# One and Two dimensional NMR Spectroscopy: Concepts and Spectral Analysis

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## Lecture – 01: Nuclear Spin

Good morning everyone, welcome for this course on one and two dimensional NMR spectroscopy: concepts and spectral analysis. I am professor Suryaprakash, served at Indian Institute of Science for nearly 44 years and superannuated as a professor and chairman 2 years back. Currently I am holding CSIR Emeritus Scientist position at SSCU. Now, let us start by asking in this course what I am going to offer for you, what is that you are going to learn in this course. First we will discuss NMR concepts right from little bit of introduction to spin physics, interaction of magnetic moment with the external magnetic field, how do we get the resonance and what are the interaction parameters etc. etc. Basic concepts including selection rules we will discuss.

Subsequently we discuss more about the interaction parameters such as chemical shift and scalar couplings. After introduction of these two parameters, we discuss extensively on these two parameters. Afterwards we will analyze one dimensional NMR spectra where I am going to take N number of examples, lot of examples to make you feel more comfortable. As we go along I will discuss spin echoes, attach proton test, inept, DEPT, etcetera, where we will try to enhance its signal intensity by polarization transfer in INEPT and DEPT. Similarly I would like to analyze spectra of large number of spin half nuclei, especially like carbon 13, fluorine, phosphorus, lithium, boron, silicon, nitrogen 15 etcetera.

After all those things we will try to analyze several one or two examples for each of these nuclei. We also discuss the relaxation, nuclear overhauser effect then I will introduce concepts of two dimensional NMR and what is a 2D pulse sequence especially pulse sequences involved in COSY, TOCSY, HSQC, DOCY, HMBC etcetera. And we will analyze lots of 2D spectra, numerous examples of 2D spectra would be analyzed like COCY, TOCSY, HSQC, HMBC, INADEQUATE spectra and everything. And finally, we will try to see how we can combine all these one and two dimensional techniques to analyze the spectrum of any given molecule and how do we assign the peaks and get the structure. This is basically you would like to achieve by the end of this course. I hope by the end of this course if you attend to all the classes you would become more comfortable in analyzing the spectra of varieties of nuclei; and by the by part of it was discussed in the previous two courses also, but in this course more focus is given for understanding the concepts and the analysis of the spectrum.

With this let us go further and for this course I have taken some references. These are the references like high resolution NMR technique book in organic chemistry by Claridge and NMR data interpretation explained by Neil Jacobson, NMR spectroscopy explained again by Neil Jacobson and multi dimensional NMR method for solution state which was edited by Gareth Morris and J.W. Emsley and we have book on organic structure from 2D NMR spectra by Leslie Field, Spin dynamic by Malcolm Leavitt and the number of public domain resources are also there.

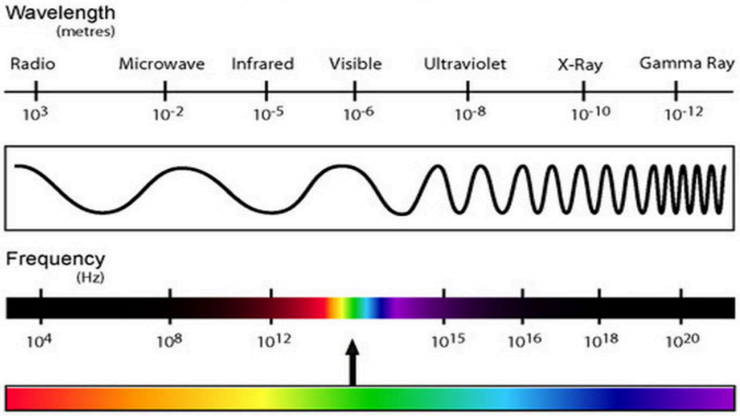
So, I would like to mention at this stage the materials taken from the books are used only for teaching purpose and not for any commercial purpose. So, lot of books have been referred, lot of spectra and information and a material that is required to be discussed have been taken from large number of books, but I would like to stress again it is only for teaching this course. So, no part of this will be copied and displayed to or distributed to anybody.

