

The three dimensional structure of proteins, ch-4-

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The three dimensional structure of protein:

- 1) Structure determined by a.a sequence.
- 2) Protein function depends on its structure.
- 3) Isolated protein exists in stable structural form/s.
- 4) Strongest interaction stabilizing a specific structure are noncovalent interactions.

Conformation:

The spatial arrangement of atoms in a protein.

Possible conformations of a protein include any structural state achieved without breaking covalent bonds.

Stability :

Tendency to maintain a native conformation.

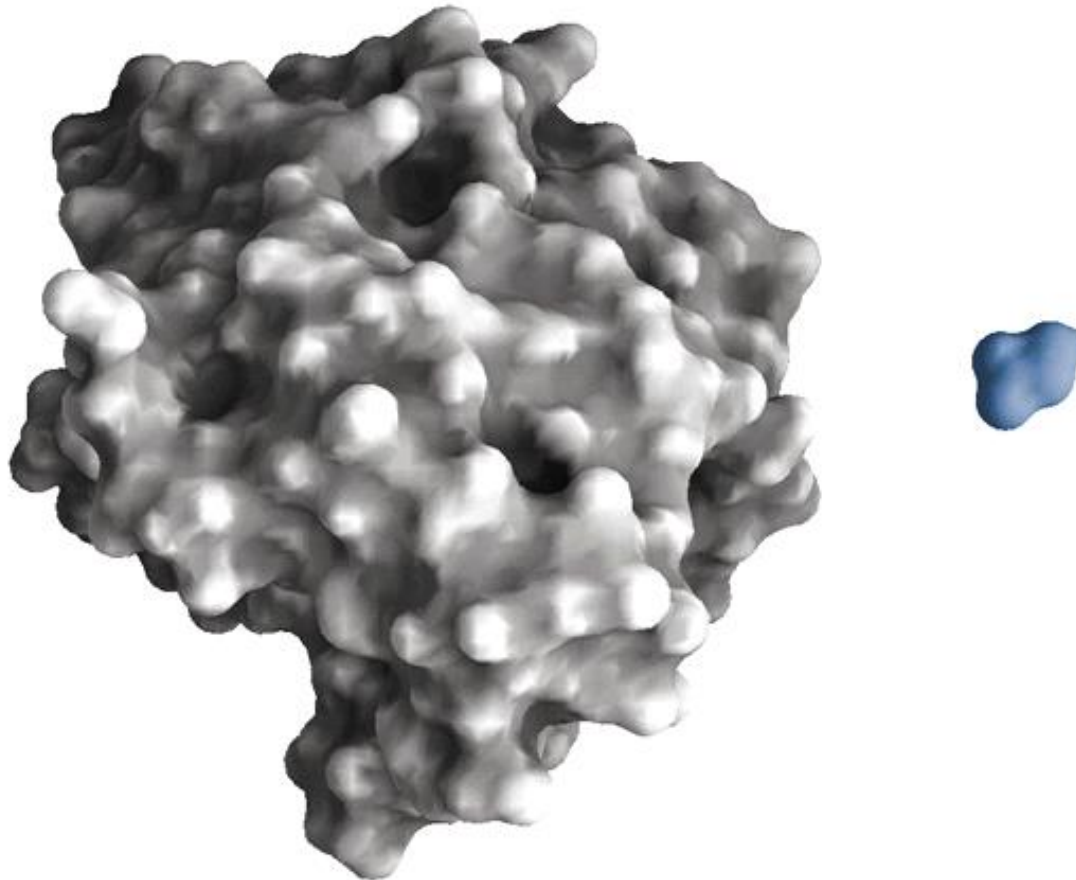
Protein structure is stabilized by → multiple weak interactions.

Hydrophobic interactions are major contributors to stabilize the globular structure of most soluble proteins.

Structure of chymotrypsin, a globular protein, relative to **glycine**.

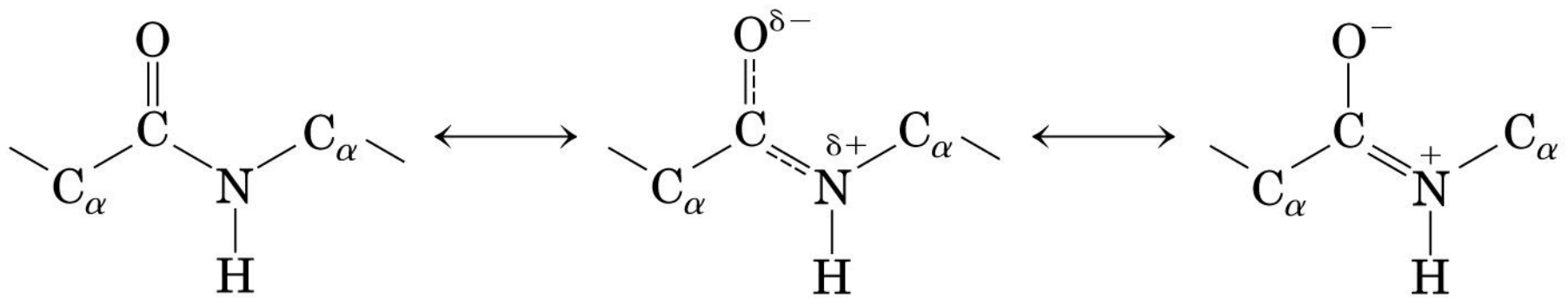
Structure obtained from protein data bank (PDB) www.rcsb.org/pdb
each structure assigned a unique 4 character identifier = PDB ID

6GCH



The planar peptide bond:

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)

α -carbons of adjacent a.a separated by 3 covalent bonds **C_α—C—N—C_α**

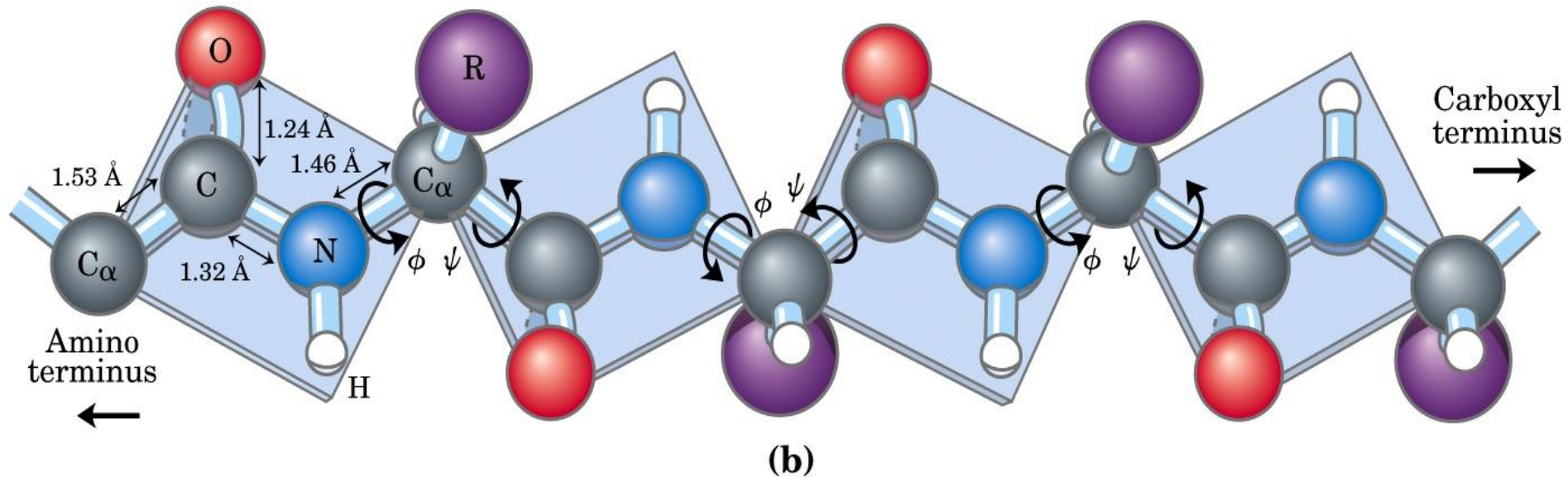
The peptide C-N bond is not free to rotate.

N - C α and C α - C bonds can rotate

bond angles Φ (phi) and ψ (psi) .

Φ and ψ are 180° when polypeptide is fully extended & all peptide groups are in the same plane.

Bond Values $-180^\circ - 180^\circ$



Secondary structure:

Local conformation of some part of a polypeptide.

α - helix

β -conformation

β -turns

α helix:

polypeptide backbone tightly wound around an imaginary axis drawn longitudinally through the middle of the helix.

R groups protrude outward from the helical backbone.

Each helical turn includes 3.6 a.a residues.

