Chapter 8

Nuclear Magnetic Resonance Spectroscopy
Introduction-NMR

• One of the most powerful techniques for studying the shape and structure of molecules

• The first NMR instrument, Varian-30 was developed in 1952

• NMR imaging technique under the name of “Magnetic Resonance Imaging, MRI” is widely used in the diagnosis of cancer and other medical problems

• It is very useful when coupled with mass spectrometer and a chromatograph

• It involves absorption of radiowaves ($\nu$ is in the order of $10^7$ Hz) by the nuclei of some atoms in the molecule that is located in a magnetic field.
• The quantity of energy involved in RF radiation is very small. It is too small to vibrate, rotate, or electronically excite an atom or molecule.

• However, RF is great enough to affect the nuclear spin of atoms in a molecule.

• As a result, spinning nuclei of some atoms in a molecule in a magnetic field can absorb RF radiation and change the direction of the spinning axis.

• In principle, each chemically distinct atom in a molecule will have a different absorption frequency (or resonance) if its nucleus possesses a magnetic moment.

• The analytical field that uses absorption of RF radiation by such nuclei in a magnetic field to provide information about a sample is NMR spectroscopy.
• NMR is a method useful for qualitative and quantitative analysis particularly of organic compounds.

• In addition, NMR is used to study chemical equilibria, reaction kinetics, the motion of molecules, and intermolecular interactions.

• Three Nobel Prizes have been awarded in the field of NMR. 1952 to the two physicists, E. Purcell and F. Bloch,. In 1991, R. Ernst and W. Anderson The 2002 Nobel Prize was awarded to three scientists for developing methods to use NMR and MS in the analysis of large biologically important molecules such as proteins.
Magnetic properties of nucleus

• To understand the properties of certain nuclei in an NMR experiment, we must assume that nuclei rotate about an axis.

• In addition, nuclei are charged. The spinning of a charged body produces a magnetic moment along the axis of rotation.

• The spinning of the charged nucleus produces an angular acceleration causing the axis of rotation to move in a circular path with respect to the magnetic field. This motion is called “precession”

• For a nucleus to give a signal in an NMR experiment, it must have a nonzero spin quantum number and must have a magnetic dipole moment.

• Nuclei with an odd number of protons or an odd number of neutrons but not both odd show magnetic properties like $^1$H and $^{13}$C
Nuclei that can be studied by NMR

- The nuclei of certain atoms act as if they are spinning and this gives them the properties of a magnetic vector.
- Common nuclei with this property are $^1$H, $^{13}$C, $^{15}$N, $^{19}$F, $^{20}$Si and $^{31}$P.
- When a nucleus of such nuclei is placed in a magnetic field it will tend to become lined up in definite directions relative to the direction of the magnetic field. For the $^1$H nucleus it is aligned in one of two directions, with or against the applied field.
- Nuclei in which the number of protons and the number of neutrons are both even have no angular momentum and do not show magnetic properties like $^{12}$C.
Nuclei that have a nuclear spin such as $^1\text{H}$, $^{13}\text{C}$, $^{19}\text{F}$, $^{31}\text{P}$ are considered as spinning charge and they create a magnetic moment while spinning, so these nuclei can be thought of as tiny magnets.

If we place these nuclei in a magnetic field, they can line up with or against the field by spinning clockwise or counter clockwise.

Alignment with the magnetic field (called $\alpha$) is lower energy than against the magnetic field (called $\beta$). How much lower it depends on the strength of the magnetic field.

Note that for nuclei that don’t have spin, such as $^{12}\text{C}$, there is no difference in energy between alignments in a magnetic field since they are not magnets. As such, we can’t do NMR spectroscopy on $^{12}\text{C}$.
In the presence of an applied magnetic field, a nucleus with $I = \frac{1}{2}$ can exist in one of two discrete energy levels. The levels are separated by $\Delta E$.

