One and Two dimensional NMR Spectroscopy: Concepts and Spectral Analysis

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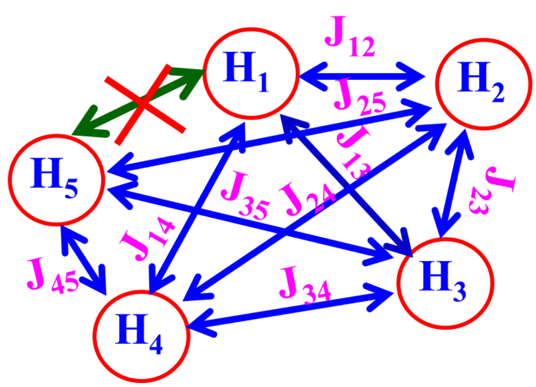
Lecture 16 Coupled spin system

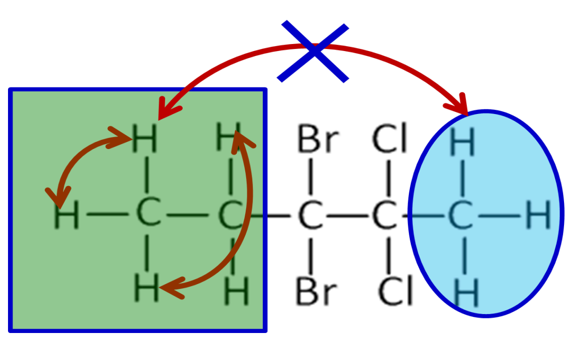
In the last couple of classes, we discussed extensively the internal interaction parameters, especially chemical shift and coupling constant. On coupling constant I gave lot of information for you about how do we get the multiplicity pattern, how do you give the nomenclature for a different multiplicity pattern for a particular proton, when it is coupled to single proton, two protons, three protons, a chemical inequivalent or coupled to chemically equivalent group of protons. And we accordingly gave a nomenclature like doublet, triplet, quarters, varieties of things. And we took a realistic example and get the information about what is the pattern we are going to get. We discussed a lot about those things. And at the same time, I gave you strength of j coupling, the information about the strength of j coupling.

One bond coupling is quite large, especially in hydrogen molecule. As the number of consecutive bonds keep on increasing between two interacting spins, J coupling keeps reducing; that is a general trend. But I gave several examples where J coupling can be extended even up to 5 bonds, 6 bonds, 8 bonds, 9 bonds also. These are rare examples, but not always observable. But remember this is general guideline, the J coupling decreases with increase in the number of consecutive bonds between two protons or between two interacting spins. But there are exceptions like this especially in the linear molecules or molecule that are in zigzag fashion, this type of coupling strength can be observed; the significant coupling strength can be observed. Further, I said I measured the coupling in a hypothetical molecule of a triplet and a quartet in a given magnetic field at 200 megahertz. The same thing when I measured at 400 megahertz, I showed you the coupling remains invariant with the magnetic field. Whereas, the chemical shift linearly changes, but coupling will not change. So, coupling is always constant in any spectrometer you measure. Whereas, chemical shift linearly changes. This is what we discussed. Several things, for several classes, we have been discussing about chemical shift and J coupling. This information is needed for you if you



want to take a deep plunge into NMR analysis of varieties of molecules and to take it further into your research. So, with this today we will continue further and see how we can analyze the spectrum of given molecules. But remember when analyzing the spectrum there are two ways. One characterization of the molecule, I give NMR spectrum you look at the peak and say there is a CH3 group, you have benzene group, you have CH2 is there. My molecule is having a phenyl group CH3 and CH2, that is fine. That is one way of doing because your idea is only to characterize the molecule. But if you really want to get the conformation information, If you want to get the structural information, then you have to really analyze the multiplicity pattern, and the complete information including the intensity pattern of the peaks. Only then analysis will be complete to get more information about the given molecule. So, that is another way of analysis for which we need to understand what is called a spin system. So, today we will start understanding the spin systems and Pople notation.

