Introduction to Physiology

Homeostasis and Cell

Guyton & Hall

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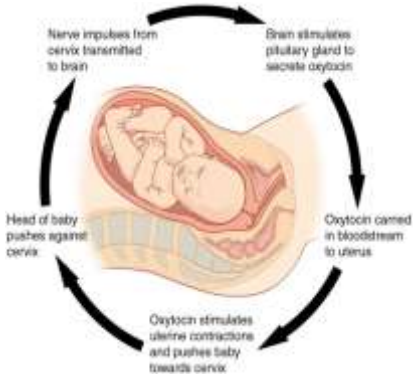
Positive Feedback Systems: Normal Childbirth

- Uterine contractions pushes baby to cervix
- Stretch-sensitive receptors in cervix send impulse to brain
- Oxytocin is released into the blood
- Contractions are enhanced and so Oxytocin release and baby pushes farther down the uterus
- Cycle continues to the birth of the baby (no stretching)



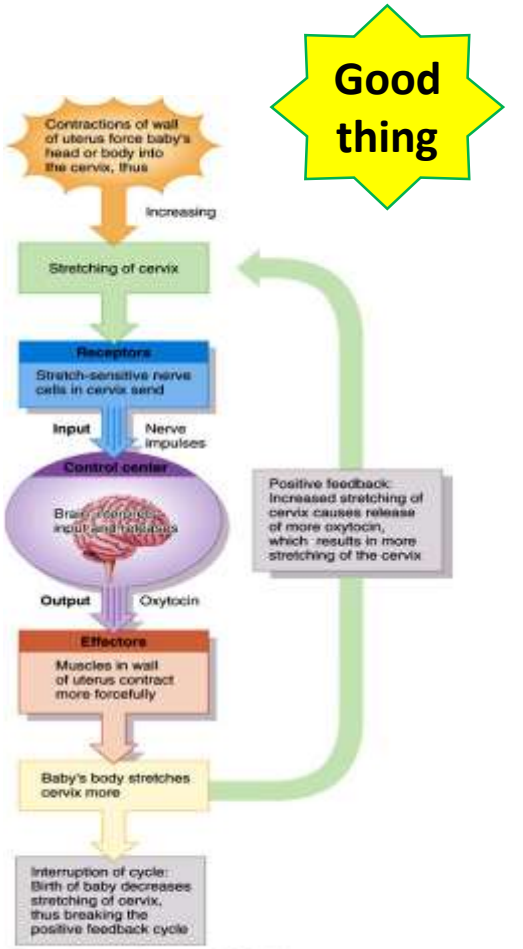
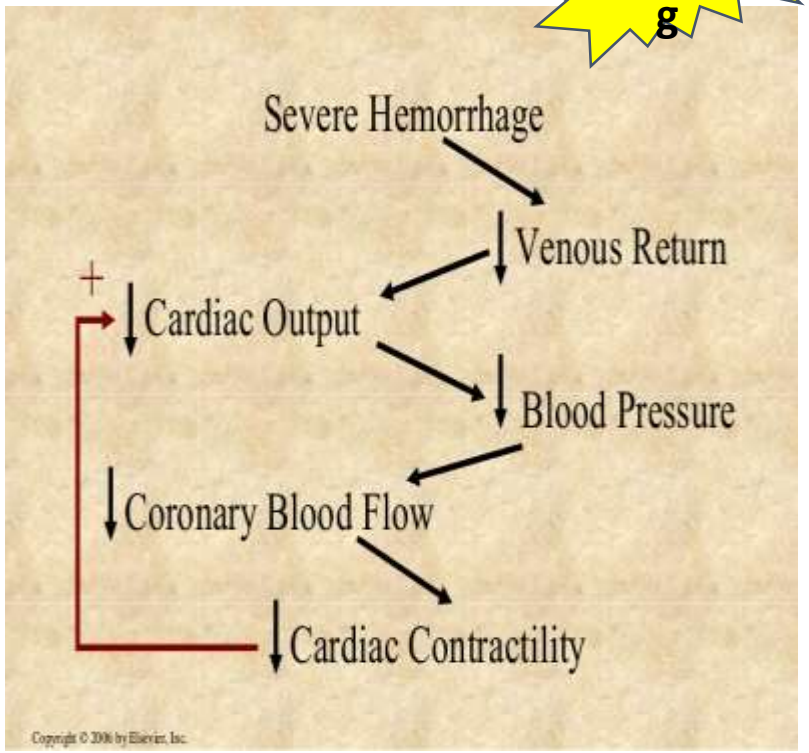


Figure 01.04 Tortora - PAP 12/e

Positive Feedback: Blood Loss

Bad thing

- Normal conditions, heart pumps blood under pressure to body cells (oxygen and nutrients)
- Severe blood loss
  - Blood pressure drops
  - Cells receive less oxygen and function less efficiently
  - If blood loss continues
    - Heart cells become weaker
    - Heart pumping decrease
    - BP continues to fall more
    - **May lead to death**



Gain” of a Control System

Gain of the Negative Feedback:

- degree of effectiveness where a control

system maintains constant conditions.

- FORMULA: Gain = Correction/Error

- EXAMPLE: Large volume of blood transfused to a person whose baroreceptor pressure control system is not functioning = from 100mm HG, it rises up to 175 mm HG.

- Same volume transfused to a person with functioning baroreceptor pressure control system = causing inc of only 25 mm Hg from normal.

- CORRECTION: 125-175= -50mm Hg

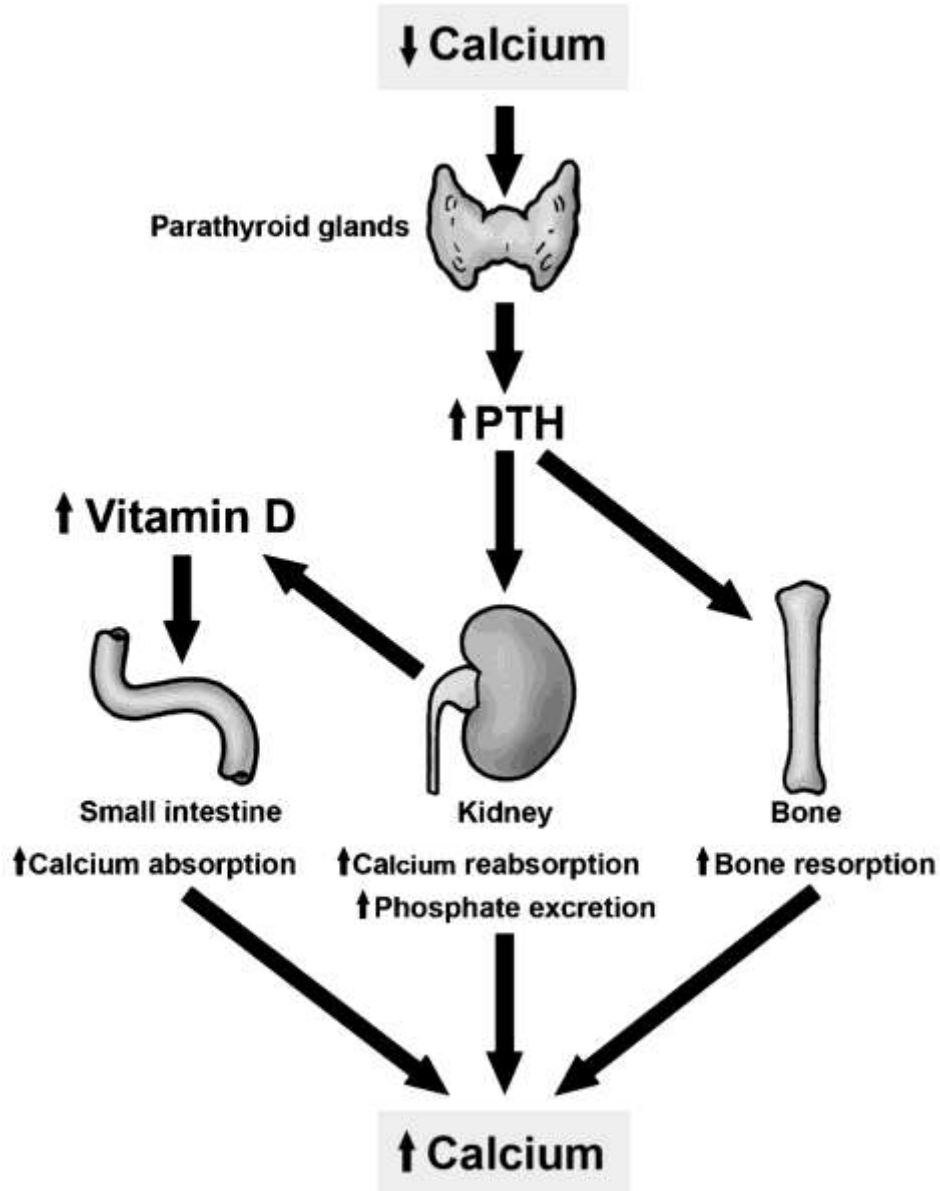
- The remaining +25mm Hg is the ERROR.

- CONCLUSION: control system is not

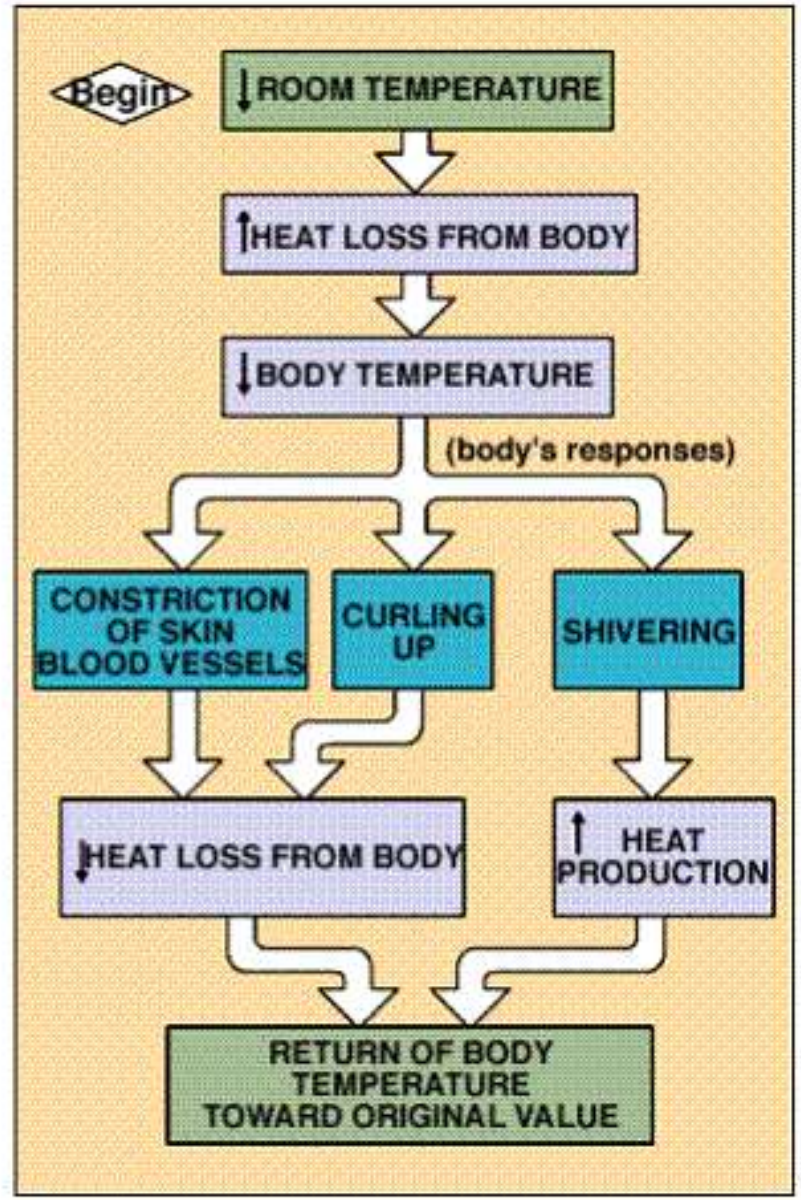
100% effective in preventing change.

Homeostatic Imbalances

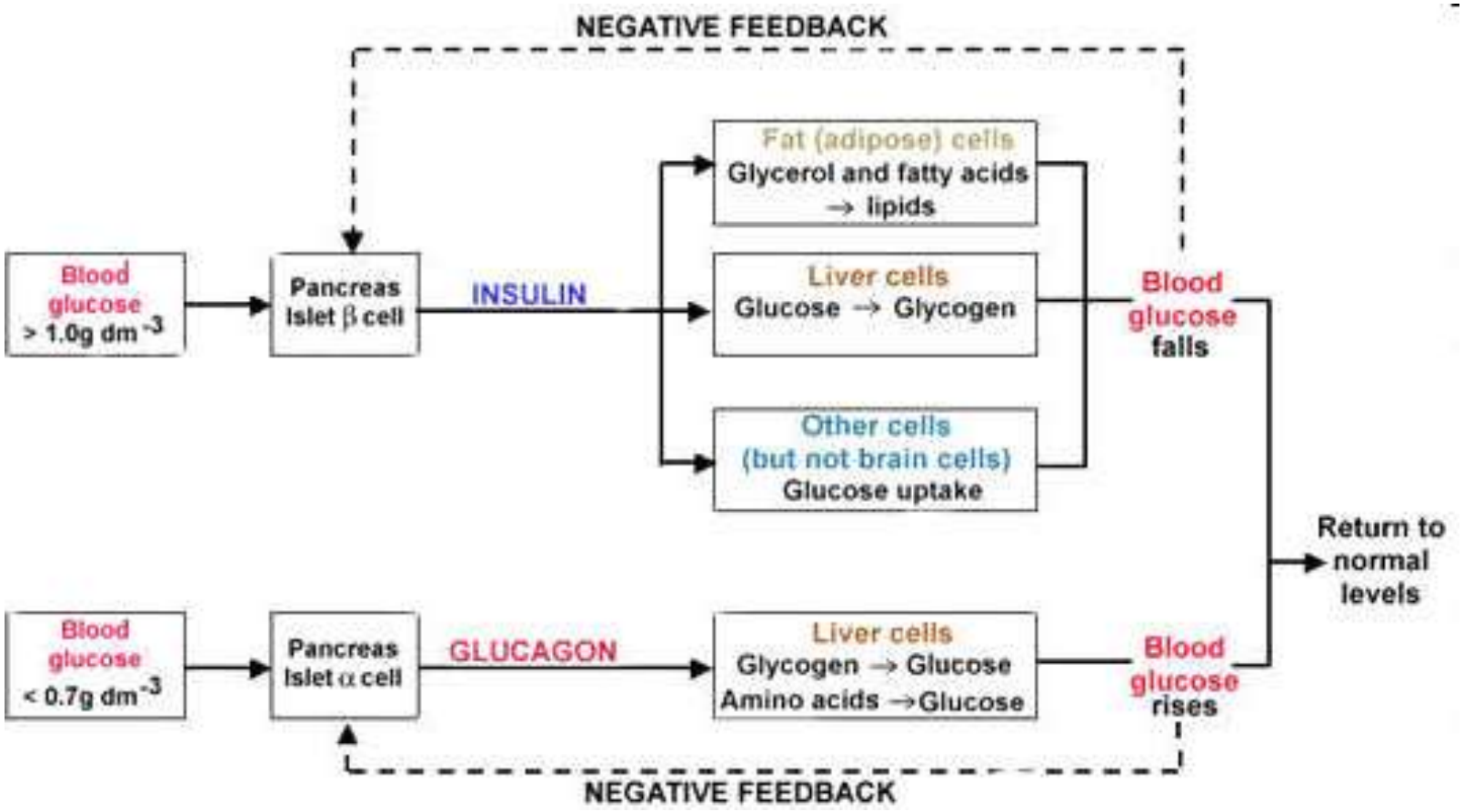
- **Normal equilibrium of body processes are disrupted**
  - **Moderate imbalance**
    - **Disorder**: any abnormality of structure and function
    - **Disease**: specific term for an illness with recognizable signs and symptoms
    - **Signs** are objective changes such as a fever, swelling or high blood pressure
    - **Symptoms** are subjective changes such as headache
  - **Severe imbalance**
    - Death

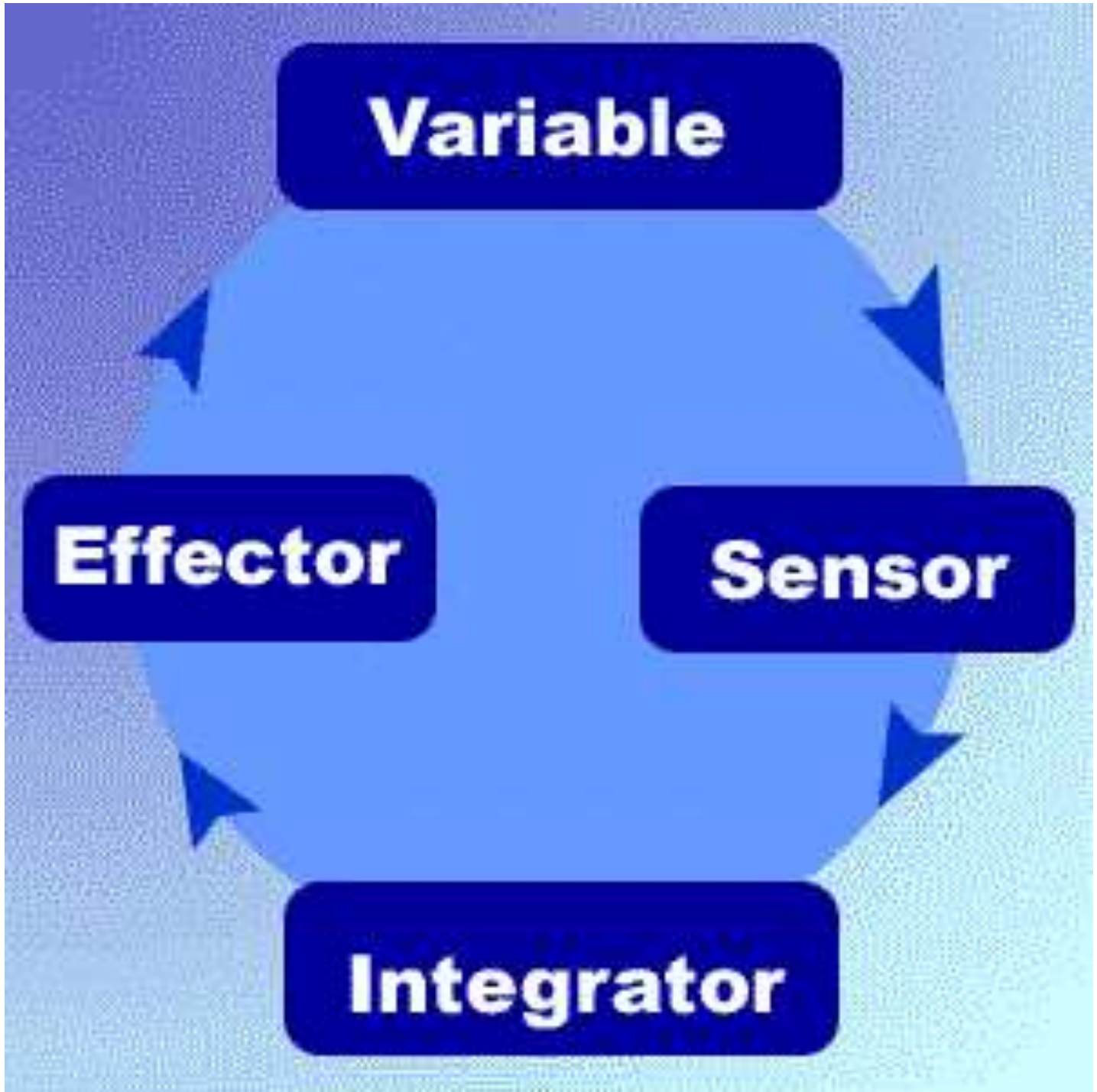

↓Calcium
Parathyroid glands
↑PTH
↑Vitamin D
Small intestine
↑Calcium absorption
Kidney
↑Calcium reabsorption
↑Phosphate excretion
Bone
↑Bone resorption
↑Calcium

Homeostatic Control System



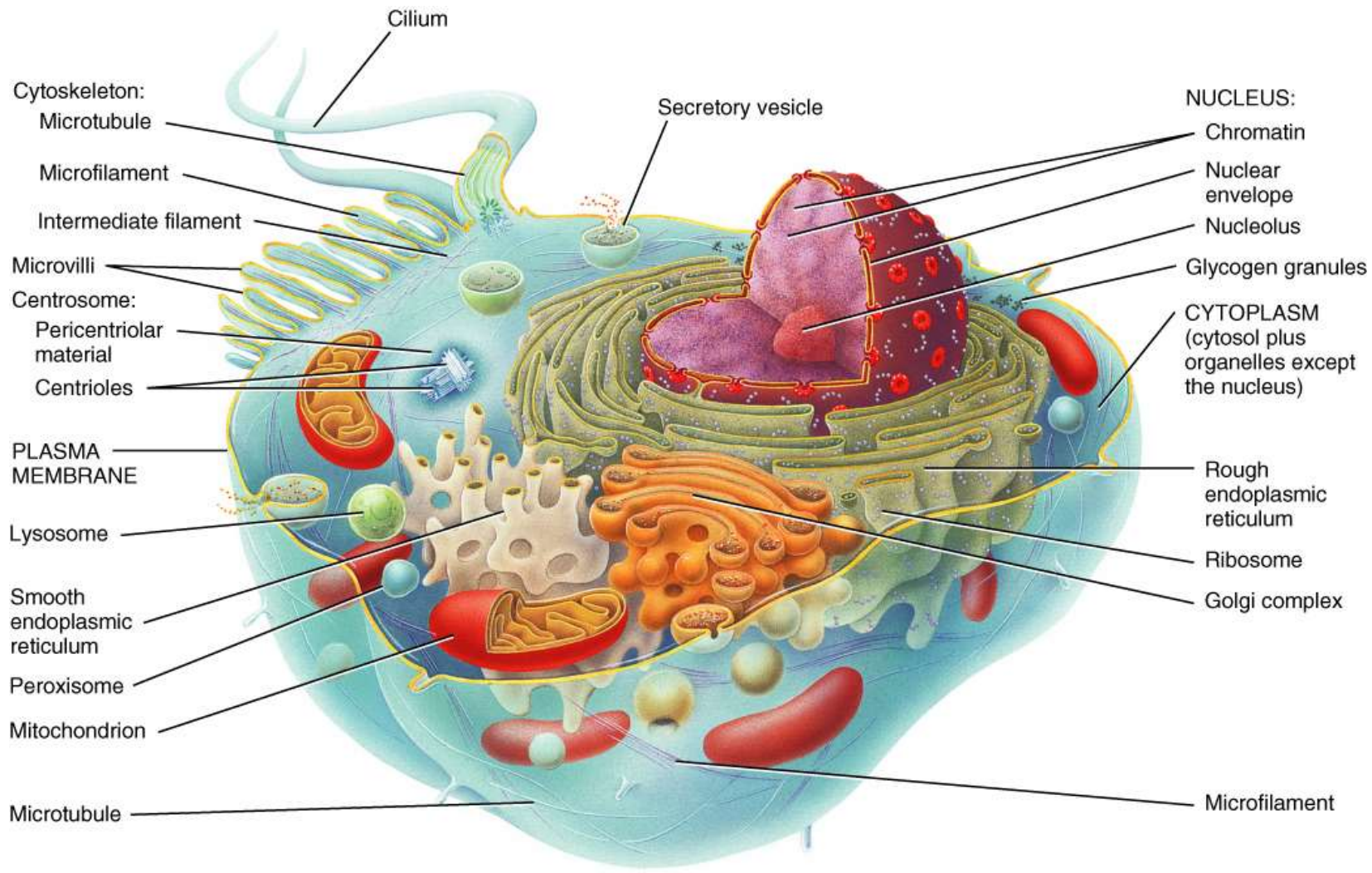
NEGATIVE FEEDBACK




Variable
Sensor
Integrator
Effector

Cell and Organelles

Fig. 03.01



Sectional view

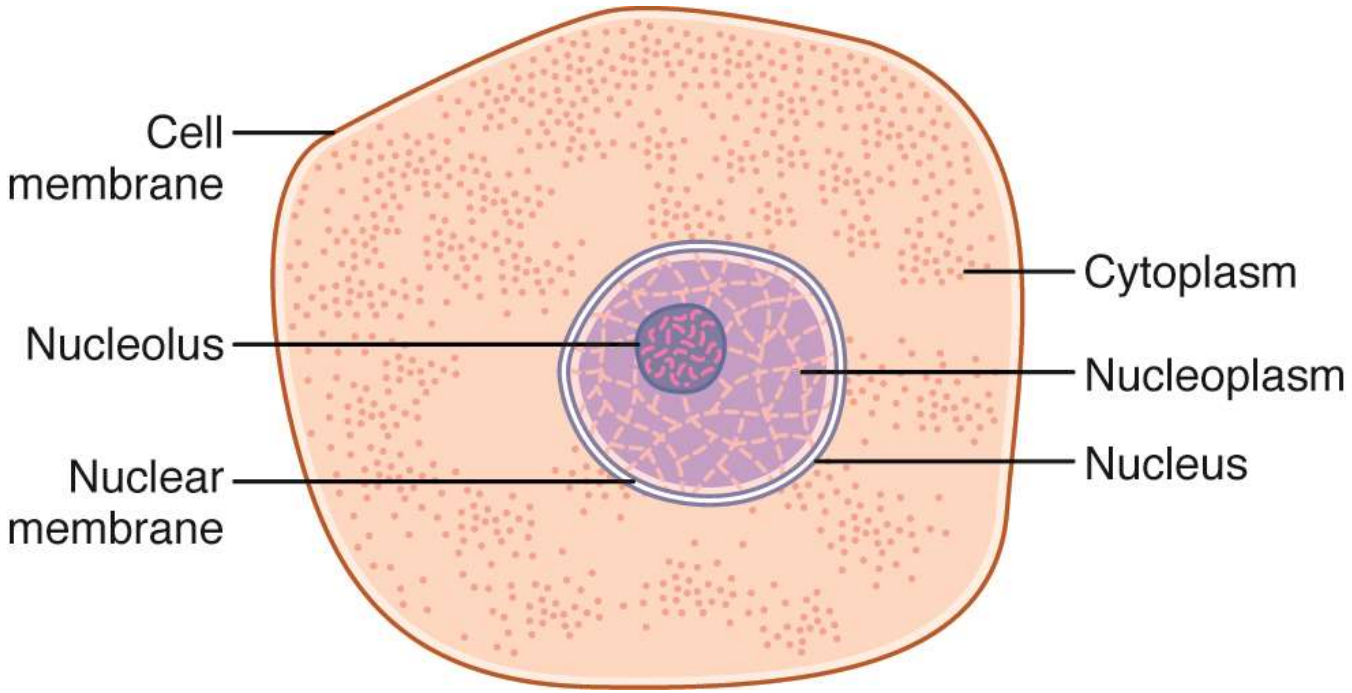

Cell membrane
Nucleolus
Nuclear membrane
Cytoplasm
Nucleoplasm
Nucleus

Figure 2-1

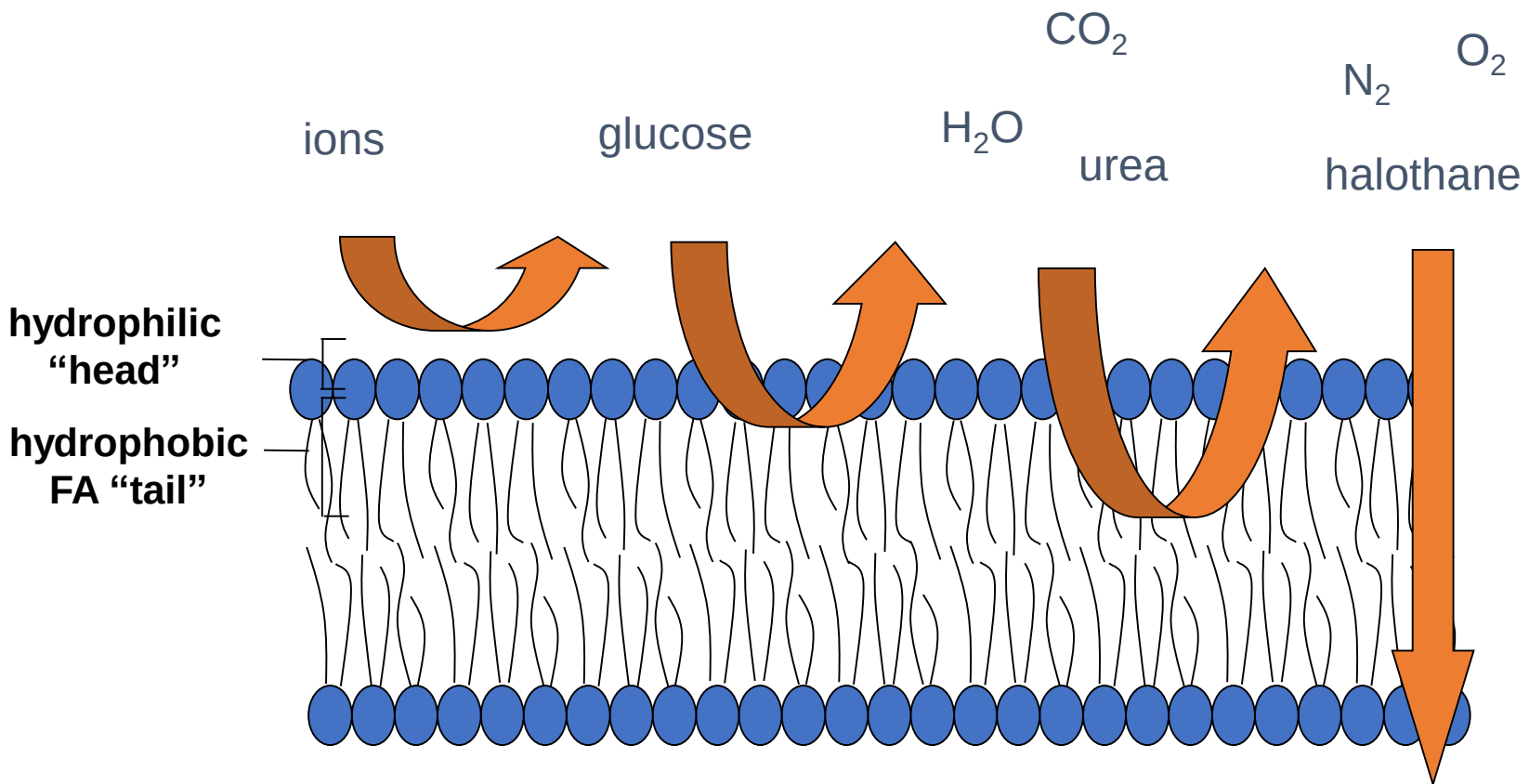
Composition of Cells

Water	...70-85% of cell mass
Ions	
Proteins	...10-20%
Lipids	...2-95%
Carbohydrates	...1-6%

Components: Plasma Membrane

LIPIDS:

- **barrier to water and water-soluble substances**
- **organized in a bilayer of phospholipid molecules**



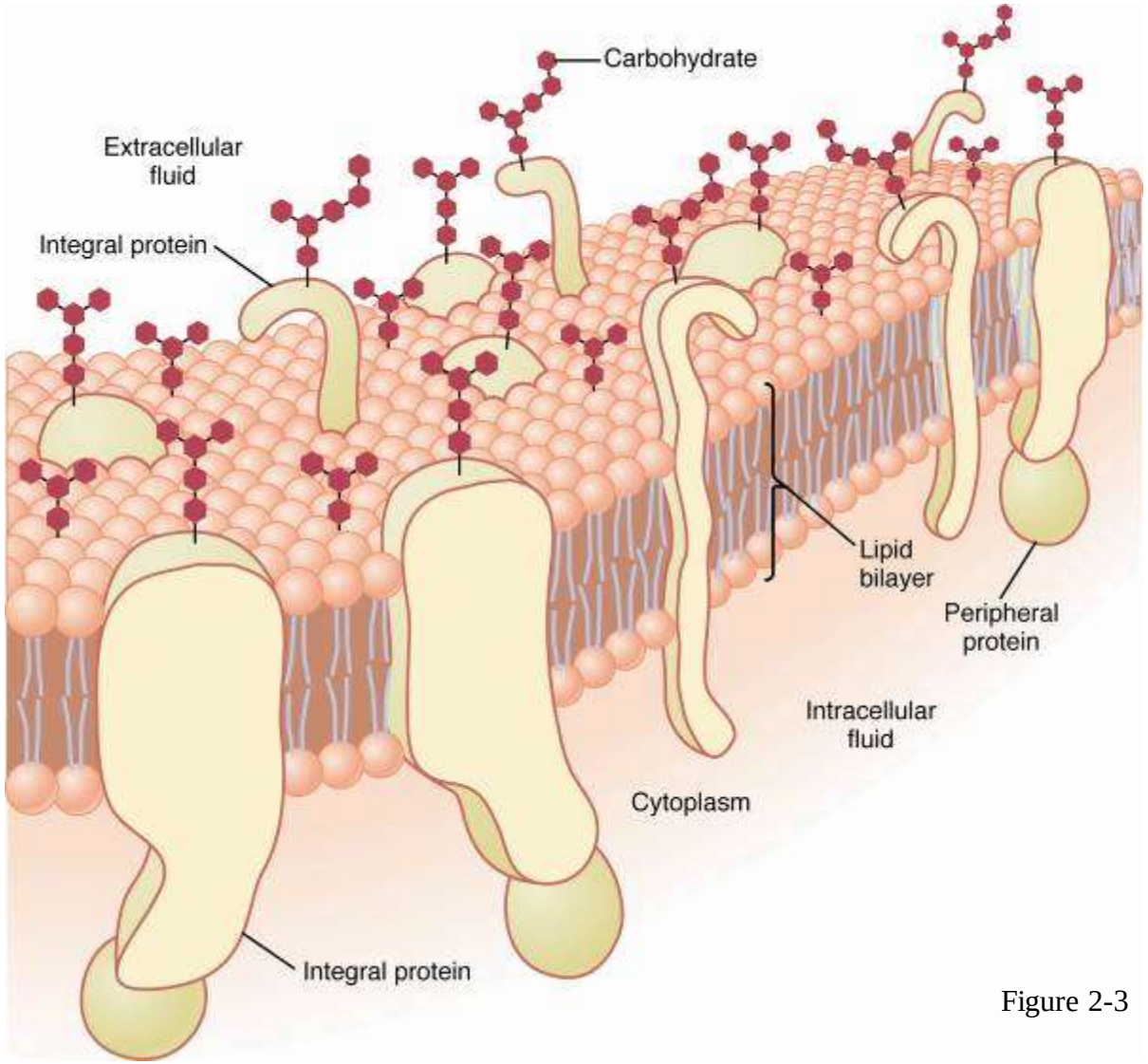
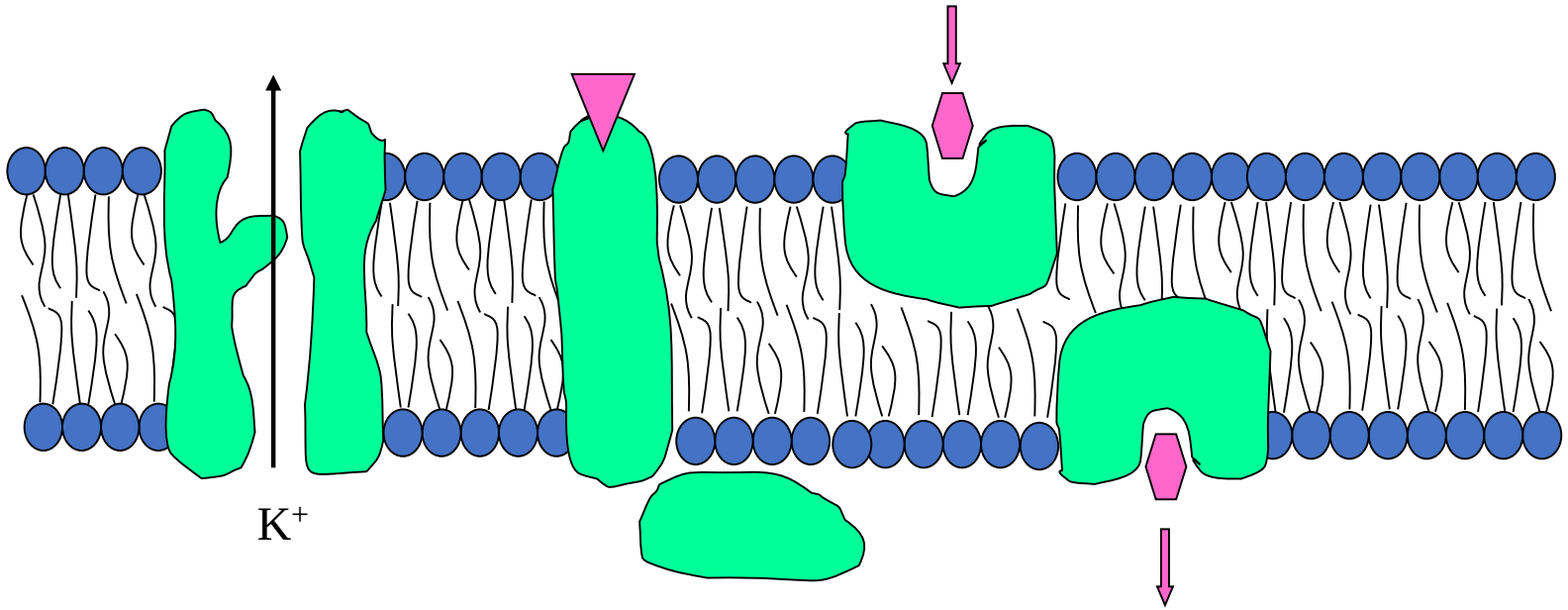

Carbohydrate
Extracellular fluid
Integral protein
Lipid bilayer
Peripheral protein
Intracellular fluid
Cytoplasm
Integral protein

Figure 2-3

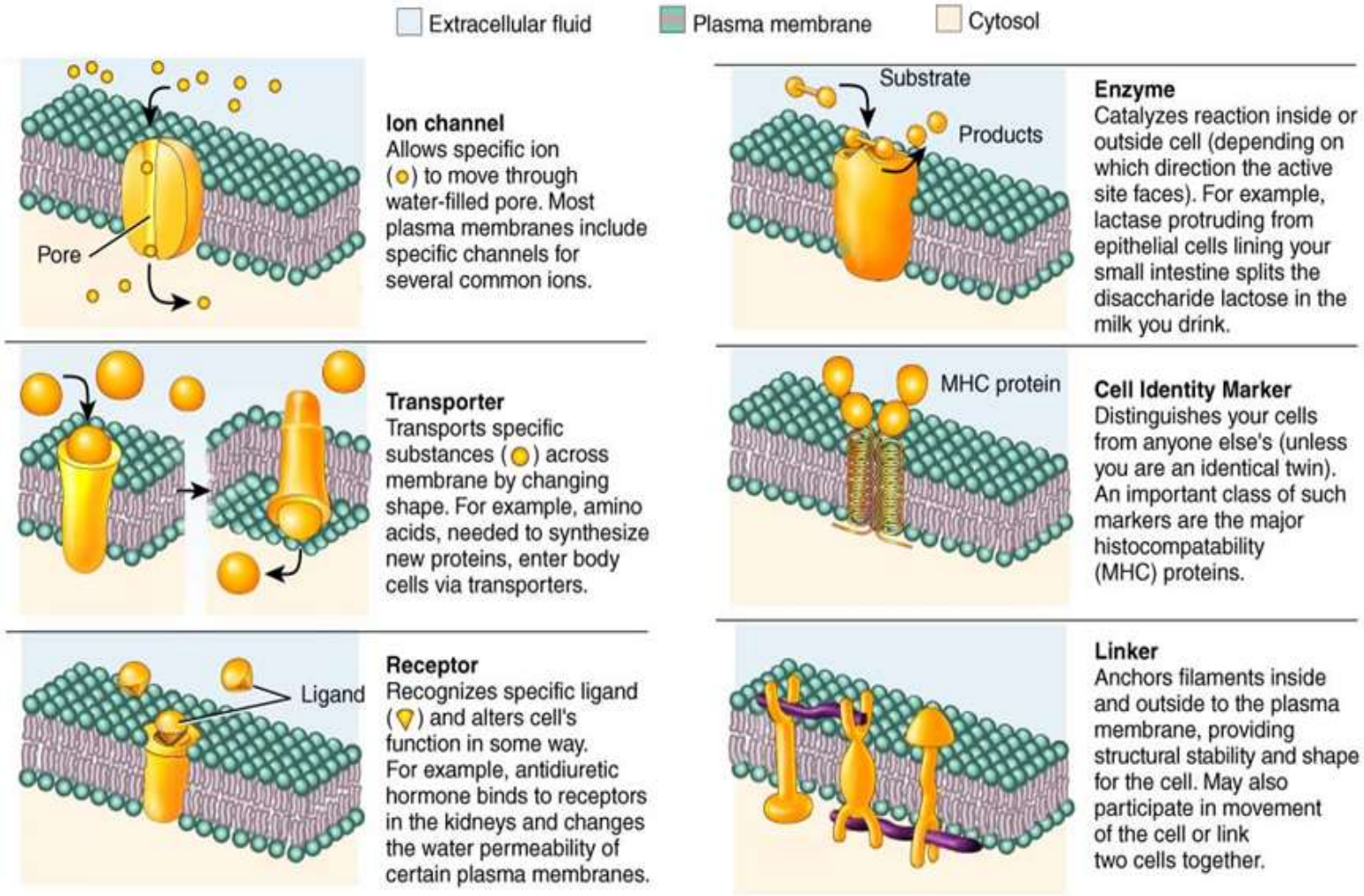
Proteins:

- provide “specificity” to a membrane
- defined by mode of association with the lipid bilayer
  - integral: channels, pores, carriers, enzymes, etc.
  - peripheral: enzymes, intracellular signal mediators



