Multinukleární NMR spektroskopie
C6800

- Materiály v ISu
- Řešené úlohy ze spektroskopie nukleární magnetické resonance

  http://nmr.sci.muni.cz
- Úlohy – vyřešit a odevzdat
- Prezentace (na konci semestru) 10-15 min na vybrané téma NMR
- Závěrečná písemná zkouška

NMR – Historical Perspective

- 1922 Electron spin observed (Stern-Gerlach)
- 1926 Nuclear spin - David Dennison (H_2)
- 1938 NMR was first observed in a molecular beam
- 1939 I. I. Rabi observes absorption of radio frequency (RF) energy by nuclei of H_2 gas
- Isidor I. Rabi Nobel prize in physics in 1944

"for his resonance method for
recording the magnetic
properties of atomic nuclei"

(1898 – 1988)

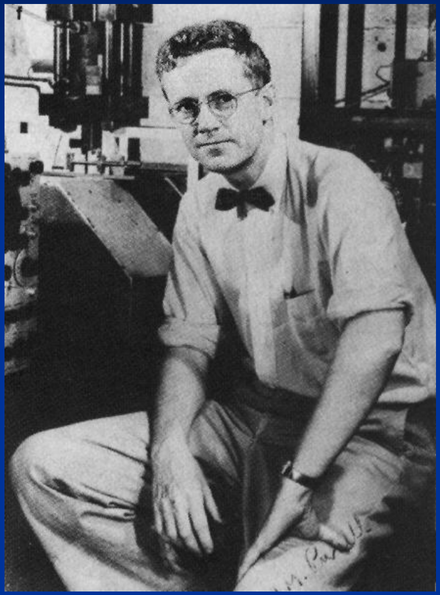
NMR – Historical Perspective

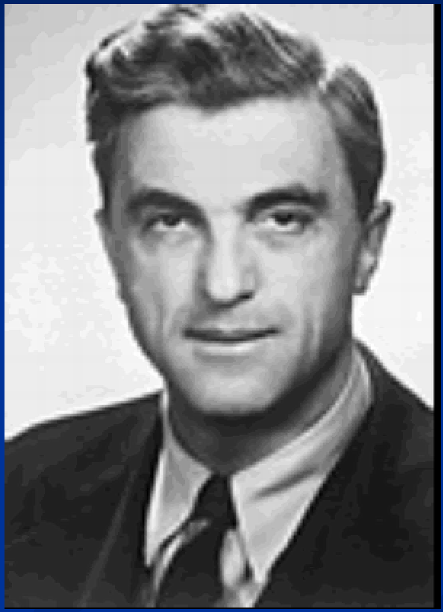
- 1945 Purcell, Torrey, Pound @ Harvard — solid paraffin
- 1945 Bloch, Hansen, Packard @ Stanford — liquid H_2O
- Varian Bros. & Russell — klystron for radars (WWII)
- 1948 Pake, van Vleck — solid state NMR
- 1950 W. G. Proctor, F. C. Yu @ Stanford

  δ - chemical shift in $^{14}NH_4{}^{14}NO_3$
- 1950 W. C. Dickinson @ MIT

  δ - chemical shift in ^{19}F
- 1952 Commercial NMR instruments used at DuPont, Shell, Humble Oil

NMR – Historical Perspective





Edward M. Purcell (1912-1997) & Felix Bloch (1905-1983)
NP in physics 1952

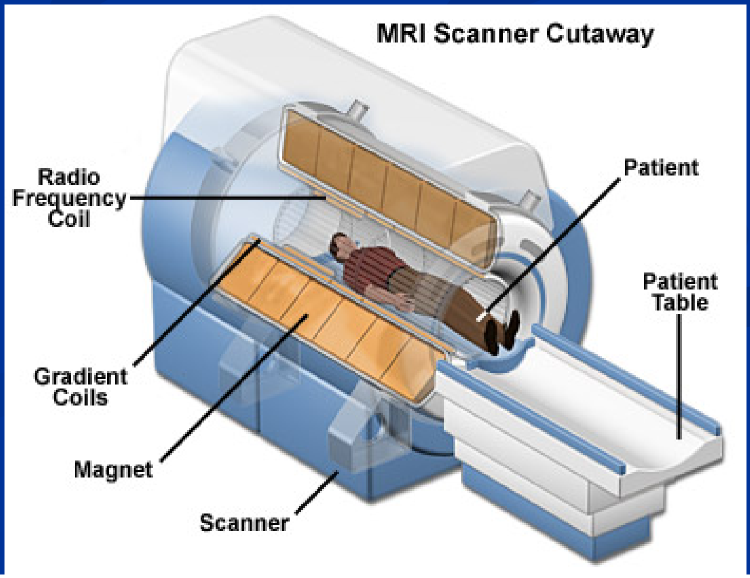
"for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"

NMR – Historical Perspective

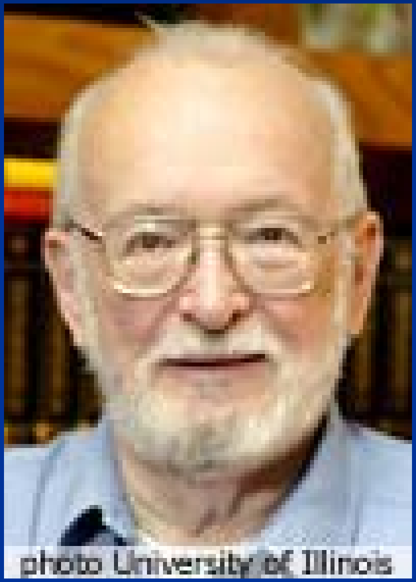
- 1952 Hahn, Maxwell @ Berkeley - J scalar coupling
- 1953 Gutowsky, McCall, Slichter @ U. of IL - J
- 1955 Bloom, Shoolery spin decoupling
- 1960 Shoolery integration
- 1966 Ernst, Anderson FT NMR at Varian
- 1968 Waugh @ MIT HR, multipulse NMR in solids

NMR – Historical Perspective

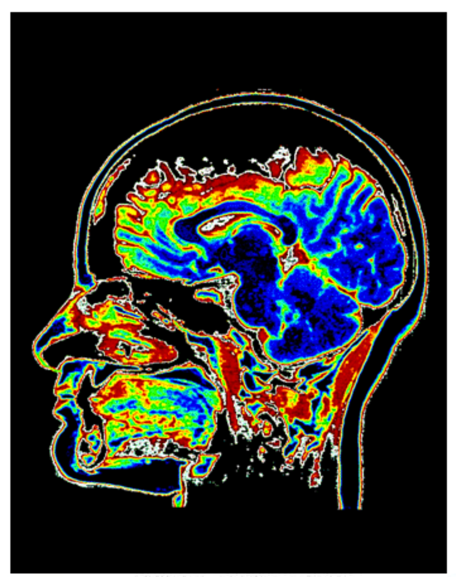
- 1971 Jeener 2D NMR
- 1971 Damadian different NMR relaxation times of tissues and tumors
- 1972 CP, HP decoupling
- 1972 The first routine ^{13}C NMR spectrometer (before mainly ^{1}H, ^{19}F, and ^{31}P NMR)
- 1973 Lauterbur MRI

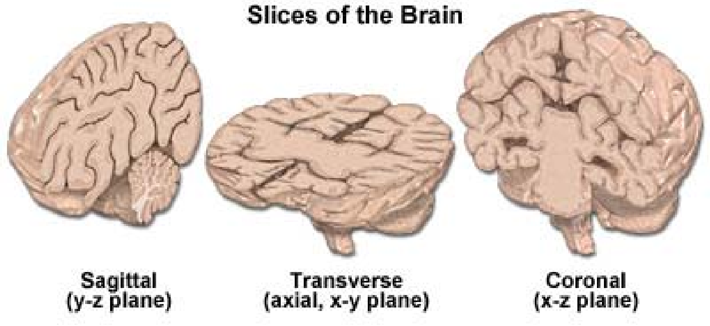

MRI Scanner Cutaway

MRI-Magnetic Resonance Imaging



Paul C. Lauterbur (1929-)





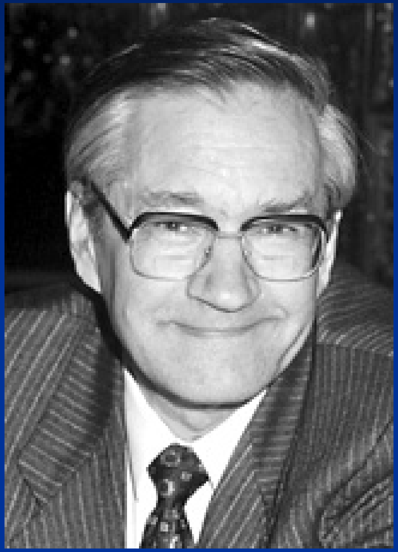
Sir Peter Mansfield (1933-)

NP in physiology and medicine 2003

NMR – Historical Perspective

- 1974/1979 R. R. Ernst 2D COSY, NOESY
- 1977 MAS
- 1981 Bax, Freeman INADEQUATE
- 1982 APT
- 1983 Freeman BB decoupling, MLEV, WALTZ
- 1990 3D and $^{1}H/^{15}N/^{13}C$ Triple resonance
- 1991 R. R. Ernst NP in chemistry
- 2001 The first commercial 900 MHz instrument
- 2002 K. Wüthrich NP in chemistry

NMR – Historical Perspective



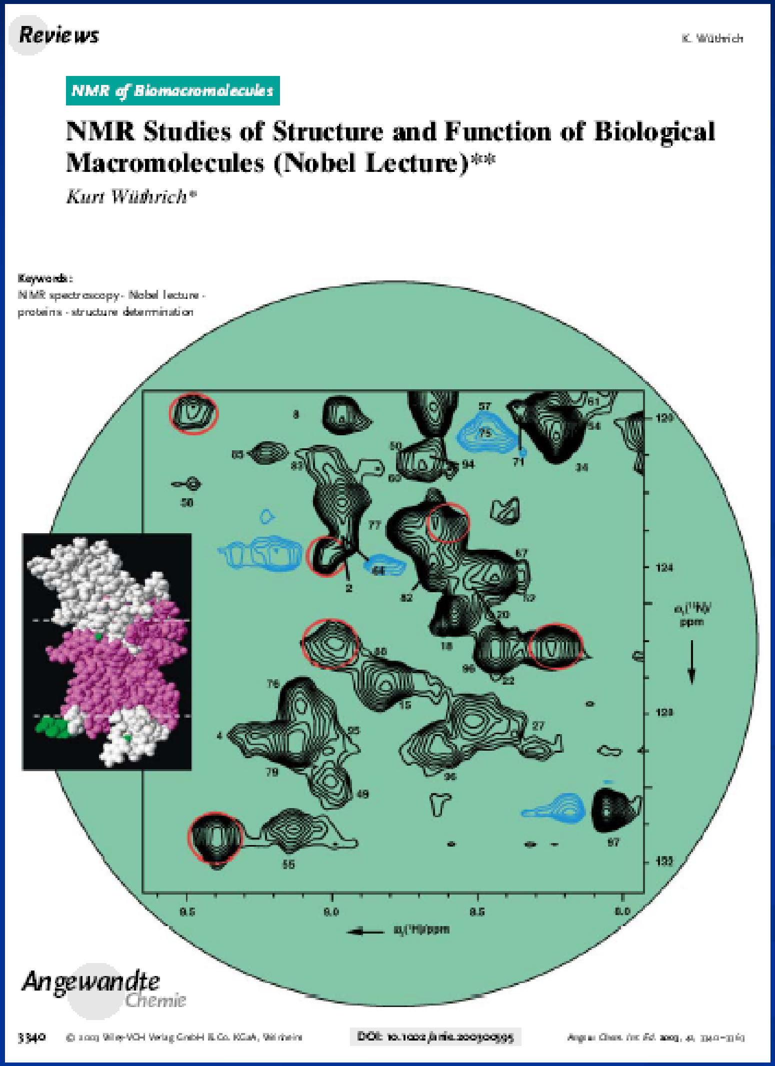
Richrad R. Ernst
(1933-)
NP in chemistry 1991

"for his contributions to the development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy"

Kurt Wüthrich
(1938-)
NP in chemistry 2002

"for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution"

NMR – Historical Perspective



Reviews

K. Wüthrich

NMR of Biomacromolecules

NMR Studies of Structure and Function of Biological Macromolecules (Nobel Lecture)**

*Kurt Wüthrich**

Keywords:
NMR spectroscopy · Nobel lecture · proteins · structure determination

Angewandte Chemie

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Nuclear Magnetic Resonance

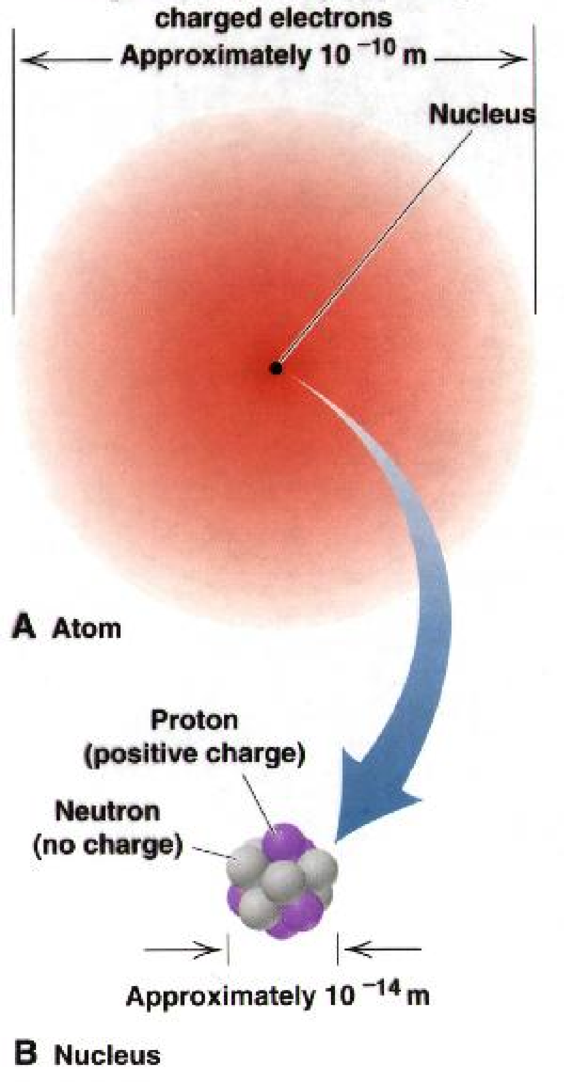
- High resolution liquid state NMR spectroscopy
- Solid state NMR spectroscopy
- High-pressure NMR
- NMR in the gas phase
- NMR spectroscopy in liquid crystalline media
- Magnetic resonance imaging (MRI)

Hyperfine Interactions

- Interactions of nuclei with the electric and magnetic fields

- Interactions between a nucleus and electrons

- Transfer of chemical (electronic) information from bonds and lone pairs to a nucleus
  - Indirect
  - Direct



Hyperfine Interactions

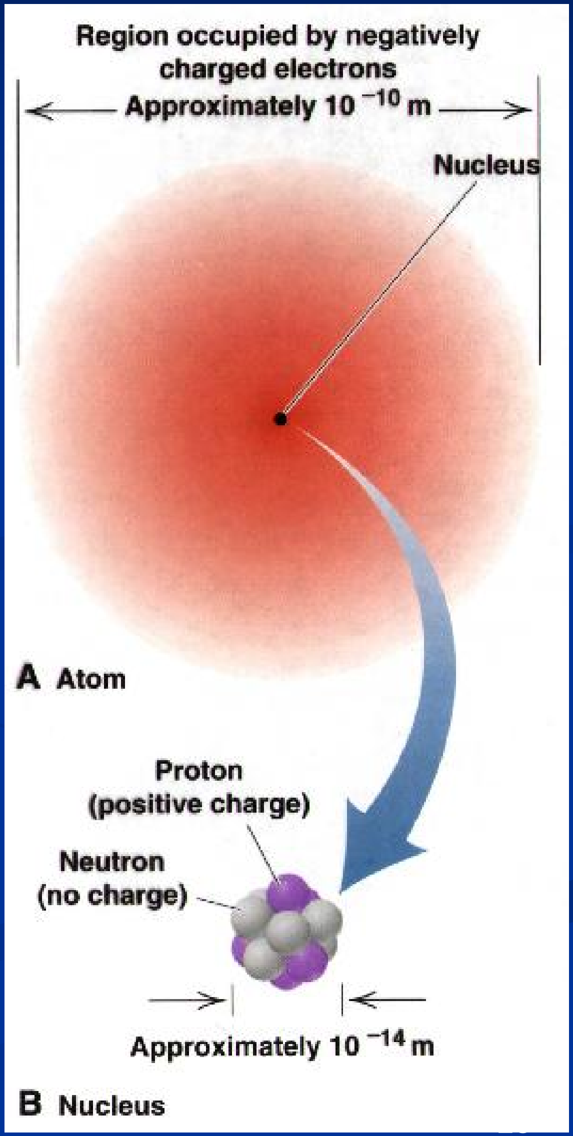
Indirect

- Electric field gradient (EFG) with nuclear electric quadrupole

- Induced magnetic field with nuclear magnetic moments (shielding)

