Biomolecules
Part1

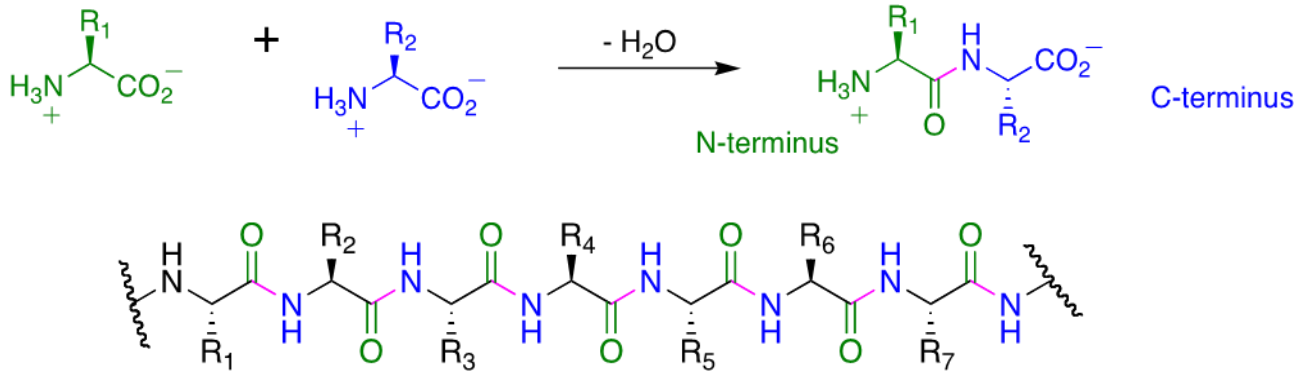
(for Semester V, CC-12)

Dr Subhra Mishra
Associate Professor
Department Of Chemistry
Kharagpur College

Biopolymer……

Biopolymers are natural polymers produced by the cells of living organisms. Biopolymers consist of monomeric units that are covalently bonded to form larger molecules.
Classification: There are three main classes of biopolymers, classified according to the monomeric units used and the structure of the biopolymer formed:
polynucleotides, Polypeptides and polysaccharides

Polypeptides: The monomeric amino acids are linked through an amide bond (the carboxylic acids of one AA with the α-amino group of a second)

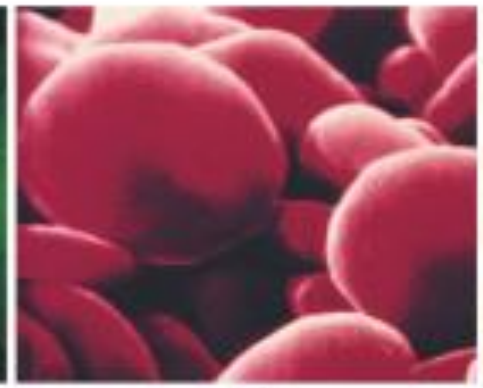


peptide (< 50 amino acids)
protein (> 50 amino acids)

Different structural and functional proteins – all made from Amino Acids

(a)

Light from the enzyme, Luciferase, that uses a chemical reaction to produce light



(b)

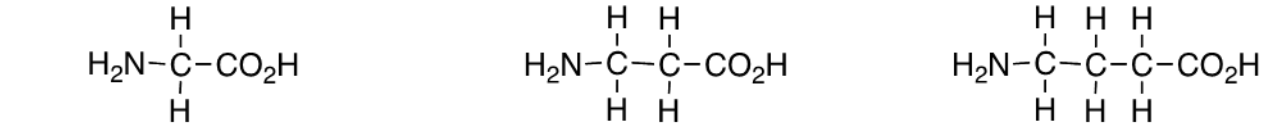
Hemoglobin (Hb) an oxygen binding protein.

(c)

Skin, horns, nails, hair, claws, feathers....all different forms of keratin, a structural protein

Proteins are linear heteropolymers of α-amino acids

Amino acids:

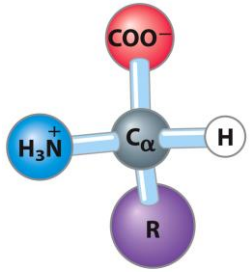


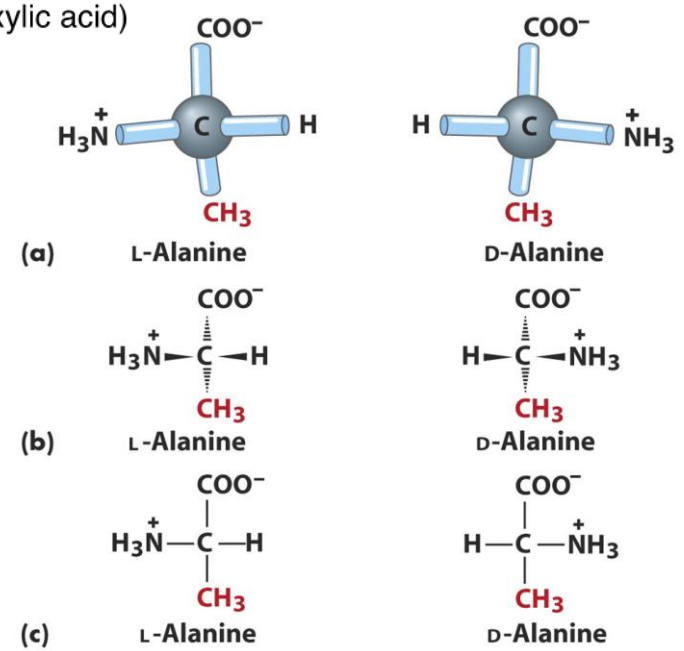
α-amino acid
(2-amino carboxylic acid)

β-amino acid
(3-amino carboxylic acid)

γ-amino acid
(4-amino carboxylic acid)

- α-Amino carboxylic acids
- The "building blocks" from which proteins are made of..



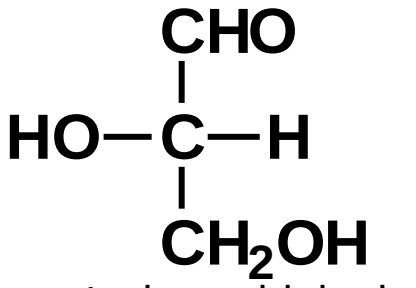


- Note: except for glycine (R = H), all α-amino acids are chiral molecules
- Amino acids share many features, differing only at the R substituent
- There are 20 genetically encoded α-amino acids found in peptides and proteins
- 19 are primary amines, 1 (proline) is a secondary amine
- 19 are "chiral", 1 (glycine) is achiral; the natural configuration of the α-carbon is L.

