Protein : structure & function

Lecture 7

Chapter 4 (part 1)

Introduction

- Proteins are major components of all cellular systems
- Proteins consist of one or more linear polymers called polypeptides
- Proteins are linear and never branched
- Different AA's are linked together via PEPTIDE bonds
- The individual amino acids within a protein are known as RESIDUES
- The smallest known P' is just nine residues long - oxytocin
- The largest is over 25,000 residues - the structural protein titin

Introduction

- Proteins are generally between 100 and 1000 residues in length.
- In the absence of stabilizing forces a minimum of 40 residues is needed to adopt a stable 3D structure in water.
- Protein sequence can be determined by systematically removing the AA's one at a time from the amino end - Edman degradation
- Now we just sequence the gene or cDNA for that protein and use the genetic code to determine the AA sequence

Each amino acid has the same fundamental structure, differing only in the side-chain, designated the R-group. The carbon atom to which the amino group, carboxyl group, and side chain (R-group) are attached is the alpha carbon (Cα).

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

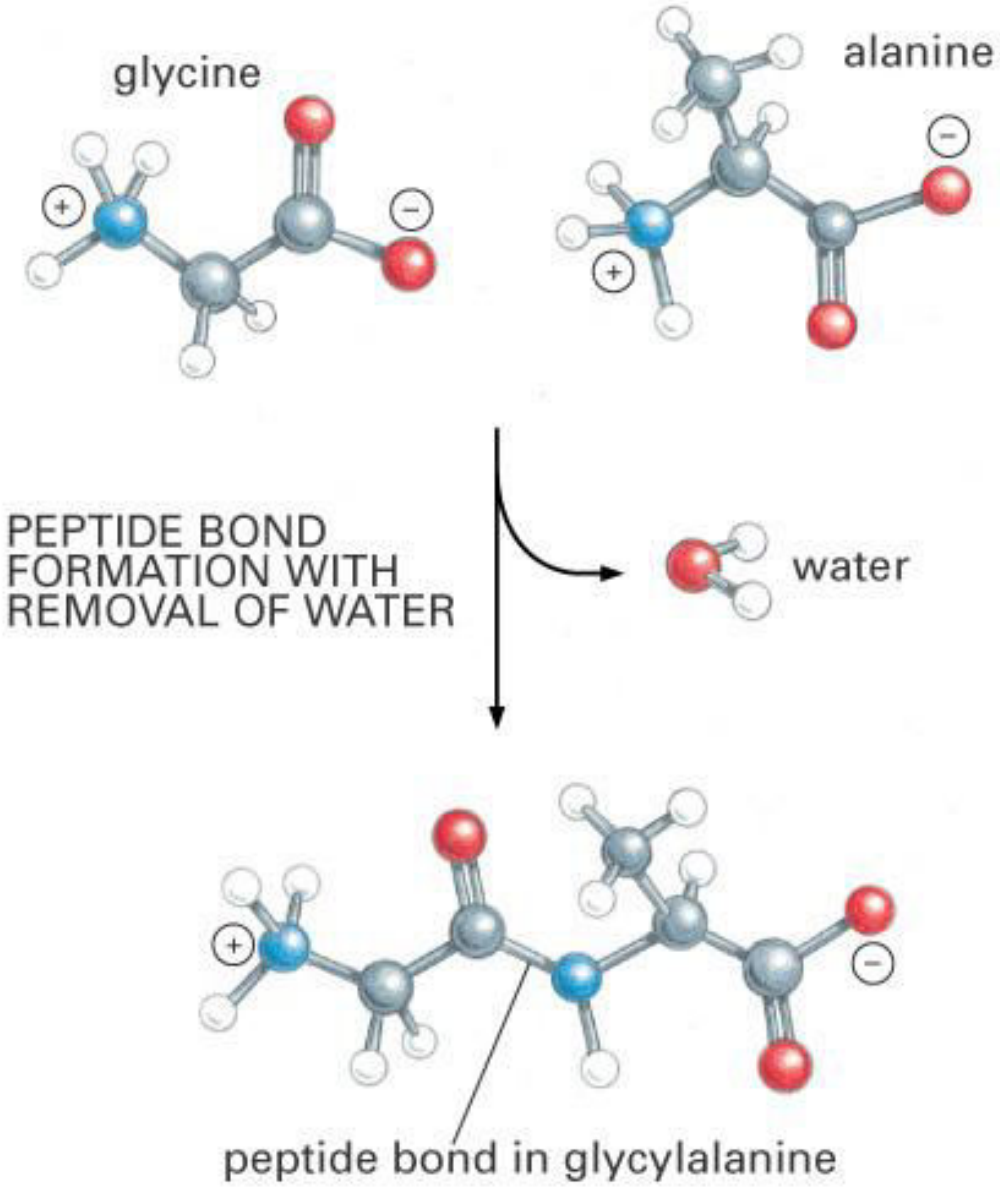
NONPOLAR AMINO ACIDS

Figure 4-3 Essential Cell Biology, 2/e. (© 2004 Garland Science)

What to learn…

- You are required to learn the structure of all 20 amino acids
- You are required to learn the spelling of all 20 amino acids
- You are required to learn the 3 letter abbreviation of all 20 amino acids
- You are required to learn the one letter abbreviation of all 20 amino acids

Peptide bond formation. Once again it is a condensation reaction



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Each AA' contributes three atoms to the polypeptide backbone. The side groups of adjacent AA's protrude in an alternating manner

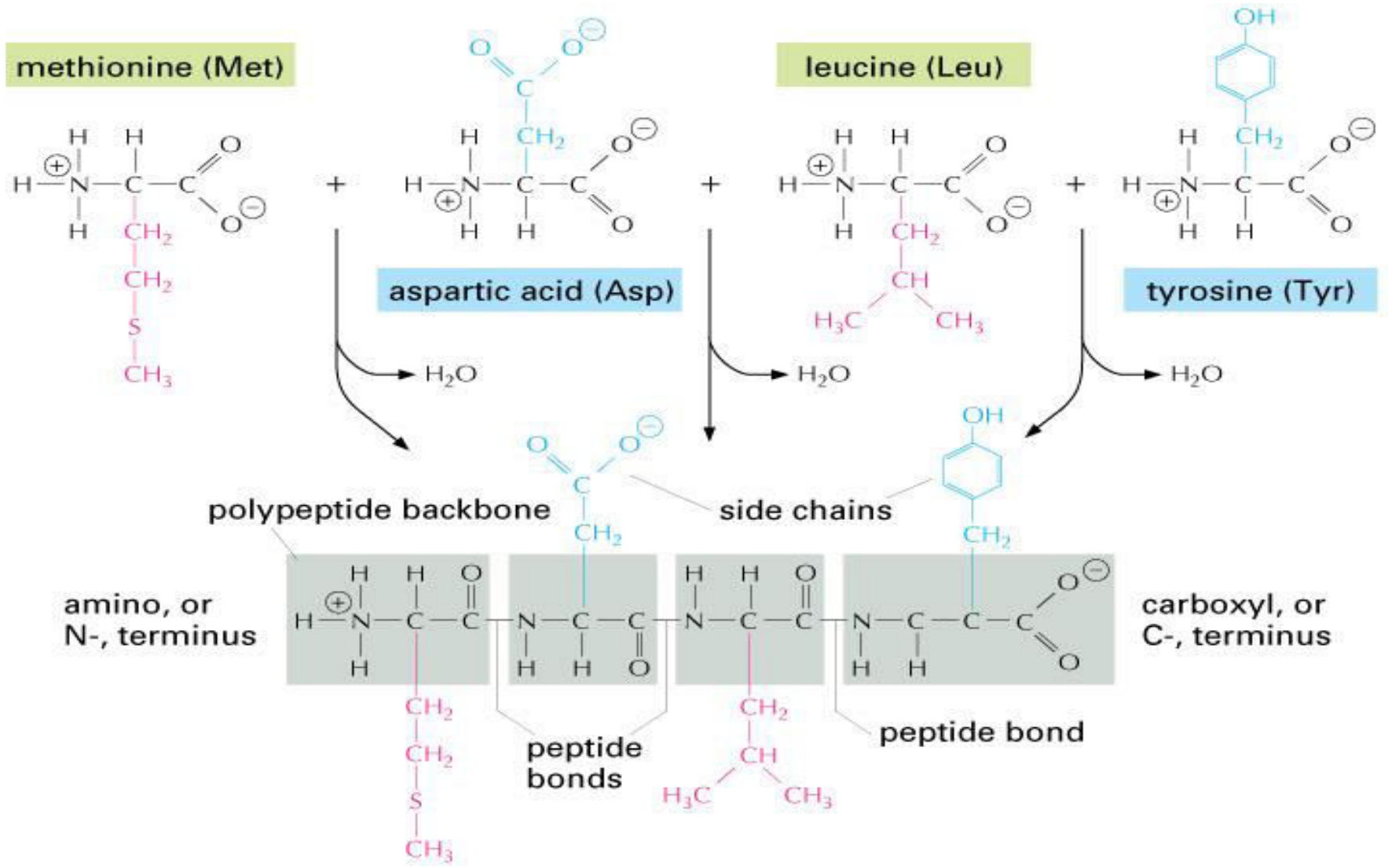
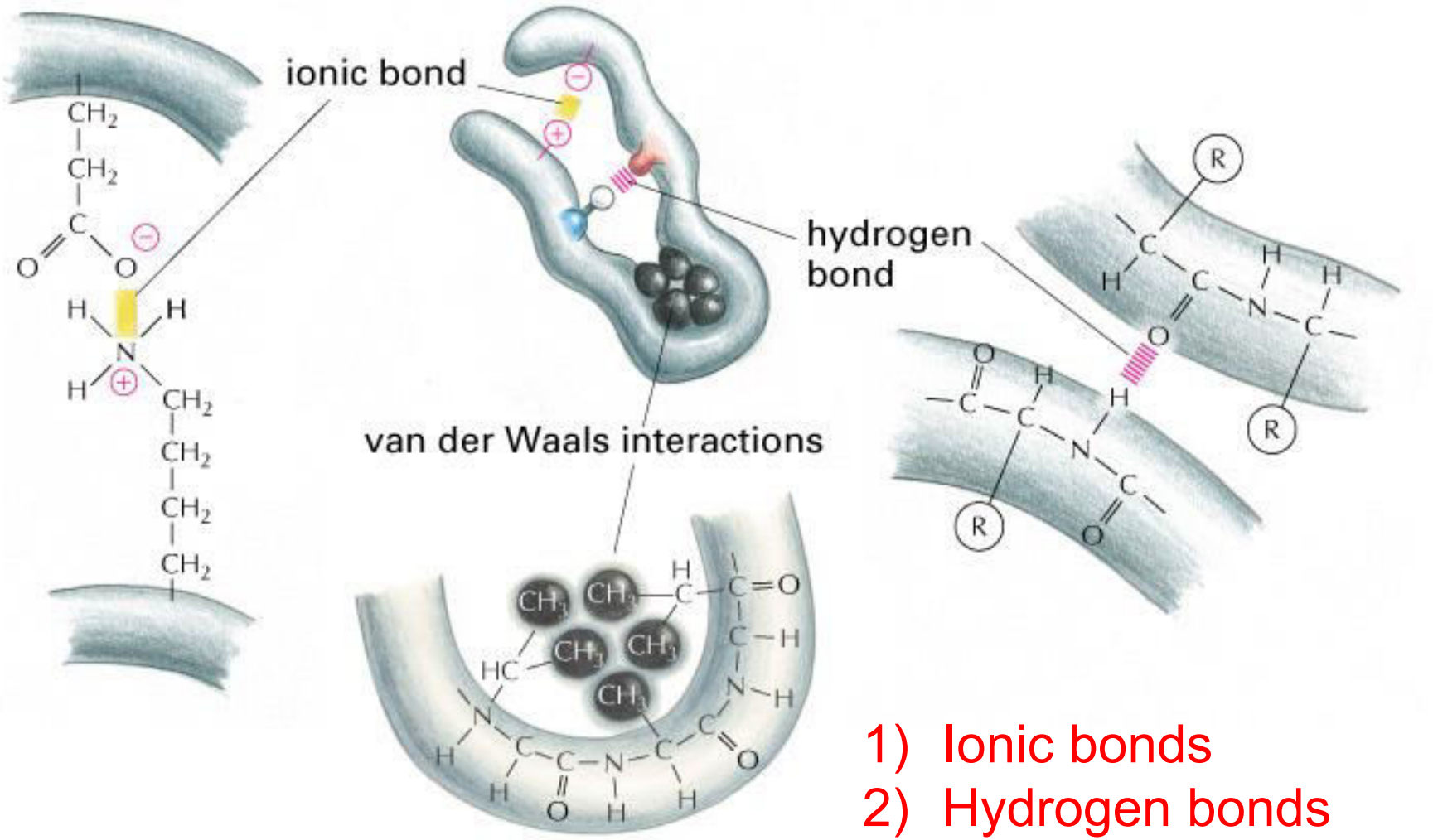


Figure 4-2 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Non-covalent bonds within and between P' chains are as important in their overall conformation and function



1) Ionic bonds
2) Hydrogen bonds
3) Van der Waals forces

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

The side groups of the linear unfolded polypeptide are intermingled. Only when correctly folded do we see the wonder of Nature!

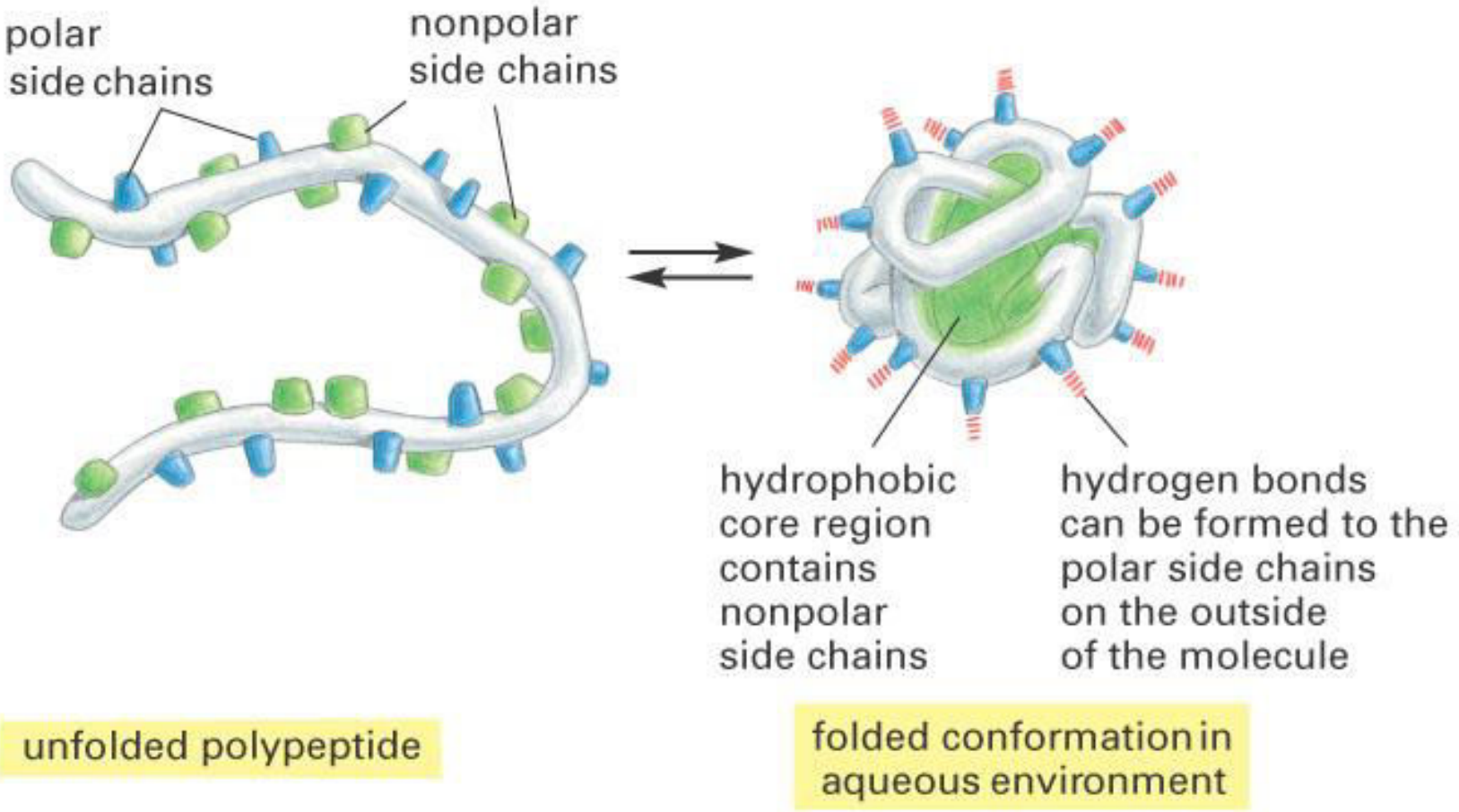
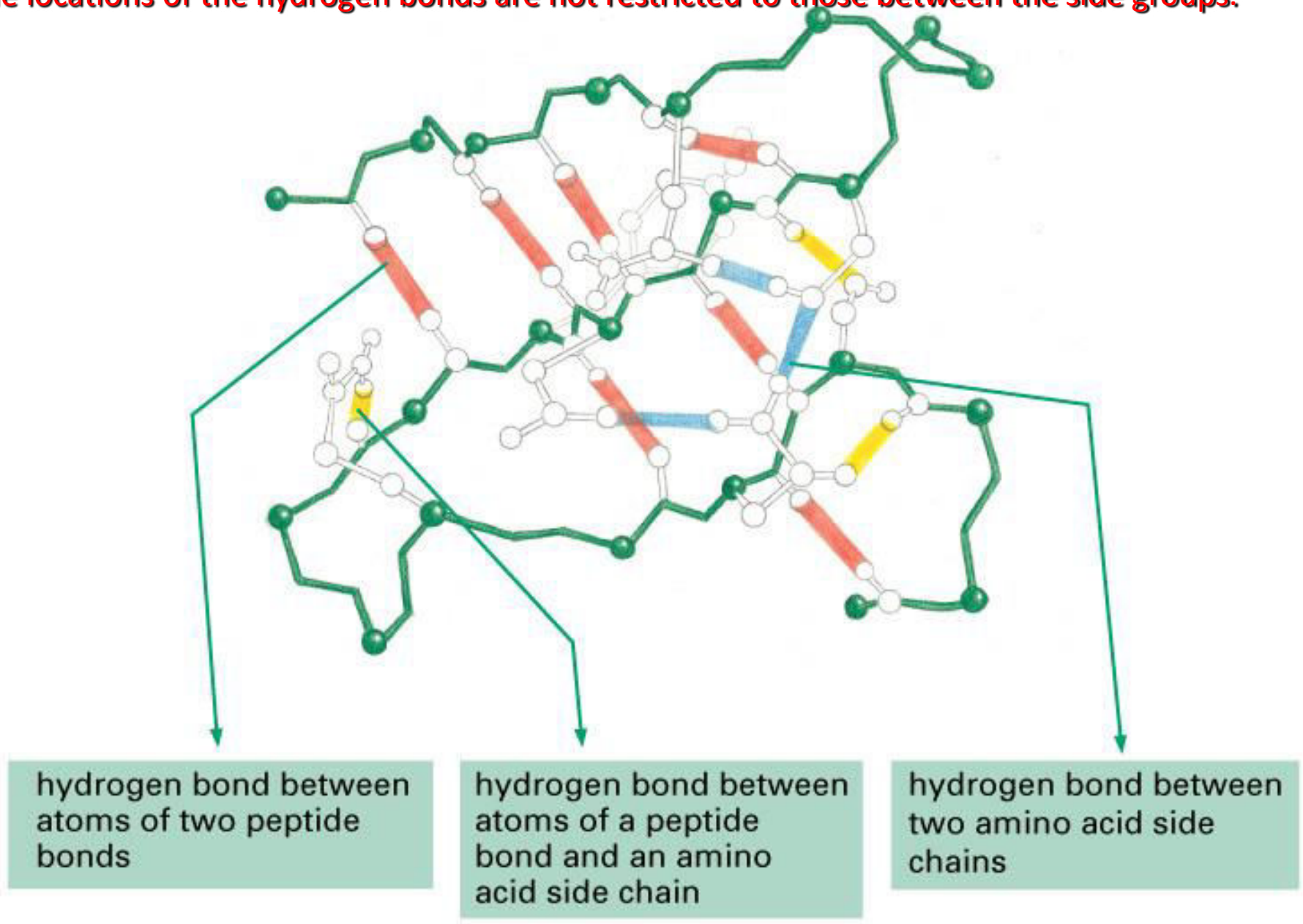


Figure 4-5 Essential Cell Biology, 2/e. (© 2004 Garland Science)

The locations of the hydrogen bonds are not restricted to those between the side groups.



