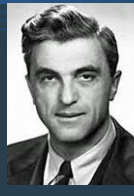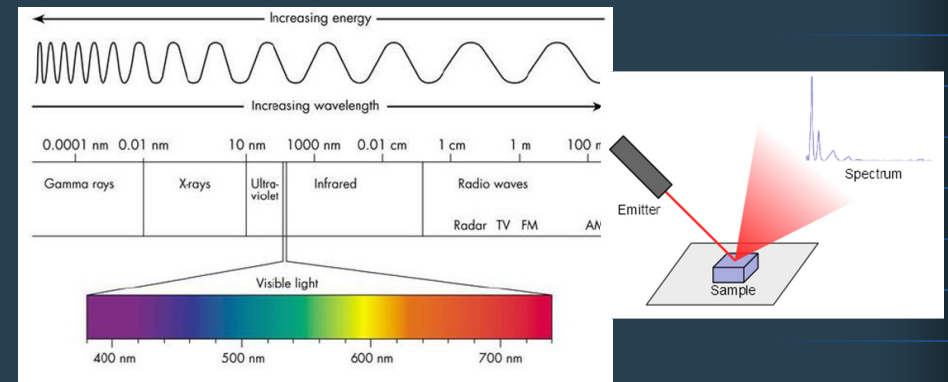**P. Zeeman**   **I. Rabi**   **F. Bloch**   **E. Purcell**

Nuclear Magnetic Resonance (NMR) spectroscopy


NMR Spectroscopy

- It is the study of interaction of radio waves with nuclei (of matter) in presence of a strong external magnetic field

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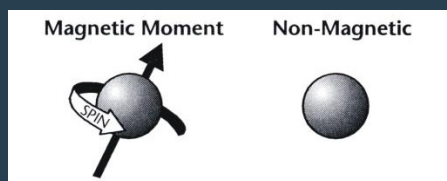# Nuclear Magnetic Resonance (NMR)
Introduction

❖ Magnetic resonance concept was introduced by P. Zeeman and I. Rabi. First crude NMR spectrometer was built by F. Bloch and E. Purcell. All of them got Nobel prizes for thier work in the magnetic resonance field.

❖ NMR spectroscopy is the study of molecular structure through the measurement of the interaction of radio waves with a collection of nuclei (matter) immersed in a strong external magnetic field.

❖ The energy of radio waves suitably matches with the energy gap between the nuclear levels. Matching condition is called resonace and it leads to nuclear transitions

❖ A molecule is an asssembly of many nuclei. Therfore, an NMR spectrum can provide the information about the molecular structure and the nuclear dynamics.
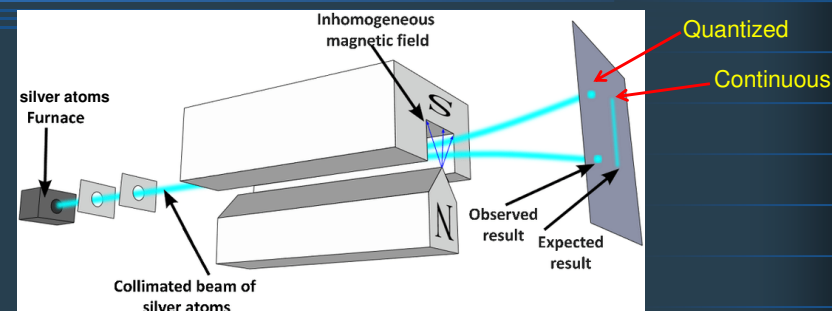

NMR Spectroscopy
Nuclear energy levels
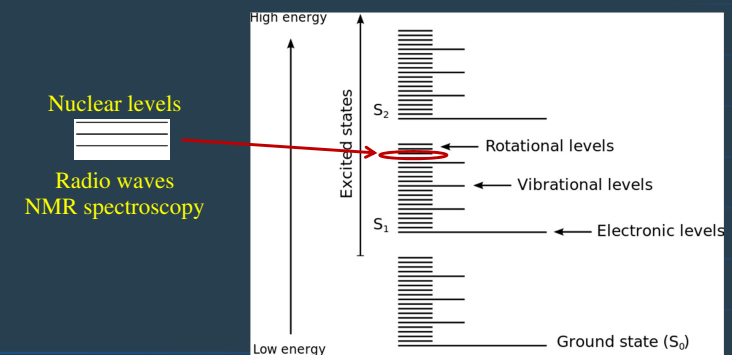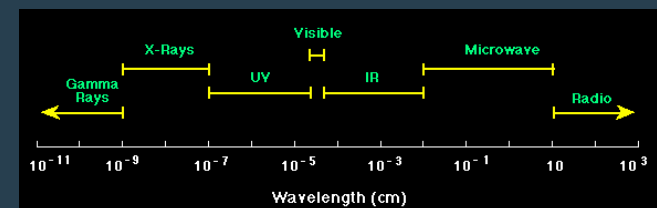
Nucleus & Nuclear spin

- Atom has nucleus and most of the atomic mass is concentrated in its nucleus.
- Nucleus can be further dissected into other important fundamental particles called protons and neutrons.
- Most of the nuclei have a spinning property (so it is a nuclear spin) – generates magnetic field.
- Nuclear spin acts as a tiny spinning bar magnet and thus it exhibits a magnetic moment.
- The magnetic characteristic of an individual nucleus is determined by its neutron-proton composition.

Magnetic Moment   Non-Magnetic

SPIN

Stern-Gerlach experiment

Spin is quantized

Inhomogeneous magnetic field

Quantized

Continuous

silver atoms Furnace

Observed result

Expected result

Collimated beam of silver atoms

- Spin multiplicity = 2I+ 1 = Allowed spin states (No. of spots on screen) where I = spin qunatum number

- Here, for Silver (Ag) nuclei ---- 2I+1=2 (means 2 spin states) ----- I=1/2
- ^{13}C, ^{1}H, ^{15}N, etc. ----- I=1/2 ----- all are called spin-1/2 nuclei

- If 2I+1=0 (or I=0), then those type of nuclei does not possess the spin property

NMR active & inactive nuclei

- Spin qunatum number, $I \neq 0$ ----- NMR active (detectable using NMR)
  $I = 0$ ----- NMR inactive (undetectable)

Only nuclei with spin number I≠0 can absorb/emit electromagnetic radiation.

nuclei		example	Spin quantum No. (I)	Magnetic Quantum no. (m)	Allowed spin states	Activity in NMR
Atomic mas	Atomic no					
odd	odd or even	^{1}H, ^{13}C, ^{19}F, ^{31}P	1/2	+1/2,-1/2	2(1/2)+1=2	NMR active
odd	odd or even	^{35}C	3/2	+3/2,1/2,-1/2,-3/2	2(3/2)+1=4	NMR active
even	odd	^{2}H, ^{14}N	1	+1,0,-1	2(1)+1=3	NMR active
even	even	^{12}C, ^{16}O, ^{32}S	0	0	2(0)+1=1	NMR inactive

- Nuclei with I=0 do not exhibit the spin property (no magnetic moment)

NMR active & inactive nuclei

- NMR active nuclei with different nuclear spin qunatum numbers (I).

