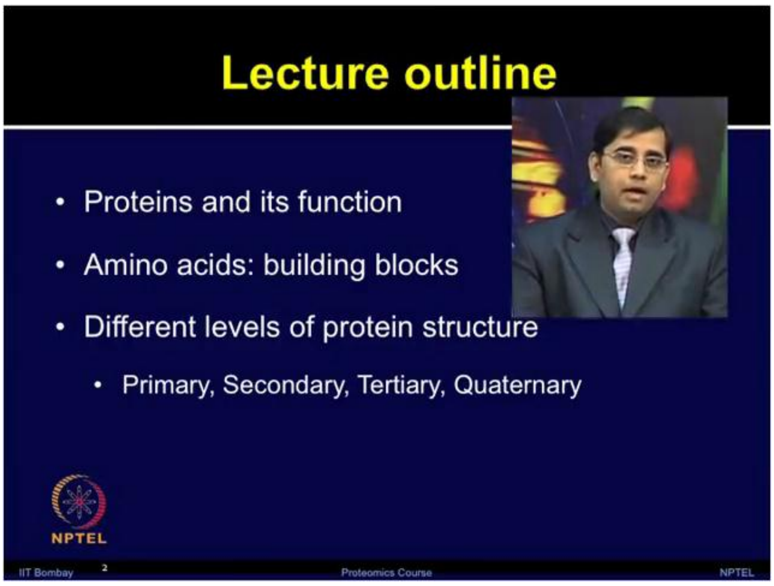
Proteomics Principles and Techniques

Prof. Sanjeeva Srivastava
Department of Biosciences and Bioengineering
Indian Institute of Technology, Bombay

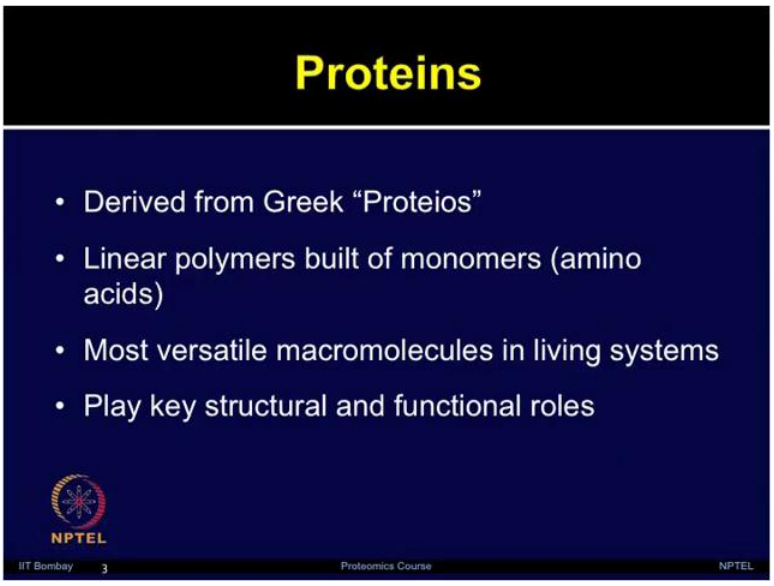
Lecture No. # 04
Proteins: Amino Acids and Structural levels of proteins

(Refer Slide Time: 00:49)



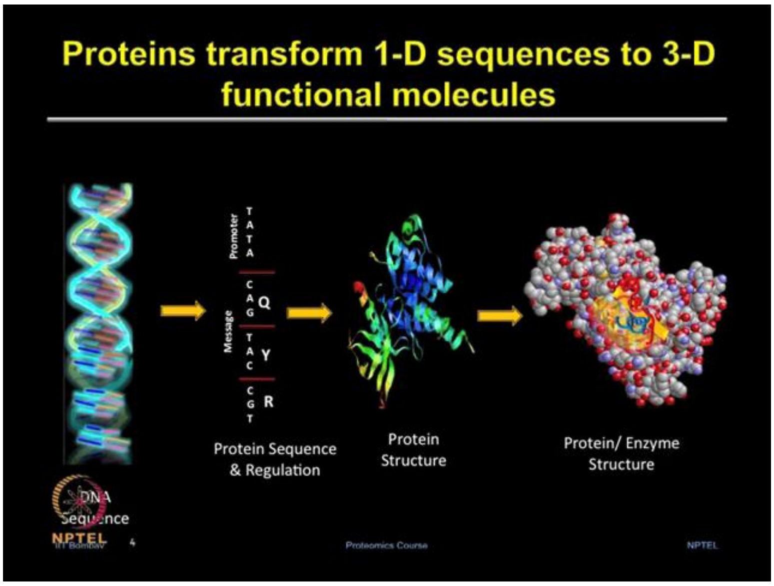
Welcome to the proteomics course; before we move on to the proteomics and discuss about what are all different techniques and concepts involved in proteomics. Let us first start the basic concepts on proteins. So, today we will talk about proteins, amino acids and structural level of proteins. Let me give you the lecture outline; we will first talk about proteins and its functions, amino acids - the building blocks, and then different levels of protein structure - primary, secondary, tertiary and quaternary.

(Refer Slide Time: 01:09)



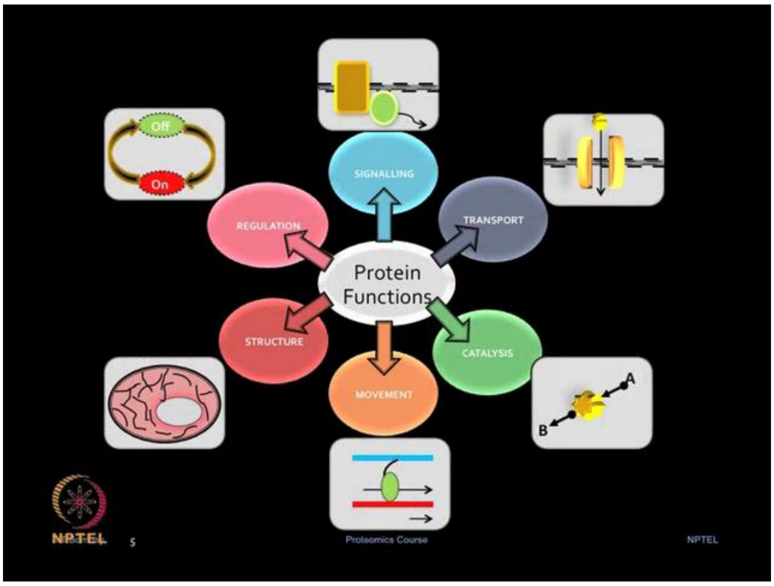
The protein term was derived from the Greek word Proteios, which means of the first rank are very important. This term were coined by scientist Berzelius in 1833. These are linear polymers, which are built of monomers or amino acids subunits. These are most versatile macromolecules in any living systems. They are crucial for very essential functions of all the biological processes, and they play very critical role both from structural, and functional point of view.

(Refer Slide Time: 01:52)



Therefore, studying about the proteins is very important. If you look at the center dogma is starting from DNA to RNA and protein, the protein can transform the one-dimensional sequence to the three-dimensional functional information. Proteins can play wide range of functional properties, because of their different functional groups, which can account for various protein functions and its activity. Protein-protein or protein-other bimolecular interactions, they are generated, because of the capability of these proteins which cannot be obtained from the any given individual protein.

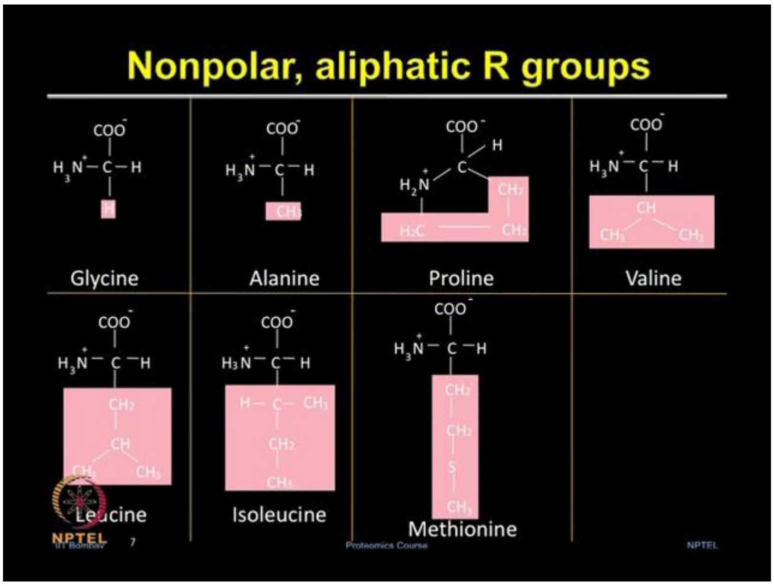
(Refer Slide Time: 02:42)



Proteins can performs various type of functions whether it is catalysis, movement, structure, regulation, signaling, transport etcetera. As you can see in this slide, various types of functions have been shown. Enzyme catalysis - the enzyme catalyze biochemical reactions by increasing the rate of reactions. Transport and the storage - proteins can transport a small molecule such as oxygen and iron. Proteins are involved in the movement with muscle contraction, if you talk about microorganism, in bacteria the chemotaxis. They are responsible for the mechanical strength. For example, in this skin and bones the collagen and keratin all of these different examples of mechanical strength proteins are also present as immunoglobulin responsible for the immunity an antibodies are used for various type of protein protei and protein ligand interactions; growth in differentiation transcription factors gene expression during growth and development. For example, nerve growth factors harborne such as insulin all of these are various examples of proteins and the various diverse functions in which they are involved.

Amino acids, the building blocks of proteins. Amino acids constitute the basic mono medic unit of proteins which are joined by the peptide bonds. The 20th standard amino acids which can be arranged in several ways, giving rise to numerous proteins having different structure and function properties. The diversity and versatility of 20 amino acids enables range of protein functions, due to the side chains which can vary in size, shape, hydrogen bounding capacity, hydrophobic characters, charge and chemicals reactivity proteins perform much diverse function as compared to the DNA.

