Proteins

Definition

- Protein from the Greek proteios, meaning primary.
- Proteins are the work horses of biological systems.
  - They play key roles in constructing and maintaining living cells
- Our genes code for proteins
- Proteins are polymers of amino acids

Proteins are:

Polypeptides + (cofactors, coenzymes, prosthetic groups, other modifications)

- Polypeptides are covalently linked α-amino acids
- Cofactors are non-amino acid components e.g. metal ions like Zn^{2+} in carboxypeptidase
- Coenzymes are organic cofactors e.g. nucleotides in lactate dehydrogenase
- Prosthetic groups are covalently attached cofactors e.g. heme in myoglobin

Roles played by proteins include

- Enzymes (biological catalysts)
- Hormones
- Storage proteins
- Transport proteins
- Structural proteins
- Protective proteins
- Contractile proteins
- Toxic proteins

Food Proteins

- Palatable
- Digestible
- Non-toxic
- Available Economically

Proteins in the Diet

- 9 of the 20 amino acids must be obtained from the diet
- These are referred to as the essential amino acids.
  - Histidine
  - Isoleucine
  - Leucine
  - Lysine
  - Methionine
  - Phenylalanine
  - Threonine
  - Tryptophan
  - Valine
- Proteins are also the major source of nitrogen in the diet

Protein Structure

- 20 Amino Acids
- Primary
- Secondary
- Tertiary
- Quaternary
- Denatured

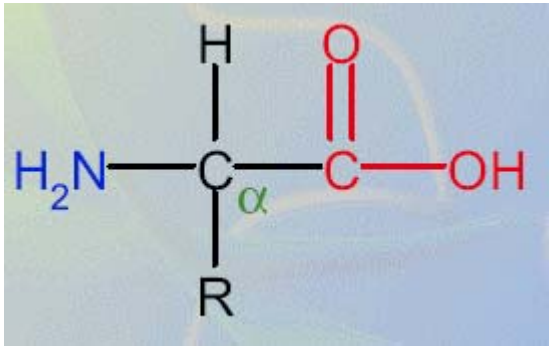
Coded in DNA

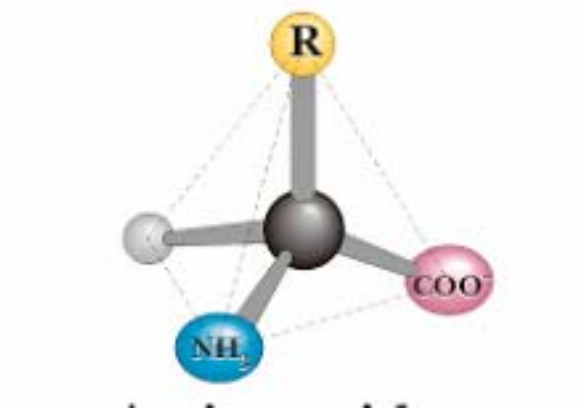
Self assembly to a single (native) structure. Depends on primary structure and solution conditions

Common in foods. Many non-native forms depending on protein structure, solution conditions (& history) and ingredient interactions

Protein Structure and Function

- Protein are polymers of α-amino acids
- The amino acids used to make proteins are 2-amino-carboxylic acids.





- The α (alpha) carbon is the carbon to which a functional group is attached.

Properties of Amino Acids

- structure and chemical functionality
- chirality
- acid-base properties
- capacity to polymerize

Properties of Amino acids

- Aliphatic chains: Gly, Ala, Val, Leu, and Ile
  - Pro?

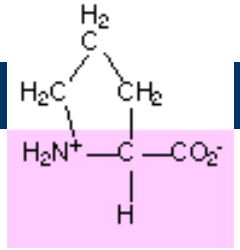
hydrophobicity →

- Hydroxyl or sulfur side chains: Ser, Thr, Cys, Met
- Aromatic: Phe, Trp, Tyr
- Basic: His, Lys, Arg
- Acidic and their amides: Asp, Asn, Glu, Gln

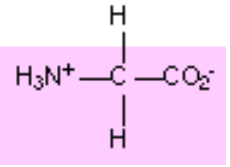
Aliphatic (alkane) Amino Acids

Hydrophobicity

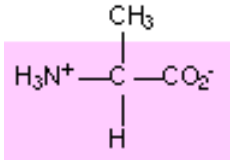
- Proline(pro, P) – cyclic "imino acid"



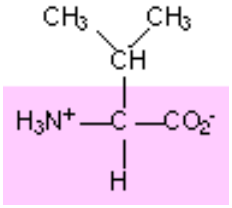
- Glycine(gly, G)– only non-chiral amino acid, not hydrophobic



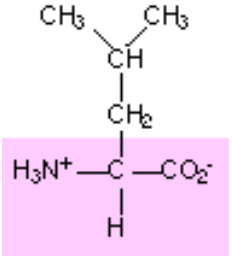
- Alanine(ala, A) – R- group = methyl-group

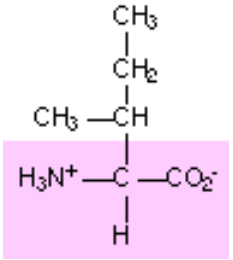


- Valine(Val, V) – Think V!