Nuclear Spins for Main Elemental Isotopes that Undergo NMR

Nuclear Spin: 1/2, 1, 3/2, 5/2, 7/2, 9/2, 5, 8   No data for synthetic elements ≥ 103

NMR instrumentation

NMR instrumentation

- HeliumPorts
- Nitrogen Ports
- Air lift
- Vacuum Chamber
- Liquid Nitrogen
- Liquid Helium
- Magnet
- Sample
- Probe
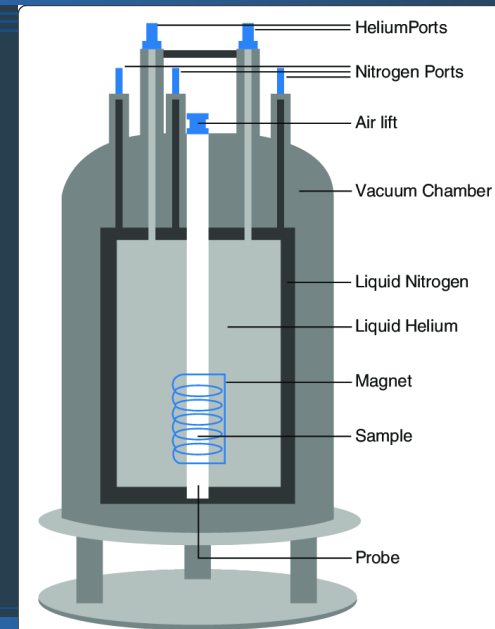
NMR instrumentation
Schematic diagram

Sample Tube · Nuclear Magnetic Resonance (NMR) Spectroscopy · RF Transmitter · Magnet · Detecter · Printer · Absorption · B_0 · Magnet Controller · Magnetic Field
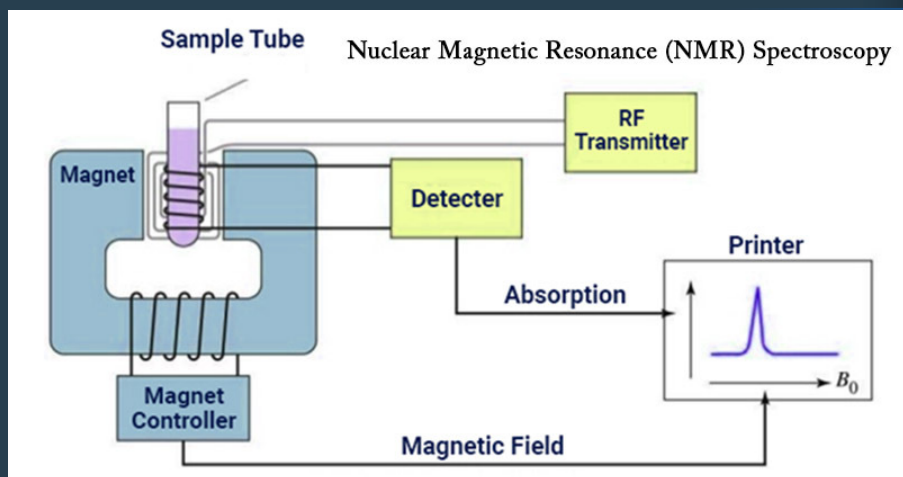
NMR spectroscopy – Principle
Under an external magnetic field

- Net magnetization (M) is zero at equilibrium in absence of an external magnetic field
- Nuclear alignment takes place under the influence of an external magnetic field (Bo)

atomic nuclei in absence of magnetic field
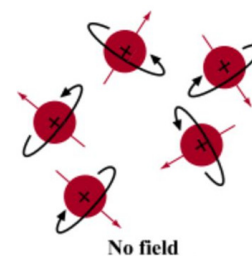
atomic nuclei in presence of external magnetic field

$+\frac{1}{2}$ or α spin states

$-\frac{1}{2}$ or β spin states

B_o

M_o

M_o = Net Macroscopic Magnetization

No field

With field

B_o
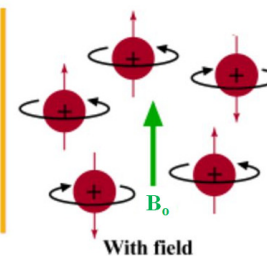
Net magnetization $M_0=0$

Net magnetization $M_0\neq0$

NMR – Principle
Under magnetic field-Nuclear energy levels

- NMR active (I≠0) nuclei adopt 2I+1 spin states under the influence of external magnetic field (Bo), each with different energy.

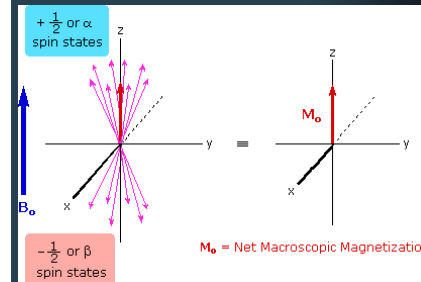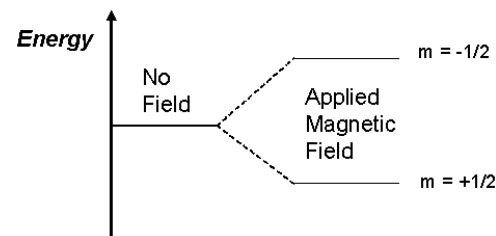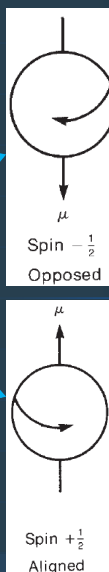Zeeman splitting

Energy Levels for a Nucleus with Spin Quantum Number 1/2

Energy

No Field

Applied Magnetic Field

m = -1/2

m = +1/2

μ
Spin $-\frac{1}{2}$
Opposed

μ
Spin $+\frac{1}{2}$
Aligned

$Lower\ state\ -\alpha = 1/2$ ------- Energy = E_α
$Upper\ state\ -\beta = -1/2$ ------- Energy = E_β

NMR – Principle
Under magneticfield – Larmor frequency

- All the NMR active spins remain at a certain angle to B_0 and it causes spins to precess around the axis of B_0 at a fixed frequency.
- The frequency of the periodic precesional motion of nuclear spins under the external magnetic field is called Larmor/precessional frequency (υ)
- It is just like the precession of a spinning top under the earth's gravitational field.
- It is also just like the earth's self rotation under the influence of Sun.
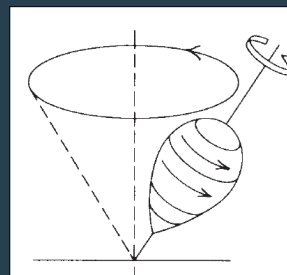
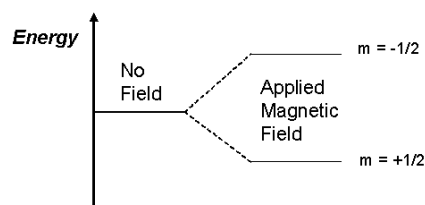$$\nu = \frac{\gamma B_0}{2\pi} = \text{Larmor frequency}$$

$$\gamma = \text{Gyromagnetic ratio}$$

precession

magnetic field   nuclear spin
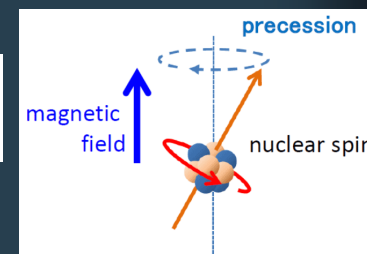
Radio frequency (RF)
Selection rules

- NMR active (I≠0) nuclei adopt 2I+1 spin states under the influence of external magnetic field (Bo), each with different energy.