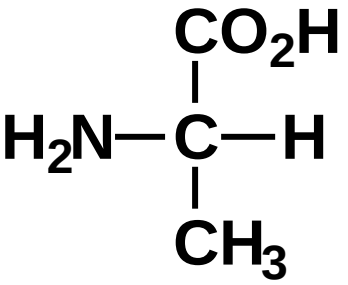
<u>Now the no.s are extended to 22</u>

- As with carbohydrates, it is traditional to use the D and L nomenclature with amino acids – based on the configuration of glyceraldehyde

- Naturally occurring amino acids generally have the same configuration as L-glyceraldehyde (S-configuration at the α-carbon):



L-glyceraldehyde

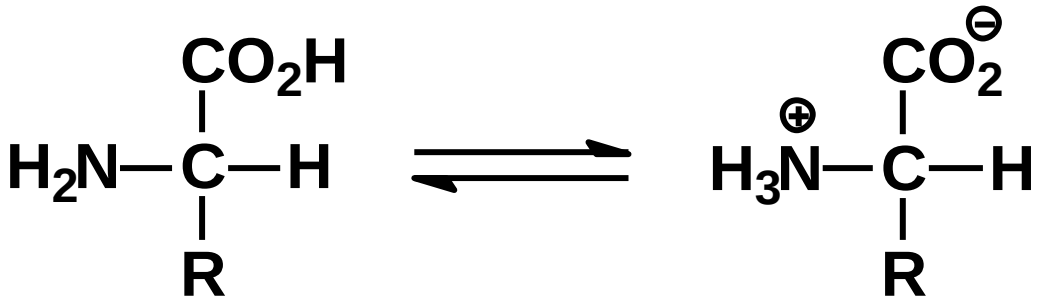


L-Alanine

D-Amino acids are found in the cell walls of bacteria. The D-amino acids are not genetically encoded, but derived from the epimerization of L-isomers

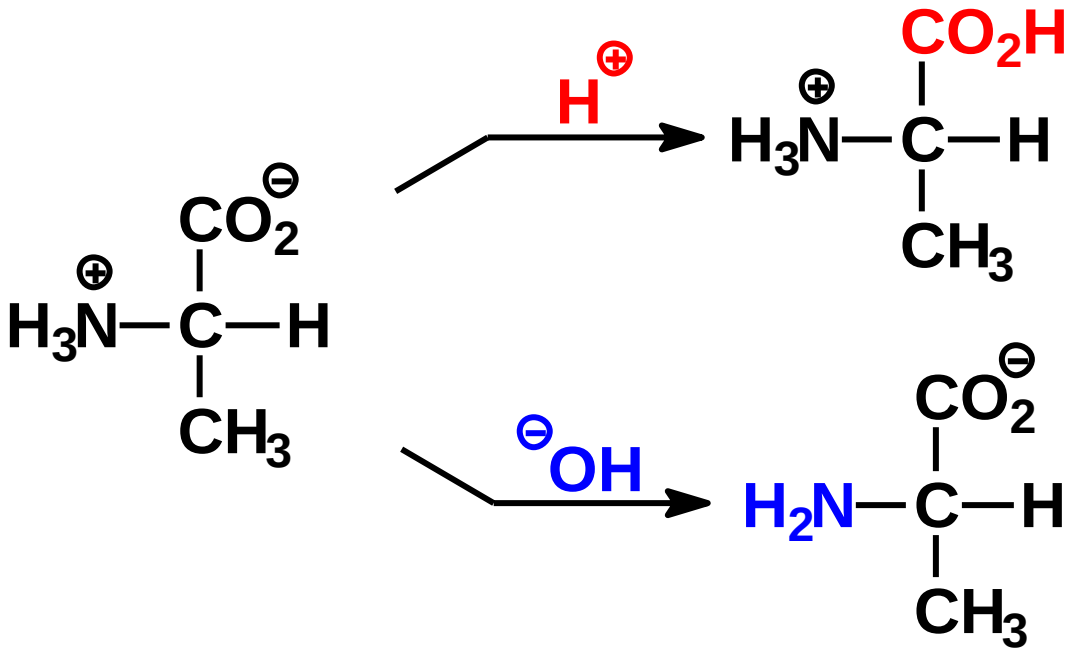
Properties of amino acids

- They decompose than melt at high temperature
- They conduct electricity in solid state
- They have high dipole moment
- Acid–Base Properties
- Since amino acids have both an acidic functionality and a basic functionality, we should expect the following equilibrium:

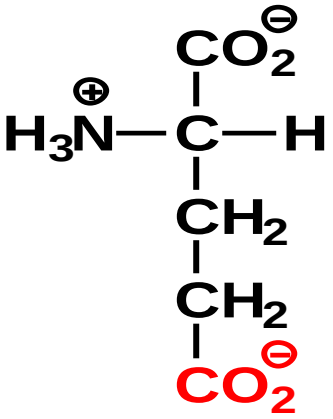


- In fact, the equilibrium lies to the right all amino acids are charged at any pH!
- Such species that are overall neutral molecules but contain charged ends are called zwitterions
- They are amphoteric in nature

- Acid–Base Properties
- Amino acids can react as either acids or bases:

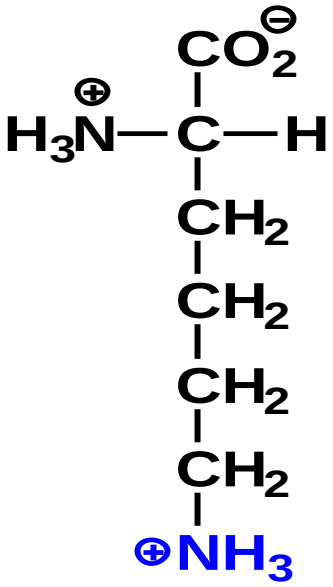


- Amino acids can also have side chains containing acidic or basic groups:



Deprotonated at physiological pH

Glutamic acid (acidic R)



Protonated at physiological pH

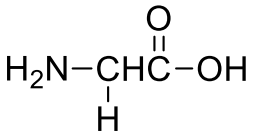
Lysine (basic R)

Amino Acids: Classification

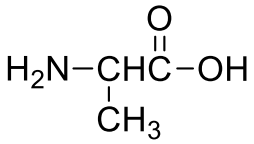
Common amino acids can be classified in five basic groups depending on their R substituents:

- Nonpolar, aliphatic (7) (hydrophobic)
- Aromatic (3) (hydrophilic or hydrophobic)
- Polar, uncharged (5) (HO-, S-, and amide containing – hydrophilic)
- Positively charged (3) (hydrophilic)
- Negatively charged (2) (hydrophilic)

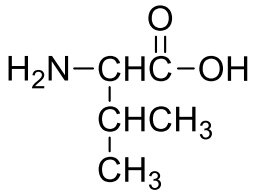
Aliphatic side chains – hydrophobic



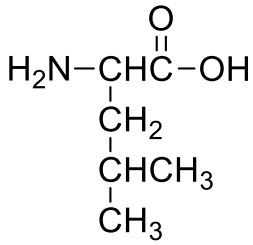
Gly, G



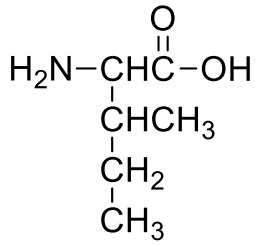
Ala, A



Val, V

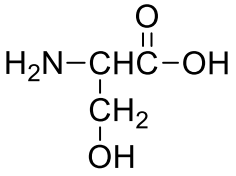


Leu, L

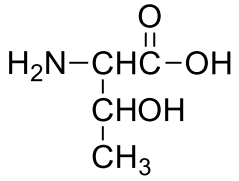


Ile, I

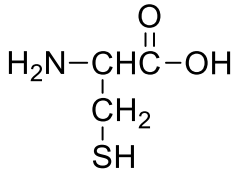
Polar side chains – text classifies as HO-, S-, and amide containing – hydrophilic



