Proteins - Many Structures, Many Functions

1. A polypeptide is a polymer of amino acids connected to a specific sequence
2. A protein's function depends on its specific conformation

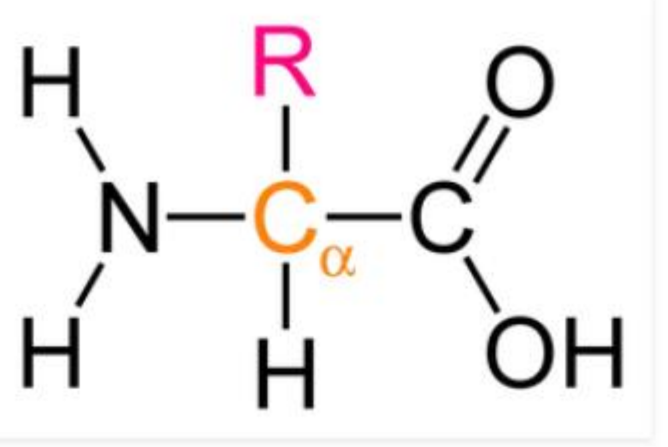
Introduction

- **Proteins** are instrumental in about everything that an organism does.
  - structural support,
  - storage
  - transport of other substances
  - intercellular signaling
  - movement
  - defense against foreign substances
  - Proteins are the main enzymes in a cell and regulate metabolism by selectively accelerating chemical reactions.
- Humans have tens of thousands of different proteins, each with their own structure and function.

- Proteins are the most structurally complex molecules known.
  - Each type of protein has a complex three-dimensional shape or conformation.
- All protein polymers are constructed from the same set of 20 monomers, called amino acids.
- Polymers of proteins are called **polypeptides**.
- A protein consists of one or more polypeptides folded and coiled into a specific conformation

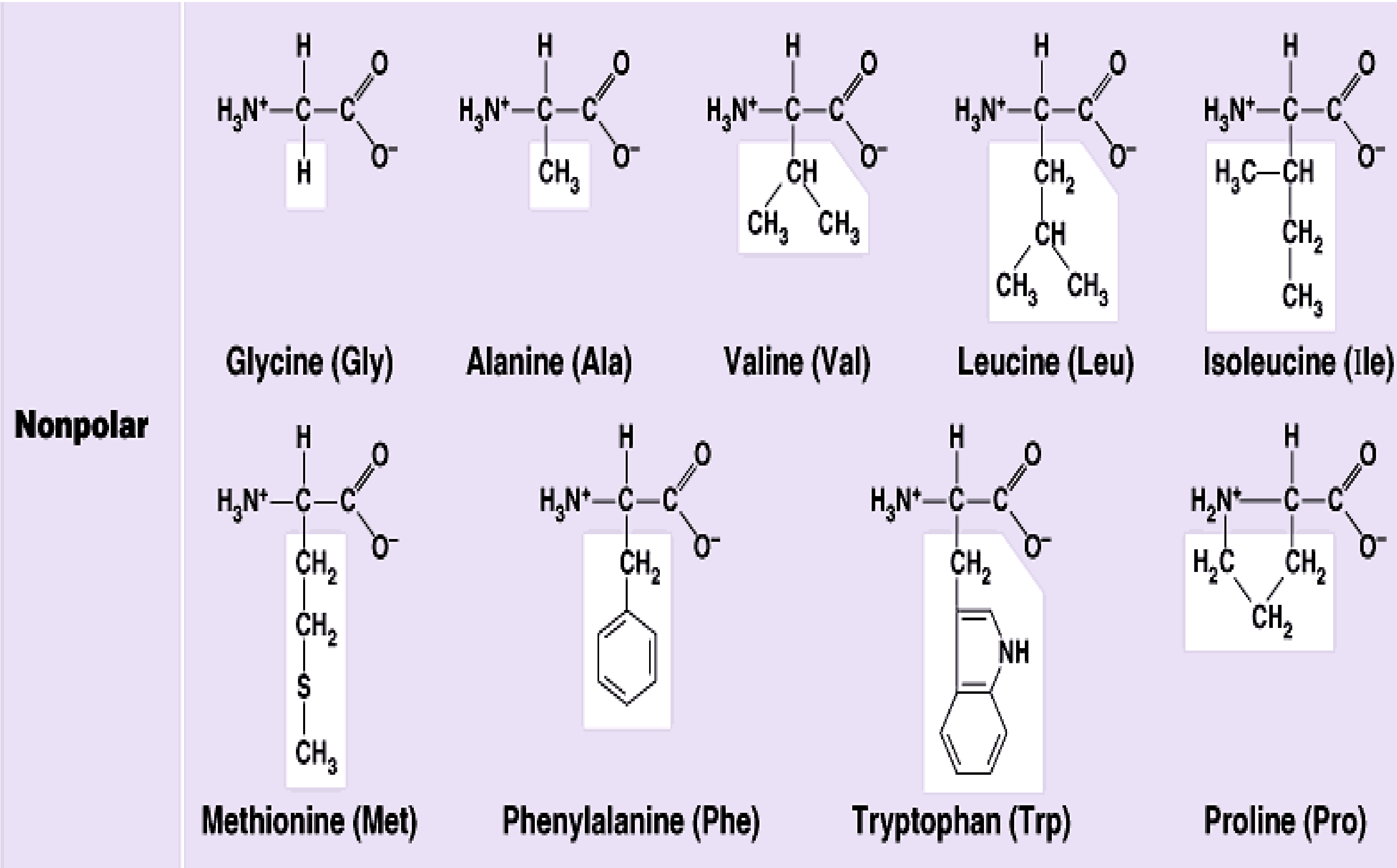
1. A polypeptide is a polymer of amino acids connected in a specific sequence

- **Amino acids** consist of four components attached to a central carbon, the *alpha carbon*.
- These components include a hydrogen atom, a carboxyl group, an amino group, and a variable R group (or side chain).
  - Differences in R groups produce the 20 different amino acids.

