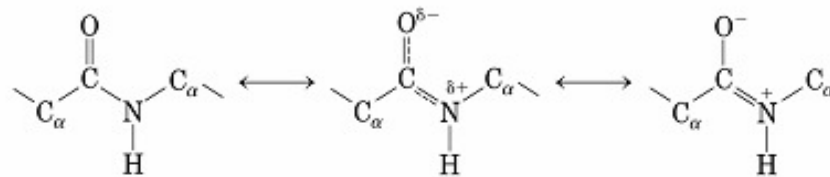


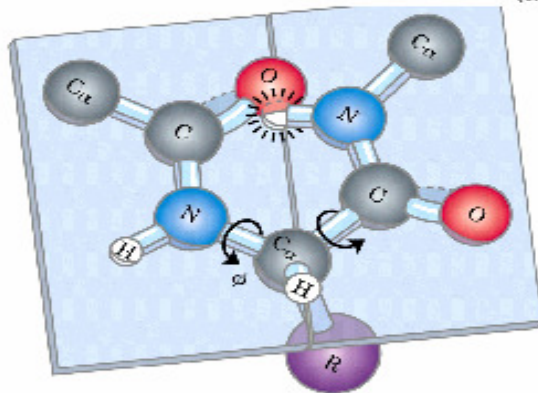
3-D Structure of Proteins

- The spatial arrangement of atoms in a protein is called its **conformation**.
- Proteins in any of their functional folded conformations are called **native** proteins.
- **Stability** - the tendency to maintain a native conformation.
- When water surrounds a hydrophobic molecule, the optimal arrangement of hydrogen bonds results in a highly structured shell or **solvation layer** of water in the immediate vicinity.

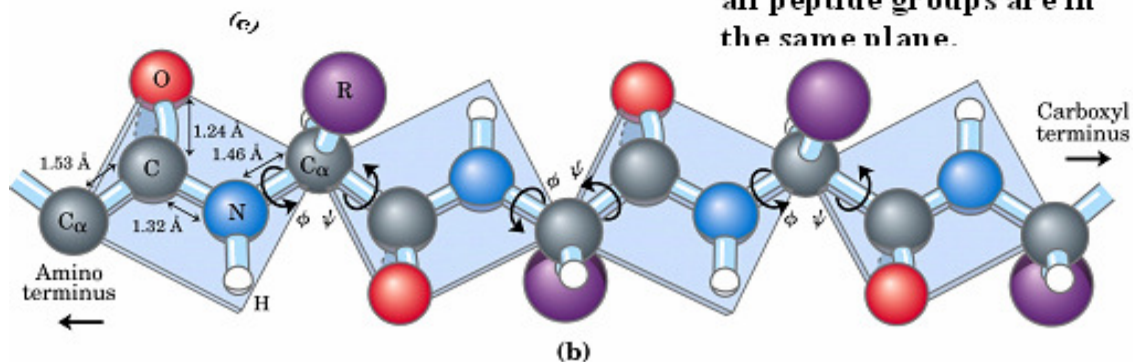
The carbonyl oxygen has a partial negative charge and the amide nitrogen a partial positive charge, setting up a small electric dipole. Virtually all peptide bonds in proteins occur in this trans configuration; an exception is noted in Figure 6-8b.



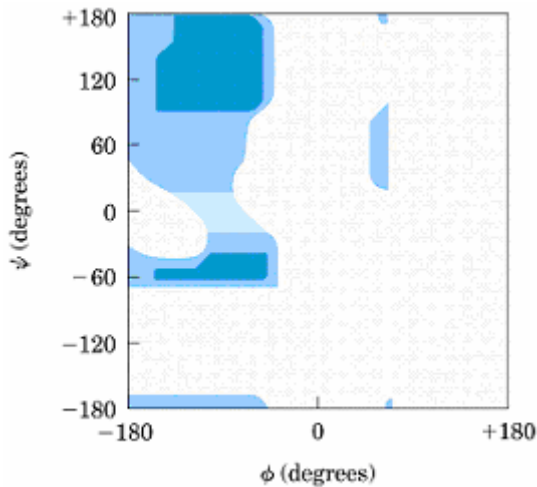
(a) By convention the bond angles resulting from rotations at C_α are labelled Φ (phi) for the N- C_α bond and Ψ (psi) for the C_α -C bond.



By convention Φ and Ψ are defined as 180° when polypeptide is in its fully extended conformation and all peptide groups are in the same plane.



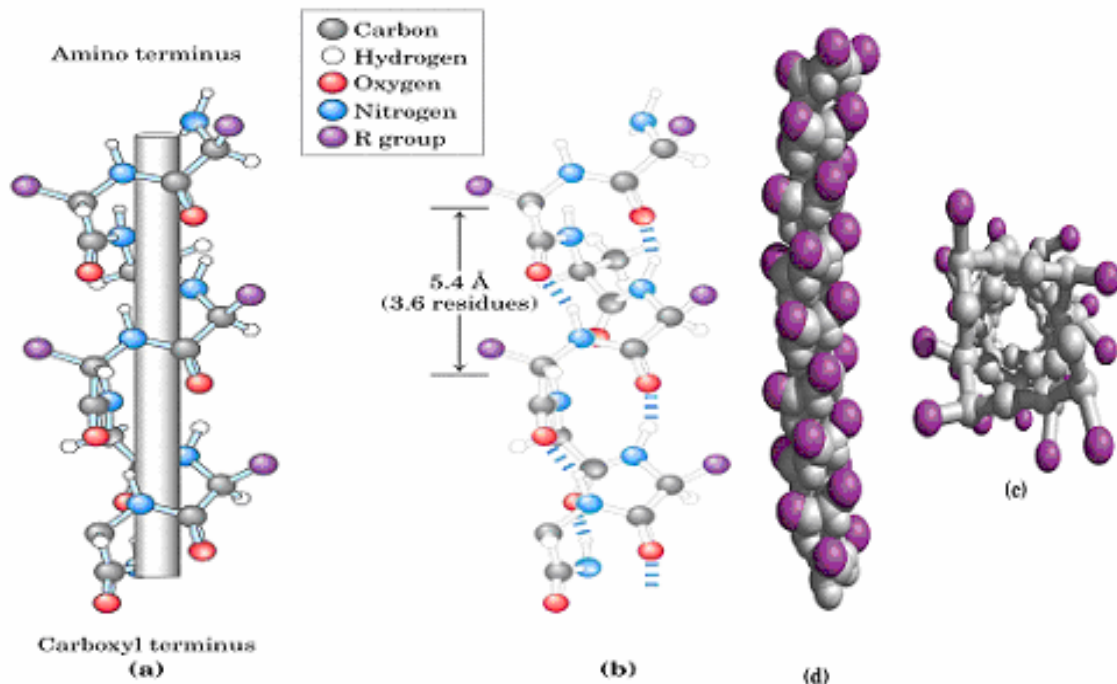
Ramachandron Plot



Allowed values for the Φ and Ψ are graphically revealed when Ψ is plotted versus Φ in a Ramachandran plot.