The lower energy level ($m = \frac{1}{2}$) has the nuclear magnetic moment **aligned with the field**; in the higher energy state ($m = -\frac{1}{2}$), the nuclear magnetic moment is aligned **against the field**.
• The energy difference between the spin being aligned with the field and against the field depends on the strength of the magnetic field applied.

• The greater the field strength the greater the energy difference

\[ \Delta E = \frac{h \gamma B_0}{2\pi} \]

where \( h \) is Plank's constant; \( \gamma \) is the magnetogyric ratio of a particular nucleus; and \( B_0 \) is the applied magnetic field.

• The fundamental rule of resonance is expressed by the Larmor equation.

• Larmor equation indicates that for a given nucleus there is a direct relationship between the frequency \( \omega \) of RF radiation absorbed by that nucleus and the applied magnetic field \( B_0 \). This relationship is the basis of NMR.
The Larmor Equation

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

\( g \) is a constant which is different for each atomic nucleus (H, C, N, etc).

\[ \nu = \left( \frac{\gamma}{2\pi} \right) B_0 \]

\( \nu \) is the frequency of the incoming radiation that will cause a transition.

\( \gamma \) is a constant which is different for each atomic nucleus (H, C, N, etc).

 Gyromagnetic ratio \( \gamma \)

 Strength of the Applied magnetic field \( B_0 \)
The principle of obtaining an NMR spectrum

• Imagine a hydrogen nucleus is spinning around its own axis
• As this nucleus is placed in an external magnetic field the magnetic energy of the nucleus will cause its magnetic field to align itself with the external magnetic field
• For a proton \(^1\text{H}\) there are only two available orientations:
  – One is aligned with the applied field (lower energy)
  – One is aligned against the applied field (higher energy)
• NMR occurs when the spinning nucleus in a lower energetic orientation in a magnetic field absorbs sufficient EMR to be excited to higher energetic orientation
• Because the energy that is required for the excitation varies with the type and environment of the nucleus, NMR can be used for qualitative chemical analysis
• When the rate of precession equals the frequency of the RF radiation applied, absorption of RF radiation takes place and the nucleus becomes aligned opposed to the magnetic field and is in an excited state.

• To get an NMR spectrum for organic compounds containing protons, the sample is first put into a magnetic field and then irradiated with RF radiation. When the frequency of the radiation satisfies Larmor equation, the magnetic component of the radiant energy becomes absorbed.

• If the magnetic field $B_0$ is kept constant, we may plot the absorption against the frequency $\nu$ of the RF radiation.
• The same experiment could be done by holding the RF frequency constant and varying \( B_0 \).

• When a nucleus absorbs energy, it becomes excited and reaches an excited state.

• It then loses energy and returns to the unexcited state. Then it reabsorbs radiant energy and again enters an excited state.

• The nucleus alternately becomes excited and unexcited and is said to be in a state of resonance. This is where the term resonance comes from in nuclear magnetic resonance spectroscopy.
• Typical common values:
  – Bo = 14,000 gaus
  – \( \mu \) and I depend upon the nucleus
  – \( \Delta E = 6.7 \times 10^{-3} \) cal /mol

• Now consider the application of radio-frequency field from a radiofrequency transmitter

• A proton in the lower energy level may absorb this energy and jump to the upper level

• When the frequency of the radio-frequency field is equal to the precession frequency of nucleus, the nucleus will absorb this energy. The nucleus at this point will be in resonance.

• This absorption process is called magnetic resonance

• Or we may say that the nucleus resonates at the proper resonance frequency
Some information about NMR spectrometry

- Compared to other spectroscopic techniques, the energy difference between the ground and excited state is not large and thus the difference between the number of protons in the low-energy and high-energy states is very small.
- This is because the energy difference between the two states is low relative to the thermal energy in the environment.
- This means that NMR is a relatively insensitive technique because the net energy—absorption by the population of low-energy protons in a sample is low.
- The wavelength of the radiation used in NMR is of low energy and is in the radiofrequency region.
- The units of energy used in NMR are in Hertz, which is a unit of frequency \((c/\lambda, \text{ where } c = 3 \times 10^{10} \text{ cm/s and } \lambda \text{ is in cm})\).
The stronger the magnetic field applied the greater the radiation frequency in Hertz (the shorter the wavelength) required to cause the spin of a nucleus to align against the field.