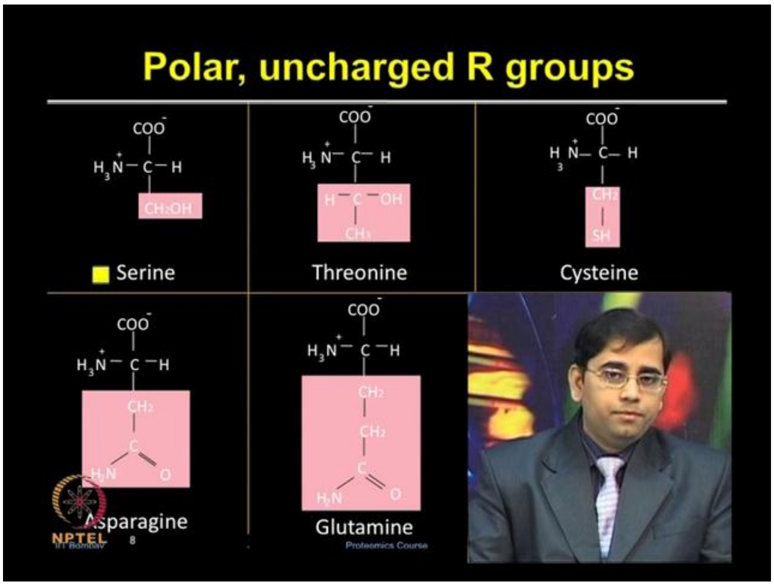
(Refer Slide Time: 05:11)



We have already studied about different amino acids in your under graduate education I will again try to refresh you on some of those concepts, but it in more nut shell. So, here I have shown various amino acids which are non-polar and aliphatic r groups starting with the glycine. If you see on the left hand side the top most which is the simplest and a chiral? Now next is alanine which can contains a methyl group, proline which have aliphatic side chains, proline has very unique feature it has no free amino group, and the side chain is bounded to the an an alpha carbon of the alpha carbon atoms.

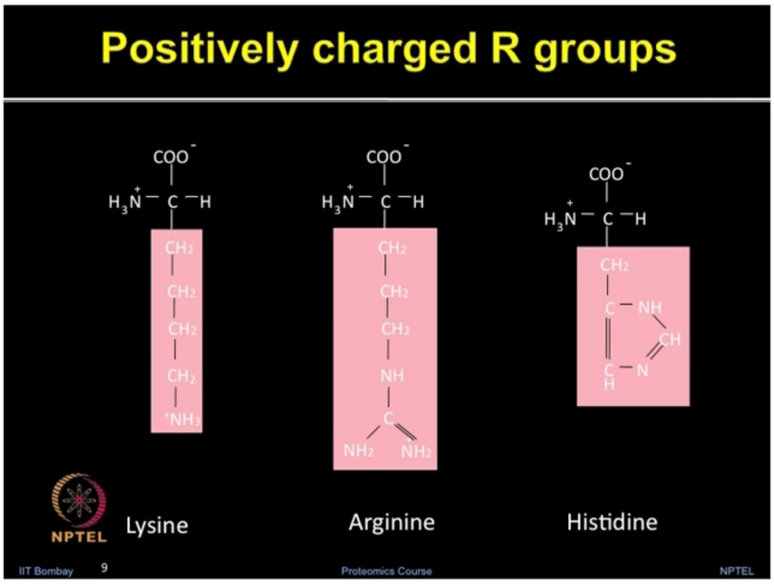
The range structure it provides more conformational restriction and therefore, proline plays very crucial role in unique properties in many functions. Valine it is branch chain amino acid leucine on the left hand side bottom panel, which is hydrophobic amino acid with isobutyl r group, isoleucine it also has the hydrophobic amino acid characteristic and it contains chiral side chain it is one of the essential amino acids. The last in the group is methyl methionine which includes ethio ether group again generally two two amino acids which contains sulfur and they play Sulfuric some critical role.

(Refer Slide Time: 07:08)



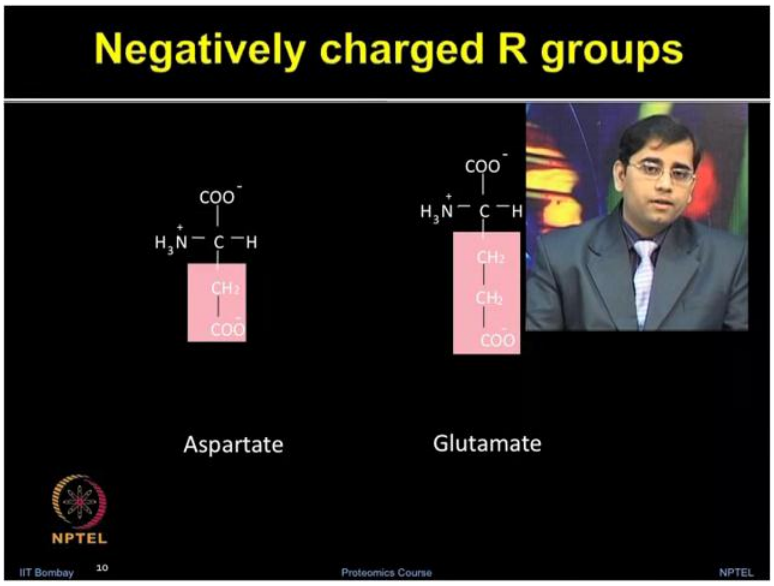
Our next category is polar uncharged r groups. Let’s start with the serine which resembles in the structure like alanine, but it contains hydroxyl group. Threonine it resembles in the structure like valine and it contains hydroxyl group, it has an addition symmetric center. Cysteine it is similar to serine, but it contains sulfhydryl or thiol group, to cysteine molecules form cysteine. Let us talk about asparagines which is shown in the left side lower panel it contains carboxamide side chains as a functional group. Glutamine this side chain called as amide of glutamic, which is form by replacing the side chain hydroxyl group glutamic acid with an amino functional group. Next category is positively charged r groups.

(Refer Slide Time: 08:26)



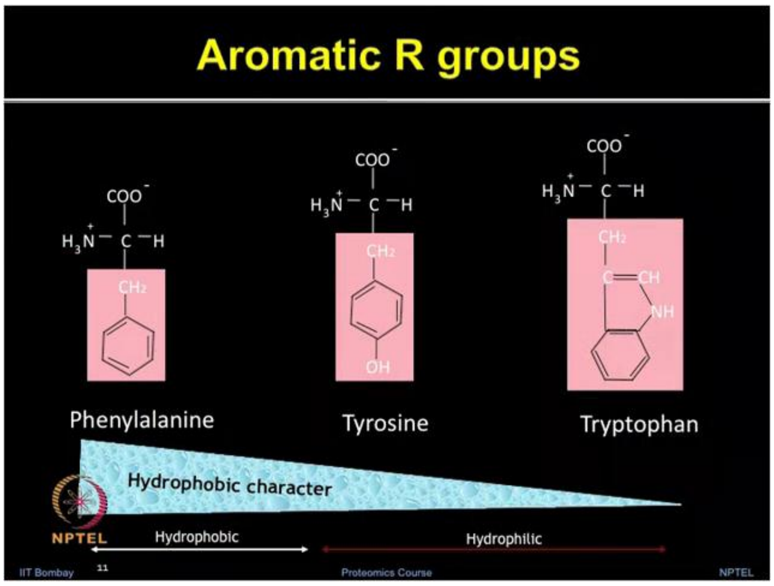
Three amino acids are here Lysine, Arginine, and Histidine. Lysine is a base it contains the cap primary amino group, where as arginine contains Gordian group, histidine it has a functional imidazole group which is aromatic ring that can be positively charged. Histidine plays very critical role in much enzymatic activity.

(Refer Slide Time: 08:53)



Next group is negatively charged r groups aspartate or glutamate or aspartic acid or glutamic acid. The name aspartate or glutamate is, because at the physiological p h the side chain of these amino acids lacks a proton present in the acid form. Therefore, these amino acids are negatively charged. Aspartate is a carboxyl ate anion of aspartic acid known as aspartate, where as the carboxyl ate anions and charge for glutamic acid are known as glutamate.

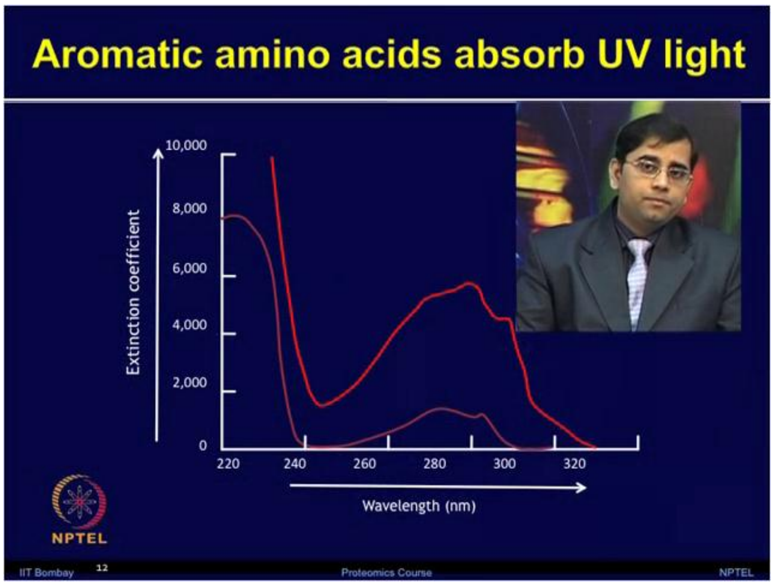
(Refer Slide Time: 09:35)



Next category is aromatic r groups. Let this one there are three aromatics phenylalanine, tyrosine, and tryptophan. Phenylalanine contains phenyl ring, tyrosine has one reactive hydroxyl group, and tryptophan contains in dole ring two rings which are fused.

Now if you look at the hydrophobic or hydrophilic characteristics phenylalanine is hydrophobic, where as tyrosine and tryptophane there are hydrophilic due to the slight chain containing hydroxyl and n h reactive groups.

