

## **Nuclear Magnetic Resonance**

References: "Methods of Experimental Physics," **20**, Academic Press, New York, pp 1–52.

CS II, pp. 481–525.

Principles of Magnetic Resonance, C. P. Slichter, Chapters 1 and 2

Nuclear Magnetic Resonance Spectroscopy, R. K. Harris, Pitman Books, London, 1983, Chapters 1 and 3

NMR is one of the most powerful spectroscopic tools for studying the structure of molecules in solution. The method exploits the magnetic nuclei in molecules and the sensitivity of their NMR transitions to

- (a) electronic environment
- (b) geometric disposition *vis a vis* other magnetic nuclei, both in terms of the number of intervening bonds and the distance directly through space
- (c) molecular motion or dynamic state

For this course, these molecules are metabolites and biological precursors, nucleic acids, proteins, membrane components, and cellular components.

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<u>Magnetic nuclei:</u>	$^1\text{H}$ , $^{13}\text{C}$ , $^{15}\text{N}$ , $^{31}\text{P}$ , $^{19}\text{F}$	$I = 1/2$
	$^2\text{H}$ , $^{14}\text{N}$	$I = 1$
	$^{23}\text{Na}$ , $^{35}\text{Cl}$ , $^{39}\text{K}$ , $^{37}\text{Cl}$	$I = 3/2$
	$^{17}\text{O}$ , $^{25}\text{Mg}$	$I = 5/2$
	$^{43}\text{Ca}$	$I = 7/2$

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NMR is also a noninvasive method<sup>1</sup> for monitoring or following cellular components, identifying them, following their concentrations, their biochemical transitions and transformations, and their metabolic states.

NMR has also recently evolved as a tool for imaging, permitting *in situ* noninvasive delineation of organs, bone, blood vessels etc.

To do NMR, the sample must be placed in a magnetic field and the spins in the sample must be magnetically polarized. There must be a source of rf to excite the spins so that they make transitions among the spin energy states.

## **Physics of NMR — Classical Picture**

### **Motion of Spin in a Magnetic Field**

Associated with a magnetic nucleus of spin  $I$ , there is a magnetic moment  $\vec{\mu}$  related to the angular momentum  $\vec{J}$  by the “gyromagnetic ratio”  $\gamma$ :

$$\vec{\mu} = \gamma \vec{J} = \gamma h \vec{I}$$

$I$  is a quantum mechanical quantity, but we can look at how classical mechanics describes the behavior of a magnetic moment. In a magnetic field,  $\vec{\mu}$  experiences a torque

$$\text{torque} = \vec{\mu} \times \vec{B}_0$$

This torque is equal to the rate of change of angular momentum  $\vec{J}$  (Newton’s law)

$$\frac{d\vec{J}}{dt} = \vec{\mu} \times \vec{B}_0$$

So in the laboratory frame of reference (x, y, z)

$$\frac{d\vec{\mu}}{dt} = \gamma (\vec{\mu} \times \vec{B}_0)$$

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<sup>1</sup> e.g., topical NMR or whole cell NMR, NMR of tissues

We can see the physical meaning of this expression by transforming to a reference frame  $(x', y', z)$  rotating about  $z$  with angular velocity  $\check{\omega}_0$  :

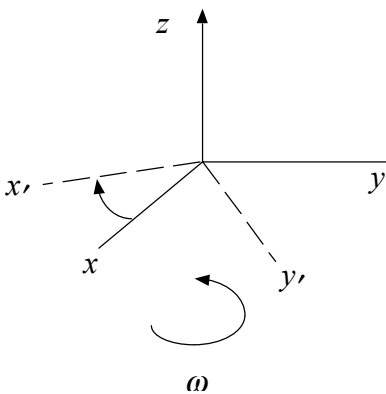


Figure 9-1

Such a transformation obeys

$$\left(\frac{d\check{\mu}}{dt}\right)_{lab\ frame} = \left(\frac{d\check{\mu}}{dt}\right)_{rotating\ frame} + (\check{\omega}_0 \times \check{\mu})$$

