

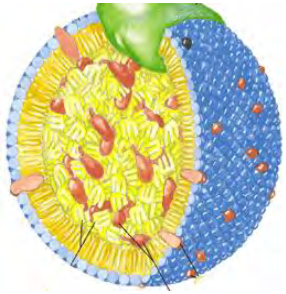


BIOCHEMISTRY REVIEW

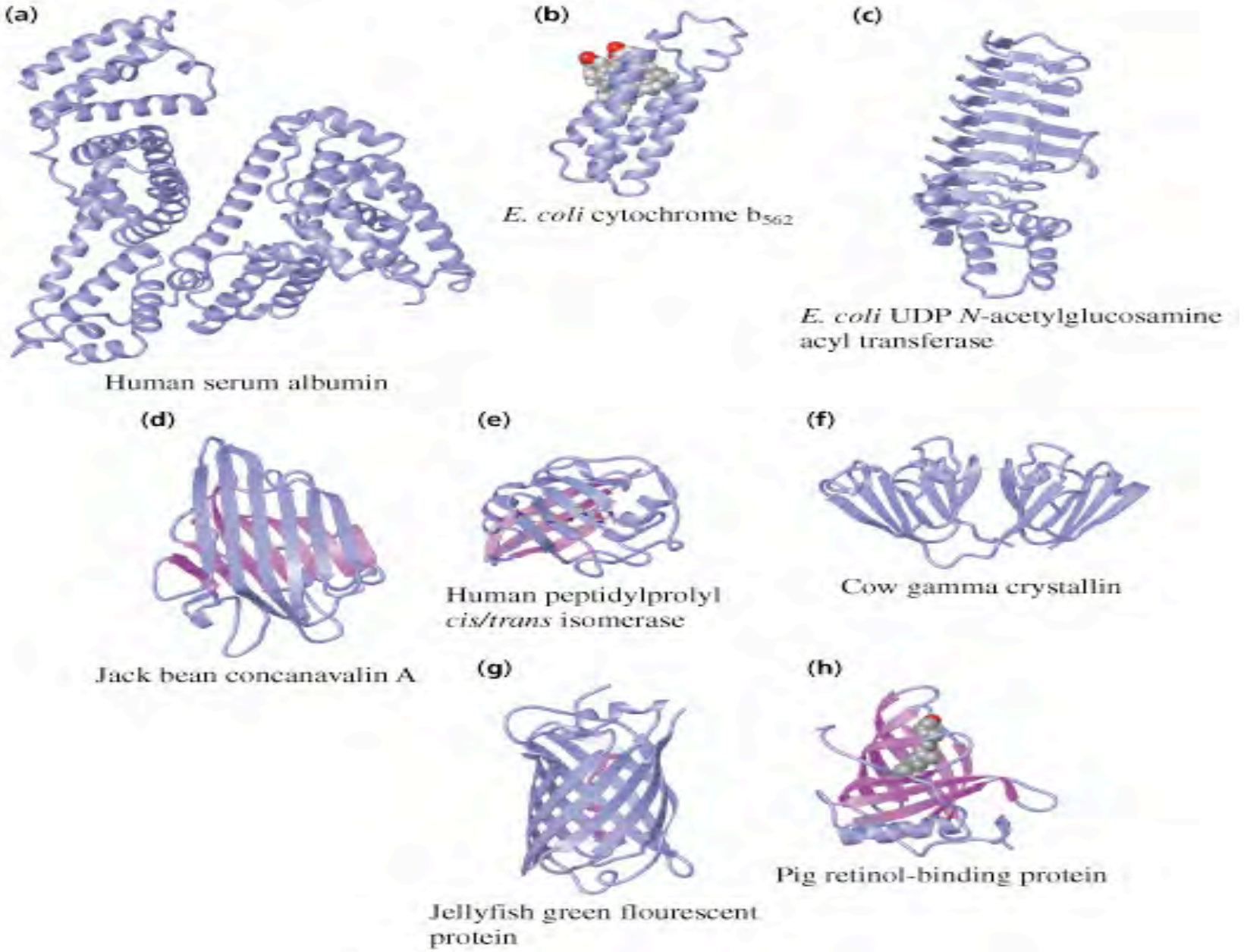
Overview of Biomolecules

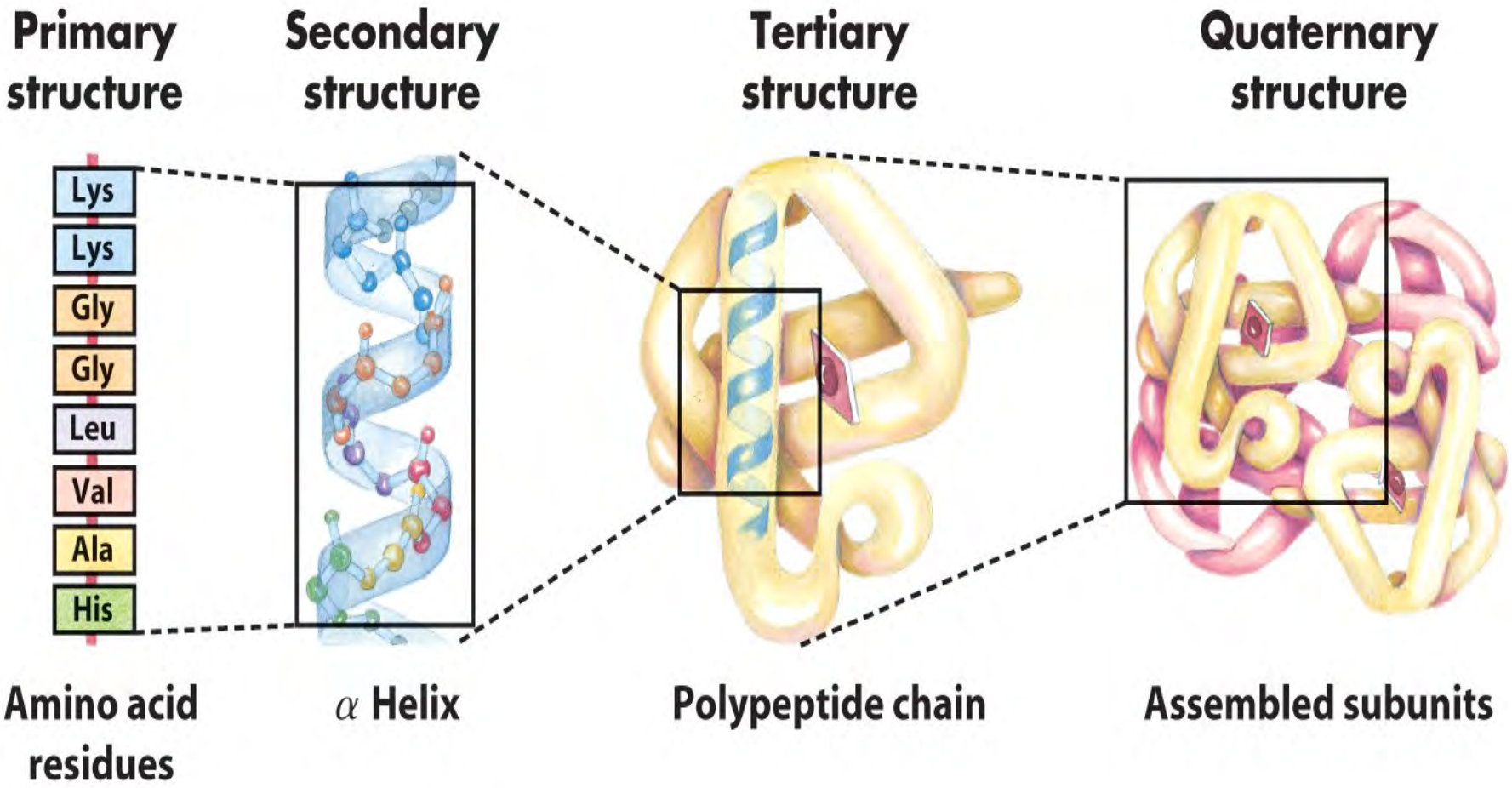
Chapter 5

Protein Conformation






(a)
(b)
(c)
E. coli cytochrome b_{562}
E. coli UDP N-acetylglucosamine acyl transferase
Human serum albumin
(d)
(e)
(f)
Human peptidylprolyl cis/trans isomerase
Cow gamma crystallin
Jack bean concanavalin A
(g)
(h)
Pig retinol-binding protein
Jellyfish green flourescent protein


Primary structure
Secondary structure
Tertiary structure
Quaternary structure
Lys
Lys
Gly
Gly
Leu
Val
Ala
His
Amino acid residues
α Helix
Polypeptide chain
Assembled subunits



Are You Getting It??



Which types of protein structure deal with the shape or spatial arrangement of the polypeptide chain(s)? ***(multiple answers)***

a) primary structure
b) secondary structure
c) tertiary structure
d) quaternary structure



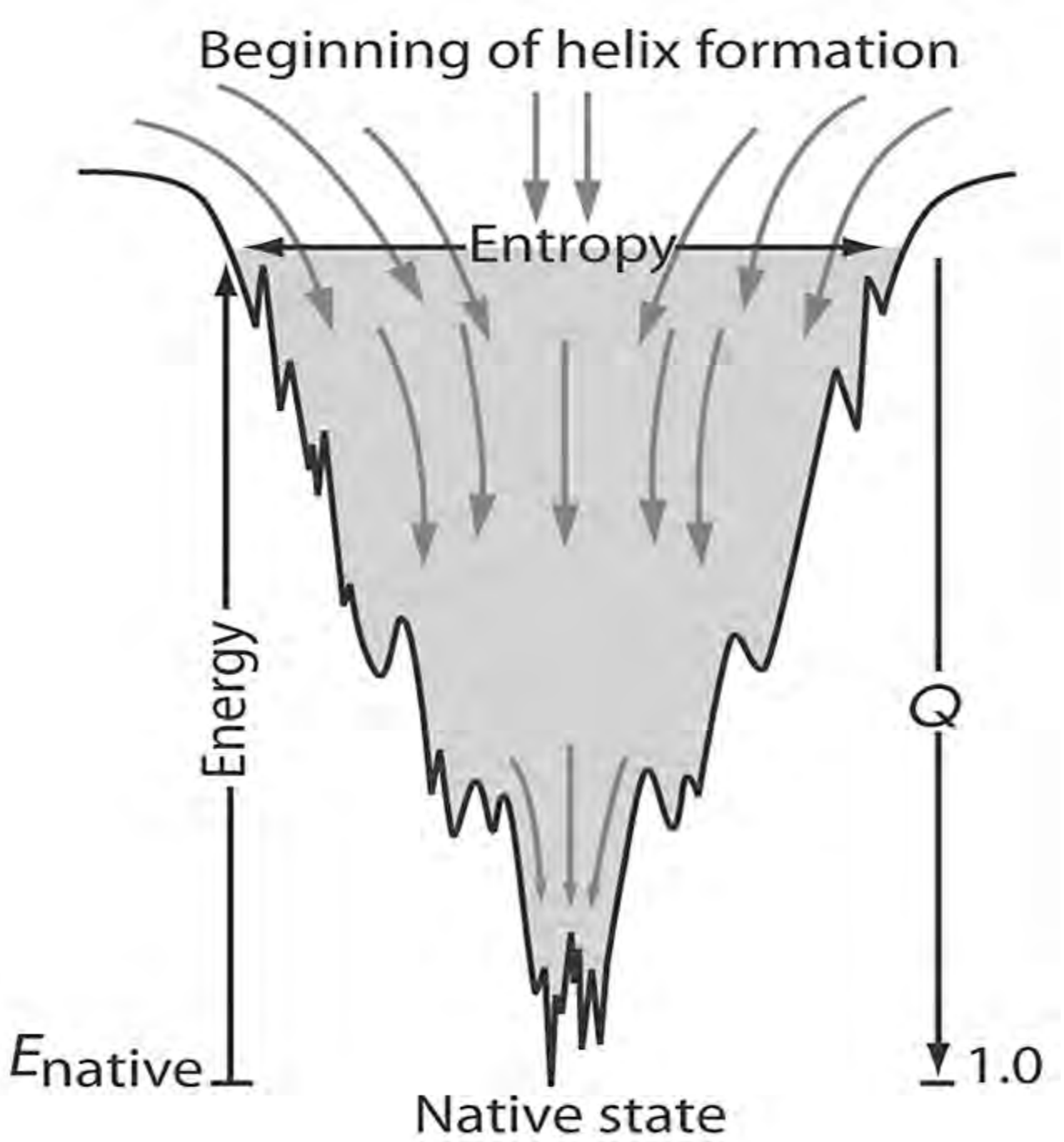
Are You Getting It??



Answer

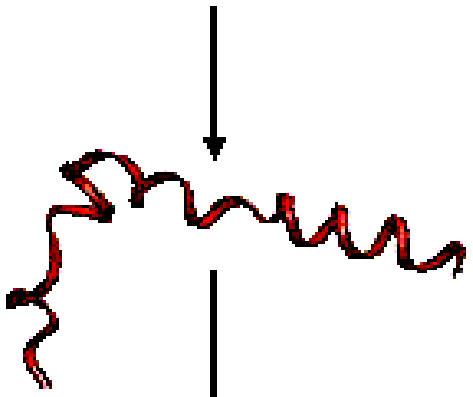
Which types of protein structure deal with the shape or spatial arrangement of the polypeptide chain(s)?

a) primary structure
b) ***secondary structure***
c) ***tertiary structure***
d) ***quaternary structure***

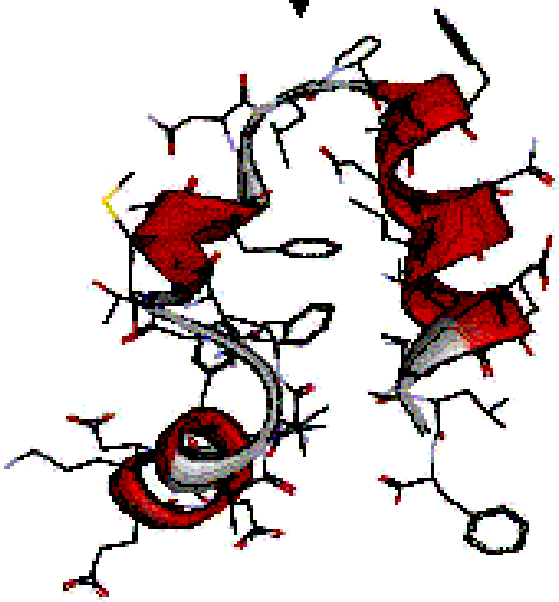

Beginning of helix formation
Entropy
Energy
Q
Enative
1.0
Native state

MET LEU SER ASP GLU ASP PHE LYS ALA VAL PHE GLY
MET THR ARG SER ALA PHE ALA ASN LEU PRO LEU TRP
LYS GLN GLN ASN LEU LYS LYS GLU LYS GLY LEU PHE

Unfolded State



Native state





Are You Getting It??



What property could be shared by two protein molecules that normally have different conformations under biological conditions? ***(multiple answers)***

a) They could have the same molecular weight.
b) They could have the same amino acid sequence.
c) They could have the same number of disulfide bonds.
d) They could have the same number of subunits.



Are You Getting It??



Answer

What property could be shared by two protein molecules that normally have different conformations under biological conditions?

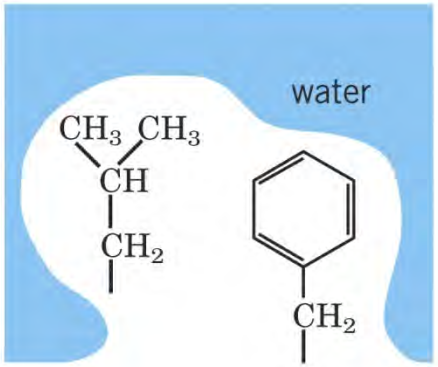
a) ***They could have the same molecular weight.***

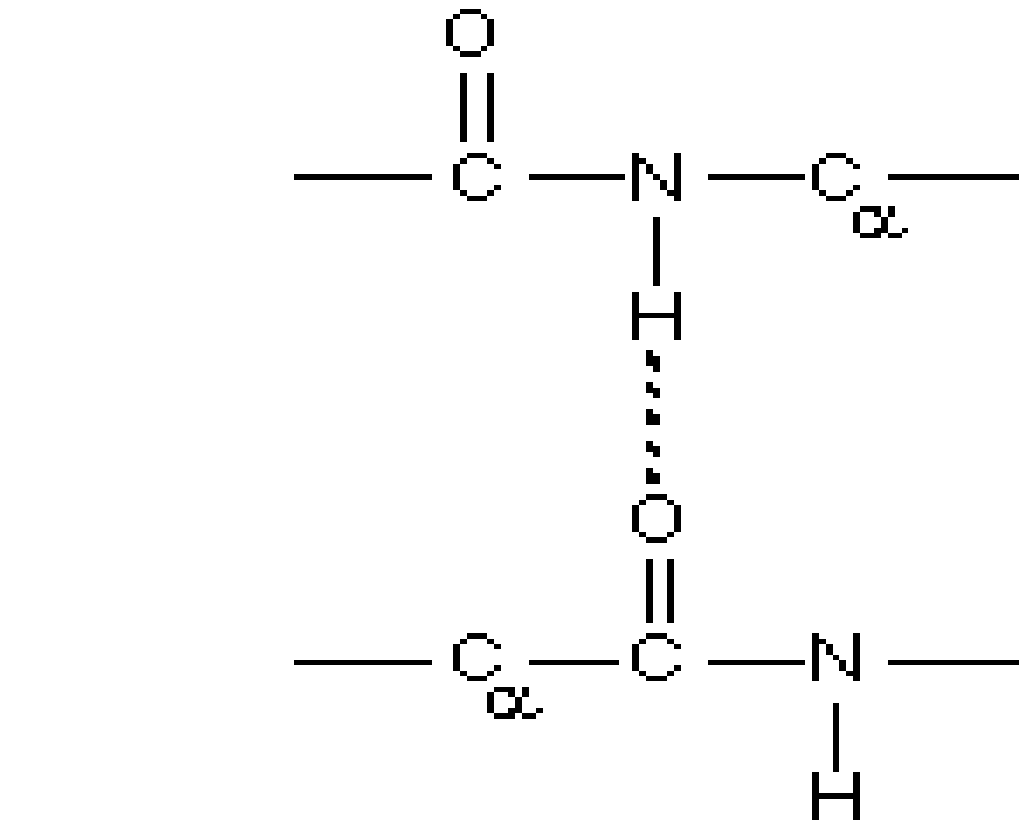
b) **They could have the same amino acid sequence.**

c) ***They could have the same number of disulfide bonds.***

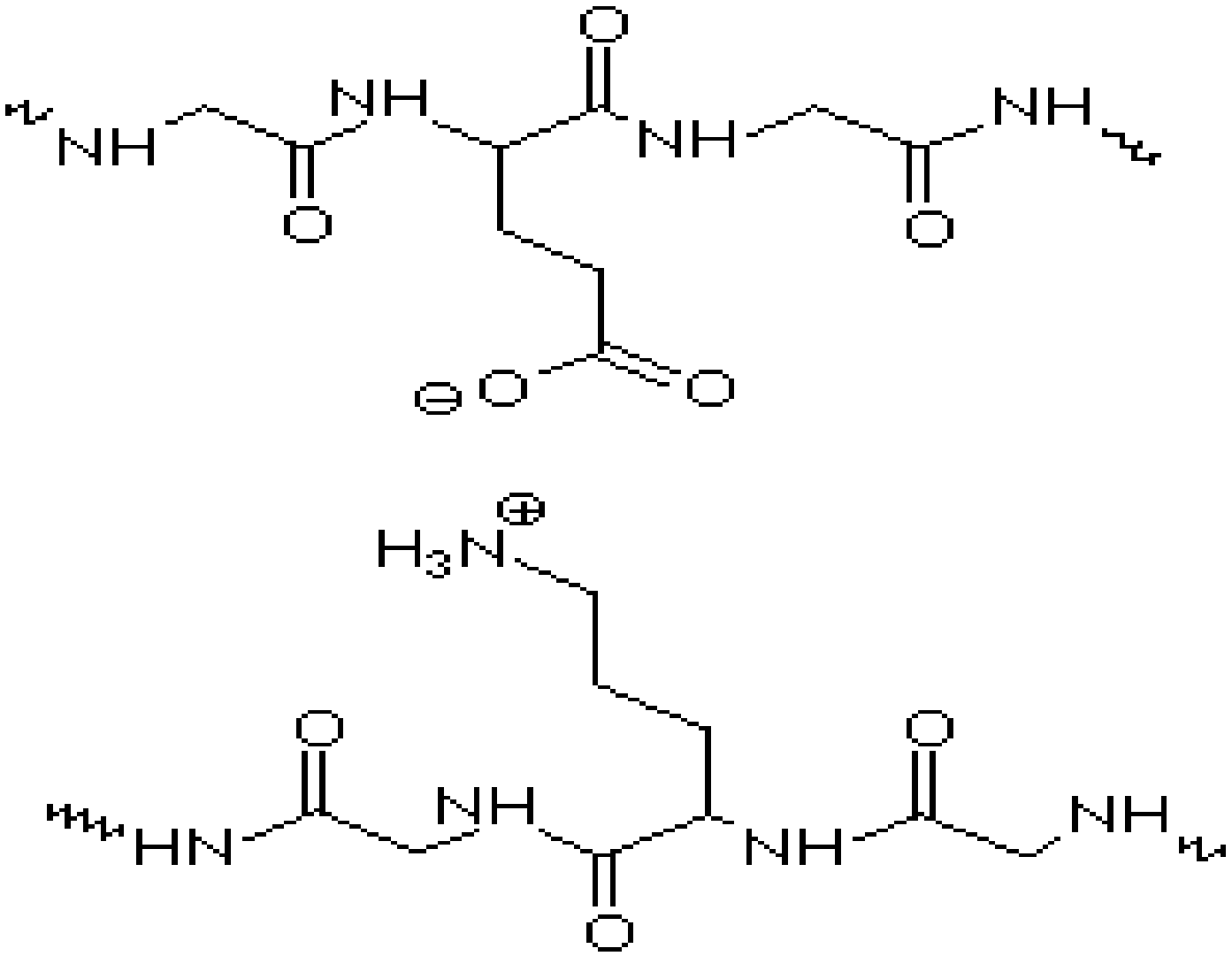
d) ***They could have the same number of subunits.***

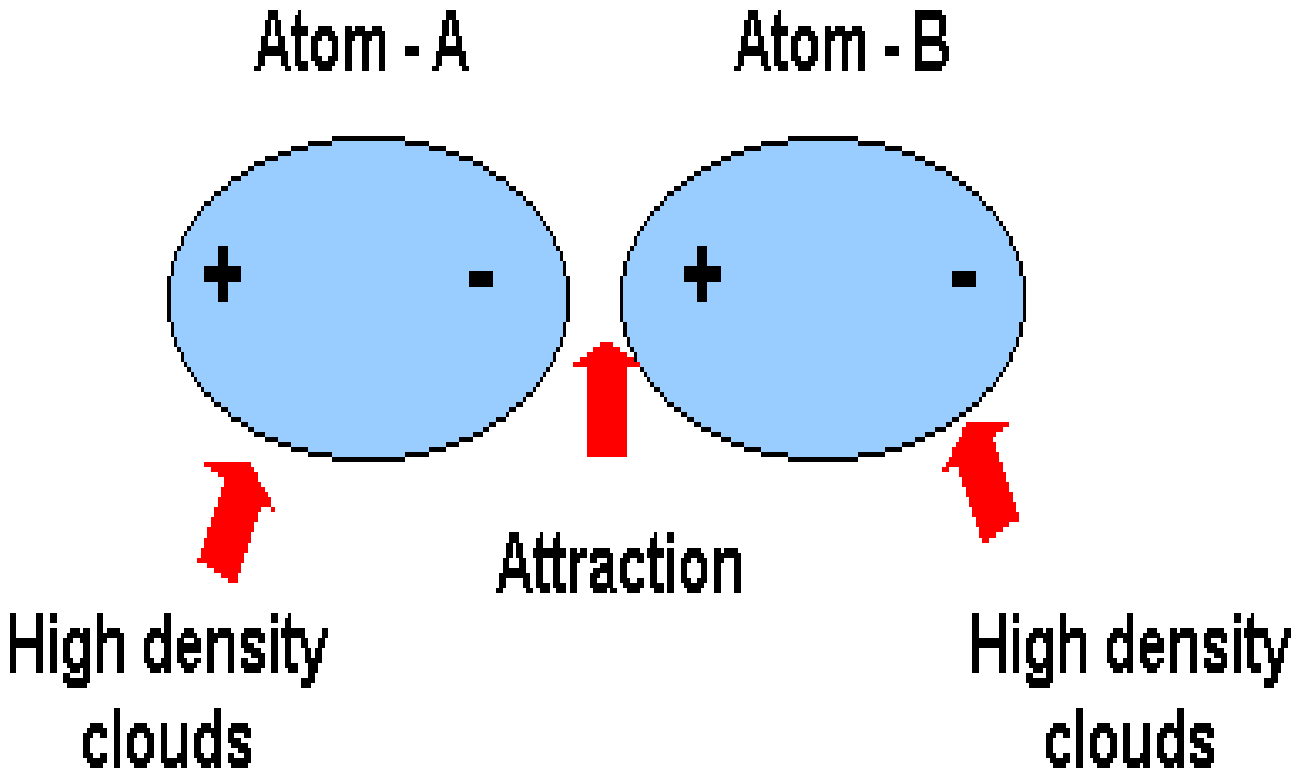
TABLE 2–5 Four Types of Noncovalent ("Weak") Interactions among Biomolecules in Aqueous Solvent

