MAGNETIC RESONANCE IMAGING: M.Sc. RAD II

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Recommended textbooks:

MRI: From Picture to Proton. DW McRobbie, EA Moore. MJ Graves, MR Prince. Cambridge University Press. My thanks to the authors for the inclusion of many modified diagrams from this book in my talk.

M. A. Brown and R. C. Semelka, *MRI Basic Principles and Applications*, Wiley-Liss, Inc. Second Edition 1999. ISBN 0-471-33062-0 (RO)

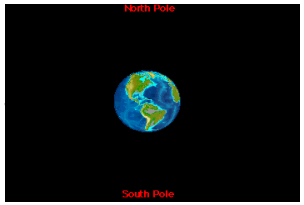
On-Line Material:

The Basics of MRI (Joseph Hornak)
http://www.cis.rit.edu/htbooks/mri/

Goes over the fundamentals of MRI + has some nice animations

MRI field strengths

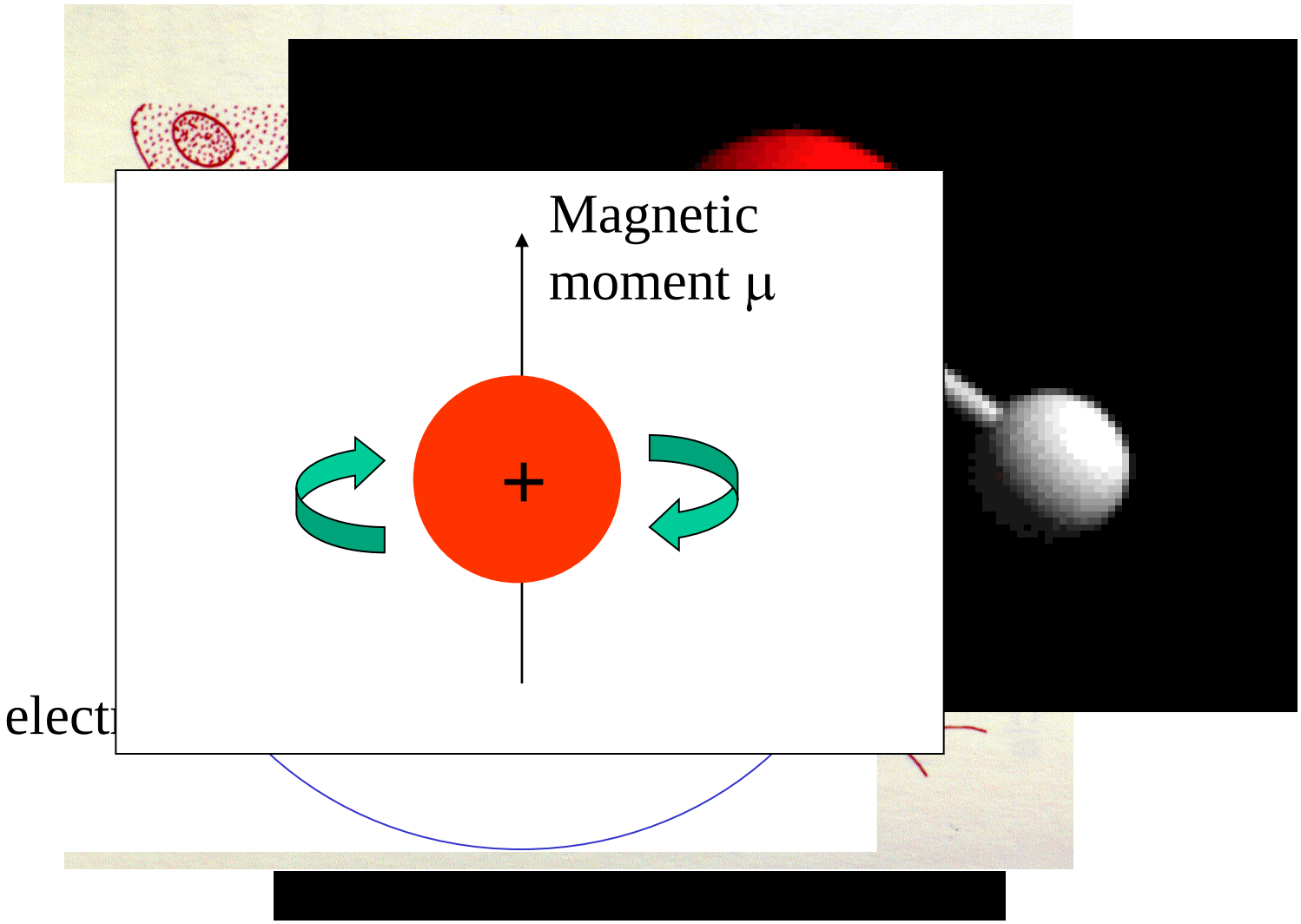
1 T= 1 Tesla = 10^4 Gauss



- 0.00005 T average Earth's field
- 1.5 T typical clinical MR scanner
- 3 T becoming standard MR in UK
- 7 T several in US; soon in Nottingham
- 9.4 T highest human MR scanner (Chicago and Minnesota, USA)

What does MRI look at?

10^{-13}m



MRI Systems

At ~£1 million, the most expensive equipment in the hospital…

Nuclear magnetic resonance (NMR) was first measured in 1945 by Purcell, Torrey and Pound. It involves the magnetic energy of NUCLEI in a magnetic field. Transitions between energy levels in this magnetic field are at a frequency given by:

Energy Difference: $\Delta E = h \upsilon$

where υ is a frequency in the radio-frequency (RF) band, and h is a constant known as Planck's constant.

NMR is usually applied to liquids and solutions, since these give well defined signals as a result of rapid molecular tumbling, which averages out inter-molecular magnetic interactions. MRI is usually used to image water in the human body. These same interactions are not averaged out in solids and so bone appears dark in MR images (in contrast to X-ray imaging).

Angular Momentum

The angular momentum (**P**) of a moving mass, m, velocity **v** and radius of rotation **r**, is given by:

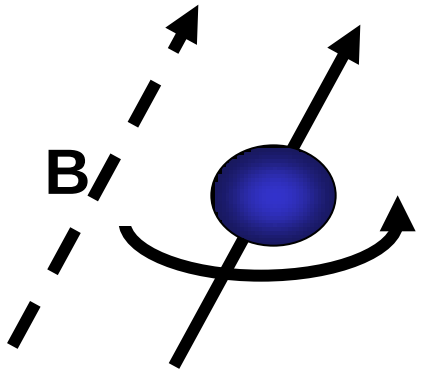
P = m**v** x **r** (bold indicates vectors and x is a cross product)

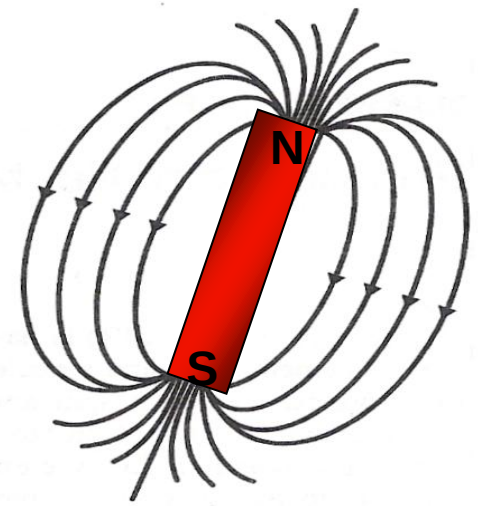
For microscopic particles Quantum Mechanics must be used to describe the particles state. The total angular momentum of a particle is then quantised and it's magnitude P can be specified using a quantum number I so that:

$P = \hbar [I(I+1)]^{0.5}$ where $\hbar = h/2\pi$ and I is either an integer or half-integer.

We are interested in nuclear spin. Nuclear spin effectively produces a magnetic dipole moment which interacts with the applied magnetic field.

A rotating hydrogen nucleus with a positive charge produces a magnetic field and acts like a bar magnet with a north and south pole.





MRI involves the measurement of a magnetic signal from the nucleus. The nucleus we measure is hydrogen which is present in tissue as water, fat and other bio-chemicals.

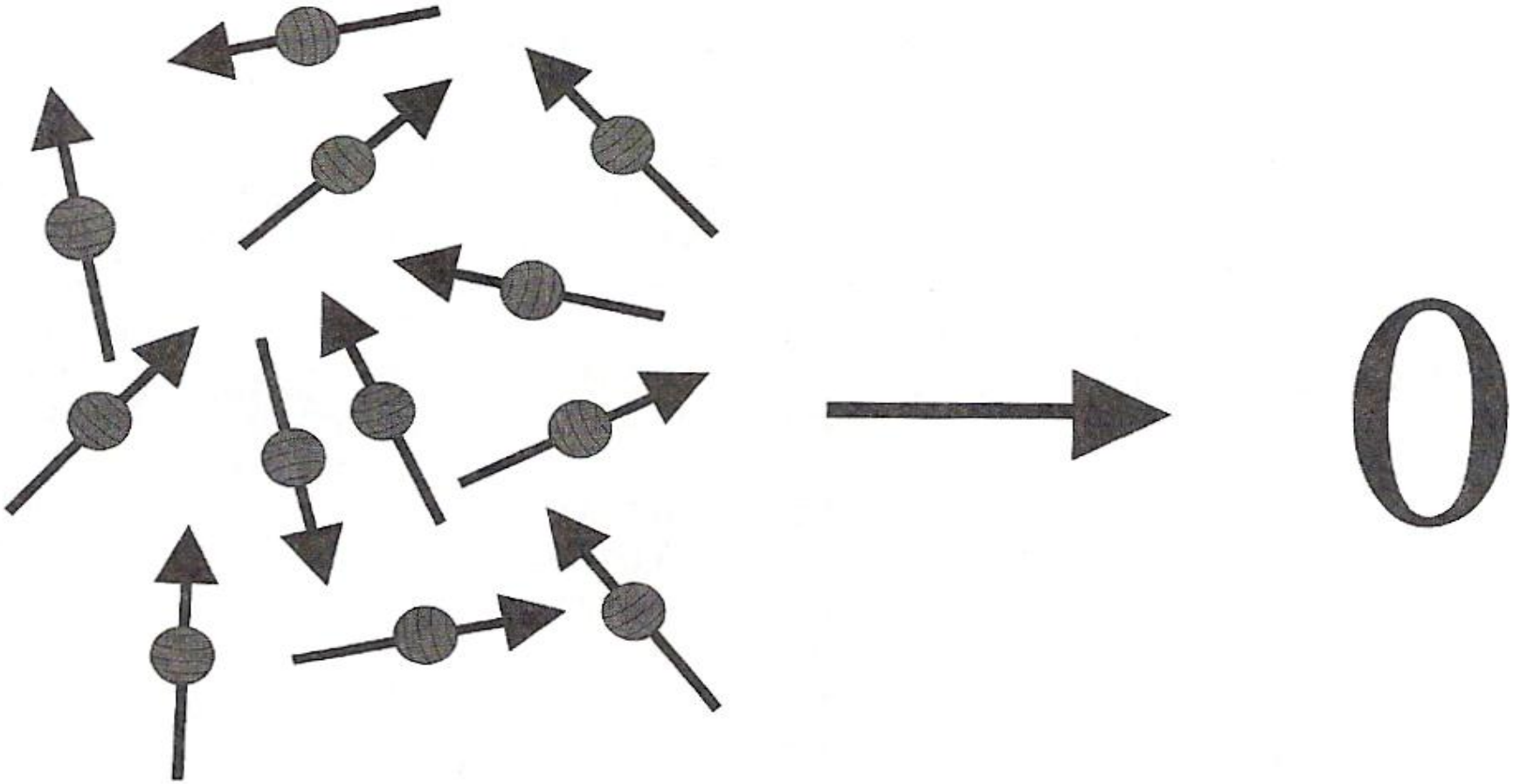
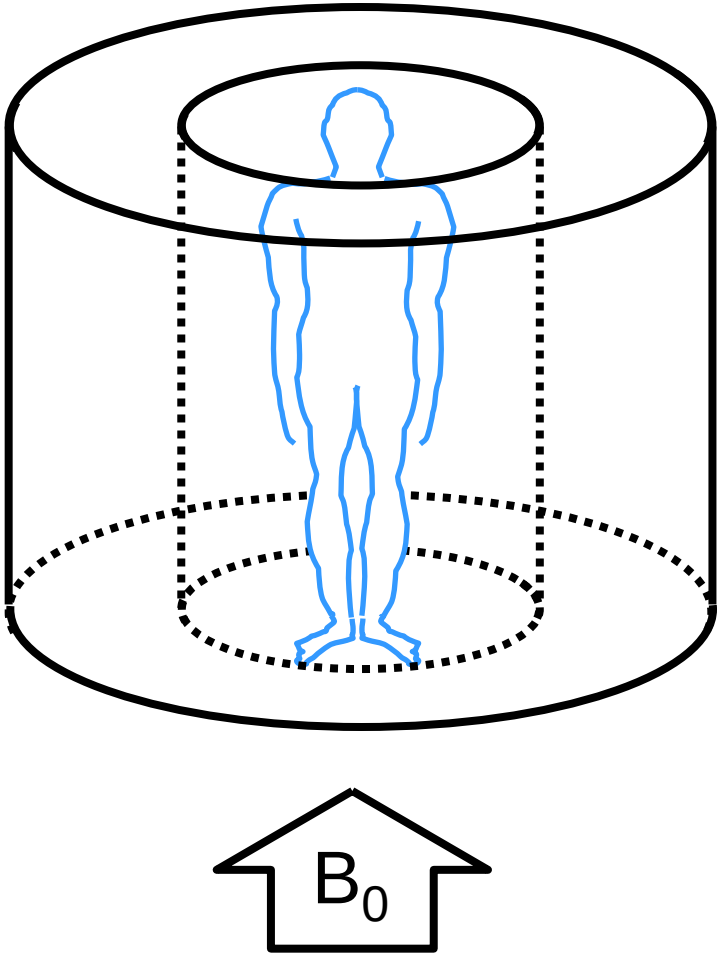
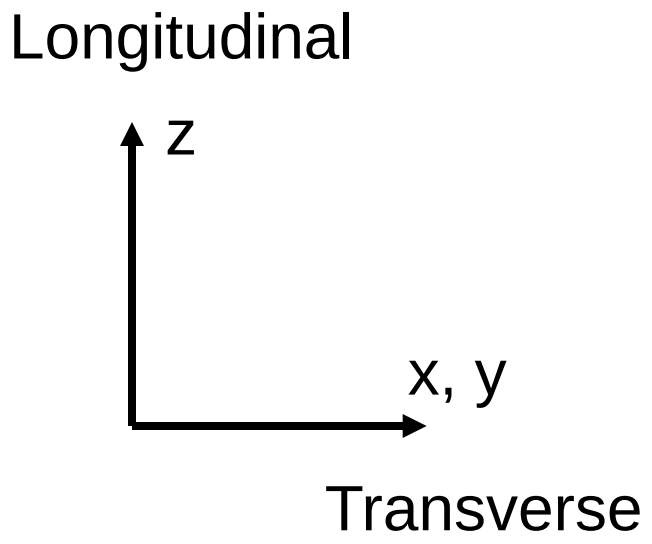


Figure 1-2. Microscopic and macroscopic pictures of a collection of protons in the absence of an external magnetic field. In the absence of a field, the protons have their spin vectors oriented randomly (microscopic picture). The vector sum of these spin vectors is zero (macroscopic picture).

Static Magnetic Field

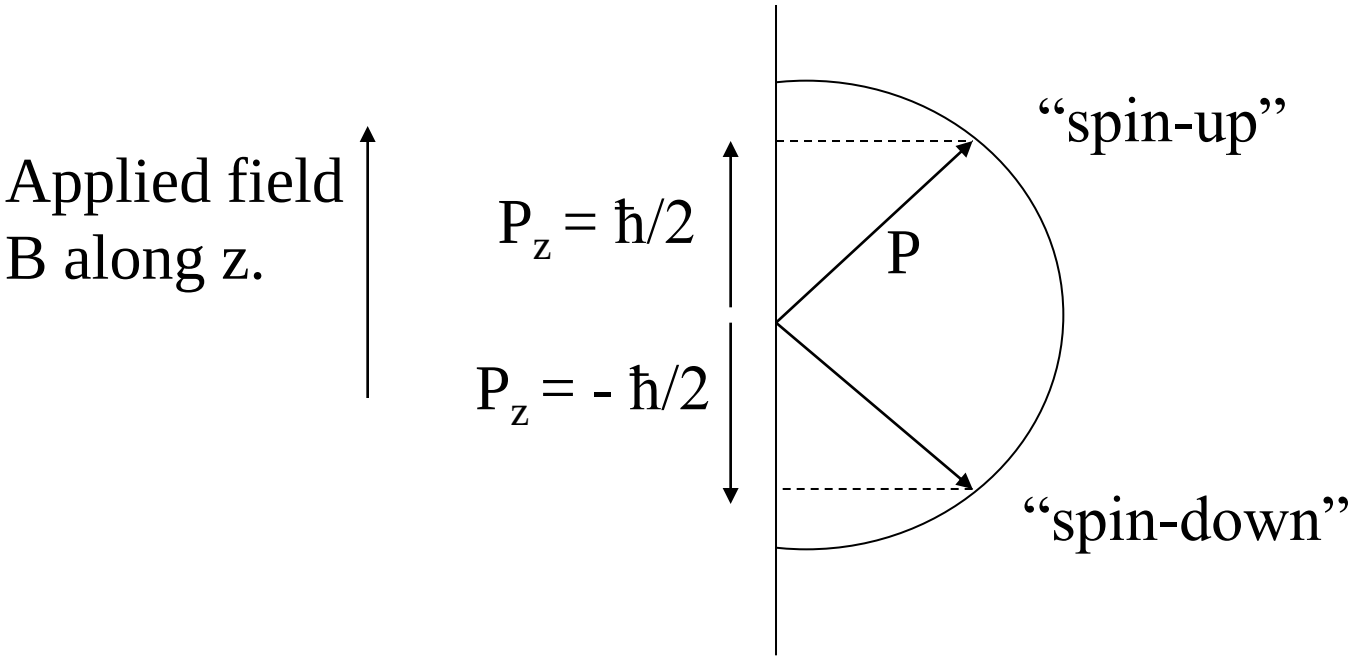




The direction of the applied magnetic field, Bo, is taken as z.

In an applied magnetic field, the nuclear "spins" take up quantised (well defined) energy states in this field with quantised values of the z-component of nuclear spin, defined by the quantum number m_z. For a "spin = ½" nucleus (hydrogen), then I = ½ and m_z = ½. Therefore:

$$P = \hbar\,[I(I+1)]^{0.5} = \hbar\sqrt{3}/2 \quad \text{and} \quad P_z = \hbar m_z = \tfrac{1}{2}\,\hbar$$



The existence of nuclear spin was suggested by Pauli in 1924 to explain why nuclei of different elements differ in spin angular momentum. In a nucleus made up of protons and neutrons the spin angular momentum combine together to give a total value of I which is either integer or half-integer. Features of this net value for I are:

(i) Nuclei with odd mass number (no.) have 1/2 integral spin

(ii) Nuclei with even mass number and even charge number have zero spin (eg. ^{12}C, ^{16}O)

(iii) Nuclei with even mass number and odd charge number have integral spin.

Nuclei with I=0 do not give an NMR signal. Nuclei with I>1/2 have short lifetimes of nuclear magnetic states and are not commonly studied.

Normally we are interested in nuclei with I=1/2 (ie hydrogen), which has two orientations in a magnetic field, B such that m_z = ½.

N.B. Charge no. = no. of electrons; Mass no. = no. of protons + neutrons

The angular momentum of the spinning nucleus produces an apparent magnetic dipole field (from a circulating current, even from neutrons!).

Nuclear magnetic moments, $\boldsymbol{\mu}$, are defined by the magnetogyric ratio, γ, such that:

$$\boldsymbol{\mu} = \gamma \mathbf{P} \qquad \text{(note } \boldsymbol{\mu} \text{ and } \mathbf{P} \text{ are vectors)}$$

γ is a property of each individual nucleus and is largest for ^{1}H.

Therefore, because **P** is quantized so is $\boldsymbol{\mu}$ and in a magnetic field, Bo, because P_z is quantised, so is μ_z .

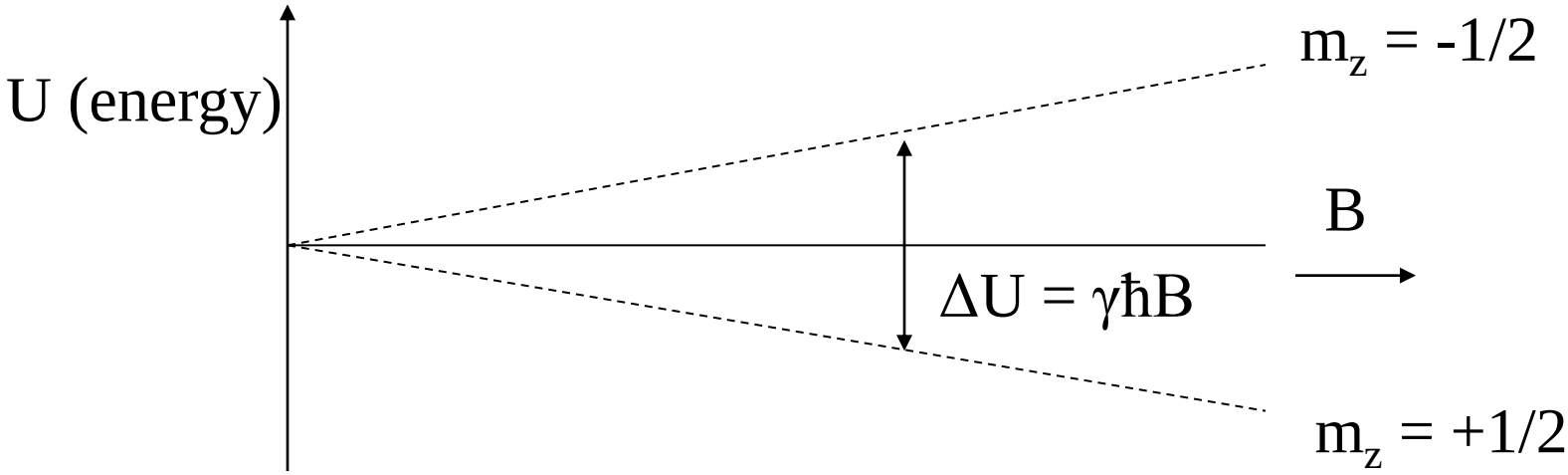
In a field of B (measured in Tesla (T), where 1 T = 10^4 Gauss) applied along the z axis, a magnetic moment $\boldsymbol{\mu}$ has an energy U given by:

$$U = -\boldsymbol{\mu}.\mathbf{B} = -\mu_z B \qquad \text{where } \mu_z \text{ is the z component of } \boldsymbol{\mu}$$

and is given by the quantum number m_z such that:

$$\mu_z = \gamma \hbar m_z \quad \text{so } U = -\gamma \hbar m_z B$$

For I = ½ (e.g. hydrogen):



Transitions occur when radiation is applied at the frequency of the energy level difference ie. $\Delta U = h f = |\gamma \hbar B \Delta m_z|$ where | | denotes magnitude. The selection rule governing the transitions is $\Delta m_z =$ 1 (ie. absorption or emission of energy).

