Hello, welcome to an NMR tutorial on NMR multiplicities and splitting our why is our signal that shape? Just to outline what we're going to talk about. I'm not going to talk about chemical shifts. I believe you're already familiar with that.

instead, I'm going to focus on splitting patterns So if we see these signals here We're going to talk about why they split, why the couplings are the size they are, why the late intensities are as you see. let's talk about how these splitting arise, what influences them, and what information we can gain from them. I'm also not going to talk about why these aromatic protons are written nearly 10 ppm. But maybe we'll come back to that in a later talk. So the format's going to be a quick summary of how NMR works. Some discussions of the origins of splitting. And then finally what influences the observed j values. So let us start with the concept of nuclear spin, which is the origin of NMR. Some nuclei have spin, and this is a fundamental property denoted by spin quantum number. This is a physics analogy, has nothing to do with the spinning of football or cricket ball, tennis ball or whatever. That said. If it helps you to think of it that way, feel free. Before we move on, I just wanted to point out that organic chemists usually talk about electrons. And although they are relevant to this topic, we're going to focusing today, at least at the start, on the nuclei. So nuclei with non-integer spins: a half, 3/2, 7/2.. Are NMR active. However, the nuclei normally of interests organic chemists are spin 1/2, which is good because it makes our lives much simpler. So examples of this include protons, the carbon-13 isotope. Fluorine and Phosphorus.

Phosphorus. A spin half nuclei has two orientations plus a half and minus a half up and down if you prefer. In the absence of a magnetic field, in theory equal quantities of each. Ijn the presence however of a magnetic field. These are aligned with and against the field, like the tools of a magnet. And you can see here, how did this energy gap grows as the magnetic field gets stronger. This is called the Zeeman effect. And this changes the equilibrium position between these two spins and creates an equilibrium where there is a small preference towards aligning with the field. And this results in a net magnetization. A radio pulse then scrambles this distribution. And energy must be lost to return to the equilibrium position. And it's this process that we record and turn into NMR spectrum. So to go over that in a little bit more detail, here we have three spin 1/2 nuclei. And we're going to add to that 2 minus 1/2 (-1/2). And this gives us a net polarization in line with the field along what we call the Z axis. I should say here the preference in real life is much smaller than that. It's maybe a 6 atom preference in a million but it's enough. Okay?

Okay? So in reality, the nuclei can't orientate just straight up Z axis and they precess around this in a circle but the bulk magnetisation is still on this axis. We then use radio frequency pulse to generate a magnetic field at 90 degrees. And this flips this orientation. So it is now in the x or y axis. It will then precess around this circular fashion, returning to equilibrium. That's the relaxation process. And in doing so it generates magnetic fields, of its own those we can record. And use for the NMR spectra. This is a bit clearer, I think in video form So here we have polarization, then flip into the y axis and precession back to the equilibrium magnetisation. So to recap, magnetic field makes our spin states inequivalent causing bulk magnetization. We then push this from equilibrium, through a radio pulse to an excited state. How does this compare to other spectroscopy? So for example, in absorption spectroscopy, we measured absorbed energy and we correlate this to the presence of bonds or electronic features. In fluorescence, we instead generate excited state and we measure a photon which is re-emitted in the relaxation process. This process is quite slow and we can only see fluorescence for some molecules. This is a sort of general feature, actually, spontaneous emission being somewhat slow and it is actually energy dependent, is dependent on the inverse cube of the energy, and NMR transitions are quite low in energy, and therefore. Spontaneous relaxation is actually very slow. Instead, relaxation occurs via interaction with other magnetic fields, be that imperfection

