CONCEPT: PROTEIN BASICS

Protein Structures

● Proteins are made by _____ amino acids

  □ A **polypeptide chain** is formed by *peptide bonds* between amino acids

    - A **multimeric** protein is made up of multiple polypeptide chains, each called a **subunit**

    - A **monomeric** protein is made up of a single polypeptide.

  □ The **polypeptide backbone** is formed with a repeating sequence of Nitrogen and Carbon atoms (-N-C-C-)

    - The **N-terminus** contains an amino group (NH_3) at it's end

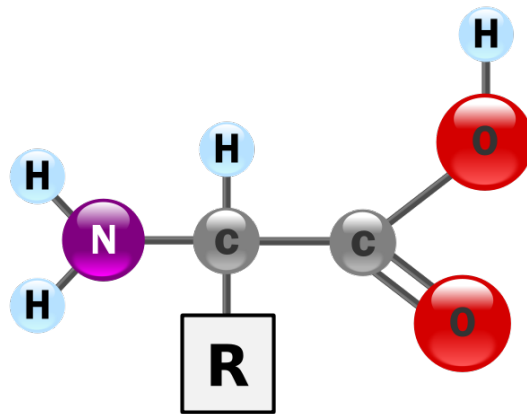   - The **C-terminus** contains a carboxyl group (COOH) at its end

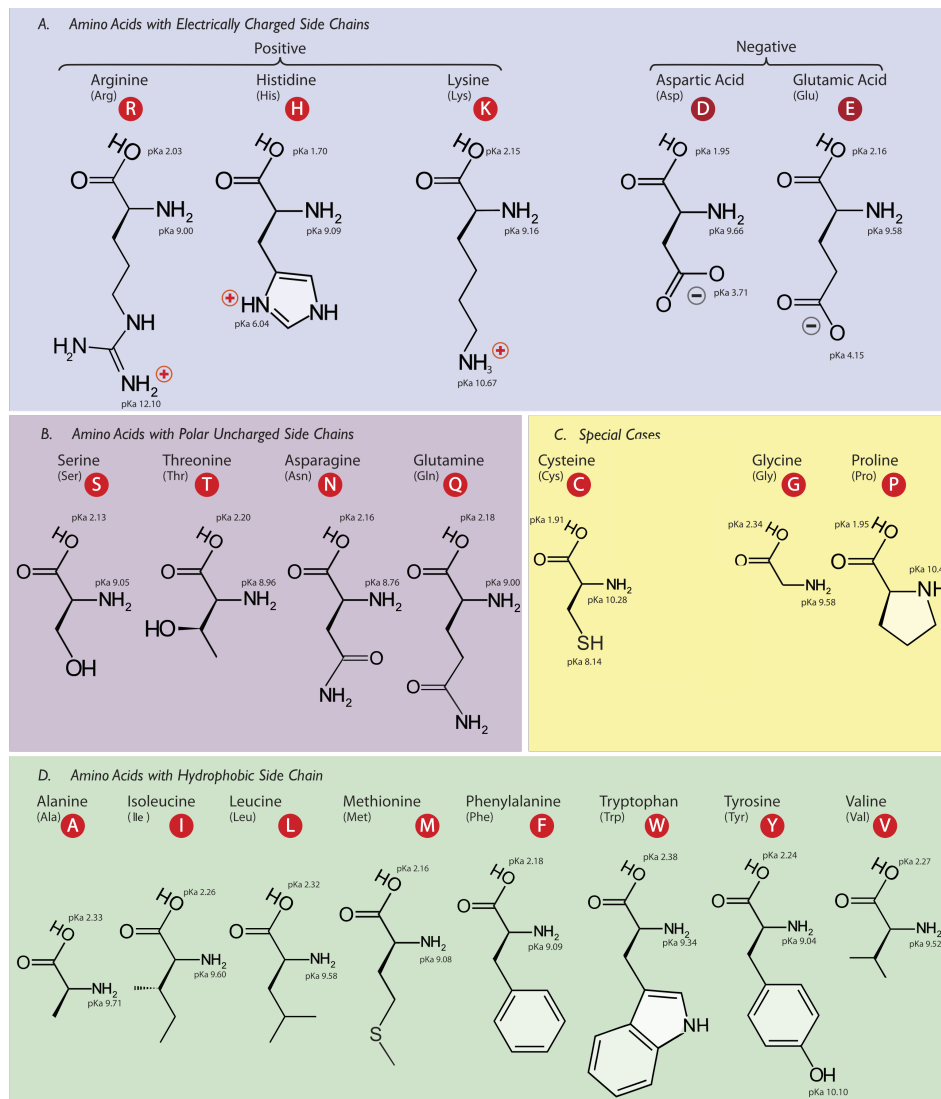**EXAMPLE:** A three amino acid polypeptide chain with N and C termini
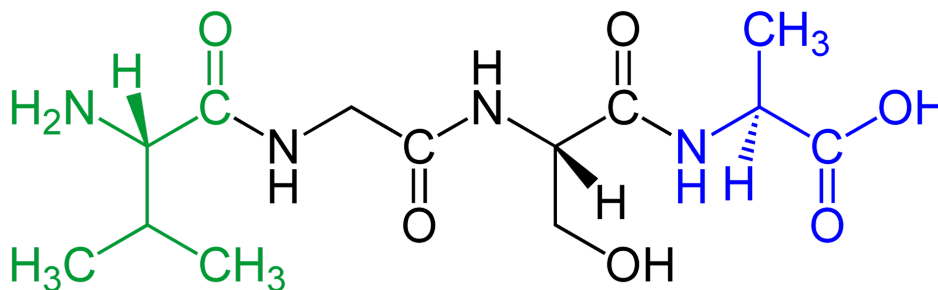
Amino Acids

