So today I'm going to go through the NMR Rules. So these are rules that are probably not going to be written down specifically in many textbooks or websites. But these are a compliation all looking through those websites and textbooks, etc. And this is a means for anybody to be able to understand how to interpret at least a 1D spectra. So these rules are just more like guidelines. They can be elaborated on further. But here I've picked out the key points. Your spectra, your proton spectra is composed of protons, otherwise known as hydrogen's. And what it does is you proton spectra is like a summary of all the other possible NMR experiments that could be run. For instance, like some 2D experiments, like your COSY experiment, for example. And what the proton spectra has the ability to do that if you are able to attempt to interpret it correctly, you can actually start to divulge further into your structure and be able to understand a little bit more than maybe directly what the proton NMR is telling you. So for instance, it can tell you what environment your proton in. Is it next to something that's electronegative or is it next to another neighbouring proton? And if so, what does that proton look like? What is really cool is the NMR produces lines? It doesn't produce a picture, so it produces something that looks like this. On the chemist has to interpret these lines by following some of these basic rules, and they end up with a picture like this. Now you're looking at the two going, yeah they don't look the same. They look different. So what I'm gonna do is I'm going to explain to you how you make this transition and that you can be able to view your picture. So moving on from there you need to know a few things: your spectra. What does it look like? So your spectra typically runs from left to right. You have a downfield region, which is located on the left-hand side, and you have an up field region that's located on the right. So let's start with the downfield region. The downfield region. This is where nuclei that absorb here are found to be what is known as deshielded. And what I mean by deshielded, Deshielded are nuclei that have had something taken away from them, removed. And in this case, we like to speak about electrons. So where electrons are pulled away from this nuclei, you find that the nuclei actually absorb in this region of spectra. Whereas its opposite is where you find upfield. These nuclei are known as shielded and shielded just means that the disturbance all these electrons is not very significant. And therefore they can be found in this region here. I would like to highlight as well, I've also called regions of the spectra as outside, as well as inside of the spectra. And what we do when we discussed this in the following slides. So things that you must remember before you start interpretating your spectra, carbon, carbon is totally neutral in this case. So just think of it as it doesn't have the desire to steal anything from anybody. And in doing so, it doesn't influence where your peak start to fall in relation to your spectra located at the bottom. Atoms however like the electronegative nitrogen, oxygen, and even some halogens, they like to steal electron density from their neighbouring protons. So like we discussed in the previous slide, if you are stealing something or you are deshielding it, you are moving in this direction of the spectra. You are moving to more of the downfield region. The same is opposite. If you are not stealing anything, for instance, like this carbon species, you are therefore staying within the upfield region of the spectra. There are two things I have written here outside, and I have also written here inside. What do I mean by this? So outside, I want you to imagine that you are somebody wearing an awful lot of clothing and you were standing outside. If I am, for instance, bigger and stronger than you, I want to take some of your clothing and then doing so, if I take some of your clothing, I'm stealing your electron density as it where. You get cold and you start to move inside of your spectra or inside a house or inside a building etc. The more layers of clothing I steal from you, the further and further inside the spectra I come. And this seems to be quite a weird technique to explain. But over the years of teaching this, I found this is actually to be quite effective for teaching people who are not chemistry related to get them to think about this inside and outside of your spectra. So rule number one, let's start with the rules. Let's make it, it's all about the rules. So your regions of your NMR. These are some things to pay attention to. So we're going to start off quite large and then we're going to break all down into the finer bits of detail. So this is us starting

quite large. Your spectra and a proton runs typically from 0 to 12 or 12 you can find is the most deshielded. Which means you're in the downfield region and 0 is where you can find the upfield region. Now, the spectra is measured in ppm, otherwise known as parts per million. You have your region, so I blocked them off in 3s. So 0, 3, 6, 8 and 12. And as you can see here by looking at this thing, the structures that I have written in these different areas, you can see you're becoming more and more electronegative as you start moving along a spectra with the most electronegative being your acid and your aldehyde. What do these two groups have in common? Well, they have this in common, the carbonyl species. That if you are familiar with your chemistry, the carbonyl species, the oxygen steals electrons from the carbon, and in doing so, it creates a pull on the bond. In doing so, you get what is known as a partial negative charge and a partial positive charge. Ignore my my really horrible attempts to draw on this. You get partial positive and a partial negative charge. This is signifying the carbon has lost something and the oxygen has