Biological Inorganic Chemistry
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Lecture – 3
Biomolecular Structure and Molecular Biology Component

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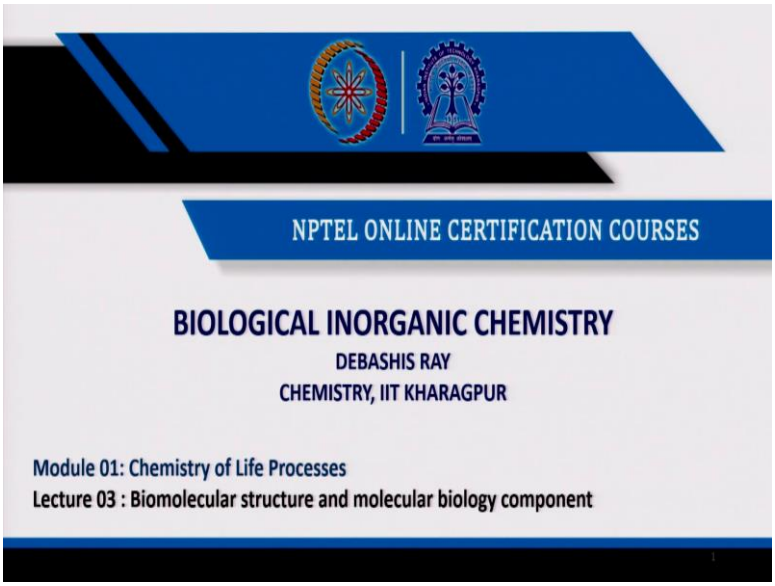

Hello, good morning everybody. So, we are in the third class of your Biological Inorganic Chemistry, where we will be talking about the third part basically of this particular module that means chemistry applied processes, where will be talking a little bit about the more biologic part, that means the biomolecular structure and molecular biology component what we should know.

So, this is basically a hybrid area of studies where we can see that the biologists can come and join for knowing these, for doing something and for publishing something as a research component. Similarly, the inorganic chemist as well as the coordination chemist can also contribute in a large amount of these informations because they know very much about the corresponding chemistry of the metal ions.

So, in this particular class, basically, will see how the different bio molecular structures are important, and how the molecular biology component is also important to understand nicely the involvement of the metal ions in biology.

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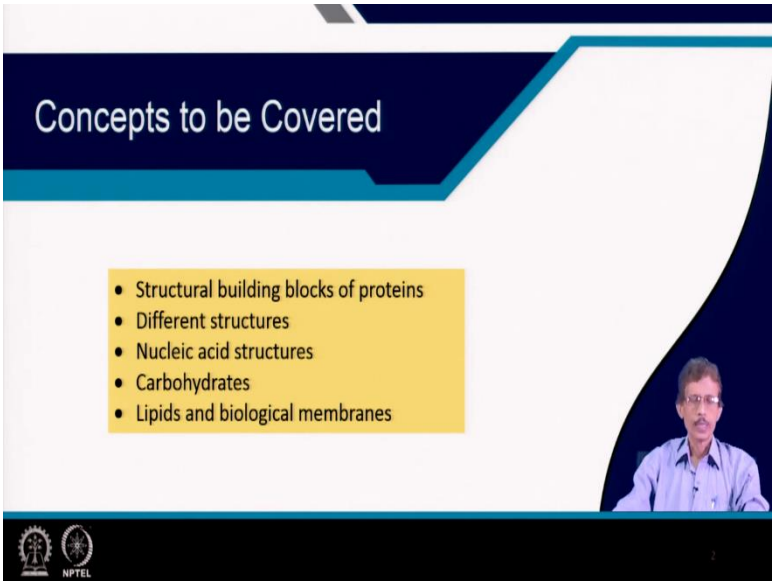

So, will be talking very quickly about the structural building blocks, where we can have the proteins because the proteins are there and we have to get by insertion of the metal ions, the corresponding metalloprotein parts. So, how proteins we have and how the metal ions will be incorporated, not all proteins will take up metal ions to give you the metal of proteins.

Similarly, we will have the metalloenzymes, so the different structures. So, structures of the proteins, structure of the metal ions centres and the final structures. Then, little bit will talk about the nucleic acid structures, because we can have the DNA and RNA molecules as well as the metal ions side by side, the carbohydrates also will take part through the involvement with that of the structures. And finally, the lipids and the biological membranes will talk about.

