

Protein Structure

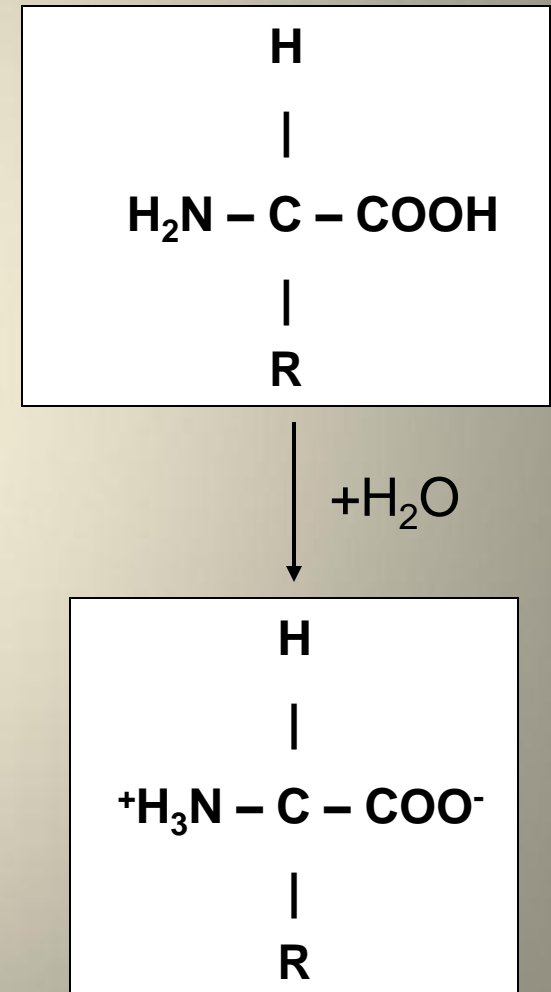
**Amino Acids, Polypeptide
Levels of Structure**

Monomer

- The single unit that makes up a protein is an amino acid
- Question: Based on its name, which 2 functional groups would be found in an amino acid?
- An amino acid is sometimes referred to as a residue

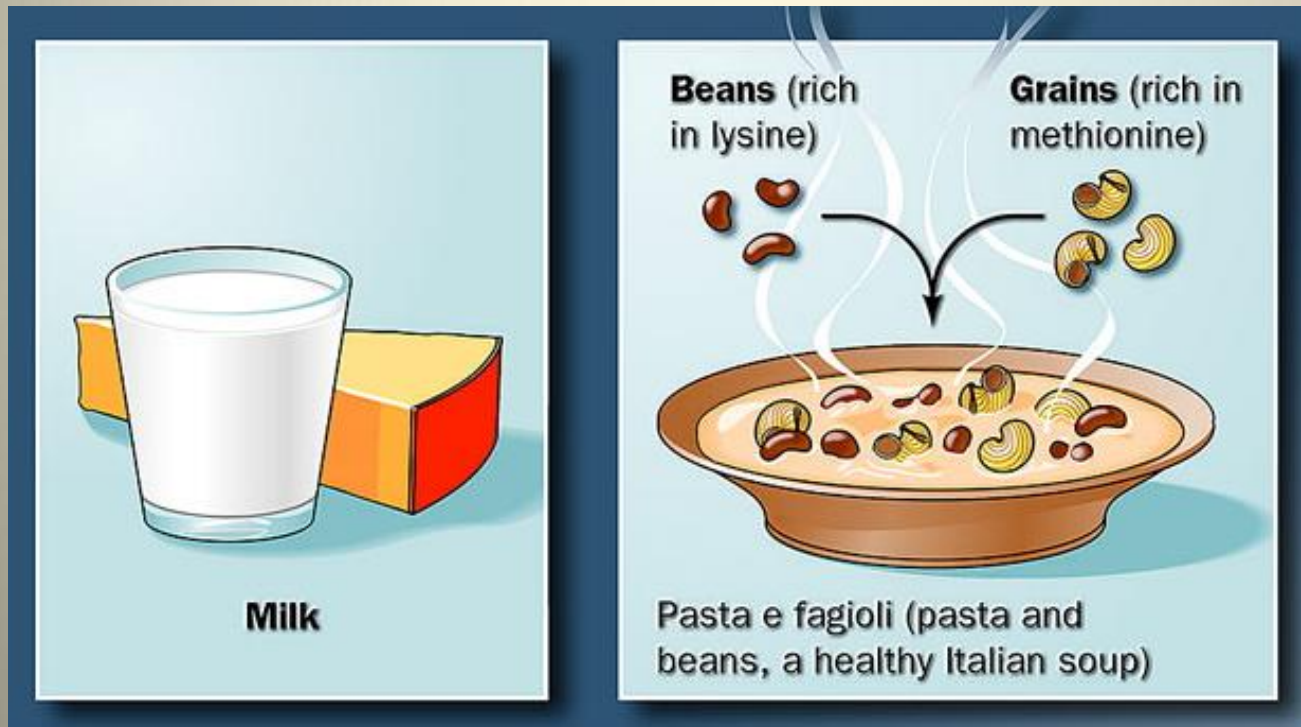
Amino acid structure

- four components attached to a central carbon:
 - amino group
 - carboxylic acid (carboxyl) group
 - hydrogen atom
 - variable R group (or side chain)
- amphiprotic: containing both acidic (COO⁻) and basic (NH₃⁺) functional groups
- observed in aqueous solution: carboxyl group donates H⁺ ion to amino group



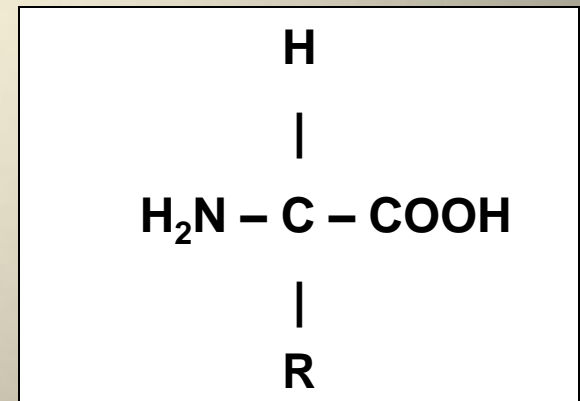
Amino acid R groups (side chains)

- differences in R groups produce the 20 different amino acids
- 8 are essential: body cannot synthesize them



