NMR Spectroscopy for Chemists and Biologists

Professor Ramkrishna V. Hosur
Department of Biosciences & Bioengineering
Indian Institute of Technology, Bombay

Lecture No. 01

Basic Concepts

Welcome to this course on NMR spectroscopy. NMR spectroscopy is one technique which has grown enormously ever since its discovery and has generated applications in all areas of science. Let me begin by showing you the pioneers who have made this technique popular and brought it to the level where it is now. Several people have contributed to it and it is continuing to grow, and we will try and see how the technique has developed, starting from a very fundamental principles and taking to the level where it is today.

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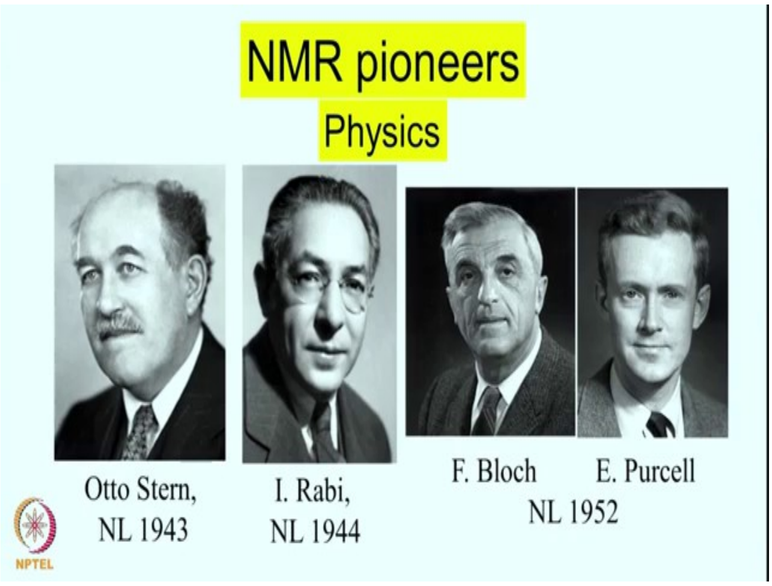

NMR pioneers

Physics

Otto Stern,
NL 1943

I. Rabi,
NL 1944

F. Bloch E. Purcell
NL 1952

If we see here, the first pioneers were Otto Stern, I. Rabi, Felix Bloch, E. Purcell; all four of them got Nobel Prize in physics. It was in the realm of physics as it started Otto Stern 1943, Rabi 1944, Felix Bloch and E. Purcell together got it in 1952.

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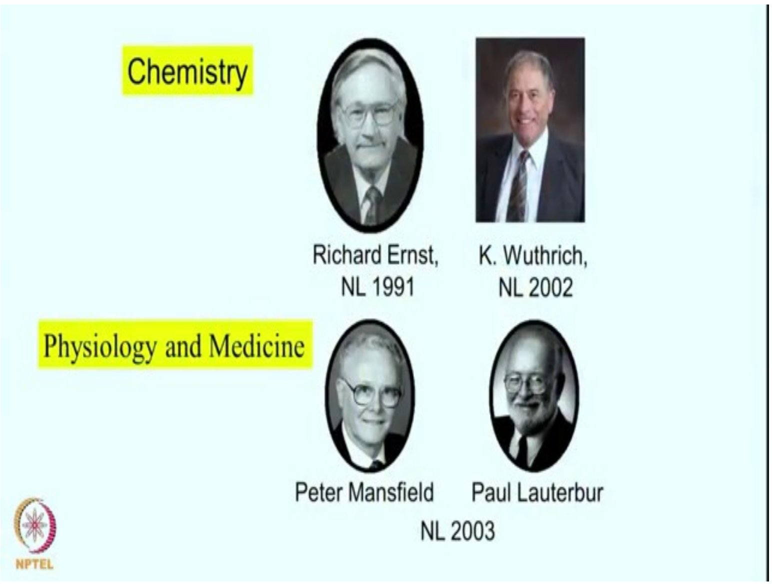

Chemistry

Richard Ernst,
NL 1991

K. Wuthrich,
NL 2002

Physiology and Medicine

Peter Mansfield

Paul Lauterbur

NL 2003

Then it was followed by two more Nobel Prizes in chemistry once in 1991 to Richard Ernst and again in 2002 to Kurt Wuthrich and parallelly, the developments are going on in different areas. Those resulted in another Nobel Prize to Peter Mansfield and Paul Lauterbur in 2003 and this time it was in physiology and medicine. So, you can see the technique has started from physics, gone into chemistry, gone into biology and physiology and medicine, so it is all encompassing.

Naturally, therefore, to study this technique in detail, we need to have a certain combination of physics, chemistry, and biology in our training, which would imply that a certain amount of knowledge of mathematics and physics and chemistry, biology are required. We will try and develop this course in that manner. What it requires is certain knowledge of mathematics with regard to the vector algebra, linear algebra, matrix algebra, differential equations, and then some quantum mechanics like Schrodinger equations, angular momentum. Some knowledge of this is required.