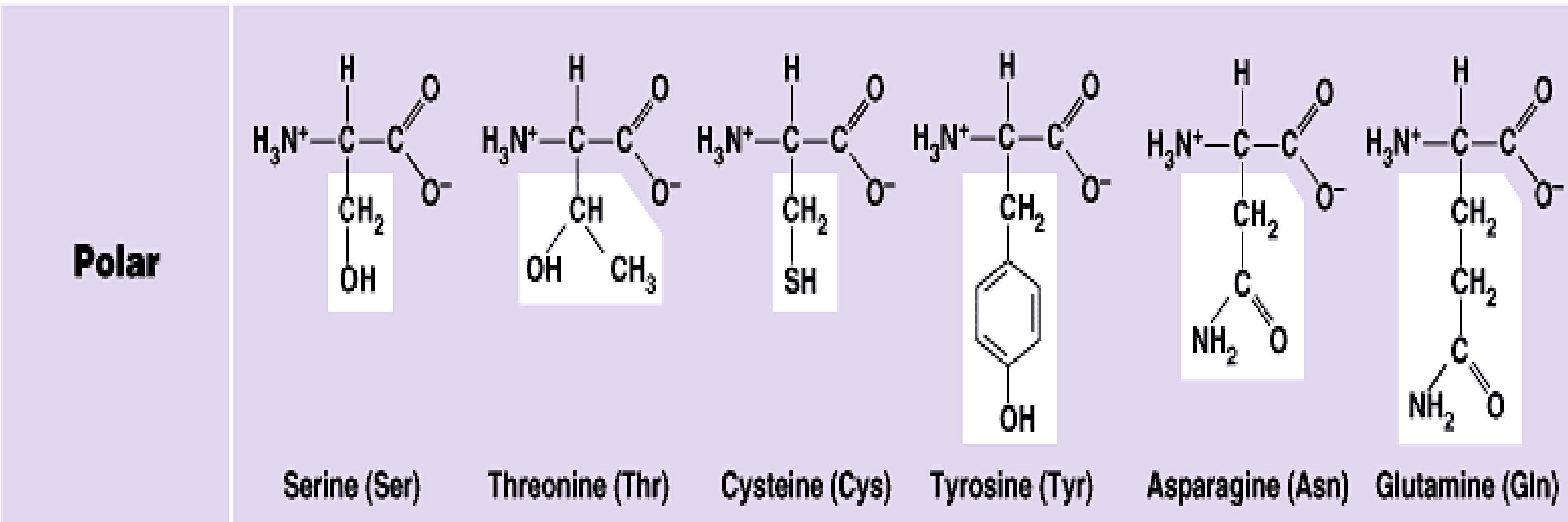


- The twenty different R groups may be as simple as a hydrogen atom (as in the amino acid glutamine) to a carbon skeleton with various functional groups attached.
- The physical and chemical characteristics of the R group determine the unique characteristics of a particular amino acid.

One group of amino acids has hydrophobic R groups.

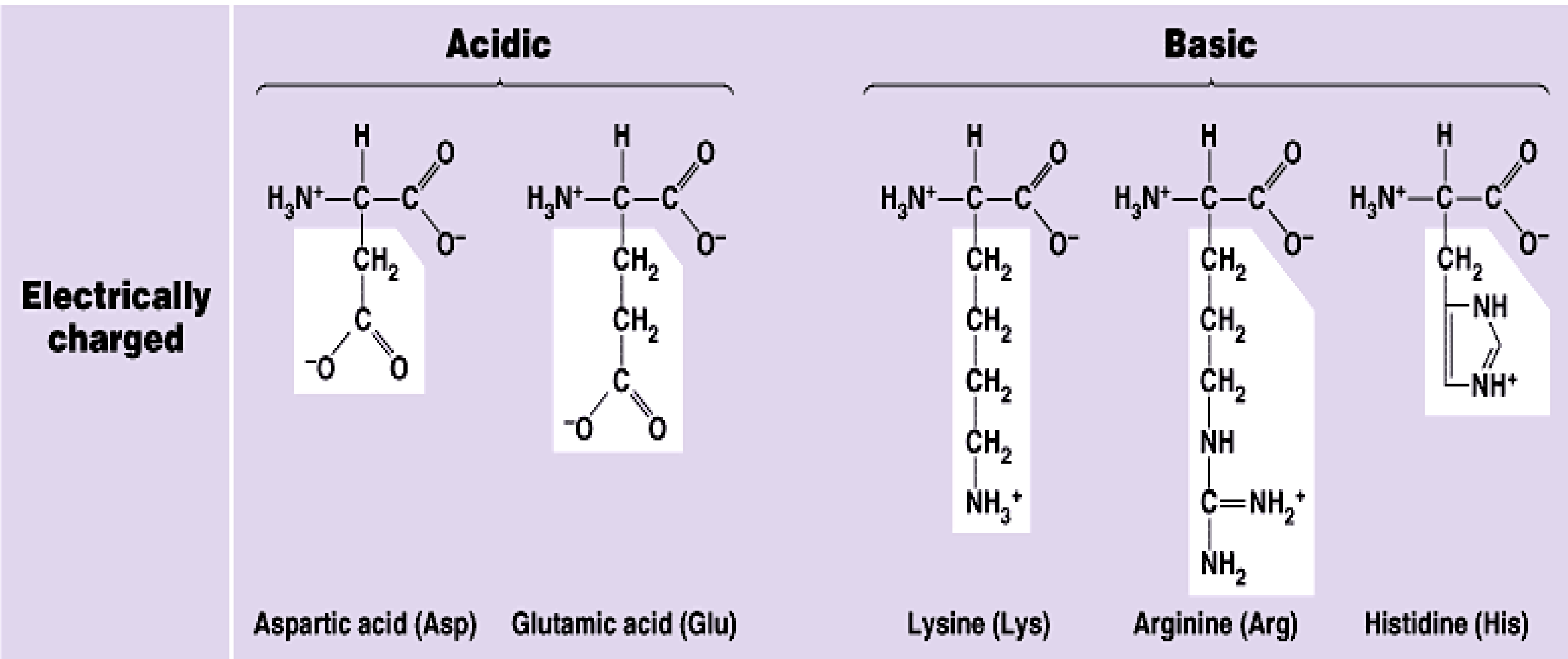


Another group of amino acids has polar R groups, making them hydrophilic.