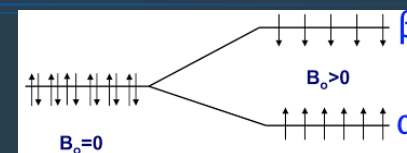- Spin-1/2 (I=1/2) nuclei will have two spin states (m=+1/2, -1/2)

Energy Levels for a Nucleus with Spin Quantum Number 1/2

Energy

No Field

Applied Magnetic Field

m = -1/2

m = +1/2

- Spin transitions occur when we supply the RF to the spins.
- The allowed spin transitions between the nuclear levels are: Δm=±1

NMR principle
Applying the radio frequency (or) RF - irrdiation

β

B_o>0

α

B_o=0

$$\nu = \frac{\gamma B_0}{2\pi} = Larmor\ frequency$$

The energy difference (ΔE) = the energy of radio waves
(or)   resonance, nuclear transitions occur
The frequency of radio waves =Larmor frequency of spins

$$\Delta E = h\nu = \frac{h\gamma B_0}{2\pi}$$

β spin

Energy separation (ΔE)

Transition between spin states gives NMR line

Energy →

α spin

Irradiation

Magnetic field strength →

CH₃

OH   CH₂

TMS
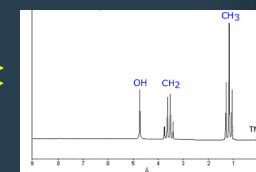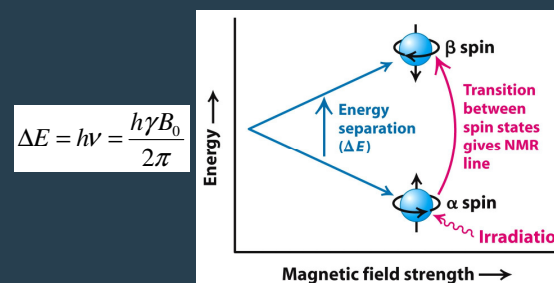
Spectrum, but not that simple

NMR Spectrum
FID & FT-NMR

- We get the time domain signal which is a free induction decay (FID).
- FID is not much informative in structural point of view.

- FID is finally transformed into the frequency domain signal using the Fourier transformation (FT) to result the characteristic NMR peaks.
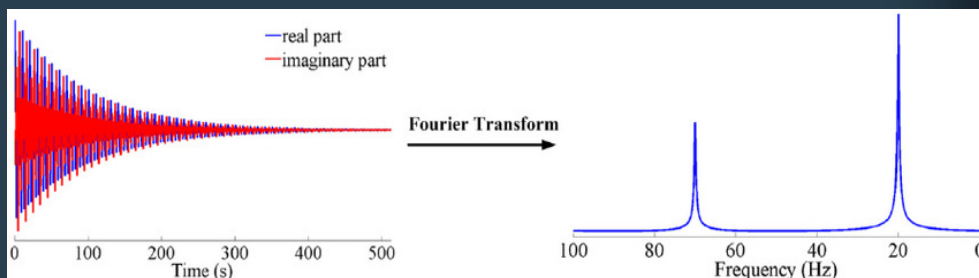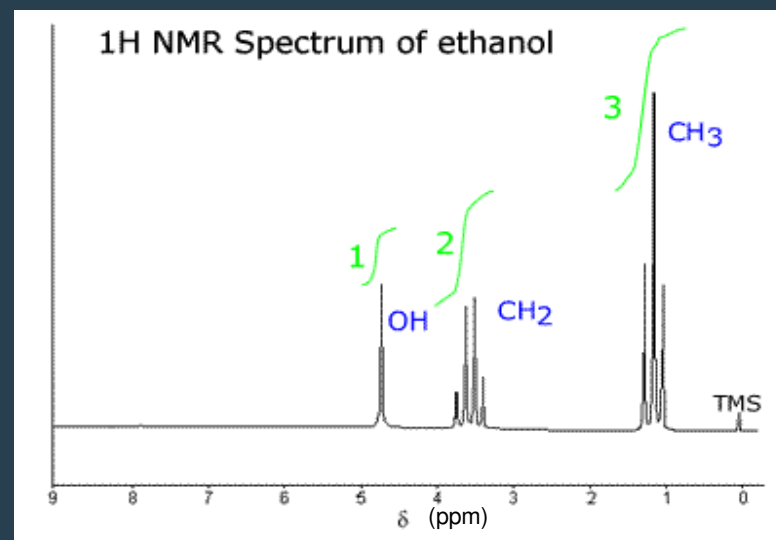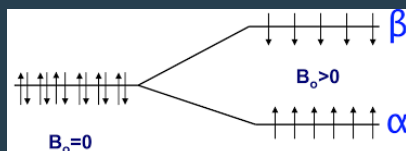

NMR Spectrum
An example: Ethanol

1H NMR Spectrum of ethanol

Boltzman distribution law
Spin population in the states

- Boltzman distribution law describes the population density in the energy levels (nuclear levels here). It is applicable to all the concepts.

$$\frac{N_{upper}}{N_{lower}} = e^{-\frac{\Delta E}{kT}}$$

$$\nu = \frac{\gamma B_0}{2\pi} = Larmor\ frequency \qquad \Delta E = h\nu = \frac{h\gamma B_0}{2\pi}$$

N_{upper} = no. of spins in the upper state

N_{lower} = no. of spins in the lower state

- As the energy gap between the nuclear levels increases, the population in the lower state increases.

Low signal intensity of NMR signals

- The external magnetic field makes the possible spin states non-degenerate in case of NMR active nuclei.

- But, the energy gap between the nuclear energy levels is still small compared to electronic or vibrational energy levels.

- Due to the less energy gap between nuclear levels, the spin population difference between the ground state (+1/2) and uppaer state (-1/2) is less.

- Transitions are made usually by the extra spins in the ground state.

- Therefore, *NMR always suffer from low signal intensities.*

Can we increase the ground state population?
Yes

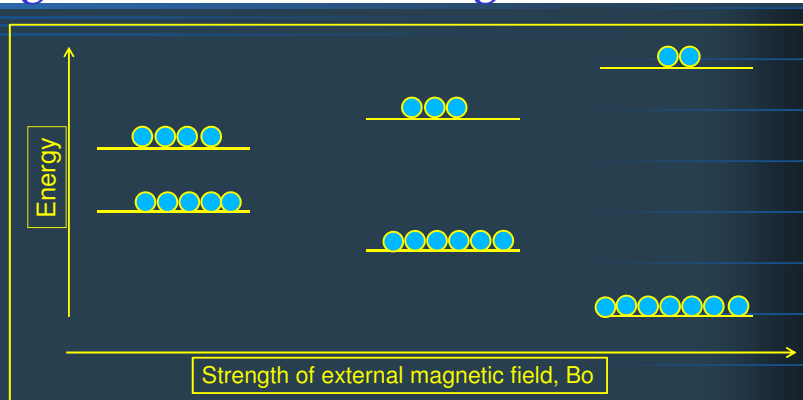$$\Delta E = \frac{h\gamma B_0}{2\pi}$$
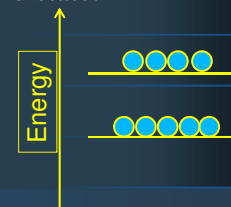
NMR signal enhancement
Strength of the external magnetic field