Nevertheless, we will try and give this knowledge at appropriate places for those who have not studied this in the past. Applications to chemistry will obviously require proper knowledge of chemistry and when it entered the area of biology, we need to understand the biological principles, when it entered physiology and medicine, of course, you also require to understand how the system works in our, in our bodies. So the, for healthcare, this has become an important technique.

I will list the important milestones in this process so that you know exactly how the technique is evolved over the years. As I said it started in the realm of physics then it entered in chemistry, then it entered in biology, and then entered in physiology and medicine and no stopping, keep counting. There may be more Nobel Prizes, who knows, as applications pick up in different areas of science. Let me first give you the major milestones of this important technique.

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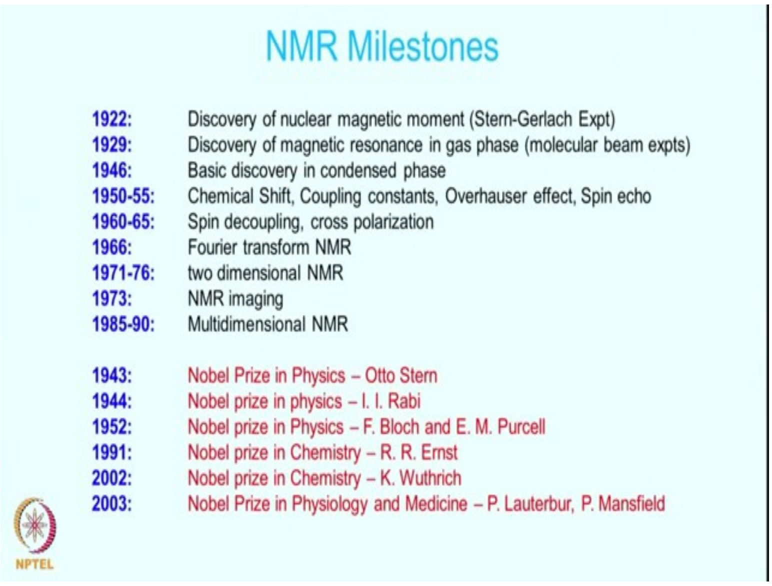

NMR Milestones

1922: Discovery of nuclear magnetic moment (Stern-Gerlach Expt)
1929: Discovery of magnetic resonance in gas phase (molecular beam expts)
1946: Basic discovery in condensed phase
1950-55: Chemical Shift, Coupling constants, Overhauser effect, Spin echo
1960-65: Spin decoupling, cross polarization
1966: Fourier transform NMR
1971-76: two dimensional NMR
1973: NMR imaging
1985-90: Multidimensional NMR

1943: Nobel Prize in Physics – Otto Stern
1944: Nobel prize in physics – I. I. Rabi
1952: Nobel prize in Physics – F. Bloch and E. M. Purcell
1991: Nobel prize in Chemistry – R. R. Ernst
2002: Nobel prize in Chemistry – K. Wuthrich
2003: Nobel Prize in Physiology and Medicine – P. Lauterbur, P. Mansfield

It started in 1922 with the discovery of nuclear magnetic moment which is a Stern-Gerlach experiment, and this actually led to the Nobel Prize to Otto Stern in 1943. And in 1929, Isaac Rabi discovered the first magnetic resonance in the gas phase in his molecular beam experiments, and that led to the Nobel Prize in 1944. Subsequently, this continued and in the condensed phase, the basic discovery was made in 1946 by two groups, one at Stanford led by Felix Bloch, other one at MIT led by E. M. Purcell, and they shared the Nobel Prize in 1952.

In the 1950s a large number of major discoveries were made. The chemical shift, you can see here, I am seeing coupling constants, Overhauser effects, Spin Eco. Each one of them is such an important technique. They revolutionized applications in various areas. Spin decoupling, 1960s, cross polarization which led to applications in solid state. Then the major breakthrough came in 1966 which is the Fourier transform NMR. This laid the foundation for the development of two dimensional NMR, NMR imaging and multidimensional NMR in the subsequent years.

The idea of this course is that the students who are taking it, they must be able to interpret the NMR spectra unambiguously have a clear appreciation of the information content in those spectra and at the end of the day they must be able to develop techniques in case they have to, for interpreting their results. Some problems they may come across in their systems and to understand and solve these problems, one may have to develop some new techniques and the course is intended to prepare the students from that point of view. Okay, so then let us start from the very basics.

We will start from the very basics and take you to the level where the technique has reached today by the end of the course. Nuclear magnetic resonance is a technique which is a consequence of some intrinsic properties of the nuclei. There are two intrinsic properties which are present simultaneously. First one is nuclear spin angular momentum and the second thing is the nuclear magnetic moment. We will look at these things in some detail.