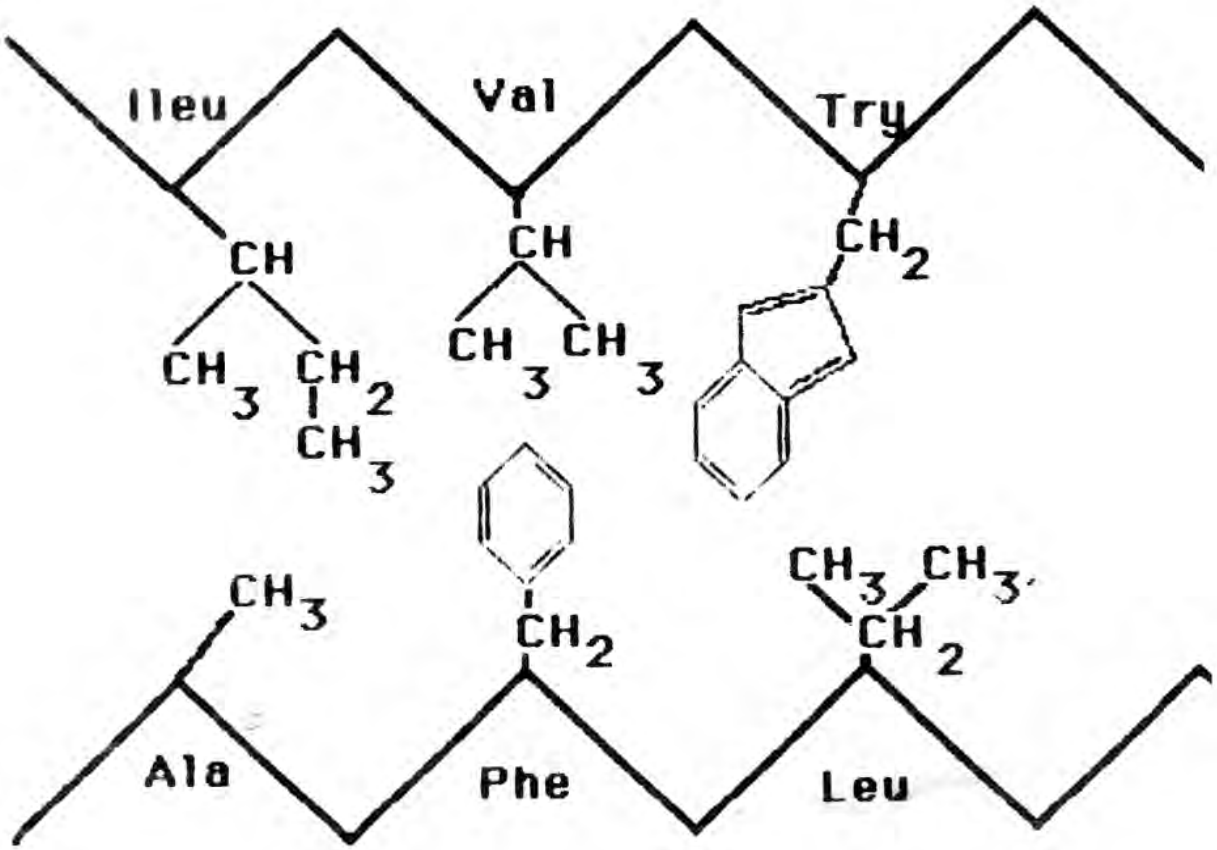
Hydrogen bonds	
Between neutral groups	
Between peptide bonds	
Ionic interactions	
Attraction	
Repulsion	
Hydrophobic interactions	
van der Waals interactions	Any two atoms in close proximity

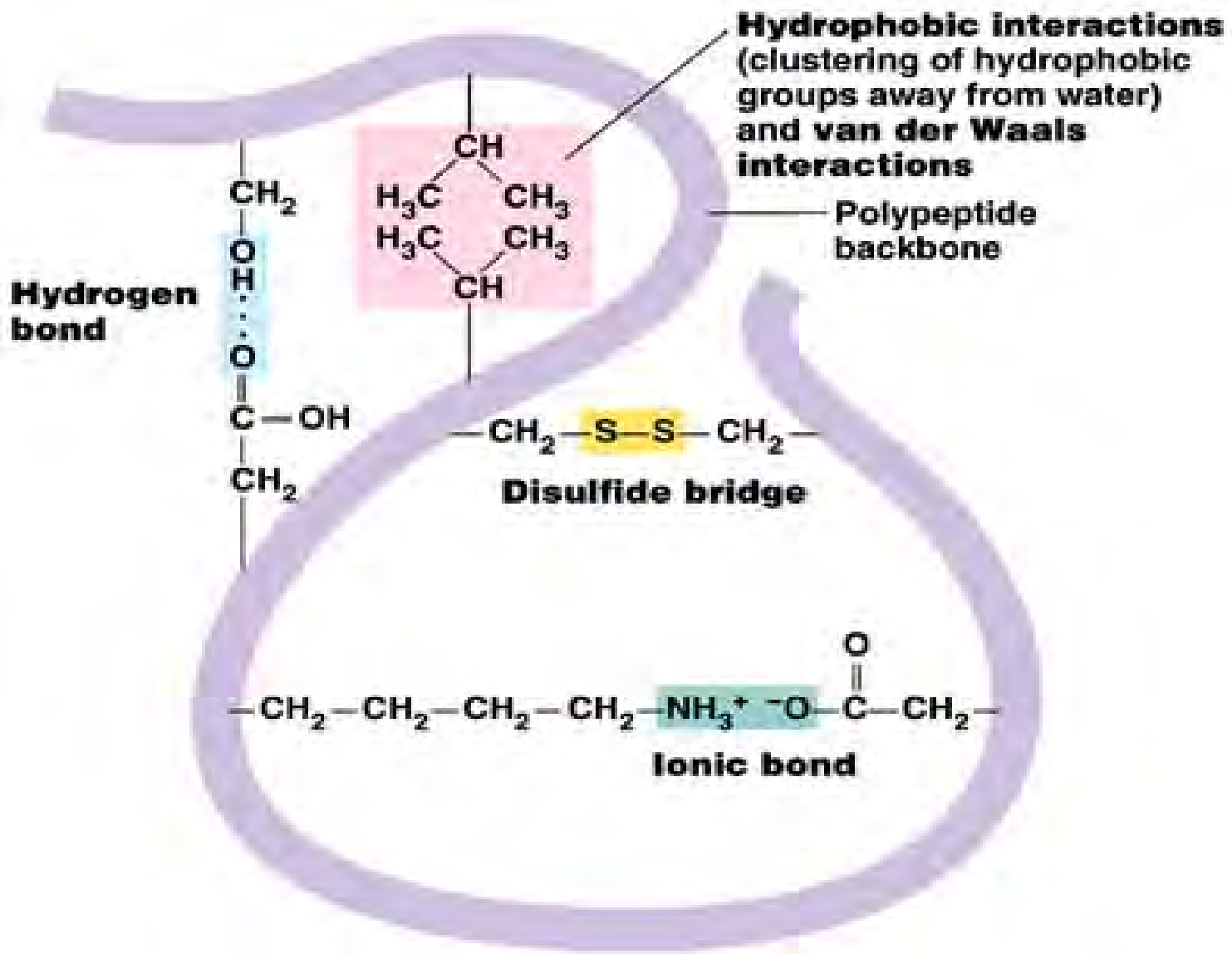


peptide backbone H-bond
(H & R-group on α-C omitted)




Atom - A
Atom - B
+
-
+
-
Attraction
High density clouds
High density clouds


Ileu
Val
Try
CH
CH
CH2
CH3
CH2
CH3
CH3
CH3
CH3
CH3
CH2
CH3
CH2
Ala
Phe
Leu


Hydrophobic interactions
(clustering of hydrophobic groups away from water)
and van der Waals interactions
Polypeptide backbone
Hydrogen bond
Disulfide bridge
Ionic bond



Are You Getting It??



Which of the following types of bonds are likely to be involved in maintaining protein conformation?
(multiple answers)

a) a peptide bond
b) a hydrogen bond
c) an ionic bond
d) an amide bond



Are You Getting It??



Answer

Which of the following types of bonds are likely to be involved in maintaining protein conformation?

a) a peptide bond
b) *a hydrogen bond*
c) *an ionic bond*
d) an amide bond



Are You Getting It??



Which types of non-covalent forces are the following amino acids likely to form within a protein?

a) alanine
b) serine
c) arginine
d) aspartate
e) glutamine



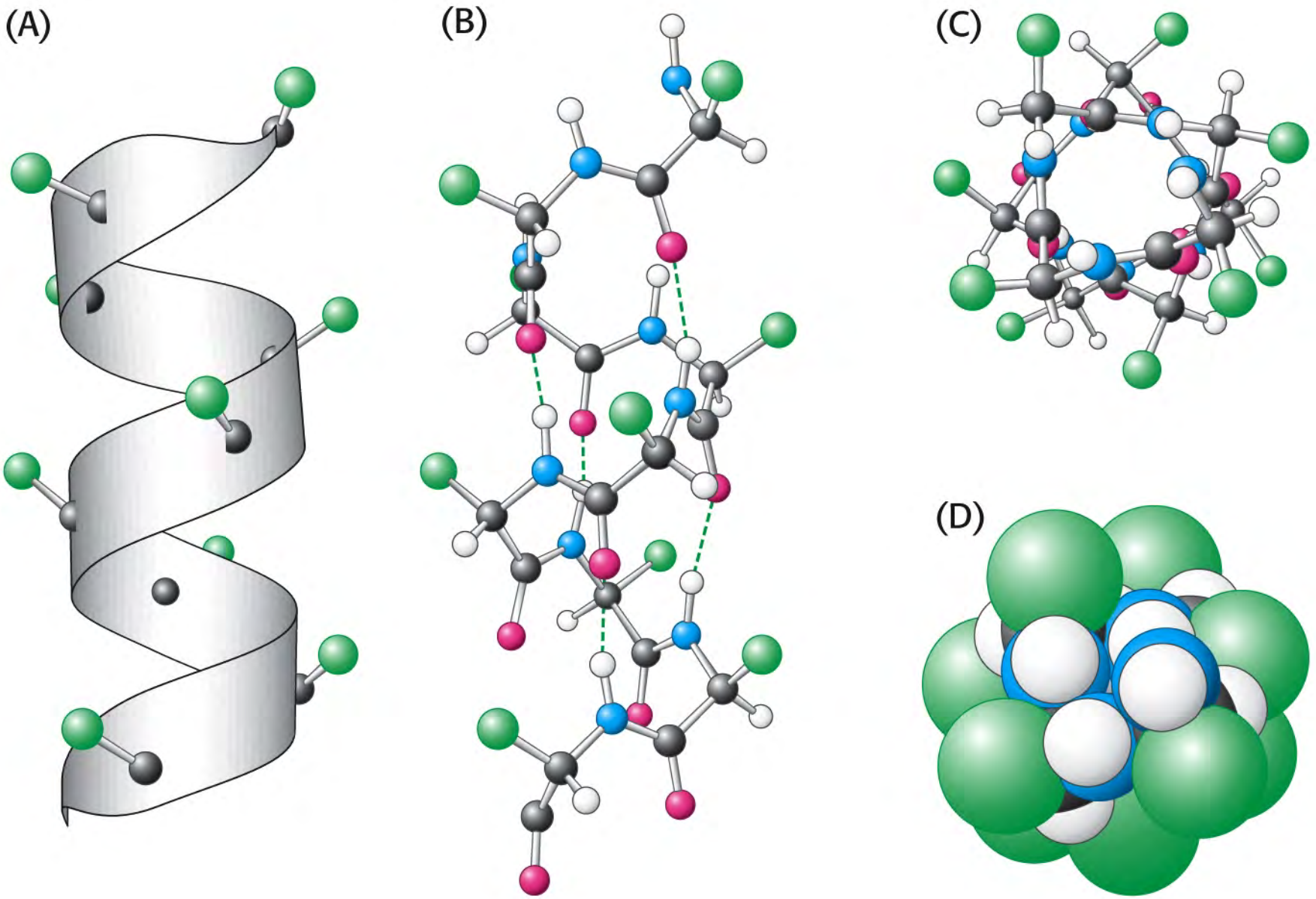
Are You Getting It??

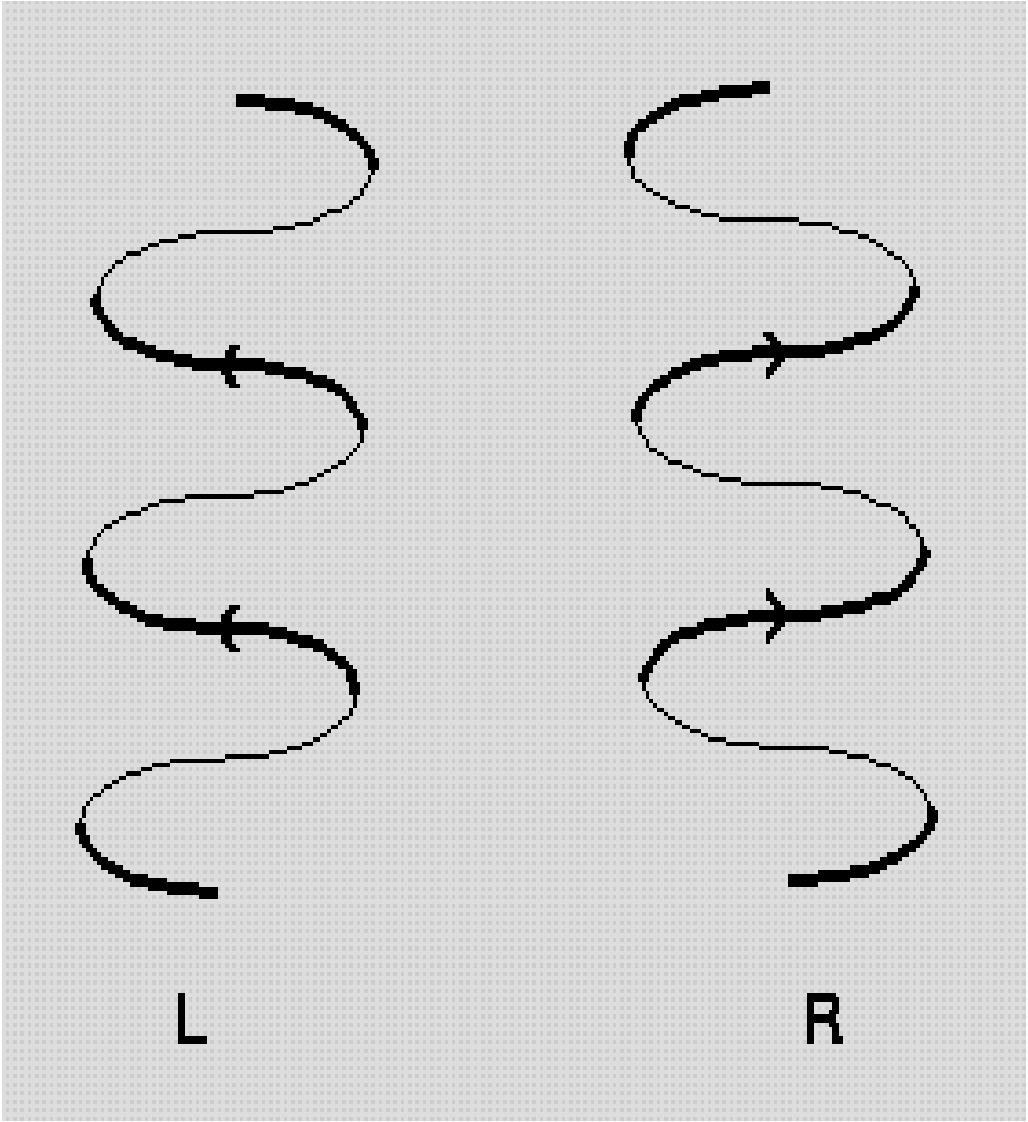


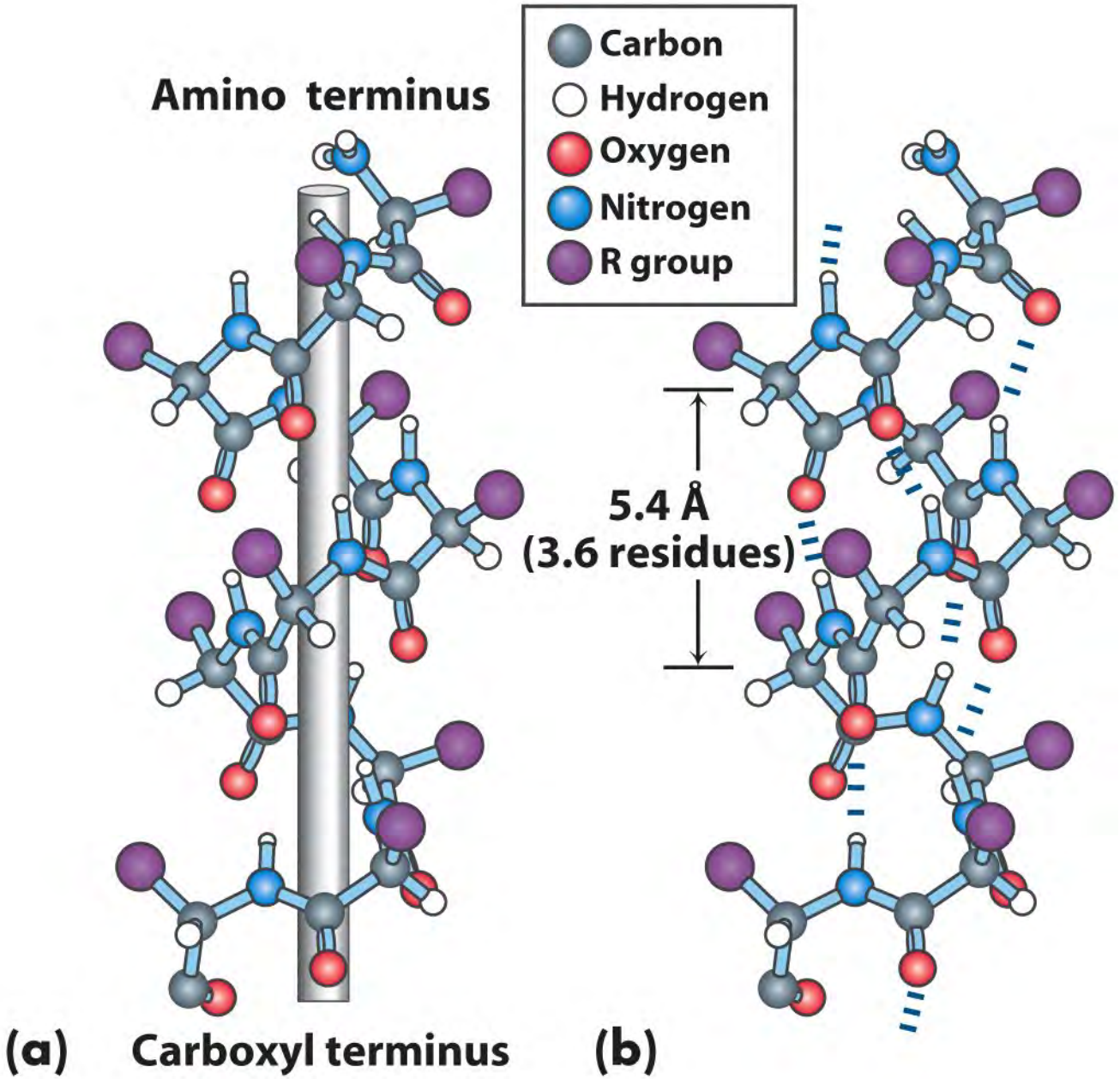
Answer

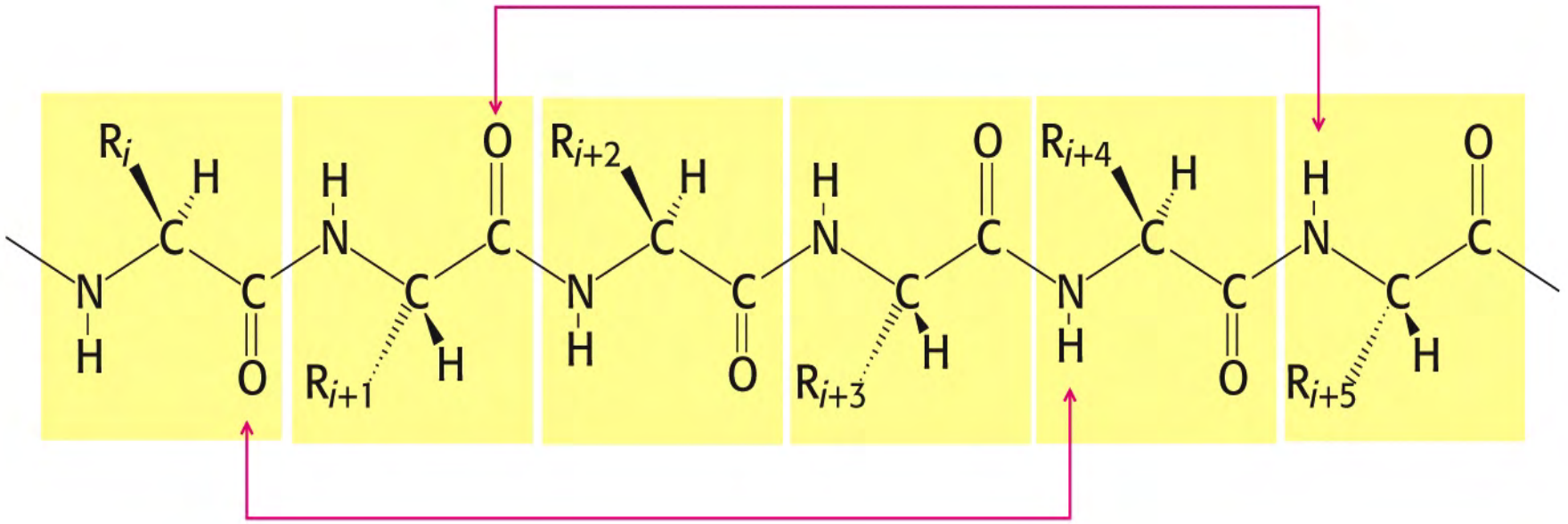
Which types of non-covalent forces are the following amino acids likely to form within a protein?

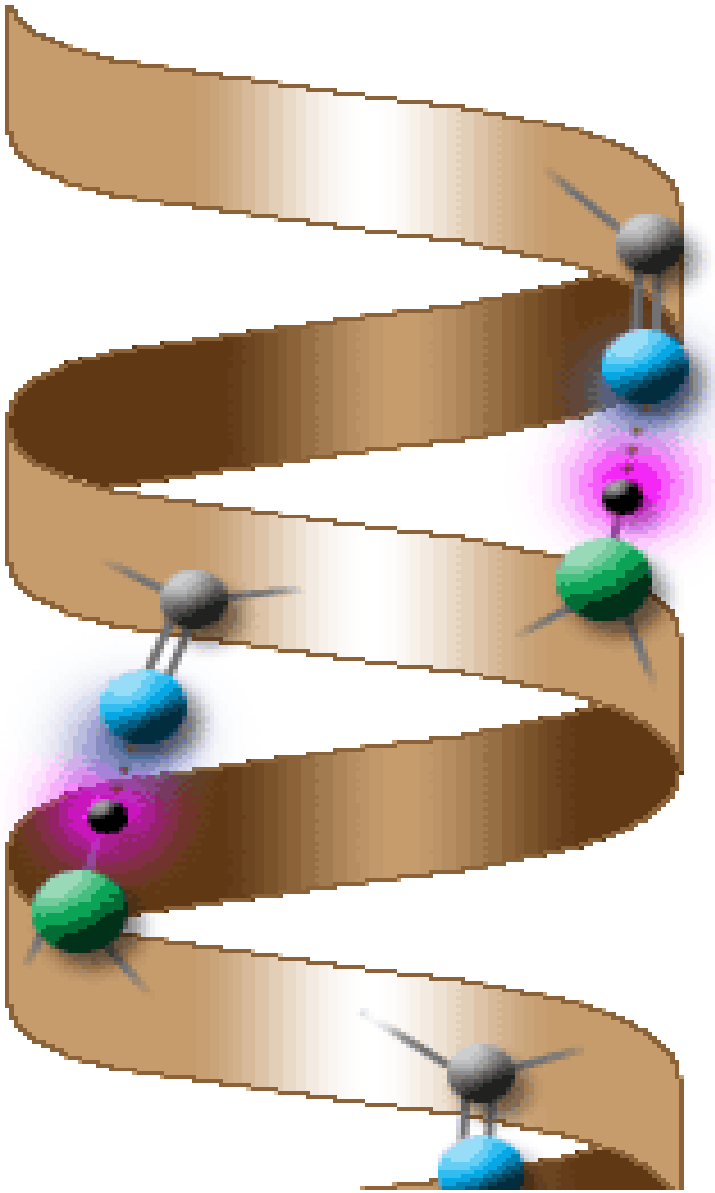
a) alanine *-hydrophobic, van der Waals*
b) serine *-hydrogen bond, van der Waals*
c) arginine *-salt bridge, hydrogen bond, van der Waals*
d) aspartate *-salt bridge, hydrogen bond, van der Waals*
e) glutamine *-hydrogen bond, van der Waals*

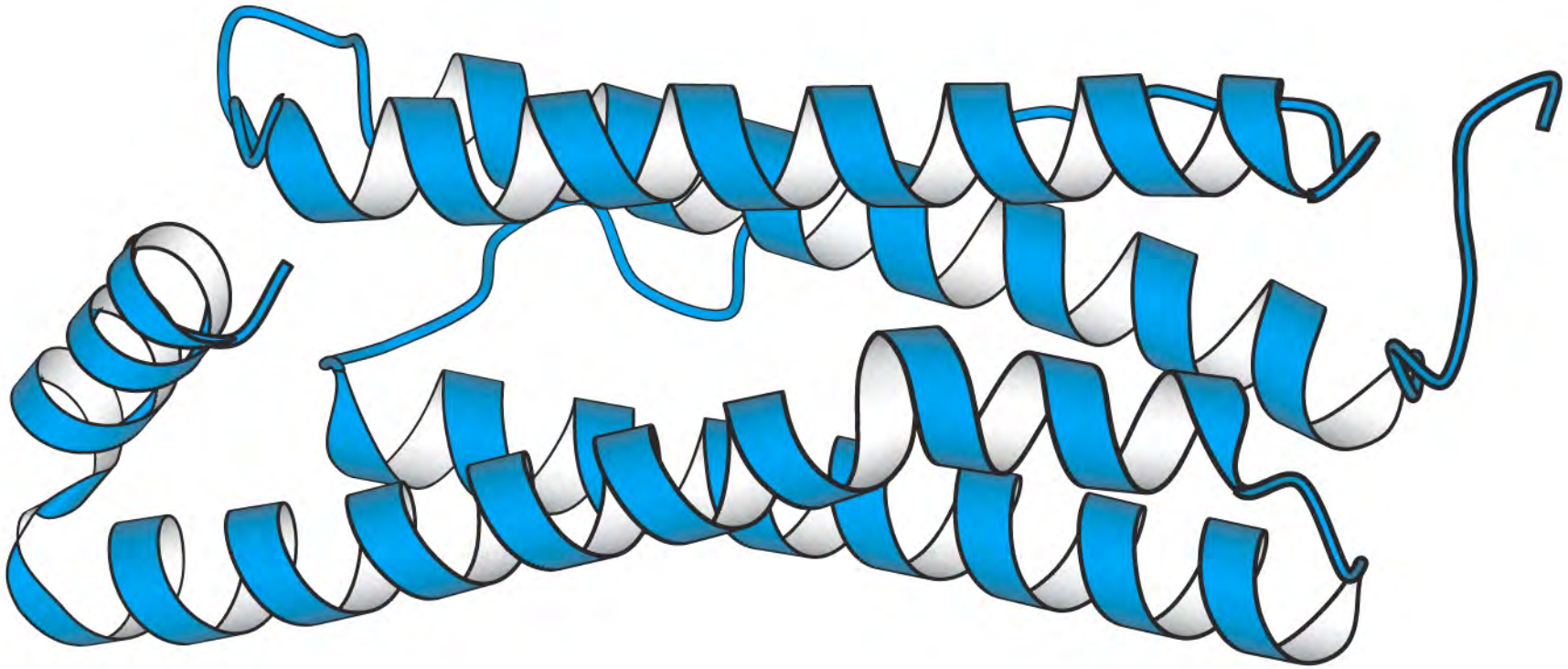

(A)
(B)
(C)
(D)


L
R


Carbon
Hydrogen
Oxygen
Nitrogen
R group
Amino terminus
5.4 Å
(3.6 residues)
(a)
Carboxyl terminus
(b)


R_i
R_{i+1}
R_{i+2}
R_{i+3}
R_{i+4}
R_{i+5}







Are You Getting It??