Hence: $f = (\gamma/2\pi)B$ or $\boxed{\omega = \gamma B}$ where $\omega = 2\pi f$ (angular frequency in radians/second).

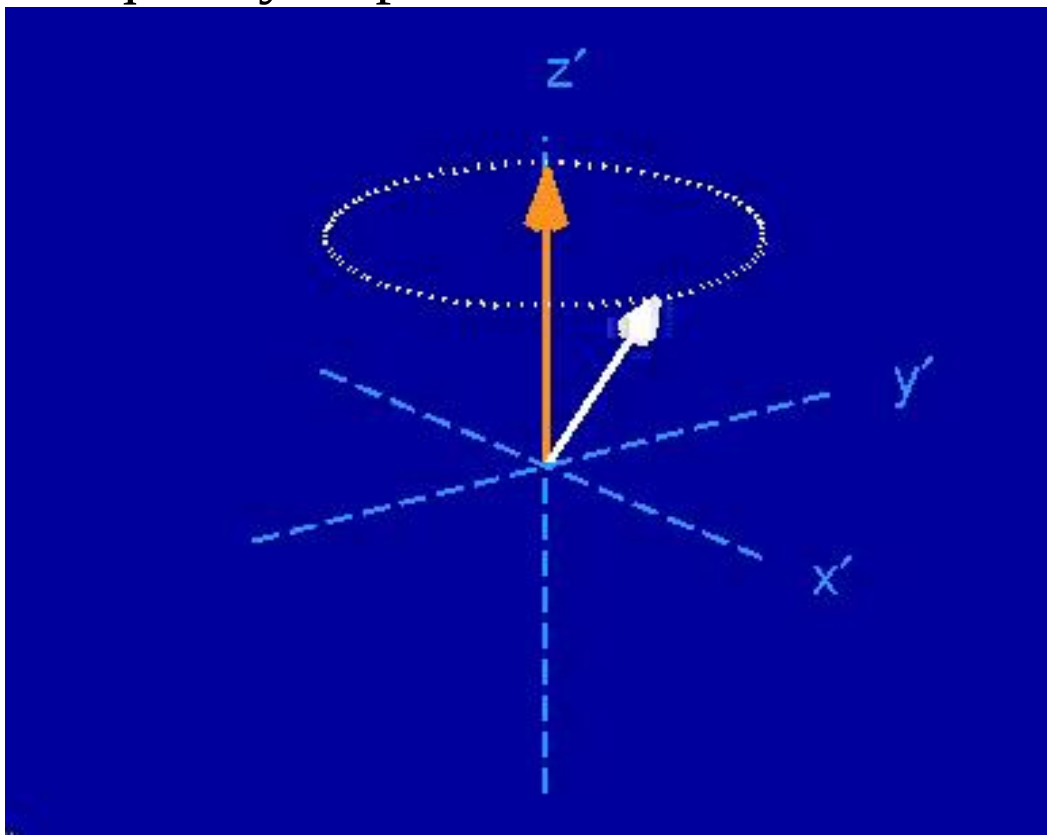
For fields in the range 1-10 T , f is in the range of 10's to 100's of MHz, ie. radiofrequencies (RF).

Larmor Precession

In a magnetic field, a magnetic moment experiences a "torque" (rotational force) given by:

$$d\boldsymbol{\mu}/dt = \gamma\, \boldsymbol{\mu} \times \mathbf{B} = \boldsymbol{\omega} \times \boldsymbol{\mu} \qquad \text{and} \quad \boxed{\omega = \gamma B}$$

μ is constant in length. The equation describes precession of **μ** about **B** as shown, where ω is the angular frequency of precession.

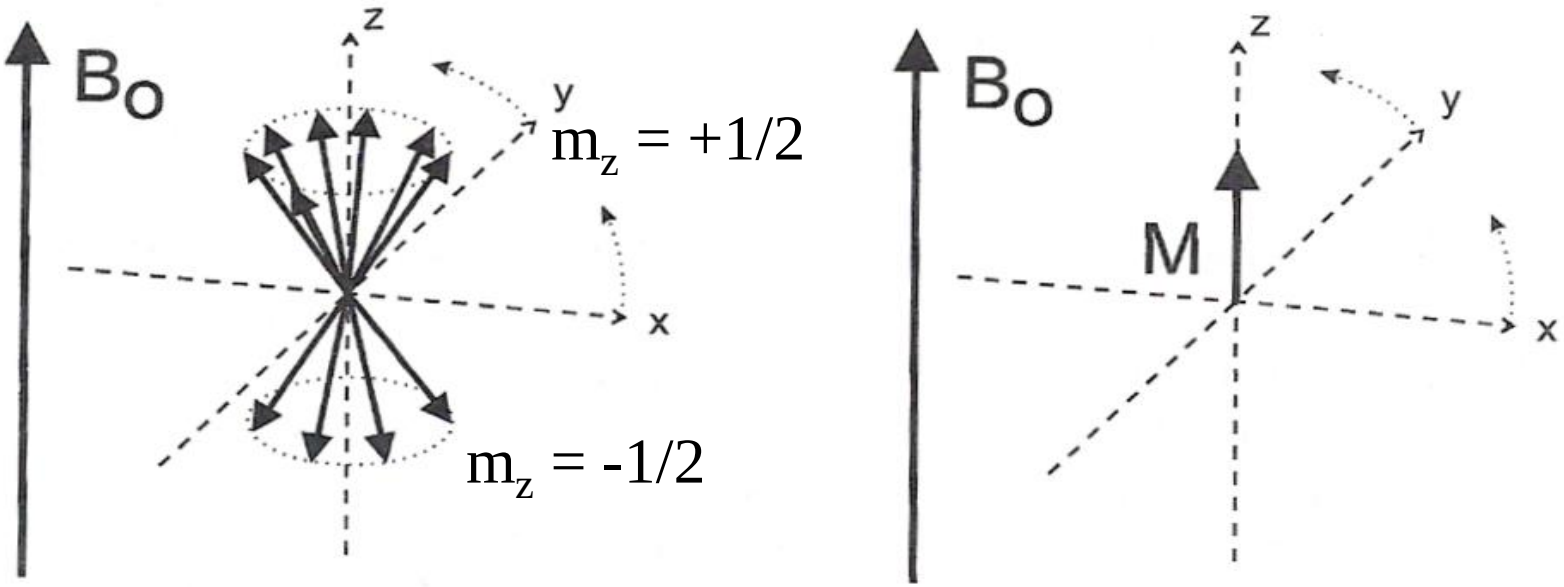


ω is known as the Larmor frequency. For Bo = 1.5 T, ω = 2π x 64 x 10^6 radians /sec.

NOTE: THIS IS THE SAME FREQUENCY AS OCCURS DURING TRANSITION BETWEEN ENERGY LEVELS

Macroscopic Magnetisation

In a magnetic field the nuclei take up "alignment" or "anti-alignment" with Bo to produce (when all the nuclear magnets are added together) a net magnetic field called the **macroscopic magnetisation, M (easier to deal with !!)**



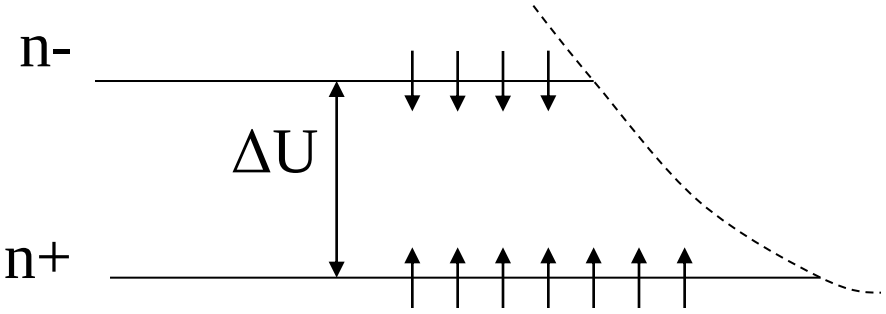
Note that the x–y component cancels because the magnetic field from individual nuclei cancel, and there are more nuclei aligned with Bo than in anti-alignment making **M** parallel with Bo.

The Boltzmann Distribution

The nuclei which align with Bo have a lower energy than those in anti-alignment. The difference in energy between the two states is proportional to Bo and defines the difference in populations of the two states (defined by the Boltzmann distribution, see below) Thermal energy tries to equalise the populations. **It is this difference that defines the size of the MR signal, therefore we need a powerful Bo producing magnet to get the most signal.**

$n-/n+ = \exp(-\Delta U/KT)$

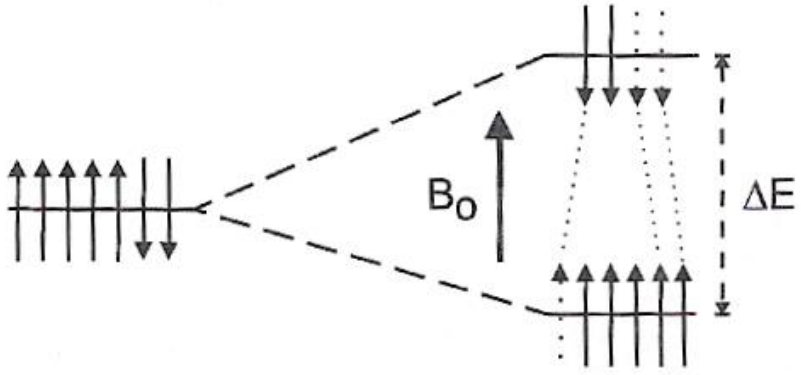
where n- and n+ are the populations of the $m_z = -1/2$ and $m_z = +1/2$ energy states; ΔU is the energy difference of the two states ($|\gamma\hbar B|$); T is temperature and K is the Boltzmann constant.



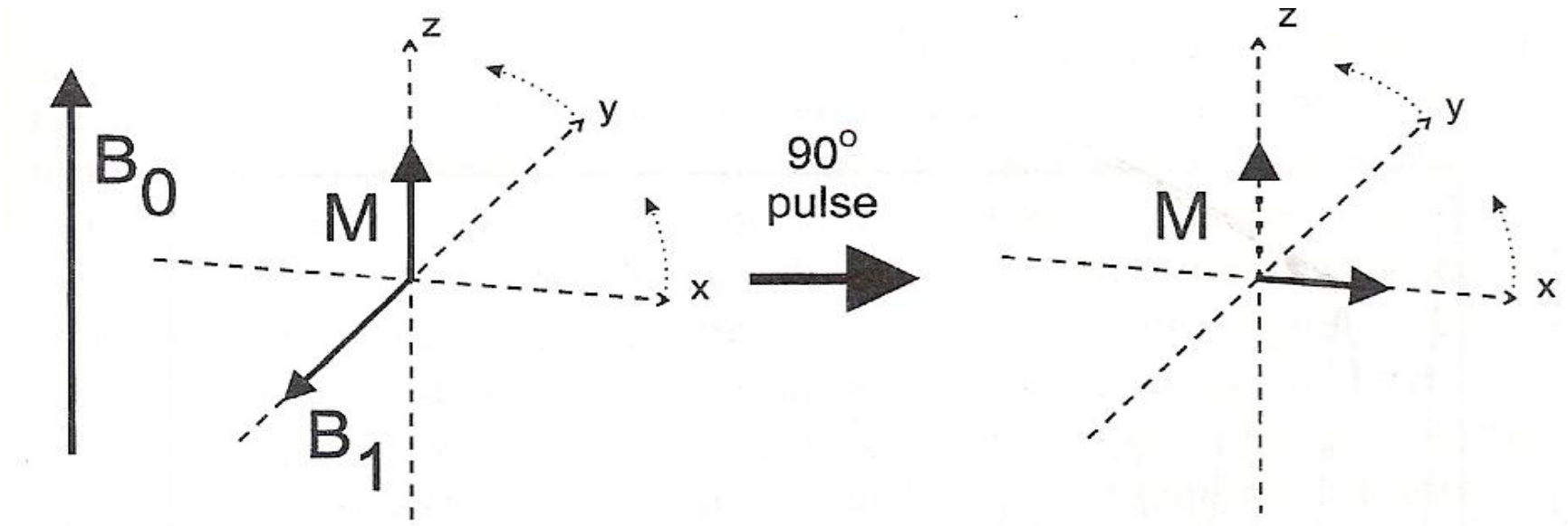
At 1.5 T the excess population is ~ 1 in 100000 because KT is much larger than ΔU.

“Exciting” an NMR Signal

In order to change state a nucleus must absorb or emit a packet of magnetic energy at the Larmor frequency (ω). When we apply an RF pulse at this frequency and energy, individual “spins” are stimulated to change energy level. Since there are more in the lower energy level, there is a net absorption of energy and the nuclear magnetic moments are “excited” to produce a NMR signal.



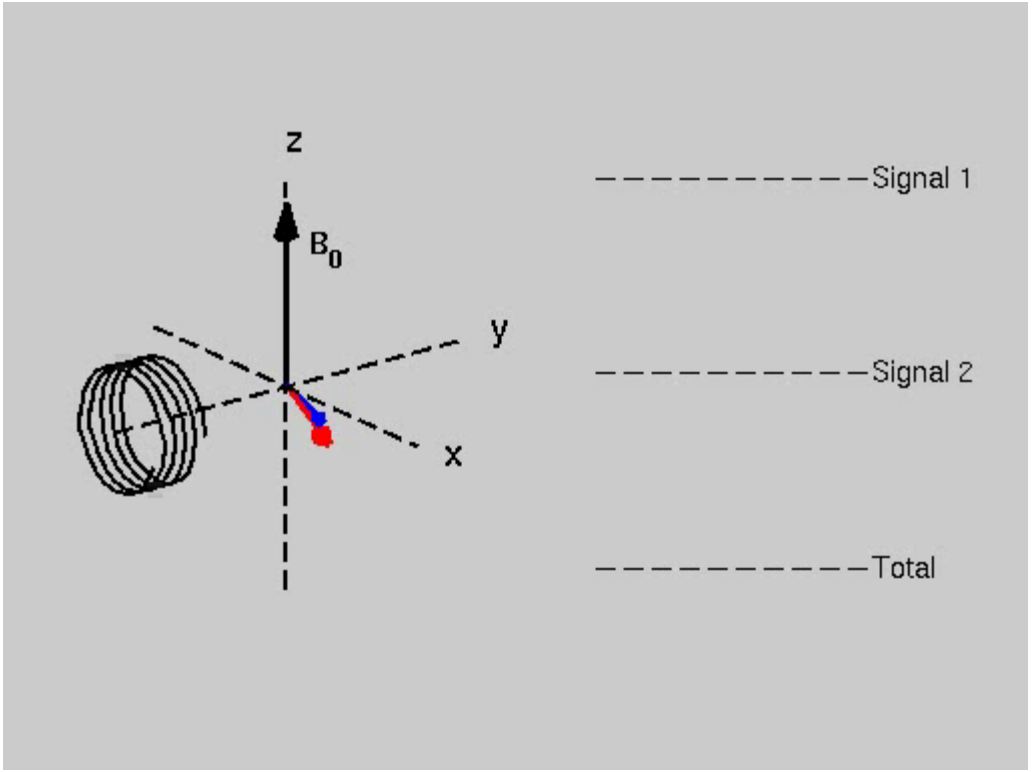
Magnetisation **M** is tipped by 90^0 by a radiofrequency pulse of magnetic energy (B_1) applied at the resonant (Larmor) frequency and of the correct duration. B_1 actually rotates at $\omega = \gamma B_o$ around the z-axis.



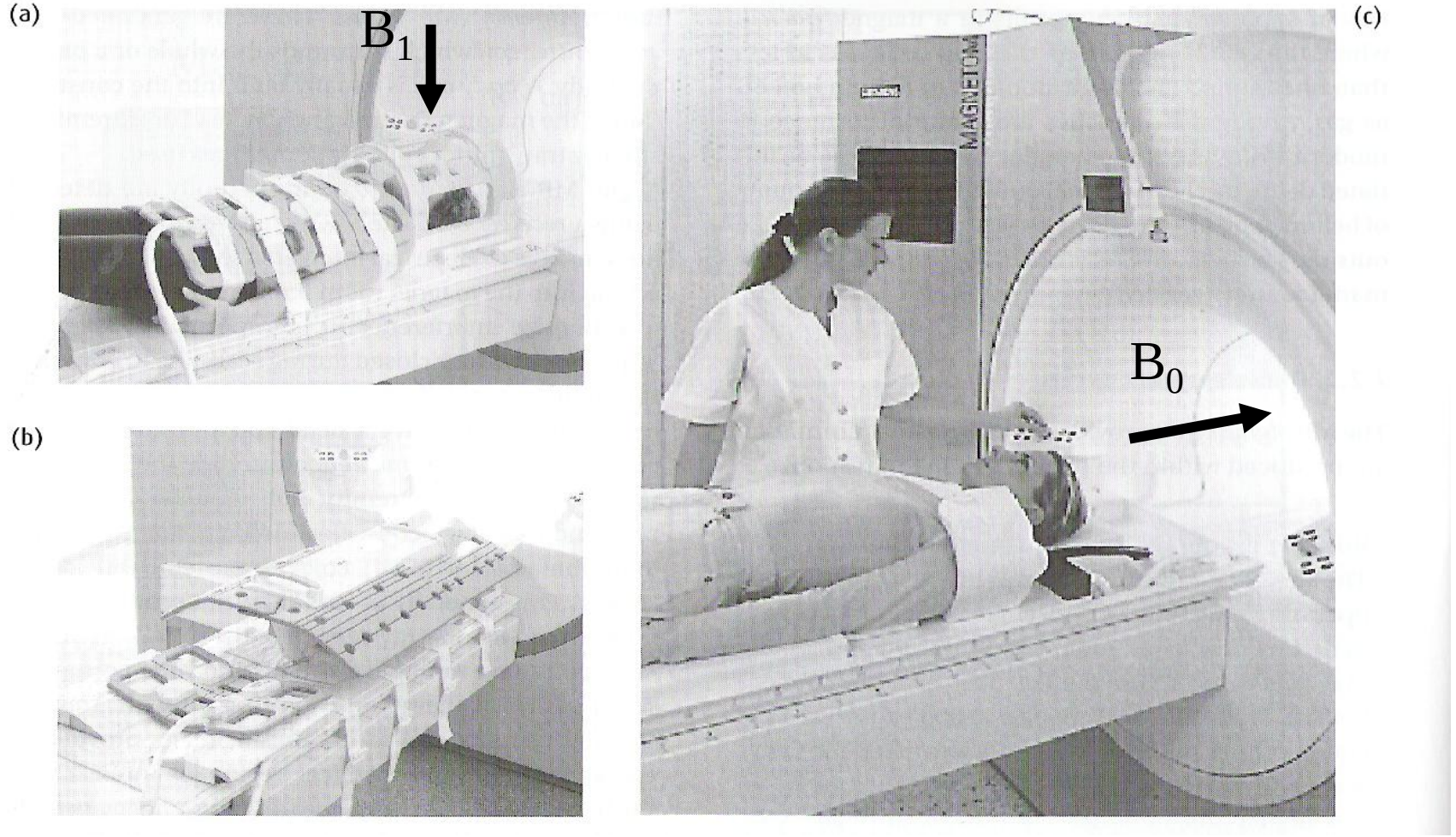
This is called a 90^0 radiofrequency (RF) pulse.

Once M is in the x-y plane, it rotates about the direction of Bo with a frequency given by $\omega = \gamma$ Bo. This produces a rotating magnetic field that can be picked up using a receiver coil. A similar "transmitter coil" was used to produce the 90^0 RF pulse.