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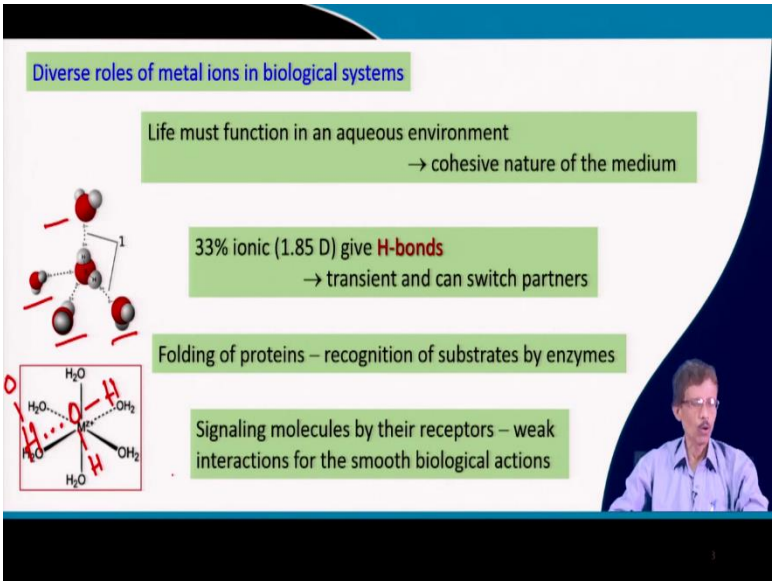

So, when we have the metal ions in biological systems, what we find that they can have different roles to play and definitely the metal ions will try to have the corresponding informations in terms of its structure as well as the reactivity, that metal ions will try to behave as a metal ion, like it will go for simple coordination chemistry at that particular point.

But the environment is much more complex, even for the environment, where you can have large amount of water molecules, because the biological environment we all know is dominated by the presence of large amount of water molecules. So, those water molecules, how those water molecules can initially interact with the metal ion centres that we all should know.

That means, if we consider the 3d ions, the iron ions, the copper ions or the zinc ions, we should also know not only the ions but the corresponding aqua species. How many water molecules will be binding to the metal ion centres? And what are the corresponding geometry of those species? And how they can react in terms of its substitution reactions or as well as the electron transfer reactions?

So, what we can see that, that it can function, the metal ion should function, our lives should also function in an aqueous environment. The way we say or the way we know that, our life is also functioning in the environment of oxygen also. We cannot survive in absence of oxygen. Likewise, always you should have the typical aqueous environment.

So, the medium, in which particular medium will be talking about all the reactivity patterns and all the reactions of these metal ions, a metal ion salts, a ferric chloride in water say or some other anhydrous salt like ferrous chloride, if we know that it will be soluble in some aprotic solvent or non-polar solvent, we will try to dissolve it in some organic solvent.

So, where the organic part will come? Obviously, the organic part will come in our life also, which are insoluble in water, insoluble in aqueous medium, which is the lipid part that we will see also. So, when we talk about the aqueous environment, the medium must have some cohesive nature.

And that cohesive nature is also important because we all know that the density water, the structure of the water and how it changes, when you can have some interactions with the different water molecules. So, this is the classic structure where we all know that this particular structure is made up of 1 central water molecule surrounded by 4 water molecules.

So, this is one, so, this, so, this water molecule we have, so 1, 2, 3 and 4. So, these water molecules, so how you can have a tetrahedral motif, we call it as a tetrahedral motif, because this oxygen and the hydrogen they have some typical characteristics, but we will know that these are responsible for hydrogen bonding interactions.

So, 1 water molecule has 2 hydrogen donors. That means they are hydrogen bond donors; they can donate hydrogen bonds for hydrogen bonding interactions with that of your adjacent oxygen of the adjacent water molecules. Similarly, what we find that other two, this the left-hand water molecules these water molecules have hydrogen.

So, those hydrogens are also pointing towards the oxygen of the central water molecule. So, these hydrogen bonding interactions are very important because all we know that there is a charge separation between oxygen and hydrogen of this typical covalent bond between oxygen and hydrogen. So, we all know that is 30 percent, 33 percent ionic in nature, that is why you have a dipole moment.

So, on the oxygen we write delta minus minus and on hydrogen we write delta plus and the delta plus. So, you have the charge delta plus on one of these hydro hydrogens of the water molecule and another hydrogen also have a delta plus charge. But these hydrogen bonding interactions or the hydrogen bonds are transient and can switch partners.

So, at one point of time, if we see that the number one that means, these two hydrogen bonds we are pointing for our understanding that they are interacting, but is a dynamic situation not

that this is very static situation. So, this water molecule can be replaced by any other hydrogen bond donor or hydrogen bond acceptor. So, new hydrogen bonding interaction can take place.

Similarly, we will also find that when we can have the X-ray structures, the protein structures, the metalloprotein structures or the metalloenzyme structures in the crystal lattice also in the solid state the two oxygen, because this oxygen, this oxygen as well as the top oxygen also, we can have in the hydrogen bonding distances.

So, what we can have? We have this H, so H we can have, so then O and H but this one also we have this another H, but if you have this another oxygen, so these oxygens, so oxygen oxygen distance is important, because hydrogen we cannot locate or we cannot find out from X ray diffraction.

