One and Two dimensional NMR Spectroscopy: Concepts and Spectral Analysis

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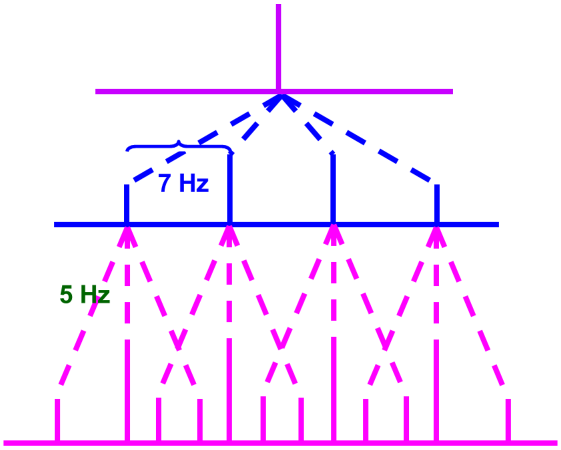
Lecture 19 Analysis of ^{1}H NMR spectra-I

Welcome all of you. Now onwards we will really take a plunge into analysis of the NMR spectrum. So, far I was giving lots of concepts about multiplicity pattern, chemical shifts, varieties of interaction parameters; and especially I showed you how we get the multiplicity pattern when the one spin is interacting with the various other spins with the different coupling strengths, whether it is chemically equivalent, chemically non-equivalent groups of coupled spins, like CH2 coupled to CH3, CH2 coupled to individual CH, and we have varieties of examples. And I also classified the coupled spin system into weak and strongly coupled. I gave the definition of what is the strongly coupled spin system and what is the weakly coupled spin system. And we took number of examples of them and I showed the spectra of strongly coupled and also weakly coupled spin systems.

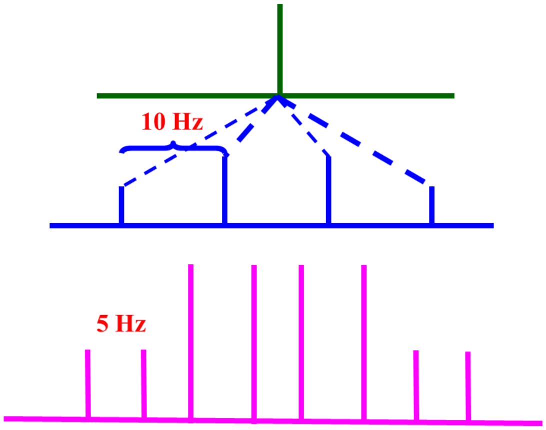
And I discussed in depth about the Pople nomenclature. It is a nomenclature given for the coupled spin system, especially spin half. Each coupled spin half is given a letter in alphabet. If it is weakly coupled, it is written with one letter in the alphabet and another letter should be far away in the alphabet order, like AX means weakly coupled. The alphabets next to each other are strongly coupled, AB is strongly coupled. And even more strongly coupled is when the chemical shifts are identical, we call it as A2. And when the chemical shifts are identical, but couplings are still be present with something else, we call it AA prime. Number of such examples are there. We can have AB, A2, AX for 2 spins. For 3 spins, we can have n number of possibilities like AMX, A3, AA prime, A double prime, AB prime, all those things we can think of, including AB2, ABC and varieties of things.

There is no point in discussing everything, which has been discussed at strech in some of the previous courses. But I just gave you few examples of how we can analyze this, how this nomenclature is important in understanding the spectral pattern, so that you know how to interpret. As I told you weakly coupled are easy to analyze. Whereas, the strongly coupled, the peak are not of equal intensity, appearance of spectrum itself is a completely different. You cannot analyze in a straight forward way, For very strongly coupled, you need to simulate, especially for 3 spins are more, you have to simulate through computers and then only you can do it. It is not possible to analyze in a straight forward way.

With this, now we will go to the analysis of the 1D spectra of some molecules. First of all, we have to create what is called a family tree approach to generate the spectrum. We can hypothetically simulate a spectrum by using a family tree approach. This is done only for weakly coupled spins case, not for strongly coupled spins. I will give an example like this. We do not go into the detail. One or two examples I will give and then we go to the real examples. For example, I will take a problem; there is a CH proton. Assume in a molecule, CH (A) proton is coupled to CH3 proton with a coupling constant of 7 hertz; and CH is also coupled to CH2 (X) with a coupling constant of 5 Hertz. That means, there are 3 groups of protons, A is coupled to M, A is also coupled to X, AM coupling is 7 hertz, AX coupling is 5 hertz. This is what I wanted to tell you. Now, we can generate the multiplicity pattern for each of them. What is the multiplicity pattern? And also I give you another information. CH3 is also coupled to CH2 with a coupling constant of 10 hertz. That means, we have 3 groups of protons coupled, maximum we can have is 3 couplings. AM, AX and MX couplings. All the information is given for you and it is weakly coupled.

