Molecular Cell Biology A

"Protein structure and pathways"

BIOX24ZL

Tuesdays 9-10:30

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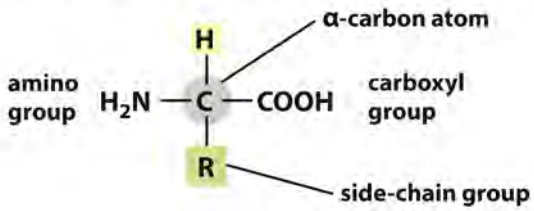
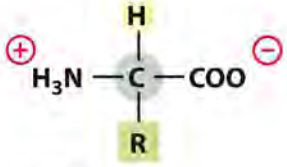
THE AMINO ACID

The general formula of an amino acid is



R is commonly one of 20 different side chains. At pH 7 both the amino and carboxyl groups are ionized.



Panel 3-1 (Part 1) Molecular Biology of the Cell 6e (© Garland Science 2015)

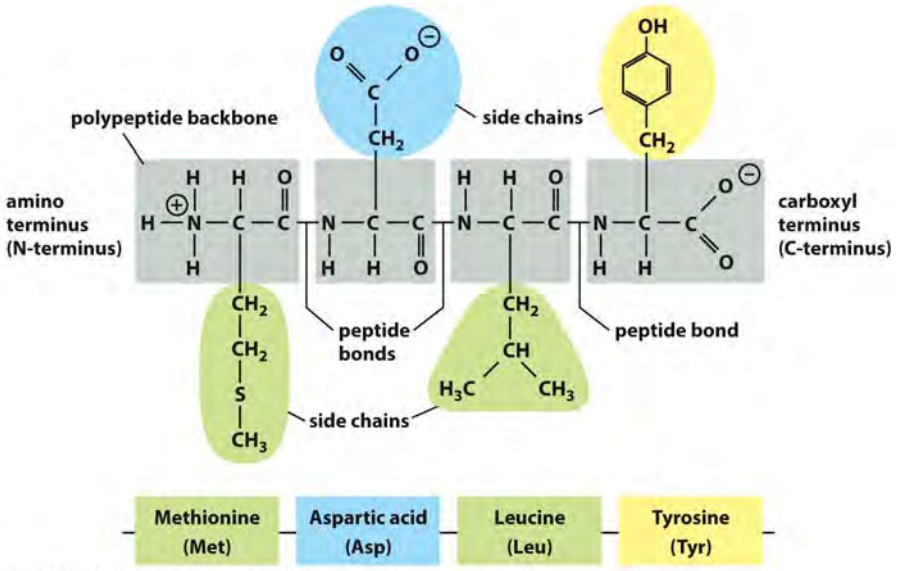
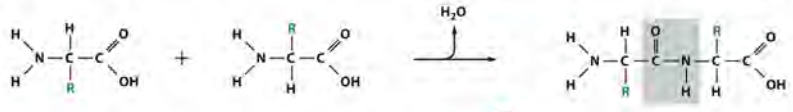


Figure 3-1 Molecular Biology of the Cell 6e (© Garland Science 2015)

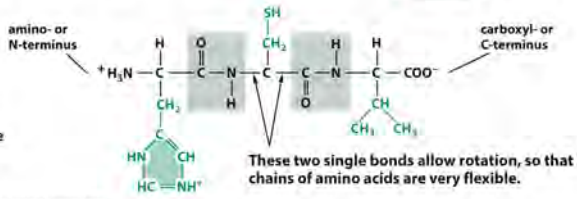
PEPTIDE BONDS

Amino acids are commonly joined together by an amide linkage, called a peptide bond.

Peptide bond: The four atoms in each *gray box* form a rigid planar unit. There is no rotation around the C–N bond.



Proteins are long polymers of amino acids linked by peptide bonds, and they are always written with the N-terminus toward the left. The sequence of this tripeptide is histidine-cysteine-valine.



These two single bonds allow rotation, so that long chains of amino acids are very flexible.

Panel 3-1 (Part 3) Molecular Biology of the Cell 6e (© Garland Science 2015)

Proteins are specified by their amino acid sequence.

- Polypeptide backbone with AA side chains
- Bond angle restricted, weak noncovalent bond: H+, electrostatic, van der Waals determine final 3D shape
- Nonpolar (hydrophobic) side chains (Leu Phe Trp Val) cluster together interior to H+ water
- Polar (hydrophilic) side chains (Asp- Arg+ His+ Gln polar) H+ bond outside, backbone interact

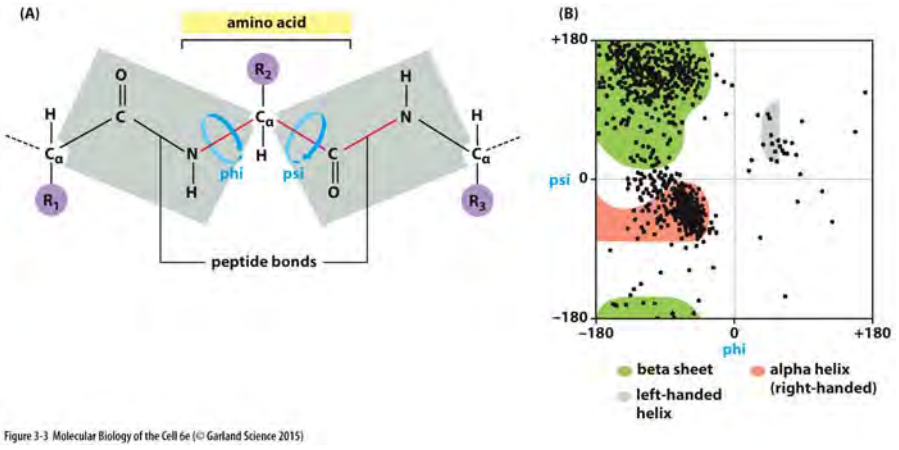
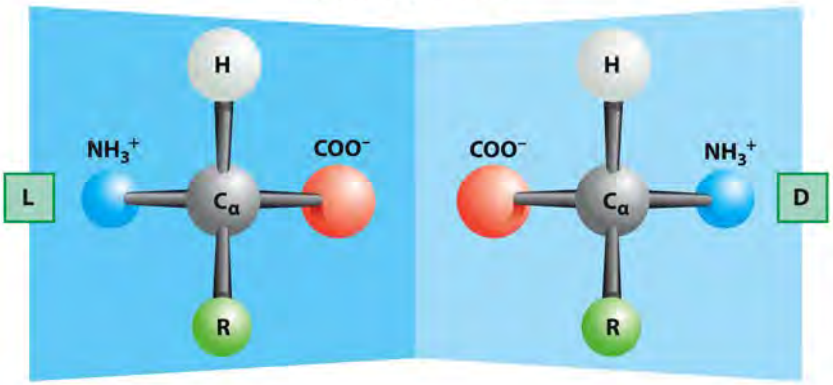


Figure 3-3 Molecular Biology of the Cell 6e (© Garland Science 2015)

OPTICAL ISOMERS

The α-carbon atom is asymmetric, which allows for two mirror images (or stereo-) isomers, L and D.



Proteins consist exclusively of L-amino acids.

