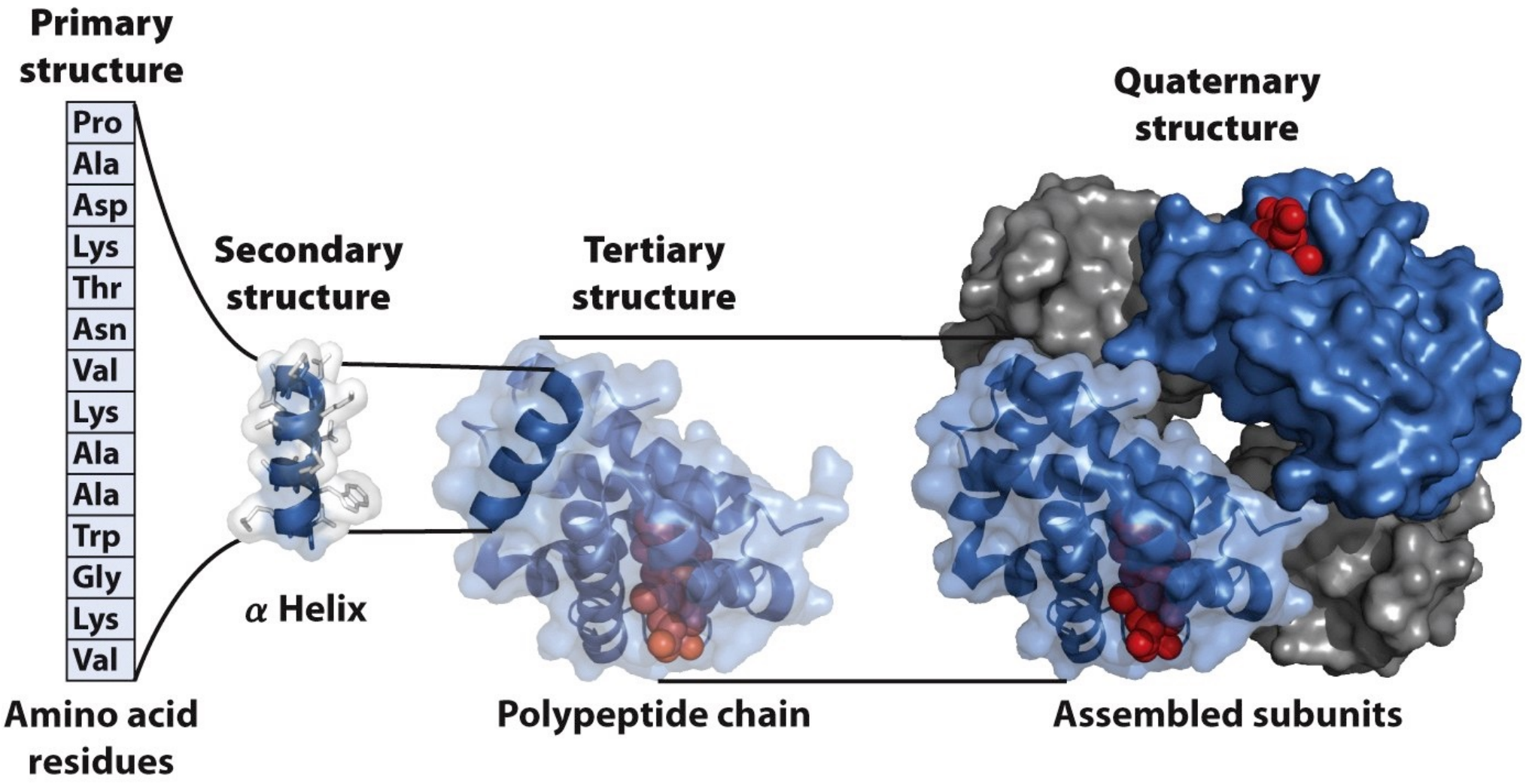
Class 4

(Ch. 3, pp. 85-89; Ch. 4, pp. 115-142)

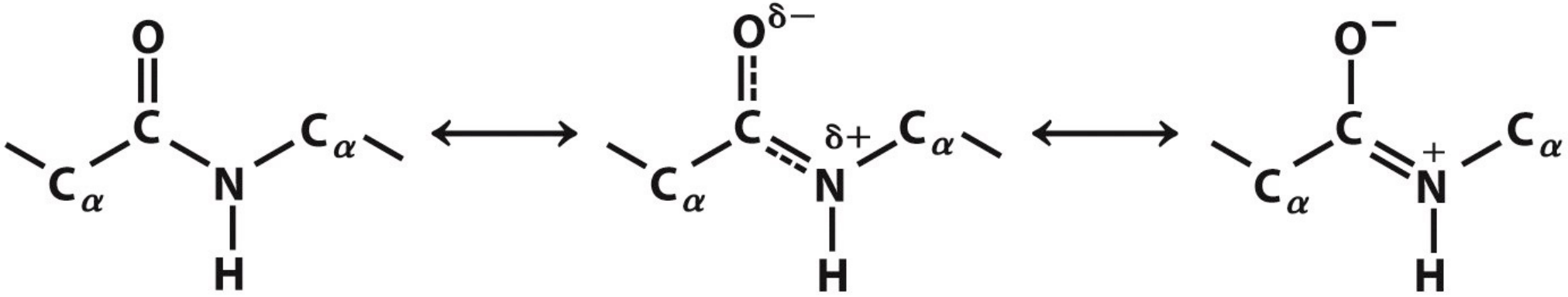
Peptide bond
&
covalent structure of proteins

Hierarchy of protein structural organization



Peptide (amide) bond formed by dehydration reaction

Peptide bond is rigid and planar



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 4–7b.

Figure 4-2a

Dihedral angles do have some rotational freedom

Defines relative conformation of two neighboring amino acids

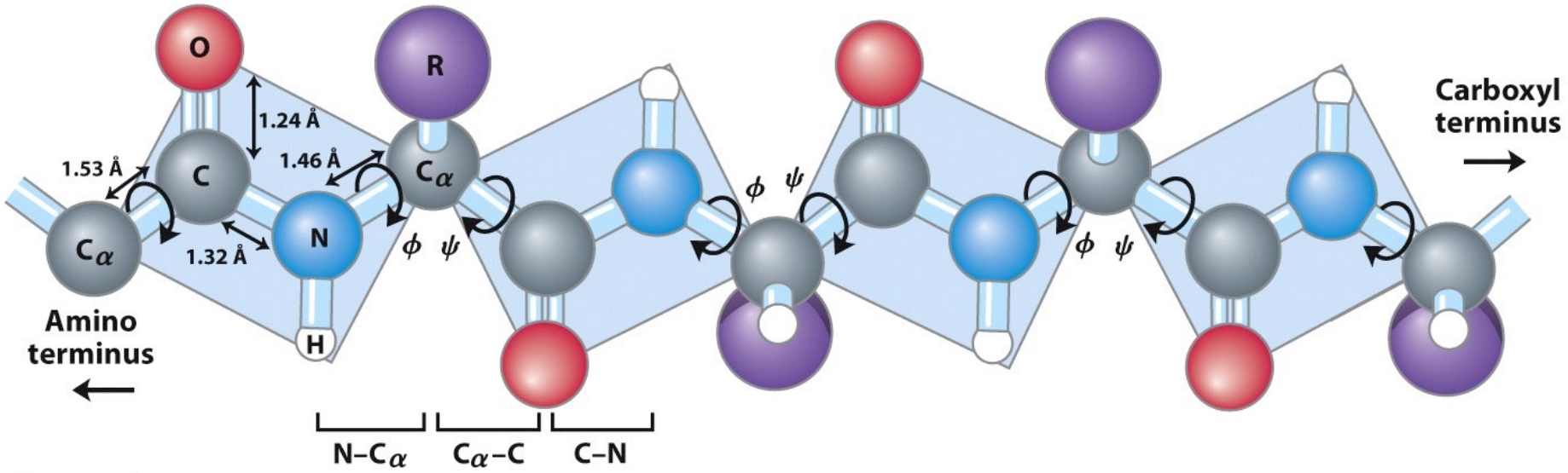
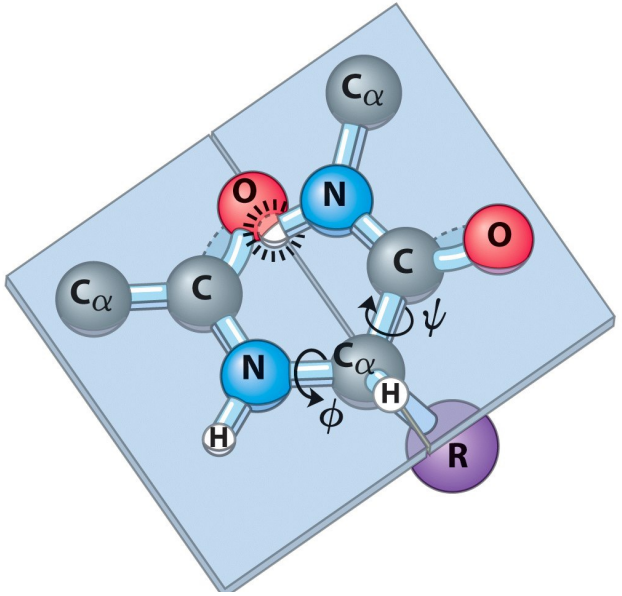