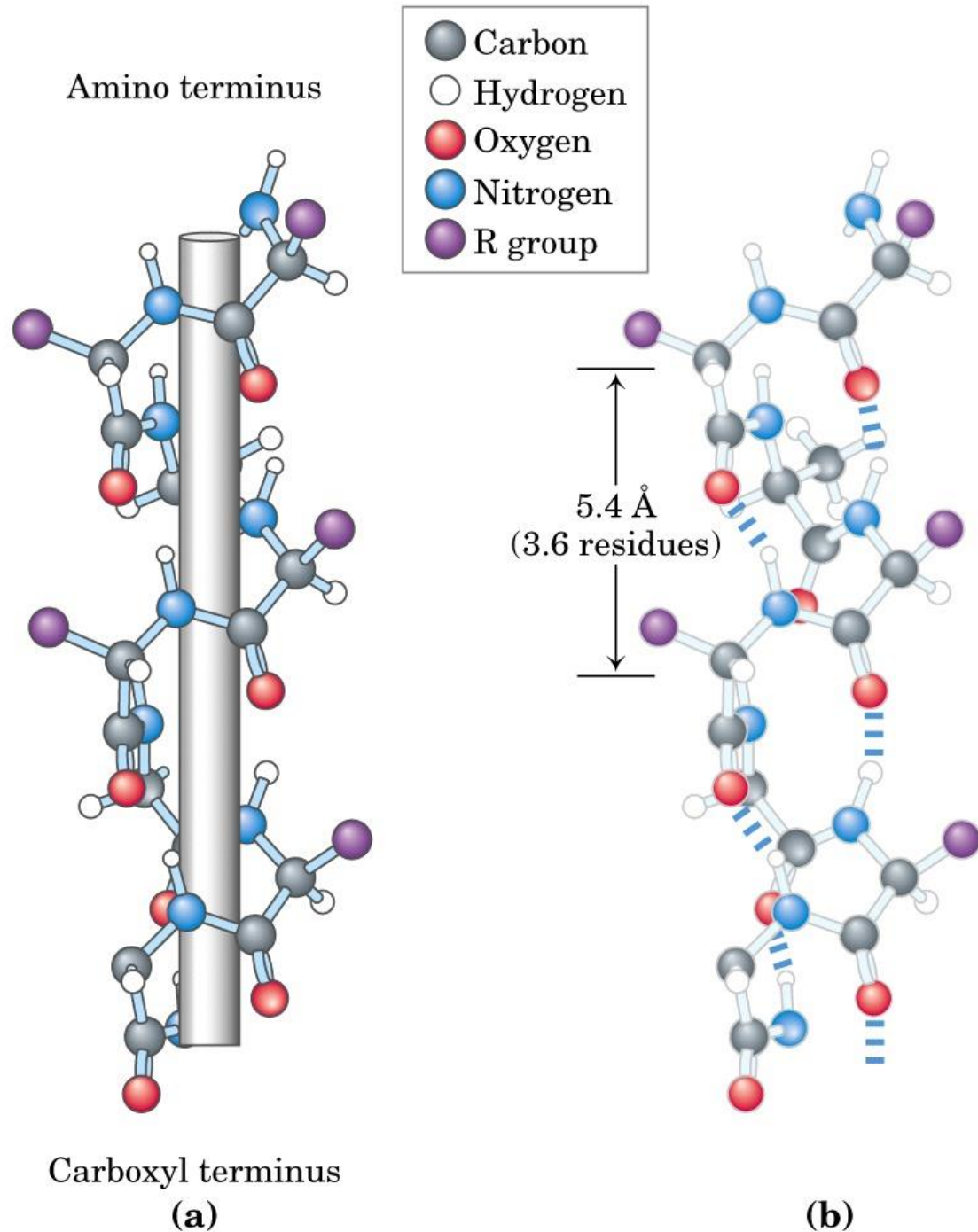
The helical twist of the α helix in all proteins is right-handed.

Models of the α helix :

Right handed helix.

Ball and stick model showing intrachain H-bonds.

The repeat unit in a single turn of the helix 3.6 residues.



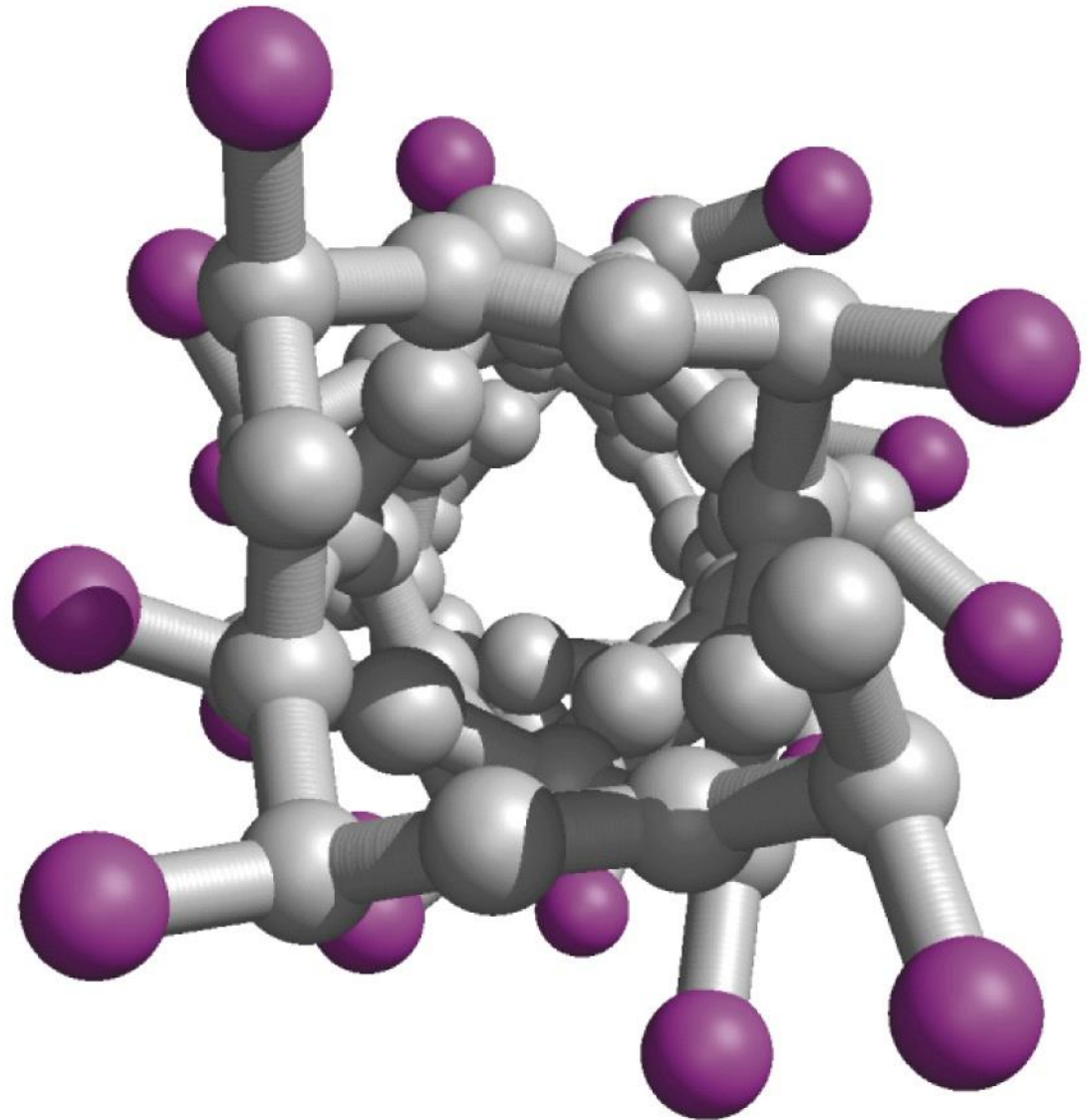
c) A view of the α - helix from one end:

PDB ID 4TNC .

Purple balls = R groups

Ball and stick model gives
false impression that
helix is hollow .

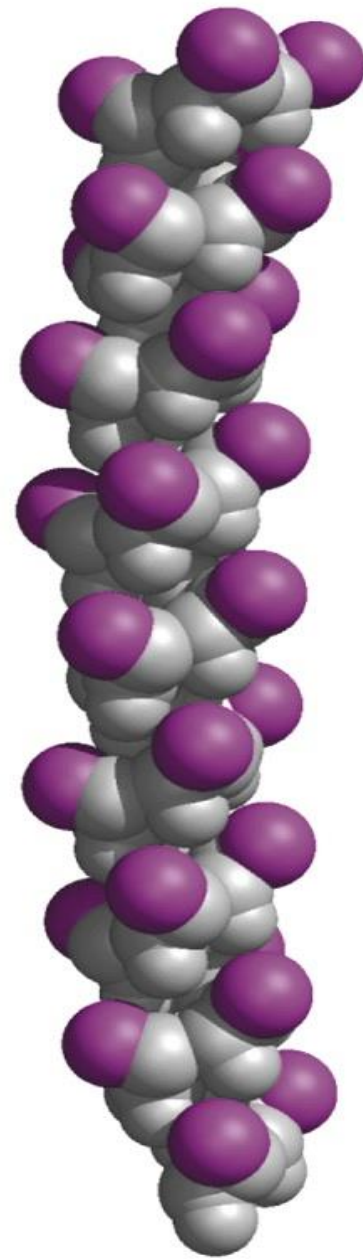
Since the balls don't
represent van der waal
radii of the individual atom.



(c)

Space filling atom:

reveals that atoms in center
are in very close contact.



(d)

a.a sequence affect α -helix stability:

If a polypeptide chain has a long block of Glu residues \rightarrow

-ve charged carboxyl groups of adjacent Glu residues \rightarrow

Strong repulsion \rightarrow no α -helix at pH 7 .

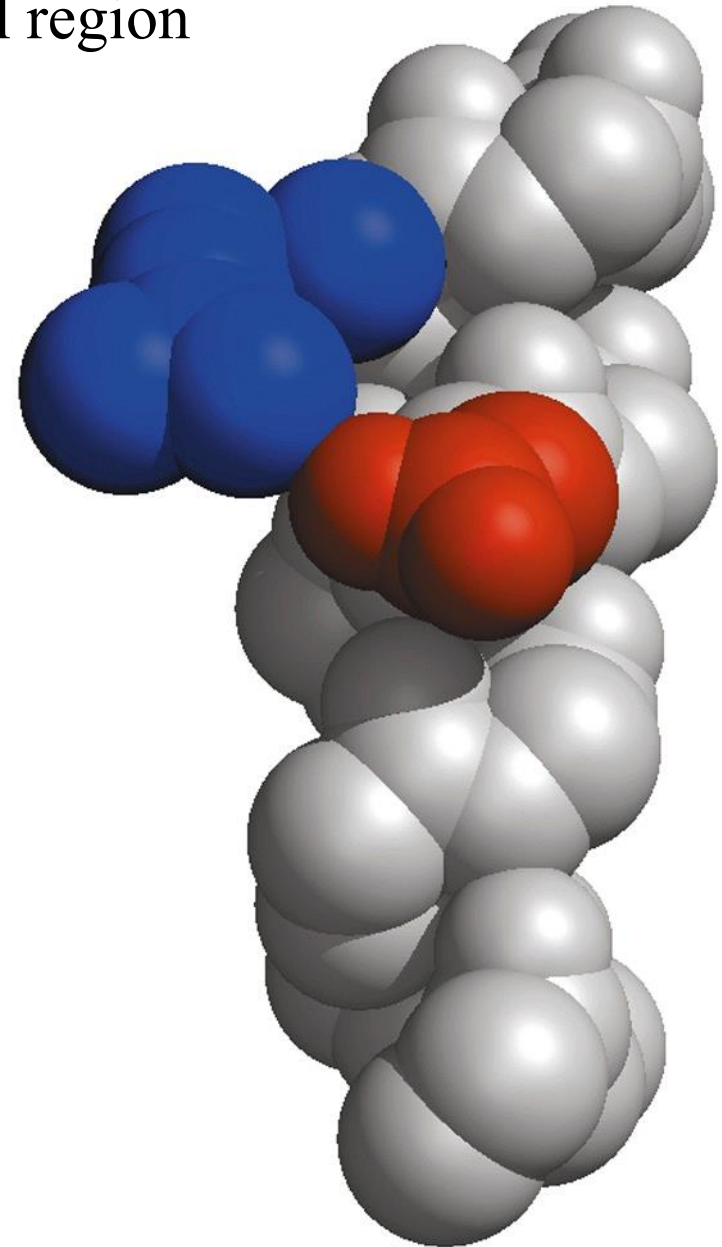
The same for Lys or arginine +ve charge .

