Fundamentals of Protein Chemistry

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Module – 01
Amino Acids and the Peptide Bond
Lecture – 01
Amino Acids – I

Welcome to this course on the Fundamentals of Protein Chemistry which will be offered by myself, Professor Swagata Dasgupta of the Department of Chemistry at IIT, Kharagpur. This course has been divided into several modules. Each week will constitute a module followed by the lectures in the specific modules. We will start off with proteins and their building blocks.

And considering the vast importance of proteins, we will be touching upon all types of proteins, protein structure; we will not go into the determination of protein structure because the course is related to protein chemistry. We will look at proteins related in terms of enzymes, in terms of metalloproteins, motor proteins, protein-ligand interactions, protein-protein interactions, protein aggregation as well as some specific topics related to protein chemistry that is important for research related to protein chemistry.

We start off with the amino acids – the major building blocks of proteins. What are these amino acids, what are the properties of these amino acids, and how are they important in an understanding of what proteins are all about, how do they affect the structure of proteins, how do they affect the properties of proteins?

These are the some of the things, we will try to understand and be able to predict to further look at the interactions that are involved in all living organisms, all the processes involved in living organisms.

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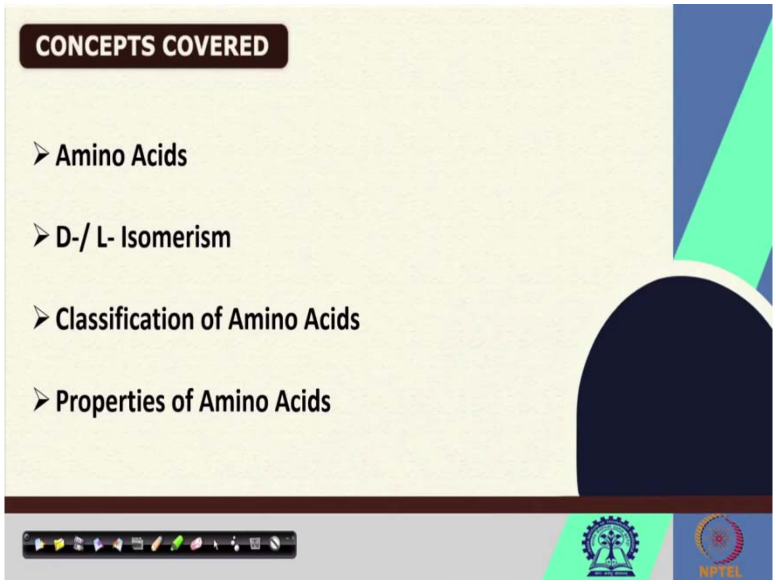

So, we start off with our understanding of the concepts that are going to be covered in this module the amino acids, the D-/L-isomerism, the classification of the amino acids, and the properties of the amino acids.

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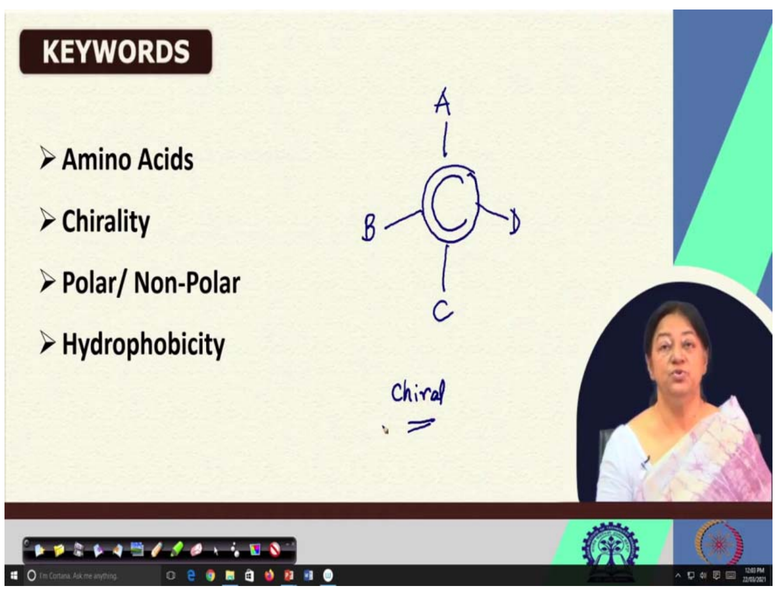

Now, we are going to understand what these specific terms mean: amino acids, chirality, polar, non-polar, and hydrophobicity in the terms of the properties of the amino acids. For example, if we want to understand what chirality is, we look at a carbon atom, a carbon atom that is the basis of all living organisms. So we have a specific carbon atom. And what we want to look at is what are the groups that are attached to this carbon atom. If they happen to be all different in nature so say we have A, B, C, D that are representing different forms of moieties, functional groups, attached to what we call this central carbon, we have what is called a chiral molecule. Now, is this chirality important in amino acids? This is what we are going to look at what we are going to try to understand.

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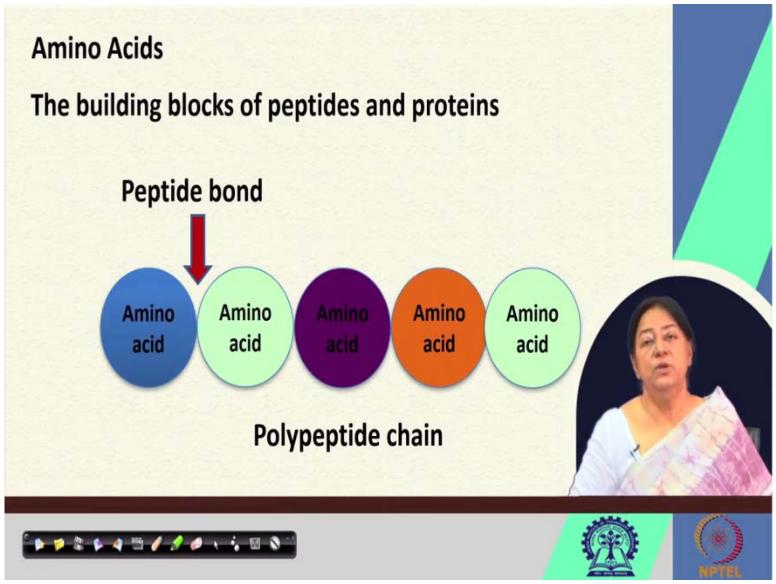

Going back to the building blocks themselves, we try and see what they constitute, what they form or how they are formed. We have the amino acids linked together. This we are going to study in the subsequent class. But when we have these amino acids linked together, we see they are of different colors representing their different properties.

