بسم الله الرحمن الرحيم

BioChemistry | Lecture 13

Amino Acids & Peptides pt.2

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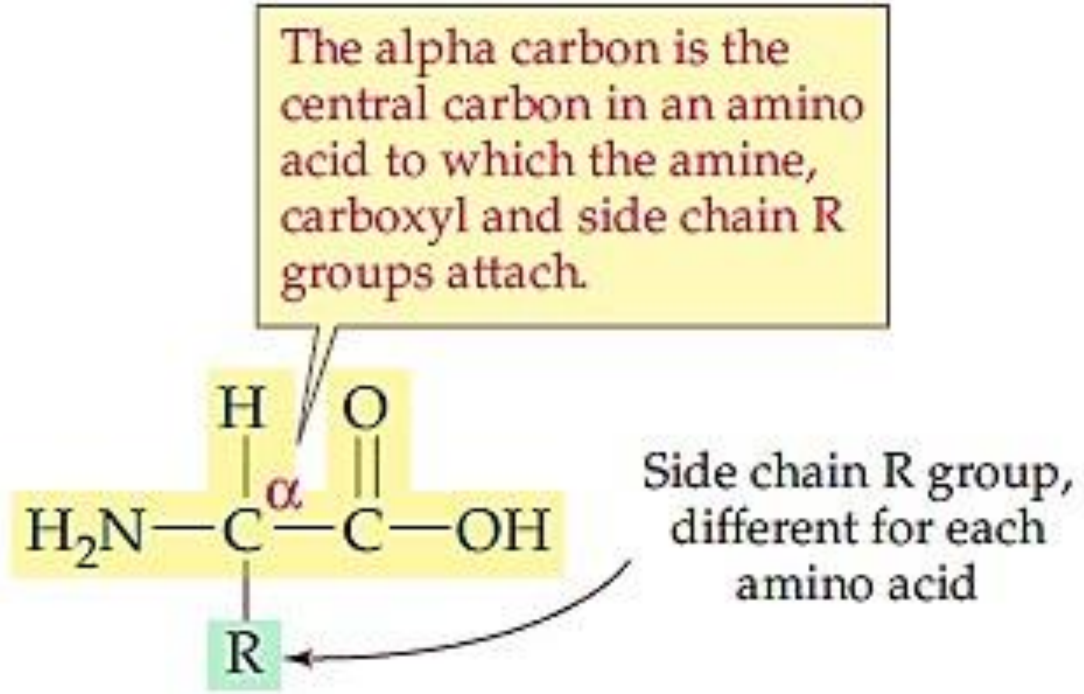
Protein structure and function

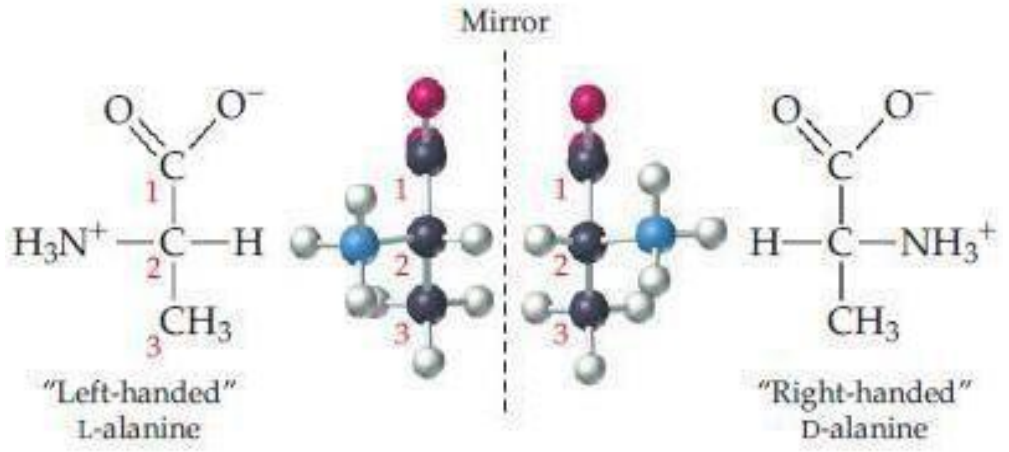
- Greek: proteios, primary (importance)
- 50 % of body's dry weight is protein
- Free vs. attached (**residue**), **D vs. L**



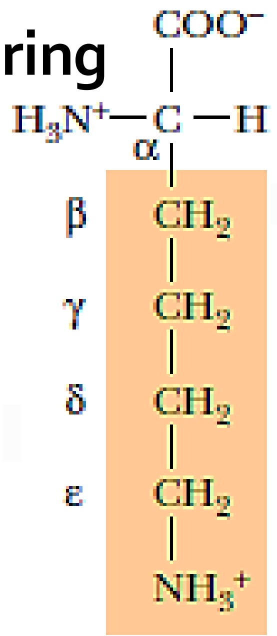
An α-amino acid

TYPE	FUNCTION	EXAMPLE
Enzymes	Catalysts	*Amylase*—begins digestion of carbohydrates by hydrolysis
Hormones	Regulate body functions by carrying messages to receptors	*Insulin*—facilitates use of glucose for energy generation
Storage proteins	Make essential substances available when needed	*Myoglobin*—stores oxygen in muscles
Transport proteins	Carry substances through body fluids	*Serum albumin*—carries fatty acids in blood
Structural proteins	Provide mechanical shape and support	*Collagen*—provides structure to tendons and cartilage
Protective proteins	Defend the body against foreign matter	*Immunoglobulin*—aids in destruction of invading bacteria
Contractile proteins	Do mechanical work	*Myosin and actin*—govern muscle movement

Alanine, a chiral molecule



Carbon Numbering



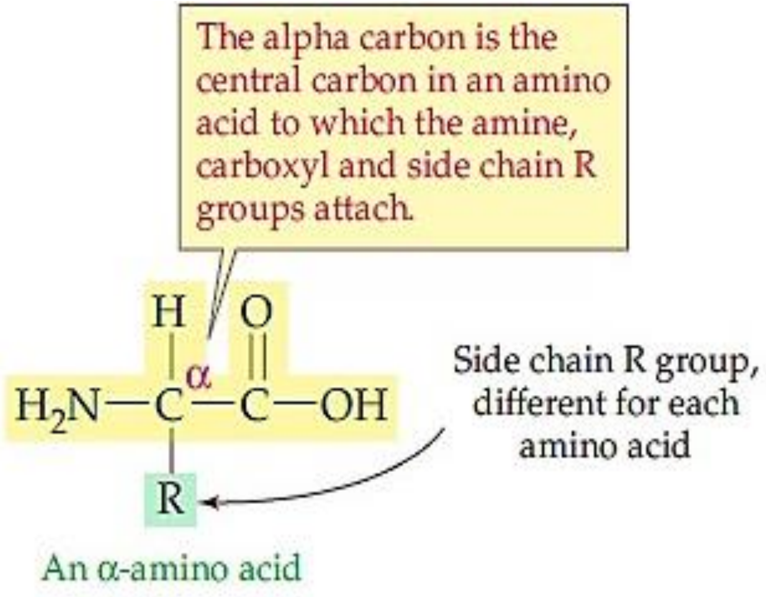
- Why it is called alpha carbon?

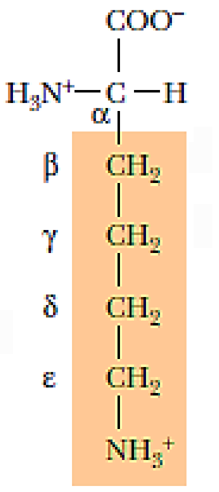
Because it is the first carbon after the carboxylic group and the numbering begin with it (alpha , beta , gama ....)

- The last carbon always can be omega.

The difference between amino acid is based on side chain

- Side chain can be Hydrogen or anything else
  - If it is hydrogen, achiral molecule will be formed like glycine
  - Otherwise, it will be chiral because the presence of four different attachments around the central carbon





- The 3 letter code depends on the first three letters of the amino acid except for (Arginine and Asparagine) and (Glutamine and Glutamic acid)

Names and codes

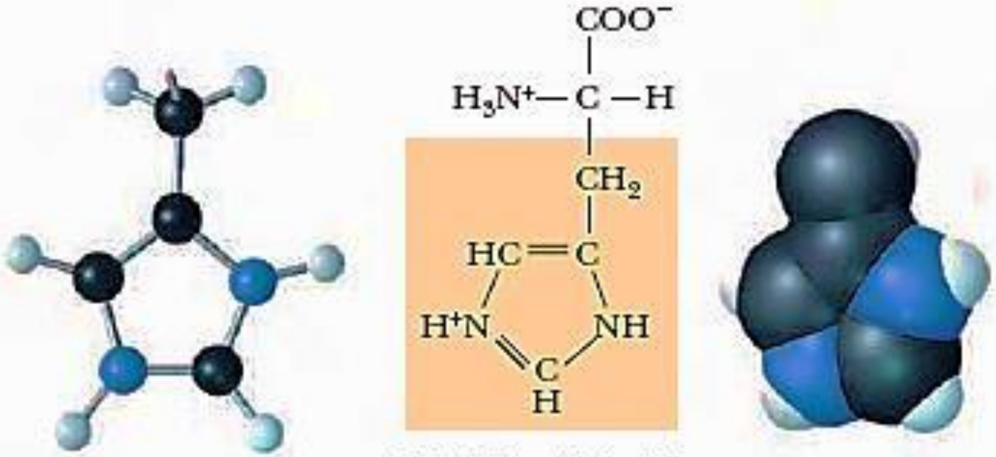
Amino Acid	3-letter code	1-letter code	Amino Acid	3-letter code	1-letter code
Alanine	Ala	A	Leucine	Leu	L
Arginine	Arg	R	Lysine	Lys	K
Asparagine	Asn	N	Methionine	Met	M
Aspartic acid	Asp	D	Phenylalanine	Phe	F
Cysteine	Cys	C	Proline	Pro	P
Glutamic acid	Glu	E	Serine	Ser	S
Glutamine	Gln	Q	Threonine	Thr	T
Glycine	Gly	G	Tryptophan	Trp	W
Histidine	His	H	Tyrosine	Tyr	Y
Isoleucine	Ile	I	Valine	Val	V

Classification (according to the polarity of R group)

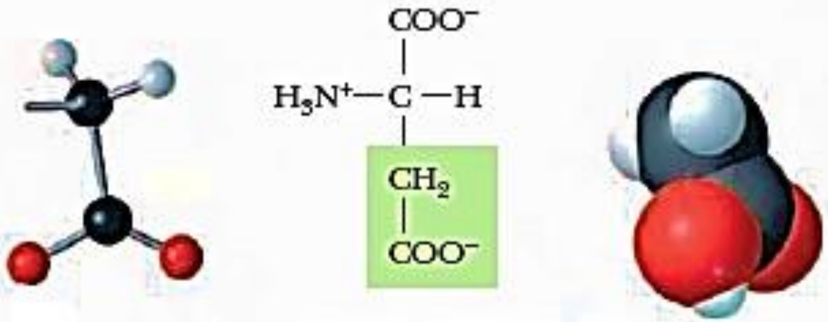
- Polar
  - Charged
  - Uncharged
- Non polar

Non-polar	Polar	Charged (positive)	Charged (negative)
Alanine	Serine	Lysine	Glutamate
Valine	Threoeine	Arginine	Aspartate
Leucine	Glutamine	Histidine	
Isoleucine	Asparagine		
Methionine	Cysteine		
Tryptophan	Tyrosine		
Phenylalanine			
Proline			
Glycine			

Polar, Charged



Histidine (His, H)



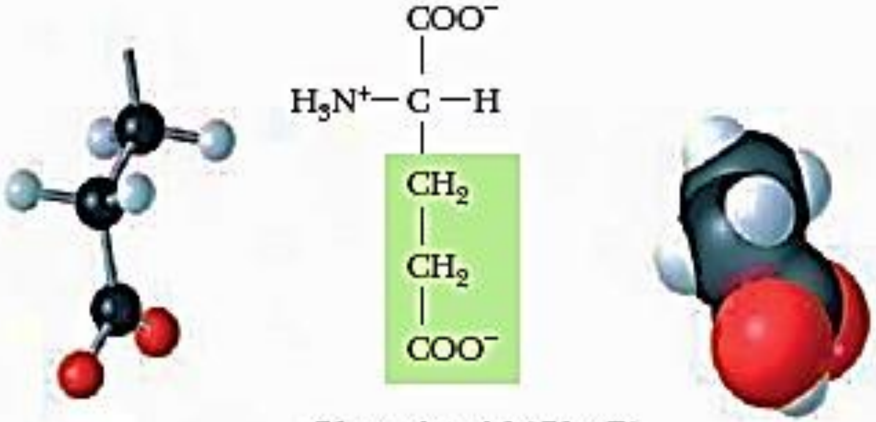
Aspartic acid (Asp, D)