Interaction between R groups of amino acids:

Asp 100 (red) and **Arg 103** (blue) in α helical region of protein Troponin C (calcium binding protein associated with muscle).

PDB ID 4TNC

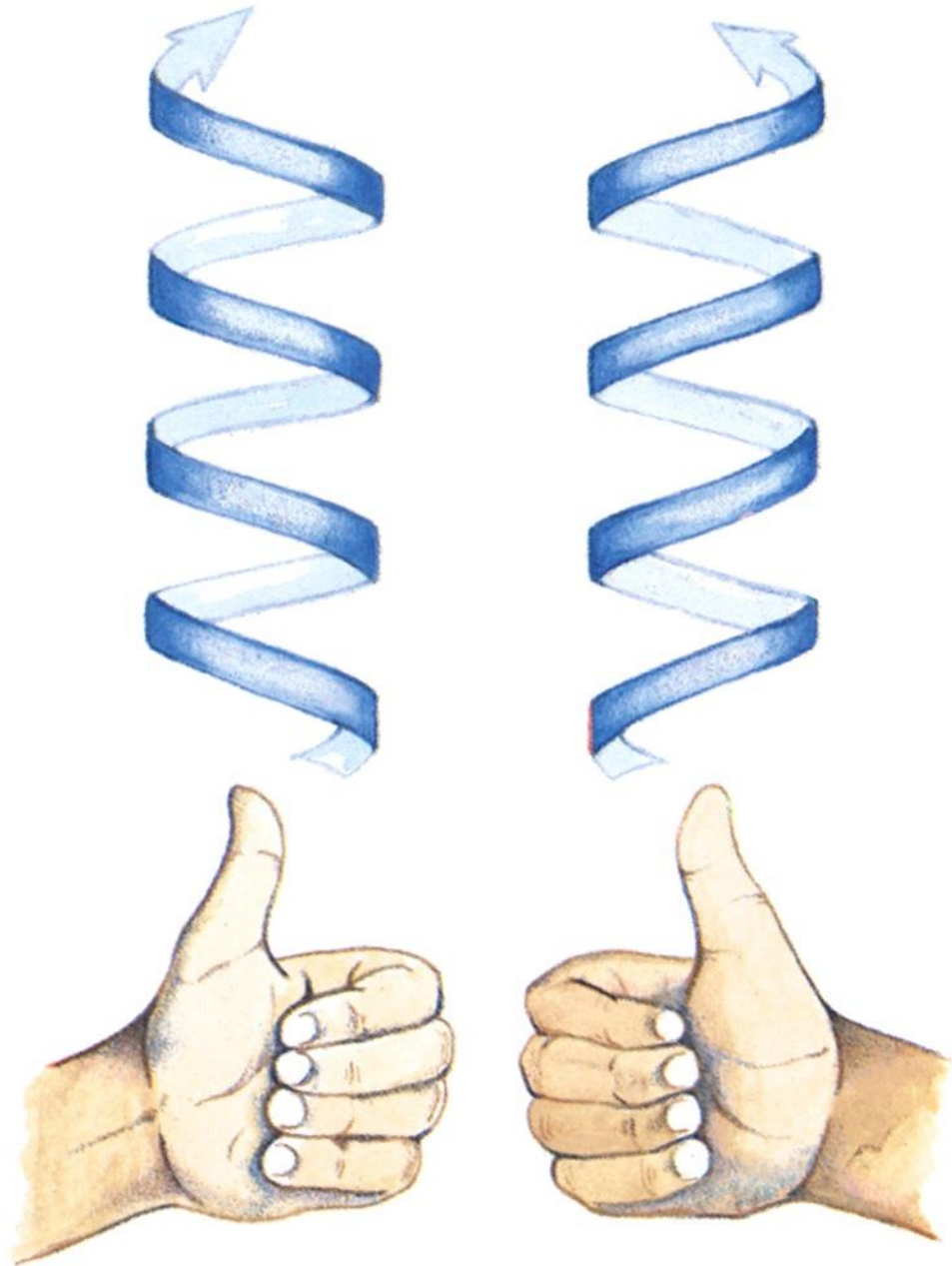
Helix of 13 residue long,
in gray = polypeptide backbone



Right handed or left handed helix ?

Counterclockwise: right-handed

Clockwise : left-handed



Proline residue is constrain in α -helix formation.

Nitrogen atom is part of a rigid ring.

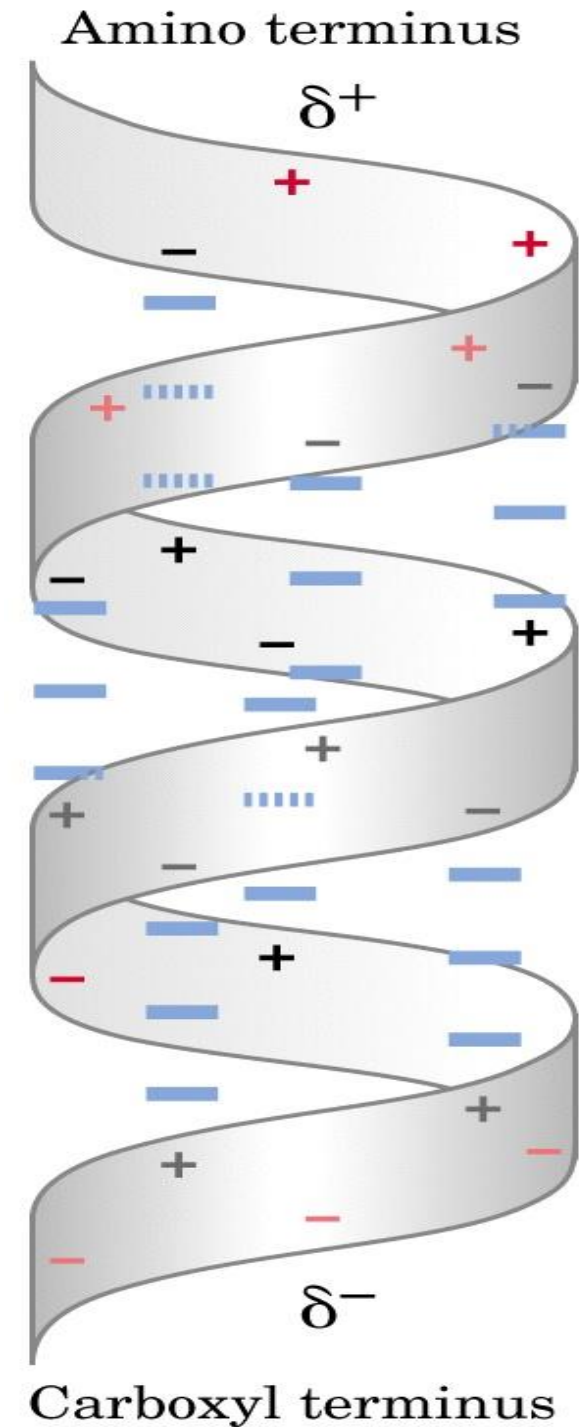
Rotation about N—C α bond is not possible.

Pro induce a kink in α helix \rightarrow destabilizing the helix.

Rarely found in α helix.

Helix dipole :

The electric dipole of a peptide bond transmitted along an α -helical segment through an intrachain H- bonds \rightarrow an overall helix dipole.



Five different kinds of constraints affect α -helix stability:

- 1) Electrostatic repulsion / attraction between successive amino acid residues with charged R groups.
- 2) Bulkiness of adjacent R groups.
- 3) Interactions between R groups spaced 3 / 4 residues apart.
- 4) Occurrence of Gly and Pro residues.
- 5) Interaction between amino acid residues at the ends of helical segment and the electric dipole inherent to the α helix.

β -conformation

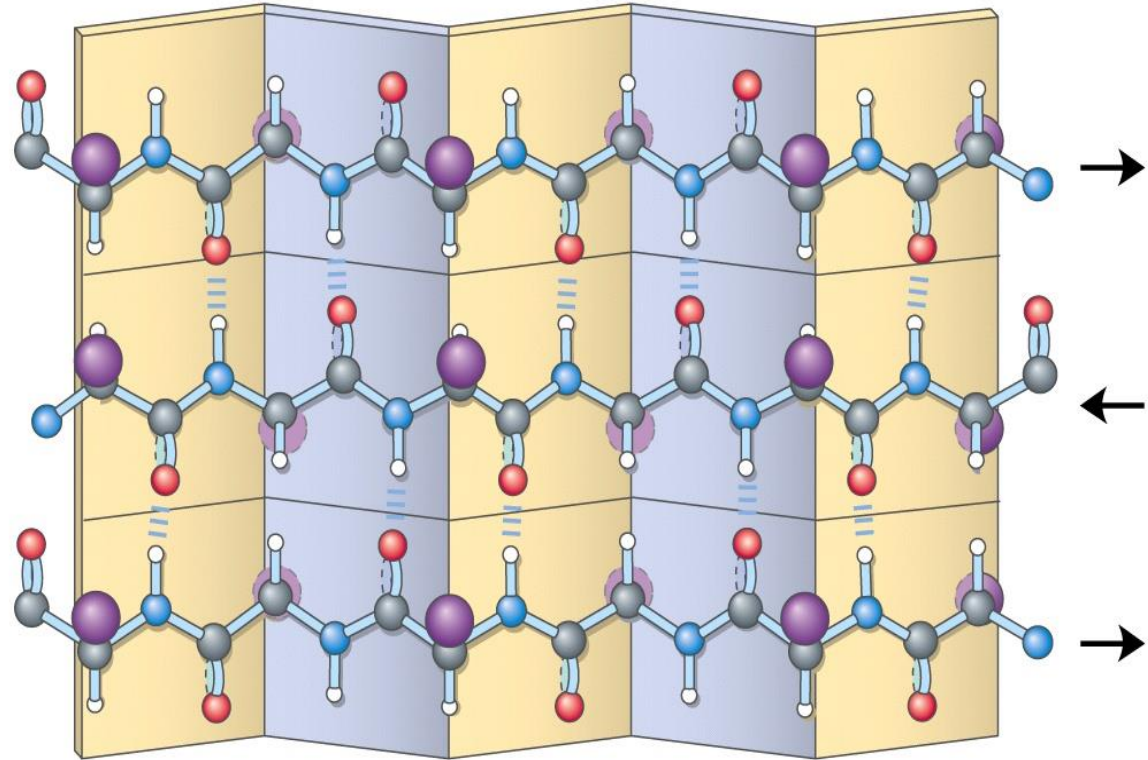
- A more extended conformation of polypeptide chains.
- Polypeptide chain backbone is extended in a zigzag not helical.
- β sheet H-bonds are formed bw adjacent segments of polypeptide chain.
- Rich in Gly, Ala e.g. β -keratins, silk , spider web.

