BIOCHEMISTRY 1

2ND CLASS

UNIVERSITY OF ANBAR-COLLOGE OF SCIENCE

BIOLOGY DEPARTMENT

2020-2021

Structures of proteins

Lecture four(4)

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References:

Harper's Illustrated Biochemistry

Lippincott Biochemistry

Lehninger Principles of Biochemistry

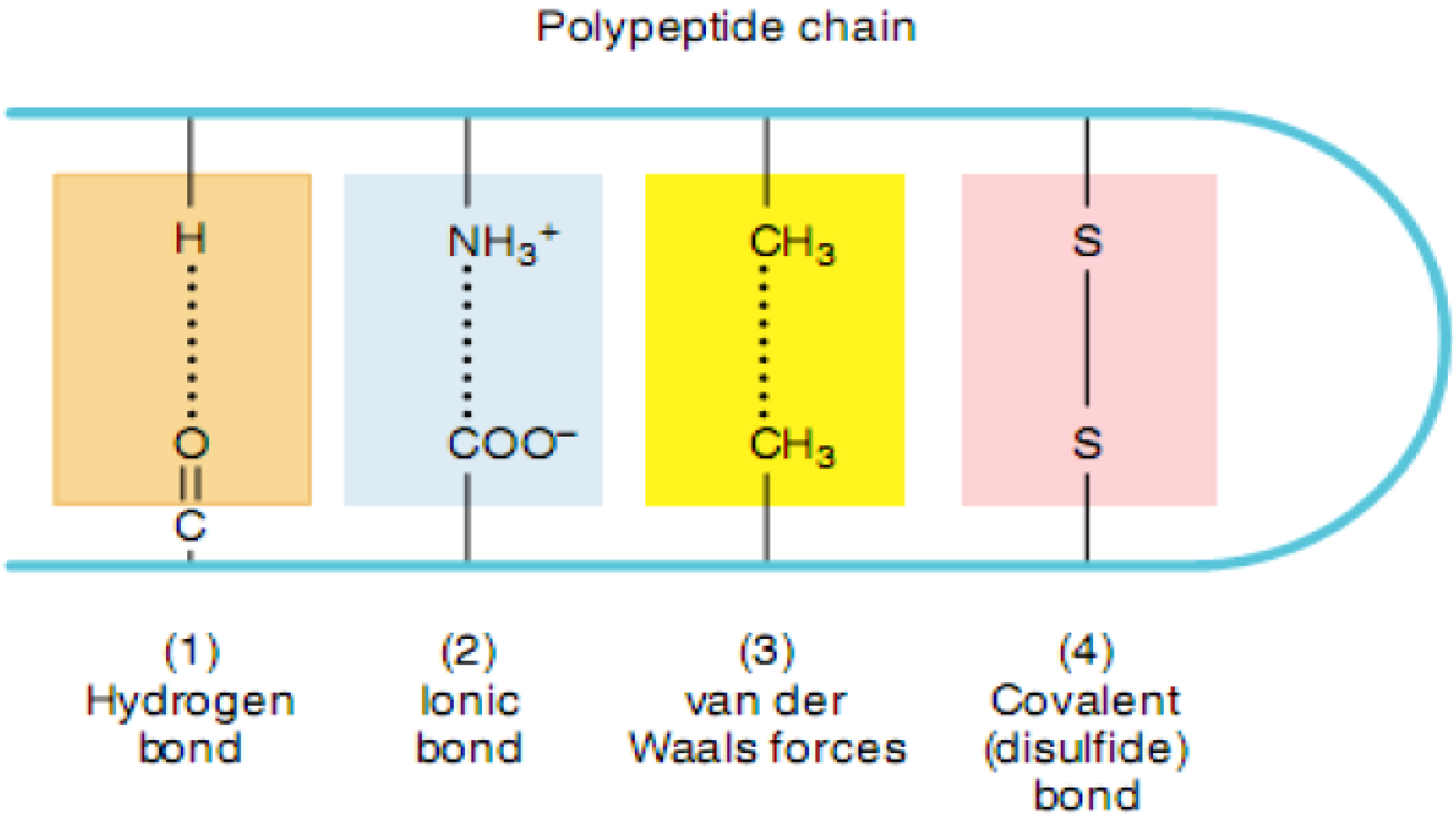
Stryer Biochemistry

Learning Objectives

- **Different structures of proteins**
- **Structures of two peptide chains conformations: alpha helix and beta pleated sheet**
- **The concept of folding, unfolding and misfolding of protein**
- **The deficiency and excess of proteins in human nutrition**

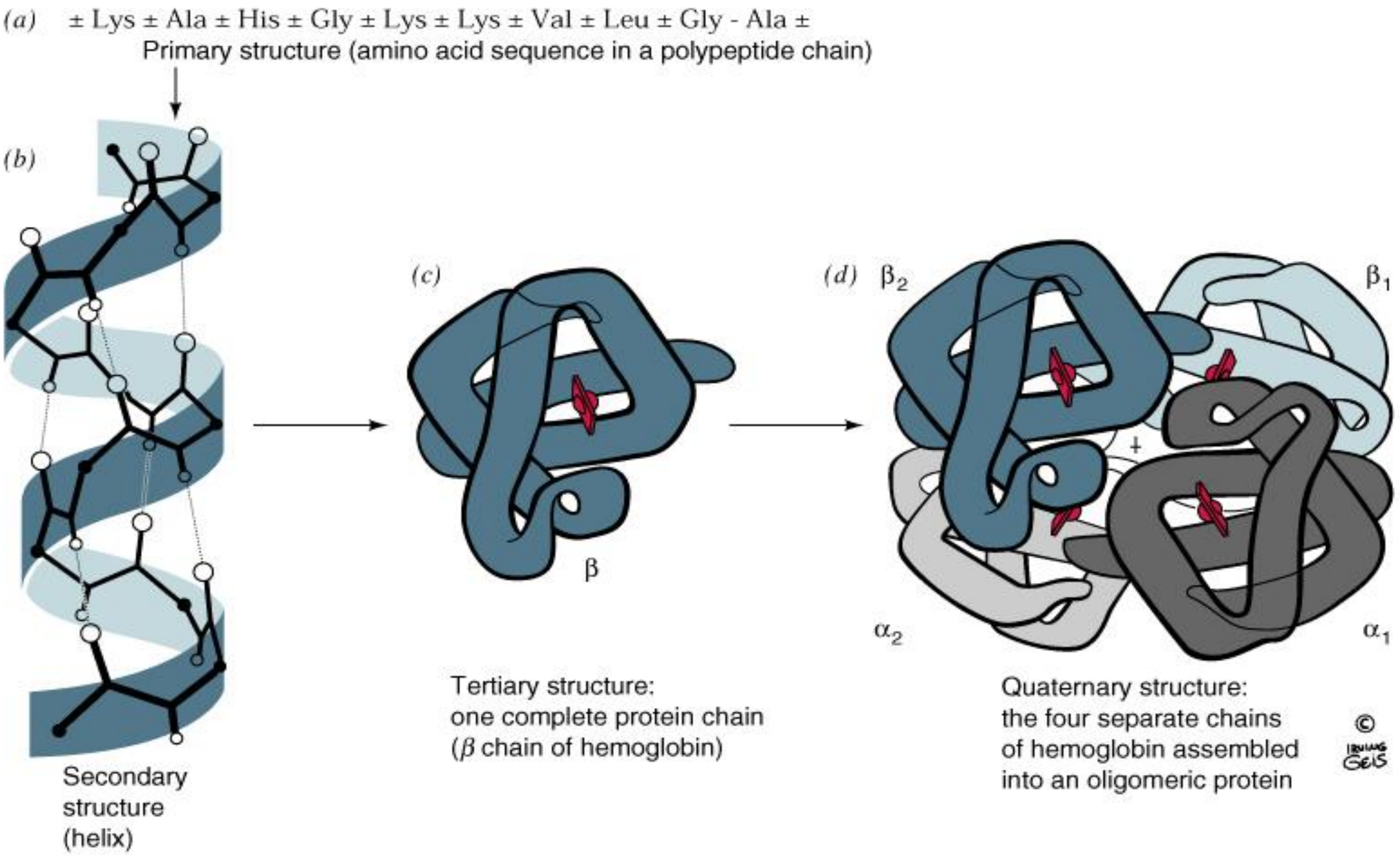
Structures of proteins

- **Simple proteins are made up of peptide bond**
- **Conjugated proteins have structures which incorporate non protein portions called prosthetic group**
- **The peptide chains of a particular protein molecule are folded in the same way. This is known as chain conformation**
- **The unique chain conformation of a given protein is influenced by many week forces (disulfide bridges, ionic bond, hydrogen bond, etc.)**