Panel 3-1 (Part 2) Molecular Biology of the Cell 6e (© Garland Science 2015)

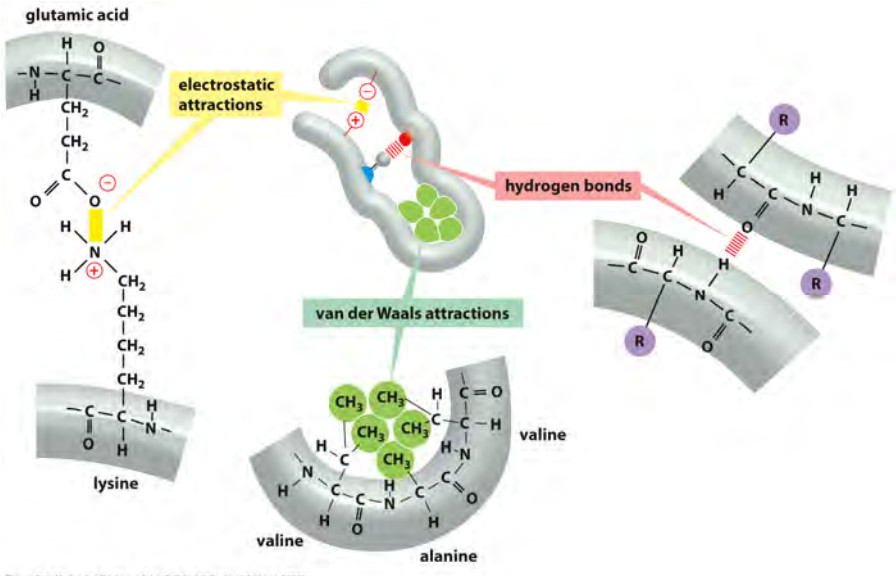


Figure 3-4 Molecular Biology of the Cell 6e (© Garland Science 2015)

AMINO ACID			SIDE CHAIN
Aspartic acid	Asp	D	negative
Glutamic acid	Glu	E	negative
Arginine	Arg	R	positive
Lysine	Lys	K	positive
Histidine	His	H	positive
Asparagine	Asn	N	uncharged polar
Glutamine	Gln	Q	uncharged polar
Serine	Ser	S	uncharged polar
Threonine	Thr	T	uncharged polar
Tyrosine	Tyr	Y	uncharged polar

POLAR AMINO ACIDS

AMINO ACID			SIDE CHAIN
Alanine	Ala	A	nonpolar
Glycine	Gly	G	nonpolar
Valine	Val	V	nonpolar
Leucine	Leu	L	nonpolar
Isoleucine	Ile	I	nonpolar
Proline	Pro	P	nonpolar
Phenylalanine	Phe	F	nonpolar
Methionine	Met	M	nonpolar
Tryptophan	Trp	W	nonpolar
Cysteine	Cys	C	nonpolar

NONPOLAR AMINO ACIDS

Figure 3-2 Molecular Biology of the Cell 6e (© Garland Science 2015)

FAMILIES OF AMINO ACIDS

The common amino acids are grouped according to whether their side chains are

- acidic
- basic
- uncharged polar
- nonpolar

These 20 amino acids are given both three-letter and one-letter abbreviations.

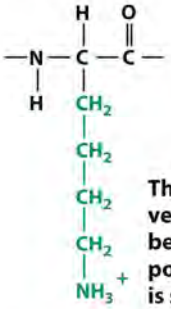
Thus: alanine = Ala = A

Panel 3-1 (Part 4) Molecular Biology of the Cell 6e (© Garland Science 2015)

BASIC SIDE CHAINS

lysine

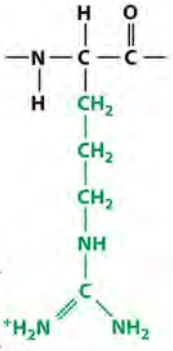
(Lys, or K)



This group is very basic because its positive charge is stabilized by resonance.

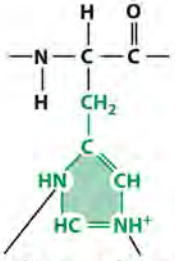
arginine

(Arg, or R)



histidine

(His, or H)



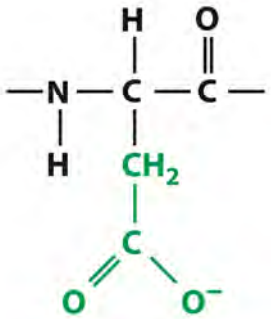
These nitrogens have a relatively weak affinity for an H^+ and are only partly positive at neutral pH.

Panel 3-1 (Part 5) Molecular Biology of the Cell 6e (© Garland Science 2015)

ACIDIC SIDE CHAINS

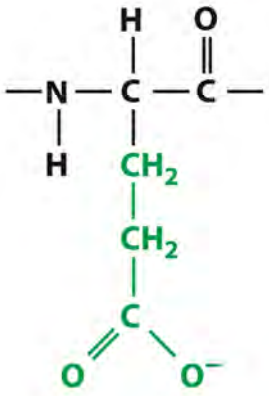
aspartic acid

(Asp, or D)

