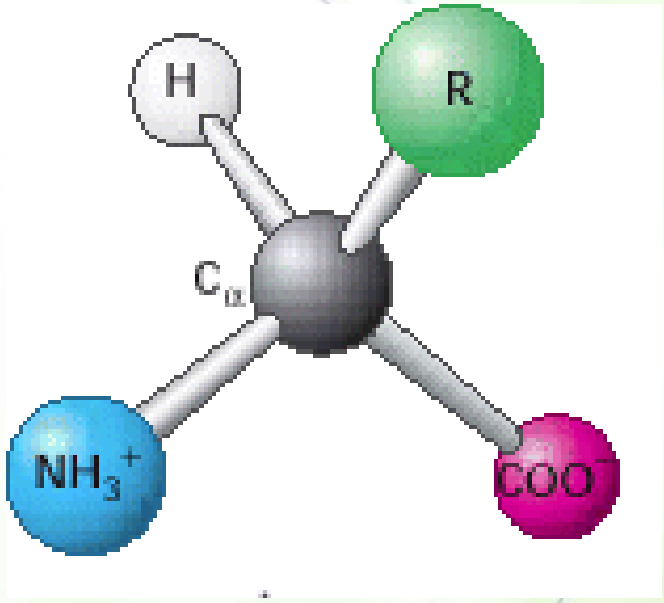
Amino acids

Summer semester 2024

General structure

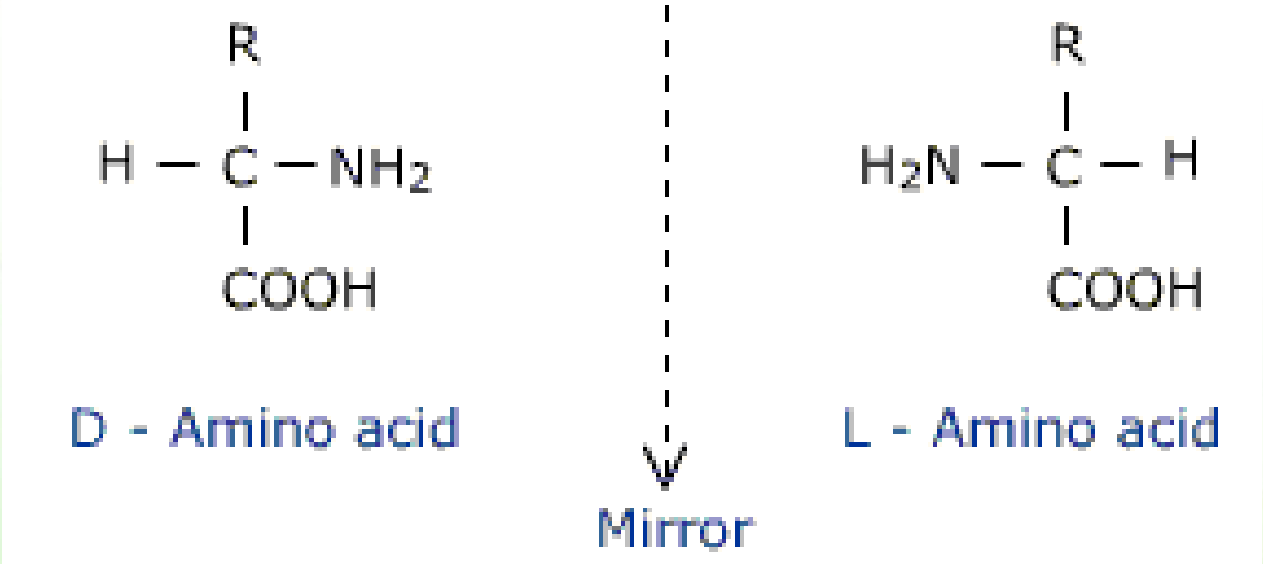
- Proteins are polymers of α-amino acids (or amino acids).
- An amino acid consists of:
  - a central carbon atom, called the α carbon, linked to four groups
  - an amino group (-NH2),
  - a carboxylic acid group (-COOH),
  - a hydrogen atom, and
  - a specific R group (the side chain)



L and D isomers

- The α-carbon atom is chiral and, thus, amino acids are chiral and can be present in two forms, L and D isomers, that are mirror-images of each other (they are enantiomers).
- Only L amino acids naturally make up proteins.

Note that the amino and carboxylic groups of all amino acids are ionized at neutral pH



The amine group of L-amino acids occurs in the left-hand side when drawn in the Fischer projection, keeping the carboxylic acid group on bottom (or top) and the R group on the top, whereas the amine group of the L-amino acids occurs on the left.

Types of amino acids

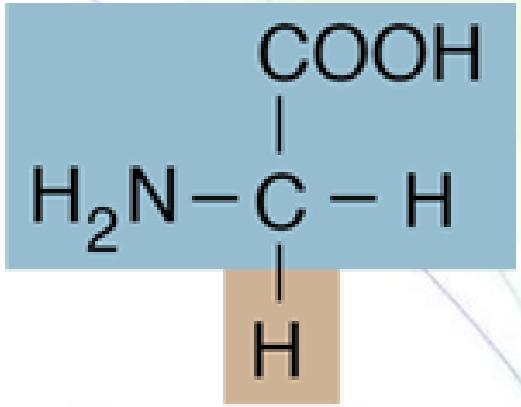
- There are twenty kinds of amino acids depending on the side chains varying in
  - Size
  - Shape
  - Charge
  - Hydrogen-bonding capacity
  - Hydrophobic character
  - Chemical reactivity

Classification (according to R group)

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

Glycine (Gly)

- Glycine is a derivative of acetic acid.



Glycine (gly)

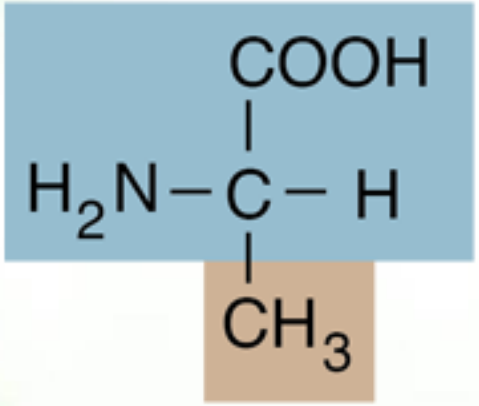
Note that the amino and carboxylic groups are normally ionized at physiological pH

Is it chiral?

Non-polar, aliphatic amino acids

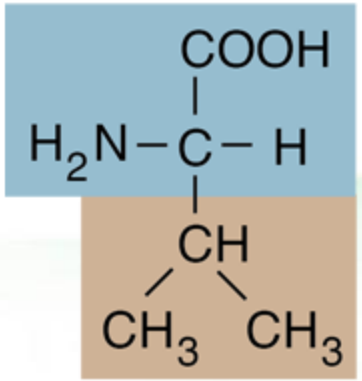
Alanine (Ala)

- Alanine, the next simplest amino acid, has a methyl group (-CH_3) as its side chain.

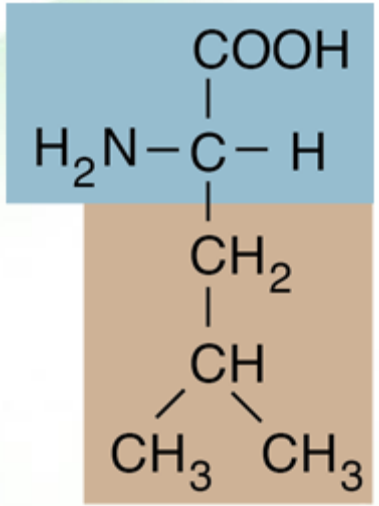


Alanine (ala)

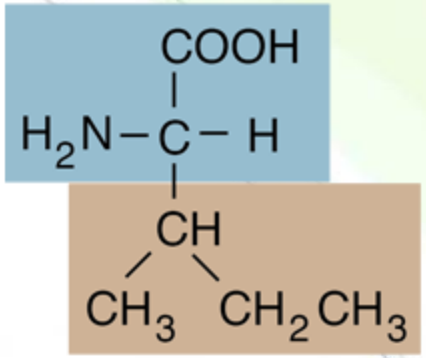
Valine (Val), leucine (Leu), and isoleucine (Ile)



Valine (val)*



Leucine (leu)*



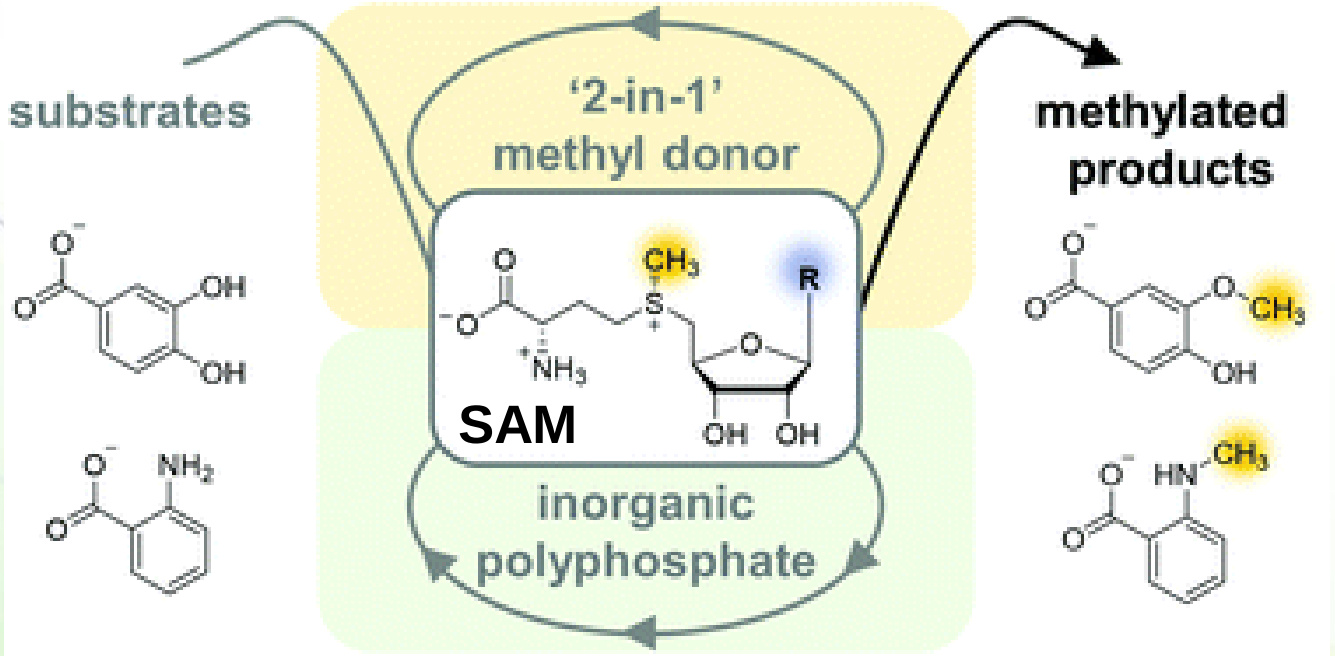
Isoleucine (ile)*

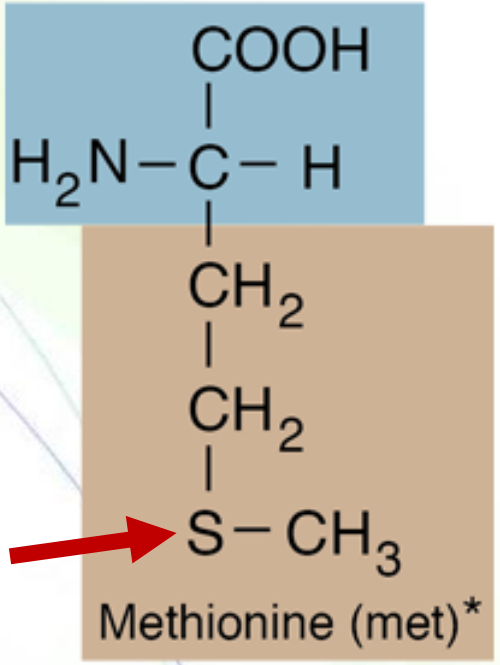
They are branched amino acids.

