Amino Acids

September 20, 2016

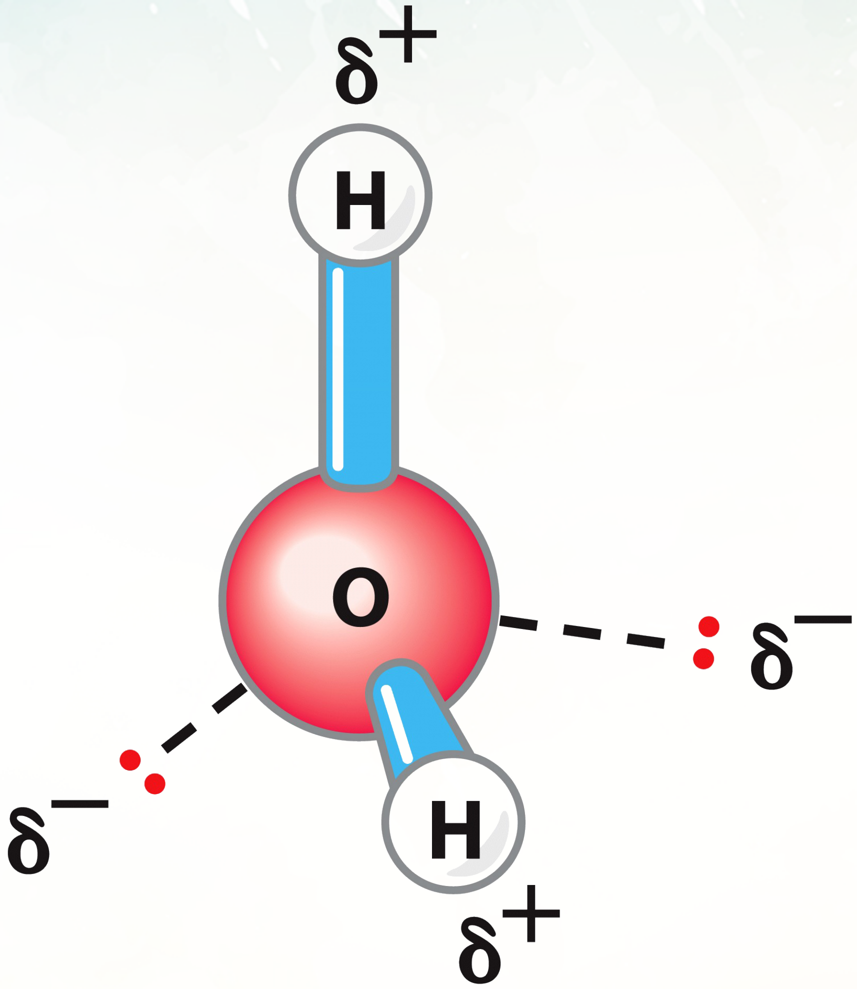
Primary Objectives

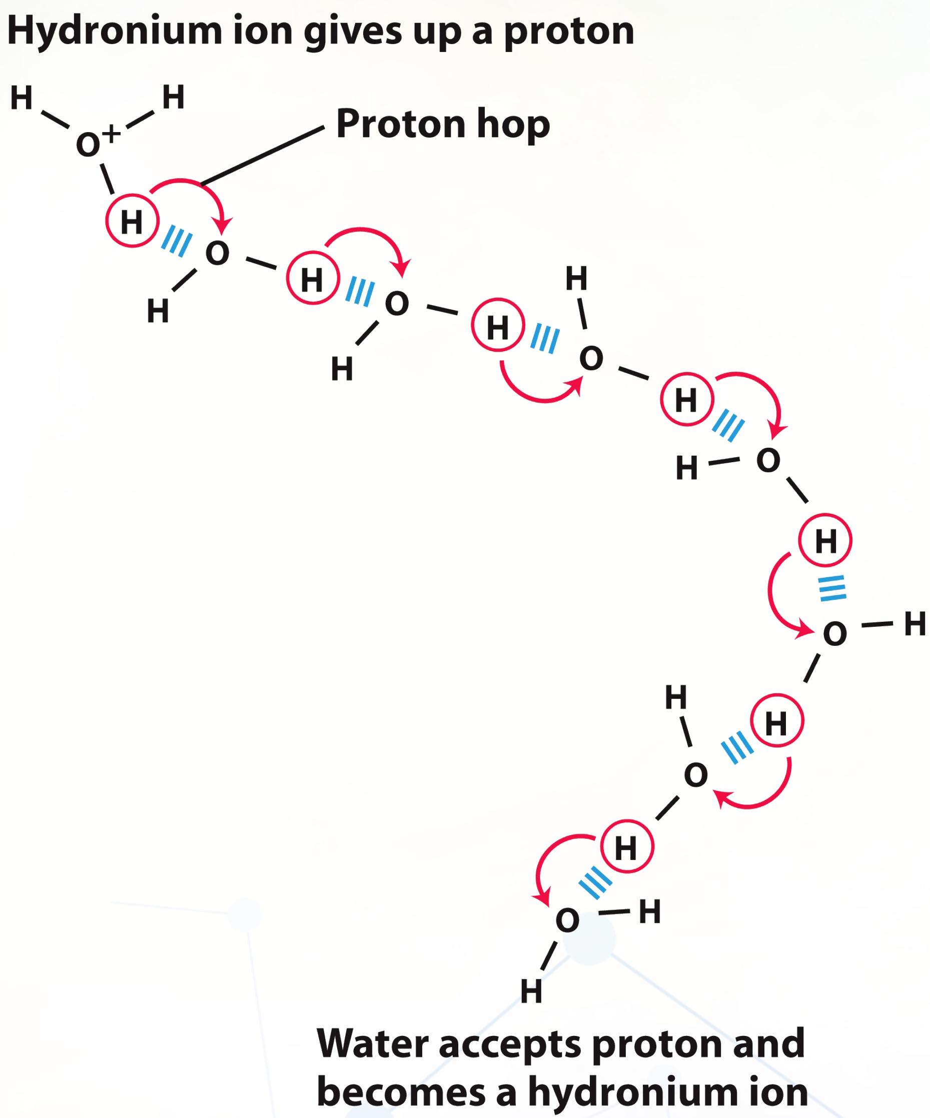
1. Understand the properties of weak acids and bases
2. Work the Henderson-Hasselbach equation to elucidate the state of molecules in a solution
3. Be able to titrate weak acids and amino acids
4. Differentiate the amino acids and learn their structures and properties

