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Biomembranes and internal cell organization

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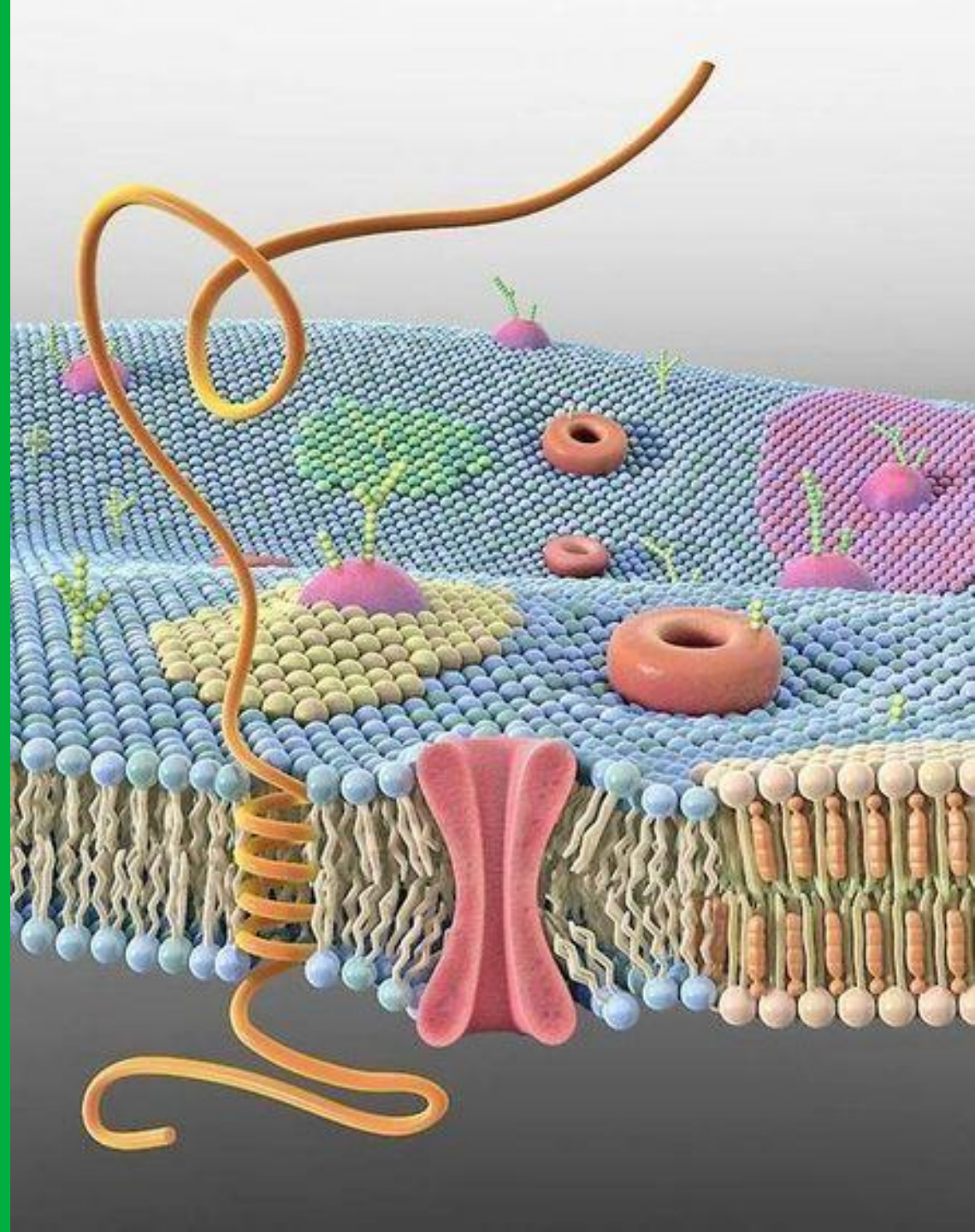


Memory system / All types of cells

– System of nucleic acids and proteins (storage and expression of genetic information)

Membrane system / All types of cells – quantitative differences

– System of biomembranes (flow of matter, energy and information)

Cytoskeletal system / Eukaryotes, analogy in prokaryotes

– System of filamentous protein structures (motility, spatial organization, communication)

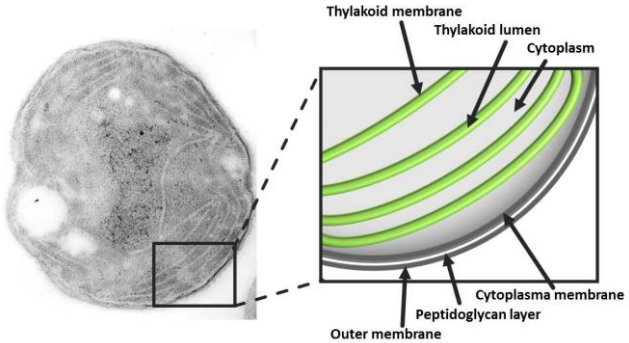
Outline

- Structure and properties of biomembranes
- Plasma membrane
- Biomembranes in prokaryotic cells
- Compartmentalization of eukaryotic cells
- Membrane fusion and vesicular transport

Structure and properties of biomembranes

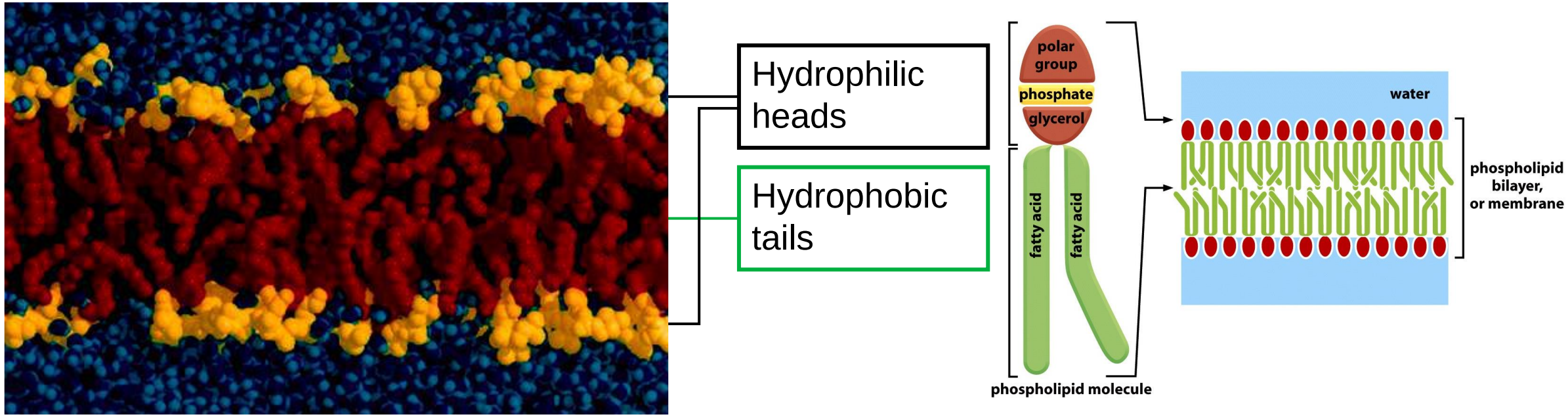
The biomembrane

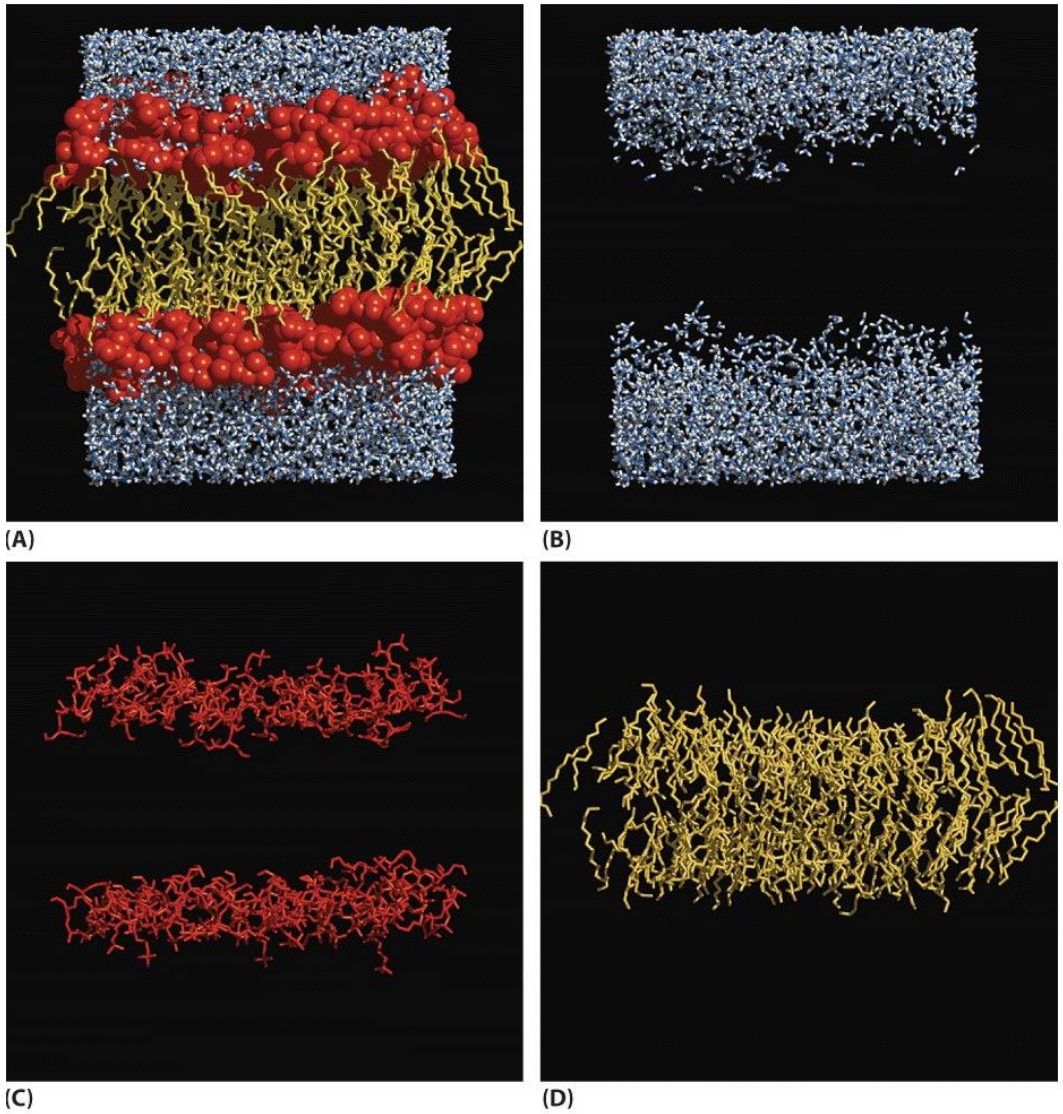
- **Lipid bilayer with embedded proteins**
- **Fluid character** – allows movement of molecules
- 5–7.5 nm thick
- **Prokaryotes**
  - **Plasma membrane**, Cyanobacteria – **thylakoids**, membrane vesicles (further reading)
  - ! Bacteria: mesosomes – invaginations of the plasma membrane (**fixation artifacts?**)
  - ! Cyanobacteria: aerotopes (gas vacuoles; formed by a single layer of !protein!)
- **Eukaryotes**
  - Plasma membrane, membrane organelles, membrane transport vesicles
  - **Compartmentalization**

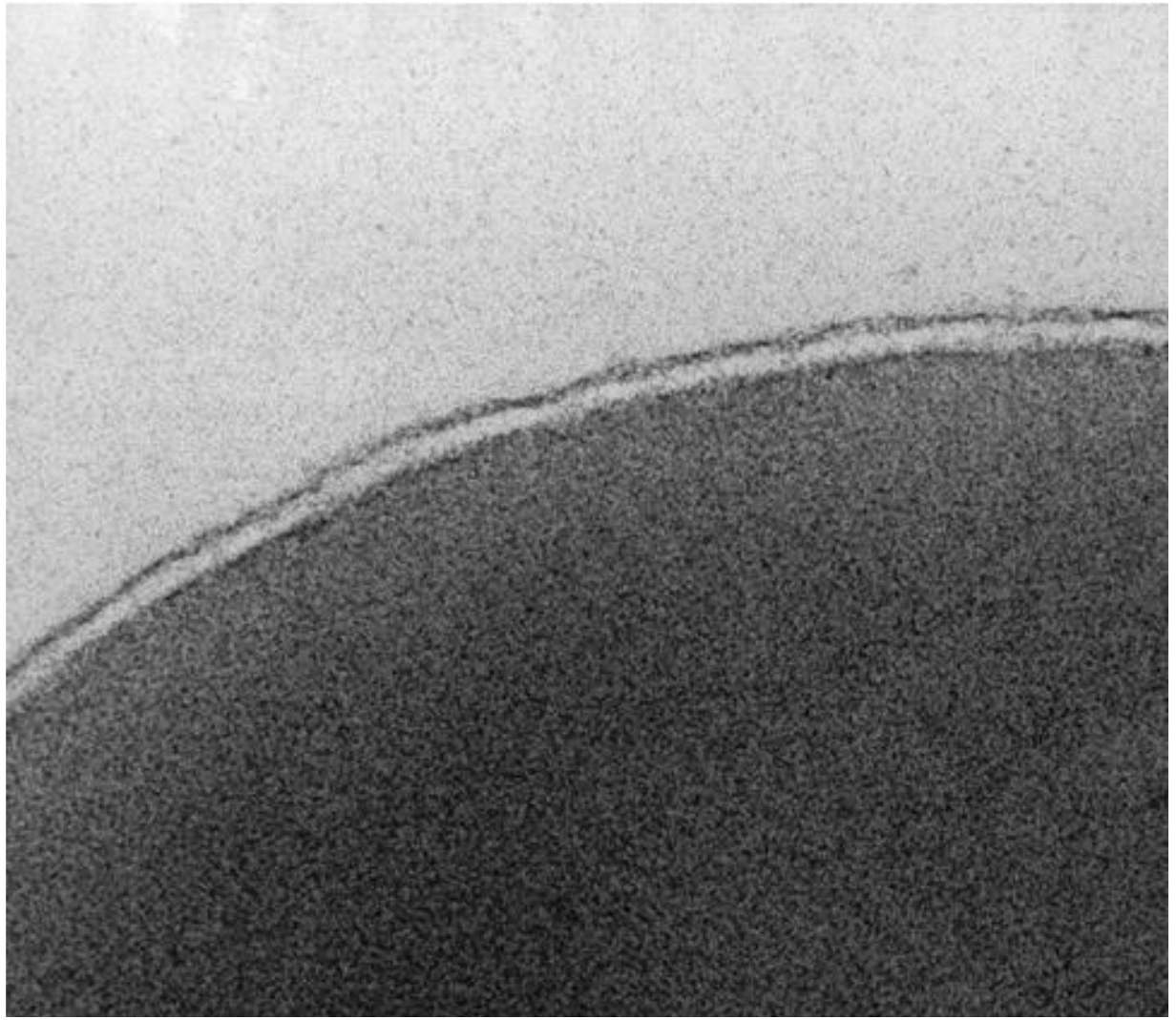


Lipid bilayer

– Universal and essential structure of biomembranes




(A)
(B)
(C)
(D)

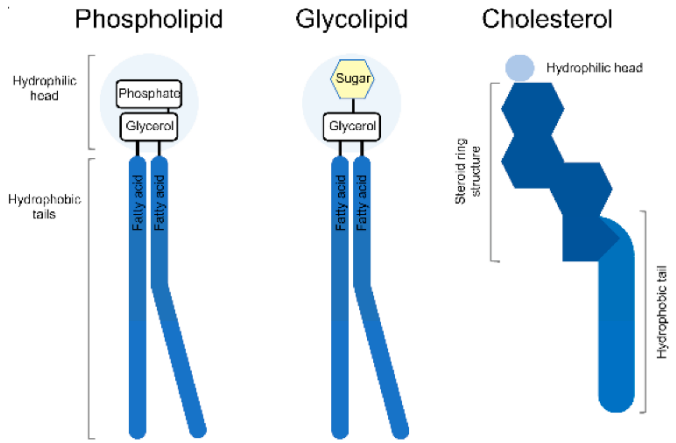


Lipid bilayer

- General structure of a membrane lipid:
  1 hydrophilic head, 1-2 hydrophobic tails

3 main types of membrane lipids:

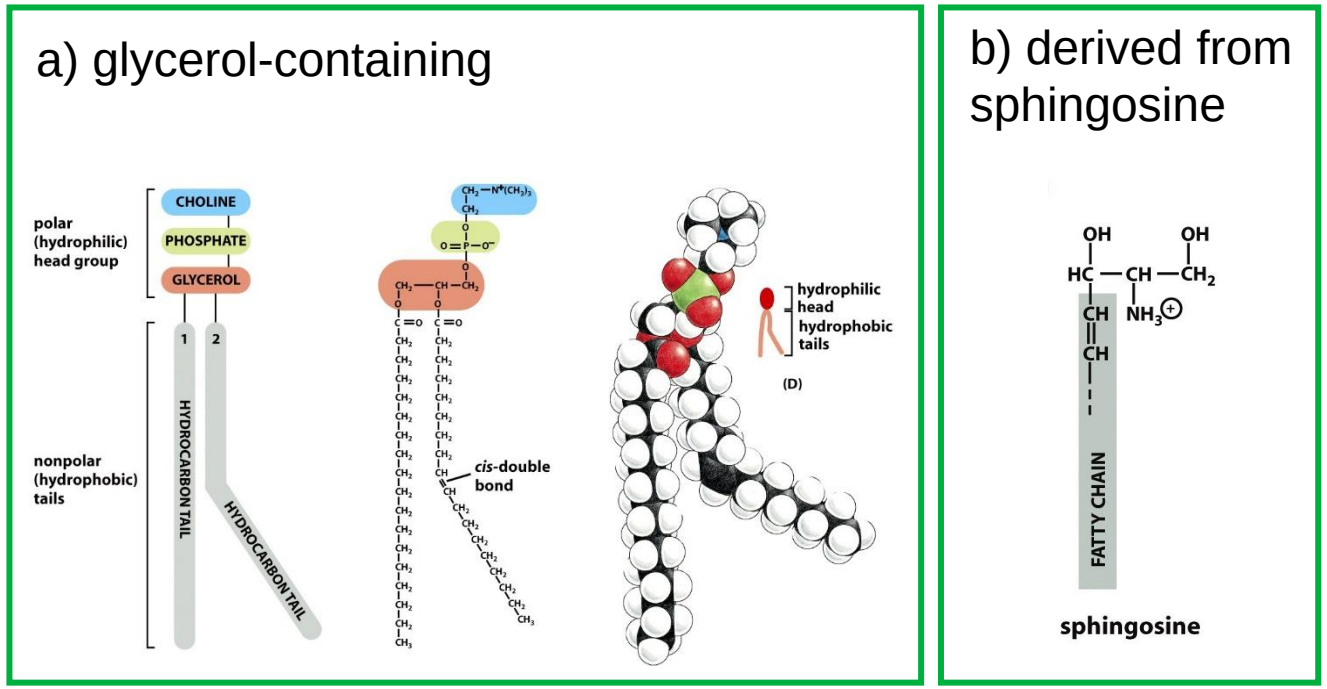
- **Phospholipids – most abundant**
- **Sterols** – regulation of fluidity
- **Glycolipids** – stability, recognition



