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Fundamentals of Biochemistry

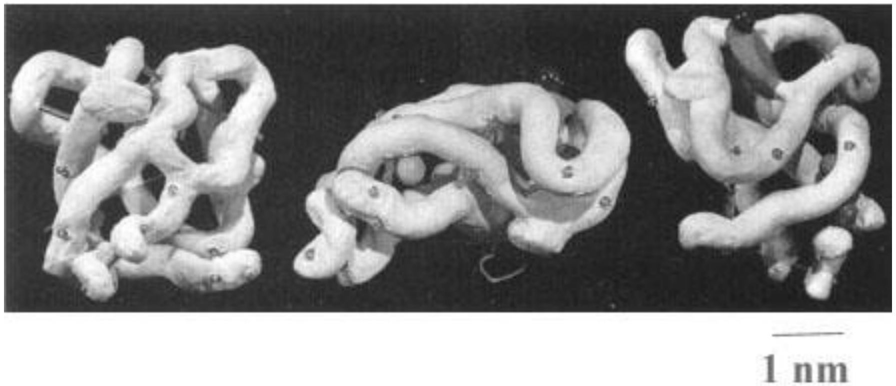
Second Edition

Chapter 6:

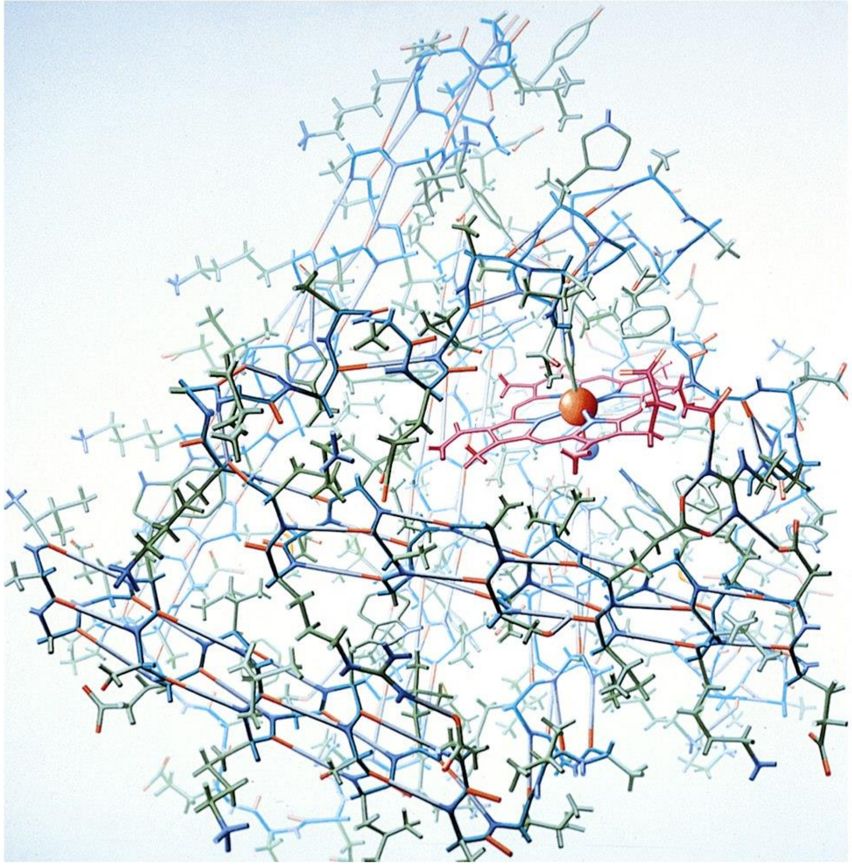
Proteins:

Three-Dimensional Structure

1958, John Kendrew



Any regularity?



Chapter 6 Opener Fundamentals of Biochemistry, 2/e

The atomic structure of myoglobin as a stick model

A sequence of amino acids to a stable functional 3D form

Levels of protein structure

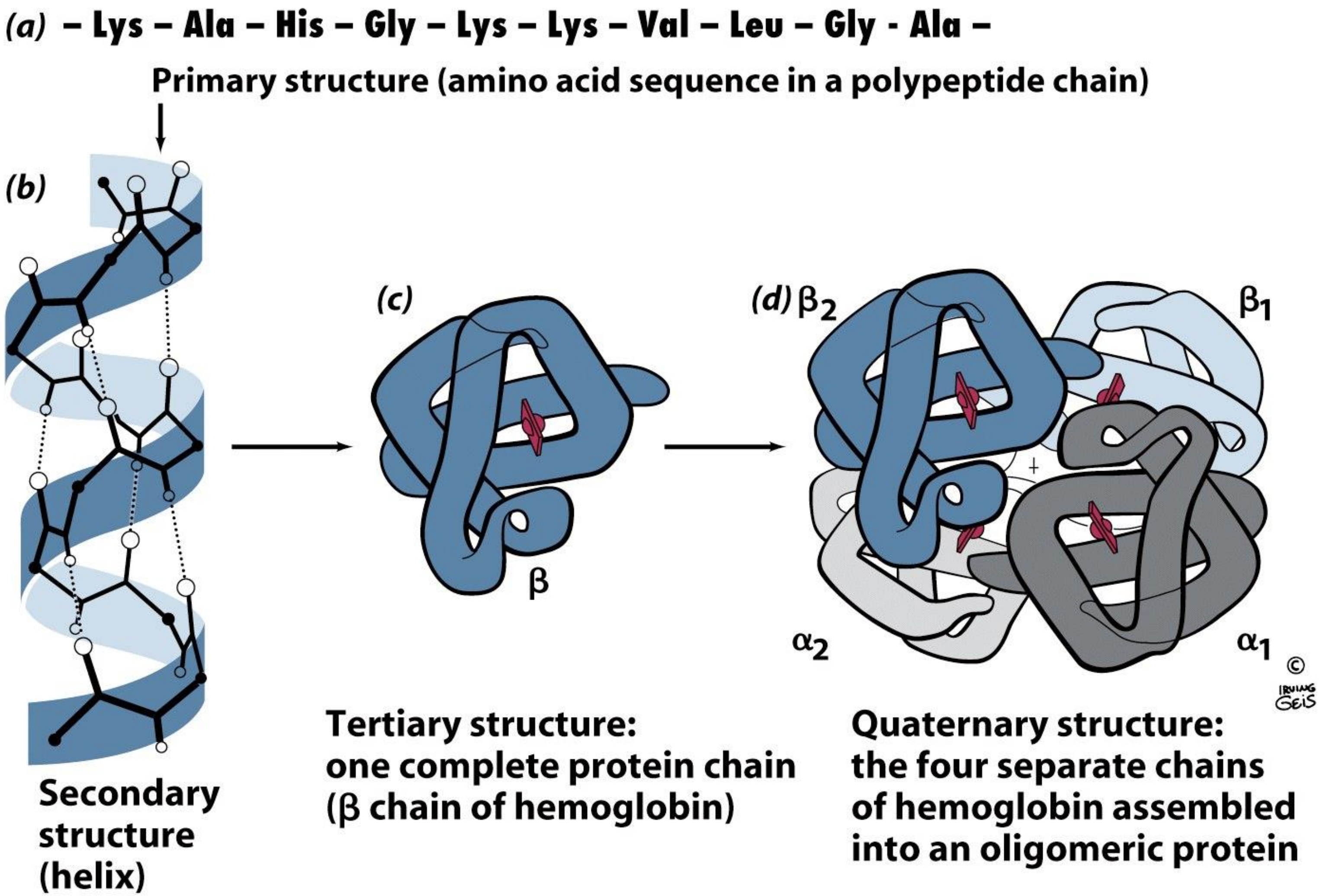
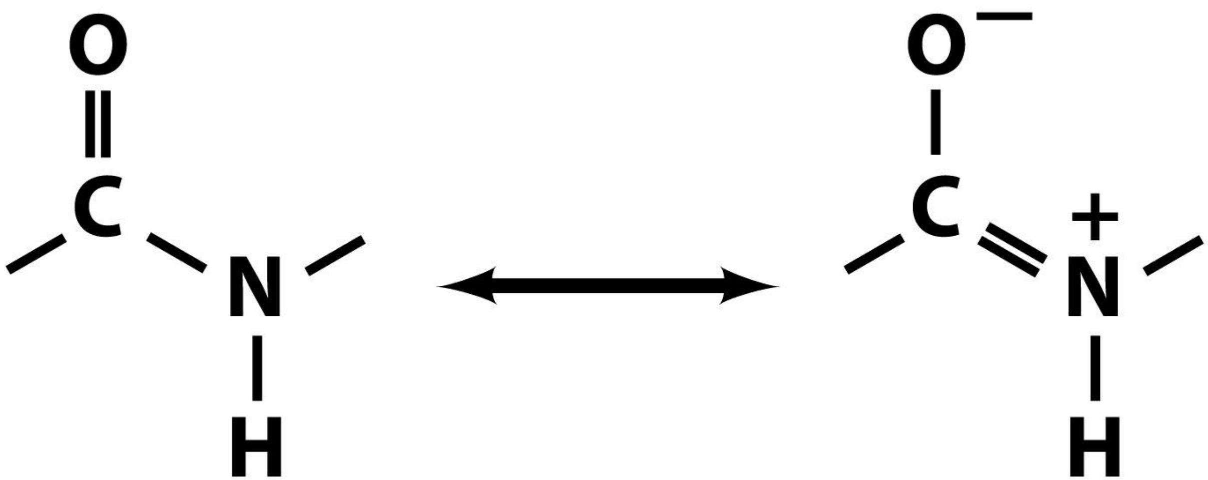


Figure 6-1 Fundamentals of Biochemistry, 2/e

Secondary structure

The peptide group: a rigid planar structure
trans conformation



Unnumbered figure pg 131 Fundamentals of Biochemistry, 2/e

~40% double bond character: due to resonance interactions:

C-N bond is 0.13 Å shorter than its single bond

C=O bond is 0.02 Å longer than that of aldehydes and ketones

Trans conformation: more stable than cis conformation

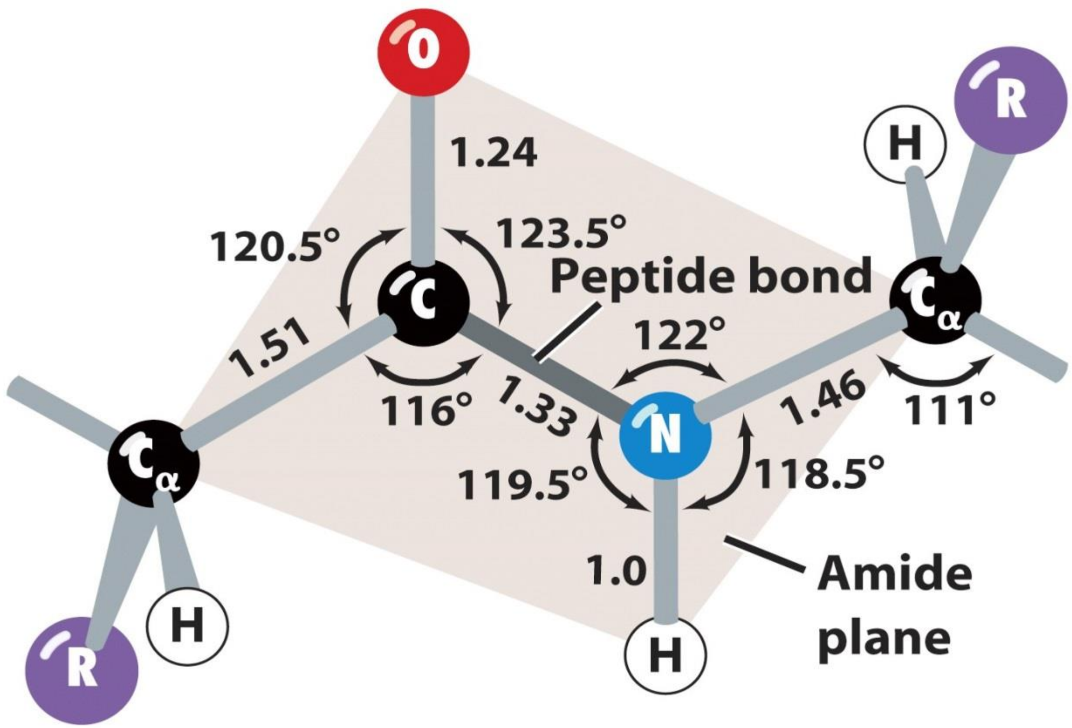


Figure 6-2 Fundamentals of Biochemistry, 2/e

Extended conformation of a polypeptide main chain: backbone

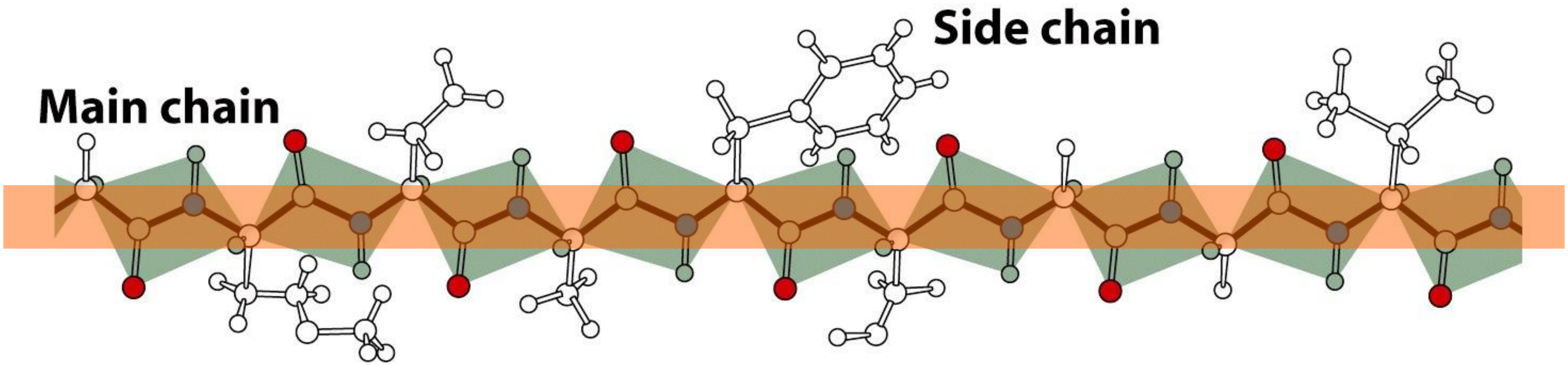


Figure 6-3 Fundamentals of Biochemistry, 2/e

The conformation of the backbone by rotation angles around the Cα-N bond and the Cα-C bond

Torsion angles of the polypeptide backbone

the Cα-N bond (Φ) 180º

the Cα-C bond (Ψ) 180º

The angles increase when rotated clockwise as viewed from Cα

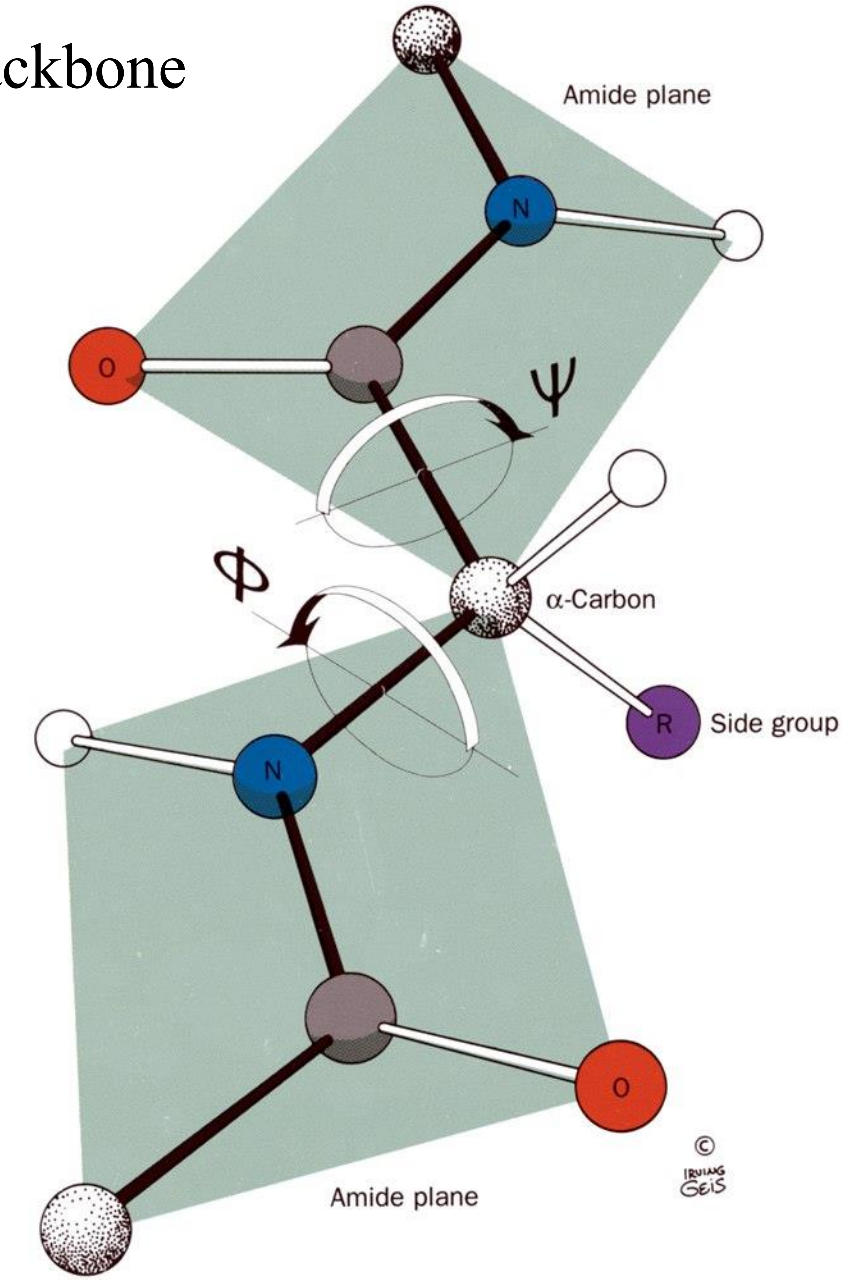


Figure 6-4 Fundamentals of Biochemistry, 2/e

Steric interaction between adjacent peptide groups

Conformational freedom is restricted

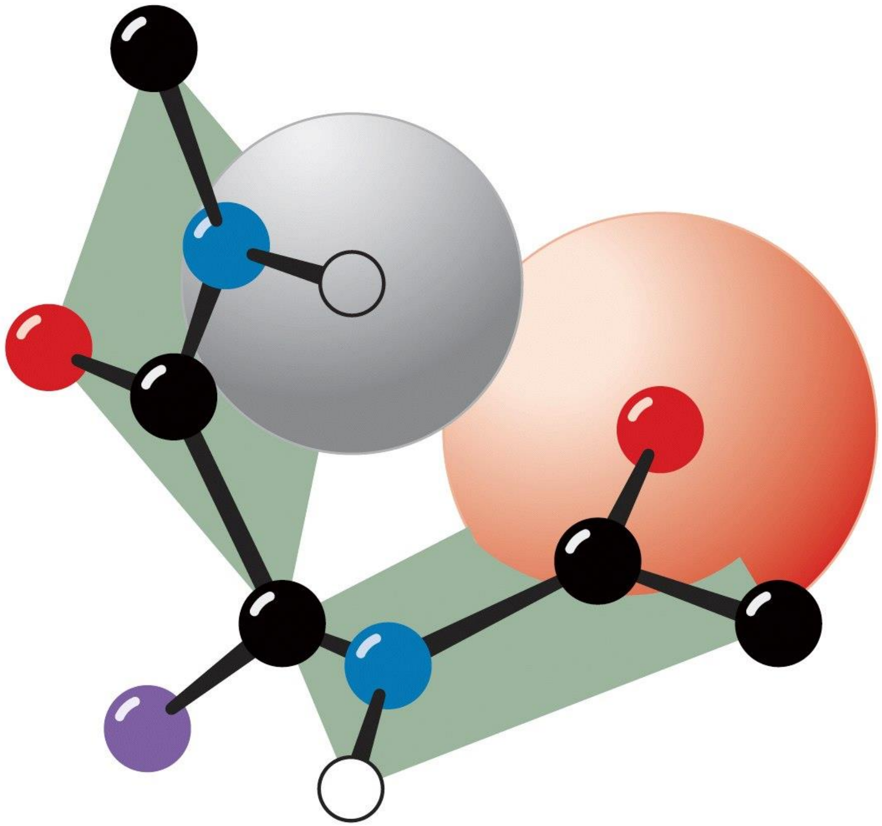


Figure 6-5 Fundamentals of Biochemistry, 2/e

The Ramachandran diagram

Calculation of sterically allowed angles/observed angles in the proteins

Blue: sterically allowed angles for all residues except Gly and Pro
Green: extreme limits for unfavorable atomic contacts
Orange circles: conformational angles of secondary structures