gained something. You have your aliphatic, which are typically your CH3, your methyls. It can be long, long chains, for instance, like heptane, hexane for instance. You then move in your region of 3 to 6 and you find that you start to incorporate some of this electronegativity through double bonds, for instance. However, was not written on this diagram is actually the heteroatoms will go to the heteroatoms fall. Heteroatoms tend to fall between the regions of 3 to 6. However, depends on what the heteroatoms attached onto that can be found closer to 3 or they can be found closer to 6. And how do we determine if something starts to move within each region? Well, we will discuss that later on. So for now, just remember the regions of the NMR. We started off with heow to start tp interpret our spectra. Moving on to the next important rule, rule number 2, peak splitting. So I said to you that the NMR can tell you how many neighbours does another proton atom contain? Is it something that doesn't contain any neighbours or something that does. And if so, what sorts of environments are they in? So right now what we're gonna do is we're going to actually start to discuss this, what's known as peak splitting. We want to find out how many neighbours and there's a general rule of thumb. The n plus one and n stands for the number of neighbouring protons. And then we add on the additional through plus one. I want to actually tell you just now that it is beyond the scope of this tutorial, to explain the shapes of these peaks, for now, we are just discussing how peak splitting occurs. So let's take our first peak for instance, here we have two. So after writing out the formula of n plus one, and we say that a equals two. Again look at this shocking. And that is the best I could do on this one. Okay? We find out that n is actually equal to one. So if this peak splits into two, we know that the number of neighbouring protons that this proton can see is 1. And is this true? Yes, it would be to look at it, it contains 1. By looking at the next, we see that it splits into 4. So using the rule of n plus one is therefore equal to 4. We know that this species has 3 neighbouring protons. And the same could be said for the last peak where it splits into 3. That it's n number is actually 2 so it contains 2 neighbouring protons. So let's now start to divulge into where do they start to fall in the spectra? So we've looked at regions, and we've also looked at how they split. So we start to talk about the electronegative atoms. And what this is, depending on the shielding and deshielding effects, depends on where they fall within the spectra. So the more electronegative, which means is taking electrons from the bond or stealing or has a greater pool of these electrons, you will find this becomes more deshielding. And I said to you deshielding fals more inside your spectra. So over in this region here or downfield, otherwise known as. So let's take our first species to look at. Here we have ourselves a CH3. CH3 is attached onto an aliphatic chain. So automatically we should be thinking in this aliphatic chain, it should fall within the aliphatic region of 0 to 3. We therefore then start to say, okay, well, what are its neighbours? So let's look at its neighbours. We have here a carbon species, this carbon species contains 2 hydrogen atoms on it. So we are drawing here. Now we use the rule of n plus one. So we know the number of n this time for these blue CH3. We know that its number of neighbours is 2. So 2 plus 1. Therefore, this peak should appear as 3. Where should it fall? Well it should fall within the region of 0 to 3.

How close to 0 to 3 is determined by what it's also attached onto. Carbon as we said before, is a has no desire to steal anything. So therefore, if there's no pulling power on this bond here, therefore, this peak should fall closer to 0 than it should do to 3. But let's take
another example. Let's start to look at these electronegative atoms. Here we have ourselves this methyl group which knows touched on to the oxygen species. Let's do what we did before. This methyl group is still an aliphatic, so it should still fall within this region of the spectrum. However, this time, let's now look at our next rule which was peak splitting. How many neighbouring protons does this group see? And here the carbon is being replaced by an oxygen. Therefore, it doesn't see any. So using the rule of n plus one, we should therefore see one single peak within this region of 0 to 3. However now the NMR can tell the difference between that this one was connected to CH2 and this one is now connected to an oxygen. So an oxygen is electronegative. It is pulling on the electrons from this bond, it is stealing what does it belong to it. And in doing so, it's starting to deshield these hydrogen atoms here. In doing so, would it be closer to 0 or wouldn't be closer to 3? Now, using our knowledge of previous, we know that it should start to move further up the spectra as in towards the downfield or inside region. And in doing so, we expect that this group should start to fall closer to 3. So taking a look at it in the next slide, we see that we do have a single peak as we discussed earlier. And the single peak is indeed actually found closer to 3. But this doesn't stop here. So let's take a look more into these electronegative atoms. You've got OH, you've NH, you've got SH. And these are known as exchangeable protons because the exchange is very rapid, we don't see these nice peaks, clean peaks that we see here. What we see is we see what is known as line broadening, or we see these fat and lazy peaks as if it were. And what this happens is this is identifying that you have an exchangeable proton in your spectra. So anytime you see something like this in your spectra, you should be flagging up by saying, hold on. Actually, I could have one of these elements present in here. And if so, which one