Figure 4-2b

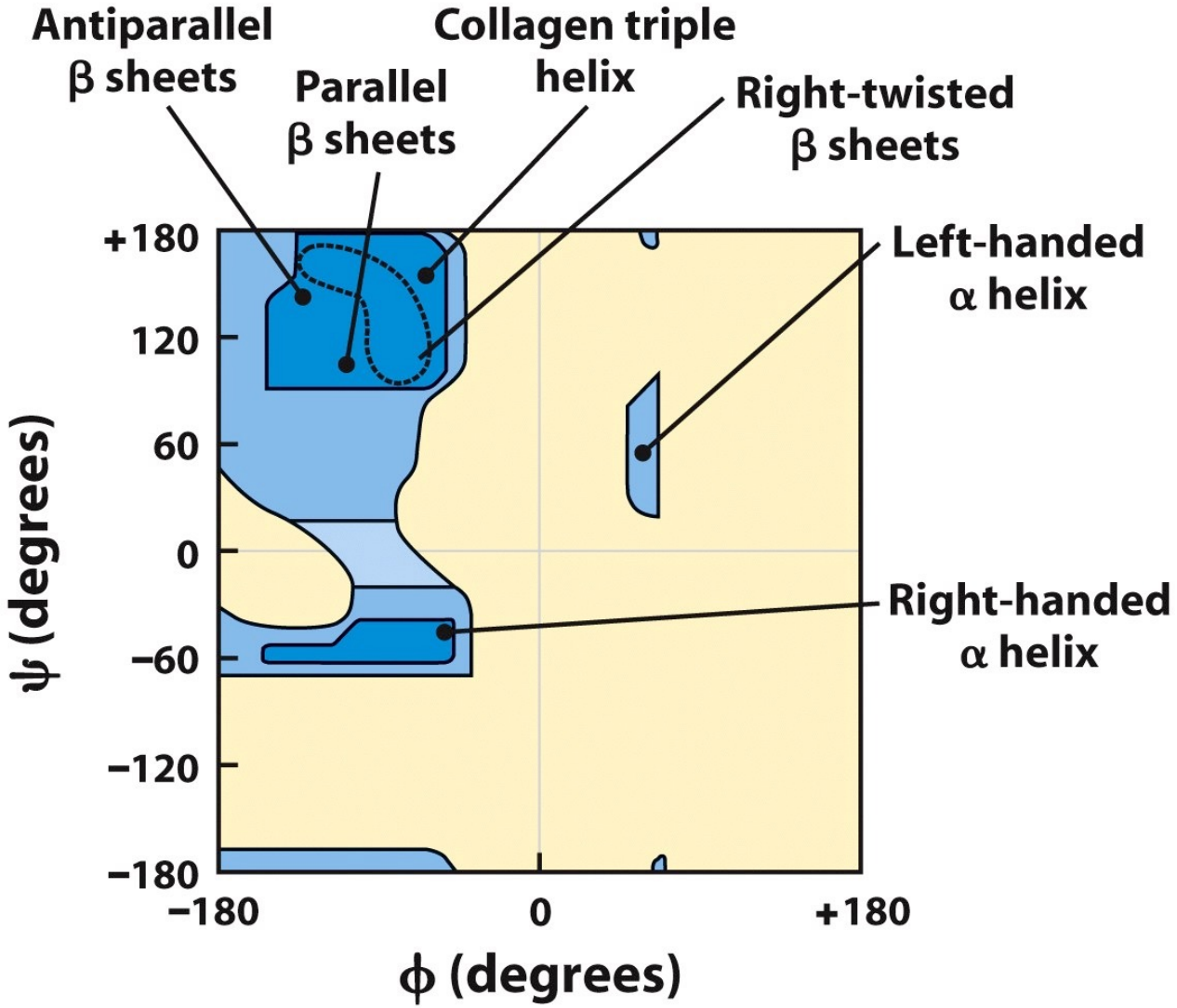
NEVER = 0 because of steric clash between adjacent amino acids

Steric hindrance of neighboring R groups favors trans configuration



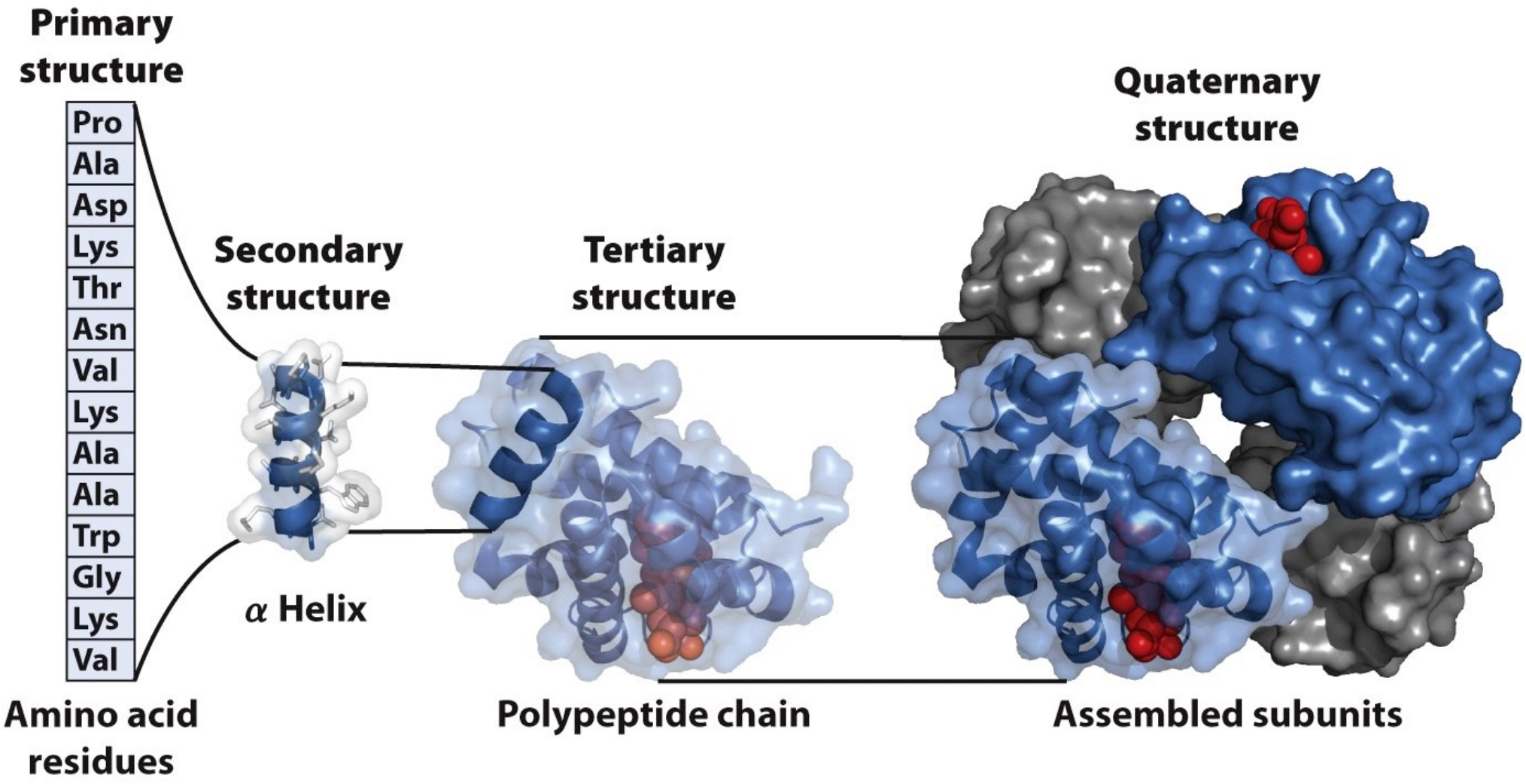
Ramachandran plot

(rotational angles adopted in proteins)



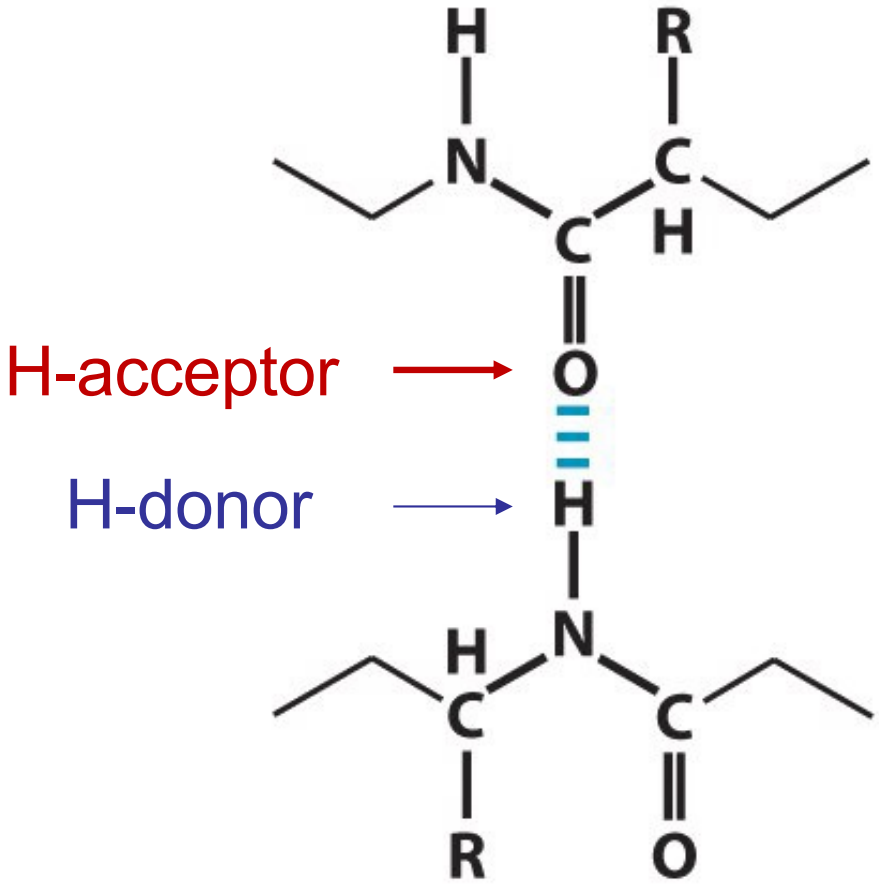
In nature, most combinations are disallowed due to steric hindrance.

