

## An Overview of Nuclear Magnetic Resonance: A Review

Lalit Kumar<sup>1</sup> and Anandveer Sindhu<sup>2</sup>

<sup>1</sup>Department of Physics, Meerut College, Meerut, INDIA

<sup>2</sup>Department of Chemistry, Meerut College, Meerut, INDIA

<sup>1</sup>Corresponding Author: lalitksuvaksh@gmail.com

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### ABSTRACT

Nuclear Magnetic Resonance (NMR) spectroscopy is the most important techniques that has been developed in the recent past decades. Matter, organic compounds and biological and non biological applications ranging from a particular cell to different organs and various tissues. has been investigated through NMR. Aspects of this technique are still under research and many functions and various applications of the NMR are still under process. This review paper is aimed at providing a general overview of the different NMR, main principles and pro and con of NMR spectroscopy. In spite of all of these we have discussed the various use of NMR in the field of science and medicine and ongoing development of NMR spectroscopy.

**Keywords--** NMR Spectroscopy, Biological Applications, Larmor Frequency

### I. INTRODUCTION

NMR spectroscopy is a non destructive technique which are used to analyse the structure of molecule by exploring its electronic orientation. This technique is widely used in industrial and in the field of medicine to detect abnormalities and fracture etc. NMR also provides the information on the molecular structure at the atomic level and it is a tool which are used to analyzing molecular dynamics and interactions at the atomic level. NMR is very powerful analytical tool which is used to provide precious result with minimal potential damage to the body tissue. NMR was first discovered in the decade of 1940. It is also beneficial to explore the structure of amorphous glasses, disease detection etc.

NMR is a spectroscopic technique which is based upon the absorption of electromagnetic radiation in the radiofrequency region by nuclei of the atoms. Proton nuclear magnetic resonance spectroscopy is used for elucidating the number of hydrogen in the various type of compounds. It is used to study a wide variety of nuclei. The nuclei which have half integer spin are NMR active and those nuclei which have zero spin are not NMR active.

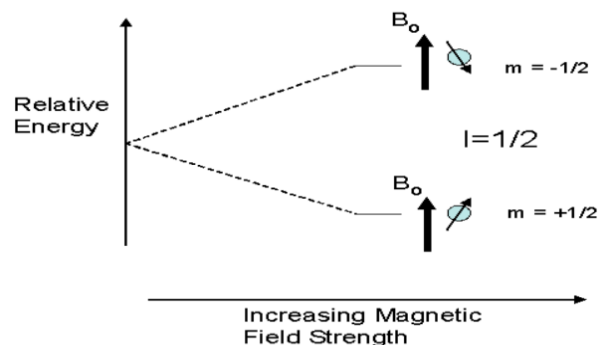


Figure 1: Energy level of proton in magnetic field

When a nucleus whose magnetic moment has the z- component  $\mu_z$  is in a constant magnetic field B, the magnetic potential energy of the nucleus is

$$U_m = -\mu_z B$$

This energy is negative when  $\mu_z$  is in the same direction as B and positive when  $\mu_z$  is opposite to B. In a magnetic field each angular momentum state of the nucleus is splitted into components. Fig 1 shows the splitting when the angular momentum of the nucleus is due to the spin of a single proton. The energy difference between the sublevels is

$$\Delta E = 2\mu_{pz} B$$

a photon of this energy will be absorbed when a proton in the lower energy state flips its spin to upper energy state. This energy will be emitted when a proton in the upper state flips its spin to fall to the lower state. The photon frequency  $\nu_L$  that corresponding to  $\Delta E$  is

$$\nu_L = \frac{\Delta E}{h} = \frac{2\mu_{pz} B}{h}$$

This is equal to the frequency with which a magnetic dipole precesses around a magnetic field. Suppose we put a sample of some substance that contains nuclei with spin of half in a magnetic field B. The spins of the most of the nuclei will become align parallel to be in spin up state because this is the lowest energy state. If we now supply electromagnetic radiation at the Larmor frequency to the sample the nuclei will receive the right amount of energy to flip their spins to the higher energy state or spin down state. This phenomenon is called Nuclear Magnetic Resonance.

