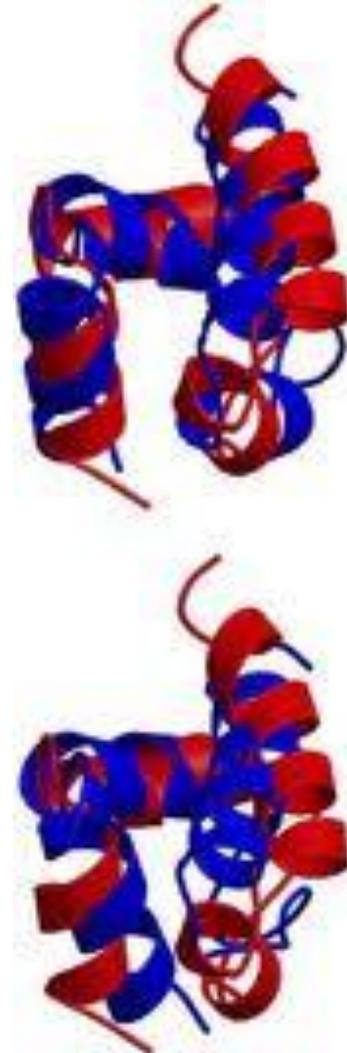
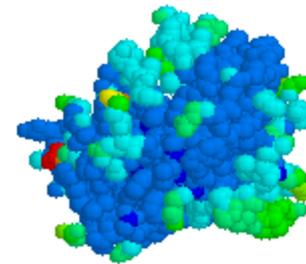
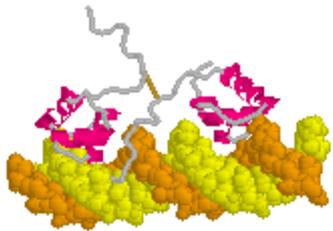


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Polypeptide & protein Structure

Protein conformation

- Many conformations are possible for proteins due to flexibility of amino acids linked by peptide bonds
- At least one major conformation has biological activity, and hence is considered the protein's **native conformation** or the **native protein**



Levels of Protein Structure

- **1° structure:** sequence and number, from N to C
- **2° structure:** the ordered 3-dimensional arrangements (conformations) in localized regions of a polypeptide chain, backbone interactions through hydrogen bonding;
 - e. g., α -helix and β -pleated sheet
- **3° structure:** 3-D arrangement of all atoms
- **4° structure:** multimeric proteins, arrangement of monomer subunits with respect to each other

Primary Structure of Proteins

- Zigzag arrangement
- R-groups
- Determination?
- 1° Sequence & 3-D conformation; relation to functional properties (MW& genetic mutations)
- Site-directed mutagenesis and structure function relationship

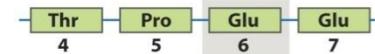
HBB Sequence in Normal Adult Hemoglobin (Hb A):

Nucleotide	CTG	ACT	CCT	GAG	GAG	AAG	TCT
Amino Acid	Leu	Thr	Pro	Glu	Glu	Lys	Ser
	3			6			9

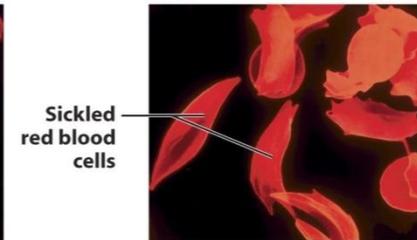
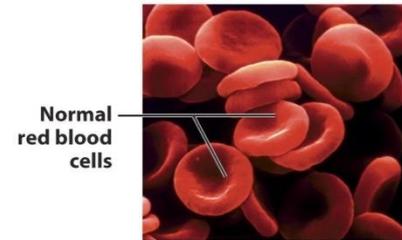
HBB Sequence in Mutant Adult Hemoglobin (Hb S):

Nucleotide	CTG	ACT	CCT	GTG	GAG	AAG	TCT
Amino Acid	Leu	Thr	Pro	Val	Glu	Lys	Ser
	3			6			9