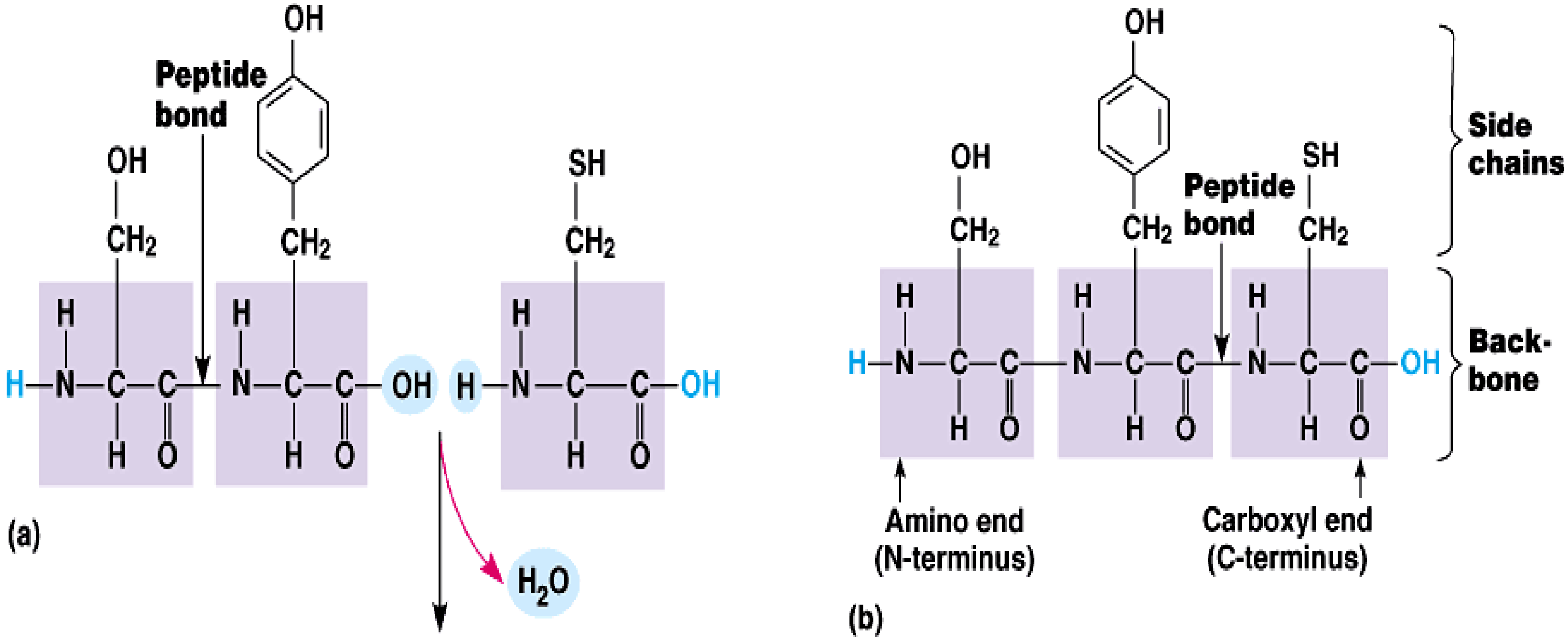
•The last group of amino acids includes those with functional groups that are charged (ionized) at cellular pH.

- Some R groups are bases, others are acids.



- Amino acids are joined together when a dehydration reaction removes a hydroxyl group from the carboxyl end of one amino acid and a hydrogen from the amino group of another.

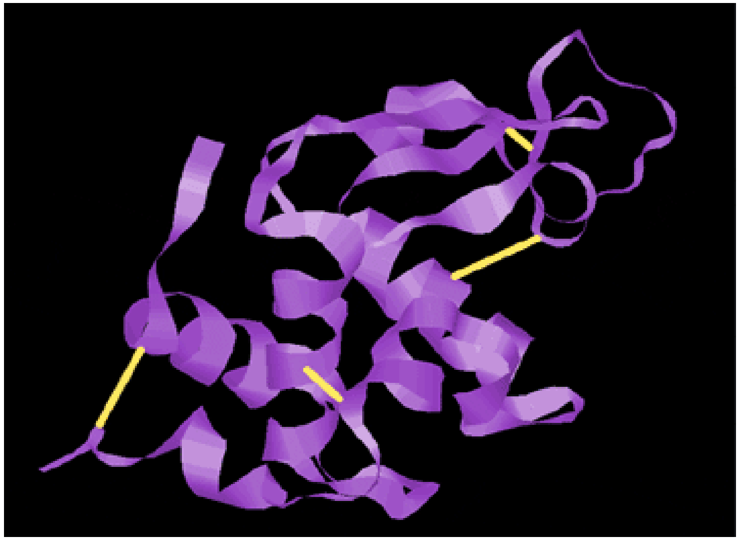
  - The resulting covalent bond is called a **peptide bond**.

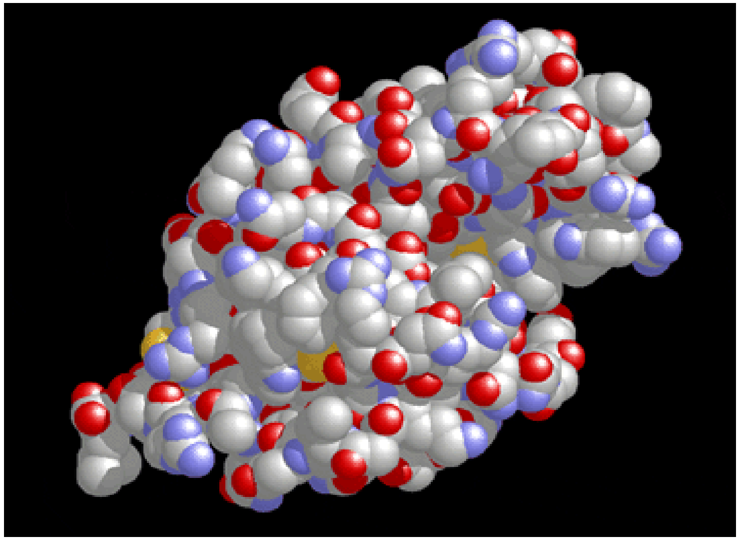


- Repeating the process over and over creates a long polypeptide chain.
  - At one end is an amino acid with a free amino group the (the N-terminus) and at the other is an amino acid with a free carboxyl group the (the C-terminus).
- The repeated sequence (N-C-C) is the polypeptide backbone.
- Attached to the backbone are the various R groups.
- Polypeptides range in size from a few monomers to thousands.