Section 1

Water and Weak Acids

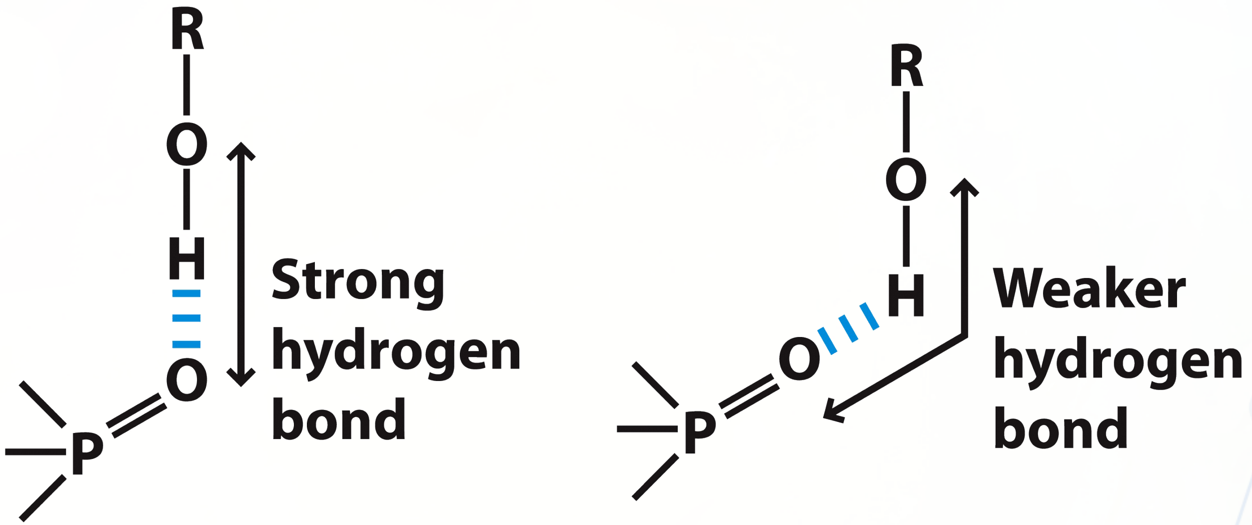
Water Forms Hydrogen Bonds





Non-covalent Interactions Govern Structure

- A single noncovalent interaction is weak
- Many interactions are strong
- The extensive interactions govern:
  - Primary & Secondary sequence
  - Macromolecular three-dimensional structure
  - Enzyme catalytic site–substrate interactions

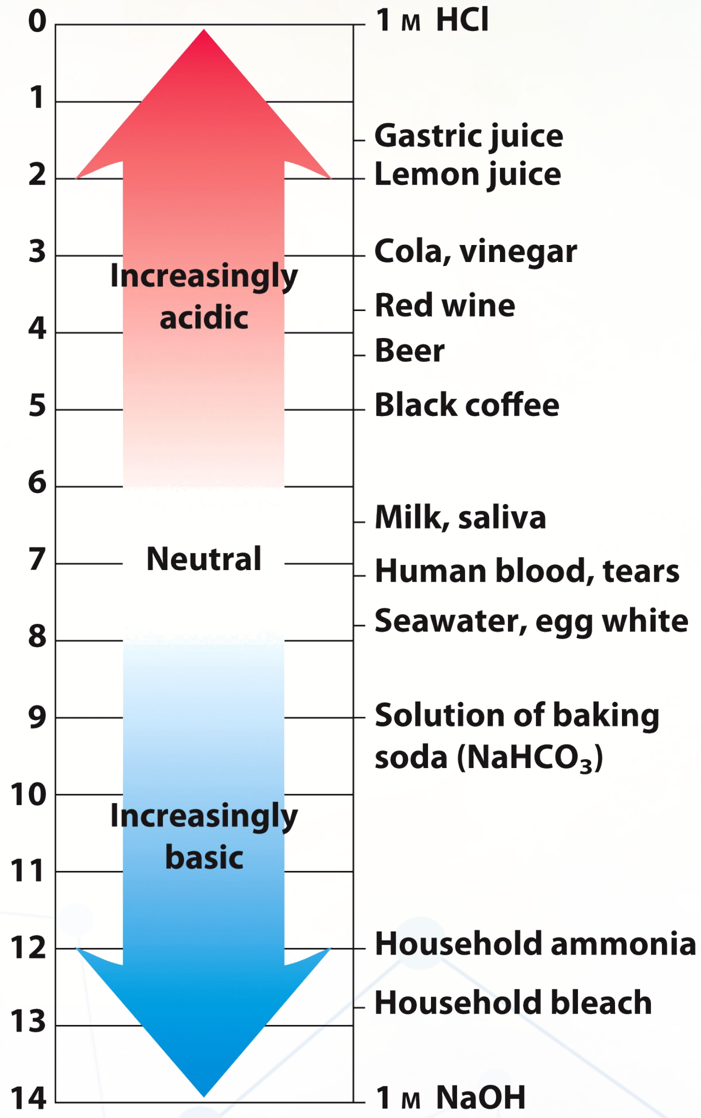


Acidity is a Measurement of A Substance's Proton Concentration

TABLE 2–6 The pH Scale

$[H^+]$ (M)	pH	$[OH^-]$ (M)	pOH*
10^0 (1)	0	10^{-14}	14
10^{-1}	1	10^{-13}	13
10^{-2}	2	10^{-12}	12
10^{-3}	3	10^{-11}	11
10^{-4}	4	10^{-10}	10
10^{-5}	5	10^{-9}	9
10^{-6}	6	10^{-8}	8
10^{-7}	7	10^{-7}	7
10^{-8}	8	10^{-6}	6
10^{-9}	9	10^{-5}	5
10^{-10}	10	10^{-4}	4
10^{-11}	11	10^{-3}	3
10^{-12}	12	10^{-2}	2
10^{-13}	13	10^{-1}	1
10^{-14}	14	10^0 (1)	0

