

Organic Chemistry In Biology And Drug Development
Prof. Amit Basak
Department of Chemistry
Indian Institute of Technology, Kharagpur

Lecture – 03 (NOTE FORM)
Amino Acids: The Building Block of Proteins

Now let us talk about these fundamental units which are called the building blocks of the molecules of life. We will start with the proteins where the building blocks are amino acids.

(Refer Slide Time: 00:45)

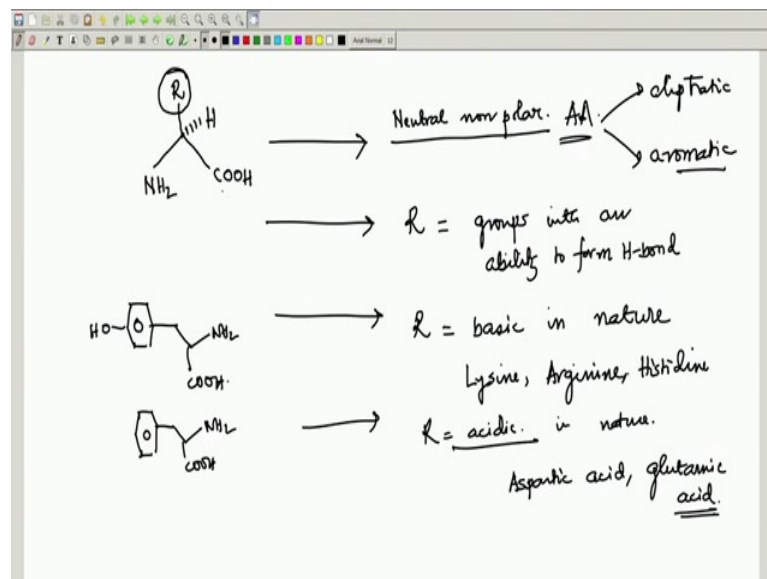
<p>1 The Amino Acids of Proteins</p> <ul style="list-style-type: none">A. General PropertiesB. Peptide BondsC. Classification and CharacteristicsD. Acid-Base PropertiesE. A Few Words on Nomenclature <p>2 Optical Activity</p> <ul style="list-style-type: none">• A. An Operational ClassificationB. The Fischer ConventionC. The Cahn-Ingold-Prelog SystemD. Chirality and Biochemistry <p>3 "Nonstandard" Amino Acids</p> <ul style="list-style-type: none">A. Amino Acid Derivatives in ProteinsB. Specialized Roles of Amino Acids
--

But, saying only amino acids is not sufficient, the amino acids have to be α amino acids. They have a special stereochemistry and that is L and hence they are designated as capital L-amino acids. Remember, capital L does not mean leavorotatory, capital L is the notation used for absolute configuration. Except glycine which does not have any side chain, other 19 amino acids belong to the L category.

And if you want to convert it into the R-S nomenclature system, then out of these 19, 18 belong to the S configuration and only cysteine (because of a priority order change over) L cysteine becomes R cysteine. So, 18 amino acids are basically S amino acids. Why I am saying this is because sometimes it is difficult for you to write the D-L system, but it is much easier to show the R-S.

So, if I ask you to write an L amino acid or different L amino acid containing peptides very quickly then the best way to do it is to just check their R-S system of the α carbon. Remember, that the α carbon is the one which is the chirality centre. However, there are few other (less in number, not many) amino acids where there is additional chiral centre. I could remember one at least right now and that is called threonine, that has got an additional chiral centre, but mostly it is only one chiral centre and that is present at the α position.

(Refer Slide Time: 02:53)



So, what is an α amino acid? Again I repeat, last time we told this, that α amino acids have a NH_2 at one carbon and the same carbon is attached to a carboxy and alongside with that you have an R-group.

Now, this has to be L configuration. So, if you want to make it L, you quickly try to make it S configuration by writing the hydrogen. Now, the hydrogen can be β or it can be α . So, which way it will be? You know that according to the priority sequence, nitrogen takes number 1, this is number 2 and the alkyl group takes number 3; except in case of cysteine, where there is a sulphur which alters the sequence. Now forget about cysteine, consider the other 18 amino acids where these are all S. So, to make it S, the hydrogen has to be α . So, this is the general structure of an L-amino acid.

Now, depending on the nature of R you have different classes of amino acids. What are those classes? Some are called neutral non-polar. So, that means, the classification is

based on this part only because that is the part which is varying in different amino acids. NH_2 is there for all amino acids except another amino acid which is called proline where this is NH and not NH_2 . So, that is a secondary amine. So, the only secondary amine containing amino acid is proline.

Now, this R can be non-polar side chain. So, they are called neutral non-polar amino acids and I will show you that this is the largest pool of the amino acids. Now, remember another thing that what we are discussing is the building blocks which makes the protein; we are talking about the amino acids which are joined together to make the proteins. So, these are called protein amino acids.

