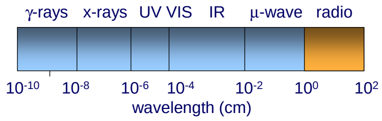
What is Spectroscopy?

- Spectroscopy is the study of the interactions between ***light*** and ***matter***.
- Here ***light*** refers to any sort of electromagnetic radiation, such as visible light, UV, IR, and radio waves.
- Depending on the ***frequency*** or ***wavelength*** of the radiation involved we will have different types of interactions with matter (molecules).

What is Spectroscopy?

- The following chart shows the ranges (wavelengths), for different types of spectroscopies.



- As you know, wavelength and frequency are inversely proportional, so higher frequencies mean shorter wavelength.

NMR Spectroscopy

NMR

NUCLEAR MAGNETIC RESONANCE

NMR Spectroscopy

NUCLEAR MAGNETIC RESONANCE

- Some property of the nucleus is used
  - Should have net free spin
  - Spin Number I = Integral multiple of ½
    - ± 1/2, 3/2, 5/2….

NMR Spectroscopy

NUCLEAR **MAGNETIC** RESONANCE

- Two Magnetic fields are generated
  - External magnet
    - Permanent Magnet
    - Electro Magnet
    - Superconducting Magnet
  - Nuclear spin generates dipoles
    - Nucleus behaves as tiny bar magnets

NMR Spectroscopy

NUCLEAR MAGNETIC **RESONANCE**

- Matching of Frequency
  - Precisional Frequency
  - Applied Radiofrequency

Spin Resonance (Magnetic Resonance)

- **Spin resonance** is a physical phenomenon resulting from the intrinsic angular momentum associated with the spin of the nucleus or electron of an atom.
- **These are of two types**
  - **Nuclear Magnetic resonance**
  - **Electron Spin Resonance**
- **Nuclear magnetic resonance** (NMR) implies that the nuclei of the atoms are in resonance, while
- **Electron spin resonance** (ESR) deals with electrons.

NMR History

- 1937 **Rabi** predicts and observes nuclear magnetic resonance
  1946 **Bloch, Purcell** first nuclear magnetic resonance of bulk sample
- 1953 **Overhauser** NOE (nuclear Overhauser effect)
- 1966 **Ernst, Anderson** Fourier transform NMR
- 1975 **Jeener, Ernst** 2D NMR
- 1985 **Wüthrich** first solution structure of a small protein (BPTI) from NOE derived distance restraints
- 1987 3D NMR + 13C, 15N isotope labeling of recombinant proteins (resolution)
- 1990 pulsed field gradients (artifact suppression)
- 1996/7 new *long range* structural parameters:
- - **residual dipolar couplings** from partial alignment in liquid crystalline media
- - projection angle restraints from **cross-correlated relaxation**
- TROSY (molecular weight > 100 kDa)

NMR History

Nobel prizes

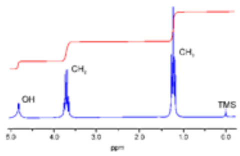
- 1944 *Physics* Rabi (Columbia)
- 1952 *Physics* Bloch (Stanford), Purcell (Harvard)
- 1991 *Chemistry* Ernst (ETH)
- 2002 *Chemistry* Wüthrich (ETH)
- 2003 *Medicine* Lauterbur (University of Illinois in Urbana), Mansfield (University of Nottingham)

NMR History

First Observation of the Chemical Shift

1H NMR spectra ethanol

Modern ethanol spectra

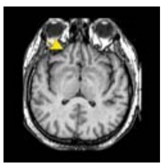


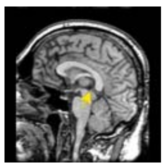
Typical Applications of NMR

1.) Structural (chemical) elucidation
  Natural product chemistry
  Synthetic organic chemistry
    - analytical tool of choice of synthetic chemists
    - used in conjunction with MS and IR
2.) Study of dynamic processes
  reaction kinetics
  study of equilibrium (chemical or structural)
3.) Structural (three-dimensional) studies
  Proteins, Protein-ligand complexes
  DNA, RNA, Protein/DNA complexes
  Polysaccharides
4.) Drug Design
  Structure Activity Relationships by NMR
5) Medicine -MRI

