Intracellular Vesicular Traffic

Every CELL must:

- **EAT**

  COMMUNICATE

- **RESPOND.**

HOW? The CELL *add/remove* transmembrane proteins:

- ***Receptors;***
- ***Ion channels;***
- ***Transporters.***

MEANS? - Elaborate internal membrane system!

ENDOCYTIC and BIOSYNTHETIC-SECRETORY pathways that envolves the ER and Golgi apparatus.

The endocytic and biosynthetic-secretory pathways

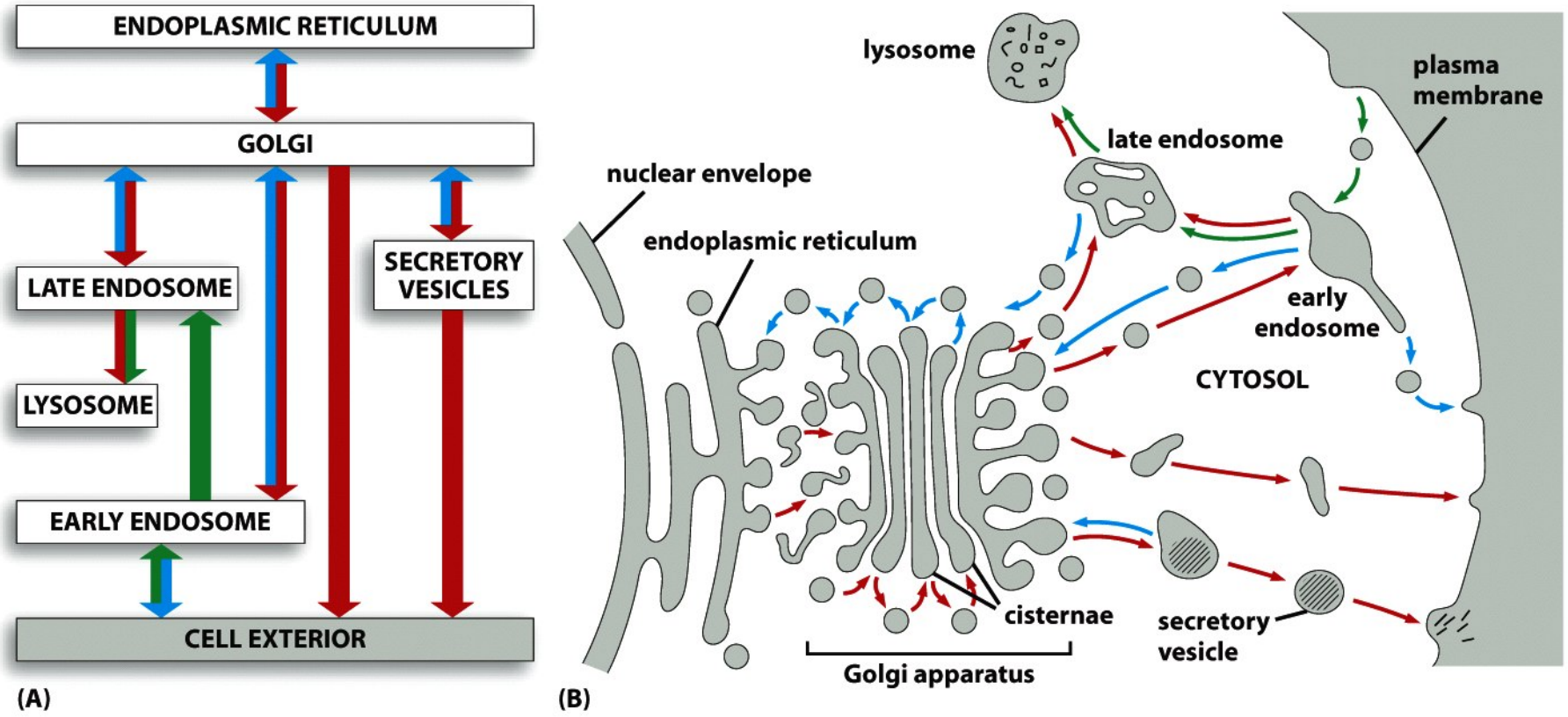


Figure 13-3 *Molecular Biology of the Cell* (© Garland Science 2008)

Different compartments;

Directed and selective transport of particular components from one membrane-enclosed compartment to another.

ISSUES

- ten or more chemically distinct, membrane-enclosed compartments;

- Transporters – vesicles;

- the vesicles MUST fuse only with the correct compartment!

How to find the DESTINATION?

SOLUTION:

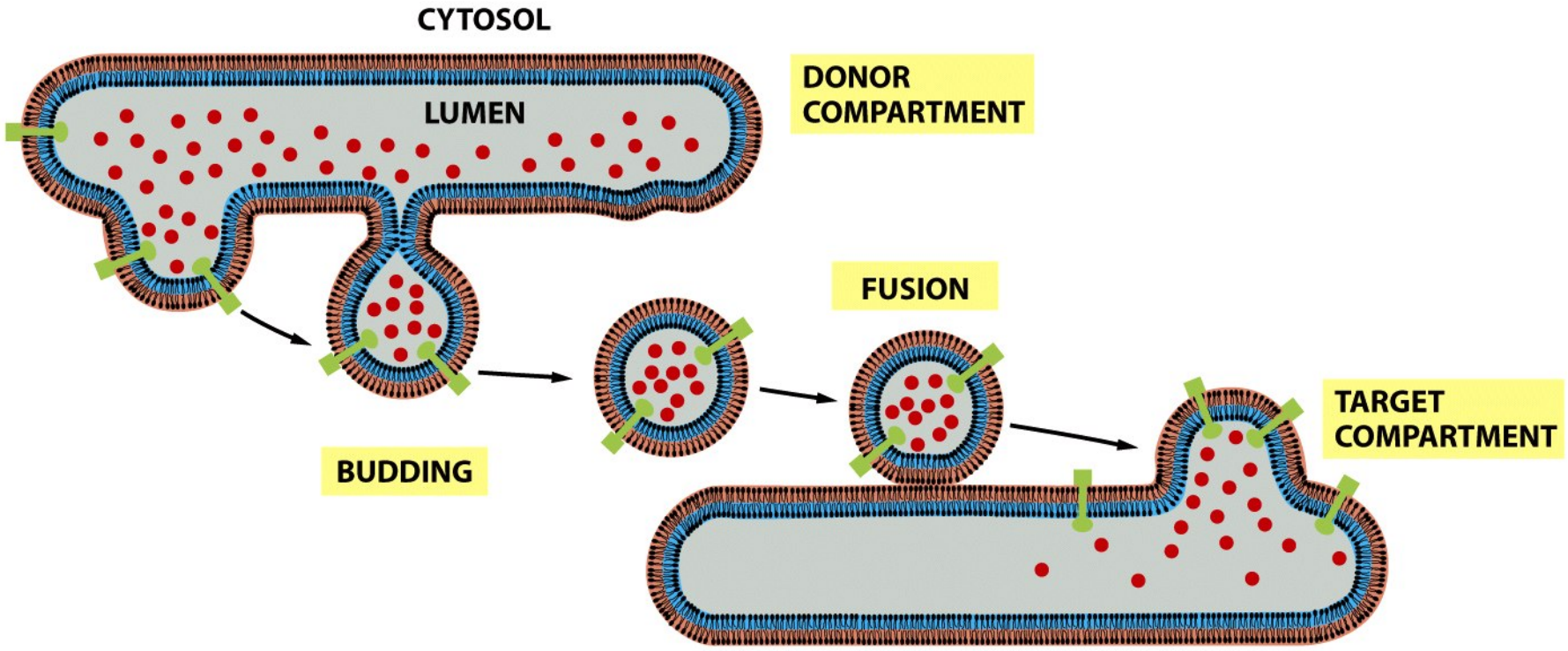
- a specific combination of marker molecules that gives each compartment its unique molecular address.

Key terms:

- Donor&acceptor compartments;

- Transport vesicles;

- Cargo.



Transport vesicles:

- *can be spherical, tubular, or irregularly shaped;*
- *bud from specialized coated regions of the donor membrane.*
- *the assembly of the coat:*
  - ✓ *helps to collect specific membrane and soluble cargo molecules for transport;*
  - ✓ *drive the formation of the vesicle.*

Transport vesicles:

- types of coated vesicles:

- ✓ ***Clathrin-coated - mediate transport from the plasma membrane and the trans Golgi network;***
- ✓ ***COPI (COat Protein) and COPII-coated - mediate transport between Golgi cisternae and between the ER and the Golgi apparatus, respectively.***

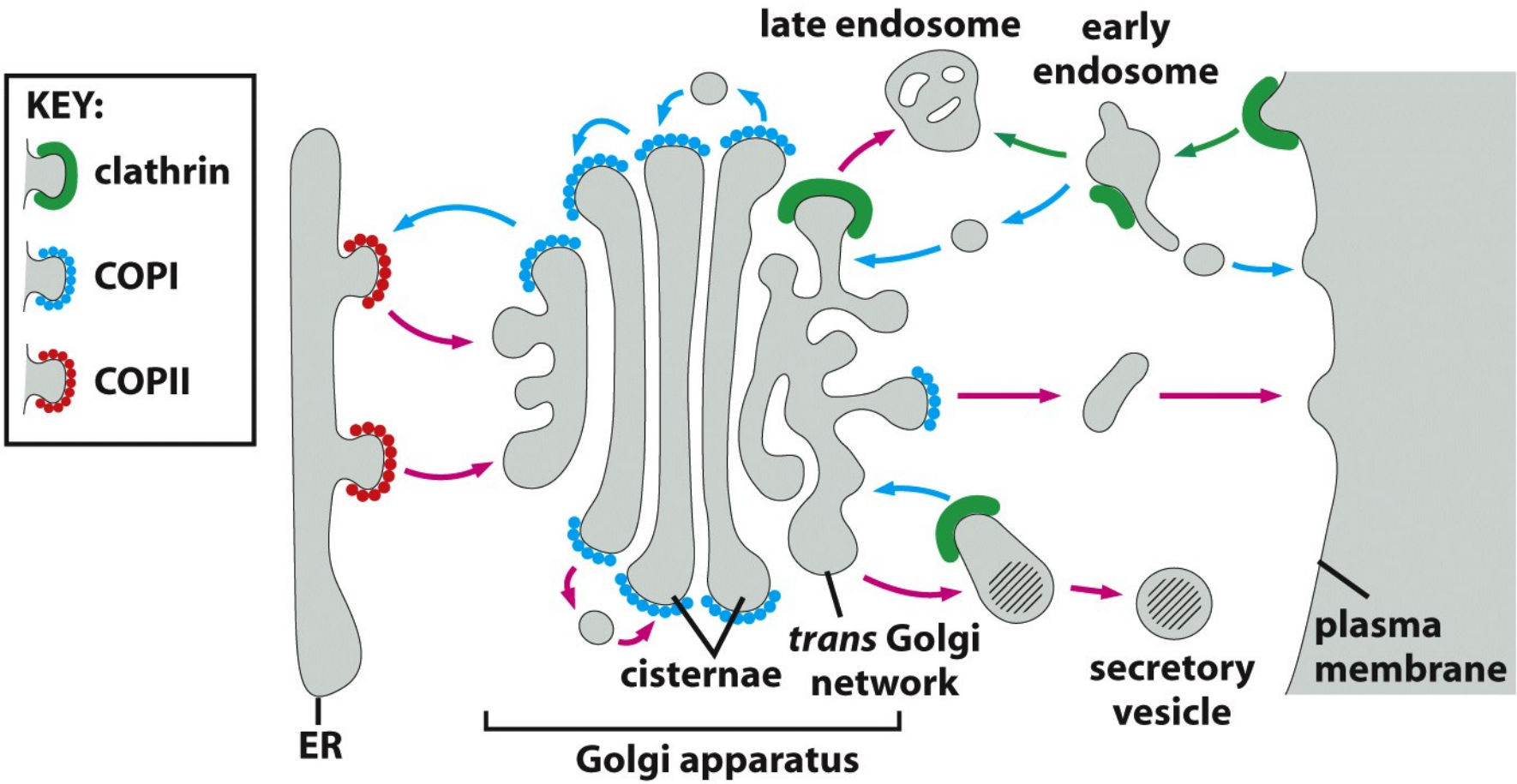


Figure 13-5 *Molecular Biology of the Cell* (© Garland Science 2008)

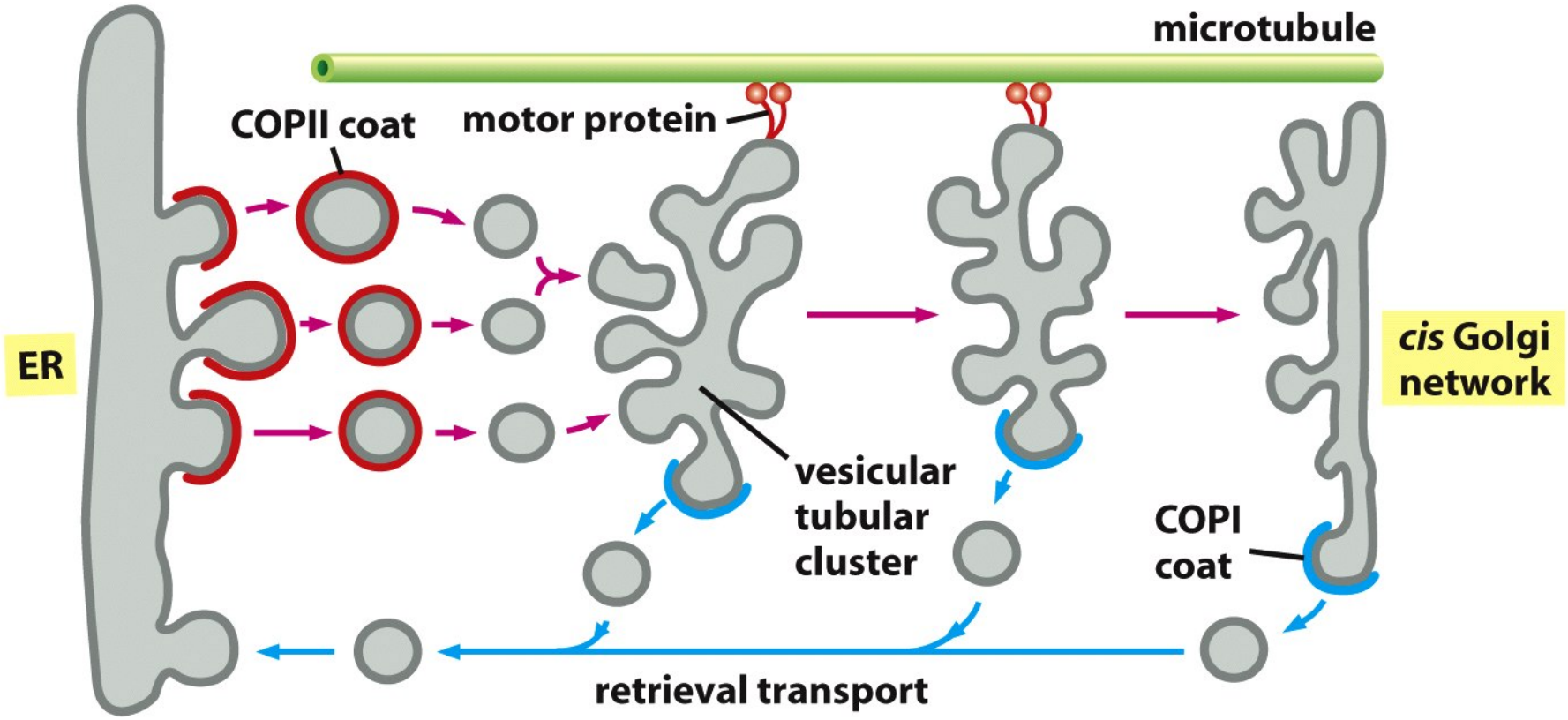


Figure 13-23b *Molecular Biology of the Cell* (© Garland Science 2008)

Coated Vesicles:

- have a distinctive cage of proteins covering their citosolic surface;

- before the vesicles fuse with a target membrane, they discard their coat, as is required for the two citosolic membrane surfaces to interact directly and fuse;

- coat proteins: clathrin-coated, COPI-coated, and COPII-coated.

ENDOCYTOSIS

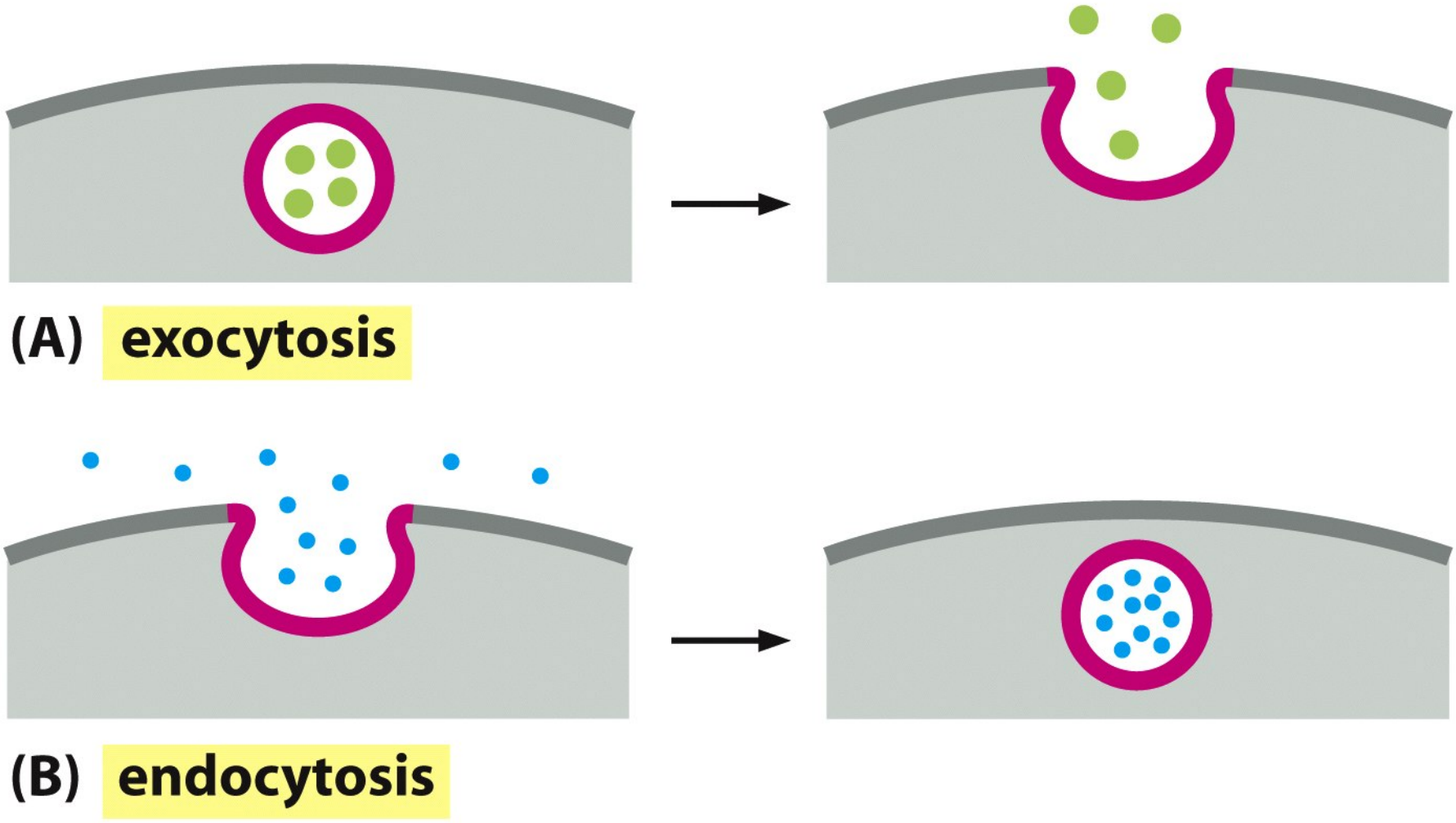


Figure 13-1 *Molecular Biology of the Cell* (© Garland Science 2008)

ENDOCYTOSIS

The process by which cells take up macromolecules, particulate substances, and, in specialized cases, even other cells.

Uptake of material into a cell by an invagination of the plasma membrane and its internalization in a membrane-bounded vesicle.

ENDOCYTOSIS

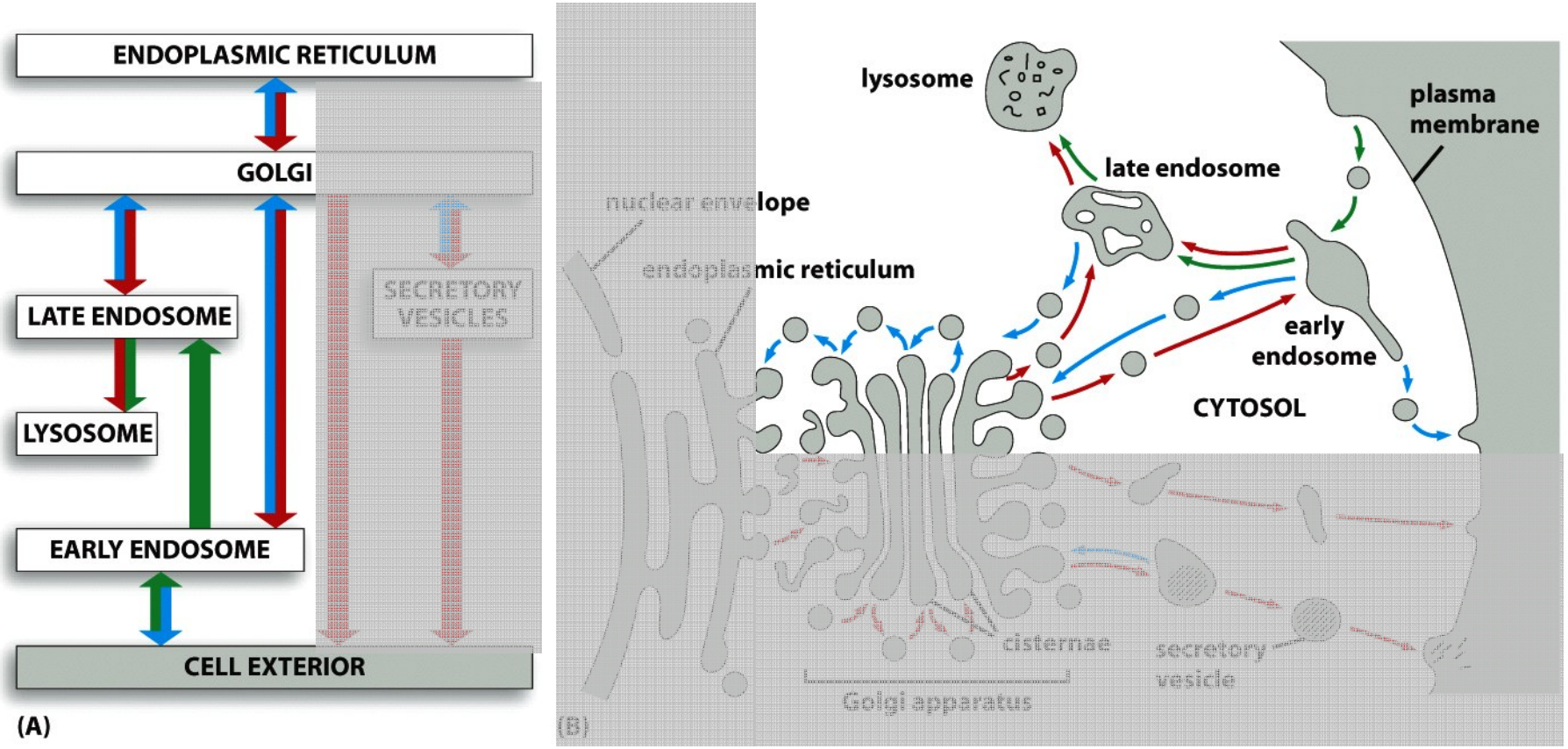
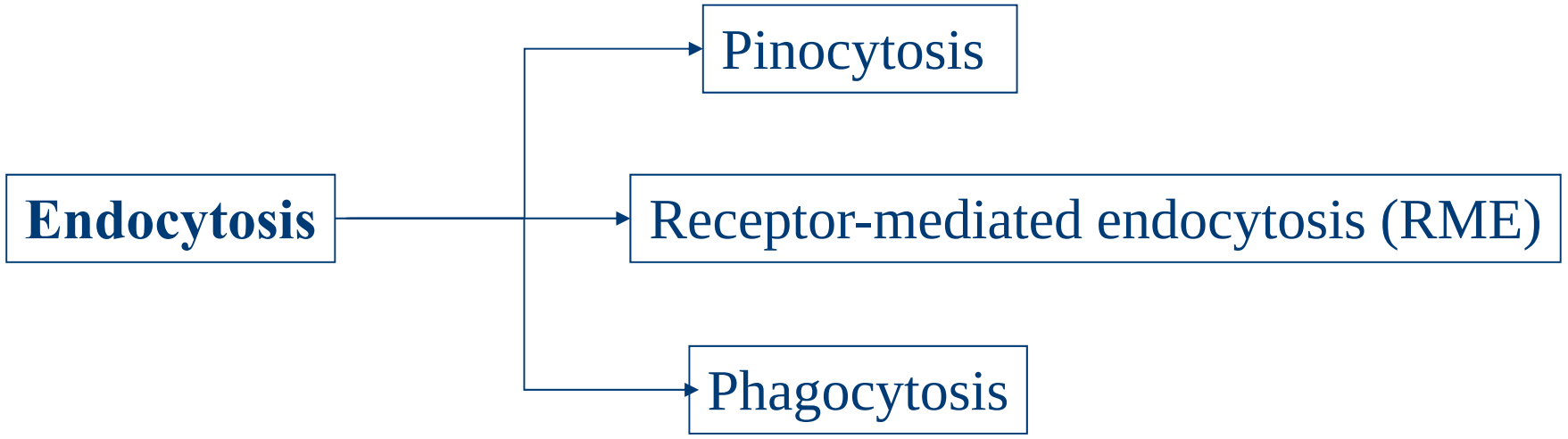


Figure 13-3 *Molecular Biology of the Cell* (© Garland Science 2008)

Ingestion by the endocytic pathway

Molecules and large bodies such as dead cells, cell debris, bacteria, viruses, etc.



