Concepts of Chemistry for Engineering
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Lecture 48
Fundamentals of NMR Spectroscopy and MRI

Hello all, my name is Arnab Datta. I am an assistant professor in Chemistry Department, IIT, Bombay. And today, we will discuss the fundamentals of a interesting spectroscopic method known as NMR. And we will also look into its application in the form of MRI. Let us start.

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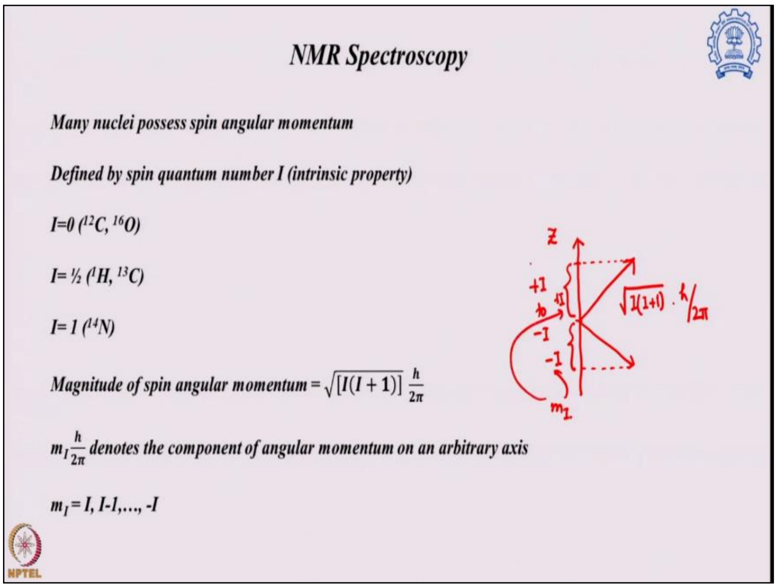

NMR Spectroscopy

Many nuclei possess spin angular momentum

Defined by spin quantum number I (intrinsic property)

$I=0$ (^{12}C, ^{16}O)

$I=½$ (^{1}H, ^{13}C)

$I=1$ (^{14}N)

Magnitude of spin angular momentum $= \sqrt{[I(I+1)]}\,\frac{h}{2\pi}$

$m_I\frac{h}{2\pi}$ *denotes the component of angular momentum on an arbitrary axis*

$m_I = I, I\text{-}1, \dots, \text{-}I$

So, most of the nuclei, we see around the world, contains an intrinsic spin angular momentum and the spin angular momentum is the main reason behind the NMR spectroscopy. So, this spin angular momentum is actually defined by the spin quantum number I, the spin quantum number I is actually how we define a spin system. The spin quantum number can have different values.

It can be zero, it can be an integer value or it can be even a number like 1/2 or 3/2. The actual value of this I depends on how many neutrons and protons are actually present inside the nuclei. If I have a nuclei with even number of atomic number and mass number, typically they give us a overall spin quantum number of zero.

But, if it deviates from it, we can have different I values, which are non-zero. The magnitude of the spin angular momentum is given by this term $\sqrt{[I(I+1)]}\,\frac{h}{2\pi}$

Whereas the value m_I can be in different forms. +I to -I, whereas, $m_I \frac{h}{2\pi}$ defines the component of the angular momentum on a arbitrary axis.

So, let us define what do I mean over there. So, we can have any particular direction. We have an spin angular momentum, which has this value $\sqrt{[I(I+1)]}\,\frac{h}{2\pi}$. However, if I want to find out what is the value at a particular axis, it is the z axis. We try to find, what is the projection of this spin angular momentum on this particular axis. and they can have only particular values and over here I am showing in such a way that it can have values from + I to - I, it can be also on the opposite direction and the projection of that is over there say - I over there it say, it is + I and defining that it is the m_I values.

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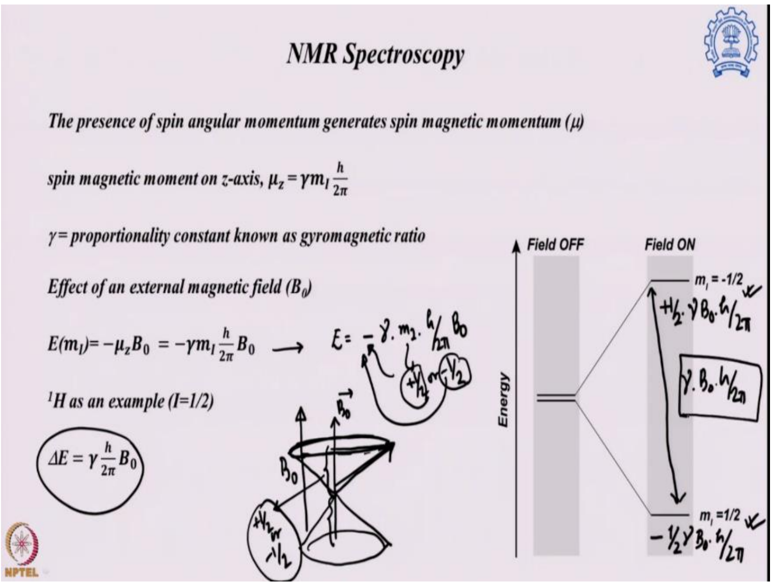