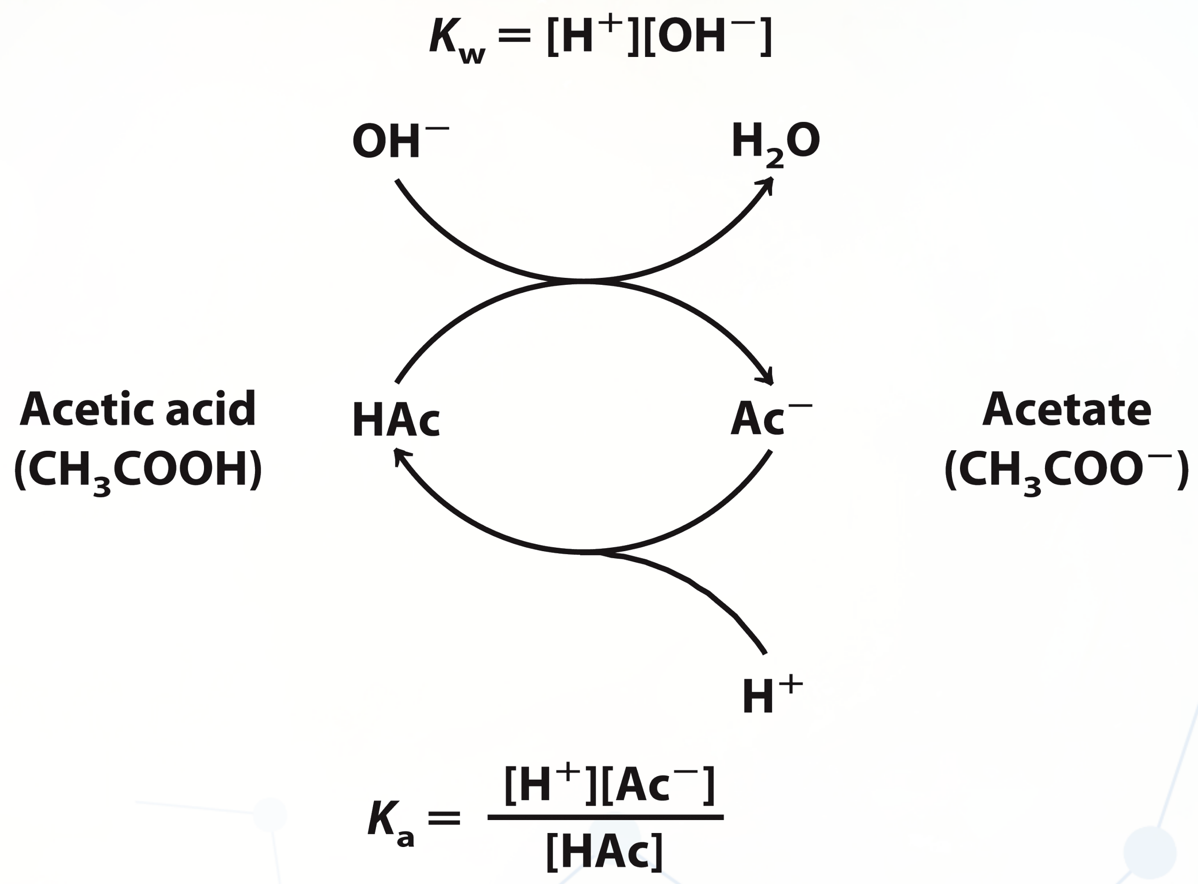
*The expression pOH is sometimes used to describe the basicity, or OH^- concentration, of a solution; pOH is defined by the expression pOH = $-\log[OH^-]$, which is analogous to the expression for pH. Note that in all cases, pH + pOH = 14.



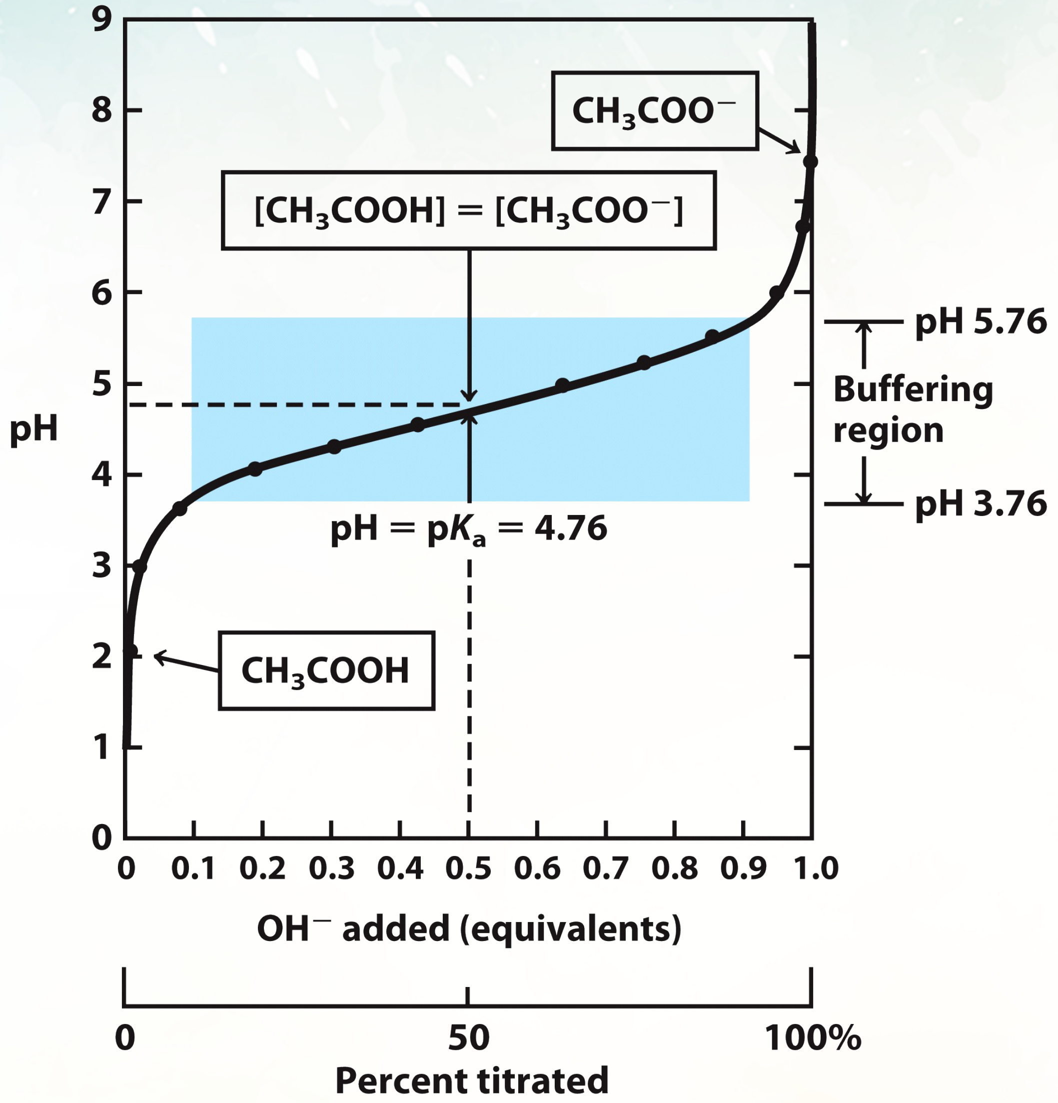
A Molecule's Ability to Lose Protons is Expressed as pK_a, Which Is Different from pH

