Biochemistry
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Lecture -04
Protein Structure -II

We continue our discussion on protein structure and protein architecture.

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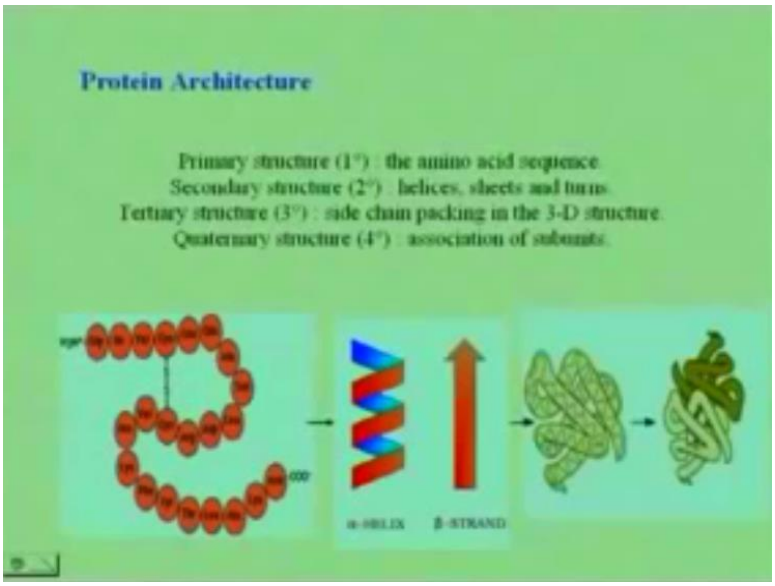

What we have here is the primary structure that we now know is just the amino acid sequence of the protein. The secondary structure that comprises helices sheets and turns something that we will be doing in more detail today. Then, we have the tertiary structure of the protein that is the side chain packing in the three-dimensional structure. This we will be doing later because we have to understand the interactions that go on into what is called the folding of the protein.

Finally, we have what is called the quaternary structure of the protein that is the association of subunits. So, I have here for you, the primary structure followed by the different elements of the secondary structure, then we have the tertiary structure of the protein and if you see this monomer subunit, it has associated with it now another subunit, where you have a connection that is not a covalent bond.

It is just an agglomeration or aggregation of these two units that is forming what is called the quaternary structure of the protein. You have to remember that there is usually no covalent

bond formation between the quaternary subunits in the quaternary structure. All proteins will have a primary structure, a secondary structure and a tertiary structure, but not all proteins will have a quaternary structure because all of them do not have a polymeric or an oligomeric structure.

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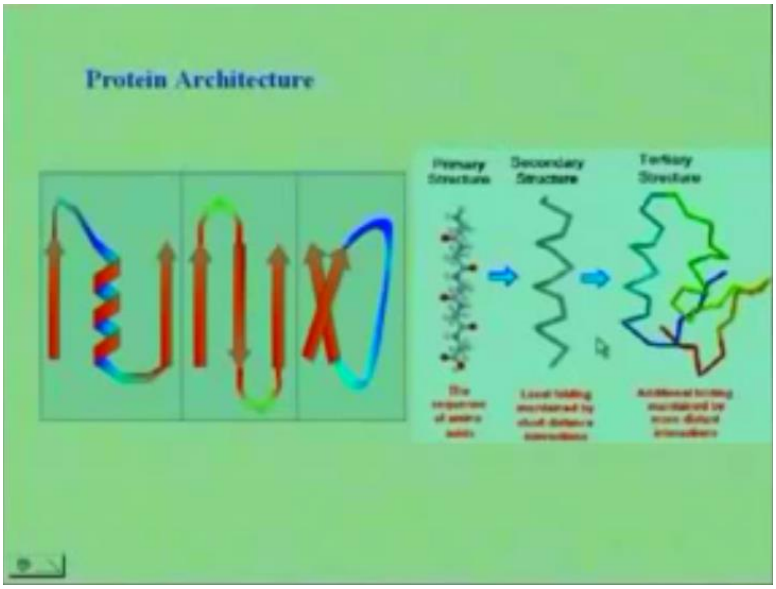

Now, this is what we consider when we consider the specific elements of secondary structure associated to form the tertiary structure. So, from the primary amino acid sequence, we go on to the helix and then we go on to the tertiary structure.

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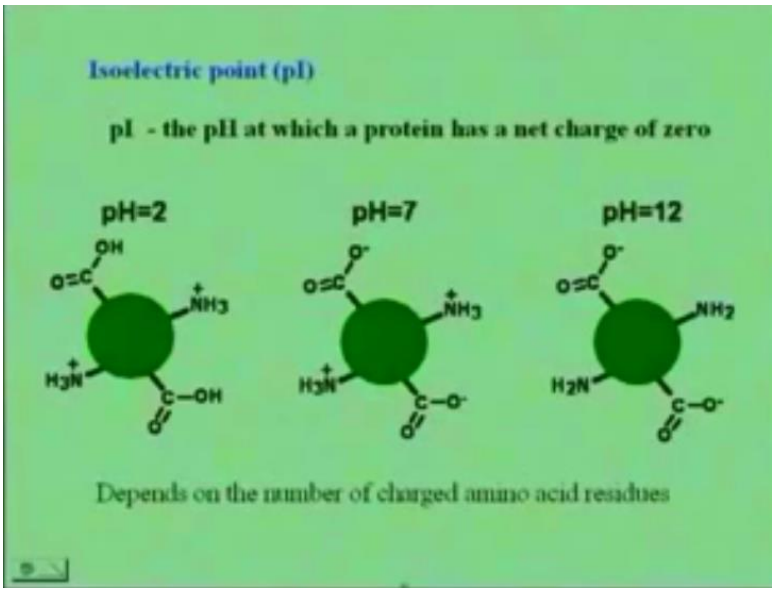

Now, if we want to understand the amino acid sequence of the protein, you now know that each amino acid is going to have its own isoelectric point, each amino acid is going to have its own definite point, where it is going to lose its protons or be zero in net charge. Now, the

isoelectric point also exists for the protein. Now what is this? This is when the pH of the protein is zero, the pH at which the net charge on the protein is zero. Now, what is that?

What do you mean by the pH at which a protein has a net charge of zero? Now, a protein is going to have a large number of amino acid residues, some of them may be acidic; some of them may be basic. So, each of them are going to lose their protons at different times. So, if we have, see at pH 2, we have all, what do we have here? We have all the side chains protonated as well as the amino and carboxylic acid terminal protonated.

We cannot say which of this may, we know that one of this has to be the terminal and we know that one of this has to be the terminal, but this may belong to a lysine and this may belong to either an aspartic acid or a glutamic acid. Now, as I increase the pH, what am I going to do? I am going to lose the carboxylic acid protons first. So, I am going to come to a point at, say in this case, I have written pH equal to 7, what is the net charge on the protein here? It is zero.

So, this would correspond to the isoelectric point of such a protein. Now, you may have another protein that has an extra NH3+ here. So, to reach a net charge of zero, I have to go even further high in the pH to achieve a net charge of zero. So, once I achieve that net charge of zero, I can then say that I have reached what is called the pI of the protein. So, as I keep on increasing or rather deprotonating all these protons that are available, I come to a very high pH, where I have lost even all the protons that were associated with the amino groups.

So, if you were to have a basic protein, what do I mean by a basic protein? I mean a protein that has a large number of lysines or arginines associated with it. The pI of that protein is going to be high. If I have an acidic proton, acidic protein rather, then what is going to happen to my pI? It is going to be a low value, why? Because, I'm going to reach a negative charge after the deprotonation of the carboxylic acid groups, I am going to achieve that at a lower pH.

