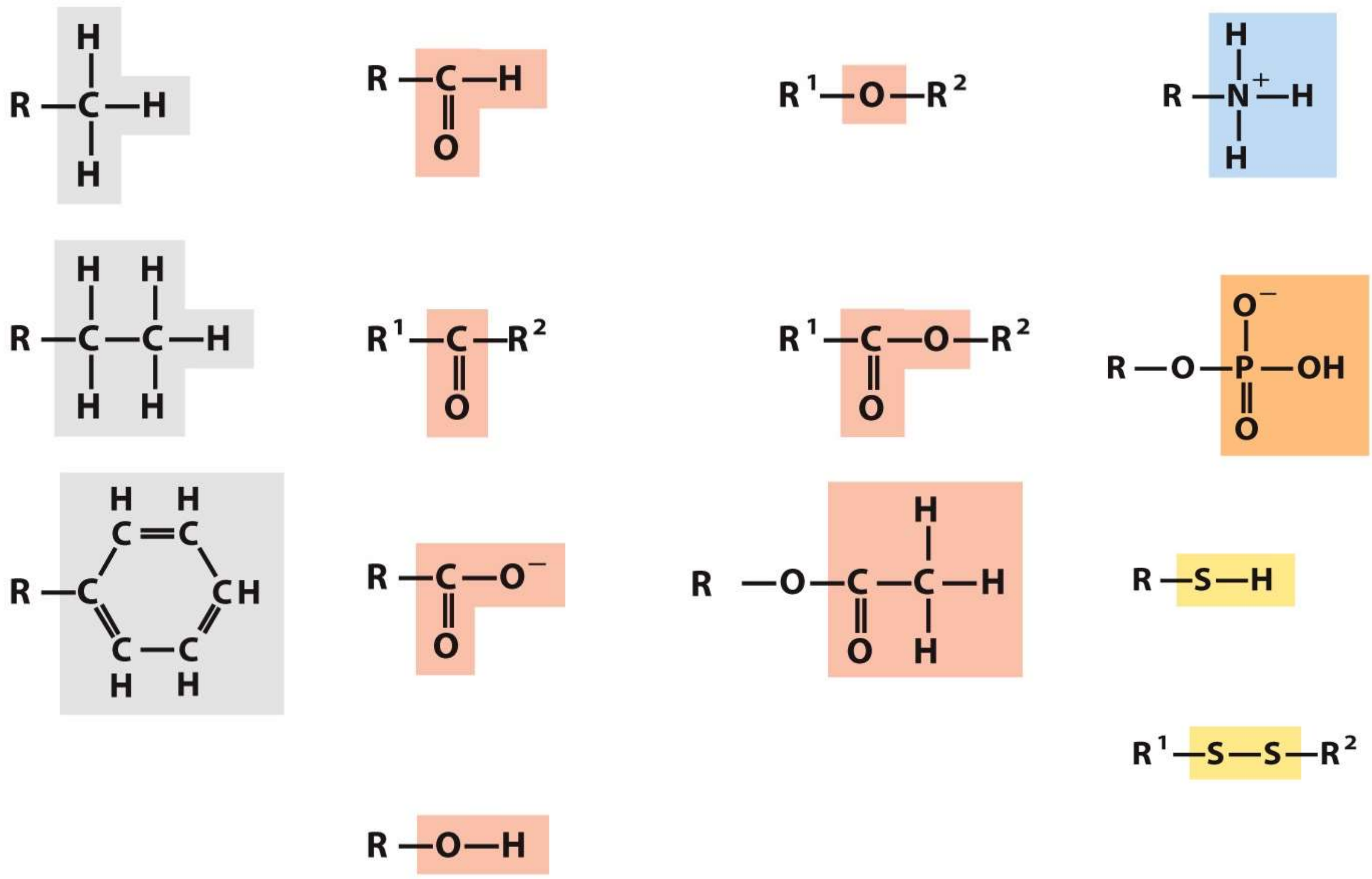
1st week

- Living organisms (domains, kingdoms, definition)
- Cellular foundation: Structure and function of the cell
- Chemical foundation: Biomolecules and building blocks

2nd week

- Three laws of thermodynamics (1, 2)
- Is a living organism at equilibrium with surrounding?
- ΔG?
- Equilibrium constant?
- ΔG°?
- Chemical coupling?
- Enzymes function as catalysts. How?

14 Organic Friends



3rd week

- Nature of intermolecular forces (IHVH)
- 4 things about water (HHOP)
- Behavior of weak acids and bases in water: pK_a
- Henderson-Hasselbalch Equation

$$K_a = \frac{[H^+][A^-]}{[HA]} = K_{eq}$$

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$

H.W: What are acidosis and alkalosis?

pH calculations!!

1. Calculate the pH of a 150 mL solution of pure water to which has been added 50 mL of 1 mM HCl.
2. Calculate the pH of a 1 L solution containing
   a. 10 mL of 5 M NaOH
   b. 10 mL of 100 mM glycine and 20 mL of 5 M HCl
   c. 10 mL of 2 M acetic acid and 5 g of sodium acetate (MW: 82 g/mol), pK_a=4.76
3. A solution is made by mixing 50 mL of 2.0 M K_2HPO_4 and 25 mL of 2.0 M KH_2PO_4. The solution is diluted to a final volume of 100 mL. What is the pH of the final solution? pK_a= 6.82
4. What is the pK_a of the weak acid HA if a solution containing 0.1 M HA and 0.2 M A^- has a pH of 6.5?

Amino Acids, Peptides, and Proteins

1. Structure and naming of amino acids
2. Ionization behavior of amino acids
3. Methods to characterize peptides and proteins

Proteins:
Main Agents of Biological Function

- Catalysis
  - enolase (in the glycolytic pathway)
  - DNA polymerase (in DNA replication)
- Transport
  - hemoglobin (transports O_2 in the blood)
  - lactose permease (transports lactose across the cell membrane)
- Structure
  - collagen (connective tissue)
  - keratin (hair, nails, feathers, horns)
- Motion
  - myosin (muscle tissue)
  - actin (muscle tissue, cell motility)

Amino Acids:
Building Blocks of Protein

- Proteins are linear heteropolymers of α-amino acids.

- Amino acids have properties that are well suited to carry out a variety of biological functions:
  - capacity to polymerize
  - useful acid-base properties
  - varied physical properties
  - varied chemical functionality

Amino Acids Share Many Features, Differing Only at the R Substituent

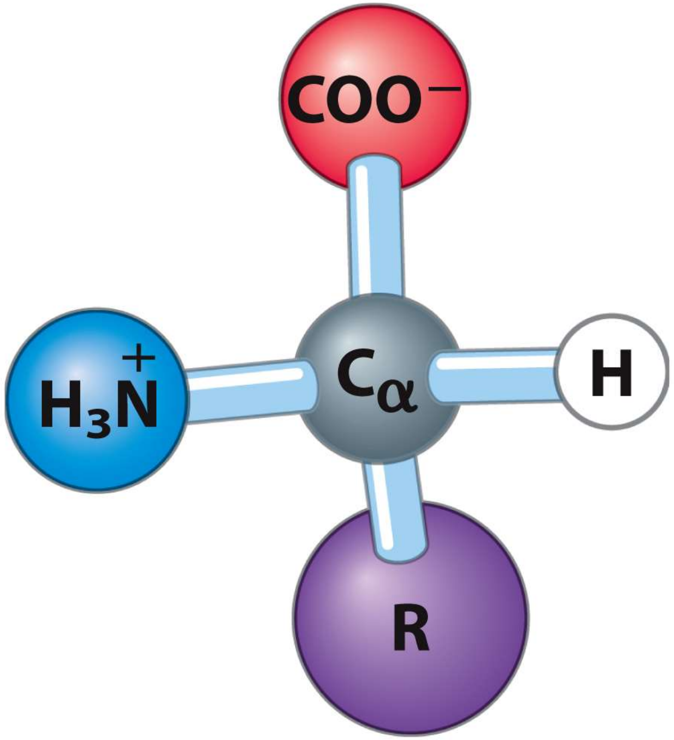


Figure 3-2
Lehninger Principles of Biochemistry, Seventh Edition

- The α carbon always has four substituents and is tetrahedral.
- All (except proline) have:
  - an acidic carboxyl group connected to the α carbon
  - a basic amino group connected to the α carbon
  - an α hydrogen connected to the α carbon
- The fourth substituent (R) is unique in glycine, the simplest amino acid. The fourth substituent is also hydrogen.