Let us start with the fundamental thing what an NMR will do. Of course, NMR is an ubiquitous technique. You can see this NMR spectroscopy applied in various branches of science starting from physics, soil science, agriculture, medicine, hospitals, functional imaging, and in unconventional applications like airport for detection of explosives, well logging, food technology, structural biology, material science, lots of areas . The areas which I have mentioned are only the tip of an iceberg. Nowadays, you can see the utility of NMR spectroscopy in every branch of science, even in engineering applications. So, it is a very powerful and ubiquitous technique. Now, when we say it is a ubiquitous technique, we can ask a question what makes NMR a ubiquitous technique, what is that which makes it so powerful. First of all, it is a non-invasive or non-destructive technique and you can study very weak interaction surrounding the nucleus, microscopic interactions or perturbations that is going on at the site of the nucleus would be studied.

And if you go to the periodic table, at least one isotope of every element of the periodic table is NMR active and can be individually studied. And it is possible to study variety of chemical, biological molecules and even materials. It is possible to obtain the structural and conformational information in all the three phases of matter like you can study NMR in solution state, solid state and also in gaseous state; but mostly NMR is practiced in solution and solid state. The dynamics of the molecules over different time scales ranging from picoseconds to microseconds or to seconds can be investigated. So, with this of course, there are lots of applications and basically this is the application oriented course where we analyze lot of spectra.

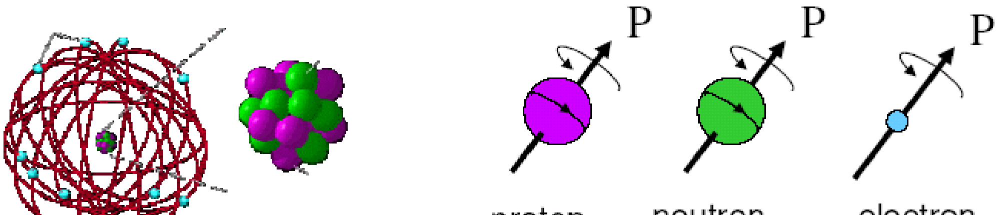
We can ask the question what NMR can do for chemists, pharmacists or biologists who basically want to utilize NMR spectroscopy for their analysis. Of course, it is used for structural elucidation. You can get the structure of natural products and synthetic products which are synthesized in the laboratory. You can study dynamic processes like you can study reaction kinetics; the study of chemical and structural equilibrium is possible. You can get biomolecular structures like. the structure of proteins, nucleic acids, polysaccharides and varieties of things can be studied.

You can use it for drug design. You can investigate structural activity relationships. It is also applied in medicine, used in medicine especially MRI, the magnetic resonance imaging where you can study metabonomics also where we can investigate biofluids, cells and tissues. With this basic introduction about utility of NMR in diverse aspects, diverse areas of science. let us start asking the question where does this NMR spectroscopy appear in the electromagnetic spectrum because this is a molecular spectroscopy. You all know in the molecular spectroscopy there are varieties of spectroscopy techniques like IR, Raman, UV, X-ray, varieties of things, right from X-ray region to RF region. Lots of spectroscopy techniques are available. Now, the question is where does NMR spectroscopy appear in this electromagnetic spectrum.



If we look at this electromagnetic spectrum starting from the gamma ray, X-ray; from right end to left end if I come, you can see there is a radio frequency region. This is where, or in this region NMR spectroscopy is practiced. If you want to study NMR spectroscopy, you will be in the RF region of the electromagnetic spectrum.