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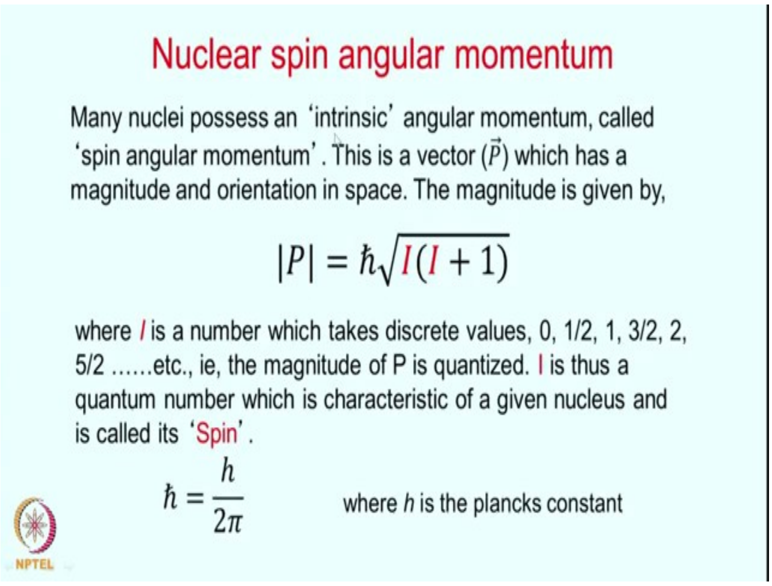

Nuclear spin angular momentum

Many nuclei possess an 'intrinsic' angular momentum, called 'spin angular momentum'. This is a vector ($\vec{P}$) which has a magnitude and orientation in space. The magnitude is given by,

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

where I is a number which takes discrete values, 0, 1/2, 1, 3/2, 2, 5/2 ......etc., ie, the magnitude of P is quantized. I is thus a quantum number which is characteristic of a given nucleus and is called its 'Spin'.

$\hbar = \frac{h}{2\pi}$ where h is the plancks constant

Many nuclei possess an intrinsic angular momentum called spin angular momentum. Notice that this nomenclature spin angular momentum is somewhat of a misnomer because it may tend to give an impression that there is something which is spinning or something is rotating. That was a concept which one had thought about because angular momentum deals with angular motions and therefore one thought that it is some kind of an angular motion which is happening. However, this is not the case here.

This is an intrinsic property and this angular momentum is a vector and it obeys all the laws of angular momentum and that is why this nomenclature has survived and it is called as spin angular momentum. The basic laws of angular momentum seem to be applicable here. It follows those laws and therefore this nomenclature has remained and so I would like to emphasize again, this has no connection with any angular motion of the nuclei within themselves and this is a vector obviously which has a magnitude and an orientation space.

The magnitude is given by this formula,

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

Where, I is a number which takes discrete values, *0, 1/2, 1, 3/2, 2, 5/2,* etc. This comes as a result of nuclear theory structure of the nuclei and so on and so forth. We are not going to go into those details. We take it that this I value takes discrete numbers *0, 1/2, 1, 3/2, 2, 5/2,* etc. So therefore it implies that the magnitude of P is quantized. It is not continuous. It can only have a certain values depending upon the value of I, I is thus a quantum number which is characteristic of a given nucleus and it is called its spin.

Every nucleus therefore has a particular I value and that is called, its spin. The nuclear structure terms, this refers to the ground state of the nucleus, so therefore we always deal within the ground state of the nucleus and the, I value there is called as their nuclear spin.

$$\hbar = \frac{h}{2\pi}$$

Where, the h is the Planck's constant. There are some empirical rules for the calculation of I. What values I take, how do we know which nucleus has, what value? As I said, this comes as the result of the nuclear theory, but there are some empirical rules which have been found to be valid which allows us to calculate the, I value for any given nucleus.

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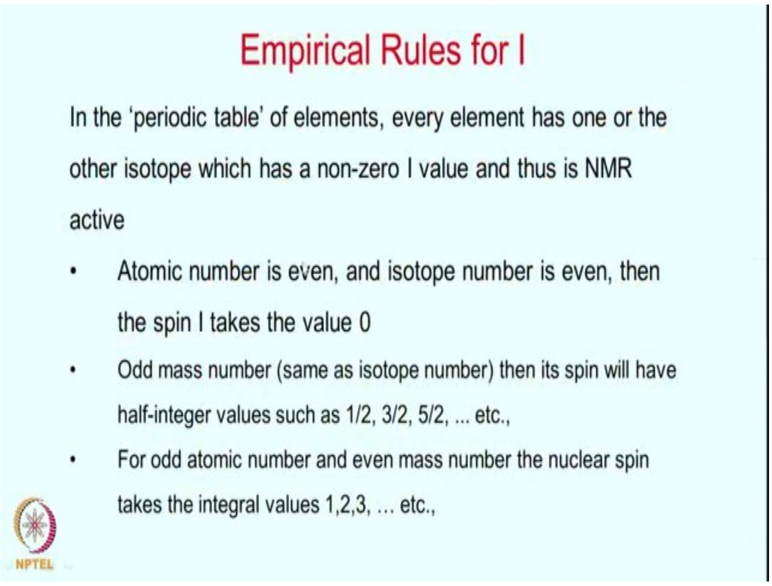

Empirical Rules for I

In the 'periodic table' of elements, every element has one or the other isotope which has a non-zero I value and thus is NMR active

- Atomic number is even, and isotope number is even, then the spin I takes the value 0
- Odd mass number (same as isotope number) then its spin will have half-integer values such as 1/2, 3/2, 5/2, ... etc.,
- For odd atomic number and even mass number the nuclear spin takes the integral values 1,2,3, ... etc.,

If the atomic number is even and the isotope number is even, then the spin *I*, takes the value 0. If the mass number is odd, then its spin will have a half integer values which is *1/2, 3/2, 5/2*, etc. For odd atomic number and even mass number, the nuclear spin value takes the integral values, *1, 2, 3,* etc.