All Amino Acids Are Chiral (Except Glycine)

Proteins only contain L amino acids

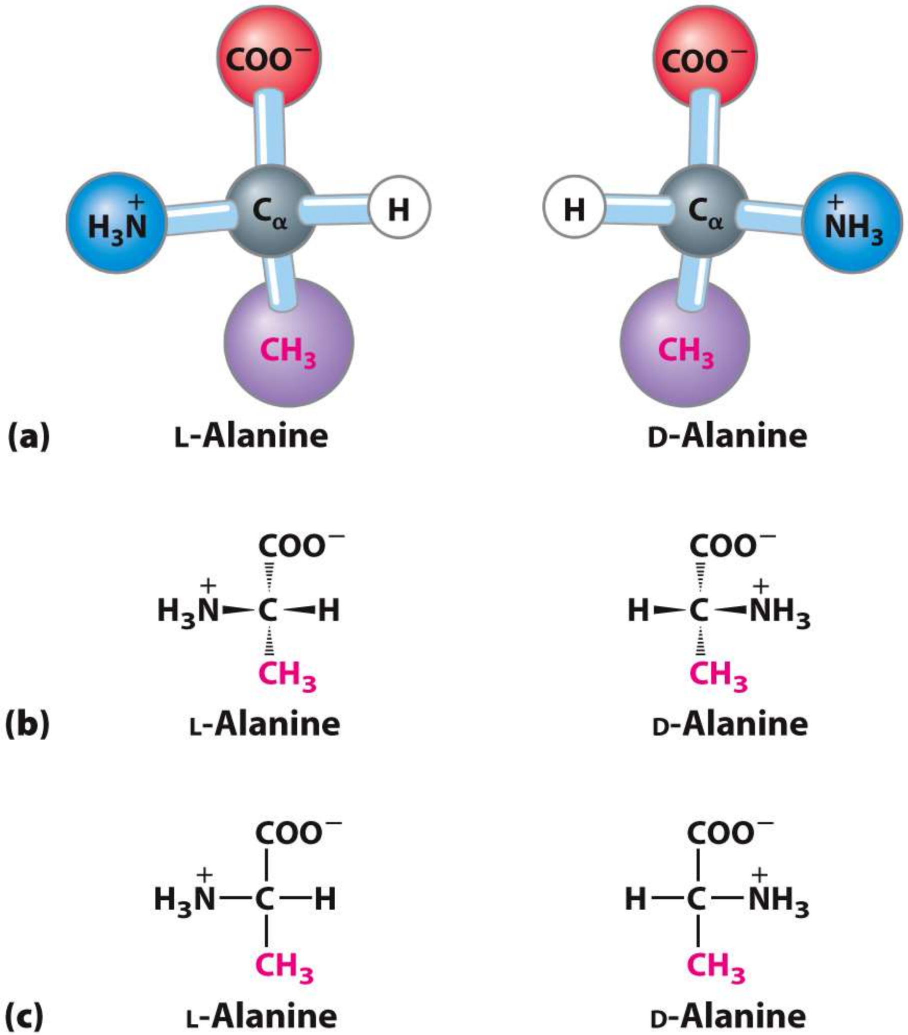


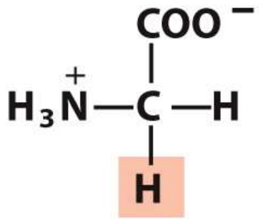
Figure 3-3
Lehninger Principles of Biochemistry, Seventh Edition

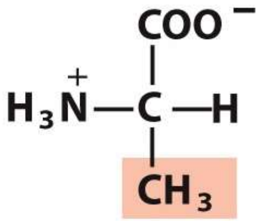
Amino Acids: Classification

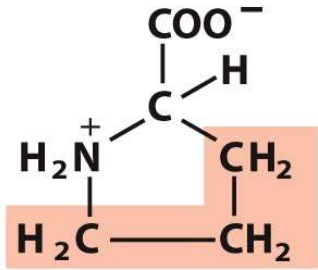
Common amino acids can be placed in five basic groups depending on their R substituents:

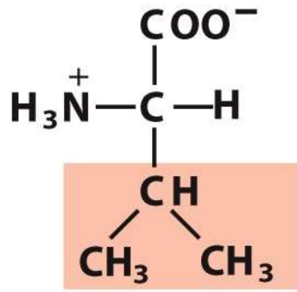
- nonpolar (7)
- aromatic (3)
- polar, uncharged (5)
- positively charged (3)
- negatively charged (2)