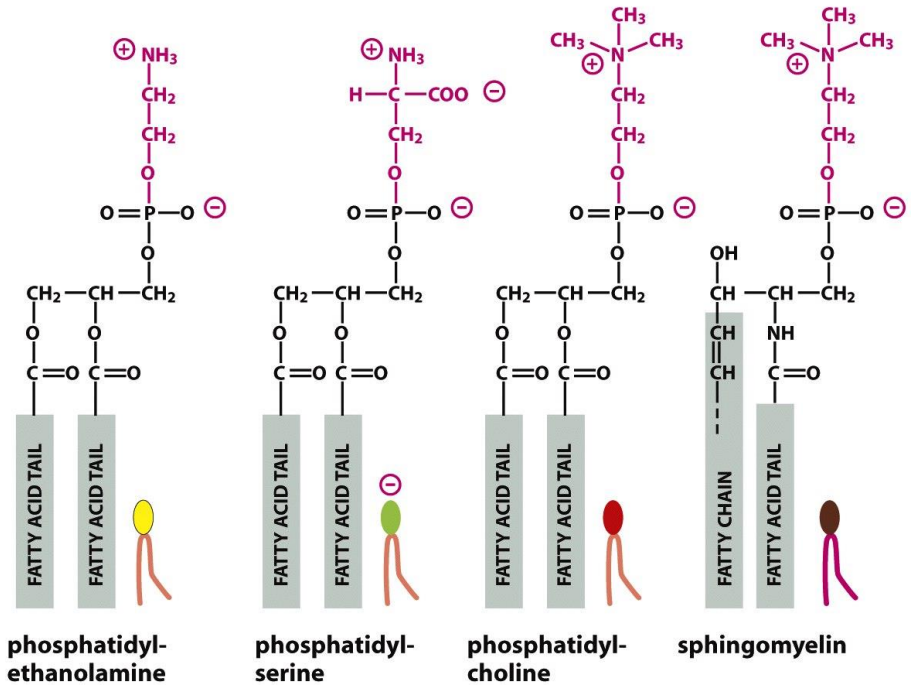
- **Asymmetric composition:** differences in the abundance of individual lipids in inner and outer layer of the bilayer

Phospholipids

– (a) **glycerolphospholipids**,
(b) **sphingophospholipids**

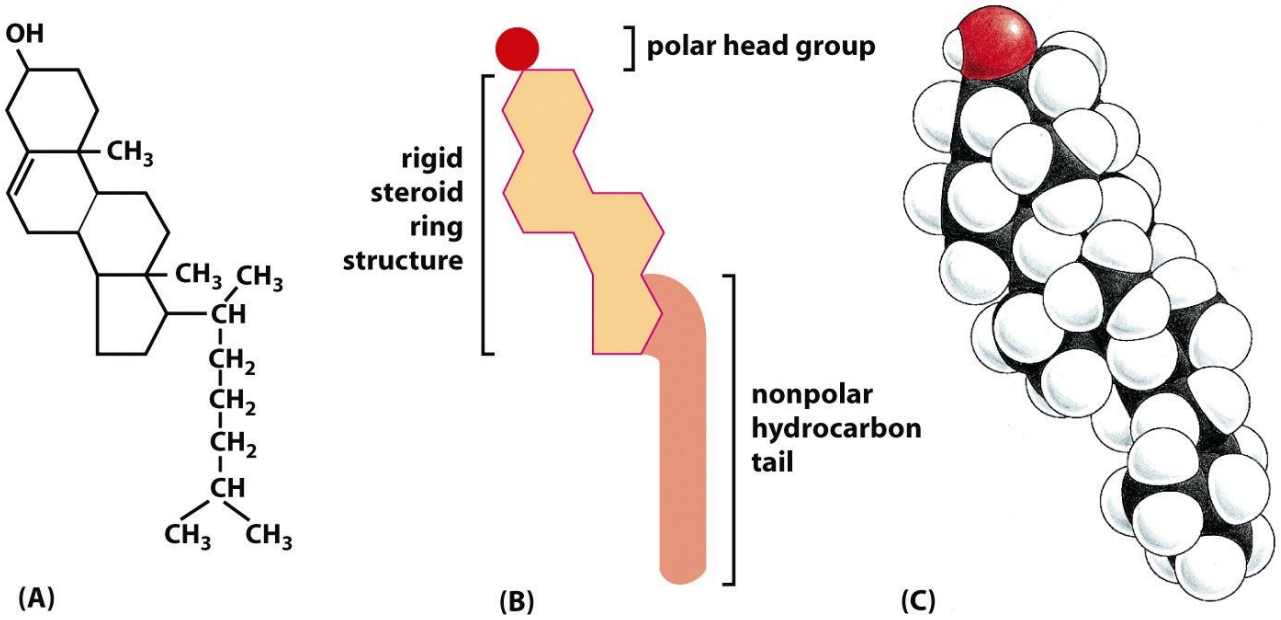


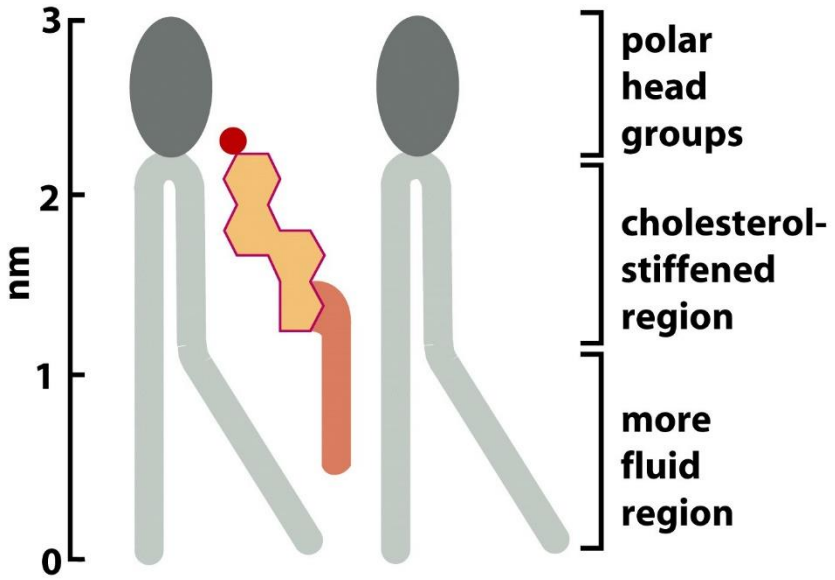
– **Major mammalian phospholipids**
(most plasma membrane mol.):



Sterols

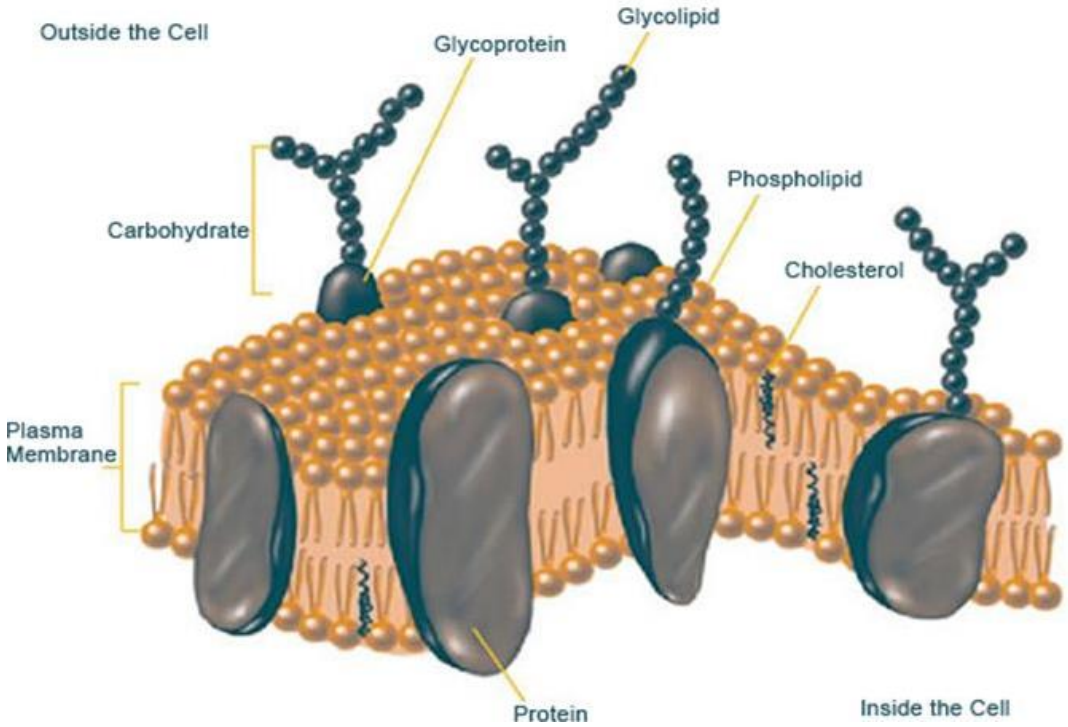
- Do not form the bilayer themselves
- **Cholesterol** – bidirectional regulation of membrane fluidity

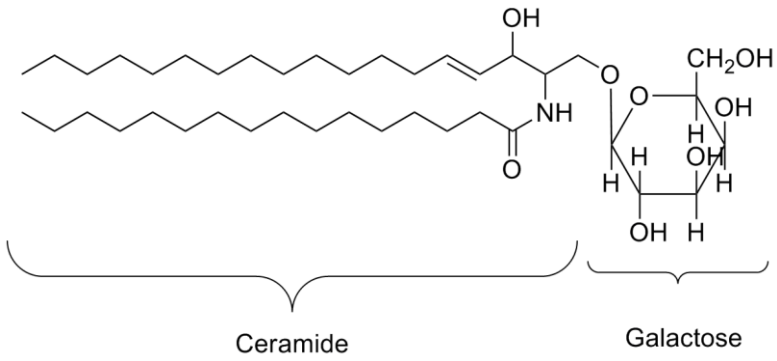




Glycolipids

- Lipids with attached carbohydrate groups (sugar)
- Appear on the membrane layer that faces extracellular space

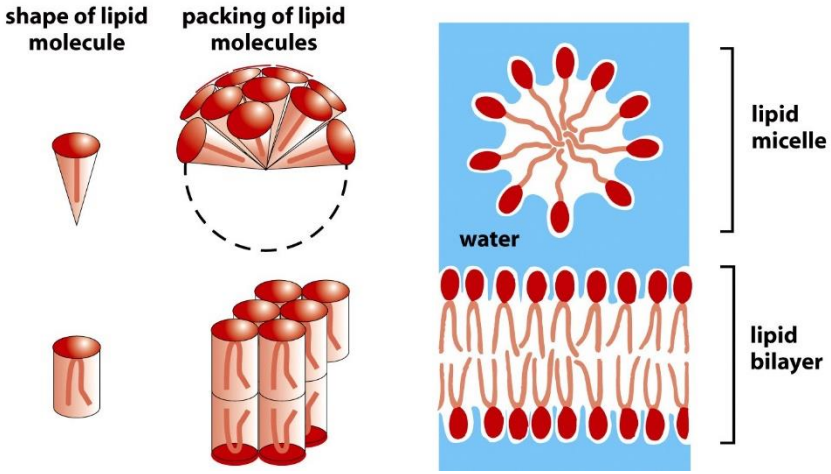


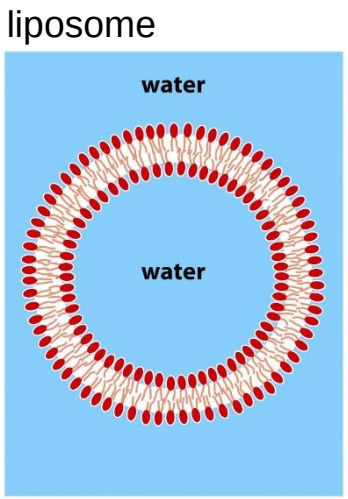


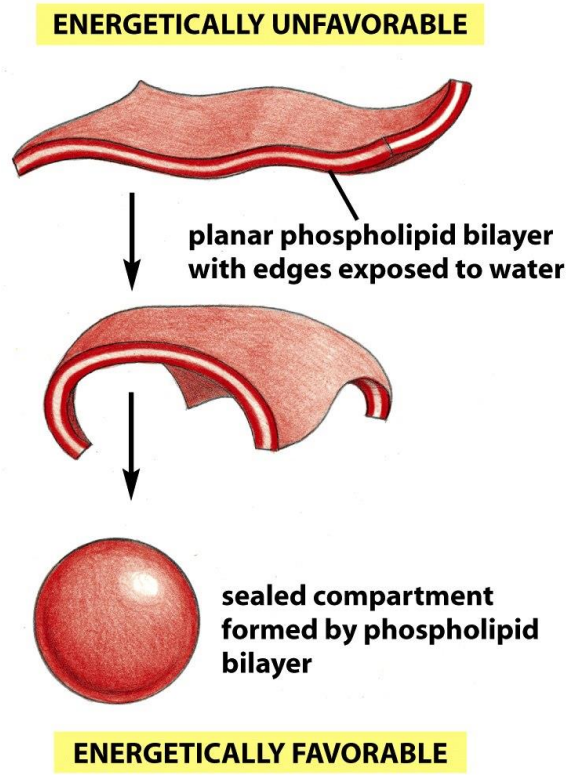
galactocerebroside

Lipids are amphiphilic

- Polar (hydrophilic) and non-polar (hydrophobic)
  → packing in an aqueous environment
- **Self-sealing nature of biomembranes**
  Spontaneously form closed structures:
  - **Liposomes**
    synthetic vesicles
  - **Micelles**
    remnants of a single lipid leaflet

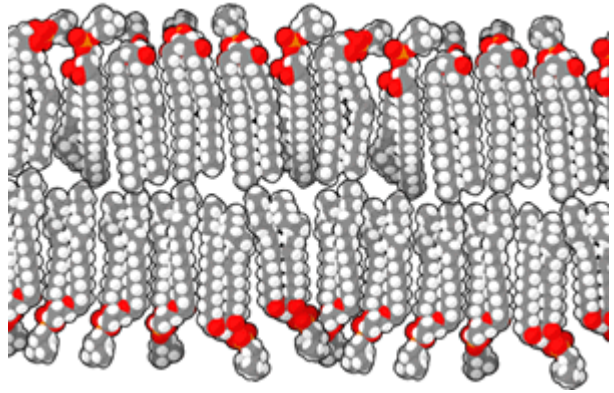






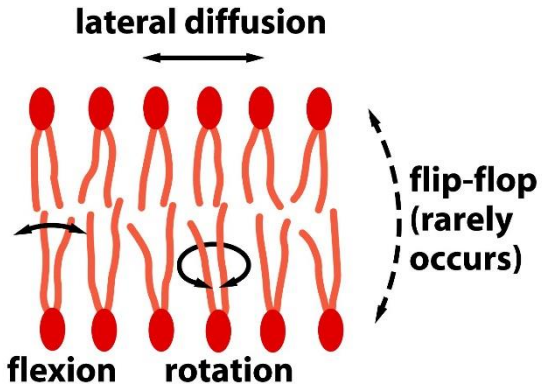
Fluidity of a lipid bilayer

- Continuous movement of the lipids



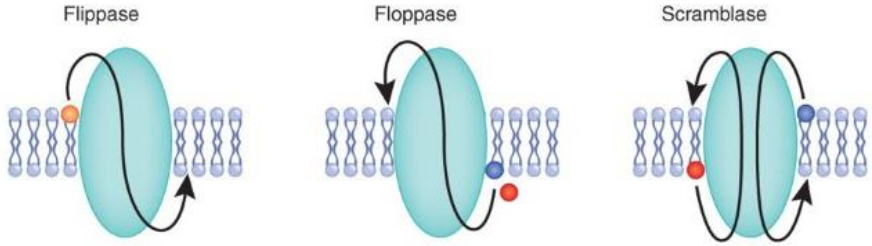
Frequent within a monolayer (leaflet)

- **Rotation**
- **Lateral diffusion**



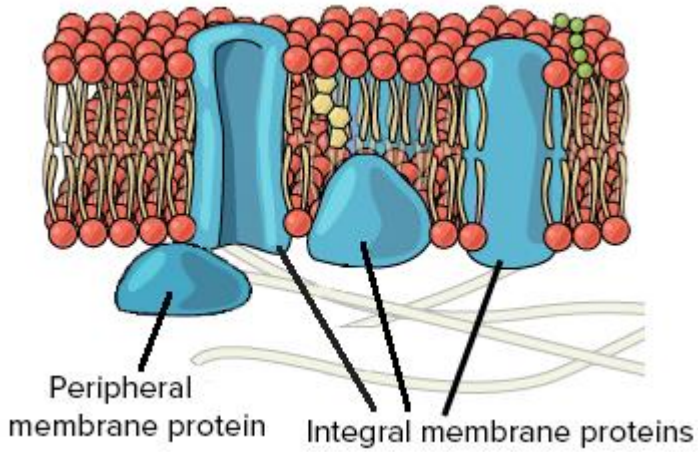
Rare between the monolayers

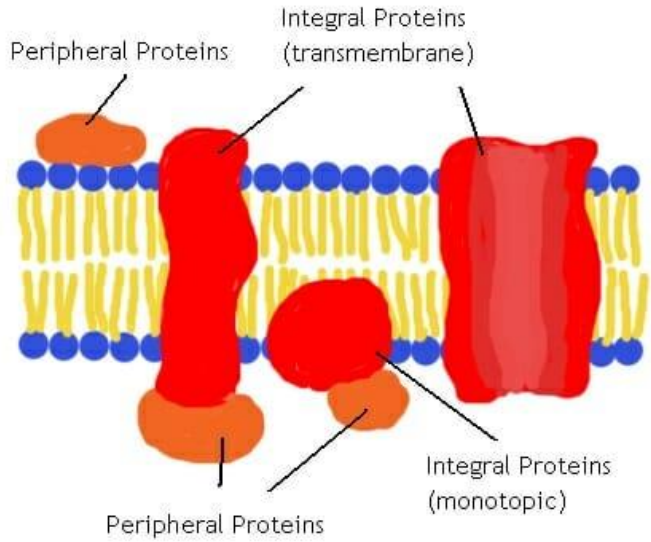
- **Flip-flop** – enzymes can catalyze rapid flip-flop: **flippase, floppase, scramblase**

