Biochemistry
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Lecture -03
Protein Structure -1

We continue our discussion on the acid base chemistry of the amino acids which we were discussing in our last class and we understood that if we have a structure such as this acid glycine, we have, basically we have our protonated NH3+ and we have our CO2-.

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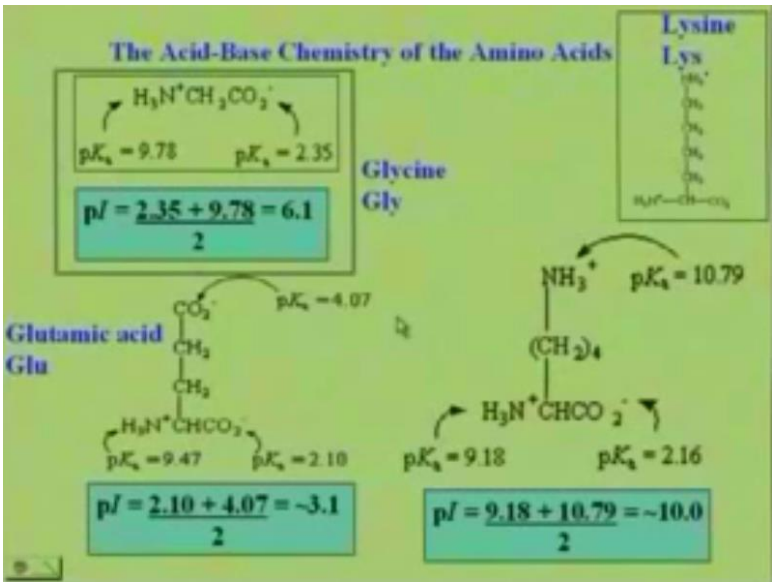

Now this is zero charge, right. Because it has reached its point where it has lost its carboxylic H+, the proton belonging to the COOH and it is yet to lose its proton attached to the amino group of the amino acid. Now, when calculating the pI you have to remember that you have to go from a +1 to a -1 charge through the 0. So, for each structure that you are considering we have to remember that if I want to go from the +1 to the 0 to the -1 these are the two steps that I have to follow.

If I want to calculate the pI of glycine, what I have to do is I have to sum up the pK1 and pK2 and the pKa's of both the acids, divide them by two to get the pI value corresponding to glycine. Now, if we go to glutamic acid then, initially my charge is +1. If all of these are protonated my charge is +1. When I lose one proton from the CO2H, which proton am I going to lose? I am going to lose the acid proton belonging to the amino acid first and not the side chain.

When I lose this proton, then what is the charge? It has a plus charge here and a minus charge here. This is still protonated. So, now I'm at the zwitterionic form. So, how do I calculate my pI? It is going to be the sum of 2.1 and 4.07 divided by 2. In the next case, suppose we have a lysine, then what happens to my lysine? Initially, what is my charge if I have an H here? It is +2. When I lose the first proton here, then this becomes COO-, but I still have a charge of +1.

Now, I have to lose the next proton. So, the next proton that is going to be lost is the amino group proton of the amino acid. Then, to calculate the pI in this case going from the +1 to 0 to -1, is going to be 9.18 + 10.79 divided by 2. So, if we just consider, the thing that you have to remember is, in calculating the pIs you have to go from a charge of +1 to -1 obviously through the 0. At the 0 is what is known as the zwitterionic form of the amino acid.

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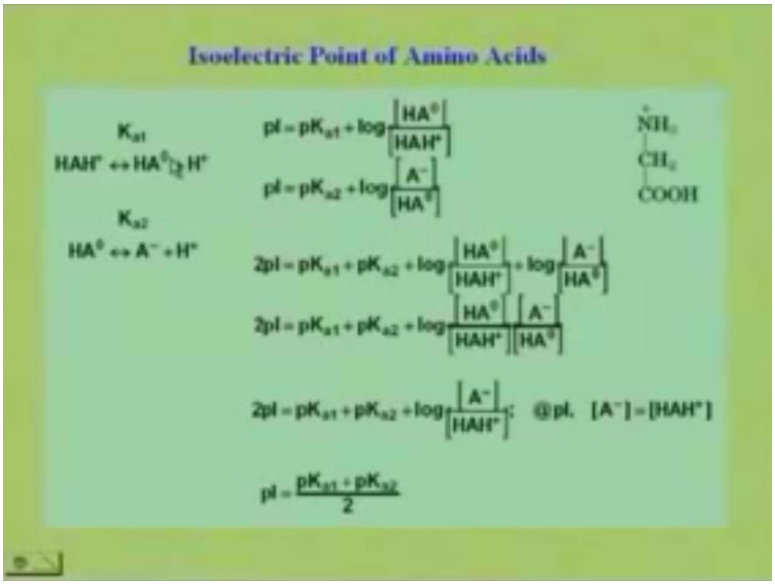

So, basically if you want to calculate the isoelectric point of the amino acids, if we just consider the simplest one that is glycine, then I have a NH3+ here and a COOH here, this H is going to be lost first, because it is a proton that is easily removed. So, when I go from an HAH+ I am going to an HA0 + H+. What is this form? It is a +1 form and I'm going to a zero form and I am losing this hydrogen first.

After I lose this hydrogen based on the Henderson-Hasselbalch equation, which I showed you last time, you can calculate what the pI form is for both Ka1 and Ka2 and when you are calculating it from Ka2, you go to the A- form, because you are losing this proton as well, you have already lost this proton. Then, if you just work through the algebra, you can find out

that the pI is actually going from the +1 to the -1 through the 0, pI is the pKas, summation of the pKas of those 2 values divided by 2.

So, all you have to do is consider the +1 form, the -1 form going through the 0 form for which you calculate the pI value of your specific amino acid.

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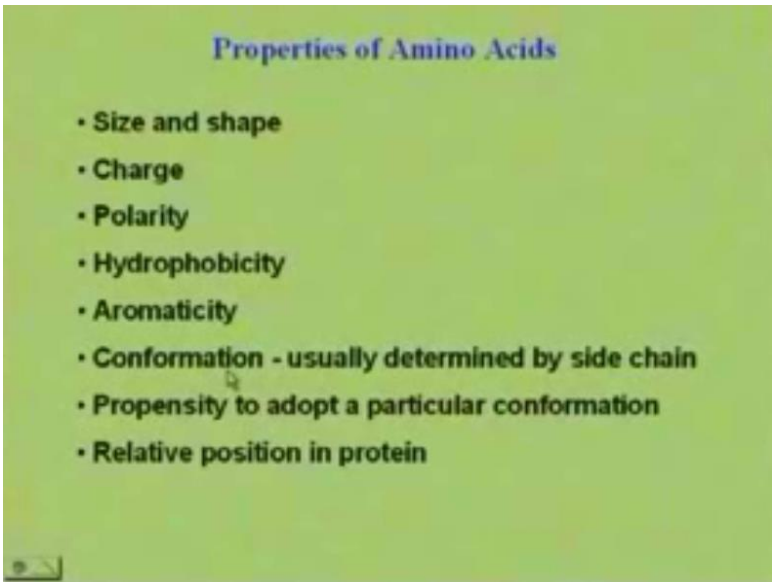

Now, we go back to the properties of the amino acids, where we have considered the size, the shape, the charge, the polarity, some of the hydrophobicity, part of the aromaticity and the conformation that is determined by the side chain this is due to the different R groups that are present and obviously the properties of these R groups.