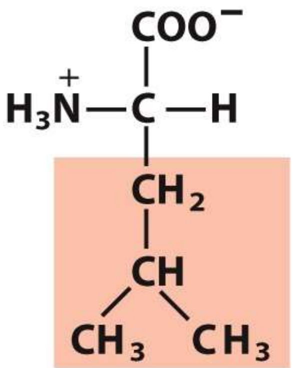
Amino Acids: Classification

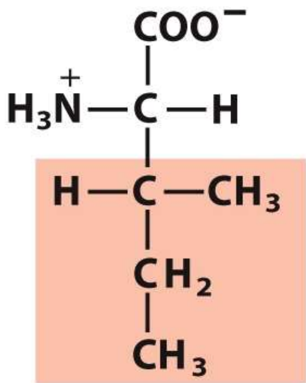


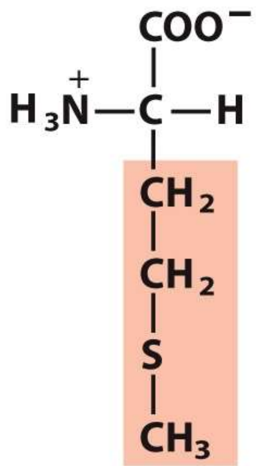




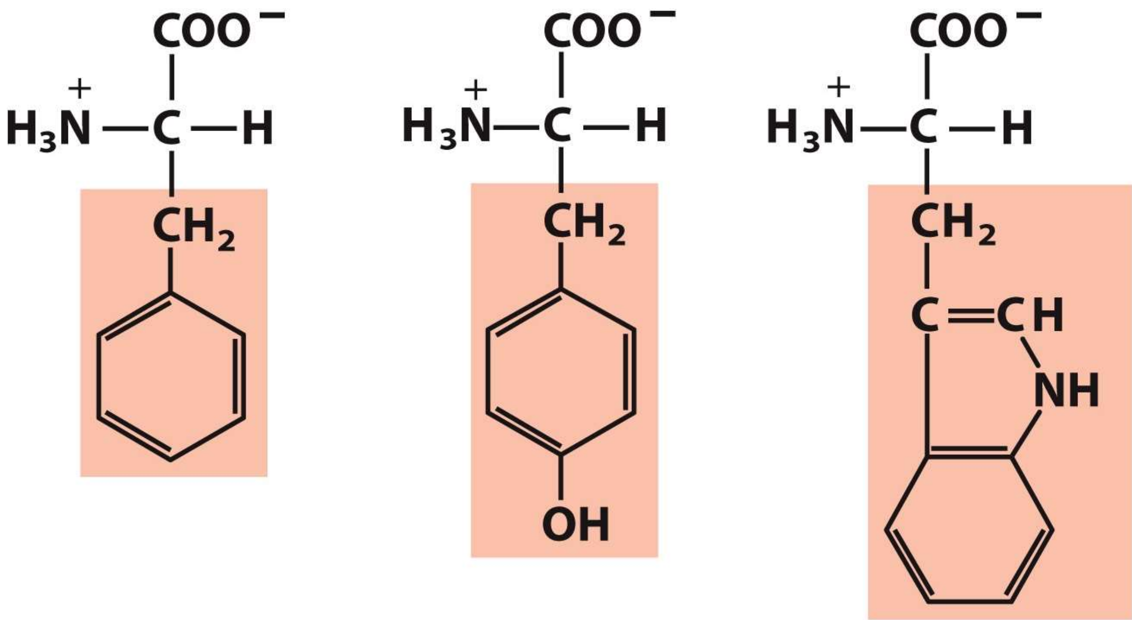






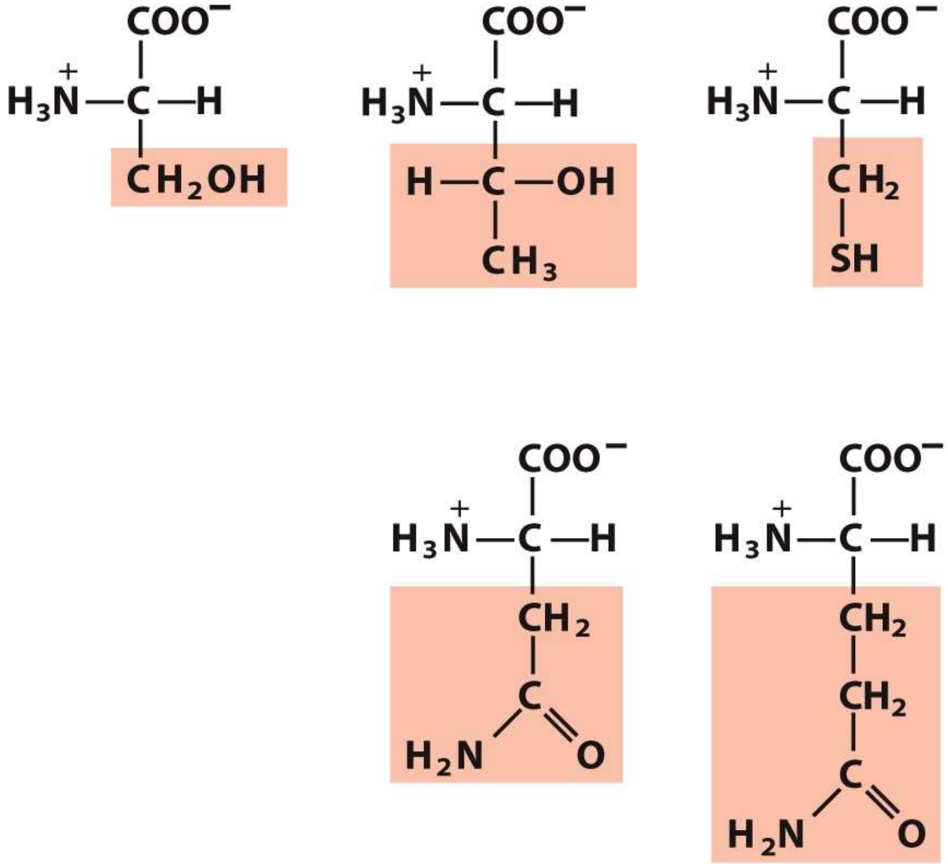


Amino Acids: Classification



These amino acid side chains absorb UV light at 270–280 nm