When I say I have to analyze the spectrum, generally they are all coupled spin systems. If they are uncoupled you get only single peak there is no interest to analyze. But if you want to analyze the spectrum, as you know the spins are coupled among themselves. In this what is a coupled spin system? What do you mean by a coupled spin system? Let us consider the group of spins like this 1, 2, 3, 4 and 5. There are 5 different protons. You can think of coupling between 1 and 2, coupling between 1 and 3, 1 and 4, 1 5, 2 5, 3 5, 4 5 all couplings you can see. For example, coupling between 1 and 5 can be 0, no problem. But it is a part of the coupled spin system. These 5 protons are called a coupled spin system. There exist couplings among themselves, among all the 5 protons; there is an interaction. Interaction strength of one of them could be 0, coupling 1 3 could be 0 or 1 5 could be 0; does not matter. But it forms part of the coupled spin system and this is called a coupled spin systems.

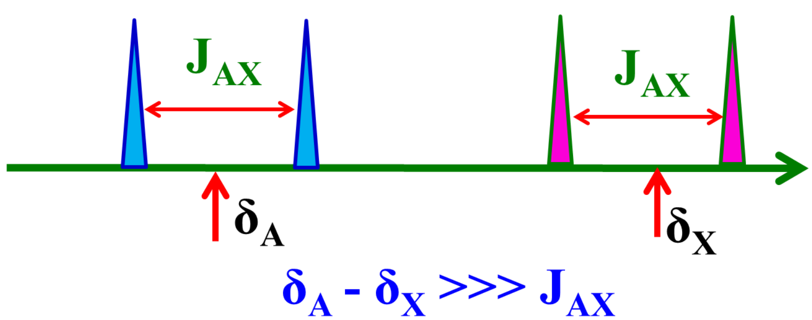


In NMR we say coupled spin system means they are part of this group, they are coupled there is coupling among themselves. And if there is another group here and there may not be coupling between this and this; then this is one spin system this is another spin system. There can be many spin systems possible; many spin system can be present in the molecule. So, this is the important concept to understand what is a coupled spin system. Coupled spin system is group of coupled spins with varieties of coupling strengths; different coupling strength could be there or one of them could be 0 does not matter. But the spins are part of the coupled group of spins; a coupled spin system. And then spin system can be classified into 2 groups one is, for example, this is just to give you an idea about what is a spin system before going further. For a hypothetical molecule I take that there is a coupling between this and this CH3 group, may be or may not be, does not matter. There is a coupling between this proton to this proton, fine, but there is no coupling between this proton to this proton because in between there is a break in the coupling. And this forms one coupled spin system this form another coupled spin system. So, in a given molecule there can be N number of coupled spin systems. This is very important when you want to understand 2D NMR like TOCSY. When I go further I will discuss these things. So, in the spin systems; this is a part of a coupled group of spin system, this is a part of coupled group of spin system. Whereas, between these two there is no coupling. So, there are two spin systems in this molecule.

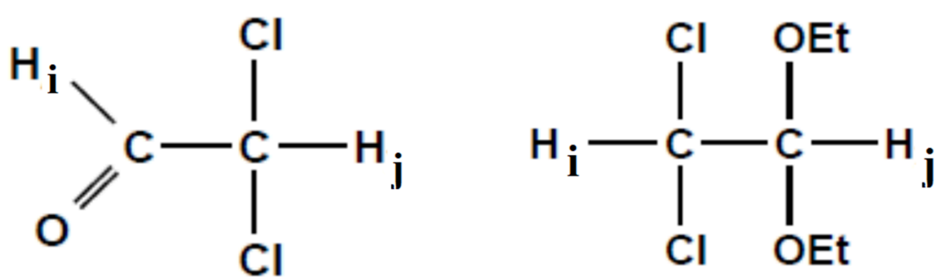
The coupled spin systems can be classified into 2 groups. What are those 2 groups? they are strongly coupled and weakly coupled. What do you mean by weakly coupled what do you mean by strongly coupled spin system? This is something which is we have to understand. What do you mean by weakly coupled and strongly coupled?

Of course, from your knowledge you can say if the interaction strength, J coupling is larger, coupling is stronger, interaction strength is larger. And you nay say coupling is very very small, then it is weakly coupled. That is common thinking, but that is not the way to understand, whether the 2 protons coupled is strongly coupled or weakly coupled. There is a different different way. One is you have to measure the chemical shift difference between the 2 coupled spins and measure the J coupling. If the chemical shift difference between 2 coupled spins is very very large compared to coupling strength then they are called weakly coupled spins. Remember, we considered the example of 2 spins; 2 different chemical shifts; one here and one here. Measure the difference in the chemical shifts and that delta delta, if the difference in the chemical shifts of these coupled spins is very very large compared to the coupling strength, which is, let us say doublet of doublet, in which case these spins are called weakly coupled.