3-D Structure of Proteins

- **Primary Structure** – basic amino acid sequence
- **Secondary Structure** – refers to the local conformation of some part of the polypeptide [α helix; β conformations]
- **Tertiary Structure** - is the overall 3-D arrangement of all atoms in a protein.
- **Quaternary Structure** – is the 3-D complexes of protein subunits.



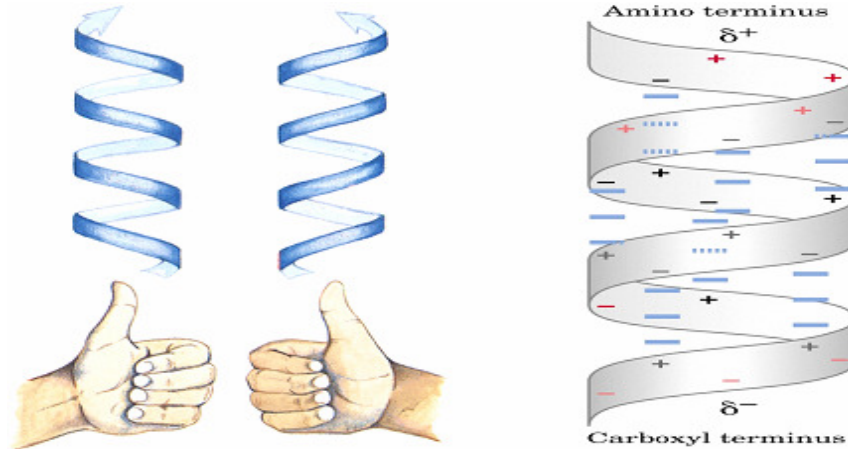
α helix – different aspects of its structure

α helix – $\Psi = -45^\circ$ to -50° ; $\Phi = -60^\circ$

Each helical turn includes 3.6 amino acid residues

The helical twist of α helix found in all proteins is right-handed.

Knowing the Right Hand from the left.



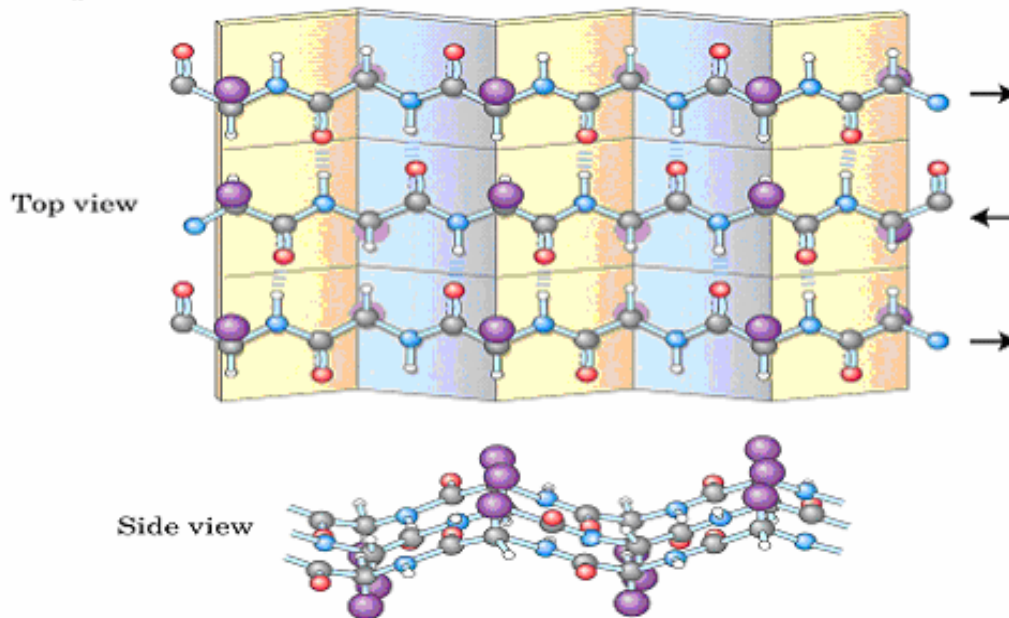
Not all polypeptides can form a stable α helix. Interactions between amino acid side chains can stabilize or destabilize this structure.

Five different kinds of constraints affect the stability of an α helix:

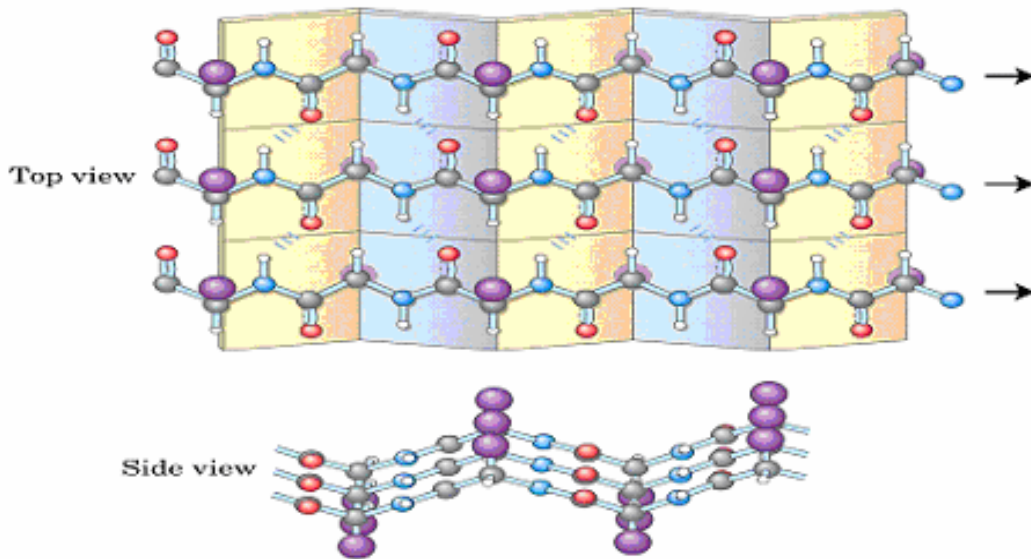
1. Electrostatic repulsion (or attraction) between successive amino acid residues with charged R group.
2. Bulkiness of adjacent R group
3. Interactions between amino acid side chains spaced three (or four) residues apart.
4. Occurrence of Pro and Gly residues.
5. Interaction between amino acid residues at the ends of the helical segment and the electric dipole inherent of the α helix.