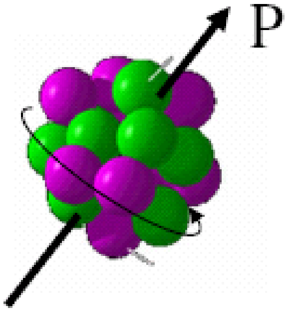
Conceptual understanding of NMR. Let us go and try to understand some concepts of NMR spectroscopy. First of all, once I say NMR spectroscopy, you cannot avoid discussing the spin of the nucleus. If you know, if you understand quantum mechanics, you already may be knowing that there is spin angular momentum of some subatomic molecules like protons, neutrons, electrons. They have spin angular momentum.



| | proton | neutron | electron |
|---|---|---|---|
| Charge q | +e | 0 | -e |
| Spin I | ½h | ½h | ½h |

For example, proton has positive charge, spin is half, neutron is charge 0, spin half, electron is negative charge, it is spin half. These are all individual particles and have their own spin. Now, what is a spin? Can we try to understand this? But remember spin is a quantum mechanical concept. There is no good classical analogy at all. You cannot question what is this? What is this spin? How do you explain that? It is not possible. Of course, we will discuss about rotation of the particles, spin is, you know, the spinning particle rotating about its own axis, etcetera, but it is all okay to some extent, but actually it is not produced by the rotation of the particle.

It is intrinsic property of the particle. It is always there even at 0 k, at 0 degrees. Then why it is called a spin is the next question; because it is described by the equations governing the angular momentum p and its vector; and it is a vector, spin is a vector, angular momentum is a vector. Now, we go to the spin of a nucleus, the spins of the individual protons and neutrons, what I said a spin half. Inside the nucleus, we have nucleons. The word nucleon means the combination of neutrons and protons. It is together called nucleons. Inside the nucleus, we have neutrons and protons. These individual protons and neutrons, combine to give an overall spin for the nucleus of any isotope of an element.



How do they combine everything? It has all been discussed in one of my previous courses of the NPTEL. One can refer to that. I do not want to go to the more details of that. But it is possible to get the nuclear spin.

But then the question comes. Do nuclei of all elements or isotopes of an elements possess nuclear spin? We can answer this question. But remember there is an empirical rule to predict NMR activity of a nuclear spin. That means, I can find out whether a given isotope of an element, whether that particular nucleus has a spin or not. Look at this table which is given here.

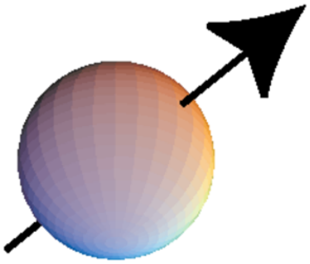
| Atomic Mass | Atomic Number | Examples of Nuclei | Total Nuclear Spin | NMR Active |
|---|---|---|---|---|
| Odd | Odd / Even | $^{1}H_{1}$, $^{13}C_{6}$, $^{15}N_{7}$, $^{31}P_{15}$ | Half integers 1/2, 3/2, 5/2 | YES |
| Even | Odd | $^{14}N_{7}$, $^{2}H_{1}$, $^{10}B_{5}$ | Integers 1, 3 | YES |
| Even | Even | $^{12}C_{6}$, $^{16}O_{8}$, $^{32}S_{16}$ | Zero | NO |

In the top row, you have atomic mass, atomic number and few examples of nuclei, total nuclear spin and last column tells me whether such nuclei are NMR active or not. If you go to the second row of this table, you will see you can come across some nuclei whose atomic mass is odd number and whose atomic number could be either odd or even; it does not matter. For example, take proton, the hydrogen atom. In NMR jargon, we call it as a proton. Henceforth, if I say proton do not get confused with the proton of the nucleus; it is nothing but a hydrogen atom. It is a convention used in NMR spectroscopy. And next you see the carbon 13, nitrogen 15, phosphorus 31. All of them have atomic mass as odd number and such nuclei are called spin half nuclei. They are called spin half nuclei. That means, they have spins equal to half integer. Here the, spins are half integer, half , 3/2 etcetera and the last column is very important to see such nuclei are NMR active. All such nuclei that possess spin are NMR active.

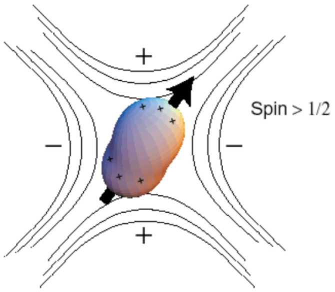
Go to the next row where atomic mass is even, atomic number is odd number and example for example, we have nitrogen 14. Also examples of deuterium and boron 10, these have integer spins like 1, 3 etc. Such nuclei are also NMR active.