So, these two oxygen and the oxygen or oxygen and the nitrogen these are important to find out the typical distance between these two centres and how strong these hydrogen bonds are, which are also important during the folding of the proteins. And these hydrogen bonding interactions are also important for recognising the substrates by enzymes.

Because, these as I told you very weakly interacting because the hydrogen bonds are very weak and they can also change their partners. So, at one point of time, the enzyme can recognise the substrate, then substrate can be activated by some reagent or some nucleophilic attack, then it is converted to the product, but the product may or may not be strongly hydrogen bonded to that particular site.

So, it will be leaving that particular site and we get the enzyme catalysed product in that particular fashion. So, what do we see there that is that your M2 plus and this M2 plus is bound to 6 water molecules. So, these M2 plus bound to 6 water molecules is the hexaco species.

It is a very simple one any M having a charge of n plus when it is binding to 6 water molecules like iron is a hexaco species of iron in the ferrou state as well as in the ferric state. So, immediately whenever you have the available water molecules there, it immediately binds or traps to that particular iron site by surrounding 6 water molecules in octahedral geometry.

So, this hydrogen bonding also is important in case of signalling many molecules by their receptors and the weak interactions for the smooth biological actions. So, not only our

covalent bond formation or coordinate bond formation, these hydrogen bonding interactions are always very important to find out the typical biological actions because the energy requirement will also be less. So, with a small energy requirement your substrate binding, product formation and release from the enzyme pocket is also taking place there.

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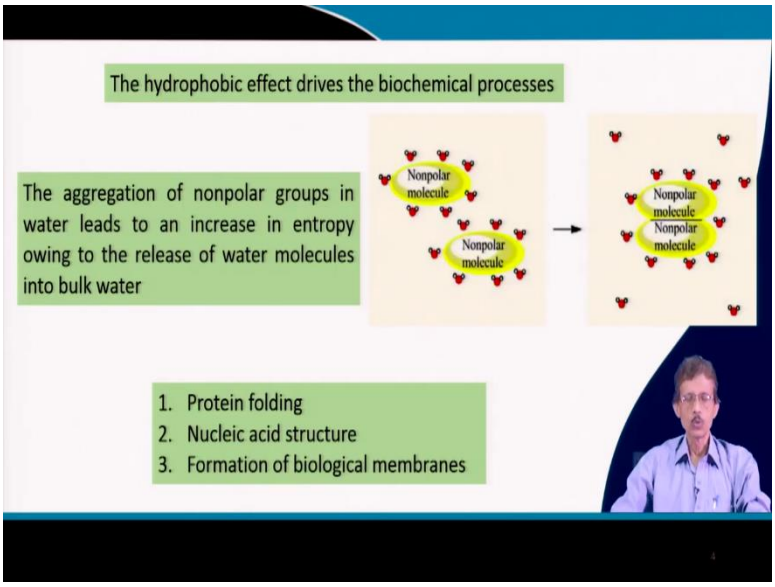

Then not only these hydrophilic interactions, that hydrogen bond formation, but also the hydrophobic effect or hydrophobic interactions are important in driving a particular biochemical reaction. Therefore, those water molecules are still there, but when you have the hydrophobic effect, the particular species or the particular environment will definitely repel a lot like the corresponding water environment or the aqueous environment.

So, here we see that if you can have a non-polar molecule, the non-polar molecules they do not have any hydrogen bonding interactions, but when it is present in the aqueous medium, the water molecules will come and try to surround it even it is a charge neutral also. So, many of these water molecules will be surrounding to individual non-polar molecules.

But these components these non-polar molecules will try to avoid these water molecules they do not like basically to have within the environment of these water molecules, but instead of that, what they like, they like to interact to each other. So, these two yellow or red species that means the non-polar part of one molecule and another non-polar part of the molecule or the molecule itself, they can come together and they can aggregate or they can agglomerate.

So, during that interaction, that means the non-polar non-polar interactions that means the aggregation process due to the hydrophobic effect, because they are repelling water

molecules. So, from this particular aqueous environment, what do you find large pool of water molecules will be released in the environment.

So, you have many water molecules, because already whatever number of molecules you have, so in the top, you have 4 plus 3, 7 here also 4 plus 3, 7. So, 7 plus 7 all 14 water molecules will then be surrounding this particular aggregate. So, non-polar groups definitely will go for aggregation and there will be release of water.

And release of water means many number of water molecules will be released that will be contributing to an increase in entropy factor, because of this release of water and those water molecules will be going to that of your bulk water environment. So, these hydrophobic interactions when you find that you can have a amino acid and this particular amino acid can have, we all know the amine group and the carboxylates are, there in the amino acid residues.

So, if we have the corresponding charged species the dipolar one so the amine function is getting protonated from the deprotonation of the carboxy end. So, it will be NH_3 plus and the carboxy end will be CO_2 minus, so is a dipolar molecule. So, dipolar molecule it is involved in peptide bond formation and then the corresponding other things are taking place also.