β -conformation of polypeptide chains.

(a) Antiparallel

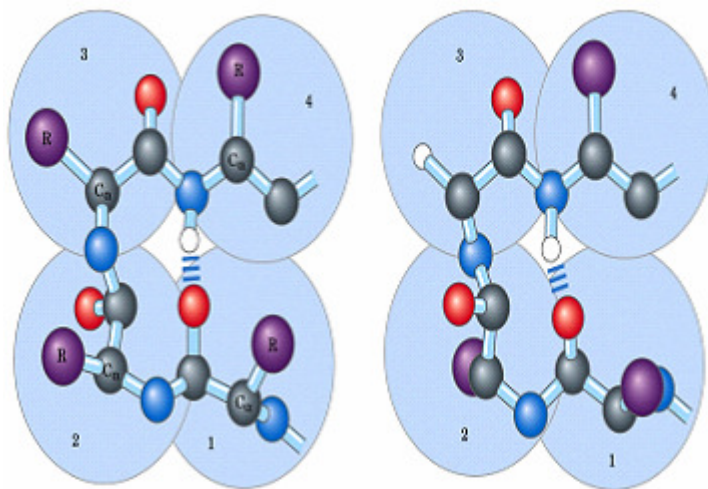


(b) Parallel



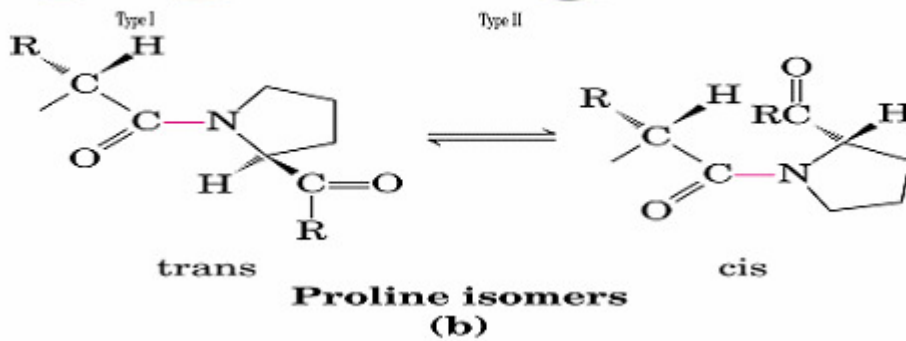
The structures are somewhat similar, although the repeat period is shorter for the parallel conformation (6.5Å versus 7Å for anti-parallel) and the H-bonding patterns are different.

β turns are common in proteins.

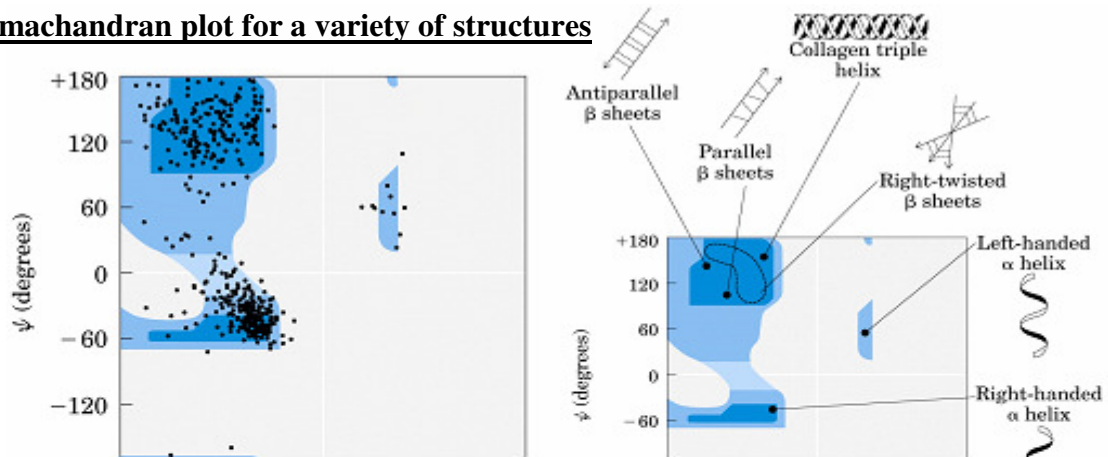


Type I β turns occur more than twice as frequently as type II.

Type II β turns always have Gly as the third residue.