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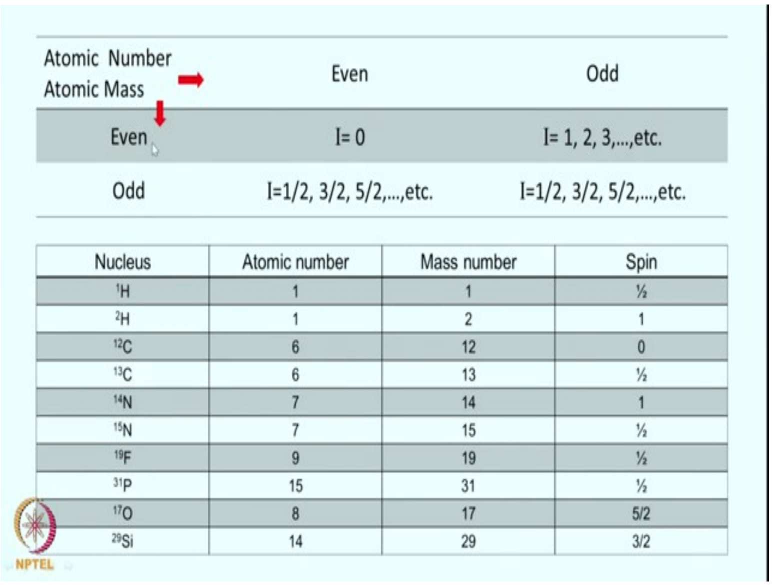

Atomic Number → Atomic Mass ↓	Even	Odd
Even	I= 0	I= 1, 2, 3,...,etc.
Odd	I=1/2, 3/2, 5/2,...,etc.	I=1/2, 3/2, 5/2,...,etc.

Nucleus	Atomic number	Mass number	Spin
^{1}H	1	1	½
^{2}H	1	2	1
^{12}C	6	12	0
^{13}C	6	13	½
^{14}N	7	14	1
^{15}N	7	15	½
^{19}F	9	19	½
^{31}P	15	31	½
^{17}O	8	17	5/2
^{29}Si	14	29	3/2

This is shown in the tabular form here, so on this you have the, even or odd atomic number and all in the rows, you have this even at odd mass number and you can see that if the mass number is even, the spin will have the values *0* or *1, 2, 3*, etc. If this is even, even it is *0*. If it is even odd, it is *1,2, and 3*.If the mass number is odd, regardless of what the atomic number is, it is always half integral values, *1/2, 3/2, 5/2*, etc. Here are a few examples of this. If you take proton (H), is atomic number is 1 mass number is 1 spin is *1/2*, deuteron atomic number is 1 mass number is 2 spin is *1*.It fits with that.

If you take carbon twelve (^{12}C), it is atomic number is 6 mass number is 12, so it has a spin *0*. That is even, even. Carbon 13(^{13}C) the atomic number is 6 mass number is odd, which is 13 therefore it has a value of *1/2*. Nitrogen 14 (^{14}N) atomic number 7 mass number 14 it is *1*, nitrogen 15 (^{15}N) the atomic number is 7, and mass number is 15 the spin is *1/2*. Fluorine 19 (^{19}F) is atomic number 9 mass number 19 so here again there is a spin of *1/2*. Phosphorus 31 (^{31}P) the atomic number 15 mass number 31 this is *1/2* again. Oxygen 17 (^{17}O) the atomic number 8 mass number 17 this is *5/2*.

Silicon 29 (^{29}Si) the atomic number 14 and mass number 29 and *3/2*. I have listed the here only, some of those isotopes and elements which are of common use. By and large, it is proton (H), deuterium (D), carbon 13 (^{13}C), nitrogen 15 (^{15}N), and ^{31}P, the ones which are used in chemistry and biology and things like ^{17}O or ^{29}Si. These are used in material science. Therefore, they come in the area of materials chemistry or condensed matter physics. So we said the angular momentum magnitude is quantized as it is a vector. It turns out, that not only the magnitude of the angular momentum quantize but also its orientation in space.

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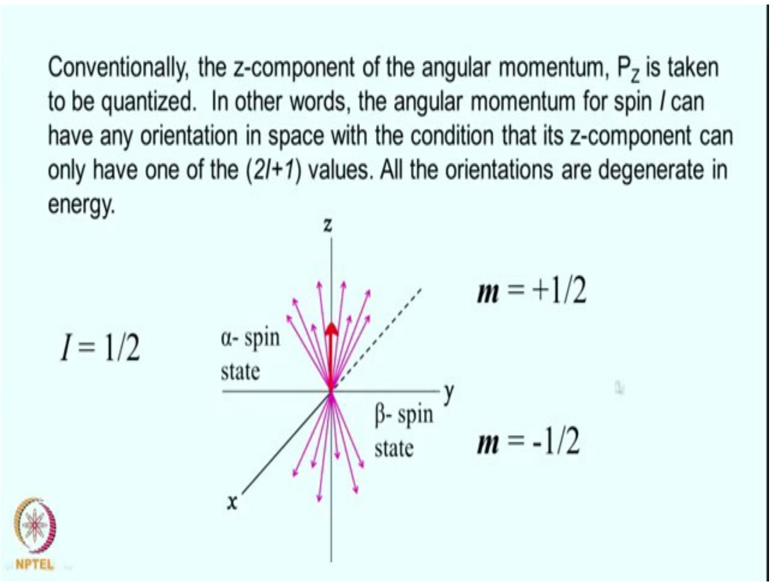