NMR Spectroscopy

The presence of spin angular momentum generates spin magnetic momentum (μ)

spin magnetic moment on z-axis, $\mu_z = \gamma m_I \frac{h}{2\pi}$

γ = proportionality constant known as gyromagnetic ratio

Effect of an external magnetic field (B_0)

$E(m_I) = -\mu_z B_0 = -\gamma m_I \frac{h}{2\pi} B_0 \longrightarrow E = -\gamma . m_I . h/2\pi\, B_0$

$+1/2$ or $-1/2$

^1H as an example (I=1/2)

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

Now, with that thing sorted out, we also found that when we have a spin angular momentum, it also generates a spin magnetic momentum. The spin angular momentum also generate a spin magnetic momentum because the spin angular momentum actually has an electrical component. So, obviously, it also gives a magnetic component around it. And this magnetic component is the reason to creation for the, is the reason for the creation of a spin magnetic moment.

And say I want to find out the spin magnetic moment. The presence of the spin angular moment also is the main reason for the creation of a spin magnetic moment. The spin magnetic moment can be also found along with a particular axis. So, over there, how much spin magnetic moment is going to generate that depends on this particular equation, shown over here.

$\mu_z = \gamma m_I \frac{h}{2\pi}$. We already knew that $m_I \frac{h}{2\pi}$, is the component of the angular momentum. And if I multiply that with this term gamma, which is a proportionality constant is gives us, how much of the angular momentum is actually transferred to the spin magnetic momentum. So, that is why this proportionality constant gamma, also known as gyromagnetic ratio.

So, it defines how much of the angular momentum is actually converts into the magnetic moment. And for each particular nuclei, this value will be constant. Each of the nuclei has their own distinct gyromagnetic ratio.

Now, when this particular spin magnetic moment sees an external magnetic field, what happens? The energy of these systems will be dependent on the magnetic fields that were producing the strength of the magnetic field and following the equation we can say the energy of that particular system in place of a magnetic field B_0 will be - $\mu_z B_0$, where μ_z is nothing but the spin magnetic moment, which is already given over there $\gamma m_I \frac{h}{2\pi}$

So, you have to just multiply B_0 into that. So, this will be the energy of a particular state with a magnetic moment where m_I is defining its nuclear spin. So, take proton as an example, where the I value can be 1/2 we like to see what is actually happening over here with respect to its energy. So, when we start with this particular spin state over here, we said field is off, that means there is no magnetic field is produced externally.

So, there is no presence of an external magnetic field. So, all the states are in the same energy. Because they cannot be differed in the absence of a field. However, at once we turn on the field, the two m_I states, because proton has a I value of 1/2, so it can have the different m_I values + 1/2 and - 1/2. And in the presence of magnetic field, it could differ in - 1/2 and + 1/2. Over here, the + 1/2 is actually lower in energy.

Why? Because as we know over here, energy is actually given by - $\gamma m_I \frac{h}{2\pi} B_0$. Now m_I can have a value of + 1/2 or - 1/2. So, if I have a + 1/2 value, because of the presence of this minus sign, that is going to be lower energy, which will have a value of - 1/2 $\gamma \frac{h}{2\pi} B_0$

Whereas when it is - 1/2 state, this - sign from this m_I value and - sign already present in the equation will combine together and give me an higher energy state, whose energy will be +1/2 $\gamma \frac{h}{2\pi} B_0$. So, that is how they splited up. And the difference of their energy if I subtract them down, it will be $\gamma \frac{h}{2\pi} B_0$, which is given over here.

Now, again, coming back to this system, why this m_I state differs, because whenever we are putting a magnetic field from outside, the magnetic moment present due to the spin state, actually start precessing around this particular magnetic field. So say if this is the magnetic field, it start precessing around. So it will look like more of like a cone, around which it is precessing. So, this particular moment is actually generated, which is also known as the larmor frequency.

So, over here, when it is precessing around this external magnetic field B 0, what is going to happen how much of the magnetic moment is actually projecting on that magnetic axis of the external magnetic field axis, that is going to be having two different values. It can be either + 1/2 or - 1/2.

And depending on that, we say we have these two particular values + 1/2 and - 1/2. So, that is the main reason behind the splitting of the magnetic spin state in the presence of a magnetic field. Otherwise the spin state cannot be differentiated. Only in the presence of magnetic field they get differentiated. So once they get differentiated, now we have a particular energy gap.

