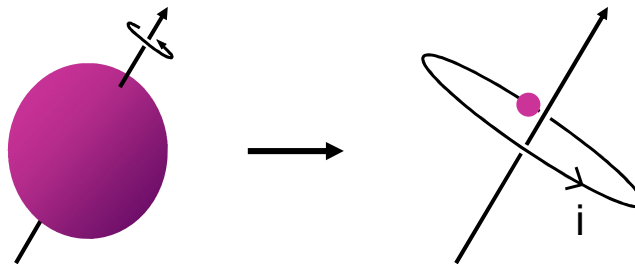


## 1. Nuclear magnetic resonance

### 1.1 Classical derivation of gyromagnetic ratio



The spin of a proton can be interpreted as a positive charge orbiting the spin axis.

And the orbiting charge can be interpreted as a current  $i$  flowing in a very small loop of wire.

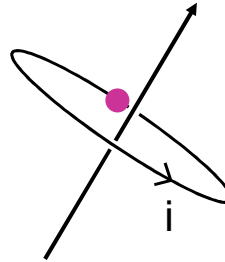
Consider charge  $e$  moving in circular orbit:

radius =  $r$   
 mass =  $m$   
 velocity =  $v = r\omega$   
 period =  $\tau$

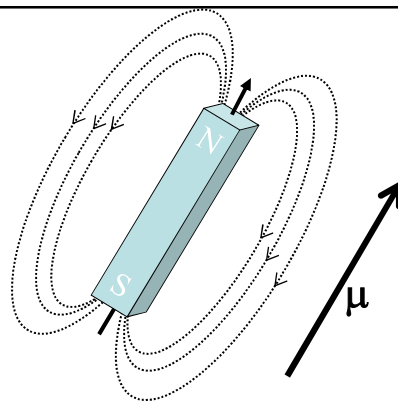
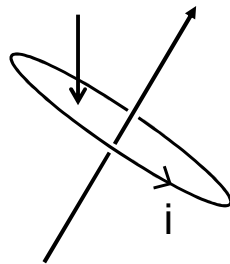
$$\Rightarrow \text{current } i = e / \tau$$

But  $v = 2\pi r / \tau$

$$\Rightarrow i = ev / 2\pi r$$



Loop area  $A$



A current loop produces a magnetic field which is the same at large distances as that of a magnetic dipole (i.e. a tiny bar magnet) at centre of loop and orientated perpendicular to plane.

For current  $i$  in loop of area  $A$ , the magnitude of the magnetic moment of equivalent dipole is given by:

$$\mu = iA$$

$$\Rightarrow \mu = (ev / 2\pi r) \cdot \pi r^2 = evr/2$$

But we have a rotating *mass* as well as rotating *charge*. And a rotating mass has *angular momentum*  $\mathbf{L}$ .

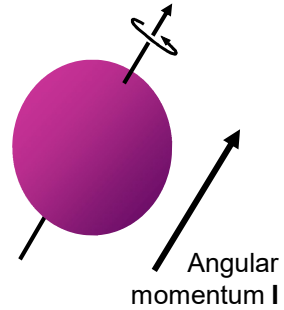
$\mathbf{L}$  has orientation and magnitude given by:

$$\mathbf{L} = \mathbf{r} \wedge \mathbf{p}$$

where  $\mathbf{p}$  = linear momentum vector =  $m\mathbf{v}$ .

$$\Rightarrow \mathbf{L} = m \mathbf{r} \wedge \mathbf{v}$$

In a circular orbit  $\mathbf{r}$  and  $\mathbf{v}$  are perpendicular:  $\Rightarrow L = mrv$



Thus ratio of magnitude of magnetic moment to magnitude of angular momentum is given by:

$$\mu/L = evr / 2mr = e/2m = \gamma.$$

$\gamma$  is called the gyromagnetic ratio.

### The story so far:

- The hydrogen nucleus (proton) can be represented as a rotating sphere with mass  $m$  and charge  $e$ .
- The mass gives rise to an *angular momentum*  $I$ , and the charge gives rise to a *magnetic moment*  $\mu$ .
- The ratio is a constant:  $\mu/I = \gamma$ .

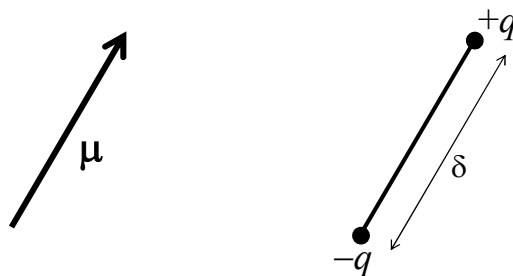
## 1.2 Effect of an external magnetic field

The **magnetic moment** is equivalent to two magnetic monopoles of opposite sign, separated by distance  $\delta$ .

Thus in vector form:  $\mu = q\delta$

where  $q$  = magnetic strength of each pole,

and  $\delta$  = vector from negative (south) to positive (north) pole.



An external magnetic field exerts a force of magnitude  $qB$  on positive pole and a force of same magnitude but opposite direction on negative pole.

Reminder: Magnetic force  $\mathbf{F} = q\mathbf{B}$

Thus there is no net translational force. But dipole experience a torque equal to sum of moments.