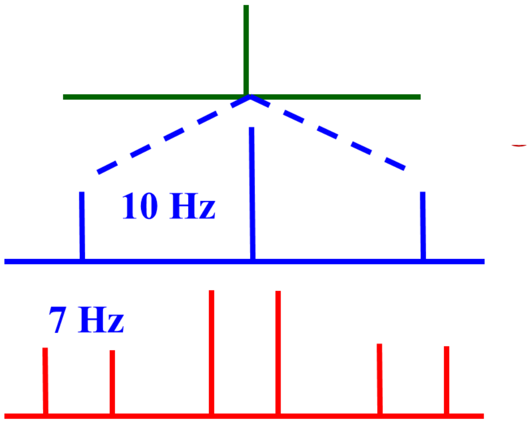


Take an example where the chemical shfits are very far away, well separated. Generate the multiplicity pattern. We can do it for one or two of them and then go to the other examples. How do you generate the multiplicity pattern for a CH proton using a family tree approach? Assume there is a CH proton which is not coupled to anything else. Then it is going to be a singlet, it is a single peak. In the absence of any coupling, CH proton gives a single line. Now, I am bringing in the coupling of A with M. Then because the CH3 protons are chemically equivalent apply 2NI+1 rule and the Pascal triangle, then you are going to get a quartet of intensity 1:3:3:1. The single peak became a quartet of 1:3:3:1 intensity. And now, each line of this quartet is also split into a triplet because A is also coupled to CH2 with a coupling of JAX. That coupling of 5 hertz is there. Then what will happen? Each line of this quartet is further split into a triplet. But remember this is 7 Hertz coupling and each of them is split into a triplet of intensity 1:2:1 with coupling of 5 Hertz. Then what is going to happen now? Look at it. Many of these lines will cross over. Now, if you start wit this, this is a triplet, 1:2:1 intensity, this peak and other one again 1:2:1 intensity, but because this separation is 7 Hertz and this separation is 5 hertz, you see there is a crossover. As a consequence, you will make mistake in analyzing multiplicity pattern. So, but you should know how to extract the multiplicity information from a given complex multiplet spectrum and again another one, another one. See this is what it is. What do you call this pattern? We already discussed which is the larger coupling. Larger coupling is a quartet and rest is triplet. This pattern is called quartet of triplets. For a CH proton, for the condition which I have given you, you are going to get quartet of triplets.



Let us go to the example of CH2 proton in the same molecule. I told you CH2 is coupled to CH3 with 10 hertz coupling and of course, it is coupled to other one CH proton with 5 Hertz. How do you generate the multiplicity pattern now? CH2 proton in the absence of any coupling is a singlet. It is split into a quartet because of CH3 with the coupling constant of 10 Hertz. Of course, intensity as you know it is 1:3:3:1; It is a quartet. It is further coupled to what? CH proton. What is that CH coupling? 5 Hertz and what is happening? CH is going to split each of these lines into a doublet, but it is a single proton. So, it is going to split each of this line into a doublet; and there is no overlap because the separation is 10 Hertz and the coupling is only 5 hertz. So, there is no question of this getting overlapped because 5 Hertz from the center 2.5 Hertz, here 2.5 Hertz here. There is no overlap, but everything is very clearly separated out and this is a doublet; this is a doublet. What do you call this pattern? Largest coupling is quartet, other is doublet. So, it is called quartet of doublets. In a hypothetical example of a molecule we can generate a spectrum like this.