But the backbone of this particular amino acid sometime we find that many of these backbones are off this non-polar character, that means the hydrophobic nature. So, hydrophobic non-polar part of the amino acid there also so, during protein folding, will have to see whether you are non-polar or hydrophobic part inside the folding or outside the folding. So, definitely this interaction can take part in your protein folding process also. And we can have that also in your nucleic acid structure.

And finally, the formation of your biological membrane because that particular point also if it is not soluble in aqueous medium, you have to repel the aqueous medium, and during that repulsion, your structure will also be changing. So, how the biological membrane will be there in presence of water molecules, when they will try to repel the water molecules or the water environment or the aqueous environment.

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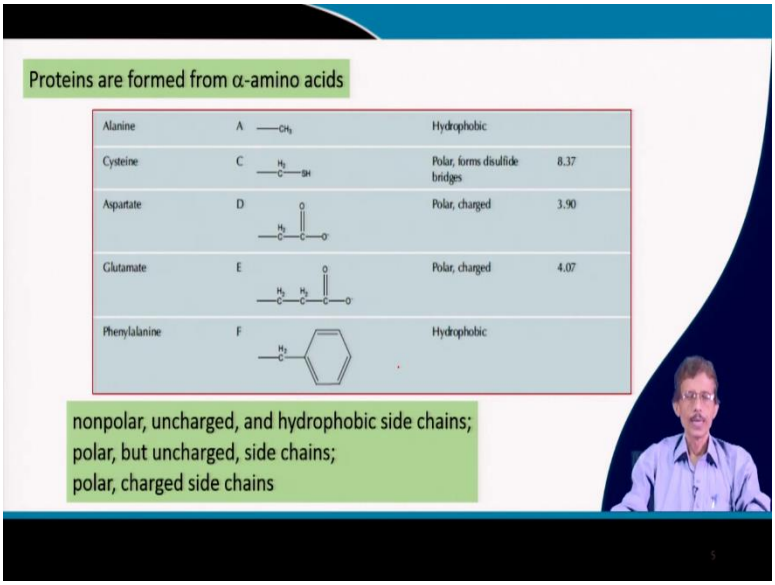

So, the protein structure, how we get the protein structure and we all know the alpha amino acids that means the alpha carbon has that particular amine function as well as carboxy function, carboxylic acid function. So, we all know the very simple example. So, I have taken five such examples of these amino acids.

And we should know also the three-letter abbreviation as well as the single letter abbreviations nowadays, because we do not spend time, we do not write writing these particular amino acids, with the three letter abbreviations but it is little bit difficult for you, but try to memorise it also.

As this how alphabetically also we can arrange also A is alanine, but earlier we used to write is A Ala. Cysteine is C also which is we earlier we write as Cys system, then aspartate, glutamate and phenylalanine. So, how we write these basically, these are the groups which we have shown at the third column, this these are shown as corresponding one as you are responding part of these as your room that R groups.

So, you have the alpha carbon and alpha carbon has the amino function as well as the carboxylic acid function and that carboxylic acid function what we can have, that that carboxylic acid function will be involved in formation of your CO NH function with that of your another NH2 function of the another amino acid giving you the peptide linkage.

So, the R groups, the R groups form the CS3 function that means the methyl function in alanine to that of your phenyl or the benzyl function, if you consider the CH2 group also for your phenylalanine function. So, when you see that in case of alanine, we are not classifying

alanine like that of your glycine, of glycine we all know that the simplest amino acid when you have the backbone is CH2.

So, when one of the hydrogen of that CH2 in glycine molecule you replace by methyl function you get the alanine. So, Ala or A, is hydrophobic in nature because the backbone basically forget about the other two parts, because those two parts will be forming your peptide linkages. So, the backbone will giving you a hydrophobic environment and that hydrophobic environment is basically will be there apart from your peptide linkage. So, it is under the category of a hydrophobic backbone bearing amino acid.

Similarly, for cysteine you have the pendant or dangling CH2SH function. That is why it is polar and it can form the disulfide bridge which is also very important for our hairs and all these the keratin formation and all these the SH function from one protein part and another SH function of the one protein part, if they coupled together giving you the oxidation and that oxidation is basically leading towards SS bond formation.

So, the disulfide bridge is taking place and that disulfide bridge formation can take up one of the protein part to another protein part and these two are coupled together, but when we talk in terms of the corresponding PK value, you see 8.37 these are the PK values on the last column. So, you can have a local rise in the pH values it is above that particular value of 8.37 you can get the corresponding deprotonation that means SH function will be S minus.

And will find also that S minus that means the cysteine residues, the cysteinate ion can be available for metal ion coordination, which is a very simple example of coordination of thiolate anion, typical inorganic thiolate, sorry organic thiolate. What we can have in the laboratory and which can be available to coordinate to your metal ion centre.