So, we are talking about protein amino acids. How many protein amino acids are there? We know that there are 20 protein amino acids, ok. But if we say how many amino acids are there in nature? Then that is thousands and thousands in number, because there are different types of amino acids which are present, which are not joined together to make the proteins. So, the question has to be very clearly understood that what is asked. How many non protein amino acids are present in nature? Then it is thousands; How many protein amino acids are present in nature? Then it is 20 and if it is asked that how many amino acids are present? Again it is countless.

We are talking about only the amino acids which are present in proteins. These amino acids are 20 in number; they are classified according to the nature of R. If R is non-polar side chain, then that is called neutral non-polar amino acids. Then R could be groups with an ability to form hydrogen bond. So, they are again neutral. Now, neutral means we are talking about the charge present in R, which is our basis for classification of neutrality. We are not talking about this NH_2 and CO_2H . Obviously, they can be ionized. So, our neutrality is based on this side chain R. So, groups with an ability to form hydrogen bond.

So, there are amino acids which contains OH, name of such amino acids are serine or threonine; or there could be amino acids which are called asparagine and another is glutamine, they are amide. They also have the ability to form hydrogen bonds, ok, but they are uncharged groups. So, when I say neutral; that means, they are uncharged. You can have R which is basic in.

And amongst this, there are three amino acids; one is the lysine another is arginine and the third one is histidine. These are the three basic amino acids. You also have R group which is acidic in nature. Acidic in nature means we are talking about strongly acidic in nature, not weakly acidic; that means, the carboxylic acids and in this category, there are two amino acids- one is aspartic acid and the other is glutamic acid.

So, these non-polar amino acids are also called hydrophobic amino acids; non-polar means they will not like water. This is the one which can form hydrogen bond. So, they like water, but their interactions are through hydrogen bond. Then the third class is where R is basic in nature and the other is the acidic amino acid where R contains a carboxylic acid functionality. Now this is one way of classification, you can have other ways of classification.

You can have aromatic amino acids; you can have aliphatic amino acids. Now, there are three aromatic amino acids; one is called phenylalanine, another is tyrosine and the third one is tryptophan. They are all hydrophobic in nature. However, one must remember that there is an index of hydrophobicity. How much hydrophobic, how much there will be water repellent, that depends on the nature of the group.

Like if I take tyrosine and phenylalanine; now, tyrosine has an R group which has OH here (a *para* hydroxyl group) and there is CH₂ and then NH₂ and CO₂H. Now, when we write these structures, we generally do not write the 3-dimensional structure because we assume that this is in the L configuration and phenylalanine is lacking that hydroxy group. So, obviously, we know that phenolic OH is slightly acidic. So, the hydrophobicity of these two amino acids will definitely be different.

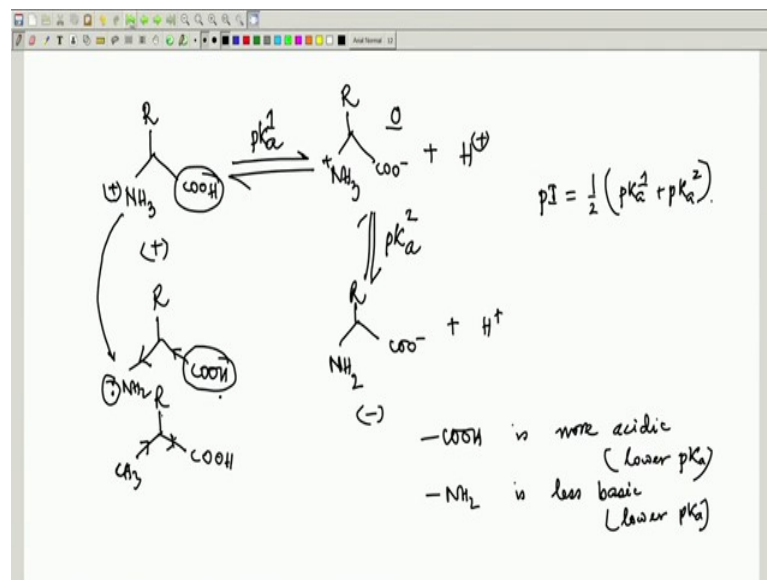
So, that is what I was pointing out there is the hydrophobicity index of all these side chains and depending on that when you have a number of amino acids then basically this hydrophobicity they can add up together and finally, make it extremely hydrophobic. So, different amino acids have different solubility profile at different pHs of solution and these all depends on the characteristics of the groups NH₂ the CO₂H and the R. So, these are the three important groups.

Now, let me talk about this first this NH₂ and CO₂H. We know that the this is an acidic group and this is a basic group. So, first thing that comes into mind that if you forget about R, then this is basically an amphoteric system, i.e it has got a basic group and an

acidic group. The issue is that both will affect each other; there is a NH_2 , there is a CO_2H ; that is not same as a molecule which is only having carboxylic acid and that is also not same with the molecule which is only having the amine.