is it? So taking care, we have the example benzoic acid. And now what we're doing is we're focusing more on this OH, now this OH, is attached on to the carbonyl species, and we said before. So let's start using our rules. Rule number one, where in a spectrum with this fall? We knew the acids fall between 8 to 12. So we're talking about this region here. That's fine. We then said, okay, peak splitting, how many neighbours does it have? And we look here to say, actually it doesn't contain any neighbours. It's got a carbon which is attached to the oxygen species. So therefore should only appear as a single peak. Because now we know the OHs are exchangeable protons. We may see a single peak, but we may also see this line broadening because the exchange of these protons are very, very rapid with the sample. And in doing so, any water So this is also another rule as well, any water that is present in the sample can also cause this exchange. So what happens is this proton becomes exchange with the water species in the sample. And in doing so, the NMR is detecting this exchange. At the exchange is rapid and you are not going to see much of a peak is a nice sharp peak. You're going to see one of these broad peaks here. So this also takes us onto our next rule. Our next rule is solvents. Now you don't want a lot of water your sample. You might see a lot of this exchange occur, might never see what it is that you're truly wanting to see in your molecule. Does it have an OH? Does it have a NH? You might not be able to see this because sometimes that line broadening can be so broad, that your peak actually merges with the baseline and it's not possible to see it. I love as well I'm also hand gestures and he can't see anything with my hands. So moving on from here, solvents. If you take one milligram of sample and you dissolve it in 500 microlitres of a given solvent. So let's, for instance, think about methanol, ethanol, chloroform, dichloromethane, DMSO, is they all contain protons on it. Which one do you think the NMR's going to be able to see? Your compound or the solvent? And the answer should be flagging to you straightway. It's definitely solvent. I mean, there's so much of it there and you'd be correct. The NMR would become completely saturated by this solvent. Now that's not really good for us because we want to be able to see our compound. So what do we do? Well, what we do in NMR is we exchange out all of these hydrogens

and we exchange it for the element deuterium. Now what is Deuterium? Deuterium is heavy hydrogen. So another little rule to remember is that proton NMR can measure spin states of a 1/2 3/2, etc And what do I mean by this? So with deuterium, deuterium contains a proton, but it also contains a neutron. And in doing so, it now has a spin state of one. Because my spin state is not 1/2 or 3/2, which is like to be seen for a proton. What happens is here is that it now becomes NMR silent. Anything that contains a deuterium, the NMR cannot read it. So this is how we manage to eliminate the presence of solvents in our sample so that we can read purely just our compound of interest. More detail into where you can find about spin solvents is, sorry, spin states and what the NMR can actually read, can be found in later on tutorials, but it's beyond the scope just now to go through this. So the next rule, another major and most important one is equivalent protons. So, so far, we've gone through our spectra. We've looked at all the different regions in the spectra. We then said, but how did our peaks look to us? How did they split 2, 3 , 4 peaks, for instance. We've then taken a look to say about exchangeable protons. So these are things that polar atoms that we see in quite an awful lot of drug molecules. And then we then started to talk about solvents where we say, well, how do we actually read from the spectra? And now what we start to look at is the equivalent protons because there are some compounds out there that have areas in it that are symmetrical. They have identical regions on it. And the NMR can actually detect these identical regions. It might not be able to distinguish the differences between both of them, but it can tell you that it's present in the sample. So let's look again at benzoic acid. Benzoic acid. If I was to draw a line of symmetry through the middle, I could see that the hydrogens are located and blue are identified and blue identical. I cannot tell the difference between this one or I cannot tell the difference between this one. So the NMR detects this and the NMR stays well, actually, I know that both of these are within the same distance to this carboxylic acid group. And therefore, I'm going to put them together. So for instance, if I'm going to draw on extra hydrogens, so let's just draw on the rest of these hydrogens onto this aromatic ring. Again with my beautiful, beautiful drawing. No laughing. So here, each one of these hydrogens, let's use the n plus one rule. How many neighbours do each of these have? And we look, and we say, this hydrogen species contains one neighbouring hydrogens species. So using the rule of n plus one, he should appear as two peaks. Let's look at this here. The number of neighboring groups is one using the rule then plus two that should appear as to Hobart cause they're both identical. The NMR merges these two together. And in doing so, it forms a peak that looks like this. This here signifying that you have two peaks. The highest peaks for now, we will not speak about just now the smaller peaks, again, beyond the scope of this NMR rules, but will be mentioned in later on tutorials. Here we can see the two major peaks that are 2, 2 peaks here. And in doing so, this is what we hypothesized. However, the NMR is able to read the two identical protons. And in doing so it creates this was known as an integration number underneath. And what it's doing is it's measured the idea of the peak. And it