And now, what we are going to consider next, is the protein structure in general, how, we have learnt how these amino acids are linked together by peptide bonds. So, when we have these linkages, what is so important about the linkages that we have to consider?

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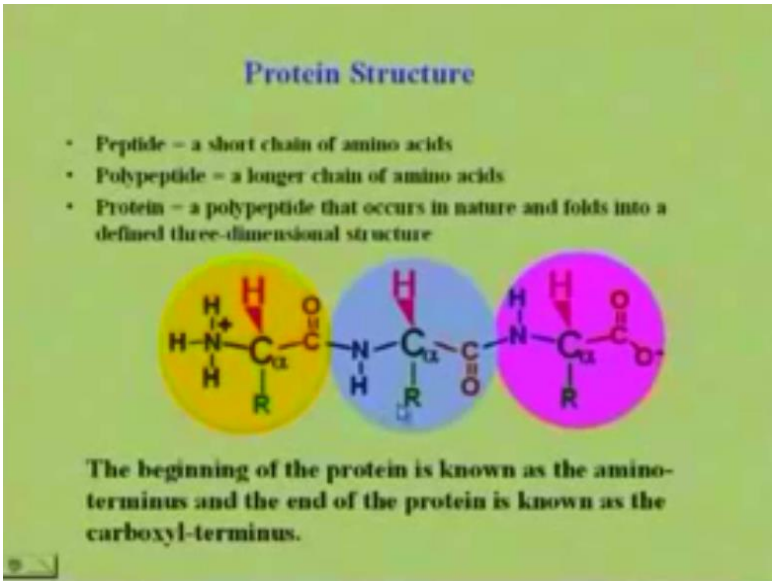

So, if we consider just the protein structure, what we have is a peptide. We now know what a peptide is because we are joining the amino acids together. Now, what is the difference between a peptide, a polypeptide and a protein? A peptide is usually a short chain of amino acids. A polypeptide is a longer chain of an amino, a set of amino acids. A protein is a polypeptide that occurs in nature and folds into a defined three-dimensional structure.

We are going to understand exactly what this means. This means that all proteins are polypeptides, but all polypeptides are not proteins, the reason being that all polypeptides may not fold into a definite three-dimensional structure, which is true for a protein. So, a protein is a polypeptide chain of a set of amino acids that are linked together by peptide bonds and it has a definite three-dimensional structure.

So, we have a peptide, we have a polypeptide and we have a protein. Now, if we look at these linkages, you can now say that when we are at a pH of 7, we have lost the carboxylic acid proton. So, a protein is always represented in this form. So, this is a tri peptide. The tri peptide at physiological pH which is pH 7, we have not lost the proton that belongs to the amino acid group, but we have lost the proton that belongs to the carboxylic acid group, which is why this is represented in this form and we always begin the protein with the amino terminus.

So, we have our amino terminus and we have our carboxylic acid terminus. So, we have now the different R groups, which are going to behave differently based on the different properties that it has.

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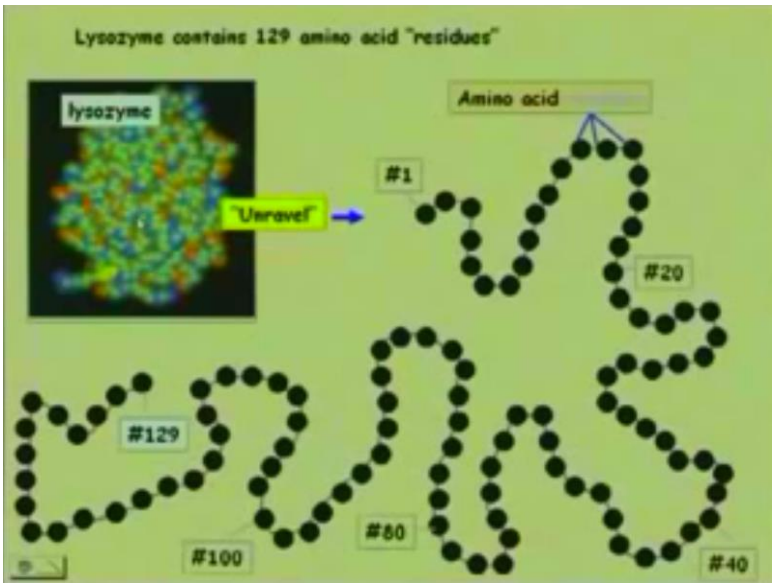

So, if we consider our one of these proteins, this is called lysozyme. If I have a protein in its three-dimensional structure and I just open it up into its polypeptide chain, I will find that it opens up into a random polypeptide chain that is, what are these bonds? These are peptide, covalent peptide bonds linking the beads that are amino acids together. So, if we now go further into the detail of this we have these amino acid residues that are linked by peptide bonds to form our polypeptide chain.

This polypeptide chain will form a protein because it is going to fold into a definite three-dimensional native structure.

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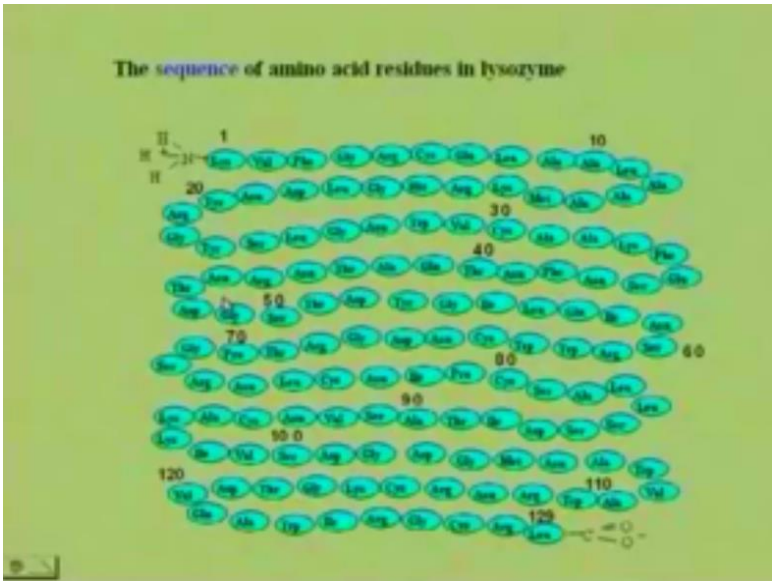

So, now if we go to the sequence of amino acid residues of this protein, what it means is that I start off with a protonated amino terminus and I end with a carboxylic acid terminus, which does not have a proton attached to it and this is the sequence of my protein. What do I know from this sequence? I know that lysine is followed by valine followed by phenylalanine followed by glycine and so on and so forth.

Now, you can recognize the three letter codes for the whole polypeptide chain that comprises the sequence of lysozyme. Now, this is going to fold into a definite structure. Now, how does it do that?