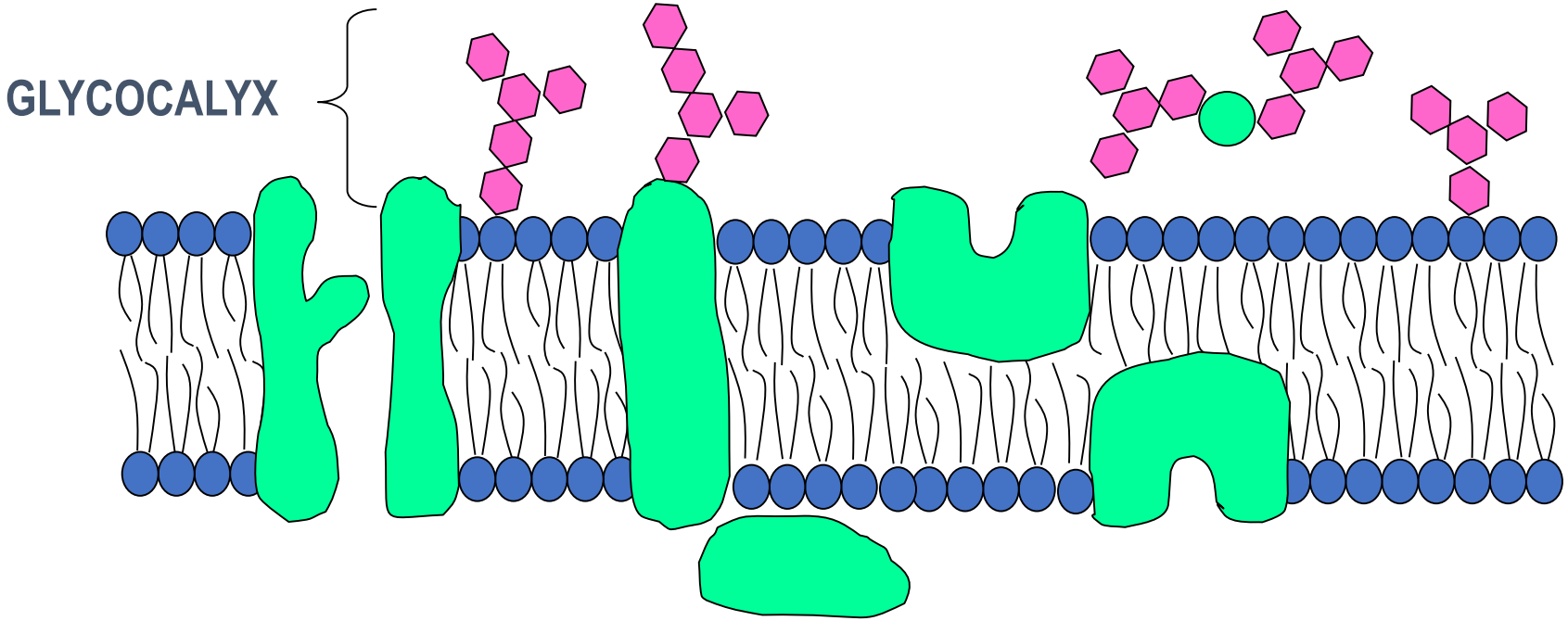
Membrane Structure	*Function*
Phospholipid Bilayer	▪ The phospholipids are arranged in a bilayer, with their polar, hydrophilic phosphate heads facing outwards, and their non-polar, hydrophobic fatty acid tails facing each other in the middle of the bilayer. ▪ This hydrophobic layer acts as a barrier to all but the smallest molecules (oxygen & Carbon Dioxide), effectively isolating the two sides of the membrane. ▪ Phospholipids can exchange position in the horizontal plane but not the vertical.
Integral Proteins	▪ Usually span from one side of the phospholipid bilayer to the other. ▪ Proteins that span the membrane are usually involved in transporting substances across the membrane (more detail below)
Peripheral Proteins	▪ These proteins sit on one of the surfaces (peripheral proteins). They can slide around the membrane very quickly and collide with each other, but can never flip from one side to the other. ▪ Proteins on the inside surface of plasma membrane are often involved in maintaining the cell's shape, or in cell motility. ▪ They may also be enzymes, catalysing reactions in the cytoplasm.
Glycoproteins	▪ Usually involved in cell recognition which is part of the immune system. They can also acts as receptors in cell signaling such as with hormones.
Cholesterol	▪ Binds together lipid in the plasma membrane reducing its fluidity as conferring structural stability

Protein functions in plasma membranes



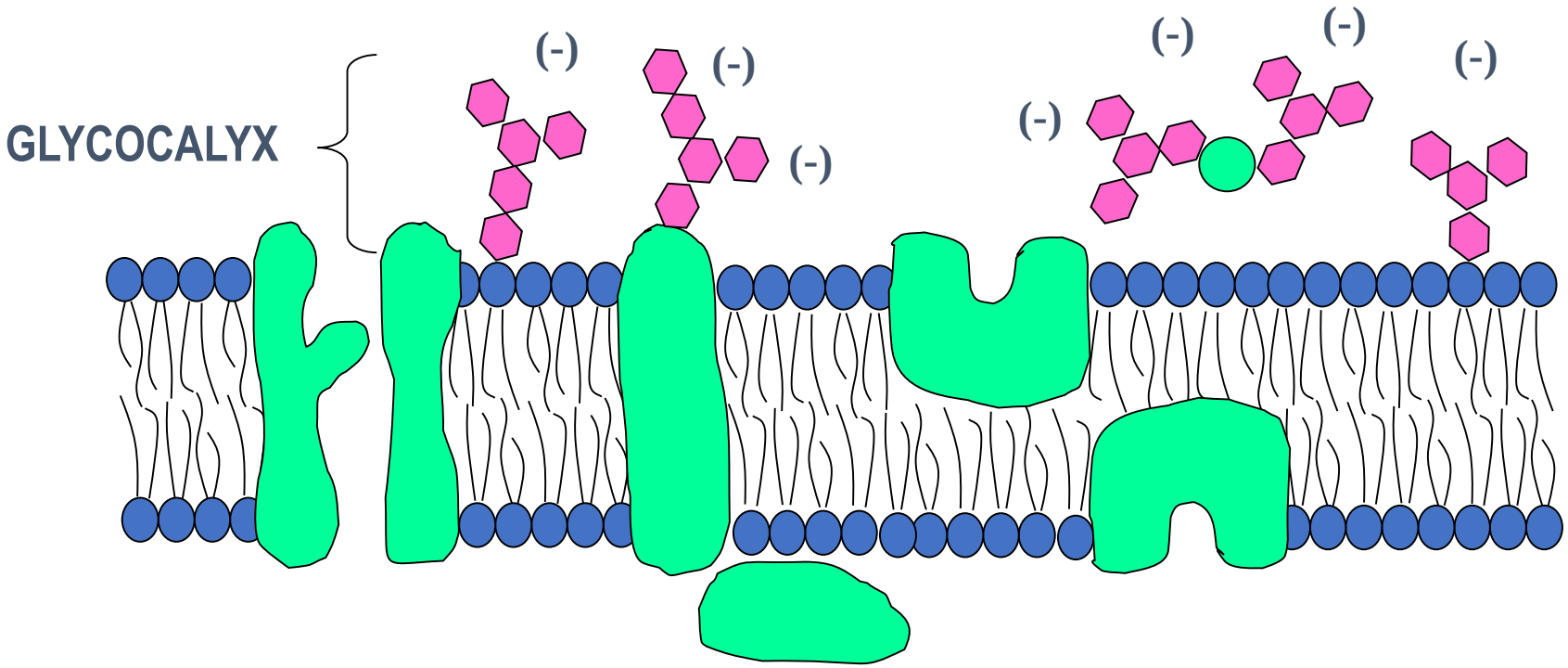
Carbohydrates:

- glycolipids (approx. 10%)
- glycoproteins (majority of integral proteins)
- proteoglycans



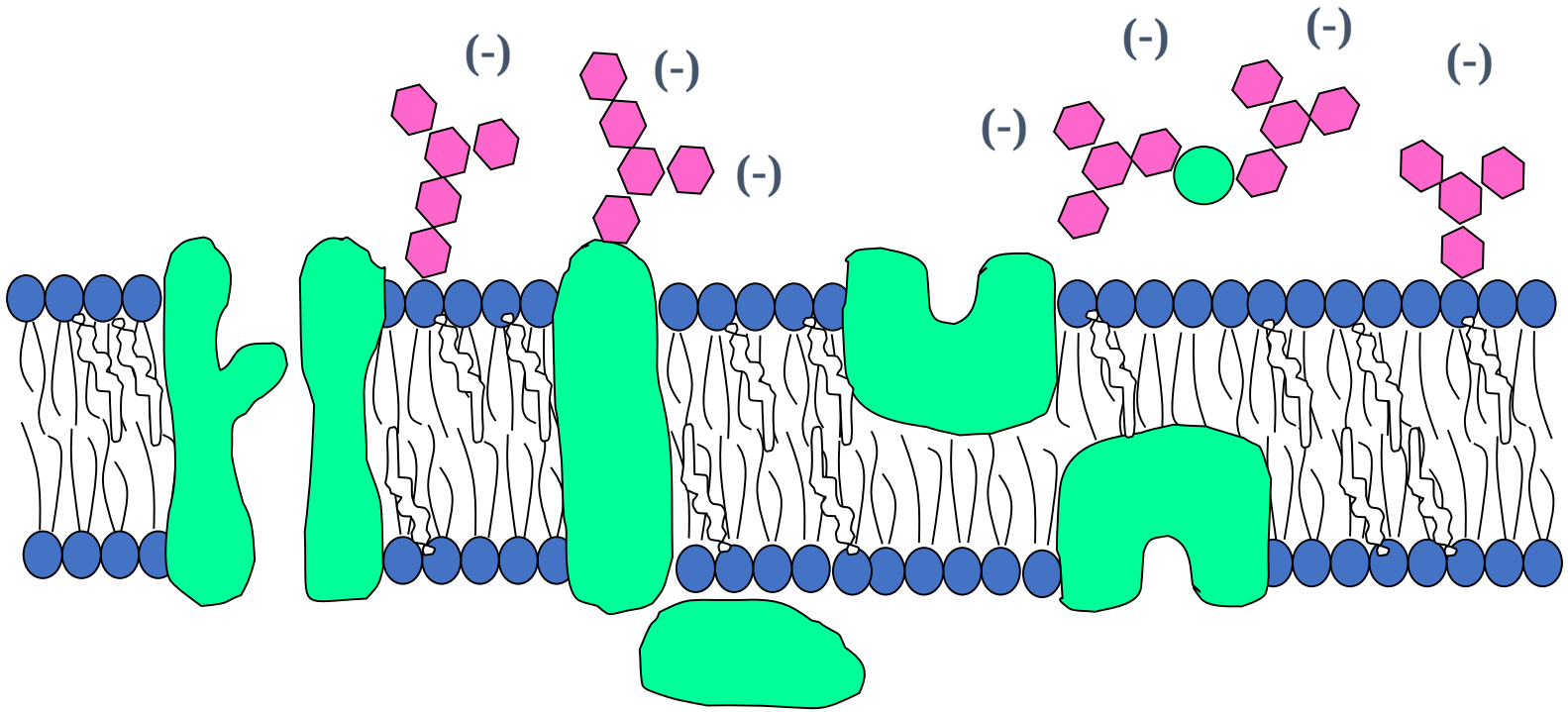
Carbohydrates

- negative charge of the carbo chains repels other negative charges
- involved in cell-cell attachments/interactions
- play a role in immune reactions



Cholesterol:

- Present in membranes in varying amounts
- Generally decreases membrane FLUIDITY and PERMEABILITY (except in plasma membrane)
- Increases membrane FLEXIBILITY and STABILITY



Cell Organelles

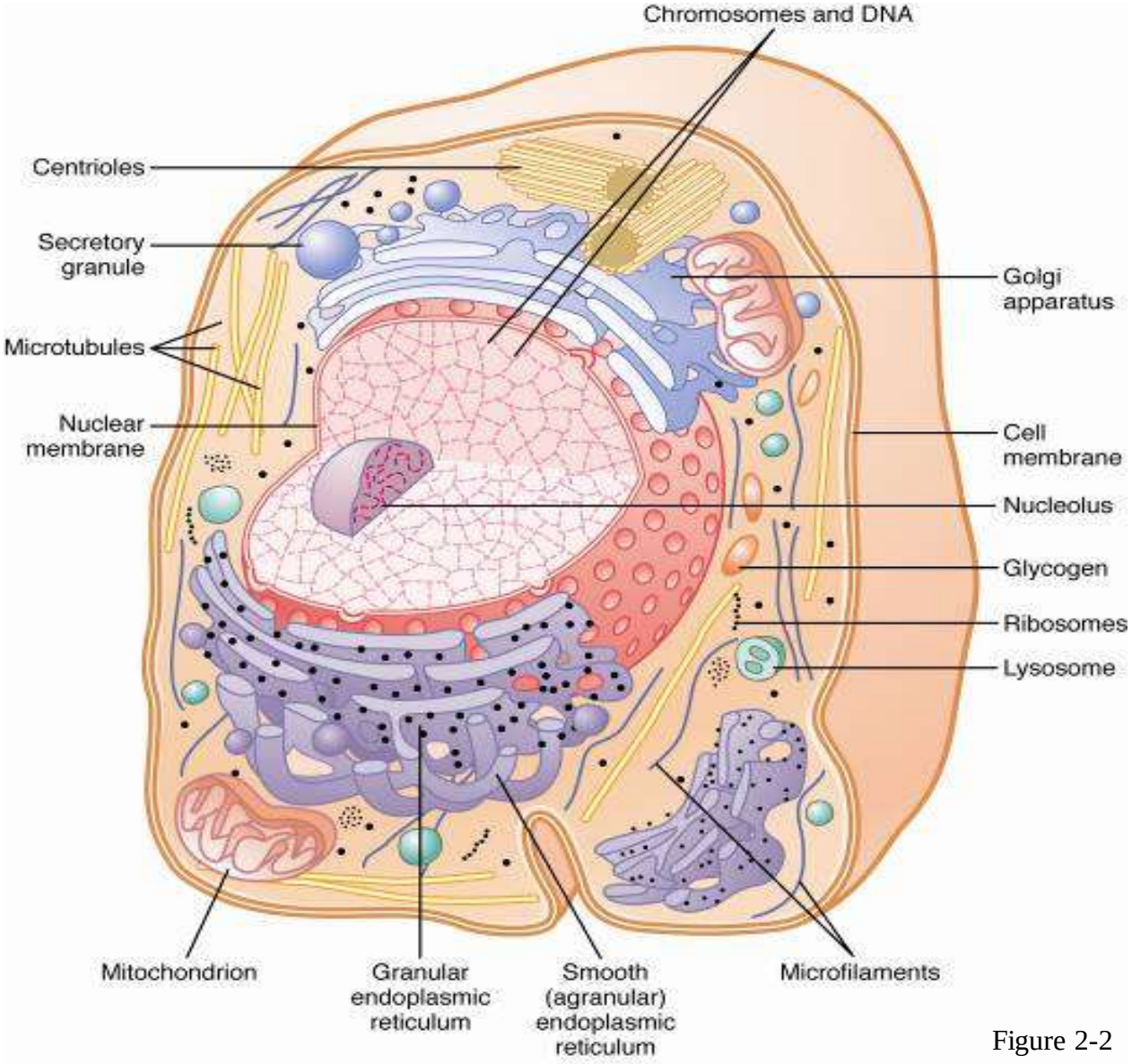


Figure 2-2

Endoplasmic Reticulum

- Network of tubular and flat vesicular structures
- Membrane is similar to (and contiguous with) the plasma membrane
- Space inside the tubules is called the endoplasmic matrix

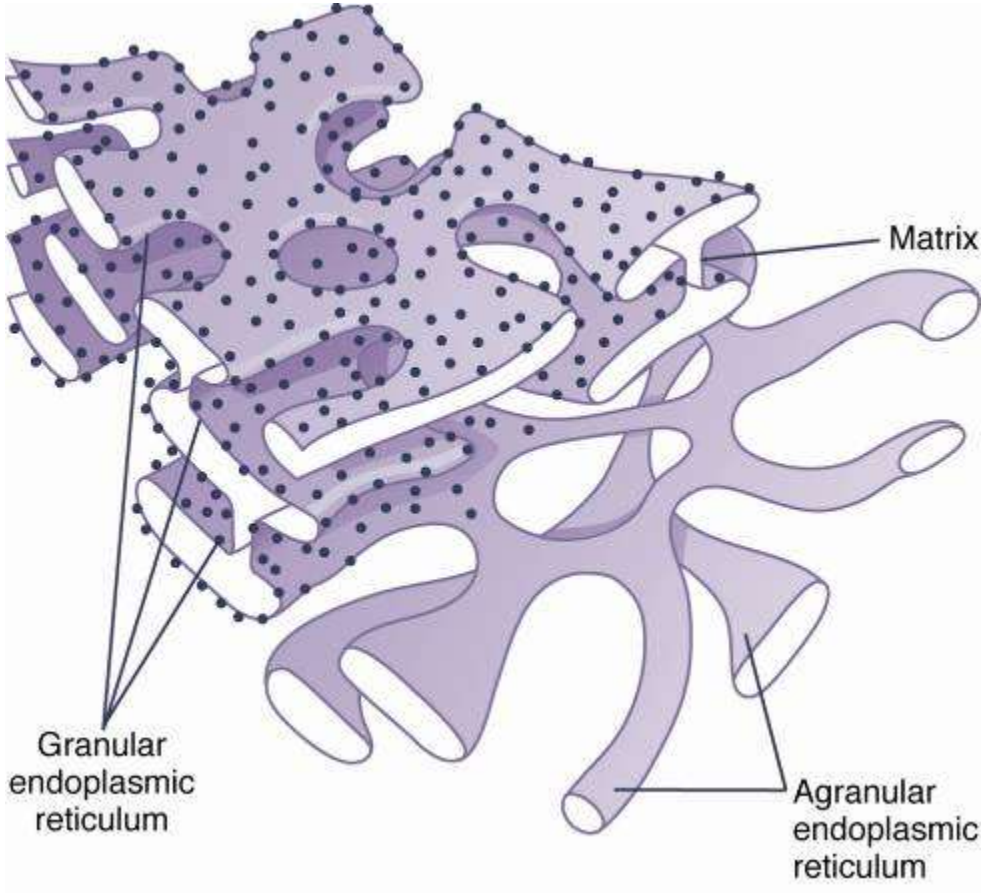


Figure 2-4

Rough Granular ER

- Outer membrane surface covered with ribosomes
- Newly synthesized proteins are extruded into the ER matrix
- Proteins are “processed” inside the matrix
  - crosslinked
  - folded
  - glycosylated (N-linked)
  - cleaved

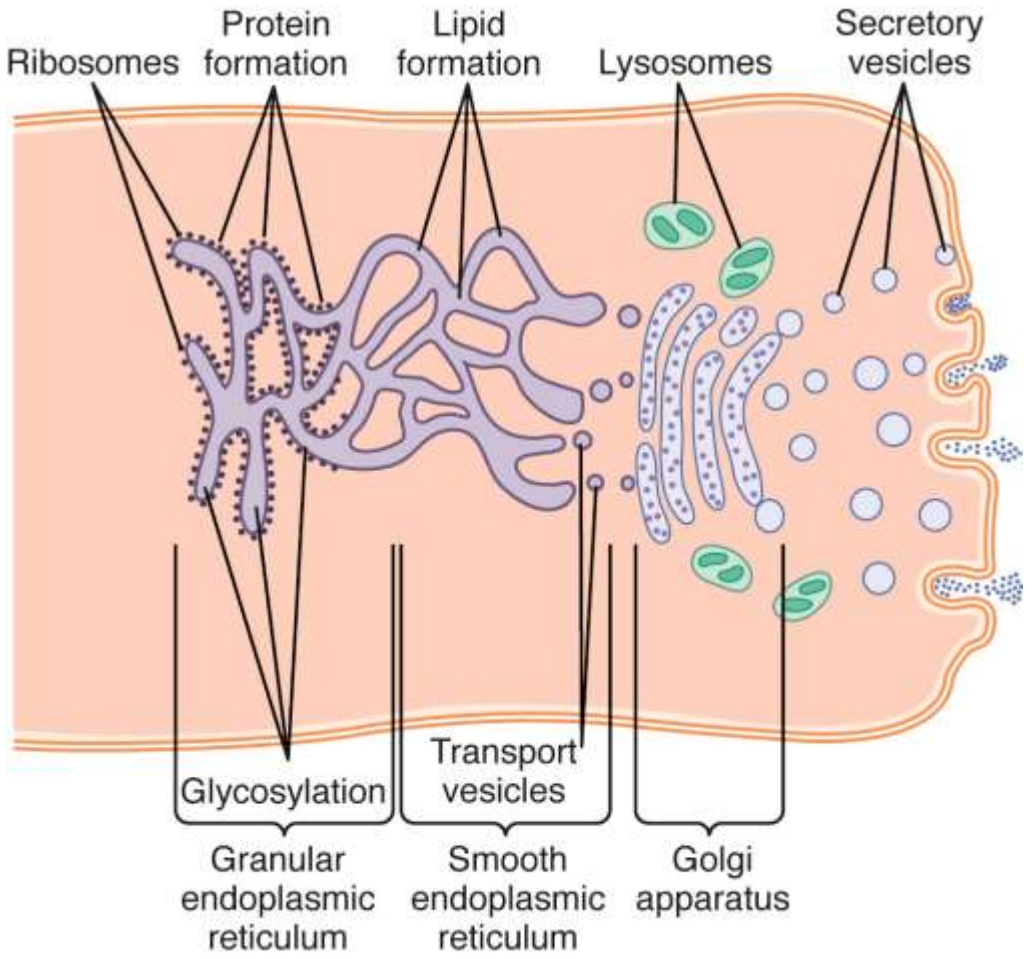


Figure 2-13

Smooth ER

- Site of lipid synthesis
  - phospholipids
  - cholesterol

- Growing ER membrane buds continuously forming transport vesicles, most of which migrate to the Golgi apparatus

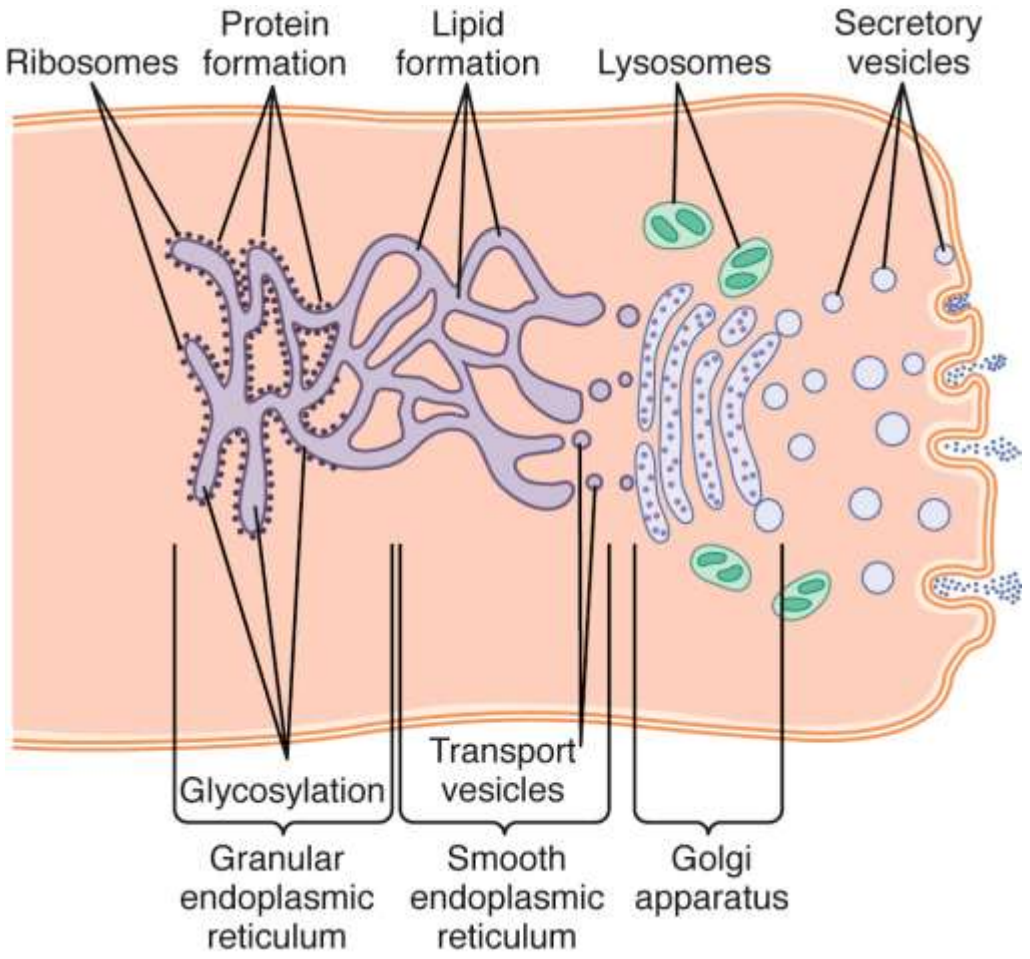


Figure 2-13

The Golgi Apparatus:

- Membrane composition similar to that of the smooth ER and plasma membrane
- Composed of 4 or more stacked layers of flat vesicular structures

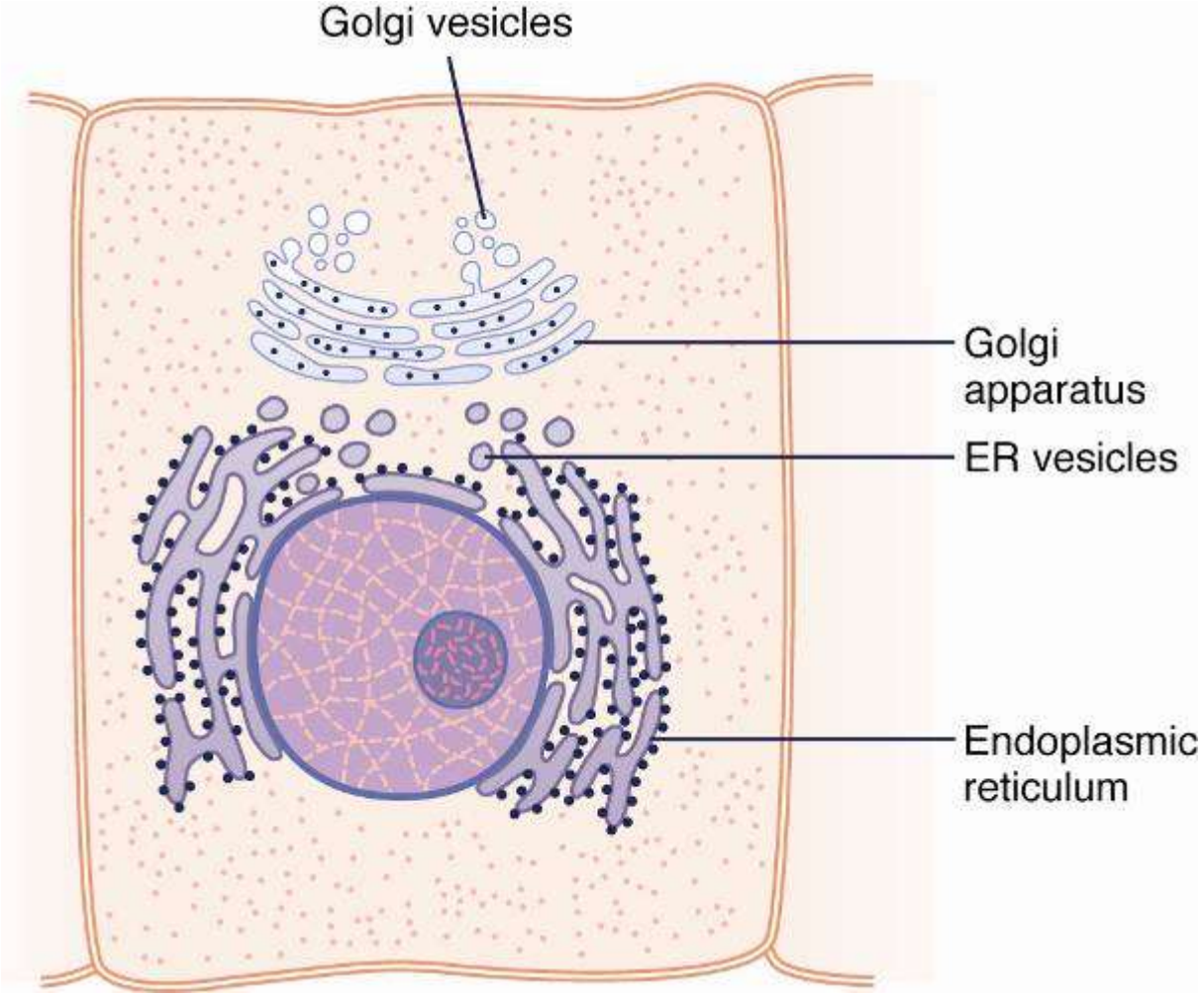


Figure 2-5

- Receives transport vesicles from smooth ER

- Substances formed in the ER are "processed"
  - phosphorylated
  - glycosylated

- Substances are concentrated, sorted and packaged for secretion.

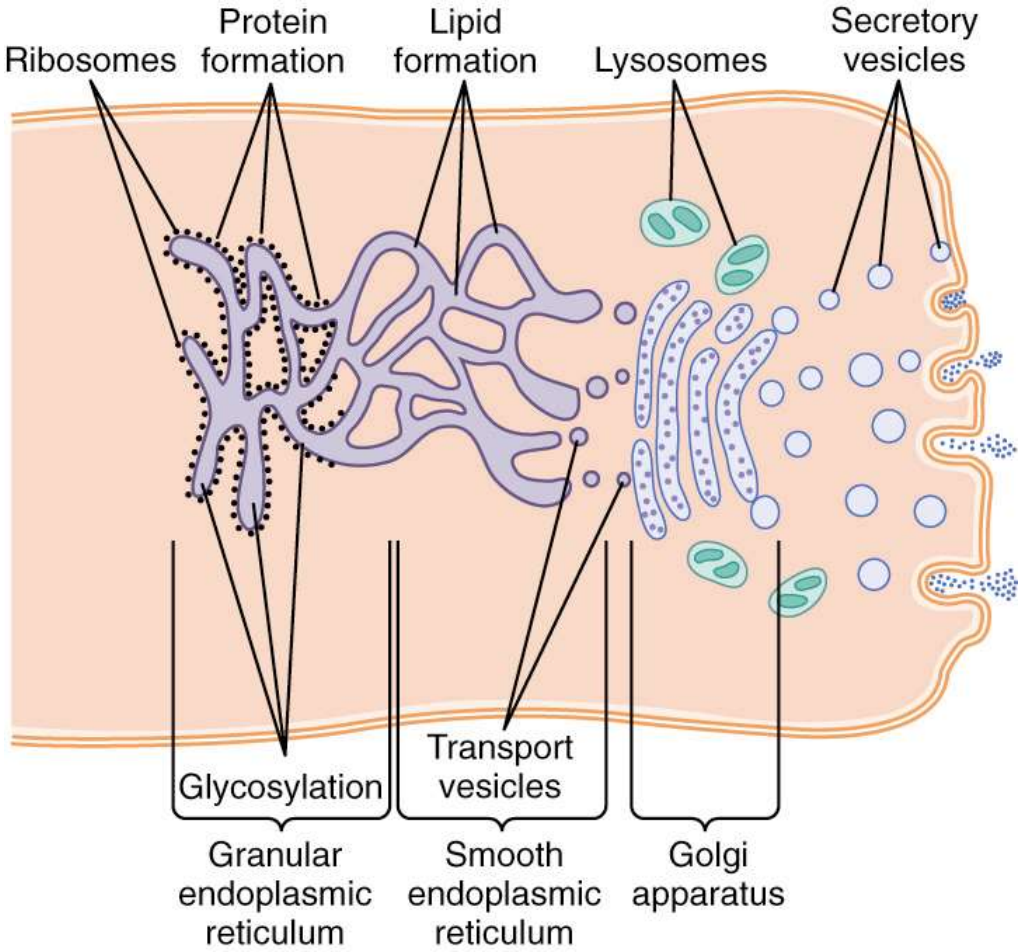


Figure 2-13

Exocytosis

Secretory vesicles diffuse through the cytosol and fuse to the plasma membrane

Lysosomes fuse with internal endocytotic vesicles

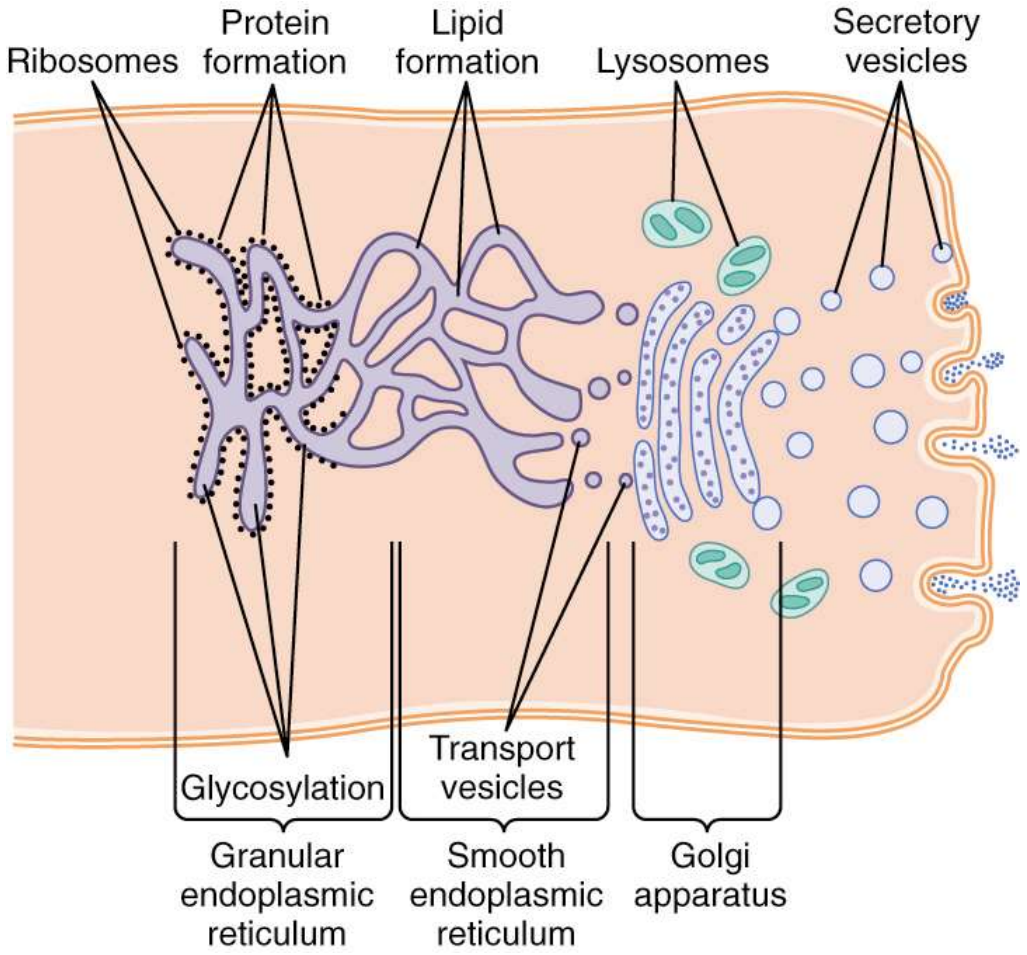


Figure 2-13

Secretion

- Secretory vesicles containing proteins synthesized in the RER bud from the Golgi apparatus

- Fuse with plasma membrane to release contents
  - constitutive secretion - happens randomly
  - stimulated secretion – requires trigger

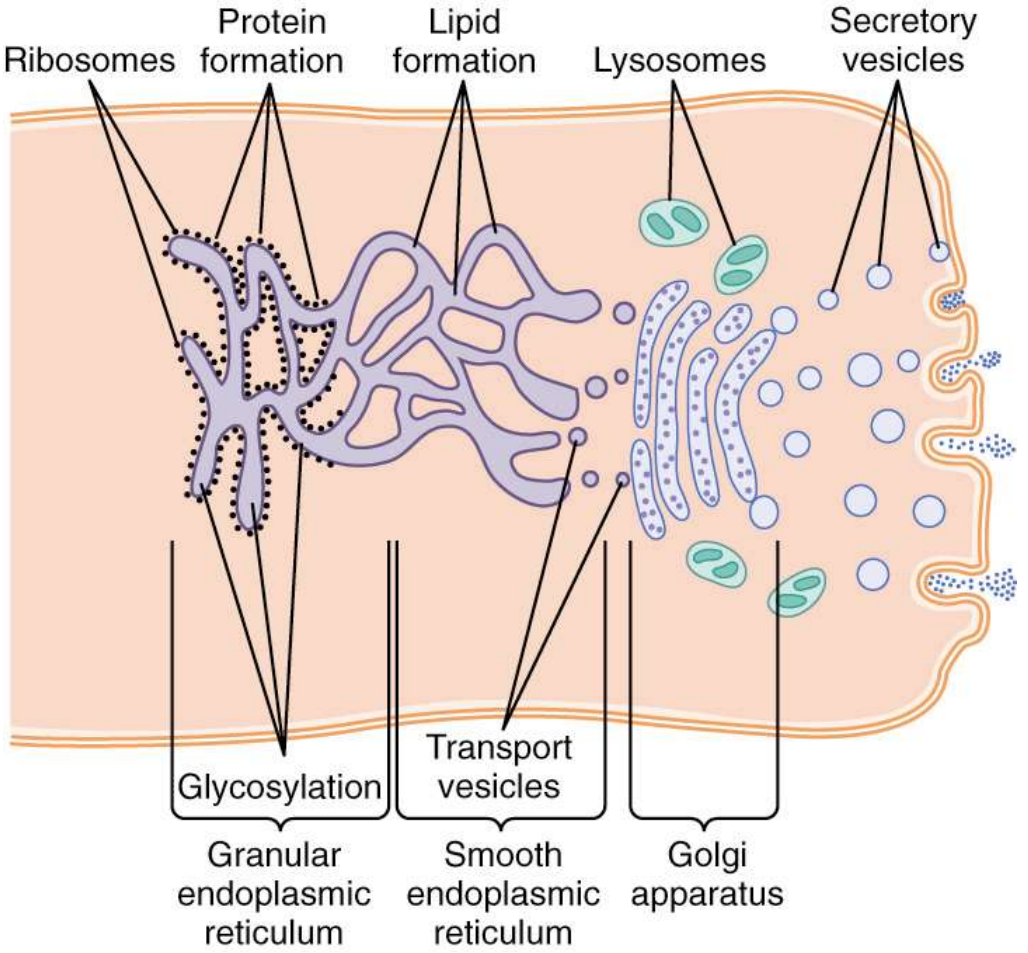


Figure 2-13

Lysosomes:

- Vesicular organelle formed from budding Golgi

- Contain hydrolytic enzymes (acid hydrolases)
  - phosphatases
  - nucleases
  - proteases
  - lipid-degrading enzymes
  - lysozymes digest bacteria

- Fuse with pinocytotic or phagocytotic vesicles to form digestive vesicles

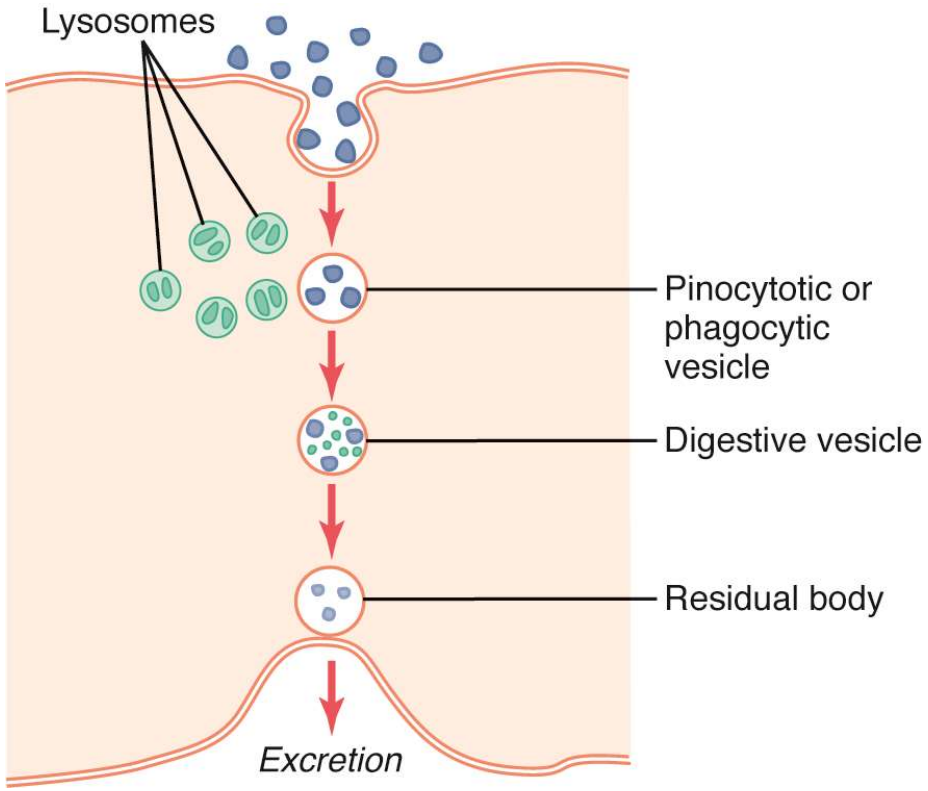


Figure 2-12

Lysosomal Storage Diseases

Absence of one or more hydrolases

- not synthesized
- inactive
- not properly sorted and packaged

Result: Lysosomes become engorged with undigested substrate

Examples:

- Acid lipase A deficiency
- I-cell disease (non-specific)
- Tay-Sachs disease (HEX A)

Peroxisomes:

- Similar physically to lysosomes

- Two major differences:
  - formed by self-replication
  - they contain oxidases

Function: oxidize substances (e.g. alcohol) that may be otherwise poisonous

Secretory Granules

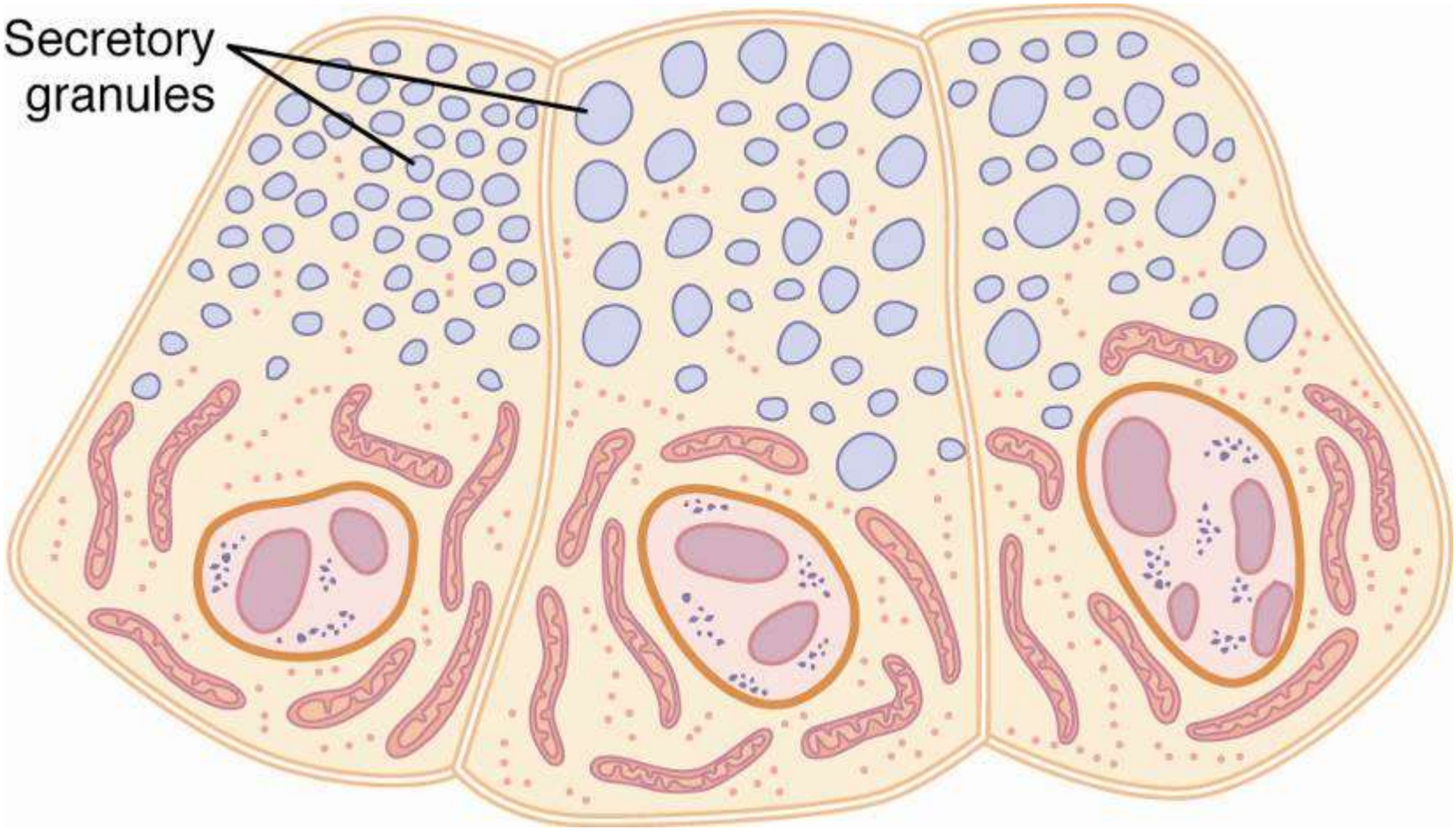


Figure 2-6

Mitochondria

<u>Primary function</u>: extraction of energy from nutrients

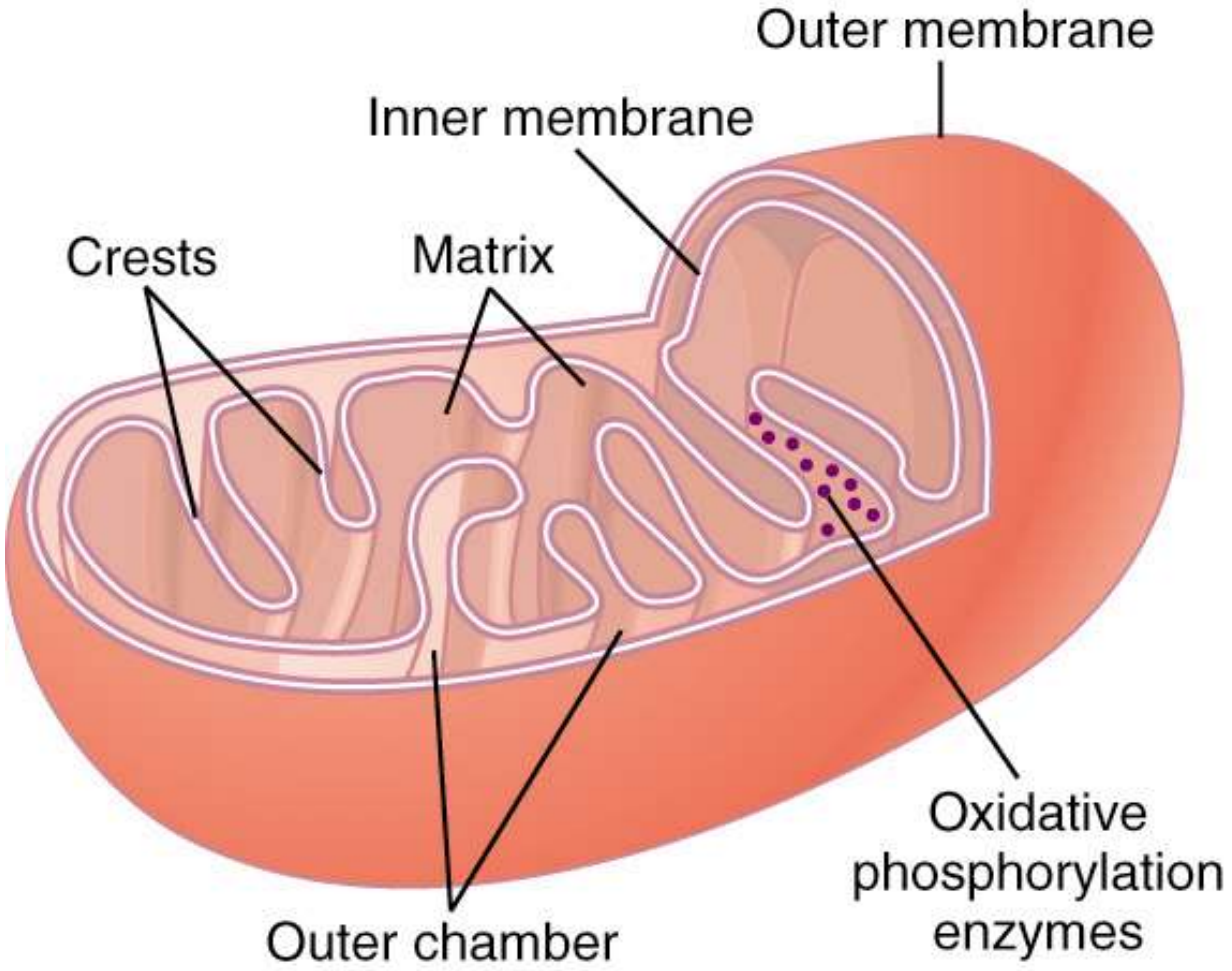


Figure 2-7

The Nucleus: “Control Center” of the Cell

The double **nuclear membrane** and matrix are contiguous with the endoplasmic reticulum

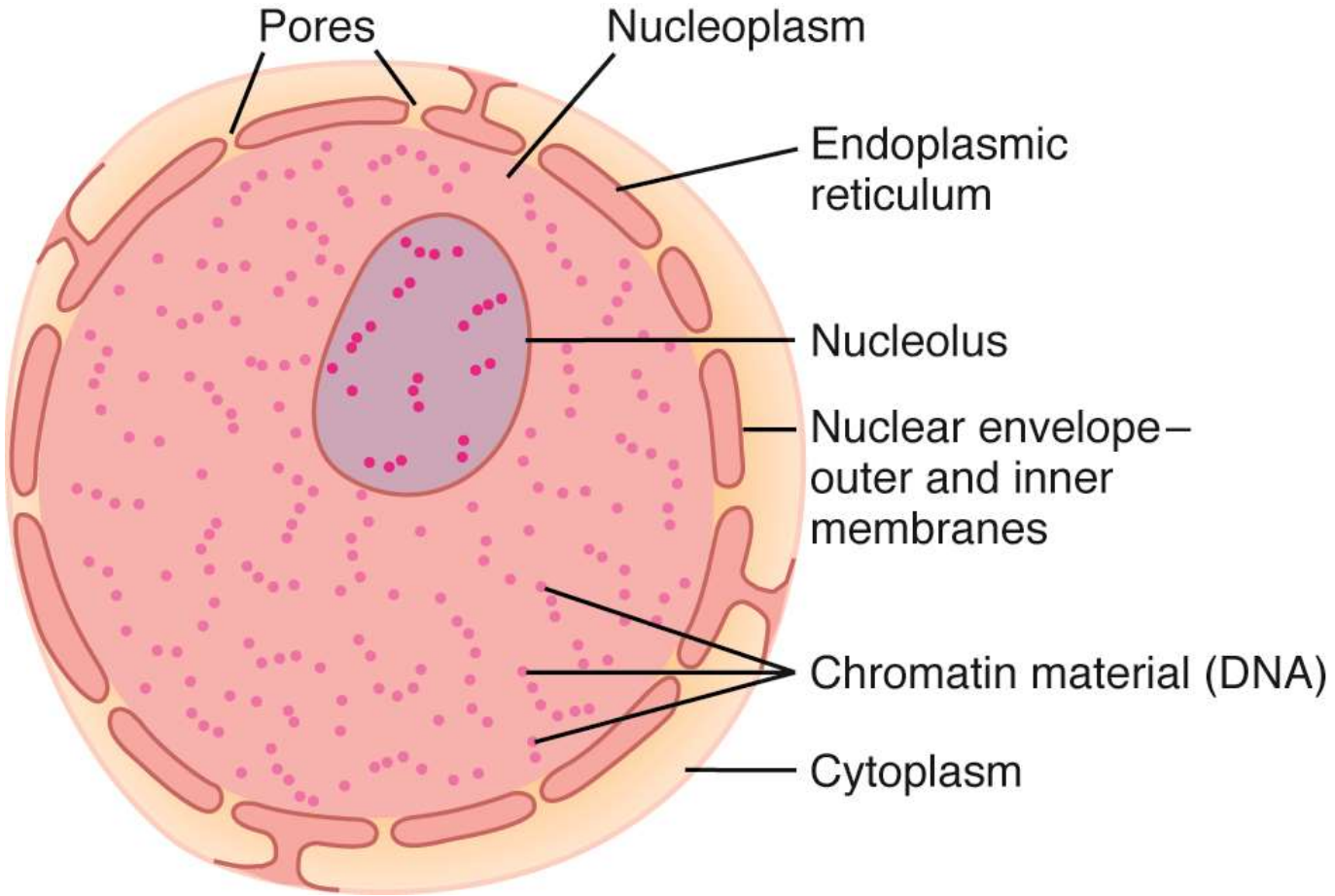


Figure 2-9

The nuclear membrane is permeated by thousands of nuclear pores

- 100 nm in diameter
- functional diameter is ~9 nm
- (selectively) permeable to molecules of up to 44,000 MW

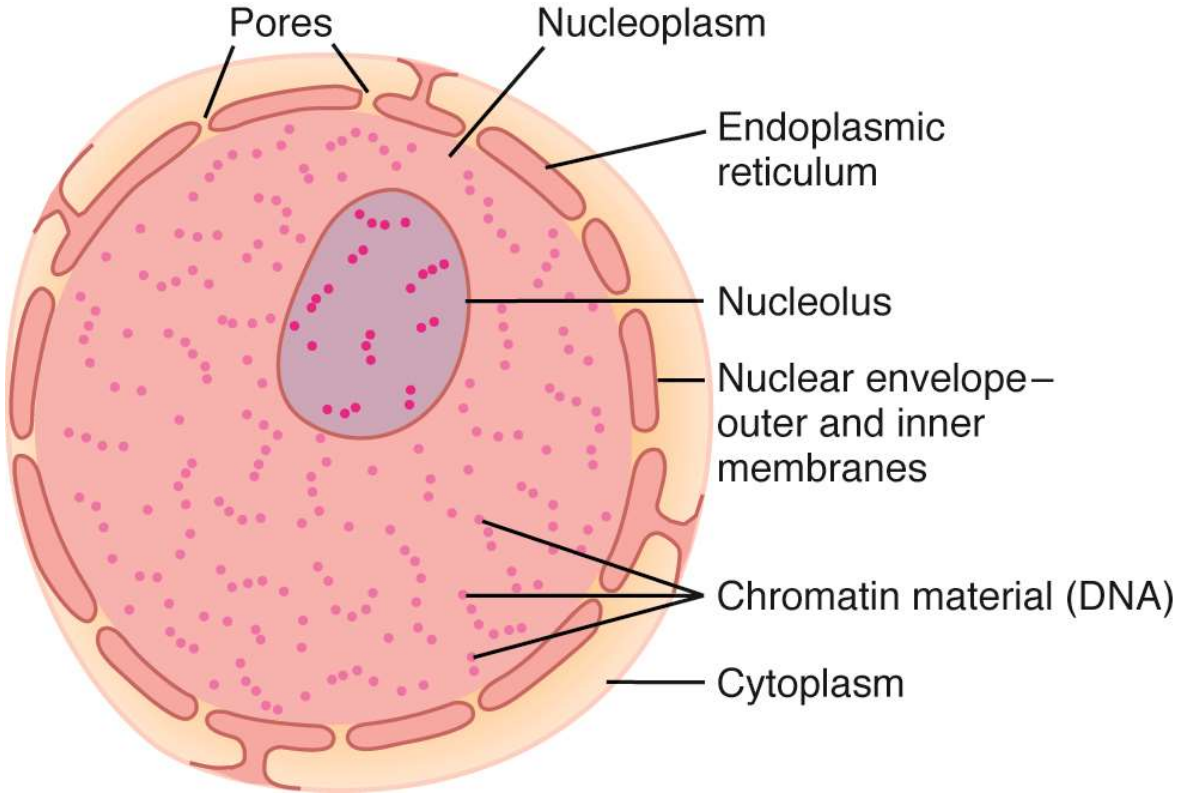


Figure 2-9

Chromatin (condensed DNA) is found in the nucleoplasm

Nucleolus

- one or more per nucleus
- contains RNA and proteins
- not membrane delimited
- functions to form the granular “subunits” of ribosomes

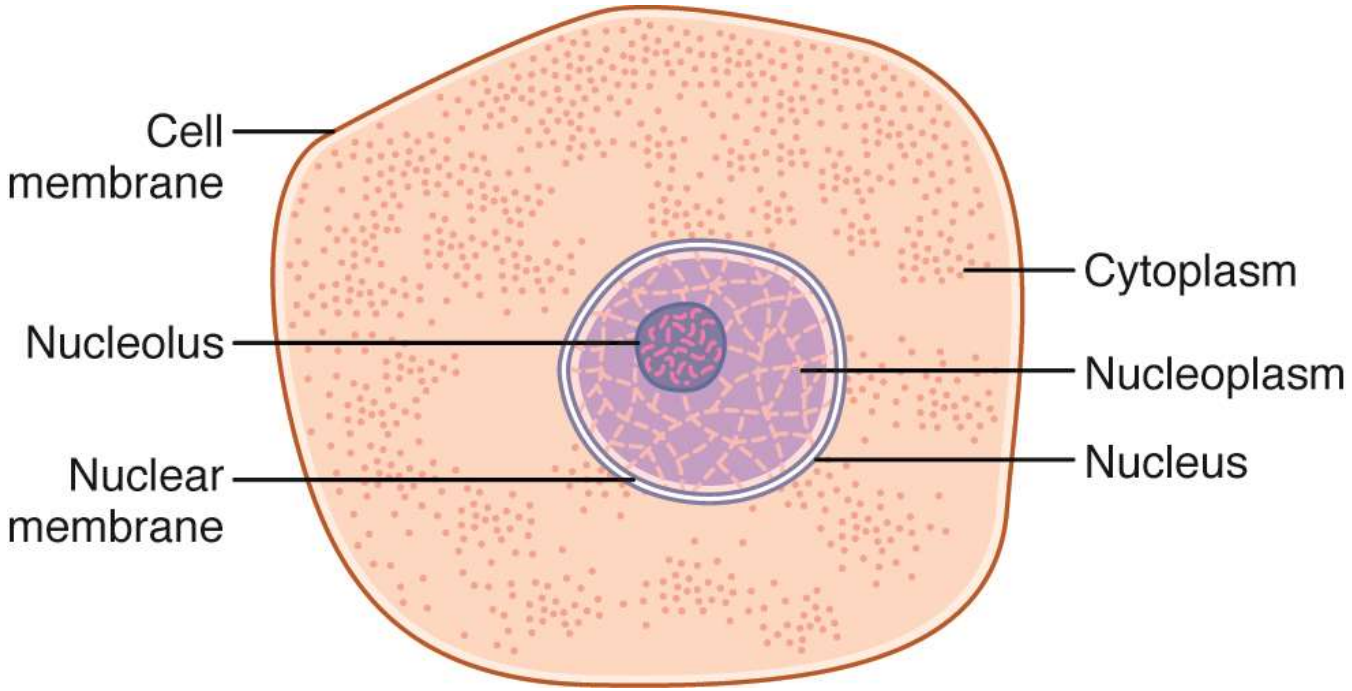


Figure 2-1

Receptor-mediated

- Molecules attach to cell-surface receptors concentrated in clathrin-coated pits
- Receptor binding induces invagination
- Also ATP-dependent and involves recruitment of actin and myosin

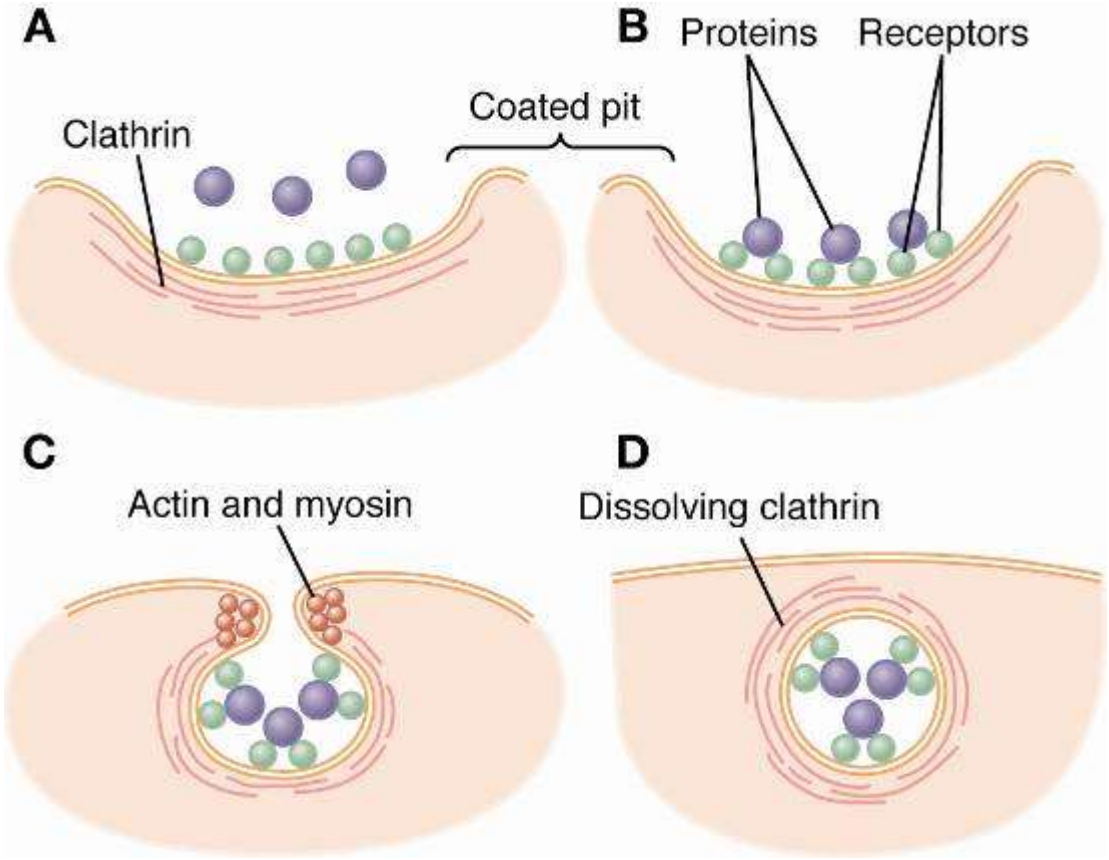


Figure 2-11

Digestion of Substances in Pinocytotic or Phagocytic Vesicles

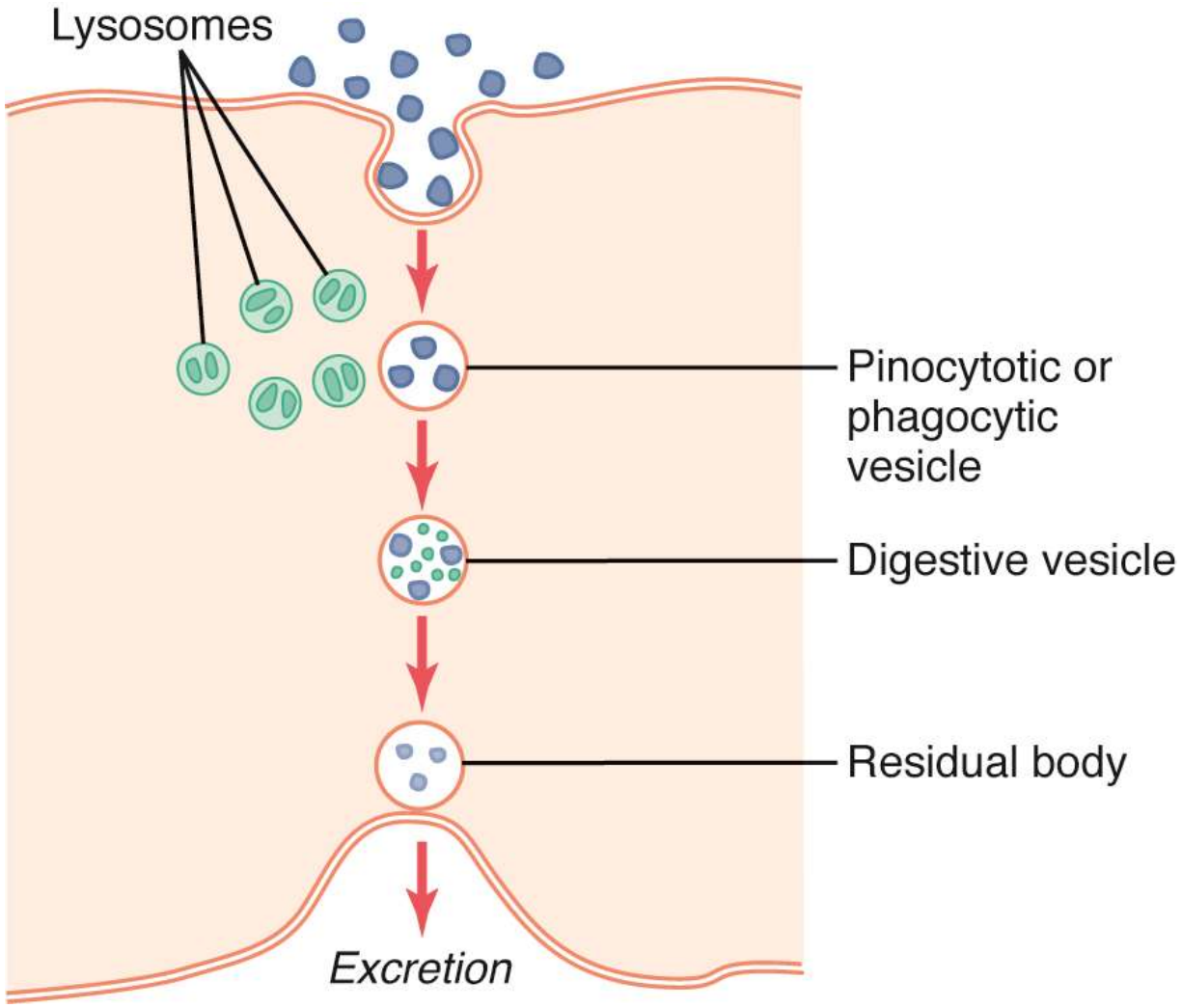


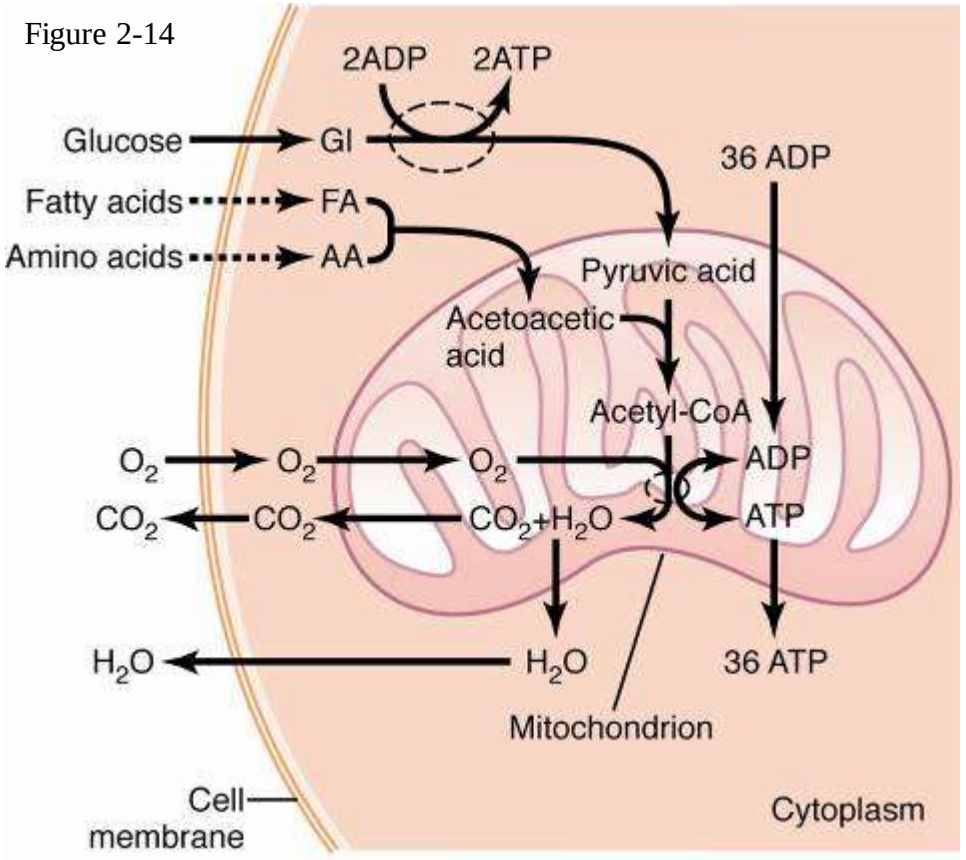
Figure 2-12

ATP production

Step 1.
- Carbohydrates are converted into glucose
- Proteins are converted into amino acids
- Fats are converted into fatty acids

Step 2.
- Glucose, AA, and FA are processed into AcetylCoA

Step 3.
- AcetylCoA reacts with O_2 to produce ATP



A maximum of 38 molecules of ATP are formed per molecule of glucose degraded.

(More in Chapter 67)

The Use of ATP for Cellular Function

- Under “standard” conditions ΔG° is only -7.3 kcal/mole
- ATP concentration is ~10x that of ADP, the ΔG is -12 kcal/mole

1. Membrane transport

2. Synthesis of chemical compounds

3. Mechanical work

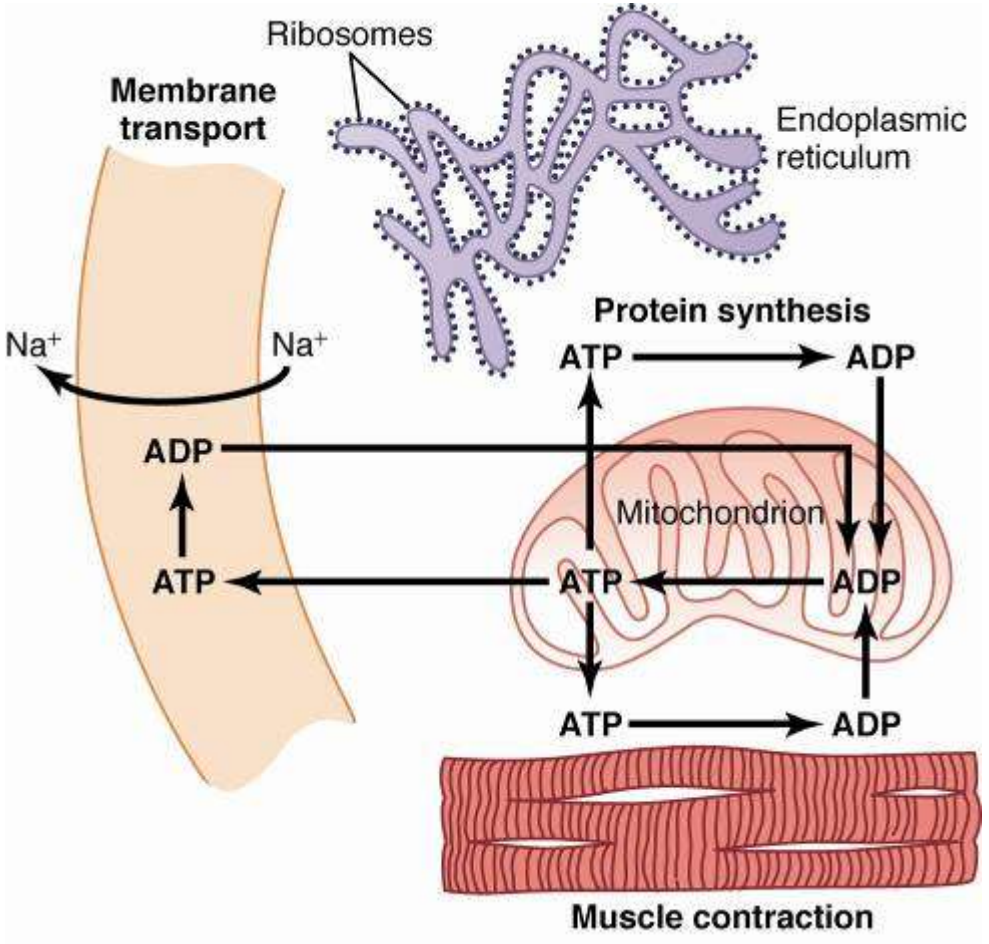


Figure 2-15

The Cytoskeleton

Intermediate Filaments:

- Comprised of cell-specific fibrillar monomers (e.g. vimentin, neurofilament proteins, keratins, nuclear lamins)

Microtubules:

- Heterodimers of α and β tubulin
- Make up spindle fibers, core of axoneme structure

Thin Filaments:

- F-Actin
- Make up “stress fibers” in non-muscle cells

Thick Filaments:

- Myosin (types I and II)
- Together with actin support cellular locomotion and subcellular transport

Cilia and Ciliary Movements:

- Occurs only on the inside surfaces of the human airway and fallopian tubes

- Each cilium is comprised of 11 microtubules
  - 9 double tubules
  - 2 single tubules

  } axoneme

- Each cilium is an outgrowth of the basal body and is covered by an outcropping of the plasma membrane.

- Ciliary movement is ATP-dependent
  (also requires Ca^{2+} and Mg^{2+})

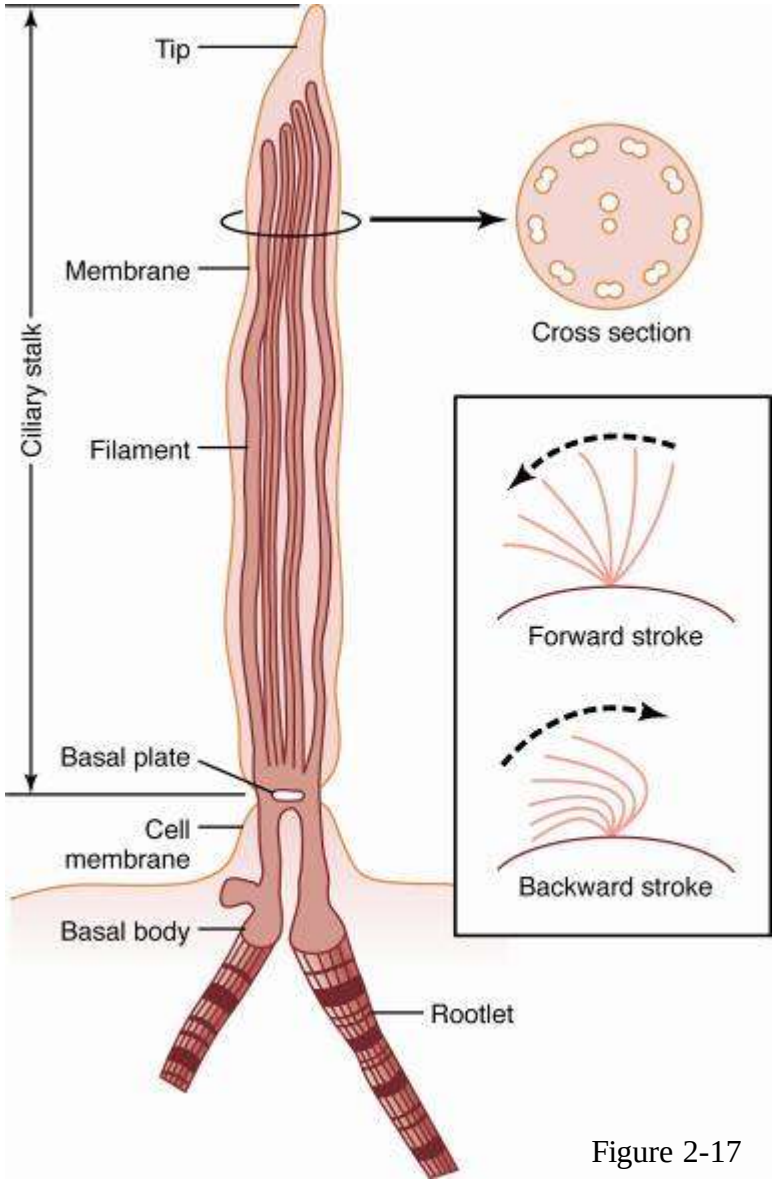


Figure 2-17

Ameboid Locomotion:

- Continual endocytosis at the “tail”and exocytosis at the leading edge of the pseudopodium
- Attachment of the pseudopodium is facilitated by receptor proteins carried by vesicles
- Forward movement results through interaction of actin and myosin (ATP-dependent)

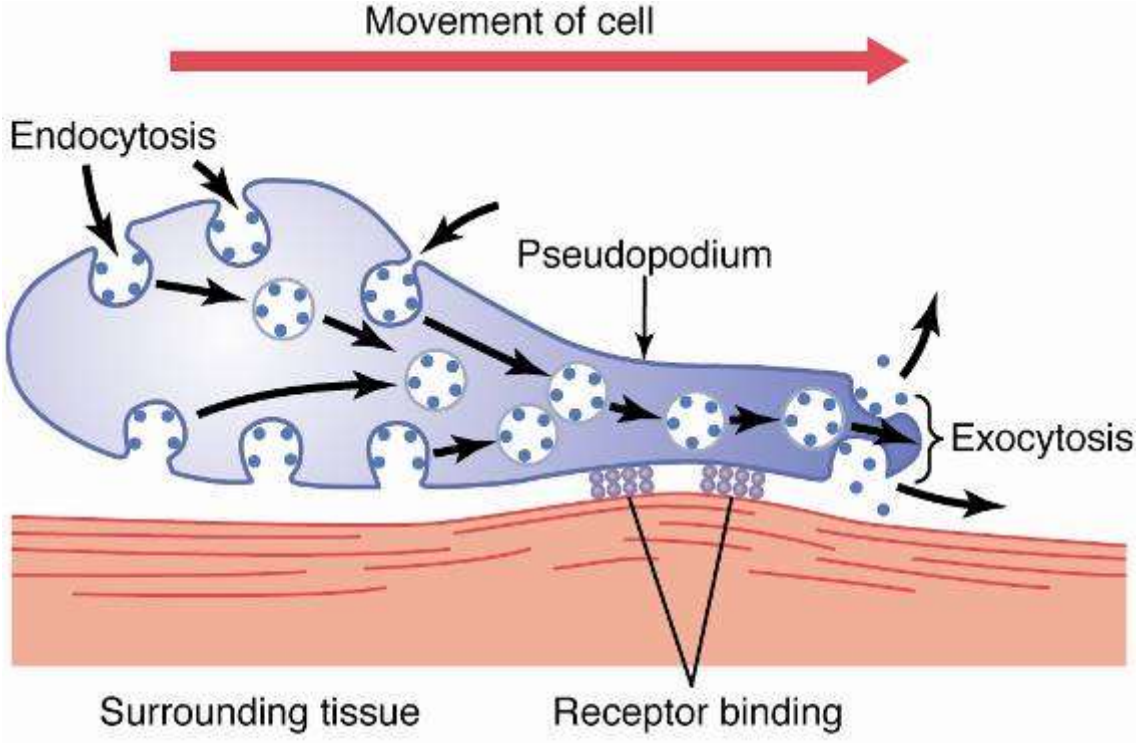
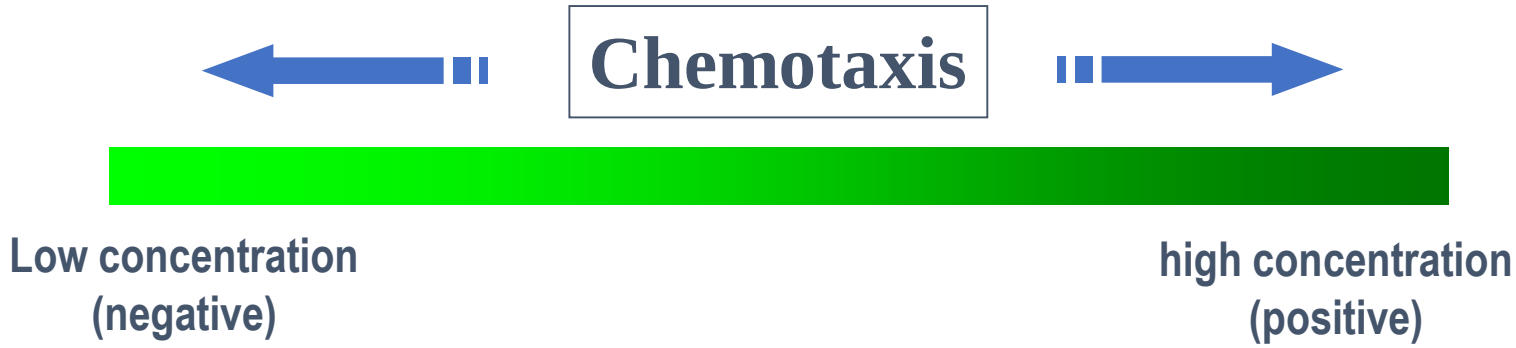
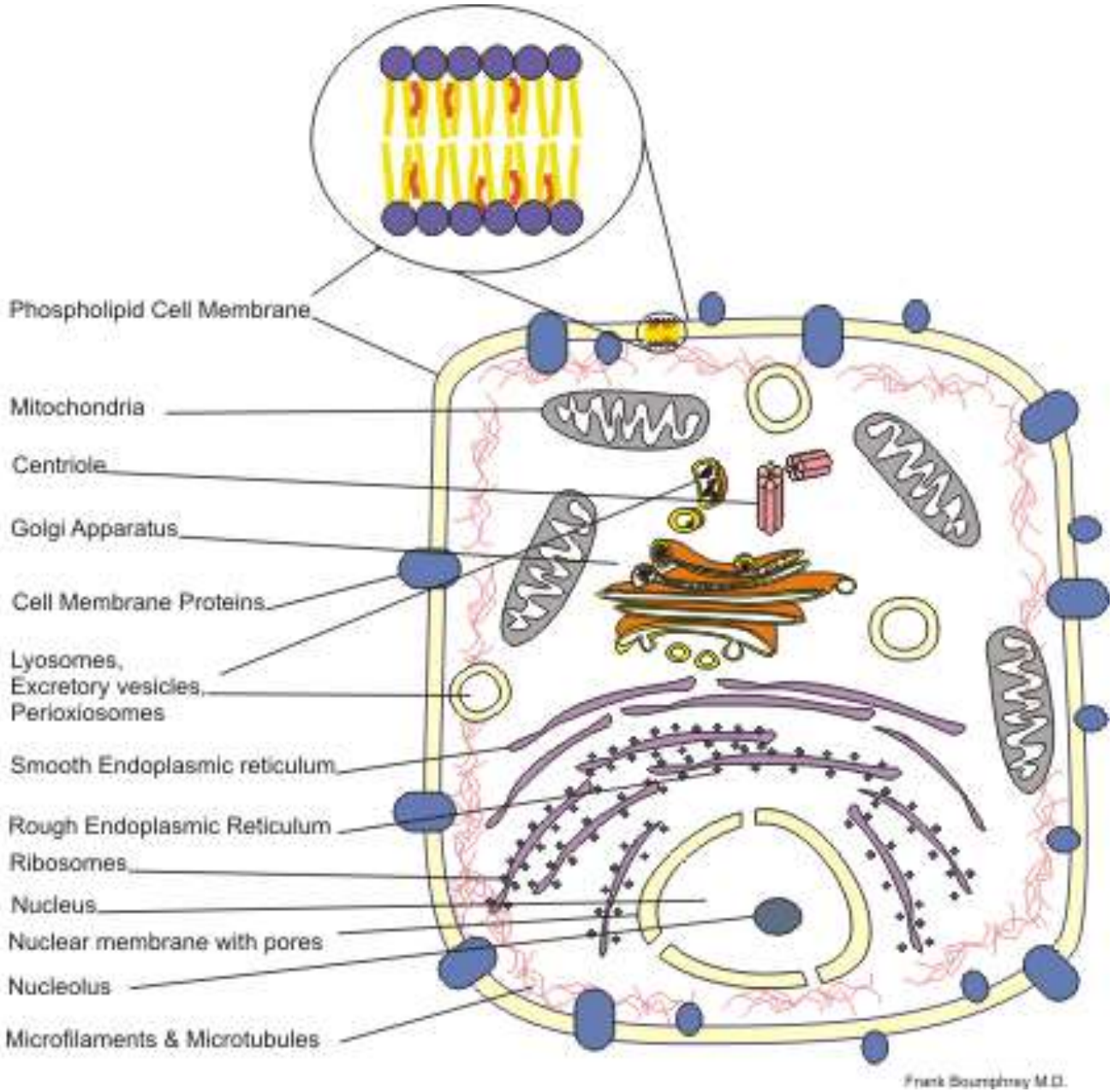
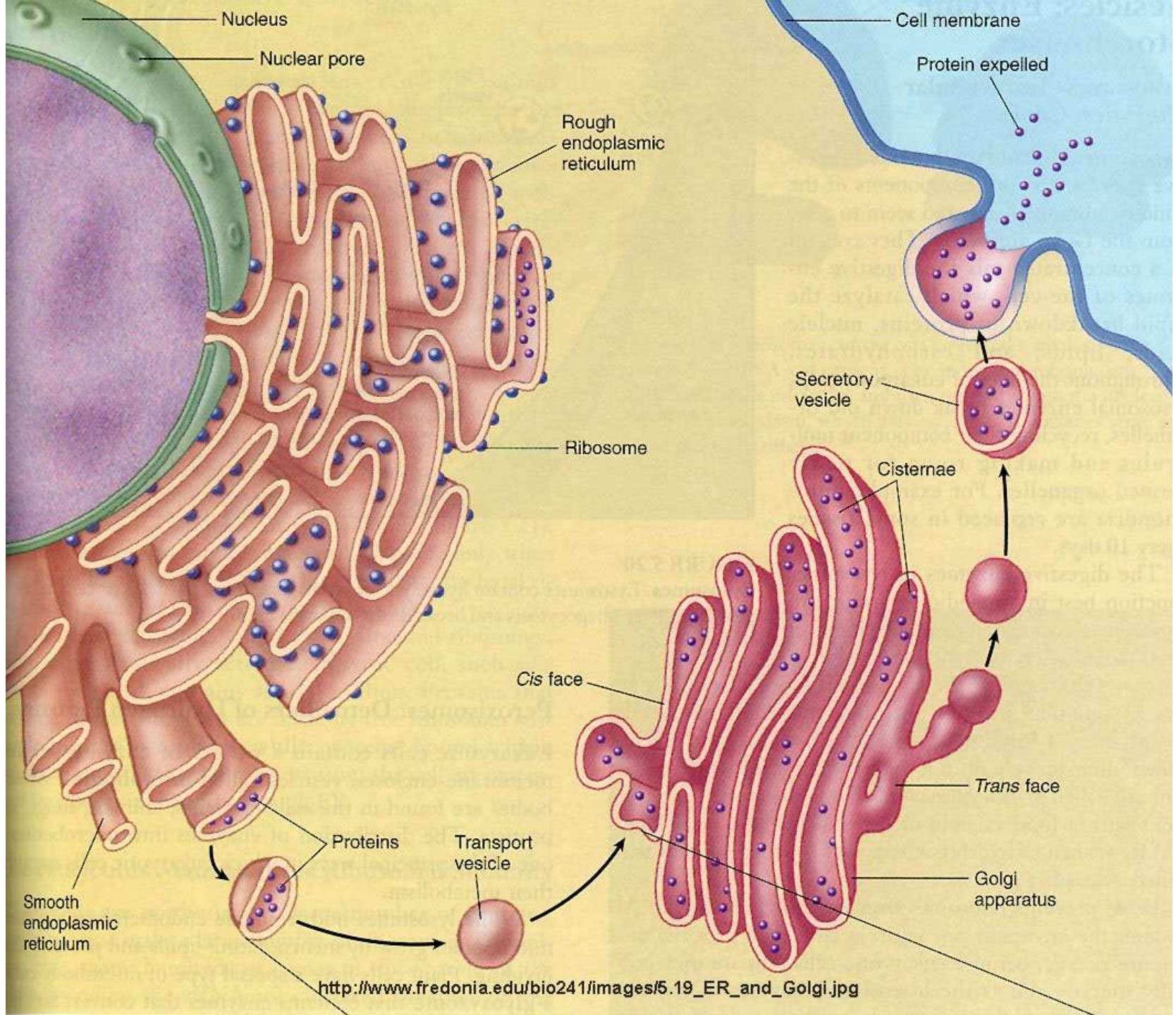


