Molecular biology of the cell
BIO 207

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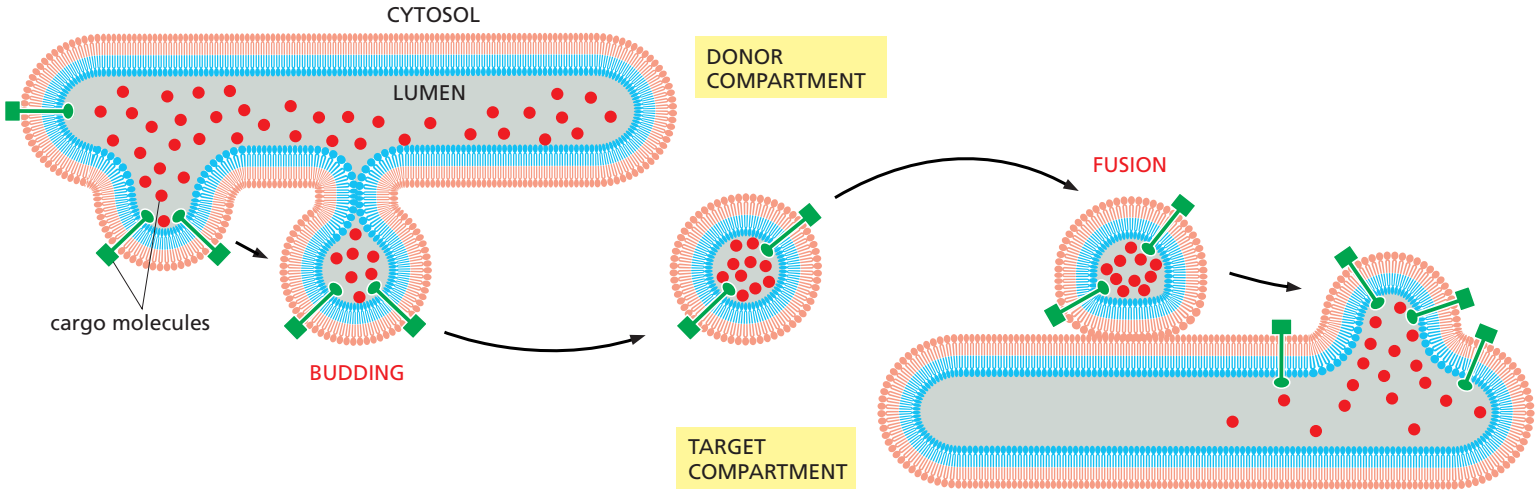
CHAPTER 13

Intracellular Membrane Traffic

IN THIS CHAPTER

Basics of vesicle transport discussed last week



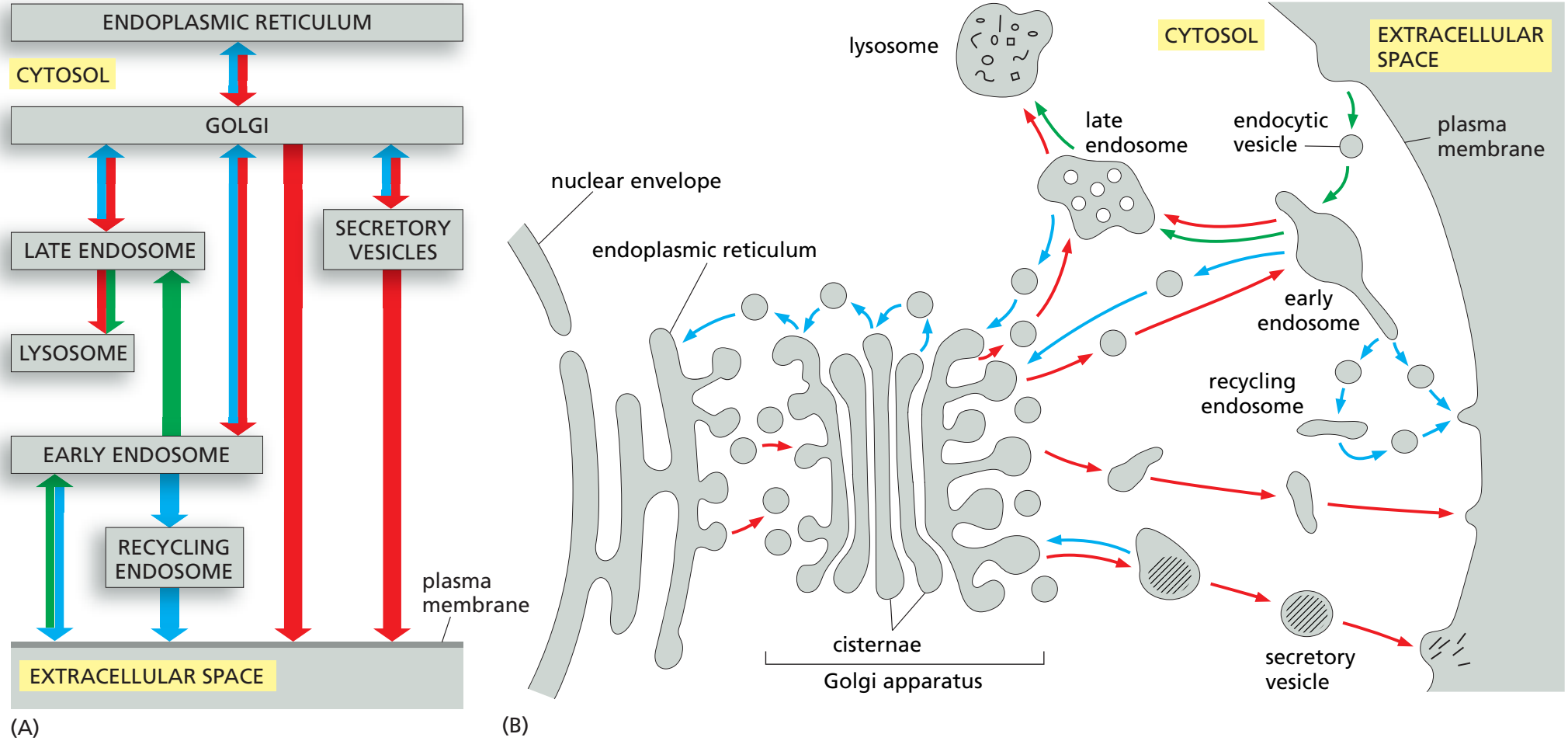
Mechanism

- Form a bud
- Detach a vesicle
- Move the vesicle optimally through the cell
- Merge the vesicle with an acceptor compartment
- Ensure that the compartments remain constant in size

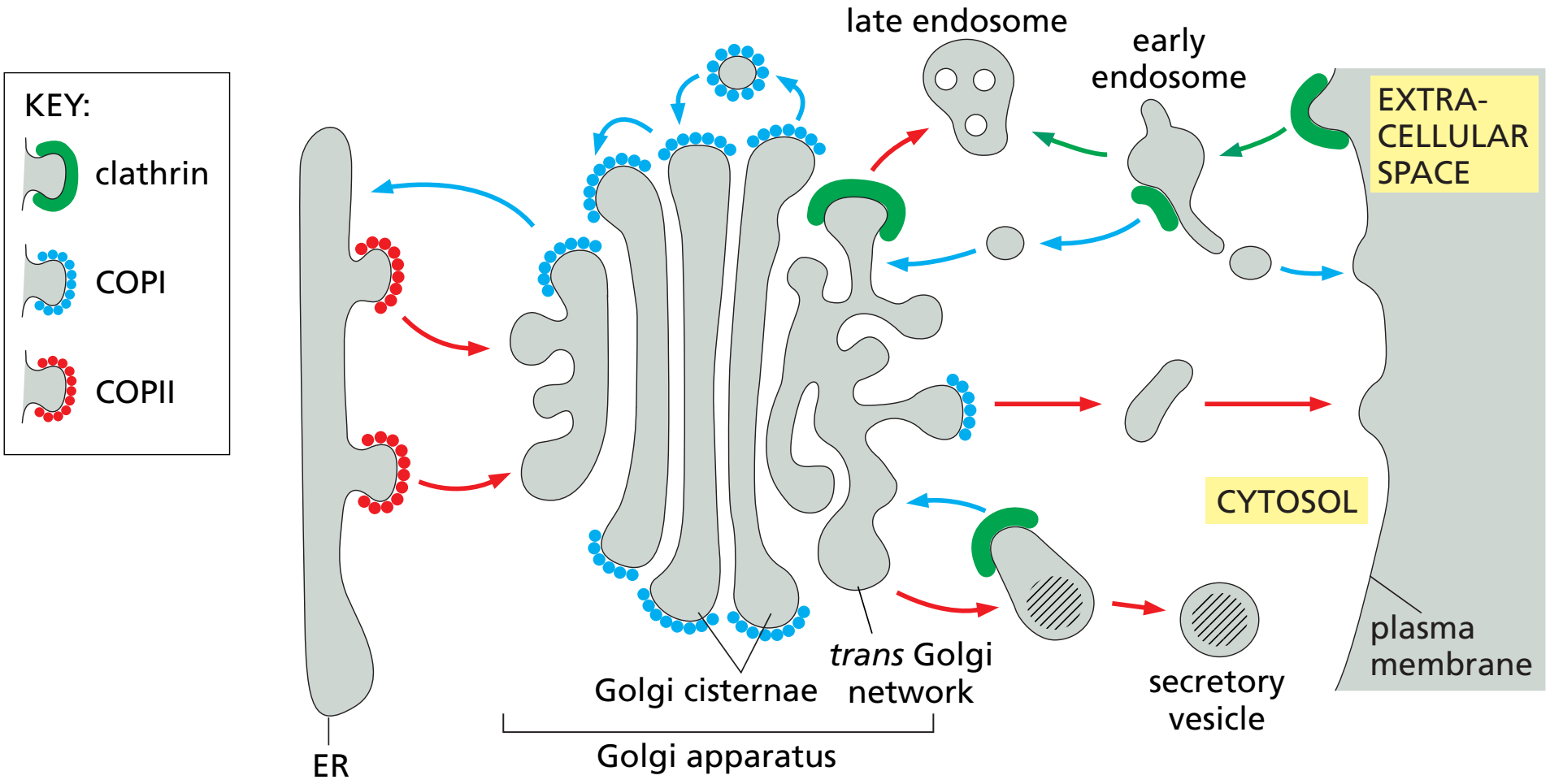
Specificity

- Put the right proteins in the nascent vesicle
- Address the vesicle to the right compartment

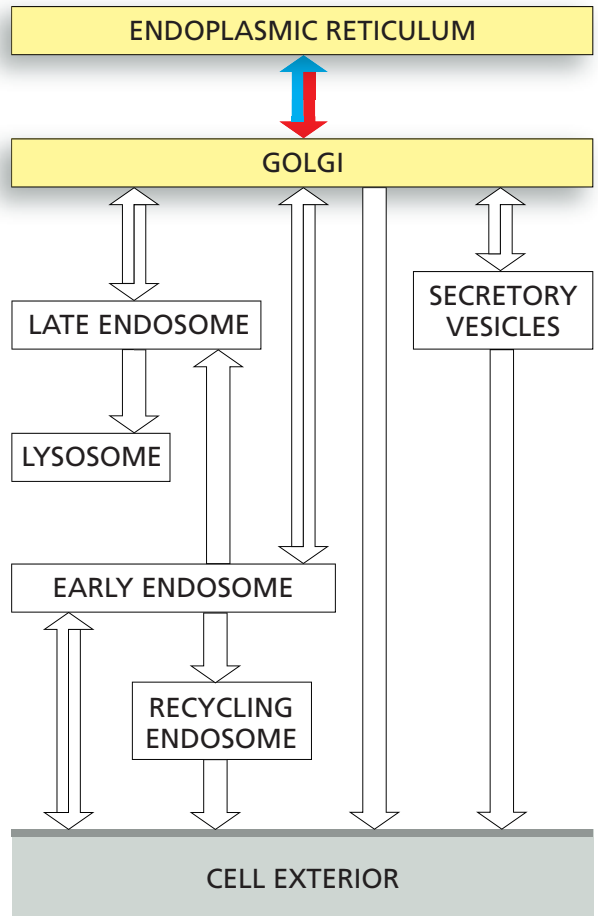
Vesicles in the secretory and endocytic pathways



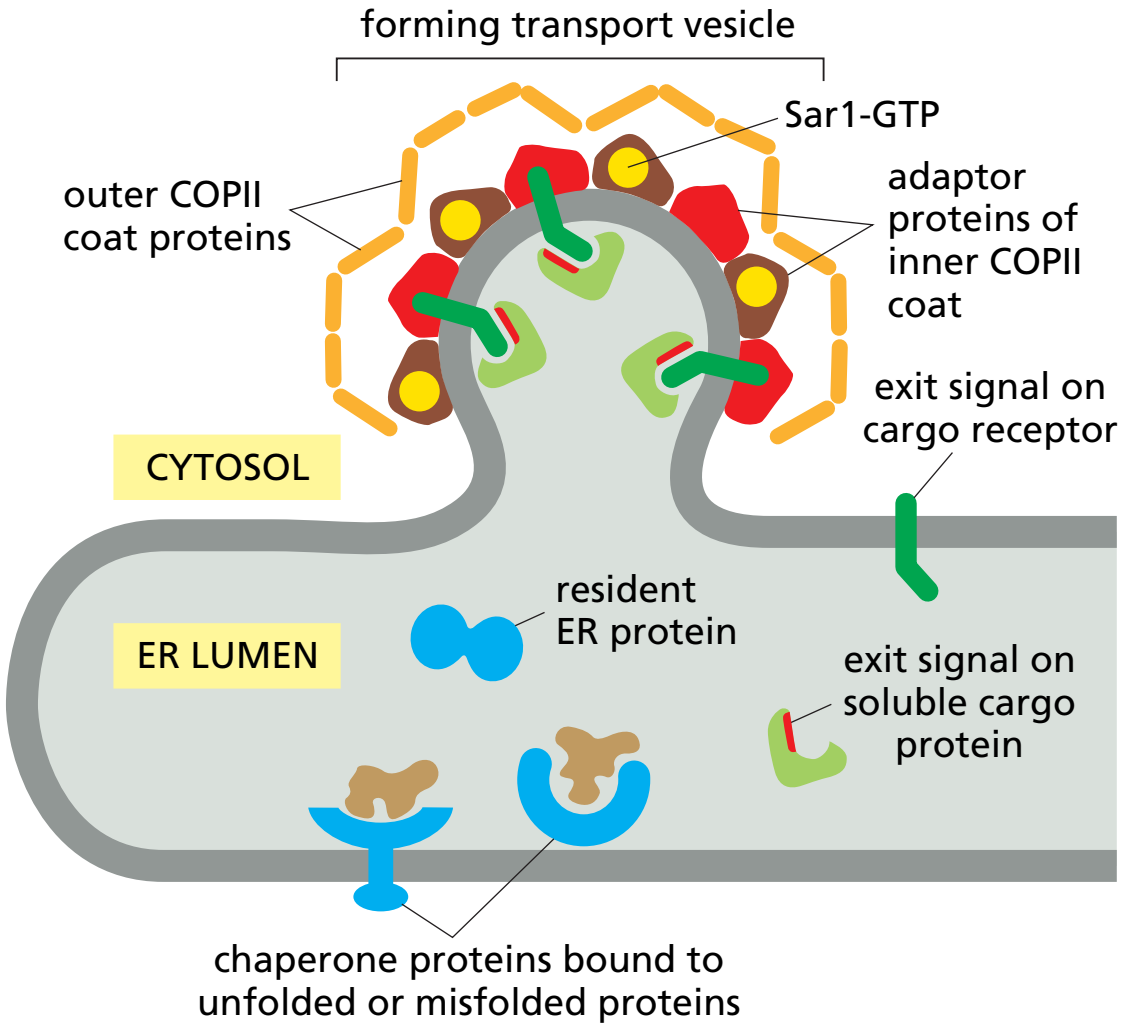
Use of different coats for different steps in vesicle traffic



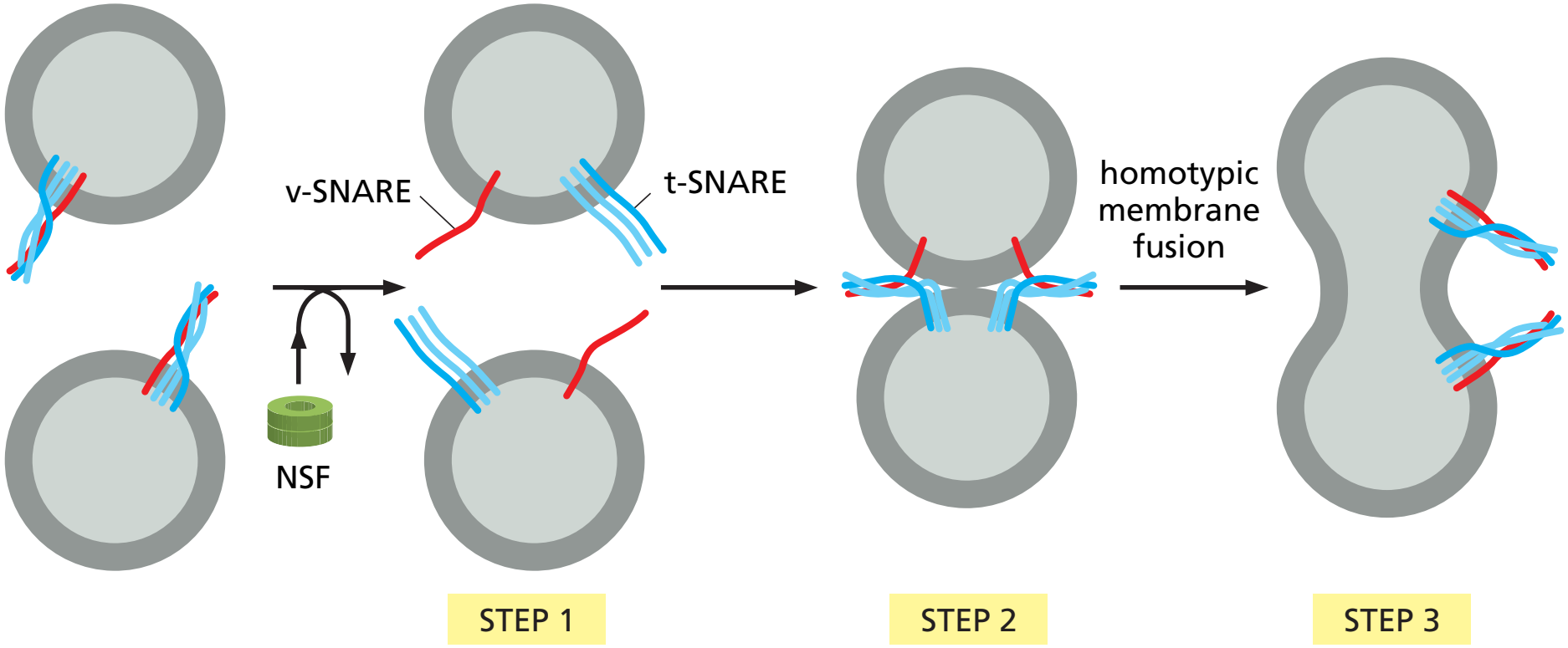
Transport between the ER and the Golgi


ENDOPLASMIC RETICULUM
GOLGI
LATE ENDOSOME
SECRETORY VESICLES
LYSOSOME
EARLY ENDOSOME
RECYCLING ENDOSOME
CELL EXTERIOR

The recruitment of membrane and soluble cargo molecules into ER transport vesicles