- Leucine(Leu, L) –

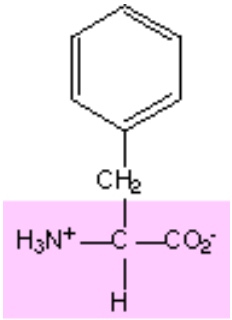


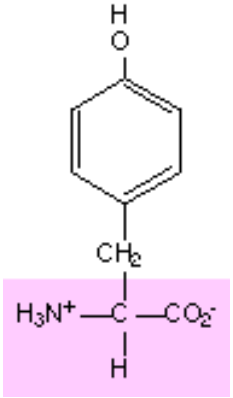


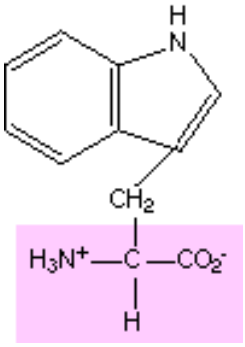
- Isoleucine(Ile, I) - 2 chiral carbons

Aromatic Amino Acids

- All very hydophobic
- All contain aromatic group
- Absorb UV at 280 nm
- Phenylalanine(Phe, F)
- Tyrosine(Tyr,Y) – -OH ionizable (pKa = 10.5), H-Bonding
- Tryptophan(Trp, W) – bicyclic indole ring, H-Bonding

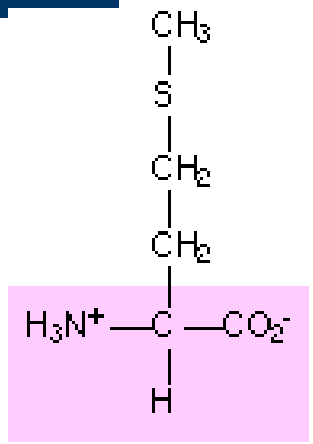




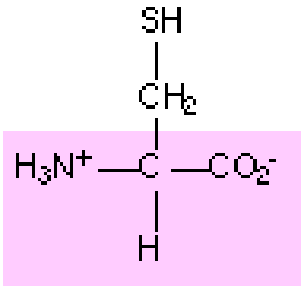


Sulfur Containing Amino Acids

- Methionine (Met, M) – "start" amino acid, very hydrophobic

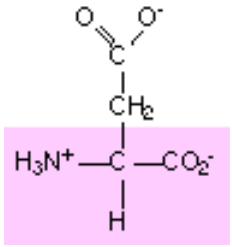


- Cysteine (Cys,C) – sulfur in form of sulfhydroyl, important in disulfide linkages, weak acid, can form hydrogen bonds.

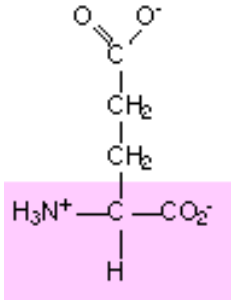


Acidic Amino Acids

- Contain carboxyl groups (weaker acids than α-carboxyl-group)
- Negatively charged at physiological pH, present as conjugate bases (therefore –ate not –ic acids)
- Carboxyl groups function as nucleophiles in some enzymatic reactions
- Aspartate –

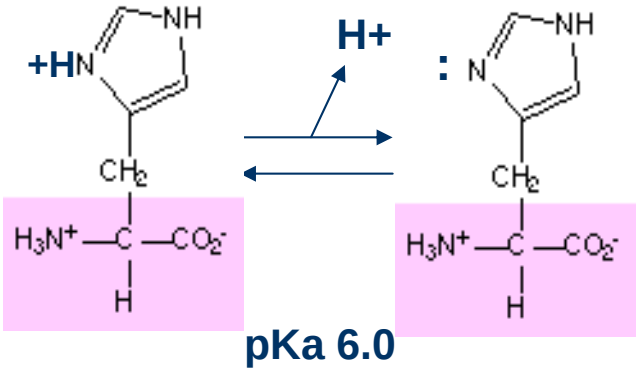


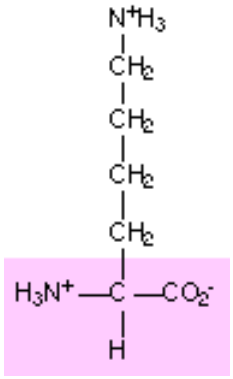
- Glutamate –

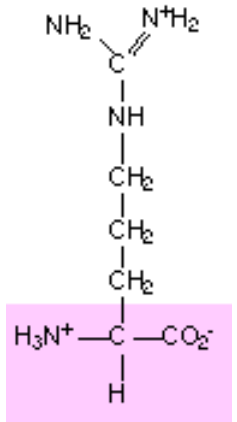


Basic Amino Acids

- Hydrophillic nitrogenous bases
- Positively charged at physiological pH
- Histidine – imidazole ring protonated/ionized, only amino acid that functions as buffer in physiol range.
- Lysine - diamino acid, protonated at pH 7.0
- Arginine - guianidinium ion always protonated, most basic amino acid