● Each amino acid in a polypeptide chain has unique properties

  □ All amino acids have the same carboxyl group, an amino group, and hydrogen

  □ The **R group** is a side chain that differs between amino acids and gives them _____ properties

    - The *polar, charged* group can form ionic bonds with other charged molecules in the cell

    - The *polar, uncharged* group can form hydrogen bonds with other molecules including water

    - The *nonpolar* group cannot interact with water

    - The *other* group consists of three amino acids, each with unique properties that do not fit into other groups

  □ Amino acids exist as **stereoisomers** because the four groups are asymmetrically arranged around the α-carbon

    - Two forms D- and L-; BUT the L forms is used in proteins

EXAMPLE: A model of the structure of each amino acid

EXAMPLE: The 20 amino acid structures, classified by group

A. Amino Acids with Electrically Charged Side Chains

Positive

Arginine (Arg) R — pKa 2.03, pKa 9.00, pKa 12.10
Histidine (His) H — pKa 1.70, pKa 9.09, pKa 6.04
Lysine (Lys) K — pKa 2.15, pKa 9.16, pKa 10.67

Negative

Aspartic Acid (Asp) D — pKa 1.95, pKa 9.66, pKa 3.71
Glutamic Acid (Glu) E — pKa 2.16, pKa 9.58, pKa 4.15

B. Amino Acids with Polar Uncharged Side Chains

Serine (Ser) S — pKa 2.13, pKa 9.05
Threonine (Thr) T — pKa 2.20, pKa 8.96
Asparagine (Asn) N — pKa 2.16, pKa 8.76
Glutamine (Gln) Q — pKa 2.18, pKa 9.00

C. Special Cases

Cysteine (Cys) C — pKa 1.91, pKa 10.28, pKa 8.14
Glycine (Gly) G — pKa 2.34, pKa 9.58
Proline (Pro) P — pKa 1.95, pKa 10.47

D. Amino Acids with Hydrophobic Side Chain

Alanine (Ala) A — pKa 2.33, pKa 9.71
Isoleucine (Ile) I — pKa 2.26, pKa 9.60
Leucine (Leu) L — pKa 2.32, pKa 9.58
Methionine (Met) M — pKa 2.16, pKa 9.08
Phenylalanine (Phe) F — pKa 2.18, pKa 9.09
Tryptophan (Trp) W — pKa 2.38, pKa 9.34
Tyrosine (Tyr) Y — pKa 2.24, pKa 9.04, pKa 10.10
Valine (Val) V — pKa 2.27, pKa 9.52

Self-Assembly and Protein Folding

● Proteins form into _____ shapes

  □ Most proteins are capable of **self-assembly**, meaning they can fold into their shape without assistance

    - Information required to specific the folding is inherent in the amino acid side chains (R group)

    - If the protein is **denatured** (unfolded) in one condition it will **renature (**reform) in proper conditions

  □ The peptide bonds in the polypeptide backbone _____ movement

    - First limit on protein folding

**EXAMPLE:** Example of denatured and renatured forms of a protein
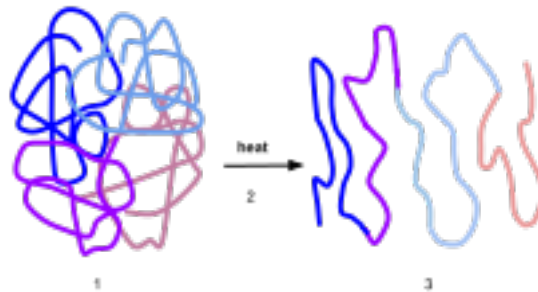
  □ The protein's **conformation** (folded shape) is determined through the properties of the amino acid R group

    - This forms with conformation with the _____ Gibbs free energy

    - The **native state** of a protein specifies a small number of conformations the protein will actually form

      - Out of 1000s of possibilities

  □ The protein's **conformation** (folded shape) is formed through noncovalent interactions

    - *Hydrogen bonds, Ionic bonds, Van der Waals interactions,* and *hydrophobic interactions*

  □ **Disulfide bonds** are stabilizing covalent bonds formed between sulfur atoms on two cysteine amino acids

EXAMPLE: Protein conformation is dictated by amino acid side chains
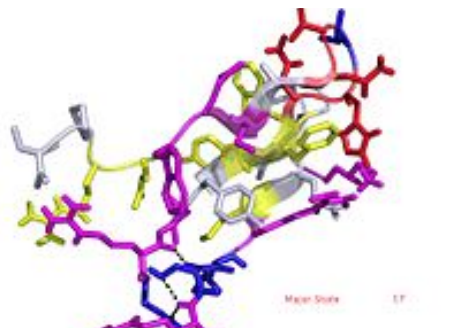
● **Chaperone** proteins are proteins that can _____ in protein folding

