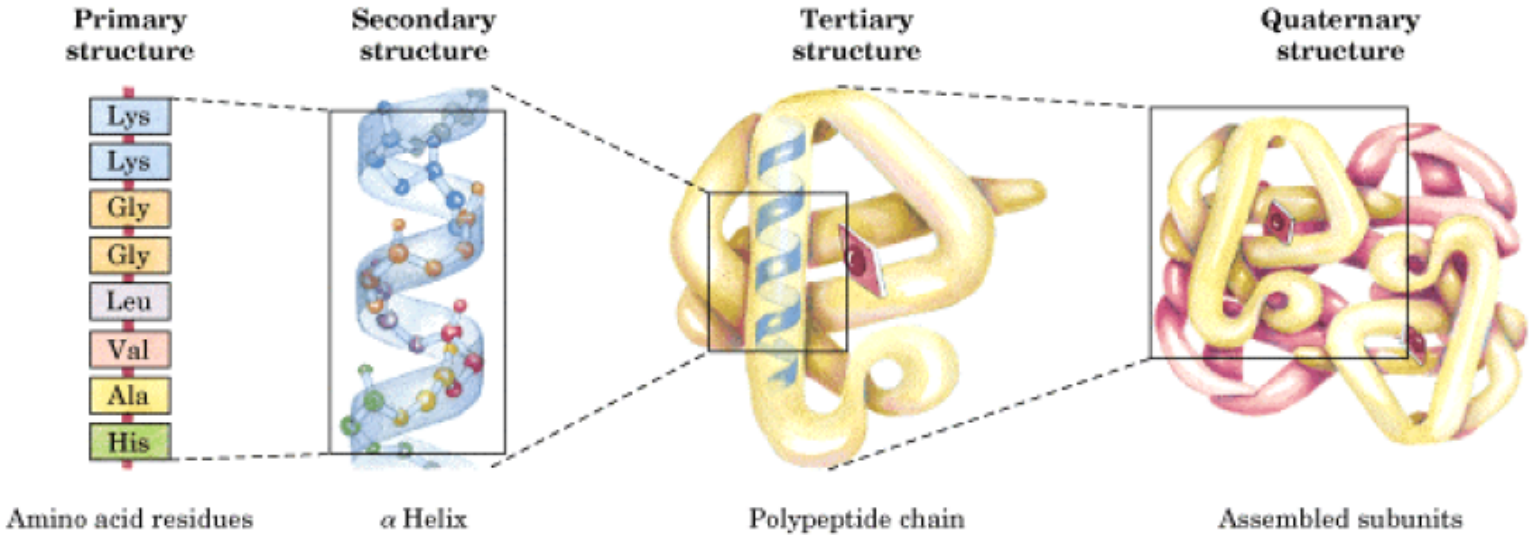
Levels of protein structure



- Primary structure is the amino acid sequence
- Secondary structure is repeating geometry (a-helix and b-strand)
- Tertiary structure is overall spatial arrangement
- Quaternary structure is arrangement of several (folded) polypeptides

Proteins

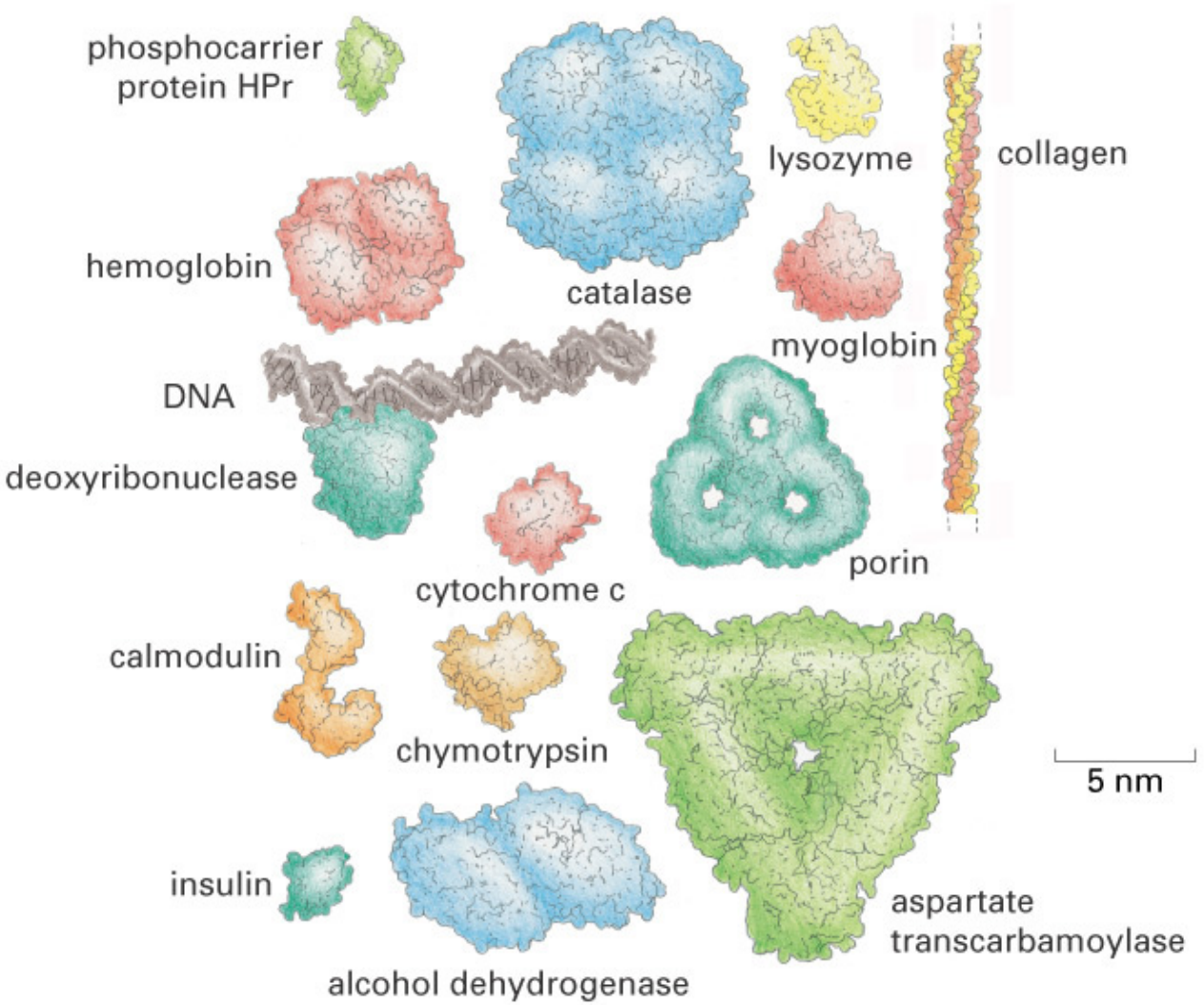


Figure 4-9 Essential Cell Biology, 2/e. (© 2004 Garland Science)

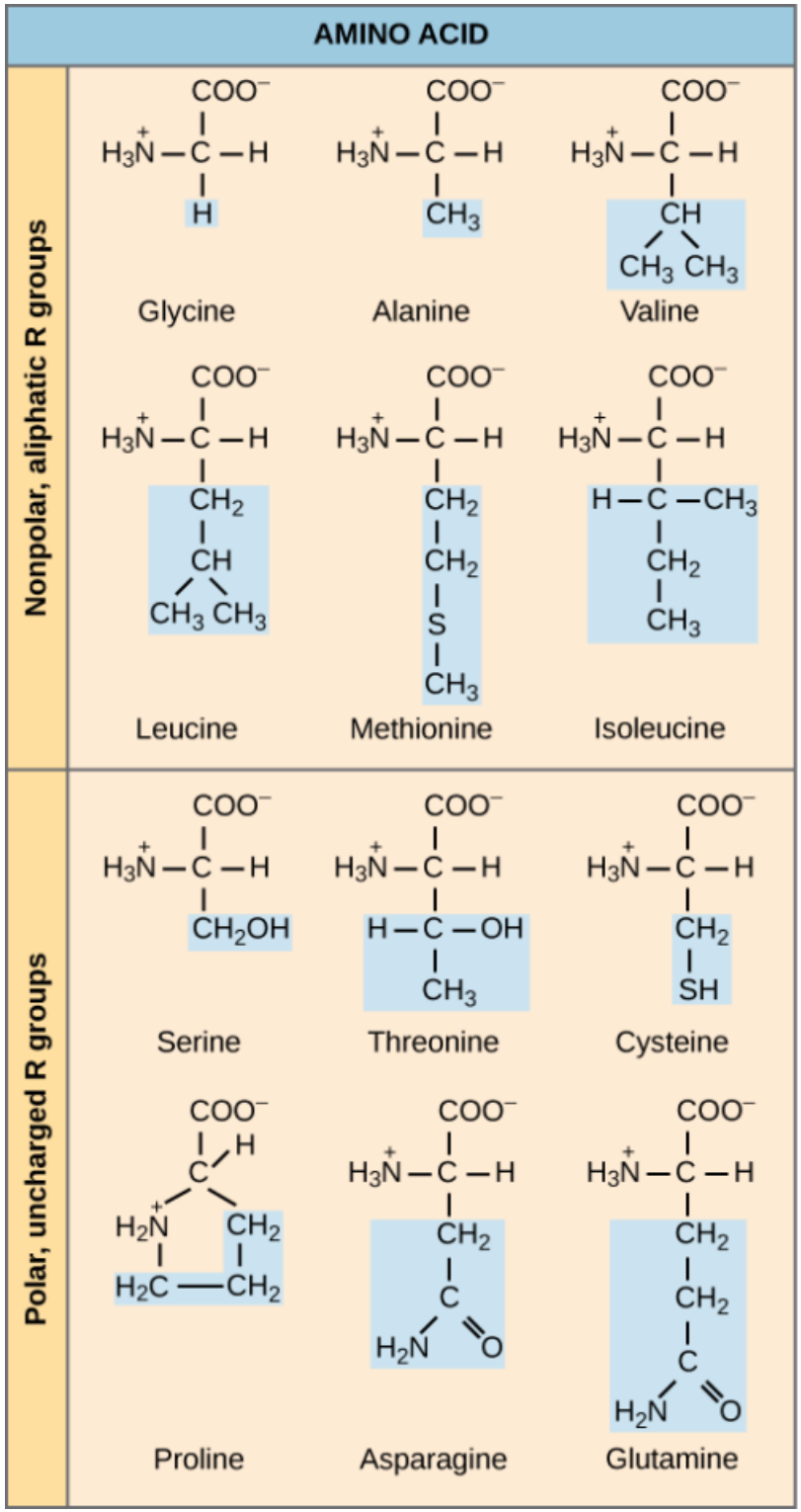
PRIMARY STRUCTURE

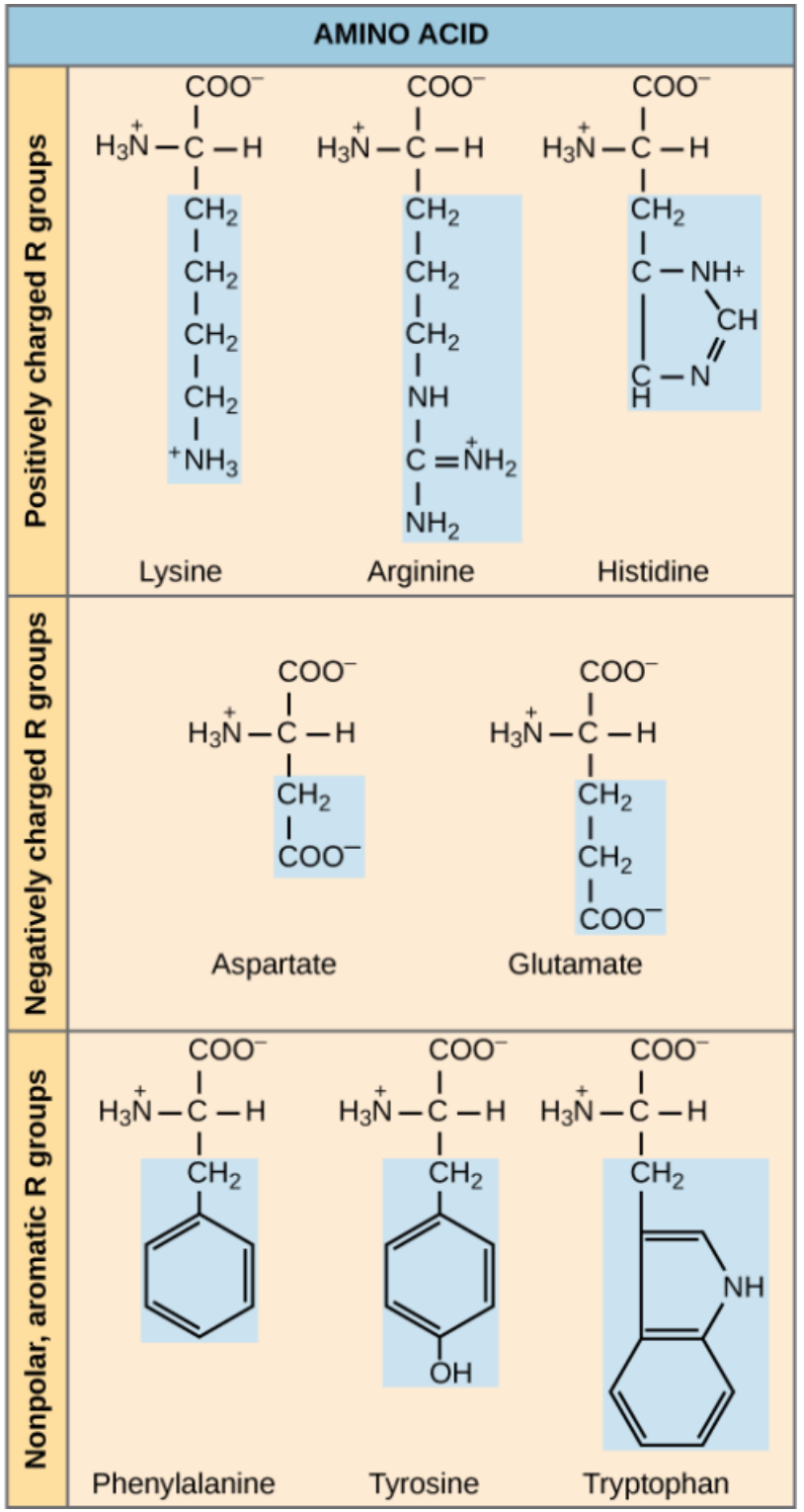
AMINO ACID			SIDE CHAIN
Aspartic acid	Asp	D	negative
Glutamic acid	Glu	E	negative
Arginine	Arg	R	positive
Lysine	Lys	K	positive
Histidine	His	H	positive
Asparagine	Asn	N	uncharged polar
Glutamine	Gln	Q	uncharged polar
Serine	Ser	S	uncharged polar
Threonine	Thr	T	uncharged polar
Tyrosine	Tyr	Y	uncharged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