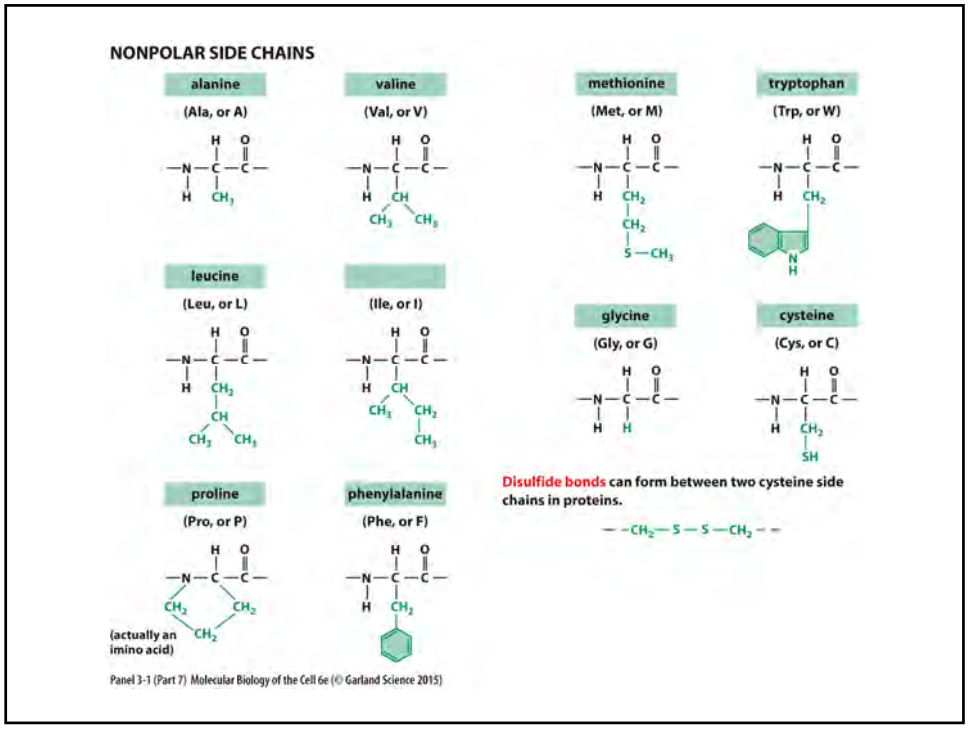


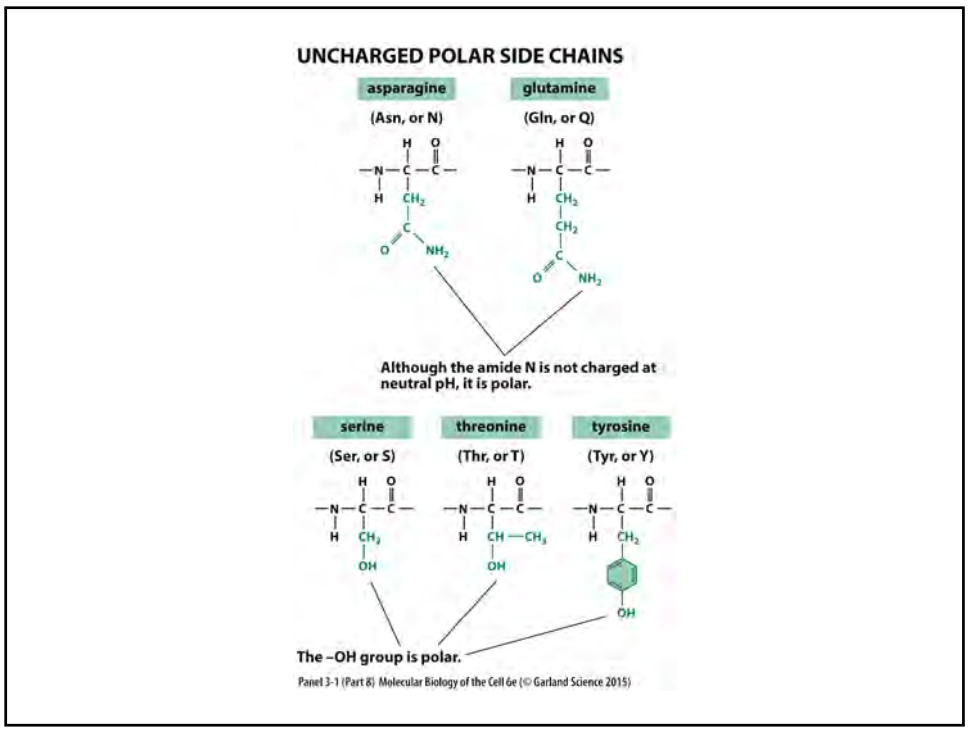
glutamic acid

(Glu, or E)



Panel 3-1 (Part 6) Molecular Biology of the Cell 6e (© Garland Science 2015)


NONPOLAR SIDE CHAINS
alanine
(Ala, or A)
valine
(Val, or V)
methionine
(Met, or M)
tryptophan
(Trp, or W)
leucine
(Leu, or L)
(Ile, or I)
glycine
(Gly, or G)
cysteine
(Cys, or C)
Disulfide bonds can form between two cysteine side chains in proteins.
proline
(Pro, or P)
phenylalanine
(Phe, or F)
(actually an imino acid)
Panel 3-1 (Part 7) Molecular Biology of the Cell 6e (© Garland Science 2015)


UNCHARGED POLAR SIDE CHAINS
asparagine
(Asn, or N)
glutamine
(Gln, or Q)
Although the amide N is not charged at neutral pH, it is polar.
serine
(Ser, or S)
threonine
(Thr, or T)
tyrosine
(Tyr, or Y)
The –OH group is polar.
Panel 3-1 (Part 8) Molecular Biology of the Cell 6e (© Garland Science 2015)

Proteins fold into unique 3D conformations of lowest energy.

- Study by denaturing noncovalent bonds (urea), allow to renature from flexible chain
- Conformation altered if interact with cell mol
- Chaperones: prevent hydrophobic aggregates making folding more reliable, assist folding
- SH2 (GTGA domains) 100AA backbone, ribbon, wire, space-filling models

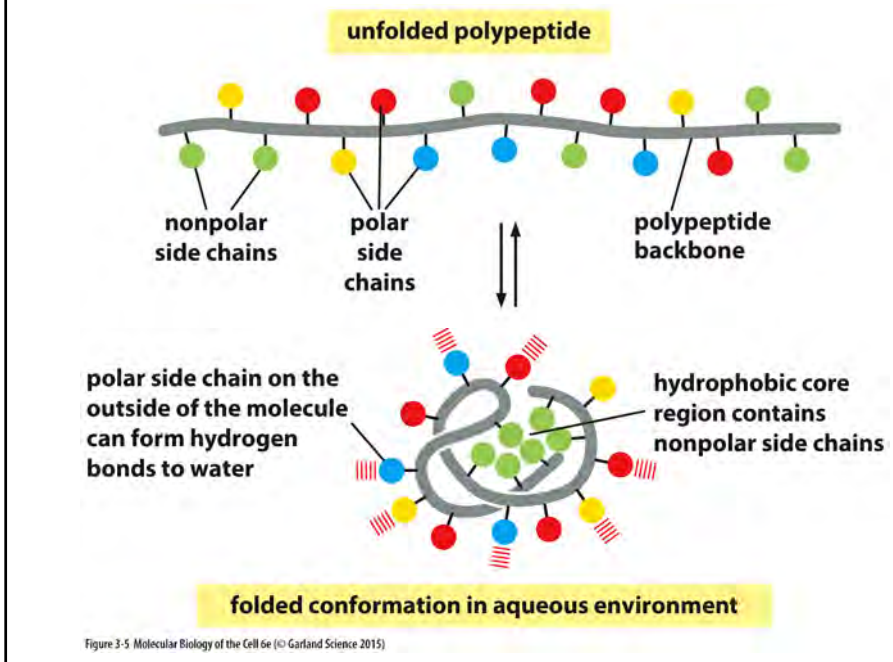


Figure 3-5 Molecular Biology of the Cell 6e (© Garland Science 2015)

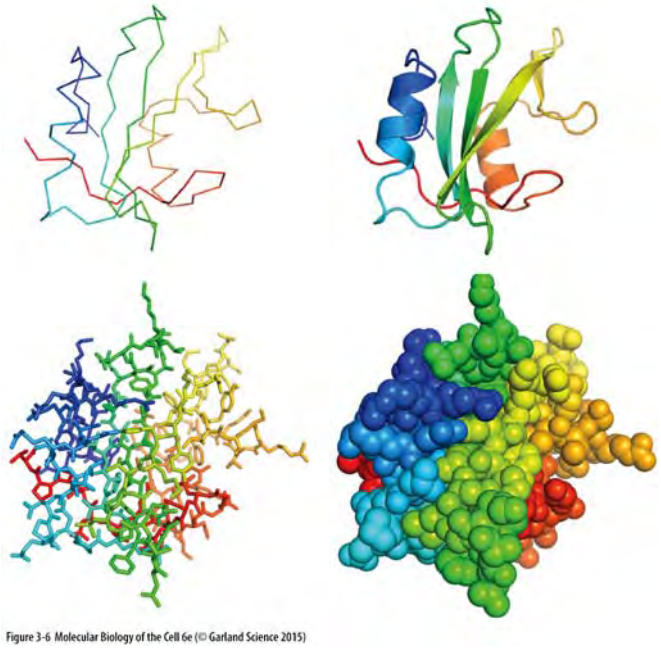


Figure 3-6 Molecular Biology of the Cell 6e (© Garland Science 2015)

Team work.