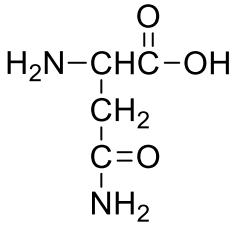
Ser, S



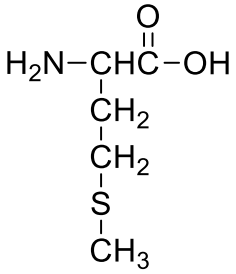
Thr, T



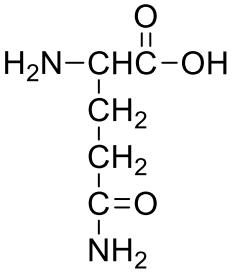
Cys, C



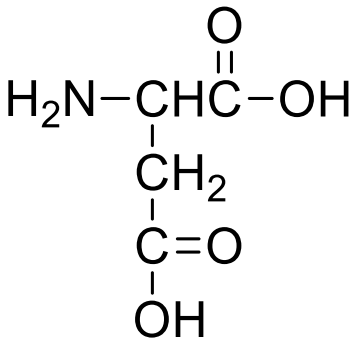
Met, M



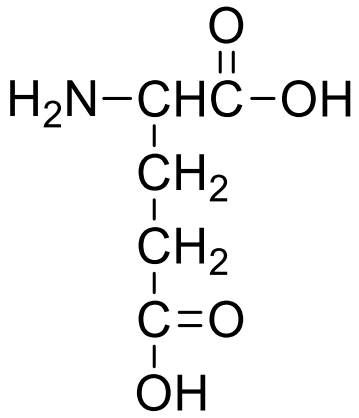
Asn, N



Gln, Q

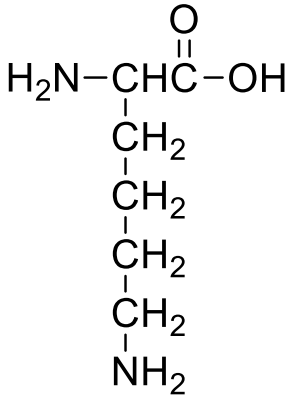


Asp, D

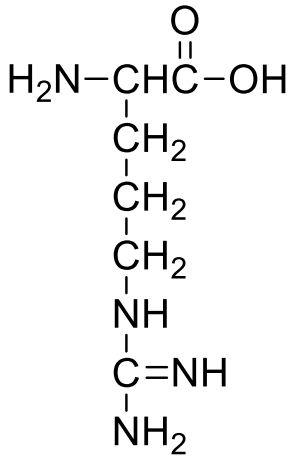


Glu, E

Acidic – hydrophilic



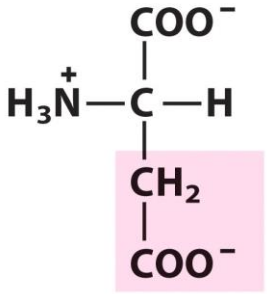
Lys, K



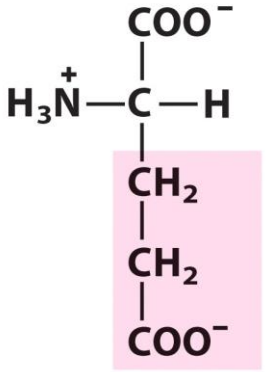
Arg, R

Basic – hydrophilic

Negatively charged R groups

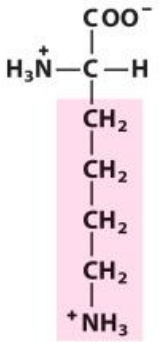


Aspartate

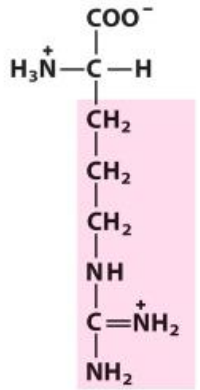


Glutamate

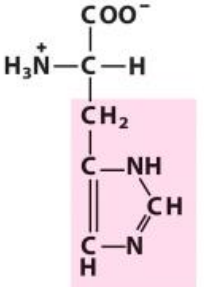
Positively charged R groups



Lysine

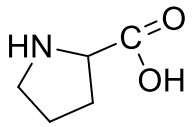


Arginine

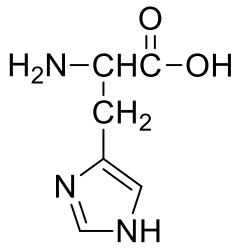


Histidine

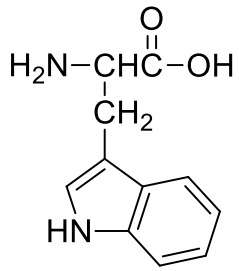
Heterocyclic/Aromatic – hydrophilic or hydrophobic