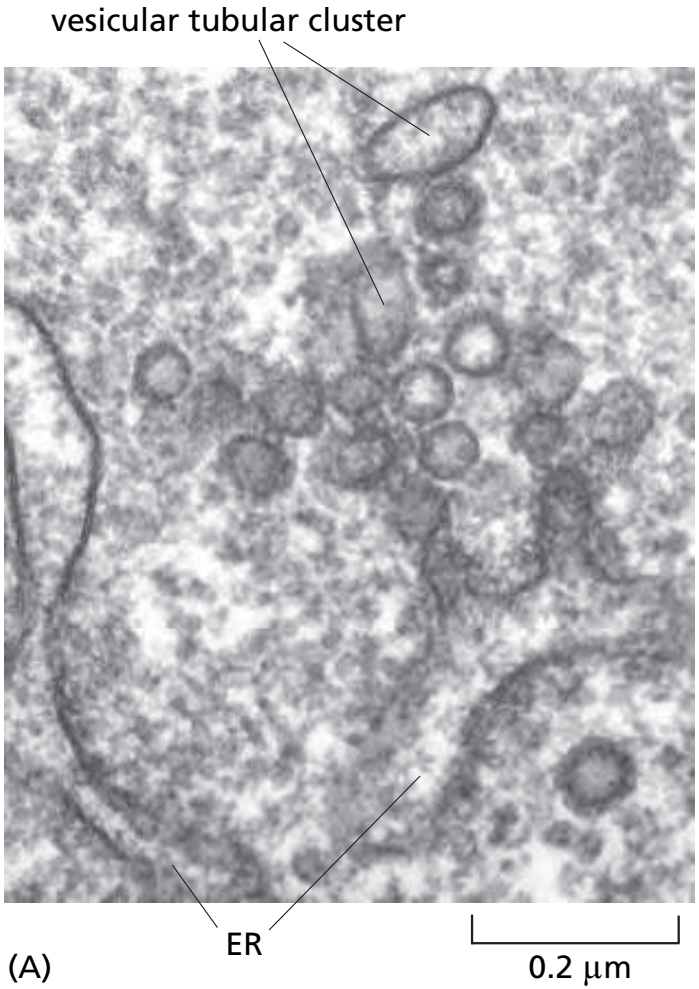


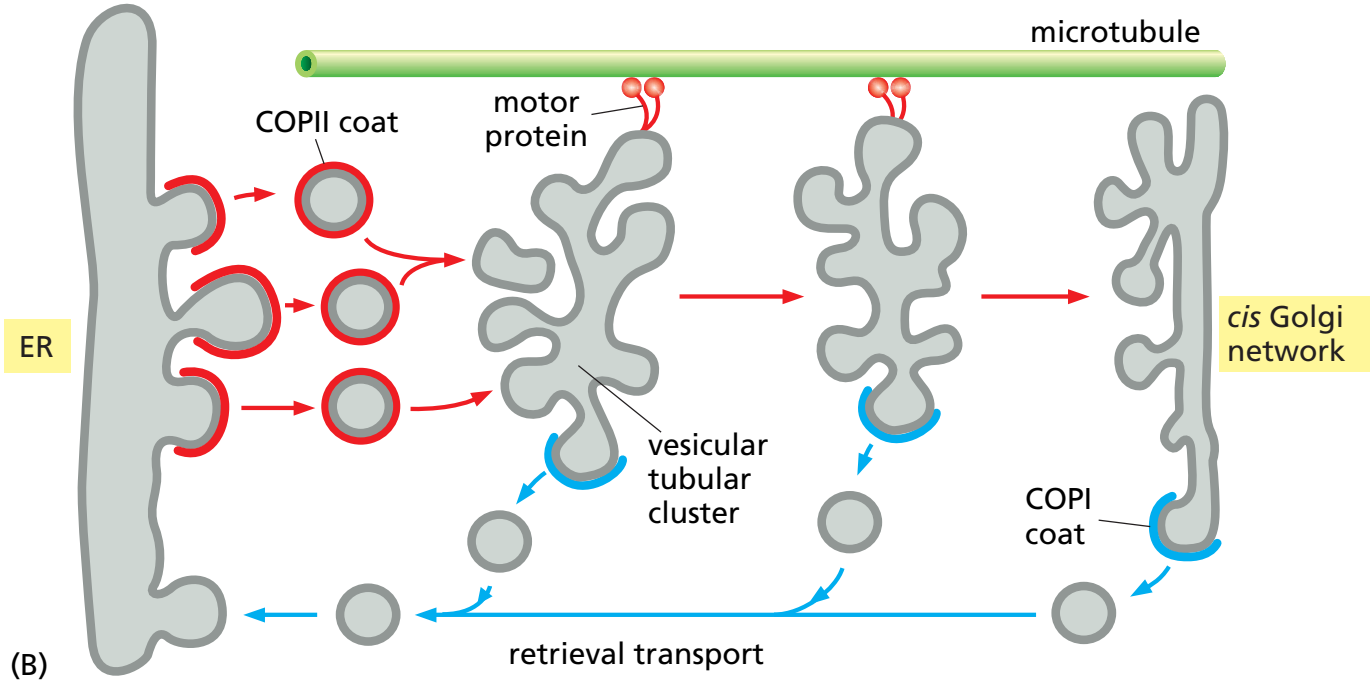
Homotypic membrane fusion to make transport more efficient



Fusion between vesicles moving to the same destination

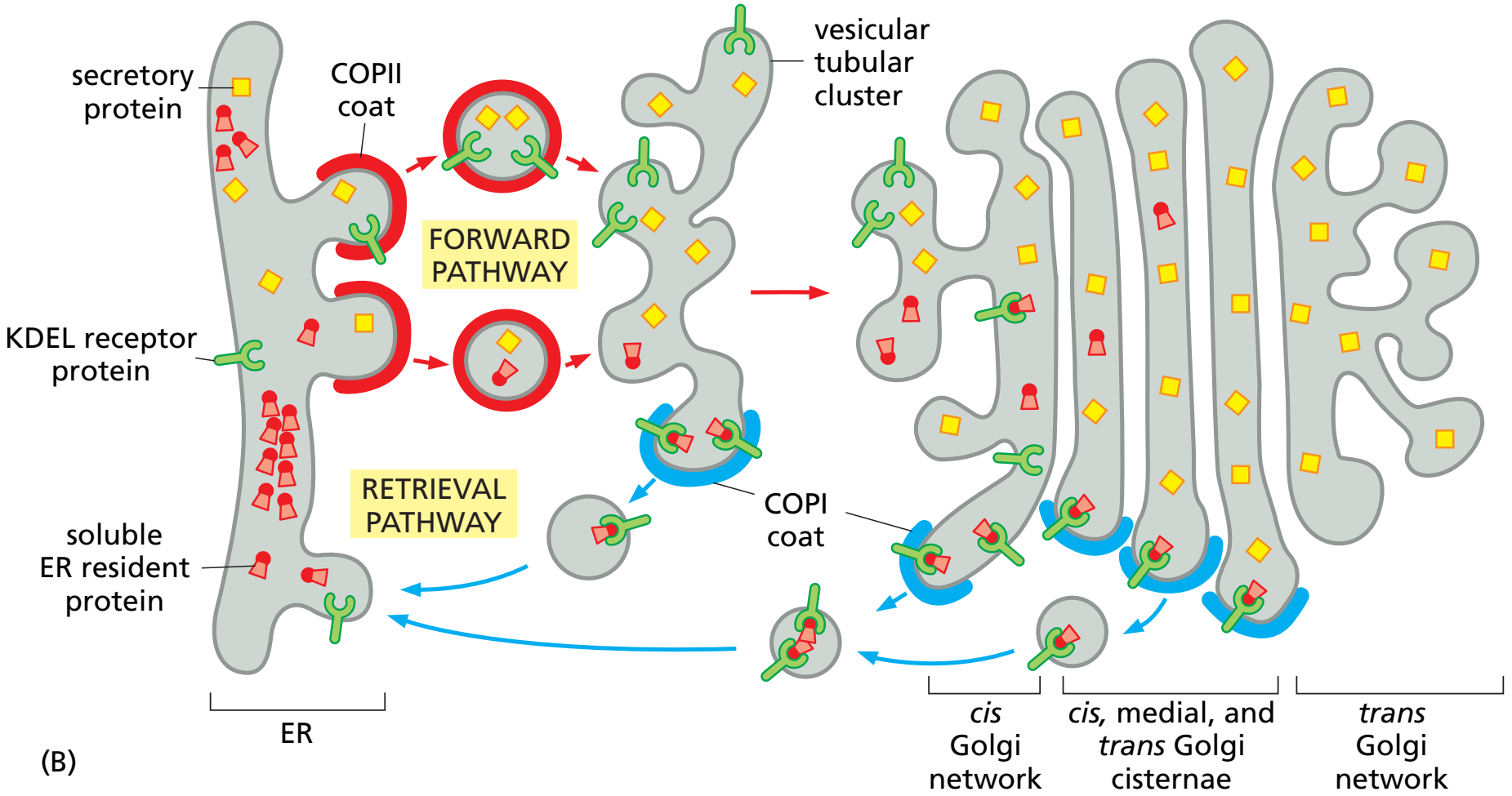
Homotypic fusion = Vesicular tubular clusters





Why is there retrograde transport from the Golgi to the ER?

Retrieval of soluble ER resident proteins



(B)

The C-terminal KDEL sequence

Biology is imperfect.
Sometimes a soluble ER resident protein is wrongfully transported to the Golgi

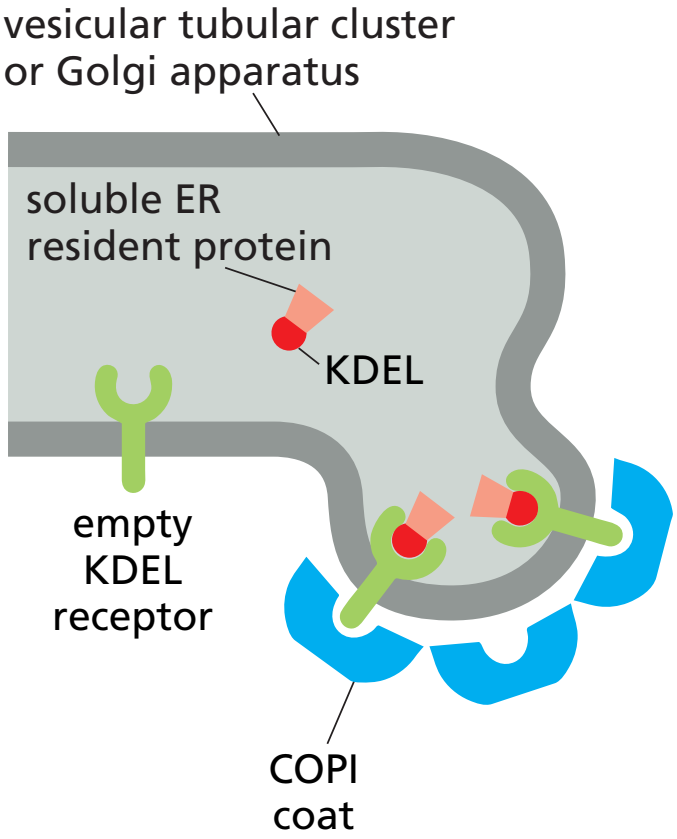
A specific amino acid sequences KDEL targets them for return

KDEL is located at the C-terminus

KDEL is also involved in retaining the ER resident protein!

Wrongfully transported ER Transmembrane proteins have retrieval signals (KKXX at the extreme C-Terminal end is an example) that directly interact with the COPI, so not via KDEL!

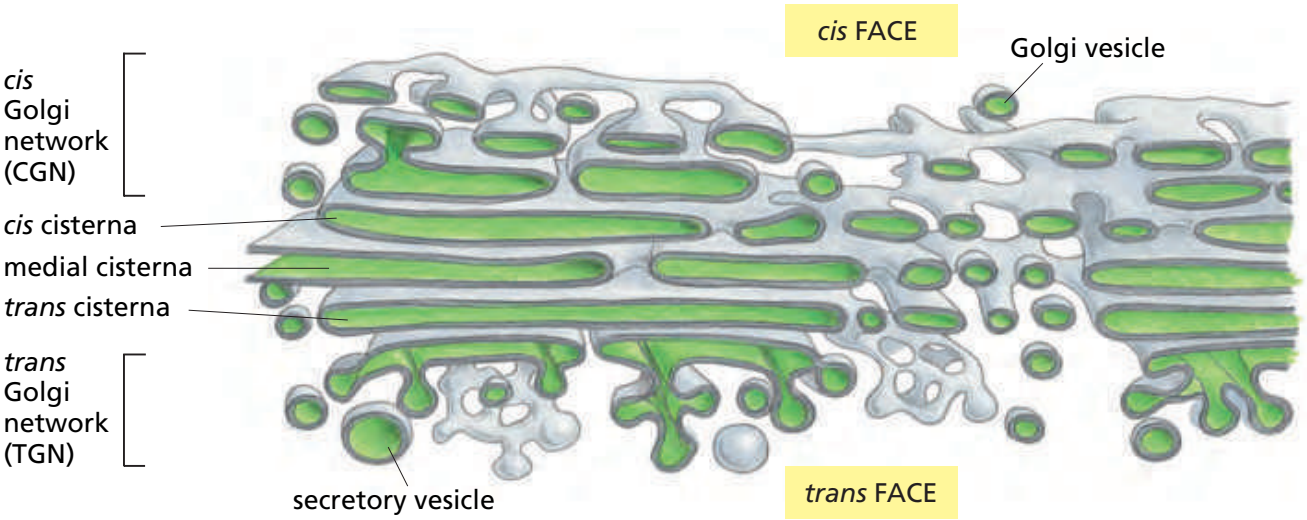
- **K**—Lysine
- **D**—Aspartic acid
- **E**—Glutamic acid
- **L**—Leucine

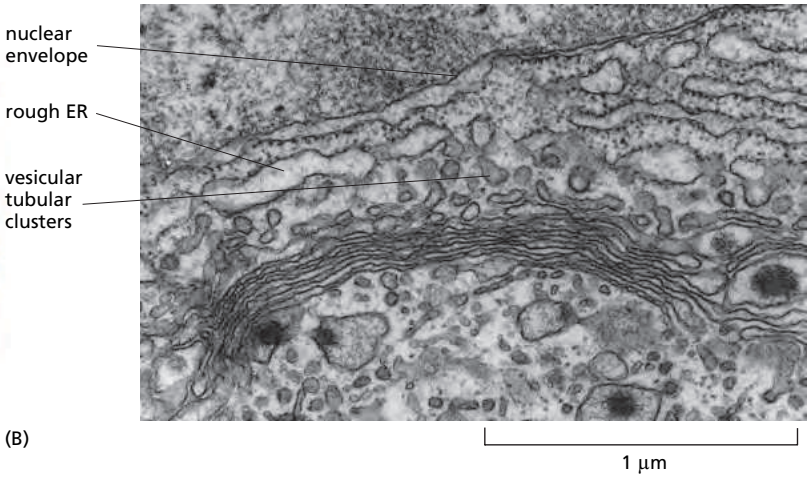


(A)

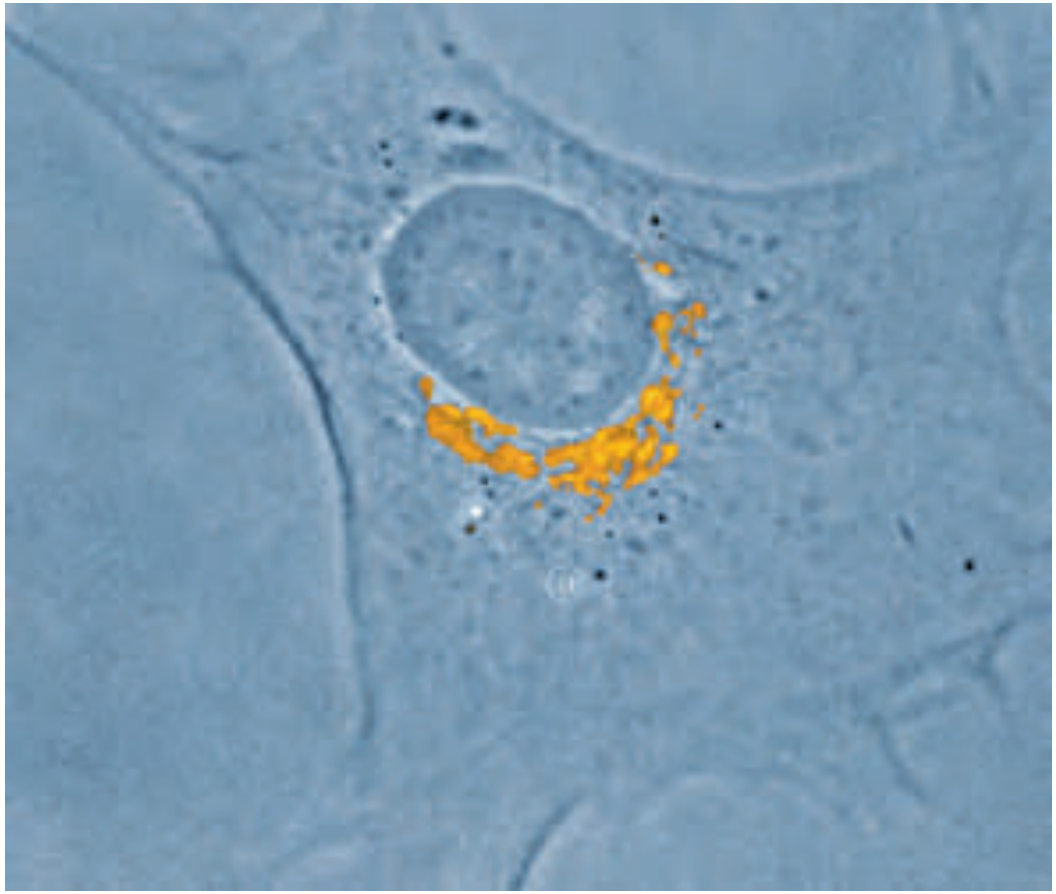
Transport through, editing and sorting of proteins in the Golgi

The Golgi apparatus

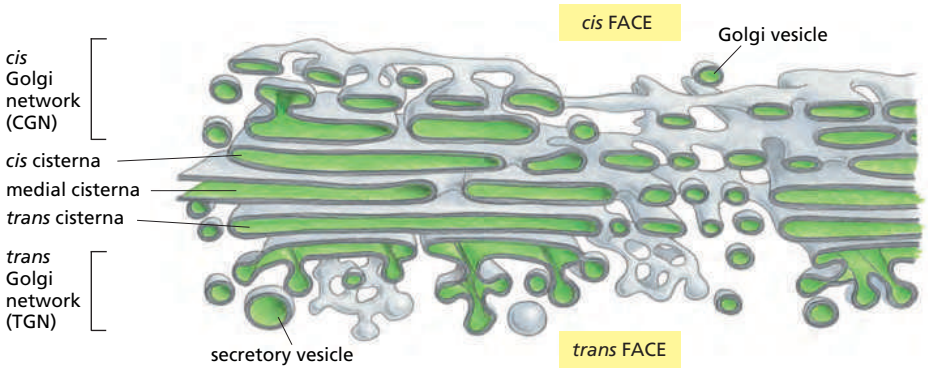


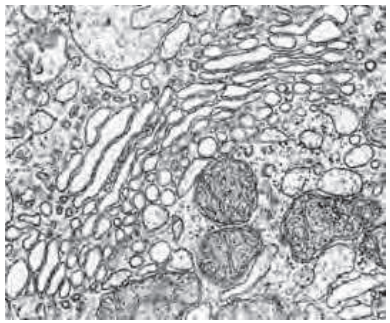


Localization of the Golgi apparatus in animal cells

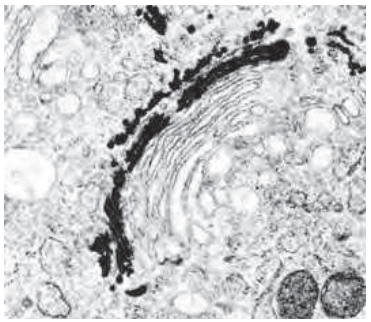


Molecular compartmentalization of the Golgi apparatus

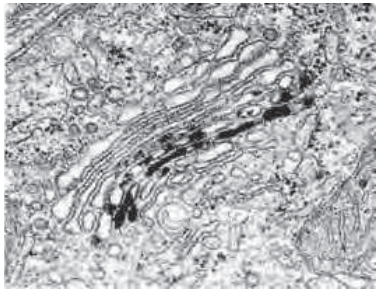




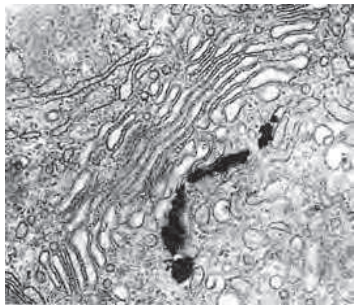
(A)
No stain



(B)
Cisternae in Cis compartment stained with Osmium

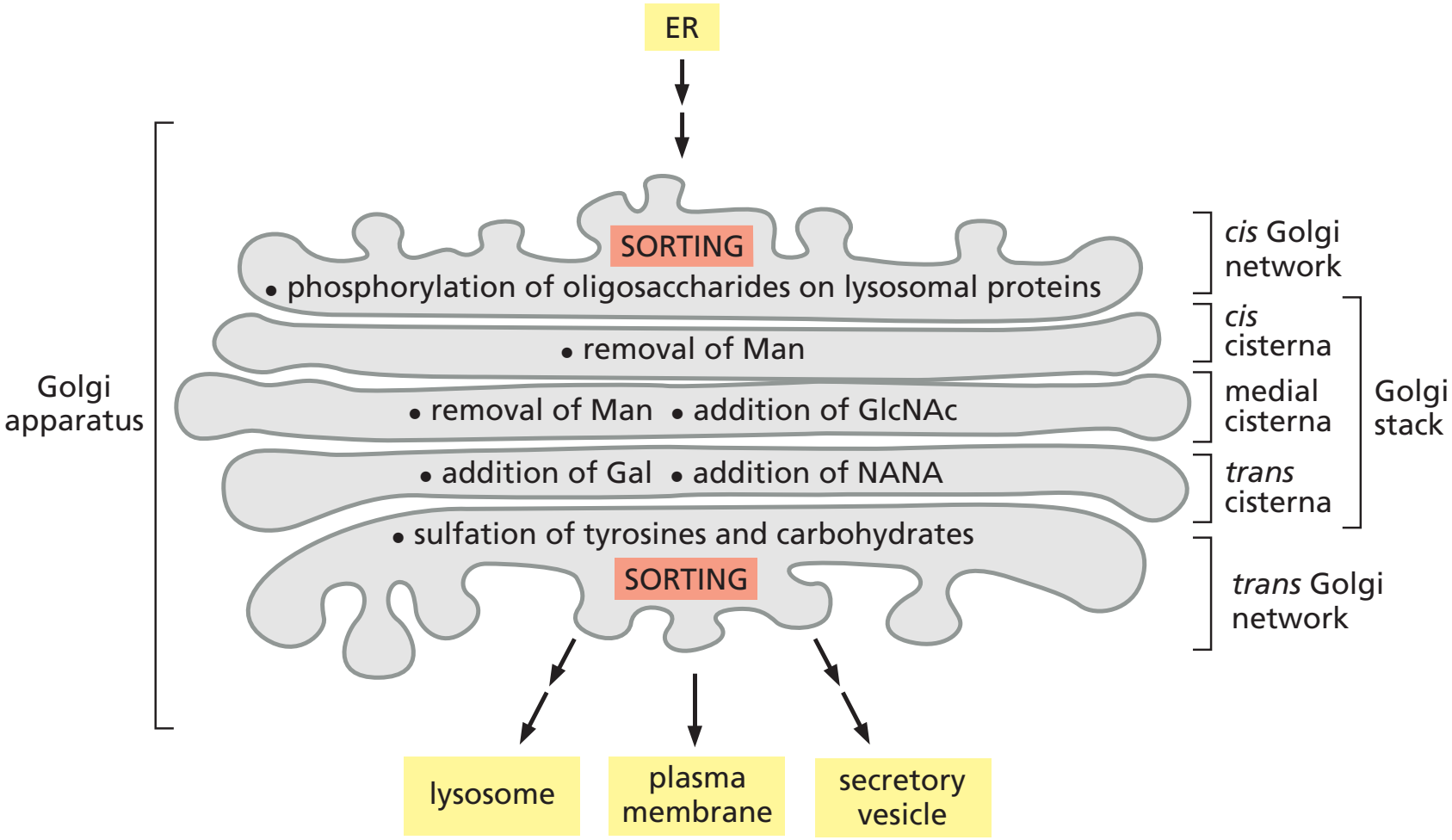


(C)
Nucleoside diphophatase
Trans cisterna



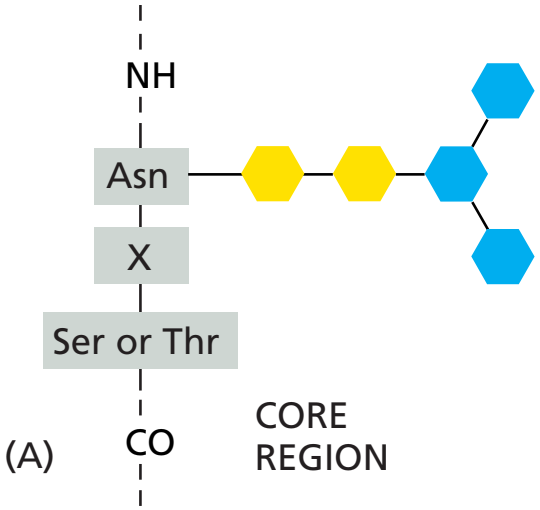
(D)
Acid phosphatase
Trans Golgi Network