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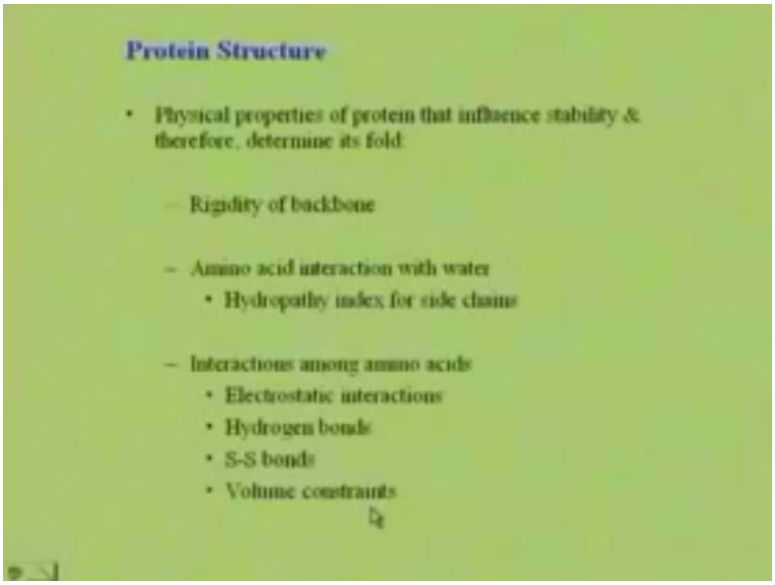

So, when we consider the protein structure, we have to consider the physical properties of the protein that influence the stability of the protein and determine its fold. okay. How does it do that? There is specific rigidity of the backbone that is essential for the structure. There are interactions of amino acid with water depending on the hydrophobicity of the amino acids. How do you determine that?

There are scales to determine that. But how is it actually, if you think of a physical interpretation what are you looking at? You are looking at a case, where you have in the side chain if you have oxygen or a nitrogen atom; it is possible for it to form a hydrogen bond. But, if your side chain contains only carbon and hydrogen, it is not possible.

So, you have a specific index called hydropathy index, which I will show you later on, that actually tells you, how the amino acids interact with water and how we can actually

determine different regions of the protein that are going to be embedded in the protein because it has a stretch of amino acids. If you have a stretch of hydrophobic amino acids, they will not be on the surface of the protein.

Then, we have to consider the interactions among the amino acids. There are going to be electrostatic interactions. How? Because we have charges on the amino acids, so, if we have charges on the amino acids, where can these electrostatic interactions arise from? For example, lysine which is a positively charged amino acid can interact with aspartic or glutamic acid which are negative amino acids, negatively charged amino acids.

So, we can have these acidic amino acids interact with the basic amino acids. We also have hydrogen bonds. Hydrogen bonds are going to be between the polar amino acid residues and the solvent or between the polar amino acid residues themselves. The next one that we already mentioned was the S-S bonds. Now, what are these S-S bonds? The S-S bonds are the disulfide linkages and they arise from the cysteine residues coming together and forming cystines.

So we have these S-S bonds and you have to remember that these are the only other covalent bonds apart from the peptide bonds that are present in the proteins. And we also have volume constraints. What do I mean by volume constraints? We have the sizes of the different amino acid side chains and obviously, there is going to be a steric hindrance, a steric hindrance into the accommodation as to how they can occur in the folded protein. So, this is what we mean by hydrophobicity scale.

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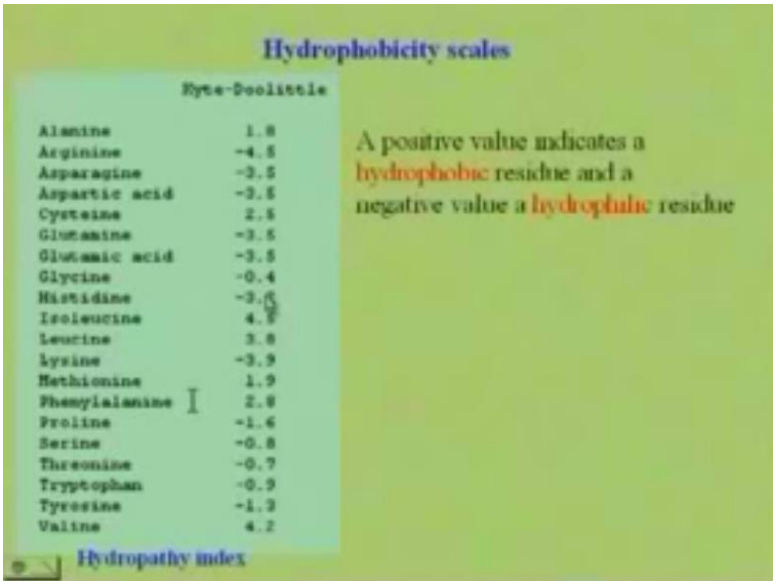

If we look at this scale, you can see just by glancing at it, this is called the Kyte-Doolittle hydropathy index. It is nothing but the scale for hydrophobicity values. What do you see here? If you just look at this, a positive value indicates a hydrophobic residue. Where do we have a positive value? We have a positive value at alanine. What is the side chain of alanine? It is just a methyl group. So, it is hydrophobic in nature.

We know that valine is also a hydrophobic residue. What is the hydropathy index for valine? It is 4.2. It is a high positive value indicating that it is hydrophobic in nature. Look at the negative ones. Lysine is a positively charged amino acid residue, it has a negative charge, a negative hydropathy index. It has a positive charge but a negative hydropathy index indicating that it is a hydrophilic residue.

It would rather remain on the surface of the protein than be embedded in the protein. Aspartic acid, arginine, glutamic acid, glutamine all of these are hydrophilic residues. And the ones that have positive values here are hydrophobic residues. Later on we are going to see how this index actually helps us in determining which stretch of amino acids are on the surface of the protein and which stretch of amino acids are embedded in the centre of the protein.

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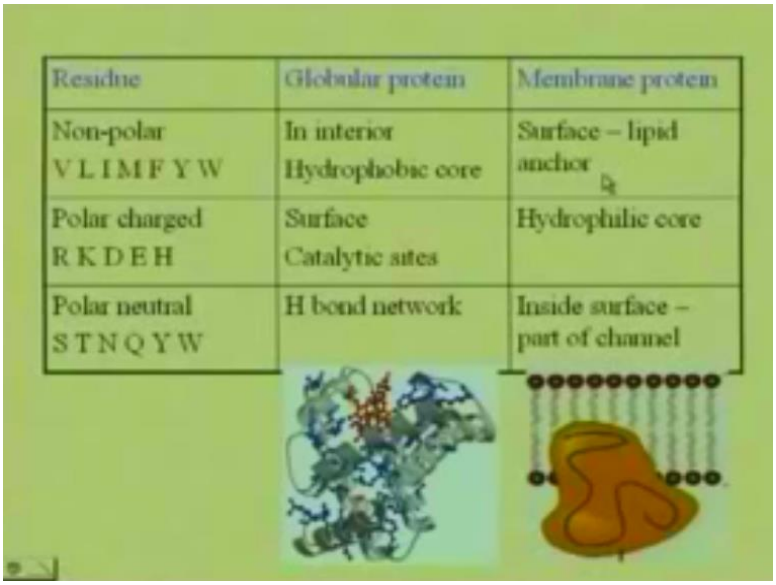

So, let's look at the structures of two proteins. This on the right hand side is a membrane protein. You can see, this is the cell membrane. What is the cell membrane? It is a lipid bi-layer. What do you have in a lipid bi-layer? You have polar head groups and hydrophobic tails. We will be studying membrane structure later on, but you all basically know that we have a cell membrane that happens to be a lipid bi-layer.