A protein's function depends on its specific conformation

- A functional proteins consists of one or more polypeptides that have been precisely twisted, folded, and coiled into a unique shape.
- It is the order of amino acids that determines what the three-dimensional conformation will be.



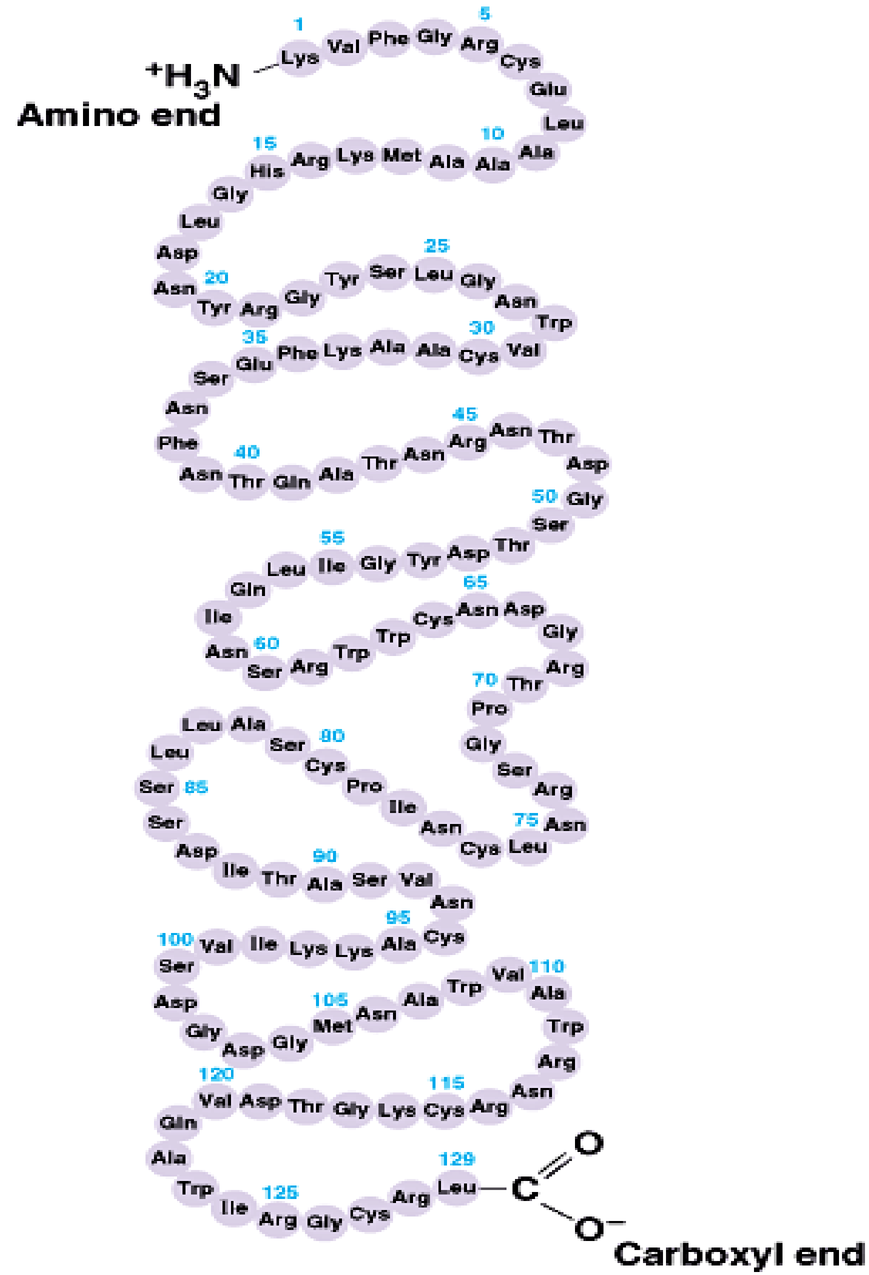


- **A protein's specific conformation determines its function**.
- In almost every case, the function depends on its ability to recognize and bind to some other molecule.
  - For example, antibodies bind to particular foreign substances that fit their binding sites.
  - Enzyme recognize and bind to specific substrates, facilitating a chemical reaction.
  - Neurotransmitters pass signals from one cell to another by binding to receptor sites on proteins in the membrane of the receiving cell.