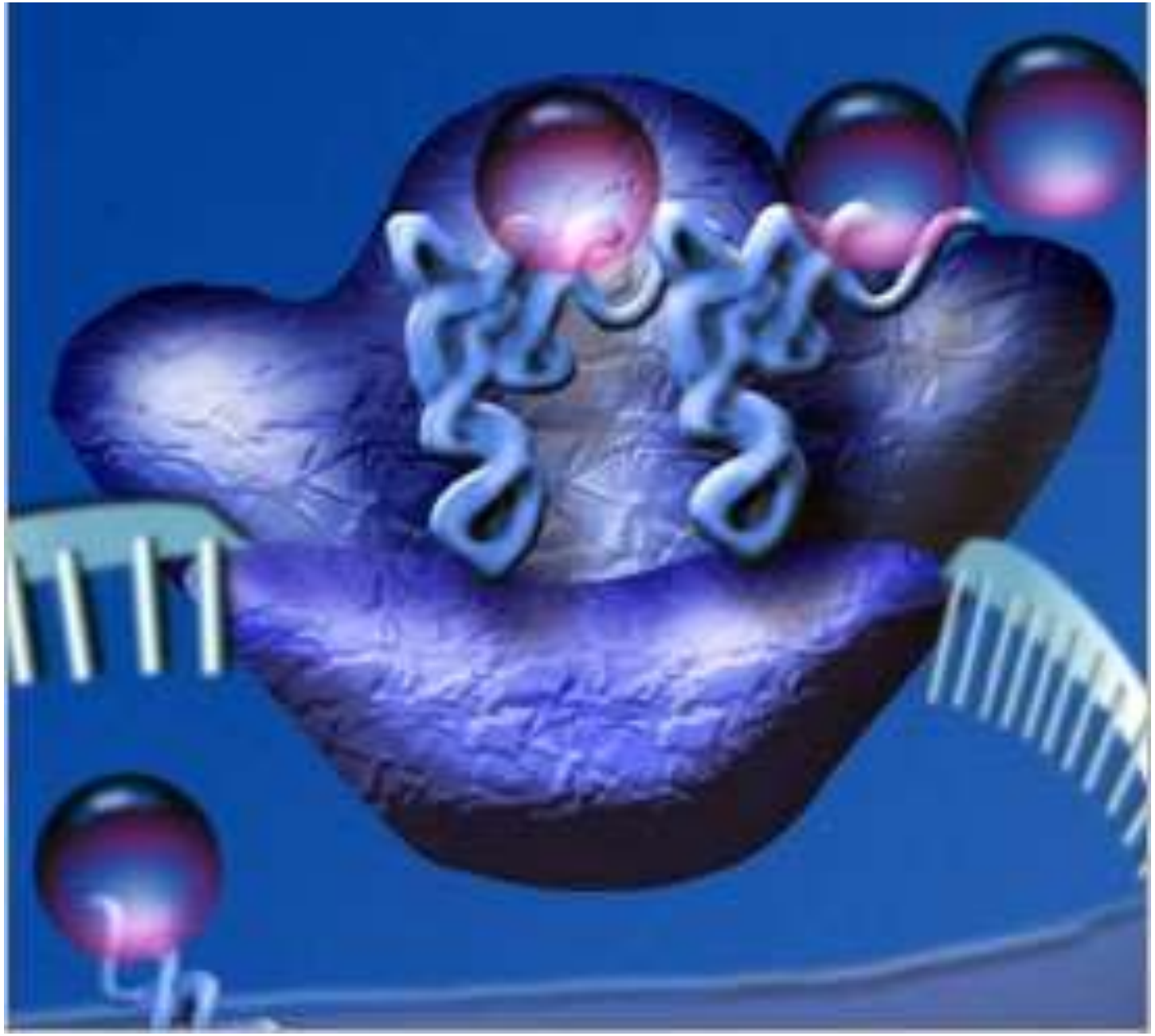
Figure 2-16

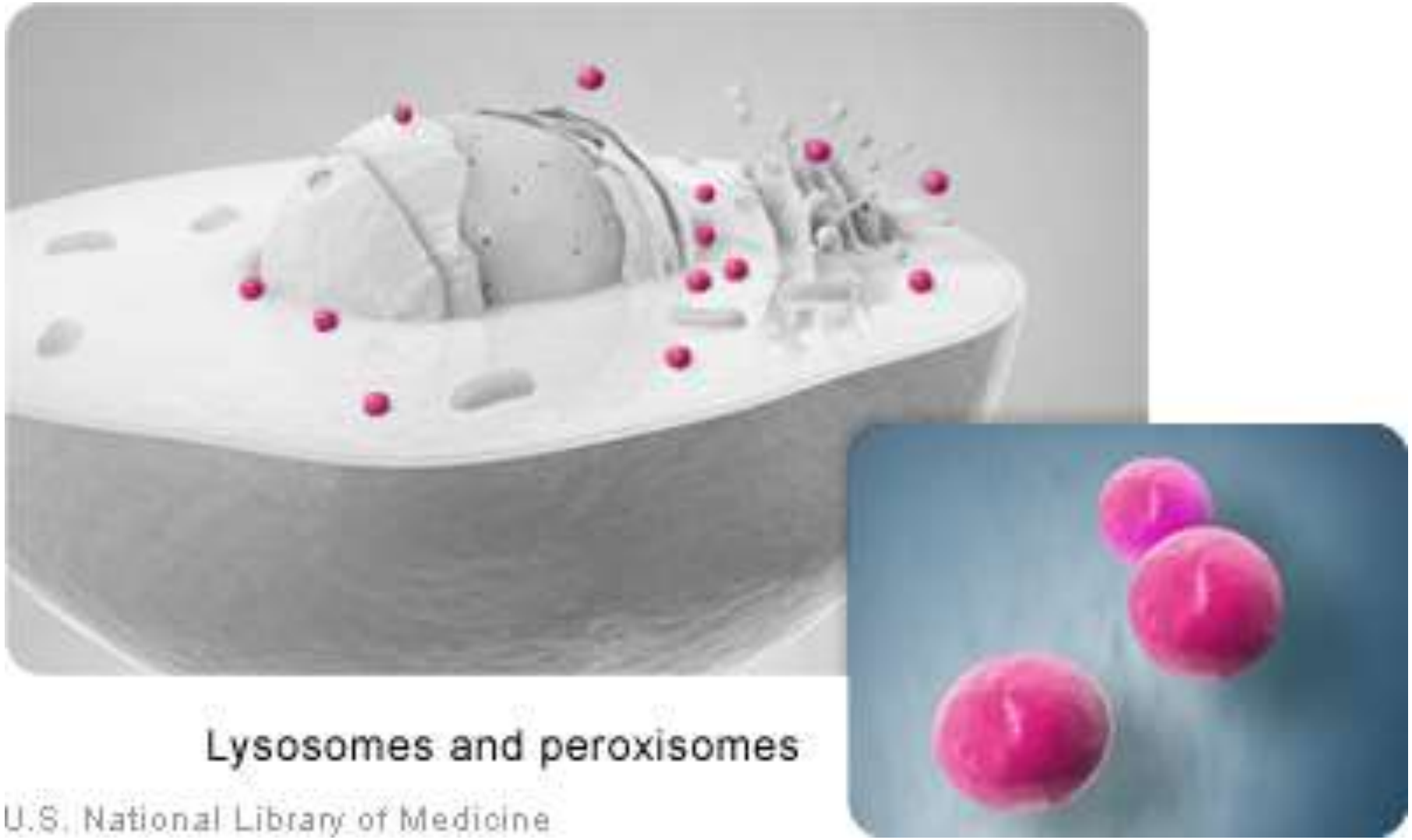
Cell movement is influenced by chemical substances…




Phospholipid Cell Membrane
Mitochondria
Centriole
Golgi Apparatus
Cell Membrane Proteins
Lyosomes,
Excretory vesicles,
Perioxiosomes
Smooth Endoplasmic reticulum
Rough Endoplasmic Reticulum
Ribosomes
Nucleus
Nuclear membrane with pores
Nucleolus
Microfilaments & Microtubules
Frank Boumphrey M.D.

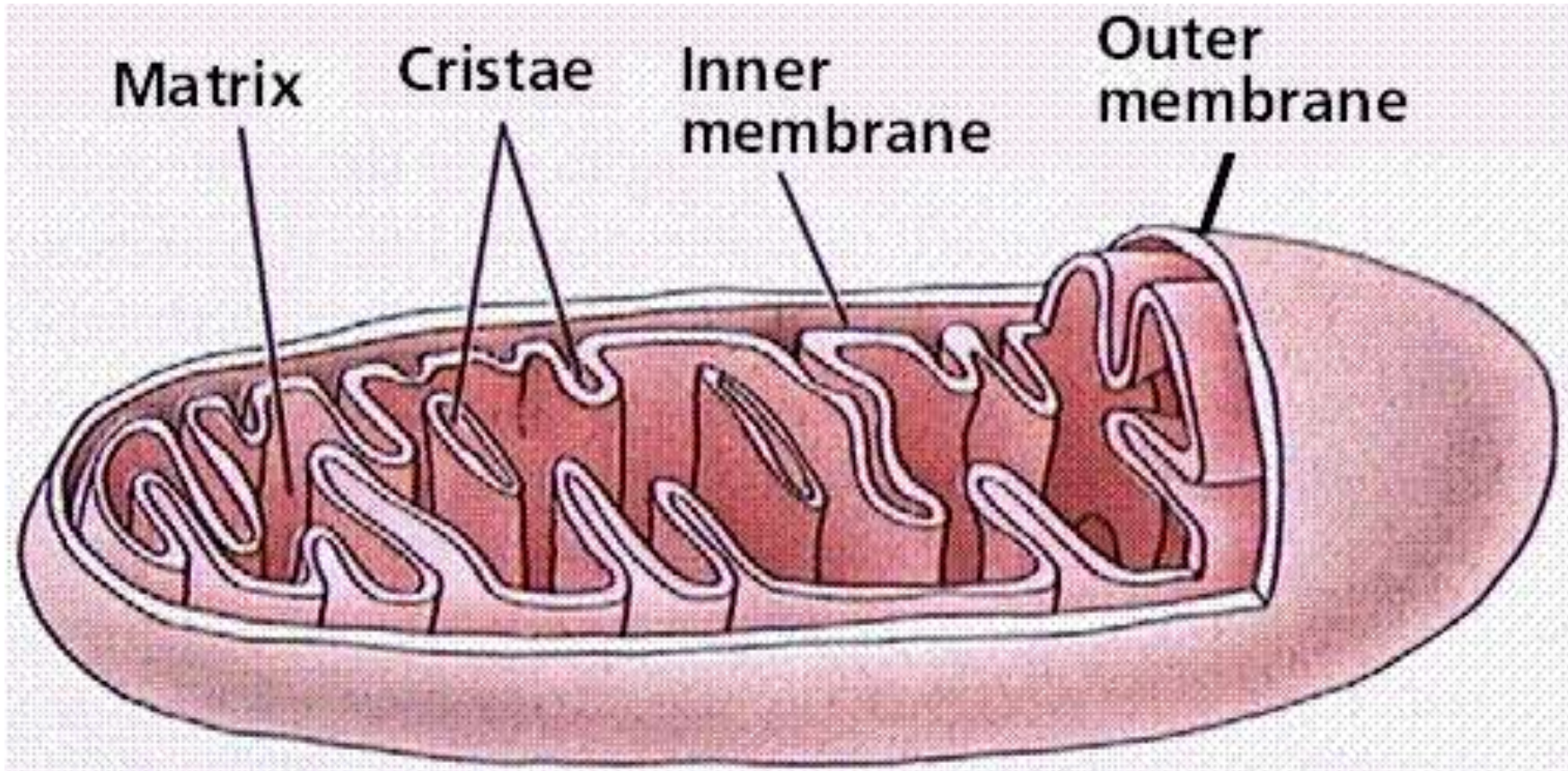

Nucleus
Nuclear pore
Rough endoplasmic reticulum
Ribosome
Cell membrane
Protein expelled
Secretory vesicle
Cisternae
Cis face
Trans face
Golgi apparatus
Proteins
Transport vesicle
Smooth endoplasmic reticulum
http://www.fredonia.edu/bio241/images/5.19_ER_and_Golgi.jpg

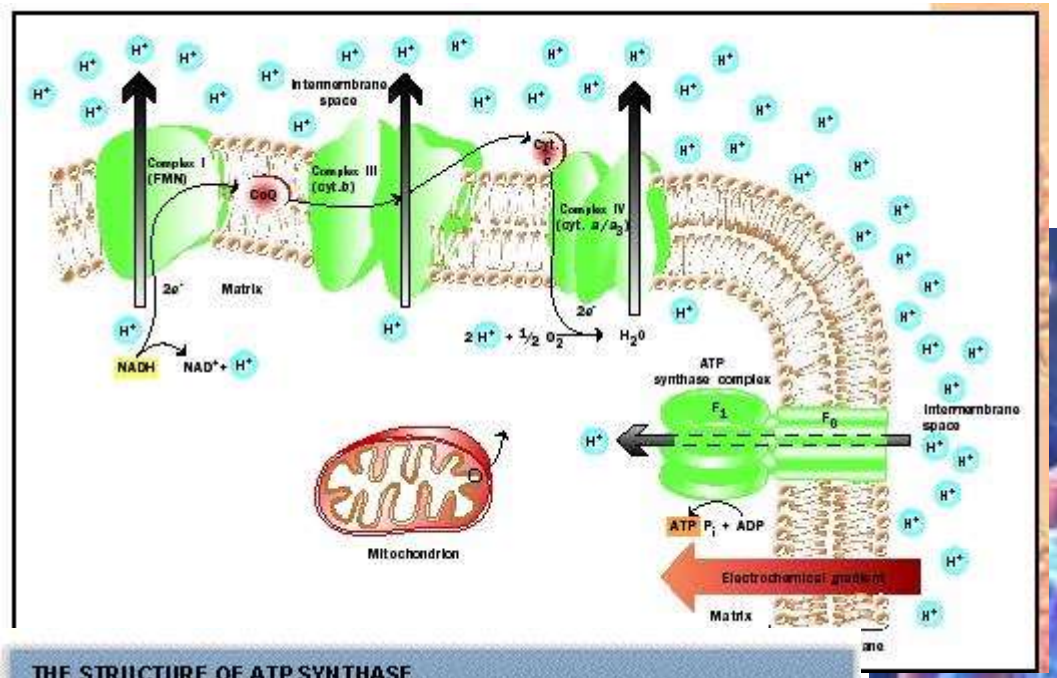


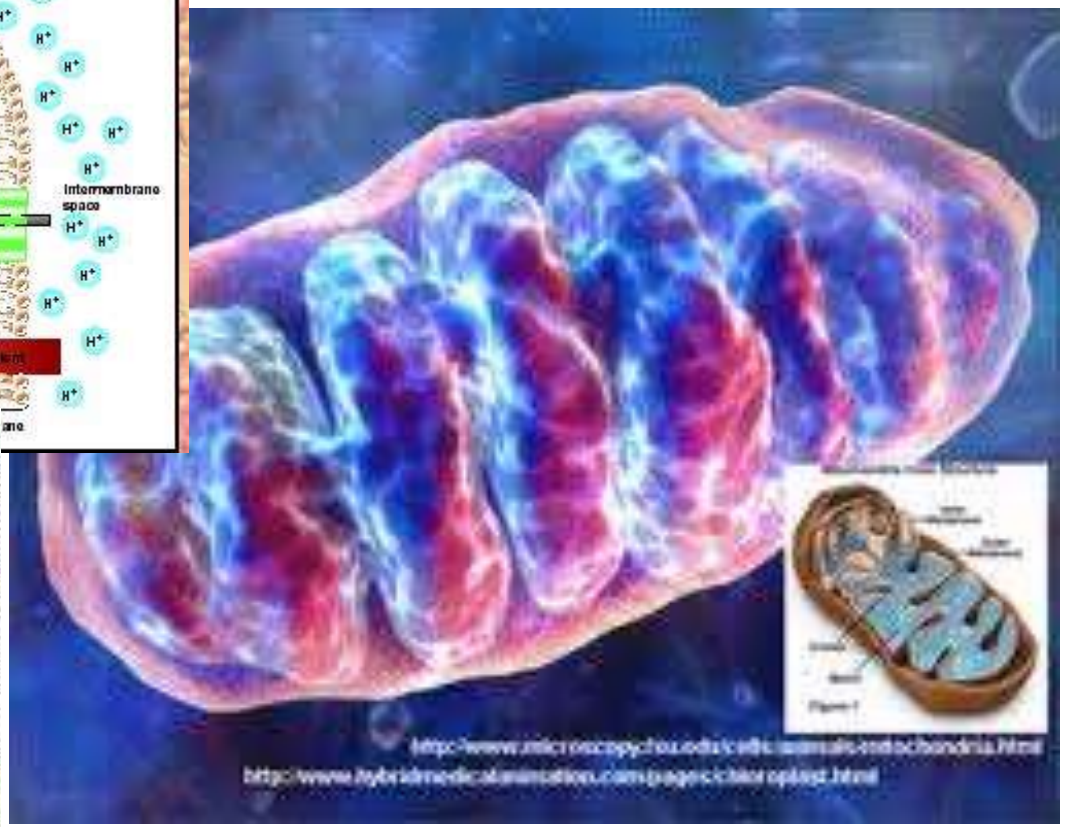


Lysosomes and peroxisomes

U.S. National Library of Medicine


Matrix
Cristae
Inner membrane
Outer membrane


Intermembrane space
Complex I (FMN)
CoQ
Complex III (cyt.b)
Cyt. c
Complex IV (cyt. a/a3)
2e⁻
Matrix
2e⁻
2 H⁺ + ½ O2
H2O
NADH
NAD⁺ + H⁺
ATP synthase complex
F1
F0
Intermembrane space
ATP
Pi + ADP
Mitochondrion
Electrochemical gradient
Matrix



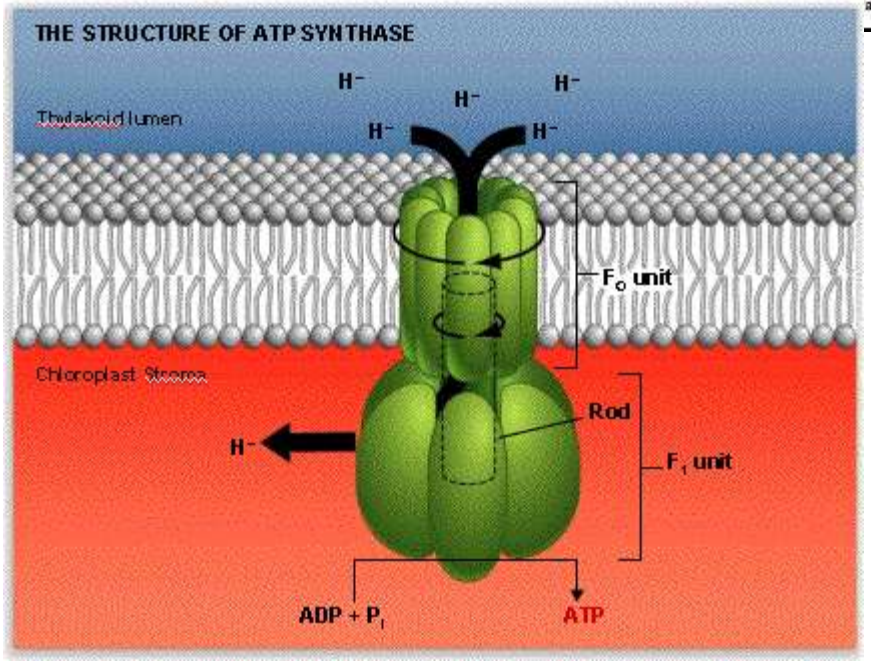
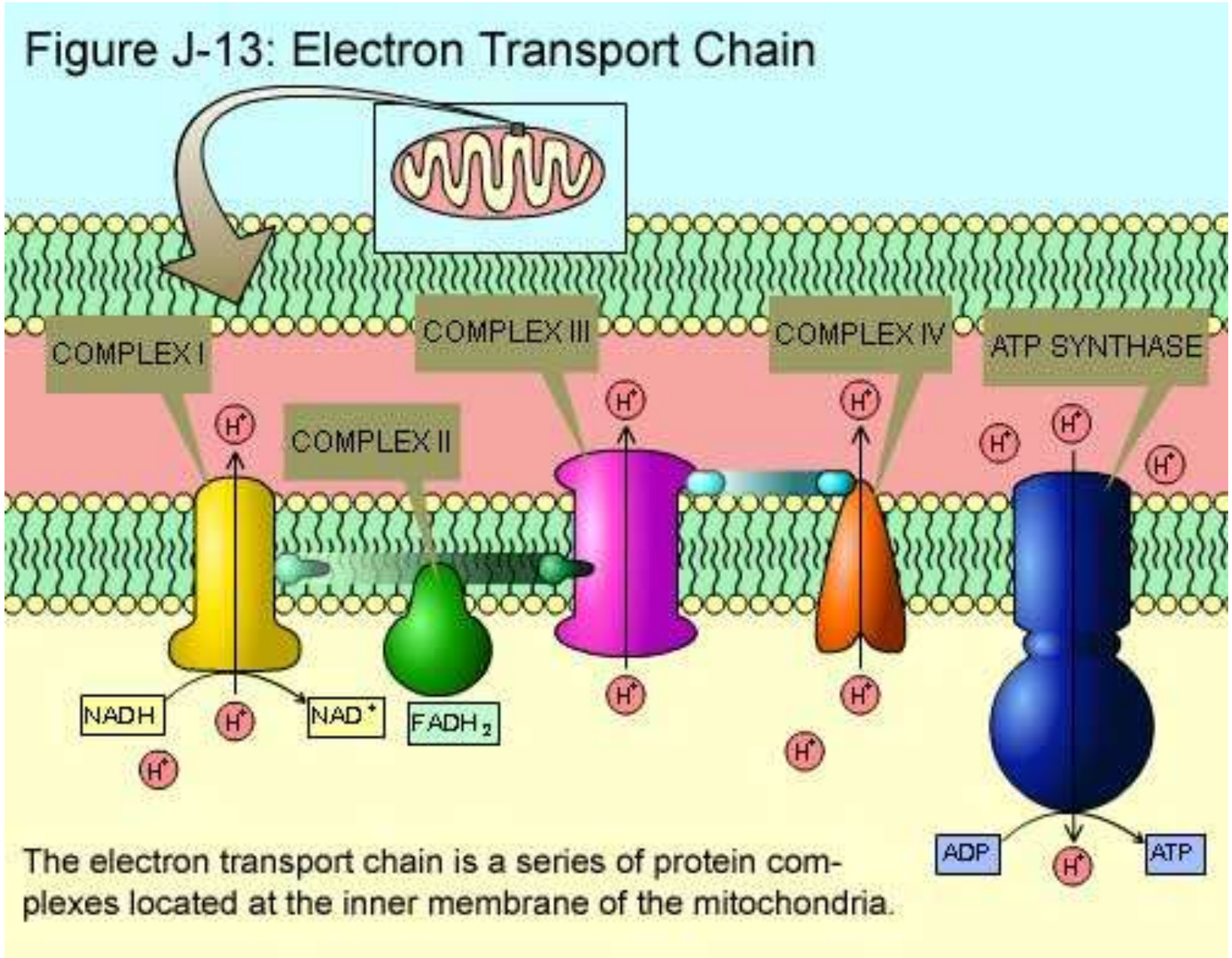
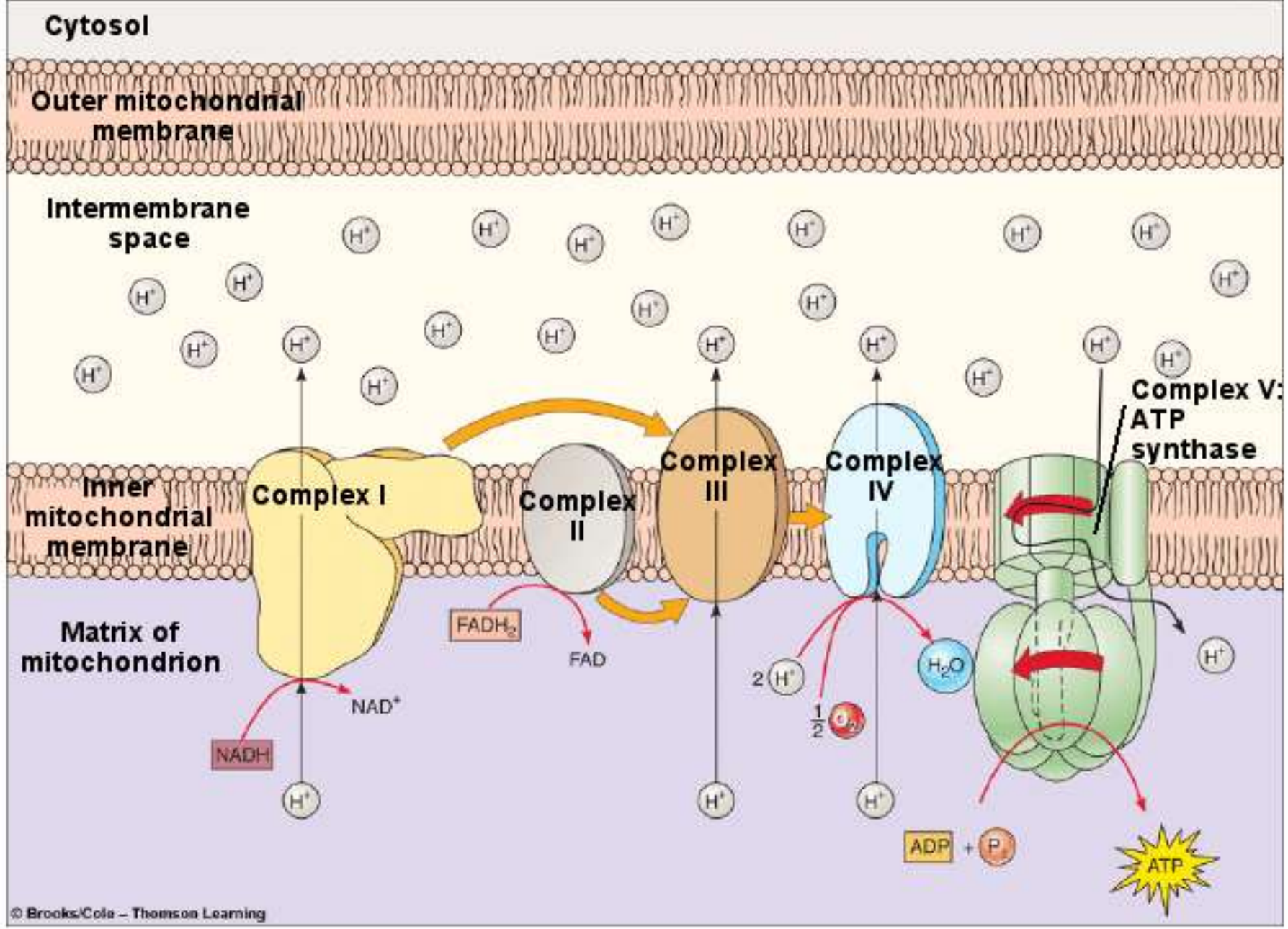

THE STRUCTURE OF ATP SYNTHASE
Thylakoid lumen
H⁻
Fo unit
Chloroplast Stroma
Rod
F1 unit
ADP + P1
ATP

Figure J-13: Electron Transport Chain

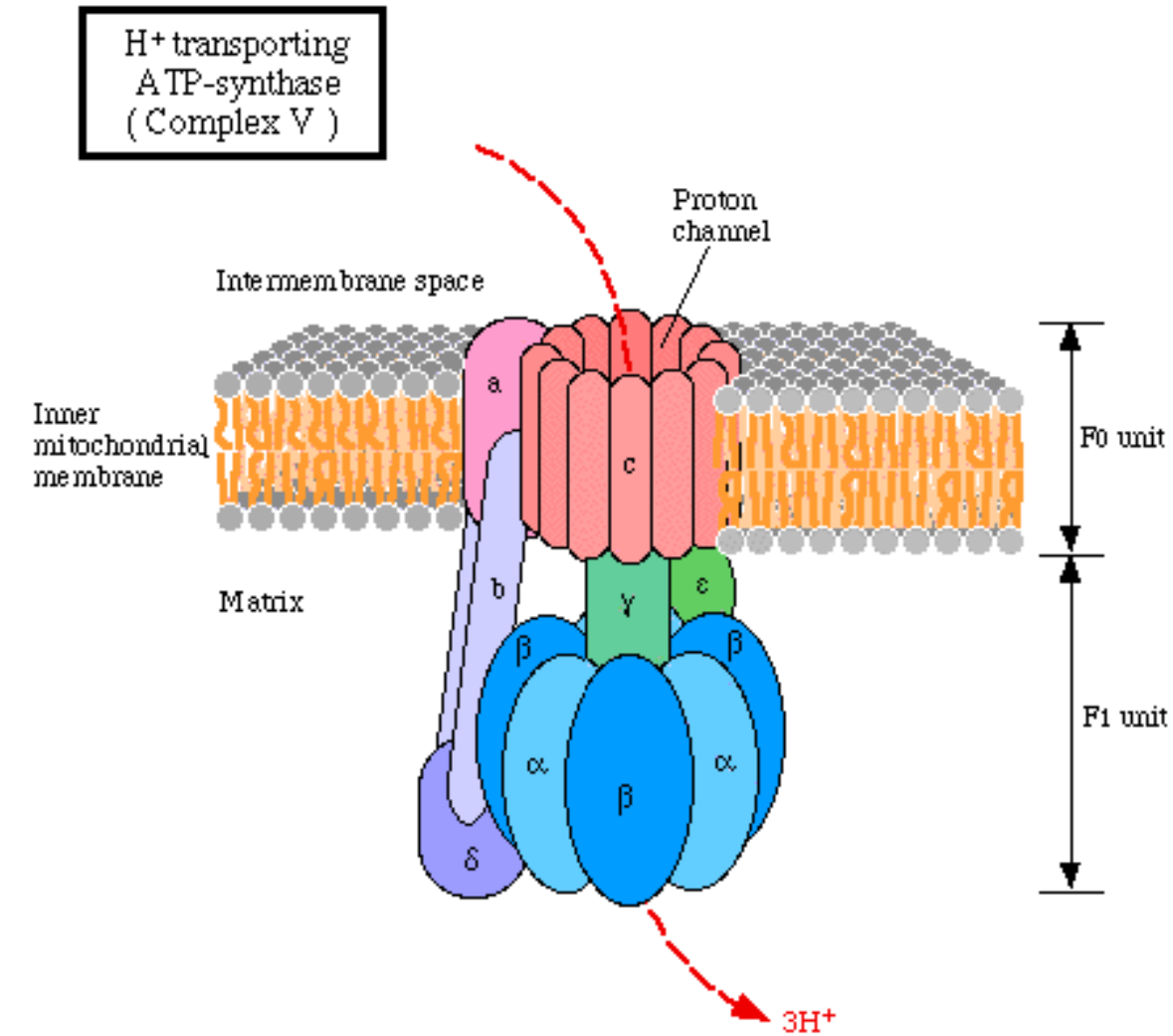


The electron transport chain is a series of protein complexes located at the inner membrane of the mitochondria.