This classification is based on pH = 7

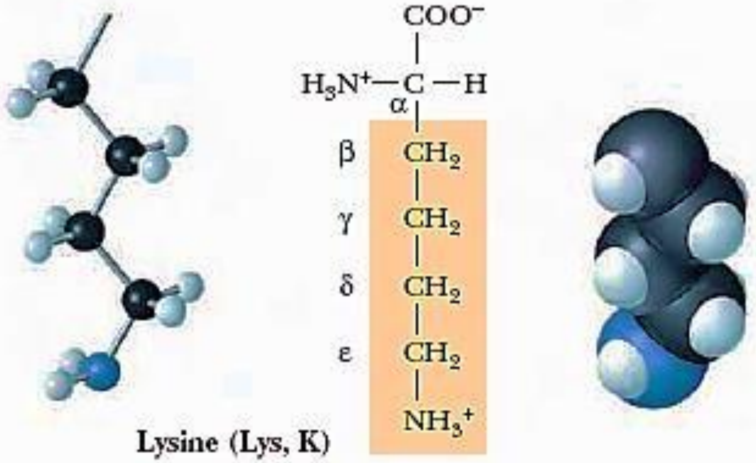
Changing pH will result in classification change

- **The charge on amino acids depends on pH.**

Arginine (Arg, R)



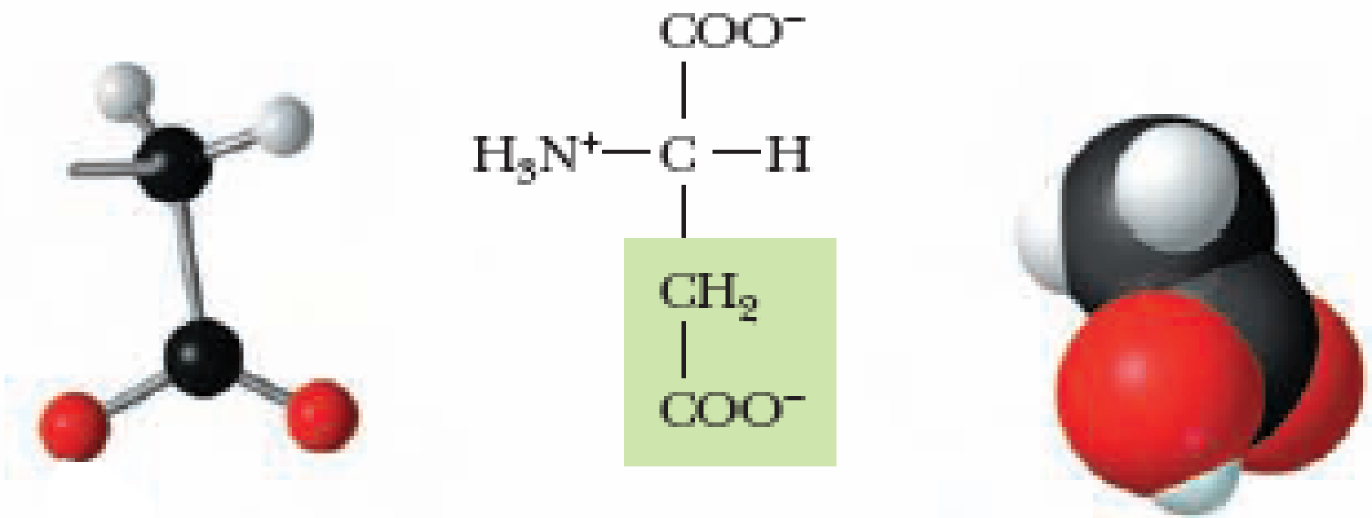
Glutamic acid (Glu, E)



Lysine (Lys, K)

Polar, Charged

(Negative, Aspartic acid)



Aspartic acid (Asp, D)

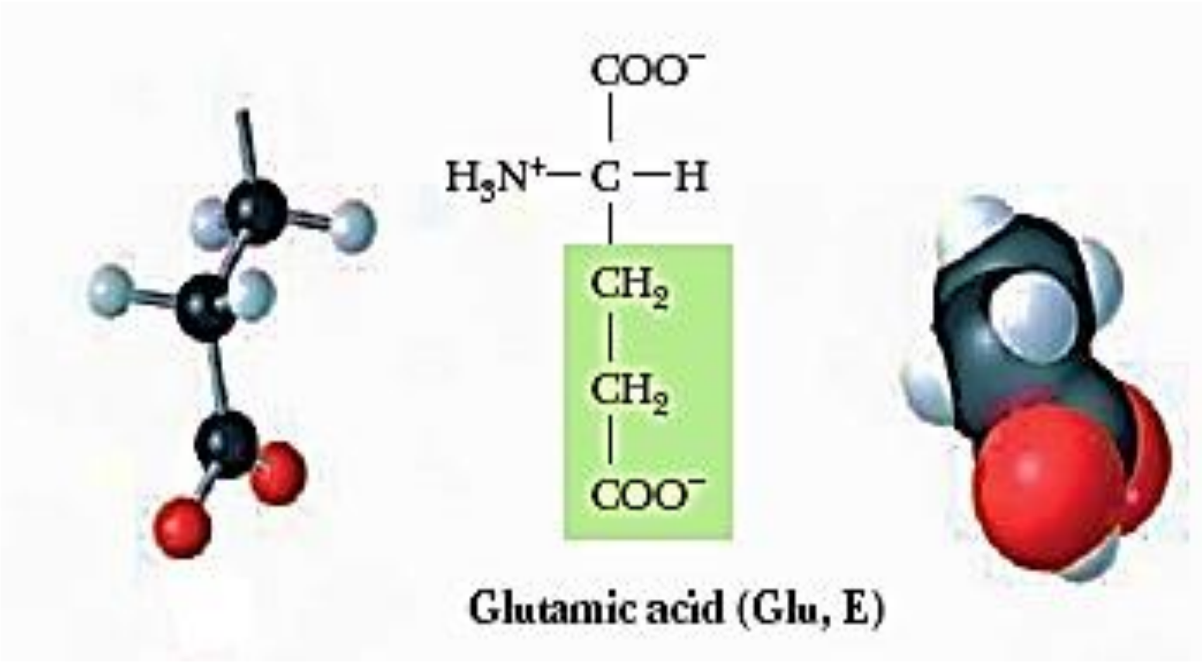
How to recognise it from

1- Name: it has “acid” in the name (Aspartate if ionised)

2- Structure: it contains carboxylic group in the side chain

Polar, Charged

(Negative Glutamic acid)

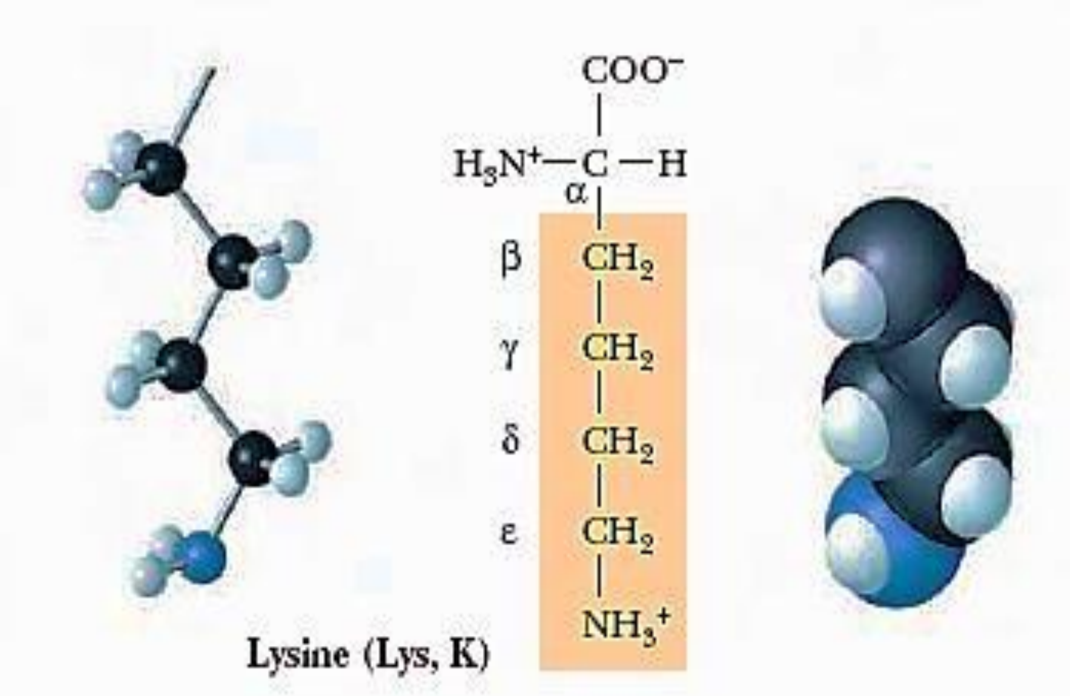


Negatively charged

- One more carbon than aspartic acid
- Aspartic acid is smaller than Glutamic acid

Polar, Charged

(Positive Lysine)

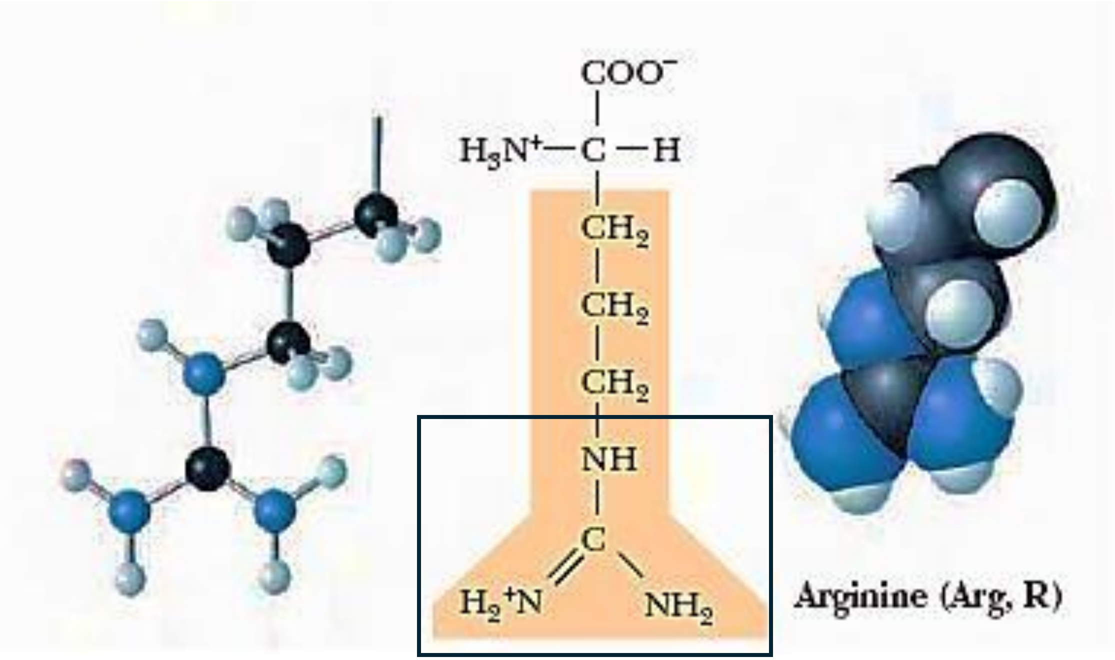


Straight line of carbon followed by amino group

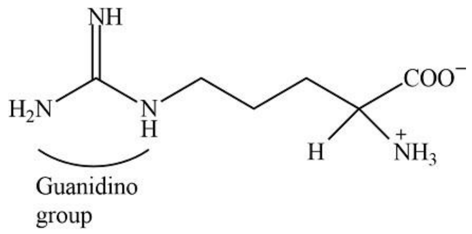
Polar, Charged

(Positive Arginine)

What is special about arginine is that it contains guanidino group, which can make resonance

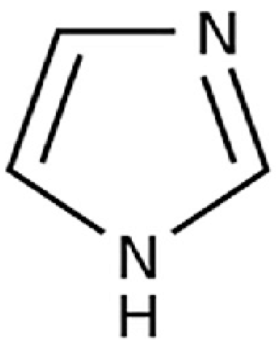


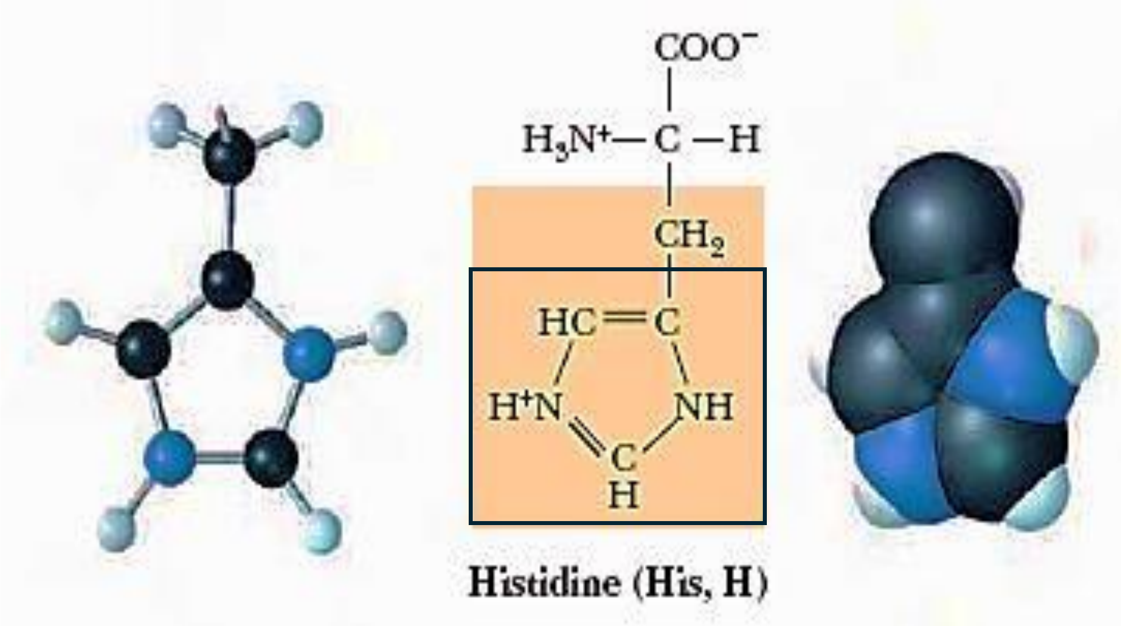
Guanidino group



Arginine

Polar, Charged
(Positive Histidine)