VESICULAR TRANSPORT

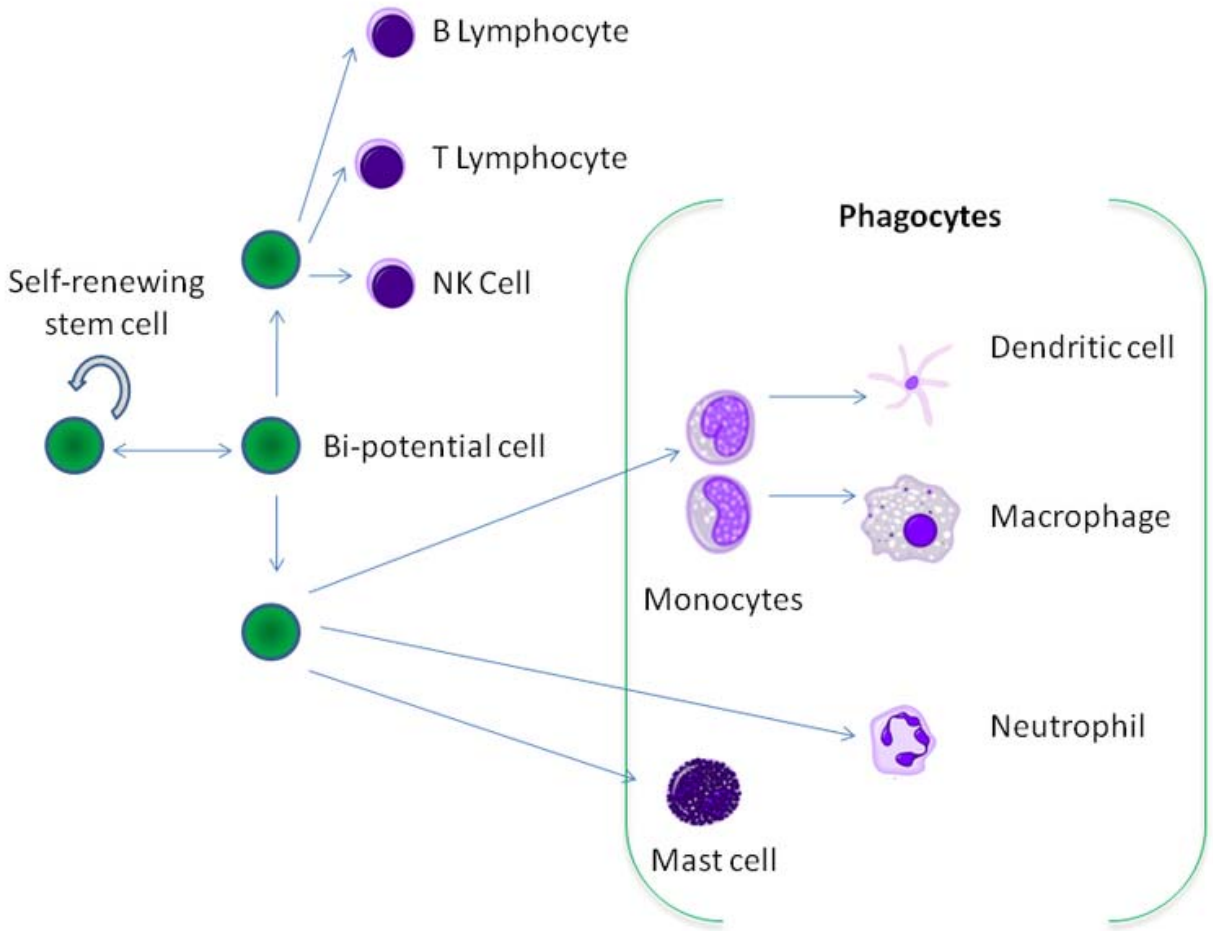
Endocytosis - distinguished on the basis of the size of the endocytic vesicles formed:

- **PINOCYTOSIS ("cell-drinking", "fluid endocytosis") - involves the ingestion of fluid and solutes via small pinocytic vesicles (about 100 nm in diameter)**
- **PHAGOCYTOSIS (“cellular eating”) - ingestion of large particles, such as microorganisms or dead cells via large vesicles called phagosomes (generally >250 nm in diameter).**
- **ENDOCYTOSIS - ingestion of smaller (than phagosome) particles**

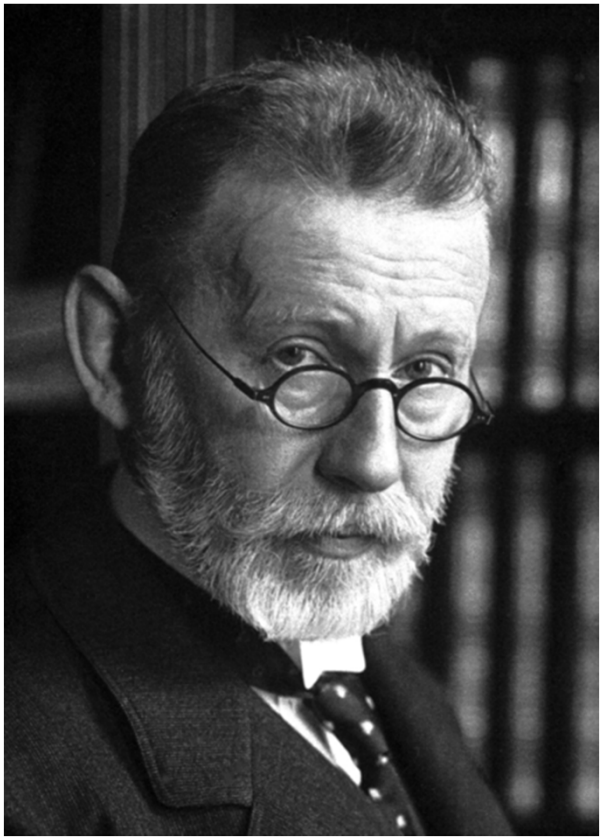
PHAGOCYTOSIS

PHAGOCYTOSIS – roles:

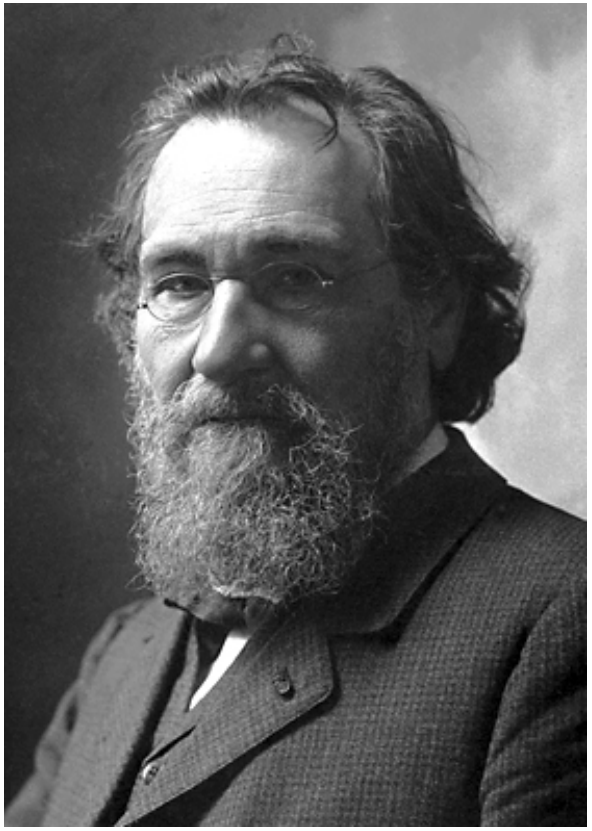
- immune defense against pathogens;
- removal of senescent cells and cells that have died by apoptosis



PHAGOCYTOSIS - Nobel Prize in Medicine in 1908



Paul Ehrlich



Ilya Ilyich Mechnikov

PHAGOCYTOSIS - Ilya Ilyich Mechnikov

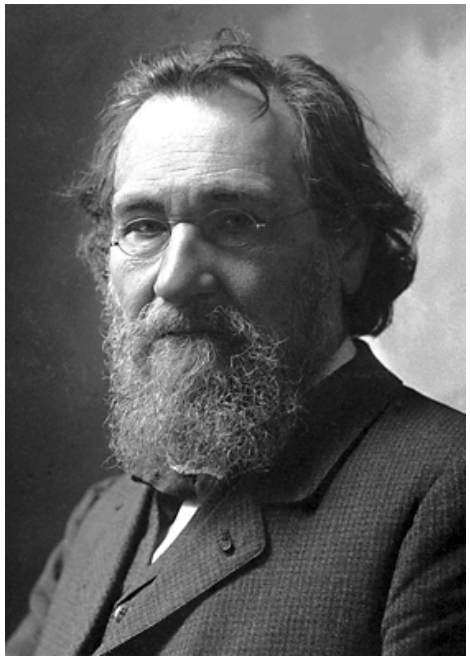
- born in Ukraine, Russian Empire;

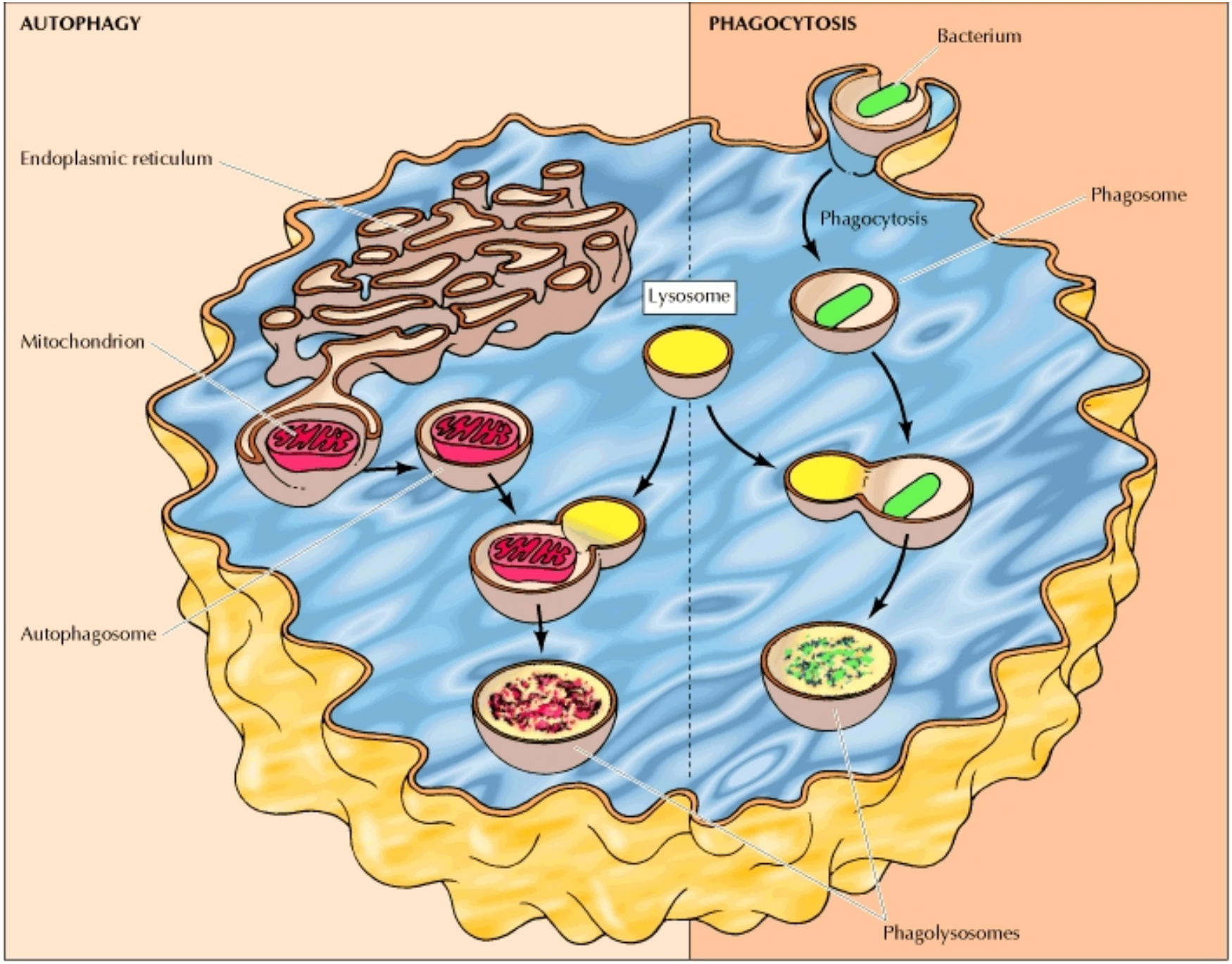
- maternal grandfather the first Russo-Jewish writer;

- Mechnikov is a translation from Romanian, since his father was a descendant of the Chancellor Yuri Stefanovich, the grandson of Nicolae Milescu – Spătar;

- The word "mech" is a Russian translation of the Romanian "spadă" (sword), which originated with Spătar;

- Nicolae Milescu - Spătar - second in rank in the army after the voivode.




AUTOPHAGY
PHAGOCYTOSIS
Bacterium
Endoplasmic reticulum
Phagocytosis
Phagosome
Lysosome
Mitochondrion
Autophagosome
Phagolysosomes

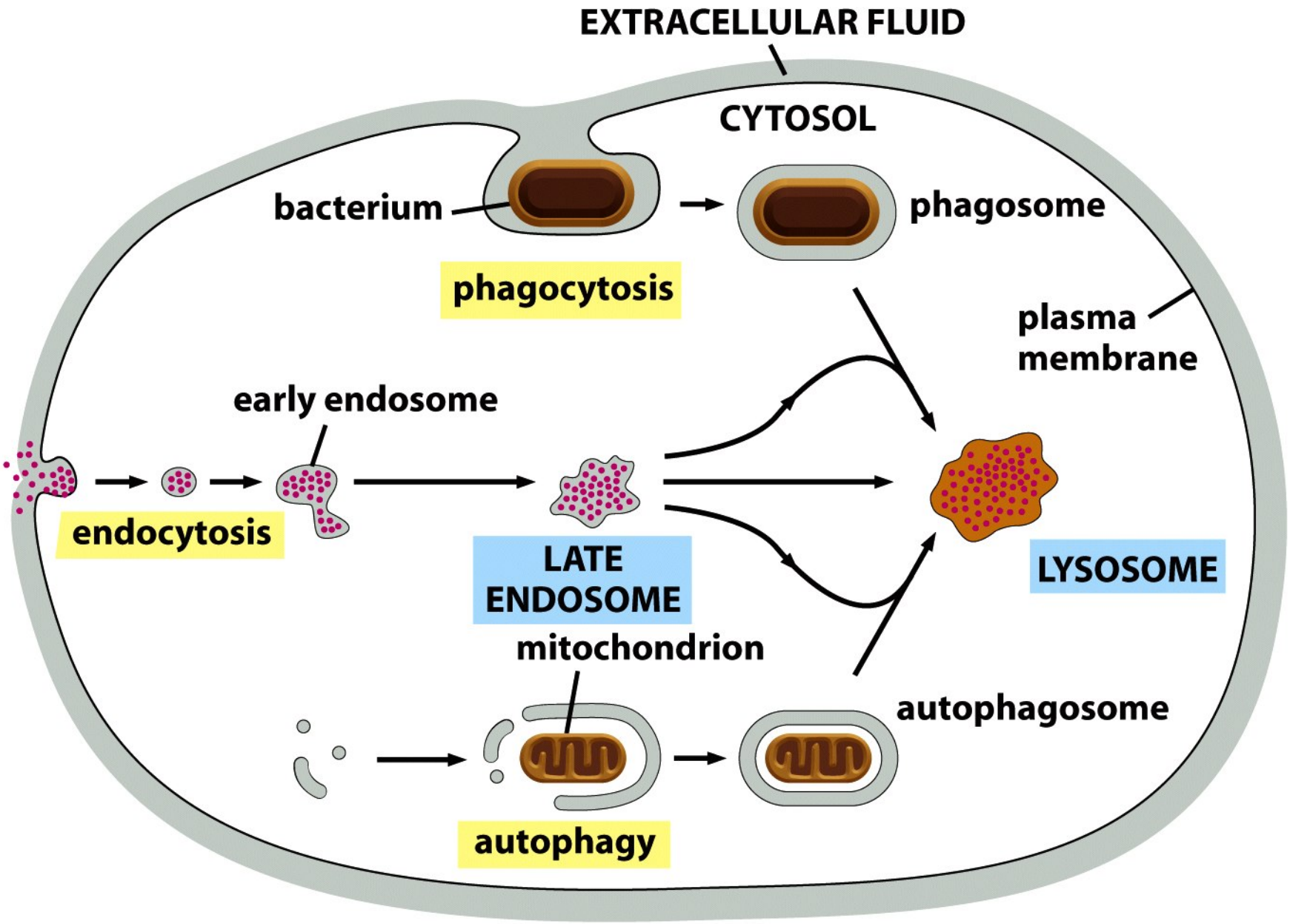


Figure 13-42a *Molecular Biology of the Cell* (© Garland Science 2008)

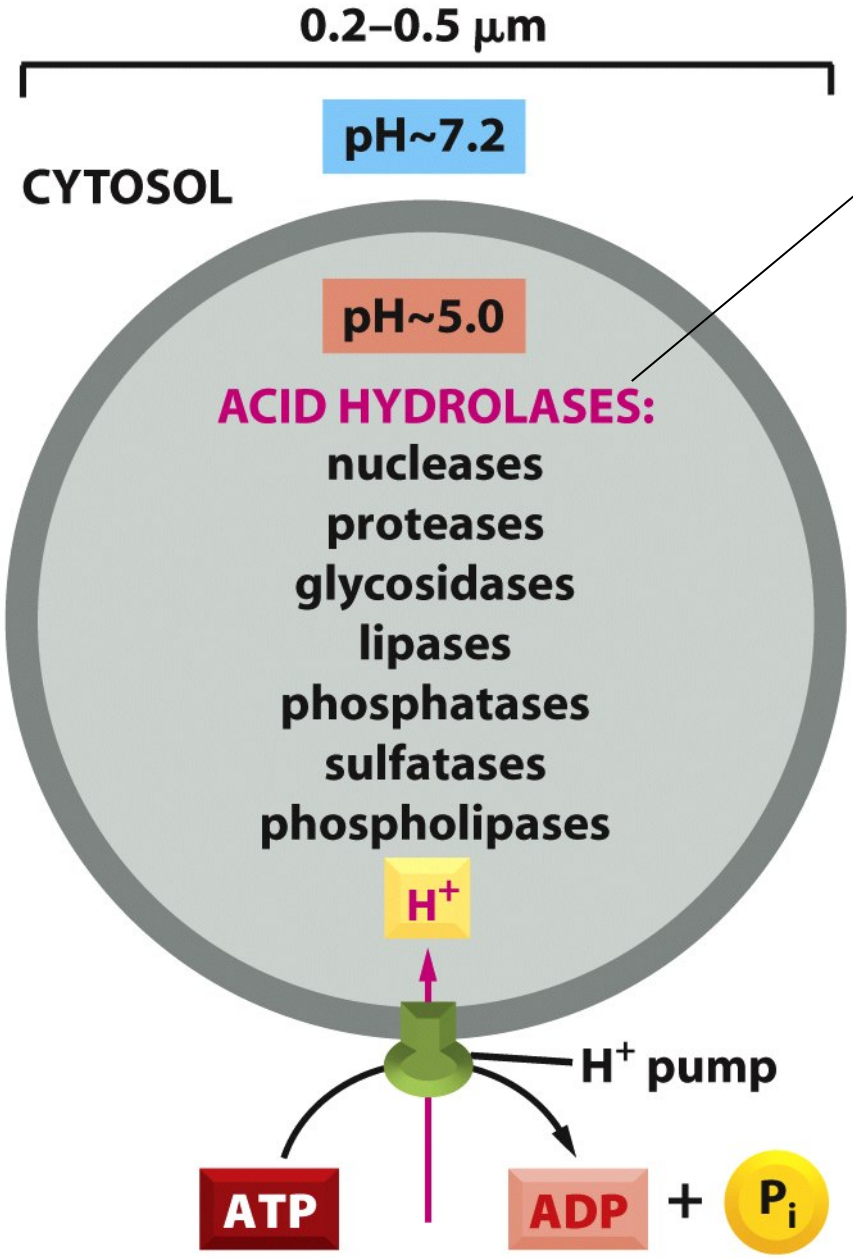
LYSOSOMES

- the principal site of intracellular digestion;

- about 40 types of hydrolytic enzymes (eg: proteases, nucleases, glycosidases, lipases, phospholipases, phosphatases, sulfatases);

- enzymes - acid hydrolases – activated by proteolytic cleavage at low pH (4.5-5).

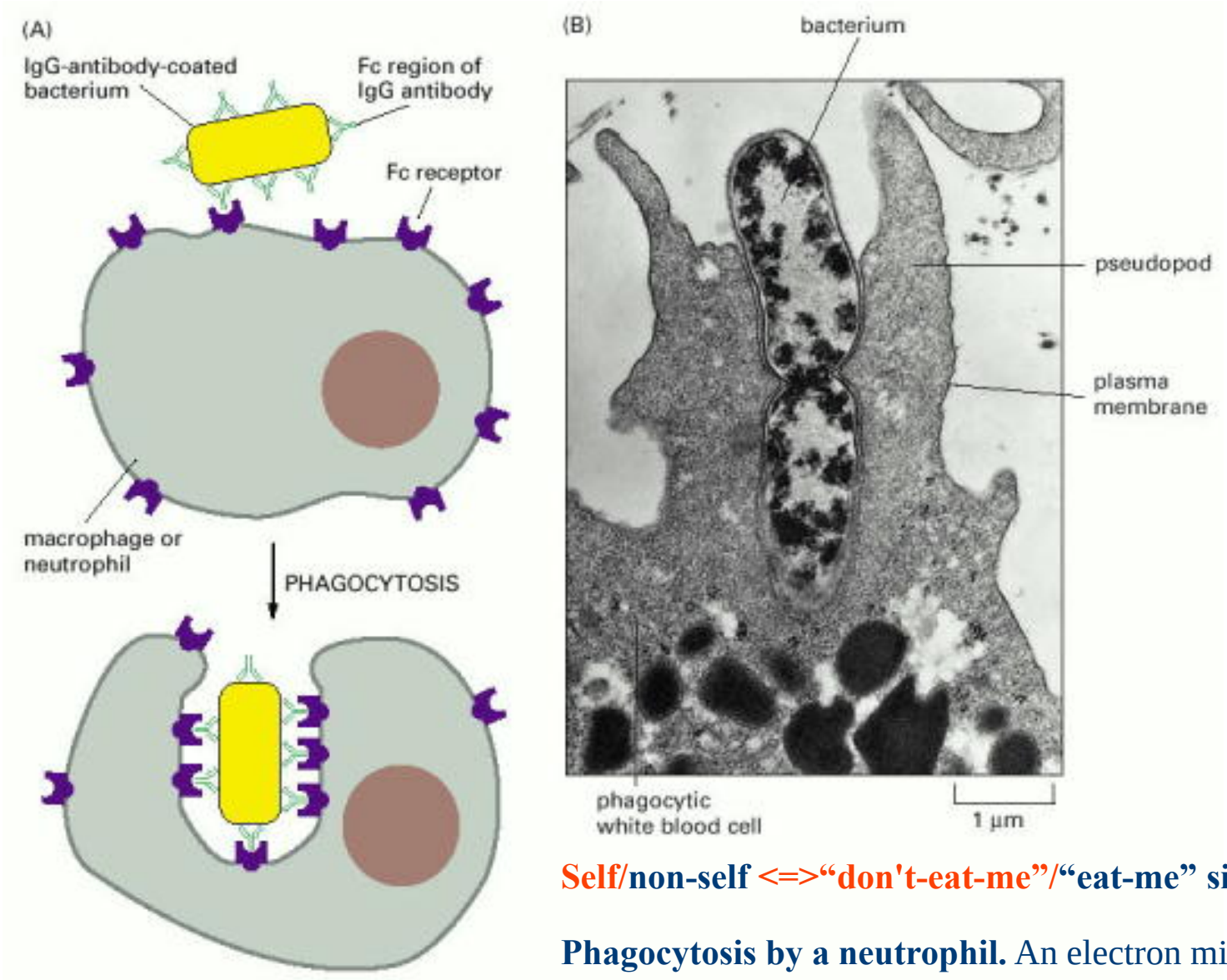
Cell – double protection against its own digestive system (mb+pH).