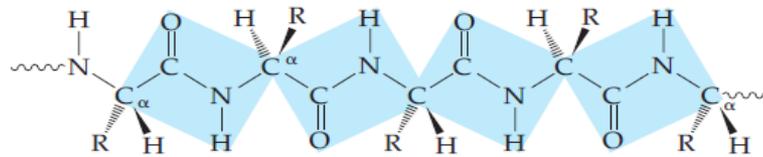
(a) Normal amino acid sequence



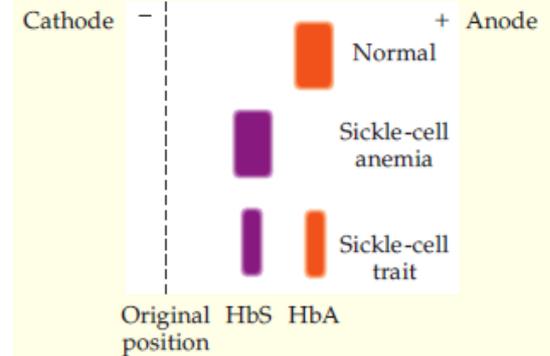
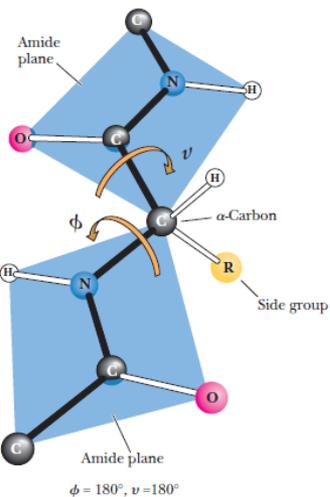
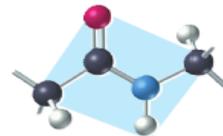
(b) Single change in amino acid sequence



Planar units along a protein chain

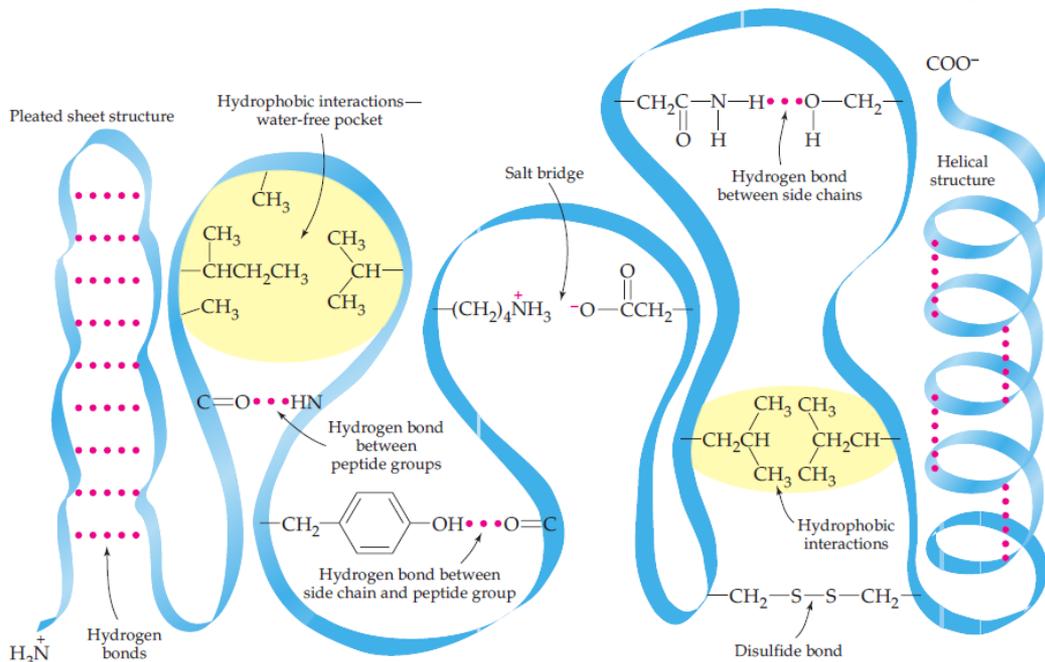
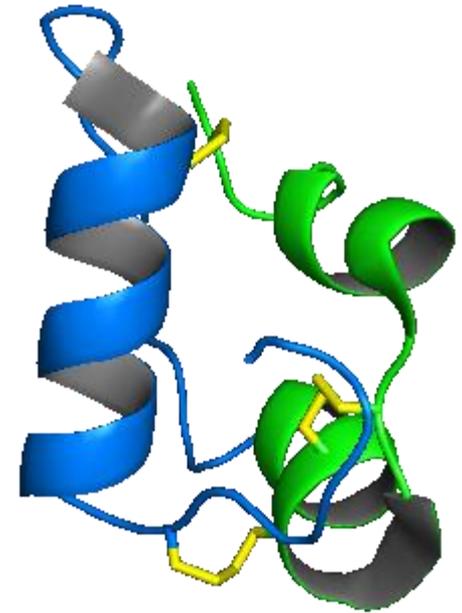
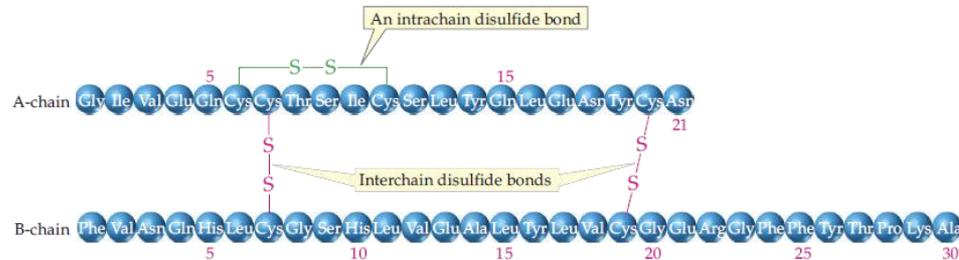