$$\Delta E = h\nu = \frac{h\gamma B_0}{2\pi}$$

$$\Delta E \ \alpha \ B_0$$
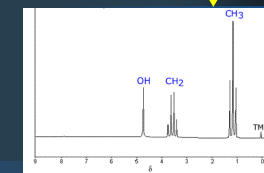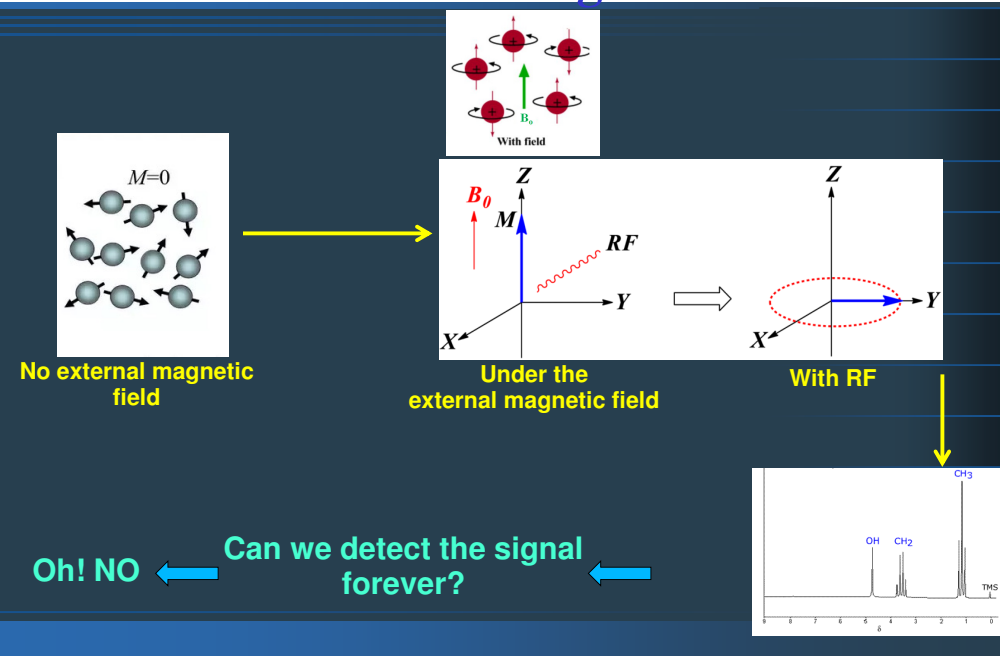
$$\frac{N_{upper}}{N_{lower}} = e^{-\frac{\Delta E}{kT}}$$

Energy

Strength of external magnetic field, Bo

- The energy gap between the nuclear levels increases as we increase the strength of the external magnetic field
- The ground state population increases as the energy gap increases.
- More the ground state population, more are the spin transitions
- More the transitions, more is the intensity of NMR signal

Total NMR Phenomenon
Let us see together

With field

$M=0$

B_0 M Z RF Y X

Z Y X

No external magnetic field

Under the external magnetic field

With RF

CH₃

OH CH₂

TMS

Can we detect the signal forever?

Oh! NO

Why does the signal decay during detection?

- We get the time domain signal which is a free induction decay (FID).
- Signal decays with time.

— real part
— imaginary part
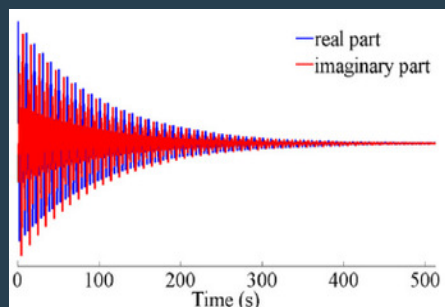
Time (s)

Why does the signal decay with time?

Saturation & Spin relaxation

- Continuous apply of the RF saturates the nuclear energy levels
- It equates the population in both the states and hence no transitions. So, the NMR signal decays with time.
- Spins need rest before the next RF pulse --------------- called **Relaxation**

B_0 M Z RF Y X

Z Y X

Energy →

Energy separation (ΔE)

β spin

Transition between spin states gives NMR line

α spin

Irradiation

Magnetic field strength →

Signal

Time
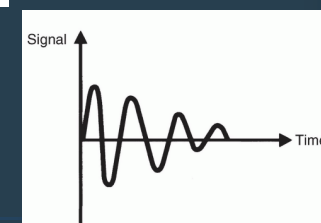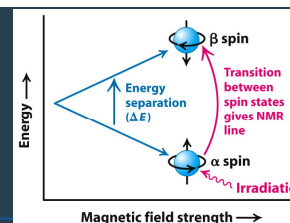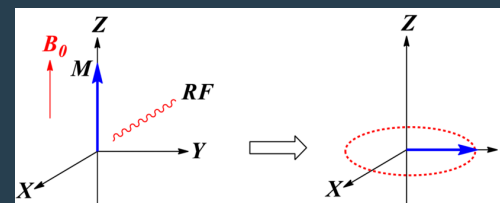
Relaxation & Types of relaxation

- ❖ Relaxation process helps spins to come back to the equilibrium state with net magnetization along the Z-axis (more population in ground state.
- ❖ This phenomenon occurs in absence of the RF.
- ❖ Relaxation mainly occurs in two ways:

- • Spin-spin (or transverse) relaxation (T_2)

- • Spin-Lattice (or longitudinal) relaxation (T_1)

    Both happen individually and simultaneously
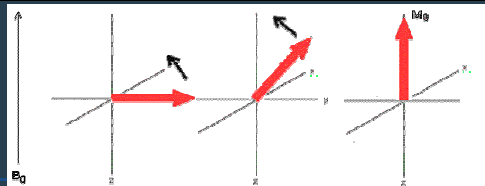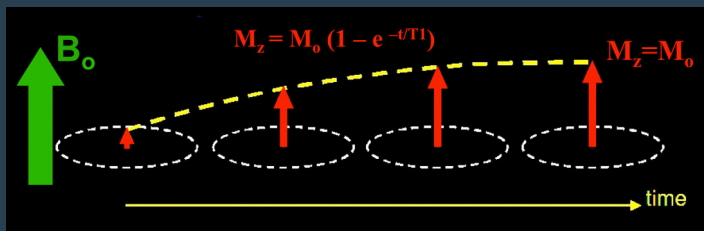
Spin-spin relaxation (T_2)

- ❖ This is also called the transverse relaxation.
- ❖ This type of relaxation occurs within the transverse plane (xy-plane)
- ❖ It is due to the dephasing of spins in the transverse plane after stopping the RF irradiation
- ❖ Dephasing of spins lead to the zero net magnetization in the xy-plane

$$M_{xy} = M_o e^{-t/T2}$$
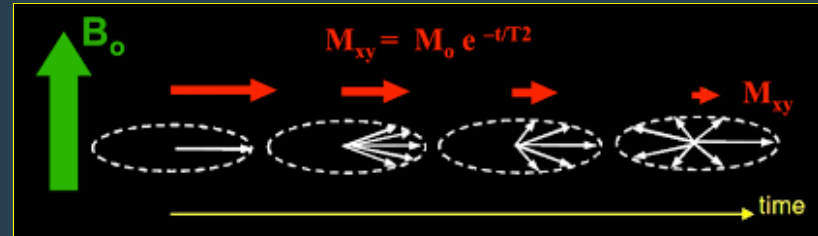
Detector

Spin-Lattice relaxation (T_1)

- ❖ This is also called the longitudinal relaxation (towards z-axis).
- ❖ This type of relaxation is due to the interaction of spins with the lattice (sorroundings).
- ❖ Spins move towards the z-axis to attain the equilibrium state

$$M_z = M_o (1 - e^{-t/T1})$$

$M_z = M_o$

Now apply an RF pulse again

Spin Relaxations

- ❖ Both type of relaxations occur independently and simultaneously

- ❖ Spin-spin relaxation (T2) is much shorter than spin-lattice relaxation (T1)

- ❖ Due to both the relaxations, spins attain the equilibrium state (spins along the z-axis)

- ❖ Then, the spins are again ready to absorb the RF to make nuclear transitions.