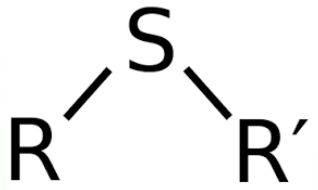
These are *essential amino acids since the body* cannot synthesize them.

Methionine (Met)

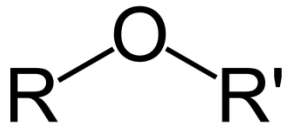
It can form S-Adenosyl-L-Methionine (SAM) which serves as a methyl donor in reactions.







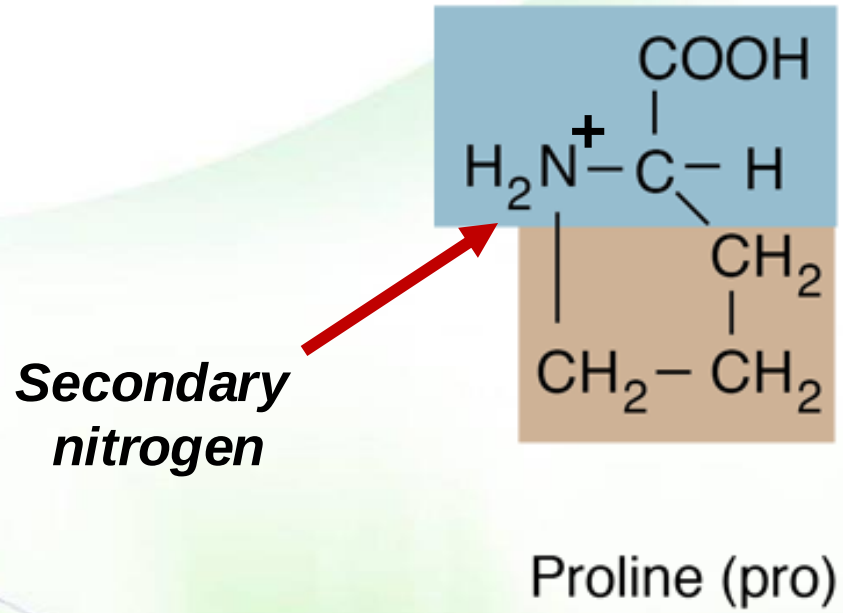
Thioether



Ether

Proline (Pro)

(the only cyclic amino acid)

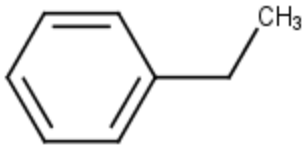


Proline (pro)

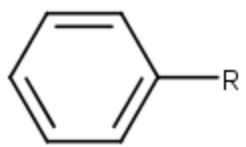
Non-polar, aromatic amino acids

Phenylalanine (Phe) and Tryptophan (Trp)

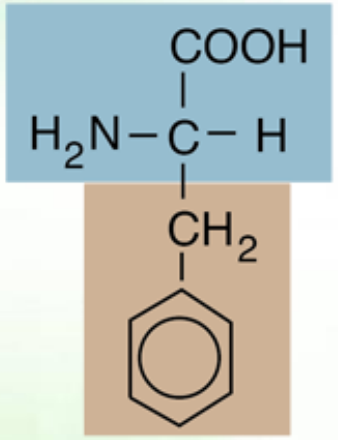
- Phenylalanine contains a phenyl ring.
- Tryptophan has an indole ring; the indole group consists of two fused rings and an NH group.



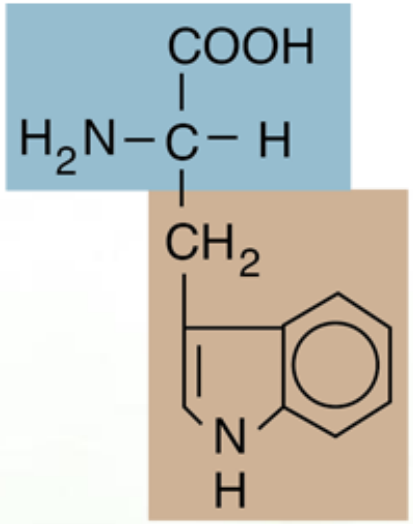
benzyl



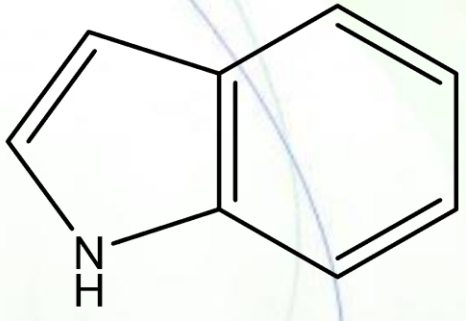
phenyl



Phenylalanine (phe)*



Tryptophan (trp)*

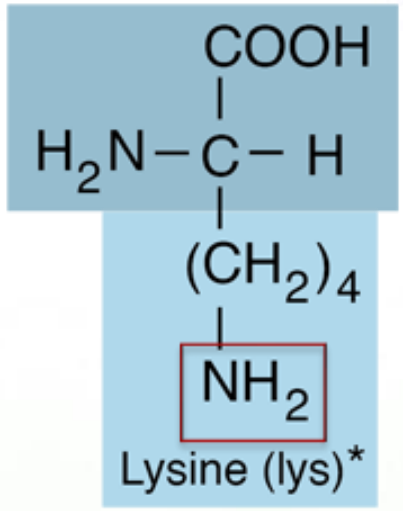


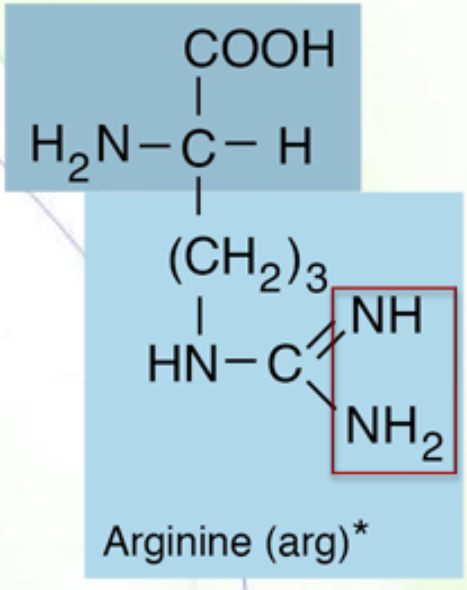
Indole

Positively-charged amino acids

Lysine (Lys) and arginine (Arg)

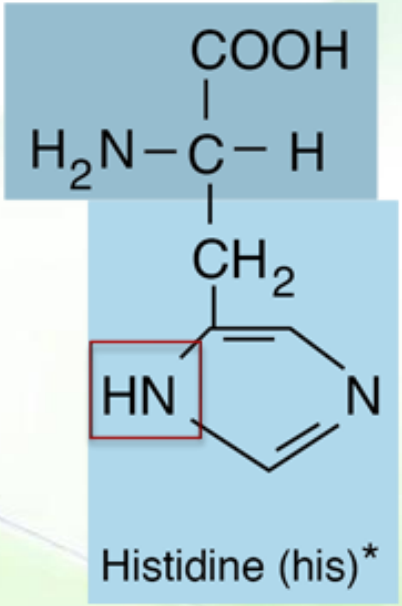
- Lysine and arginine have relatively long side chains that terminate with groups that are positively charged at a neutral pH.
- Lysine ends with a primary amino group and arginine by a guanidinium group.

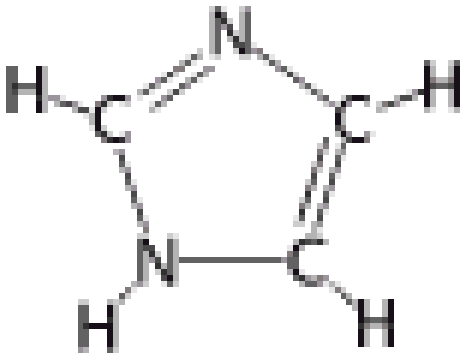




Histidine (His)

- Histidine contains an imidazole group, an aromatic ring that also can be positively charged.



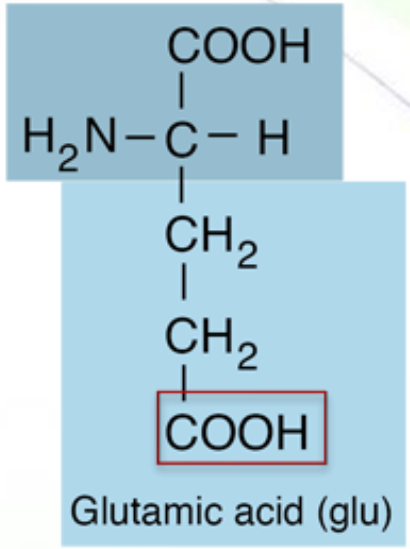


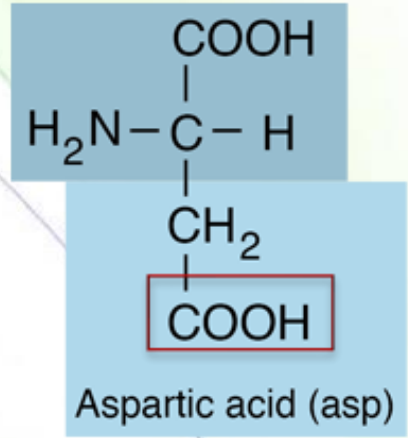
Imidazole

Negatively-charged amino acids

Aspartic acid (Asp) and glutamic acid (Glu)

- Two amino acids contain acidic side chains: aspartic acid and glutamic acid.
- These amino acids are often called aspartate and glutamate when they are charged.