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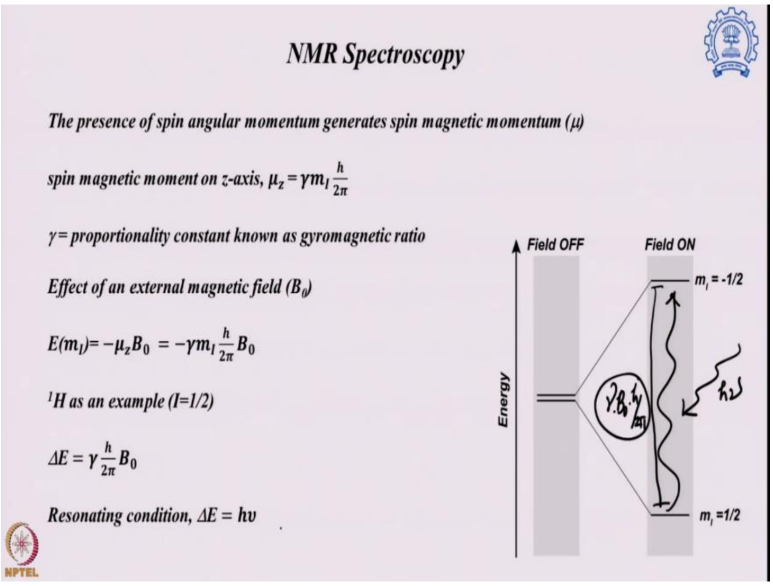

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^1H as an example ($I=1/2$)

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

Resonating condition, $\Delta E = h\upsilon$

And we can go from the ground state to the excited state. If I can give an electromagnetic radiation whose energy perfectly matches that energy gap that we have created, which is nothing but $\gamma \frac{h}{2\pi} B_0$.

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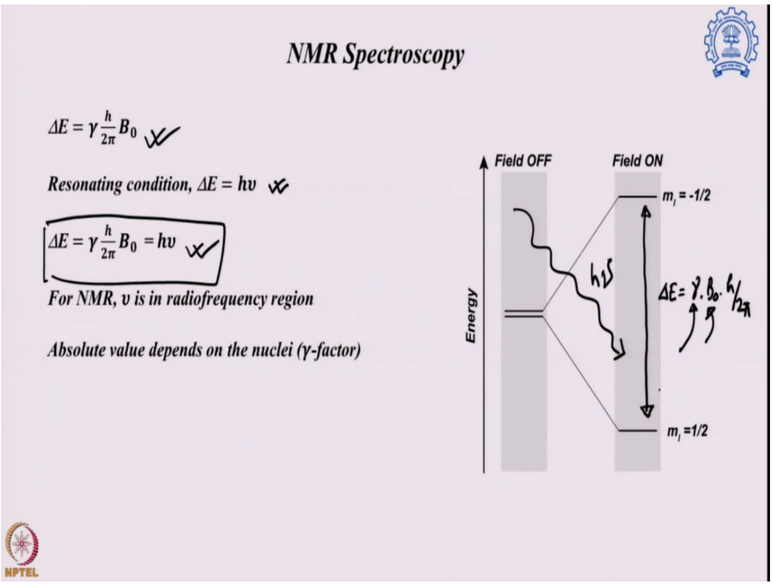

NMR Spectroscopy

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

Resonating condition, $\Delta E = h\upsilon$ ✓

$\boxed{\Delta E = \gamma \frac{h}{2\pi} B_0 = h\upsilon}$ ✓

For NMR, υ is in radiofrequency region

Absolute value depends on the nuclei (γ-factor)

And when these two actually can be equated, we can say the resonating condition has been met. So, again just telling that thing one more time. So, once this energy gap is created in the presence of the magnetic field, this energy gap is $\gamma \frac{h}{2\pi} B_0$, you can see that this full system is depending on two factors. One is the B_0, the strength of the magnetic field, one is the gamma(γ) the gyromagnetic ratio, which is actually a property of the nuclei itself.

And this part is going to equate with the resonating condition, we can actually match that with an external electromagnetic radiation, which can bring the ground state nuclear spin to the upper state by flipping it and when they match, we have the resonating condition, which says that it is going to be equal to hν. And as we just said the difference of this energy state depends on two factors, the gamma value and the B_0 value.

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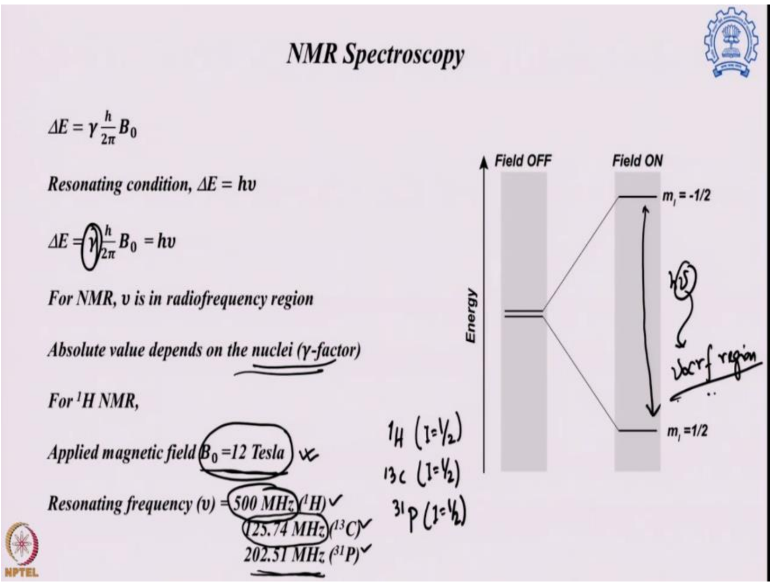