One planar unit

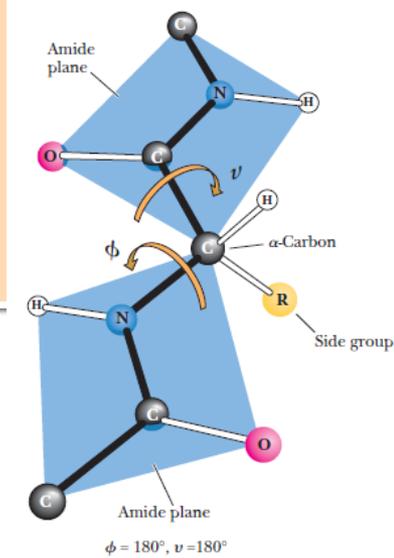
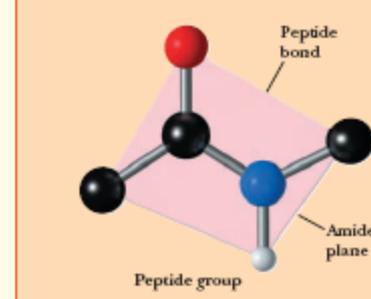
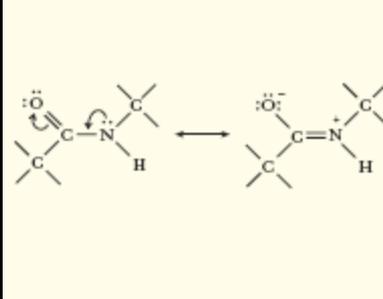


Shape-Determining & stabilizing Interactions in Proteins

- Is it ordered or spaghetti?
- Hydrogen, ionic, covalent, & hydrophobic

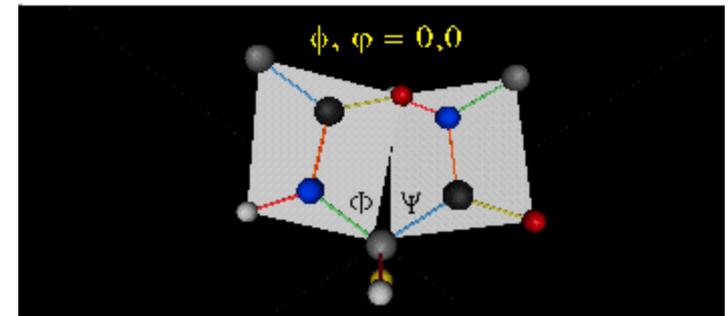


Secondary Structure

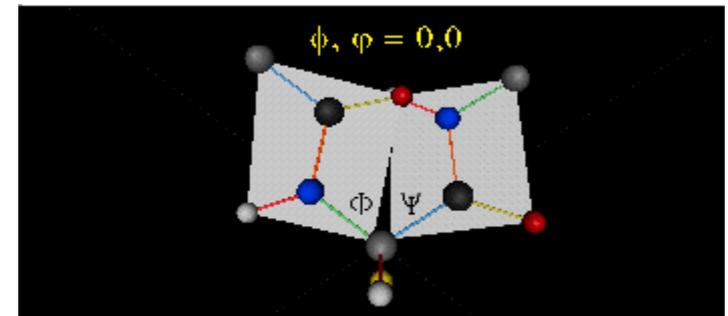


- What is the secondary structure of proteins? "folding of the backbone"
- What are the bonds that have a free rotation? What is the implication? These angles repeat themselves in regular secondary structures
- Two main kinds: α -helix and β -pleated sheet
- They are periodic; their features repeat at regular intervals
- Stability of secondary structure

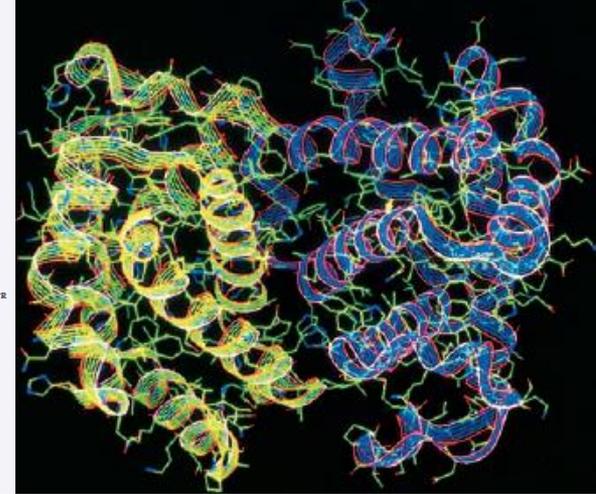
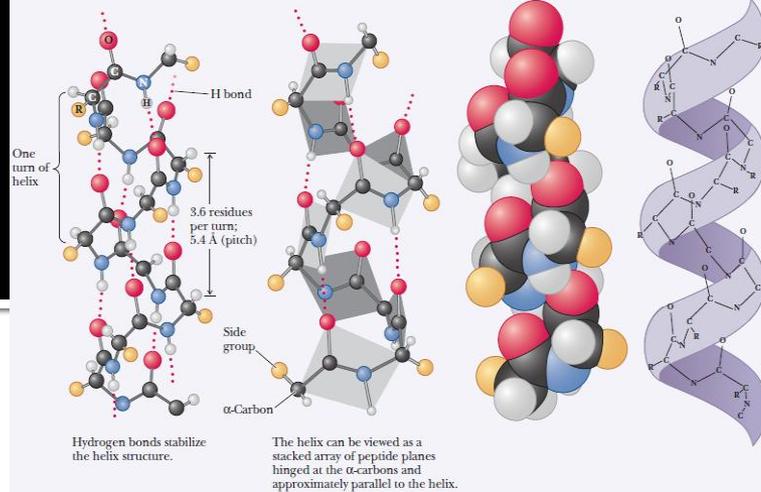
Rotation around phi (ϕ)