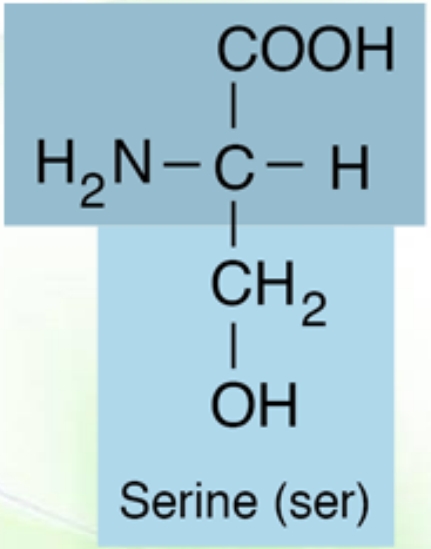


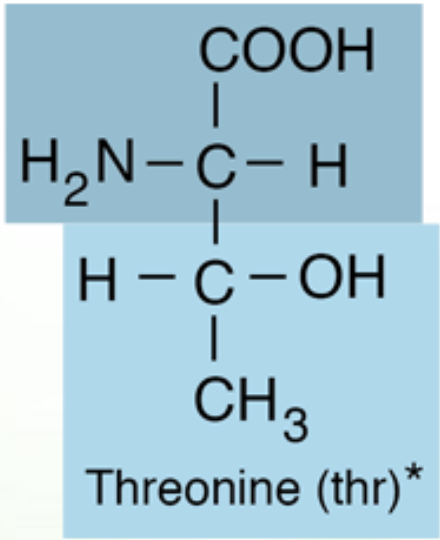


Polar, hydrophilic, neutral amino acids

Serine (Ser) and threonine (Thr)

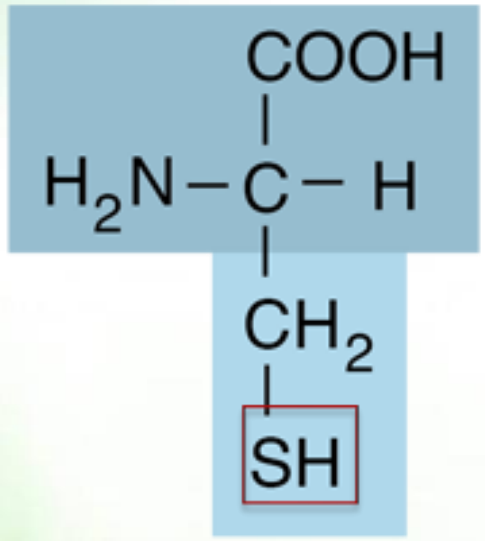
- Serine and threonine, contain aliphatic hydroxyl groups.
- The hydroxyl groups on serine and threonine make them hydrophilic and reactive.





Cysteine (Cys)

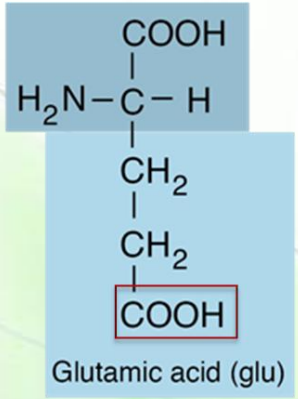
- Cysteine contains a sulfhydryl or thiol (-SH), group.
- The sulfhydryl group is reactive.



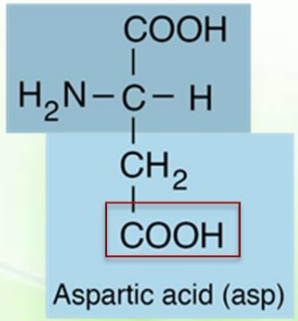
Cysteine (cys)

Asparagine (Asn) and glutamine (Gln)

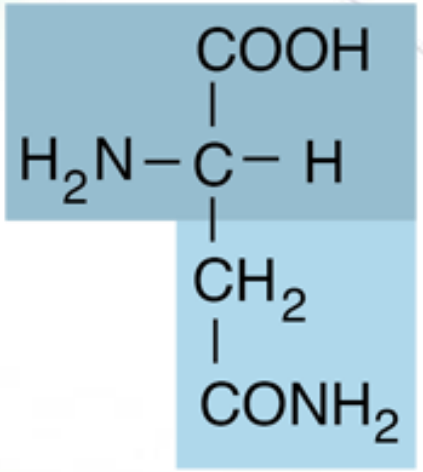
- Asparagine and glutamine are uncharged derivatives of aspartate and glutamate.
- Each contains a terminal carboxamide in place of a carboxylic acid.



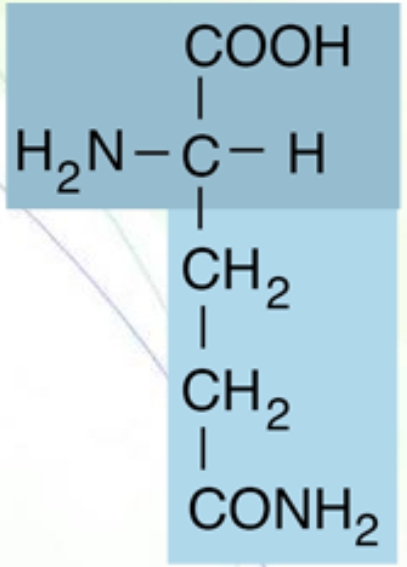
Glutamic acid (glu)



Aspartic acid (asp)



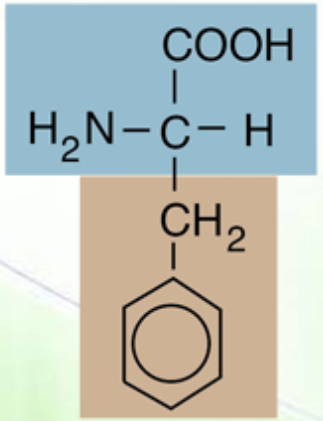
Asparagine (asn)



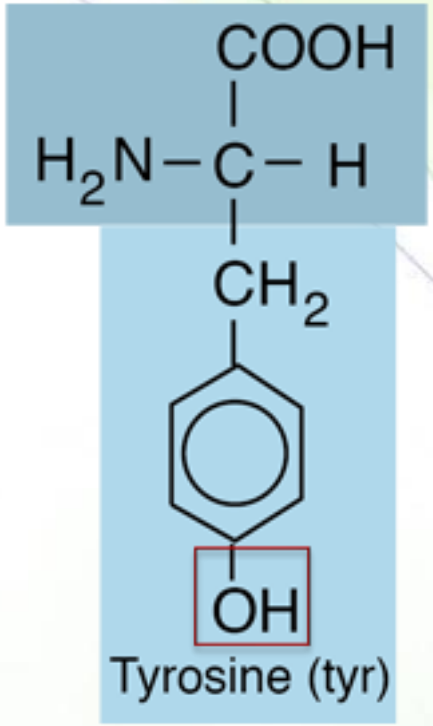
Glutamine (gln)

Tyrosine (Tyr)

- The aromatic ring of tyrosine contains a hydroxyl group.
  - It is derived from phenylalanine.
- This hydroxyl group is reactive.



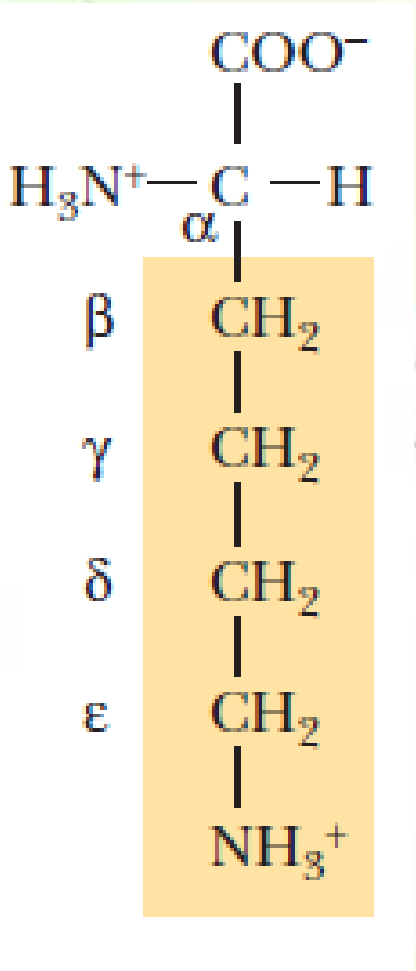
Phenylalanine (phe)*



Tyrosine (tyr)

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.



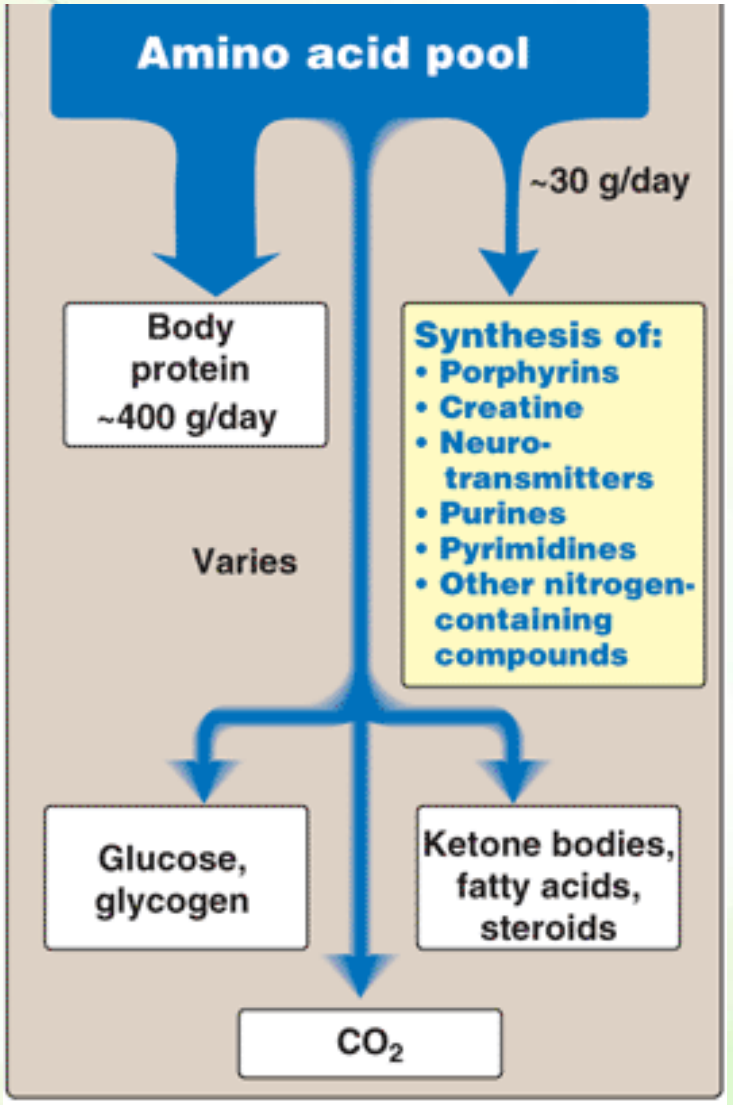
Questions

- Two amino acids are negatively-charged:
- The following amino acid is achiral:
- …etc.