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The 3D folding of a P' is governed solely by the sequence of the AA's. Under some physiological conditions & in vitro many P's can reversibly unfold and refold

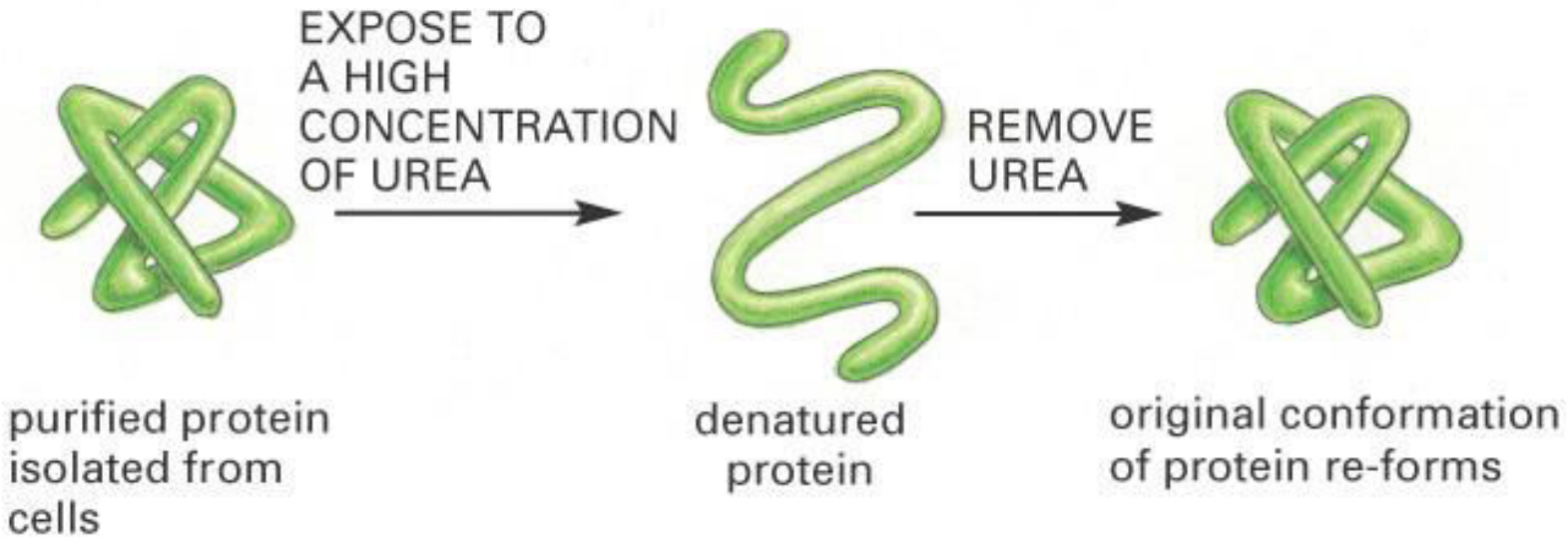


Figure 4-7 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Posttranslational modifications of P's

- Various AA's are modified by enzymes after their incorporation into polypeptides
  - Addition of phosphate groups
  - Addition of methyl groups
  - Addition of hydroxyl groups
  - Formation of disulfide bonds
    - we learn more about these later…

cURRENT tOPICS - Prions

- Prions cause diseases, but they aren't viruses or bacteria or fungi or parasites.
- They are simply proteins, and proteins were never thought to be infectious on their own. Organisms are infectious, proteins are not.
- ‘Mad cow’ epidemic that hit England in 1986
- Scrapie in sheep and goats has the same basis.

Prions

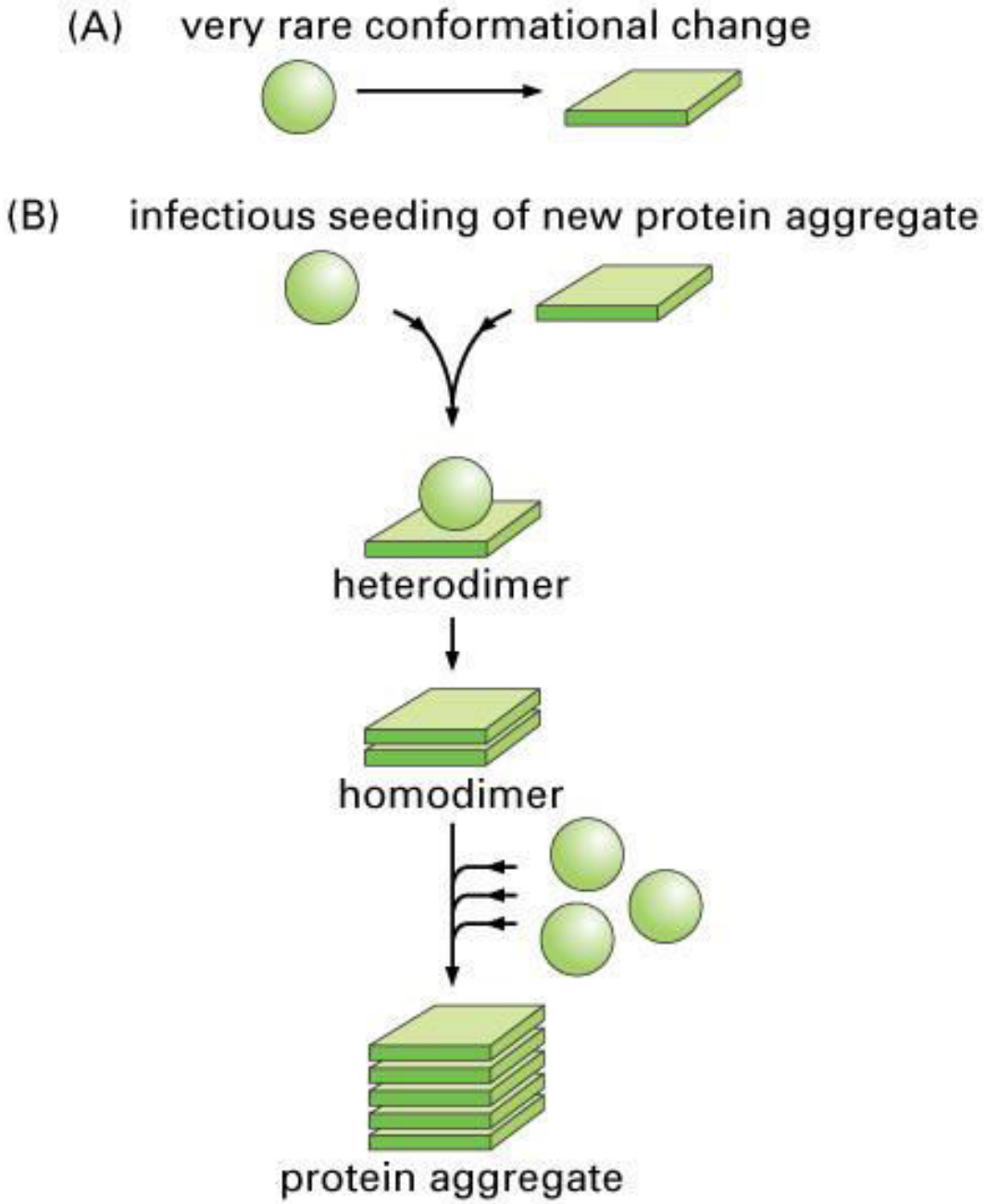


Figure 4-8 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Shapes & Sizes of Proteins

- There are more varieties of Proteins in a cell than any other macromolecule
- Filamentous & Globular
- Large & Small

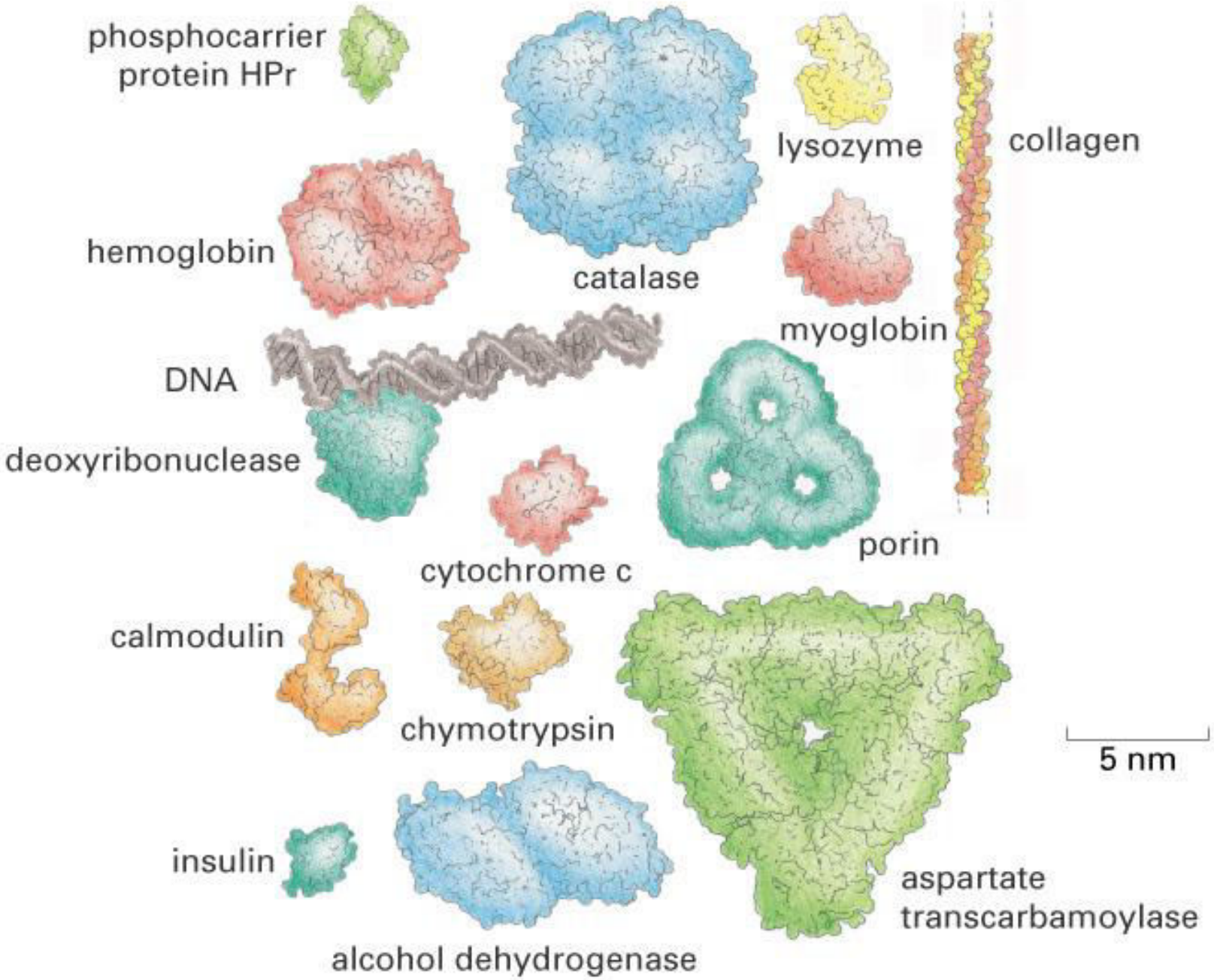


Figure 4-9 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Secondary Structure

- The 2^{O} Structure of P's is defined as the localized folding of domains of the polypeptide chain
- α-helices
- β-sheets
- β-barrels
- coiled-coils

Right-handed α-sheets

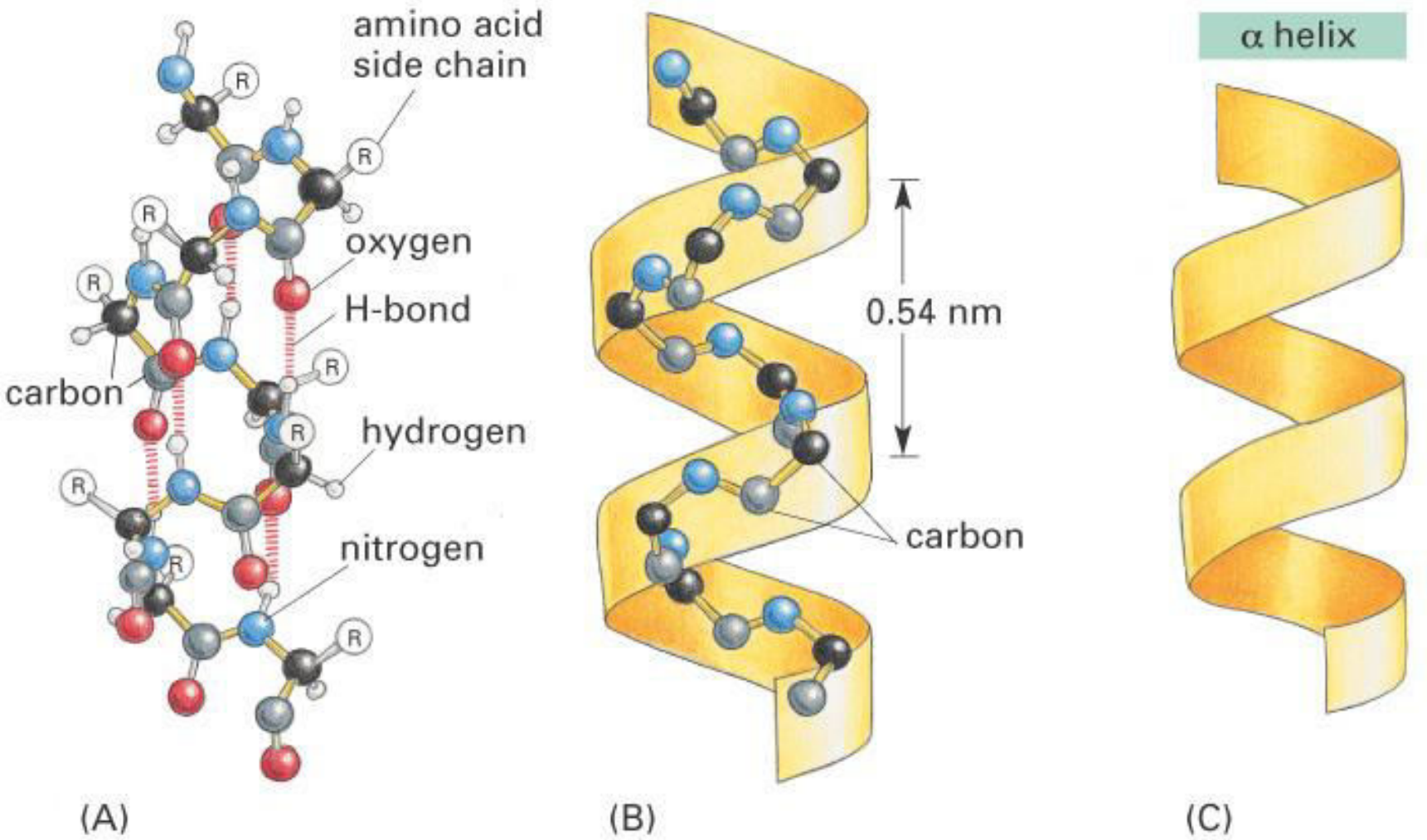
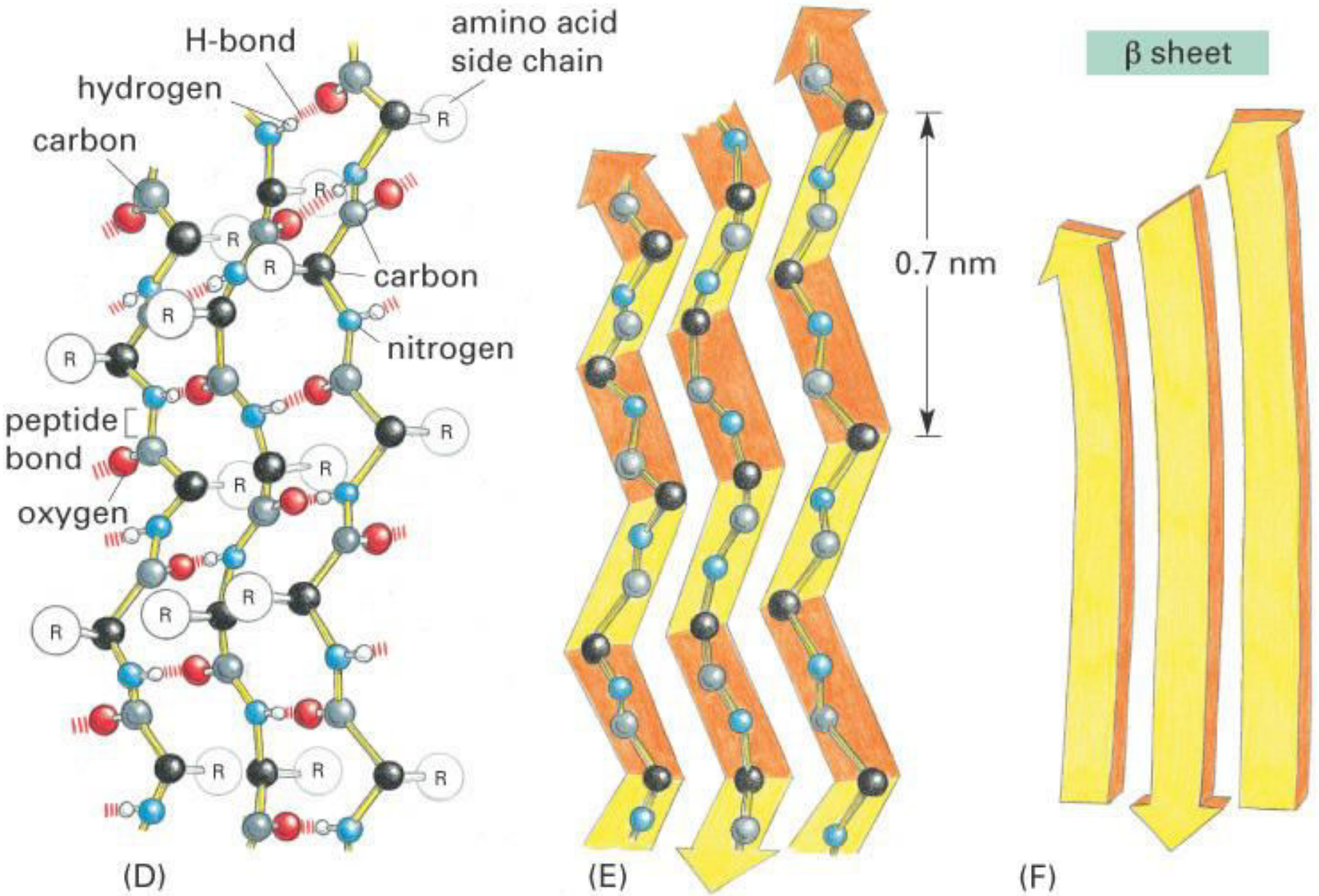