## II. NMR INSTRUMENTATION

**1. Sample Holder:** It is a glass tube which is 8 to 9 cm long and 0.3 cm in diameter. It is typically made of borosilicate glass and have thin walled and it holds the sample dissolve in a suitable solvent.

**2. Permanent Magnet:** This type of magnet provide homogenous magnetic field of the order of 5200 MHz. Now a days most NMR magnets are of the superconducting type and NMR magnet range in field strength varies from 6 to 24 tesla.

**3. Magnetic Coils:** These coils induced magnetic field when current passes through the magnetic coil. NMR uses a large magnet to probe the intrinsic spin property of atomic nuclei.

**4. Sweep Generators:** It is a piece of electronic test equipment and behaved as a function generator which creates an electrical waveforms with a linearly varying frequency and a constant amplitude.

**5. Radio frequency Transmitter:** It is an electronic device which produces the radio waves with an antenna, transmitter itself generate a radiofrequency alternating current which is applied to the antenna. This create a signal which is used to excite proton in the imaging field.

**6. Radio Frequency Receiver:** A radio receiver coil that detects radio frequency emitted as nuclei relax to a lower energy level. Range of radio frequency lies from 20 KHz to 300 GHz. This is between the upper limit of audio frequencies and the lower limit of infrared frequencies.

**7. Read out System:** A computer that analysis data received.

### *Relaxation Process*

This is the process involve some non radiative transitions by which a nucleus in an upper transition state returns to the lower spin state. There are three kind of relaxation process.

**Spin- Spin relaxation:** It is due to mutual exchange of spins by two precessing nuclei which are very close to each other. Basically each precessing nucleus is associated with a magnetic vector component rotating in a plane perpendicular to the field. If this small rotating magnetic field is the same as required to induce a transition in the neighbourhood proton then mutual exchange of spin takes place. Consequently transfer of energy takes place from one nucleus to another. The speed of energy among the nuclei is responsible for line broadening which makes NMR spectra of solids highly interesting.

**Spin Lattice Relaxation:** In this phenomenon transfer of energy takes place from the nucleus in its higher energy states to the molecular lattice. Here energy is transferred to the component of the lattice for the translational, vibrational and rotational energy levels. This process involve a short time therefore responsible for broadening of absorption peaks. This process is responsible for keeping the excess of nuclei in the lower energy states and it is essential condition for NMR phenomenon.

**Quadrupole Relaxation:** This relaxation phenomenon occurs for those nuclei which have nuclear spin greater than half. The nuclei due to anisotropic interaction between non spherical, electrical quadrupole nuclei etc is responsible for asymmetric positive charge distribution on the nuclei. these nuclei possesses electric quadrupole moment and relax rapidly and display broad signals. This process of deactivation of nuclei is called electric quadrupole relaxation.

## III. TYPES OF NMR SPECTROSCOPY

- 1. Gel Phased NMR:** This type of spectroscopy was first introduced in the year 1996. From this type of spectroscopy information from the liquid or Gel phase can be obtained. Solvent system can be manipulated to obtain various type of information. Plants, microbes, clay organic complexes, vegetables can be analysed by this type of spectroscopy.
- 2. Solution state NMR:** It provide the highest resolution data and comprehensive molecular information about soluble compounds.
- 3. Solid State NMR:** This type of NMR is traditionally used for dried samples packed into a rotor. It is used to determine the chemical structure, 3D structure and dynamics of solids and semi solids. The nuclear spin interactions and the effects of magnetic fields and radiofrequency pulses on nuclear spin in solid states NMR are the same as liquid state NMR spectroscopy.  $C^{13}$  is the most commonly detected nucleus in the solid state for the environmental sample. Due to low sensitivity of  $C^{13}$  detection, cross polarization is generally used to enhance the  $C^{13}$  signal. Solid state  $C^{13}$  NMR provides excellent overview of environment and distribution of carbon with in a sample. Phosphorus and Nitrogen NMR spectroscopy have great potential to understand nutrient cycles.