(Refer Slide Time: 10:24)

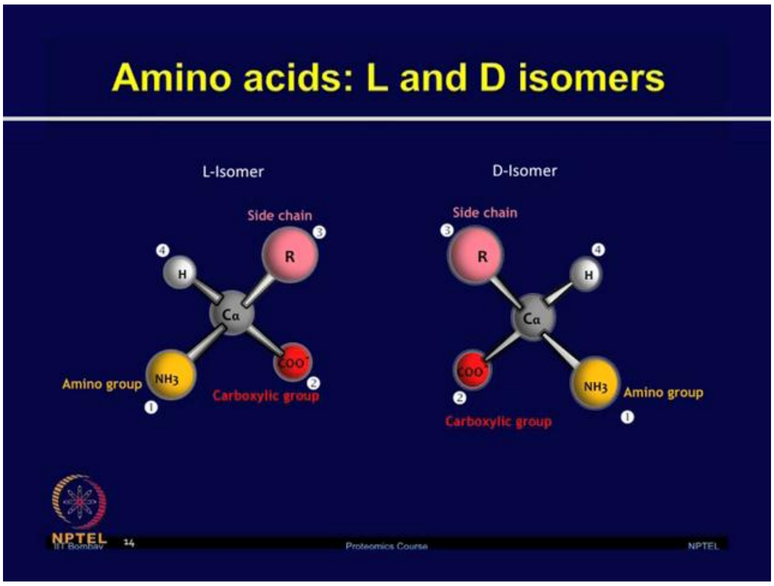


Aromatic amino acids have unique property they can absorb UV light. All the three amino acids which we just discussed tryptophane, tyrosine, and phenylalanine they can absorb UV light. Tryptophane absorption at 280 nanometers, tyrosine at 276 nanometer phenylalanine it absorbs light less strongly and at the shorter wavelength. The light absorption at 280 nanometers is used for the protein concentration determination.

I will refresh some of the concepts discussed in the amino acid structures and properties in following animation. Amino acids are the building blocks or monomers that make a protein; they consist of a central alpha carbon atom bonded covalently to an amino group, a carboxyl group, a hydrogen atom and a variable slide chain called as r group. Amino acids are the basic monomeric constituents of protein found in varying amount depending upon the type of protein.

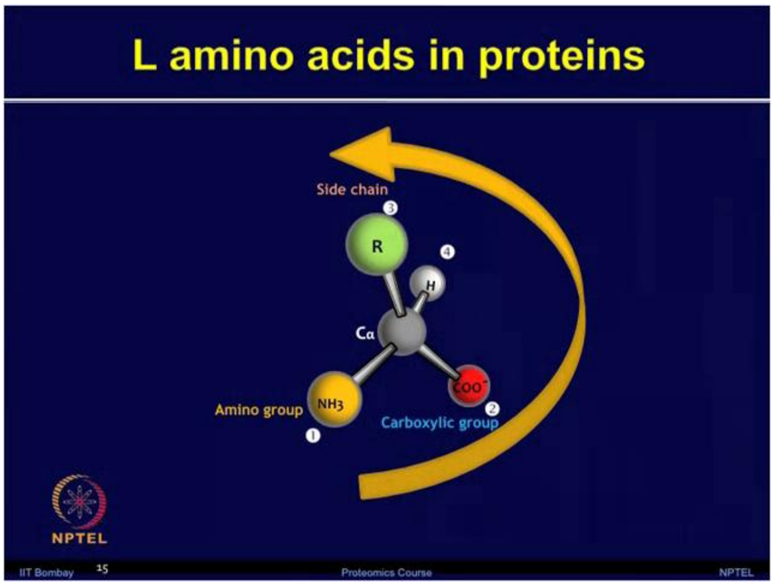
They are classified based on the properties on their slide chains or r groups which vary in size structure and charge. Polarity of silde chain is one of the main basisi for the classification. Amino acids having no polar aliphatic slide chains including glycine, alanine, proline, valine, leucine, isoleucine, and methionine essential amino acids are those that cannot be synthesized de novo in the organism and therefore, must be included in the diet. Non-essential amino acids on the other hand can be synthesized from various precursors' serine, theronine, aspargine; glutamine and cysteine consist of polar, but uncharged slide chains. Lysine, arginine, histidine these have positively charged slide chains aspartic acid and glutamic acid are polar and egatively charged amino acids. Tryptophan tyrosine phenylalanines are all essential amino acids having an aromatic slide chains. After having discussed the different type of group of amino acids, let us look at the basic constituents of amino acids and different iso forms which it can form.

(Refer Slide Time: 13:55)



Amino acids having the four different groups which are connected to the alpha carbon atom, it can form two mirror images which can exist in l or the d isomers which are shown in the slide here. The alpha amino acids are tiral they could be r or s configurations in the amino acid depending upon the priority groups, but only l amino acids are present in the proteins.

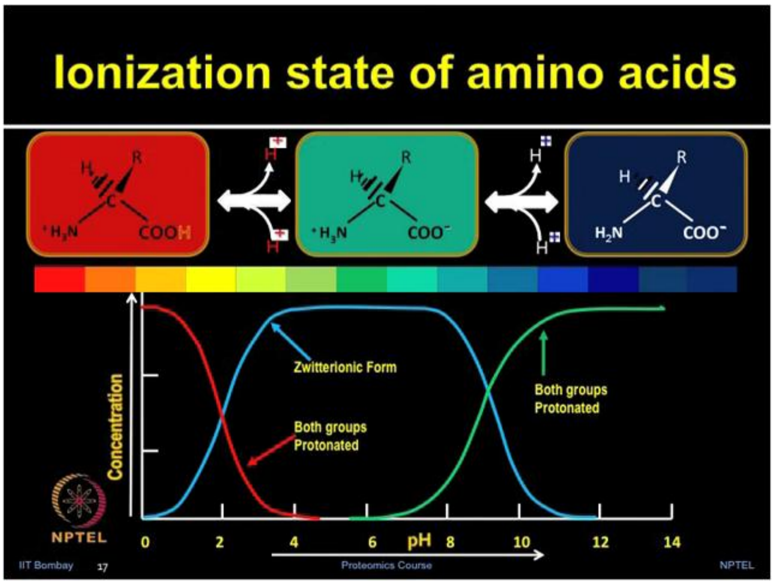
(Refer Slide Time: 14:25)



All the l amino acids have s configuration, which describes the counter clockwise direction as shown here, from highest to the lowest priority groups, which is an indicative of chiral center with the s configurations. Some of the isomerism properties of amino acids will be discussed in following animations. Before learning about the isomerism let us first know what is chirality. The term chirality arises from the Greek term cheer meaning, handedness just like the two hands are non super imposable mirror images of each other. Amino acid molecules are also non super imposable due to their chiral alpha carbon center.

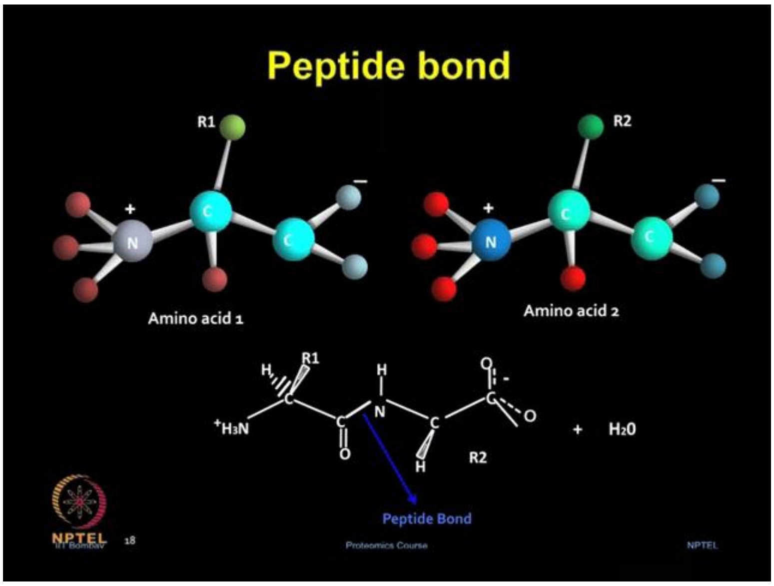
All amino acids except glycine contained an s symmetric center, which makes him chiral in nature due to which they can rotate the plane of polarize light. The two enantiomers designated as d and l rotate the plane of polarization in opposite directions. The two enantiomers of amino acid are non super imposable mirror images, due to the a special arrangements of four different groups about the chiral carbon atom. Rotation of either isomer about it is central axis will never give rise to the other isomeric structure. Let's now talk about ionizations state of amino acids. The ionization state of amino acids varies with it is ph.

(Refer Slide Time: 16:37)

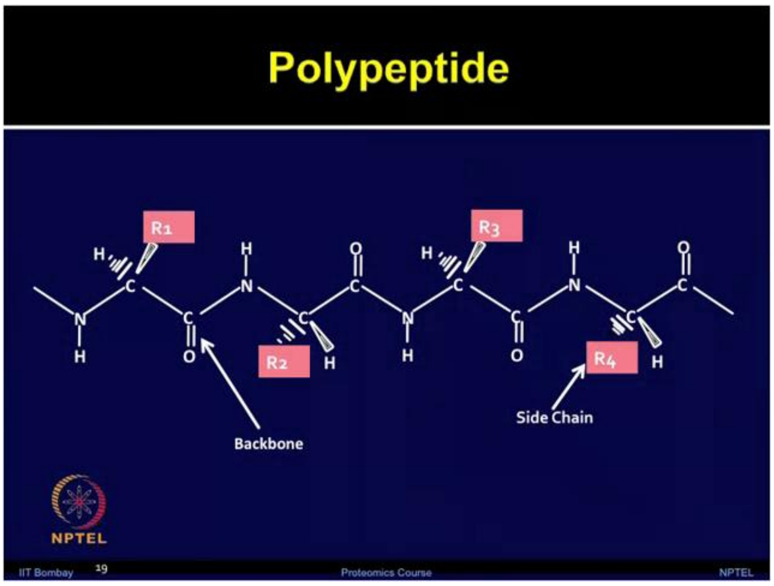


In the acidic solution if you follow the slide from left to right, the amino group is protonated n h three plus carboxylic group is undissociated c double o h. At the neutral ph amino acids exist as dipolar ions or zwitter ions. Amino group is protonated n h three plus and carboxylic group is denoted c double o minus. Now this dipolar form can exist till ph 9. Now when you move to the basic p h, the protonated amino group loses its proton and forms n h 2.