Oligosaccharide processing in Golgi compartments

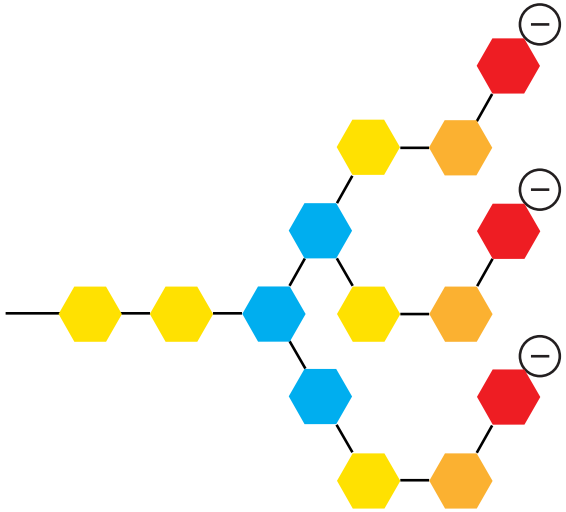


Glycosylation in the Golgi

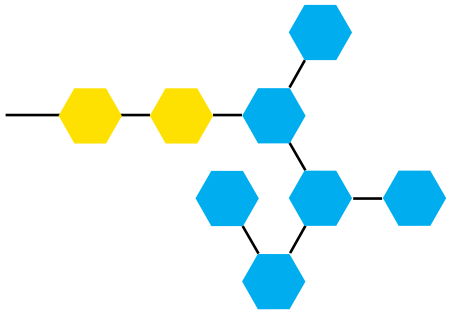
The two main classes of asparagine-linked (*N-linked*) oligosaccharides found in mature mammalian glycoproteins



(A)



(B) COMPLEX OLIGOSACCHARIDE



(C) HIGH-MANNOSE OLIGOSACCHARIDE

KEY

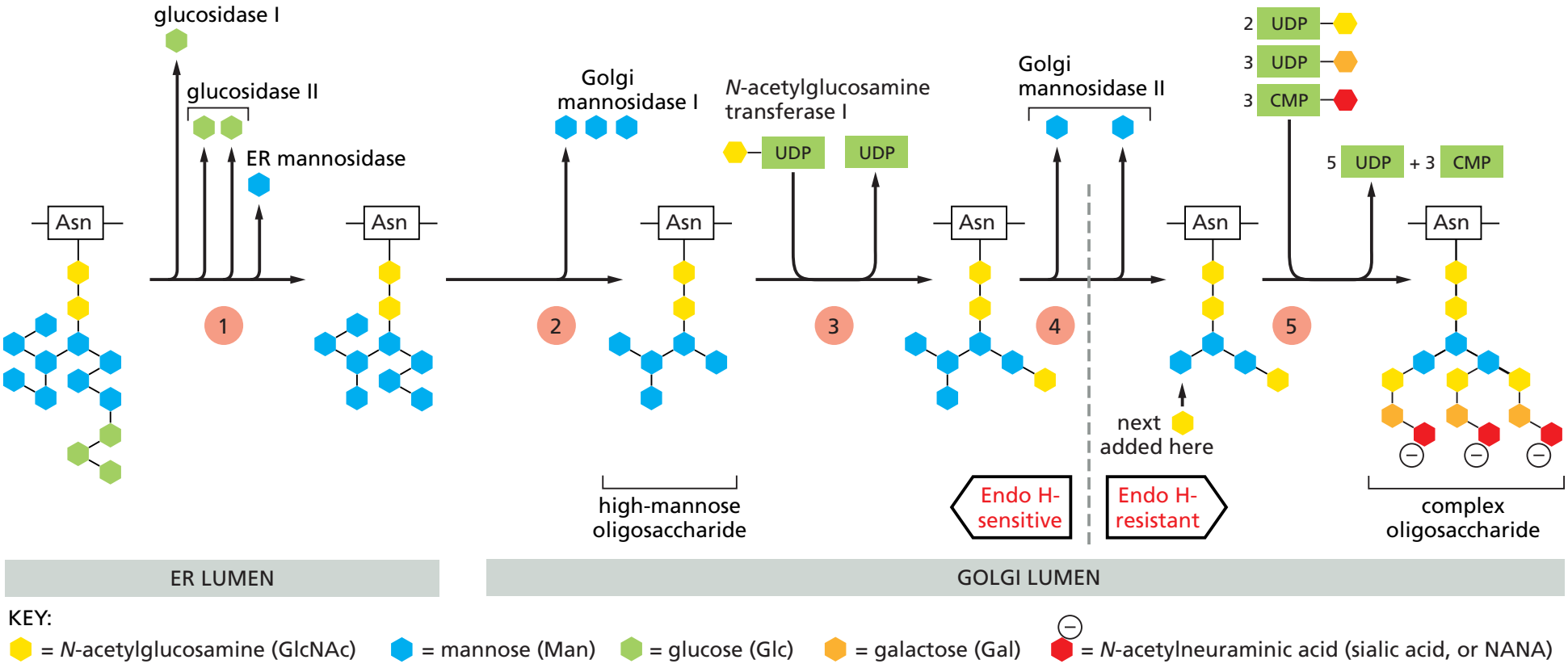
= *N*-acetylglucosamine (GlcNAc)

= mannose (Man)

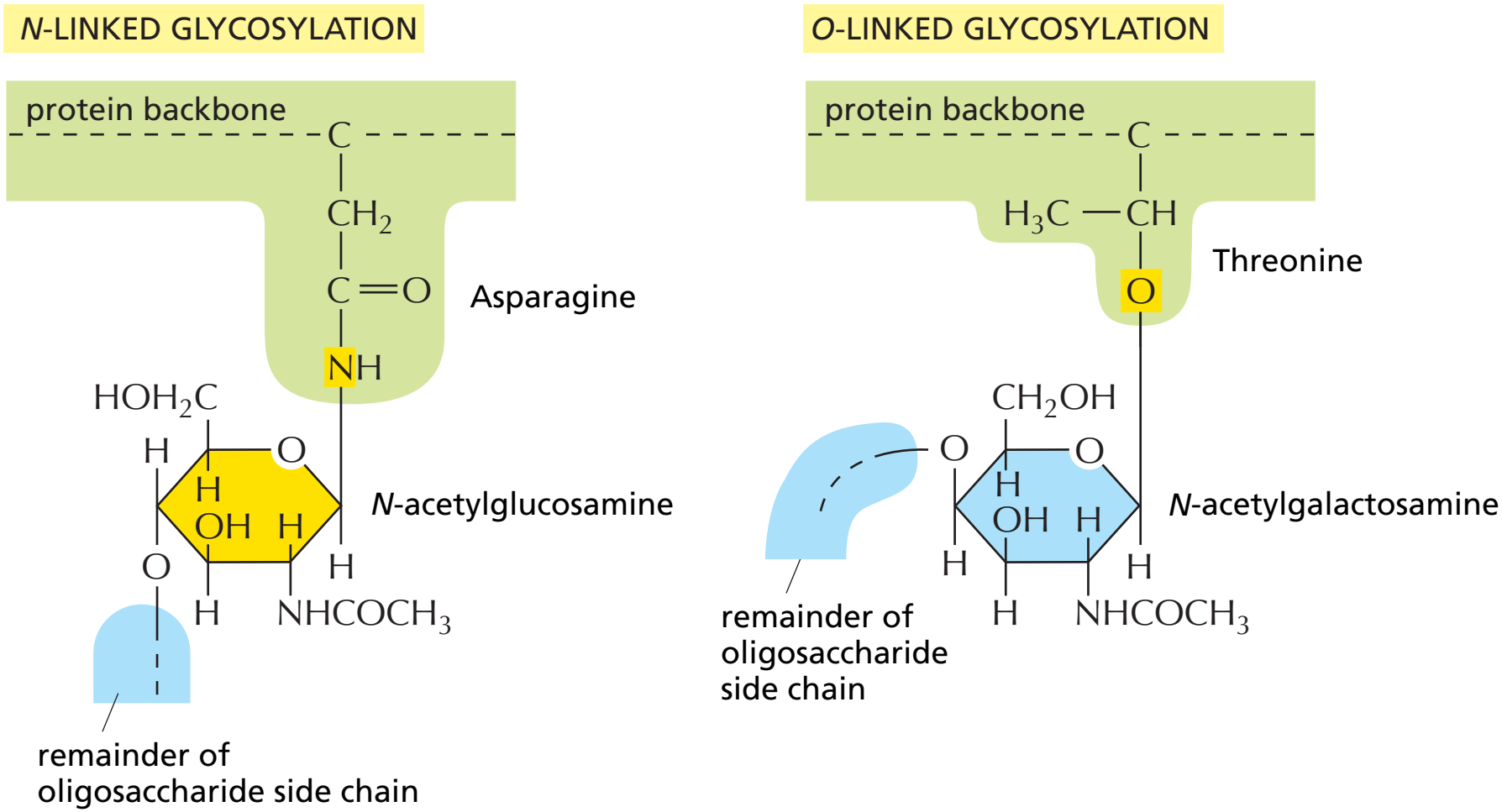
= galactose (Gal)

= *N*-acetylneuraminic acid (sialic acid, or NANA)

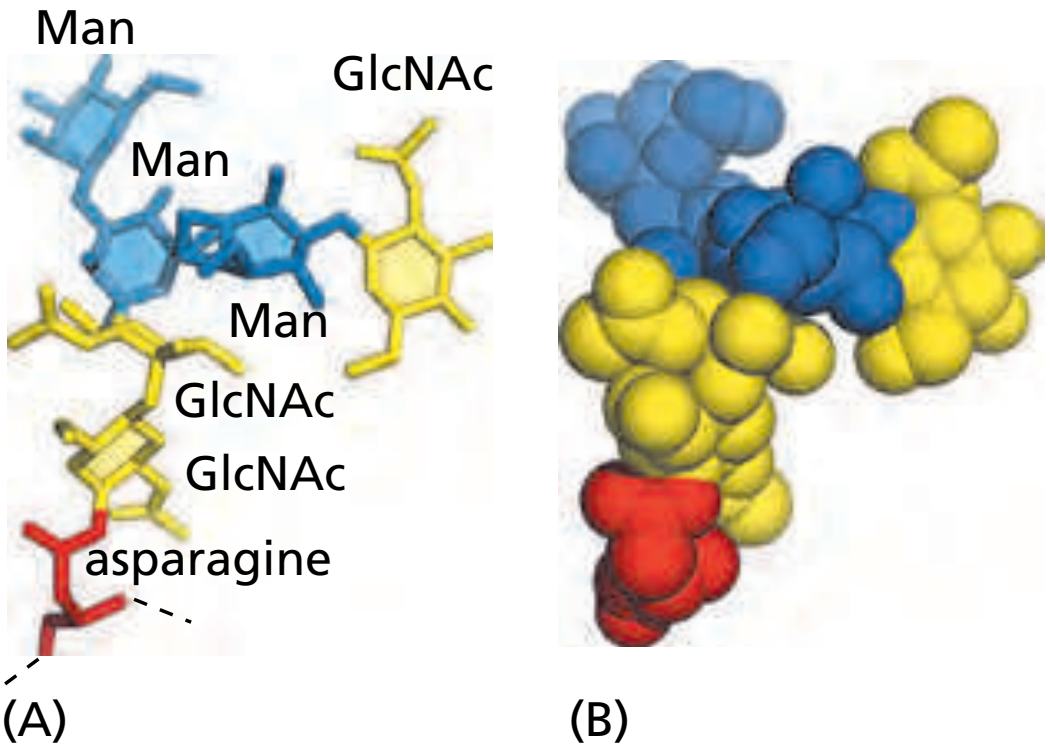
Oligosaccharide processing in the ER and the Golgi apparatus



N- and *O-linked* glycosylation



Purposes of glycosylation



The three-dimensional structure of a small *N-linked* oligosaccharide

Promoting folding (ER)

Solubilizing proteins

Protecting proteins (Membrane proteins facing extracellular milieu)

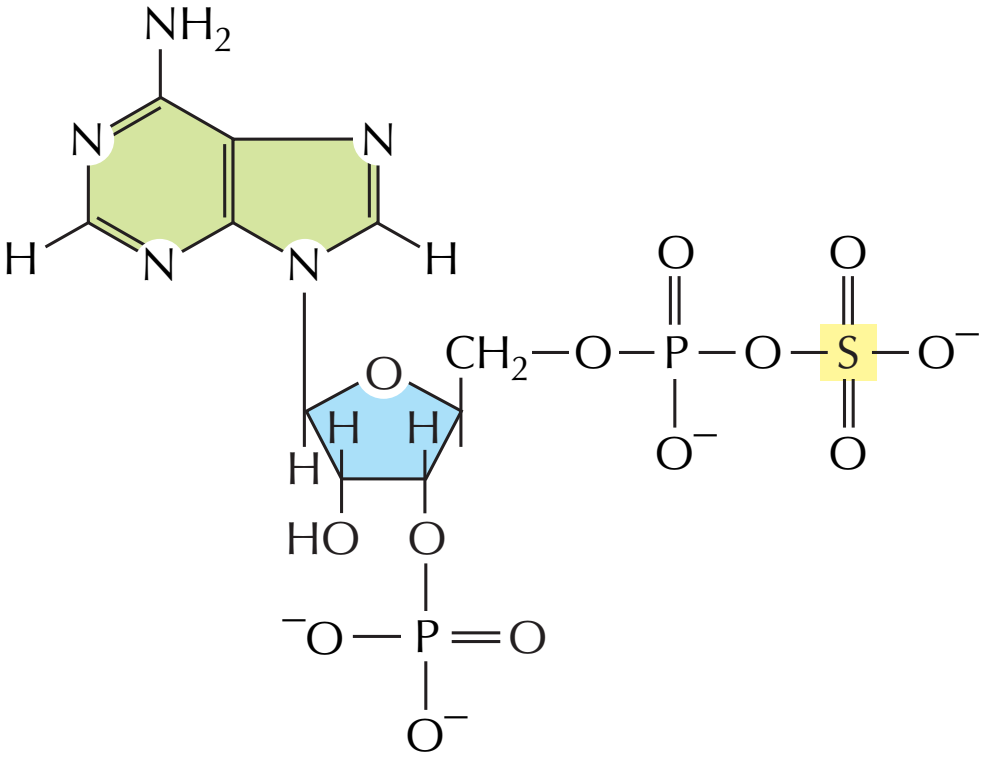
Roles in cell-cell recognition

Protein interactions

Protection against pathogens (Intestine & Lung)

Proteins that interact with sugar groups are called lectins

The structure of PAPs



3′-phosphoadenosine-5′-phosphosulfate
(PAPS)

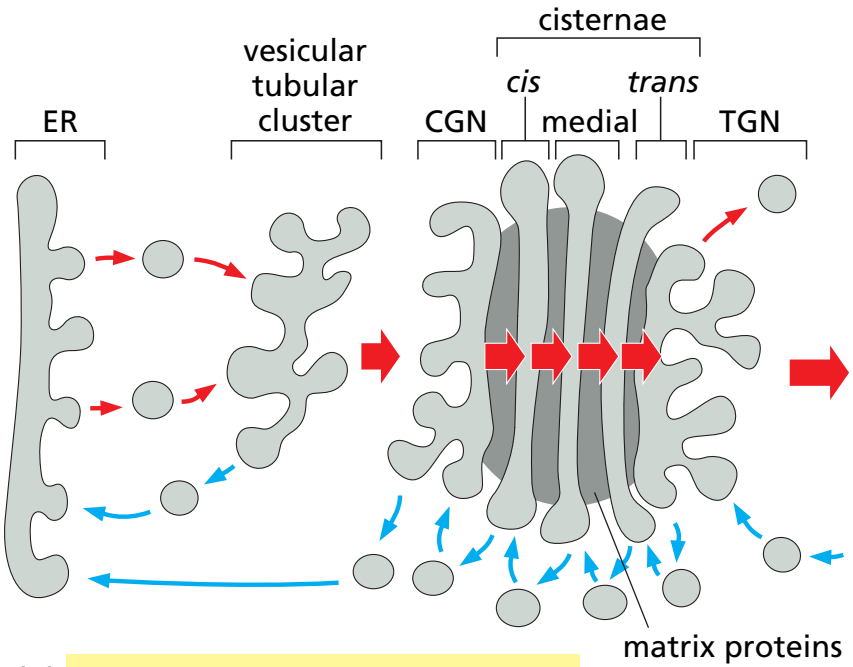
Important for addition of sulfate groups on glycosaminoglycans -> Sulfation

These are long chains of repeating disaccharide units (discussed later in the course, Chapter 19)

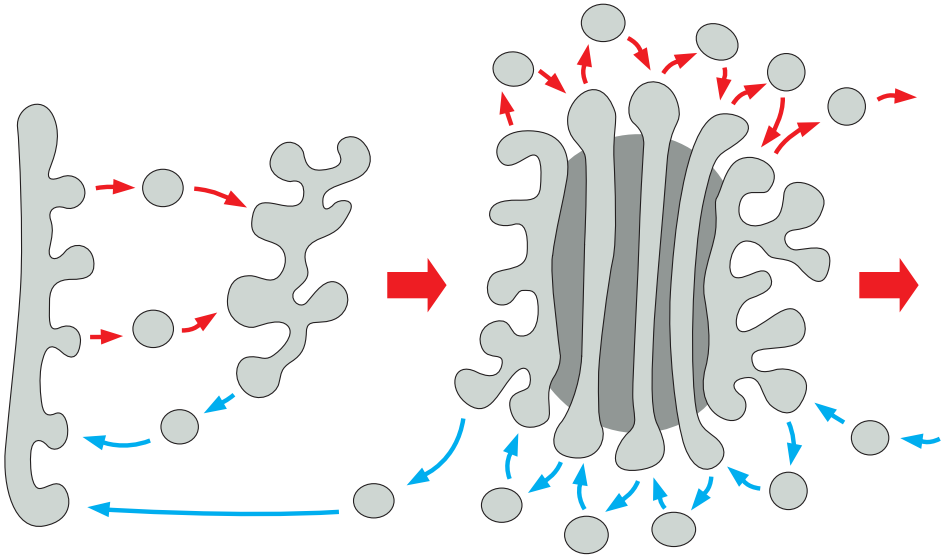
It is added in the trans golgi network

Important for extracellular matrix

Two possible models explaining the organization of the Golgi apparatus and how proteins move through it