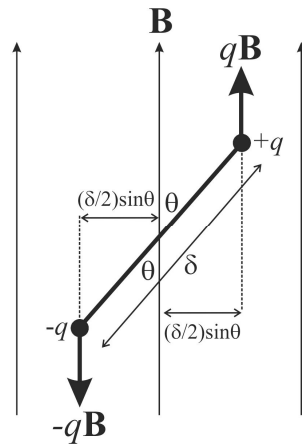
Reminder:

Moment = force  $\times$  perpendicular distance

$$T = qB (\delta/2) \sin\theta + qB (\delta/2) \sin\theta$$

$$\Rightarrow T = qB\delta \sin\theta$$

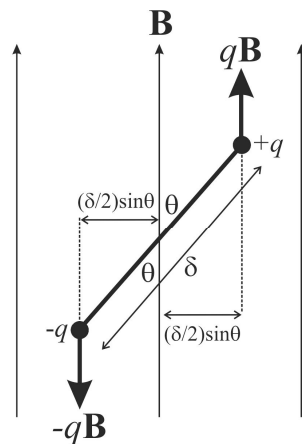
$$\Rightarrow T = \mu B \sin\theta \quad (\text{Since } \mu = q\delta)$$



The torque is represented by a vector  $\mathbf{T}$  perpendicular to both  $\boldsymbol{\mu}$  and  $\mathbf{B}$ :

$$\mathbf{T} = \boldsymbol{\mu} \wedge \mathbf{B}$$

Its direction is such that  $\boldsymbol{\mu}$  tends to align with  $\mathbf{B}$  (right hand corkscrew rule).



But what happens if  $\mu$  cannot align with  $\mathbf{B}$ ?

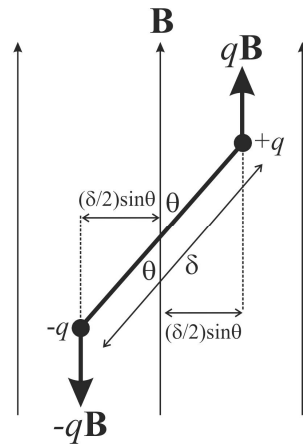
Since  $\mathbf{T} = \mu \wedge \mathbf{B}$  and  $\mu = \gamma \mathbf{I}$ :

$$\Rightarrow \mathbf{T} = \gamma \mathbf{I} \wedge \mathbf{B}$$

However, from Newton's second law of motion:

$$\mathbf{T} = \frac{d\mathbf{I}}{dt} \quad (\text{equivalent to } \mathbf{F} = d\mathbf{p}/dt)$$

$$\Rightarrow \frac{d\mathbf{I}}{dt} = \gamma \mathbf{I} \wedge \mathbf{B}$$



Thus the *change* in  $\mathbf{I}$  occurs in a direction perpendicular to both  $\mathbf{I}$  and  $\mathbf{B}$ .

$$d\mathbf{I} = \gamma \mathbf{I} \wedge \mathbf{B} dt$$

In time  $dt$ , tip of vector  $\mathbf{I}$  moves through an angle  $d\phi = dI / (I \sin\theta)$

$$\Rightarrow d\phi = \gamma \mathbf{I} \wedge \mathbf{B} dt / (I \sin\theta)$$

$$\Rightarrow d\phi = \gamma I B \sin\theta dt / (I \sin\theta) = \gamma B dt$$

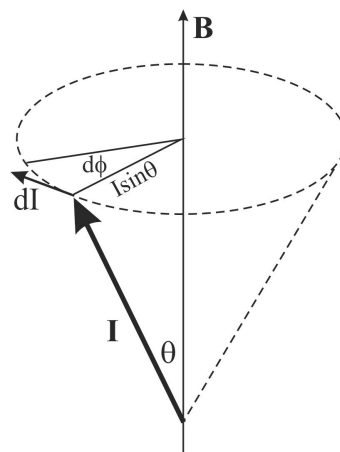
Thus the angular frequency  $\omega_0$  is given by:

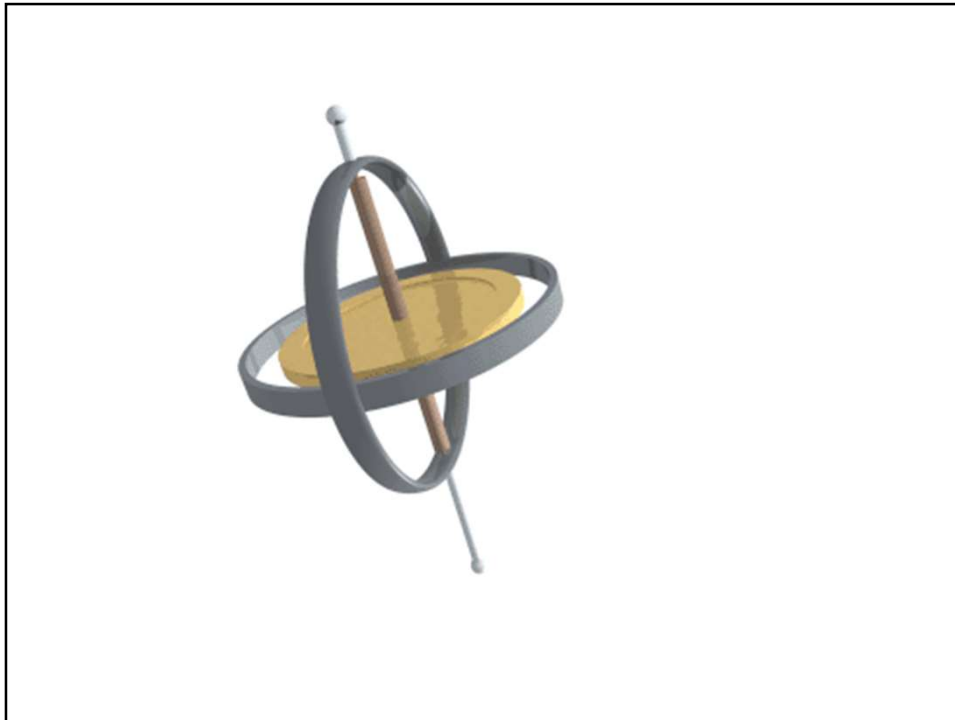
$$\omega = d\phi/dt = \gamma B$$

or  $f = \gamma B / 2\pi$

Thus  $\mu$  precesses around  $\mathbf{B}$ , maintaining constant  $\theta$ .