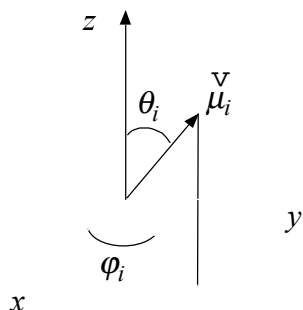
$$\therefore \left(\frac{d\check{\mu}}{dt}\right)_{rotating\ frame} = \gamma(\check{\mu} \times \check{B}_0) - (\check{\omega}_0 \times \check{\mu}) = \gamma\check{\mu} \times \left(\check{B}_0 + \frac{\check{\omega}_0}{\gamma}\right)$$

This last result shows that  $\check{\mu}$  is stationary in the rotating frame for which  $\left(\check{B}_0 + \frac{\check{\omega}_0}{\gamma}\right) = 0$ , i.e. for  $\check{\omega}_0 = -\gamma\check{B}_0 = \check{k}\omega_0$  where  $\omega_0$  is called the Larmor frequency.

Conversely, and more importantly, this shows that  $\check{\mu}$  “precesses” or rotates about a static magnetic field, with frequency  $\omega_0 = -\gamma B_0$ .

### An Ensemble of Isolated $\mu_i$ s in $\vec{B}_0$ : The Concept of Magnetization

There are many spins in the sample. Even for a sample where all the spins are the same, same  $\gamma$ , chemically identical,

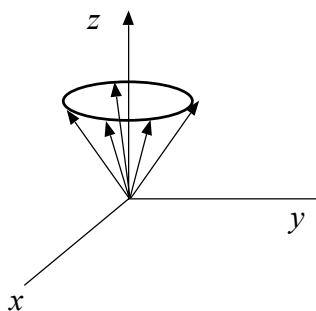


$\theta_i$  and  $\varphi_i$  are uncorrelated from one spin to another.

$$\text{Energy} = -\mu_i B_0 \cos \theta_i = -\vec{\mu}_i \cdot \vec{B}_0$$

$$\varphi_i = \text{arbitrary}$$

so that for all spins with the same  $\theta_i$ , hence same energy, random  $\varphi_i$ .



at thermal equilibrium

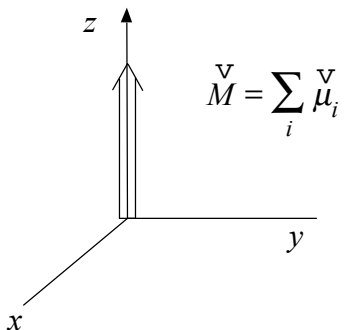
$$M_x(\theta) = \sum_i \mu_{xi} = 0 \quad M_x = \sum_{\theta} M_x(\theta) = 0$$

$$M_y(\theta) = \sum_i \mu_{yi} = 0 \quad M_y = \sum_{\theta} M_y(\theta) = 0$$

$$M_z(\theta) = \sum_i \mu_{zi} \quad M_z = \sum_{\theta} M_z(\theta)$$

Result: at thermal equilibrium, any bulk magnetization present is along the z axis.  $\vec{M}_z$  will be nonzero for  $\theta \neq 90^\circ$ . (Quantum mechanics will establish what values of  $\theta$  are allowed).

This is important because in an NMR experiment, we can follow only macroscopic magnetization.



In general, all spins with the same  $\gamma$  but different chemical environments, and all spins with different  $\gamma$  contribute to  $\vec{M}$  (may not be able to excite them all at the same time).

### Phenomenon of Magnetic Resonance

Consider one of these spins that make up  $\check{M}$  in the magnetic field. It will be precessing about  $\check{B}_0$  with angular frequency  $\check{\omega} = \gamma \check{B}_0$ .

