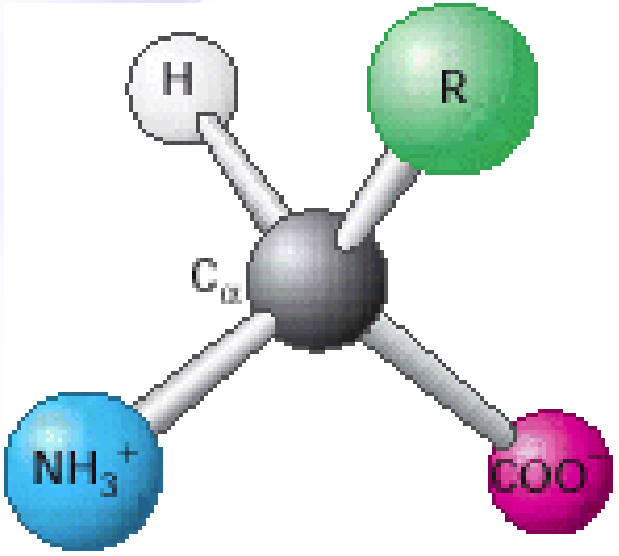
Amino acids

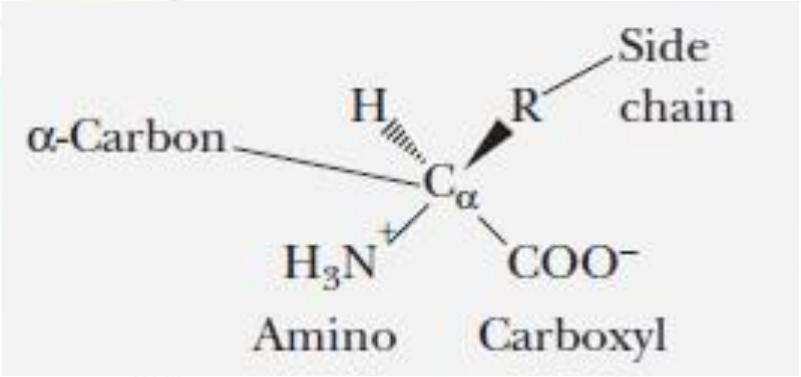
Dr. Diala Abu Hassan

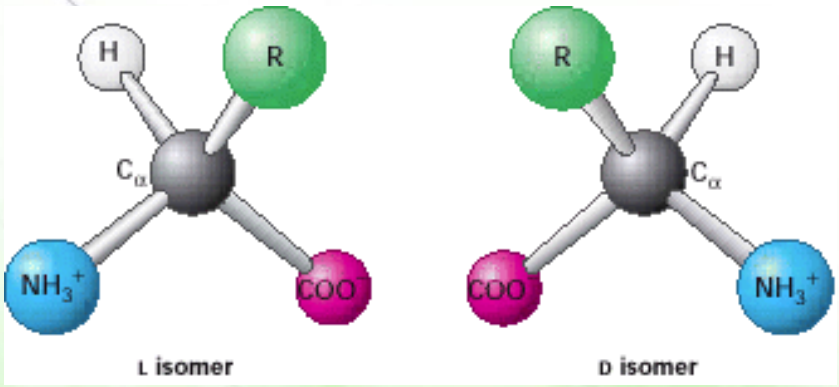
Campbell and Farrell's Biochemistry, Chapters 3 (pp.66-76)

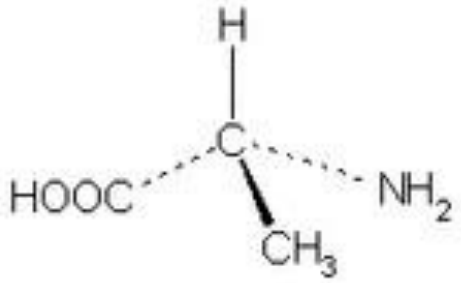
General structure

(Chiral carbon)

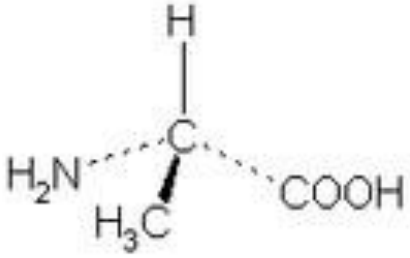




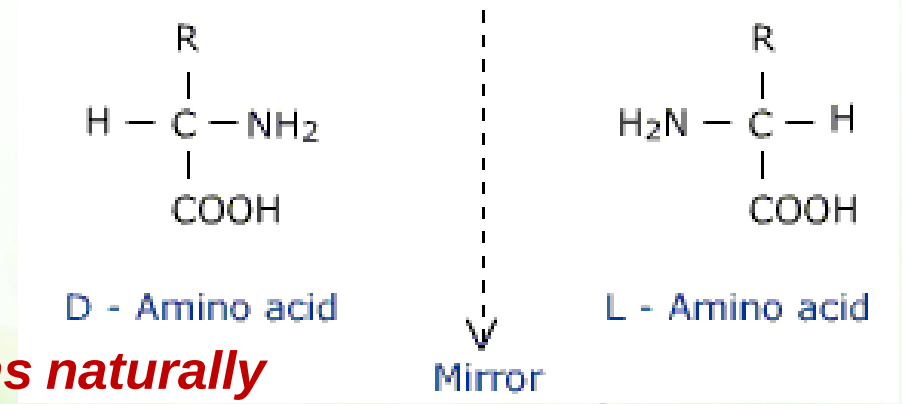




D-Amino acid

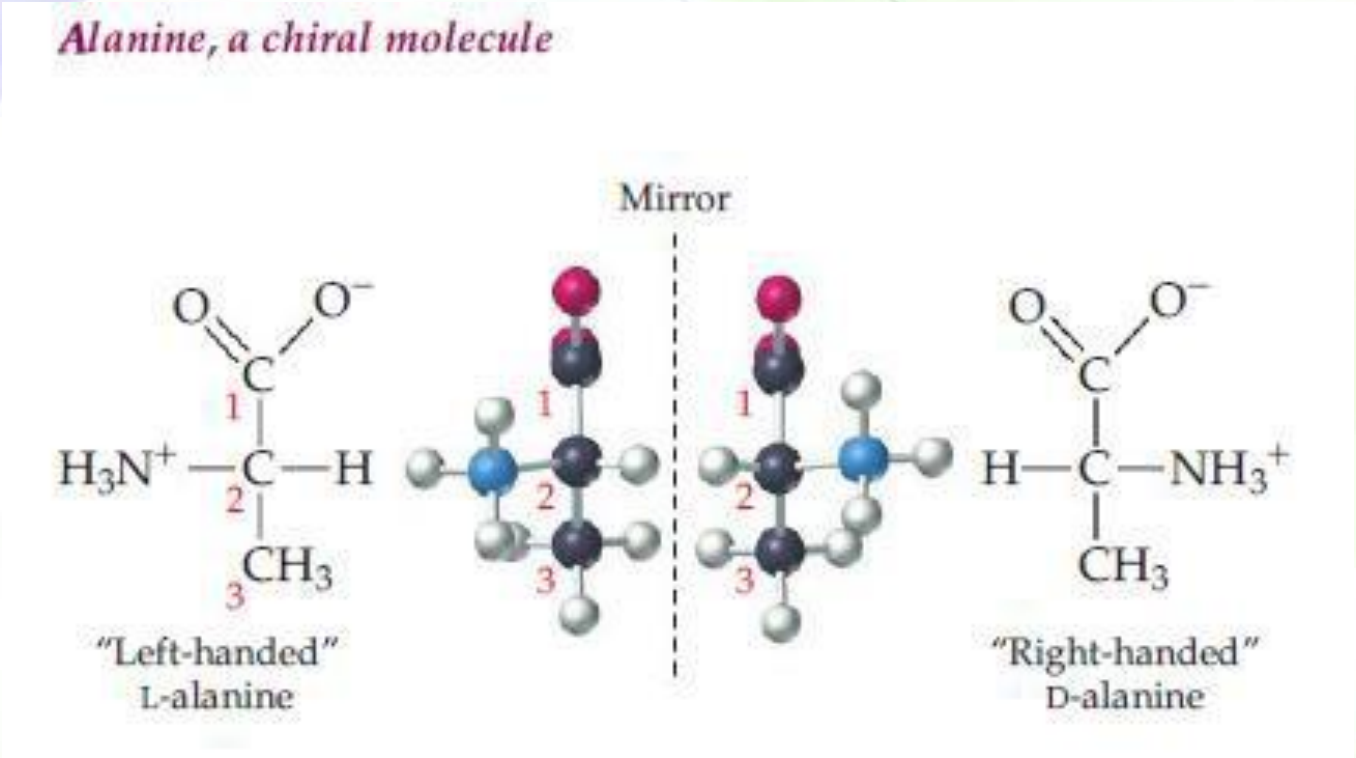


L-amino acid



The amino acids that occur in proteins naturally are all of the L form.

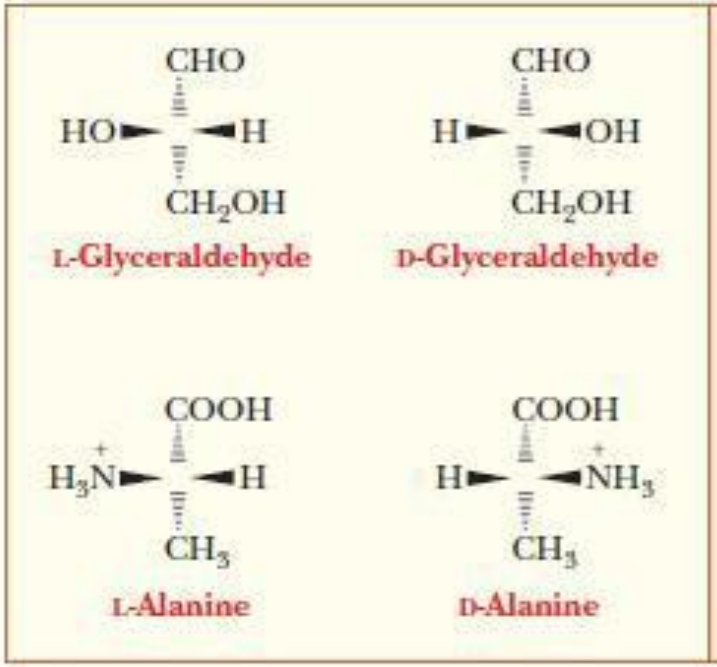
Amino acid stereoisomers or optical isomers

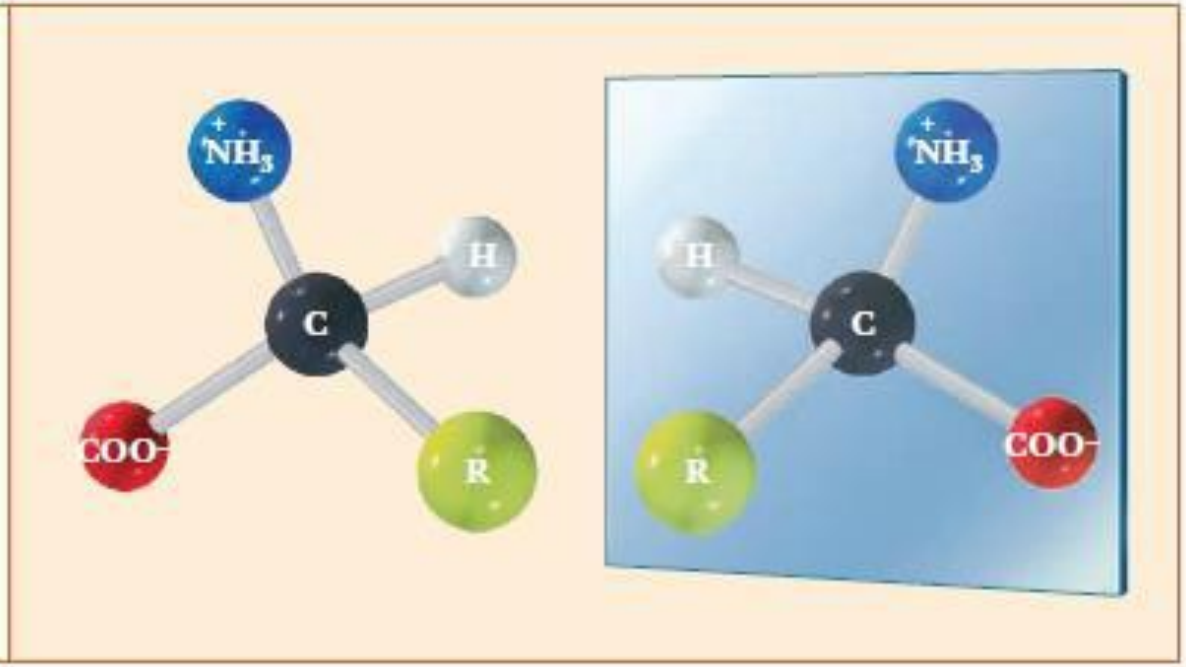


The amino acids in proteins are not superimposable on their mirror images (with the exception of glycine).