So, I am going to have or the protein is going to have a net charge that is zero at a lower pH than would a basic protein. So, that is what we mean by, when we consider the pI of the protein and you understand that it depends on the number of charged amino acid residues. So, it is going to depend upon the number of lysine, arginine, aspartic acid, glutamic acid that

you have in the protein, because that is, where you are going to associate the charges that are going to be essential in understanding, how you can actually determine what the pI of the protein is.

So, if you have a polypeptide, you can determine what the pI is, from just the knowledge of what is the content of the polypeptide. You know the number of charges. You know you have to come to a net charge of zero to attain the pI.

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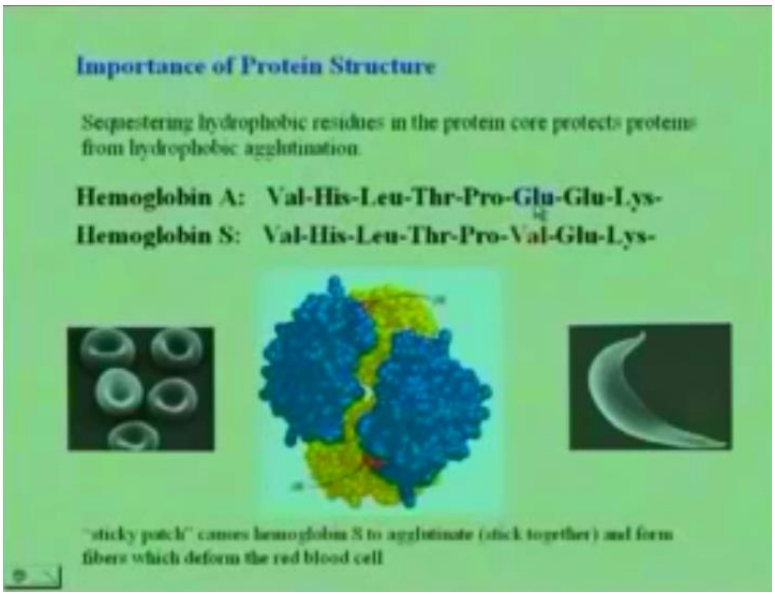

Now, when we consider the charge importance or the importance of the protein structure so to speak, I just have this one slide that shows you how detrimental a very slight change in the structure might achieve. Now, you have all heard of sickle cell anemia. This is what happens to your red blood cells, which are originally circular in shape; they become sickle shaped if you happen to have this sickle cell anemia.

Now, this is the beta chain of hemoglobin. For now, let us consider it is the polypeptide sequence of one of the chains that is present in hemoglobin. What do you see here is everything is the same except this glutamic acid. It has become valine. The rest of the protein chain is exactly the same. It has 174 amino acid residues and this is the sole change that makes this round red blood cell this. Now, what is essentially happening here?

You have a glutamic acid. A glutamic acid is a charged amino acid residue. It would prefer to be on the surface of the protein. Now, when I say it would like to be on the surface of the protein, why is that? It is because, it has a negative charge associated with it; it would like to

associate with the solvent around it. Now, when I change it to a valine, what am I doing? I am making it a hydrophobic amino acid residue that does not like to be on the surface at all.

So, what is happening here is, you see this is hemoglobin, this is the beta chain, the blue ones are the beta, the yellow ones are the alpha. So, what do I have here? I have the quaternary structure of hemoglobin that is comprised of four subunits, two of them are alpha type and two of them are beta type. The one that is marked in red here is the valine. Now what happens? Because the glutamic acid was on the surface, this valine is now on the surface.

So what happens? If another hemoglobin molecule comes here and this bottom one of the next hemoglobin molecule sticks with this one, sticks means it forms a hydrophobic interaction because it wants to be away from the solvent. So eventually what do you get? You get a fiber. Because what is going to happen, you are going to have another amino, you are going to have hemoglobin that is going to stick to the bottom of this one.

So, you are eventually going to get fibers and these fibers are what form the sickle cell. This was the first molecular so called disease that was determined to be solely on the amino acid sequence of the protein. So, you see how important understanding the whole protein structure is. It is just a single property of that amino acid that results in such a detrimental effect to your red blood cell forming the fibers to form your sickle cell anemia.

And the reason being that the glutamic acid that was on the surface is now, no longer there, you have valine which would prefer to be away from the solvent.

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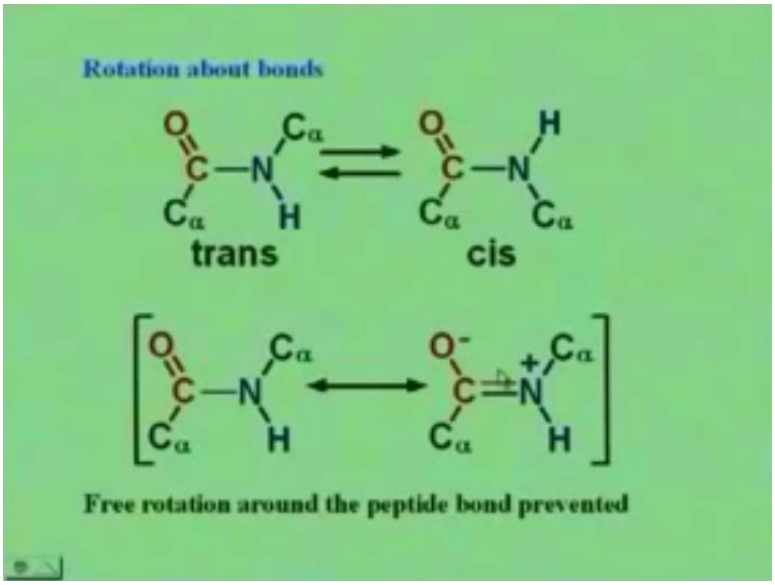

So now, we have our amino acids that are linked by the peptide bonds. Now, this is what we say when we have a partial double bond character to the peptide bond. Now, what do we have in this case? This is the C alpha. This is the C alpha of the next amino acid and to it or to both of them are attached side chains. This is trans in nature, because the C alphas are on two opposite directions. I can have a cis peptide also.

But what happens to a cis peptide? I have the C alphas on the same side and if I have C betas on top of this, what is going to happen? There might be a steric clash, which is the reason, why you have more trans peptide bonds than you have cis peptide bonds. Also, we have prevention of rotation about this single peptide bond due to the formation of this partial double bond. How is this being formed?

You have the lone pair on nitrogen, so it forms this partial double bond and because of its partial double bond character what do you do? You impose rigidity. It is not as flexible as the other single bonds in the peptide chain.

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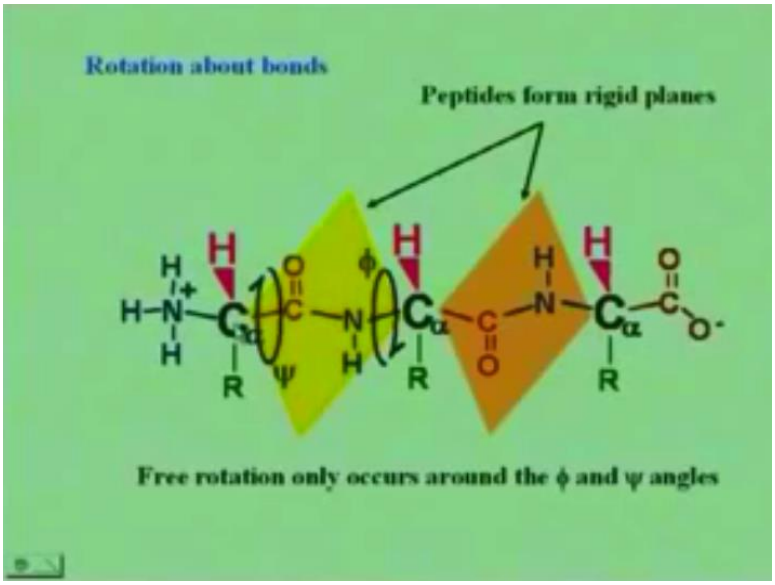

What are these other single bonds? These are the other single bonds that are going to amount for the rotation around these single bonds. And what do we have here? We have the peptides that form two rigid planes here. Why are we calling these rigid planes? Because of the partial double bond character that restricts rotation about the C-N peptide bond. What do we have here? We have free rotation about which other bonds then, the Phi and the Psi angles.