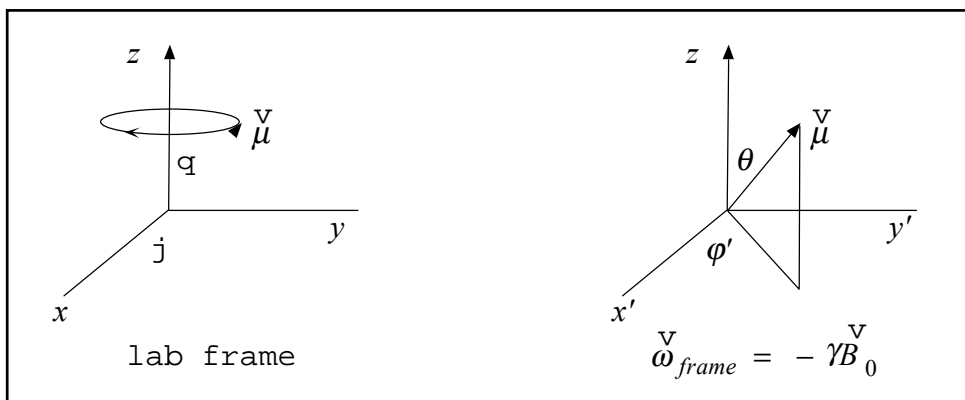
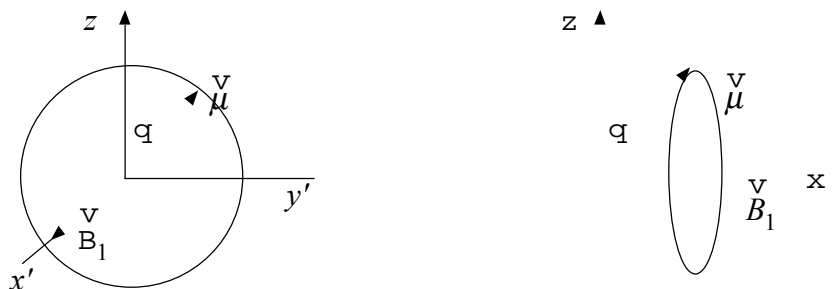


Figure 9-2

Then  $\check{\mu}$  is stationary in the frame, rotating with  $\check{\omega} = -\gamma \check{B}_0$ .

Now if we impose a magnetic field  $\check{B}_1$  (with  $\|\check{B}_1\| \ll \|\check{B}_0\|$  typically) in the  $xy$  plane such that it rotates with the same angular velocity and sense as  $\check{\mu}$ , then  $\check{B}_1$  is also stationary in this rotating frame.

Say that  $\check{B}_1$  is along the  $x'$  axis. Then in the rotating frame, there will be a torque on  $\check{\mu}$  given by  $\check{\mu} \times \check{B}_1$  and  $\check{\mu}$  will precess about  $\check{B}_1$  in the rotating frame with angular velocity  $\check{\omega}_1 = i \omega_1 = -\gamma \check{B}_1$ . This is the phenomenon of magnetic resonance. If  $\omega_1$  differs substantially from  $\omega_0$ , the spin is scarcely perturbed by  $\check{B}_1$ .



Generalizing to the behavior of the ensemble again, if the resonance condition  $\omega_1 = \omega_0$  is met, all spins will precess about  $\vec{B}_1$  in the rotating frame. Thus with a  $\vec{B}_1$  “pulse” of the proper length, we can turn the equilibrium magnetization  $\vec{M}_z$  into the  $xy$  plane or even invert it:

If  $\theta = 0$  initially

$$\omega_1 t_{\pi/2} = \frac{\pi}{2}, \quad t_{\pi/2} = \frac{\pi}{2\omega}, \quad \text{and } \vec{\mu} \text{ is in } xy \text{ plane}$$

$$\omega_1 t_{\pi} = \pi, \quad t_{\pi} = \frac{\pi}{\omega}, \quad \text{and } \vec{\mu} \text{ is inverted} \\ \text{(opposed to field)}$$