Figure 4-10 part 1 of 2 Essential Cell Biology, 2/e. (© 2004 Garland Science)



Anti-parallel β-sheets

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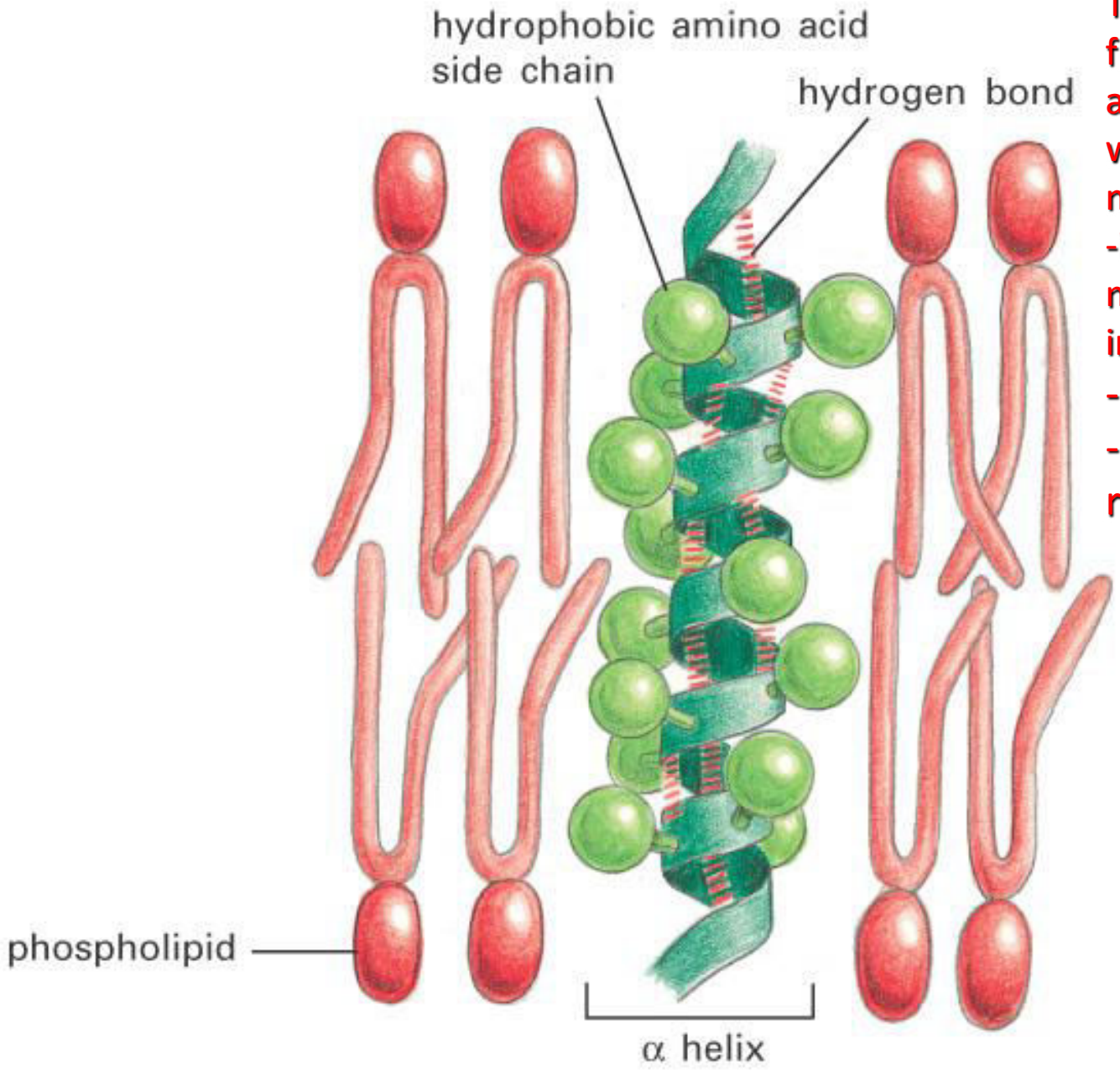
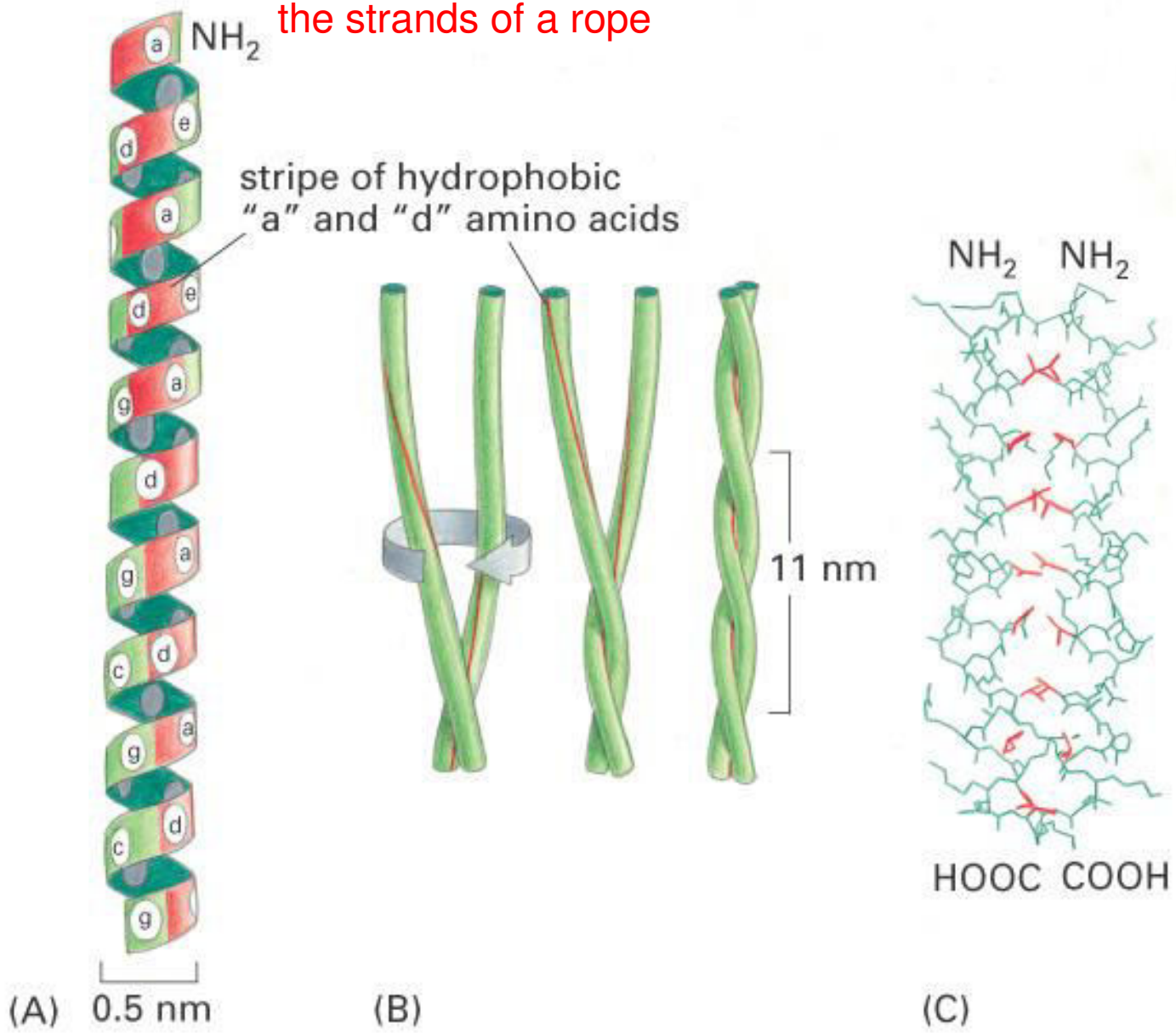


The helix is fundamental in allowing P's to sit within the plasma membrane
-it is the foundation of many many very important P's
- Visual Pigments
- Immune cell receptors

Figure 4-15 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Coiled-coil - in which 2-6 alpha-helices are coiled together like the strands of a rope



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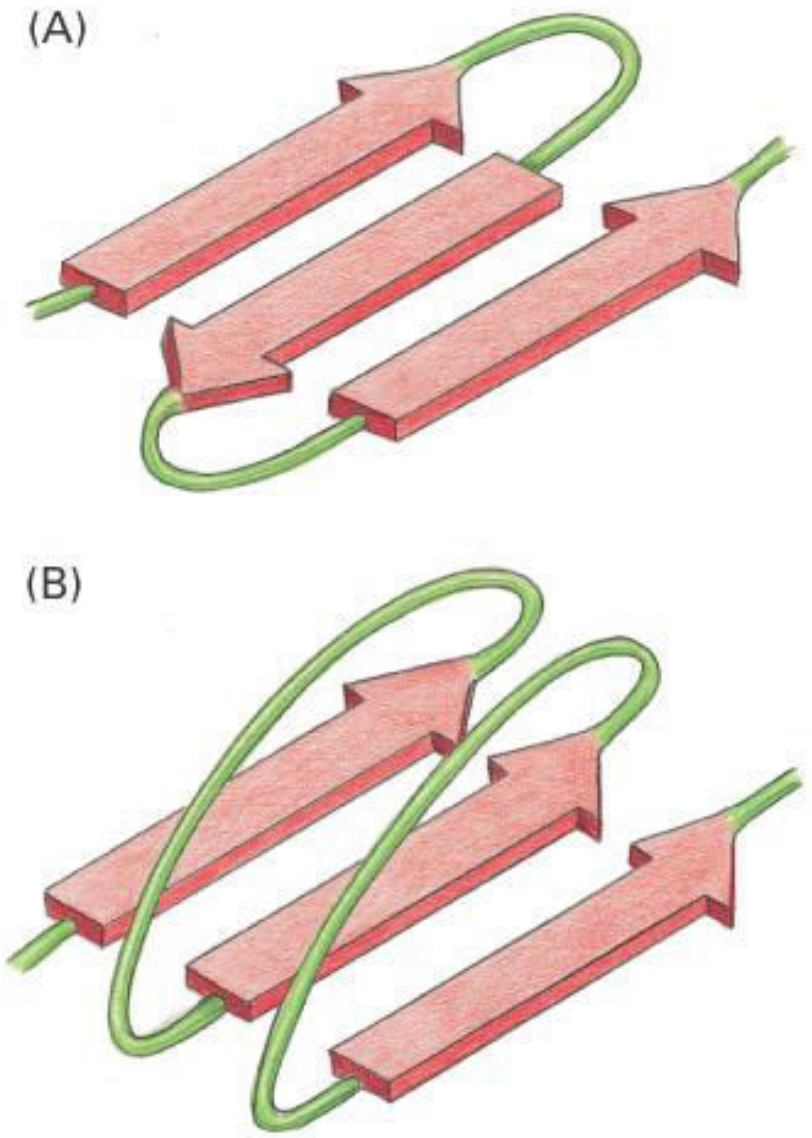
Parallel and anti-parallel sheets



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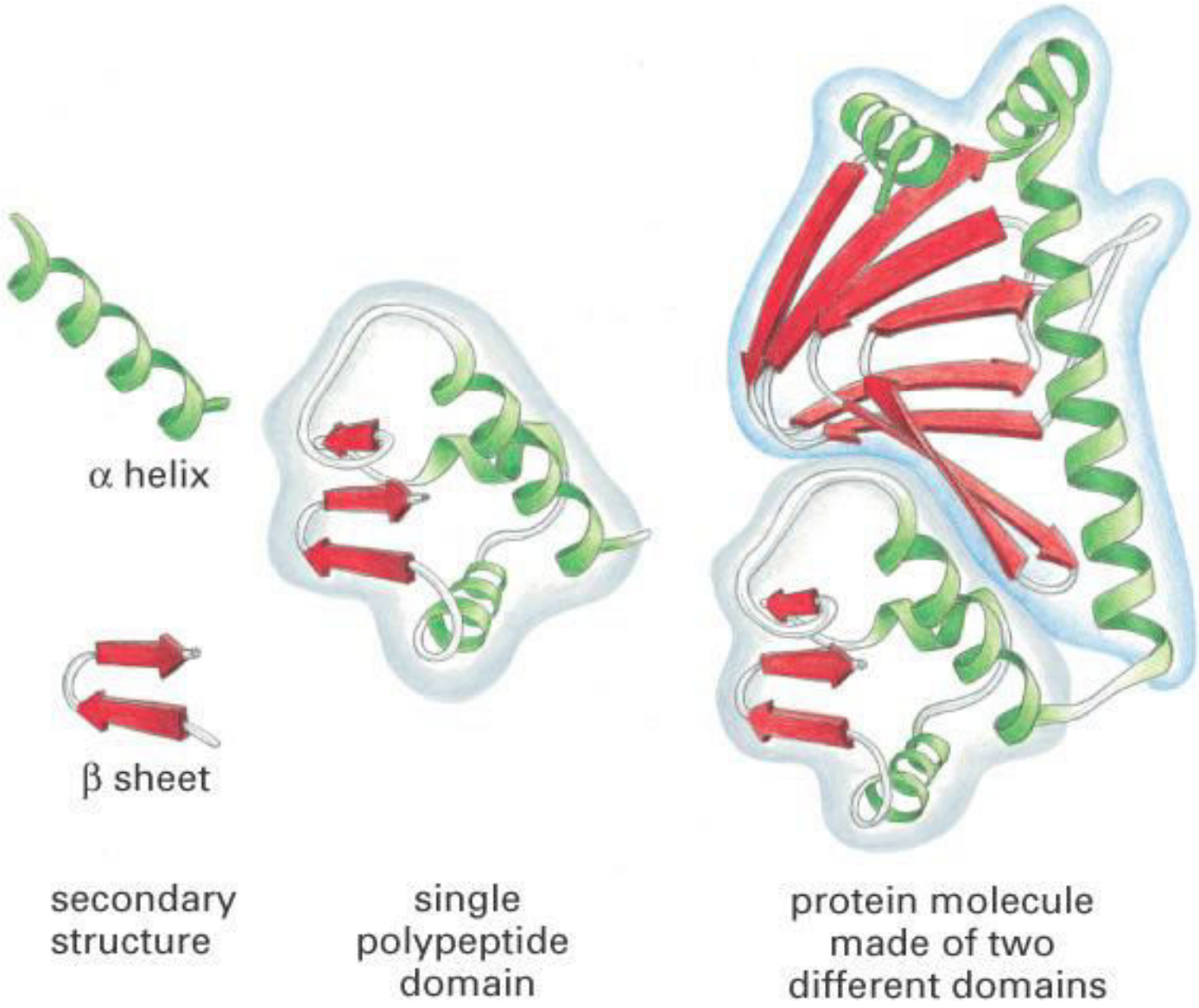
Individual Protein domains may and generally do consist of a combination of secondary structures



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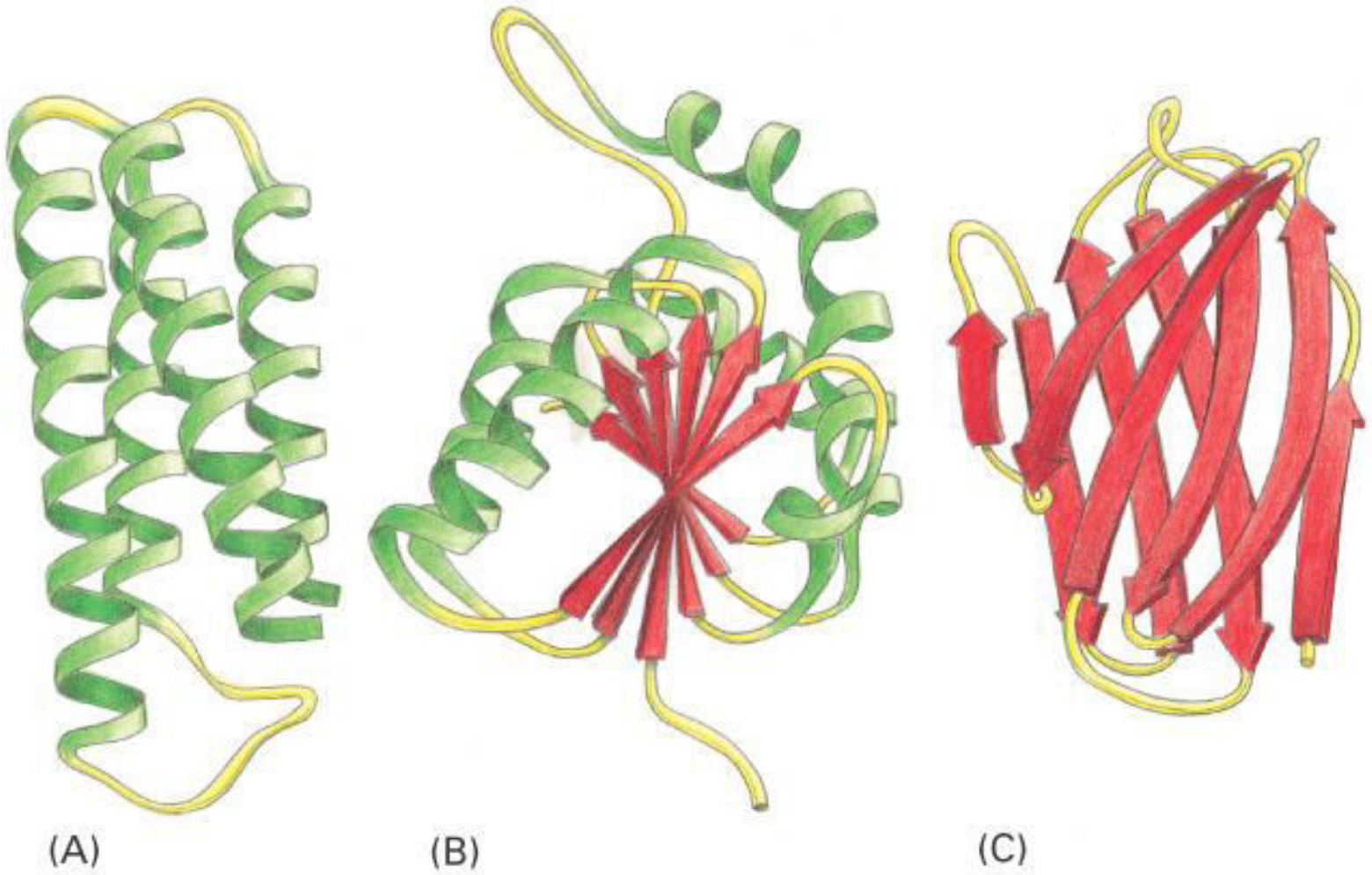