That means, what I am pointing out is that whether the acid strength or the basic strength will remain very similar like the ordinary aliphatic or aromatic carboxylic acids or whether the amine will have similar basicity like what is present in aliphatic or aromatic amines? So, that is the question. Now, what happens here in this case?

(Refer Slide Time: 12:31)



So, what happens here that if you take an amino acid, and place it into an acidic solution of say pH 1, then this is the form that it is going to take. We are considering that this R is a neutral hydrophobic group; it does not have any acid or basic group.. So, this will be present as NH_3 plus and CO_2H .

Now, if you start raising the pH to a certain level, since this molecule has to dissociate hydrogen- one is this carboxy, another is this NH_3 plus. So, NH_3 plus can go to NH_2 and CO_2H can go to CO_2 minus, but since carboxylic acid proton is the stronger acid, so, first this proton will be lost. So, that ionization will take place and this will be R.

Now, suppose the equilibrium constant for this is expressed in terms of pK_a . What is pK_a ? That is the dissociation constant of this carboxylic acid because you have a proton that is liberated; dissociation constant is an equilibrium constant of this process, the

negative logarithm of the equilibrium constant is the dissociation constant; lower pK_a means higher acid strength. So, as you raise the pH you have this dissociation. So, it goes to a form where there is no net charge, the amount of positive and negative charge is same.

Now, if you further increase the pH, then what happens? Then this NH_3^+ will lose the hydrogen and you have a second dissociation. And the second dissociation will have another dissociation constant. So, suppose this is pK_{a1} and we call it pK_{a2} , ok. So, this is what exactly happens as you raise the pH from a very acidic zone to say up to pH 12. Now, this has got a net negative charge, this has got a net positive charge and this has got a net 0 charge.

I told you last time that there is a particular pH where this form (which is electrically neutral) is the dominant form and it is called the zwitter ionic form and that pH is called the isoelectric point. And the isoelectric point means a pH at which it is electrically neutral; it is given by the average of this $pK_{a1} + pK_{a2}$.

Now, before I go into this pI, again the basic question I asked is that what is the effect of this NH_3^+ on this CO_2H or what is the effect of this CO_2H on this NH_2 ? That means, how do they interfere with each other? Now, we know that NH_3^+ is an electron withdrawing group or forget about NH_3^+ ; if you take this molecule, only the normal NH_2 (not the zwitter ionic form), and CO_2H and R, and now you ask yourself that what is the effect of this NH_2 on this?

Now, nitrogen is more electronegative than carbon. So, there will be an inductive effect on this side. If there is inductive effect on this side, that will be transmitted to the second bond and that means, there is electron withdrawal. This carbon is trying to pull electron from this carbon and that will enhance or that will facilitate the release of the hydrogen from this; that means, if I have suppose a methyl R and then CO_2H .

In case of methyl, it is the other way around, actually methyl pushes electrons on this side and that ultimately is transmitted to this carbon. In this case the opposite effect is happening and here if electron is pumping towards this carbon, then there will be less tendency of this oxygen to release the hydrogen because nobody wants that concentration of a charge on a particular atom; the more delocalized it is that is better.

So, this H will be released at a pH which will be higher than this hydrogen because this hydrogen release will be facilitated by the electron withdrawal of the nitrogen.

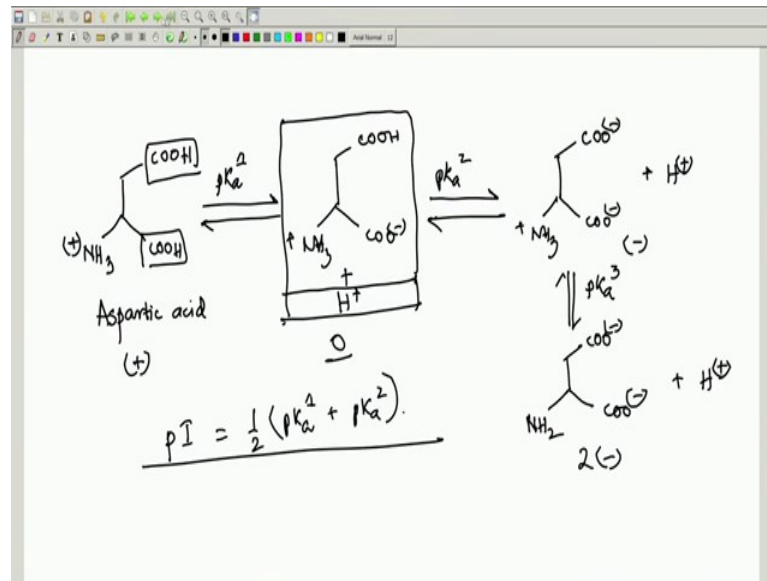
So, what is the ultimate effect? The ultimate effect that the pK_a of the carboxylic acid will be lower than the normal pK_a of acetic acid or propionic acid, these type of aliphatic acids. So, alpha amino acids, the carboxylic acid has a lower pK_a and that means, the carboxylic acid is a stronger acid; lower pK_a means it is a stronger acid.