On the other hand and of course, we can find out what is the condition for that weakly coupled. J by delta delta should be extremely smaller, very much smaller than 1; that means, this is large, this separation is very very large. This is the condition then J by delta is very very small, of the order of 0.1, 0.01, 0.001 will be there. Smaller this value is, more and more weakly coupled are the spins. On the other hand in the case of the strongly coupled the chemical shift difference delta delta between 2 coupled spins is less than 1 or at times approximately equal to coupling constant itself. Then such spins are called strongly are coupled spins. please remember when the chemical shift difference between 2 coupled spins is sufficiently larger than J coupling, where the parameter J by delta delta is very very smaller than 1, then they are called weakly coupled spins. Whereas, in this case when the chemical shift difference is approximately equal to J or which very very much smaller than J, if the condition J by delta delta is approximately equal to or greater than 1, then it is called strongly coupled spin system. This is the way you have to classify the spin systems. Then you may ask me a question so what how does it matter for us whether the spins are weakly coupled or strongly coupled. It defines the type of spectrum you get. The spectrum for strongly coupled spins will be different than this weakly coupled. Consider example of 2 protons, if they are weakly coupled you get 1 type of spectrum. If they are strongly coupled you get another type of spectrum. Both are 2 protons only, coupled between themselves, but the type of spectrum you see is different. That depends upon coupling strength and chemical shift difference.



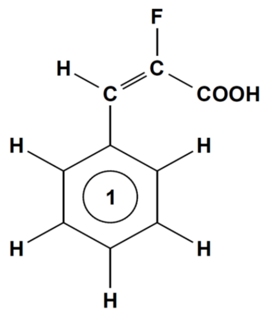
So, this is an example of two coupled spin system, A and X. It is called AX spin system. The spectrum I am showing you here. This is the chemical shift of A, this is the chemical shift of X. Each is a doublet that we have been seeing. Already I explained to you this separation is larger; this is J coupling. And now measure the separation between this and this, the chemical shift of A and the chemical shift of X you can measure; and measure the difference delta A minus delta X. And if this is very very larger than this, this is the type of pattern you are going to get. This is called a weakly coupled spin system. These 2 protons are weakly coupled here, provided this delta A minus delta X is very much larger than this coupling; The J coupling is what is important thing. See the chemical shift difference. This are weakly coupled protons; a weakly coupled spectrum appears like this. What are the weakly coupled spins, this is the general rule. Remember delta delta by J should be very much greater than 1 or if you take the reverse of that, J over delta delta, this should be very much smaller than 1. Usually it is not always the case. The general convention is if chemical shift difference over J is larger, 50 times more, for example I measure the delta delta difference between these 2 protons, chemical shift difference and also measure the J coupling divide 1 by other, and if this value is more than 50, this ratio, then it is weakly coupled spin sytem. If you take the reverse of that, if I take J coupling divide by the difference in chemical shift; if this value is much much smaller, and is of the order of 0.01 or 0.02; or even smaller; they are called weakly coupled spins. So, this is the condition for that. The homolecular weakly coupled spins,

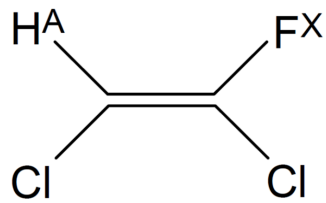


I will

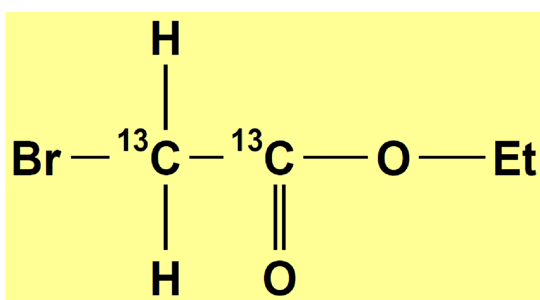
give an example like this. It is a simple molecule, where we have 2 protons. I and J. What is the J coupling between this and this? It is already been measured, around 2.9 Hertz. Let us say you are measuring you take the spectrum of this in a 500 mega hertz spectrometer 3.75 ppm take 4 for calculation, 4 ppm in 500 MHz is 2000 Hertz; and this is 2.9 Hertz. 2.9 or 3 by 2000 you take, this is much much smaller than 1. Obviously it is a weakly coupled spin system because the coupling here is much much smaller than the chemical shift difference between these 2 protons. It is one example of weakly coupled spin system.