Direct

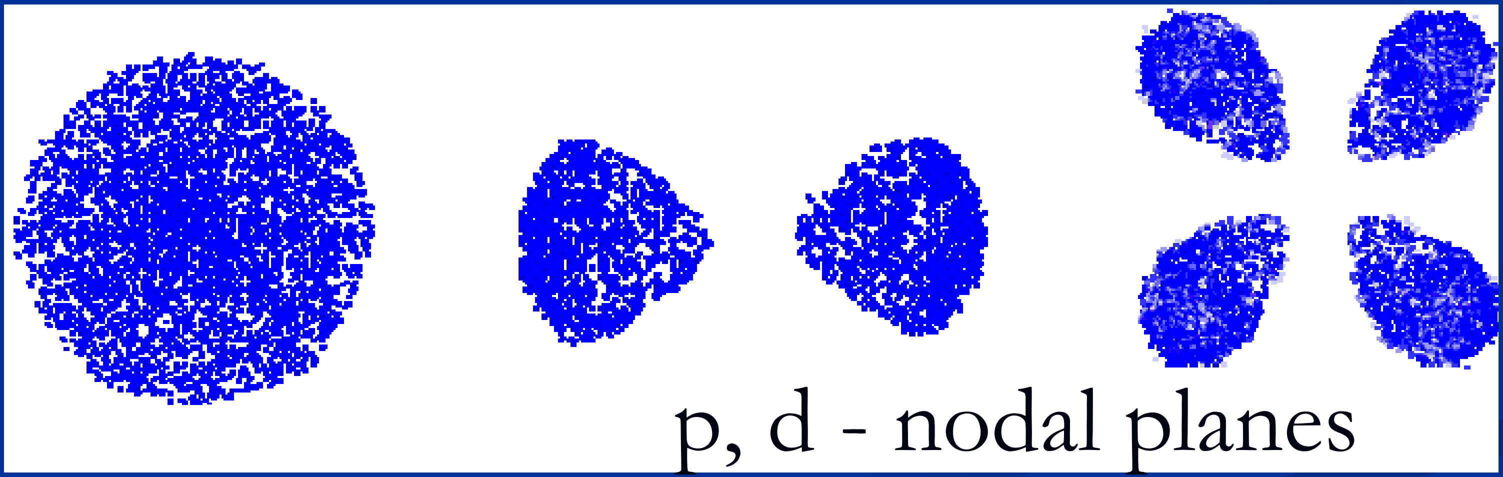
- s-electrons within nuclei, polarization of bonding spins (J-coupling)



Direct Interactions

ONLY s-electrons can interact with nuclei

ONLY s-electrons have non-zero electron density at a nucleus


p, d - nodal planes

Relationship Between Wavelength, Frequency and Energy

- Speed of light (c) is the same for all wavelengths

  $c = 2.9979\ 10^{8}\ \ \mathrm{m\ s^{-1}}$

- Frequency (ν), the number of wavelengths per second, is inversely proportional to wavelength:

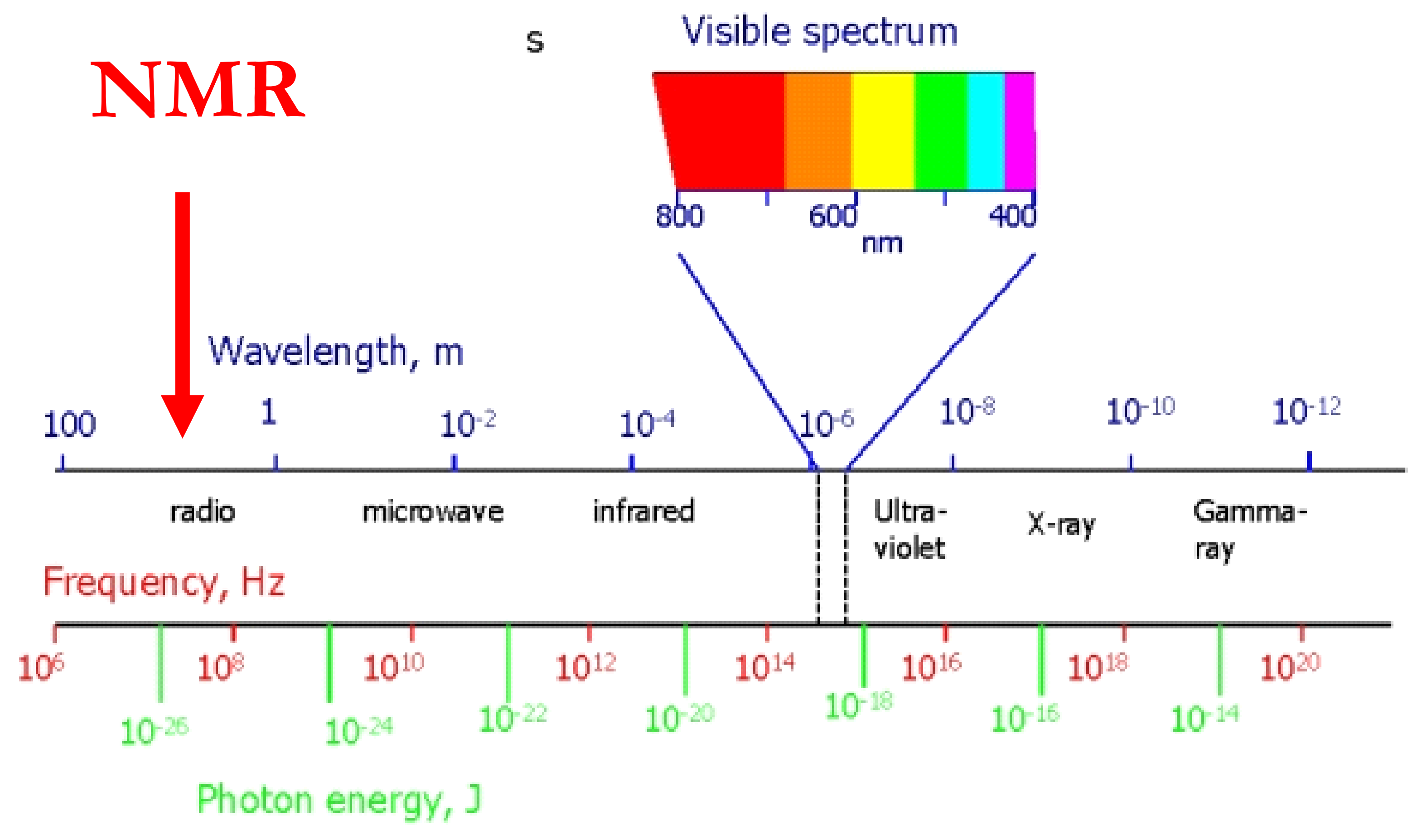
  $$\nu = c/\lambda$$

- Energy of a photon is directly proportional to frequency and inversely proportional to wavelength:

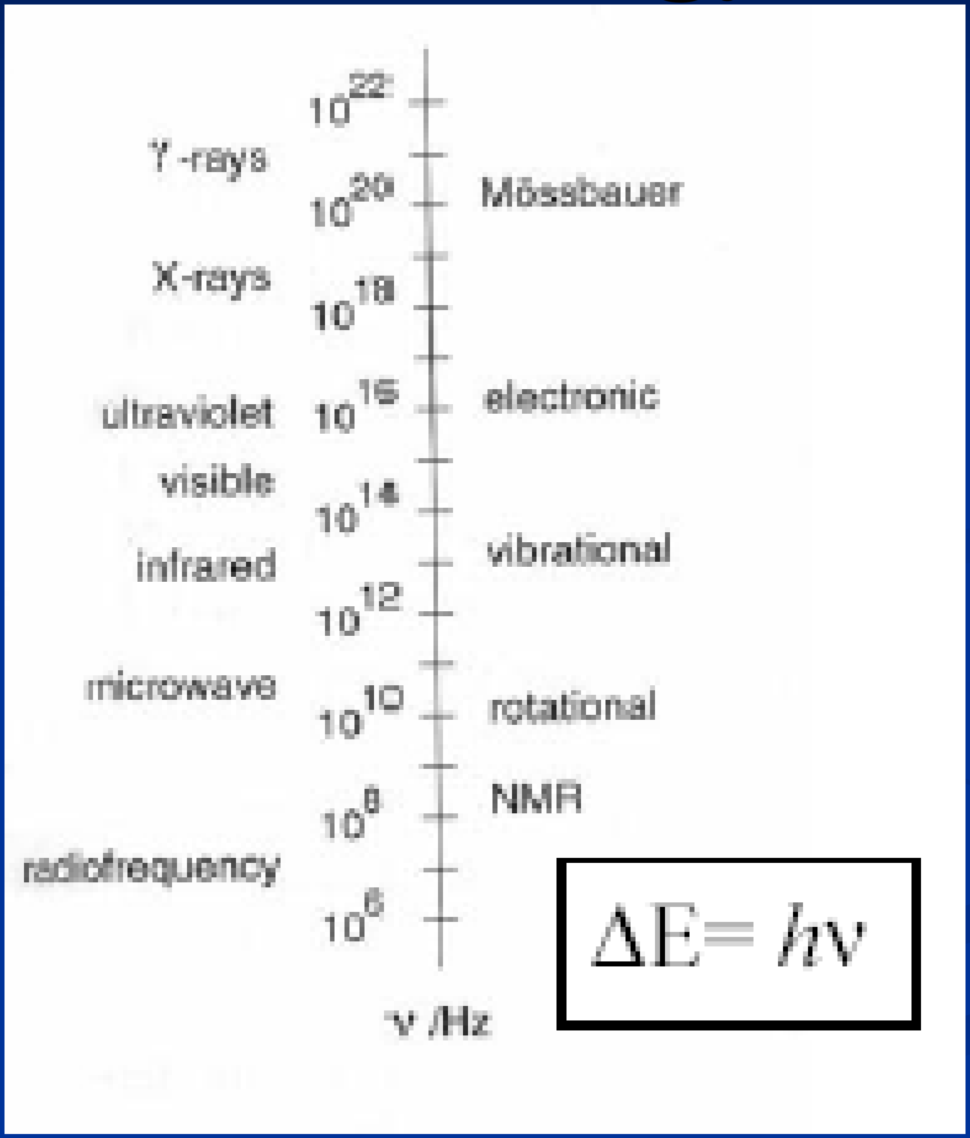
  $$E = \mathrm{h}\nu = \mathrm{h}c/\lambda$$

  h = Plank's constant = $6.626176\ 10^{-34}$ J s

Electromagnetic Radiation



Method Energy Scale



$$\Delta E = h\nu$$

Energy Scale Conversion Factors

	Hz	**eV**	**$J\ mol^{-1}$**
Hz	1	$4.136\ 10^{-15}$	$3.990\ 10^{-10}$
eV	$2.418\ 10^{14}$	1	$9.649\ 10^{4}$
$J\ mol^{-1}$	$2.506\ 10^{9}$	$1.036\ 10^{-5}$	1

Isotopes

Isotopes = a set of nuclides of an element, same Z, different A
there is about 2600 nuclides (stabile and radioactive)
340 nuclides found in nature
270 stabile and 70 radioactive

Monoisotopic elements:
^{9}Be, ^{19}F, ^{23}Na, ^{27}Al, ^{31}P, ^{59}Co, ^{127}I, ^{197}Au

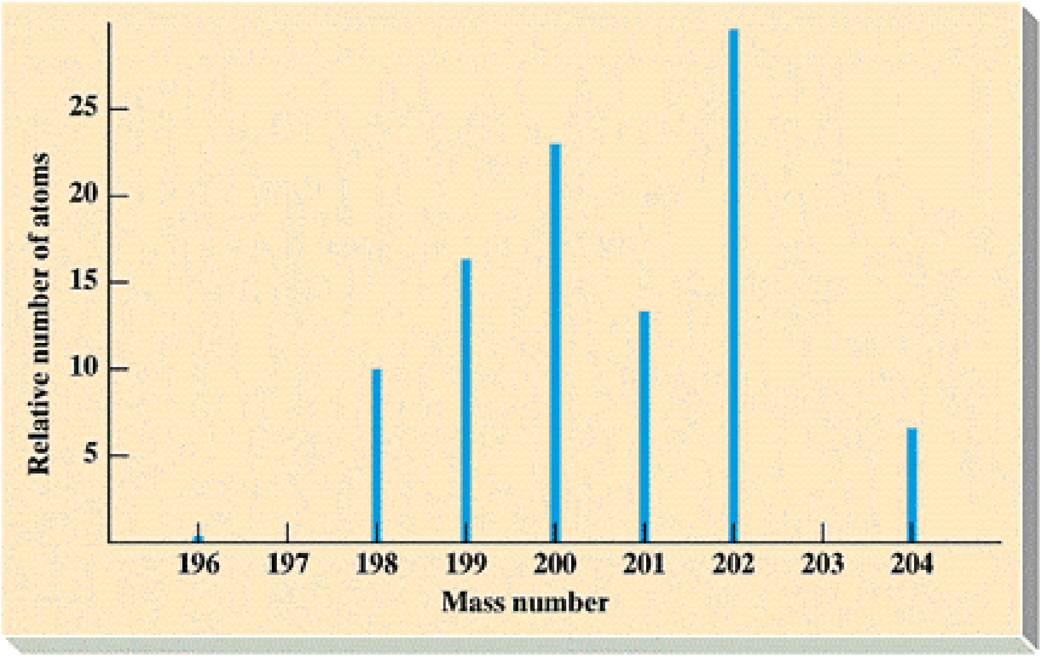
Polyisotopic elements:
^{1}H, ^{2}H (D), ^{3}H (T)
^{10}B, ^{11}B
Sn has the highest number of stabile isotopes – 10

112, 114, 115, 116, 117, 118, 119, 120, 122, ^{124}Sn

Natural Abundance, %

Isotopic Compositions of the Elements

^{A}Hg	*I*	NA%
196	0	0.146
198	0	10.02
199	1/2	16.84
200	0	23.13
201	3/2	13.22
202	0	29.80
204	0	6.850



Mass number, *A*

Natural Abundance, %

Isotopic Compositions of the Elements

^{1}H	99.985	^{16}O	99.759
^{2}H	0.015	^{17}O	0.037
		^{18}O	0.204
^{12}C	98.89		
^{13}C	1.11	^{32}S	95.00
		^{33}S	0.76
^{14}N	99.63	^{34}S	4.22
^{15}N	0.37	^{36}S	0.014

Variability in Isotopic Compositions

	Natural Abundance, %	
Isotope	Range	Average
^{10}B	18.927 - 20.337	19.9 (7)
^{11}B	81.073 - 79.663	80.1 (7)
^{16}O	99.7384 - 99.7756	99.757 (16)
^{17}O	0.0399 - 0.0367	0.038 (1)
^{18}O	0.2217 - 0.1877	0.205 (14)

Nuclear Spin

electron spin $s = ½$

proton and neutron $I = ½$

nuclear spin $I = z ½$ **z = integer 0, 1, 2, 3, ...**

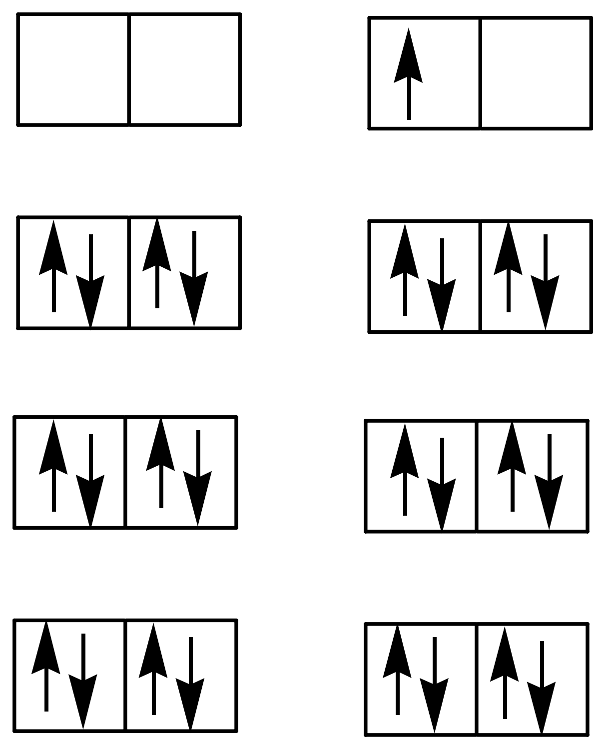
Number of protons, *Z*	**Number of neutrons, *N***	***I***
even	even	0
odd	odd	integer
even	odd	multiples of ½
odd	even	

Nuclear Spin

protons and neutrons are Fermions, obey Pauli exclusion principle

^{12}C

$I = 0$



^{13}C

$I = ½$

n p n p

Nuclear Spin

- even – even: $I = 0$ ^{4}He, ^{12}C, ^{16}O, ^{20}Ne, ^{24}Mg, ^{28}Si, ^{32}S, ^{36}Ar, ^{40}Ca

- odd – odd: I = integer

ONLY ^{2}H, ^{6}Li, ^{10}B, ^{14}N, ^{40}K, ^{50}V, ^{138}La, ^{176}Lu

- even – odd and odd – even:

I = multiples of ½

^{13}C ½, ^{17}O 5/2, ^{33}S 3/2

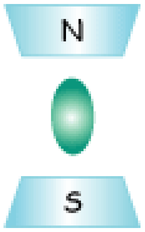
Nuclear Spin

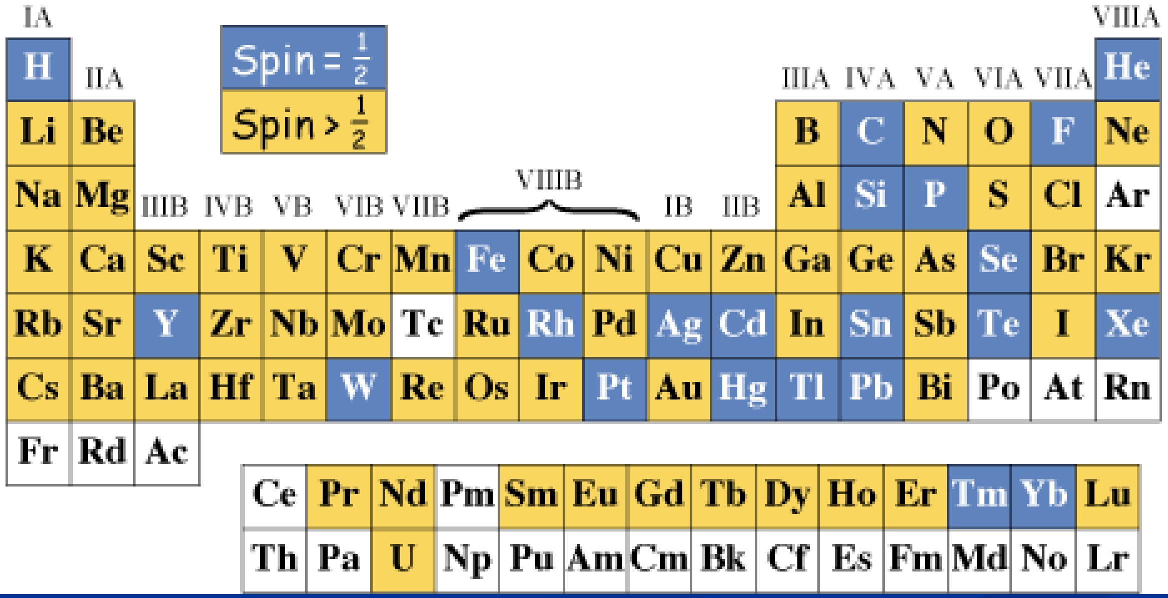
Number of protons *Z*	Number of neutrons *N*	Number of nuclides
even	even	168
odd	odd	8
odd	even	50
even	odd	57

Allowed Nuclear Multipole Moments as a function of Spin I

	$l = 0$	$l = 1$	$l = 2$	$l = 3$	$l = 4$
Spin	monopole	dipole	quadrupole	octapole	hexadecapole
$I = 0$	electric	0	0	0	0
$I = \frac{1}{2}$	electric	magnetic	0	0	0
$I = 1$	electric	magnetic	electric	0	0
$I = \frac{3}{2}$	electric	magnetic	electric	magnetic	0
$I = 2$	electric	magnetic	electric	magnetic	electric

Nuclear Magnetic Dipole Moment couples to magnetic field

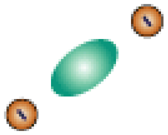




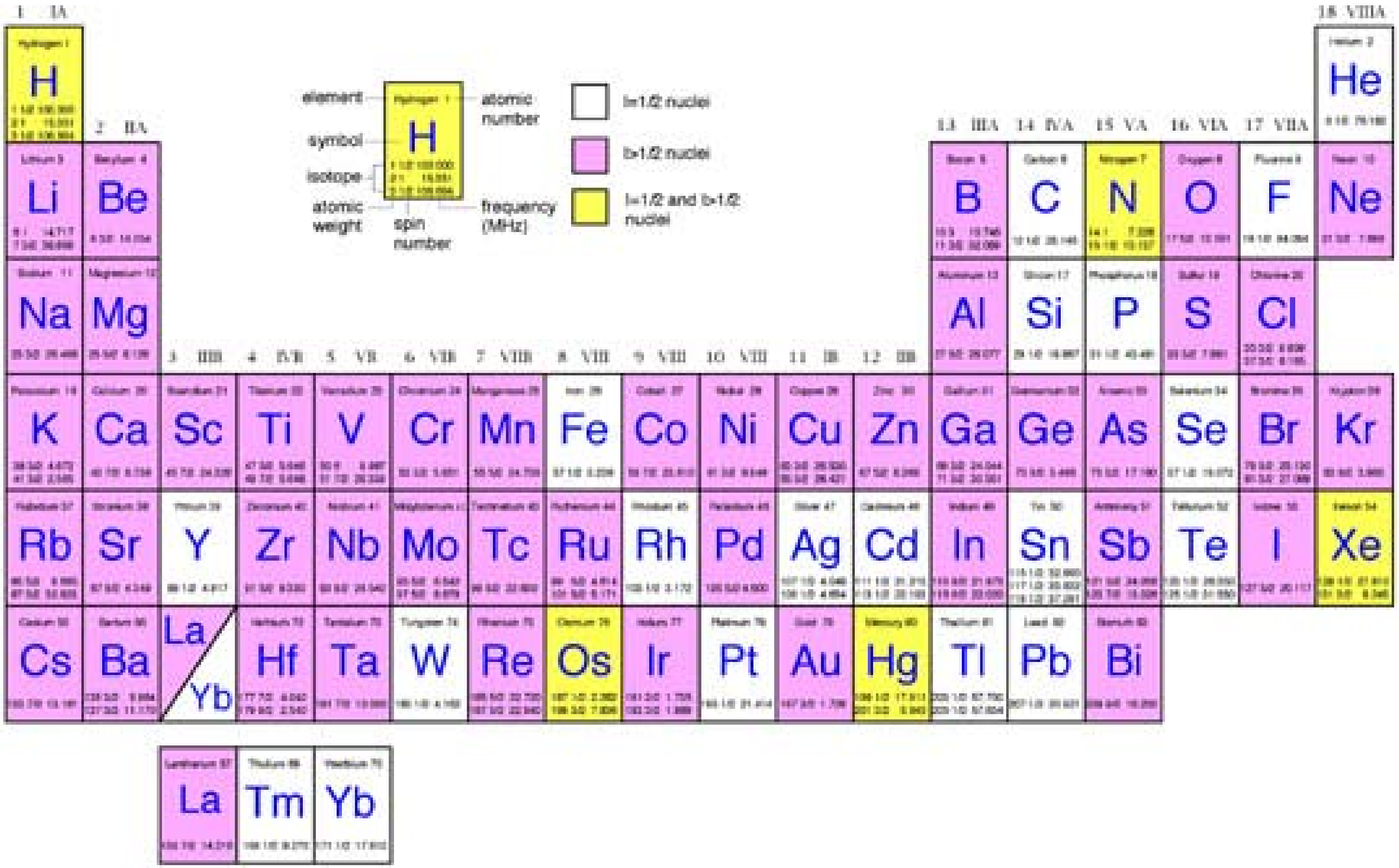
IA	IIA	IIIB	IVB	VB	VIB	VIIB	VIIIB			IB	IIB	IIIA	IVA	VA	VIA	VIIA	VIIIA
H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Rd	Ac															

Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Nuclear Electric Quadrupole Moment couples to electric field gradient



Elements Accessible by NMR



Nuclear Spin

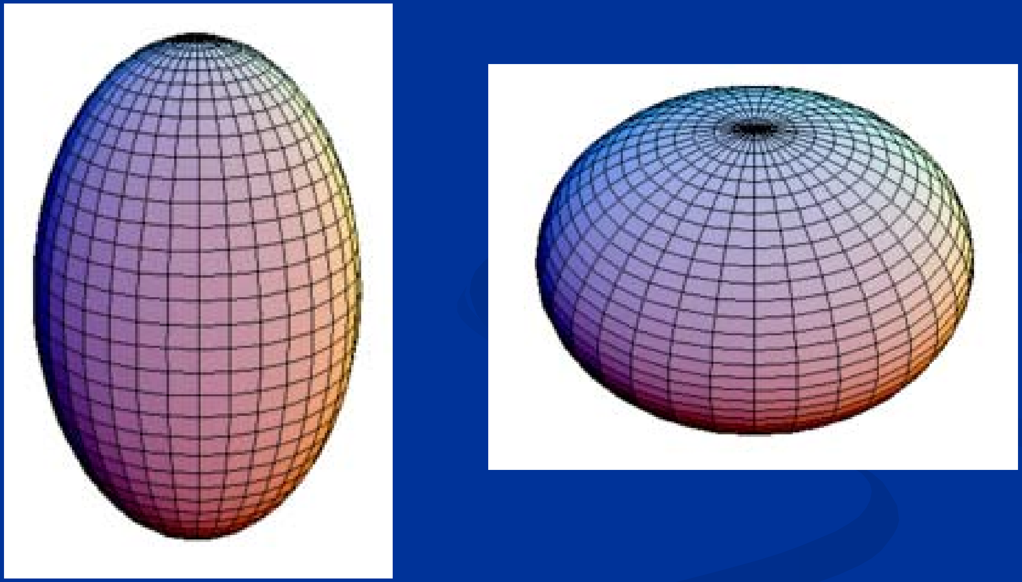
- NO stable nucleus has spin 2
- the highest value of spin for a stable nucleus is 7 ^{176}Lu
- unstable nuclei

  highest integral spin 16 - isomer ^{178}Hf
  highest half-integer 37/2 - isomer ^{177}Hf)

Nuclear Spin

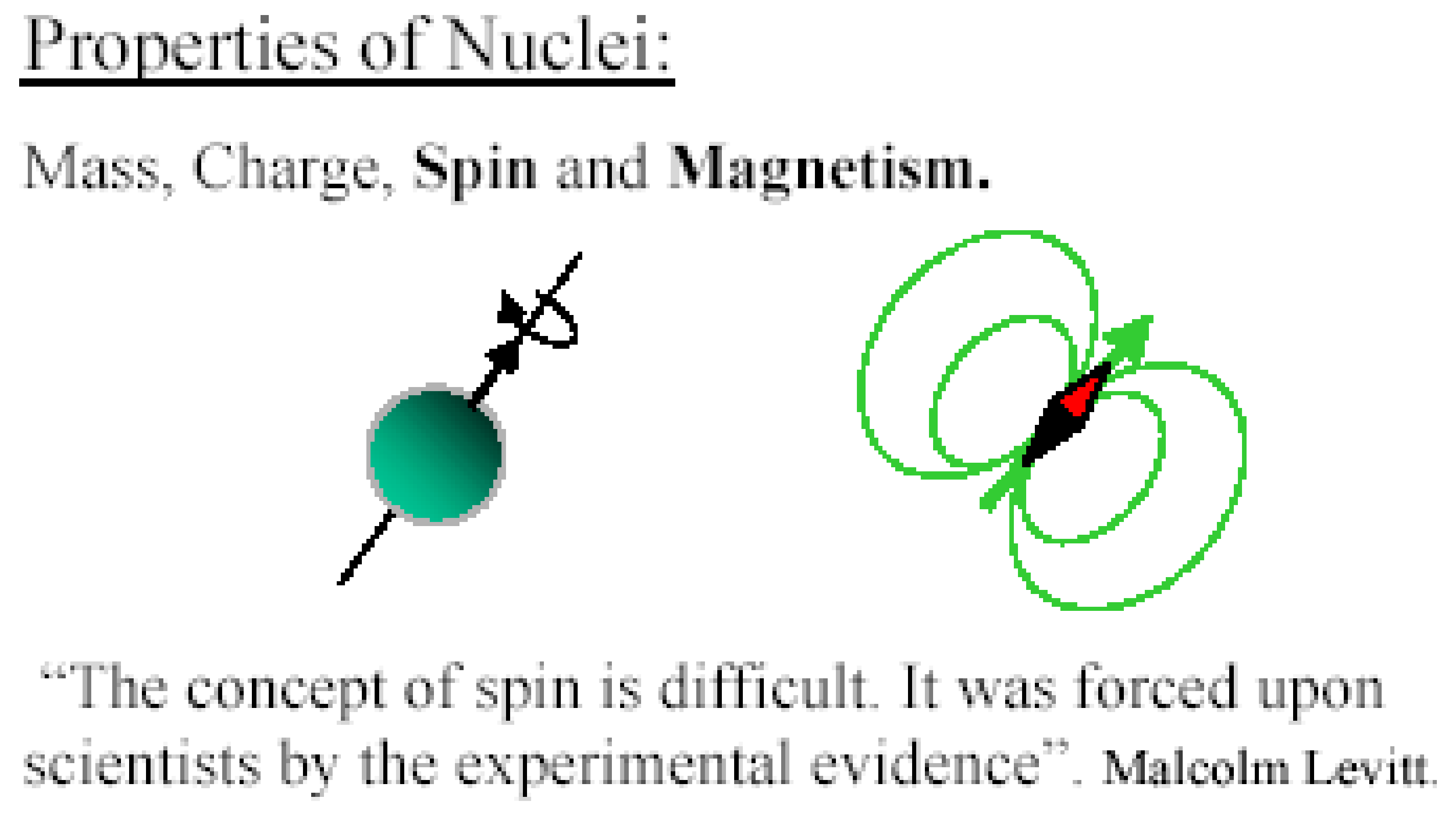
- Nuclei with spin ½ - a spherical charge distribution
- Nuclei with *I* > ½ - nonspherical charge distributions

(prolate or oblate)



- All nuclei with non-zero spins – magnetic moments (μ)
- Nonspherical nuclei - an electric quadrupole moment (e*Q*)

Nuclear Spin

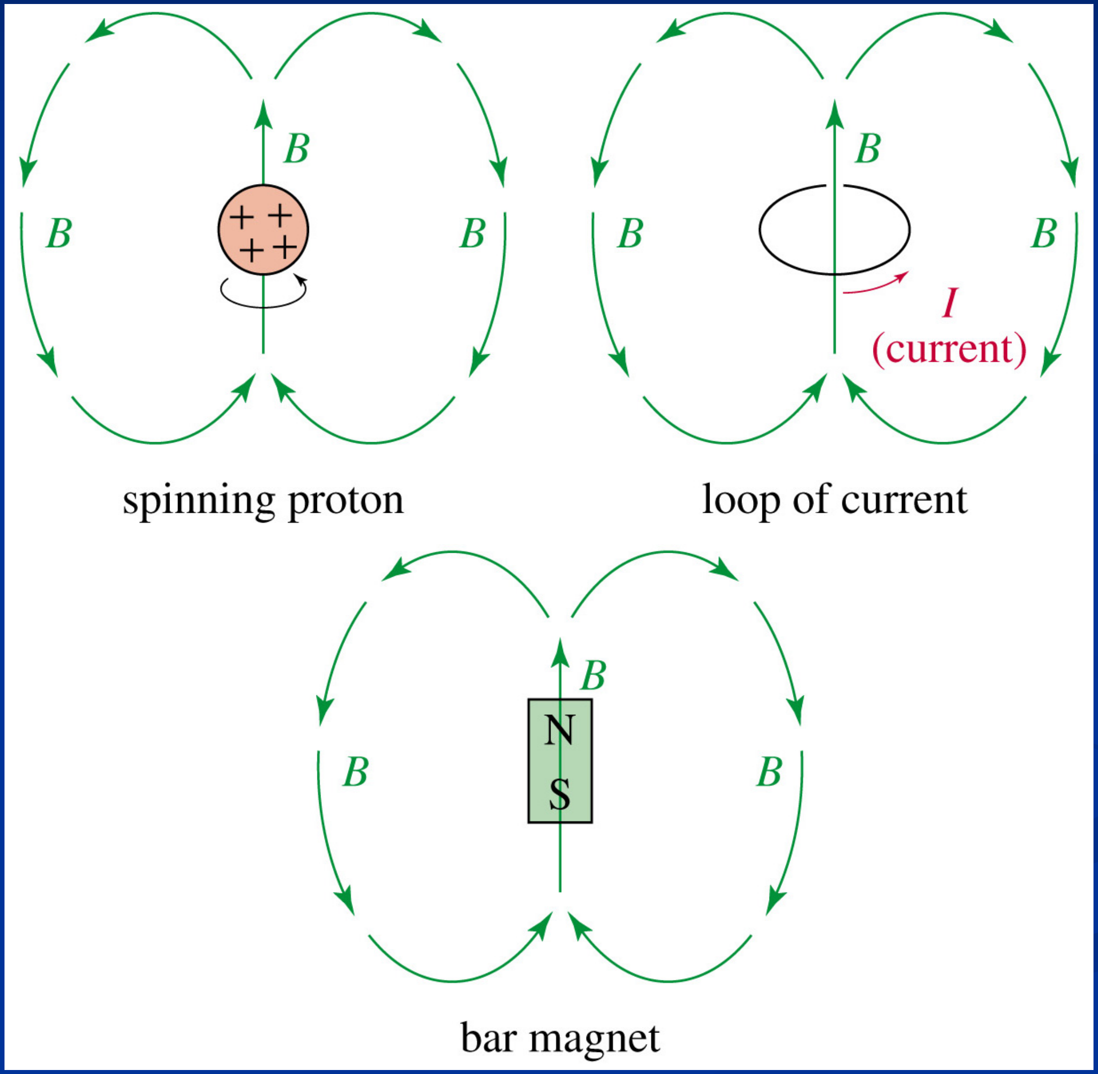


Properties of Nuclei:

Mass, Charge, **Spin** and **Magnetism.**

“The concept of spin is difficult. It was forced upon scientists by the experimental evidence”. **Malcolm Levitt.**

Nuclear Spin



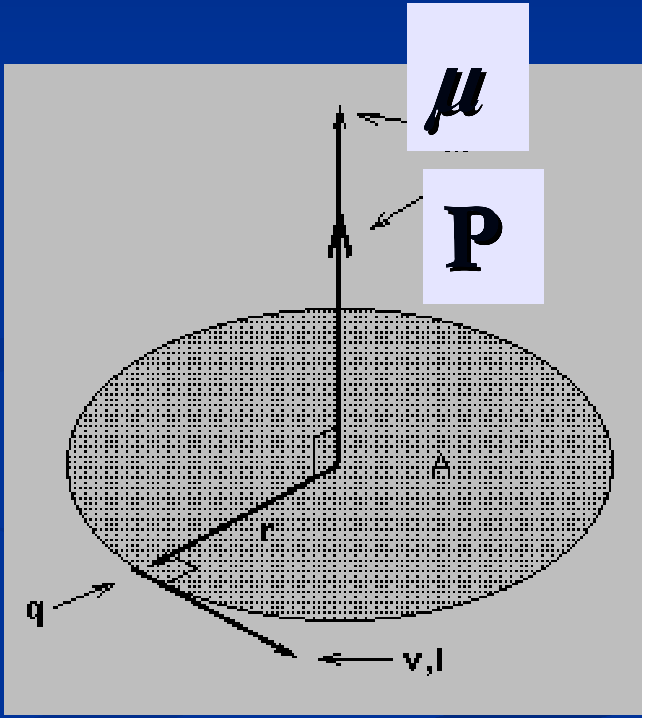
Nuclear Spin

Nuclear spin = Spin angular momentum, *P (vector)*

Spin quantum number *I*
Magnetic quantum number m_I

Magnitude of *P* is quantized:

$$P = \frac{h}{2\pi}\sqrt{I(I+1)}$$



Direction with respect to the magnetic field B_0 is quantized:

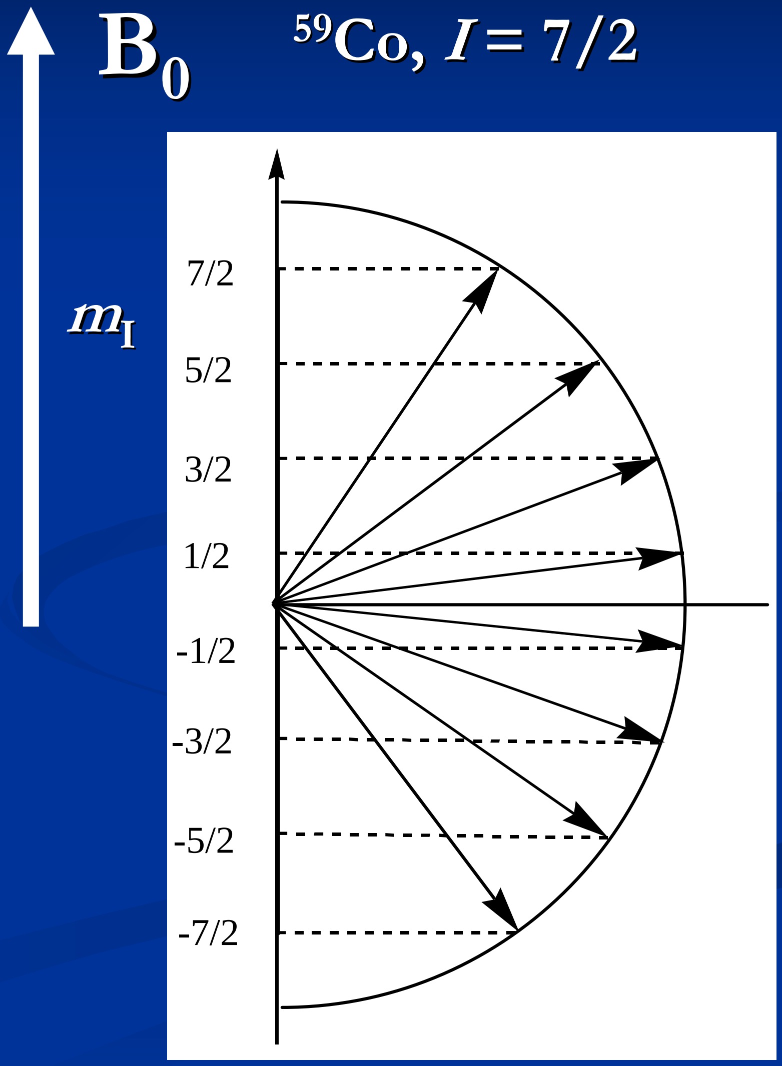
$$P_z = \frac{h}{2\pi} m_I$$

Spin Angular Momentum, *P*

$$P = \frac{h}{2\pi}\sqrt{I(I+1)}$$

$$P_z = \frac{h}{2\pi} m_I$$

^{59}Co, $I = 7/2$



I = Nuclear spin quantum number

$I = 0, ½, 1, 3/2, 5/2, 3, 7/2,.....$

m_I = Nuclear spin magnetic quantum number

Multiplicity, M $2I + 1$ values

$m_I = I, I\text{-}1, I\text{-}2, ..., \text{-}I\text{+}2, \text{-}I\text{+}1, \text{-}I$

$$\cos\theta = \frac{P_z}{P} = \frac{m_I}{\sqrt{I(I+1)}}$$

Spin Angular Momentum, *P*

$$P = \frac{h}{2\pi}\sqrt{I\left(I+1\right)}$$

I	$[I(I+1)]^{½}$
½	0.866
1	1.414
3/2	1.936
5/2	2.958
3	3.464
7/2	3.969
4	4.472
9/2	4.975

Spin Magnetic Moment, μ

The electrons, nucleons (protons, neutrons) and some nuclei possess intrinsic magnetism, which is not due to a circulating current.
Permanent magnetic moment similarly as spin angular momentum.

Magnetic moment, μ, is directly proportional to the spin angular momentum, P:

$$\mu = \gamma \; P$$

γ is the gyromagnetic (magnetogyric) ratio

Magnetogyric Ratio

γ - the magnetogyric ratio is the ratio of the nuclear magnetic moment μ to the nuclear angular momentum P.

$$\mu = \gamma \ P$$

γ - Important characteristic of nuclei

[rad T^{-1} s^{-1}]

Spin Magnetic Moment, μ

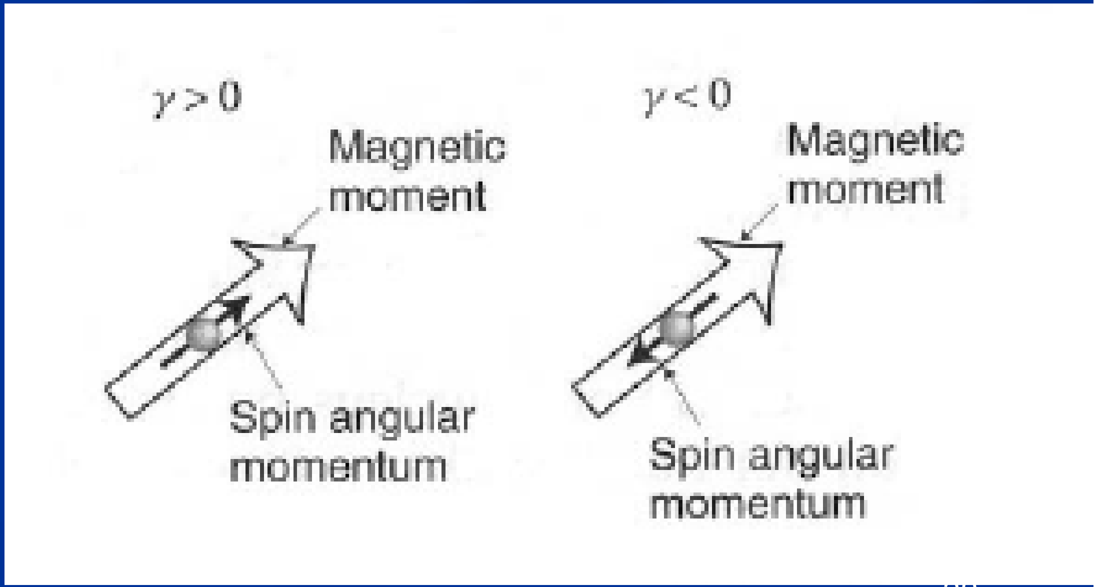
$$\mu = \gamma P = \gamma (h/2\pi) [I(I + 1)]^{½}$$

$$\mu_z = \gamma P_z = \gamma (h/2\pi) m_I$$

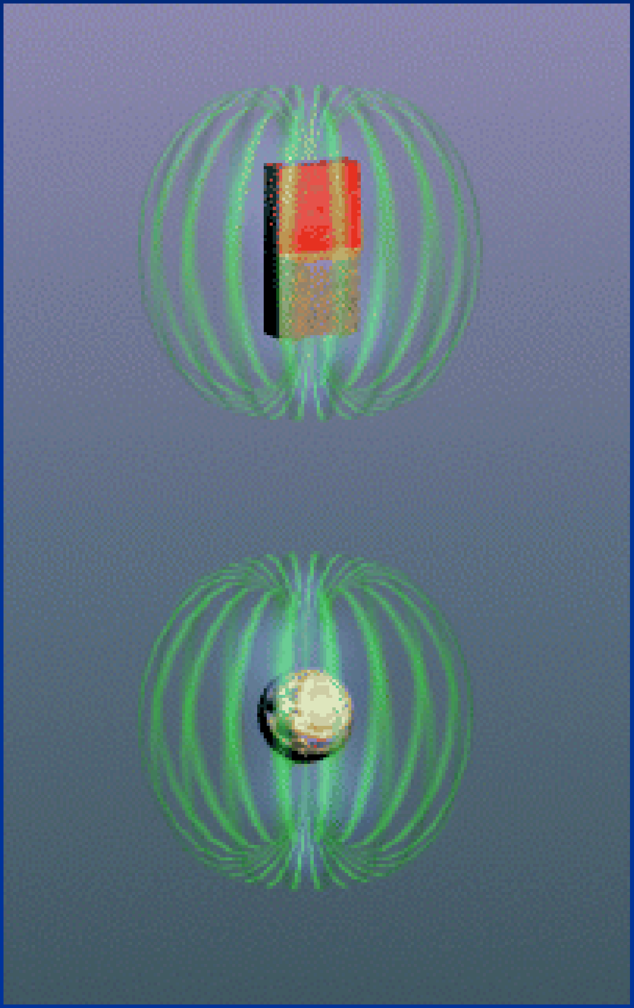
Nucleus	^{1}H	^{2}H	^{13}C	^{15}N	^{19}F	^{29}Si	^{31}P
γ [10^{-7} rad $T^{-1}s^{-1}$]	26.75	4.11	6.73	-2.71	25.18	–5.32	10.84

electron

$$\gamma_e = 17\ 609\ 10^7 = 658\ \gamma(H)$$

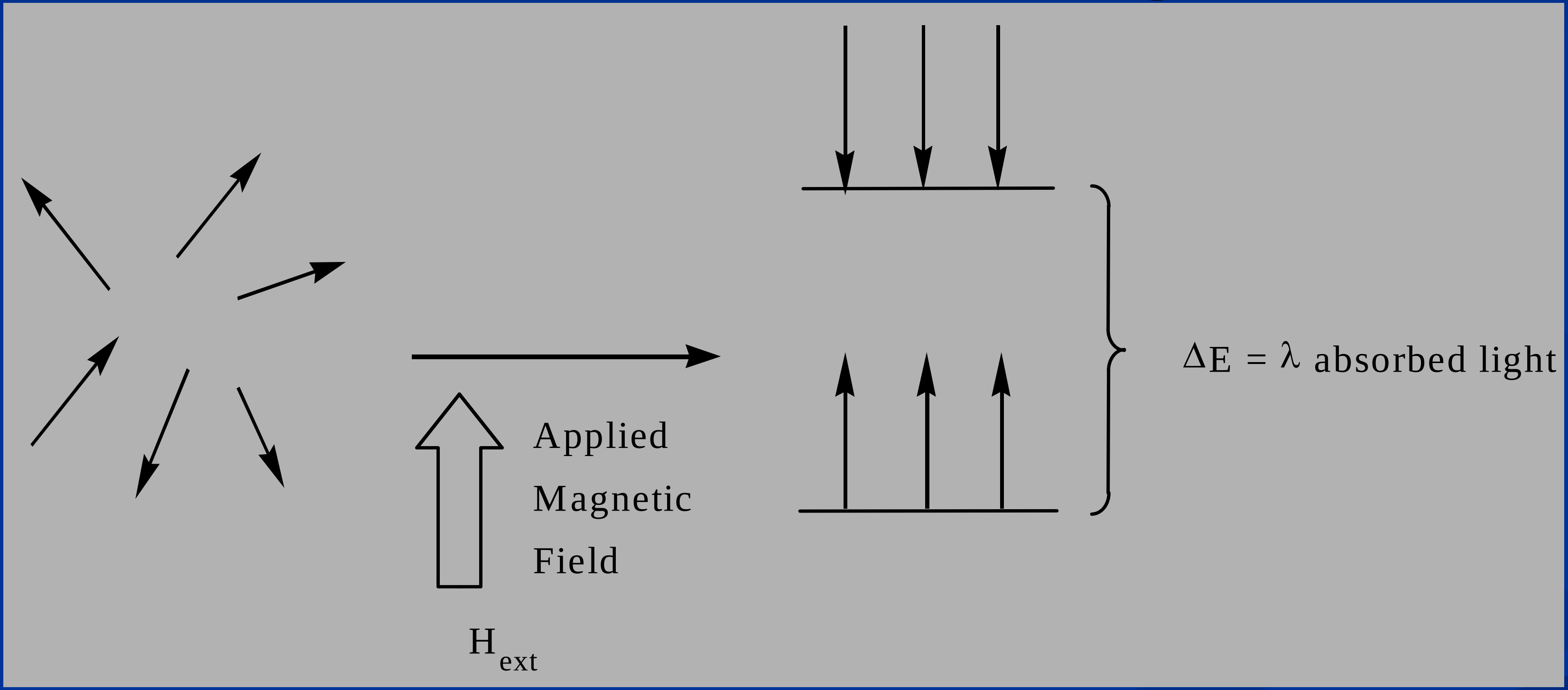


Nuclear Spin in Magnetic Field



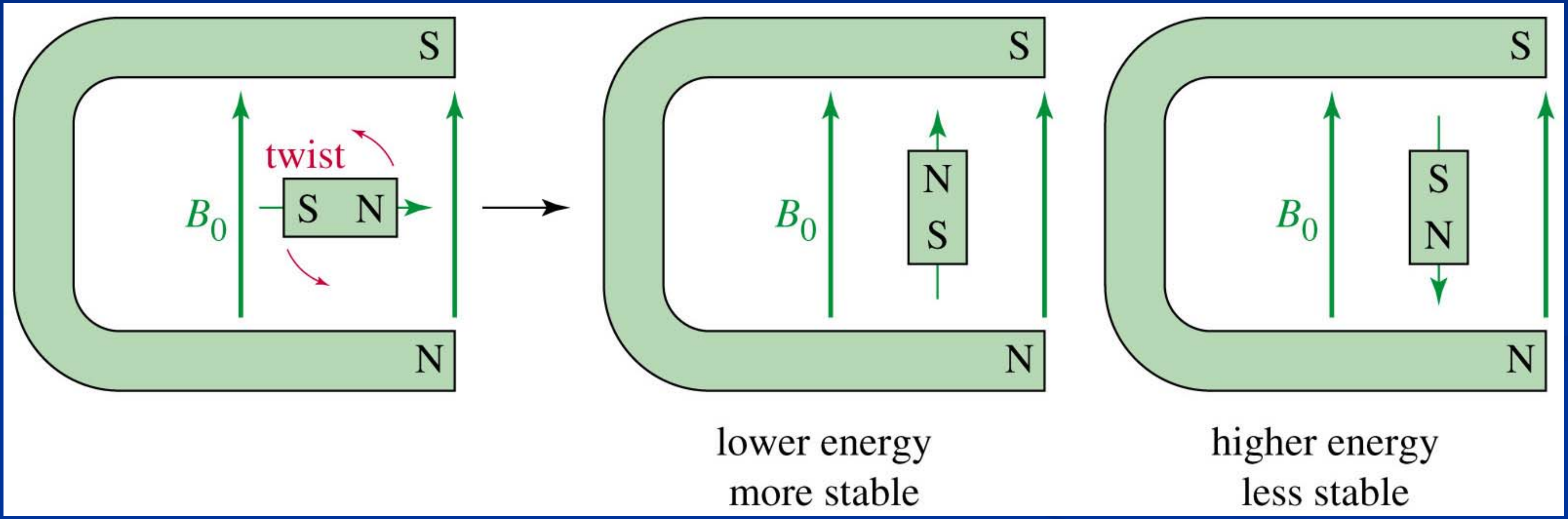
Nuclear Spin in Magnetic Field

Random orientation **Alignment**



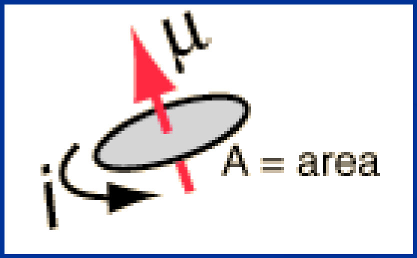
No Field **Magnetic Field**

Nuclear Spin in Magnetic Field



Nuclear Spin in Magnetic Field

- An angular momentum is associated with each rotating object
- A nuclear spin possesses a magnetic moment arising from the angular momentum of the nucleus
- The magnetic moment is a vector perpendicular to the current loop
- In a magnetic field (B) the magnetic moment behaves as a magnetic dipole