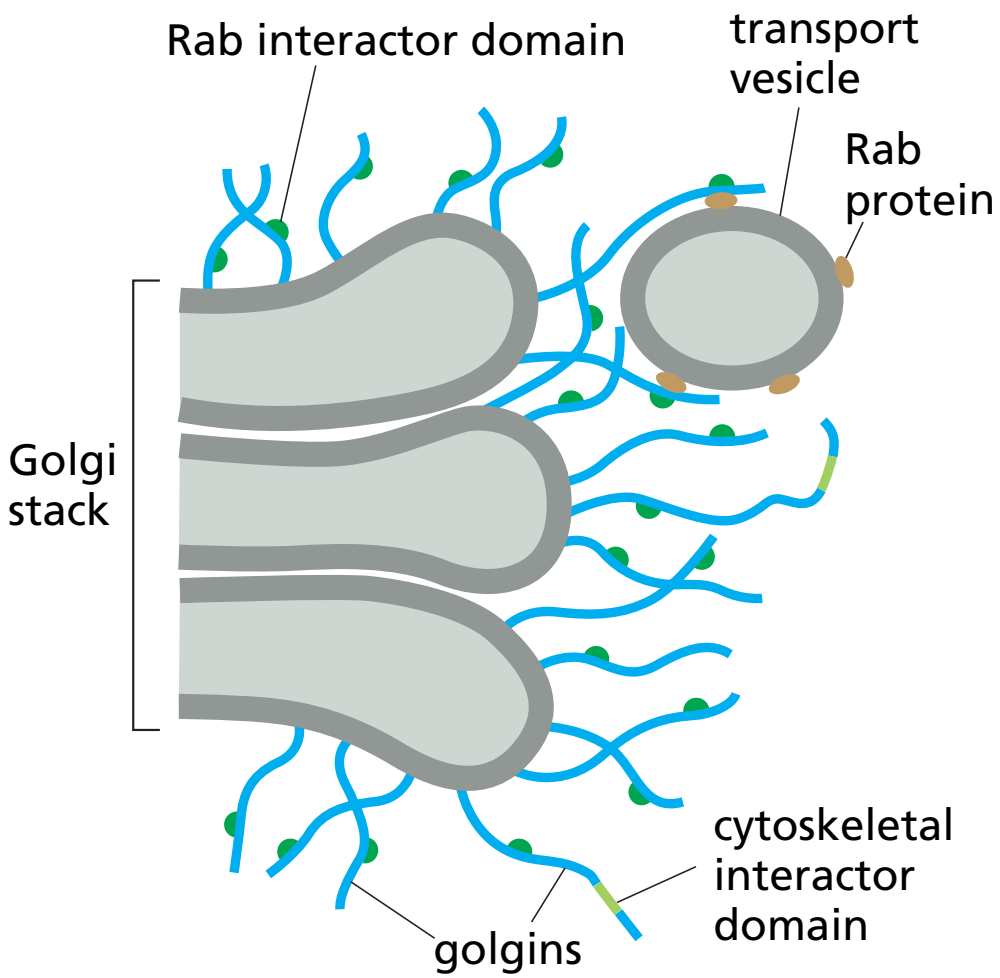


(A) CISTERNAL MATURATION MODEL



(B) VESICLE TRANSPORT MODEL

A model of golgin function



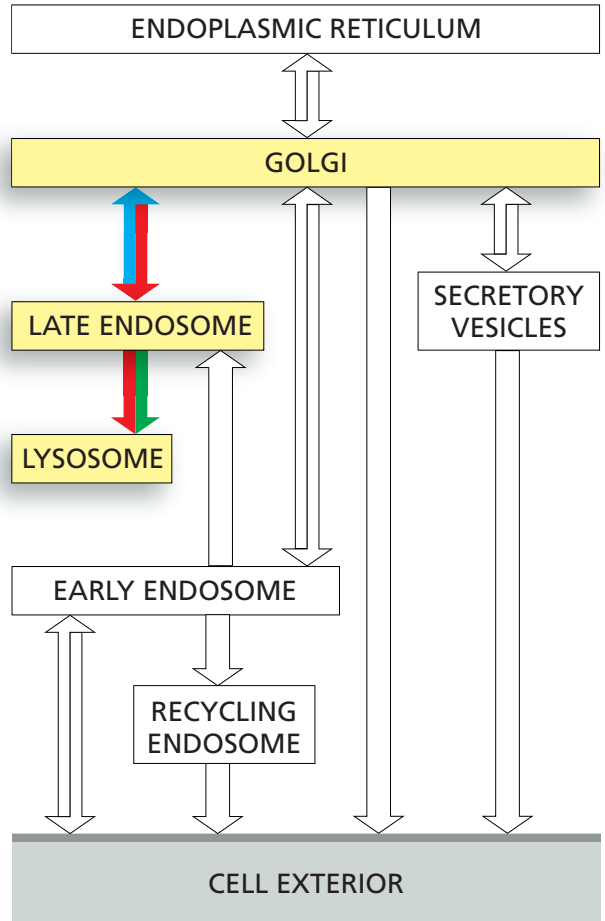
Golgin is important for organizing the golgi stack and retaining vesicles near the golgi

Golgins stick out 100-400 nM and make a “forest”

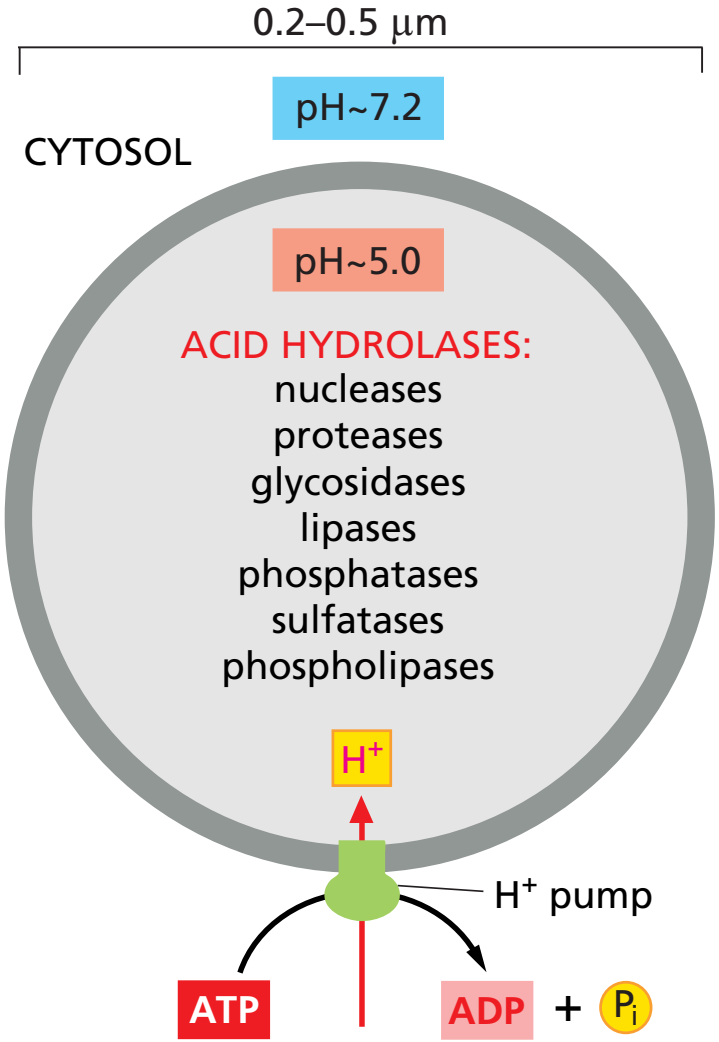
Other cytoskeletal microtubule and internal golgi matrix proteins are also involved.

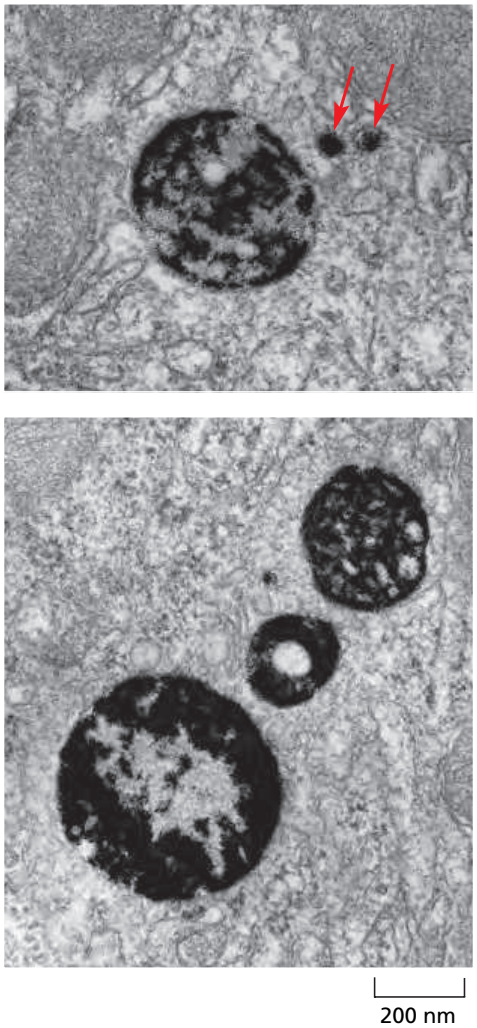
Figure 13–36 **A model of golgin function.** Filamentous golgins anchored to Golgi membranes capture transport vesicles by binding to Rab proteins on the vesicle surface.

Transport from the Golgi to the late endosome and lysosome

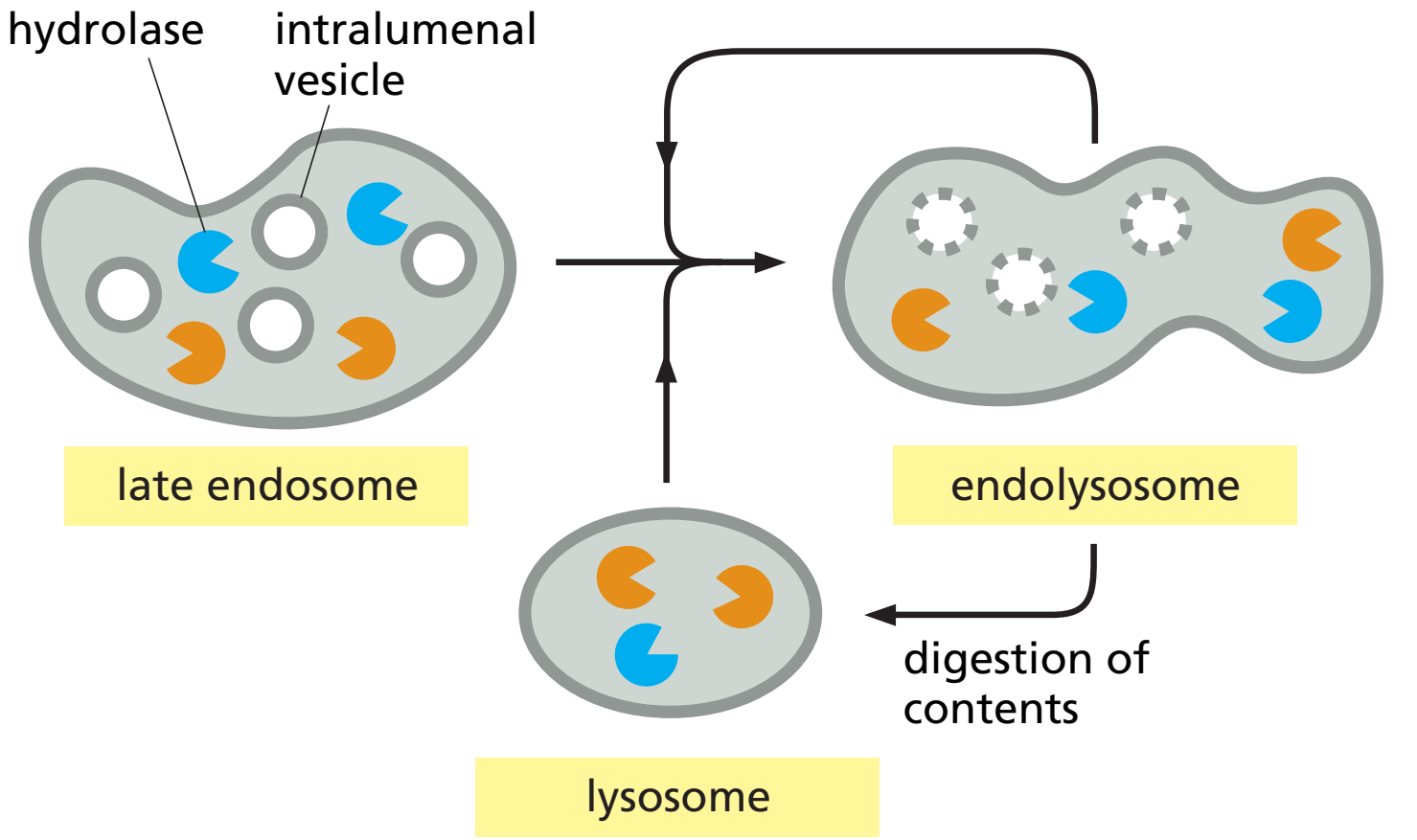

ENDOPLASMIC RETICULUM
GOLGI
LATE ENDOSOME
LYSOSOME
SECRETORY VESICLES
EARLY ENDOSOME
RECYCLING ENDOSOME
CELL EXTERIOR

Lysosomes

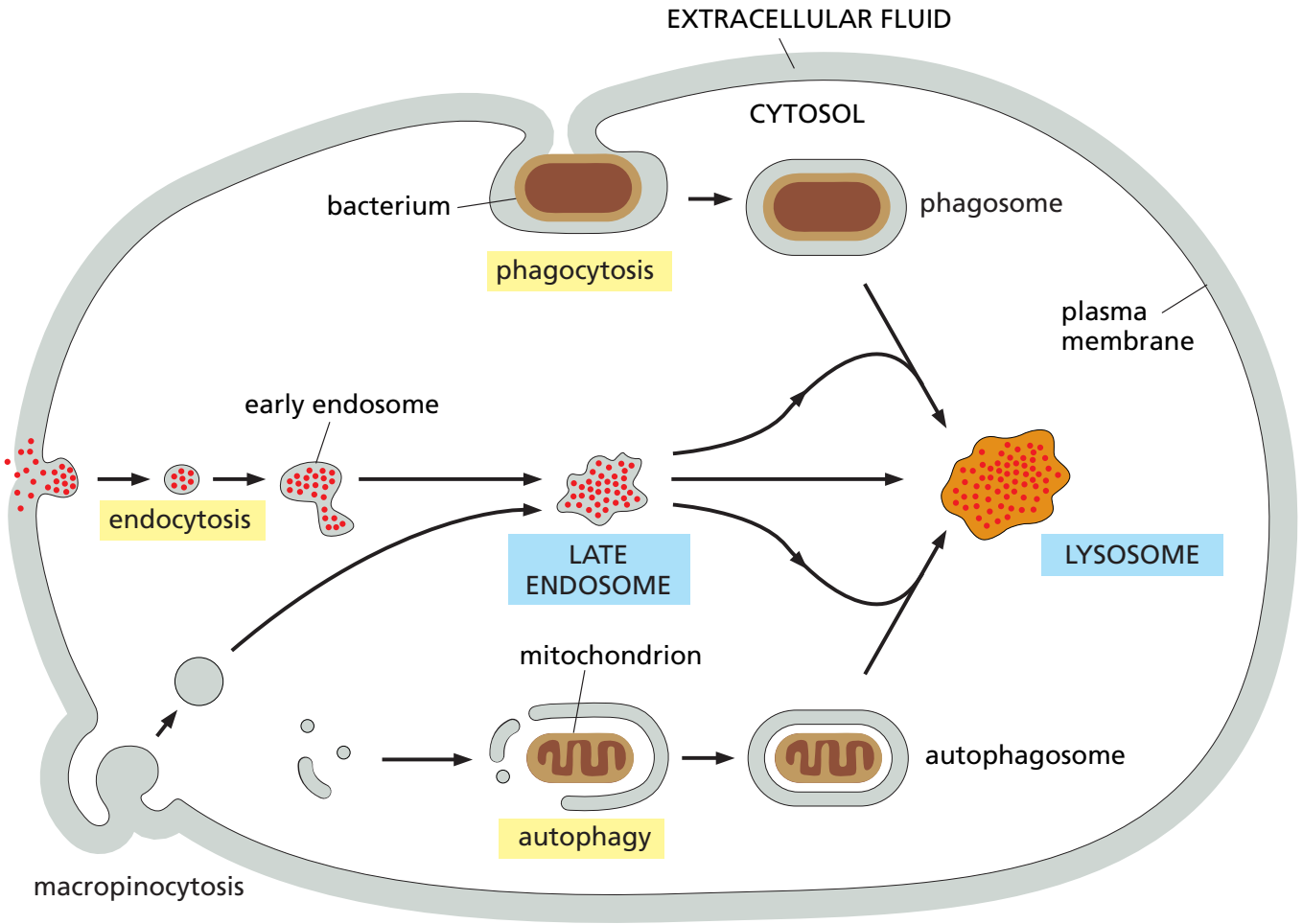

0.2–0.5 μm
pH~7.2
CYTOSOL
pH~5.0
ACID HYDROLASES:
nucleases
proteases
glycosidases
lipases
phosphatases
sulfatases
phospholipases
H+
H+ pump
ATP
ADP
+
Pi


200 nm

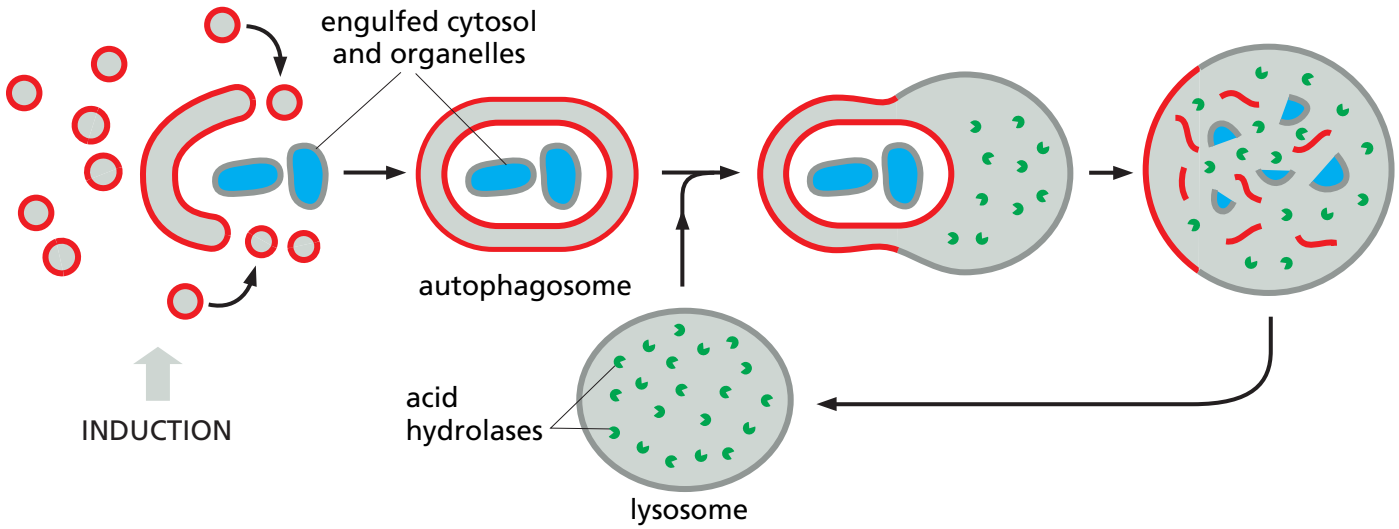
A model for lysosome maturation



Four pathways to degradation in lysosomes



A model of autophagy

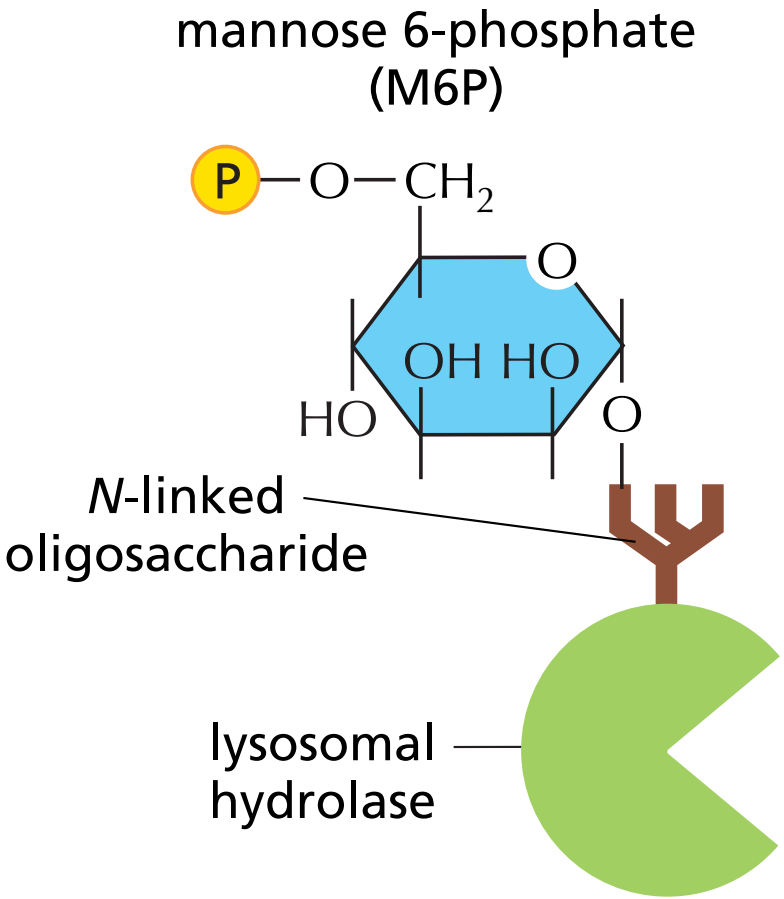


(A)

(B)

How are lysosomal hydrolases recognized in the trans golgi network?