We will see what these properties are all about as well. And when we try and understand what these connections are, we will see that these are the peptide bonds. These peptide bonds linked these amino acids together, link these amino acids together and form what is called a polypeptide chain.

Now, when we look at these beads on this necklace to find out how they interact with each other, how they fold, we will see the multitude and the various properties that are possible for the polypeptide chain, for the protein. Now, what are these amino acids constituted of?

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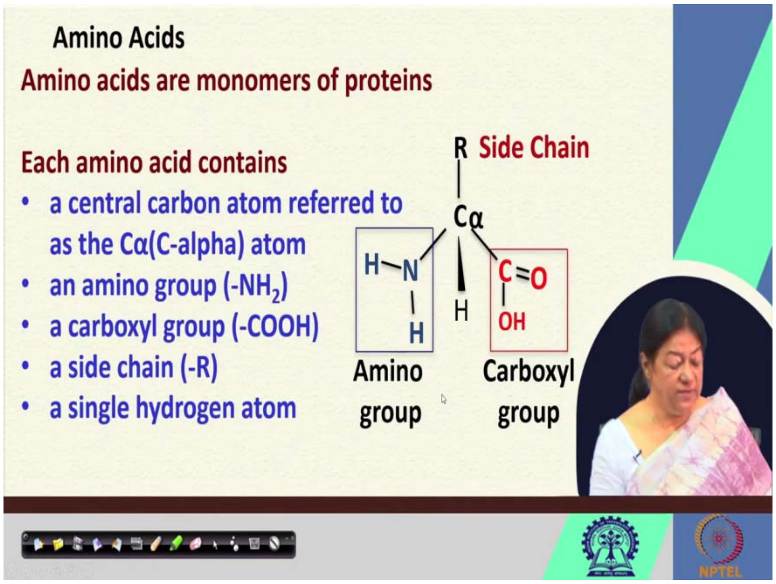

They are monomers of proteins as we found out the building blocks of proteins in the polymer that is the polypeptide chain. Each amino acid contains a central carbon atom known as the C-alpha, referred to as the C-alpha carbon atom, an amino group the NH 2, a carboxylic acid group that is the COOH, a side chain referred to as R in general, and a single hydrogen atom.

That means, if we look at this central carbon atom that we have here, if we look at the central carbon atom we see the central C-alpha carbon atom that is connected to what an amino group represented by the NH 2, a carboxylic acid group represented by the C double bond O, -OH, the side chain, and the hydrogen. Now, we realize that this R group is variable in nature. What does this mean? It means that this R group can be several types which we will see in a few slides.

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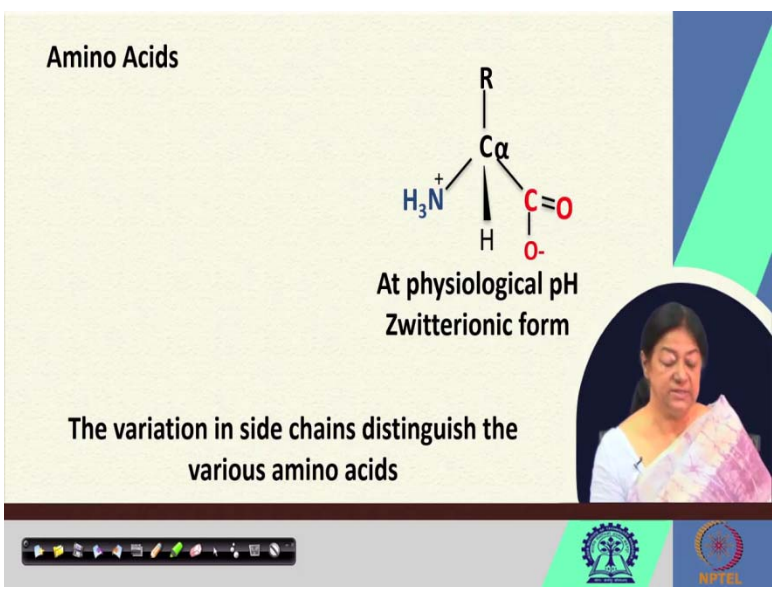

Now, a representation of an amino acid is usually given in what we called a zwitterionic form. Now, the variation in the side chains as I just mentioned, distinguish the various types of amino acids and at physiological pH which is 7.4, there is an ionization. An ionization of the carboxylic acid that is going to lose its proton and become COO minus and the NH 2 that we saw as the amino group is going to remain as NH 3 plus.

This is what is called the zwitterionic form. In addition, when we look at the R group that we have here that may also have variations, what are these variations, and how are they important in an understanding of the properties of amino acids.