in the NMR field, or the presence of other magnetic fields from other nuclei nearby. So this seems like a good time to mention spin, spin coupling Spin half nuclei within a certain range can interact with each other. And this happens through electrons and therefore through bonds. Let me give you a quick example of what that looks like, here we have hydrogen molecule. And in the absence of any magnetic field, we can see that these actually prefer to be in an antiparallel spin state because this allows them to spin paired with the electrons on each side of the bond better If we then add an atom to the bond and go to this germinal type system I'll explain what that means in a moment, Then the principle is the same, but you want parallel spins which is favored. If you take it an atom further. You then end up back in an antiparallel system So the range of this varies. But wto bond, which are called germinal couplings, and three bond, called vicinal couplings, are common for protons. Where orbital overlaps is better, Like in conjugated pi systems, the information is transmitted between nuclei better and you can get longer range four or five bond couplings. And because all of these pair of spins still still have themselves +1/2 and -1/2 spin states, They then cause a split in the signal. I'll now talk about what that means So to depict the simplest possible example. Coupling within a hydrogen molecule. In the absence of a magnetic field, which we can see. Here, the spins are degenerate and the energy is the same. Applying a magnetic field splits these. Since NMR measures transitions, there is one transition here and there's a single line which is a singlet So if we then introduced the other atom so now we have two hydrogen atoms, which is a hydrogen molecule. There are now multiple transitions available. So you can go from here to here. There is a feature that you generally only see single quantum number transitions. So here you're going from plus one to 0 if you adopt the halfs and minuses. And so this is allowed, but you're not, at least in this system, going to be seeing that. As a result of this. The nuclei being identical means that the transitions within the more complex splitting are actually all identical. This still gives you singlet. Let us look now at an AX system. The A and X just meaning the chemical shifts of the two protons are quite different. This is a three bond vicinal coupling. All of this bit is as before. So we have splitting caused by the magnetic field, resulting in transitions between spin states. Both of our nuclei of interest here on the same diagram, but don't couple them. Then we can see each in this case gives a different translation. These are two signals with different chemical shifts. However, if we look at the transactions available to atom A, which is here in green, in green. And then the transitions available to atom X, purple here, and purple here, although they are not different between the purple and the greens, both of the greens are equivalent transitions and both of the purple are quivalent transitions, they have the same energy. And so only singlet is observed for each nuclei. And so you see two singlets, at different chemical shifts. Now let's consider what happens if we couple these. So in the absence of the magnetic field, because our nuclear spins like to pair with the electrons, as previously described, this is the lowest energy spin configuration. Its Anti parallel.

When we apply a strong magnetic field, The preference will still be to align both of the spins with field. However, because it gives us a less favorable spin interaction with our electrons, this is a little bit less favorable than was previously. On the other hand, both of the antiparallel arrangements are a little bit more favorable than they would previously have been. And then the alignment of both spins against the magnetic field is unfavorable because you're having to overcome both the unfavorable alignment with the magnetic field and the unfavorable electron pairing. The result of this distortion is that if we look at the two green lines for the A system and the two purple lines with the X system, we will see that there is now a pair of inequivalent transitions for each And this results in each nucleus gives us, giving us two lines. So we see a doublet, different chemical shifts for each. If we consider the energy of that. As a happens, the distortion of each of of these configurations, from the uncoupled energy value is a quarter of J. Now, if we start by considering atom A, you can see that for this transition, this antiparallel state is 1/4 J more favorable than before coupling And this state here

where both spins are aligned against the field, is a quarter of a j less favorable. Result of this is that the overall size of the transition, is 0.5 J larger. We then compare this to the other transition. Exactly the opposite is happening. This alignment with the field is a quarter of a J less favorable than previously, where this antiparallel arrangement is a quarter of J more favorable. The result of this is that the energy of this transition is half J less. This means difference between the two lines in total equals J. And what you can also see from this diagram, if you consider instead x, is that although the transitions themselves and the resulting chemical shifts are different from the observed for A. The difference between the two lines produced is going to be the same. So you also end up with the J value as difference between these two lines. And as a result, when you see your signal. It will also be a doublet, and it will have the same J value and these are coupled. Let's take an example using ethyl acetate here, common solvent. And I have simulated the spectra. And we'll start with this acetyl group here you can see a proton. We can count 1,2,3 bonds, there are no spin half nuclei within three bonds. discounting the small prevalence of carbon-13. And as a result, these three coupled to each other, but that all cancels out and we see a singlet, a single transition everywhere. If we were instead, to take the other methyl group, here: Again, you can ignore the equivalent nuclei: 1,2,3 This couples to these two protons here. These are equivalent to each other, not to this. Now if we look at how we can arrange the spins of these two protons, we have the parallel and in line with field configuration, that's the lowest energy. And we have against the field configuration, that's the highest energy. But there are actually, there is an intermediate level and there are two ways to achieve it, because these states are degenerate. Because it can only be achieved in twice as many ways. This transition occurs twice as often. So when we look at the lines, we get intensity patterns and it goes 1-2-1 and gives us a triplet. If we then use these methylene protons here. So you focus on this one. Again, ignore the proton, that is equivalent.