Rotation around psi (ψ)



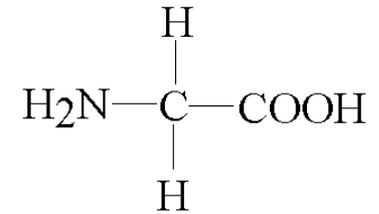
The α -helix



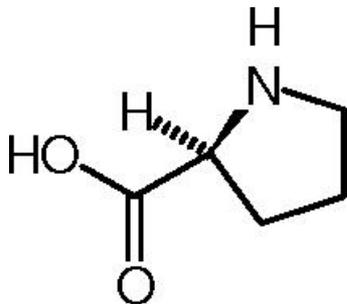
- Same segment
- H-bonds are parallel
- C=O binds N—H four residues away
- linear arrangement of H-bonds (maximum strength & stability)
- Turns occur every 3.6 residues,
- Right handed, clockwise
- The pitch (linear distance between points on successive turns) is 5.4 Å
- Proteins vary in their α -helical structures
- What factors affect the helix (specific amino acids, electrostatic repulsion, steric repulsion)

Amino acids NOT found in α -helix

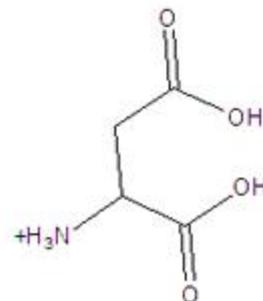
- Glycine: too small & entropically expensive (high flexibility)
- Proline
 - No rotation around psi bond
 - No hydrogen bonding of α -amino group
- Close proximity of a pair of charged amino acids with similar charges



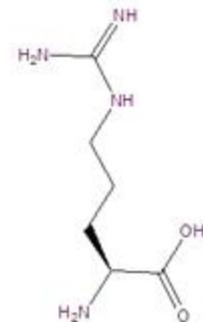
glycine



L-proline

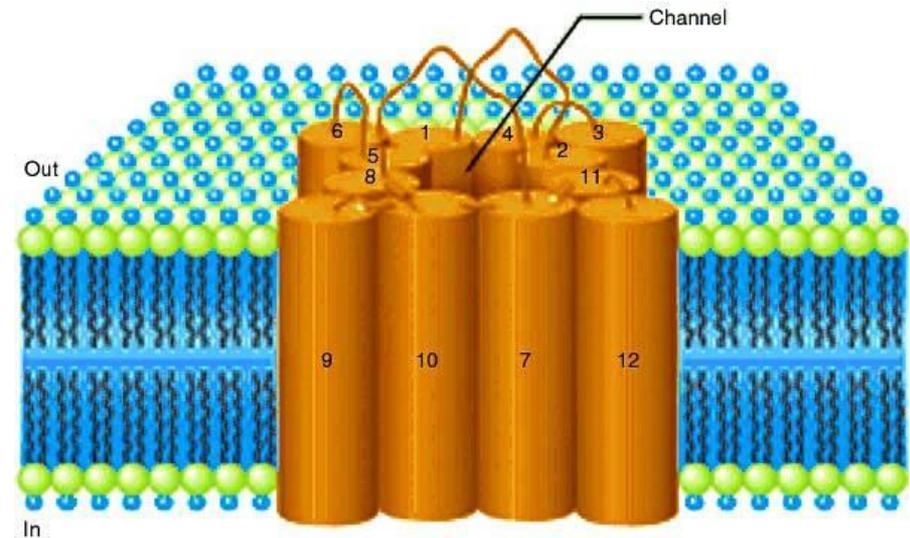
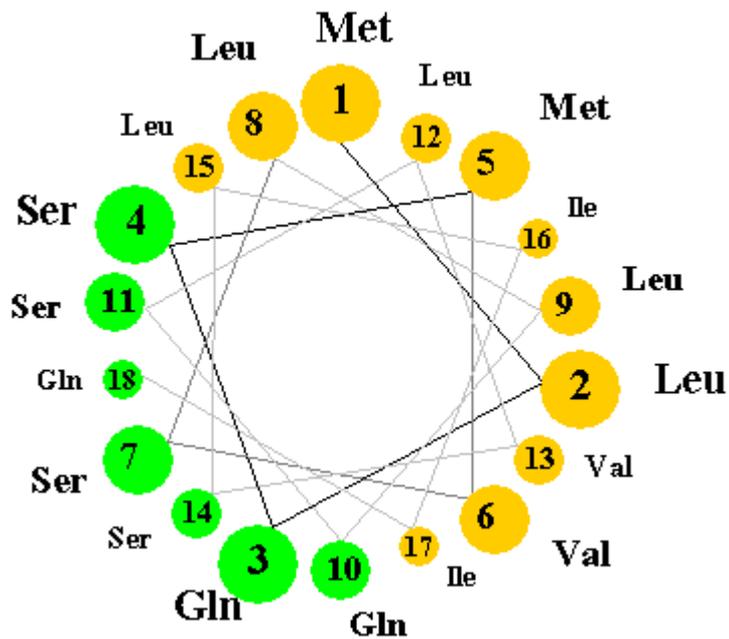
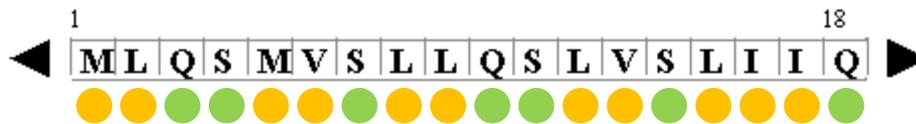