Take another example like this. This proton and this proton coupling is about 5.6 Hertz and let us say same 500 MHz. This is approximately 1 ppm. 5.6 over 500; see almost 100 times smaller. 0.01, the ratio 0.01 is very small. So, this is also weakly coupled. So, if you want to find out either strongly coupled or weakly coupled then it is going to be J over delta delta difference you have to calculate and find out its ratio and this one above 500 mega hertz and above this is weakly coupled even in 100 mega hertz they are weakly coupled. Why I am telling frequency of the spectrometer here, as I told you chemical shift difference linearly varies with the magnetic field. The same strongly coupled if I go to very very high magnetic field, because the chemical shift difference becomes larger, it may become weakly coupled. Remember strongly coupled will become weakly coupled at a very high magnetic field strength, because the chemical shift shift difference becomes larger. Or weakly coupled at a very high magnetic field can become strongly coupled at low magnetic field. This is important thing you should remember.

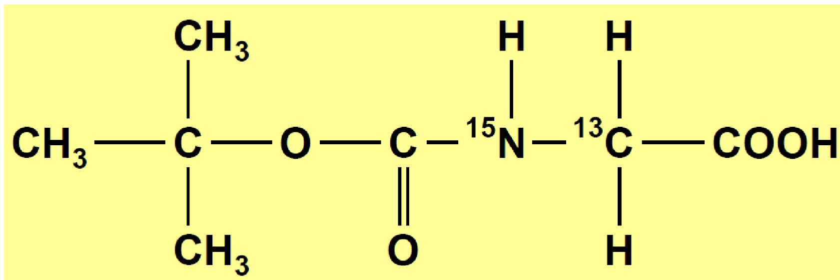




Take an example of a molecule like this. This is heteronuclear coupled fluorine and proton. The question is are they weakly coupled? or they strongly coupled? Remember you are looking at the heteronuclei fluorine and proton. If I take, let us say, 500 MHz spectrometer, the proton comes at 500 MHz. Where does fluorine come? the fluorine will resonate at let us say 470 MHz. What is the difference between them? 30 MHz. That means the chemical shift difference is 30 MHz. Whereas this coupling is of the order of 10 hertz or 15 hertz; that is all. Fery small value, whereas chemical shift separation is 30 mega hertz. 30 into 10 to the power of 6, huge separation in the chemical shift. The megahertz resonating frequency is nothing but the chemical shift, because that is where you are looking at. And of course I already discussed with you the chemical shift is the difference between the resonant frequency of the reference with respect to your peak divided by the spectrometer frequency. So this spectrometer frequency difference is 30 megahertz that means heteronuclear coupled spins are always weakly coupled. Remember this point, heteronuclear coupled spins are always weakly coupled, because the chemical shift separation is of the order of several megahertz.