**Table 1: Commonly Studies Nuclei in Solid State NMR Spectroscopy**

Nuclei	Spin Quantum Number	Natural Abundance	Applications
H <sup>1</sup>	1/2	99.9%	Organic materials, lipids proteins etc
H <sup>2</sup>	1	0.015%	Carbohydrate, proteins etc
Li <sup>7</sup>	3/2	92.4%	Lithium ion batteries etc
Be <sup>9</sup>	3/2	100%	Coordination complexes etc
B <sup>11</sup>	3/2	80.1%	Abnormal growth of tissues etc
C <sup>13</sup>	1/2	1.1%	Organic and biological compounds etc
N <sup>15</sup>	1/2	0.37%	Proteins ceramics etc
O <sup>17</sup>	5/2	0.037%	Water, carbohydrate, protein, ceramics etc
F <sup>19</sup>	1/2	100%	Organic materials etc
Al <sup>27</sup>	5/2	100%	Aluminosilicate, Zeolites etc
Si <sup>29</sup>	1/2	4.7%	Zeolites, minerals etc
P <sup>31</sup>	1/2	100%	Phosphate, nucleic acid, assay purity in chemistry

#### IV. IMPORTANT FEATURES IN NMR SPECTROSCOPY

- Chemical Shift (CS):** In an atom, electron revolves around the nucleus and movement of electron creates a magnetic field in and around the nucleus. This created magnetic field is different in the direction as compared with the outer applied magnetic field therefore any change in the magnetic field causes corresponding change in the spectrum of NMR. This sum of the shift is controlled by nature of the motion of the electrons in its surrounding atoms and molecules. This phenomenon is known as chemical shift (CS). A reference compound is needed to measure CS and differentiate magnetically equivalent nuclei present in a molecule. The CS of the carbon nuclei is determined by the electron density surrounding the nucleus. CS is influenced by hybridisation and electronic effects. CS also depends upon electro negativity of nearby atoms and when the electro negativity of nearby atoms increases then CS also increases, CS also depends upon number of pie bonds in adjacent atoms.

Vanderwaal's deshielding play a crucial role in chemical shift. Electron cloud of a bulky group will tend to repel the electron cloud surrounding the proton. Therefore such a proton will be deshielded and will resonate at slightly higher frequency.

Anisotropic effects and hydrogen bonding also play an important role in chemical shift. Tetramethylsilane (TMS) is the most convenient reference for measuring chemical shift. It is chemical inert and has 12 protons all are magnetically equivalent. It has low boiling point and is readily remove from the system.

- Shielding and Deshielding of Nucleus:** When the effective magnetic field experience by the

nucleus is less than that of applied magnetic field then the nucleus is said to be shielded. The signal for shielded proton appears up field. When the effective magnetic field experience by the nucleus is more than that of applied magnetic field then the nucleus is said to be deshielded. The signal for deshielded proton appears down field. The deshielded of protons is caused when it is surrounded by electronegative atoms. Ethylenic, aromatic and aldehyde protons are highly deshielded.

- Spin-Spin Splitting:** Splitting occurs only between nuclei with different chemical shift. The coupling interaction takes place between the neighbouring protons, most often through bonds and results in the splitting of spectral lines. Coupling also takes place between protons on the same carbon atom provided these are in stereo chemical different environment.
- Hydrogen Bonding:** It causes deshielding of proton. Greater the degree of hydrogen bonding, greater the downfall shift. Basically extent of hydrogen bonding decreases on dilution and so the deshielding.
- Coupling Constant:** The coupling constant is a measure of the coupling interaction between the nuclei. the spacing between the lines with in a coupled multiplet is constant. This constant distance, called coupling constant is denoted by J and is expressed in Hz.
- Equivalence of Protons:** A set of chemically equivalent protons are also magnetically equivalent and they possesses the same frequency and only one characteristic spin spin interaction with the nuclei of the neighbouring group. All the three protons of methyl group are equivalent because all the three protons have the same time average chemical environment and hence the same resonance frequency.