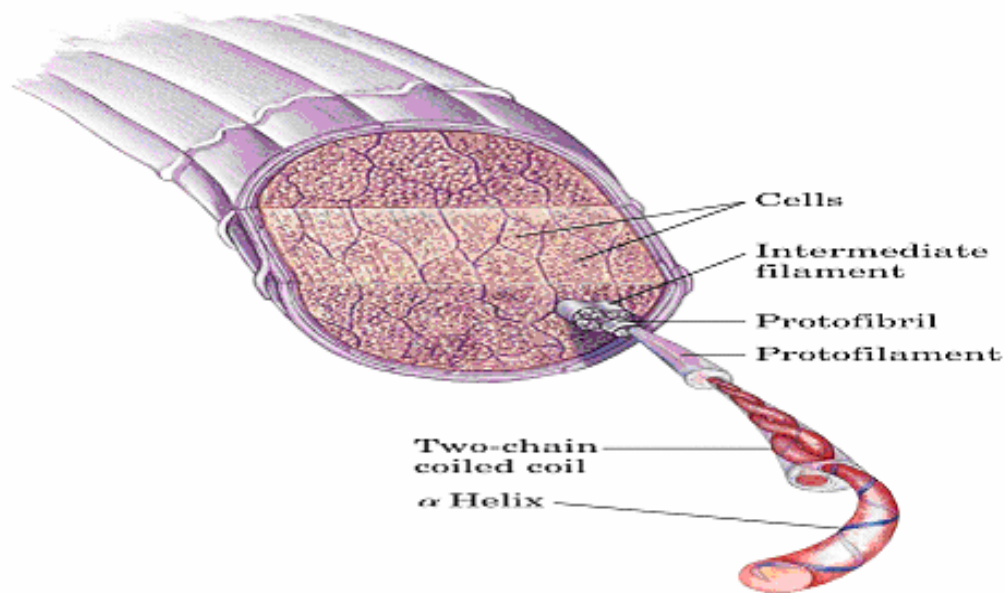
Ramachandran plot for a variety of structures



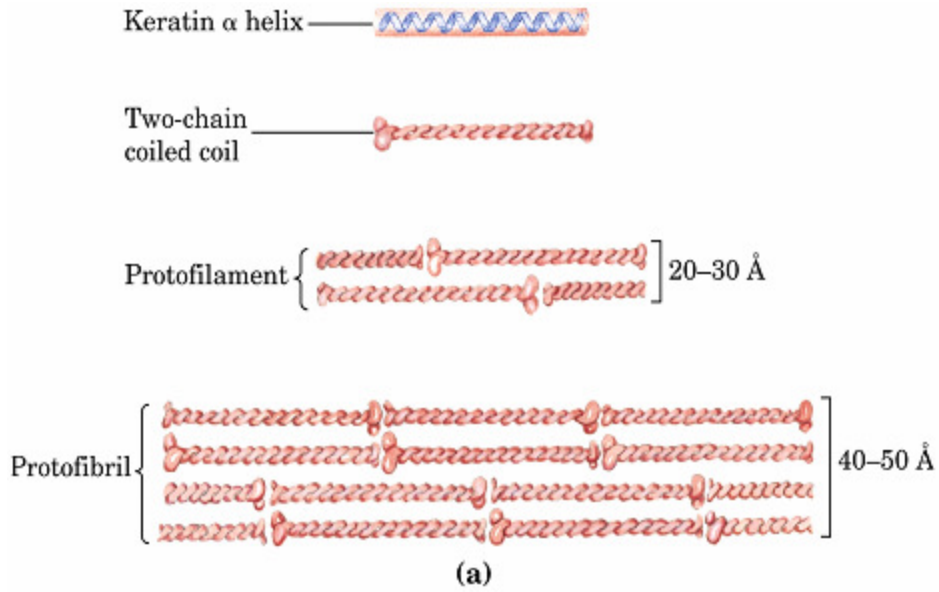
Secondary Structures and Properties of Fibrous Proteins

Structure	Characteristics	Examples of occurrence
α Helix, cross-linked by disulfide bonds	Tough, insoluble protective structures of varying hardness and flexibility	α -Keratin of hair, feathers, and nails
β Conformation	Soft, flexible filaments	Silk fibroin
Collagen triple helix	High tensile strength, without stretch	Collagen of tendons, bone matrix

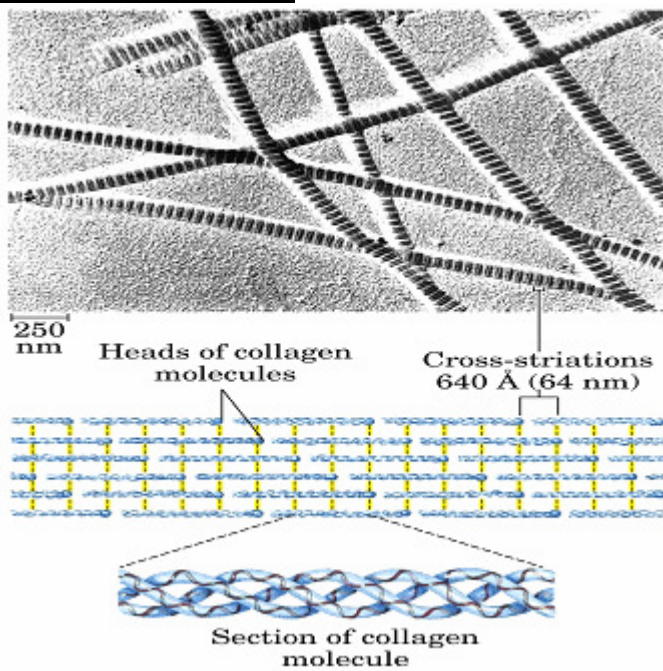
Structure of hair



Cross section of a hair (b)