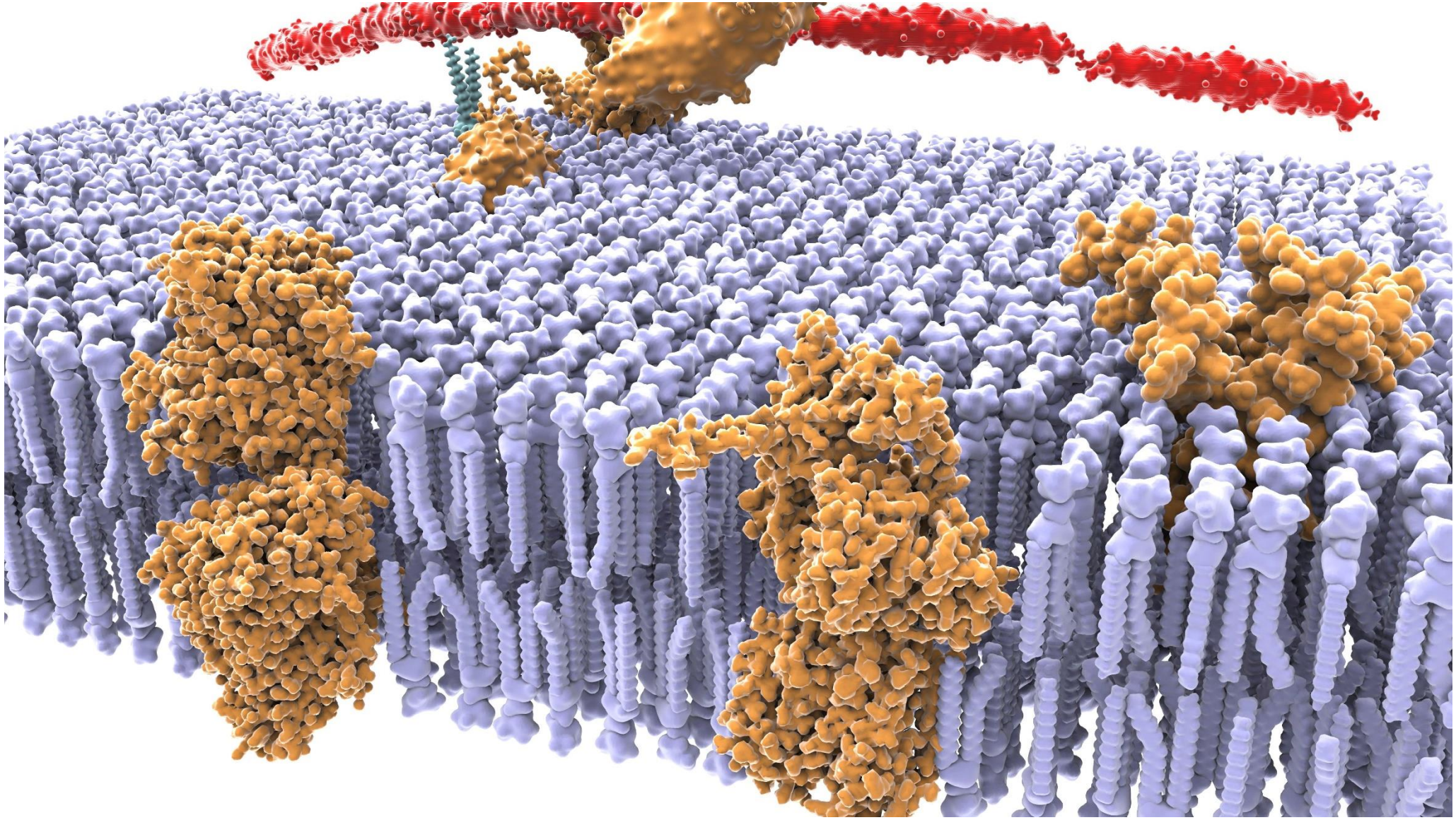


Membrane proteins

- **Integral monotypic proteins**
  - Localized at one side of the bilayer (span only one leaflet)
  - Most often bound by covalent bonds
- **Transmembrane proteins** (integral polytypic)
  - Span the bilayer (even multiple times)
  - Hydrophobic polypeptide regions inserted within the bilayer
  - Hydrophilic regions may be present at both sides of the bilayer
- **Peripheral membrane proteins**
  - Noncovalent interactions with integral proteins





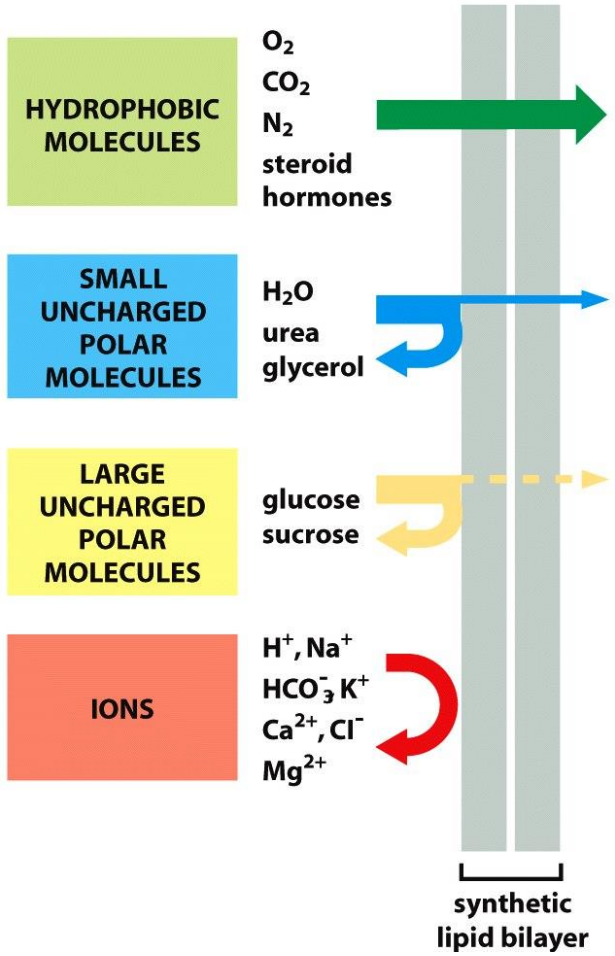


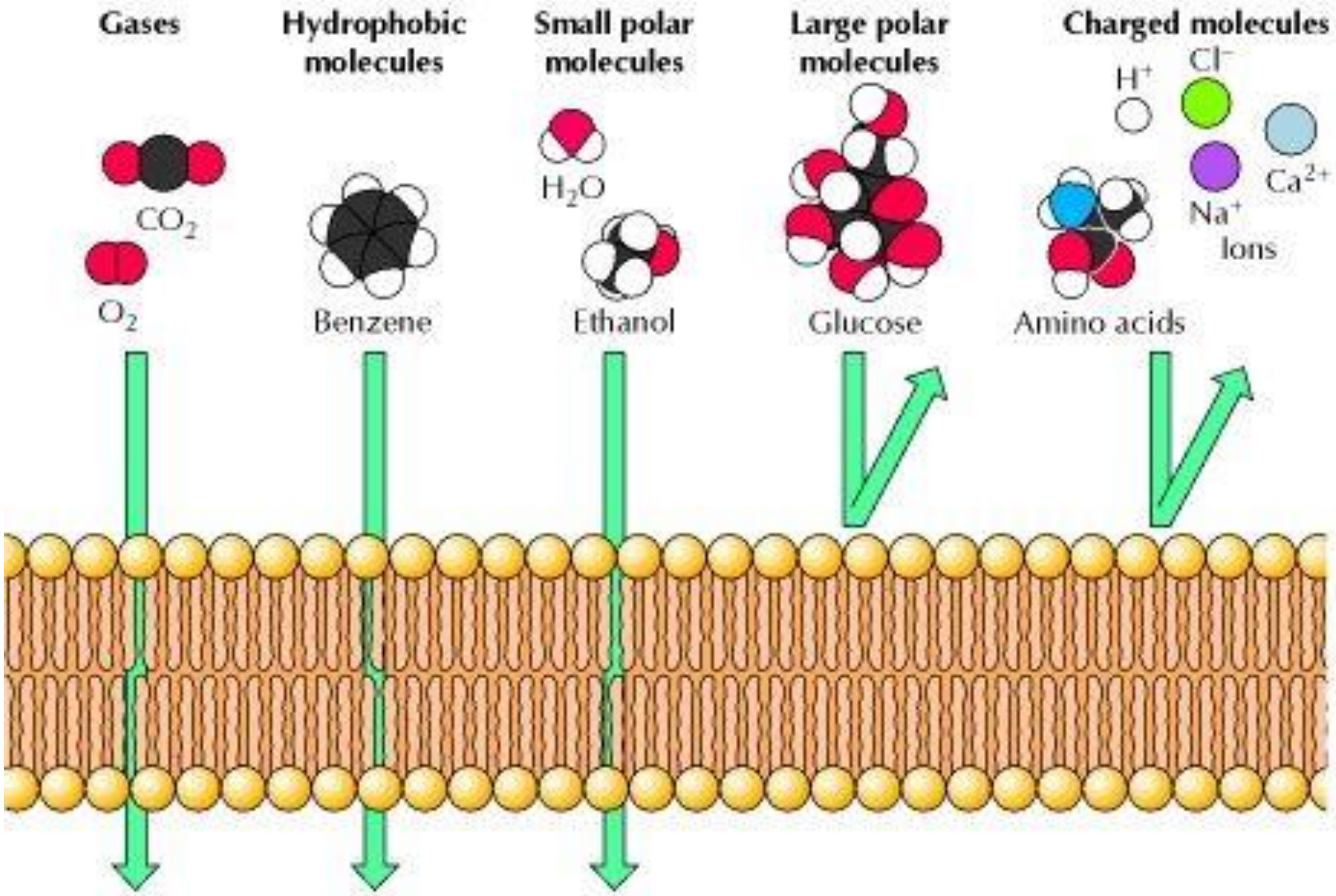
Essential biomembrane functions

- Creates a **barrier** between inner and outer environment
- Regulates **communication** between the cell and surrounding environment: transport of molecules and information (signaling)
- Cell **motility and growth** (animal cells)
- Intracellular **compartmentalization** (eukaryotes)
  - Organelles with different environment (pH, concentration of molecules) can cooperate in one cell

Membrane transport (protein-free bilayer)

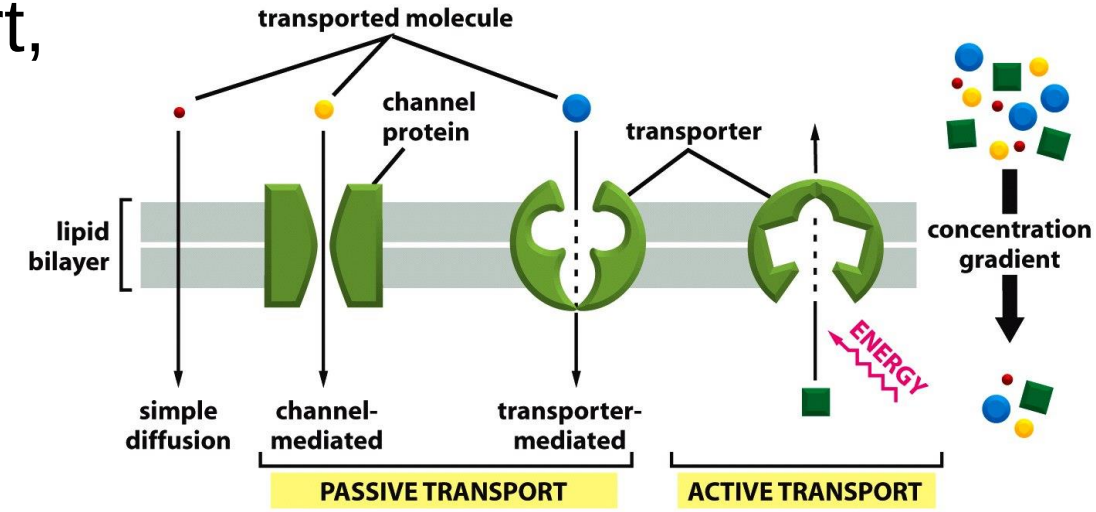
- **Semipermeable** – different permeability to classes of molecules:
- **Small nonpolar molecules** – free diffusion
- **Small uncharged polar molecules** – slow diffusion; H_2O – water channels/aquaporins
- **Large uncharged polar molecules** – impermeable
- **Ions** – **highly impermeable**




Gases
Hydrophobic molecules
Small polar molecules
Large polar molecules
Charged molecules
CO_2
O_2
Benzene
H_2O
Ethanol
Glucose
H^+
Cl^-
Ca^{2+}
Na^+
Ions
Amino acids

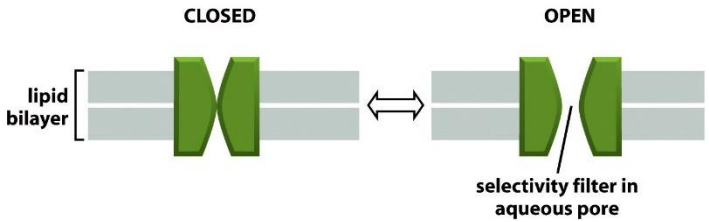
Membrane transport mechanisms

- **Diffusion**: passive transport, a substance follows concentration gradient
- **Channel-mediated**: passive transport, closed/open conformations
- **Transporter-mediated**: passive or active, conformational change mediates transport
- Endocytosis/exocytosis – transport using membrane vesicles

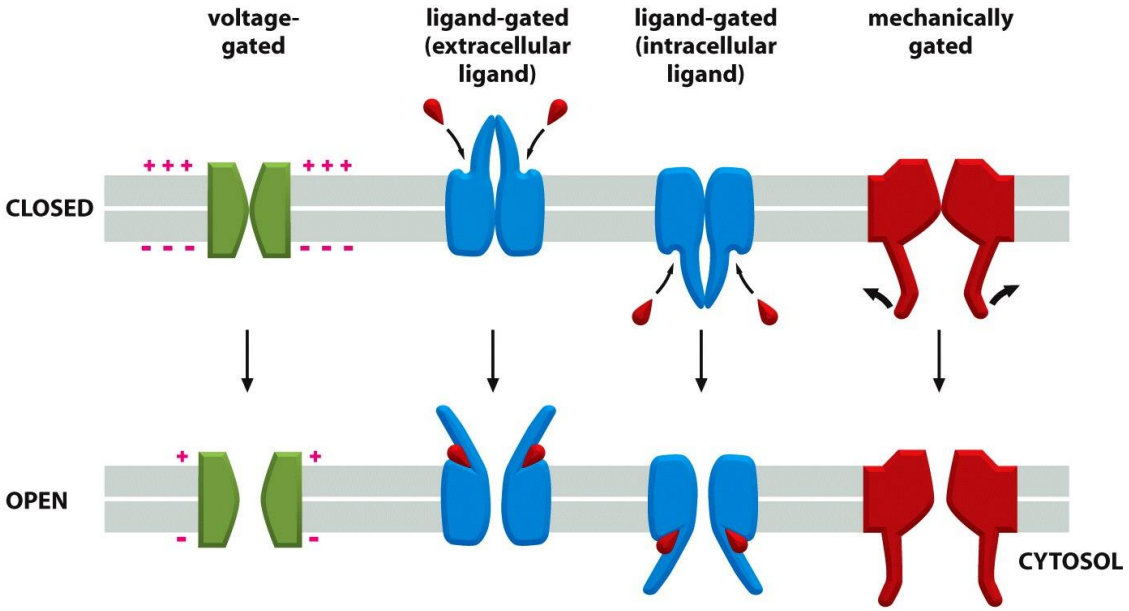


Channel-mediated transport

Ion channels

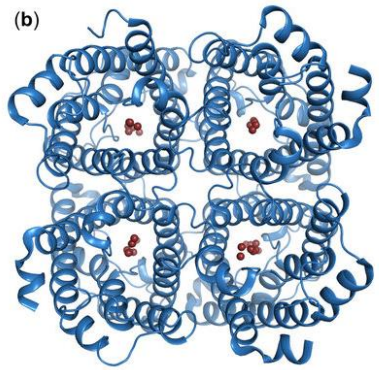


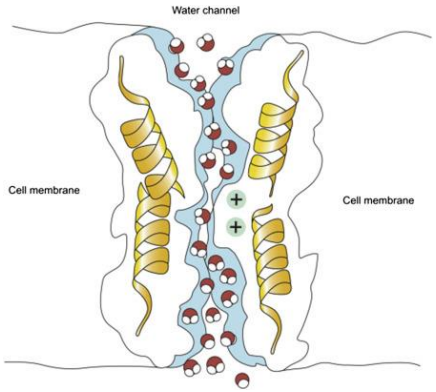
- Ion selectivity
- **Gating** – closed/open conformation regulated by different mechanisms



Aquaporins / bacterial water channels

- Rapid passage of water molecules

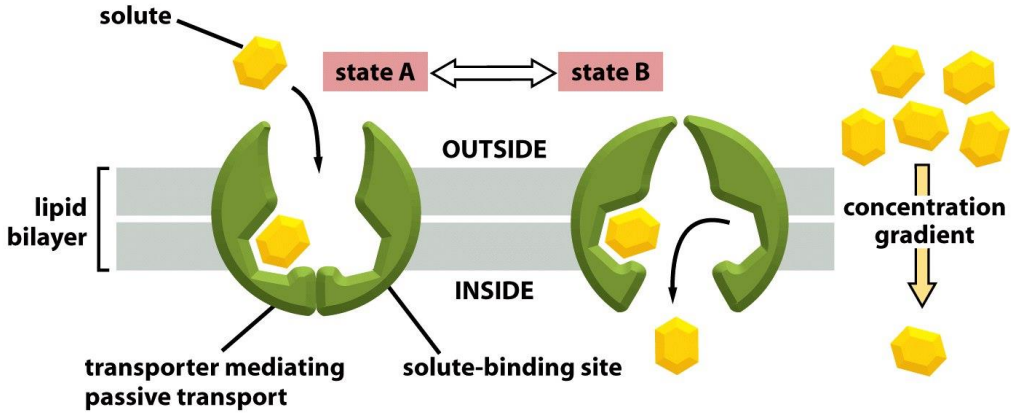




Transporter-mediated transport

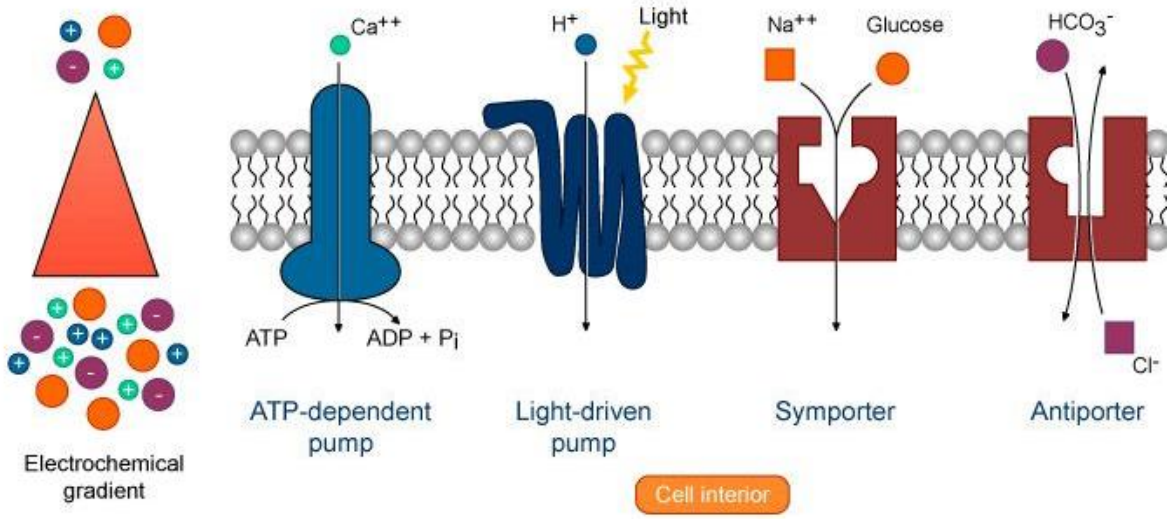
Passive (downhill)