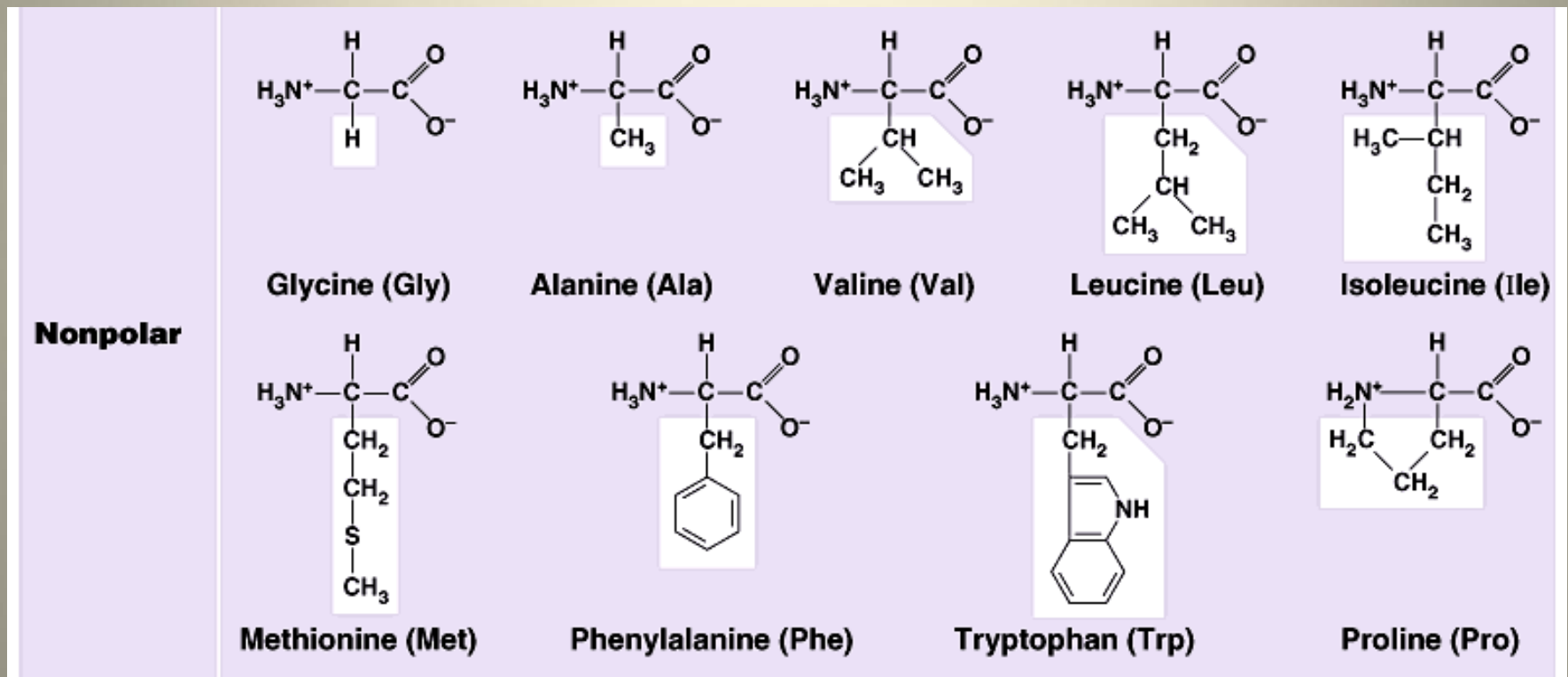
Amino acid R groups (side chains)

- physical and chemical characteristics of the R group determine the unique characteristics of an amino acid
- amino acids are classified into 4 groups based on their R groups:
 - Nonpolar
 - Polar
 - Acidic
 - basic



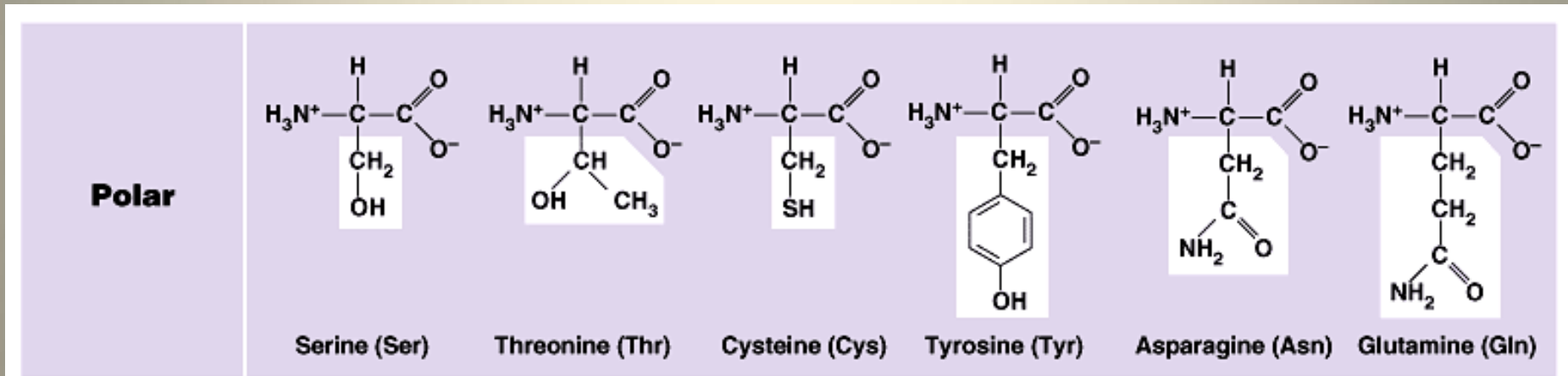
Nonpolar amino acids has hydrophobic R groups