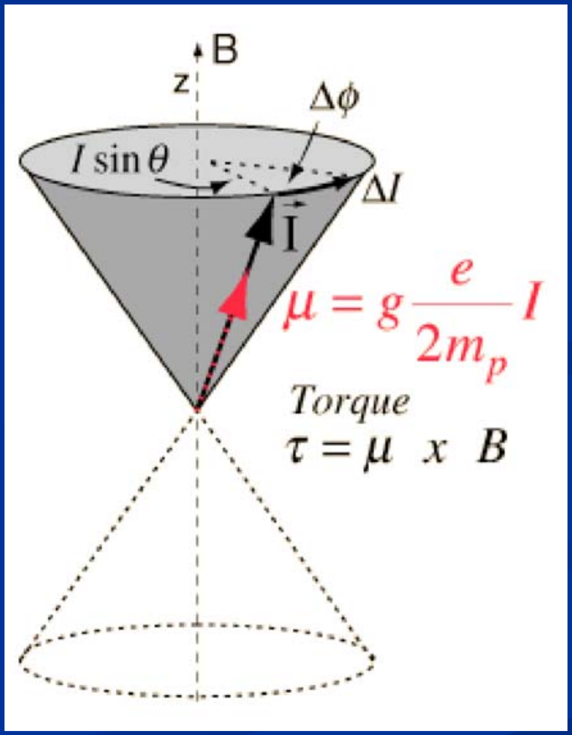
$$\mu = i\,A$$

Nuclear Spin in Magnetic Field

In B_0, a magnetic moment is directed at some angle w.rt. B_0 direction

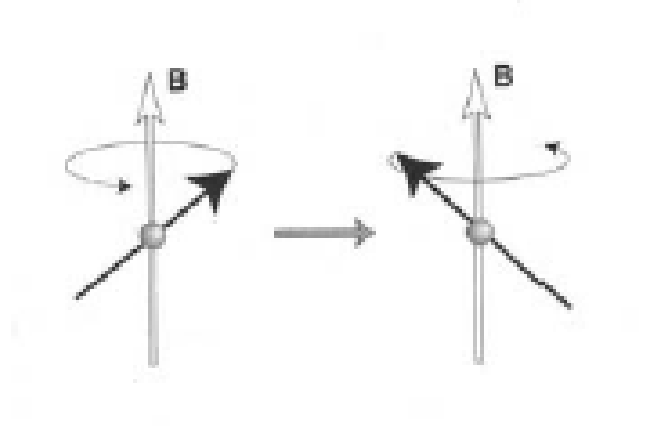
the B_0 field will exert a torque on the magnetic moment. This causes it to precess about the magnetic field direction

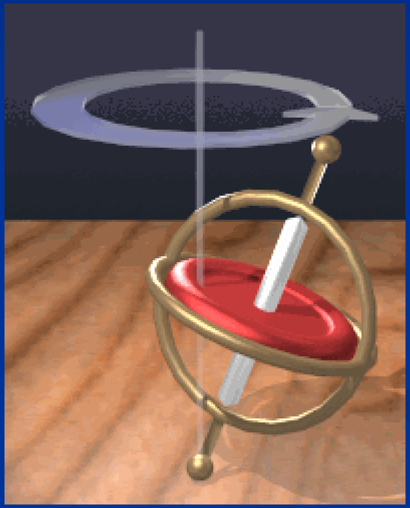
Torque is the rate of change of the nuclear spin angular momentum

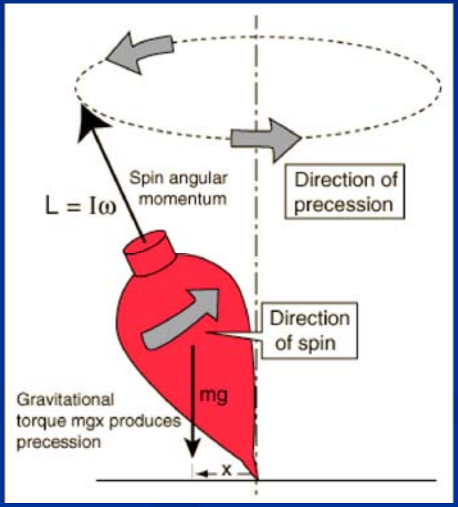


Nuclear Spin in Magnetic Field

Spin precession in the external magnetic field.







Quantum description of precession shows that the frequency of the motion is:

$$\omega_0 = -\gamma\, B_0 \text{ [rad s}^{-1}\text{] or } \nu_0 = -\gamma\, B_0 / 2\pi \text{ [Hz]}$$

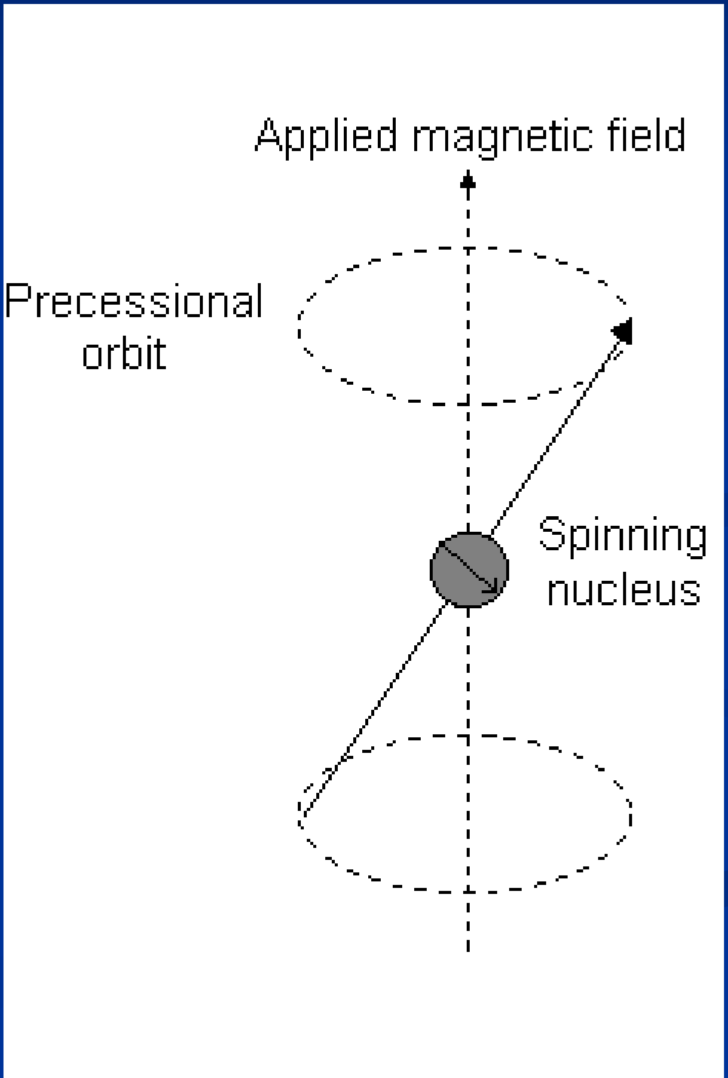
It is called the Larmor frequency (if $\gamma > 0$ then $\nu_0 < 0$)

Larmor Frequency

$\omega_0 = -\gamma B_0$ [rad s^{-1}]

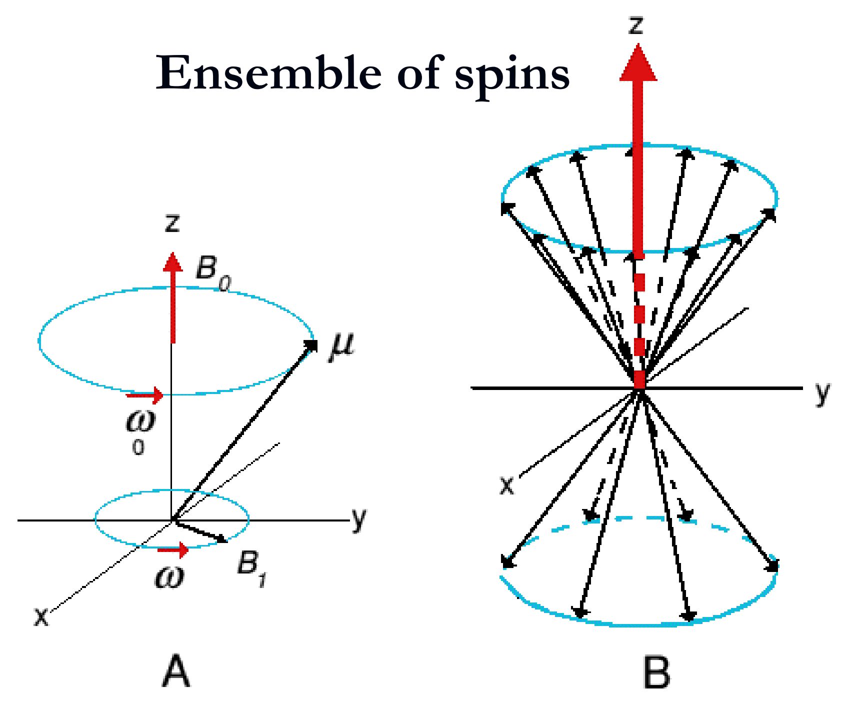
$\nu_0 = -\gamma B_0 / 2\pi$ [Hz]

$$\boxed{\nu_0 = -\frac{\gamma B_0}{2\pi}}$$



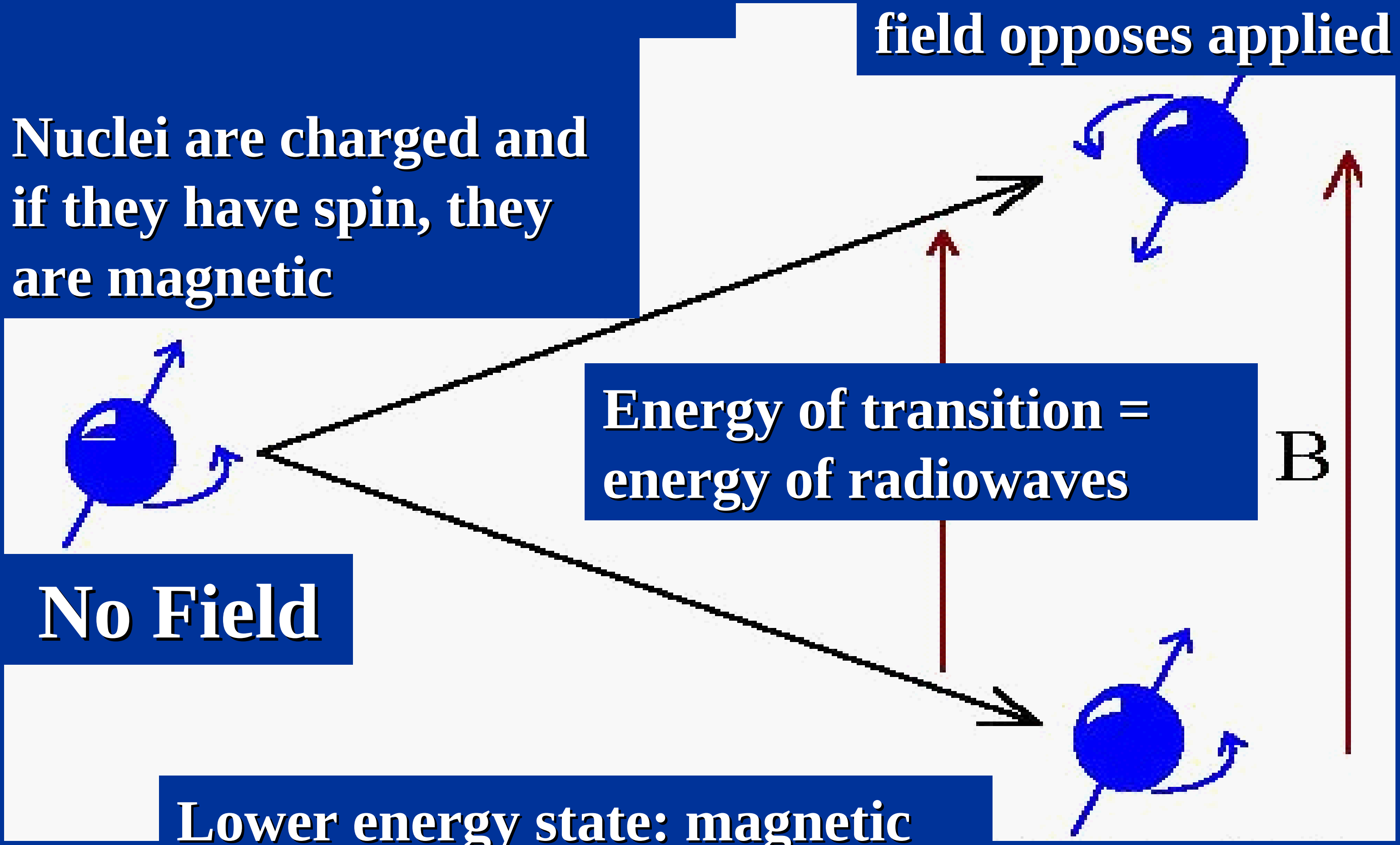
Larmor Frequency

Sir Joseph Larmor
(1857-1942)



$$\omega_0 = -\gamma\, B_0 \text{ [rad s}^{-1}\text{] or } \nu_0 = -\gamma\, B_0 / 2\pi \text{ [Hz]}$$

Nuclear Zeeman Effect - Splitting



Higher energy state: magnetic field opposes applied field

$m_{\mathrm{I}}\ -\frac{1}{2}$

Nuclei are charged and if they have spin, they are magnetic

Energy of transition = energy of radiowaves

Applied Magnetic Field = B_0

No Field

Lower energy state: magnetic field aligned with applied field

$m_{\mathrm{I}}\ +\frac{1}{2}$

Nuclear Spin in Magnetic Field

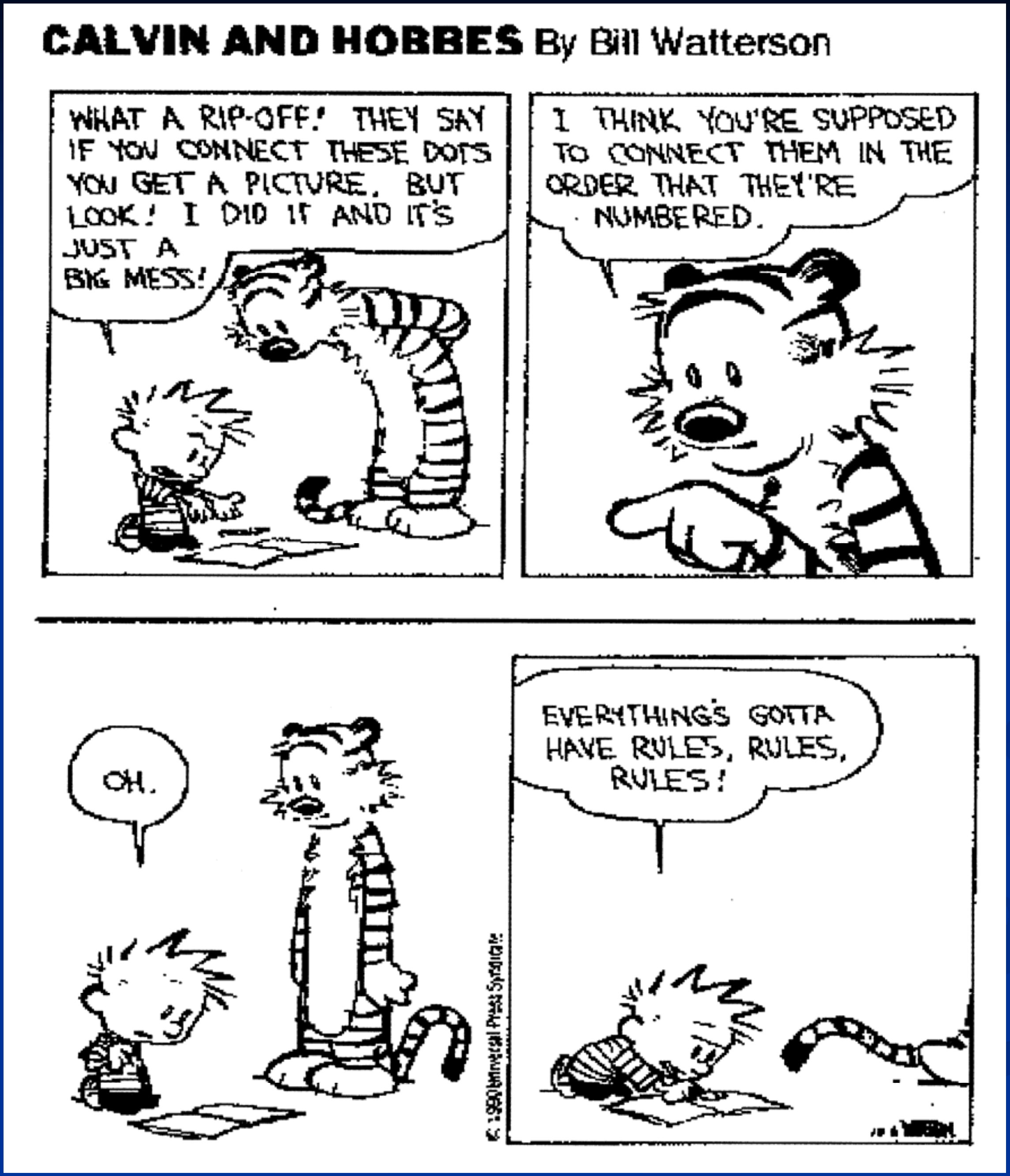
The magnetic energy depends on the interaction between the magnetic moment and B_0 field:

$$E_{mag} = -\mu \cdot B_0 \quad \text{(scalar product)}$$

$$E_{mag} = -\mu_z B = -\gamma P_z B$$

$$E_{mag} = -m_I \hbar \gamma B$$

NMR selection rule $\Delta m_I = \pm 1$


CALVIN AND HOBBES By Bill Watterson
WHAT A RIP-OFF! THEY SAY IF YOU CONNECT THESE DOTS YOU GET A PICTURE. BUT LOOK! I DID IT AND IT'S JUST A BIG MESS!
I THINK YOU'RE SUPPOSED TO CONNECT THEM IN THE ORDER THAT THEY'RE NUMBERED.
OH.
EVERYTHING'S GOTTA HAVE RULES, RULES, RULES!
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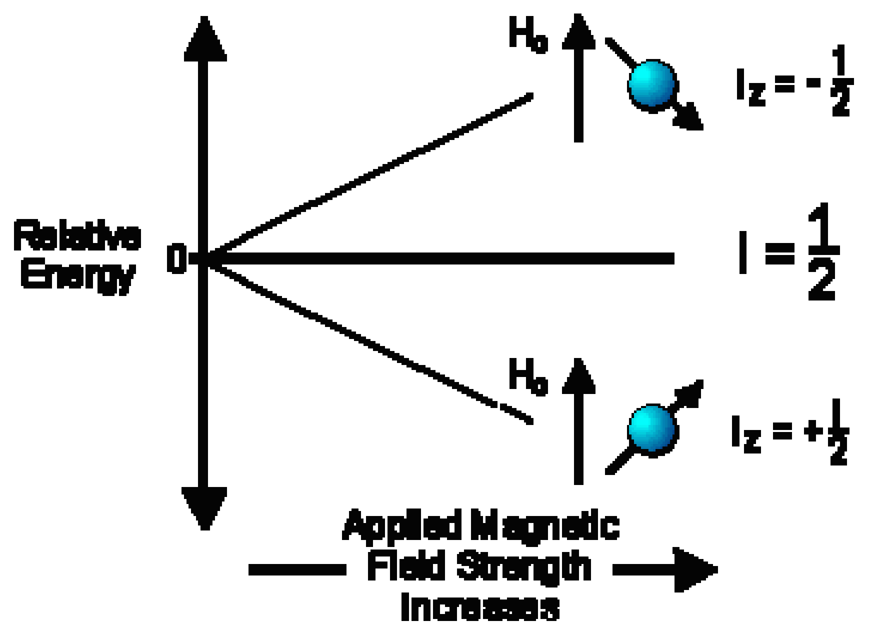
WATTERSON

Spin in Magnetic Field

$I = ½$

$E_{m=-1/2}$

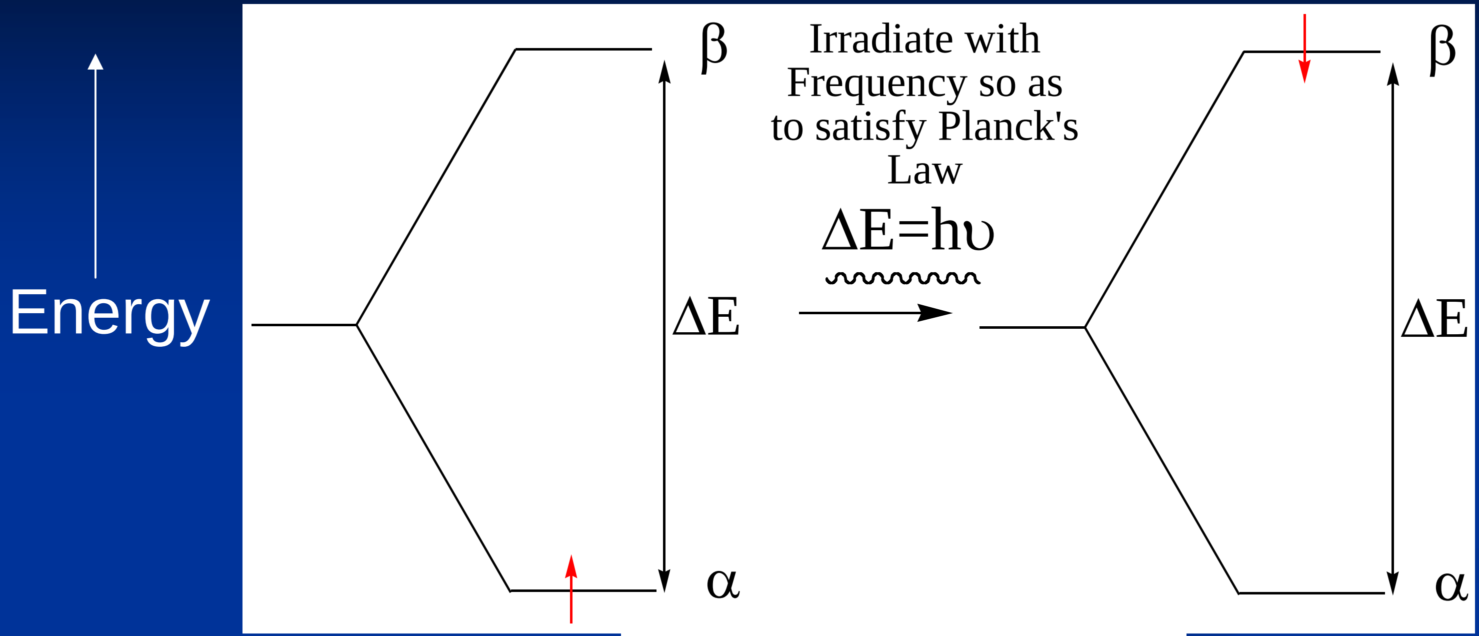
$E_{m=1/2}$



$$\Delta E_{mag} = E_{m=-1/2} - E_{m=1/2} = \Delta m_I \, \hbar \, \gamma \, B = h \, \nu \;\Rightarrow\; \nu = \gamma \, B/2\pi$$

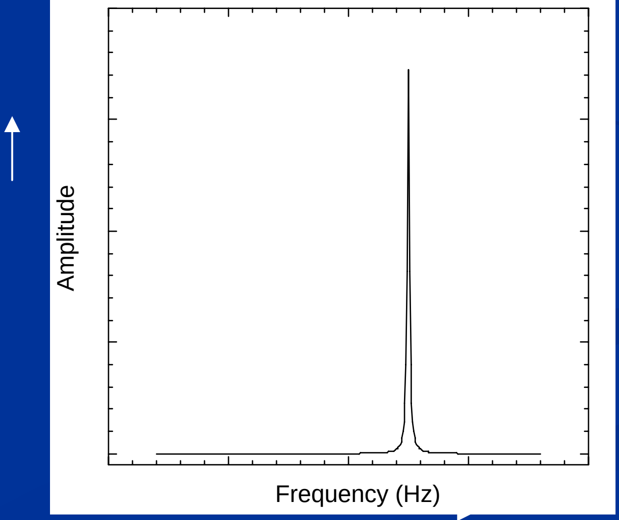
The frequency of the electromagnetic radiation that corresponds to the energy difference between the two energy levels is equal to the precessional frequency of the nuclei.

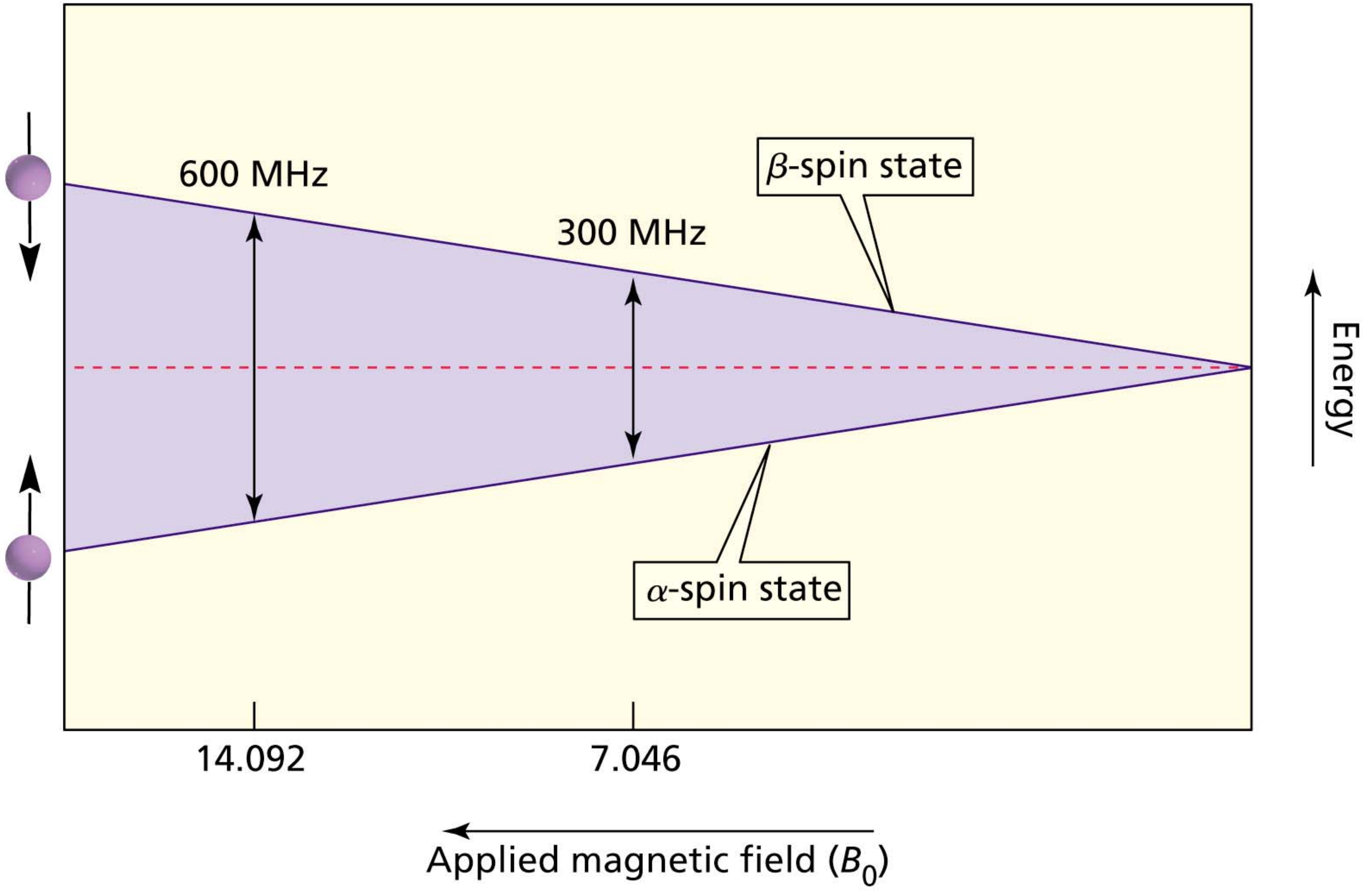
Excitation of NMR Spin



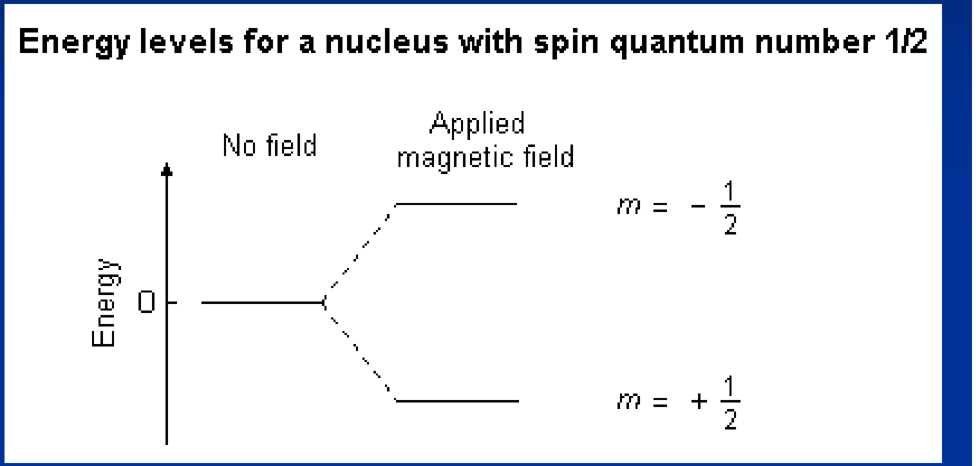
Irradiate with Frequency so as to satisfy Planck's Law

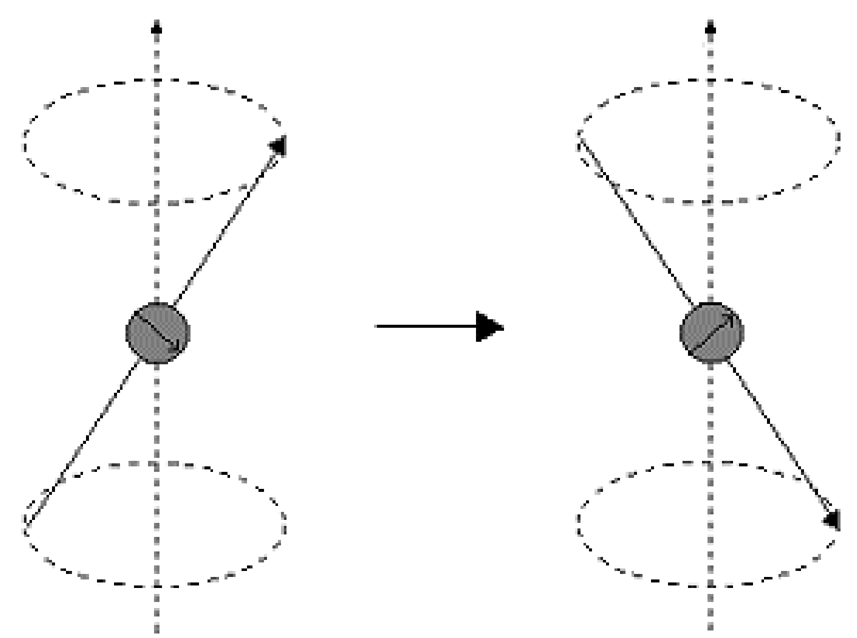
$\Delta E = h\upsilon$




600 MHz
300 MHz
β-spin state
α-spin state
Energy
14.092
7.046
Applied magnetic field (B_0)

Energy Levels for *I* = ½

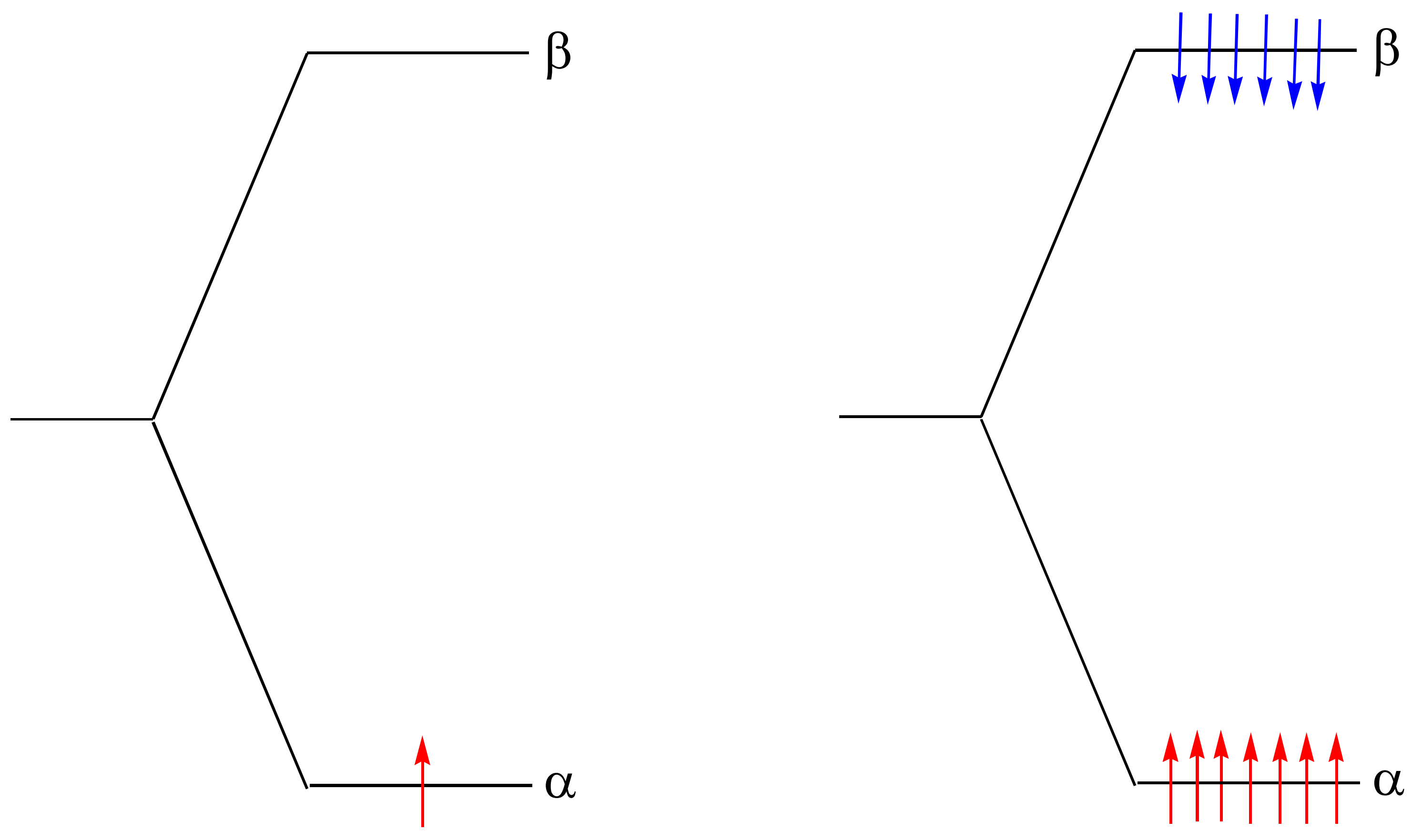

Energy levels for a nucleus with spin quantum number 1/2



$$\Delta E_{mag} = E_{m=-1/2} - E_{m=1/2} = \Delta m_I\, \hbar\, \gamma\, B = h\, \gamma\, B/2\pi$$