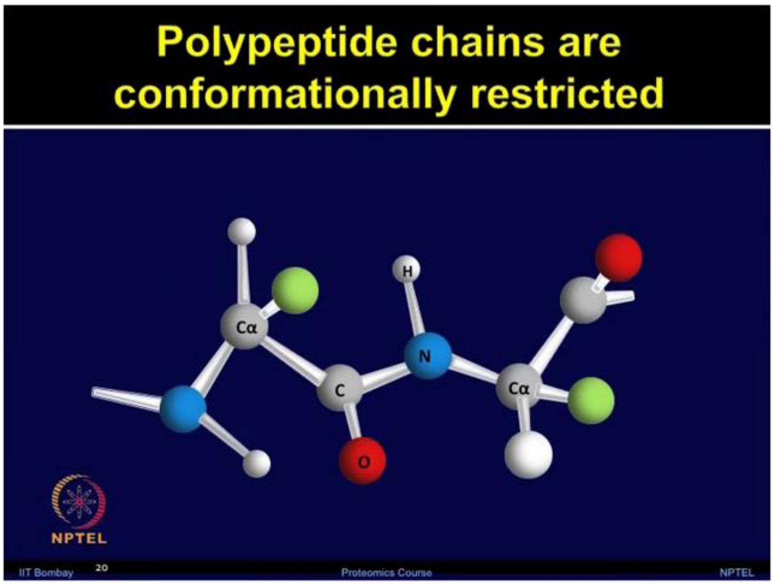
(Refer Slide Time: 17:30)



(Refer Slide Time: 17:58)

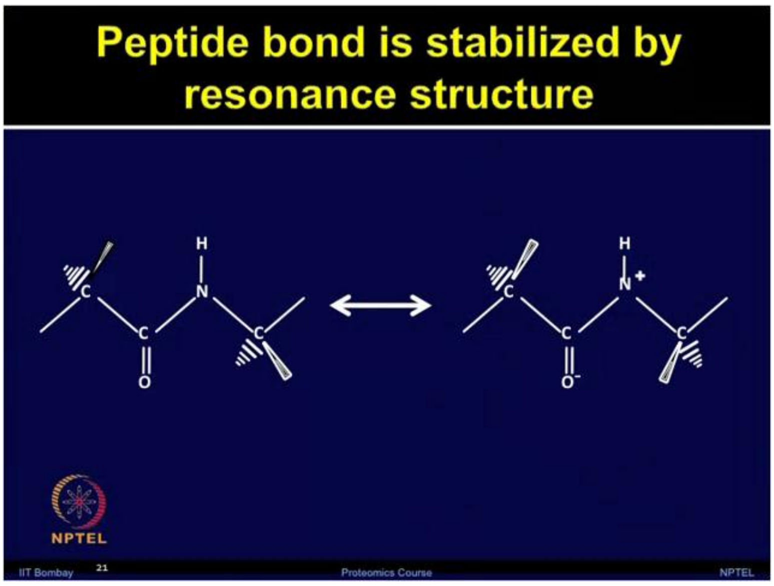


(Refer Slide Time: 18:06)



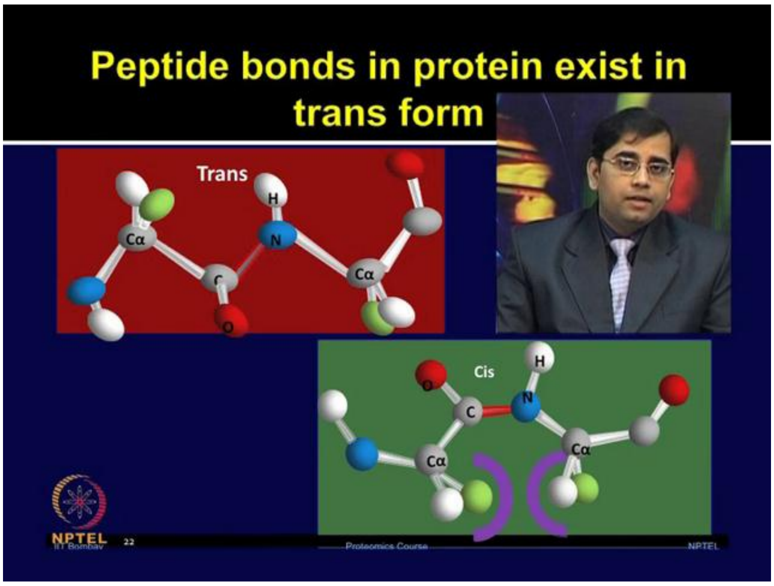
Let us now talk about peptide bonds. Peptide bond can link amino acid to for the polypeptide proteins. The alpha carboxylic group of one amino acid link to the alpha amino group of another amino acid. As you can see here these two amino acids are forming the bond and peptide bond is formed with accompanying loss of water molecule. Many amino acids are lined together they for a polypeptide, as you can see in the slide the multiple peptide bonds are present. The polypeptide chains are conformation ally restricted therefore, peptide bond is planar amino acid pairs they are linked by peptide bonds, and all the 6 atoms lie in the same plane. As you can see here, alpha carbon oxygen, nitrogen, hydrogen and another alpha carbon.

(Refer Slide Time: 18:30)



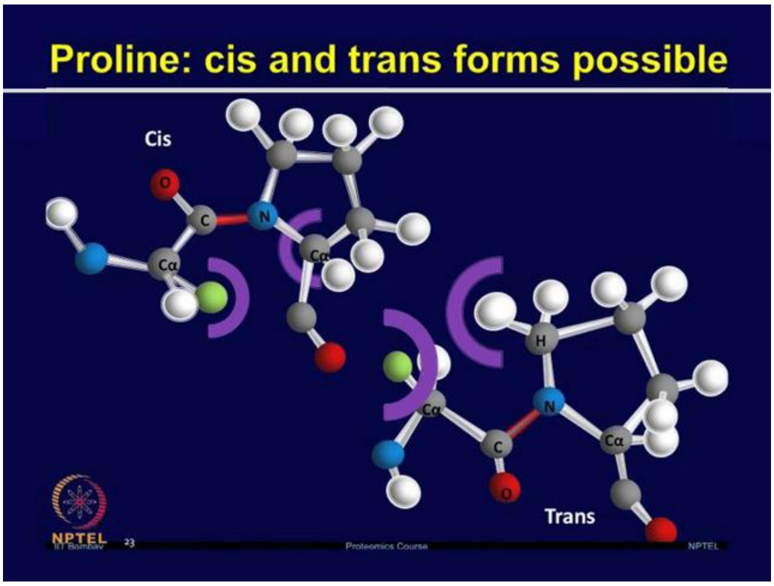
Peptide bonds can be stabilized by the resonance structure. Peptide bond is rigid, because of their partial double bond character which arises due to the resonance structures present in peptide bond. Now there could be tow forms cisform and the transform, but peptide bonds in protein exist in the transform.

(Refer Slide Time: 18:55)



If you see the top panel the Trans configuration the two c alpha on the opposite side of the peptide bonds. This configuration is allowing less steric clashes whereas, if you look at the bottom panel the cis configuration there are two alpha carbons on the same side of peptide bond. So, there is ore probability of having steric clashes therefore, peptide bond in protein exist in the transform. Toproline proline is unique amino acid as we discussed earlier.

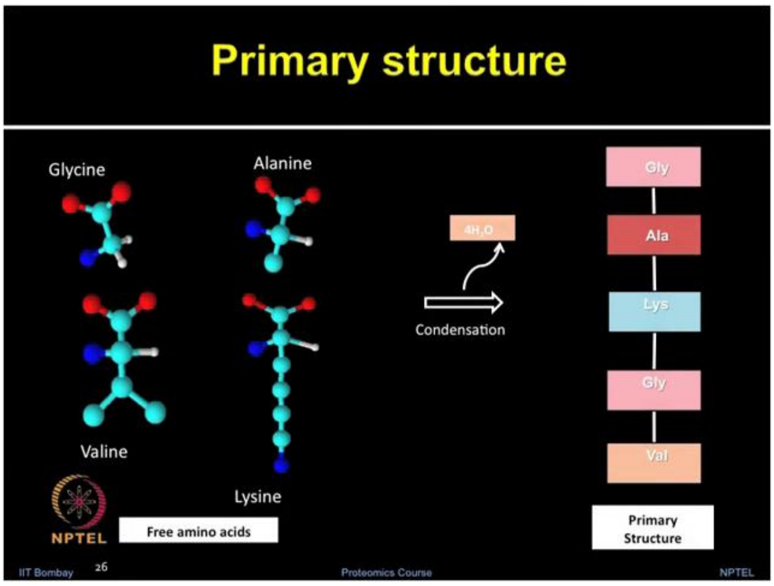
(Refer Slide Time: 19:35)



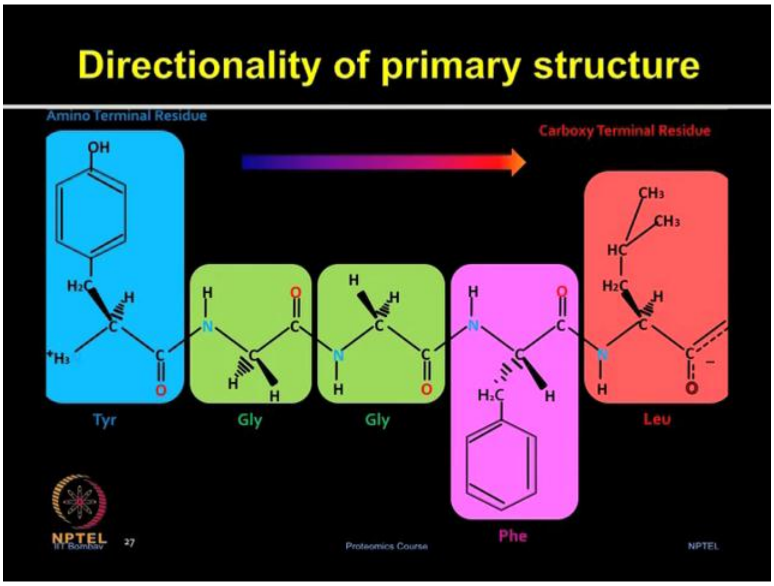
Proline with peptide bonds it can form both cis and the transforms. So, as you can see here it can avoid the steric clashes and both cis and Tran's configurations are possible. So, some of the concepts of peptide bonds will be described in the following animation. Amino acids are the building blocks or monomers that makeup proteins. Amino acids are oriented in a head to tail fashion and link together such that the carboxyl group of one amino acid combines with the amino group of another amino acid. Two amino acids join together by means, of such a condensation reaction with the loss of water molecule forms a dipeptide. Many such amino acids link together and form polypeptide. The peptide bond is rigid due to its partial double bond character, which arises from the resonance structure; however, the bonds between the alpha carbon and amino and carboxyl groups are pure single bonds that are free to rotate.

Now let us move on to different structure level of proteins starting with the primary structure. Amino acid constitutes the basic monomeric unit f proteins, and they are joined together by the peptide bonds. These 20 standard amino acids can be arranged in several ways and therefore, it can give rise to unique structural and functional properties.