Conventionally, the z-component of the angular momentum, P_Z is taken to be quantized. In other words, the angular momentum for spin *I* can have any orientation in space with the condition that its z-component can only have one of the (*2I+1*) values. All the orientations are degenerate in energy.

What does it mean that, for any vector you will have three components along the *x, y* or *z* axis and it turns out that one of the components of P takes discrete values as given by this equation.

$$P_q = m\hbar$$

Where, *q* is equal to *x, y* or *z*. One of them is quantized; other can be any continuous value. One of the components is quantized. The number m takes discrete values, *I, I –1, I –2,…. –I* for a given value of spin I that means there will be total of *2I* + *1* values and this number m is called the magnetic quantum number and sometimes it is also called as azimuthal quantum number.

What does it mean? Conventionally the *z* component of the angular momentum, P_z is taken to be quantized. We could have chosen other ones also but it has been a convention to use a *z* component as the one which is quantized and therefore we always say it *z* component is only some discrete values. So for any spin *I*, the orientation can be such that does that *z* component can have anyone of the two *I* + *1* values. For*, I =1/2, 2I+1=2.*

Therefore, there will be two orientations in space. This is indicated here. There is various, arrows which are there, this represents the orientations of the different spins. Some are with

$m=\frac{1}{2}\wedge m=\frac{-1}{2}$

In each case they are of different a place. But the component along the *z* axis for all of them is the same. This is the *z* component which is here and the *x* components or the *y* components can be anything, which is why you are having so many vectors here.

Similarly,$m=\frac{1}{2}$, the *z* component is, the same for all of these orientations, which is $\frac{-1}{2}\hbar$

The *x* and the *y* component can be anything. Therefore we say one of the components is quantized. The other components are not quantized. Let me show you this more explicitly. You also notice here that all these vectors which are drawn, they have a certain angle with respect to the *z* axis. I will show you, why you can immediately guess it, why you should be. So I will explicitly show in the next slide.

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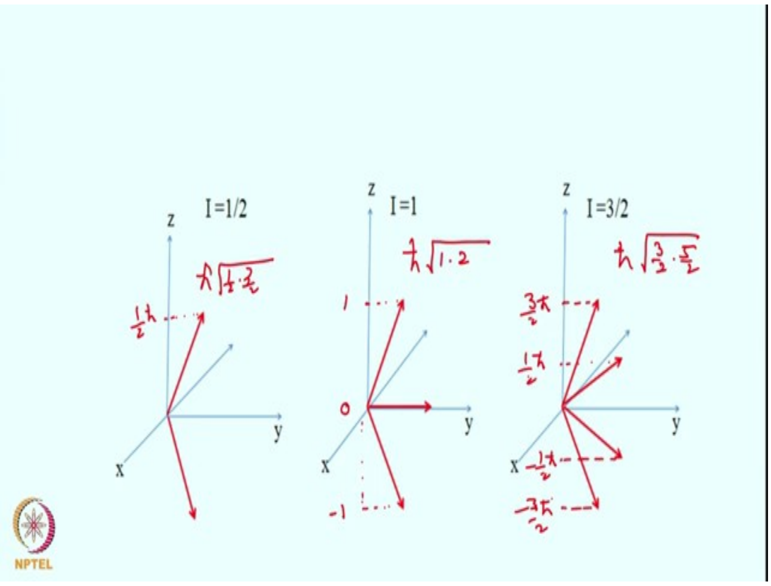

This is the case for$I=\frac{1}{2}$. I have shown only one vector here. This is the case for *I=1*. There are three orientations possible. I have only shown on one vector. Again, there be many vectors and for ¿$\frac{3}{2}$, there will be four vectors. So what are these, why are, why is this an angle and what is the angle between them? So this can be seen by recognizing that the magnitude of this vector is $\hbar\sqrt{\frac{1}{2}\cdot\frac{3}{2}}$ for$I(I+1)$. And the *z* component here is$\frac{1}{2}\hbar$. The two values are not the same. Therefore, the length of the vector and the z component are not the same. Therefore, there is an angle in this which is dictated by the ratio of this, the $\cos\theta=\frac{\frac{1}{2}}{\sqrt{\frac{3}{2}}}$, for the case$I=I+1$

This length of the vector is $\hbar\sqrt{\frac{1}{2}}$. So this $\sqrt{2}$ and the *z* component for this is *1*. The *z* component for this orientation is *0*. And if I went to draw the *z* component here, for this the, it is-1. Similarly, for $I=\frac{3}{2}$, *I* will have the magnitude $\frac{\frac{3}{2}*5}{2}I(I+1)$ and the *z* component for this is $\frac{3}{2}\hbar$and $\frac{1}{2}\hbar$ and $\frac{-1}{2}\hbar$ and $\frac{-3}{2}\hbar$. So therefore all of them have different orientations in space, because the *z* components are different compared to the magnitude of the angular momentum.