The values for the strength of the applied magnetic field are in the range 14000-140000 Gauss (1.4-14 Tesla).

A proton in the ground state will absorb radiation having a frequency of ca 60 mHz at 1.4 T and ca 600 mHz at 14 T.

NMR instruments are described in terms of the frequency at which they cause protons to resonate; thus a 600 mHz instrument is one which causes protons to resonate at a frequency of ca 600 mHz.

At higher magnetic field strength, greater sensitivity is obtained because of the greater difference in the populations of the higher and lower energy states.

For a 60 mHz instrument the population difference between the ground and excited state for a proton is ca 1 in 100000, whereas for a 600 mHz instrument the population difference is ca 1 in 10000, i.e. about a 10-fold increase in sensitivity.
Instrumentation

All NMR units consist of five basic components, namely:
1. a sample holder
2. a large capacity magnet
3. a radio-frequency generator
4. a sweep system
5. an RF detector and recorder system.

• The general arrangement of these components is shown below
A Simplified 60 MHz NMR Spectrometer

1. a sample holder
2. a large capacity magnet
3. a radio-frequency generator
4. a sweep system
5. an RF detector and recorder system.
The NMR Spectrometer
The sample holder

• The sample holder is situated in a sample probe located at the intersection of the planes of the applied magnetic field, the applied radio-frequency field, and the detector radio-frequency field, all three of which are mutually perpendicular.

• It is a small tube about 5 mm O.D., is composed of glass or some other chemically inert material, and is transparent to RF radiation.

• It is about 3 in. long and contains approximately 0.5 ml of the liquid.
The Permanent Magnet

- The magnet must be of a large capacity (approximately 14,000 G) and must be capable of producing and maintaining a strong homogeneous field for an extended period of time.
- Since the homogeneous field (1 part in $10^8$) requirement is critical that any slight temperature variation would change the physical dimension of the magnet and thus the field homogeneity, thermostatically control systems are utilized.
The Radio-frequency Generator

- A radio-frequency oscillator is used to produce the RF radiation.
- The RF coil is wound around the sample probe in such a manner that the field plane is perpendicular to the plane of the applied magnetic field and the plane of the detector RF field.
- The oscillator must yield the same degree of precision as the magnet, i.e., about part in $10^8$ for high resolution applications.
The Sweep System

• The resonance energy may be obtained by
  – either changing the applied magnet field (field sweeping) and holding the RF field constant,
  – or by changing the applied RF field (frequency sweeping) and holding the applied magnetic field constant.

• The many difficulties which may be encountered when attempting to vary a magnetic field of a large permanent magnet are avoided by superimposing a small variable magnetic field (usually furnished by a set of Helmholtz coils) on top of the permanent magnetic field.
The Detector and Recorder

• The detector is an RF coil, the field of which is perpendicular to both the applied RF and magnetic fields.
• It detects the radiation which is absorbed and subsequently reemitted by the sample.
• From the detector the signal passes to a pre-calibrated recorder.
Sample handling

• A dilute solution (about 2 to 10%) is normally used
• If we want to study protons in the sample, the ideal solvent should contain no additional protons.
• Carbon tetrachloride meets this requirement
• Deuterated chloroform, CDCl₃, or deuterated benzene are preferably used
• Deuterated solvents may give a small additional peak for a residual proton impurity
• Deuterium oxide (deuterated water) is also available for samples soluble only in aqueous solutions
• A 5-mm OD glass tube serves as a sample container. It is held by a propeller (rigid) arrangement so that it can be spun by a jet of compressed air
The absorption Spectrum