Similarly, for aspartate you have the dangling CO minus group apart from your two peptide linkages from left and the right. So, you have the dangling, so, that is why the R groups you should focus our attention you should concentrate on that, that what R groups are important and whether R group has can function as a ligand or R group can have some effective donor function or effective donor group to coordinate to your metal ion centre.

Similarly, glutamate and that of your phenyl alanine that is also again hydrophobic because you do not have any function attached to that particular phenyl ring or the CH2 function which will be available for metal ion coordination, but if the para position of these is

converted to that of your OH function, we all know that we getting as the tyrosine. The tyrosine can have metal ion coordination.

So, will have three categories of these sorts of amino acids or long list of 20 amino acids you can have and the recently discovered one is your cystine1, selenocysteine 1 that SH group is replaced by a CH function. So, altogether we will have 21 amino acid.

So, they are nonpolar uncharged and hydrophobic side chains, they can have polar, but uncharged again and side chains. So, some groups are there so that ultimately finally, it is not uncharged, then polar and charged side chains. So, you can have the S minus, CO minus and all these you can have the corresponding side chains.

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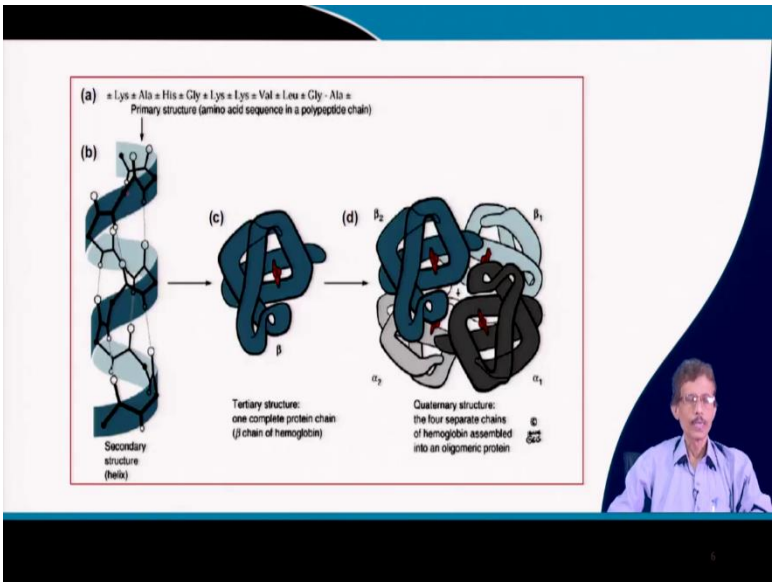

Now, we will see quickly that how these particular amino acids, the three letter abbreviations again we are going back to three letter abbreviations. So, these basically are coupled together, so different amino acids we are coupling together. So, these are linked by peptide bonds. So, peptide bond with lysine, alanine, histidine, glycine, lysine, lysine, valine, leucine, glycine, alanine.

So, any of these amino acid residues from the list of 20 amino acids can be used for your peptide bond formation on both ends. So, we get the primary structure, so is nothing but a polypeptide chain. So, when two amino acids one glycine is coupled with another glycine, we get gly gly, which is the typical dipeptide, one peptide bond, but it is a two amino acids you can call it as a monopeptide also, that one peptide bond is there, but two amino acids are there.

Similarly, we can have a dipeptide, we can have a tripeptide and all these things. And most of the cases, the nature of these donor groups are so aligned, if you have the donor groups available from the backbone of the polypeptide chain, then only will be able to trap the metal ion, because our ultimate goal is how to trap the metal ion.

So, we get the primary structure then we can have the in B the category B we can have the corresponding structure as the secondary structures sorry. The secondary structure will discuss definitely, so secondary structure. Now, the hydrogen bonding thing will come into play and hydrogen bonding can take place and that hydrogen bonding interacts and can give you a helical structure, which is after primary will have the secondary structure.

Then the typical coiling can take place, which is your one complete protein chain, and will be labelling as the beta chain. How we configure, which is a alpha and which is your beta will see shortly. And that is one part of that particular component which is the beta chain of haemoglobin which is similar to that of your monomeric part of myoglobin and when four such units, four such units in terms of two alpha type and two beta type that means alpha 1 alpha 2 and beta 1 beta 2 are assembled together, we get the quaternary structures.

But you have separate chains of these particular units and they are assembled in oligomeric protein. So, the final structure of haemoglobin is a quaternary structure, but myoglobin has a tertiary structure. So that we will see how these are developed. So, these are the very primary informations and the primitive informations for getting these structures.