Polypeptide chain
H
O
C
NH_3^+
COO^-
CH_3
CH_3
S
S
(1) Hydrogen bond
(2) Ionic bond
(3) van der Waals forces
(4) Covalent (disulfide) bond

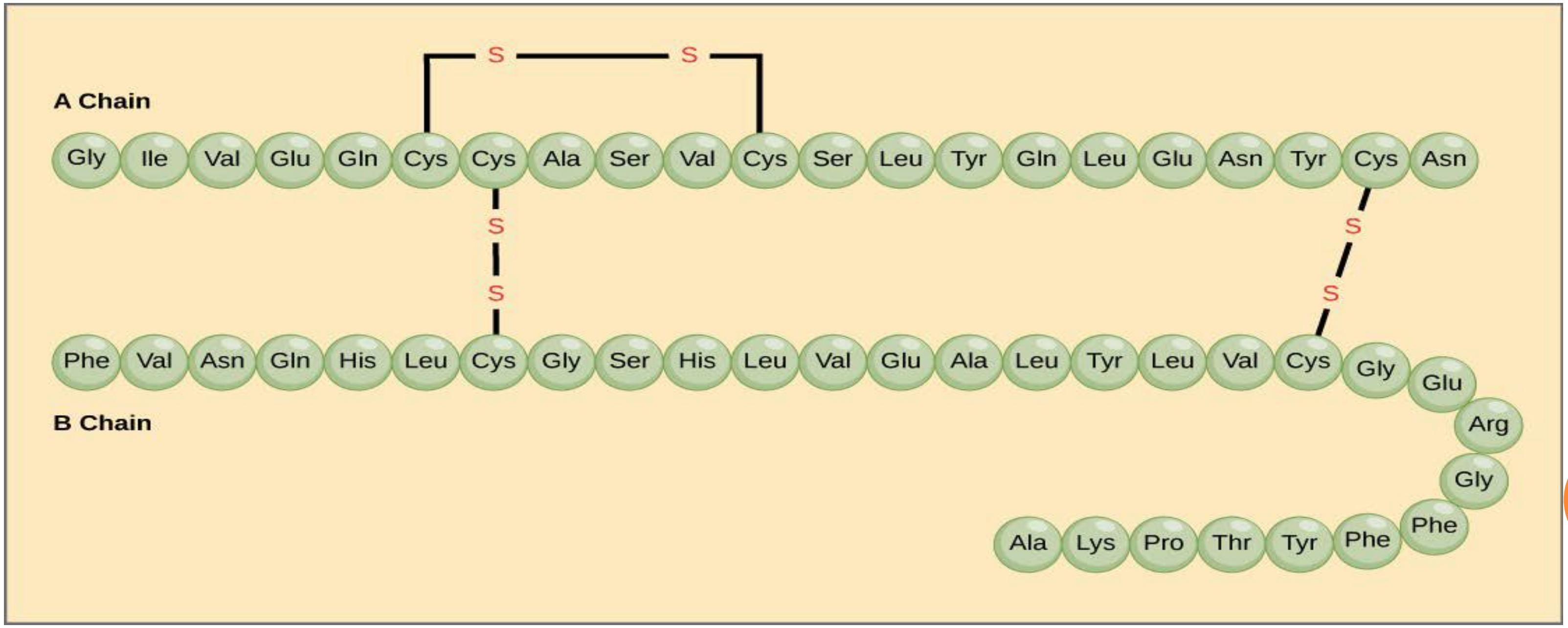
Levels of protein structure

- The sequence of a protein is determined by the DNA of the gene that encodes the protein (or that encodes a portion of the protein, for multi-subunit proteins).
- A change in the gene's DNA sequence may lead to a change in the amino acid sequence of the protein. Even changing just one amino acid in a protein's sequence can affect the protein's overall structure and function.
- To understand how a protein gets its final shape or conformation, we need to understand the four levels of protein structure: primary, secondary, tertiary, and quaternary


(a) ± Lys ± Ala ± His ± Gly ± Lys ± Lys ± Val ± Leu ± Gly - Ala ±
Primary structure (amino acid sequence in a polypeptide chain)
(b)
Secondary structure (helix)
(c)
β
Tertiary structure: one complete protein chain (β chain of hemoglobin)
(d)
β2
β1
α2
α1
Quaternary structure: the four separate chains of hemoglobin assembled into an oligomeric protein
© Irving Geis

Primary structure

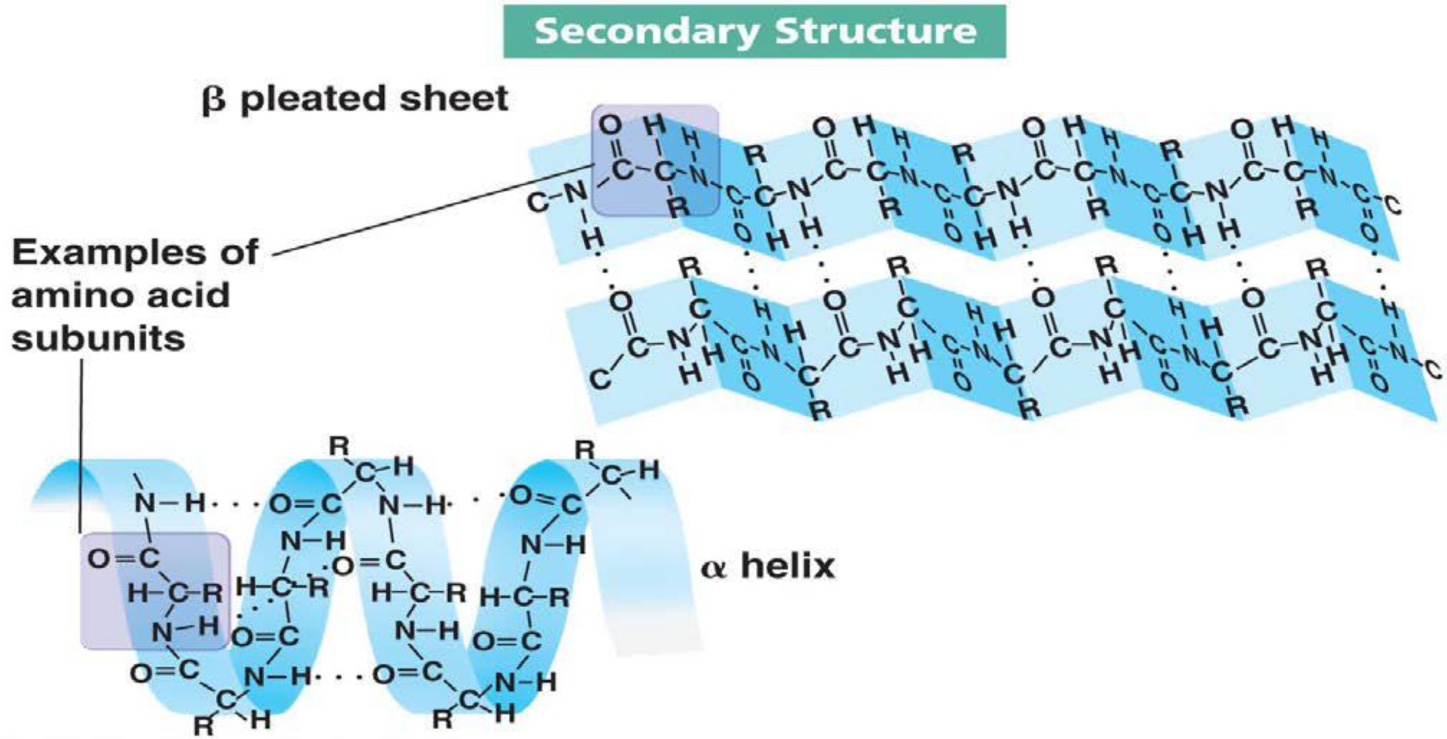
The simplest level of protein structure, primary structure is simply the sequence of amino acids in a polypeptide chain.
The hormone insulin has two polypeptide chains A, and B. The sequence of the A chain, and the sequence of the B chain can be considered as an example for primary structure.