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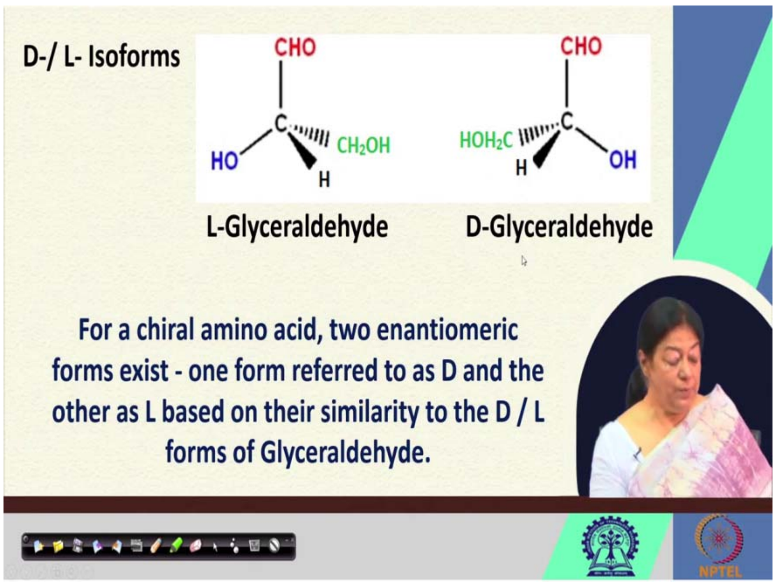

Now, there are different isoforms. What are these isoforms? Let us first understand the isoforms, and then we will go on to the properties of the amino acids. As we saw in the previous slide, we had a C-alpha and we had four different substituents on this carbon atom – we had the NH 2, we had the COOH, we had the H, and we had an R group.

Now, if we have a chiral form, it means that the R, the NH 2, the H and the C O H these are all different just as I mentioned in the A B C connect C D connected to the central carbon making these chiral in nature. The only achiral one that we can have is if R is also H which we will see in a moment.

So, when we look at the different forms of the amino acids, they are actually based on their similarity to the D and L isoforms of glyceraldehyde. If we look at the two diagrams given here, the central carbon that is in the middle in black has four different groups attached to it. So does the one on the right.

But the representation is such that we call the this one on the left as L-glyceraldehyde, and the one on the right D-glyceraldehyde. This was a nomenclature given for glyceraldehyde following which the nomenclatures for the amino acids were also made.

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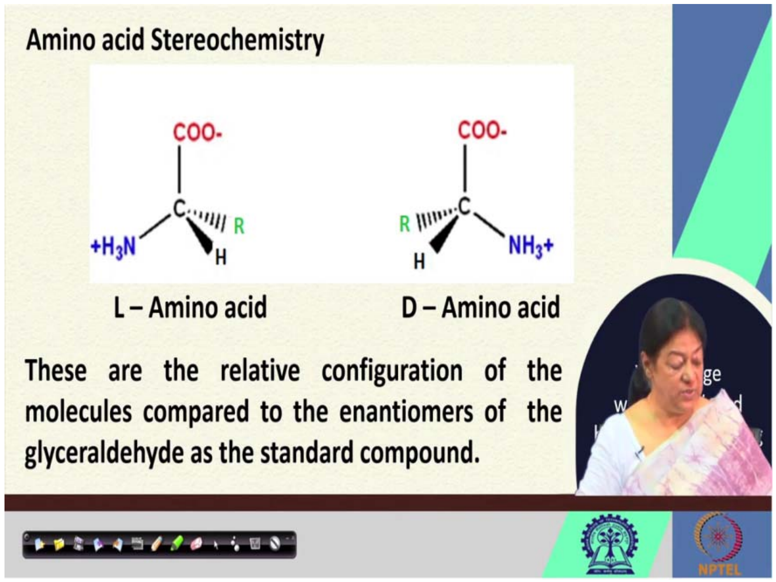

Now, when we look at the amino acid nomenclature, again we have the L-amino acid and we have the D-amino acid. The representations here that we can see are related also to the R and S groups or R and S nomenclature that you have would have learned in organic chemistry. So, when we look at the amino acid stereochemistry, we have the L-amino acid, we have the D-amino acid the representation of where the R group where the NH 3 plus group actually are oriented the stereochemistry.

So, these are the relative configurations of the molecules that as I mentioned were compared to the enantiomers of the glyceraldehyde considering that as the standard compound. So, each of the amino acids that we will see will have a D form and will have an L form these are the stereochemistry of the amino acids that we see.

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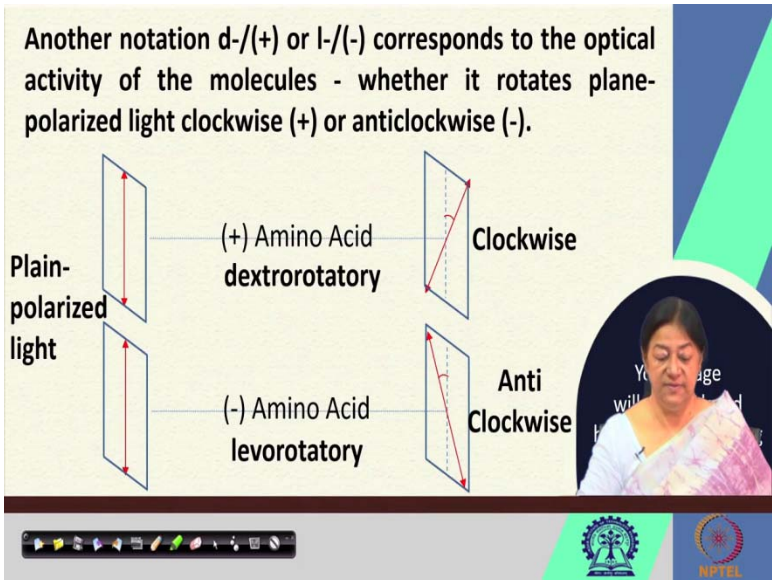

Another rotation is given by a dextrorotatory set and a levorotatory set because they can rotate what is called plane polarized light. What is this related to? This is related to the optical activity of the molecules. The optical activity of the molecules tells us whether it rotates the plane polarized light to the left or to the right, is it clockwise or is it anti clockwise.