   □ One group is the **molecular chaperones** that assist in stabilizing unfolded or partially folded proteins

   - Bind to short segments of the protein substrate

   - Prevent aggregation of unfolded, or misfolded proteins

   - Hsp70 is an example

   □ The second group is the **chaperonins**, which form small folding chambers to sequester unfolded proteins

   - The sequestering allows the protein to refold without influence from molecules or water in cytosol

   - Contain a cylindrical folding core, and regulated by protein "lids" that allow proteins in and out

   - Hsp60 is an example

   □ Chaperones _____ proteins from energy provided by ATP hydrolysis

   □ Misfolded proteins results in diseases like Parkinson's, and Alzheimer's

EXAMPLE: Structure of a chaperonin
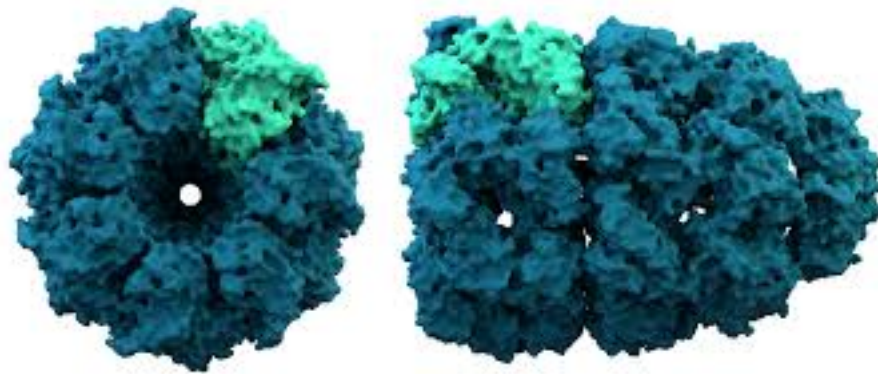
Four Protein Models

● There are four ways to present a protein's structure

   □ The **backbone** model presents the overall organization of the polypeptide chain

   □ The **ribbon** model shows the polypeptide backbone folding

   □ The **wire** model shows the polypeptide backbone and the amino acid side chains

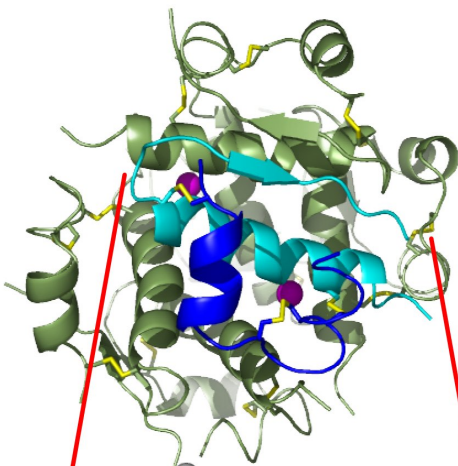   □ The **space-filling** model shows a contour map of the protein's surface
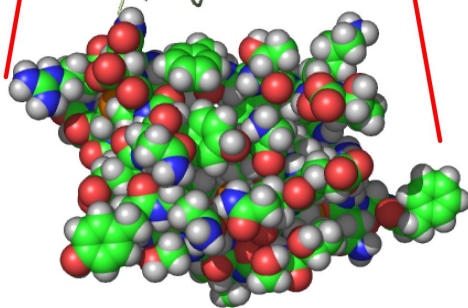
EXAMPLE: Four models of protein folding
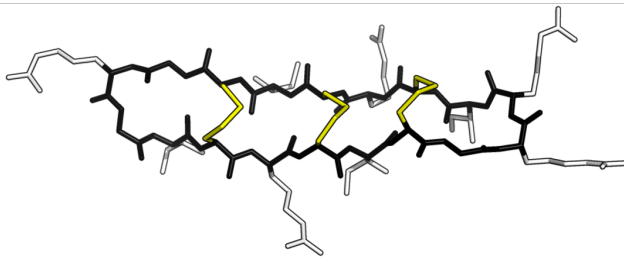
Backbone model

Ribbon model

Wire model

Space Filling model

PRACTICE

1. Which of the following is false about the R group of amino acids?
    a. They give polypeptide chains unique properties
    b. They assist in forming complex protein structures
    c. They control the stereoisomer form of the amino acid
    d. They can be nonpolar

2. A protein C-terminus is named that way because it contains what molecule?
    a. An extra carbon
    b. A COOH group
    c. A CH_3 group
    d. A Chloride

3. A protein's conformation is formed through all but which of the following?
   a. Hydrophobic Interactions
   b. Disulfide bonds
   c. Covalent bonds between carbons
   d. Noncovalent bonds between R groups

4. Which of the following protein models would you use if you wanted to gain an idea of what the surface of a protein looked like?
   a. Backbone
   b. Ribbon
   c. Wire
   d. Space-Filing