Secondary structure

secondary structure, refers to local folded structures that form within a polypeptide due to interactions between atoms.

The most common types of secondary structures are the α helix and the β pleated sheet. Both structures are held in shape by hydrogen bonds, which form between the carbonyl O of one amino acid and the amino H of another.



α-Helix

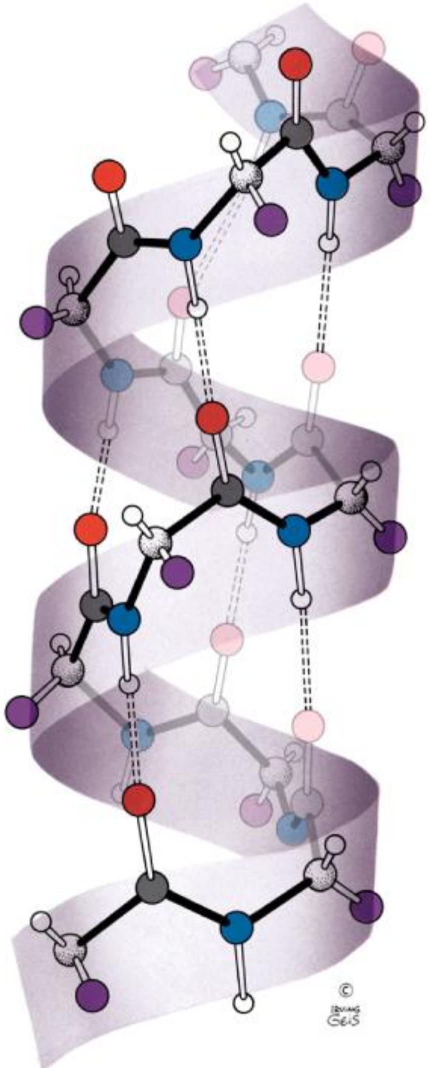
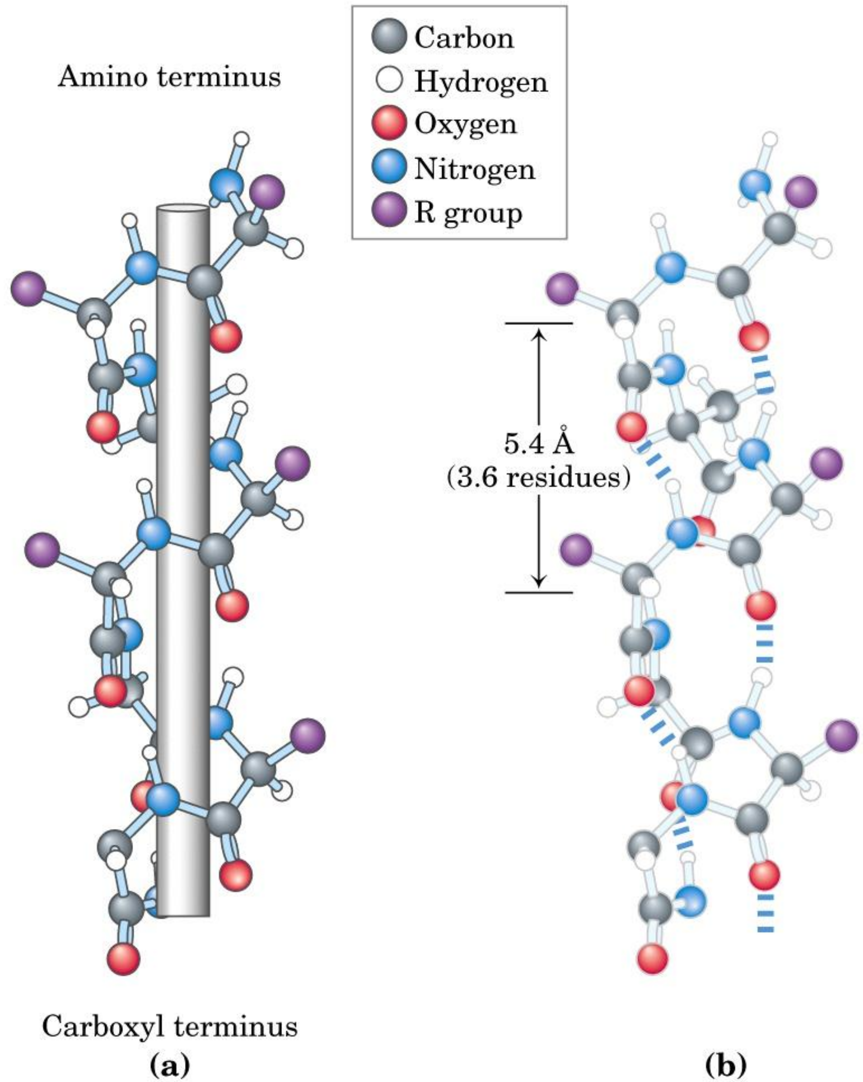
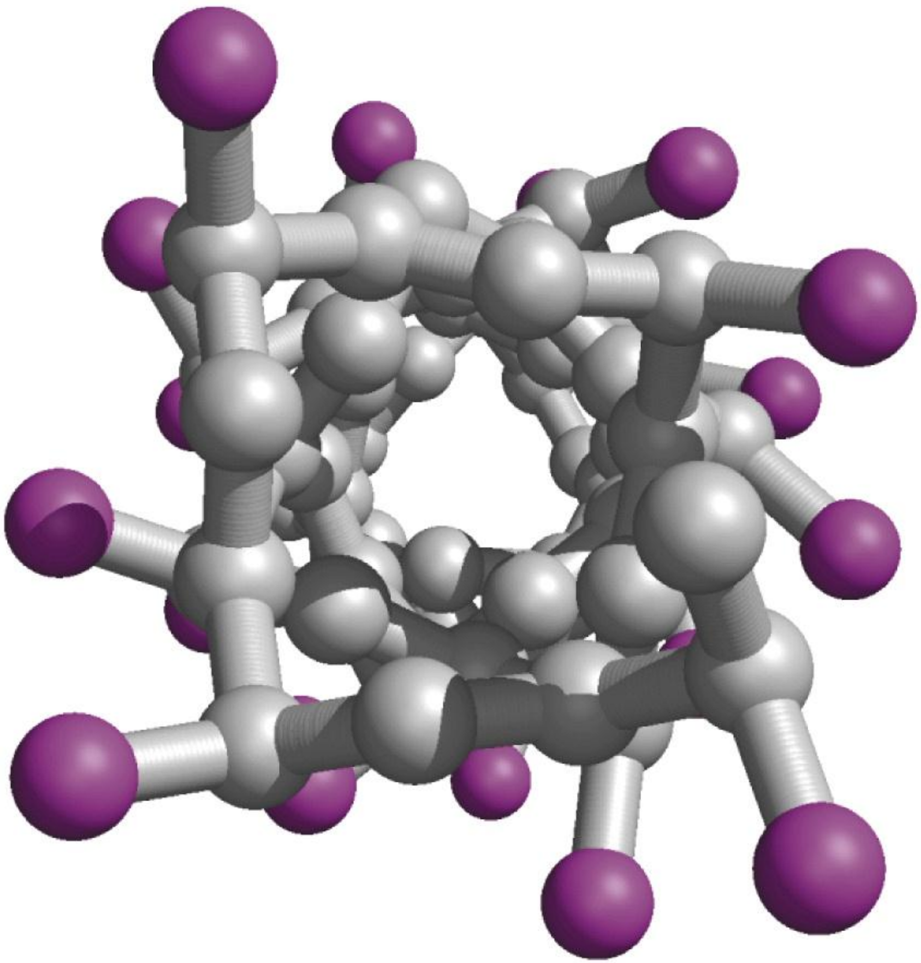


Figure 6-7. Key to Structure. The α helix.
[Figure copyrighted by © Irving Geis.]