β -conformation of polypeptide chains: β -pleated sheets

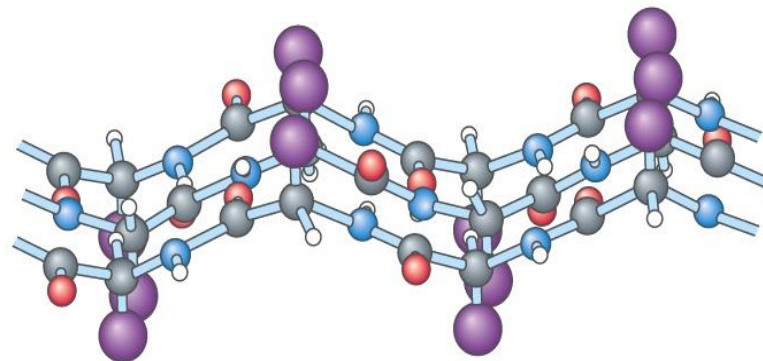
(a) Antiparallel

Antiparallel:
N-terminal to C-terminal orientation of adjacent chains is inverse.

Top view



Side view

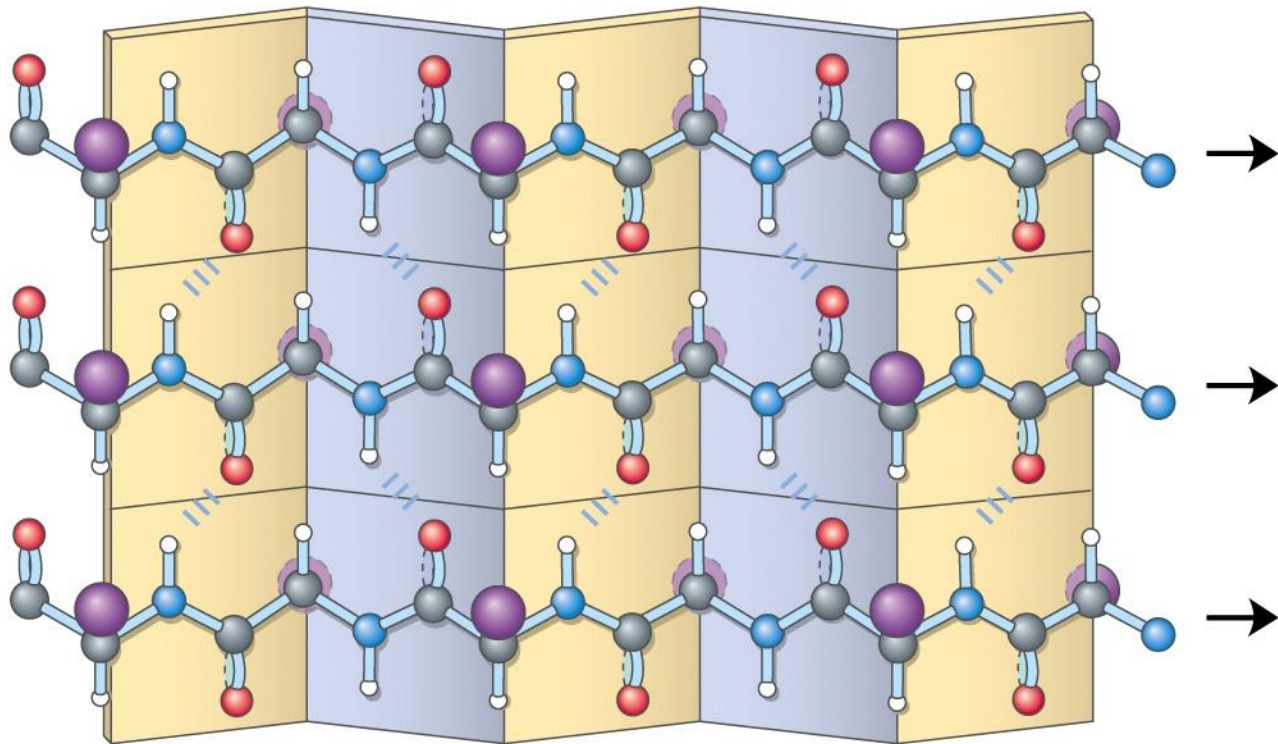


Parallel β -sheet :

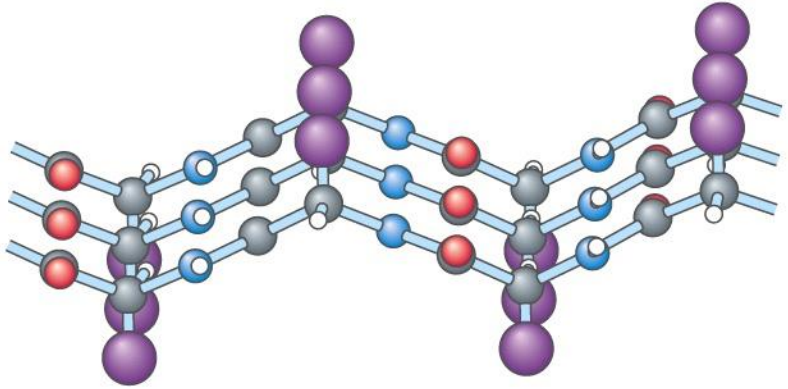
(b) Parallel

H-bonding patterns
are different
than antiparallel.

Top view



Side view



β -turns

In globular proteins with compact structure 1/3 of the a.a residues are in turns /loops where polypeptide chain reverses direction.

β -turns = connecting elements linking successive runs of α helices and β sheets.

Connect the ends of adjacent segments of antiparallel β sheet.

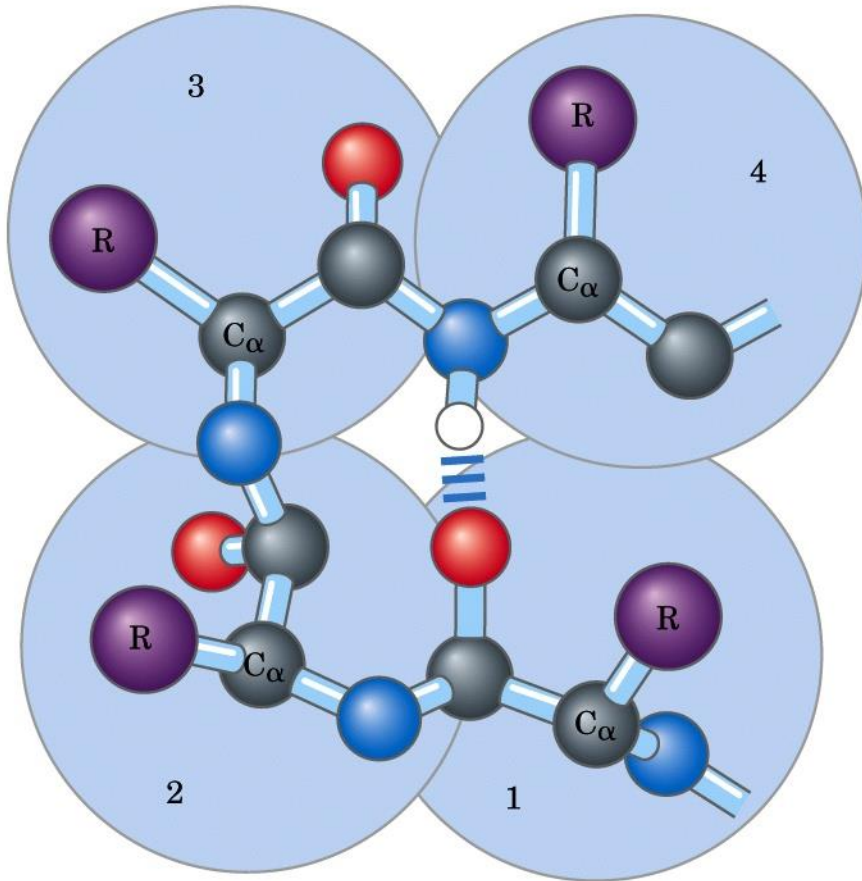
β -structure = 180° turn involving 4 a.a residues.