And, I explained in the last class how we can such a rotation, how do we define it? We define it by 4 atoms. For example, if I want to define the Phi angle, how do I define it? I define it by the C, the N, the C alpha and the C. What does it mean? It means that if I construct a plane that has the points C, N, and C alpha on it and if I construct another plane that has N, C and C alpha on it, then the angle between those two planes is going to give me the Phi angle.

Similarly, I can get the Psi angle that is going to be the angle between the planes that have N, C alpha, C and C alpha, C, N.

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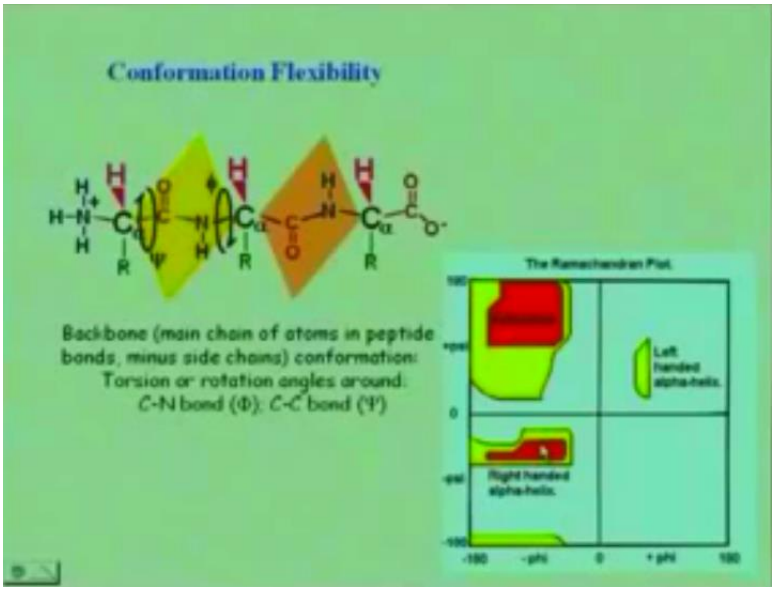

So, we have our Phi, Psi rotations and this gives rise to what is called The Ramachandran Plot, which I explained last time, where we have definite locations for the alpha- helix and the beta sheet. We will understand how these locations are restricted in the Phi, Psi values based on the geometry that they have.

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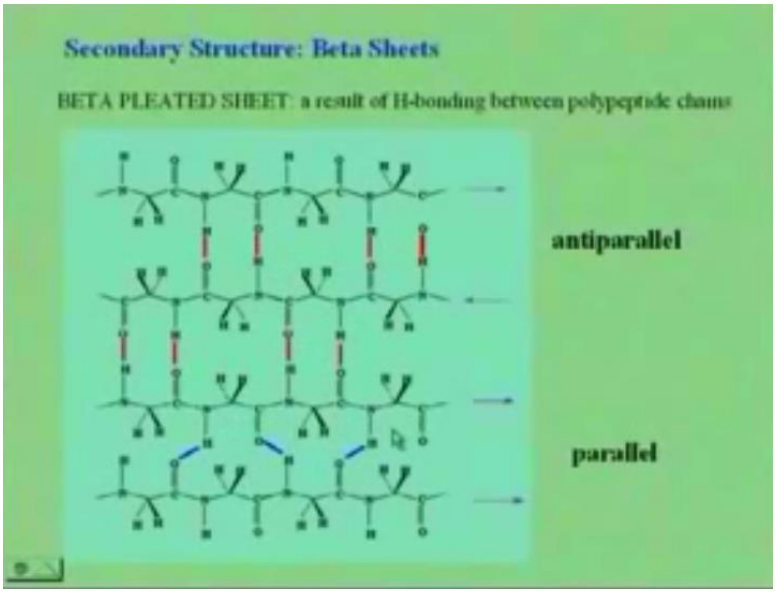

This is what is called a beta sheet. Now, when you look at a beta sheet you can straight away even if you did not have these arrows here, you should be able to tell me in which direction the polypeptide chain is going, why? Because you know that you always begin with an N. So, you have an N, a C alpha followed by a C. So, what is this amino acid? It is a glycine. In fact, all of them are glycine, it is just for a simple representation.

So, what do we have here? We have N, C alpha, C - N, C alpha, C. So, my protein chain is in this direction. What about the next one? If I go from here, I have N, C, and C alpha. That's the wrong direction. What is my right direction? N, C alpha, and C, that's my backbone. N, C alpha, C. So, what is the direction of my polypeptide chain? It is opposite to the previous one. It is antiparallel, fine? Look at the bottom two strands that we have here. I have N, C alpha, C, so it is going from left to right.

In the bottom chain, bottom strand also has N, C alpha, C, so, it is also going from left to right. So, I have a parallel strand here. I have two parallel strands here and I have two antiparallel strands here. So, it is just the direction of the beta strand that is going to determine whether it is an antiparallel beta sheet or it is a parallel beta sheet. Now, very carefully look at the hydrogen bonding between the sheets.

Now, when we speak of secondary structure, there are two types of secondary structure that are important. They are the alpha-helix and the beta sheet. Both of these have hydrogen bonds that associate them. Now, if we go back here and look at our antiparallel beta sheet and the parallel beta sheet, what you see here is different types of hydrogen bonding. If you look carefully, you will be able to distinguish the difference.

What is the difference? This N, C alpha, C, is a single amino acid. If we look at what it is hydrogen bonding with, this is going in the opposite direction from right to left. So I have N, C alpha the C. Is this the same amino acid or a different amino acid? It is the same amino acid. What about this? So, I have the N of this amino acid linked with the O of another amino acid on another strand and the same amino acid is going to have its amino NH linked with the carboxylic O of the other amino acid.

So, we have an amino acid N, C alpha, C on top and on the second strand, I also have N, C alpha, C here and the hydrogen bonds are between the same set of amino acids. Look at the difference in the parallel sets. What do we have there? In the parallel set, you see, we have our chains in the same direction; our strands are in the same direction. So, what do I have on the top strand here? I have my N go to C alpha then to C.

In the bottom strand, I also have my N, C alpha, and C. This has a hydrogen bond with this amino acid and the CO of this amino acid here, has a hydrogen bond with another amino

acid. Do you see the difference? The hydrogen bonding in the first case, let us look at this again, we have N, C alpha, C. My NH and my CO bond with the same amino acid. In the second case, my NH and CO bond with two different amino acids.

So, when you have the bond of an amino acid in a beta strand, hydrogen bond, the amino acid, hydrogen bond with two different amino acids, it is a parallel beta strand. When you have the amino acid bond with hydrogen bonds with the same amino acid it is an antiparallel beta strand. So, this is the hydrogen bonding difference between the two.