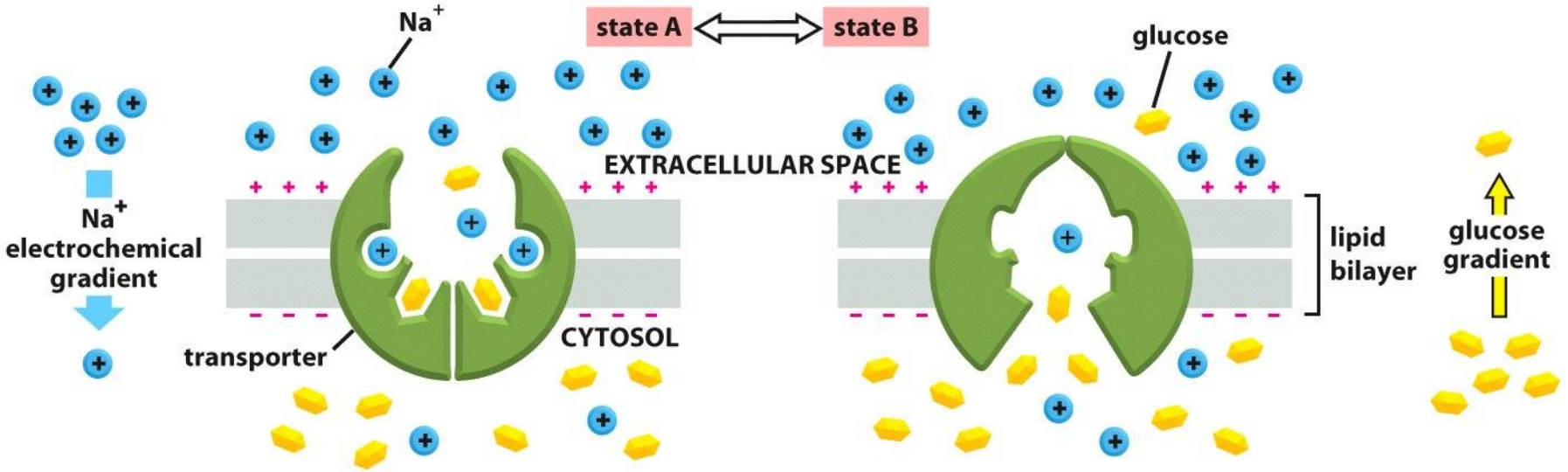
- Binding of a solute induces conformation changes



Active (uphill)

- **Primary:** ATP-driven or light-driven pumps
- **Secondary:** symport vs. antiport
  - Coupled transport; e.g. symport of glucose by Na+ gradient

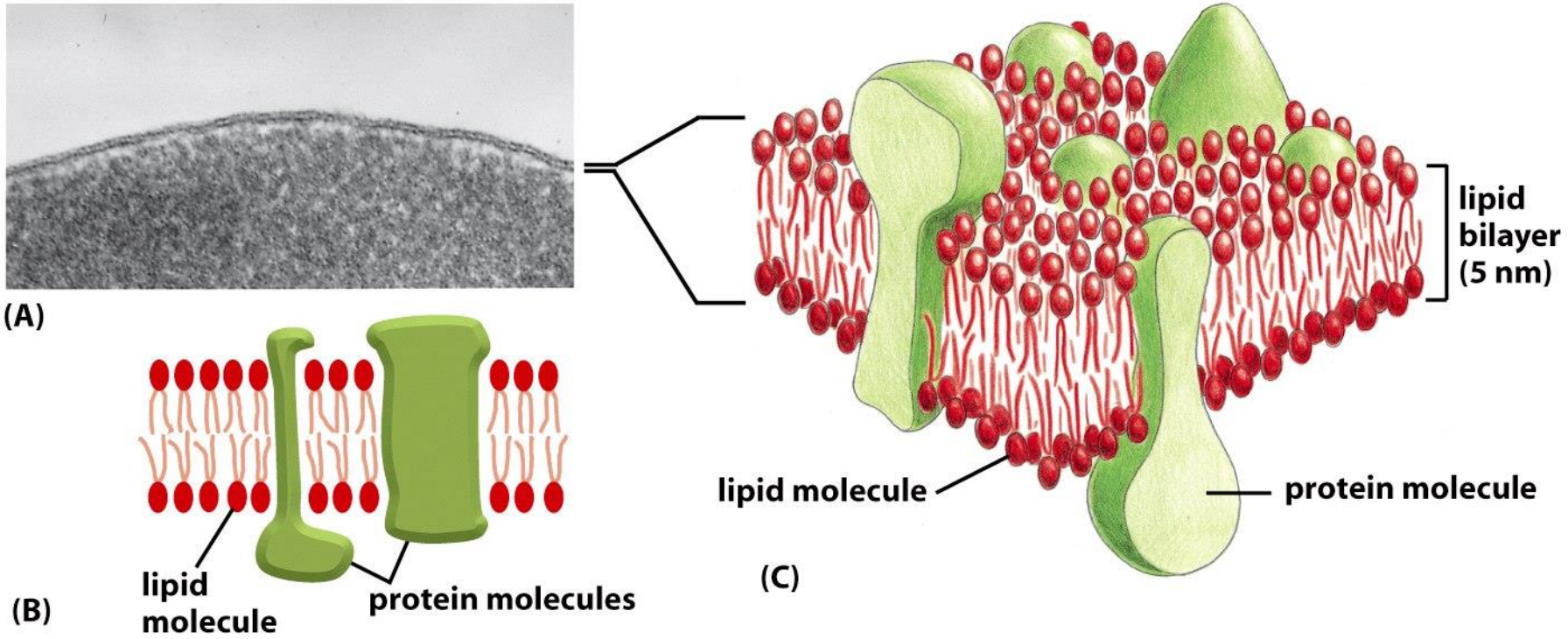




Symport of glucose: Sodium-dependent glucose cotransporter in enterocytes

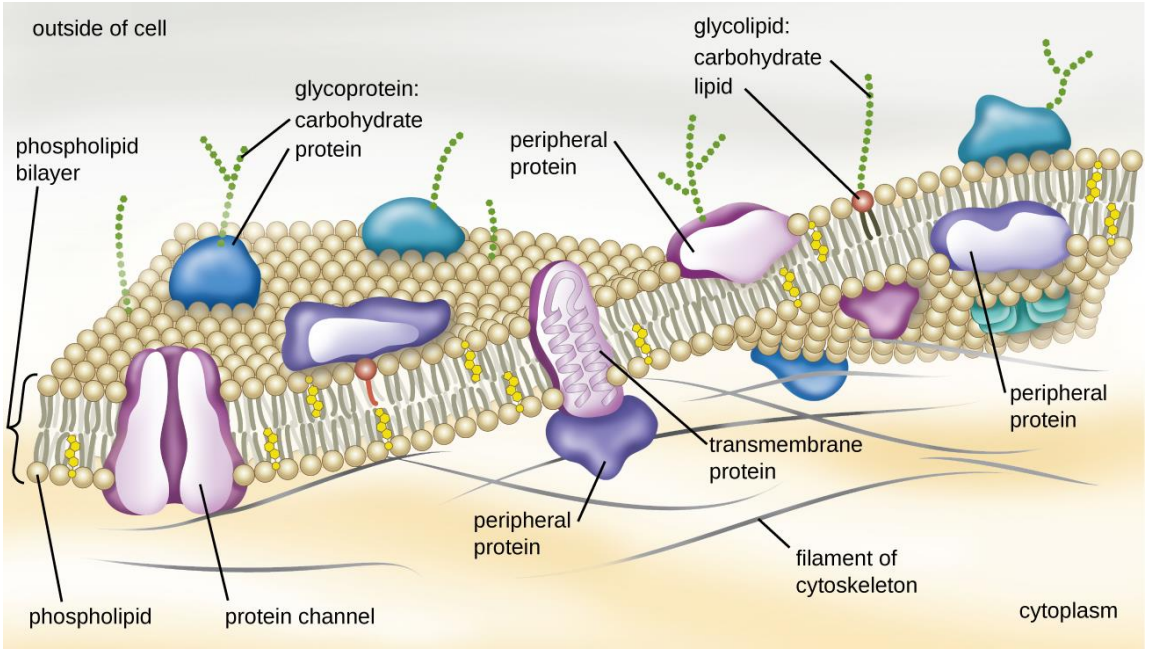
Plasma membrane

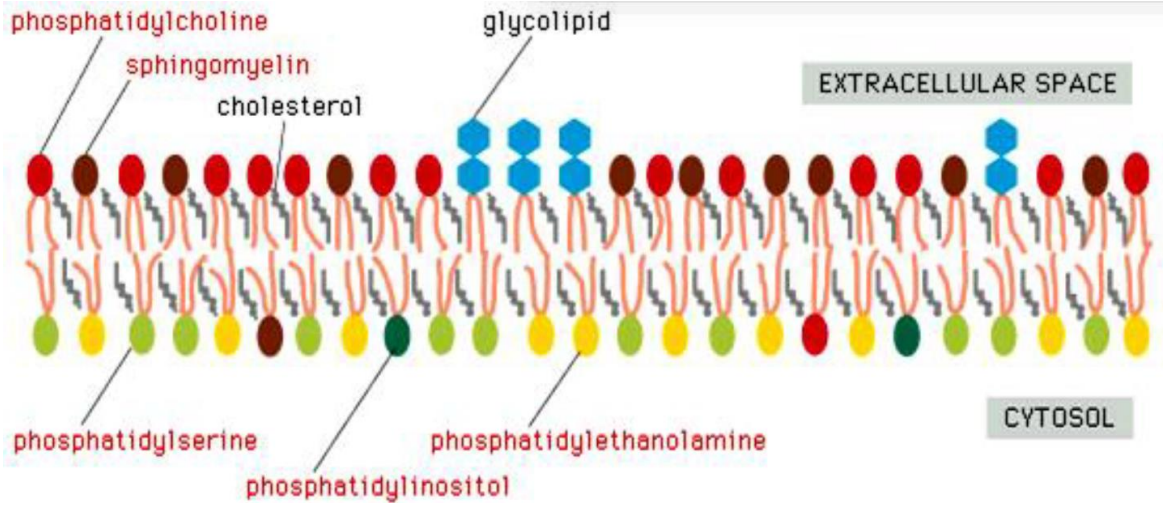
Shows a prototypical biomemebrane structure



Plasma membrane

- A barrier, regulating flow of substances, energy and information
- **Asymmetric composition – important functional roles**
  - **Carbohydrates** of glycoproteins and glycolipids **always point outside the cell**: cell recognition and cell-cell interactions
  - **Reflecting cell health**: phosphatidylserine exposure (outside) during apoptosis – “eat me signal” – cell engulfed by macrophages





Lipid rafts

- Plasma membrane microdomains, tightly packed lipids and proteins
- Thicker and **highly organized** – move freely in the membrane
- Animal cells – rich in **sphingolipids and cholesterol**
- Plant cells – rich in **phytosterols**
- **Signaling organization centers**
  - Close interactions of protein receptors and their effectors
  - Compartmentalization of signaling components
- Two major types: **planar lipid raft** and **caveola**

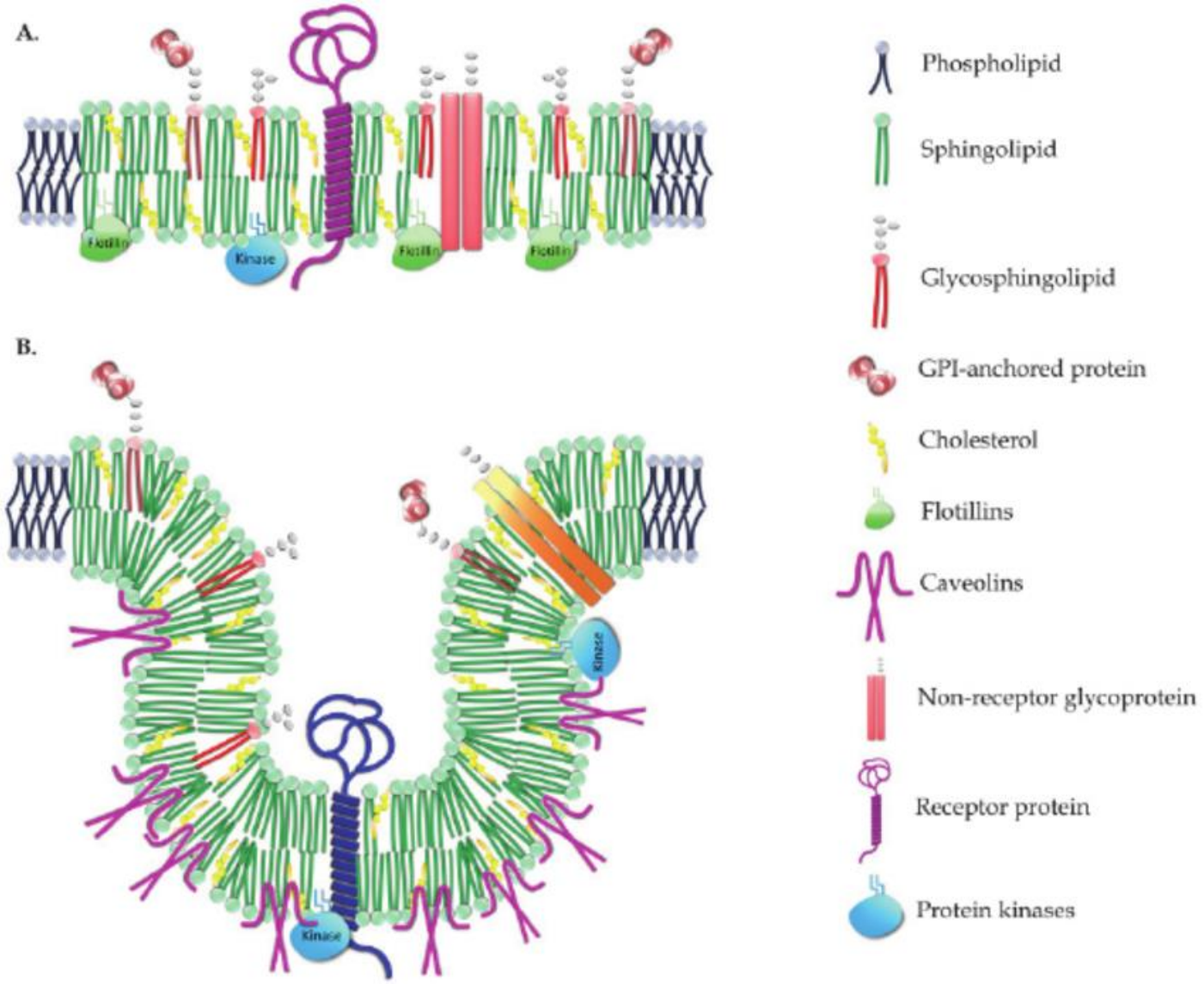
Lipid rafts

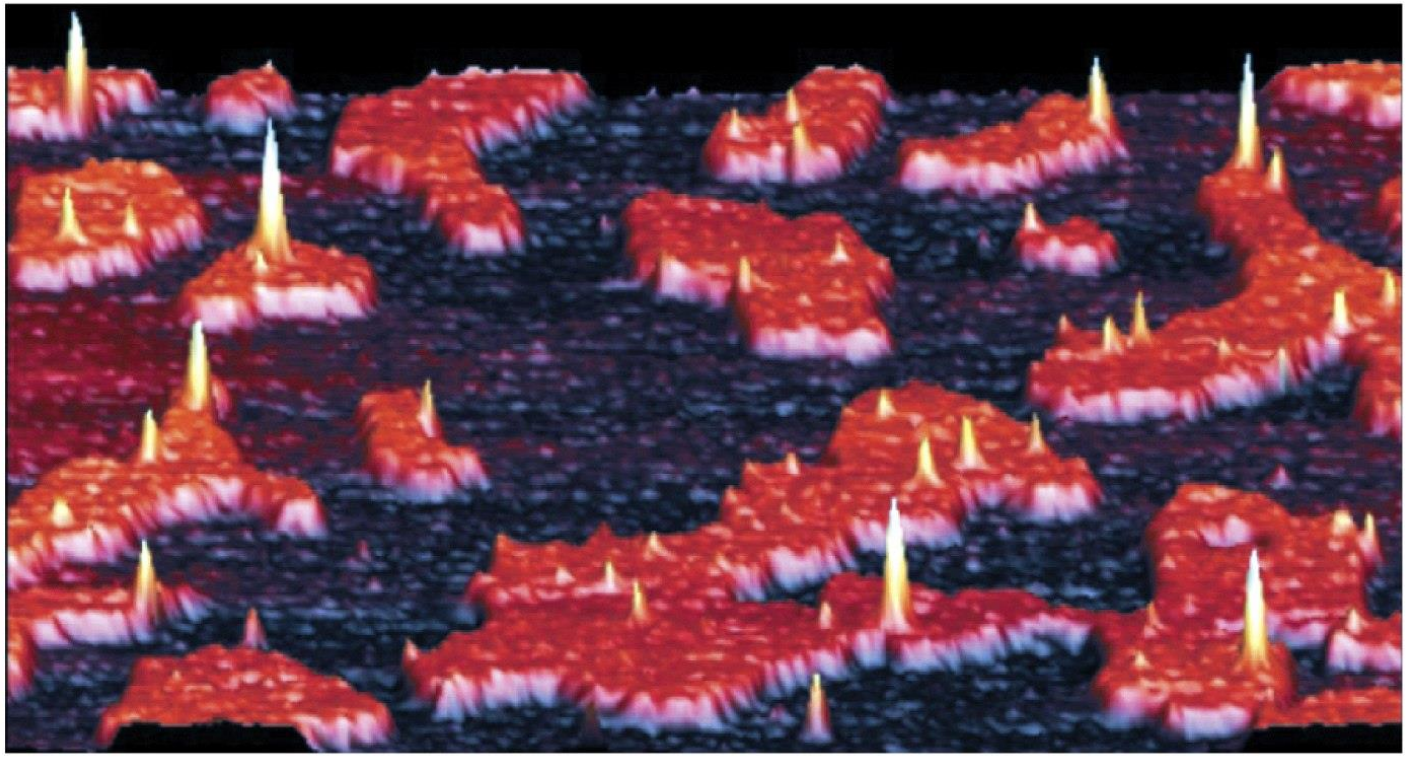
Planar lipid raft

- Flotillin-rich

Caveola

- Caveolin-rich
- Caveolin – scaffold protein important for formation of the invaginations