Latin *laevus* and *dexter,* meaning "left" and "right," respectively, (the ability to rotate polarized light to the left or the right).

Amino acid stereoisomers

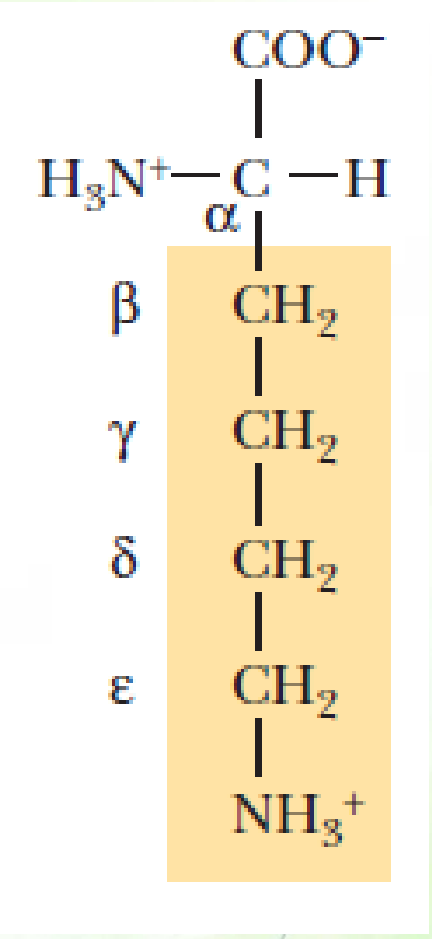




D-amino acids occur in nature, in bacterial cell walls and in some antibiotics, but not in proteins.

Designation of carbons

- Side-chain carbon atoms are designated with letters of the Greek alphabet, counting from the α-carbon. These carbon atoms are, in turn, the β-, γ-, δ-, and ε-carbons.
- If a carbon atom is terminal, it is referred to as the ω-carbon.



Types of amino acids

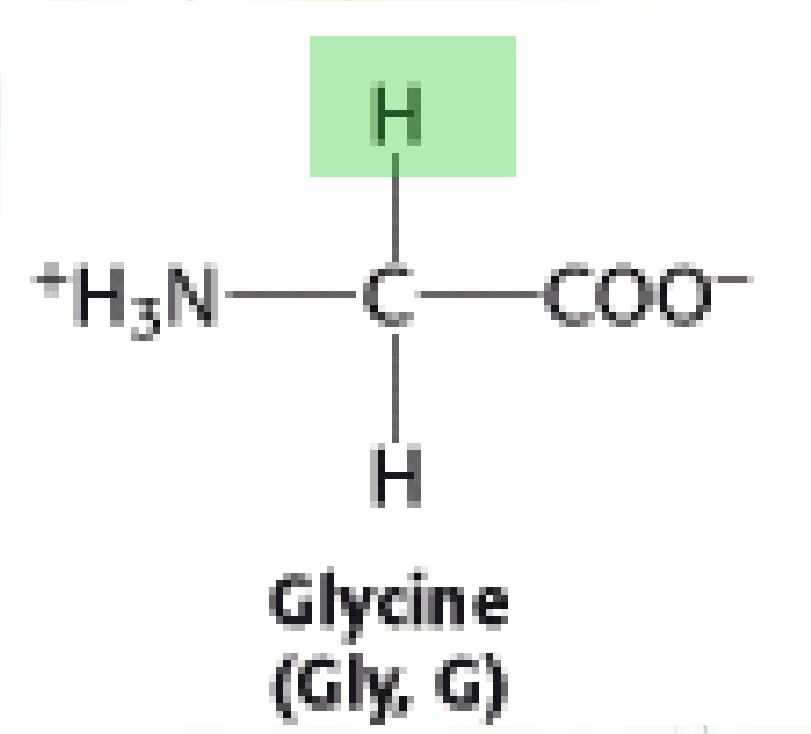
- There are twenty kinds of amino acids depending on the side chains varying in
  - Size
  - Shape
  - Charge
  - Hydrogen-bonding capacity
  - Hydrophobic character
  - Chemical reactivity

Classification (according to the polarity of R group)

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			

Glycine

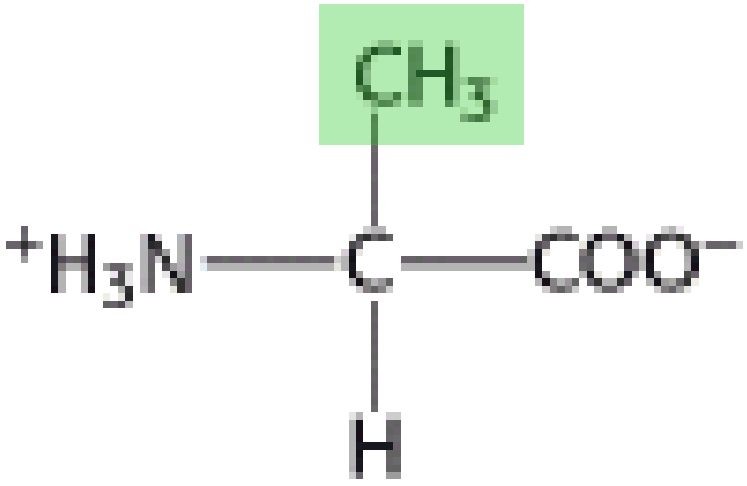
- Glycine is a derivative of acetic acid.
- It could be considered a derivative of ethylamine.



Is it chiral?

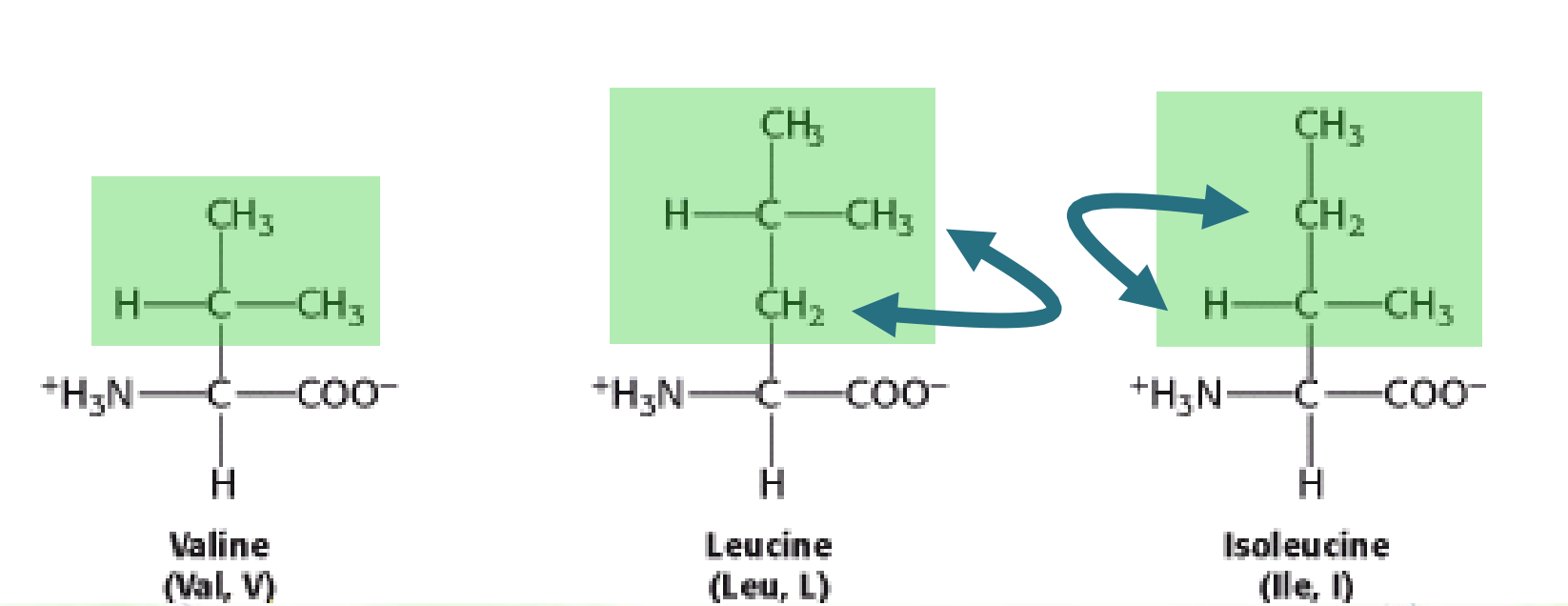
Non-polar (aliphatic amino acids)

Alanine



Alanine
(Ala, A)

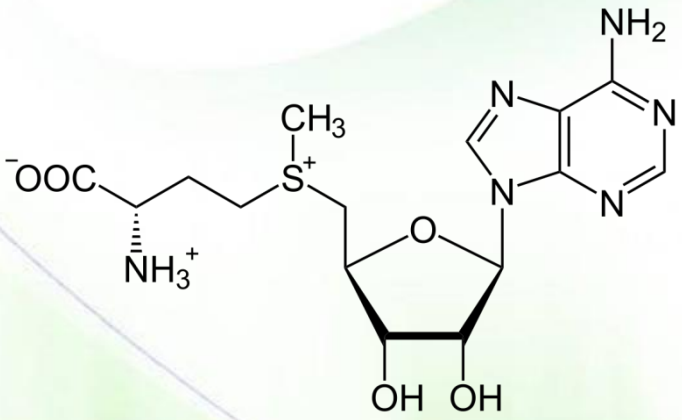
Valine, leucine, and isoleucine

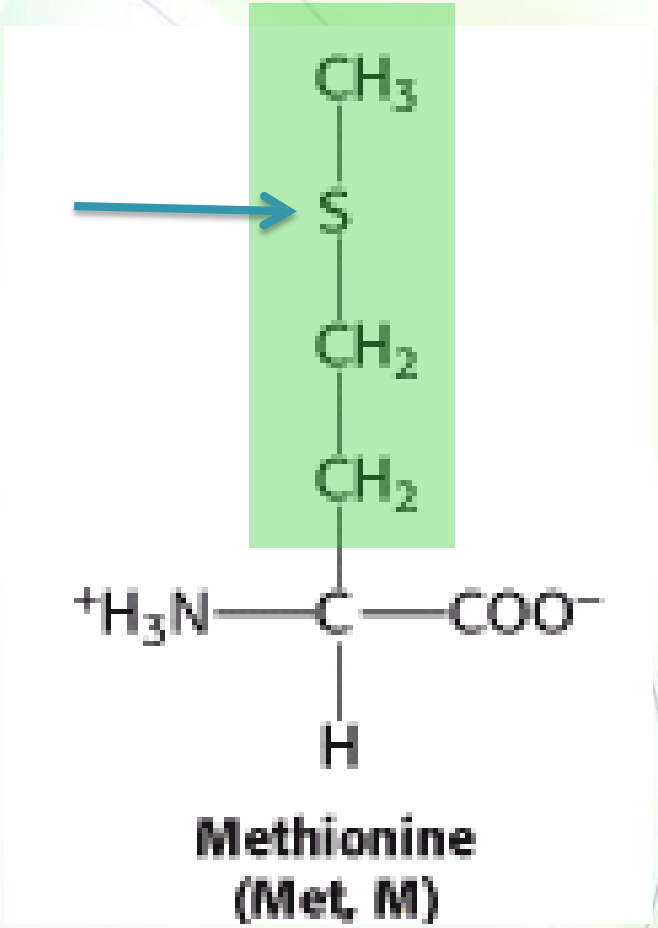


They are branched amino acids.
These are *essential amino acids in the sense that the body* cannot synthesize them.

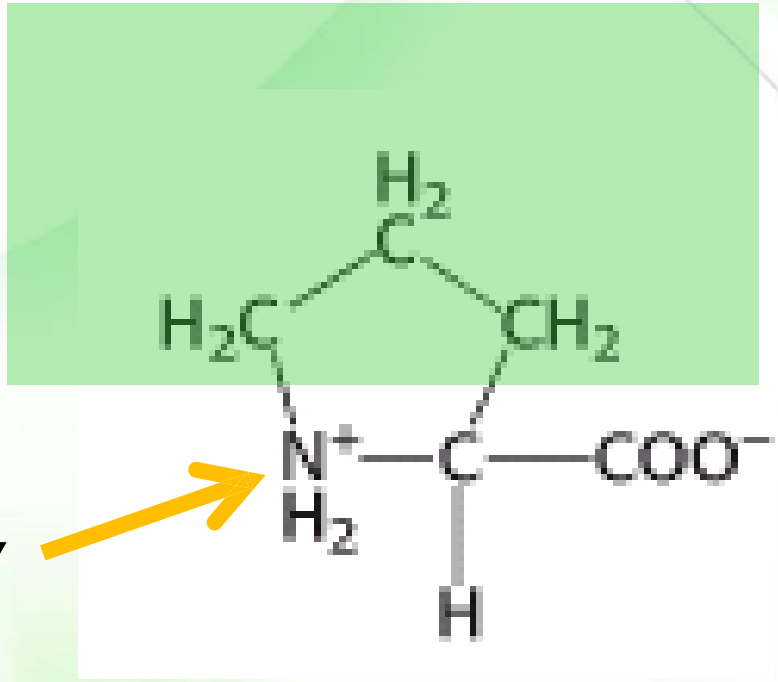
Methionine

It can react to form S-Adenosyl-L-Methionine (SAM) which servers at a methyl donor in reactions.