Structure of β -turns:

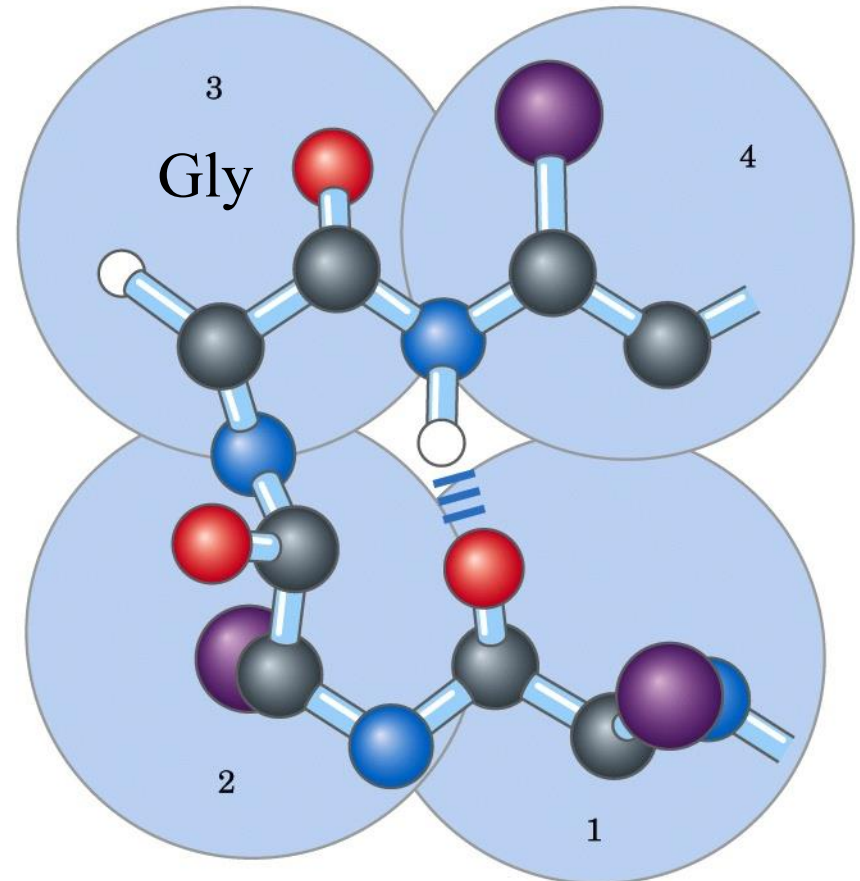
Type I twice as common as type II.

Type II has always Gly as third residue.

The H bond bw 1st and 4th a.a , no H-bonding bw 2nd and 3rd



Type I



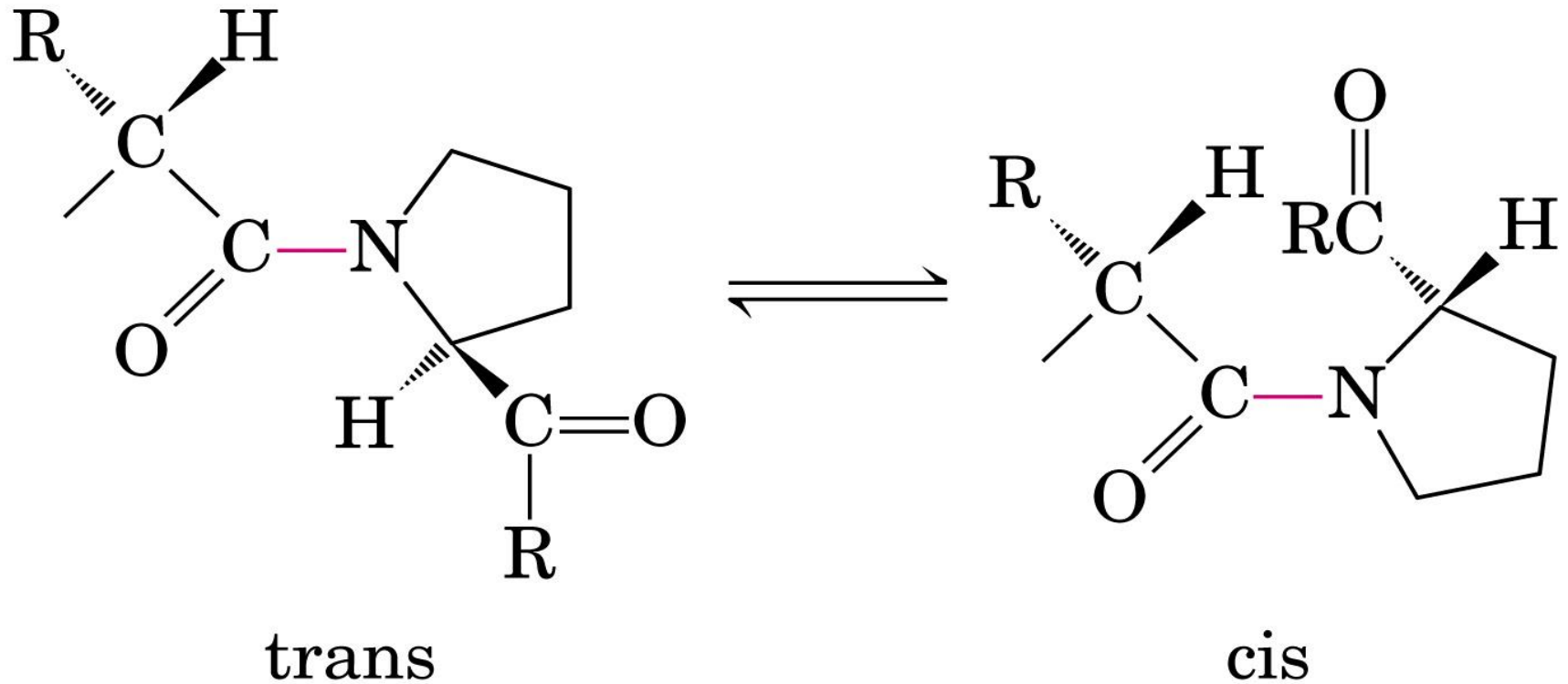
Type II

β Turns
(a)

Trans and Cis isomers of a peptide bond :

Over 99% are in trans.

Gly and Pro residues occur often in β -turn.



Proline isomers
(b)

Secondary structure:

The arrangement of a.a residues in a polypeptide segment. In which each residue is spatially related to its neighbors in the same way.

Tertiary structure:

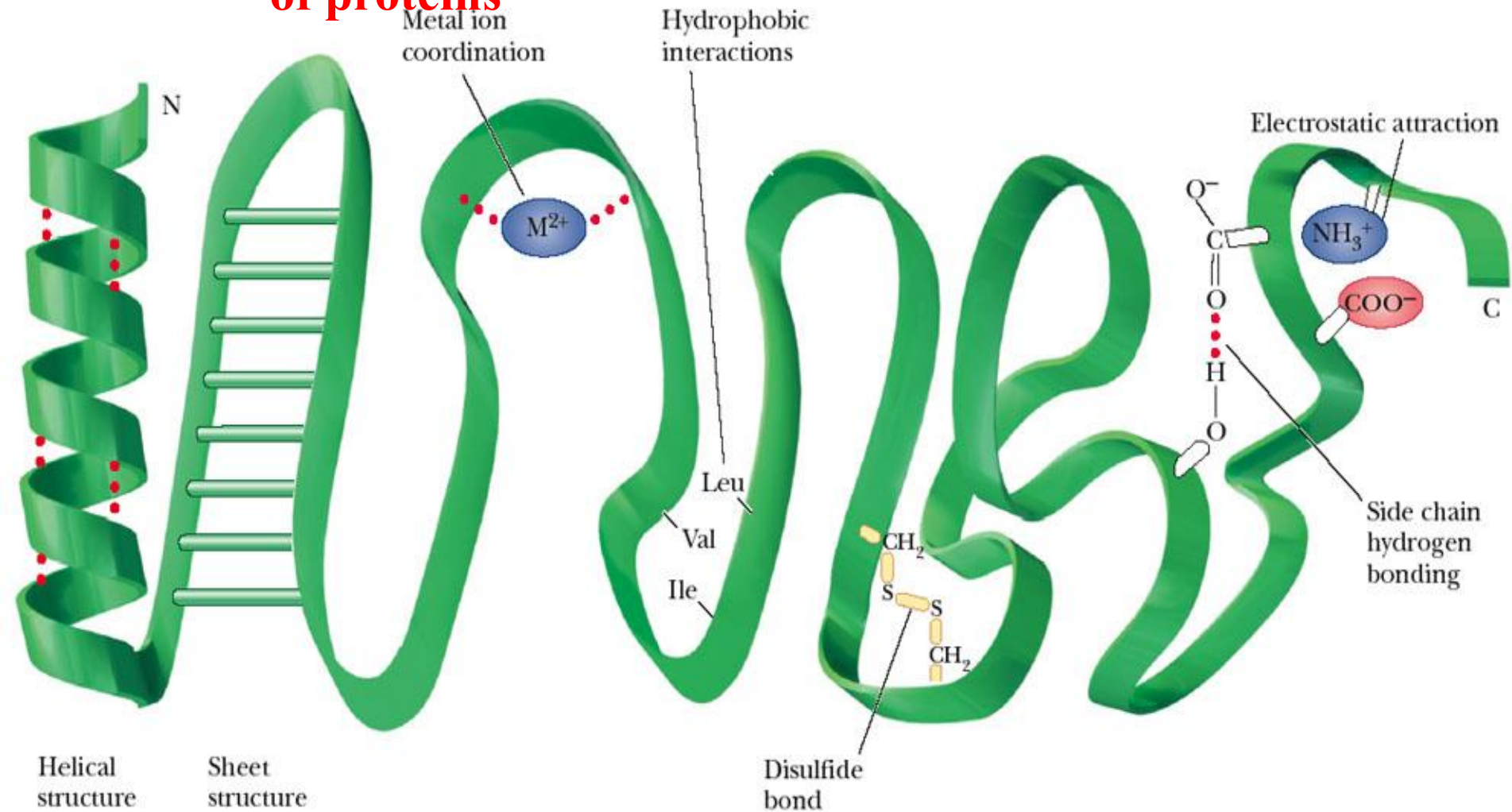
The overall three-dimensional arrangement of all atoms in a protein. Two general structures of protein based on tertiary structure fibrous, globular.