CYTOSOL

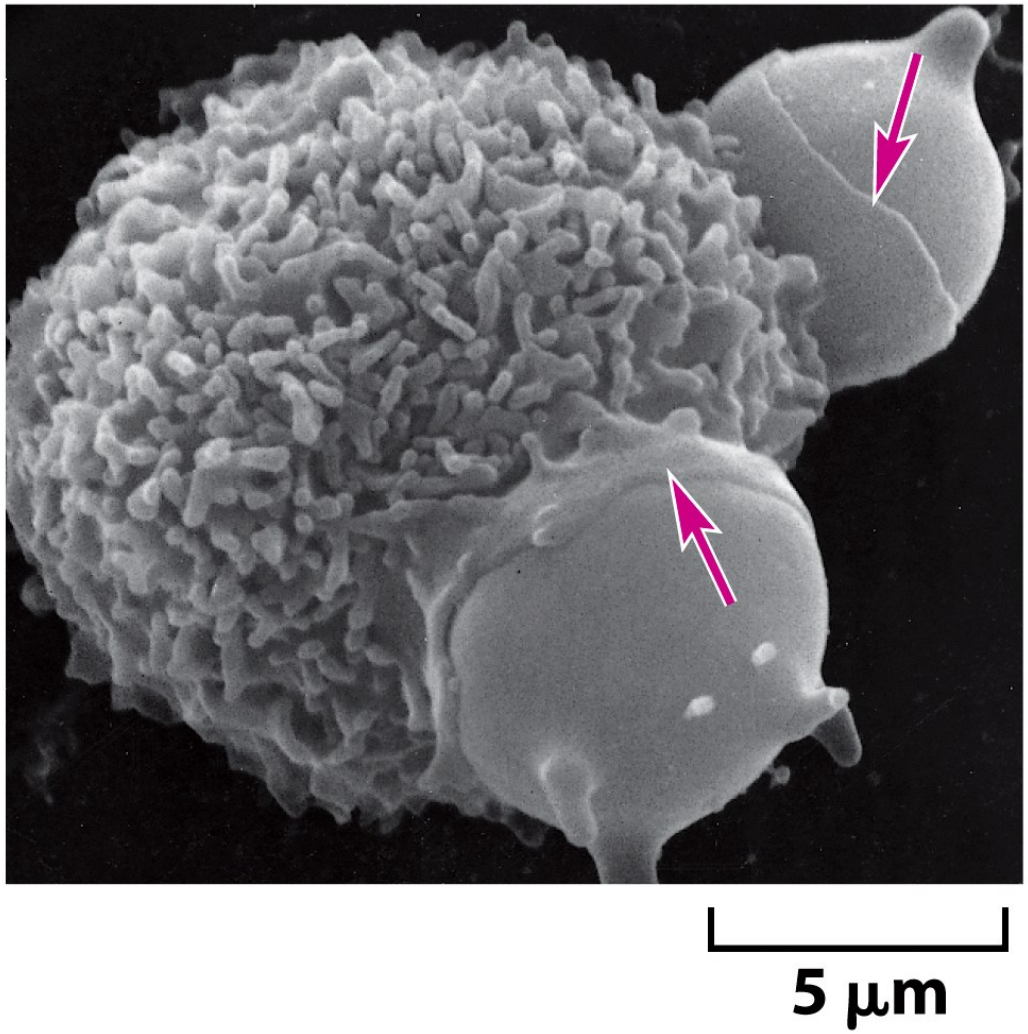
amino acids, sugars, and nucleotides

Figure 13-36 *Molecular Biology of the Cell* (© Garland Science 2008)



Self/non-self <=>"don't-eat-me"/"eat-me" signals

Phagocytosis by a neutrophil. An electron micrograph of a neutrophil phagocytosing a bacterium, which is in the process of dividing.



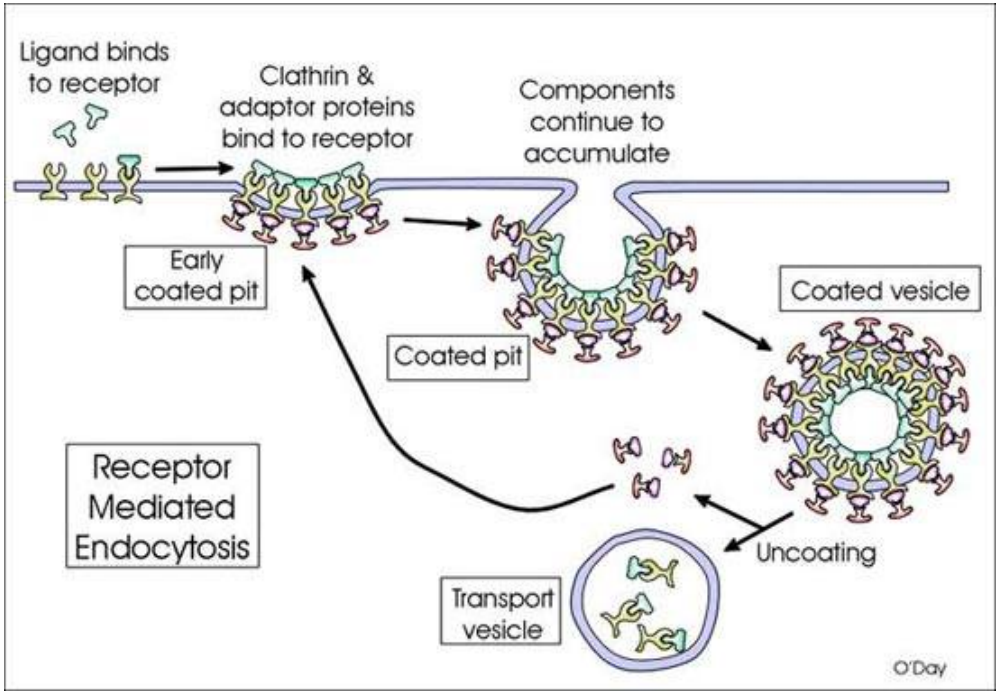
Self (but bad) <=>“eat-me”

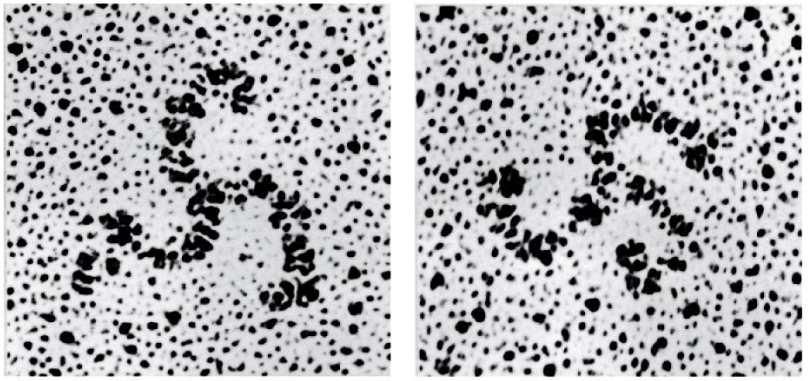
The self-signals are altered!!!

Phagocytosis by a macrophage. An electron micrograph of a **macrophage** phagocytizing two chemically altered RBC.

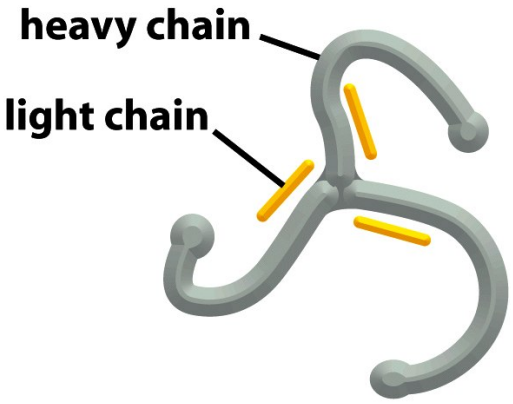
Figure 13-46 *Molecular Biology of the Cell* (© Garland Science 2008)

Uptake of Bacteria by Phagocytes





(A)



(B)

CLATHRIN-coated Vesicles:

- the major protein – clathrin;

- each clathrin subunit – three large and three small polypeptide chains => three-legged structure = triskelion;

- assemble into a basketlike convex framework => coated pits.

Receptor-mediated endocytosis (RME)

CLATHRIN-coated Vesicles:

- the major protein – clathrin;

- adaptor proteins:

– form a discrete second layer;

– bind the clathrin-coat to membrane;

– trap various transmembrane proteins (eg.: cargo receptors);

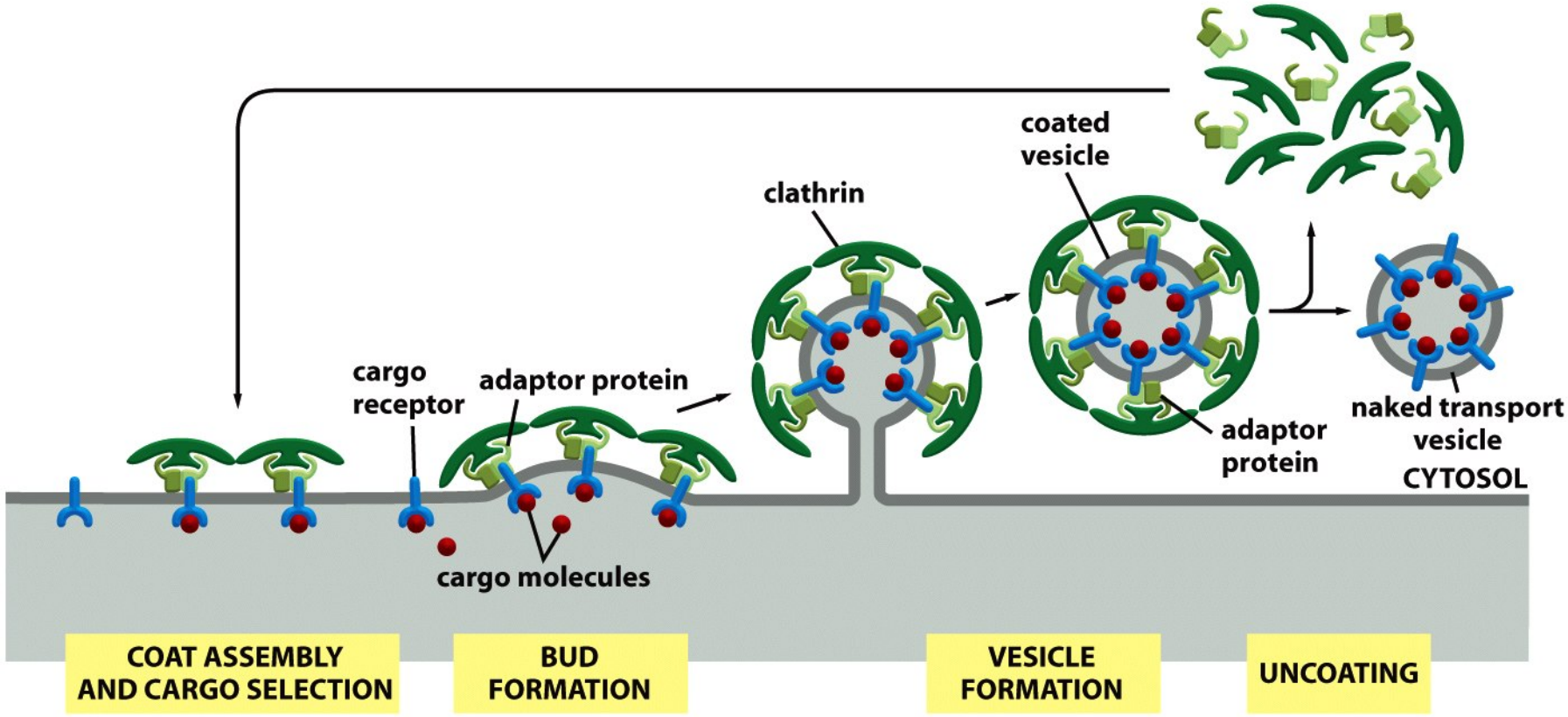


Figure 13-8 *Molecular Biology of the Cell* (© Garland Science 2008)

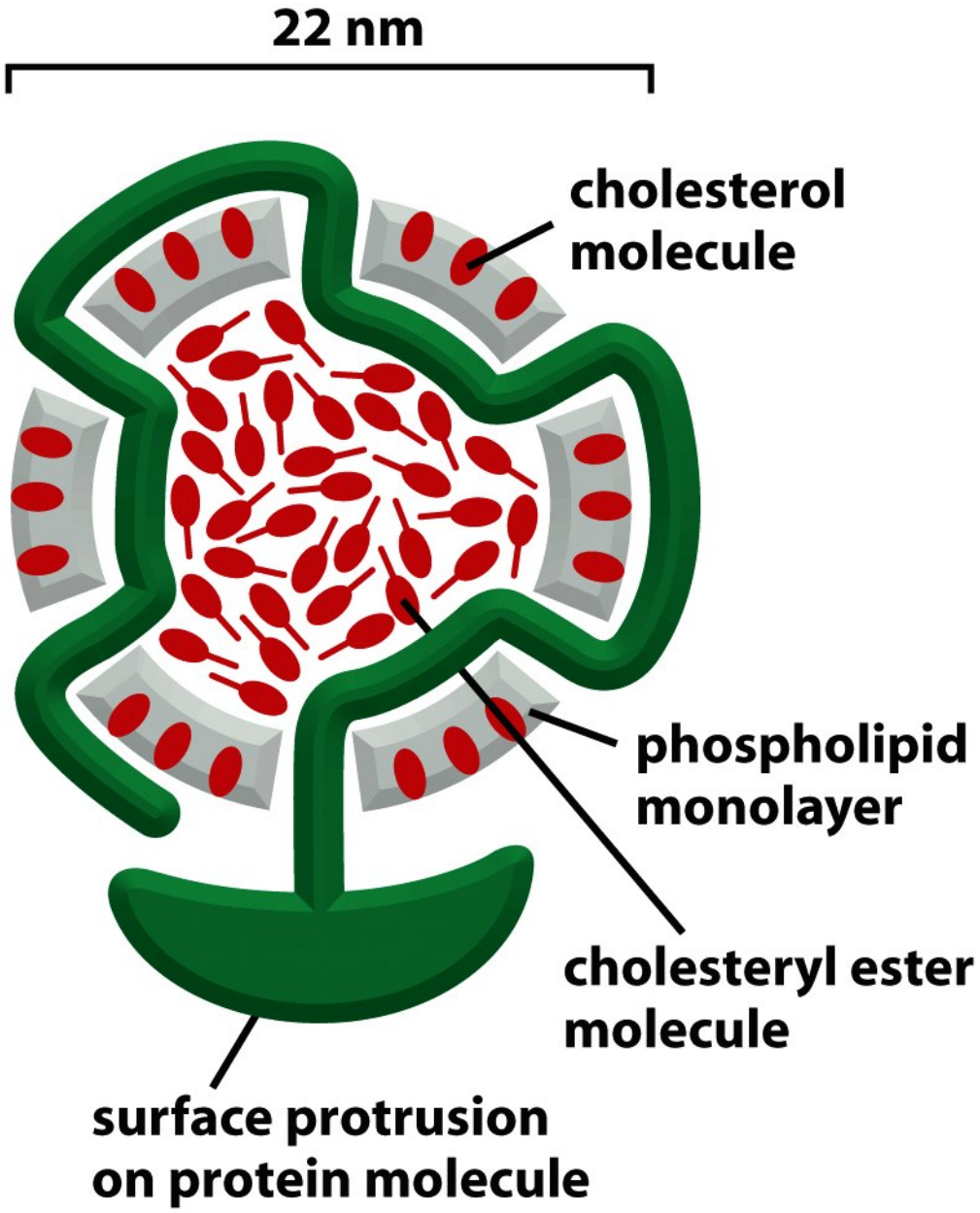


Figure 13-50 *Molecular Biology of the Cell* (© Garland Science 2008)

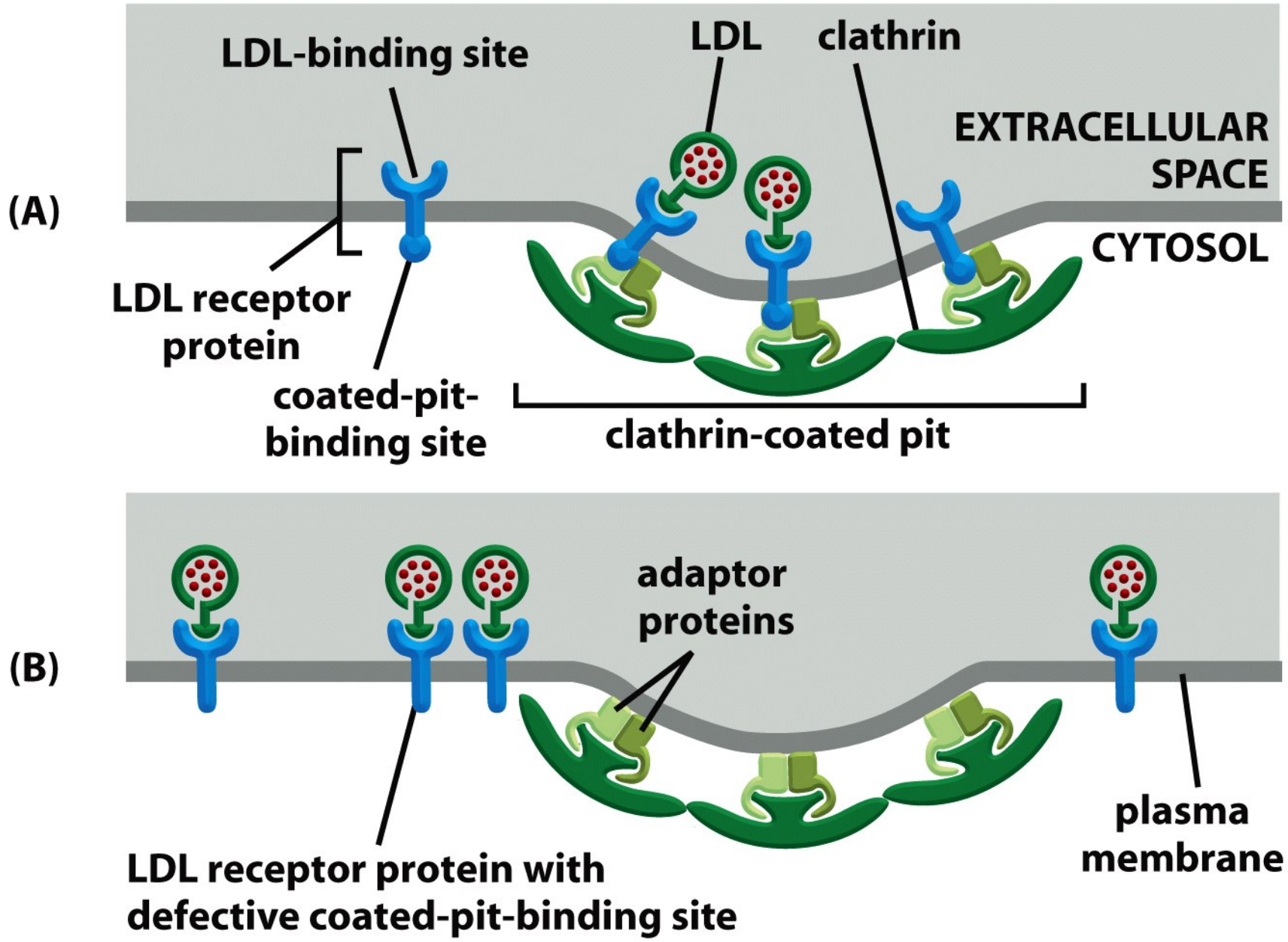
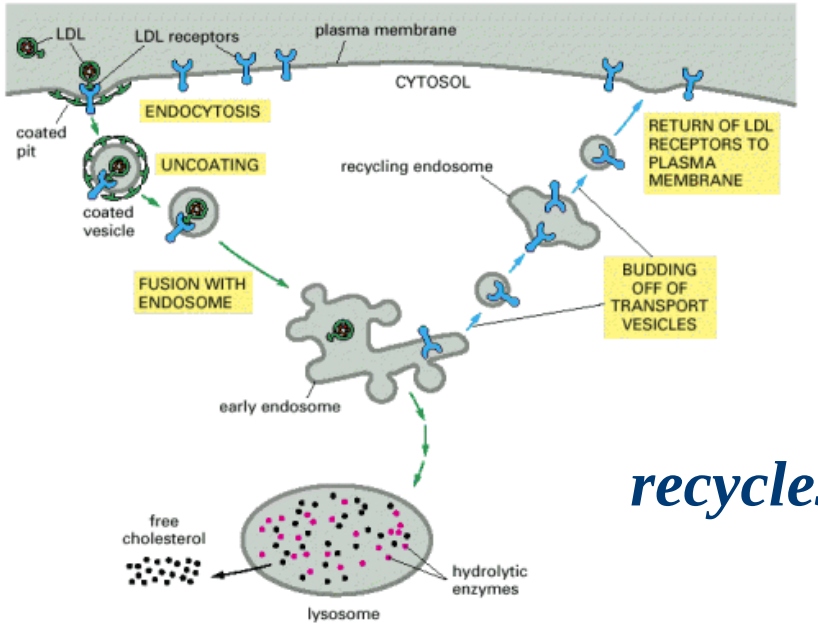
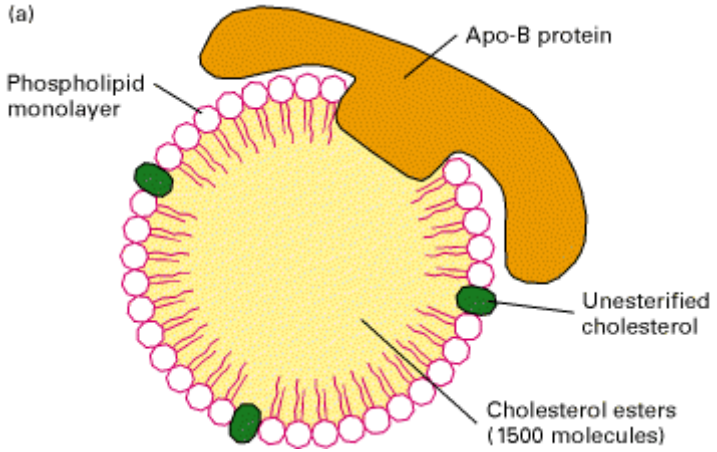