(Refer Slide Time: 21:48)

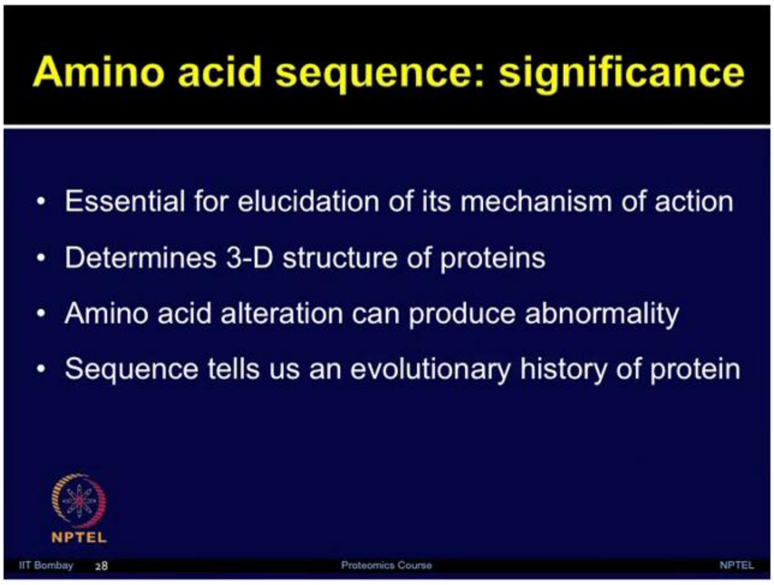


(Refer Slide Time: 22:12)



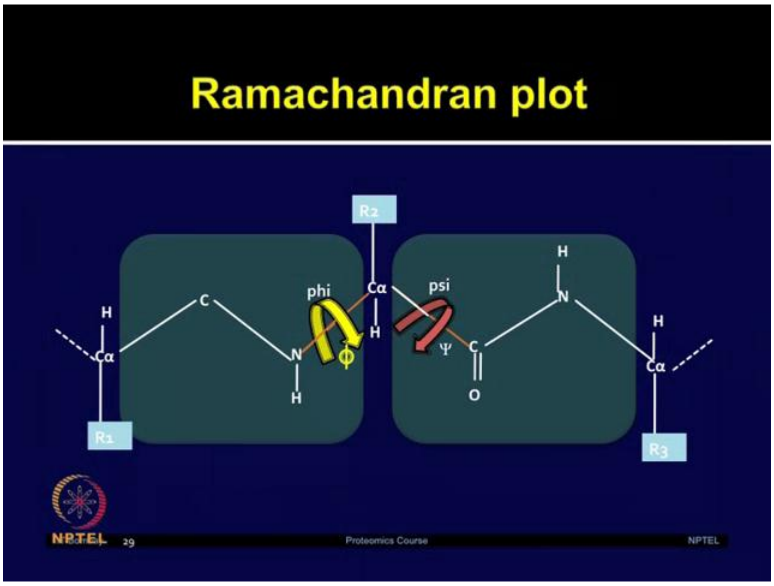
So, primary structure refers t the sequence of amino acids. As you can see on the left slide different amino acids can come together, and the linear sequence amino acids constitutes the primary structure with loss of water molecule. Now what is the directionality of primary structures? The polypeptide chain has polarity. So, one end is alpha amino group, and other end is alpha carboxyl group. The amino marks the beginning of any polypeptide chain. So, what is the significance of amino acid sequence as we discussed this represent the primary structure?

(Refer Slide Time: 22:33)



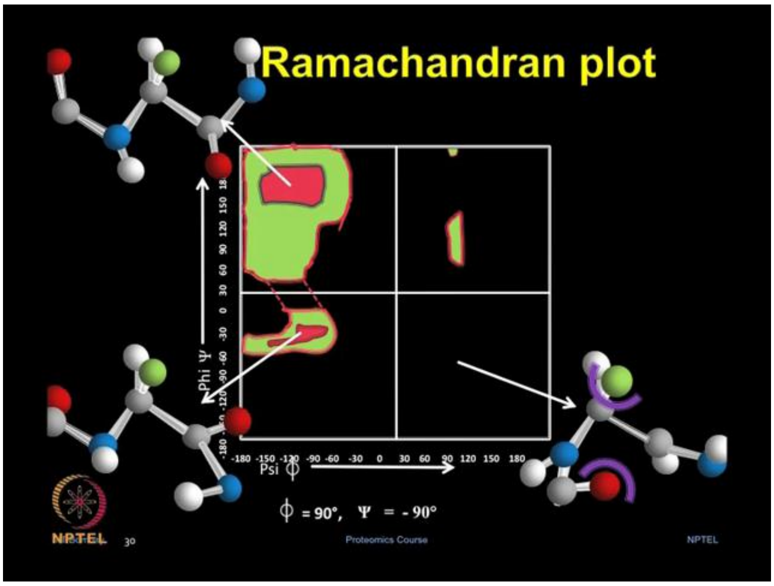
The amino acid sequence is essential for elucidation of it is mechanism action. And enzymes catalytic action can be determined it determines 3 dimensional structure of the proteins links in the functional 3 dimensional protein structure and the genetic message obtained from the dna. The amino acid alterations can produce various type of disease abnormality for example; cystic fibrosis change on only one amino acid can give rise to the abnormality. And these amino acid sequences can also tell us various type of evolutionary aspect of the protein. So, various type of information can be obtained from amino acid sequences.

(Refer Slide Time: 23:25)

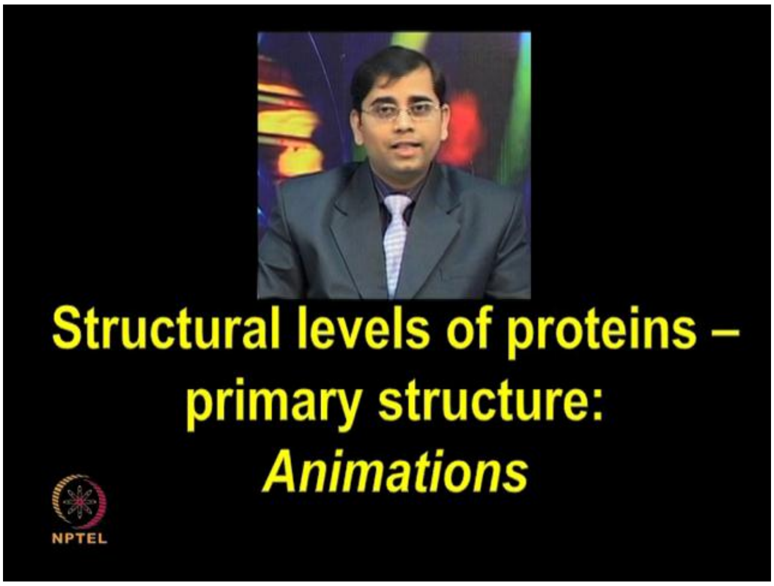


Now, let us move o to concept of Ramachandran plot, but before that it is important to know about the phi and the psi angles. As you can see here in the slide rotation of two single bonds adjust structure of each amino acids in polypeptides. The phi angle between the nitrogen and the alpha carbon atom, and the psi angle between alpha carbon and carbonyl carbon. This phi and psi angles determine the path of polypeptide chain all the combination of phi and psi angles are not possible. So, the allowed combinations can be viewed on two d plot which is known as the Ramachandran plot or Ramachandran diagram.

(Refer Slide Time: 24:41)



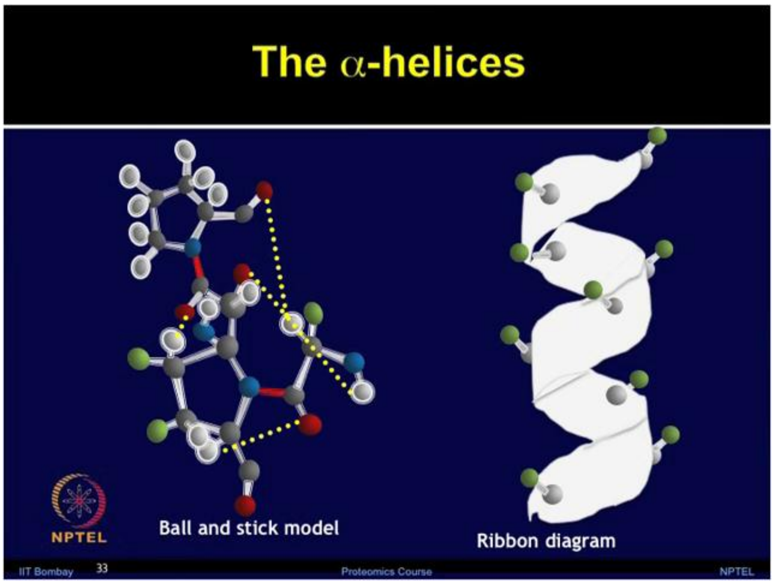
(Refer Slide Time: 25:03)



There could be many possibilities of various type of combination, but all the combinations are not allowed, because of the steric hindrances and collision between the various atoms. Therefore, steric exclusion can be powerful governing factor for organizing such plot. Now you can see it more clearly in this slide the Ramachandran plot where most favorable regions are shown in the dark green color, and less favored regions are shown in the light green. The structural level of proteins the primary structure few concepts will be discussed in following animation.