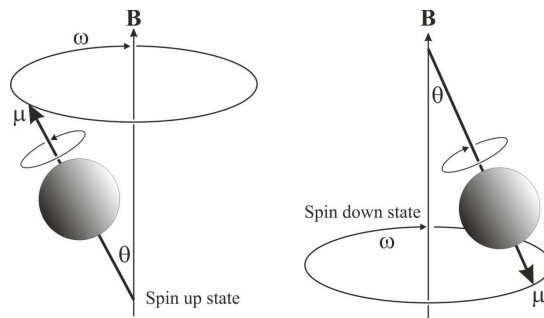
This is known as the Larmor Precession Frequency.





### The story so far:

- The hydrogen nucleus (proton) can be represented as a rotating sphere with mass  $m$  and charge  $e$ .
- The mass gives rise to an *angular momentum*  $I$ , and the charge gives rise to a *magnetic moment*  $\mu$ .
- The ratio is a constant:  $\mu/I = \gamma$ .
- A magnetic moment at an angle  $\theta$  with an external field experiences a torque which tries to align it with field.
- If the moment cannot align, the torque causes moment to precess at frequency  $\omega_0 = \gamma B$ .

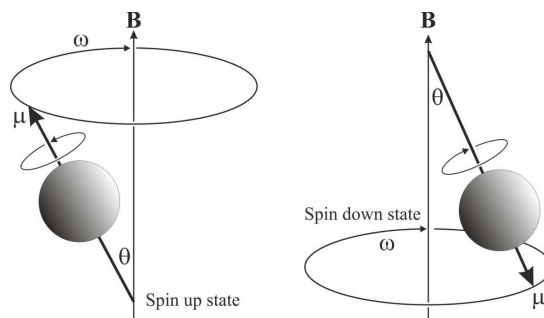


From rules of quantum mechanics:

- The magnetic moment  $\mu$  of proton cannot align exactly with a magnetic field – it can only occupy one of two states: “spin up” and “spin down” (both at  $54.7^\circ$  to  $\mathbf{B}$ ).
- The spin down state requires slightly more energy. The difference in energy is:

$$\Delta E = hf = \gamma h B / 2\pi$$

where  $h$  = Planck's constant.



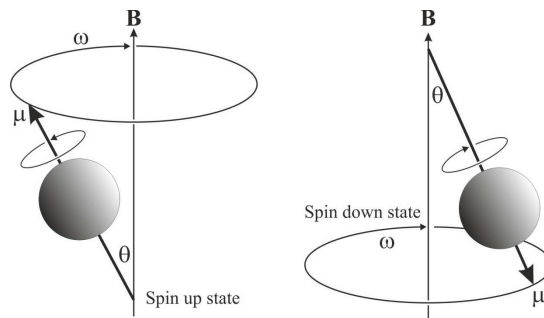
- When  $\mathbf{B}_0$  is applied an equilibrium will be established with more nuclei in lower energy “spin up” state.

The ratio of numbers in two states is given by the Boltzmann distribution:

$$\frac{n(\text{spin up})}{n(\text{spin down})} = \exp\left(\frac{\Delta E}{kT}\right) = \exp\left(\frac{\gamma h B}{2\pi k T}\right)$$

where  $k$  = Boltzmann's constant, and  $T$  = absolute temperature of spin system.





For protons in a 1 Tesla magnetic field at 20°C:

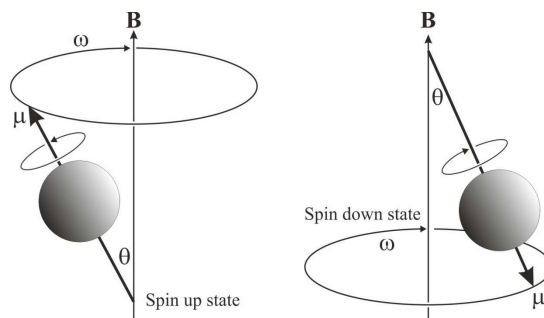
$$\Rightarrow \Delta E \approx 2.83 \times 10^{-26} \text{ J} \quad \text{and} \quad kT \approx 4.05 \times 10^{-21} \text{ J}$$

$$\Rightarrow \Delta E / kT \approx 7 \times 10^{-6}$$

For small  $x$ :  $\exp(x) \approx 1 + x$

$$\Rightarrow \exp(\Delta E/kT) \approx 1 + (\gamma \hbar B / 2\pi kT) \approx 1 + 7 \times 10^{-6}$$

Therefore  $\exp(\Delta E/kT)$  is very near unity. The excess of protons in a spin up state is  $\approx 7 \times 10^{-6}$ .



Every gram of water contains about  $10^{23}$  H-nuclei (protons). In B field of 1 Tesla, magnetic moment of each proton will precess at Larmor frequency equal to:

$$\omega_0 = \gamma B = 2.67 \times 10^8 \text{ radians/s}$$

in either the *spin-up* or *spin-down* state.

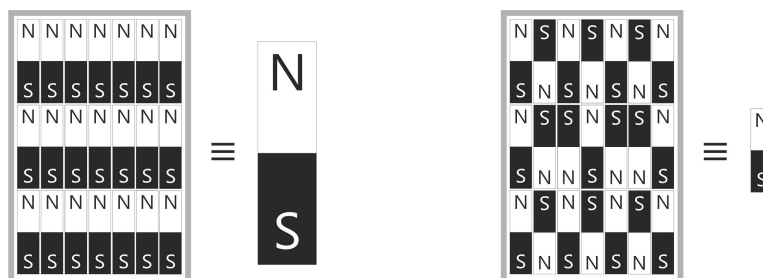
A small majority (7 protons per million) will occupy the lower-energy spin up state.

Values of  $\gamma$  cannot be predicted for all nuclei by the classical analysis presented above (needs quantum mechanics). Only a few nuclei with “spin” will have a magnetic moment and hence can give rise to a nuclear magnetic resonance signal (section 1.4).