- Hydrophobic R groups



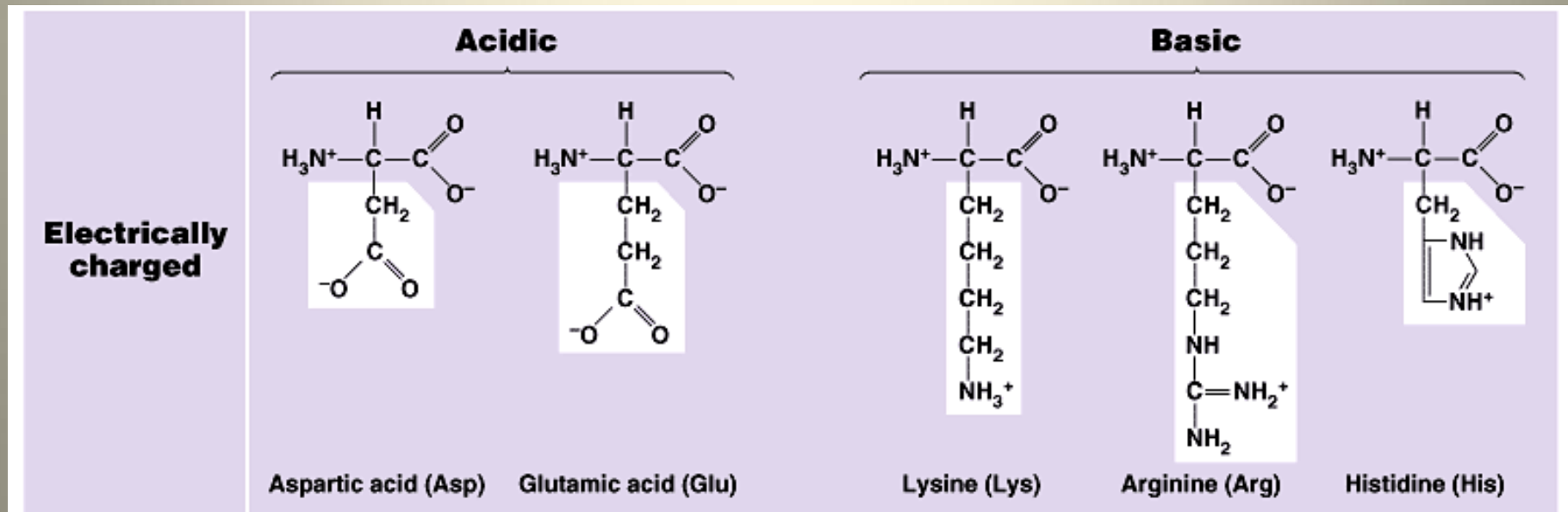
Polar amino acids

- Polar R groups
- hydrophilic



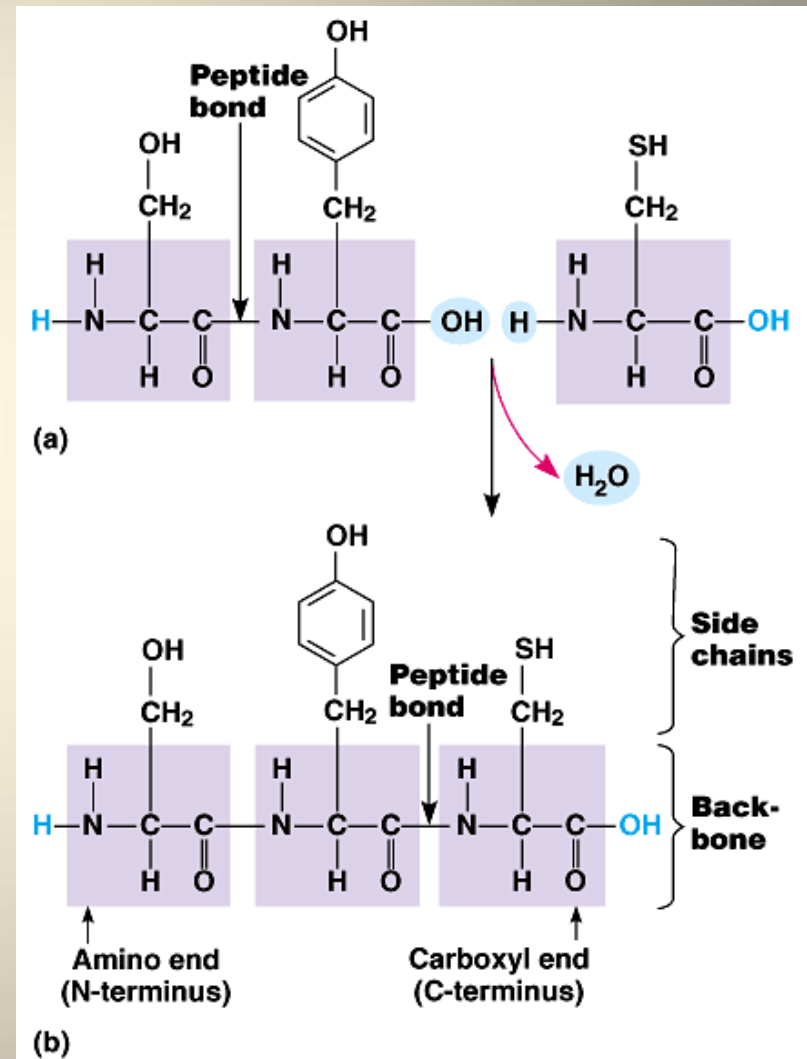
Acidic and Basic Amino Acids

- Amino acids with charged (ionized) functional groups at cellular pH can be either:
 - Acidic: carboxylic acid, negative charge
 - Basic: amino, positive charge



Forming a Polypeptide

- A chain of amino acids linked by a **peptide** bond (amide functional group)
- Formed by dehydration synthesis: hydroxyl group from the carboxyl end of one amino acid and a hydrogen from the amino group of another



Forming a Polypeptide

- Question: What is name of the new functional group formed?
- Peptide bond: links between amino acids
- Growth of polypeptide is from N to C-terminus

Protein shape determines function

- The order of amino acids determines the three-dimensional conformation (shape) of a protein
- Specific conformation determines function
- Function depends on its ability to recognize and bind a molecule

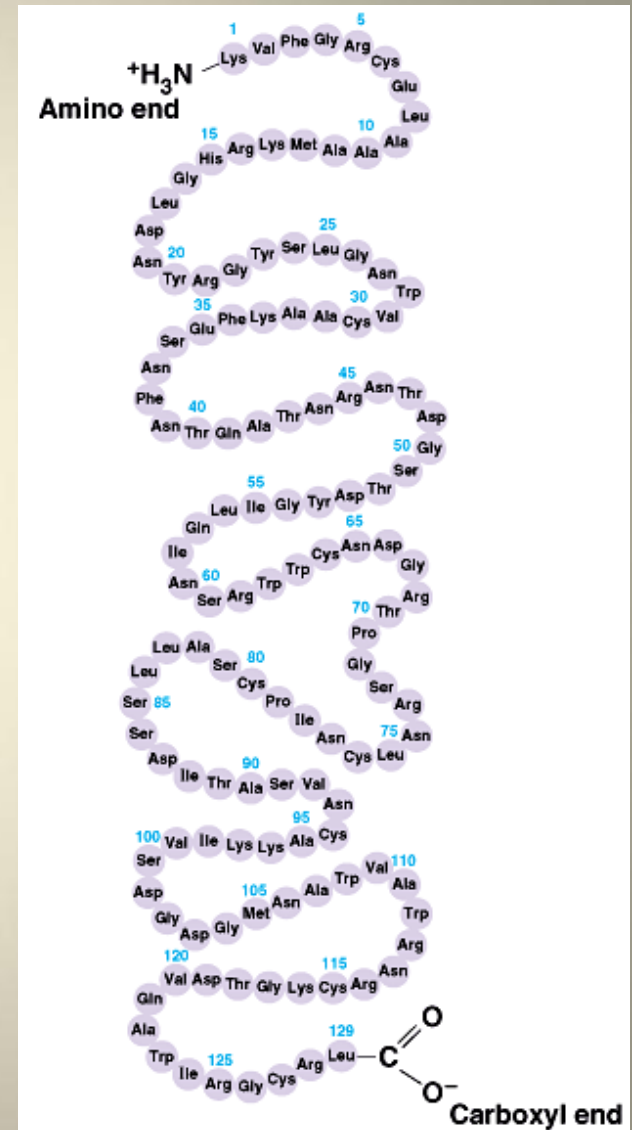
Amino acids → conformation → function

Levels of protein structure

- **Primary, Secondary, and Tertiary** structures: are used to organize the folding within a single polypeptide
- **Quaternary** structure involves two or more polypeptides that make a protein