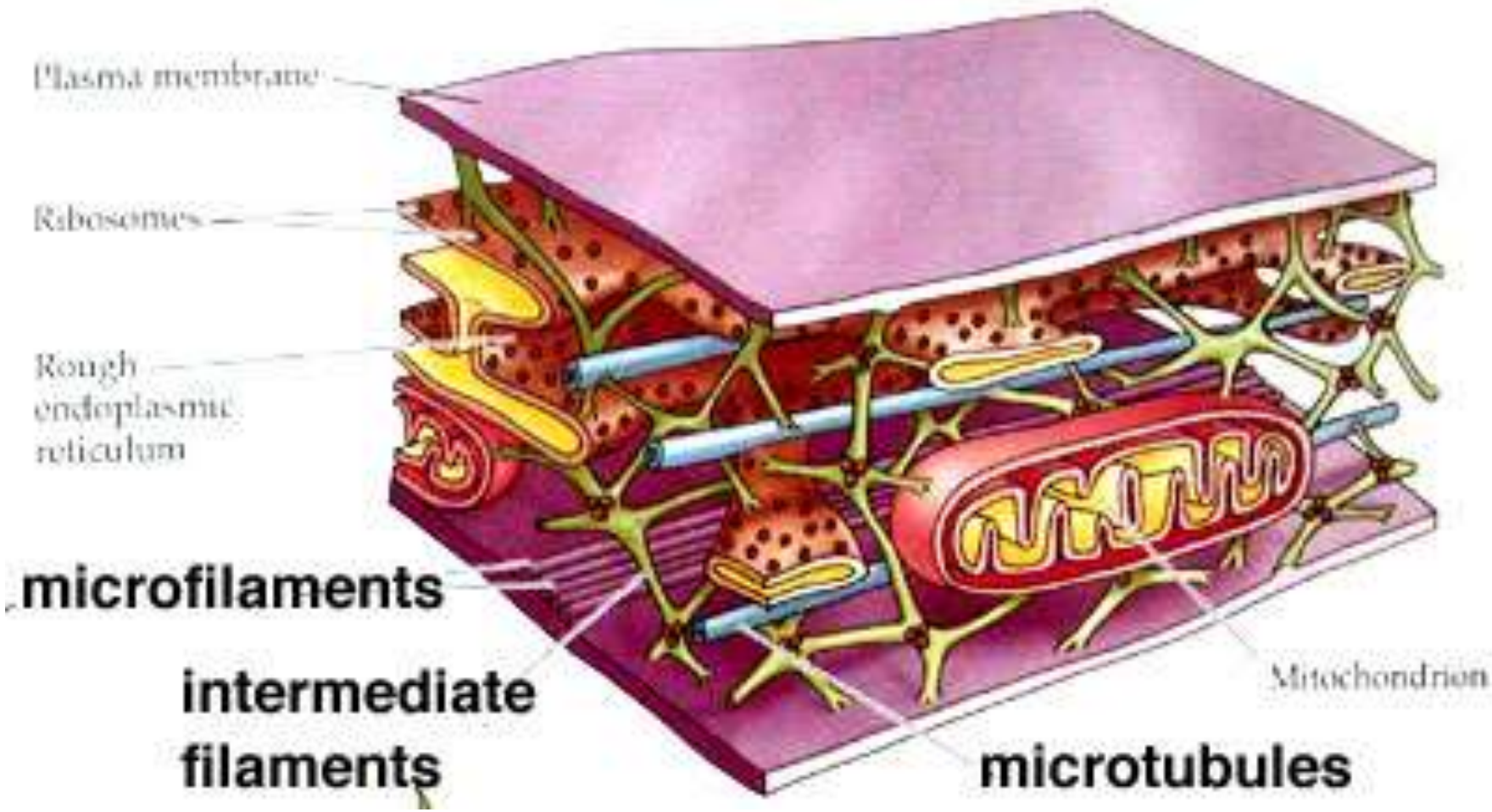


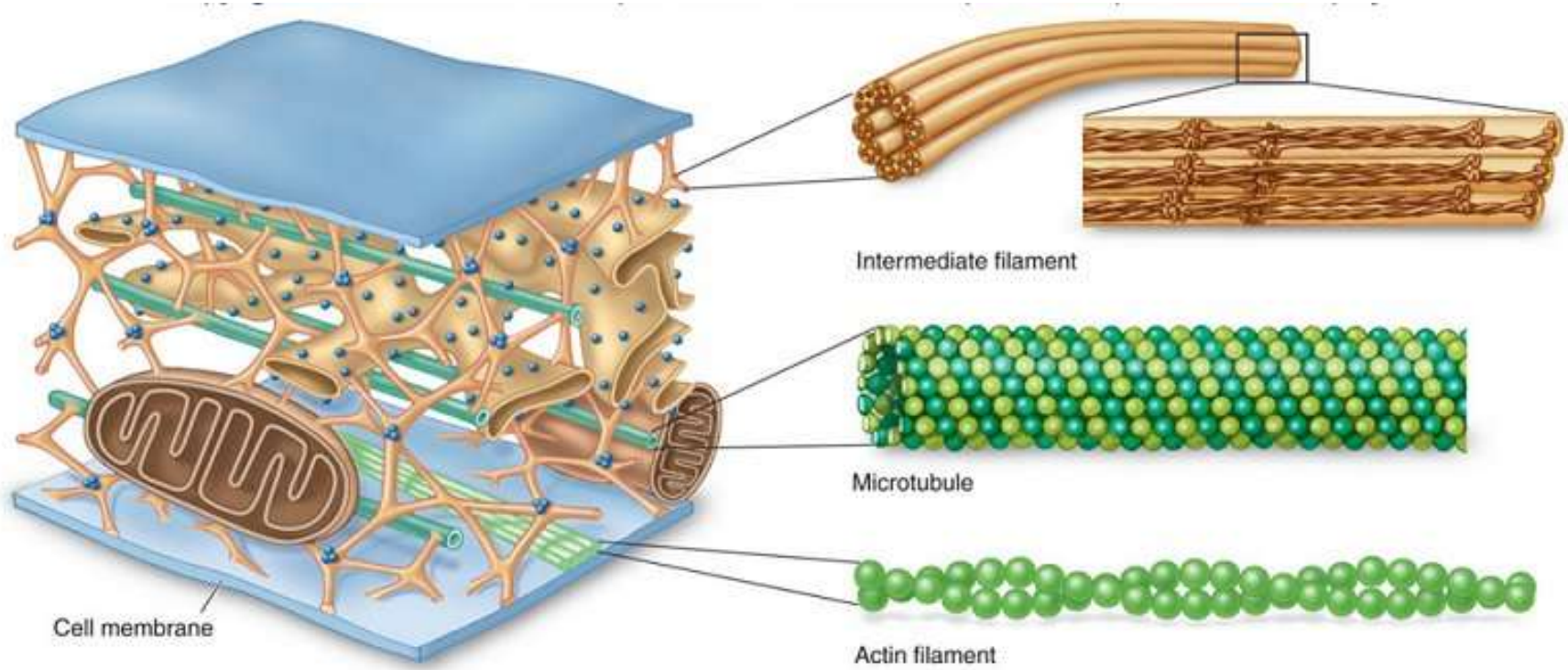
(a)

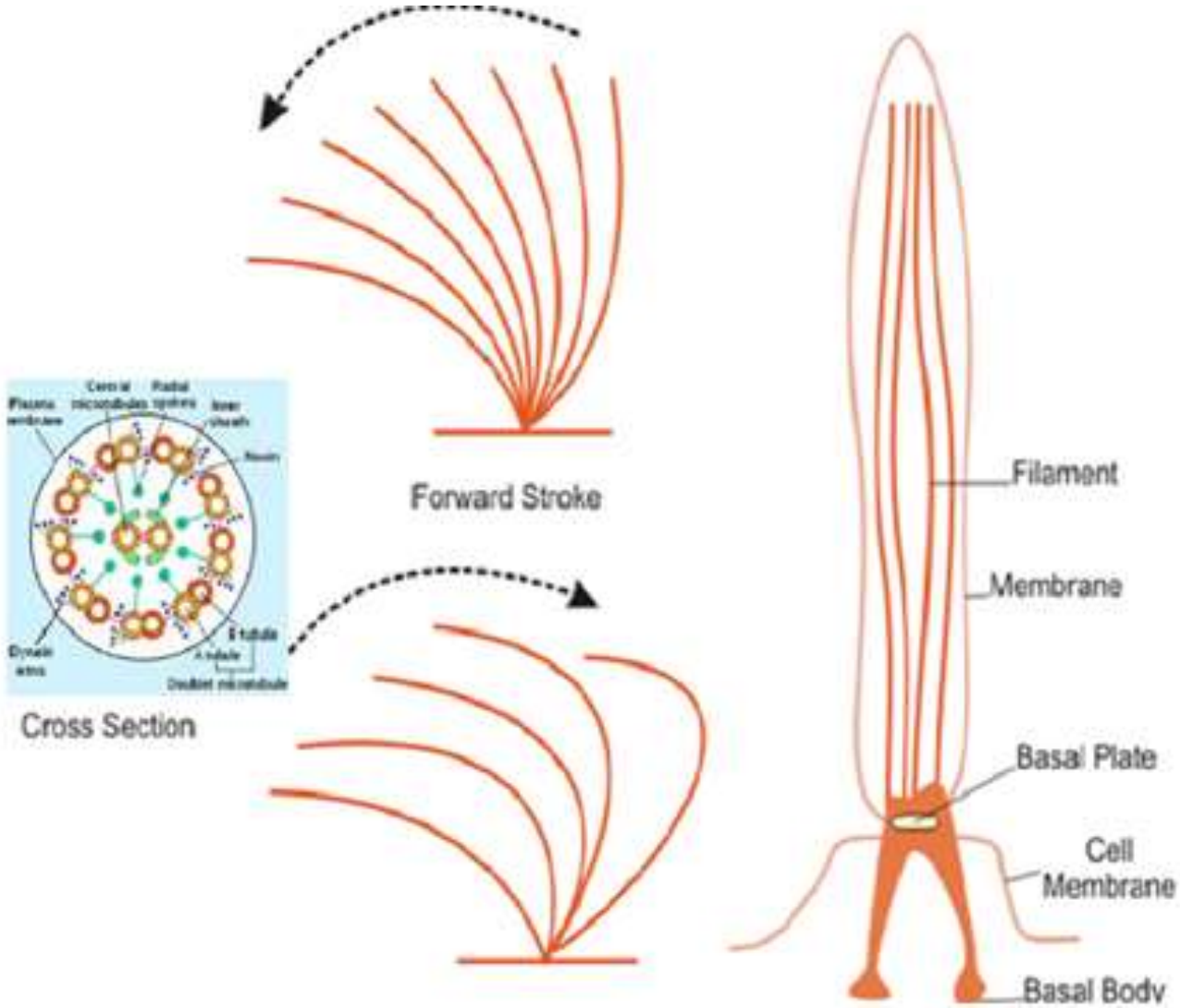
Fig. 7-10a(2)
Page 149

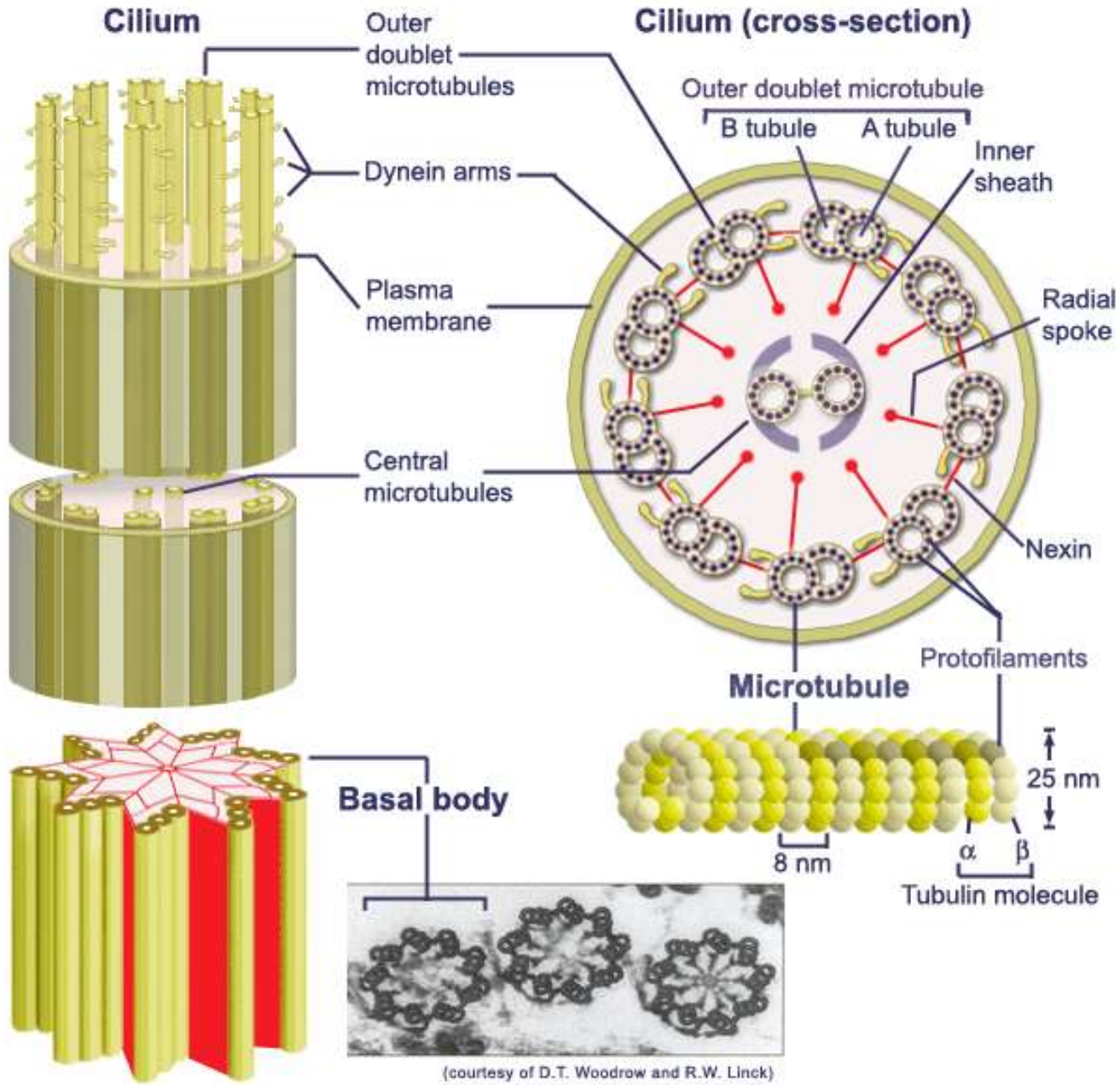

H+ transporting
ATP-synthase
(Complex V)
Proton
channel
Intermembrane space
Inner
mitochondrial
membrane
Matrix
a
c
b
γ
ε
β
β
α
β
α
δ
F0 unit
F1 unit
3H+
03110 5/26/99

Cytoskeletal Structures

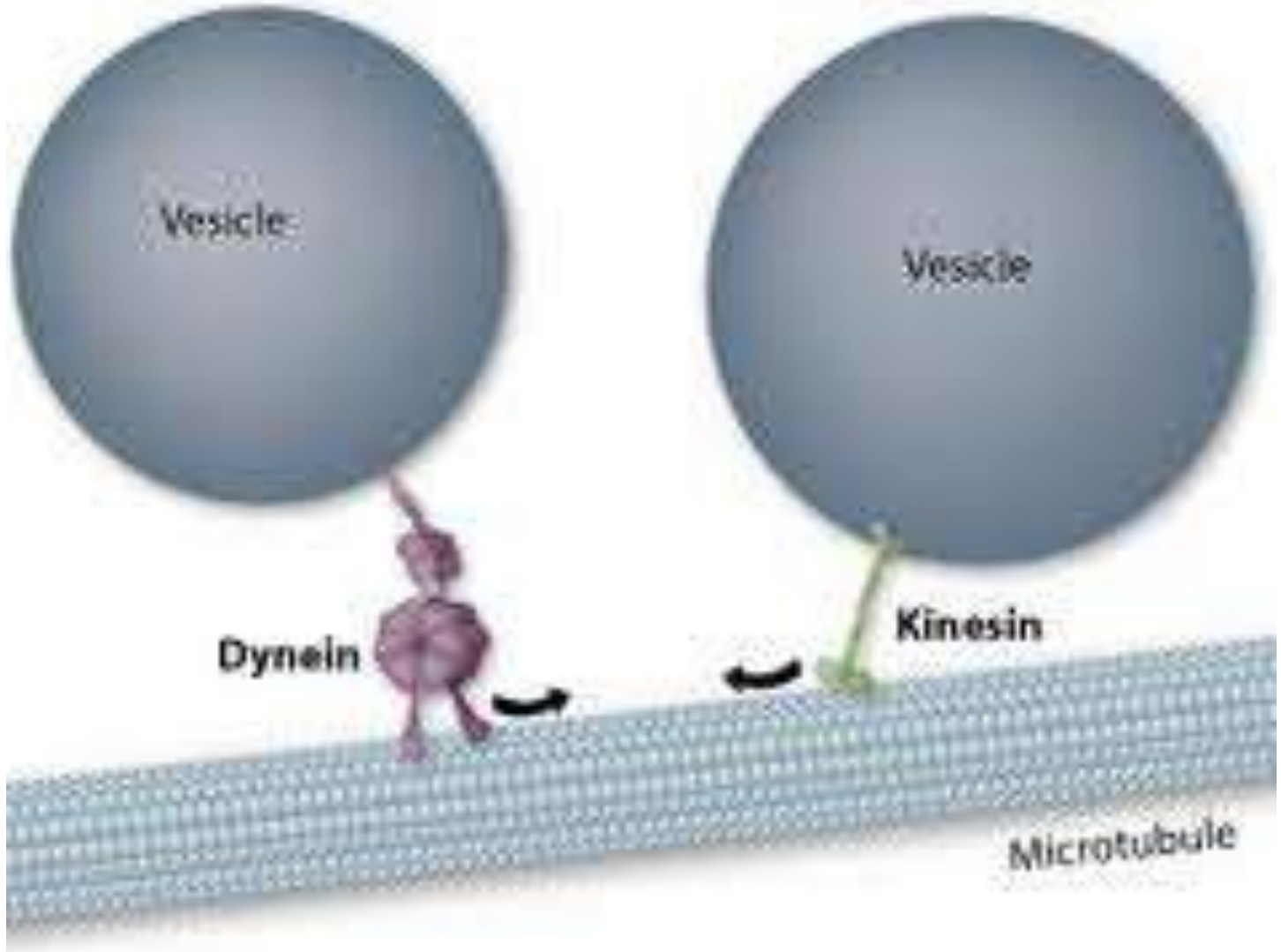

Plasma membrane
Ribosomes
Rough endoplasmic reticulum
microfilaments
intermediate filaments
Mitochondrion
microtubules

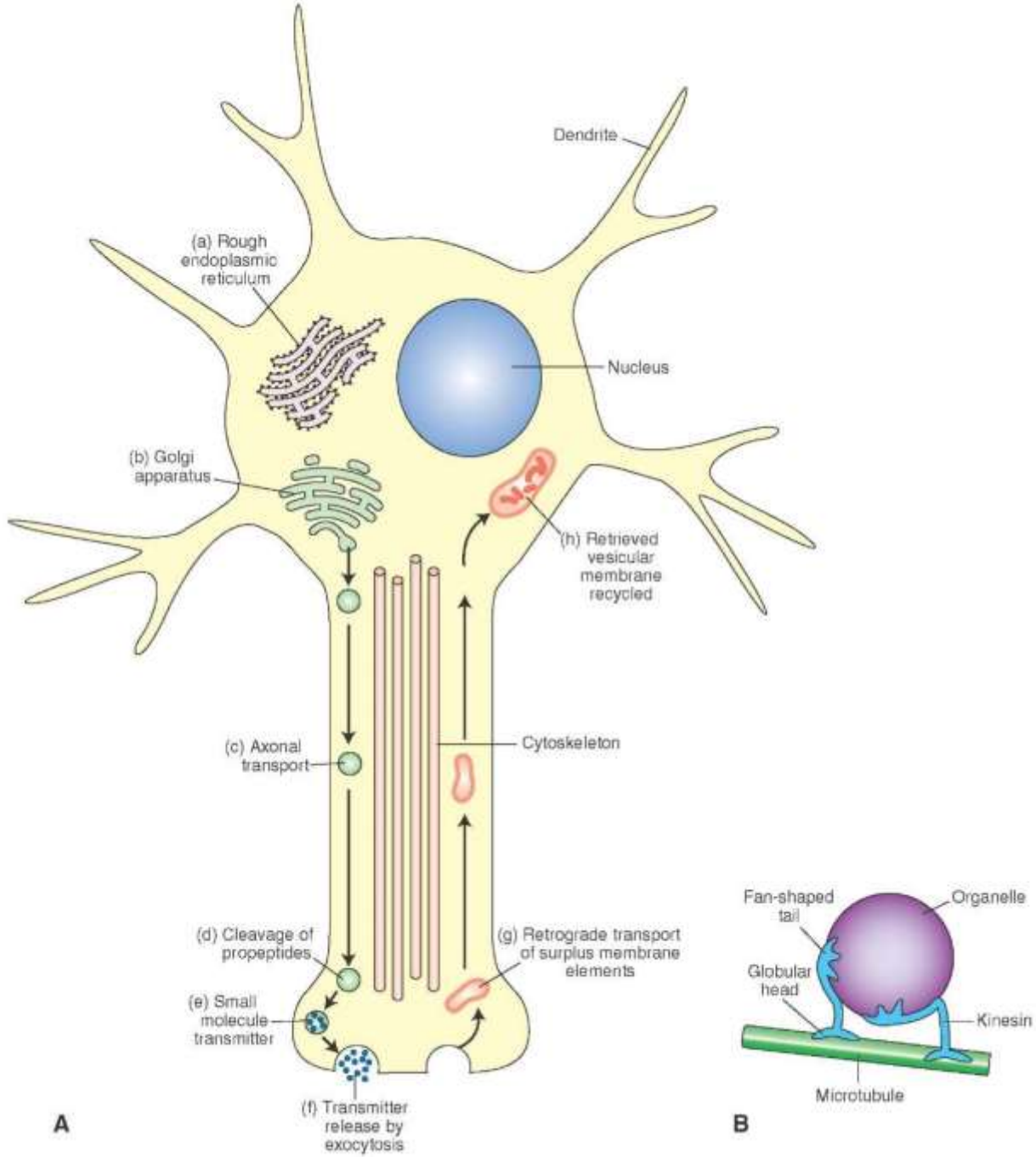

Intermediate filament
Microtubule
Actin filament
Cell membrane

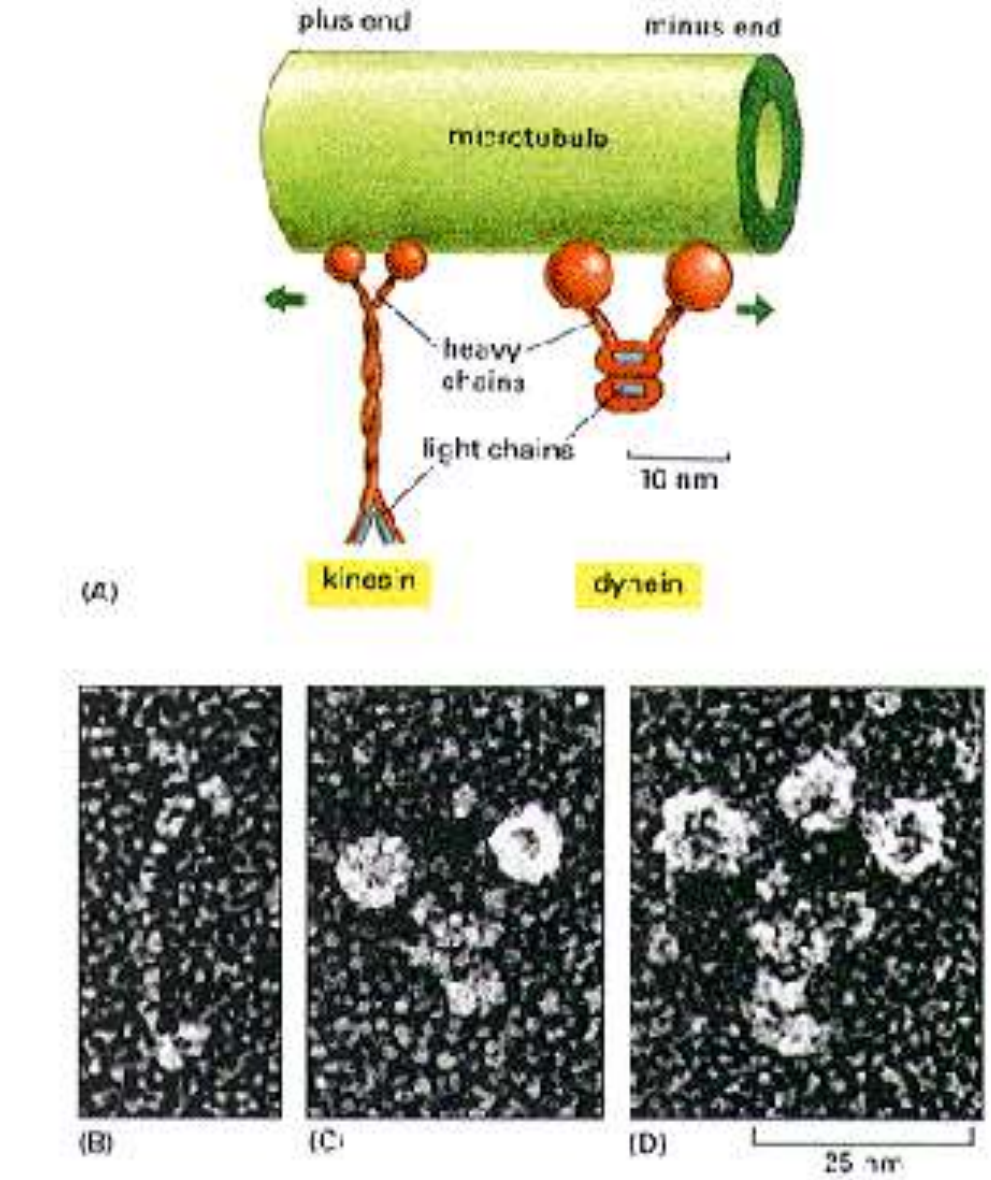

Forward Stroke
Cross Section
Filament
Membrane
Basal Plate
Cell
Membrane
Basal Body


Cilium
Outer doublet microtubules
Dynein arms
Plasma membrane
Central microtubules
Basal body
Cilium (cross-section)
Outer doublet microtubule
B tubule
A tubule
Inner sheath
Radial spoke
Nexin
Protofilaments
Microtubule
25 nm
8 nm
α
β
Tubulin molecule
(courtesy of D.T. Woodrow and R.W. Linck)

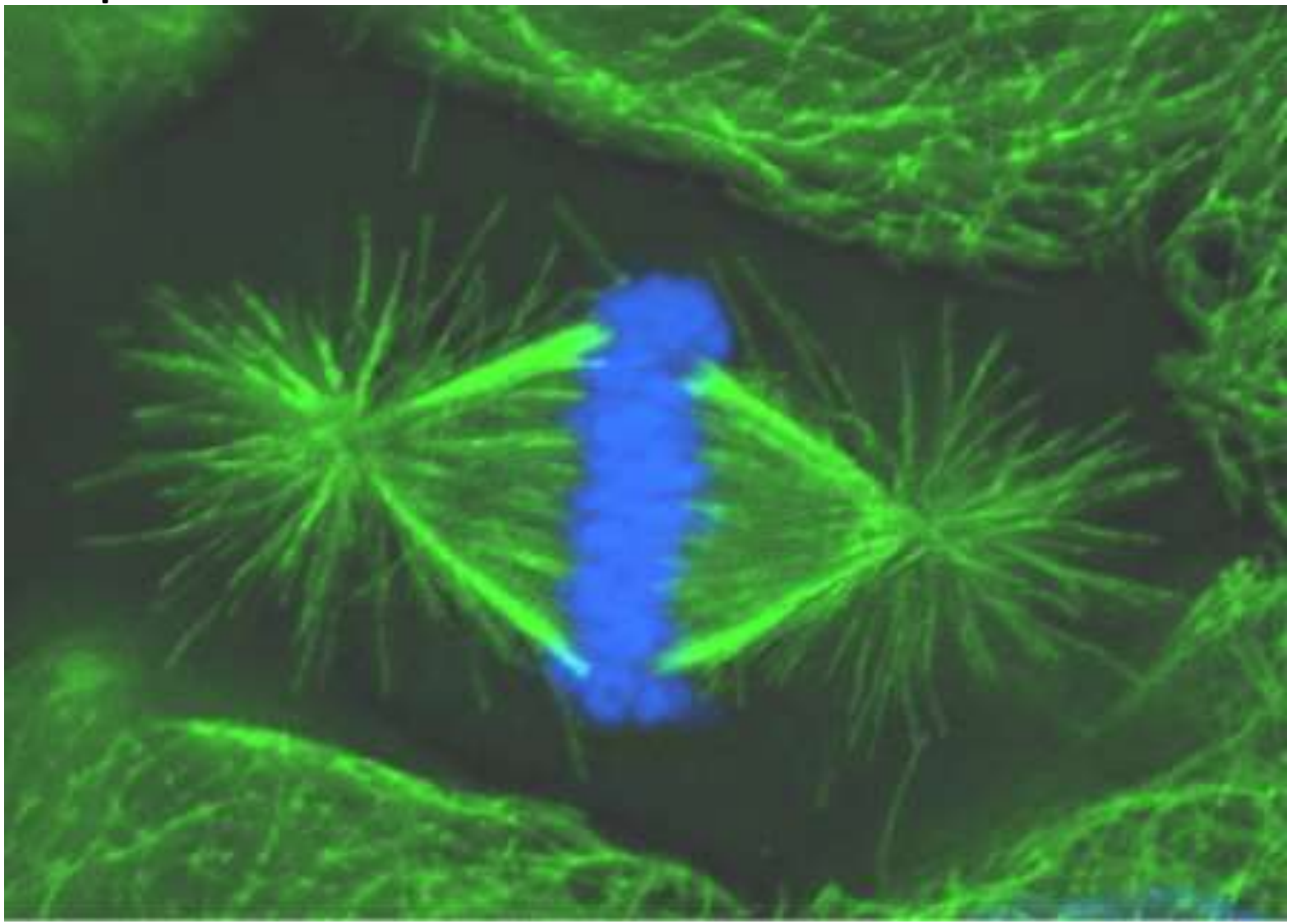
Vesicles Travel Cellular Highways



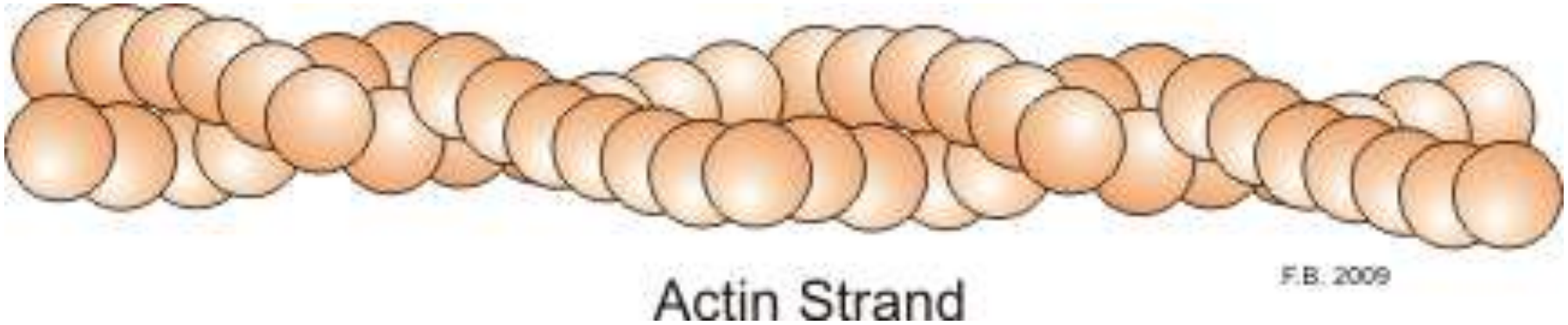

Dendrite
(a) Rough endoplasmic reticulum
Nucleus
(b) Golgi apparatus
(h) Retrieved vesicular membrane recycled
(c) Axonal transport
Cytoskeleton
(d) Cleavage of propeptides
(g) Retrograde transport of surplus membrane elements
(e) Small molecule transmitter
(f) Transmitter release by exocytosis
A
Fan-shaped tail
Organelle
Globular head
Kinesin
Microtubule
B

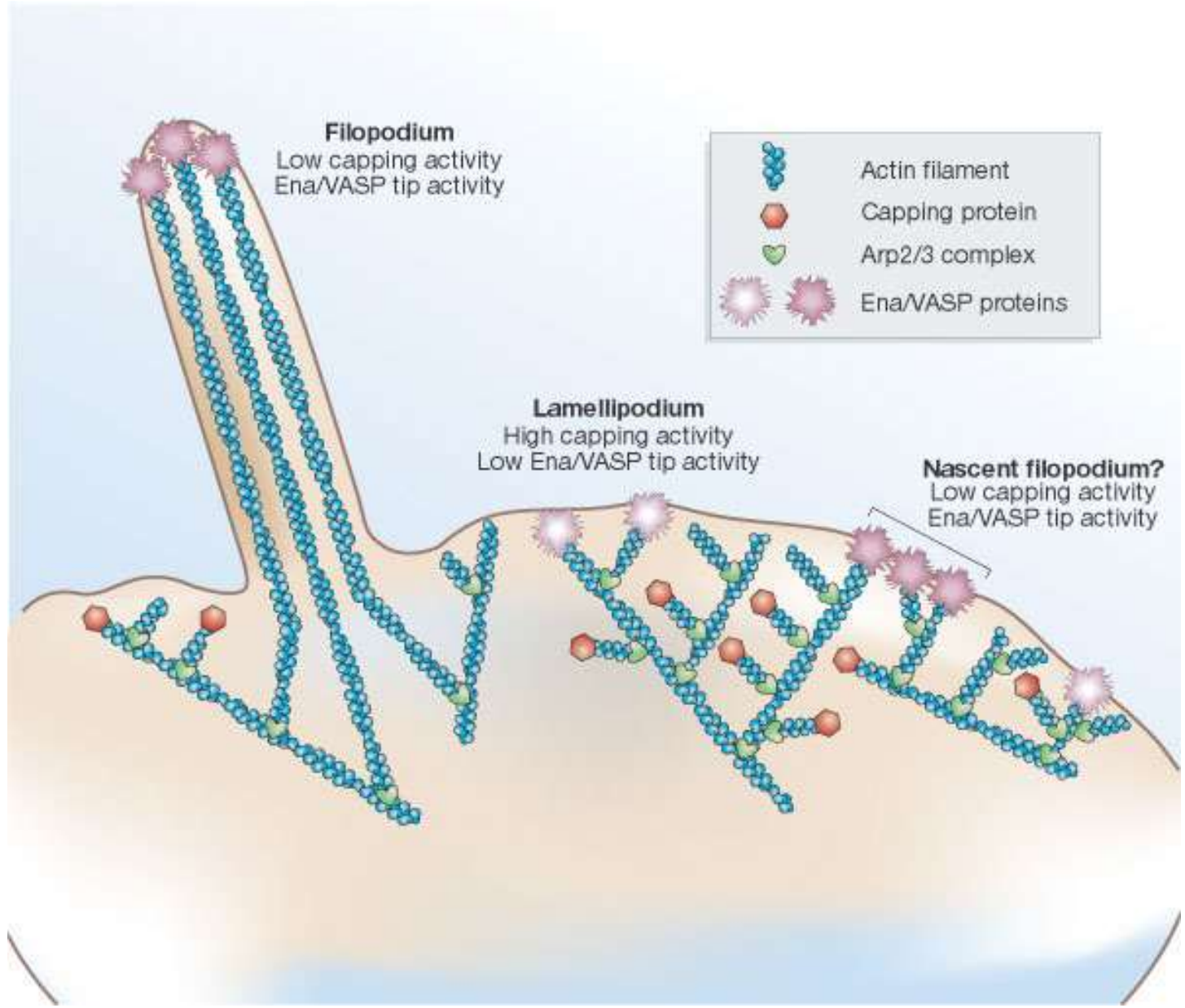

plus end
minus end
microtubule
heavy chains
light chains
10 nm
(A)
kinesin
dynein
(B)
(C)
(D)
25 nm

Mitotic spindle



Actin filaments



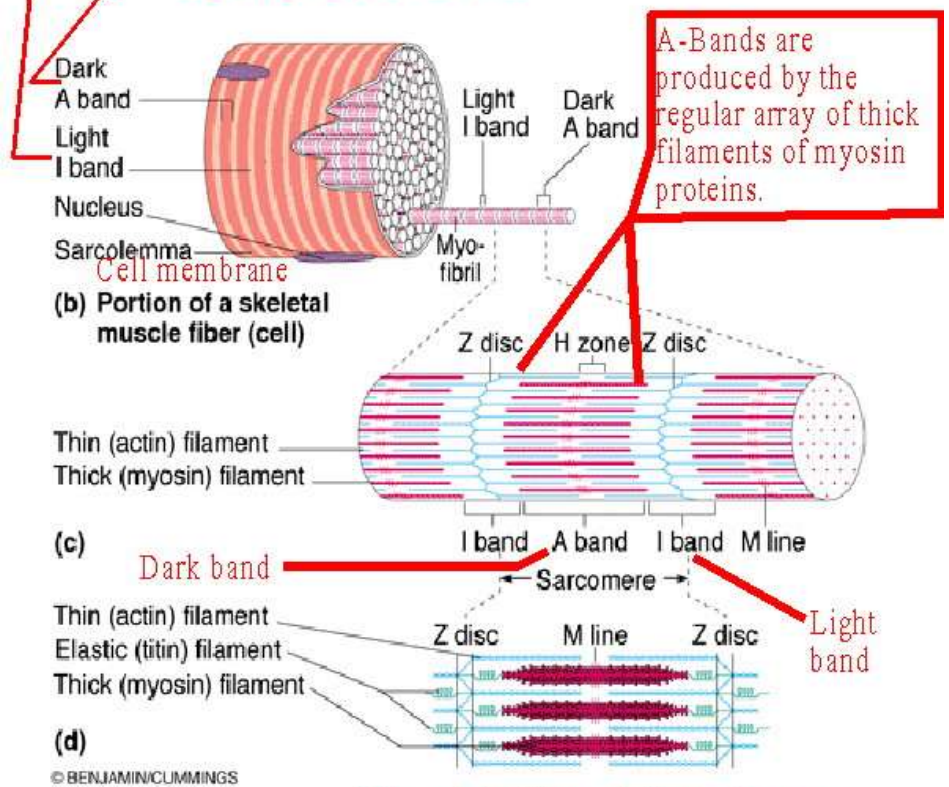

Filopodium
Low capping activity
Ena/VASP tip activity
Actin filament
Capping protein
Arp2/3 complex
Ena/VASP proteins
Lamellipodium
High capping activity
Low Ena/VASP tip activity
Nascent filopodium?
Low capping activity
Ena/VASP tip activity

Structural Elements of a Muscle Cell

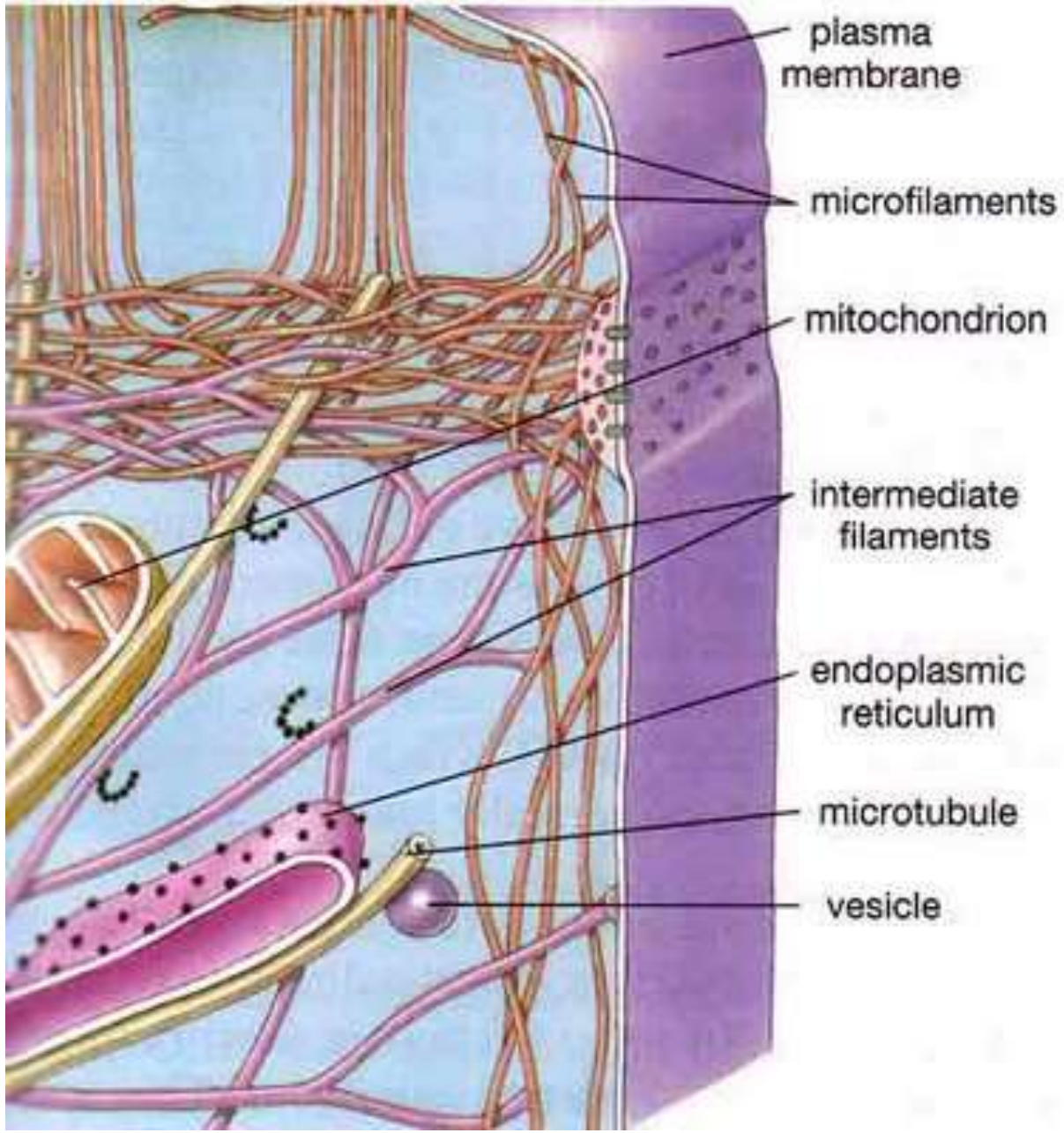
I Band - I stands for isotropic meaning the light passes through this area evenly. These are the light bands between the dark striations.

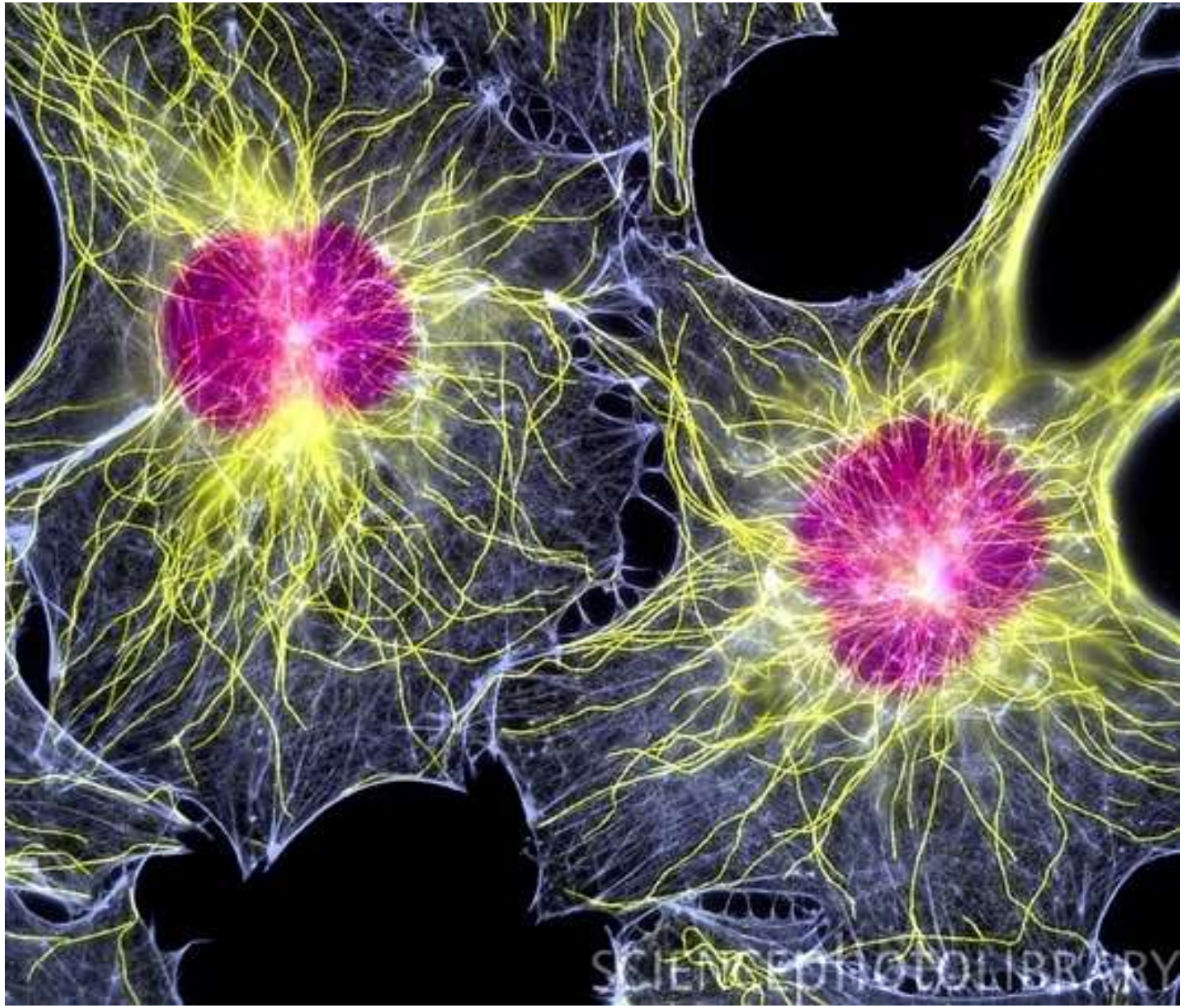
Striations = A Bands, for anisotropic (not isotropic) meaning the light does not pass evenly, it is refracted. These are the dark striations.