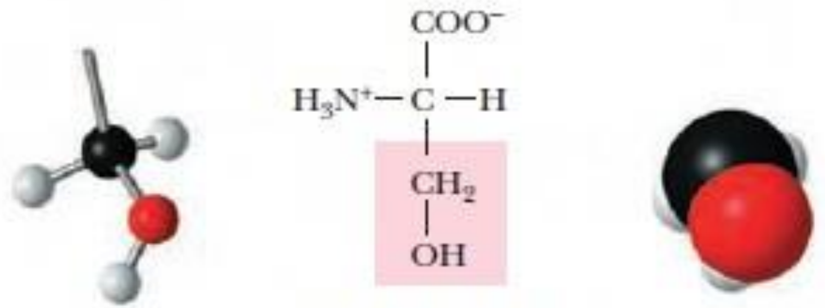


Imidazole group

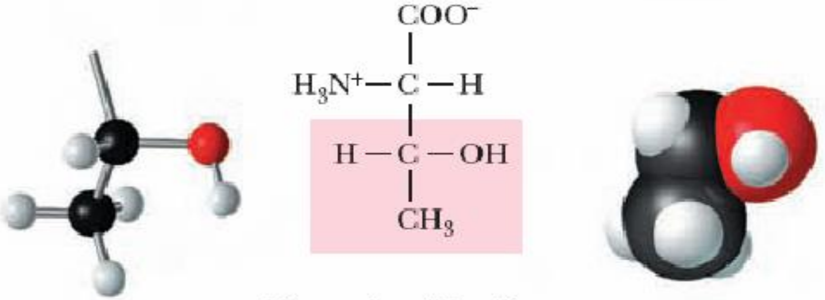
What is special about histidine is the five membered ring

Polar, Uncharged

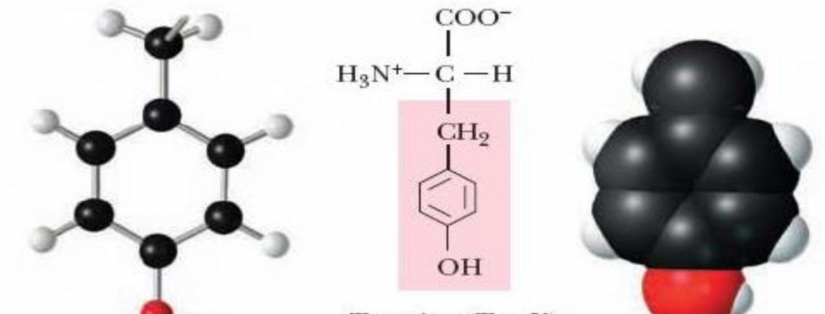
What creates polarity in side chains
Oxygen , Nitrogen and Sulfur



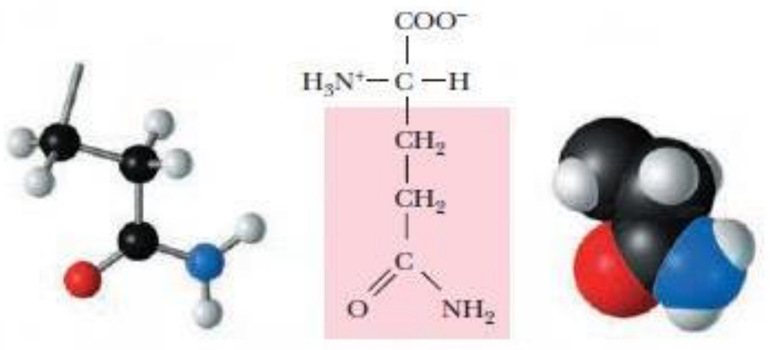
Serine (Ser, S)



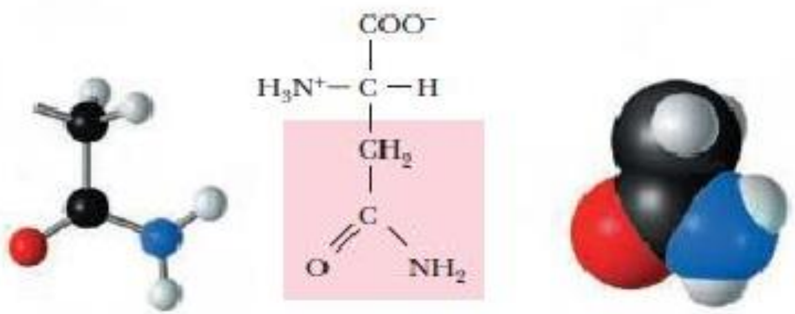
Threonine (Thr, T)



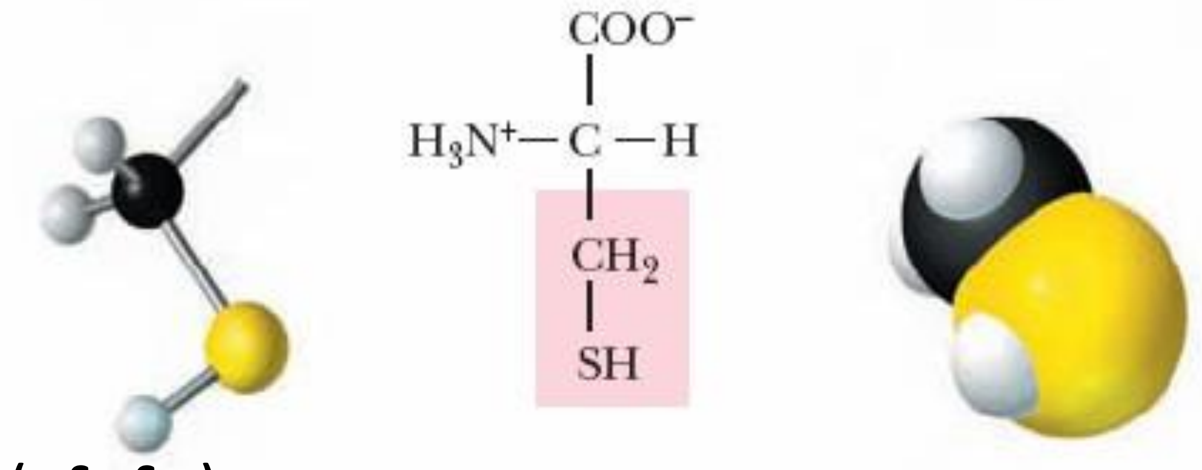
Tyrosine (Tyr, Y)



Glutamine (Gln, Q)



Asparagine (Asn, N)



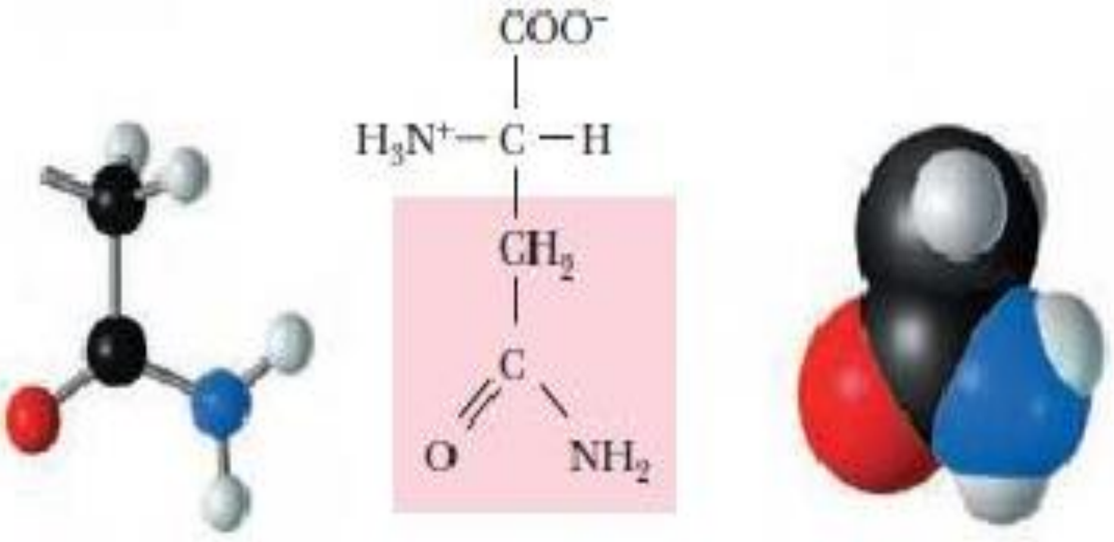
(—S—S—)

Cysteine (Cys, C)

Polar, Uncharged (Asparagine)

- OH is the responsible for the acidity in COOH
- H+ has left.
- Removing of O- from aspartic acid will result in the loss of acidity and forming of carbonyl group.
- Carbonyl group won't be stable, so it will bind to:
  - 2 carbons to form ketone
  - Hydrogen to form aldehyde
  - OH to form carboxylic acid
  - **Nitrogen to form amide group as in asparagine**

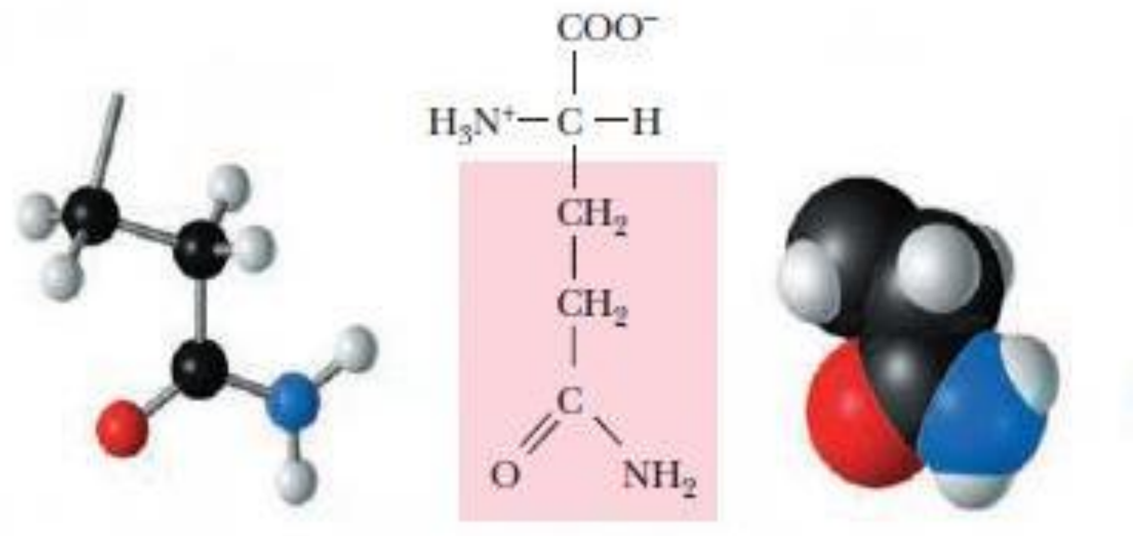
We can synthesize asparagine from aspartic acid in our bodies in an amidation reaction



Asparagine (Asn, N)

Polar, Uncharged (Glutamine)

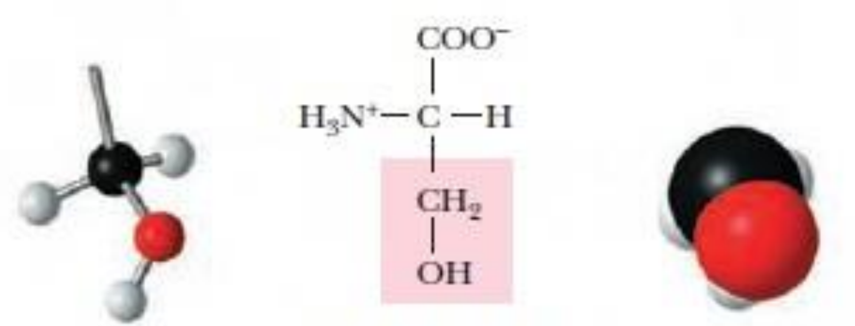
Same as asparagine



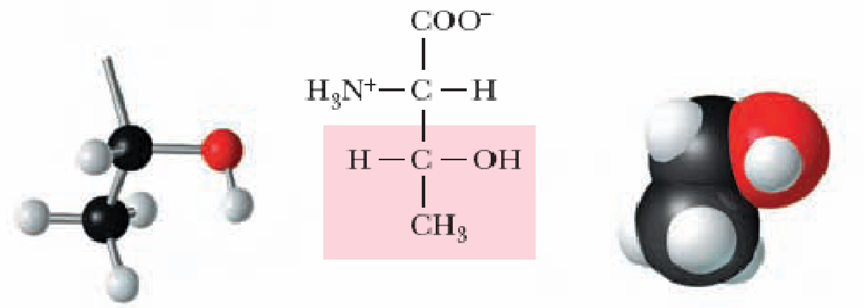
Glutamine (Gln, Q)