Which of the following pairs of amino acid residues would you expect to form ionic bonds?

- A. Glutamic acid and glutamine
- B. Arginine and lysine
- C. Tryptophan and tyrosine
- D. Tyrosine and glutamine
- E. Lysine and glutamic acid

Which of the following stretches of amino acid residues would you expect to find in the interior of protein molecules?

- A. Ala-Val-Leu-Ile-Trp
- B. Ala-Asp-Asp-Tyr-Arg
- C. Phe-Glu-Gln-Glu-Asn
- D. Gly-Tyr-His-Arg-His
- E. Gly-Lys-Ser-Pro-Thr

Proteins form common patterns (alpha helix, beta sheet) by backbone H bond.

- Alpha helix: keratin in skin hair, N-H (up) H bond to C=O (down) 4 away, turn every 3.6, C end part neg, N part pos, membrane proteins inside H bond each other, outside nonpolar
- Beta sheet: fibroin in silk, H bond between diff chains, R alternate up down, protein core rigid
- Beta sheet run in parallel (same orientation) or anti-parallel (fold back on itself) directions
- Coiled coil alpha helix 2-3 chains, nonpolar on one side inward so twist around each other

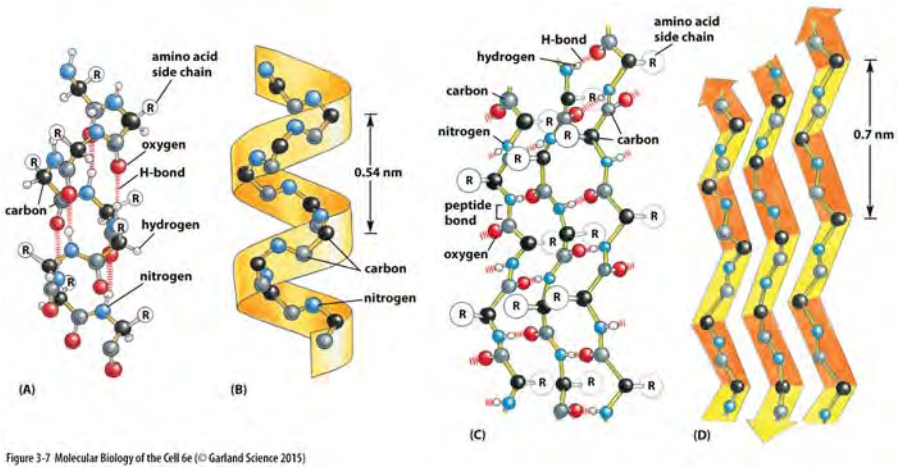


Figure 3-7 Molecular Biology of the Cell 6e (© Garland Science 2015)

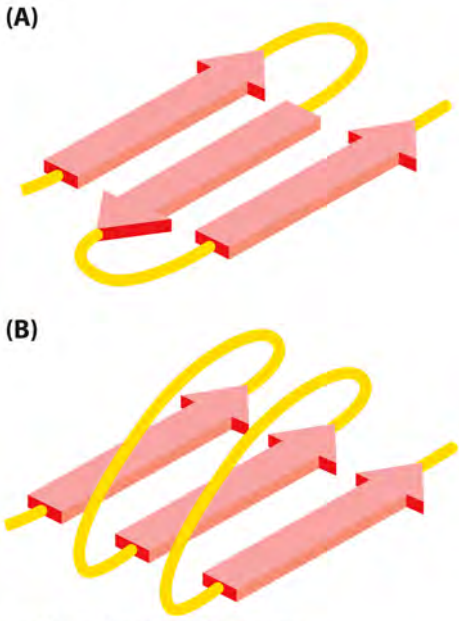


Figure 3-8 Molecular Biology of the Cell 6e (© Garland Science 2015)

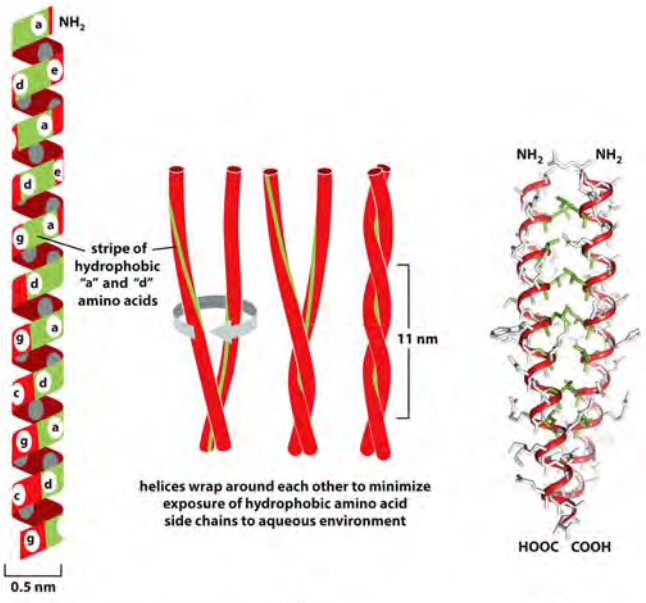


Figure 3-9 Molecular Biology of the Cell 6e (© Garland Science 2015)

Proteins are characterized by four (plus one) levels of structure.

- Primary structure: AA sequence
- Secondary structure: alpha helix, beta sheet
- Tertiary structure: 3D peptide organization
- Quaternary structure: multiple peptide chains
- Domains: part of chain into stable modules, e.g. Src Kinase SH2 SH3 regulate C-term kinase
- 20^n possible seq but evolution selects for only 1 in a billion for its stable structure

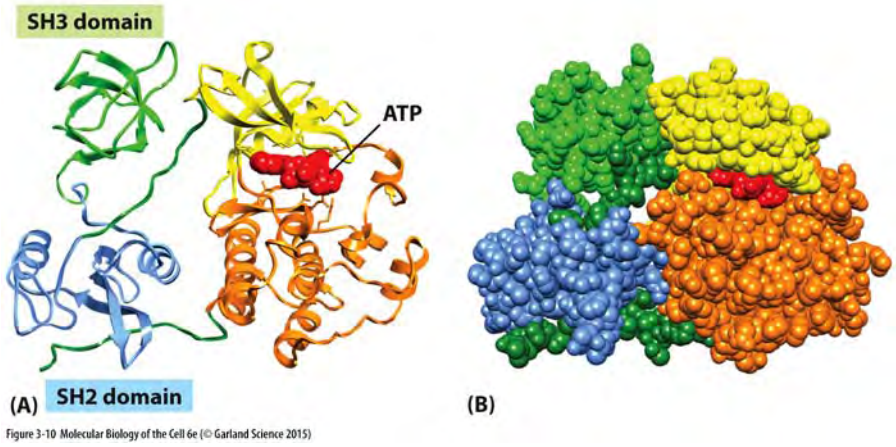


Figure 3-10 Molecular Biology of the Cell 6e (© Garland Science 2015)