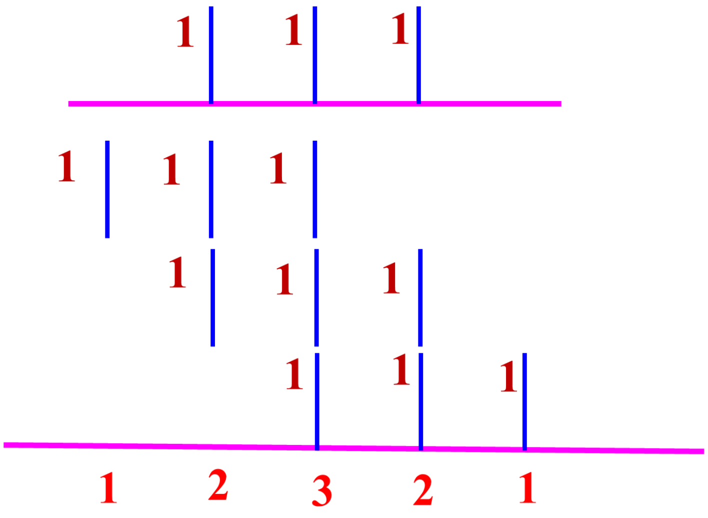
Of course, multiplicity for the CH3 group also we can do finish with that. CH3 is coupled to CH2 and CH. In the absence of the coupling again CH3 is a triplet.



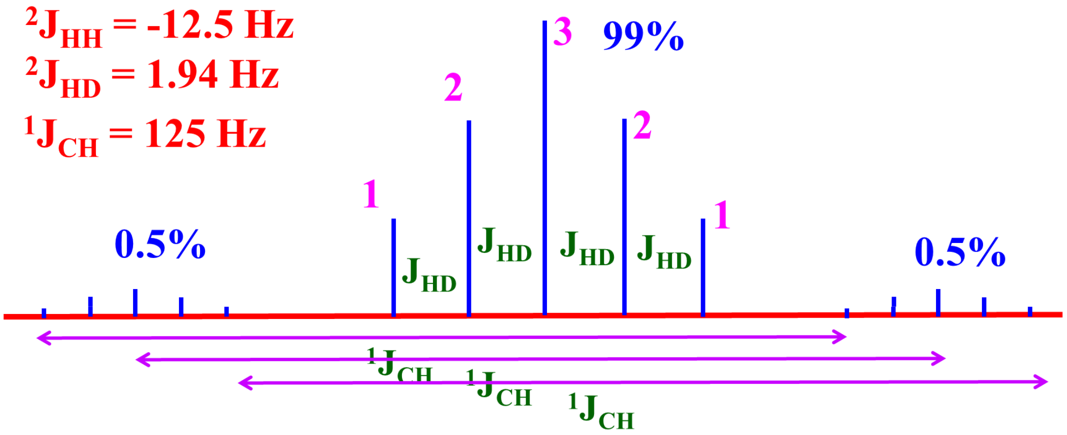
Now, I am going to bring the coupling to CH2 of 10 hertz. So, this line is going to become a triplet, very clear it is going to become a triplet. What will happen now? This CH3 is also coupled to CH. CH will split each of this line into a doublet and that separation is 7 Hertz; this is 10 hertz. So, you can work it out and now it is going to be a very simple pattern. It is triplet of doublets. And this separation gives you 7 Hertz and here to a separation gives you larger coupling 10 Hertz. So, this pattern is called triplet of doublets. Very easily you can generate like this. Of course, we can generate all this like this. I don't want to go to this, another example.

I will go into another example where we can synthesize. We will go to a real example where I am simulating proton, deuterium and carbon 13 spectra of a molecule called CH2D2; dideutro methane. We have to synthesize this spectrum, or we can simulate it. Remember this molecule has 3 NMR active nuclei which are the, proton spin is half carbon 13 spin half and deuterium spin is 1. There are 3 nuclei in CH2D2; small molecule. There are 3 NMR active nuclei and what are the couplings you can think of? One is there can be a coupling between proton and deuterium; there can be a coupling between carbon and deuterium, and there can also be a coupling between carbon and proton. So, 3 different couplings are there and all the 3 are heteronuclei will not worry about the chemical shift differences; one comes at proton frequency; other carbon frequency; one at deuterium frequency. All are different. So, individually we can take the spectrum for each of these nuclei. So, with this I give you some idea just for the simulation purpose. The one bond coupling JCH is 125 hertz and 2 bond proton-proton coupling is 12 Hertz. And of course, if I know this J_{CH} I can calculate JCD. I will tell you later when we go further. Of course, I already discussed when I discussed the coupling constant. So, I discussed quite a bit about HH coupling and everything. May be I did not work it out with an example. We will come to that later. Possibly in this analysis I will discuss later. We will see that. When I have a JCH, I can calculate JCD or if I have JCD I can calculate JCH. So, I can give an example of JCD is this thing and JCH is given. With this I will generate the spectrum. Remember I am telling you natural abundance of carbon is 1.1 percent; very weak in intensity, because in 100 molecules 99 molecules are carbon 12. I told you, only 1 molecule is carbon 13. That gives us the very weak intensity they are called satellites we can discuss that also later.