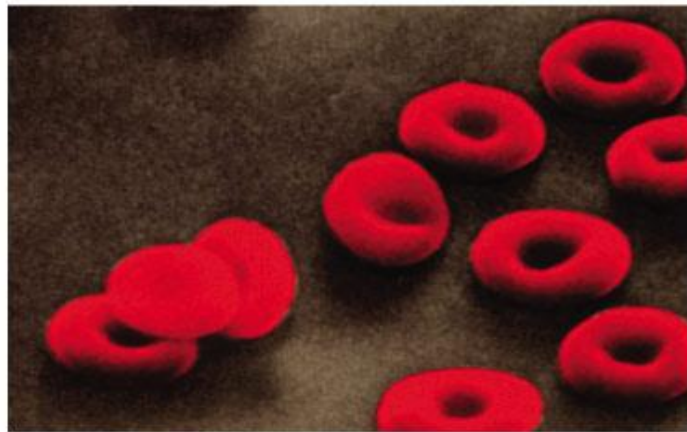
Primary Structure

- unique sequence of amino acid (also known as residue)
- sequence determined by DNA
- a slight change in primary structure can affect a protein's conformation and ability to function



Example: Sickle Cell Anemia

- abnormal hemoglobin develop because of a single amino acid substitution (change)
- causes hemoglobin to crystallize, deforming the red blood cells and leading to clogs in blood vessels.



10 μ m

Val His Leu Thr Pro Glu Glu
1 2 3 4 5 6 7

(a) Normal red blood cells and the primary structure of normal hemoglobin



10 μ m

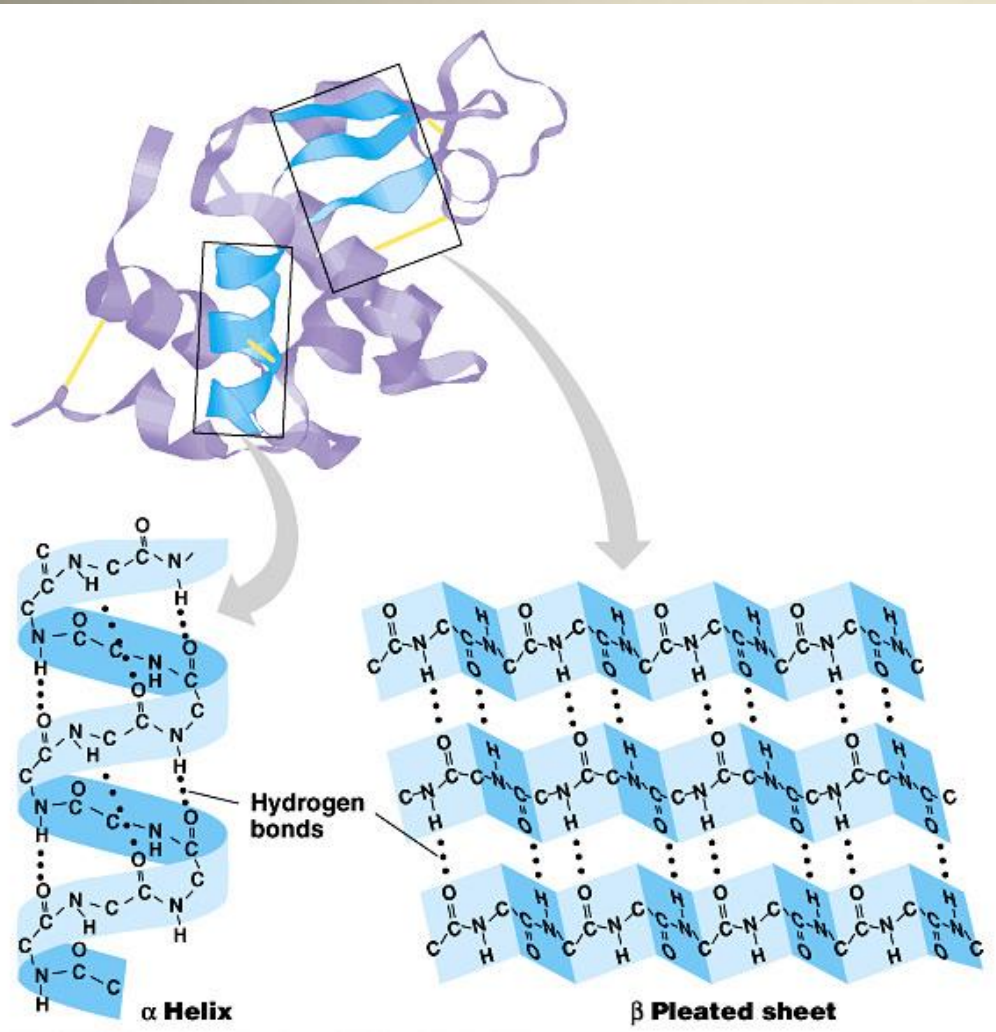
Val His Leu Thr Pro Val Glu
1 2 3 4 5 6 7

(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

Origami: Protein Structure

- Paper model of GFP (by PDB-101)
- Follow instructions for steps 1 and 2 only

Secondary Structure



- results from **hydrogen bonds** at **regular intervals** along the polypeptide **backbone**
 - typical shapes:
 - alpha helix (coils)
 - beta pleated sheets (folds)
- Not found in all proteins

Linus Pauling (1901-1994)

- Discovered the alpha helical structure of protein in 1951
- Back story:
<https://paulingblog.wordpress.com/2011/03/09/the-alpha-helix/>
- Original PNAS article published in 1951
- Analysis of the alpha helix and beta sheet work of Pauling (Eisenberg, 2003)
<http://www.pnas.org/content/100/20/11207.full.pdf>