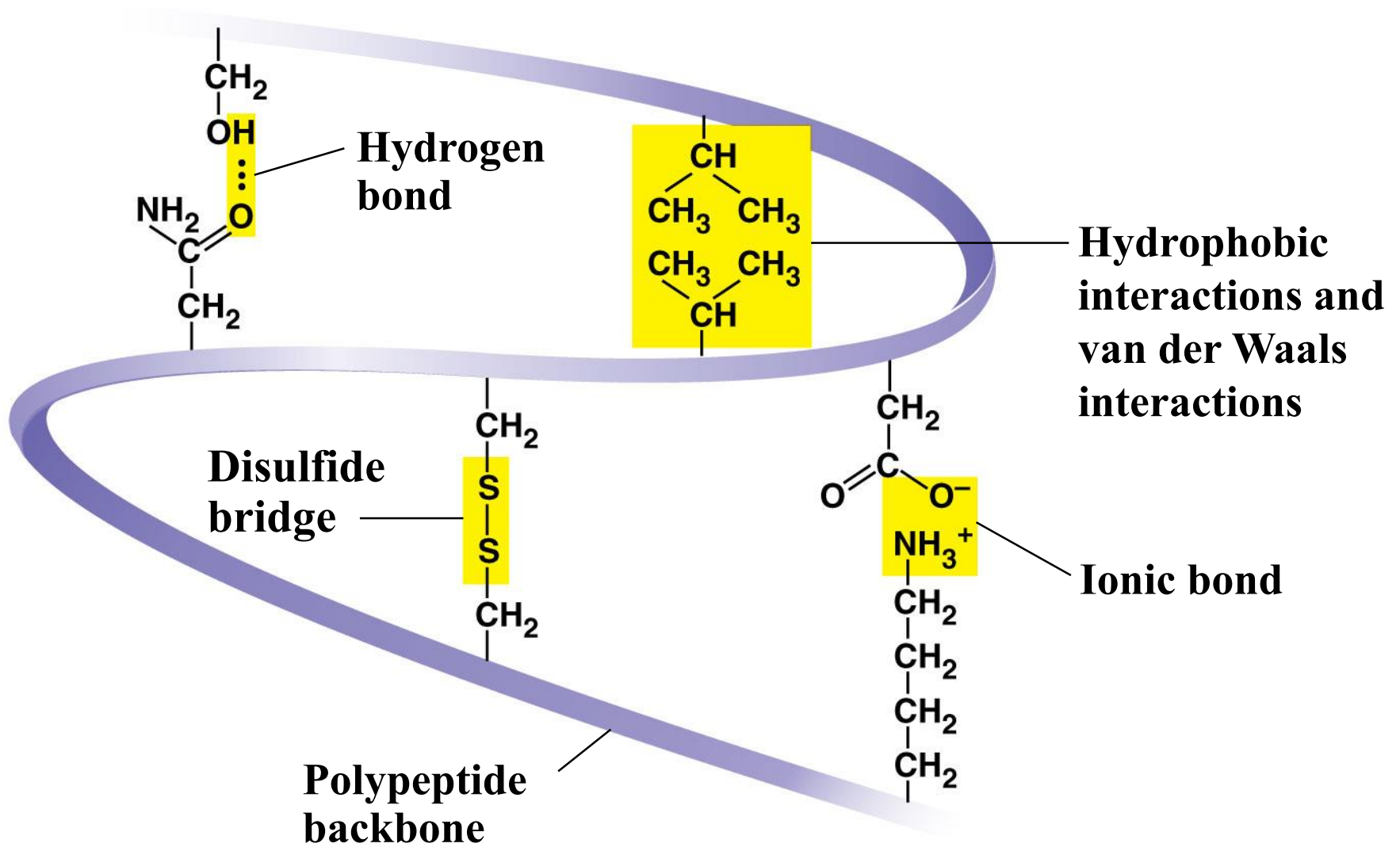
Quaternary structure:

The arrangement of protein subunits / chains in the three dimensional complexes.

Interactions bw the subunits of the multisubunit / multimeric proteins.

Forces that stabilize the tertiary structure of proteins





Protein classification:

1) Fibrous proteins:

polypeptide chains arranged in long strands / sheets.

(single type of 2nd structure) + (provide support, shape, strength,

Globular proteins:

polypeptide chains folded into spherical / globular shape.

(several types of 2nd structure) + (enzymes and regulatory proteins). Water soluble

Fibrous proteins:

α -keratin, collagen, silk fibroin.

- The fundamental structural unit: a simple repeating element of secondary structure.
- All insoluble in water (high conc. hydrophobic a.a. residue in interior and surface of protein).

table 6-1

Secondary Structures and Properties of Fibrous Proteins

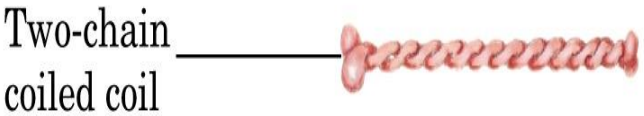
Structure	Characteristics	Examples of occurrence
α Helix, cross-linked by disulfide bonds	Tough, insoluble protective structures of varying hardness and flexibility	α -Keratin of hair, feathers, and nails
β Conformation	Soft, flexible filaments	Silk fibroin
Collagen triple helix	High tensile strength,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

α-keratin : (strength)

- Constitute most of the dry wt. hair, wool, nails, claws, horn, skin.
- Part of larger family intermediate filament proteins (IF), found in cytoskeleton of animal cells, all have structural functions.

Structure of Hair :

Elongated right handed α-helix



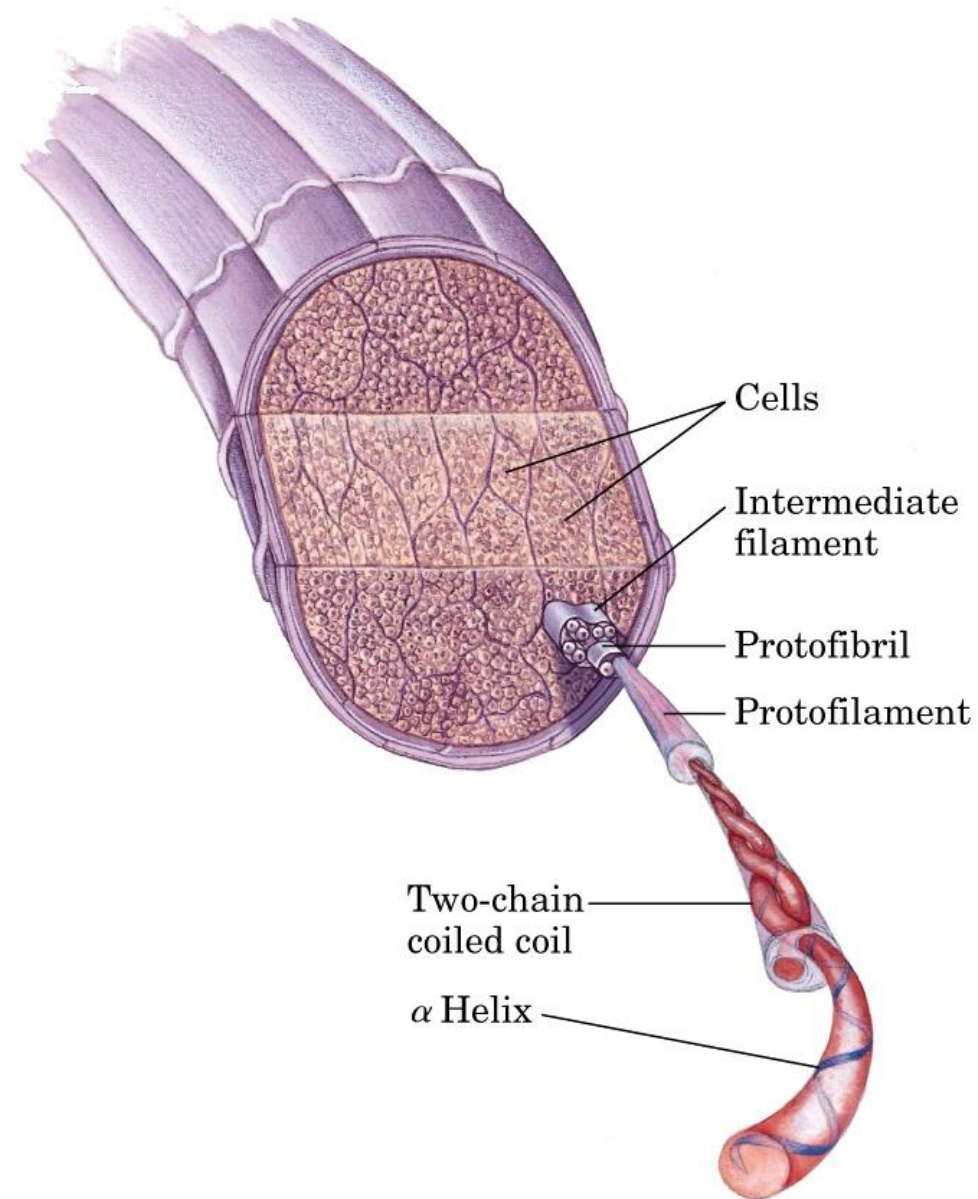
(a)

Hair:

an array of many α -keratin filaments / many coiled coils.

The surfaces where the two helices touch are made by hydrophobic a.a residues, R groups meshed together in interlocking pattern. Permitting close packing of the polypeptide chains.

α -keratin is rich in hydrophobic residues Ala, Val, Leu, Ile, Met and Phe.



Cross section of a hair
(b)