• As previously stated, the proton, \( ^1H \), nuclei may possess only one of two possible energy states.
• The transition from the low to high energy corresponds to the absorption process, while that from the high to the low to an emission.
• If an equal population of the nuclei existed at the two energy levels, the energy lost by emission would equal the energy gained by absorption and nothing could be measured.
• This is not the case.
• A very slight (approximately 0.001 %) excess of nuclei exists in the lower energy spin state. It is this slight excess upon which nuclear magnetic resonance depends.
In the classical NMR experiment, the instrument scans from "low field" to "high field".
Each different type of proton comes at a different place. You can tell how many different types of hydrogen there are in the molecule.
Peaks integration

Not only does each different type of hydrogen give a distinct peak in the NMR spectrum, but we can also tell the relative numbers of each type of hydrogen by a process called integration.

Integration = determination of the area under a peak

The area under a peak is proportional to the number of hydrogens that generate the peak.
Benzyl acetate

The integral line rises an amount proportional to the number of H in each peak.

\[ 55 : 22 : 33 = 5 : 2 : 3 \]

simplest ratio of the heights
Benzyl acetate (FT-NMR)

Actually:

\[
\frac{58.117}{11.3} = 5.14
\]

\[
\frac{21.215}{11.3} = 1.90
\]

\[
\frac{33.929}{11.3} = 3.00
\]

METHOD 2

digital integration

Modern instruments report the integral as a number.

Integrals are good to about 10% accuracy.
Magnetic Shielding

- If all protons absorbed the same amount of energy in a given magnetic field, not much information could be obtained.
- But protons are surrounded by electrons that shield them from the external field.
- Circulating electrons create an induced magnetic field that opposes the external magnetic field.
The applied field induces circulation of the valence electrons - this generates a magnetic field that opposes the applied field. Valence electrons shield the nucleus from the full effect of the applied field. The fields subtract at the nucleus.
Shielded Protons

Magnetic field strength must be increased for a shielded proton to flip at the same frequency.
All different types of protons in a molecule have a different amounts of shielding.

They all respond differently to the applied magnetic field and appear at different places in the spectrum.

This is why an NMR spectrum contains useful information (different types of protons appear in predictable places).
The chemical shifts of nuclei are measured (and defined) relative to a standard nucleus.

A popular standard for proton NMR is tetramethylsilane (TMS), which has the chemical formula $\text{Si(CH}_3\text{)}_4$.

In this compound all 12 hydrogen nuclei are chemically equivalent; that is, they are all exposed to the same shielding and give a single absorption peak.

The chemical shift for other hydrogen nuclei is represented as follows:
Delta Scale

Chemical shift, ppm $\delta =$ \[ \frac{\text{shift downfield from TMS (in Hz)}}{\text{spectrometer frequency (in MHz)}} \]

For 60 MHz:
- 600 Hz: 10
- 480 Hz: 9
- 360 Hz: 8
- 240 Hz: 7
- 120 Hz: 6
- 0 Hz: 5

For 300 MHz:
- 3000 Hz: 10
- 2400 Hz: 9
- 1800 Hz: 8
- 1200 Hz: 7
- 600 Hz: 6
- 0 Hz: 5

TMS
Shielding and deshielding of the nuclei

- In terms of NMR, within a given molecule, the electronic and steric environment of each nucleus produces a shielding effect against the external field $B_0$.

- As the screening effect increases, the nuclei are said to be shielded.

- On a continuous wave instrument operating at fixed frequency, the intensity of the field $B_0$ has to be increased in order to obtain resonance.

- Signals to the right of the spectrum are said to be resonant at high field. Signals observed to the left of the spectrum correspond to deshielded nuclei and are said to be resonant at low field.
Peaks are measured relevant to TMS

Rather than measure the exact resonance position of a peak, we measure how far downfield it is shifted from TMS.