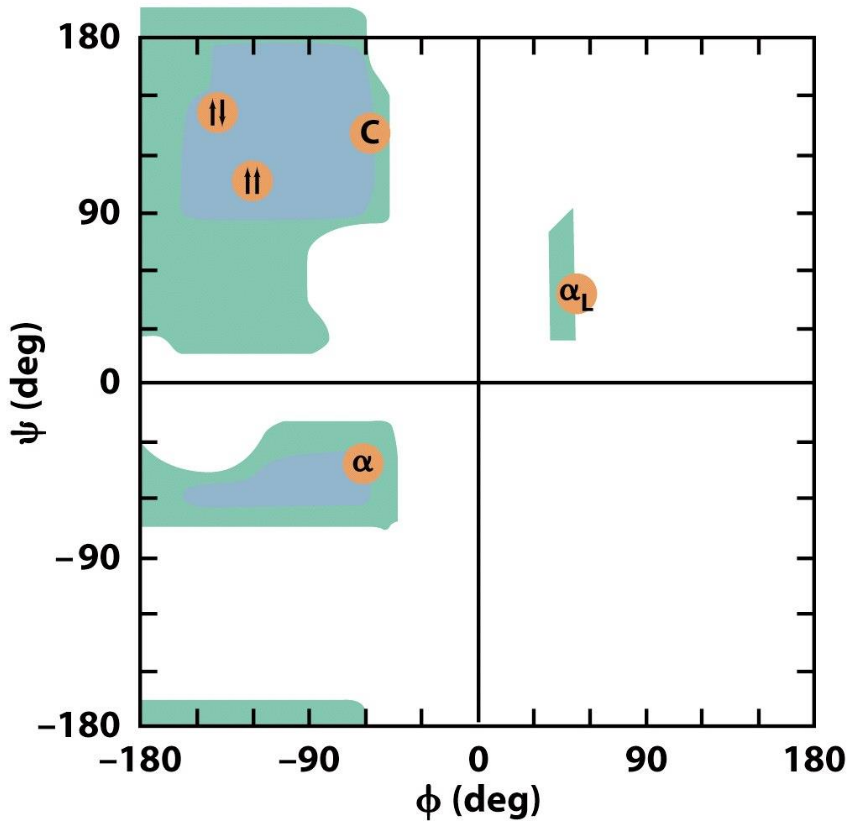
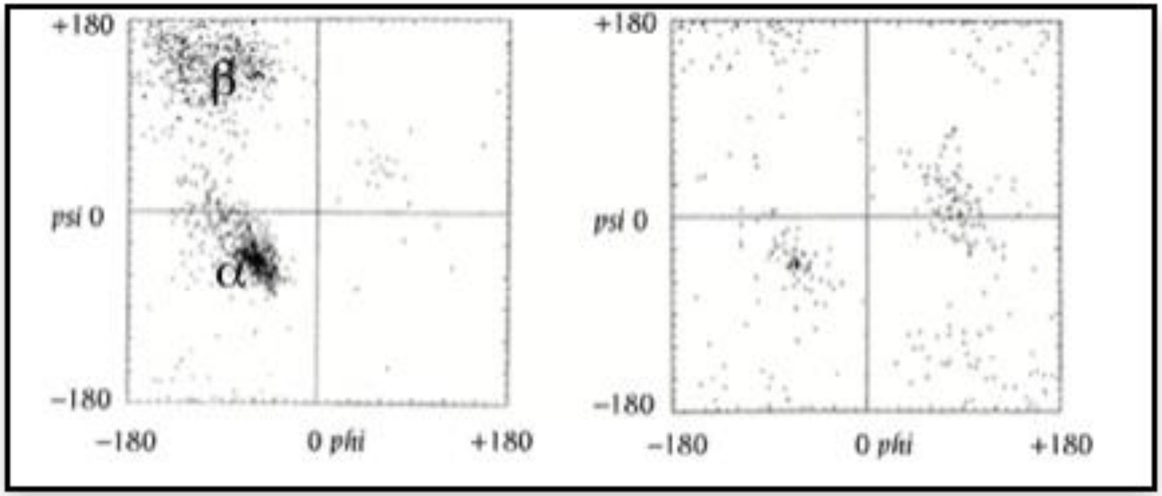
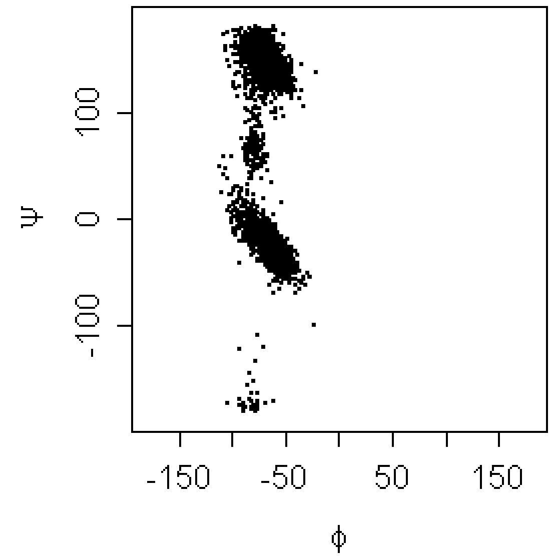


Figure 6-6 Fundamentals of Biochemistry, 2/e

Gly


+180
β
psi 0
α
−180
−180
0 phi
+180
+180
psi 0
−180
−180
0 phi
+180

Proline


100
0
-100
ψ
-150
-50
50
150
ϕ

Regular secondary structure

- α helix
- β sheet
- turns

The α helix

- right handed helical
- 3.6 residues/turn
- 1.5 Å/residue
- 5.4 Å/turn (pitch)
- diameter: 12 Å

- intra chain H bonds
- C=O of the nth residues
- N-H of the (n+4)th residue

- side chains project outward

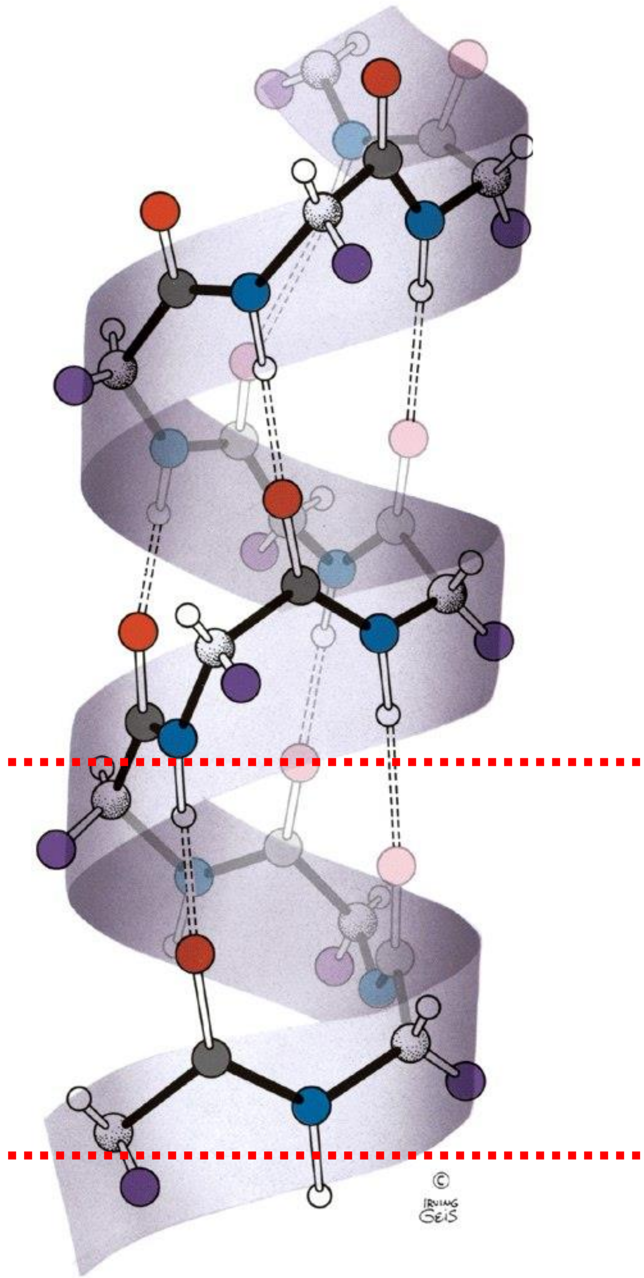


Figure 6-7 Fundamentals of Biochemistry, 2/e

Space-filling model of α helix

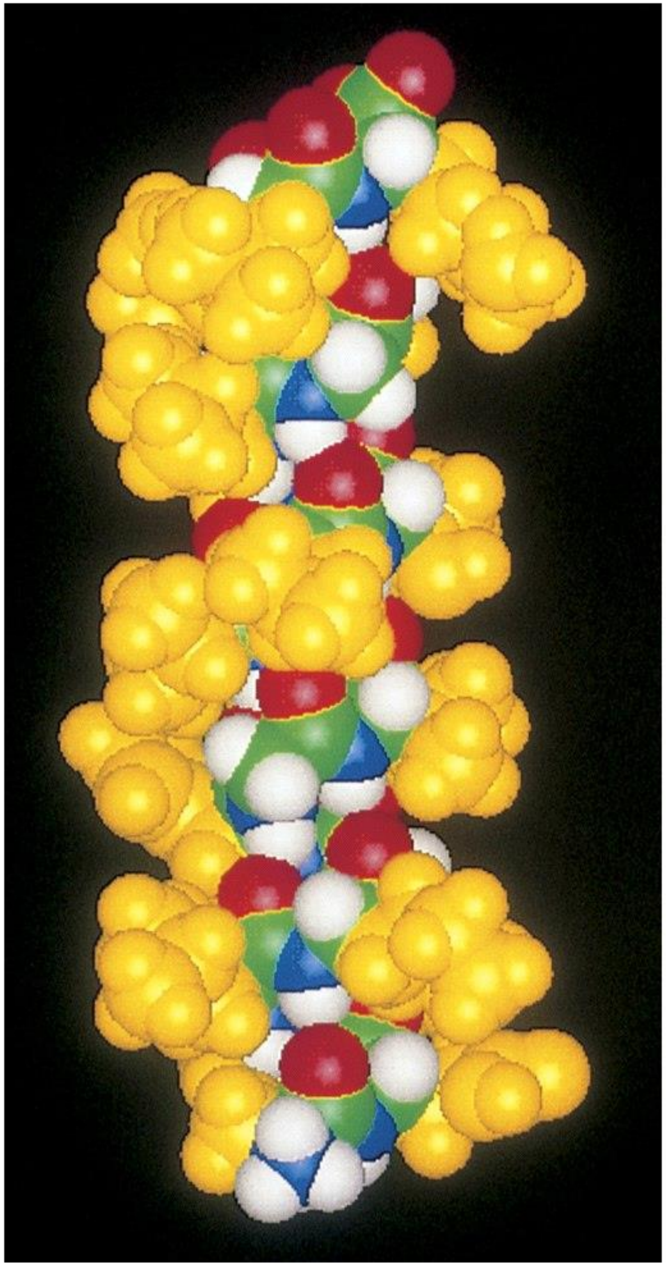


Figure 6-8 Fundamentals of Biochemistry, 2/e

β sheets

extended structure: pleated sheets

inter chain H bonds

H-bond difference

Antiparallel is more stable than parallel

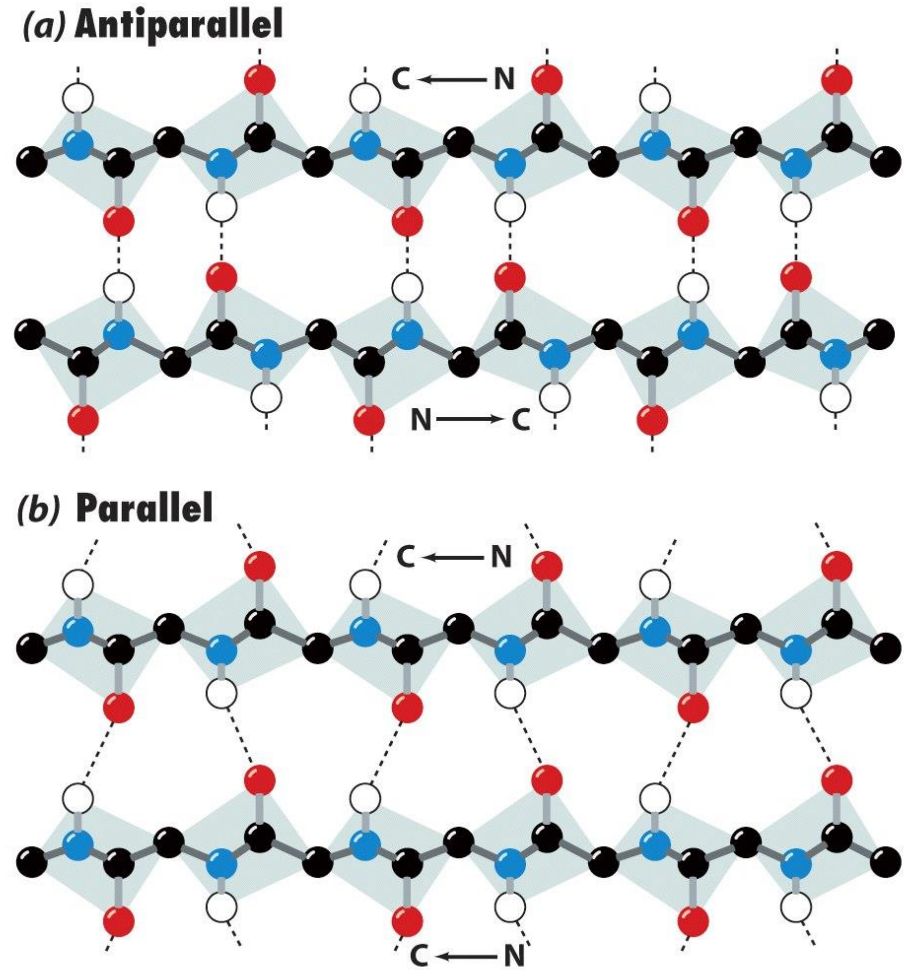


Figure 6-9 Fundamentals of Biochemistry, 2/e

Pleated appearance
(not fully extended)