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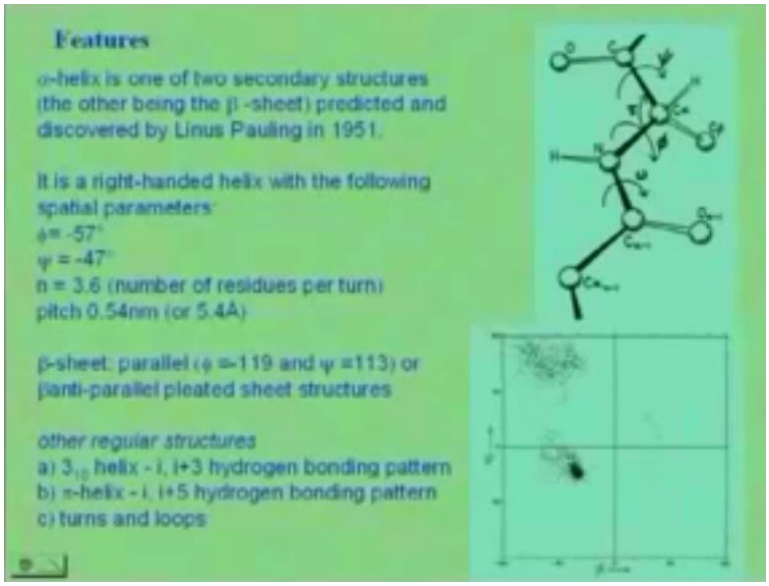

What about the alpha-helices? When we speak of alpha-helices that is another type of secondary structure that also has specific Phi, Psi angles that we have to consider that are -57 and -47. What am I talking about? Where is this? On the Ramachandran Plot. So, this would be a typical Ramachandran plot for a protein, where what do you see, you see some alpha helices, some in the beta sheet regions and some here, which are usually glaicy.

The ones on the right-hand side with positive 5 are usually glaicy. Now let us look at this chain here. When we look at the chain, which direction am I going in? From top to bottom or from bottom to top? You can say from what? You can say from the location of the nitrogen, the C alpha and the C. So, we know this is the C N, C alpha, C. So I am going from the bottom to the top.

And, we now know what type of angles we are considering? We have a 5 angle, we have a psi angle and omega angle is the angle of the peptide bond. So, this omega angle is usually

trans. So, it is usually 180 degrees. You can at times get a cyst peptide bond, at that point omega will be close to zero. Now, let us look at the hydrogen bonding pattern of helices. Now, when we have a helix we are going round.

We are forming a spring. These are two numbers that you might want to remember, which we will be doing again later on. N is 3.6 for a normal alpha helix. I will explain what I mean by a normal alpha helix in a moment. For this, it means that this is the number of residues per turn. You understand that the helix looks like a spring. So, it is going to have number of turns associated with it.

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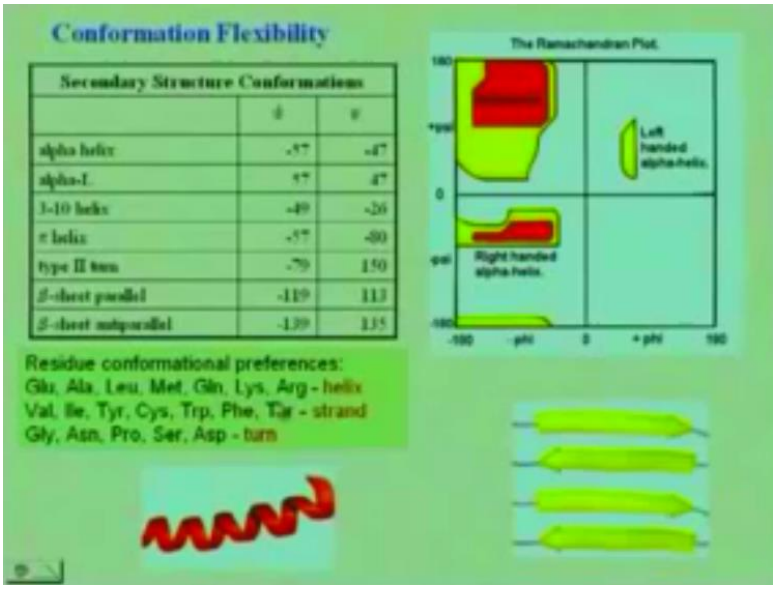

Ok, now these are features of the secondary structure conformations and you now know what are parallel beta sheet is and what are anti parallel beta sheet is and these are the corresponding 5-side locations where you might see them. But, usually we know that the right hand helix is here, a beta sheet is here, this is a left hander beta helix or mostly as I mentioned Glycine because it is the most flexible amino acid. And these I showed you last time also where we have residue conformational preferences.

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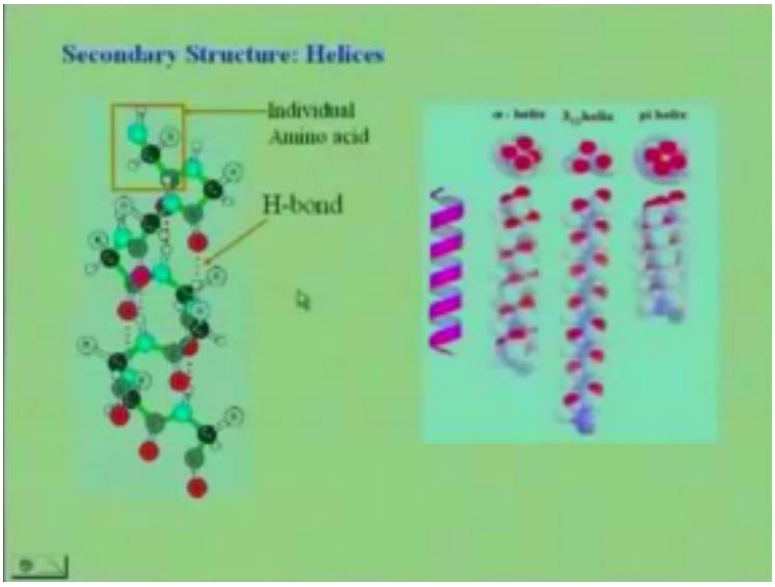

Now, we come to the secondary structure called the helices. We have a specific individual amino acid here. Now, if we were to follow the direction of the poly peptide chain, follow it very carefully and you can see in which direction it is going. The nitrogens are in blue. The oxygens are in red. And these are the R groups that are in grey, circled in grey here. So, I have my nitrogen here.

What is this? This is C alpha, because I have the R group connected to it. This is my C O, so I am going from the top down. Why? This is the amino acid, N, C alpha, C. What comes after that N, C alpha, C. right? N, C alpha, C and then what is next N, C alpha, C and what is after that? N, C alpha, C. You have to remember you are going round. So you are traversing a helix. As you traverse a helix, you are going from one point to the next point. So, as you go from one point to the next point you have certain turn associated with it.

For this particular one that I have drawn the direction of propagation is down. What is that make my helix? It is going in this direction and down. So, it is a right hander helix. If it were going up it would be a left hander helix. You have to follow the poly peptide chain, follow it with your hands and fingers and see, you following the poly peptide chain. In this case, where is your nitrogen? It is here, then is your C alpha, then is your C. So, you are going that way.

If you are going that way and the direction of propagation is down, then you are going that way down. So, what helix is it? Right hander. If you are going this way, your poly peptide chain and your direction of propagation is this, it is a left hander helix. So, you understand that this, that has been drawn here, is a right hander helix. You have to follow the poly

peptide chain. Follow its direction of propagation. How do you follow the poly peptide chain?

You look at where N, C alpha, C is. That is all you have to do. N C Alpha C, N C alpha C, N C alpha C, you follow the whole chain, look at which direction it is going. All you have to do is follow the spring. Once you follow the spring, you can determine in which direction it is going and you find out that this happens to be a right hander helix and it has specific connectivity. What is that connectivity? We see connectivity in the term, in the form of hydrogen bonds much like we saw in beta sheets.

But, these hydrogen bonds, sort of link that spring together. So we don't have an extended poly peptide chain. We have a helix. These are the different types of helices you can have. You can have what is called an alpha helix, what is called a 3 10 helix, what is called a pi helix. I will explain these terms. But, basically what you would have to need to know is what an alpha helix actually is.