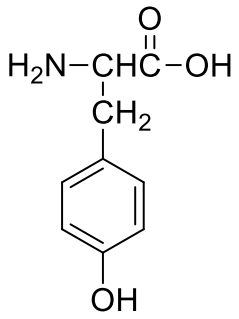
Pro, P



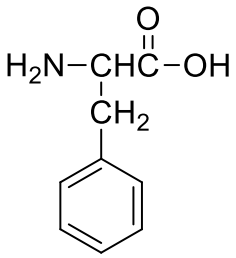
His, H



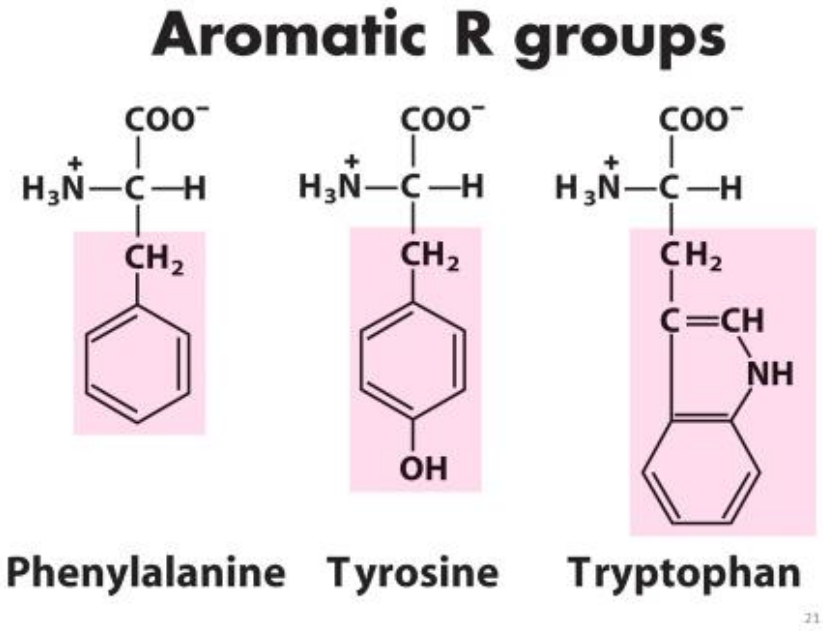
Trp, W



Phe, F



Tyr, Y



Hydrophobic

Other derived amino acids……

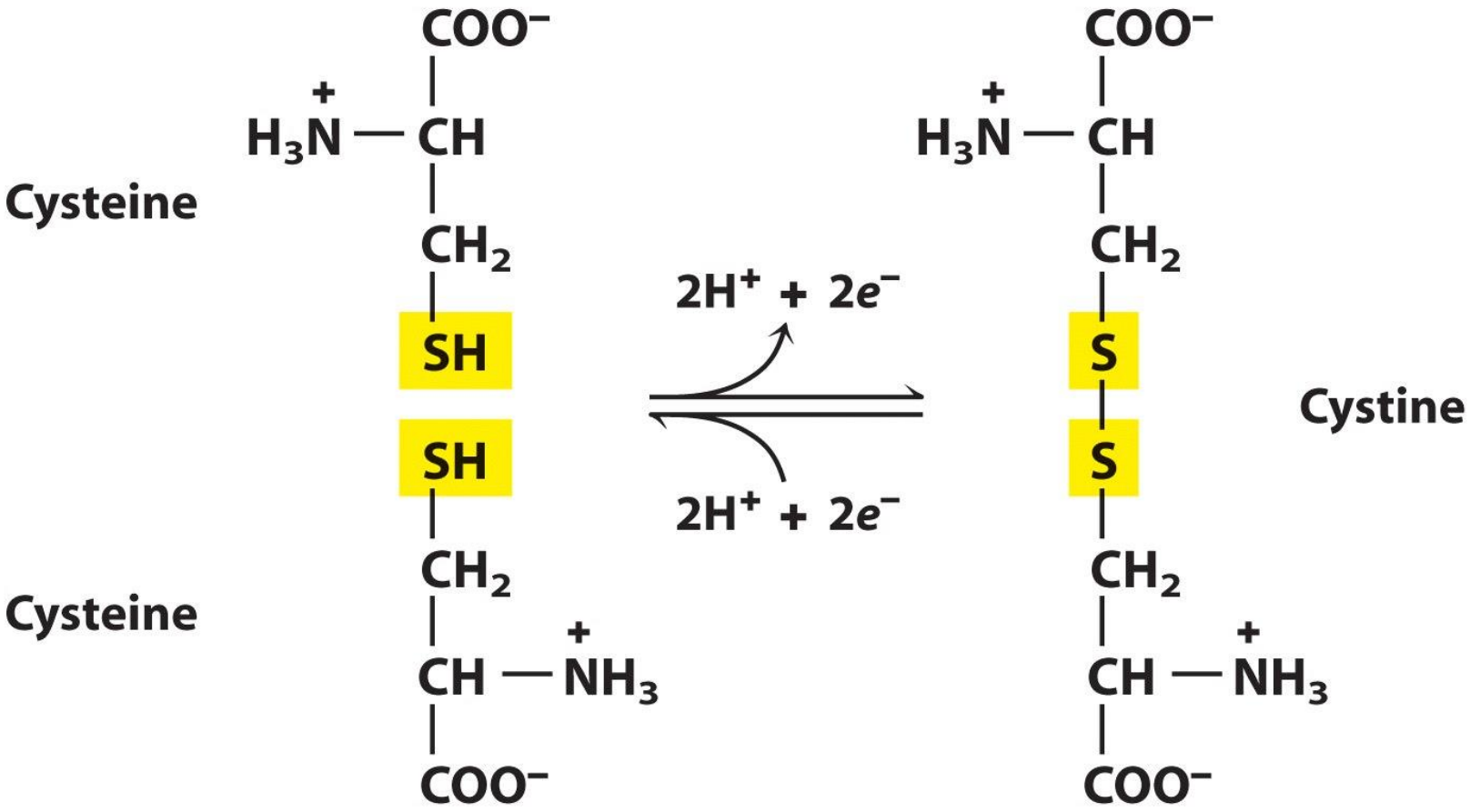


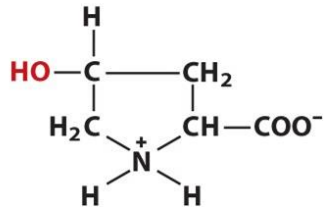
TABLE 3–1 Properties and Conventions Associated with the Common Amino Acids Found in Proteins

Amino acid	Abbreviation/ symbol	M_r*	pK_a values: pK_1 (—COOH)	pK_2 ($—NH_3^+$)	pK_R (R group)	pI	Hydropathy index†	Occurrence in proteins (%)‡
Nonpolar, aliphatic R groups								
Glycine	Gly G	75	2.34	9.60		5.97	−0.4	7.2
Alanine	Ala A	89	2.34	9.69		6.01	1.8	7.8
Proline	Pro P	115	1.99	10.96		6.48	1.6	5.2
Valine	Val V	117	2.32	9.62		5.97	4.2	6.6
Leucine	Leu L	131	2.36	9.60		5.98	3.8	9.1
Isoleucine	Ile I	131	2.36	9.68		6.02	4.5	5.3
Methionine	Met M	149	2.28	9.21		5.74	1.9	2.3
Aromatic R groups								
Phenylalanine	Phe F	165	1.83	9.13		5.48	2.8	3.9
Tyrosine	Tyr Y	181	2.20	9.11	10.07	5.66	−1.3	3.2
Tryptophan	Trp W	204	2.38	9.39		5.89	−0.9	1.4
Polar, uncharged R groups								
Serine	Ser S	105	2.21	9.15		5.68	−0.8	6.8
Threonine	Thr T	119	2.11	9.62		5.87	−0.7	5.9
Cysteine§	Cys C	121	1.96	10.28	8.18	5.07	2.5	1.9
Asparagine	Asn N	132	2.02	8.80		5.41	−3.5	4.3
Glutamine	Gln Q	146	2.17	9.13		5.65	−3.5	4.2
Positively charged R groups								
Lysine	Lys K	146	2.18	8.95	10.53	9.74	−3.9	5.9
Histidine	His H	155	1.82	9.17	6.00	7.59	−3.2	2.3
Arginine	Arg R	174	2.17	9.04	12.48	10.76	−4.5	5.1
Negatively charged R groups								
Aspartate	Asp D	133	1.88	9.60	3.65	2.77	−3.5	5.3
Glutamate	Glu E	147	2.19	9.67	4.25	3.22	−3.5	6.3

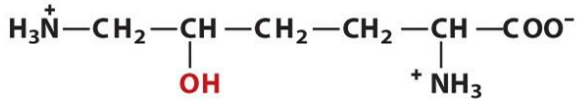
Margaret Oakley Dayhoff
1925–1983

Invented the One Letter Amino Acid Code.