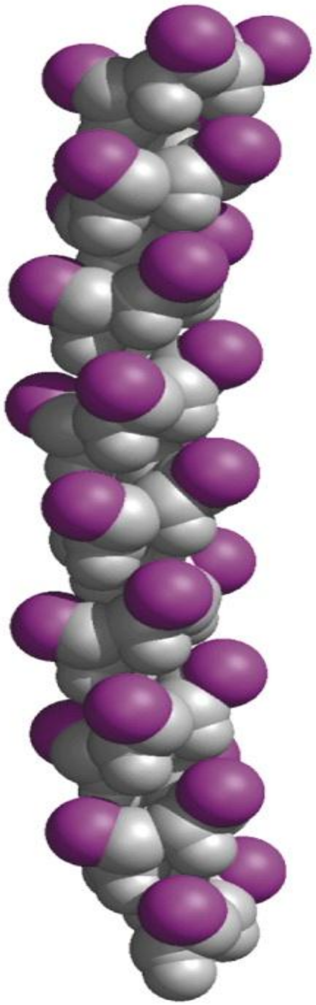


α-Helix as viewed from one end



(c)

A space feeling model of α- Helix



(d)

β-Sheet

β-pleated sheet consists of peptide chains arranged side by side which resembles a piece of paper folded into many pleats

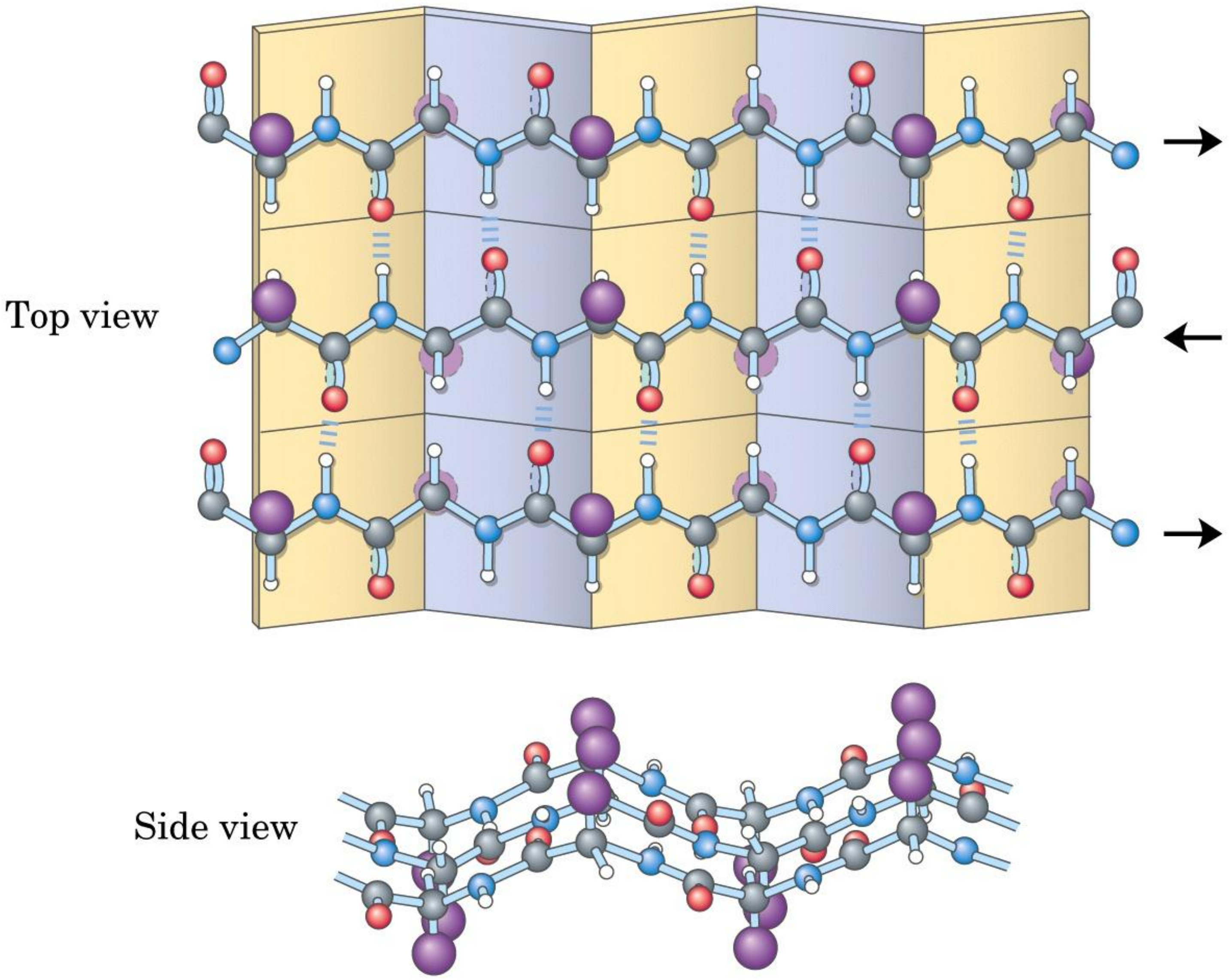
- Like a helix, the β-sheet uses the full H-bonding capacity of the polypeptide backbone

- HOWEVER, H-bonding occurs BETWEEN neighboring peptide chains, rather than within one.

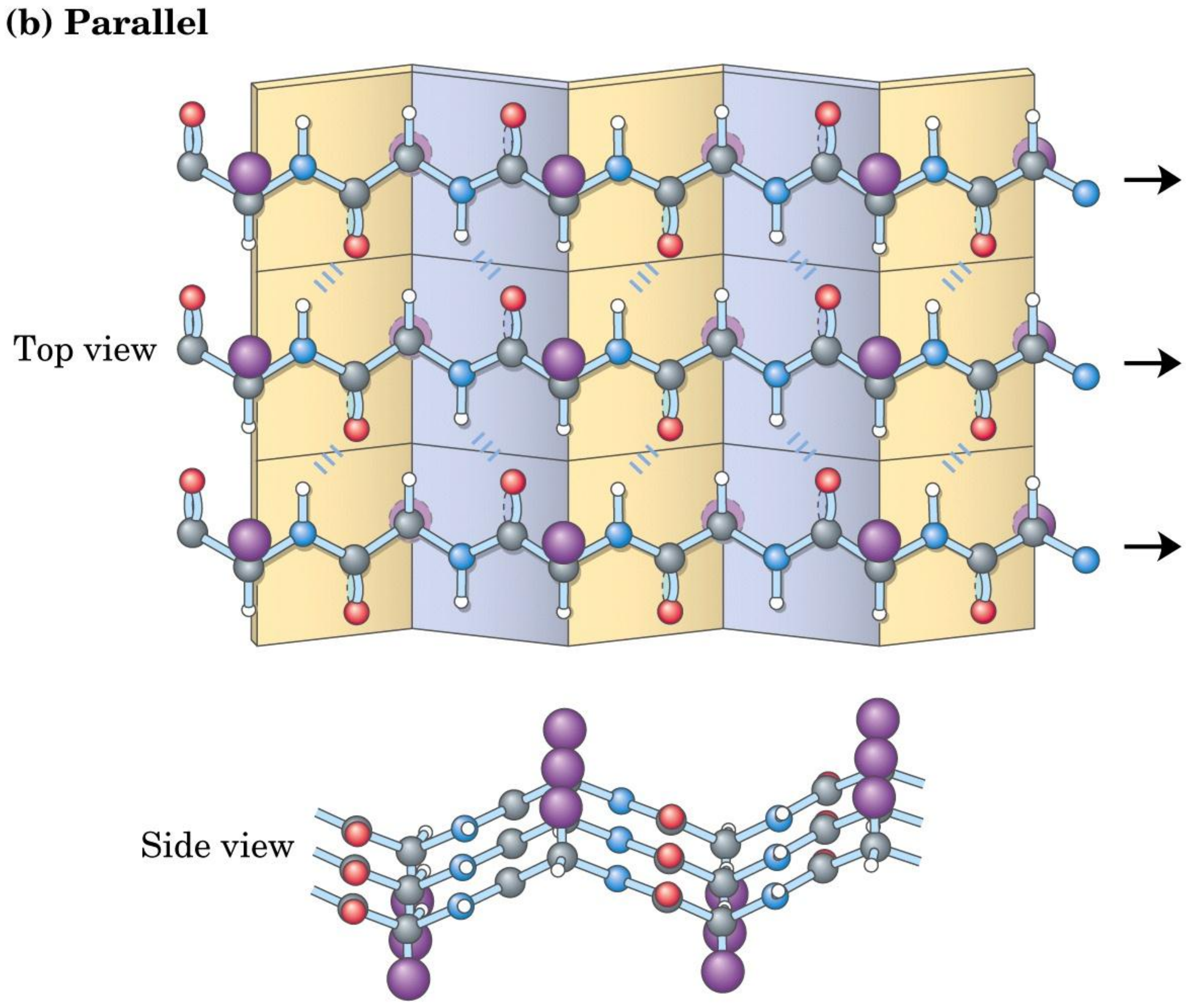
- R-groups extend above and below the plane of the sheet