AMINO ACID
Nonpolar, aliphatic R groups
Glycine
Alanine
Valine
Leucine
Methionine
Isoleucine
Polar, uncharged R groups
Serine
Threonine
Cysteine
Proline
Asparagine
Glutamine


AMINO ACID
Positively charged R groups
Lysine
Arginine
Histidine
Negatively charged R groups
Aspartate
Glutamate
Nonpolar, aromatic R groups
Phenylalanine
Tyrosine
Tryptophan

A peptide bond

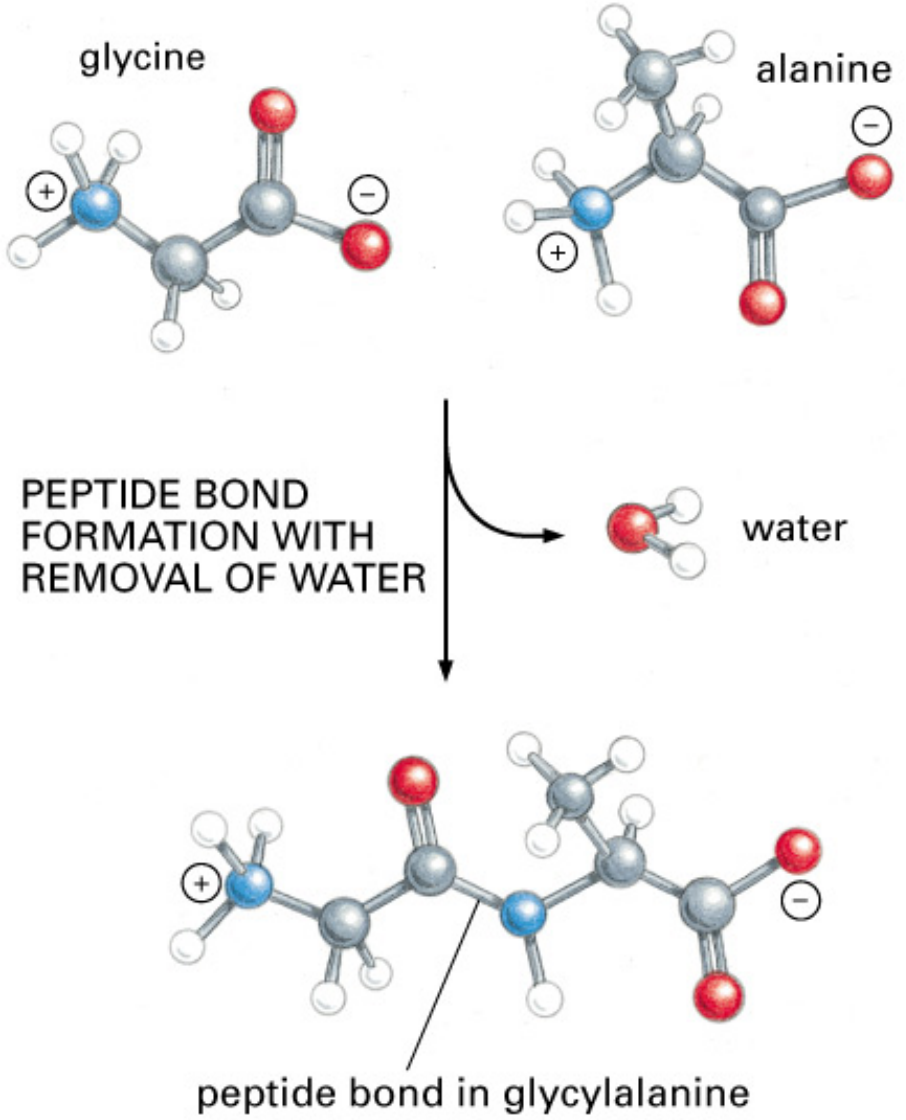


Figure 3–1. Molecular Biology of the Cell, 4th Edition.

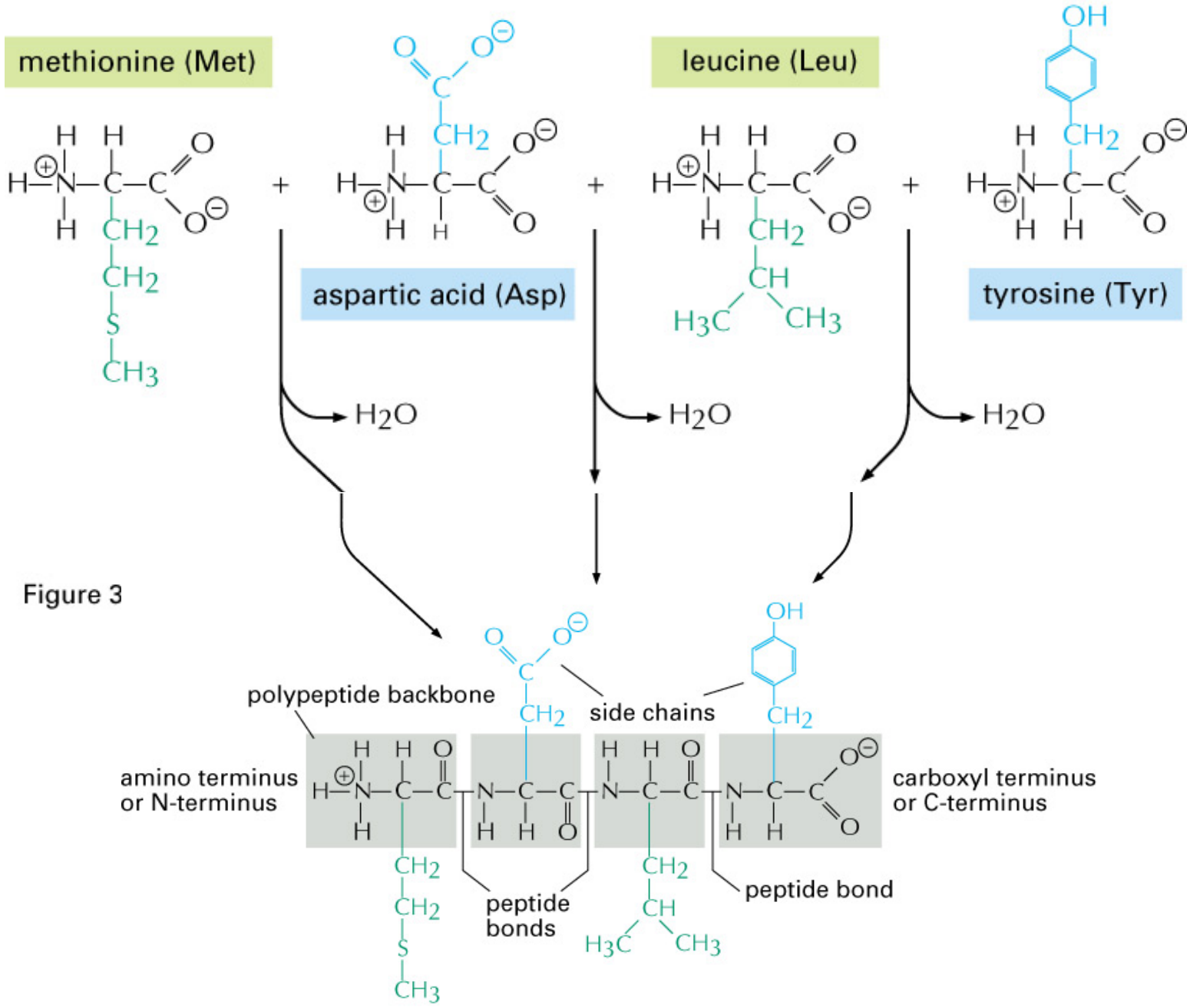


Figure 3

Figure 3–2 part 2 of 3. Molecular Biology of the Cell, 4th Edition.

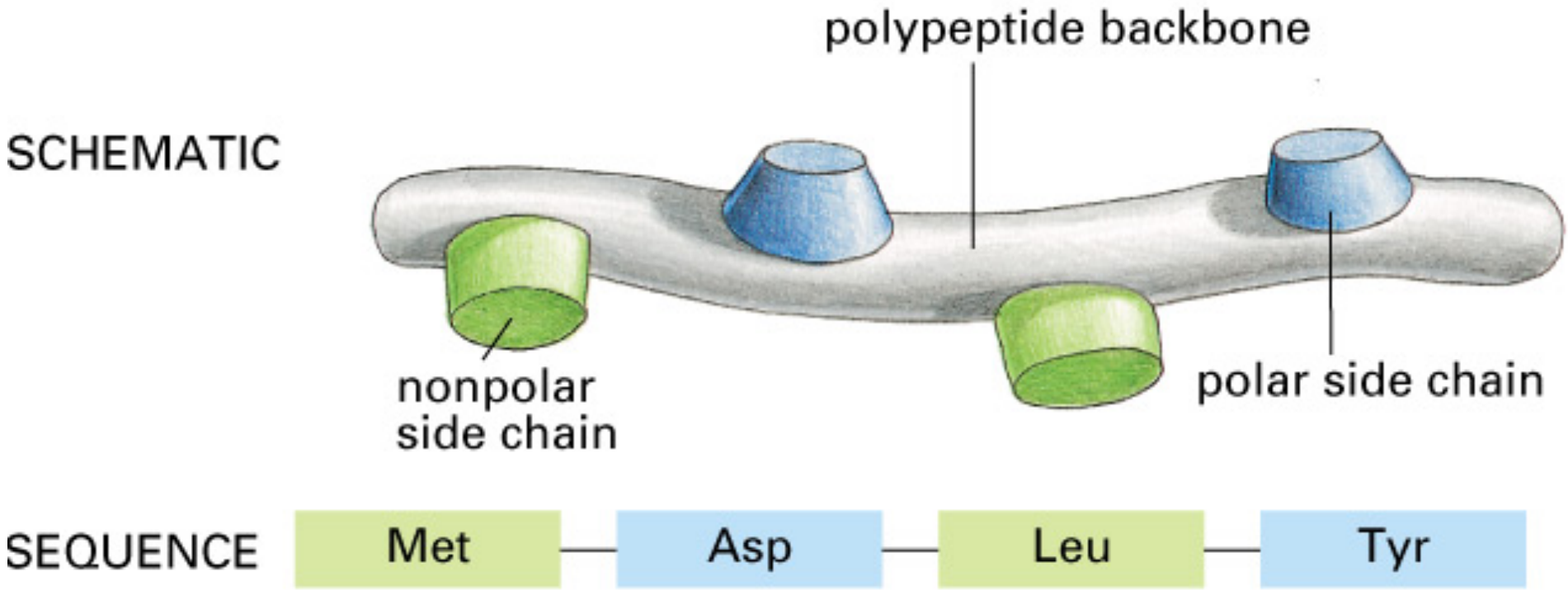
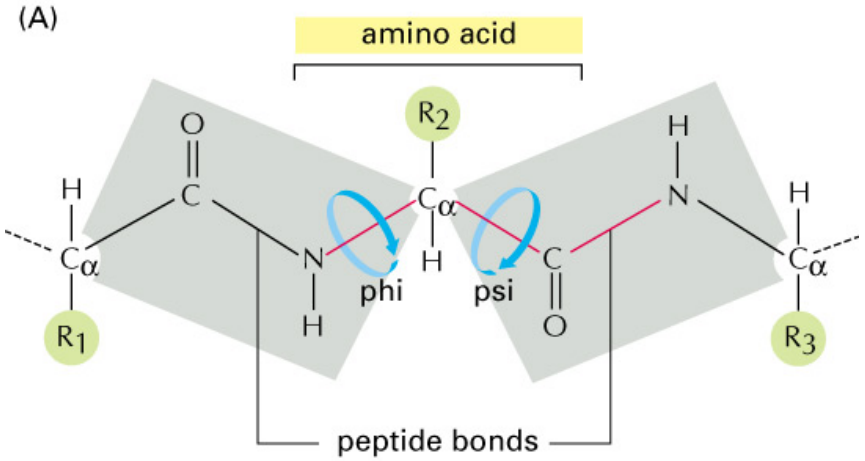


Figure 3–2 part 3 of 3. Molecular Biology of the Cell, 4th Edition.