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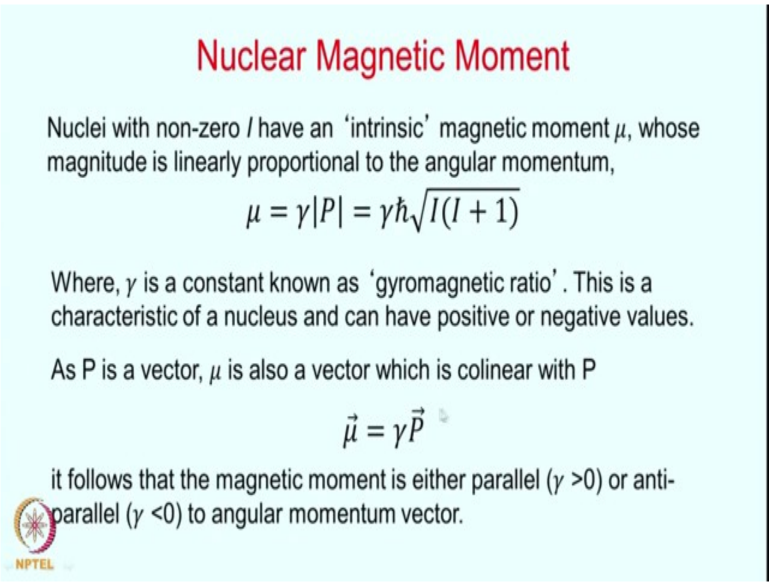

Nuclear Magnetic Moment

Nuclei with non-zero I have an 'intrinsic' magnetic moment μ, whose magnitude is linearly proportional to the angular momentum,

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

Where, γ is a constant known as 'gyromagnetic ratio'. This is a characteristic of a nucleus and can have positive or negative values.

As P is a vector, μ is also a vector which is colinear with P

$$\vec{\mu} = \gamma\vec{P}$$

it follows that the magnetic moment is either parallel (γ >0) or anti-parallel (γ <0) to angular momentum vector.

Now turn to the other important property of the nucleus which I mentioned in the beginning and that is the nuclei with non-zero magnetic moment. There is the magnetic moment and only those which have the magnetic moment of course are NMR active. Nuclear with non-zero *I* value have an intrinsic magnetic moment. We represent as μ and whose magnitude is linearly proportional to the angular momentum. So

$$\mu = \Upsilon \vee P \vee ¿$$

Where, P is the magnitude and therefore it is called the

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

The Υ is a constant known as gyromagnetic ratio. This is characteristic of nucleus, can have positive or negative values. Once again, this comes from the theory of a nuclear structure and we simply take what is the result that is coming from there and P is a vector as we said earlier, it can have certain orientations and therefore

$$\vec{\mu} = \Upsilon\vec{P}$$

Now both these now are written as vectors, so it follows that depending upon whether Υ is positive or negative, the magnetic moment is parallel to the angular momentum or antiparallel to the angular momentum vector. That is an important factor and here are some of the values of certain nuclei of the magnetic moments and the magnetogyric ratios. In early days, the aim of the NMR experiment was to measure the magnetic moments people use to measure the magnetic moments of all the different kinds of nuclei.

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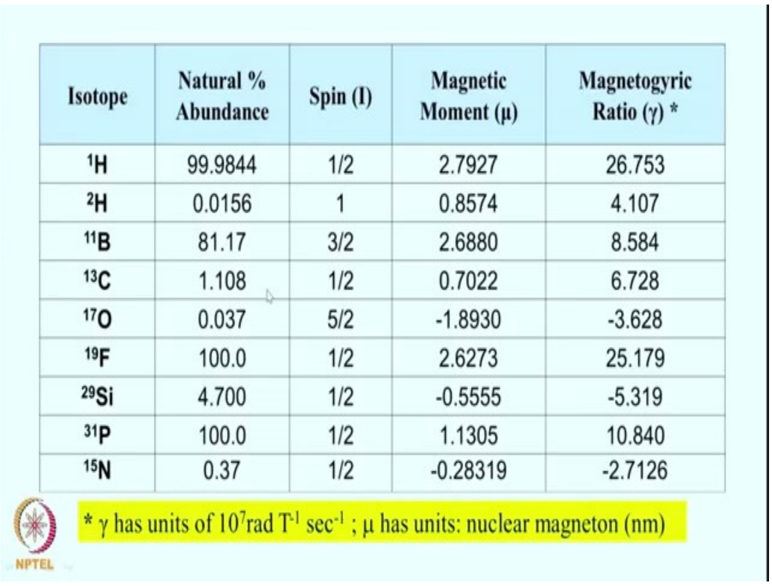