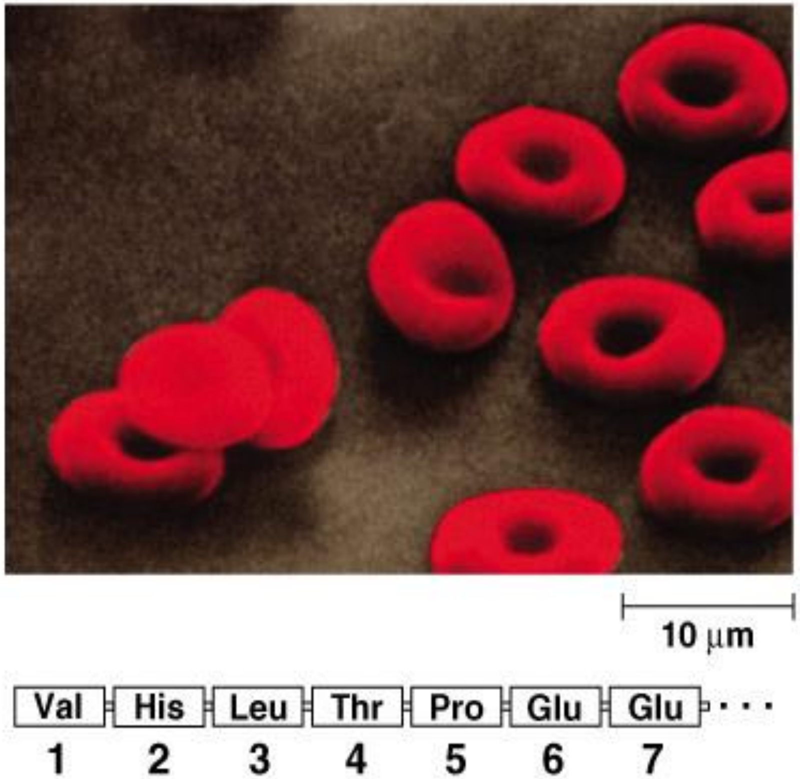
Levels of Protein Structure

1. Primary structure
2. Secondary structure
3. Tertiary structure
   - are used to organize the folding within a **single** polypeptide.
4. Quarternary structure arises when **two or more** polypeptides join to form a protein.

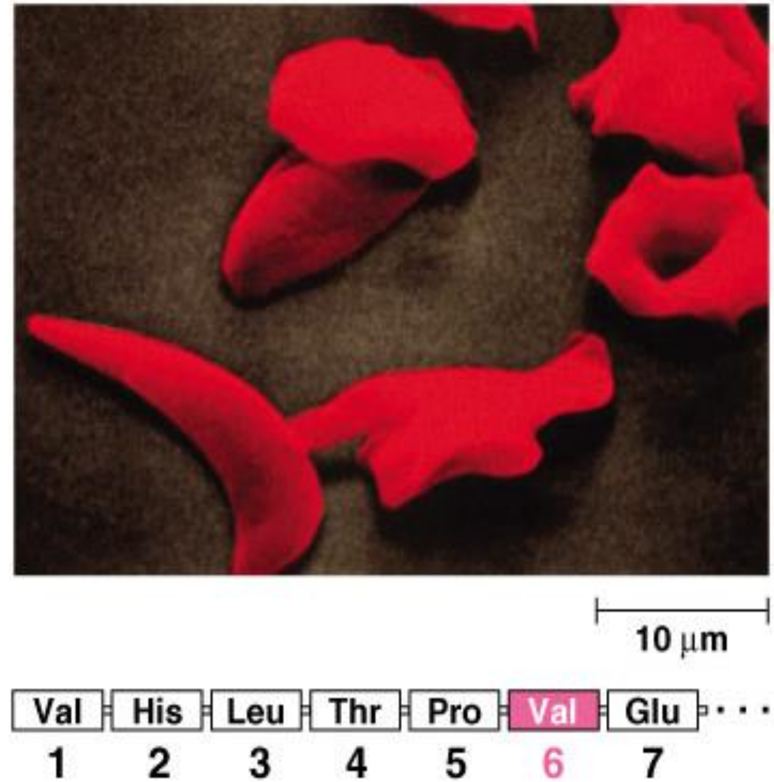
- The **primary structure** of a protein is its unique sequence of amino acids.
  - Lysozyme, an enzyme that attacks bacteria, consists on a polypeptide chain of 129 amino acids.
  - The precise primary structure of a protein is determined by inherited genetic information.



- Even a slight change in primary structure can affect a protein’s conformation and ability to function.
- In individuals with sickle cell disease, abnormal hemoglobins, oxygen-carrying proteins, develop because of a single amino acid substitution.
  - These abnormal hemoglobins crystallize, deforming the red blood cells and leading to clogs in tiny blood vessels.