Dihedral angles define secondary structure



Secondary structures are stabilized by H-bonds between backbone amide groups

(R-groups not DIRECTLY involved but do influence)



Right handed α-helix

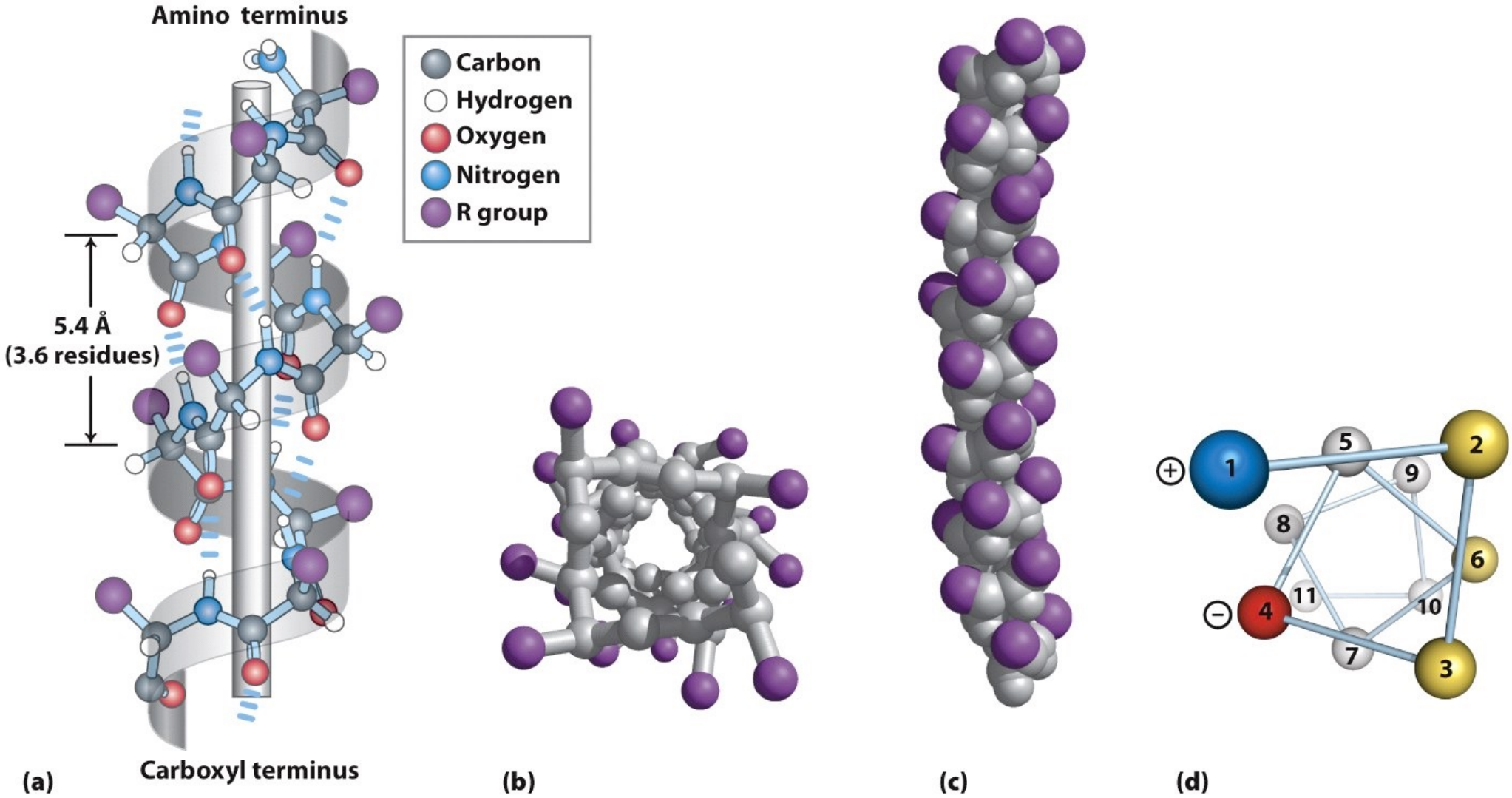


Figure 4-4

RBC glucose transporter (GLUT1)

speeds up glc uptake 50,000 fold

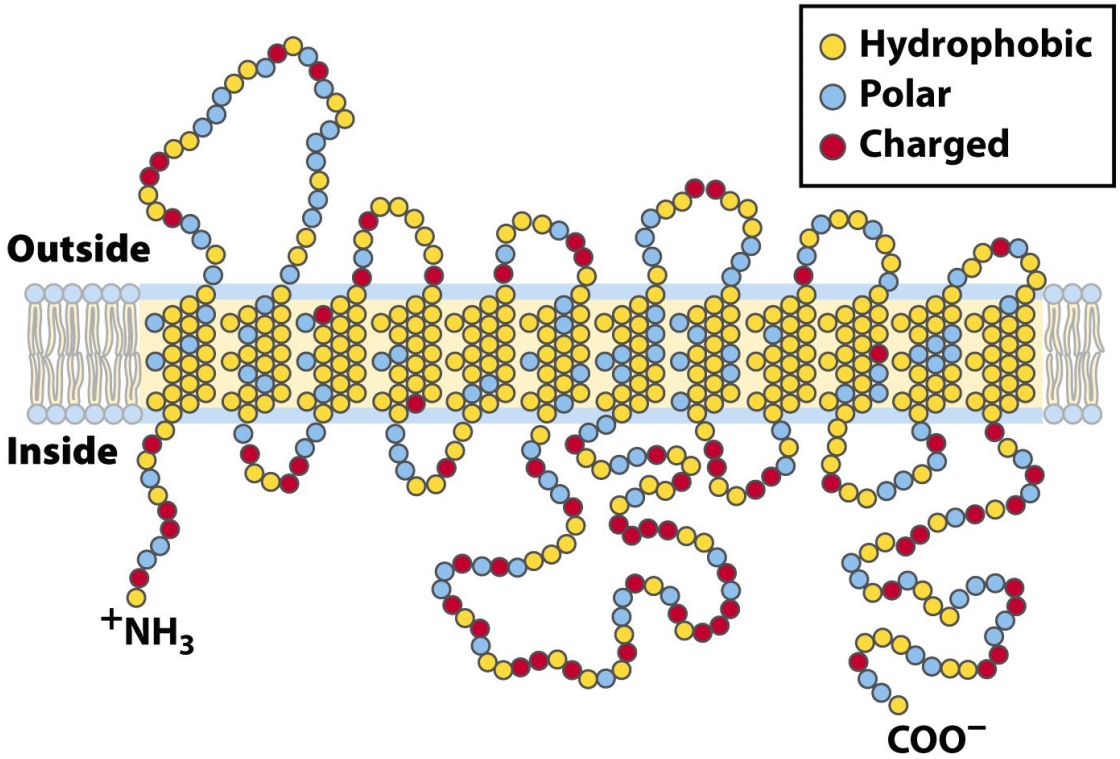


Figure 11-29a
Lehninger Principles of Biochemistry, Fifth Edition
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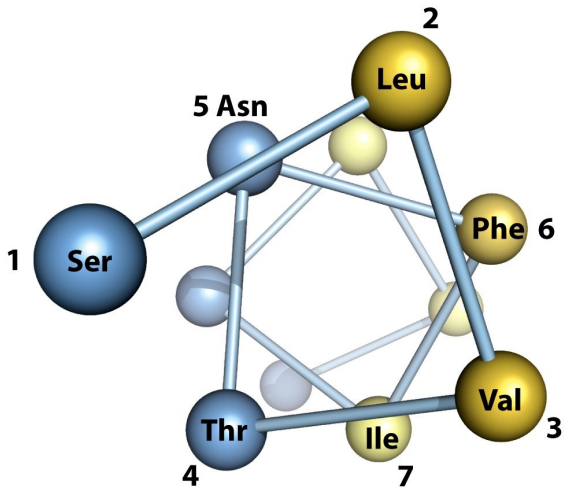

Figure 11-29b
Lehninger Principles of Biochemistry, Fifth Edition
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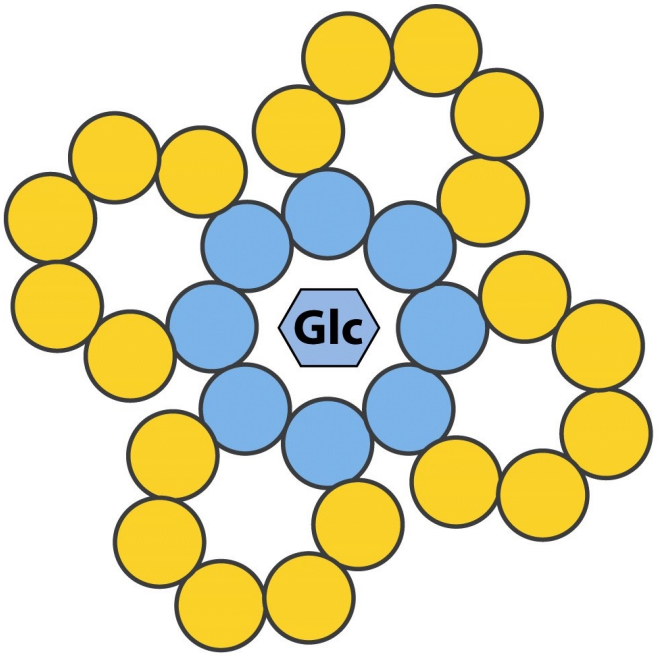