A lipid is basically a polar head group with hydrophobic tails. If we look at the structure of a solvent protein, a protein in just a polar solvent then, there are going to be specific characteristics of the residues that are on the surface of the protein. For example, if we look at this chain, it is a hydrophobic chain. So, what do I expect on the surface of this membrane protein?

Hydrophobic amino acid residues, a polar residue on the surface will not interact favorably with the hydrophobic tail of the lipid. So, you will have preferably hydrophobic interactions here, but if you are looking at this protein what do I expect? I expect the hydrophobic amino acid residues to interact among themselves, in the center of the protein and on the surface, I am going to expect polar residues, which are just the reverse of what I would expect for a membrane protein.

So, any protein that is embedded in the membrane would rather have a hydrophobic surface to it, because it can interact with the hydrophobic tails of the lipid bi-layer and a globular protein, as this is called, that would be in the solvent would rather have its hydrophobic residues buried in the centre of the protein. Now, since you know the characteristics of the

amino acids and I give you a list of amino acids, you should be able to tell me, where each one occurs.

So, if I just have a list up here, we have a globular protein that is this, and we have a membrane protein that is this. Okay? I look at non-polar residues. I have given the single letter codes for the amino acids here. So we have Valine, Leucine, Isoleucine, Methionine, Phenylalanine, Tyrosine and Tryptophan. In a globular protein, they prefer to be in the interior to form the hydrophobic core. So, they are somewhere here.

The polar charged residues in this case, are on the surface. And they form the catalytic sites. So, where are they? They are on the surface of the protein. And the polar neutral ones would preferably form the hydrogen bonding network. So, if we look at a globular protein and we look at the specific types of amino acid residues, we know to some extent where they might be located in a protein.

If we look at the membrane protein on the other hand, the non-polar residues are not in the interior. They are on the surface. Why? Because they interact with the lipid. Because, they have to anchor themselves to the lipid and this hydrophobic tail would not want a polar to interact with a polar residue. So, the non-polar residues would preferably be on the surface in the case of a membrane protein.

The polar charged groups would rather be in the core of the protein because they want to be as away from the surface as possible. So, instead of a hydrophobic core, which you find in globular proteins that are in solvents, you have a hydrophilic core for the membrane proteins and the polar neutral parts would form the inside surface of the part of the channel. Now, what do I mean by the part of the channel?

Now suppose, on the bottom we have the inside of the cell and on the surface, I have the outside of the cell. This is a cell membrane. So, if I have a protein that actually integrates through the membrane, which we will study later on, then what do I expect? I expect that the salts inside the cell or the salts from outside the cell, there has to be a channel that goes in and out and if you are to transport, say sodium ions or potassium ions, would it prefer hydrophilic environment or hydrophobic environment? It would prefer hydrophilic environment.

So, it makes sense that for the lipid, the inside surface of the lipid has this pattern of hydrophilic amino acid residues that are eventually going to allow the passage of the transport of ions from the inside to the outside or from outside to inside. If you had a hydrophobic core in here, it would be extremely difficult for you to allow this transfer to occur. So, in the membrane proteins, we have the surface hydrophobic amino acid residues that are going to link up or form interactions with the hydrophobic tails of the lipid valor (()) (20:58).

And inside we have a hydrophilic core, we have a surface, a hydrophilic surface that allows the transport of ions in and out of the cell. So this is very clear to understand once you know the characteristics of amino acid residues and also you know the characteristics of protein, whether you are talking about the globular protein or you are talking about the membrane protein.

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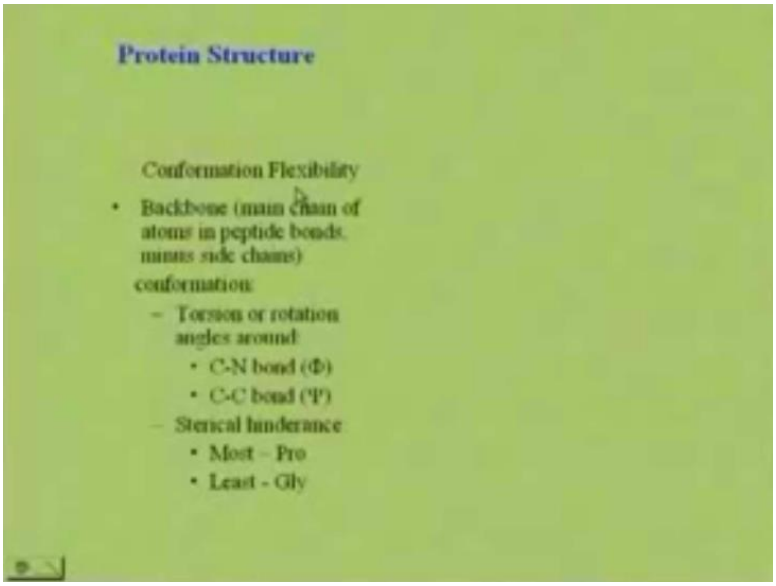

So, now if we consider the protein structure, we have to remember that there is conformational flexibility. What do I mean by that? How is the protein poly peptide chain formed? It is formed by the linking of amino acid residues.

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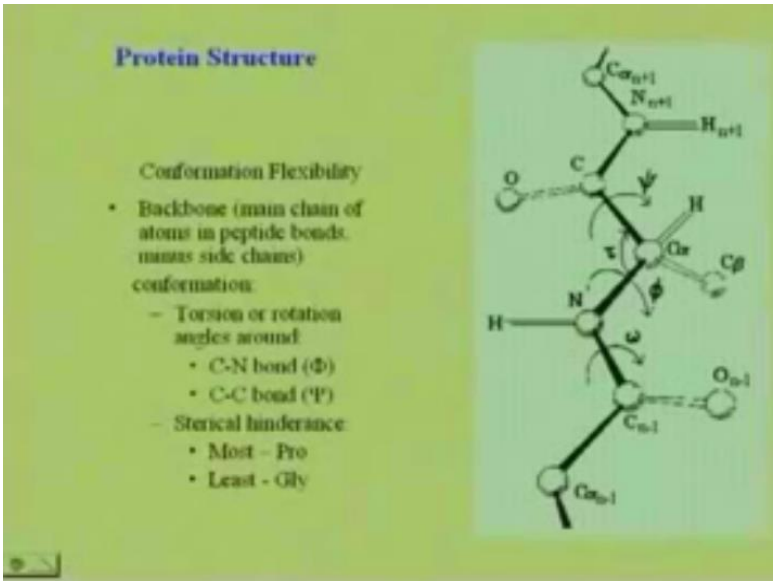

Once you link the amino acid residues together we have a lot of geometrical consideration that we have to make. Now, I am going to go step by step in understanding these geometrical considerations. Here, I have the C Alfa carbon atom. What is the C Alfa? It is to which the amino group is linked and the carboxylic O is linked. Follow the chain, the black, the one in black is what is called the back bone. That is where we have our linkages. So, where does my protein actually begin?