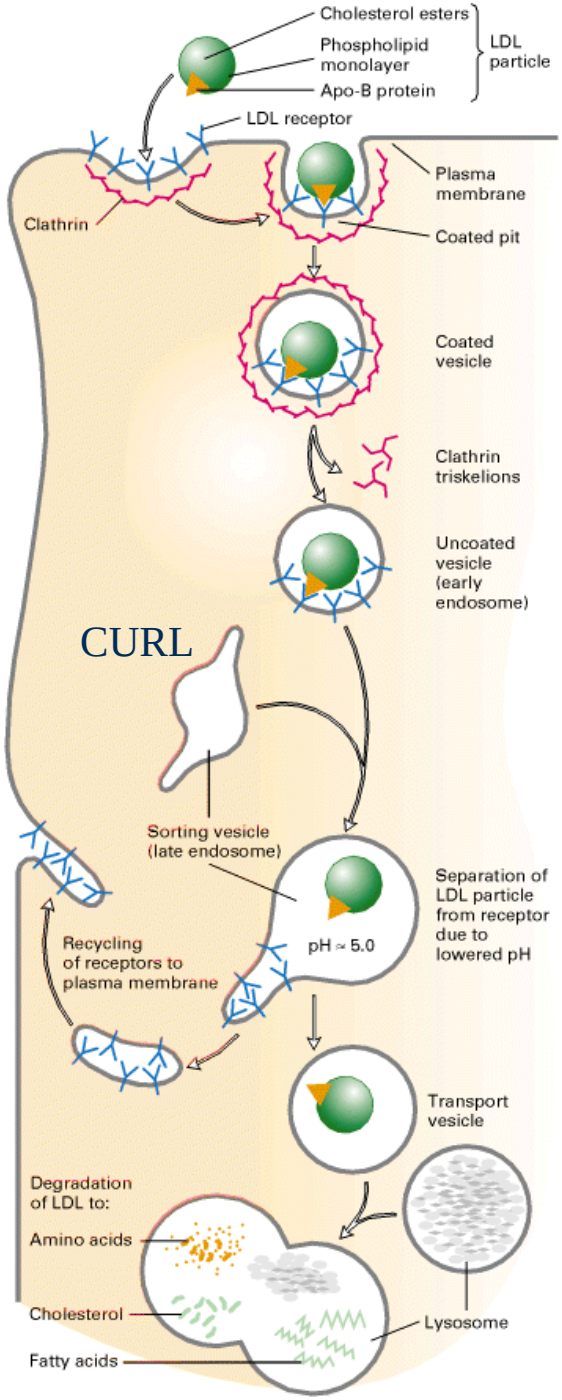
Figure 13-51 *Molecular Biology of the Cell* (© Garland Science 2008)

Receptor-Mediated Endocytosis of LDL (low-density lipoproteins)

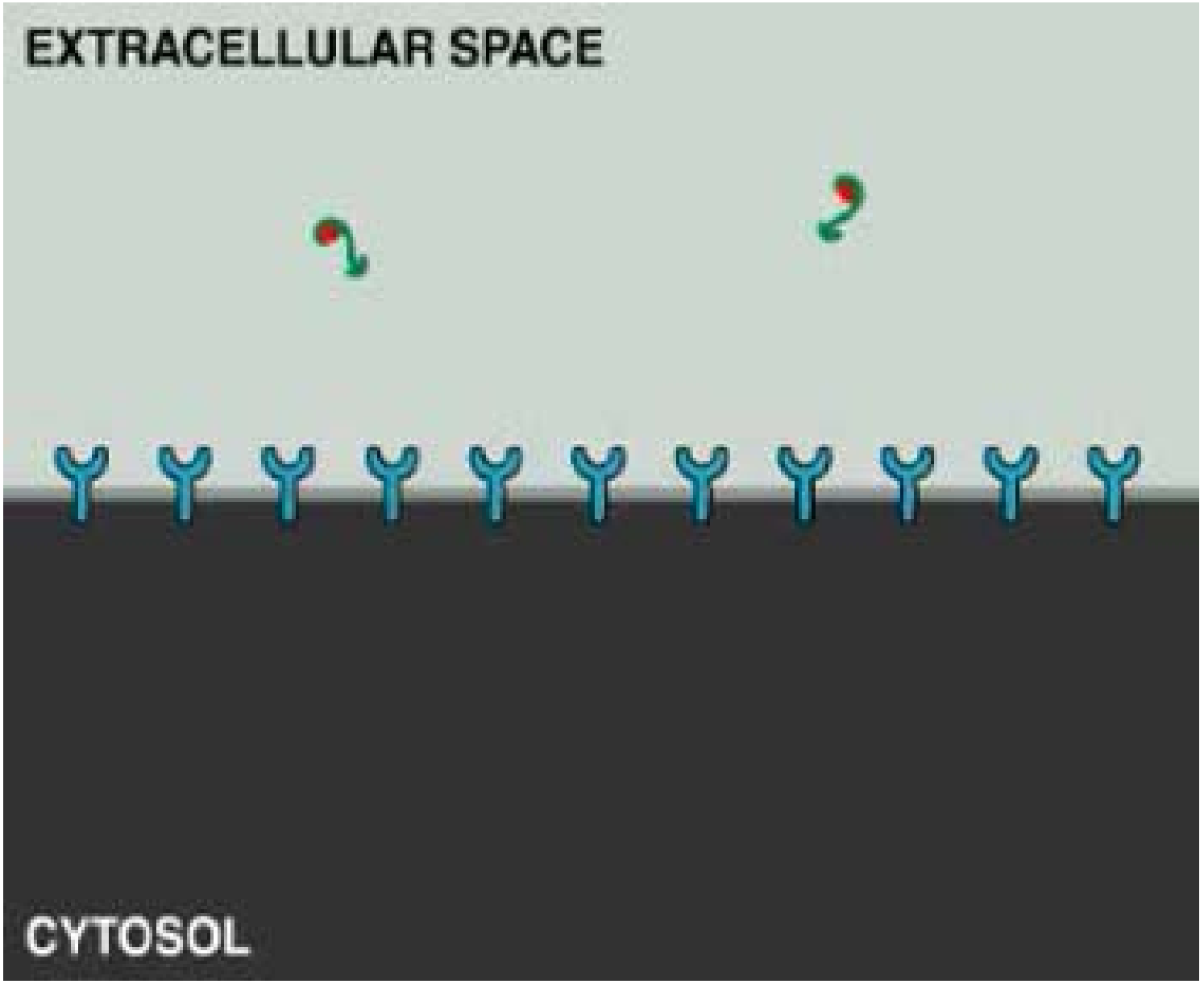


recycles the receptors





Receptor-Mediated Endocytosis of LDL (low-density lipoproteins)

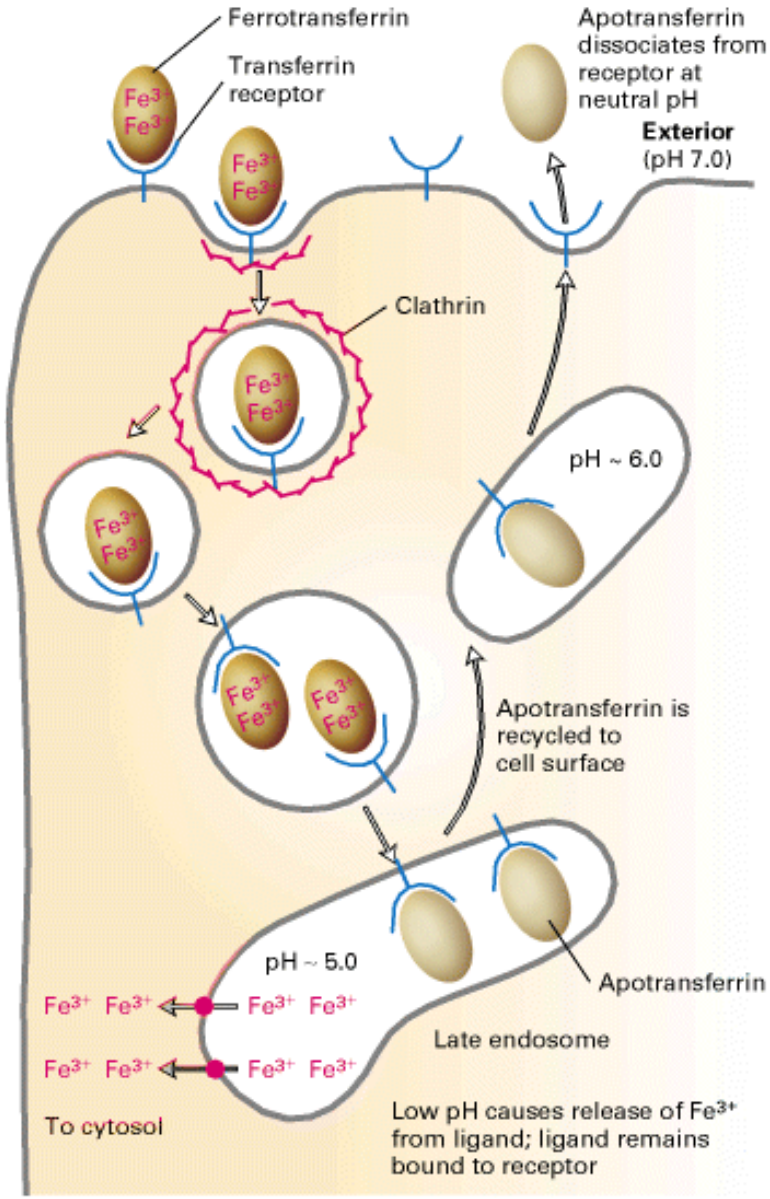


Receptor-Mediated Endocytosis - Iron Uptake

Transferrin = a soluble protein that carries iron in the blood.

Apotransferrin = iron-free transferrin

recycles the receptors and ligands!!!



Cell Junctions, Cell Adhesion, and the Extracellular Matrix

Are critical for every aspect of the organisation, function and dynamics of multicellular structures.

The mechanisms of cohesion govern the architecture of the body.

Cells may:

- **cling to one another - cell-cell junctions;**
- **be bound together by extracellular matrix (ECM).**

“Key players”:

- CELLS (Cytoskeleton and specific membrane proteins)

- ECM (complex network of proteins and polysaccharide chains)

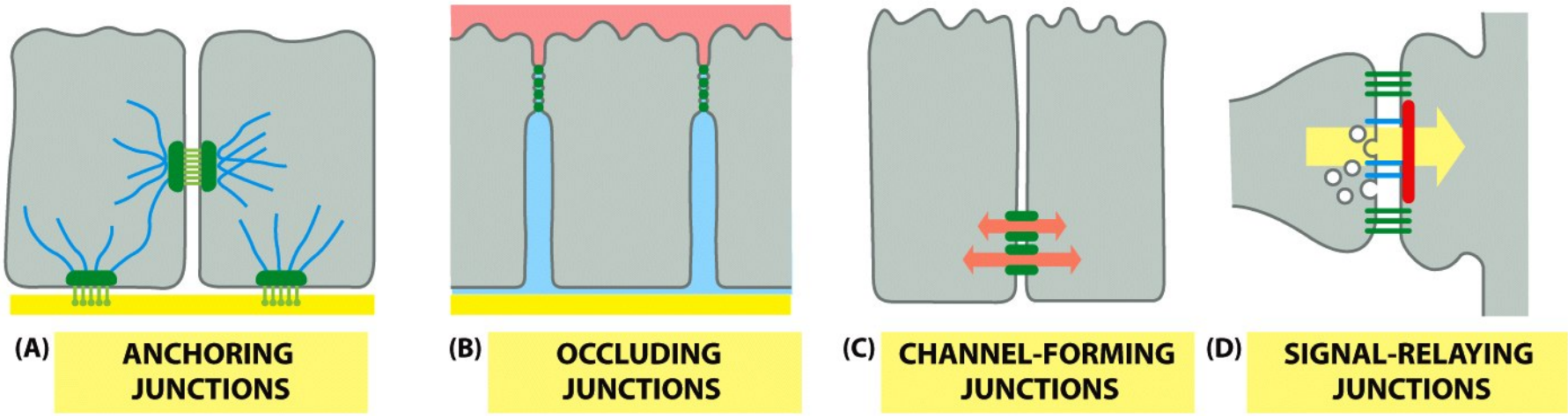
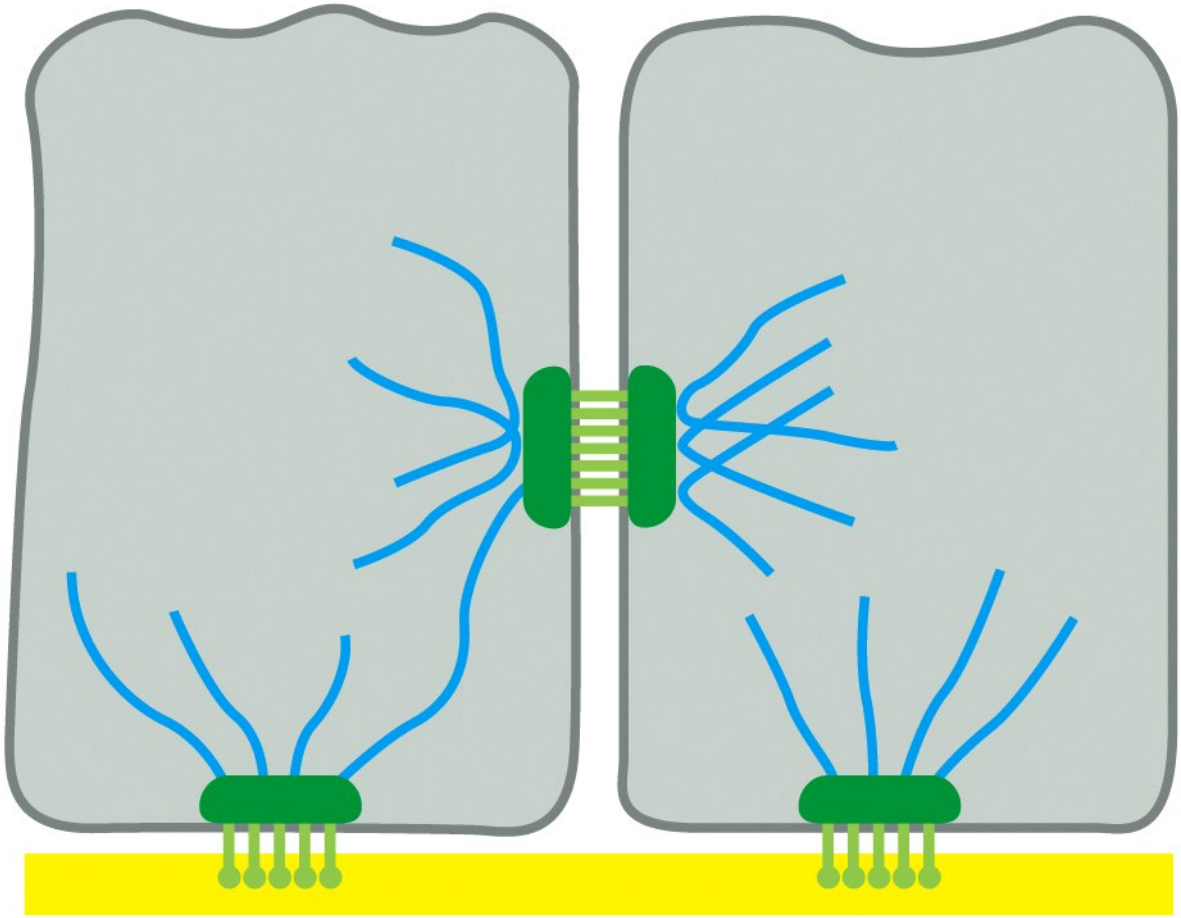


Figure 19-2 *Molecular Biology of the Cell* (© Garland Science 2008)

Table 19–1 A Functional Classification of Cell Junctions

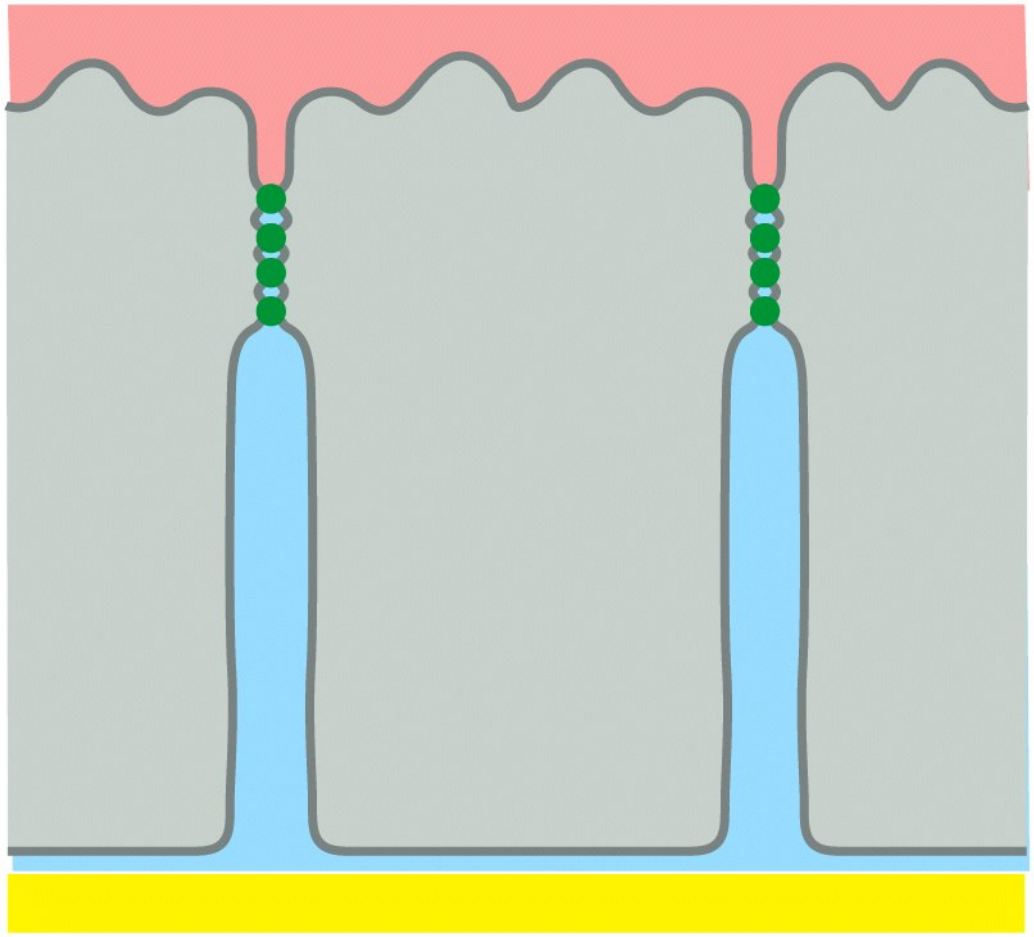
ANCHORING JUNCTIONS
Actin filament attachment sites
1. cell–cell junctions (adherens junctions)
2. cell–matrix junctions (actin-linked cell–matrix adhesions)
Intermediate filament attachment sites
1. cell–cell junctions (desmosomes)
2. cell–matrix junctions (hemidesmosomes)
OCCLUDING JUNCTIONS
1. tight junctions (in vertebrates)
2. septate junctions (in invertebrates)
CHANNEL-FORMING JUNCTIONS
1. gap junctions (in animals)
2. plasmodesmata (in plants)
SIGNAL-RELAYING JUNCTIONS
1. chemical synapses (in the nervous system)
2. immunological synapses (in the immune system)
3. transmembrane ligand–receptor cell–cell signaling contacts (Delta-Notch, ephrin-Eph, etc.). Anchoring, occluding, and channel-forming junctions can all have signaling functions in addition to their structural roles

Table 19-1 *Molecular Biology of the Cell* (© Garland Science 2008)



ANCHORING JUNCTIONS

Figure 19-2a *Molecular Biology of the Cell* (© Garland Science 2008)



OCCLUDING JUNCTIONS

Figure 19-2b *Molecular Biology of the Cell* (© Garland Science 2008)

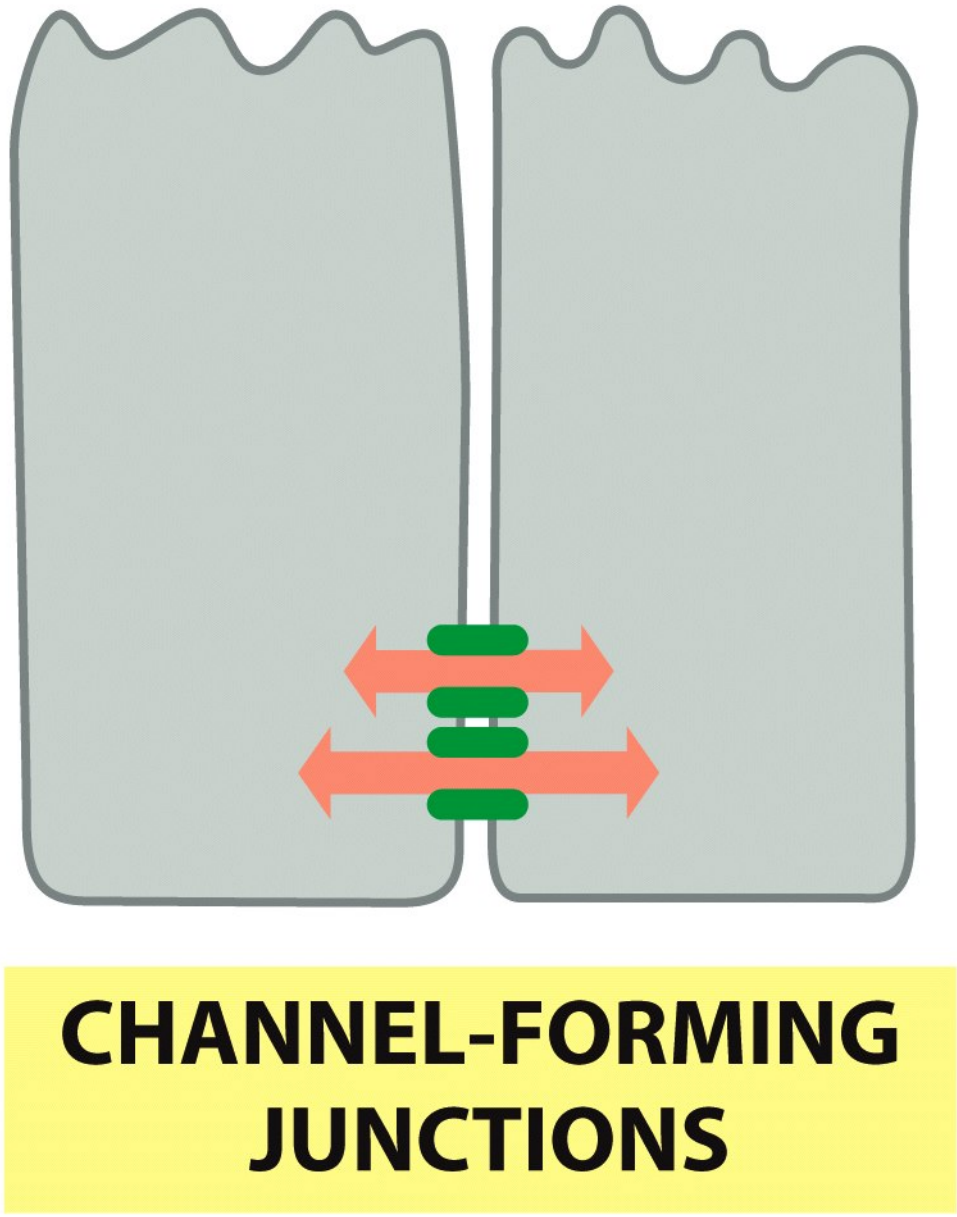


Figure 19-2c *Molecular Biology of the Cell* (© Garland Science 2008)