Now, go to the last row, atomic mass is even number, atomic number is also an even. Examples like carbon 12, oxygen 16, Sulphur 32. You can see carbon 12 atomic mass is even, atomic number is also even. Such nuclei have nuclear spin 0. That means such nuclei, if you look at the last column, tells me they are not NMR active. They are called

NMR silent nuclei. You cannot study NMR of such nuclei. Now, we have, as I said half integer spins, integer spins and spin 0.



Let us see spin half nuclei. Spin half nuclei have a charge distribution which is spherical in shape and their behavior is easy to understand and we call such spin of nuclei as a dipole as if it has two poles of a magnet. Spin half nucleus can be treated like a tiny magnet. So, they are called dipoles. And if you consider nuclei with spin greater than half like this, they have non spherical charge distribution. Look at this one, here negative, negative and positive, positive.



There are four poles, quadrupole. These are four poles, and such type of this is non spherical. So, such type of nuclei are called quadrupolar nuclei and they possess electric quadrupole moment and their behavior is slightly difficult to understand compared to spin half nuclei.

Now, with this let me introduce to you something about what is called a spin quantum number and a magnetic quantum number. This is a very important concept you require to understand to know the concept of NMR. For example, if I have to consider any nucleus, there are two quantum numbers associated with it. The spin angular momentum of the nucleus. Nuclear spin angular momentum has two quantum numbers, One is spin quantum number I, other is magnetic quantum number m. This magnetic quantum number has constant magnitude and direction. These two are very important and these two quantum numbers will determine the properties of the nucleus. If you take any nucleus, these two quantum numbers are enough to define or to understand the properties of the nucleus.

Now, we can also talk about the magnitude of this nuclear spin angular momentum which is given by spin quantum number I. The angular momentum, if I consider its magnitude, is given in terms of the spin quantum number by a simple equation which is P, is equal to h cross root of I into I plus 1.

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

Do not worry about how we derive everything. It is just an equation I am giving you. Please take it. What is h cross? Of course, we all know h is a Planck's constant , and h cross is h divided by 2 pi; the h cross is equal to h divided by 2 pi.

Now, the z component of the spin angular momentum is quantized in a given magnetic field. It is always quantized. You all know in quantum mechanics quantization etcetera. So, z component of the spin angular momentum P is given as Pz is equal to m into h cross.

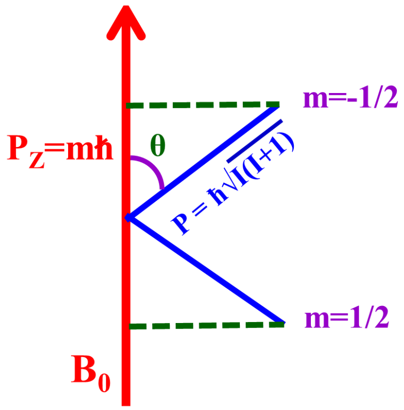
$$P_z = m\hbar$$

What is m now? m is called the magnetic quantum number. The m is a magnetic quantum number, which is related to spin angular momentum; the z component of the spin angular momentum. Now, the magnetic quantum number m in turn depends on what is called spin quantum number I. I told you about spin quantum number and I told you about m. They are all related to spin angular momentum P. Now, the magnetic quantum number m is related to I and it takes the values from minus I to plus I in steps of 1.

For example, if I take I is equal to equal to 1, we start with minus 1; add 1; becomes 0; add 1 it will become plus 1. So, that means it has 2I plus 1 possible orientations. For example, consider the nuclei with spin half, the spin half nuclei; that is what we are going to deal with most of the time. As I said there are 2 possible orientations because it takes the value from minus 1 to plus I, including zero. If I is equal to half it is minus half then add 1 for it, then it will become plus half. So, that means spin half nuclei have only 2 possible orientations.

