Proteins

- Proteins are polymers
- Amino acids linked into a peptide chain

- Formation of a peptide bond (dehydration synthesis)

metastable bonds

- How to brake a peptide bond?
  Amide hydrolysis - adding water
Bottom-Up picture of Protein Structure

(a) Primary structure
- Ala - Glu - Val - Thr - Asp - Pro - Gly -

(b) Secondary structure
\[ \alpha \text{ helix} \]
\[ \beta \text{ sheet} \]

(c) Tertiary structure

(d) Quaternary structure

Domain
Helices and Sheets

β-Sheet

α-Helix
### One Classification of Proteins

1. **Fibrous Proteins**
   - mostly structural proteins
   - an elongated, unidimensional structure
   - Ex: keratin, collagen,

2. **Membrane Proteins**
   - reside within the cellular & intracellular membrane
   - transport molecules in and out of the cell
   - Ex: rhodopsin, G proteins,

3. **Globular Proteins**
   - short chains packed into a compact 25-40Å globule
   - closely folded structure
   - water soluble proteins
   - Ex: egg albumin, hemoglobin, many enzymes

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<th>PROTEINS</th>
<th>SEQUENCES</th>
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### Protein Structure Models

- **Structure Models**
  - **Globular Proteins**: Quasi-random sequences
    - Short chains packed into a compact globule
  - **Membrane Proteins**: Blocks
    - Hydrophilic and hydrophobic regions
  - **Fibrous Proteins**: Repeats
    - Repeated units in sequence
Structural Classes of Globular Proteins/Domains

1. “pure”-α - a core built exclusively from alpha-helices
2. “pure”-β - a core built exclusively from (mostly antiparallel) beta-sheets
3. “mixed”-α/β - mixture of “pure”-α and “pure”-β
4. α+β - built from combinations of β-α-β motifs

Further: Simplified Models of Protein Structures

Level of Simplification
Usefulness: classification and outlining their typical features
Quasi-cylindrical core

Quasi-spherical core

Most Common!!!

Quasi-flat core

The core is hydrophobic in water-soluble globular and fibrous proteins and it is hydrophilic in membrane proteins
α-proteins - Helix Bundle

Fold composed of several parallel/antiparallel helices

helix-turn-helix motif

3-helix bundle

4-helix bundle

Cytochrome c'  
Hemerythrin  
Coat protein  
*Tobacco mosaic virus*
α-proteins – Globin fold

Common fold
A bundle of 8 helices, connected by rather short loop regions

myoglobin

No 360° turns

No loop crossings
Quasi-spherical polyhedron model

The geometry of any helix packing can be described by a polyhedron, where each vertex corresponds to half of the helix.

Typical protein chain envelopes its core as if taking a continuous path along the sides of a quasi-spherical polyhedron.

Quasi-spherical polyhedron model

Several packing arrangements

right- (-60° between helices) often
left- (+60° between helices) rare
Close packing –”Ridge into Groove”

Ridges of one helix fit into grooves of an adjacent helix

Ridges at the surface of the alpha helix

“i+4”     “i+3”
**α/β-proteins**

Regular secondary structure sequence: α-β-α-β-α-β- ...
Parallel beta sheets, and parallel helices
Usually with two hydrophobic cores

**Tim Barrel fold**

Triose-phosphate isomerase
Right-handed superhelix

The active site is located in the funnel on the cylinder axis, the one where the N-termini of the helices are directed.
**α/β-proteins - α/β-horseshoes**

Similar to TIM barrel fold, but the beta circle inside the alpha helix is not complete

![Diagram of α/β-horseshoe structure]

- 17 beta-strands
- 16 alpha helices

Placental ribonuclease inhibitor
α/β-proteins
Rossman fold

A beta layer is sandwiched between two alpha helix layers

The location of the active site
**α+β-proteins**

a). αβ-plaits – regular alternation of α- and (even number of) β-regions

b). “usual” α+β proteins – irregular alternation of α- and β-regions

a). αβ-plaits

\[ \alpha-\beta-\beta-\alpha-\beta-\beta-\alpha-\ldots \text{ OR } \alpha-\beta-\beta-\beta-\alpha-\beta-\ldots \]

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Ribosomal protein S6

Ferredoxin fold

[Diagram of protein structure]
α+β-proteins – OB fold
(oligonucleotide-binding fold)

b). “usual” α+β proteins

β-β-β-α-β-β-α-α-…

Staphylococcus nuclease