Receiver coil →



MRI Scanner and RF coils being strapped around the patient

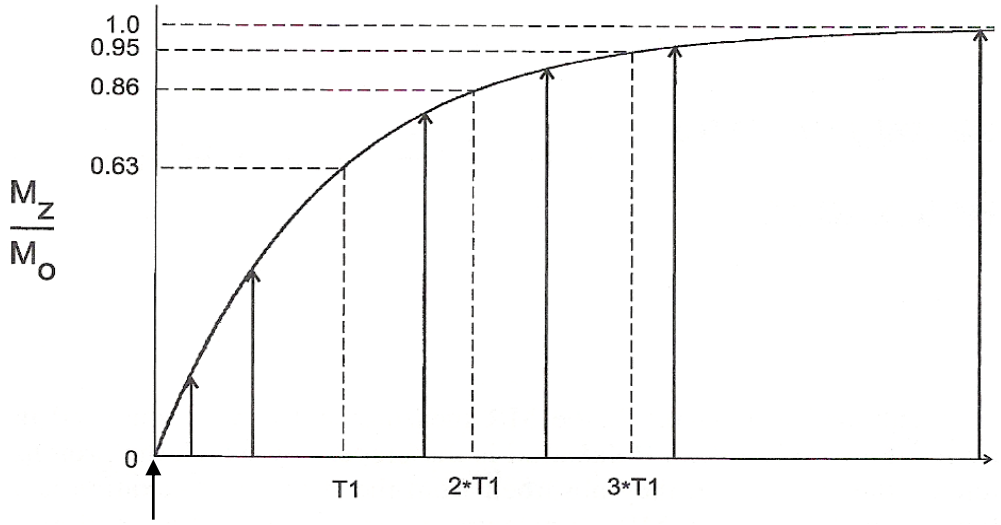


Relaxation to Equilibrium

Following the 90^0 RF pulse, nuclei exchange energy with each other by exchanging packaged photons of energy oscillating at the Larmor frequency. These are generated by molecular motion (driven by the heat energy of temperature; molecules being slightly magnetic) and cause the “spins” to dephase in the x-y plane (signal decays) and also cause the macroscopic magnetisation, **M**, to reform in alignment with Bo. These two processes occur at different rates and are referred to as **relaxation** back to equilibrium.

SPIN-LATTICE RELAXATION (T1)

After the RF pulse, the magnetisation gradually realigns with Bo in a time characterised as the spin-lattice relaxation time, T1 (typically a second or so, but varies depending on the type of tissue that the water is within). The hydrogen nuclei (spins) lose their magnetic energy to the surroundings (called the lattice). The amount of magnetisation aligned with Bo (applied along the z-axis) at any time point is known as M_z.



This signal recovery is an exponential curve.

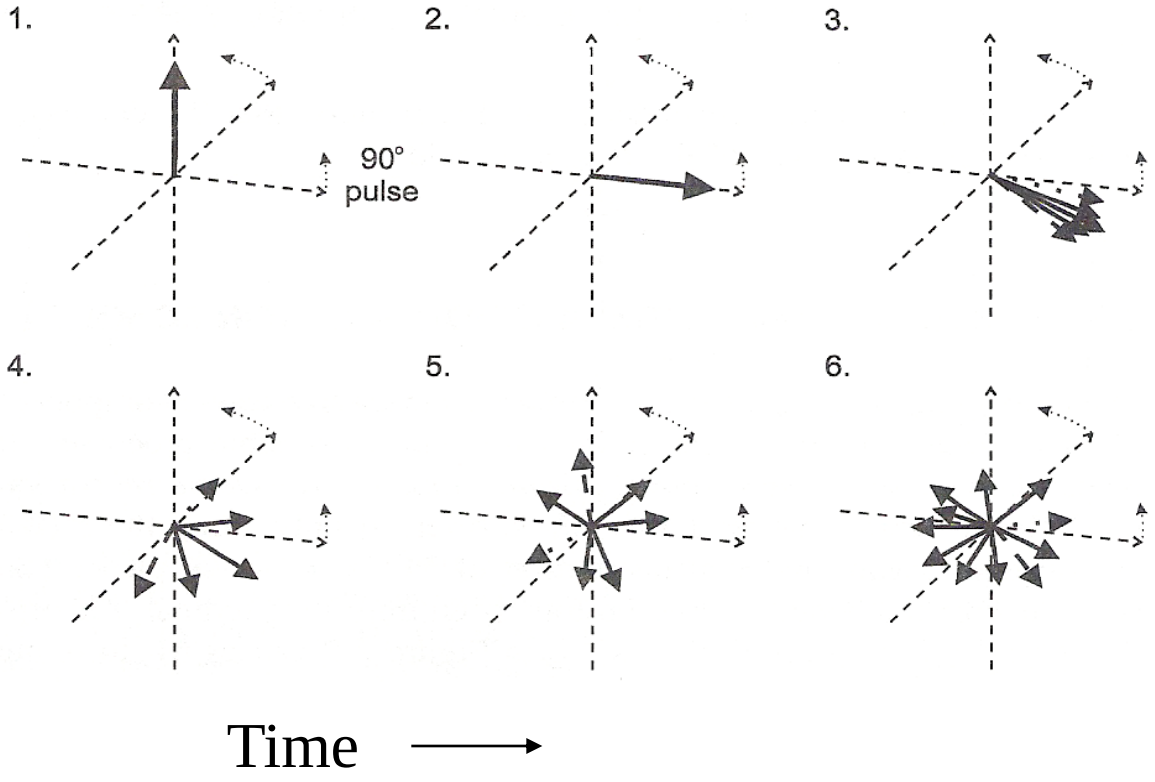
T1 relaxation only occurs after the spins (as represented by **M**) have been perturbed from alignment with Bo. It requires molecular motion that generates oscillating fields at ω that cause the population of the energy levels to return to normal as defined by the temperature of the sample. The equation for recovery of **M** along z, M_z, following a 90^0 RF pulse is:

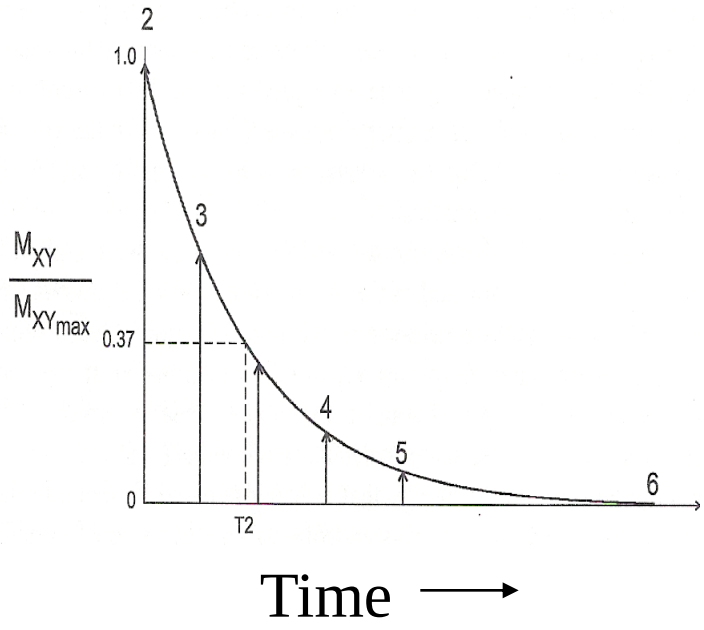
$$M_z(t) = \mathbf{M} [1- \exp (-t/T1)]$$ where t is time after RF pulse

i.e. ~2/3 of M has recovered in a time T1. T1 varies in different tissue and is in the range of 100's of milliseconds to a few seconds.

SPIN-SPIN RELAXATION (T2)

The MR signal that is in the x-y plane (M_{xy}) also evolves by decaying away at an exponential rate defined by the spin-spin relaxation time, T2. T2 also varies between water in various tissues and is typically 50-100 milliseconds. The amount of magnetisation in the x-y plane is M_{xy} and it decays exponentially with time.





The rate at which M_{xy} is lost is given by the following equation:

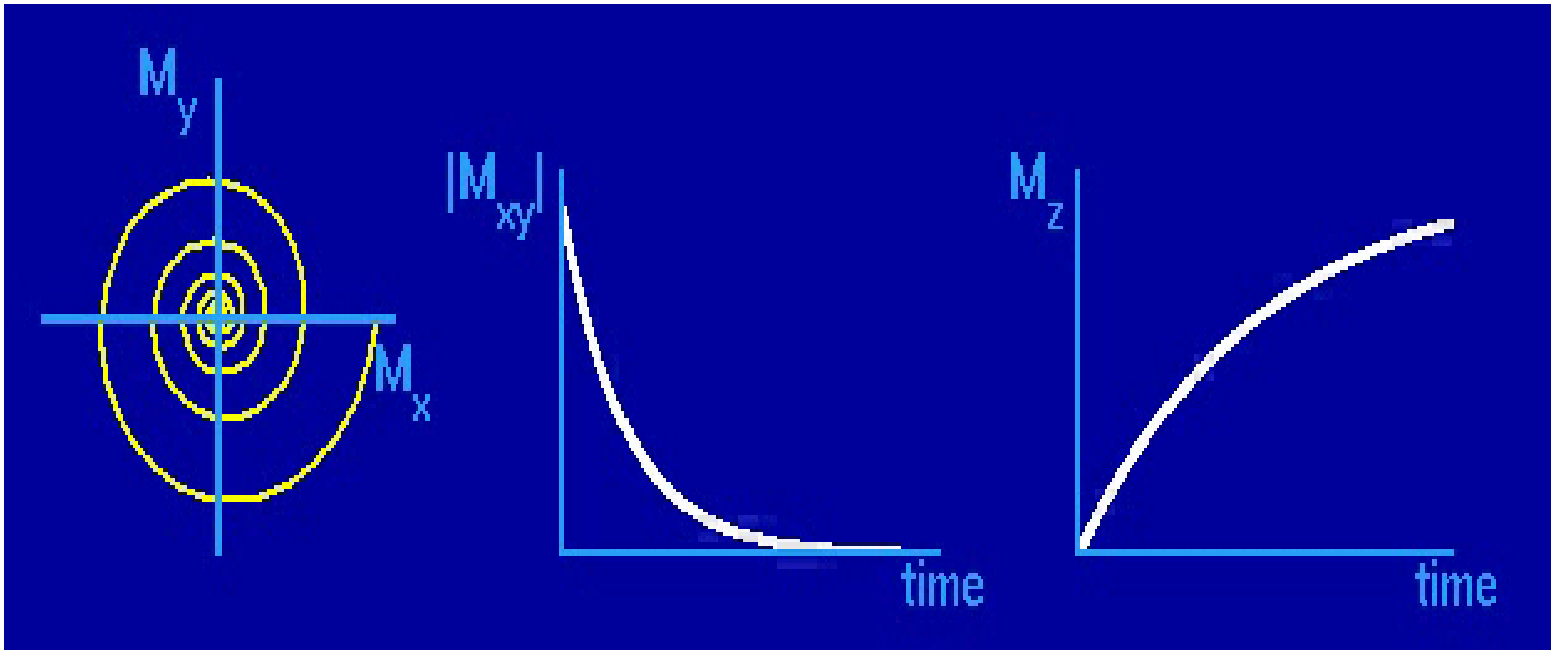
$M_{xy} = \mathbf{M} \exp(-t/T2)$ where t is time after the RF pulse.

T2 relaxation is caused by two effects:

(A) Relaxation caused by an exchange of energy between nearby spins through exchanging energy photons (packets) at the Larmor frequency. They act like coupled oscillators and following the energy exchange between many neighbouring spins, they become dephased with each other and the M_{xy} signal gradually decays.

(B) The presence of nearby magnetic molecules cause magnetic field perturbations that add or subtract from Bo. Since the frequency of M_{xy} rotation following the 90^0 RF pulse is at the Larmor frequency (as defined by Bo), the range of Bo fields experienced by different spins means that individual components of M_{xy} are rotating at different speeds causing a reduction in M_{xy} as the spins dephase with each other.

Relaxation to Equilibrium



T2 (looking along z-axis).

T2

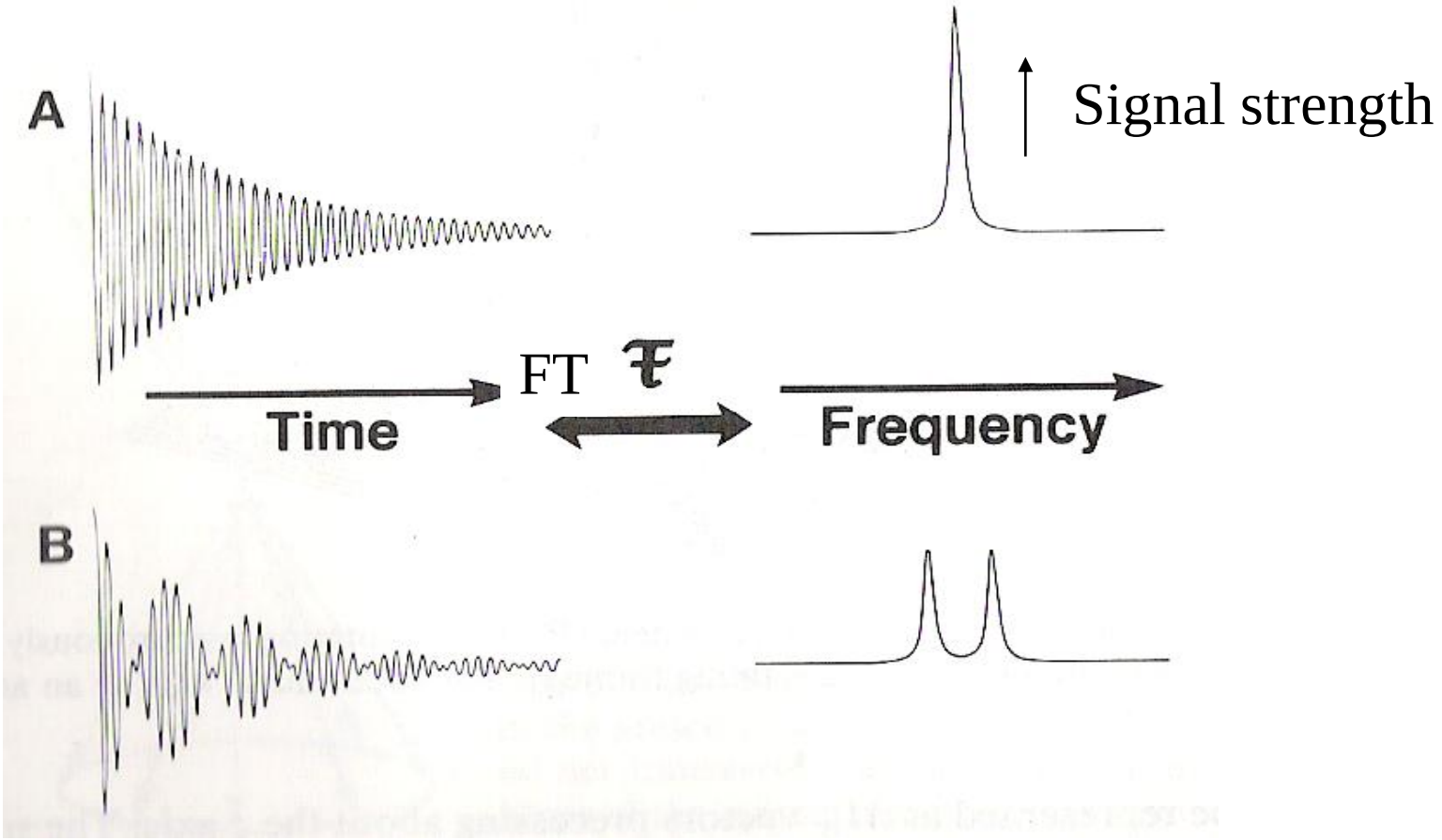
T1

In liquids, molecules are rapidly tumbling and the magnetic effect of neighbouring molecules may be cancelled out on the time scale of the NMR measurement. This leads to long T2 values and enables MRI to be performed.

In solids (e.g. hydrogen in bone) averaging by molecular tumbling is limited leading to very short T2 values. MRI cannot usually see the signal from bone because it is too short.

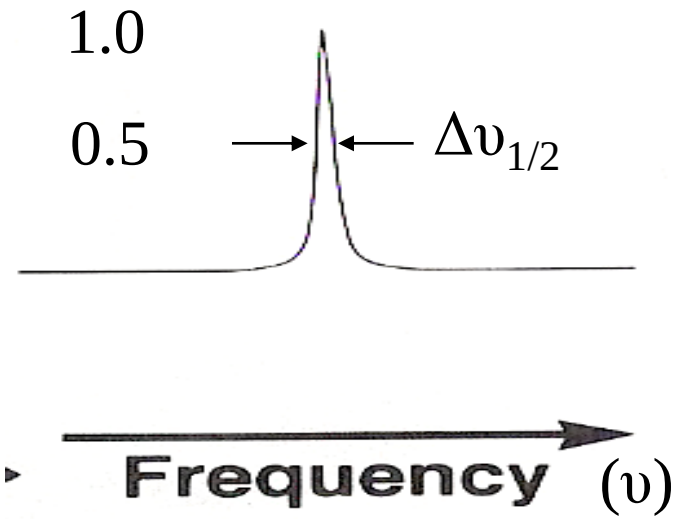
Because T2 has two mechanisms c.f. T1 relaxation, then $T2 << T1$. However, in pure liquids they can be of similar magnitude.

The signal picked up by RF receiver coil (the decay of M_{xy}) is sent to a computer where it is digitised (into numbers) and analysed to determine the strength and distribution of it's frequency components. This analysis procedure is called Fourier Transformation (FT) and produces a "spectrum" of the frequency distribution.



The width of the spectral line generated from a single type of nucleus is inversely related to T2 by the equation:

$T2 = 1/\pi\Delta\upsilon_{1/2}$ where $\Delta\upsilon_{1/2}$ is the half-height line-width of the resonance. If T2 is longer, the "resonance line-width" is narrower.



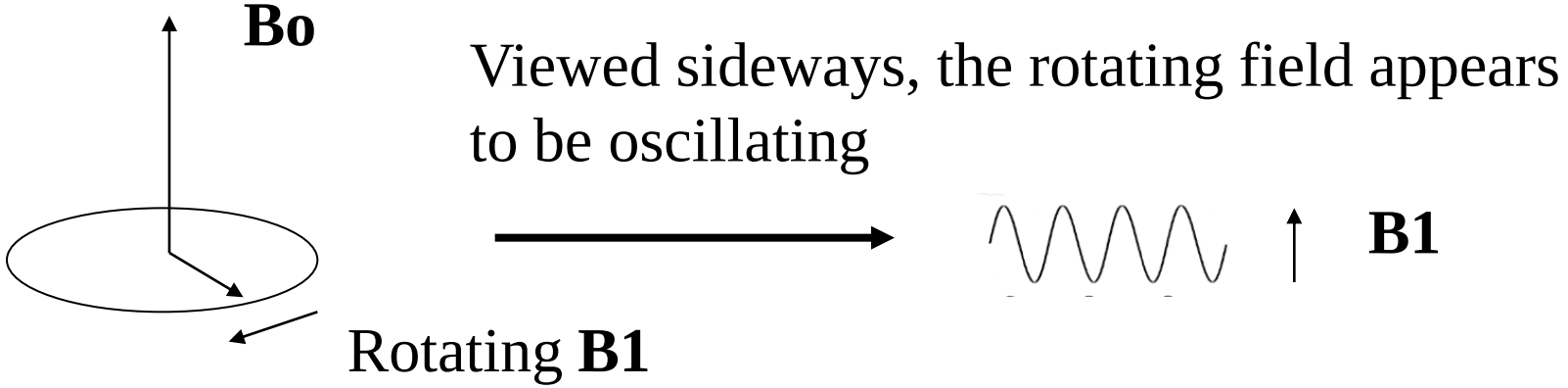
Because T2 is an exponential decay, the resonance line is shaped like a "Lorentzian" curve (FT of exponential).

Bloch Equations

The Bloch equations describe the motion of **M** in the presence of any magnetic fields (including Bo and the RF field, B1). They may be summarised as:

$$d\mathbf{M}/dt = \gamma\, \mathbf{M} \times \mathbf{B}$$

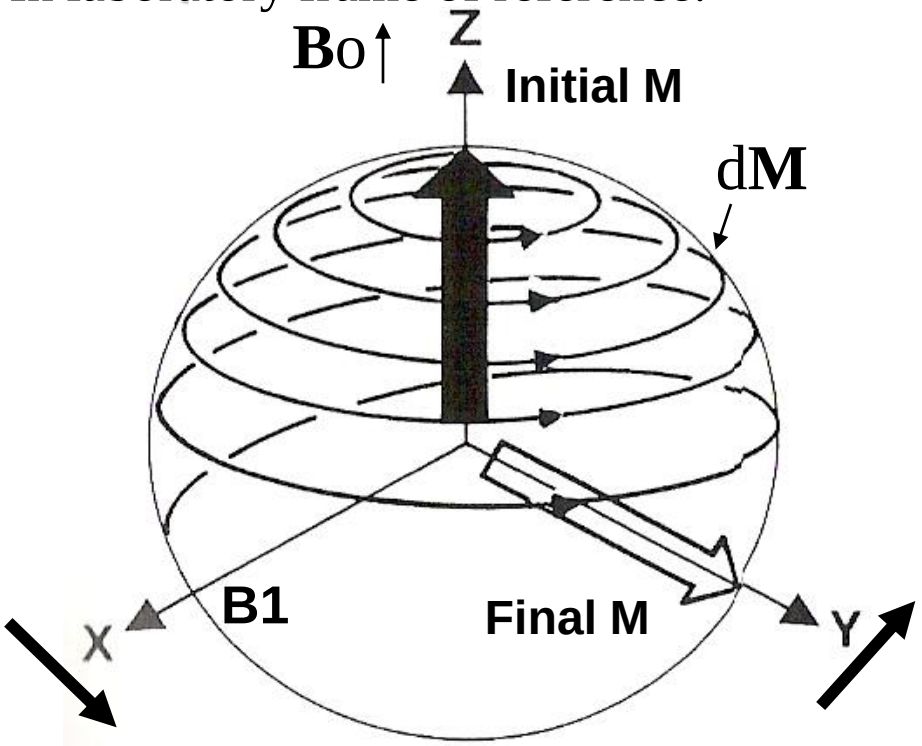
B may be fixed **(Bo)** or oscillating (**B1**; which is the same as rotating in the x-y plane around the z-axis). Hence, **M** will move perpendicular to both it's present position (staying the same size) and the direction of any applied **B** field.