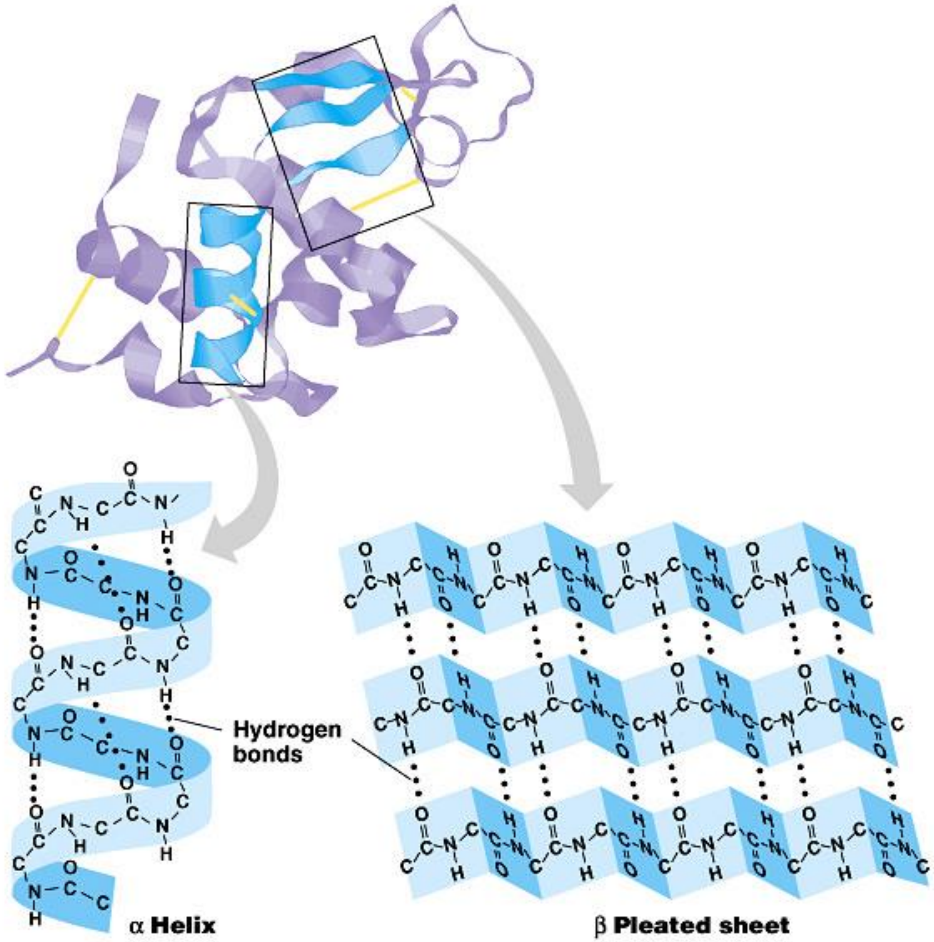


(a) Normal red blood cells and the primary structure of normal hemoglobin



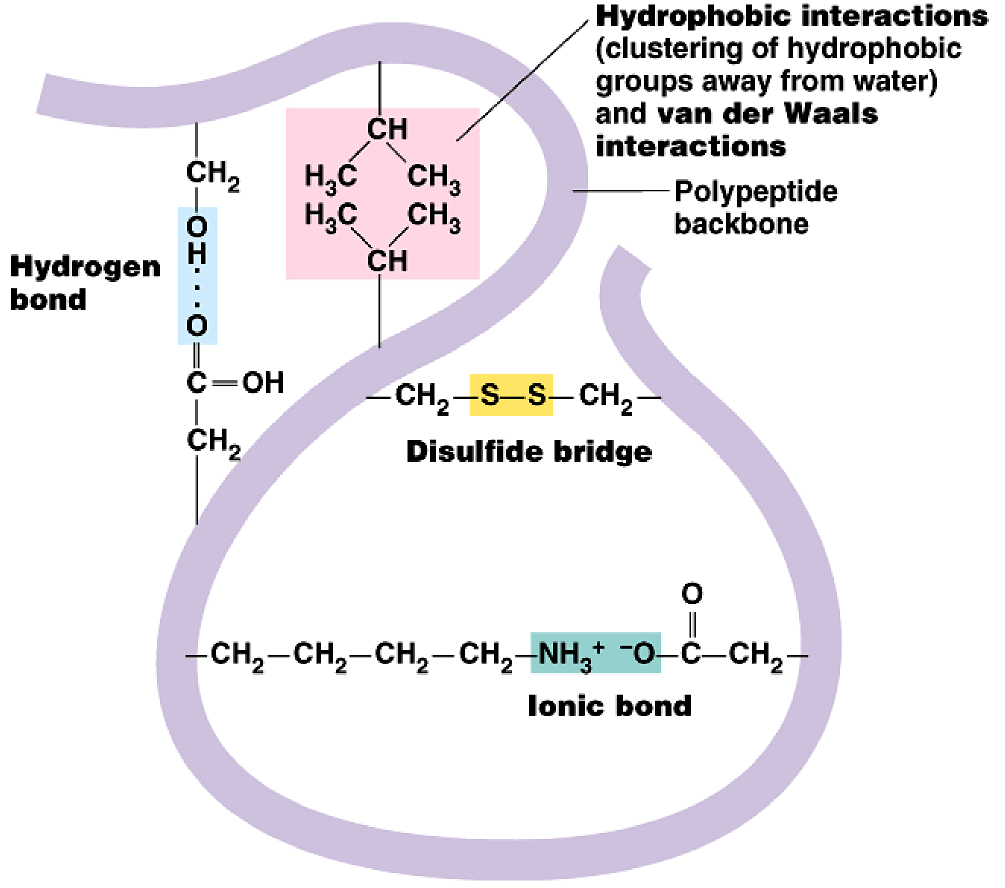
(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

- The **secondary structure** of a protein results from hydrogen bonds at regular intervals along the polypeptide backbone.
  - Typical shapes that develop from secondary structure are coils (an alpha helix) or folds (beta pleated sheets).

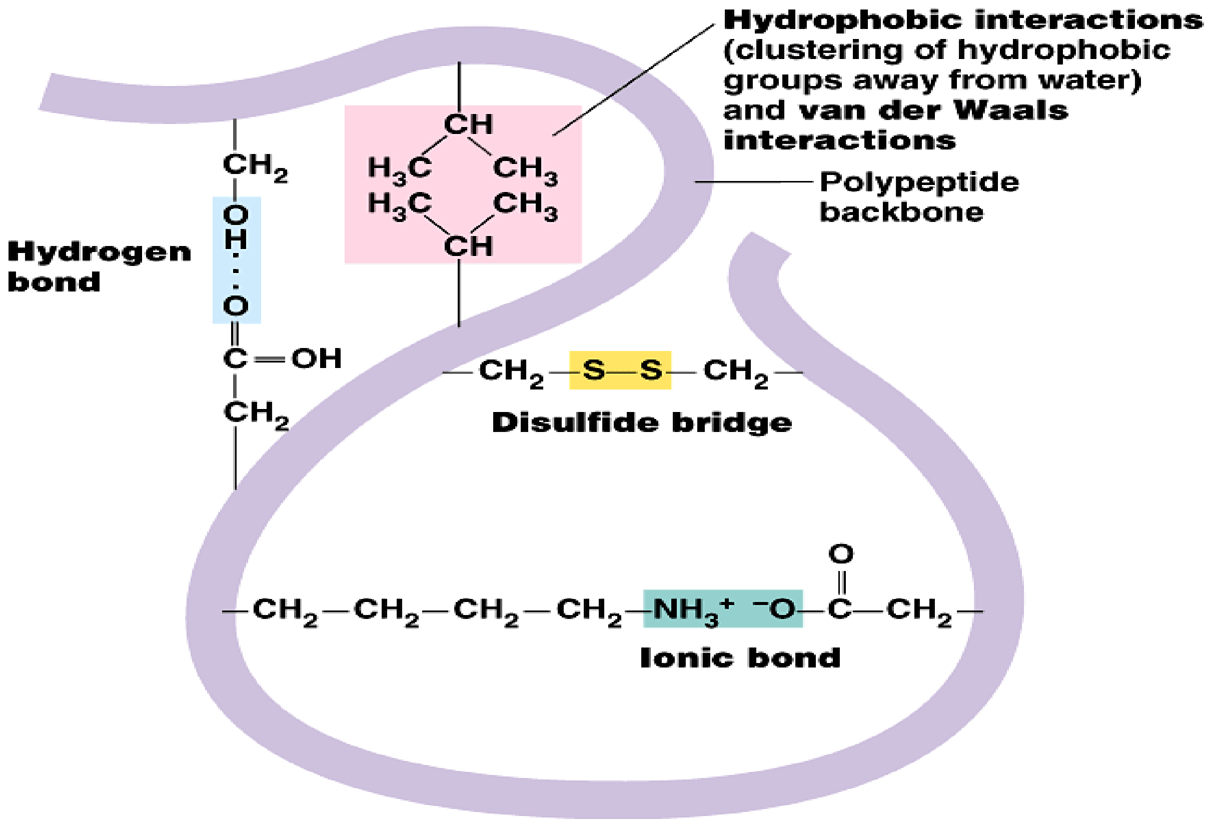


- The structural properties of silk are due to beta pleated sheets.
  - The presence of so many hydrogen bonds makes each silk fiber stronger than steel.