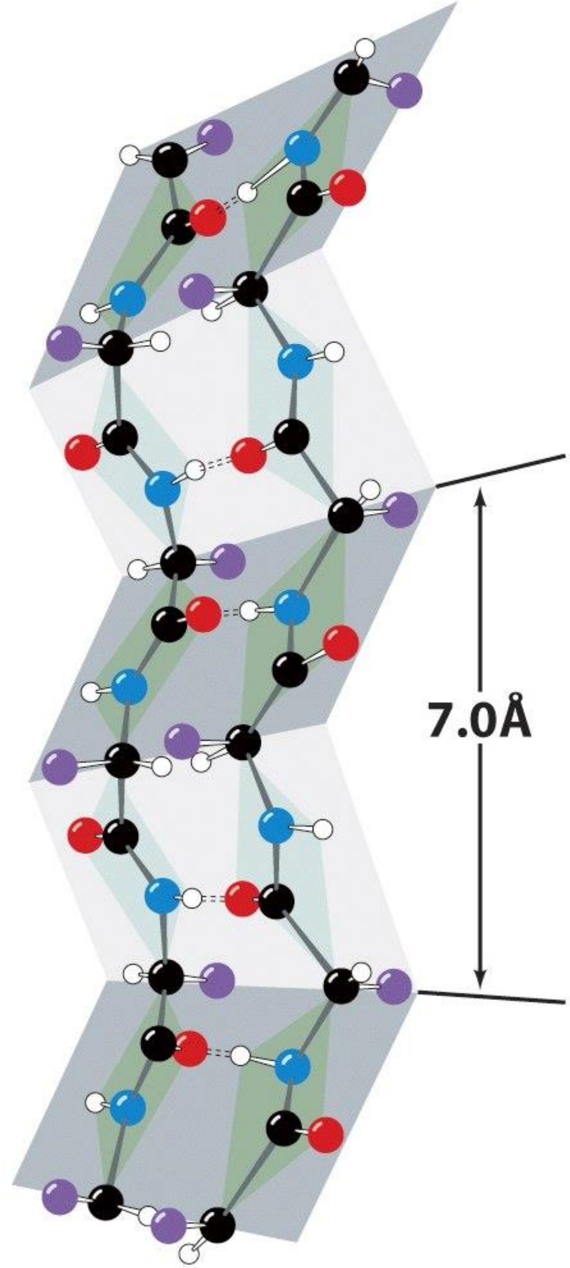


Figure 6-10 Fundamentals of Biochemistry, 2/e

Space filling model

average of 6 strands

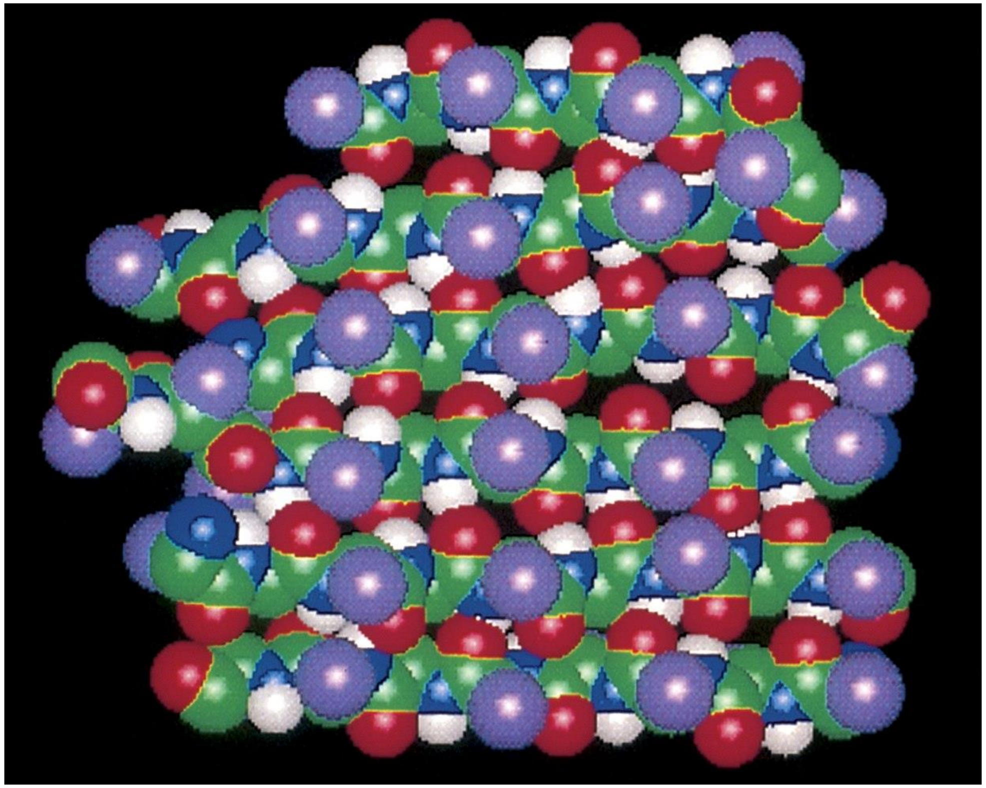
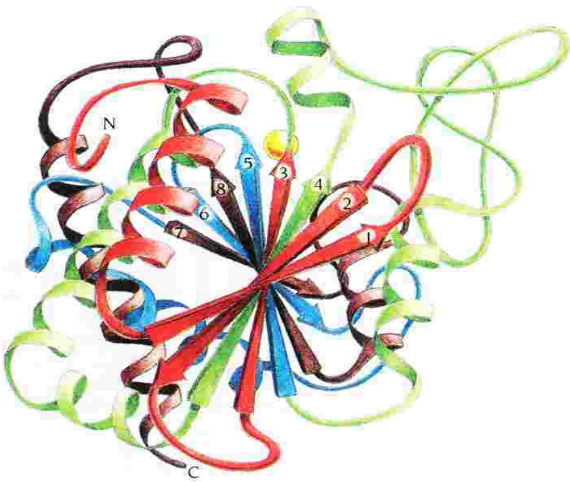
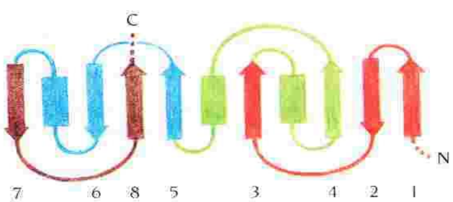


Figure 6-11 Fundamentals of Biochemistry, 2/e

Diagram of a β sheet in bovine carboxypeptidase A

Mixed: parallel and antiparallel
Right-handed twist
Complex topology (connectivity)





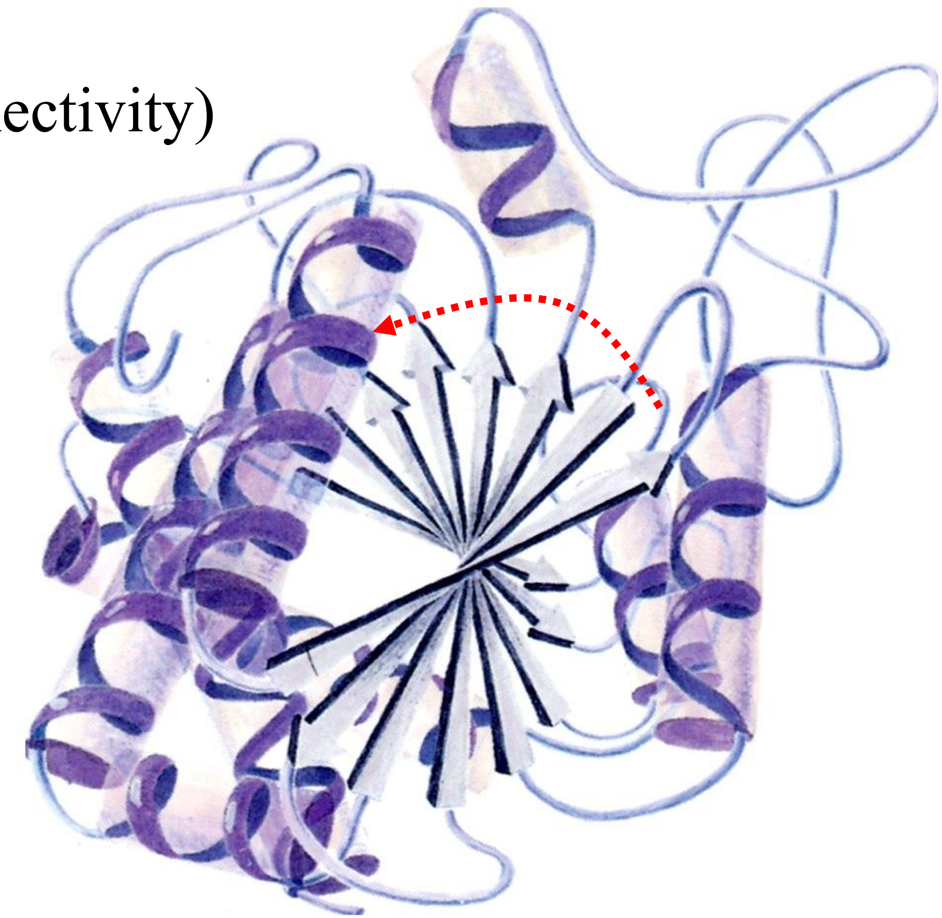


Figure 6-12 Fundamentals of Biochemistry, 2/e

Connections between adjacent strands in β sheets

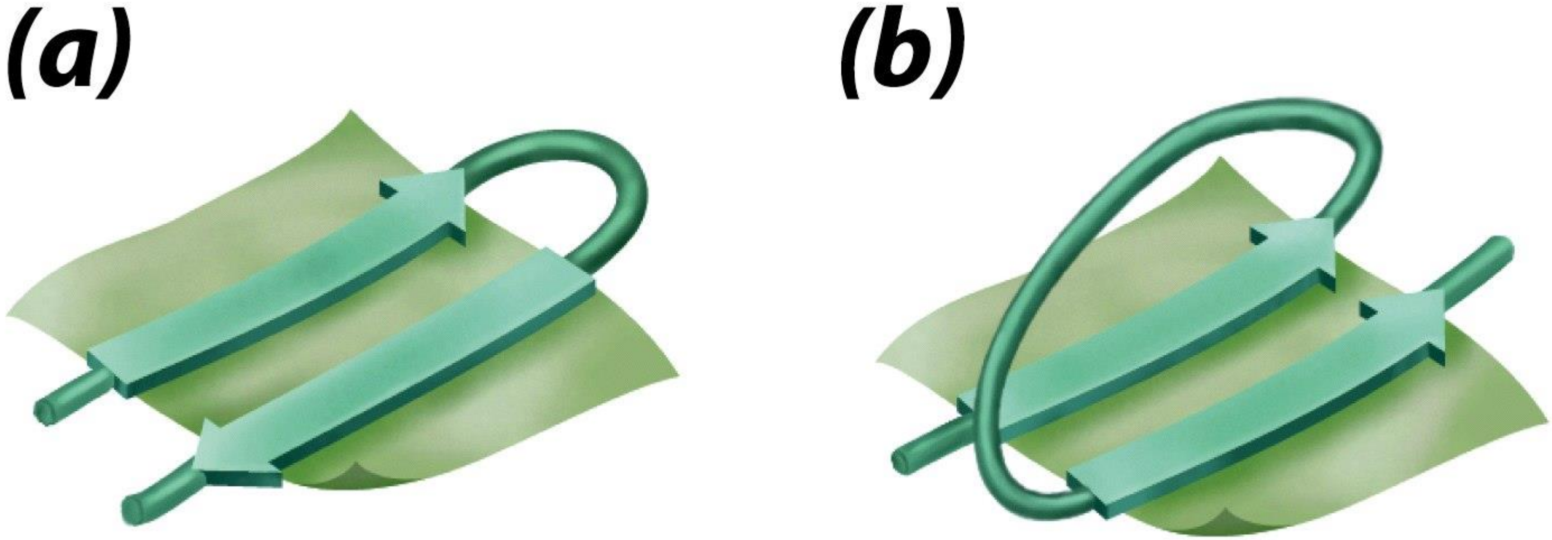


Figure 6-13 Fundamentals of Biochemistry, 2/e

C. Fibrous proteins

fibrous proteins: stiff, elongated, fibrous, insoluble
globular proteins: compact, highly folded, globular, soluble
some proteins have both regions