The Rotating Reference Frame

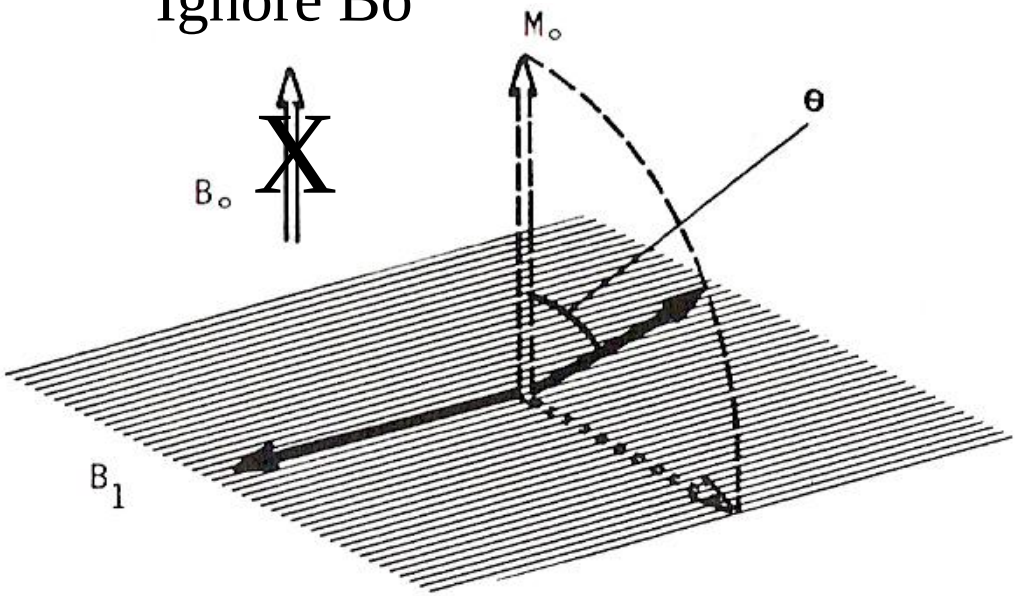
The motion of **M** during an RF pulse is complicated (a spiral). We simplify it by imagining that we are in a frame of reference that is rotating about Bo at the same rate as **M**. Motion during and following a 90^0 RF pulse is simplified because in this frame of reference we can ignore the effect of Bo.

In laboratory frame of reference:

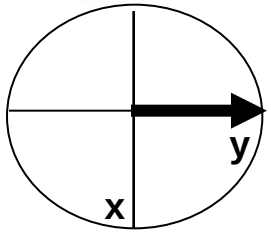


In rotating reference frame:

Ignore Bo

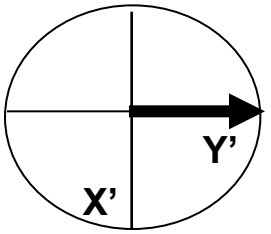


After pulse looking down on the x-y plane:



M rotates

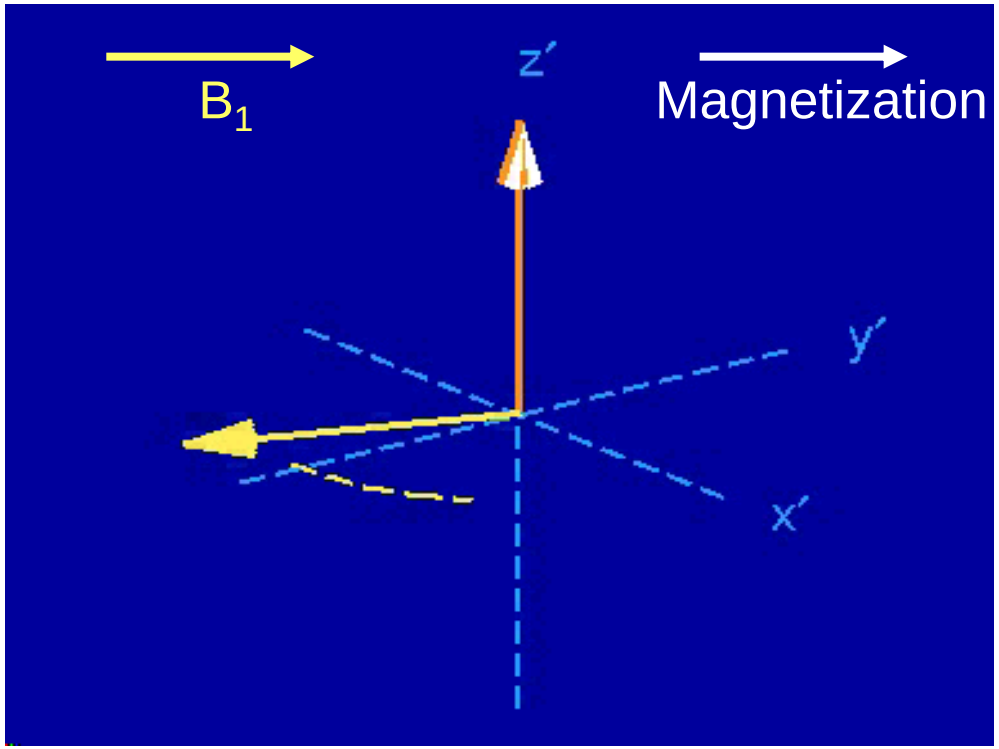
After pulse in the rotating frame:



M static

Signal Excitation

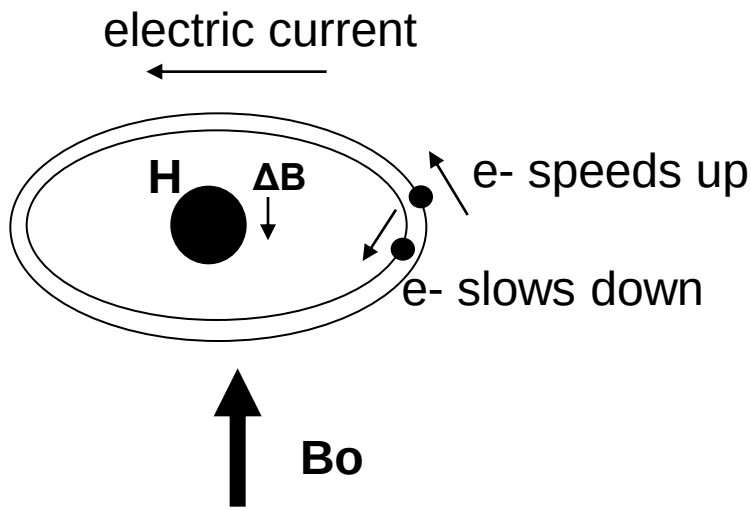
- Transverse RF field (B_1) rotates at γB_0 about z-axis



Chemical Shift

When a substance is placed in a magnetic field it becomes magnetised by two effects: (a) bulk macroscopic effect, which is usually diamagnetic and reduces the field within the sample; (b) a local microscopic effect called the chemical shift effect.

These cause shifts in the resonance frequency of the hydrogen nucleus by alteration in the rotation of electrons in their orbital shells in response to the application of a magnetic field. An electric current is generated that opposes the main field Bo causing the nucleus to experience a reduced magnetic field. The more electrons that surround the nucleus, the greater the effect. For example, a hydrogen connected to an oxygen atom has fewer surrounding electrons (Oxygen attracts them strongly) compared to the hydrogen in a $–CH_2$ or $–CH_3$ group.



The screening effect of the electrons is expressed as:

$$B = Bo\ (1- \sigma\ )$$

where σ is the shielding constant. The effect on individual nuclei depends on the distribution of electrons surrounding the nucleus, which in turn depends on surrounding atoms and atomic bonds. The difference in σ for nuclei in various positions within molecules causes shifts in resonance frequencies known as chemical shifts, which are measured in parts per million (ppm) to make them independent of field strength. It allows different molecules to be distinguished.
The frequency of the resonance line (from above) is given by expressing it relative to the Larmor frequency ($\upsilon_o$in Hz):

$\upsilon_j = \upsilon_o\ (1- \sigma_j)$ and the chemical shift is: $(\upsilon_j - \upsilon_o)/\ \upsilon_o = \Delta\upsilon_j/\upsilon_o = -\Delta\sigma_j$

Note: a positive chemical shift produces a lower frequency of resonance as denoted by the minus sign above.

Therefore, a frequency offset of -300Hz in a magnet with a Larmor frequency of 100MHz ($\omega = \gamma$ Bo) corresponds to a chemical shift ($-\Delta\sigma$) of +3ppm. The intensity (area) of the resonance is proportional to concentration of each substance.

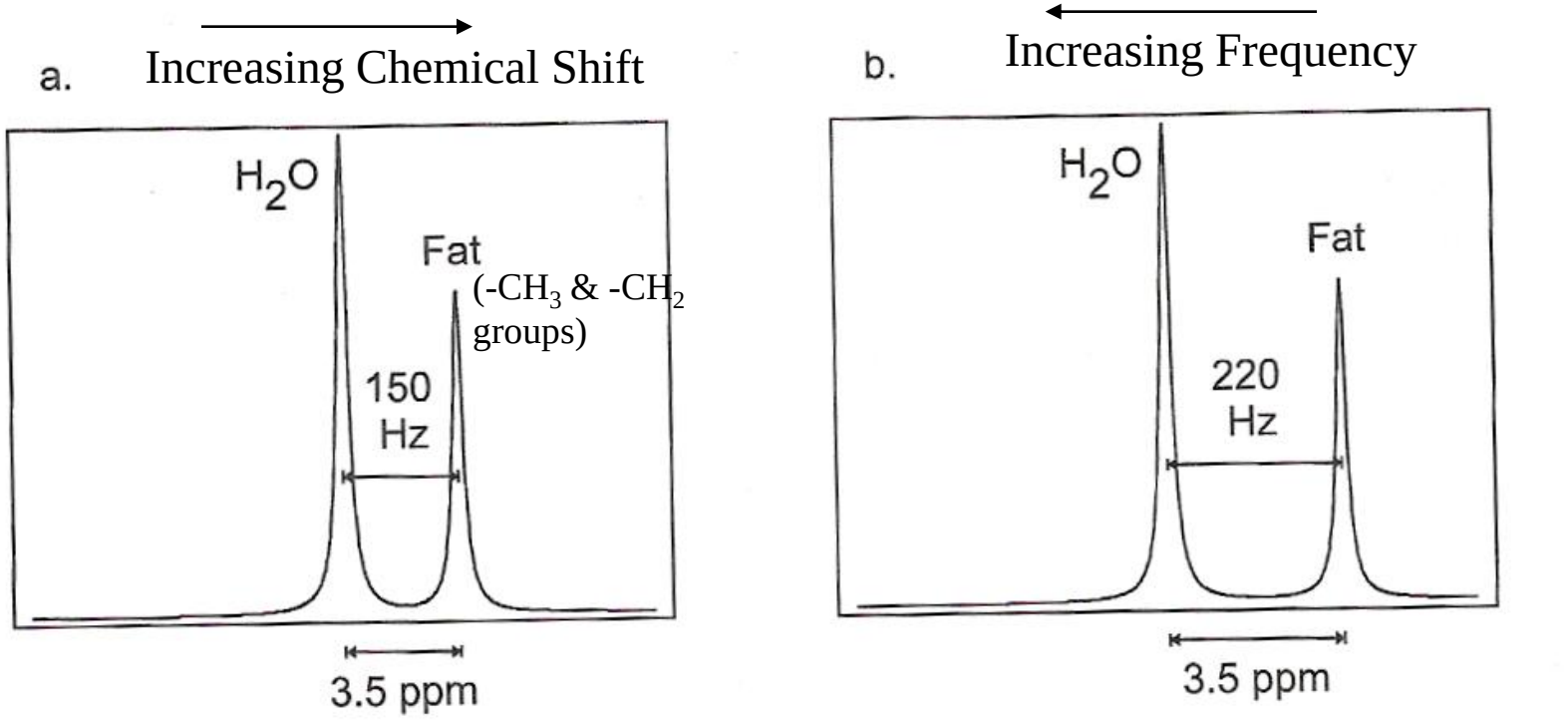


Figure 2-5. Spectrum of water and fat at 1.0 T (*a*) and 1.5 T (*b*). The resonant frequencies for water and fat are separated by approximately 3.5 ppm, which translates to an absolute frequency difference of 150 Hz for a 1.0 T magnetic field (42 MHz) or 220 Hz at a magnetic field of 1.5 T (63 MHz).

NMR Sensitivity and Other Nuclei

Any nucleus with a nuclear spin of ½ is visible by NMR. The NMR signal strength depends on the difference in populations between energy levels (ie. Boltzmann distribution).

$$n-/n+ = \exp(-\gamma\hbar Bo/KT)$$

The NMR signal strength increases with:

(i) Field strength , Bo

(ii) Magnetogyric ratio, γ

(iii) Decreasing temperature, provided that the substance remains a liquid.

The overall signal will also depend upon:

(i) The number of nuclei within the receiver coil of the NMR system (spectrometer).

(ii) The isotopic abundance of the nucleus (eg. ^{13}C is NMR visible but is only present at a natural abundance of approx. 1%.

For equal atomic concentrations and sample volumes the quantity $|\gamma^3 C|$ is defined as the nuclear receptivity (actual NMR sensitivity) where C is the natural abundance. This sensitivity is quoted relative to hydrogen eg.:

Isotope	^{1}H	^{13}C	^{19}F	^{31}P
Receptivity	1	1.8×10^{-4}	0.83	0.067

This does not take into account the biological abundance of each nucleus.

Table 1-1 Constants for Selected Nuclei of Biological Interest

Element	Nuclear Composition: Protons	Nuclear Composition: Neutrons	I	Gyromagnetic Ratio γ (MHz T^{-1})	% Natural Abundance	ω at 1.5 T (MHz)
^{1}H, **Hydrogen.**	1	0	1/2	42.5774	99.985	63.8646
^{2}H, Deuterium	1	1	1	6.53896	0.015	9.8036
^{3}He	2	1	1/2	32.436	0.000138	48.6540
^{12}C	6	6	0	0	98.90	0
^{13}C	6	7	1/2	10.7084	1.10	16.0621
^{14}N	7	7	1	3.07770	99.634	4.6164
^{15}N	7	8	1/2	4.3173	0.366	6.4759
^{16}O	8	8	0	0	99.762	0
^{17}O	8	9	5/2	5.7743	0.038	8.6614
^{19}F	9	10	1/2	40.0776	100	60.1164
^{23}Na	11	12	3/2	11.2686	100	16.9029
^{31}P	15	16	1/2	17.2514	100	25.8771
^{129}Xe	54	75	1/2	11.8604	26.4	17.7906

Source: Adapted from Ian Mills, ed., *Quantities, Units, and Symbols in Physical Chemistry*, IUPAC, Physical Chemistry Division, Blackwell, Oxford, UK, 1989.

Uses of MR Measurements of Other Nuclei (MR Spectroscopy; MRS)

Firstly Carbon-12 and Oxygen-16 have no nuclear spin and, hence, give no signal. Nitrogen-14 has a nuclear spin of 1 (twice that of hydrogen) but has very short relaxation times so cannot be seen.

Useful Nuclei measured from localised regions in-vivo:

Phosphorous-31 in Phosphocreatine, Adenosine Tri-Phosphate (ATP), Phosphodiesters and Inorganic Phosphate: enables high-energy phosphate metabolism to be studied e.g during and following ischaemia.

Hydrogen MRS: Measures lactate, choline, creatine and N-acetyl-aspartate (NAA) in-vivo (brain). Compounds altered in brain and other organs in diseased states.

Carbon-13: 1% natural abundant. Labelled glucose (C-13 enriched) used as a tracer to follow metabolic cycle in tissue.

Flourine-19: No natural abundance; used as a tracer when tagged to pharmaceuticals.

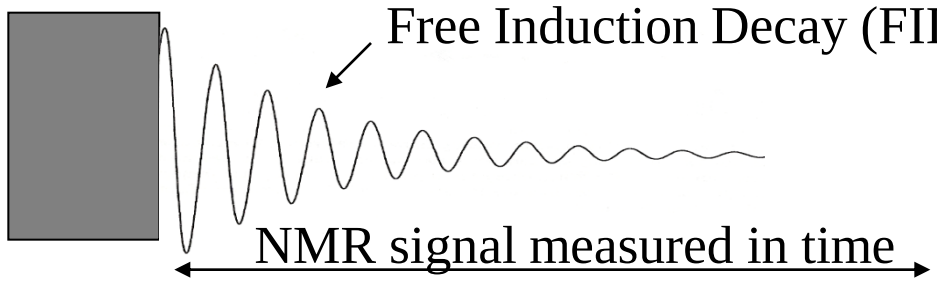
Sodium-23: Difficult to distinguish intracellular and extra-cellular. Therefore, can be only used to see region of stroke damage where ion homostasis (concentration balance) is perturbed.

Gaseous Helium-3 and Xenon-129: Used as gas contrast agents when “magnetised”.

Pulsed and Fourier Transform NMR

In modern NMR machines an RF pulse is used to excite the NMR signal.

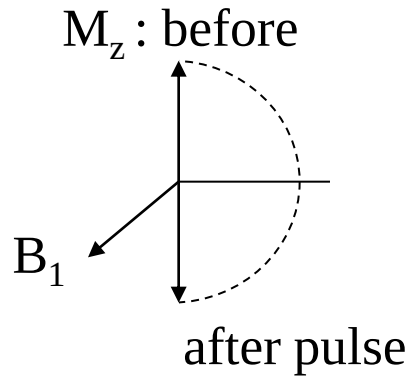
90^0 RF pulse
10-100μs



The RF frequency is set close to the Larmor frequency of the nucleus. In the rotating frame, the macroscopic magnetisation will rotate around B_1at a rate of $\omega_1 = \gamma B_1$ during the pulse. At the end of a pulse of duration τ then **M** will have precessed by $\gamma B_1\tau$ radians.

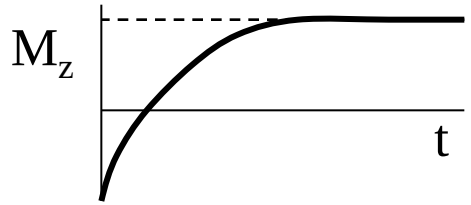
For a 90^0 pulse: $\tau = \pi / 2\gamma B_1$

For a 180^0 pulse: $\tau = \pi / \gamma B_1$ behaves like:



A 180^0 pulse is followed by spin-lattice relaxtion only, back towards the Boltzmann energy level distribution (**M**):

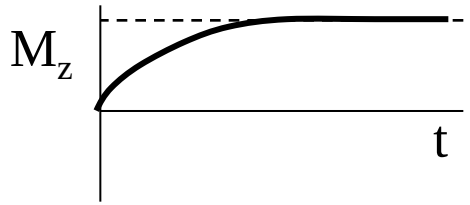
$$M_z(t) = \mathbf{M} [1 - 2 \exp (-t/T1)]$$



A 90^0 pulse is followed by spin-spin or "transverse" relaxation of the form:

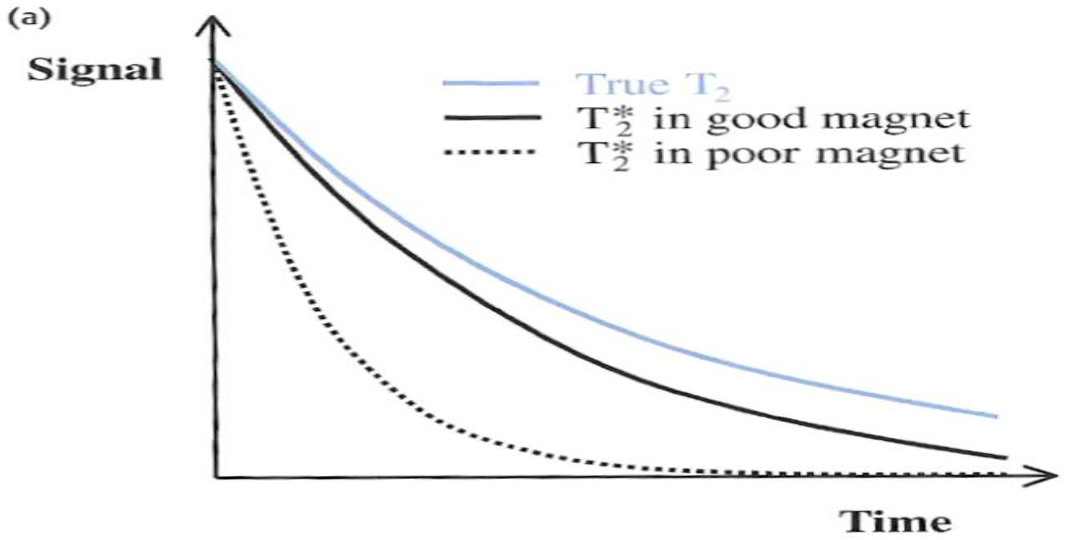
$$M_{xy}(t) = \mathbf{M} \exp (-t/T2)$$

$$M_z(t) = \mathbf{M} [1 - \exp (-t/T1)]$$

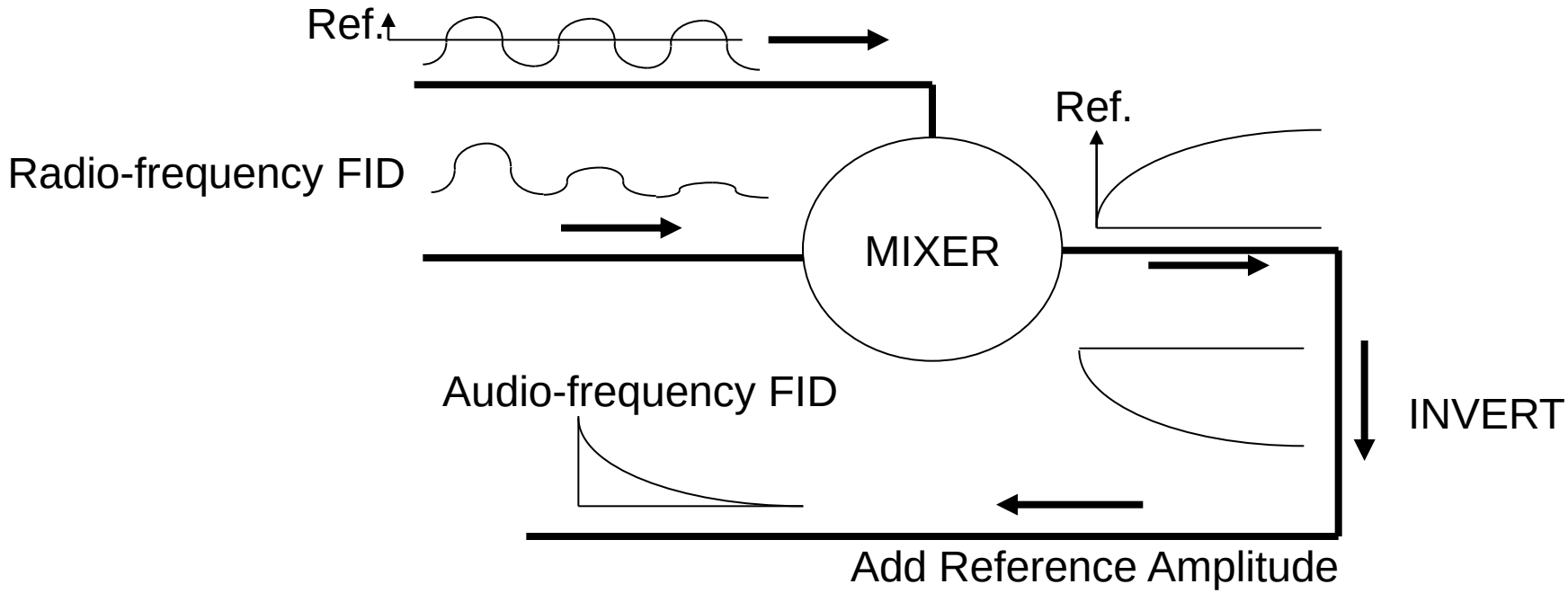


The NMR signal following the RF pulse is initially all in phase along an axis in the rotating frame, but gradually as the spins evolve at different frequencies (due to different chemical shifts and perhaps non-uniformities in the main magnetic field) the signal decays as the spins get out of phase with each other. This decaying signal is known as the Free Induction decay (FID: see a previous slide). The individual signals also decay in strength as spin-spin relaxation occurs.