Figure 11-29c
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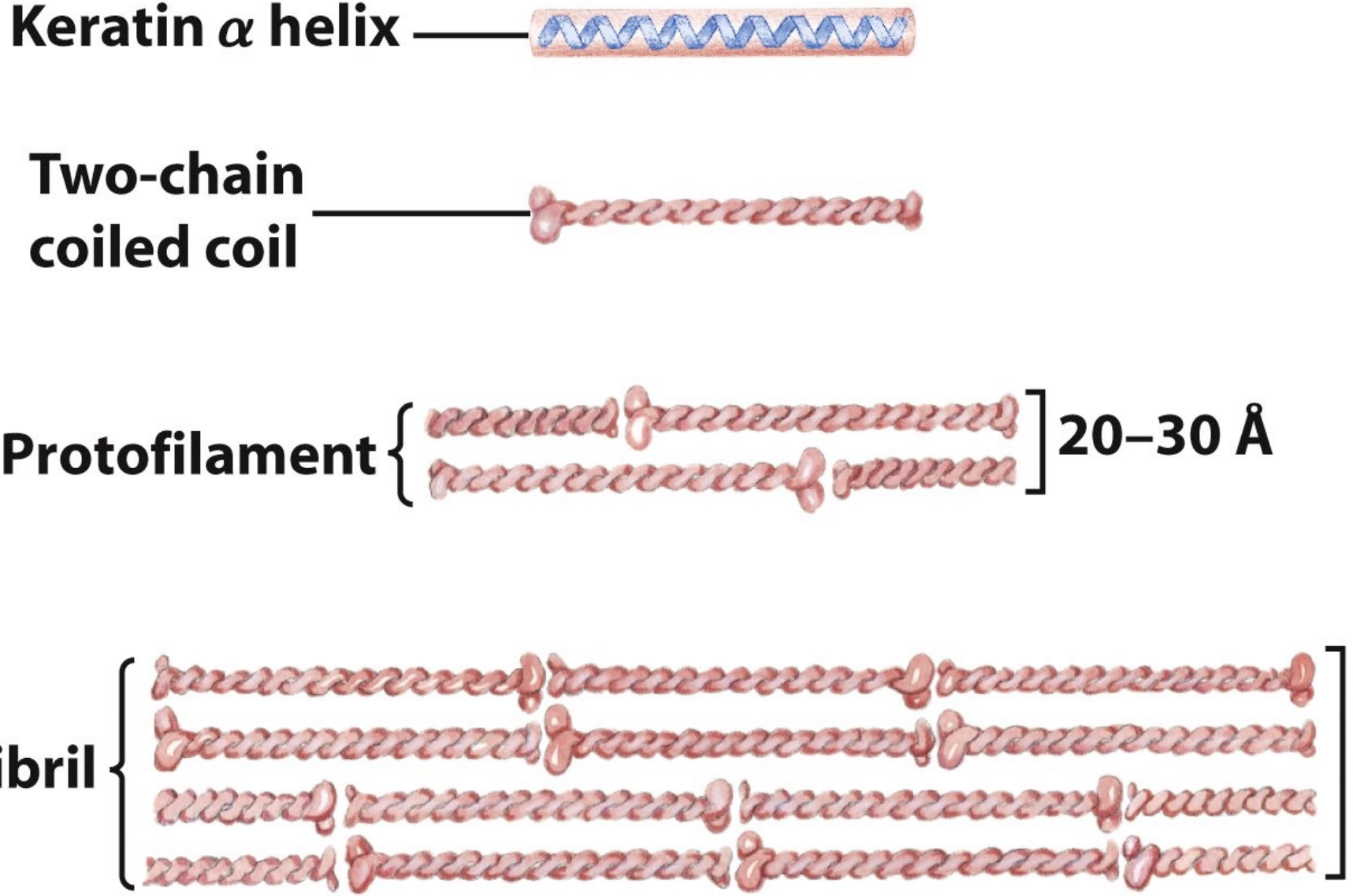
Keratin - helix of 2 helices

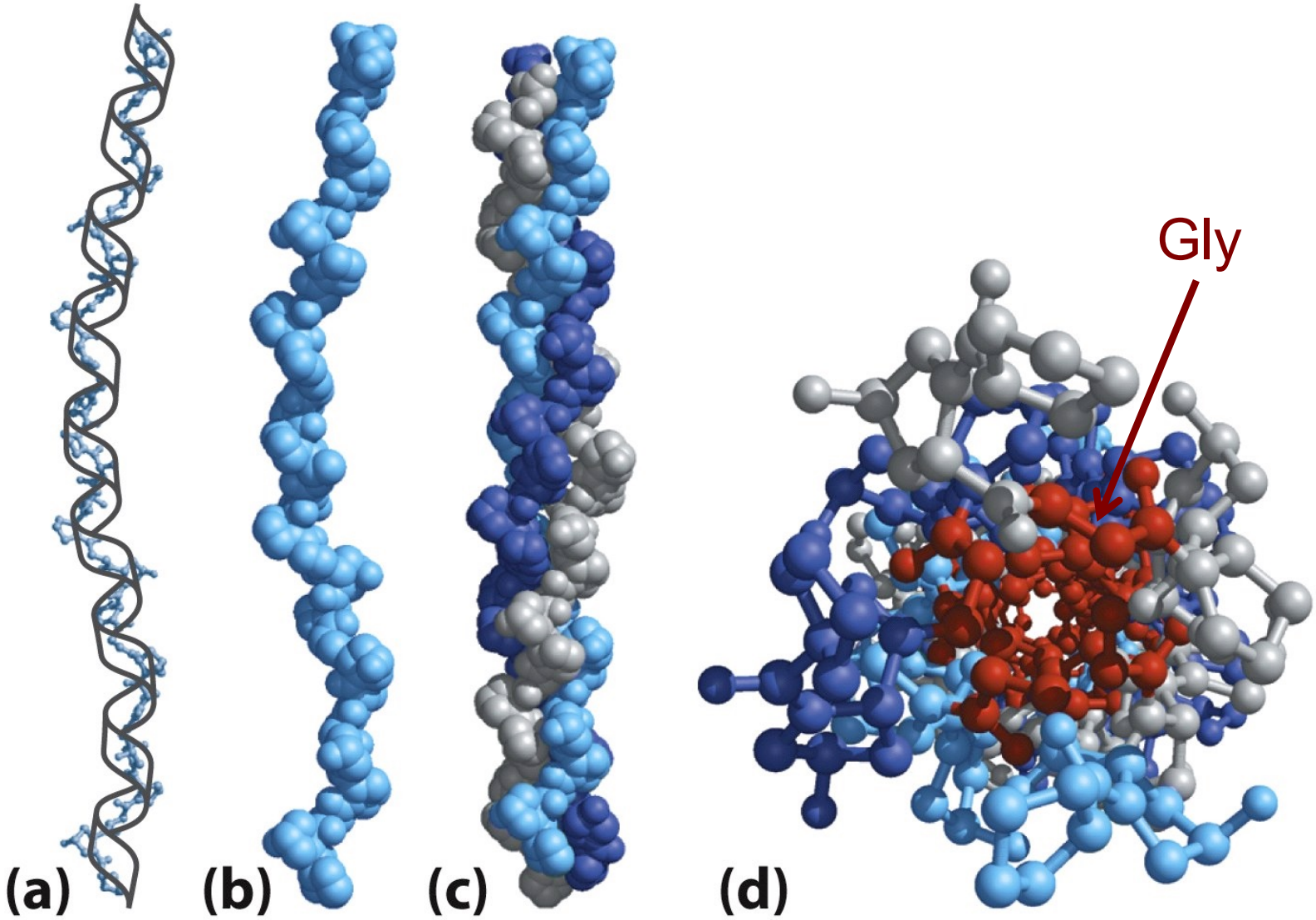


Propensity of amino acids to form α–helix

TABLE 4–2 Propensity of Amino Acid Residues to Take Up an α-Helical Conformation

Amino acid	ΔΔ*G*° (kJ/mol)*	Amino acid	ΔΔ*G*° (kJ/mol)*
Ala	0	Leu	0.79
Arg	0.3	Lys	0.63
Asn	3	Met	0.88
Asp	2.5	Phe	2.0
Cys	3	Pro	>4
Gln	1.3	Ser	2.2
Glu	1.4	Thr	2.4
Gly	4.6	Tyr	2.0
His	2.6	Trp	2.0
Ile	1.4	Val	2.1