## V. APPLICATIONS OF NMR SPECTROSCOPY

### 1. Application of NMR in Food Analysis:

- NMR is a rapid fast and analytical method that is used to study moisture in food and analysing the components of oil, protein and carbohydrates.
- Together with Fourier Transform Spectroscopy it is also used to food analysis including oil, red wine, honey, milk, fruits and vegetables.
- NMR has been widely used in the analysis of edible oil. It is also playing an important role in identification the origin of fats, monitoring the oxidation process, determining the oil content of foods and identifying adulteration of edible fats.
- $H^1$  and  $C^{13}$  NMR spectroscopy has been applied to analysis of refined edible oil from various plant sources and such type of spectroscopy have been widely used to analysis of various fatty acids.
- NMR has been widely used to identify oxidation products.
- NMR has been used to qualitatively and quantitatively analysis of wine chemical components to distinguish wine waste on grape variety, geographic origin and year of production.
- NMR has been used for the analysis of fermentation and adulteration.
- In recent years NMR has been widely used to study the metabolic spectra of milk and various dairy products.
- Information obtained by NMR spectroscopy provides the knowledge about environment of various food compounds including evaluation of microbiological, physical and chemical quality of foods.

### 2. Application of NMR in Medicine and Dentistry:

- The ability to analyse abnormal behaviour in the cell or metabolism allow scientists to detect the metabolite based biomarkers associated with cancer.
- NMR is widely used to identify breast cancer at an early stage. mammogram cannot differentiate between small cancer and a spot however with NMR this distinction is possible.
- Clinical proton NMR imaging has been widely used for the analysis of brain and central nervous system.
- Proton NMR imaging can be used for the detection of vascular obstruction.

- Proton NMR imaging of the kidney provide the detail information regarding anatomy and the function of the kidney.
- NMR is a nice tool for identifying different type of human disorder and disease such as T.B , pneumonia and malaria can be easily diagnosed.
- NMR is widely used to investigate Parkinson disease and cardiovascular disease and neuro disorder such as bipolar, major depression etc.
- NMR can be used to demonstrate bone marrow and finding any disorders in the same.
- Another major advantage of NMR is its lack of ionisation and therefore individual have the safety from the same.
- NMR has particular use for certain body areas such as brain where it produce very detailed and definite images showing delineation between grey and white matter.
- NMR techniques provides good images of fatty tissues.
- The advancements of proteomics in dentistry have brought a revolution in the management of oral diseases and analysis of molecular changes during the reconstruction of oral tissues.

### 3. Application of NMR in Drug Designing and Development:

- NMR has proved to be a valuable tool in pharmaceutical research. It also provide information on the three dimensional structure of small molecules.
- Unique ability of NMR provides information about the structure and confirmation of ligands molecules.
- Drug NMR spectroscopy had been utilised in various field such as evaluation of the content of residual solvents, observation of the course of degradation of a drug and determination of the level of impurities and elucidation of their structure.
- NMR used in the evaluation of drug performance and in elucidation of the basic mechanism of drug action.
- $N^{15}$  NMR is used to test the binding of drugs to  $N^{15}$  level proteins.
- Drug NMR spectroscopy has wide applications in the identification of the drugs and determination of the composition of multi component drugs and it is also used to determine the isomeric composition too.

### 4. Application of NMR in Chemistry:

- Detection of hydrogen bonding: The extent of hydrogen bonding varies with



the solvent, concentration of the solution and the temperature. Intra molecular hydrogen bonding also shifts the absorption downfield.