said the number of protons equating to this sample is two. So it's telling you that not only is there, each one of these has one neighbour, because the n plus one, but also its two protons are counting for. And because they have managed to merge together, they must be identical. This might look a little bit weird by looking at it from this sort of perspective. So let's take it back a notch. Let's look here. Here we have the starting molecule that we saw in the very first slide. We have an OH and we have an NH2 and they're located para substituted, which means 1 and 4 position of the ring. Like we did previous, if I draw a line of symmetry down so we can see that they're identical protons. And here, the red protons are within the same distance to the OH. And the blue protons are within the same distance to the NH2. And you can agreed by looking at it. The blue and red ones are not identical. They are different environments based upon these groups that are attached on either side. The NMR can read this. And the NMR then says, okay, the red ones have one neighbour. The blue ones have one neighbour. Using the n plus one rule, they appeared as two. And here the integration value, like we spoke about just in the previous slide, is saying to you that there are two protons making up a

sample. But the protons have only one neighbour between them. Again, let's divulge and let's look at some more examples. So here. We have ourselves the aromatic signals. So here the NMR has the ability to identify substitution patterns on an aromatic ring. So aromatics, like we said before, we look between the ages of six to eight on the spectrum. How far they fall within this region depends on what they're connected to. So here we have our aromatic benzene ring, and now we're going to start to look at substitution patterns when each one of these rings. But first, let's look at it here. So the

first thing to do is when you get a structure, start to identify all the protons are not spectra. And what to do is categorize them, which ones are the same and which ones are not the same. So here we have a methoxy group attached onto our aromatic ring. The red protons are closest to the methoxy group. So appear as one group. The blue protons, you cannot identify the difference between either in the same environment. So this is group number two, and the green ones are group number three. The green one is on its own. Now using the n plus one rule, the protons in red have one neighbour, the blue, and therefore appears as two. The blue protons have two neighbours, the red and the green, and what therefore appear as three. And the green protons have two neighbors, although they are identical, but it still has two neighbors with therefore appear as three. So that's fine. However, something about the order at which they fell. Why did the blue burns come first? Why was it followed by the green and why was it followed by the red? So what we can do is we can actually take a look at another example here to help us. So here what we've got is, we've got ourselves, our acid again, but this time that we have now made it an ester for the sake of. So we know how to start to categorize these. So these are categorized into groups and the details of which will be given because we've just discussed them here. So the splitting is identical. Look at the splitting. The red continues to, the green contains three and the blue contains three, the same as can be found in this example here. However, look at the order. Why has the order changed? And this is where we start to look at electronics. What is the substituted group doing to that ring? The oxygen contains a lone pair. And in doing so, this lone pair feeds into the ring. When it feeds into the ring, it creates a partial positive and a partial negative charge. The partial positive on the oxygen. And the oxygen will now resemble to Barnes to your right. We do like so. That's the best I could do for the ring on this one. And in doing so, because the arrows have moved onto the next neighbouring position, we have ourselves a slightly negative charge. So, what we can say is that there are more electrons present in this position than there are thats now attached to the oxygen. Through the resonance structure, if we start to keep drawing this, we will find that the negative charge can then move again and therefore now be found on the four position on the ring. So what happens is, is that when you have this electron donating species, as you see here, the positions that are affected are positions: ortho and position para. And in doing so, if you are giving electrons, so you're giving clothing to that species, they should fall more within the up field region of their spectra, six than they would do to eight because they had been given electron density. The meta position, which was located by the blue protons are not affected by this group being added. And in doing so, it remains higher up in the spectra are more downfield and spectra than the other two peaks. So let's take a look at its opposite. A carbonyl species should be said likes to pull electrons. Doing so, if there is a pulll of electrons, we again get this partial positive and partial negative charge. The oxygen now in this case gains the negative charge and the carbon species gains the partial positive charge. And in doing so, it's saying here, now, that the ortho position has lost electron density and the oxygen has gained. If we keep moving these electrons known as resonance around the ring. We can therefore see that it's the ortho and para positions that become most effected by this group. However, the electron density is poor at these regions in comparison to its electron donating species where they were rich. The sites therefore they are most effected are the ortho and are the para. Because the ortho is in closer proximity to the carbonyl group, it appears higher-up. Whereas you would find actually the blue and the green protons. These groups would actually be quite close together. And here I've just