Nucleus	f (at B = 1T)	Relative sensitivity
$^1\text{H}$	42.6 MHz	100
$^{19}\text{F}$	40.0 MHz	83
$^{23}\text{Na}$	11.3 MHz	9.3
$^{31}\text{P}$	17.3 MHz	6.6

Relative sensitivity = relative to that of an equal number of protons, and depends on  $\gamma$ .

### 1.3 Net magnetisation vector



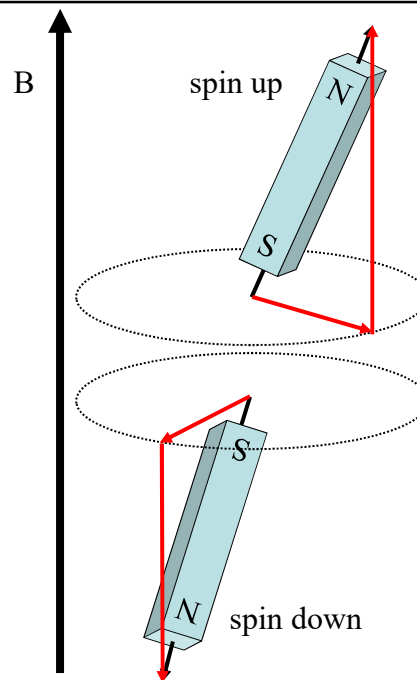
Consider a box of 21 identical magnets.

If all are aligned in same direction, the net magnetic field will be 21 times larger than field of one magnet.

If 11 are aligned in one direction, and 10 in the other, the net magnetic field will be equivalent to that of just one magnet.

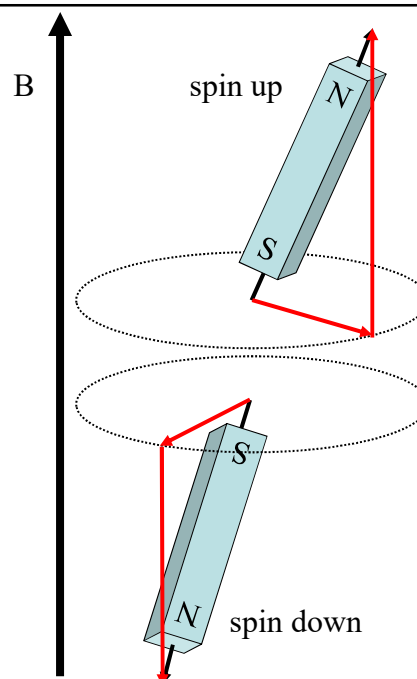
The total field produced by adding magnetic moments of billions of hydrogen nuclei in a sample of water is called the *net magnetisation vector*  $\mathbf{M}$ .

A small majority (7 per million) of those nuclei will occupy lower-energy spin-up state, and therefore there is net component pointing upwards (in same direction as  $\mathbf{B}$ ).



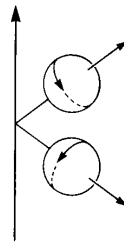
The perpendicular ( $xy$ ) components of magnetic moments for both spin up and spin down states add up to zero.

Thus  $\mathbf{M}$  will be aligned with  $\mathbf{B}$  (along  $z$  axis).



### The story so far:

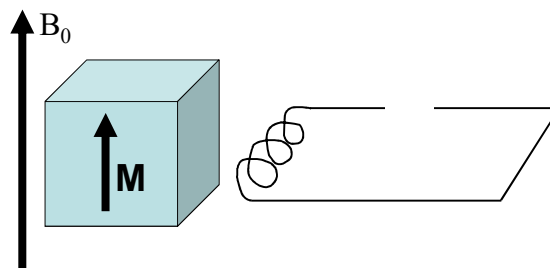
- Hydrogen nuclei (a single proton) have a "magnetic moment", equivalent to that of a tiny bar magnet.
- The rules of quantum mechanics prevent this moment from aligning exactly with an external field. Instead a proton aligns in either the "spin up" or "spin down" state.
- Because the moment cannot align exactly, the moment experiences a torque which causes moment to precess at a frequency  $\omega_0 = \gamma B$ .
- Slightly more protons occupy the "spin up" state than the "spin down" state, and therefore a sample containing a very large number of nuclei will have a *net magnetisation*  $\mathbf{M}$  which aligns with  $\mathbf{B}$ .



Nuclear alignment in a magnetic field

## 1.4 Nuclear magnetic resonance

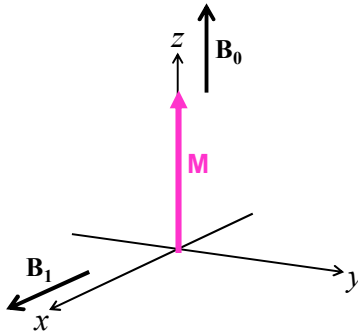
Suppose that the orientation of the net magnetisation  $\mathbf{M}$  can be changed so that it induces a current in a nearby coil of wire.



Let's assume it is possible to change orientation of  $\mathbf{M}$  using a second external magnetic field.

Main external field =  $\mathbf{B}_0$

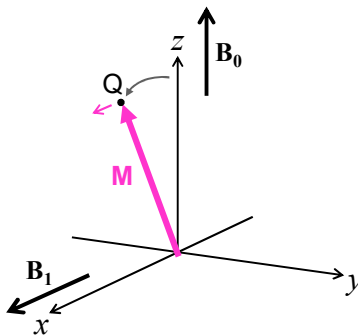
Second (much weaker) applied field =  $\mathbf{B}_1$  ( $B_1 \ll B_0$ )



Initially net magnetisation  $\mathbf{M}$  will be aligned parallel to  $\mathbf{B}_0$  along  $z$  axis.