Figure 4-20 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Nature is known for reusing structures

- Proteins are no exception. Here two very similar P's are built on a common theme but perform very different functions…

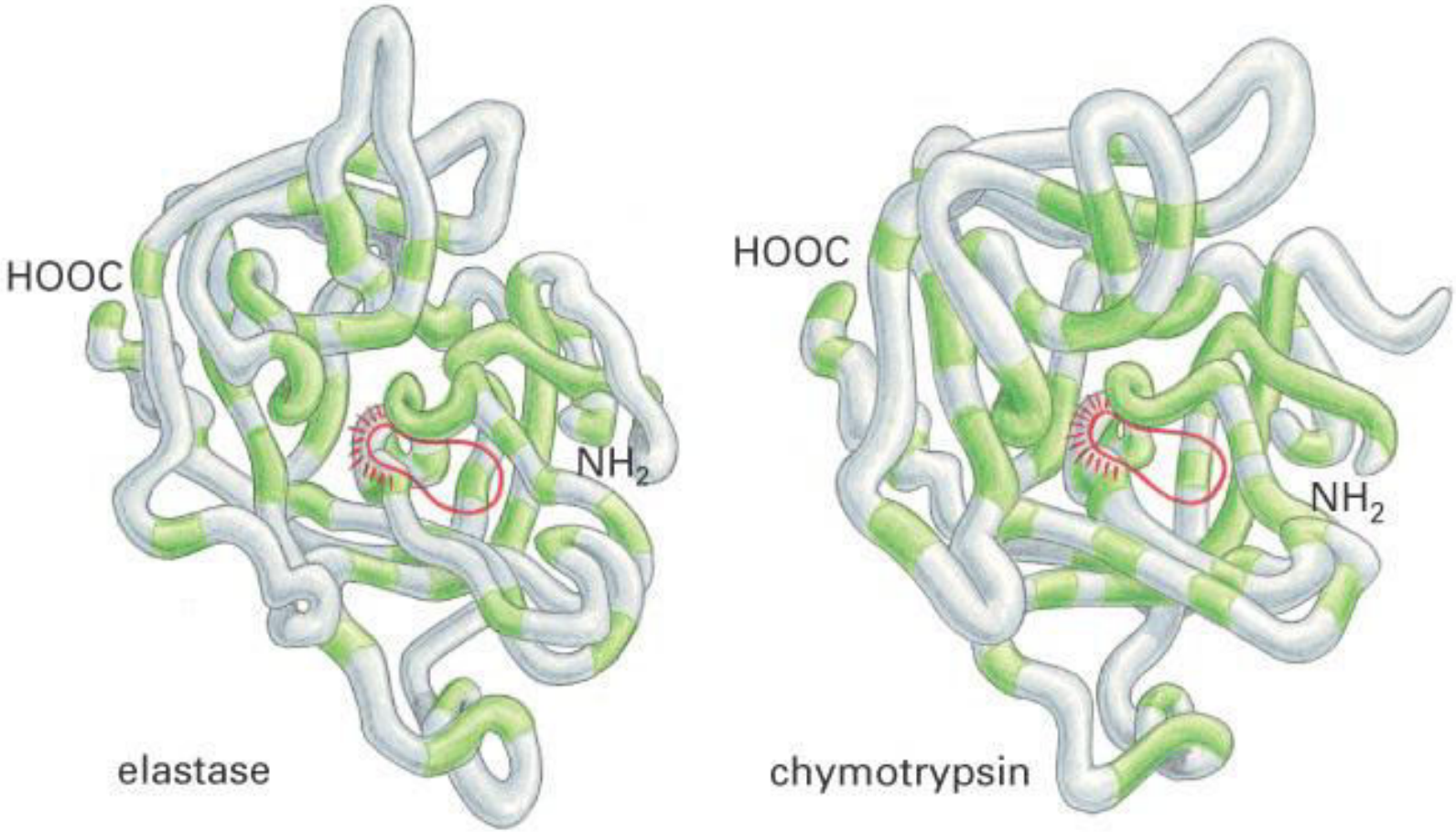
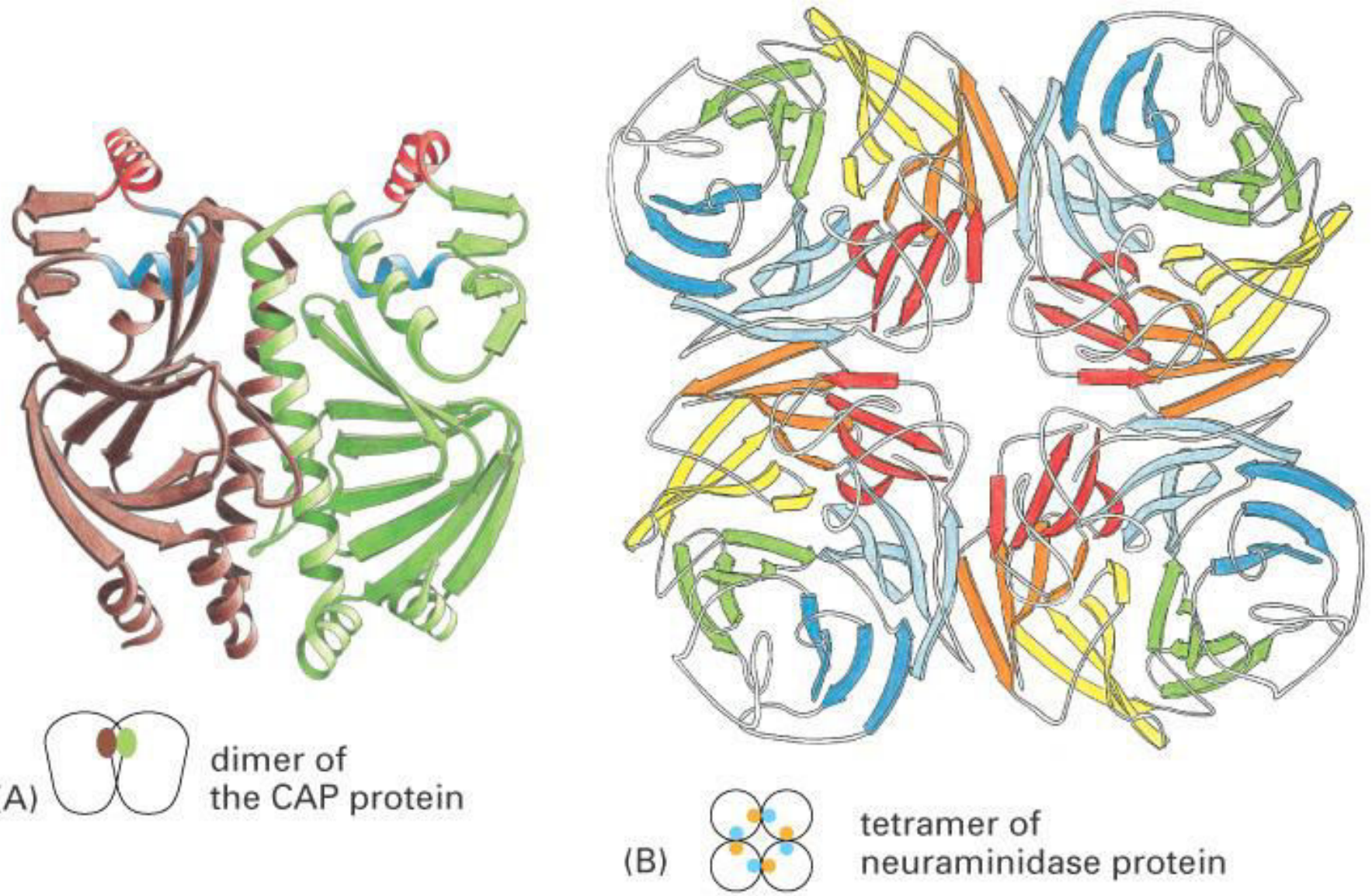


Figure 4-21 Essential Cell Biology, 2/e. (© 2004 Garland Science)

•In other instances identical, or nearly identical, polypeptides are used in the final Proteins



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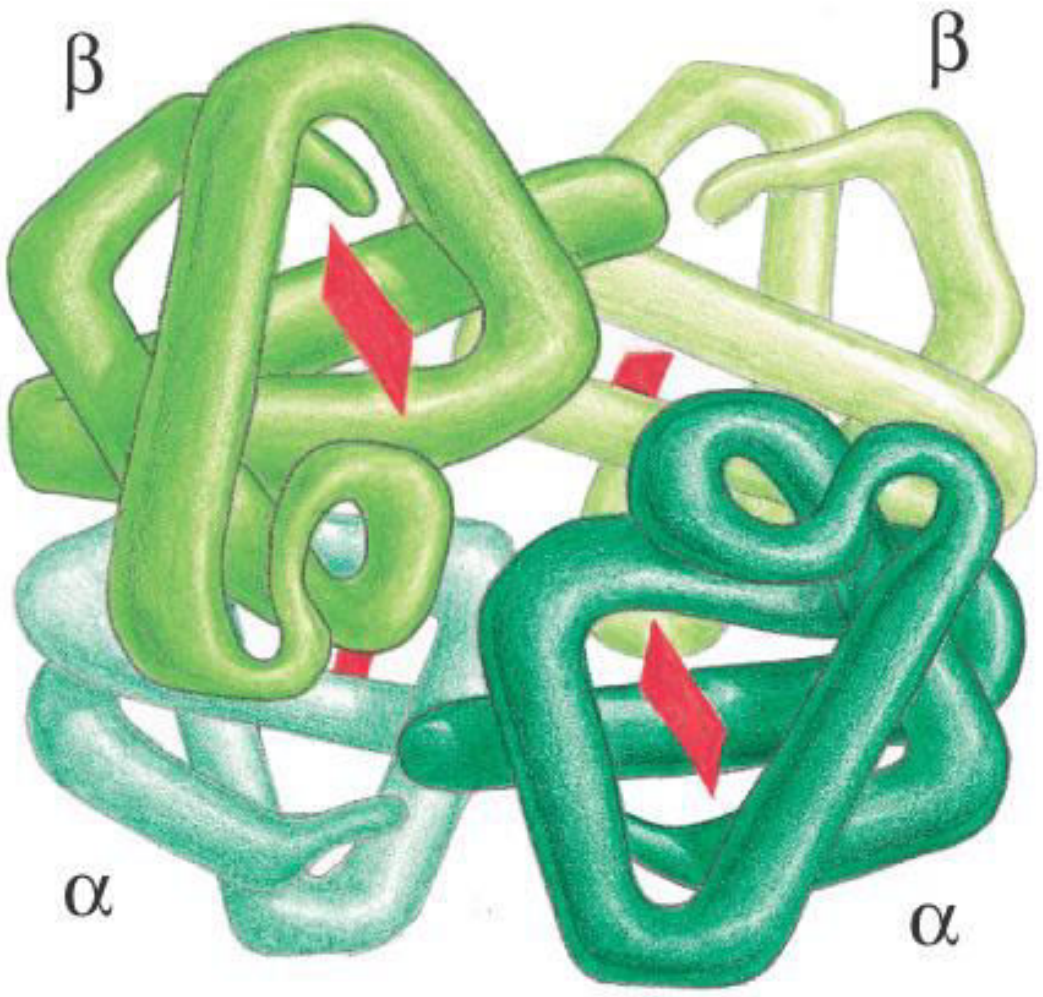
Haemoglobin - is the iron-containing oxygen-transport metalloprotein in the red blood cells of the blood in vertebrates and other animals



Here we see the use of two different polypeptides made by different genes

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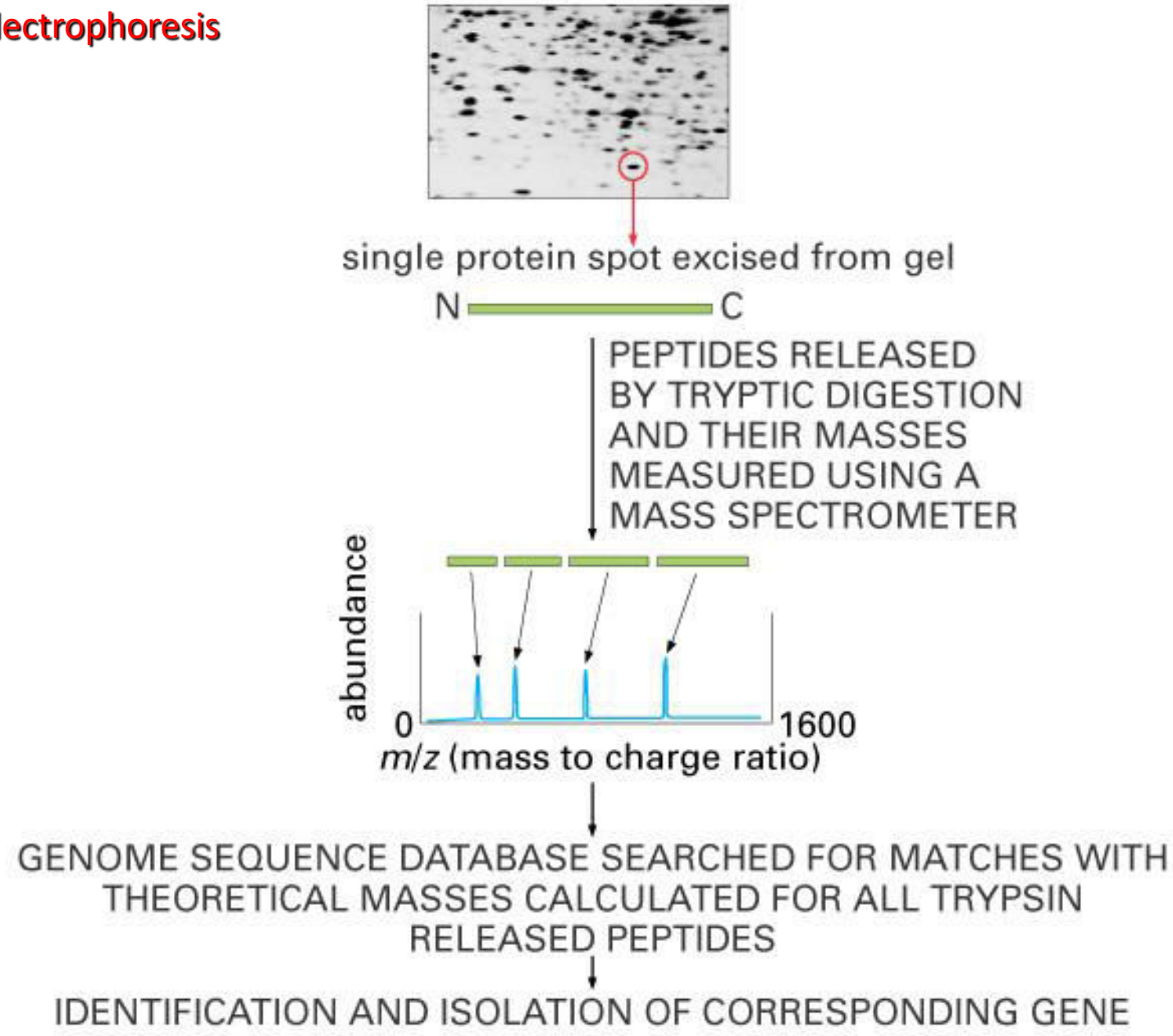
Experimental Procedures

2D gel electrophoresis



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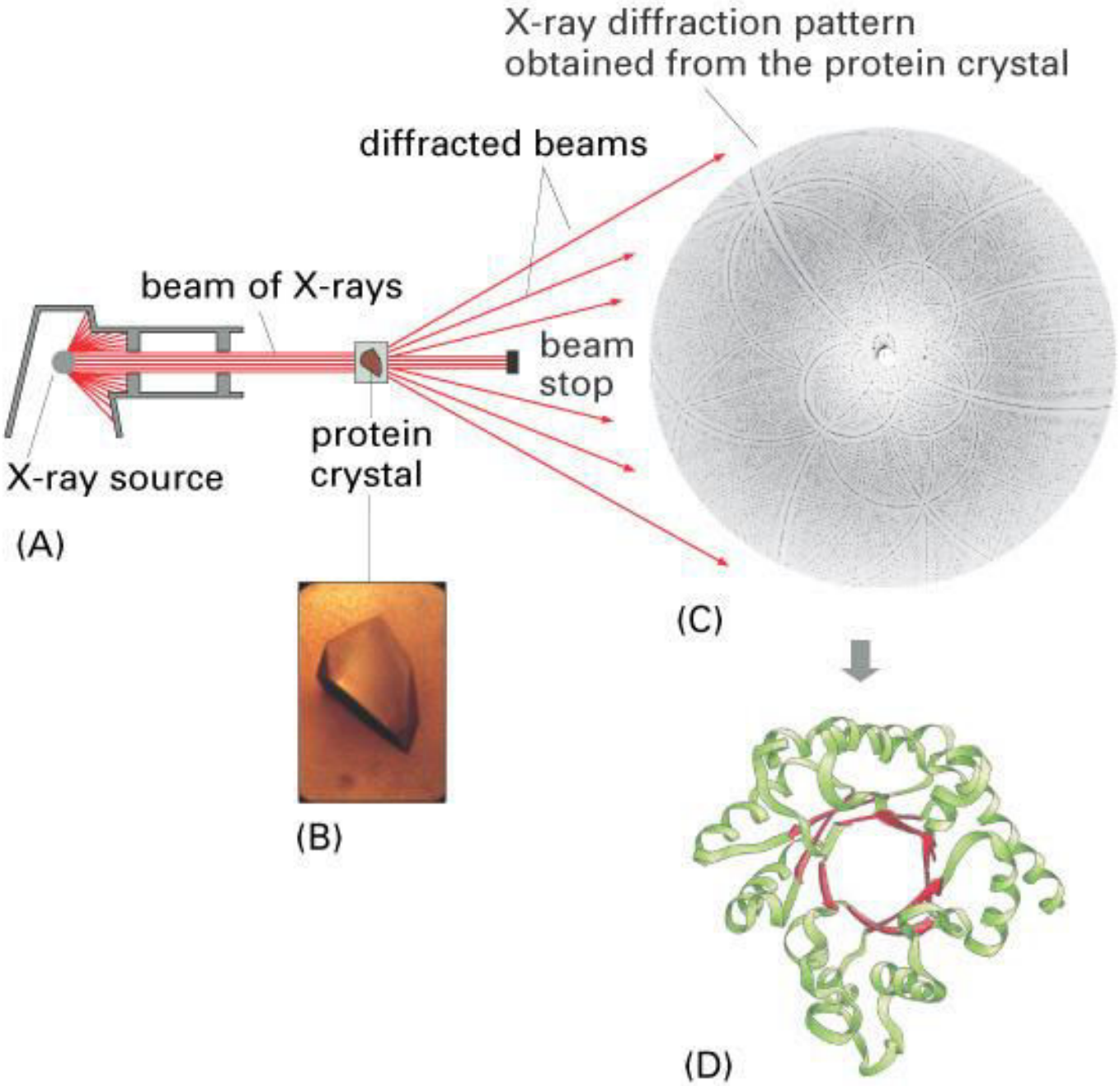