$\Delta E = (6.626\ 10^{-34}\ \mathrm{J\ s}\ \ 26.75\ 10^{7}\ \mathrm{rad\ T^{-1} s^{-1}}\ 11.743\ \mathrm{T})/2\pi = 3.313\ 10^{-25}\ \mathrm{J}$
very small energy difference

Energy Levels for *I* = ½



Boltzmann Distribution

The excess of nuclei on the lower energy level is given by Boltzmann distribution:

$$N_{\uparrow\downarrow}/N_{\uparrow\uparrow} = \exp(-\Delta E/k_B T) = \exp(-\hbar\,\gamma\,B\,/k_B T)$$

$$= \exp(-3.313\ 10^{-25}/\ 4.101\ 10^{-21}) = \exp(-8.078\ 10^{-5}) = 0.99991922$$

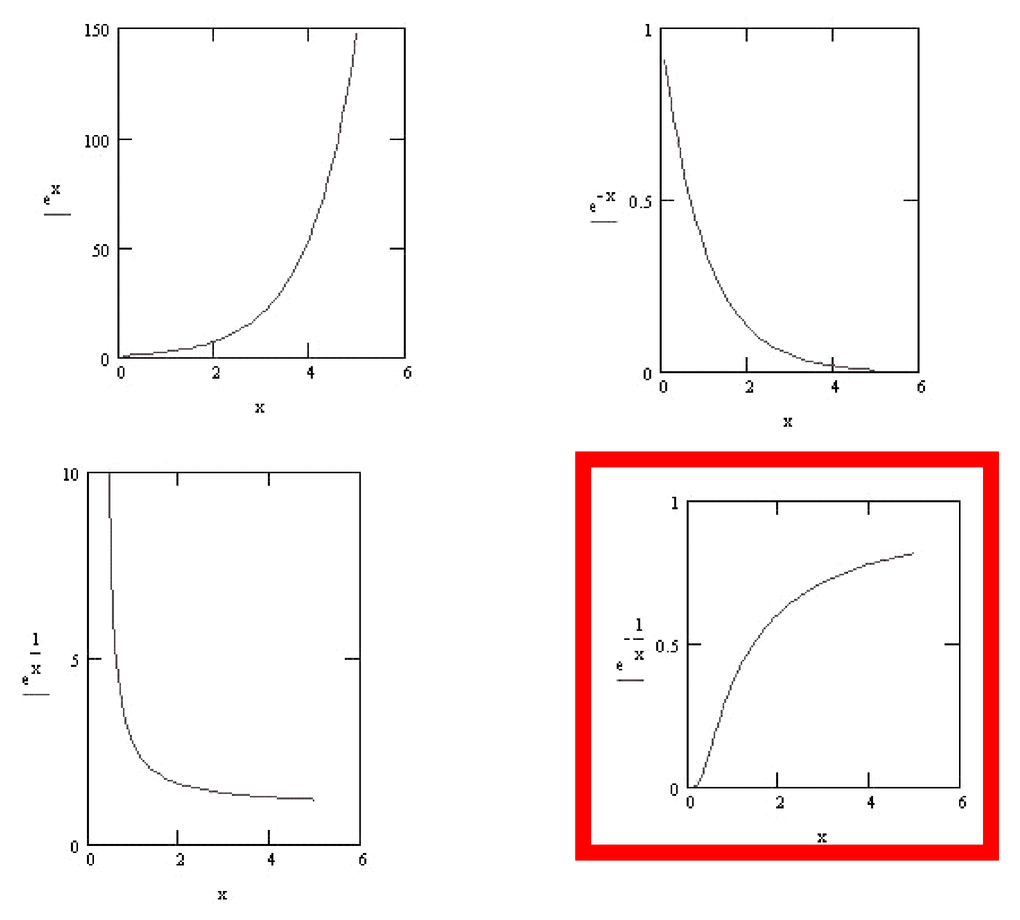
If $N_{\uparrow\uparrow}$ = 1 000 000 then $N_{\uparrow\downarrow}$ = 999919

Only 81 out of million ^{1}H nuclei contribute to NMR signal at 500 MHz!

$\hbar = 1.055\ 10^{-34}$ J s
$\gamma_H = 26.75\ 10^7$ rad $T^{-1}s^{-1}$
B = 11.7433 T (500 MHz)
$k_B = 1.3807\ 10^{-23}$ J K^{-1}
T = 297 K

Boltzmann Distribution

$$N\uparrow\downarrow / N\uparrow\uparrow = \exp(-\Delta E/k_B T) = \exp(-\hbar\,\gamma\, B\,/k_B T)$$



the stronger the field and the higher the magnetogyric ratio, the larger the population difference

the higher the temperature, the smaller the population difference

Boltzmann Distribution

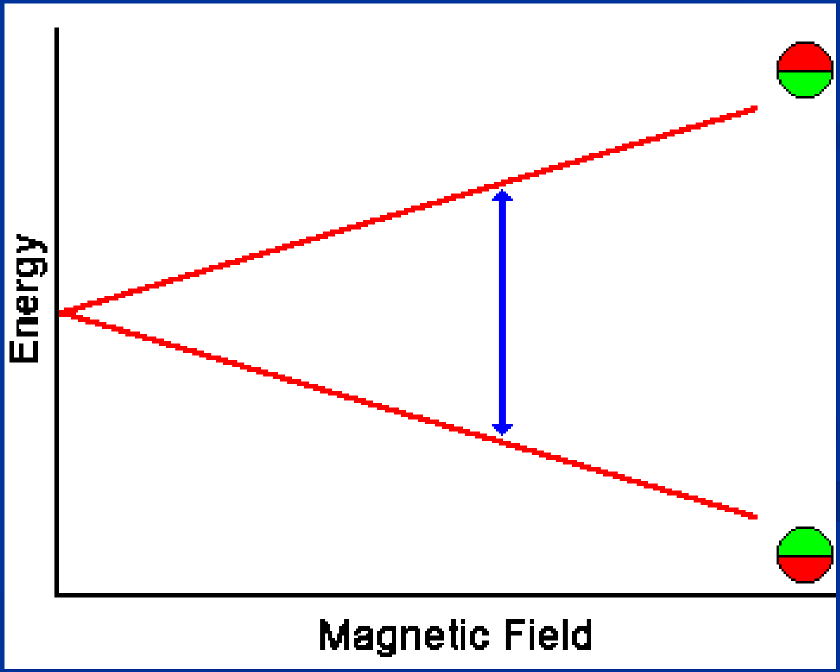
The higher the field,

the larger the energy difference,

the larger the population difference,

the larger the net magnetization,

and the bigger the NMR signal



Nuclear Magnetic Resonance (NMR)

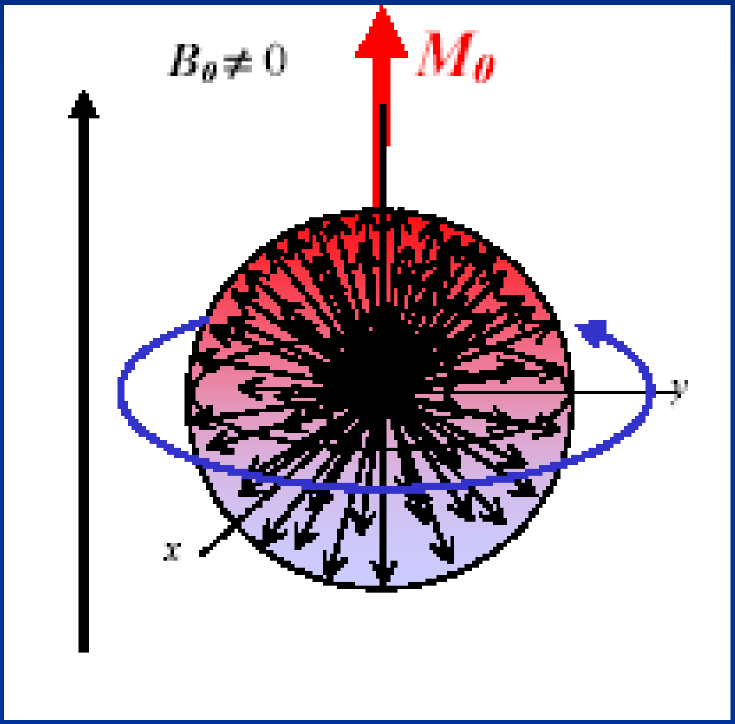
- **Nuclear** – spin ½ nuclei (e.g. protons) behave as tiny bar magnets.

- **Magnetic** – a strong magnetic field causes a small energy difference between + ½

  and – ½ spin states.

- **Resonance** – photons of radio waves can match the exact energy difference between the + ½ and – ½ spin states resulting in absorption of photons as the protons change spin states.

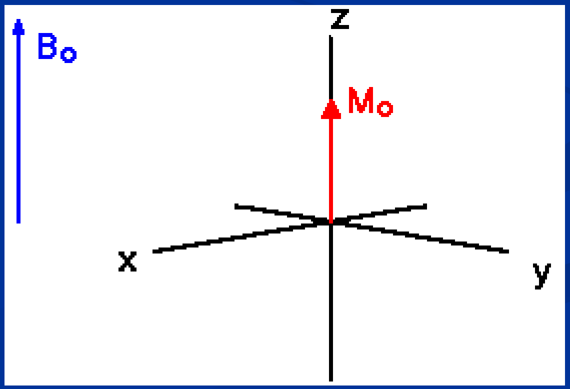
Magnetization



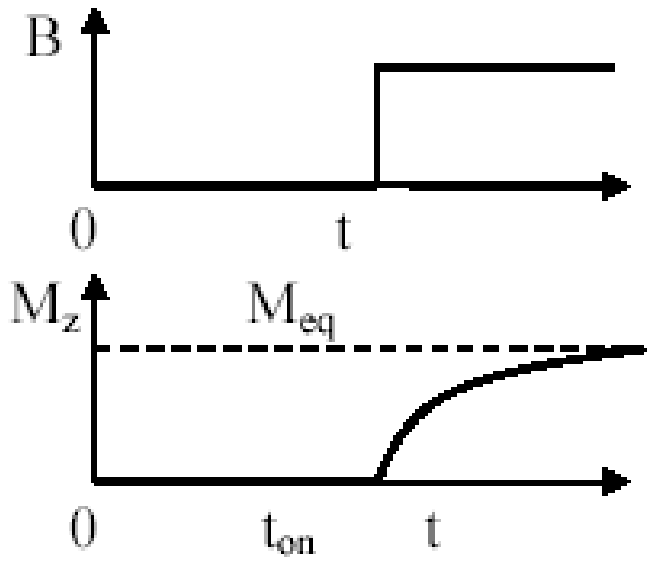
In-Field

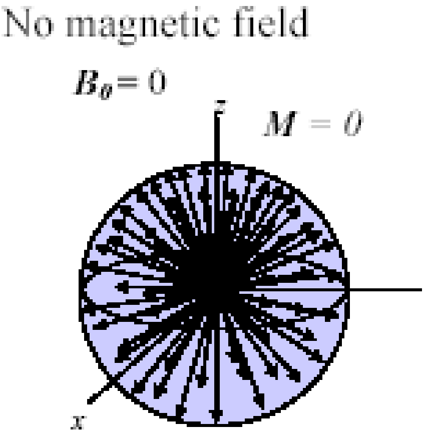
More nuclei point in parallel to the static magnetic field.
The macroscopic magnetic moment, M_0

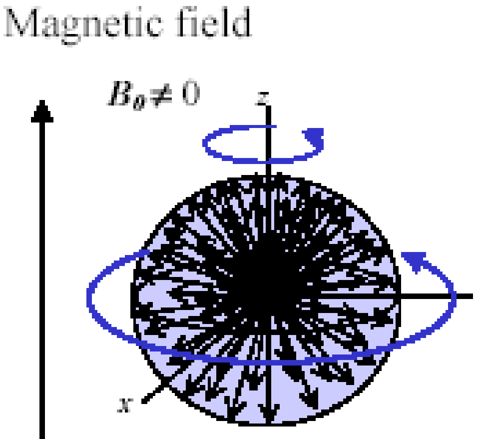
$$M_0 = \Sigma\, \mu_i$$



Longitudinal Magnetization

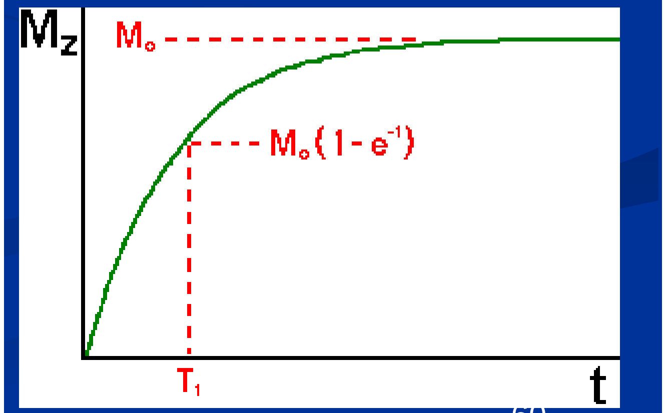



No magnetic field


Magnetic field

$$\frac{d}{dt}M_Z = R_1(M_{eq}-M_z) = \frac{1}{T_1}(M_{eq}-M_z)$$

$$M_z(t) = M_{eq}\left(1-e^{\frac{-(t-t_{on})}{T_1}}\right)$$



Spin-Lattice Relaxation Time

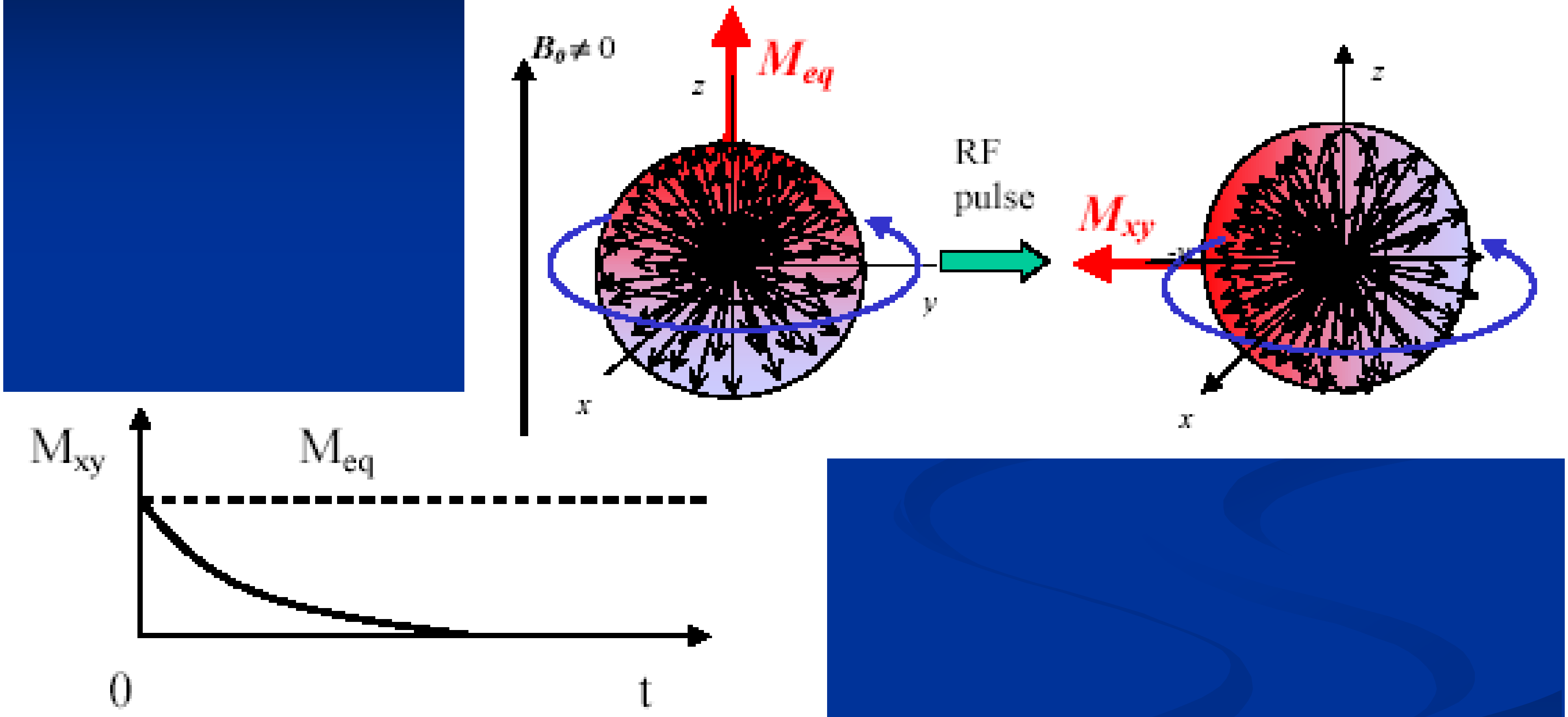
$R_1 = 1/T_1$ [Hz] longitudinal relaxation rate constant