Fibrous proteins: keratin, collagen

keratin: structural proteins of hair, horn, nails, feathers
α keratins in mammals (α-helical)
β keratins in birds and reptiles (β-pleated)

α keratins in mammals: over 30 variants

X-ray diffraction pattern resembles that of α helix
5.1 Å spacing
coiled coil structure: left-handed

Coiled coil structure

7-residue pseudorepeat
Nonpolar at a and d

3.5 residue repeat per turn
Inclined ~18° relative to one another

Interdigitated side chains

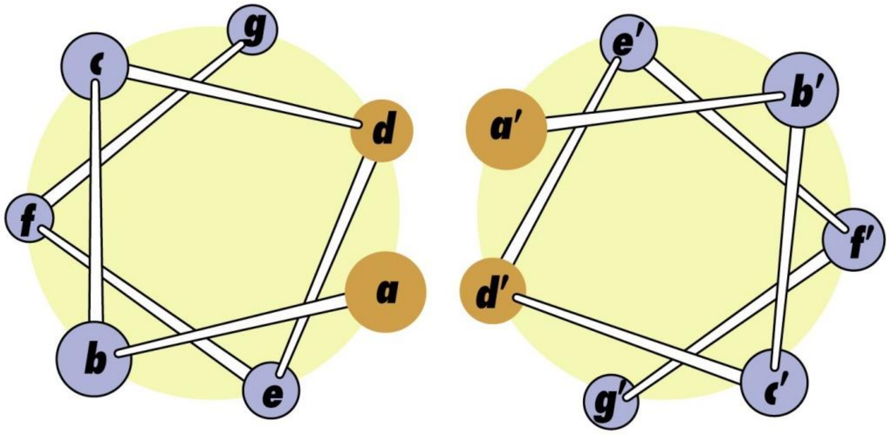


Figure 6-14a Fundamentals of Biochemistry, 2/e

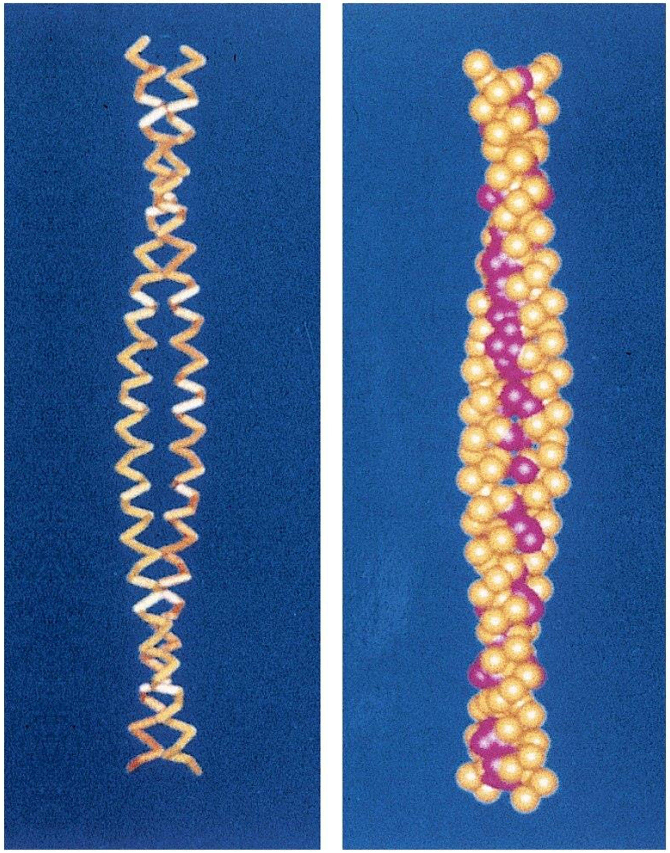
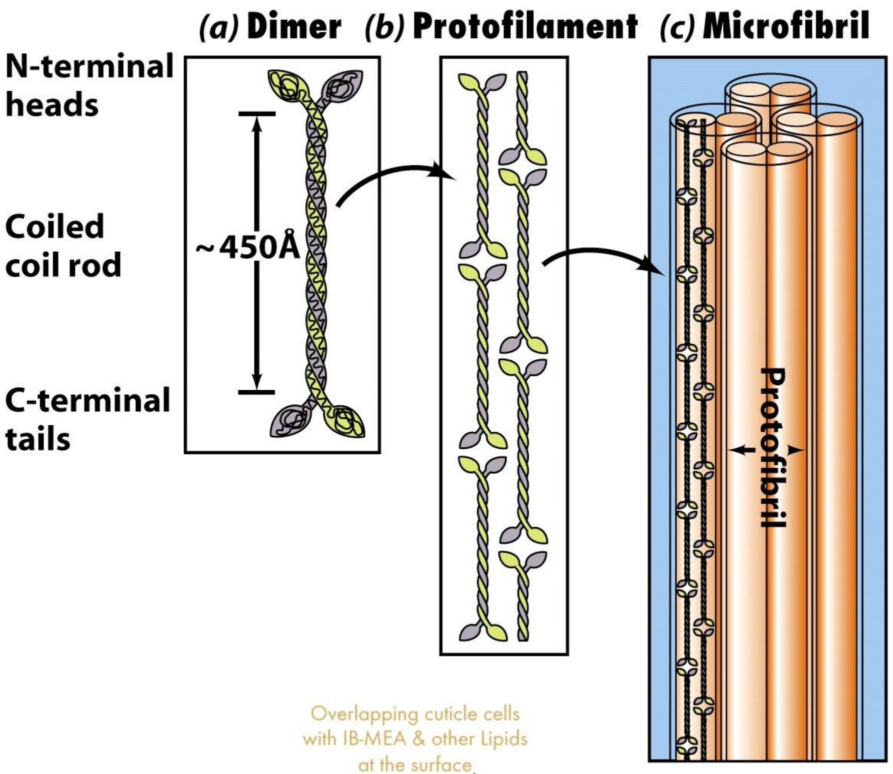


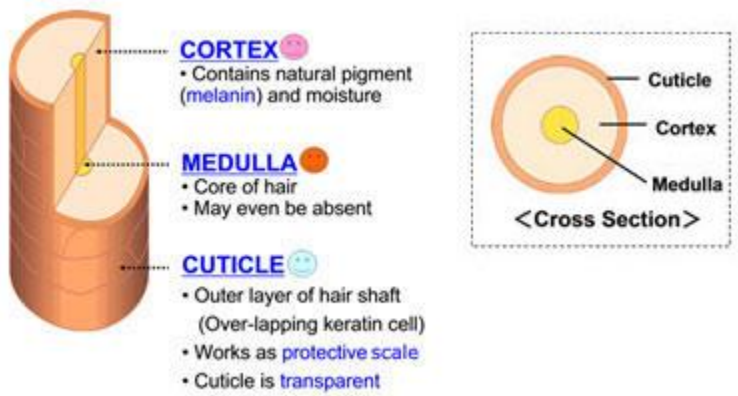
Figure 6-14b Fundamentals of Biochemistry, 2/e

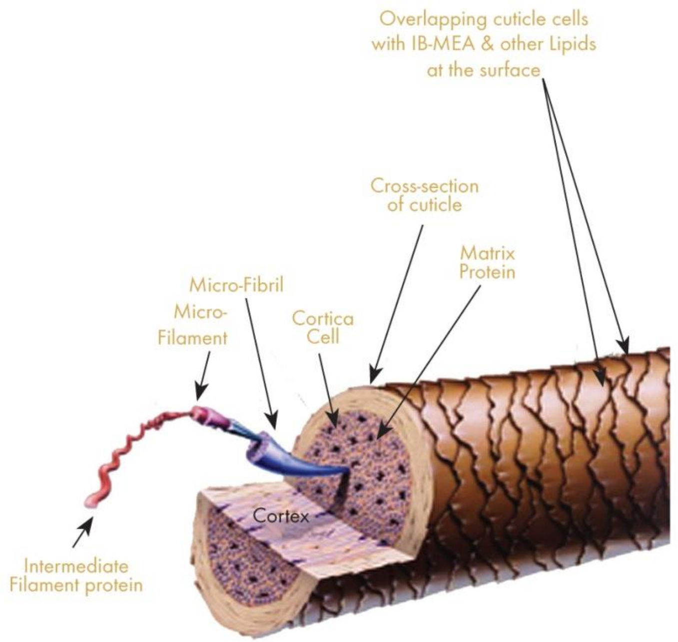
High order α keratin structure

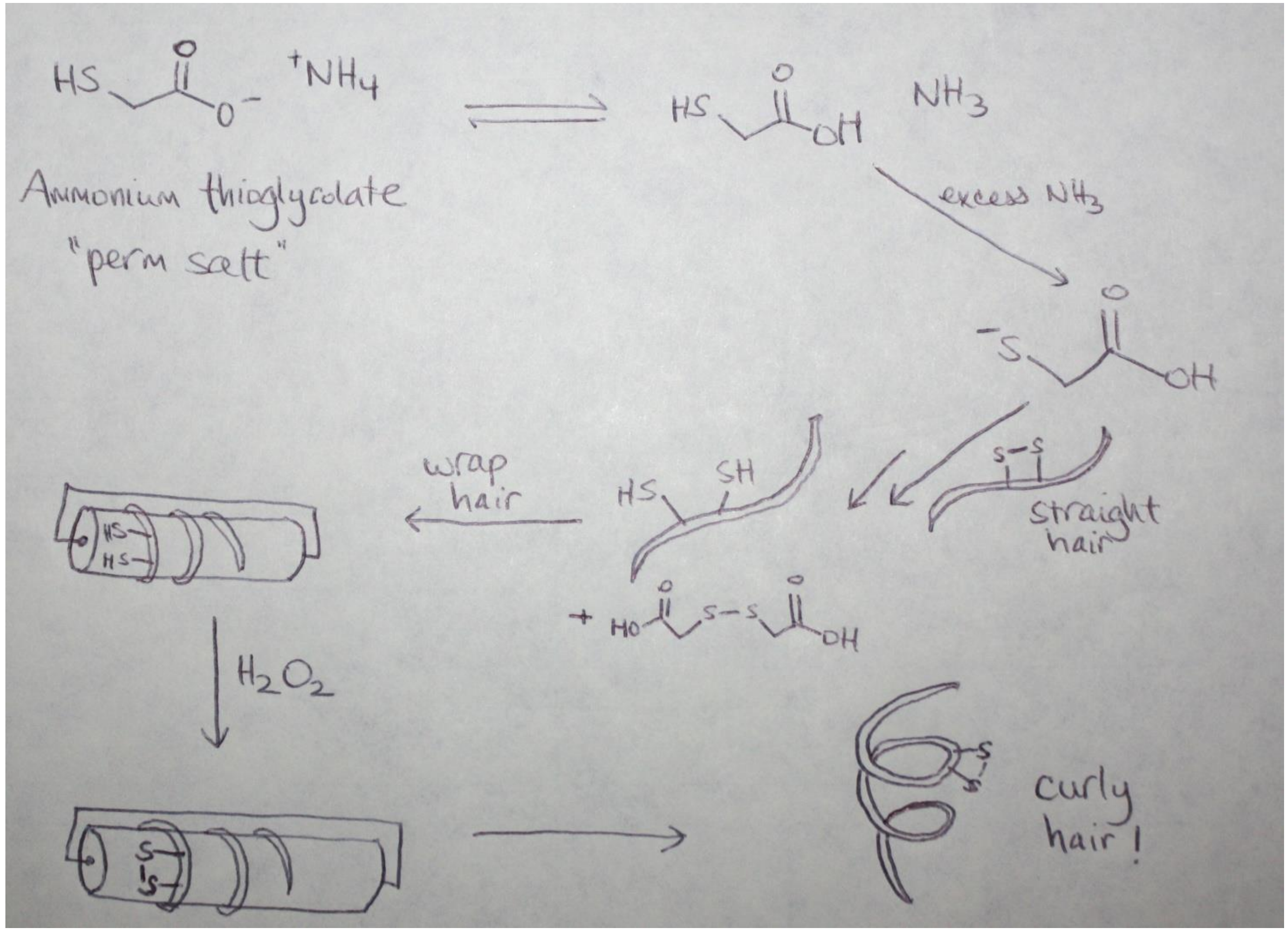
Dimeric coiled coil
Head to tail association: protofilament
Dimerized protofilaments: microfibril

Rich in Cys
disulfide bond
depending on the content: hard and soft
Permanent waves
reduction & oxidation









The chemistry of perms. Reference: J. Soc. Cosmet. Chem. **1996**, 47, 48-59.