Chemists originally thought no other compound would come at a higher field than TMS.
Protons in a Molecule

Depending on their chemical environment, protons in a molecule are shielded by different amounts.
The shift observed for a given proton in Hz also depends on the frequency of the instrument used. Higher frequencies give larger shifts in Hz.
The chemical shift

The shifts from TMS in Hz are bigger in higher field instruments (300 MHz, 500 MHz) than they are in the lower field instruments (100 MHz, 60 MHz).

We can adjust the shift to a field-independent value, the “chemical shift” in the following way:

\[
\text{chemical shift} = \delta = \frac{\text{shift in Hz}}{\text{spectrometer frequency in MHz}} = \text{ppm}
\]

This division gives a number independent of the instrument used.

A particular proton in a given molecule will always come at the same chemical shift (constant value).
The Chemical Shift (Also Called $\delta$) Scale

- Here’s how it works. We decide on a sample we’ll use to standardize our instruments.
- We take an NMR of that standard and measure its absorbance frequency.
- We then measure the frequency of our sample and subtract its frequency from that of the standard.
- We then then divide by the frequency of the standard. This gives a number called the “chemical shift,” which does not depend on the magnetic field strength. Why not? Let’s look at two examples.
Imagine that we have a magnet where our standard absorbs at 300,000,000 Hz (300 megahertz), and our sample absorbs at 300,000,300 Hz. The difference is 300 Hz, so we take

\[
\frac{300}{300,000,000} = \frac{1}{1,000,000}
\]

and call that 1 part per million (or 1 ppm)
• Now let's examine the same sample in a stronger magnetic field where the reference comes at 500,000,000 Hz, or 500 megahertz.

• The frequency of our sample will increase proportionally, and will come at 500,000,500 Hz.

• The difference is now 500 Hz, but we divide by 500,000,000 (500/500,000,000,000 = 1/1,000,000, = 1 ppm).
• If the sample nucleus is **upfield** it means that $\delta$ is positive and that the sample is more highly shielded than the reference.

• When downfield, $\delta$ is negative and the reference is more highly shielded than the sample.

• The unit of the chemical shift is **ppm**.

• This is not a concentration unit but is the ratio of numerator and denominator in the above equation, i.e., it is the difference in the magnetic field of the sample, $H_S$, and the magnetic field of the reference, $H_r$, divided by the magnetic field of the reference.
The chemical shift

• If NMR were suitable only for detecting and measuring the presence of hydrogen or carbon in organic compounds, it would be a technique with very limited usefulness. There are a number of fast, inexpensive methods for detecting and measuring hydrogen and carbon in organic compounds.

• According to the NMR experiment, protons in different chemical environments within a molecule absorb at slightly different frequencies.

• This variation in absorption frequency is caused by a slight difference in the electronic environment of the proton as a result of different chemical bonds and adjacent atoms.

• The absorption frequency for a given proton depends on the chemical structure of the molecule.
• This variation in absorption frequency is called the chemical shift.

• The same type of chemical shift occurs for carbon in different chemical environments within a molecule.

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• The same type of chemical shift occurs for carbon in different chemical environments within a molecule.
Suppose that we take a molecule with several different "types" of hydrogen atoms, such as the molecule ethanol, CH$_3$CH$_2$OH.

This molecule has hydrogen atoms in three different chemical environments: the three hydrogen atoms in the terminal CH$_3$,

The two hydrogen atoms in the CH$_2$ group,

and the one in the OH group.

Consider the nuclei of the different types of hydrogen. Each one is surrounded by orbiting electrons, but the orbitals may vary in shape and the bonds vary in electron density distribution.

This changes the length of time the electrons spend near a given type of hydrogen nucleus.

Let us suppose that we place this molecule in a strong magnetic field $B_0$. The electrons associated with the nuclei will be rotated by the applied magnetic field $B_0$. 
• This rotation, or *drift*, generates a small magnetic field which opposes the much larger applied magnetic field $B_0$.

• The nuclei are *shielded* slightly from the applied magnetic field by the orbiting electrons.