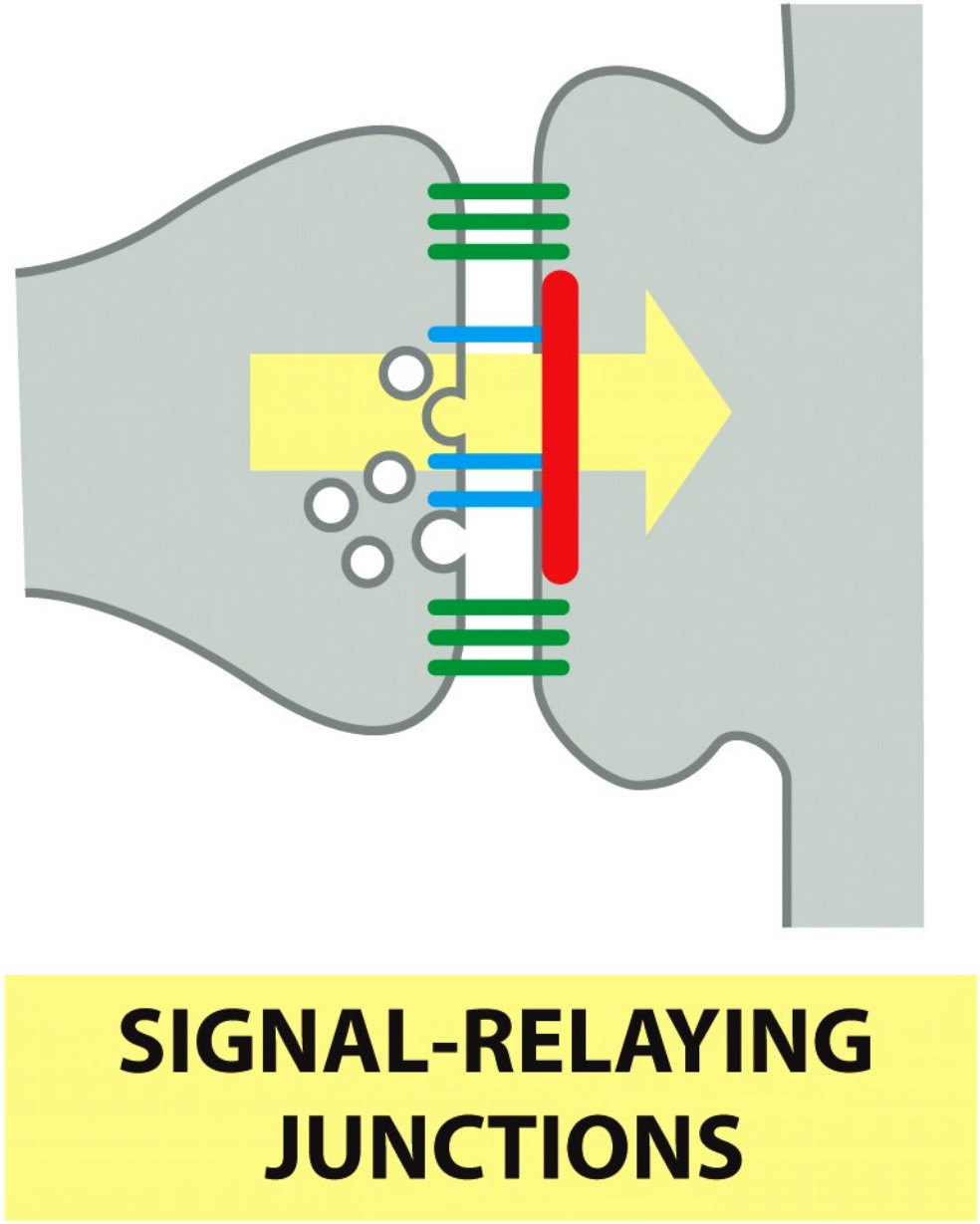


Figure 19-2d *Molecular Biology of the Cell* (© Garland Science 2008)

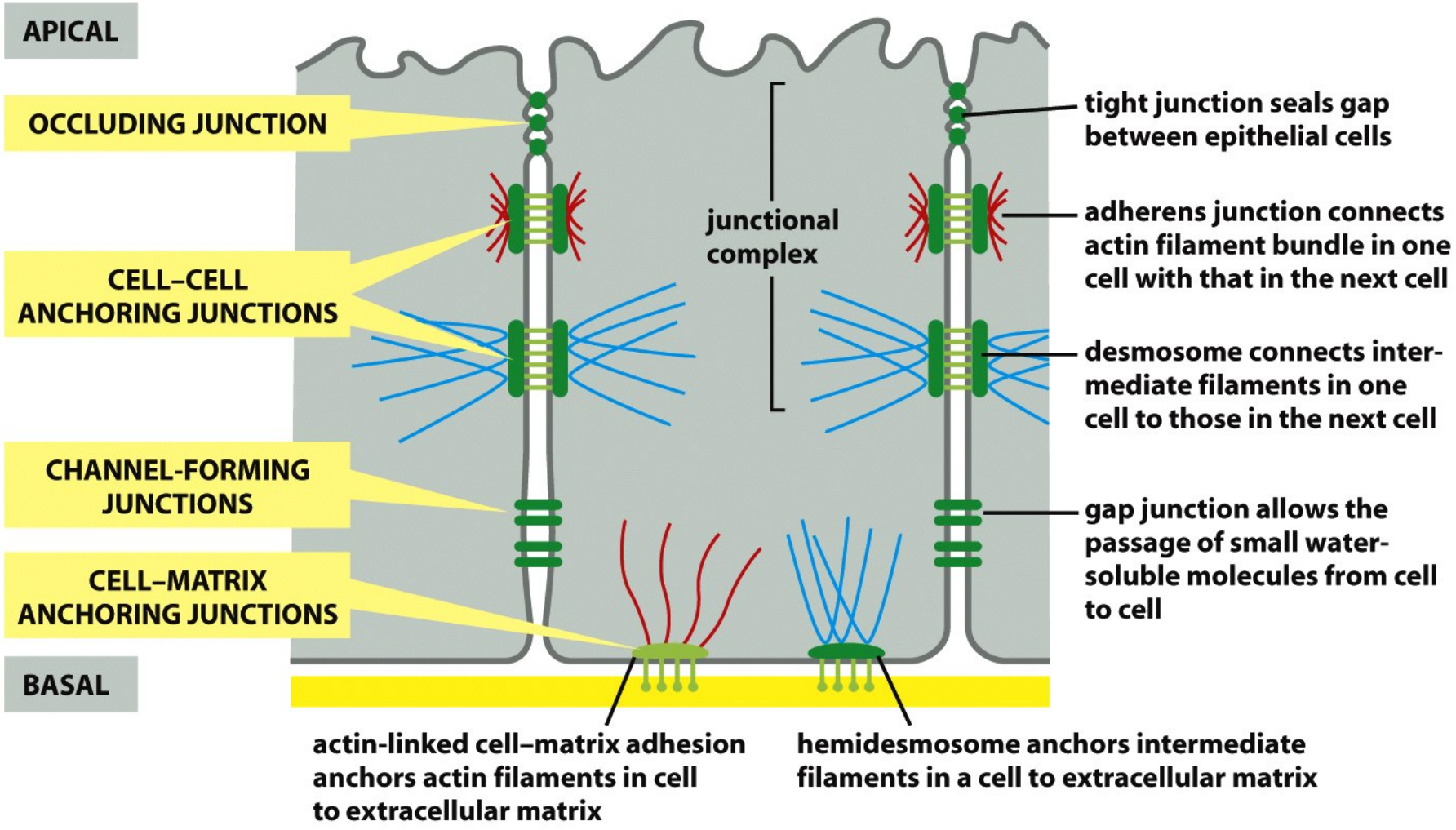


Figure 19-3 *Molecular Biology of the Cell* (© Garland Science 2008)

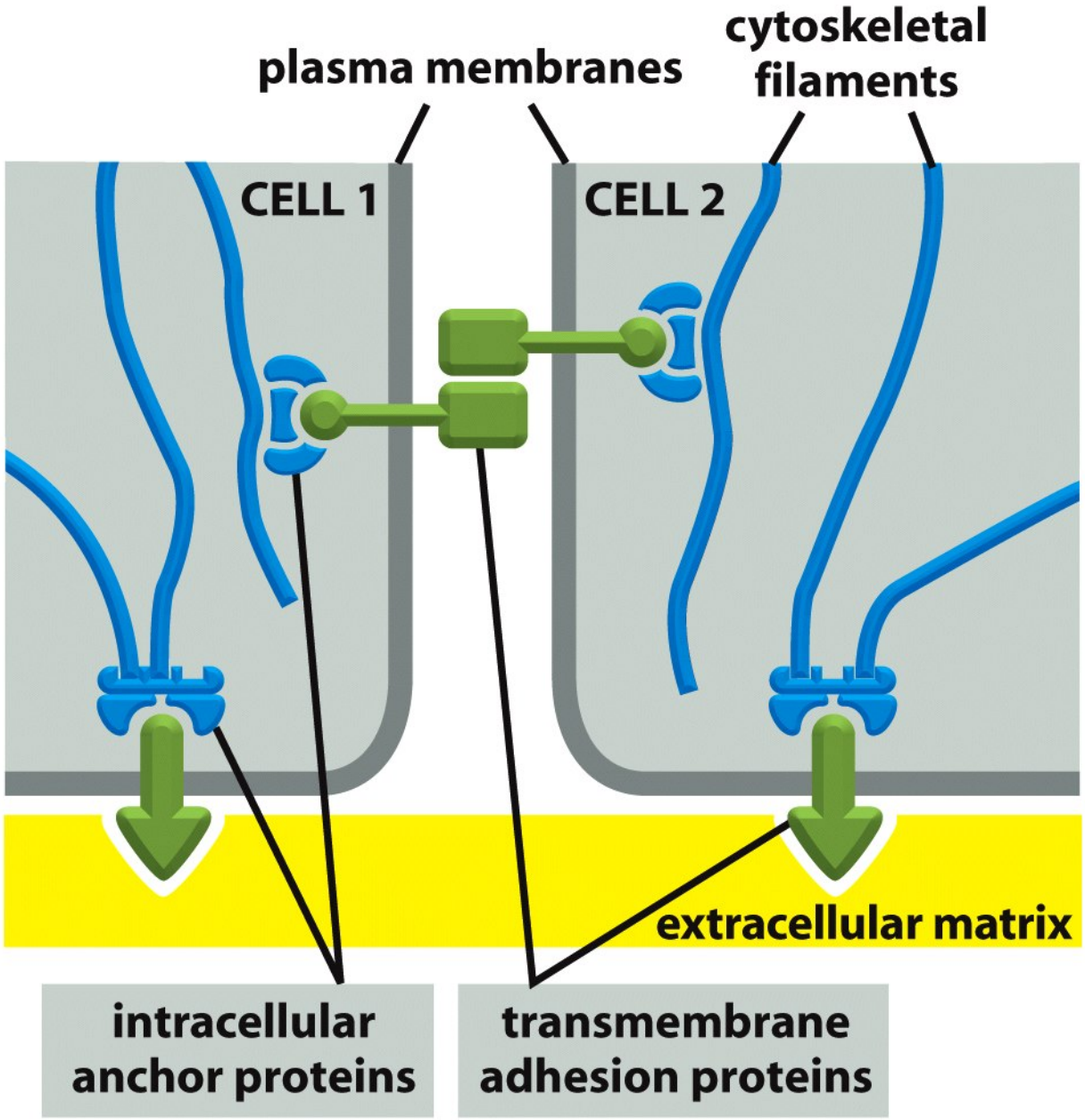


Figure 19-4 *Molecular Biology of the Cell* (© Garland Science 2008)

Table 19–2 Anchoring Junctions

JUNCTION	TRANSMEMBRANE ADHESION PROTEIN	EXTRACELLULAR LIGAND	INTRACELLULAR CYTOSKELETAL ATTACHMENT	INTRACELLULAR ANCHOR PROTEINS
Cell–Cell				
adherens junction	cadherin (classical cadherin)	cadherin in neighboring cell	actin filaments	α-catenin, β-catenin, plakoglobin (γ-catenin), p120-catenin, vinculin, α-actinin
desmosome	cadherin (desmoglein, desmocollin)	desmoglein and desmocollin in neighboring cell	intermediate filaments	plakoglobin (γ-catenin), plakophilin, desmoplakin
Cell–Matrix				
actin-linked cell–matrix adhesion	integrin	extracellular matrix proteins	actin filaments	talin, vinculin, α-actinin, filamin, paxillin, focal adhesion kinase (FAK)
hemidesmosome	integrin α6β4, type XVII collagen (BP180)	extracellular matrix proteins	intermediate filaments	plectin, dystonin (BP230)

Table 19-2 *Molecular Biology of the Cell* (© Garland Science 2008)

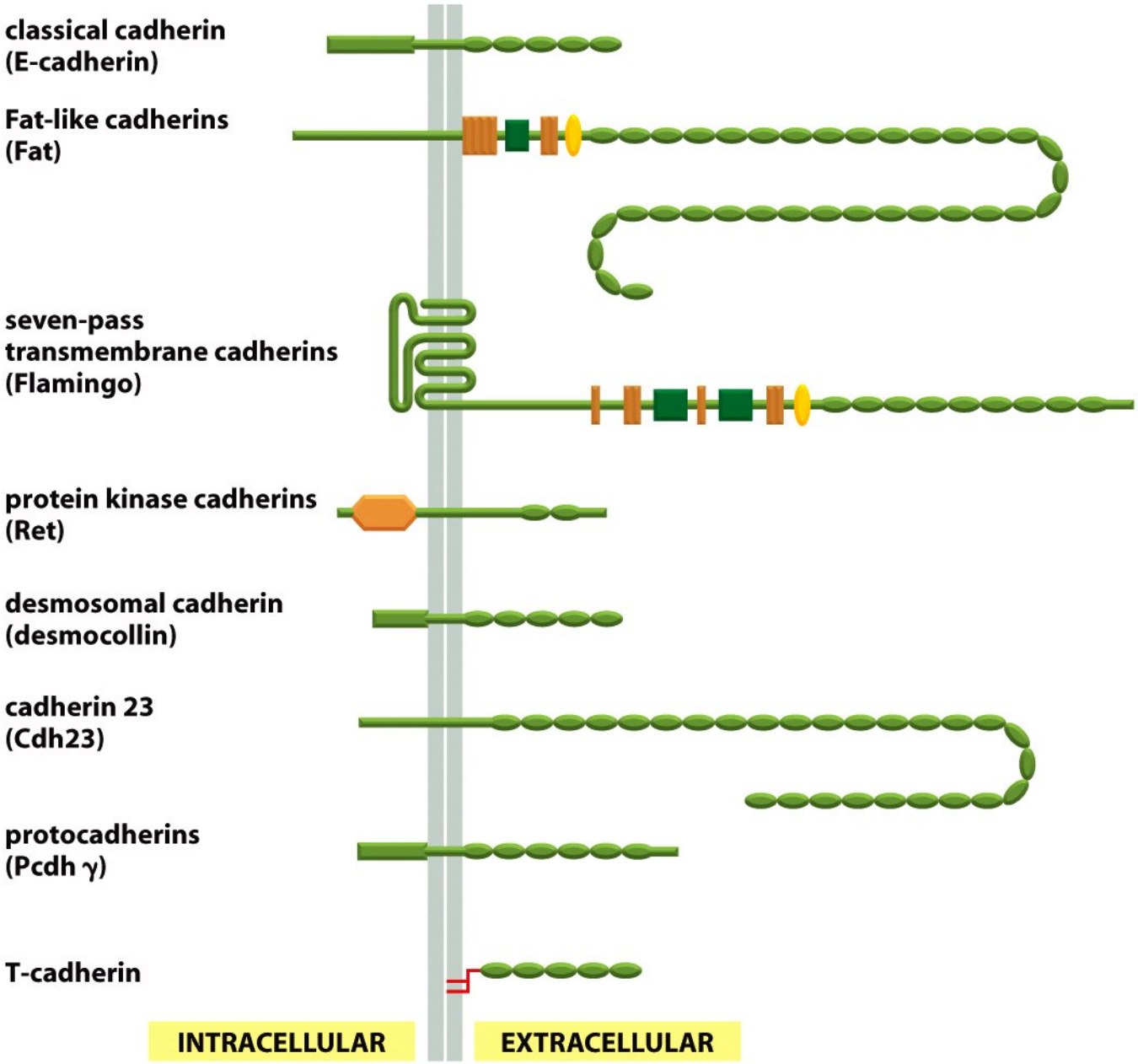


Figure 19-7 *Molecular Biology of the Cell* (© Garland Science 2008)

Table 19–3 Some Members of the Cadherin Superfamily

NAME	MAIN LOCATION	JUNCTION ASSOCIATION	PHENOTYPE WHEN INACTIVATED IN MICE
Classical cadherins			
E-cadherin	many epithelia	adherens junctions	death at blastocyst stage; embryos fail to undergo compaction
N-cadherin	neurons, heart, skeletal muscle, lens, and fibroblasts	adherens junctions and chemical synapses	embryos die from heart defects
P-cadherin	placenta, epidermis, breast epithelium	adherens junctions	abnormal mammary gland development
VE-cadherin	endothelial cells	adherens junctions	abnormal vascular development (apoptosis of endothelial cells)
Nonclassical cadherins			
Desmocollin	skin	desmosomes	blistering of skin
Desmoglein	skin	desmosomes	blistering skin disease due to loss of keratinocyte cell–cell adhesion
T-cadherin	neurons, muscle, heart	none	unknown
Cadherin 23	inner ear, other epithelia	links between stereocilia in sensory hair cells	deafness
Fat (in *Drosophila*)	epithelia and central nervous system	signal-relaying junction (planar cell polarity)	enlarged imaginal discs and tumors; disrupted planar cell polarity
Fat1 (in mammals)	various epithelia and central nervous system	slit diaphragm in kidney glomerulus and other cell junctions	loss of slit diaphragm; malformation of forebrain and eye
α, β, and γ-Protocadherins	neurons	chemical synapses and nonsynaptic membranes	neuronal degeneration
Flamingo	sensory and some other epithelia	cell–cell junctions	disrupted planar cell polarity; neural tube defects

Table 19-3 *Molecular Biology of the Cell* (© Garland Science 2008)

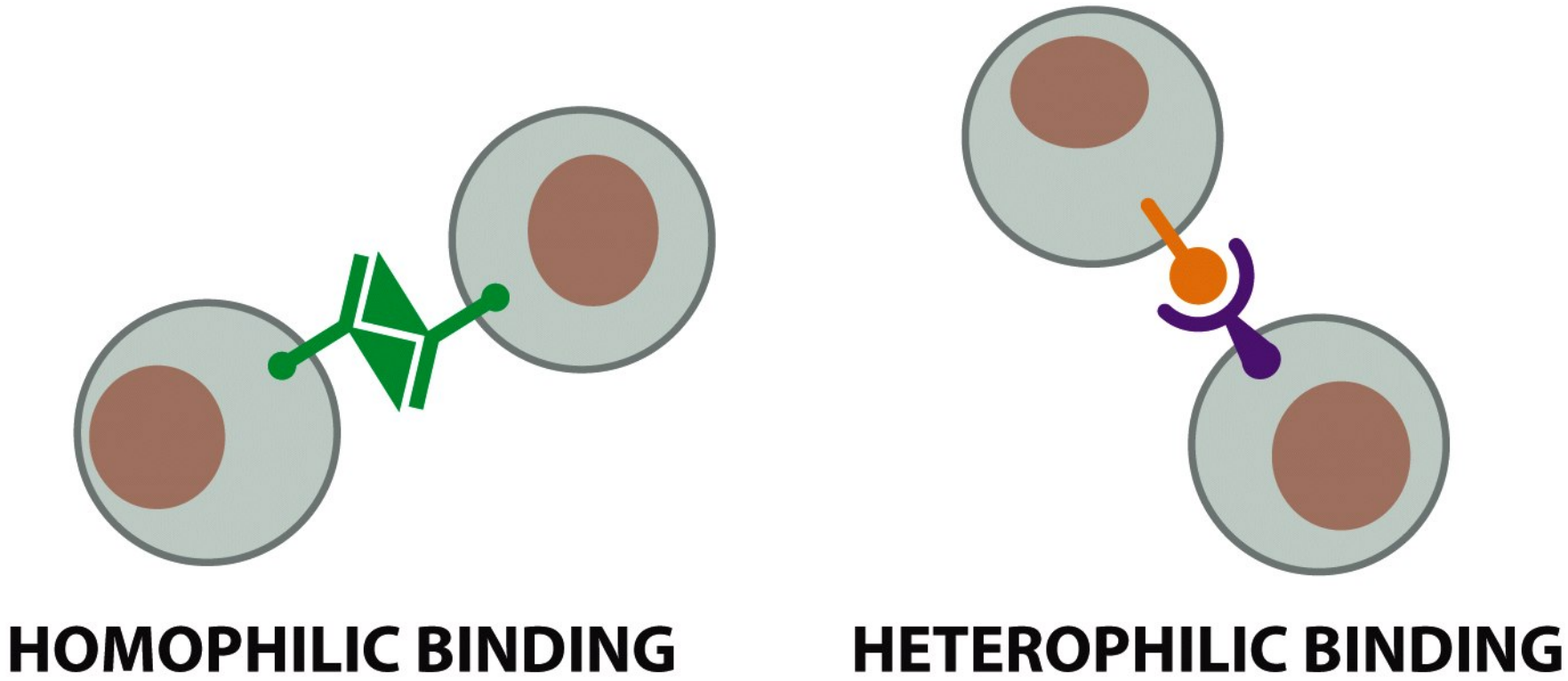


Figure 19-8 *Molecular Biology of the Cell* (© Garland Science 2008)

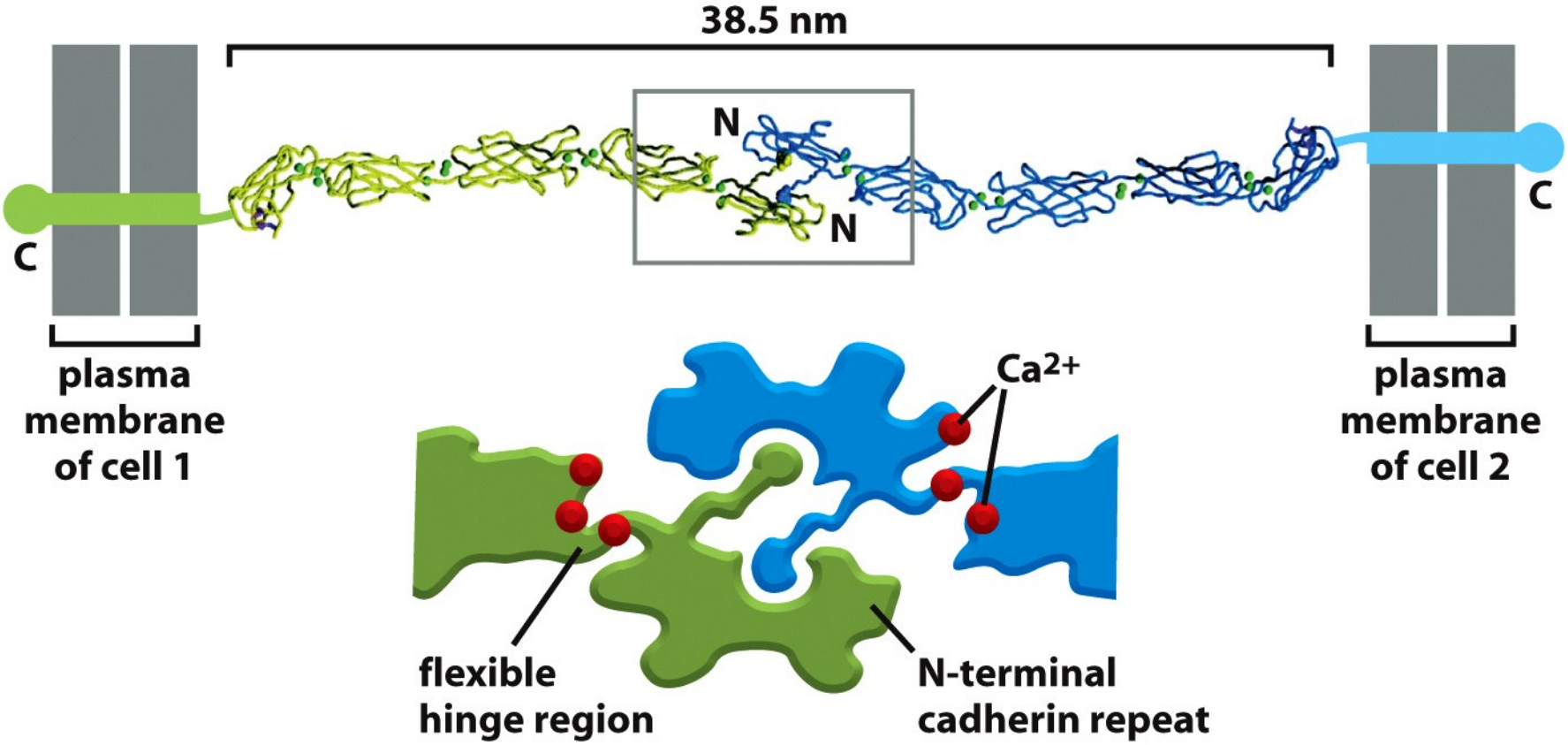


Figure 19-9a *Molecular Biology of the Cell* (© Garland Science 2008)