aspartic acid



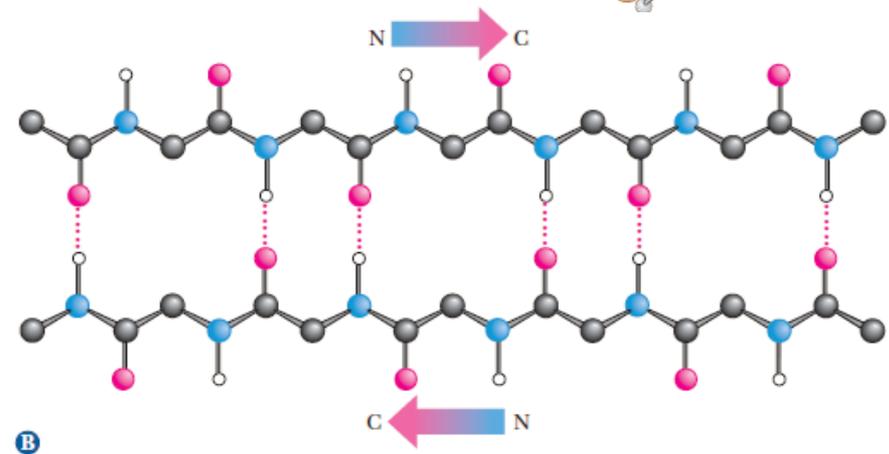
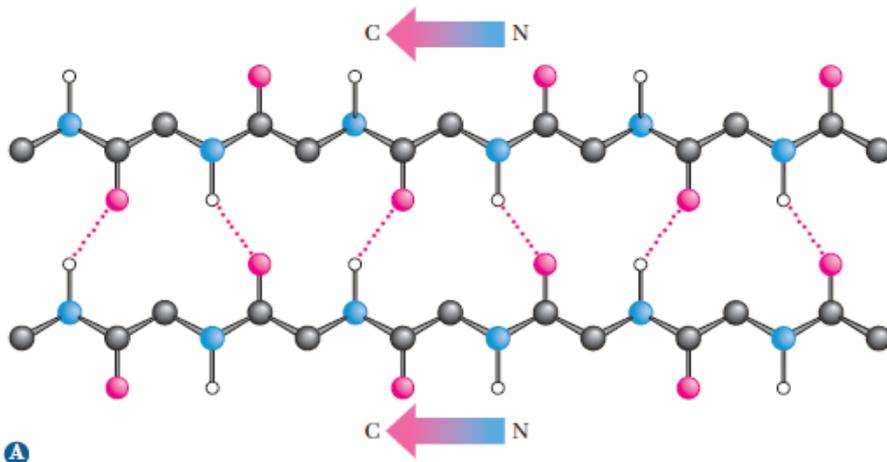
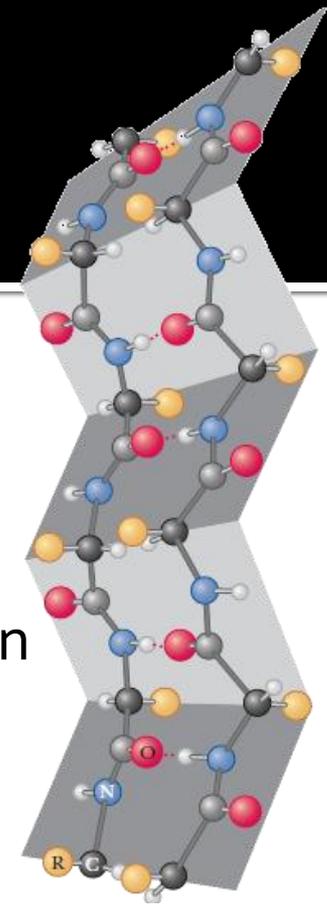
arginine