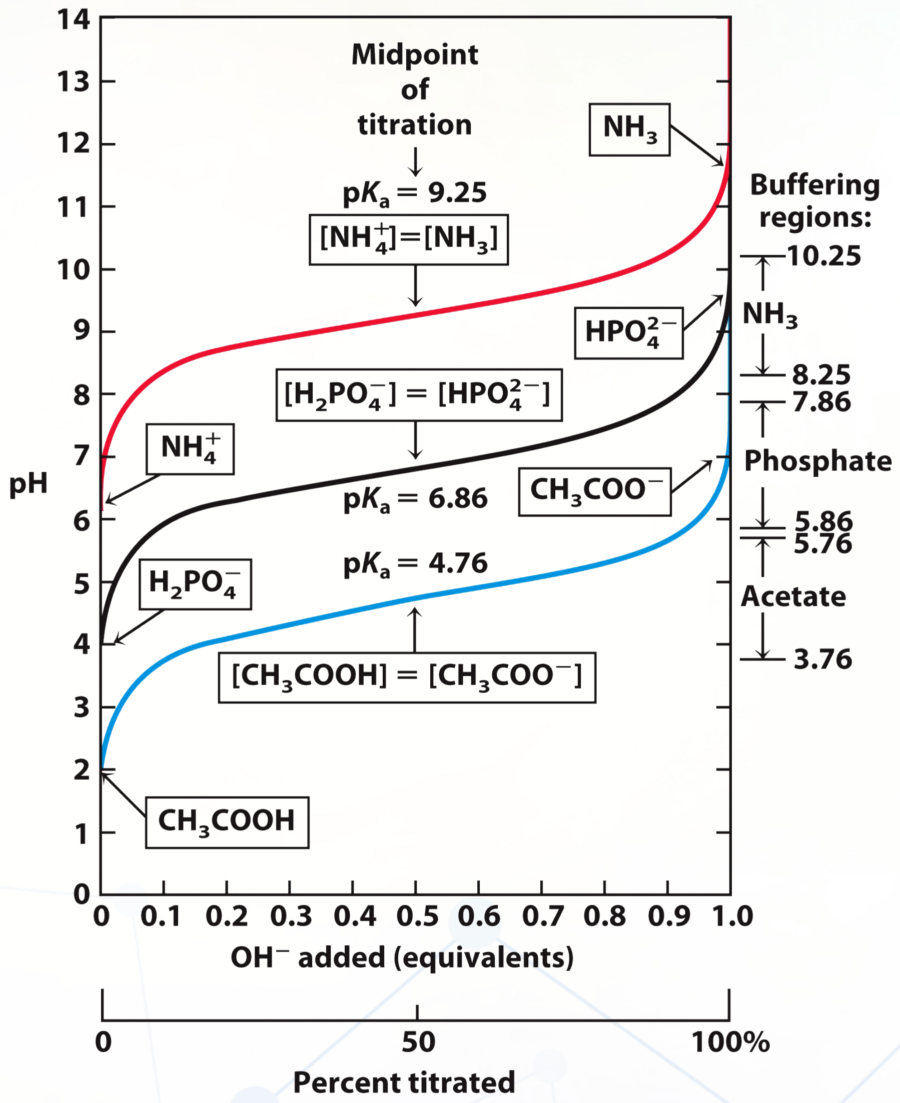
$$pH = -\log[H^+]$$

$$pK_a = -\log(K_a)$$



Titration of a Weak Acid Visually Relates the pK_a to the pH





The Henderson-Hasselbach (H-H) Equation Mathematically Relates the pK_a to the pH

- In biochemistry, we generally aren't dealing with strong acids and bases
  - More interested in weak acids and bases such as amino acids

$$\mathrm{pH} = \mathrm{pK}_a + \log\left(\frac{[\mathrm{A}^-]}{[\mathrm{HA}]}\right)$$

IN-CLASS EXERCISE

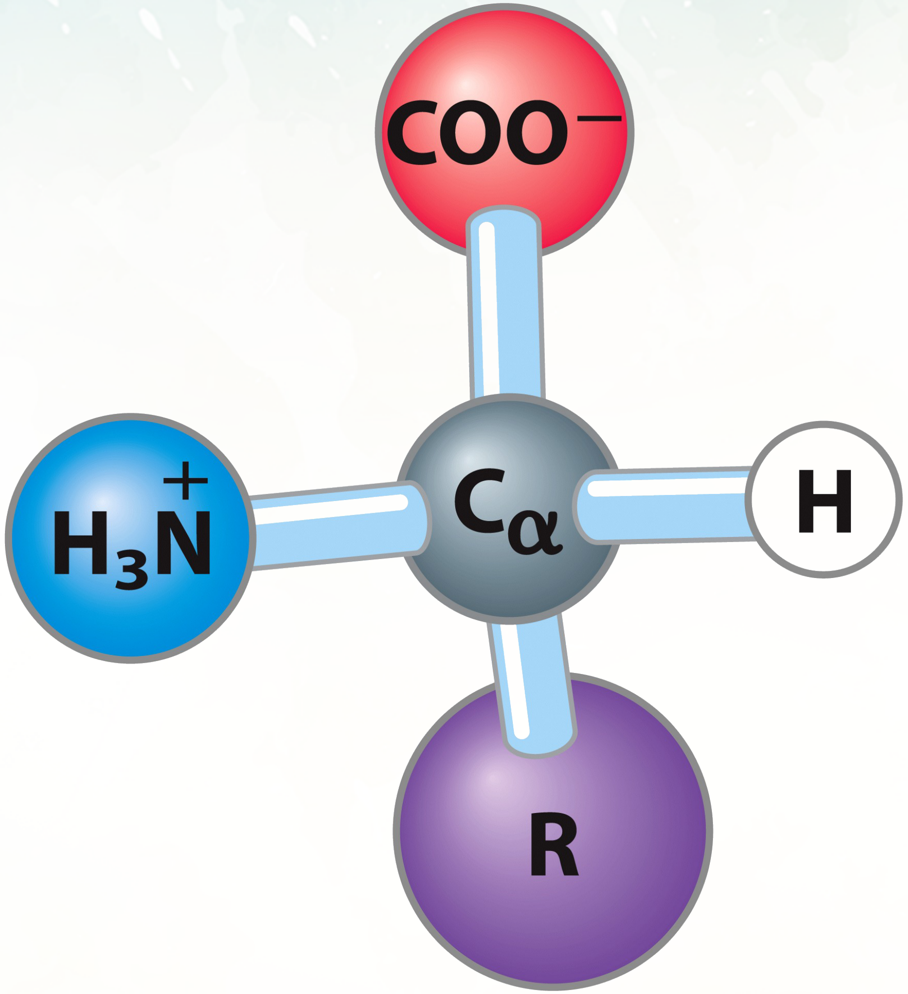
The pH of a solution at equilibrium is 4. There is only one acid in the solution, with a known pK_a of 2.