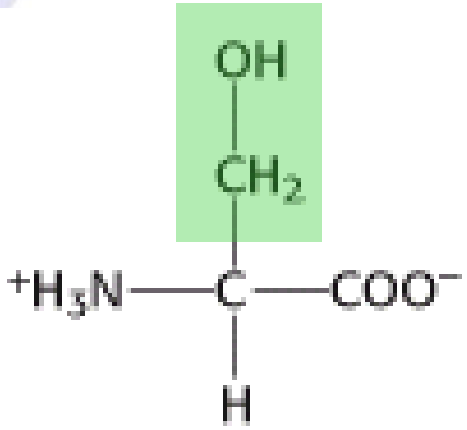
Proline (imino acid)



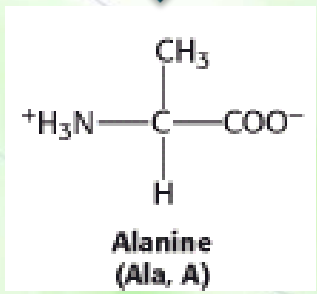
Secondary nitrogen

Polar amino acids

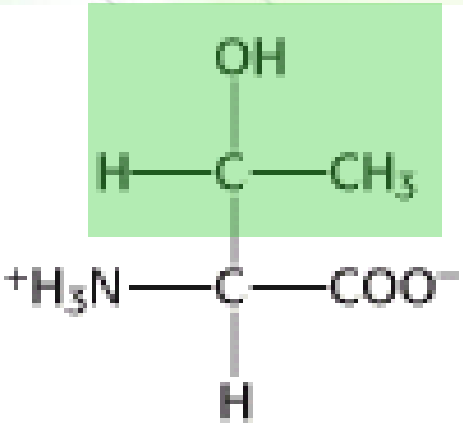
Serine and threonine



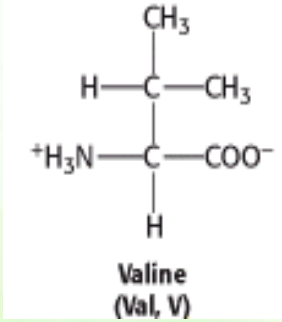
Serine
(Ser, S)



Alanine
(Ala, A)

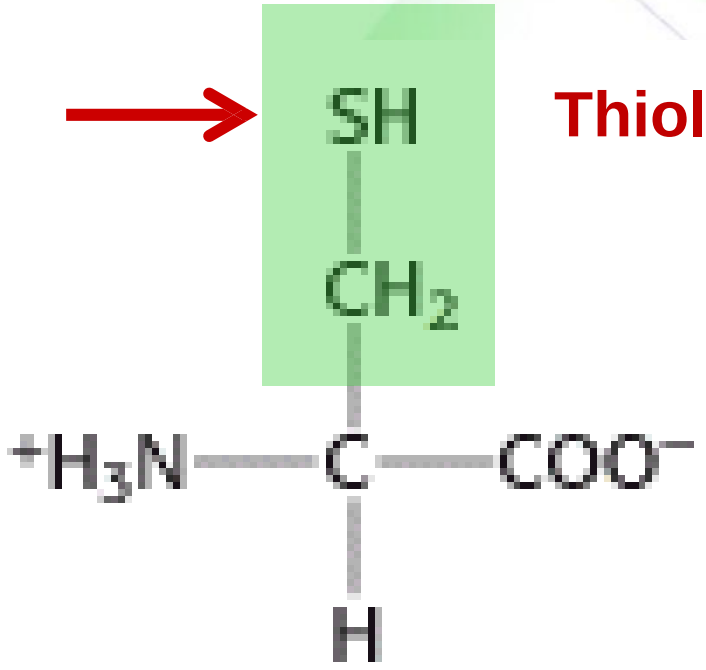


Threonine
(Thr, T)



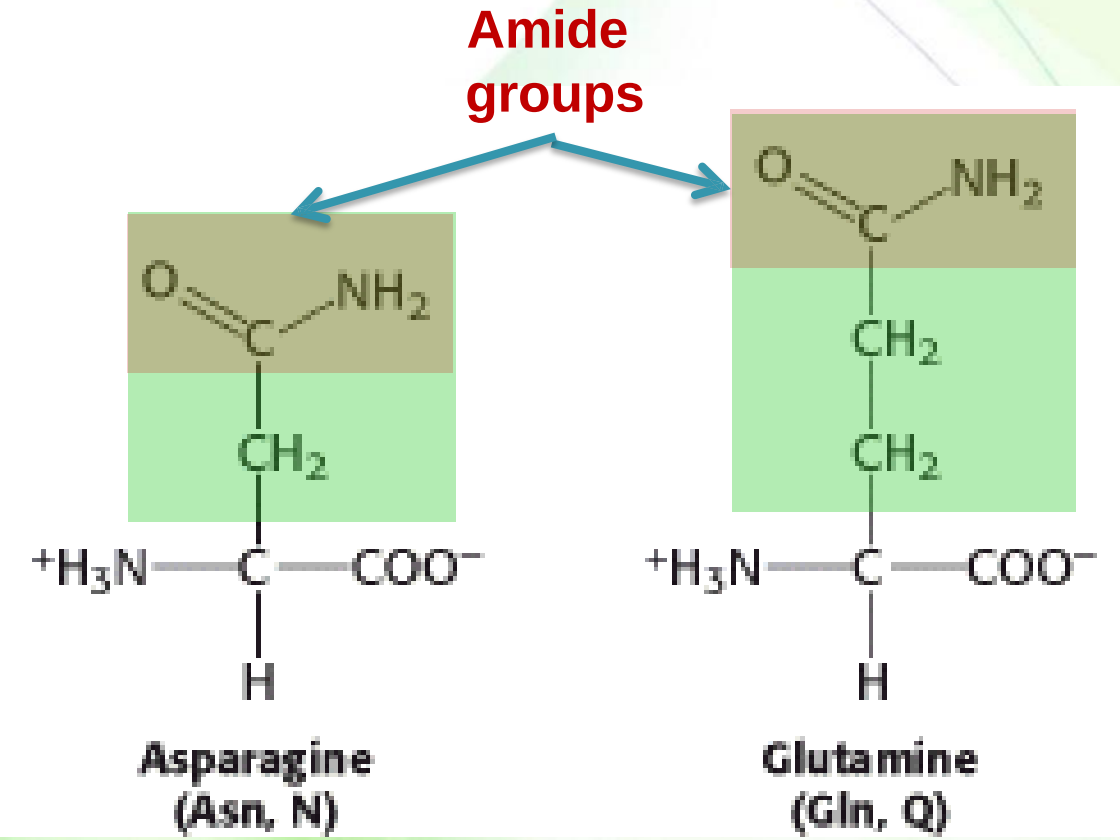
Valine
(Val, V)

Cysteine (Cys, C)



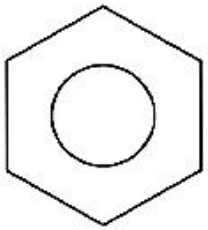
Thiol group

Asparagine and glutamine



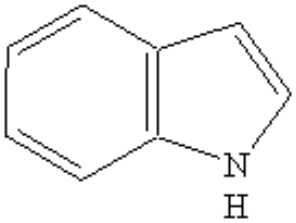
Aromatic amino acids

Phenylalanine, tyrosine, Tryptophan

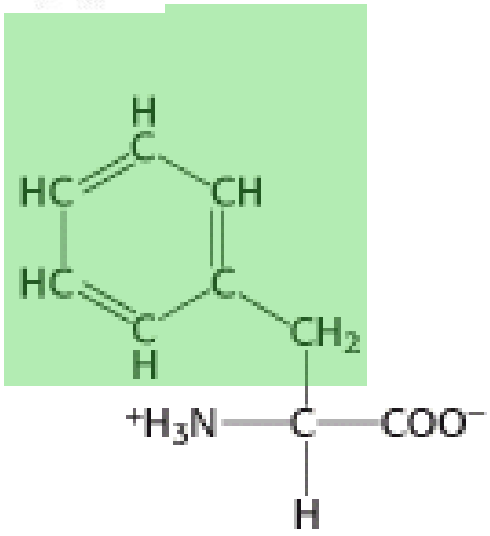


Benzene

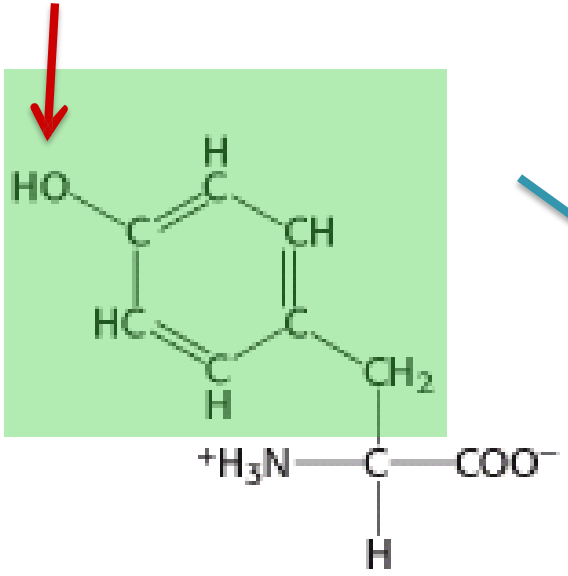
C_6H_6



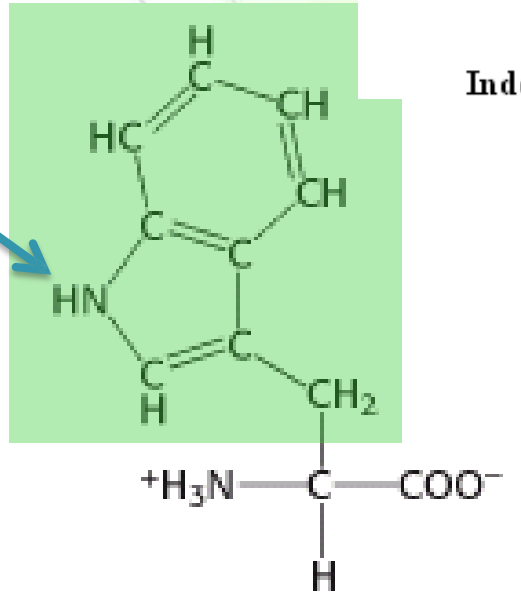
Indole



Phenylalanine
(Phe, F)