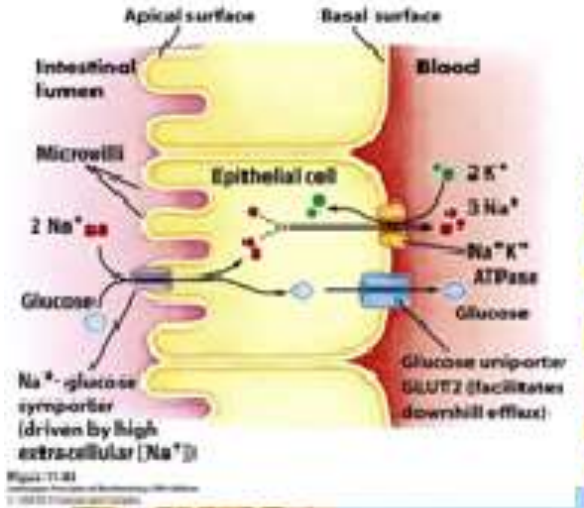
A-Bands are produced by the regular array of thick filaments of myosin proteins.

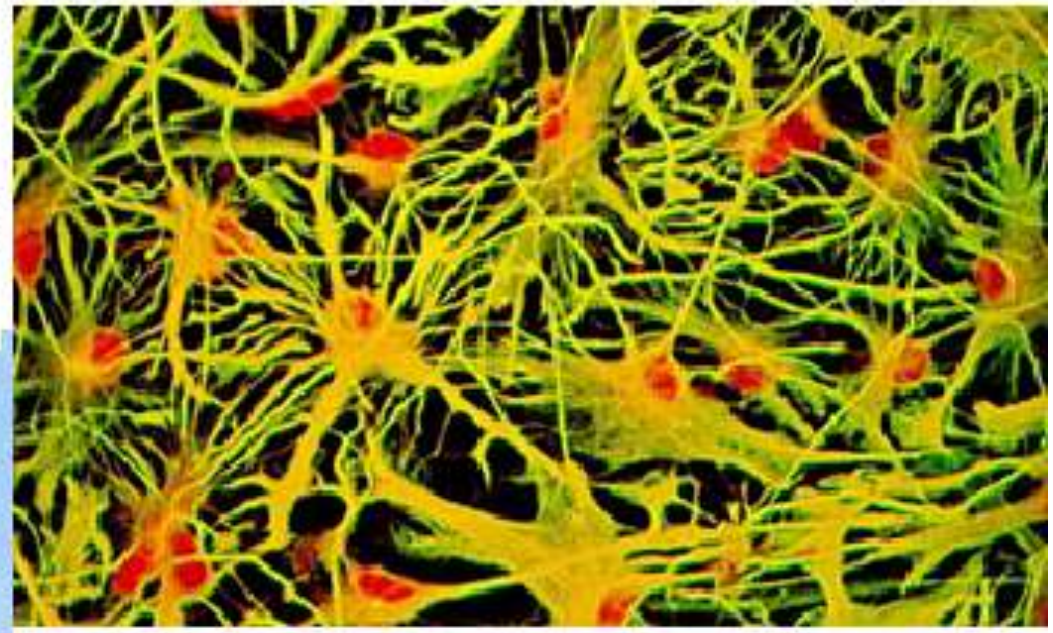


Although the filaments themselves run longitudinally along the myofibril, the A and I bands run perpendicularly to the myofibril, produced by the stacking of the filaments.

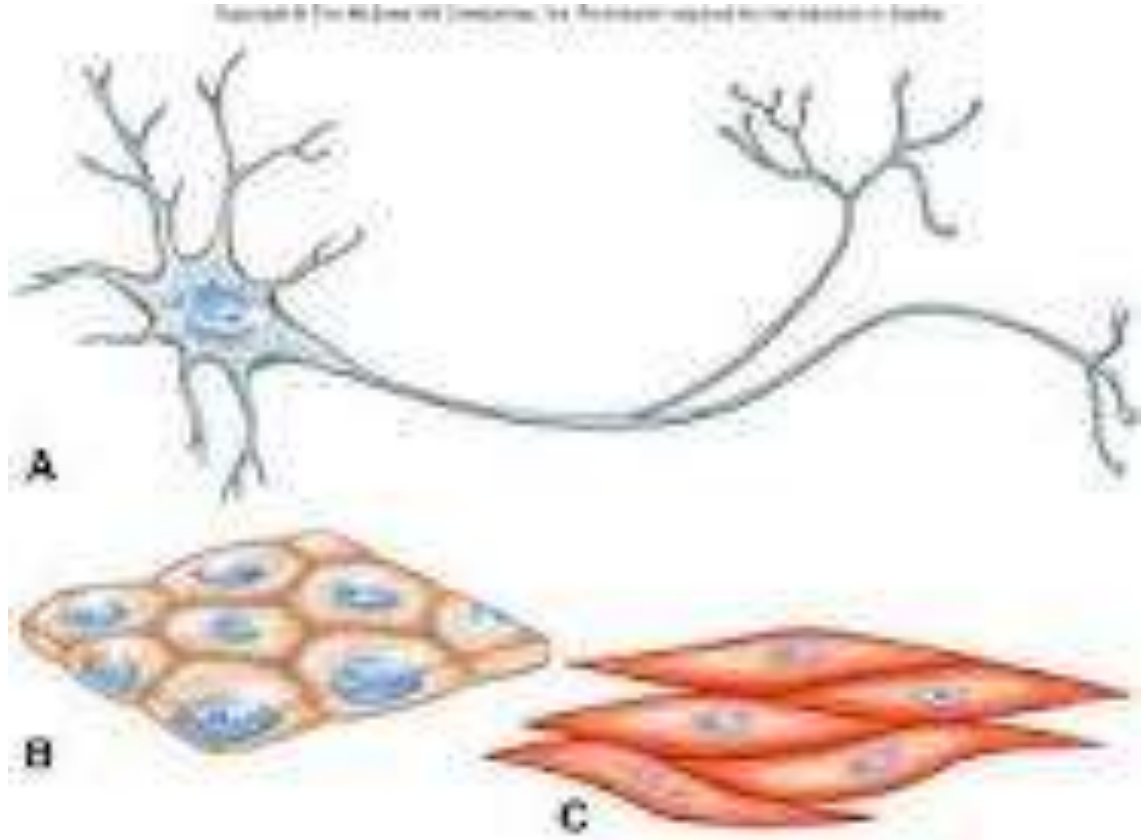

plasma membrane
microfilaments
mitochondrion
intermediate filaments
endoplasmic reticulum
microtubule
vesicle

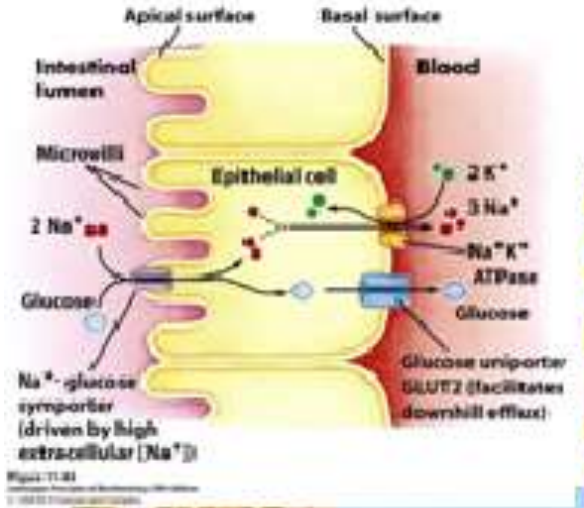

SCIENCE PHOTO LIBRARY

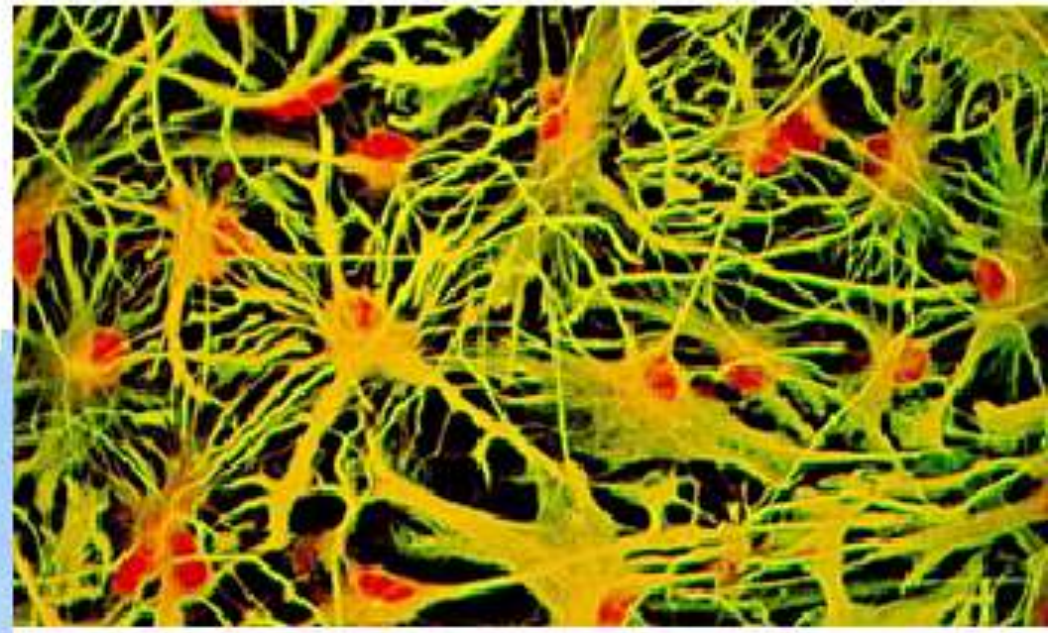

Apical surface
Basal surface
Intestinal lumen
Blood
Microvilli
Epithelial cell
2 K+
3 Na+
2 Na+
Na+K+ ATPase
Glucose
Glucose
Na+-glucose symporter (driven by high extracellular [Na+])
Glucose uniporter GLUT2 (facilitates downhill efflux)

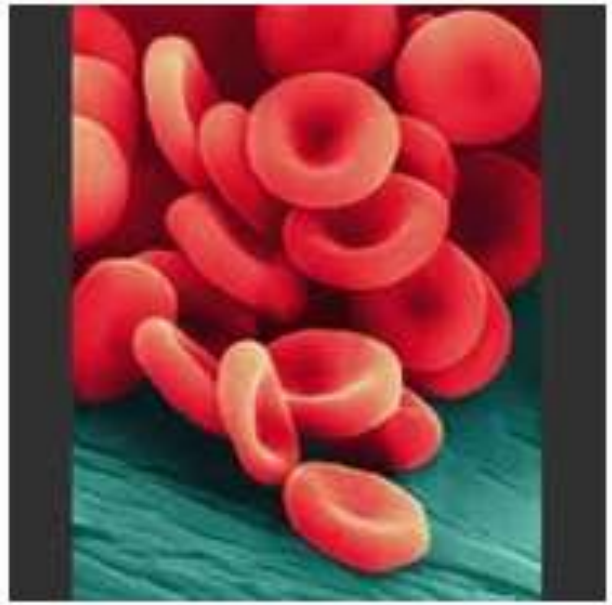


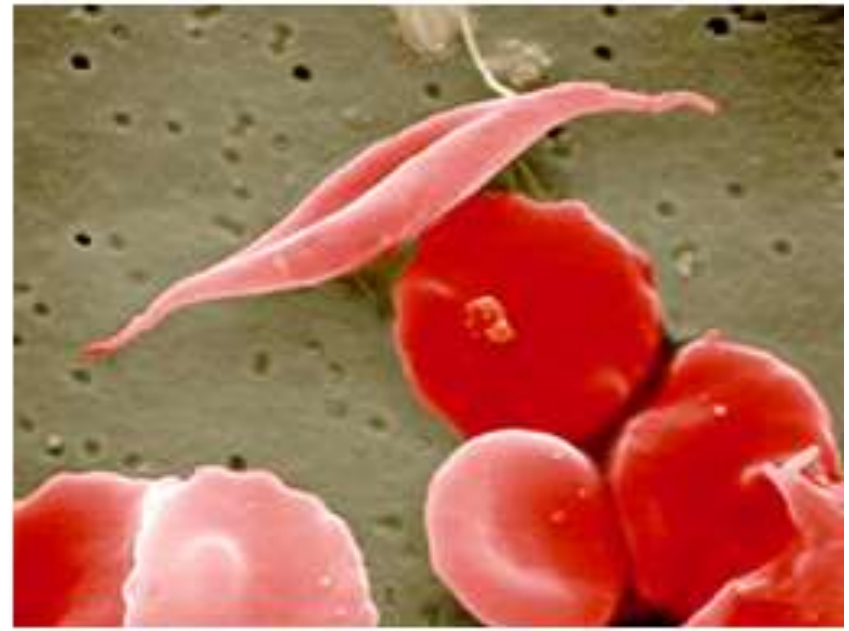
THE IMPORTANCE OF CELL SHAPE FOR FUNCTIONS


A
B
C

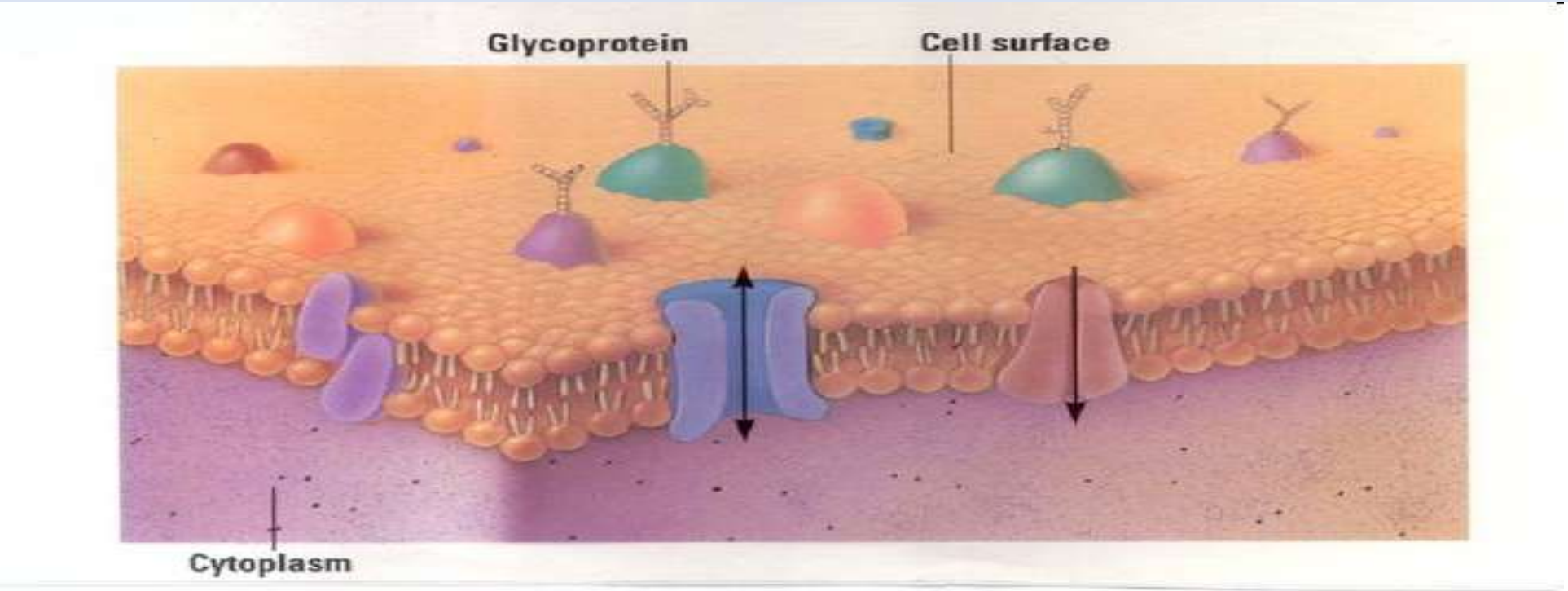

Apical surface
Basal surface
Intestinal lumen
Blood
Microvilli
Epithelial cell
2 K+
3 Na+
2 Na+
Na+K+ ATPase
Glucose
Glucose
Na+-glucose symporter (driven by high extracellular [Na+])
Glucose uniporter GLUT2 (facilitates downhill efflux)



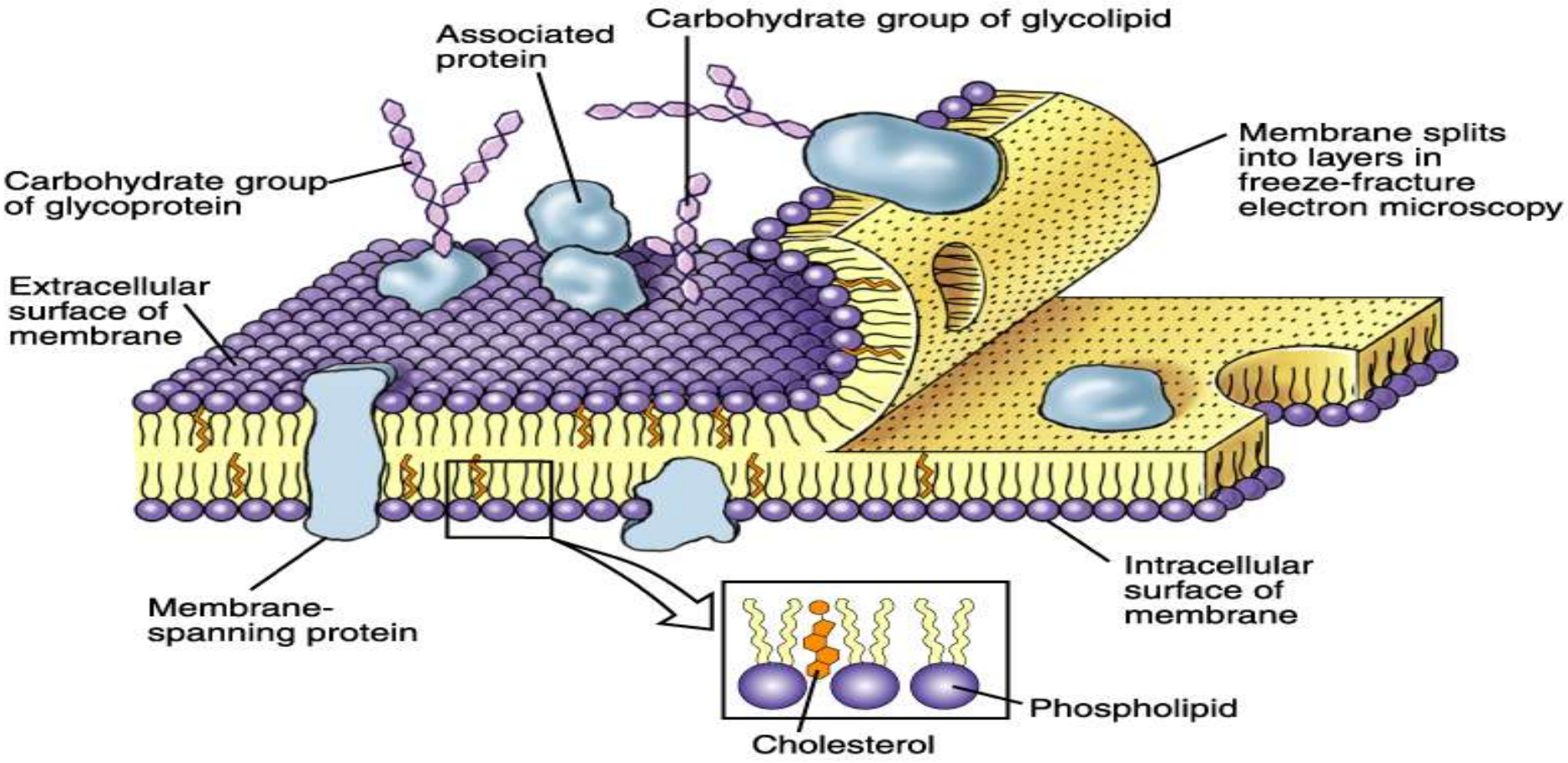


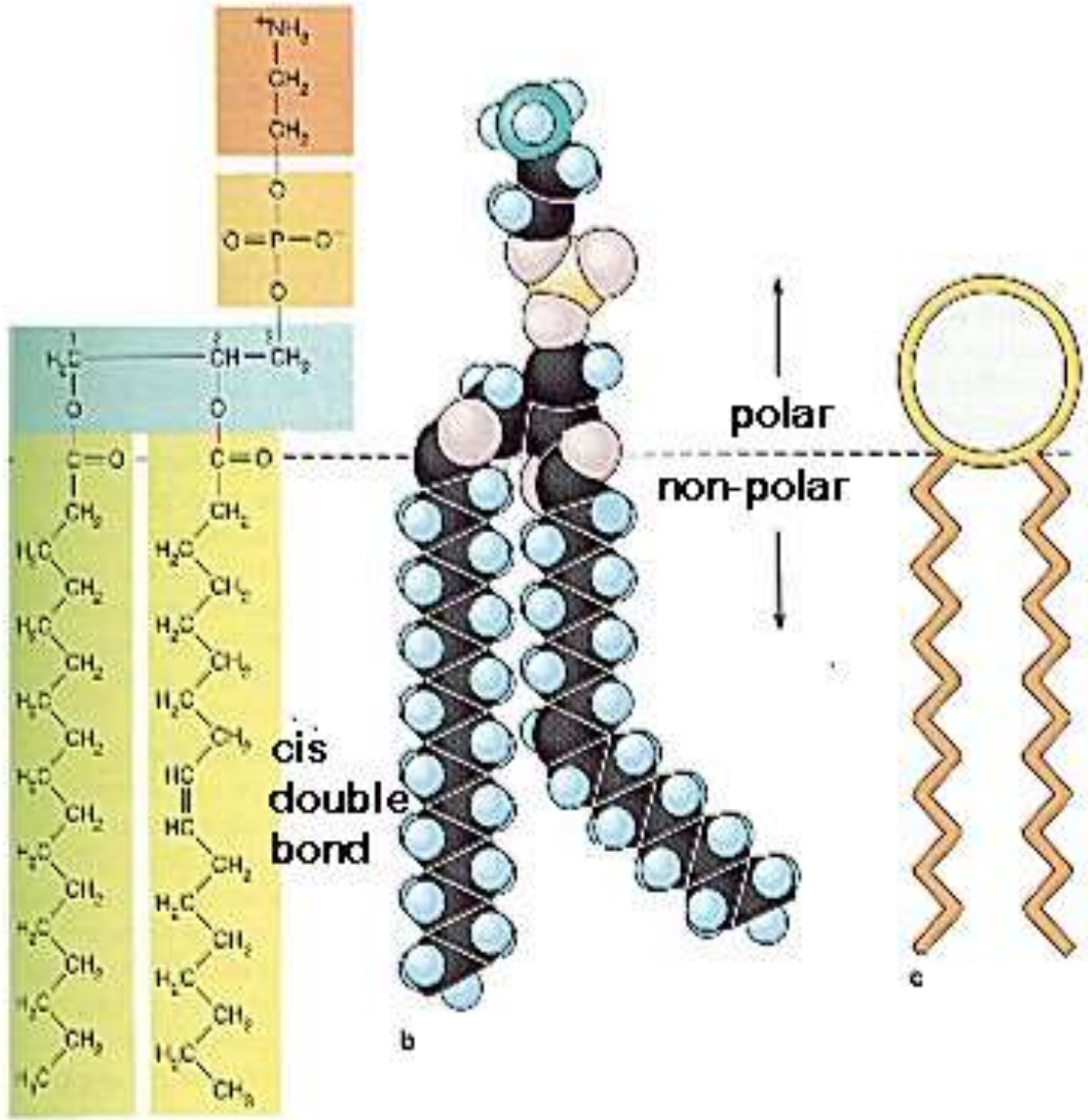


Structure of Plasma membrane

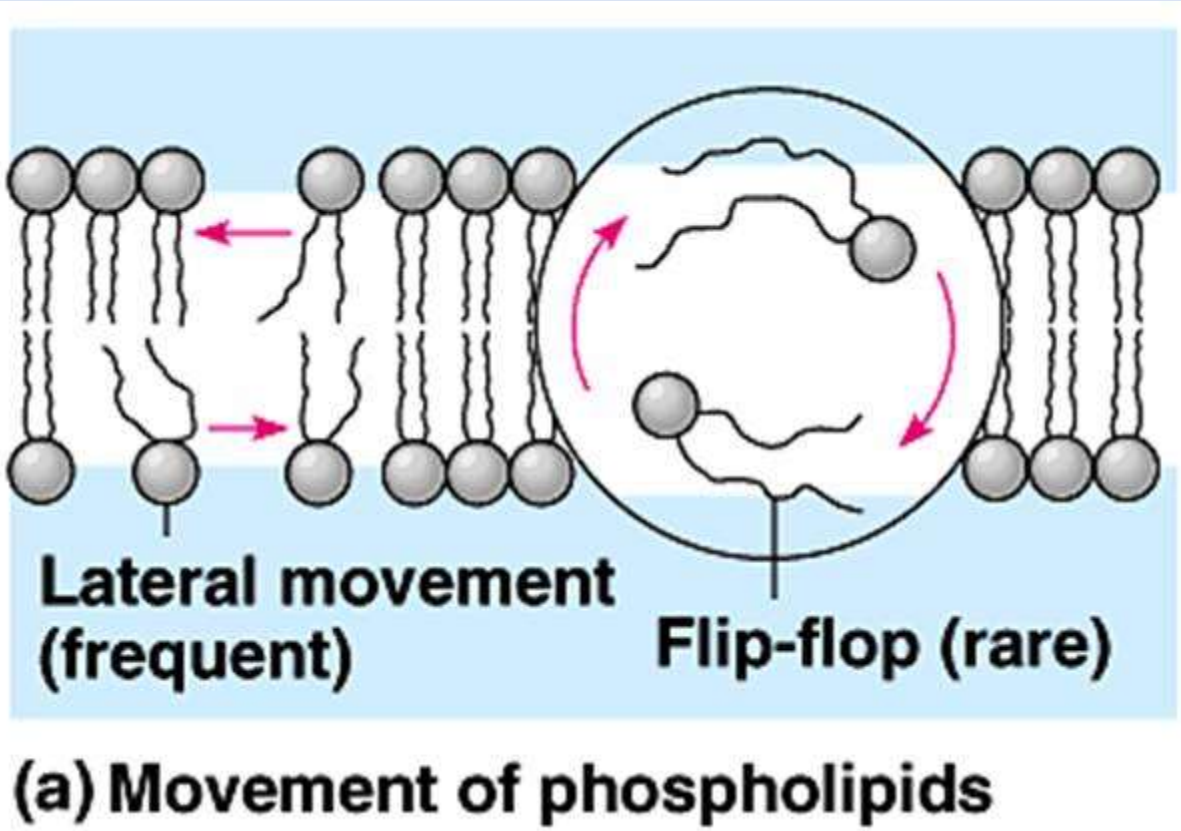


Lipids in Plasma membrane

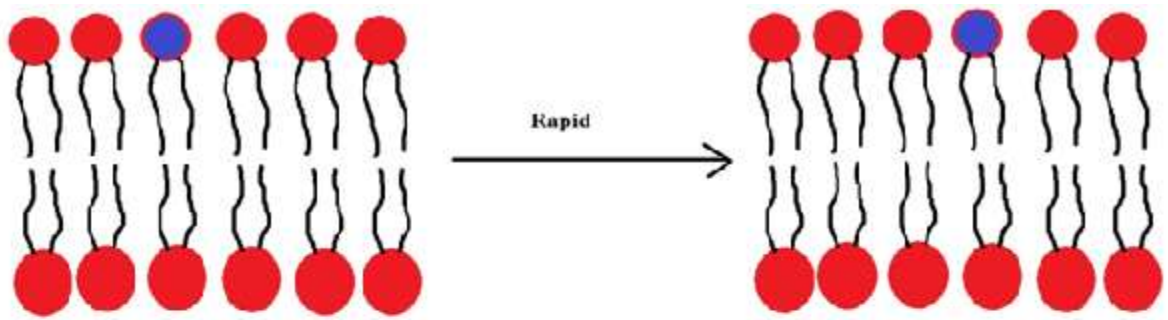



cis
double
bond
polar
non-polar
b
c

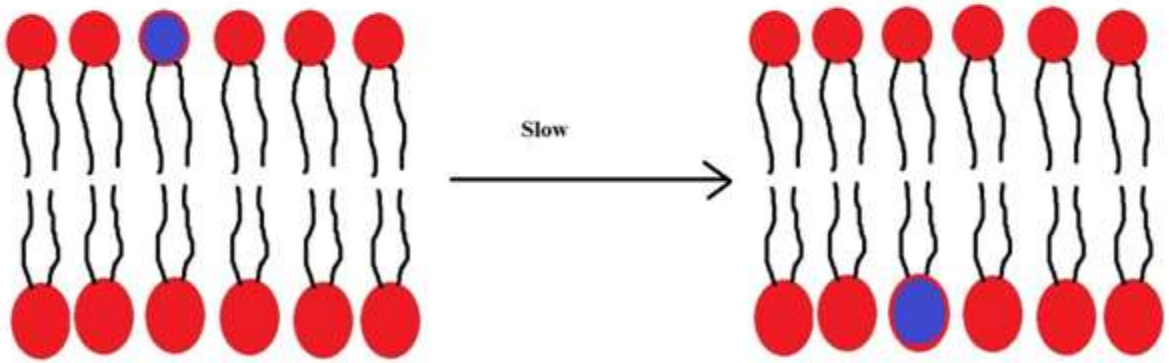
Movements of lipid molecules



Movements of lipid molecules

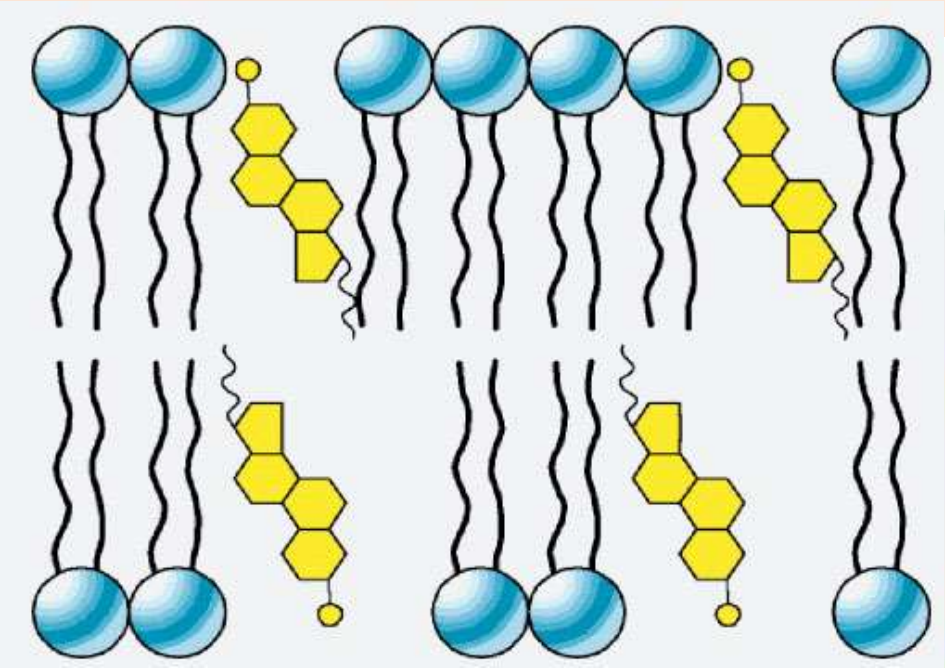


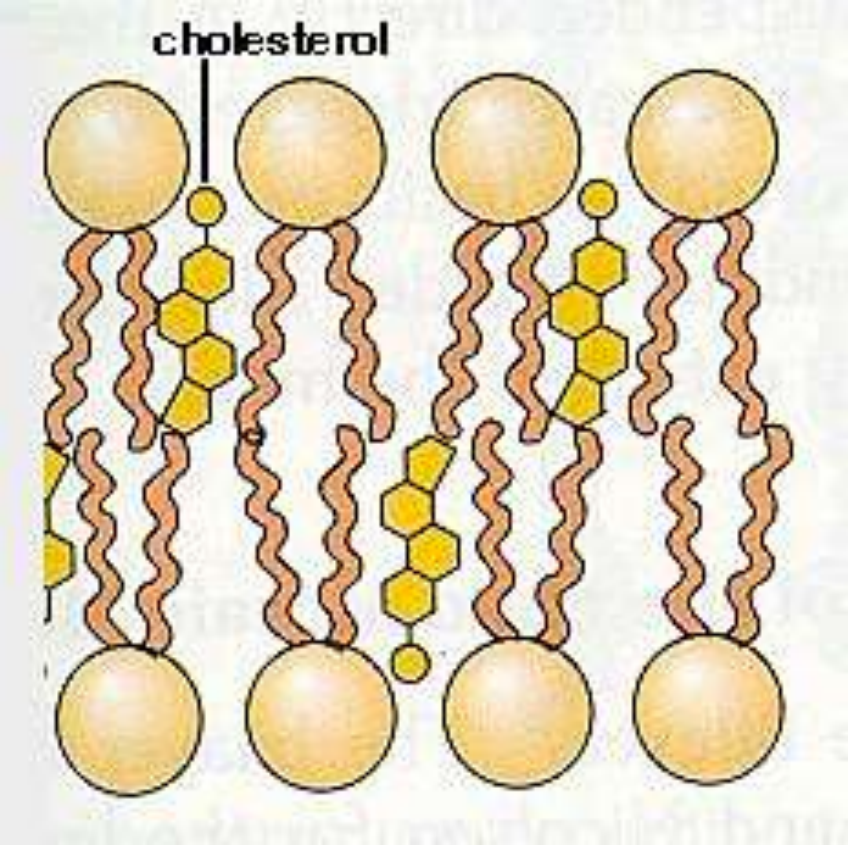
Lateral Diffusion



Flip Flop Diffusion

Cholesterol in plasma membranes



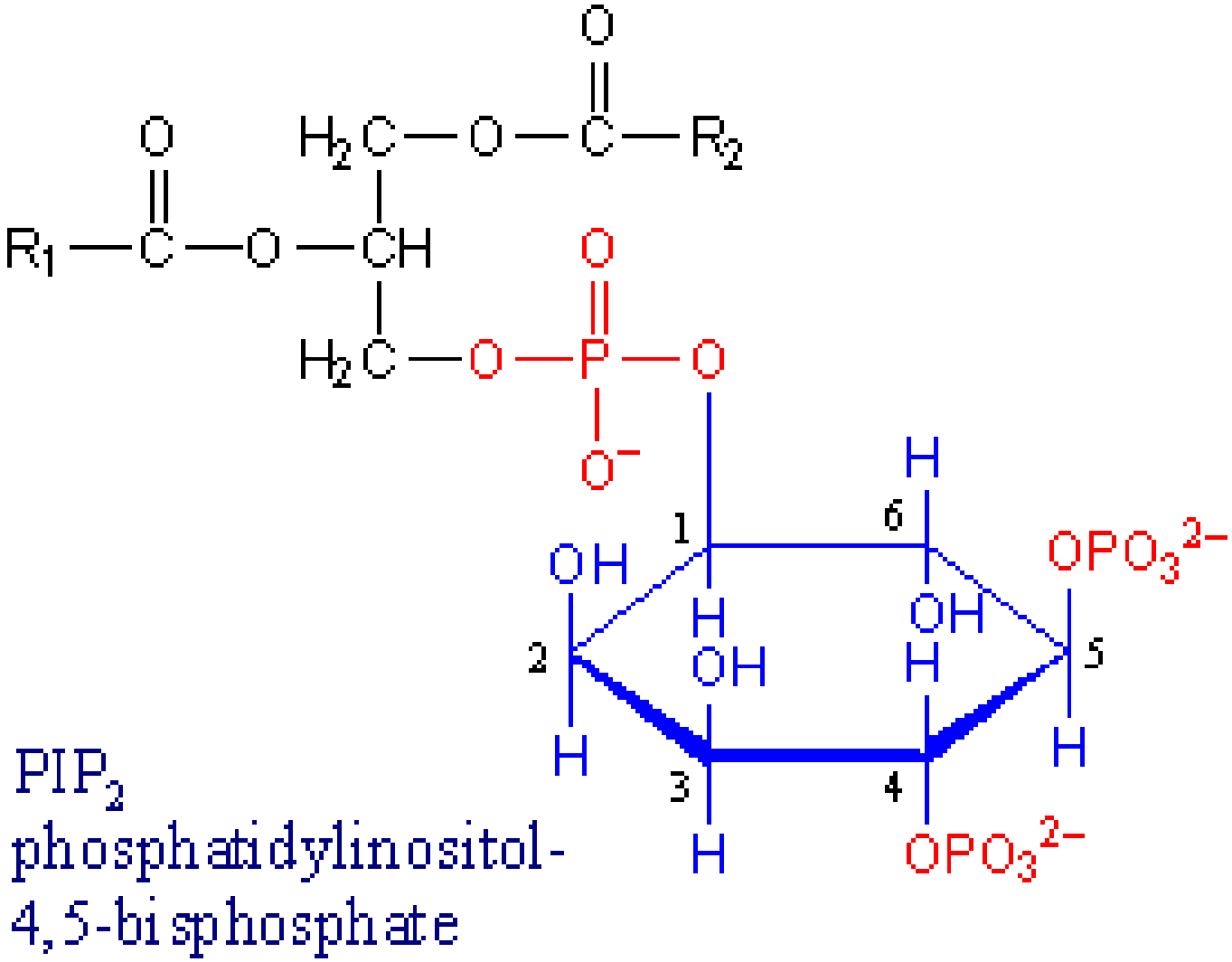


Cholesterol in plasma membranes

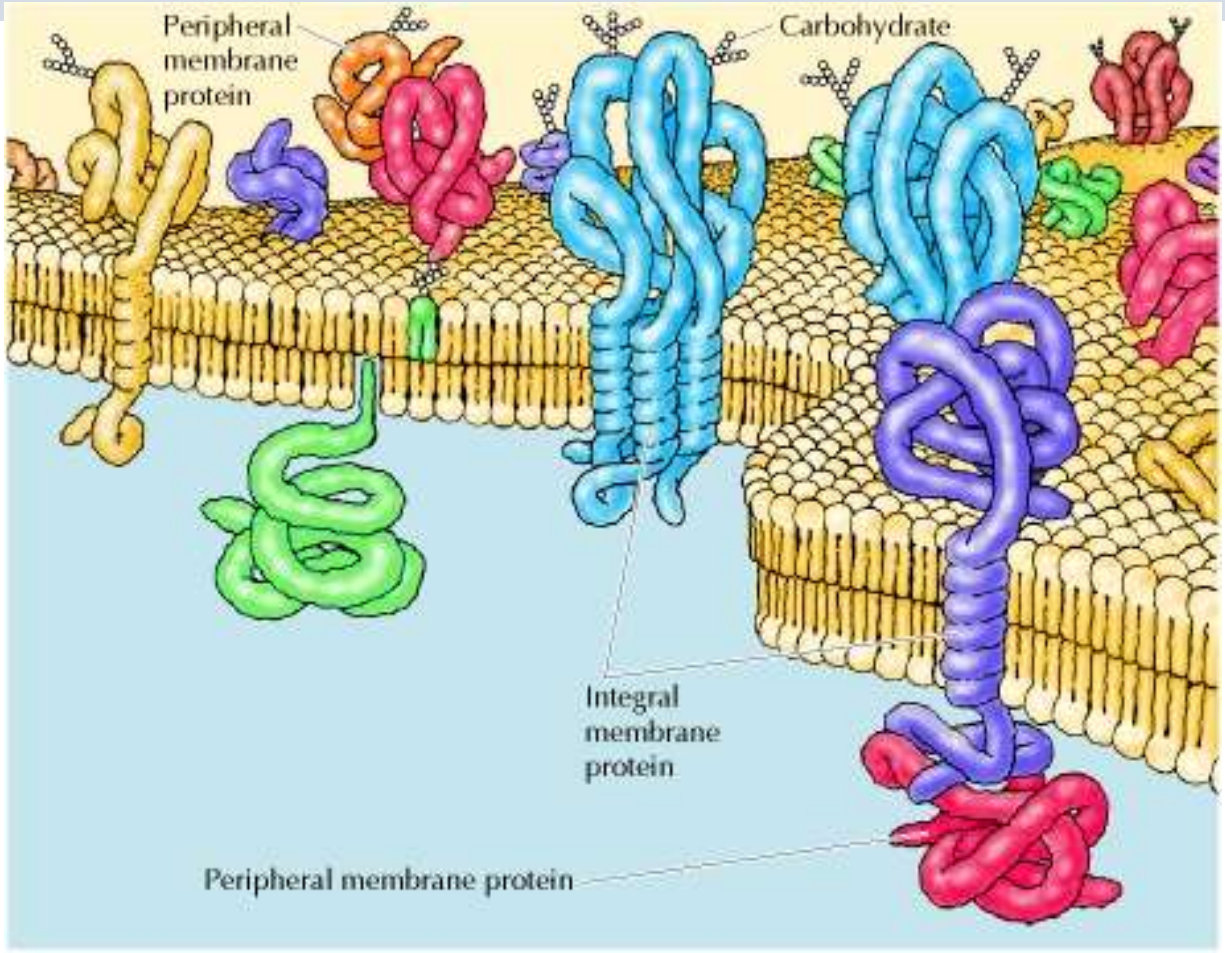
- Increase firmness and integrity of cell membrane (50% of Cell membrane structure)
- cholesterol helps to separate phospholipids, so the fatty acid chains can't come together and crystallize