1. What is the ratio of base to acid ($[A^-]/[HA]$)?
2. What percentage of acid, at equilibrium, exists as a base?

Section 2

The Amino Acids

General Structure of an Amino Acid Centers Around the Cα



- 20 different common amino acids
- The α-carbon always has four substituents and is tetrahedral
- All (except proline) have:
  - An acidic carboxyl group
  - A basic amino group
  - An α-hydrogen connected to the α-carbon
- All (except for glycine) have a chiral center at the α-carbon
- The fourth substituent (R) is unique
  - In glycine, the fourth substituent is also hydrogen and thus, is not chiral

Table 3-1 is a Useful Reference Table

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

			pK_a values					
Amino acid	**Abbreviation/ symbol**	**M_r***	**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

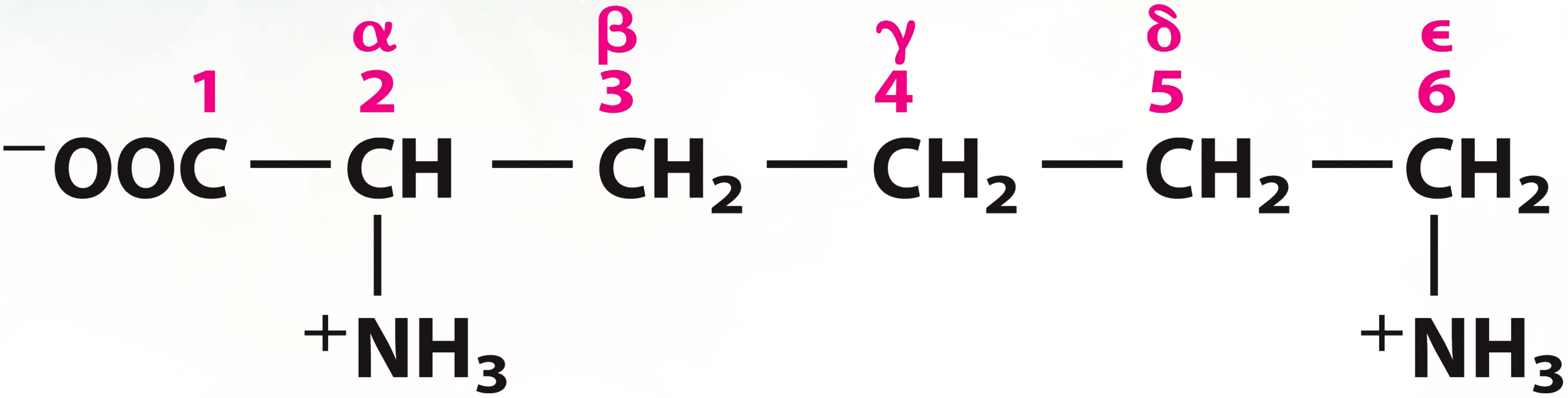
*M_r values reflect the structures as shown in Figure 3–5. The elements of water (M_r 18) are deleted when the amino acid is incorporated into a polypeptide.

†A scale combining hydrophobicity and hydrophilicity of R groups. The values reflect the free energy (ΔG) of transfer of the amino acid side chain from a hydrophobic solvent to water. This transfer is favorable ($\Delta G < 0$; negative value in the index) for charged or polar amino acid side chains, and unfavorable ($\Delta G > 0$; positive value in the index) for amino acids with nonpolar or more hydrophobic side chains. See Chapter 11. From Kyte, J. & Doolittle, R.F. (1982) A simple method for displaying the hydropathic character of a protein. *J. Mol. Biol.* 157, 105–132.

‡Average occurrence in more than 1,150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed.), pp. 599–623, Plenum Press, New York.