T_1 [s] longitudinal relaxation time

spin-lattice relaxation time

enthalpy

Transverse Magnetisation



$$\frac{d}{dt}M_{xy} = -R_2 M_{xy} = \frac{-1}{T_2}M_{xy} \quad M_{xy}(t) = M_{eq}e^{\frac{-t}{T_2}}$$

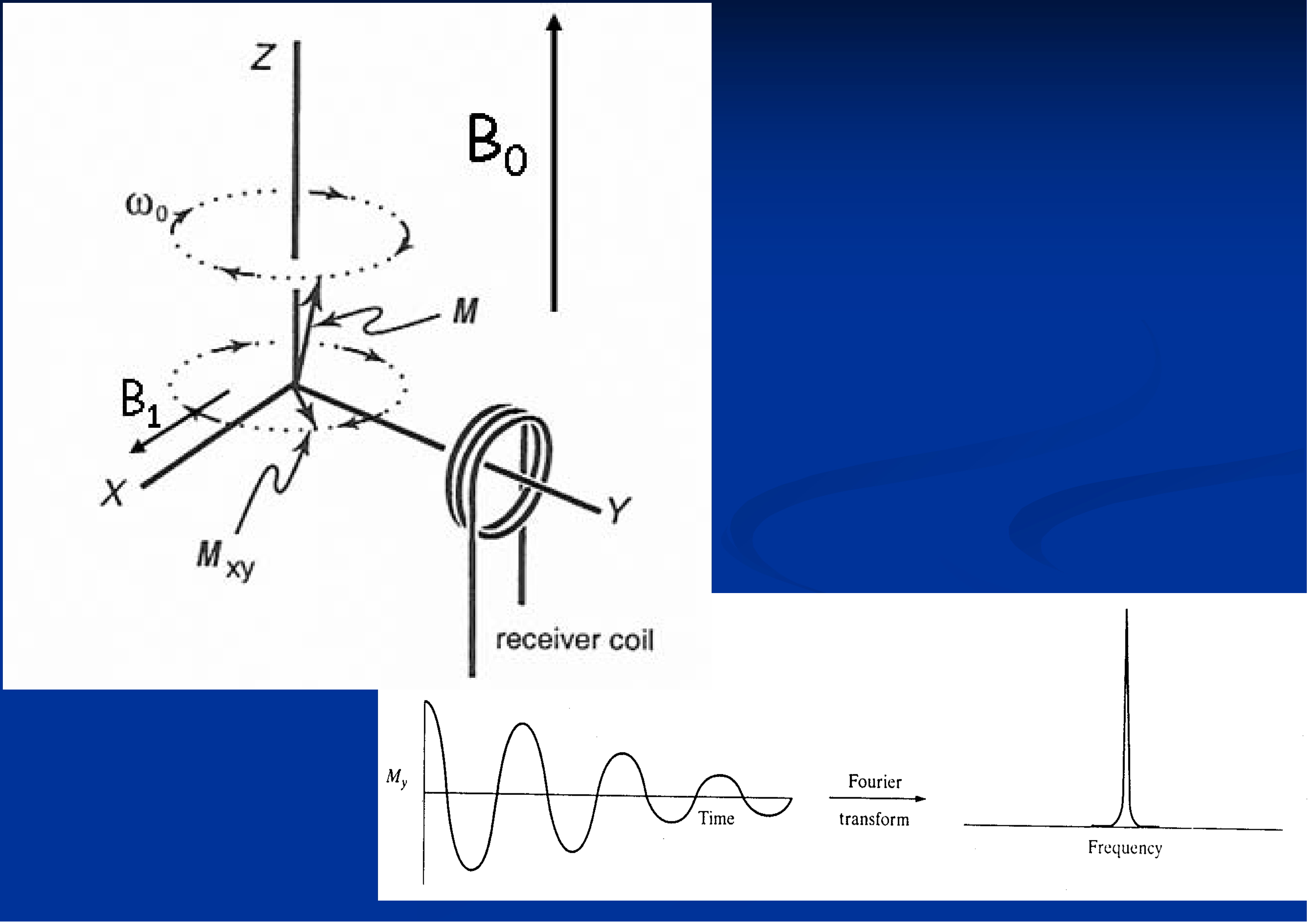
Spin-Spin Relaxation Time

$R_2 = 1/T_2$ [Hz] transverse relaxation rate constant

T_2 [s] transverse relaxation time constant

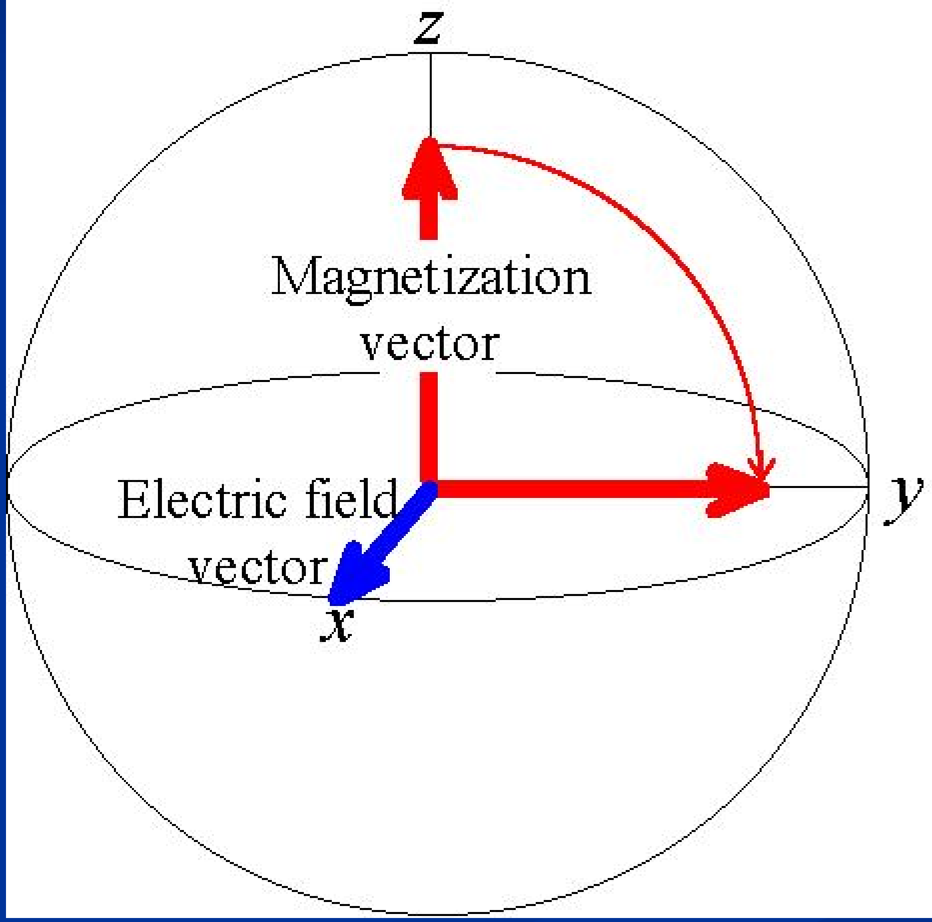
spin-spin relaxation time

entropy

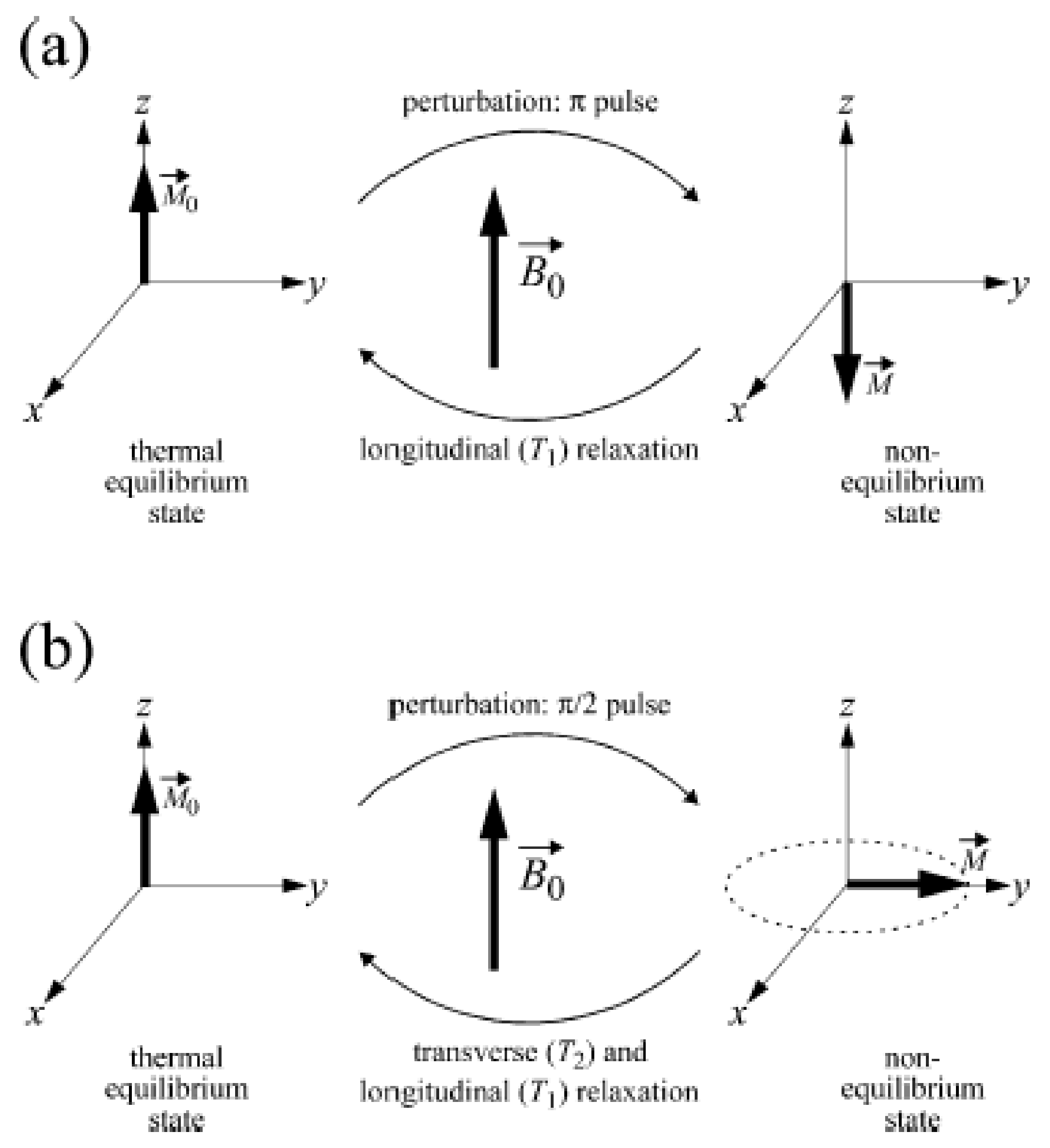

Z
B0
ω0
M
B1
X
Mxy
Y
receiver coil
My
Time
Fourier
transform
Frequency

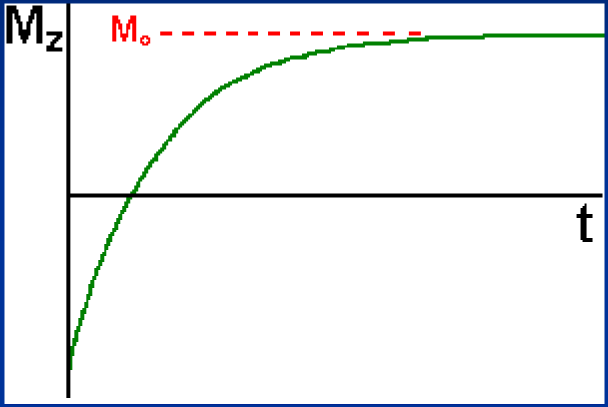
Effect of a 90°x pulse

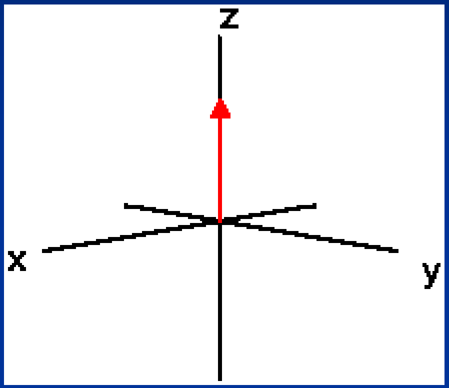
The magnetization vector is rotated to the y axis



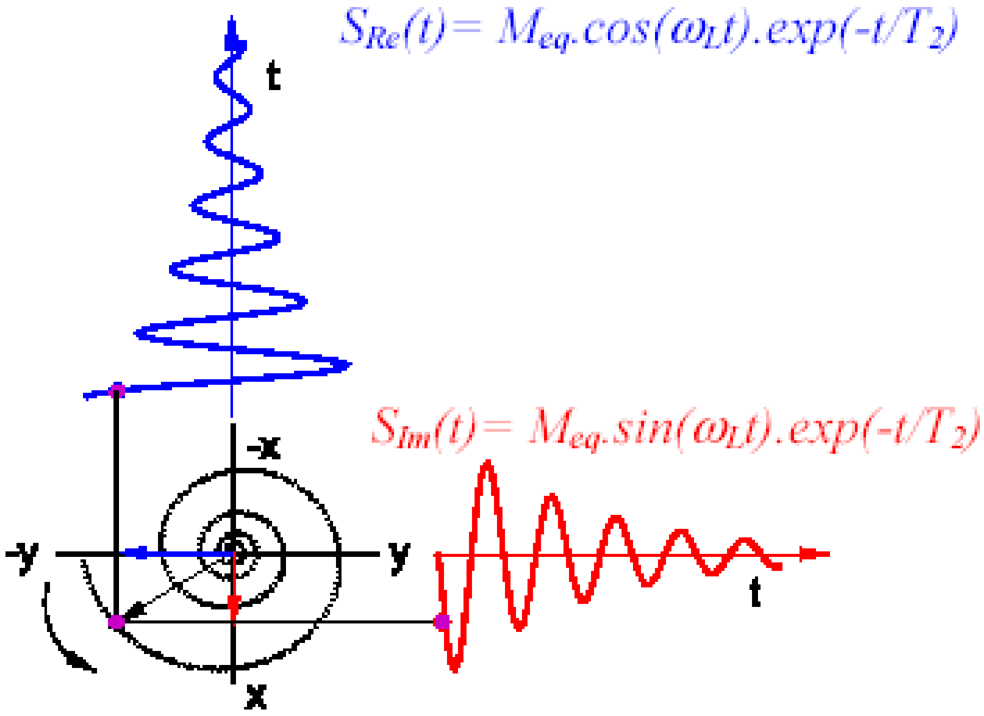
Relaxation


(a)
z
$\vec{M}_0$
y
x
thermal equilibrium state
perturbation: π pulse
$\vec{B}_0$
longitudinal (T_1) relaxation
z
y
x
$\vec{M}$
non-equilibrium state
(b)
z
$\vec{M}_0$
y
x
thermal equilibrium state
perturbation: π/2 pulse
$\vec{B}_0$
transverse (T_2) and longitudinal (T_1) relaxation
z
$\vec{M}$
y
x
non-equilibrium state


M_z
M_o
t


z
x
y

Free Induction Decay FID



$$S_{Re}(t) = M_{eq}.\cos(\omega_L t).\exp(-t/T_2)$$

$$S_{Im}(t) = M_{eq}.\sin(\omega_L t).\exp(-t/T_2)$$

$$S(t) = S_{Re}(t) + iS_{Im}(t)$$

$$= [\cos(\omega_L t) + i\sin(\omega_L t)]\exp(-t/T_2)$$

$$= \exp(i\omega_L t)\exp(-t/T_2) = \exp[-(1/T_2 - i\omega_L)t]$$