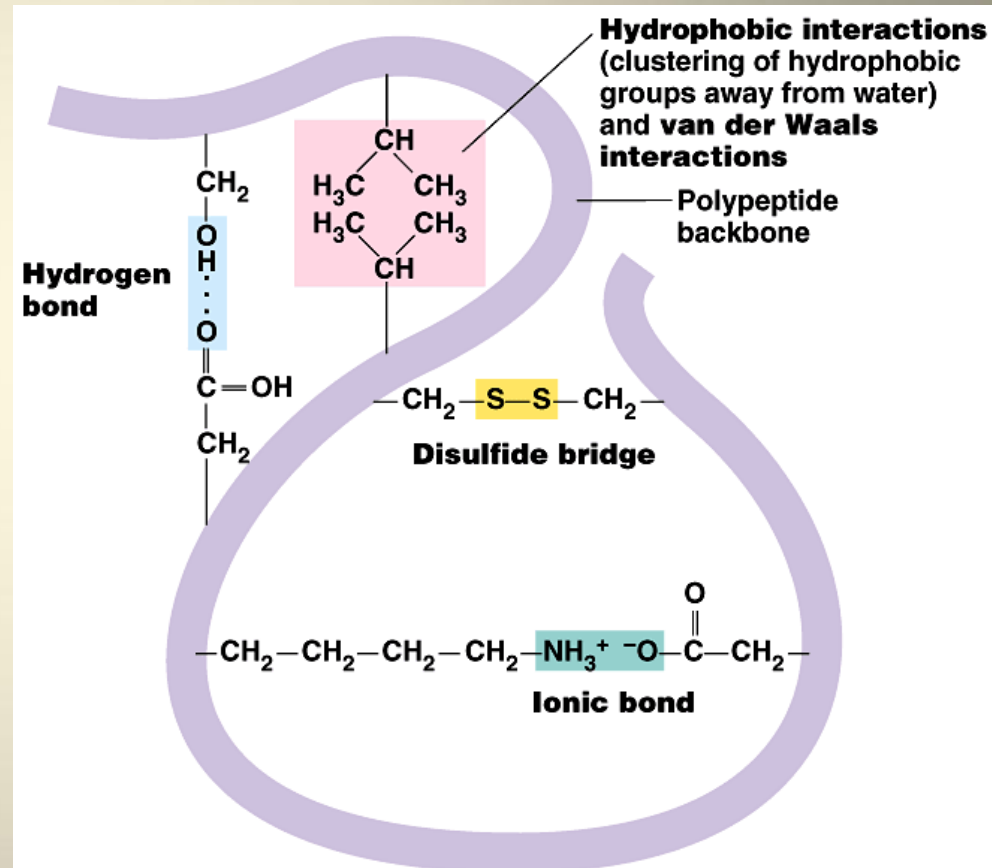
Origami: Protein Structure

- Complete steps 3 and 4 only

Tertiary Structure

Interactions between:

- R groups and R groups
- R groups and backbone



Tertiary Structure

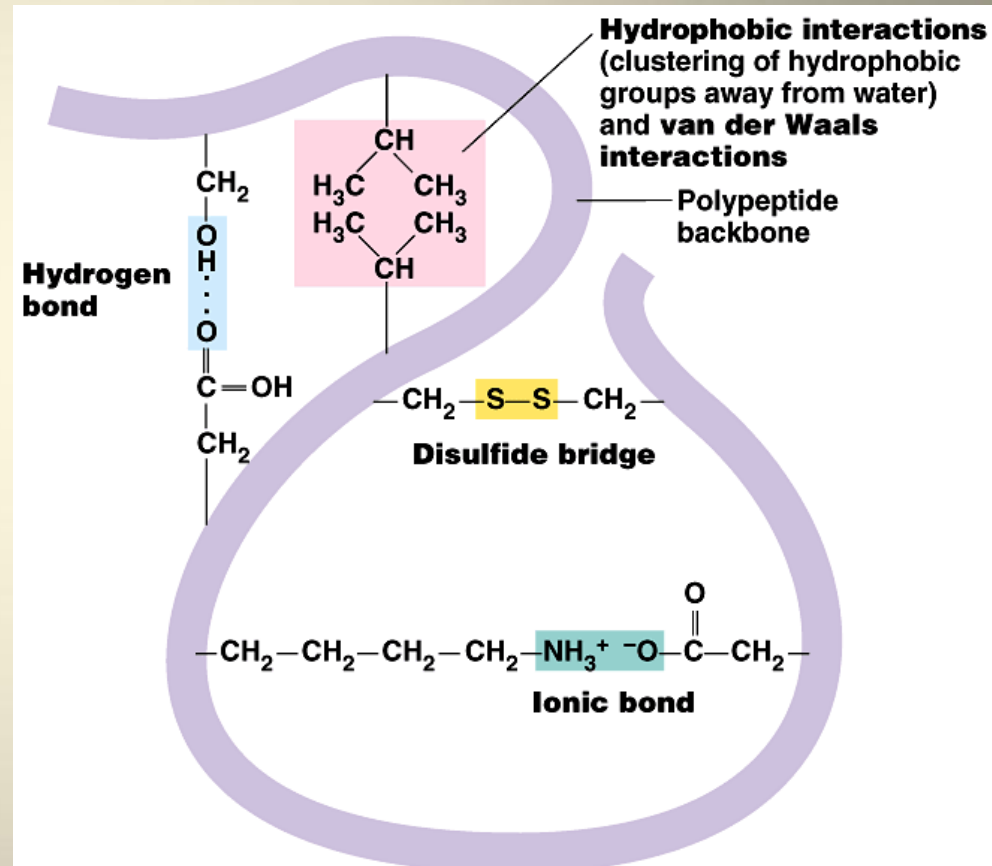
Types of interaction include all different types of intermolecular forces of attraction:

- Between polar / charged amino acids:

- Hydrogen bonds
- Dipole-dipole
- Ion-dipole

- Between nonpolar amino acids:

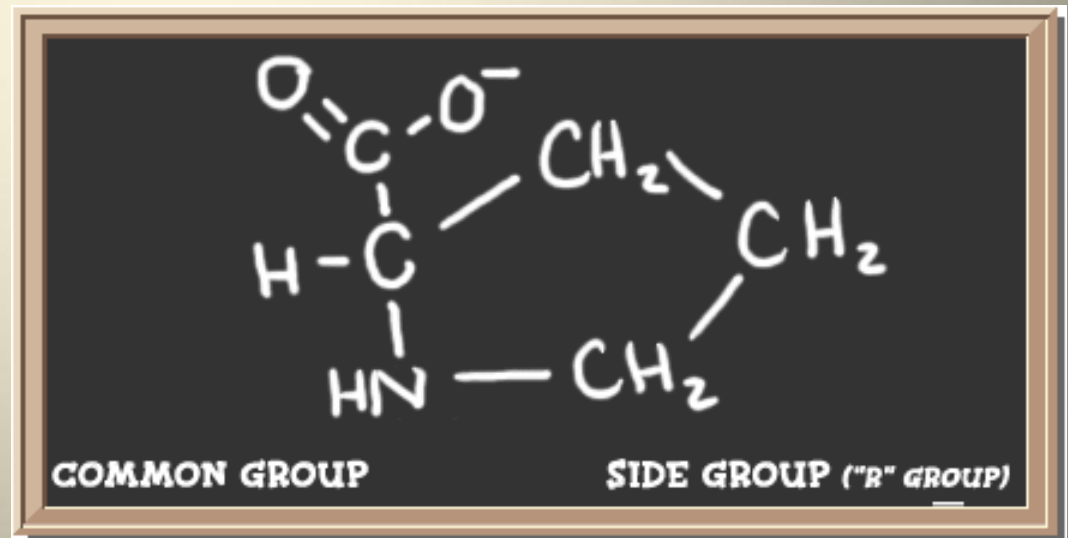
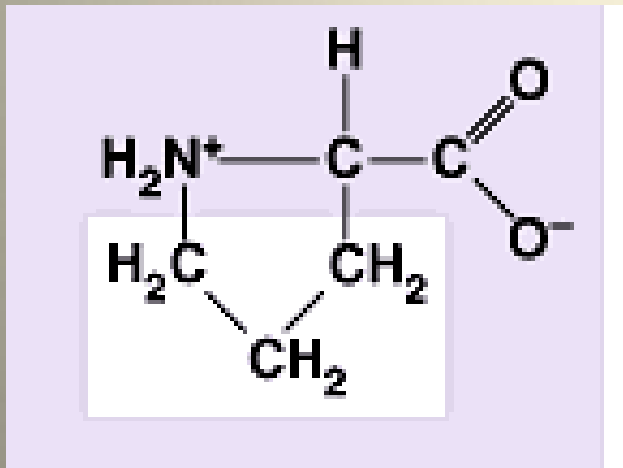
- Hydrophobic interactions (often in interior of protein)