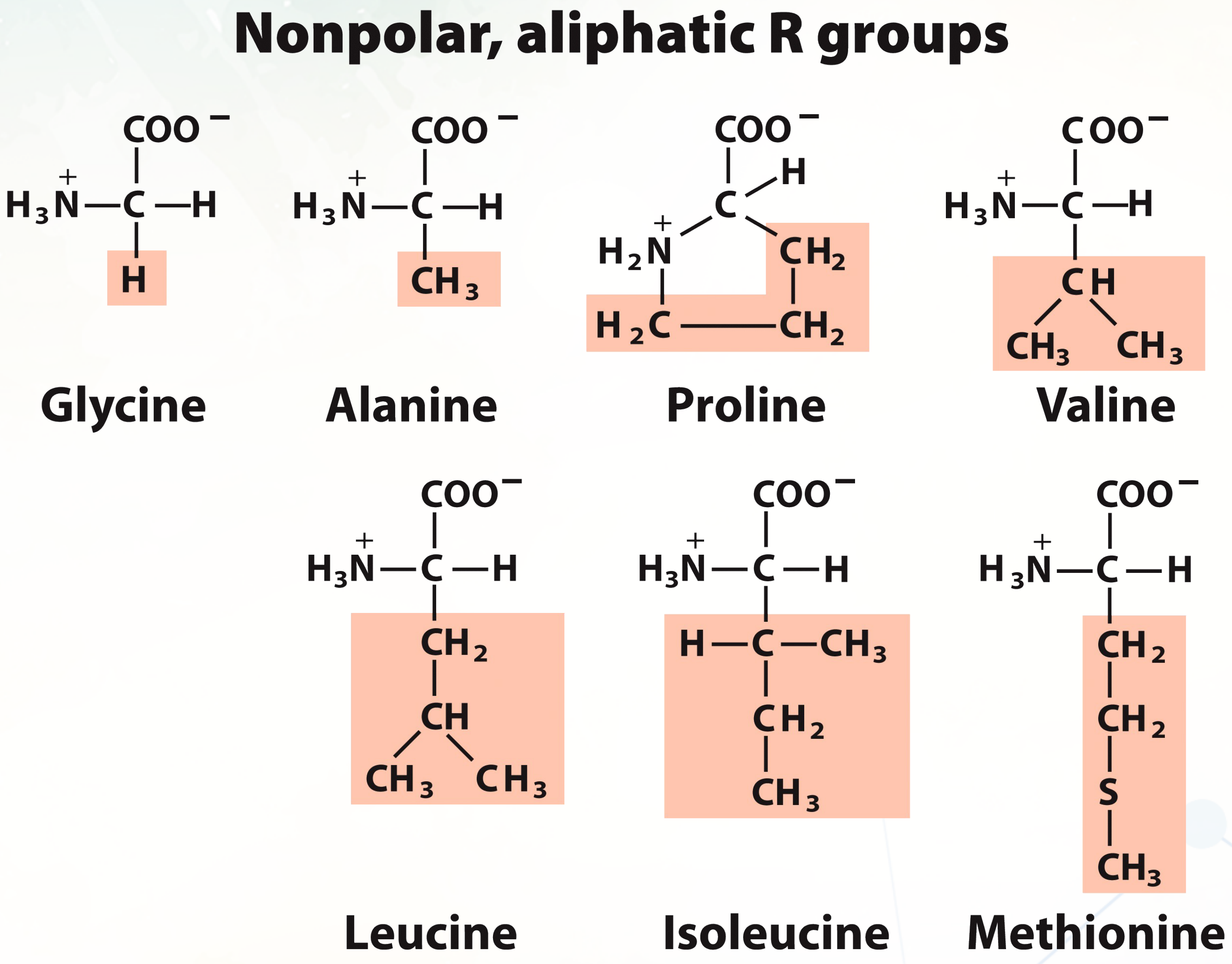
¶Cysteine is generally classified as polar despite having a positive hydropathy index. This reflects the ability of the sulfhydryl group to act as a weak acid and to form a weak hydrogen bond with oxygen or nitrogen.