So, if we look at plane polarized light that is shown on a plus amino acid that is dextrorotatory, and a minus amino acid that is levorotatory, what we will see is we will see a clockwise rotation of the plane polarized light, or an anti clockwise rotation of the plane polarized light giving us optical activity.

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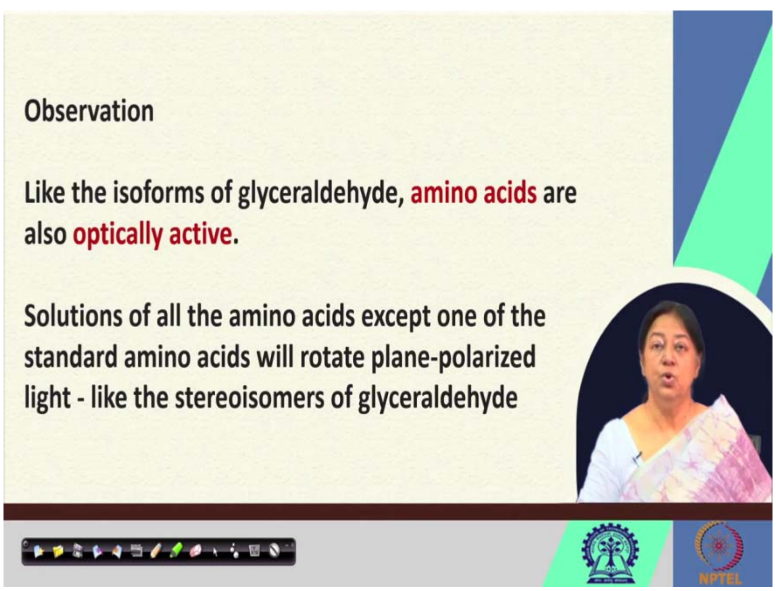

So, what are the observations that we see? The observations are that like the isoforms of glyceraldehyde, the amino acids are also optically active. The solutions of all the amino acids except one of the standard amino acids will rotate plane polarized light – like the stereoisomers of glyceraldehyde.

Now, which is the one that does not rotate plane polarized light, it will be one that is achiral in nature. So, when we look at the R group substitutions, we will see that there will be two substituents or two moieties that are the same that will relate or tell us that this is the molecule that is not going to be able to rotate plane polarized light.

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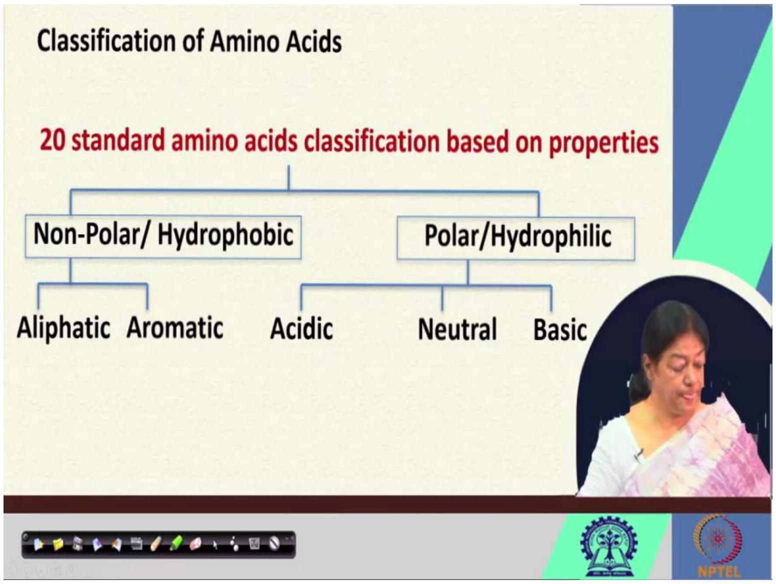

The amino acids, there are 20 standard amino acids. They can be classified based on their properties. What are these properties? They could be hydrophobic in nature, non polar. The atoms that comprise the R-group can be carbon, hydrogen, nitrogen, oxygen, and sulfur. So, a combination of these can give us a variety of R-groups that are going to determine the properties, going to determine their classification.

So, if we have an R-group that is comprised only of carbon and hydrogen we would render it hydrophobic in nature. But if it so happened that the side chain also had an oxygen, nitrogen, or a sulfur, then we would render it polar or hydrophilic in nature. Now, the hydrophobic ones can be aliphatic, can be aromatic. The hydrophilic ones can be acidic, can be neutral, can be basic.

And obviously, depending upon the type of properties that each of these amino acids have we are going to see different types of interactions, different types of steric interactions, and different types of say Van der Waals, hydrophobic, possibility of interaction in electrostatic interactions, or hydrogen bonding which is extremely important in proteins.

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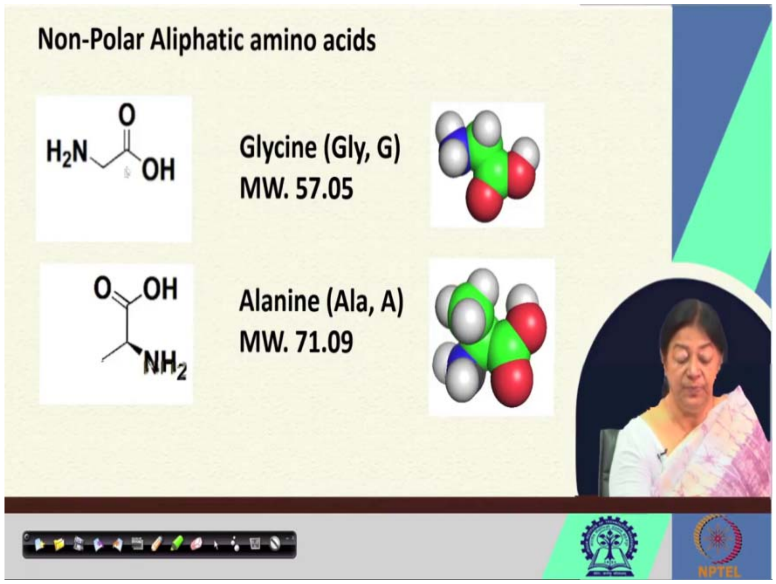

So, if we look at the non-polar aliphatic amino acids what is there on the left is a so we see that we have the NH 2 and the C double bond OH. Now, what happens well is when we look at this so this is the alpha carbon. So, when we look at the alpha carbon, we see that we had an hydrogen attached, there is again another hydrogen attached, making glycine the only achiral amino acid which means that this will not rotate plane polarized light.