The requirement that no two atoms overlap limits greatly the possible bond angles in a polypeptide chain



Each amino acid contributes three bonds (red) to the backbone of the chain. The peptide bond is planar (gray shading) and does not permit rotation. Rotation can occur about the Cα-C bond, whose angle of rotation is called psi (ψ), and about the N-Cα bond, whose angle of rotation is called phi (ϕ)

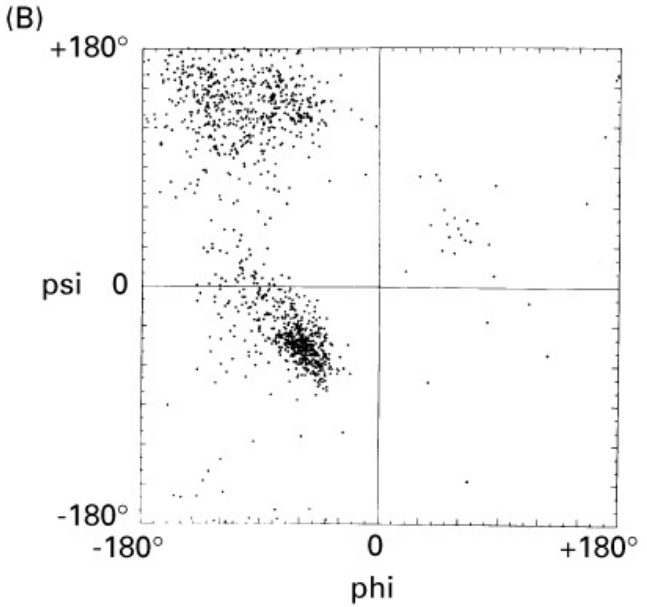
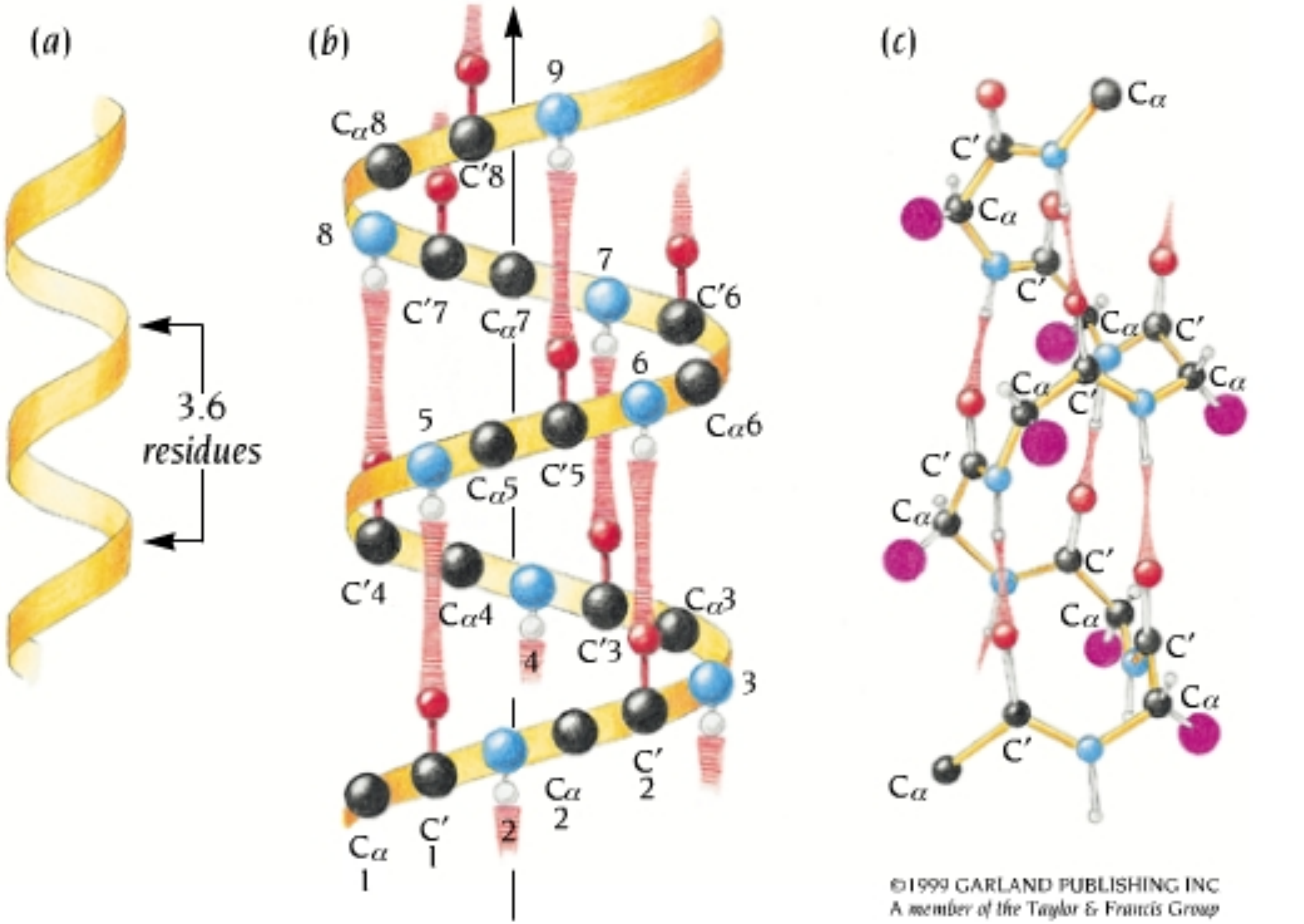


Figure 3–4. Molecular Biology of the Cell, 4th Edition.

The conformation of the main-chain atoms in a protein is determined by one pair of ϕ and ψ angles for each acid. Because of steric collisions between atoms within each amino acid, most pairs of ϕ and ψ angles do not occur. Each dot, in the Ramachandran plot shown here, represents an observed pair of angles in a protein. In α-helices, the backbone dihedral angles, ϕ and ψ have repeating values of -60°and -40° respectively.

SECONDARY STRUCTURE



The α helix is one of the major elements of secondary structure in proteins.

Main-chain N and O atoms are hydrogen-bonded to each other within α helices. (a) Idealized diagram of the path of the main chain in an α helix. Alpha helices are frequently illustrated in this way. There are 3.6 residues per turn in an α helix, which corresponds to 5.4 angstrom (1.5 angstrom per residue). (b) The same as (a) but with approximate positions for main-chain atoms and hydrogen bonds included. The arrow denotes the direction from the N-terminus to the C-terminus. (c) Schematic diagram of an α helix. Oxygen atoms are red, and N atoms are blue. Hydrogen bonds between O and N are red and striated. The side chains are represented as purple circles.

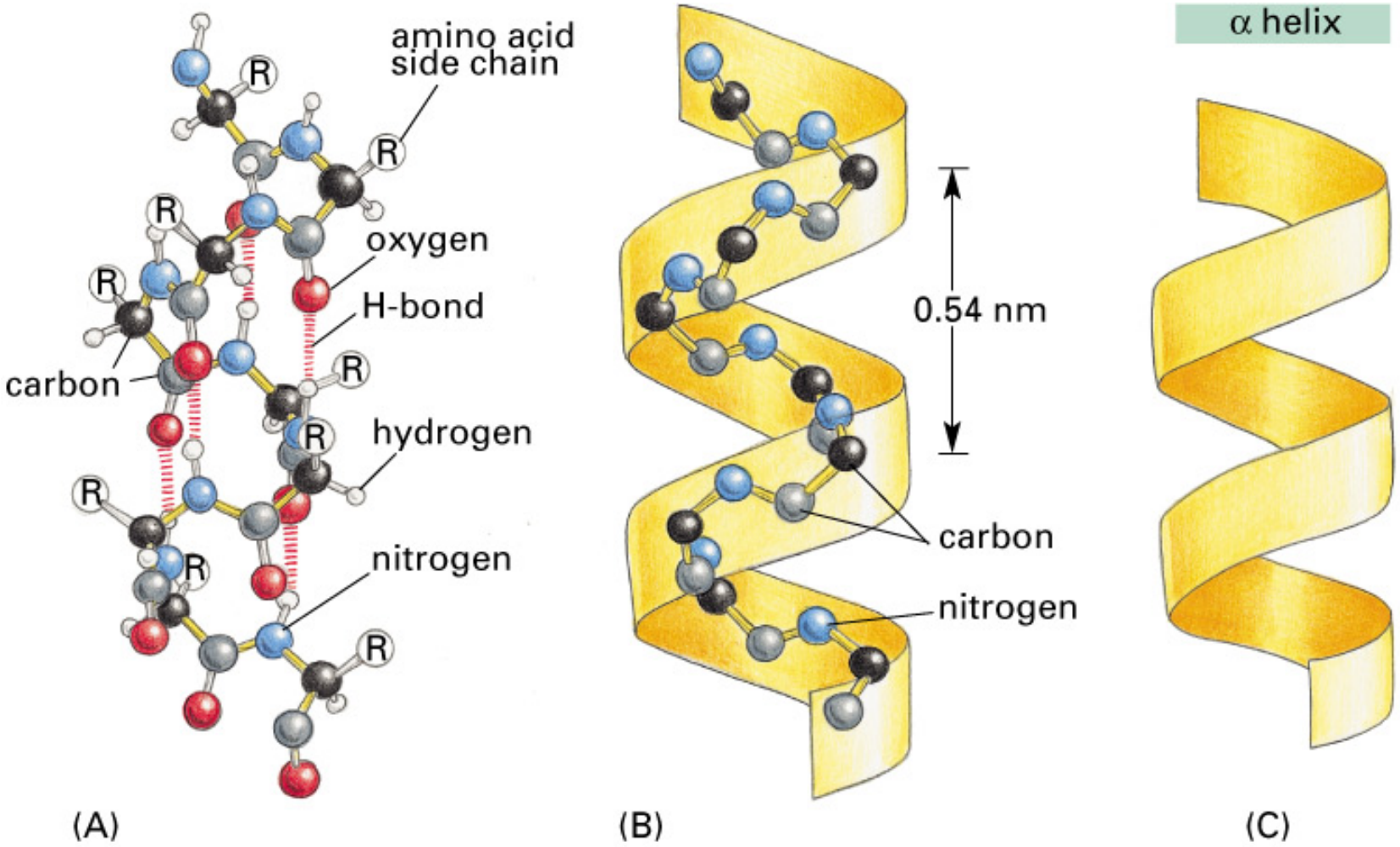


Figure 3–9 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

The α-helix. The NH of every peptide bond is hydrogen-bonded to the CO of a neighboring peptide bond located four peptide bonds away in the same chain

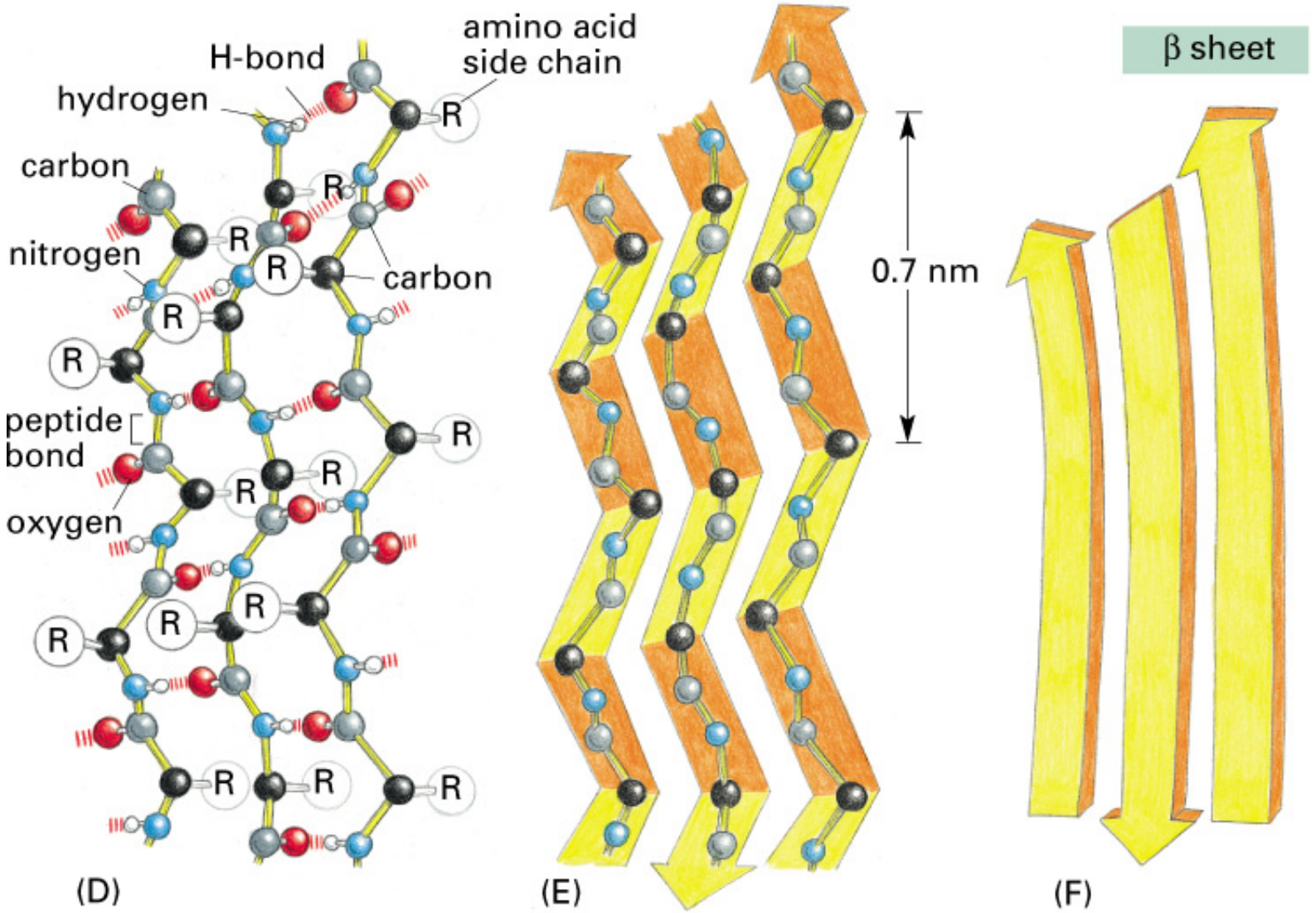


Figure 3–9 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

The b-sheet. The individual peptide chains (strands) in a b-sheet are held together by hydrogen-bonding between peptide bonds in different strands