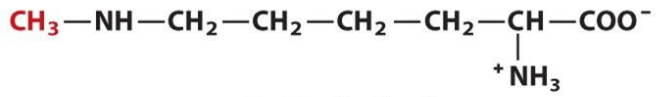
Other uncommon amino acids……



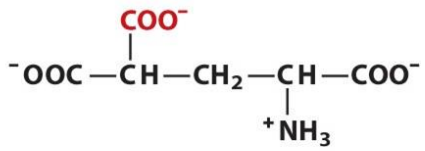
4-Hydroxyproline



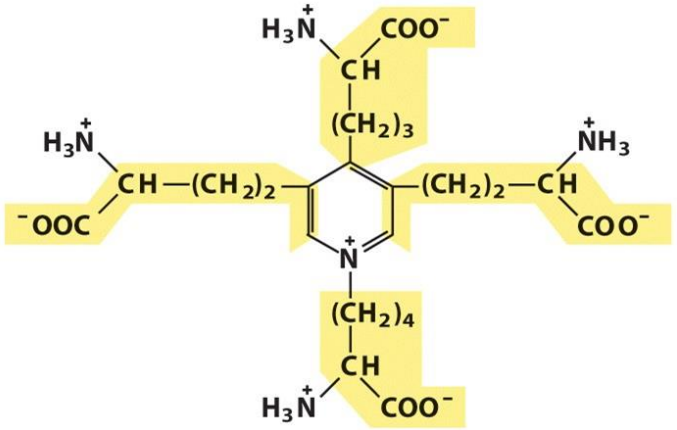
5-Hydroxylysine



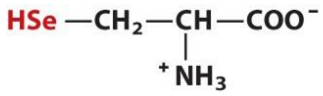
6-*N*-Methyllysine



γ-Carboxyglutamate

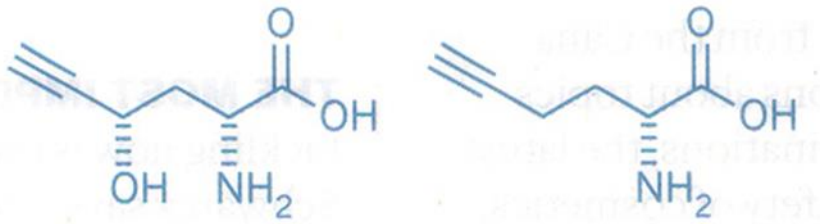


Desmosine

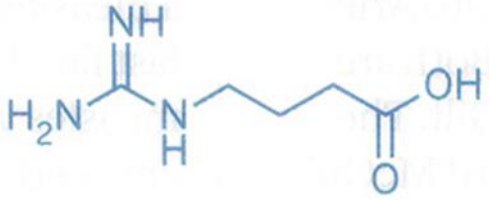


Selenocysteine

Some toxic amino acids…..



New toxic amino acids



γ-Guanidinobutyric acid

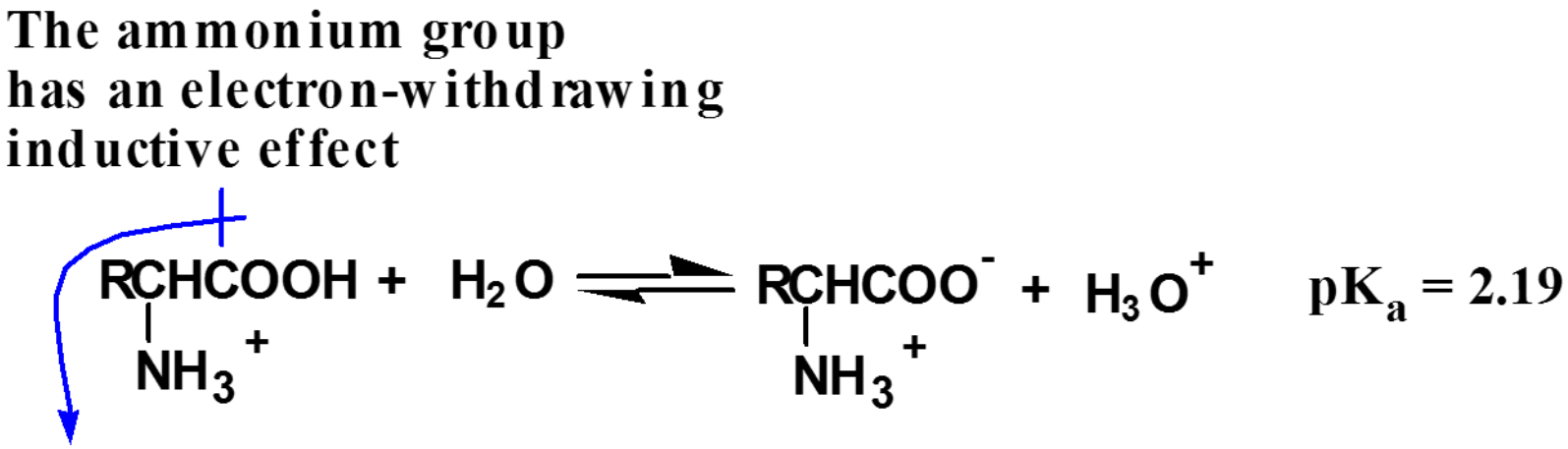
A search for compounds producing Yunnan Sudden Unexplained Deaths found related to eating a mushroom

Some essential amino acids……..

There are certain amino acids which are essential for growth of human being but are not synthesized by the body itself …called as Essential amino acids (10), examples are-V, F,I,L,M,T,W,H,K,R

Acidity of α-COOH Groups

- The average pKa of an α-carboxyl group is 2.19, which makes them considerably stronger acids than acetic acid (pKa 4.76)
- The greater acidity is accounted for by the electron-withdrawing inductive effect of the adjacent -NH3+ group

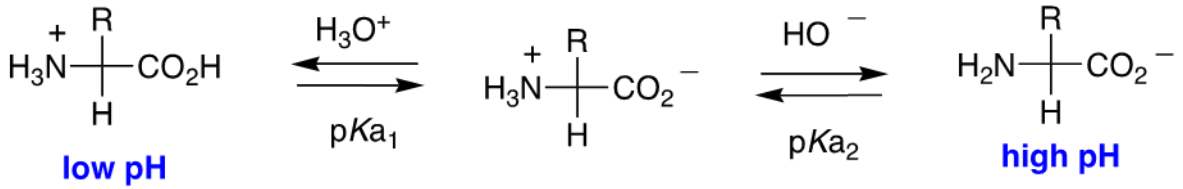


Acid-Base Behavior of Amino Acids……

Amino acids exist as a zwitterion: a dipolar ion having both a formal positive and formal negative charge (overall charge neutral).

Amino acids are amphoteric: they can react as either an acid or a base. Ammonium ion acts as an acid, the carboxylate as a base.

