

Beyond Primary Structure of Proteins

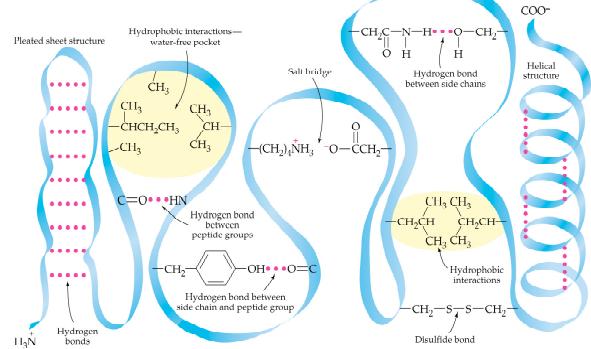
Secondary, Tertiary and Quaternary Structure

Shape determining interactions in Proteins

1. **Hydrogen Bonds**
2. **Ionic attractions between R groups** - the ionic attractions between the acidic and basic side chains – also known as the salt bridges.
3. **Hydrophobic Interactions between the R groups** – caused by dispersion forces caused by the momentary uneven distribution of electrons. The resulting groups cluster together like oil droplets giving it the name hydrophobic interaction.
4. **Covalent Sulfur-Sulfur bonds** – The amino acid Cysteine has side chain containing the – SH group that reacts to form the sulfur-sulfur bonds –S-S- called the disulfide bond.

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Secondary Protein Structure

Secondary Protein Structure is caused by a repeating pattern hydrogen bonds between atoms that are part of the backbone of the protein.

There are two types of secondary structure –

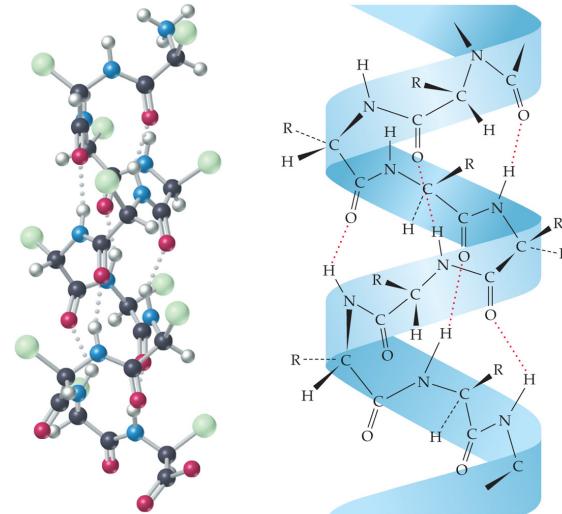
- α Helix
- β Sheet

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α Helix:

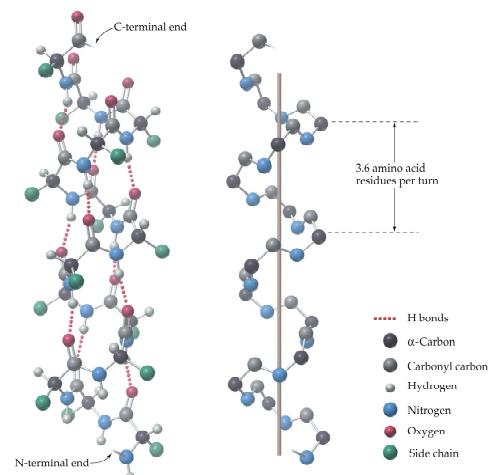
- A single chain of coiled in a spiral right handed twist is known as the α Helix .
- This resembles a telephone cord.
- It is stabilized by hydrogen bonds that lie along the length of the chain.
- The R groups extend out of the chains.