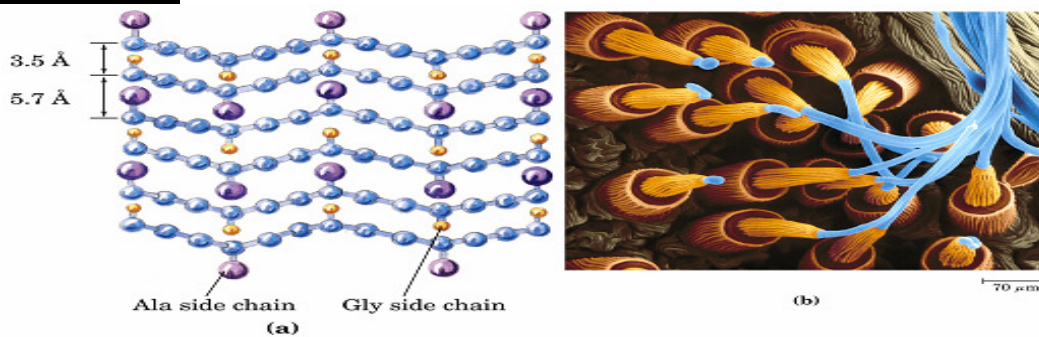


Structure of Collagen

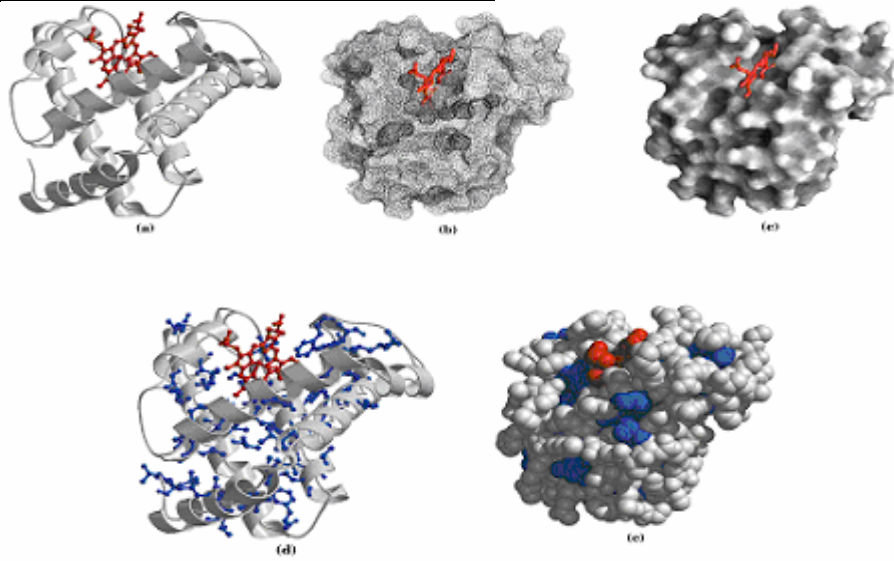


- Like all the α -keratins, collagen has evolved to provide strength.
- Found in connective tissue such as tendons, cartilage, the organic matrix of bone, cornea of the eye.
- It is left-handed and had three amino acid residues per term.

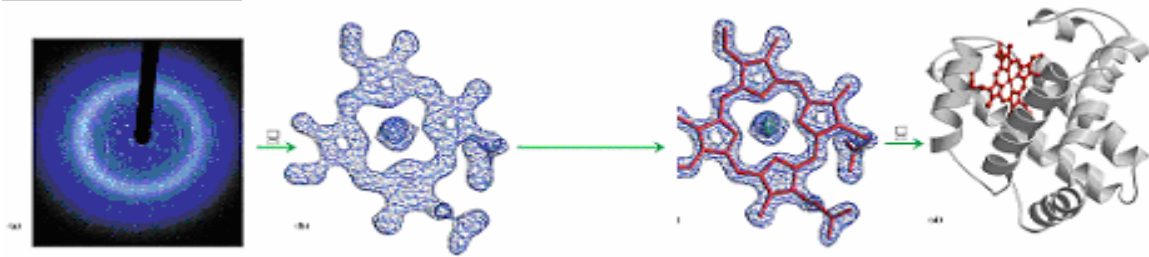
Structure of Silk



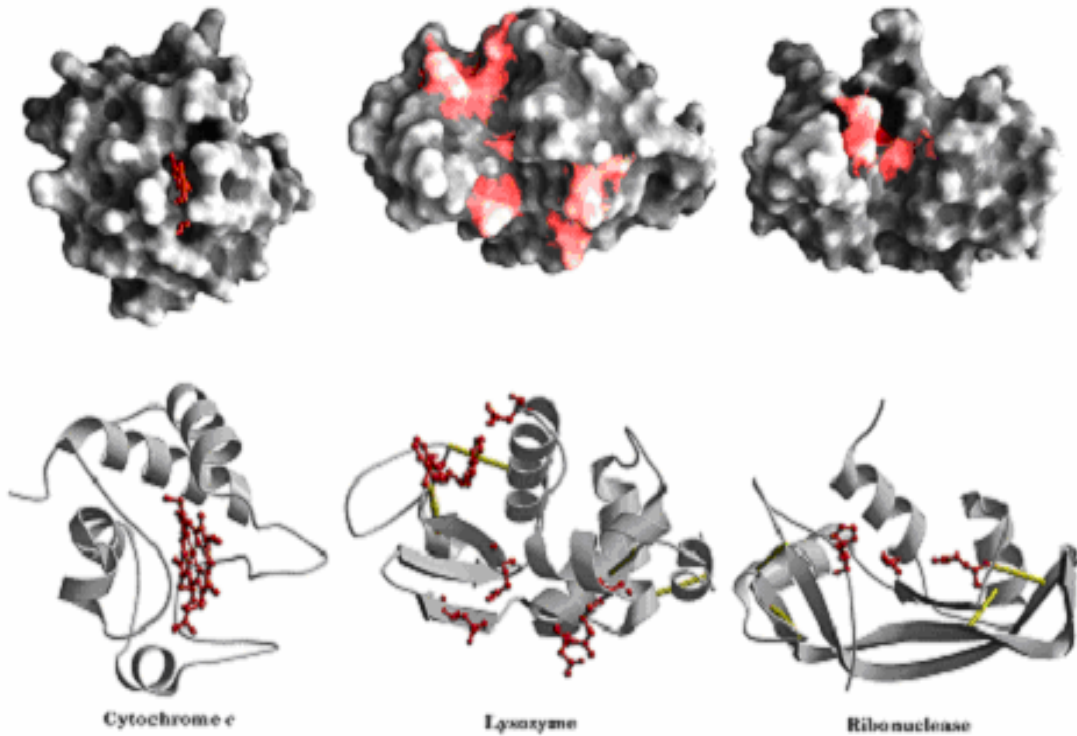
Tertiary structure of sperm whale myoglobin



X-ray Diffraction



3-D structure of some small proteins.