Isoelectric point (pI): The pH at which the amino acid exists largely in a neutral, zwitter ionic form (influenced by the nature of the side chain)



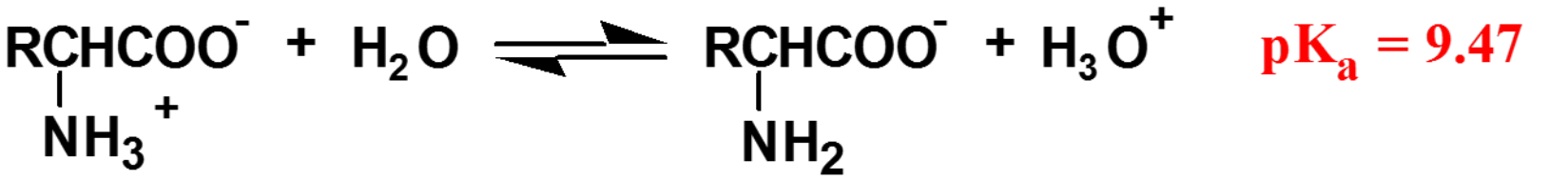
Side Chain COOH Groups

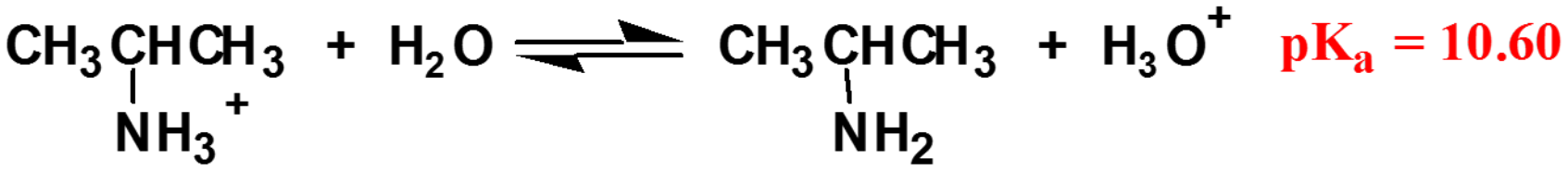
- Due to the electron-withdrawing inductive effect of the α-NH_3^+ group, side chain -COOH groups are also stronger than acetic acid
  - the effect decreases with distance from the α-NH_3^+ group-- compare:

α-COOH group of alanine (pK_a 2.35)
β-COOH group of aspartic acid (pK_a 3.86)
γ-COOH group of glutamic acid (pK_a 4.07)

Acidity of α-NH3+ Groups

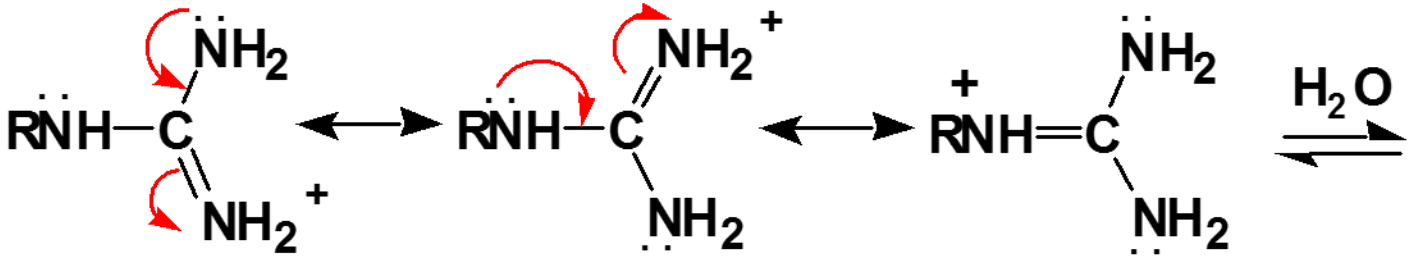
- The average value of pKa for an α-NH3+ group is 9.47, compared with a value of 10.76 for 1° alkylammonium ions

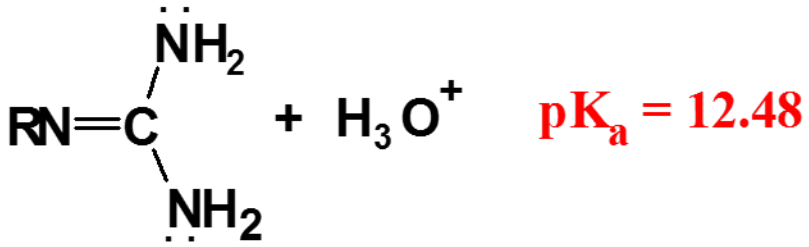




Basicity of Guanidine Group

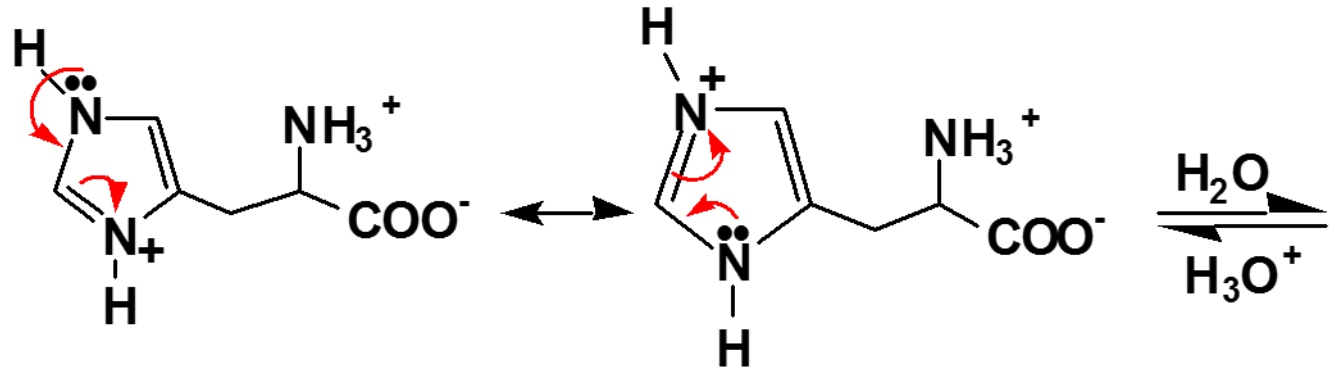
the side chain of arginine contains a guanidine group