Specialized and uncommon amino acids

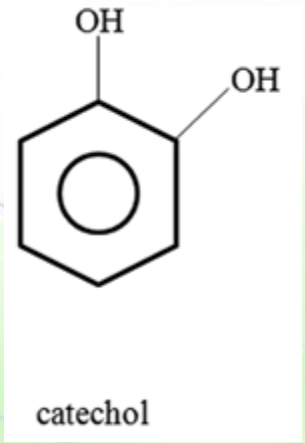
Biological significance of amino acids

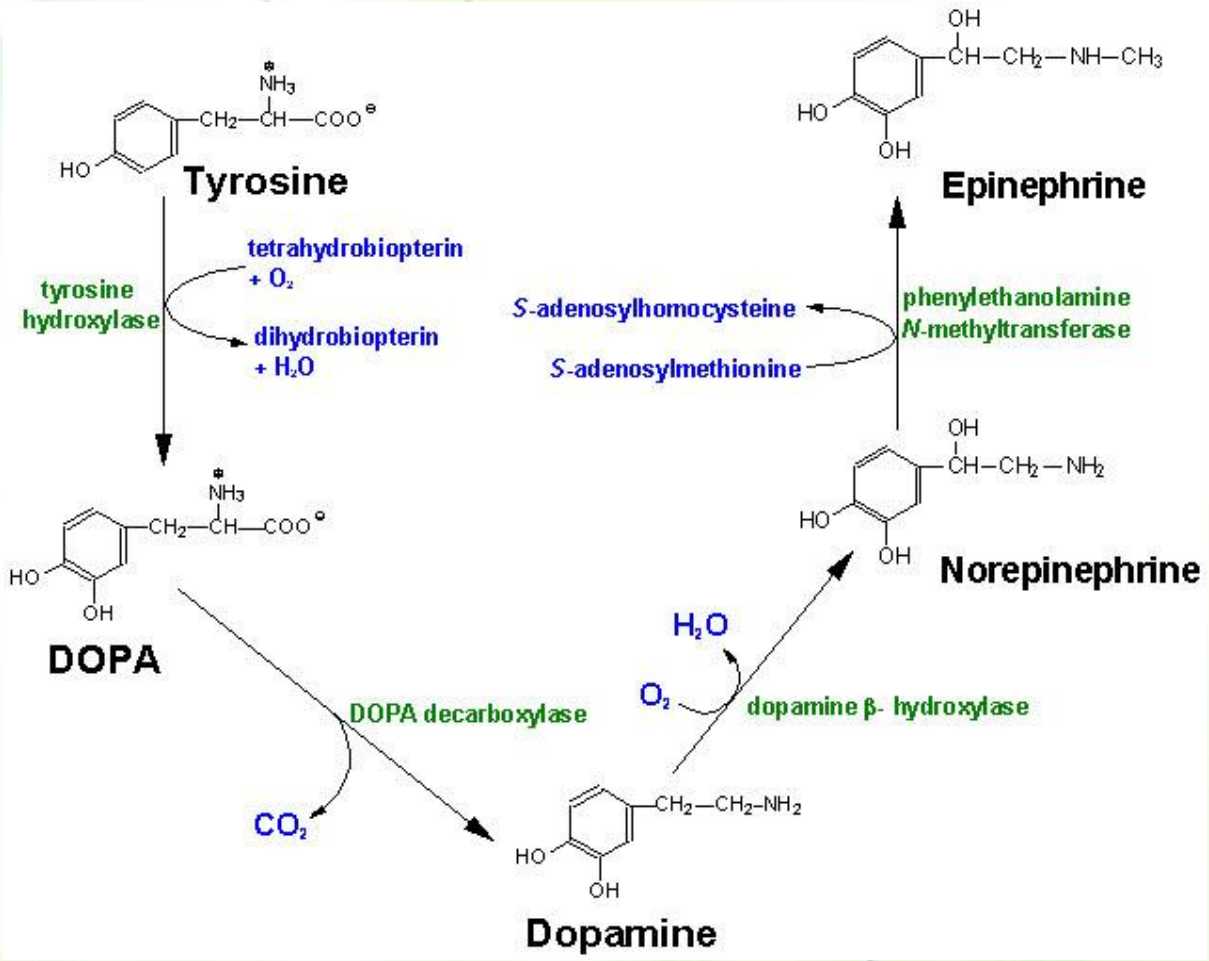
- α-nitrogen atom of amino acids is a primary source for many nitrogenous compounds:
  - Hormones
  - Neurotransmitters
  - Biologically active peptides



Tyrosine (1)

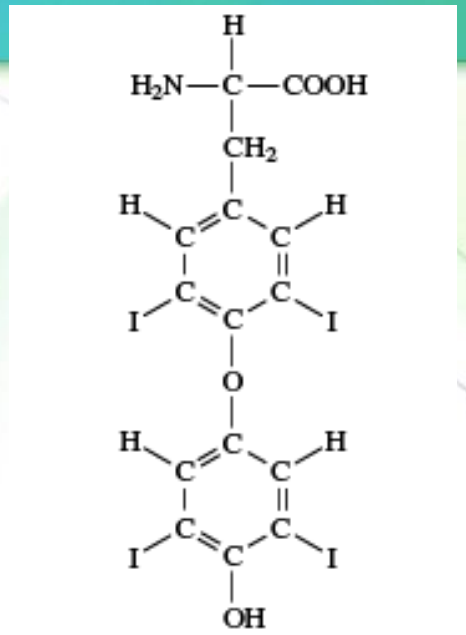
- It is converted into catecholamine neurotransmitters.
  - Dopamine
  - Norepinephrine
  - Epinephrine
    - flight or fight

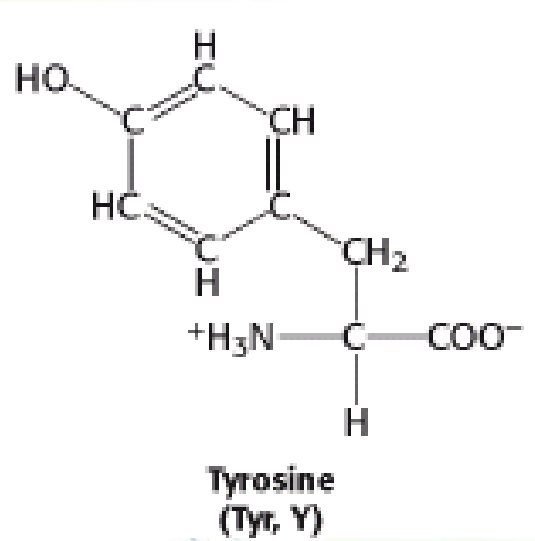


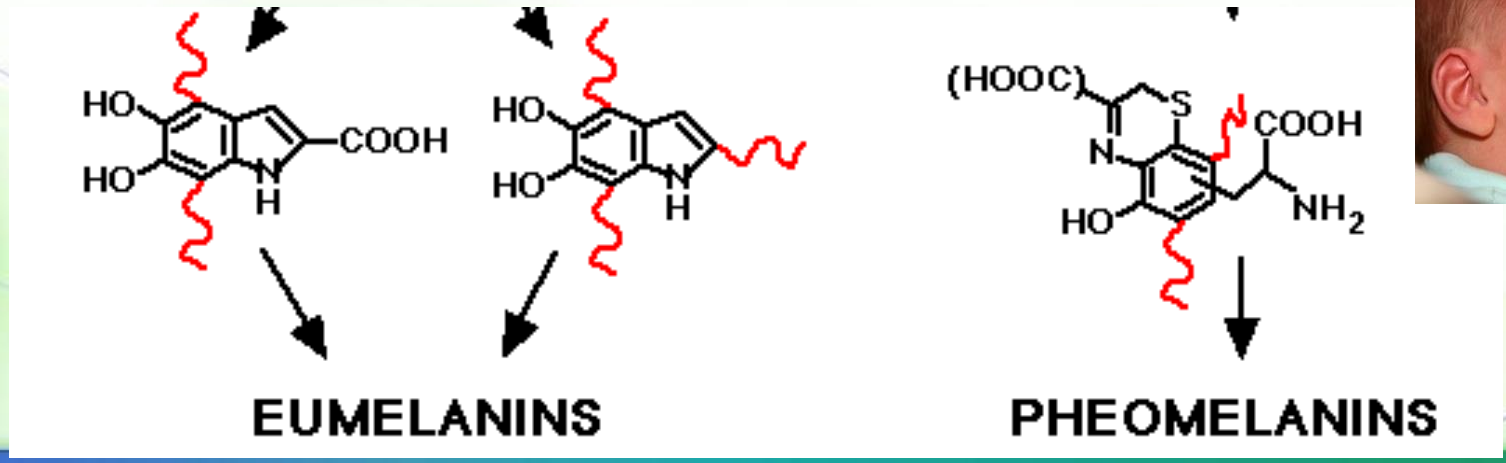


Tyrosine (2)

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

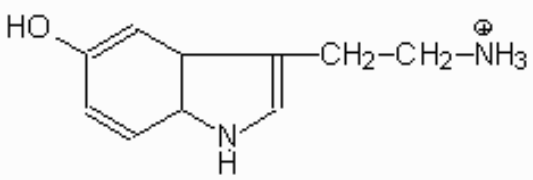




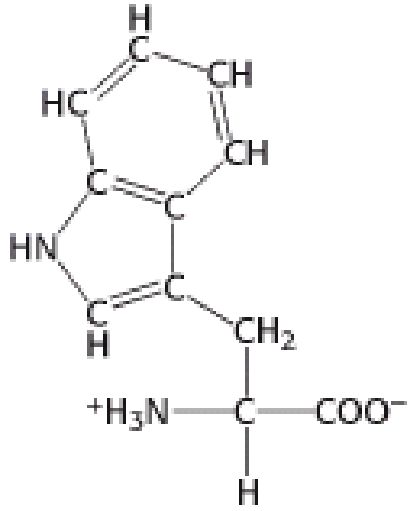


Tryptophan

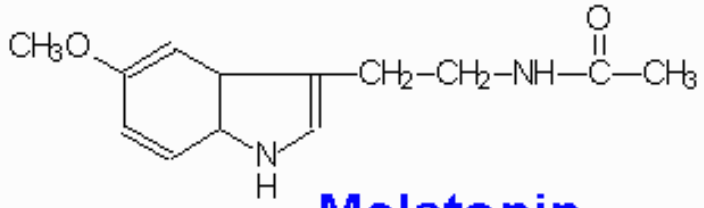
- Tryptophan serves as the precursor for the synthesis of Neurotransmitters
  - Serotonin (neurotransmitter-sedative)
  - Melatonin (day-night cycle)