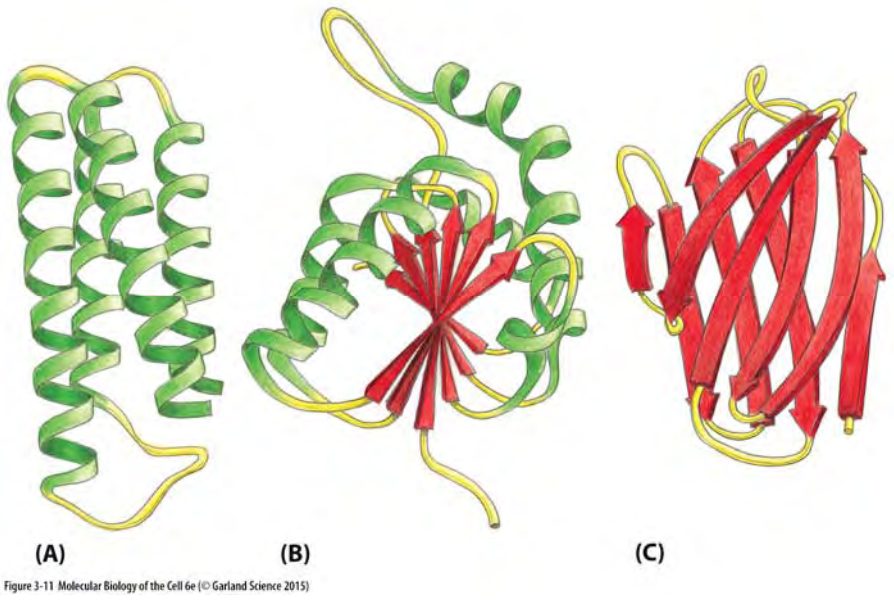


Figure 3-11 Molecular Biology of the Cell 6e (© Garland Science 2015)

Protein diversity result from reuse of same modules as homologs.

- Families of protein from duplicated mutations
- Diff AA seq (25% same) still similar structure due to small number of characteristic shapes
- Pattern matches in signature seq allow identification with proteins of known function
- Domain shuffling forms new proteins from existing motifs, binding sites mutated for diff ligands, N-C terms at opposite or same ends

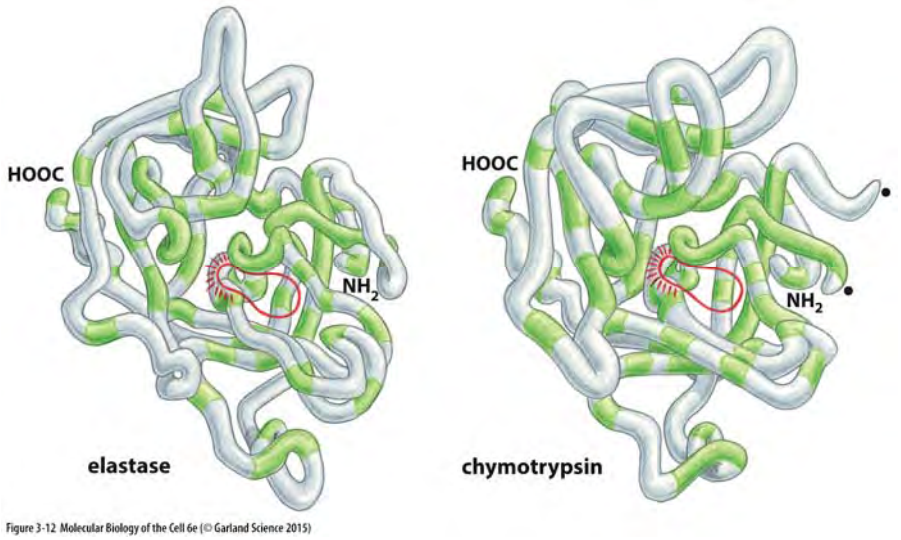


Figure 3-12 Molecular Biology of the Cell 6e (© Garland Science 2015)

Only green are identical AAs.

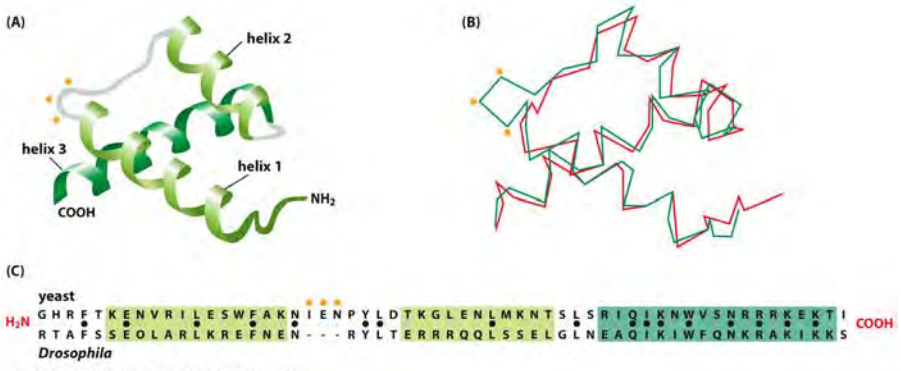


Figure 3-13 Molecular Biology of the Cell 6e (© Garland Science 2015)

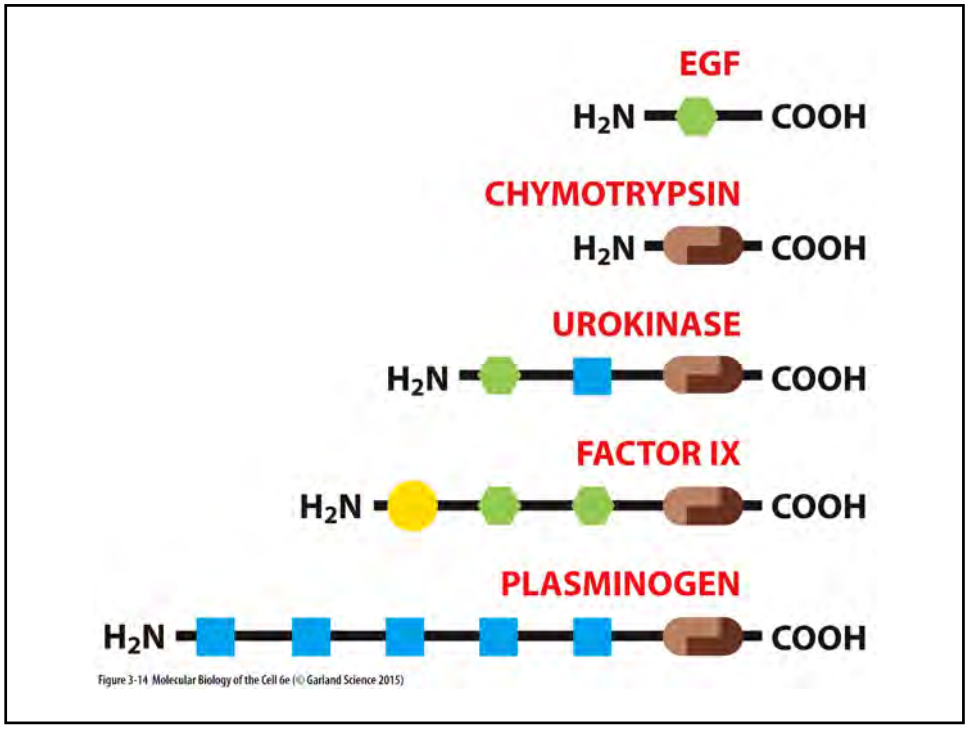


Figure 3-14 Molecular Biology of the Cell 6e (© Garland Science 2015)