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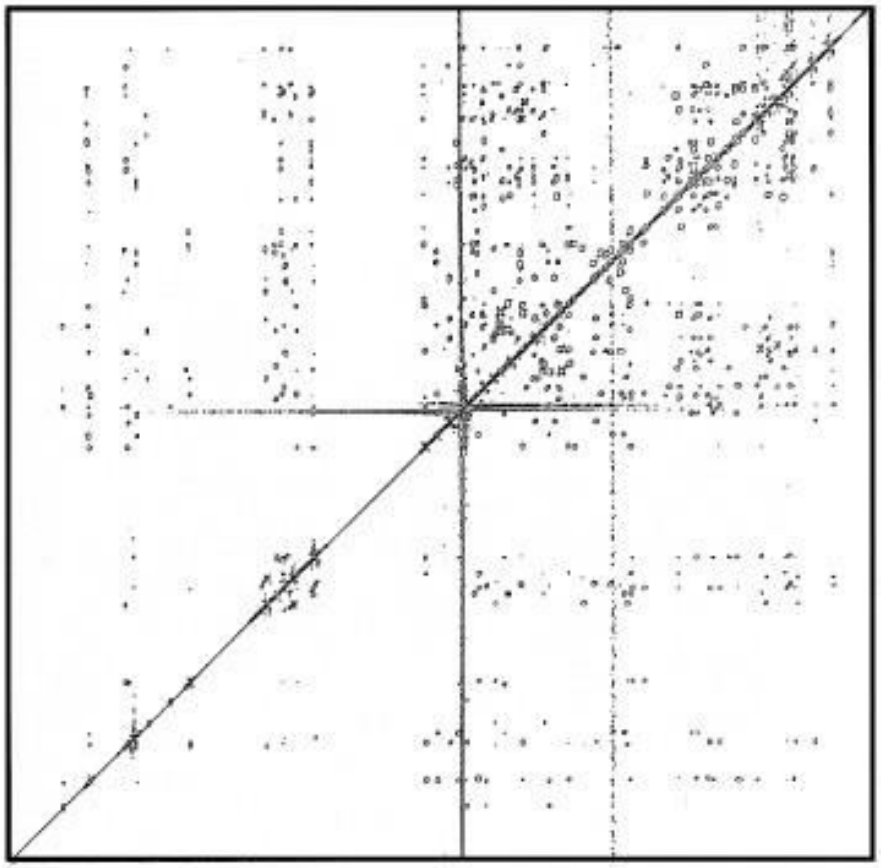
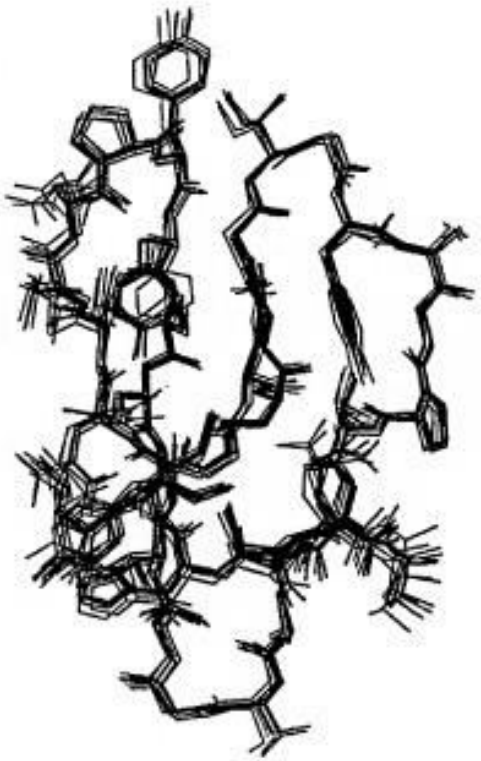
Nuclear magnetic resonance is used to elucidate the structural rigidity of P's



(A)



(B)

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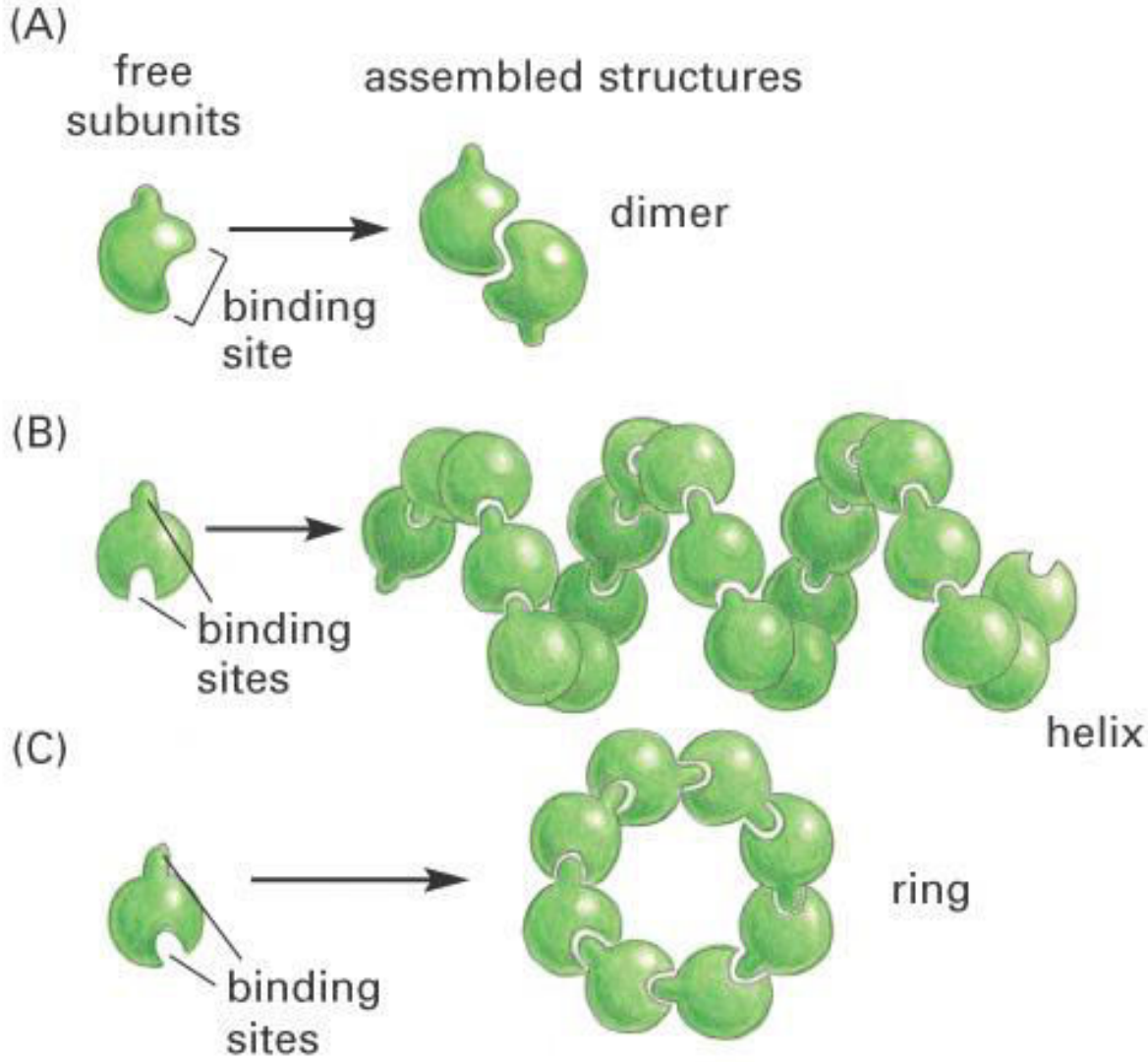
Protein: structure and function 2

Lecture 8

Chapter 4 (remainder)



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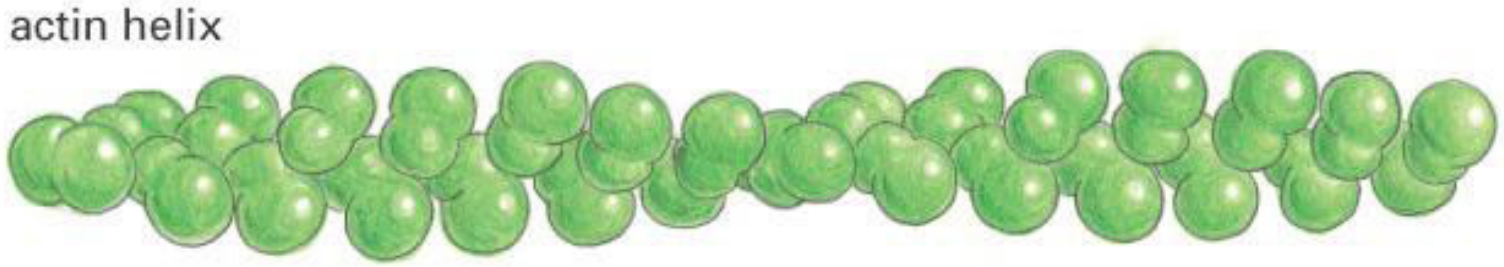

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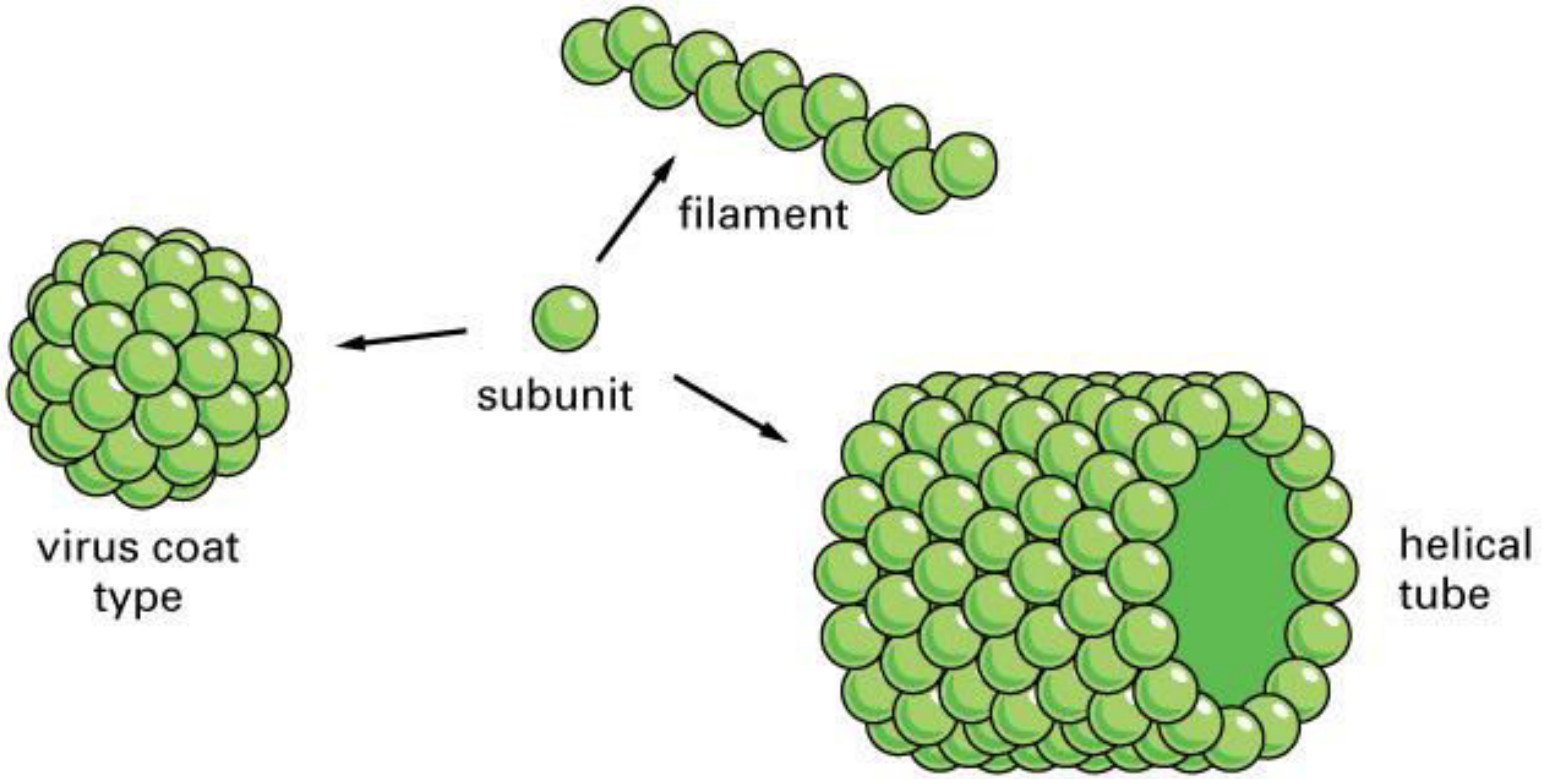

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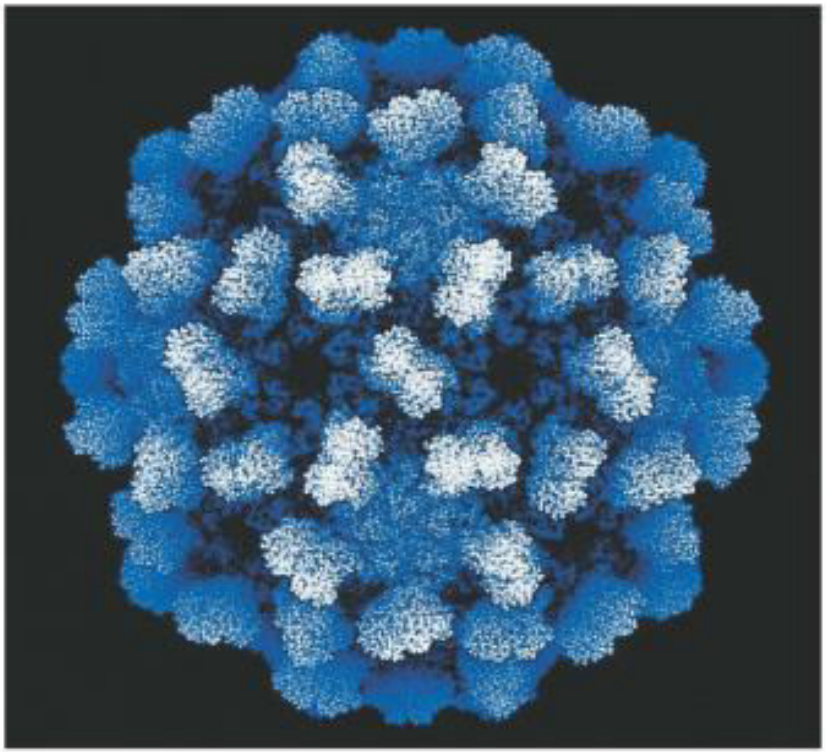

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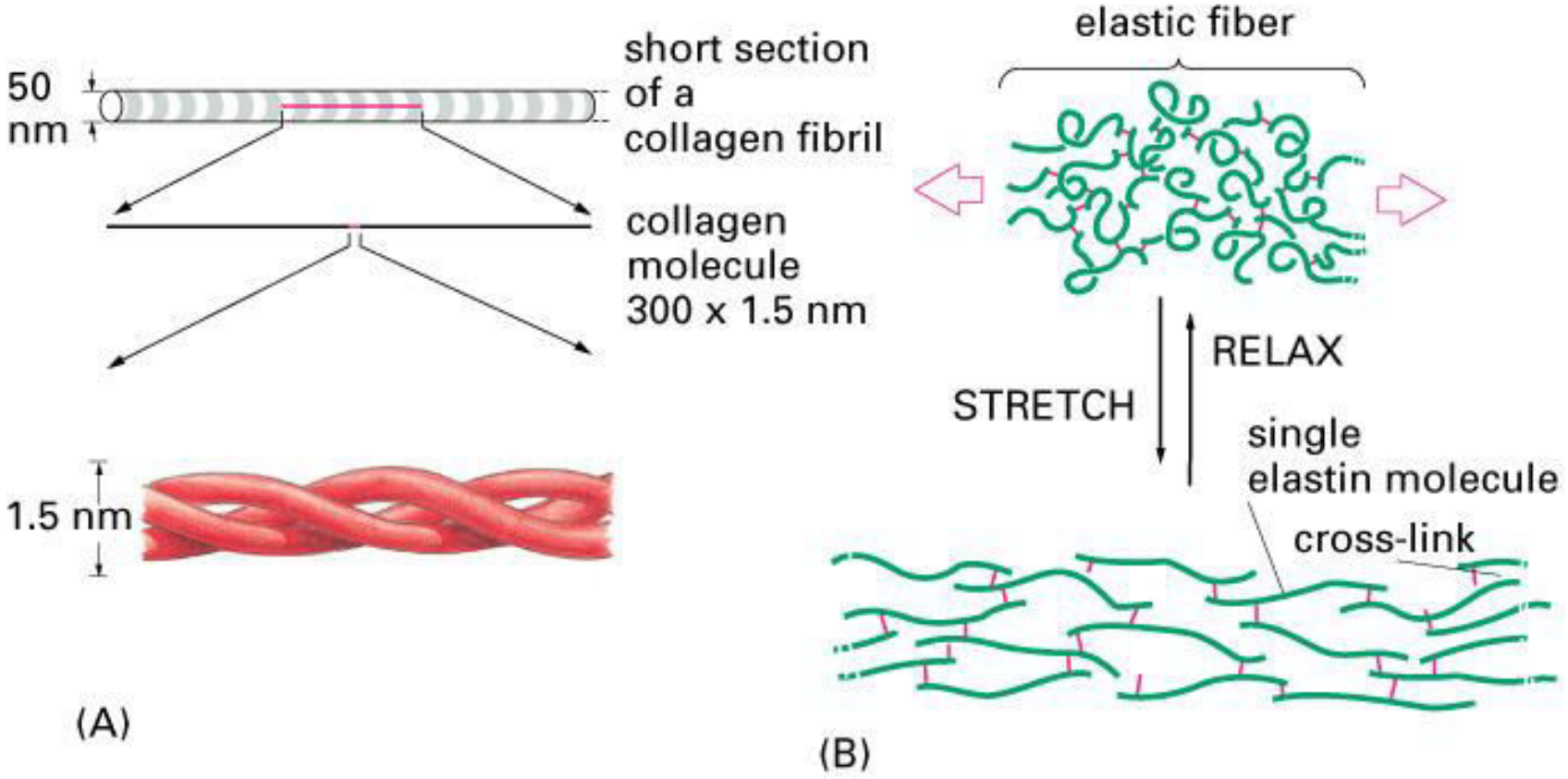