Helps preventing extremes and maintaining consistency of membrane

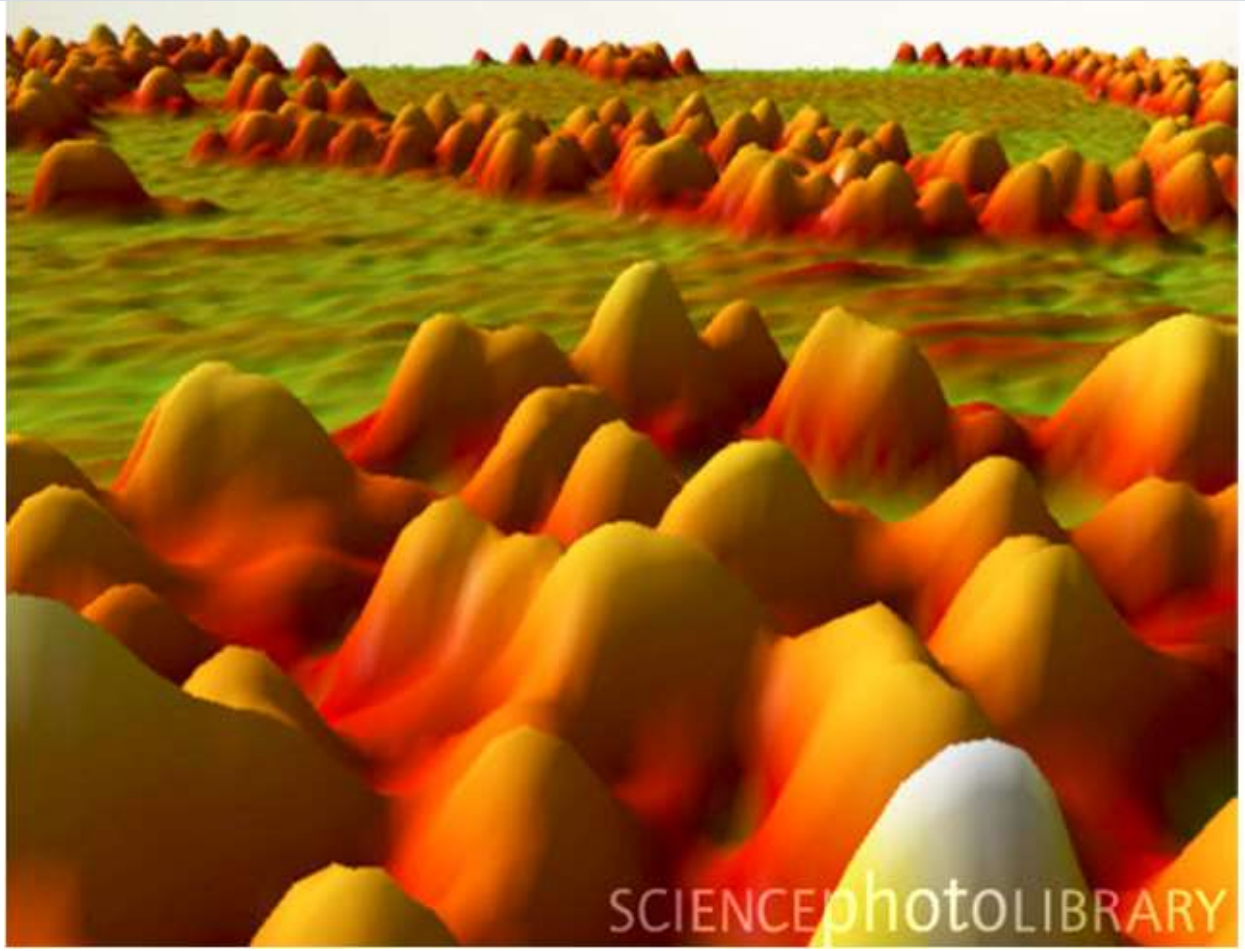
Functional Phospholipids in plasma membranes



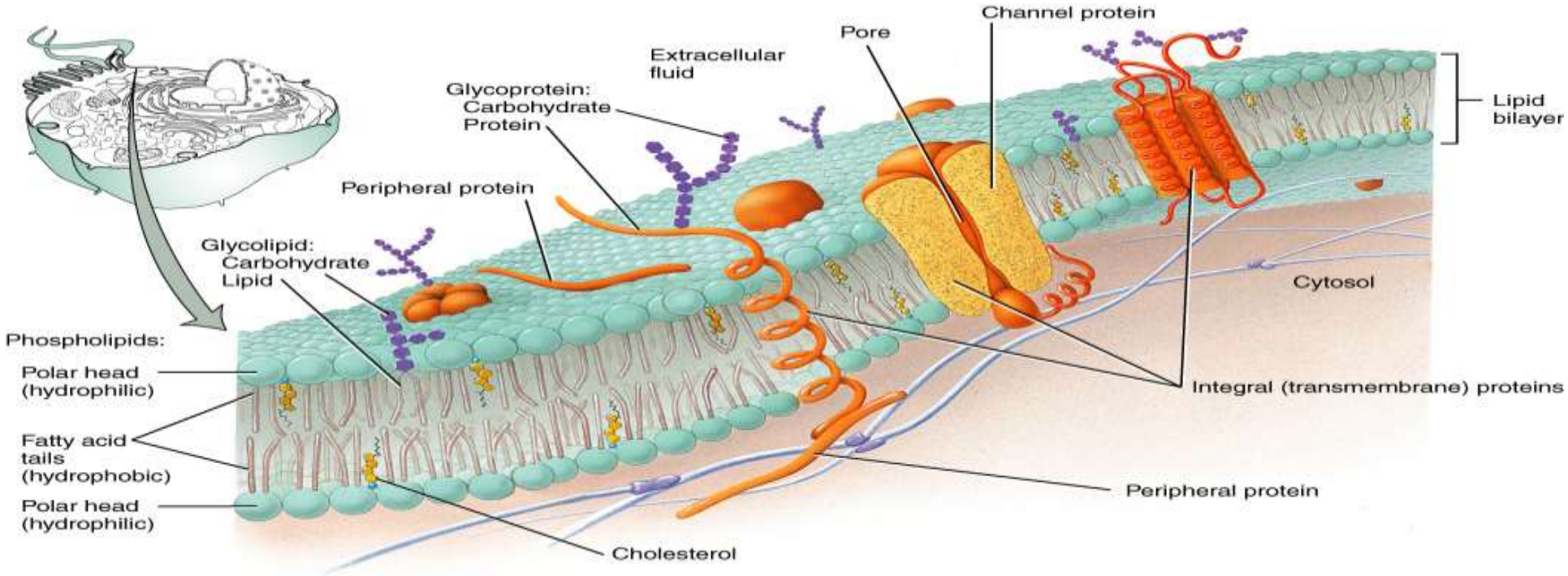
Proteins in plasma membranes



Proteins in plasma membranes

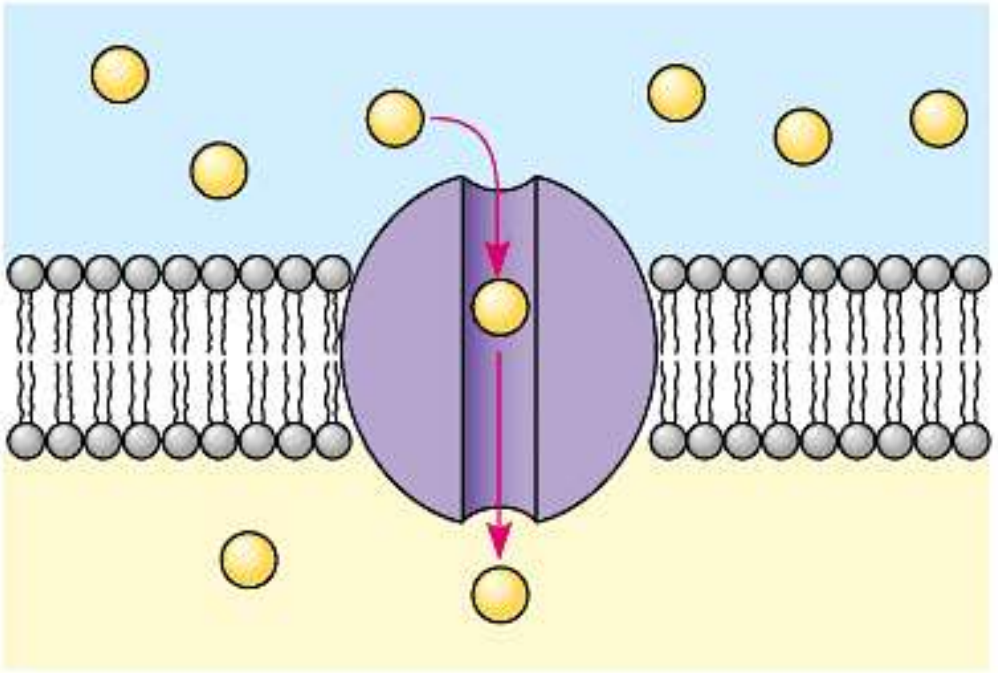


Protein functions in plasma membranes



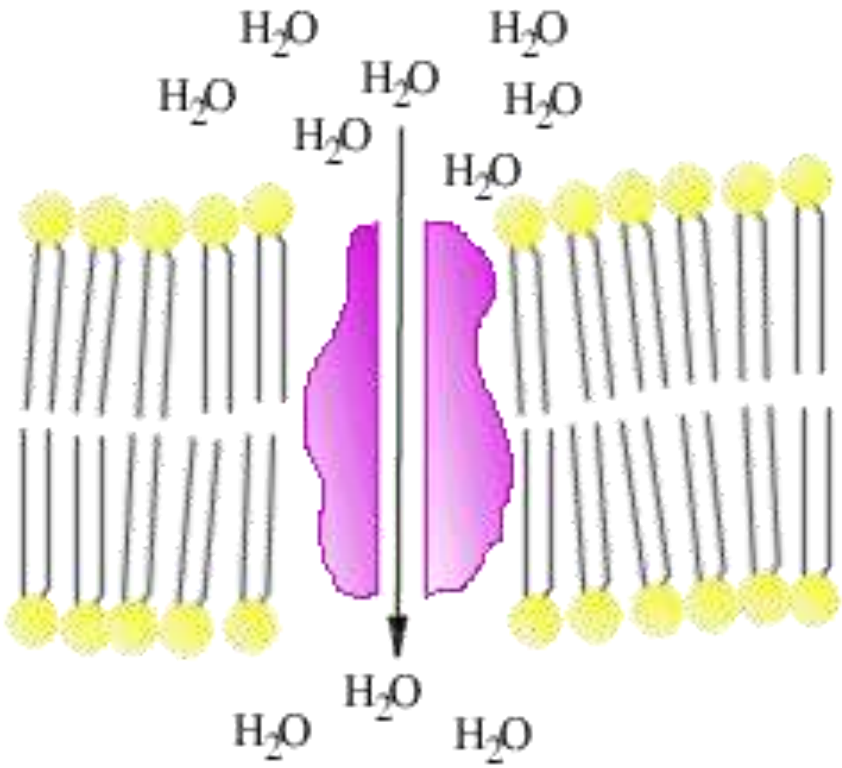
Chan

Channels

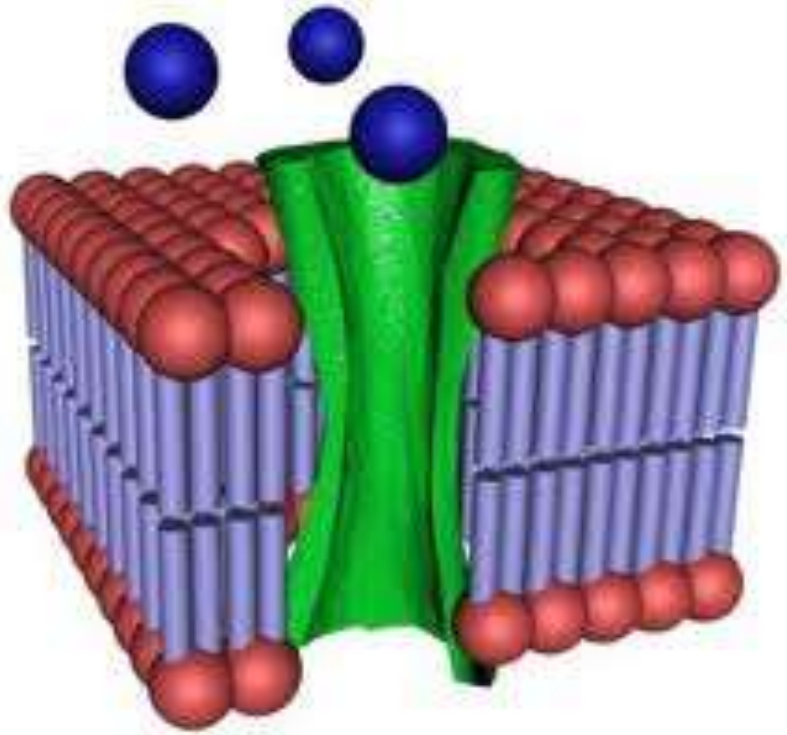


(a)

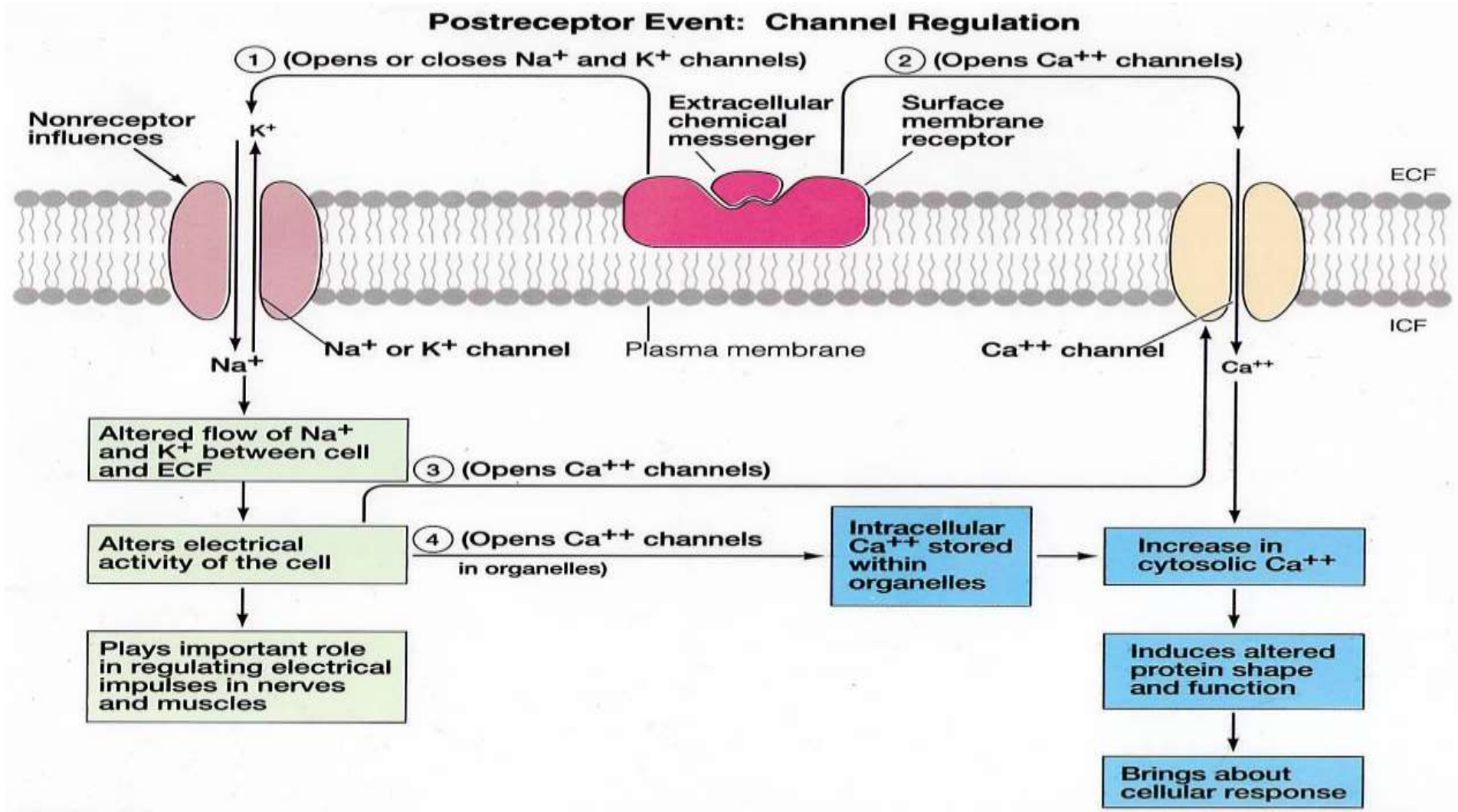
Channels



Diffusion through a protein channel

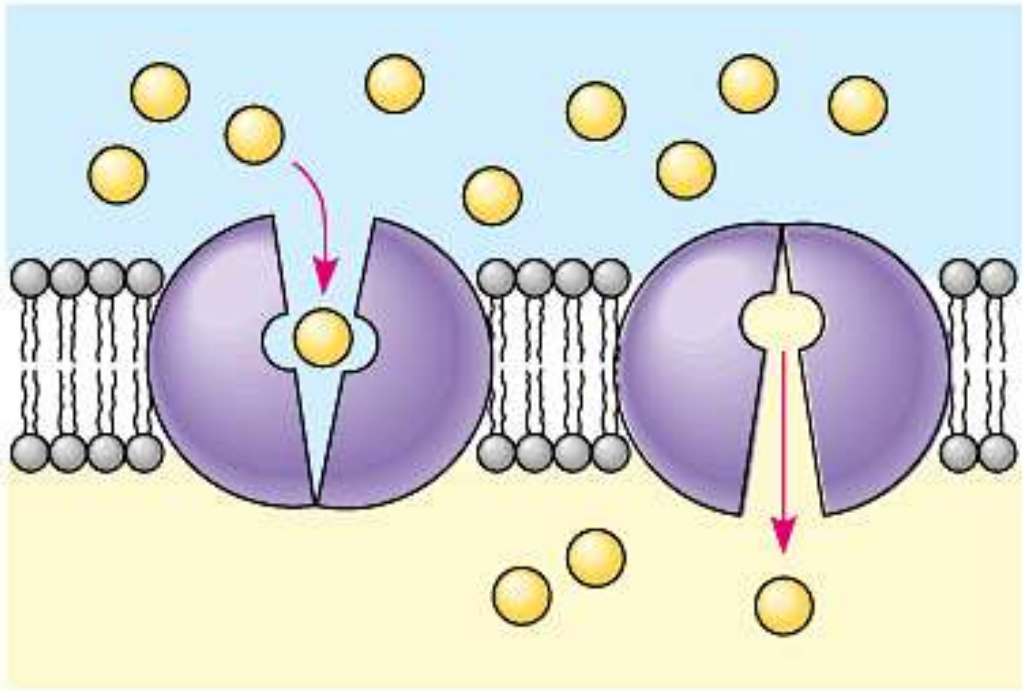


Chemical gated Channels



Chan

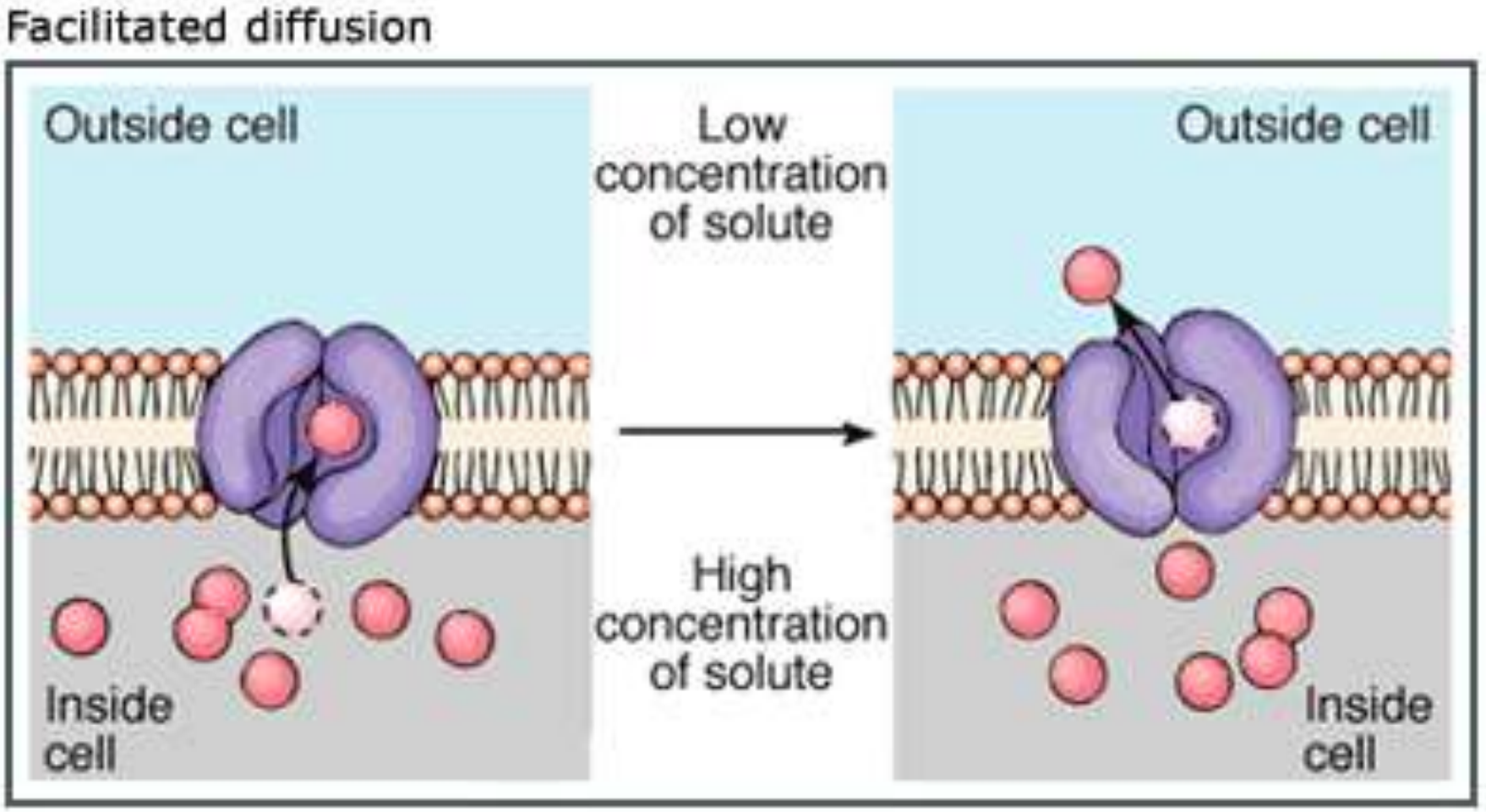
Carriers (Transporters)



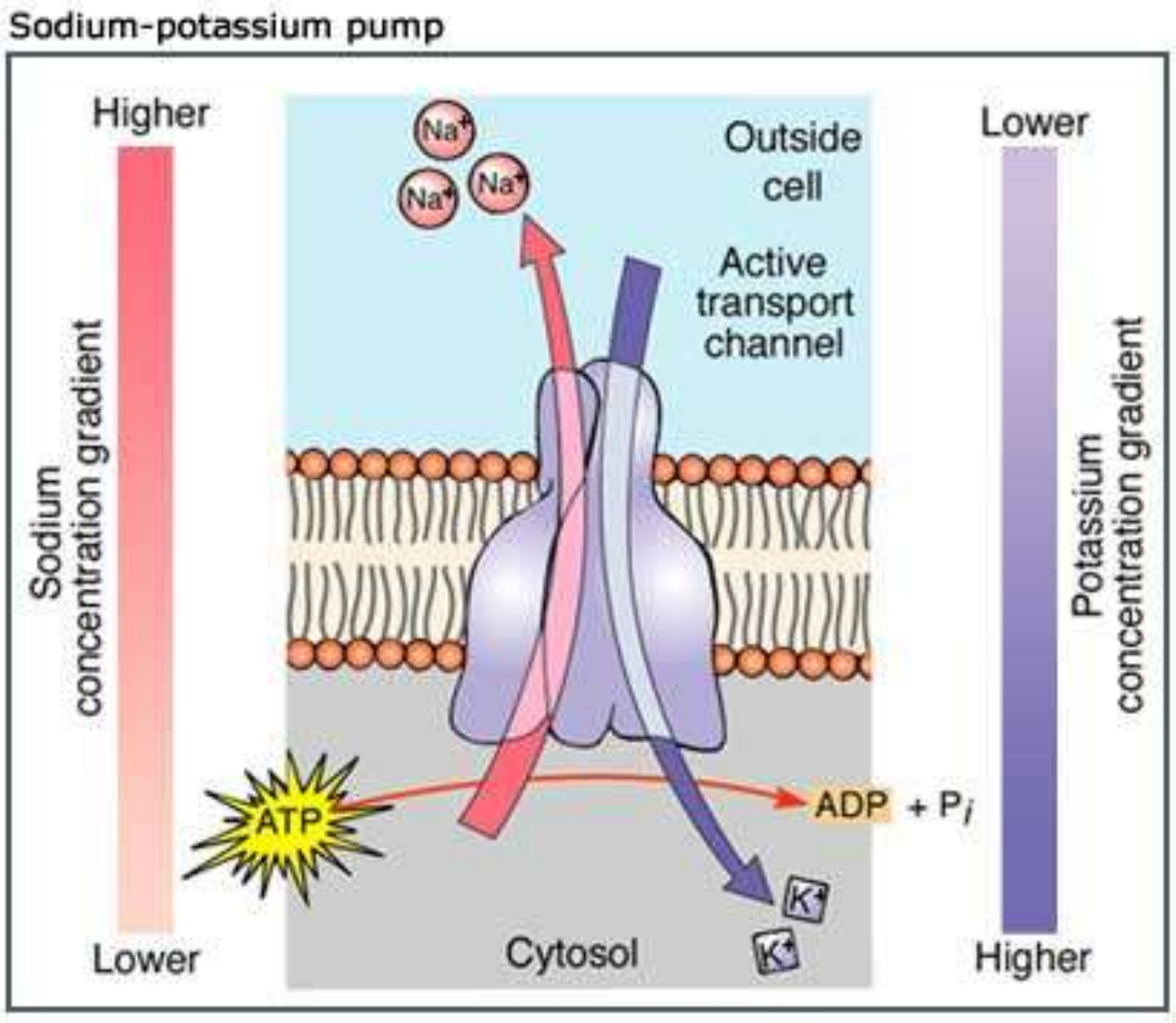
(b)

C

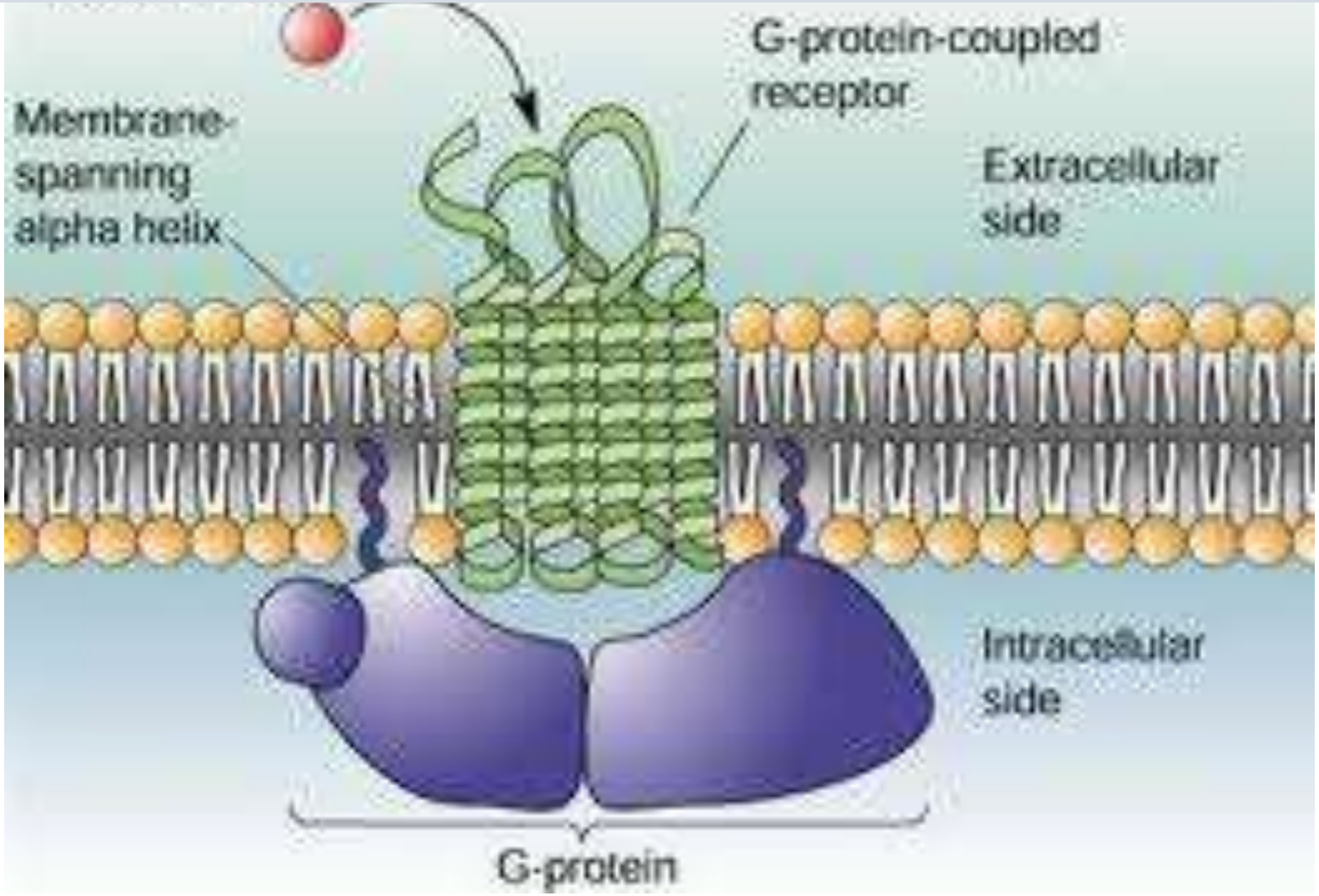
Carriers (Transporters)



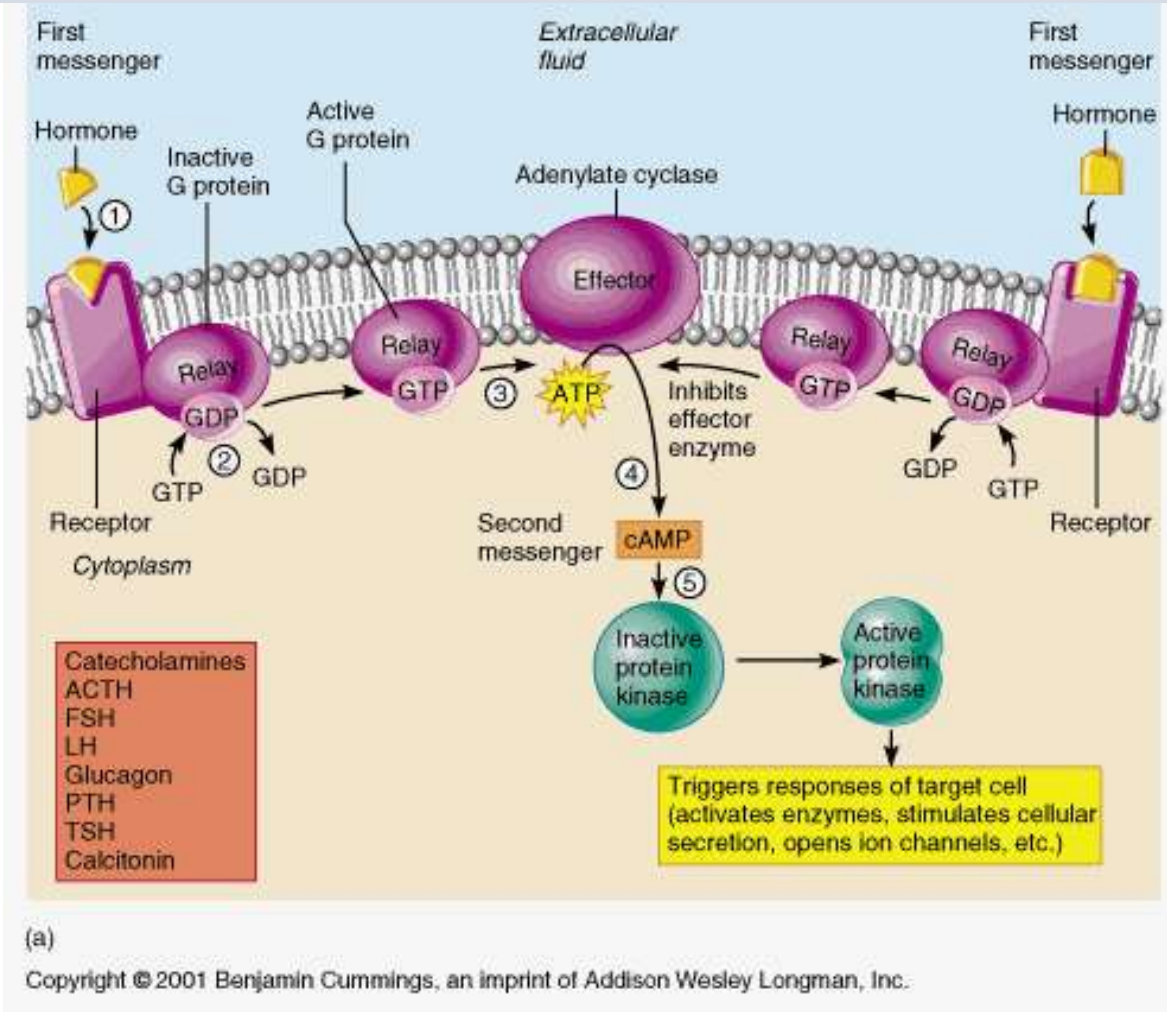
ATP dependent Carriers

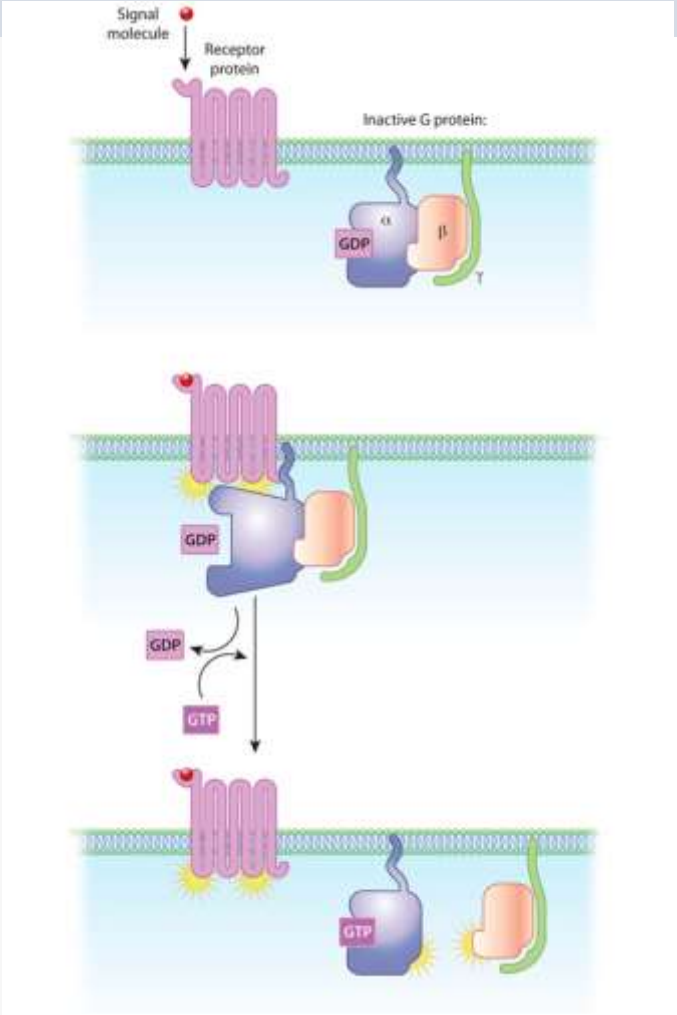


Receptors

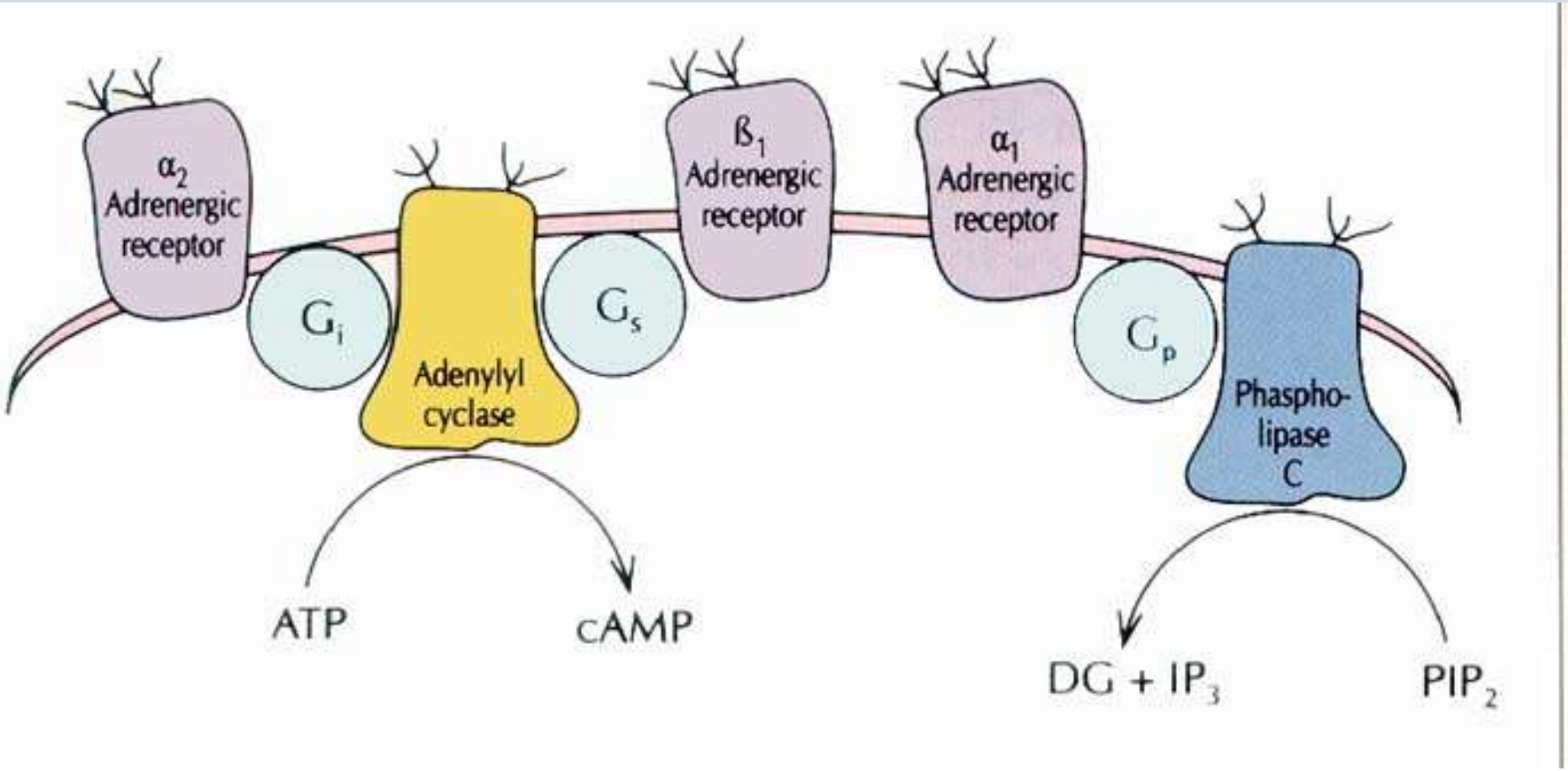

G-protein-coupled
receptor
Membrane-
spanning
alpha helix
Extracellular
side
Intracellular
side
G-protein