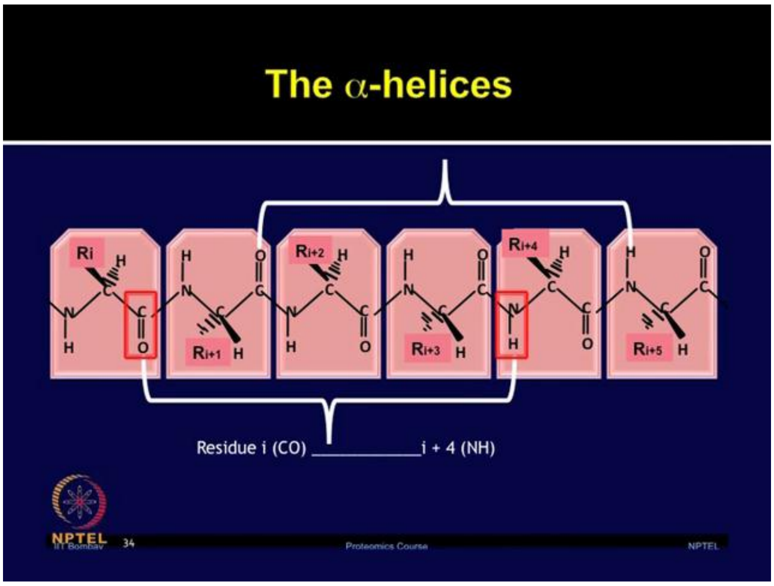
(Refer Slide Time: 25:32)

(Refer Slide Time: 25:58)

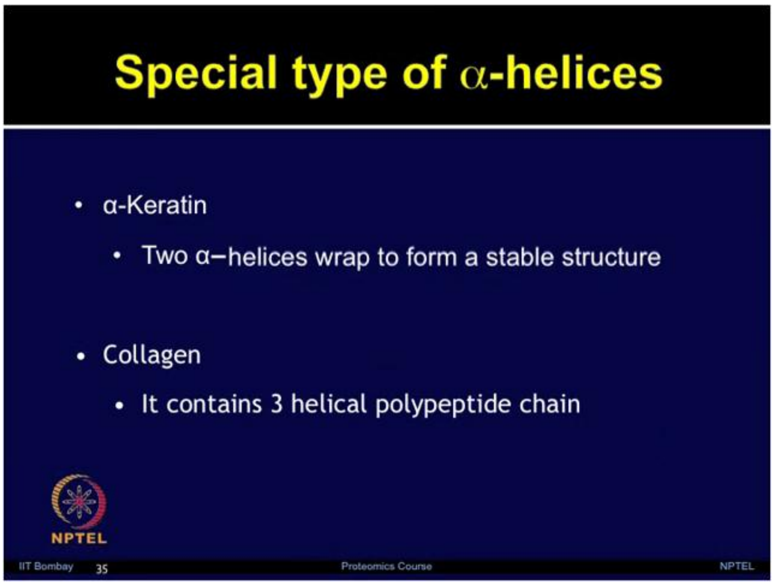


Amino acids are joined together in a head to tail arrangement by means, of peptide bonds with the release of water molecules. This linear sequence of amino acids constitutes the primary structure. Let us now discuss about secondary structure, which refers to locally folded regions. The folding of polypeptide or protein chain in to regular structures like alpha helices, beta sheets turns and loops all this represent the secondary structures. Let us first start with the alpha helices. So, proteins have variable helix content alpha helix shows rod like a structure, it has main chain and a side chain is tightly coiled around helical axis and a side chain is extended outward away from the helical axis. As you can see in the ribbon diagram on the right side and the ball and stick model on left side.

(Refer Slide Time: 26:36)

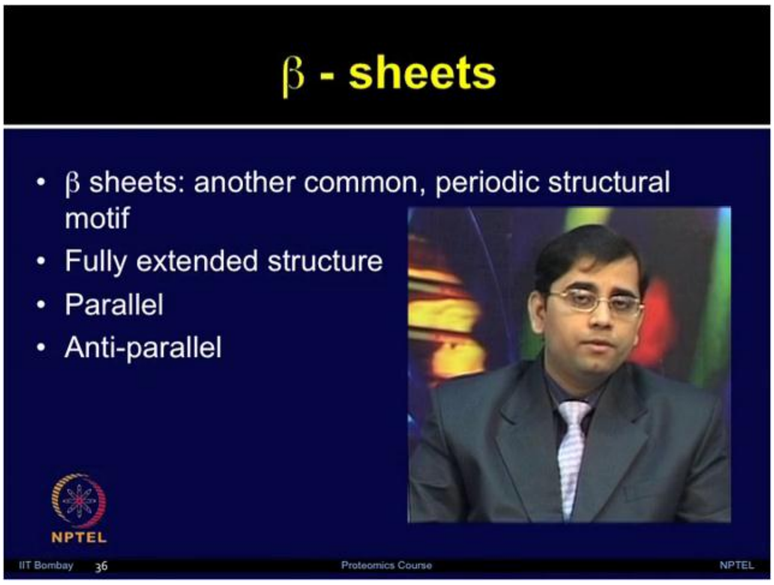


(Refer Slide Time: 27:08)



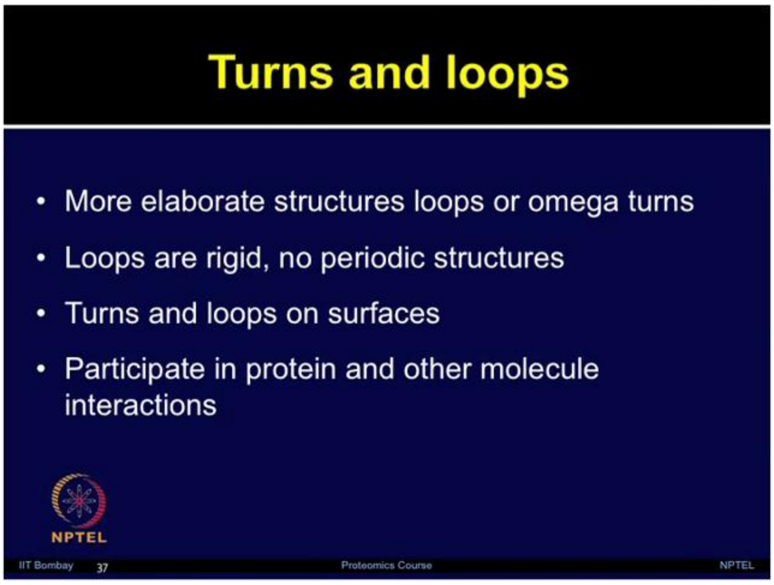
Specific hydrogen bonds stabilizes helical core. The alpha helix can be stabilized by the hydrogen bond. So, the carbonyl group of each amino acid with n h group of amino acid which are four residues ahead in the sequence they form these hydrogen bonds, as you can see in this figure here. There are a special type of alpha helices were two alpha helices can wrap up or three alpha helices can come together. So, the first example is alpha keratin where two alpha helices can wrap to form a stable structure it is primary component of hair and consist of two helical soil around each other and forms a left handed super helix which is known as the coiled coil.

(Refer Slide Time: 27:50)

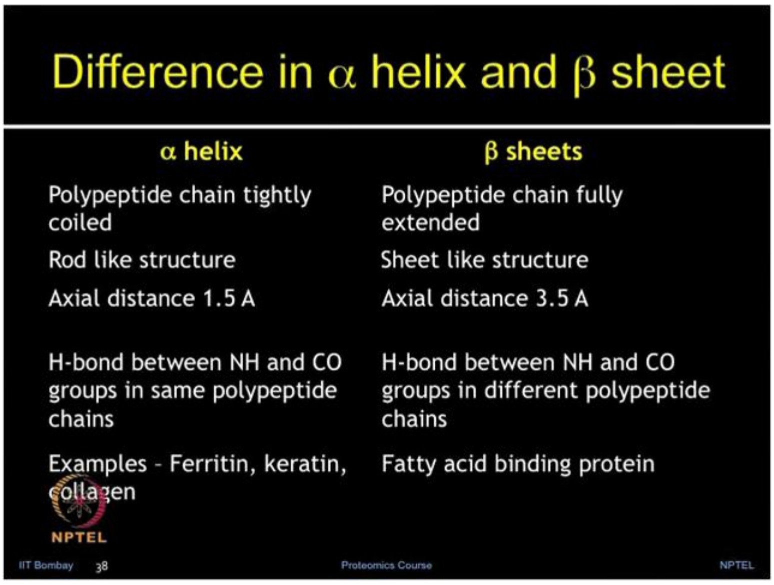


Another example is collagen which is fibrous component of skin bone etcetera. It is also most abundant in mammals; it contains three helical polypeptide chains. Beta sheet another common periodic structure motive which was discovered by scientist Pauling and Corey, it is fully extended structure unlike the tightly coiled alpha helices. It can be two having two directions the parallel or anti parallel. Parallel when they are running in the same direction and anti parallel when they are running in the opposite direction.

(Refer Slide Time: 28:24)

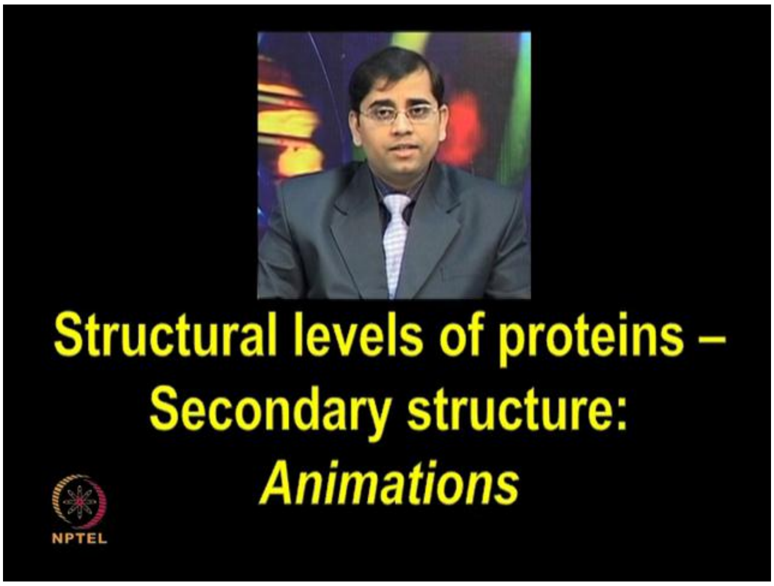


(Refer Slide Time: 28:56)



Another category of secondary structures are turns and loops. These are more elaborate structures loops or omega turns, which also perform chain reversal loops are rigid well defined these are not periodic structures. The turns and loops are present on surface and participate in various important properties of proteins, another biomolecule interactions. The difference in alpha helix and beta sheet is summarized in this slide. The alpha helix polypeptide chain is tightly coiled whereas; in beta sheet it is fully extended. Alpha helix rod like structure and beta sheets sheet like structure. The axial distance between adjacent amino acids is 1.5 angstrom whereas; it is 3.5 angstrom in beta sheets.