Typical Applications of NMR

- ***MRI images of the Human Brain***

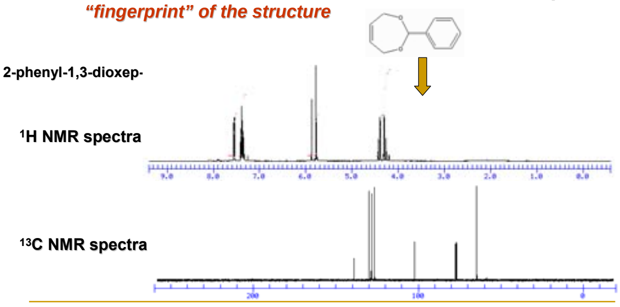




NMR Spectra

Each NMR Observable Nuclei Yields a Peak in the Spectra

"fingerprint" of the structure

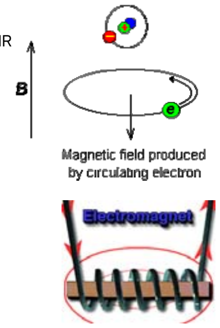


Electro Magnetic Theory

Basic Concept

A Direct Application to NMR

A moving perpendicular external magnetic field will induce an electric current in a closed loop



An electric current in a closed loop will create a perpendicular magnetic field

Electro Magnetic Theory

Basic Concept

Faraday's Law of Induction

- If the magnetic flux (Φ_B) through an area bounded by a closed conducting loop changes with time, a current and an emf are produced in the loop. This process is called induction.
- The induced emf is:

$$\xi = -\frac{d\Phi_B}{dt}$$

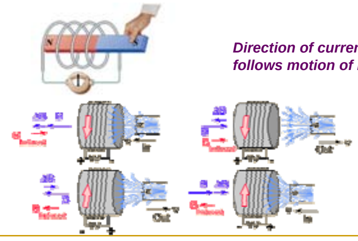
Simple AC generator

Electro Magnetic Theory

Basic Concept

Lenz's Law

- An induced current has a direction such that the magnetic field of the current opposes the change in the magnetic flux that produces the current.
- The induced emf has the same direction as the induced current



Direction of current follows motion of magnet

Concept of Spin

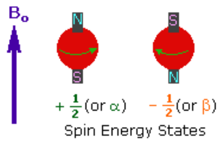
- Spin is a fundamental property of all elementary particles and is typically viewed as the intrinsic angular momentum.
- Both electrons and nuclei possess spin, and these spins precess around the direction defined by an applied magnetic field.
- The frequency of precession scales with the applied field and is roughly 1,000 times faster for electrons.

Concept of Spin

- **1.** A spinning charge generates a magnetic field, as shown by the animation on the right. The resulting spin-magnet has a magnetic moment (**μ**) proportional to the spin.

Concept of Spin

- **2.** In the presence of an external magnetic field (**B0**), two spin states exist, **+1/2** and **-1/2**.
The magnetic moment of the lower energy +1/2 state is aligned with the external field, but that of the higher energy -1/2 spin state is opposed to the external field. Note that the arrow representing the external field points North.



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The Gory Details

- Only nuclei with ***spin number*** (***I***) **≠ 0** can absorb/emit
- electromagnetic radiation.
  - Even atomic mass & number ⇒ ***I* = 0** (^{12}C, ^{16}O)
  - Even atomic mass & odd number ⇒ ***I* = *whole integer***
  - (^{14}N, ^{2}H, ^{10}B)
  - Odd atomic mass ⇒ ***I* = *half integer*** (^{1}H, ^{13}C, ^{15}N, ^{31}P)
- The ***spin states*** of the nucleus (***m***) are ***quantized***:

$$m = I, (I - 1), (I - 2), \ldots, -I$$

- Properly, ***m*** is called the ***magnetic quantum number***

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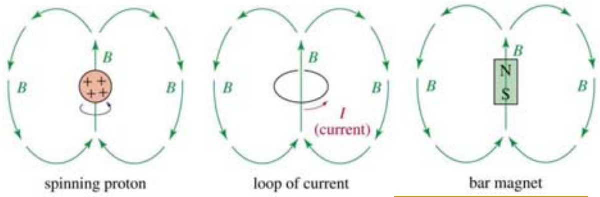
Nuclear Spin

- A nucleus with an odd atomic number or an odd mass number has a nuclear spin.
- The spinning charged nucleus generates a magnetic field.



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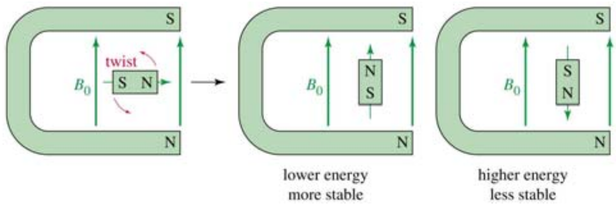
External Magnetic Field

When placed in an external field, spinning nuclei act like bar magnets.