1,2,3 Split by three equivalent spin 1/2 nuclei. Same principle holds, but this time, there is one more way of arranging these spins so you can have two aligned with the field and one against, or two against and one with, and again, these can be achieved in more ways. So now you have a pattern that goes 1-3-3-1, and this is a quartet. Now, we really don't want to have to construct spin diagrams every time we need to understand that intensity pattern. Fortunately, we don't have to: we can use Pascal's triangle. So this is a scheme where the sum of the two numbers directly above gives the number below. So if you want, you can draw the 0 here, 0 plus one gives 1+1 = 2, and so on. Four plus 6 gives 10, 10+5 gives 15 15 plus 20 gives you 35. And in principle, so on all the way down to infinity. As it happens, we can take each number and we can consult the triangle. Consult the row equal to one more than the number of protons we have splitting. So n plus one, the doublet you have one proton splitting. Two lines: row 2. You can see a one-to-one ratio. You can instead actually just looked are actually the number of lines. So triplets, row 3. And you can see one-two-one. And this continues all the way down. A quintet is row 5, 1-4-6-4-1 and so on. You really not going to see very much beyond this distribution in terms of splittings that are a single level don't involve further coupling. So in fact, you might already, if you're looking particularly closely, have been a bit thrown by the sextet. This is because the Sextet should arise from five equivalent protons. Now you can't attach five protons to a carbon and you actually can't draw a symmetrical molecule. That splits five protons. So if I was to give you an example here and say this is CH3, this is CH2 and R There's just no way. That actually these are equivalent So I have got this particular signal simulated from butanol And it's this proton here. And it couples twice there, to give you a triplet and three times here to give you a quartet And this signal can also be considered a triplet of quartets where the J values are close enough that they overlap to give you this sextet. And in fact, this is a sort of general principle. You can construct signals to this way. So two doublets if they are separated by the j value. So you have another coupling of the same J value add up to give you a triplet.

Two triplets = quartet. And you can see you can add the line intensities and get correct numbers. So a quartet arising from interactions with three protons.

Here. There we have it, is equivalent to double of triplets. And you can actually see this if you replace one of the protons with a fluorine you're seeing coupling to the same number of spin half nuclei. But this J value is quite different, and what results is a doublet of triplets. Where here we had a quartet.

Origins. are the same, the differences are in the J values. And in fact all of these composite signals, doublets of doublets, doublets of triplets, triples of quartets wherever, are constructed in this fashion. I just want to leave the slide with a particularly beautiful example. This comes from Anstey group in Davidson College. And I'm just going to mark out there is two quartets here, they're easy enough to see, but I will just mark them anyway. And why I want you to do is easy enough. In your head is just imagine that you move all of these. One place. I think it's quite easy to convince yourself that what in fact you'd see is a quintet with the correct intensity distribution. So we now understand, I hope where J values, the splittings come from, but what controls there magnitude? Why do we sometimes get large J values and other times small? Well, as we've already said, the spin pairing is mediated by the electrons in the intervening bonds. Good orbital overlaps provide strong interactions and larger J values. Weaker interactions and long-range couplings are usually weaker and give low J values. Now, the relationship between Dihedral angle and J value for vincinal coupling, so that's this 1-2-3 bonds coupling, Is described by the Karplus equation.The Dihedral angle is just the angle between these two. And we can see for very low values, 0, the overlap is good. These are parallel and you big J value somewhere around 13. If however you flip this proton here 90 degrees. Orbital overlap here is really quite poor. And you end up with a much lower J value, something around 2.5 perhaps. However, as we push on back up to 180, again, this is an antiperiplanar arrangement. This is favorable for overlap and we get nice big J values. Something I'm going to come back to in a later tutorial. I'll mention just briefly here, is that NMR is a slow technique. So what you usually, although not always observe, is actually an average of conformations. And in the case of a chain like this, the observed j value is consistent with an average of the most common conformations. The conformations the molecule spends the most time in. And I'll be 60-180-300 degree conformations. So you end up with a J value, actually somewhere around seven. If however it was fixed in a ring system, then it wouldn't be able to rotate. And we would be able to tell a lot about the arrangement of protons from the J value. And just in general, coupling constants tell us a great deal about spatial arrangements. There are some other things that matter: electrons on a carbon adjacent to an electronegative element are pulled in closer and they're less available to Facilitate coupling. This results in lower J values. So here we have good overlap between this oxygen and carbon-hydrogen, so on. And as a result, it really inhibits the coupling and you end up with a low J value between these two. If you actually take the same geometrical arrangement between the hydrogens here, but you move the oxygen into position where it's less able to interfere, you've got much larger J value. And I would point out though this is still considerably smaller than you'd have if the oxygen was gone entirely. So geometry still matters. The better conjugated the withdrawing group, the stronger than the effect. Bond length is also important. So this shorter pi bond here is able to transmit information between the nuclei more effectively. Than the sigma bond that you have in between here. And there's a big difference in theJ value As a result. Angle strain can be considered a kind of special case of the geometry story. But here, this is illustrated quite well by the series of cyclo alkenes. You can see for the more smaller rings the more strained configurations, the protons are kept in an almost a V-shape. And if you imagine that there's very little opportunity for the bonds to really overlap in this arrangement. But as you make the ring larger, this angle, the theta and theta prime angles, shrink and the overlap is improved and you

go from a J of 0.5-2.0 to right up to a much more sizable 8.8 to 10.5 Hertz observed in this system here, Cyclohexene.

