Introduction to Biophysical Chemistry

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Magnetic Resonance Spectroscopy.

Nuclear Magnetic Resonance. I.

Nuclear Magnetic Resonance

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.

Nuclear Magnetic Resonance

Magnetic nuclei:

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

Nuclear Magnetic Resonance

NMR is also a noninvasive method[1] 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" γ:

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

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

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

Physics of NMR: Classical Picture

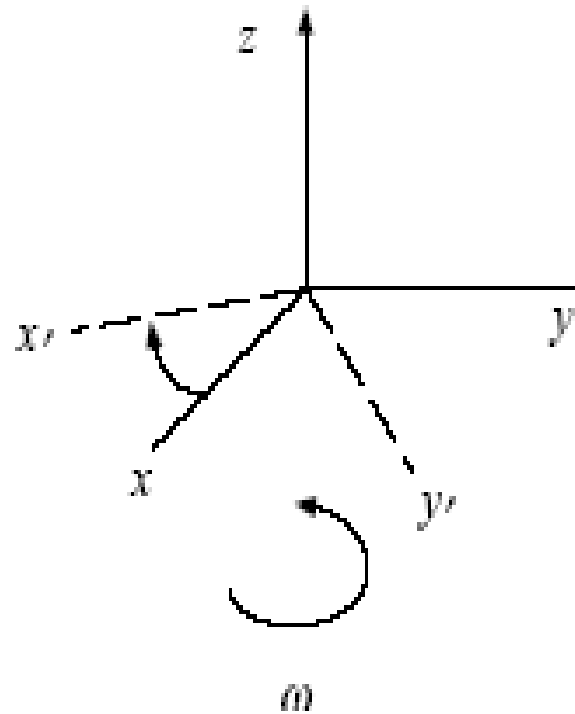This torque is equal to the rate of change of angular momentum $\vec{J}$ (Newton's law)

$$\frac{d\vec{J}}{dt} = \vec{\mu} \times \vec{B_0}$$

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

$$\frac{d\vec{\mu}}{dt} = \gamma \left(\vec{\mu} \times \vec{B_0} \right)$$

Physics of NMR: Classical Picture

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

Physics of NMR: Classical Picture

Such a transformation obeys

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

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

Physics of NMR: Classical Picture

This last result shows that $\overset{v}{\mu}$ is stationary in the rotating frame for which $\left(\overset{v}{B_0} + \dfrac{\overset{v}{\omega_0}}{\gamma} \right) = 0$,

i.e. for $\overset{v}{\omega_0} = -\gamma \overset{v}{B_0} = \overset{v}{k}\omega_0$ where ω_0 is called the Larmor frequency.

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

Nuclear Magnetic Resonance

An Ensemble of Isolated $\vec{\mu}$ 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 γ, chemically identical,
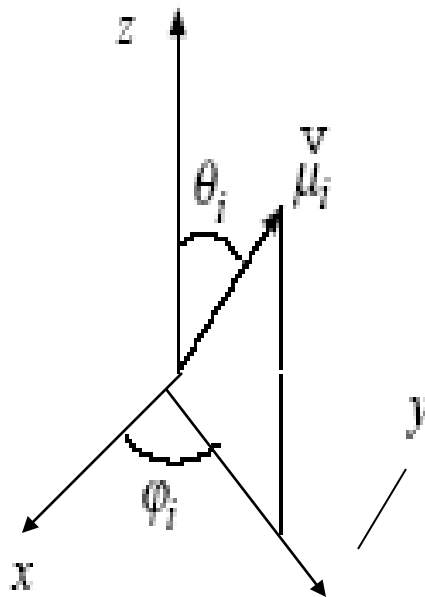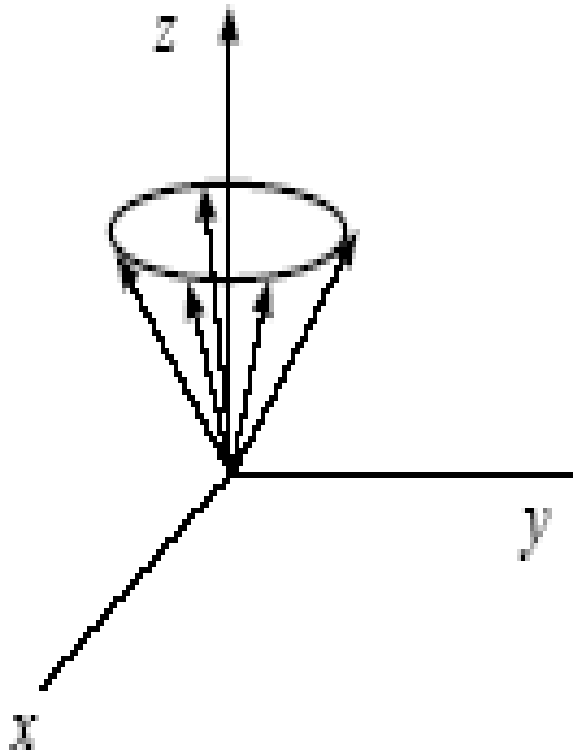