These just tell you how many turns there are. Because they look, kind of different. You see there are about four atoms here in red. How many are they here? 3. And, here there are just about 5, one peeking out there.

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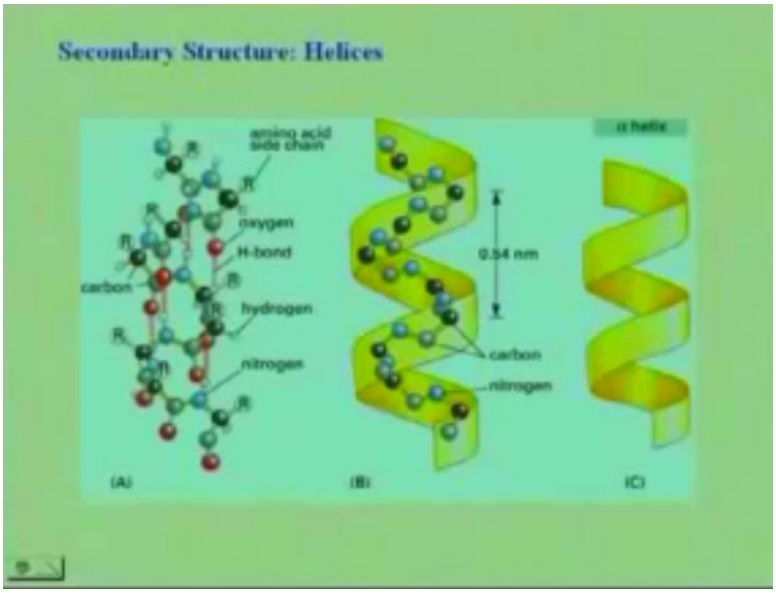

Now, let us look at this. Now, again we are looking at the same thing. We have N C Alpha C. So, this is the traversing of the chain. So, the poly peptide chain is now shaped like this. It is shaped like a helix. And what do I have along the helix? I have the carbon of or let start with

the nitrogen. We have the nitrogen of the amino acid, we have the C alpha of the amino acid, and we have the C of the amino acid.

So, we have the two carbons and we have the nitrogen. Now, this is what is called the pitch. What is a pitch? It is for one complete rotation the height that the helix of the poly peptide chain has traversed. It is just like a screw. You have a pitch of a screw. So, the helix should also have a pitch because it is also a spring, so, it is basically rotation of the poly peptide chain and you have what is called the pitch.

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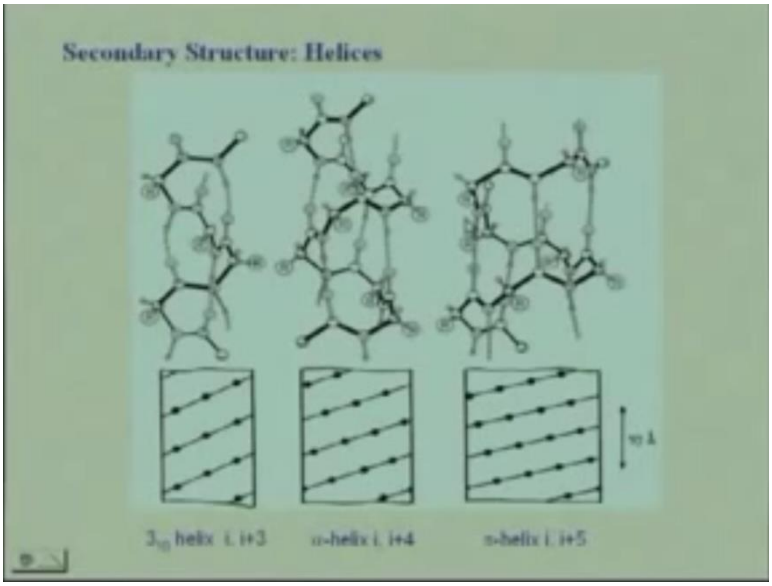

Now if we look at the pitch of these helices, what I mentioned before was, what we called a 3-10 helix and an alpha helix and a phi helix. The difference between these is the hydrogen bonding. They all form hydrogen bonds. It is just with whom they are forming the hydrogen bonds. So, in the helix or 3 10 helix, we have a hydrogen bond formation from the ith residue to the i+ third residue. That is what 3 10 helix means. And, 3 10 tells you that you have 3 residues per turn and there are 10 atoms in those, in that turns rather.

So, what is the 3 10 stand for? The 3 stands for 3 residues in a turn, and the 10 stands for the 10 atom in the turn. And the hydrogen bonding of the helix is from the ith residue to the i+ third residue. We look at the normal alpha helix now. In this alpha helix, which is the one that is the most common, which is why it is just called an alpha helix, the hydrogen bonding pattern is slightly different. You have the hydrogen bonding from the ith residue to the i+ fourth residue.

So, if you can just imagine what the turn would look like. So, you have basically a poly peptide chain that is rotating, it is like a spring. You have a hydrogen bonding between the CO and the NH of the backbone. In the 3-10 case, it is from i to i+3. In the normal alpha helix, it is i to i+4 and in the phi helix, which is extremely rare you have i to i+5. Now, the nomenclature for the 3-10 helices can also be written for the alpha helix. In this case, it is 3.6 residues per turn and 13 atoms.

So, if you were to write it in the same manner, instead of writing 3 10, we would write 3.6-13. But, that is not quite necessary for what we are doing right here. What you need to understand is the difference in the different types of helices is solely due to the difference in the hydrogen bonding pattern. So, basically this makes the sort of a tighter helix. This is slightly looser than that and this is even looser because, what you are doing is you are increasing the pore.

If you have a hydrogen bonding from an i to an i+3, you have a tighter helix. So, the inside cylindrical part is smaller. If you have from i to i+4 it is slightly larger and i to i+5 is even larger. So, basically you can see how this diameter gets larger.

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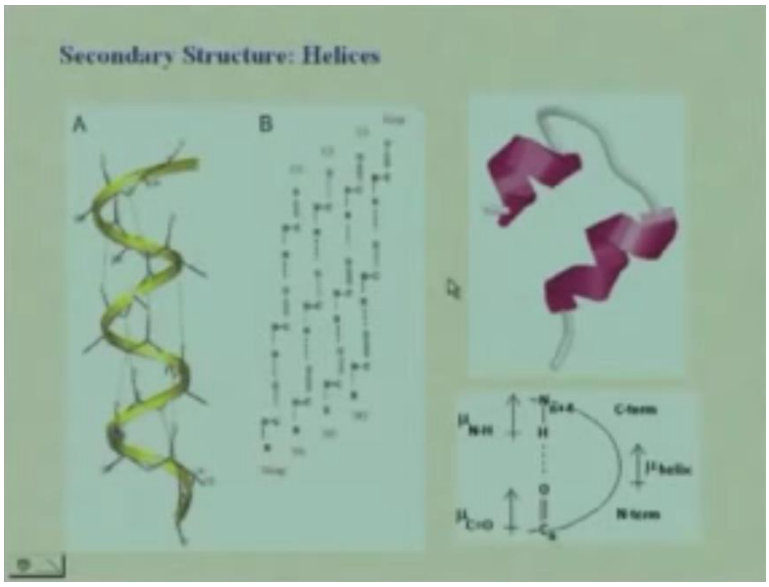

So, this shows you the hydrogen bonding pattern even better. The normal alpha helix that I mentioned has i to i+4. That is the hydrogen bonding pattern. So, what does this look like? You can see the C double bond O here. So, we have NC double bond O. What has been drawn here? It is just the N and C double bond O. Where is the C alpha? It is in between here. Right How is the amino acid? It is N C Alpha C.