Just one more thing I wanted to mention. This is true for homonuclear couplings. If were heteronuclear couplings, for example, the hydrogen fluorine coupling. We saw earlier, you do have to consider the nature of the other atom as well. So fluorine will tend to produce larger couplings. Aside from any other considerations. Now we have looked at, both intensities and J values with regard to the information they give us and how they inform us. But conductivity of a molecule, I'd like to introduce a formalism which is generally very useful. And this is the splitting tree. So the idea is that we mark the lines in our signal and we measure the gaps between them. And this gives us our J values, seven. And we can see that this one matches. We recognize the shape of the signal. Intensity pattern is correct.

Intensity pattern is correct. This is a triplet. If we alternatively wanted to draw it as a doublet, of doublets it, say this is seven. And as it turns out, this is also seven. that's why its a triplet. Here we can see that we're layering our couplings in the tree. To give you an example with J values are not the same, Here we have central green proton here, It has two ortho couplings here. Small coupling. And if we wanted to find the large doublet, here, that would be the center point between these two signals that are split from it. However, we don't need to actually measure the center point because that spacing is the same as the spacing here. So we can take these lines. as the spacing here, and measure this, and that is our second J value for 7.5 Hertz. We then move around to another signal. This could be either red or blue. We have a large ortho coupling and a small meta coupling. Here is our small meta coupling. And again, we don't need to look for centre points. We can measure the gap here, same as that gap there This gives us our larger coupling of eight Hertz, same with that gap there. For a slightly more complicated example, this looks a lot like a sextet. But there are only 4 coupling protons. So this is a bit alarming because we know there should be five to get the correct intensity pattern But then if we look at the intensities for a sextet We should have 10 and 5 and 1. And you can see the signal is not twice the size, of that one. And in fact, this is not a sextet, its a doublet of quartets So there is our quartet J value, we can distinguish that this is the quartet from the intensity pattern. And then to identify the second quartet, we can see that here we have the first two lines of the quartet. We would expect another three here. However, what we have is four. And this is because the first line of the second quartet is being added on top. And so here is our J value, which is the equivalent of This space. You don't have to use the edges. So you could equally use that. Let's look at different quartets now. This one has a small coupling, and the large one, it looks much more like double of cortex. Again, here's our small coupling it is 3.5 hertz. And then we have a huge coupling And it's much easier in this case for us to pick them out. These are all equivalent. They will all give as our second doublet coupling. Here. You may have noticed that this is not technically a doublet of quartets. Actually it should be a doublet of doublet of doublets of doublets, with our large coupling from this geminal coupling here, And then axial-equatorial and equatorial-equatorial couplings to these other protons. However, these J values are close enough that they overlap and we get something that looks like this doublet quartets. Another doublet of quartets. This time, the doublet is the smaller coupling. So again, so this is a proper doublet of quartets this time. We have axial-equatorial coupling, we would expect this to be small. Remember that the angle is not ideal for orbital overlap and so the J values are relatively small here. And here is the first line in our first Quartet. But instead of having a three beside it, we have another one. And this means that this is the second quartet. And this time, this is our doublet splitting. And if we want our quartet splitting, actually going to have to go to here, And it's this space. And it gives us a larger J value. And so we have three same examples of the same signal here. And we can distinguish what they are and their connectivity from them, from the shapes and the J values. Here's yet another example. This differs from the

previous, only in flipping Whether the doublet or the quartet has the larger or smaller J value. And you can see you end up with a completely different pattern. Again, we're something that looks like a sextet, but isn't. And here, the larger of the couplings is our doublet. And the axial-equatorial and equatorial-equatorial, couplings that end up looking like a quartet are small. So there is our quartet J value. And here again is our doublet J value. And these signals can be distinguished and you can distinguish these connectivity patterns from each other based on these signals. So we're getting really quite a lot of detail about how the atoms in our molecule are arranged with one another. There are limits. There are limits to what you like to be able to personally work out. I would suggest not bothering with this one. For example. There are also limitations that you should bear in mind. When you take real spectral data. These are simulated, and so they work out perfectly. There are other factors. Measured J values rarely match exactly because the lanes are varied thickness and they can become distorted. We can have other protons underneath and they can display other phenomena that we will cover in later talks such as roofing, second-order effects. That said, when you get good spectral data, it is quite often the case that you end up with quite distinct complex signals that you can interpret and tell you really quite a lot about how the molecule is connected. And this is the real advantage of NMR. There other techniques that can inform us on functional groups are overall molecular properties. What the NMR gives us is the connectivity. I am of course available for questions. But here are some other resources I think you might find useful.