NMR Spectroscopy

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

Resonating condition, $\Delta E = h\upsilon$

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

For NMR, υ is in radiofrequency region

Absolute value depends on the nuclei (γ-factor)

For ^1H NMR,

Applied magnetic field B_0 =12 Tesla ✓

Resonating frequency (υ) = 500 MHz (^1H) ✓
125.74 MHz (^{13}C) ✓
202.51 MHz (^{31}P) ✓

^1H ($I = 1/2$)
^{13}C ($I = 1/2$)
^{31}P ($I = 1/2$)

So, generally we actually use a magnetic field strength around 12 Tesla. So, typically we use a magnetic field strength around 12 Tesla. With that amount of magnetic field we created enough space such a way that this space can be covered with a hν where the ν is actually belongs to the radio frequency region.

So, that says that this energy gap is actually pretty low, because radio frequency is one of the weakest electromagnetic radiation with respect to energy. So, if we look back again. So, it is an electromagnetic radiation can be the important factor to bring the lower magnetic spin state to the higher magnetic spin state, where the spin can be flipped.

Now, the other important factor as we just discussed, is the gamma factor, which actually says that, how much the energy gap will be the nuclei itself will have a say, because each nuclei has their own gyromagnetic ratio. And over there we can say if I use the same magnetic field 12 Tesla, the energy gap will be different for different nuclei and over there, I am taking example of three different nuclei.

So, we have taken their three different nuclei ^{1}H, ^{13}C, and ^{31}P, each of them has one common thing, all of them has a nuclear spin of 1/2. So, that means, in presence of magnetic field, they will all split between + 1/2 and - 1/2. If I use the same magnetic field of 12 Tesla, their energy gap will different.

Why they will be different? Because, the gamma value. The gamma value of these three different nuclei's are different. and we can see the proton has the highest gyromagnetic ratio has an energy gap that can be covered with a radio frequency of 500 Mega Hertz whereas, 13

C is way too weaker than it and it requires only 126 Mega Hertz. The 31 P is stronger than 13 C, but weaker than^{1}H, as per the value of the gyromagnetic ratio of that particular nuclei and we have a resonating frequency of 202.5 Mega Hertz.

So, over there we can say that the overall energy gap will differ in two different the overall energy gap between the different nuclear spin state in the presence of magnetic field will be dependent on two different factors. One is the external magnetic field, its strength and the second is the gyromagnetic ratio, which will be intrinsic property of the nuclei itself.

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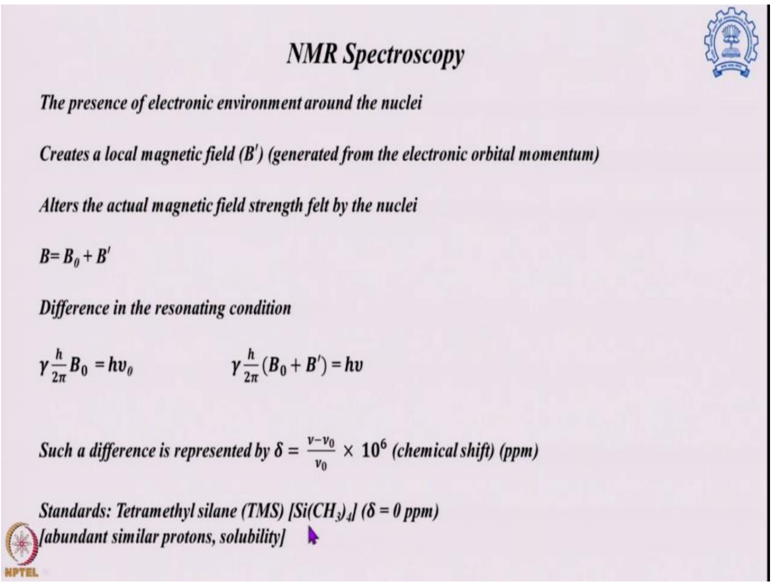

NMR Spectroscopy

The presence of electronic environment around the nuclei

Creates a local magnetic field (B') (generated from the electronic orbital momentum)

Alters the actual magnetic field strength felt by the nuclei

$B = B_0 + B'$

Difference in the resonating condition

$$\gamma \frac{h}{2\pi} B_0 = h\upsilon_0 \qquad \gamma \frac{h}{2\pi}(B_0 + B') = h\upsilon$$