- ❖ Therefore, there must be a time gap ($5T_1$) between each RF-pulse

- ❖ We can have many RF-pulses (many scans) with proper time gaps and NMR signal can be obtained until it is good.

How do we get the NMR signal?
## What are contributing for the signal?

❖ NMR signal is the result of spin transitions with the RF irradiation under the external magnetic field.

❖ During this process, many interactions take place in the spin system.

❖ Interactions are mainly four types:
- Chemical shift interactions ⎤
- Spin-spin coupling ⎦ — Our main focus
- Dipolar interactions (through space; strong in solid state)
- Quadrupolar interactions

---

1. Chemical shift interactions
Chemical shift

❖ These interactions occur between the nuclear spins and the external magnetic field.

❖ Nuclear spins ------- we stick to ^1H nuclei (called protons)----- ^1H NMR

❖ Ethanol (CH_3CH_2OH) has ^1H nuclei, but all of them do not possess the same Larmor frequency.

❖ It was historically observed in 1951 with the detection of three different signals for ethanol in its ^1H NMR sectrum.

❖ It was soon realized that those three signals correspond to three different sets of ^1H nuclei in ethanol (CH_3, CH_2, OH).
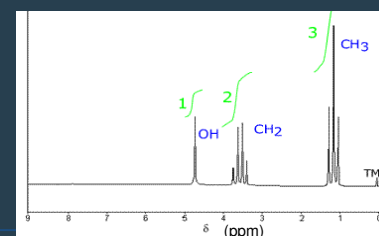
Chemical shift

❖ Though all 6-H's are ^1H nuclei (protons), three different signals are obtained.

❖ It is attributed to three diffferent chemical envoronments for protons of ethanol (it opened gates for chemists to use NMR to identify structures)

❖ The shift in the resonance frequency of the nuclei due to their different chemical environments is called the chemical-shift.
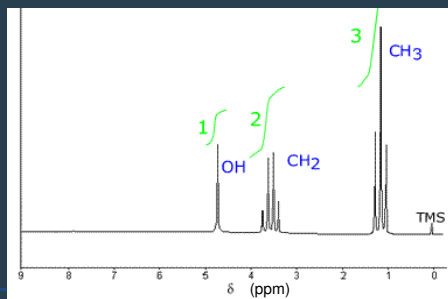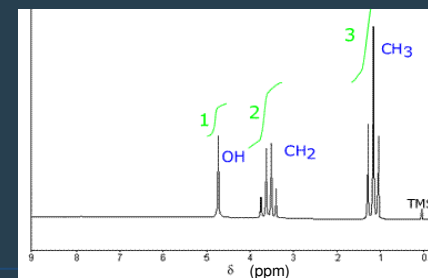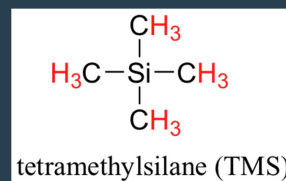

Ethanol
NMR spectrum

Chemical shift
Reference compound

❖ Measuring the Larmor frequency of a group of ^1H nuclei (protons) in absolute frequency units is not required.

❖ Instead, the differences in frequency are measured with respect to some reference.

❖ Tetramethylsilane (TMS) is the universally accepted reference compound for ^1H NMR.

❖ TMS has 12 equivalent protons, all are connected to electropositive Si-atom. All the protons are highly sheilded by electron cloud and it is always taken at zero chemical-shift.

tetramethylsilane (TMS)

Ethanol
NMR spectrum

Measurement of chemical shift

❖ Instruments with a 1.4 T magnet are usually called 60 MHz instruments.

1.4 T -------- 60 MHz

2.3 T -------- 100 mHz

7.0 T -------- 300 MHz

14.1 T ------- 600 MHz

$$\nu = \frac{\gamma B_0}{2\pi}$$

❖ As we increase the strength of the magnetic field, the resolution and the signal intensities are high.

❖ If we record spectra for a sample on 100 MHz or 600 MHz, basic set of peaks are same but with different resolution.

❖ However, the corresponding peak frequencies (in Hz on x-axis) are different.

❖ This leads to desirability of using units which are field-independent.

Measurement of chemical shift
Hz- scale

❖ Plotting with respect to frequency units (Hz) leads different frequency values for a same peak on different magnetic field NMR instruments.

$$\delta = \frac{\text{(Frequency shift from Me}_4\text{Si in Hz)}}{\text{(Spectrometer frequency, MHz)}}$$
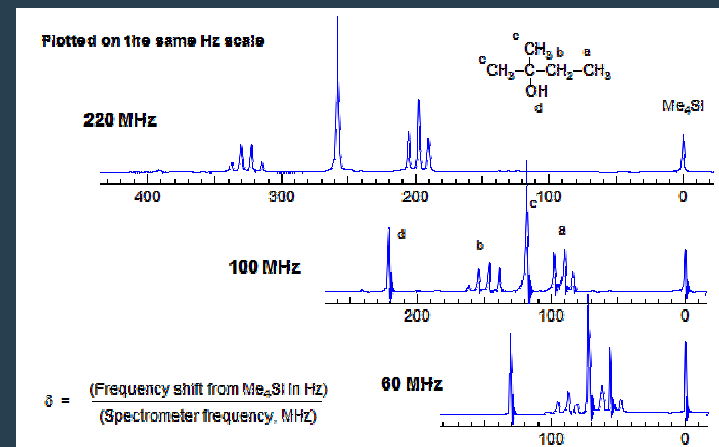
❖ But, it is good to have similar resonance value on x-axis for a particular peak irrespective of the instrumental frequency or the magnetic field.

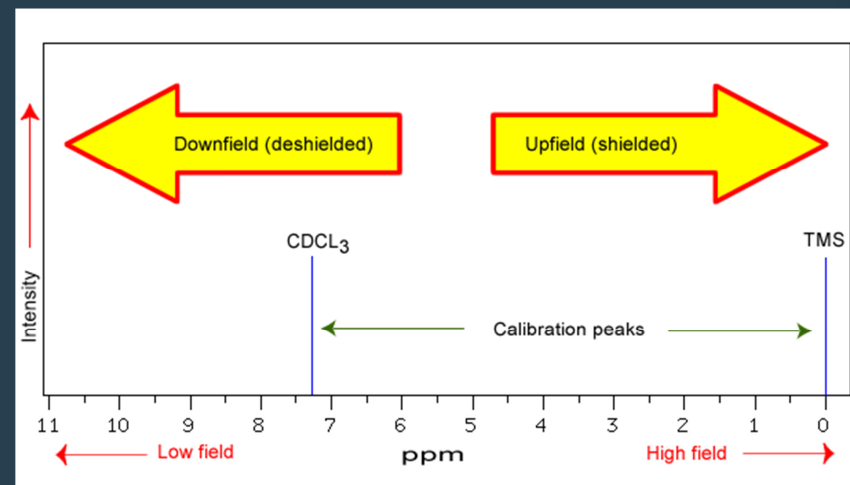---

Measurement of chemical shift
δ-scale(in ppm)

$$\text{chemical shift } (\delta) = \frac{\nu_x - \nu_{ref}}{\nu_0}$$

ν_x = frequency of the signal (Hz)

ν_{ref} = frequency of the TMS (Hz)

ν_0 = frequency of instrument (MHz)

❖ Now, a single peak has the same ppm value on x-axis irrespective of the instrumental frequency.