• The extent of the shielding depends on the movement of the electrons caused by the magnetic field (not by the simple orbiting of the electrons).

• A shielded nucleus resonates or absorbs at a lower frequency than an unshielded nucleus. This change in frequency of absorption because of shielding is the chemical shift.

• Instead of one absorption signal for the protons in ethanol, we would predict three absorption signals at slightly different frequencies.
Absorption of $\text{CH}_3 \text{ CH}_2 \text{ OH}$
• The chemical shifts of nuclei are measured (and defined) relative to a standard nucleus.

• A popular standard for proton NMR is tetramethylsilane (TMS), which has the chemical formula Si(CH$_3$)$_4$.

• In this compound all 12 hydrogen nuclei are chemically equivalent; that is, they are all exposed to the same shielding and give a single absorption peak.

• The chemical shift for other hydrogen nuclei is represented as follows:
The NMR Spectrum

less shielded
lower field (downfield)

more shielded
higher field (upfield)

increasing magnetic field strength \( (B_0) \)
Number of Major Absorption Peaks

• The number of major absorption peaks in an nmr spectrum equals the number of *different types* of protons which exist in the molecular compound.

• The protons within the molecule which possess the same magnetic environment are said to be *equivalent* and will absorb at the same applied field strength.

• Protons with different magnetic environments will absorb at different applied field strengths and are *non-equivalent*.

• The equivalency or non-equivalency of protons in any given molecule is determined by the type and character of its bonding to adjacent atoms and in some cases to a group of atoms.
• Hydrogens bonded to different atoms are non-equivalent.
• For example, in methyl alcohol, CH₃OH, the hydrogens bonded to the carbon are not equivalent to that one which is bonded to the oxygen and two major absorption peaks will be obtained.
• Because of the tetrahedral nature of the carbon atom, the three hydrogens in the methyl group are equivalent to each other and appear as a single major absorption peak in an nmr spectrum.
• The other major absorption peak arises from the OH bonding
• The two hydrogens in a CH$_2$ group are equivalent to each other.
• Three major absorption peaks would be expected from CH$_3$-CH$_2$-OH;
• One from the CH$_3$ group, one from the CH$_2$, group, and one from the OH group.
• At times it is necessary to consider not only the atom to which the hydrogen is bonded but also any bonds which are once or twice removed from this primary bond.

• For example, the bonding of the CH₃ hydrogens in a CH₃-CH₂- group will not be equivalent to the bonding of the CH₃ hydrogens in a CH₃-O- group.

• The compound methyl ethyl ether, CH₃-O-CH₂-CH₃ will show three major absorption bands—one for the hydrogens of the methyl group with the CH₃- O bond, one for hydrogens of the methyl group with the CH₃-CH₂- bond, and one from the hydrogens of the CH₂ group.

• On the other hand, diethyl ether, CH₃-CH₂-O-CH₂-CH₃, shows only two major bands.
• Bonding to atoms which are twice removed must also be considered. For example, all of the groups of hydrogen atoms in CH$_3$-CH$_2$-CH$_2$-OH are non-equivalent and four major absorption peaks will be observed.

• In the benzene molecule all six hydrogens are equivalent since the bonding of all six to the carbon atoms is identical. Only one peak will be observed.

• A substitution on one or more of the positions of the benzene ring will upset this equivalency -the extent of change depends upon the number and/or nature of the substituted group(s).