Suppose, this is just part of the chain, we are looking at this particular amino acid here, I have this NH, what is this NH? It was the part of the NH2 originally. This is the C Alfa, which is the one to which the amino group is attached and the carboxylic group is attached. So, this forms part of one amino acid in the chain. What do I have linked to C Alfa? I have the R group. On one side you have the hydrogen, what makes it asymmetric?

You have the hydrogen, you have the R group, you have the NH2 group, you have the COOH group. So, this is part of my amino acid, which is now present in the protein structure. I am not looking at it isolated; it is part of the protein structure. So. now I have what are called torsion angle. I am going to explain what torsion angles are to you in a minute, where we are looking at rotations about bonds. What are these rotations?

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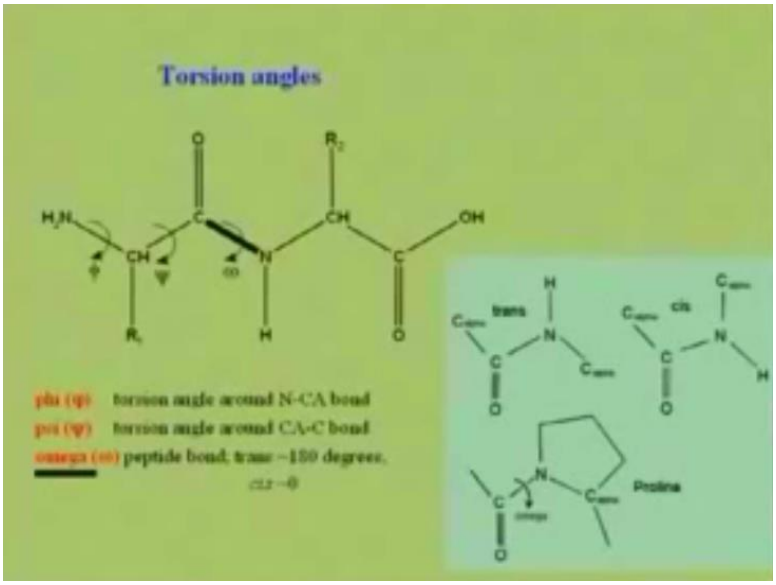

These torsion angles actually define the rotation about the single bonds that are present. Now you recognize this, what is this? this is amino part of the chain that I have drawn here. What is this? This is the C Alfa to which is attached the R group. This is the C double bond O, what was attached here originally and OH, which has lost its H with this amino group H to form the peptide bond. Now, this peptide bond actually has a partial double bond character to it.

You can see it is drawn thicker. Why is that so? Because there is a lone pair on nitrogen, that actually can be donated to this bond here, where this loses a CO-. So what do we have here? A partial double bond character. Now, in the partial double bond character what will this impart to the poly peptide chain? It will impart rigidity. Right? What do I mean by rigidity? It will not allow rotation about the poly peptide chain about the peptide bond. It will restrict the rotation, because it is now partially double bonded in character.

If I look at this, this is free to rotate. It is a single bond. It can rotate freely. Similarly, this can rotate freely. This can rotate freely. This has some restrictions due to the partial double bond character. Why do we have partial double bond character? Because of the lone pair of nitrogen that results in a partial double bond here. Now, if we look at the disposition of the C Alfa residues, what is this? This is residues number 1, R1. This is residues number 2, R2. So what is this C? This is the C Alfa of R2. This is the C Alfa of R1.

If I look at this, this is my C Alfa. This is my C double bond O. This is my NH. This is my C Alfa of the next. Which is R1 now? This is R1. How do you know it is R1? Because its tail is carboxylic acid. NH is the beginning of the next one. It has to be. So this is R2. So, if this is

R1 and this is R2, what sort of orientation is this? Trans. If I rotate about the peptide bond, what can I have this become? Cyst. So, normally you can have a trans, in very rare cases you have cyst.

Now, why do I call them rare cases? If you look, you just have to see the C Alfa here, what is attached to the C Alfa? The rest of the side chain. So what might happen here? Steric hindrance, a clash of the side chain unless they are very small. So, what would I expect? I would expect the peptide bond to be preferably trans in nature.

So, now there are different definitions for the torsion angles. But, before I get into telling you or explaining to you what torsion angles are or dihedral angles are, I am going to explain some geometry to you.

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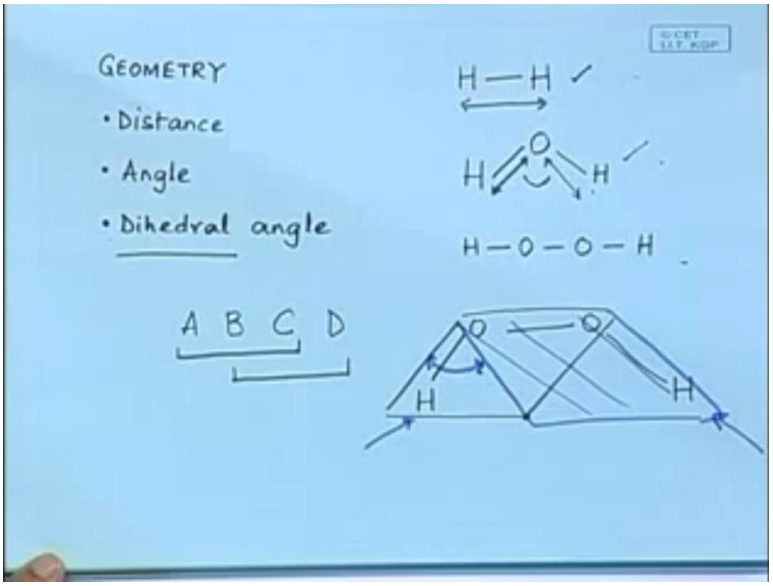

So, we will go to our page here and what I am going to show you is, if we have the geometry of any compound, see I want to tell you what the geometry of hydrogen is, what information do you need? You need just the distance between the 2 hydrogen atoms. That is all the information you need. Because, if you know where the one is located you can find out where the other one is just by knowing what the distance between the 2 atoms is. So, all you need in this case is this distance.

If you were to go to water, where you would look at H O H. It is not sufficient if I give you distances. If I tell you this H is this distance away from the oxygen and this H is this distance

away from the oxygen, that does not suffice because I have to tell you what the angle between the H O H is, if you have to get the correct geometry of the water molecule.

So, when you have a diatomic molecule the distance is fine. If you have a tri atomic molecule what you need? You need 2 distances and an angle. Fine? Now, what is this dihedral angle? Suppose you have 4 atoms - A, B, C and D. You know that a plane is defined by a minimum of 3 points. So, I can define a plane using the atoms A, B and C. I can define another plane using the atoms B, C and D. So, now I have 2 planes. The angle between these 2 planes is what is your dihedral angle is.