1 ppm=220 Hz

1 ppm=100 Hz

1 ppm=60 Hz

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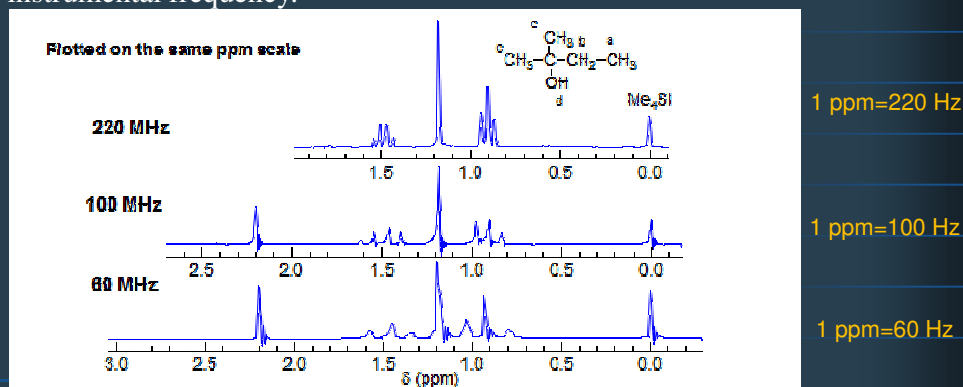
¹H NMR chemical shift scale

Shielding effect

❖ When a nucleus is surrounded by electron density, then the nucleus is shielded from the influence of the applied magnetic field (Bo).

❖ Electopositive elements pushes more electrons towards protons (^1H) by +ve I-effect. For example 'Si' atom in TMS (12 protons are highly shielded).

❖ Shielded proton signals appear at lower part of the **δ-scale.** Proton signals of TMS are hence placed at zero ppm (TMS protons are highly shielded).

tetramethylsilane (TMS)
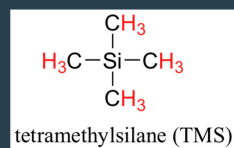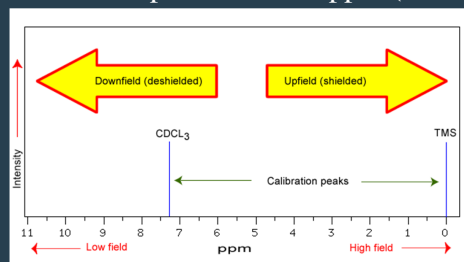
Deshielding effect

❖ When a nucleus is surrounded by less electron density, then the nucleus is deshielded and more open to the applied magnetic field (Bo).

❖ Electonegative elements withdraw electrons from protons (^1H) region by negative I-effect. For example halogens or oxygen etc.

❖ Deshielded proton signals appear at upper part of the **δ-scale.**
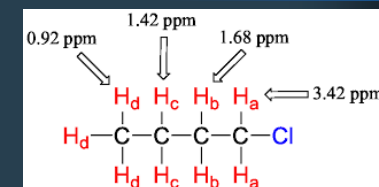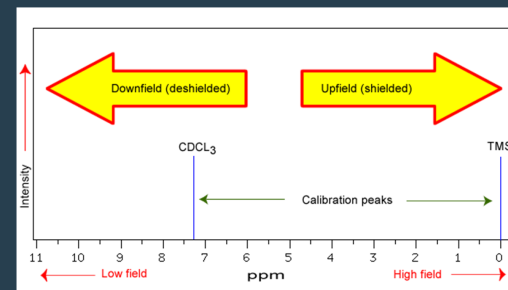
Factors influencing the ^1H chemical shift

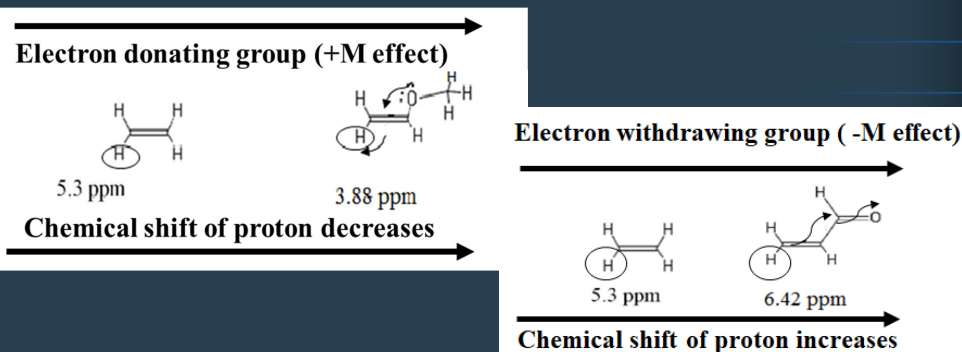### 1) Electronegativity of neighboring nuclei

The neighboring electronegative groups deshield and increase the chemical shift of protons (H). More the electronegativity of the group, more is the chemical shift of protons

Electronegativity Increases				
CH_4	CH_3I	CH_3Br	CH_3Cl	CH_3F
0.23 ppm	2.16 ppm	2.68 ppm	3.05 ppm	4.26 ppm
Chemical shifts of Proton Increases				

Factors influencing the ^1H chemical shift

2) Resonance effect

Resonance or conjugation reduces the electron cloud around the protons (H) and de-shields them. More the resonance, more is the chemical shift of protons
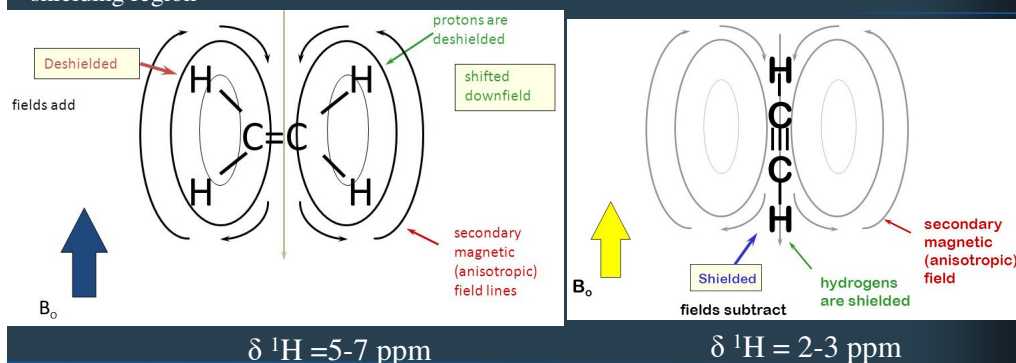

Electron donating group (+M effect)

5.3 ppm   3.88 ppm
Chemical shift of proton decreases

Electron withdrawing group (-M effect)

5.3 ppm   6.42 ppm
Chemical shift of proton increases

Factors influencing the ¹H chemical shift

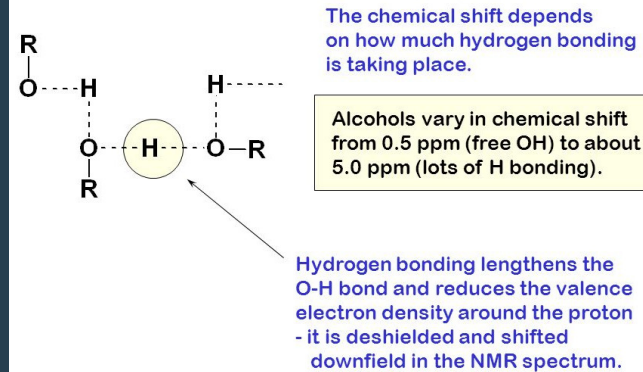**3) Chemical shift anisotropy (or) Magnetic field anisotropy**

The electron circulation around the proton is varied with the orientation of the molecule in the external magnetic field (Bo). The anisotropic electron circulation induces the different extent of local magnetic field which depends on the orientation of protons in the shielding region and deshielding regions.