Suppose another magnetic field  $\mathbf{B}_1$  is then applied along  $x$  direction.

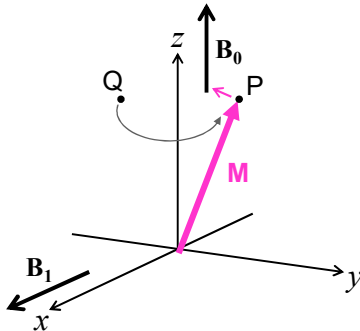
When a magnetic moment is not parallel to an external field, it will precess around the field direction at rate  $\omega = \gamma B$ .



Thus  $\mathbf{M}$  will begin to precess around  $x$  axis, moving it away slightly from  $z$  axis towards point Q.

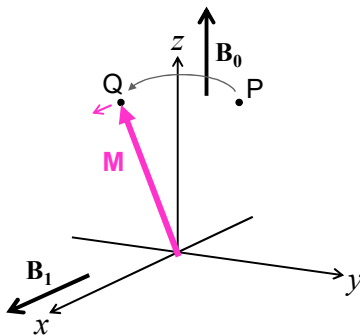
Then  $\mathbf{M}$  is no longer parallel to  $\mathbf{B}_0$ , and will precess around the  $z$  axis too.

Since  $\mathbf{B}_0 \gg \mathbf{B}_1$ , precession around  $z$  axis is much faster.



Thus **M** will precess very quickly around  $z$  axis away from point Q.

At point P the slow precession around  $x$  causes **M** to move towards  $z$  axis.



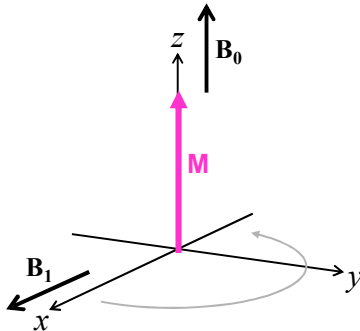
Thus **M** will precess very quickly around  $z$  axis away from point Q.

At point P the slow precession around  $x$  causes **M** to move towards  $z$  axis.

But very quickly, **M** is again near point Q, and then slow precession around  $x$  cause **M** to move away from  $z$  axis again.

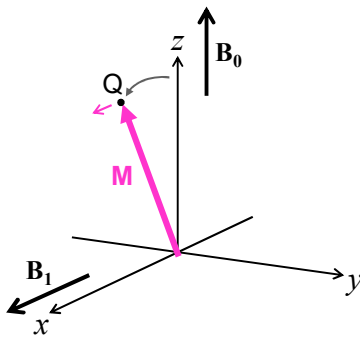
The combined effect of both precessions prevents **M** from moving far from  $z$  axis.

Since **M** will not move much, very little signal will be detected by coil.

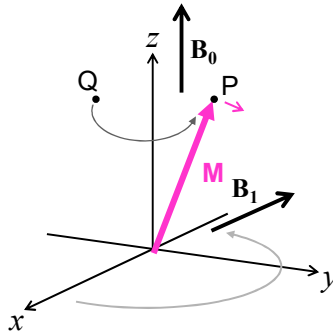


Let's try something else to move  $\mathbf{M}$  away from the  $z$  axis.

Suppose we rotate  $\mathbf{B}_1$  around  $\mathbf{B}_0$  at same frequency as precession around the  $z$  axis (i.e. at Larmor frequency).



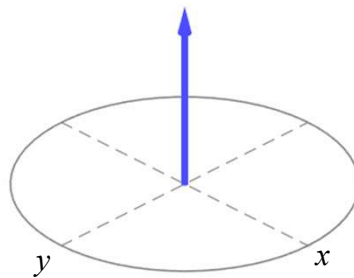
When  $\mathbf{B}_1$  points along  $x$  axis,  $\mathbf{M}$  will attempt to precess around  $x$  axis as before towards point  $\mathbf{Q}$ , and then also precess around  $z$  axis.



However, while rapid precession about  $z$  axis moves  $\mathbf{M}$  from point  $\mathbf{Q}$  to  $\mathbf{P}$ , the field  $\mathbf{B}_1$  will *also* have rotated (at same frequency) so that it now points along *minus*  $x$  direction.

So  $\mathbf{M}$  will now try to precess around *minus*  $x$  direction. This will cause  $\mathbf{M}$  to move *further* away from  $z$  axis!

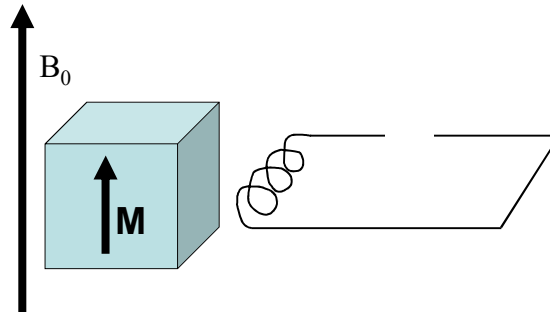
Blue arrow =  $\mathbf{B}_0 + \mathbf{B}_1$   
Pink arrow =  $\mathbf{M}$



Thus  $\mathbf{M}$  spirals away from  $z$  direction into  $xy$  plane!

This only occurs when  $\mathbf{B}_1$  field is rotated at Larmor frequency (hence the term “resonance”).



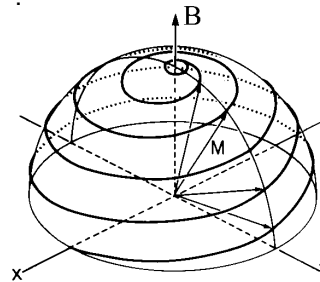


Suppose our coil near sample is sensitive to changes in magnetic field in  $x$  or  $y$  direction. When  $\mathbf{M}$  is tilted into  $xy$  plane, coil experiences a magnetic field which varies sinusoidally at Larmor frequency, which induces a small alternating current to flow. This is signal we use to make MRI images.