And in case of the NH₂, we talk about the basicity and when you talk about basicity we try to say that what happens to this dissociation? Which means this is the pK_a of NH₃ plus transforming to NH₂. What happens to that? If that pK_a is higher, that means, its basicity is increasing; if the pK_a is lower that means, its basicity is decreasing and acidity is increasing.

So, now, in this case what happens? This is the carboxylic acid; we know if we just consider this structure, it tries to withdraw electrons because there is a CO₂H where carbonyl is an electron withdrawing group. So, if it tries to withdraw electrons, the chances that this lone pair will be donated to a proton will be less. Basicity of the amine depends on how easily this lone pair can be donated to a proton. Thus this donation of electron lone pairs will be more difficult in the presence of an electron withdrawing group like carboxylic acid.

So, ultimately what is happening? The bottom line is that in α amino acids, the carboxylic acid is more acidic; that means, lower pK_a and the NH₂ is less basic. What does it mean? Again, that means, that it will have a lower pK_a than the normal NH₂, for example methyl amine or propyl amine. I will show you the chart of these different carboxylic acids and the amines and what are their pK_as; we will go to that, but before that, we will talk a little bit about this R group and the isoelectric point.

(Refer Slide Time: 20:39)



Now, suppose there is a carboxy group in the side chain. So, how to know the the isoelectric point of this molecule? This amino acid is called aspartic acid. Now, aspartic acid, if you take it in a acid medium like pH 1 then it will be a present in this form NH₃ plus and CO₂H. Now, what will happen if you try to raise the pH add alkali slowly? These acids are stronger than the NH₃ plus. So, one of these acids will now lose proton. Question is which acid will lose the proton first.

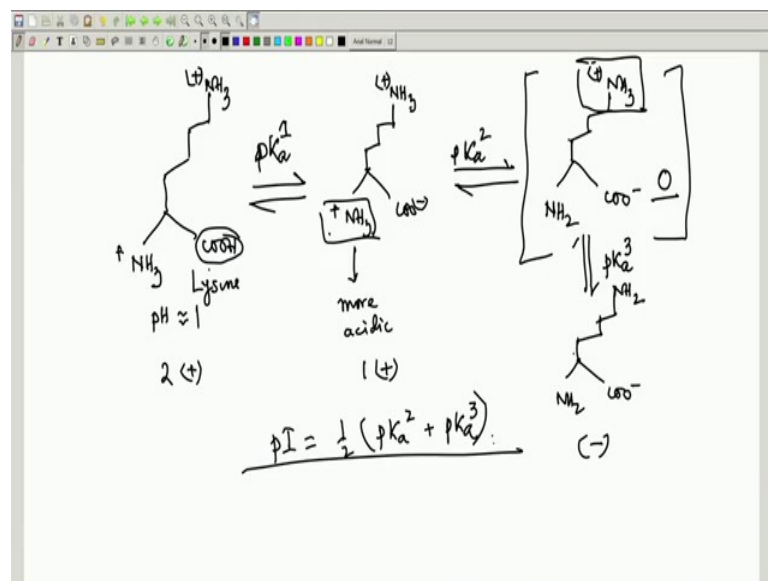
Now, previously I just said that in the α amino acid, the α carboxy group is stronger acid than the normal aliphatic acids. So, that means, this will have a lower pK_a than this one. So, as you raise the pH, the first dissociation will happen from this α -carboxylic group. So, α -carboxylic group will become CO₂ minus and the other will remain CO₂H. So, this is the first dissociation.

The second dissociation now will occur from the other carboxylic group; CO₂ minus (from the side chain carboxylic acid) and then this is NH₃ plus and this is CO₂ minus plus H plus; but still you have one more acidic proton. So, if you again raise the pH, suppose pH 12 (suppose you do not know what is the pK_a of this NH₃ plus), although generally the highest pK_a is what is for guanidine which is around 12 or 13. So, that is why I am saying that suppose the pH is raised to 12 then what will happen? Surely this is going to lose the hydrogen and you get CO₂ minus.

So, these are the three dissociations that you have which are pK_{a1} , pK_{a2} and pK_{a3} . Now, so, calculate the charges of each species. In this case, you have a net positive charge, in this case you have the zwitterion; so a net charge of 0, in this case you have a net negative charge (two negatives and one positive). So, one negative charge and in this case, two negative charges.