θ_i and φ_i are uncorrelated from one spin to another.

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

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

Nuclear Magnetic Resonance

so that for all spins with the same θ_j, hence same energy, random φ_j.
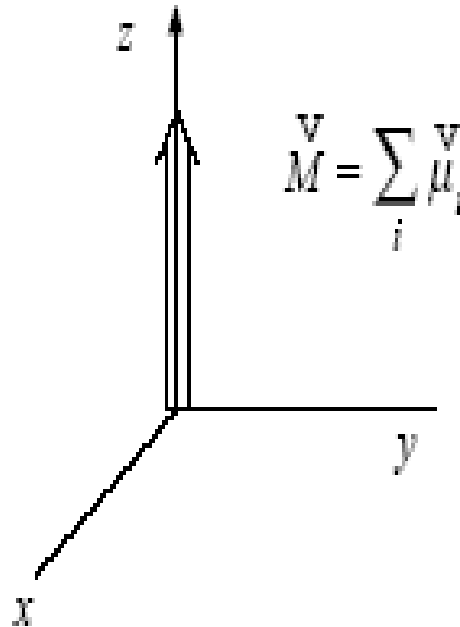

at thermal equilibrium

Nuclear Magnetic Resonance

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

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

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

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

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

$$\overset{v}{M} = \sum_i \overset{v}{\mu_i}$$

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

Phenomenon of Magnetic Resonance

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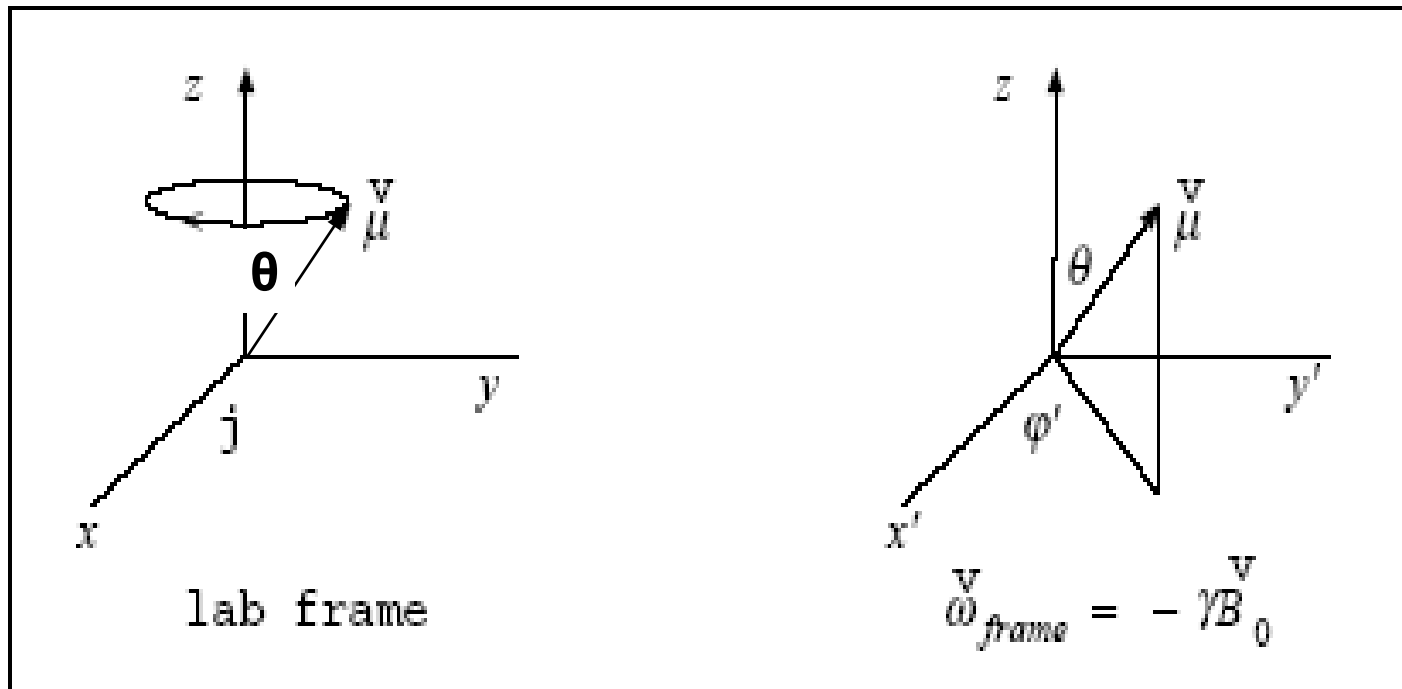
Phenomenon of Magnetic Resonance