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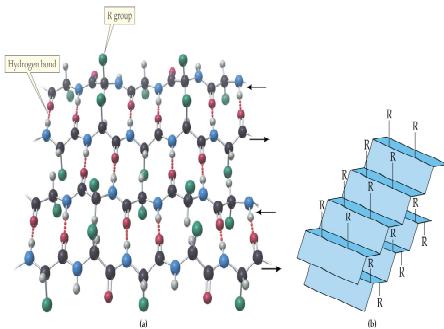
β Sheet:

- The polypeptide chains are held in place by hydrogen bonds between pairs of polypeptide units.
- The protein backbone bends at the α carbons giving the β sheets has a planer corrugated structure.
- The R groups extend above and below the sheet.

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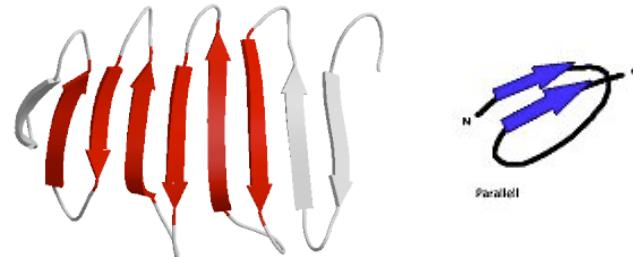
- The protein chains usually lie side by side so that alternating chains run from the N-terminal end to the C-terminal end and from the C-terminal end to the N-terminal end (known as the anti parallel arrangement).



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- (b) A pair of stacked pleated sheets illustrates how the R groups point above and below the sheets.

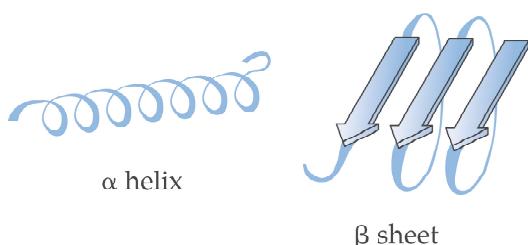
β sheets



Parallel

Antiparallel

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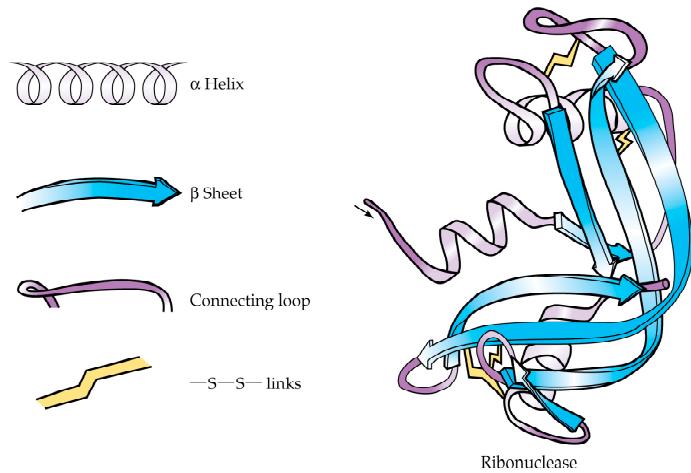
These are the 2 types of secondary structure.

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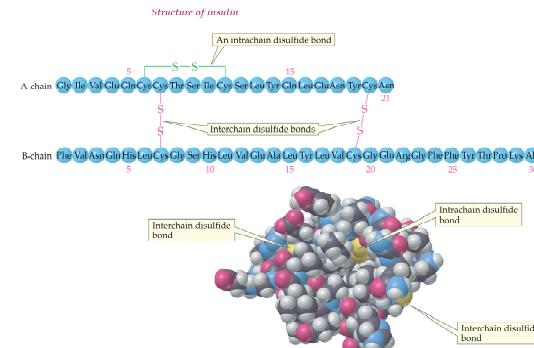
Tertiary Protein structure

- The overall shape that results from folding of the protein is called the tertiary structure of the protein.
- The tertiary structure includes the unique arrangement of secondary structures that are found in proteins.
- Tertiary structure generally depends on hydrophobic interactions, salt bridges, and disulfide bonds.