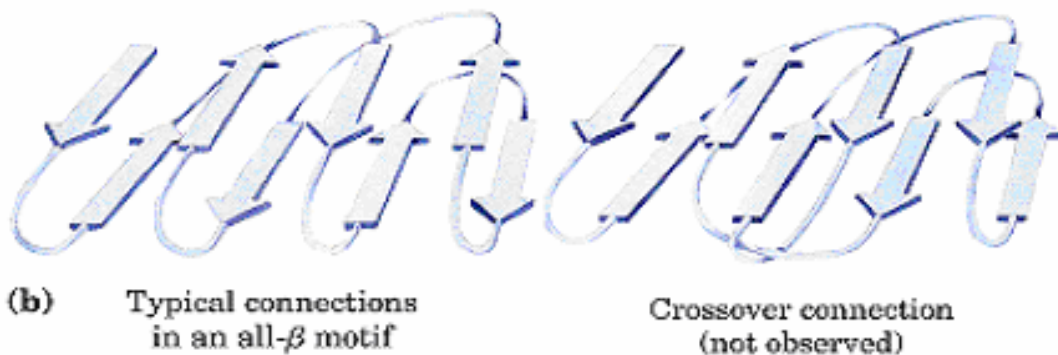


Approximate Amounts of α Helix and β Conformation in Some Single-Chain Proteins*

Protein (total residues)	Residues (%)	
	α Helix	β Conformation
Chymotrypsin (247)	14	45
Ribonuclease (124)	26	35
Carboxypeptidase (307)	38	17
Cytochrome <i>c</i> (104)	39	0
Lysozyme (129)	40	12
Myoglobin (153)	78	0

*Portions of the polypeptide chains that are not accounted for by α helix or β conformation consist of bends and irregularly coiled or extended stretches. Segments of α helix and β conformation sometimes deviate slightly from their normal dimensions and geometry.

- **Supersecondary structures**, also called **motifs** or simply **folds**, are particularly stable arrangements of several elements of secondary structure and the connections between them.
- **Class and Fold** – are purely structural
- **Family** – similar structure and function
- **Superfamily** – little primary sequence similarity, but make use of same major structural motif and have functional similarity





(c) Right-handed connection
between β strands



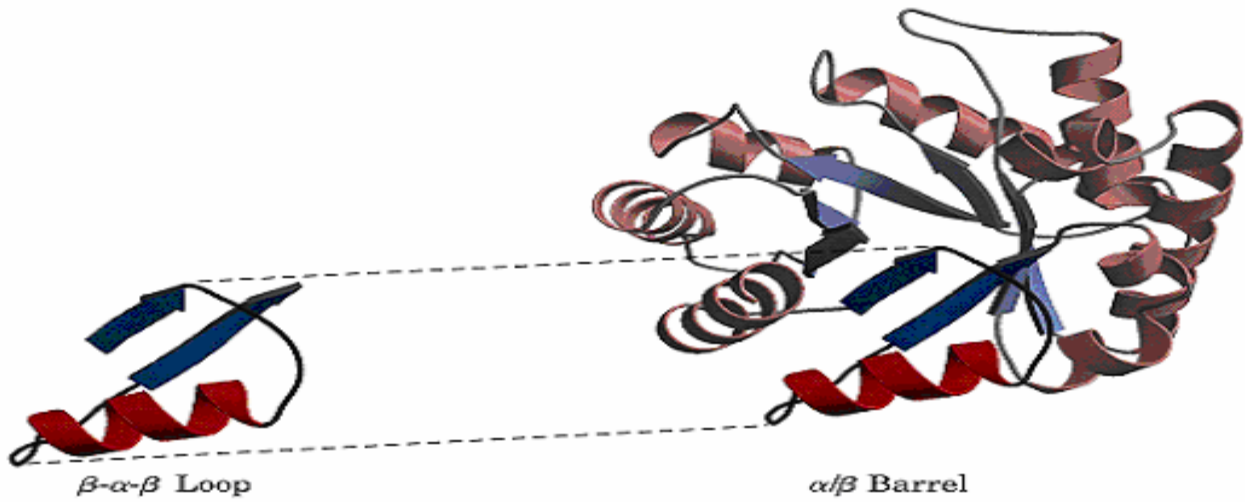
Left-handed connection
between β strands
(very rare)



(d) β Barrel



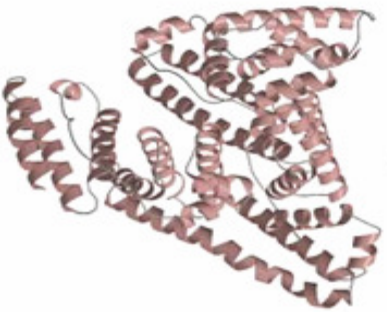
Twisted β sheet



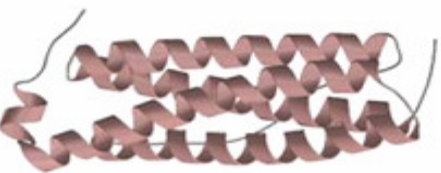
β - α - β Loop

α/β Barrel

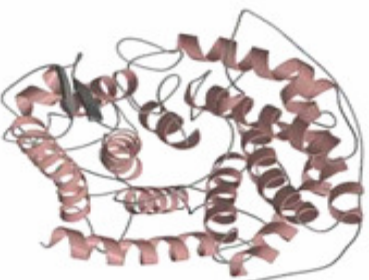
All α



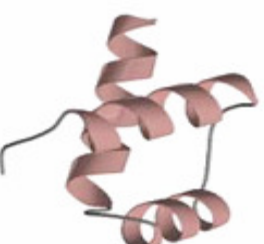
la06
 Serum albumin
 Serum albumin
 Serum albumin
 Human (*Homo sapiens*)



1b6f
 Ferritin-like
 Ferritin-like
 Ferritin
 Bacterioferritin (cytochrome b_7)
Escherichia coli



1gai
 α/α toroid
 Glycosyltransferases of the
 superhelical fold
 Glucoamylase
 Glucoamylase
Aspergillus awamori, variant x100



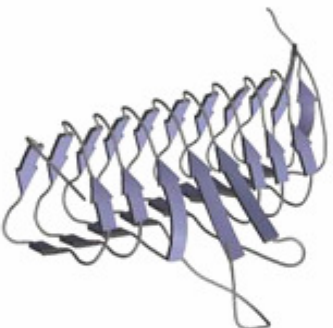
1enh
 DNA-binding 3-helical bundle
 Homeodomain-like
 Homeodomain
 Homeodomain
 engrailed Homeodomain
Drosophila melanogaster