Then $\vec{\mu}$ is stationary in the frame, rotating with $\vec{\omega} = -\gamma \vec{B_0}$.

Now if we impose a magnetic field $\vec{B_1}$ (with $\|\vec{B_1}\| \ll \|\vec{B_0}\|$ typically) in the xy plane such that it rotates with the same angular velocity and sense as $\vec{\mu}$, then $\vec{B_1}$ is also stationary in this rotating frame.

Phenomenon of Magnetic Resonance

Say that $\vec{B}_1$ is along the x' axis. Then in the rotating frame, there will be a torque on μ given by $\vec{\mu} \times \vec{B}_1$ and μ will precess about $\vec{B}_1$ in the rotating frame with angular velocity $\vec{\omega}_1 = i\,\omega_1 = -\gamma\,\vec{B}_1$. This is the phenomenon of magnetic resonance. If ω_1 differs substantially from ω_0, the spin is scarcely perturbed by $\vec{B}_1$.
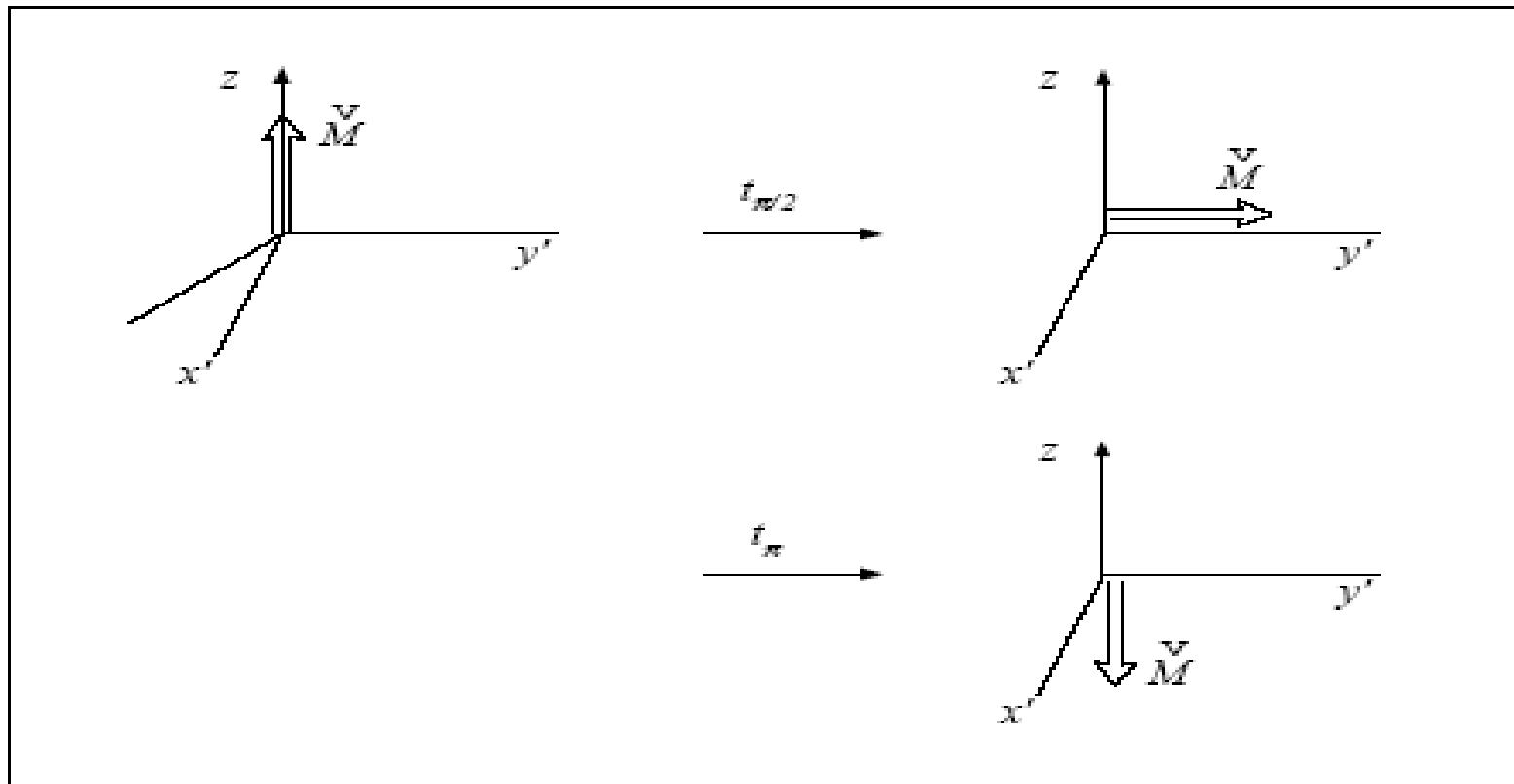