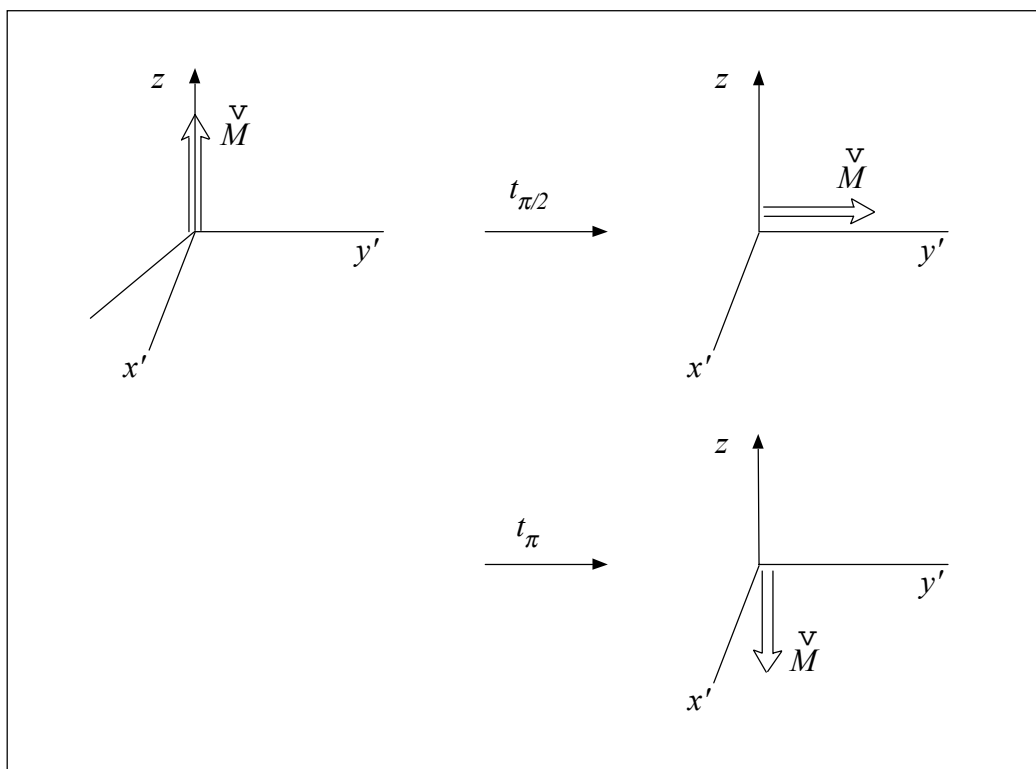


Figure 9-3

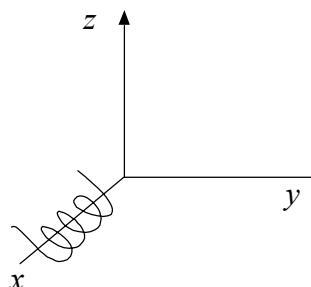
In the classical picture, magnetic resonance = absorption of rf power by the spin when the resonance condition  $\omega_1 = \omega_0$  is met.

Time behavior of magnetization is given by the Bloch equations.

$$\begin{aligned}\frac{d\vec{M}}{dt} &= \gamma \vec{M} \times \vec{B} - i \frac{M_x}{T_2} - j \frac{M_y}{T_2} - \frac{(M_z - M_0)}{T_1} \\ \frac{dM_x}{dt} &= \gamma (M_y B_0 + M_z B_1 \sin \omega_{rf} t) - \frac{M_x}{T_2} \\ \frac{dM_y}{dt} &= \gamma (M_z B_1 \cos \omega_{rf} t - M_x B_0) - \frac{M_y}{T_2} \\ \frac{dM_z}{dt} &= -\gamma (M_x B_1 \sin \omega_{rf} t + M_y B_1 \cos \omega_{rf} t) - \frac{(M_z - M_0)}{T_1}\end{aligned}$$

### How to Generate Rotating Fields

Linearly polarized rf can be resolved into two circularly-polarized components.