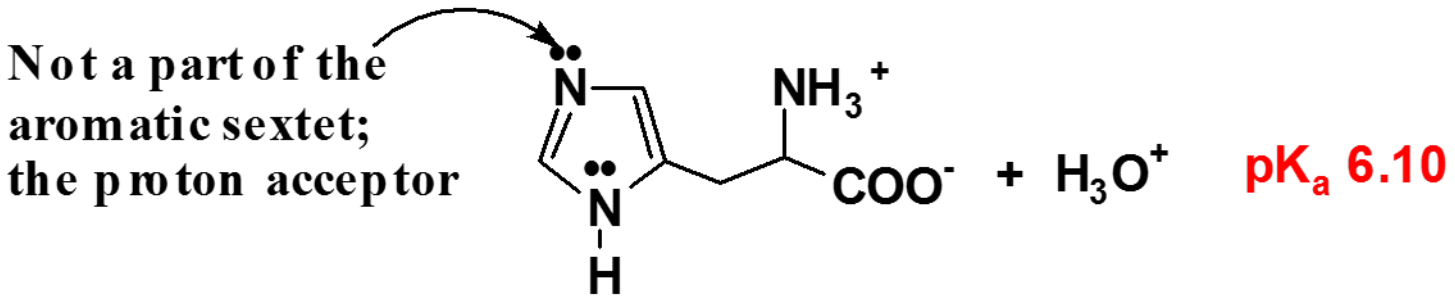




The Imidazole Groups of His

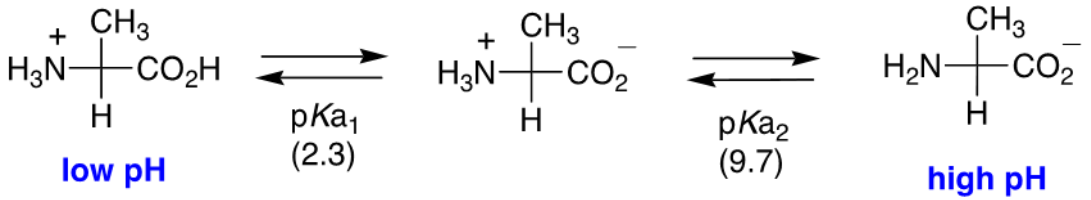
The imidazole group is a heterocyclic aromatic amine





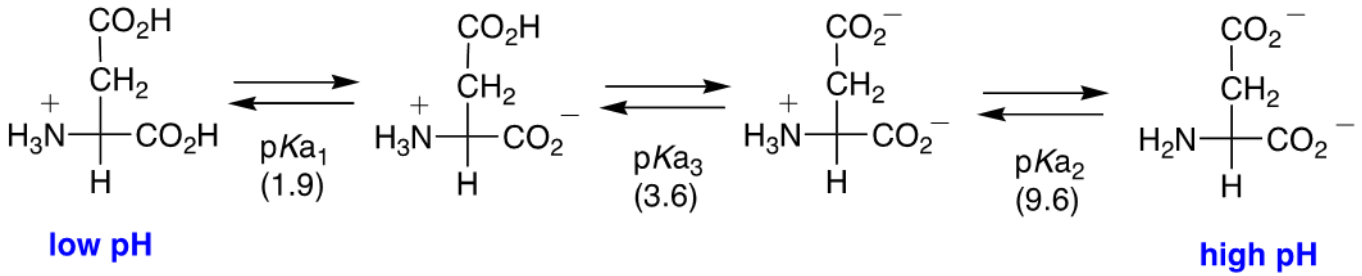
$$pI = \frac{pKa_x + pKa_y}{2}$$

Note that the a_x and b_y are between amino acid pK's where the net charge is zero. It is interesting to find the pI of amino acids with acidic and basic R groups.



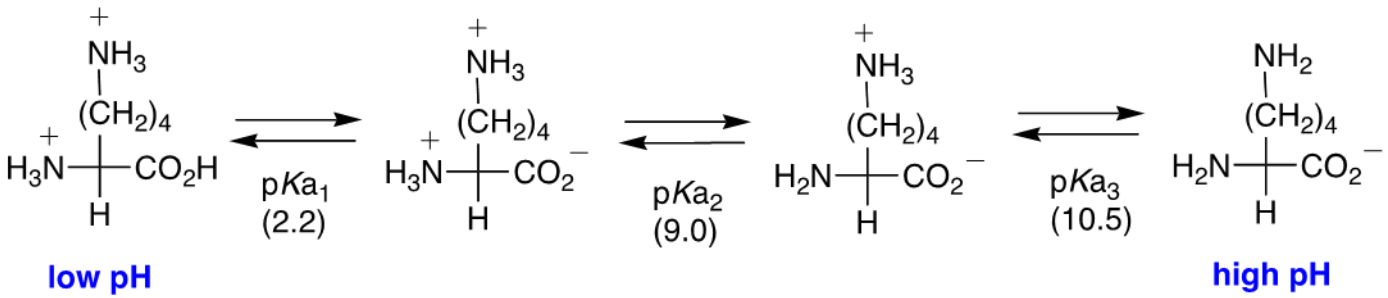
$$pI = \frac{pKa_1 + pKa_2}{2}$$

$$pI = 6.0$$



$$pI = \frac{pKa_1 + pKa_3}{2}$$

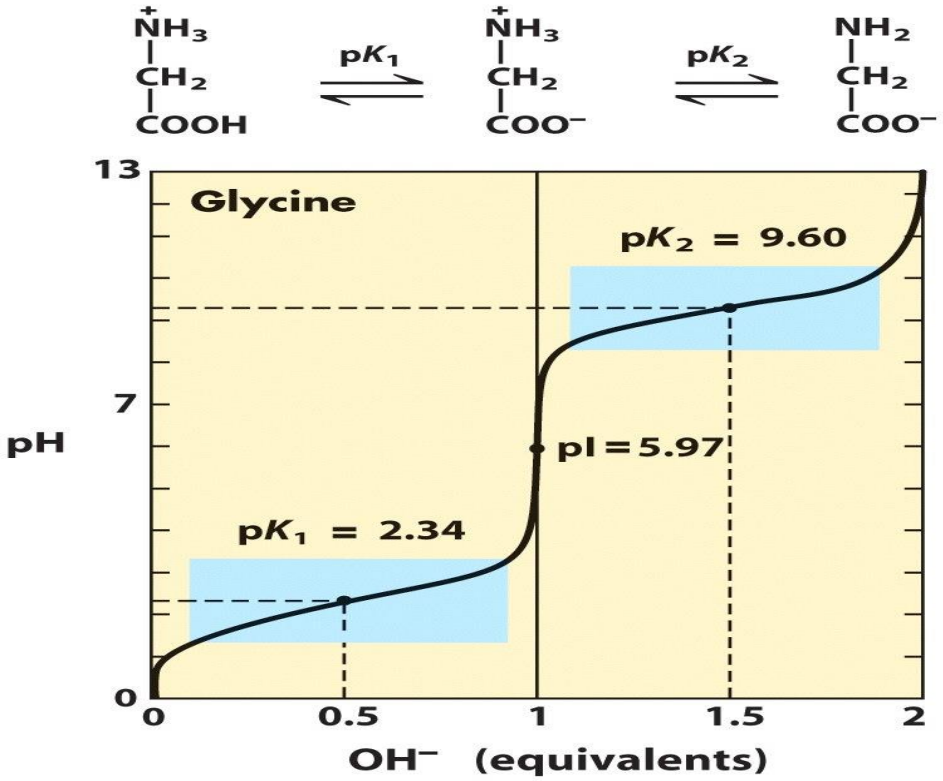
$$pI = 2.7$$



$$pI = \frac{pKa_2 + pKa_3}{2}$$

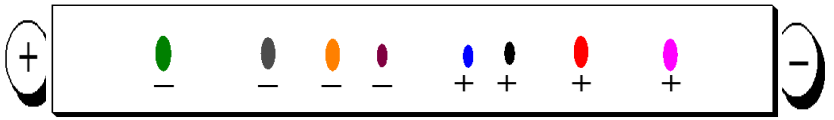
$$pI = 9.7$$

Glycine Acid/Base Titration and electrophoresis



Electrophoresis: the process of separating compounds on the basis of their electric charge