And go to the spin 1 nuclei. There are 3 orientations I is equal to 1. Start with minus I; then it is minus 1, 0 and plus 1. If you go to 3/2 nuclei spin 3/2, there are 4 possible orientations which is given by minus 3/2 minus, to plus 3/2. Start with I is equal to -3/2, add 1, it becomes minus half; add 1; becomes plus half; add 1 more becomes 3/2. So, for spin 3/2 there are 4 possible orientations. Like this you can work out for the spin of any given nuclei what are the possible orientations. The quantization direction for the magnetic quantum number $m_I$, especially for spin ½.

Now, there are 2 possible orientations I said for mI, which is $m_I$ is equal to half when it is plus half, the spin angular momentum orients in the direction of the field. When mI equal to minus half, it orients opposite to the direction of the field. There are 2 possible orientations. This is the magnetic field, for mI is equal to plus half the orientation is like this, for mI is minus half, the orientation is like this. And there are only 2 possible orientations. Ofcourse, course, for M is equal to for I, equal to 1 we have 3 orientations then we have 1 like this 1 like this 1 like this there are 3 possible orientations. So, like this we can work out the quantization directions for any magnetic quantum number mI. And for the mI is half, as I said there are only 2 orientations; one is called plus half other is called minus half. In NMR jargon we call it spin up state and other is spin down state. The plus half is spin up state and minus half is spin down state. Conventionally spin up state is called alpha state and spin down state is called beta state. Remember when I am talking in future when I am analyzing the spectra etcetera, if I say alpha state and beta states you should immediately understand when I say alpha state, it is a spin up state beta state is a spin down state. These are the 2 possible orientations for spin half. And of course, we can get the magnitude of the spin angular momentum for each of these orientation directions.



For example, we know Mz which is equal to m into h cross. I told you already and I know p is equal to this thing. Simply use the trigonometry rule and you can find out what is this. It is very easy to calculate this thing. So, I am not going to the details of that because it has already been discussed in two of the earlier courses.

Now, I will go into what is called the nuclear magnetic moment, μ. it is a vector. Again it is a very important term; this is what is very important in understanding NMR spectroscopy. Let us start understanding charged nucleus which is undergoing rotation with an angular frequency omega which is given by 2 pi υ. It creates a magnetic field that is called B. And it is like this, the spin is rotating like this whether it is clockwise or anti clockwise does not matter. You can treat it like a small tiny bar magnet because it generates a magnetic field and we call this as one is a north pole and other is a south pole here and that is why we call it as a dipole.

This is applicable only for spin of nuclei. For, of course, spin greater than half I told you, it is a quadrupolar spin we have 4 poles. So, it cannot be treated like a dipole. So, I can say if I am dealing with a spin half nucleus, I can treat the nuclear spin like a tiny magnet. So, with this when I say nuclear spin, I can treat like a tiny magnet. You all know in your school days when I say it is a magnet I can define a magnetic moment. So, nuclear spin, since I can treat it like a tiny magnet, has a magnetic moment μ; also called dipole moment; it is a magnetic moment μ; and μ is a vector. I can easily understand μ in the vectorial representation. So, if I consider magnetic moment μ also it is proportional to spin angular momentum p which is given by a simple equation mu is equal to gamma into p.

$$\mu = \gamma P$$

It is a simple expression what is gamma here? the gamma is called a gyromagnetic ratio and interestingly it is constant for a given nucleus. If I take the hydrogen atom or proton, it has one gamma value; go to carbon-13; nitrogen-15, different nuclei have different gamma. But for a given nucleus that gamma is a constant. So, now, I substitute this mu I knew what is p already, I have written already you know p, p is equal to h cross into root of i into i plus 1, earlier I wrote. Now μ is this equation.

$$\mu = \gamma\hbar\sqrt{I(I+1)}$$

Now, I put I is equal to 0 here, what will happen? then μ becomes 0, that means there is no magnetic moment. So, that means, if nucleus has no spin it has no magnetic moment. Since the magnetic moment is very important, as I go ahead further I will tell you, in understanding the concept of NMR, the interaction of the magnetic moment with the external magnetic field is a criterion to see NMR spectroscopy. if μ is 0; no NMR. That means, if I is 0, no magnetic moment. When there is no magnetic moment there is no NMR spectroscopy. That is the reason why in the table I told you for the nucleus with even atomic number and even atomic mass, the I was 0. And I said such nuclei are NMR silent nuclei. That is what it isl because of this they have no magnetic moment and they cannot interact with the external magnetic field.