Amino Acids: Classification



These amino acids side chains can form hydrogen bonds.
Cysteine can form disulfide bonds.

Cysteine Can Form Disulfide Bonds

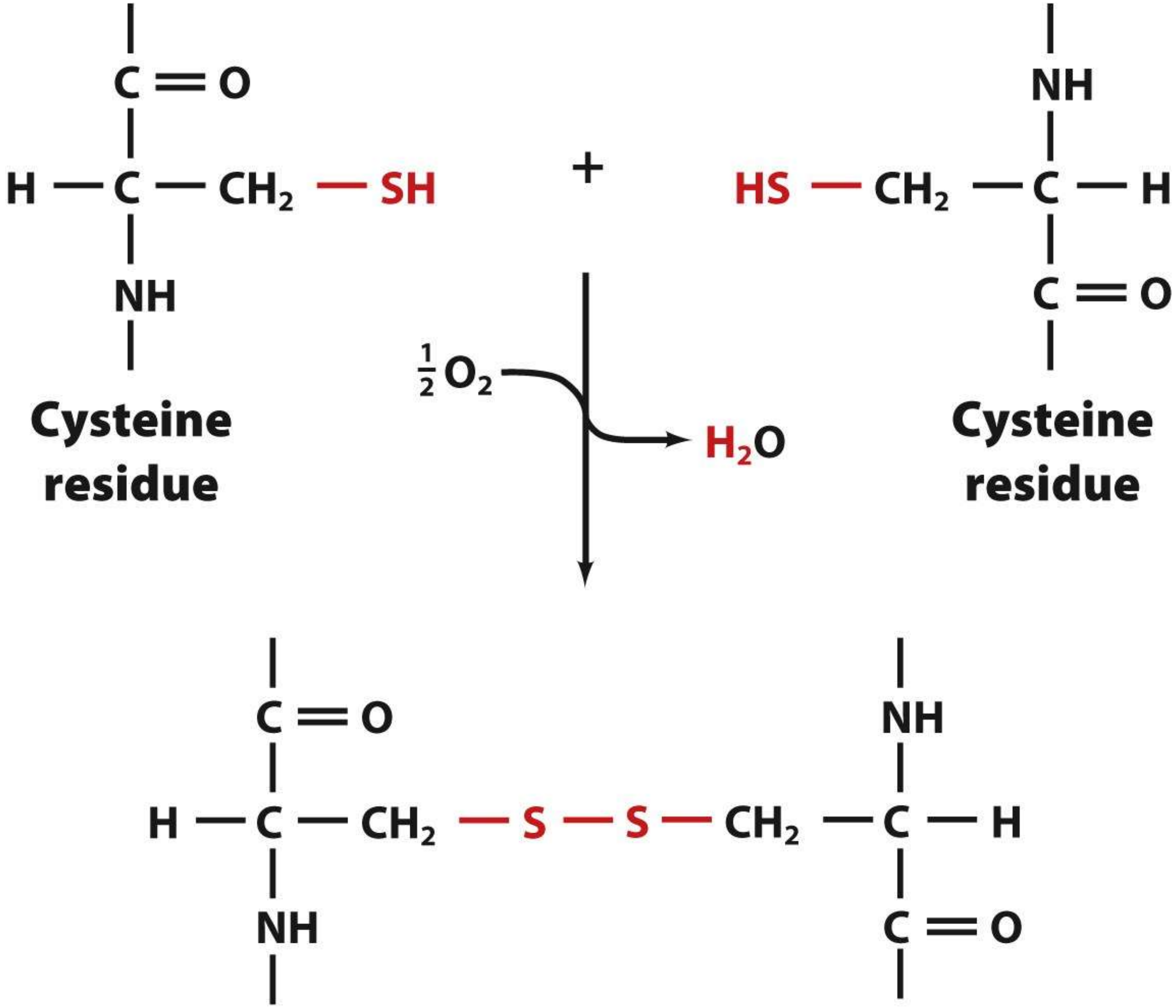
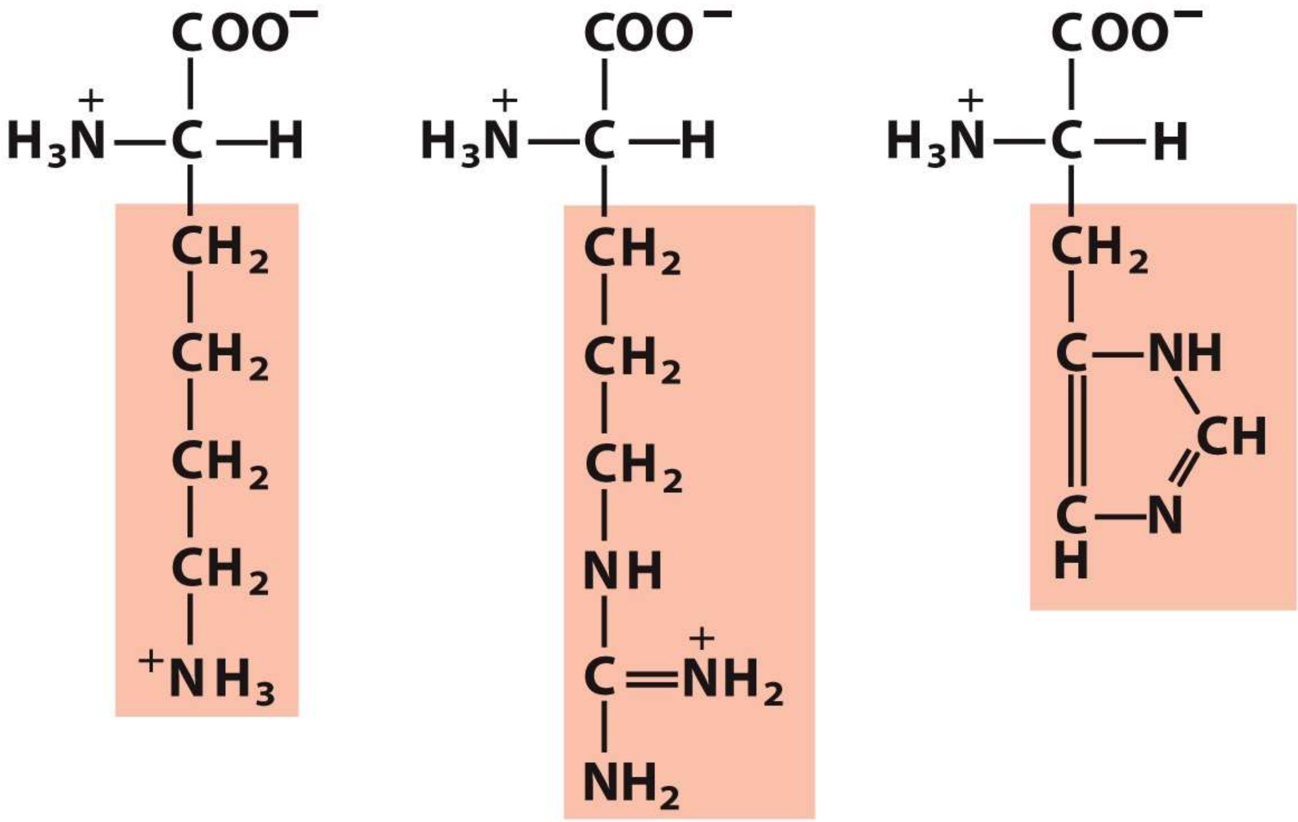
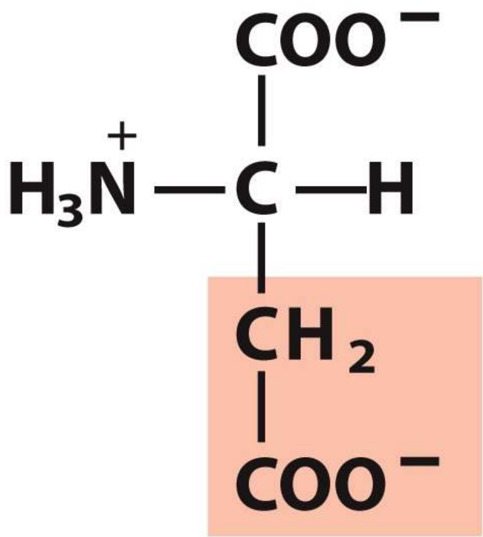