Polar, Uncharged

(End with OH
Serine , Threonine and Tyrosine)

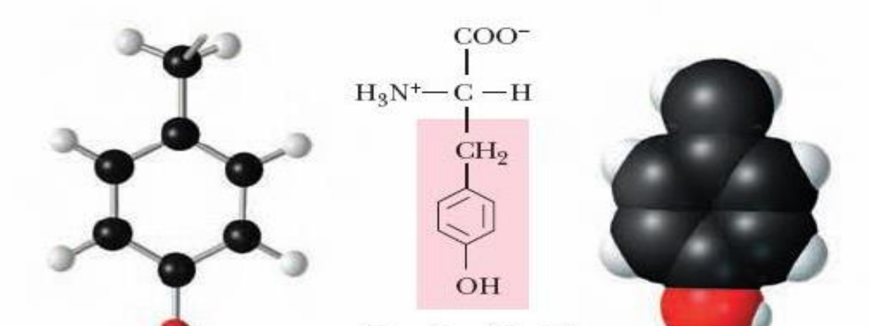


Serine (Ser, S)



Threonine (Thr, T)

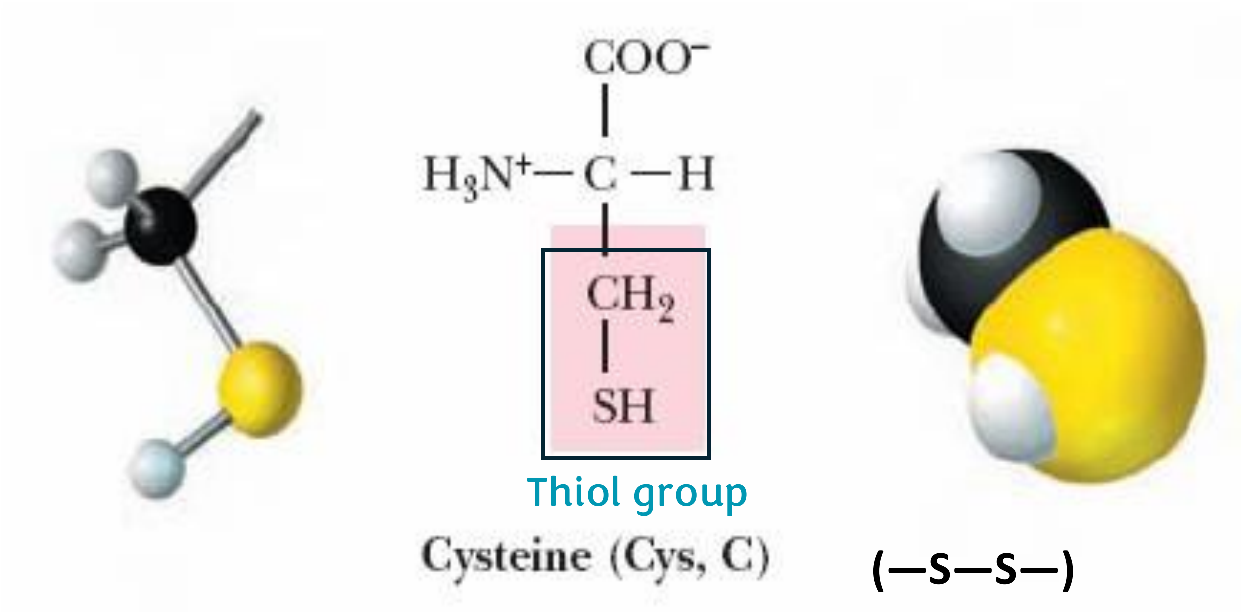
- It pairs phenyl group which is benzene ring
- Benzene ring alone is non polar
- But with binding to OH it becomes polar



Tyrosine (Tyr, Y)

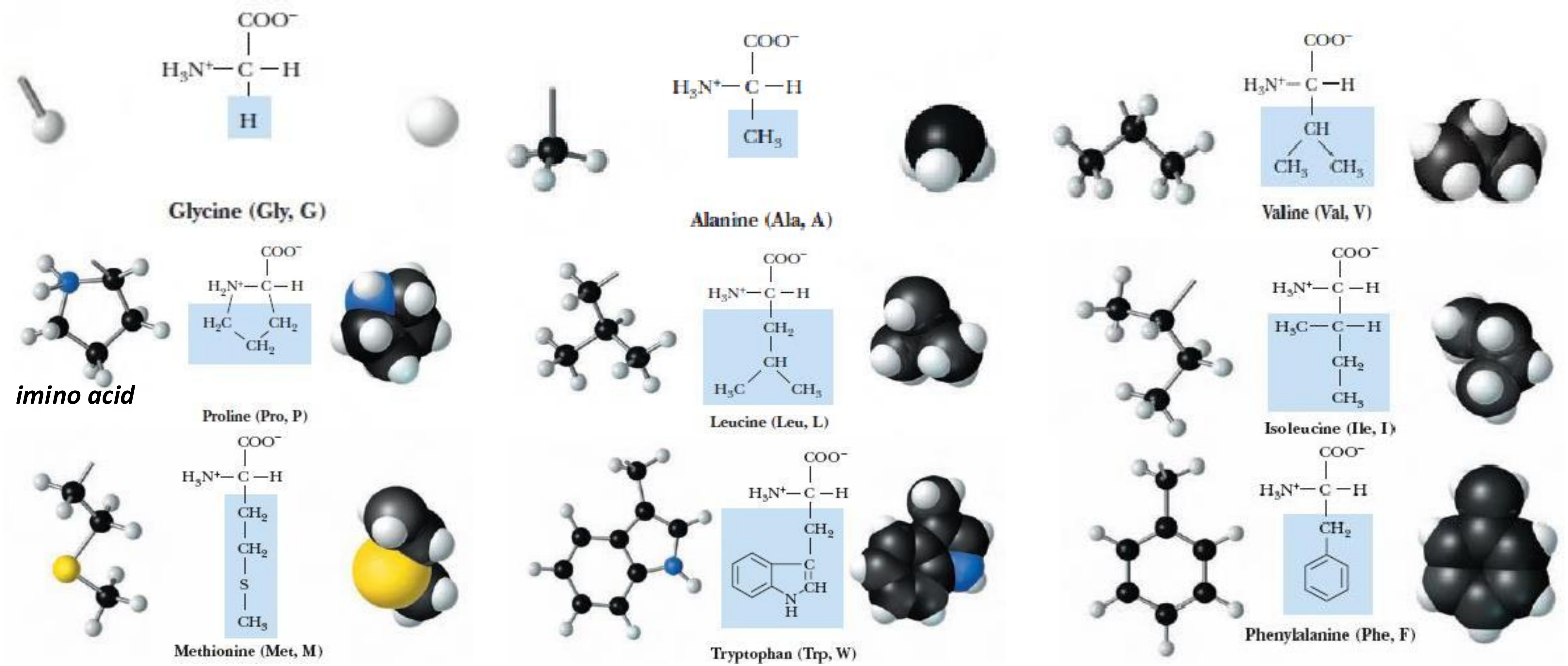
Polar, Uncharged
(Cysteine)

- It has thiol group which is a peripheral sulfhydryl group
- It is important in the tertiary structure of protein
- 2 cysteine can make a bond by leaving of the 2 hydrogen which make the sulfur very reactive
- They will form disulfide bond or disulfide bridge



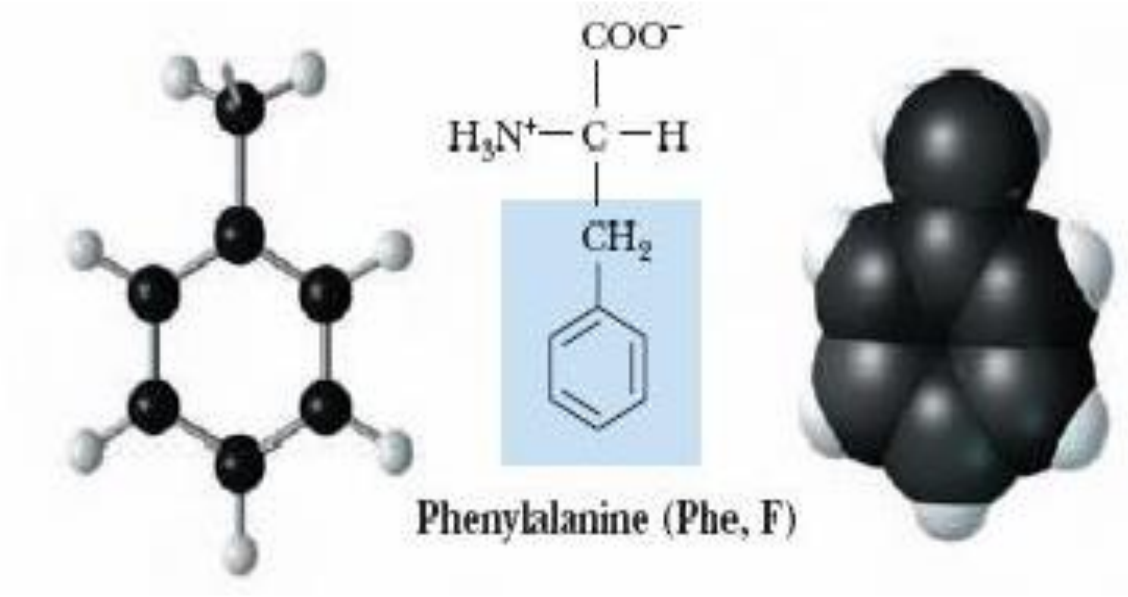
- These bonds are represented in proteins in different numbers
- It is very important for proteins binding to be tight and not loose and to be specific as in antibodies and antigens

Non-polar, Uncharged



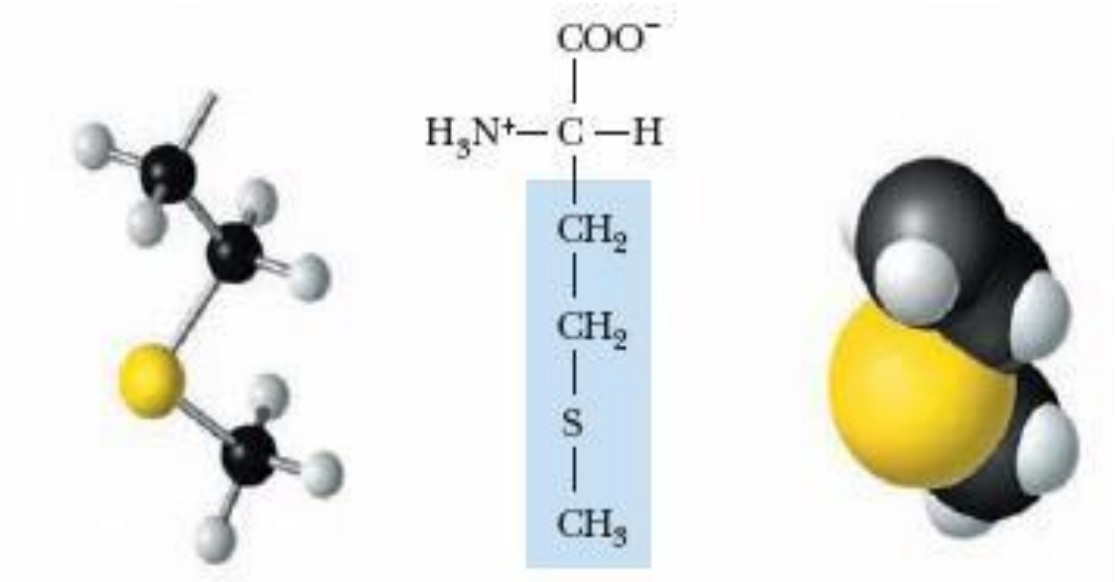
Non-polar, Uncharged (Phenylalanine)

- Removing OH group from tyrosine will give us phenylalanine
- It is named alanine because removing of phenyl group will result in alanine



Non-polar, Uncharged
(Methionine)

- It is different from cysteine by having a Sulfur attached to two sides of carbon

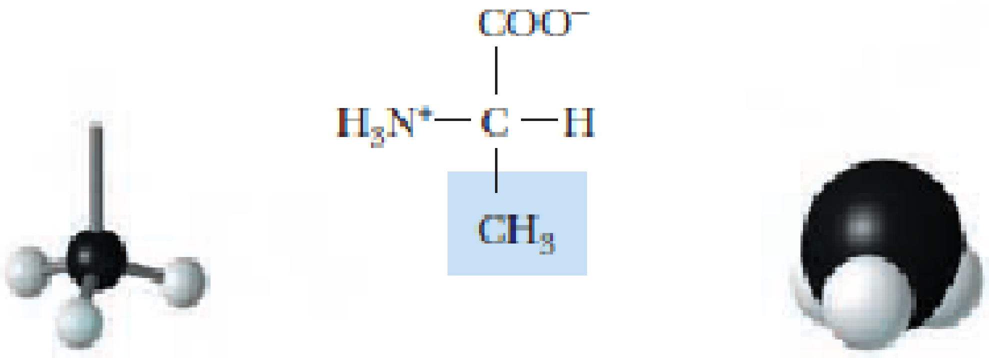


Methionine (Met, M)