(Refer Slide Time: 29:42)

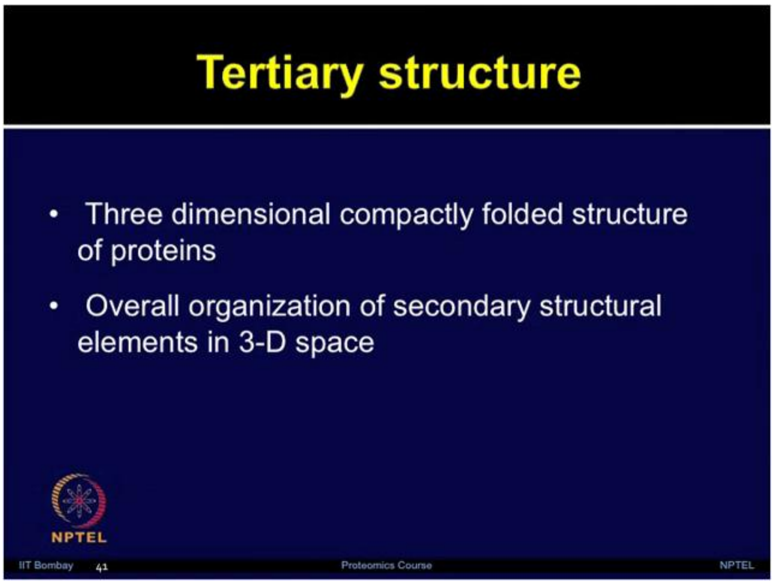


In alpha helix hydrogen bond between n h and c o groups in same polypeptide chains whereas, in beta sheets it is in different polypeptide chains. Alpha helix example, include ferritin, keratin, collagen etcetera. In beta sheet it is fatty acid binding protein. Some of the properties of secondary structures will be described in following animation. The folding of the primary structure into the secondary is governed by the permissible rotations about the phi and psi angles, not all value of these angles lead to historically favorable confirmations. The Ramachandran plot they defines these regions of favorability. Amino acids along the polypeptide backbone interact through hydrogen bonds, leading to the secondary structures. The alpha helix has intra chain hydrogen bonds between the hydrogen of n h and oxygen of c o in every fourth residue.

Most alpha helices are right handed still the confirmation is energetically more favorable here; you can see more energetically favorable alpha helix structure. The amino acid proline which has a cyclic side chain does not fit into the regular alpha helix structure and there by limits flexibility of the backbone. It is commonly referred to as the helix breaker; alpha helices can also wind around each other, to form a stable structure. Such that there hydrophobic residues are buried inside while there polar side chains are it is poles to the aqueous environment. Alpha keratins the major protein component of here consist of two such coiled coils forming a left handed super helix. Collagen which is the fibrous component of skin muscles etcetera, consist of three such coiled alpha helices. It has a characteristics recurring amino acid sequence of glycine, proline, hydroxyproline, with glycine appearing at every third residue. Beta pleated sheets discovered by Pauling and Corey is another common secondary structure with periodic repeating units, it is composed of two or more polypeptide chains, with their side chains oriented above and below the plane. It is an extended structure with hydrogen bonds between the chains stabilizing it.

Amino acids in parallel beta sheets which run in the same direction interact with two different amino acid on the adjacent strand through the hydrogen bonds. Amino acids in anti parallel strands on the other hand interact with only one amino acid on an adjacent strand. Almost all proteins exhibit a compact globular structure, which is possible only if there are turns or loops between the various regions. Beta turns which are the most commonly observed turn structure, consist of rigid well defined structures that usually lie on the surface of the protein molecule and interact with other molecules.

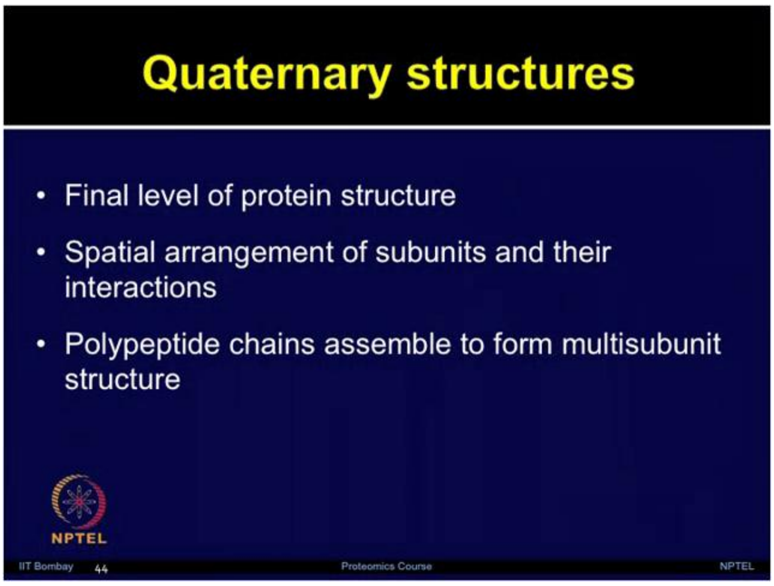
(Refer Slide Time: 34:38)



Let us now move on to tertiary structure which refers to overall folded structure. n m r and axilla crystallography provides detail three dimensional structures. The 3 dimensional structures is compactly folded structure of proteins and it represents overall organization of secondary structural elements in 3 d space. The numerous interactions which stabilized the tertiary structure of proteins, we will take myoglobin as an example, and describe some of the properties of tertiary structure in following animation Amino acids located far apart on the polypeptide chain interact with each other by means, of hydrogen bonds electrostatic interactions disulphide etcetera, which allows the protein to fold three dimensionally in the space giving rise to the tertiary structure. Protein folding takes place such that the hydrophobic residues are buried inside the structure, while the polar residues remain in contact with the surroundings.

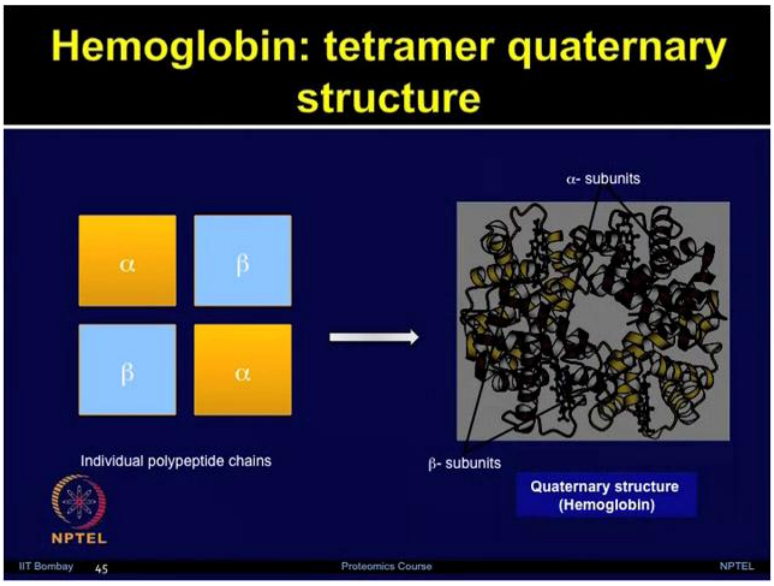
The tertiary structure of myoglobin determined by John Kendrew clearly revealed that the nature of amino acid side chains dictate the location in the tertiary structure. The hydrophobic residues are found buried inside this structure, while the polar amino acids are present in the surface. 70 percent of main chain of myoglobin is folded into alpha helices with the rest being present in the form of turns and loops which are essential to provide it a compact structure. And what is quaternary structure. It refers to interaction between individual protein subunits in a multi subunit complex.

(Refer Slide Time: 37:10)

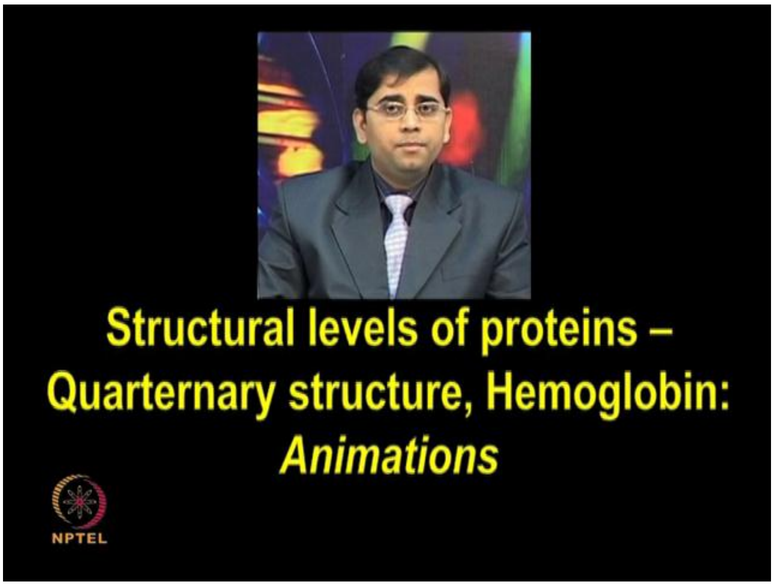


So, quaternary structures represent final level of protein structure, which is special arrangement of subunits and their interactions. The polypeptide chains assemble to form multi subunits structure and each polypeptide chain is known as subunit. The different examples, such as d n a binding co protein of bacteriophage lambda which is representing simple quaternary structure then we have classical example of hemoglobin.

(Refer Slide Time: 37:44)



(Refer Slide Time: 38:02)

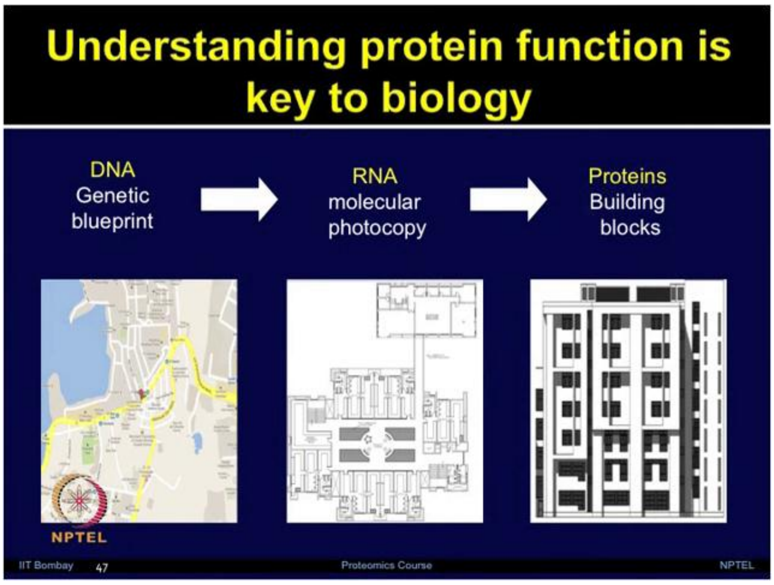


So, let us look at hemoglobin the tetramer quaternary structure. It has two alpha subunits and two beta subunits. The individual polypeptide chains they come together and form quaternary structure. Properties of quaternary structures and some details about human hemoglobin and comparison of myoglobin hemoglobin will be discussed with following animation. Different subunit or polypeptide chains interact with one another and are held together by means, of ionic electrostatic in the van der Waals etcetera interactions. Such multi subunit proteins having a quaternary structure, which is the final level of protein stricture.