Collagen: a triple helix

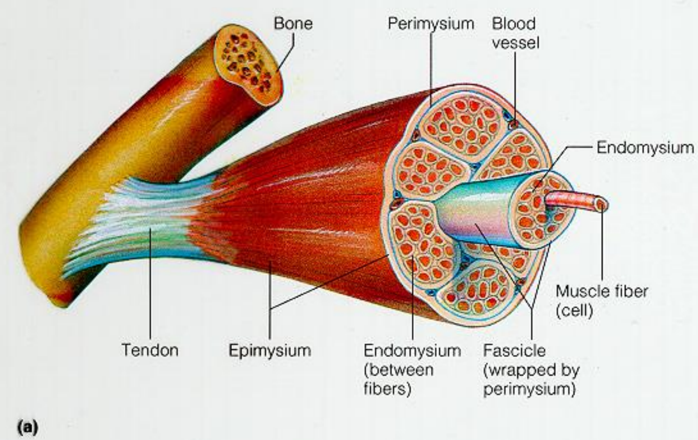
Left-handed polypeptides twisted into
right-handed superhelical structure

Most abundant vertebrate protein
Major connective tissue protein
(muscle, tendons, ligaments, skin)
>33 genetically distinct chains
assembled into >20 collagen varieties
in different tissues

Type I collagen
two α1(I) + one α2(I) chains
molecular mass ~285 kD
a width of ~14 Å
a length of ~3000 Å

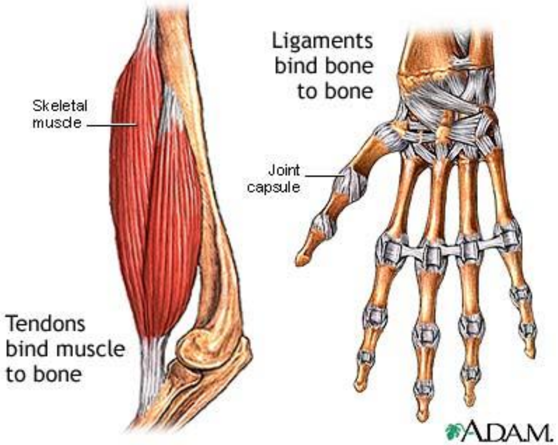
Figure 6-16 Fundamentals of Biochemistry, 2/e

Connective tissue wrappings of skeletal muscle (Figure 9.1a)

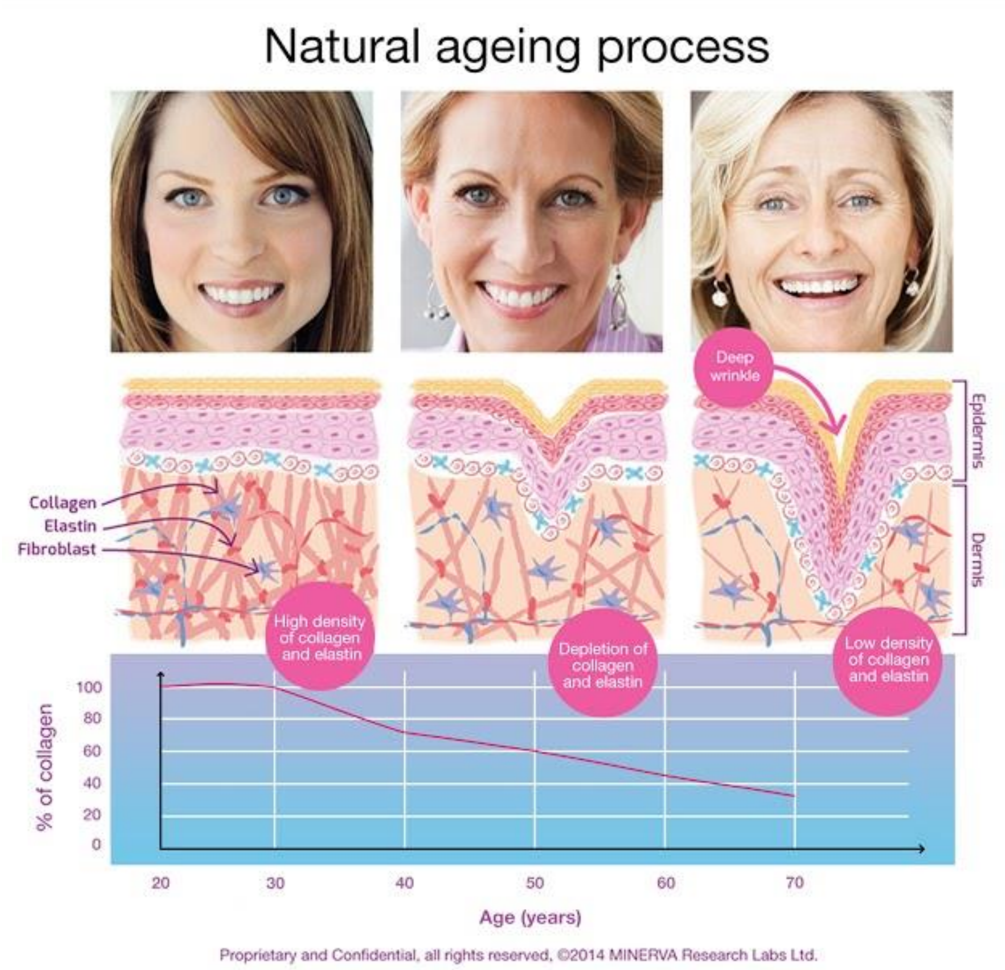


epimysium, perimysium, endomysium: collagens
muscle fiber: consists of myofibrils (actin, myosin)

Tendon and ligament

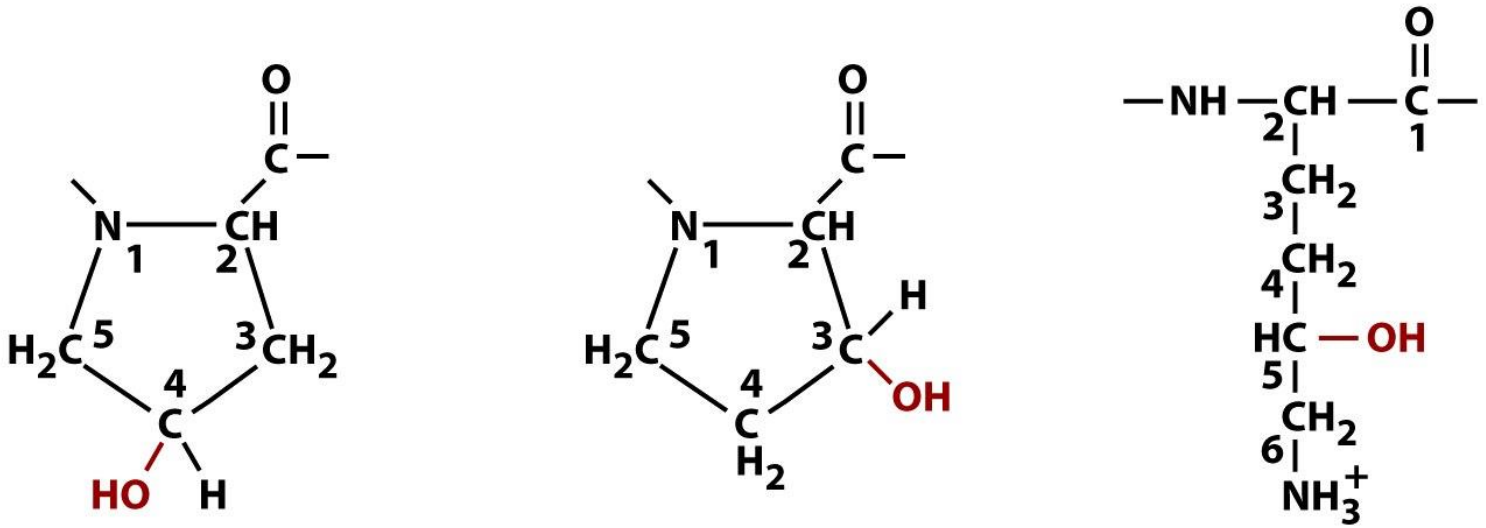


Skin collagen



Collagen polypeptide composition

~1/3: Gly
15-30%: Pro
The others: 4-OH Pro, 3-OH Pro, 5-OH Lys
Typical polypeptide: Gly - x - y (over ~1000 residues)



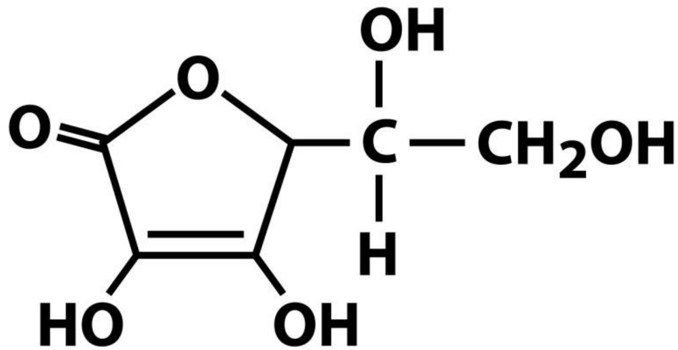
4-Hydroxyprolyl residue (Hyp) **3-Hydroxyprolyl residue** **5-Hydroxylysyl residue (Hyl)**

Unnumbered figure pg 140a Fundamentals of Biochemistry, 2/e

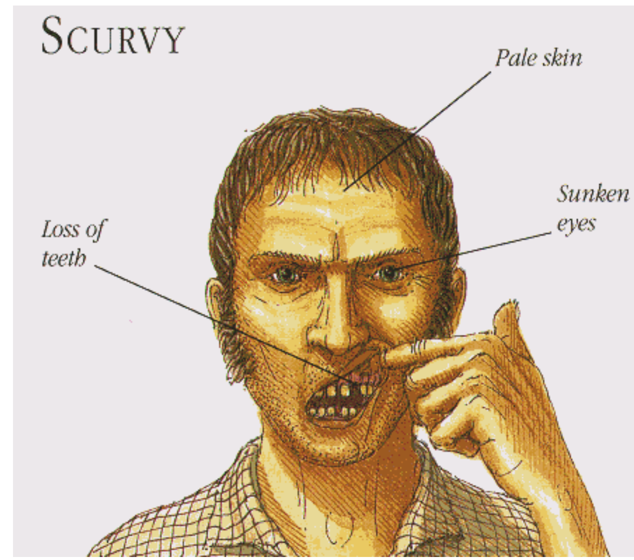
Hydroxylation after protein synthesis

prolyl hydroxylase

ascorbic acid as a cofactor



Ascorbic acid (vitamin C)