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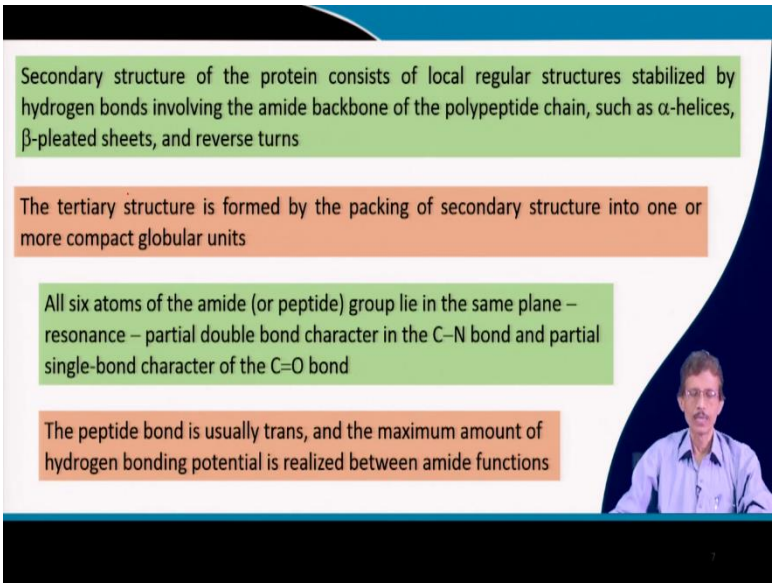

So, hydrogen bonds are definitely there to stabilise this secondary structure just now, what we have seen the left-hand side of your secondary structure, the helical structure. Then you have the amide backbone, the chain and such as the alpha helices, beta pleated sheets and the reverse turn. So, these are the three types of that particular binding you can have you can have the chains from alpha helices, beta sheets and the reverse turns, the hairpin turns we can have.

Then we just now we have seen the tertiary structure and the tertiary structures are formed from the packing of secondary structure into one or more compact globular units or the globular forms. So, all six atoms in the amide backbone should be in the same plane and they are resonance stabilised and partial double bond character in the CN bond can be achieved. We know that in the peptide, if they are in resonance.

So, their resonance the CN bond is in resonance with the CO bond. So, we find that that the corresponding single bond character will be increased for the CN and the double bond character of the CO will be reduced. So, that is why we have the resonance stabilised peptide structure. They so one of these oxygens will be pointing in this direction and one will be in the opposite direction. So, will have the transient orientation.

And the maximum amount of hydrogen bonding potential is reduced, is realised basically between the amide function, so how these amide functions are there because the amide CO that means this CO function of these, these oxygen is the hydrogen bond acceptor, and if you have the corresponding CH functions or the NH functions available, those are hydrogen bond donors.

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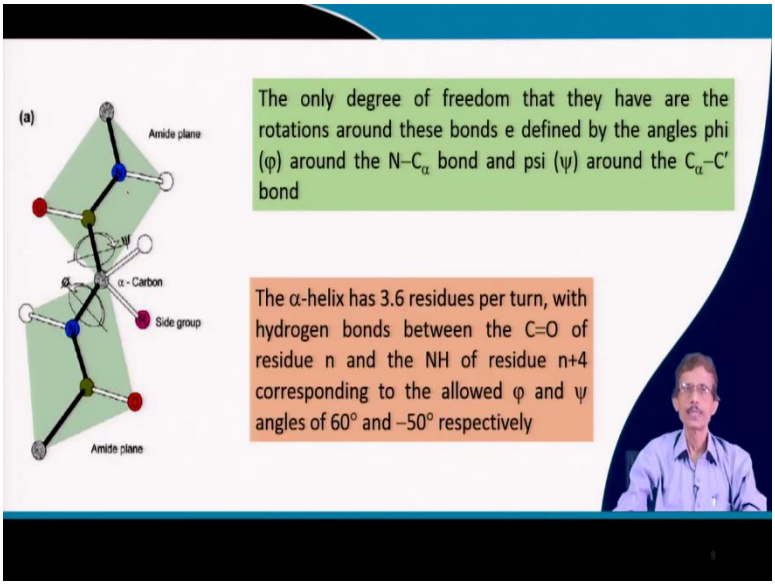

So, those hydrogen bond acceptors and hydrogen bond donors basically giving you this particular type of arrangement, where you have the basic amide plane and basic amine plane containing this alpha carbon, that alpha carbon is there. So, one of these amide plane containing the six atoms, the six atoms at the top and the six atoms at the bottom they are plane basically.

So, if you have this plane and if you have another plane, so basically around this carbon which is your alpha carbon, so these two planes can rotate basically. So, because this is the fixed, the resonance stabilized planar part of the peptide unit and another resonance stabilised planar part of the peptide unit, but these two can rotate through that particular carbon. So, that carbon is the tetrahedral carbon.

So, around that tetrahedral carbon you can have two types of rotations and is these are designated by two angles. So, one is the phi and another is the psi angles. So, that basically tells us the degree of freedom and the bonds is defined by the angles phi around NC alpha and angle phi between C alpha and C prime bond.

So, how we get these particular informations and these bonds is important, that we can have two types of these angles and those angles basically tells us that we where we can have that turn. So, the if the alpha helix has 3.6 residues part turn with hydrogen bond between the CO of the residue and the NH function of the residue n plus 4.