Lipid rafts visualized by atomic force microscopy

Localization of membrane proteins

– Restricted to specific domains also by:

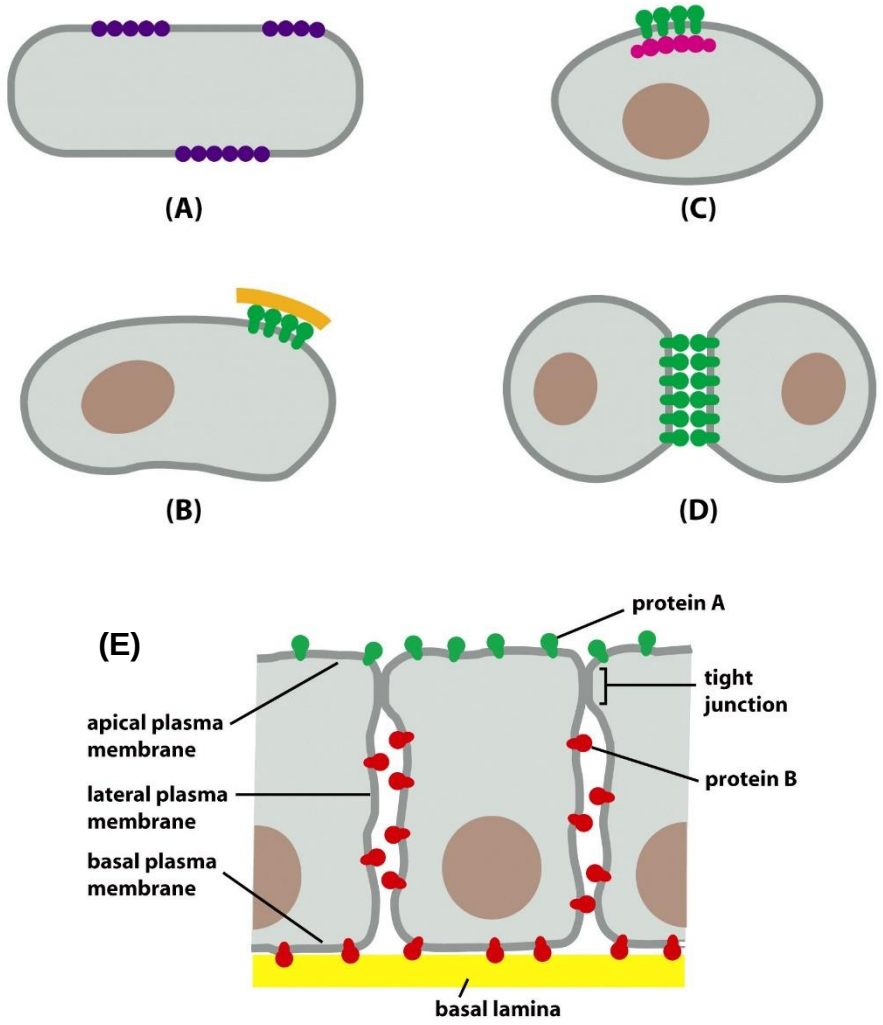
(A) **aggregation** (e.g., bacteriorhodopsin)

(B) **interactions with ECM** (e.g., integrins)

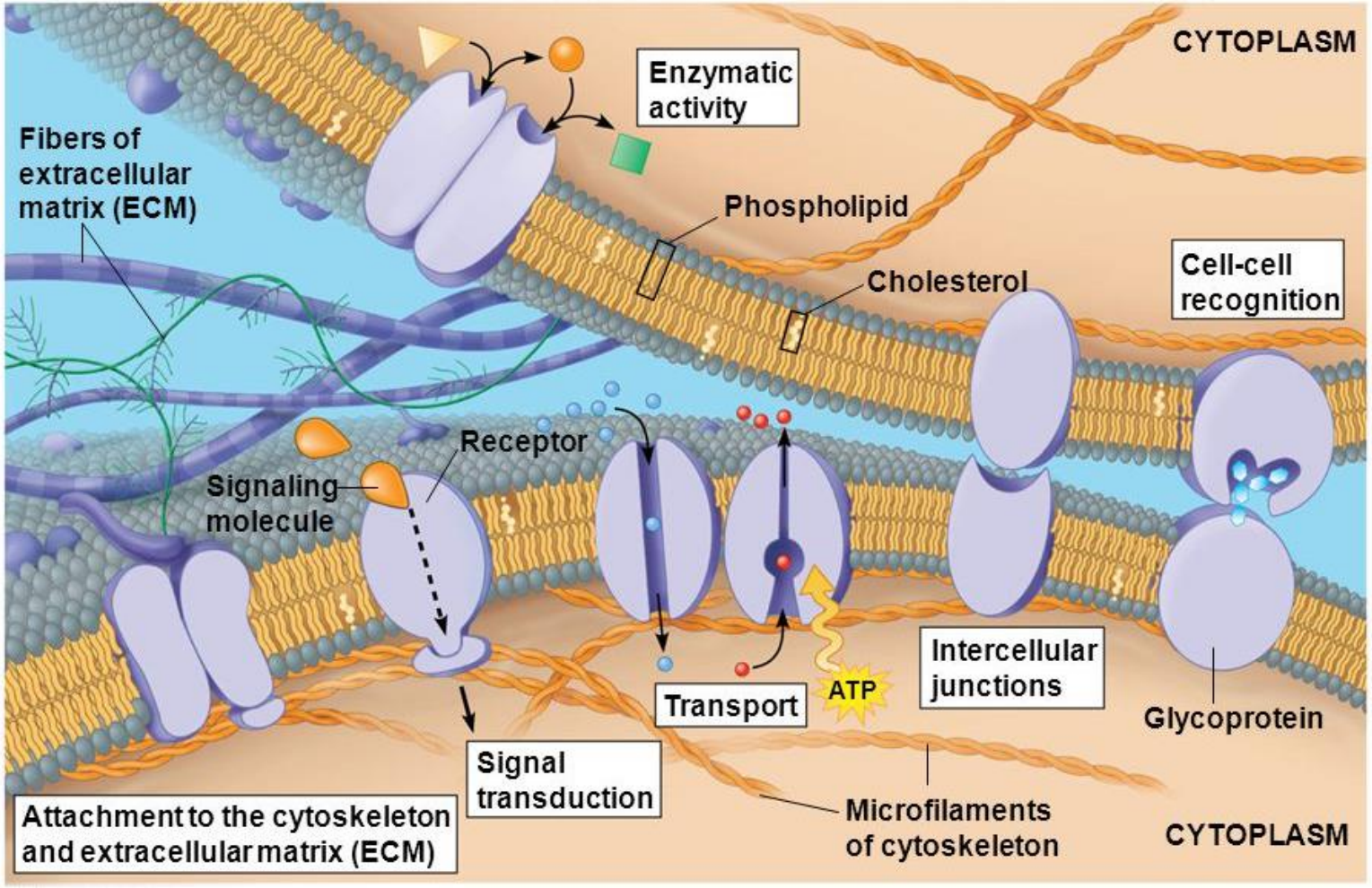
(C) **interactions with cytoskeleton** (e.g., E-cadherin to actin via catenin)

(D) **intercellular protein-protein interactions** (e.g., E-cadherin)

(E) **tight junctions** (specialized intercellular junctions; e.g., in entorocytes)



Functions of membrane proteins



Osmosis


OSMOSIS
The movement of ~~solvent molecules~~ *cats* through a membrane into a region of ~~higher solute~~ *lower cat* concentration.

Osmosis

- Semipermeable plasma membrane
- **Solvent (water) can freely enter the cell** (diffusion & !aquaporins/water channels)
- **Solutes mostly impermeable**
- **Solvent tends to equalize the solute concentrations on the two sides of the plasma membrane**

- **Osmotic effects**

Osmotic effects

Osmotic gradient (concentration of solute inside vs. outside the cell)

Hypotonic solution (>)

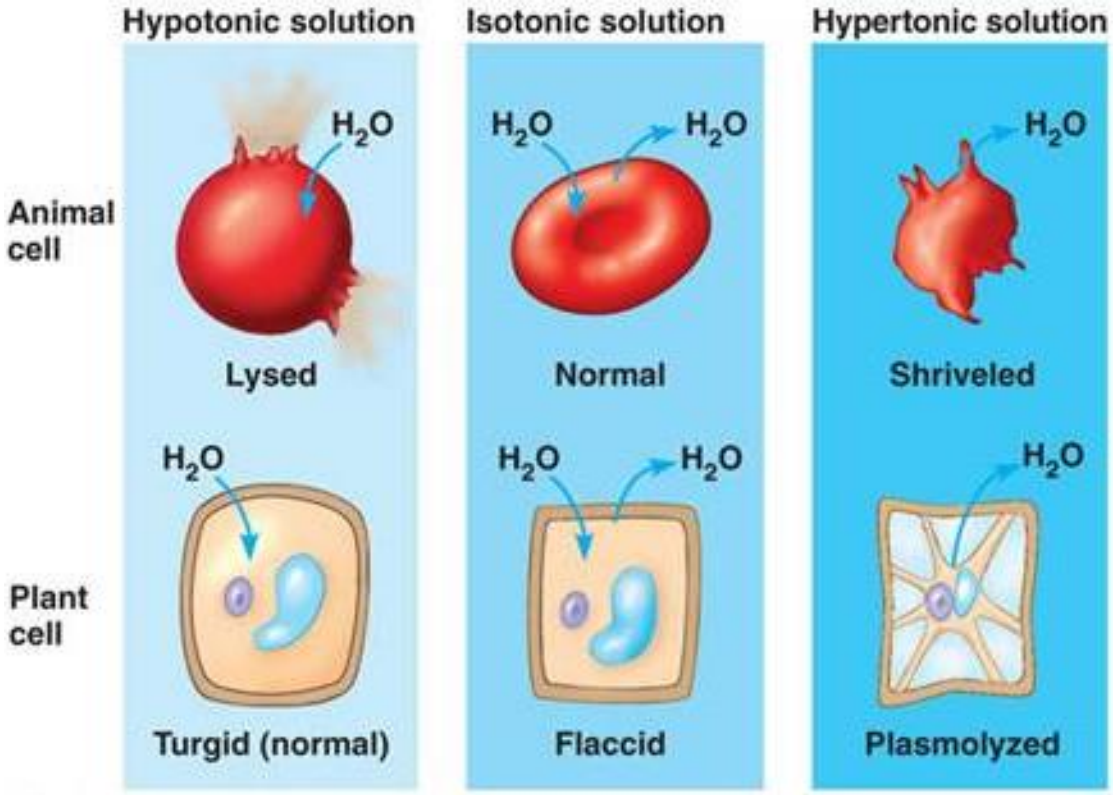
- Water enters the cell, increased volume
- **Animal cells: plasmoptysis/osmotic lysis** (in erythrocytes **osmotic hemolysis**)

Hypertonic solution (<)

- Cell loses water, reduced volume of cytoplasm
- **Animal cells: plasmorhisis** (shrinkage)
- **Plant cells: plasmolysis**

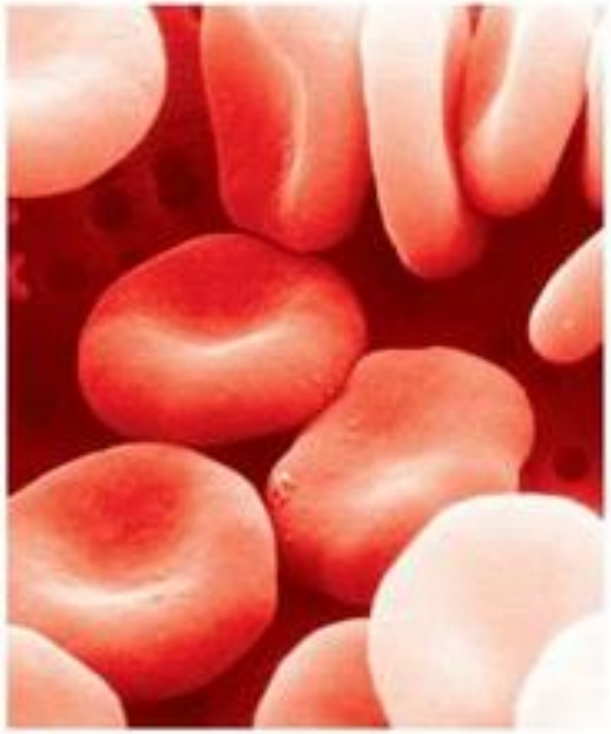
Isotonic solution (=)

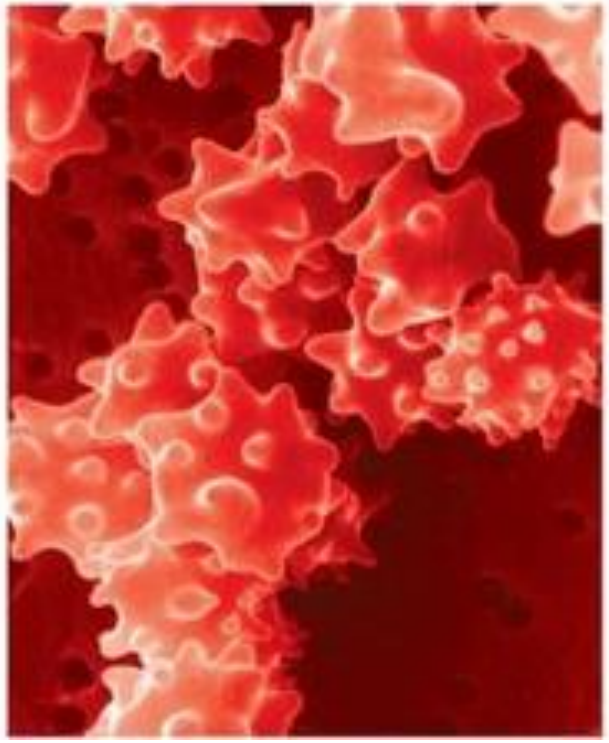
- Water passes the membrane in both directions



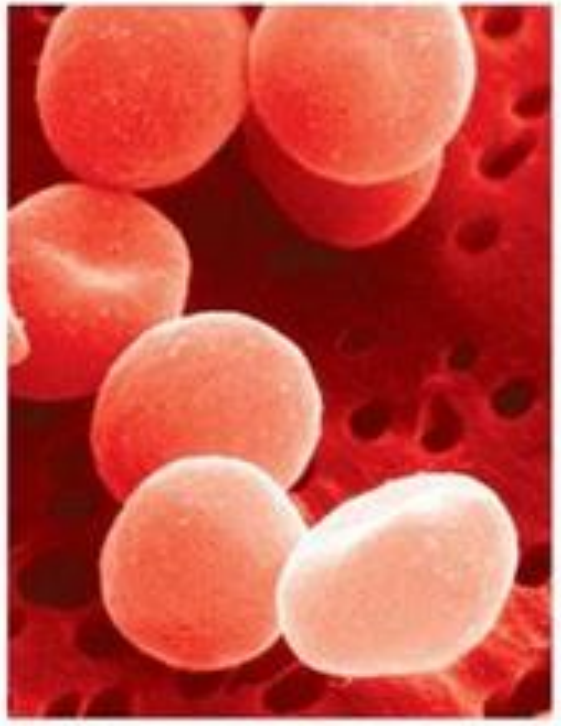
Red blood cells under different osmotic pressure

?





echinocytes



spherocytes

Biomembranes in prokaryotes

Prokaryotic cells

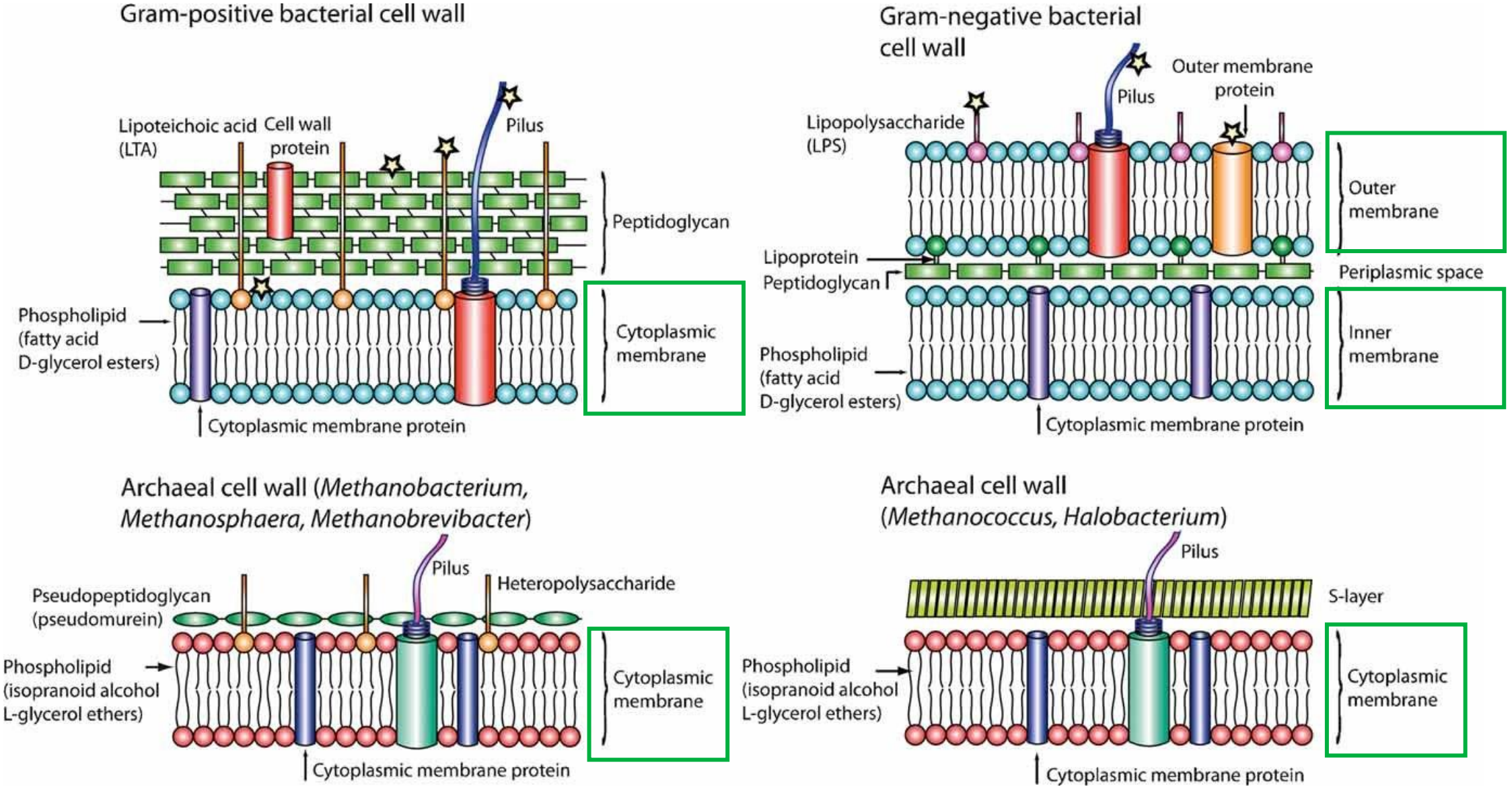
- **Plasma membrane** covered by cell wall (peptidoglycan)