Which is a property of an α-helix? ***(multiple answers)***

a) Any amino acid sequence can form an α-helix.
b) A protein molecule could be composed entirely of α-helix.
c) A protein molecule could contain 3 segments of α-helix.
d) All α-helices have the same number of amino acids per turn.
e) Two molecules of the same protein could have different amounts of α-helix.



Are You Getting It??



Answer

Which is a property of an α-helix?

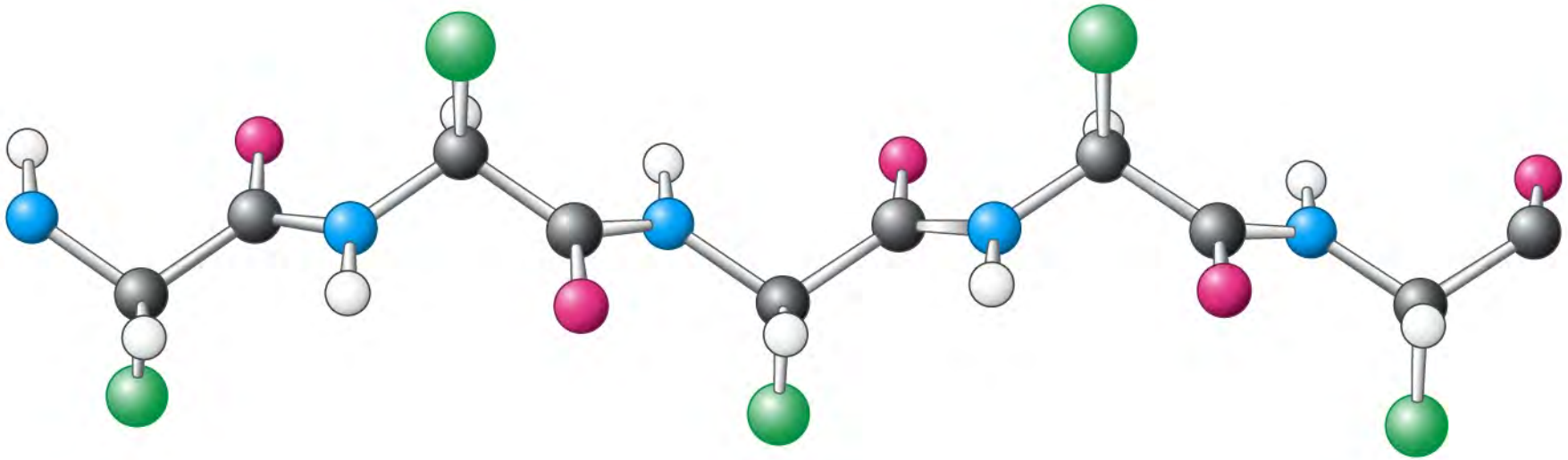
a) Any amino acid sequence can form an α-helix.

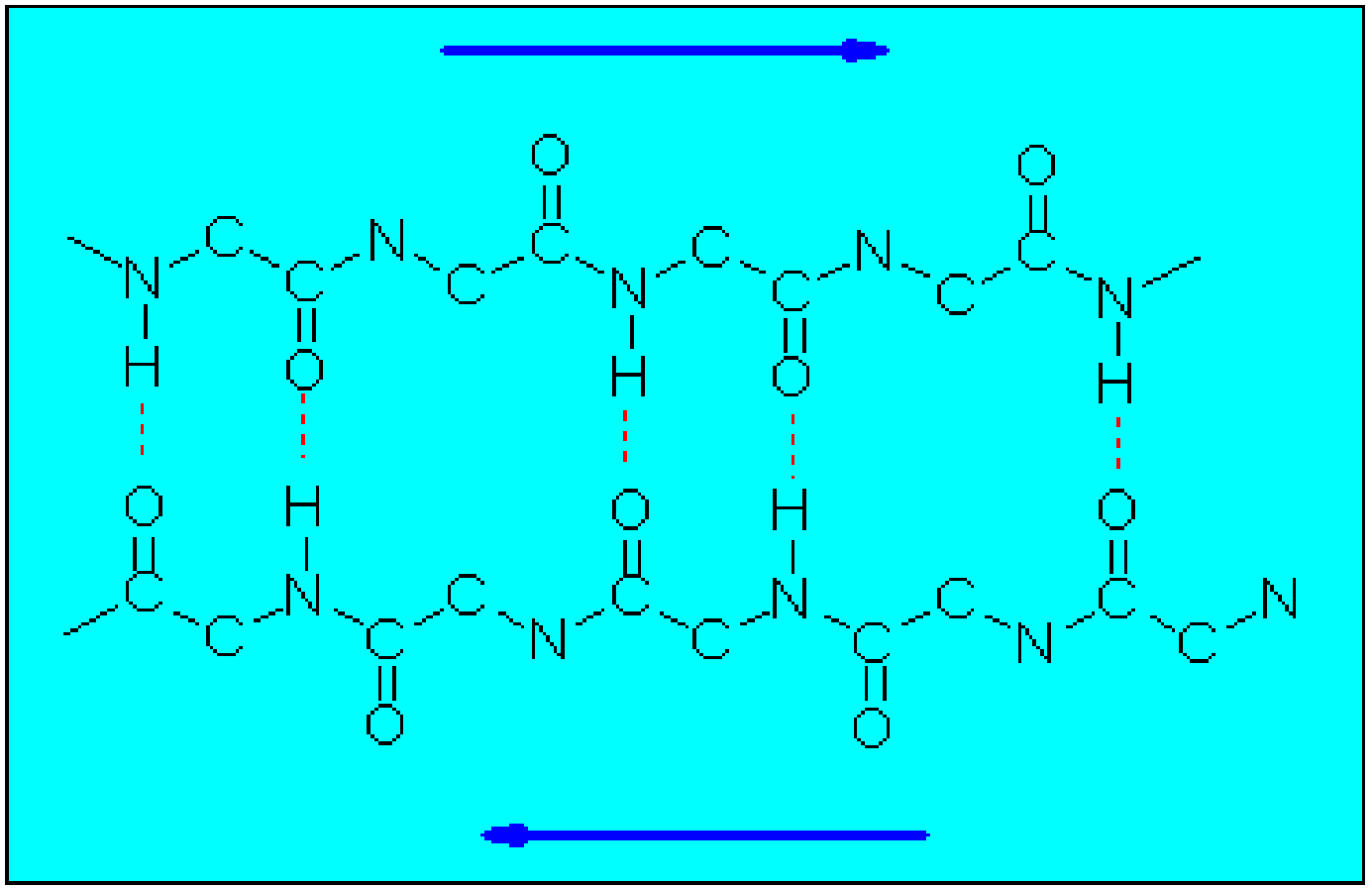
b) ***A protein molecule could be composed entirely of α-helix.***

c) ***A protein molecule could contain 3 segments of α-helix.***

d) ***All α-helices have the same number of amino acids per turn.***

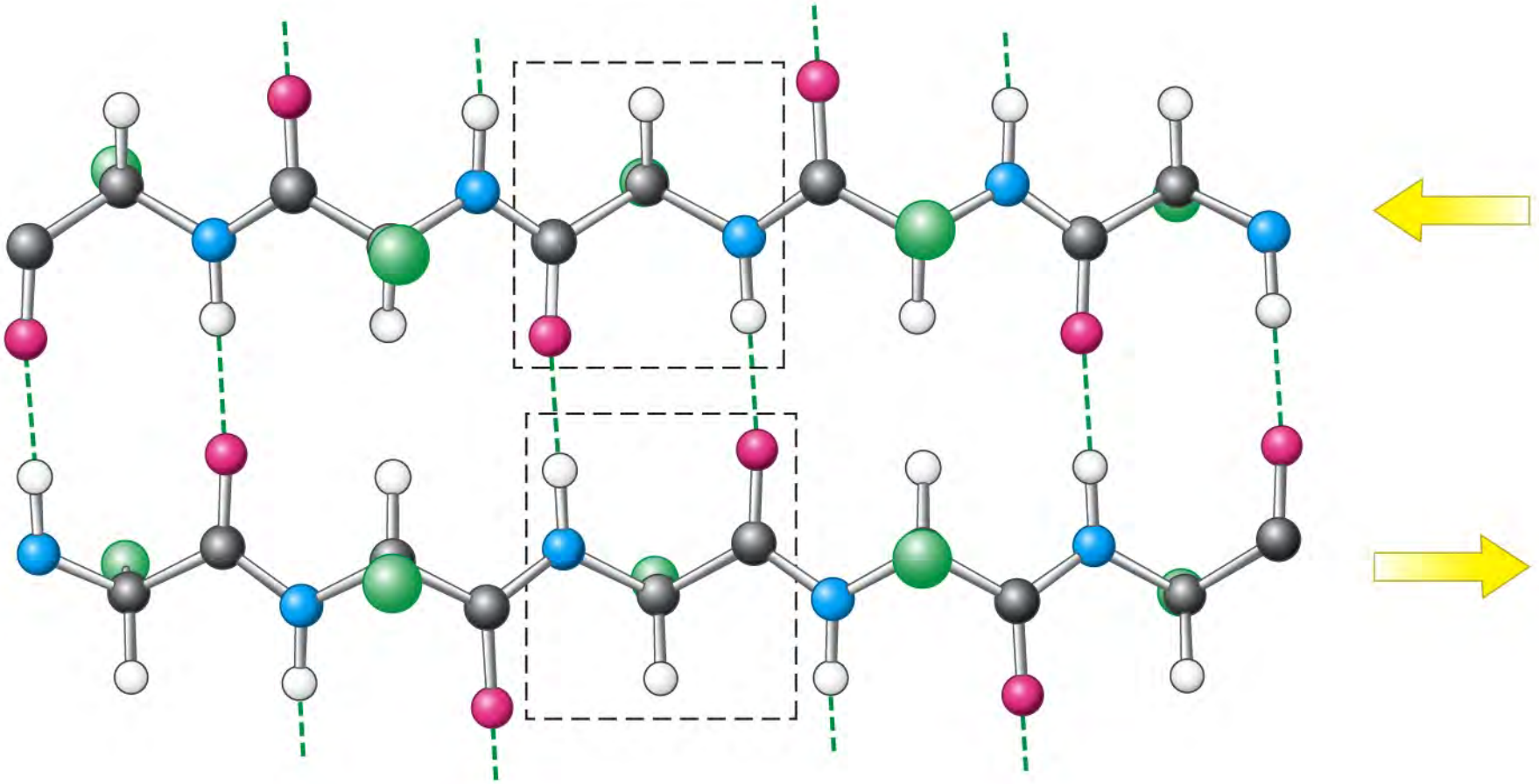
e) Two molecules of the same protein could have different amounts of α-helix.





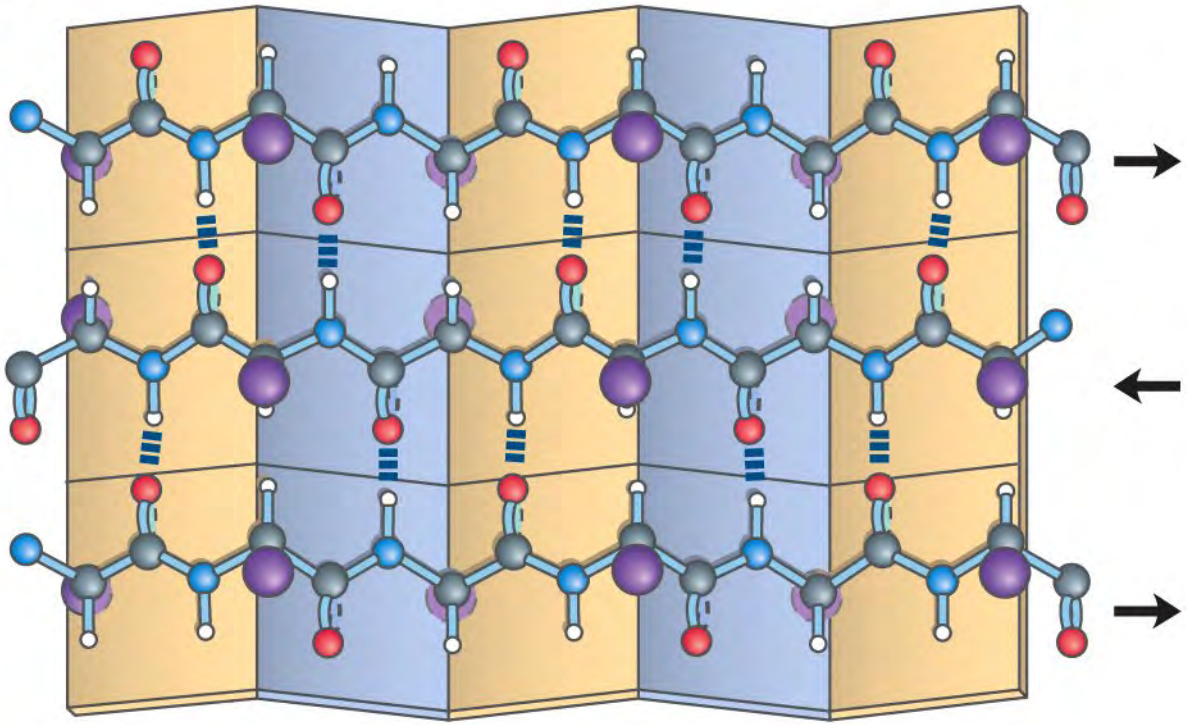
Direction of the polypeptide chain

Hydrogen bond

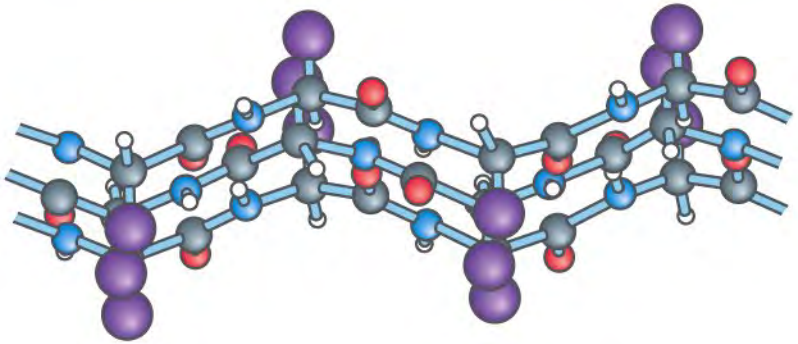


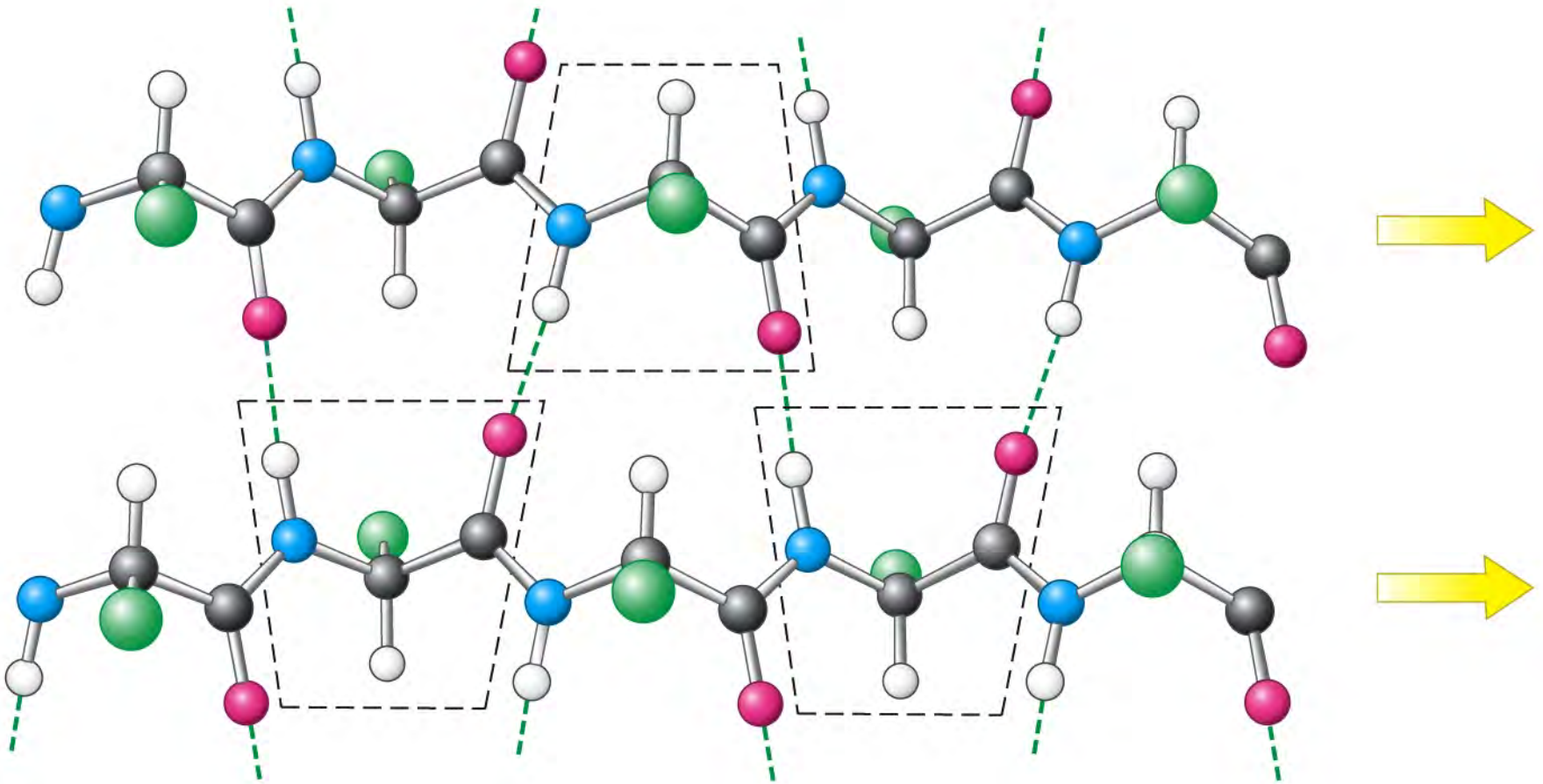
(a) Antiparallel

Top view



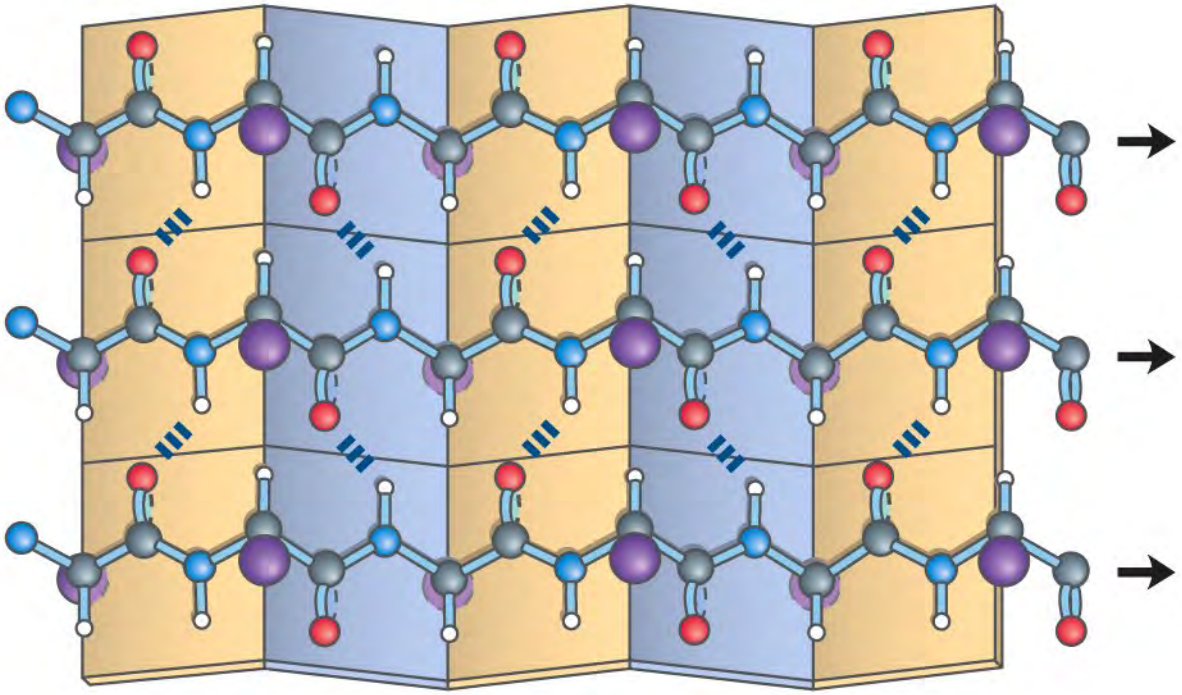
Side view



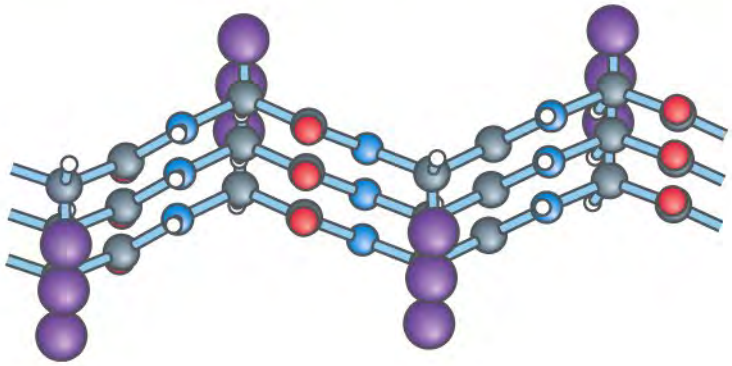


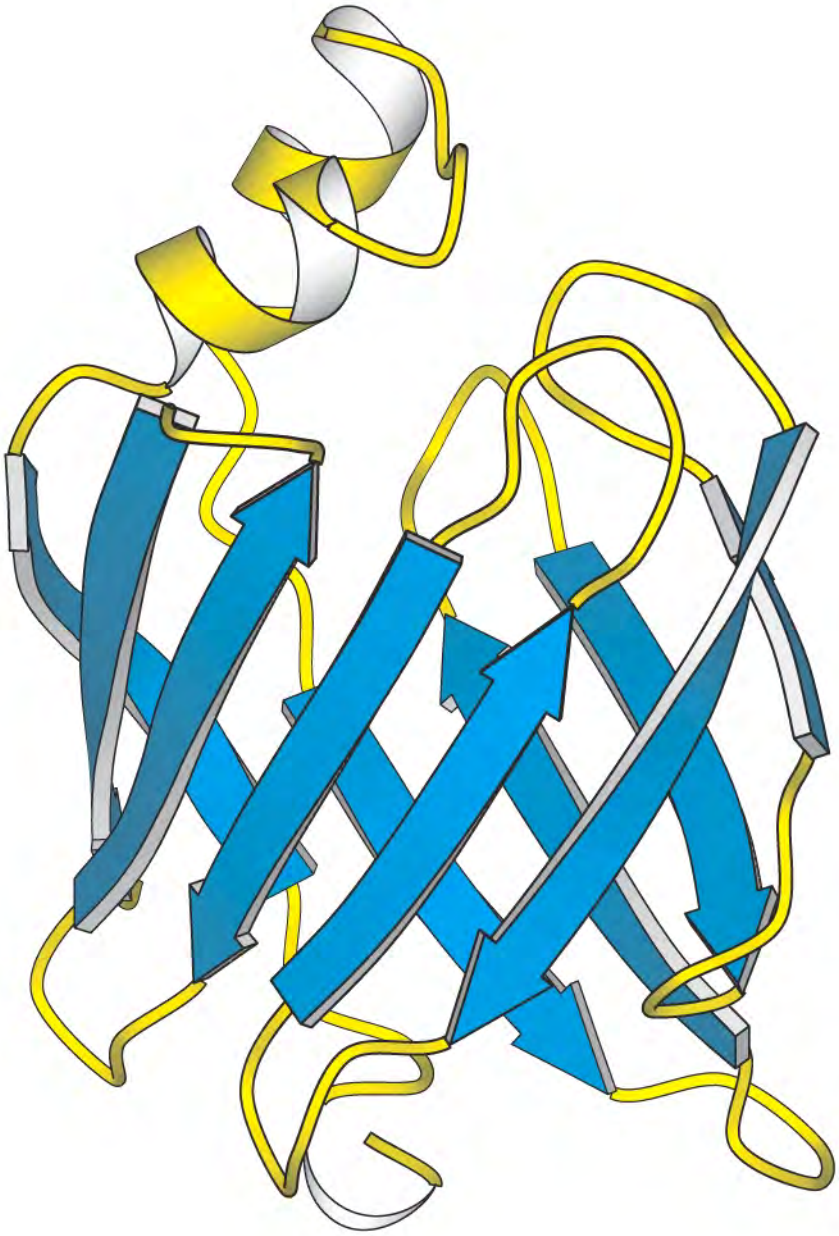
(b) Parallel

Top view



Side view







Are You Getting It??



Which is a property of a β-pleated sheet? ***(multiple answers)***

a) A β-pleated sheet is maintained by non-covalent bonds.
b) A β-pleated sheet can form only in a multimeric protein.
c) A β-pleated sheet always has a parallel configuration.
d) A β-pleated sheet can form only with certain amino acid sequences.
e) A β-pleated sheet always contains the same number of chains.



Are You Getting It??