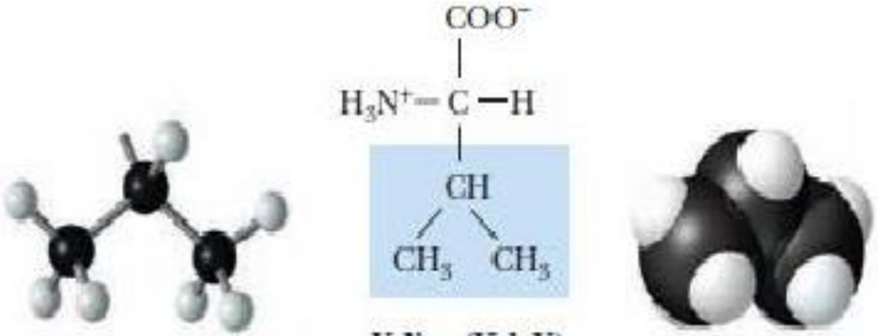
- Not required to differentiate between leucine and isoleucine
- Valine , Leucine and Isoleucine are branched amino acids

Non-polar, Uncharged

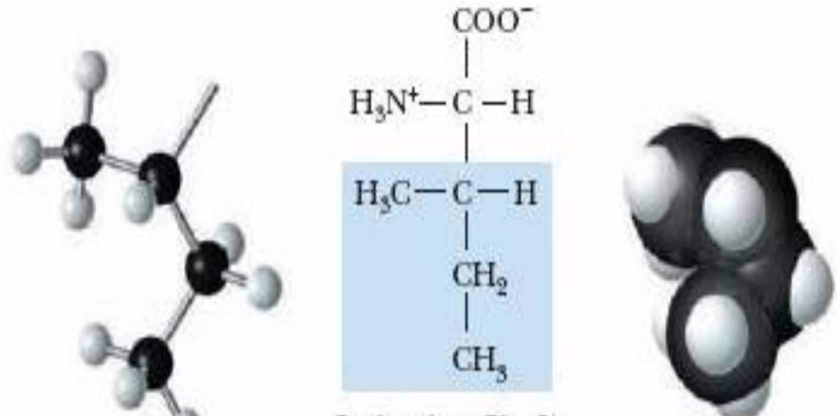
(Alanine , Valine , Leucine and Isoleucine)



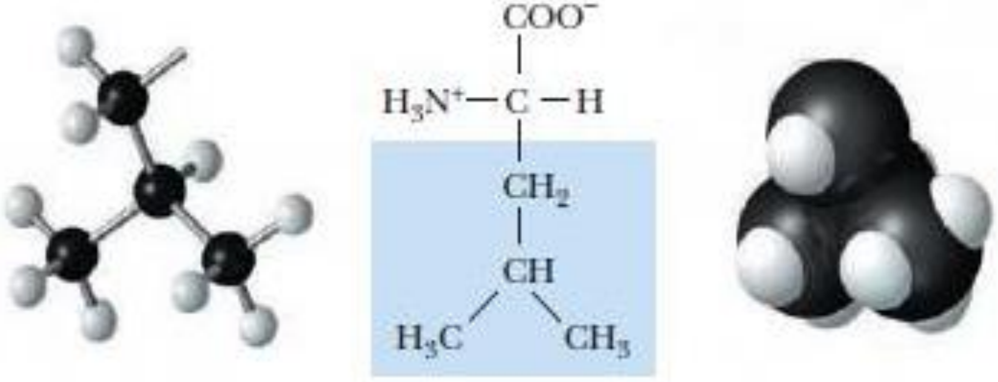
Alanine (Ala, A)



Valine (Val, V)

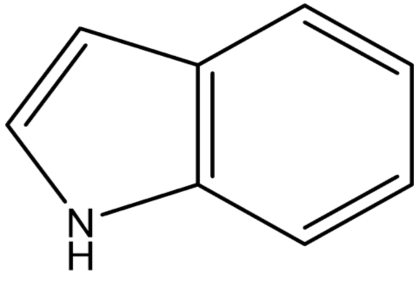


Isoleucine (Ile, I)



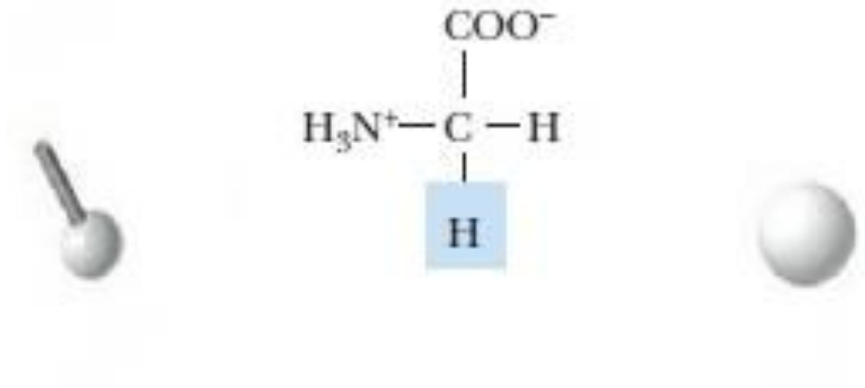
Leucine (Leu, L)

Non-polar, Uncharged
(Glycine and Tryptophan)



Indole

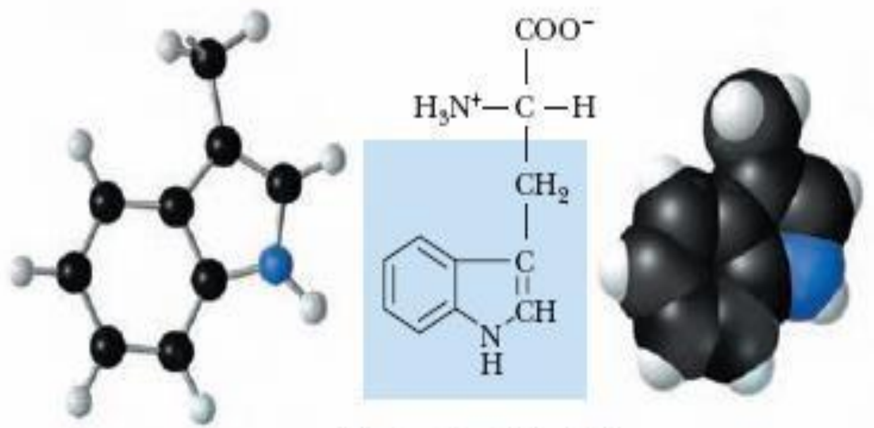
- The simplest amino acid
- Achiral



Glycine (Gly, G)

- The largest and bulkiest amino acid
- How to know that it is the biggest amino acid?

It contains Indole ring (5 membered and 6 membered rings)

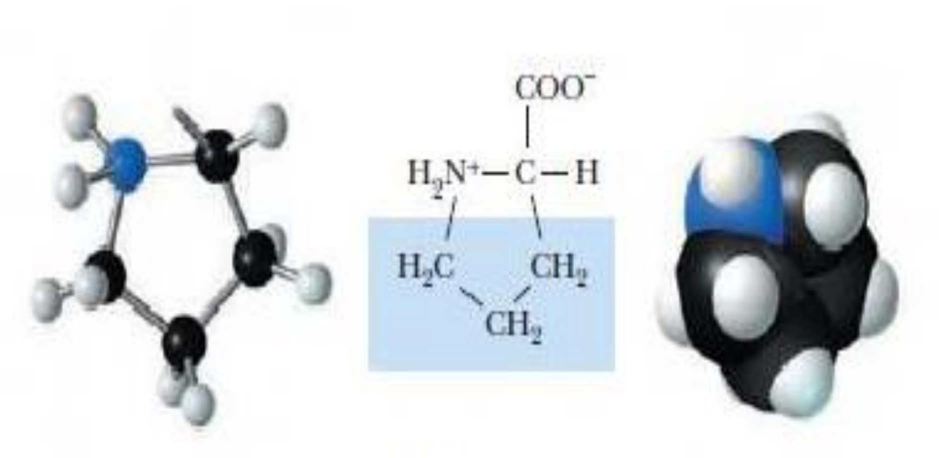


Tryptophan (Trp, W)

Non-polar, Uncharged (Proline)

- Why it is called imino acid?

Because the nitrogen in its backbone forms a cycle with side chain which forms secondary nitrogen

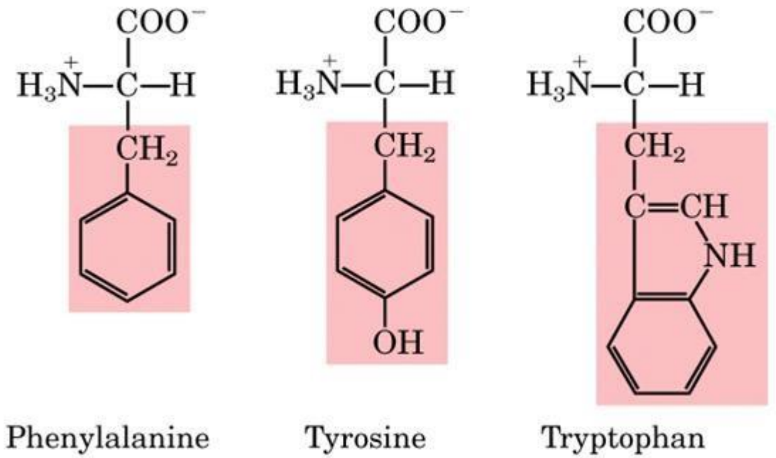


imino acid Proline (Pro, P)

- Clinical relevance:
  - It is no longer a site for hydrogen bonding
  - It produces kinks
  - It is found in turns in proteins unless it interrupts a regular sequence like in secondary structures, it disrupts their regularity

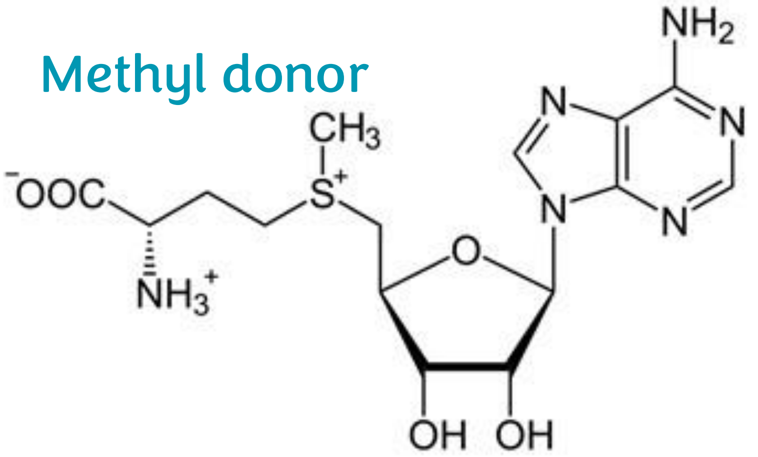
Important notes

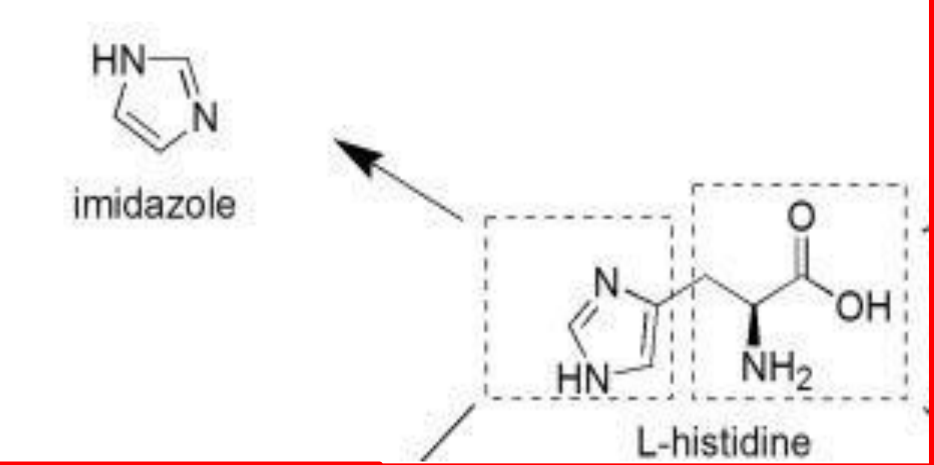
Aromatic amino acids



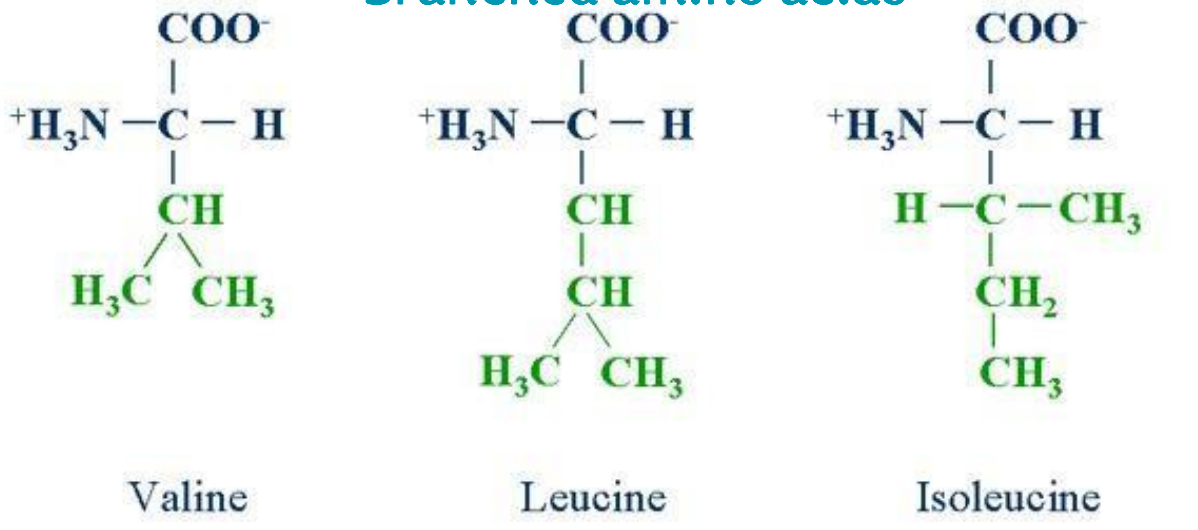
SAM (S Adenosyl Methionine)