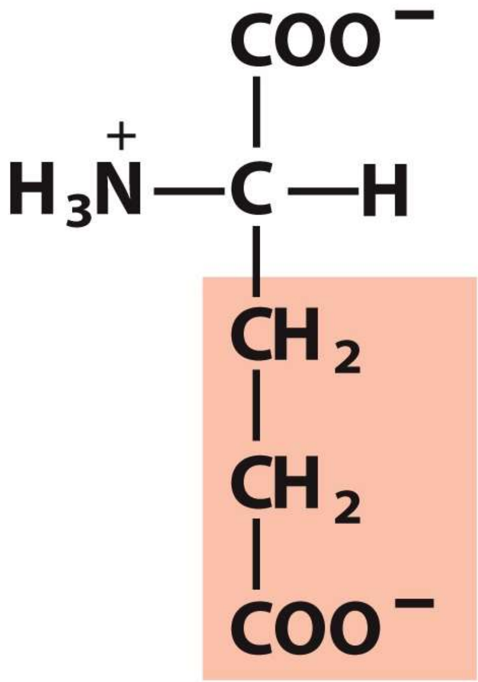
Figure 4-6

Amino Acids: Classification



Amino Acids: Classification



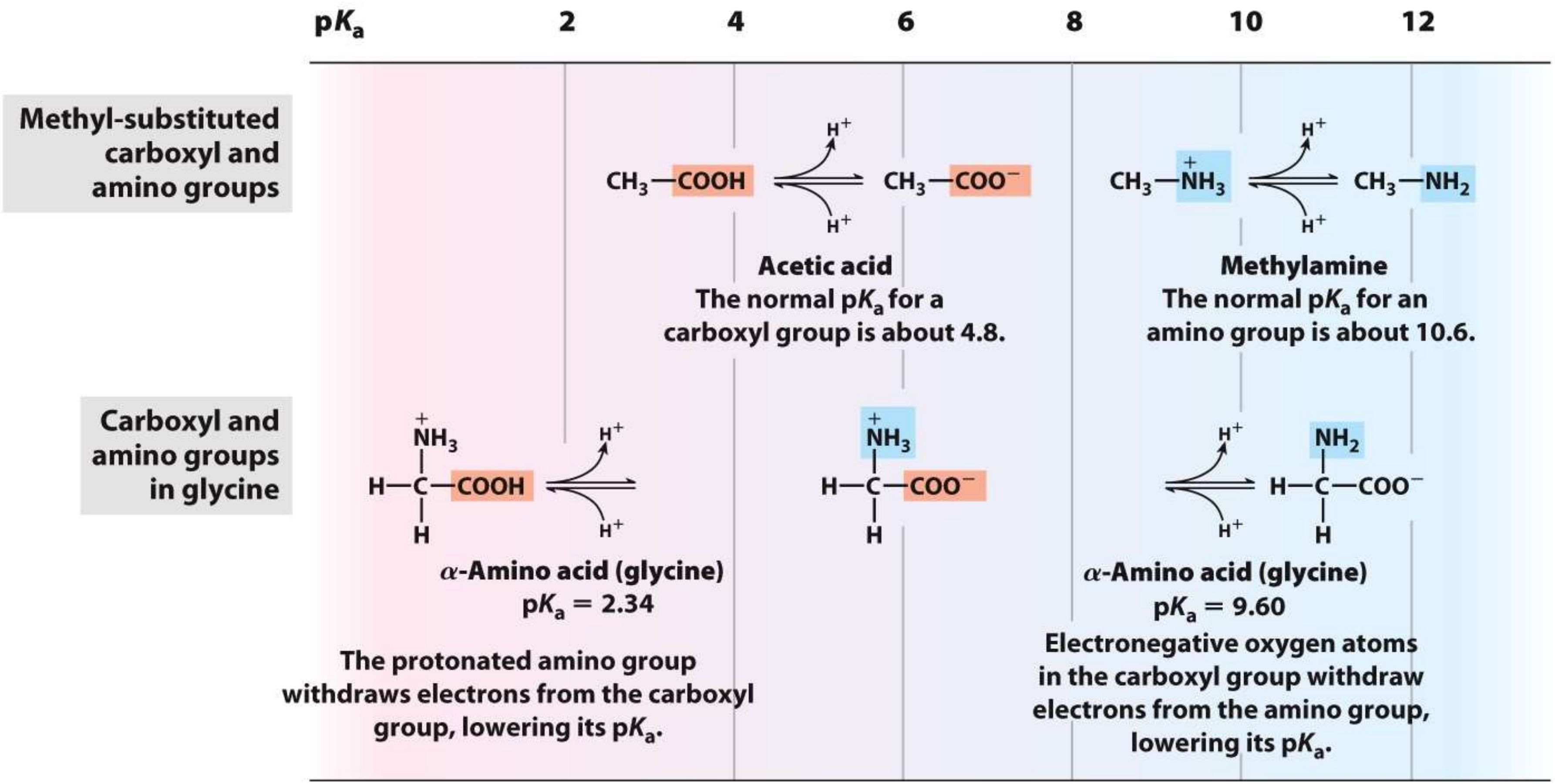


Ionization of Amino Acids

- Amino acids contain at least two ionizable protons, each with its own pK_a.
- The carboxylic acid has an acidic pK_a and will be protonated at an acidic (low) pH: $-COOH \leftrightarrow COO^- + H^+$
- The amino group has a basic pK_a and will be protonated when basic pH (high) is achieved: $-NH_4^+ \leftrightarrow NH_3 + H^+$
- At low pH, the amino acid exists in a positively charged form (cation).
- At high pH, the amino acid exists in a negatively charged form (anion).
- Between the pK_a for each group, the amino acid exists in a zwitterion form, in which a single molecule has both a positive and a negative charge.

Chemical Environment Affects pK_a Values

α-carboxyl group is much more acidic than in carboxylic acids.
α-amino group is slightly less basic than in amines.



Amino Acids Carry a Net Charge of Zero at a Specific pH (the pI)

- Zwitterions predominate at pH values between the pK_a values of the amino and carboxyl groups.
- For amino acids without ionizable side chains, the Isoelectric Point (equivalence point, pI) is:

$$pI = \frac{pK_1 + pK_2}{2}$$

- At this point, the net charge is zero.
  - AA is least soluble in water.
  - AA does not migrate in electric field.

Amino Acids Can Act as Buffers

Amino acids with uncharged side chains, such as glycine, have two pK_a values:

- The pK_a of the α-carboxyl group is 2.34.
- The pK_a of the α-amino group is 9.6.

As buffers prevent change in pH close to the pK_a, glycine can act as a buffer in two pH ranges.