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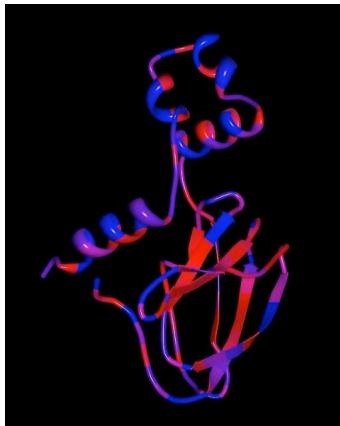


The structure of the peptide hormone insulin is strongly influenced by two disulfide bonds that connect two separate polypeptide chains.

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Tertiary Structure-Hydrophobicity

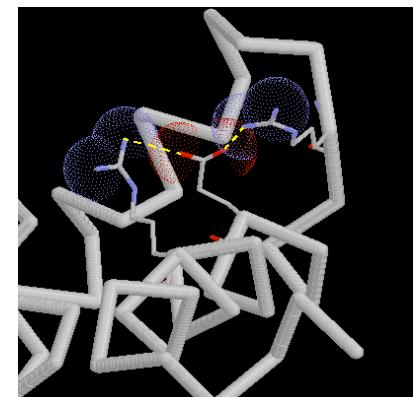
- A model of VHL protein with backbone recolored by hydrophobicity (red = most, blue = least hydrophobic). Data from Min, JH, Yang, H, Ivan, M, Gertler, F, Kaelin Jr, WG, Pavletich, NP. Structure of an HIF-1alpha-pVHL complex: hydroxyproline recognition in signaling. *Science*. 296, 5574, 1886-1889. 2002 (wiki commons)



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Tertiary Structure-Salt Bridge or Ionic interaction

- Positively charged side group is attracted to a negatively charged side group.
- This ionic interaction (like that in an ionic bond) holds different regions of the protein near each other.
- It is not clear how important these are in determining protein structure.



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Quaternary Protein Structure

When two or more polypeptide units associate to form a single three dimensional protein the combined structure is called a quaternary protein structure. The molecules are held together by noncovalent and, less frequently, covalent bonds.

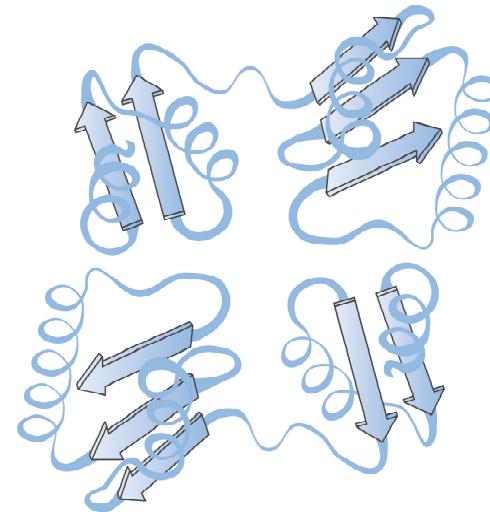
Hemoglobin and collagen are such examples of proteins with quaternary structure, as are .

Egg white is composed of a globular protein while spider web is composed of a fibrous protein.



Fibrous and Globular Proteins

- **Fibrous proteins** are tough, insoluble proteins in which chains form fibers.
 - Wool, hair, and fingernails are examples of fibrous proteins known as α keratin . α Keratins is made of mainly α helix. The hardness and flexibility comes from the presence of disulfide bonds and increases with its number.
 - Natural silk is made of fibroin, a fibrous protein composed entirely of β sheets.
 - Collagen is a fibrous protein that is composed of helices wrapped around each other.
- **Globular Proteins** are water soluble proteins whose chains are folded into compact globe like structures. Their structures are not regular. They contain sections of α helix and β sheets. They contain hydrophilic side chains that gives them water solubility allowing them to travel through the blood stream.
 - Hemoglobin is an example of a globular protein
- **Membrane Proteins** proteins that exit in the membranes of cells. The pass information across the cell membrane and transfer materials from one side of the membrane to the other.

