Proteins

Proteins are naturally occurring peptides with 40 or more amino acid residues.

The function and the shape of a protein is described by their structure

4 levels of protein structure:
- Primary
- Secondary
- Tertiary
- Quaternary

• Primary Protein Structure
  - The linear sequence of amino acids in a protein chain.
  - Determines secondary and tertiary structures.

Primary structure of human insulin

• Secondary Protein Structure
  - Regularly repeating pattern of folding along the primary structure.
  - Determined by hydrogen bonding between amide groups of amino acid residues in the chain.

\[ \text{H-C = O} \quad \text{H-N} \]

- Three basic types of secondary structure:
  - Random - portions of all protein strands w/ secondary structure
  - \( \alpha \)-helix – keratin, myosin, epidermin, fibrin.
  - \( \beta \)-pleated sheets – found extensively only in silk protein.

\( \alpha \)-helix

- Right handed spiral corkscrew.
- Formed from H-bonding
- Gives rise to fibrous proteins

The primary structure of human myoglobin; an oxygen storage protein in muscles
Four representations of the $\alpha$ helix protein structure. (a) Arrangement of protein backbone. (b) Backbone arrangement with hydrogen-bonding shown. (c) Backbone atomic detail shown. (d) Top view of an $\alpha$-helix showing that amino acid side chains (R groups) point away from the long axis of the helix.

$\beta$-pleated Sheet

- Zig-zag sheet of parallel chains
- Formed by H-bonding
- Chain run in opposite directions
- Also gives rise to fibrous proteins

Two representations of the $\beta$ pleated sheet protein structure. (a) A representation emphasizing the hydrogen bonds between protein chains. (b) A representation emphasizing the pleats and the location of the R groups.

The secondary structure of a single protein often shows areas of a helix and $\beta$ pleated sheet configurations, as well as areas of random coiling.

Proteins having only primary and secondary structure are considered Fibrous proteins, or long rod-shaped or string like molecules that intertwine to form fibers

Common Fibrous Proteins

$\alpha$-helix
- Keratins (elastic; found in hair, nails and skin)
- Myosin (muscle)
- Epidermin (skin)
- Fibrin (blood clots)

$\beta$-pleated Sheet
- $\beta$-keratins (strong thin fibers in silk and webs)

Common Fibrous Proteins Con’t

Collagen Helix

Variation on the $\alpha$-helix

A tri-left handed coiled helix that is very ridged and strong.

Most abundant protein in vertebrates (cartilage, bone and tendons)
Tertiary Protein Structure

- The specific 3-D shape of a protein resulting from interactions between “R” groups of amino acid residues.

“R” group interactions include:
1. Disulfide bridges – between cystiene residues.
2. Salt bridges – ionic bonds between acidic and basic residues.
3. Hydrogen bonds – between polar residues

Affect of intermolecular forces

Human insulin, a small two-chain protein, has both intrachain and interchain disulfide linkages as part of its tertiary structure.

Globular proteins—spherical shaped proteins that form stable suspensions in water, or are water soluble (hemoglobin, enzymes).

Myoglobin contains a Heme prosthetic group. The heme group consists of an Fe$^{2+}$ interlocked within a nitrogen ring structure. The Fe$^{2+}$ ion in the protein easily oxidizes to FeO, acting as an oxygen storage protein in muscle cells.

An example of a common protein having a globular tertiary structure is Myoglobin

Myoglobin is a conjugated protein rather than a simple protein.
- Simple proteins – contain only amino acid residues.
- Conjugated proteins – contain amino acid residues and other organic or inorganic components (prosthetic groups).
Types of Other Conjugated Proteins

<table>
<thead>
<tr>
<th>Class</th>
<th>Prosthetic group</th>
<th>Specific example</th>
<th>Function of example</th>
</tr>
</thead>
<tbody>
<tr>
<td>hemoproteins</td>
<td>iron acid</td>
<td>hemoglobin</td>
<td>carton of O2 in blood</td>
</tr>
<tr>
<td>lipoproteins</td>
<td>lipid</td>
<td>lipoprotein</td>
<td>oxygen transfer in muscles</td>
</tr>
<tr>
<td>glycoproteins</td>
<td>carbohydrate</td>
<td>glycoprotein</td>
<td>antibody</td>
</tr>
<tr>
<td>phosphoproteins</td>
<td>phosphor group</td>
<td>phosphoprotein</td>
<td>enzyme</td>
</tr>
<tr>
<td>nucleoproteins</td>
<td>nucleic acid</td>
<td>nucleoprotein</td>
<td>enzyme complex</td>
</tr>
<tr>
<td>metalloproteins</td>
<td>metal</td>
<td>metalloprotein</td>
<td>storage complex for iron</td>
</tr>
</tbody>
</table>

Quaternary Protein Structure

- The arrangement of multi protein subunits held together by intermolecular forces that form a larger protein resulting in a stable 3-D structure.
- Subunits are polypeptides that have primary, secondary, and tertiary structure.
- Hemoglobin is a well-known example.