Amino Acid Numbering Convention Differs from Regular Atomic Numbering

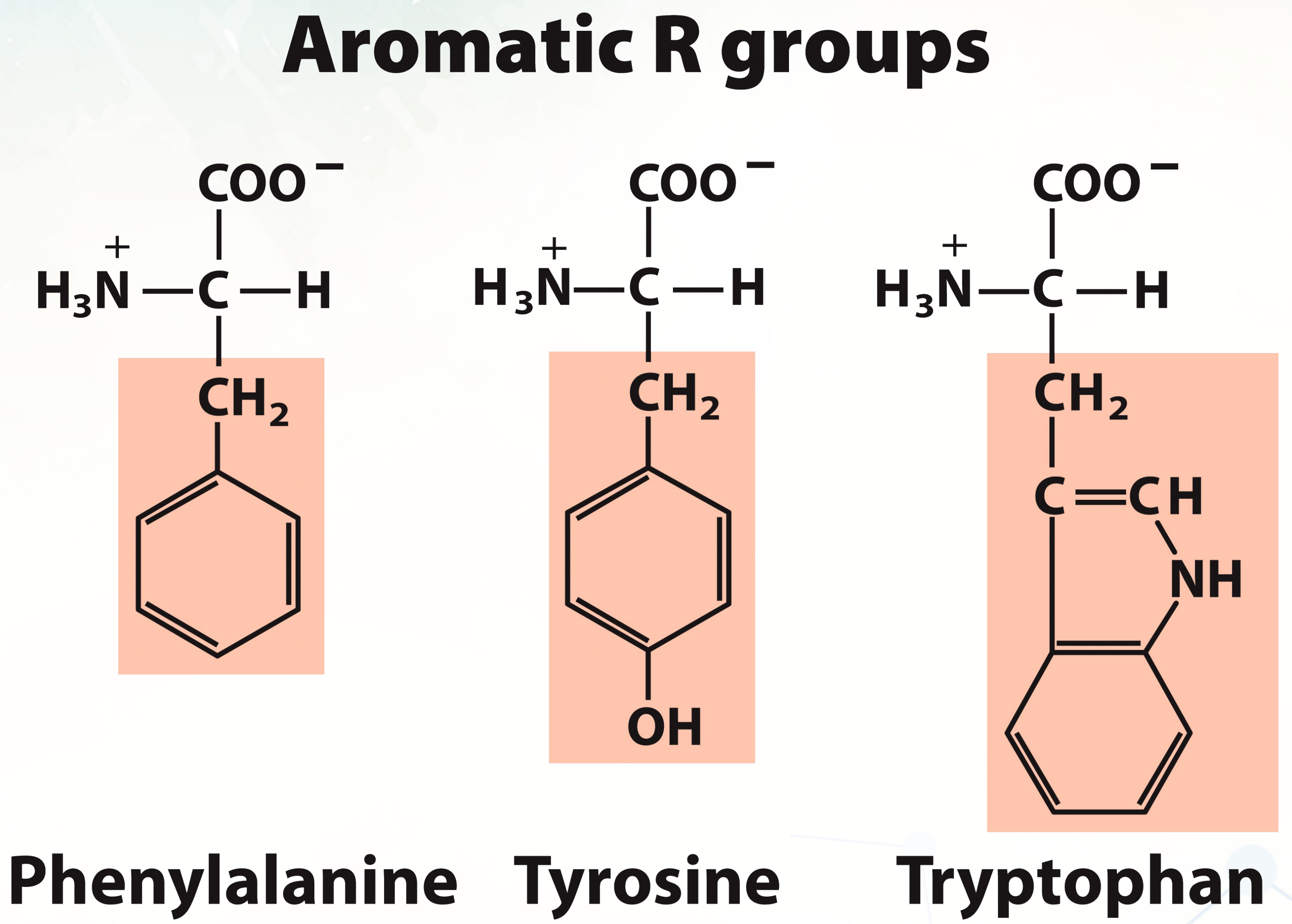


Lysine

Nonpolar, Aliphatic Amino Acids Are Very Stable

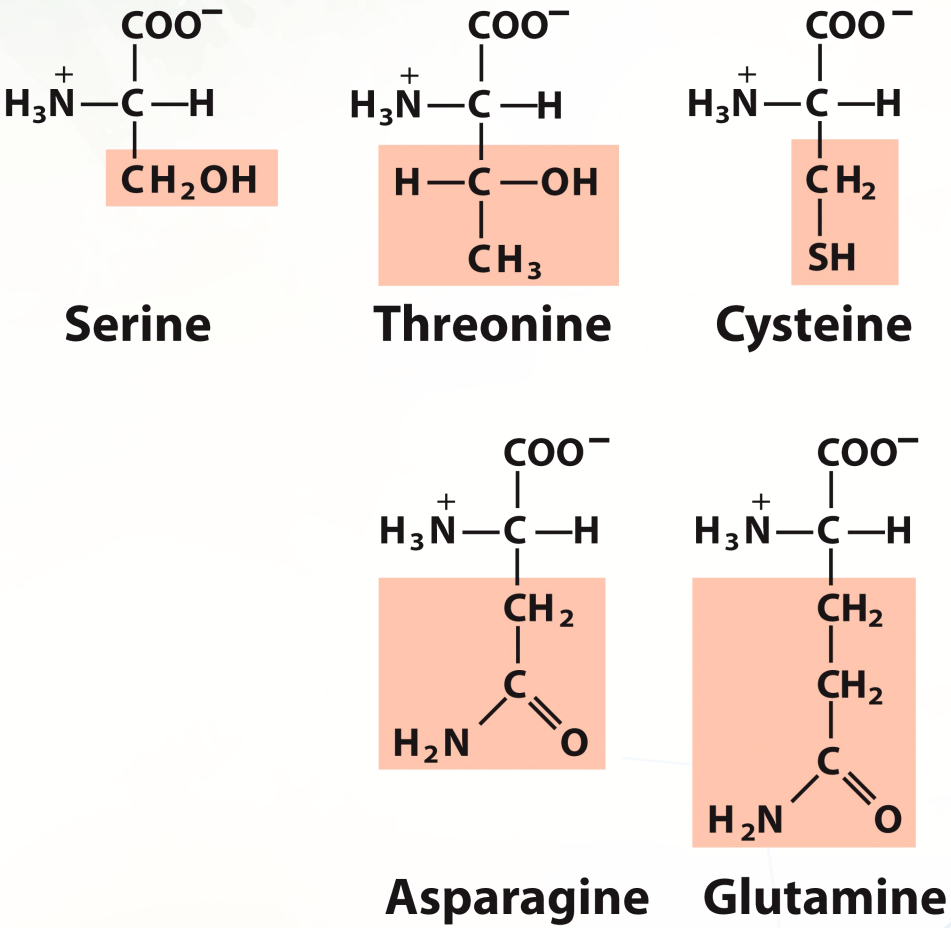


Aromatic Amino Acids Absorb Ultraviolet Light



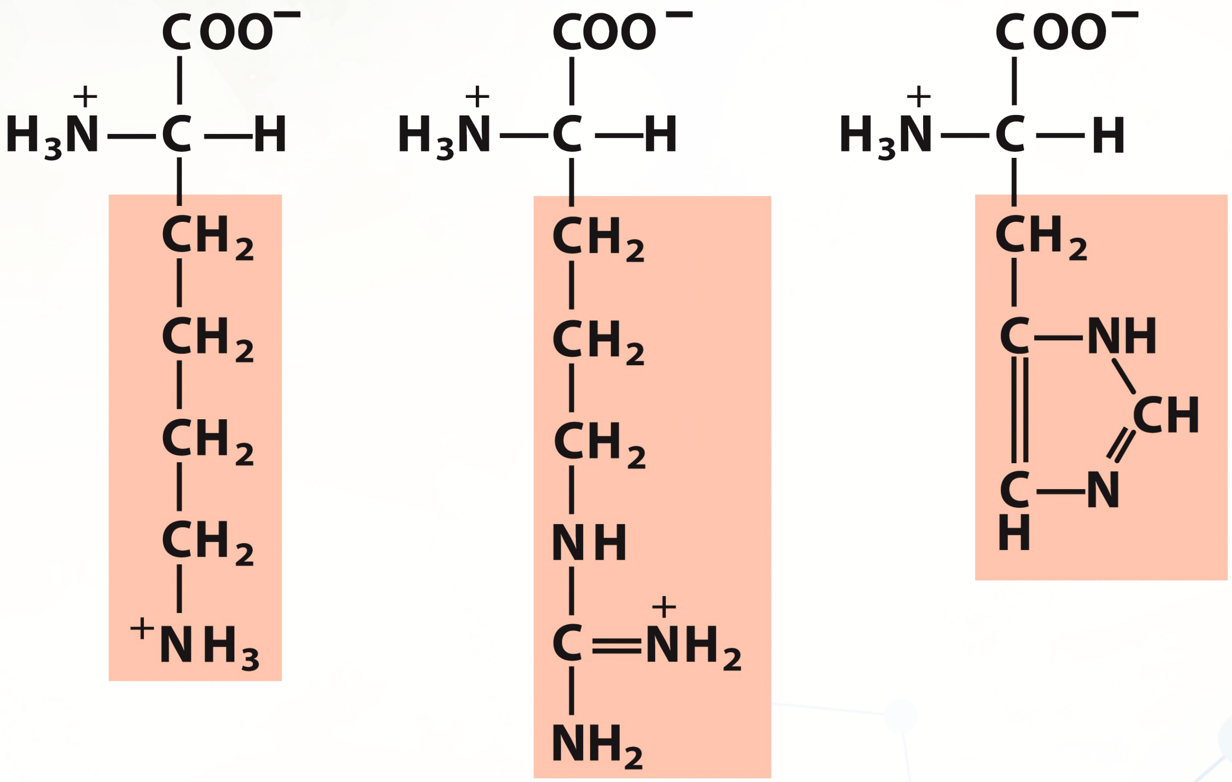
Polar, Uncharged Amino Acids Easily Form Hydrogen Bonds