For obvious reasons, the  $\mathbf{B}_1$  signal which causes  $\mathbf{M}$  to tilt into  $xy$  plane is known as a  $90^\circ$  pulse.

Thus if  $\mathbf{B}_1$  is applied until  $\mathbf{M}$  is tilted by  $90^\circ$  :

- $\Rightarrow M_z = 0$
- $\Rightarrow M_{xy}$  is a rotating RF field which will induce a signal in a suitable coil.



**Example:** For how long must a  $\mathbf{B}_1$  field of  $30 \mu\text{T}$  be applied to produce a  $90^\circ$  pulse?

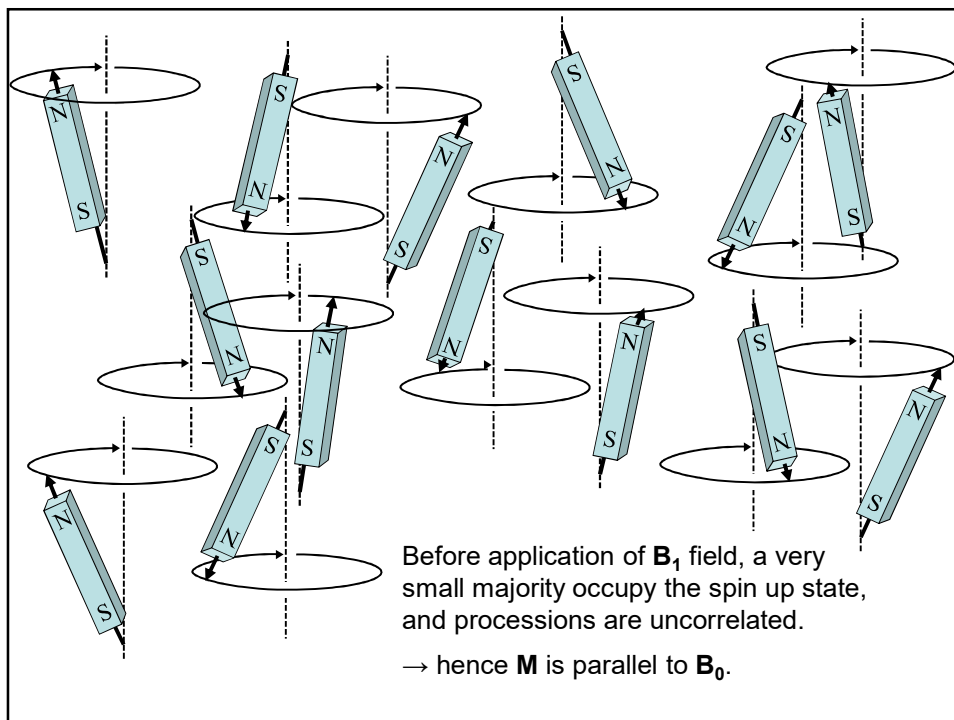
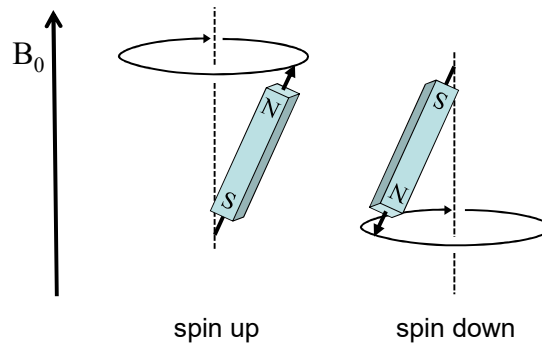
Consider precession away from the  $z$  direction due to the  $\mathbf{B}_1$  field:

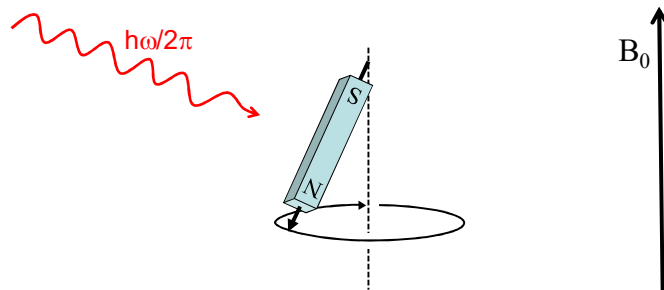
$$\omega = \gamma B = \text{angle (in radians) per unit time} = \theta/\tau$$

$$\tau = \theta/\gamma B_1 = (\pi/2)/(267 \times 10^6 \times 30 \times 10^{-6}) = 196 \times 10^{-6} \text{ s.}$$

### What is the effect on individual magnetic moments (spins)?

Every magnetic moment ("spin") in an external field is always continuously precessing in either spin up or spin down state.



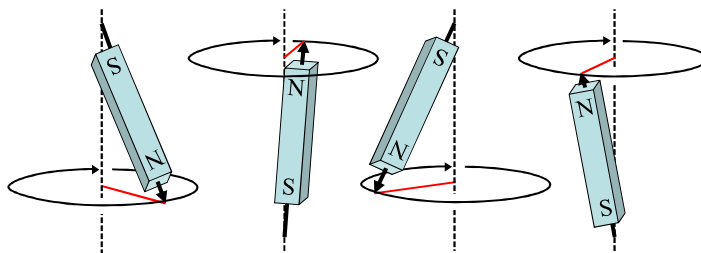


When  $\mathbf{B}_1$  is applied, some protons absorb quantum of energy ( $\hbar\omega/2\pi = \gamma\hbar B/2\pi$ ) causing them to switch from spin-up to higher energy spin-down state.

This reduces the vertical component of  $\mathbf{M}$ , which we denote as  $M_z$ .