Such a difference is represented by $\delta = \frac{\nu - \nu_0}{\nu_0} \times 10^6$ *(chemical shift) (ppm)*

Standards: Tetramethyl silane (TMS) [$Si(CH_3)_4$] ($\delta = 0$ ppm)
[abundant similar protons, solubility]

Now, how the NMR spectroscopy can be used to understand the property of a molecule. So, whenever we produce an external magnetic field and try to see how it is affecting the splitting of the different nuclear spin state, there is one more thing can be important. And that is each of the nuclear in a molecule is present around electron field. And different molecule different nuclei, not all the time their environment is same.

And depending on the environment, they can have a little bit more electron density or less electron density, coming from the structure of the molecule. And those electronic environment around the system also creates a local magnetic field, which is generated because those electrons are present in an orbital. And orbital generates an orbital magnetic momentum, which actually creates a local magnetic field, which is given over here as $B^/$ and this local magnetic field can come around the system along with the external magnetic field.

So, when we have the external magnetic field B_0, this local magnetic field $B^/$ can also come into there. And they will combine to give the actual magnetic field actually felt by the nuclei. So, this B dash can be positive or negative, depending on the orientation of the electron. And the actual resonating condition will be different now. So, in a condition where there is almost negligible electronic effect, what do we expect that the resonating condition will be met with $\gamma \frac{h}{2\pi} B_0$, because B_0 is the magnetic field that is they are experiencing, and that can be resonated with $h\nu_0$. υ_0 is a condition where it matches the energy gap created by this magnetic field B_0.

However, in a molecule, the presence of the electronic environment creates an external magnetic field, which gives us this value $B^/$. So, altogether the actual magnetic field the molecule is experiencing is that $B_0 + B^/$. And if we now want to resonate that cannot be happening at $h\nu_0$. It needs a totally different value.

Which is given by ν. So, this will be the new resonating condition to balance the presence of this extra local magnetic field and the difference where and this new condition where we actually resonating this ν can be differentiated with respect to the υ_0, where it should be in the absence of magnetic field and it can be given by this term delta which is given by this expression which is $\delta = \frac{\upsilon - \upsilon_0}{\upsilon_0} X\ 10^6$.

So, why this particular expression? Because $\frac{\upsilon - \upsilon_0}{\upsilon_0}$ is giving an idea no matter what is the B_0 or external magnetic field I am using if I use this particular expression that will be independent of what is the strength of the external magnetic field.

So, this will be a more of a universal number, this delta value will be particularly constant at any particular condition all around the world. So, that is why it is known as chemical shift. And that is a universal factor when we are expressing that with this particular expression. And over there, I multiply that by 10 to the power 6, because the υ_0 has a value of 500 Mega Hertz if you are talking about a proton, whereas the difference comes in the unit of Hertz. So Mega Hertz is 10^6 Hertz and the difference is Hertz.

So we multiply that with 10^6, so we can have a number that we can play with very easily. So you have a number like 5 or 6 rather than $5 \text{ X } 10^{-6}$. So that is why you multiply that to 10^6. And that is why there is a unit comes around with that which name as ppm (parts per million), which is not really an unit because over there you can see $\frac{\upsilon - \upsilon_0}{\upsilon_0}$ it should be dimensionless quantity and it is.

But we still considered this ppm written around it so that it can remind us that it actually gets multiplied by 10^6 or by a million numbers so that we can get this particular value. So that is known as chemical shift. And again, coming back to that this chemical shift is totally dependent how much local magnetic field I am creating. And that is why this delta value is nothing but a detector of what is the chemical environment around the system.

Now, the unique thing is that this particular delta value is going to be constant for a particular group in a particular molecule. And if we want to measure different molecules at a time, we also need to know what is the υ_0 value. So, we need a standard molecule, which we exactly know it has such a electronic field present around it that it cancel each other out and there is the local magnetic field is almost negligible it only feels the magnetic field created by the external one.

So one of such molecule is tetramethyl silane. In short form it is known as TMS which is nothing but a silica bound with four methyl groups. And this molecule gives us a delta value of zero. So that means if I am doing an experiment and use tetramethyl silane, we know exactly where we should expect to see that graph. And in that graph, the signal is going to come at delta equal to 0 ppm.

And why it is very easy to use? Because it has a very good solubility in all different kinds of solvents. And all the same time, we do not need to use a lot of this particular standard because it has 12 protons present there which are all in the similar environment. So, we always got a very good signal even with a minute amount of this standard. So, that is why this tetramethyl silane is used as a common standard all around the world, especially for the proton and also for the 13 C NMR spectroscopy.