So, now, what will be the isoelectric point, pI ? Now, basically pI is taken as the average of the two pK_a values on the left and right side of the neutral form or of the zwitter ionic form. Now, the zwitter ionic form is this one. So, this is the zwitter ionic form excluding the H and on the left is the uni-positive one and on the right is the uni-negative one. So, pI will be half of pK_{a1} plus pK_{a2} , so, this is your pI . Interestingly, the third dissociation constant does not take part in the formula of the pI .

(Refer Slide Time: 24:53)



Now, take the other type of amino acid where there is a basic side chain. You will see exactly the reverse of what we have seen earlier; in case of aspartic acid it is the average of the first two dissociations (the pK 's) and in case of basic amino acids, where you have a basic group here, like this, let me count the carbons 1, 2, 3, 4, 5, 6, 7. So, this is NH_3^+ plus, this is the lysine in the fully protonated form when pH is say approximately 1. So, this is what lysine is. It will be present in that form.

Now, if you raise the pH again now, you do not have any problem since there is only one carboxy group. So, that is what is going to ionize. So, you will get NH_3^+ plus and this will

be CO_2 minus and that will be 6 carbon (1, 2, 3, 4, 5, 6) and that will be NH_3 plus ok. Next, you again raise the pH. So, now, you have a dissociation constant here and the pK_a value of this carboxy group that is pK_a1 . So, that belongs to this carboxy group. Then as you raise the pH, now there are two acidic hydrogens here; this is NH_3 plus, that is also NH_3 plus. So, the question you have to decide is which one will come first?

Now, we have already told that this amine becomes less basic in an α amino acid because of the carboxylic group withdrawal of the carboxylic group. If it is less basic that means, the other one is more basic; you have to just go step by step; if it is less basic that means, its hydrogens is more acidic. So, these hydrogens are more acidic; why? Because this amine is less basic. So, this is the hydrogen that is going to be lost resulting in the formation of NH_2 and COO minus and then this NH_3 plus will undergo dissociation with dissociation constant of pK_a2 .

Now, you have another hydrogen which can be dissociated. So, you raise the pH and the corresponding dissociation constants will be the pK_a3 (pK_a3 is for this ammonium species). So, that will be NH_2 and then you have COO minus. So, you have to always count 6 carbons including the carboxy in lysine. So, these are all the three forms now.

So, now, you just count the charges. This has got two positive charges, this has got one positive charge, and this has got no charge, (i.e, 0). So, that is a zwitterion and this has got a negative charge. Now, what did I say? Last time I said that to know the pI of a system, you first consider which is the zwitterion? Now this is your zwitterion, and then you take the pK_a values from the left side and from the right side. So, now, in this case pI will be half of $\text{pK}_a2 + \text{pK}_a3$. I think this should be clear to you.

Now, this is very important because here we are talking about amino acids; if you have now here peptide, a dipeptide or a tripeptide, where there are different ionizable groups, that will also have an isoelectric point. An isoelectric point is very important because this is related to the movement of the system in an electric field. So, if you want to separate three molecules which have got three different pIs, you can separate them by applying a voltage and then keeping the pH at certain point where one amino acid does not move; that means, that pH is kept at pI where the other amino acid will move because that will have some charges (because if pH does not match the pI). So, pI is a very important

concept in peptide chemistry, even amino acid separation, peptide, protein separation. Now, let us just show some of these slides very quickly.

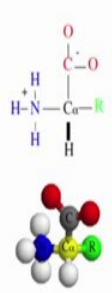
(Refer Slide Time: 30:15)

Amino Acids are zwitterions

In the physiological pH range (5-8), the α -carboxyl and α -amino groups of amino acids are completely ionized

- Compounds with this property are referred to as **zwitterions** (or dipolar ions or ampholytes)
- Zwitterions can act as either an acid or a base

α -carboxyl groups have pK_a s near 2.2 while α -amino groups have a pK_a near 9.4



The slide contains two diagrams of an amino acid zwitterion. The top diagram is a Fischer projection showing a central carbon atom (C α) bonded to a hydrogen atom (H) on the left, a hydrogen atom (H) on the right, a carboxylate group (COO⁻) at the top, and an R group at the bottom. The nitrogen atom (N⁺) is shown to the left of the C α atom. The bottom diagram is a ball-and-stick model of the same molecule, with carbon atoms in grey, oxygen atoms in red, hydrogen atoms in white, and the nitrogen atom in blue. The R group is represented by a green sphere.

The amino acids are the building blocks of proteins. amino acids can exist as zwitterions. This is the C- α as it is shown here, it is connected to R. This is the L configuration in the Fischer projection formula; L is the one where the amine group is on the left side of the vertical bond and the carboxy should be at the top because Fischer projection formula demands that the number 1 carbon or the most oxidized carbon should be kept at the top of the vertical position (Refer Time: 30:51).