The presence of field in-homogeneities in the magnetic field is usually taken into account by modifying the T2 relaxation time by making it shorter. The effective T2 is called T2* .

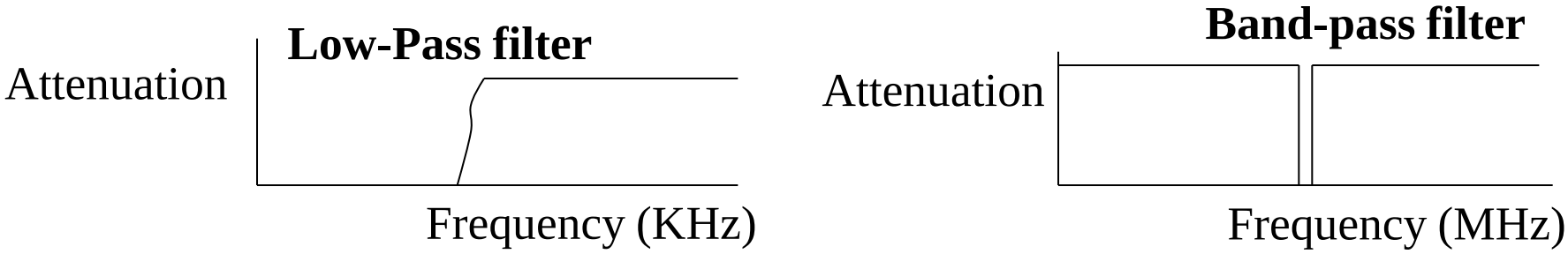


The FID signal is measured by the receiver coil. The signal is amplified by a pre-amplifier and then "mixed" with a carrier frequency which is at the same frequency as the RF pulse which was applied. This produces a signal at the frequency difference between the signals.
"Mixing" signals in this way is achieved by amplifying the difference between the NMR signal and a reference signal at the carrier frequency, and then subtracting a baseline value (equal to the magnitude of the reference signal).

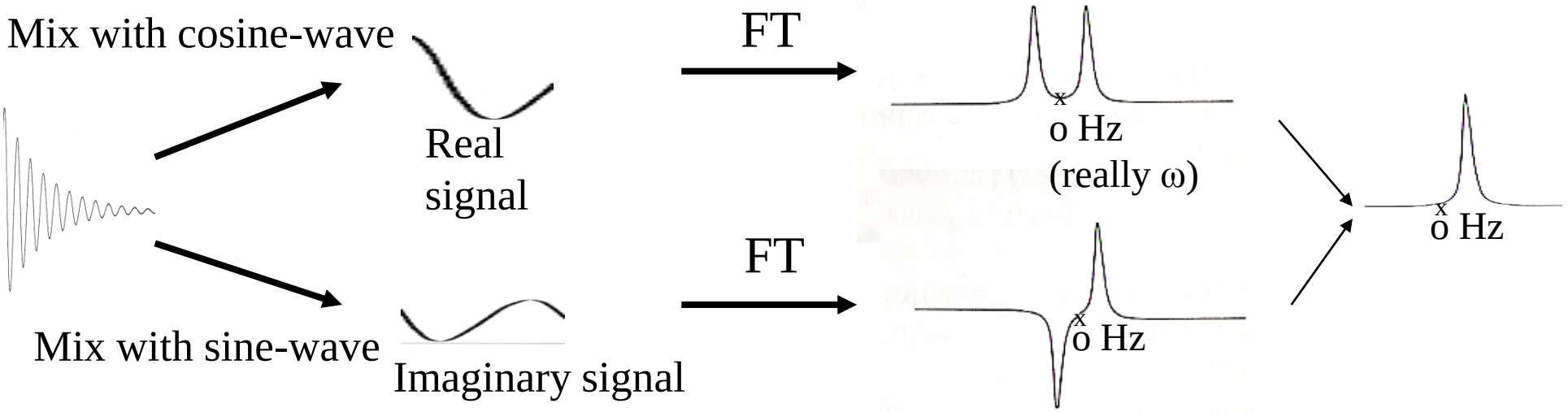


The net effect is to produce an "on-resonance" signal ie. oscillations of the signal at the carrier frequency have been removed leaving a signal with only low frequency modulations at the difference of the FID and reference signals (similar to AM radio !!). This is also known as demodulation, and allows us to use audio-frequency electronics to filter and then sample the signal using an analogue to digital converter (ADC).

The filter can be set to remove noise at high frequencies and can be a "low-pass" design which is simple to make (i.e. let through signals below 50 KHz and block-out higher frequencies). Without demodulation, a notch filter would be required with a sharp response close to the resonant frequency. The audio-frequency is much easier to digitally sample than the corresponding RF signal.



Furthermore, by choosing the phase of the reference signal, we can select either the in-phase signal component (absorption) or the out-of-phase component (dispersion). This is known as phase-sensitive detection (PSD) and from one input signal (the FID), we can get two outputs by mixing it with a cosine and sine wave respectively. These signals are known as the "real" and "imaginary" signals. A change from resonance is seen as an audio-frequency modulation. The new FID must then be analyzed to investigate it's frequency components by using a Fourier Transform (FT). This allows any function in time to be expressed as a distribution of frequency components (the spectrum). PSD also allows negative and positive signals to be distinguished from each other.

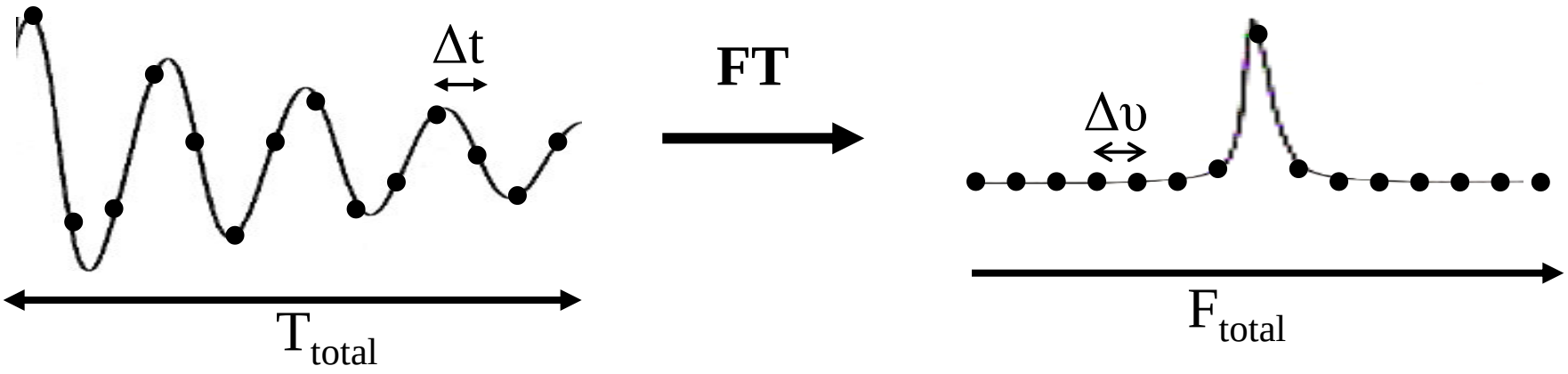


The theory works the other way around and allows you to predict the time function if you know the frequency components. The mathematical operation required by an FT is an integration:

$$f(t) = \int_{-\infty}^{\infty} F(\upsilon) \exp(i 2\pi\upsilon t)\, d\upsilon$$

$$F(\upsilon) = \int_{-\infty}^{\infty} f(t) \exp(-i 2\pi\upsilon t)\, dt$$

These functions are continuous, but in an NMR machine the signal has been digitised for computer storage using the ADC. Therefore a discrete Fourier Transform is applied which relies on summations of sines and cosines.



Data Sampling

Usually 2^N time data points are sampled in both real and imaginary signals (making $2*2^N$). If the time interval between sampling is Δt then the discreteness with which the frequency distribution is sampled $\Delta \upsilon$ is given by:

$$\Delta \upsilon = 1 / 2^N \Delta t = 1 / T_{total}$$

For two frequencies to be resolved by an FT, one must have evolved at least an extra 2π relative to the other by the end of T_{total}.

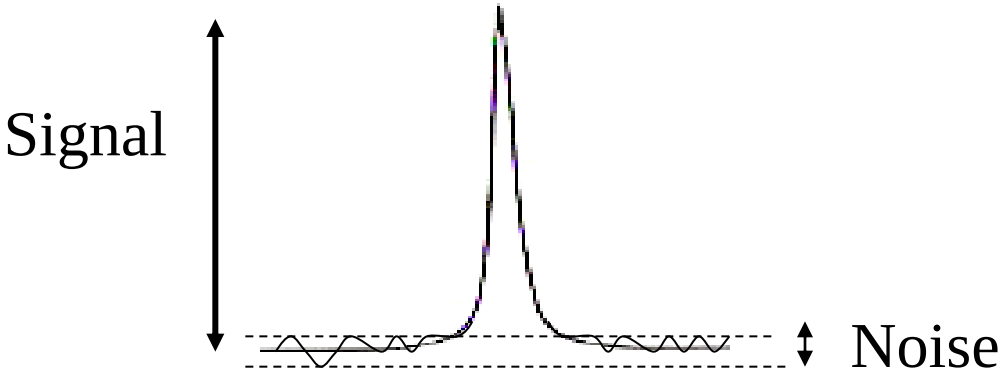
This equation is derived from the Nyquist Theorem, which prevents signal aliasing (see below). $\Delta \upsilon$ is chosen to resolve all the different frequencies that may be present in the FID. Discrete Fourier transforms give the same number of points as an output as was input. The total frequency width that can be sampled is then:

$$F_{total} = 2^N / 2^N \Delta t = 1 / \Delta t$$

Δt is chosen to cover the frequency range expected from the sample (eg. 100μs for 10 KHz range of frequencies), and the audio-frequency filter is chosen to be slightly higher to let all the frequencies be sampled without interference of noise of a higher frequency. Because of PSD the bandwidth of signals covered is 5 KHz relative to ω. Without the audio-filter, noise would be sampled and, although too high to be correctly assigned by the FT, would be "aliased" into the spectrum. The Nyquist Theorem states that the highest frequency that can be correctly assigned by a discrete FT must have been sampled at least twice per cycle to prevent aliasing, providing the basis for the above equation for F_{total} .

Signal and Noise

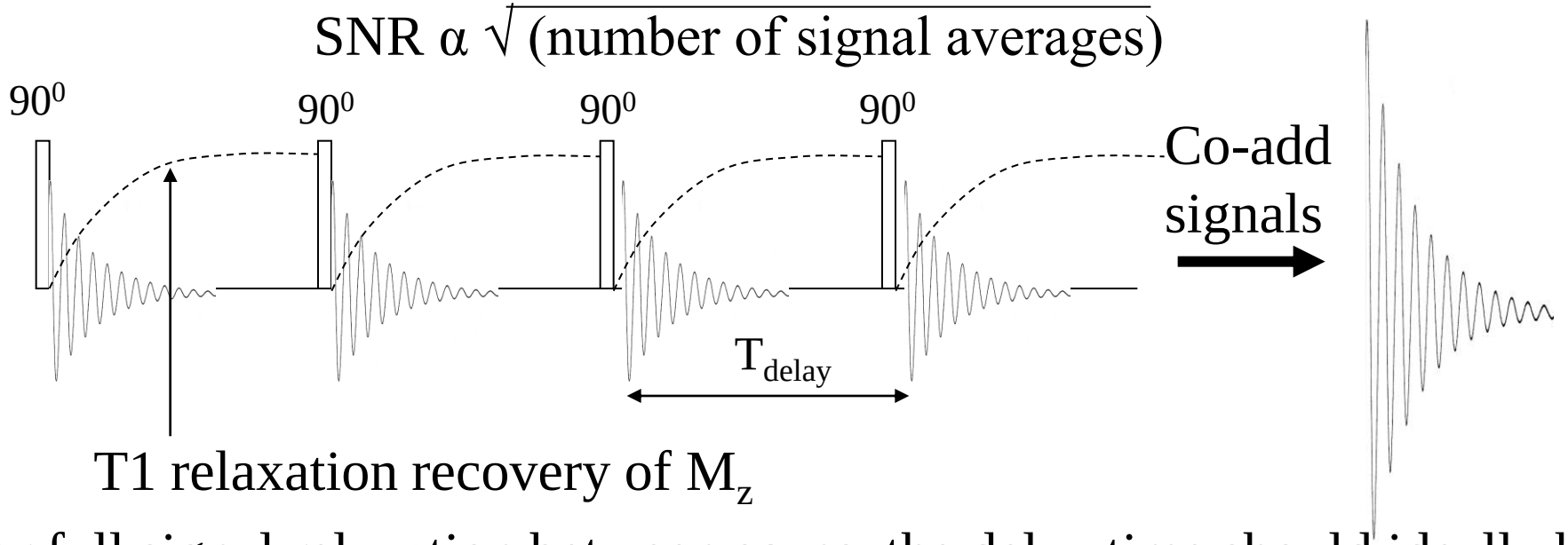
In addition to the NMR signal, the receiver coil always picks up RF noise which is generated by the surroundings (principally the thermal oscillations of atoms within the sample and receiver coil itself). This noise is random and depends on the effective electrical resistance of the coil and sample (which adds resistance to the coil because they are closely coupled) , and their respective temperatures. The signal to noise ratio (SNR) is used as a measure of the size of a spectrum relative to noise.



SNR = Signal/Noise

Noise is completely random and two noise signals added together result in a $\sqrt{2}$ increase in noise level. Since NMR signals co-add linearly, co-addition of the results of multiple identical sequences results in an improvement in S/N ratio according to the formula:

$$SNR \alpha \sqrt{(number\ of\ signal\ averages)}$$



For full signal relaxation between scans, the delay time should ideally be greater than 5 x T1. However, the sequence may be repeated more quickly by using an RF pulse which creates a rotation (spin flip angle) of less than 90^0 . The optimum is given by the Ernst angle, α_E where:

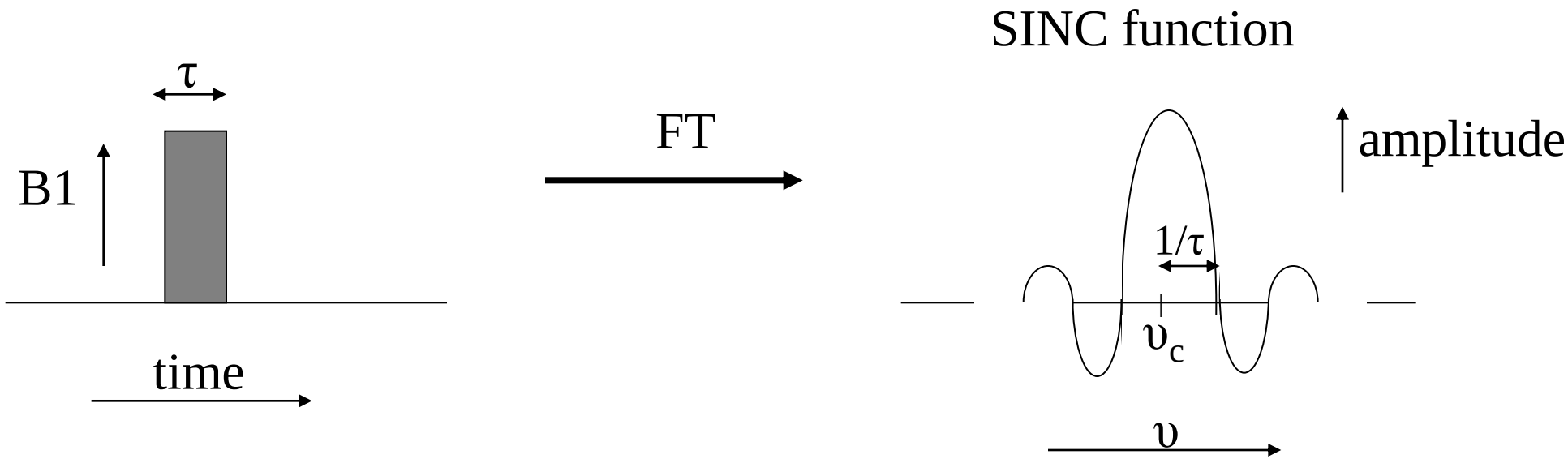
$$\cos(\alpha_E) = \exp(-T_{delay}/T1)$$

The SINC Function

Fourier analysis shows that a short rectangular RF pulse has a range of frequency components, centred upon υ_c given by the equation:

$$\sin [\ \pi(\upsilon-\upsilon_c)\tau\ ] / \pi(\upsilon-\upsilon_c)\tau = \text{SINC}\ (\pi(\upsilon-\upsilon_c)\tau)$$

For an RF pulse of duration τ:



Therefore, the pulse must be sufficiently short to cover the desired width of the spectrum to be obtained. For example, a pulse of 10μs duration will cover a frequency range of 10^5 Hz.

MR Imaging: Basic Theory

MRI provides the spatial distribution of the nucleus of interest. For protons they show the density of free tissue water and fat (-CH_3 and --CH_2 groups). In contrast to X-rays, bones appear dark and soft-tissue appears bright.

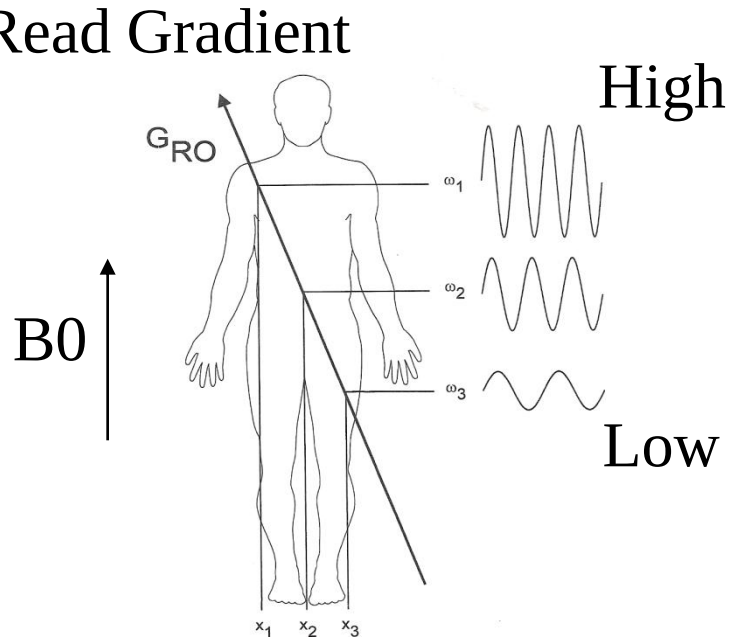
In pathology, the tissue generally increases in water density as tissue structure is degraded, and the T1 and T2 of pathological tissues are increased over normal values. The main advantage of MRI is that this contrast between normal/abnormal tissue is good compared with other techniques.

A second advantage is that MRI is safe and non-invasive. There are no physical hazards such as radiation or electrical hazards. It is non-invasive since it does not require the subject to damaged in any way, and so people may be repetitively scanned. Disadvantages are that the scans generally last at least 0.5 hour and the machines themselves are quite expensive (approx. £2 million including installation costs).

SPATIAL INFORMATION

To obtain spatial information, we excite the MR signal and then measure it whilst it evolves in a magnetic field gradient. The gradient causes nuclei (spins) in different positions to experience different magnetic fields separating them out along the frequency axis of our analysed signal (frequency spectrum). By measuring the frequency we can assign position to the hydrogen nuclei.