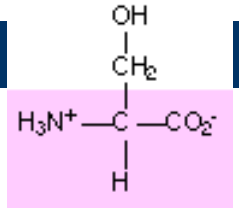




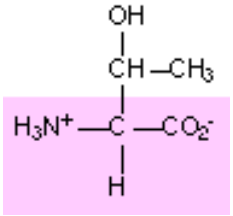


Polar Uncharged Amino Acids

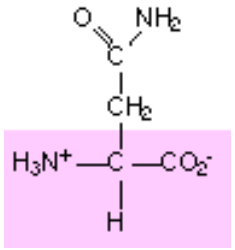
- Serine(Ser, S) – looks like Ala w/ -OH



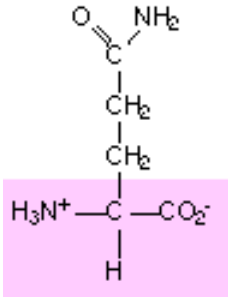
- Threonine(Thr, T) – 2 chiral carbons



- Asparagine(Asn, N) – amide of aspartic acid



- Glutamine (Gln, Q) – amide of glutamic acid



Other Amino Acids - in proteins

Result from “post-translational” modifications examples:

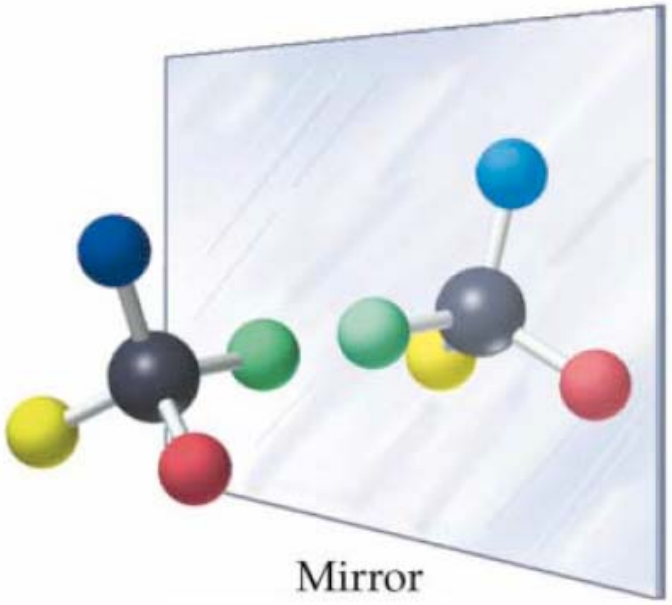
- Hydroxylysine, hydroxyproline - collagen
- Carboxyglutamate - blood-clotting proteins
- Pyroglutamate - bacteriorhodopsin
- Phosphorylated amino acids - signaling device
- D- alanine, D-glutamic acid: bacterial cell wall polypetides
- γ-aminobutyric acid: neurotransmitter
- Homoserine: intermediate in amino acid metabolism
- Ornithine: intermediate in arginine synthesis

Functional significance

- Hydrophobic amino acids: encountered in the interior of proteins shielded from direct contact with water
- Hydrophillic amino acids: generally found on the exterior of proteins as well as in the active centers of enzymes
- Imidazole group: act as either proton donor or acceptor at physiological pH
  - Reactive centers of enzymes
- Primary alcohol and thiol groups: act as nucleophiles during enzymatic catalysis
  - Disulfide bonds