So, n is 1 amino acid residue, then another 3 amino acid, then you go to the fourth one. So, n plus 4 1. So, these two will be involved in hydrogen bonding interactions and then phi and psi

values are very important in the range of 60 degree to minus 50 degrees is important and these particular ranges basically will also dictate the pleat structure of the protein chain. And with respect to these two we have a famous Indian scientist GN Ramachandran. So, GN Ramachandran plot is also important to have an understanding about these structures.

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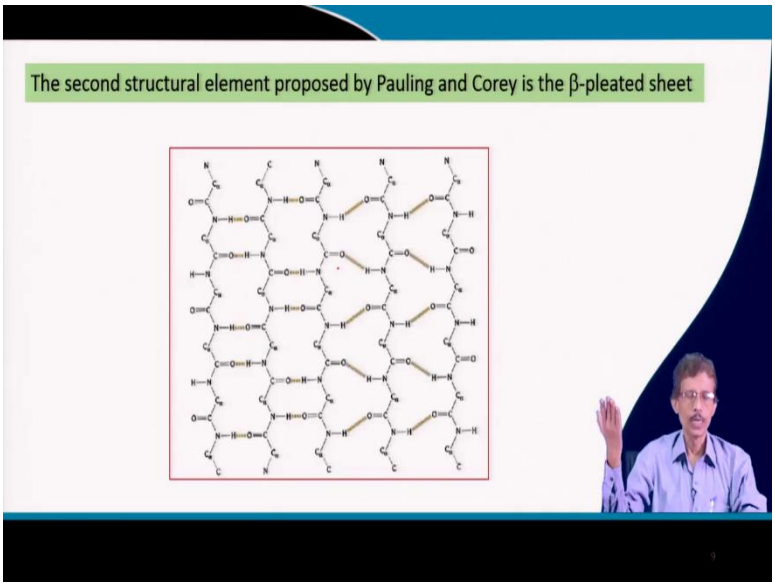

So, that particular one that means, when you have these two angles and this particular Ramachandran plot, we can have some good idea about the structure. Then Pauling and Corey these two people, these two scientists basically talked about the beta pleated sheet. So, this is another kind of hydrogen bonding interactions, which is responsible for the formation of the beta pleated structure, so is the pleat like structure.

So, you can have the planar units, the planar units can have two types of hydrogen bonding interactions, one is say you see the typical horizontal interaction and another is angularly up and angularly down. So, angularly up and angularly down things. So, these basically these sorts of things can basically give rise to these particular types of arrangements.

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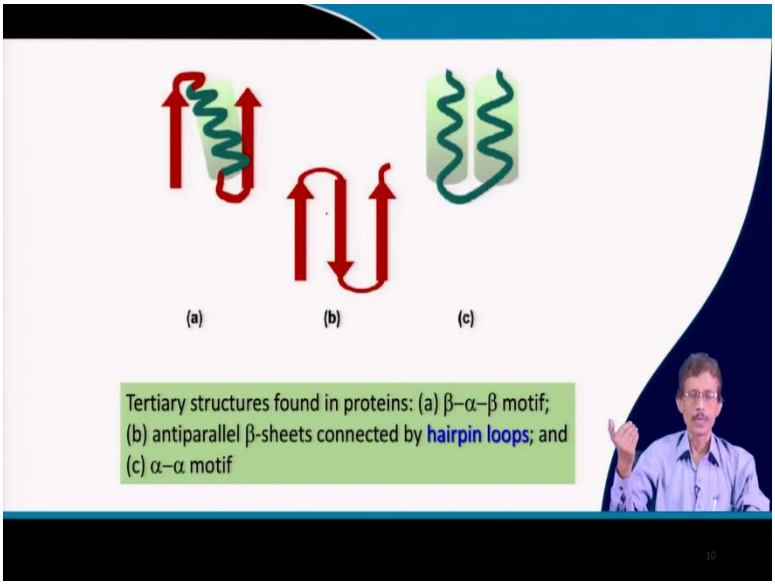

So, we can have three types of arrangements one is a and that is b and other is c. So, the individual parts, the individual parts of these components are getting stabilised. How they are stabilised, because all are made of amino acids only, those are our useful ligands, which will be available for trapping the metal ions.

So, those basically are very important how we get this particular one. So, when we get these structures, not that quaternary structure is after secondary structure that tertiary structure. So, we can have it in the protein, the beta-alpha-beta motif, so this the red part is your beta, then the curly part is your alpha part, and then again beta part. So, they can be in the same direction or they can be in the opposite direction.

That is why you have the b, the anti-parallel beta sheets, no alpha is their only beta sheets connected by you have a loop. So, the hairpin loops are there, but when two alpha, alpha-alpha things are connected, beta-beta-beta is connected then alpha-alpha is connected, though we have the alpha-alpha motif. So, these are basically the cartoon diagrams for knowing these structures and knowing these particular motifs, how we can get this.