The amino acid is N because there is the amino terminus on one side, the carboxylic acid terminus on the other side and in between is C alpha. So, the representation is just in this fashion to show you what? To just show you the hydrogen bonding pattern. So, if I have the first amino acid here, which one is it supposed to link with? The 5th one. Okay, If this is amino acid 1, 2, 3, 4, 5, why did I come here and not there? Because I am turning. It is a helix.

So, number 2 should have a link with number 6. So, 2, 3, 4, 5, 6. What do we have the hydrogen bond in between? The NH of this and the CO of 2, in this case, the one with 2 and 2+4 that is 6. It is the 2nd amino acid number 2. What is contributing to the hydrogen bonding here? The CO of residue number 2 and the NH of residue number 6. If I go to 1, it is the CO of 1 and the NH of 5. If I go to number 3, what is it? It is the CO of 3 and the NH of 7.

Now, what do you notice here? You notice something that all the COs are pointing in the same direction. What does that mean? It means that this alpha helix can have what is called a dipole associated with it. All of you know what a dipole is. It imparts a polarity to this due to the fact that all the COs in this helix have to point in the same direction if they are to form this hydrogen bond, which is specific for an alpha helix.

So, we have basically the end terminus of the helices, it is called, because we are going in this direction to the C terminus of the helix, we have an overall dipole that is from the N term to the C term. Why do we have it? We have it, because we have the hydrogen bonding pattern of the helix. This hydrogen bonding pattern of the helix is going to impart what? It is going to impart polarity to the helix and because of this polarity in the helix, we have all the Os pointing in the same direction, we have dipole associated with that and we have the helix dipole in that direction.

Usually, when you have 2 helices like on this diagram here, they are anti-parallel usually. The reason being that the dipole cancels one another out, because you wouldn't want the protein to be Polar in that sense. Usually, when you have helices they are anti parallel in nature, so that it can counter act the dipole that is associated with the alpha helix. So, what have I shown here in pink? These are alpha helices, that are connected by just some part of the polypeptide chain.

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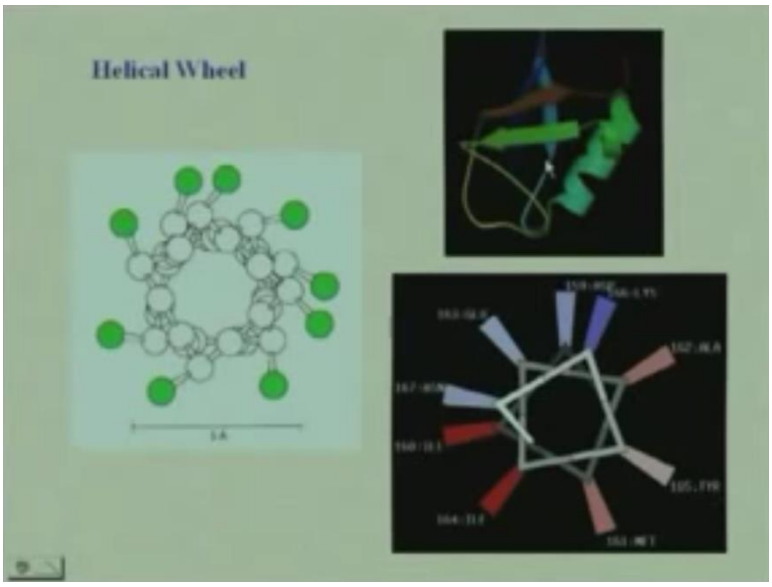

Now, we are going to learn a bit more about helices, something called a helical wheel and you are going to construct a helical wheel. Now, if you look at the diagrams here, this is the picture of the protein. What do I have here? I have a strand. This is the strand of a particular beta sheet and these are just connectors, the ones that look like worms, coils. This is an alpha helix. Now, if I look at the alpha helix and I know that surrounding here I have solvent.

I have particular residues that are sticking out from the helix. All my R groups are sticking out from the helix. If I look at my helix now and I say that this part is associated with the solvent and this part is associated with the core of the protein. What do I expect these amino acids types to be? They should be hydrophobic in nature and the ones that are sticking out on this side should be hydrophilic in nature.

So, if I consider every turn, say I have one residue here, the 5^{th} residue is here, i and i+4. So, if I have a hydrophilic residue sticking out here, the 5^{th} residue should also be hydrophilic in nature and so on because and so forth. Because my helix is a surface helix and in here, I expect hydrophobic types of residues because this is facing the central core of the protein. On the surface, I expect hydrophilic amino acid residues because it is facing the solvent.

So now, if you look down the helix, I am looking down the helix and these are all my backbone atoms, the ones that are in white. What are they? They are the N, C alphas, the Cs and so on. The green ones are the R groups. Now, what happens to my R groups they are all surfaced around here? So, what I should expect is this set or say any set, say for example, let

us consider this set should be one type and this set should be another type, why? because I am looking down the helix now.

If I am looking down the helix all the ones that are on one side here inside facing the protein all of them should be hydrophobic in nature and all these ones should be hydrophilic in nature. That's exactly what happens. This is an example for a typical helical wheel that you could construct and also, you'll also have to construct one. Where we are looking at the helix here, and the ones that are in blue are hydrophilic in nature.

How can you say that? I have asparagines here. I have glutamic acid here. I have aspartic acid here and lysine here. What are these? These are all hydrophilic in nature. What about the ones here? It has isoleucine, methionine, tyrosine to some extent and alanine. What are all these? They are all mostly hydrophobic in nature. So, if I just give you a picture of the helical wheel that is here you can straight away tell me which part is going to face the solvent, why? because you know the characteristics of the amino acids.

So, all these blue ones are going to be here outside and all the red ones are going to be inside. All the red ones are going to be inside, why? because they are hydrophobic in nature and all the blue ones are going to be outside because they are hydrophilic in nature, they will interact with the solvent.

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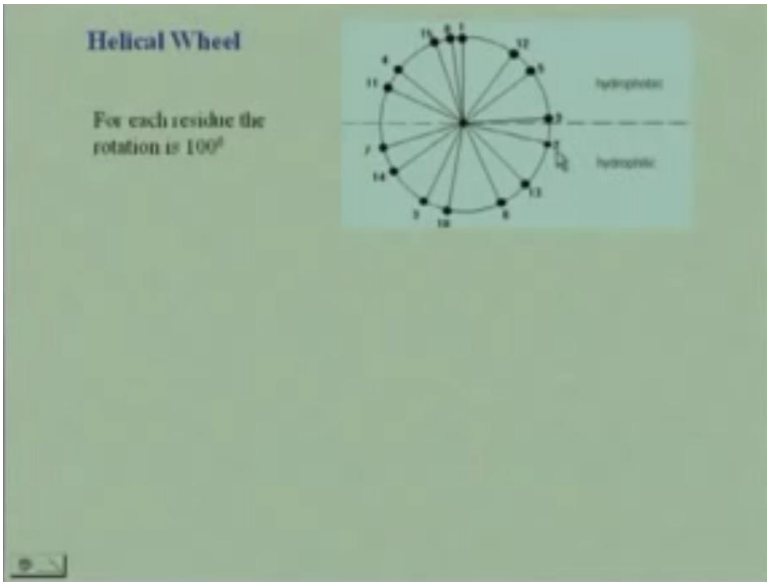

So, how do you construct the helical wheel? This is how you construct the helical wheel. For each residue, now, you have 3.6 residues per turn or usually we say that there are 4 residues

per turn. Now, if you are to construct the helical wheel, then we would put residue number one say on the top. For every residue, there is a rotation about 100. So, my next residue is going to come here. That is residue number 2.