Methyl donor

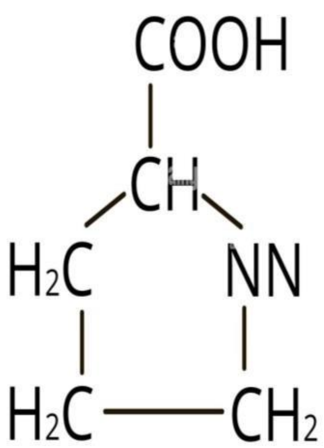


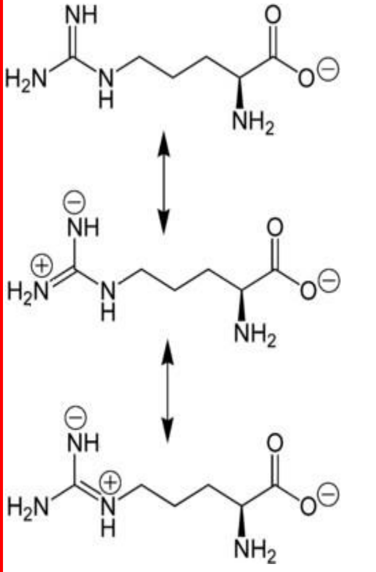


Branched amino acids



Proline

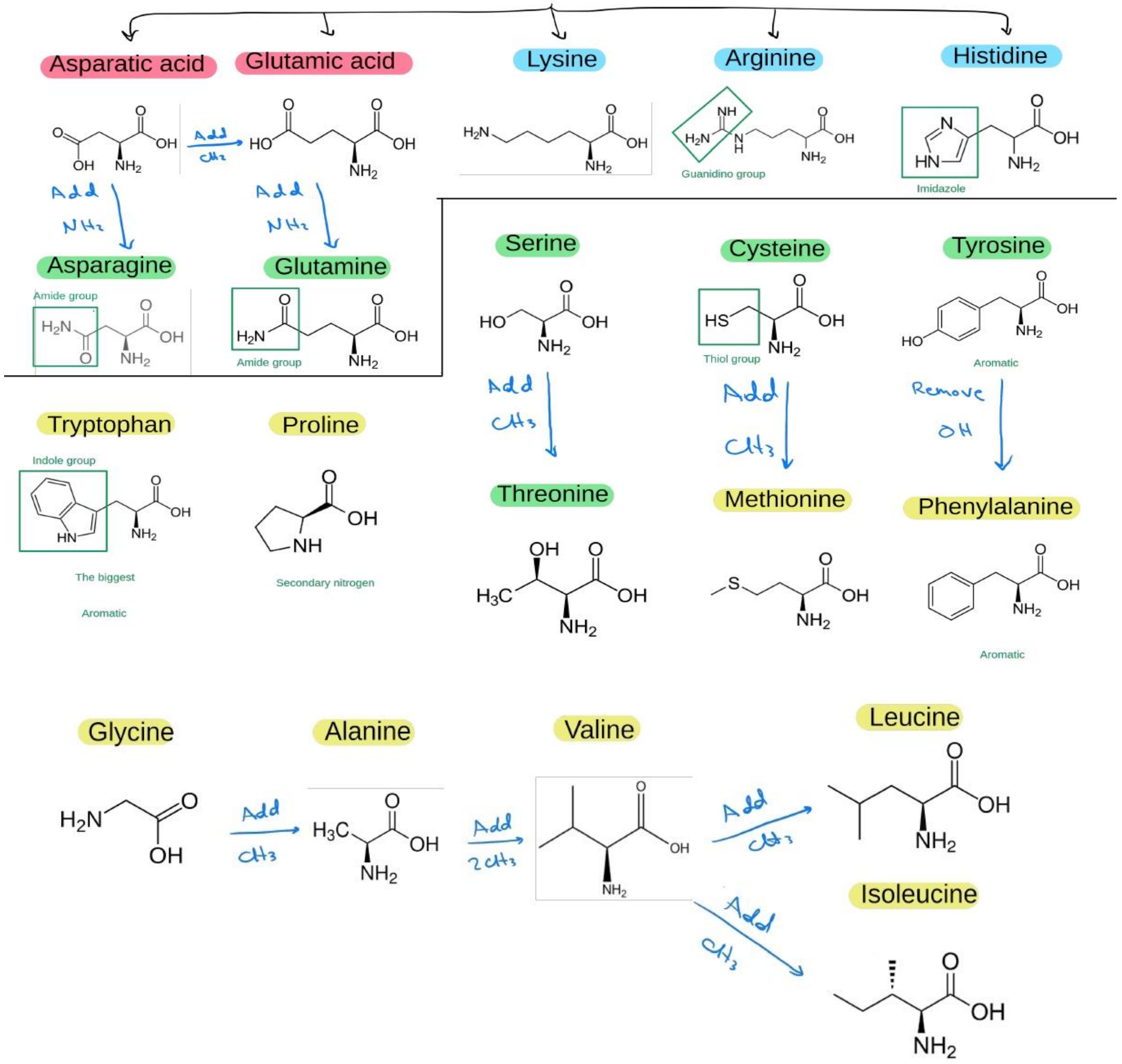




Body deals with them in the same way metabolically

Amino Acids

Polar, charged (acid)
Polar, charged (basic)
Polar, uncharged
non polar



Titration Of Amino Acids

- What is Titration?

Titration is the process where a charge equalizes another charge

- All 20 amino acids share a carboxylic and an amine group on their backbone, both of which are ionizable.
- What determines whether the carboxylic group and amine group are ionized is:

1. Their pKa value
2. The pH of the solution

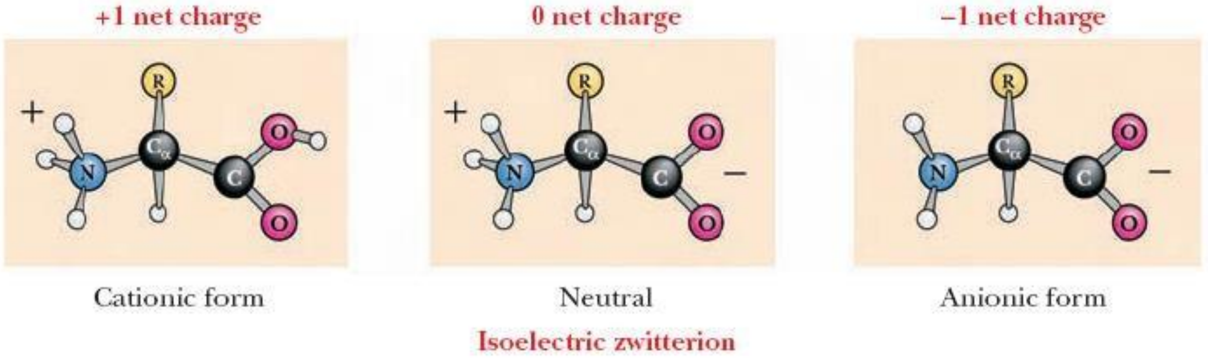
- When increasing the pH value, the carboxylic group ionizes first and then the amine group, (i.e. Carboxylic group donates its proton at a lower pH value than the amine group). This is because carboxylic group is acidic and amine group is basic
- In 7 of the 20 amino acids, the side chain also plays a role in the ionization process. (including the 5 charged amino acids).
- The pKa value of the carboxylic group in the **backbones** of all 20 amino acids is almost 2. While the pKa value of the amine group in the **backbones** of all 20 amino acids is almost 9. (For the sake of the exam, we consider them exactly 2 and 9 respectively).

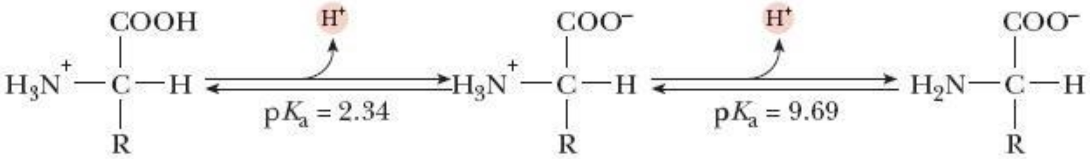
Titration Of Amino Acids

- At pH=2, 50% of carboxylic acids of the backbones are in the ionized form (deprotonated) (COO-) and 50% are not ionized (protonated) (COOH). At pH levels below 2, most carboxylic groups are **protonated** (COOH) , so it contributes to **neutral** charge, at pH levels above 2, most carboxylic groups are **deprotonated** (COO-), so it contributes to **-1** charge.
- At pH=9, 50% of amine groups of the backbones are in the ionized form (protonated) (NH3+) and 50% are not ionized (deprotonated) (NH2). At pH levels below 9, most amine groups are **protonated** (NH3+) , so it contributes to **+1** charge, at pH levels above 9, most amine groups are **deprotonated** (NH2), so it contributes to **neutral** charge.
- For example: What is the total charge of the amino acid at pH=13: Carboxylic group is deprotonated (hence it contributes to -1 charge). Amine group is deprotonated (hence it contributes to neutral charge). So total charge is -1.
- Note: in the above example we didn't consider the charge of the side chain, which is correct for 15 of the 20 amino acids(i.e. the uncharged amino acids). The other 5 amino acids, we need to consider the pKa of the side chains as well (i.e. the charged amino acids, which are: Aspartic acid, Glutamic acid, Lycine, Arginine, Histidine)
- For Aspartic acid and Glutamic acid, the pKa of the carboxylic acid in side chain is 4. At pH levels below 4, most carboxylic groups are protonated (COOH) , so it contributes to neutral charge, at pH levels above 4, most carboxylic groups are deprotonated (COO-), so it contributes to -1 charge.
- For example: what is the total charge of Aspartic acid at pH=6: Carboxylic group of the backbone is deprotonated (hence it contributes to -1 charge). Amine group of the backbone is protonated (hence it contributes to +1 charge). While the Carboxylic group of the **side chain** is also deprotonated, (so it contributes to -1 charge) So total charge is -1.

Titration of amino acids: what is an isoelecrtic point (pI)?

Isoelectric point is a state when an amino acid is titrated until the total charge of this amino acid is zero