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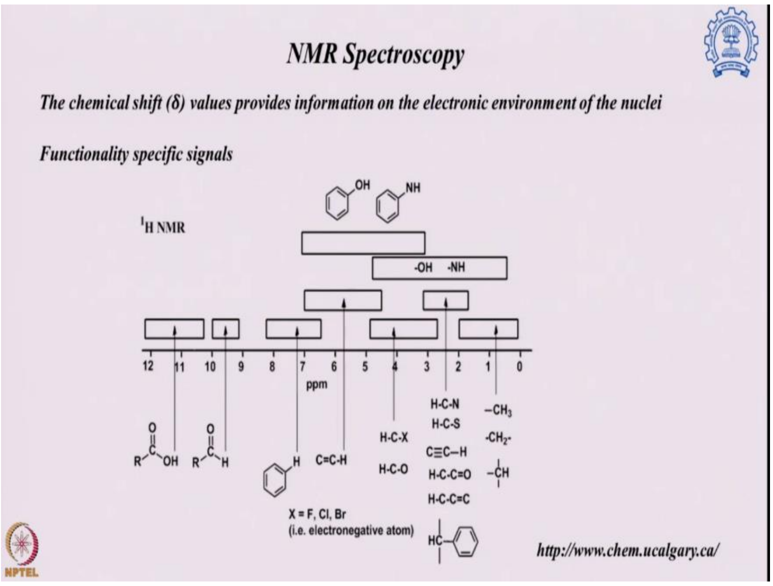

NMR Spectroscopy

The chemical shift (δ) values provides information on the electronic environment of the nuclei

Functionality specific signals

http://www.chem.ucalgary.ca/

The chemical shift values as we just discussed is actually gives us an idea what is the electronic environment around the molecule. Especially around the nucleus we are discussing. For examples say we are talking about proton NMR. So, what we found for different compounds what we have produced, what we have extracted over the years, all of them, we can record a proton NMR and for each particular group, we can find a region, where this particular signal comes out.

And those are kind of the signature region for these particular groups. For an example, we can start with this alkane groups and we can see the alkane groups comes around the delta PPM value between 0 to 2. Whereas, whenever I put an alkyne group over here or an alkene group or a ketone group you can see they actually moved towards a little bit higher value of delta. So, it says that, if you have this kind of electron withdrawing groups or electron rich environment, then you are expected to have a shift in the delta value.

Similarly, if we have an aromatic group you can see it is way shifted towards almost 6.5 to 8.5 region. So, it is actually a signature region for aromatic compounds. If you have an acid group, you can see it shifted farther beyond 10 ppm region. So, each of these region is actually signifying the presence of one particular proton in a chemical environment.

So, that is why this chemical shift values, can be a testament for the presence of particular groups. So, with respect to that we can easily follow and find out not only whether this particular group is present or not, and even can follow that change during an experiment. So, that is why NMR spectroscopy is a very powerful tool for the structure elucidiation of different compounds.

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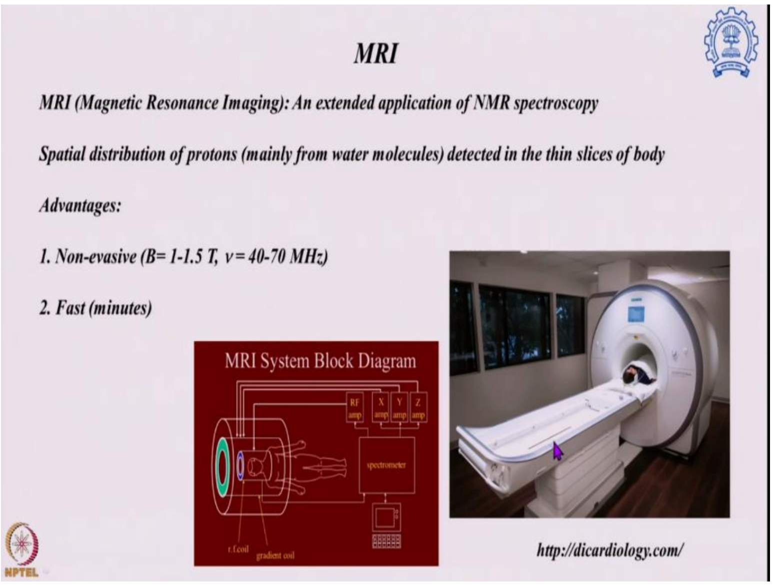

MRI

MRI (Magnetic Resonance Imaging): An extended application of NMR spectroscopy

Spatial distribution of protons (mainly from water molecules) detected in the thin slices of body

Advantages:

1. Non-evasive (B= 1-1.5 T, ν = 40-70 MHz)

2. Fast (minutes)

MRI System Block Diagram

http://dicardiology.com/

Now, we come to the second part of this NMR spectroscopy, which is an application, which is known as MRI or Magnetic Resonance Imaging. MRI is quite a common term nowadays in the medical field, because whenever we get injured in our body, we generally try to do an MRI scan and it actually gives us an idea what is actually happening around our body.