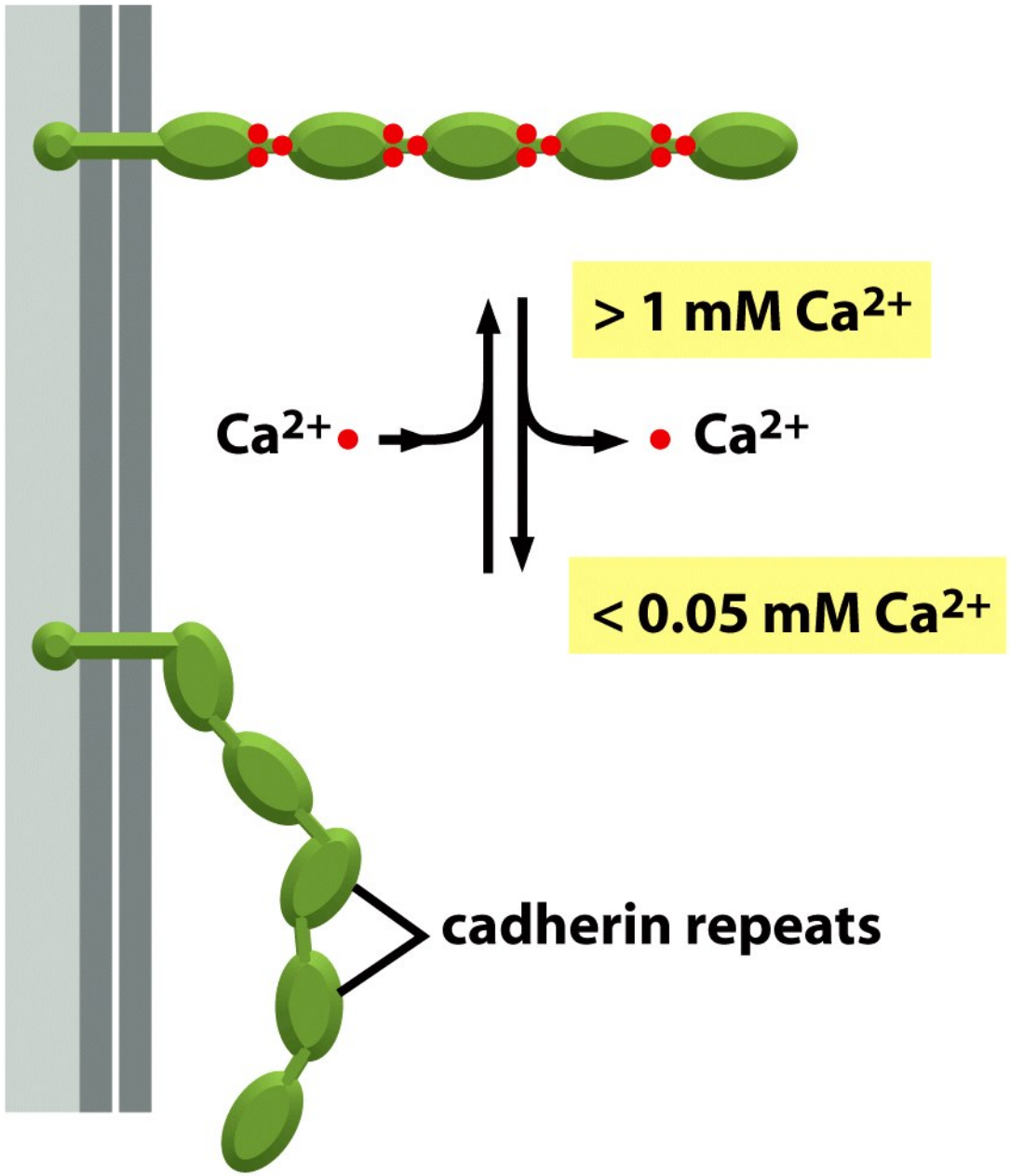


Figure 19-9b *Molecular Biology of the Cell* (© Garland Science 2008)

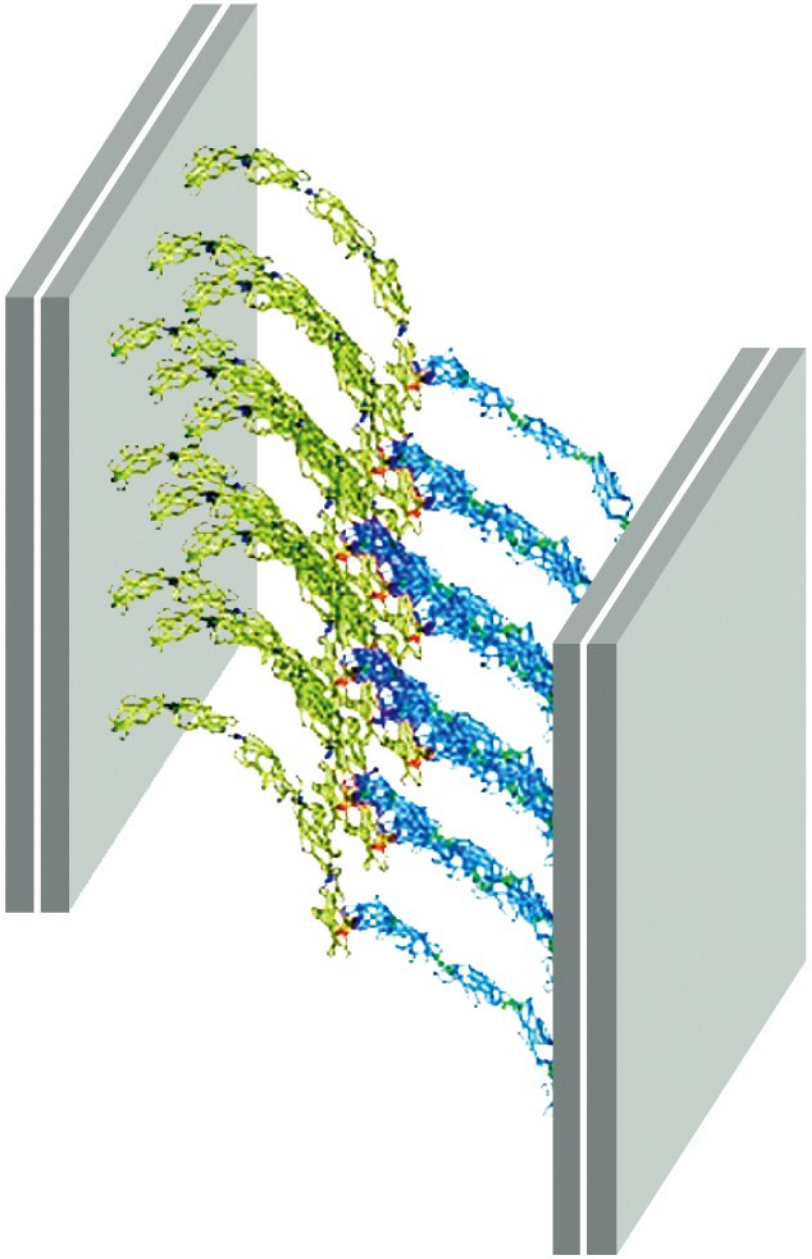


Figure 19-9c *Molecular Biology of the Cell* (© Garland Science 2008)

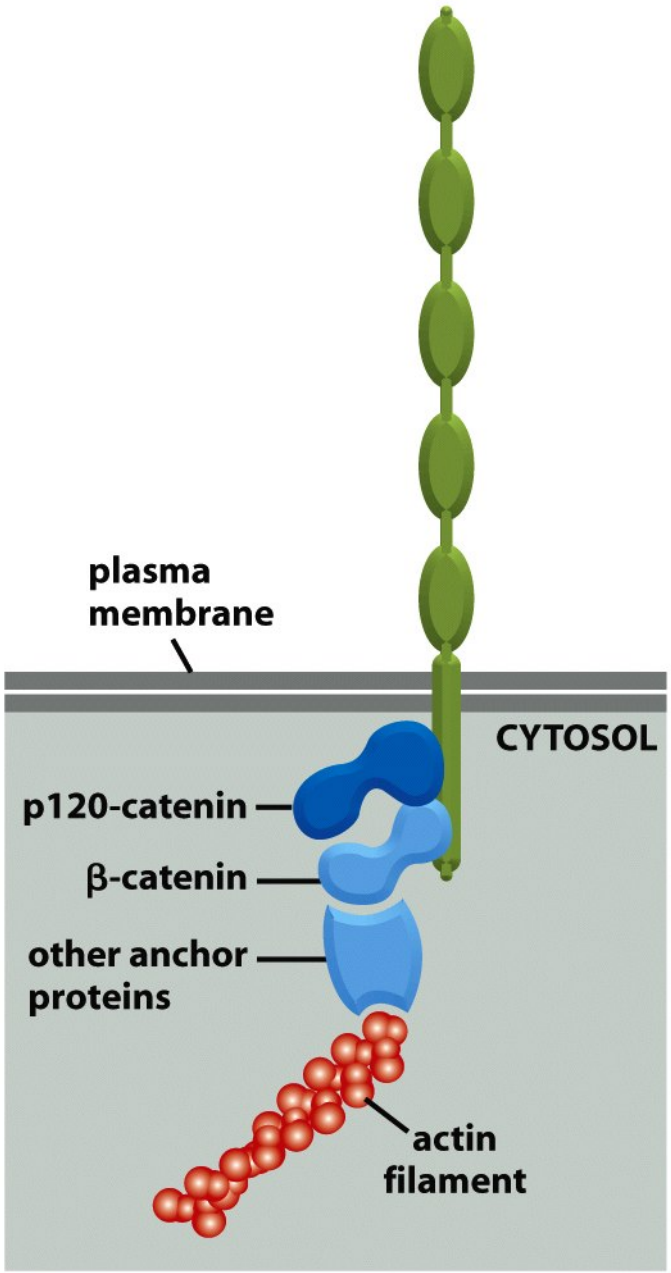


Figure 19-14 *Molecular Biology of the Cell* (© Garland Science 2008)

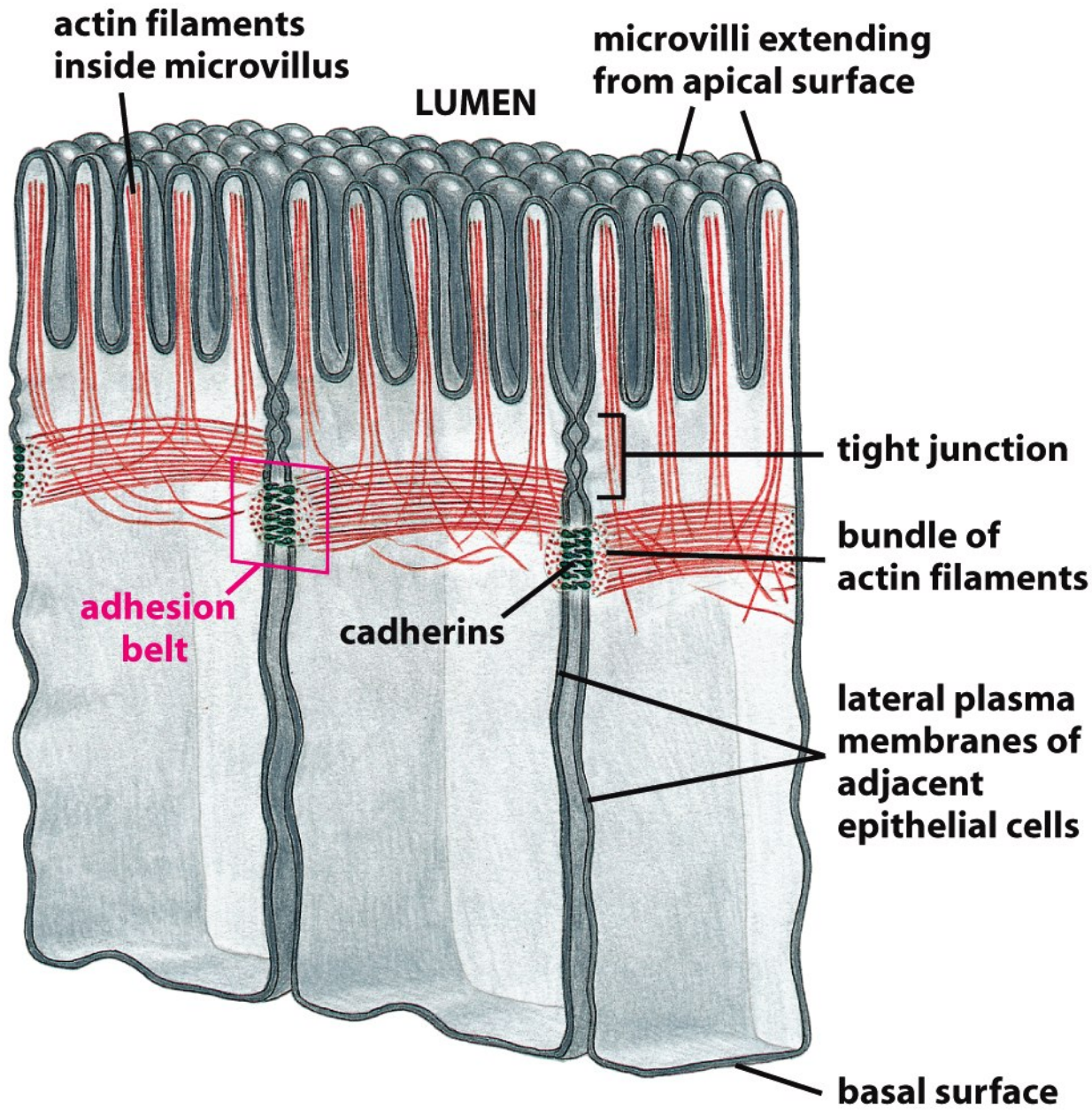


Figure 19-15 *Molecular Biology of the Cell* (© Garland Science 2008)

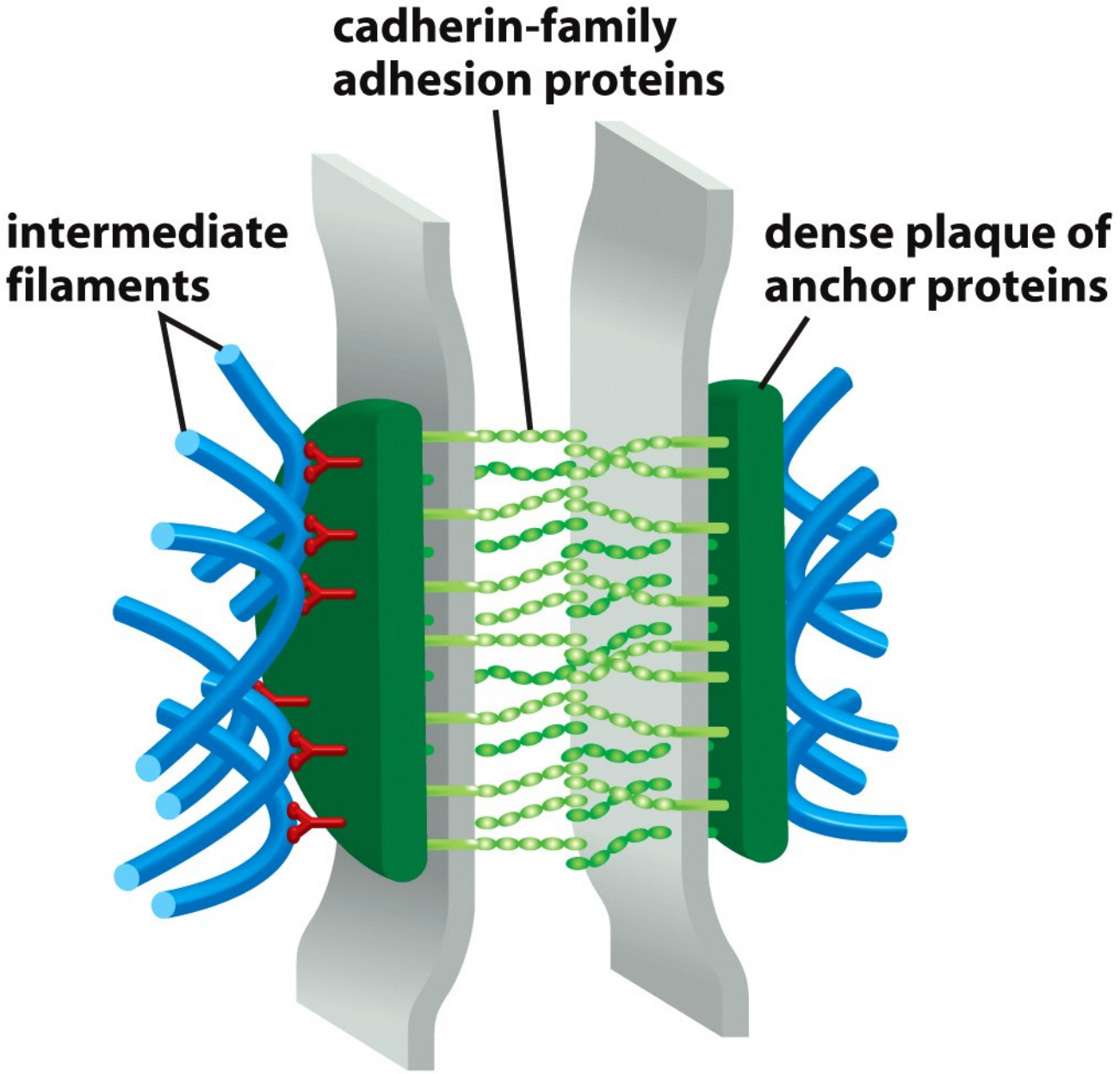


Figure 19-17a *Molecular Biology of the Cell* (© Garland Science 2008)

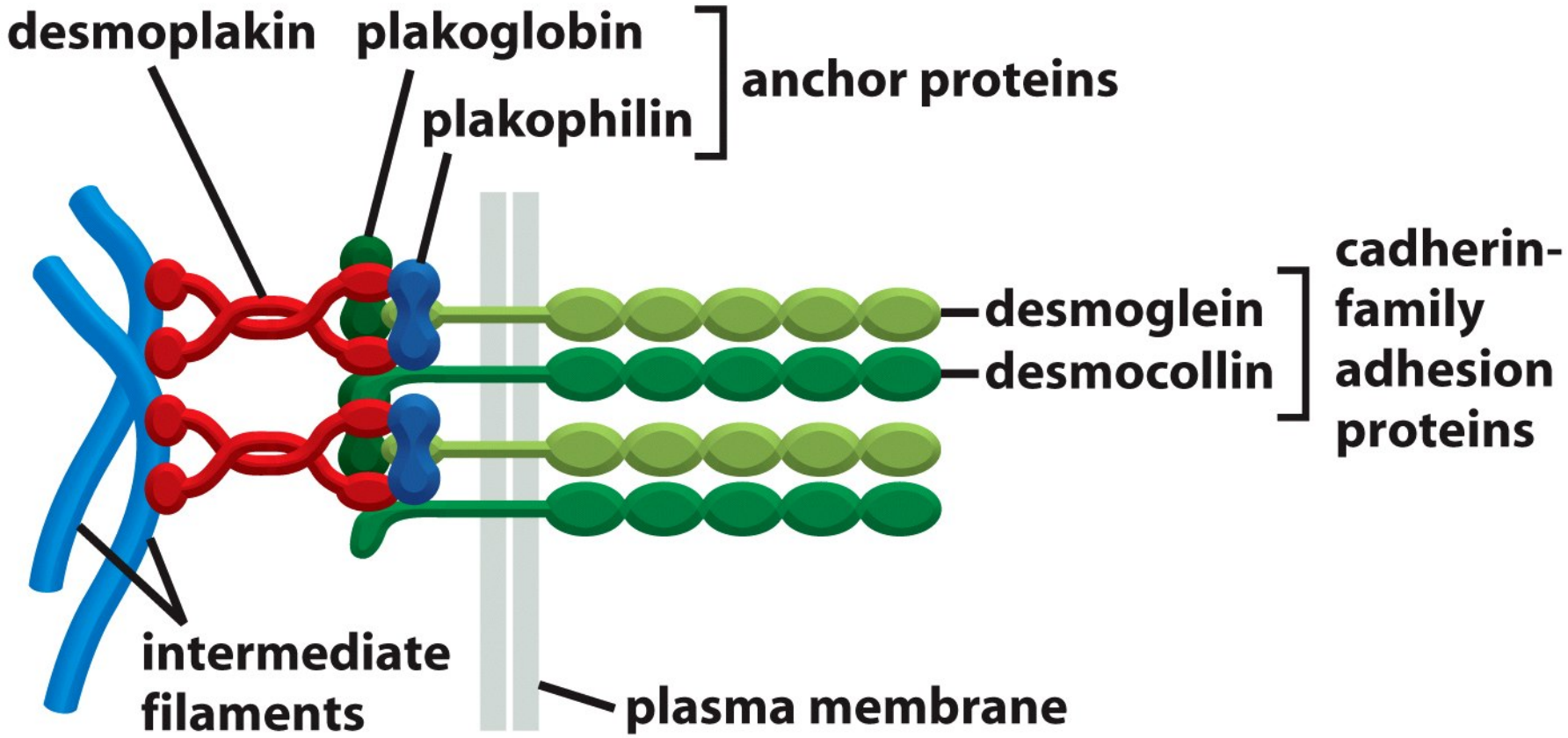


Figure 19-17b *Molecular Biology of the Cell* (© Garland Science 2008)

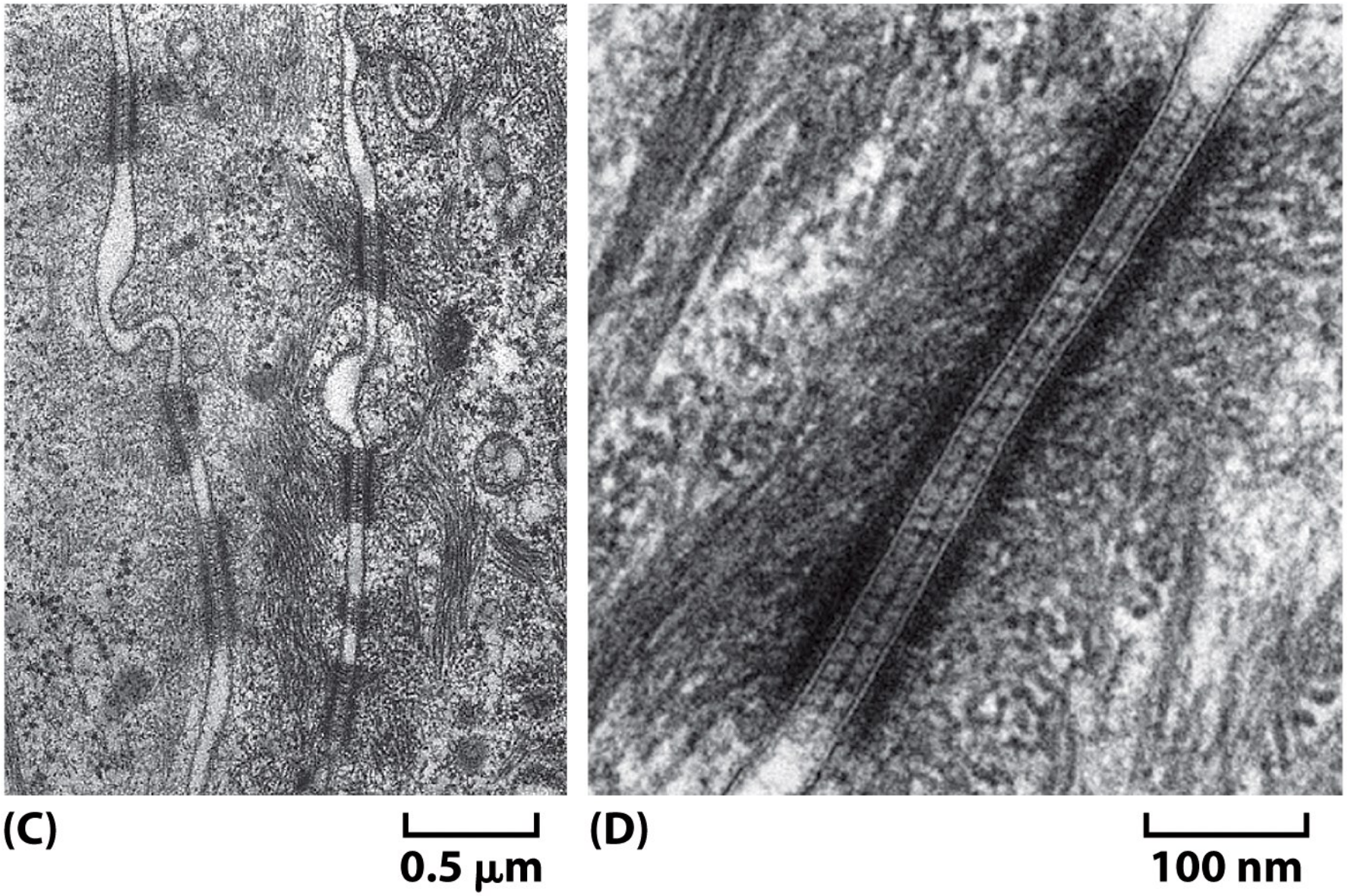


Figure 19-17c, d *Molecular Biology of the Cell* (© Garland Science 2008)