$$2B_1^x \cos \omega_0 t = 2B_1^x \frac{e^{i\omega_0 t} + e^{-i\omega_0 t}}{2} = B_1^x \left( \begin{array}{cc} \uparrow & \uparrow \\ \text{anti-} & \text{clockwise} \\ \text{clockwise} & \end{array} \right)$$

### Physics of NMR: Quantum Picture

For a nuclear spin with spin quantum number  $I$  given by  $\vec{J} = \hbar \vec{I}$  there is a magnetic moment operator

$$\vec{\mu} = \gamma \hbar \vec{I}$$

The Hamiltonian for the Zeeman interaction between a quantum-mechanical magnetic moment and a magnetic field is lifted from the classical expression:



$$H_z = -\check{\mu} \cdot \check{B} = -\mu_z B_0 = -\gamma \hbar I_z B_0 \quad \text{where} \quad \check{B} = \check{k} B_0$$

$$E_z = \langle H_z \rangle = -\gamma \hbar B_0 \langle I_z \rangle \quad \text{where} \quad E_z = \text{Zeeman energy}$$

$$= -\gamma \hbar B_0 m_I$$

$m_I$  = quantum number associated with  $2I + 1$  allowed projections of  $\check{I}$  on  $B_0$  or  $z$  axis

$$m_I \in \{-I, -I+1, \dots, I-1, I\}$$

This is the difference from the classical picture ... not all values of  $\theta$  are allowed.

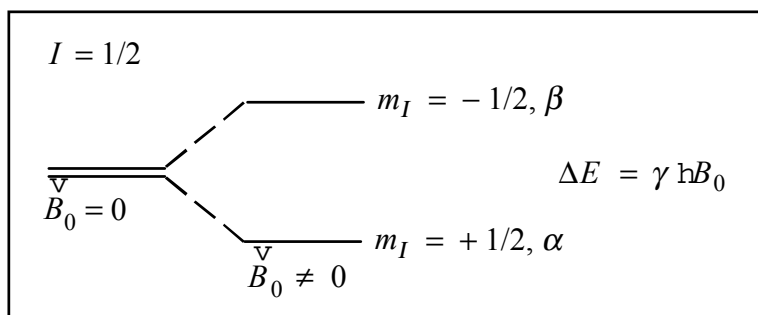
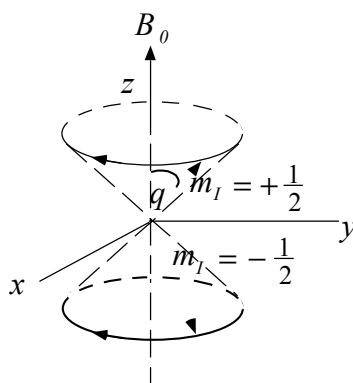


Figure 9-4

$\alpha$ ,  $\beta$  are names commonly given to the spin states. They aren't further specified, unlike spatial wavefunctions (their physical origin is in nuclear structure), and don't need to be:

1.  $\alpha$ ,  $\beta$  are eigenstates of the Hamiltonian, therefore we can use them to find energy levels.
2. They are a complete eigenbasis, i.e. any state of the system can be described by a linear combination of  $\alpha$  and  $\beta$ .
3. Spin and spatial degrees of freedom are independent (to good approximation) so we can ignore spatial wavefunctions when doing NMR calculations.

**NMR**

Transitions of spin between two states

$$\alpha \rightarrow \beta$$

$$\beta \rightarrow \alpha$$

To have a transition,  $\underline{\mu}$  must interact with  $\vec{B}_1$  and  $\omega_1$  must satisfy the Bohr relation

$$\Delta E = \gamma \hbar B_0 = \hbar \omega_1 \quad \text{or} \quad \omega_1 = \omega_0$$

The interaction of  $\underline{\mu}$  with  $\vec{B}_1$  must result in a nonvanishing matrix element between the two states involved in the transition.

$$I_{i \rightarrow f} \propto \left| \int \psi_f^* \underline{\mu} \psi_i d\tau \right|^2$$