Gram-negative bacteria

- **Additional outer membrane, periplasmic space**

Gram-positive bacteria, Archea

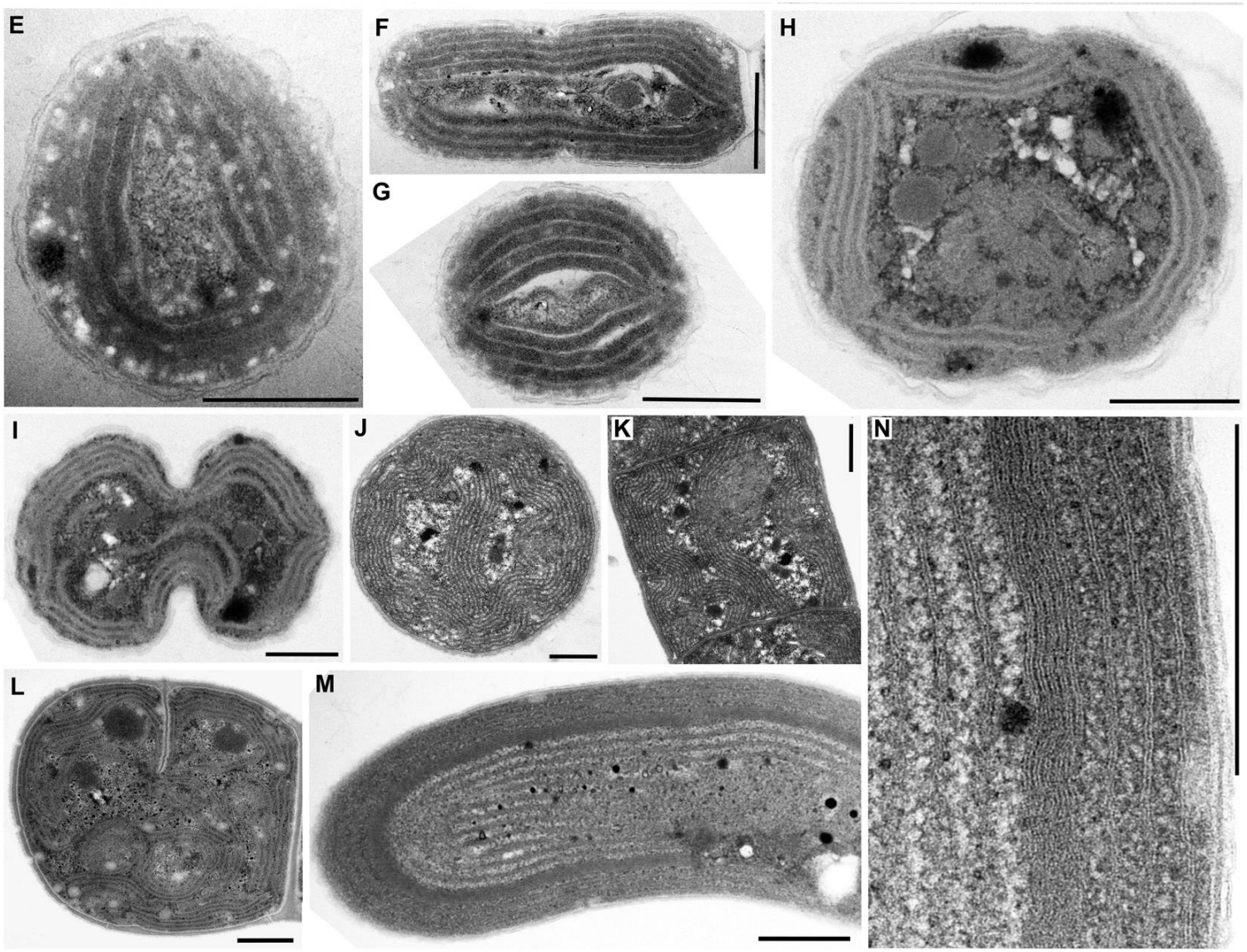
- **Single plasma membrane**
- Bacteria: thicker cell wall
- Archea: different cell wall composition – pseudopeptidoglykan


Gram-positive bacterial cell wall
Lipoteichoic acid (LTA)
Cell wall protein
Pilus
Peptidoglycan
Phospholipid (fatty acid D-glycerol esters)
Cytoplasmic membrane
Cytoplasmic membrane protein
Gram-negative bacterial cell wall
Pilus
Outer membrane protein
Lipopolysaccharide (LPS)
Outer membrane
Lipoprotein
Peptidoglycan
Periplasmic space
Phospholipid (fatty acid D-glycerol esters)
Inner membrane
Cytoplasmic membrane protein
Archaeal cell wall (Methanobacterium, Methanosphaera, Methanobrevibacter)
Pilus
Heteropolysaccharide
Pseudopeptidoglycan (pseudomurein)
Phospholipid (isopranoid alcohol L-glycerol ethers)
Cytoplasmic membrane
Cytoplasmic membrane protein
Archaeal cell wall (Methanococcus, Halobacterium)
Pilus
S-layer
Phospholipid (isopranoid alcohol L-glycerol ethers)
Cytoplasmic membrane
Cytoplasmic membrane protein

Cyanobacteria

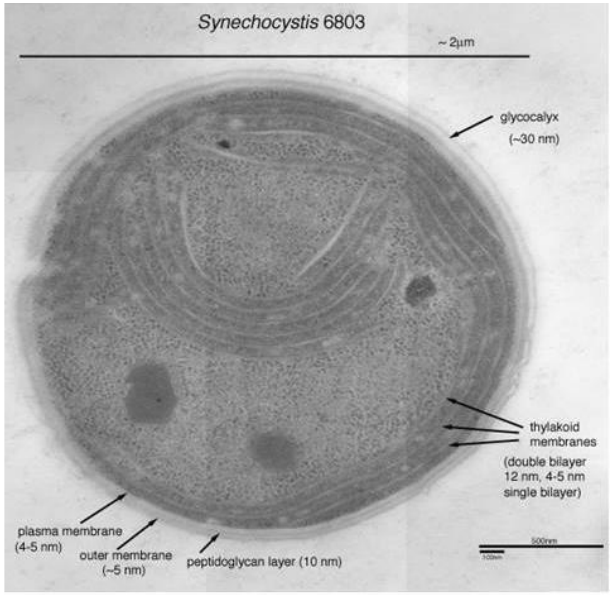
- **Thylakoids**

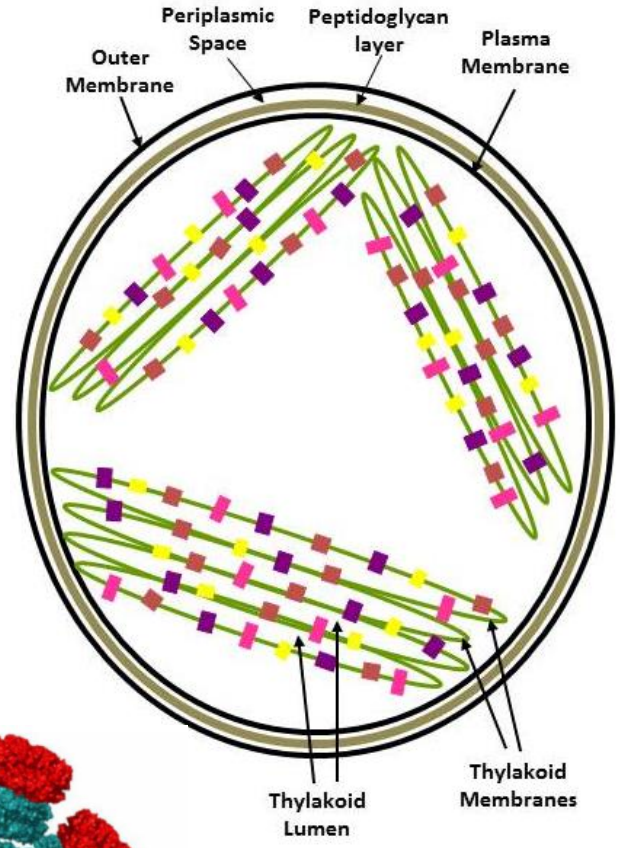
  “photosynthetic membranes”



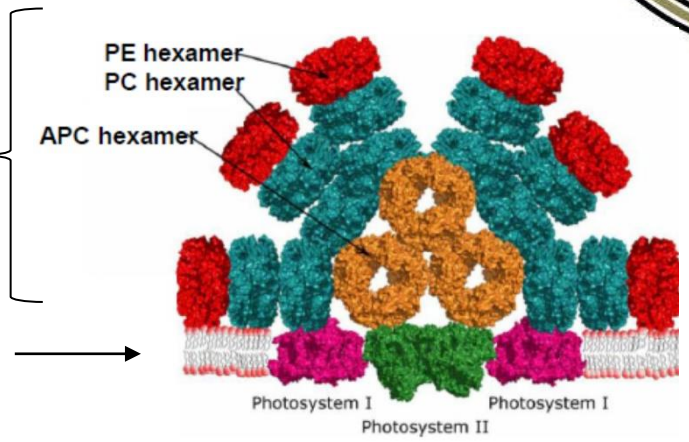
Cyanobacteria

- **Thylakoids – membrane compartments with photosynthetic pigments:**
  phycobilins, carotenoids, various forms of chlorophyll



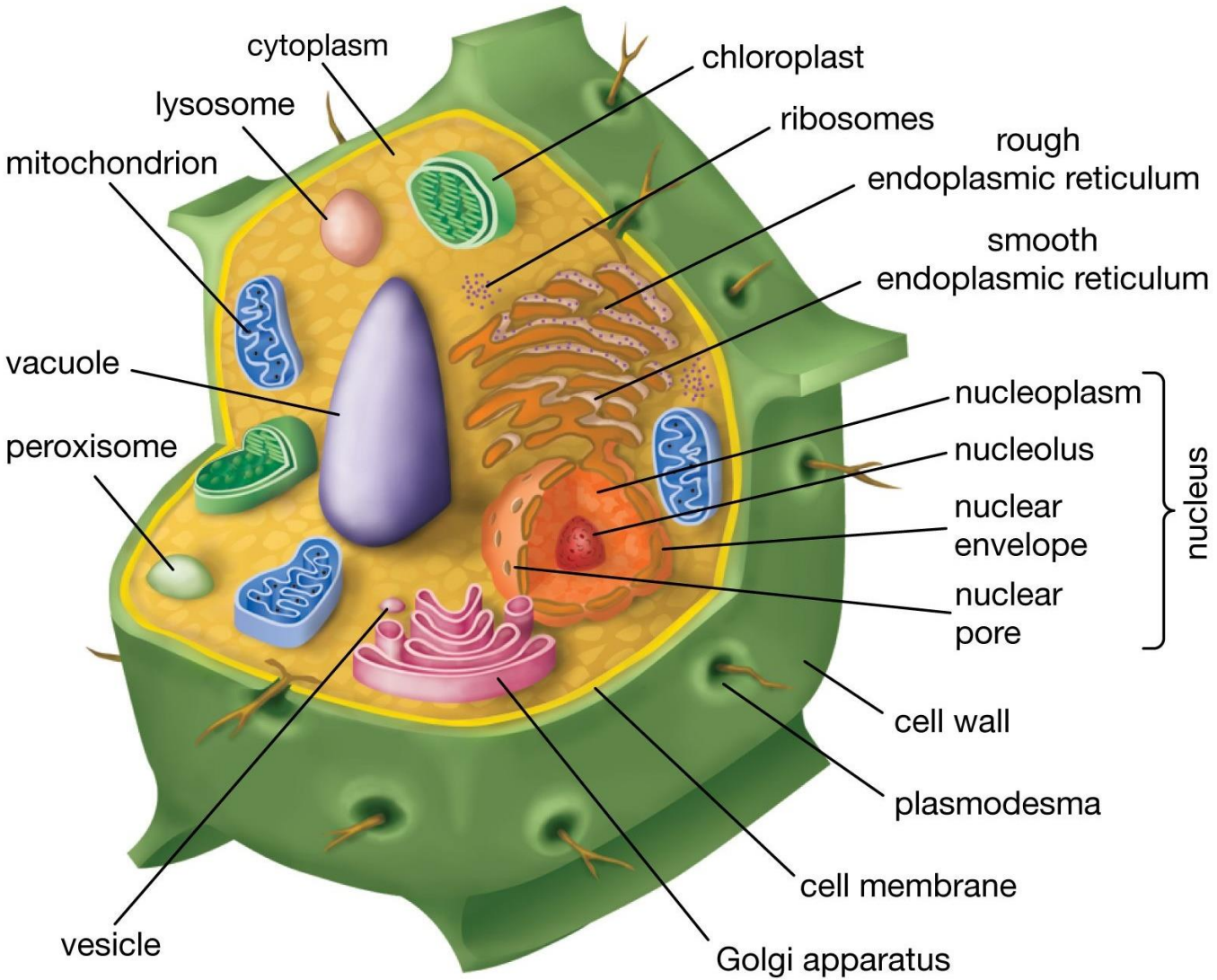


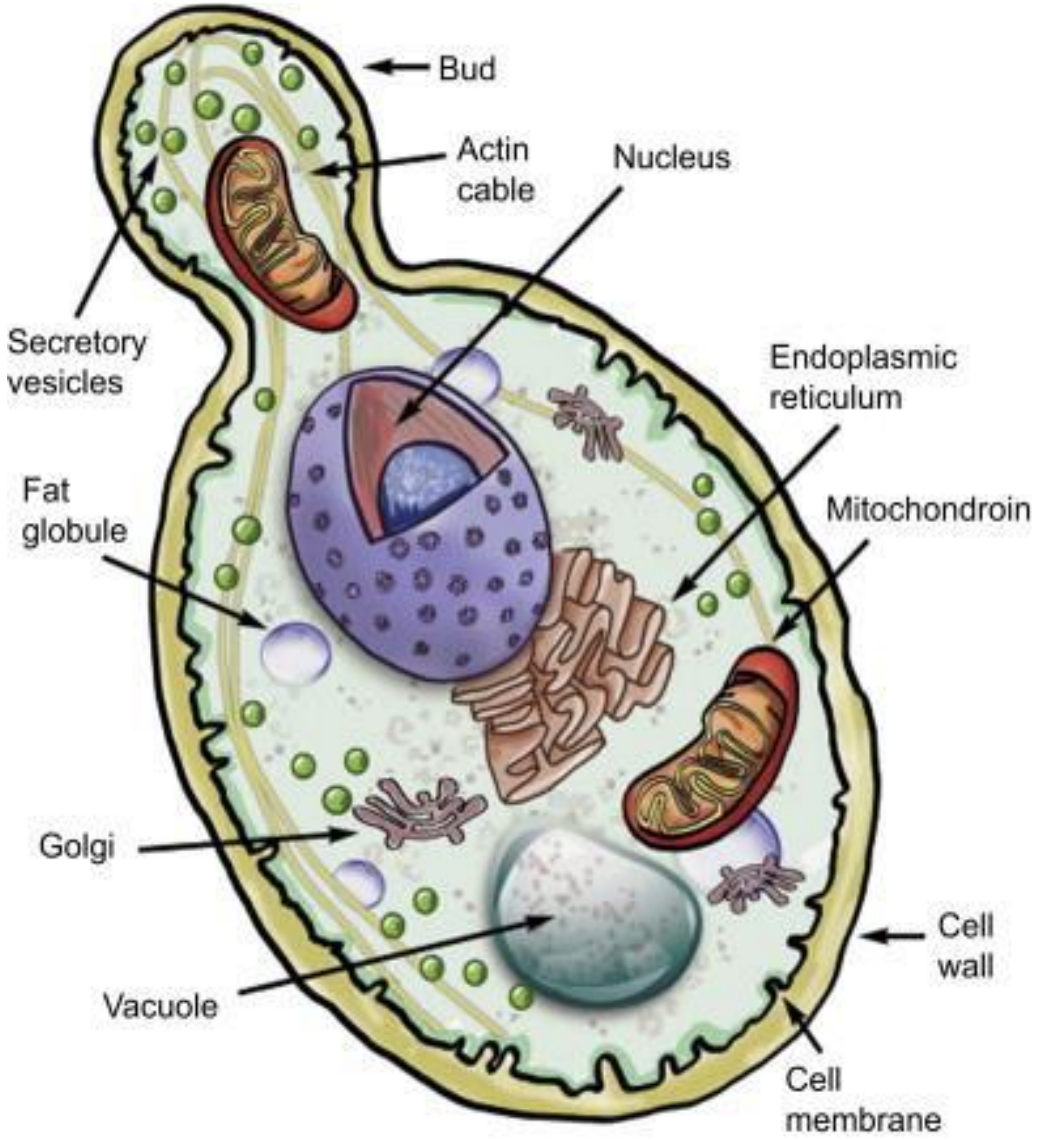
phycobilisome

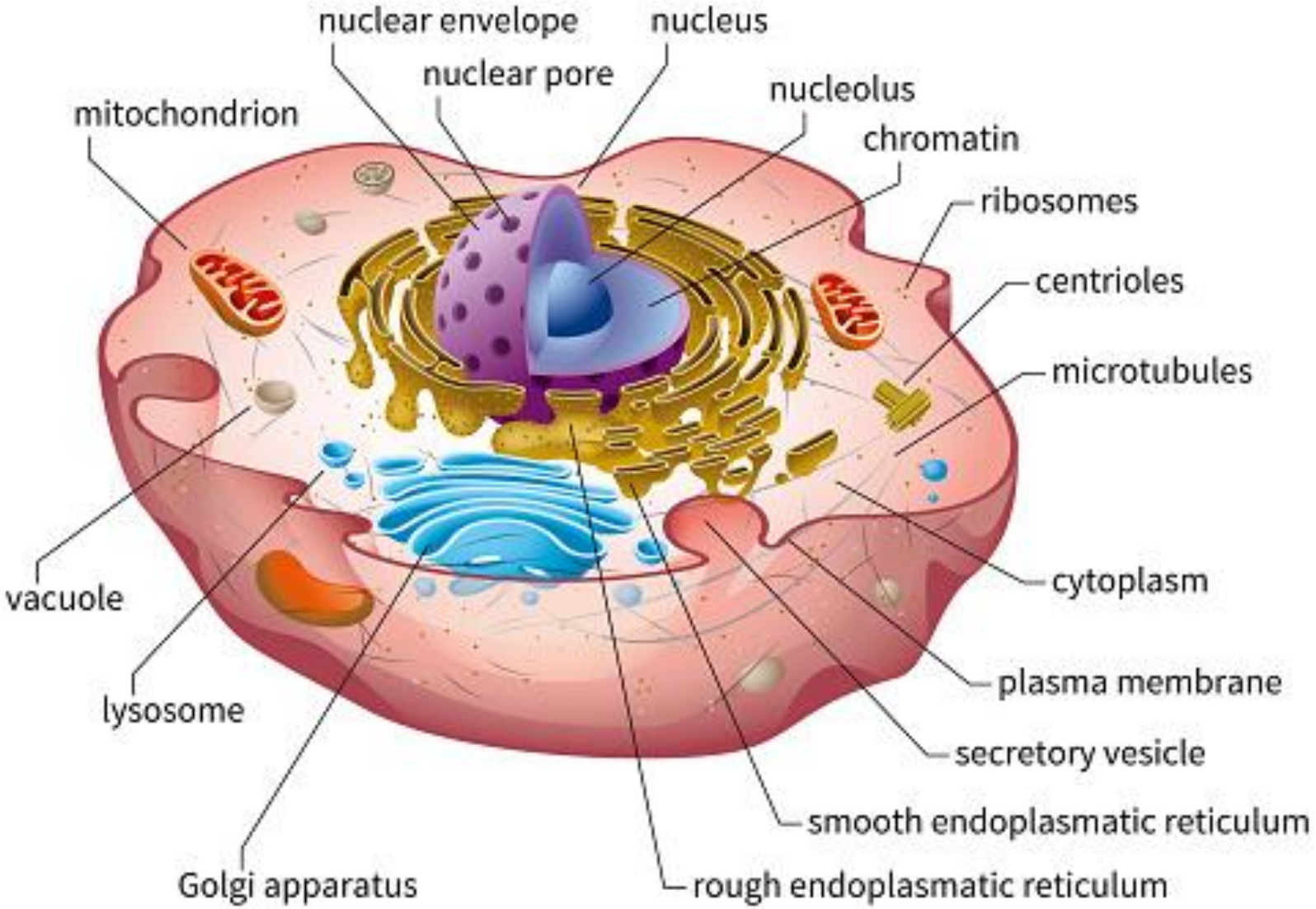


thylakoid membrane →

Compartmentalization of eukaryotic cells


cytoplasm
lysosome
mitochondrion
vacuole
peroxisome
vesicle
chloroplast
ribosomes
rough endoplasmic reticulum
smooth endoplasmic reticulum
nucleoplasm
nucleolus
nuclear envelope
nuclear pore
nucleus
cell wall
plasmodesma
cell membrane
Golgi apparatus