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Precession

- To explain everything in NMR we have to refer to rotation, and Hz are not the best units to do this. We define the ***precession*** or ***Larmor*** frequency, ω_o, in radians:

$$\omega_o = 2\pi\nu_o \quad \Rightarrow \quad \omega_o = \gamma B_o \text{ (radians)}$$

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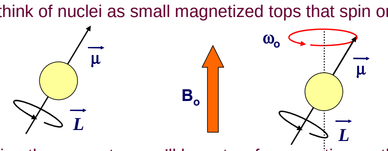
Precession

- With what precession is ω_o related to? One thing we left out of the mix was the ***angular momentum***, ***L***, asociated will all nuclei (magnetic or not).
- We can think of nuclei as small magnetized tops that spin on their axis



- After turning the magnet on we'll have two forces acting on the spins. One that tries to turn them towards $\mathbf{B_o}$, and the other that wants to maintain their angular momentum. The net result is that the nuclei spins like a top

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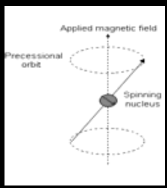
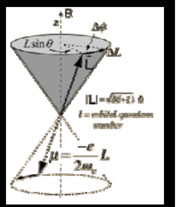
Theory of Magnetic Resonance

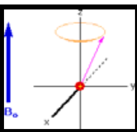
Classical Description

- *Spinning particle precesses around an applied magnetic field*

A Spinning Gyroscope
in a Gravity Field

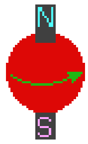






Theory of NMR

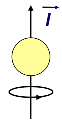
Quantum Description



Nuclear Spin (think electron spin)

- Nucleus rotates about its axis (spin)
- Nuclei with spin have angular momentum (p) or spin

1) total magnitude



$\hbar\sqrt{I(I+1)}$

1) quantized, spin quantum number I

2) 2I + 1 states: $I, I\text{-}1, I\text{-}2, \ldots, -I$

$I=1/2$: $-1/2, 1/2$

3) identical energies in <u>absence</u> of external magnetic field

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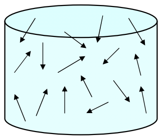
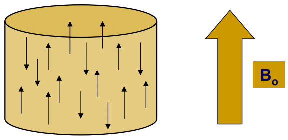
Magnetic Alignment

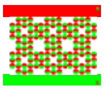
$\uparrow = \gamma h / 4\pi$



In the absence of external field,
each nuclei is energetically degenerate

Add a <u>strong</u> external field (B_o) and the nuclear magnetic moment: aligns with (low energy) against (high-energy)





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Quantum Description

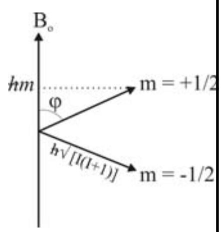
Spins Orientation in a Magnetic Field (Energy Levels)

- Magnetic moment are no longer equivelent
- Magnetic moments are oriented in *2I + 1* directions in magnetic field

- **Vector length is:** $\hbar\sqrt{I(I+1)}$
- **Angle (φ) given by:** $\cos\varphi = \sqrt{\dfrac{m}{I(I+1)}}$
- **Energy given by:** $E = -\dfrac{m\mu}{I} B_o$

where,

B_o – magnetic Field
μ – magnetic moment
***h* – Planck's constant**



For I = 1/2

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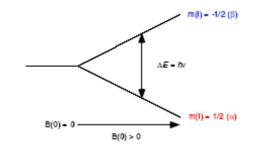
Quantum Description

Net Magnetization

Spins Orientation in a Magnetic Field (Energy Levels)

- Magnetic moments are oriented in one of two directions in magnetic field (for *I* =1/2)



- Difference in energy between the two states is given by:

$\Delta E = \gamma h B_o / 2\pi$

where:

B_o – external magnetic field
h – Planck's constant
γ – gyromagnetic ratio

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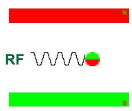
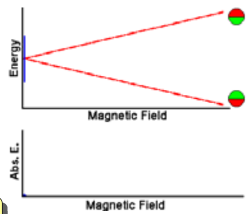
Quantum Description

Net Magnetization

Spins Orientation in a Magnetic Field (Energy Levels)

- Transition from the low energy to high energy spin state occurs through an absorption of a photon of radio-frequency (RF) energy