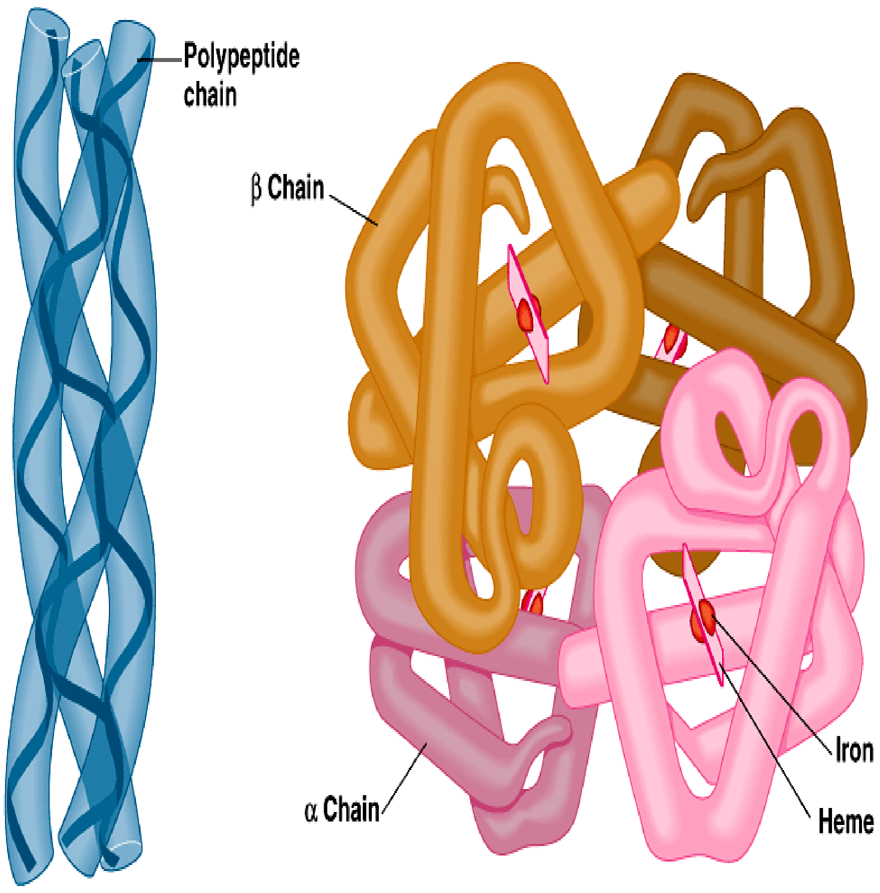
- **Tertiary structure** is determined by a variety of interactions among R groups and between R groups and the polypeptide backbone.
  - These interactions include hydrogen bonds among polar and/or charged areas, ionic bonds between charged R groups, and **hydrophobic interactions** and **van der Waals interactions** among hydrophobic R groups.



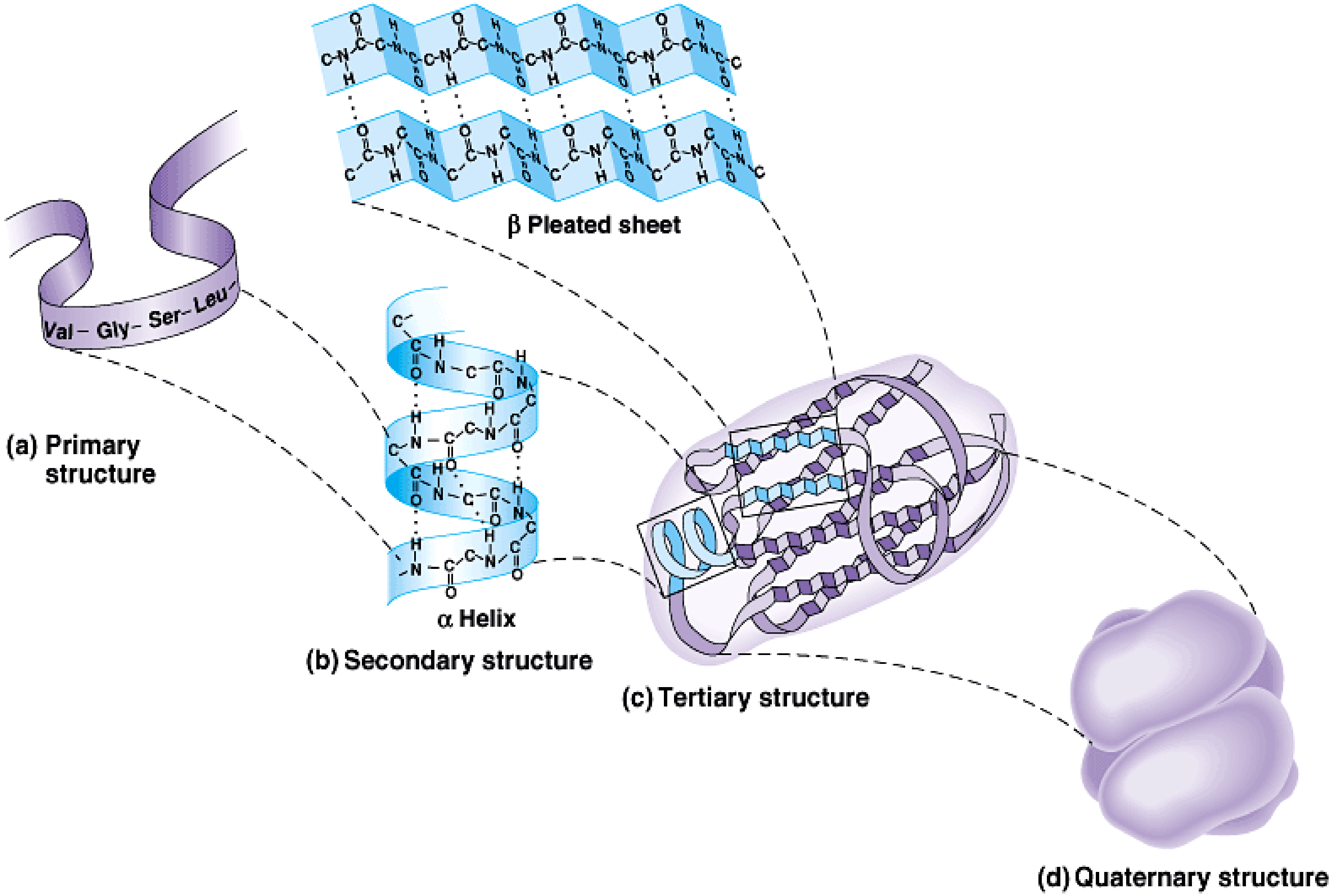
- While these three interactions are relatively weak, **disulfide bridges**, strong covalent bonds that form between the sulfhydryl groups (SH) of cysteine monomers, stabilize the structure.