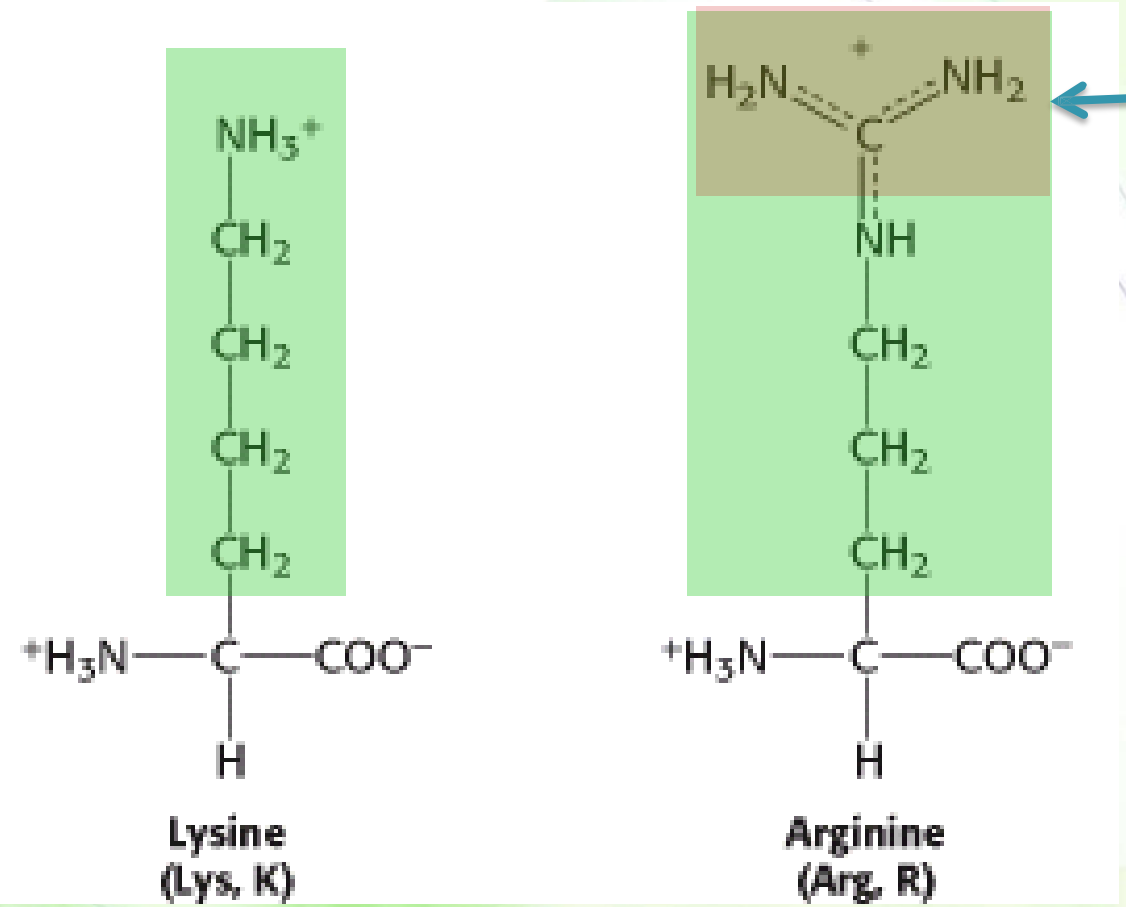
Tyrosine
(Tyr, Y)



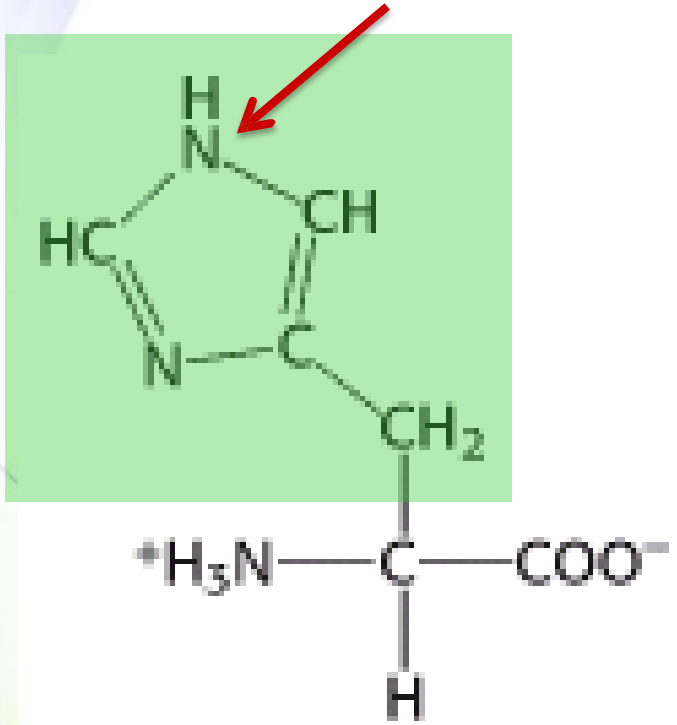
Tryptophan
(Trp, W)

Positively-charged amino acids (Basic amino acids)

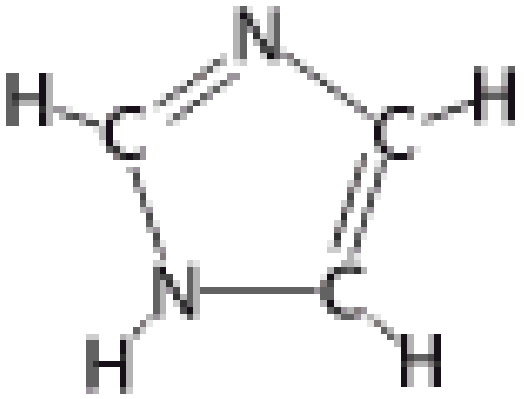
Lysine and arginine



Histidine



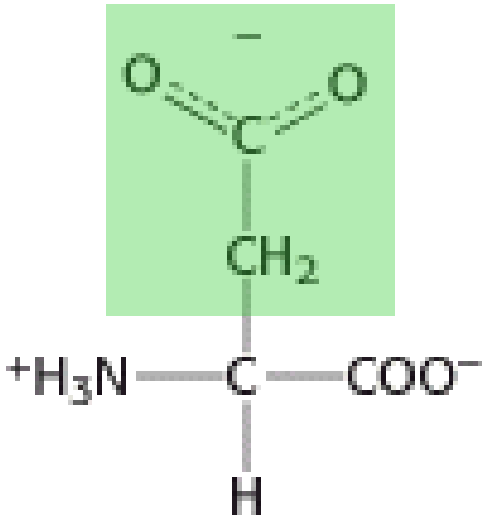
Histidine
(His, H)



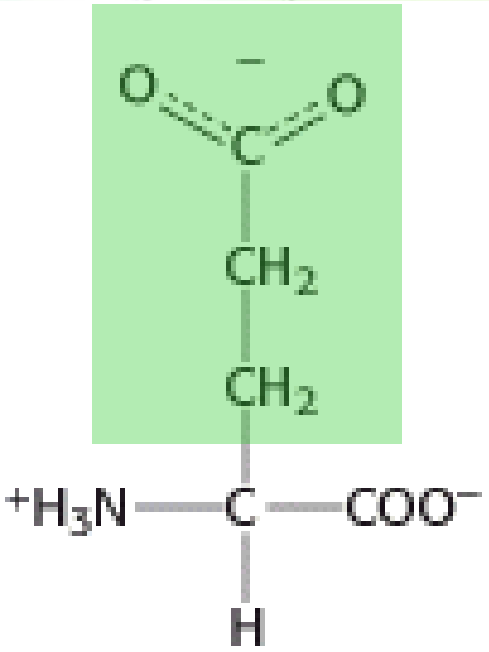
Imidazole

Negatively-charged amino acids (Acidic amino acids)

Aspartic acid and glutamic acid



Aspartate
(Asp, D)



Glutamate
(Glu, E)

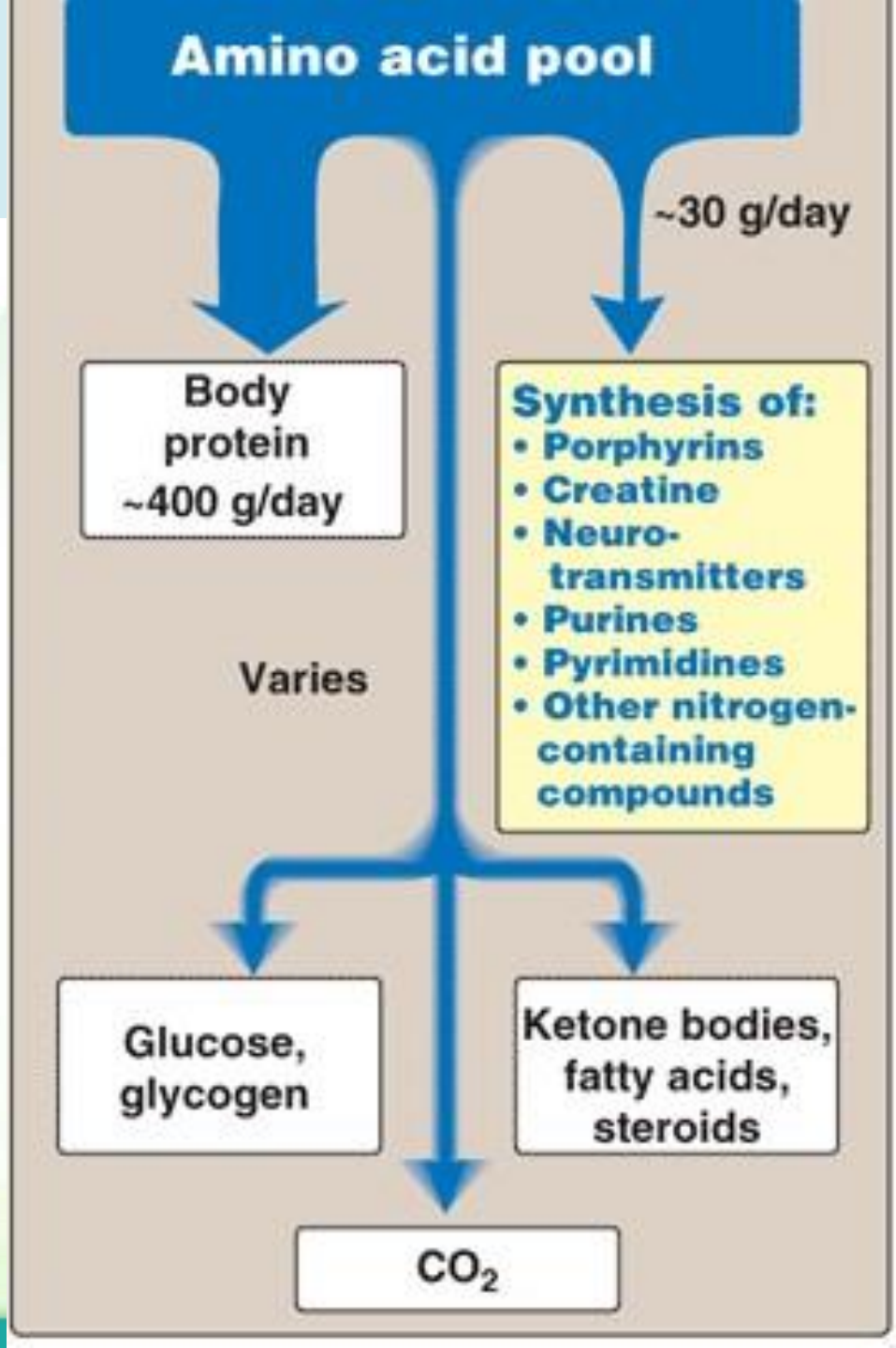
Answer these questions

1. Two amino acids are negatively-charged_____ and _____
2. The following amino acid is achiral_____
3. What is the amino acid that is a secondary amine?
4. Give examples on amino acids that contain an OH group in their side chains.
5. Name 2 amino acids that share a functional group in their side chain

Specialized and uncommon amino acids

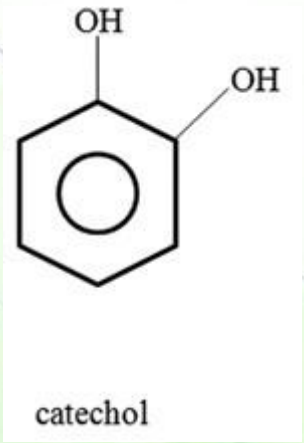
Biological significance of amino acids

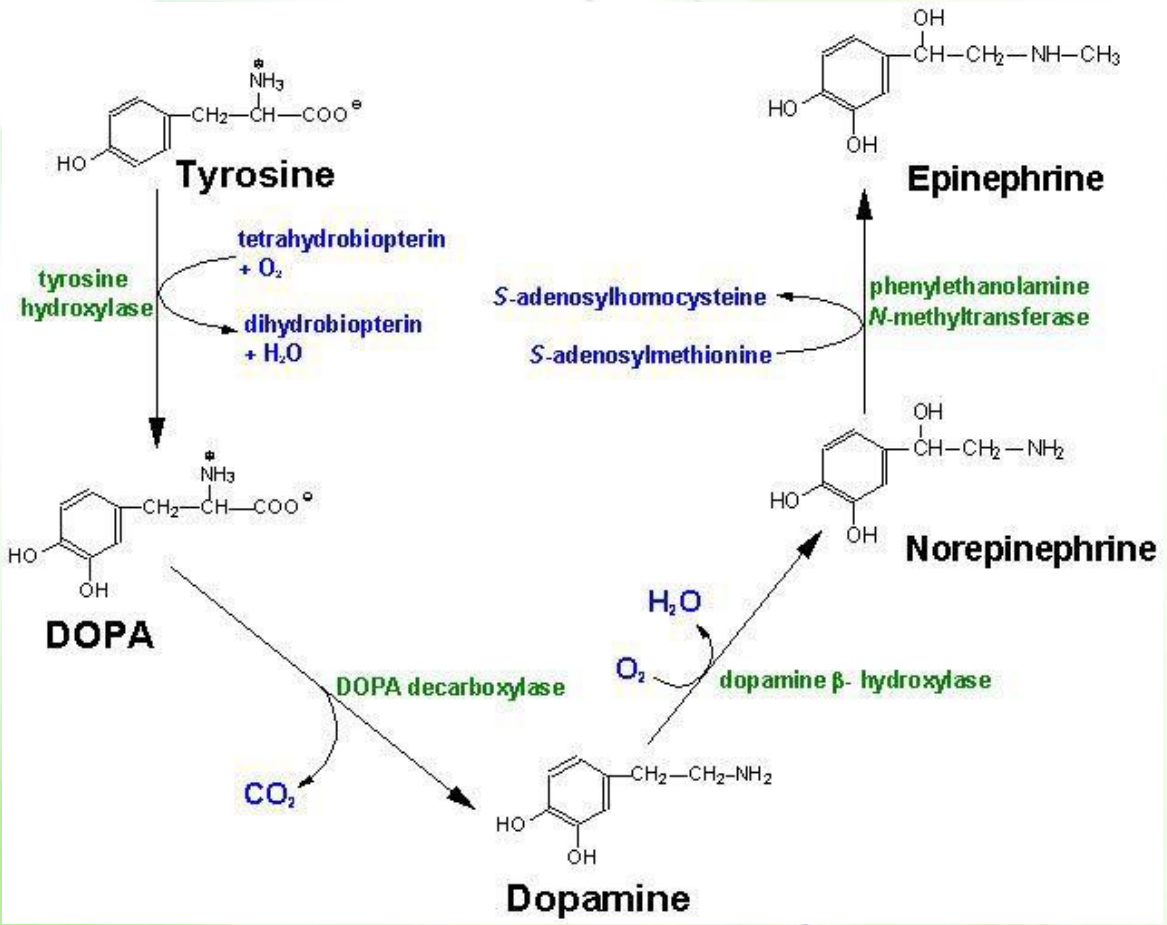
- α-nitrogen atom of amino acids is a primary source for many nitrogenous compounds:
  - Hormones
  - Neurotransmitters
  - Biologically active peptides



