Structure of Proteins

3D structure determined by amino acid sequence
Structure - Function
Native structure of a protein = functionally, folded conformation

Protein conformation stabilized by
1.
2.

Chymotrypin
Glycine
Structure of Proteins

3D structure determined by amino acid sequence

Structure - Function
Native structure of a protein = functionally, folded conformation

Protein conformation stabilized by
1. disulfide bonds
2. weak noncovalent interactions (H-bonds, hydrophobic & ionic)

Chymotrypin

Glycine
3D Structure of Proteins

Primary structure =
Peptide bond is rigid and planar

The carbonyl oxygen has a partial negative charge and the amide nitrogen a partial positive charge, setting up a small electric dipole. Virtually all peptide bonds in proteins occur in this trans configuration; an exception is noted in Figure 4–8b.
3D Structure of Proteins

Primary structure = amino acids linked together
Peptide bond is rigid and planar

The carbonyl oxygen has a partial negative charge and the amide nitrogen a partial positive charge, setting up a small electric dipole. Virtually all peptide bonds in proteins occur in this trans configuration; an exception is noted in Figure 4–8b.
Secondary Structure of Proteins

Important elements -

Basic types of secondary structure: Helices, Sheets, Turns and Coils

$\alpha$ Helices
Secondary Structure of Proteins

Important elements - steric clashes & H-bonding

Basic types of secondary structure: Helices, Sheets, Turns and Coils

α Helices
Secondary Structure of Proteins

α Helices
Ionic interaction between R groups of AAs three residues apart

Arg →

Asp
Secondary Structure of Proteins

β sheets
Backbone is extended into a zigzag structure
Arranged side-by-side to form a structure (pleats)
Important Forces =

(a) Antiparallel

Top view

Side view

Layering of ≥2 sheets
R groups must be small (Gly, Ala)

(b) Parallel

Top view

Side view
Secondary Structure of Proteins

\(\beta\) sheets
Backbone is extended into a zigzag structure
Arranged side-by-side to form a structure (pleats)
Important Forces = H-bonds and steric clash

(a) Antiparallel

Top view

Side view
Layering of \(\geq 2\) sheets
R groups must be small (Gly, Ala)

(b) Parallel

Top view

Side view
Secondary Structure of Proteins

**β turns**
Occur frequently in globular proteins, 180° turn involving 4 Aas
Used to:
1. Reverse direction of polypeptide chain
2. Connect α helices/β sheets and within β sheets

Important forces:

Amino acids used:
Gly - because it is small and flexible
Pro - because of cis conformation of peptide bond forms a tight turn

Proline isomers

(a) β Turns
**Tertiary Structure**

Overall 3D arrangement of all atoms in a protein
Long range contacts between AAs in a single polypeptide chain
Quaternary Structure

Long range contacts between AAs in a different polypeptide chain
Fibrous Proteins

Mainly structural role

**TABLE 4-1** Secondary Structures and Properties of Fibrous Proteins

<table>
<thead>
<tr>
<th>Structure</th>
<th>Characteristics</th>
<th>Examples of occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>α Helix, cross-linked by disulfide bonds</td>
<td>Tough, insoluble protective structures of varying hardness and flexibility</td>
<td>α-Keratin of hair, feathers, and nails</td>
</tr>
<tr>
<td>β Conformation</td>
<td>Soft, flexible filaments</td>
<td>Silk fibroin</td>
</tr>
<tr>
<td>Collagen triple helix</td>
<td>High tensile strength, without stretch</td>
<td>Collagen of tendons, bone matrix</td>
</tr>
</tbody>
</table>
**Fibrous Proteins**

**α-Keratins**
Found in: mammals, provide strength
Hair, wool, nails, claws, quills, horns, hooves, skin

\[\text{Keratin } \alpha\text{ helix} \]

Two-chain coiled coil

\[\text{Protofilament} \quad 20-30 \text{ Å}\]