Serotonin
(5-hydroxytryptamine)



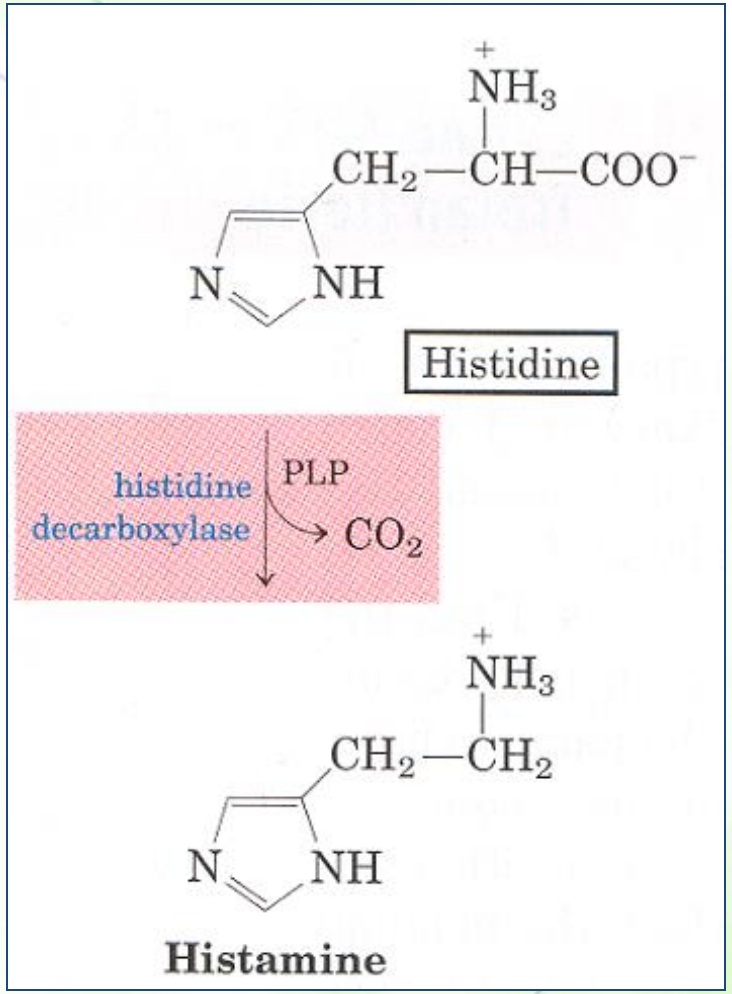
Tryptophan
(Trp, W)



Melatonin

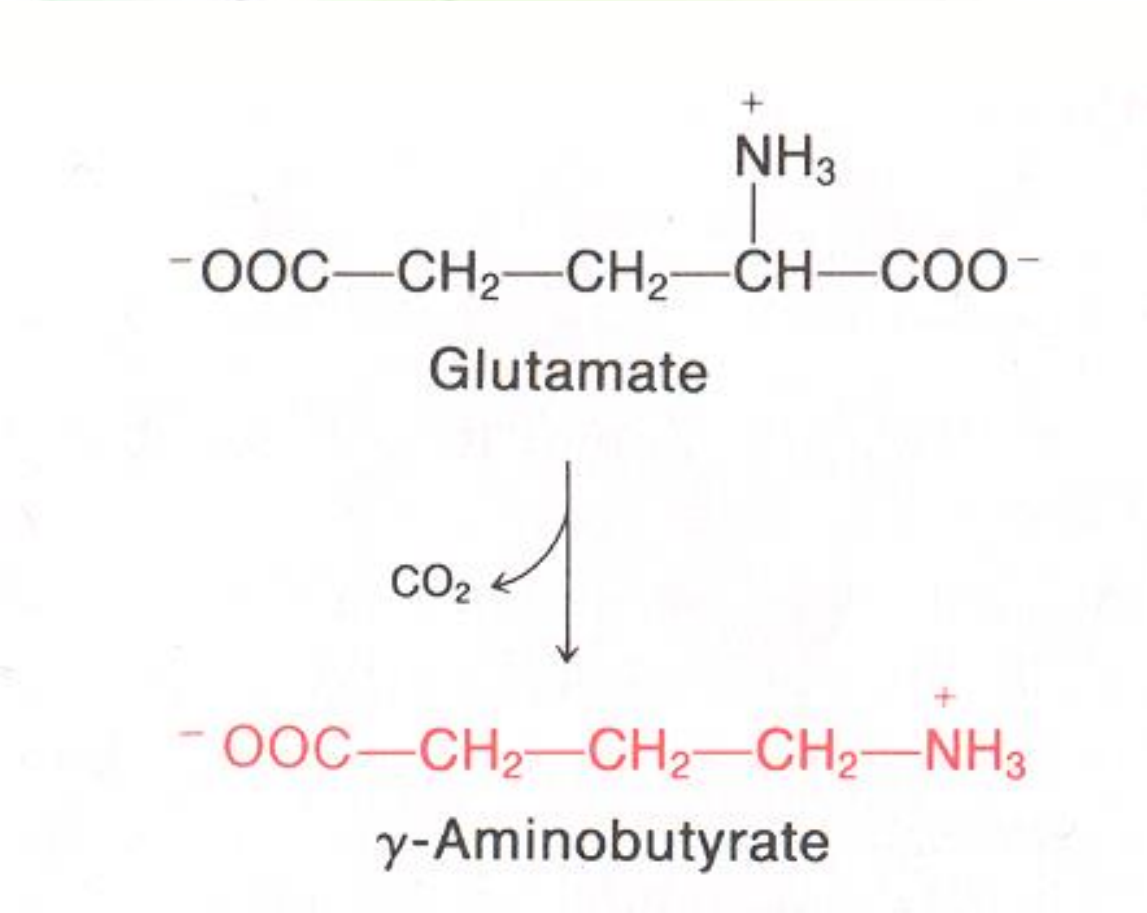
Histamine

- Acts as a neurotransmitter
- Causes allergic symptoms (a major causes for asthma)



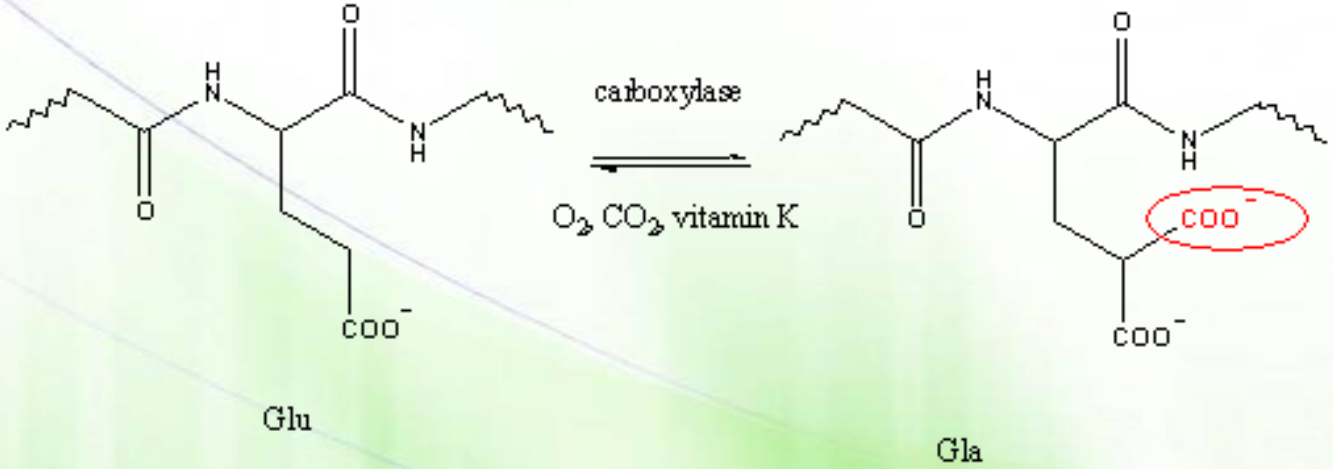
Glutamate

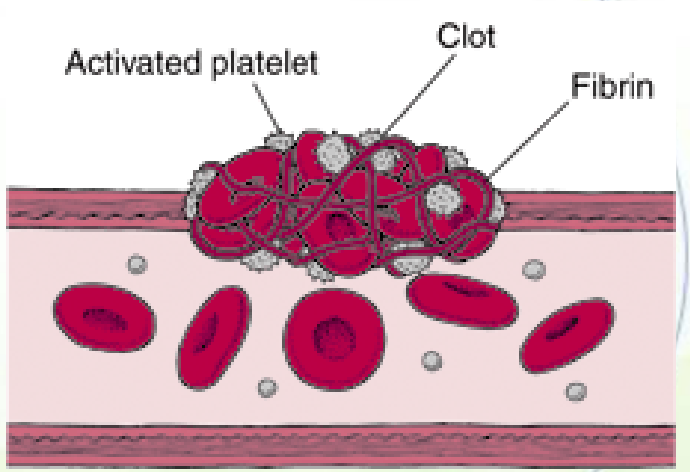
- It is a precursor of γ-aminobutyric acid (GABA), an inhibitory neurotransmitter.
- It has relaxing, anti-anxiety and anti-convulsive effects.