Ethylene protons are in the deshielding region where as Acetylene protons are in the shielding region

$\delta\ ^1H = 5\text{-}7$ ppm

$\delta\ ^1H = 2\text{-}3$ ppm

Factors influencing the ¹H chemical shift

4) Hydrogen bonding

The chemical shift depends on how much hydrogen bonding is taking place.

Alcohols vary in chemical shift from 0.5 ppm (free OH) to about 5.0 ppm (lots of H bonding).

Hydrogen bonding lengthens the O-H bond and reduces the valence electron density around the proton - it is deshielded and shifted downfield in the NMR spectrum.
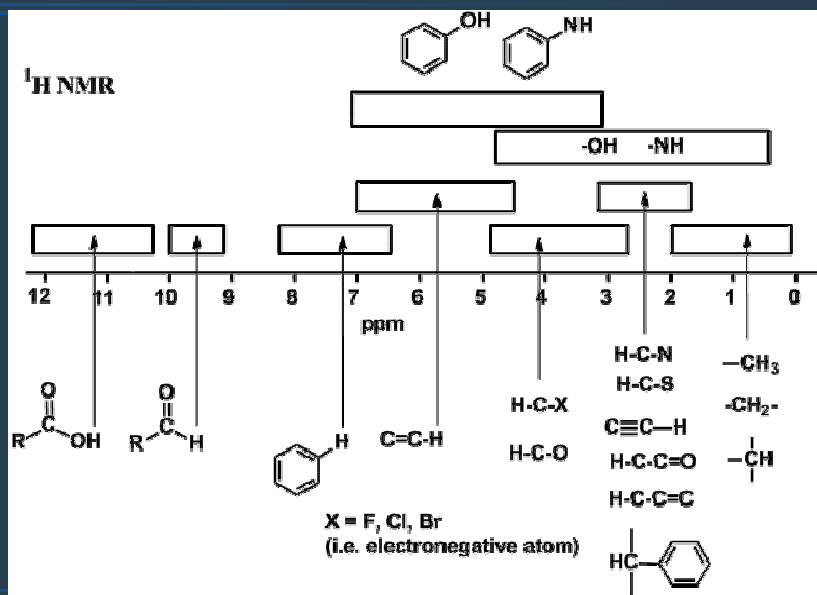
Hydrogens involved in hydrogen bonding are highly deshielded and their peaks appear at higher chemical shift region

There are also other factors like solvent, temperature, concentration etc.

# ¹H – chemical shift values

Splitting of NMR signals------why?

❖ Due to different chemical shift values of 3-sets of hydrogens, we get three different signals at different places on the scale.

❖ But, what is the reason for splitting of each peak?

❖ Does it give any important information for us?
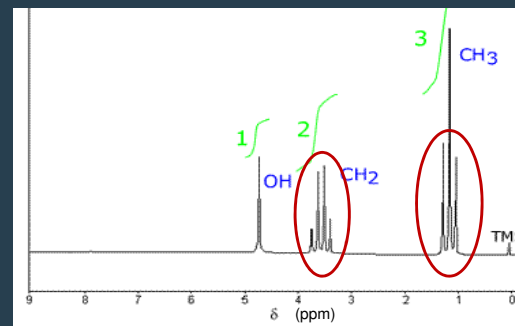
Ethanol NMR spectrum

2. Spin-spin coupling interactions (or) J-coupling

❖ Spin-spin coupling is also called the J-coupling and it takes place among spins through chemical bonds

❖ Often, the ^{1}H NMR (and other) gives multiplets instead of sharp singlets.

❖ The interaction between the spins of neighboring nuclei in a molecule may cause the splitting of NMR signals. This is known as spin-spin coupling.
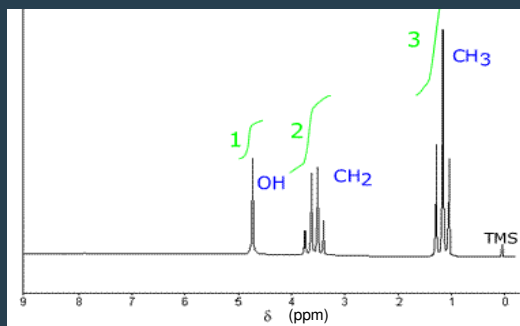

Ethanol
NMR spectrum
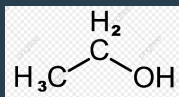
Spin-spin coupling

❖ Spin-spin coupling gives an important information about the number of protons which are present on the neighboring directly bonded carbons.

❖ The simple rule (for spins of I=1/2) to define the splitting of a particular signal corresponding to same type of protons (same chemical environment) is (n+1).

Here n=no. of protons on the next carbon ($CH3\text{-}CH2\text{----}$)

❖ If the protons under monitoring on one carbon have protons (on carbons) on both sides, then the rule is $(n_1+1)(n_2+1)$.

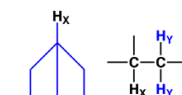n1, n2 are number of protons on carbons on both sides ($CH3\text{-}CH2\text{-}CH2\text{--}$)

Spin-spin coupling
Splitting of signals
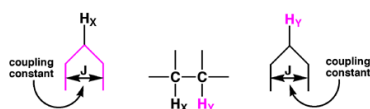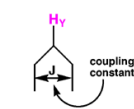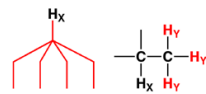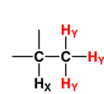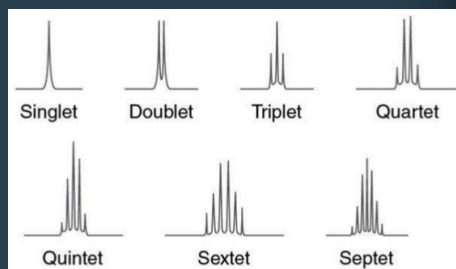
^{1}H NMR of Ethanol

❖ The molecular formula of ethanol is CH_3CH_2OH. It has three sets of chemically equivalent protons (CH3, CH2 and OH). So we can expect three singlet signals in total.

❖ But due to the spin-spin coupling between different sets of protons, singlet signals undergo splitting.

❖ Methyl protons (CH3) have two neighboring protons on the methylene carbon (CH2). So the signal of CH_3 protons is (n+1) = 2+1 = 3 ------ triplet.

❖ Methylene protons (CH2) have three neighboring protons on the methyl carbon (CH3). So the signal of CH_2 protons is n+1 = 3+1 = 4 ---- quartet. (not considering the proton of –OH due to the rapid proton exchange process).