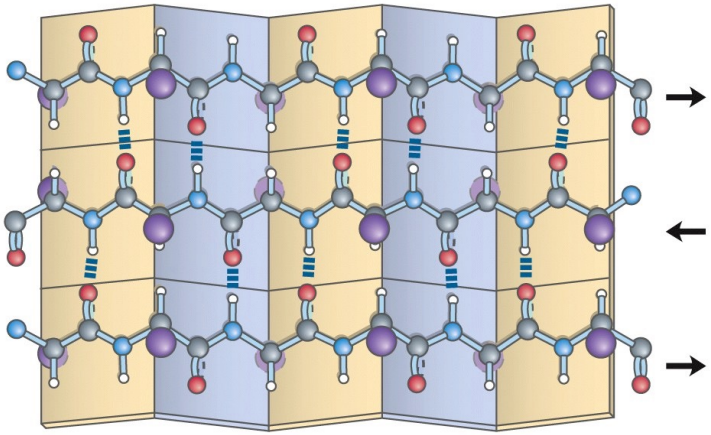
Collagen – an exception to the rule
Helix of 3 helices



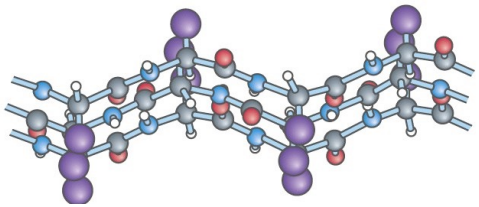
ß-sheets

Antiparallel

Top view

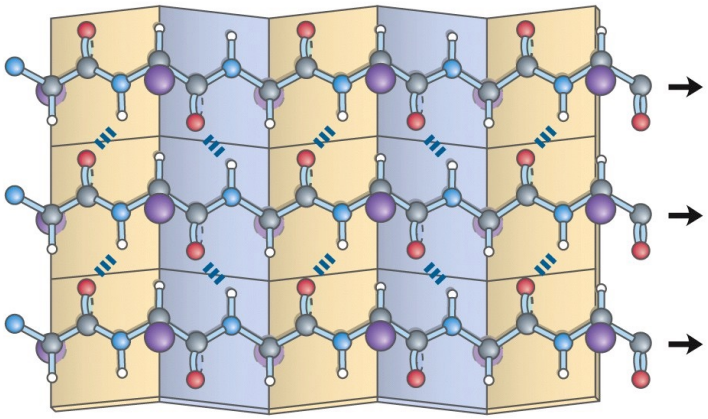


Side view

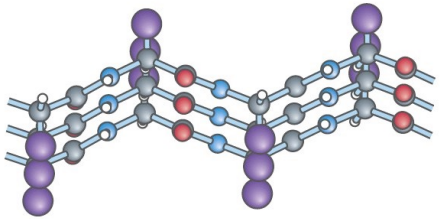


Parallel

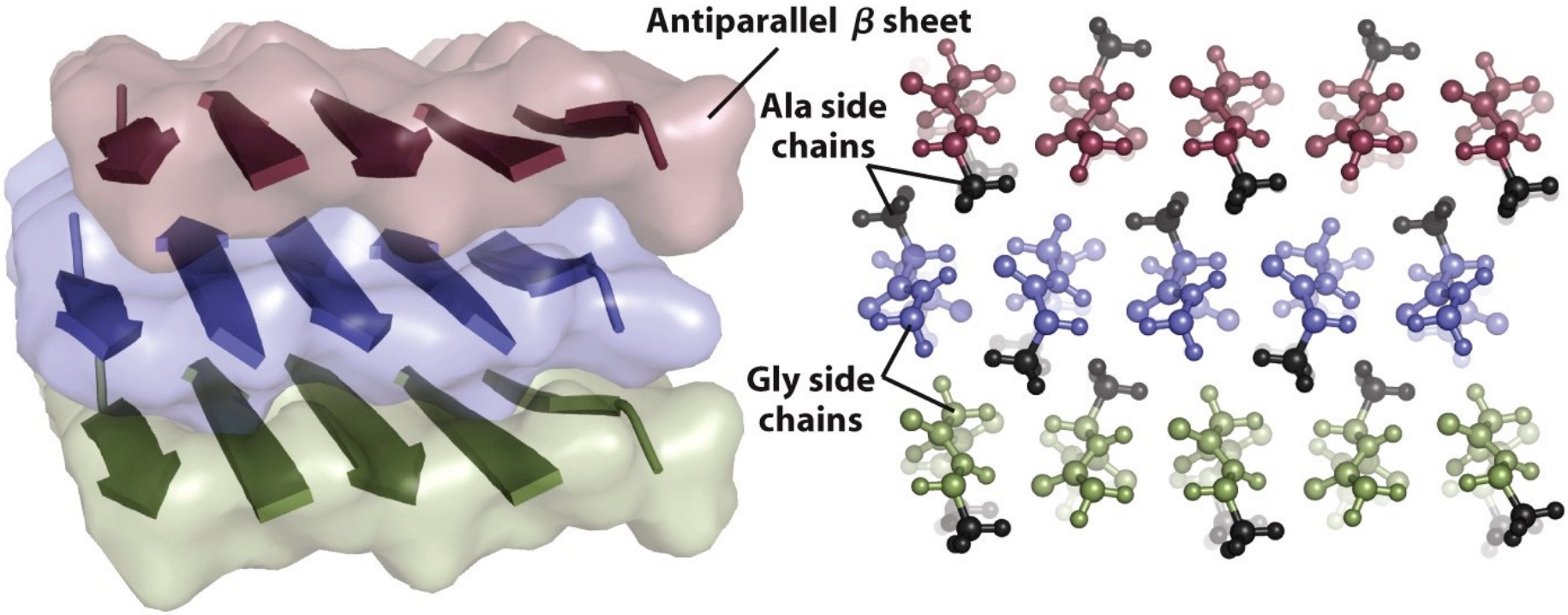
Top view



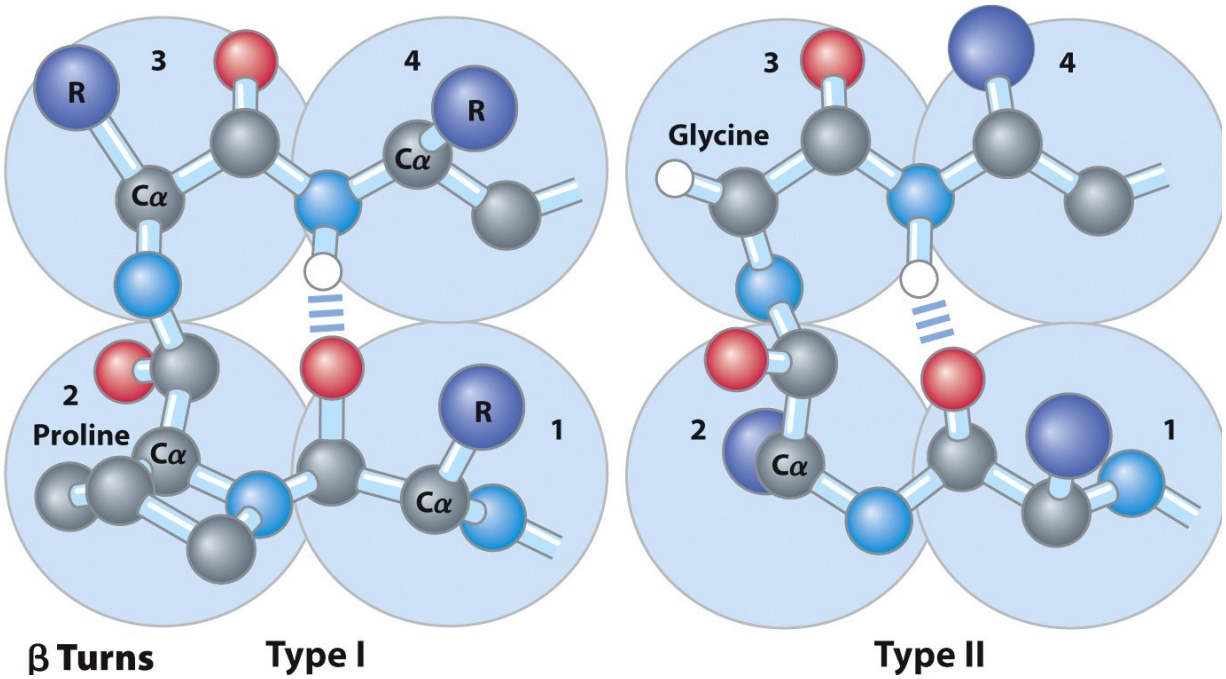
Side view