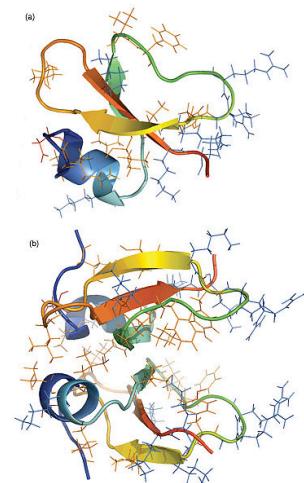


- <http://upload.wikimedia.org/wikipedia/commons/0/07/Hb-animation2.gif>
- http://upload.wikimedia.org/wikipedia/commons/b/ba/Hemoglobin_t-r_state_ani.gif

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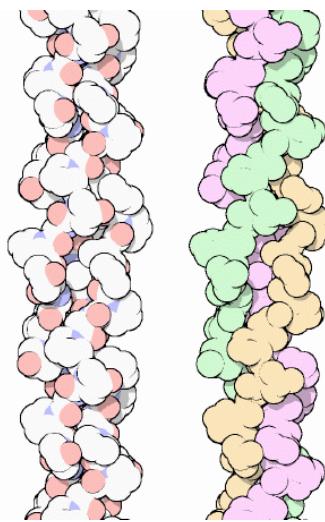
Quaternary Structure- Hydrophobic Interactions

Monomeric and dimeric representations of HBD-2. shown as cartoons in rainbow colouring from N- to C-terminal, with line representations of cationic residues in blue, hydrophobic residues in orange, and anionic residues in red. (wiki commons)
Hydrophobic interactions often have a role in determining the quaternary structure of proteins.



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- Collagen is a protein with very important quaternary structure. (Its quaternary structure is at the core of its usefulness.)
- Collagen
- Gives shape to noses and ears
- Support Tendons and skin.
- Provides the protein structure that underlies the our teeth and bones.
- ¼ of all of the protein in a body is collagen.
- Chains of about 1400 amino acid residues, that fit together and connect by hydrogen bonds.
- Contain one altered protein that nee
- http://www.pdb.org/pdb/static.do?p=education_discussion/molecule_of_the_month/pdb4_1.html



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Conjugate Proteins

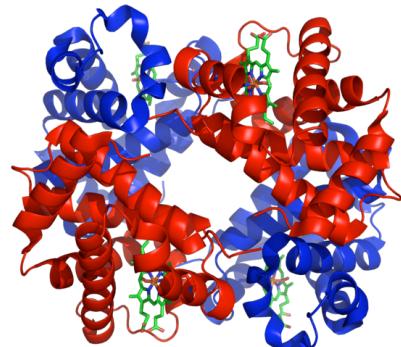
Proteins can be simple or conjugate.

The simple proteins contain only amino acid residues for example ribonuclease.

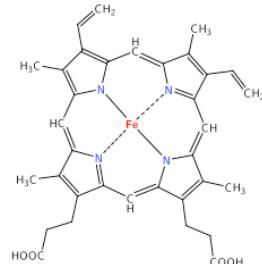
Conjugate proteins contain other non amino acid non protein group for example myoglobin and that has a heme group attached to its polypeptide chain.

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Hemoglobin is a conjugate protein.



Hemoglobin Protein + Hemes



Heme

Conjugated Proteins

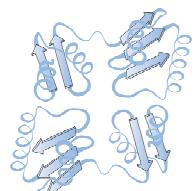
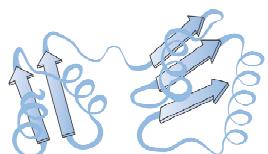
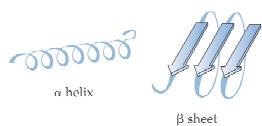
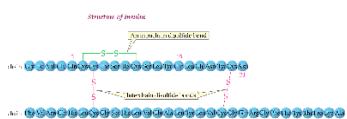
TABLE 18.5 Some Examples of Conjugated Proteins