On the right hand side, we have what is called a space filling model of glycine. The blue atoms represents nitrogen, the red atom represents oxygen. This is what these and the green ones are carbon, and the grey ones are hydrogen. This is a typical way of representation.

Now, when we look at the space filled model, we can straight away say for the one on the bottom right that we have here that here is the C double bond here, here is the COH. Now, we have the alpha carbon here and we have the NH 2 attached here. And what is attached at this point here, we see there is a C and there are three hydrogen atoms making this a CH 3. And what is this amino acid? This is alanine.

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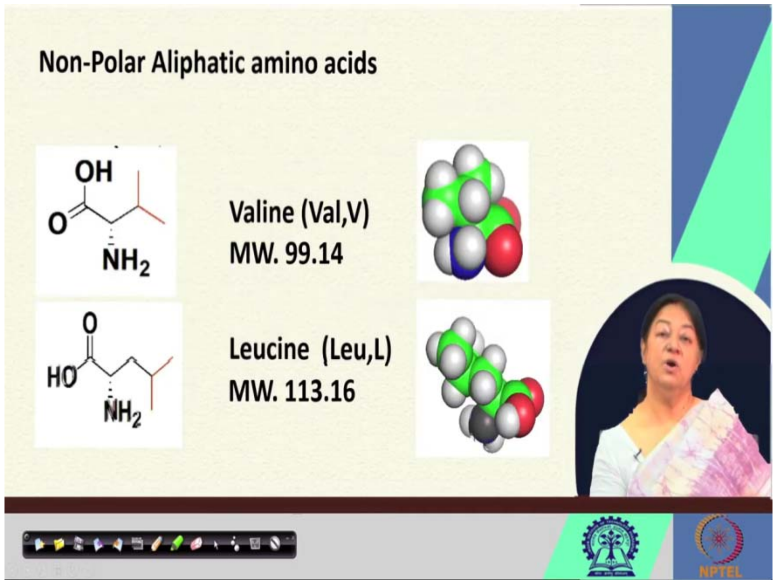

So, similarly, we can look at all the different other types of amino acids. We have valine, we have leucine. If we look if we're looking at these amino acids right now, we notice that the side chains that have been written do not have any other color associated with them. There is no blue nitrogen, no red oxygen, and the sulfurs are usually in yellow.

So, there is no such heteroatom as we would call it. This means that these are aliphatic in nature because they are not they are not aromatic as we just straight chain compounds, and they are non-polar in nature.

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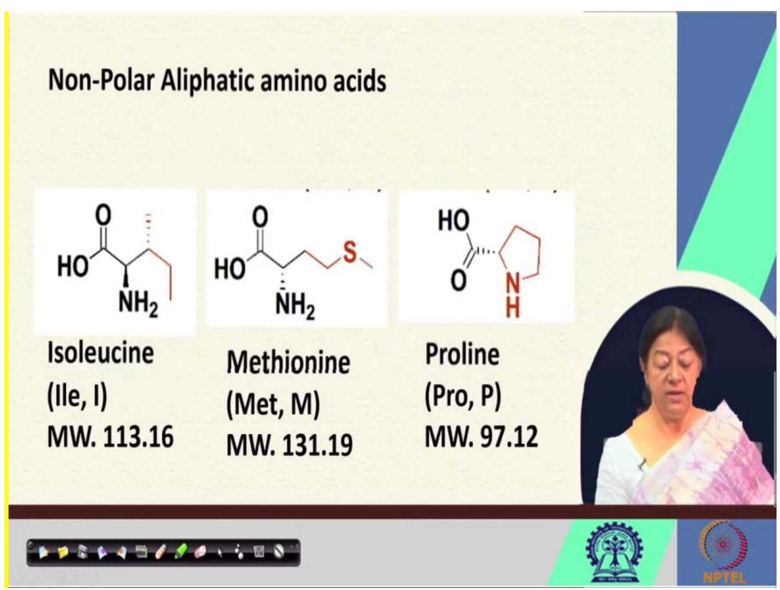

Similarly, we can have aliphatic amino acids. Now, we have isoleucine, methionine, proline which is very unique in its representation because it folds back upon itself in its side chain forming what is known as an imino acid.

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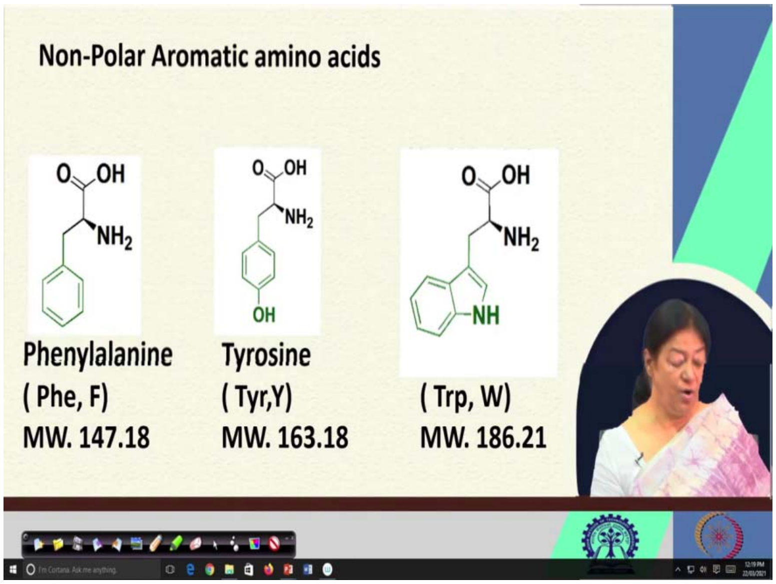

Now, when we look at the non-polar aromatic amino acids, we see that we have aromatic moieties, we have a phenylalanine, we have a tyrosine, we have a tryptophan. And we will see how these molecules or how these amino acids contribute to a very important spectroscopic property of proteins.