Amphipathic α helices



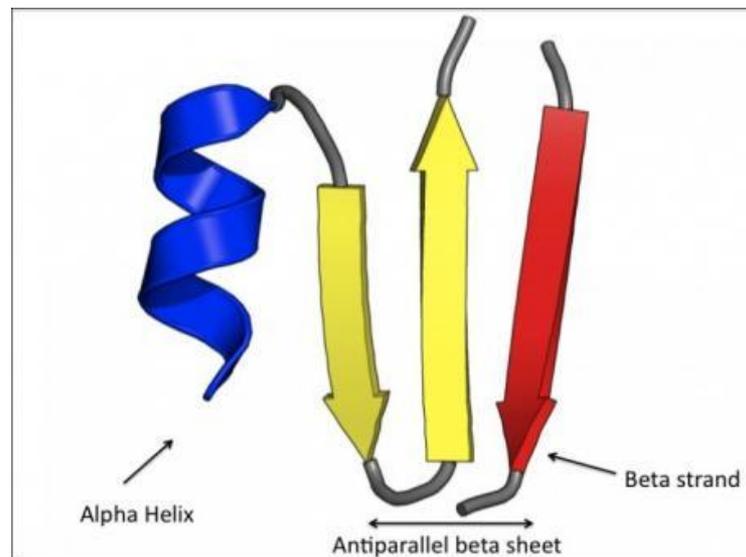
The β -sheets

- Backbone is almost completely extended
- R groups extending above and below the sheet
- H-bonds are *intra-chain* or *inter-chain* bonds
- Perpendicular to the direction of the protein chain
- Parallel vs. anti-parallel
- Zigzag structure



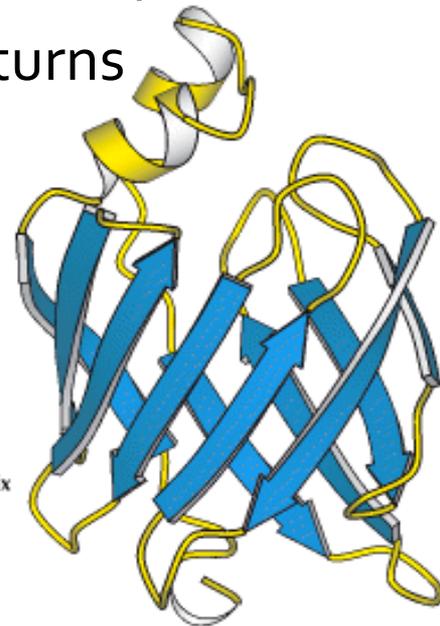
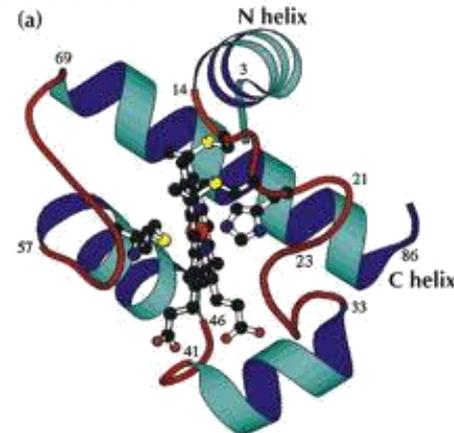
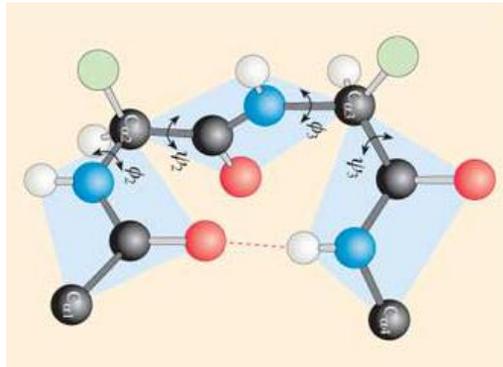
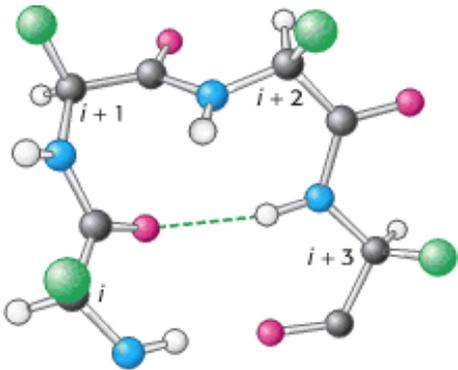
How many β strands can a β sheet have?