Answer

Which is a property of a β-pleated sheet?

a) ***A β-pleated sheet is maintained by non-covalent bonds.***

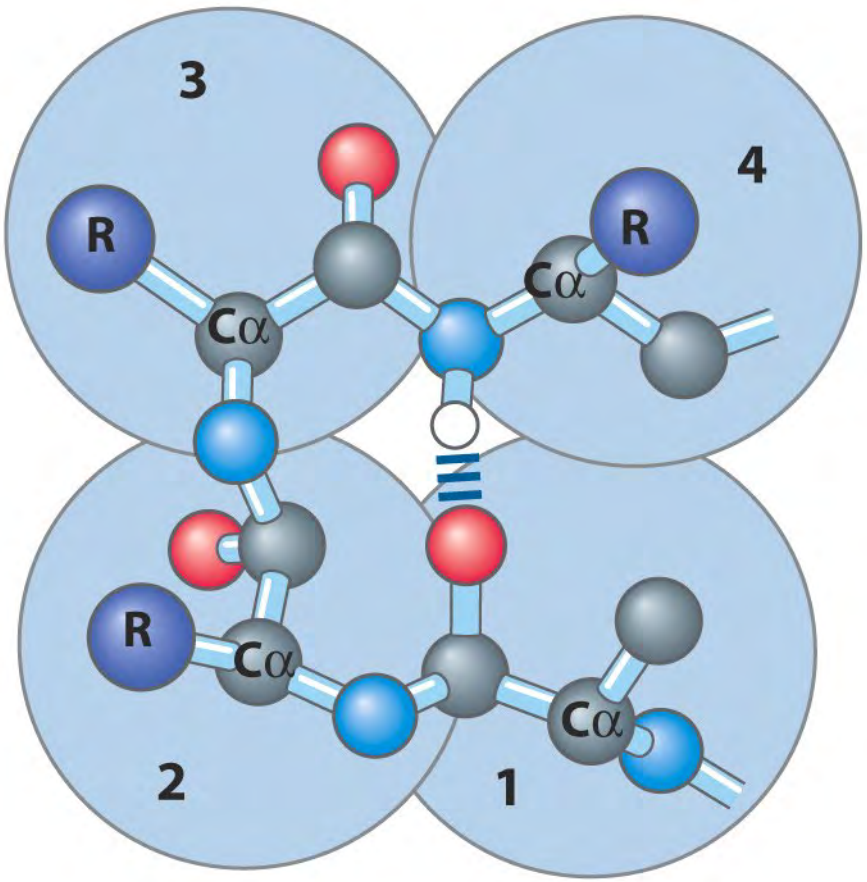
b) **A β-pleated sheet can form only in a multimeric protein.**

c) **A β-pleated sheet always has a parallel configuration.**

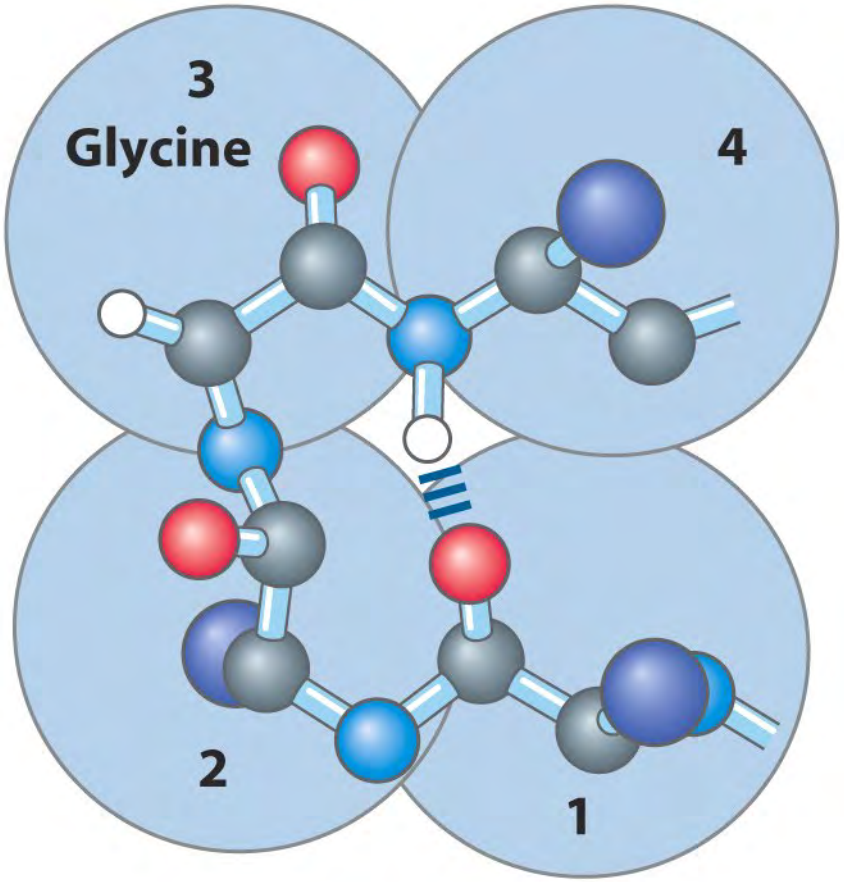
d) ***A β-pleated sheet can form only with certain amino acid sequences.***

e) **A β-pleated sheet always contains the same number of chains.**

(a) β Turns



Type I



Type II

TABLE 3.3 Relative frequencies of amino acid residues in secondary structures

Amino acid	α helix	β sheet	Turn
Ala	**1.29**	0.90	0.78
Cys	**1.11**	0.74	0.80
Leu	**1.30**	1.02	0.59
Met	**1.47**	0.97	0.39
Glu	**1.44**	0.75	1.00
Gln	**1.27**	0.80	0.97
His	**1.22**	1.08	0.69
Lys	**1.23**	0.77	0.96
Val	0.91	**1.49**	0.47
Ile	0.97	**1.45**	0.51
Phe	1.07	**1.32**	0.58
Tyr	0.72	**1.25**	1.05
Trp	0.99	**1.14**	0.75
Thr	0.82	**1.21**	1.03
Gly	0.56	0.92	**1.64**
Ser	0.82	0.95	**1.33**
Asp	1.04	0.72	**1.41**
Asn	0.90	0.76	**1.28**
Pro	0.52	0.64	**1.91**
Arg	0.96	0.99	0.88

Note: The amino acids are grouped according to their preference for α helices (top group), β sheets (second group), or turns (third group). Arginine shows no significant preference for any of the structures.

After T. E. Creighton, *Proteins: Structures and Molecular Properties*, 2d ed. (W. H. Freeman and Company, 1992), p. 256.

TABLE 4–2 Approximate Amounts of a Helix and b Conformation in Some Single-Chain Proteins

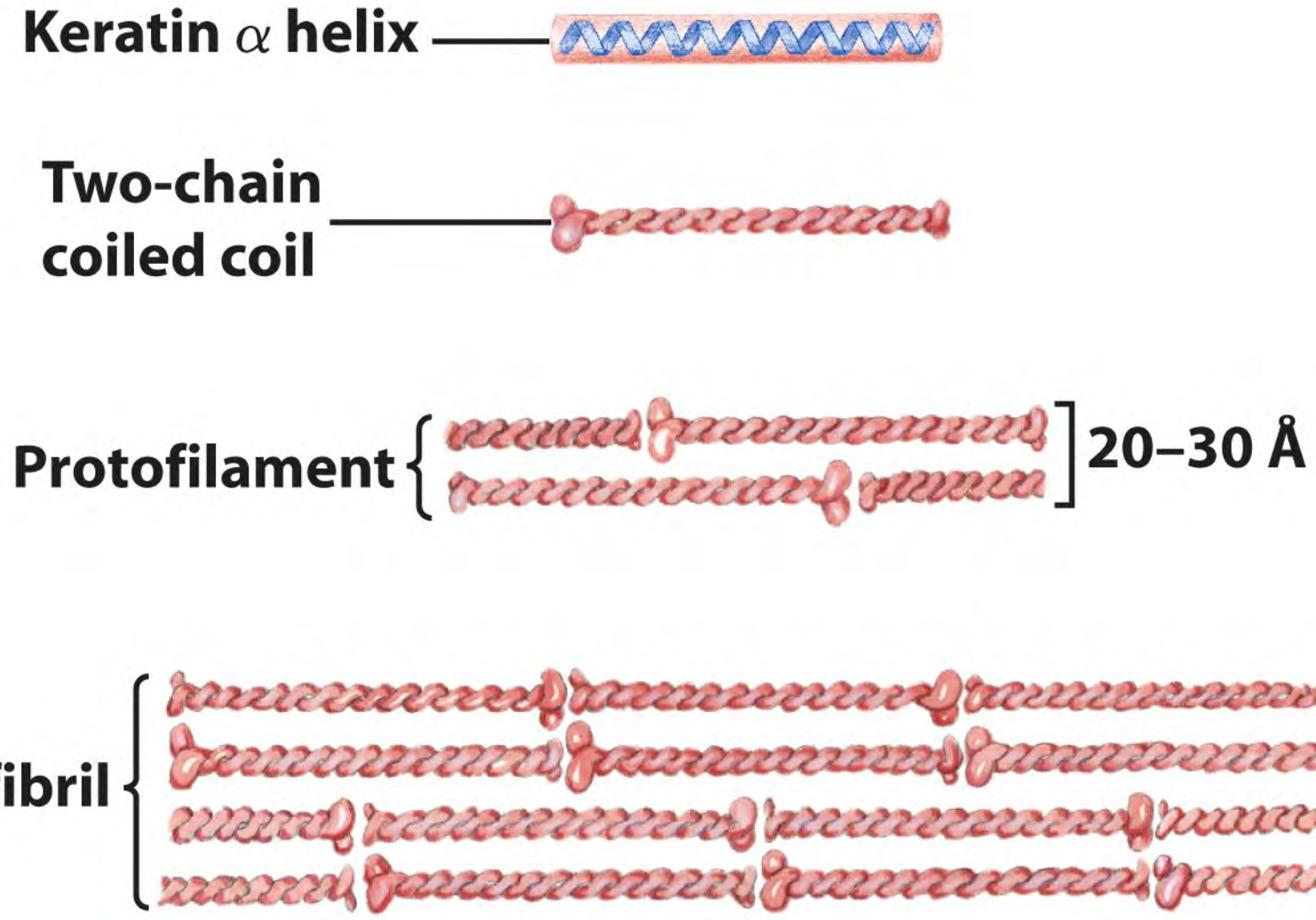
	Residues (%)*	
Protein (total residues)	*α Helix*	*β Conformation*
Chymotrypsin (247)	14	45
Ribonuclease (124)	26	35
Carboxypeptidase (307)	38	17
Cytochrome *c* (104)	39	0
Lysozyme (129)	40	12
Myoglobin (153)	78	0

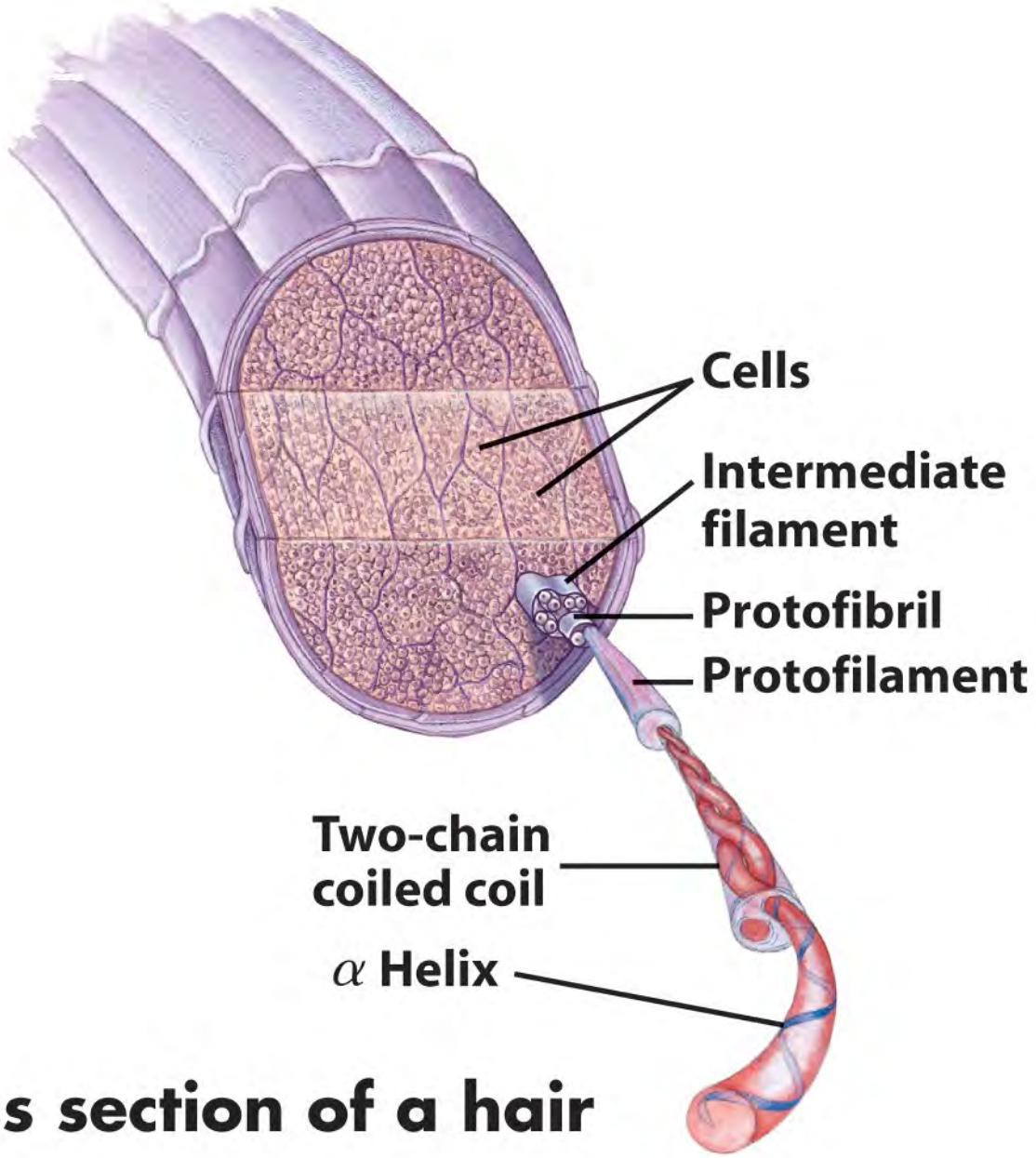
Source: Data from Cantor, C.R. & Schimmel, P.R. (1980) *Biophysical Chemistry,* Part I: *The Conformation of Biological Macromolecules,* p. 100, W. H. Freeman and Company, New York.

*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.

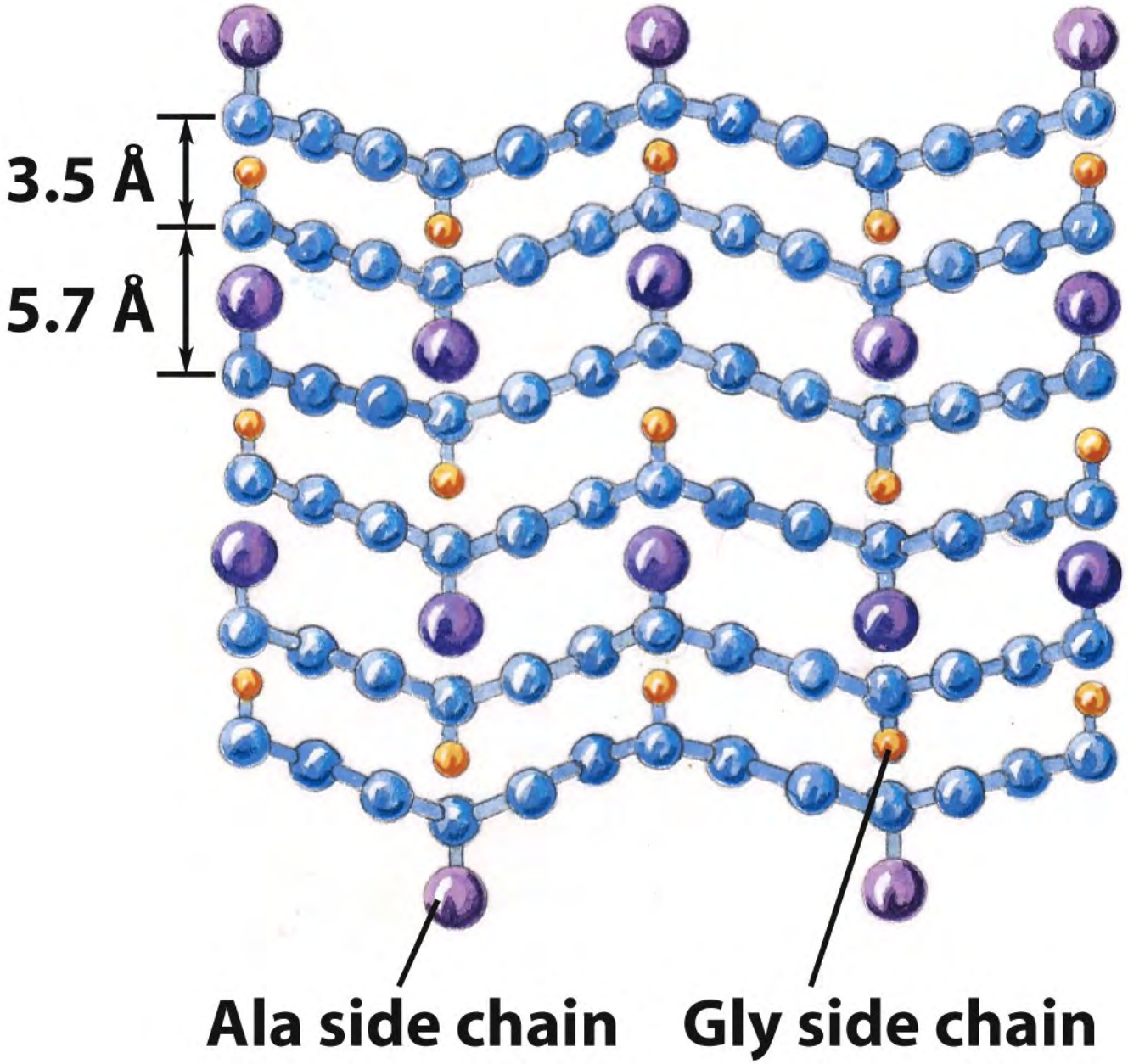
TABLE 4-1 Secondary Structures and Properties of Fibrous Proteins

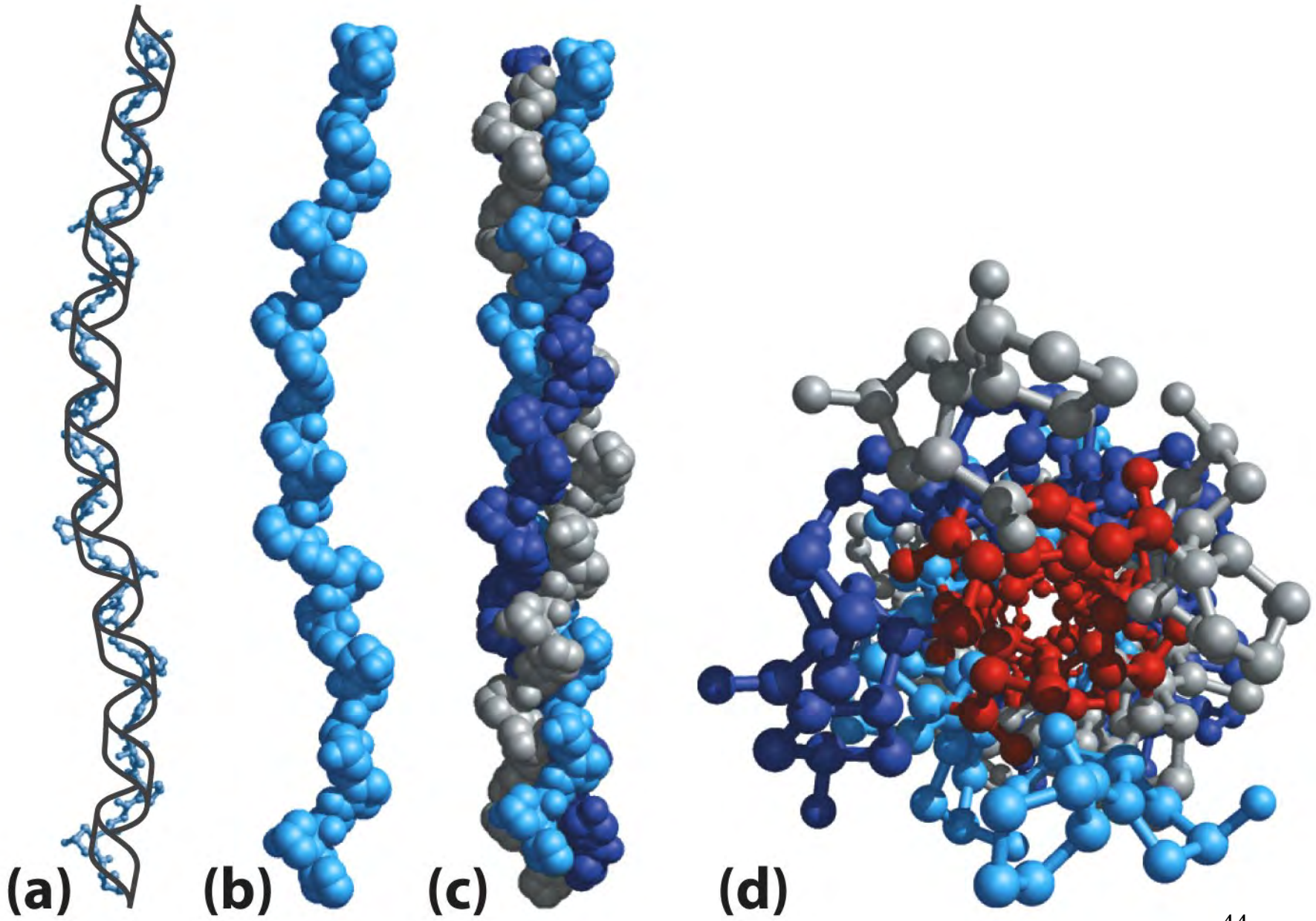
Structure	*Characteristics*	*Examples of occurrence*
α Helix, cross-linked by disulfide bonds	Tough, insoluble protective structures of varying hardness and flexibility	α-Keratin of hair, feathers, and nails
β Conformation	Soft, flexible filaments	Silk fibroin
Collagen triple helix	High tensile strength,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