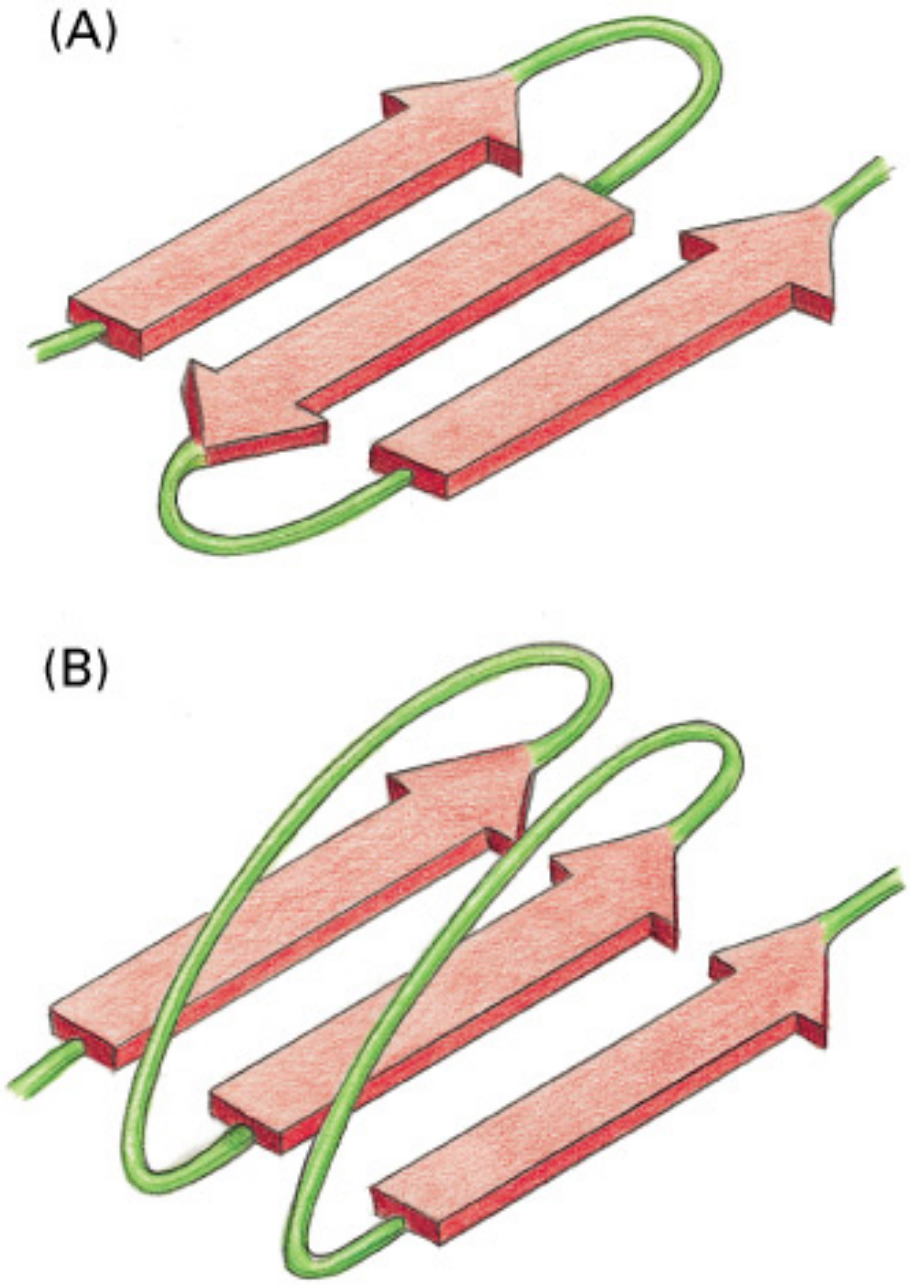


Figure 3–10. Molecular Biology of the Cell, 4th Edition.

TERTIARY STRUCTURE

Proteins fold into a conformation of lowest energy

Three types of noncovalent bonds that help proteins fold

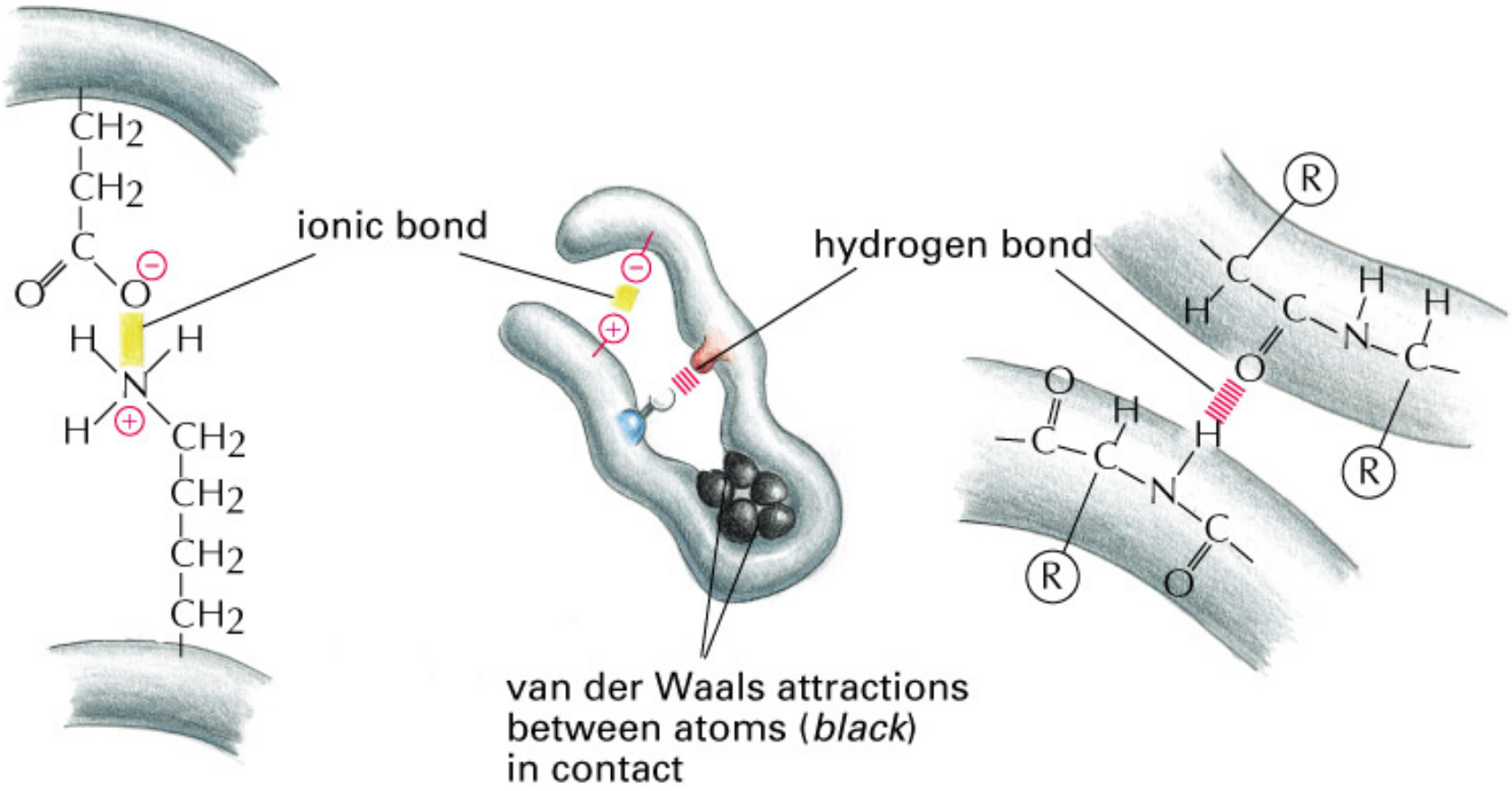


Figure 3–5. Molecular Biology of the Cell, 4th Edition.

A protein folds into a compact conformation

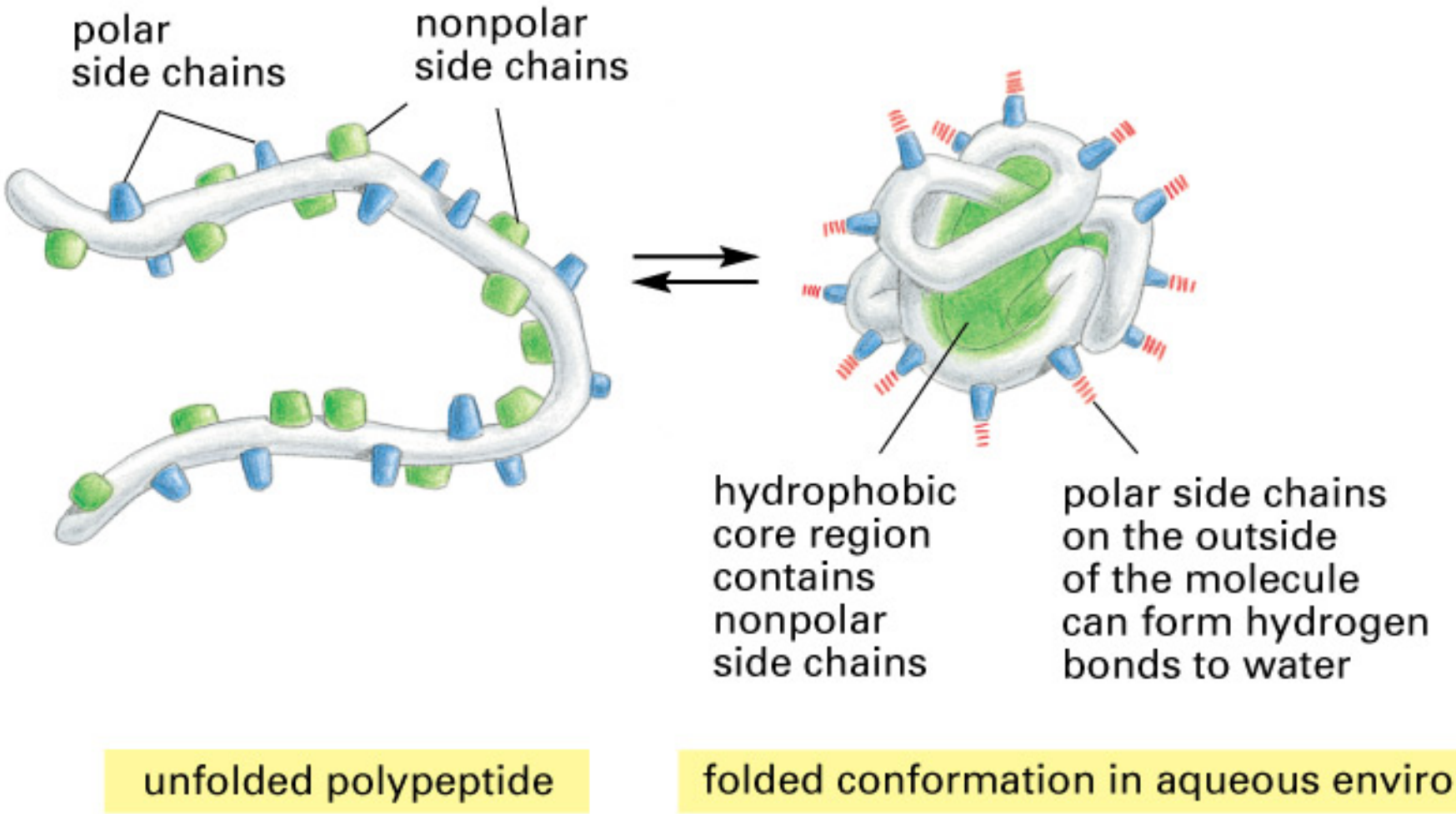


Figure 3–6. Molecular Biology of the Cell, 4th Edition.

