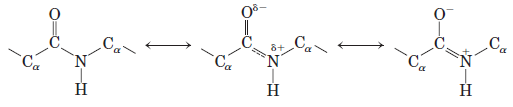
**Three-Dimensional Structure of Proteins**

**Overview of Protein Structure**

* Every protein has a three-dimensional structure that reflects its function.

**The Peptide Bond Is Rigid and Planar**

* Peptide bonds are important for primary structure of proteins.
* Peptide bond (**Fig. 4-2)**.



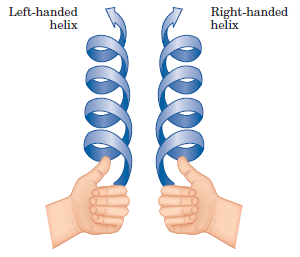
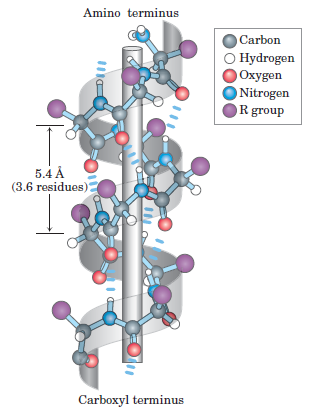
* has some double-bond character due to resonance.
* cannot rotate freely.
* has trans position (O and H atoms).
* is rigid and planar.

**Protein Secondary Structure**

* Secondary structure refers coiled primary structure by H bonds.
* H bonds are formed between C=O and N-H groups of the peptide bonds.
* The most common regular secondary structures are the  helix, the**** conformation and  turns.

**The  Helix Is a Common Protein Secondary Structure**

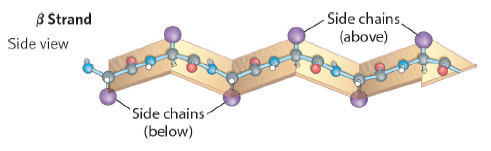
* Polypeptide chain is a helical structure called the ** helix** (right-handed) **(Fig. 4-4)**.



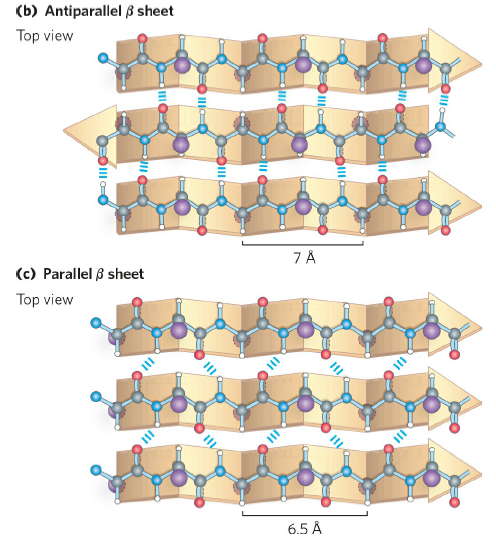
* R groups of the amino acid residues protrude outward from the helical backbone.
* The repeating unit is a single turn of the helix, which extends about 5.4 Å (Ångström, is equal to 0.1 nm) and each helical turn includes 3.6 amino acid residues.
* Amino acid sequence affects stability of the  helix.

**The  Conformation Organizes Polypeptide Chains into Sheets**

* Polypeptide chain is extended into a zigzag rather than helical structure called a ** sheet**.



* Hydrogen bonds form between adjacent segments of polypeptide chain within the sheet.
* The R groups of adjacent amino acids protrude from the zigzag structure in opposite directions.
* The adjacent polypeptide chains in a**** sheet can be either parallel or antiparallel (having the same or opposite amino-to-carboxyl orientations, respectively) **(Fig. 4-6)**.