Quaternary Structure of Hemoglobin

Hemoglobin consists of 2 α subunits that are identical and β subunits that are also identical, each containing a heme group.

- Arterial, or oxygenated, hemoglobin is called oxyhemoglobin (red)
- Venous, or unoxygenated, hemoglobin is called deoxyhemoglobin (purple/blue)
- Methemoglobin is formed when the Fe (II) is oxidized into Fe(III) which is brown (dried blood)

Inhalation of some substances act as poisons due to their absorption by the lung tissues and reactivity with the heme group of hemoglobin on red blood cells.

CO and CN− are two substances that can react with the heme group rendering it useless.

This results in oxygen starvation and eventually death.

Protein Size

<table>
<thead>
<tr>
<th>Protein</th>
<th>Molecular weight (kDa)</th>
<th>Number of amino acid residues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>6,000</td>
<td>51</td>
</tr>
<tr>
<td>Cytosochrome c</td>
<td>16,000</td>
<td>104</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>49,000</td>
<td>191</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>65,000</td>
<td>574</td>
</tr>
<tr>
<td>Hesokinase</td>
<td>96,000</td>
<td>730</td>
</tr>
<tr>
<td>Gamma globulin</td>
<td>176,000</td>
<td>1120</td>
</tr>
<tr>
<td>Myosin</td>
<td>800,000</td>
<td>6100</td>
</tr>
</tbody>
</table>

© 2000 Thomsen - Molecular Cell Science
Protein Hydrolysis
– Heat and acid or base can completely hydrolyze proteins.

\[
\text{protein} + \text{H}_2\text{O} \rightarrow \text{smaller peptides} \rightarrow \text{amino acids}
\]

– This is an important process in protein digestion.

Protein Denaturation
= Disruption of the intermolecular forces within a protein leading to the loss of the proteins native state (normal, biologically active structure of a protein)
– The process by which a protein loses its characteristic quaternary, tertiary, and secondary structure.
– Leads to a loss of biological activity (function).

Causes of Protein Denaturation:
1. Heat and UV light
   Disrupts intermolecular forces by adding kinetic energy
2. Change in pH
   Disrupts h-bonds and salt interactions. Could lead to complete hydrolysis.
3. Addition of inorganic salts (detergents)
   Disrupts the h-bonds, hydrophobic interactions and ionic attractions
4. Presence of organic solvents
   Disrupts H-bonds in proteins a probably forms new ones with proteins

Selected Physical and Chemical Denaturing Agents.

<table>
<thead>
<tr>
<th>Denaturing agent</th>
<th>Mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>heat</td>
<td>disrupts hydrogen bonds by making molecules vibrate no colder produces coagulation; as in the boiling of an egg</td>
</tr>
<tr>
<td>microwave radiation</td>
<td>causes violent vibrations of molecules that disrupt hydrogen bonds</td>
</tr>
<tr>
<td>ultraviolet radiation</td>
<td>operates very similarly to the action of heat (e.g., sunburning)</td>
</tr>
<tr>
<td>violent whipping or shaking</td>
<td>causes molecules to globular shapes to extend to longer lengths, which then rearrange (e.g., beating egg white into meringue)</td>
</tr>
<tr>
<td>detergent</td>
<td>affects hydrogen bonds and salt linkages</td>
</tr>
<tr>
<td>organic solvents (e.g., ethanol, 2-propanol, acetone)</td>
<td>interfere with hydrogen bonds, because these solvents also can form hydrogen bonds; quickly denatures proteins in bacteria, killing them (e.g., the disinfectant action of 70% ethanol)</td>
</tr>
<tr>
<td>strong acids and bases</td>
<td>disrupt hydrogen bonds and salt bridges; prolonged action leads to actual hydrolysis of peptide bonds</td>
</tr>
<tr>
<td>salts of heavy metals (e.g., salts of \text{Hg}^{2+}, \text{Ag}^{+}, \text{Pb}^{2+})</td>
<td>metal ions combine with —SH groups and form covalent salts</td>
</tr>
<tr>
<td>reducing agents</td>
<td>oxidize disulfide linkages to produce —SH groups</td>
</tr>
</tbody>
</table>