β-Sheet

(a) Antiparallel



β-Sheet



Pleat of β-Sheet

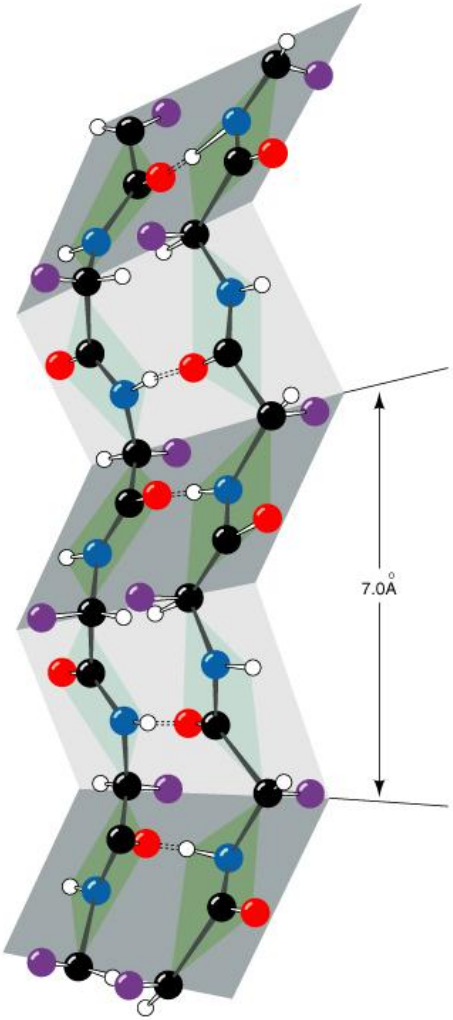


Figure 6-10. Pleated appearance of a ß sheet.
[Figure copyrighted © by Irving Geis.]

Secondary structures…

- Helices and sheets can be combined in various ways

- Some proteins have mainly a-helices, some have mainly b-sheets, but most have both

Secondary structure: fibrous proteins

- Water insoluble
- Usually physically tough
- Usually static: provides mechanical support to individual cells and entire organisms
- E.g., collagen, keratin

Examples of secondary structure…

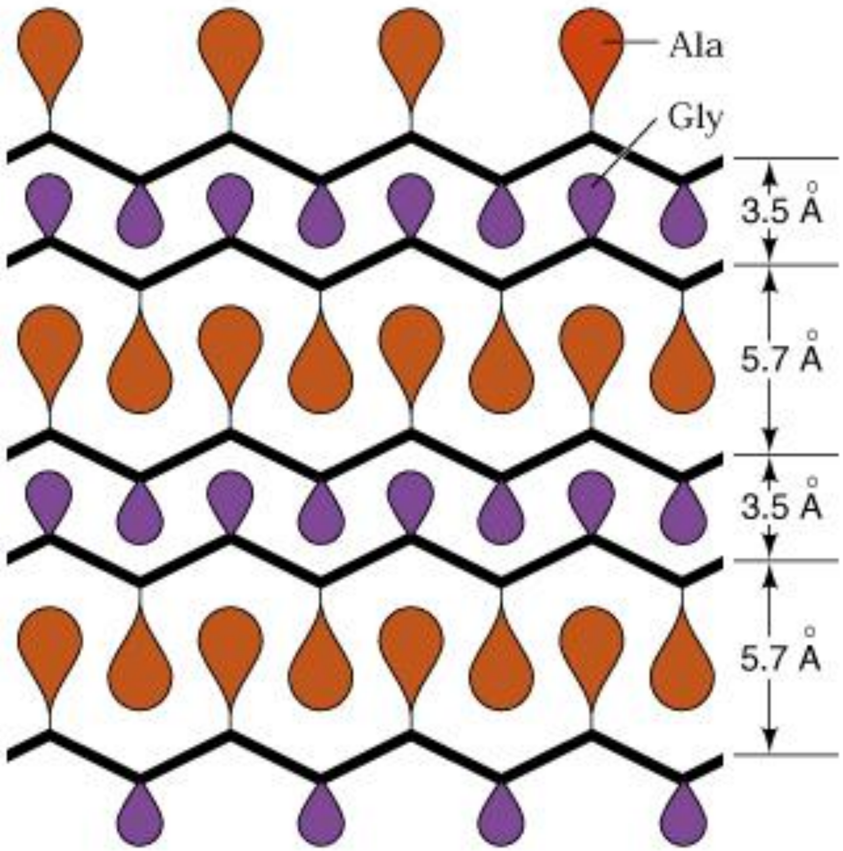
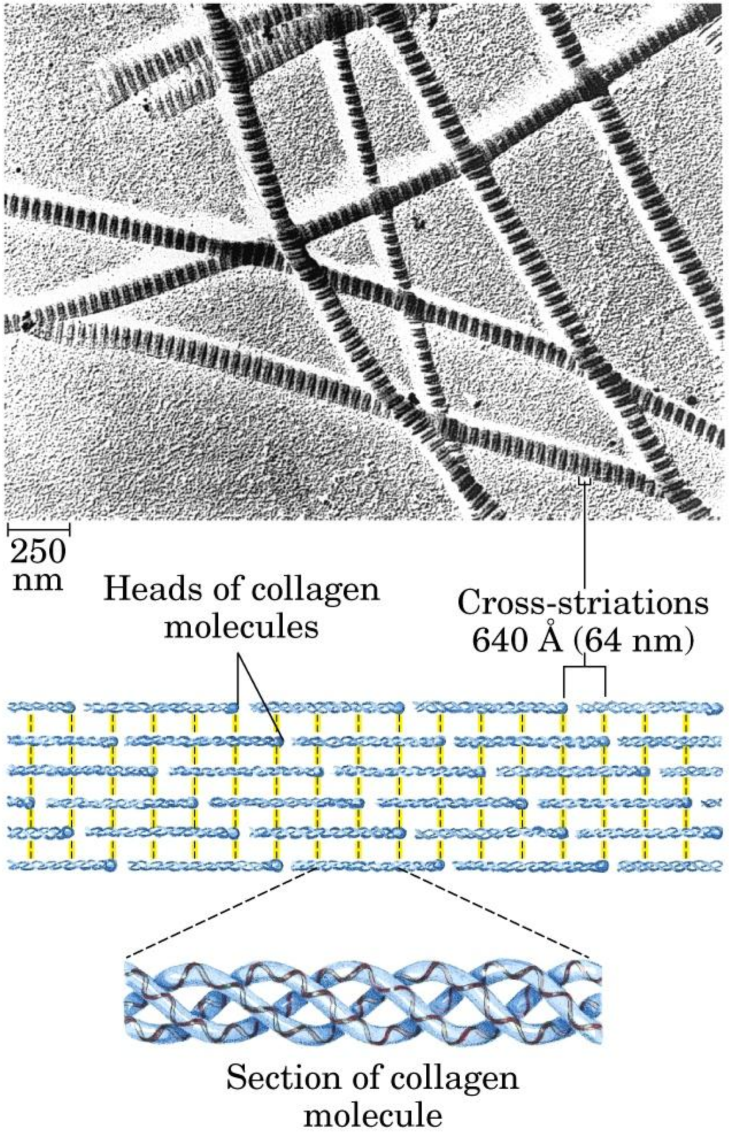


Figure 6-16. Schematic side view of silk fibroin ß sheets. [Figure copyrighted © by Irving Geis.]