- May also involve bonds formed between amino acid R-groups
- Ionic bonds formed between charged amino acids
- Covalent bonds
 - Disulfide bridge: formed between the sulfhydryl groups (SH) of cysteine amino acids

Tertiary Structure: Proline kink

- Proline is the only amino acid in which the R group is attached to the amino group
- Forms a natural kink in the polypeptide
- Helps to shape tertiary structure



Tertiary Structure: Proline kink

- Forms a natural kink in the polypeptide backbone
- Helps to shape tertiary structure

Video (0:58):

<https://www.youtube.com/watch?v=qt4iUa5OZQc>

- All proteins will have a tertiary structure since this is where we would first see a protein's function

- Conformation determines function

Amino acids → conformation → function

Categories of Protein function

Function	Example
Structural support	Collagen
Storage	Albumin (egg white)
Transport	Hemoglobin
Hormonal	Insulin
Receptor	Nerve cell receptors
Contractile	Actin and myosin
Defensive	Antibodies
Enzymatic	Digestive enzymes

Origami: Protein Structure

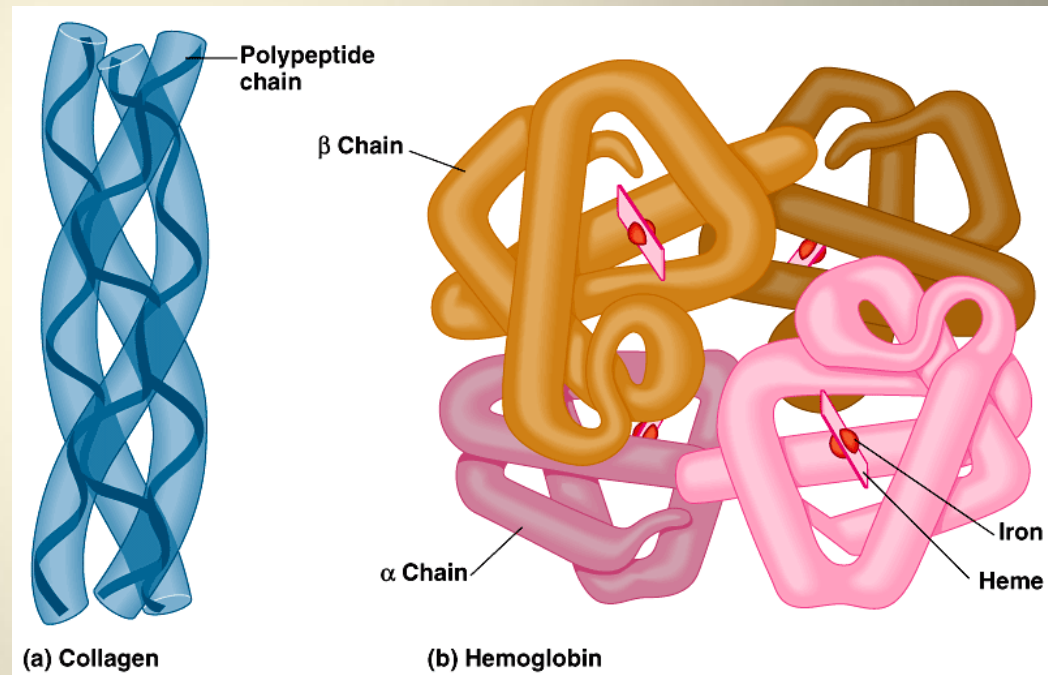
- Complete Step 5

Quaternary Structure

- Some, but not all, proteins will have a fourth level of structure that involves:
 - Interactions (aggregations) between two or more polypeptide chains
- Each chain is often referred to as a subunit
- Not found in all proteins
- Protein function would be evident at this level

Quaternary Structure

- aggregation of two or more polypeptide subunits
- Forms 2 types of proteins: globular and fibrous

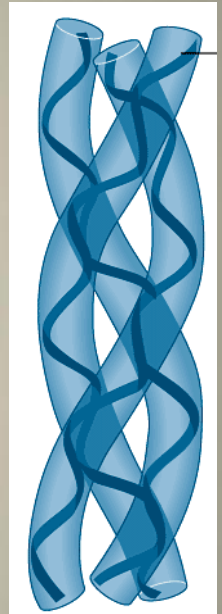
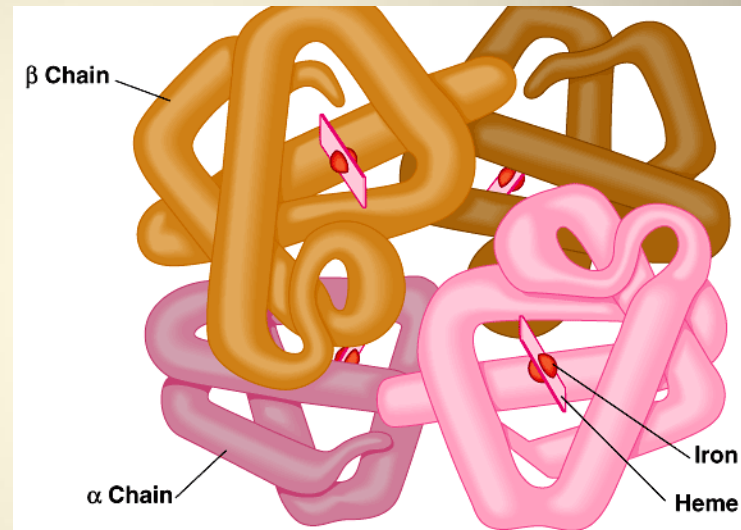