• The presence of double or triple bonds may cause a non-equivalency
Areas Under Absorption Peaks

- *Area* under an nmr absorption peak is directly proportional to the number of equivalent protons which are causing the peak.
- The instruments are equipped with an electronic integrator.
- The integral curve is recorded on the vertical axis of the recorder chart simultaneously with the absorption curves.
- The relative areas of the peaks are determined by the heights of the integral curves at the respective frequencies.
- These data are then reduced to a whole number ratio and may be used for quantitative determination or for the elucidation of structure.
Consider a spectrum of ethyl alcohol

\[
\begin{array}{ccc}
H & H & H \\
HC - & C - & OH \\
H & H & \ \\
a & b & c
\end{array}
\]

in which the height of the integration curves shows a ratio of \(a:b:c = 7.71 : 5.24 : 2.58\). This reduces to a 3:2:1 ratio.
Figure 10-4  Schematic diagram of nmr absorption curve fractions showing the use of an integral recorder. The heights of the integral curves show that the ratios of the areas of $a:b:c:d:e$ are $3.3:24:4:14:12$. 
Spin-spin coupling (Splitting)

• The signals in the NMR spectra don’t appear as single lines, sometimes they appear as multiple lines.

• This is due to $^1\text{H} - ^1\text{H}$ coupling (also called spin-spin splitting or J-coupling).

• Imagine we have a molecule which contains a proton (let’s call it $\text{H}_A$) attached to a carbon, and that this carbon is attached to another carbon which also contains a proton (let’s call it $\text{H}_B$). It turns out that $\text{H}_A$ feels the presence of $\text{H}_B$.

• Since these protons are tiny little magnets, they can be oriented either with or against the magnetic field of the NMR machine.
• When the field created by $H_B$ reinforces the magnetic field of the NMR machine ($B_0$) $H_A$ feels a slightly stronger field, but when the field created by $H_B$ opposes $B_0$, $H_A$ feels a slightly weaker field. So, we see two signals for $H_A$ depending on the alignment of $H_B$.

• The same is true for $H_B$, it can feel either a slightly stronger or weaker field due to $H_A$’s presence. So, rather than see a single line for each of these protons, we see two lines for each.

For this line, $H_B$ is lined up **with** the magnetic field (adds to the overall magnetic field, so the line comes at higher frequency)

For this line, $H_B$ is lined up **against** the magnetic field (subtracts from the overall magnetic field, so the line comes at lower frequency)

$H_A$ is split into two lines because it feels the magnetic field of $H_B$.

$H_B$ is split into two lines because it feels the magnetic field of $H_A$. 
• Each hydrogen nucleus of an organic molecule is spinning and is magnetic.
• Since the axis of rotation of the nucleus may be with or against the applied magnetic field, the magnetic field of the nucleus may be parallel with or opposed to the applied magnetic field.
• With reference to a molecule of ethyl alcohol, 
  \[
  \text{H} \quad \text{H} \\
  \text{HC} - \text{C} - \text{OH} \\
  \text{H} \quad \text{H}
  \]
• The spinning of the hydrogen on the \( \text{OH} \) group causes a small magnetic field which may be with or against the applied magnetic field.
• This spinning interferes with the spinning of the adjacent $CH$, group causing the effective field of the $CH$, group to change slightly.

• The $CH$, hydrogens which are adjacent to the hydrogen spinning with the field absorb at a slightly different frequency from that of the $CH$, hydrogens which are spinning against the field.

• The number of possible spin combinations, and the relative numbers of each combination, and thus the fine absorption spectra are predictable.
A. For a single functional group the number of bands = \((n + 1)\) where \(n\) is the number of equivalent hydrogens on the adjacent group. See methyl alcohol or methyl ethyl ketone examples in the Table

B. If the protons of the two adjacent groups are not equivalent to each other, the multiplicity of bands will be \((n_1 + 1)(n_2 + 1)\) where \(n_1\) and \(n_2\) are the number of equivalent protons on the first and second groups, respectively. See the ethyl alcohol and 1-chloropropane examples in the Table
C. If all the carbon atoms of a group such as $CH_3$ or a compound such as in $H_3C-CH_3$ are equivalent, splitting will not occur.