Key
 PDB identifier
 Fold
 Superfamily
 Family
 Protein
 Species

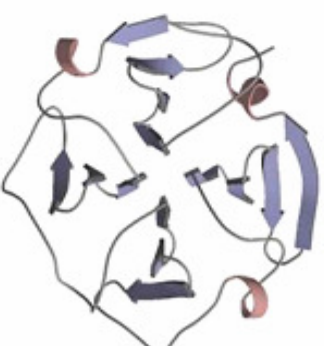
All β



Ihee
 α -Amylase inhibitor
 α -Amylase inhibitor
 α -Amylase inhibitor
 HOE-467A
Streptomyces tendae 4158



1lxa
 Single-stranded left-handed β helix
 Trimeric LpxA-like enzymes
 UDP N-acetylglucosamine acyltransferase
 UDP N-acetylglucosamine acyltransferase
Escherichia coli



1pex
 Four-bladed β propeller
 Hemopexin-like domain
 Hemopexin-like domain
 Collagenase-3 (MMP-13),
 carboxyl-terminal domain
 Human (*Homo sapiens*)



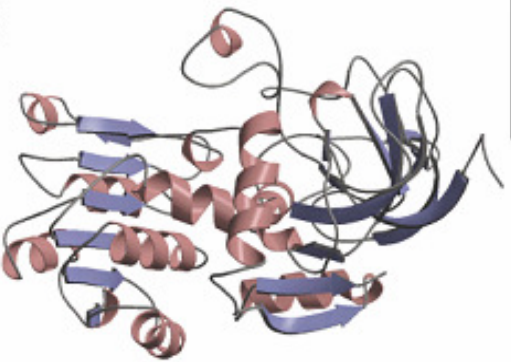
Ijpe
 β -Prism II
 α -D-Mannose-specific plant lectins
 α -D-Mannose-specific plant lectins
 Lectin (agglutinin)
 Snowdrop (*Galanthus nivalis*)



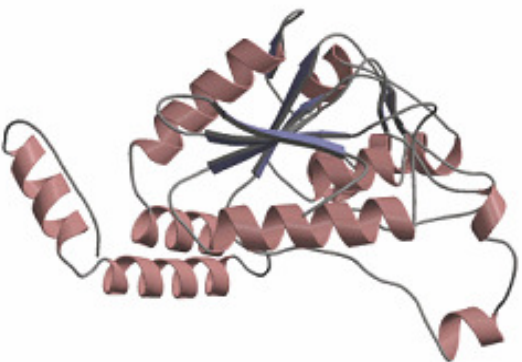
1cd8
 Immunoglobulin-like β sandwich
 Immunoglobulin
 Antibody variable domain-like
 CD8
 Human (*Homo sapiens*)

Key
 PDB identifier
 Fold
 Superfamily
 Family
 Protein
 Species

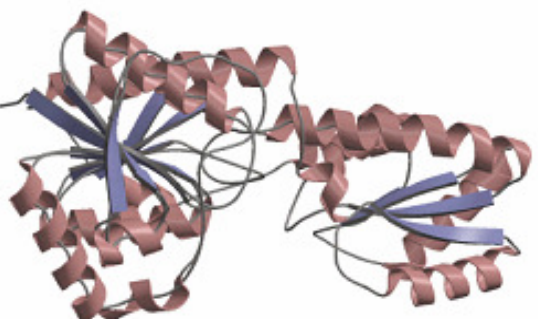
α/β



1deh
NAD(P)_i-binding Rossmann-fold domains
NAD(P)_i-binding Rossmann-fold domains
Alcohol/glucose dehydrogenases,
carboxyl-terminal domain
Alcohol dehydrogenase
Human (*Homo sapiens*)



1dub
Crotonase-like
Crotonase-like
Crotonase-like
Enoyl-CoA hydratase
Rat (*Rattus norvegicus*)



1p1k
Phosphofructokinase
Phosphofructokinase
Phosphofructokinase
Phosphofructokinase
Phosphofructokinase
Escherichia coli

α and β
segments
are
interspersed
or alternate

Key
PDB identifier
Fold
Superfamily
Family
Protein
Species

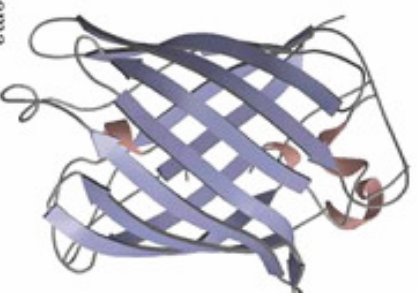
$\alpha + \beta$



2pil
Pilin
Pilin
Pilin
Pilin
Neisseria gonorrhoeae



1syn
Thymidylate synthase
Thymidylate synthase
Thymidylate synthase
Thymidylate synthase
Escherichia coli



1ema
Green fluorescent protein
Green fluorescent protein
Green fluorescent protein
Green fluorescent protein
Green fluorescent protein
Jellyfish (*Aequorea victoria*)



1u9a
Ubiquitin-conjugating enzyme
Ubiquitin-conjugating enzyme
Ubiquitin-conjugating enzyme
Ubiquitin-conjugating enzyme
Human (*Homo sapiens*)

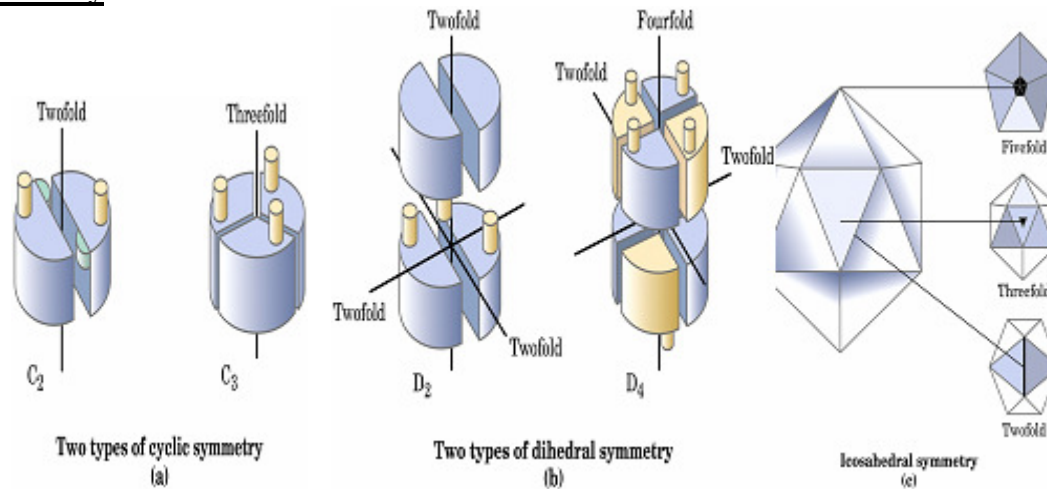
Key
PDB identifier
Fold
Superfamily
Family
Protein
Species