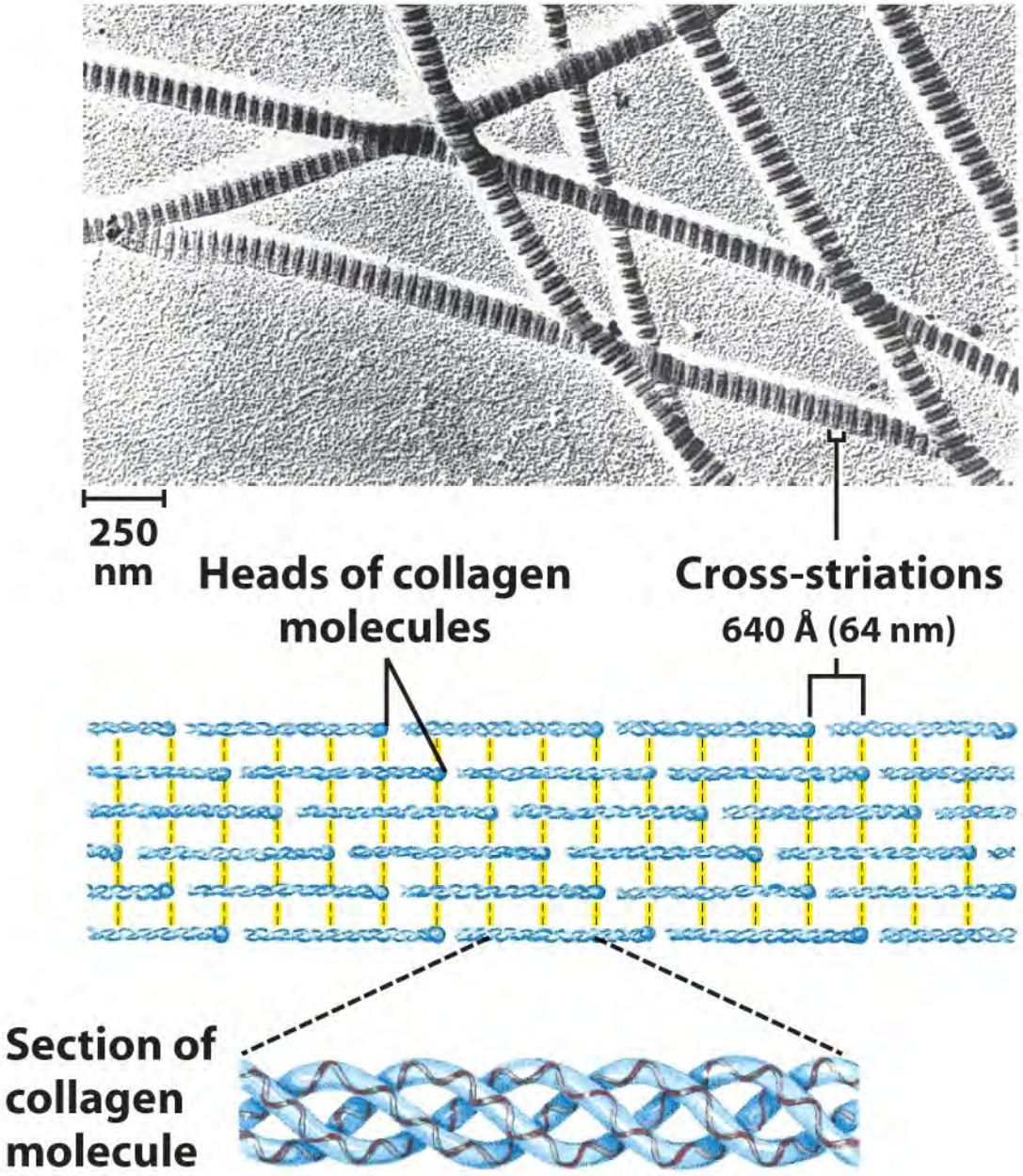

Keratin α helix
Two-chain coiled coil
Protofilament
20–30 Å
Protofibril

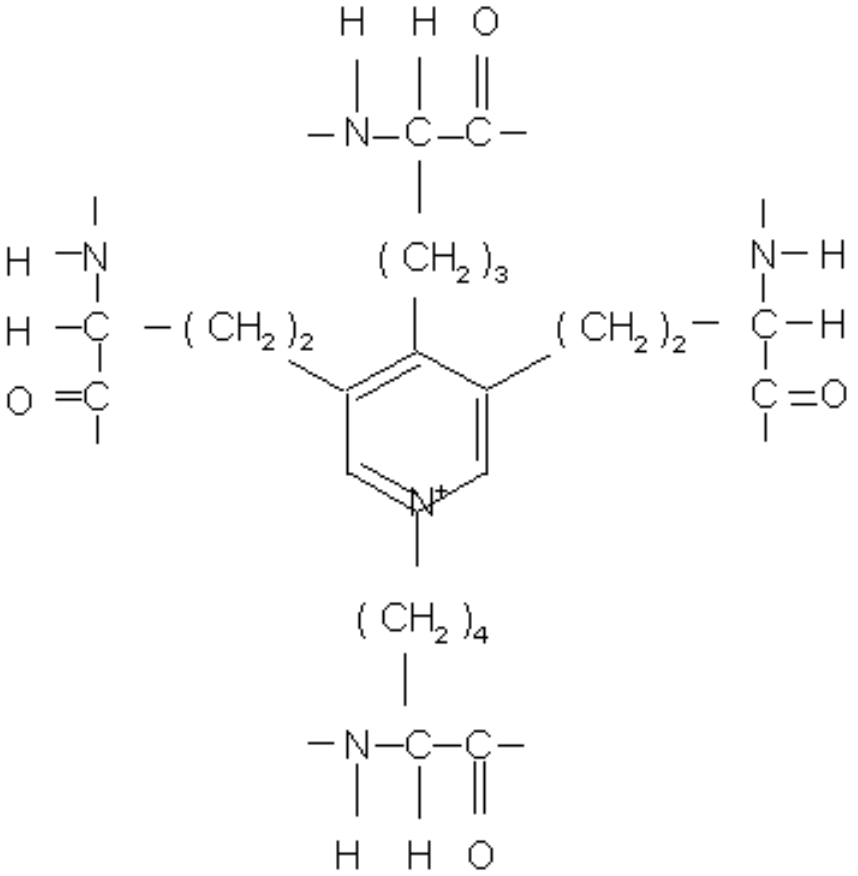


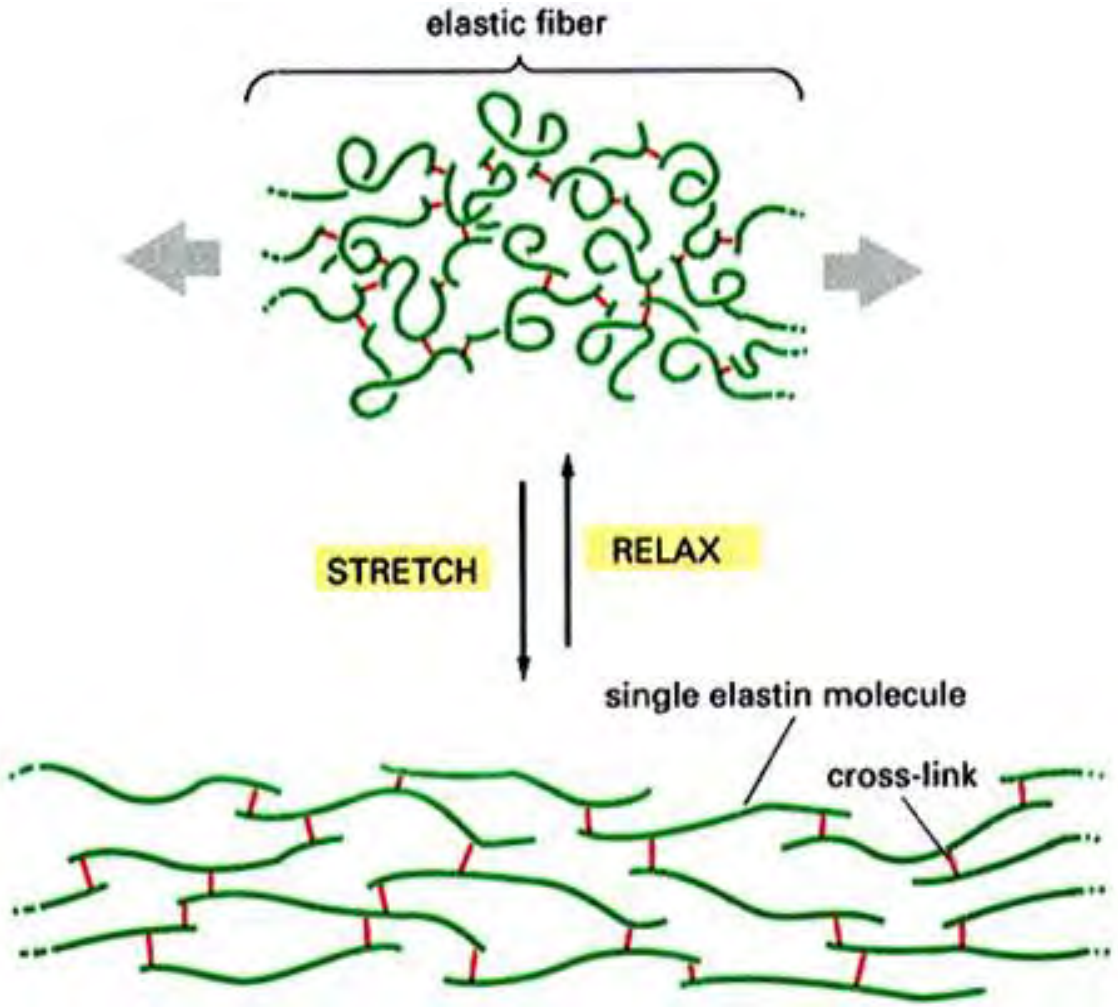
Cross section of a hair

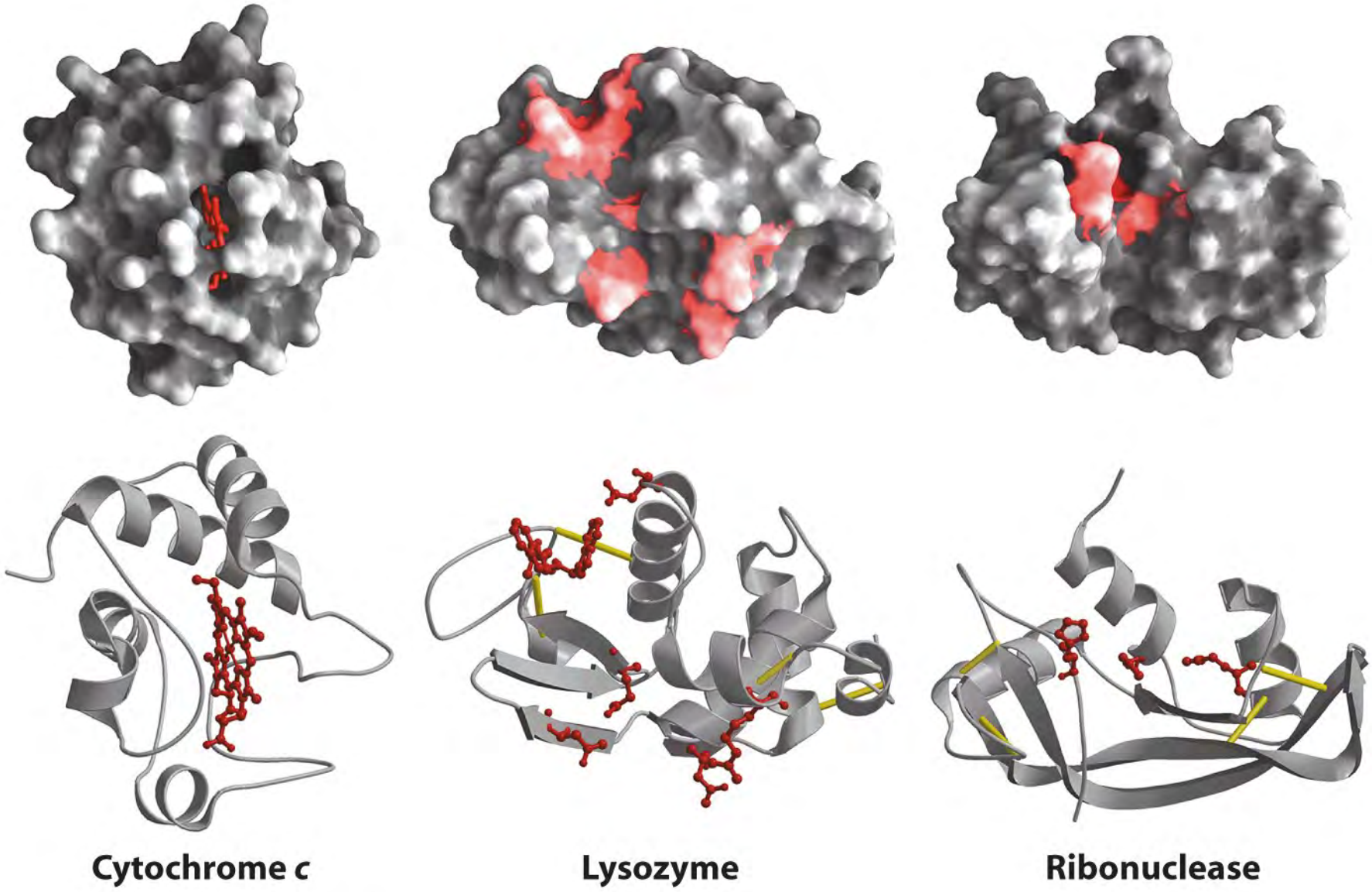

3.5 Å
5.7 Å
Ala side chain
Gly side chain

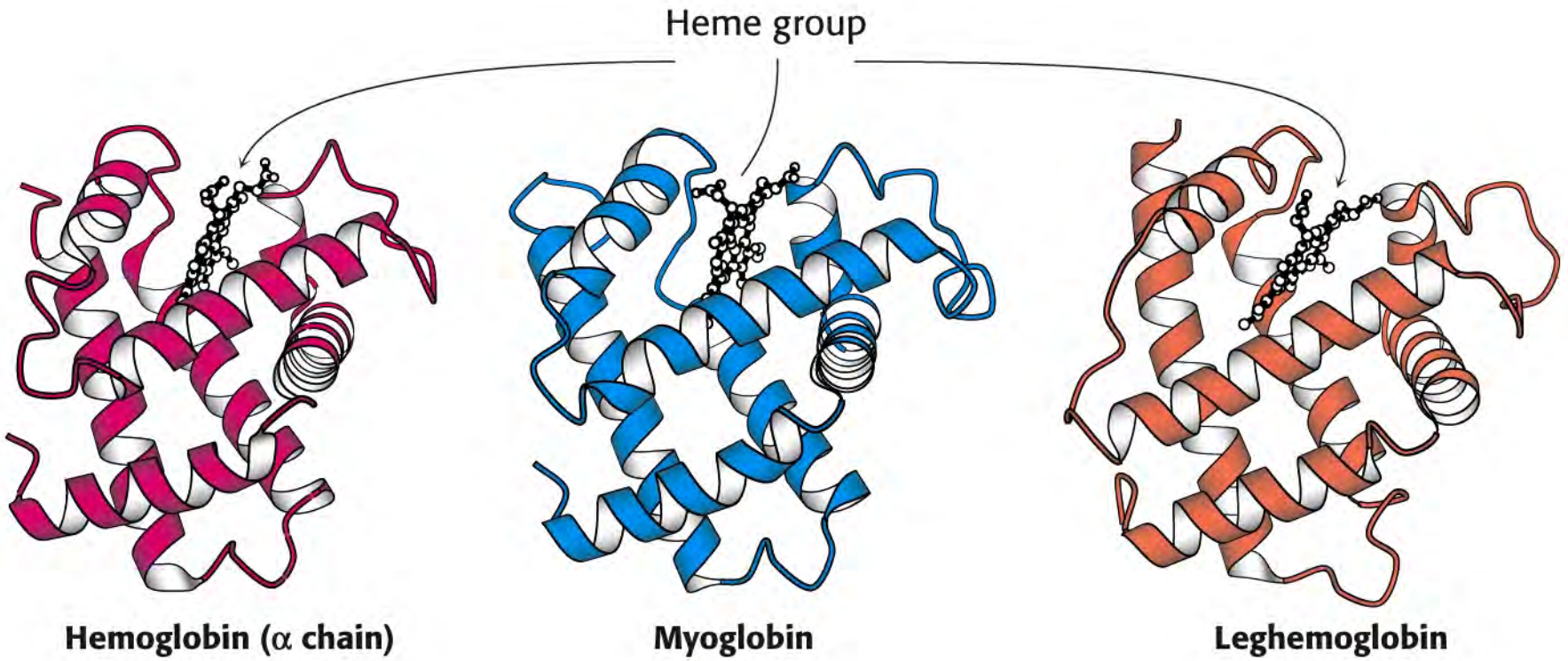

(a)
(b)
(c)
(d)

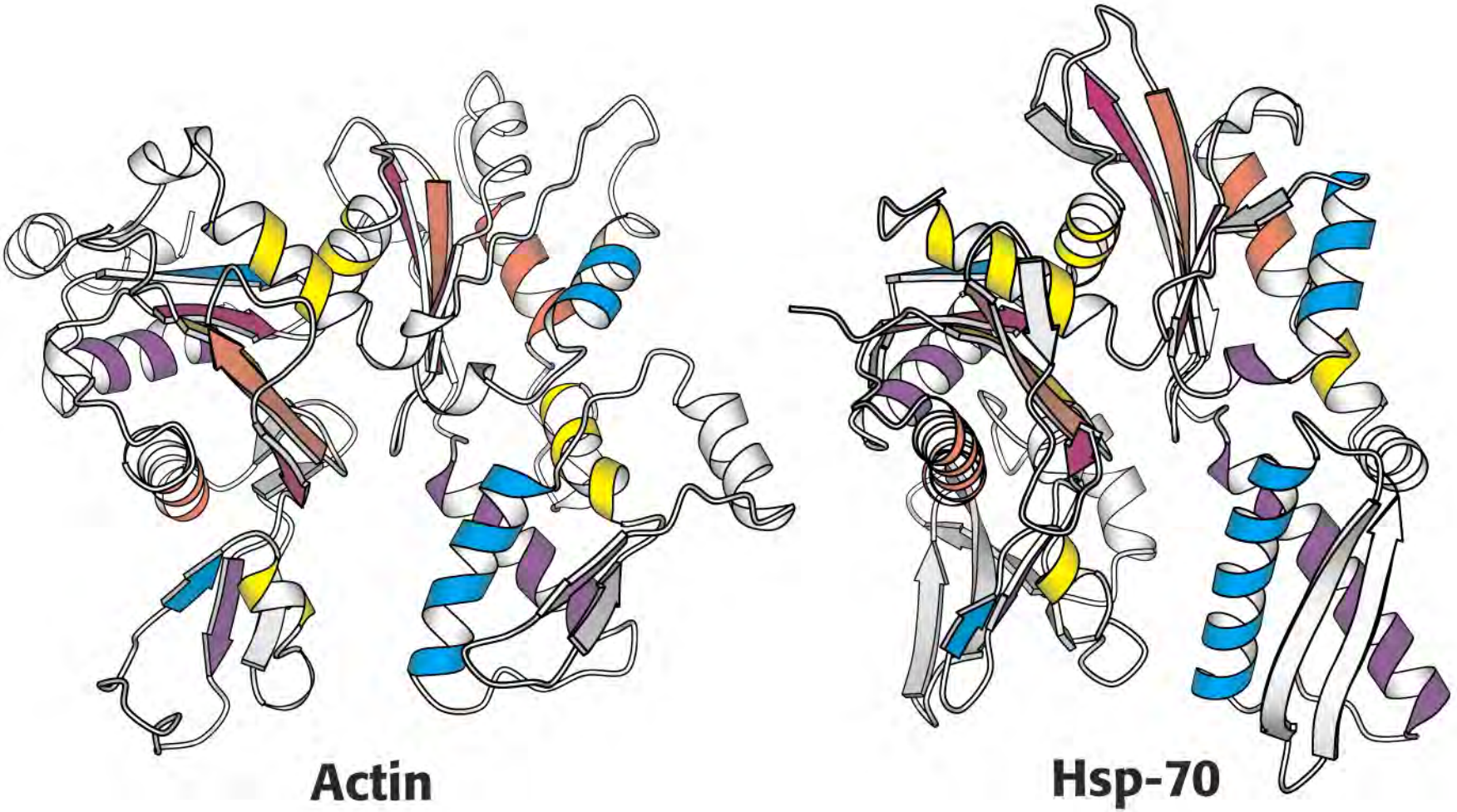

250
nm
Heads of collagen
molecules
Cross-striations
640 Å (64 nm)
Section of
collagen
molecule

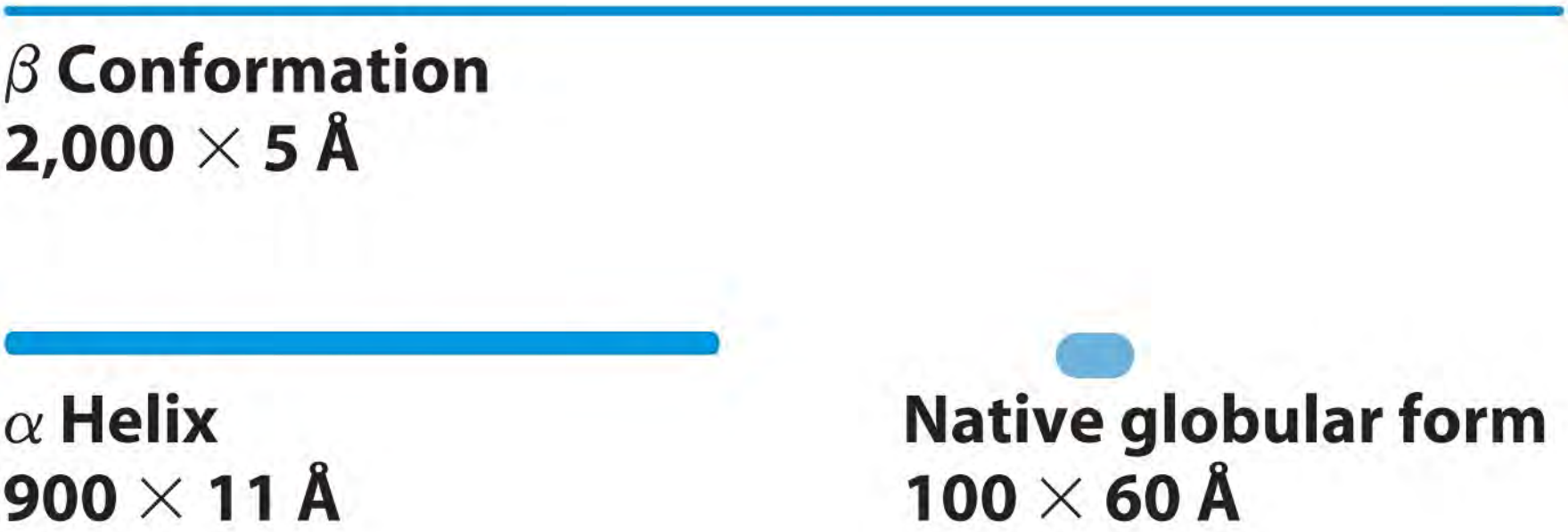



elastic fiber
STRETCH
RELAX
single elastin molecule
cross-link


Cytochrome *c*
Lysozyme
Ribonuclease


Heme group
Hemoglobin (α chain)
Myoglobin
Leghemoglobin


Actin
Hsp-70


β Conformation
2,000 × 5 Å
α Helix
900 × 11 Å
Native globular form
100 × 60 Å



Are You Getting It??



Which property is shared by both fibrous proteins and globular proteins? ***(multiple answers)***

a) Both types of proteins have secondary structure.
b) Both types of proteins can be composed entirely of β-pleated sheet structure.
c) Both types of proteins have similar functions.
d) Both types of protein contain covalent and non-covalent bonds.
e) Both types of proteins have similar shapes.



Are You Getting It??



Answer

Which property is shared by both fibrous proteins and globular proteins?

a) Both types of proteins have secondary structure.

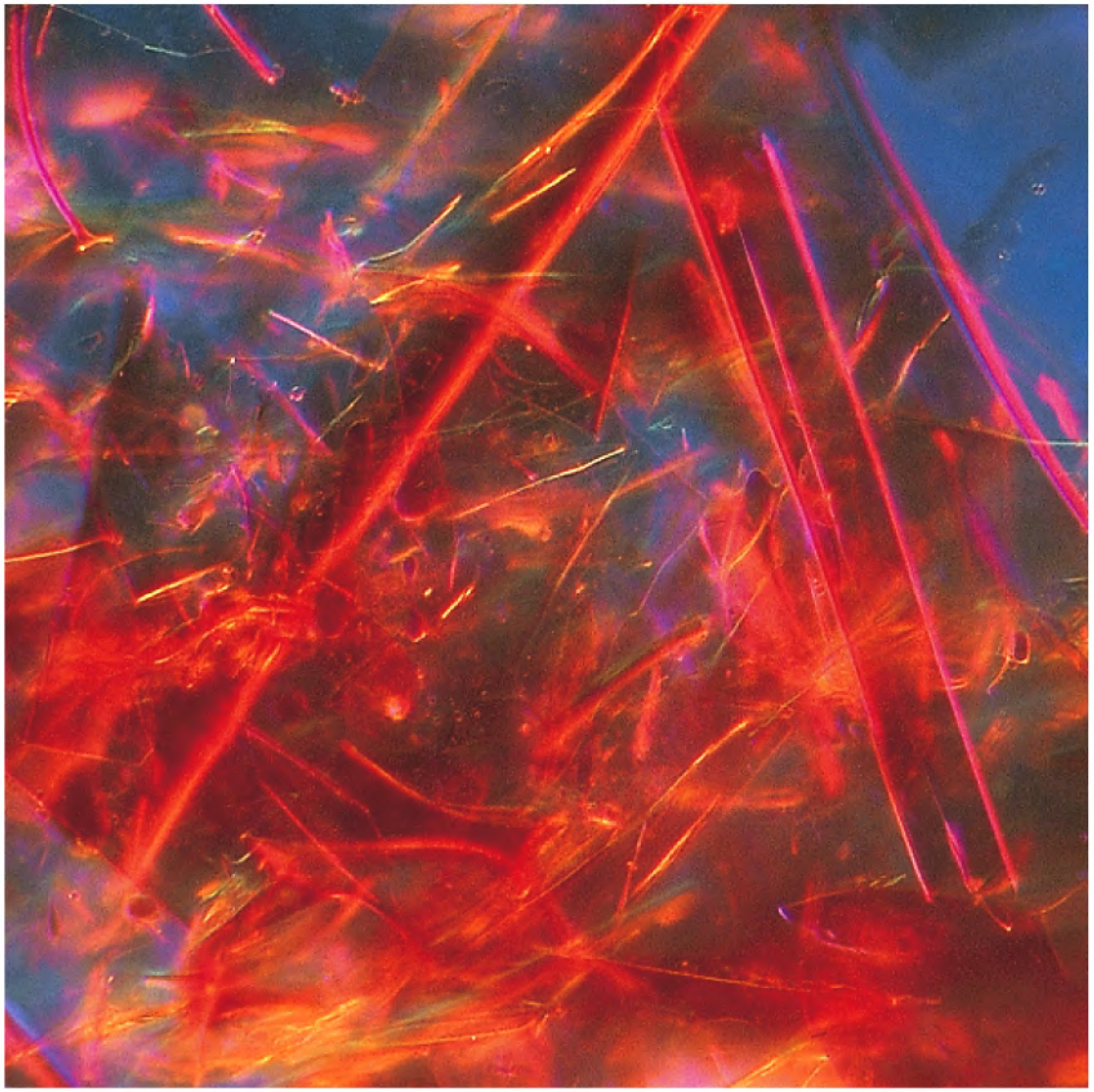
b) Both types of proteins can be composed entirely of β-pleated sheet structure.

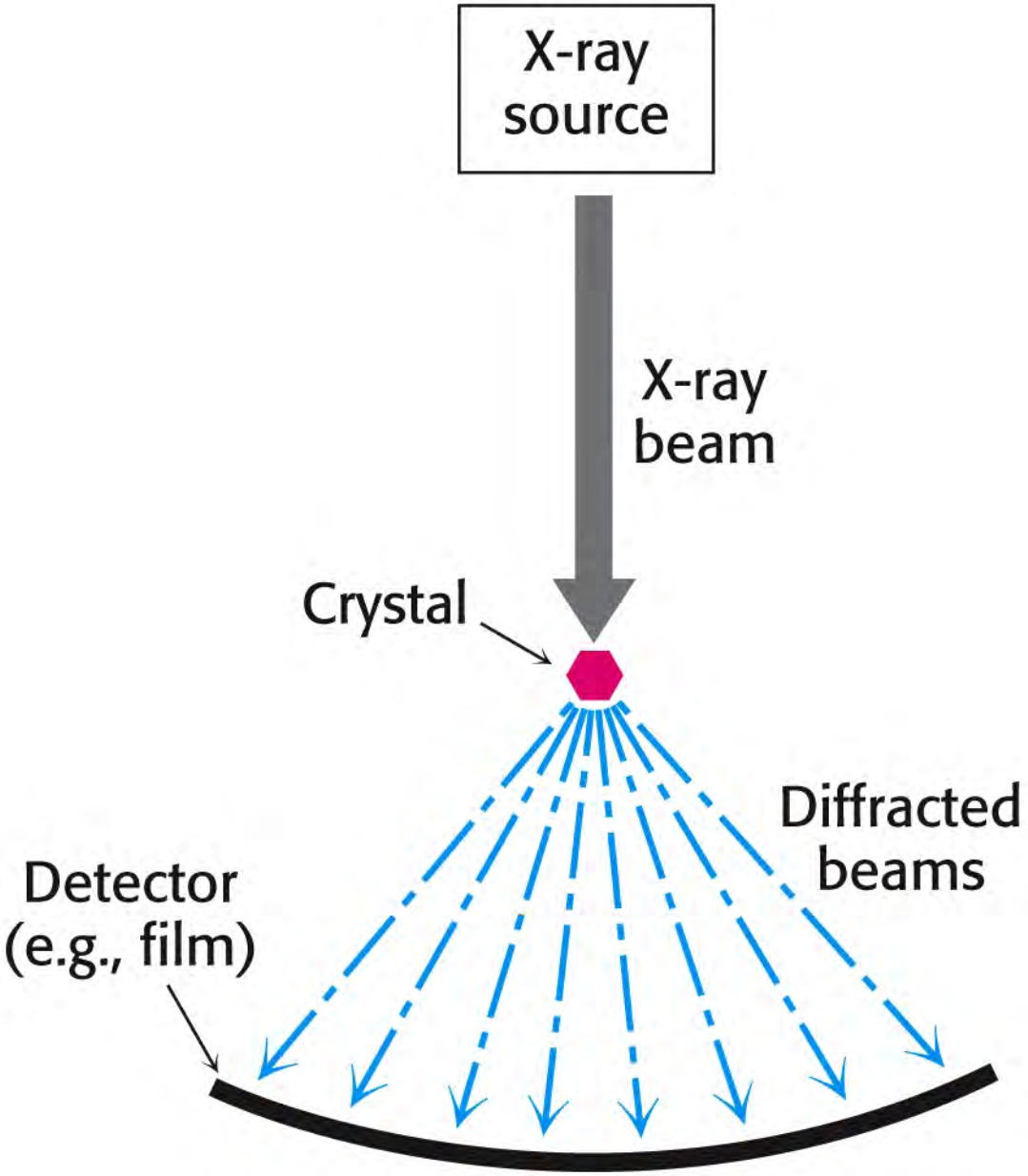
c) Both types of proteins have similar functions.

d) Both types of protein contain covalent and non-covalent bonds.

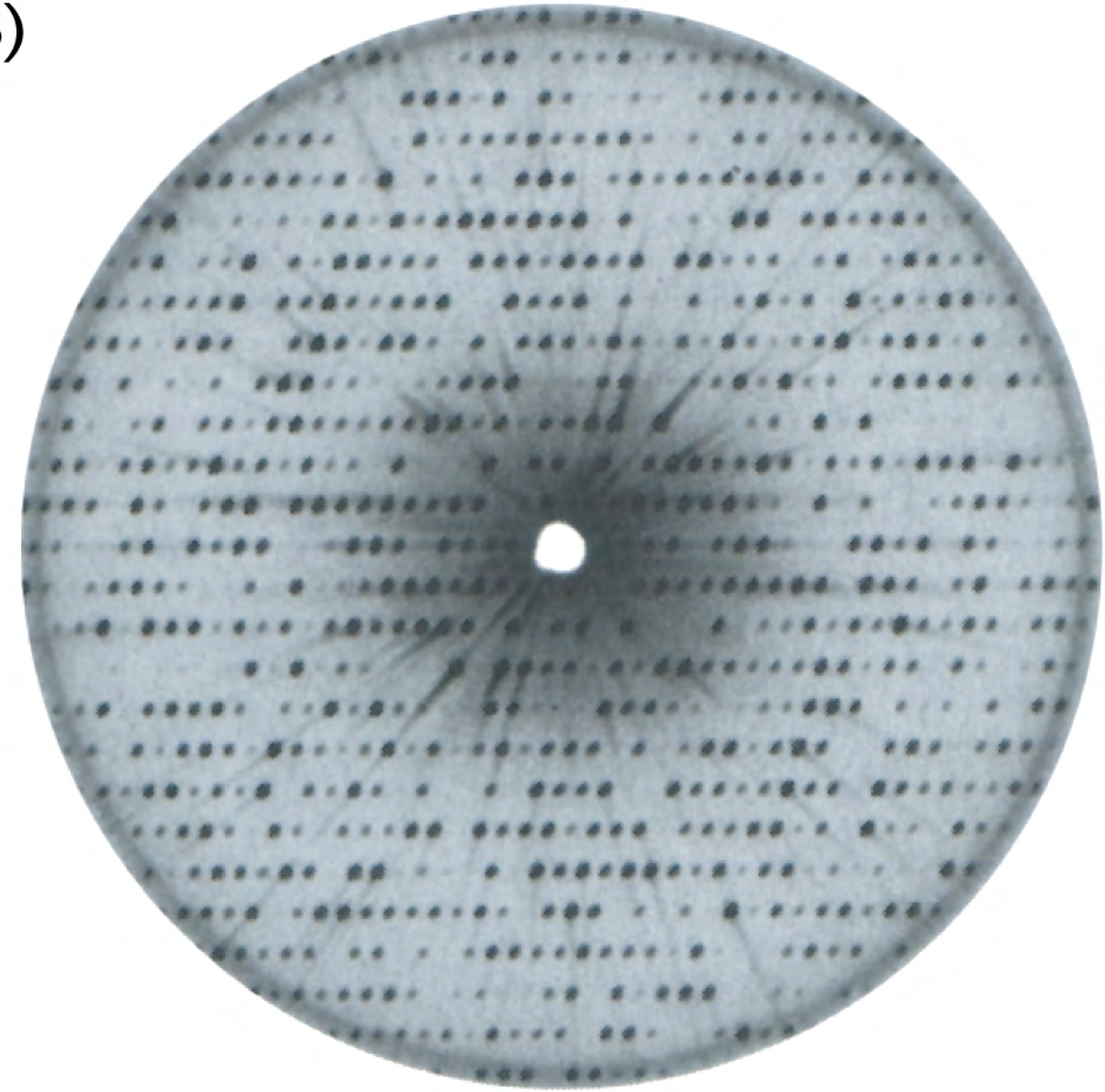
e) Both types of proteins have similar shapes.