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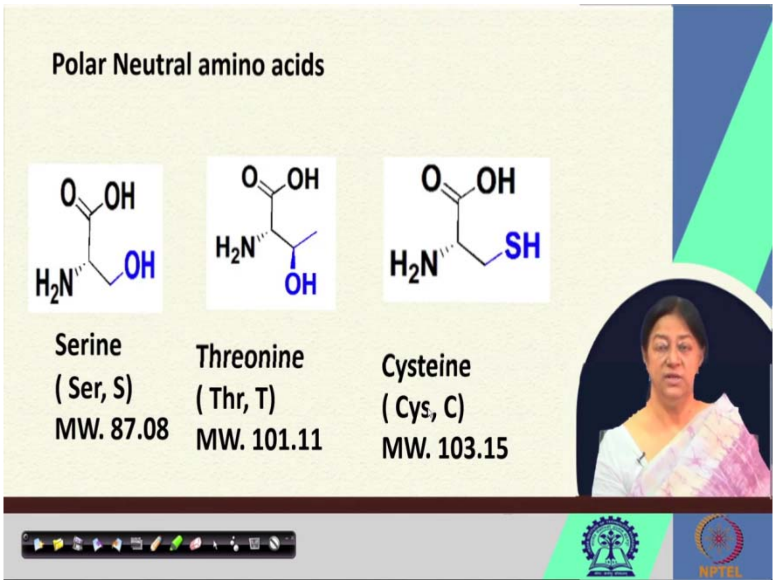

The polar neutral amino acids we see now we have now an addition of an oxygen here in the side chain or the sulfur in case of cysteine. What does this mean? This mean this means that the property is going to change of the amino acids. Their interactions are going to change, and the way they are involved in the protein is going to change.

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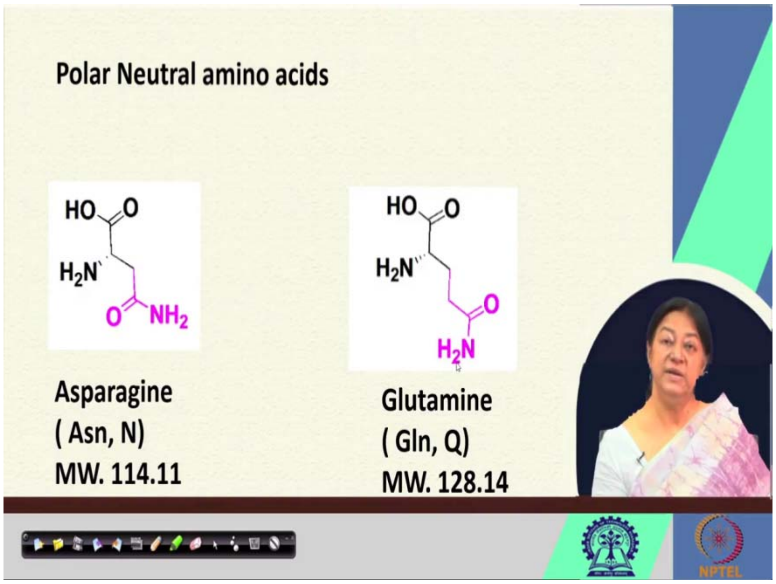

Other polar neutral amino acids important for hydrogen bonding are asparagine and glutamine. What we see here is we these are the amide containing moieties. So, we see a C double bond O and an NH 2. Similarly, we see the same for asparagine. This is derived from aspartic acid; this comes from glutamic acid.

Now, what is important about these types of amino acids we can see is their involvement in hydrogen bonding interactions which makes them important in their presence in proteins.

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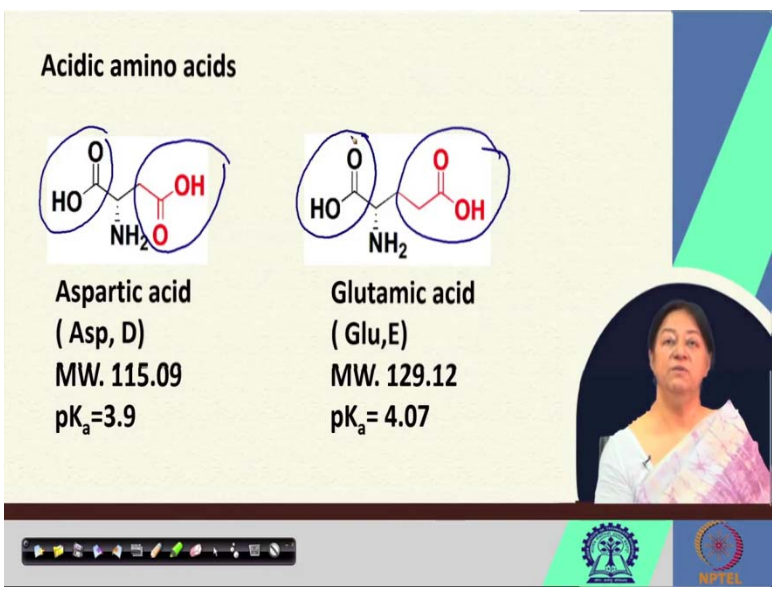

The acidic amino acids that the acid forms of the amides that were just shown aspartic acid and glutamic acid. What do we see here? We see C double bond O OH, C double bond O OH. Now, if we look at this these two of these amino acids, we see they are acidic amino acids because in addition to the carboxylic acid group that we see here there is also, so this is one of the carboxylic acid groups that was inherent for the amino acid.