Hemoglobin is a heterotetramer composed of two alpha and two beta chains. The alpha globin gene locus resides on chromosome 16 with each gene contributing to the synthesis of the alpha globin chain. The beta globin gene lcus resides on chromosome 11 and consist of all genes that are expressed from the time of embryonic development of hemoglobin, to that of adult beta globin gene. The globin chains are synthesized by ribosome’s in the cytosol.

Every sub unit of hemoglobin is bound to a prosthetic group known as heme. This consist of a central iron atom in it is surrounded by a complex organic ring structure known as protoporphyrin. The heme group is essential for the oxygen binding property of hemoglobin. The iron atom forms 6 coordinate bonds 4 of which are to the nitrogen atom of porphyrin 1 to histidine side chain in the globin subunit. And the other being the binding side for oxygen. X ray crystallography is the very useful visualization technique that facilitates the determination of 3 dimensional coordinates of atoms in a protein. Myoglobin was the first protein whose structure was determined by x ray crystallographic studies. Where a bean of x ray was passed through the crystals of myoglobin. Some part of the beam was found to pass straight through, while the others were scattered in different directions. These scattered beams were detected by means, of an x ray film. After the spot intensity calculations it provided an electronic density map of the protein.

(Refer Slide Time: 45:50)



The protein was found to consist of a single polypeptide chain having 8 alpha helices along with a heme group in the centre similar, to the hemoglobin. Myoglobin found largely in muscle tissues has been found to be structurally similar to the alpha subunit of hemoglobin. The alpha helix arrangement of both proteins has been found to be the same with the recurring structures being known as globin fold. The hemoglobin chain having 141 amino acids and myoglobin having 153 residues have also been found to have very high sequence homology. Despite the similarities, there oxygen binding capacities are different. Myoglobin functions largely as an oxygen binding protein that stores additional supply of oxygen in muscle tissues, while hemoglobin search to transport of oxygen. Myloglobin binds strongly to the oxygen and acts as an oxygen storage protein rather than transport it shows 50 percent saturation at a pressure as low as two torr and get saturated even under low oxygen pressure conditions, which prevail in the muscle.

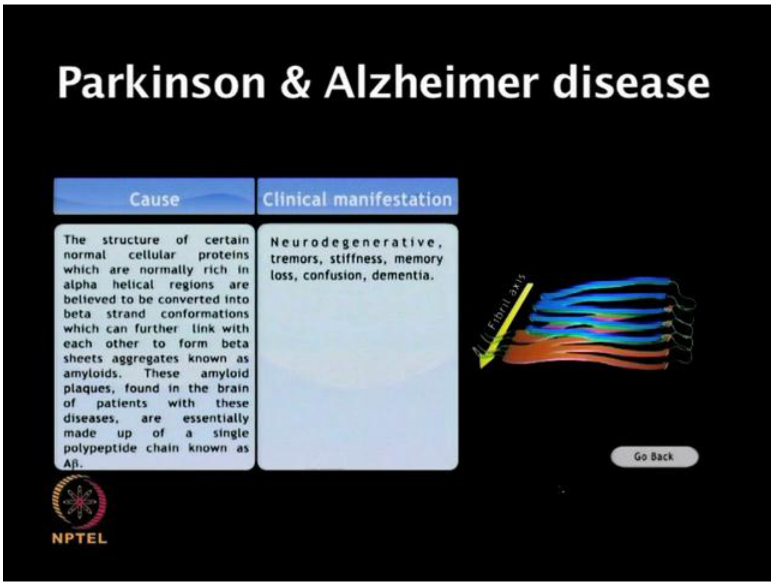
Myoglobin can use only 7 percent of the oxygen carrying capacity as opposed to hemoglobin, which ca utilized nearly 90 percent of the oxygen carrying capacity. Unlike hemoglobin which has a sigmolick oxygen binding curve myoglobin has a hyperbolic curve, which indicates that it binds to oxygen irrespective of the surrounding partial pressure of oxygen in the tissue. After discussing various properties of amino acids and different level of structural proteins, primary, secondary, tertiary and quaternary not necessary stress upon why understanding protein function is key to biology.

So, this is the result as due to the protein malfunction therefore, all the current drugs they are either targeting the protein function or they are proteins themselves which demonstrate the significance of estering about proteins. Let me describe you the slide where I have shown the various bio molecules of ventral dogma d n a, r n a and protein for example, of you look at the map here where I t is located in powai area. So, it is like d n a which is the genetic blueprint, it contains only information. Now if you want to make a building in this area it is you have to define area which is like r n a molecule, which is a molecular photocopy and it is used on the site of the construction by the site contractors. Now proteins are like the building, which you want to create on that site these are the building blocks are building materials, they are brakes and motors are engines of biology.

So, it shows you how various types of biomolecules have the significance, but it is the proteins which ultimately define the function. The malfunction of the proteins can result into various diseases, and some of the diseases will be described in the following animation. A large number of mutations have been described in the global gene. The mutation causing sickle cell anemia, is the single nucleotide substitution of a to t, in the codon for amino acid set of the beta chain. This change converts a glutamic acid residue in the corresponding amino acid sequel replacement of the glutamine residue by valine creates a sticky hydrophobic contact point at position 6 of the beta chain. These sticky spots cause deoxy hemoglobin molecules to associate abnormally with each other leading to clumping of the cells, their oxygen carrying capacity is greatly reduced and these patients require frequent. Thalassemia is the result of abnormality then hemoglobin synthesis, deficiency in beta globin synthesis results in beta thalassemia notation of single base from g to a in an intron of beta globin gene, generates a new splice site.

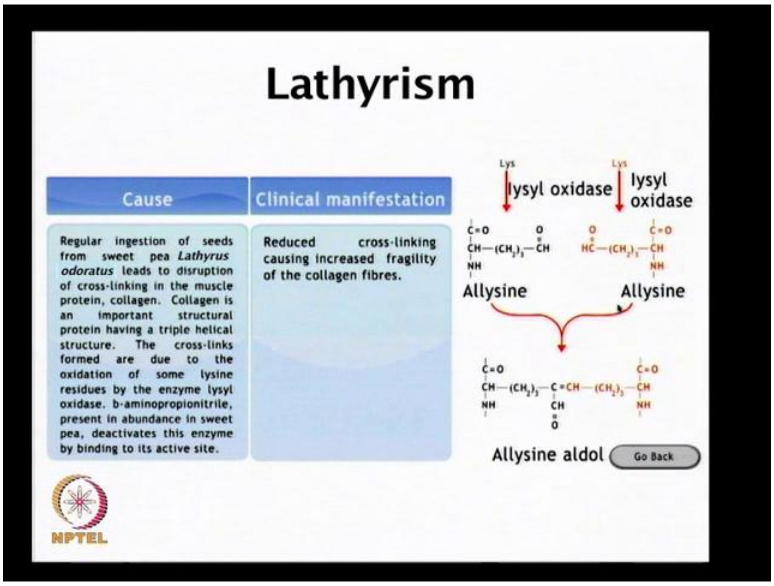
The resulting m r n a contains a stop cod on for the upstream and leads to premature translation termination there by producing apparent protein; deficiency then alpha globin synthesis due to inactivation of 1 or all the 4 alpha globin gene results in the alpha thalassemia results in the alpha thalassemia.

(Refer Slide Time: 50:10)



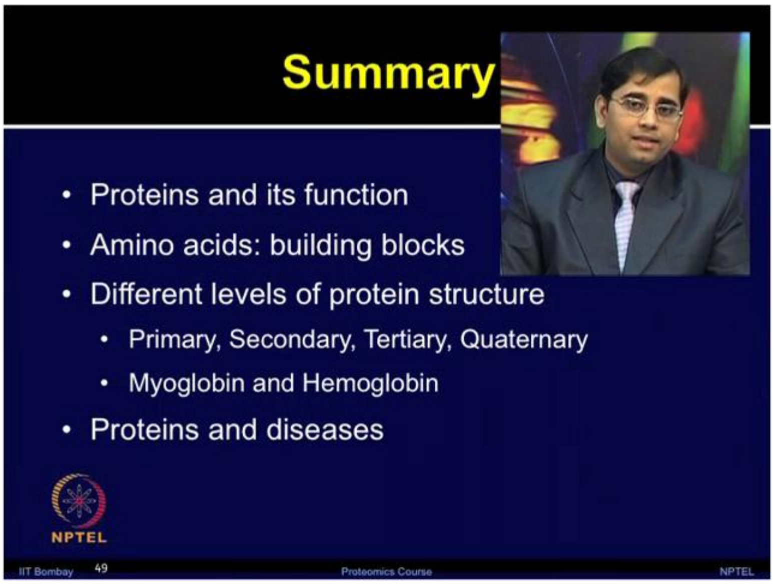
Parkinson and Alzheimer disease the stricture of certain cellular proteins, which are normally rich in alpha helical regions, are believed to be converted into beta strand conformation which can further link with each other to form beta sheet aggregates known as Amyloids. These amyloid plaques are found in the brain of the patients with these diseases are essentially made up of a single polypeptide chain. The clinical manifestation includes neurodegenerative, tremors, stiffness, memory loss, confusion, dementia, and etcetera.

(Refer Slide Time: 51:08)



Lathyrism cause is a regular ingestion of seeds from sweet pea, Lathyrus Odoratus which leads to disruption of cross linking in the muscle protein collagen. Collagen is an important structural protein having a triple helical structure, the cross links formed are due to the oxidation of some lysine residues by the enzyme lyslyl oxidase. Beta aminopropionitrile present in abundance in sweet pea deactivates this enzyme by binding two its active site. The clinical manifestation includes reduced cross linking causing increased fragility of the collagen fibers.

(Refer Slide Time: 52:00)



Summary today we talked about proteins ad nits function. We refreshed concepts on amino acids, which are the building blocks; we have talked about different levels of protein structures, primary, secondary, tertiary and quaternary. We discussed in more detail about Myoglobin and hemoglobin the model proteins. And then briefly we touched upon significance of Histedine proteins. And it is malfunction may result into various diseases. We will continue our discussion on some basic concepts of proteins in the next class thank you.