- **Quarternary structure** results from the aggregation of **two or more** polypeptide subunits.
  - Collagen is a fibrous protein of three polypeptides that are supercoiled like a rope.
    - This provides the structural strength for their role in connective tissue.
  - Hemoglobin is a globular protein with **two copies of two kinds** of polypeptides.

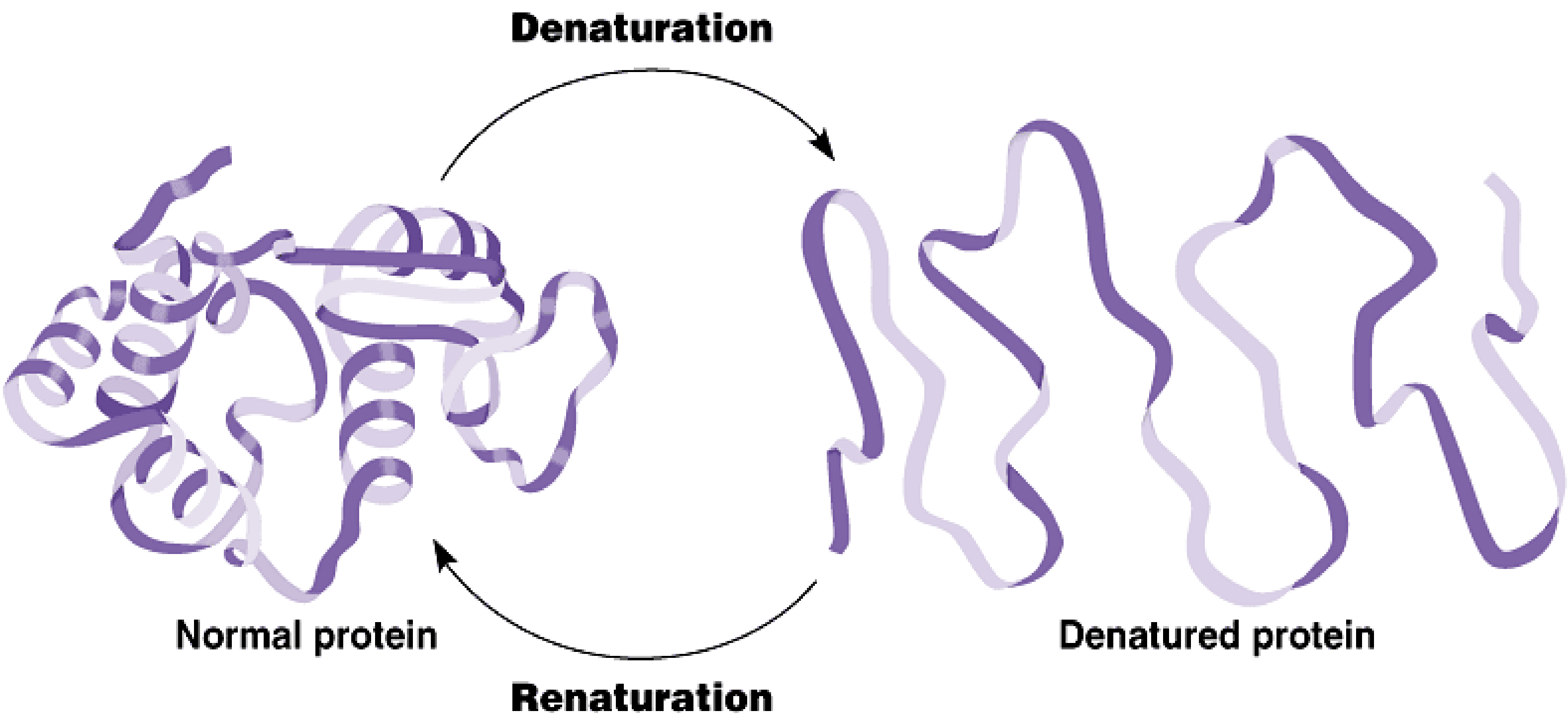


(a) Collagen (b) Hemoglobin



β Pleated sheet
Val – Gly – Ser – Leu –
(a) Primary structure
α Helix
(b) Secondary structure
(c) Tertiary structure
(d) Quaternary structure

- A protein’s conformation can change in response to the physical and chemical conditions.
- Changes in pH, salt concentration, temperature, or other factors can unravel or **denature** a protein.
  - These forces disrupt the hydrogen bonds, ionic bonds, and disulfide bridges that maintain the protein’s shape.
- Some proteins can return to their functional shape after denaturation, but others cannot, especially in the crowded environment of the cell.
  - Usually denaturation is permanent


Denaturation
Normal protein
Denatured protein
Renaturation