So, it says α carboxyl groups have pK_a s near 2.2; you know what is the pK_a of acetic acid? It is about 4.7. So, you see that it is so much acidic, so, always remember that these points are on logarithmic scale. So, if there is a jump of 1 unit; that means, that becomes 10 times more acidic or less acidic. So, that also should be kept in mind because sometimes we forget, if we say that something has a pK_a of 4 another is 3 we think that they are pretty close. Actually not close one is 10 times more acidic than the other because it is a logarithmic scale.

(Refer Slide Time: 31:37)

Chirality

- Amino acids (except glycine) have a tetrahedral C_{α} bonded to four different chemical groups
 - Consequently, amino acids are optically active or chiral
- Common amino acids are all **L stereoisomers**
 - Amino acid configuration uses the D,L system while synthetic chemistry generally uses the R,S system
- “CO-R-N” mnemonic useful for distinguishing L and D stereoisomers
 - Looking down the H – C bond, CO-R-N spelled clockwise indicates the L stereoisomer

L-amino acid

D-amino acid

I have talked about chirality that these are all having L-configuration and that translates into S except cysteine; cysteine is an R amino acid; L cysteine is R amino acid. Now this is a very global question that why nature has picked up only the L amino acids and not the D amino acids.

Now, we are not trying to tell anything here about the reason because all are speculations, but one thing I will just point out because you may face different types of interviews and vivas where it might be asked to you that do all naturally occurring amino acids belong to the L series? Again, I repeat the question whether all naturally occurring amino acids belong to L series or not?

The answer is that a majority is L, but they are instances where amino acids can be D. And, when we talk about bacterial cell wall structure, we will see that bacteria in order to survive itself from the onslaught of outside agents, it has made some amino acids which are in D configuration. So, that when there is D configuration, it cannot be recognized by the foreign organism. Well, that is a very interesting point. So, some D amino acids are there, it is not totally excluded.

(Refer Slide Time: 33:21)

Classification of Amino Acids

- Amino Acids are classified or grouped according to the physicochemical properties of their R-group
 - Voet & Voet presents one common classification scheme based upon polarity
- Polarity** is defined as *the magnitude of the dipole induced in the presence of an external electromagnetic field.*

Classification schemes are an aid to recalling structure and properties of amino acids

Amino acids grouped by Polarity (at neutral pH).

So, I will just want to make one more point that is why chirality is so important? Classification of amino acids, I have already told you.

(Refer Slide Time: 33:23)

Non Polar Amino Acids

R-group is a hydrocarbon (also includes Trp & Met)

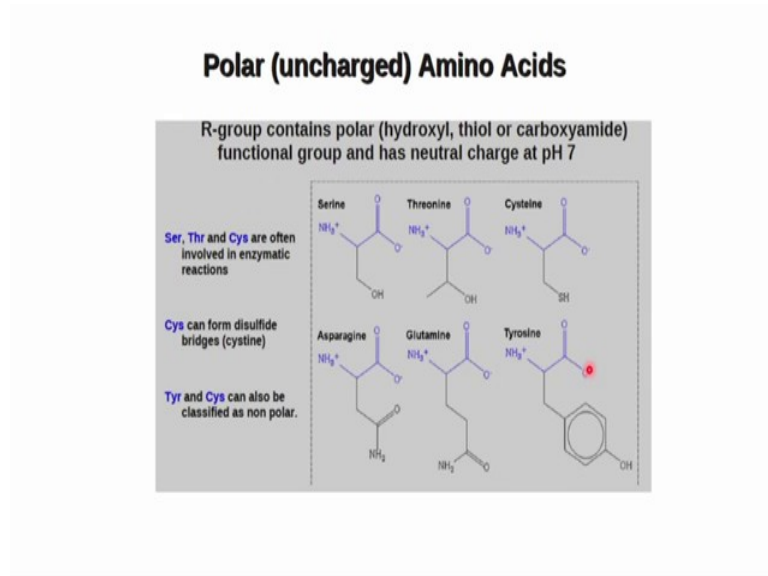
Aromatic amino acids absorb UV light

Proline R-group is covalently bonded to α -amine

Glycine can also be classified as polar uncharged

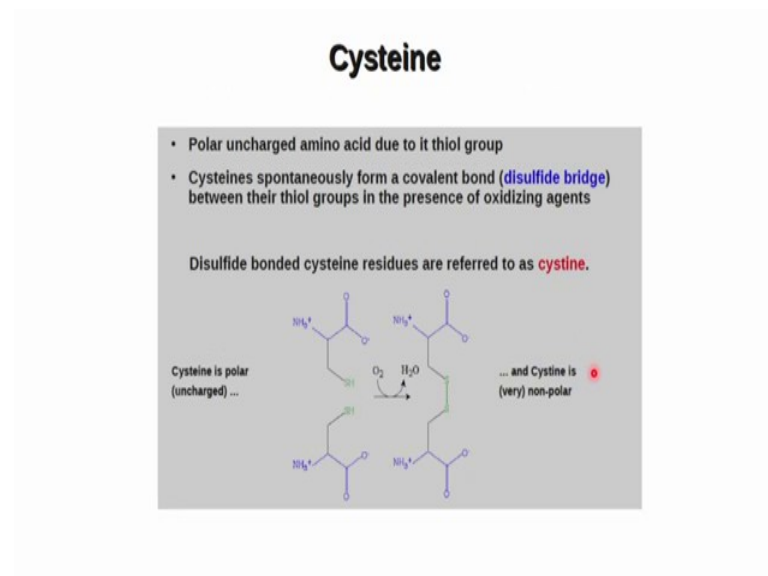
Non-polar amino acids.