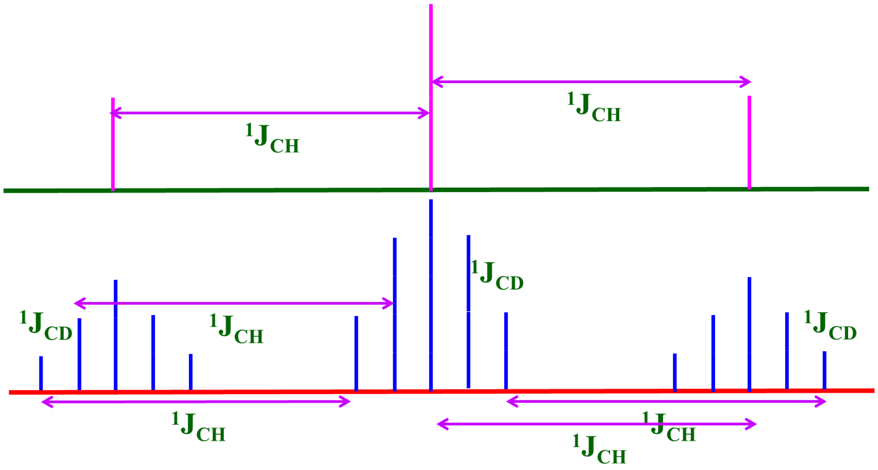
If I look at the proton spectrum of this molecule, it experiences 2 types of couplings. One is proton can coupled to carbon, JCH is there. The proton can couple to deuterium. JHD is there. There are 2 couplings; and what is a pattern we are going to get for the proton spectrum? you should understand by now. Of course, when I am looking for proton deuterium is 100 percent, because it is deuterated. I am looking at a deuterated one. It will split this proton into how many lines? remember deuterium spin is 1. These carbon and proton are spin half nuclei, deuterium spin is 1. So, what will happen? Put simply 2NI+1 rule; N is equal to 1, there are 2 deuterium; 2 into 2 plus 1, you will get 5 lines. So, coupling of proton with deuterium gives 5 lines. Of course, intensity pattern is different here, that can also be worked out later. But how you work out intensity? this is a different type of Pascal triangle. There is also a Pascal triangle similar to what is there for spin half nuclei. For spin 1, spin by 3/2 also is there, very easily we can work it out here.



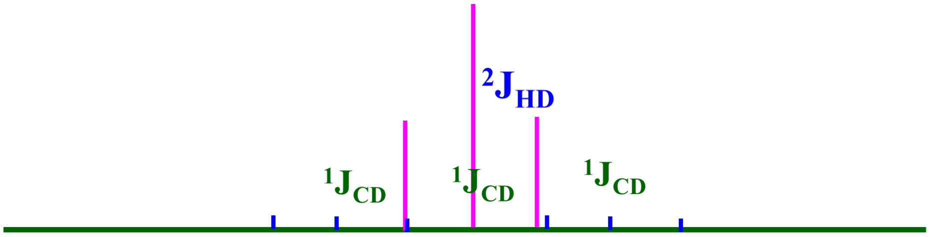
Let us say one proton is split into three lines of equal intensity by 1 deuterium; because 2 times spin is 1 it splits into 3 lines of equal intensity. 1 deuterium will split into 3 lines, what will happen to the other deuterium? the other deuterium will split each of this line into 3 lines. So, this is the center of these 3 lines. From this 3 lines, from this 3 lines now work out the intensity. It turns out to be 1 2 3 2 1 intensity ratio. That means if proton is coupled to 2 deuterium, you are going to get 5 lines. But what is the intensity pattern? intensity is 1 2 3 2 1. That is what you are going to get. If the proton is coupled to two deuteriums, you are going to get 5 lines of intensity 1 2 3 2 1. And this how the spectrum of proton coupled to two deuterium comes.