Typical polypeptide: Gly - x - y (x: Pro, y: Hyp)

Pro prevents forming α helix structure

(lack of backbone N-H)

Why Gly is so frequent

every 3rd residues in the crowded center

N-H of each Gly generates H-bond with C-O of X (Pro)

The bulky and relatively inflexible Pro and Hyp

confer rigidity on the entire assembly

viewed from N-terminal

H-bonds in white color

(between Gly N & Pro O)

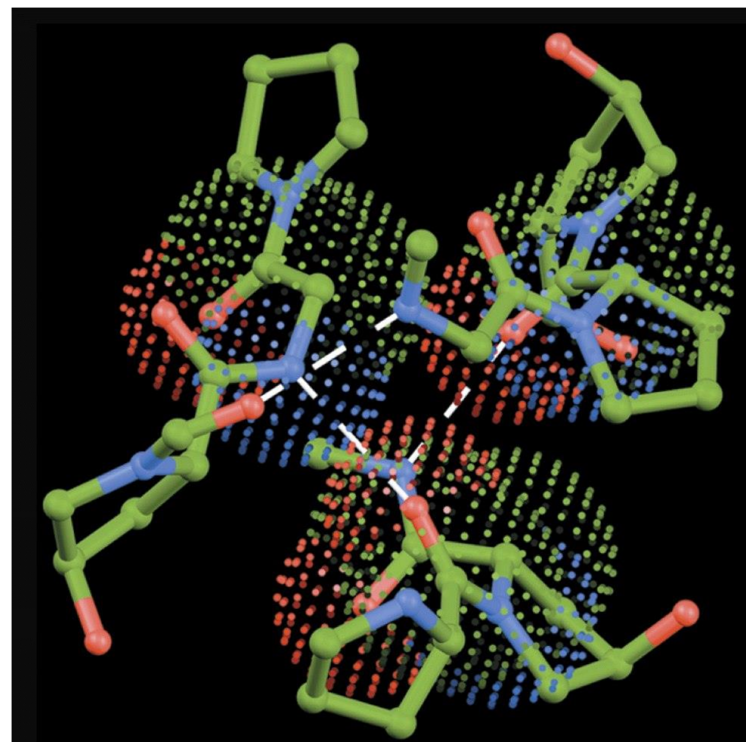
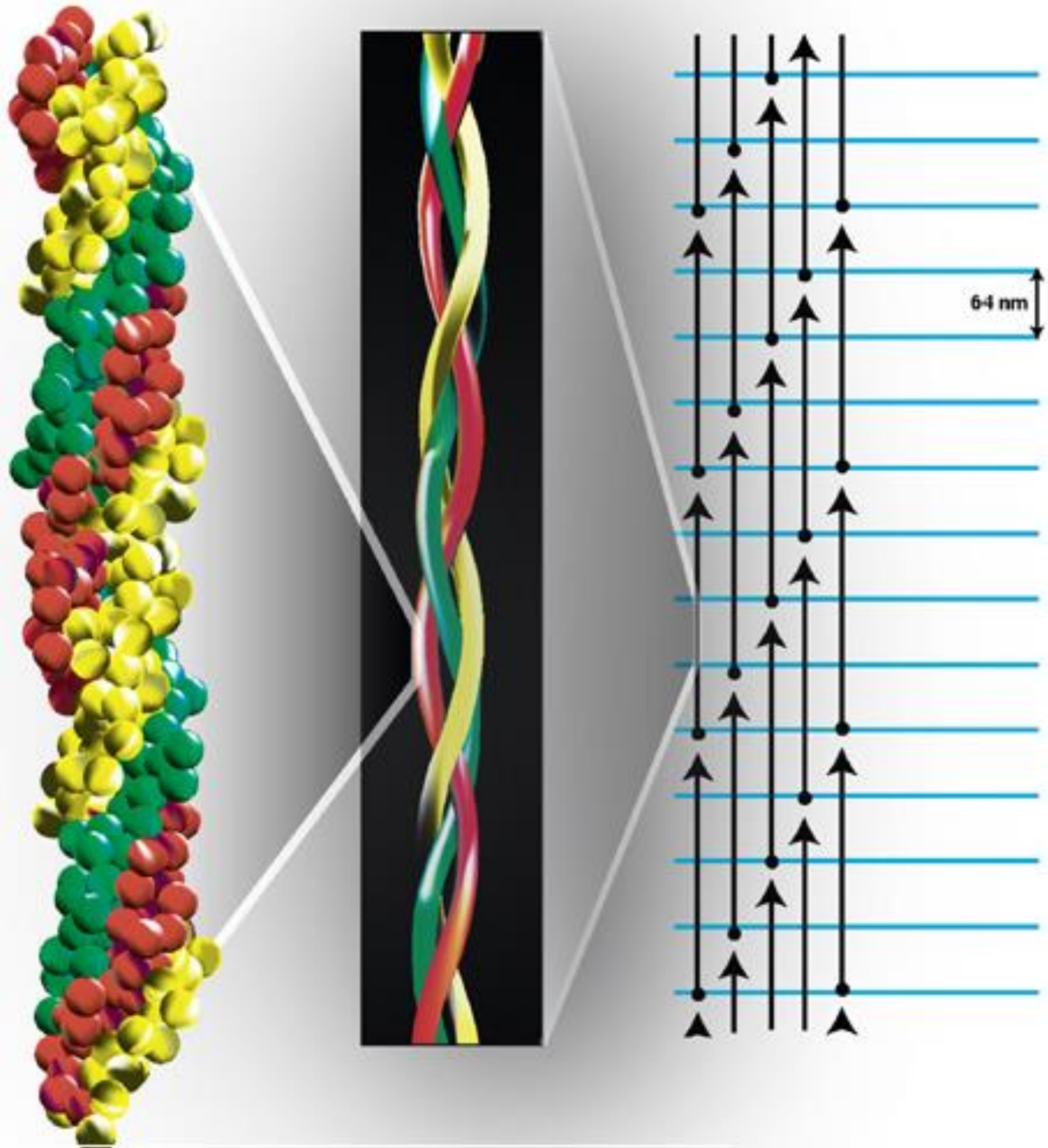


Figure 6-17b Fundamentals of Biochemistry, 2/e



6·4 nm

Cross-linking side chains in collagen

Devoid of Cys
Occur near the N- and C- termini (Lys & His)
Lysyl oxidase
Increased cross-linking with age

Collagen diseases
[Lathyrism]()
[Osteogenesis imperfecta]()
[Ehlers-Danlos syndrome]()

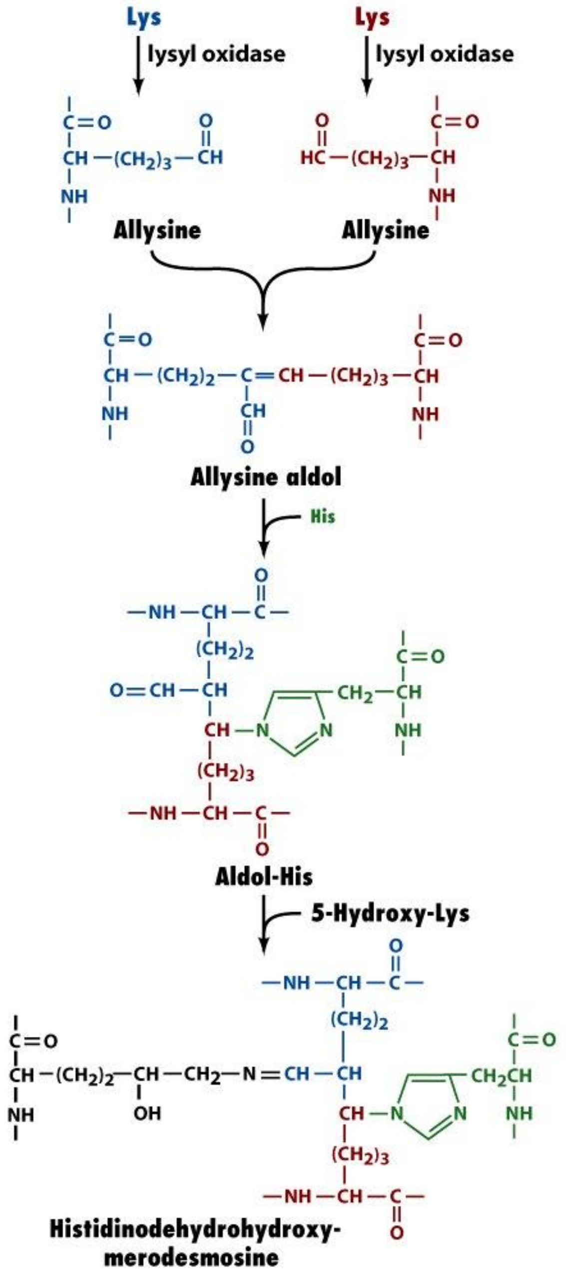
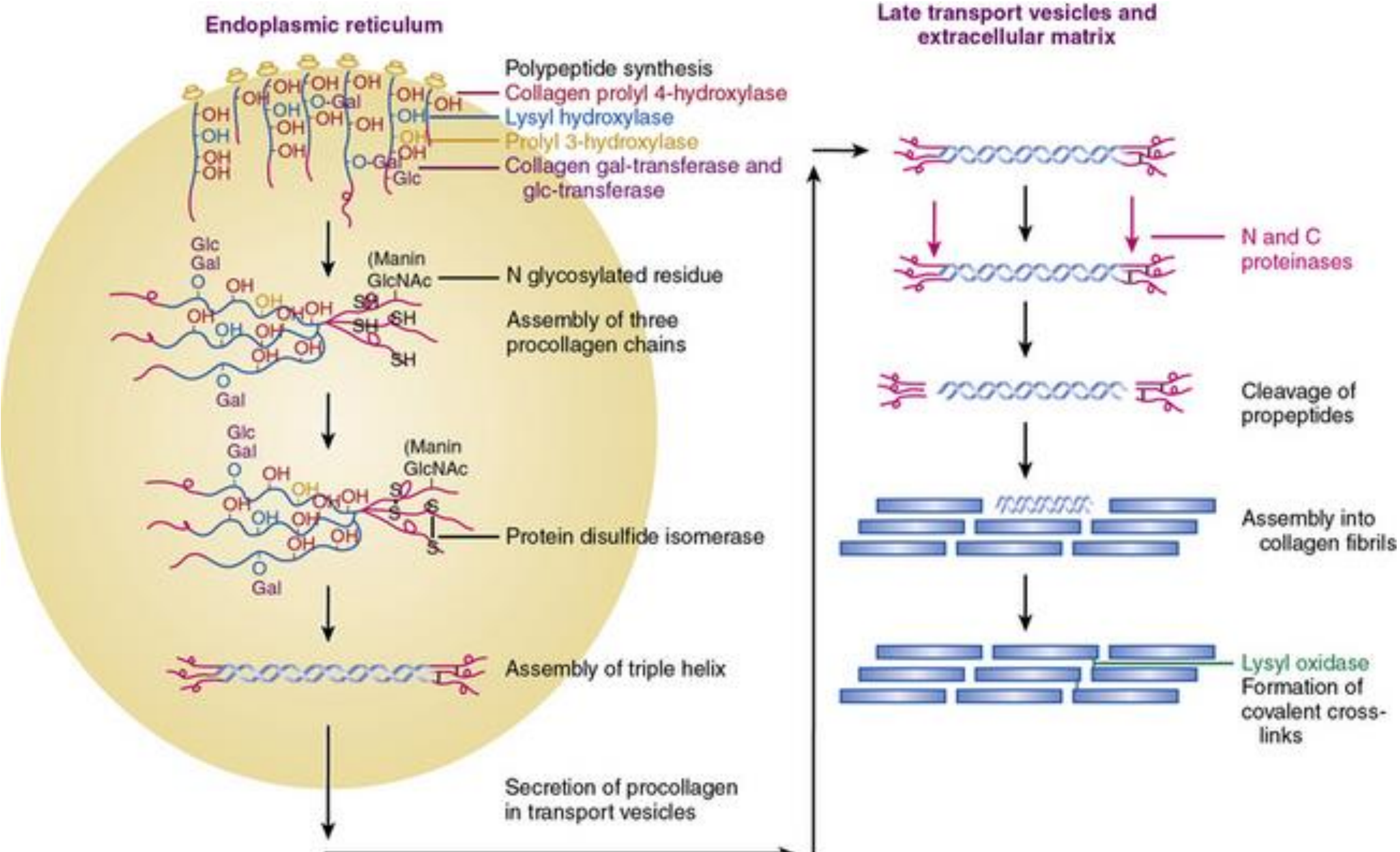