The gradients are applied by pulsing electrical current through gradient producing coils. The gradient is turned off by removing the current. Gradient switching on and off produces the sound made by MRI scanners.

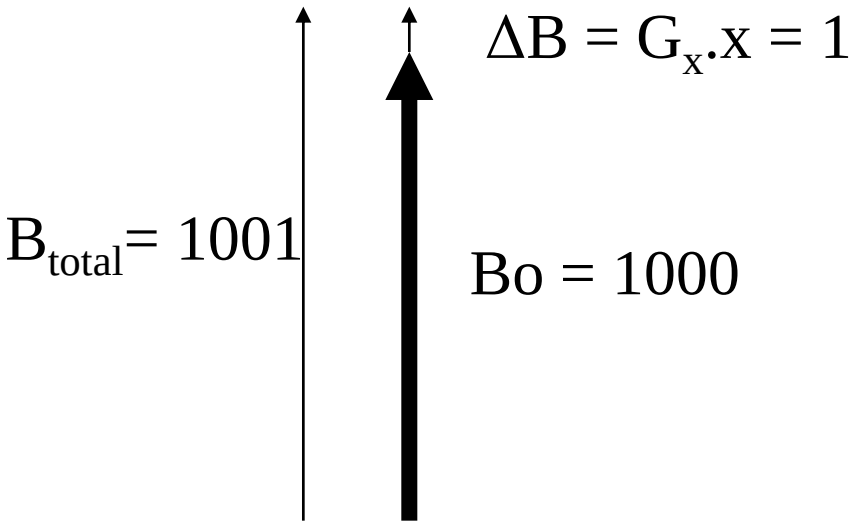


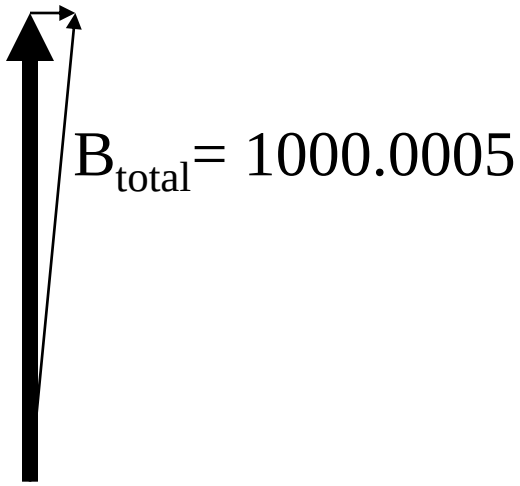
Gradients

The gradient coils produce magnetic fields that linearly vary across the bore of the MR scanner and (for max. effect) are of the form:

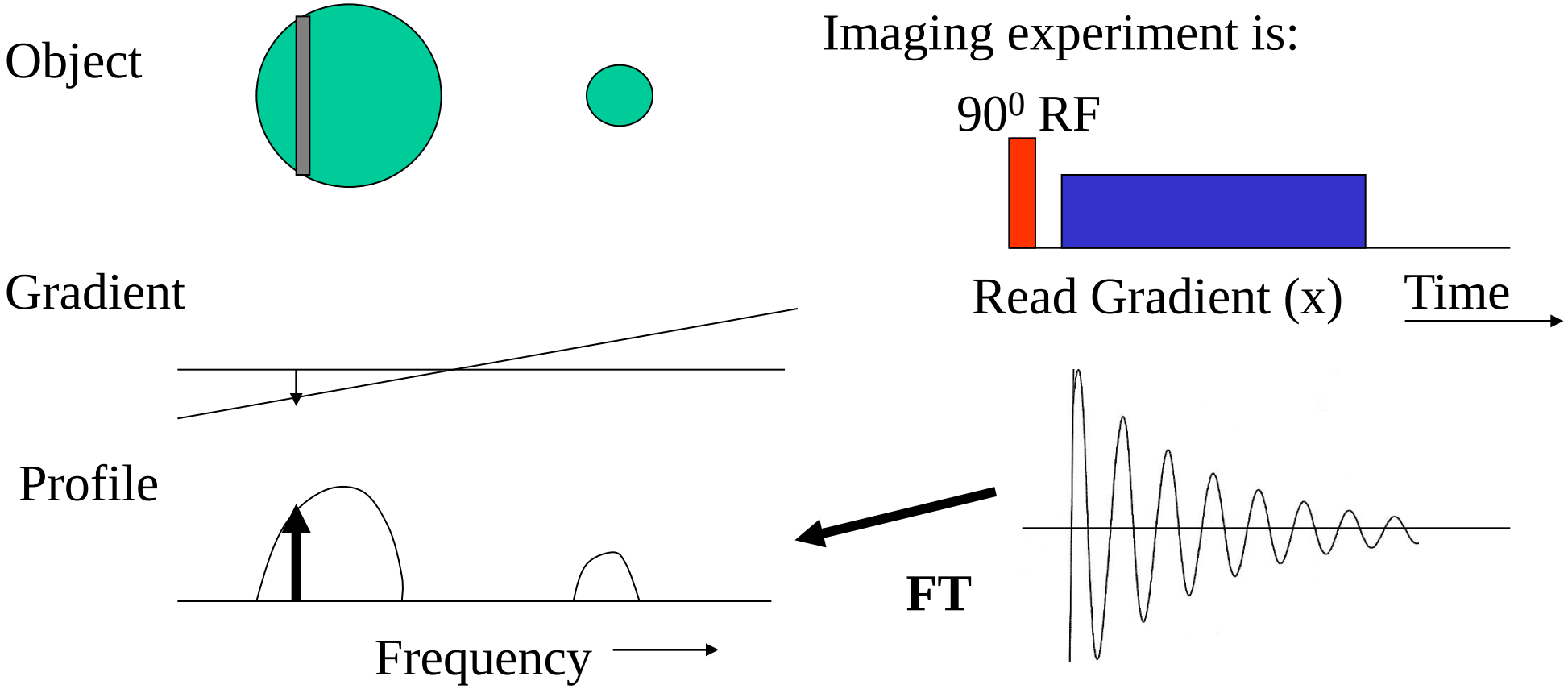
$$G_z = dB_z/dz \qquad G_y = dB_z/dy \qquad G_x = dB_z/dx$$

i.e the additional field is always parallel to Bo (z) and adds or subtracts from this field.



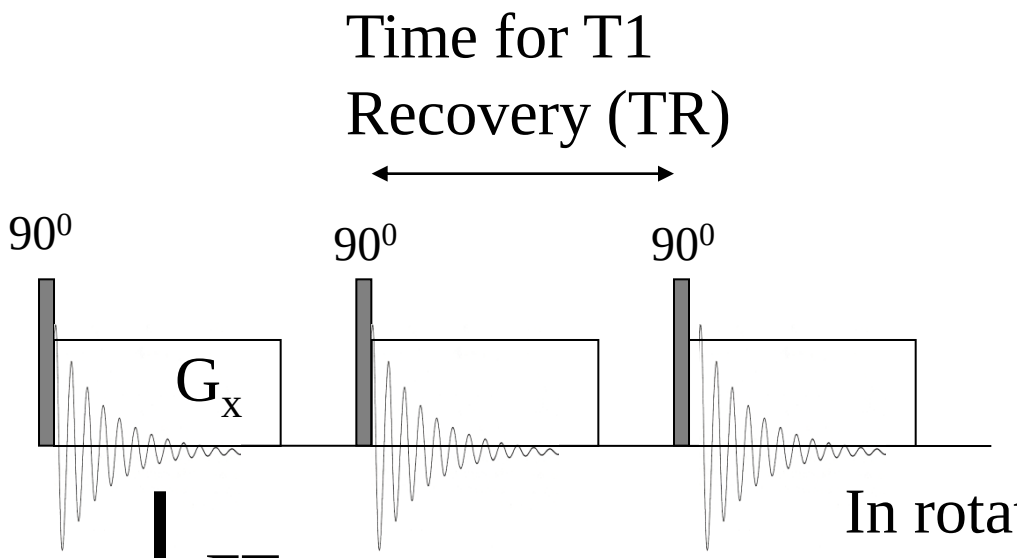


In the presence of a gradient, NMR spins will resonate at a frequency determined by their position i.e.: $\omega = \gamma B = \gamma (Bo + x. dB_z/dx)$



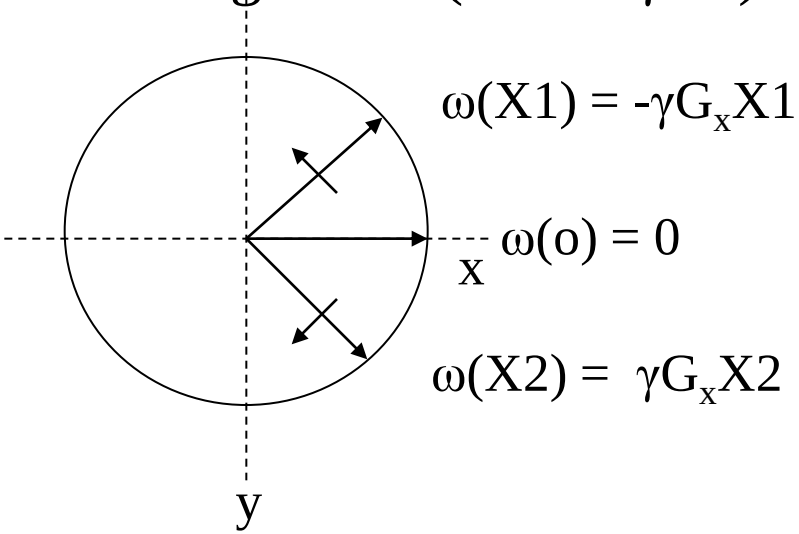
In a field gradient, if the range of resonant frequencies within an object were analysed, a spatial projection profile of the object would be obtained. The profile shows the number of spins at each resonant frequency and hence the total number within strips of the object oriented perpendicular to the field gradient.

The imaging sequence is then as shown below.



Profile of object along x axis (υ)

In rotating frame (at $\omega = \gamma Bo$):



Gradient Echoes

The NMR signal in the presence of gradients can be described by the equation:

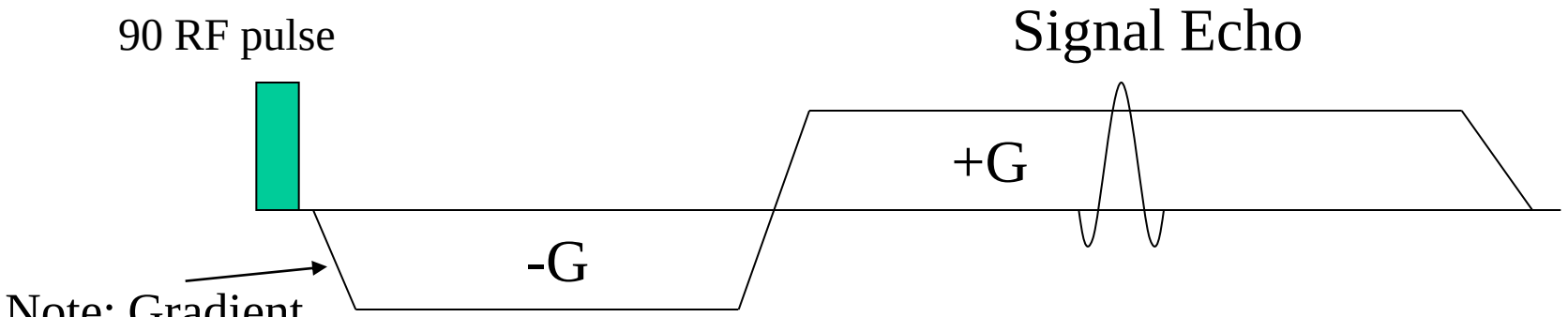
$$S(t) = \iiint M(x,y,z) \exp\left[i \int_0^t (\omega + \gamma x G_x + \gamma y G_y + \gamma z G_z) dt \right] dx\, dy\, dz$$

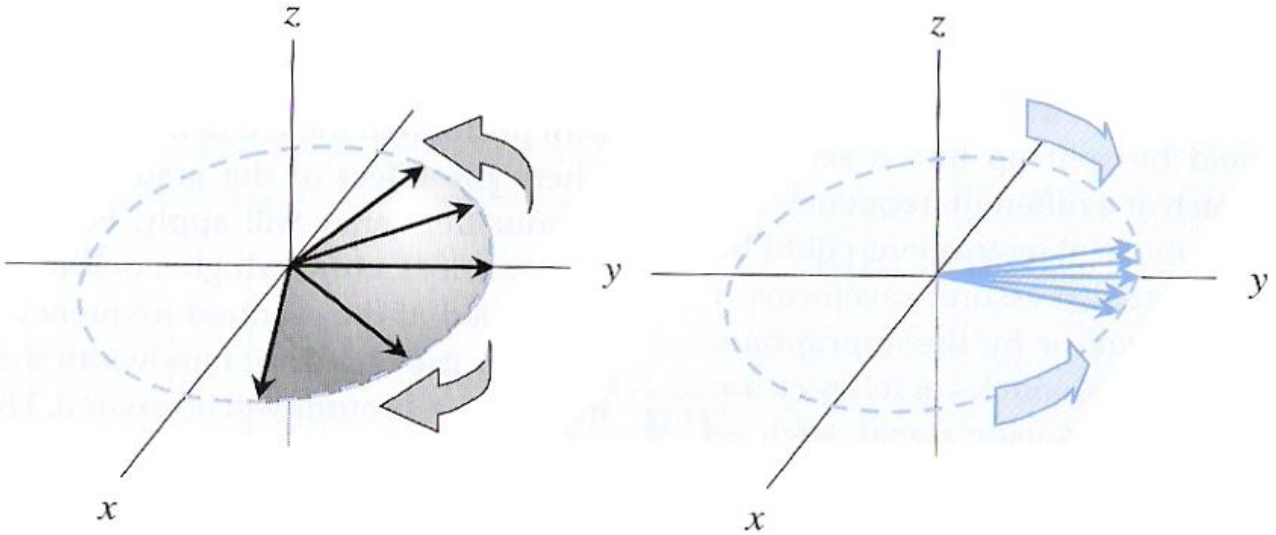
where M(x,y,z) is the spatial distribution of **M**.

For example, for one spin at $x = x_1$, $y = 0$, $z = 0$, in the presence of a single gradient, G_x, the signal at time t in the rotating reference frame (allowing us to ignore ω) is:

$$S_{x1} = M(x_1,0,0) \exp(i\Phi) \qquad \text{where } \Phi = \int_o^t \gamma\, x_1 G_x\, dt$$

One problem is that the imaging gradient cannot be turned on immediately after the 90^0 pulse, since the gradient has a finite rise time caused by gradient coil inductance. Therefore, the first sample points occur in a gradient that is changing in size, and are thus incorrect. The solution is to use a "Gradient Echo".



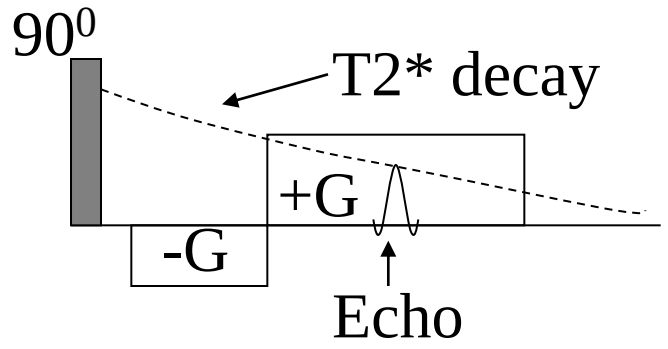


At the gradient echo time, the (gradient x time) integral is zero for all spins (at all x positions) and an echo is formed e.g.

$$\Phi = \int_{o}^{t} \gamma \, x_1 G_x \, dt = 0$$

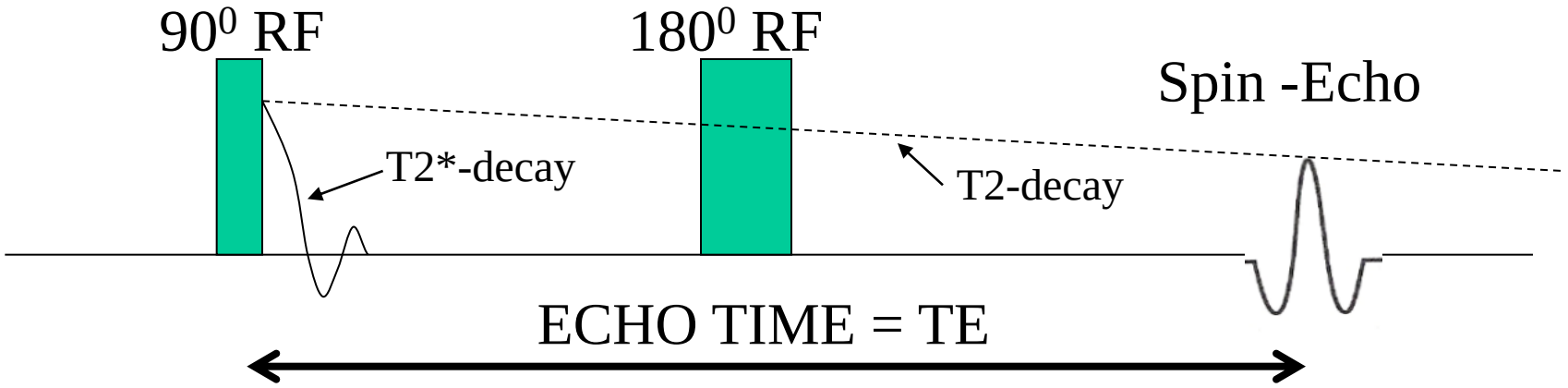
The NMR signal is sampled on BOTH sides of the echo without distortion (ie. in a constant gradient). A "magnitude" FT (square root of [real FT]^2 + [Imaginary FT]^2) gives a profile and uses information from both the real and imaginary signals sampled with phase sensitive detection.

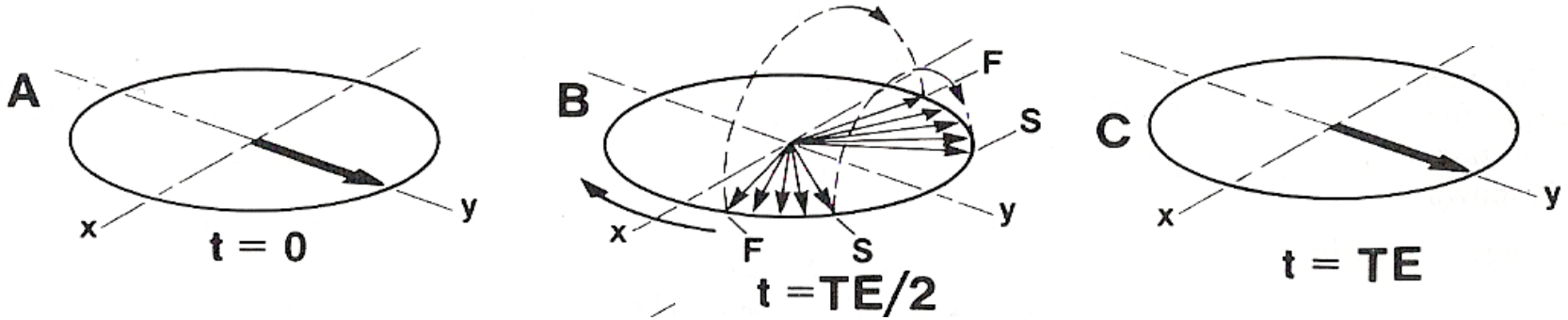
One problem with gradient echoes is that magnetic non-uniformity causes de-phasing of the spins all the time between the 90^0 pulse and the formation of the echo. Therefore, the signal has decayed by the T2* process.



The Refocusing 180^0 RF Pulse

The signal after a 90^0 can decay rapidly due to Bo non-uniformity (T2* decay) and chemical shift evolution.. A "pan-cake" flipping RF pulse (180^0) causes spins to re-phase into a spin echo at time TE. The effect of Bo field non-uniformity is removed and the height of the echo is determined by T2 not T2*.

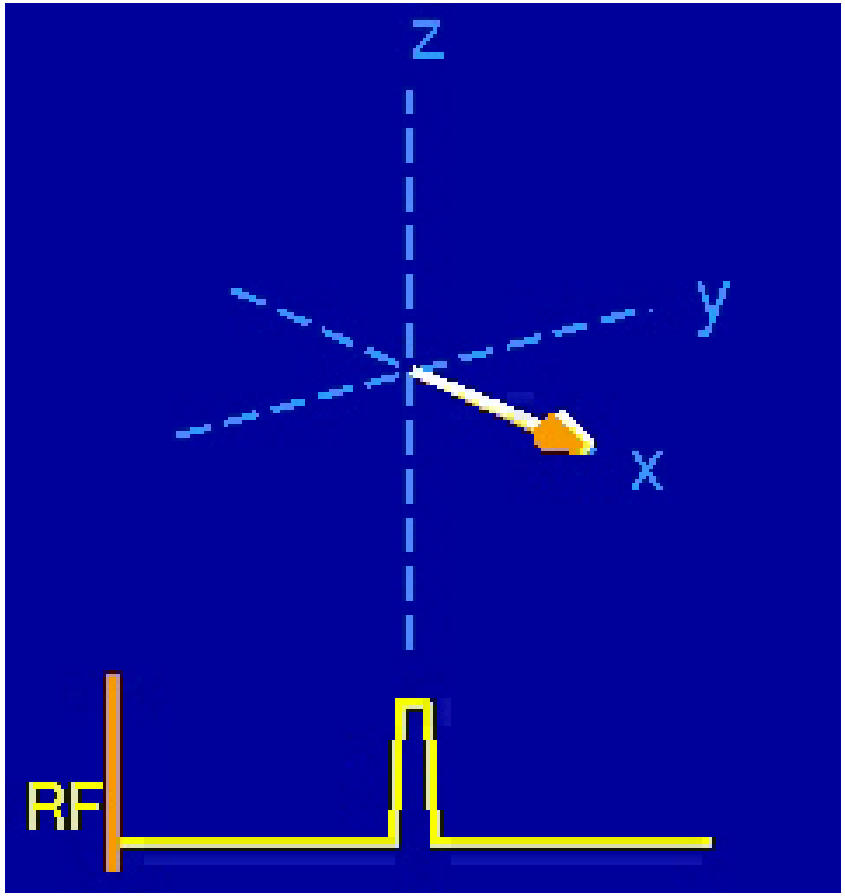




"Pancake flip"

F=Fast; S =Slow

The Refocusing 180^0 RF Pulse



The spin echo recovers any signal loss which is due to signal evolution which proceeds at the same rate before and after the 180^0 RF pulse. Hence signal decay is recovered from:

(i) Field non-uniformity, which remains constant and must be allowed to proceed for an equal time either side of the 180^0 pulse. Hence, the sequence is 90^0-TE/2-180^0-TE/2-echo and the echo is formed at TE.

