close to the center) means large wavelength
- Large k (close to edge) means small wavelength



https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/k-space/