γ- carboxyglutamate (Gla)

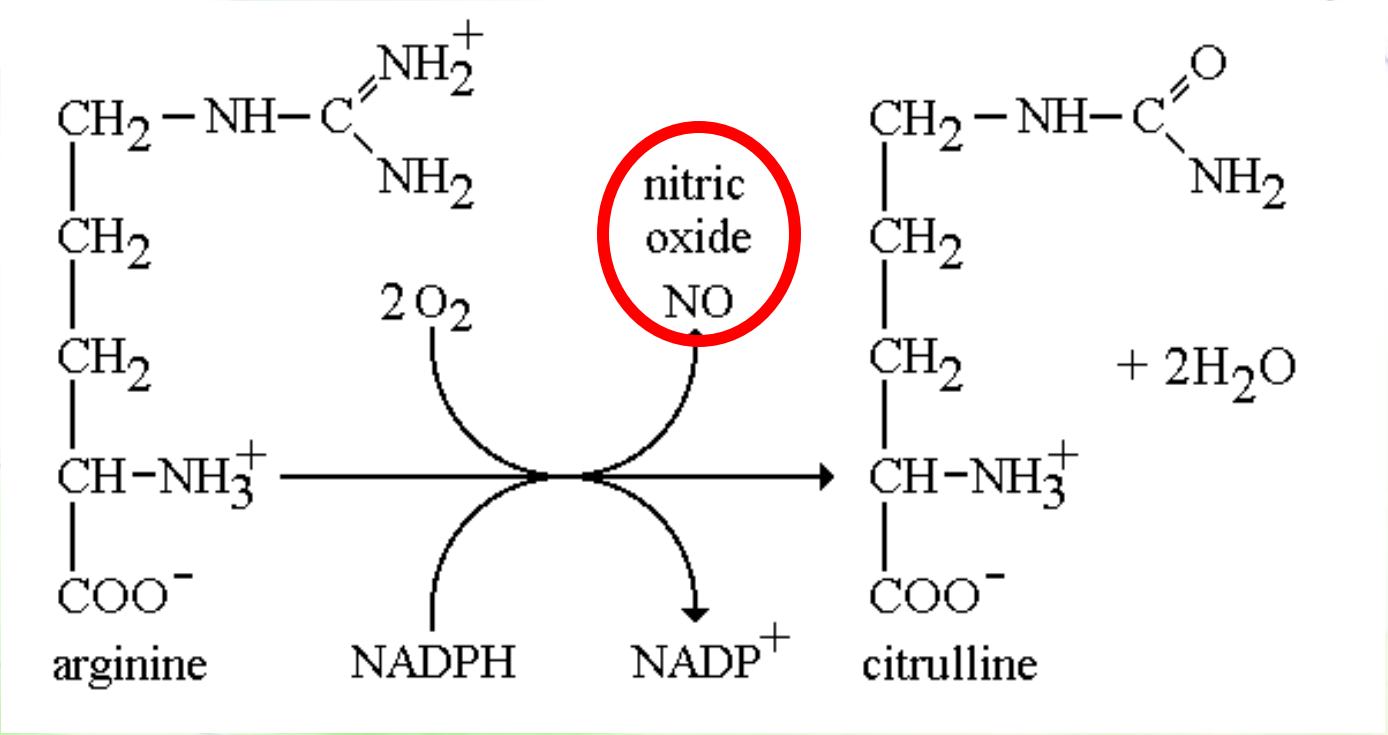
- The glutamate residues of some blood proteins factors are carboxylated to form γ- carboxyglutamate (Gla) residues.
  - Vitamin K is essential for the process
- This carboxylation is essential for blood clotting.





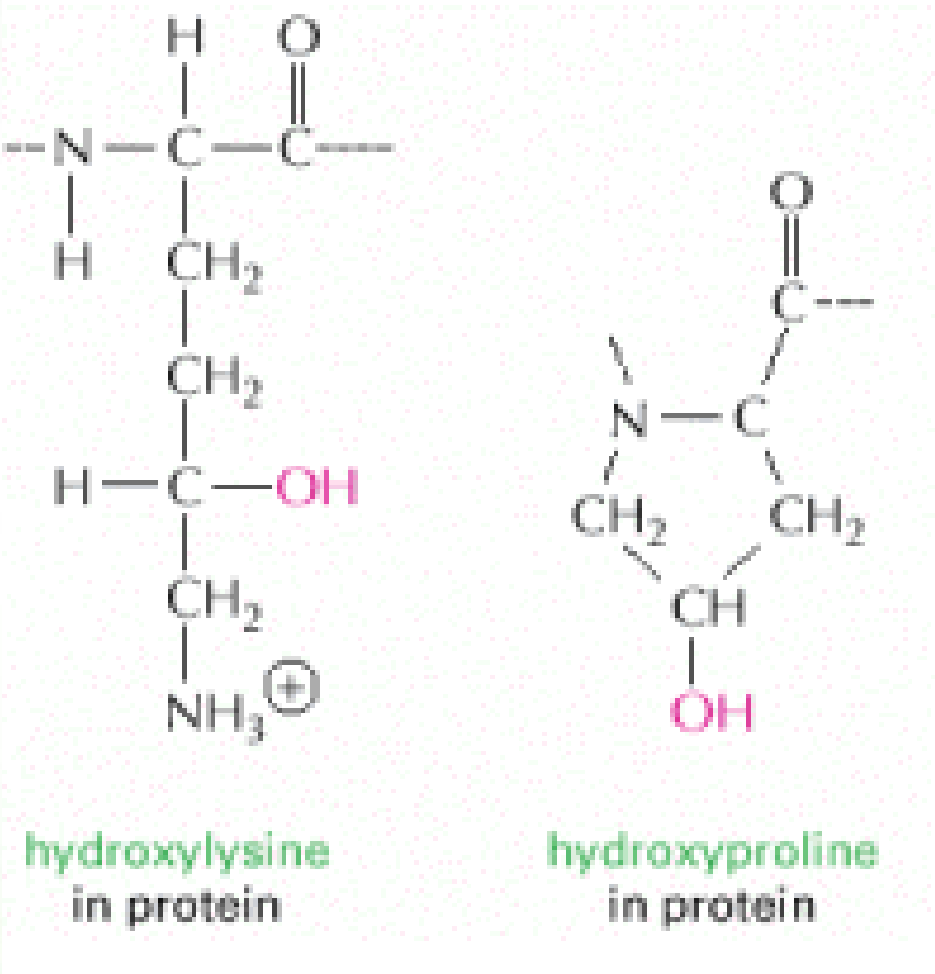
Arginine

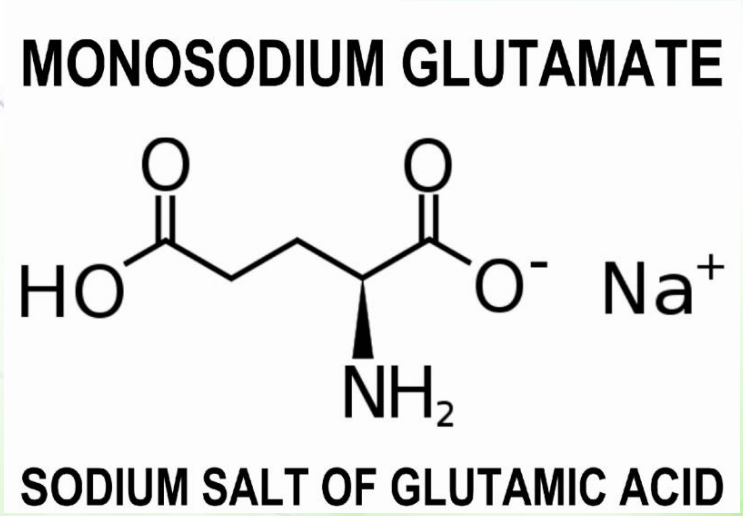
- L-arginine is the precursor of nitric oxide (NO)
- NO functions:
  - Vasodilation, inhibition of platelet adhesion, anti-inflammatory



Hydroxylysine and hydroxyproline

- Lysine and proline are hydroxylated and are part of collagen structure.
- Both are modified after protein synthesis.





Biochemical applications: Monosodium glutamate (MSG)

Glutamic acid derivative

Flavor enhancer, Asian food.

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

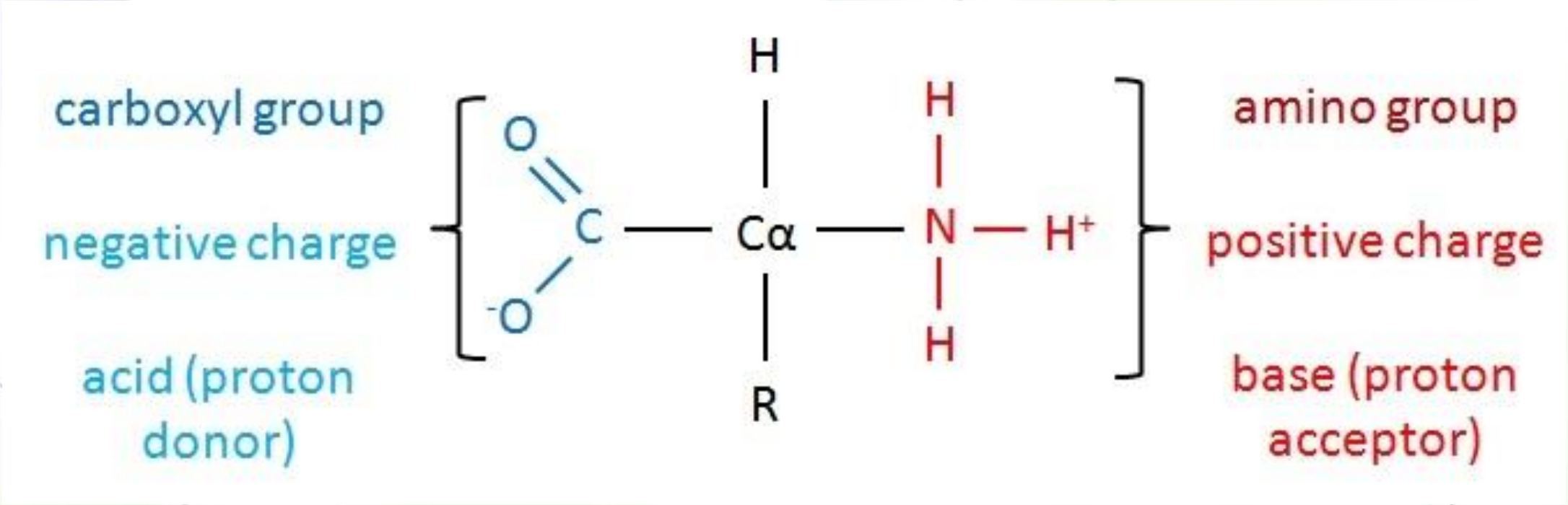
Chinese restaurant syndrome.

QUIZ

- What is special about (example: proline)?
- An acidic amino acid is_____ charged at physiological conditions.
- Name 2 amino acids that share a functional group in their side chain.

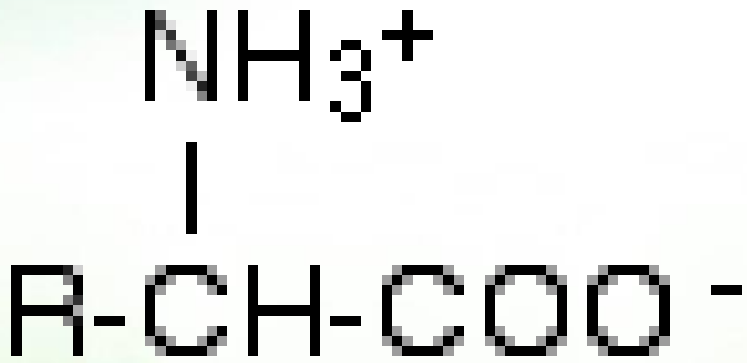
Ionization of amino acids

Why do amino acids get ionized?