(Refer Slide Time: 33:25)




Then, the polar uncharged all these classifications are there.

(Refer Slide Time: 33:27)



(Refer Slide Time: 33:33)

Amino Acid	Residue	3-letter Code	1-letter Code	R-group	pK	Frequency (%)
Nonpolar						50.1
Glycine	Glycyl	Gly	G			7.1
Alanine	Alanyl	Ala	A			8.3
Proline	Prolyl	Pro	P			4.7
Valine	Valyl	Val	V			6.9
Leucine	Leucyl	Leu	L			9.7
Isoleucine	Isoleucyl	Ile	I			6.0
Tryptophan	Tryptophanyl	Trp	W			1.1
Phenylalanine	Phenylalanyl	Phe	F			3.9
Methionine	Methionyl	Met	M			2.4
Polar uncharged						24.0
Serine	Seryl	Ser	S			6.5
Threonine	Threonyl	Thr	T			5.3
Cysteine	Cystyl	Cys	C	8.4		1.4
Asparagine	Asparagyl	Asn	N			4.0
Glutamine	Glutamyl	Gln	Q			3.9
Tyrosine	Tyrosyl	Tyr	Y	10.5		2.9
Polar charged						25.9
Histidine	Histidyl	His	H	6.0		2.3
Lysine	Lysyl	Lys	K	10.5		5.9
Arginine	Arginyl	Arg	R	12.5		5.5
Aspartate	Aspartyl	Asp	D	3.9		5.4
Glutamate	Glutamyl	Glu	E	4.1		6.8



This is the other thing which also is very important. Although you may find it to be little bit annoying that you have to know what are the symbols of these amino acids; like for elements we have symbols. We have symbol H for hydrogen; everything has a symbol; Na is sodium.

So, in case of amino acids which are 20 in number, we have names for those amino acids. Glycine, alanine, proline, etc; but if suppose I ask you to write a structure of a decapeptide, ok; then how to write this decapeptides? You have to write alanine, then suppose valine, then again alanine, then glycine. So, your whole page cannot accommodate a single decapeptide (if you start writing the full word of the amino acid). So, what is the option then? We have to use some symbols for these amino acids.

Then people started thinking of a 3-letter word corresponding to each amino acid; like glycine was gly; alanine was ala; proline pro. Again if there are thirty amino acids then there is a problem. Using these 3 letter codes, how to write these 30 amino acids in a single in a width of a single page? That becomes really difficult and 30 is a small number. Some amino acids are 100s or 200s or even much greater number of amino acids; some proteins are like that; they contain large number of amino acids.

So, ultimately IUB that is the International Union of Biologists, said that one will have to use this 1-letter code for the amino acids; just like our elements in the periodic table that we have. The elements have a symbol; the amino acids also have a symbol. However,

there is a slight problem here. The problem is that there are many amino acids. If you take the first letter of the amino acid as the symbol you will see there are degeneracy like G; glycine is G and then glutamic acid is also G. So, now, which one will get G?

So, it has been decided that first you start with this glycine and assign it G, alanine is A, P is proline, no problem. First letter gives the symbol; valine is V, leucine is L, isoleucine is I. Now, the problem starts tryptophan. Tryptophan is W. Tryptophan is W because there is another T somewhere, that is threonine. Threonine we have given the T already (reserved for threonine), so, tryptophan is W. And then phenylalanine, but you have already given P to proline. So, phenylalanine, as if the pronunciation starts with phenyl, phenyl means as you are starting with F. So, they said that let us put F for phenylalanine, ok.

Methionine is M, no problem and then you have serine S, threonine T, as I said cysteine is C, no problem; aspartic acid again is A, asparagine is a problem because alanine has got the A you have reserved A for alanine. So, asparagine is N and then glutamine is Q. Now, they say that glutamine some people in the English world they say “glutamine” means they do not say glutamine. So, as if there is a phonetic sound of Q there. So, that is why they say glutamine is Q and then tyrosine is Y, they say they took the second letter of tyrosine that is Y.

And then your histidine H; lysine K, it is because you have already reserved L for leucine. So, lysine is K and then arginine its pronunciation is like R arginine. So, you have R. These are as I said the mnemonic device; arginine if you forget try to again think arginine means R as you have starting to pronounce it, so, that gives R. Aspartic acid some people in the English world say “aspartic acid”; they do not actually put stress on the T as if there is a D (aspartic acid). So, the D is for aspartic acid and glutamate means glutamic acid is E.