Nuclear Magnetic Resonance
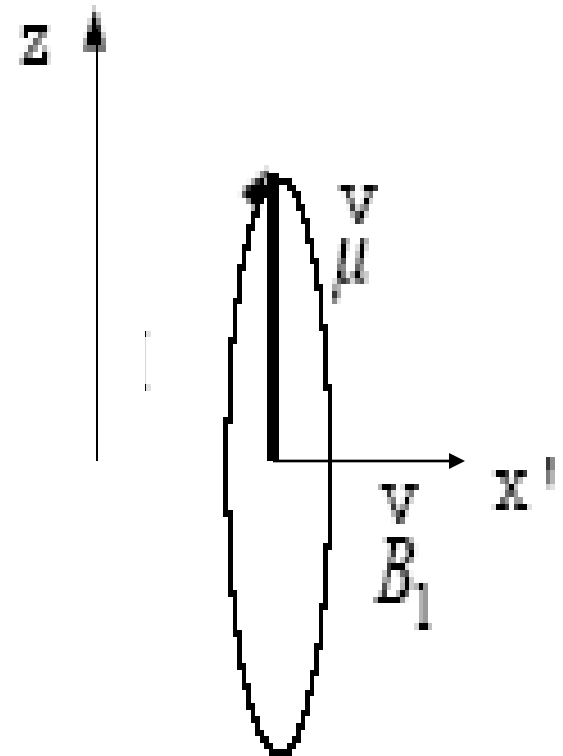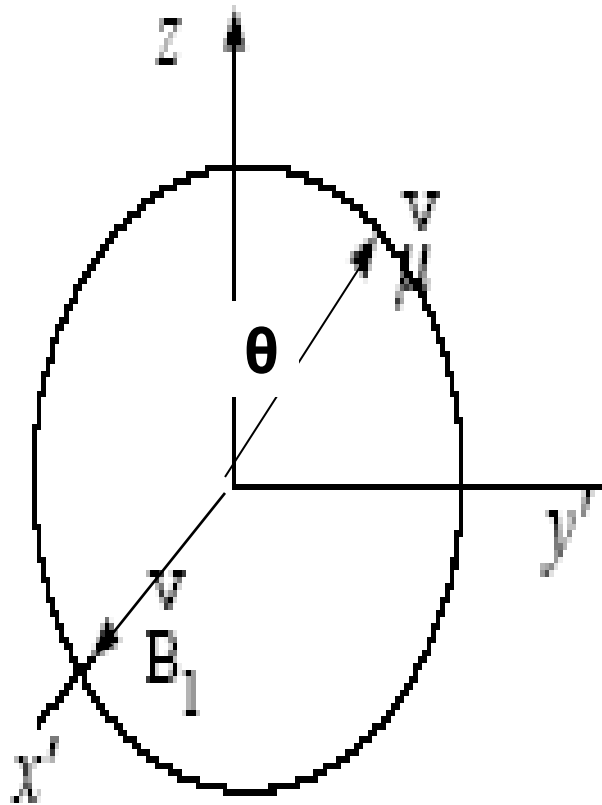
Generalizing to the behavior of the ensemble again, if the resonance condition $\omega_1 = \omega_0$ is met, all spins will precess about $\vec{B}_1$ in the rotating frame. Thus with a $\vec{B}_1$ "pulse" of the proper length, we can turn the equilibrium magnetization $\vec{M}_z$ into the xy plane or even invert it:

$$\text{If} \quad \theta = 0 \quad \text{initially}$$

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

$$\omega_1 t_\pi = \pi, \qquad t_\pi = \frac{\pi}{\omega_1}, \quad \text{and} \quad \vec{\mu} \text{ is inverted}$$

$$\text{(opposed to field)}$$

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

Bloch equations

Time behavior of magnetization is given by the Bloch equations.