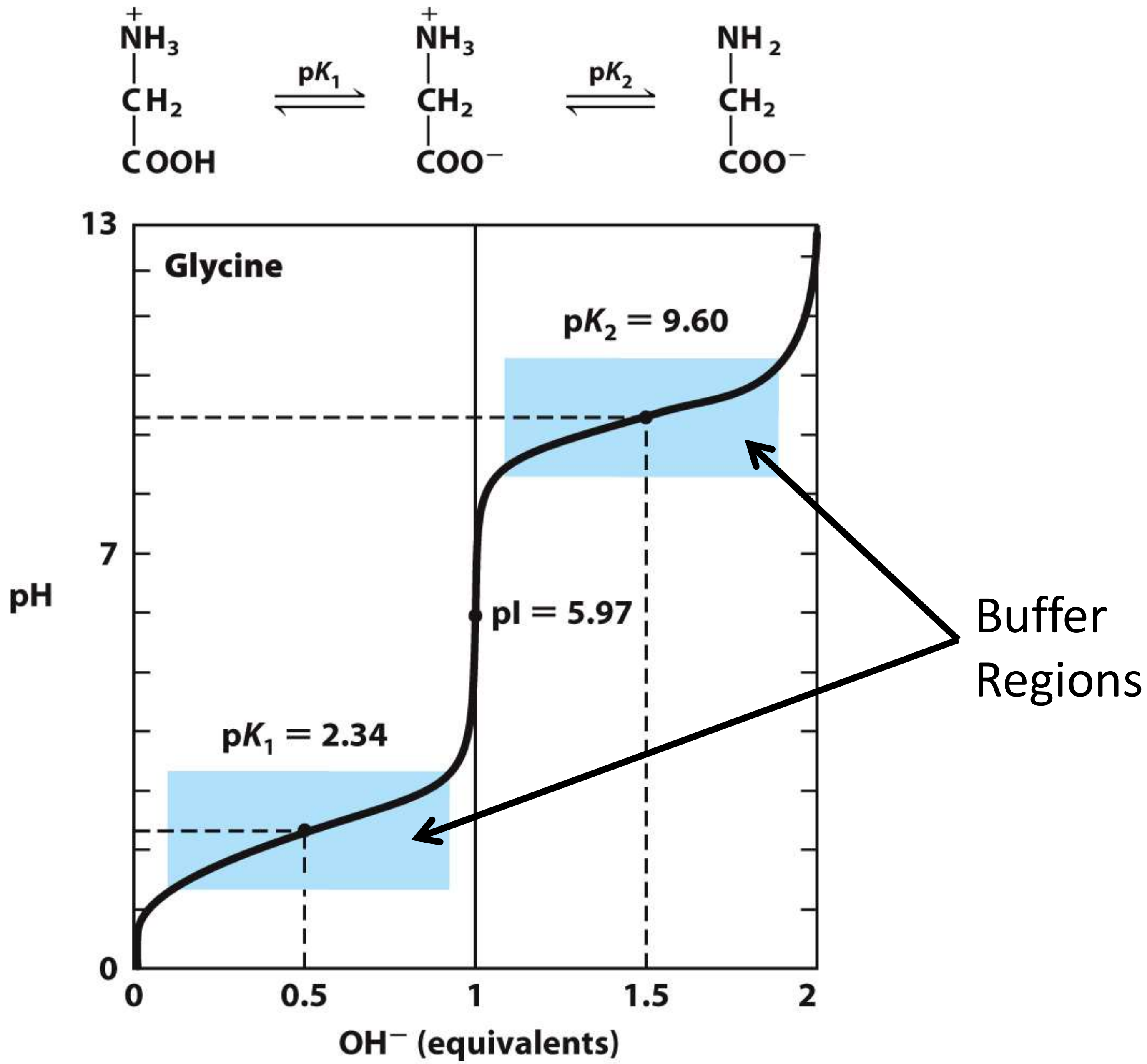
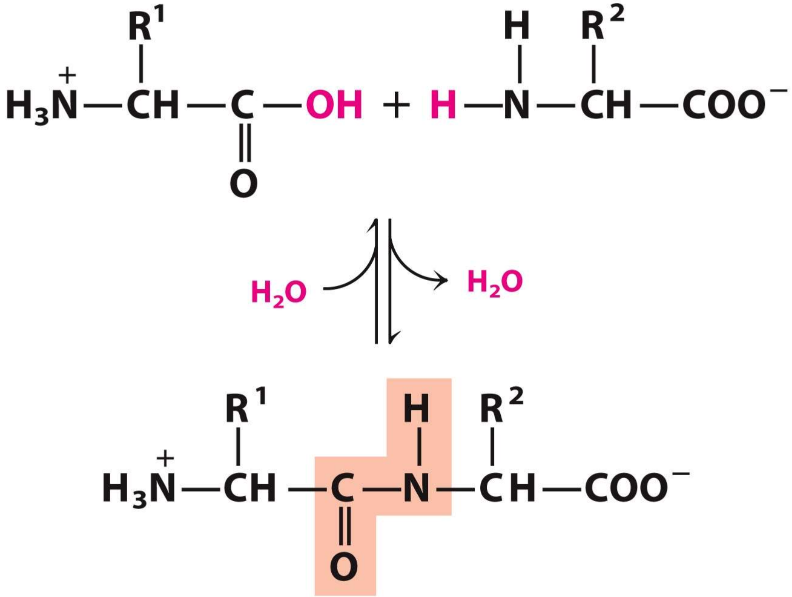


Figure 3-10

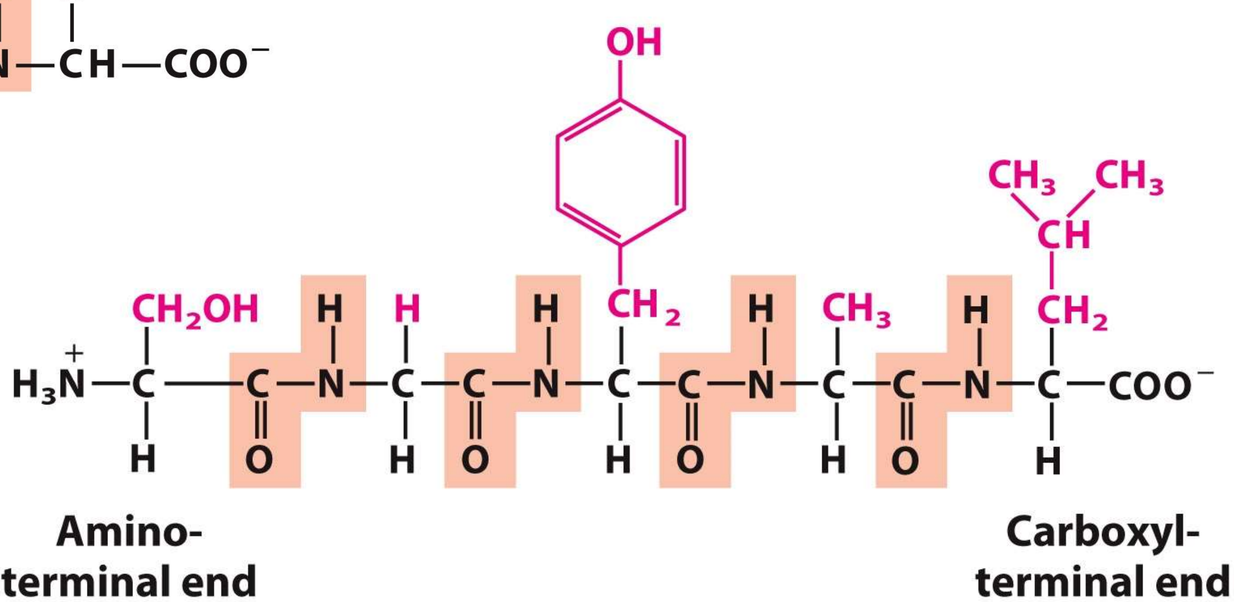
Lehninger Principles of Biochemistry, Seventh Edition

Amino Acids Polymerize to Form Peptides

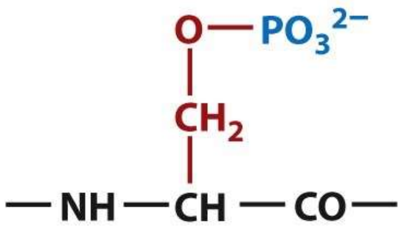
Amino acids → peptides → proteins



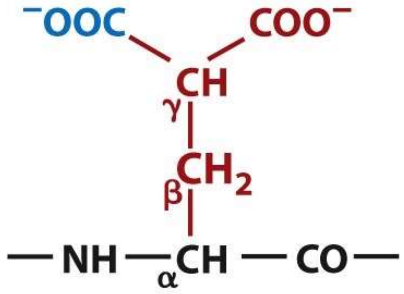
- serylglycyltyrosylalanylleucine
- Ser-Gly-Tyr-Ala-Leu
- SGYAL