Examples of secondary structure…



Examples of secondary structure

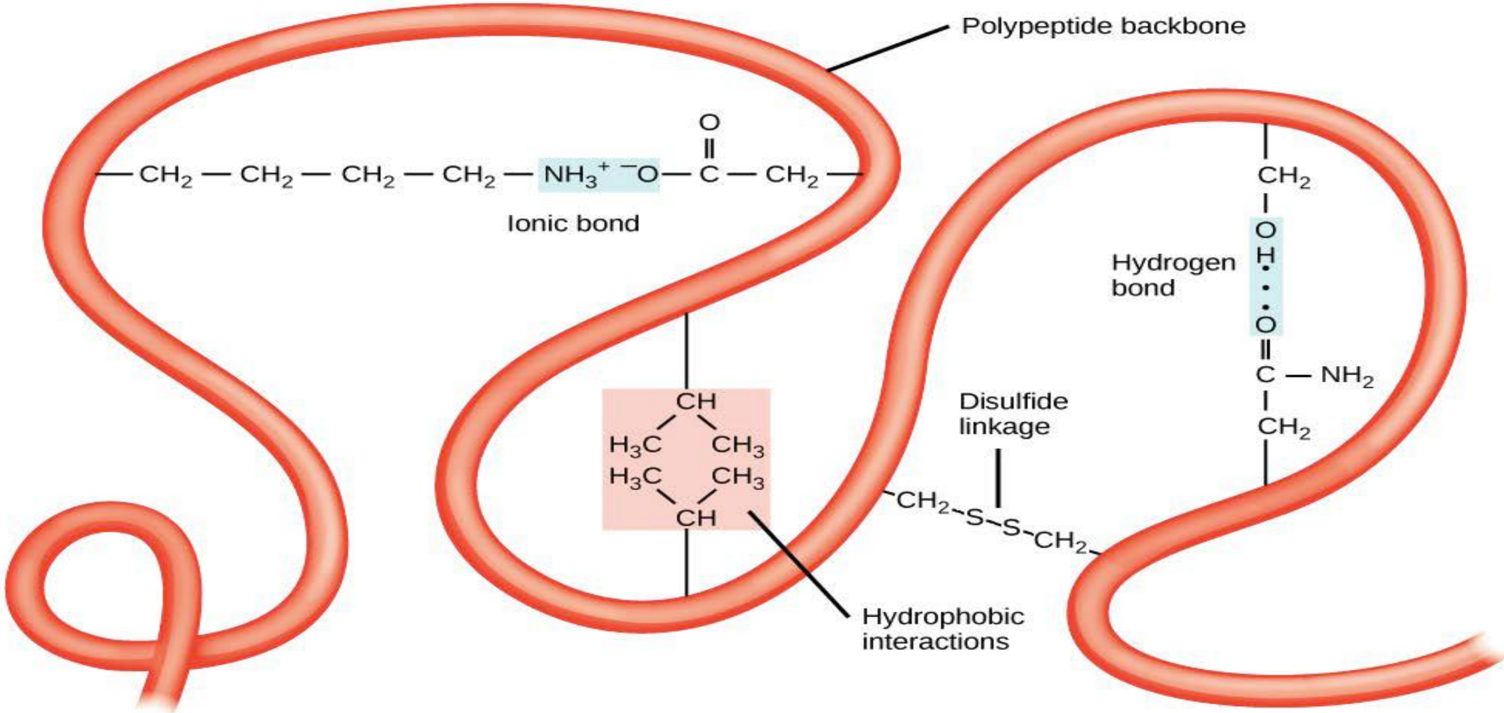
The collagen triple helix. Left-handed polypetide helices are twisted together to form a right-handed superhelical structure.

Tertiary structure

The overall three-dimensional structure of a polypeptide is called its **tertiary structure**. The tertiary structure is primarily due to interactions between the R groups of the amino acids that make up the protein.

Important to tertiary structure are **hydrophobic interactions**, in which amino acids with nonpolar, hydrophobic R groups cluster together on the inside of the protein, leaving hydrophilic amino acids on the outside to interact with surrounding water molecules.

Also, **Disulfide bonds**, covalent linkages between the sulfur-containing side chains of cysteines, are much stronger than the other types of bonds that contribute to tertiary structure

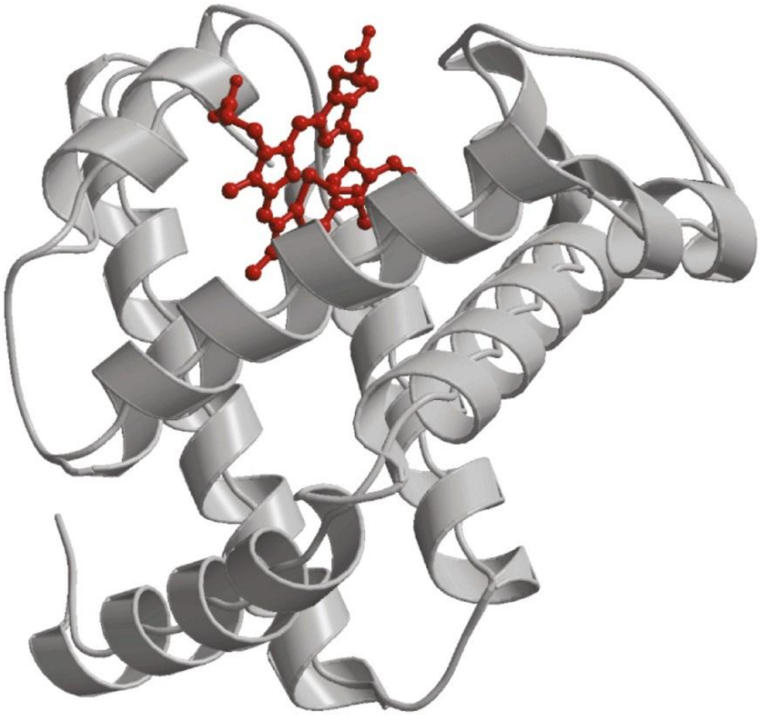


- Refers to the complete three dimensional structure of entire polypeptide. Usually involves the packing of structural elements (a-helix, b-pleated sheet, etc.)