So, in MRI which is nothing but a particular kind of NMR where we actually follow the proton NMR and the proton NMR we follow from the water molecule because water molecule is quite common in a biological system and then we try to find out what is the behavior of the proton in a particular region generally in thin slices of our body and over there we try to find in three dimensional orientation, how the protons are behaving and over there, we try to mostly find out the behavior of the proton under this particular condition, where we put the external magnetic field of 1 to 1.5 Tesla.

You can imagine that it is almost 10 times lower than that 12 Tesla we used for a 500 Mega Hertz NMR machine. So, over here the resonating condition made with much more lower energy with 40 to 70 Mega Hertz of radio frequency. The NMR at the same time, these are non-evasive techniques because we are not using very strong magnetic field or very strong radio frequency which can affect our body, otherwise. At the same time this NMR experiment, we can find out what is happening in the water, very quick, from seconds to minutes. So it is a fast and rapid diagnostic tool.

So, this is a diagram, how the MRI actually looks like. So over here, this is where we put ourselves in and over there you can find two different coils one actually contains the magnetic field, the other one is the radio frequency coil. And we use both the magnetic field and radio frequency coil, simultaneously, to get the idea of what is happening about the water around our body. And this is how it looks like from the outside, the MRI instrument.

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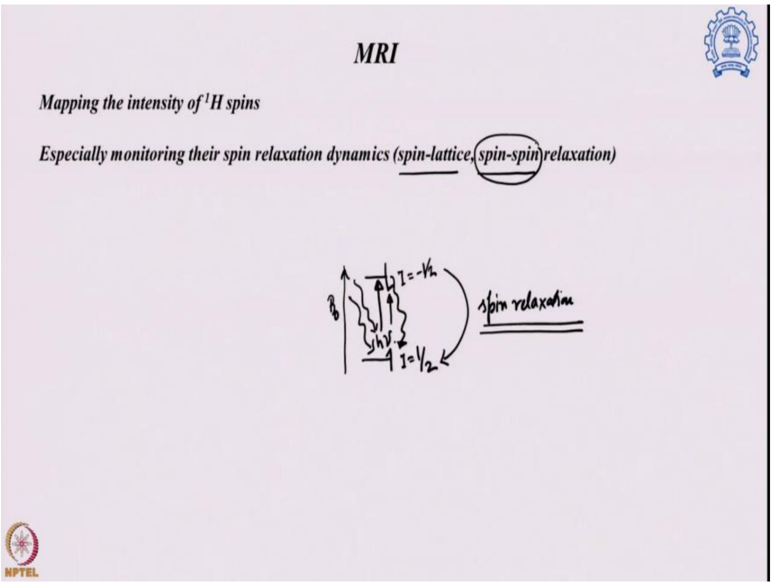

MRI

Mapping the intensity of ^1H spins

Especially monitoring their spin relaxation dynamics (spin-lattice, spin-spin relaxation)

Now, when we look into the proton NMRs of water molecule, in MRI, we actually generally try to look into their intensity and we look into the intensity by following what happens to their relaxation dynamics. So, what do I mean by relaxation dynamics? So, whenever we actually put in external magnetic field the two states splits up I equal to 1/2, I equal to - 1/2. And whenever we excite that with electromagnetic radiation, some of the spin flips and go to the excited state, from + 1/2 to - 1/2. And then it relaxes back again. And then we give the electron radiation so that it can go back again. So, this process continues.

So, when the high energy state nuclear magnetic spin state comes down to the ground state, it is known as the spin relaxation. And this spin relaxation can give me an idea how the proton is behaving. Because this spin relaxation is dependent on its environment, because it can relax us through these two different methodologies, spin lattice and spin-spin interaction.

Spin lattice is the interaction between the spin and the other environment that electrical environment around it. Whereas the spin-spin relaxation happens when there is another spin moment present around it. So, with this particular system, it gets relaxed and we can follow what is actually happening. And that is what we do in MRI.

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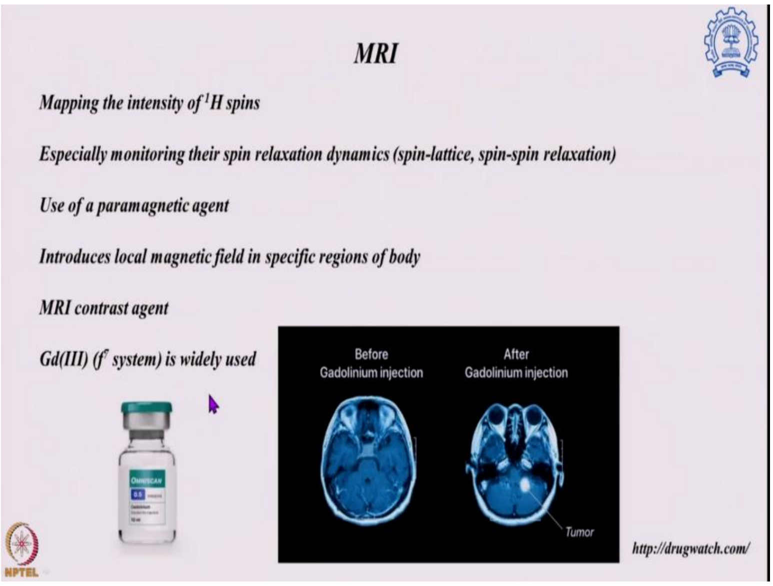