Hydrogen bonds in a protein molecule

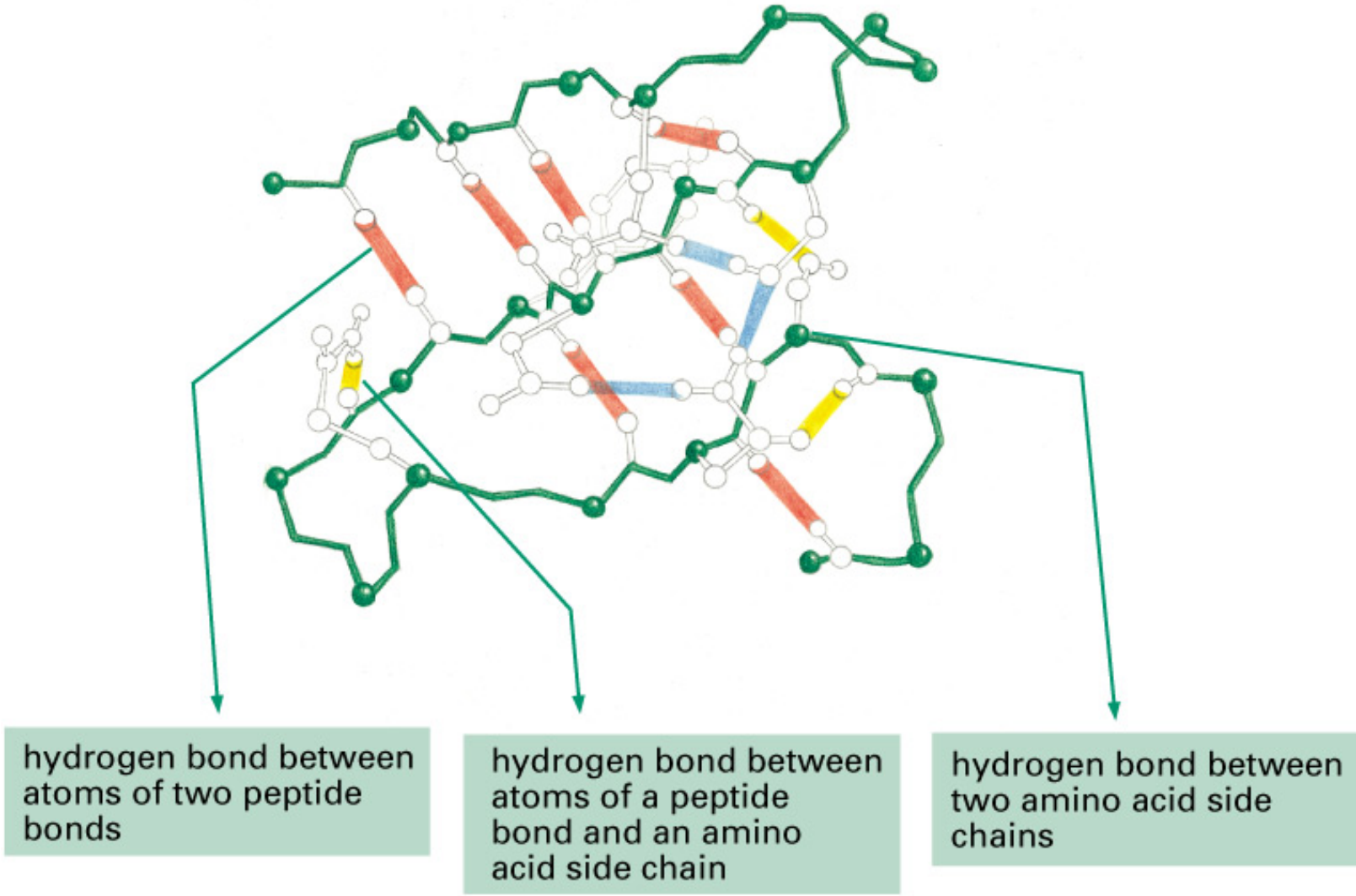


Figure 3–7. Molecular Biology of the Cell, 4th Edition.

A protein domain is a fundamental unit of organization

domains - structural units that fold more or less independently of each other

The Src protein

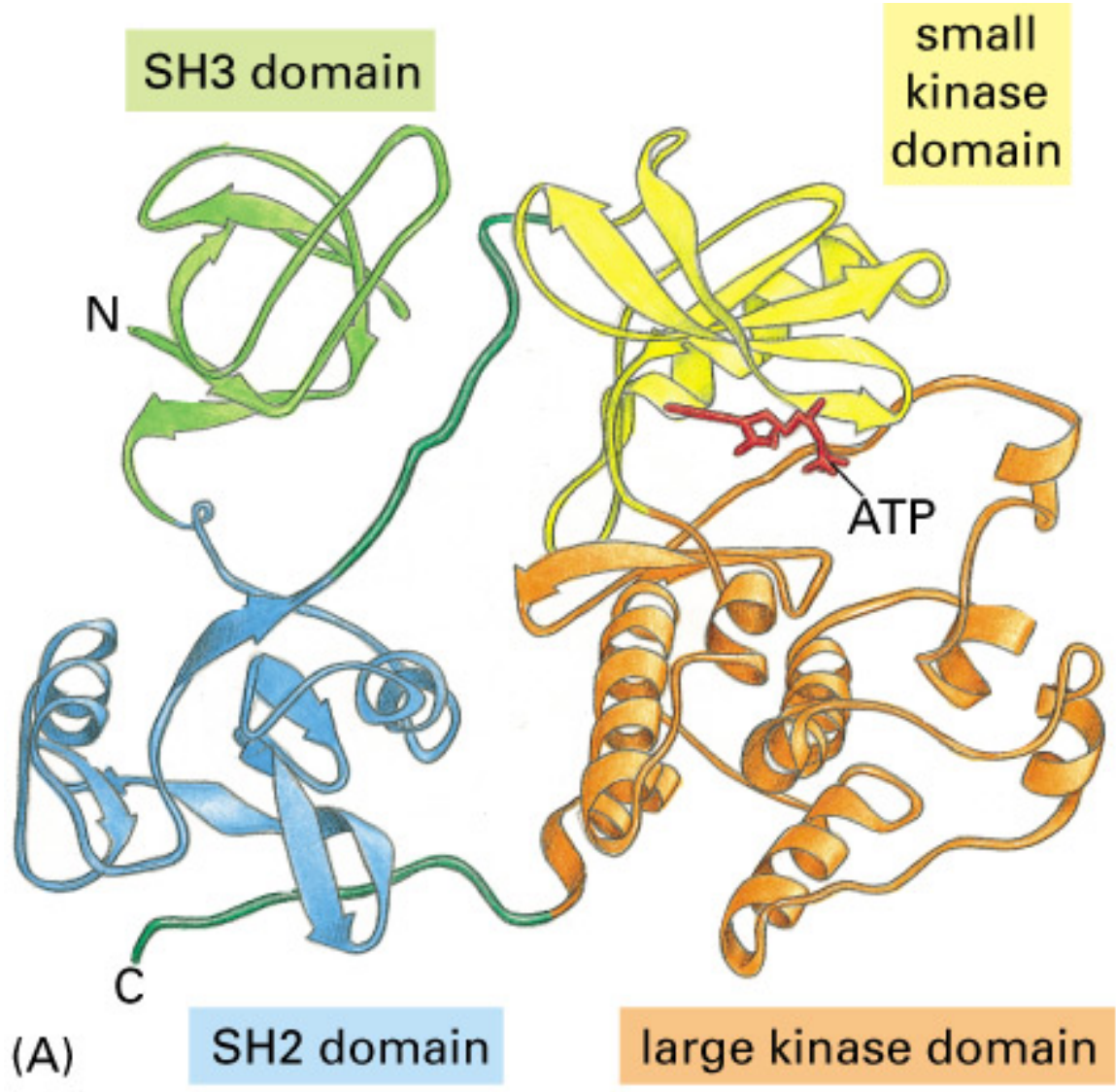
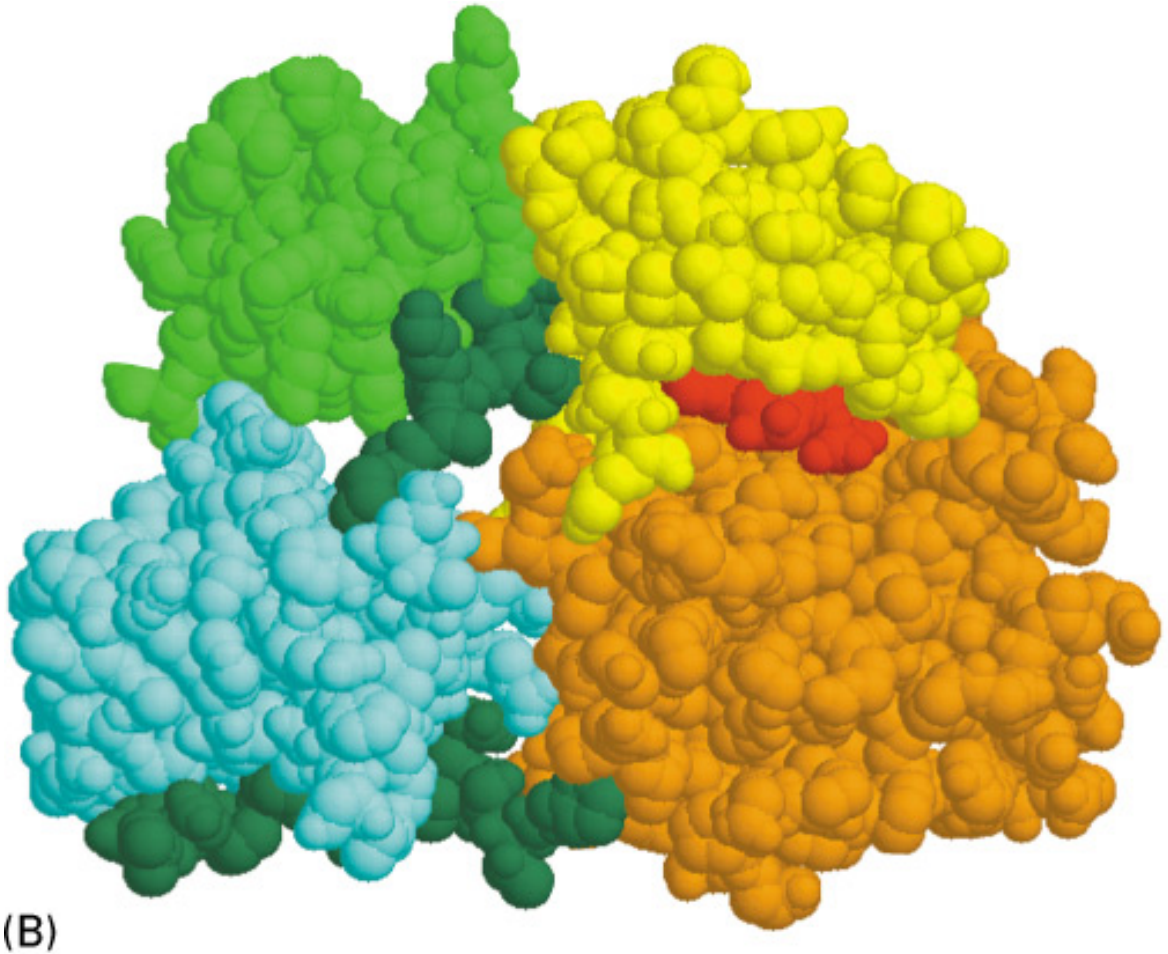


Figure 3–12 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

The Src protein



(B)

Figure 3–12 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

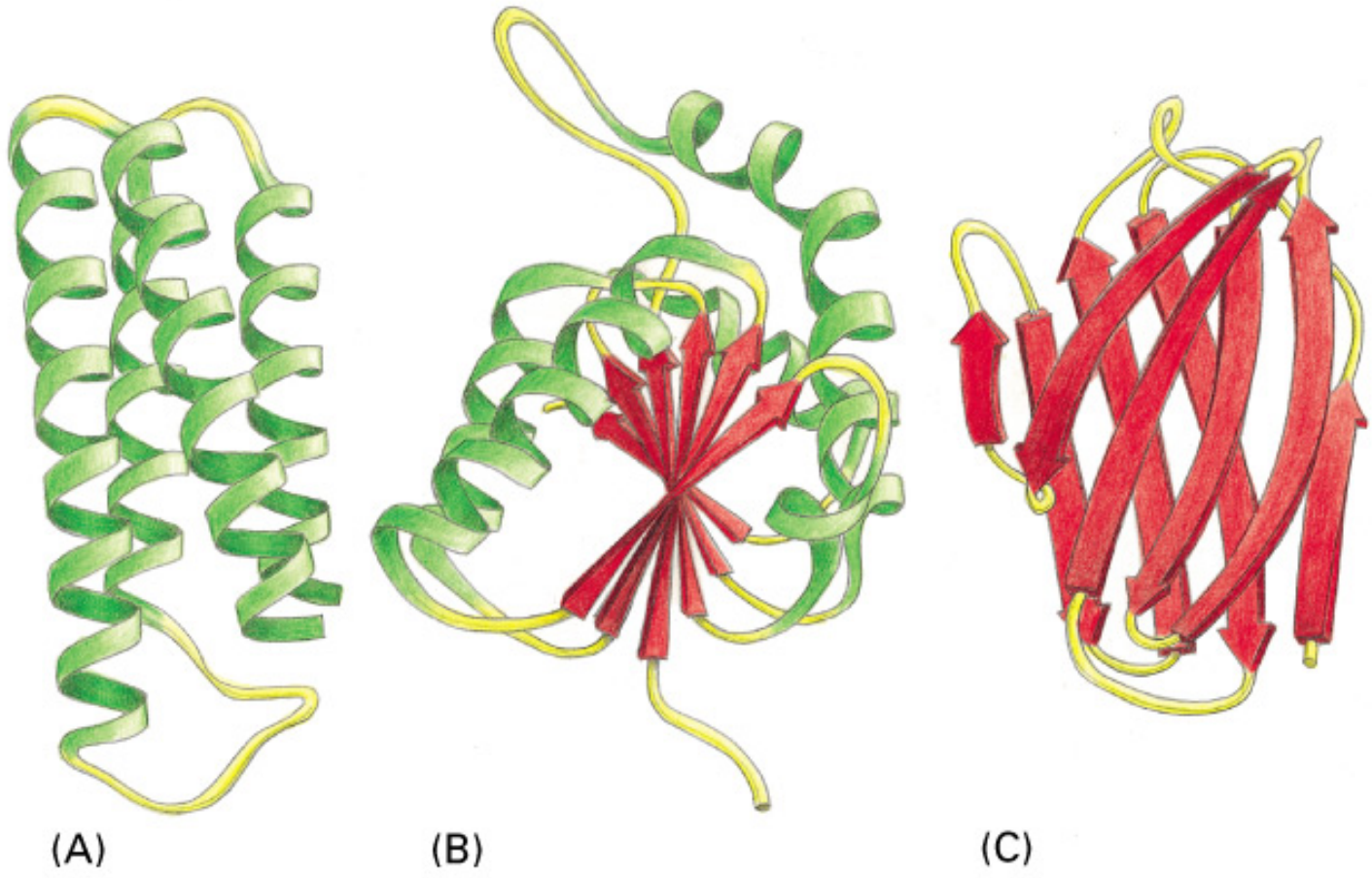


Figure 3–13. Molecular Biology of the Cell, 4th Edition.