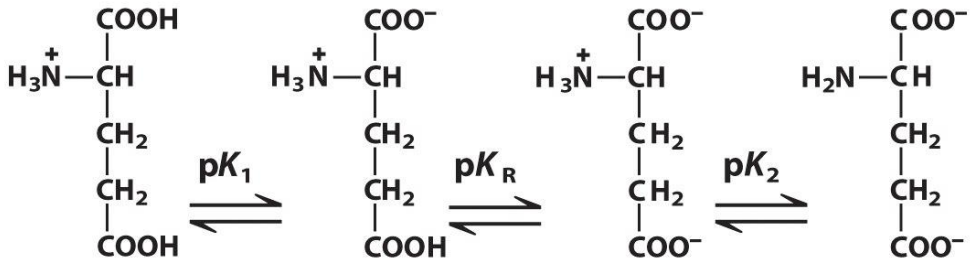
electrophoresis of amino acids can be carried out using paper, starch, agar, certain plastics, and cellulose acetate as solid supports

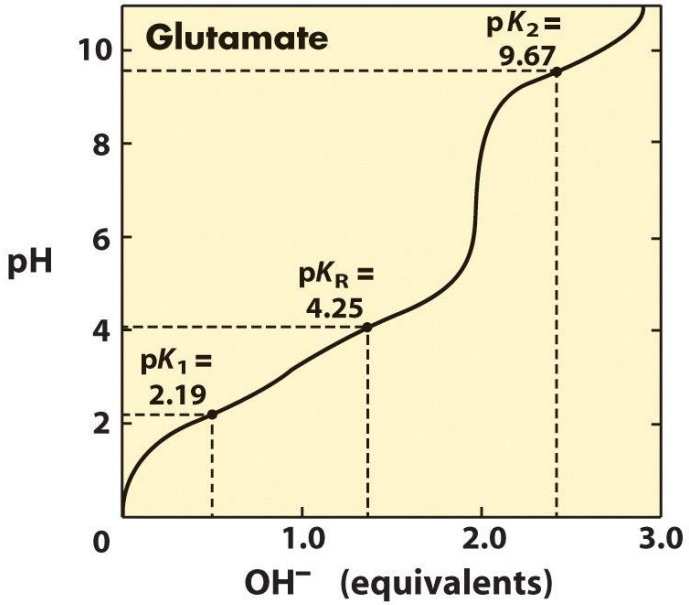


Electrophoresis

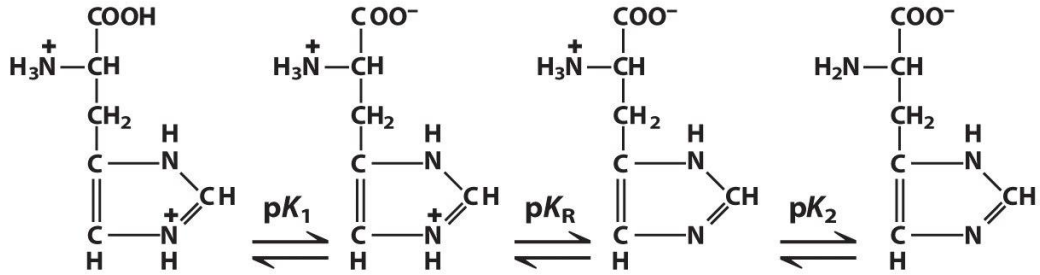
- a sample of amino acids is applied as a spot on the paper strip
- an electric potential is applied to the electrode vessels and amino acids migrate toward the electrode with charge opposite their own
- molecules with a high charge density move faster than those with low charge density
- molecules at their isoelectric point remain at the origin
- after separation is complete, the strip is dried and developed to make the separated amino acids visible

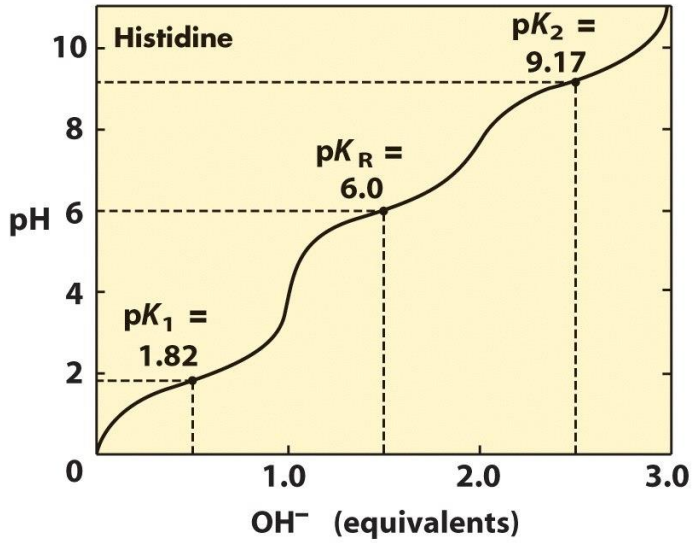
Few acid base titration curves……





Glutamate has 3 pKa's





Histidine has 3 pKa's

In summary……

How to Calculate the pI When the Side Chain is Ionizable

- Identify species that carries a net zero charge
- Identify pK_a value that defines the acid strength of this zwitterion: (pK_2)
- Identify pK_a value that defines the base strength of this zwitterion: (pK_1)
- Take the average of these two pK_a values

What is the pI of histidine?

Isoelectric Point (pI)

Nonpolar & polar side chains	pK_a of α–COOH	pK_a of α–NH_3^+	pK_a of Side Chain	pI
alanine	2.35	9.87	----	6.11
asparagine	2.02	8.80	----	5.41
glutamine	2.17	9.13	----	5.65
glycine	2.35	9.78	----	6.06
isoleucine	2.32	9.76	----	6.04
leucine	2.33	9.74	----	6.04
methionine	2.28	9.21	----	5.74
phenylalanine	2.58	9.24	----	5.91
proline	2.00	10.60	----	6.30
serine	2.21	9.15	----	5.68
threonine	2.09	9.10	----	5.60
tryptophan	2.38	9.39	----	5.88
valine	2.29	9.72	----	6.00

Acidic Side Chains	pK_a of α–COOH	pK_a of α–NH_3^+	pK_a of Side Chain	pI
aspartic acid	2.10	9.82	3.86	2.98
glutamic acid	2.10	9.47	4.07	3.08
cysteine	2.05	10.25	8.00	5.02
tyrosine	2.20	9.11	10.07	5.63

Basic Side Chains	pK_a of α–COOH	pK_a of α–NH_3^+	pK_a of Side Chain	pI
arginine	2.01	9.04	12.48	10.76
histidine	1.77	9.18	6.10	7.64
lysine	2.18	8.95	10.53	9.74

Compare Amino Acids to Simple Carboxylic Acids and Amines