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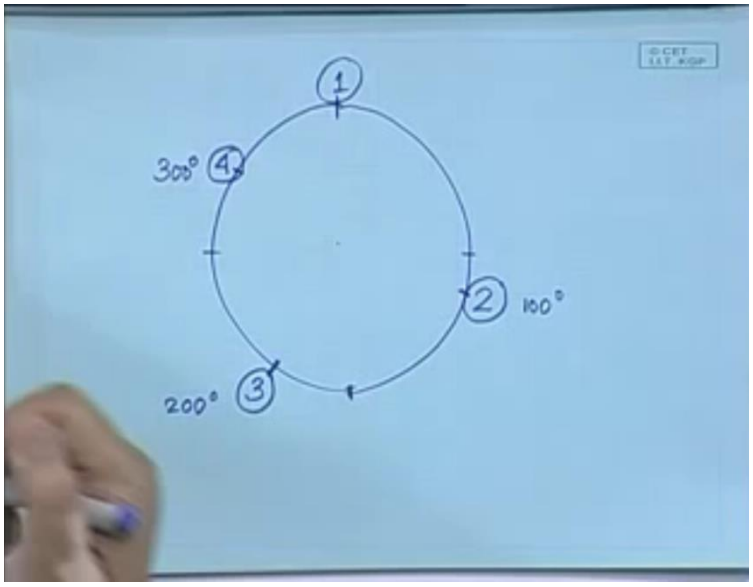

Let me just draw it out for you here. If I want to construct my helical wheel, what am I going to have? I am going to have residue one here. You know more or less where you have your 90 degree. So, 100 degrees is going to be somewhere here. We have the center. So residue number one is here and residue number 2 is here. Where is residue number 3 going to be? This is 180. It is going to be around 200. So, it is going to be somewhere here.

Where is residue number 4 going to be? This is at 100 degrees and this is at 200 degrees. Now my 4th one is going to be at 300. This is approximately 300. So, this is residue number 4 and then you can go on.

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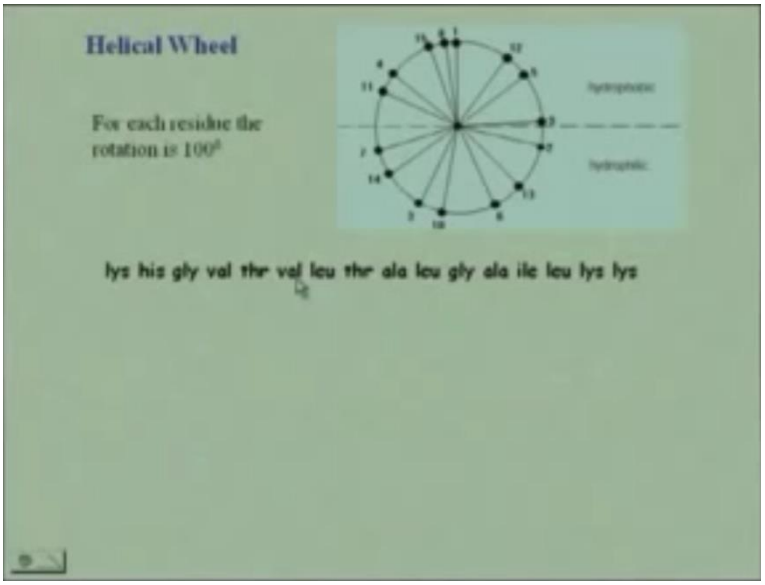

Now, if I have to construct a helical wheel for this. Let us construct it. So, for one I have lysine. You copy down the sequence that we have here. It is lysine, histidine, glycine, valine, threonine, valine, leucine, threonine, alanine, leucine, glycine, alanine, isoleucine, isoleucine, leucine, lysine and lysine.

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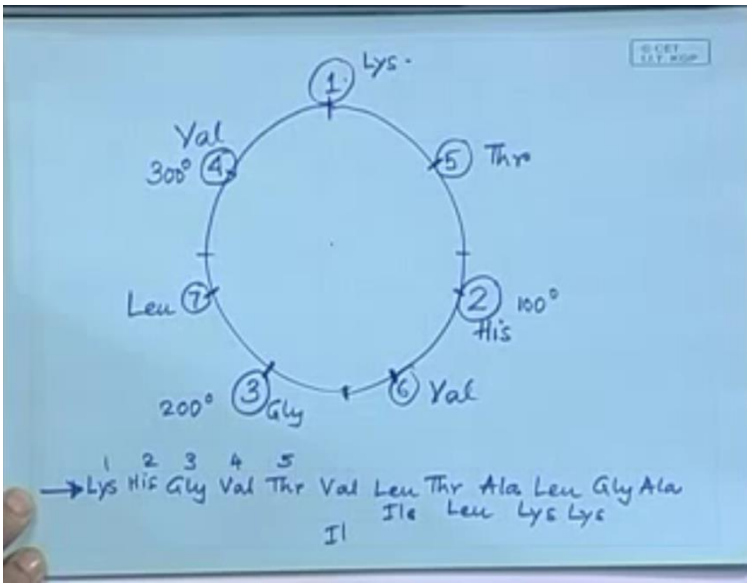

Now, where is residue number one going to be? It is going to be up here. Residue number 2 is histidine. So, this will be histidine. Residue number 3 is glycine. So, this is going to be glycine. Residue number 4 is valine. Where is residue number 5 going to be? It is going to be at 400, which is 40 degrees after this. So, it is somewhere here. So, this is going to be residue number 5, which is threonine. So, what can you do?

You can construct the helical wheel. Where is residue number 6 going to be? It is somewhere here. This is going to be valine. Residue number 7 is going to be somewhere here. That is going to be leucine. So, what can you do? You can construct the whole helical wheel. What do you need to know? All you need to know is this sequence and you need to know that for every residue the rotation is 100 degrees. That is the sufficient information for you to construct the helical wheel.

Once you construct your helical wheel, you can from the wheel itself predict which part is going to be outside and which part is going to be inside if it were to fold into a protein. So, you can actually say which part is going to be hydrophilic in nature and which part is going to be hydrophobic in nature.

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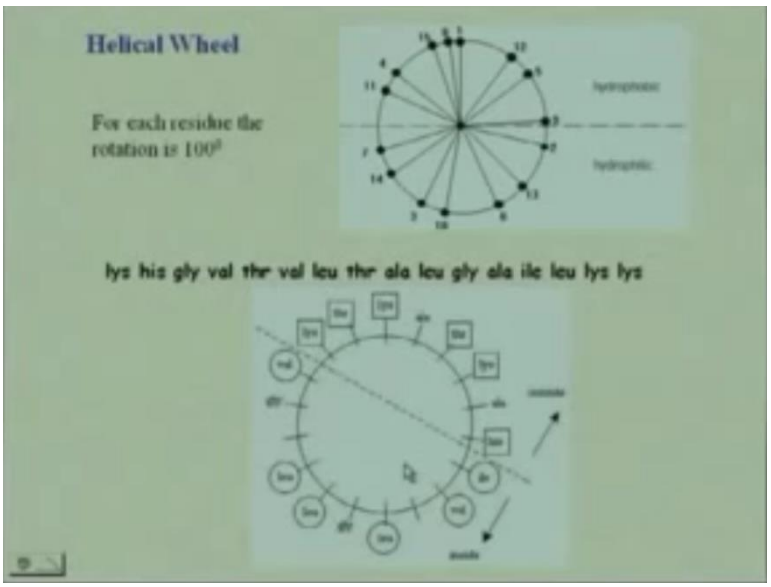

So, if you plot this helical wheel with its whole construction, this is what it is going to look like. Now, if we look at what is drawn here, you should have some of these at least. We have lysine, histidine, glycine, valine, threonine and so on and so forth. So, you know how to construct a helical wheel. Now, when you construct this helical wheel we say, we have a dotted line here.