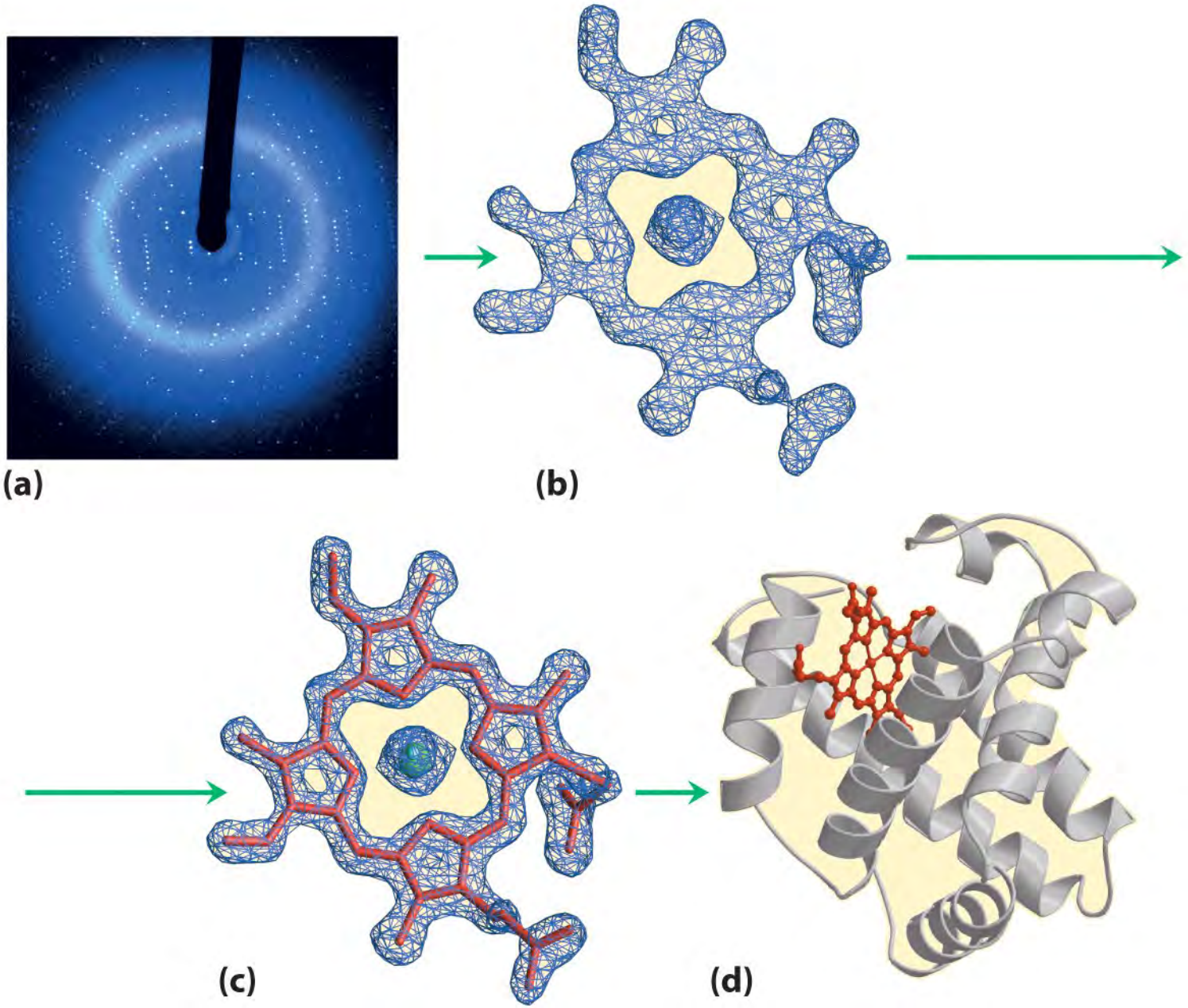
(A)

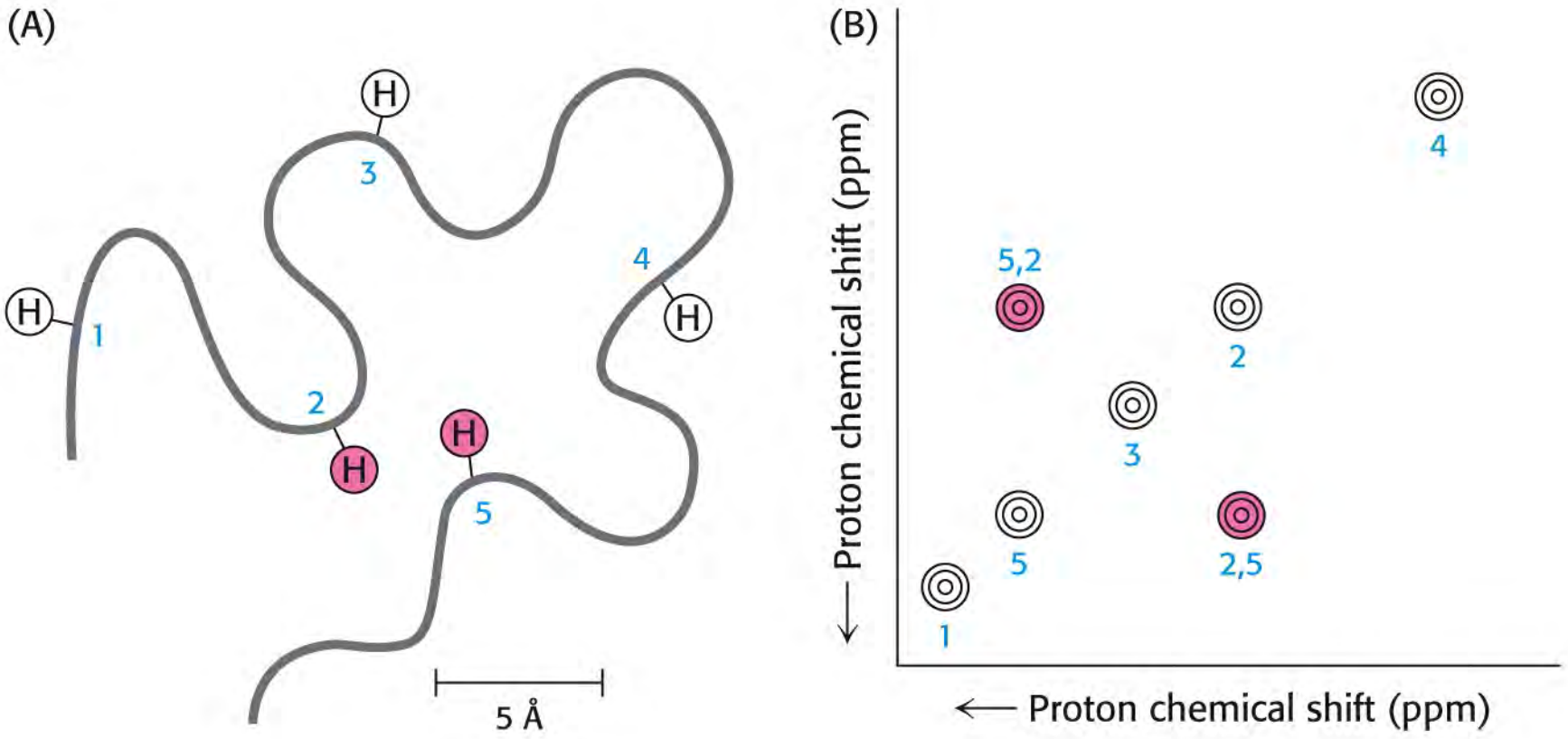


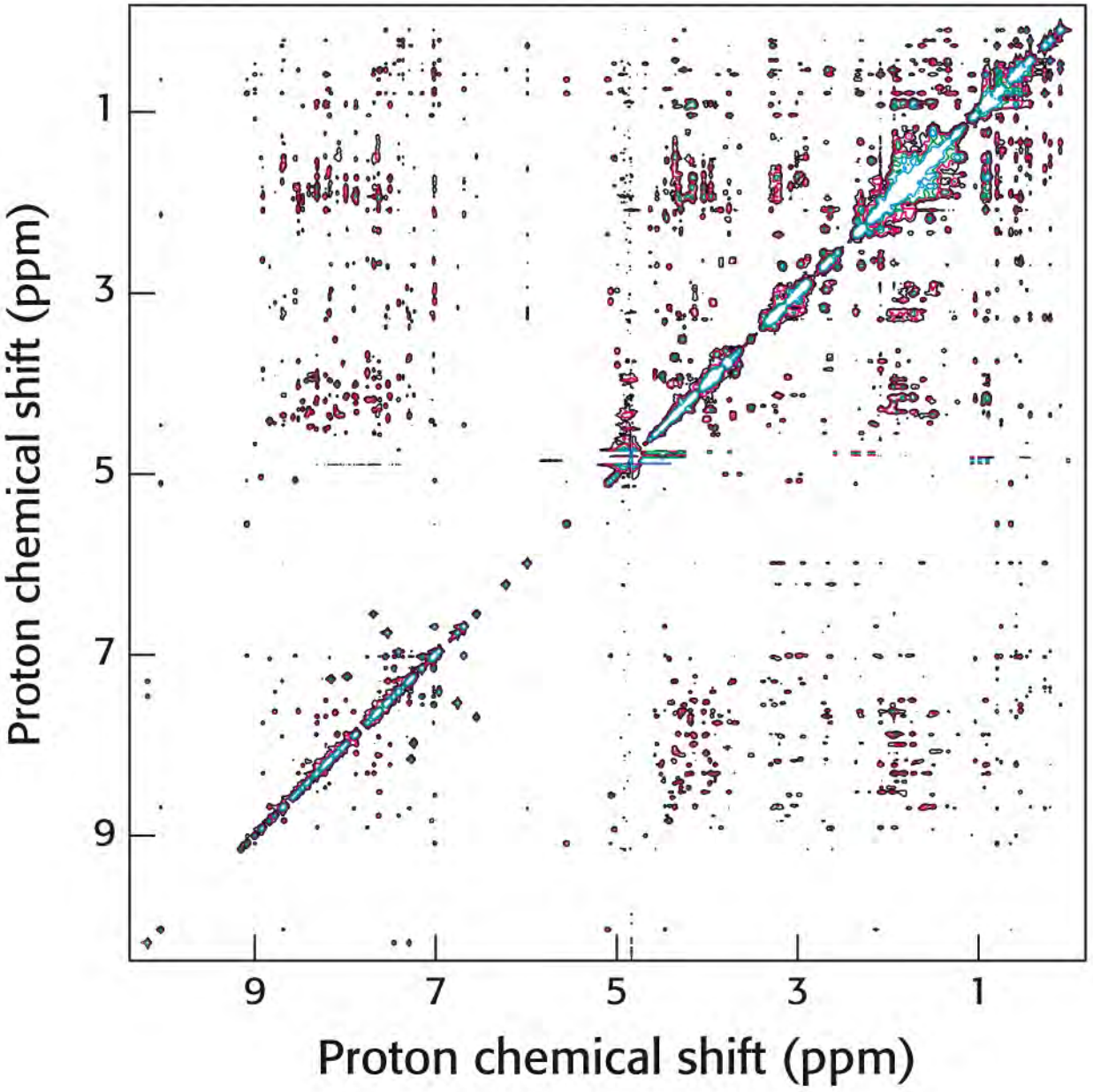

X-ray source
X-ray beam
Crystal
Diffracted beams
Detector (e.g., film)

(B)

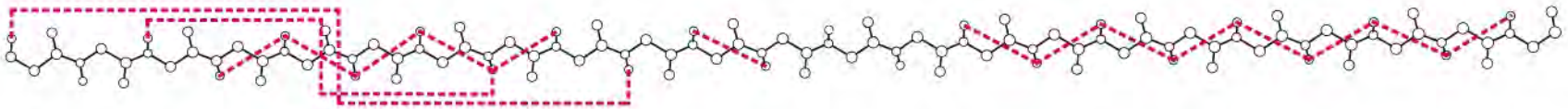



(a)
(b)
(c)
(d)

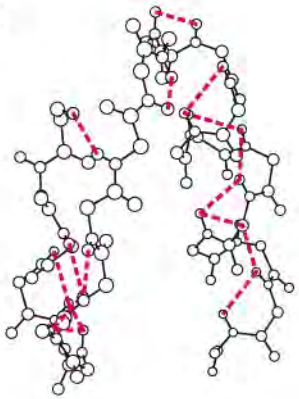

(A)
H
3
4
H
H
1
2
H
H
5
5 Å
(B)
4
5,2
2
3
5
2,5
1
Proton chemical shift (ppm)
Proton chemical shift (ppm)


Proton chemical shift (ppm)
1
3
5
7
9
9
7
5
3
1
Proton chemical shift (ppm)

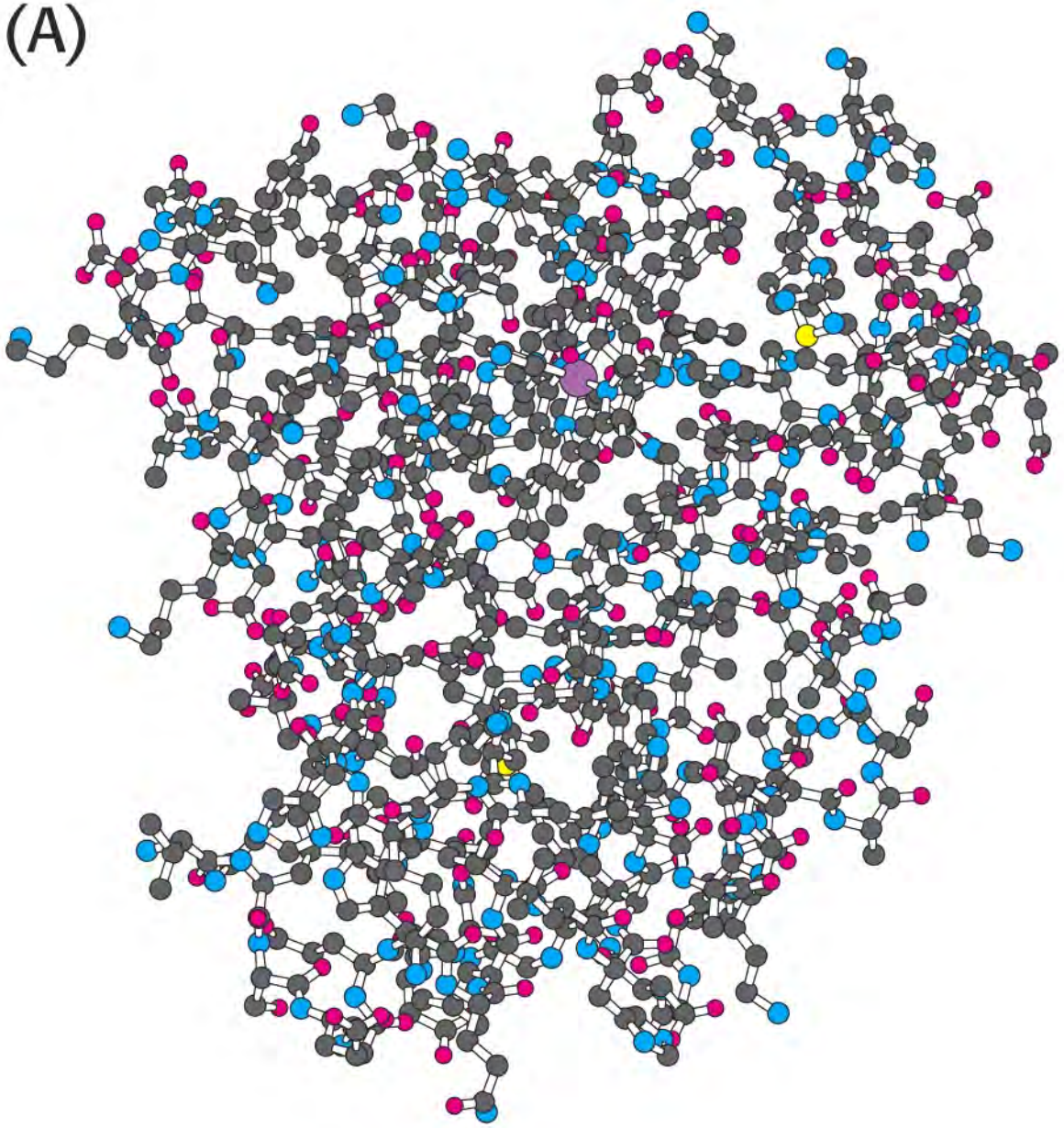
(A)



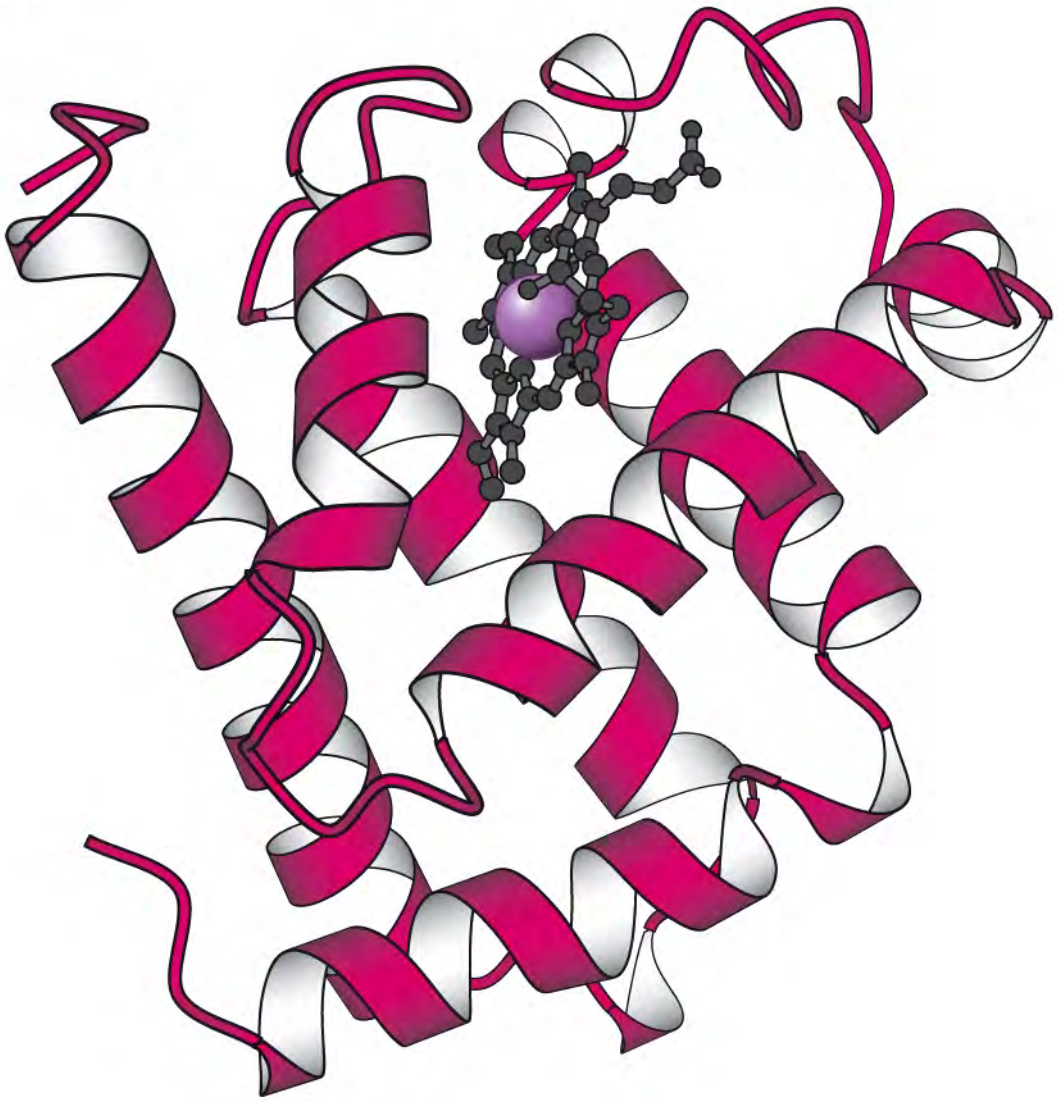
(B)



Calculated structure


(A)

(B)





Are You Getting It??



A protein contains many aspartates (Asp) and alanines (Ala). Which will be a characteristic of its tertiary structure?

a) Ala will be on the protein's surface while Asp will be in the interior.
b) Asp will be on the protein's surface while Ala will be in the interior.
c) Ala and Asp will be evenly distributed throughout the protein.
d) The protein will fold into a random conformation.



Are You Getting It??



Answer

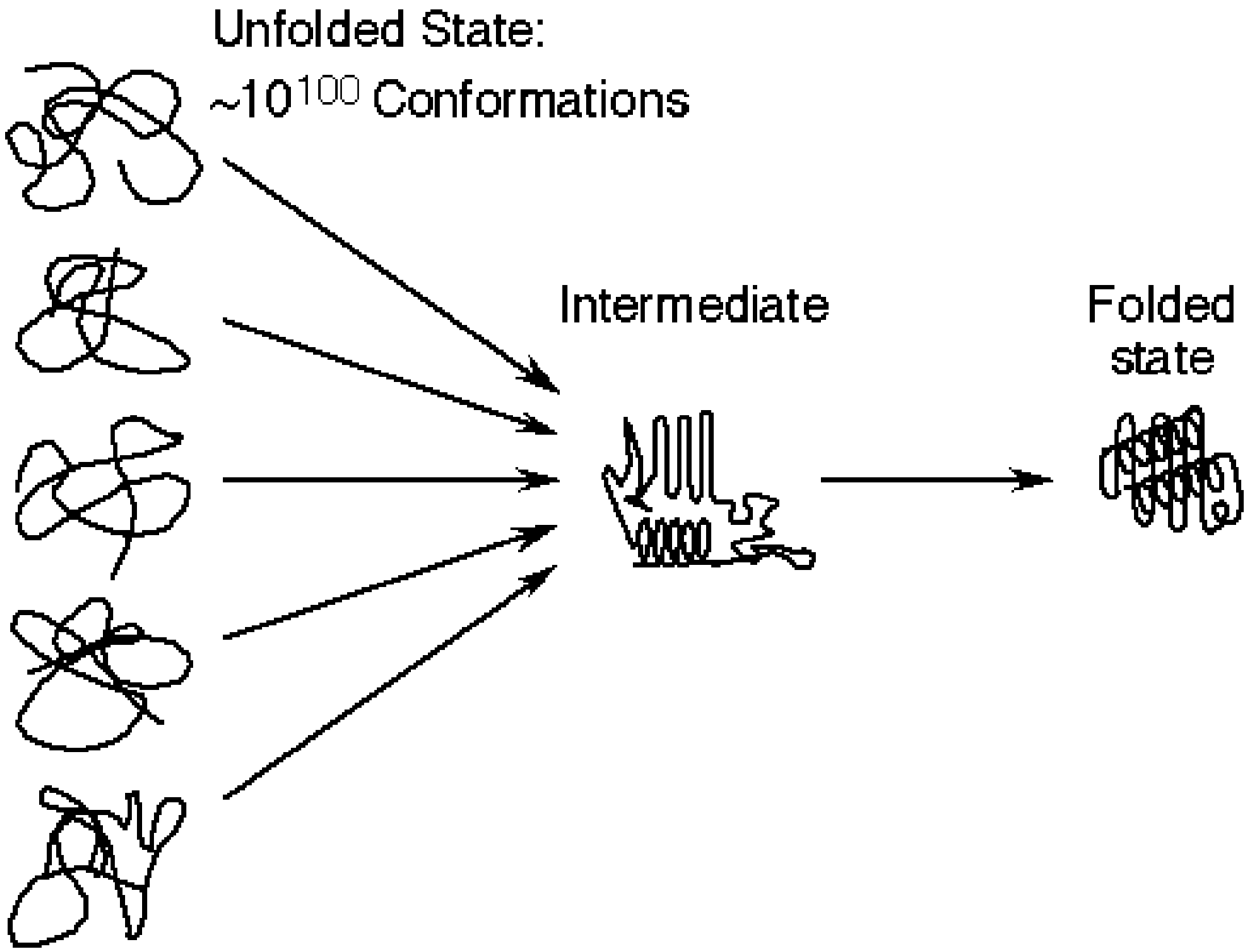
A protein contains many aspartates (Asp) and alanines (Ala). Which will be a characteristic of its tertiary structure?

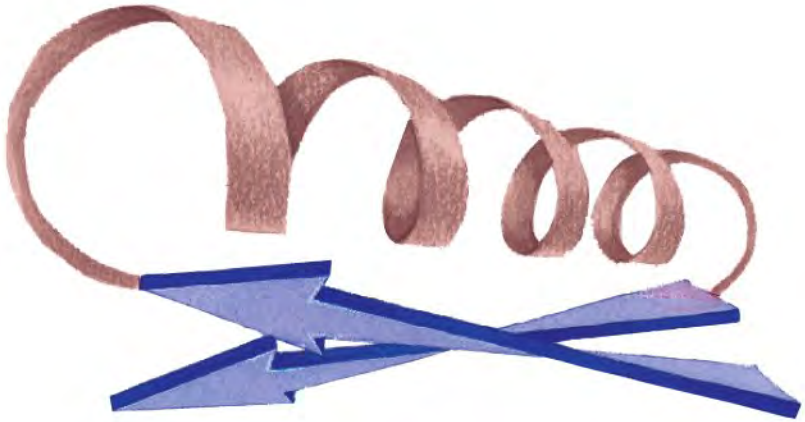
a) Ala will be on the protein's surface while Asp will be in the interior.

b) Asp will be on the protein's surface while Ala will be in the interior.

c) Ala and Asp will be evenly distributed throughout the protein.

d) The protein will fold into a random conformation.