We can have an example. Suppose, let us take hydrogen peroxide. That is an example of ABCD. What do I have with H-O-O here? I will have 1 plane. Let us do it with another color. If I consider BCD, which is O-O-H, what do I have? I have 2 planes. One is this plane that I have here and one is the plane behind that I have drawn there. Do I have the angle between the 2 planes? I do. This angle is my dihedral angle.

So, what do you have? When you are defining the geometry for just 2, you just need the distance. When you are defining it for 3 atoms, you need 2 distances and an angle. I don't need to give you a dihedral angle here because it does not occur. I do not need to give you an angle in the first case because it is not necessary. But, when I come to the dihedral case, I need everything, I need the distance, I need the angle and also need the dihedral angle.

What angle do I need? I need to know the H-O-O angle on that plane. I need to know the O-O-H angle on this plane. I also need to know the dihedral angle to exactly know the disposition of this H and this H with respect to the oxygen and oxygen. That's exactly what we are going to do here.

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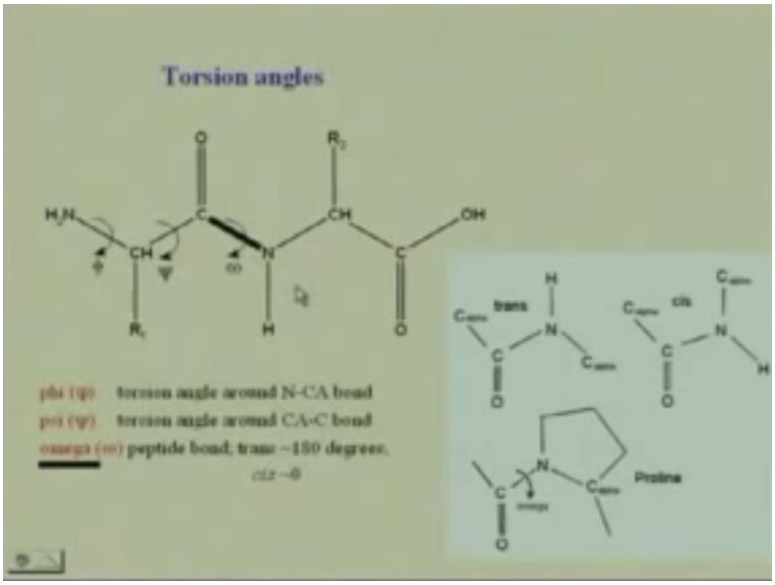

So, now if I consider my torsion angle here, I have a torsion angle that is defined by the rotations, say, I have the phi angle that is defined by rotation about the NC alpha bond. What does that mean? This is my N, this is my C alpha. It is similar to the hydrogen peroxide that I showed you, where these are actually the 2 oxygens. Now, when you always mention a polypeptide chain, you speak about the backbone.

So, what are my 4 atoms here? The C, the N, the C alpha and the C that belongs to the next amino acid. This is the C of the previous one which is this amino acid and it is this one. Why is this one amino acid? Because this has an amino group here, a C alpha group here and a carboxylic group here. So, this has to be one amino acid. This is the previous amino acid. It has to be because it begins with the amino terminal, the C alpha and the C carboxylic group and of this amino acid.

So, when I am talking about in similar cases that I mentioned about the hydrogen peroxide, I have to have 4 atoms that are going to define my torsion angle or the angle between the planes. Now, what are these? What are my points here? A, B, C, D. I have a plane that is going to define A, B, C. What is this plane? It defines C, N, C alpha. What is the next plane? It's N, C alpha, C. The angle between those 2 planes is the phi angle.

If I want to define rotation about the N, C alpha, then I must to go one atom before it and one atom after it. It's just like doing H-O-O-H. Right? What is my definition? I have to have 2 planes, planes that contain atom numbers 1, 2, 3 and another plane that contains atom

numbers 2, 3, 4. So, here I have my C, N, C alpha, C. That's how you define a phi angle. What does that mean? C-N-C Alpha-C, I have 2 planes.

That is C, N, C alpha in one plane and N, C alpha, C in next plane. The angles between these 2 planes is the phi angle. Similarly, you can define a psi angle. The psi angle is the angle between the C alpha and C angle. So, what are the 4 atoms that I have here? It's N, C alpha, C, N. What are the 2 planes that I have here? It's N, C alpha, C and C alpha, C, N.

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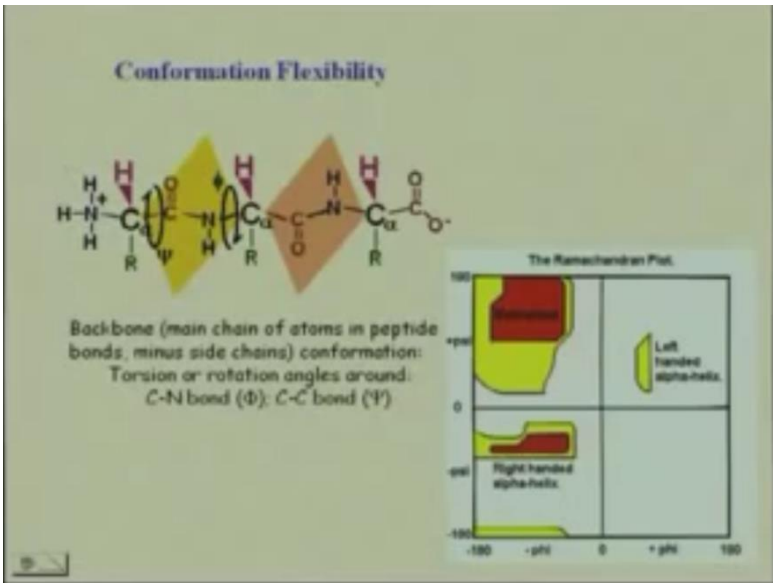

You have to look at this. Let's look at this now. What do I have? This is my backbone. Do you recognize the backbone? What have I marked in these 2 planes? What is this bond? The peptide bond. This also forms the plane. I can also have a dihedral that defines this. But why do I don't consider it that importantly? Because it has a partial double bond character. There are restrictions to its rotations.

So, it is less flexible. It is more rigid. But that does not mean you cannot rotate. You do get a Trans and a sis. So, what is this rotation about this bond? It's N, C alpha, C, N. If you remember that when you have C alpha and C it is the psi angle. So, what are my planes? N, C alpha, C is one plane and C alpha, C, N is the other plane. I have my psi angle. What is my phi angle? It is the rotation about the N, C alpha. So, what are my 4 atoms in this case?

It's C, N, C alpha, C. What are my 2 planes? It's C, N, C alpha and N, C alpha, C. So, I define specific phi, psi angles that define the geometry of the polypeptide chain, the amino acid disposition. Now if I rotate this, what is rotating along with it? It's the R chain. The R

has rotated along with it. If I rotate this, what is happening? This is also moving. So, my whole polypeptide chain is going to have large dependence on phi, psi angles.

So, if I go through the whole polypeptide chain, each amino acid is going to have a phi, psi angles associated with it. What can I do with this phi, psi angles? You can do a lot. We will be studying the structure of proteins in a lot of detail. Now, if you plot the phi, psi angles you get what is called the Ramachandran plot, which an extremely important plot in protein structure is and we are proud that it was G. N. Ramachandran, who actually pointed this out.