What is this dotted line telling me? It is telling me that these are mostly hydrophilic in nature. So this is going to be the outside. These are mostly hydrophobic in nature. So, they are going to be on the inside. It is very simple construction but it gives you a lot of information. All you need to know is just the sequence of the protein. Once you know the sequence of the protein, you can then construct a helical wheel.

Say, I said, this sequence forms a helix. You have to tell me which part of the helix is inside and which part is outside. It is very simple to say that. All you need to know is that for every residue that you go, you have to go 100 degrees. And then, obviously you have to know the types of the amino acid residues to know that you have to know which ones can hydrogen bonds and which ones cannot hydrogen bonds.

Now, what happens at times, is this line does not have to be at the center as you can see it is not here. It may be just up here just saying that most of it is buried or most of it is inside, but a little part is outside. In the next class, we can see how all of it can be inside. So, when we are looking at this helical wheel, we can straight away say that we have an outside region and an inside region based on the types of amino acids that we have.

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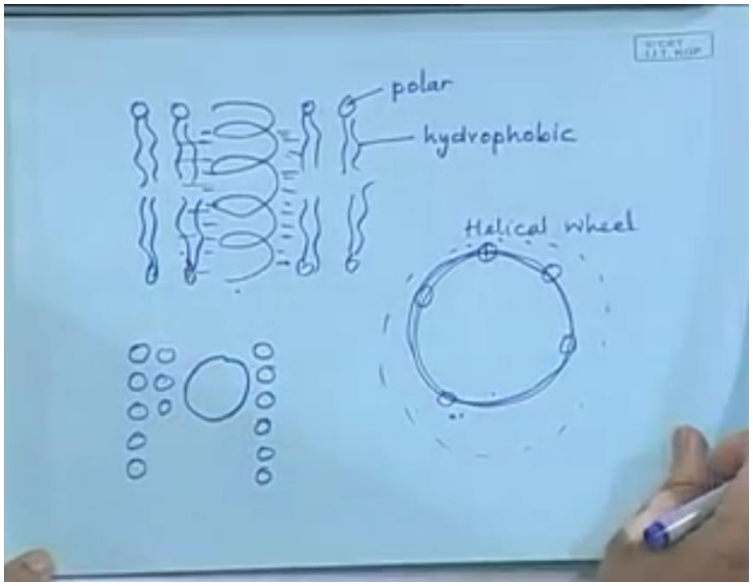

Now, if we are to look at a helical wheel for a membrane protein, what do we have in a membrane? We have something like this. If I have a helix here, what should I get when I construct a helical wheel? If I construct a helical wheel, say this is my helical wheel and I have my different residues like 1, 2, 3, 4, and 5 and so on and so forth, what do I expect on the surface here? What are these? Hydrophobic.

What are these? Polar. If I am looking at the side here, so, I have my interactions here in the helix and here, my interactions have to be with the hydrophobic tails of the lipids. So, what do I expect my helical wheel to comprise of? All hydrophobic residues. Does that make

sense? It does because you have to have hydrophobic interactions. If you do not have hydrophobic interactions, then this helix will not stay here at all.

It cannot, because the helix has to have the favorable interactions with the lipid tails that are hydrophobic in nature and the surface of the helix has to be hydrophilic in nature. So, if I construct a helical wheel for this helix, I would not have a distinction where I would get an outside and an inside, I would get all hydrophobic. So, if you do get all hydrophobic it means that your helix is part of a membrane.

Now, if we have it such that I have 4 helices here say, if I am looking from the top down, these are my polar heads, say, and I have my helix here. That is also possible.

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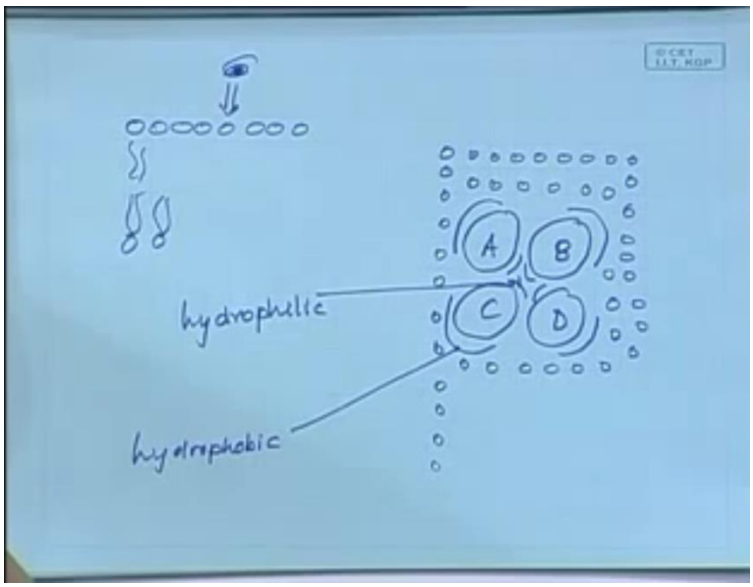

Because you have to remember that your surface actually looks like this. If we look at the membrane, it looks like this from the top. This is a cross section. If I place my eye here and then I look at the surface actually which are all lipids, all polar heads of lipids. I have say, 4 helices in the protein that is embedded in there.

If I construct a helical wheel for A, B, C and D, my helical wheel is going to be such that this part is going to be hydrophobic, why? because it is interacting with the hydrophobic tails of the lipids that are down there. What about this region? The inside region, hydrophilic. That's exactly what you see in such types of proteins. Why is it convenient to have this part, hydrophilic? So that it can transport ions and this part is hydrophobic.

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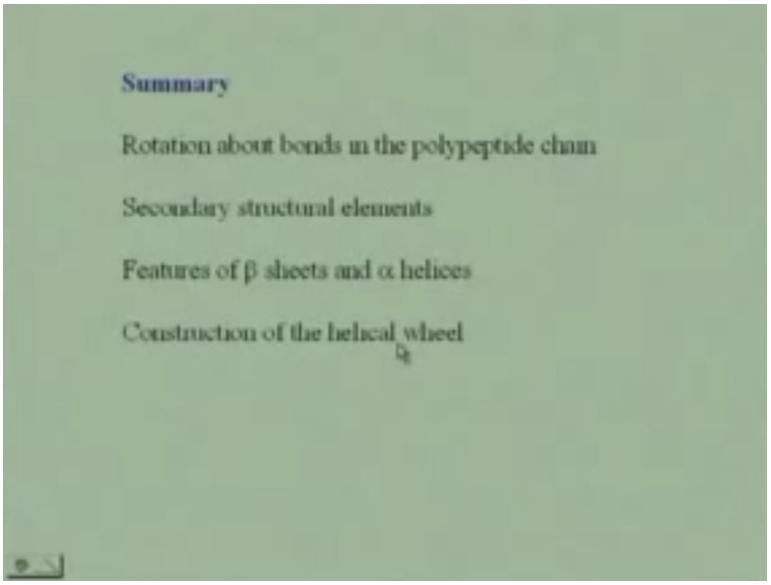

What we learnt today? We have rotations about the bonds in the polypeptide chains that give rise to the phi, psi angles. And we know that the omega angle is also present in the proteins but we rather have a trans-peptide than a sis-peptide, due to the restricted rotation because of the partial double bond character of the peptide bond. Then we have the secondary structural elements that we talked about where we look at the features of the beta sheets and the alpha helices.

What are the features of the beta sheets that we looked at? Their parallel and the anti-parallel and the differences in the hydrogen bonding patterns. Then, for the alpha helices we looked at the hydrogen bonding patterns of the alpha helices and we learnt how to construct a helical wheel that is going to exactly tell us where our helix is located. We'll stop here today. Thank You.