drawn a blue followed by green, but it could be highly close together, even maybe merge/overlap with one another. So let's take a look at some more. Here we have started to add on some groups. So here we have a methoxy that we learned before was electron donating. So it feeds electrons into the ring. A methyl group, a carbon, is virtually neutral. So it doesn't take, but it has the option to give, but just a little bit give. And we found that if stuff wants to get electrons into the ring, we found that the positions that are most affected, are ortho signified by O and Para. And therefore what we see here is the site that is most affected because the oxygen is more electronegative than the CH3, that the position that would be the most affected are the protons signified in red. Are they siginfied in a good way or a bad way? Well if they had been given electrons, it's a good way. So here we've shown that they fall lower down in comparison to its blue counterparts. Let's take another example. So here we have electron donating, feeding electrons into the ring. And we have an electron withdrawing, taking away from the right. We said that the ortho and para positions where the most affected by this. And which one is the most effective? Well, we see here that the blue protons have electron density sucked away from it. So it would appear more towards eight. And the ortho, or the red protons are being given electrons, so good fall more towards six. And you can actually see this by the spectrum here, that the gap between these two have become quite large, signifying to the reader, the viewer of this, is looking at it going, okay. There are two different environments. Two very different environments, one is pulling electrons severely and the other not so. We will then take a look at our last example here. So these all so far we've been talking about para position that's great, but not everything falls on para position, not everything falls on meta, not everything falls an ortho. So now we just want to look at another example. Here we have these two same groups. So remember donating. and we have withdrawing. And now we want to see what which protons and most effected. Again, always drawing the hydrogens first. So we've drawn them in. We identify the different ones and similar ones. And here I've color coded red, purple, pinky sort of colour, blue, and green. We then look and say, okay, which ones are affected? So by donating, we have a negative charge in this position and a negative charge in this position. Because this group is para, we also have a negative in this position. The position that remains unaffected by this methoxy group is the blue protons. We then take a look at the electron withdrawing species. So in this case our ester and we say the one that is most effective is ortho. So this site also now gets a positive. This site here also now gets a positive charge. And this site here also gets a positive charge. So what can clearly be seen here is that the blue protons are the ones least affected. Because they are least affected. We know that they should be more up field or closer to six than the others. Here we have, which one comes first in the spectra? So we have the option here of the purple, pink or the green, Which one was to come first? This site here, the green protons, are furthest away from the methoxy group and therefore having least influence compared to its ortho counterparts. In doing so, then the green protons has the most effected by this electron withdrawing species and therefore, would appear higher up in the spectra or more downfield. The same, therefore, is true for when we start speaking, about these two protons. The red proton, is least influenced by this withdrawing group because it's furthest away yet still the charge is carried and the same therefore can be said by this species here, by the purple one. The methoxy and the ester group are both ortho to this group here. So you have donation and pulling away of these protons. So therefore the group, therefore it becomes the more effected looks to be like the red, because it's furthest away. Is a good or a bad thing? Well, actually in this example is actually quite hard to tell. Again, you would probably get merging of these two peaks together. But here I've said that the red would fall first, followed by the pink/purple color. In reality, these could be merged together because they both contain these two charges. Both of them are within ortho to this methoxy group. However, this one is also ortho to its electron withdrawing group. So it depends on the strength of which electrons are being pushed in to which the strength of the electrons being pulled back out. So here they can be found, so they are written red and purple or pink, but they can be

found in either way. So I hope far this is just a guideline to the basic of NMR interpretation and it follows these set of rules. And like I said before, these rules, they're not referenced because they are taken for many books and many years of studying. But the information that they're on the World Wide Web is vast. So so take a look at some of these. But like I said, these sets of rules are to help people, even of the non-chemistry nature, to be able to start to understand how does the NMR starts to interpret your spectra. That depends on your background. You may not be a chemist, but some point you might actually have to look at some of these spectra and be able to have a rough idea. Help your chemistry. You might actually be the only one on your project. So I think that these are very worthwhile rules to be able to understand your proton NMR spectra. For any additional topics that were mentioned here, but we're not going
into detail can be found further in some of our tutorial section. This talk was brought to you by WCAIR, University of Dundee.