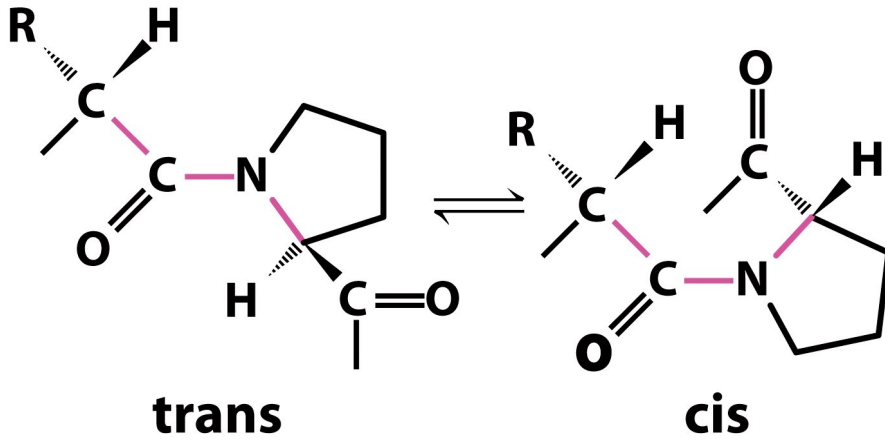


Silk fibroin

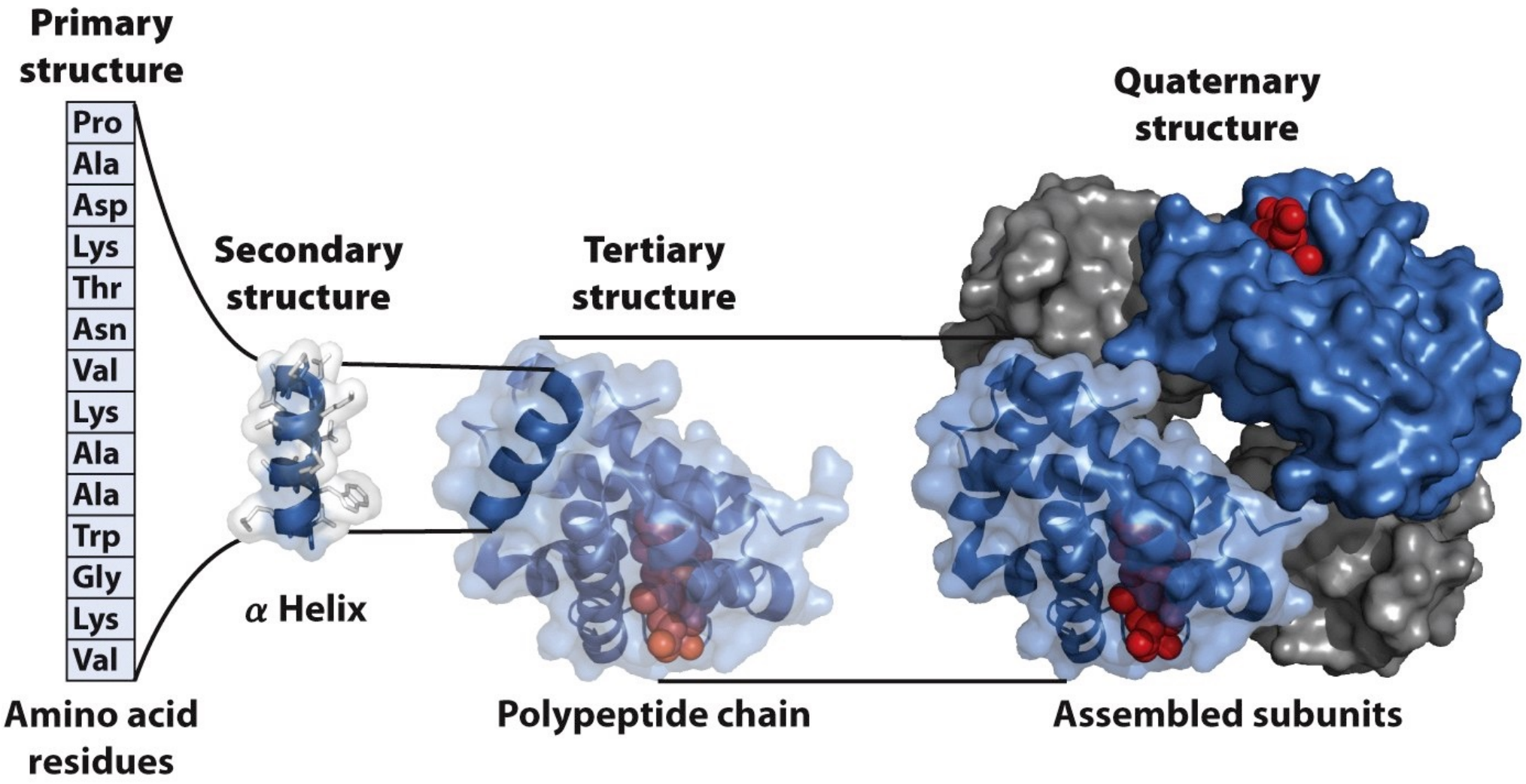


ß turns connect ß sheets

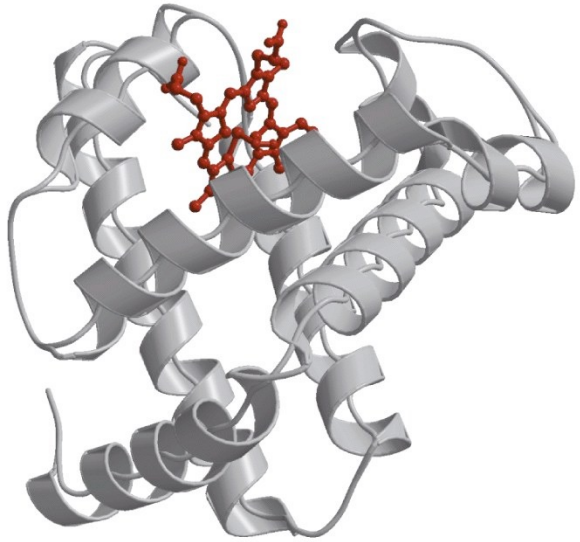




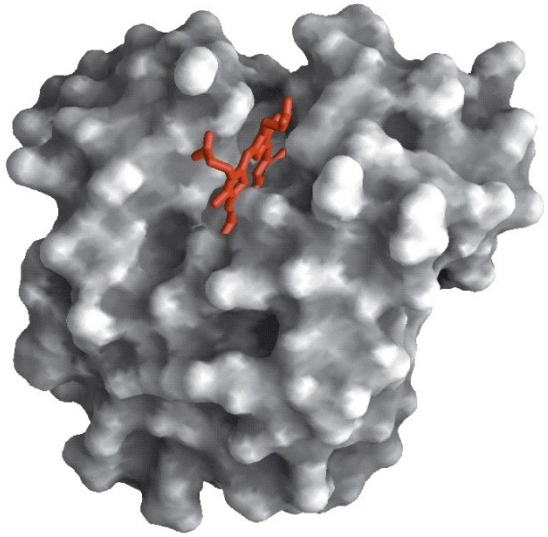
Tertiary structure – superfolding of backbone into 3D shape



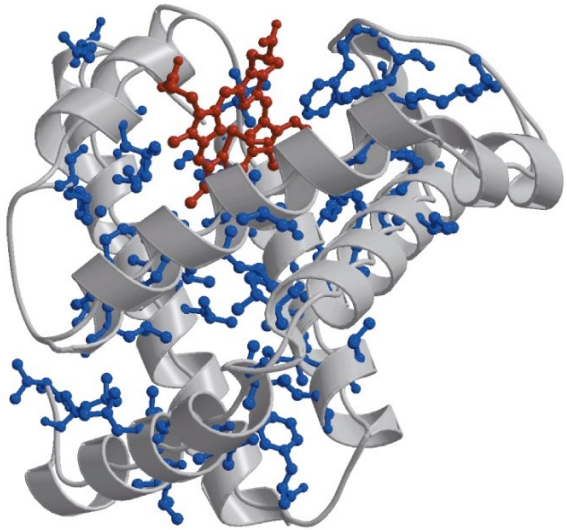
Sperm whale myoglobin



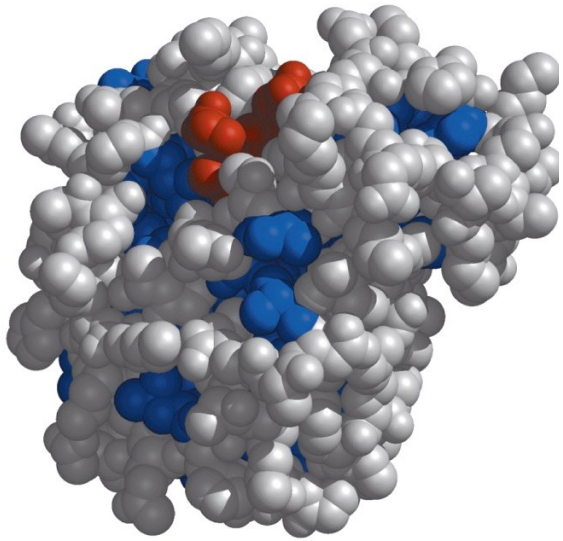
(a)



(b)



(c)



(d)