MRI

Mapping the intensity of ^1H spins

Especially monitoring their spin relaxation dynamics (spin-lattice, spin-spin relaxation)

Use of a paramagnetic agent

Introduces local magnetic field in specific regions of body

MRI contrast agent

Gd(III) (f^7 system) is widely used

http://drugwatch.com/

However, we generally use a parametric agent, which creates a huge amount of local magnetic field. And that helps us to understand what is actually happening when this parametric sample present near the system, we are diagnosing. And these are known as MRI contrast agent, because they actually create a very good contrasting, when they are present.

For an example, one of the system we use very regularly is the Gd(+3) system. Gadolinium is an F block element which has seven unpaired electrons in its +3 oxidation state, so seven unpaired electron, which has a huge local magnetic field. And you can see over here I am showing. It is a MRI of a brain. And over there, there is a tumor over here, but we cannot see it very properly. Although we can see there is a difference when you are doing the MRI. But you cannot see it very precisely exactly what is happening. But once we inject this gadolinium system near to it, it actually clearly shows what is happening over there.

Because of the presence of this strong local magnetic field. The water molecules over here, behave differently compared to the other parts. And that actually creates the contrast. And over there we can easily see that tumor over here. So that is the effect of MRI contrast agent, which actually nothing but creates a local magnetic field around it. And generally, this gadolinium f^7 system is the most common one, that we actually use during an MRI.

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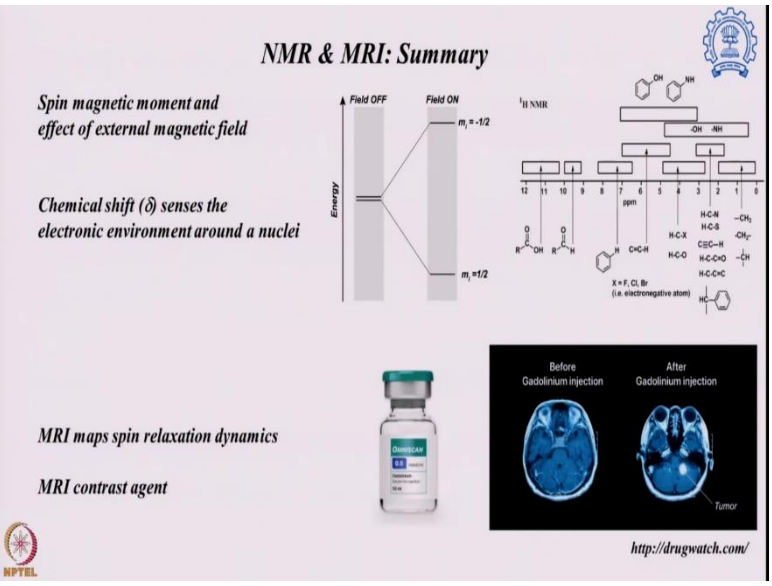

NMR & MRI: Summary

Spin magnetic moment and effect of external magnetic field

Chemical shift (δ) senses the electronic environment around a nuclei

MRI maps spin relaxation dynamics

MRI contrast agent

http://drugwatch.com/

So that we will come to the summary of our this segment. We start with the NMR, which is nothing but a study of the spin magnetic moment and how it behaves when we create an external magnetic field around it. The spins actually deviate with respect to its spin quantum number, and it can go to + I to - I values. The most common one is proton, which actually goes to + 1/2 to - 1/2 state.

And this energy gap depends on the strength of the magnetic field and also the gyromagnetic ratio. So that is why this difference is also very specific for particular nuclei, we can find out what is the energy gap, because that is not only dependent on the external magnetic field, but also the local magnetic field created by the electronic environment. And that is why the actual resonating condition differs by a small amount.

And that difference we actually express with this expression of this chemical shift or delta value. And over there, these delta values are quite specific for different groups. So with respect to that we can not only define a particular group, but we can also follow their changes during the course of a reaction.

MRI is one of the nice examples where we actually use it for diagnostic tools very regularly and very widely all over the world. Which actually nothing but monitors the spin relaxation dynamics around different biological system. Over there during this MRI, we actually use a MRI contrast agent, which is a system with a lot of unpaired electrons like gadolinium with seven unpaired electrons, which actually creates a strong local magnetic field which helps us to see the environment much better in absence of that.

So that is why it is known as the MRI contrasting agent, which actually gives us a much better visualization when it is present. So with respect to that, we would like to conclude this section of this NMR and its application over here. Thank you.