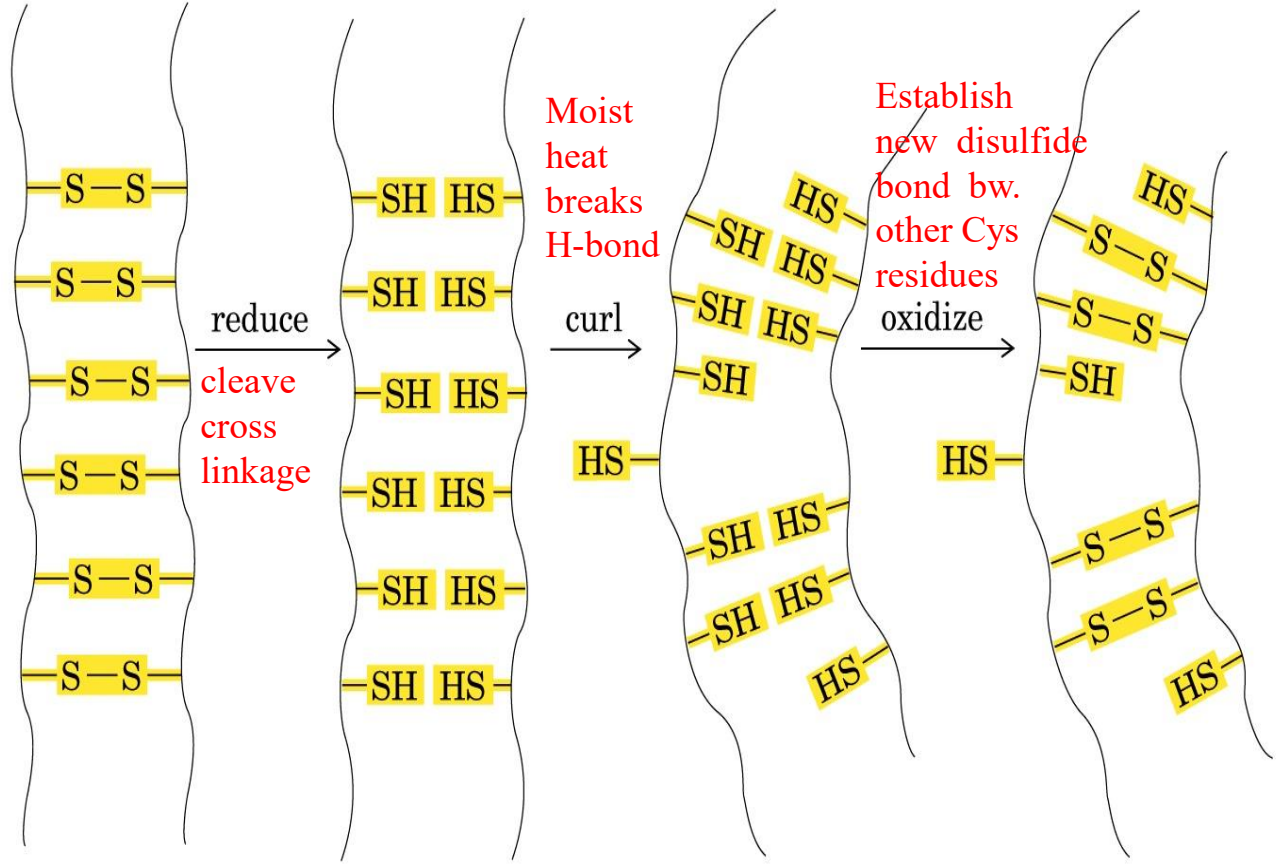
Strength of fibrous proteins enhanced by covalent cross links bw polypeptide chains within the multihelical ropes.

Stretchability

the basis of permanent waving.

Heat stretches the hair.

A permanent wave is not really permanent since hair grows replacing old.



Collagen:

-Found in connective tissue cartilage
(bone matrix).

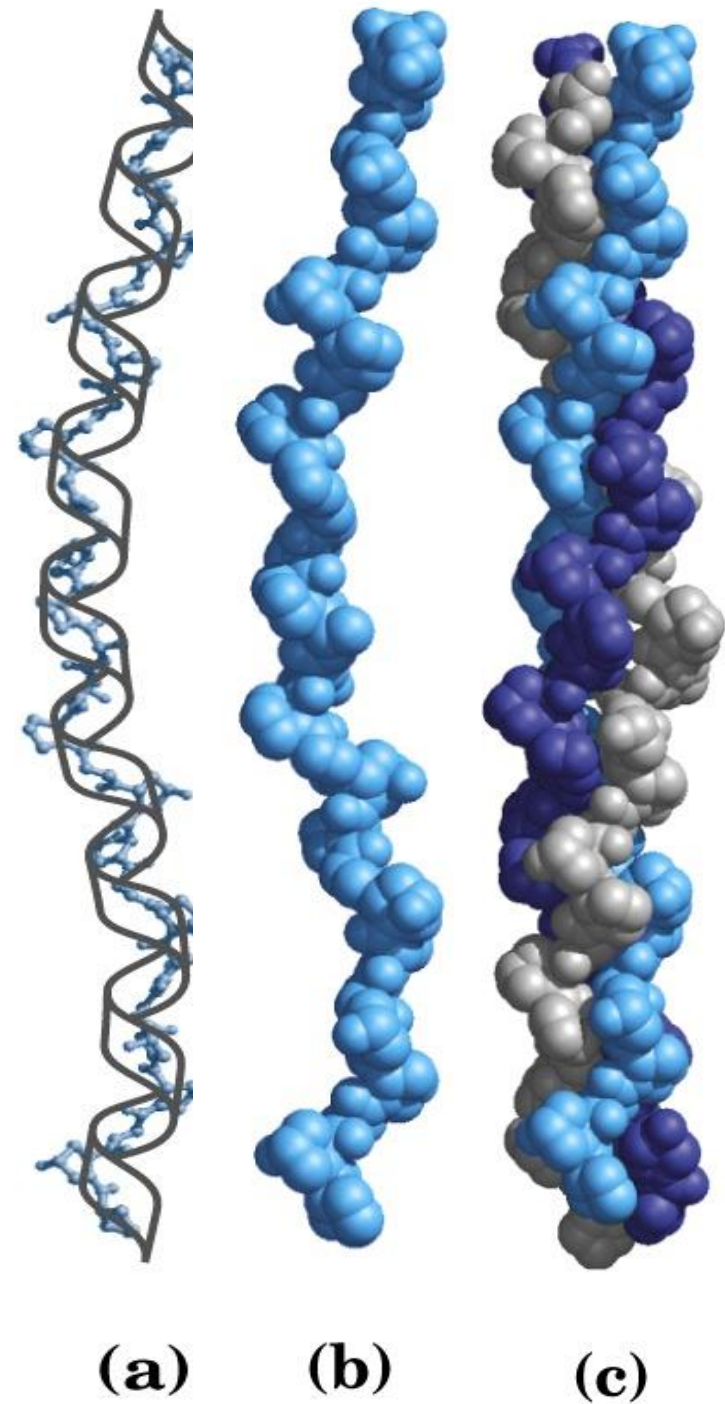
-Left handed, 3 a.a per turn. Coiled coil (3
separate polypeptide chains called α chains.

a) α chain with repeating secondary structure
of the tripeptide Gly-X-Y repeats

X often Pro, Y often 4-Hyp

b) Space filling model.

c) Three of the helices.



Ball stick model:

Three stranded collagen superhelix from end. Gly = red

Center is not hollow, but very tightly packed

Gly cant be replaced for its role

in the collagen triple helix.

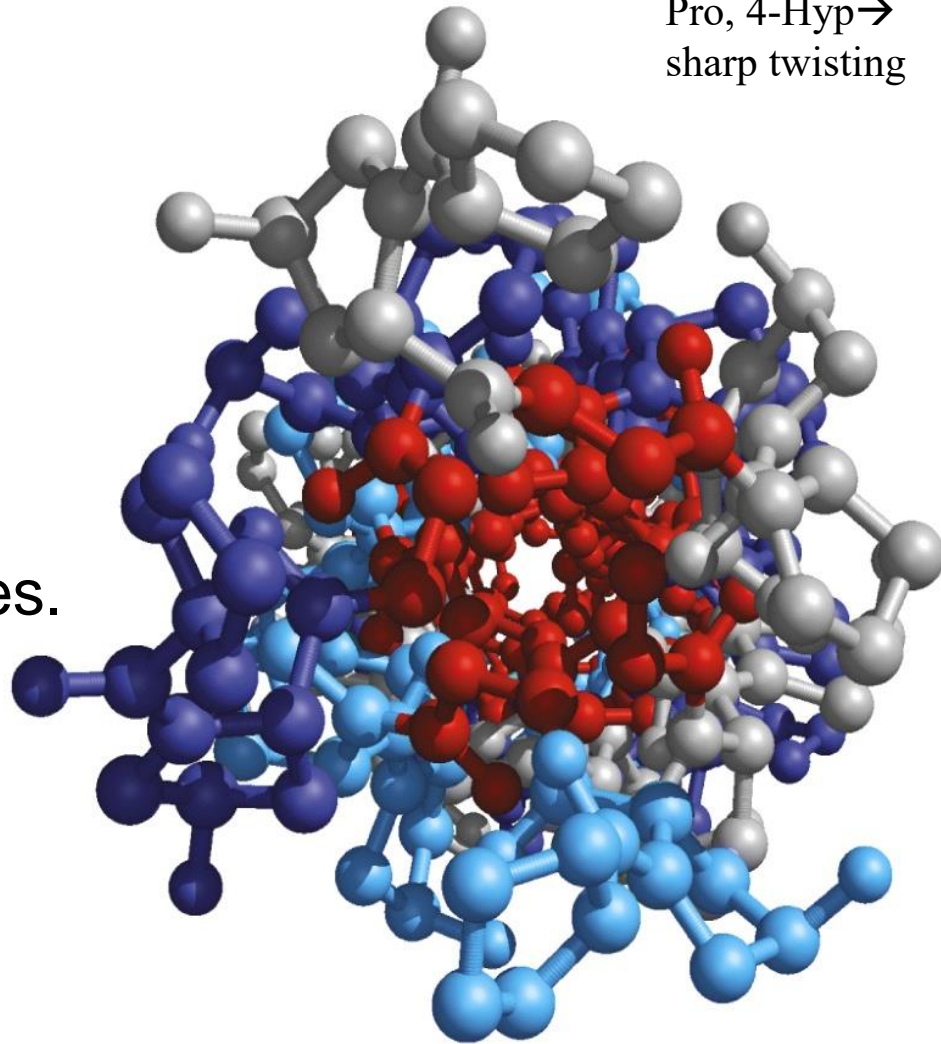
Substitutions with a.a (larger R , Cys

or Ser

Osteogenesis imperfecta →

abnormal bone formation in babies.