The structure of mannose 6-phosphate on a lysosomal hydrolase

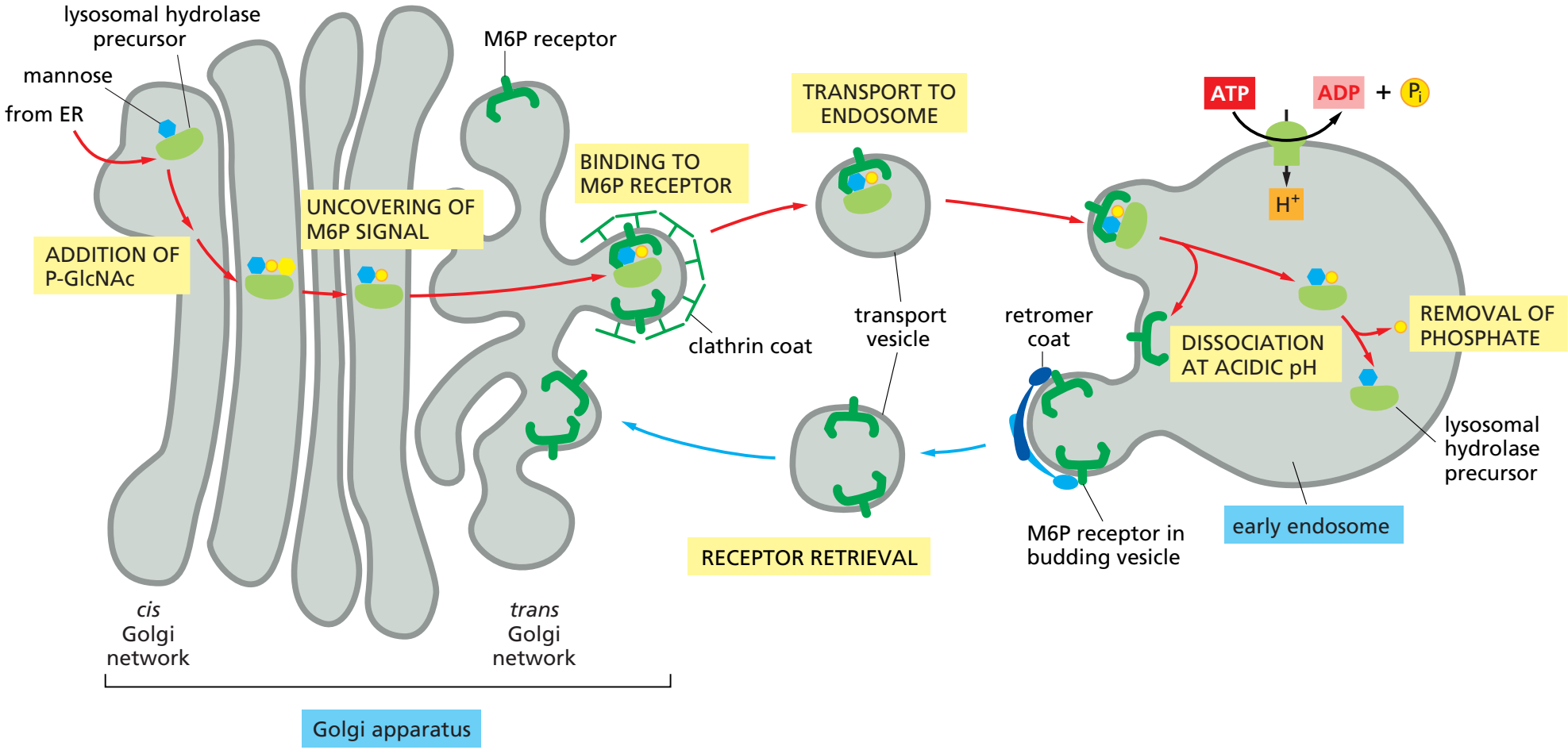


M6P added to N-linked oligosaccharide in the cis-golgi network

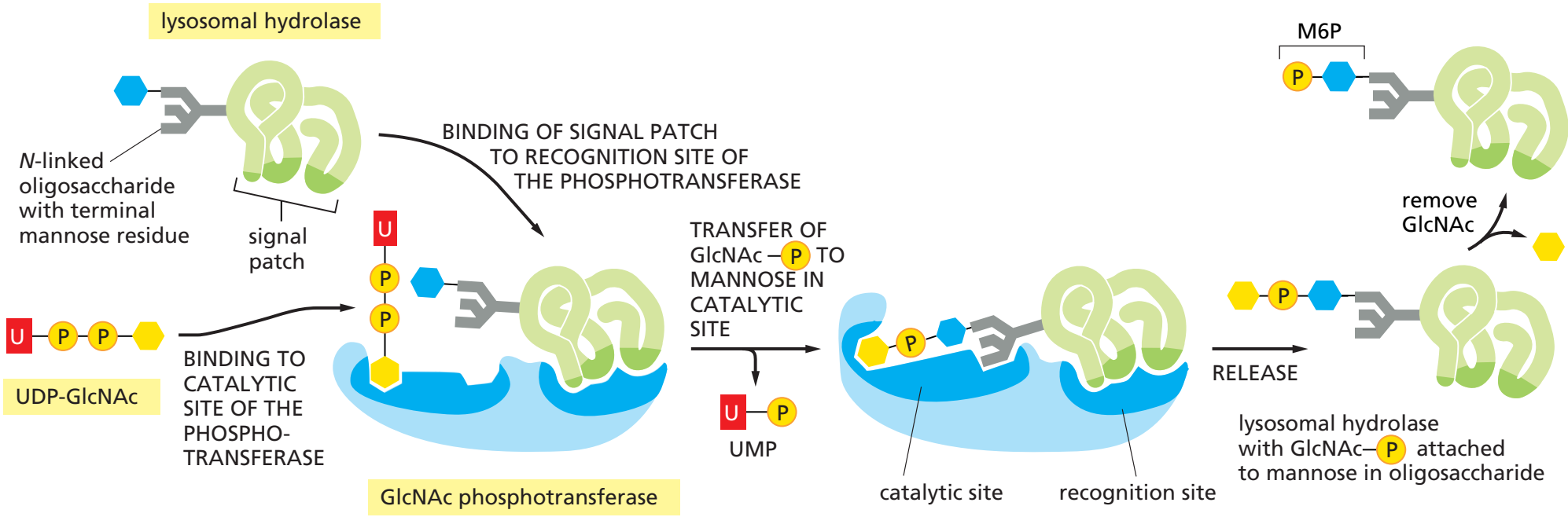
M6P interacts with the M6P receptor
-> The pH 6.5-6.7

M6P is released at pH 6 and lower (in the lysosomal pH)

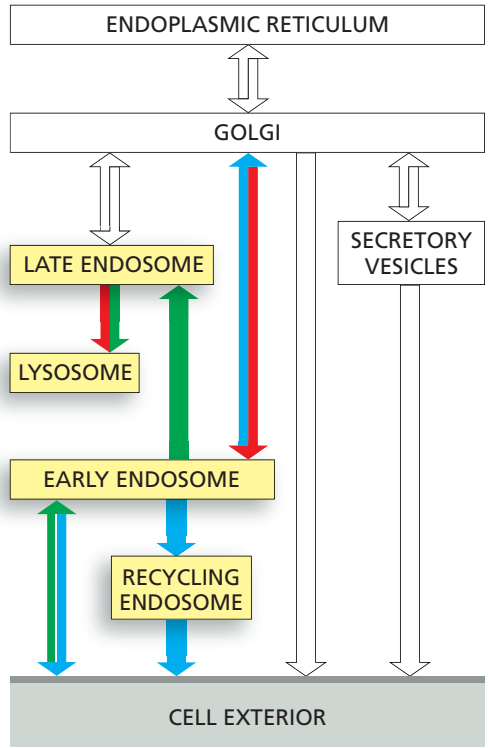
The transport of newly synthesized lysosomal hydrolase to endosomes



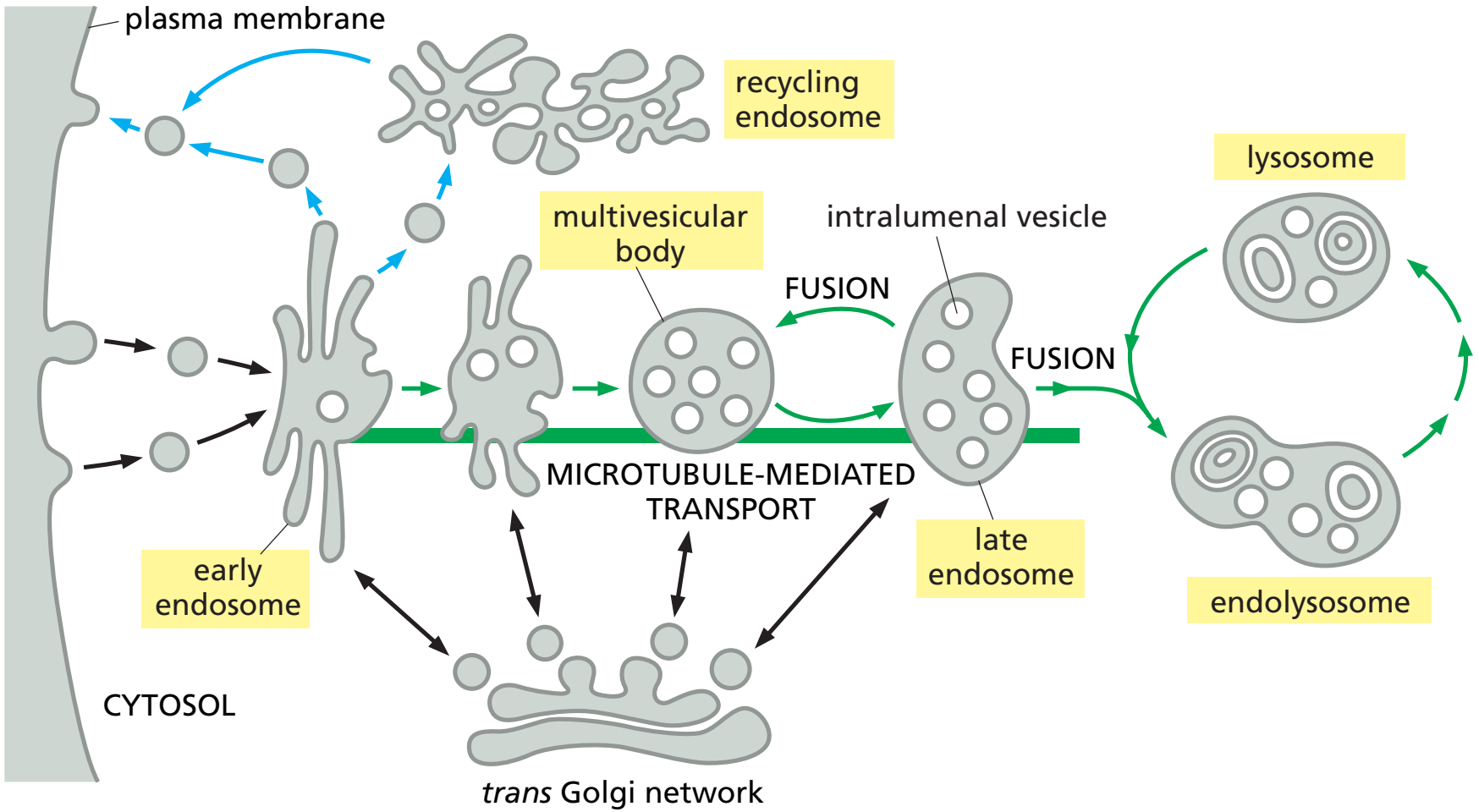
The recognition of a lysosomal hydrolase



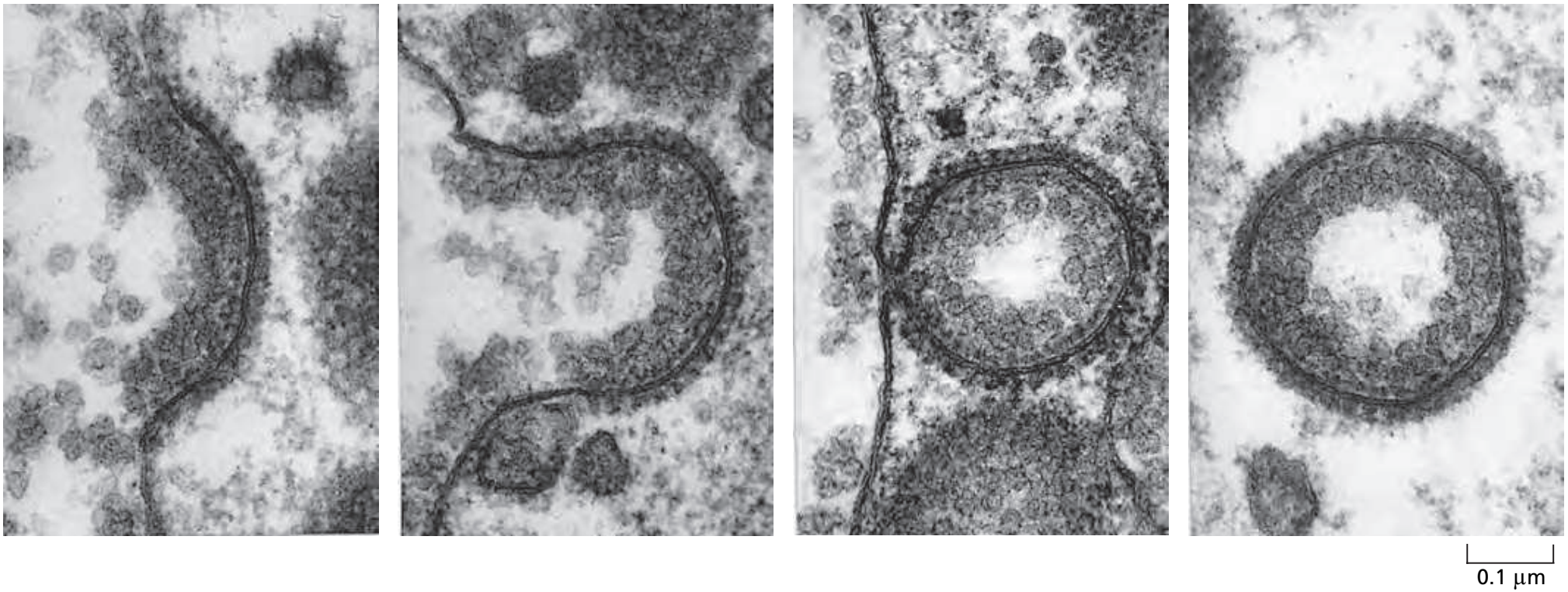
Endocytosis


ENDOPLASMIC RETICULUM
GOLGI
LATE ENDOSOME
SECRETORY VESICLES
LYSOSOME
EARLY ENDOSOME
RECYCLING ENDOSOME
CELL EXTERIOR

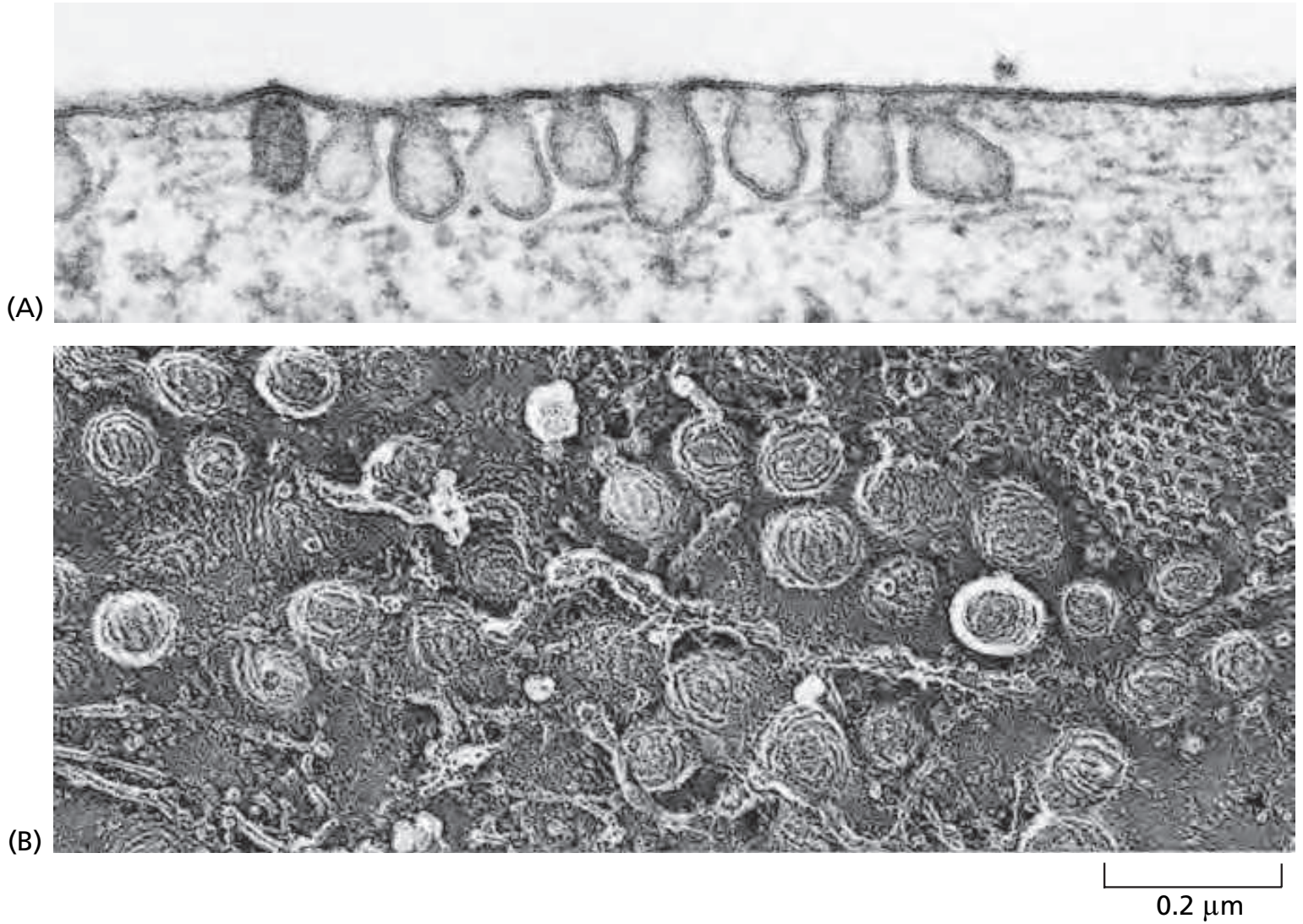
Endosome maturation: the endocytic pathway from the plasma membrane to lysosomes