But in addition we see that the side chain also has an amino acid has a carboxylic acid associated with it, similarly for glutamic acid which has. Now, how does this change the property? It does in an important way because this can be involved in electrostatic interactions.

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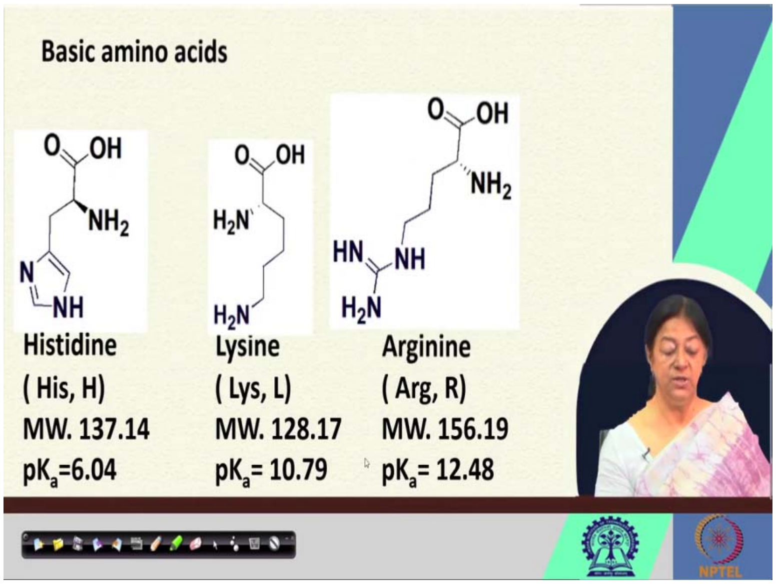

So, when we look at the different types, we can also see that there are basic amino acids. Here in addition to the NH 2 that we have, we also see additional NH 2 groups making these basic amino acids that are also going to be involved in electrostatic interactions and also change the properties of the proteins in a manner that is important for the function, very important for a lot of enzymatic reactions as well.

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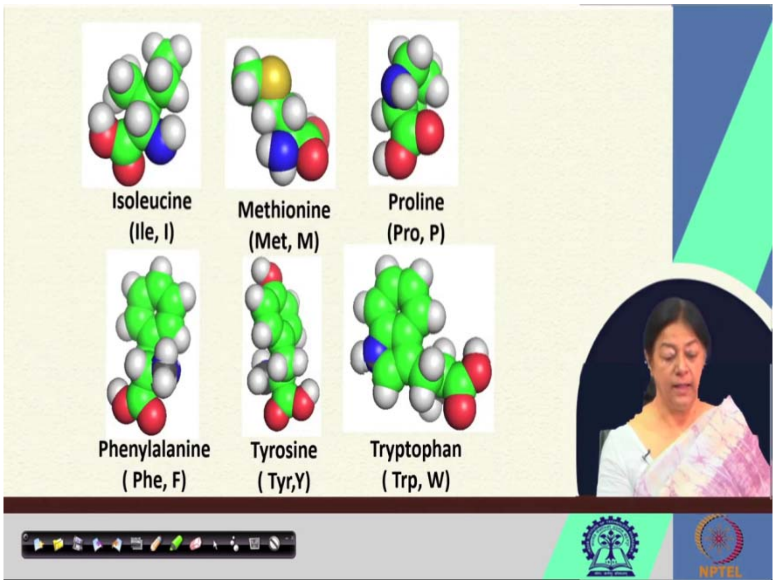

So, if we look at the space fill models of some of these as we mentioned, so when we look at this particular amino acid the one in the middle in the top here, there is a yellow atom. And the representative size gives you an idea of how they are space filled. So, now if we have a protein with the number of amino acids connected together by the peptide bond which we we will see shortly, we will see that there are steric involvements too.

And the aromatic amino acids that are given in the bottom row here show how bulky they can get when we have the aromatic ring involved in the protein polypeptide chain. So, an understanding of these properties is important to realize how these amino acids interact with each other, interact in forming the peptide bond and in the overall polypeptide chain.

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There is also a classification based on nutritional requirement we have essential amino acids and non-essential amino acids.

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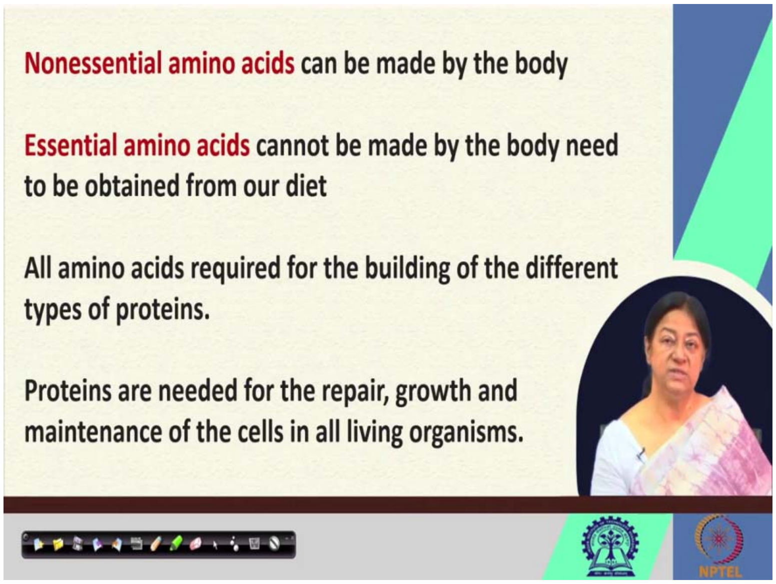

A listing, based on what? Based on how or why or should we have them in our diet. The non-essential amino acids are something that are synthesized in the body. The essential amino acids cannot be made and must be taken as nutritional supplements. So, they have to be obtained from our diet.