Structures of other globular proteins

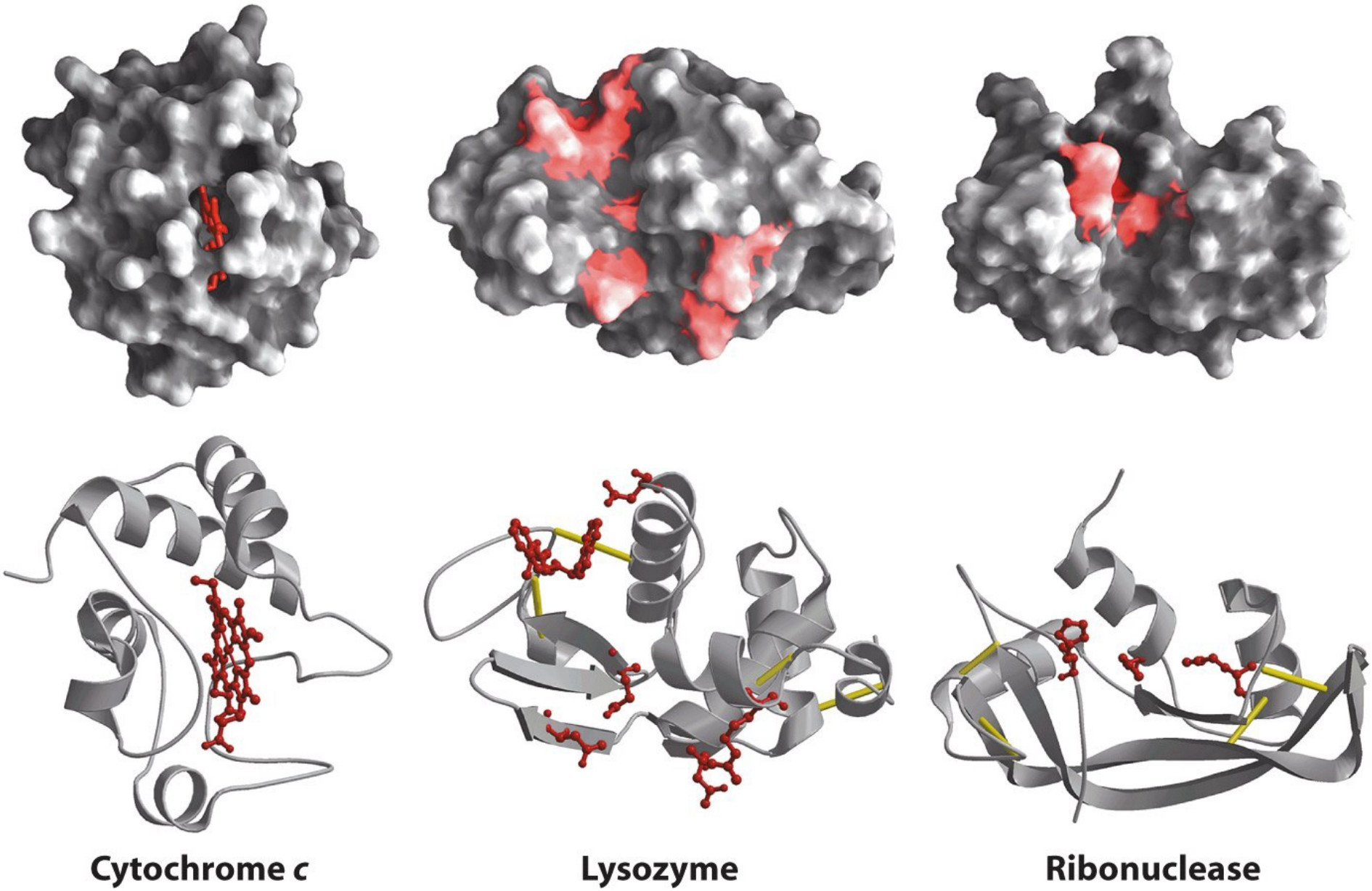
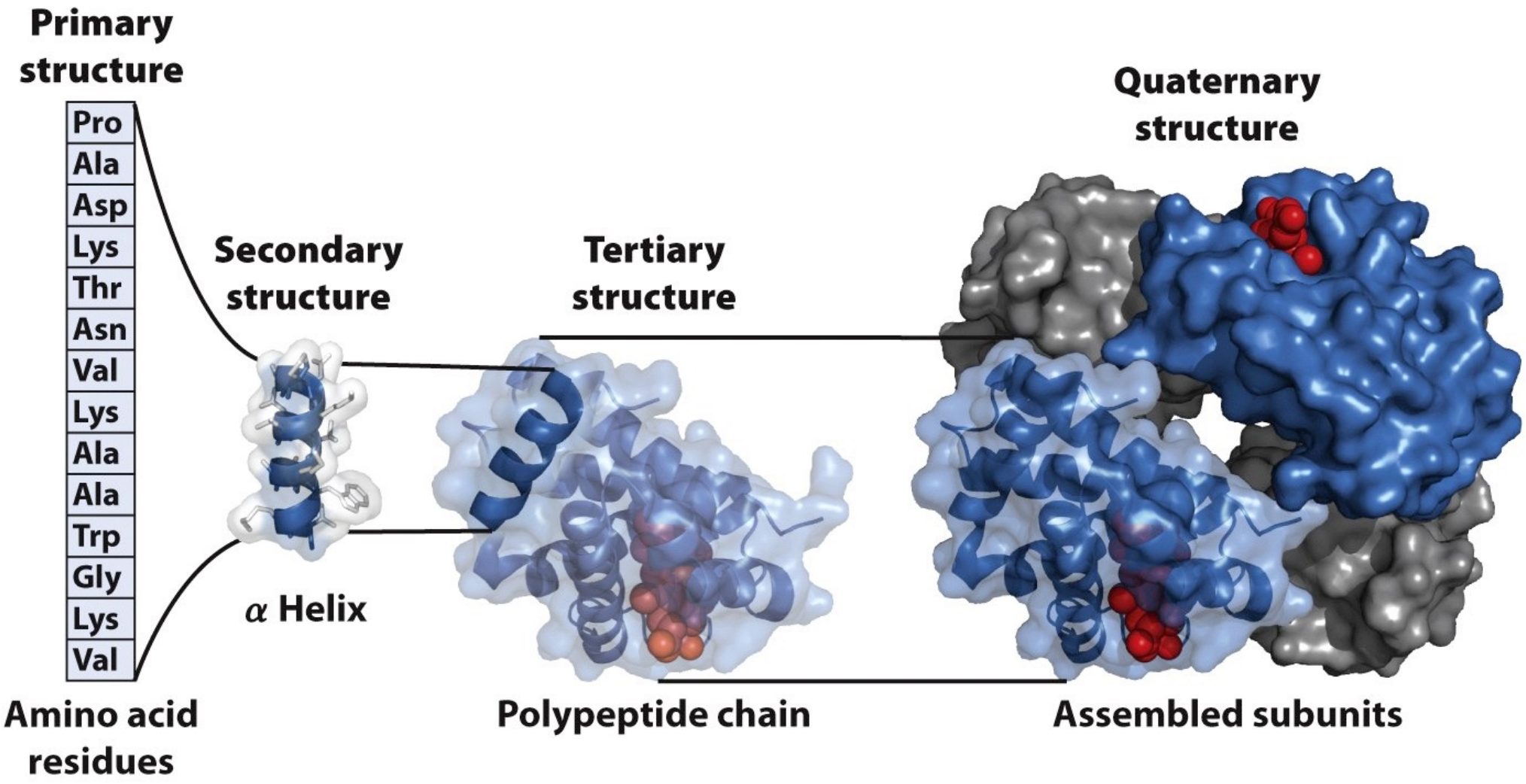


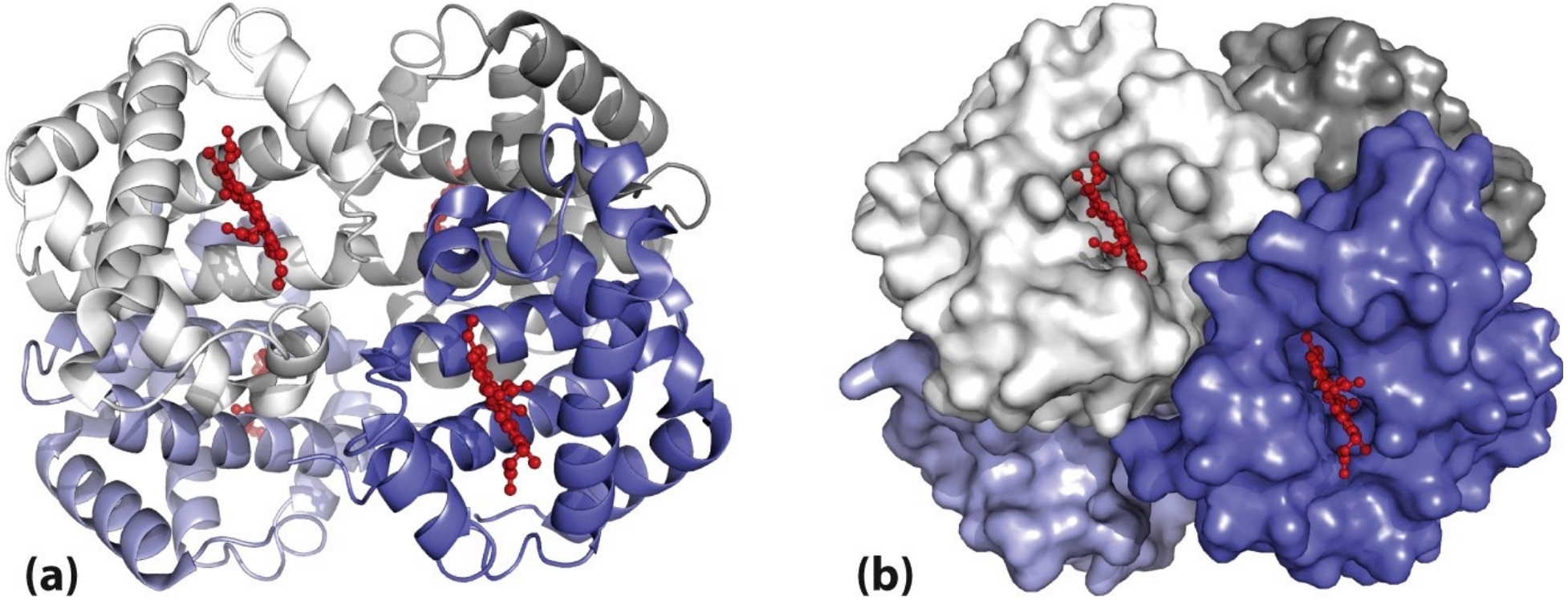
Figure 4-18, Lehninger 4th ed.