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{B} - \vec{i}\frac{M_x}{T_2} - j\frac{M_y}{T_2} - \frac{(M_z - M_0)}{T_1}$$
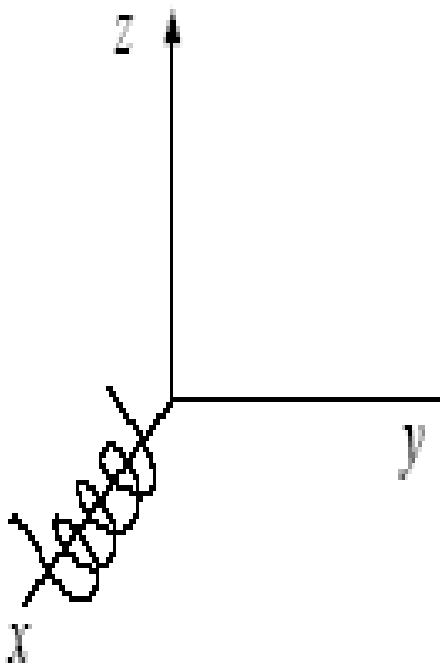
$$\frac{dM_x}{dt} = \gamma\left(M_y B_0 + M_z B_1 \sin \omega_{rf} t\right) - \frac{M_x}{T_2}$$

$$\frac{dM_y}{dt} = \gamma\left(M_z B_1 \cos \omega_{rf} t - M_x B_0\right) - \frac{M_y}{T_2}$$

$$\frac{dM_z}{dt} = -\gamma\left(M_x B_1 \sin \omega_{rf} t + M_y B_1 \cos \omega_{rf} t\right) - \frac{(M_z - M_0)}{T_1}$$

How to generate rotating fields?

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

$$2B_1^x \cos \omega_0 t = 2B_1^x \frac{e^{i\omega_0 t} + e^{-i\omega_0 t}}{2} = B_1^x \left(e^{i\omega_0 t} + e^{-i\omega_0 t} \right)$$

anti-clockwise   clockwise

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:

Physics of NMR: Quantum Picture

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

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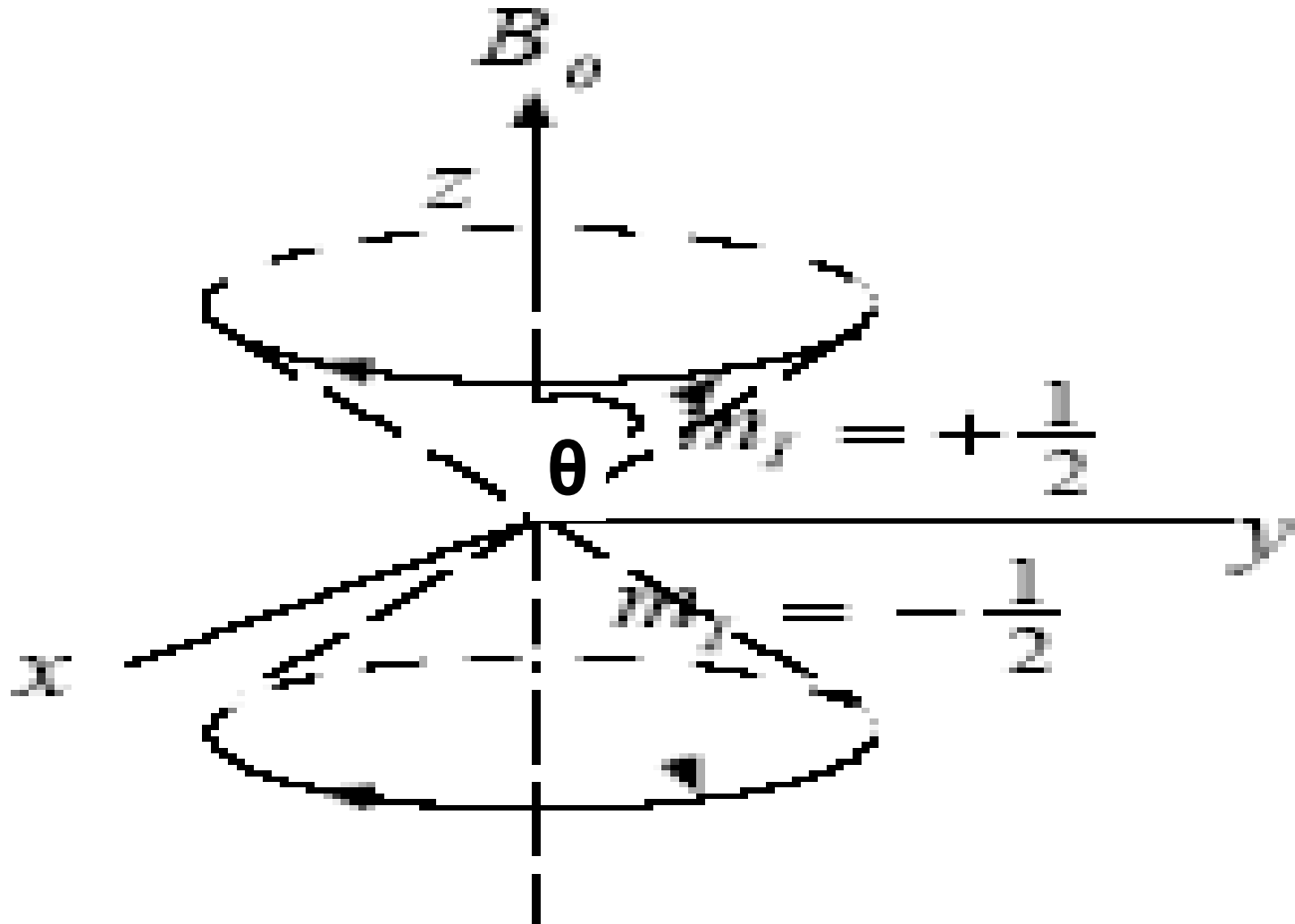
$$= -\gamma \hbar B_0 \, m_I$$

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

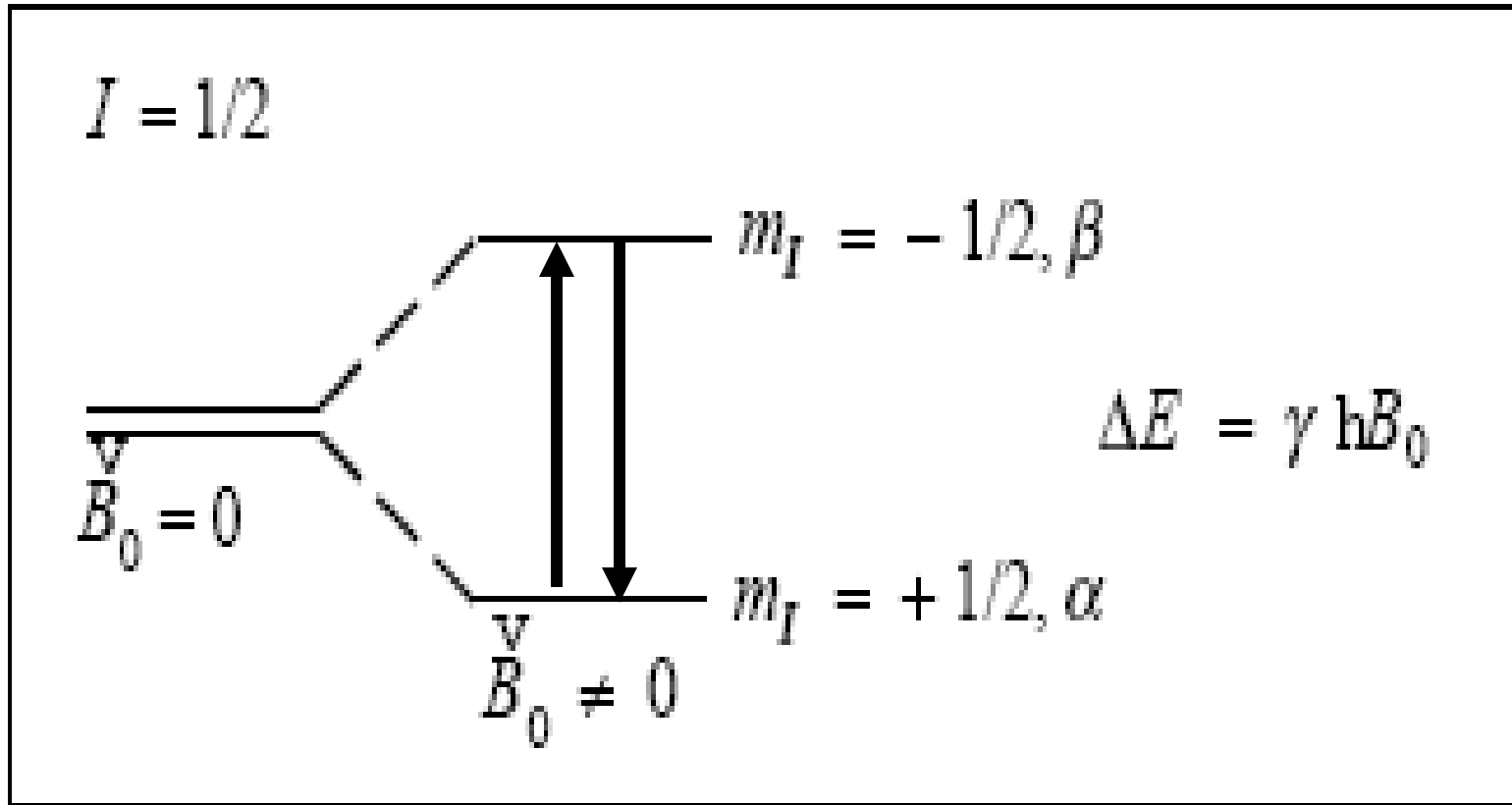$$m_I \in \{-I, \; -I+1, \; \text{к}, \; I-1, \; I\}$$