And all amino acids that we saw are required for the building of the different types of proteins. And we will realize the importance of the proteins as we go along in this course because they are needed for all living organisms, for the repair, the growth and the maintenance of the cells in our body.

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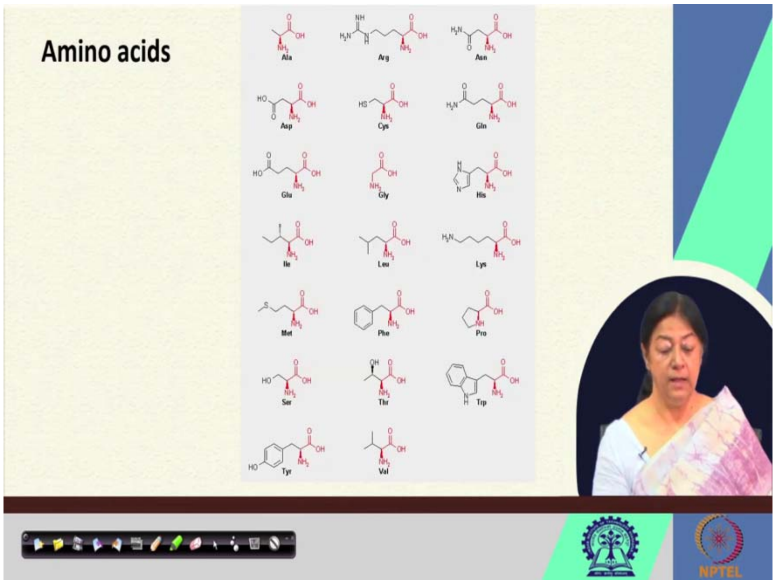

So, the amino acids if we group them together, we will see the all the different types that we just saw, all the different properties that we are going to look at.

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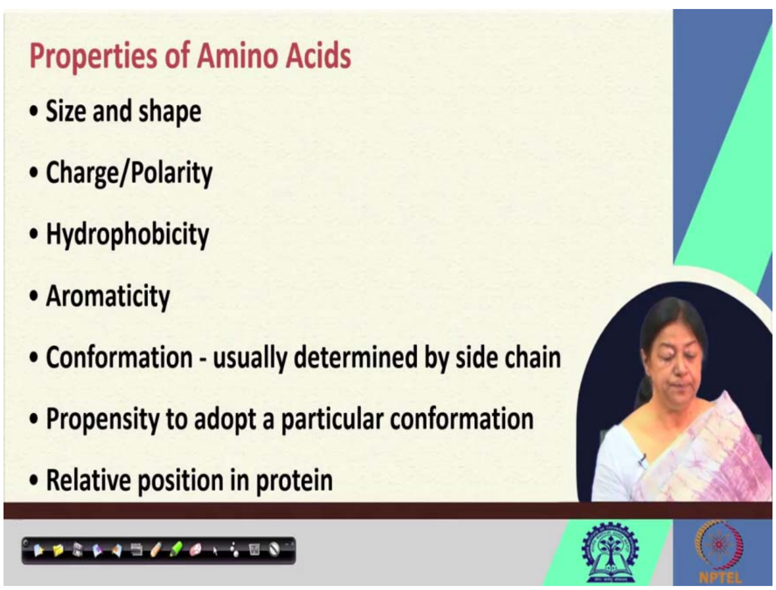

What are these properties? We saw differences in size and shape, differences in charge/polarity, in hydrophobicity, aromaticity, the conformation that actually is determined by the side chain, also the propensity which we will see later as we study protein structure, and the relative position in proteins.

What do we mean by these terms? How are the size and shape going to affect the protein chain? How is the charge or the polarity or the hydrophobicity of the side chain going to be important in the polypeptide chain in the overall interactions of the polypeptide chain or the protein?

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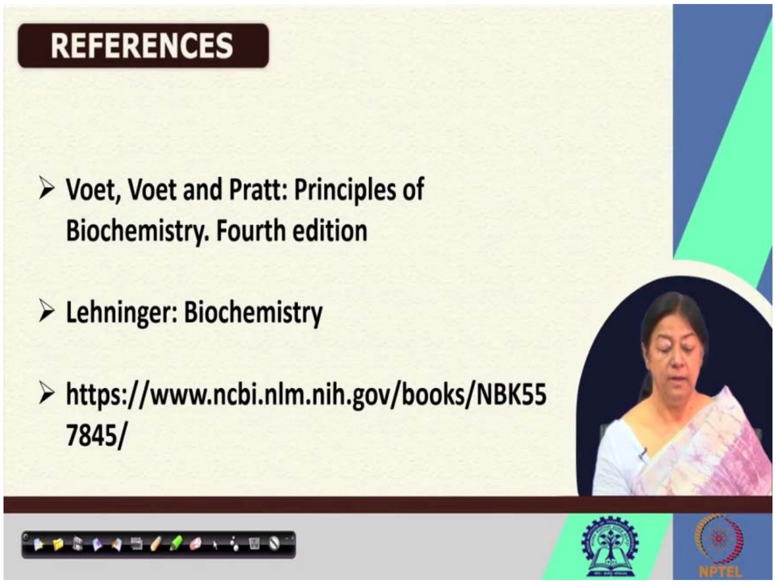

The books that will be followed for the course mainly Voet, Voet and Pratt, the Principles of Biochemistry. There is also Lehninger also Stryer, and some internet availability. But most of it will be covered will be there in relative books. There is also a book by Creighton that is Proteins, which I will give as a reference as we go along in this course.

Thank you.