Now, if I come to the gamma value, it is constant for a given nucleus and different nuclei have different gamma and it is a simple SI unit. It is given by some number into radian per second per second per tesla. For example, if I take proton, it has a value 26.753 into the 10 to the power of 7 radians per tesla per second. If you go to the carbon 13; gamma is nearly 4 times smaller, it is 6.728 into the 10 to the power of 7 radians per tesla per second. So, with this we will now try to understand how the nuclear magnetic moment interacts, how the interaction of different nuclei is taking place in the magnetic field or in other words how the magnetic moments do interact in an external magnetic field. This concept is very important.

And before that I want to tell you what is the gyromagnetic ratio. I said it is a constant \ for any given nucleus, fine. This can also be worked out; and gamma is given by a simple equation. That is gamma is equal to e divided by 2 into mc. The e is the charge and m is the mass, and of course c is the velocity of light. We know nuclei with higher mass have lower gamma; look at this, mass is in the denominator that means as you go to heavier and heavier isotopes gamma becomes smaller and smaller. That means, if you understand that among all the stable isotopes of all the elements of the periodic table, proton has a lowest mass and has highest gyromagnetic ratio. That is the important concept. Remember among all the NMR active nuclei, the one which has a highest gyromagnetic ratio is proton compared to any other nuclei.

So, now we will understand what is the difference between proton and carbon 13. Both are spin half nuclei; that is spin quantum number is a half, then the magnetic quantum number is minus half and plus half. Then what is the difference? both are same. The difference is in gamma. If you look at gamma, it is equal to e over 2 into mc. Now, m is different as a consequence what happens? μ is different gamma is different.

So, μ is equal to is equal to gamma into p. So, although both proton and carbon 13 have the same spin quantum number I, the same magnetic quantum number $m_I$, their magnetic moment μ is different. These two have different magnetic moments; that is why different nuclei having different magnetic moments can individually be studied. So, all nuclei with different gyromagnetic ratio can be individually studied. That is the beauty. If you go to the periodic table there are so many elements in the periodic table, many of them, if not all of them have at least one isotope of each of the element, which is NMR active. That means, every element of the periodic table can be individually studied by NMR.

These are the characteristic properties of some of some selected nuclei I have given here. What is most important look at the proton and its abundance and spin and finally, gamma. This is the one which has the highest gamma. As you keep going down here you can see different natural abundance is there, spins are different, and then magnetic moments are different. This is just for the information. So, commonly investigated nuclei in chemistry and biology are the proton, carbon, nitrogen, phosphorus and fluorine. All of them are interestingly spin half nucleus. Very very easy for us to understand. The spin half nuclei are easy to understand. Whereas, if you want to go to inorganic chemistry and material science we study boron, aluminium, O17 etcetera. They are all having spin greater than half. Of course, silicon is spin half, but other nuclei have spin greater than half. So, these are all the things.

Now the time is getting over. So I have discussed few fundamentals today. Right now we stop here. Next time, in the next class I am going to discuss about Zeeman interaction. Basically, what I tried to tell today is; I introduced the concept of the spin quantum number, magnetic quantum number, possible orientations, quantization directions for different mI, which depends upon spin quantum number I. For example, for spin I is equal to half, you have two possible orientations; one is plus half or the other is minus half. The plus half orients in the direction of the field and minus half orients in the direction opposite to the field.

And then different nuclei have different gamma. As a consequence there are different magnetic moments. So, they can be individually studied. The gamma has a particular unit which is radians per tesla per second. Then different nuclei have different gamma, although I is same, m is same for different nuclei. But gamma makes them different. As a consequence different nuclei can be individually studied. So, with this I am going to stop here. We will come back and continue in the next class. Thank you very much.