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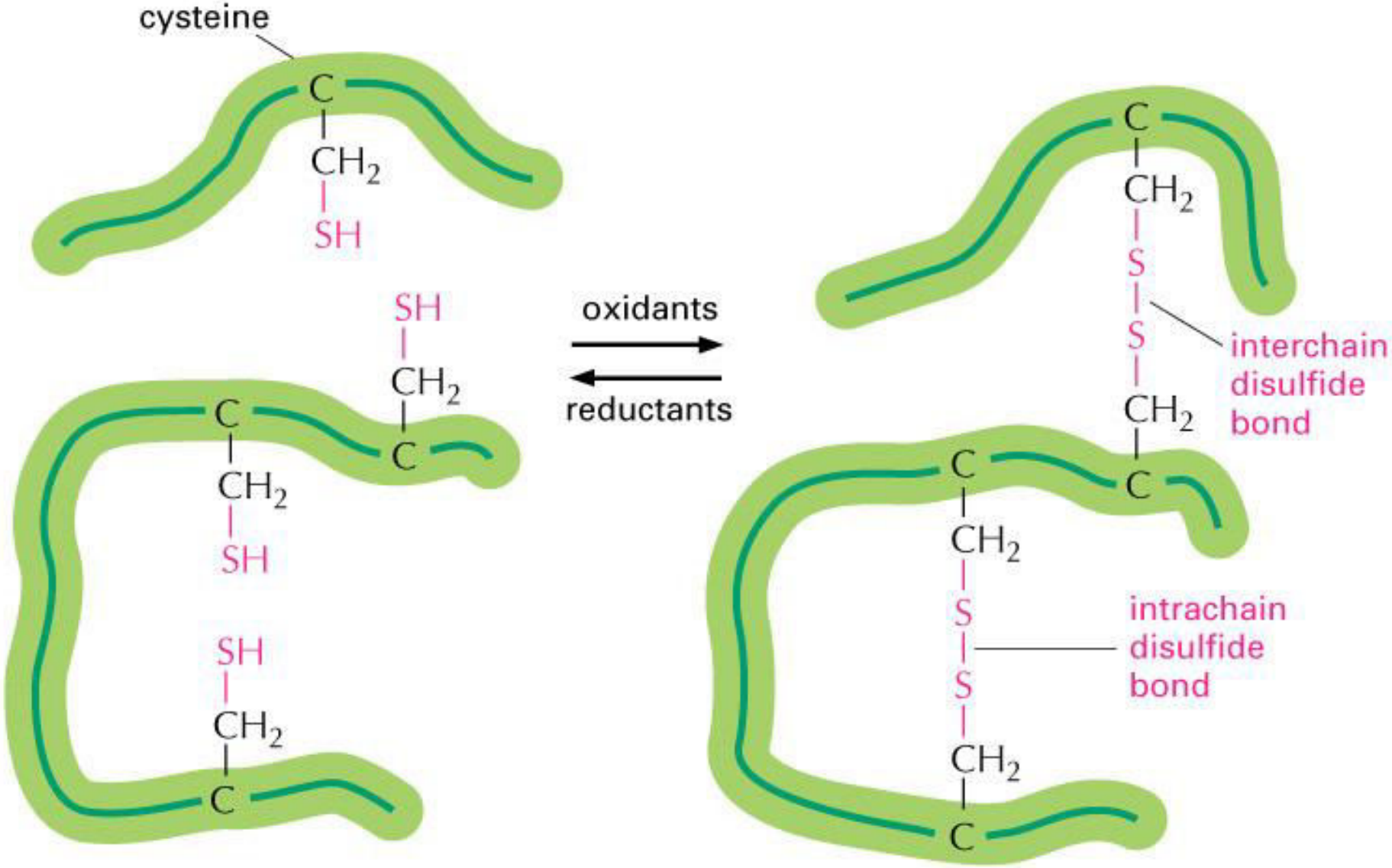

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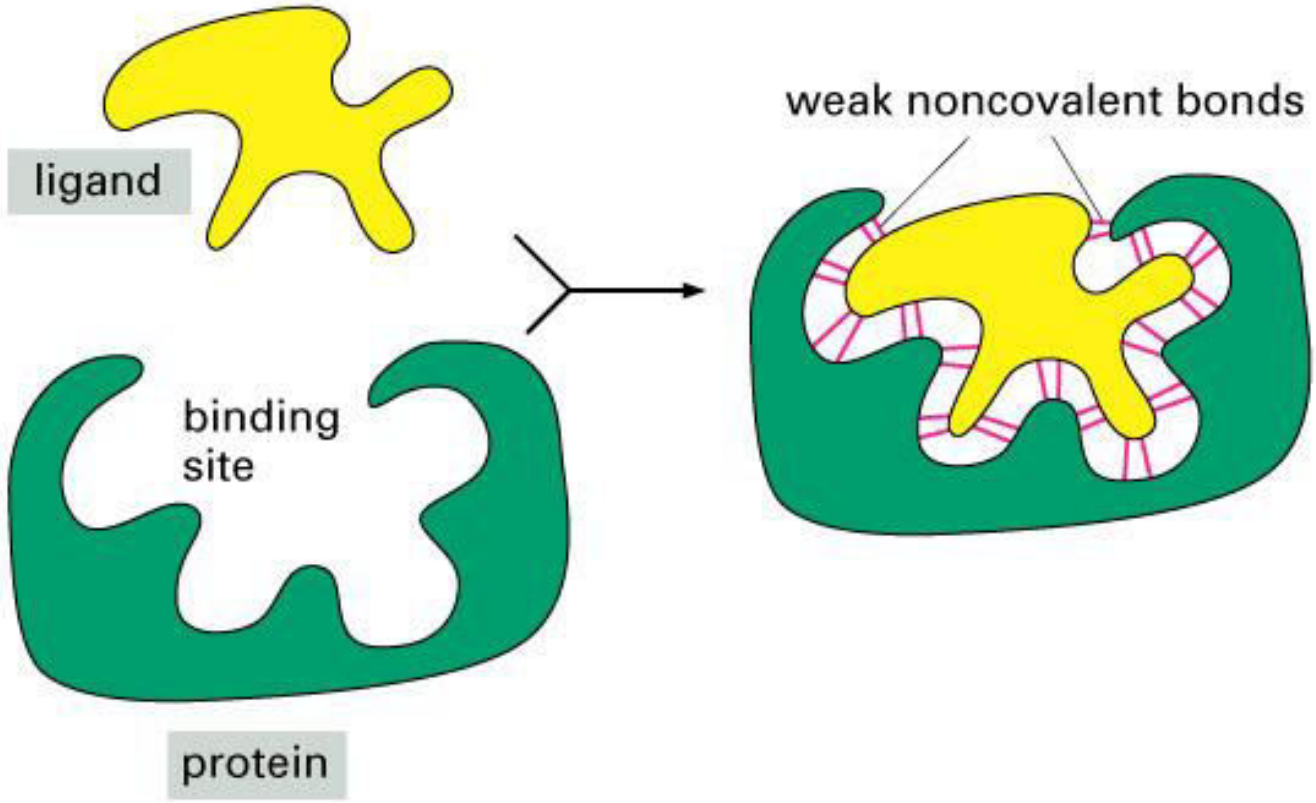

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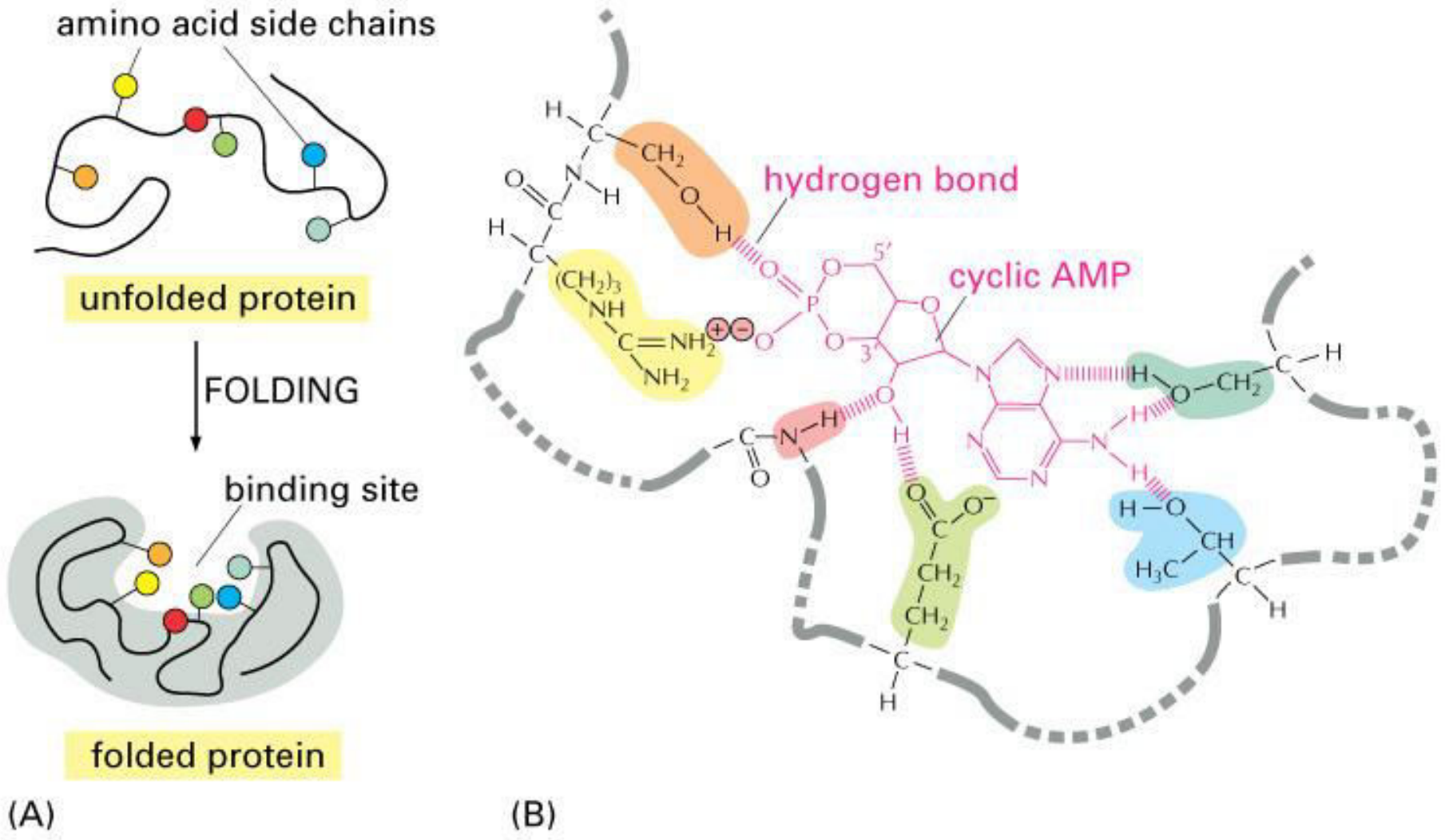

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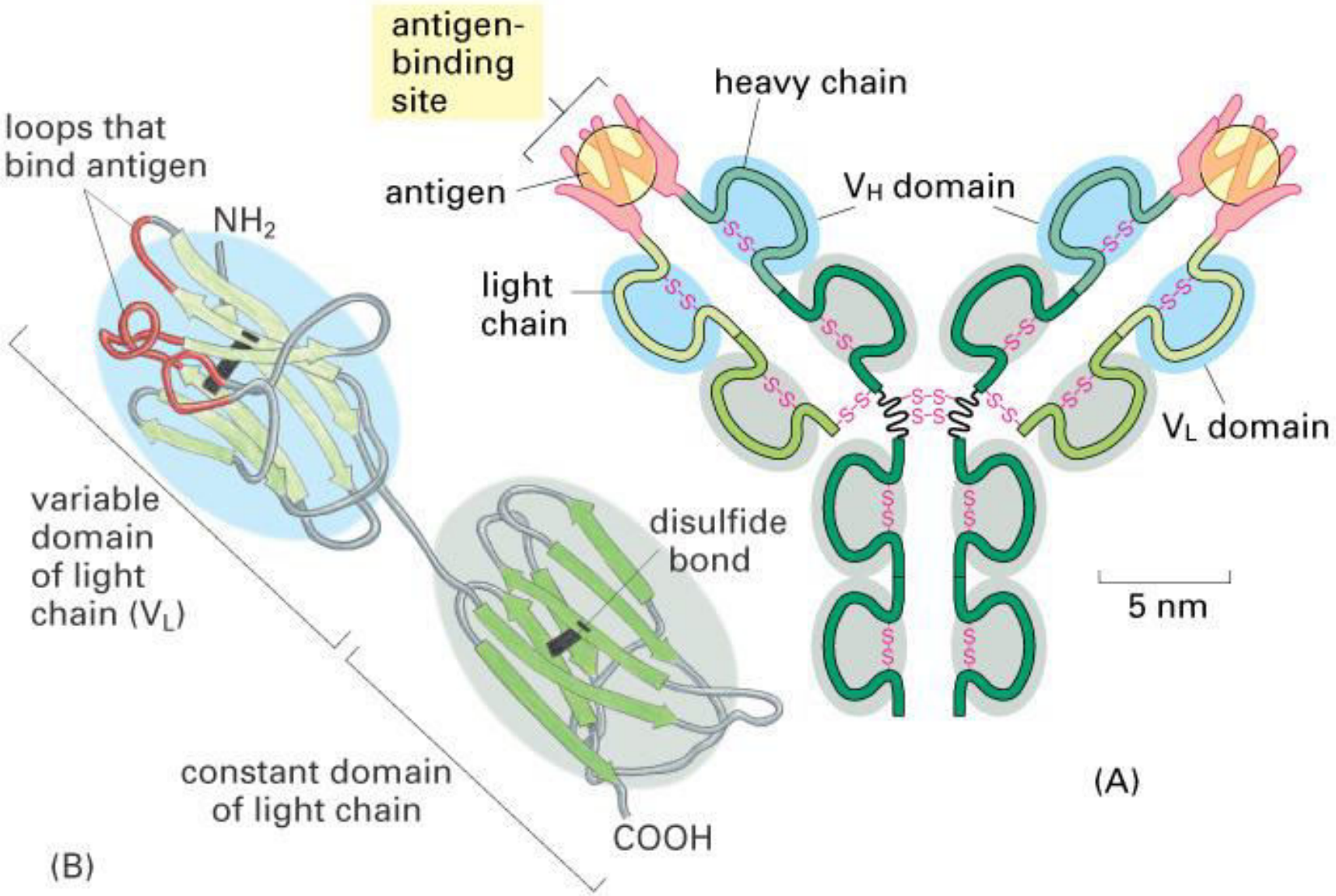

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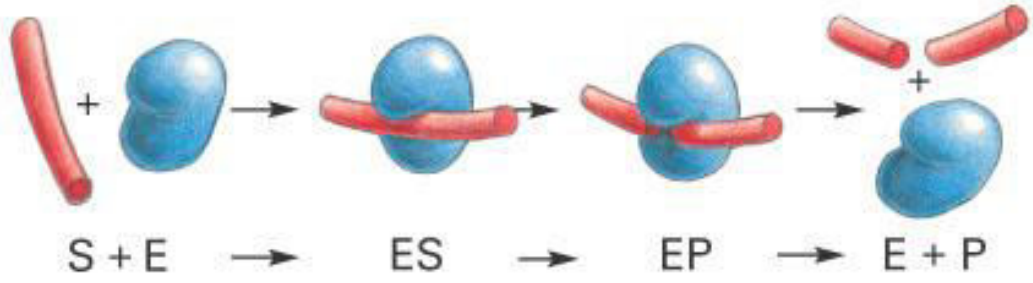
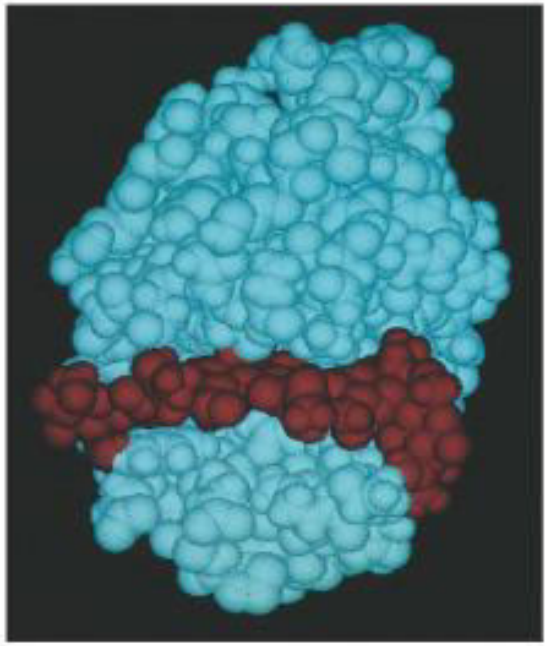


(A)



(B)

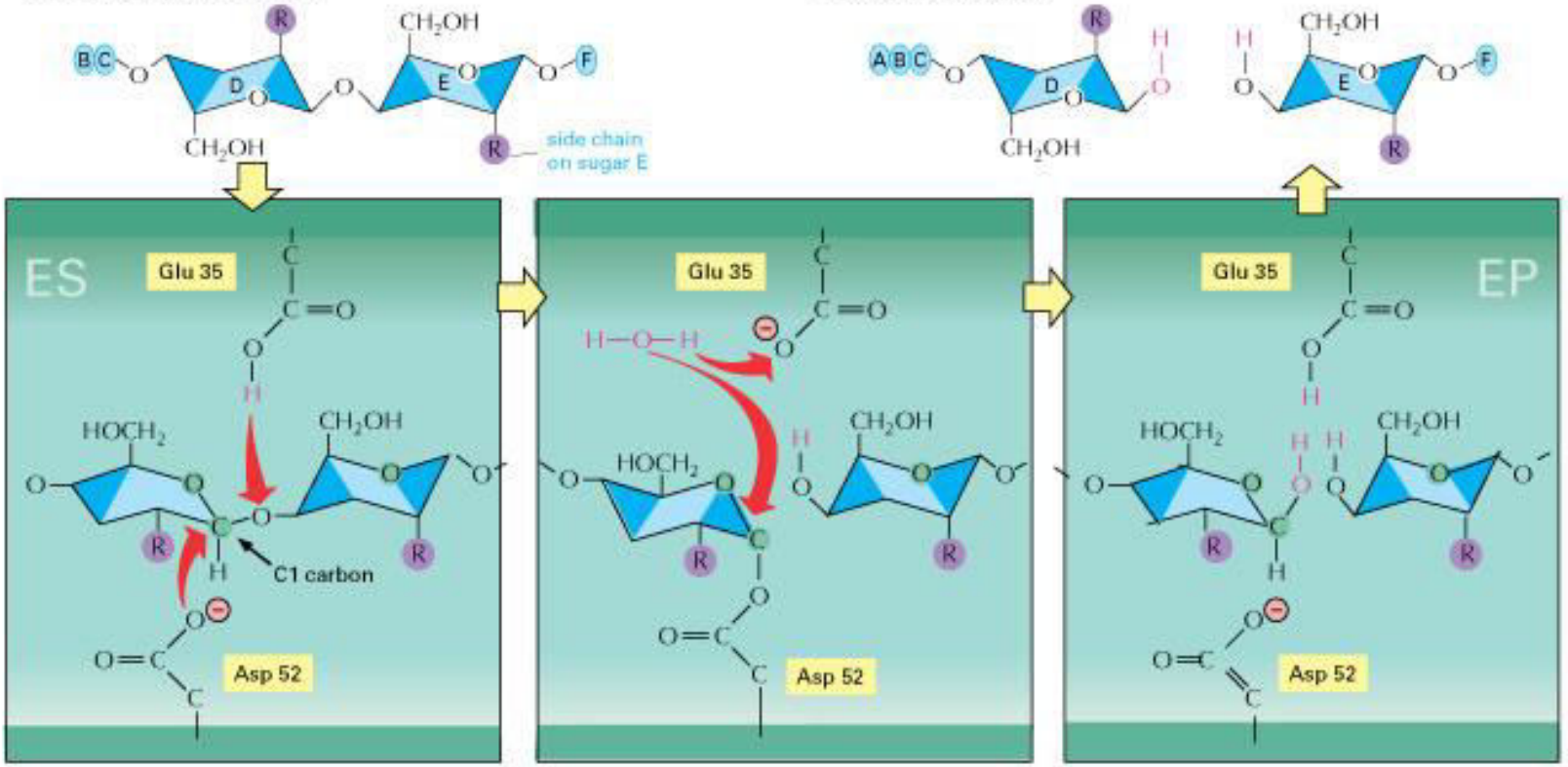
Figure 4-33 Essential Cell Biology, 2/e. (© 2004 Garland Science)

substrate

This substrate is an oligosaccharide of six sugars, labeled A–F. Only sugars D and E are shown in detail.

products

The final products are an oligosaccharide of four sugars (*left*) and a disaccharide (*right*), produced by hydrolysis.