Tertiary structure: globular proteins

- Structurally complex
- Usually dynamic
- Usually compact (tightly folded), roughly spherical
- Can be water-soluble
  - If so, characteristically have hydrophobic interior and hydrophilic surface
- Can be water-insoluble (e.g., bound to biological membrane)

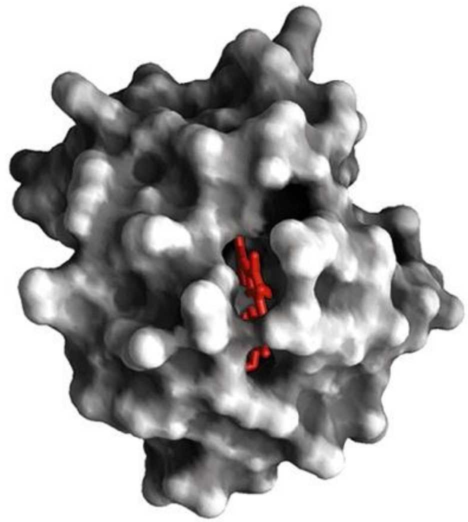
Examples of Tertiary structure…

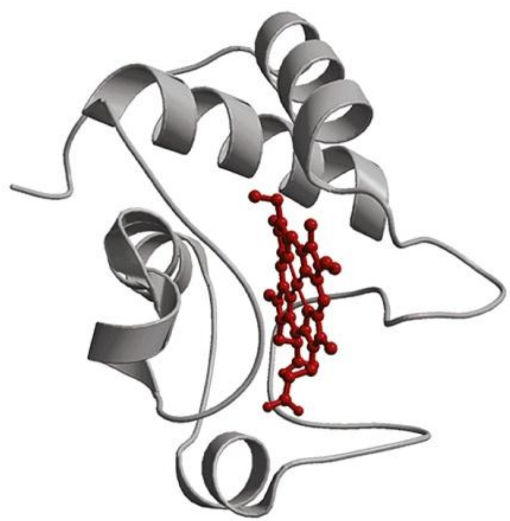


(a)

sperm whale myoglobin

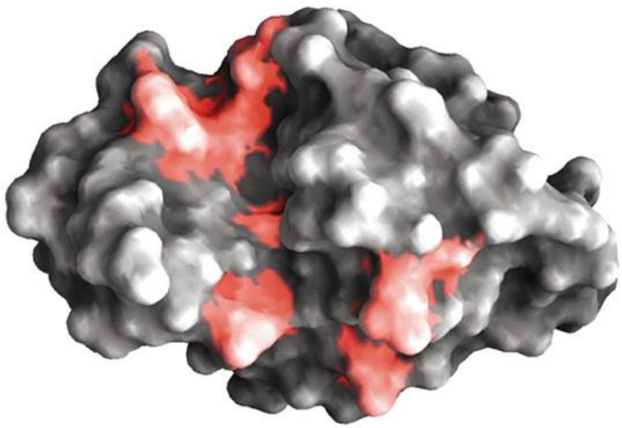
Examples of Tertiary structure…

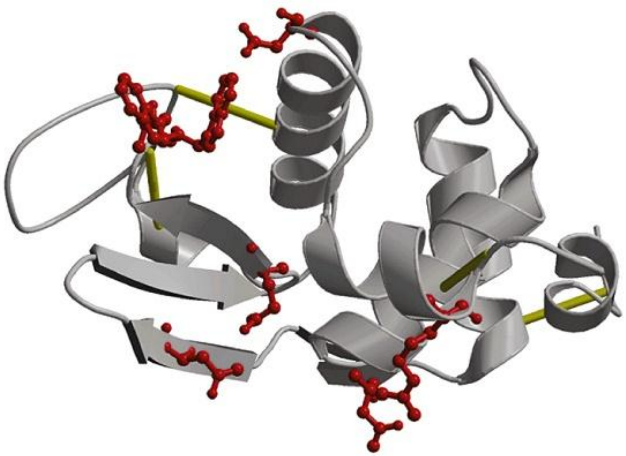




Cytochrome *c*

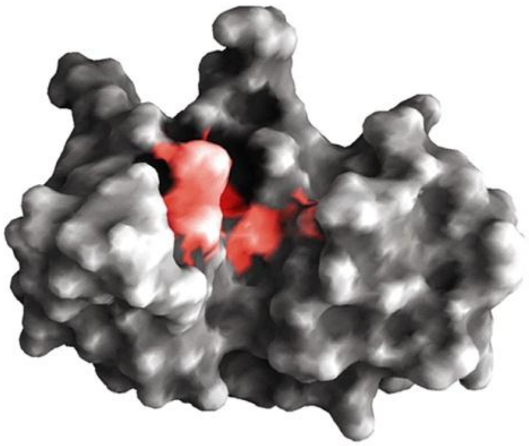
Examples of Tertiary structure…

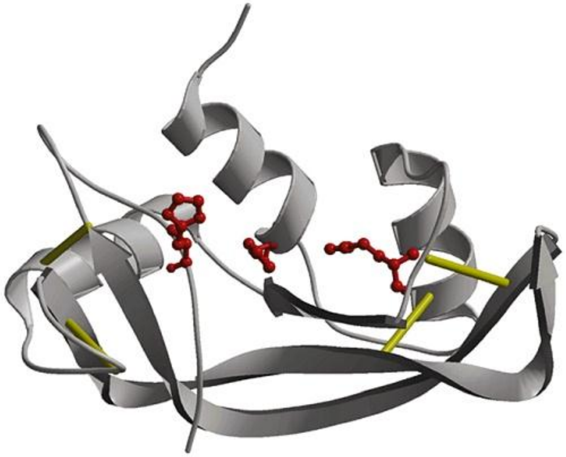




Lysozyme

Examples of Tertiary structure…





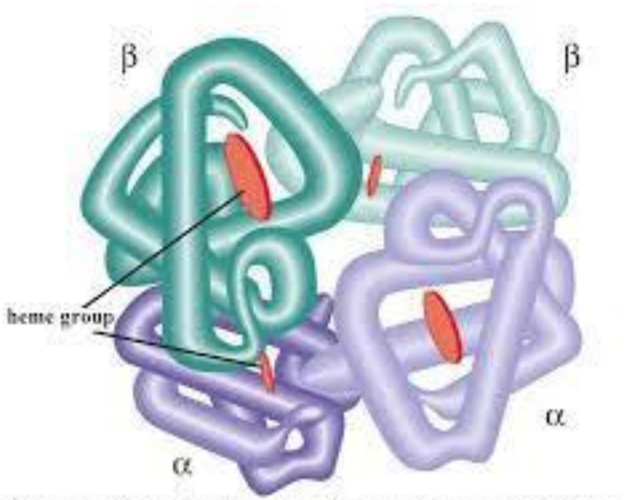
Ribonuclease

Quaternary structure

When multiple polypeptide chain subunits come together, then the protein attains its quaternary structure.

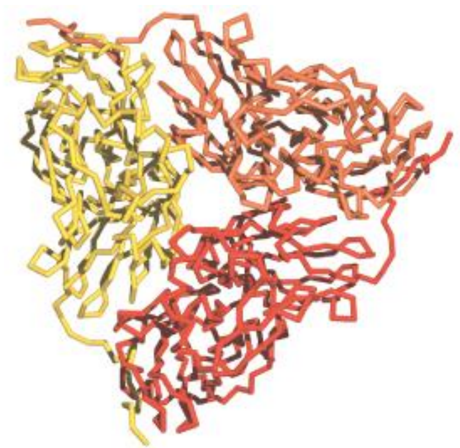
An example for quaternary structure is hemoglobin.

The hemoglobin carries oxygen in the blood and is made up of four subunits, two each of the α and β types.



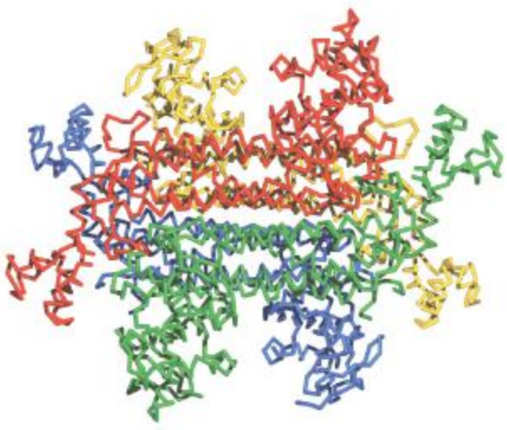
Quaternary Protein Sructue: Three-dimensional assembly of subunits

Quaternary structure of proteins



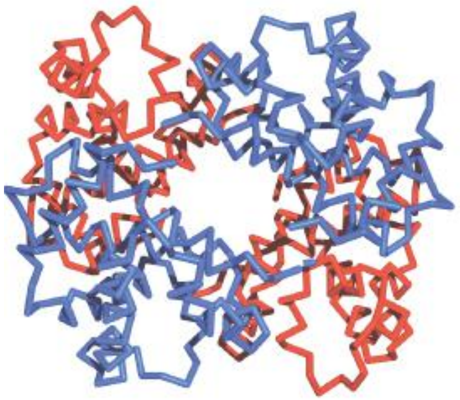
(a)