Now, this you must remember, these 20 symbols. Once you have this one letter now, it is easy to write; the thirty will be completed within few dimensions. So, this is the way the amino acids are represented when you want to know the sequence of amino acids in a peptide shell. So, that I wanted to say.

(Refer Slide Time: 38:33)

Free amino acids have 2 (or more) acid/base groups and produce complex acid/base titration curves

eg. amino acid without ionizable R group

(+1) (0) (-1)

And then this I have already told.

(Refer Slide Time: 38:35)

- **Isoelectric point** is the pH at which the total charge of the amino acid (peptide or protein) is zero
- For amino acids without ionizable R groups, the pI is the average of the pKa's

$$\text{pH} = \text{pK} + \log \frac{[\text{A}^-]}{[\text{HA}]}$$
$$\text{pI} = \frac{1}{2}(\text{pK}_i + \text{pK}_j)$$

These are how to do the pKals, pI values how to know that.

(Refer Slide Time: 38:37)

Peptide Bonds

- Amino acids polymerize via **condensation** reactions
 - Carboxylate group of residue 1 forms a covalent bond with the amine group of residue 2
- Linear polymers of amino acids have an **amino (N)** and **carboxyl (C)** terminus
 - Living organism always synthesizes proteins from N to C terminus

Peptide Bond

(Refer Slide Time: 38:41)

Amino Acid Polymers

- (1) **residue** - an amino acid (or peptide unit) in an oligopeptide, polypeptide or protein
- (2) **oligopeptide*** - short polymer of residues linked by peptide bonds; up to 10-20 residues.
- (3) **polypeptide*** - longer polymer of residues linked by peptide bonds; larger sizes
- (4) **protein*** - one or more polypeptide chains

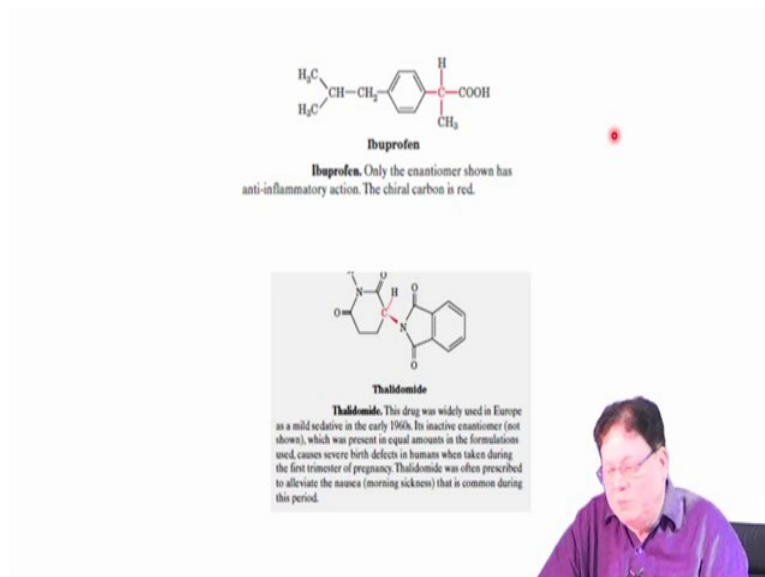
Full name:
Alanyltyrosylaspartylglycine

This I want to show you the importance of this chirality.

The chirality is very important. We say that our biological world is a L world means it is made of L amino acids. Whether there is a D world somewhere in the universe, that is a debatable issue; but this L is very important.

If you have a drug which is chiral and if you take a mixture of L and D, our body is chiral, all the materials are chiral and they have L configuration and the sugars have D configuration. So, now, there will be different type of interactions with the drug.

(Refer Slide Time: 39:31)



So, even if I take a drug in the racemic form, I have two different L and D forms of the drug and the interactions of the drug with the molecules in our body will be different. One who knows stereochemistry (coming from organic chemistry background) knows that if I have a drug which is having a plus and minus variety, then if the plus drug interacts with the L protein (protein made up of L amino acids) the plus minus compound interacts with the same protein differently.

Sometimes interactions may be extremely dangerous and there was one incident where there was a drug which was called thalidomide, which has got a chiral centre at this carbon and it was sold as a racemic mixture.

(Refer Slide Time: 40:19)



And when it was given to pregnant women and then the babies born from them did not have developed organs like the hands (which are not there); in some children, legs are missing; although it is not shown here, some of these children also have missing fingers in the hands and also in the legs. These are called teratogenic compounds.

So, this shows the importance of chirality. That is why whenever we make a peptide, whenever we are trying to make a protein or peptide (a new molecule), we must focus our attention on the chirality also.

Thank you.