In the enzyme–substrate complex (ES), the enzyme forces sugar D into a strained conformation, with Glu 35 positioned to serve as an acid that attacks the adjacent sugar–sugar bond by donating a proton (H^+) to sugar E, and Asp 52 poised to attack the C1 carbon atom.

The Asp 52 has formed a covalent bond between the enzyme and the C1 carbon atom of sugar D. The Glu 35 then polarizes a water molecule (*red*), so that its oxygen can readily attack the C1 carbon atom and displace Asp 52.

The reaction of the water molecule (*red*, completes the hydrolysis and returns the enzyme to its initial state, forming the final enzyme–product complex (EP).

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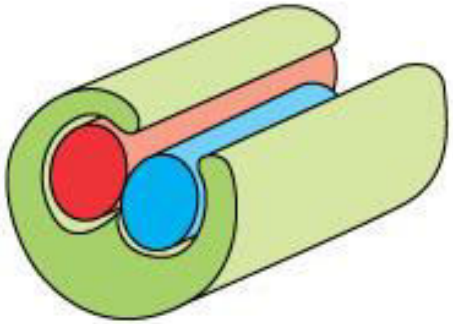
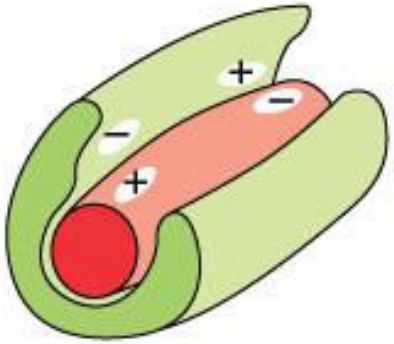
(A)



enzyme binds to two substrate molecules and orients them precisely to encourage a reaction to occur between them

(B)



binding of substrate to enzyme rearranges electrons in the substrate, creating partial negative and positive charges that favor a reaction

(C)

enzyme strains the bound substrate molecule, forcing it toward a transition state to favor a reaction

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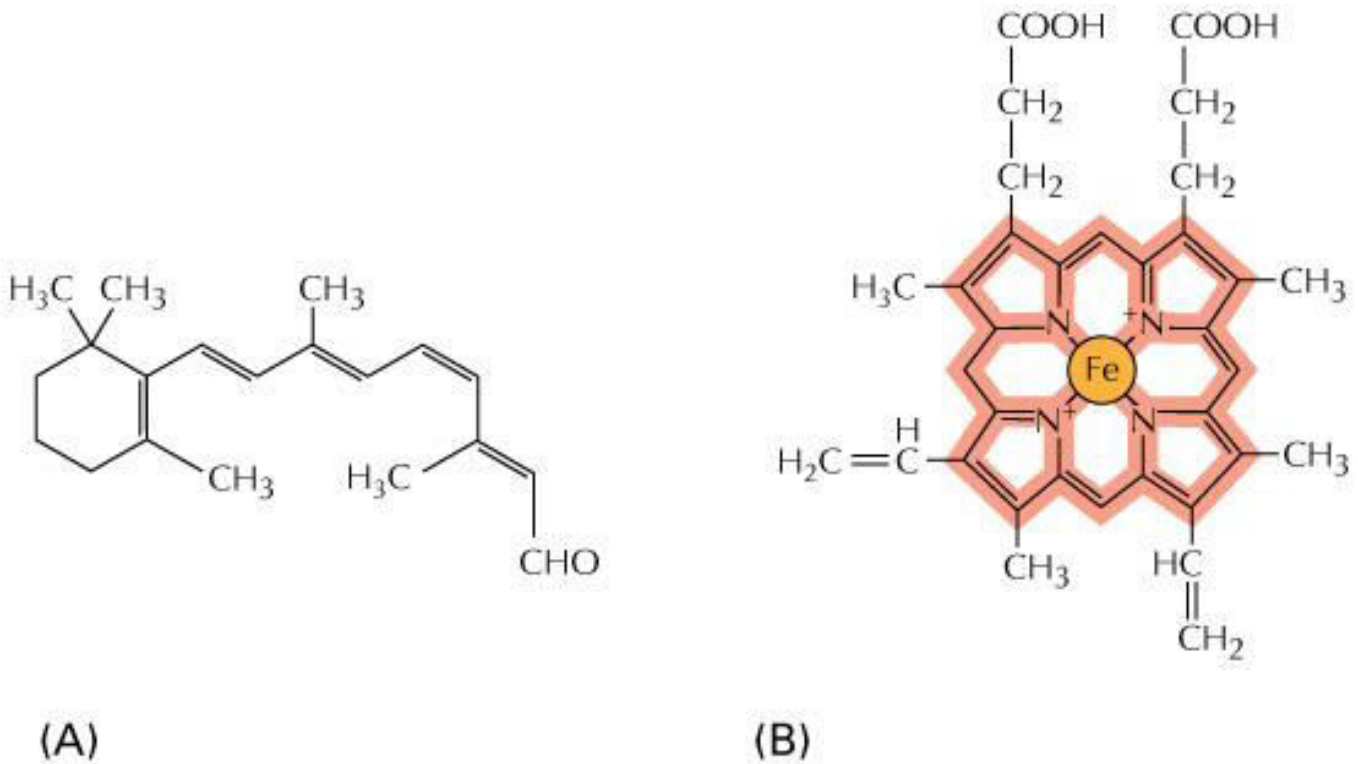

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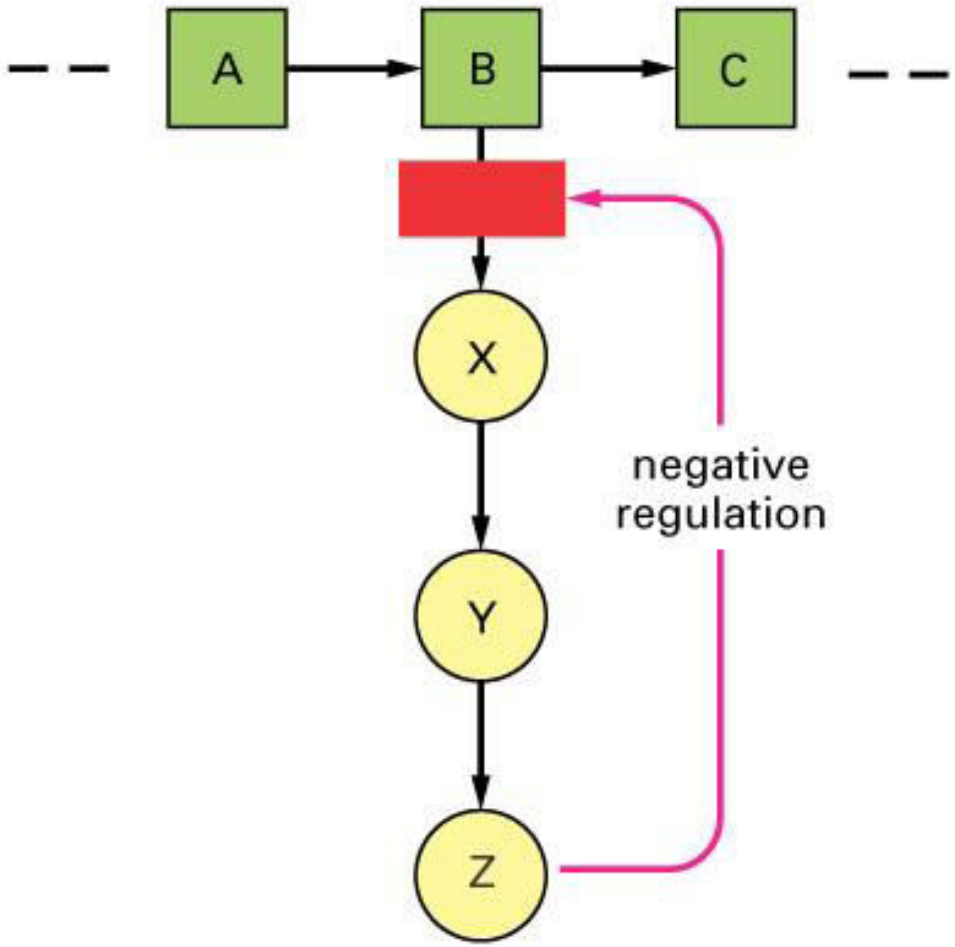

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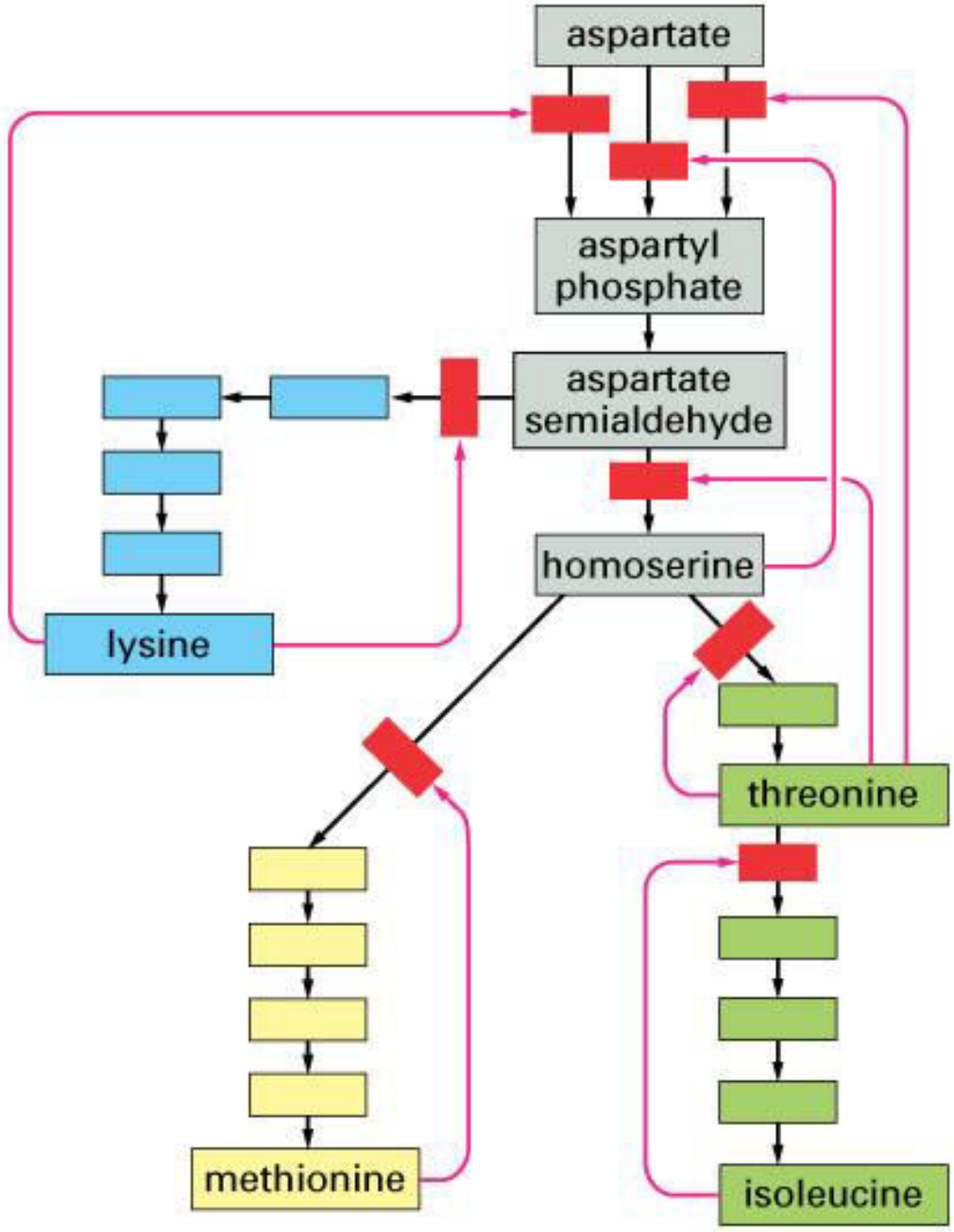

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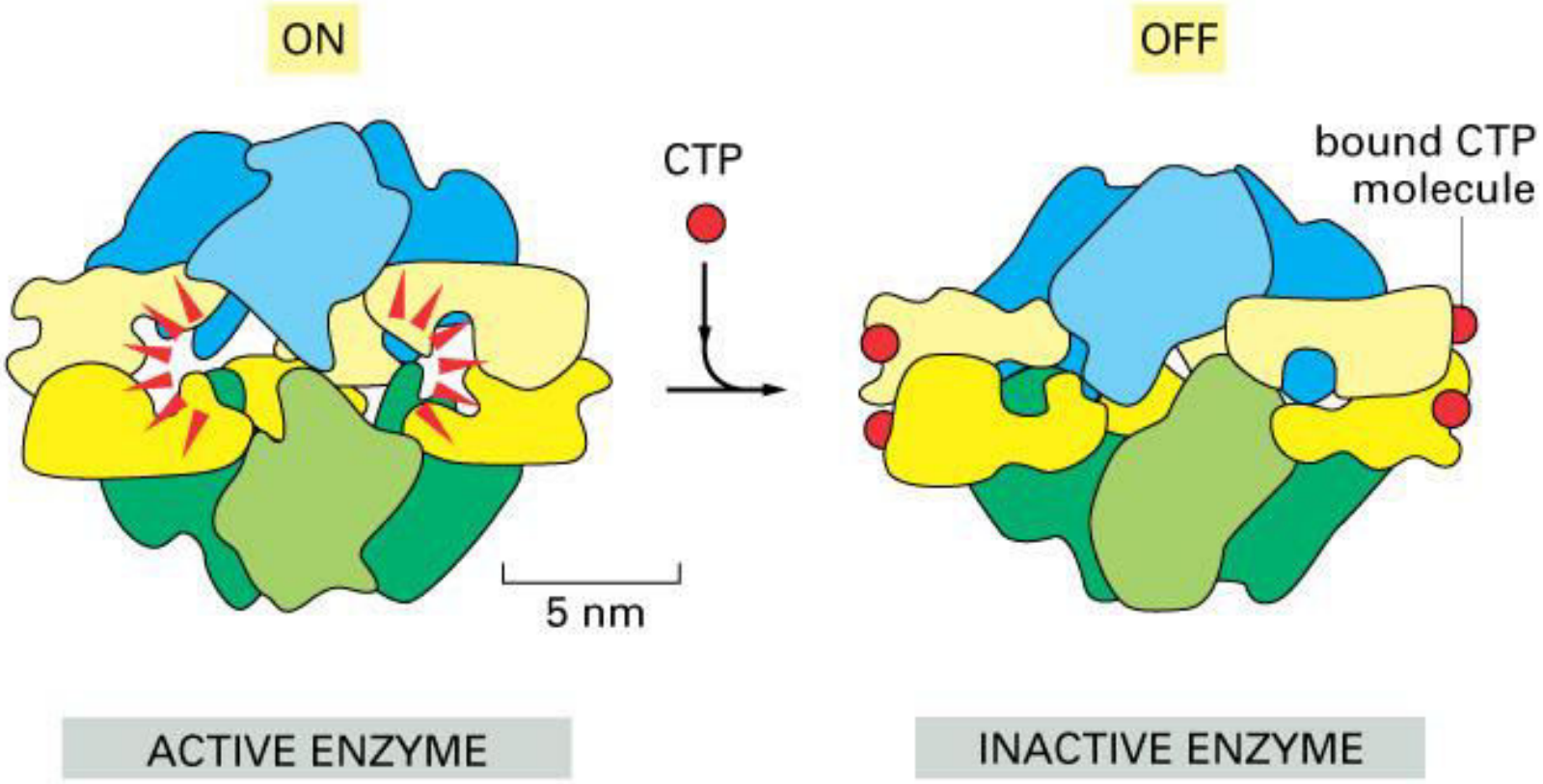

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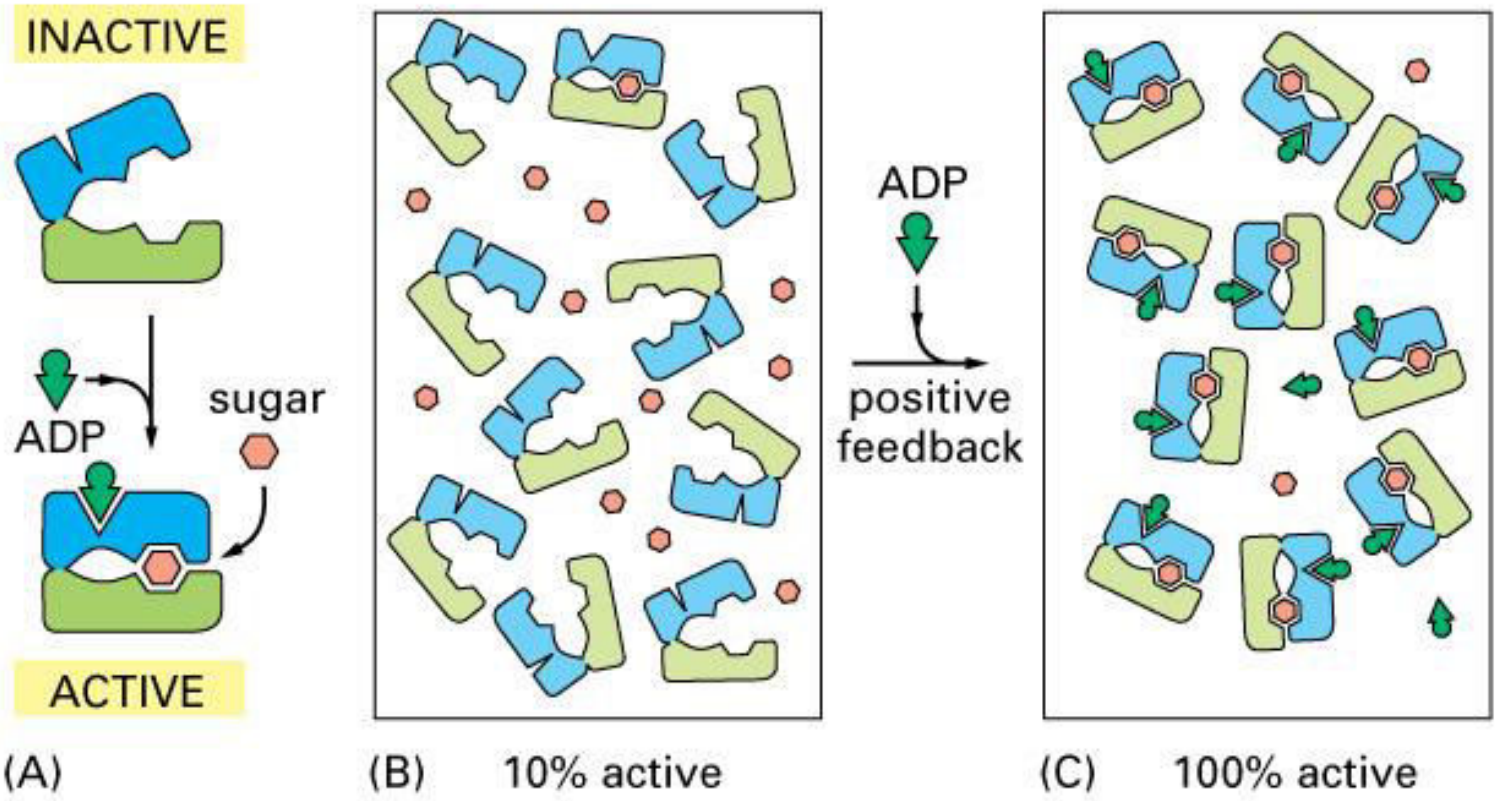