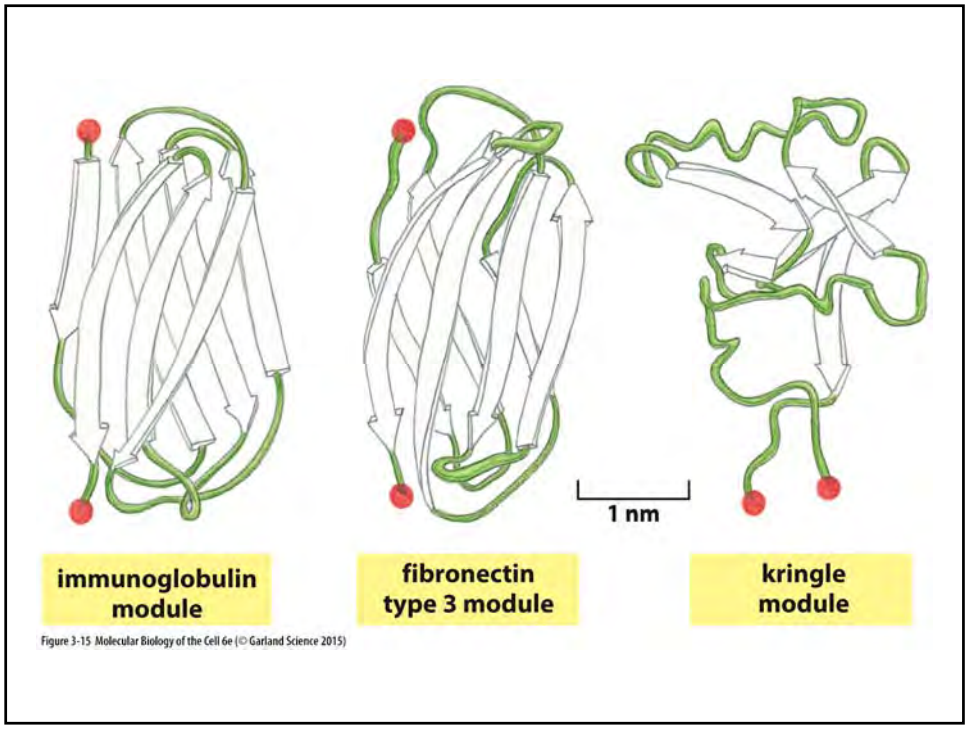


Figure 3-15 Molecular Biology of the Cell 6e (© Garland Science 2015)

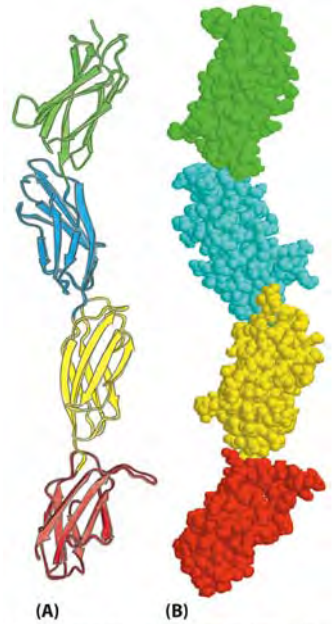


Figure 3-16 Molecular Biology of the Cell 6e (© Garland Science 2015)

Diversity of protein structures allow for adaptability.

- Half of domains shared between all organisms only 5% of 2-domain combos shared ev recent
- Humans: similar genes vastly shuffled domains
- Binding sites noncovalent interactions with other polypeptides lead to multi-chain proteins
- Repeat helical filaments common, e.g. actin
- Fibrous proteins span large distance in extracellular matrix, e.g. collagen triple helix
- Unstructured chains allow stretch, e.g. elastin

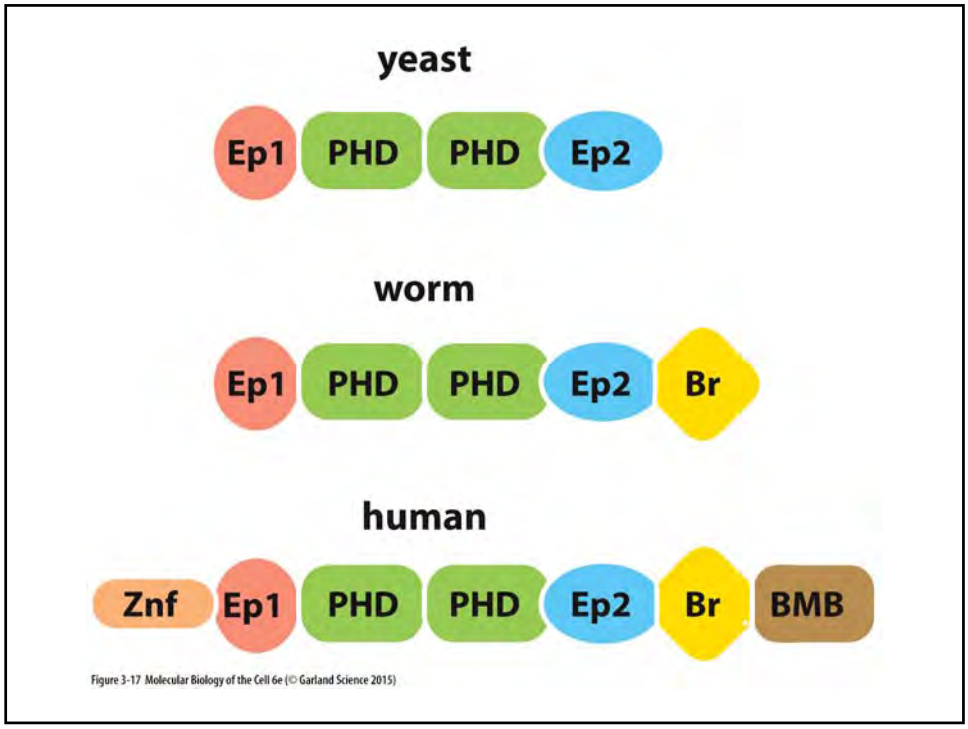


Figure 3-17 Molecular Biology of the Cell 6e (© Garland Science 2015)