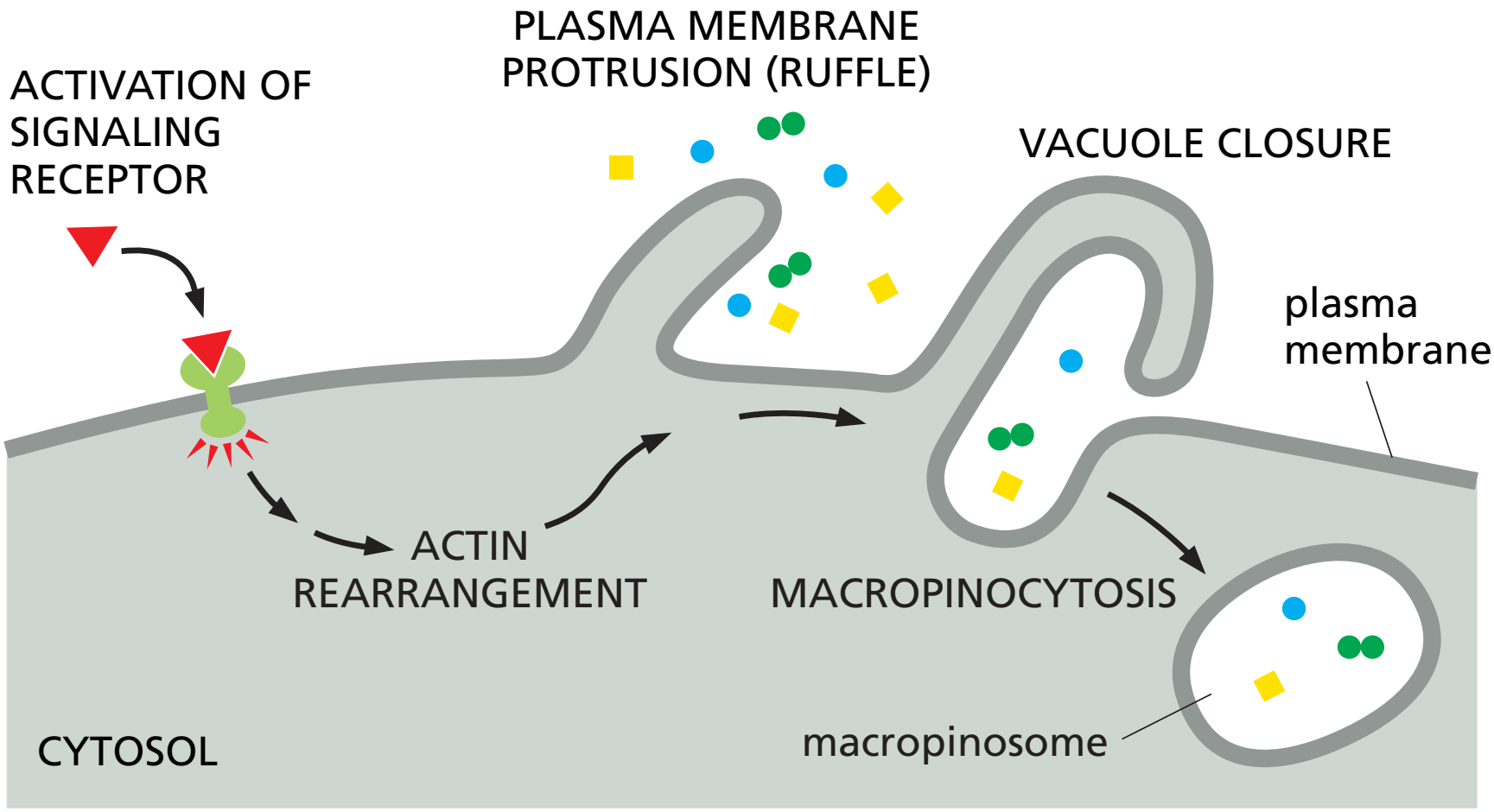
The formation of clathrin-coated vesicles from the plasma membrane



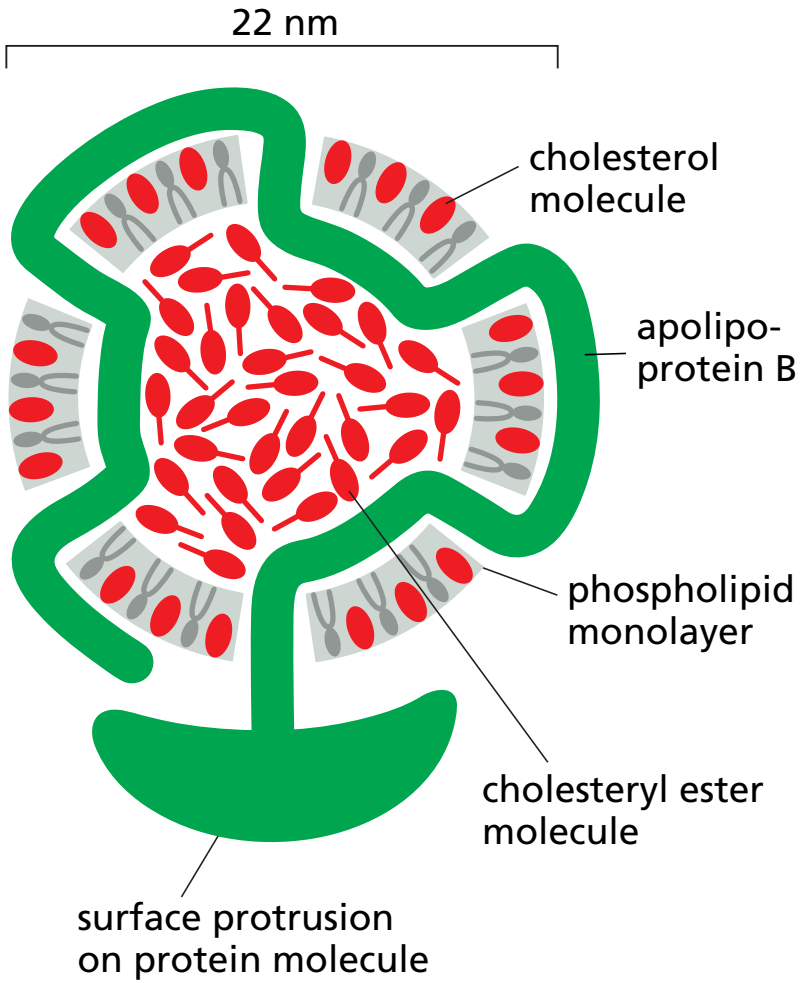
Caveolae in the plasma membrane of a fibroblast



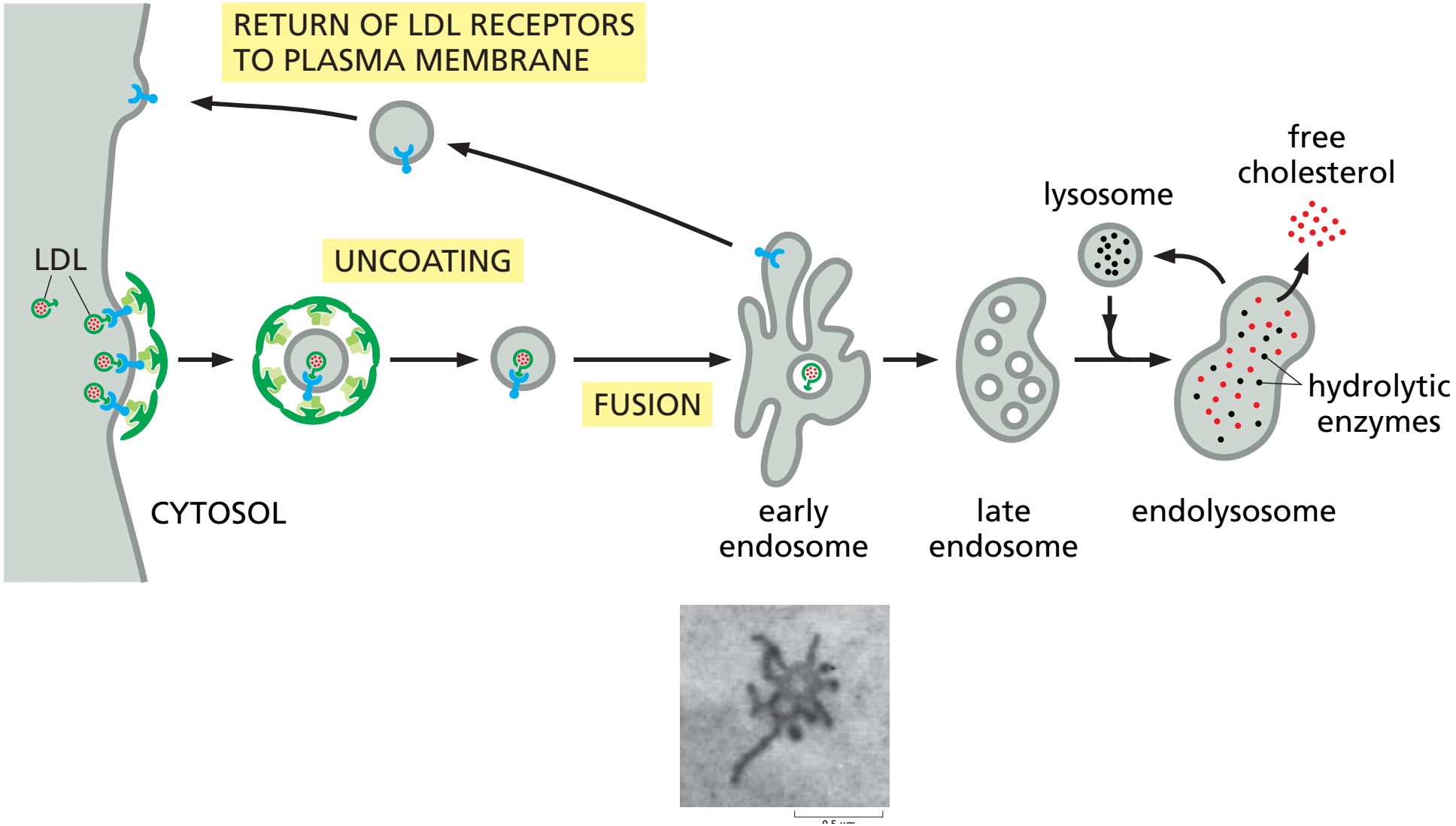
Schematic representation of macropinocytosis



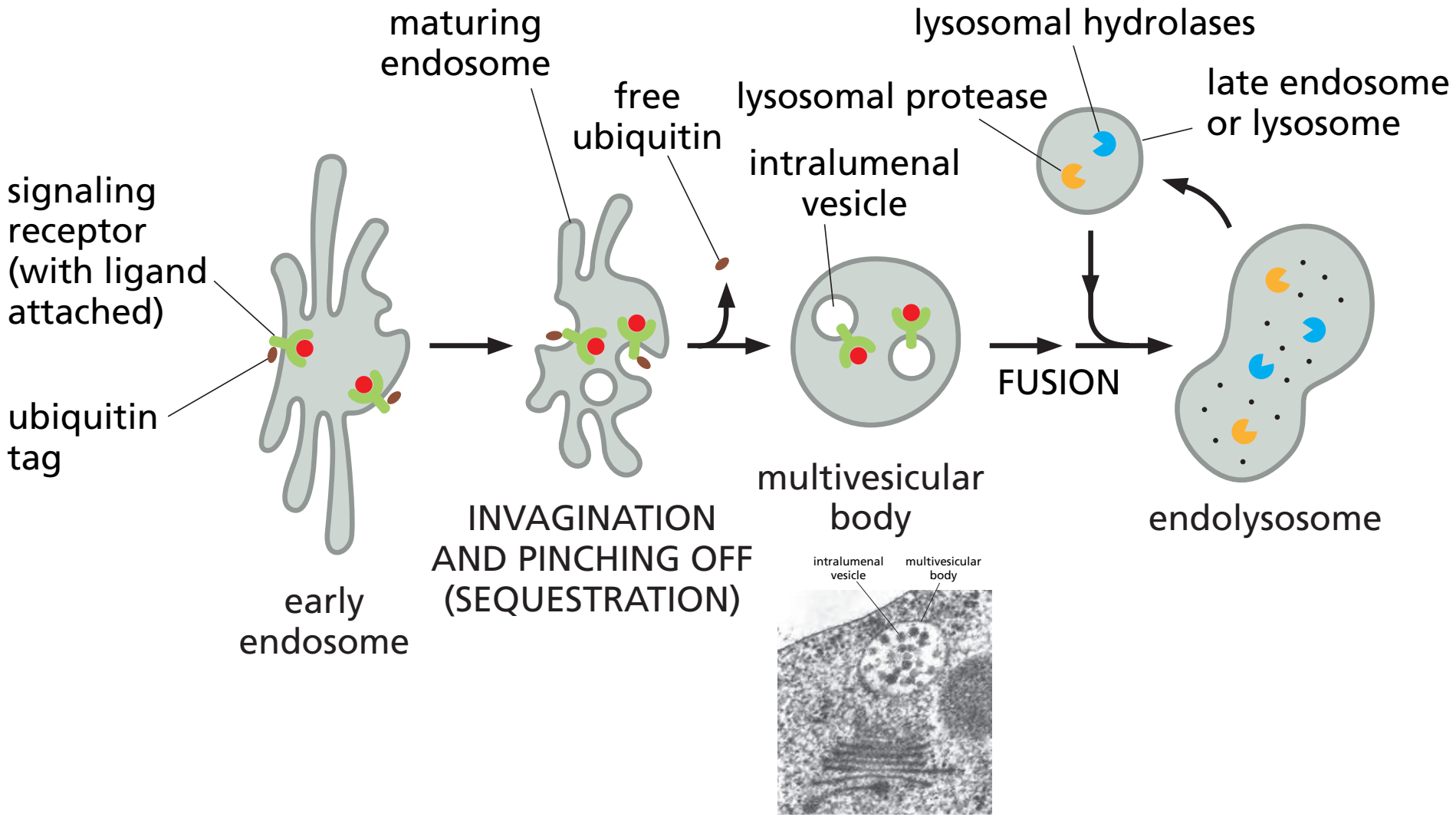
A low-density lipoprotein (LDL) particle



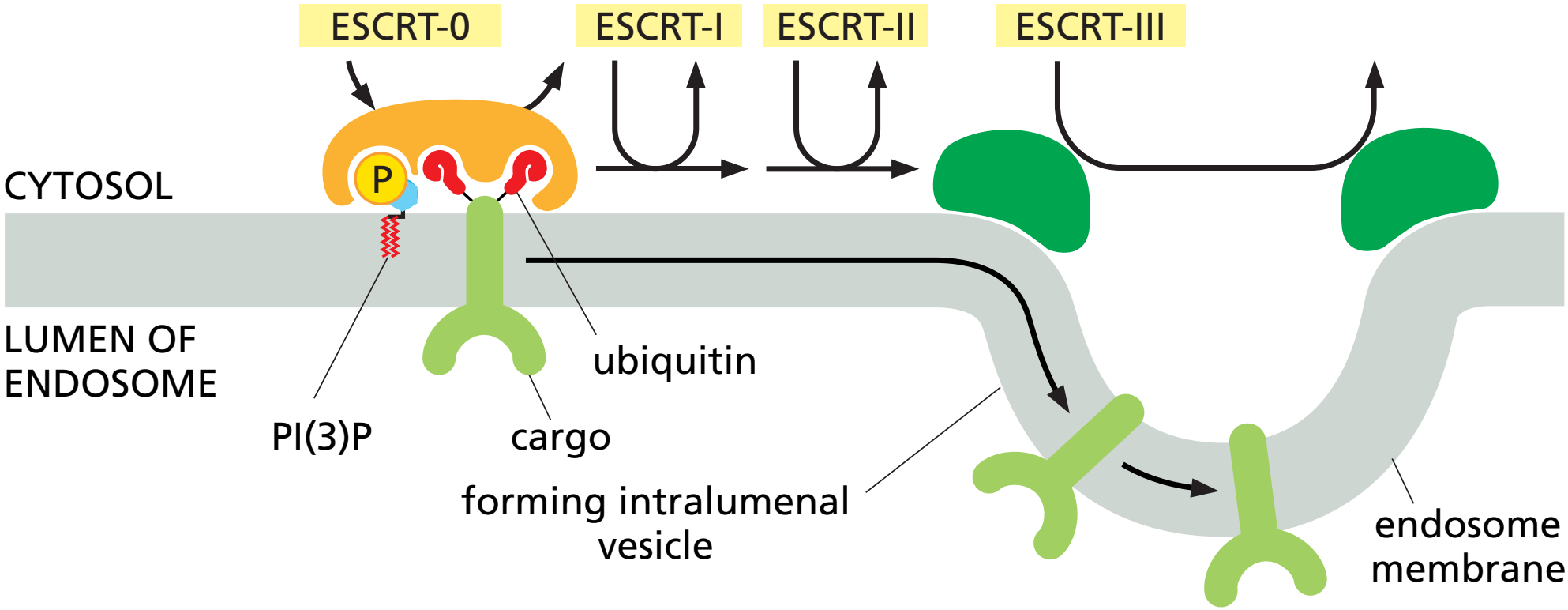
The receptor-mediated endocytosis of LDL



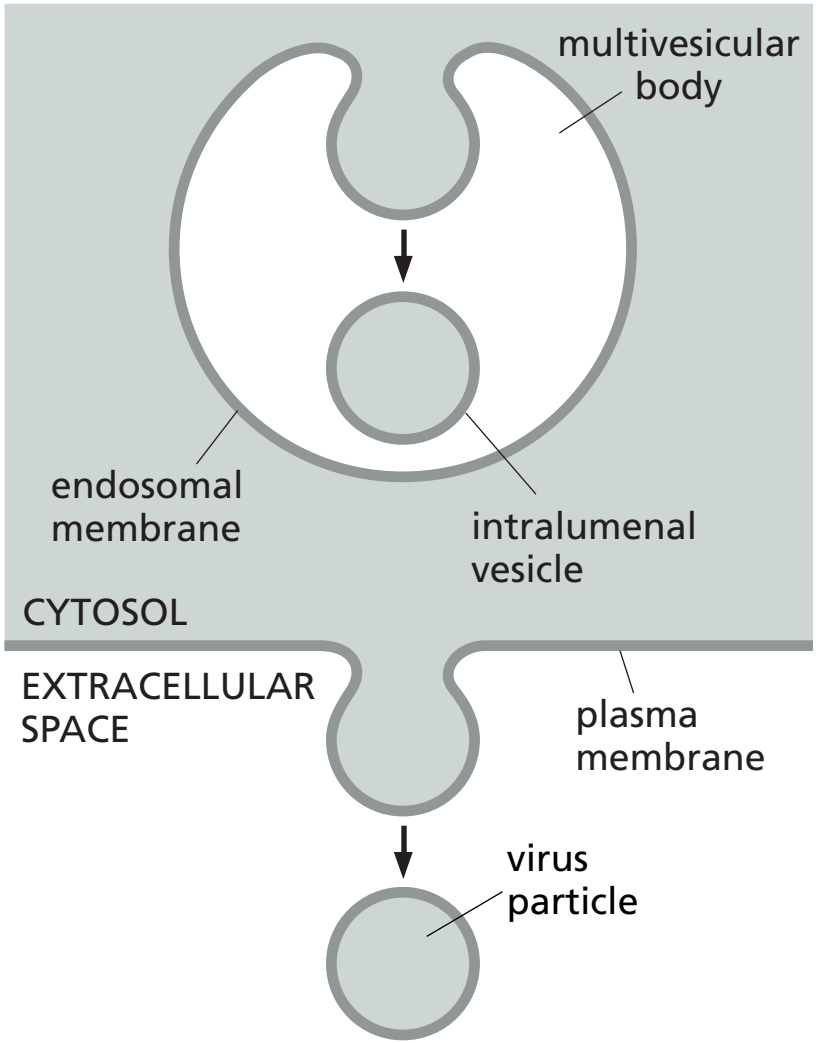
The sequestration of endocytosed proteins into intralumenal vesicles of multivesicular bodies



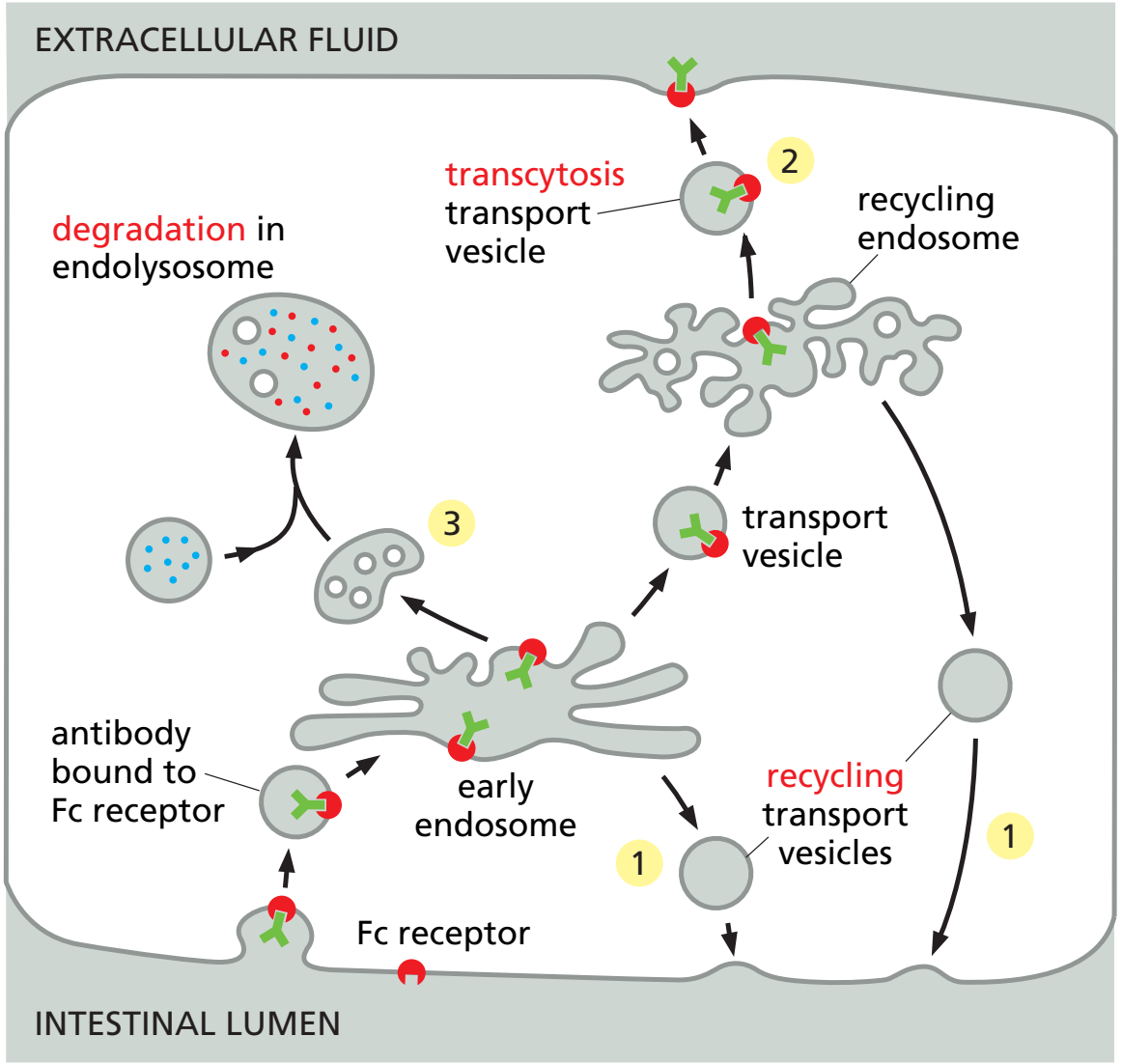
Sorting of endocytosed membrane proteins into the intralumenal vesicles of a multivesicular body