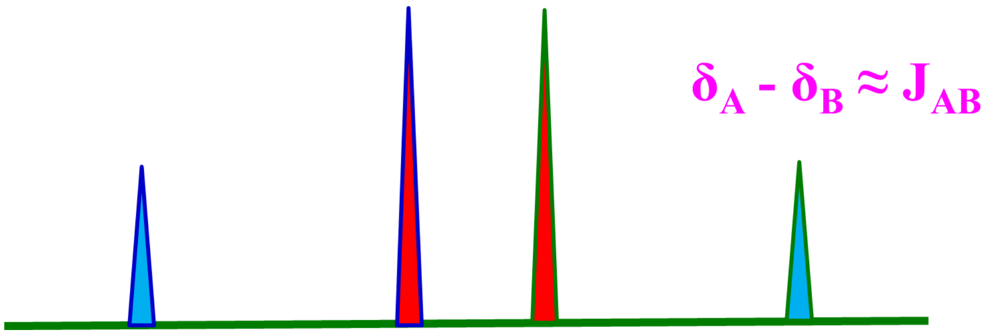


What happens in a labeled molecule? for example I consider a molecule like this two carbons are labeled labeled, means enriched. The abundance is point 1.1 percent somehow after labeling it is 100% abundant. When there is 100% abundance, there is a coupling between carbon and carbon, don't worry about it. Proton I am decoupling I will do, I will tell you what is decoupling everything later. I don't bring in the coupling of proton to carbon I see only carbon-carbon coupling. The carbon-carbon coupling is 67 Hertz. One bond coupling is very large. But look at the chemical shift difference, 141 ppm. Even if you take, let us say 400 MHz proton spectrometer, hundred MHz is the resonating frequency of carbon hundred into 141, y ousee it is 14,100. What is the peak separation, the J coupling? this is only 67 Hz. So it is a weakly coupled. So even in a labeled system homo nuclear coupling is so small and chemical shift separation is so large, this can be a weakly coupled spin system.

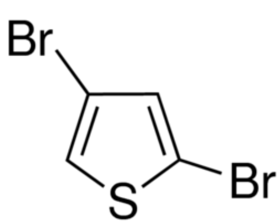


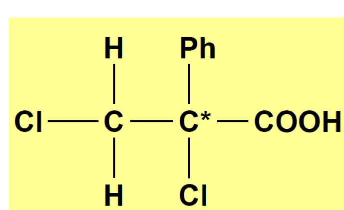
We will go to the other example like this here heteronuclear again nitrogen 15 and carbon 13 are labeled. I am removing the coupling with proton. Consider only coupling of carbon with nitrogen and the coupling between carbon nitrogen is 14 Hertz, that is all. But what is the resonating frequency? if I take 400 MHz spectrometer, the carbon is at hundred MHz, nitrogen 15 resonates comes at 40 MHz, because I told you gamma of nitrogen is 10 times smaller compared to proton and the carbon 13 gamma is 4 times smaller compared to proton. So the resonating frequency of nitrogen 15 in a 400 mega spectrum it is 40 megahertz whereas carbon is 100 megahertz. So what is the difference? then 100 minus 40, it is 60 MHz is the difference. So the chemical shift difference is 60 MHz, whereas coupling is only 14 Hertz. This is an example very heteronuclear spins even when they are labeled like this, are weakly coupled. This is a classic example of a heteronuclear weakly coupled spin system in the labeled molecule like carbon 13 and nitrogen 15; both are labeled now.

We go to the example of strongly coupled spins. So far we discussed about weakly coupled systems. Let us take the example of strongly coupled spins. I told you the definition already. The requirement for spins to be strongly coupled, if I have to say they are strongly coupled, the chemical shift difference between them must be very much smaller than the coupling between them or at the most of the order of coupling, that is what the condition I put in. Then they are strongly coupled. Go back to the same equations J by delta delta, earlier in the other case, it should be very much smaller than 1. But in this strongly coupled case it should be greater than 1. Whereas, if you take the reverse of it, the chemical shift over J; in the weakly coupled case, I said it should be very much larger than 1, but it should be very much smaller than 1; the reverse of it is a strongly coupled case; you understand the chemical shift difference between two coupled spins if you measure, and take the coupling constant, take the ratio of the chemical shift difference over the J coupling, if you take, if that ratio is very much smaller than 1 then they are strongly coupled. Of course you can take the other way. Measure the coupling and divide by chemical shift difference, that then it should be larger than 1. This is the condition for the nuclear spins to be strongly coupled. Then I say these nuclear spins are strongly coupled.