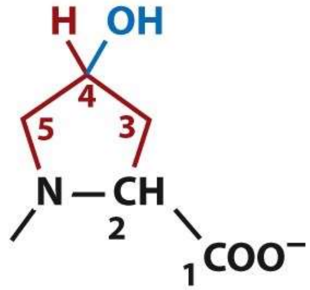
Modified Amino Acids in Proteins



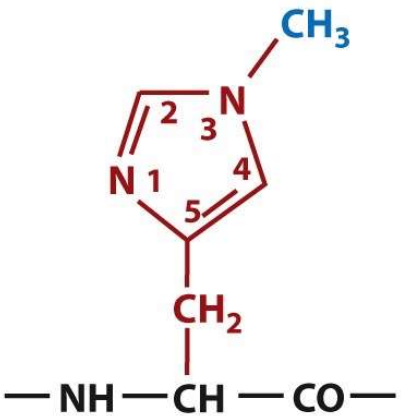
O-Phosphoserine



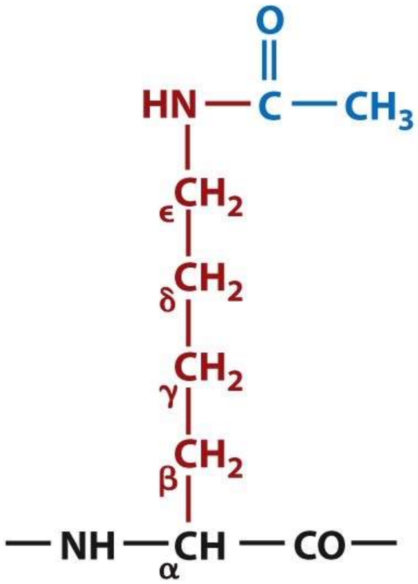
γ-Carboxyglutamate



4-Hydroxyproline

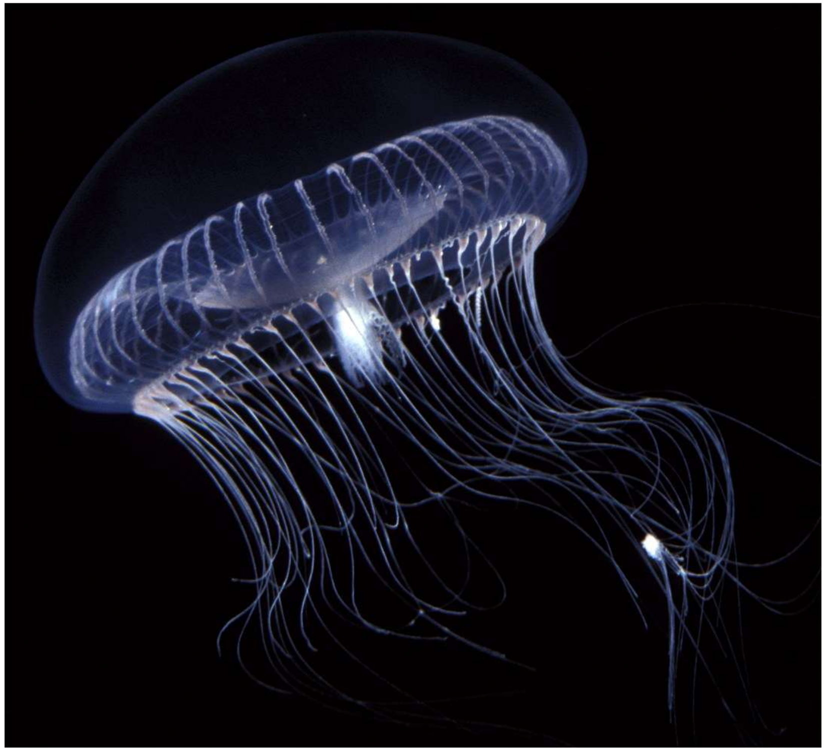


3-Methylhistidine

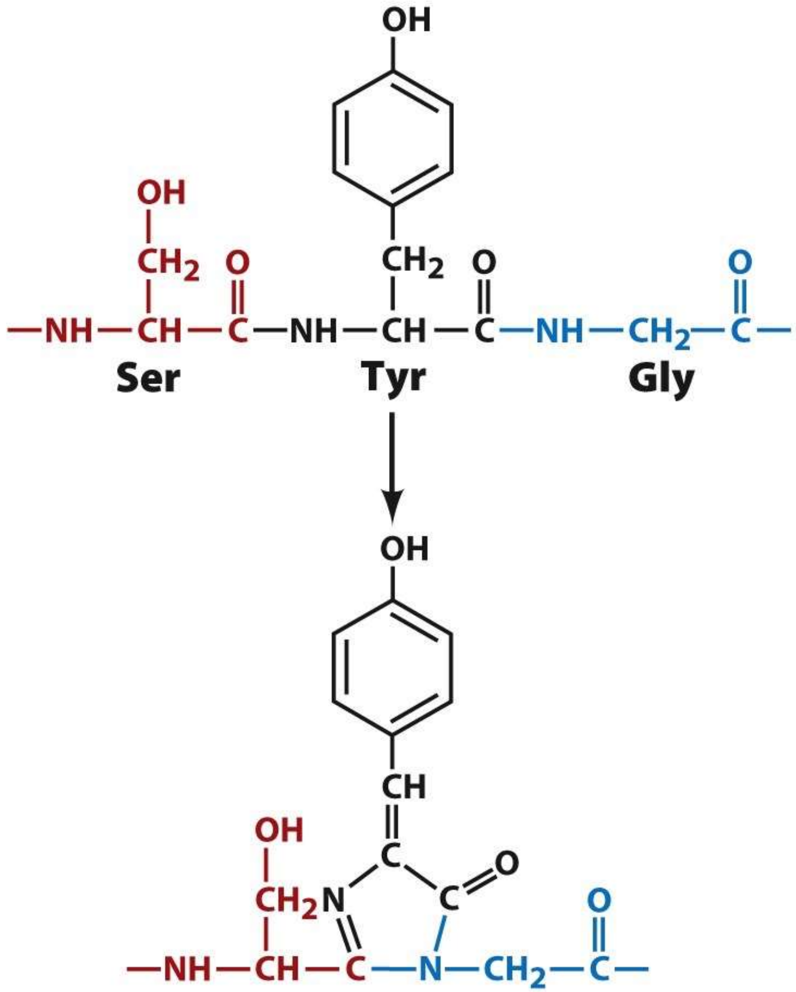


ε-*N*-Acetyllysine

Green Fluorescent Protein



Box 4-3a
Dr kevin Raskoff



Fluorophore of green fluorescent protein

Biologically Active Amino Acid Derivatives

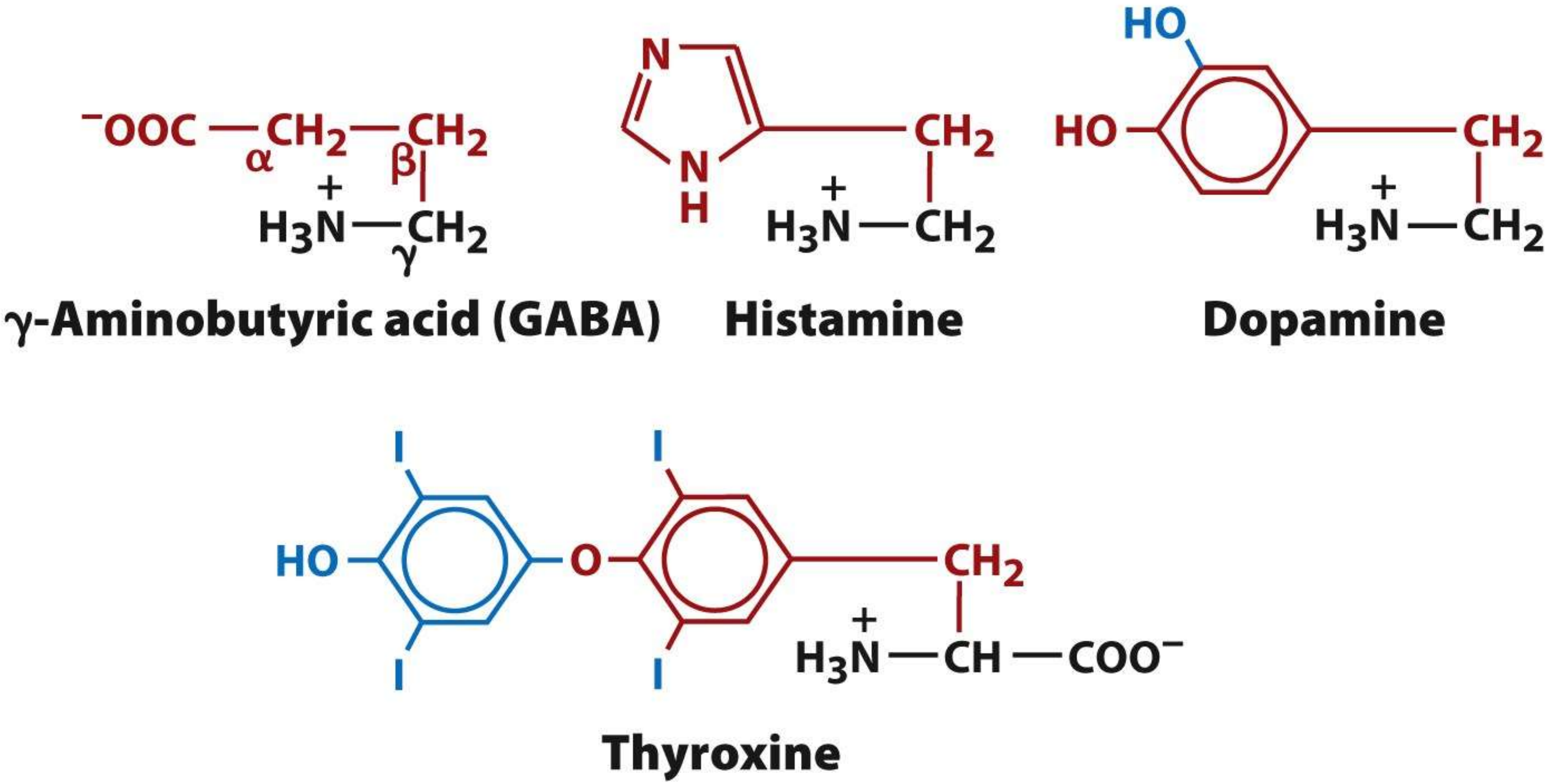


Figure 4-15

Common Questions About Peptides and Proteins

What is its sequence and composition?

What is its three-dimensional structure?

How does it achieve its biochemical role?

How is its function regulated?

How does it interact with other macromolecules?

How is it related to other proteins?

Where is it localized within the cell?

What are its physico-chemical properties?

A Mixture of Proteins Can Be Separated

- Separation relies on differences in physical and chemical properties:
  - charge
  - size
  - affinity for a ligand
  - solubility
  - hydrophobicity
  - thermal stability
- Chromatography is commonly used for preparative separation in which the protein is often able to remain fully folded.

Column Chromatography

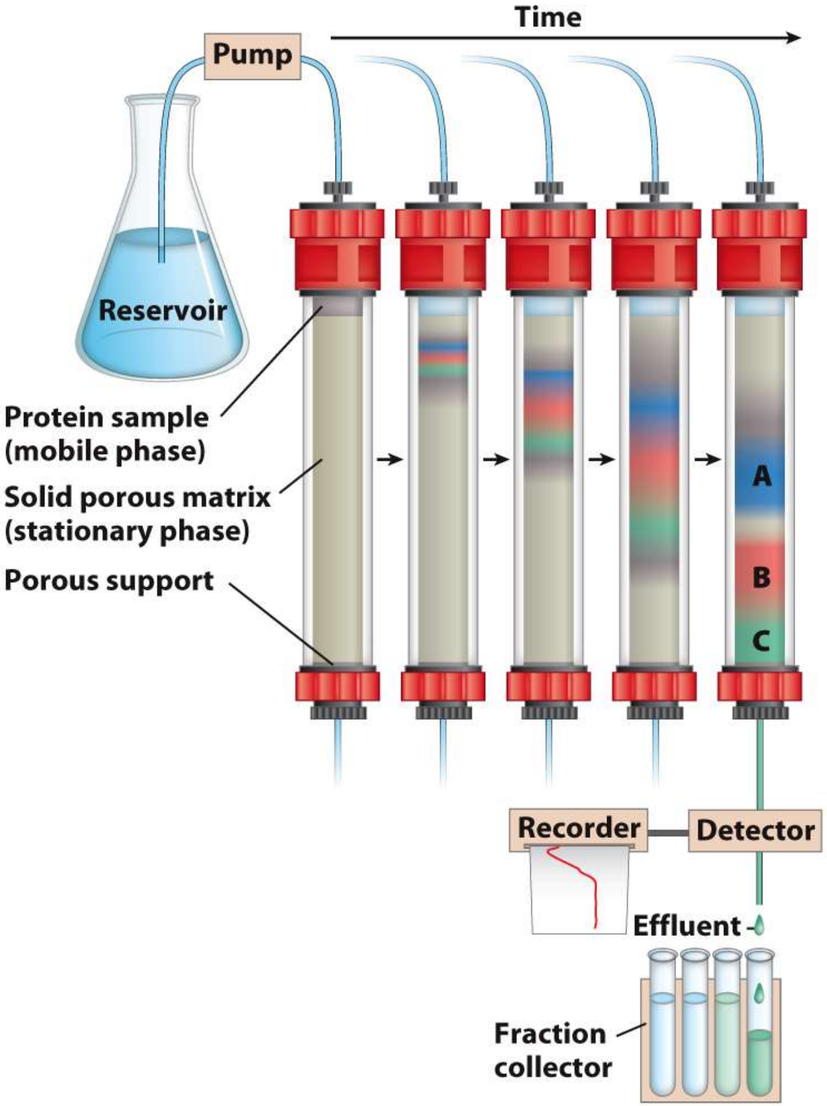


Figure 3-16
Lehninger Principles of Biochemistry, Seventh Edition

- Column chromatography allows separation of a mixture of proteins over a solid phase (porous matrix) using a liquid phase to mobilize the proteins.
- Proteins with a lower affinity for the solid phase will wash off first; proteins with higher affinity will retain on the column longer and wash off later.