Ribbon models of three different protein domains

PROTEIN FOLDING

How does a protein chain achieves its native conformation?

As an example, E. coli cells can make a complete, biologically active protein containing 100 amino acids in about 5 sec at 37°C.

If we assume that each of the amino acid residues could take up 10 different conformations on average, there will be 10^{100} different conformations for this polypeptide.

If the protein folds spontaneously by a random process in which it tries all possible conformations before reaching its native state, and each conformation is sampled in the shortest possible time (~10^{-13} sec), it would take about 10^{77} years to sample all possible conformations.

There are two possible models to explain protein folding:

In the first model, the folding process is viewed as hierarchical, in which secondary structures form first, followed by longer-range interactions to form stable supersecondary structures. The process continues until complete folding is achieved.

In the second model, folding is initiated by a spontaneous collapse of the polypeptide into a compact state, mediated by hydrophobic interactions among non-polar residues. The collapsed state is often referred to as the 'molten globule' and it may have a high content of secondary structures.

Most proteins fold by a process that incorporates features of both models.

Molecular chaperones help guide the folding of many proteins

A current view of protein folding

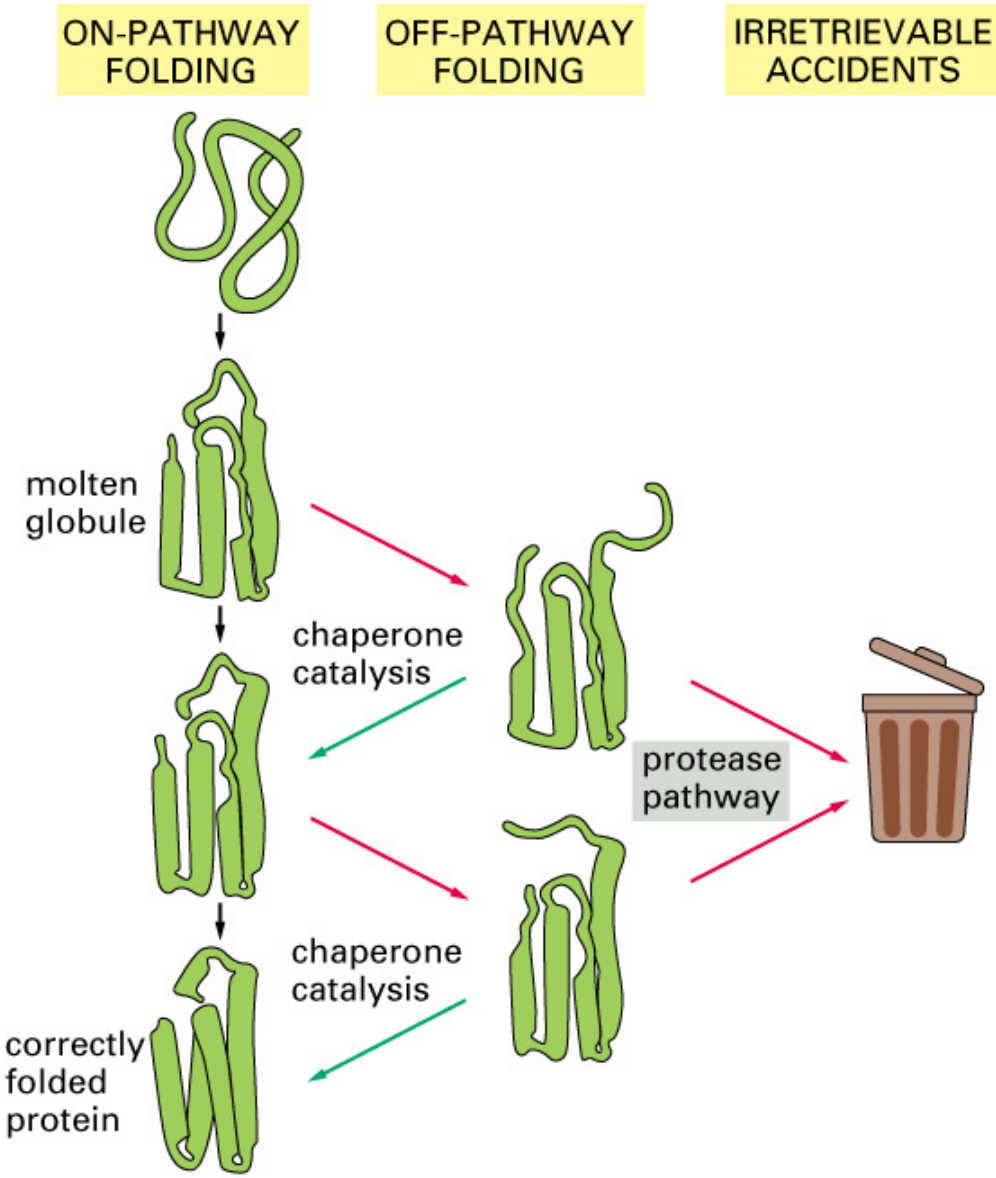


Figure 6–82. Molecular Biology of the Cell, 4th Edition.

Processive protein digestion by the proteasome

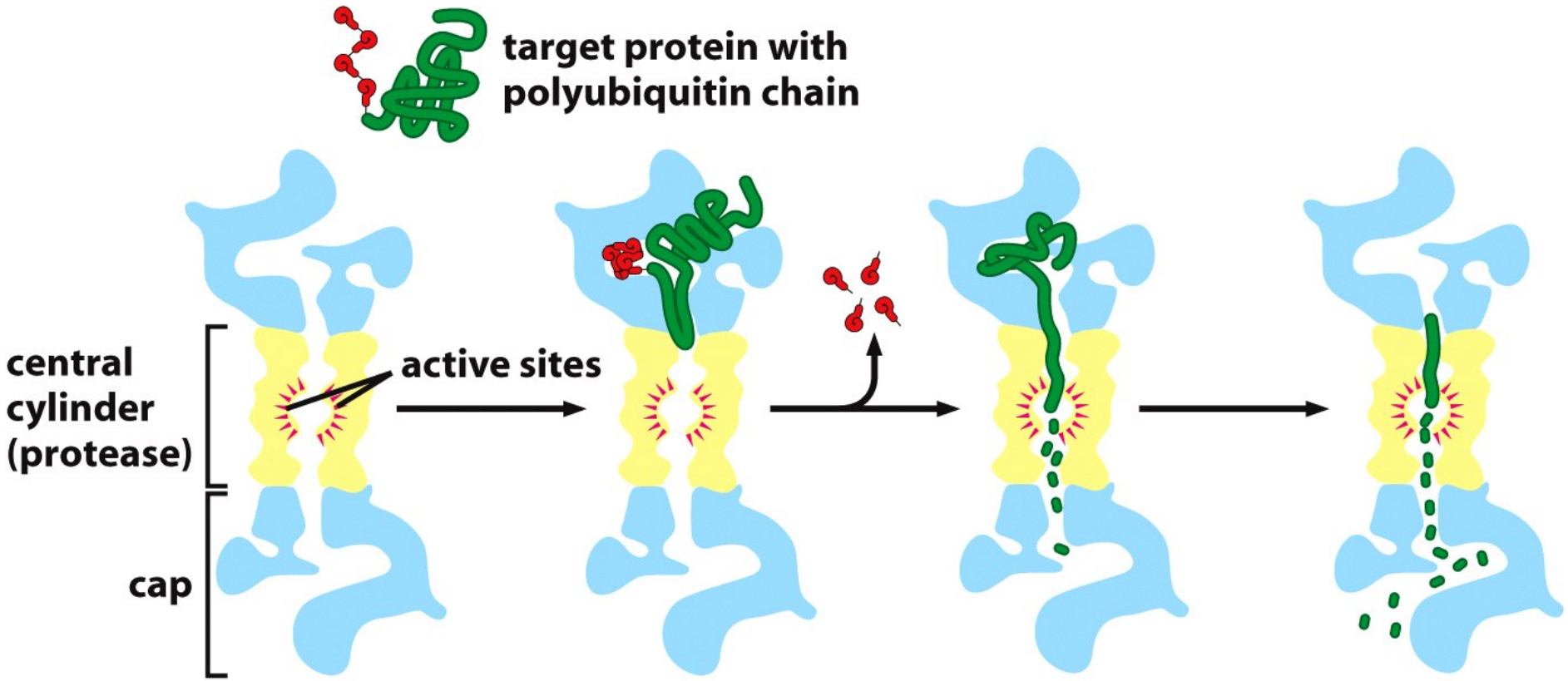


Figure 6-90 *Molecular Biology of the Cell* (© Garland Science 2008)

Sequence homology searches can identify close relatives

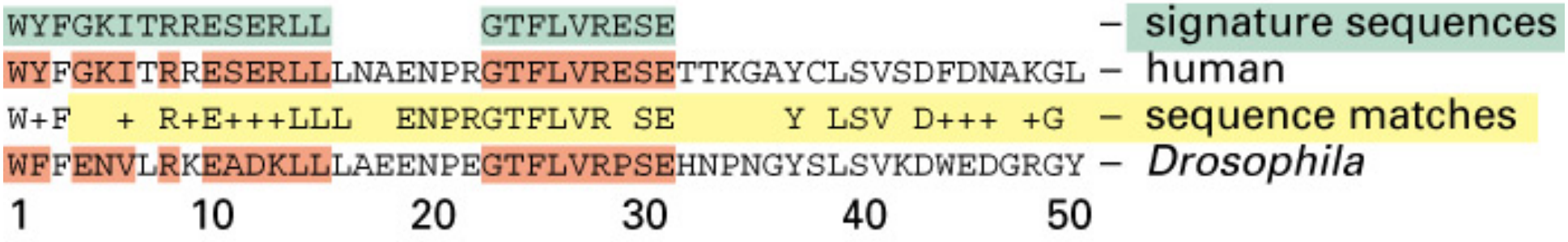


Figure 3–17. Molecular Biology of the Cell, 4th Edition.

The first 50 amino acids of the SH2 domain of 100 amino acids compared for the human and *Drosophila* Src protein

Multiple domains and domain shuffling in proteins

Quaternary structure

Larger protein molecules often contain more than one polypeptide chain

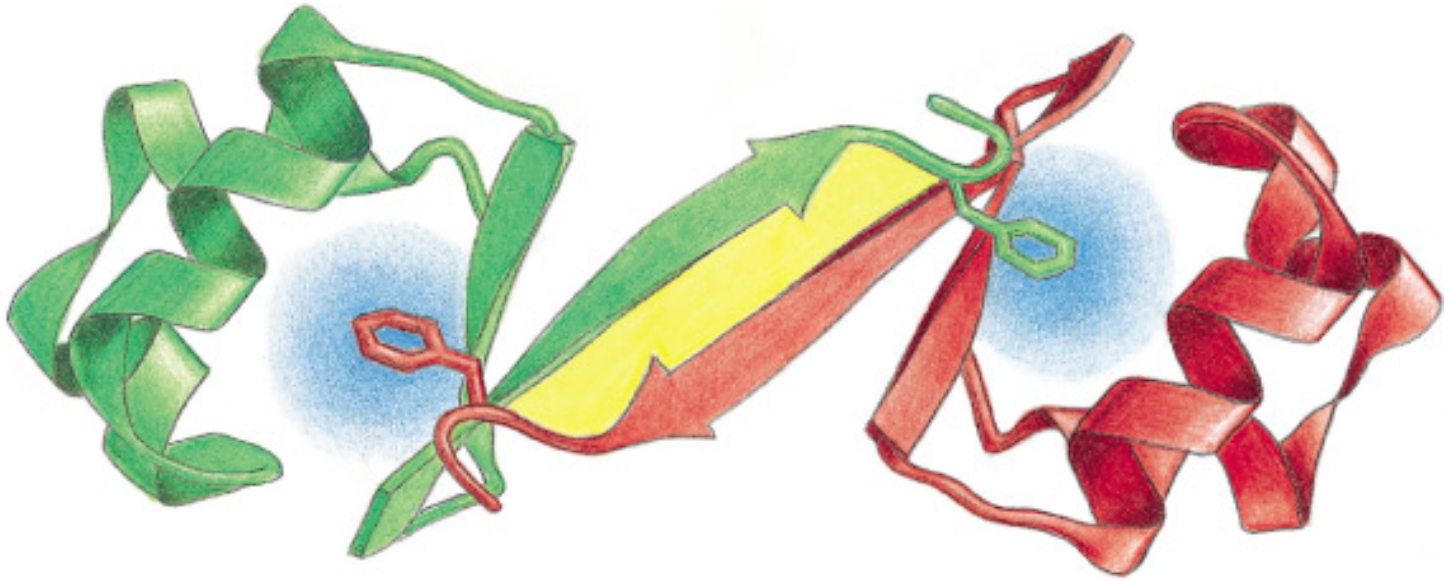


Figure 3–21. Molecular Biology of the Cell, 4th Edition.