And this should be the proton spectrum if I simulate it. Now, what happens to carbon 13? carbon 13 can also couple to proton with a coupling constant of 125 Hertz. But remember abundance of this carbon is 1 percent only, very small 1.1 percent. As a consequence each of this line because of carbon split into 2 lines, like 2 pentets. This is a pentet. There will be 2 pentets separated 1 this side and 1 this side. You are going to get peaks like this. You are going to get satellites like this. You see small peaks, this is because of coupling with proton with deuterium this is coupling with carbon proton coupling. This is what happens and now measure the separation of one of this peak to another peak, it is going to be JCH coupling. measure from this to this any of the corresponding line on the other side of the satellite, it gives you JCH coupling. So, this is how you are going to get the coupling information, you understood. So, each line of this thing is further split and this is what the proton spectrum is like this. This how the proton spectrum is going to split.

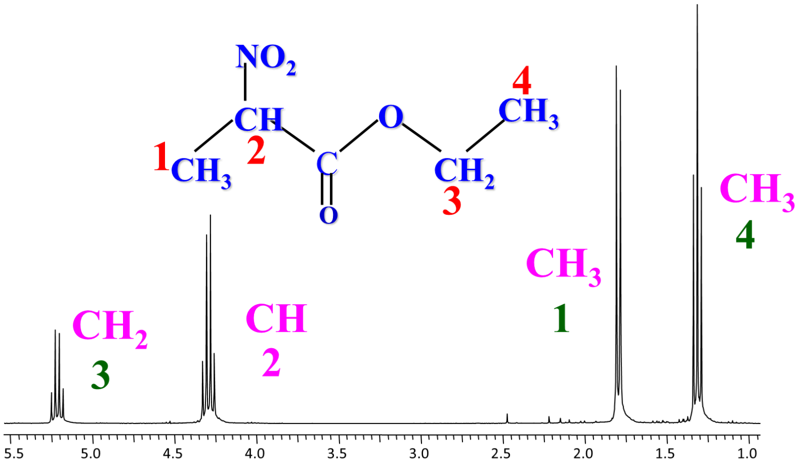


Let us look at the carbon 13 spectrum of CH_2D_2. How does the carbon spectrum comes? very easy. The carbon is split into a triplet because of 2 chemically equivalent protons. We have to get the intensity pattern 1:2:1. A triplet you are going to get. Then each line of the triplet is split into a pentet pattern because of deuterium coupling. This is what happens. So, CH coupling is there CD coupling both are there. As a consequence you are going to get a pattern like this. The overall pattern is 1 2 3 2 1 intensity quintet you are going to get; and the 13C spectrum really is like. This is a triplet because of $^1J_{CH}$ coupling, the direct coupling between carbon and proton. And each of this is further split because of the deuterium coupling is like this. And this how the pattern you are going to get if you take the carbon 13 spectrum of this molecule. you will get 15 lines. This centre of this to centre of this gives you JCH. Any two adjacent lines you take here, you are going to get JCD. Alright and this is 1JCD and this is JCH.