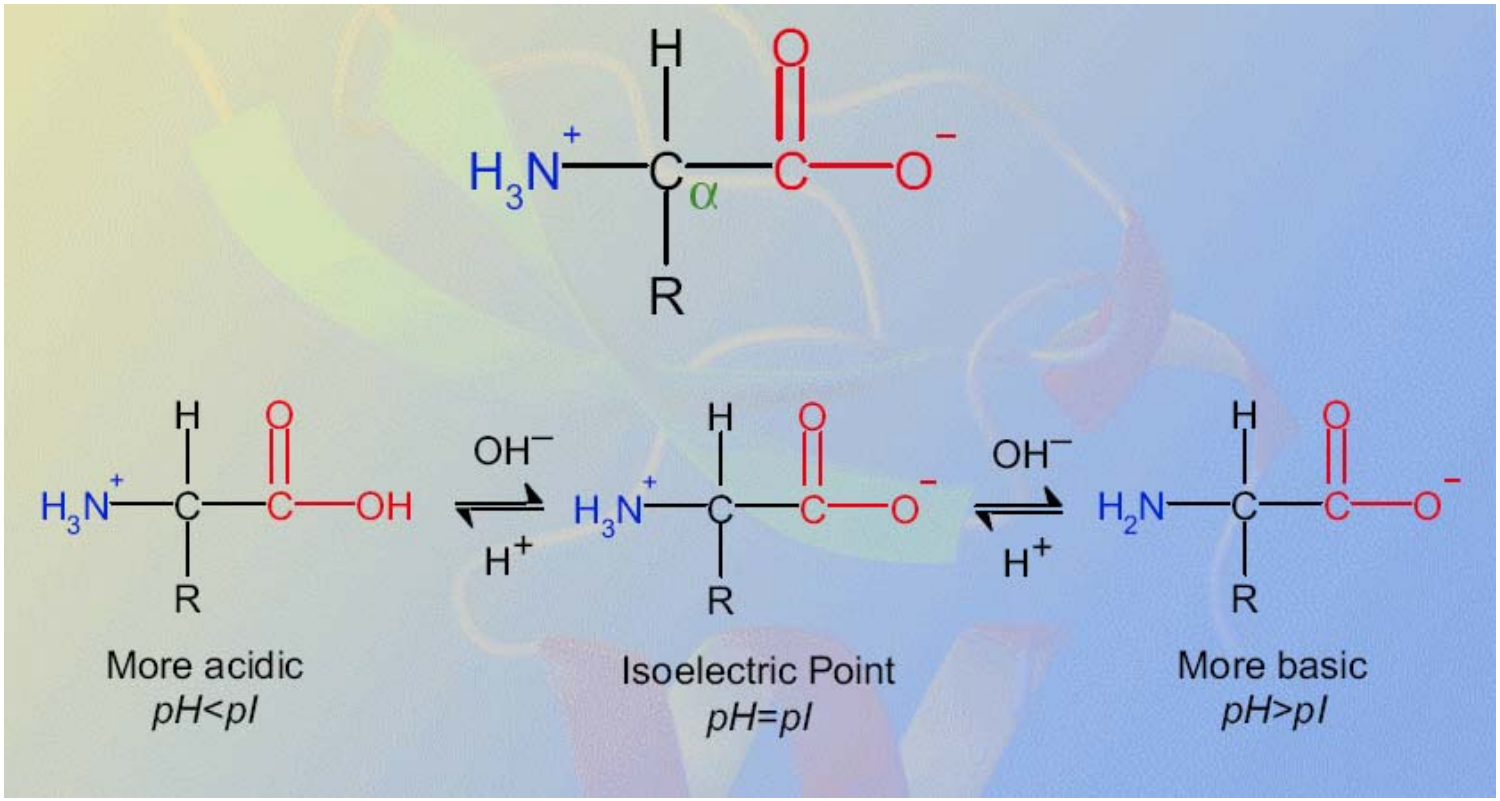
Stereochemistry of Amino acids

- Amino acids are *chiral* (asymmetric)
  - Presence of an asymmetric carbon atom
- Natural proteins are made only from left-handed amino acids



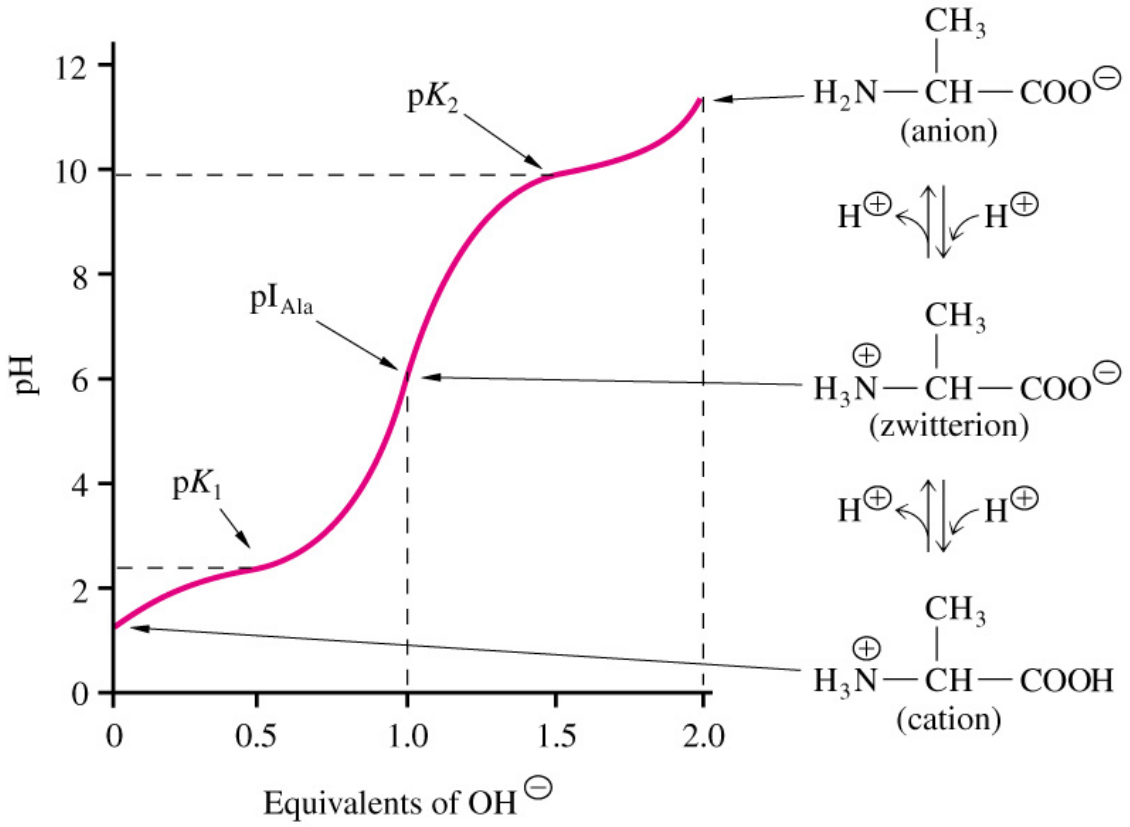
Acid-Base Properties of amino Acids

- Amino acids are zwitterions:



Amino acid	pKa1 (α - COO^-)	pKa2 (α - $^+NH3$)	pKaR R= side chain	pI
Alanine	2.35	9.69		6.02
Arginine	2.17	9.04	12.48	10.76
Asparagine	2.01	8.8		5.41
Aspartic acid	2.09	9.82	3.86	2.97
Cysteine	1.96	10.28	8.18	5.07
Glutamine	2.17	9.13		5.65
Glutamic acid	2.19	9.67	4.25	3.22
Glycine	2.34	9.78		6.06
Histidine	1.82	9.17	6	7.58
Isoleucine	2.36	9.68		6.02
Leucine	2.36	9.64		6
Lysine	2.18	8.95	10.53	9.74
Methionine	2.28	9.21		5.75
Phenylalanine	1.83	9.24		5.53
Proline	1.99	10.06		6.3
Serine	2.21	9.15		5.68
Threonine	2.71	9.62		6.16
Tryptophan	2.38	9.39		5.89
Tyrosine	2.2	9.11	10.07	5.65
Valine	2.32	9.62		5.97

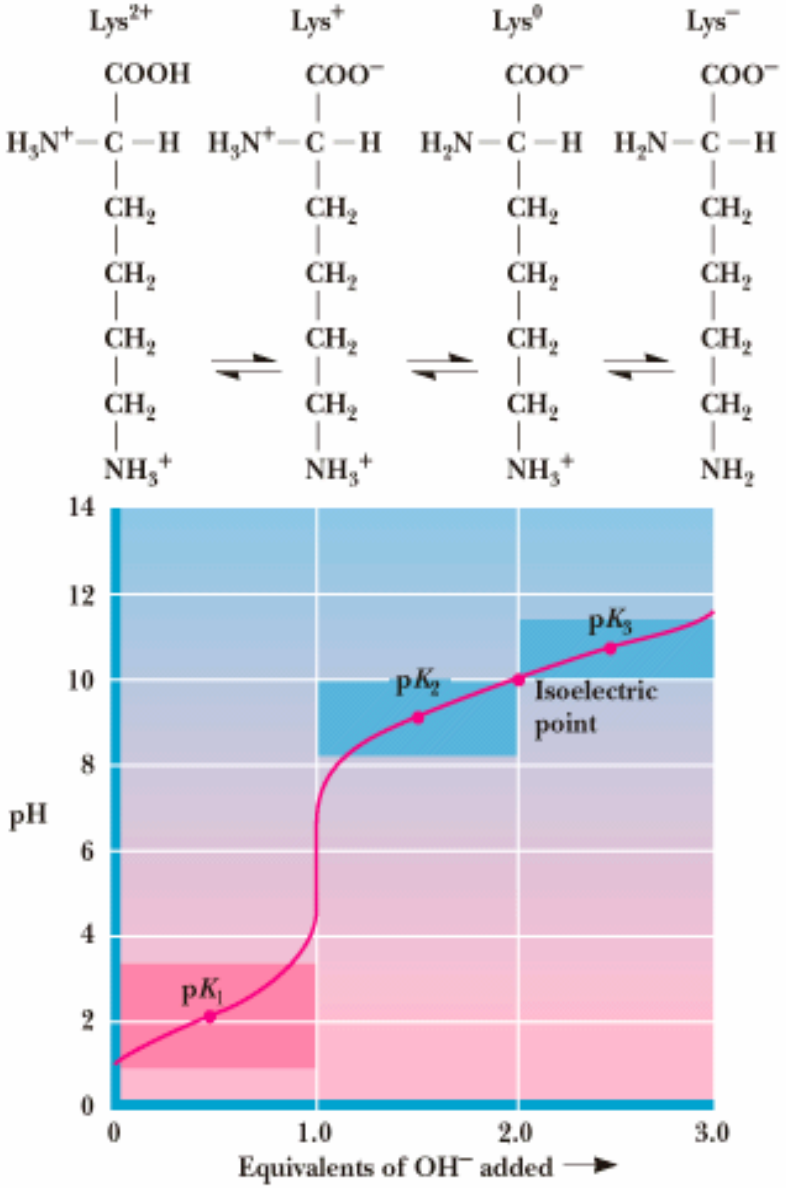
Acid-base titration

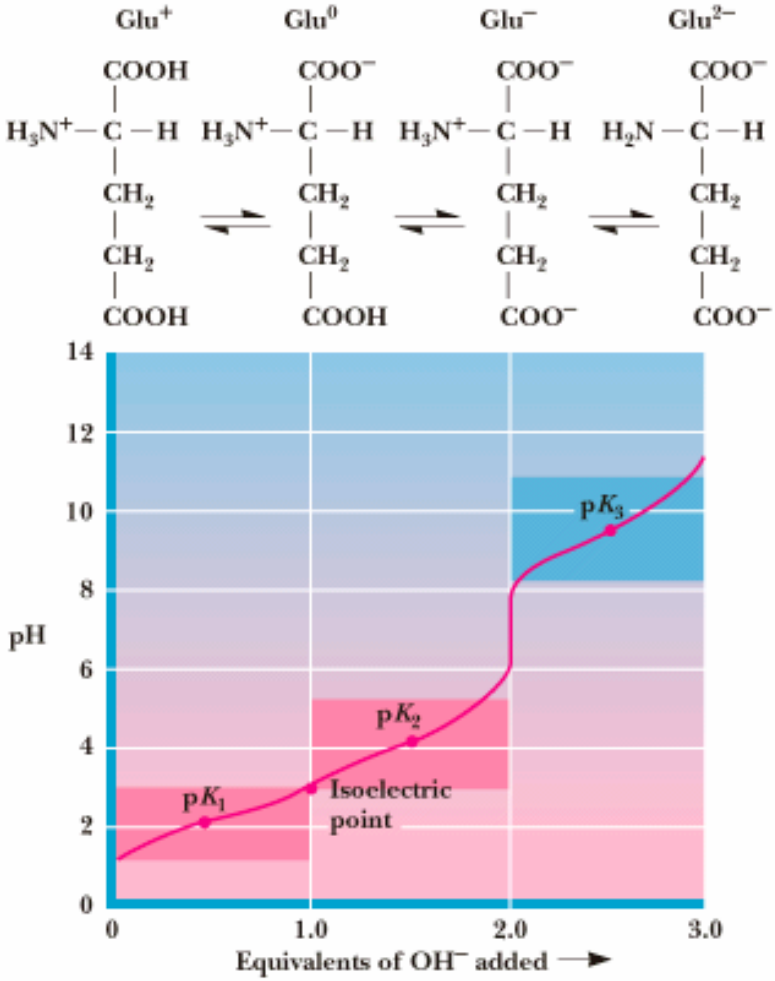


pK_1 carboxylic acid = 2

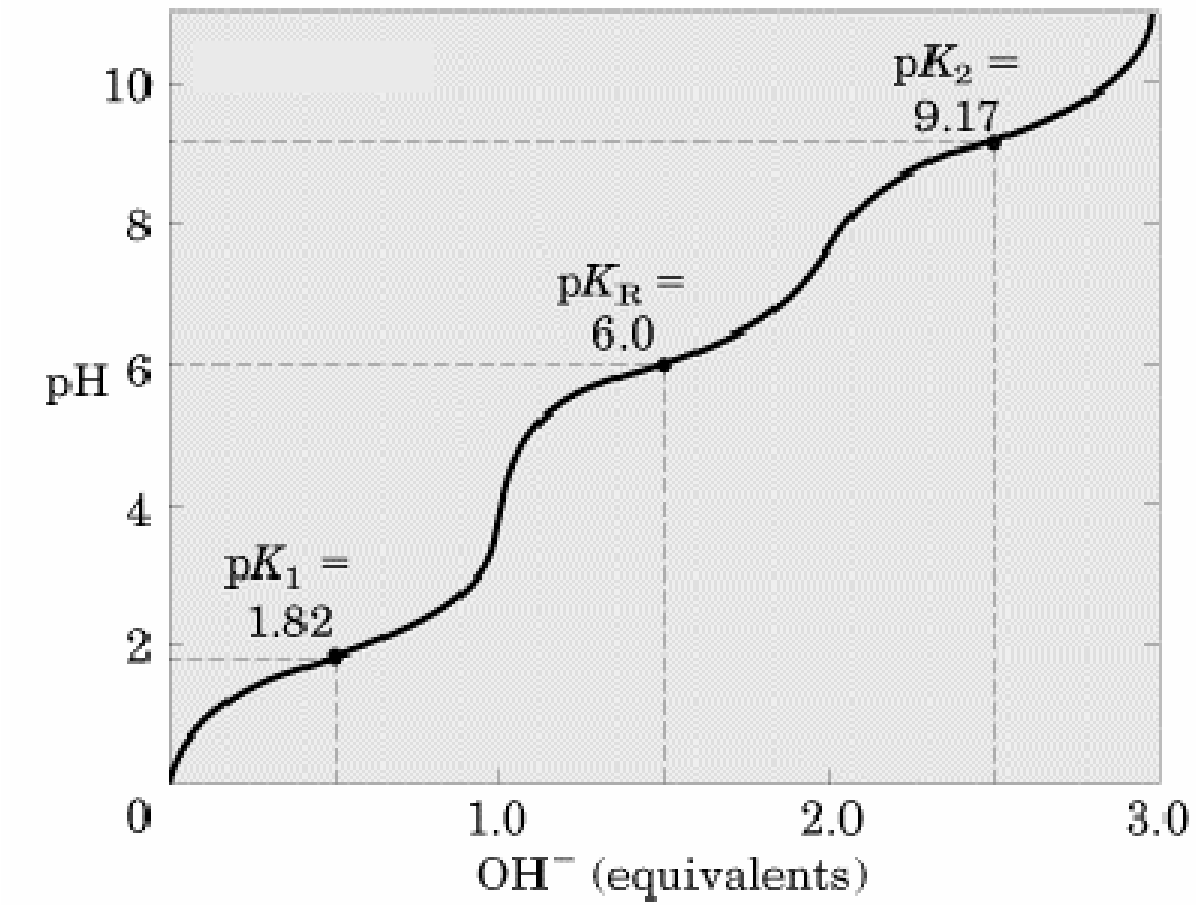
pK_2 amino group = 10

$pI = (pK_1 + pK_2)/2$


Lys2+
Lys+
Lys0
Lys−
COOH
COO−
H3N+—C—H
H2N—C—H
CH2
NH3+
NH2
pH
14
12
10
8
6
4
2
0
pK3
pK2
Isoelectric point
pK1
0
1.0
2.0
3.0
Equivalents of OH− added


Glu+
Glu0
Glu−
Glu2−
COOH
COO−
H3N+—C—H
H2N—C—H
CH2
pH
14
12
10
8
6
4
2
0
pK3
pK2
Isoelectric point
pK1
0
1.0
2.0
3.0
Equivalents of OH− added