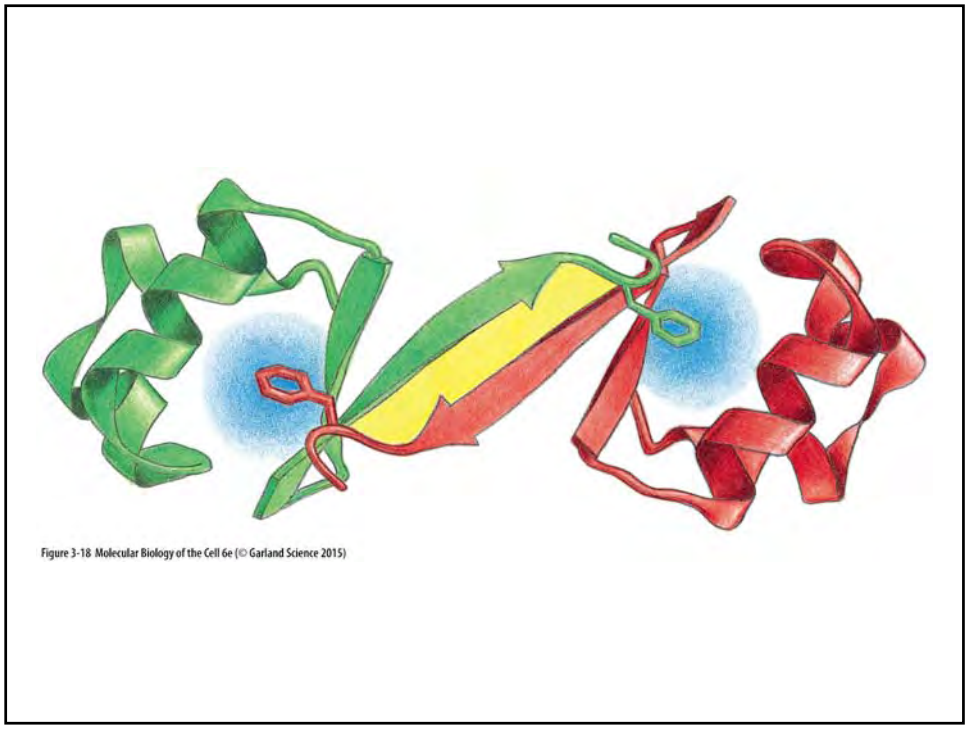


Figure 3-18 Molecular Biology of the Cell 6e (© Garland Science 2015)

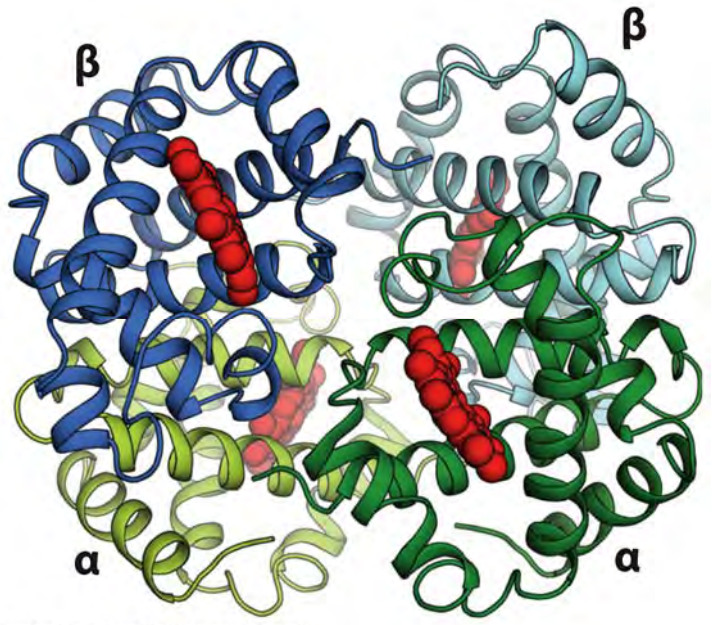


Figure 3-19 Molecular Biology of the Cell 6e (© Garland Science 2015)

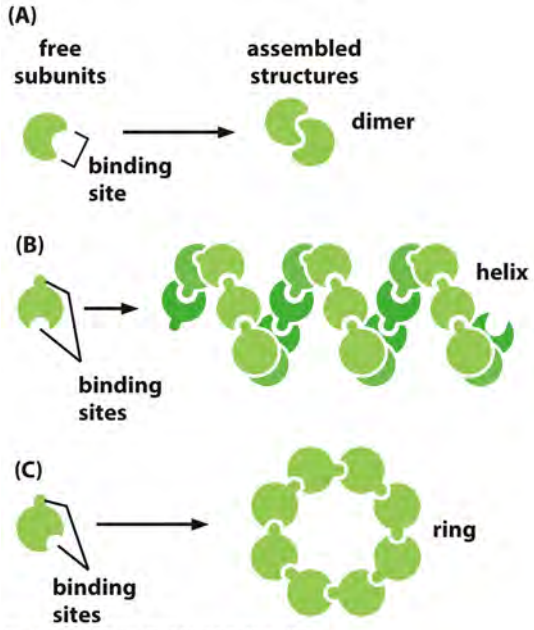


Figure 3-20 Molecular Biology of the Cell 6e (© Garland Science 2015)

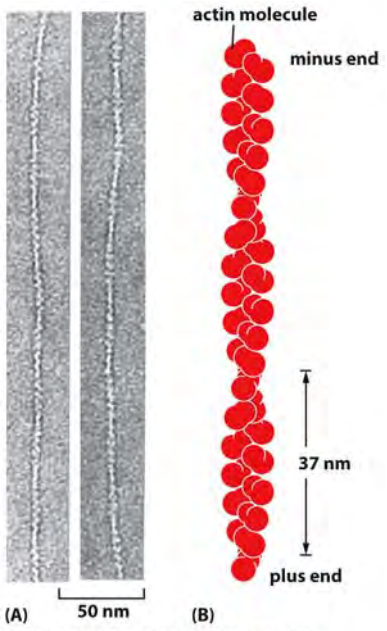


Figure 3-21 Molecular Biology of the Cell 6e (© Garland Science 2015)

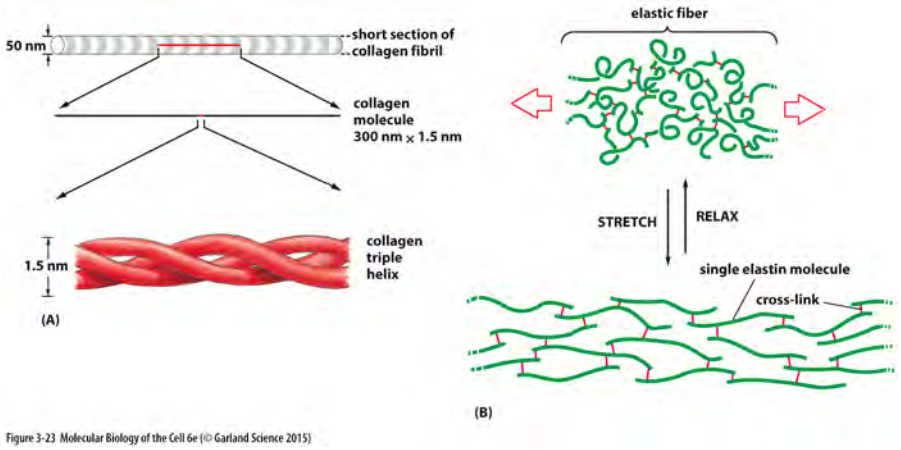


Figure 3-23 Molecular Biology of the Cell 6e (© Garland Science 2015)

Protein assemblies are formed by various means.