This is the difference from the classical picture ... not all values of θ are allowed.

Physics of NMR: Quantum Picture

Physics of NMR: Quantum Picture

$I = 1/2$

$m_I = -1/2, \beta$

$B_0 = 0$

$\Delta E = \gamma \hbar B_0$

$m_I = +1/2, \alpha$

$B_0 \neq 0$

Physics of NMR: Quantum Picture

α, β 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. α, β 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 α and β.

3. Spin and spatial degrees of freedom are independent (to good approximation) so we can ignore spatial wavefunctions when doing NMR calculations.

Physics of NMR: Quantum Picture

<u>NMR</u>

Transitions of spin between two states

$$\alpha \rightarrow \beta$$

$$\beta \rightarrow \alpha$$

To have a transition, μ; must interact with $\vec{B}_1$ and ω_1 must satisfy the Bohr relation

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

Physics of NMR: Quantum Picture

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

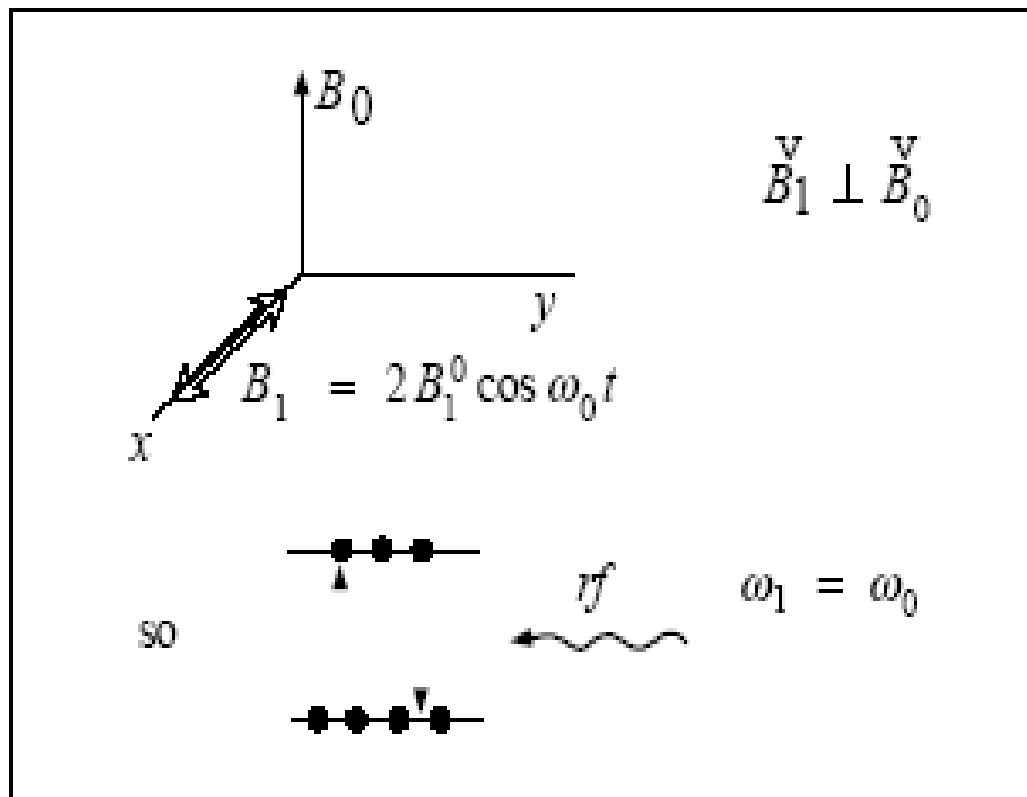$$I_{i \to f} \propto \left| \int \psi_f^* \overset{Y}{\mu} \psi_i \, d\tau \right|^2$$