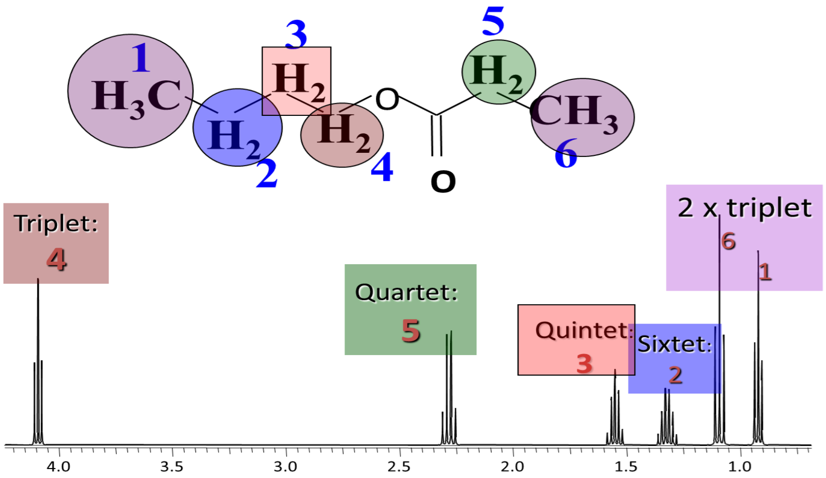


Now we will see the deuterium spectrum of this molecule, another nuclei. We already saw how carbon spectrum comes, we saw how the proton spectrum comes. Let us now try to understand the deuterium spectrum. The deuterium spectrum is a triplet because of protons. Of course, and spin half nuclei, it will be a triplet. And each line of the triplet is further split into a doublet because of carbon 13. It appear as satellites see now I give you a value for JHH, JHD and JCD. Just see that if you simulate how this spectrum comes. First of all it is going to be a triplet. The deuterium coupling to proton will be a triplet and the coupling is very small. You know JHD coupling is only 1.94 Hz. But I have written like this just to make you understand. I got a triplet, but what is happening? each line of this triplet? it is split by carbon 13 and then this what happens. It is a satellite, but remember this carbon 13 is a doublet gives a satellite and this coupling is quite large larger than this. So, it appears as if it is overlapped, moves on either side. See each of this line is split into doublet with a very weak intensity peaks. They are called satellites. The real spectrum of deuterium is like triplet and 3 satellites on either side; and they appear as satellites. So, very simple, how you know looking at the spectrum of the simple molecule, the molecule appears simple, CH_2D_2, but look at the spectrum. We are going to get carbon 13 spectrum, which is different type, proton is different type, and the deuterium spectrum is different. All are different because the spins are different. One is low abundant carbon 13, that appears as satellites, when you look at proton deuterium is going to give of quintet, when you look at deuterium proton will split this into triplet and each of these lines, carbon splits them into triplet. When you directly observe carbon, it is a different question. The satellite question does not arise when you observe carbon. The proton splits this into triplet and each line of the triplet splits into a quintet because of deuterium. The fantastic way of understanding the spectrum of very simple molecule; 3 different nuclei give the 3 different type of spectrum.

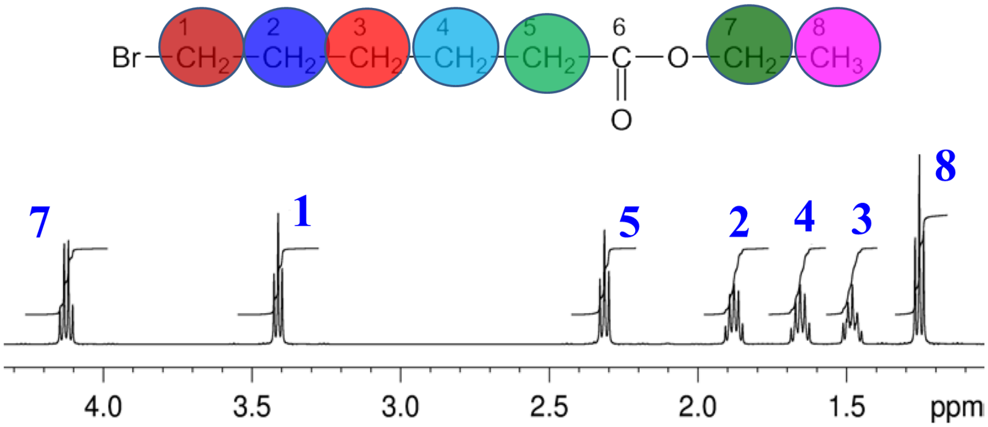
Now, we will go to the first order analysis of the real spectrum. I am looking at the spectrum of a molecule like this; hypothetical or real molecule, does not matter.



And this is the spectrum. Now, how do we interpret it I have started with a very simple molecule just to make you understand. And of course, you should use your knowledge of chemistry like chemical shift and coupling constant to interpret this one. Where does CH3 come? I have always been telling you when I discussed about the chemical shift also, I told you CH3 is more shielded. It comes to the high field normally, unless it is attached to oxygen or nitrogen like that. CH3 will always resonat at the higher field. One peak coming here is a CH3, that is my assumption. How do you know it is CH3? If it is CH3 and if it is coupled to CH2 it has to be a triplet, correct! it has to be a triplet. So, as a consequence I would say this is a CH3 which is coupled to the CH2. Why not this CH3? There are 2 CH3 here. But remember this CH3 is attached to CH. That will only split this into a doublet. This CH will split this CH3 into a doublet. Since it is a triplet this cannot be this CH3. Yhis has to be CH3 proton 4. I can easily assign. That number 4 I can assign for this peak. Then obviously, other CH3 I know. This is has to be other CH3 because this is coupled to CH and it has to be doublet. So, this is a proton 1. Then what is the next one? It is CH2. Other is CH. Interestingly both of them will give rise to quartet because CH3 will split this into quartet. This CH3 will split this into quarter. There are 2 quartets. Now, tell me which is the CH2, which is CH. First you have to think of this separation and the separation of one of them should match with the coupling between CH2 and CA3. And this separation and separation of one of this J coupling should match. That is another CH3. We can identify. The simplest possible way is look at the intensity. This is 1:2. Obviously, this has to be CH2, double the intensity. This is proton 3. This is proton 2, because intensity is half of that. Another way is you measure the separation, here J coupling. See which one matches, whether this or this. Then you know what is that one. Very easily you can make the analysis. So, you can look at the chemical shift, look at the intensity pattern, and look at the multiplicity patterns, measure the coupling. Using all these information you can analyze this spectrum very easily. And if you analyze this, this is how it comes. This is proton 1, this is proton 2, this is proton 3, this is proton 4. Very easily we can analyze this one.