- β sheets can form between many strands, typically 4 or 5 but as many as 10 or more
- Such β sheets can be purely antiparallel, purely parallel, or mixed
- Proline tends to disrupt β strands



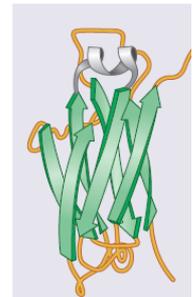
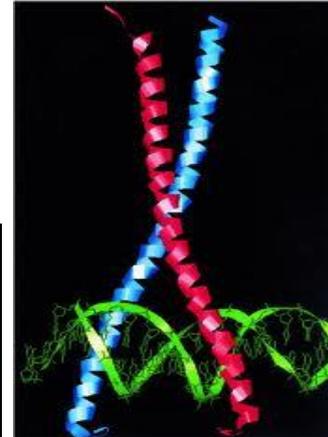
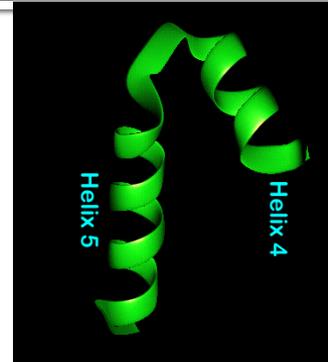
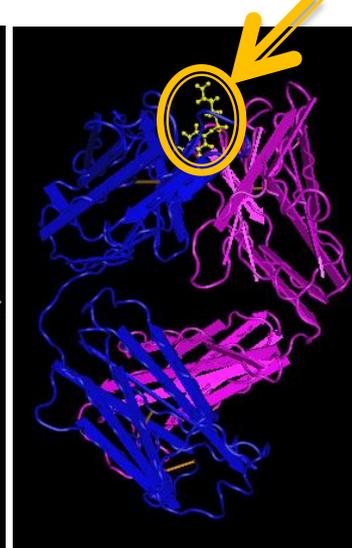
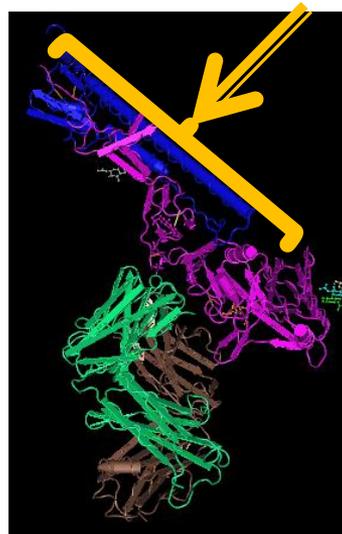
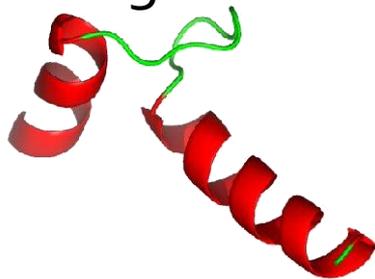
Others regular ones: Turns & loops

- Turns
 - Compact, U-shaped secondary structures
 - Also known as β -turn or hairpin bend
 - What are they used for? How are they stabilized?
 - Involve 4 amino acids (H-bond: C=O of 1 & N-H of 4)
 - Glycine and proline are commonly present in turns
- Loops do not have regular structures



Super-secondary structures: Motifs & Domains

- A motif: a small portion of a protein (typically less than 20 amino acids)
 - In general, motifs may provide us with information about the folding of proteins, but no biological function
- Domains; protein conformations with similar functions, 100–200 residues, fold independently of the rest of the protein
 - leucine zipper
 - Immunoglobulin fold