Protofibril

Strengthened by: Disulfide bonds

Cross section of a hair
Fibrous Proteins

α-Keratins
Permanent waving of hair
1. Reduce disulfide bonds
2. Moist heat breaks H-bonds and causes uncoiling of α helix
3. Remove reducing agent, add oxidizing agent, new S-S bonds
Fibrous Proteins

Collagen
α helices, left-handed helix with 3 amino acids per turn

35% Gly, 11% Ala, 21% Pro/4-Hyp
(Gly-X-Y) repeat with X as Pro and Y as 4-Hyp
Coiled-coil, three separate polypeptides called α chains are supertwisted

Provide strength (stronger than ??)
Connective tissue (tendons, cartilage, organic matrix of bone, cornea)
Fibrous Proteins

Collagen

Rigid and brittle bones caused by:
Crosslinks in collagen fibrils over time

Gly-X-Y repeat important - single change results in disease

Osteogenesis imperfecta - abnormal bone formation in babies
Ehlers-Danlos syndrome - loose joints

Both diseases involve: mutation of Gly to a different amino acid
Fibrous Proteins

Silk
Fibrous protein of silk = Fibroin
Secondary structure present: β sheets
Forces involved: H-bonds between different sheets

Made by: insects and spiders
Silk does not stretch because it is already highly extended
Fibrous vs. Globular Proteins

\[ \beta \text{ Conformation} \]
\[ 2,000 \times 5 \text{ Å} \]

\[ \alpha \text{ Helix} \]
\[ 900 \times 11 \text{ Å} \]

Native globular form
\[ 100 \times 60 \text{ Å} \]
Globular Proteins

\(\alpha\) helices and \(\beta\) sheets and \(\beta\) turns and \ldots\ldots
doncovalent interactions

Arrangement of different secondary structural elements:
Compact conformation
Folding provides structural diversity

Globular proteins = enzymes, transport proteins, motor proteins, regulatory proteins, immunoglobulins, etc.

First understanding of globular proteins came from:
x-ray structure of myoglobin (oxygen-binding protein in muscle)

![Single polypeptide chain](attachment:image.png)
Globular Proteins

Other important forces in globular proteins:

_________________ aa
Globular Proteins

Other important forces in globular proteins:
Hydrophobic interactions

(d)
Globular Proteins

Well-studied example: Myoglobin
Flat heme group rests in crevice of protein
Globular Proteins

Variety of Tertiary Structures

Cytochrome c
- Respiratory chain in mitochondria
- Heme

Lysozyme
- Egg white and human tears
- Cleaves polysaccharides
- Disulfide bond

Ribonuclease
- Enzyme secreted by pancreas
- Hydrolyzes RNA
- Disulfide bond
Protein Denaturation & Folding
AA sequence determines tertiary structure

Importance of native structure
Loss of structure = loss of function

Native state; catalytically active.

Unfolded state; inactive. Disulfide cross-links reduced to yield Cys residues.

Native, catalytically active state. Disulfide cross-links correctly re-formed.
Protein Denaturation & Folding
Rapid stepwise folding
Protein Denaturation & Folding

Defects in folding may lead to disease

AA mutation in CFTR - cystic fibrosis

**BUT** No AA mutation (except in inherited forms) just misfolding in (PrP) Prion Protein
Protein Denaturation & Folding

Proteins undergo assisted folding
“molecular chaperones” assist in folding

1. DnaJ binds to the unfolded or partially folded protein and then to DnaK.
2. DnaJ stimulates ATP hydrolysis by DnaK. DnaK–ADP binds tightly to the unfolded protein.
3. In bacteria, the nucleotide-exchange factor GrpE stimulates release of ADP.
4. ATP binds to DnaK and the protein dissociates.

To GroEL system
What type of protein has an extended shape?

A. Fibrous

B. Globular

C. Tertiary

D. Chaperone