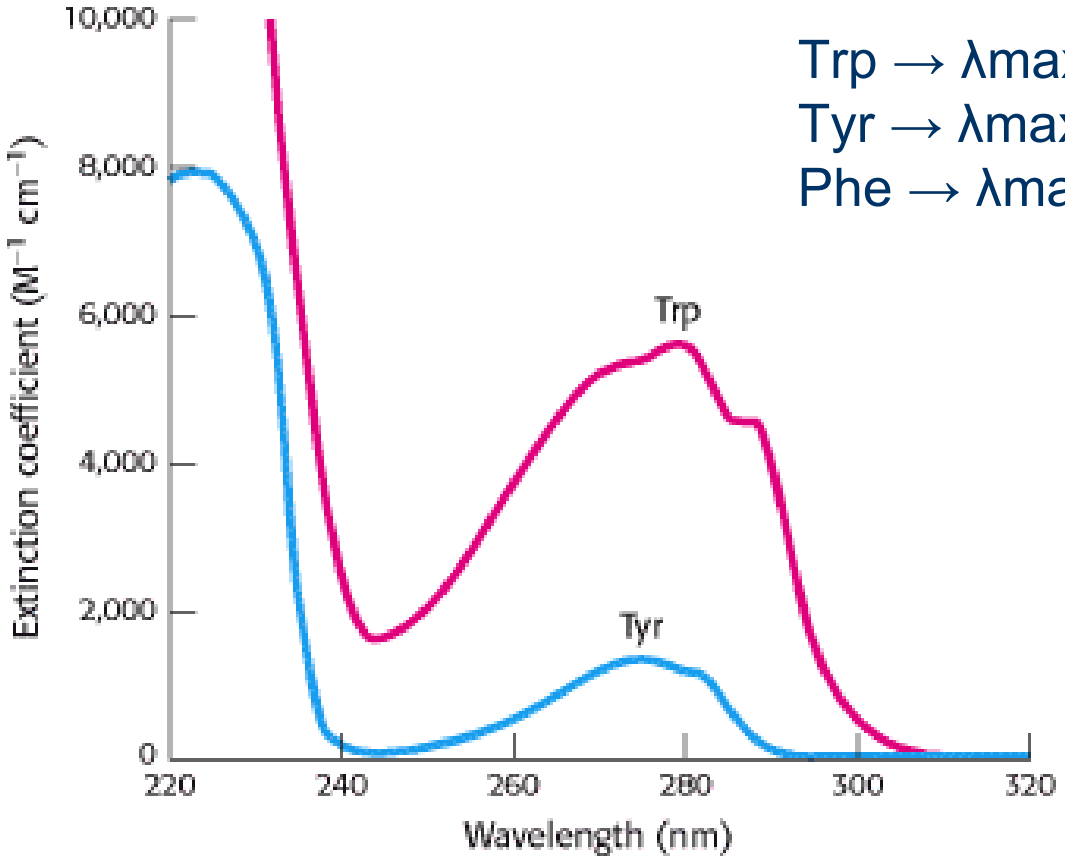
Titration Curves



Amino Acids Differ in Their Acid-Base Properties

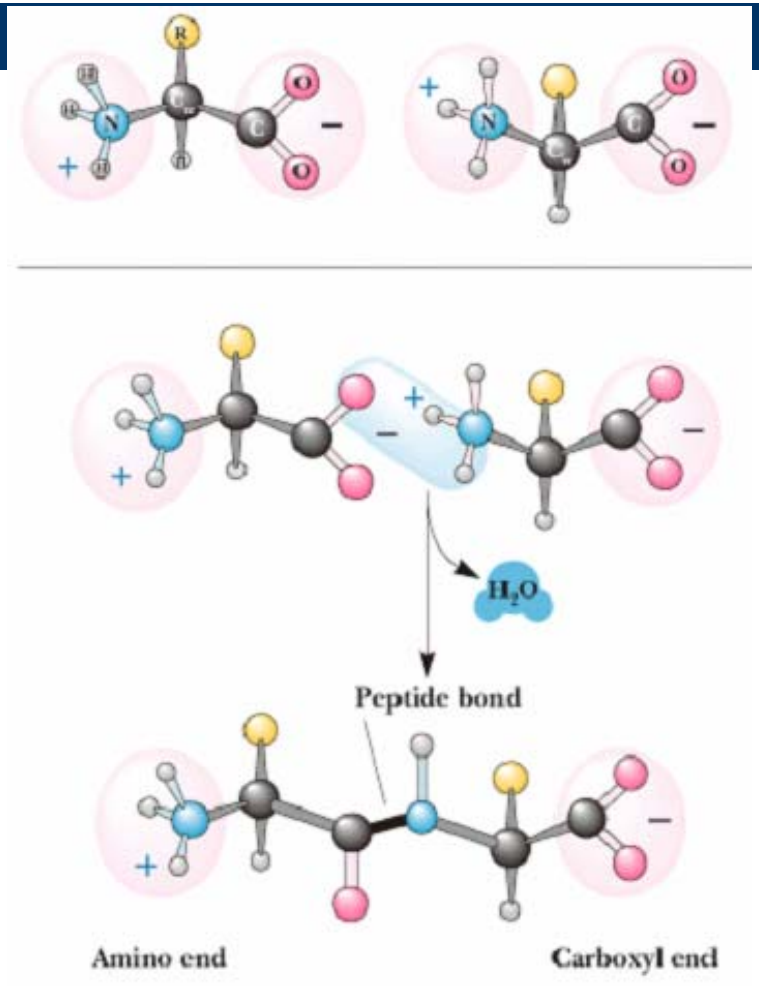
- Amino acids with an ionizable R group have more complex titration curves, with three stages corresponding to the three possible ionization steps
- The additional stage for the titration of the ionizable R group merges to some extent with the other two.
- The isoelectric points reflect the nature of the ionizing R groups present.

Absorption spectra of Aromatic amino acids