Lambda cro repressor showing "head-to-head" arrangement of identical subunits

DNA-binding site for the Cro dimer

ATCGCGAT
TAGCGCTA

The “head-to-tail” arrangement of four identical subunits that form a closed ring in neuraminidase

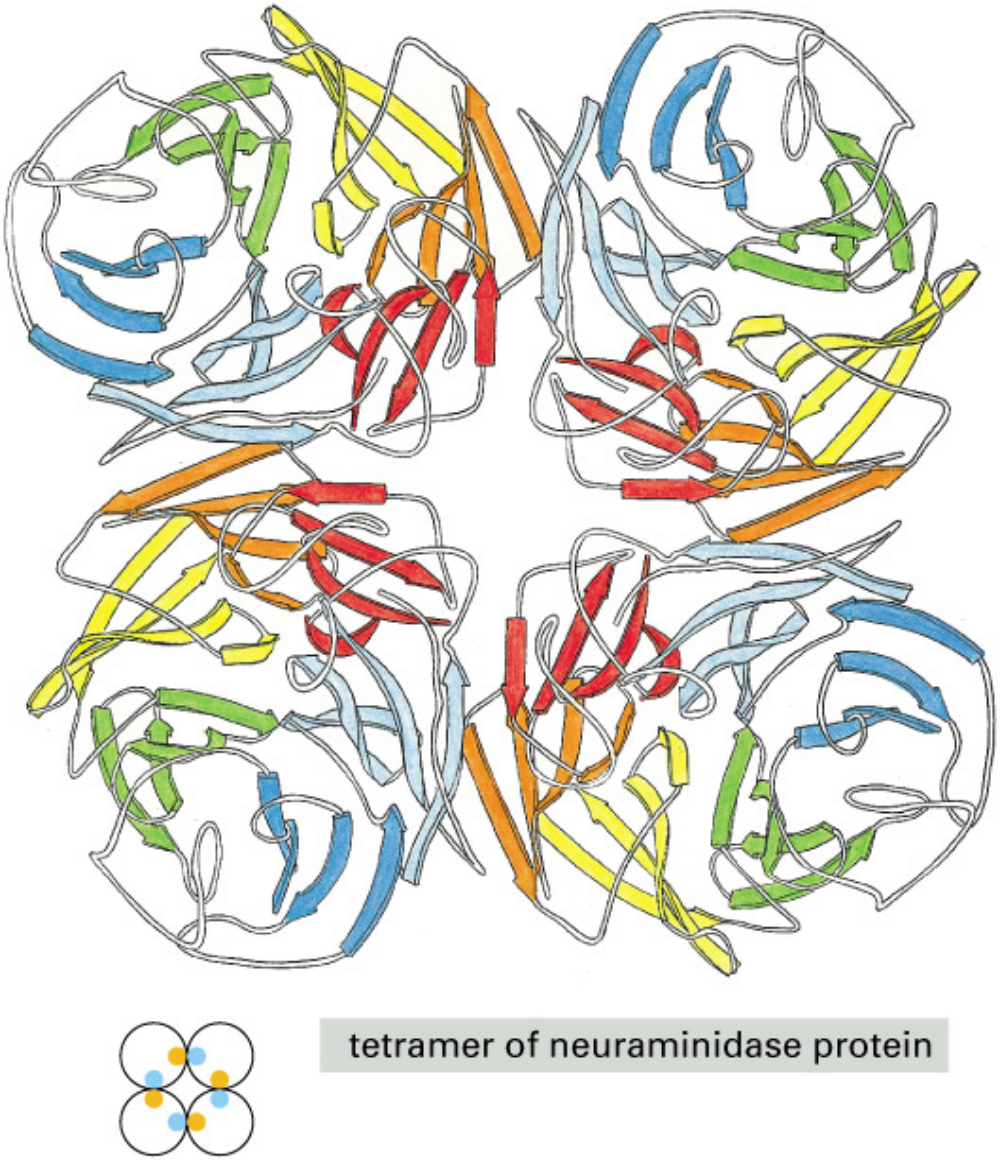


Figure 3–22. Molecular Biology of the Cell, 4th Edition.

HEMOGLOBIN

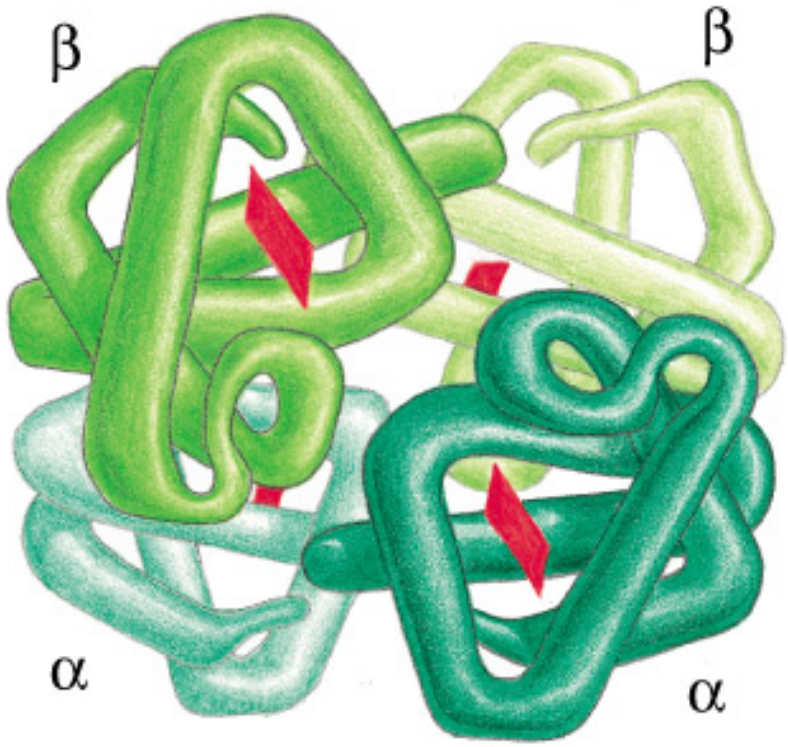


Figure 3–23. Molecular Biology of the Cell, 4th Edition.

A symmetric assembly of two different subunits

A collection of protein molecules, shown at the same scale

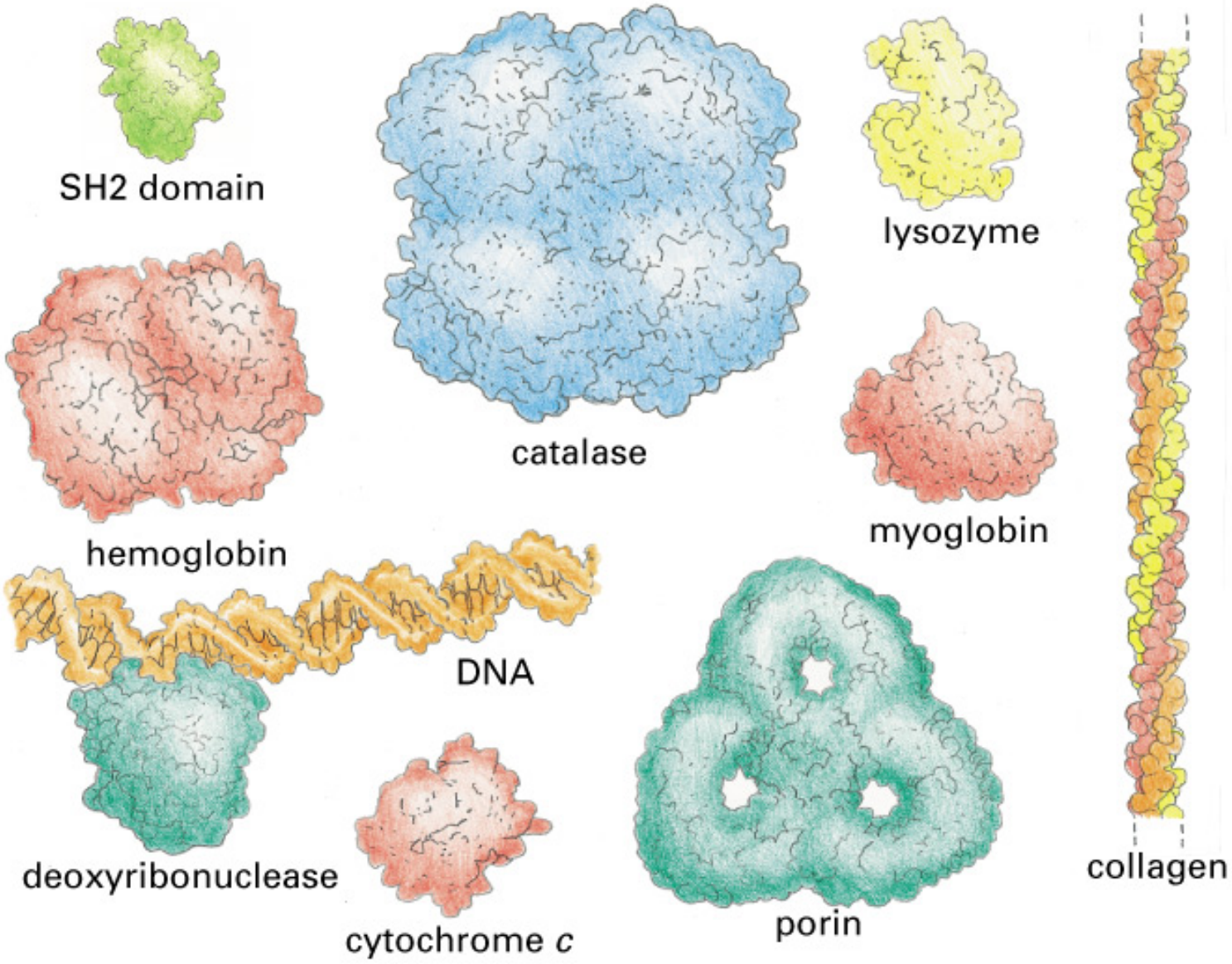


Figure 3–24 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

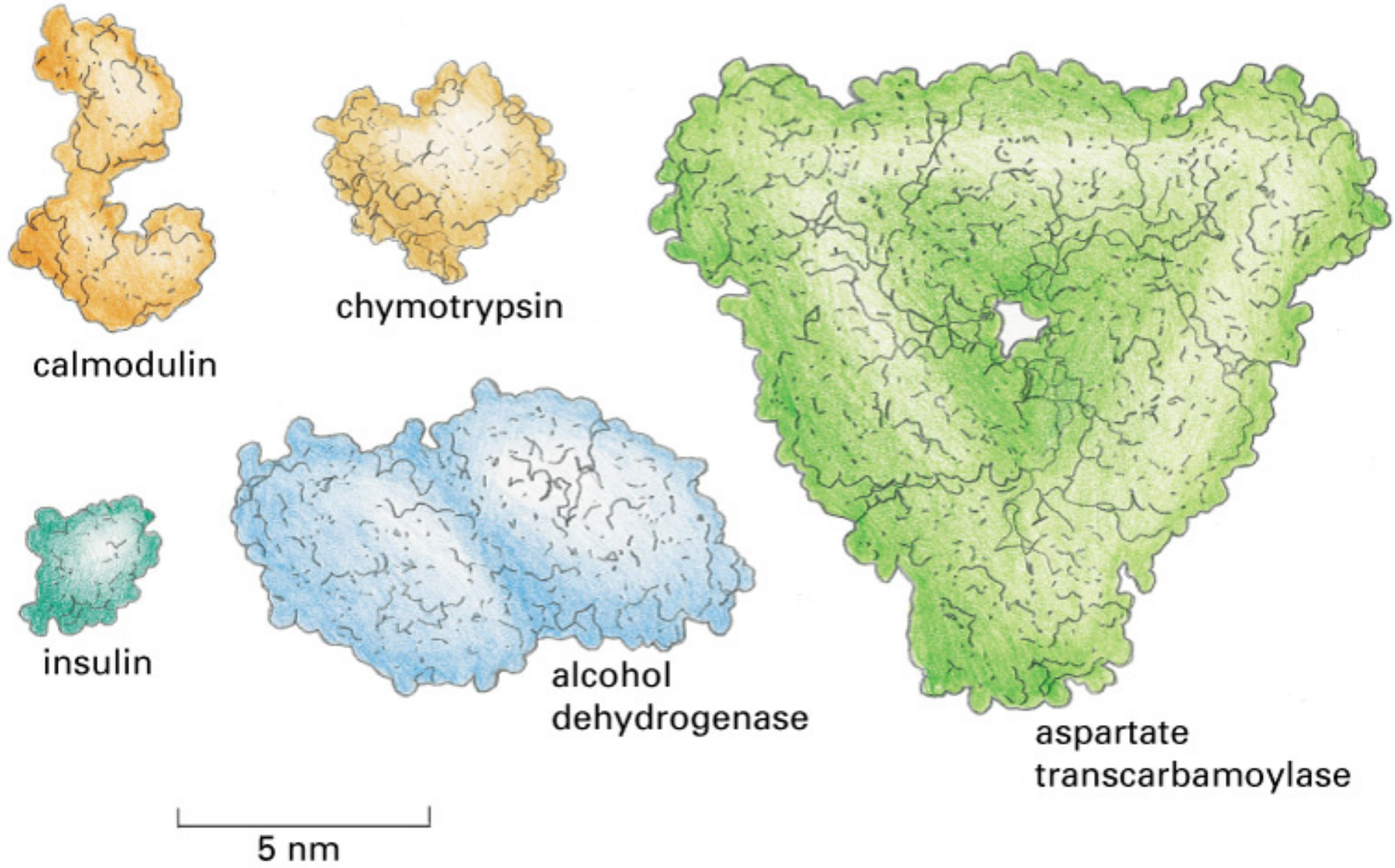


Figure 3–24 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Some proteins form long helical filaments