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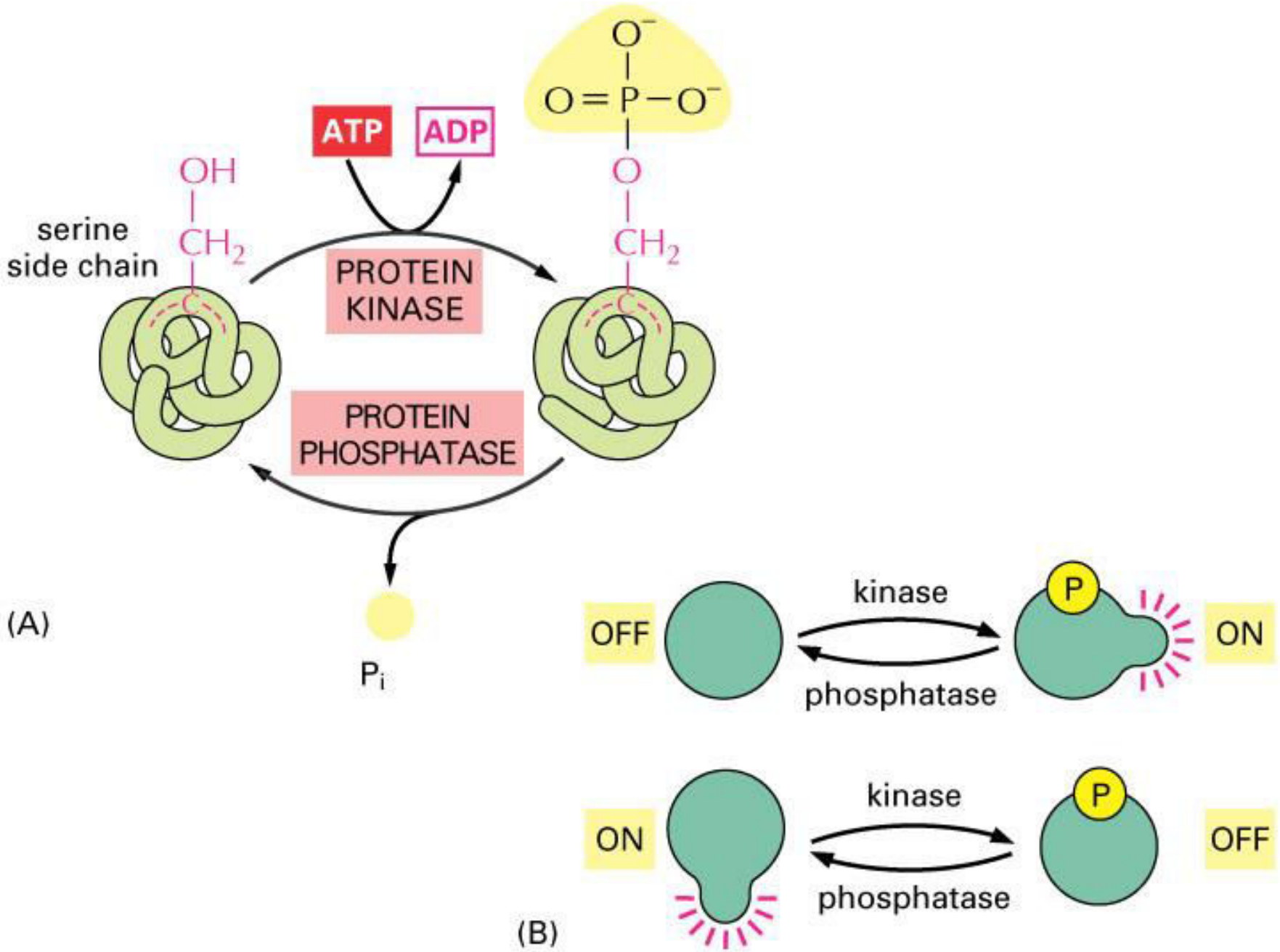

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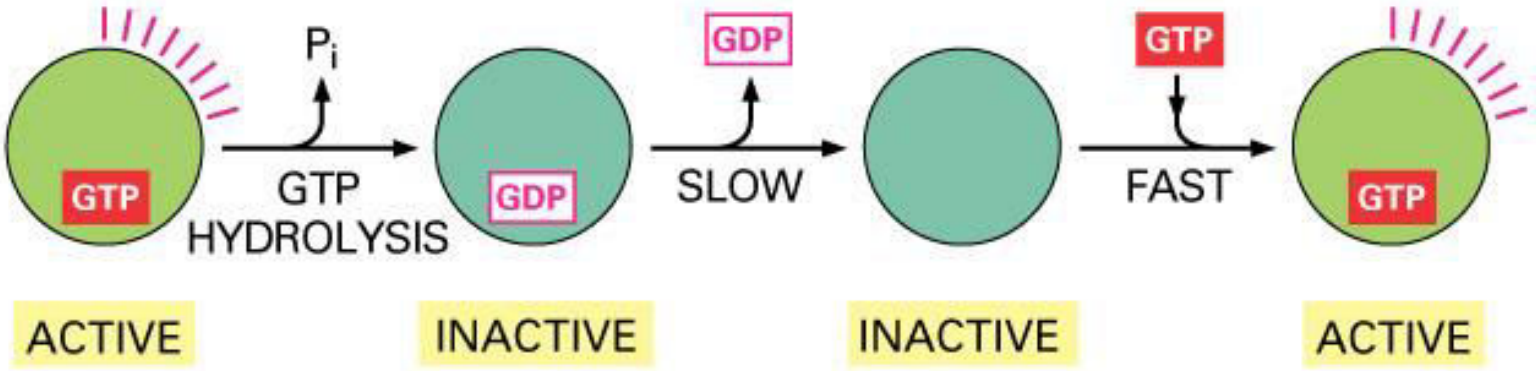

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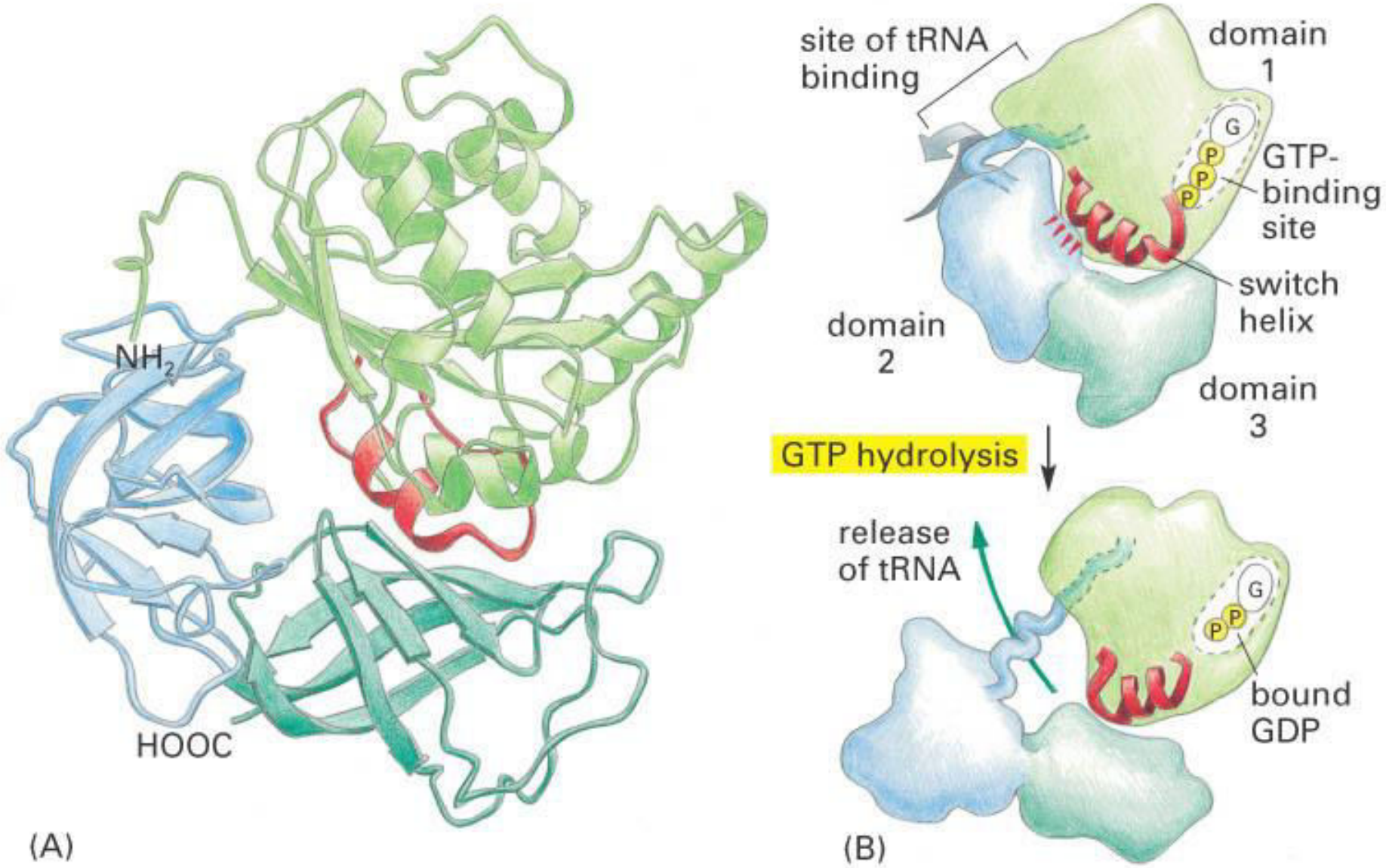

Figure 4-43 Essential Cell Biology, 2/e. (© 2004 Garland Science)

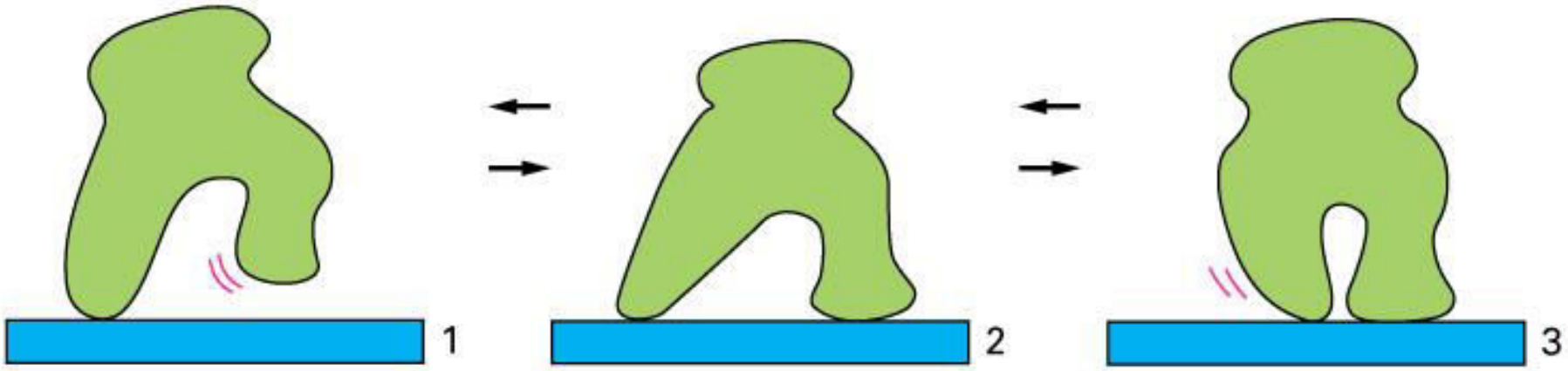

Figure 4-44 Essential Cell Biology, 2/e. (© 2004 Garland Science)

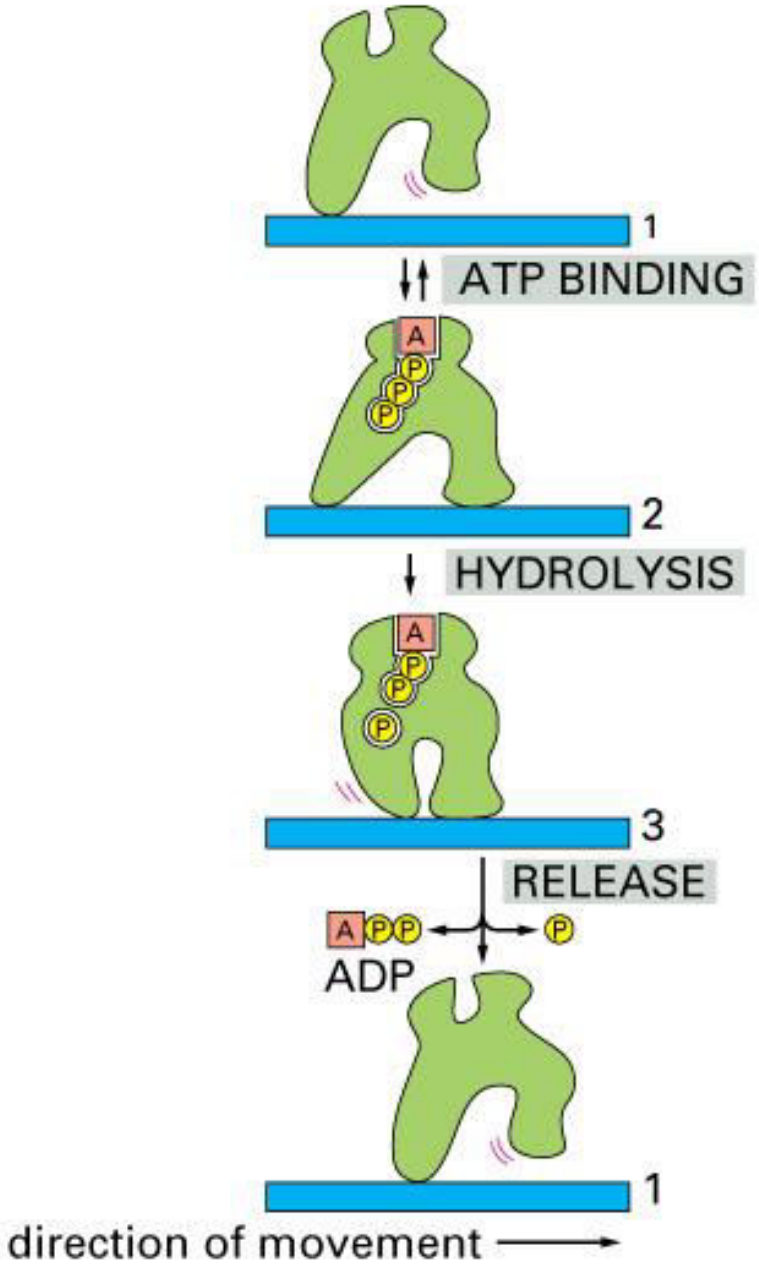

Figure 4-45 Essential Cell Biology, 2/e. (© 2004 Garland Science)

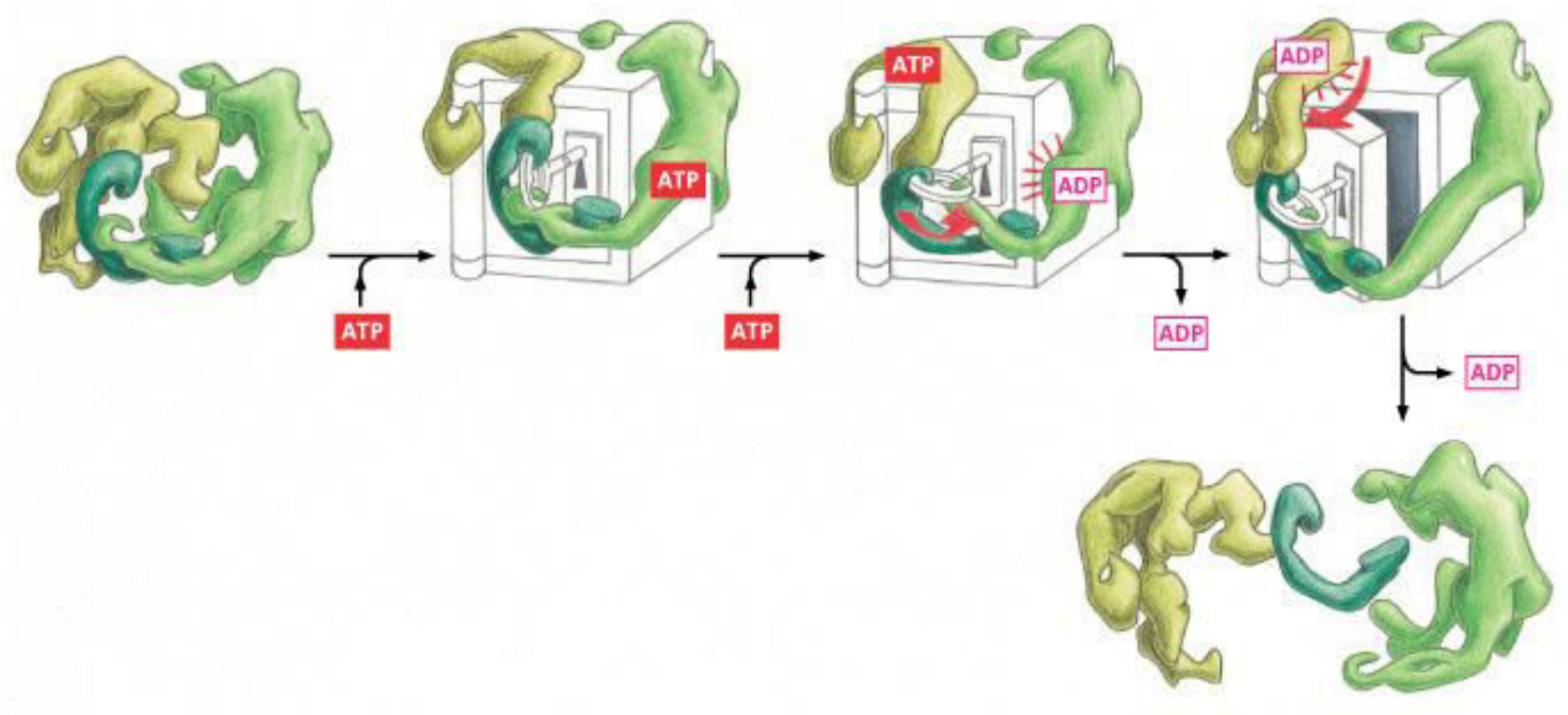

Figure 4-46 Essential Cell Biology, 2/e. (© 2004 Garland Science)