And he has a landmark pare where he showed that the definite geometry of phi, psi angle that are defined here belong to specific regions of what is known as the Ramachandran plot today, and this is a must for any protein structure that is solved. You have to have a correct Ramachandran plot for that protein.

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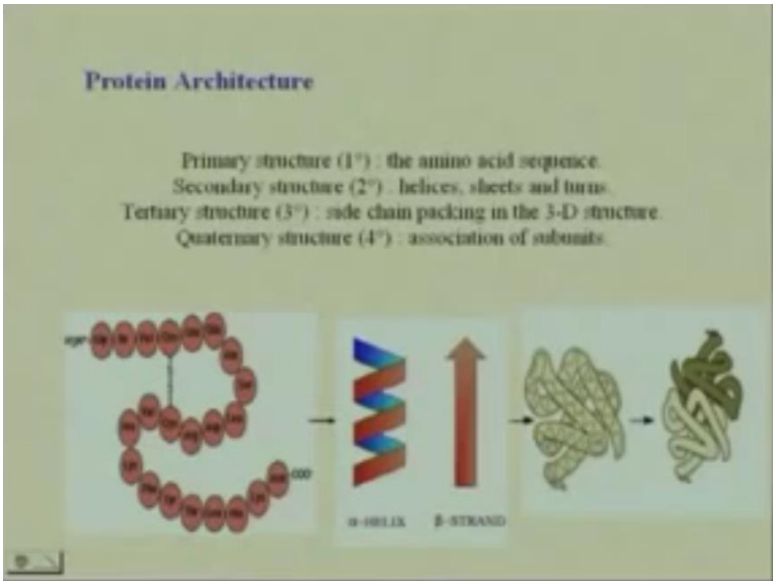

Now, this is what we mean by a protein structure. We have the primary structure, we have the secondary structure, we have the tertiary structure and we have the quaternary structure and you have to know exactly what each of these mean. The primary structure is the amino acid sequence like I showed you for lysine. It is nothing, but just the sequence of amino acids which give you no information about the structure. You only get the structure once you folded it.

What do we have next? We have the secondary structure. What is this? This is the primary structure. What have I shown here? What are these linkages? They are peptide linkages. This

is a disulfide linkage and these are the only 2 covalent linkages that I have in my protein structure and this is my amino terminal. It has to be and this is my carboxylic terminal. So, this is the amino acid sequence of the polypeptide chain.

Now, this sequence you found out with the phi, psi angles can bend or be flexible in any direction. So, you can have something that looks like this. It's the helix, because you can have it rotate. You have flexibility to the polypeptide chain. So the polypeptide chain can rotate and it can form what is called an alpha helix. It can also form what is called the beta strand.

So, when we want to form a total polypeptide or rather a protein structure, it is just a linking of all these types of different secondary structures together. So, we are basically building up this chain from bits and pieces of helices and some what we call turns or random coils that link these 2 together. If these 2 are in the same protein, they would be just linked together by another part of the polypeptide chain. Fine. So, we get what is called the tertiary structure. What is this?

It is the side chain packing in the 3 dimensional structures. Now this could be a specific unit what is called as sub unit. What do you mean by a sub unit? You all know what a monomers and dimers are. Now, if you have a dimeric protein, it means you have 2 monomer units link up together, not covalently, non-covalently. They just associate with one another. So, you have what is called a dimeric structure.

For example, hemoglobin is a tertiary structure. It has a quaternary structure. It has 4 sub units. What does that mean? It means it has 4 such monomeric units that form the protein. All proteins will have a primary structure, a secondary structure and a tertiary structure but not all proteins will have a quaternary structure. You only have a quaternary structure if you are not monomeric in nature.

If you happen to be a monomeric protein, then there is only primary, secondary and tertiary. But if there are number of sub units that have to link together, then you have what is called a quaternary structure.

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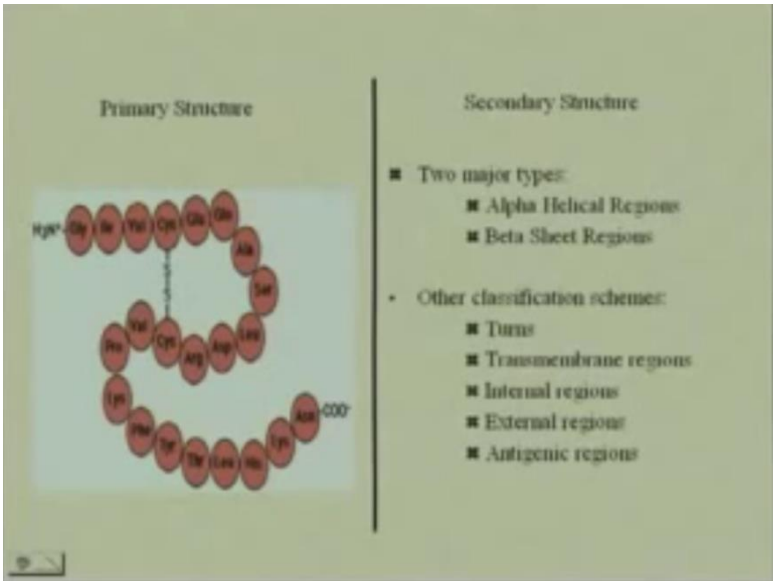

This is our primary structure. This is our secondary structure. The main 2 major types of secondary structures are alpha helices and beta sheets. I showed you on the previous slide a beta strand. Now, when beta strands link together, they form beta sheets. We will understand what these sheets are. There are other classification schemes, which we will not go into right now. But, we have to remember that apart from the primary structure, all the structure we are going to talk about do not have any covalent linkage.

So, we see an alpha helix or something that looks like an alpha helix, but there is no covalent linkage between the polypeptide chains in forming the alpha helix which is extremely important. When you are forming the secondary structure that is alpha helix or beta sheets, the only non-covalent interaction that is important in this case is hydrogen bonds.

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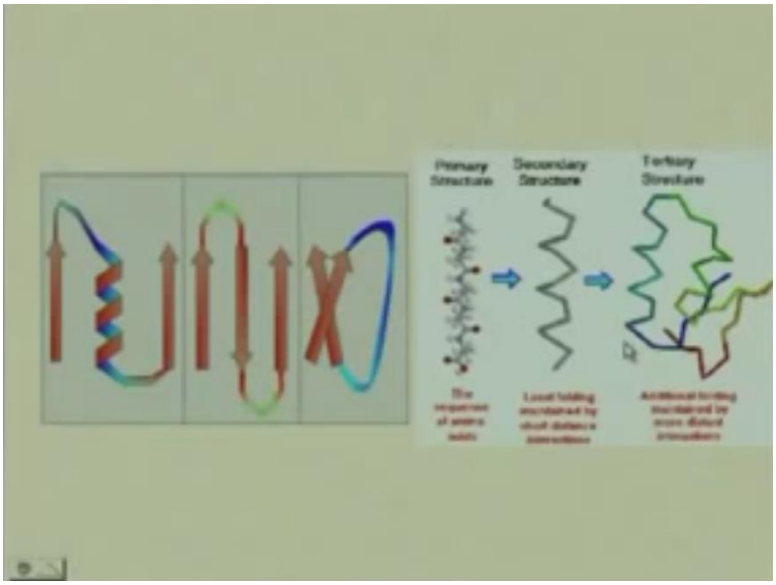

So, this is what we consider when we are linking them up. What do I have here? I have a beta strand. So, this is my polypeptide chain now. What terminal is this? It's amino. You look at it and you should tell me where the protein begins. It has to begin here, because the arrow is pointing in this direction. So, this has to be the amino terminus of the protein. You are going up then. What is this? This is the beta strand. What does it now form? An alpha helix.