Nitritite reductase



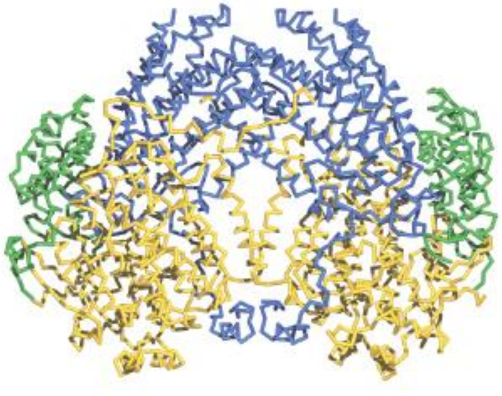
(b)

E. Coli fumarase



(c)

Human hemoglobin



(d)

Bacterial methane hydroxylase

Folding, unfolding and misfolding of protein

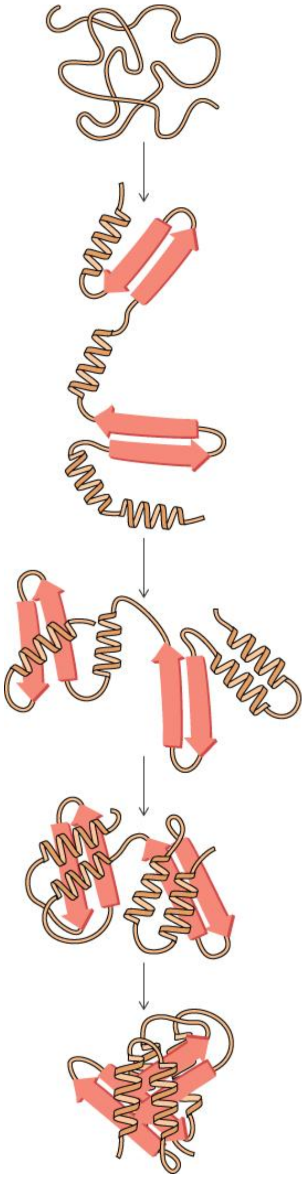
- A protein that is folded into its normal physiologically active chain conformation is in its **native state**.

- **Denaturation** occurs when a native protein unfolds owing to cleavage of disulfide bridges or disruption of the weak attractive forces. It may be **reversible** or **irreversible.**

- Protein can be denatured by heat, extremes of pH, certain organic solvents such as alcohol, acetone, certain solute like urea, or by exposure of the protein to detergents.

Denatured proteins are usually non-functional

Model of protein folding



Protein misfolding and diseases

- There are at least 15 human diseases in which amyloid fibers accumulate (as a result of misfolding of proteins).
- Amyloid diseases result in a variety of different clinical presentations, including Alzheimer’s disease.
- All the proteins involve in these diseases undergo conformational alteration to a common structure in the amyloid fibril.

Importance of structure:
one example of protein misfolding

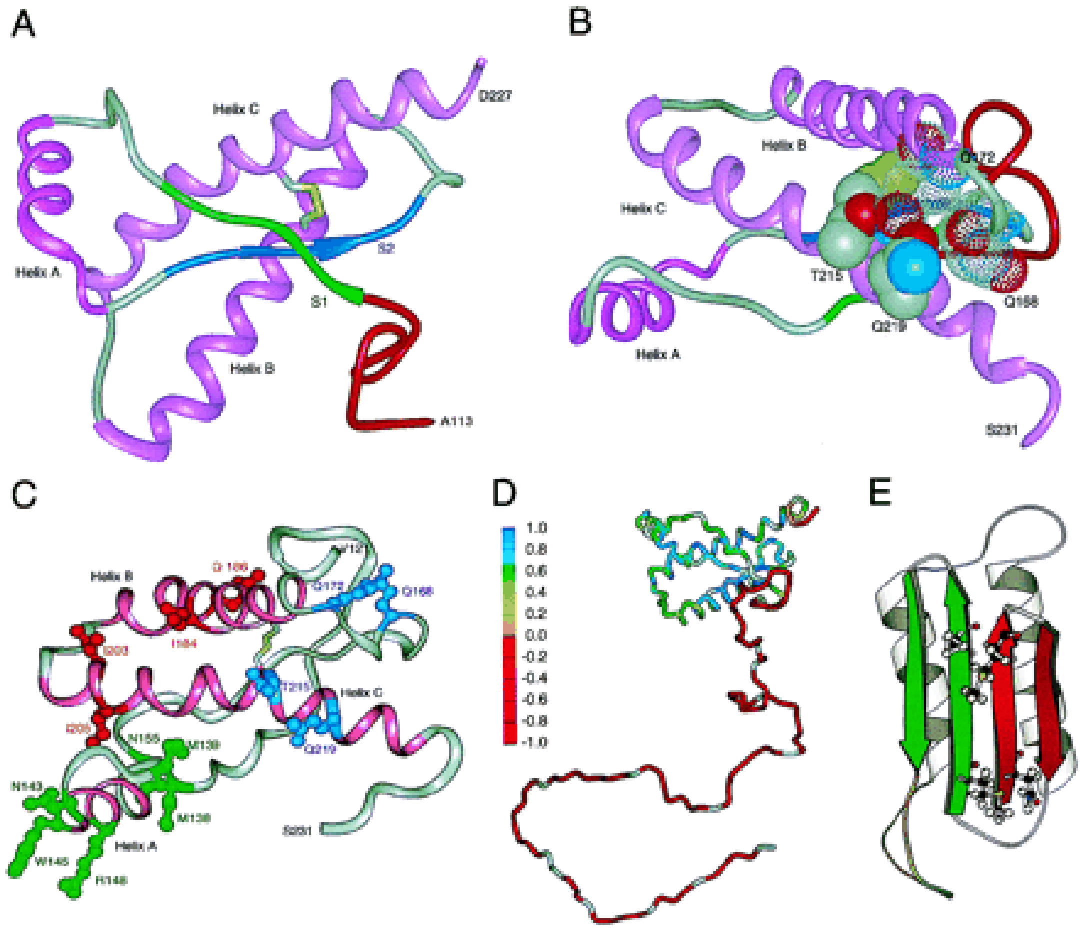
- Prion diseases
  - “misfolded” protein appears to be causative agent of many rare degenerative brain diseases in mammals

Prions…

- Stanley Prusiner was awarded the 1997 Nobel Prize in Physiology or Medicine for his work on “prions”

- Prion: name derived from *proteinaceous* and *in*fectious
  - current definition: proteinaceous infectious particle that lacks nucleic acid
- Prion diseases are invariably fatal neurodegenerative diseases, including bovine spongiform encephalopathy (BSE), scrapie of sheep, and Creutzfeldt-Jakob disease (CJD) of humans.
- البريونات هي السبب في اعتلالات الدماغ الاسفنجية المعدية مثل الاعتلال الدماغي الاسفنجي البقري وقعاص الغنم.تؤثر على بنية الدماغ او الانسجة العصبية وهي امراض قاتلة.

Structures of prion proteins



Taken from: Prusiner, 1998. *Proc Natl. Acad. Sci. USA* 95:13363-13383.

Prion diseases…

- May be present as genetic, infectious, or sporadic disorders

- All involved modification of the prion protein (PrP)

- Prions are transmissible particles, devoid of nucleic acid, and apparently composed exclusively of a modified protein.

Prion diseases

- The normal cellular PrP (PrP^C) is converted to modified protein through a posttranslational process during which it acquires a high b-sheet content.

- Normal soluble form thus converted to insoluble form.

Collagen Diseases

- Scurvy
- Brittle bone disease

Deficiency of Protein in Human

- Growth Failure
- Kwashiorkor سوء التغذية ونقص البروتين
- Marasmic Kwashiorkor
- Muscle wasting

Excess of Protein in Human

Stress in kidney

Excess of Protein in Human

Stress in kidney

References:

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