Tyrosine (1)

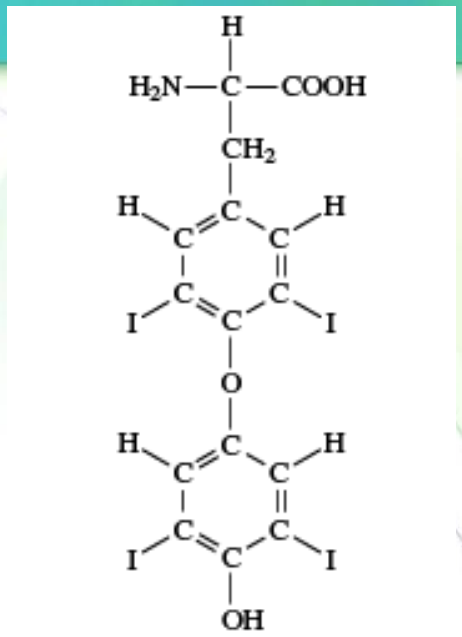
- It is converted into catecholamine neurotransmitters
  - Dopamine
  - Norepinephrine
  - Epinephrine
    - flight or fight



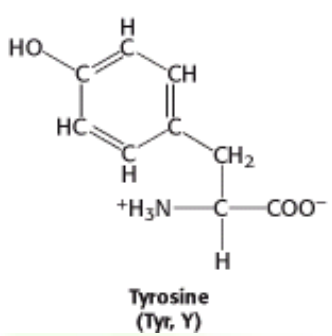


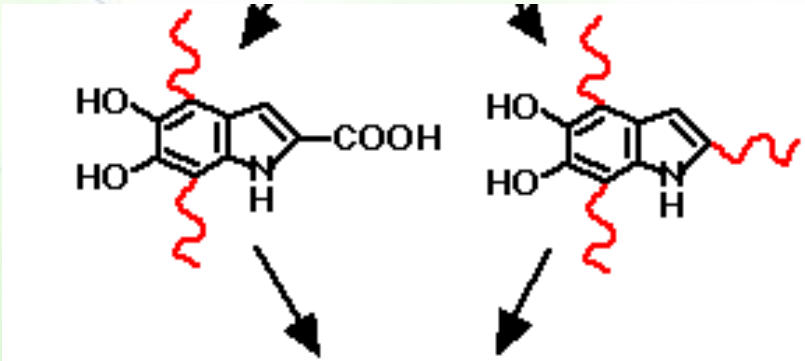
Tyrosine (2)

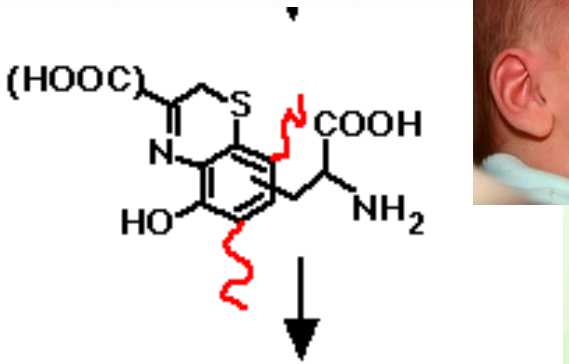
- Tyrosine is converted into
  - Melanin (skin color)
  - Thyroxine (hormone)



thyroxine (Thy)
occurs only in the hormone protein
thyroglobulin: I=iodine

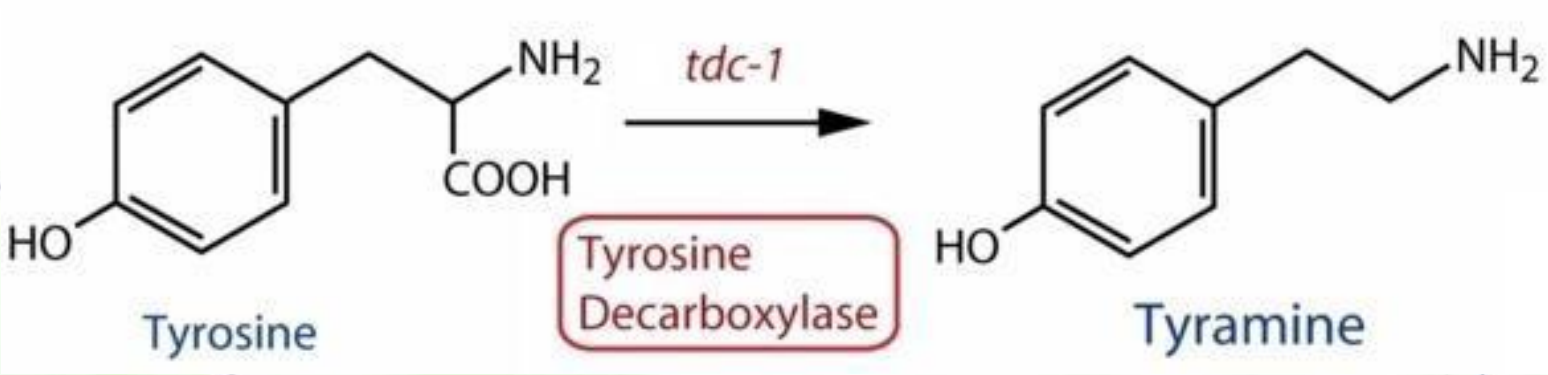






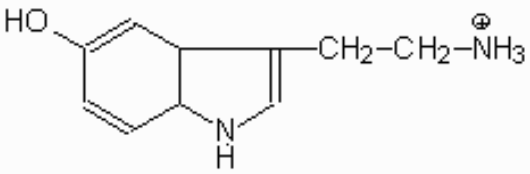
Tyrosine and life

- Cheese contain high amounts of tyramine, which mimics epinephrine; for many people a cheese omelet in the morning is a favorite way to start the day.

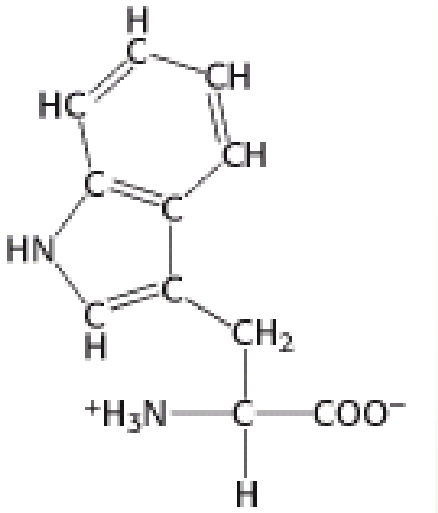


Tryptophan

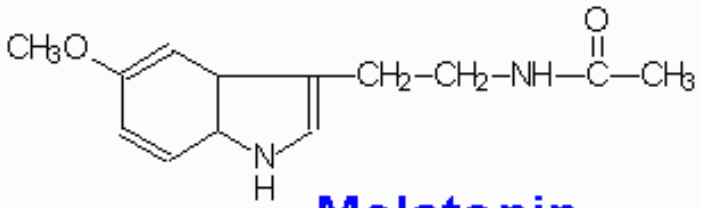
- Tryptohpan serves as the precursor for the synthesis of Neurotransmitters
  - Serotonin (neurotransmitter-sedative)
  - Melatonin (day-night cycle)



Serotonin
(5-hydroxytryptamine)



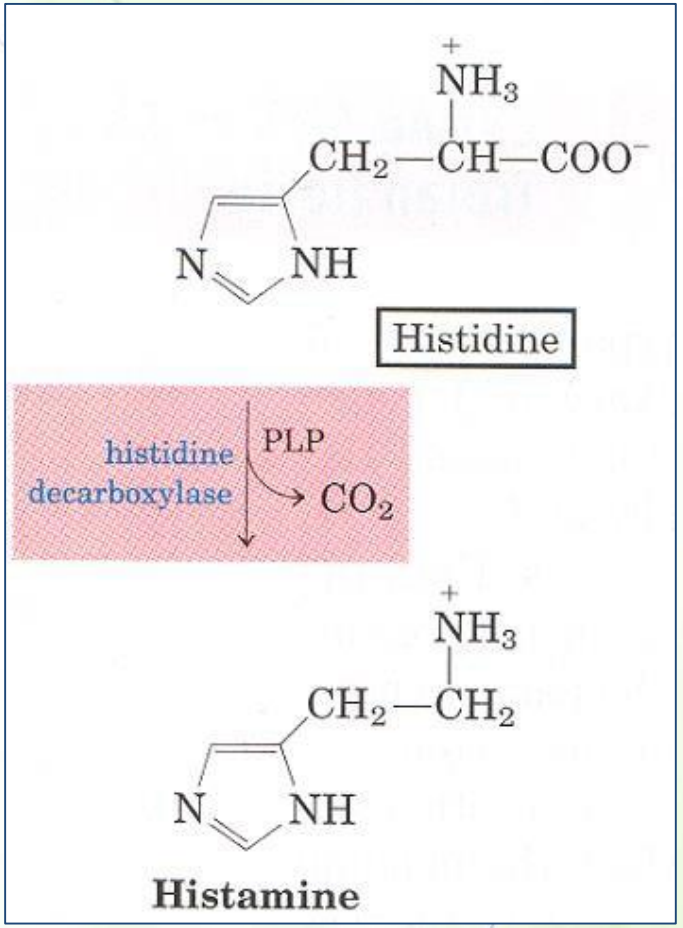
Tryptophan
(Trp, W)



Melatonin

Histamine

- Regulates physiological function in the gut
- Acts as a neurotransmitter
- Causes allergic symptoms (a major causes for asthma)
- Contributes to inflammatory response
- Causes constriction of smooth muscle

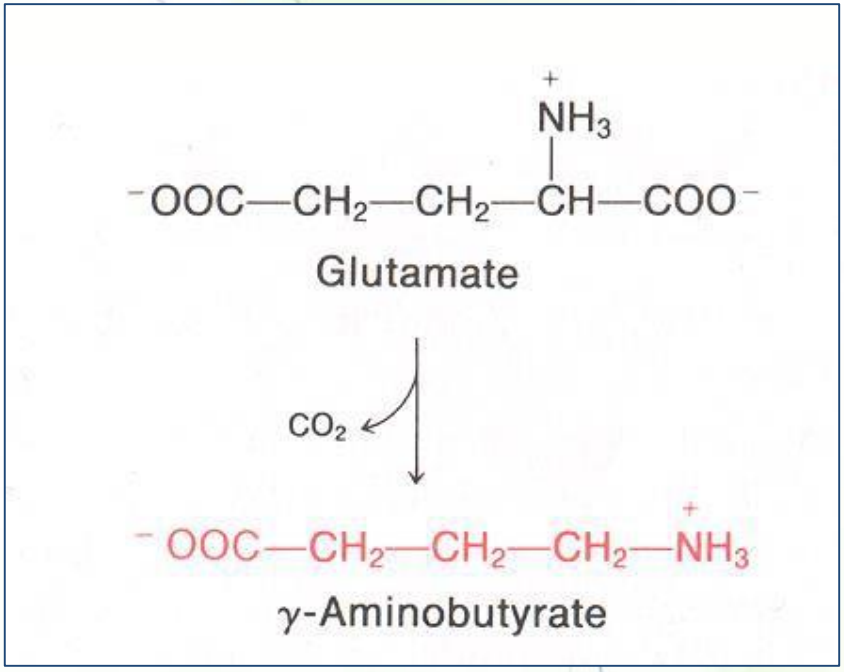


Glutamate

- Is a precursor of γ-aminobutyric acid (GABA)
- **Inhibitory neurotransmitter (CNS) that reduces neuronal excitability.**