Next we will go to another molecule. What is other molecule? this one. This spectrum is simple. Again this is a first order analysis. Remember it is a first order analysis means spins are weakly coupled, they are not strongly coupled. So, first order analysis means straightaway you can get the chemical shift and coupling constants. The direct assignment can be made without resorting to numerical simulations or anything. That means, first count the number of individual chemically inequivalent protons. In the molecule there are 1 2 3 4 5 6, there are 6 groups of protons in the molecule. How many groups of peaks are there? There are 6 groups of peaks here. You can understand now and start interpreting. Of course, these 2 have to be triplets, this CH3 and this CH3. Why it is a triplet? because each of the CH3 is attached to CH2. This CH2 will split this into a triplet, this CH2 will split this into a triplet. There are 2 triplets at the high field. As a consequence this has to be 2 CH3s. Which is 1 and which is 6 that is a matter, that we have to discuss. As I already told you have to look at the separation, the J coupling. of this and this match with other one with which it is coupled to. You can extract that information, easy to analyze. If let us say both of them are equal, J coupling, still if you want to know which is which, there are ways to analyze. When you go ahead further we can find out by using COSY and other 2 dimensional techniques. But we do not have to go to that one. It is a fairly simple molecule, straightaway we can get this information. ok. Now what is the next easiest analysis you can make. The easiest analysis next is 5, because 5 is coupled only to CH3. When it is coupled to CH3, what is the pattern you expect for 5? it has to be a quartet. Where is the quartet here? The only quartet is here. This has to be proton 5. All others are not quartets, their multiplicity is different. Now come to other, these 3 protons how do you interpret it. What about this one? that can coupled to this 3, proton 3; CH2. And it has to be a triplet. Where is the triplet you can think of. Wee one is of course this triplet. It is methyl we know that where is other triplet? We can think it is here, and also very interestingly it is attached to oxygen. As a consequence it has to move to the down field. Very easily you can assign this one. So, this has to be, my first guess is. this would be proton 4. I have assigned 1, assigned 6, this is a proton 5, this is a proton 4. Now what are left? Protons 2 and 3. In the 2 and 3 which one is more complex? 2 or 3? Look at it, which is more complex. The more complex is proton 2, why? the reason is this proton 2 is split into a quartet because of the CH3 and each line of the quartet is split into a triplet because of proton 3. So, it is a more complex pattern. What about this one? this one is split into a triplet because of this, and each line of the triplet is further split in the to triplet because of this. So, more complex pattern is this, of the two. Obviously, I will say this is proton 2. Compared to this, this is less complex, I would say this is proton 3. So, now, we can easily interpret just by looking at the multiplicity patterns. And we know where the peaks will resonate. So, very easily this sextet has to be proton 2, this quintet has to be proton 3, and this has to be proton 2 and this is 5. That is what I said. So, very easily we could interpret this molecule. A very simple molecule fairly easy to interpret. This is a first order analysis of the proton spectra.