(ii) The same applies for evolution due to chemical shifts between fat and water.

(iii) If equal gradients are applied either side of the 180^0, this evolution will also be re-focussed.

The signal amplitude at TE is given by: $M_{xy}(TE) = M \exp(-TE/T2)$

The echo time relative to the 90^0 pulse is referred to as TE.

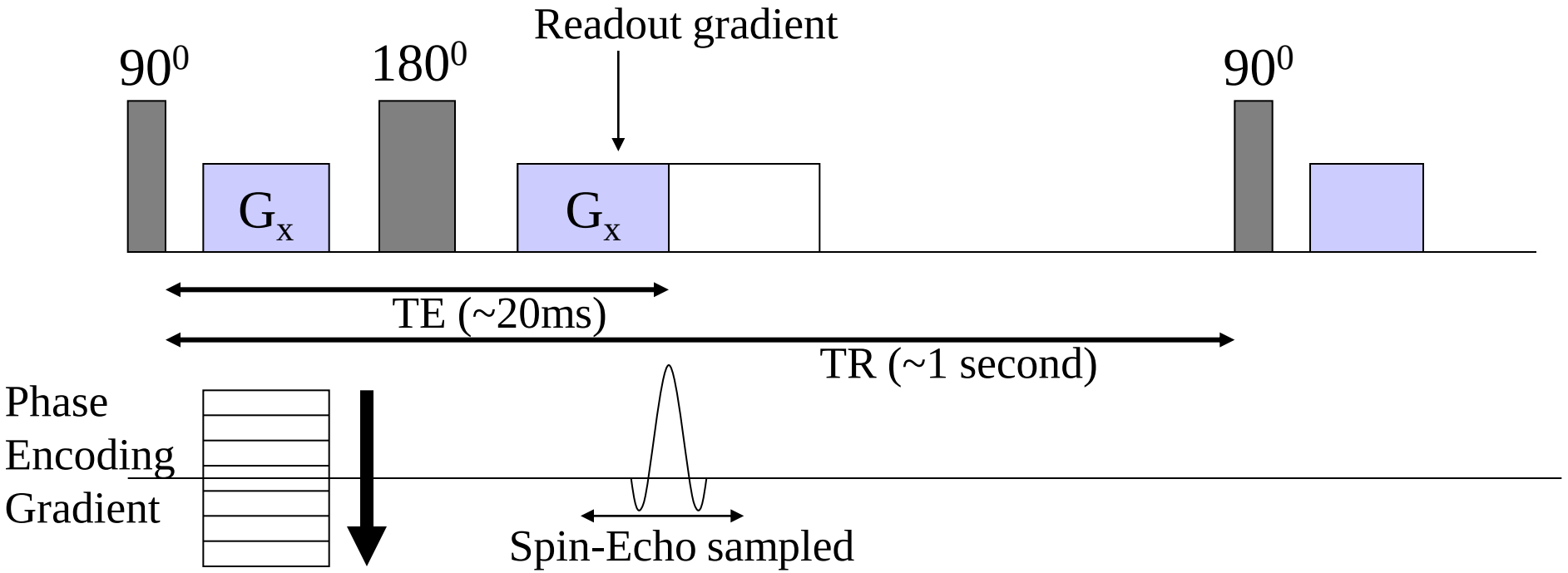
Repetitive application of the 180^0 pulse train is known as a Carr- Purcell-Meiboom- Gill (CPMG) experiment, and generates a series of spin echoes. The envelope of the echoes decays at a rate defined by T2, and the echo heights (or their corresponding spectra) can be used to measure T2 using the equation:

$$\ln (M_{xy}(2n\tau)/\mathbf{M}) = -2n\tau/T2$$

where each echo occurs at $2n\tau$ where $\tau = TE/2$ and n is an ascending integer. (ln = natural logarithm). The above ratio is plotted against $2n\tau$ and the slope of the straight line obtained is equal to -1/T2. Spin echoes enable T2 to be measured and not T2* which is responsible for signal decay following a single 90^0 pulse and does not contain pure biological information (it also depends on the uniformity of the magnet).

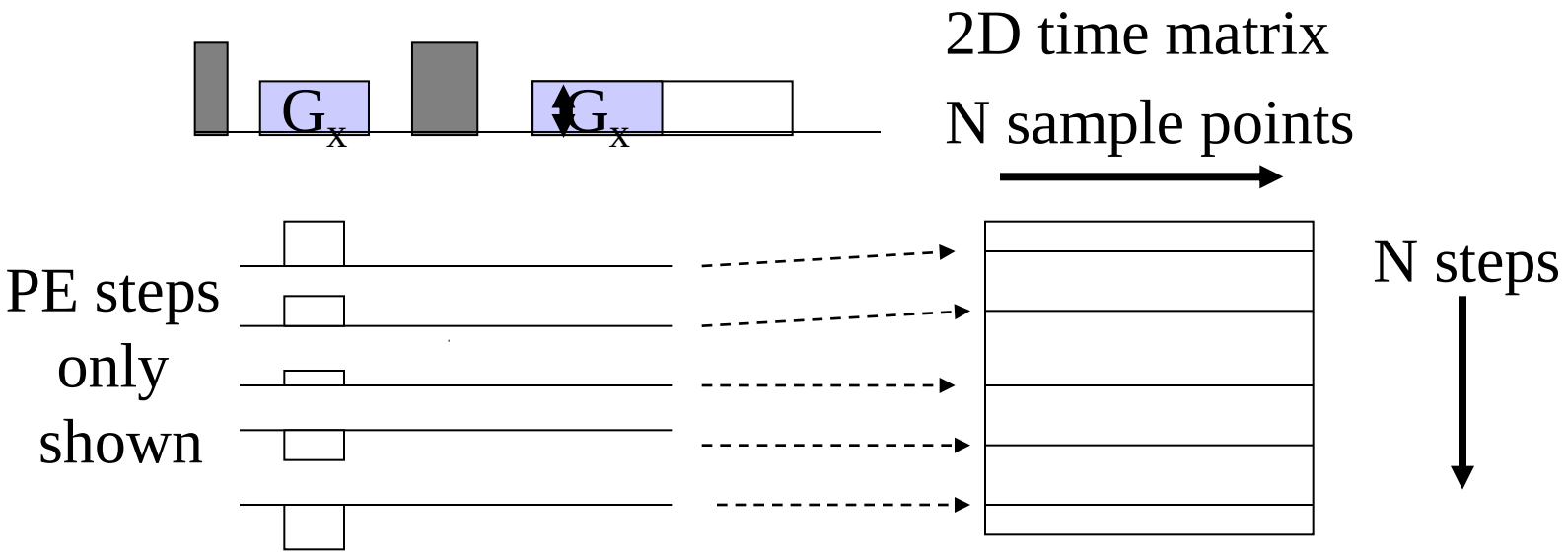
2DFT or Spin-Warp Imaging

In the 2DFT MR imaging method, the following gradient and pulse sequence is used:



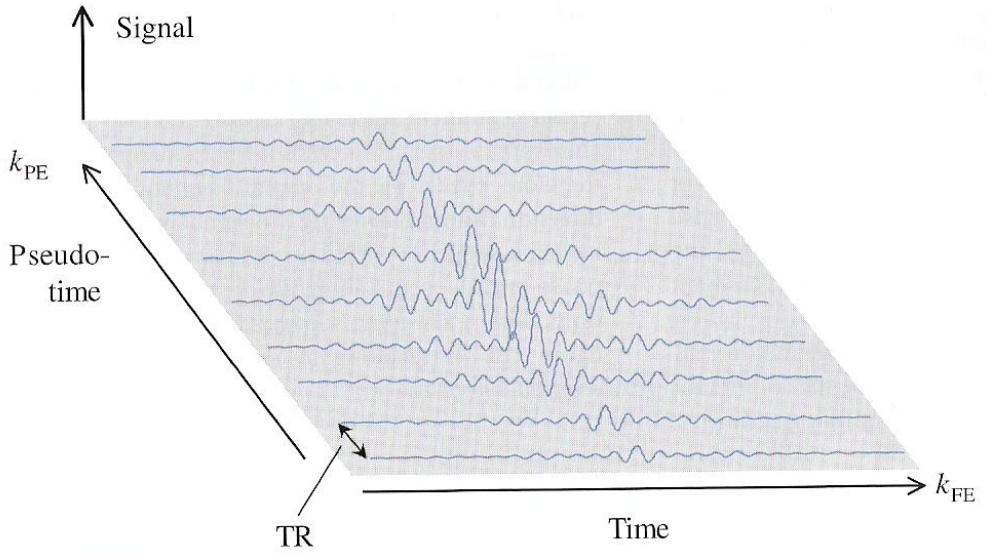
G_y decremented in successive shots

The 180^0 pulse creates a spin echo, and equal G_x gradients on either side of the 180^0 ensure a gradient echo is co-incident with the spin echo (note that two gradients must be of the same sign, rather than with a gradient echo where they are of opposite sign and the areas [blue] must be equal up to TE). FT of this echo signal would give a projection along x. Instead of rotating this gradient in successive scans, a G_y gradient is stepped in even decrements from $+G_y$ to $-G_y$. To form an N x N image matrix, this must be performed in N steps. This is called phase-encoding (PE), and the G_y gradient is called the phase-encoding gradient. The G_y gradient creates a spin echo FID in "pseudo-time", the second axis of the 2D time array that is built up when each of the successive signals is put into successive rows of the 2D matrix.



Why does this work ?

The signal evolution along the read axis involves successive sampling in time in a constantly applied G_x gradient. The signal evolution in the G_y gradient only occurs during a ***fixed*** time following the 90^0 pulse. To make this 2^{nd} axis experience the same progression of signal evolution, then G_y must be stepped in amplitude in successive shots of the scan so that a spin echo is gradually formed along this 2^{nd} axis.



A 2DFT is applied to obtain the image. This involves FT along all the rows of the 2D time matrix, and then FT along all the columns. Therefore, 2N FT's are performed to get the image. Because N PE steps are needed, the total scan time is N x TR i.e. 256 seconds for a 256 x 256 image with TR = 1 second.

Image Resolution.

The image resolution along the read axis, λ_x , is given by:

$$2\pi/\lambda_x = \gamma G_x t_s$$

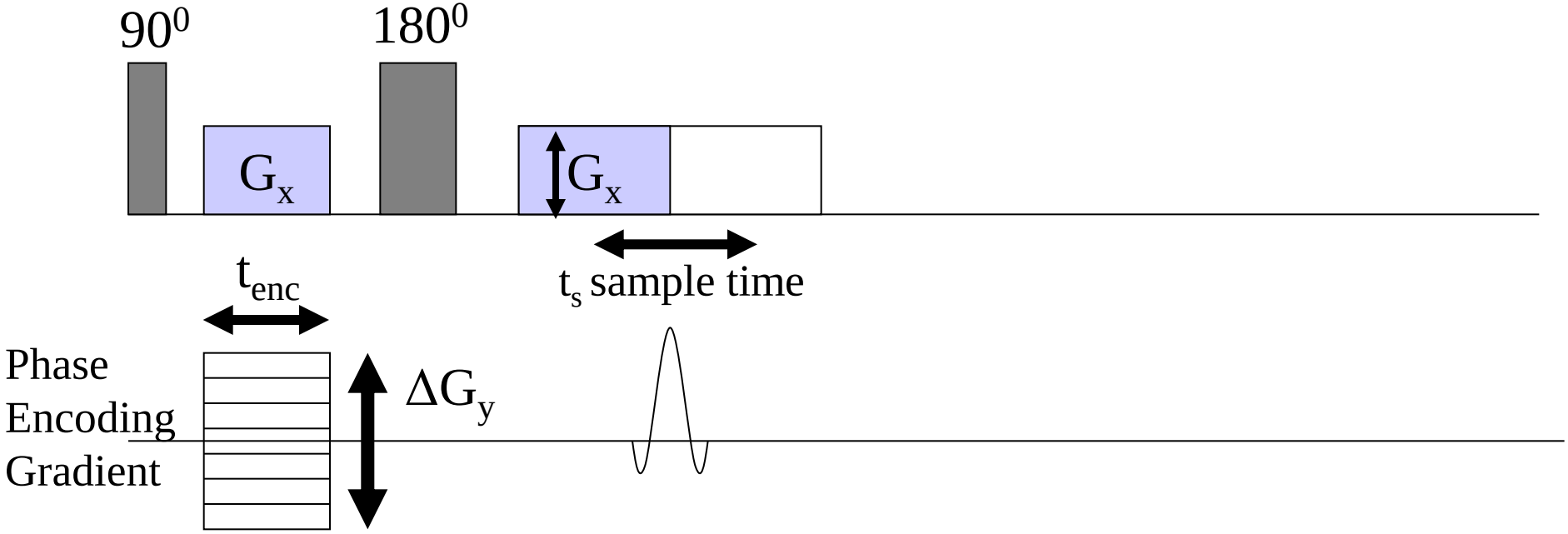
where t_s is the total time for which the echo signal is sampled. The resolution along the phase encoding axis is usually made to equal that along the read axis. This is achieved by equalising the (gradient x time) areas according to the recipe:

$$G_x t_s = \Delta G_y t_{enc}$$

The phase-encoding resolution is given by:

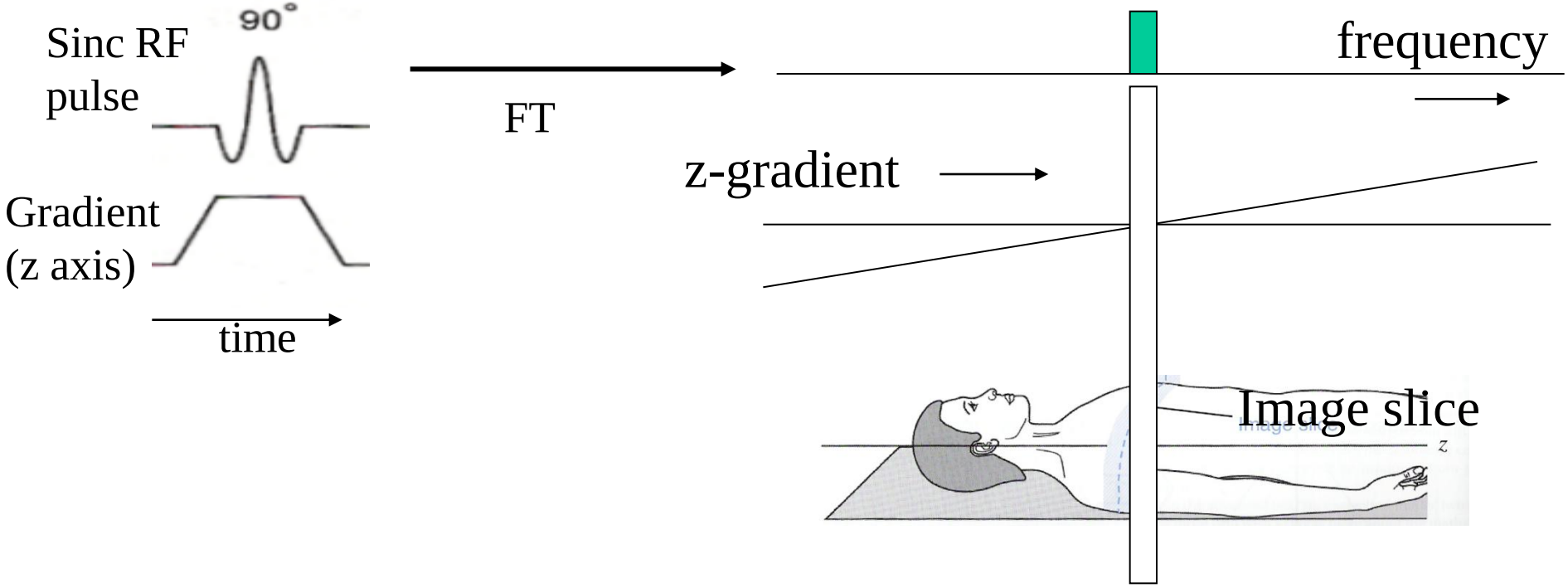
$$2\pi/\lambda_y = \gamma \Delta G_y t_{enc}$$

These values ensure a phase shift evolution between successive image pixels along both axes of 2π during the scan.



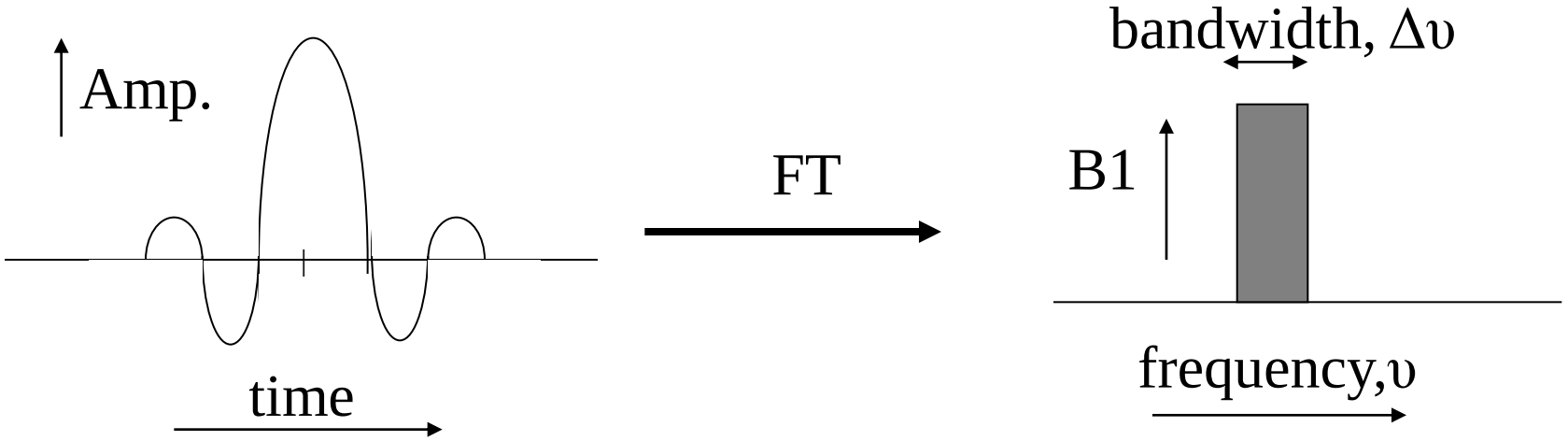
SLICE SELECTION

To select a slice of the object (along z axis), an RF pulse with a limited range of frequency components is applied in conjunction with a z-field gradient. Only the nuclei that are resonating within the bandwidth of the RF pulse respond by tipping through 90^0. The RF pulse is modulated in amplitude as a function of time to achieve this limited bandwidth: a (Sin x/x) function is used (called a SINC).



Only the NMR spins within a thin slice (thickness Δz) interact with the frequency components of the pulse (in a bandwidth $\Delta\upsilon$) and are tipped through 90^0 into the x-y plane. All other spins remain aligned with Bo. For a typical SINC pulse of 5 milliseconds duration, $\Delta\upsilon$ is 1 KHz. The slice thickness is defined by: $2\pi\Delta\upsilon = \Delta\omega = \gamma\, G_z\, \Delta z$

RF amplitude
SINC function

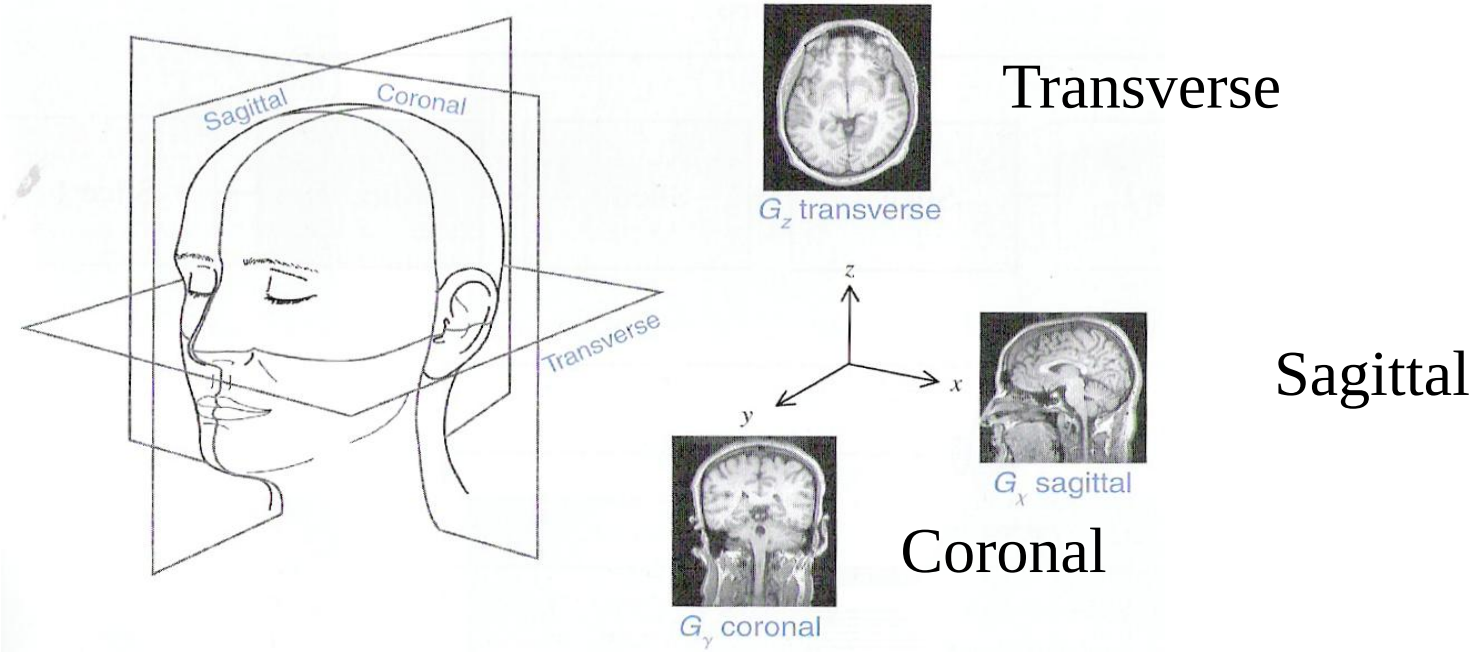


To decrease the slice thickness either G_z is increased or $\Delta\upsilon$ is reduced. Since a longer SINC pulse has a narrower bandwidth, this may be achieved by making the SINC pulse duration longer.