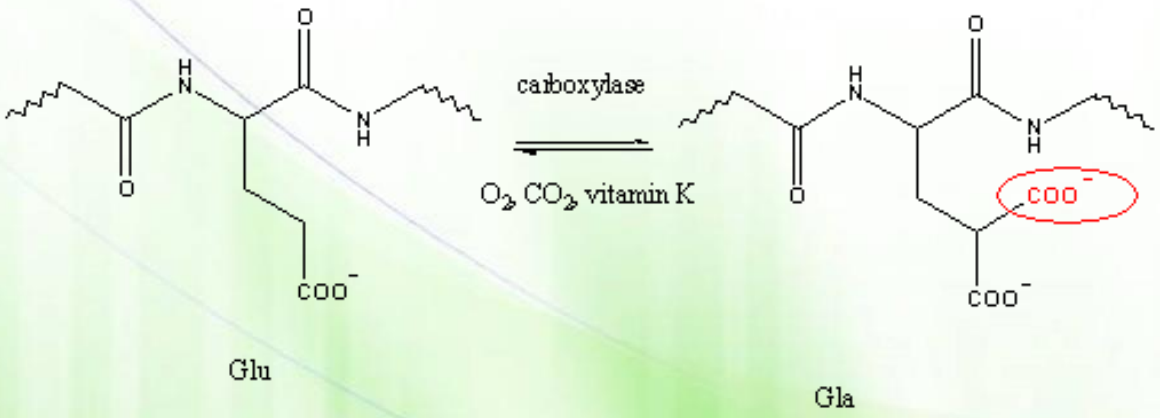
GABA is synthesized in brain because it does not cross the BBB.

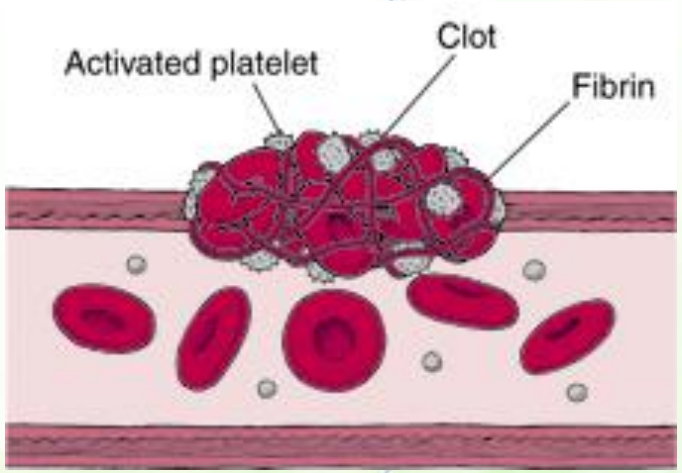
GABA have relaxing, anti-anxiety, and anti-convulsive effects.



γ- carboxyglutamate (Gla)

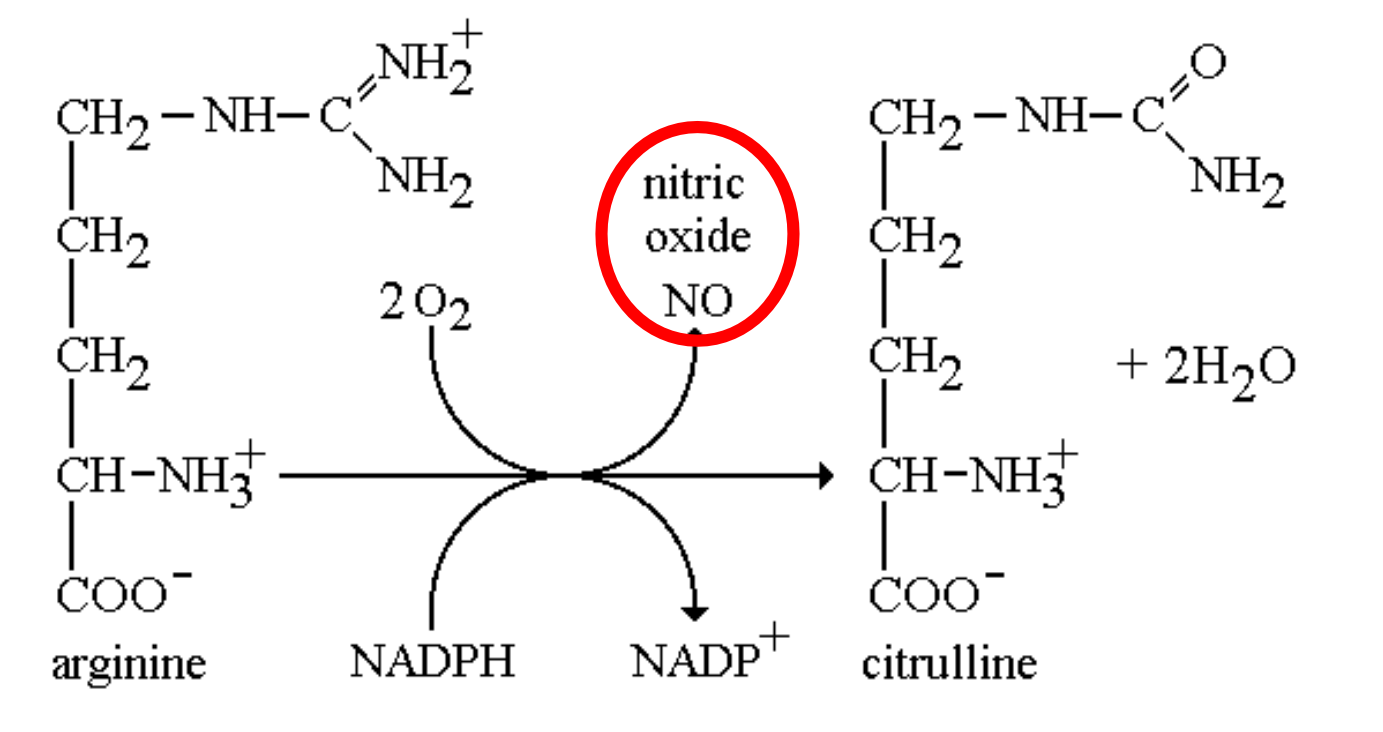
- The glutamate residues of some clotting factors are carboxylated to form γ- carboxyglutamate (Gla) residues.
  - Vitamin K is essential for the process
- This carboxylation is essential for the function of the clotting factors.





Arginine

- L-arginine is the precursor of nitric oxide (NO)
- NO functions:
  - Vasodilation, inhibition of platelet adhesion, inhibition of leukocyte adhesion, antiproliferative action, scavenging superoxide anion (anti-inflammatory)

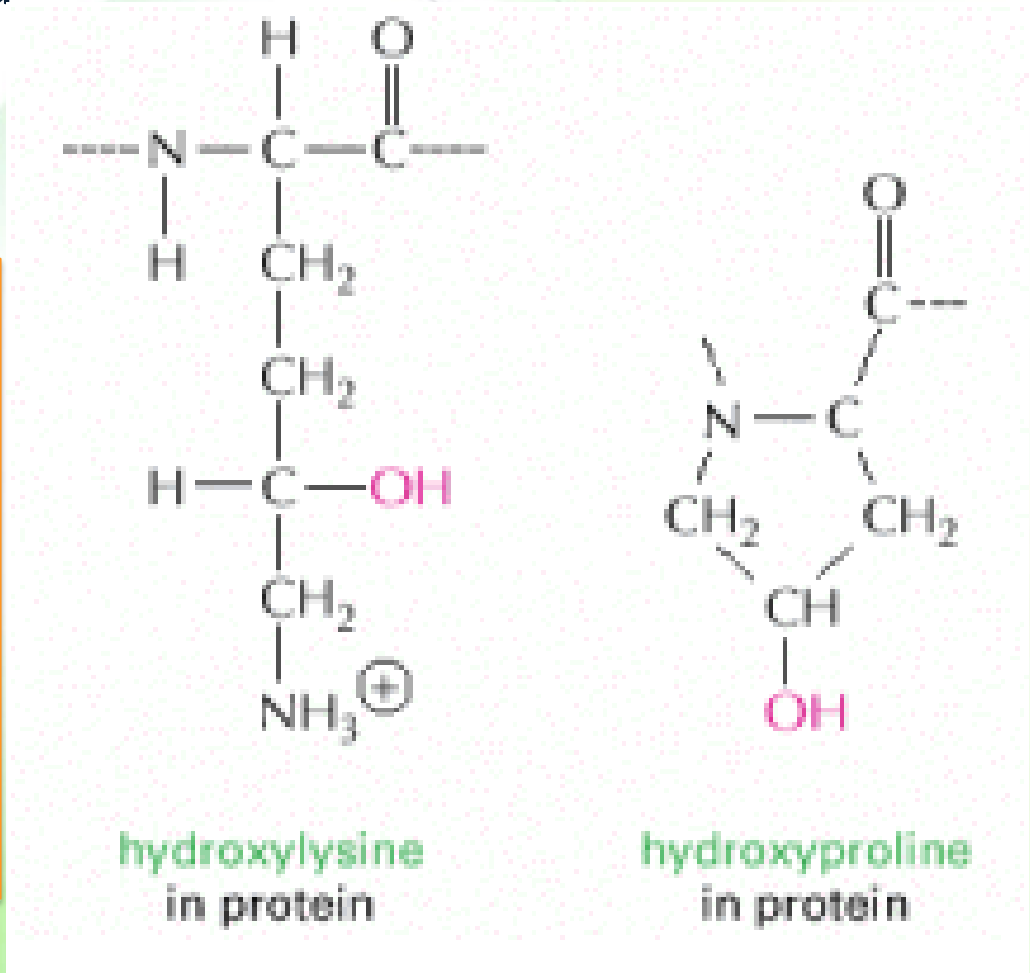


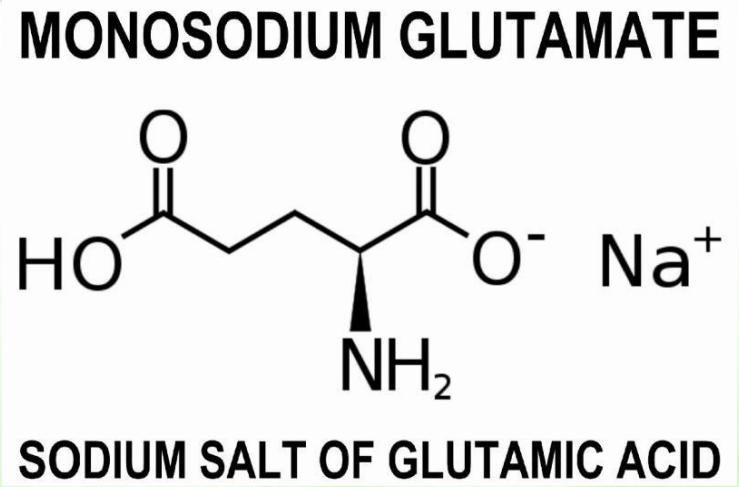
Lysine and proline

- Both are hydroxylated and are part of collagen structure.

Derived from the common amino acids.

Produced by modification of the parent amino acid after protein synthesis, posttranslational modification.





Biochemical applications: Monosodium glutamate (MSG)

Glutamic acid derivative

Flavor enhancer, Asian food.