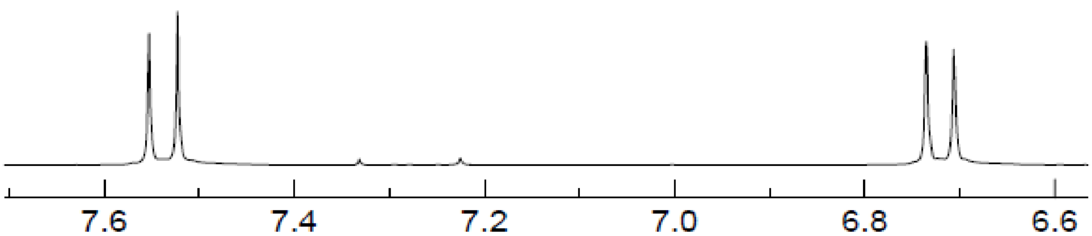


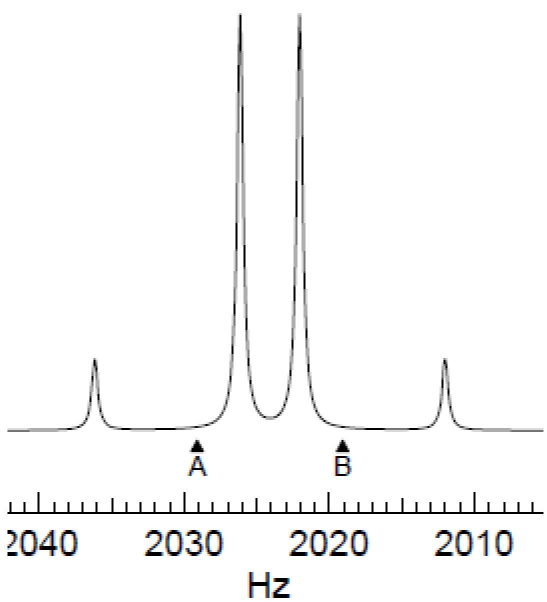
Two strongly coupled spin case. I will tell you what is AB, AX, everything today itself, as we go ahead further. A spectrum of a strongly coupled two protons is like this. Co you find the difference? what did we see in the weakly coupled case for A and X, two two lines of equal intensity, four lines we got. All were of equal intensity. I gave you an example of AX coupled, just couple of slides back. I showed you for a weakly coupled example this is chemical shift of A and this is chemical shift of X. This is J_{AX} and and I said it is a weakly coupled two spin case. Look at this strongly coupled. Qhat is the difference you see? The central lines are more intense than outer lines. Of course these two lines are of equal intensity; these two lines are of equal intensity, identical intensities. But between central line and the outer lines intensity, there is enormous difference. Not only that, it can so happen, it can be even more larger and outer lines can be even more weaker. That depends upon the ratio of chemical shift difference over J coupling. What is its value if it becomes smaller and smaller and smaller, then the pattern keeps changing. Not only that the intensity pattern keeps changing, you understand the difference. In the strongly coupled case, the same two spins if I consider the spectrum is completely different. What you see for weakly coupled and strongly coupled are different. But remember in the strongly coupled case you cannot analyze the spectrum so easily. All peaks are not of uniform intensity and just like you did for the example of three weakly coupled, I measure the chemical shift of A, I measure the center chemical shift of X and measure the separation. Get the coupling constant. This is called straight forward analysis. That is called a first-order analysis. That is easy in the weakly coupled case; but in the strongly coupled case this way of first order analysis is not possible.





An example of strongly coupled spins is like this. There are two protons here, this and this. For example two protons are coupled with the coupling of 1.6 Hertz; and chemical shift difference is 4 Hz. You see very small value, even if you go to 500 MHz, it is only 10 Hertz. If you take the Delta Delta or J, if you take it is 1.6. This is not very much smaller than 0.001. That is what we should get for weakly coupled, it is very large value they are almost comparable, J coupling and chemical shift separation here are almost comparable. That is why they are strongly coupled even at 500 MHz. In this molecule these two protons are strongly coupled. Now I consider this one, I will not bother about carbon 13. Of course carbon 13 carbon carbon 13, we showed in the previous example. Now I consider the protons here, here two protons if you consider they are not equivalent; they are different. The chemical shift difference is there, but then the J coupling is much smaller and a chemical shift separation is also much smaller in this example.

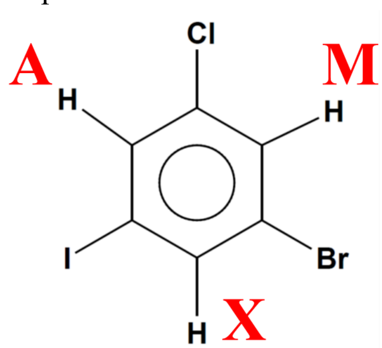


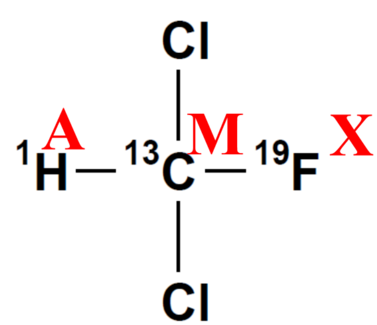


So I didn't give the values here but this is also strongly coupled these two protons are also strongly coupled like here. And again these two protons gives rise to a spectrum which \

are of different intensities. All the peaks are not of equal intensities. So this is what I was wanted to tell you about the strong and weakly coupled spin system, okay.