Figure 6-18 Fundamentals of Biochemistry, 2/e

Collagen fibril formation



Major Collagen Molecules			
Type	Molecule composition	Structural features	Representative tissues
Fibrillar collagens			
I	$[\alpha\ 1(I)]_2\ [\alpha\ 2(I)]$	300-nm-long fibrils	Skin, tendon, bone, ligaments, dentin, interstitial tissues
II	$[\alpha\ 1(II)]_3$	300-nm-long fibrils	Cartilage, vitreous humor
III	$[\alpha\ 1(III)]_3$	300-nm-long fibrils; often with type I	Skin, muscle, blood vessels
V	$[\alpha\ 1(V)]_3$	390-nm-long fibrils with globular N-terminal domain; often with type I	Similar to type I; also cell cultures, fetal tissues
Fibril-associated collagens			
VI	$[\alpha\ 1(VI)][\alpha\ 2(VI)]$	Lateral association with type I; periodic globular domains	Most interstitial tissues
IX	$[\alpha\ 1(IX)][\alpha\ 2(IX)][\alpha\ 3(IX)]$	Lateral association with type II; N-terminal globular domain; bound glycosaminoglycan	Cartilage, vitreous humor;
Sheet-forming collagens			
IV	$[\alpha\ 1(IV)]_2\ [\alpha\ 2(IV)]$	Two-dimensional network	All basal laminaes

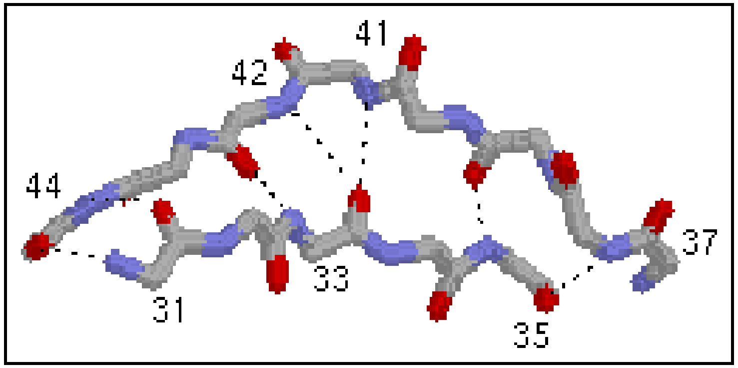
As of 2003, there were more than 28 different types of collagen identified

Nonrepetitive protein structure
in globular proteins

<u>Irregular structures: coil</u>
less ordered than α helix & β sheet
different from random coil (disordered in denatured state)

<u>Variations in standard secondary structure</u>
β bulge

<u>Turn and loops</u>



Propensity (P) of a residue
to occur in regular secondary structure

Useful for predicting the secondary str
of proteins with known a.a.

Table 6-1 Propensities of Amino Acid Residues for α Helical and β Sheet Conformations

Residue	P_α	P_β
Ala	1.42	0.83
Arg	0.98	0.93
Asn	0.67	0.89
Asp	1.01	0.54
Cys	0.70	1.19
Gln	1.11	1.10
Glu	1.51	0.37
Gly	0.57	0.75
His	1.00	0.87
Ile	1.08	1.60
Leu	1.21	1.30
Lys	1.16	0.74
Met	1.45	1.05
Phe	1.13	1.38
Pro	0.57	0.55
Ser	0.77	0.75
Thr	0.83	1.19
Trp	1.08	1.37
Tyr	0.69	1.47
Val	1.06	1.70

Source: Chou, P.Y. and Fasman, G.D., *Annu. Rev. Biochem*. **47,** 258 (1978).

Table 6-1 Fundamentals of Biochemistry, 2/e

Reverse turns (β bends) in polypeptide chains

Occur at protein surfaces

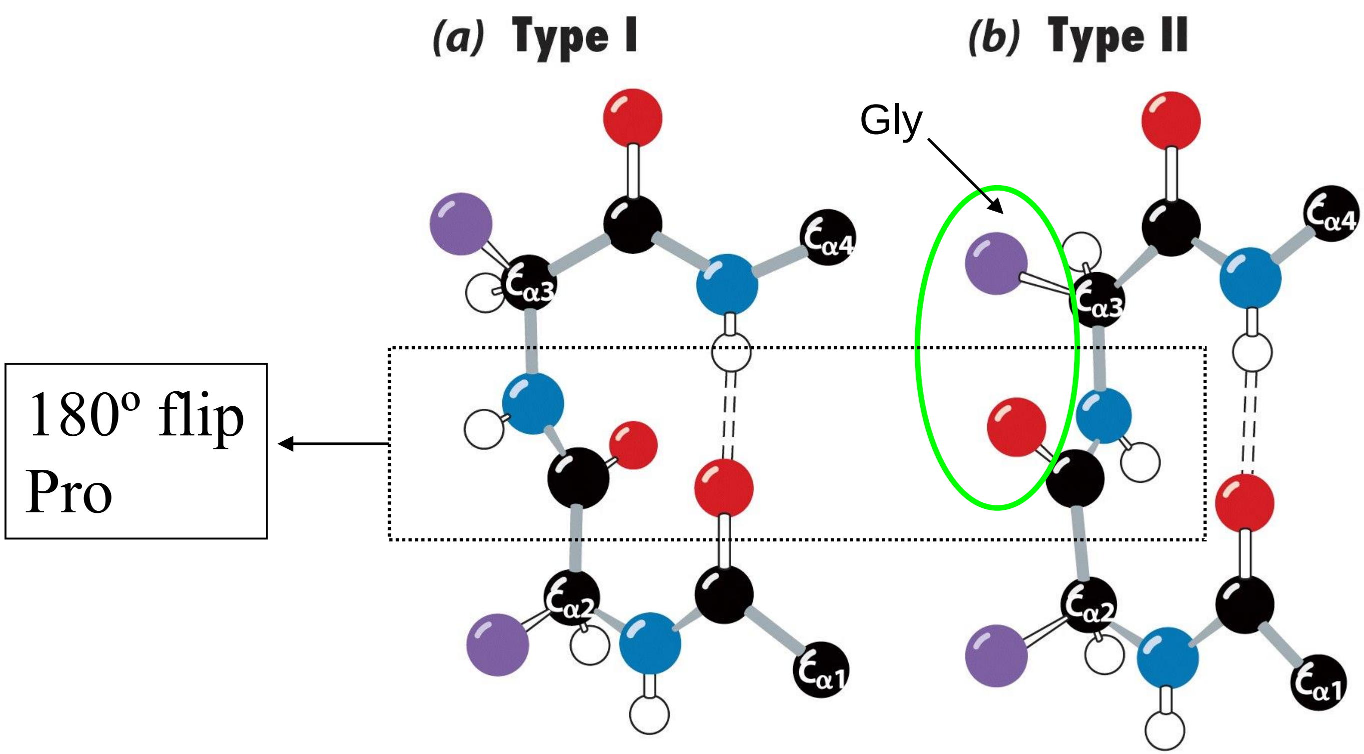


Figure 6-19 Fundamentals of Biochemistry, 2/e

Ω loops: extended loops of 6-16 residues

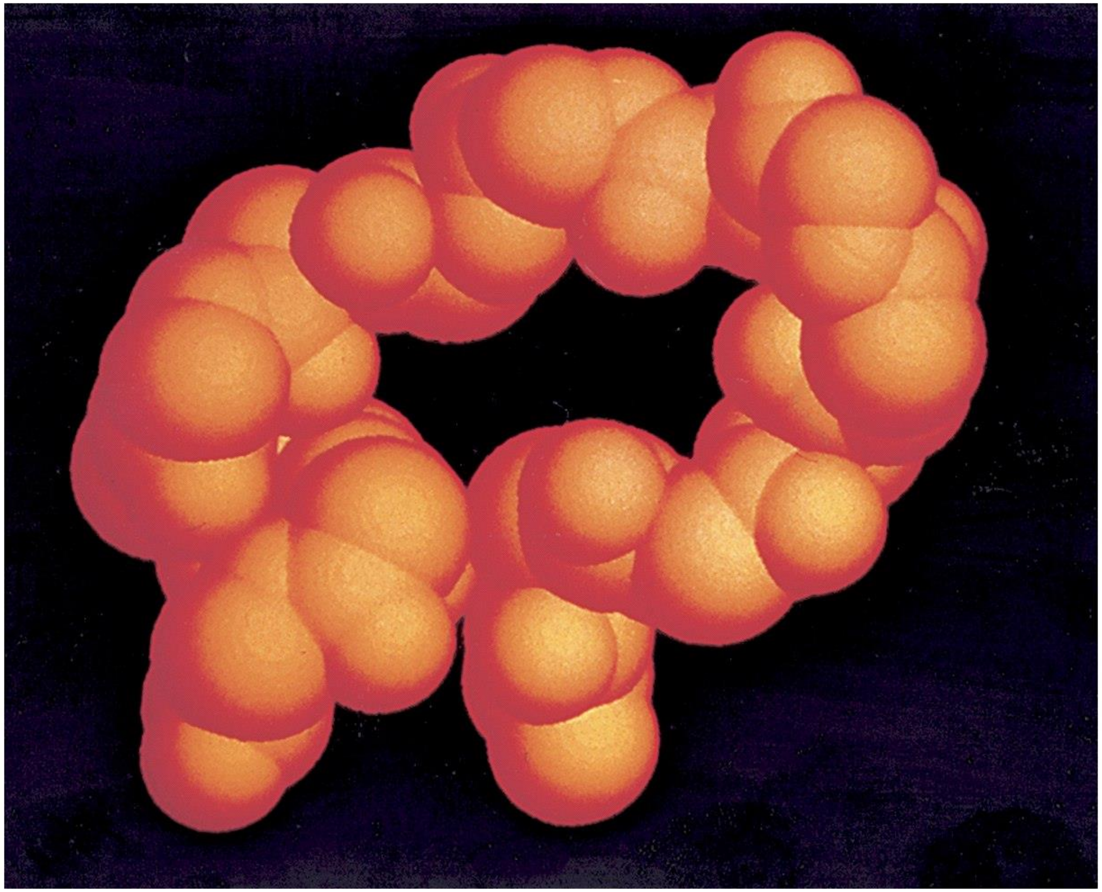


Figure 6-20 Fundamentals of Biochemistry, 2/e