We go to a slightly bigger molecule. As the molecule size increases the complexity becomes more and more. Look at this molecule, where do you start with? Always count the number of chemically inequivalent protons. There are 1, 2, 3, 4, 5, 6, 7/ I have numbered it, there are 7 groups of protons. Which are the 7 here? See 1, 2, 3, 4, 5, 6, 7 very easily you can find out. Very fact they are well separated, the chemicals shifts are far away separated among themselves I would say it is weakly coupled. So, first order analysis should be possible to do. We will assume first order analysis we can do. Now, what is the first one you can think of? Always look for the high field. High field is CH3. This CH3 is coupled to this CH2 and becomes a triplet. So, this is a triplet. This has to be proton 8, my first guess is right. Then this one will become what? has to be a quartet. Where is a quartet you can think of in this case? All the multiplicity pattern is more except this one, which is a quartet. This has to be proton 7. This also agrees with the our chemistry information, because it attaches C= O, and O. This is electronegative, it will withdraw electrons, get more deshielded, comes at the low frequency region. I am sorry, this id high frequency region, low field region is this. So, easily you know you assign 8 and assign 7. What are remaining? Remaining you can assign. Think carefully one of them, look at this proton. This is coupled to only this one. What is the pattern you think of for it? It has to be a triplet, because this is coupled only to this and nothing else. And further it is attached to bromine which is electronegative. So, it comes to the down field, low field region and in the low field you see where is the triplet? This is the only triplet possible. So, my first guess is this could be proton one. I have aassigned 8, 7 and 1. What is the remaining thing you can think of? Where is another triplet? Look at this one. This is one possibility. This is coupled only to this and nothing else. There is no long range coupling. So, this also has to be a triplet, it is split into triplet because of proton 4. Where is the next triplet? See here I will say this is proton 5, that is also correct. So, I could assign all these things very easily. Next interesting point comes. This proton becomes triplet because of this, becomes triplet because of this. Each of the CH2s here experiences coupling with the other two CH2s sitting on either side. Look at this molecule; this CH2 is split into triplet because of this and each line of this triplet is split into another triplet because of this. Look at this one, this is again split sitting between two CH2s. Again this will become triplets of triplet. What about this one? This is sitting between two CH2s. As a consequence this also becomes triplet of triplets. See this is a pattern you are going to get for these. Almost identical patterns. Look at this one. Now, how do you say which is 2, which is 3 and which is 4? What is the logic you apply? Pattern is similar. All of them are independent, but there is a difference in the chemical shift. But wh chemical shift come? Of course, you can apply the induction effect, because of this, it will be low field and this is further low field, like that you can start. For this one induction effect, this will be next, like that. You can apply some chemistry and find out using the induction effect what is what. We will make a rough guess using our chemistry knowledge and find out what is what.

This is the first my assumption 8 CH3, then this is 7. That is what I said. it is a quartet, this is a triplet, and I said this is 1, because it is only a triplet, that is also correct. Then I said this is a triplet 5, because there is only possibility for a triplet. Then I said this is triple of triplet, I put this as 2 because I assume there is a more induction effect, comes to down field that is also possible. Then I said this is 4, this comes down field because of induction effect this is more electronegative here. So, I would say this one and the last one I would say this is coming here, because this is far away from bromine, C=O. So, it resonates here. This is my assignment. However, to make sure my assignment is correct or not, there one way. What you have to do is selective decoupling; each proton breaks the coupling of one of them with the other and find out where is the change you are observing in the spectrum. That was thing which people used to do, about 30 or 40 years back. Nowadays it is not done. That you can easily identify by what is called two-dimensional NMR. Then you will easily come to know which is coupled to which and you can find out and track it and easily, and we can make the assignment. We will come to that, when I come to 2 D NMR later.

But right now what I wanted to tell you is in a weakly coupled spin system like this. If you just have the spectrum like this just find out the number of chemically inequivalent protons; look at the multiplicity pattern, apply your knowledge of little bit of chemistry, electron negativity, electron donating group is there or withdrawing group is there, whether it is shielded or deshielded, use some idea. And then third point measure the intensity of the peaks, then easily you can make the assignment. So, this is what we did and we can go further and start making the assignment. Since the time is up I am going to stop here. We will take lot more examples tomorrow or in the next class. But for today what I wanted to tell you is we really jumped into the analysis of the proton spectrum. This is the main aim of this course to make you more comfortable. If a spectrum is given of any nuclei for that matter how do you interpret it? what is the idea you have to do? how do you go ahead in interpreting? Rhis is what I wanted to discuss. And we simulated the spectrum using a family tree approach for some hypothetical molecules. And I took the CH_2D_2, a simple molecule with three different nuclei. They are two spin half and one spin one. We simulated the spectrum for each of them. We saw how when it is coupled to other nuclei spectrum changes what type of spectra we get for carbon, proton and deuterium we observed. And then realistic examples of some of the molecules I took. Started with the simple molecule, then little bit complexity keeps increasing. We will go ahead further. We will take few more examples as the complexity increases how it comes we will see. Finally, of course, by the end of this course you must be comfortable enough to interpret the spectrum in a better way. I will stop at this stage. Thank you very much.