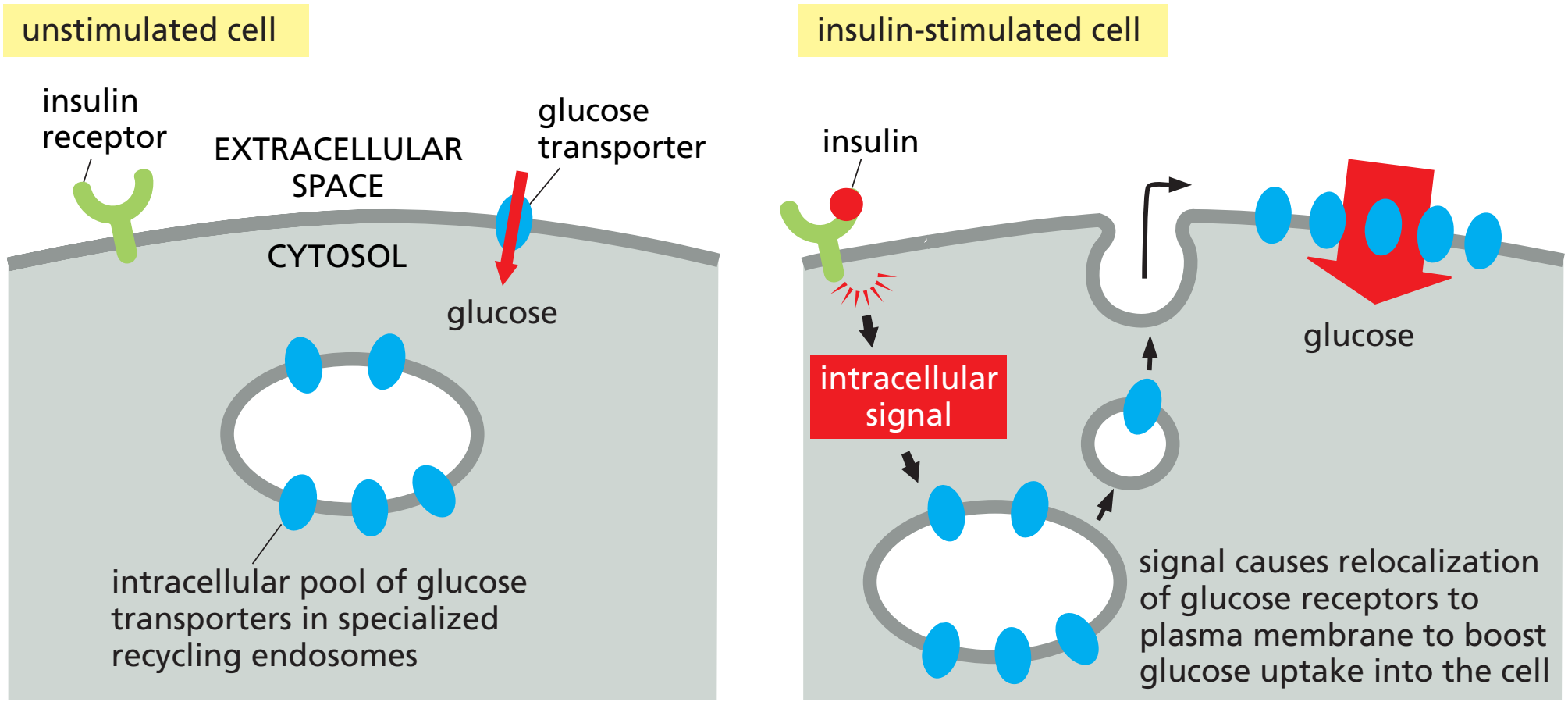
Conserved mechanism in multivesicular body formation and virus budding



Possible fates for transmembrane receptor proteins that have been endocytosed



Storage of plasma membrane proteins in recycling endosomes



Phagocytosis by a macrophage

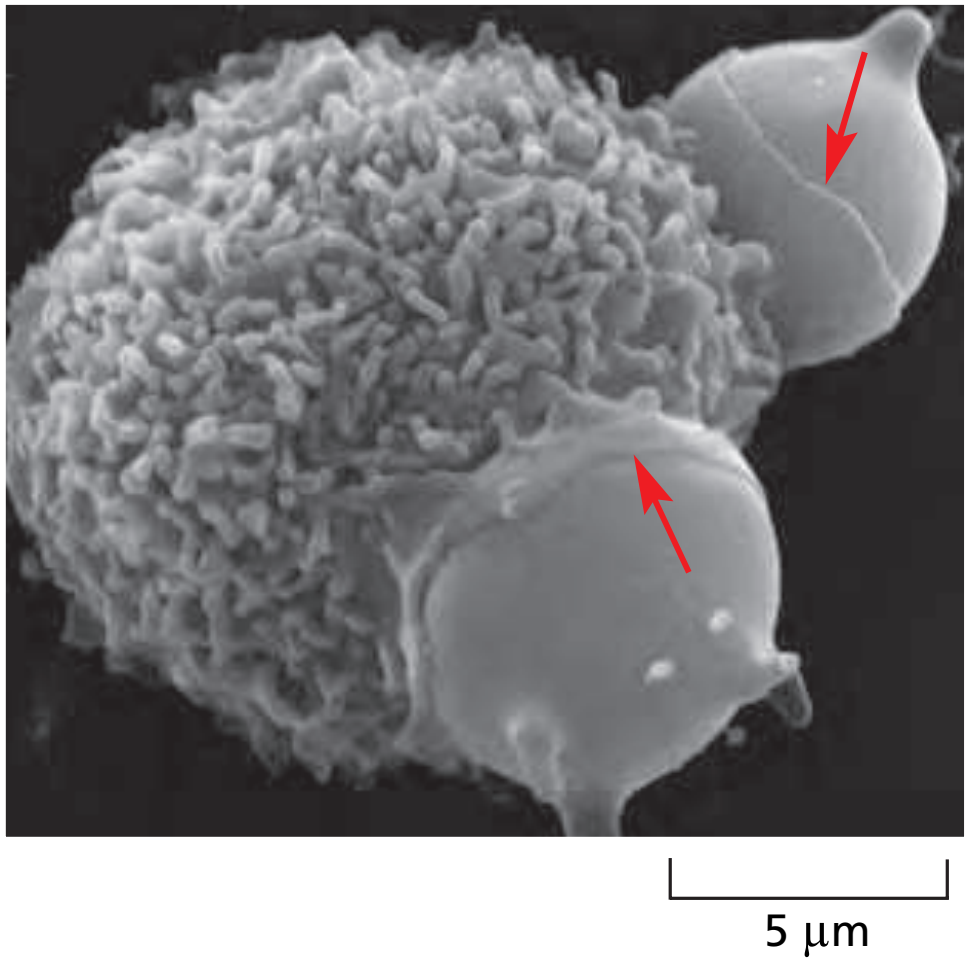
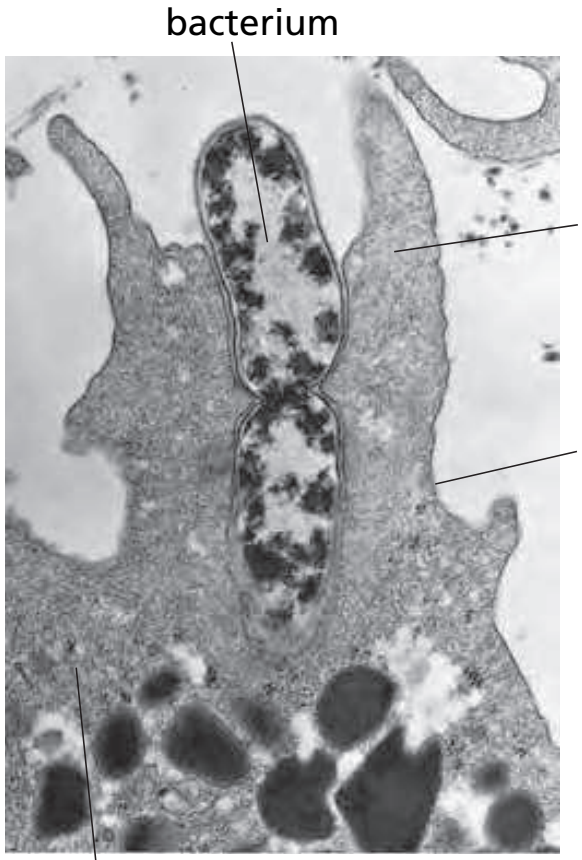
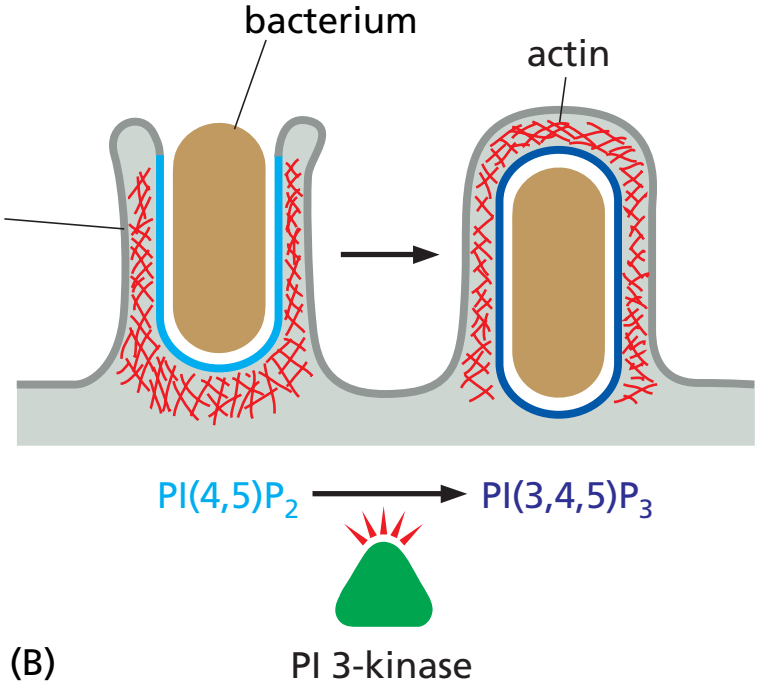


Figure 13–60 Phagocytosis by a macrophage. A scanning electron micrograph of a mouse macrophage phagocytosing two chemically altered red blood cells. The *red arrows* point to edges of thin processes (pseudopods) of the macrophage that are extending as collars to engulf the red cells. (Courtesy of Jean Paul Revel.)

A neutrophil reshaping the plasma membrane during phagocytosis

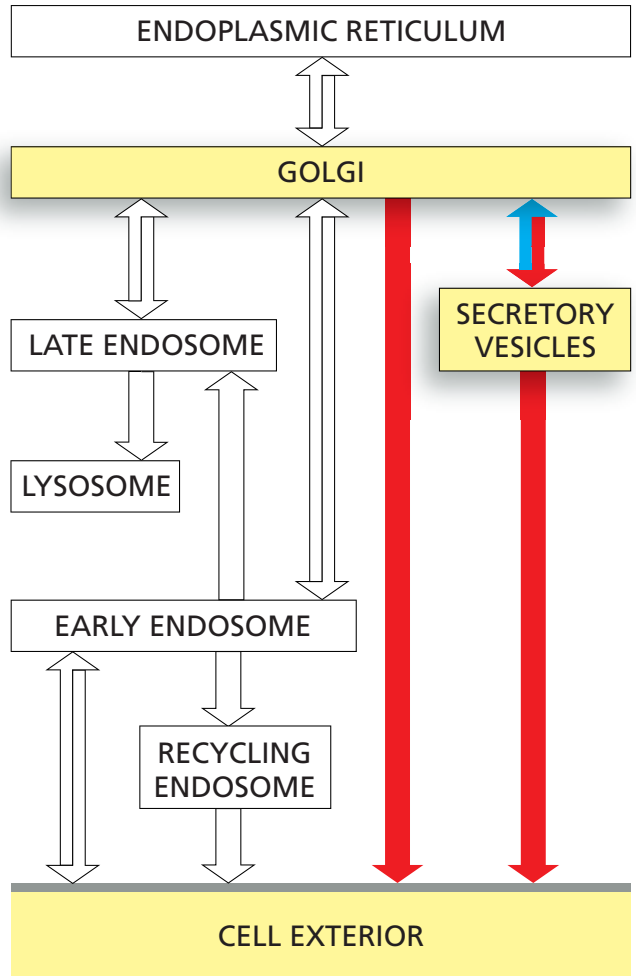


(A)

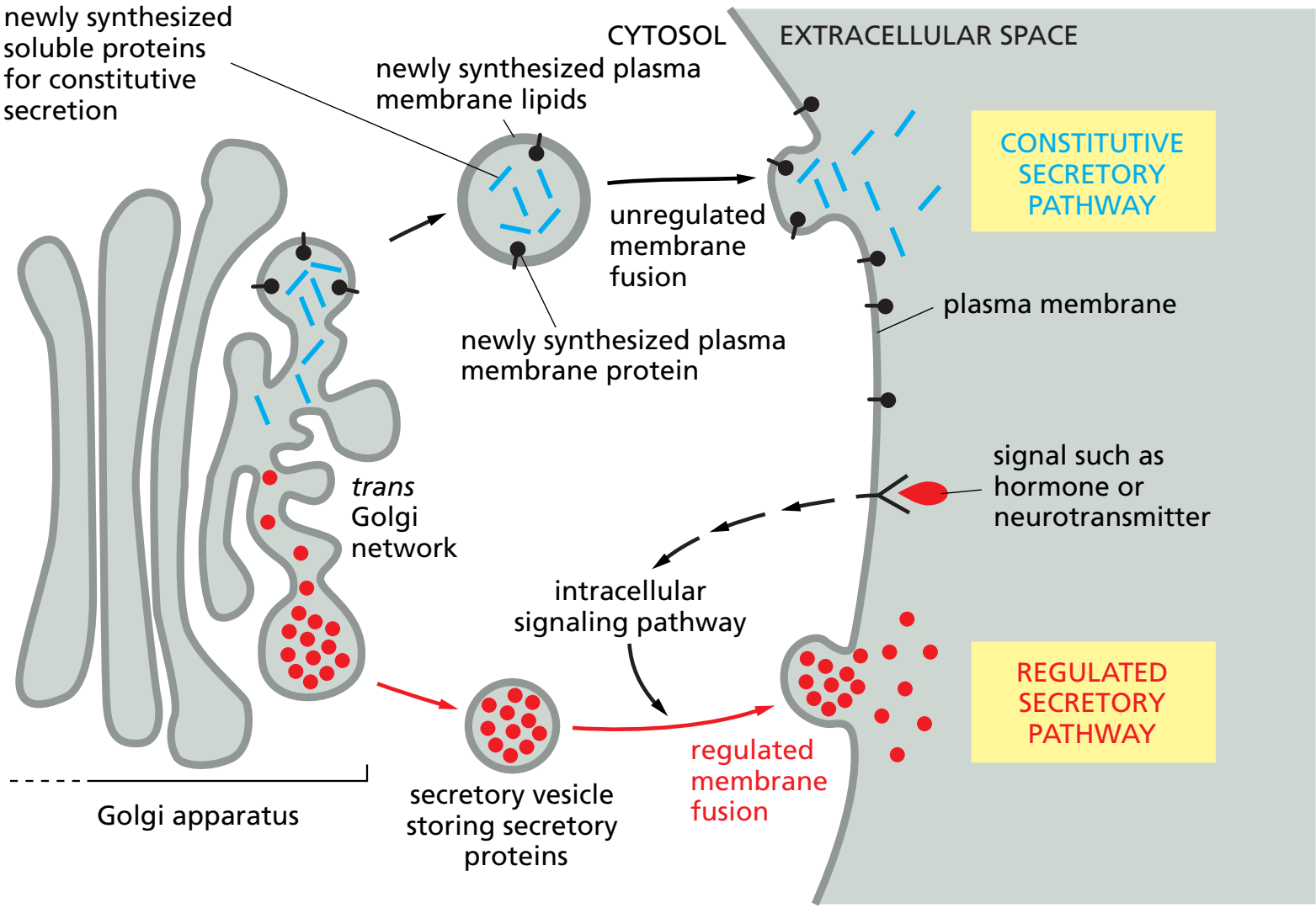


(B)

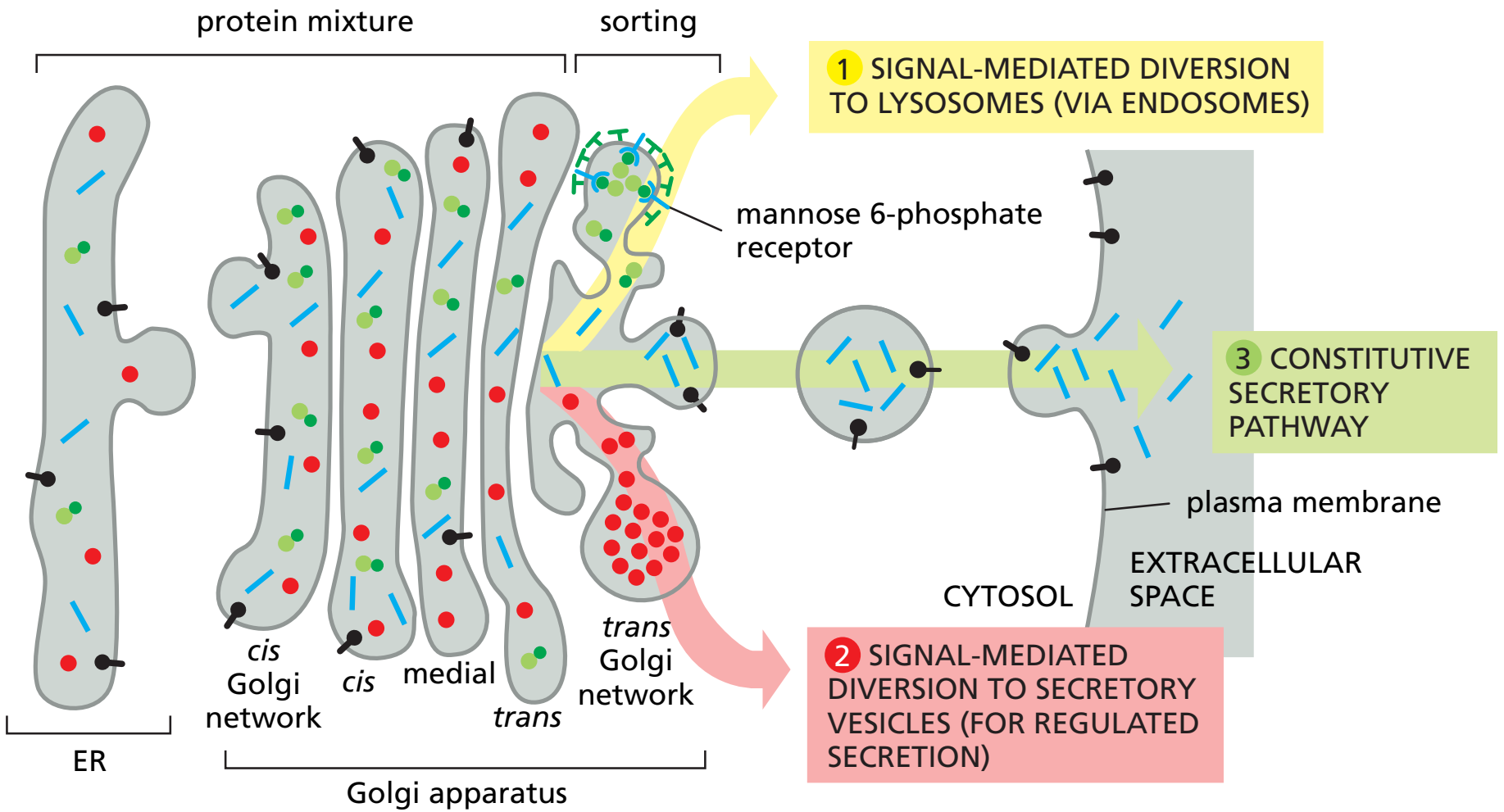
Exocytosis


ENDOPLASMIC RETICULUM
GOLGI
LATE ENDOSOME
LYSOSOME
SECRETORY VESICLES
EARLY ENDOSOME
RECYCLING ENDOSOME
CELL EXTERIOR

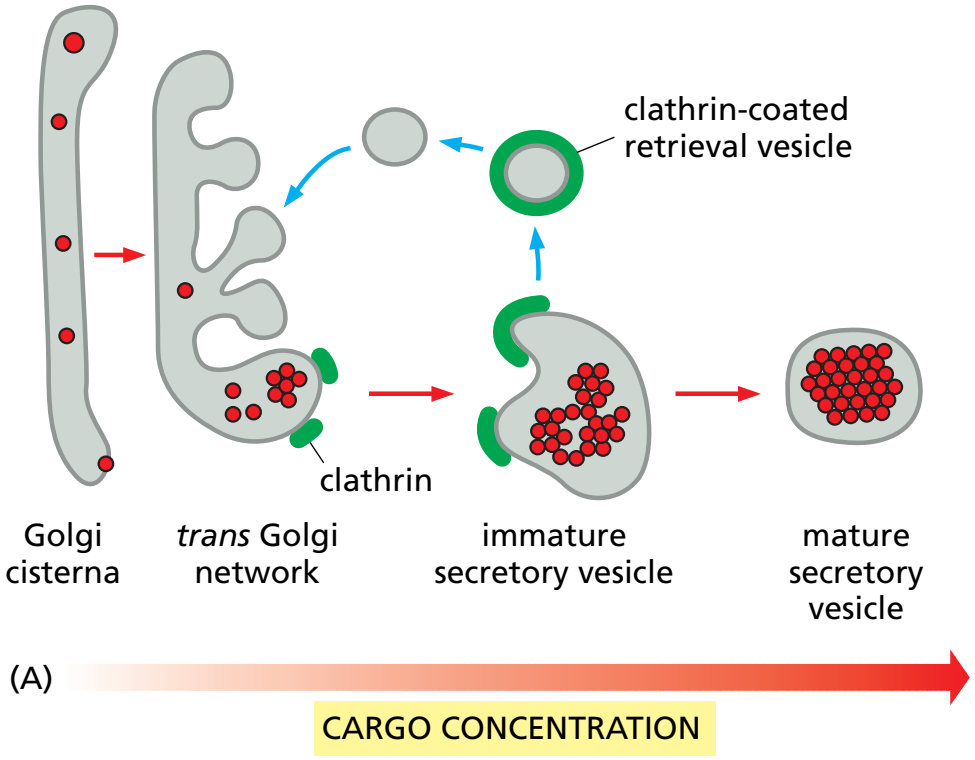
The constitutive and regulated secretory pathways