Frequency of absorption: $\nu = \gamma B_o / 2\pi$

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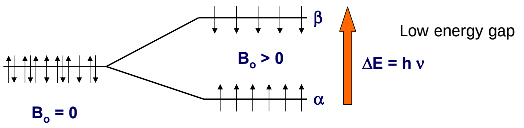
Quantum Description

Net Magnetization

NMR Signal (sensitivity)

- The applied magnetic field causes an energy difference between the aligned (α) and unaligned (β) nuclei
- NMR signal results from the transition of spins from the α to β state
- Strength of the signal depends on the population difference between the α and β spin states



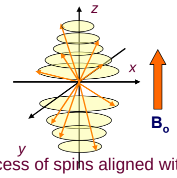
- The population (N) difference can be determined from the Boltzmman distribution and the energy separation between the α and β spin states:

$$N_\alpha / N_\beta = e^{\Delta E / kT}$$

Classical Description

Net Magnetization

- Where does the net magnetization comes from? In order to figure it out we translate all the spins to the origin of the coordinate system. We'll see something like this:

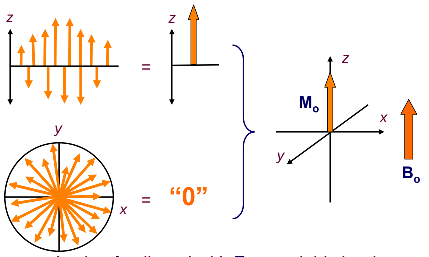


- We'll have a slight excess of spins aligned with **Bo**, but at any angle with respect to **z**. The distribution is proportional to **Na / Nb**.

Classical Description

Net Magnetization

•If we decompose the **m** vectors in **z** and **<xy>**, we get

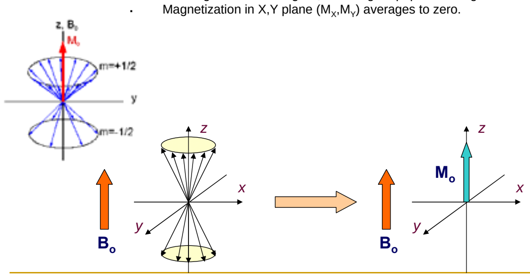


The net magnetization ***is*** aligned with **Bo**, and this is what we use in NMR.

Classical Description

Net Magnetization

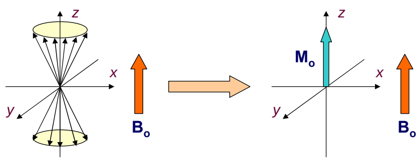
- Nuclei either align with or against external magnetic field along the z-axis.
- Since more nuclei align with field, net magnetization (M_o, M_Z) exists parallel to external magnetic field.
  - Net Magnetization along +Z, since higher population aligned with B_o.
  - Magnetization in X,Y plane (M_X,M_Y) averages to zero.



Net Magnetization

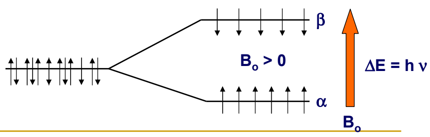
Classic View:

- Nuclei either align with or against external magnetic field along the z-axis.
- Since more nuclei align with field, net magnetization (M_o) exists parallel to external magnetic field



Quantum Description:

- Nuclei either populate low energy (α, aligned with field) or high energy (β, aligned against field)
- Net population in α energy level.
- Absorption of radio-frequency promotes nuclear spins from α → β.

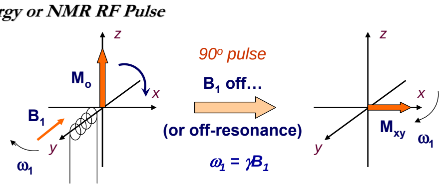


Resonance

Absorption of RF Energy or NMR RF Pulse

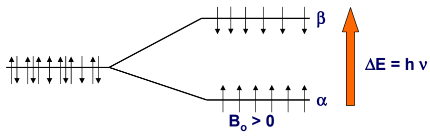
Classic View:

- Apply a radio-frequency (RF) pulse a long the y-axis
- RF pulse viewed as a second field (B_1), that the net magnetization (M_o) will precess about with an angular velocity of ω_1
- precession stops when B_1 turned off



Quantum Description:

- enough RF energy has been absorbed, such that the population in α/β are now equal
- No net magnetization along the z-axis



Please Note: A whole variety of pulse widths are possible, not quantized dealing with bulk magnetization