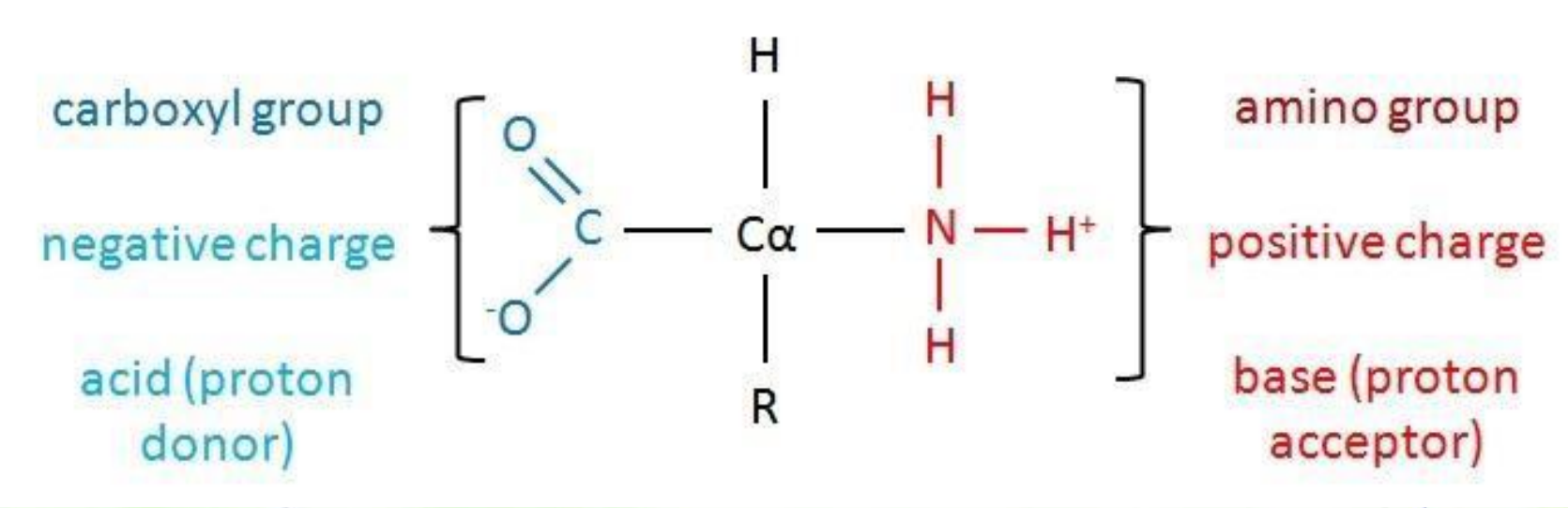
MSG causes a physiological reaction in some people (chills, headaches, and dizziness)

Chinese restaurant syndrome.

topyaps.com
www.zazzle.com

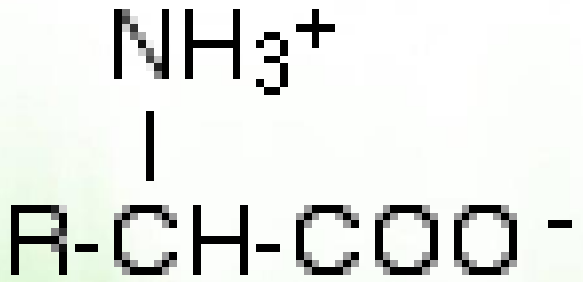
Ionization of amino acids

Why do amino acids get ionized?



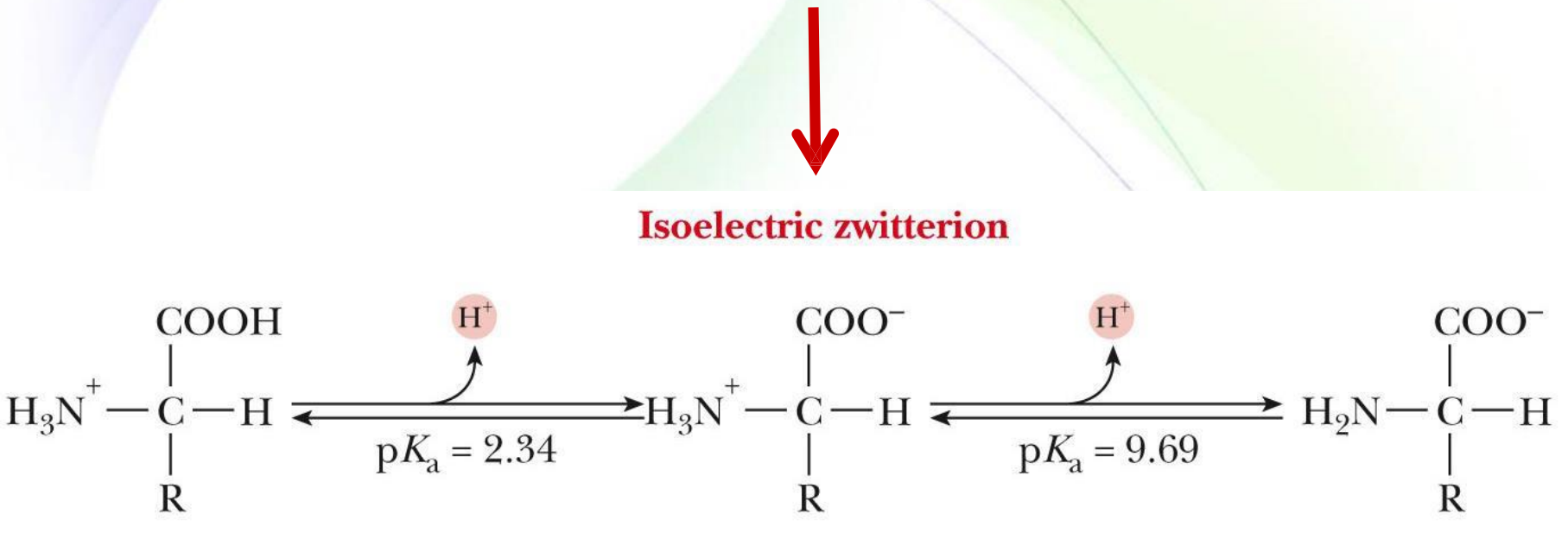
Zwitterion and isoelectric point

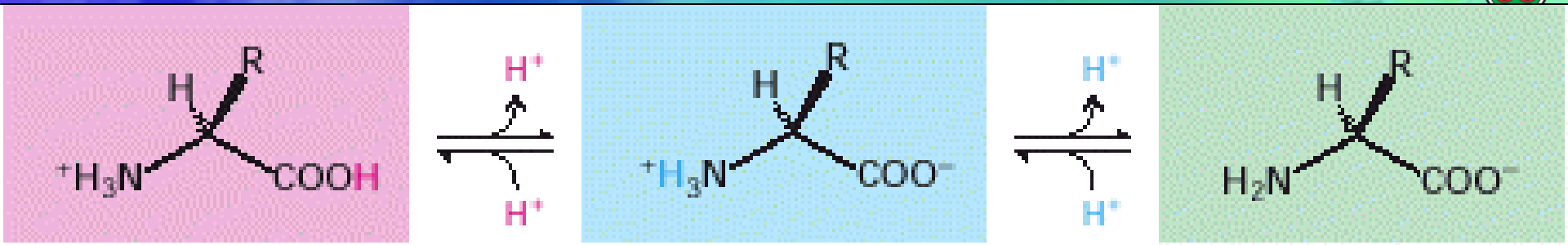
- At physiological pH, amino acids (without ionizable groups) are electrically neutral
- Zwitterion: a molecule with two opposite charges and a net charge of zero

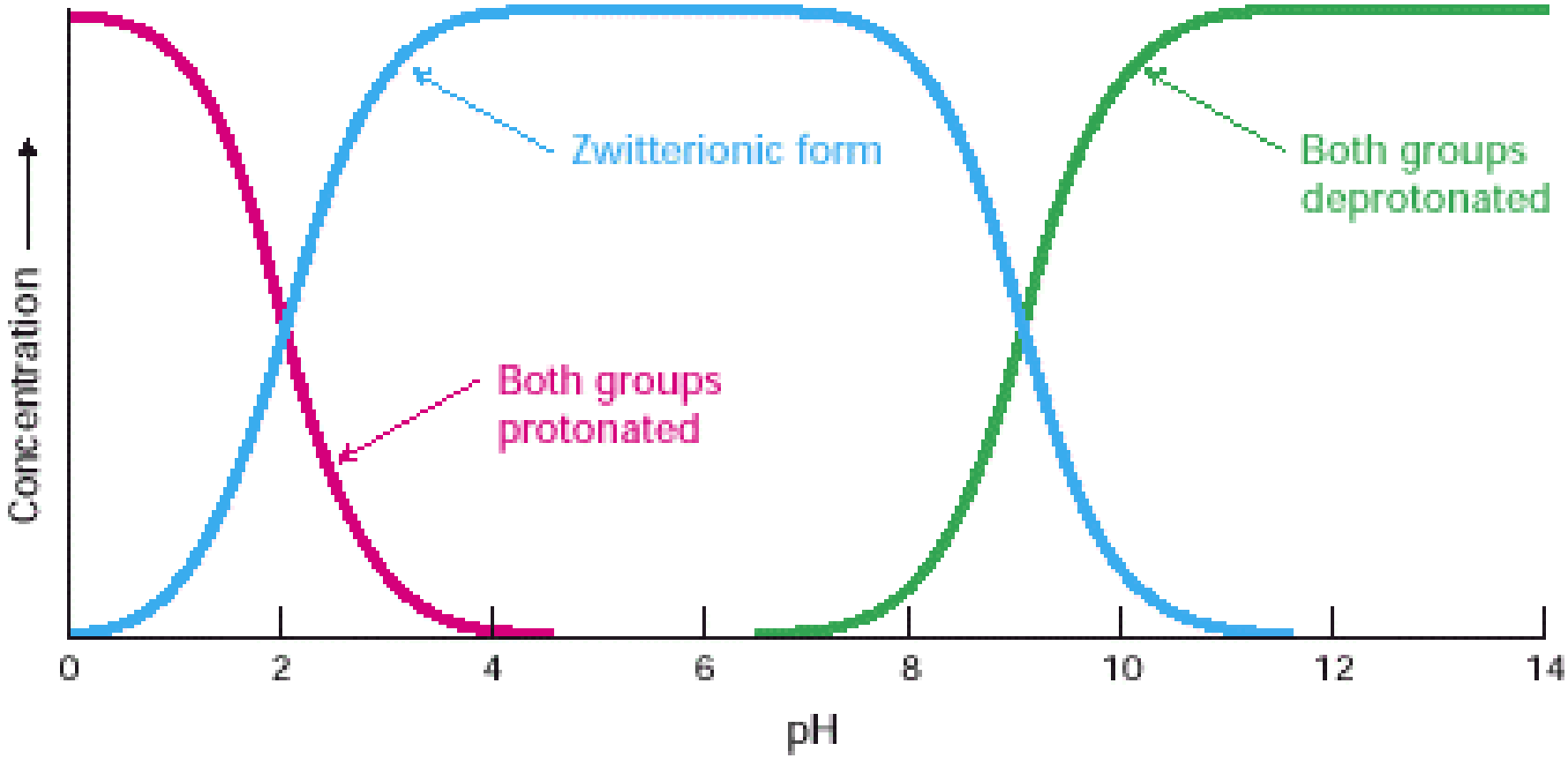


a zwitterion

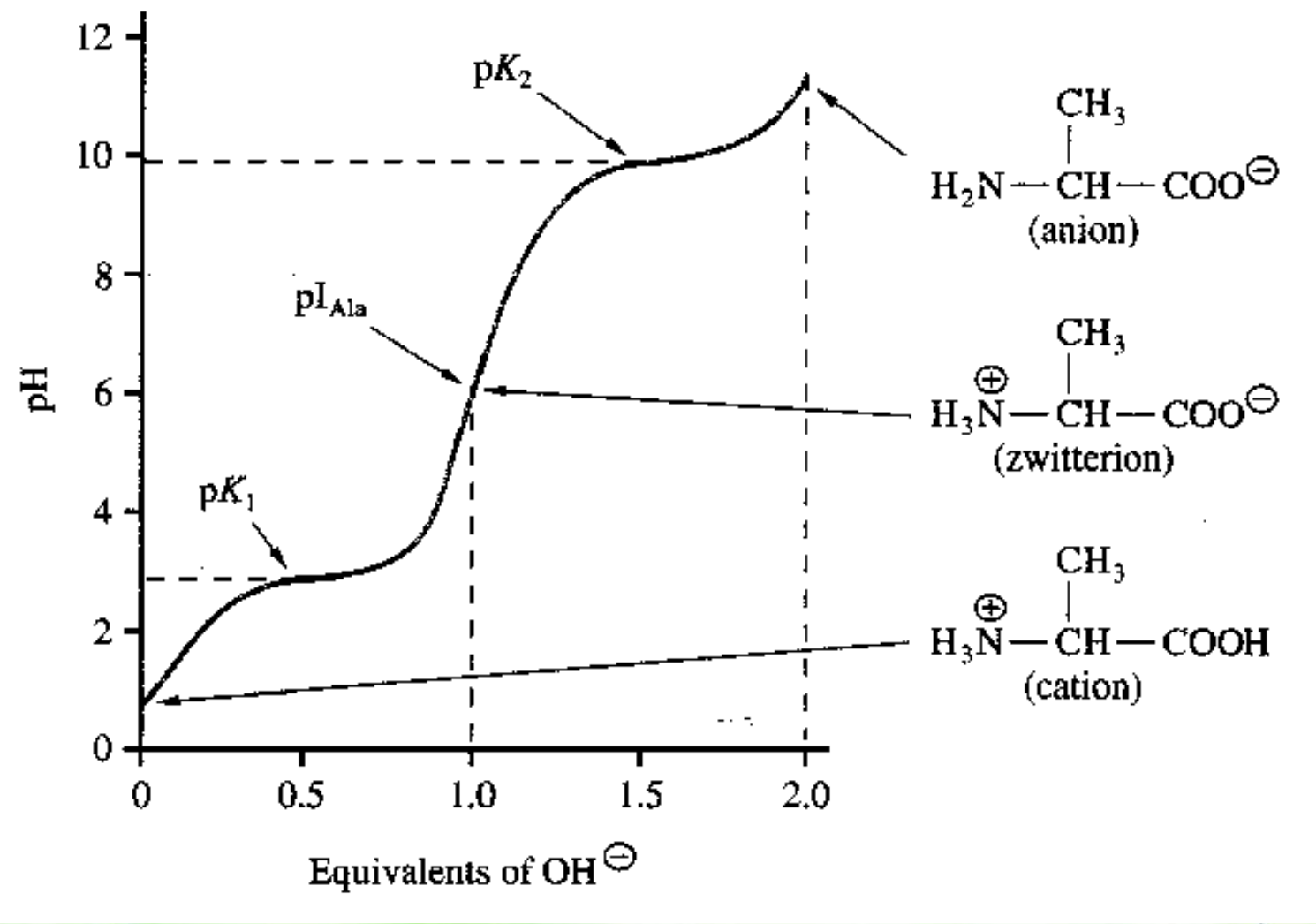
Effect of pH


Isoelectric zwitterion
COOH
H+
COO−
H+
COO−
H3N+ — C — H
H3N+ — C — H
H2N — C — H
R
R
R
pKa = 2.34
pKa = 9.69