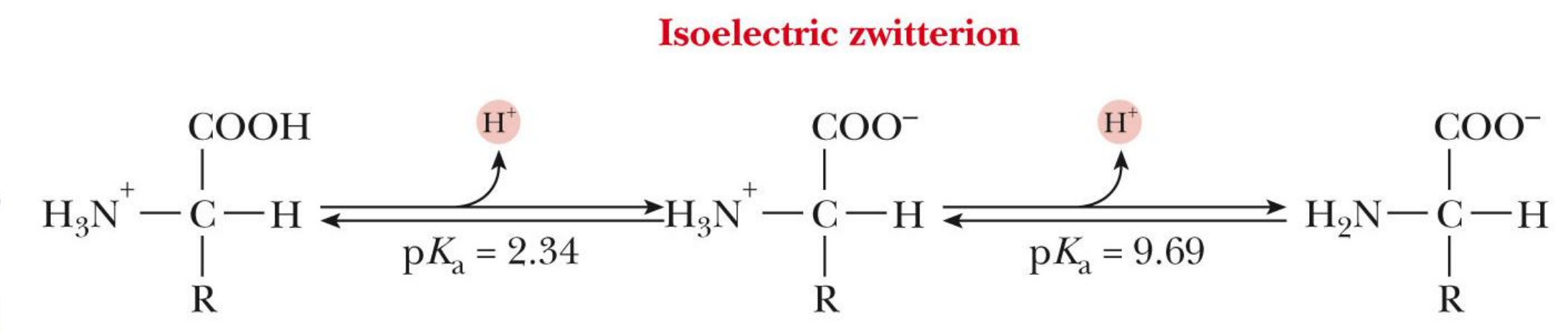
Zwitterion and isoelectric point

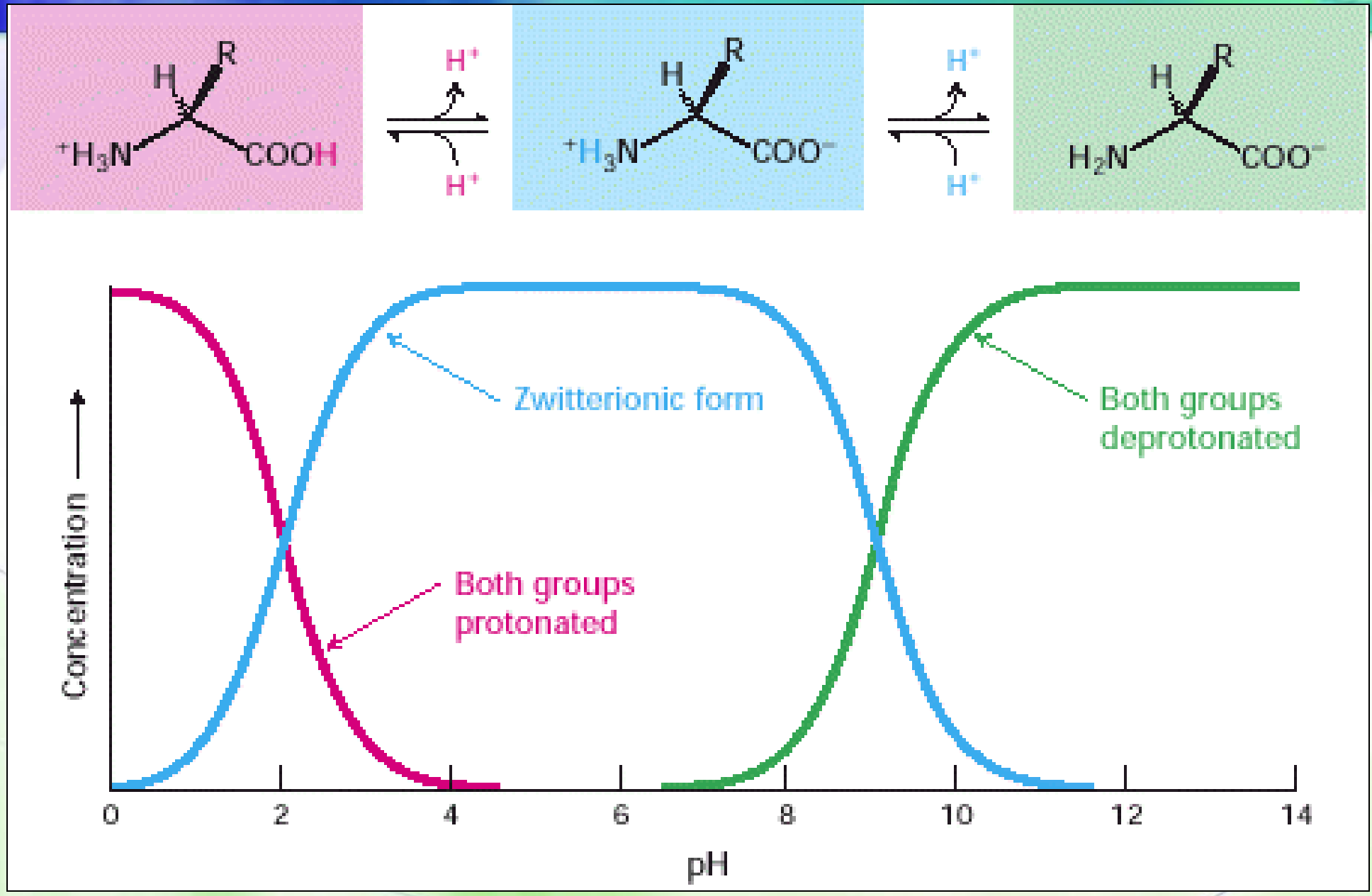
- At physiological pH, amino acids (without ionizable groups) are electrically neutral.
- Zwitterion: a molecule with two opposite charges and a net charge of zero.



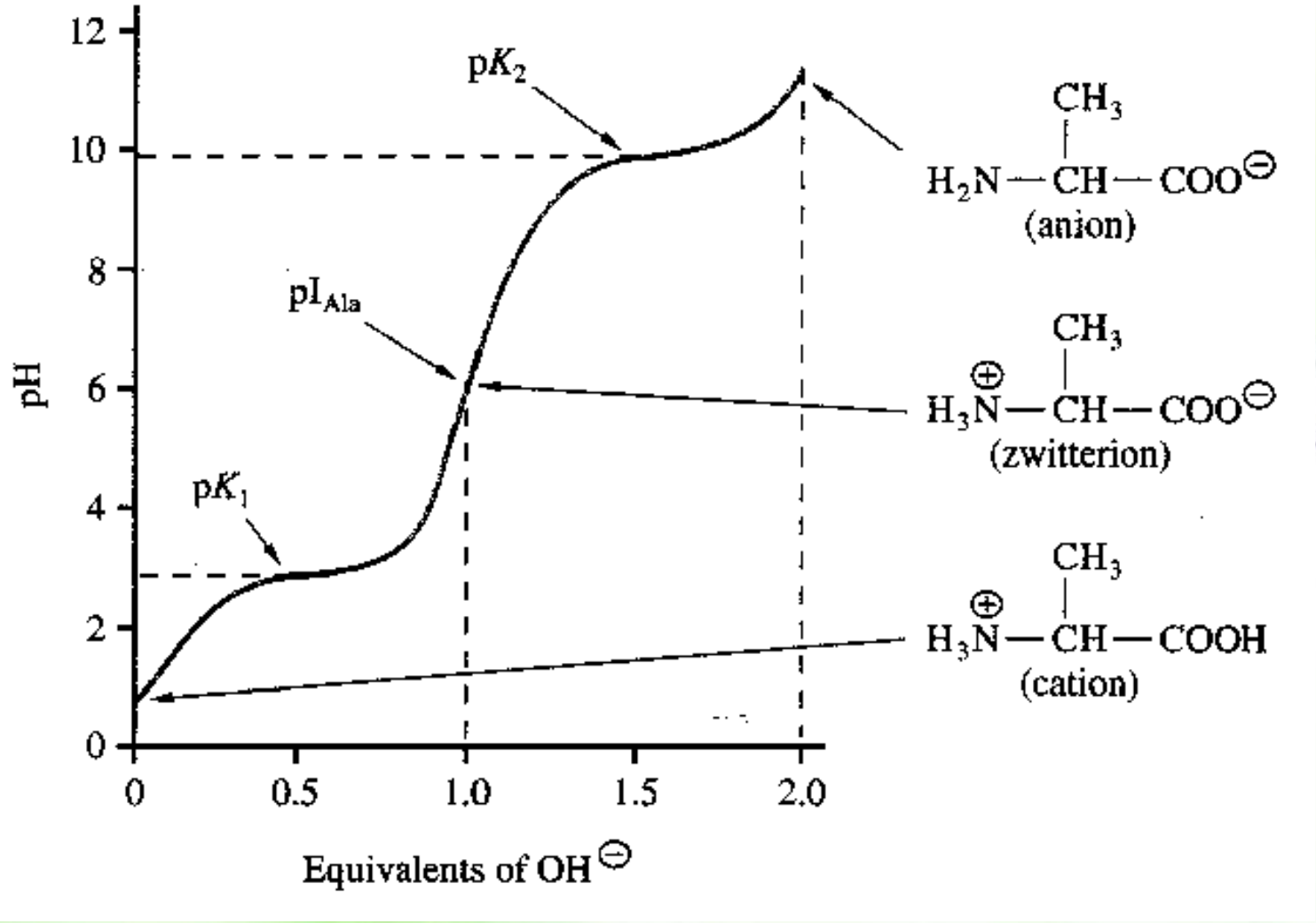
a zwitterion

Effect of pH


Isoelectric zwitterion
COOH
H_3N^+—C—H
R
H^+
$pK_a = 2.34$
COO^-
H_3N^+—C—H
R
H^+
$pK_a = 9.69$
COO^-
H_2N—C—H
R


H
R
+H3N
COOH
H+
H+
H
R
+H3N
COO−
H+
H+
H
R
H2N
COO−
Concentration
Zwitterionic form
Both groups
protonated
Both groups
deprotonated
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 isoelectric point or pI is the pH where the net charge of a molecules such as an amino acid or protein is zero.
- For the nonpolar and polar amino acids with two pKa's, the isoelectric point is calculated by taking the average of the pKa's of the carboxyl group and the amino group.