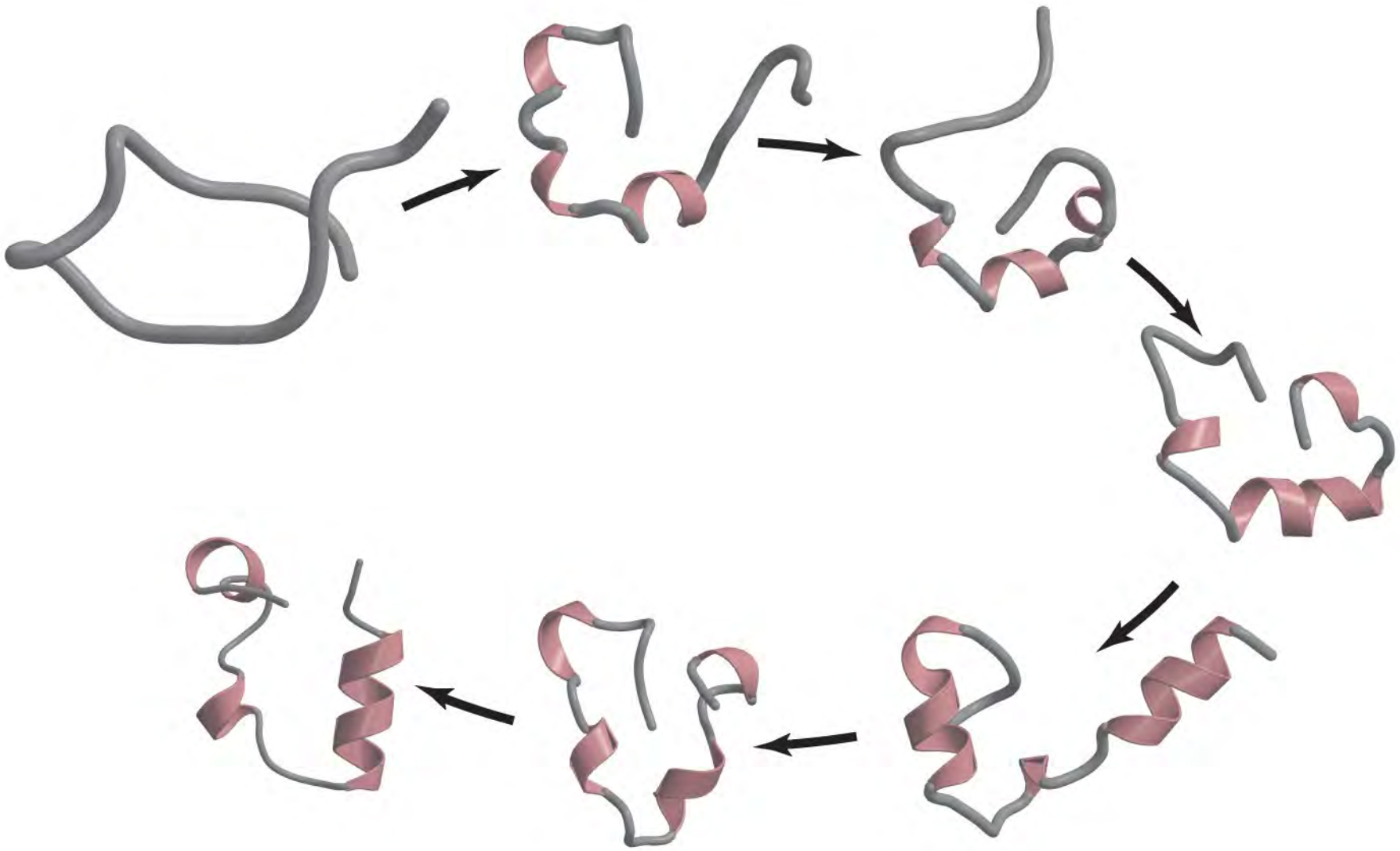

Unfolded State:
~10^100 Conformations
Intermediate
Folded state

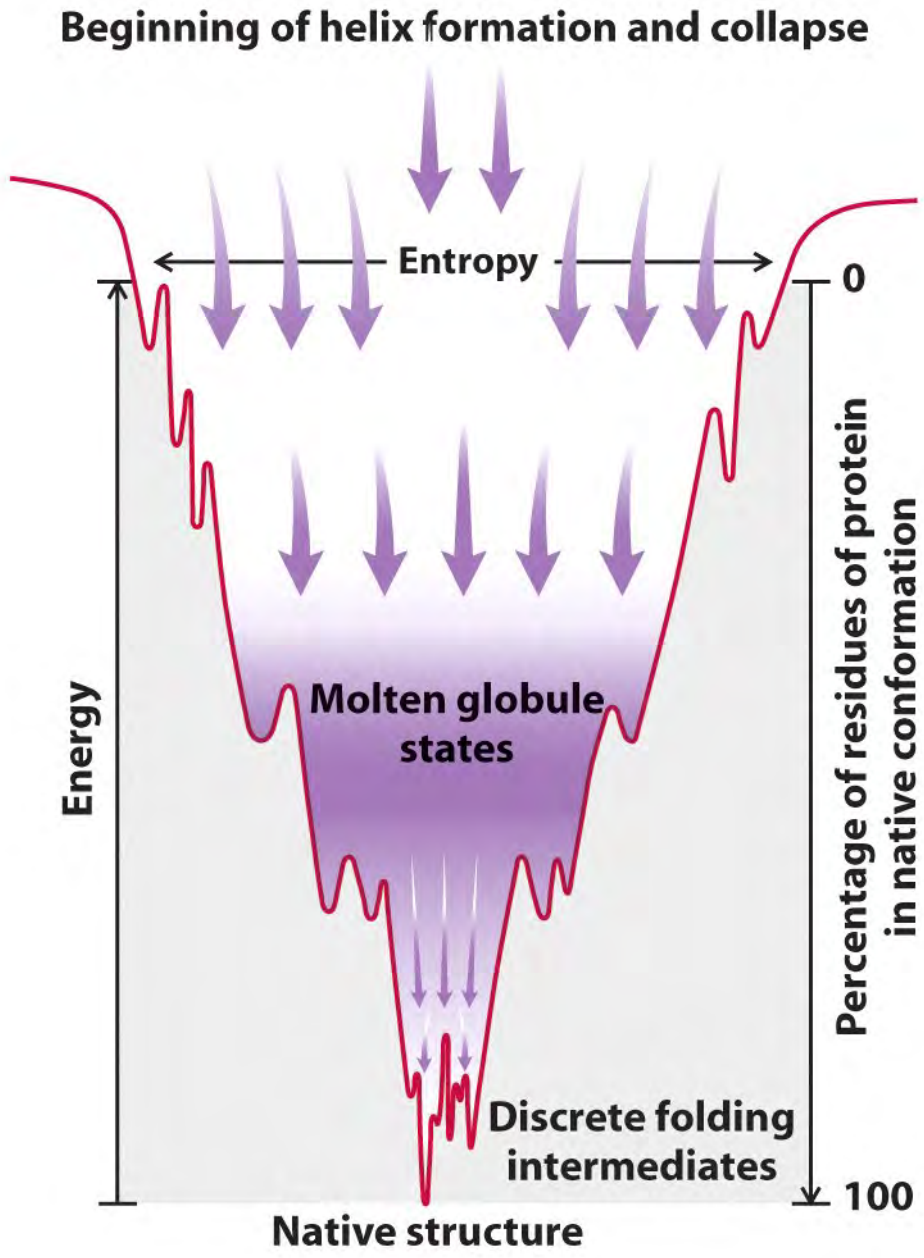


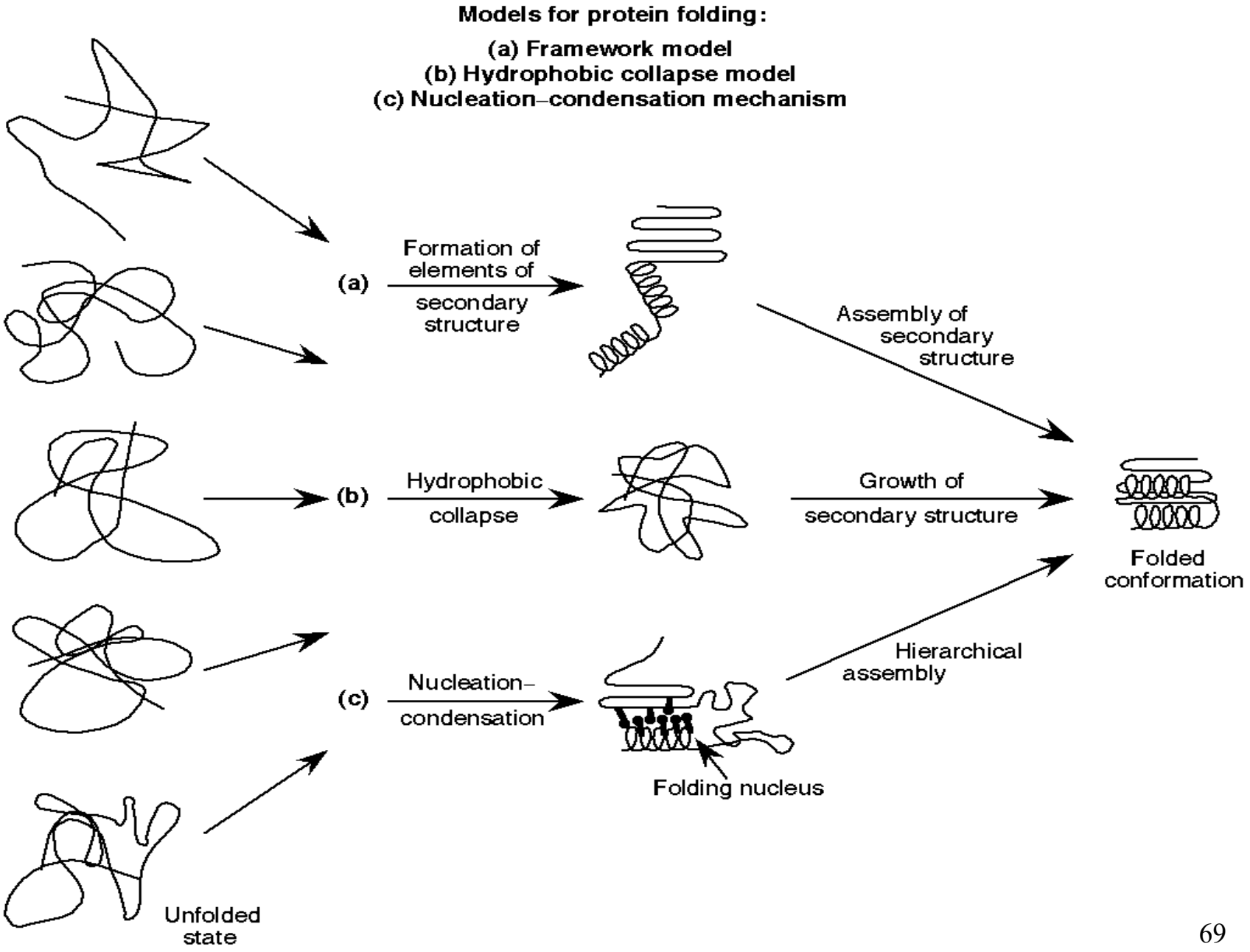
β-α-β **Loop**



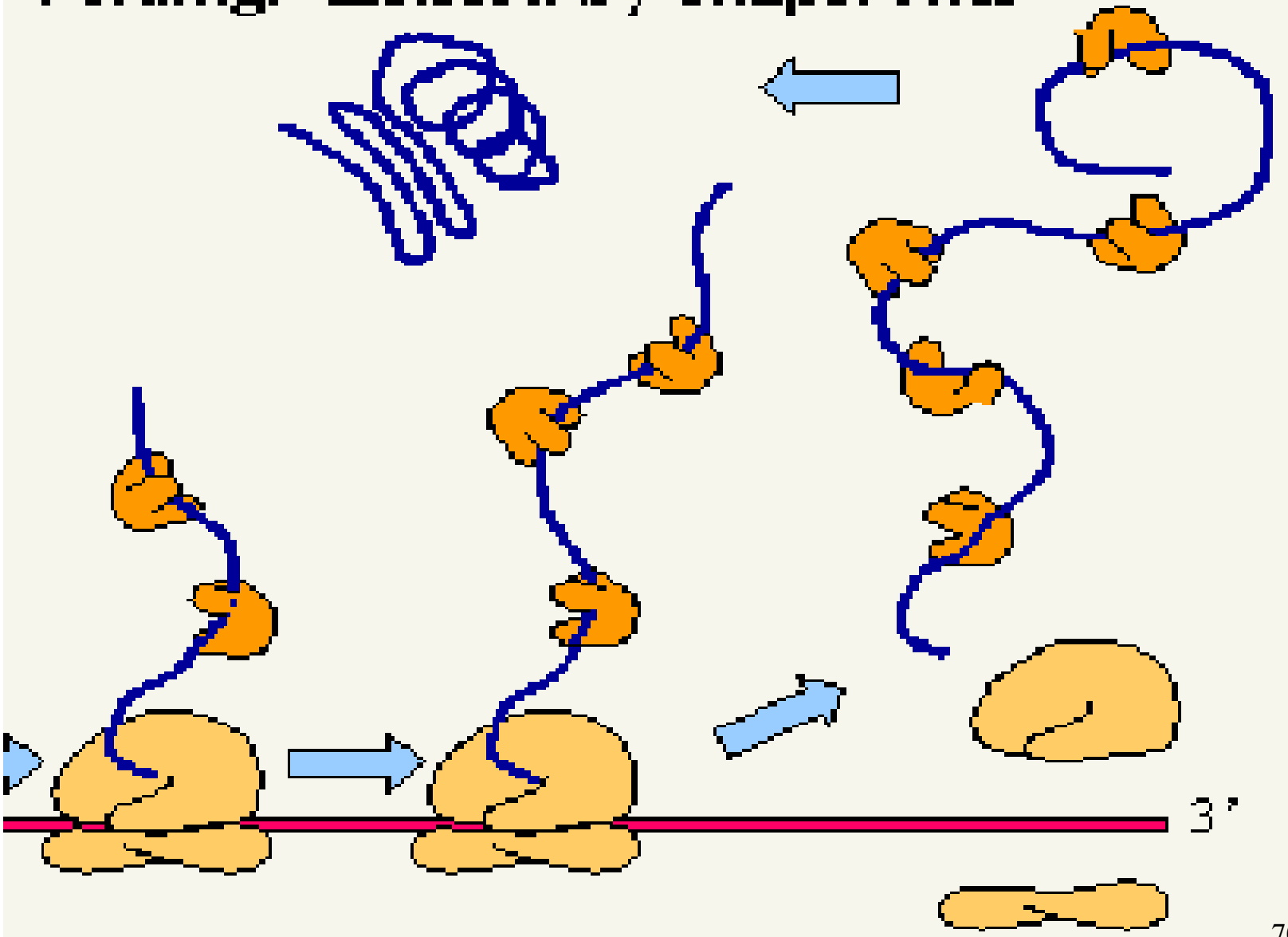
α-α **Corner**

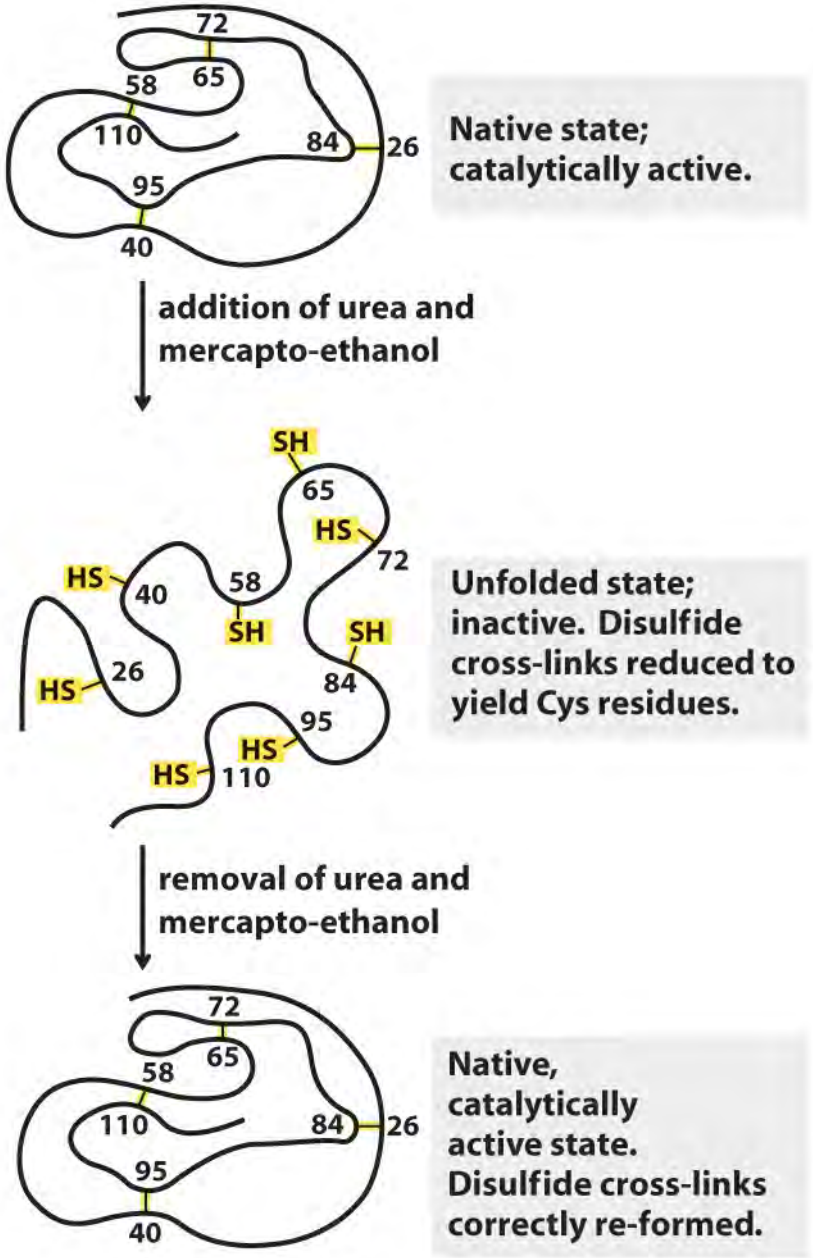



Beginning of helix formation and collapse
Entropy
0
Energy
Molten globule states
Percentage of residues of protein in native conformation
Discrete folding intermediates
100
Native structure


Models for protein folding:
(a) Framework model
(b) Hydrophobic collapse model
(c) Nucleation–condensation mechanism
(a)
Formation of elements of secondary structure
Assembly of secondary structure
(b)
Hydrophobic collapse
Growth of secondary structure
Folded conformation
(c)
Nucleation–condensation
Hierarchical assembly
Folding nucleus
Unfolded state

Folding: assisted by chaperones




72
65
58
110
84
26
95
40
Native state; catalytically active.
addition of urea and mercapto-ethanol
SH
65
HS
72
HS
40
58
SH
SH
26
HS
84
95
HS
HS
110
Unfolded state; inactive. Disulfide cross-links reduced to yield Cys residues.
removal of urea and mercapto-ethanol
72
65
58
110
84
26
95
40
Native, catalytically active state. Disulfide cross-links correctly re-formed.



Are You Getting It??



Which is a characteristic of protein tertiary structure and protein folding? ***(multiple answers)***

a) All proteins fold spontaneously into their proper shape.
b) Tertiary structures tend to be high-energy shapes.
c) Primary structure determines tertiary structure.
d) Denaturation breaks hydrogen bonds and peptide bonds.
e) Two different proteins can have similar tertiary structures.



Are You Getting It??



Answer

Which is a characteristic of protein tertiary structure and protein folding?

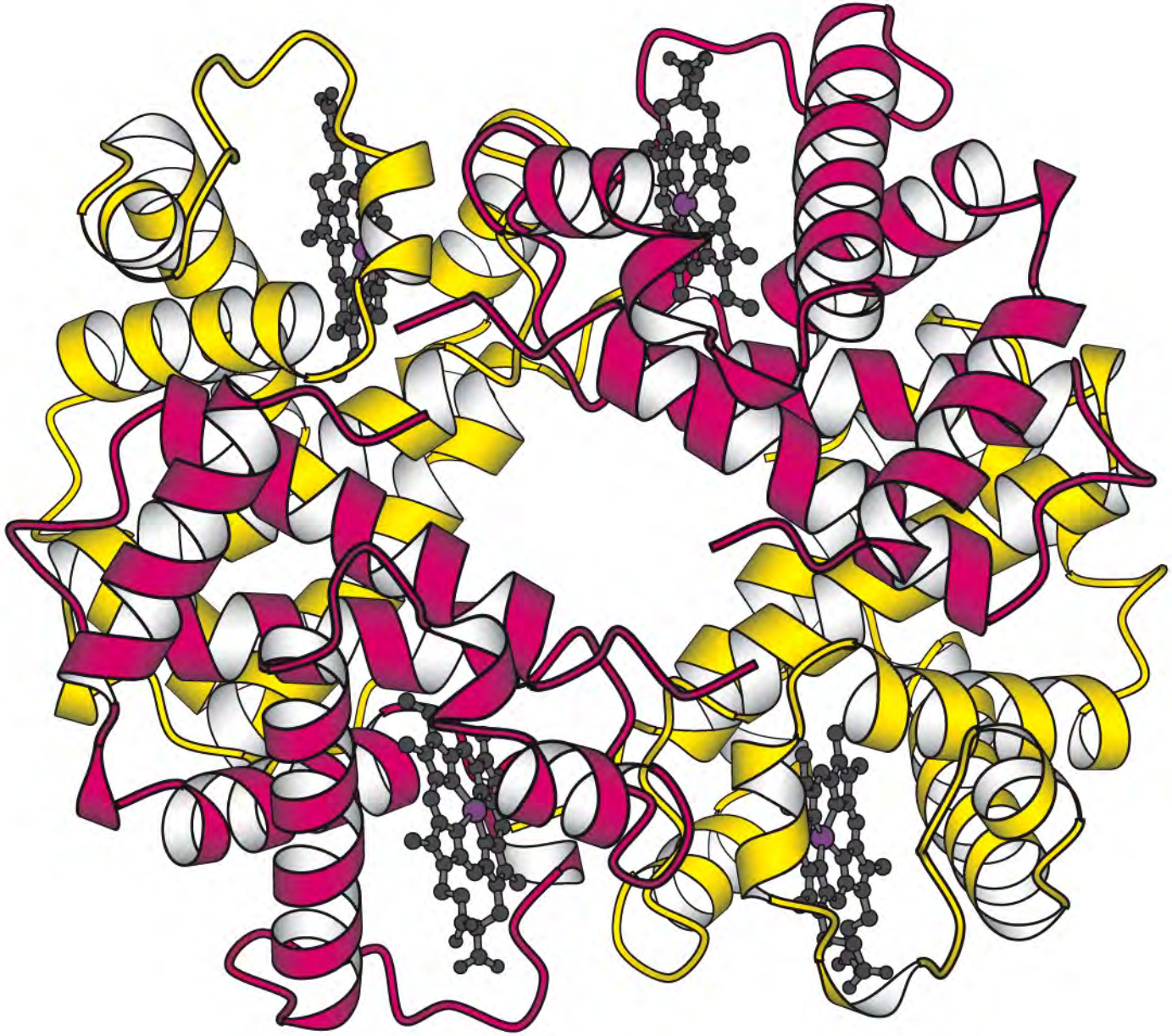
a) All proteins fold spontaneously into their proper shape.

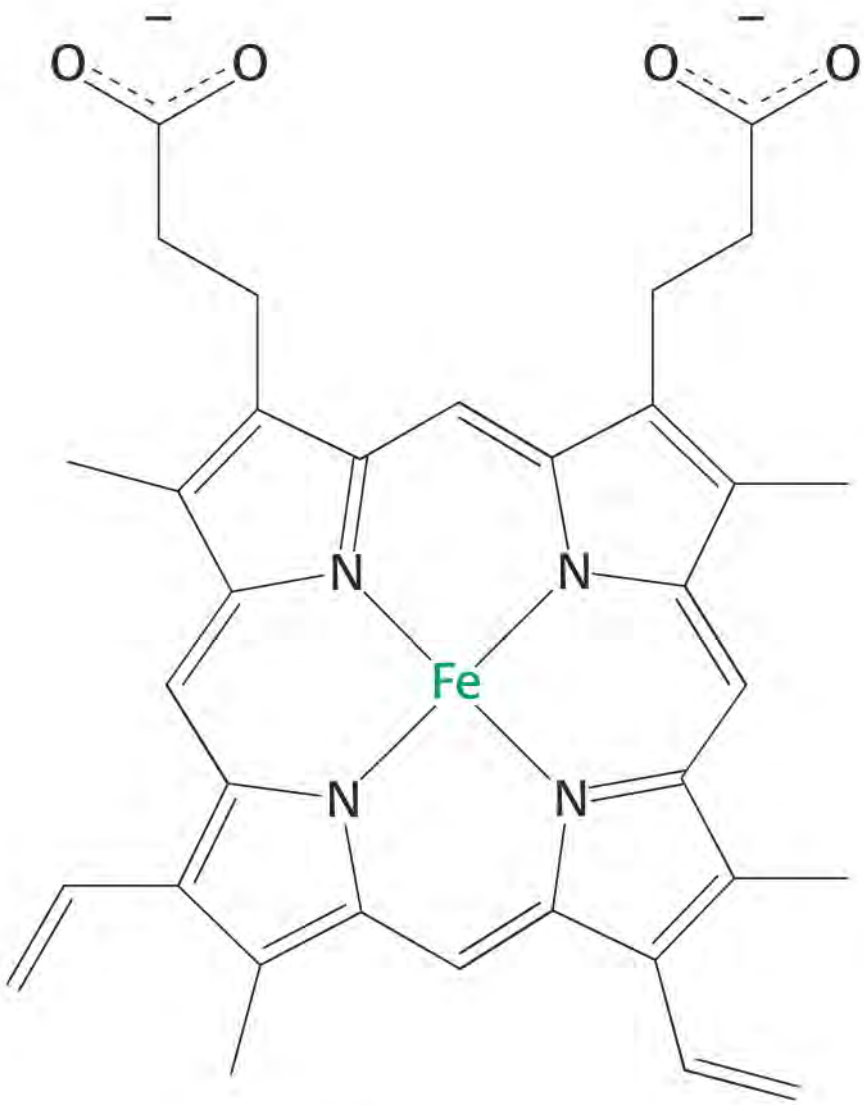
b) Tertiary structures tend to be high-energy shapes.

c) Primary structure determines tertiary structure.