Bud
Actin cable
Nucleus
Secretory vesicles
Endoplasmic reticulum
Fat globule
Mitochondroin
Golgi
Cell wall
Vacuole
Cell membrane


nuclear envelope
nucleus
nuclear pore
nucleolus
mitochondrion
chromatin
ribosomes
centrioles
microtubules
vacuole
cytoplasm
lysosome
plasma membrane
secretory vesicle
smooth endoplasmatic reticulum
Golgi apparatus
rough endoplasmatic reticulum

Animal cell	Plant cell	Fungal cell
Plasma membrane	Plasma membrane	Plasma membrane
Glycocalyx	Cell wall	Cell wall
Nucleus	Nucleus	Nucleus
Endoplasmic reticulum	Endoplasmic reticulum	Endoplasmic reticulum
Golgi apparatus	Golgi apparatus	Golgi apparatus
Lysosomes	Vacuoles	Vacuoles
Peroxisomes	Peroxisomes	Peroxisomes
-	Glyoxysomes	Glyoxysomes
Mitochondria	Mitochondria	Mitochondria
-	Chloroplasts	-

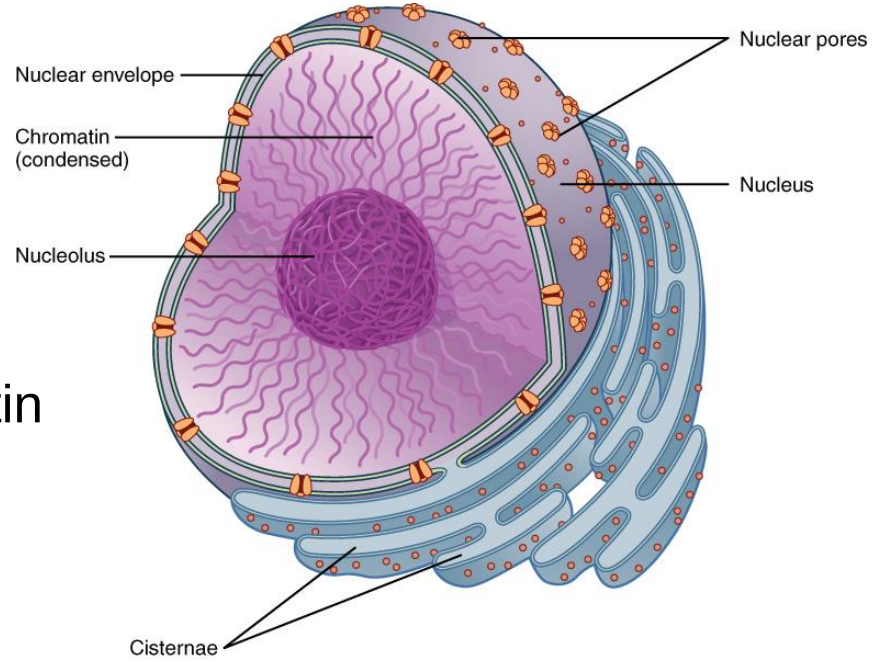
Borders of the cell, interaction with its surrounding environment	*Catabolism*
Storage and expression of the genetic information, anabolism	*Energy metabolism, apoptosis*

Brief overview of cellular compartments and their function

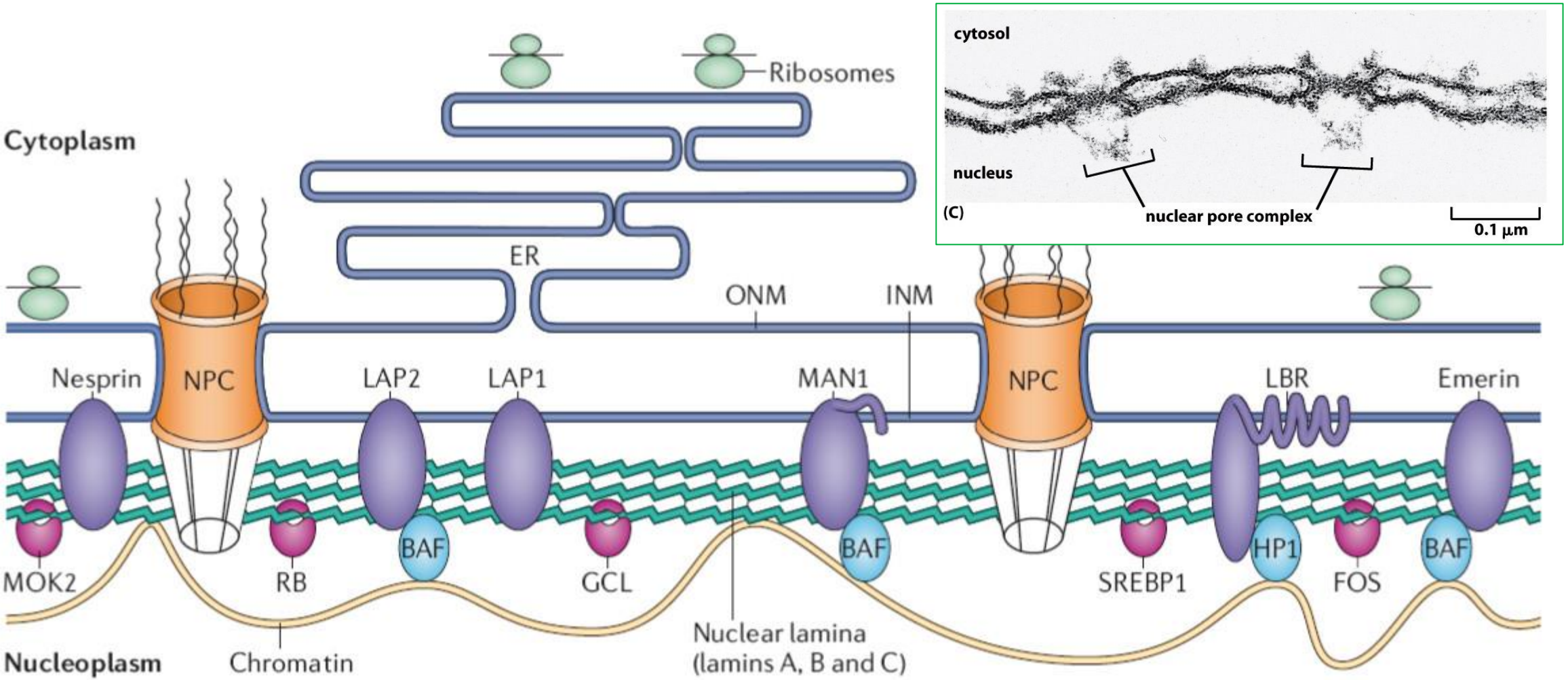
- **Cytosol**: protein synthesis, signaling and metabolic pathways
- **Nucleus**: genome, DNA and RNA synthesis
- **Endoplasmic reticulum (ER)**: lipid synthesis, synthesis of secreted and integral membrane proteins, Ca^{2+} regulation
- **Golgi apparatus**: posttranslational modification of proteins, modifications of lipids, cargo sorting to the secretory pathway
- **Mitochondrion**: ATP synthesis (OXPHOS)
- **Chloroplasts**: ATP synthesis and carbon fixation (photosynthesis)
- **Lysosomes/vacuoles**: degradation of molecules / organelles (autophagy), turgor in plants/fungi
- **Peroxisomes, glyoxysomes**: oxidation of long chain fatty acids (β-oxidation), detoxification of various harmful compounds
- **Membrane vesicles**: transport of cargo between organelles/to PM, endosomes, exosomes…

Nucleus

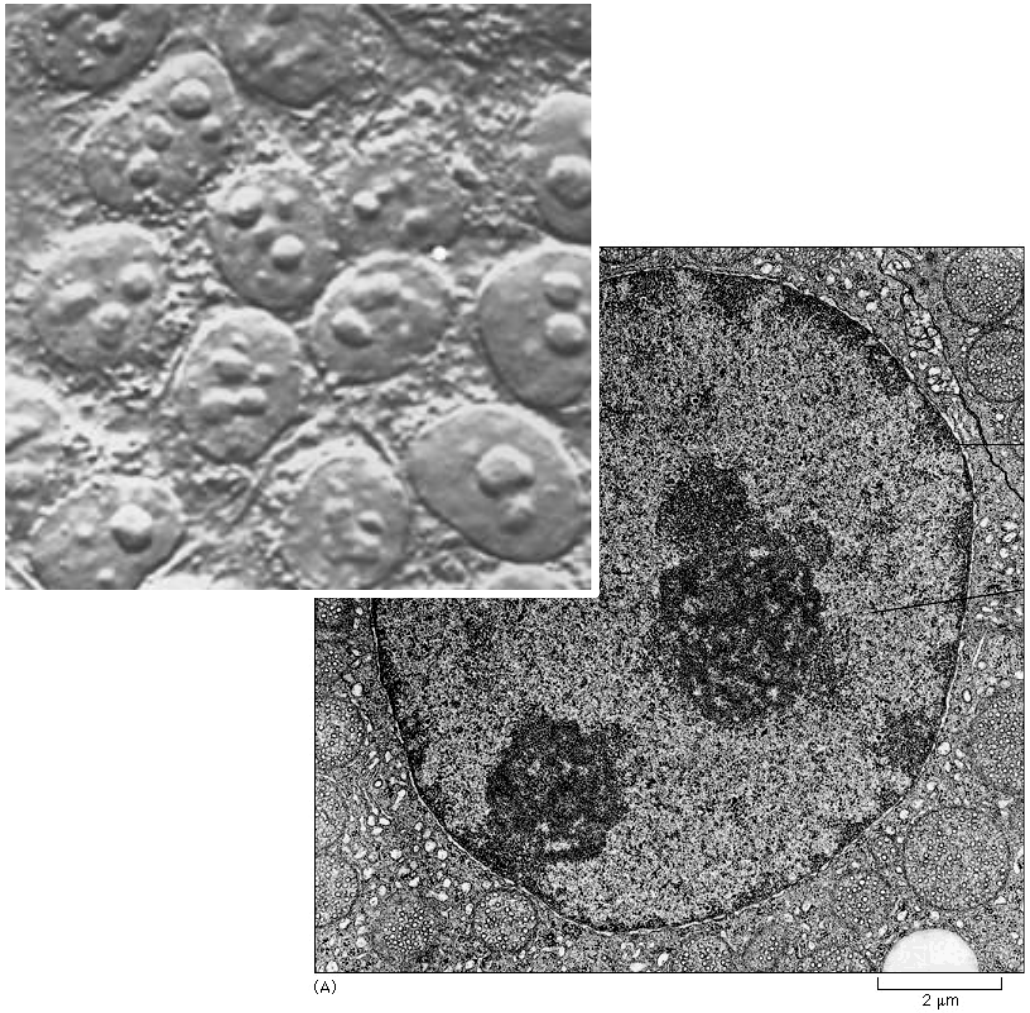
- Central organelle, spherical shape, (missing in mammalian RBC)
- Genome – **chromatin (DNA+histones)**, **replication, transcription**
- **Nuclear envelope**
  - Double-membrane structure:
    outer membrane – perinucler space – inner membrane
  - Contains **nuclear pores** (transport of larger molecules)
  - Continues into ER – perinuclear space joined with the lumen of ER
  - Inner membrane interacts with **nuclear lamina** and chromatin
- **Nucleolus**
  - Most commonly single, but several possible in one nucleus
  - rRNA genes, nascent ribosome assembly

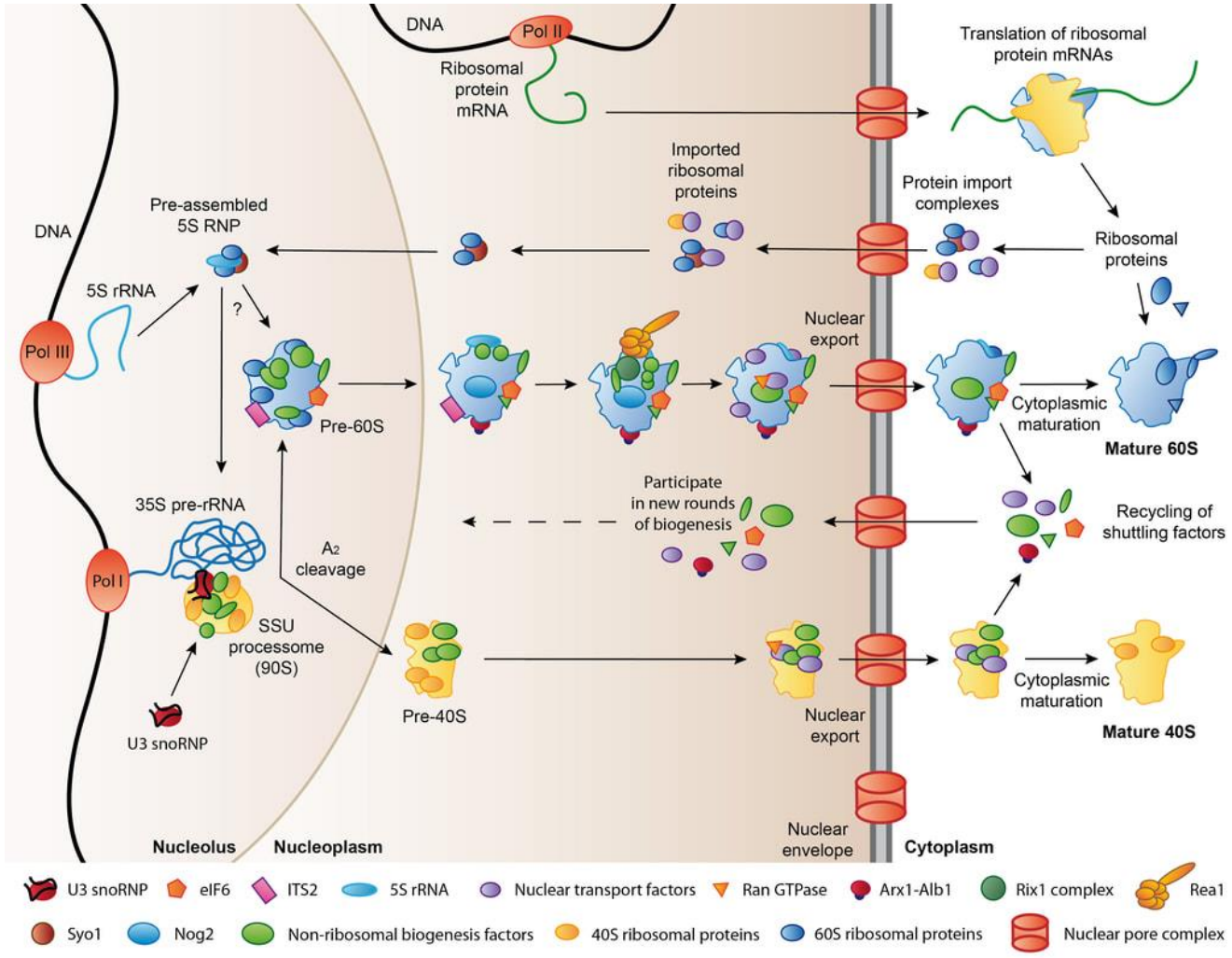


Nuclear envelope – ER, nuclear pores and lamina



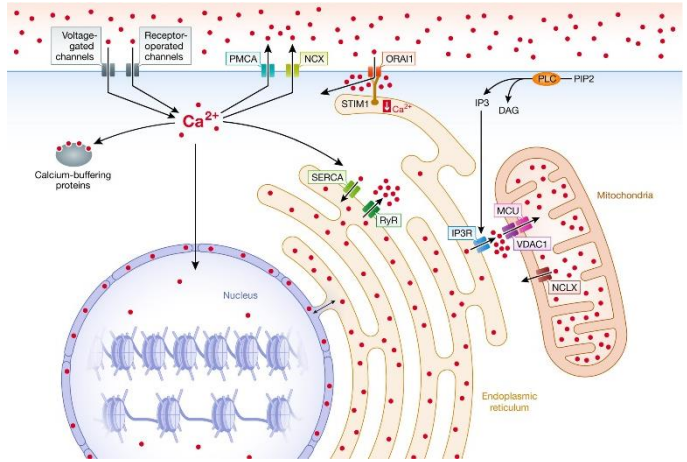
Nucleolus – rRNA transcription & ribosome assembly