α and β regions
are somewhat
segregated

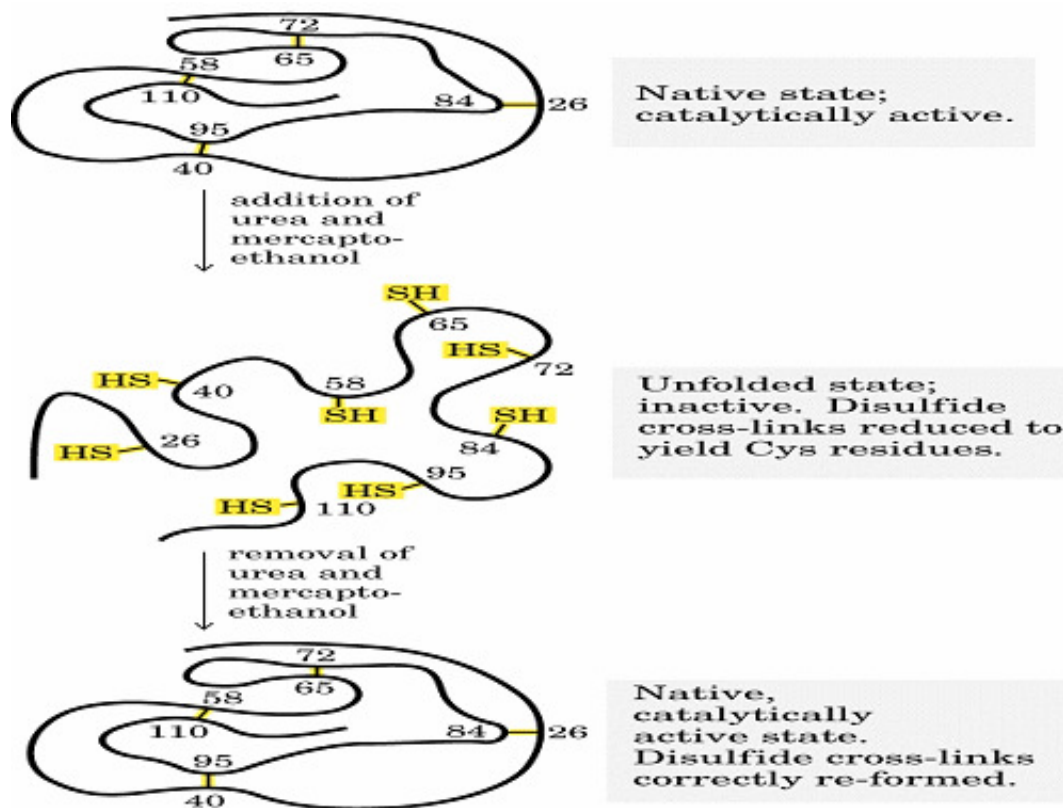
Quaternary Structure

- **Multimer** – multi-subunit protein – from 2 to 100 subunits
- **Oligomer** – multimer with few subunits
- **Protomer** – multimer with repeating structural unit

Symmetry

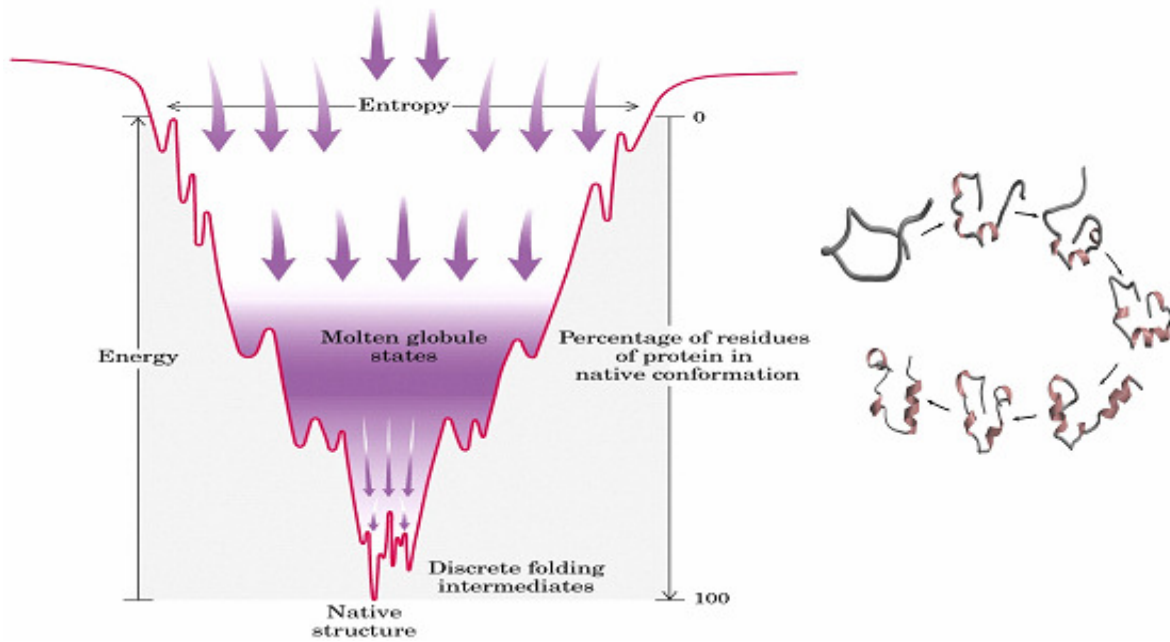


Renaturation of unfolded, denatured ribonuclease



A simulated folding pathway

Beginning of helix formation and collapse



Chaperons in protein folding