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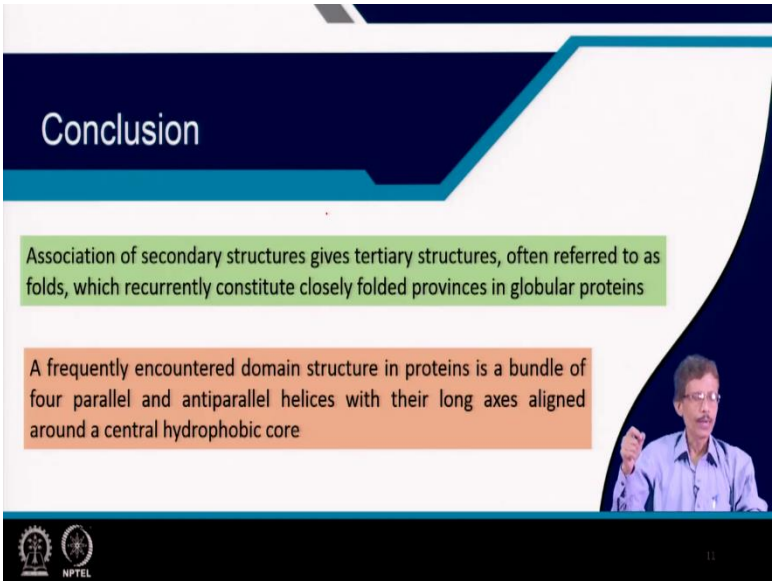

So, that way basically what we can have, how we conclude this particular part of our understanding that how we have water molecules in the aqueous medium, and how these water molecules are important in taking us to environment where we always talk about hydrogen bonding interactions, not only the hydrogen bonding interactions with the substrate molecule or some other important molecules, but also in the protein chain when you have the peptide bonds. So, the possibility of hydrogen bonding are there.

So, always try to remember that if you have CH function, NH function or OH functions these are the most basic functions what we can have. Similarly, we can have the SH function, a CH function, the selenium hydrogen bonds are there. So, you can have the electronegativity differences or hydrogens attached to those electronegative atoms can function as good donors. So, you can have the typical hydrogen bonding interactions.

So, we just follow for the association and those associations for the secondary structures basically give the tertiary structures and those tertiary structures when you have the folding the beta sheets and the alpha folding, we considered as they are typically the folds and those closely folded provinces basically, the regions, basically gives us the typical final structures of your different globular proteins.

So, within these globular proteins a domain we can have, so, frequently encountered domain structure is nothing but a bundle of four parallel and anti-parallel helixes is commonly occurring things because we are trying to find out the nature only, how nature is doing everything for us, all these things for us we try to discover the nature only.

So, this part of chemistry is basically nothing but knowing the nature. So, we see that you have four parallel or antiparallel helixes are there and long axis aligned around the central hydrophobic cores. So, if you have a hydrophobic core, you can have the different helixes present. And that is why the reactivity pattern and that tunnelling of water molecules, sometimes will find that water molecules are moving from one point to the other due to the presence of this particular hydrophobic core and the final structures.

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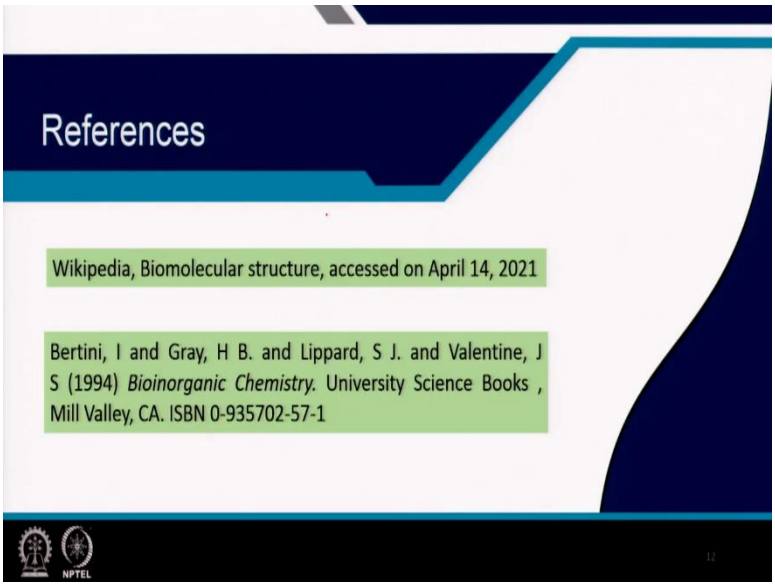

So, what we can follow basically all that they basically most of the classes will just consider that go read first the Wikipedia page, what we know about the biomolecular structures, the exact definition is nothing but the textbook type of definitions and all these things are there. And one book basically, again that Bioinorganic Chemistry book of Lippard, Valentine, Gray and Bertine. So, thank you all for this part. Thank you all.