Isotope	Natural % Abundance	Spin (I)	Magnetic Moment (μ)	Magnetogyric Ratio (γ) *
^{1}H	99.9844	1/2	2.7927	26.753
^{2}H	0.0156	1	0.8574	4.107
^{11}B	81.17	3/2	2.6880	8.584
^{13}C	1.108	1/2	0.7022	6.728
^{17}O	0.037	5/2	-1.8930	-3.628
^{19}F	100.0	1/2	2.6273	25.179
^{29}Si	4.700	1/2	-0.5555	-5.319
^{31}P	100.0	1/2	1.1305	10.840
^{15}N	0.37	1/2	-0.28319	-2.7126

* γ has units of 10^{7}rad T^{-1} sec^{-1} ; μ has units: nuclear magneton (nm)

Of course they have measured and here is the summary of some of those nuclei which are for relevance to us in the context of chemistry, biology and material science. Proton which has the a 100% almost 100% natural abundance, most abundant nuclei and this has a spin of half and it has a magnetogyric ratio *26.753*. Deuterium is very low, natural abundance *0.01* percent, and therefore this is extremely, and this has spin of *1*, this also we saw earlier ^{11}Boron is spin of $\frac{3}{2}$ it is 81 percent natural abundance and it has the magnetogyric ratios as indicated here.

^{13}Carbon is 1.1 percent natural abundance, the spin of$\frac{1}{2}$. ^{17}Oxygen is 0.037 percent abundance,$\frac{5}{2}$. ^{19}F is a 100%; this is of course very abundant nucleus. Silicon is 4.7 percent, so these ones have $\frac{1}{2}$ each and all of these. ^{31}P is 100 percent abundant, spin of $\frac{1}{2}$ and ^{15}N is spin of $\frac{1}{2}$ but 0.37% natural abundance. Therefore, some of these nuclei are very abundant and therefore they will be the most sensitive nuclei from the point of observation of signal in NMR and for those which are lower abundant nuclei, some special things that are required.

Of course this will be discussed as we go along and notice here for ^{17}Oxygen their magnetic moment is negative. Likewise, for ^{15}Nitrogen it is negative for silicon also it is negative for all others. This gyromagnetic ratio is positive and therefore magnetic moment and angular momentum are collinear and they are the same orientation whereas for these ones they are collinear but they have opposite orientation. Magnetic momentum and angular momentum have opposite orientation.

This will have an effect with regard to the interaction energies and we will see as we look at the interactions between the nuclei and externally applied magnetic fields, which is an integral part of the NMR spectrometer. Now we see what happens to these nuclear spins. We talked about the nuclear spins in isolation, the nuclear spin, suppose we put them in a magnetic field. They have a magnetic moment and therefore there will be certain interaction with the magnetic field.

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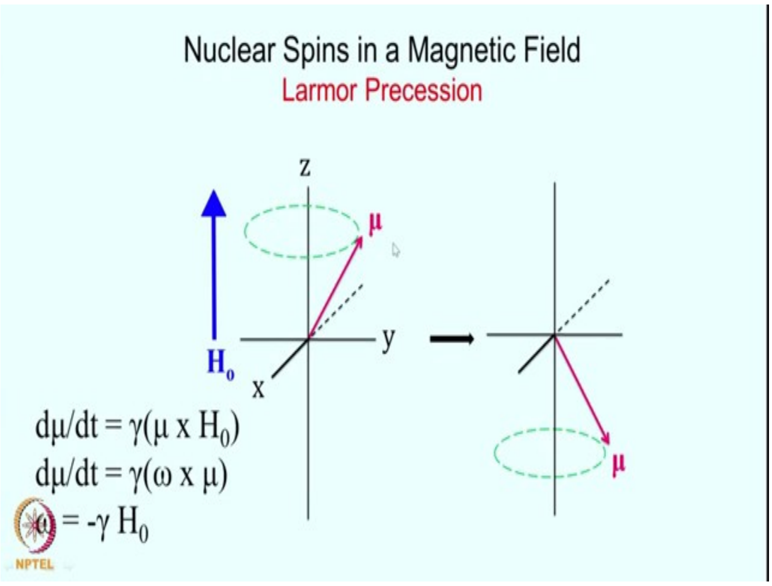

Nuclear Spins in a Magnetic Field

Larmor Precession

$d\mu/dt = \gamma(\mu \times H_0)$

$d\mu/dt = \gamma(\omega \times \mu)$

$\omega = -\gamma H_0$

So what does the magnetic field do? Since it is a magnetic dipole, it induces a torque. It applies force on the two dimensions on the two edges of their magnetic dipole and which results in a torque so it will; it will induce a motion in this nuclear magnetic moment and tries to cause a motion because of the torque. However, since the magnetic moment has a definite orientation in space, it cannot align itself with respect to the magnetic field access. Typically, the magnetic field is applied along the z axis. It cannot orient itself with respect to that. It induces a motion which is called as a processional motion and that is called as Larmor precession.

The nucleus if it is oriented here, it will move in this fashion. It exhibits the motion along this circle here. And this is called as a processional motion and nucleus which is oriented in this direction will also move and this will exhibit a motion in this circle. Along the circle, the edge will represent the motion along this circle here. This is also the processional motion. Here I can say the two orientations because this is typically true for $I=\frac{1}{2}$, but if$I=1$, there will be three such orientations and all of them will move around the magnetic field axis with a particular speed.