❖ Single proton of –OH is presently a singlet due to no coupling with other protons (due to the proton exchange process in alcohols, otherwise it also splits into triplet due to –CH2).
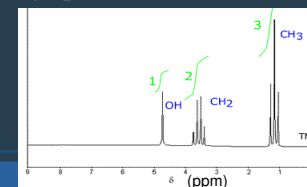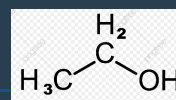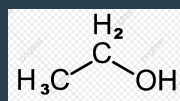
Ethanol
^{1}H NMR spectrum

¹H NMR of Ethanol

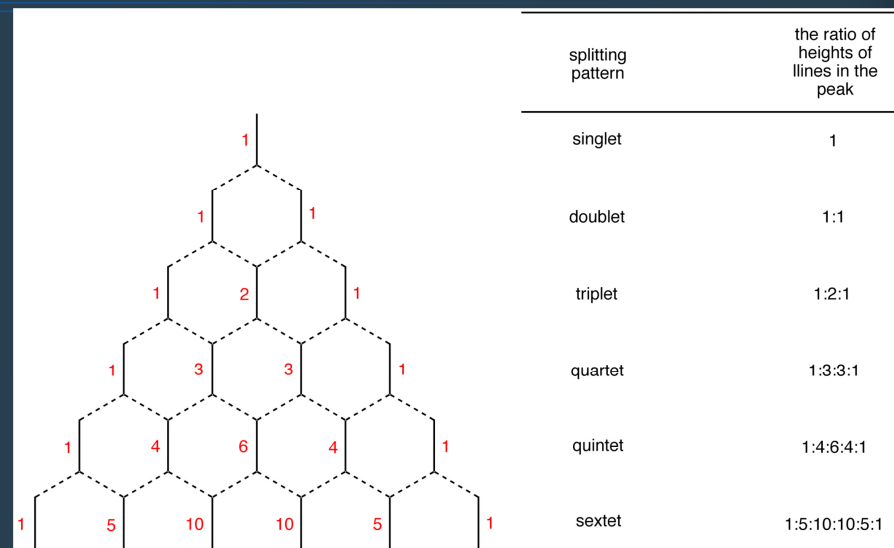- The single proton in the –OH group has more chemical shift value. It is due to the attachment to a more electronegative oxygen atom. That is, proton is highly deshielded.
- CH2 protons (quartet) have more chemical shift value than –CH3 protons. It is because, the CH2 protons are is more close to the electronegative oxygen atom and are more deshielded.
- CH3 protons are comparitively shileded (less chemcal shift value) due to no close electron withdrawing group.
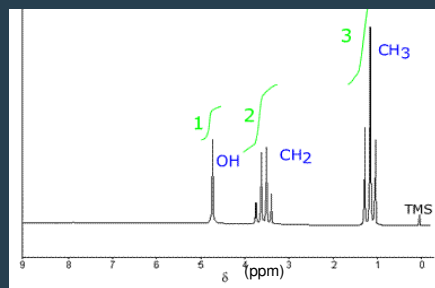
Ethanol
¹H NMR spectrum

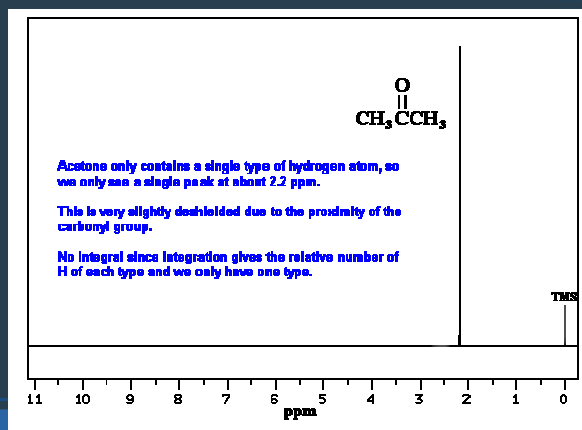# Splitting of signals follow the Pascal triangle

splitting pattern	the ratio of heights of llines in the peak
singlet	1
doublet	1:1
triplet	1:2:1
quartet	1:3:3:1
quintet	1:4:6:4:1
sextet	1:5:10:10:5:1

¹H NMR example spectra

- There are six protons (H) in Acetone molecule (two –CH3 groups). So, we can expect two separate signals for protons of two equivalent –CH3 groups.
- But, due to the same chemical environment, both the –CH3 protons are treated as a single set of protons. That is, all the 6-protons are equivalent.
- Hence, we get a single signal for all the 6-protons

CH_3CCH_3

Acetone only contains a single type of hydrogen atom, so we only see a single peak at about 2.2 ppm.

This is very slightly deshielded due to the proximity of the carbonyl group.

No integral since integration gives the relative number of H of each type and we only have one type.

¹H NMR of ethyl acetate

- There are three different sets of protons in ethyl acetate. They are (CH3, CH2 and CH3) from left to right (in the structure).
- CH3 protons attached to C=O group obtain a singlet with no splitting. It is due to no protons on neighboring carbon of C=O.
- Signal for CH2 protons appears at higher chemical shift value. It is due to the direct bonding with more electronegative oxygen

Ethyl acetate
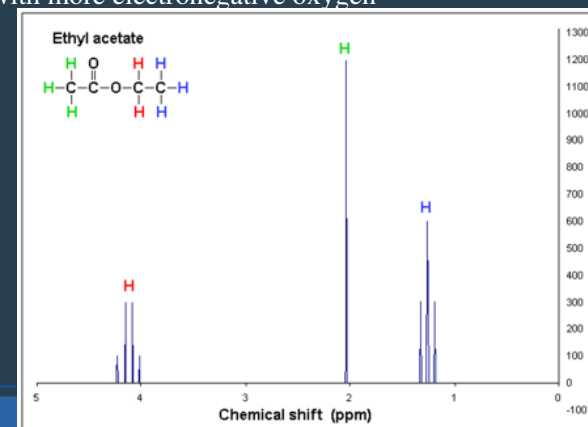
Chemical shift (ppm)

¹H NMR of 1-bromopropane

- ❖ There are three different sets of protons in this molecule. They are (CH3, CH2 and CH2) from left to right (in the structure).
- ❖ The CH2 protons (triplet) connected to bromine (electronegative) appear at high chemical shift value.
- ❖ The middle CH2 group is surrounded by two different sets of protons (five, CH3 and CH2). But, it is not just $(5+1) = 6$ ---------sextet (wrong)
- ❖ Since protons on both sides of middle CH2 are different, it is actually $(n_1+1)(n_2+1) = \{(2+1)(3+1)\} = (3)(4) = 12$ lines (called as quartet of triplet, each peak of a triplet would become a quartet)

H₃C---CH₂---CH₂--Br
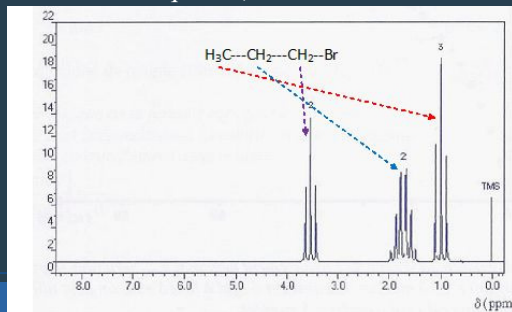
Applications of NMR

NMR Spectroscopy: A unique spectroscopic tool

Reference books

- ❖ "Introduction to spectroscopy" by Pavia.

- ❖ "Organic spectroscopy" by William Kemp.

- ❖ "A Complete Introduction to Modern NMR Spectroscopy" by Macomber.

Thank you