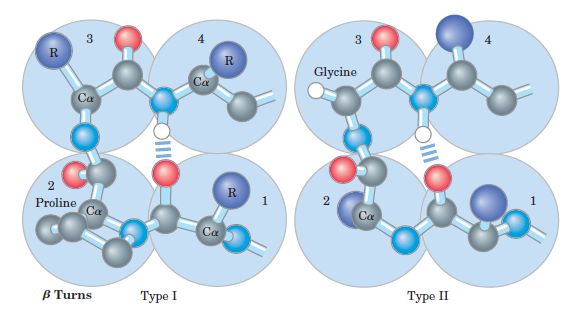




* Repeat period is shorter for the parallel conformation (6.5 Å, vs. 7 Å for antiparallel) and the hydrogen-bonding patterns are different (in-line or not in-lane).

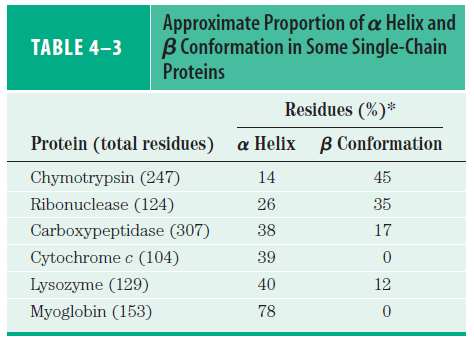
** Turns Are Common in Proteins**

*  turns connect the ends of two adjacent segments of an antiparallel  sheet **(Fig. 4-7)**.

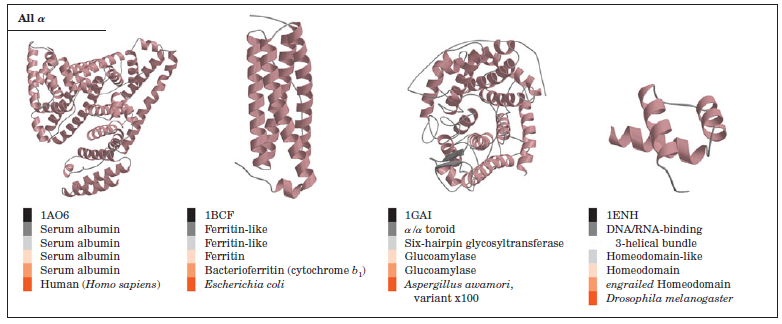
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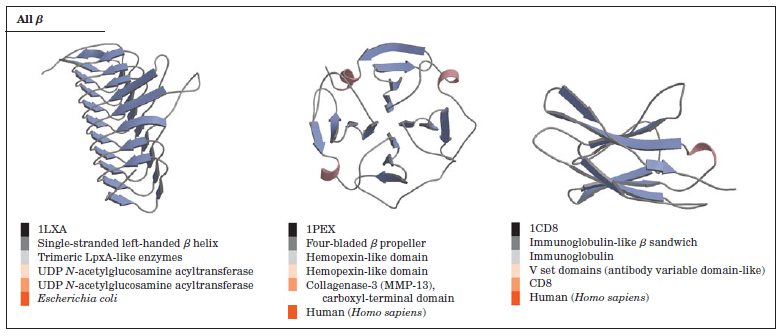
**4.3 Protein Tertiary and Quaternary Structures**

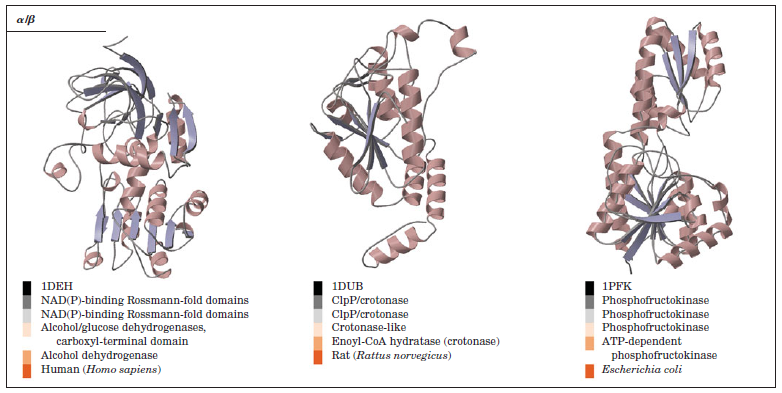
* **Tertiary structure** describes three-dimensional folding by noncovalent weak interactions between R groups (and sometimes by covalent bonds such as disulfide crosslinks).
* is the complete three-dimensional structure of a polypeptide chain.
* **Quaternary structure** results from noncovalent interactions and disulfide bonds between R groups of two or more polypeptide chains (identical or different) having tertiary structure.
* Proteins are classified into two major groups according to their structure.
* **fibrous proteins** have polypeptide chains arranged in long strand or sheets.
* insoluble in water, high concentration of hydrophobic amino acid residues (example : -keratin in hair, collagen in bone).
* **globular proteins** have polypeptide chains folded into a spherical or globular shape.
* soluble in water (example : enzymes, transport protein).
* a variety of tertiary structures **(Table 4-3)**.