- Disulfide bonds (SH cysteine) cross-links proteins together in extracellular environ only, reducing (provide electrons) to separate
- Protein subunits assemblies, e.g. icosohedral viral capsid
- Self assembly: tobacco mosaic virus, ribosome
- Irreversibility: cannot self assemble after proteolytic cleavage, mitochondria

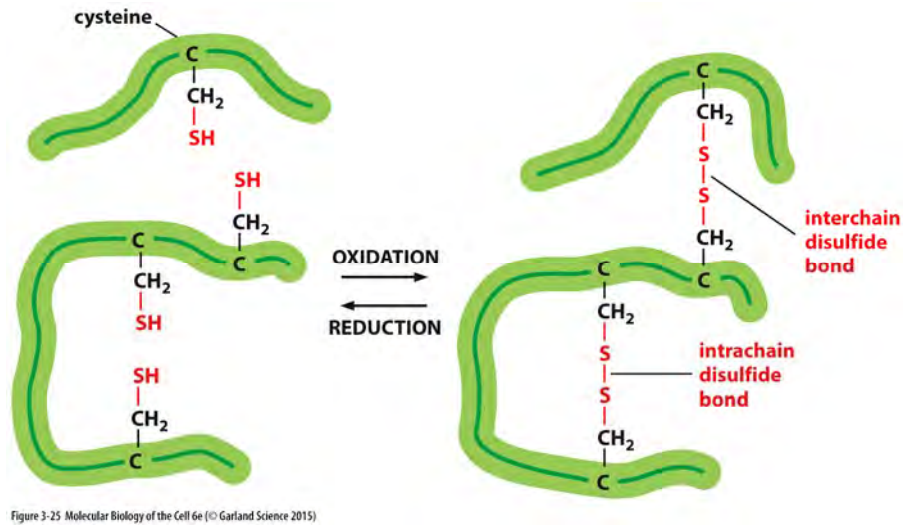


Figure 3-25 Molecular Biology of the Cell 6e (© Garland Science 2015)

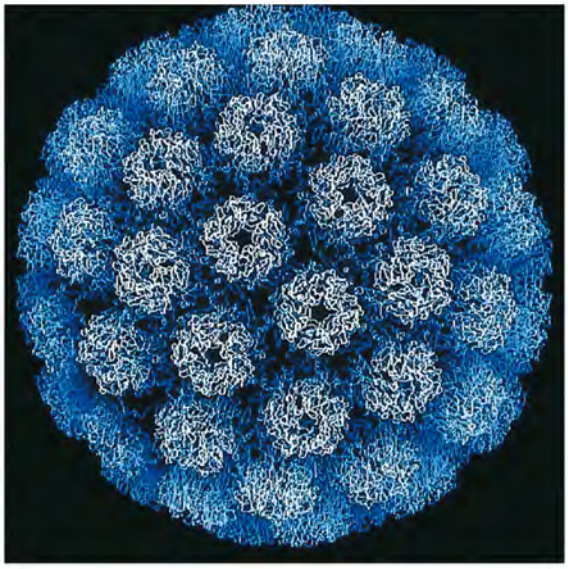


Figure 3-27 Molecular Biology of the Cell 6e (© Garland Science 2015)

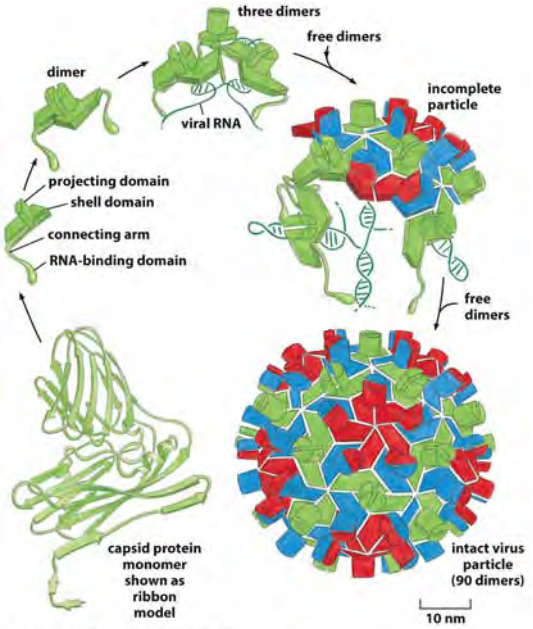


Figure 3-28 Molecular Biology of the Cell 6e (© Garland Science 2015)

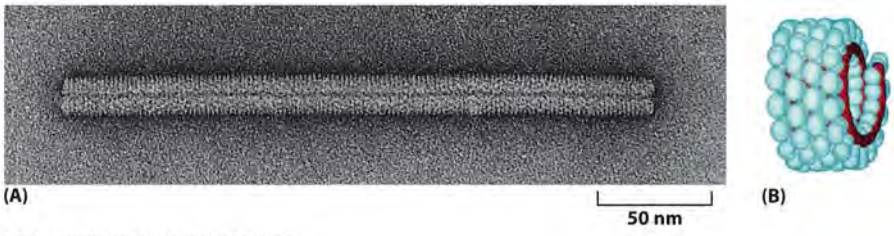


Figure 3-29 Molecular Biology of the Cell 6e (© Garland Science 2015)

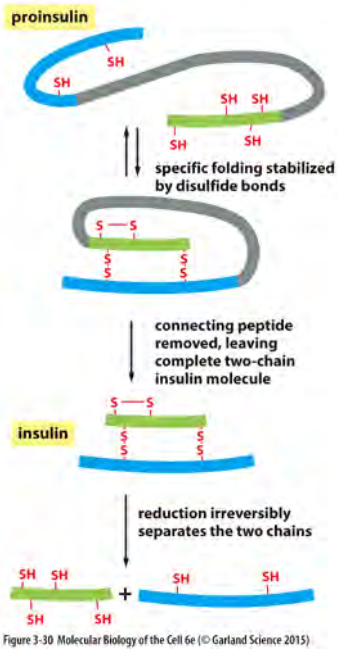


Figure 3-30 Molecular Biology of the Cell 6e (© Garland Science 2015)

Team work.

Protein secondary structure elements such as α helices and β sheets constitute the major regular folding patterns in proteins. With regard to these elements, …

- A. the folding patterns result from hydrogen-bonding between the N–H and C=O groups in the polypeptide backbone.
- B. a certain short amino acid sequence always adopts the same secondary structure.
- C. hydrogen-bonding between the amino acid side chains defines the type of secondary structure.
- D. only a few specific amino acid sequences can adopt these repetitive structures.
- E. All of the above.

You have purified a multisubunit extracellular protein that has several interchain disulfide bonds. Which of the following chemicals would you add to your purified protein mixture if you wanted to eliminate the disulfide bonds?

- A. NaCl, a salt
- B. DTT, a reducing agent
- C. H_2O_2, an oxidizing reagent
- D. SDS, an ionic detergent and denaturing agent
- E. Tris, a buffering agent