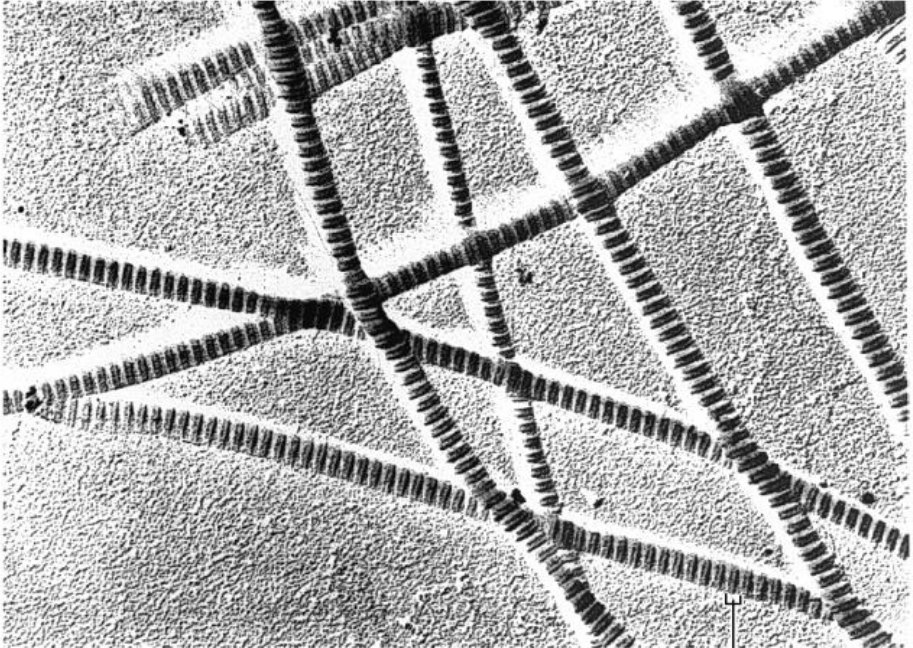
Pro, 4-Hyp →
sharp twisting



(d)

Structure of Collagen fibrils:

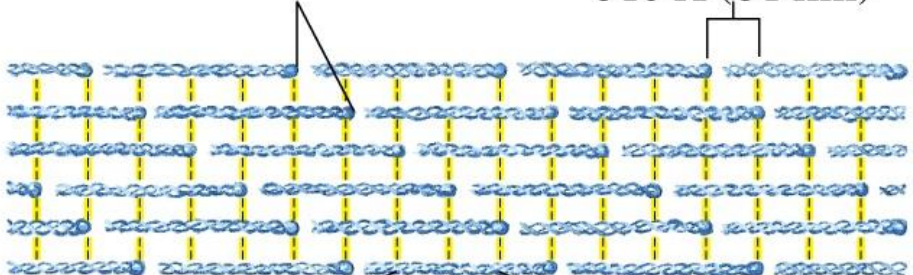
- Collagen a rod-shaped molecule.
- Three helically intertwined α -chains with different sequences.



250 nm

Heads of collagen molecules

Cross-striations
640 Å (64 nm)



Section of collagen molecule

Scurvy:

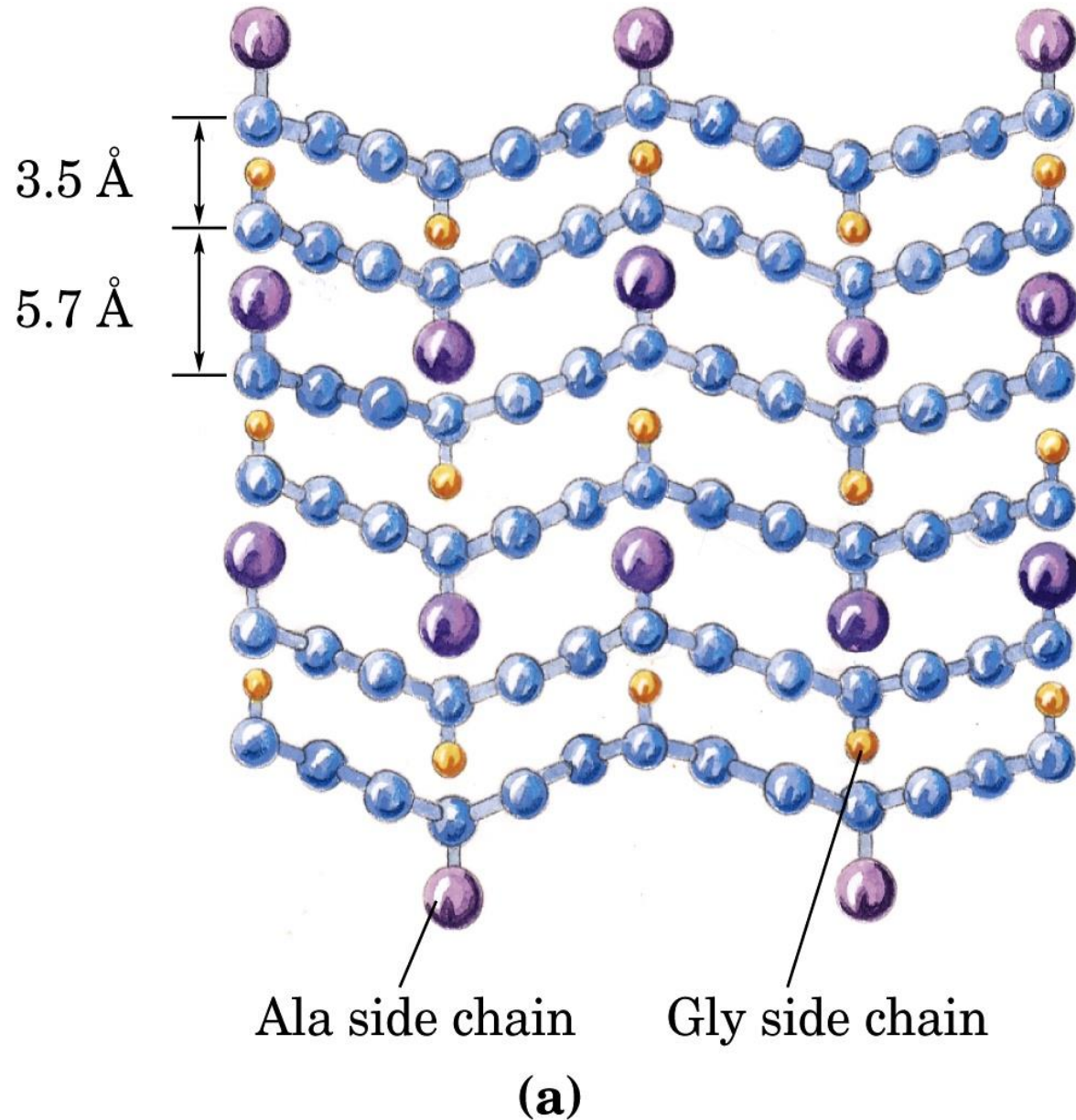
- Lack of Vitamin C / ascorbic acid.
- Required for hydroxylation of Pro / Lys in collagen.
- Inability to hydroxylate the pro at Y position when Vit C is absent
→ collagen instability and connective tissue problem.
-

Silk fibroin:

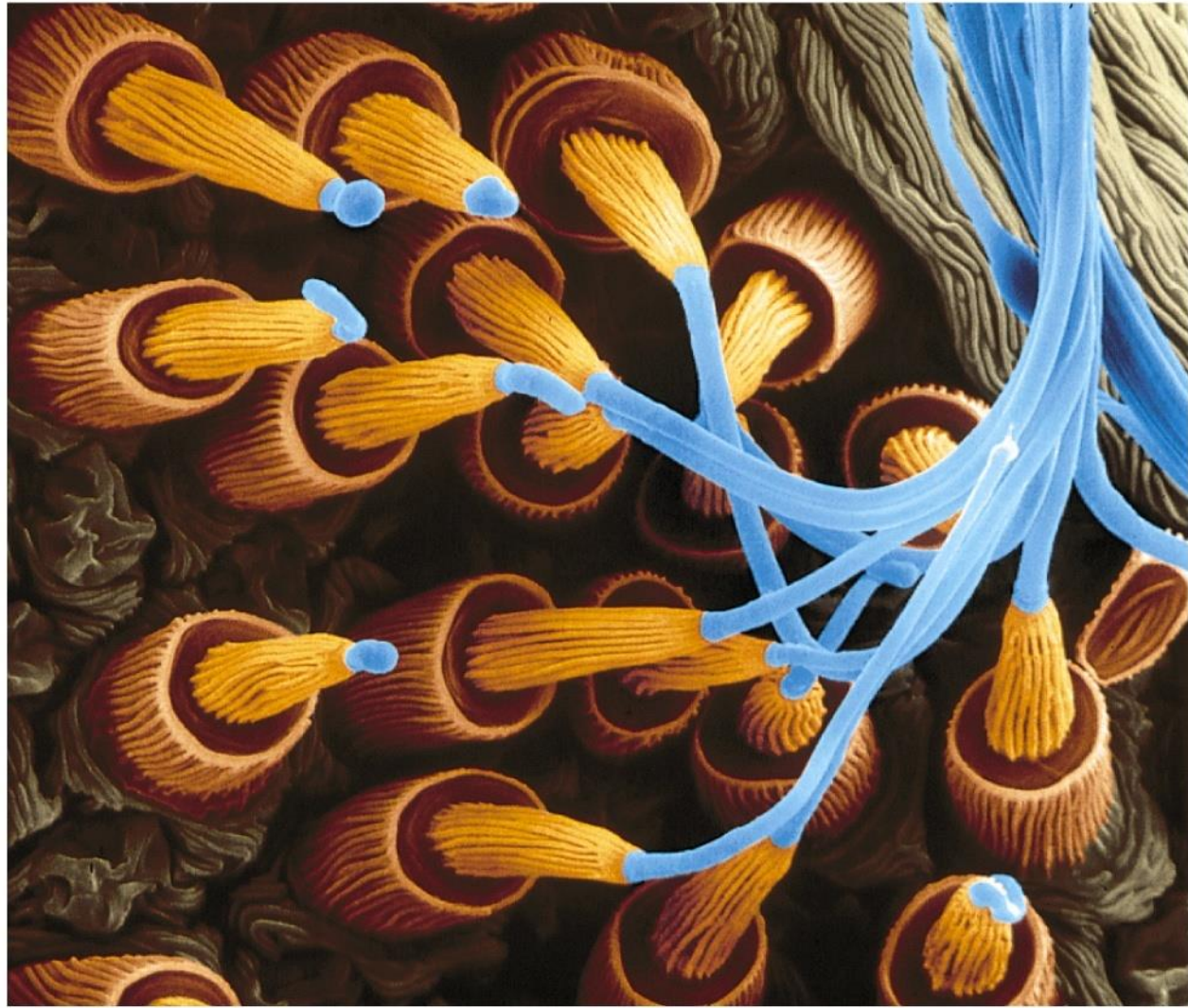
- Produced by insects and spiders.
- Polypeptide chains in β -conformation.
-

Structure of silk:

Fibroin consist of layers of anti parallel β -sheets



Fibroin strands emerging from spinnerets of a spider (colorized electron micrograph)



70 μm

(b)