- Detection of aromaticity: Signal for the aromatic protons appear at a very low field than that observe even for benzene.
- Distinction between Cis-Trans isomers and conformers.
- Detection of electronegative atom or group.
- Detection of some double bond character due to resonance.
  - Identification of structural isomers.

## VI. CONCLUSION

### *Advantages of NMR*

- No ionisation radiation is involved in the process which limit the users and samples to exposure to radioactivity.
- Sample can be recovered fully and can be used for other application too.
- Samples being analysed by NMR spectroscopy do not require sample preparation except dissolving in suitable deuterated solvents.
- We can investigate the dielectric constant, the polarity and any other property of the solvent.
- With a suitable computer apparatus we can calculate the whole 3D structure of proteins and enzymes.

### *Disadvantages of NMR*

- NMR spectroscopy requires expensive equipments and their installation is costly and difficult.
- Magnetic field used to generate NMR image with resistive and superconducting systems are sensitive to radiofrequency interference and may damage the computer tape or other objects in the surrounding environment.
- NMR imaging are not to be safe to those person who are suffering with heart disease or metal implants.
- NMR imaging is highly time consuming in comparison of X- ray and CRT.
- NMR is less sensitive than mass spectroscopy and determining the structure for higher molecular weight molecules is a major problem.
- This type of spectroscopy is applicable for only those nuclei which have a magnetic moment.

## REFERENCES

- [1] Kaiyyum A. Bhaldar, Vipul M. Patil and Sachinkumar V. Patil. (2021). *International Journal of Creative Research Thoughts*.
- [2] Komal Zia, Talal Siddiqui & Zohaib Khurshid. (2019). *European Journal of Dentistry*.
- [3] A.J Simpson, M.J Simpson & R. Soong. (2012). *Environmental Science and Technology*.
- [4] Adwin D Becker. (2000). *High resolution NMR*. (3<sup>rd</sup> ed.).
- [5] Metin Balci. (2005). *NMR spectroscopy*.
- [6] Y.R Sharma. (2008). *Elementary organic spectroscopy*. S Chand Publications.
- [7] Arthur Beiser. (1995). *Concepts of modern physics*. (5<sup>th</sup> ed.).
- [8] Bernd Reif, Se ash Brook & M Hong. (2021). *Nature review*.
- [9] Ultriike Holzgrable. (2010). *Progressing nuclear magnetic resonance spectroscopy*.
- [10] Neeraj Upmanyu, Gopal garg, Archana Dolly & Pradeep Mishra. (2007). *E-J Chm review article*.
- [11] M Heller & H Kessler. (2001). *Pure Applied Chemistry*.
- [12] M Mayer & B.Mayer. (2001). *Journal of American Chemical Society*.
- [13] Sahibzada H A, Khurshid Z, Khan R & S. Salivary. (2017). *PMC free article*. PubMed.
- [14] Khurshid Z, Zafar M S, Khan R S, Najeeb S, Slowey P & D, Rehman. (2018). *Adv Clin Chem*.
- [15] E Mark, Ladd, Peter Bacherd et al. (2018). *Progress in nuclear magnetic resonance spectroscopy*.
- [16] Takuyaf Segawa & Ryuji Igarashi. (2023). *Progress in nuclear magnetic resonance spectroscopy*.
- [17] Yael Ben-Tal, Patrick J et al. (2022). *Progress in nuclear magnetic resonance spectroscopy*.
- [18] Emil Ljungberg, Nikou L. Damestani et al. (2021). *Progress in nuclear magnetic resonance spectroscopy*.
- [19] Sara Osman. (2023). *Nature*.
- [20] V.Vitali & F.Torricela. (2023). *Scientific reports*.
- [21] G.A. Nagana Gowda & Daniel Raftery. (2018). *National Library of Medicine PUB MED*.