CLASS OF PROTEIN	NONPROTEIN PART	EXAMPLES
Glycoproteins	Carbohydrates	Glycoproteins in cell membranes (Section 24.7)
Lipoproteins	Lipids	High- and low-density lipoproteins that transport cholesterol and other lipids through the body (Section 25.2)
Metalloproteins	Metal ions	The enzyme cytochrome oxidase, necessary for biological energy production, and many other enzymes
Phosphoproteins	Phosphate groups	Milk casein, which provides essential nutrients to infants
Hemoproteins	Heme	Hemoglobin (transports oxygen) and myoglobin (stores oxygen)
Nucleoproteins	RNA (ribonucleic acid)	Found in cell ribosomes, where they take part in protein synthesis

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Primary, Secondary, Tertiary, and Quaternary Structure of Proteins



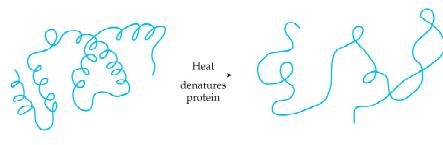
Protein Denaturation

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Denaturation

- **Denaturation:** When the structure of the proteins is broken down, to the point that the protein can no longer perform its function. The protein unfolds, and loses its natural form.



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Protein Denaturation

- Heat



- Acids or Bases



- Detergents
- Hydrophobic Surfaces
- High Salt Concentrations



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Breaking Apart the Protein Chains

Hydrolysis:

Protein hydrolysis is the reverse of peptide bond formation and the peptides are broken down to amino acids. Digestion is an example of protein hydrolysis.

In the laboratory the protein can be hydrolyzed by heating with hydrochloric acid or NaOH.

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A Protein Denaturation Disease

Mad Cow Disease (Creutzfeldt-Jakob disease)

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Mad Cow Disease

- A disease that is transmitted from cattle to humans.
- It quickly causes the brain to degenerate.
- It creates open spaces in the brain giving it a sponge-like appearance.
- It was not possible to find a usual pathogen for this disease.
- It appears that it is transmitted by a single protein.

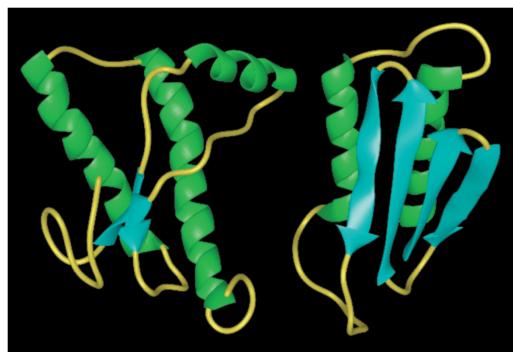
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A Disease Passed on by a Denatured Protein

- Prions (Pree-ons) Proteinious Infectious Particles
- Normal Prion Protein is Found in the Brain. – an abnormally folded version of this protein is found in infected meat.
- Consumption of the abnormal protein leads to large amounts of the abnormal protein in the brain.
- The abnormal protein makes its way to the brain.
- In the brain, the misfolded protein causes the normal proteins to misfold, so that they match the misfolded proteins.

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Theorized Structure of Normal and Abnormal Prion Protein Folds



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Protein Plaques

- The change from helices to sheets, allows the prion proteins to stack, and form a solid within brain cells.
- This is not that different from the current model of Alzheimer's Disease.

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Coping with Mad Cow Disease

- Don't eat meat that comes from the brains of cattle or sheep.
- Sterilize by heating contaminated objects in a sodium hydroxide solution.
- What does the NaOH do that heating alone will not?

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Chapter 18 Topic Summary

- Introduction to Proteins
- Amino Acids
- Primary, Secondary, Tertiary, and Quaternary Structure of Amino Acids
- Protein Denaturation

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