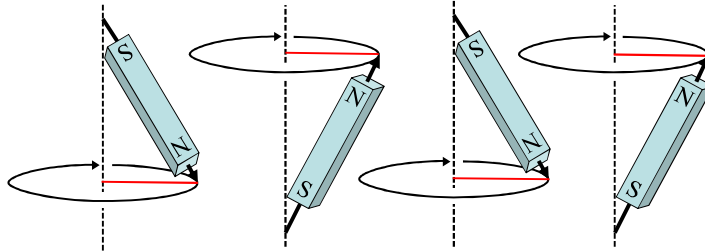
Following  $90^\circ$  pulse, equal numbers of protons are in the spin up and spin down states, and  $M_z = 0$ .

Before  $\mathbf{B}_1$



Before application of  $\mathbf{B}_1$  field, the precessions of the spins are uncorrelated.

After  $\mathbf{B}_1$



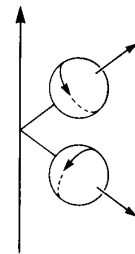
The  $\mathbf{B}_1$  field also encourages magnetic moments to precess *in phase with each other*, so all point in same direction at same time.

Thus horizontal component of  $\mathbf{M}$ , denoted as  $M_{xy}$ , is no longer zero.

Reduction in  $M_z$  and growth of  $M_{xy}$  has effect of rotating  $\mathbf{M}$  into  $xy$  plane.

### The story so far:

- Every Hydrogen nucleus effectively contains a tiny bar magnet (magnetic moment). In an external  $\mathbf{B}_0$  field, rules of quantum mechanics demand that these adopt either a “spin up” or “spin down” state.



Nuclear alignment in a magnetic field

- Because the moment (“spin”) cannot align exactly with  $\mathbf{B}_0$ , each moment experiences a torque which causes it to precess at the Larmor frequency  $\omega_0 = \gamma B_0$ .
- The total field  $\mathbf{M}$  due to all spins aligns parallel with  $\mathbf{B}_0$ , although fields of individual spins cannot.
- $\mathbf{M}$  can be realigned away from  $\mathbf{B}_0$  direction by adding another  $\mathbf{B}_1$  field which rotates at exactly the Larmor frequency.

## 1.5 Relaxation

If the precessing spins remain in phase and do not lose energy, we will detect a continuous signal.

However, in practice there are two mechanisms which cause the signal to decay. These are known as *relaxation mechanisms*.

### a) Spin-Lattice Relaxation (Longitudinal)

This causes return of relative populations of spin states to their original (non-equal) distribution, and the re-growth of  $\mathbf{M}$  along  $z$  axis. This involves *loss of energy* from the nuclear spins to their molecular environment (lattice).

The behaviour of  $M_z$  is described by:

$$\frac{dM_z}{dt} = \frac{M_0 - M_z}{T_1}$$

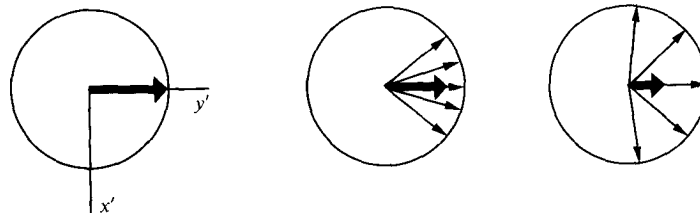
where  $T_1$  = the longitudinal relaxation time  
and  $M_0$  = initial steady state magnetisation of  $\mathbf{M}$ .

This has solution:  $M_z = M_0 [1 - \exp(-t/T_1)]$

The switch between spin states (and return to equilibrium) is caused by transfer of energy to molecular environment ("lattice"), and is more likely to occur when nucleus is able to move freely. Thus  $T_1$  is shorter in liquids than in solids.

In solutions: 100 ms  $\rightarrow$  10 sec  
In solids: Several minutes

*b) Spin-Spin Relaxation (Transverse)*



This causes decay of  $xy$  component of  $\mathbf{M}$ , when individual spins no longer precess in phase with each other.

If they precess at slightly different speeds, they will eventually be pointing in random directions again, and  $xy$  component of  $\mathbf{M}$  will be zero. This is called loss of "phase coherence".

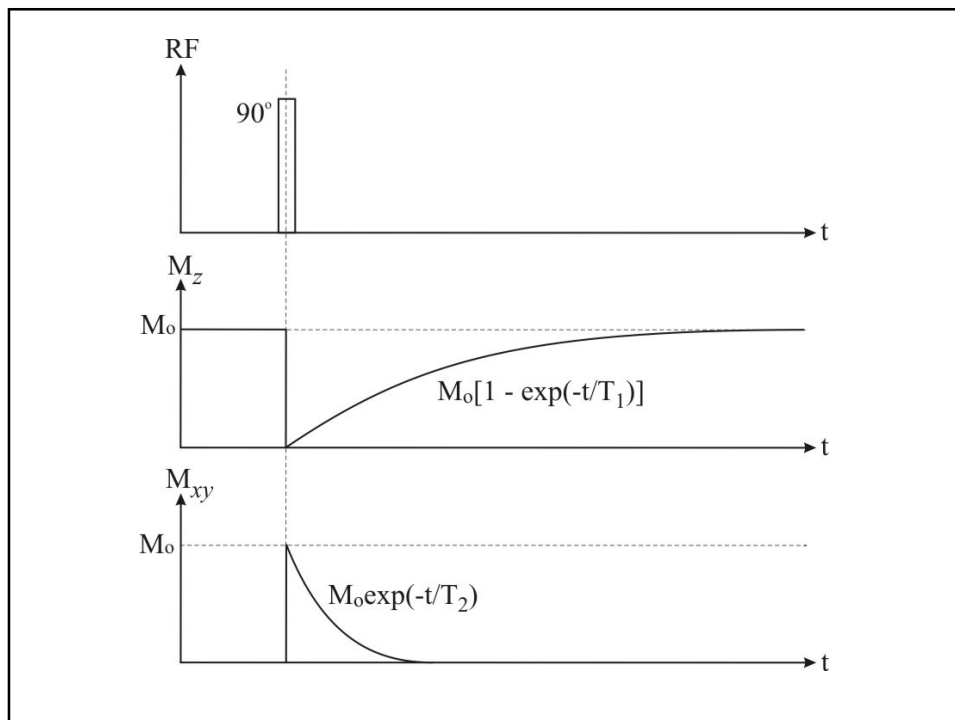
Note that there is *no loss of energy* (no change in spin-up/spin-down distribution). Different field strengths for different nuclei leads to different precession rates ( $\omega = \gamma B$ ).