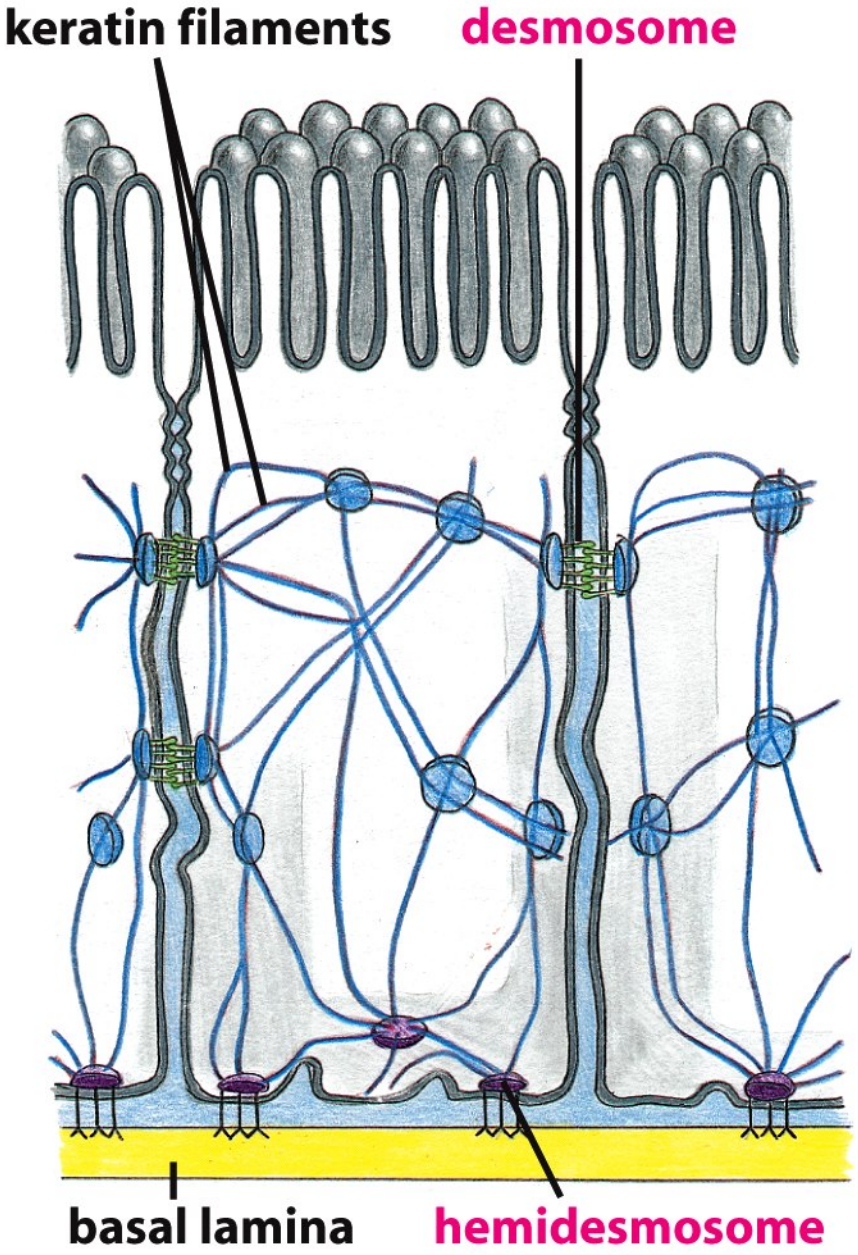


Figure 19-18 *Molecular Biology of the Cell* (© Garland Science 2008)

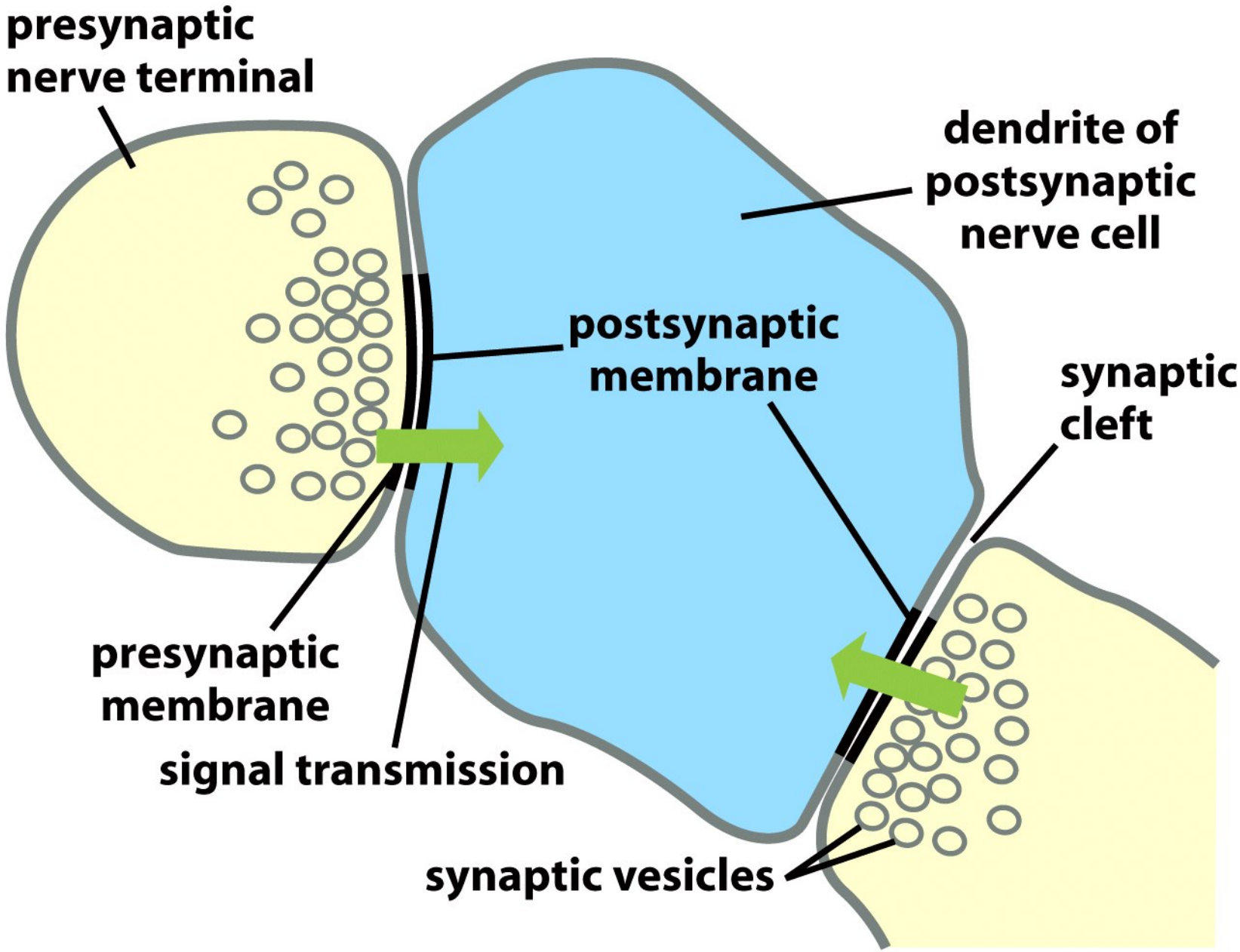


Figure 19-22b *Molecular Biology of the Cell* (© Garland Science 2008)

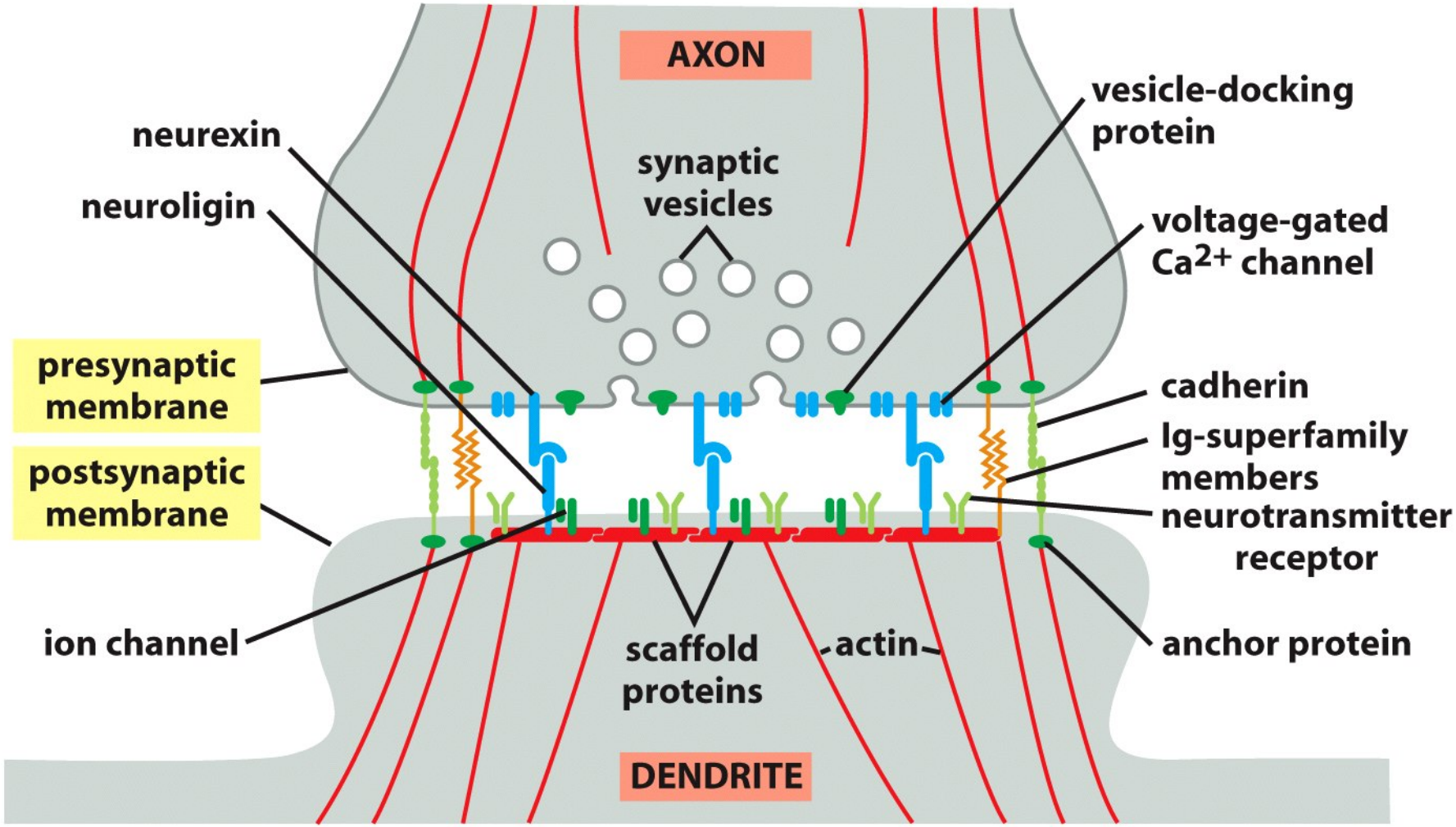


Figure 19-22c *Molecular Biology of the Cell* (© Garland Science 2008)

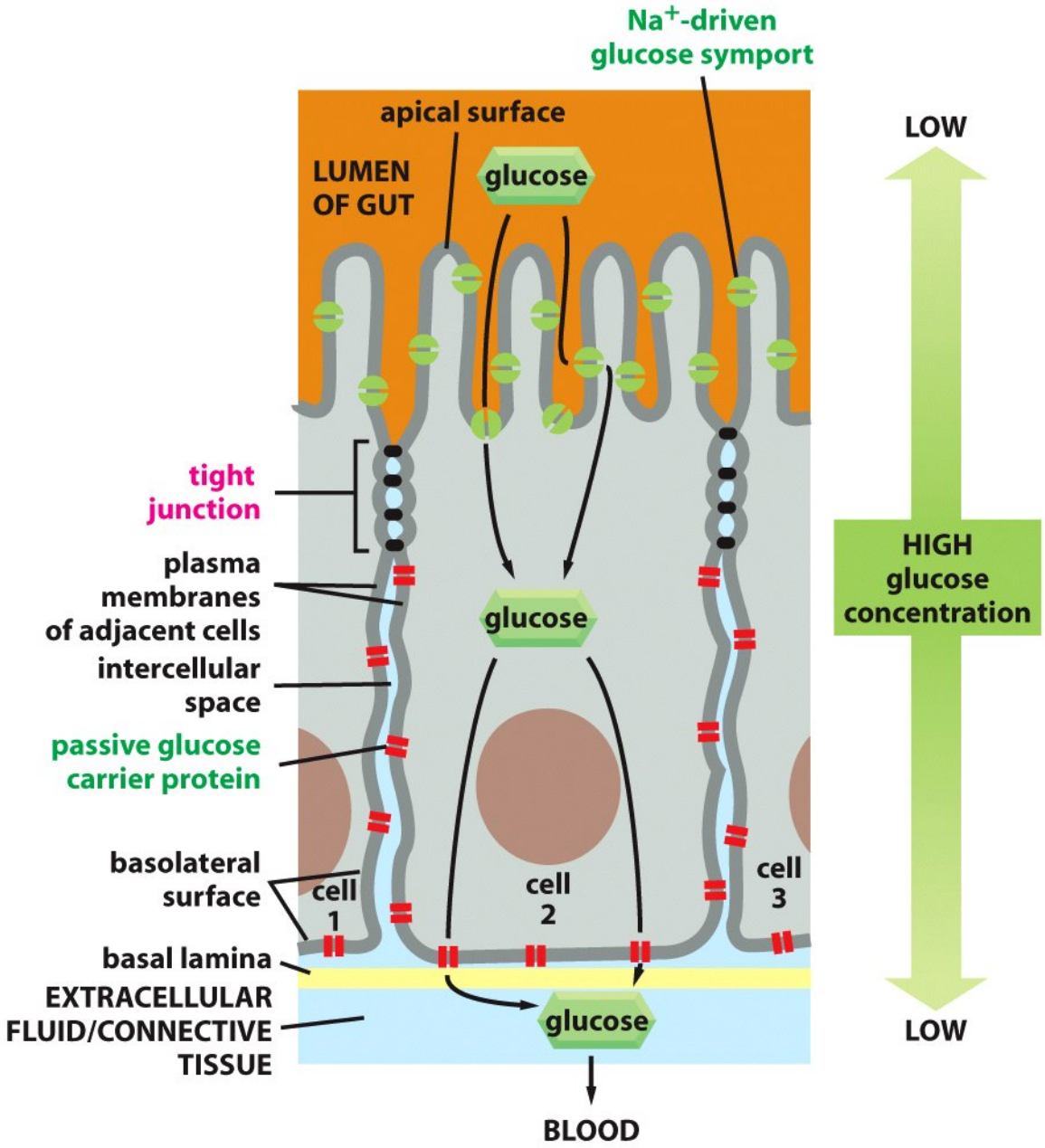


Figure 19-23 *Molecular Biology of the Cell* (© Garland Science 2008)

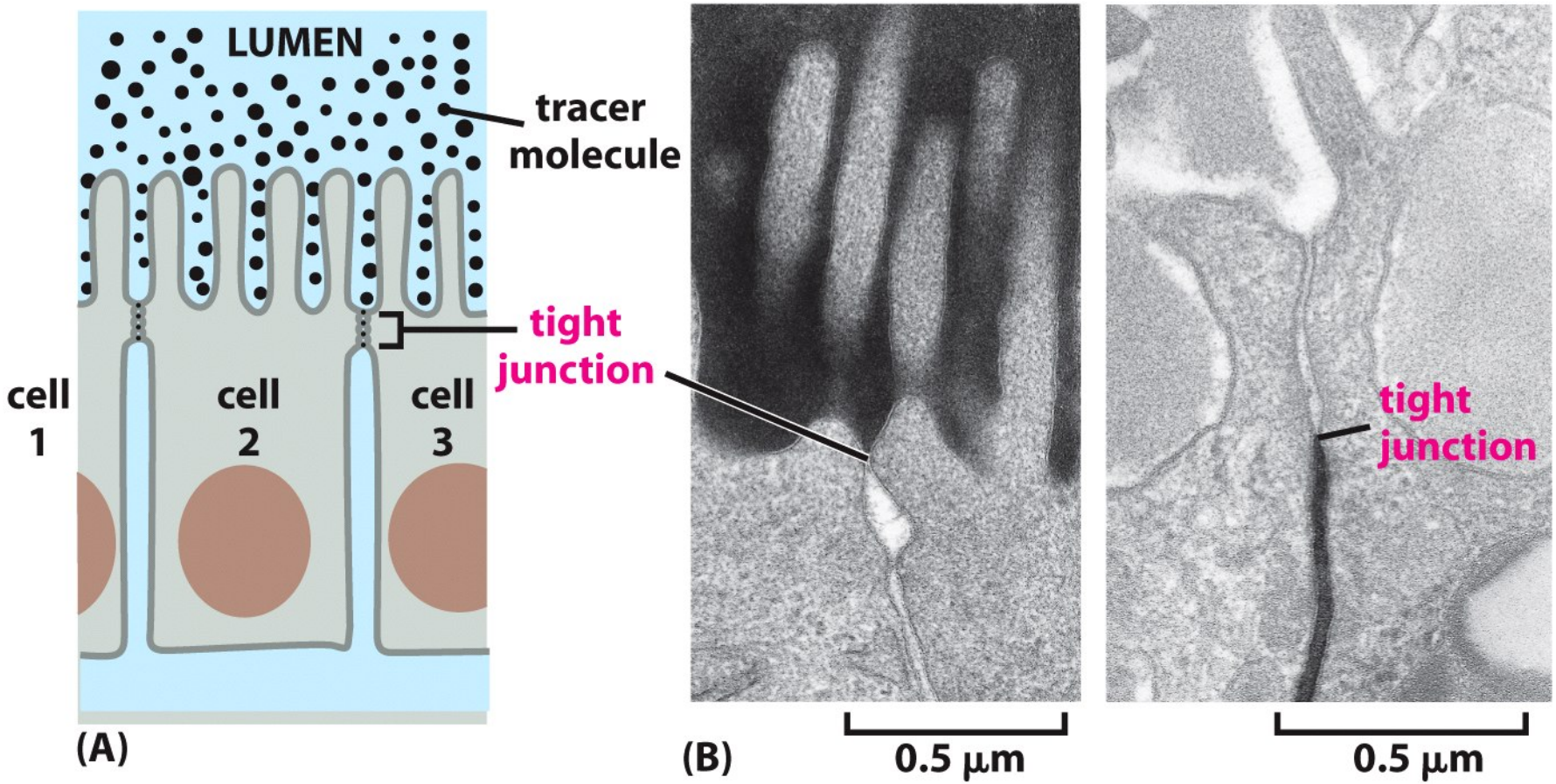


Figure 19-24 *Molecular Biology of the Cell* (© Garland Science 2008)

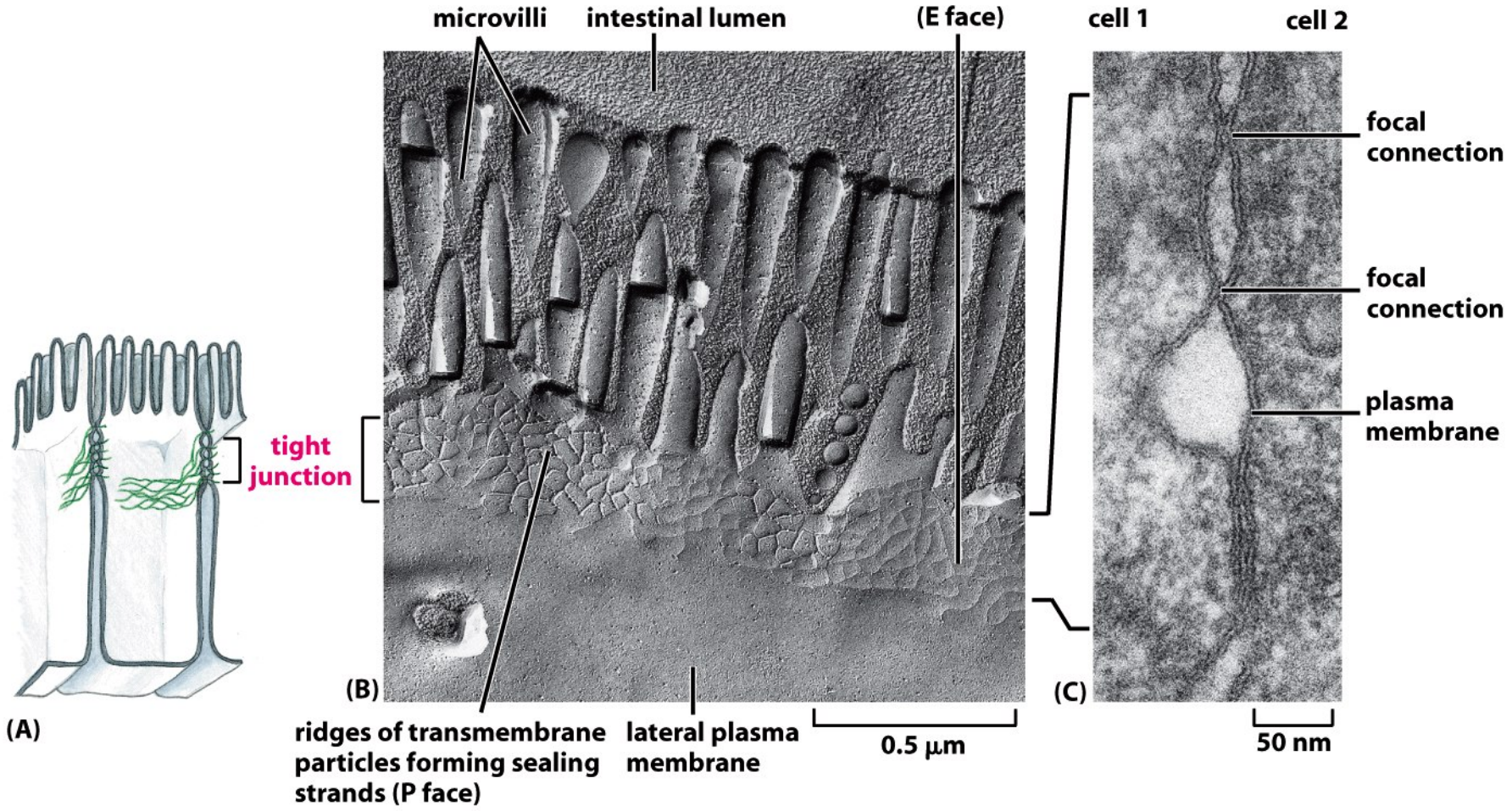


Figure 19-25 *Molecular Biology of the Cell* (© Garland Science 2008)

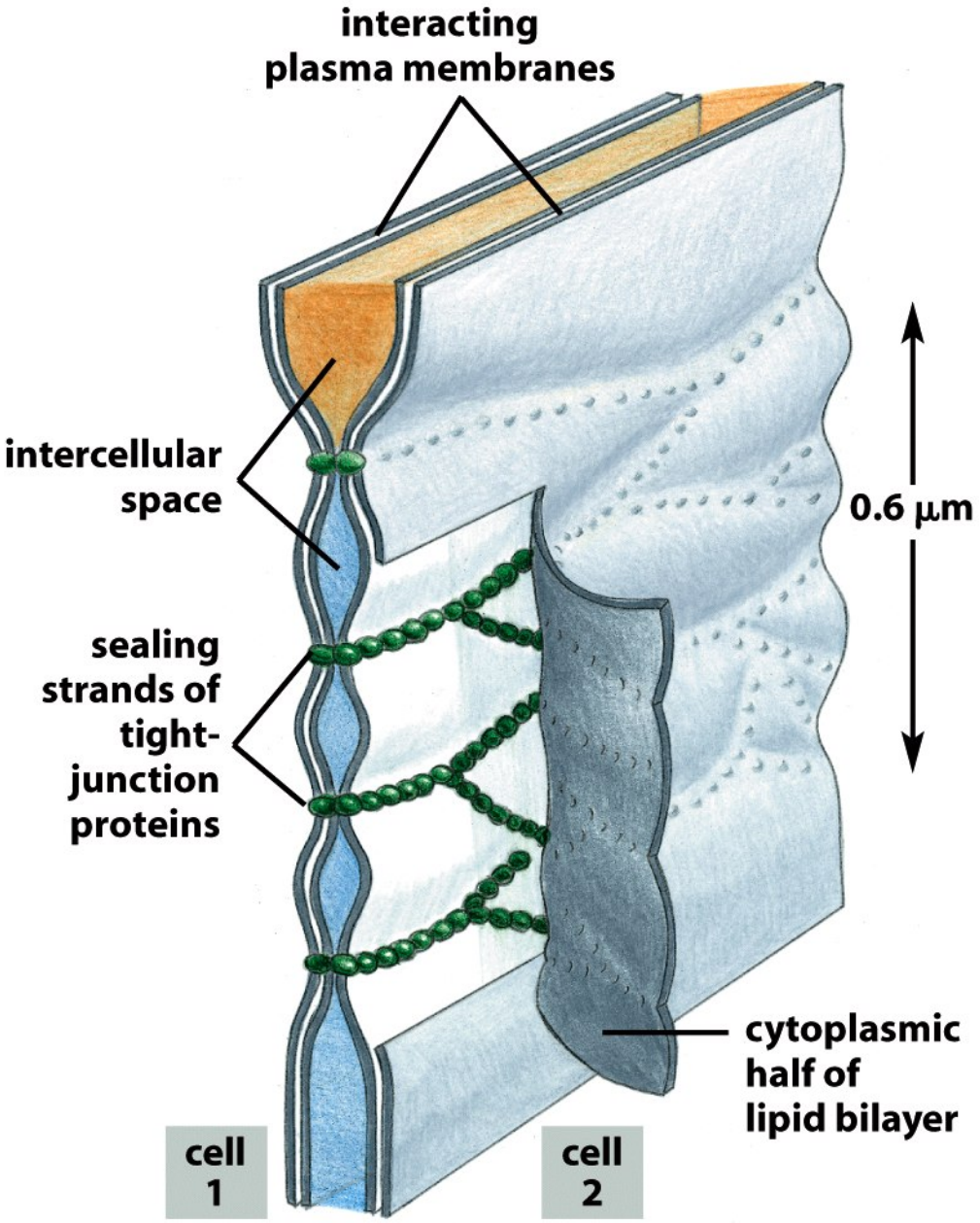


Figure 19-26a *Molecular Biology of the Cell* (© Garland Science 2008)