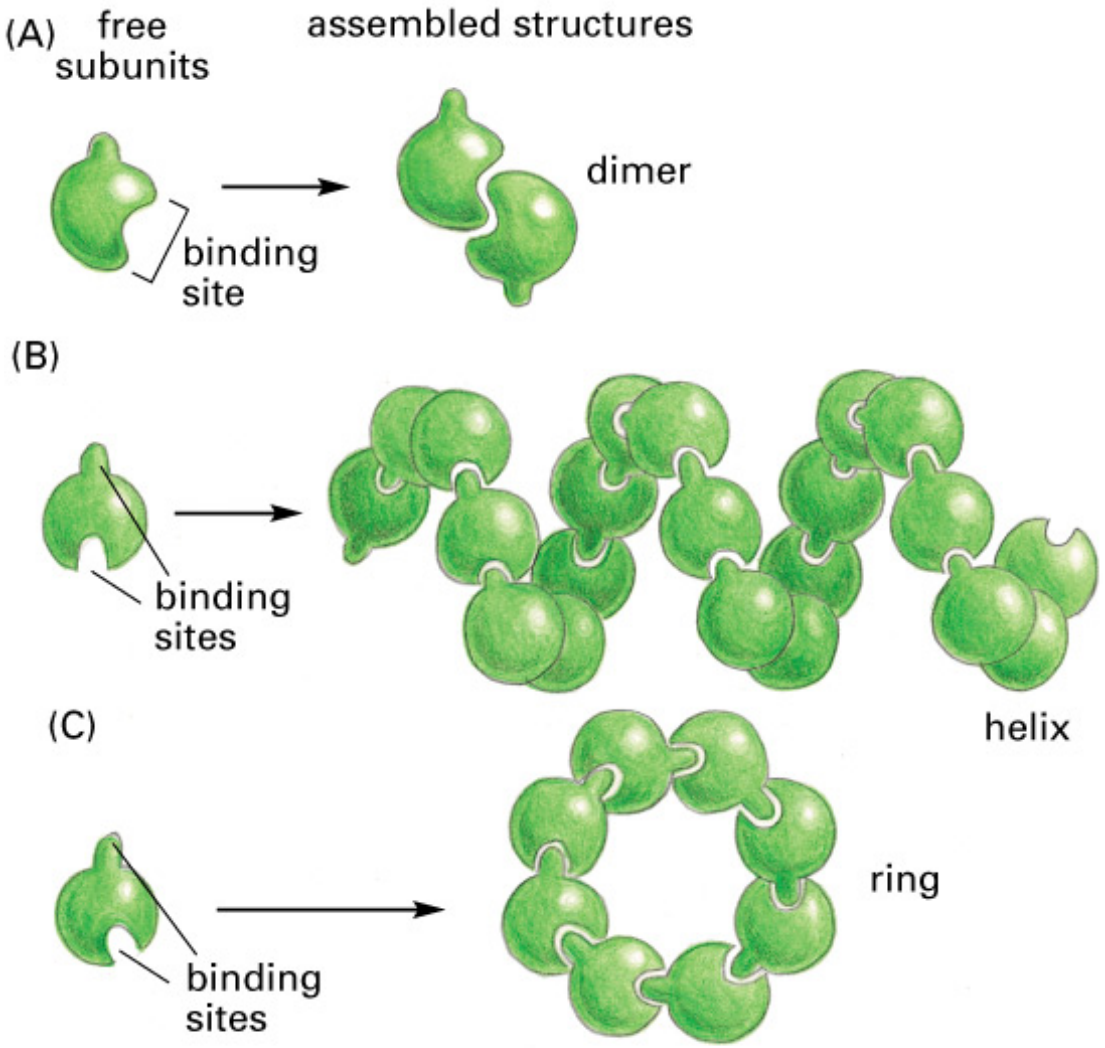


Figure 3–25. Molecular Biology of the Cell, 4th Edition.

Protein Assemblies

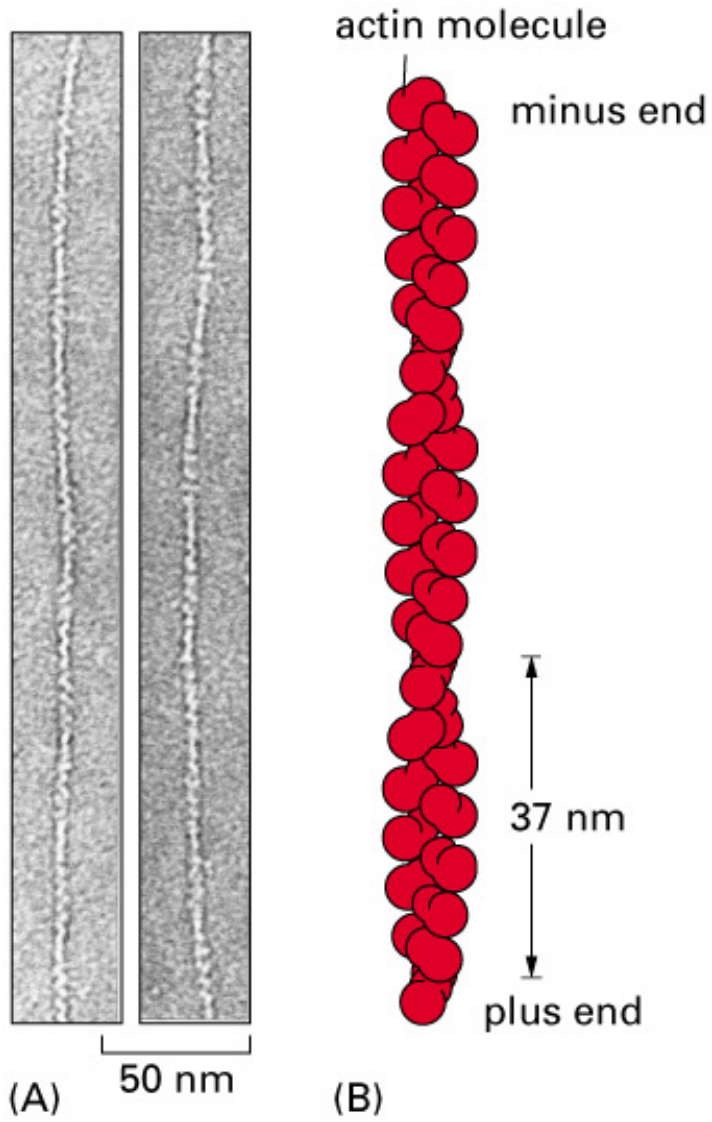


Figure 3–26. Molecular Biology of the Cell, 4th Edition.

Helical arrangement of actin molecules in an actin filament

Extracellular proteins are often stabilized by covalent cross-linkages

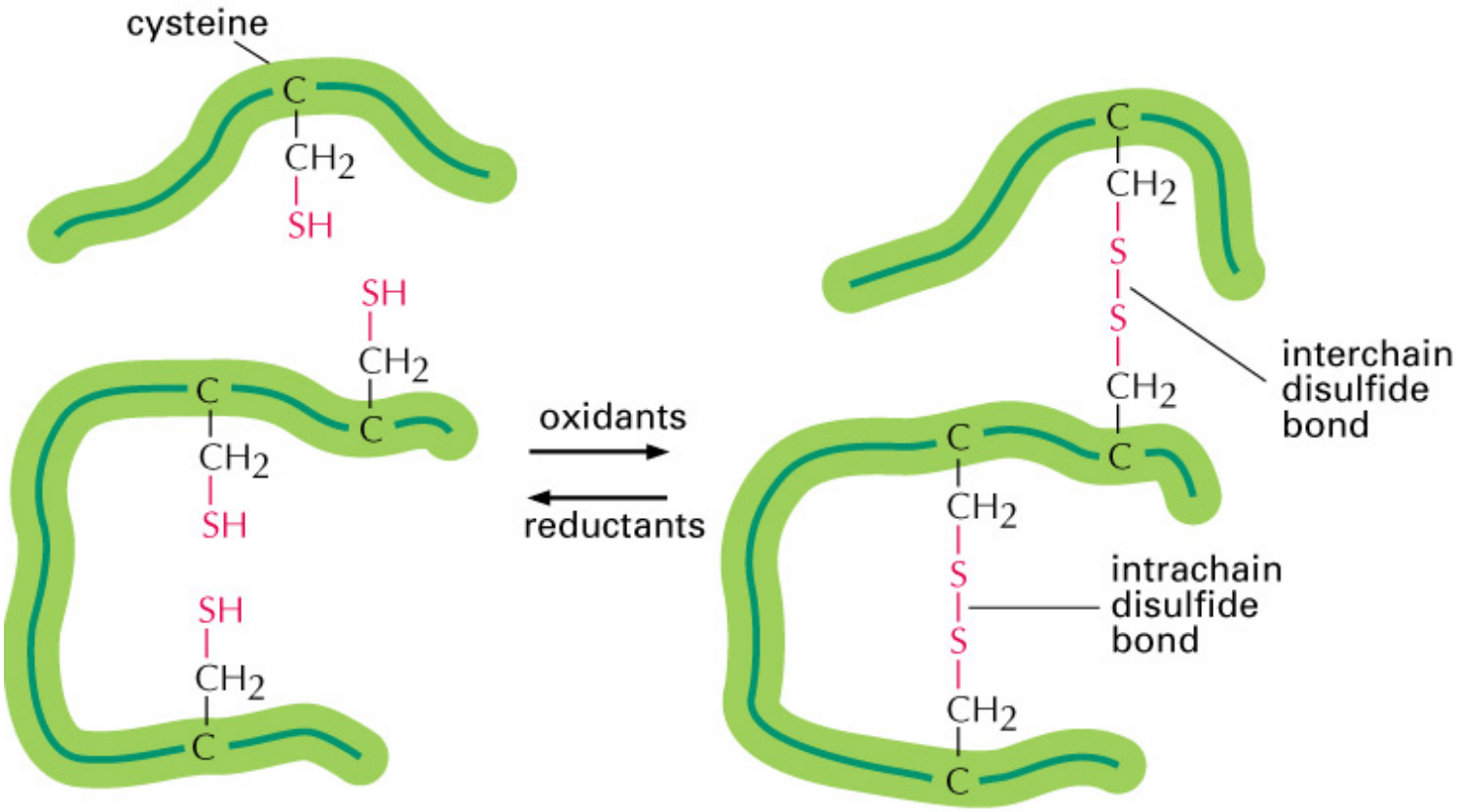


Figure 3–29. Molecular Biology of the Cell, 4th Edition.

Disulfide bonds

Proteolytic cleavage in insulin assembly

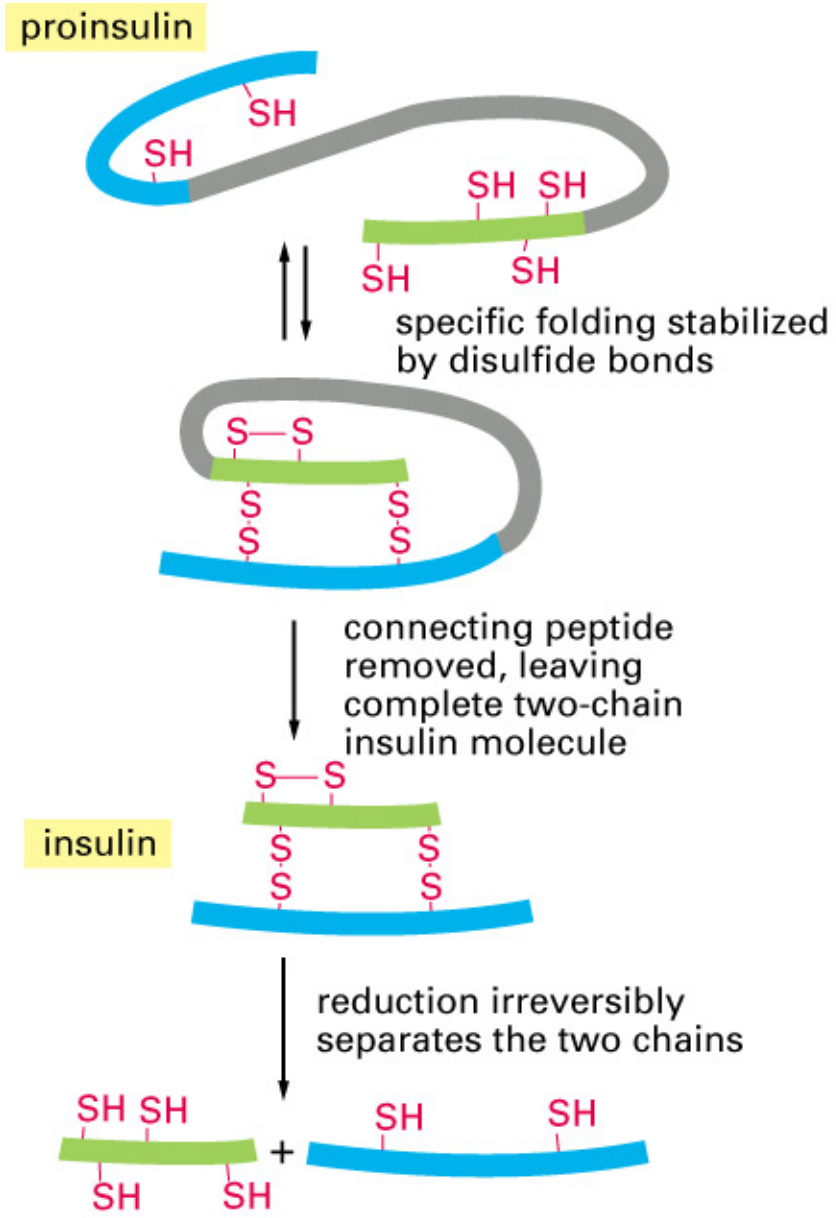


Figure 3–36. Molecular Biology of the Cell, 4th Edition.