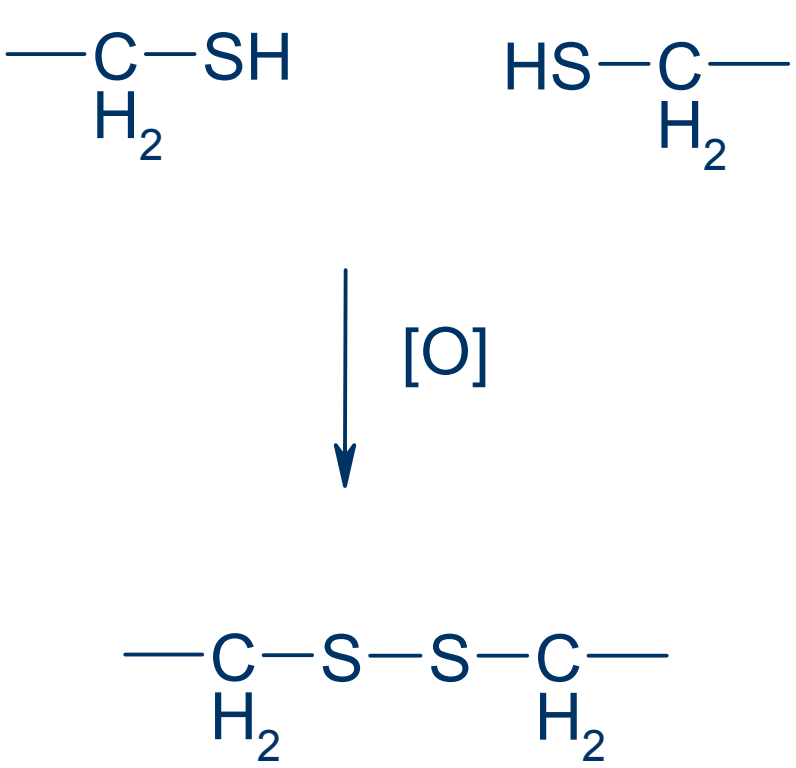


Trp → λmax of 278nm
Tyr → λmax of 275nm
Phe → λmax of 260nm

Peptide Bond Formation



Disulfide bridge



- Two cysteine molecules under oxidizing conditions

Disulfide bond

- Disulfide bonds between Cys residues stabilize the structures of many proteins.
- Although Cys is a polar AA, the disulfide-linked residues (Cystine) are strongly hydrophobic.

Other Reactions

- Ninhydrin
  - Purple, blue or violet derivatives, 570nm
  - Yellow for proline, 440 nm
- Phenylisothiocyanate
- Dansyl chloride