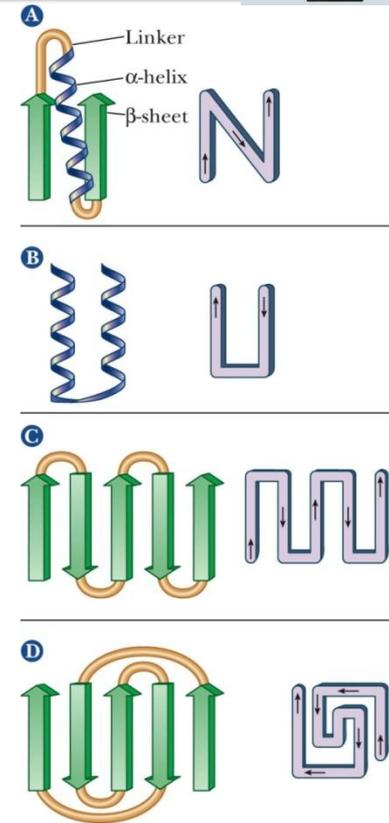
Super-secondary structures

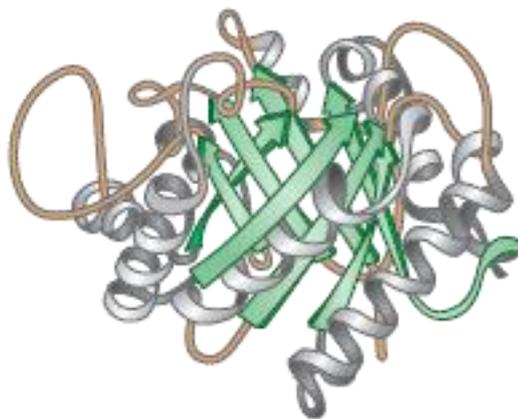
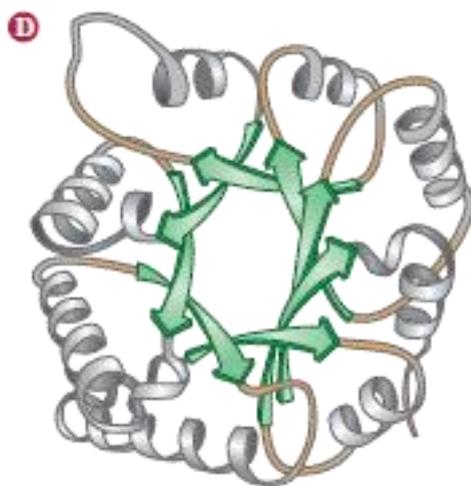
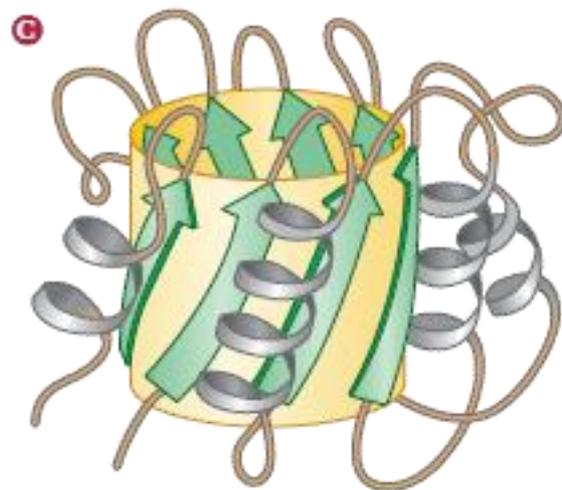
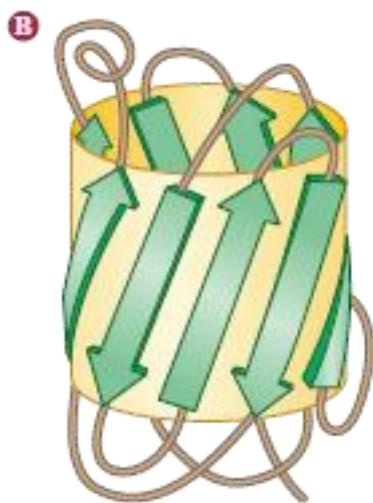
α -Helices and β -Sheets



A combination of α - and β -sections:

- **$\beta\alpha\beta$ unit:** (parallel)
- **$\alpha\alpha$ unit:** (helix-turn-helix), anti-parallel
- **β -meander:** anti-parallel sheets, series of tight reverse turns
- **Greek key:** repetitive, anti-parallel sheet doubles back on itself
- **β -barrel:** created when β -sheets are extensive enough to fold back on themselves





Fibrous Proteins

α -keratins,
bundles of α -
helices

- Contain polypeptide chains organized approximately parallel along a single axis:
 - Consist of long fibers or large sheets
 - Mechanically strong
 - Insoluble
 - play an important structural role
- Examples are
 - Keratin
 - Collagen
 - fibroin

Fibroin, β -sheets,

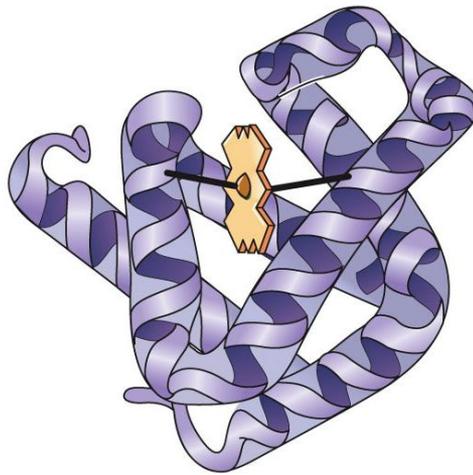


Globular Proteins

- Folded to, a more or less, spherical shape
 - Soluble
 - Polar vs. non-polar, exterior vs. interior
 - Most of them have substantial sections of α -helix and β -sheet



Filament
(four right-hand
twisted protofilaments)



Myoglobin, a globular protein