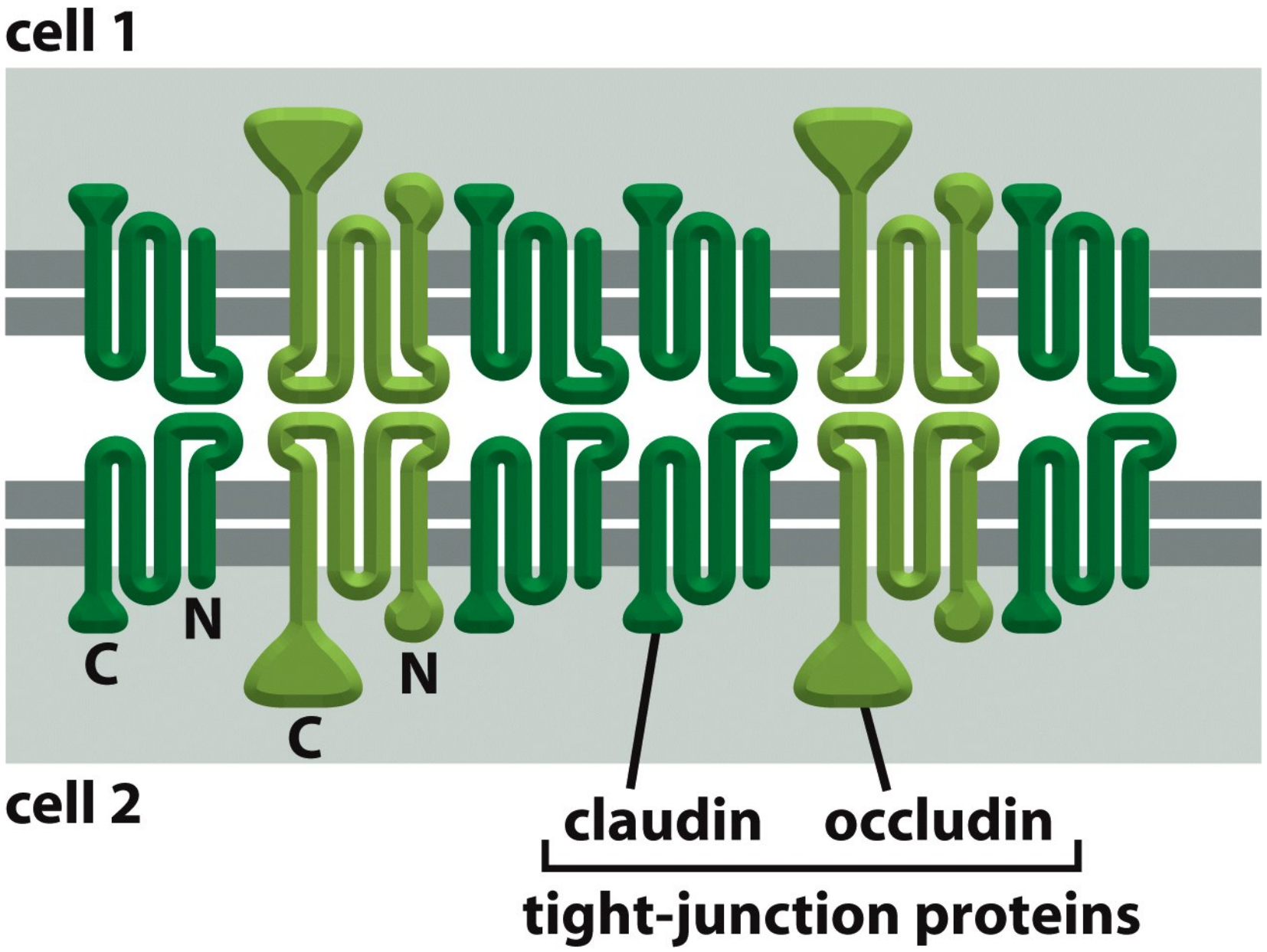


Figure 19-26b *Molecular Biology of the Cell* (© Garland Science 2008)

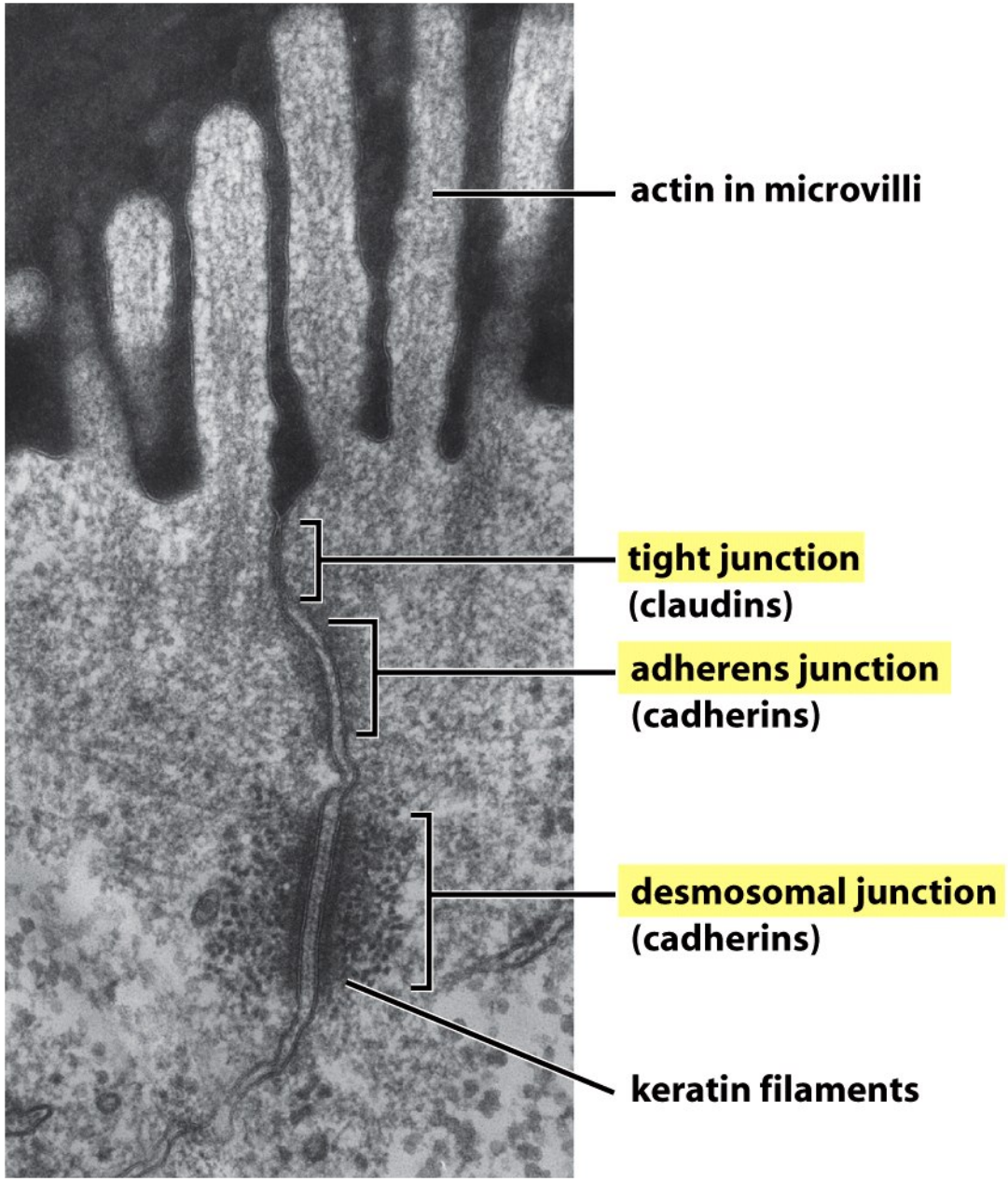


Figure 19-27 *Molecular Biology of the Cell* (© Garland Science 2008)

Figure 19-28 *Molecular Biology of the Cell* (© Garland Science 2008)

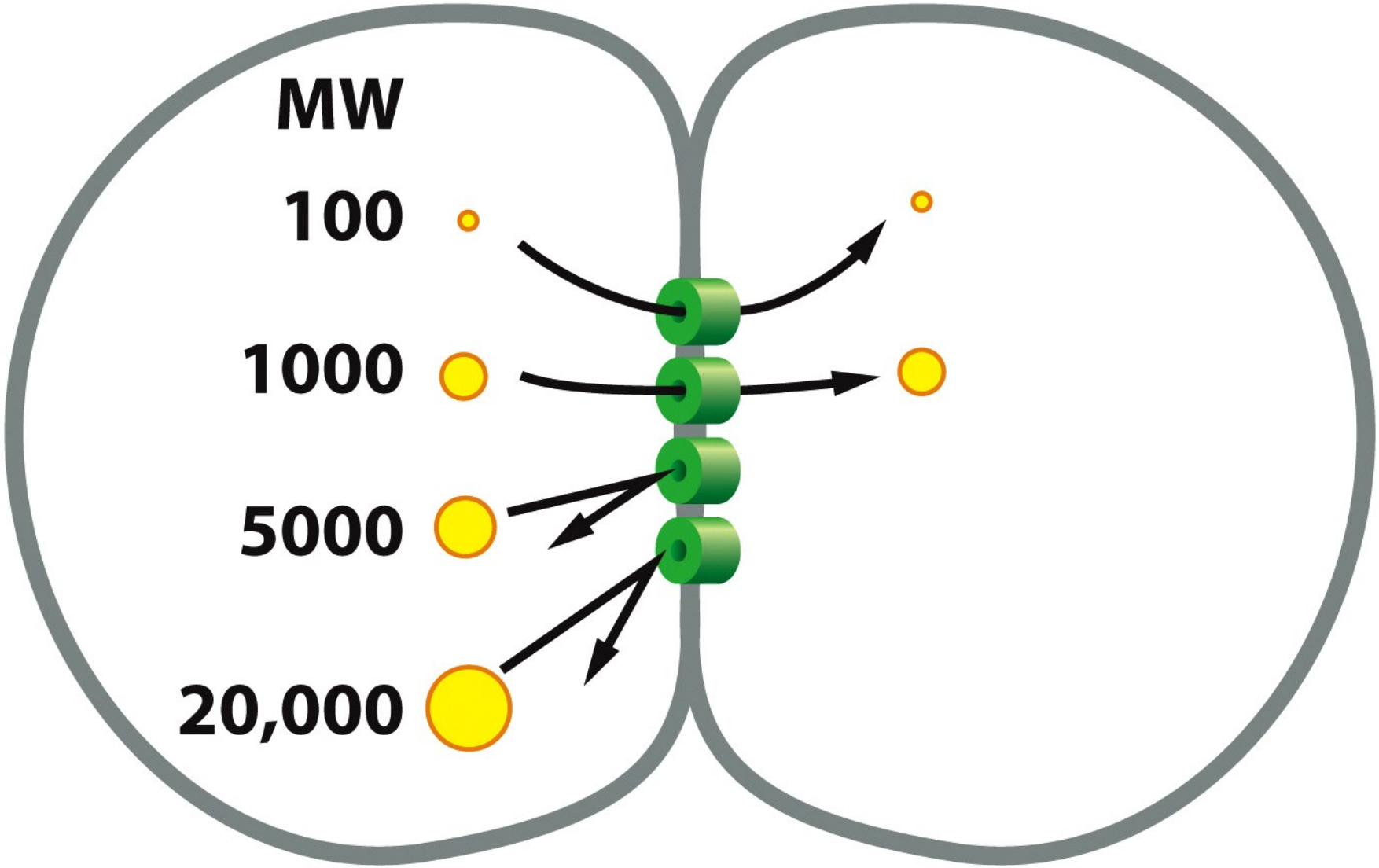


Figure 19-33 *Molecular Biology of the Cell* (© Garland Science 2008)

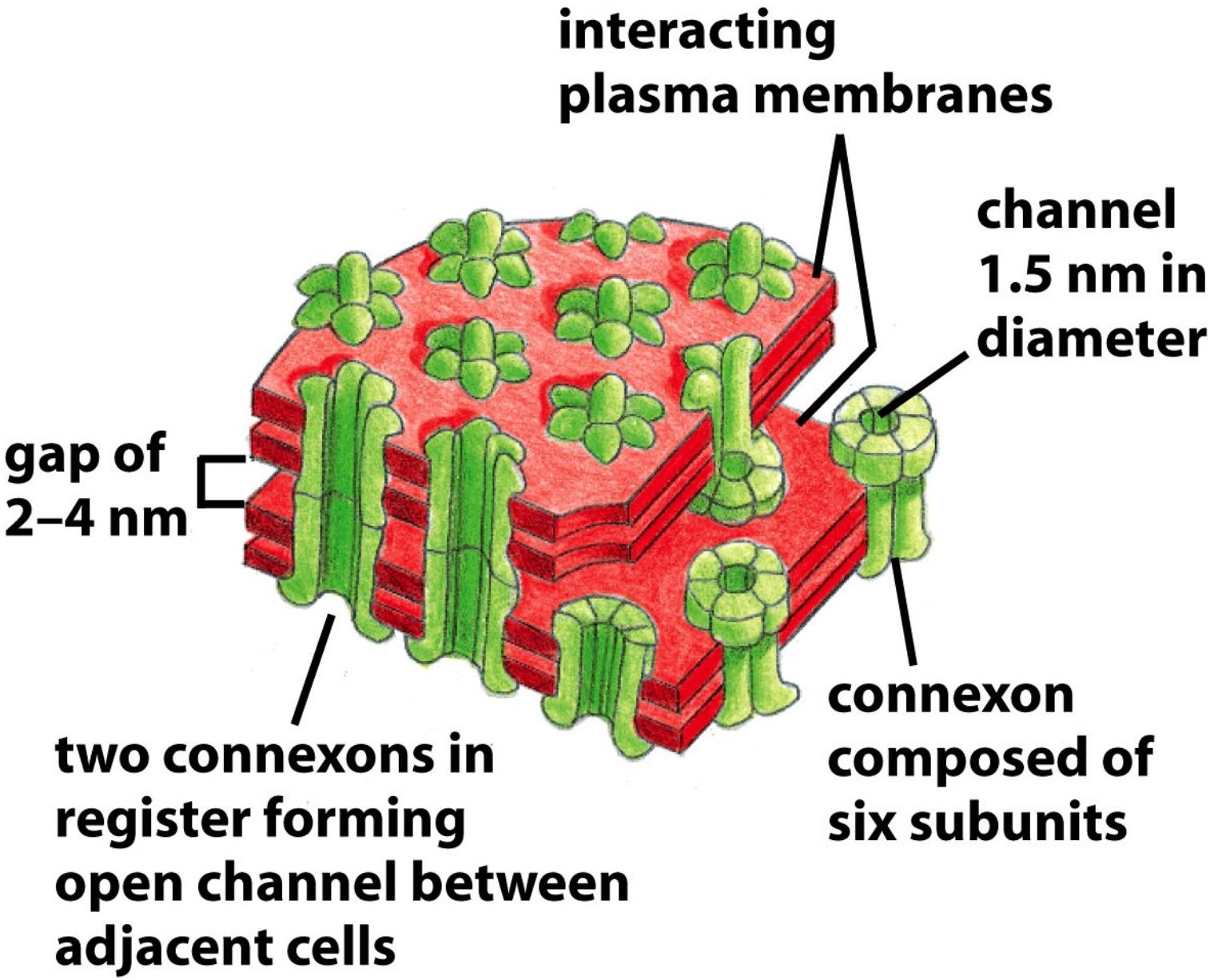


Figure 19-34a *Molecular Biology of the Cell* (© Garland Science 2008)

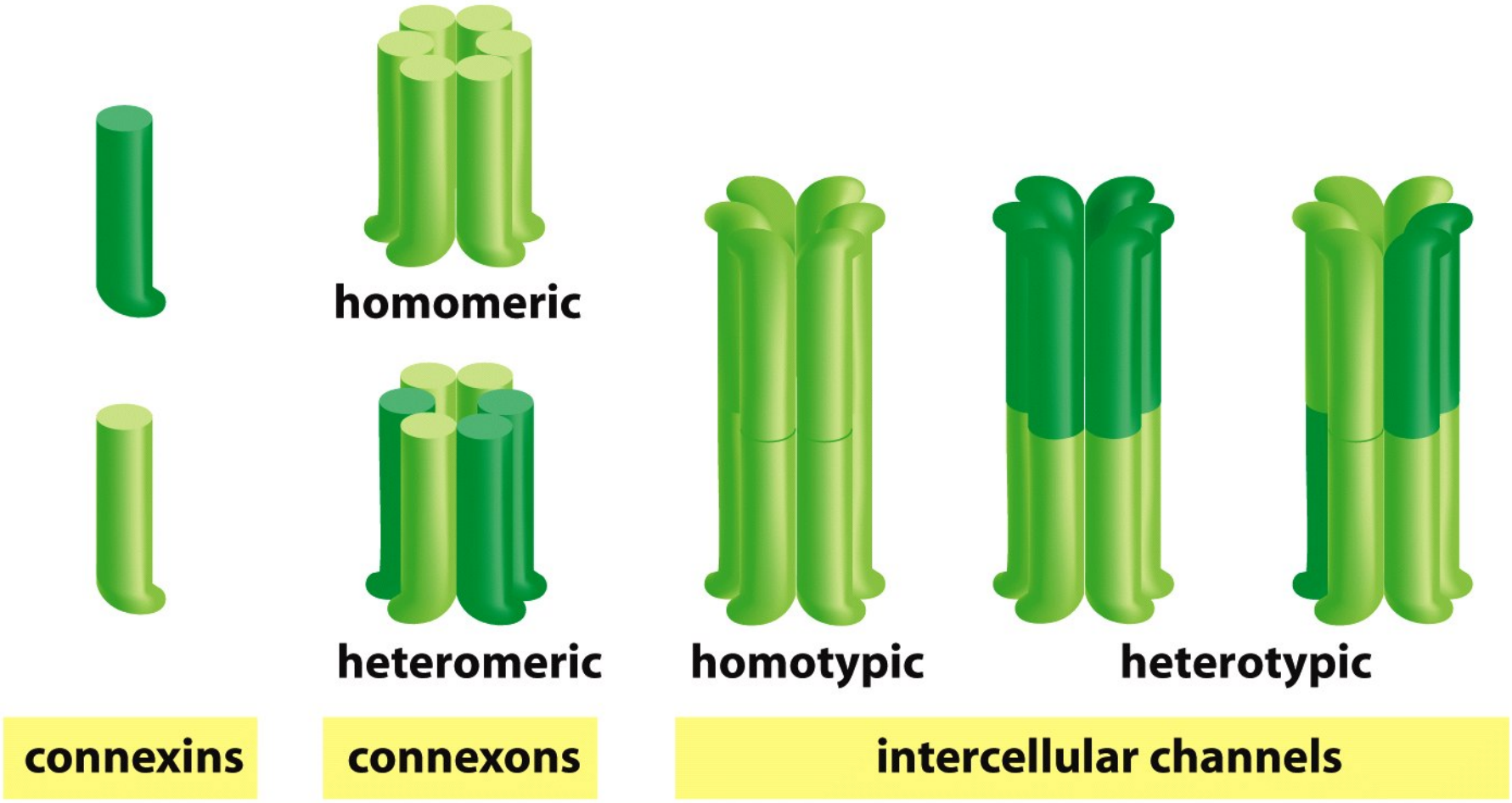


Figure 19-34b *Molecular Biology of the Cell* (© Garland Science 2008)

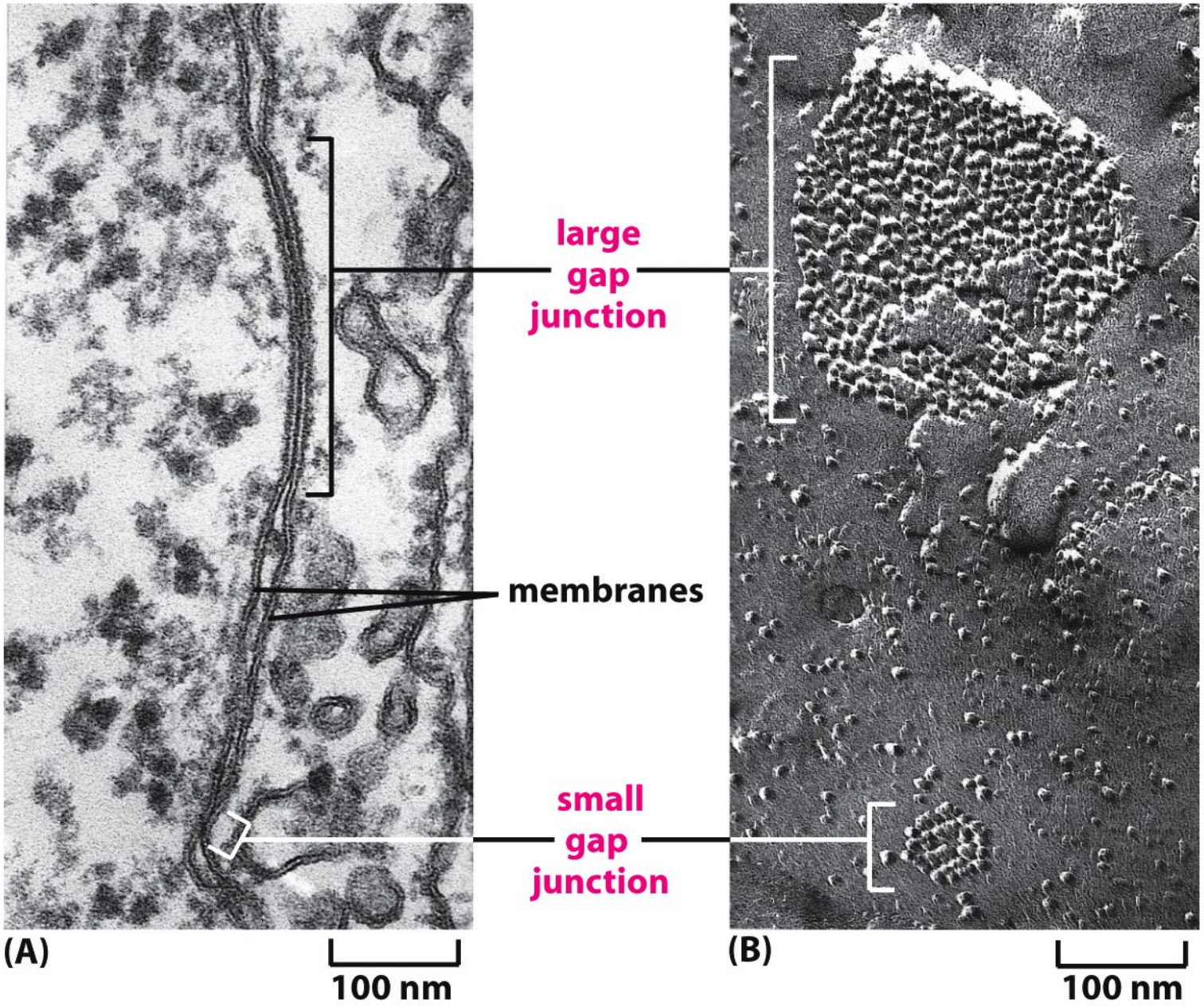


Figure 19-35 *Molecular Biology of the Cell* (© Garland Science 2008)