Polar, uncharged R groups



Positively Charged R Groups Donate Protons at High pH

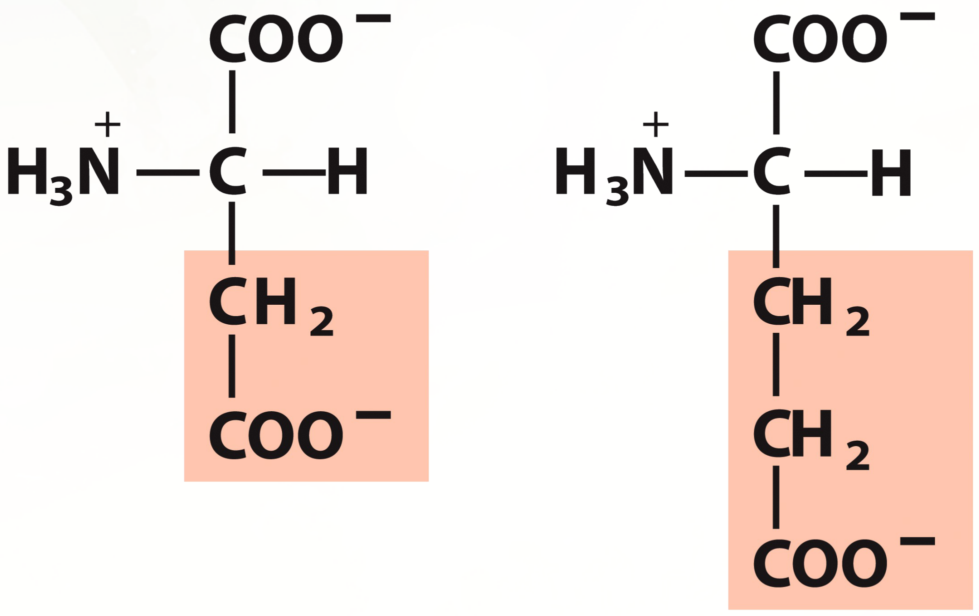
Positively charged R groups



Lysine　　Arginine　　Histidine

Negatively Charged Amino Acids Donate Protons at Low pH

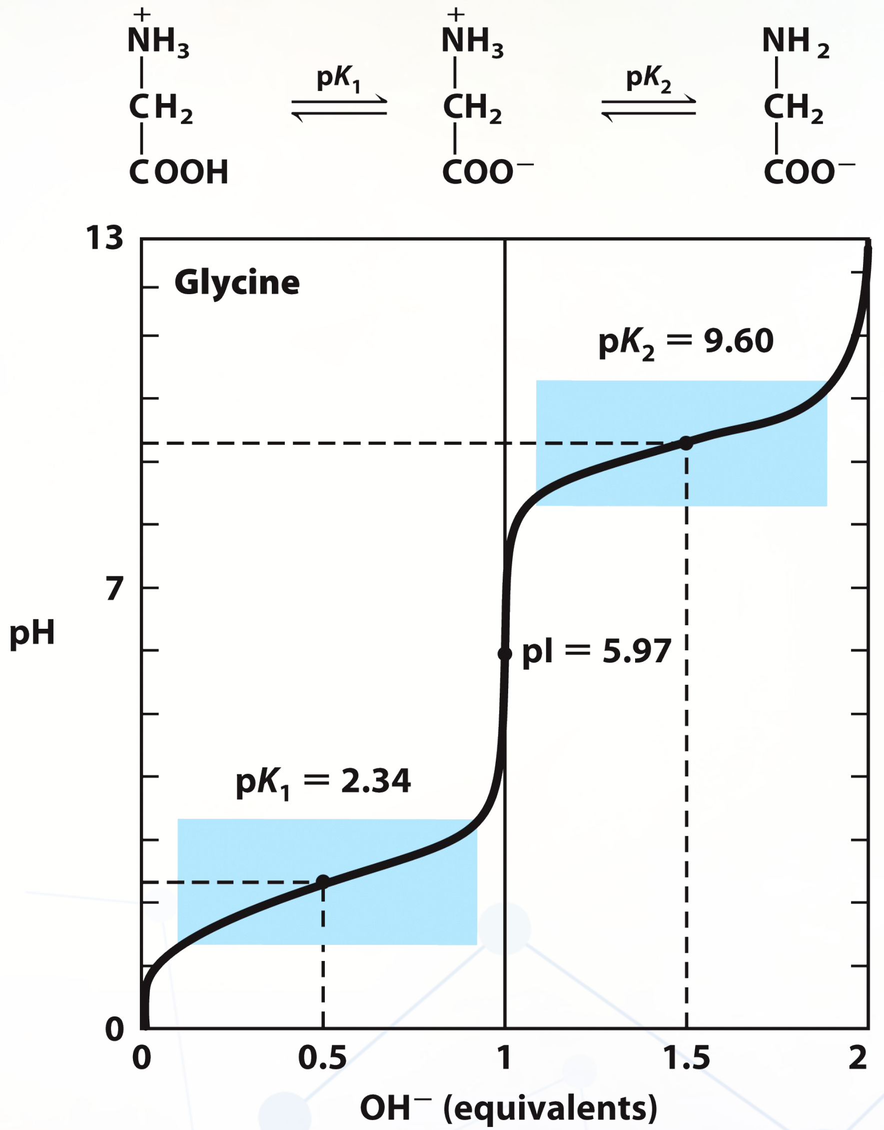
Negatively charged R groups



Aspartate   Glutamate

Titration of Amino Acids Follow the Same Concepts as Titration of Weak Acids

- At acidic pH, the carboxyl group is protonated (COOH) and the amino acid is in the cationic form (NH_3^+)
- At neutral pH, the carboxyl group of glycine is deprotonated but the amino group is protonated
  - The net charge is zero
- At alkaline pH, the amino group is neutral –NH2 and the amino acid is in the anionic form



pI Defines the pH When an Amino Acid is Neutral

- The isoelectric point defines the pH when an amino acid is likeliest to exist with an overall charge of 0

$$\mathrm{pI} = \frac{\mathrm{pK}_{positive} + \mathrm{pK}_{zero}}{2}$$

IN-CLASS EXERCISE

- Draw a titration curve for the titration of glutamate
- Be sure to label all parts:
    - Axes
    - All pKa
    - All pI
    - The curve itself

The pK_a Depends on the Chemical Environment