That is the angular frequency and this is the processional frequency. Now any such motion is described, interaction is described this by this kind of an equation. Where $\frac{du}{dt}$ change with the time. Magnitude does not change. It is only the orientation that changes and that is given by this equation,

$$\frac{du}{dt}=\Upsilon(\mu x H_0)$$

This is a Larmor Precession motion which is described by classical physics. Now any angular motion of this type is, is written by an equation of this type, you have angular frequency. If you have an angular frequency for, $\vec{\mu}$ then you write

$$\frac{du}{dt}=\Upsilon(\omega x \mu)$$

Here the motion is assumed to be in the in the anticlockwise sense.

This equation tells you that. Now both are representing the same where one case you actually have taken into account the field, in other case are represent in terms of the frequency of motion. Now therefore, if you compare this,

$$\omega=-\Upsilon H_0$$

So if I consider the motion as clockwise, so you get the minus sign here. This by comparingthese two I get the $\omega=-\Upsilon H_0$

That would imply that I have a clockwise motion here for that nuclear magnet.

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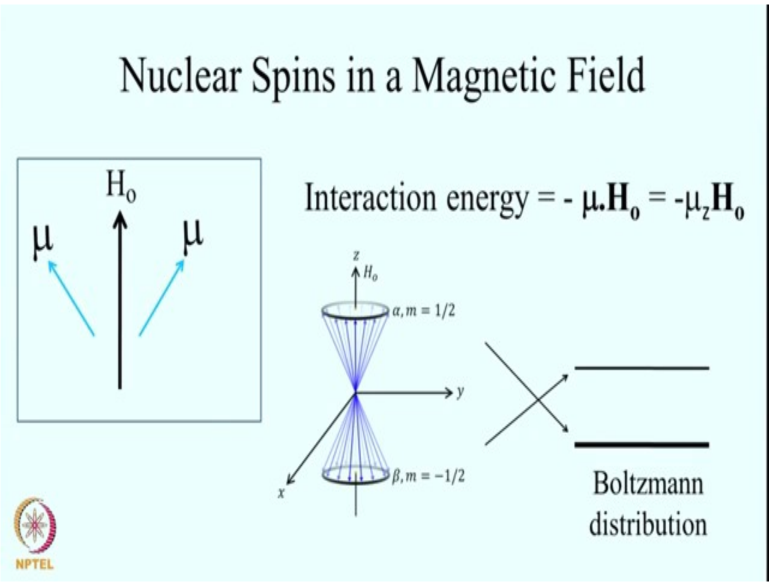

Nuclear Spins in a Magnetic Field

Interaction energy = - $\mu . H_0$ = -$\mu_z H_0$

Boltzmann distribution

The same thing now can be represented in another fashion that is use it use it for a spin$\frac{1}{2}$. This is shown more explicitly here. We have two orientations in space as indicated

$m=\frac{1}{2} \wedge m=\frac{-1}{2}$ These states are represented conventionally as α and the β states for the two spin system. The interaction energy is given by this and kind of an equation.

$$Interaction\,energy=\mu . H_0=-\mu_z H_0$$

This is a vector and this is the vector here and therefore if you take the dot product of this, you get $-\mu_z H_0$, now, note that is the minus sign here.

Now, if α is the state which you are considering, m is positive, so therefore μ_z is positive and then therefore the energy here becomes less compared to what it was in the absence of the field and that is indicated by the minus sign. Therefore, this goes down in the energy compared to what it was in the absence of the field, and this is state which is minus of here. Therefore, μ_z will be negative because the negative, this will have a negative z component. This will be negative. Therefore, this interaction energy becomes positive. Therefore, this one goes up in the energy.

The two states earlier, the two orientations were degenerate in the earlier case. In the absence of the field, when you apply, field this degeneracy gets lifted because of the interaction between the magnetic moment and the field. And once this is lifted, the two energy states will get separated like this and now therefore the spins will have to redistribute themselves between the two states. If you have an ensemble, which consist of trillions and trillions of nuclear spins and they will be populated in these two energy states and that follows what is called the Boltzmann distribution.

Typically, one thing that we have, we have nuclear spins which have the spin of ½ of *1*, one uses what is called is the Fermi-Dirac statistics. But if there is a spin of *1*, often one uses Bose-Einstein statistics. But here we will see that we can use Boltzmann statistics for both kinds of spins. And this has the, this is the consequence of the fact that this energy difference is very small compare to the sample temperatures what might we have, we will discuss that later. So for all the spins we can discuss the distribution of the spins in terms of Boltzmann statistics, and this has important implications for the signal strength.

So I think with this we will stop here we have covered the basic aspects of the properties of the nuclei. We talked about spin angular momentum and nuclear magnetic moment; both are intrinsic properties of the nucleus because, that is how the nucleus structure tells us. And these are quantized, angular momentum is quantized, nuclear magnetic moment can take also certain specific values.

It can else certain orientations in space. In the absence of any external magnetic field the all the orientations are degenerate. When you apply your field, the degeneracy gets lifted and the different orientations have different energies. The spins in an ensemble get distributed according to the Boltzmann statistics. This will have important implications for the signals that we will observe and that will be discussed later. Thank you.