Separation by Charge: Ion Exchange

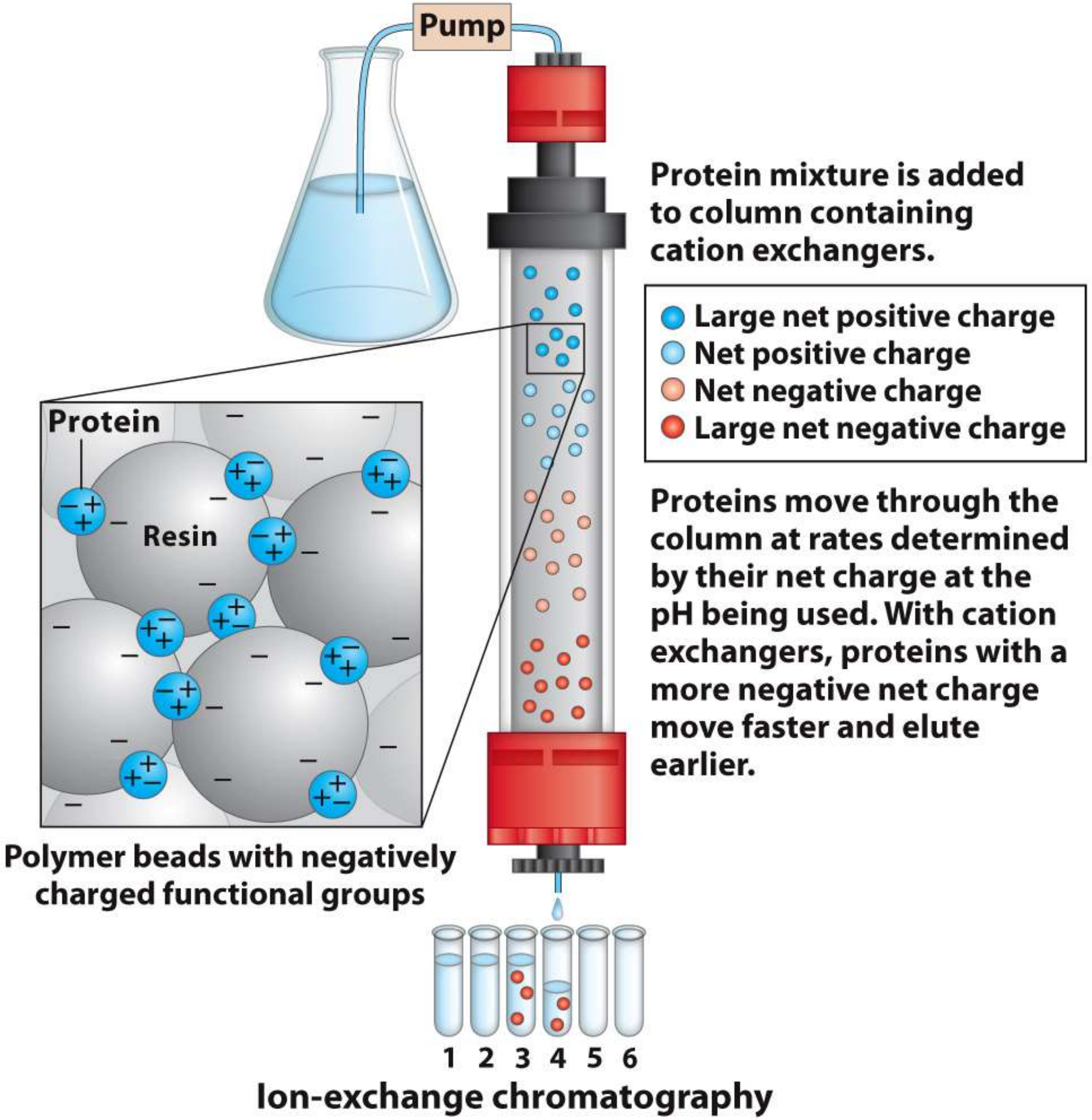


Figure 3-17a

Lehninger Principles of Biochemistry, Seventh Edition

Separation by Size: Size Exclusion

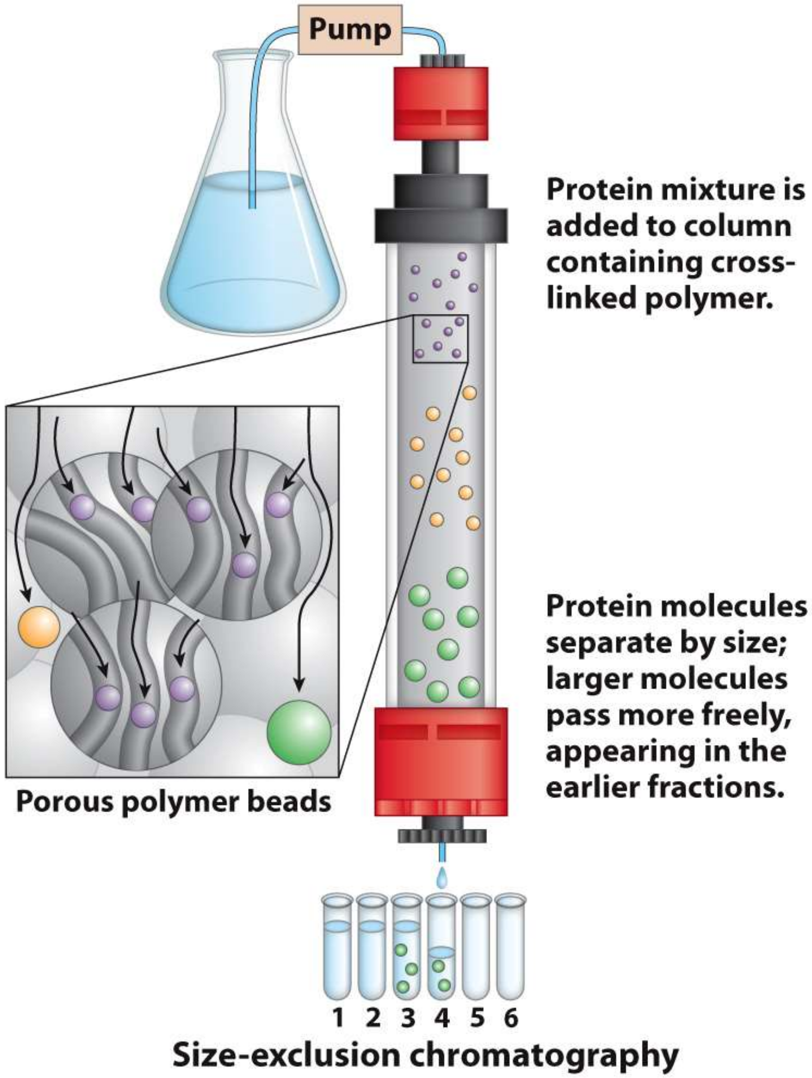


Figure 3-17b
Lehninger Principles of Biochemistry, Seventh Edition

Separation by Binding: Affinity

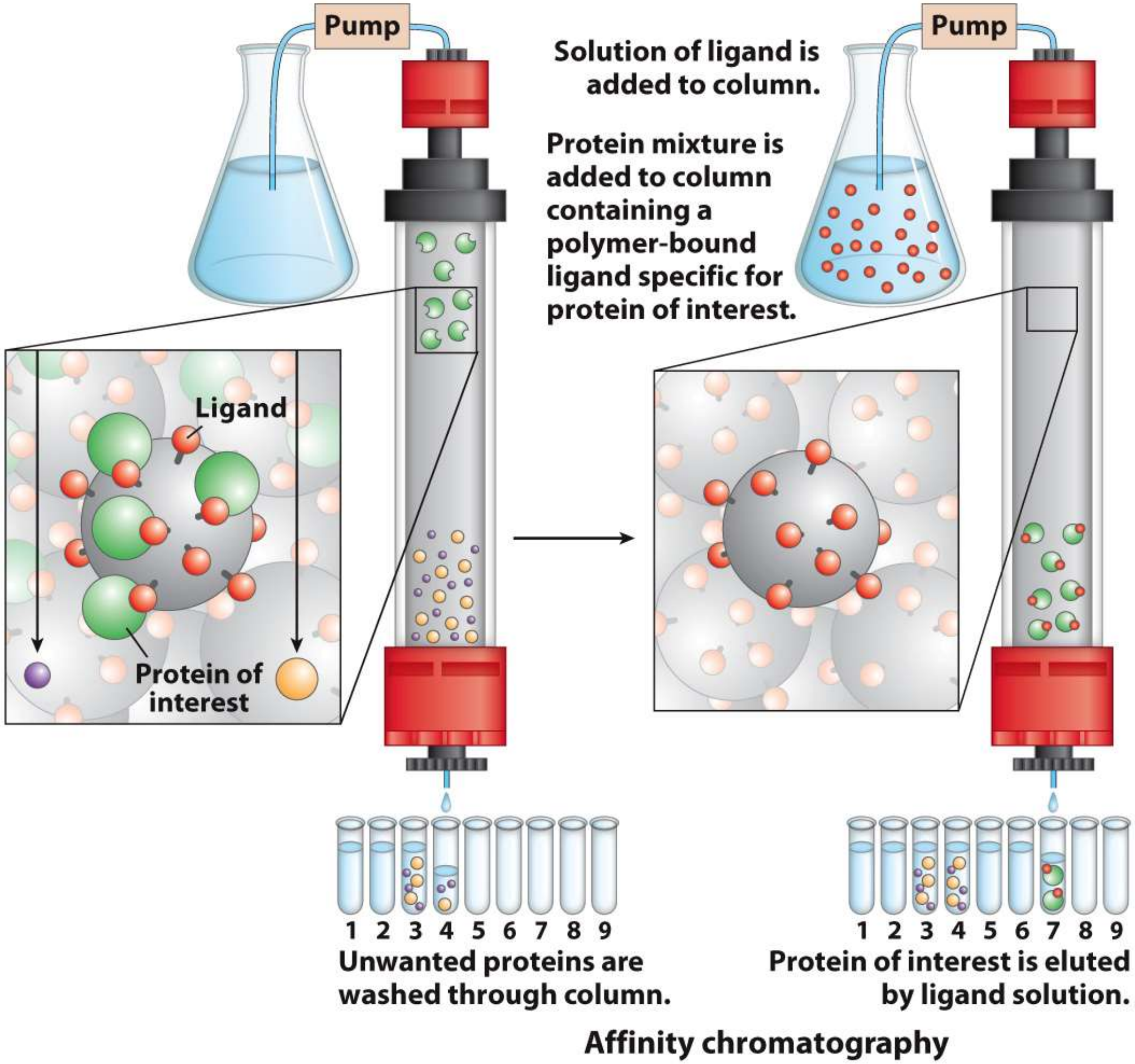


Figure 3-17c

Lehninger Principles of Biochemistry, Seventh Edition

Summary

- many biological functions of peptides and proteins
- structures and names of amino acids found in proteins
- ionization properties of amino acids and peptides
- methods for separation and analysis of proteins