If you carefully observed or if you have understood already, I used certain nomenclature when I was talking about weakly coupled two protons I use the letters A and X, I said AX spin system. if you have noticed it when I was discussing about weak coupled spin case I use the letters A and B. I didn't use A and X. There is a reason for it. always we have to mention weakly coupled and strongly coupled by a certain nomenclature. There is a method for it you can't write a letter B and say it is weakly coupled. You can't write a X and say it is strongly coupled, No that's not possible. There is a notation, there is a way we can say the spins are strongly coupled or weakly coupled. This is what is called pople notation. I told you you have to understand this if you know the Pople notation you know whether the spectrum when you are analyzing you say whether the spins are strongly coupled or spins are weakly coupled. And how do you put your nomenclature for this?

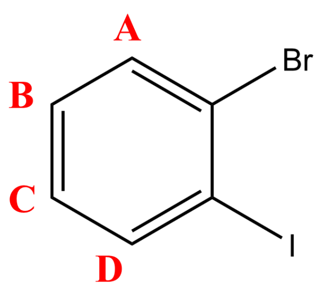


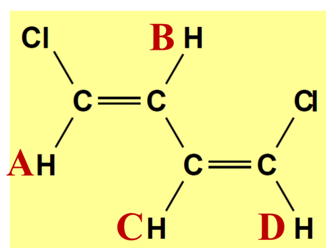


Each spin half nucleus of a coupled spin system, I am talking about spin half nuclei, I am not worried about spin one will discuss that later, of the coupled spin system is assigned a Roman alphabet. What is a Roman alphabet? like it A B C D E F G up to XYZ. All 26 characters you can consider. And then each proton or group of protons is given a letter. And then for a weakly coupled spin system, the letters are assigned that are far away in the alphabet order. Look at this one, A and X. I put it as X, X is far away from A in the alphabet order. That means they are weakly coupled. For a weakly coupled the letter should be far away in the alphabet order. If I put A and B, the letter is immediately next to that. That is strongly coupled. So for weakly coupled the letters to be assigned are far away in the alphabet order. And such a spectra are called first order spectra. The spectrum what you are going to get is first order, The first order means straight forward analysis is possible. The straight forward analysis is possible for weakly coupled. That means looking at the spectrum I can measure the chemical shftss and coupling constants fairly easily without going into more complications. Where as in the strongly coupled case, the spins are given the letters that are very close in the alphabet order. For example here, if you go here, AB is strongly coupled. ABC is strongly coupled. Here A and X are weakly coupled, A M and X if you consider, they are also weakly coupled, because M is far away from A and X is far away from M, and A and X are again far away. They are weakly coupled. AB is strongly coupled, ABC is strongly coupled. This is how you have to put a nomenclature for the coupled spin system, first order and second order. The weakly coupled spins gives you first order spectrum, the straightforward analysis possible and strongly coupled spins gives second order. There is no way you can analyze in the straightforward way. You have to use quantum mechanical calculations Although I showed you simple two spin case, we get like this, four line pattern with two central lines of higher intensity than the two outer lines. But then, even the intensity we have to calculate. It is not easy, you have to do some mathematical analysis. So the second order spectra are not easy to analyze. You have to do the quantum mechanical calculations or numerical simulations you have to do. So that is the thing you must understand for strongly coupled and weakly coupled spin system. How do you put the letters and this is called Pople nomenclature, The nomenclature is very simple to mention. What does the nomenclature you can think of for weakly coupled spins. If you have a two weakly coupled protons it can be AX, if there are three weakly coupled protons you can call it AMX, four weakly coupled protons AMPX, etc. And in general, as I said spectrum of even AX spin system four lines we can analyze, AMX gives 12 lines we can analyze; AMPX gives you 32 lines, that is also easy to analyze. Very easy straightforward analysis gives you the chemical shifts and coupling constants. No difficulty. We can easily analyze. The weakly coupled three spins for example is like this, because of different substitutions here the chemical shifts of all the three protons are entirely different.