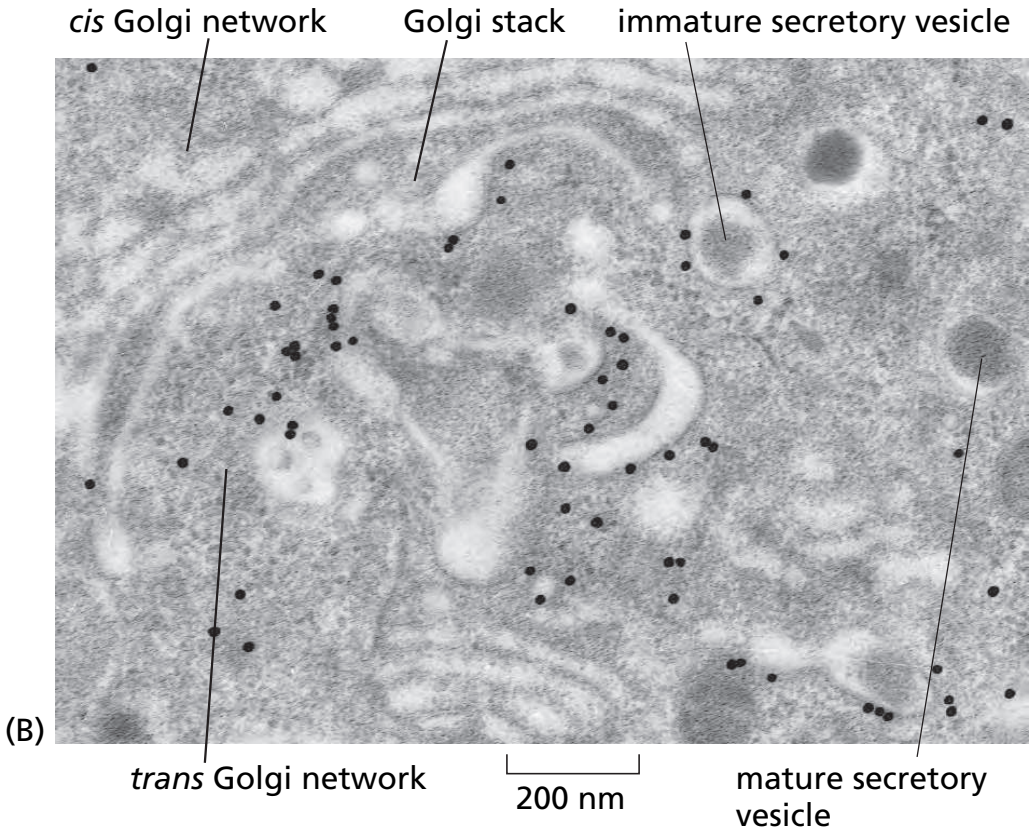


The three best-understood pathways of protein sorting in the *trans* Golgi network

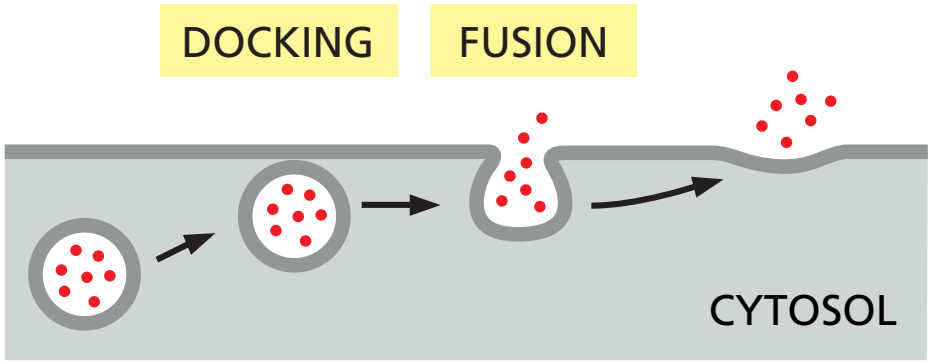


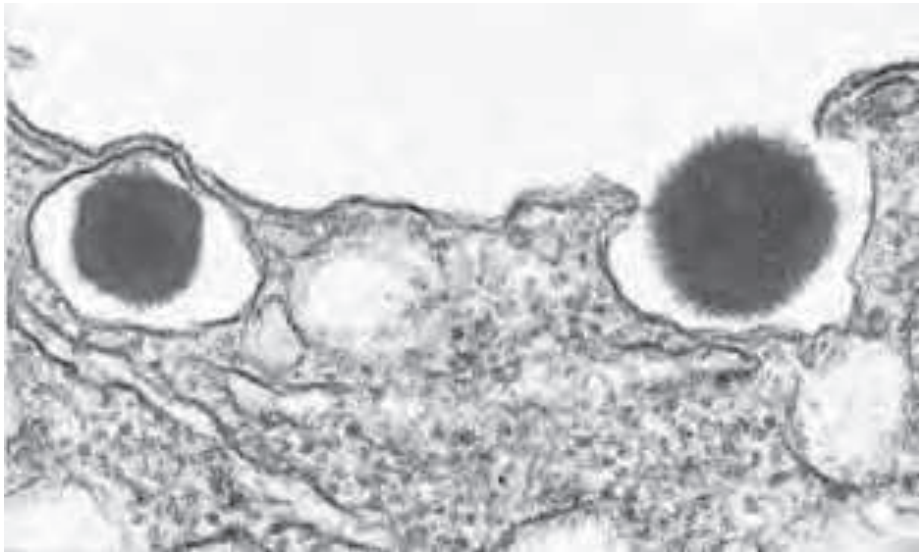
The formation of secretory vesicles



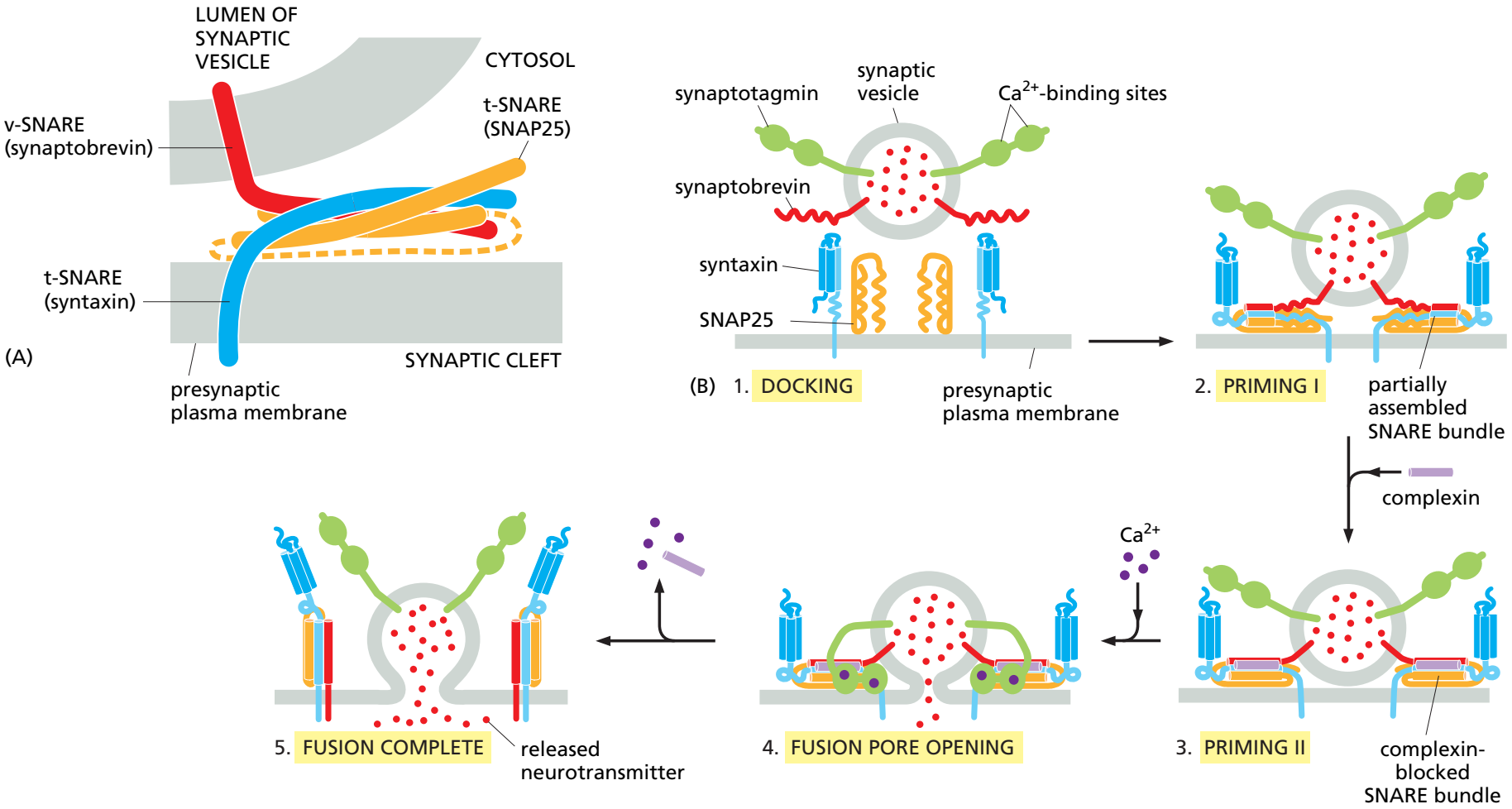


Exocytosis of secretory vesicles

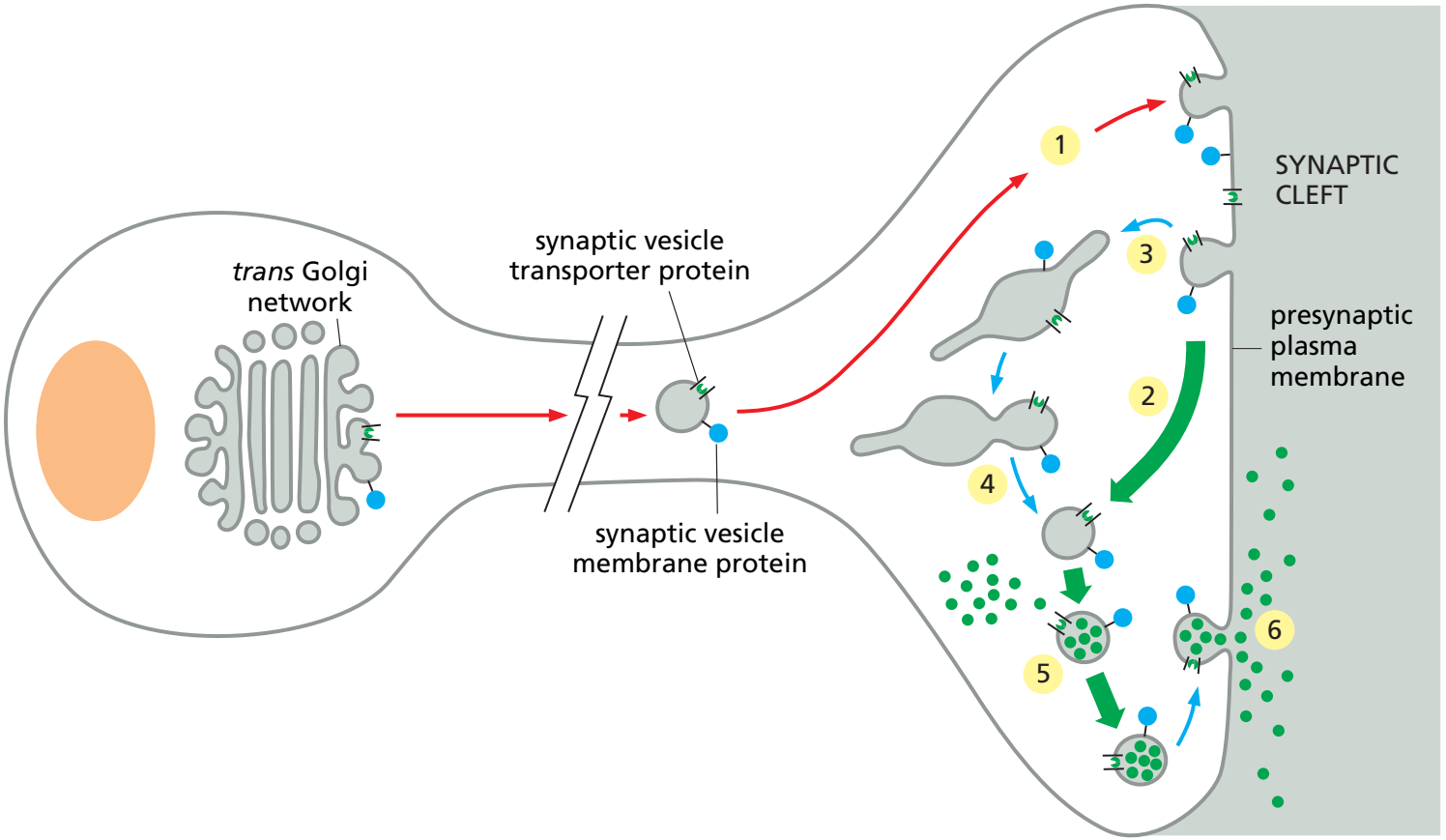




Exocytosis of synaptic vesicles

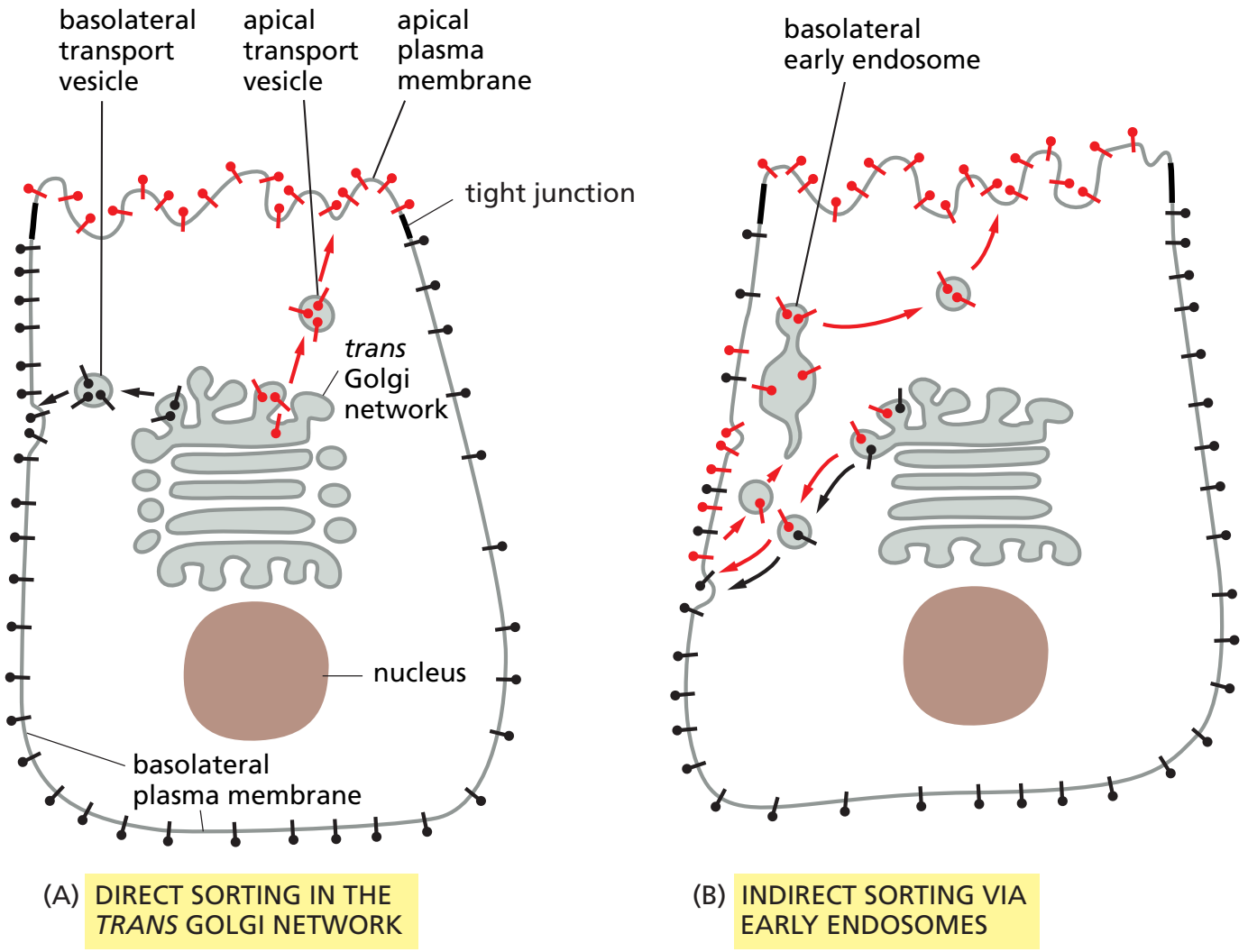


The formation of synaptic vesicles in a nerve cell



1. DELIVERY OF SYNAPTIC VESICLE MEMBRANE COMPONENTS TO PRESYNAPTIC PLASMA MEMBRANE
2. ENDOCYTOSIS OF SYNAPTIC VESICLE MEMBRANE COMPONENTS TO FORM NEW SYNAPTIC VESICLES DIRECTLY
3. ENDOCYTOSIS OF SYNAPTIC VESICLE MEMBRANE COMPONENTS AND DELIVERY TO ENDOSOME
4. BUDDING OF SYNAPTIC VESICLE FROM ENDOSOME
5. LOADING OF NEUROTRANSMITTER INTO SYNAPTIC VESICLE
6. SECRETION OF NEUROTRANSMITTER BY EXOCYTOSIS IN RESPONSE TO AN ACTION POTENTIAL

Two ways of sorting plasma membrane proteins in a polarized epithelial cell



(A) DIRECT SORTING IN THE *TRANS* GOLGI NETWORK

(B) INDIRECT SORTING VIA EARLY ENDOSOMES

Summary

Transport and Retrograde transport between ER and Golgi

Endocytosis & Lysosomes

Exocytosis