Origami: Protein Structure

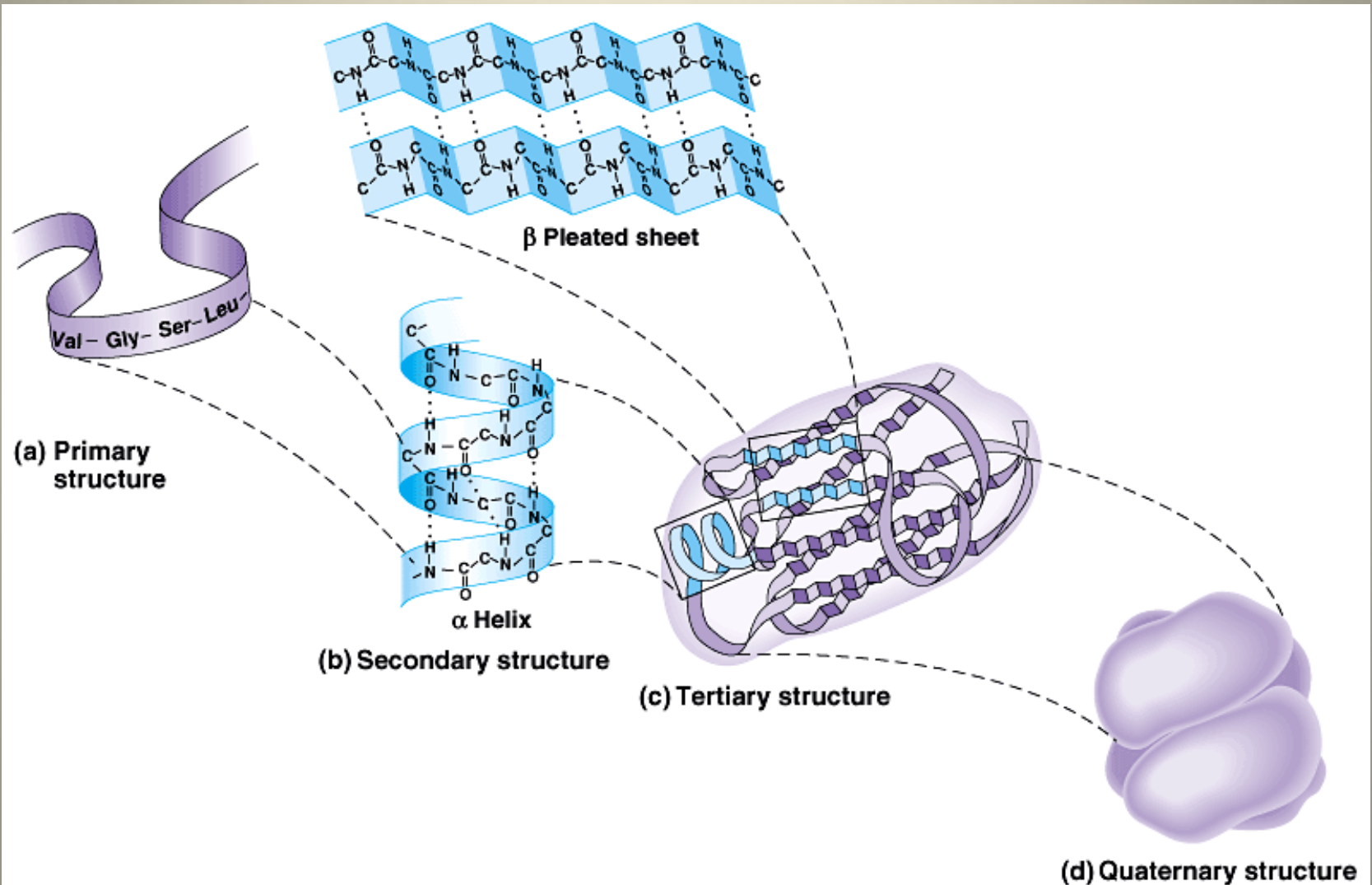
- What can you do now with your GFP paper
- protein to demonstrate the quaternary level?

Quaternary Structure

- Globular protein
 - Water soluble
 - Compact, spherical
 - e.g. hemoglobin
- Fibrous protein
 - Water insoluble
 - Threadlike
 - e.g. collagen: 3 polypeptides, supercoiled like a rope, provides structural strength for role in connective tissue



Levels of Protein Structure



Protein Folding

- Occurs spontaneously
- Aided by chaperone proteins (chaperonin)
- Provide ideal environment for folding