One is here, other is here, other is here. Very well separated peaks. Each of them will be split. A will split because of M and X will give four line pattern. This gives four line pattern, this gives four line pattern. But remember they are far away separated. This is far away separated from this, this is far away separated from this, and these are further separated far away in an example like this in this molecule. These three protons form weakly coupled AMX spin system because three protons, homonuclear, are weakly coupled spin system. For example in this case, I have taken three spins coupled among themselves, three nuclei, A is proton, M is carbon and F is Fluorine. Of course, all the three heteronuclei. I already told you the resonating frequencies are separated by several MHz as a consequence heteronuclei are always weakly coupled. When I say this proton carbon fluorine are coupled among themselves. These spins you can call it AMX spin system, weakly coupled. So it is a heteronuclear three spin weakly coupled. It is a homonuclear three spin weakly coupled. But two main conditions for either of them is chemical shift separation should be very much larger than the J coupling. That is what we are seeing in both he examples.

If you go to the nomenclature for a strongly coupled spin system how do we give the nomenclature I said, AB, ABC, ABCD, etc and the spectrum of strongly coupled spins cannot be analyzed by first order methods. I told you already. I showed you the peaks are of not identical intensity, there will be different intensitities and the chemical shifts cannot be obtained easily/ The individual chemical shifts you don't get, you get only the difference of chemical shifts. I know what is the difference between chemical shift of A and B, but I do not know the chemical shift of A, and I do not know the chemical shift of B. It is not possible to obtain,





A simple example of a strongly coupled spin in this molecule these four protons are strongly coupled called ABCD. This is another example ABCD, strongly coupled all the four protons here are strongly coupled because the chemical shift separation among themselves are much much smaller compared to J coupling. So this is how all the protons here are strongly coupled. Okay so far we discussed for the individual protons, both individual heteronuclei, how we can give nomenclature for homonuclear and heteronucleic spins for both weakly coupled strongly coupled spins, fine.

You can ask me a question what happens if there is a chemical equivalence? what happens if there is a magnetic equivalence? what happened if there are groups of spins like CH2 CH3 group? how do you put the nomenclature? How does that NMR spectrum come? Ghere are nomenclatures for that also. We will come to that later, we will discuss. That is an extensive discussion. We can do but at the moment this is a time is getting over. I am going to stop here today. I introduced to you about what is a spin system, what is a coupled group of spin system. I said there can be N number of protons coupled among themselves, N number of nuclei both homonuclear nuclei can be coupled among themselves. That forms a coupled spin system. One of the coupling can be 0, doesn't matter but it must be a part of the coupled system. If you consider three protons 1 2 & 3; 1 2, 1 3 and 1 3 are coupled. One of the coupling may be 0; but there could be 1 3 coupling may be there, 1 2 may be 0, but that is a part of the system because 2 3 coupling is still there 1 3 coupling is there; so that is a coupled spin system.

The coupled system can be divided into two groups, classified into two groups, strongly coupled and weakly coupled. Weakly coupled is the one where chemical shift separation is larger than the coupling constant. The strongly coupled is the one, where the chemical shoot separation is smaller or almost equal to coupling j coupling between the interacting spins. And then weakly coupled spins, I said easy to analyze straight forward analysis of the spectrum is easy. All the peaks are of equal intensity. All the multiplicity lines which are split because of various couplings. Whereas in strongly coupled case intensity of the peaks are not of equal intensity, and strongly coupled case cannot be analyzed in the first order way. In the strongly coupled case you cannot get the chemical shifts, the individual chemical shifts. You can get only the difference in chemical shifts. Whereas in the weakly coupled case chemical shifts and j coupling can be obtained in a straightforward manner, very easy. And I said the nomenclature for the weakly coupled spins are the letters tjat are far away in the alphabet order. In the roman alphabet each spin half nuclei is given a roman alphabet and weakly coupled means the letter should be far away in the alphabet order, strongly coupled means that they should be close to each other, like AB, ABC, ABCD are strongly coupled. The weakly coupled nomenclature are, AX, AMX, AMPX. I took the examples of couple of molecules to show you how the chemical shift separation will be there, how the j coupling between them are there; how they are strongly coupled or weakly coupled. We understood in the given exam[les, whether the spins are srongly coupled or weakly coupled. With with this I am going to stop here. With this I have given you Pople nomenclature. We will continue with the Pople nomenclature and type of the spectra we get for strong and weakly coupled cases, when we have chemical equivalence, when there are group of equivalent spins etc in the next class. Thank you very much