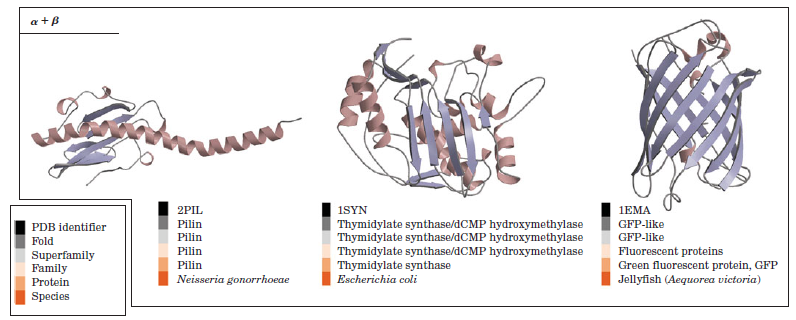


* To understand a complete three-dimensional structure, it is needed to analyze its folding.
* There are four classes of protein structure:
* all 
* all 
* /  (with  and  segments interspersed or alternating)
*  + (with  and  regions somewhat segregated). **(Fig. 4-22)**.





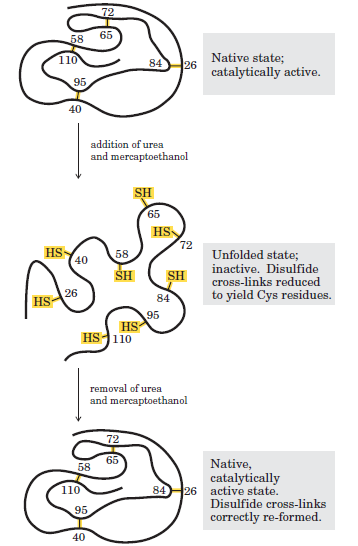






**4.4 Protein Denaturation and Folding**

* A loss of three-dimensional structure sufficient to cause loss of function is called **denaturation**.
* Most proteins can be denatured by breaking the weak interactions (primarily hydrogen bonds).
* Denaturation agents are
* heat, pH, organic solvent (alcohol or acetone), solutes (urea, detergents).
* Denaturated globular proteins can regain their native structure and their biological activity which is called **renaturation (Fig. 4-27)**.





**Polypeptides Fold Rapidly by a Stepwise Process**

* Proteins are assembled from amino acids at very high rate.
* E.coli cells can make a complete, biologically active protein molecule containing 100 amino acid residues in about 5 seconds at 37 oC.
* However, the synthesis of peptide bonds on the ribosome is not enough; the protein must fold.
* How does the polypeptide chain arrive at its native conformation?
* Let’s assume
* each of the amino acid residues could take up 10 different conformations on average, giving 10100 different conformations for the polypeptide.
* its native and biologically active form would take about 1077 years.
* Protein folding is not a completely random, trial-and-error process. There must be shortcuts.
* A native protein has one folded conformation stabilized largely by weak interactions.
* thermodynamically the most stable, having the lowest Gibbs free energy.
* As our understanding of protein folding and protein structure improves,
* increasingly sophisticated computer programs for predicting the structure of proteins from their amino acid sequence are being developed.
* Not all proteins fold spontaneously as they are synthesized in the cell.
* Folding for many proteins is facilitated by the action of specialized proteins called **chaperones**.
* are facilitating correct folding pathways or providing microenvironments.
* Protein misfolding is a substantial problem in all cells.
* The misfolding causes or contributes to the development of serious disease.