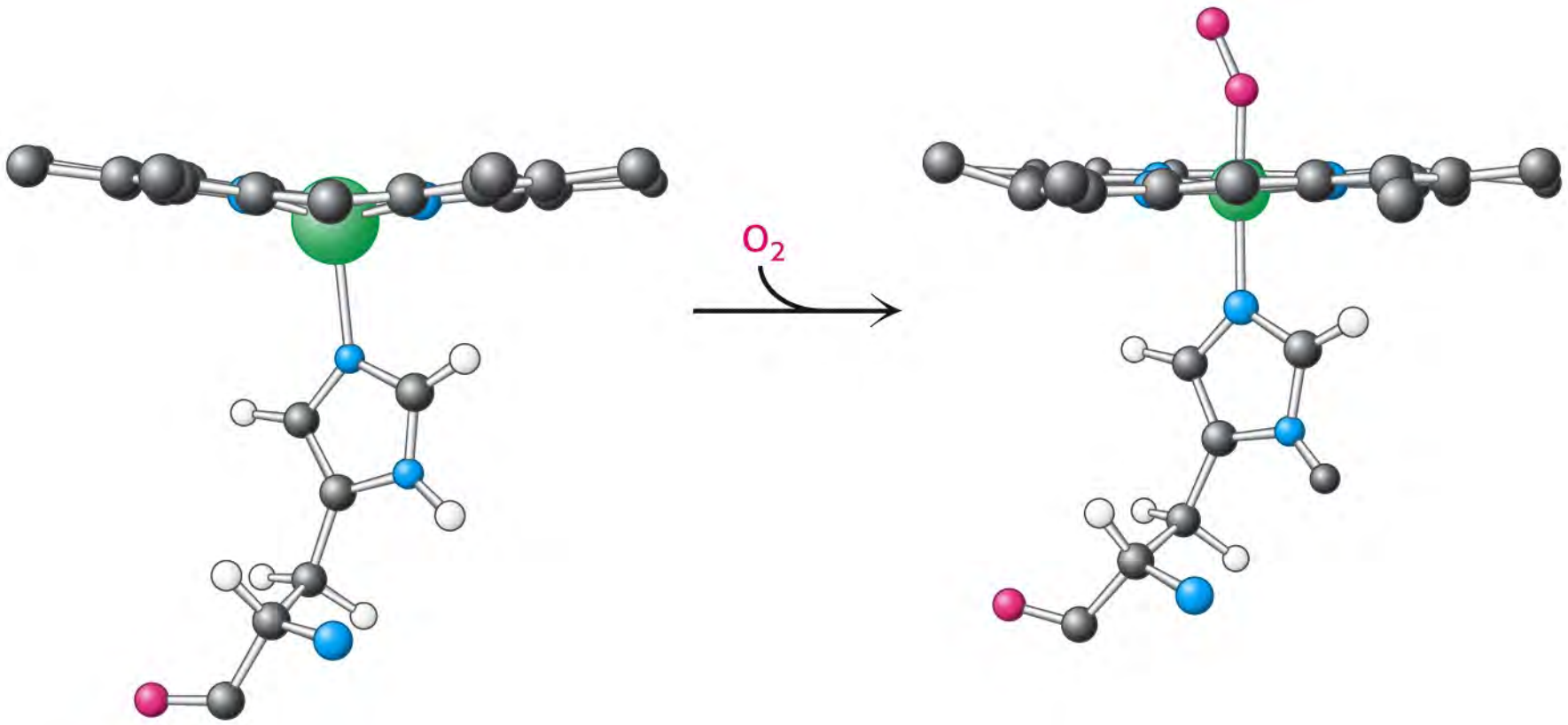
d) Denaturation breaks hydrogen bonds and peptide bonds.

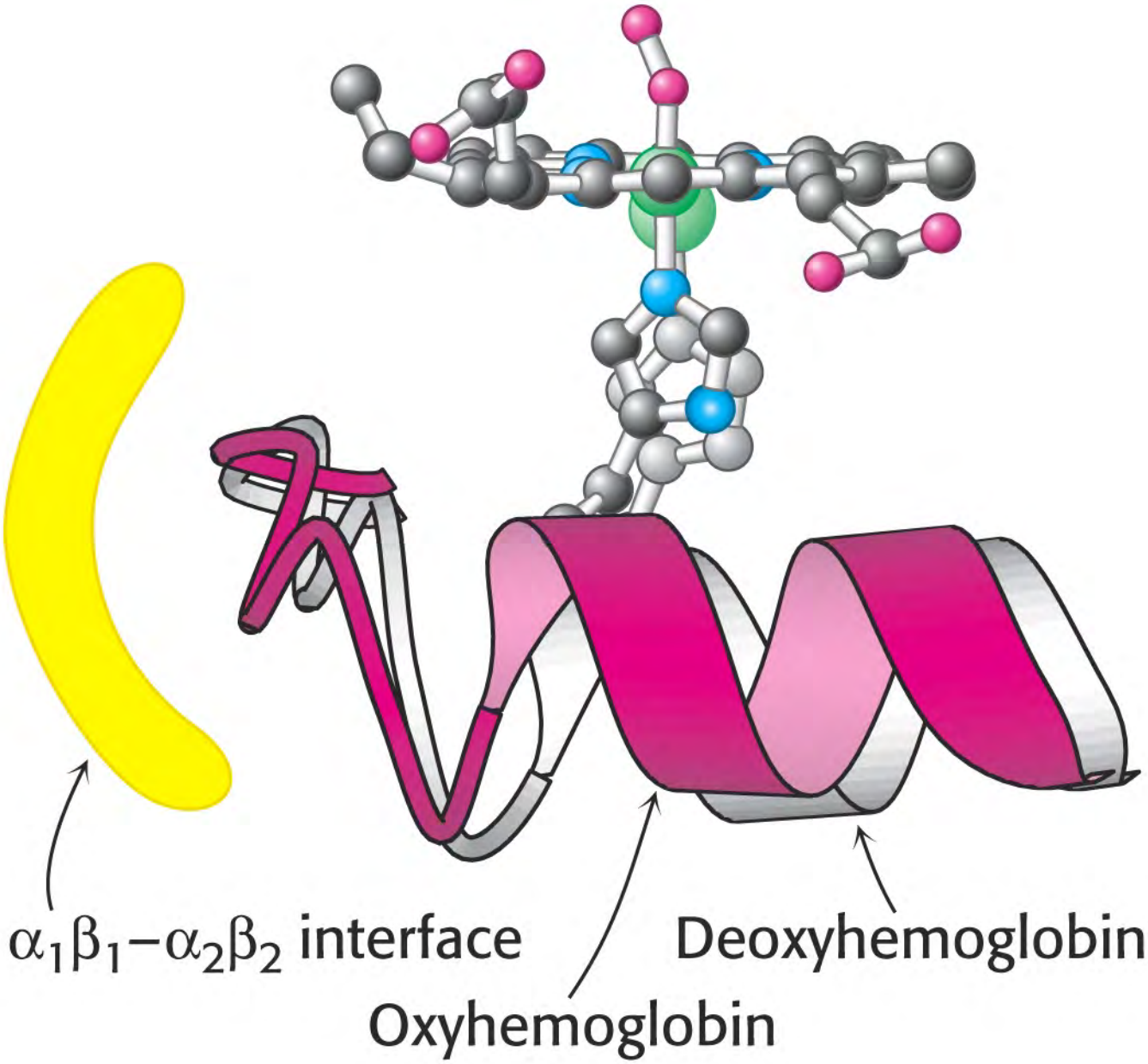
e) Two different proteins can have similar tertiary structures.

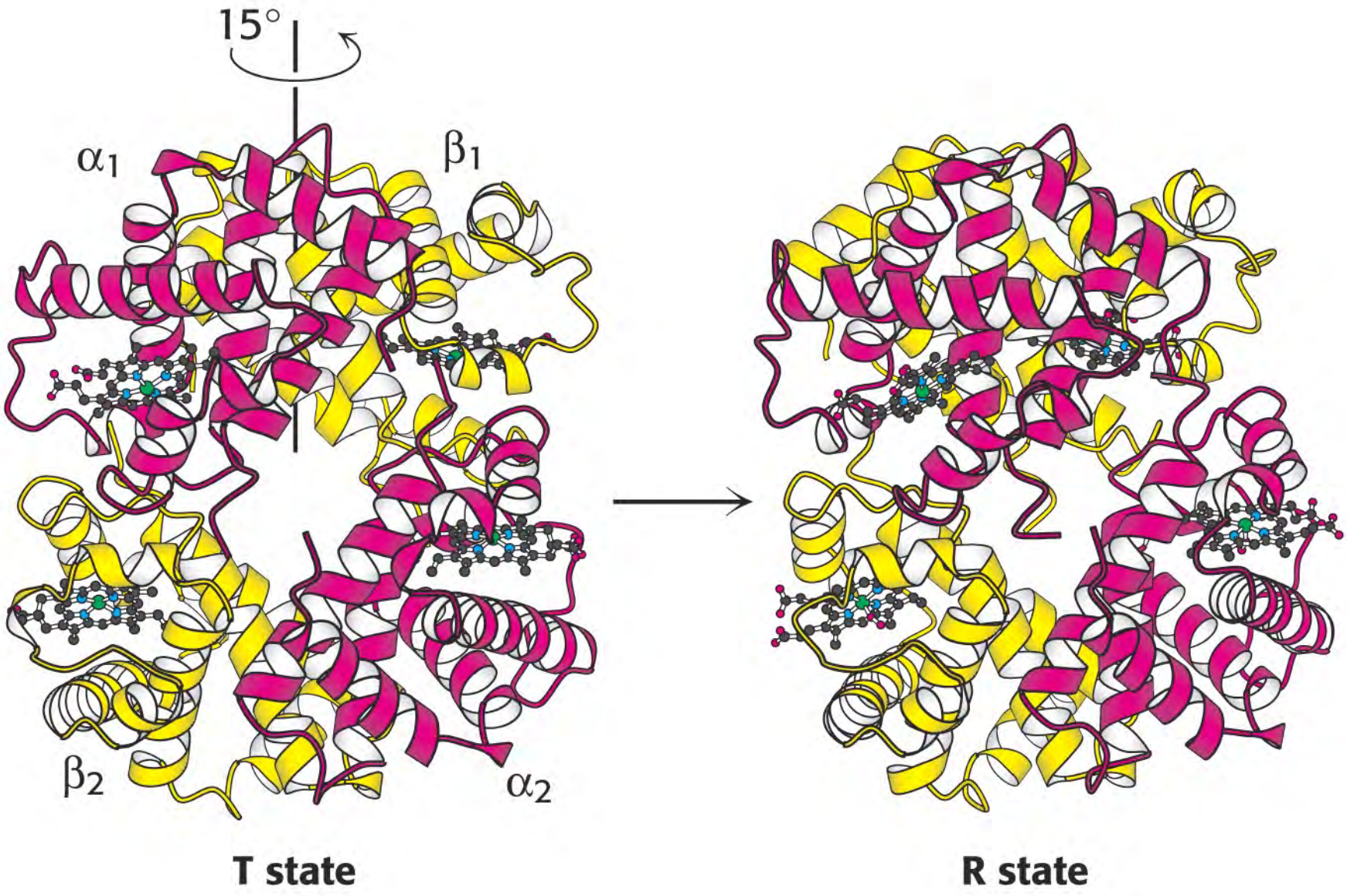


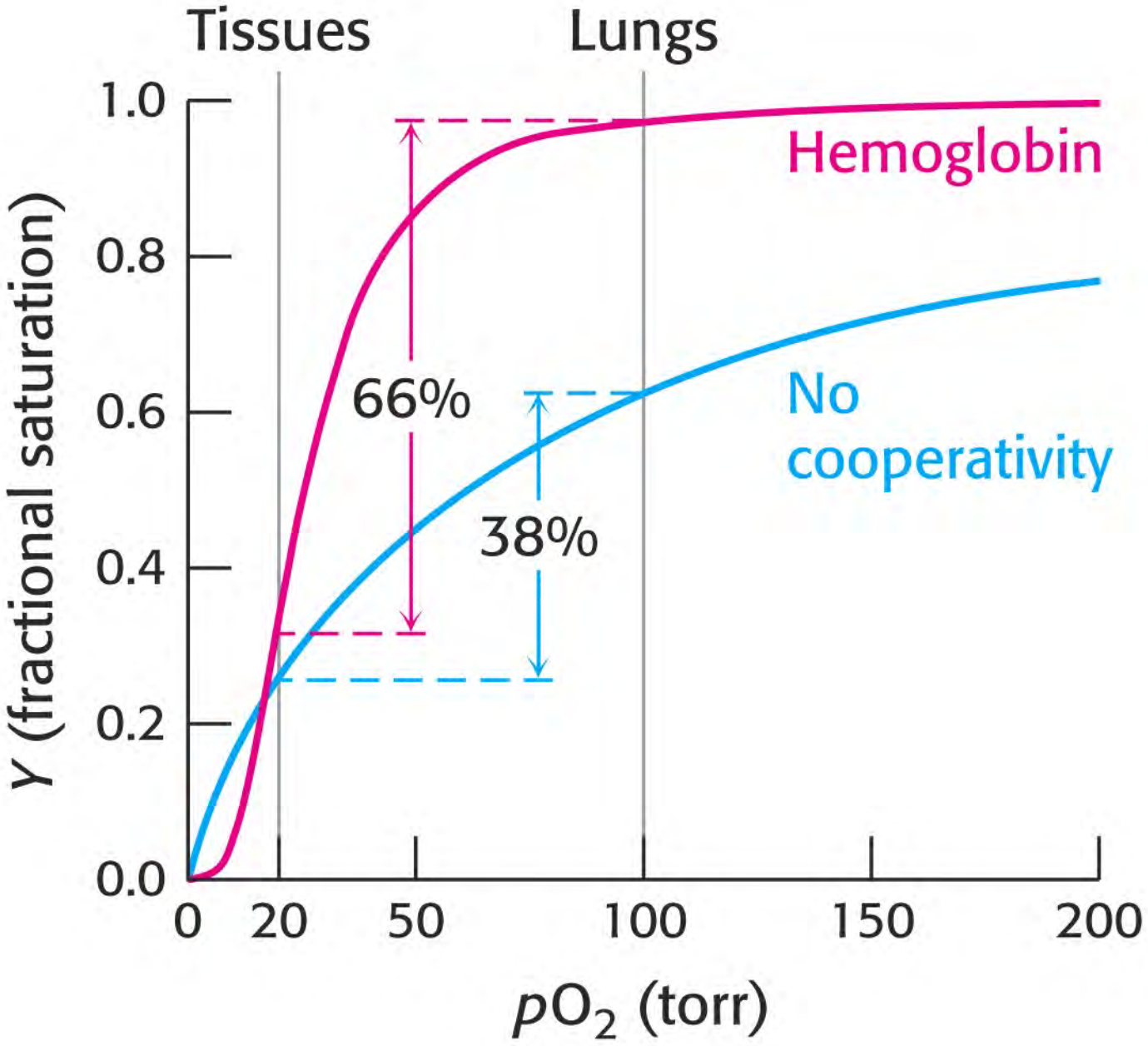


Heme
(Fe-protoporphyrin IX)


O_2


$\alpha_1\beta_1$–$\alpha_2\beta_2$ interface
Deoxyhemoglobin
Oxyhemoglobin


15°
α1
β1
β2
α2
T state
R state


Tissues
Lungs
1.0
0.8
0.6
0.4
0.2
0.0
Y (fractional saturation)
Hemoglobin
No
cooperativity
66%
38%
0
20
50
100
150
200
pO2 (torr)



Are You Getting It??



Protein A is a **multimeric** protein while **Protein B** is a **single polypeptide chain**. Which characteristics could be possessed by **Protein A**, **Protein B**, or both proteins?

a) The protein has quaternary structure.
b) The protein has tertiary structure.
c) The protein shows cooperative binding.
d) The protein contains multiple disulfide bonds.
e) The protein contains multiple salt bridges.



Are You Getting It??



Answer

Protein A is a multimeric protein while Protein B is a single polypeptide chain. Which characteristics could be possessed by Protein A, Protein B, or both proteins?

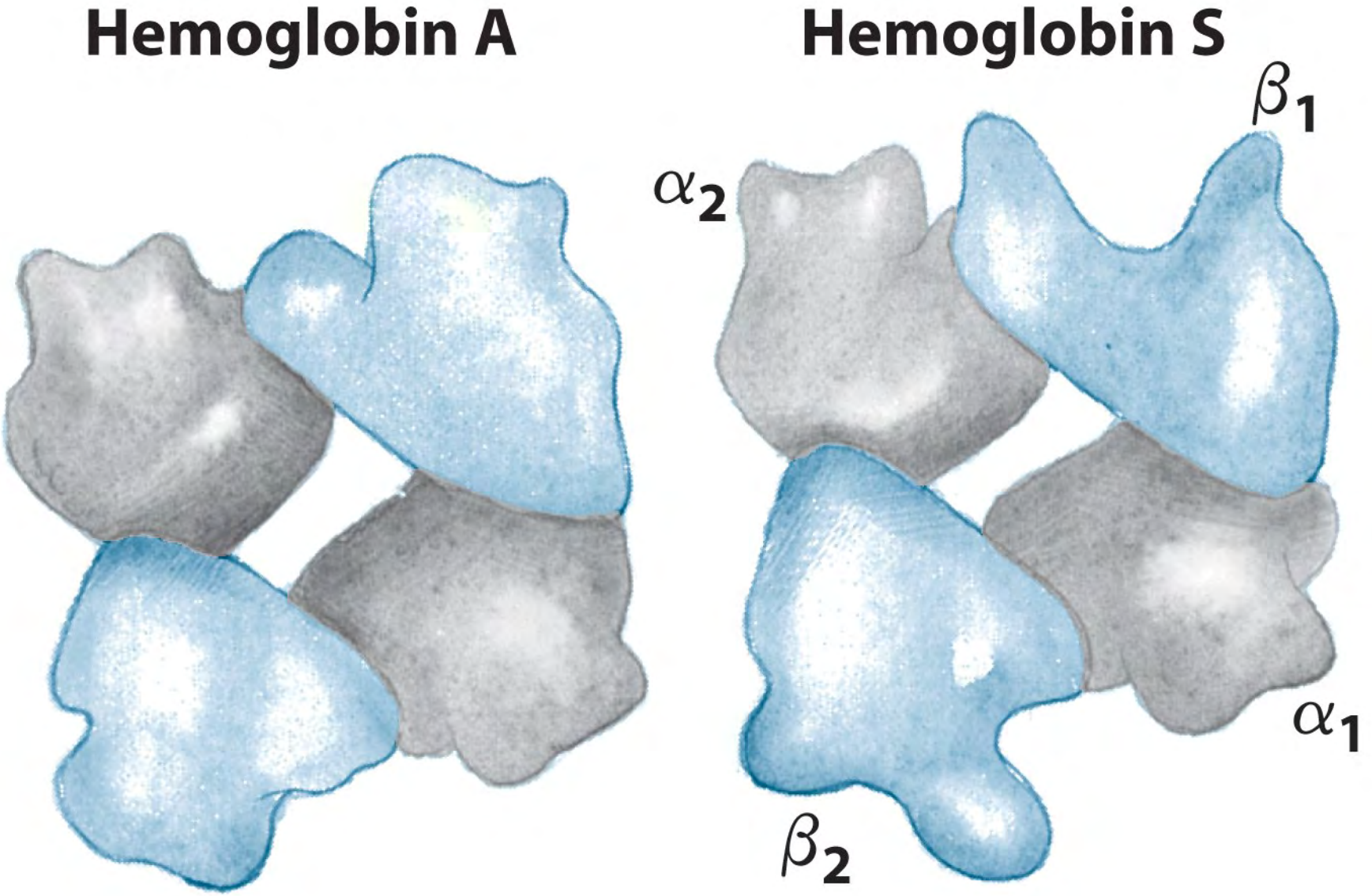
a) The protein has quaternary structure. ***Protein A***

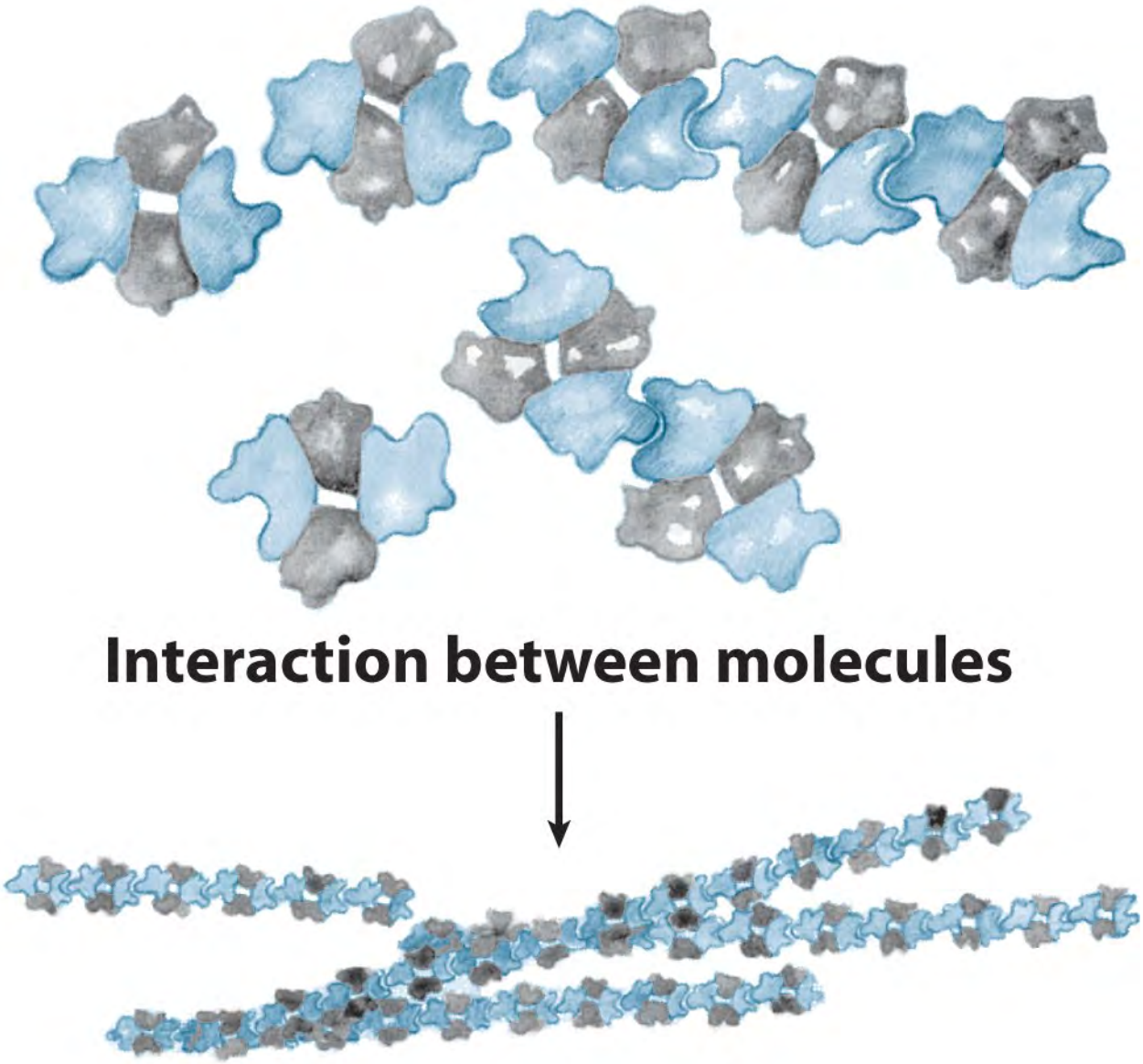
b) The protein has tertiary structure. ***Both***

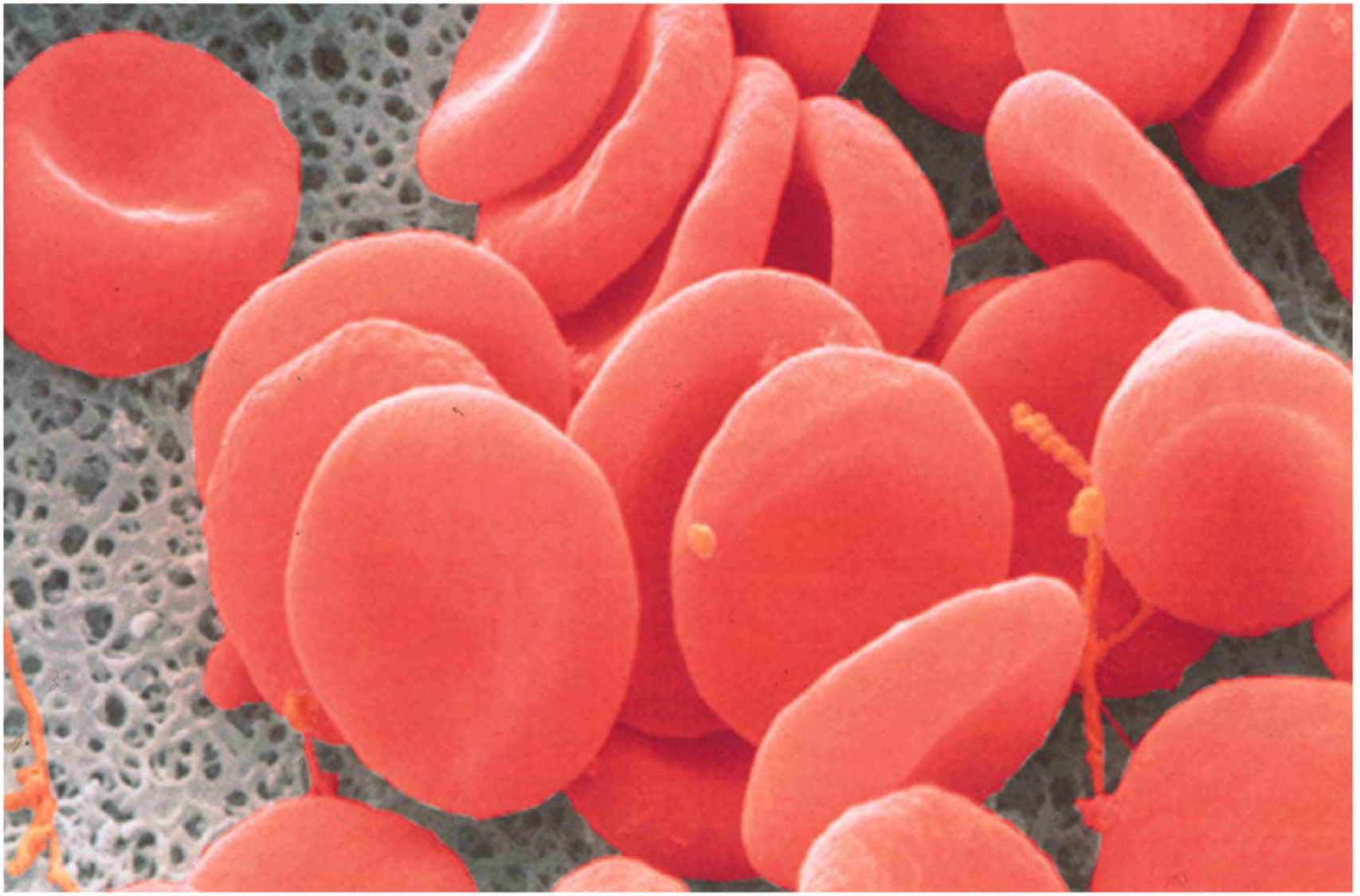
c) The protein shows cooperative binding. ***Protein A***

d) The protein contains multiple disulfide bonds. ***Both***

e) The protein contains multiple salt bridges. ***Both***


Hemoglobin A
Hemoglobin S
β1
α2
α1
β2


Interaction between molecules
Strand formation


2 μm