Then it forms another beta strand. So, together this is going to form a polypeptide chain structure or folded structure. If I go to the second case, what do I have? This is my amino part. It goes up, it comes down, it goes up again. So, what do I have here? I have 3 beta strands that form a beta sheet. Then, what do I have here? I have again protein that begins here, and then I have just one huge loop that has no characteristic structure to it.

That is possible. It is not necessary that you are always going to have specific hydrogen bonds that form the alpha helix or the beta sheets. But, what we have here? We can have different sorts of linkages. This is what a polypeptide chain. It is just a linkage of the amino acid residues one after the other. Now, if I take a necklace of beads and I drop it on the table, what is it going to form? It is going to have some structure.

If I pick it up again and drop it again, it is going to have some other structure. But, the protein will always fold into the same structure every time. So, every time you drop that necklace of beads you are going to get the same one, which is extremely unlikely if you are going to do it by hand. So, what do we have? What is the primary structure? It is a sequence of amino acid residues. What is the secondary structure? It is the local folding.

The alpha helix is local folding. What is it maintained by? It is maintained by short distance interactions. In this case, hydrogen bonds only. When we consider the tertiary structure, it is additional folding that is maintained by more distant interactions. What do you mean by that? Suppose, I have 1 polar amino acid here and I have another polar amino acid on this side, it is likely that they are going to form a hydrogen bond.

So, what is going to happen? They are going to come together. What about the disulfide linkages? I can have a disulfide linkage between say residue number 1 and residue number 78. What does that make this? It means that the distant parts of the protein structure come together. Right. So, by coming together you form the overall structure.

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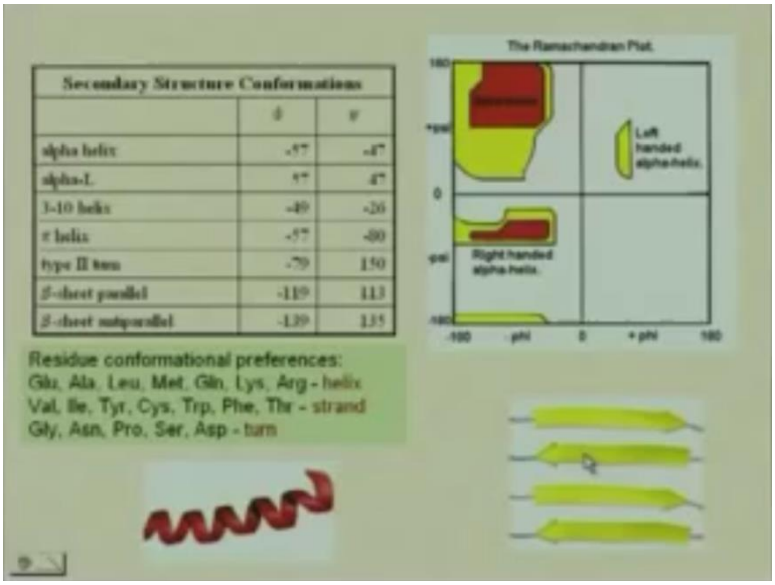

So, what do we have here? We have different secondary structure conformations. What do you mean by secondary structure conformations? You can have an alpha helix. We know what an alpha helix is. We are going to go into more details of alpha helix to understand their hydrogen bonds. This is the preferred phi and psi angles of alpha helix. Where is it located? It is here. What do I mean by a right handed alpha helix?

See that I have a right handed alpha helix and a left handed alpha helix. What do you mean by a right handed alpha helix? We mean that the helix can actually go in 2 directions. It could go up or down.

Now, if this is the direction of propagation and this is the way your polypeptide chain goes, this is a right handed helix. If you consider your left hand and this is the polypeptide chain and the direction of propagation is this, this is the left handed alpha helix. Left handed alpha helices are very rare in protein. You do not generally see them. You just have right handed alpha helices. Can you tell the conformations of the amino acids that you see?

You always see L amino acids. So, if we look at the alpha helix, usually when we mention the alpha helix we do not say it as a right handed alpha helix because by default it is. What is this region? This is the preferred region for the alpha helix in proteins. This is the preferred region for beta sheets in the proteins. Now, this is what we mean by a beta sheet. What are these? They are beta strands. These beta strands have formed the beta sheets.

Now in between these beta strands, in the blank space, I could have anything. I could even have a helix because it is just one part of the polypeptide chain linking with some other part of the polypeptide chain. But, the difference between alpha helix and beta sheet is the alpha helix has to be contiguous. I cannot have the part of the alpha helix here and the rest in the other part of the protein. That is not possible.

When I have an alpha helix and it begins at the residue number 16 and continues to residue number 30 that means, residues from 16 to 30 will all form a part of the alpha helix. But, if I have a beta sheet, I can have residue 3 to 17, residue 40 to 46. It does not matter. They just form beta strands that are part of the same beta sheet. That is possible when we are looking at this.

Now, when I consider my beta sheet here and my right handed alpha helix here, then what do I have? I have specific bonding characteristics that are linking my secondary structures. There are different types of secondary structure conformations that I have listed here. I have called a beta sheet parallel or anti parallel. Now, you can say by the name itself what that might mean. What might it mean? It might mean that the strands are parallel to one another.

What do I have here? I have an anti-parallel beta sheet, why? because one of my strand is in this direction and the other is in this direction then, the next one is in that direction and then, I have one in this direction. So this would be an anti-parallel beta sheet. Now, what I have listed here is some residue conformation preferences. What does that mean? It means that these residues would like to be in an alpha helix.

They prefer to be alpha helices. These residues prefer to be I strand and there are certain other residues that prefer to be in turns. What are turns? Turns are going to link the 2 secondary structural elements together. So what we did learn today was how we can look at the geometry of the polypeptide chain. We have definite definition for the polypeptide chain, in terms of the different torsion angle. What are these torsion angles?

One was that we learnt the peptide plane would be planar in nature because of the double bond characteristic, due to the partial double bond character of the peptide bond. That makes it rigid. Why does it make it rigid? Because of this partial double bond. But, we can have

rotation about the other single bonds that are present. These form the phi and the psi angles. Rotation about these gives definite conformation considerations that I have to make and what are these?

They give rise to specific secondary structural considerations. So, I have my primary structure that is linked by peptide bonds. I have my secondary structure, which we only learn the alpha helix and the beta sheet. Alpha helix and the beta sheet will have definite phi and psi angle that they correspond to and they would form a hydrogen bonding network something that we do in the next class. Thank you.