Receptors & G proteins



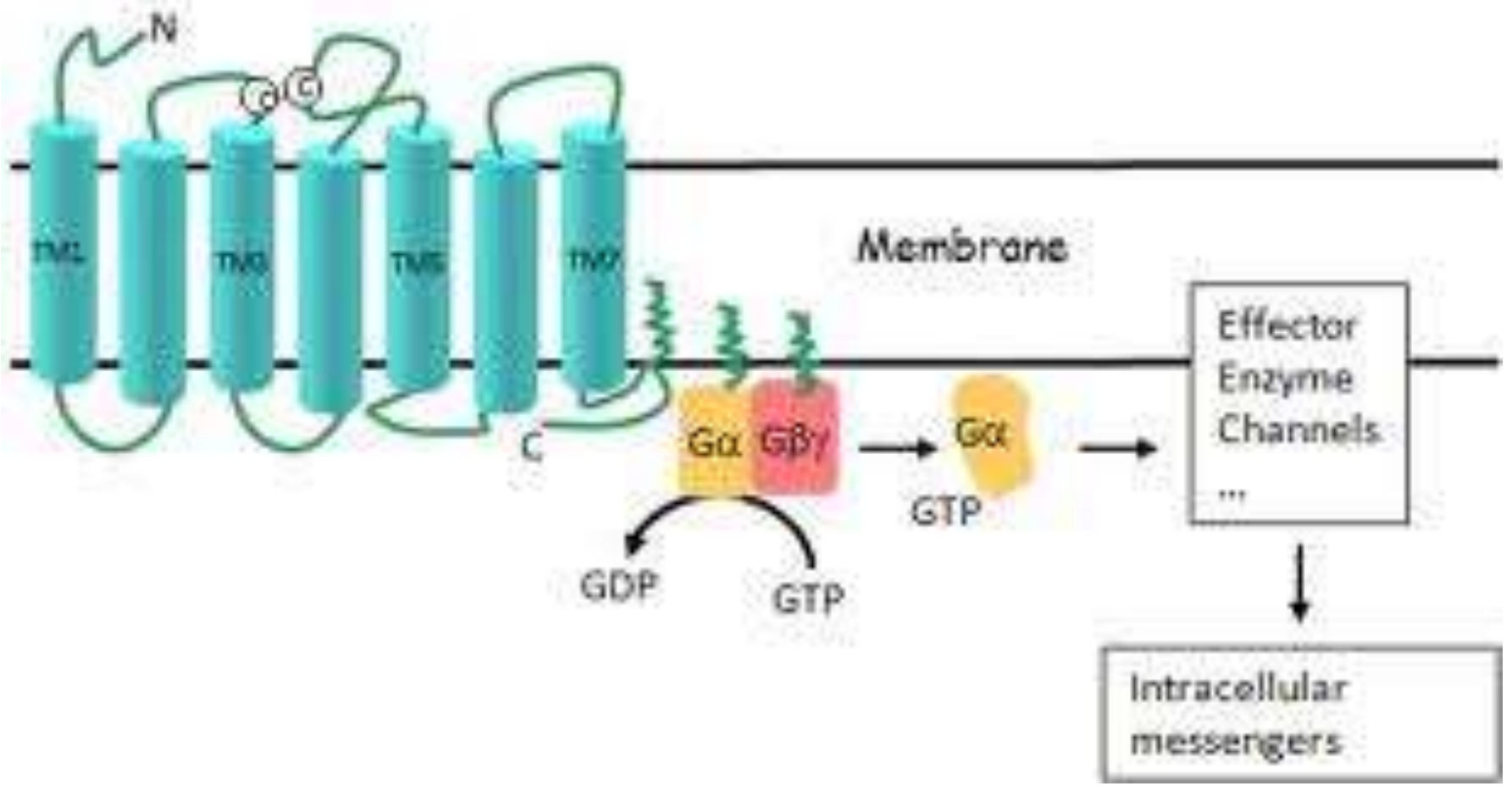


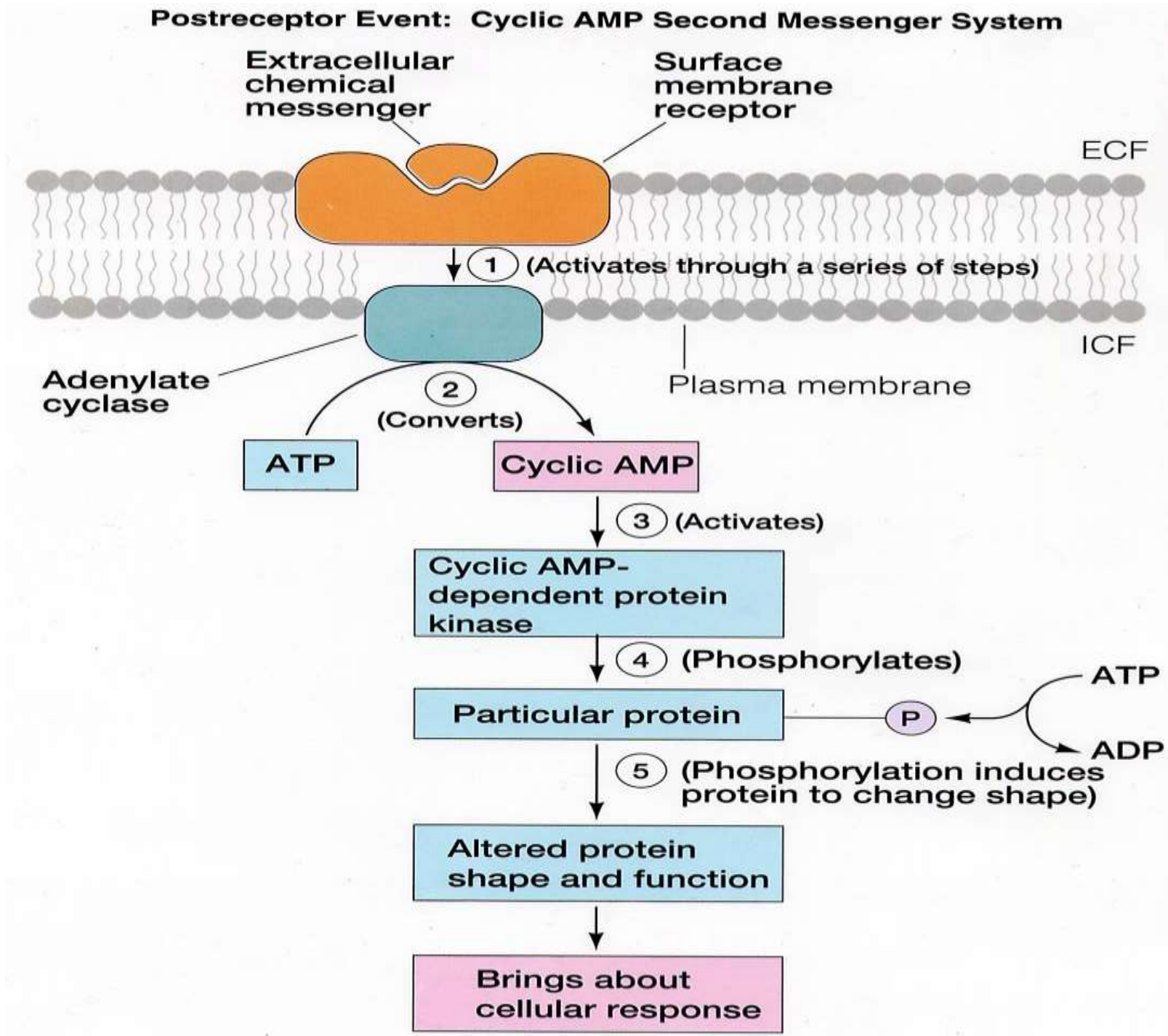
Receptors & G proteins

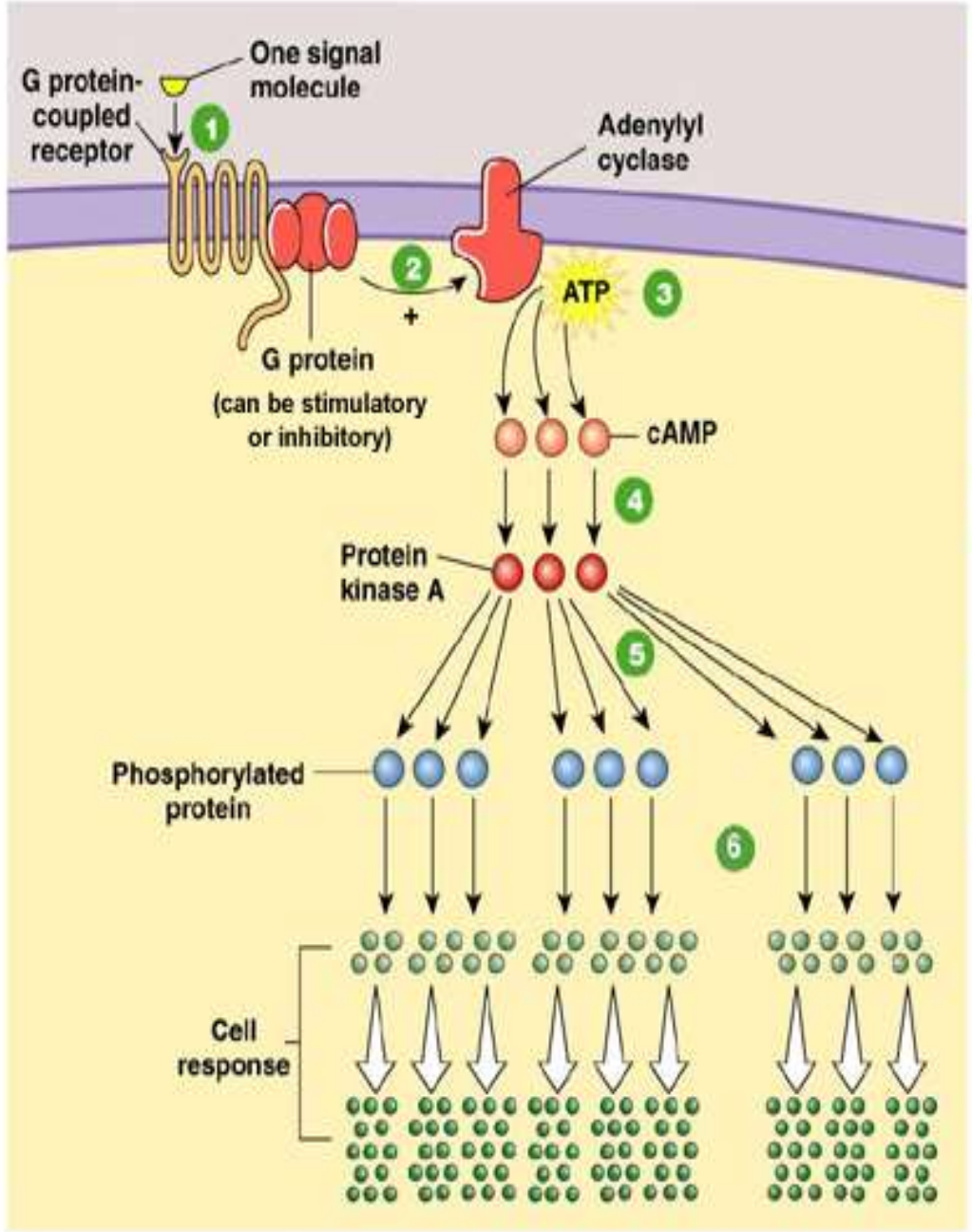


Enzymes

Receptors & Enzymes

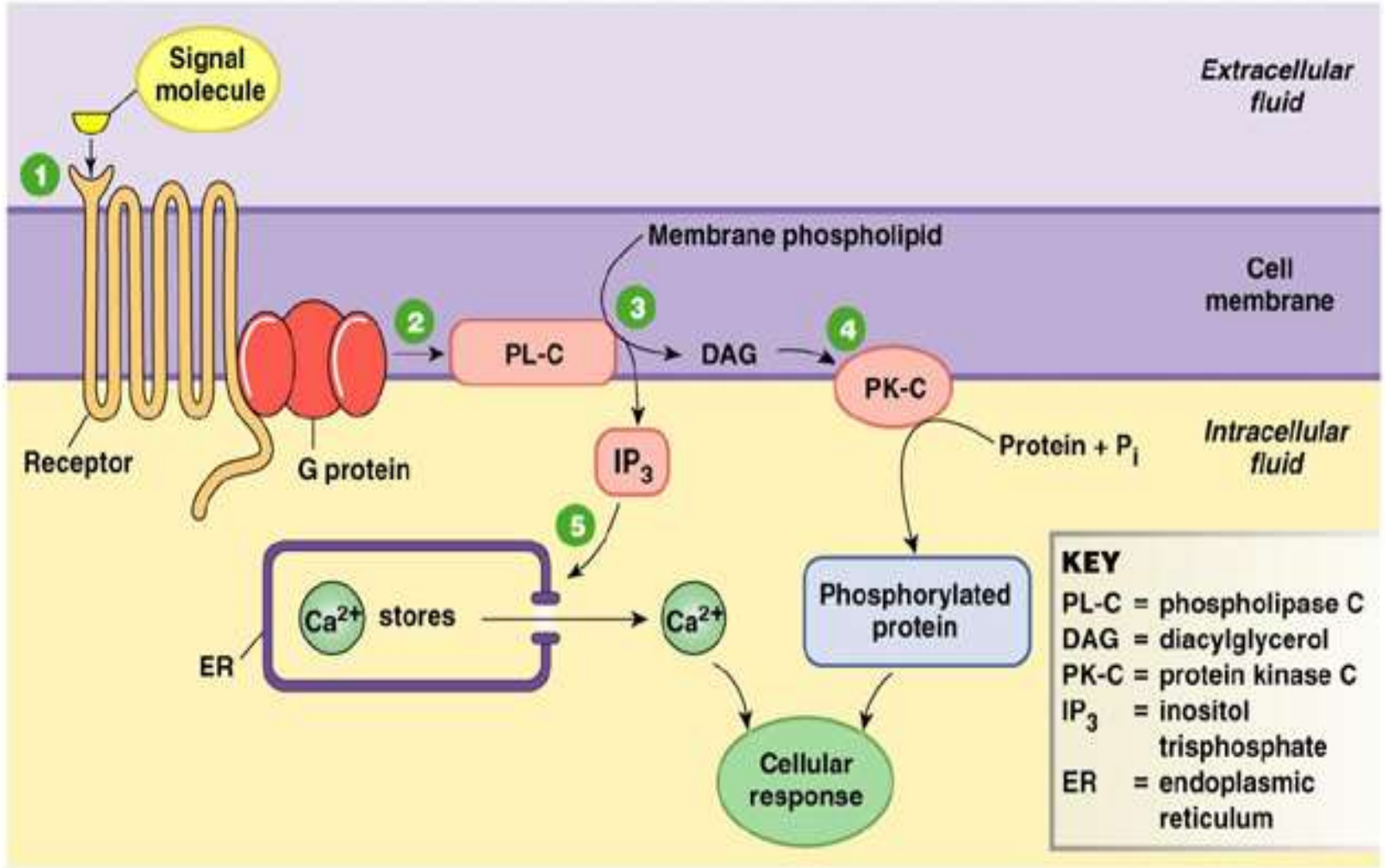



Postreceptor Event: Cyclic AMP Second Messenger System
Extracellular chemical messenger
Surface membrane receptor
ECF
1 (Activates through a series of steps)
ICF
Adenylate cyclase
Plasma membrane
2 (Converts)
ATP
Cyclic AMP
3 (Activates)
Cyclic AMP-dependent protein kinase
4 (Phosphorylates)
ATP
Particular protein
P
ADP
5 (Phosphorylation induces protein to change shape)
Altered protein shape and function
Brings about cellular response



1. Signal molecule binds to G protein-linked receptor, which activates the G protein.
2. G protein turns on adenylyl cyclase, an amplifier enzyme.
3. Adenylyl cyclase converts ATP to cyclic AMP.
4. cAMP activates protein kinase A.
5. Protein kinase A phosphorylates other proteins, leading ultimately to a cellular response.
6. Note how the initial signal is amplified.

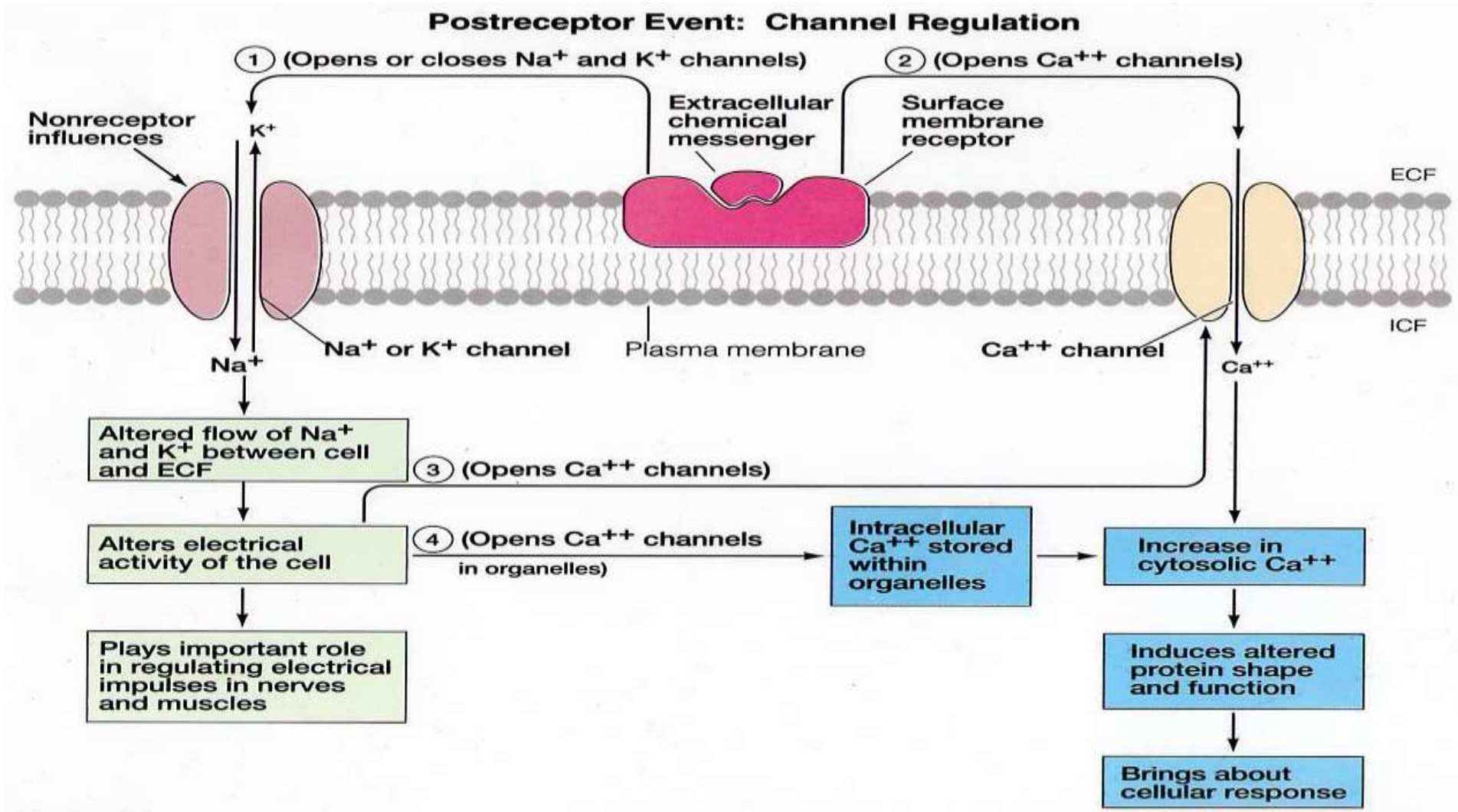
Fig. 6-11



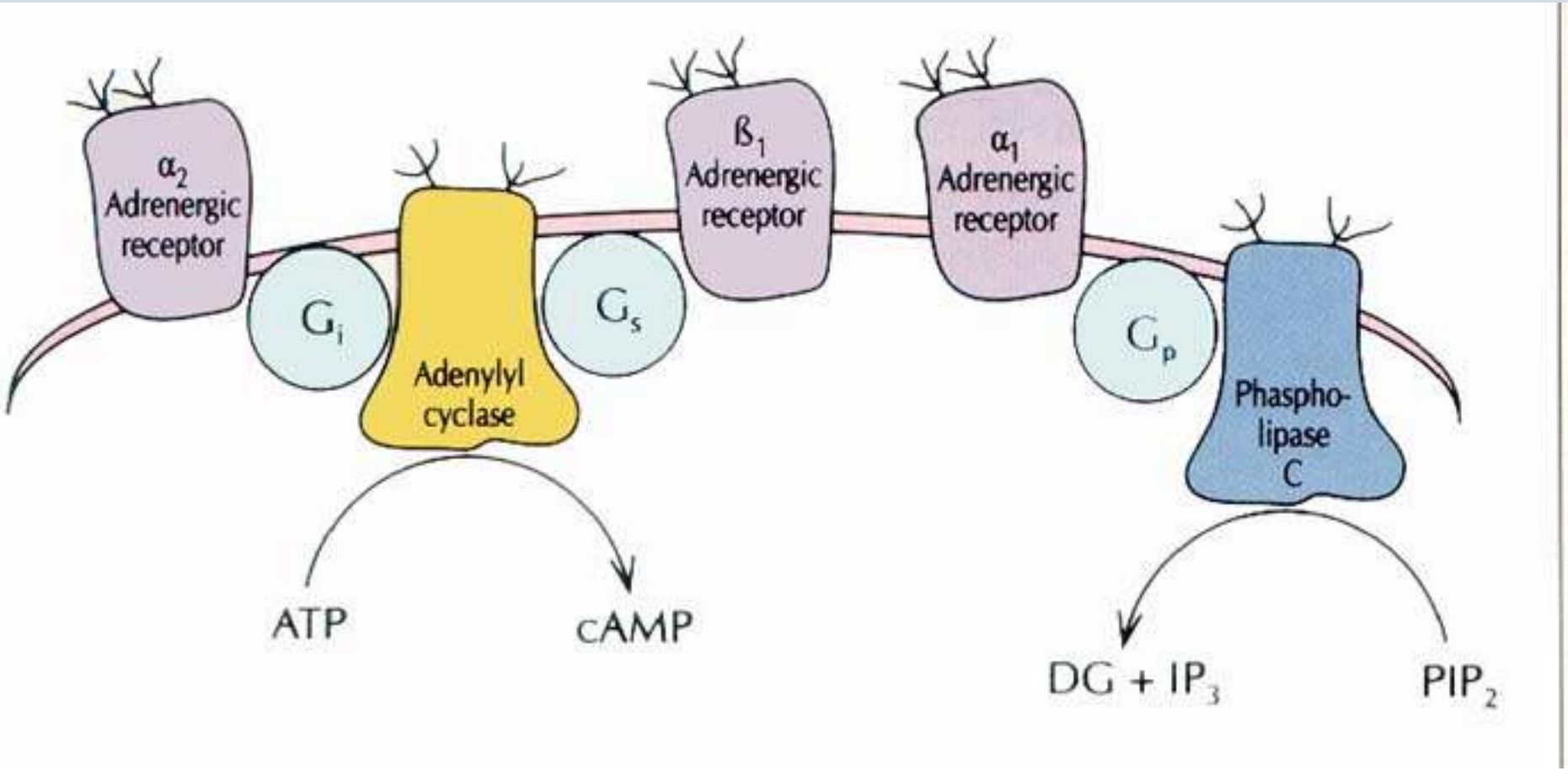
1. Signal molecule activates receptor and associated G protein.
2. G protein activates phospholipase C (PL-C), an amplifier enzyme.
3. PL-C converts membrane phospholipids into diacylglycerol (DAG), which remains in the membrane, and IP_3, which diffuses into the cytoplasm.
4. DAG activates protein kinase C (PK-C), which phosphorylates proteins.
5. IP_3 causes release of Ca^{2+} from organelles, creating a Ca^{2+} signal.

Fig. 6-12

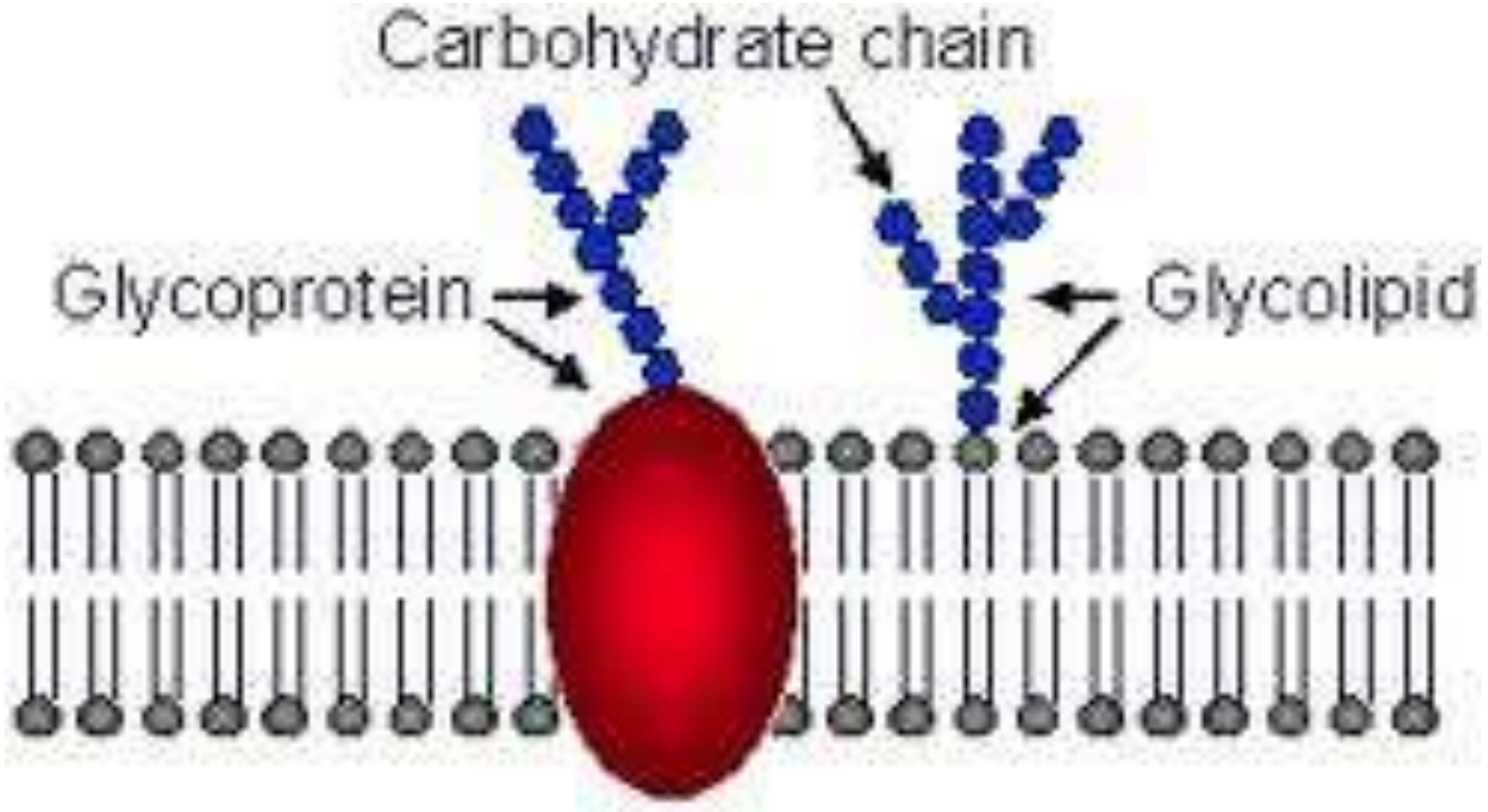
Receptors & Channels

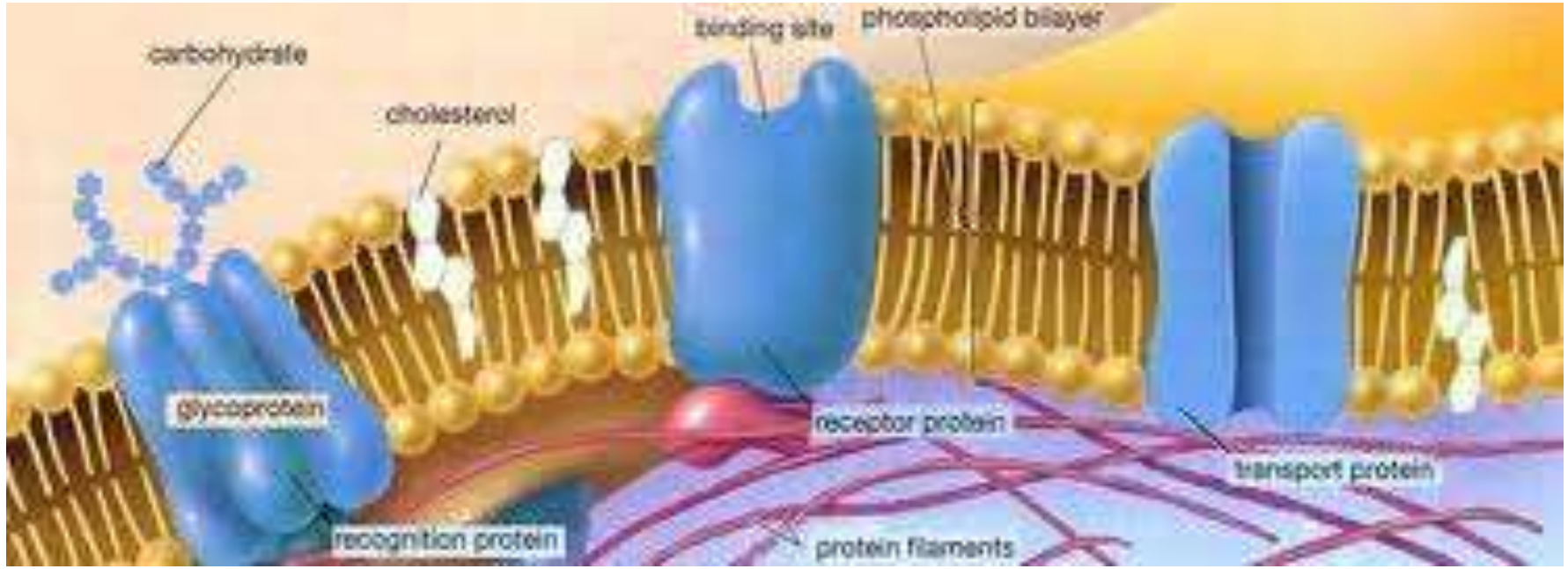


Receptors & G proteins

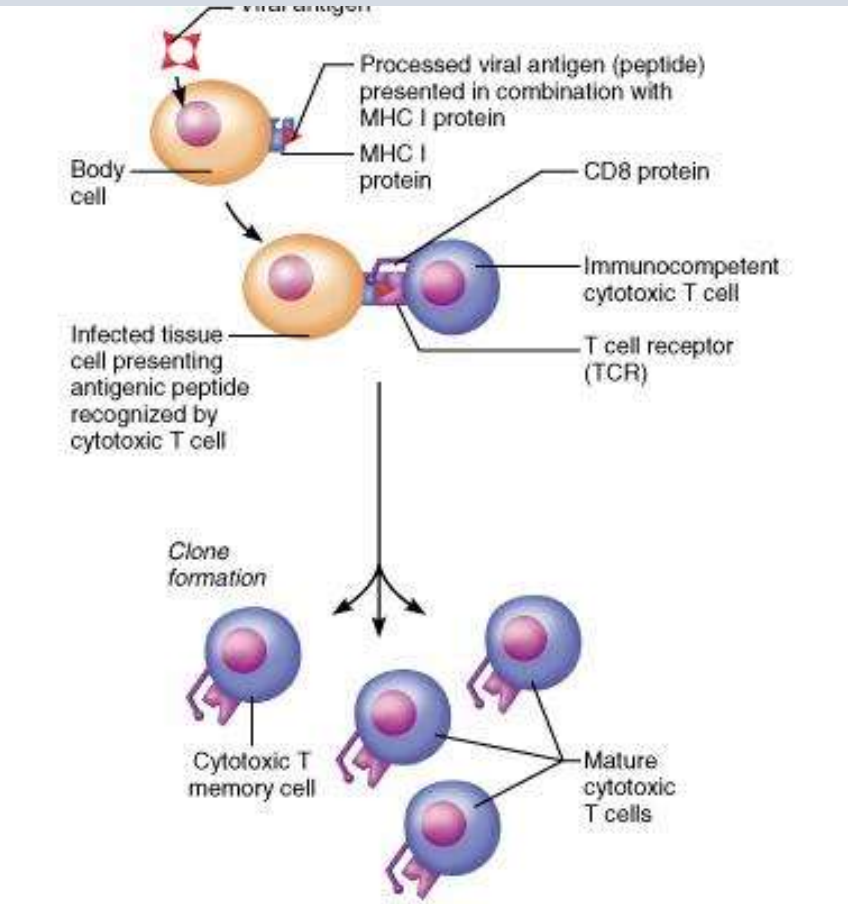


Cell Identity Markers

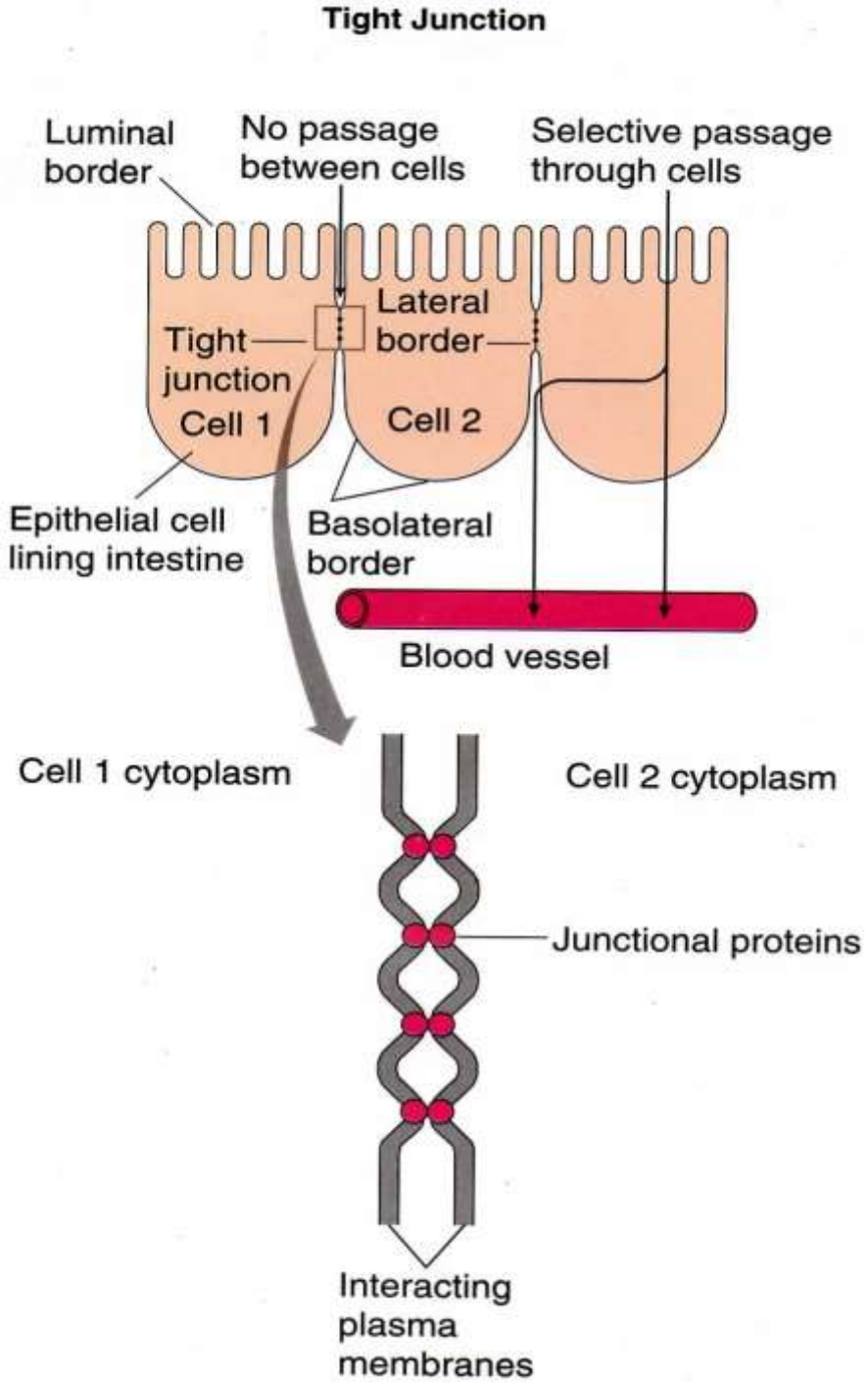



carbohydrate
cholesterol
binding site
phospholipid bilayer
glycoprotein
receptor protein
transport protein
recognition protein
protein filaments

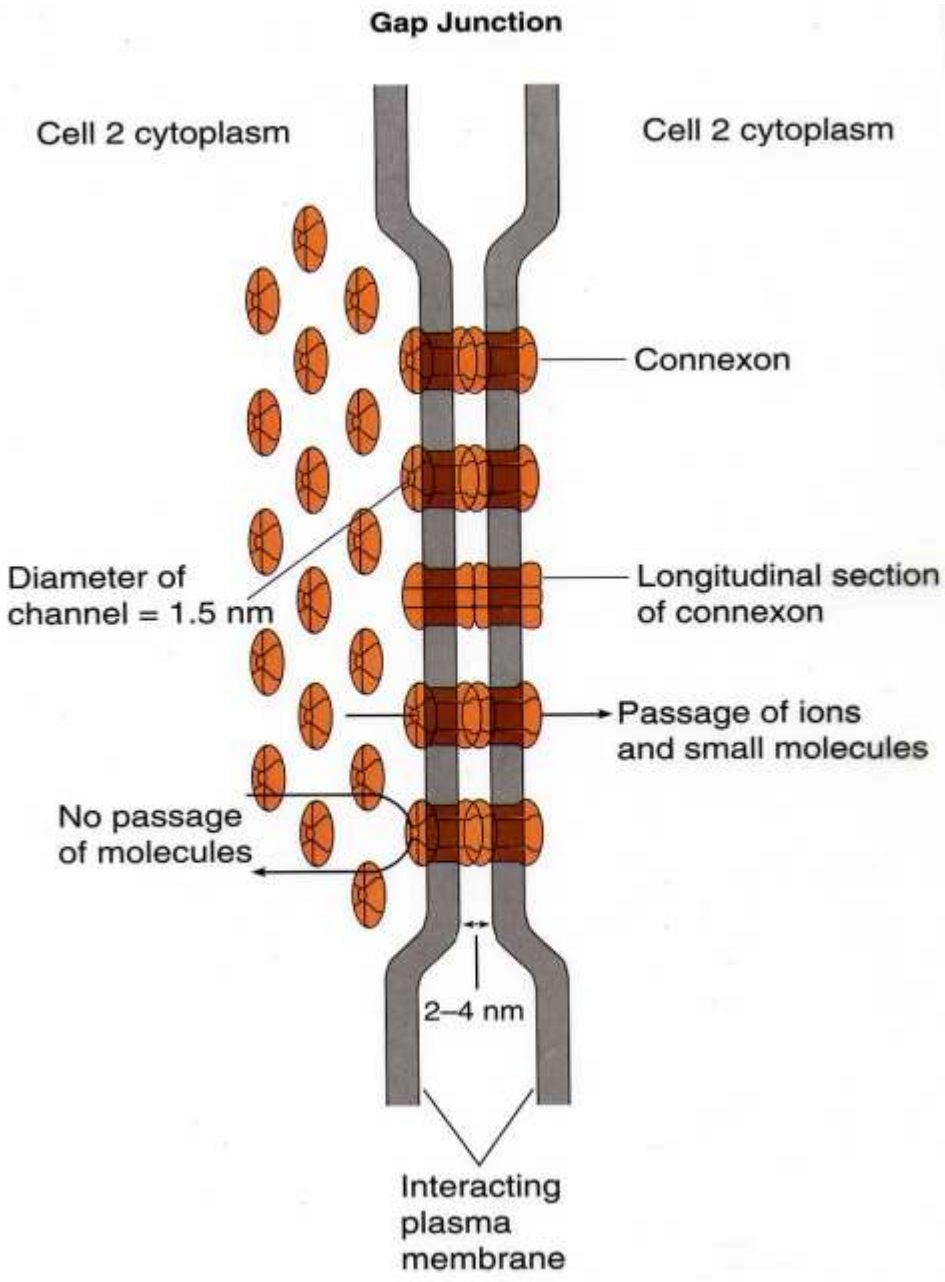
Cell Identity Markers



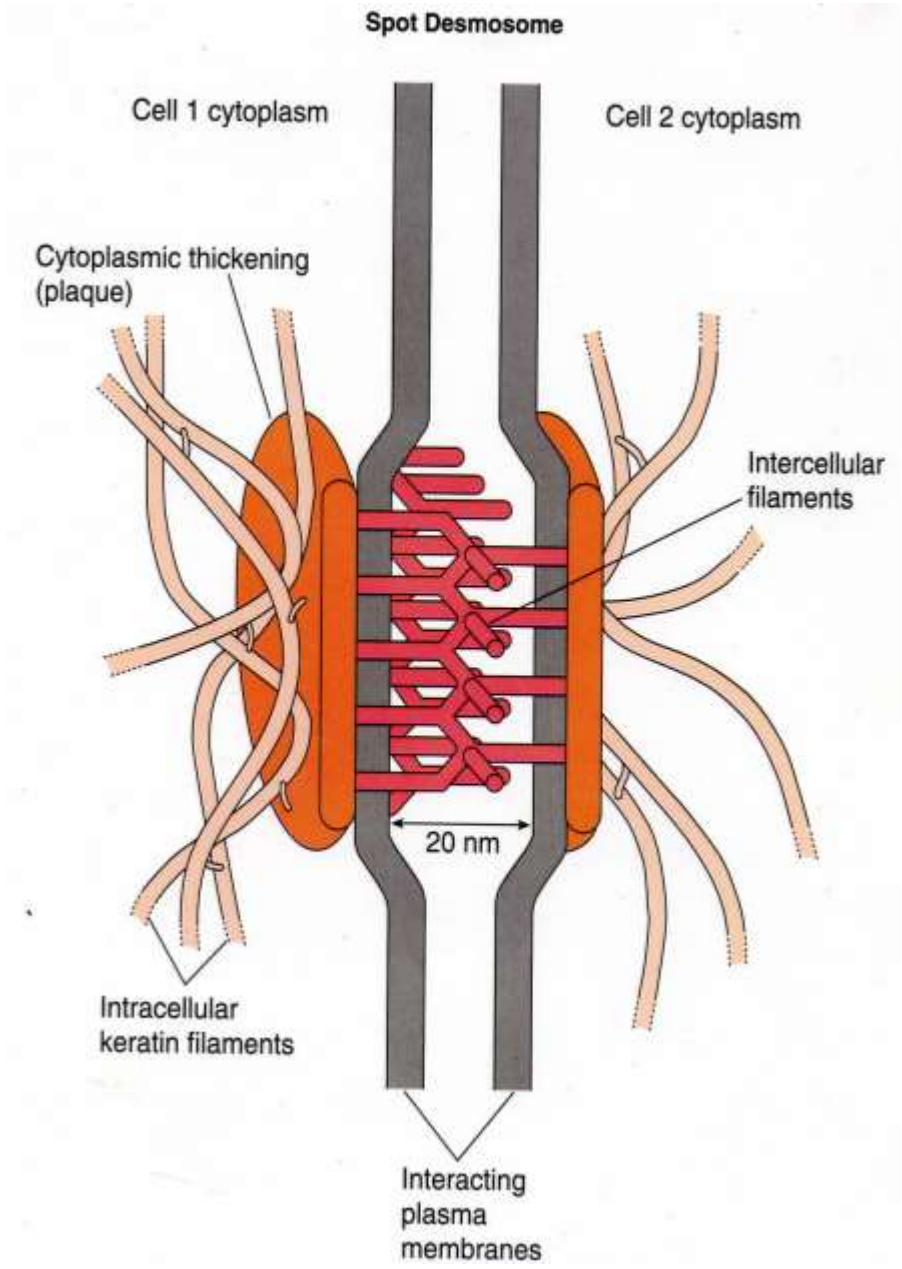
Linkers



Tight Junction



Gap Junction



Desmosome

(Adhering Junction)

Functions of Plasma Membrane Proteins