Thus  $M_{xy}$  decays according to: 
$$\frac{dM_{xy}}{dt} = \frac{-M_{xy}}{T_2}$$

where  $T_2$  = the transverse relaxation time. This has solution:

$$M_{xy} = M_0 \exp(-t/T_2)$$

This is caused by variation in local magnetic field and coupling between adjacent spins.



Note that  $T_2$  is always less than  $T_1$  (and typically  $< 100$  ms). The greater the spread in values of  $\omega_0$ , the more rapidly  $M_{xy}$  decays.

Since  $T_2 < T_1$ , transverse component of  $\mathbf{M}$  decays more quickly than longitudinal component recovers.

Following a  $90^\circ$  pulse (when  $\mathbf{M}$  is tilted into  $xy$  plane), a coil placed near sample will experience magnetic field which varies sinusoidally at Larmor frequency.

The horizontal component  $M_{xy}$  induces signal  $s(t)$  in coil known as the free induction decay (FID).

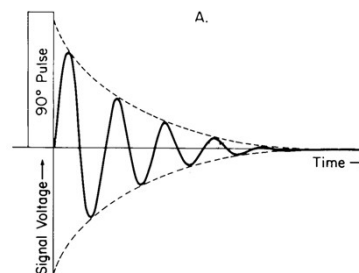
$$s(t) = A \cos \omega_0 t \cdot \exp(-t / T_2^*)$$

where  $T_2^*$  is smaller than inherent  $T_2$  of sample because of additional systematic effects, primarily field inhomogeneity  $\Delta B$ .

$T_2^*$  is described by:

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{\gamma \Delta B}{2}$$

Amplitude  $A$  is proportional to number of nuclei in sample.





## 1.6 Chemical shift

Applied field  $\mathbf{B}_0$  can induce electronic currents in atoms/molecules which produce a further small magnetic field in vicinity of given nucleus.

Thus the effective field  $\mathbf{B}_{\text{eff}}$  at nucleus is given by:

$$\mathbf{B}_{\text{eff}} = \mathbf{B}_0 (1 - \sigma)$$

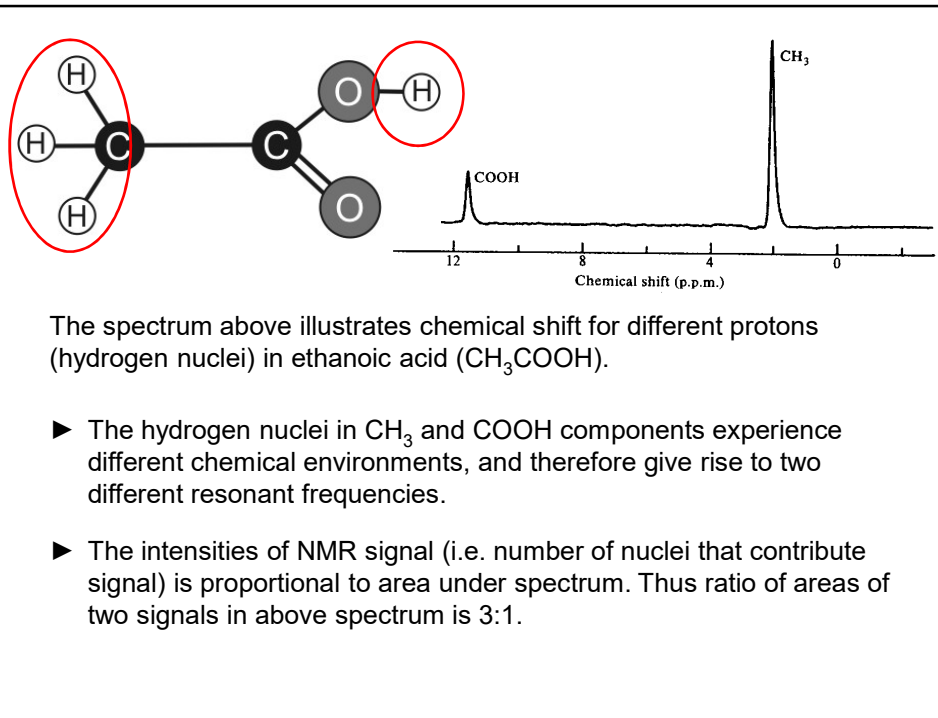
*Shielding constant*  $\sigma$  is typically  $\sim 10^{-6}$  to  $10^{-3}$ .

It is dependent upon electronic environment of nucleus, and thus identical nuclei in different chemical environments give rise to signals at different frequencies.

The difference between an observed resonance frequency and an arbitrary reference frequency is called the *chemical shift*.

Chemical shift is conventionally expressed in dimensionless units of parts per million (p.p.m.) relative to the reference frequency:

$$\text{Chemical shift} = \frac{f - f_{\text{ref}}}{f_{\text{ref}}} \times 10^6 \text{ p.p.m.}$$



NMR spectroscopy of  $\text{P}^{31}$  nuclei is commonly used to study human metabolism. Phosphorous nuclei in adenosine triphosphate (ATP), phosphocreatine (PCr) and inorganic phosphate (Pi) provide a broad range of different resonances due to chemical shift.