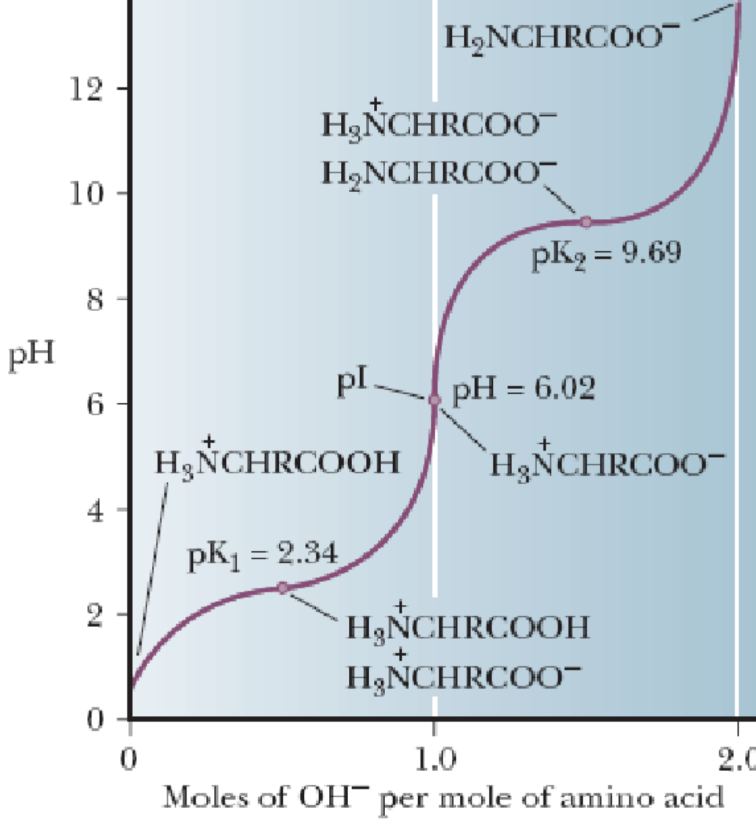


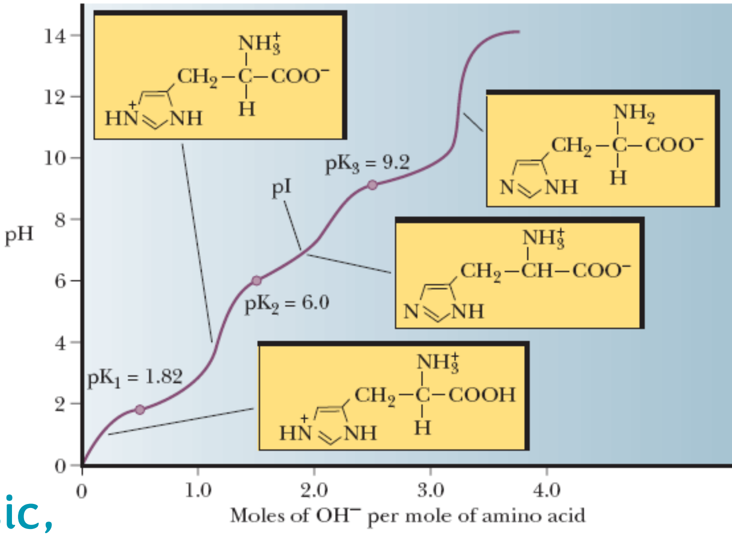


Zwitterion form

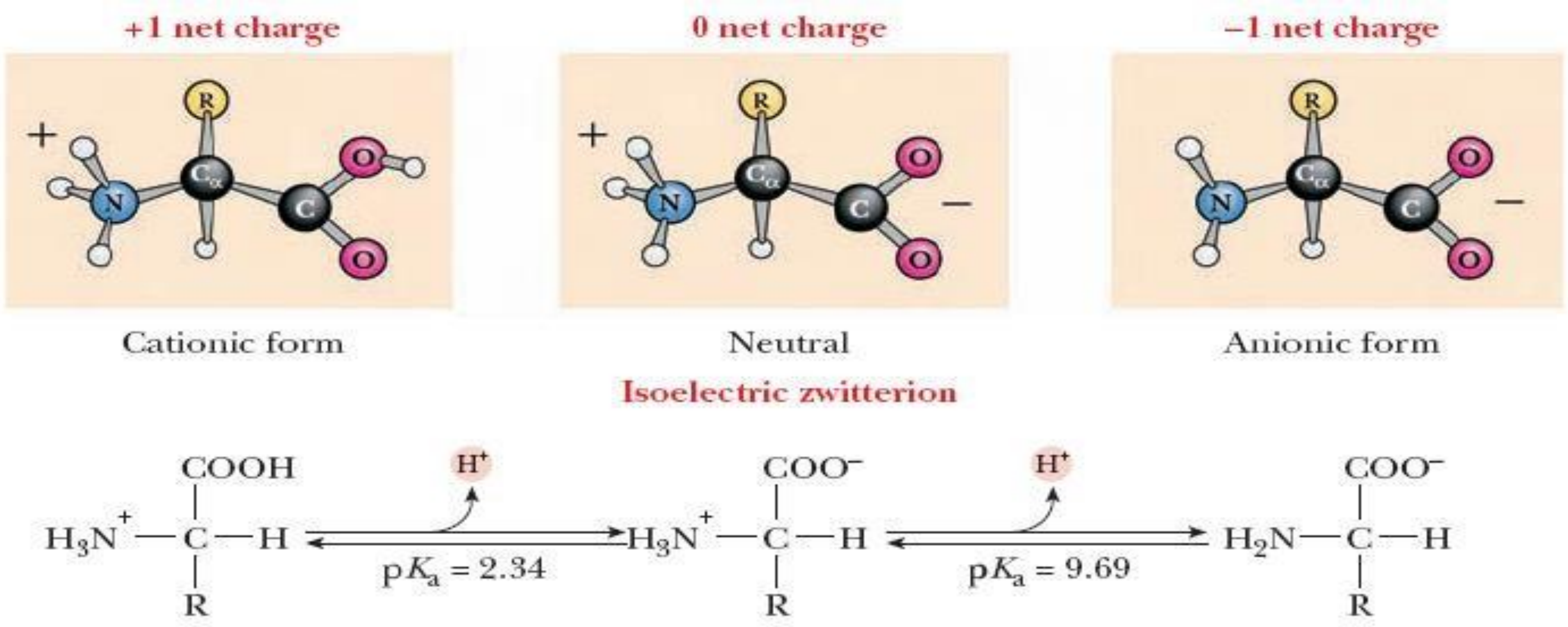
$$pI = \frac{pK_{a1} + pK_{a2}}{2}$$

- In order to calculate isoelectric point we use this formula. Which means that for 15 of the 20 amino acids (the uncharged amino acids), the pI value is 5.5. (2+9)/2. → at pH =5.5, total charge is zero.
- While for the charged amino acids, We need to look at their structure.
- For Lysine, the pKa of the amine group in the side chain is around 10
- For Arginine, the pKa of the amine group in the side chain is around 12
- For Histidine, the pKa of the amine group in the side chain is 6 although it is basic, so it is very close to the physiological pH, making it physiologically crucial

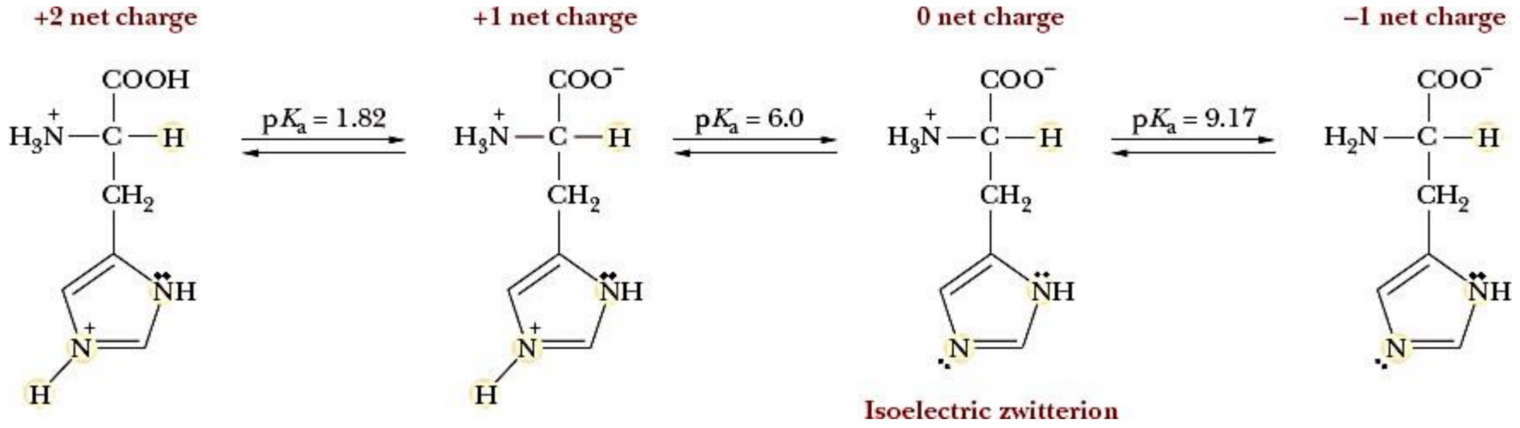


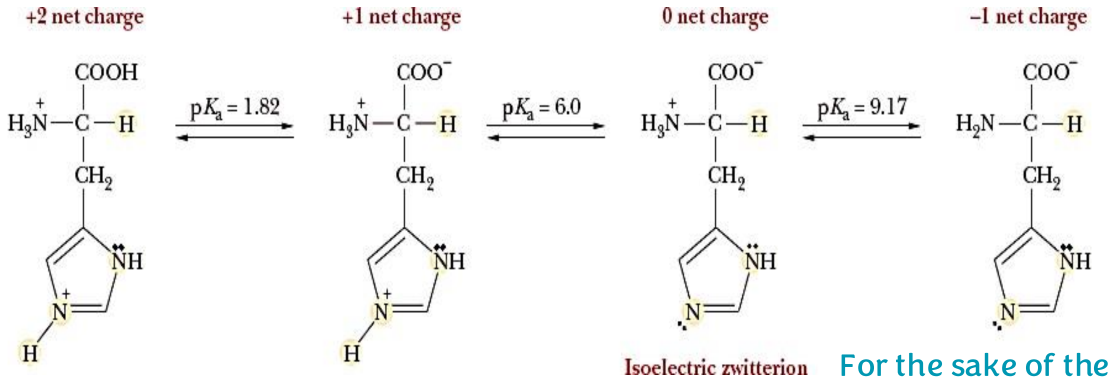


- In order to calculate the isoelectric point of an amino acid, we need to look at the zwitterion form.
- Zwitterion form is when a molecule has a total charge of zero
- For the uncharged amino acids that only have 2 ionizable groups, as pH increases and crosses the first pKa value (2), the carboxylic group loses its proton. When pH crosses the second pKa value (9), the amine group loses its proton. Hence the zwitterion form for uncharged amino acids is when pH is between the 2 pKa values (between 2 and 9). That's how we got the isoelectric point formula, since net charge is zero In the zwitterion form.



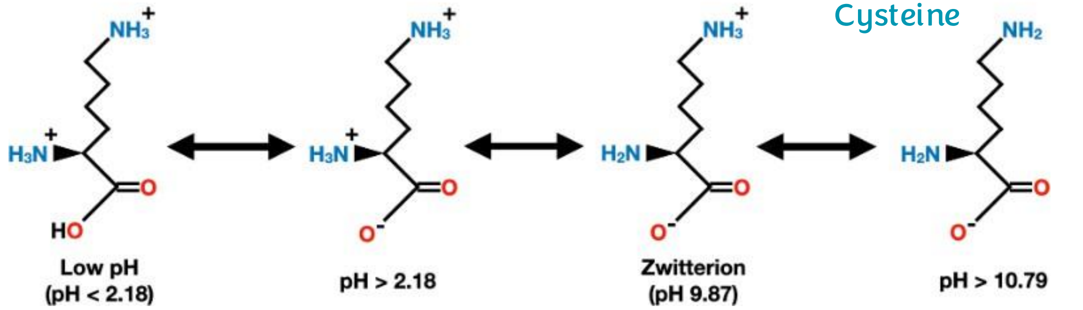
- For charged amino acids that have 3 ionizable groups(we have 3 pKa values) we need to look at them:
- For example: Histidine: when pH is below 2, Carboxylic group is neutral, amine of the backbone and the amine of the side chain are positive. Total charge is +2. As pH increases and we cross the first pKa value, carboxylic group donates its proton and becomes negative. Total charge becomes +1. When we cross the second pKa value (at pH =6), the amine group of the side chain loses its proton and becomes neutral, so total charge is zero, so this is the zwitterion form. In order to calculate the isoelectric point, we know it is between the second and third pKa values, so we calculate their average,(6+9)/2 =7.5. When we cross the third pKa value, total charge becomes -1. You can use the same method to find the isoelectric point of the rest of the charged amino acids.



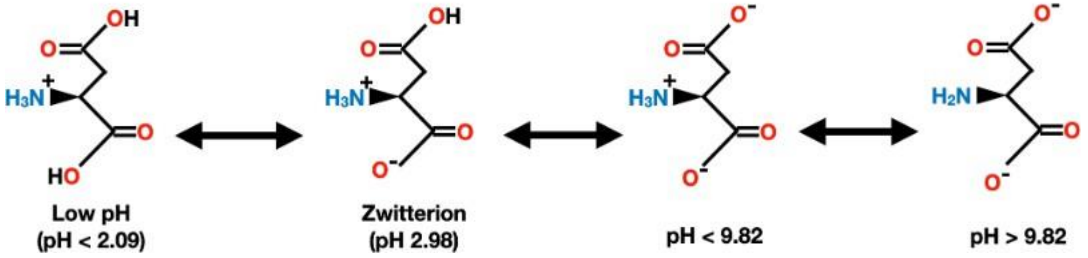


For the sake of the exam, ignore the pKa value of the side chains for Tyrosine and Cysteine

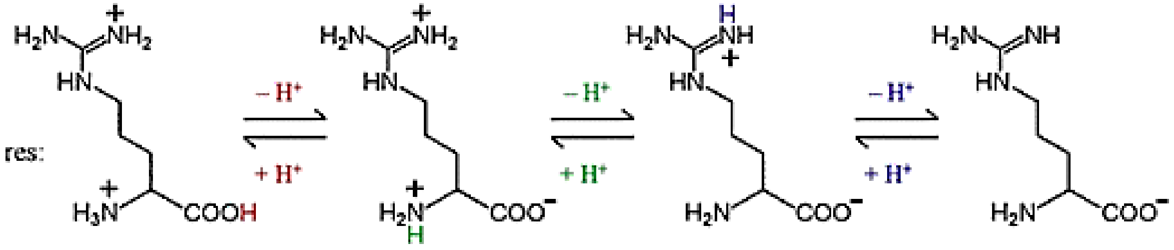
Lysine as a Zwitterion



Aspartic Acid as a Zwitterion



Amino Acid	Abbreviation 3-Letters	Abbreviation 1-Letter	pK1 -COOH	pK2 $-NH_3^+$	pKR R group	pI
Alanine	Ala	A	2.34	9.69	-	6.00
Arginine	Arg	R	2.17	9.04	12.48	10.76
Asparagine	Asn	N	2.02	8.80	-	5.41
Aspartic Acid	Asp	D	1.88	9.60	3.65	2.77
Cysteine	Cys	C	1.96	10.128	8.18	5.07
Glutamic Acid	Glu	E	2.19	9.67	4.25	3.22
Glutamine	Gln	Q	2.17	9.13	-	5.65
Glycine	Gly	G	2.34	9.60	-	5.97
Histidine	His	H	1.82	9.17	6.00	7.59
Isoleucine	Ile	I	2.36	9.60	-	6.02
Leucine	Leu	L	2.36	9.60	-	5.98
Lysine	Lys	K	2.18	8.95	10.53	9.74
Methionine	Met	M	2.28	9.21	-	5.74
Phenylalanine	Phe	F	1.83	9.13	-	5.48
Proline	Pro	P	1.99	10.60	-	6.30
Serine	Ser	S	2.21	9.15	-	5.58
Threonine	Thr	T	2.09	9.10	-	5.60
Tryptophan	Trp	W	2.83	9.39	-	5.89
Tyrosine	Tyr	Y	2.20	9.11	10.07	5.66
Valine	Val	V	2.32	9.62	-	5.96