H
R
^+H_3N
COOH
H^+
H^+
H
R
^+H_3N
COO^-
H^+
H^+
H
R
H_2N
COO^-


Zwitterionic form
Both groups deprotonated
Both groups protonated
Concentration
0
2
4
6
8
10
12
14
pH

Example 1 (alanine)



$$pH = pK_a + \log \frac{[\text{conjugate base}]}{[\text{weak acid}]}$$

Isoelectric Point

- The pH where the net charge of a molecules such as an amino acid or protein is zero is known as isoelectric point or pI.
- For the nonpolar and polar amino acids with two pKa's, the isoelectric point is calculated by taking the numerical average of the carboxyl group pKa and the a-amino group pKa.

$$\mathrm{pI} = \frac{\mathrm{p}K_{\mathrm{a1}} + \mathrm{p}K_{\mathrm{a2}}}{2}$$

Ionization of side chains

- Nine of the 20 amino acids have ionizable side chains.
- These amino acids are tyrosine, cysteine, arginine, lysine, histidine, serine, threonine, and aspartic and glutamic acids.
- Each side chain has its own pKa values for ionization of the side chains.

pI of amino acids

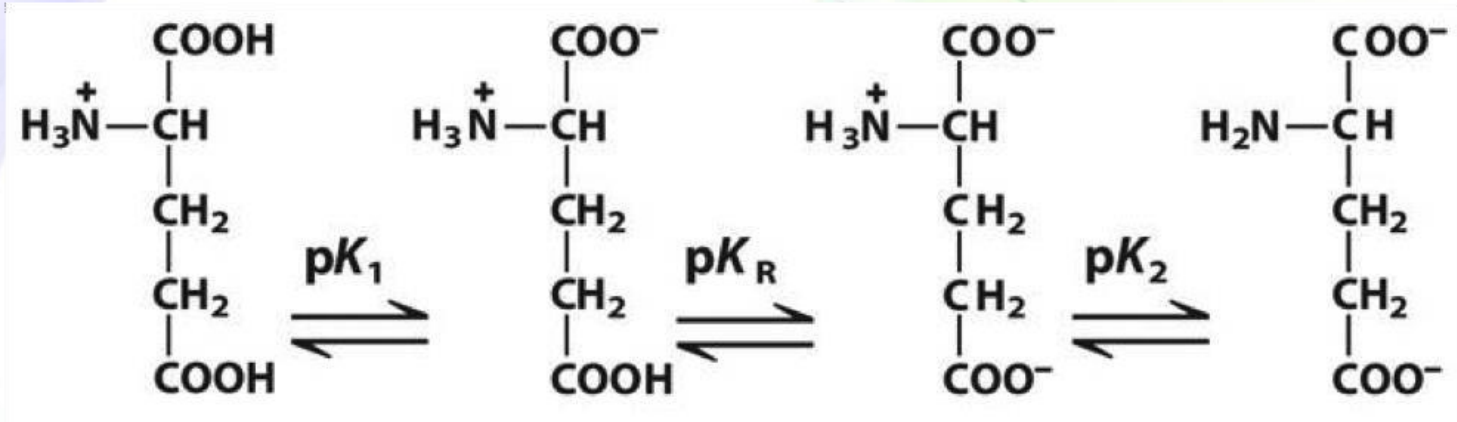
Amino Acid	Side Chain pK_a [3]	pI
Arginine	12.5	10.8
Aspartic Acid	4.0	3.0
Cysteine	8.0	5.0
Glutamic Acid	4.1	3.2
Histidine	6.0	7.5
Lysine	11.0	10

Let's consider pKa of -NH_2 = 9 and pKa of –COOH = 2 for all amino acids

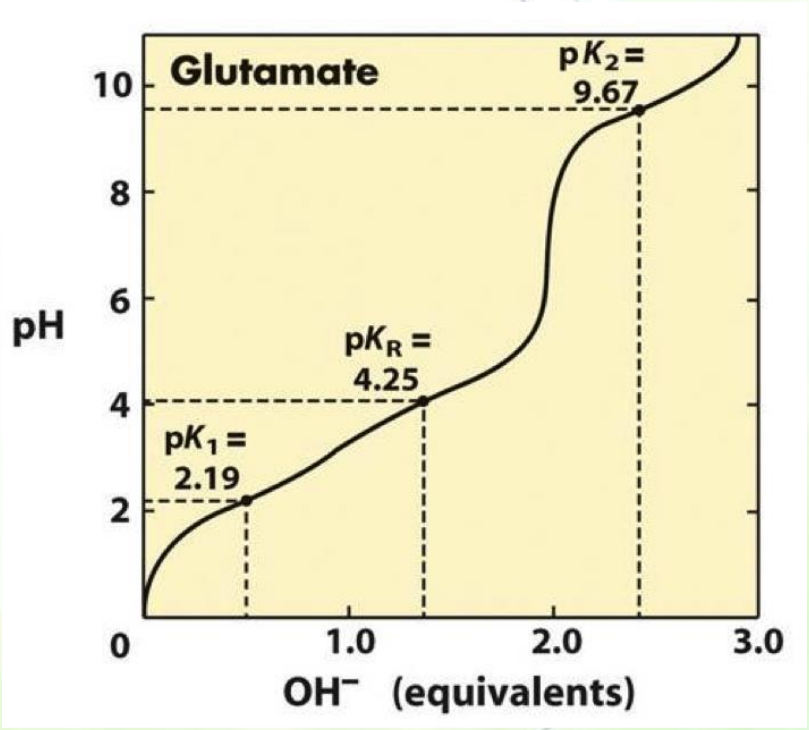
Calculation of pI of amino acids with ionizable R groups

- The isoelectric point for these amino acids is calculated by taking the average of the pKa's of the groups with same charge when ionized
- In this case, the total charge on the groups with like charge must equal one (1) so that it can be balanced by the one (1) opposite charge present on the molecule

Example: Glutamate

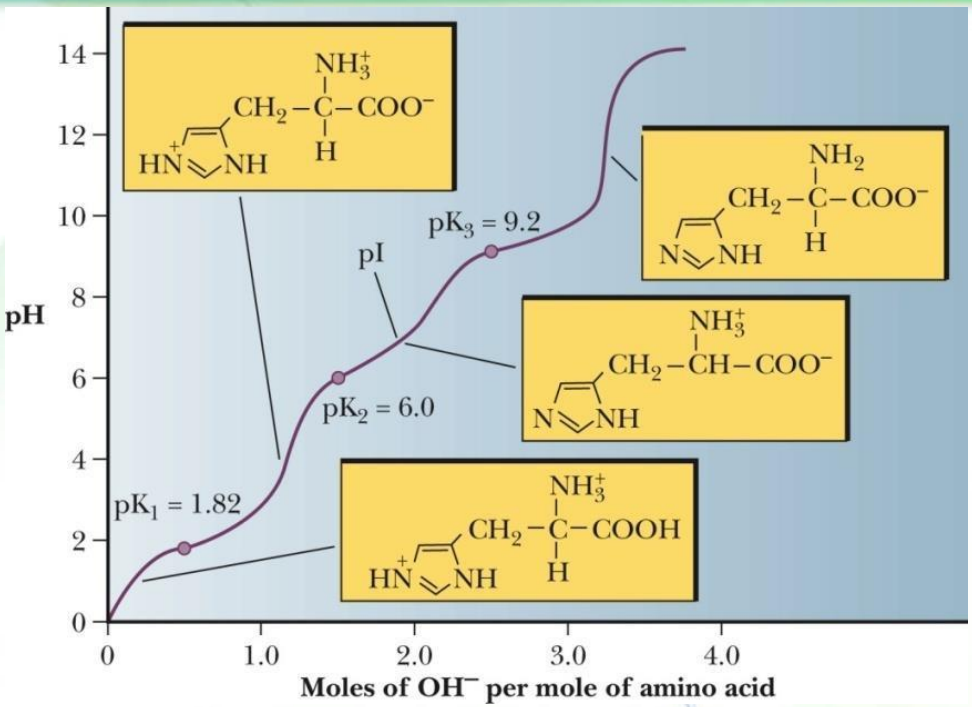


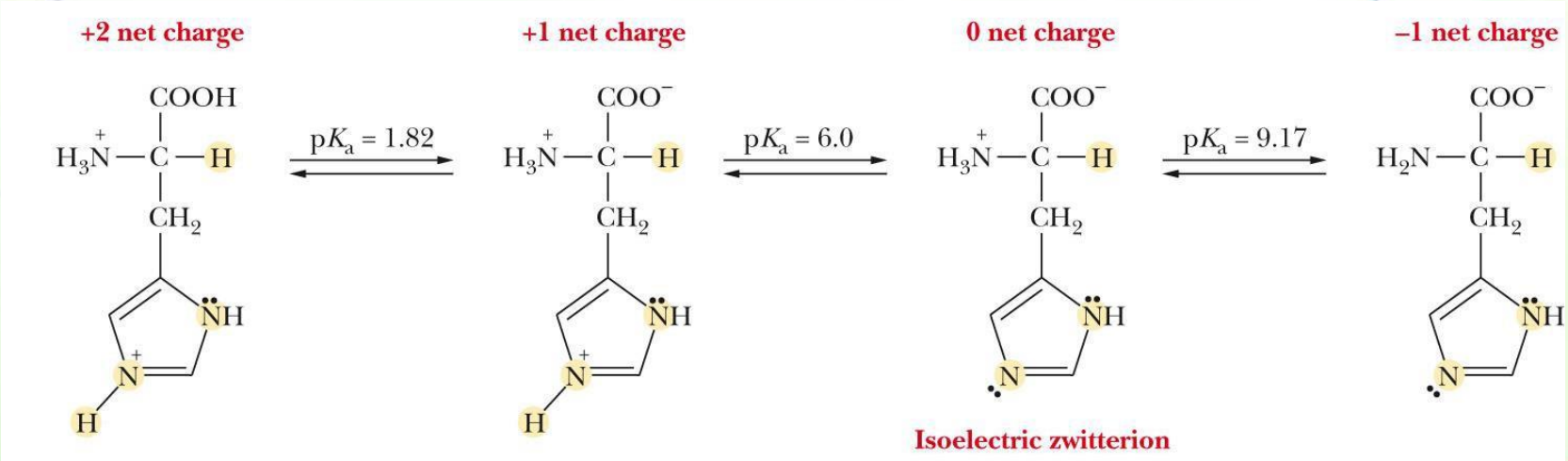
- To calculate the isoelectric point of Glu, the pKa's of the two carboxyl groups are averaged.



Histidine

- pI = ~7.5 (The imidazole group can be uncharged or positively charged near neutral pH).





Questions

1. Draw the titration curve of histidine.

2. What is the ratio of conjugate base/acid of glutamate at pH 4.5?

3. What is the total charge of lysine at pH 7?

What do you need to know?

- The names of amino acids
- The special structural features of amino acids
- Their abbreviations or designations
- The uncommon amino acids, their precursor and function (if any)
- The pKa of groups
  - not exact numbers, but which ones are acidic, basic, or near neutral