We can expand  $\underline{\mu}$  in terms of  $\alpha$  and  $\beta$  to see what this requirement means:

$$\underline{u}_z = \begin{matrix} \alpha & \beta \\ \alpha & \left( \begin{array}{cc} 1/2 & 0 \\ 0 & -1/2 \end{array} \right) \beta \end{matrix} \gamma \hbar \quad \underline{u}_x = \begin{pmatrix} 0 & 1/2 \\ 1/2 & 0 \end{pmatrix} \gamma \hbar$$

$$\underline{u}_y = \begin{pmatrix} 0 & -i/2 \\ i/2 & 0 \end{pmatrix} \gamma \hbar$$

Therefore only transverse Zeeman terms  $\mu_x B_{1,x} + \mu_y B_{1,y}$  can induce transitions between  $\alpha$  and  $\beta$ .

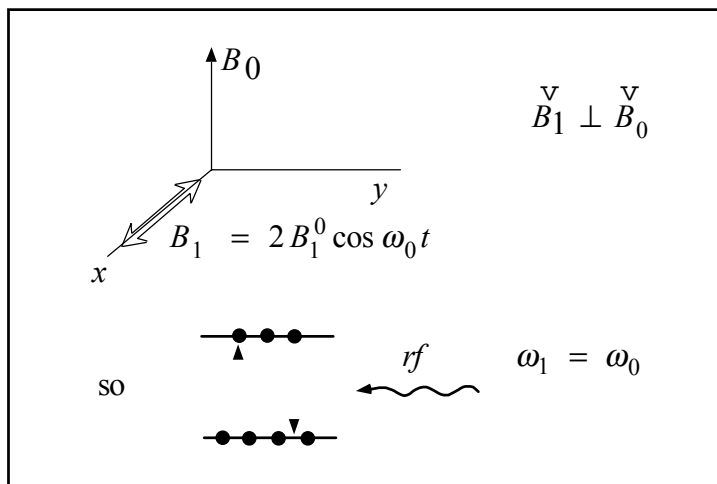
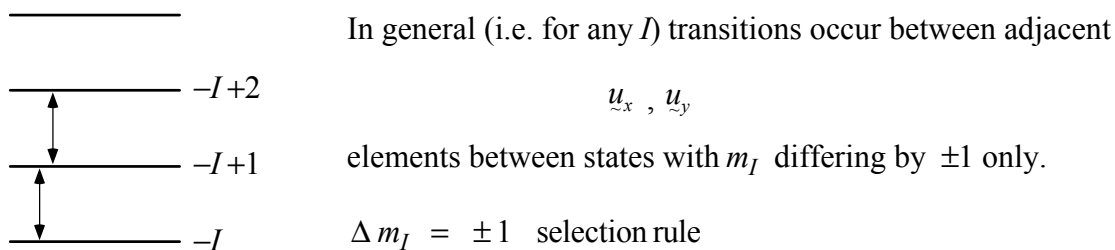


Figure 9-5



Return to  $I = \frac{1}{2}$

We can answer the question that classical treatment could not ... what is the equilibrium magnetization?  $M_z$  is nonzero due to unequal (thermal) population of  $\alpha, \beta$  states

$$\begin{aligned}
 n_\alpha + n_\beta &= N \quad (\text{normalization}) \\
 M_0 &= n_\alpha \langle \mu_z \rangle_\alpha + n_\beta \langle \mu_z \rangle_\beta \\
 &= \frac{1}{2} \gamma \hbar (n_\alpha - n_\beta) \\
 &= \frac{1}{2} \gamma \hbar N \frac{1 - e^{-\gamma \hbar B_0 / kT}}{1 + e^{-\gamma \hbar B_0 / kT}} \approx \frac{N}{4kT} \gamma^2 \hbar^2 B_0
 \end{aligned}$$

This last result is the Curie Law. The slight excess population in  $\alpha$  at thermal equilibrium also means that stimulation of transitions by resonant RF causes *net absorption* since the transition rate in each direction is proportional to the population of the initial state.