We can expand $\underset{\sim}{\mu}$ in terms of α and β to see what this requirement means:

$$
\underset{\sim}{u_z} = \begin{array}{cc} & \begin{array}{cc} \alpha & \quad \beta \end{array} \\ \begin{array}{c} \alpha \\ \beta \end{array} & \begin{pmatrix} 1/2 & 0 \\ 0 & -1/2 \end{pmatrix} \end{array} \gamma\, \mathrm{h}
\qquad
\underset{\sim}{u_x} = \begin{pmatrix} 0 & 1/2 \\ 1/2 & 0 \end{pmatrix} \gamma\, \mathrm{h}
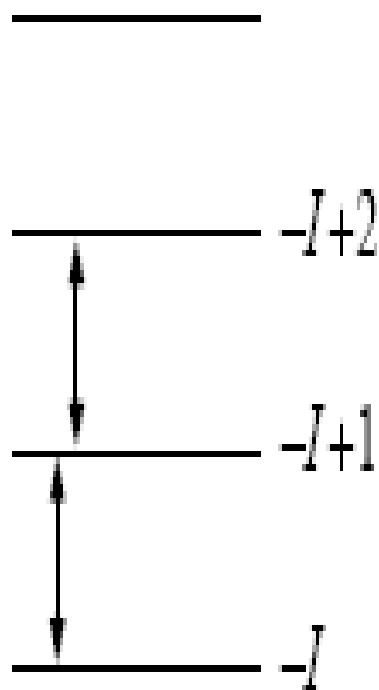$$

$$
\underset{\sim}{u_y} = \begin{pmatrix} 0 & -i/2 \\ i/2 & 0 \end{pmatrix} \gamma\, \mathrm{h}
$$

Physics of NMR: Quantum Picture

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

Physics of NMR: Quantum Picture

In general (i.e. for any I) transitions occur between adjacent

$$u_x \, , \, u_y$$

elements between states with m_I differing by ± 1 only.

$-I+2$

$-I+1$

$-I$

$\Delta m_I = \pm 1$ selection rule

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

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 α, β states

$$n_\alpha + n_\beta = N \quad \text{(normalization)}$$

$$M_0 = n_\alpha \langle \mu_z \rangle_\alpha + n_\beta \langle \mu_z \rangle_\beta$$
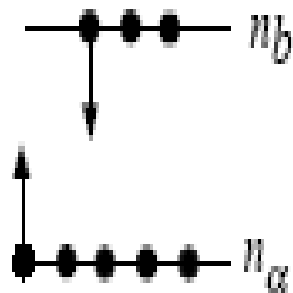
$$= \frac{1}{2} \gamma h \left(n_\alpha - n_\beta \right)$$

$$= \frac{1}{2} \gamma h N \frac{1 - e^{-\gamma h B_0 / kT}}{1 + e^{-\gamma h B_0 / kT}} \simeq \frac{N}{4kT} \gamma^2 h^2 B_0$$

Physics of NMR: Quantum Picture

This last result is the Curie Law. The slight excess population in α 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.

$$\frac{n_{\beta}^{0}}{n_{\alpha}^{0}} = e^{-\Delta E / k_B T}$$

Reading assignment

 Eisenberg and Crothers (EC), Chapter 13, pp. 604-617.

 Kensal E. van Holde, W. Curtis Johnson, and Pui Shing Ho, "Principles of Physical Biochemistry" (Second Edition 2006), Chapter 12, pp. 535-578.