Slice Selection: A SINC pulse also requires a "refocussing gradient"; a gradient of equal negative amplitude following the pulse applied for half the pulse duration. This ensures that all the M_{xy} signal starts in-phase across the selected slice.

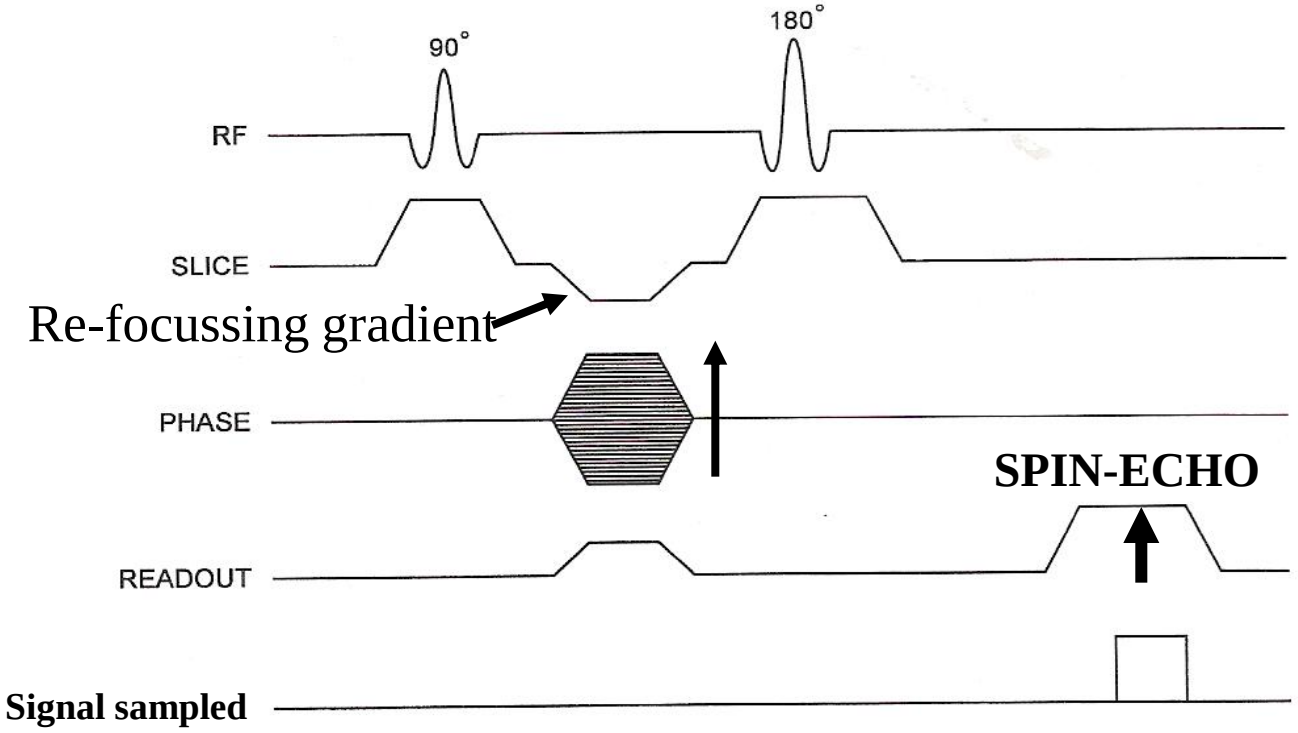
Slice position is varied by changing the carrier frequency of the RF pulse by $\delta\upsilon$ according to the equation: $\delta z = 2\pi\, \delta\upsilon / \gamma\, G_z$ where δz is the slice displacement.

The slice can be oriented along any axis, but the read and phase-encoding gradient directions must be altered accordingly.



The complete Spin-Warp (2DFT) imaging sequence

The 180^0 pulse is made slice selective. The readout gradient must be balanced on either side of the 180^0. The echo signal is sampled. A 2DFT is used to construct the image.



Repeat after TR seconds, with incremented PE gradient ,until all lines of data have been collected.

SUMMARY

$$\omega_0 = \gamma.B_0$$

$\Delta\omega = \gamma.\Delta B$ and $\Delta B = x.G_x$ (or similar for y or z); for frequency difference between 2 points, slice thickness, slice displacement from centre

$\omega_1.t = \gamma.B_1.t = \pi/2$ (90^0 pulse); or π (180^0 pulse);

$\Delta\omega.t = \gamma.\Delta B.t = \gamma.\ x.G_x.t = 2\pi$ (to resolve 2 points by FT)

Gradient Calculations for Resolution and Slice Thickness

Suppose we wanted to produce a 256 x 256 image with a field of view of 25.6 cm (i.e. resolution of 1mm suitable for the human head) and with a slice thickness of 2mm.

Let us chose:

t_s = 8 ms

t_{enc} = 4 ms

slice selection with a 5ms SINC, $\Delta\upsilon$ = 1 KHz

γ = 4.27 x 2π x 10^7 radians. $Tesla^{-1}$. $seconds^{-1}$

The gradients required are:

$$G_x = 2\pi/ \lambda_x \gamma t_s = 2\pi/ 10^{-3}*4.27*2\pi*10^7*8*10^{-3}$$

$$= 0.0029\ T.m^{-1} \text{ or } 2.9\ mT.m^{-1}$$

$$\Delta G_y = 2\pi/ \lambda_y \gamma t_{enc} = 2\pi/ 10^{-3}*4.27*2\pi*10^{7}*4*10^{-3}$$

$$= 0.0059 \text{ T.m}^{-1} \text{ or } 5.9\text{mT.m}^{-1}$$

i.e. G_y must be stepped in 256 decrements from ~3 mT m^{-1} to ~ - 3 mT m^{-1}

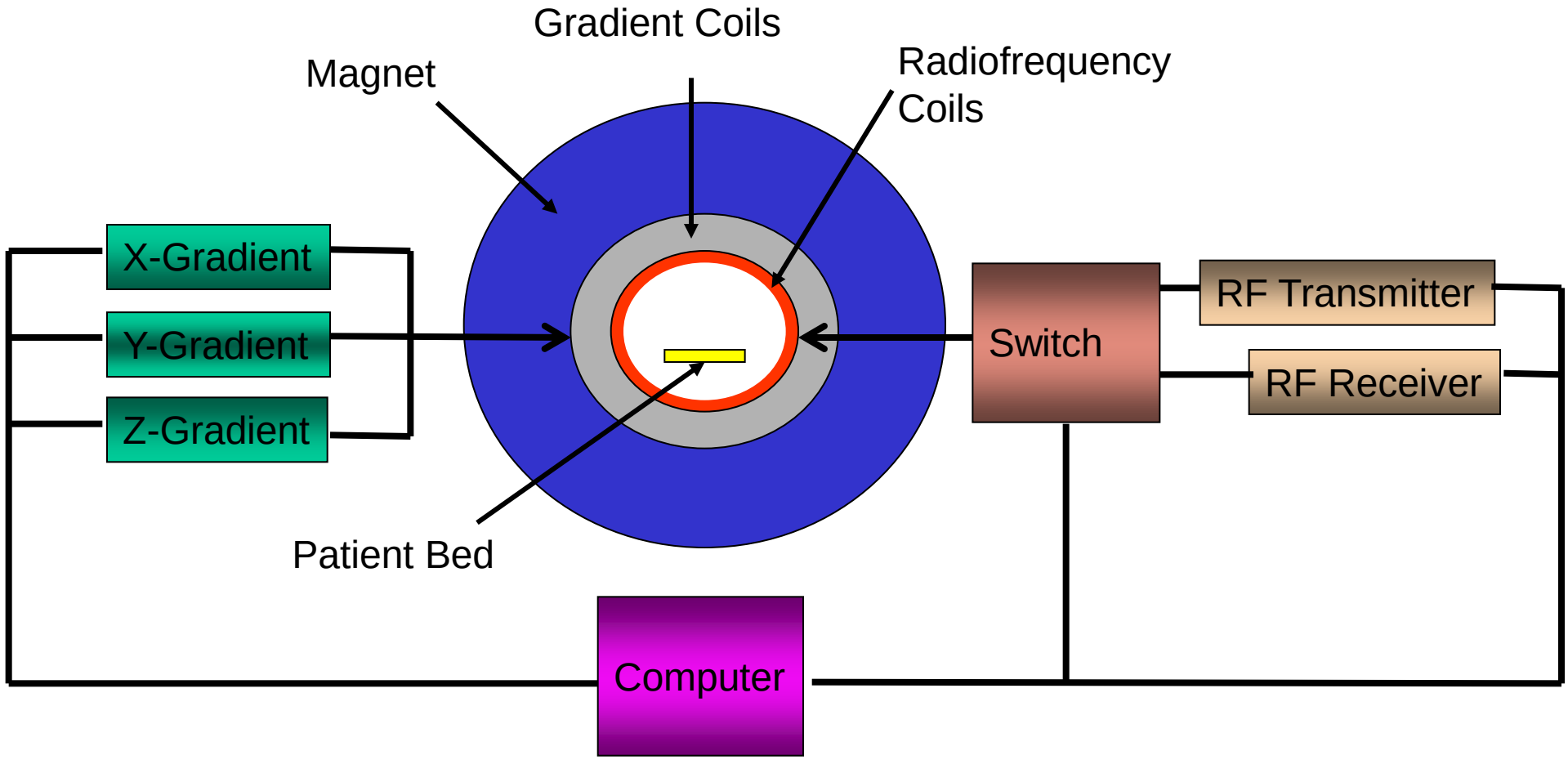
For slice selection:

$$G_z = 2\pi\Delta\upsilon/\gamma\Delta z = 10^{3}*2\pi/4.27*2\pi*10^{7}*2*10^{-3}$$

$$= 0.012 \text{ T.m}^{-1} \text{ or } 12 \text{ mT.m}^{-1}.$$

Note: (i) Image resolution improves (λ is smaller) if G_x, G_y, t_s or t_{enc} are increased. (ii) Slice thickness decreases if Gz is increased or $\Delta\upsilon$ is reduced (by lengthening RF pulse).

Block diagram of the key components of an MRI system



System Components

Magnet: The magnet usually has a 1m bore. Smaller systems are used for head-only scanning or animal research. The field strength is in the range 1.5 to 9 Tesla (64 to 400 MHz for proton resonance). The Earth's magnetic field is approx 0.5 Gauss ($1T = 10^4$ Gauss). There are 3 main types:

(i) Electromagnet (0.1 to 0.5 T); expensive in electricity to run, and tend to be unstable in field strength. Solenoid winding.

(ii) Permanent magnet (0.1 to 0.5 T); heavy and of a horseshoe design.

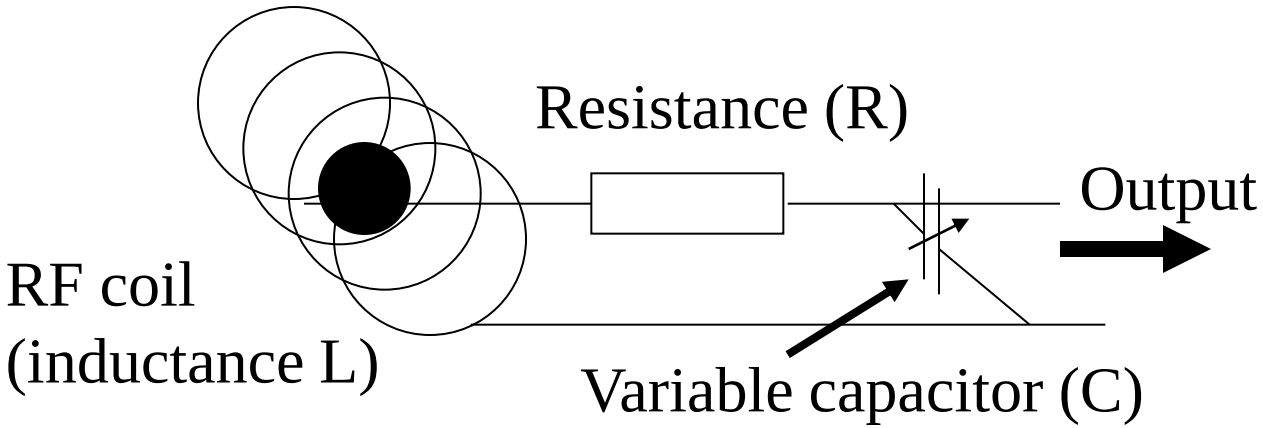
(iii) Superconducting magnet**.** Solenoid of wire cooled to -270 ^{0}C by immersion in a liquid helium jacket which keeps the wire cold by boiling at 4 ^{0}K. A refrigerator on the top re-cycles helium gas into liquid again. This is the most common type of magnet since it is very stable and can achieve higher field strengths eg. 9 T. The magnet usually has approx 50 km of superconducting wire carrying approx 200 Amps which flow continuously around a closed loop without needing a power supply. Periodic helium re-fills are needed.

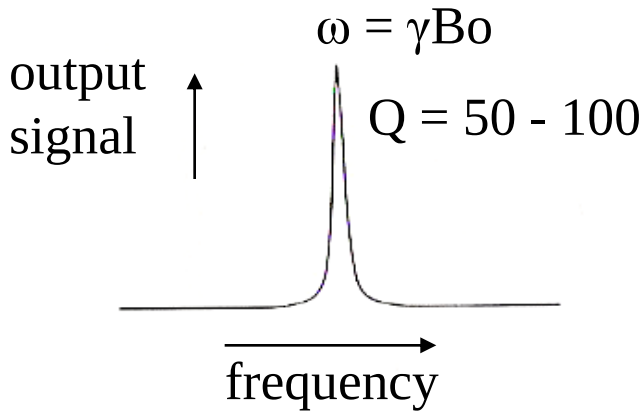
Shim Coils: To make the magnet as homogeneous as possible, and to adjust for changes in the magnetic field produced by the body itself, shim coils carrying small currents are used to "flatten" the magnetic field. These currents are often calculated and automatically applied by the MR system.

Gradient Coils: These produce the linear magnetic field gradients, and should produce a gradient over the field of view of the system. They should have a low inductance so that gradient producing currents can be rapidly switched on and off. Gradient switching is responsible for the audible noise generated by MRI scanners which can be quite loud.

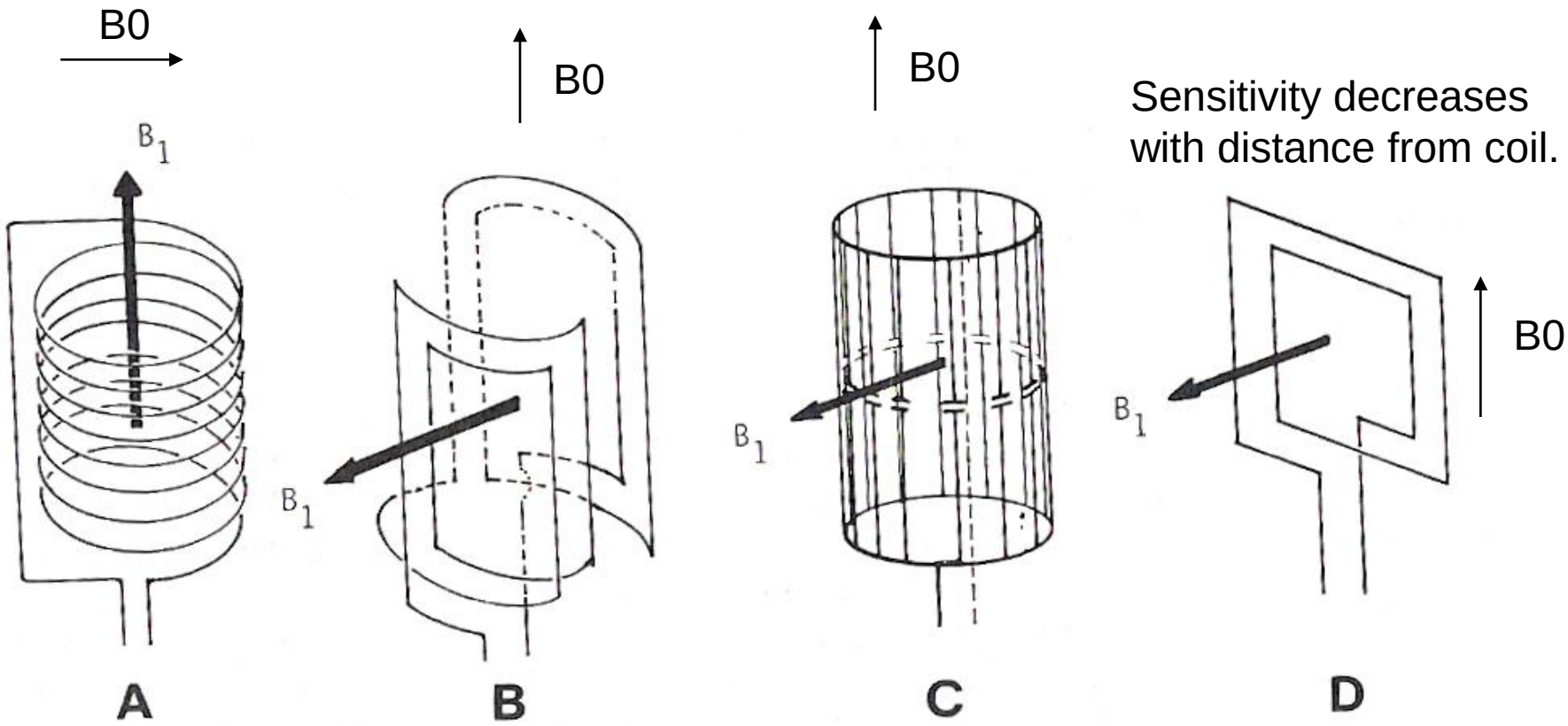
RF Coils: These are used to apply the RF pulses and to detect the much weaker NMR signals from the sample. To increase sensitivity, they are always "tuned" circuits (using variable C) set at the Larmor resonance frequency. Volume coils enclose the object and are designed to give a uniform response over the field of view. Surface coils consist of loops that are placed over the region of interest if it is on the periphery of the body, and although they are not uniform, are very sensitive. This can be used to produce images of approx twice the spatial resolution or greater. They are often used to image the spinal column and limbs.

Tune C to make $\omega = 1/\sqrt{LC}$. The MR signal is multiplied up by a factor $Q = \omega L/R$.





Various RF coil types. Note that the B1 field is always applied perpendicular to the direction of B0. A, B and C are all designed for RF uniformity. The surface coil, being closer to the tissue of interest, detects more signal that can be used to obtain higher resolution.



The four types of RF coil used in MRI: (A) solenoid, (B) saddle coil (C) birdcage coil and (D) surface coil

The RF coil must first handle a powerful RF pulse for signal excitation (typically 1Kwatt), and then be able to detect NMR signals of a few micro-volts and pass these to a sensitive pre-amplifier. An RF switch is used to isolate the high power transmitter amplifier from the sensitive receiver pre-amplifier.

Receiver System: This consists of the main receiver RF amplifier, demodulator and phase sensitive detector, audio filter circuit, and analogue to digital converter. The purpose of the last three were explained in the FT section.

Computer System: This consists of a central processor for performance of FT's (sometimes an array processor), devices for data storage, an image display processor and image display screen. The computer controls the RF pulse and gradient and shaping. The actual pulse sequence is usually timed out using another control processor (the gradient and RF controller) having been programmed by the computer. The imaging sequence may be triggered through the computer to freeze the effects of cardiac or respiratory motion.

RF and Magnetic Screen: The magnet is often placed in an iron box or between two large iron plates in order to reduce the influence of spreading magnetic fields on the surrounding environment. The recommendation is that the public should not be exposed to persistent fields of greater than 5 Gauss. Approximately 10 to 50 Gauss have a strong distortional effect on TV screens can affect heart pacemakers, and can wipe credit cards. Some magnets are self-shielded using a second set of coils external to the main magnet. The opposing set of magnet coils outside of the magnet reduces the spread of the field (self-shielding).

The RF screen is usually incorporated into the magnetic shield if it exists. It is made of copper and completely encloses the system. It is designed to prevent external RF noise from entering the system and being picked-up by the RF coil (this would reduce S/N ratio). It also prevents the RF pulses generated in the system from "polluting" the external environment. Any connections to the outside world must be filtered to remove noise as they enter the RF shielded room to prevent conduction into the system (eg. gradient cables, physiological monitoring etc.).