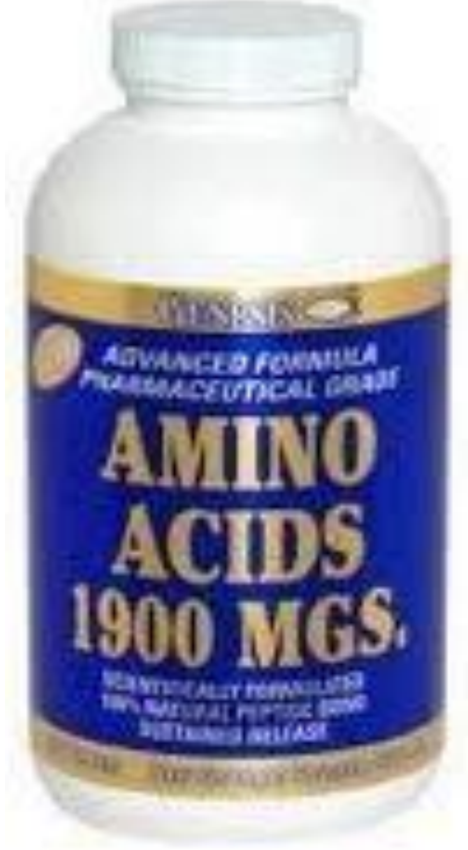


Is it the same in proteins? No

Dissociating Group	pK_a Range
α-Carboxyl	3.5-4.0
Non-α COOH of Asp or Glu	4.0-4.8
Imidazole of His	6.5-7.4
SH of Cys	8.5-9.0
OH of Tyr	9.5-10.5
α-Amino	8.0-9.0
e-Amino of Lys	9.8-10.4
Guanidinium of Arg	~12.0

- When an amino acid is free in solution, it can donate its proton freely at a certain pH value (pKa value), but when it is bound to other amino acids, the power of donating Is proton changes. For example, the pKa of the alpha carboxylic group is 3.5-4 in proteins, although it was initially 2 in amino acids, and the amine group is 8-9 in proteins, although it was initially 9. This means both carboxylic group and amine group are getting closer to the physiological pH of our body
- The imidazole of histamine in proteins became very close to the physiological conditions of our bodies. That's why hemoglobin that contains histamine works as a buffer in the blood.

Amino Acids & life



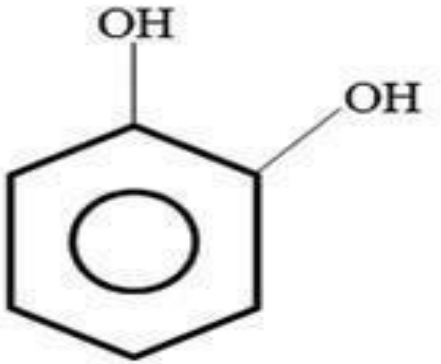
Posttranslational modification of Amino Acids

Proteins we eat gets degraded in the GI tract into amino acids, dipeptides and tripeptides. At the level of intestines, dipeptides and tripeptides also get digested into free amino acids. So only free amino acids reach the blood. Amino acids can be modified by the following reactions

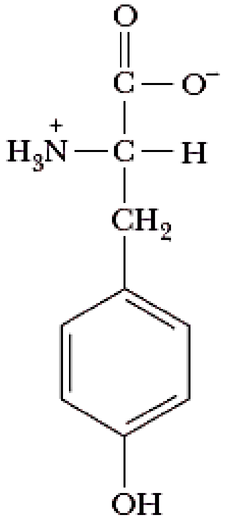
- Hydroxylation (-OH)
- Carboxylation (-COOH)
- Methylation ($-CH_3$)
- Formylation (-CH=O)
- Acetylation (CH_3CO)
- Phosphorylation ($-PO_3^{2-}$)

- These modifications significantly extend the biologic diversity of proteins by altering their solubility, stability, catalytic activity, and interaction with other proteins

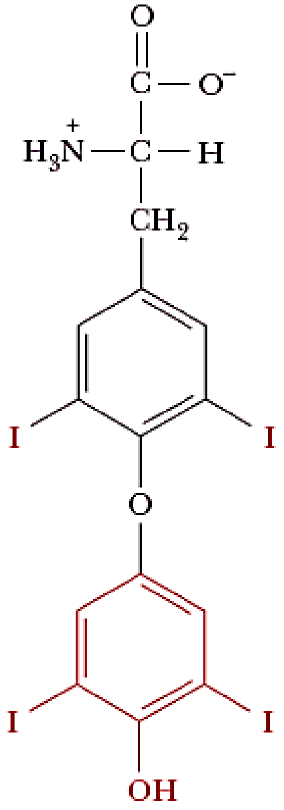
Tyrosine



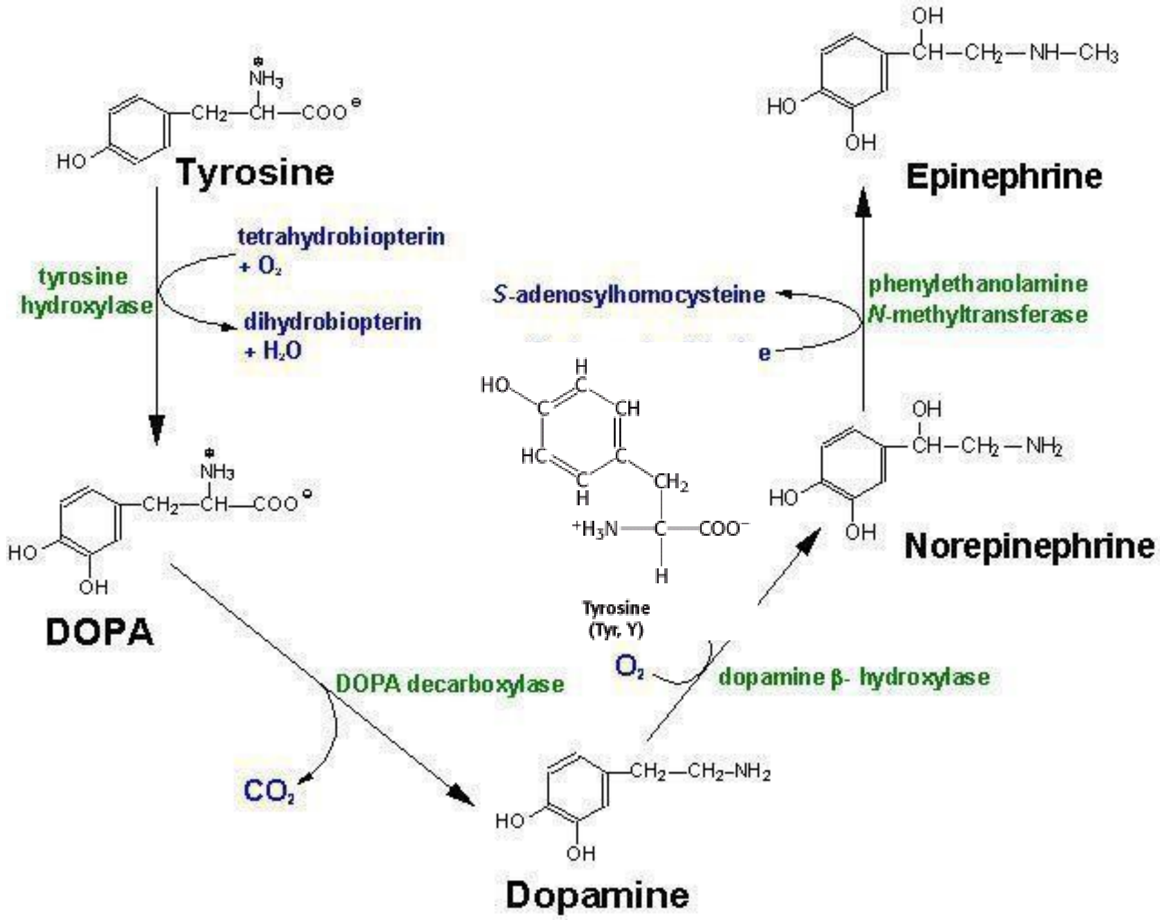
catechol

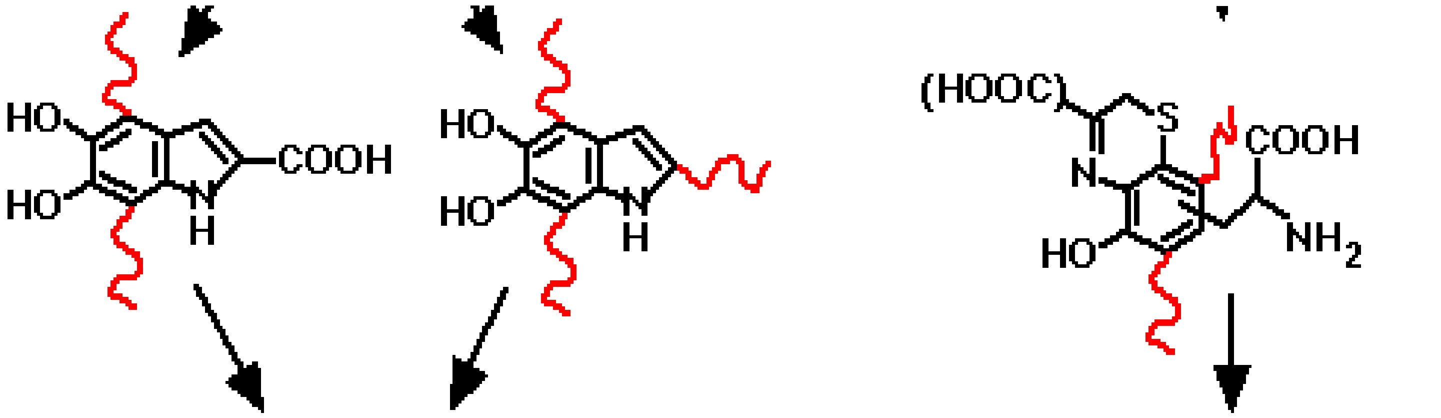


Tyrosine



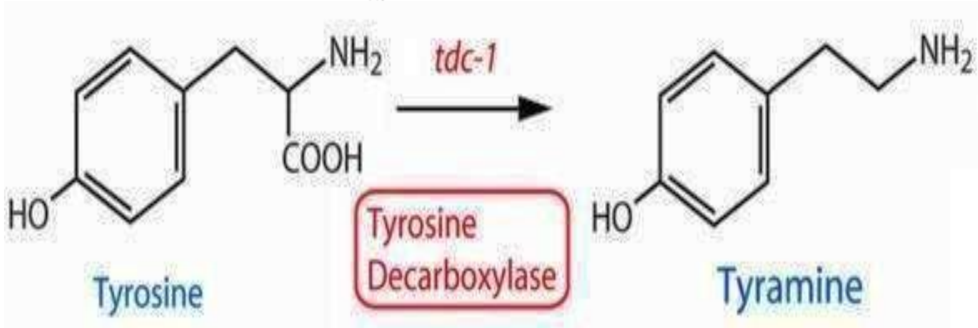
Thyroxine





EUMELANINS

PHEOMELANINS



Tyrosine

Tyrosine has a benzene ring connected to a hydroxyl group in its side chain.

- If we add another benzene ring connected to a hydroxyl group and then iodinated it, we will get the thyroid hormones, if we add 3 iodines → T3. If we add 4 iodines→T4
- Tyrosine itself is not essential, I can be synthesized from the essential amino acid (phenylalanine), by adding a hydroxyl group through the enzyme phenylalanine hydroxylase.
- If we add another hydroxyl group through the enzyme tyrosine hydroxylase, we get dihydroxyphenylalanine (DOPA).
- If we remove the carboxylic group from DOPA (decarboxylation), we get dopamine
- Hydroxylation of Dopamine gives norepinephrine which gives epinephrine
- All these hormones are called amino acid derived hormones
- Melanin(which is used as skin pigment=صبغة الجسم) is also derived from tyrosine
- Tyrosine is considered to increase the activity status of the body
- Tyramine is similar in structure to tyrosine, but without the carboxylic group. It is formed from tyrosine by the enzyme tyrosine decarboxylase, (however it is not produced in our body), instead found a lot in cheese. It has a similar function to tyrosine, increasing the activity of the body.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

الدّنيا دار العمل، أمّا الآخرة فهي دار الجزاء وفيها اللّقاء ..

اللّهمّ إنّا نسألك الهُدى والتقى والعَفاف والغِنى