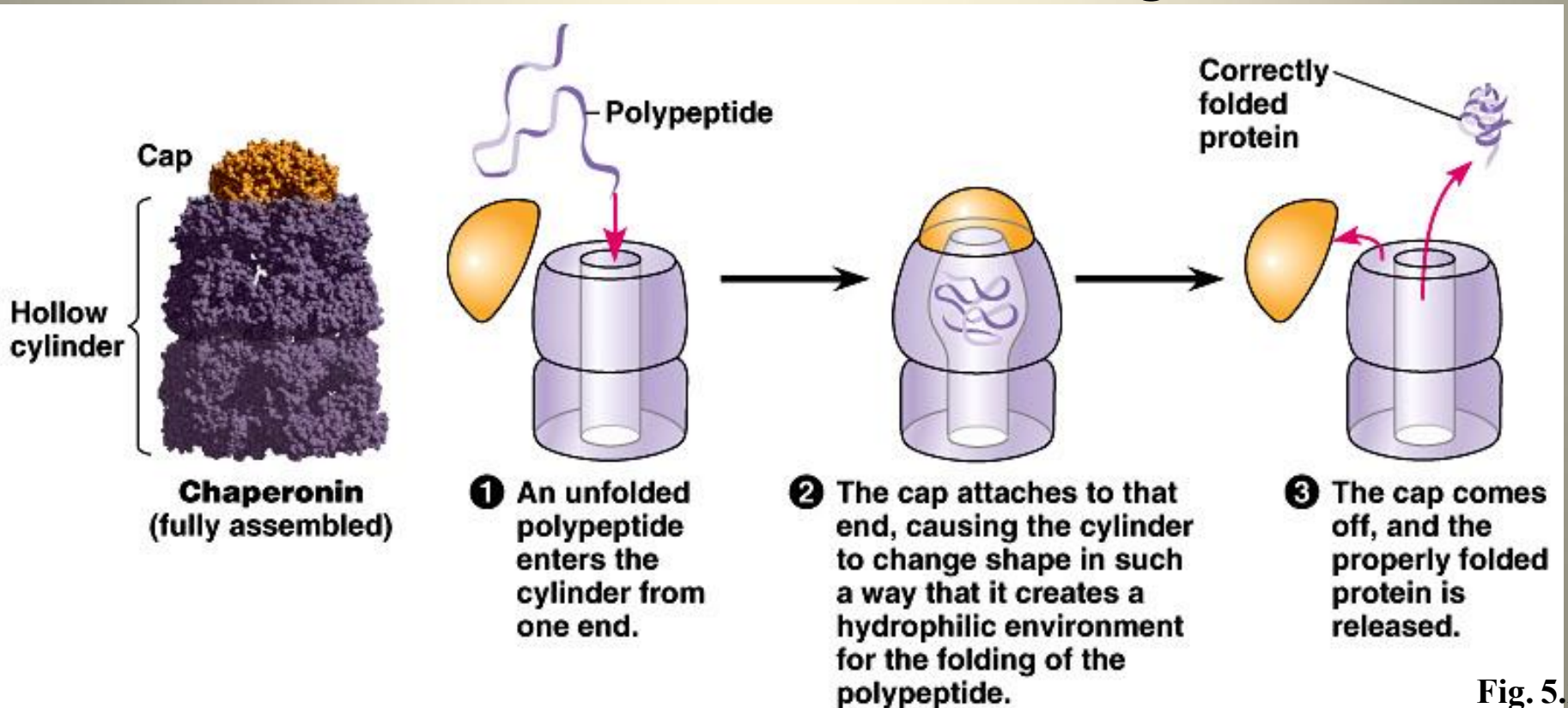


Fig. 5.26

Tutorial: Protein Folding

- http://www.wiley.com/legacy/college/boyer/0470003790/animations/protein_folding/protein_folding.htm

Conformational Change

- Changing the shape of a protein
- Reversible
- Does not disrupt a protein's function but rather is what defines the protein's function
- Change occurs in response to the physical and chemical conditions.

Example of conformational change

- Carrier protein

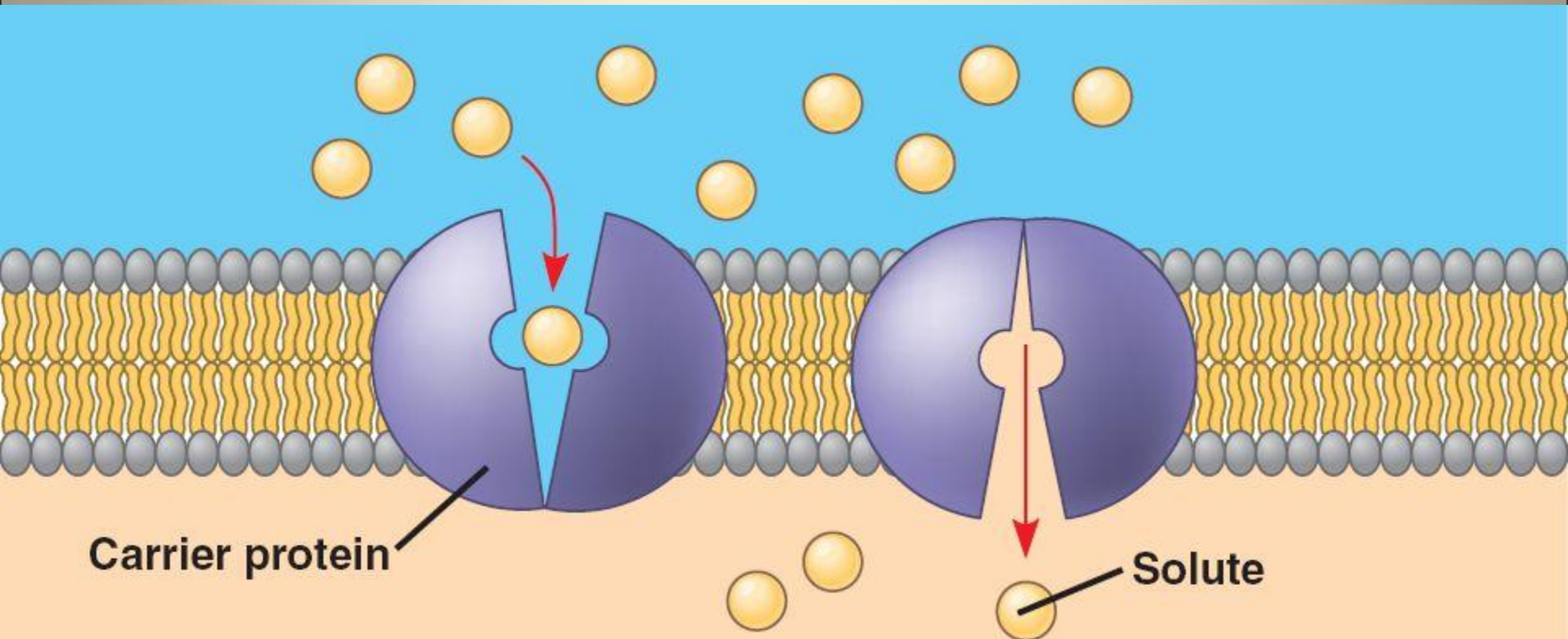
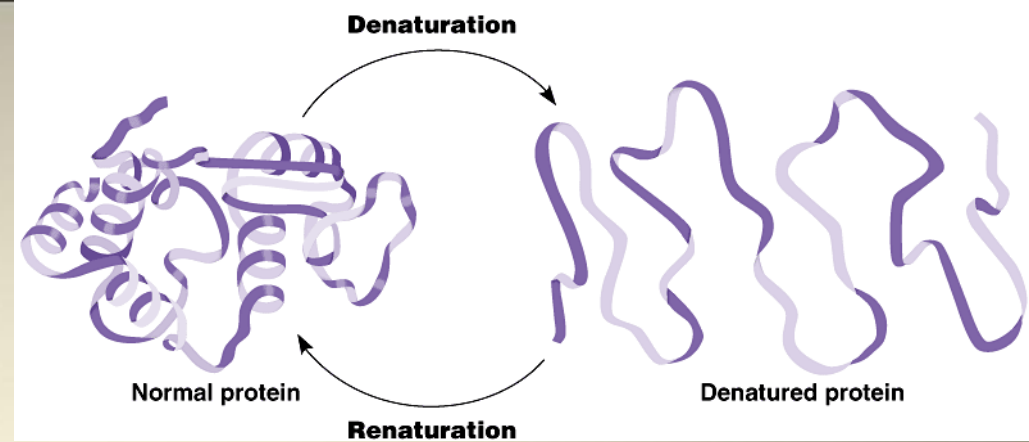


Fig. 8.14

Denaturation



- A change in the shape of the protein that disrupts protein function.
- Alterations in the environment (pH, salt concentration, temperature etc.) disrupt bonds and forces of attraction.
- Some proteins can return to their functional shape after denaturation (renaturation), but others cannot, especially in the crowded environment of the cell.

Protein Denaturation Video



McGraw Hill **Protein Denaturation**

The assembly of irreversibly denatured protein molecules results in formation of a solid gel. The gel entraps water molecules inside the white into a semi-solid structure, which holds its shape under normal conditions.

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Function and Binding

- Protein shape (conformation) determines function

Amino acids → conformation → function

- Function depends on its ability to recognize and bind a molecule

Amino acids → conformation → function → binding

X-ray crystallography

- determines protein conformation
- requires protein in the form of a crystal
- pattern of diffraction of crystal can be used to determine the location of the atoms to build a computer model of its structure