Disulfide bonds (covalent) form between two cysteines under oxidative conditions

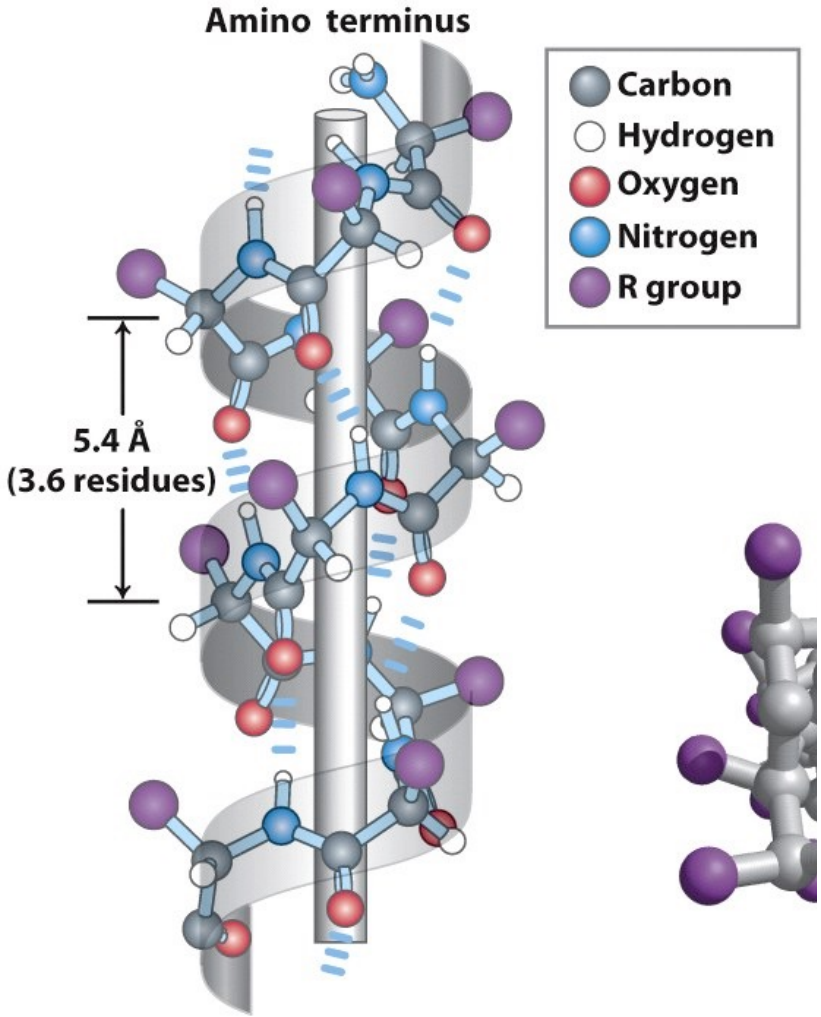
Quaternary structure – only for multimeric proteins

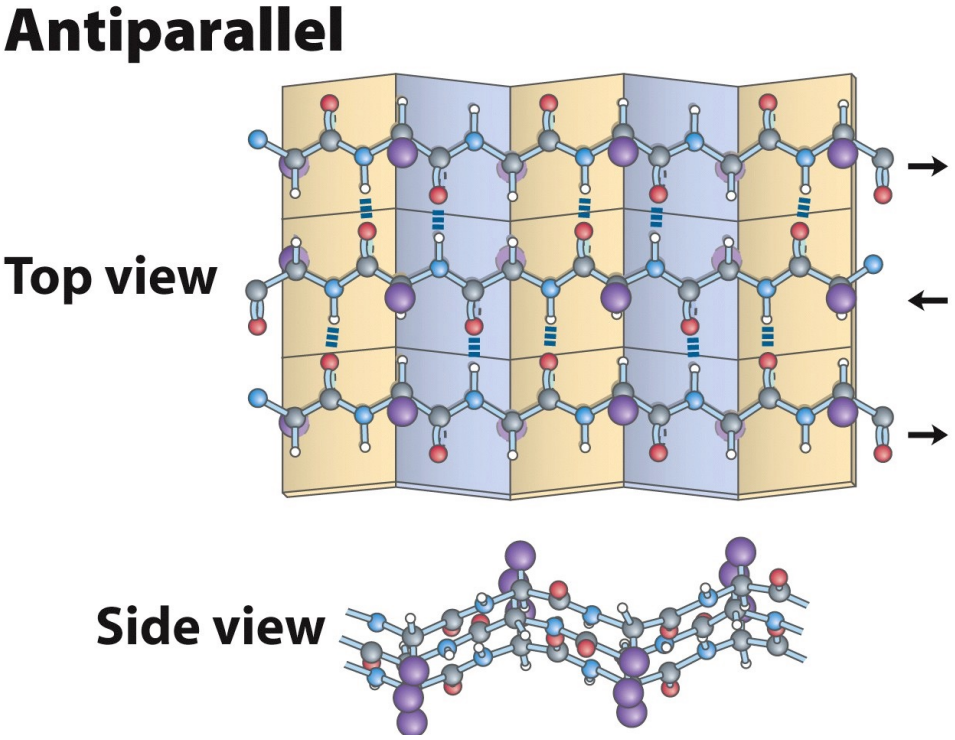


Hemoglobin is a tetramer (dimer of dimers)

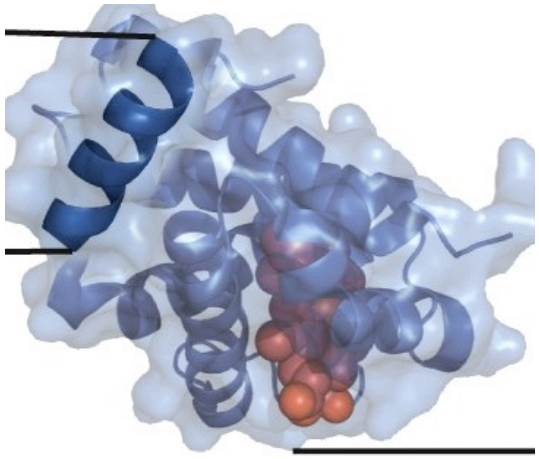


Secondary structures are stabilized by H-bonds between backbone amide groups





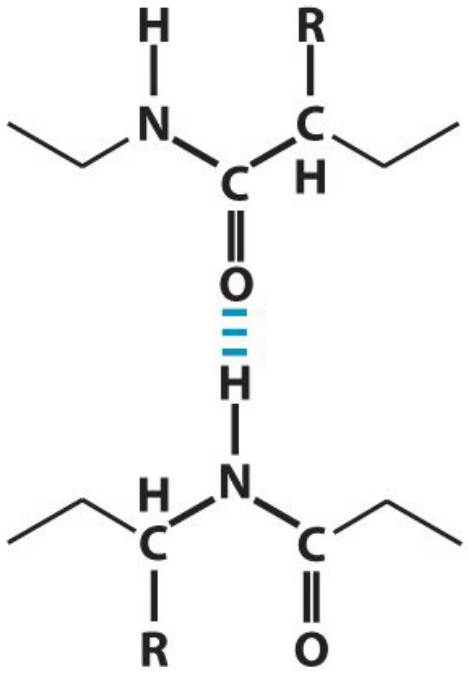
Interactions that stabilize tertiary structure



	Bond energy (kcal/mol)
1. H bonds	2-5
2. Ionic interactions	10-20
3. Hydrophobic interactions	1-3
4. Van der Waals interactions	1
5. Disulfide bonds (only covalent one)	80

H-bonds

- H bond donor and acceptor within 3 Å of each other.
- Involves backbone and side chain groups (in tertiary structure).
- Involves polar residues (if on surface of protein, can H bond with water).
- Individually weak, but additive effect – so significantly stabilizing.



Ionic interactions

- Charge-charge interactions (salt bridge formation)
- Strongest of non-covalent bonds.
- Charged amino acids usually found on surface of protein and thus interact with ions in solution.

Hydrophobic interactions

- Very important
- Involve non polar groups.
- Individually weak, but additive.
- Driven by entropy – maximize disorder in universe! (this will hopefully make more sense when we discuss thermodynamics of protein folding)

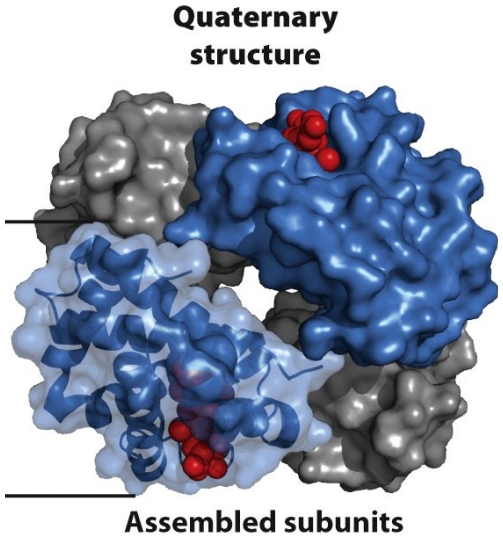
Van der Waal's interactions

- Weak attractive forces between electrically neutral molecules which have permanent or induced dipoles (additive).

Disulfide bonds (strong covalent)

- Usually few Cys in proteins, so not too many disulfide bonds (but small proteins utilize disulfide bonds to confer stability (ex. lysozyme, ribonuclease A).

Quaternary structure stabilized by all of the below EXCEPT disulfide bonds!



	Bond energy (kcal/mol)
1. H bonds	2-5
2. Ionic interactions	10-20
3. Hydrophobic interactions	1-3
4. Van der Waals interactions	1
5. Disulfide bonds (only covalent one) (not involved in quaternary structure)	80