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

Ionization of side chains

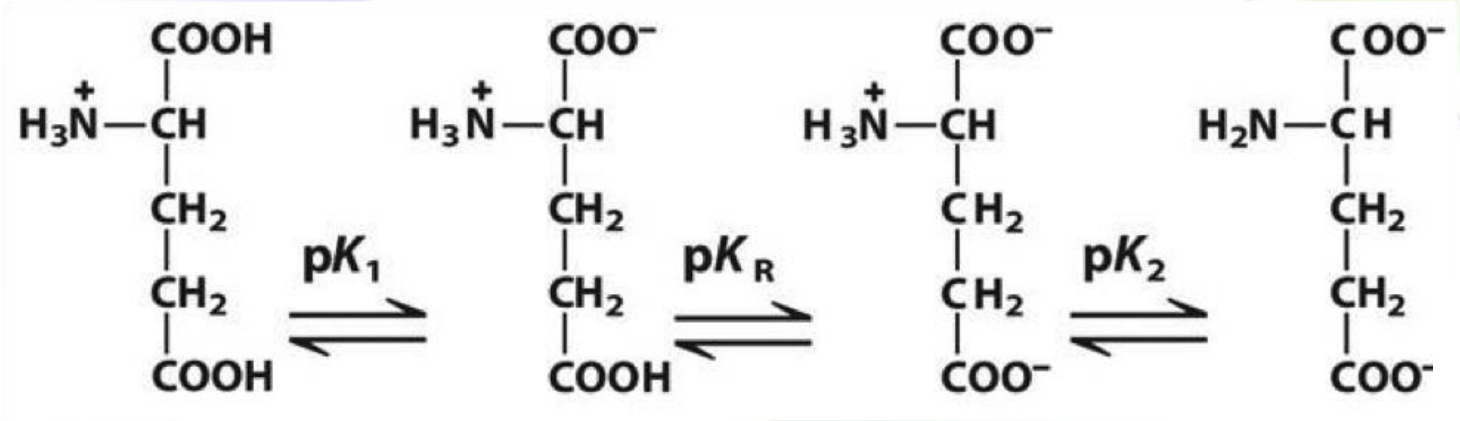
- 7 of the 20 amino acids have ionizable side chains near physiological pH.
- These amino acids are tyrosine, cysteine, arginine, lysine, histidine, and aspartic and glutamic acids.
- Each side chain has its own pKa values for ionization of the side chains.

pI of amino acids

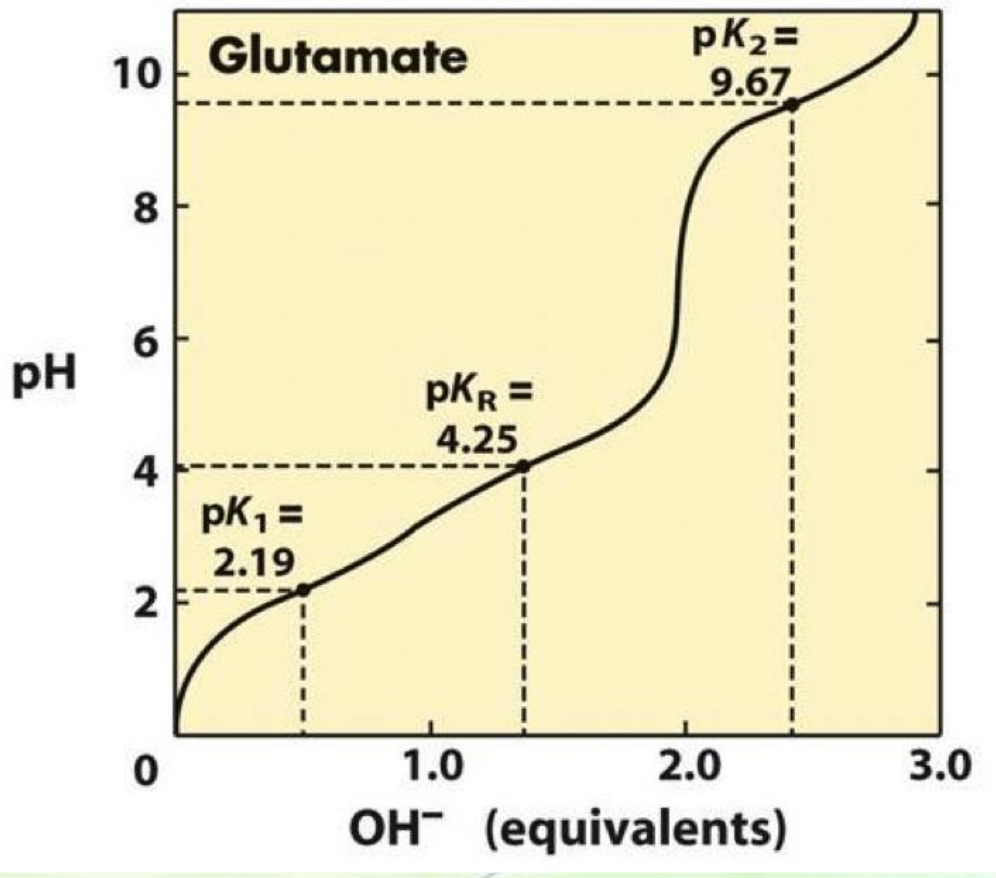
Amino Acid	Side Chain pK_a (approx.	pI
Arginine	12.5	10.8
Aspartic Acid	4.0	3.0
Cysteine	8.0	5.0
Glutamic Acid	4.1	3.2
Histidine	6.0	7.5
Lysine	11.0	10
Tyrosine	10.0	9.5

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

Example: Glutamate



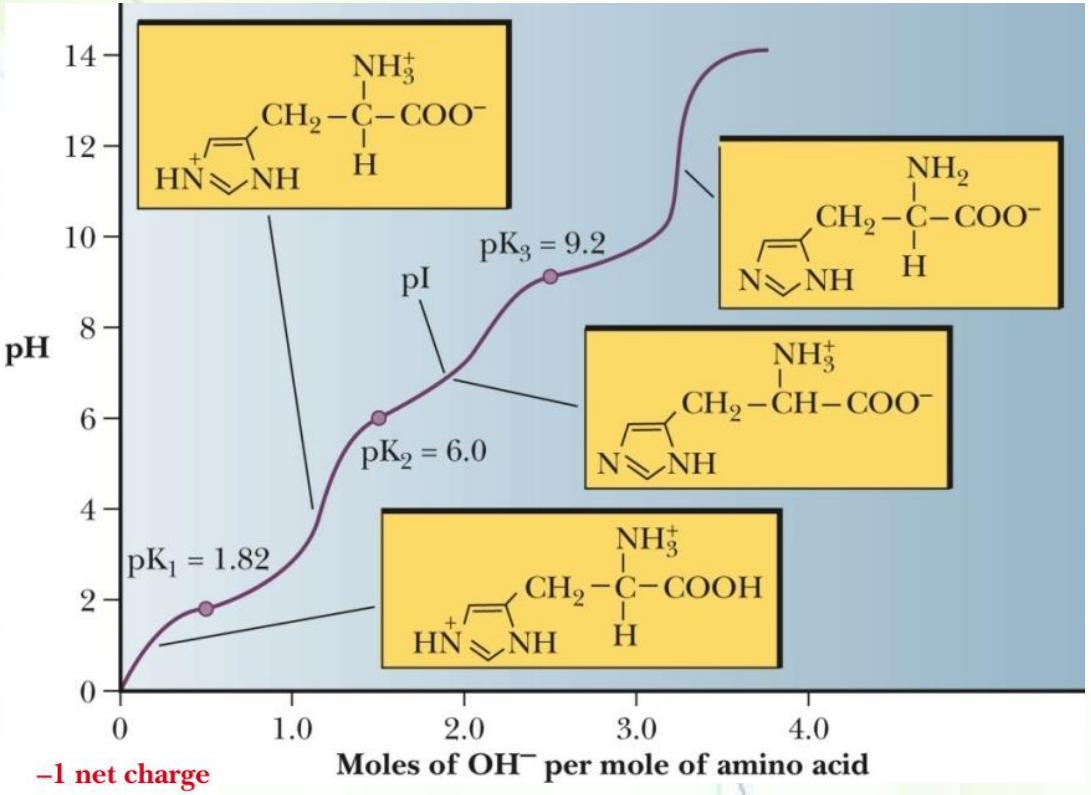
- To calculate the isoelectric point of Glu, the pKa's of the two carboxyl groups are averaged.

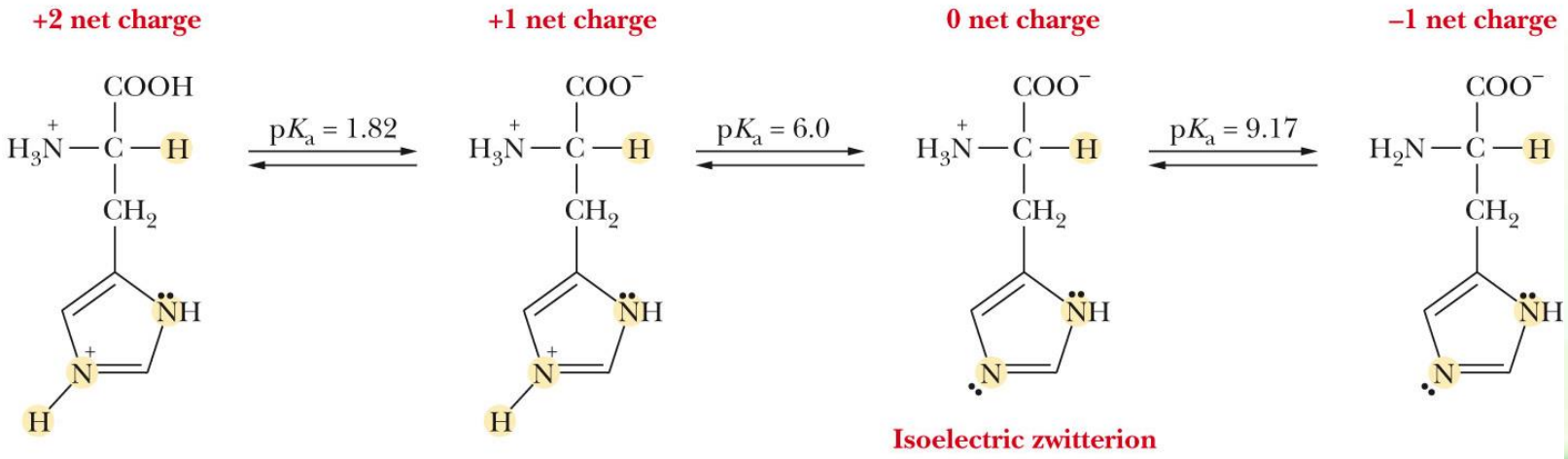


Histidine

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

Note that the pKa's of the side chains are different when amino acids are part of proteins.





Questions

- Draw the titration curve of histidine.
- What is the ratio of conjugate base/acid of glutamate at pH 4.5?
- 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