D. The protons of the aromatic hydrogens on the substituted benzene ring are often non-equivalent. Complex splitting patterns may occur.
• The number of peaks which will actually be seen depends upon the resolution of the instrument.
• The splitting pattern of isobutyl alcohol and normal butyl alcohol can be seen in the Figures below.
NMR absorption spectrum of normal butyl alcohol
NMR absorption spectra of ethyl alcohol. The numbers designate the relative areas of the groups in the low resolution spectrum and of the peaks within a functional group in the high resolution spectrum.
• The absorption position of a particular functional group will vary with the applied magnetic field strength but the magnitude of separation which is caused by spin-spin coupling is independent of the applied field strength.

• This spacing is called the spin-spin coupling constant, is denoted by the symbol, J, and has the units of frequency in cycles per second, cps.
• There is no coupling between hydrogens on the same carbon.
• The constant, J, is from 6-8 cps between the hydrogens on adjacent carbons and decreases rapidly as the distance between the carbons increases.
• The areas of the peaks which arise from spin-spin splitting are in direct ratio to the number of possibilities of each of these peaks being observed.
• For example, the relative areas of the -CH, -\textit{CH}_2, and -OH groups in ethyl alcohol should be in the ratio of 3:2:1, respectively.
• Upon higher resolution where splitting occurs, the three bands of the -\textit{CH}_3 triplet would exist in an area ratio of 1:2:1 and the quartet of the -\textit{CH}_2 group would have a ratio of 1:3:3:1. See last Figure above.
Analytical applications

• The procedures are limited to structure determinations involving nuclei which possess either an odd mass number such as the proton or an even mass number with an odd atomic number such as the deuterium.

• The nmr spectroscopy techniques are applied primarily to liquid samples.

• The absorption bands for solids are generally too wide and instruments are not sensitive enough for gaseous samples without instrumental modification.

• Liquid sample sizes range from 0.1 to 0.4 ml.

• If the sample itself is a liquid it may be determined directly; if not, it may be dissolved in a suitable solvent.

• The minimum concentration which may be detected in a liquid is approximately 1%.

• The choice of a liquid solvent is made on the basis of its purity, chemical stability and volatility.
13C NMR

13C signals are 6000 times weaker than 1H because:

1. Natural abundance of 13C is small (1.08% of all C)

2. Magnetic moment of 13C is small

3. The chemical shift range is larger than for protons (0-200 ppm)
Because of its low natural abundance (0.0108) there is a low probability of finding two $^{13}\text{C}$ atoms next to each other in a single molecule.

\[ ^{13}\text{C} - ^{13}\text{C} \quad \text{Coupling not probable} \]

Spectra are determined by many molecules contributing to the spectrum, each having only one $^{13}\text{C}$ atom.

However, $^{13}\text{C}$ does couple to hydrogen atoms (I = 1/2)

\[ ^{13}\text{C} - ^{1}\text{H} \quad \text{coupling} \quad \text{Very common} \]
ETHYL PHENYLACETATE

$^{13}\text{C}$ coupled to the hydrogens
Qualitative Analysis

• nmr would offer little information which is not available by other less expensive methods.
• The nmr is primarily applied in organic chemistry and is used in the elucidation of the structure of and identification of organic molecules.
• As we have seen, the chemical shift yields information as to the types of hydrogens which are present,
• whereas the spin-spin splitting yields information concerning the nature of the neighboring groups.
• These two features, combined with the fact that the relative areas of absorption peaks are in direct proportion to the number of equivalent hydrogens in each group, make nmr a powerful structure identification tool.
Quantitative Analysis

- The fact that the areas of nmr absorption peaks are in direct proportion to the types of hydrogens which are causing the respective peaks is the basis for the nmr quantitative analysis of organic liquids.
- These areas may be rapidly determined with the integration recorders.
- In order for quantitative procedures to be applied, the components must be known.
- In addition, each component of the mixture must provide at least one absorption band which is isolated from the absorption bands of any other components.
- Impure samples may be determined by the addition of a known pure compound as an internal standard.
- Quantitative applications have been used to elucidate chain length or the percentage of hydrogen in a pure compound.
- The degree of saturation in a compound of known chain length and known percentage composition may be calculated.