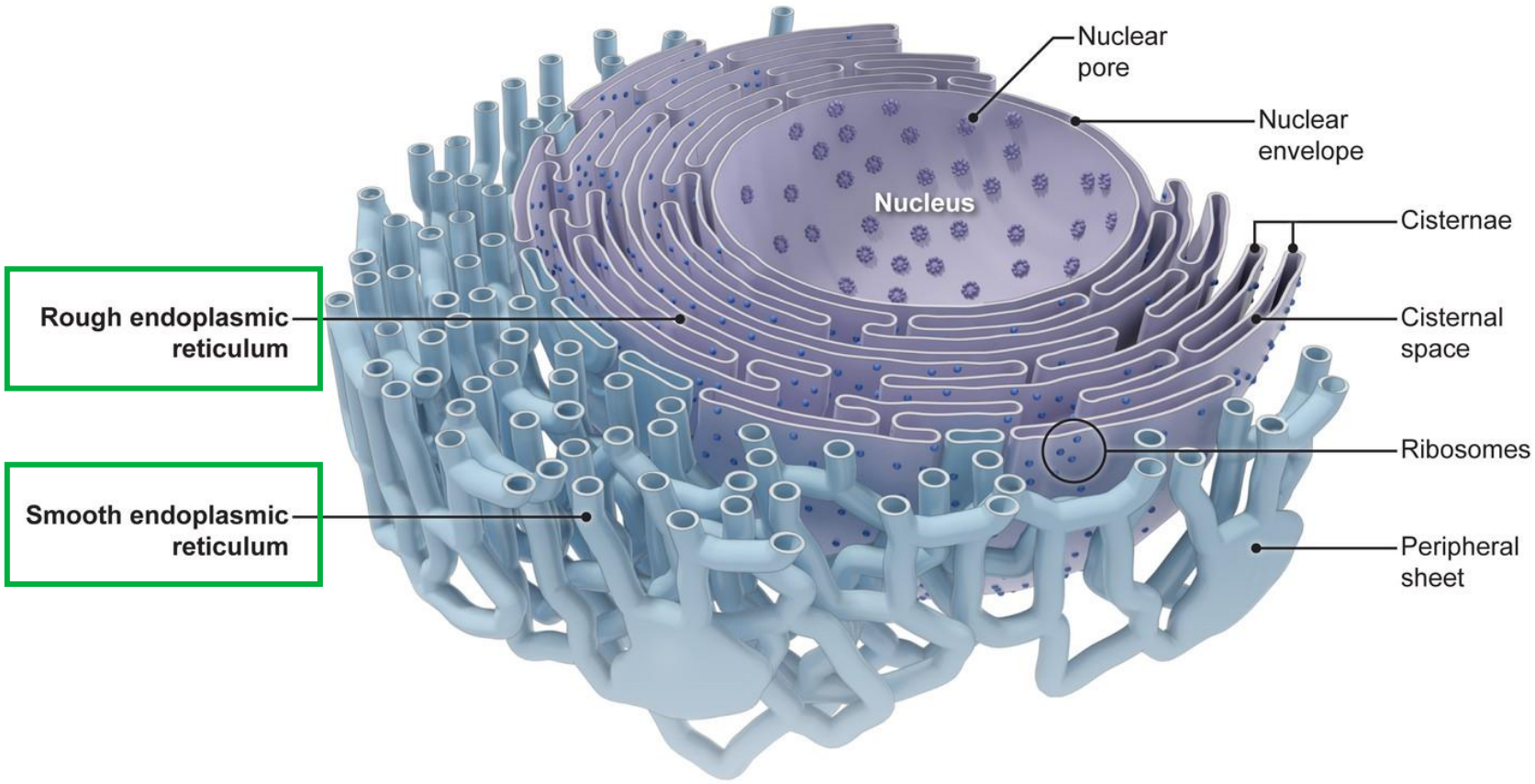


Endoplasmic reticulum (ER)

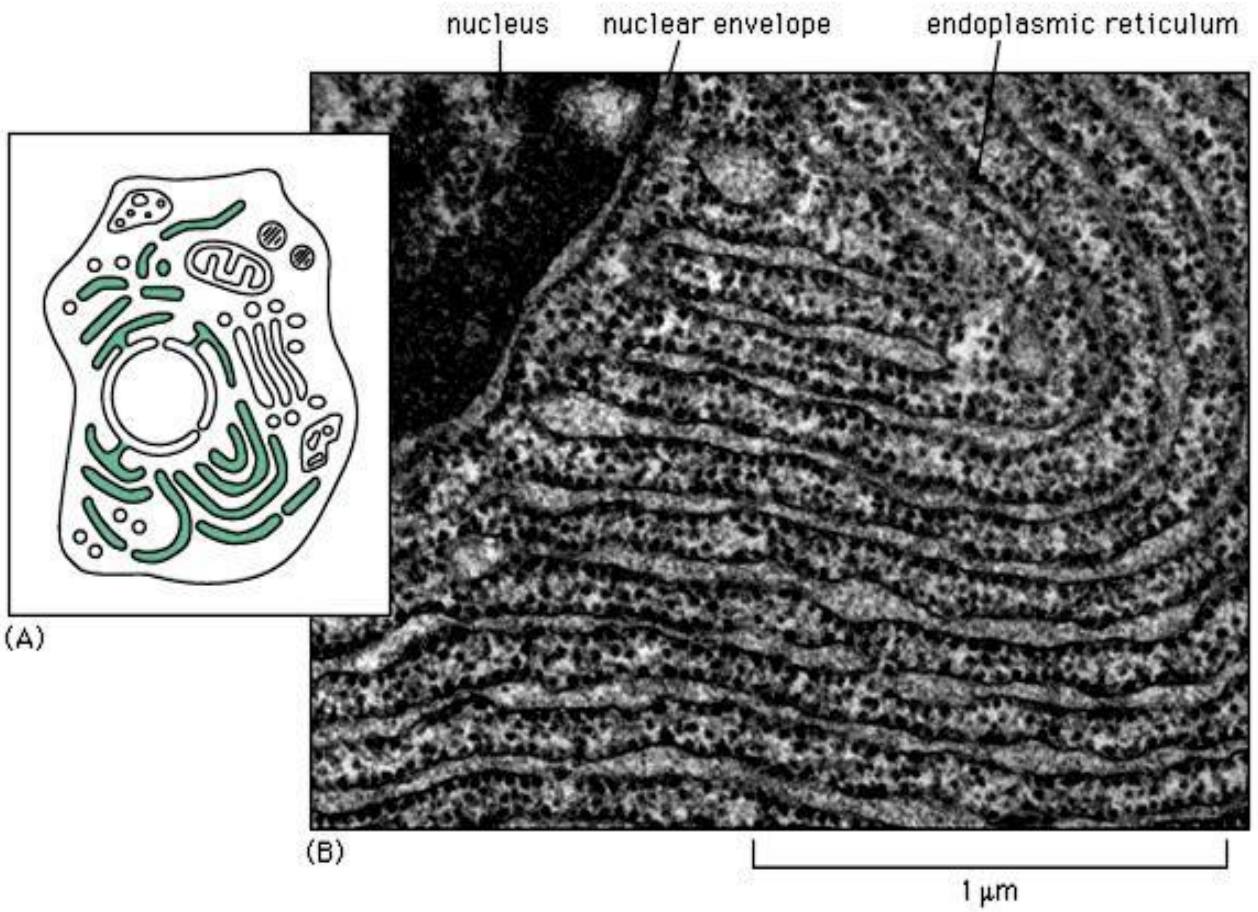
- Network of cisternae and tube-like membrane structures, joined with perinuclear space
- **Rough ER:** cisternae with attached ribosomes, **protein synthesis and posttranslational modifications**
- **Smooth ER:** tubes w/o ribosomes, **synthesis of lipids, phospholipids, steroids**
- **Calcium (Ca^{2+}) storage and homeostasis**
  - Ca^{2+} signaling; mitochondria overload – apoptosis

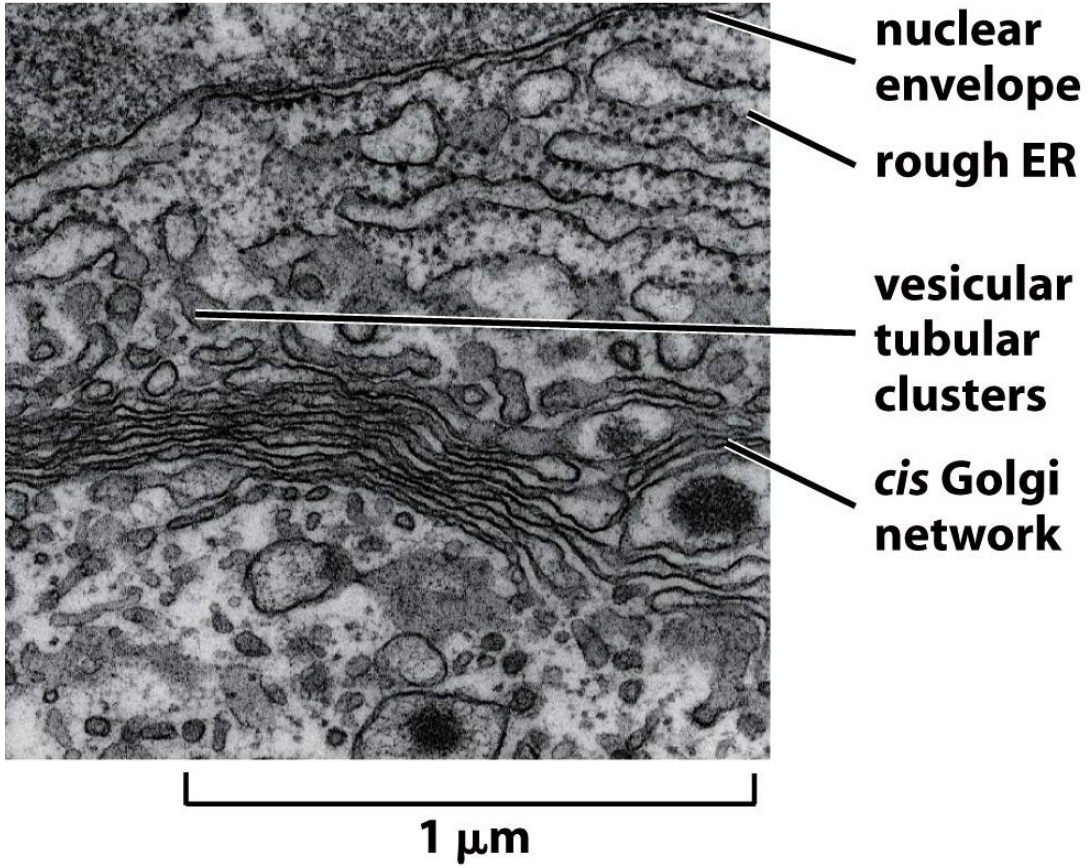


ER

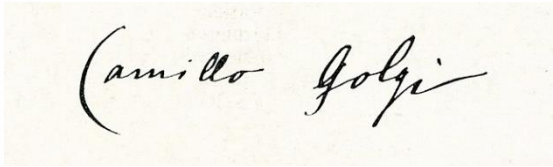

Nuclear pore
Nuclear envelope
Nucleus
Cisternae
Rough endoplasmic reticulum
Cisternal space
Ribosomes
Smooth endoplasmic reticulum
Peripheral sheet

ER


nucleus
nuclear envelope
endoplasmic reticulum
(A)
(B)
1 μm


nuclear envelope
rough ER
vesicular tubular clusters
cis Golgi network
1 μm

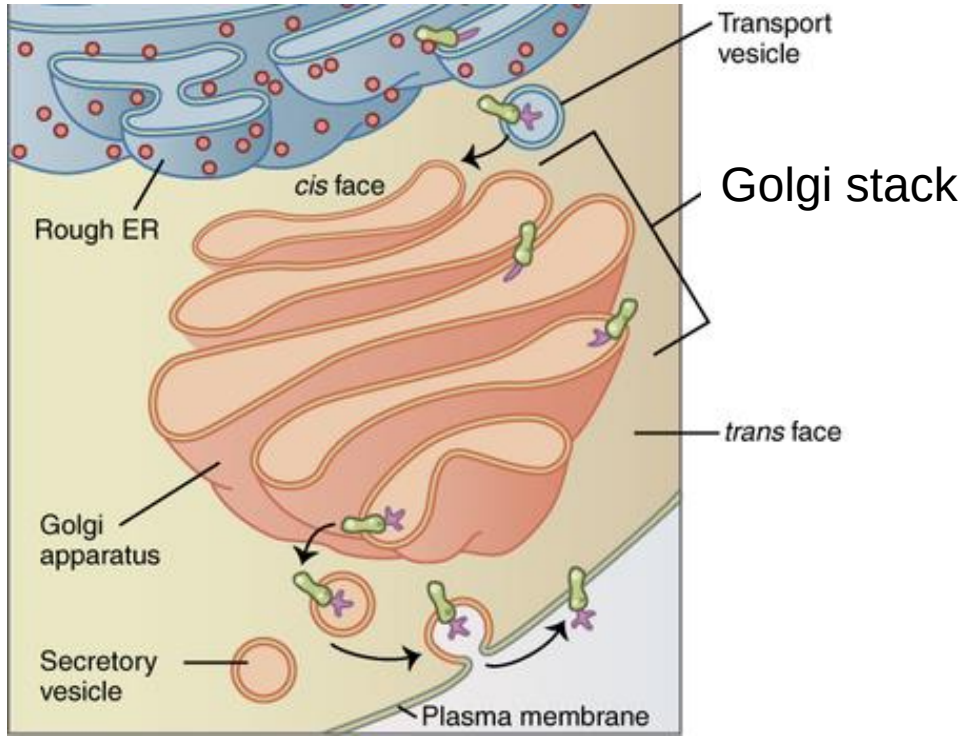
Golgi apparatus (GA)



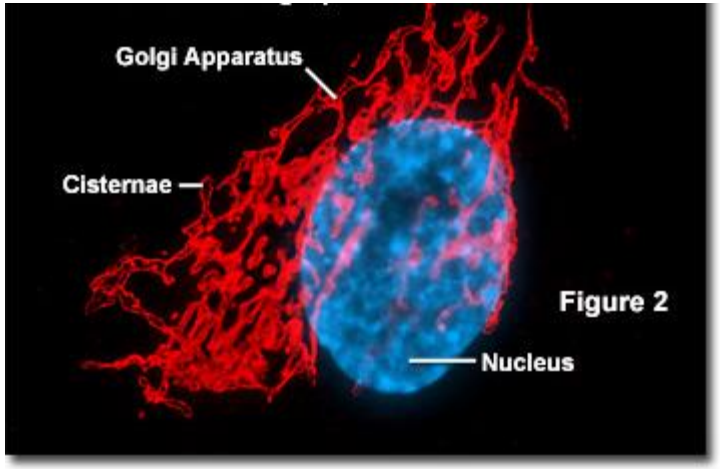
- Network of membrane cisternae and membrane-bound vesicles
- **Modifications of proteins and lipids, packaging into vesicles:** sorting for their transport

Functional polarization:

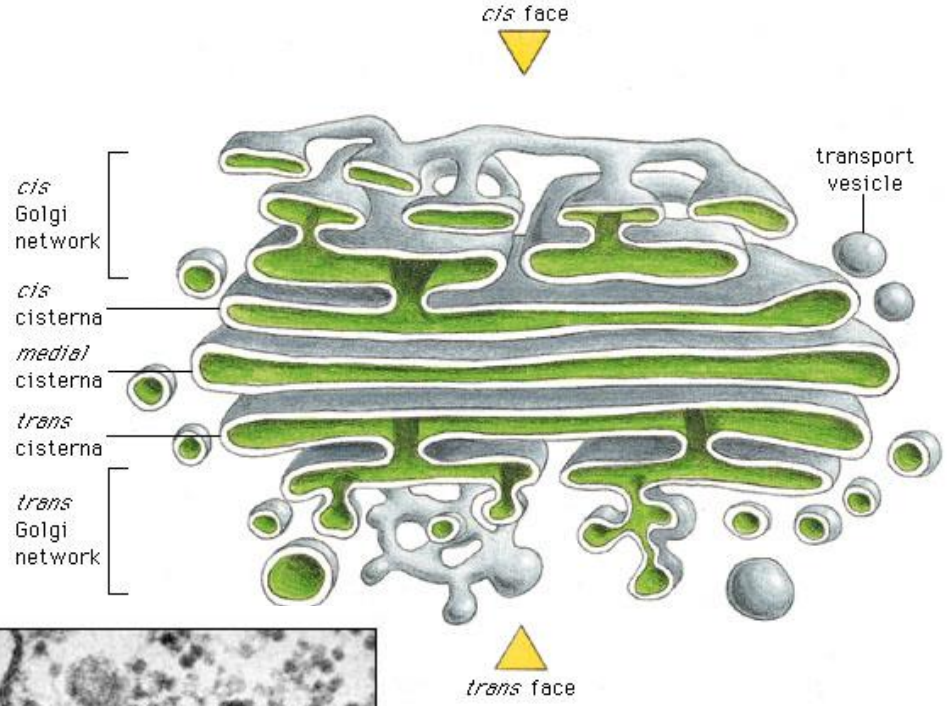
- ***cis* face** (facing ER) vs ***trans* face**
- several **Golgi stacks** per cell
  - Animal cells: up to 100; plant cells: different distribution

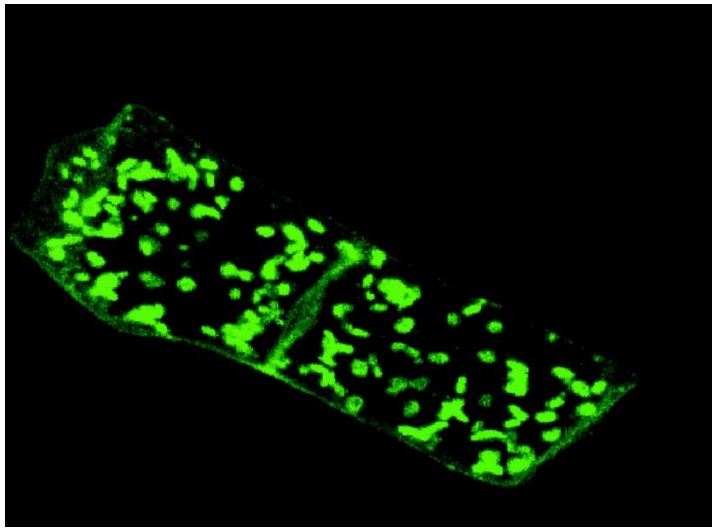


Golgi apparatus (GA)



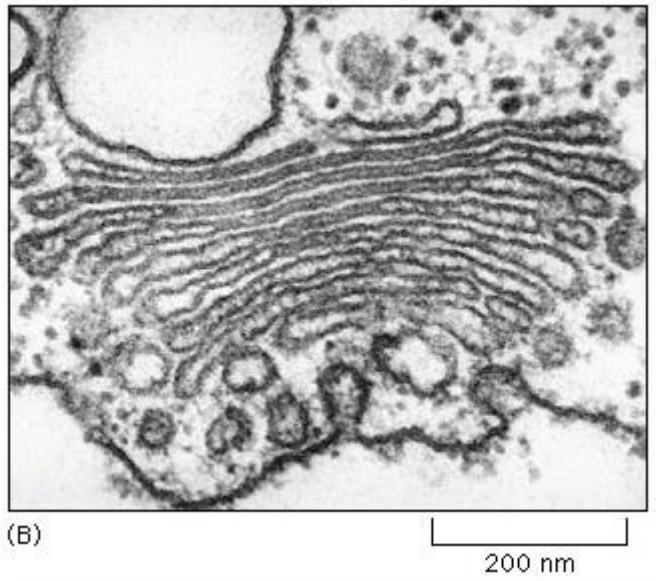
Animal cell





Plant cells

Golgi stacks distributed throughout the cell

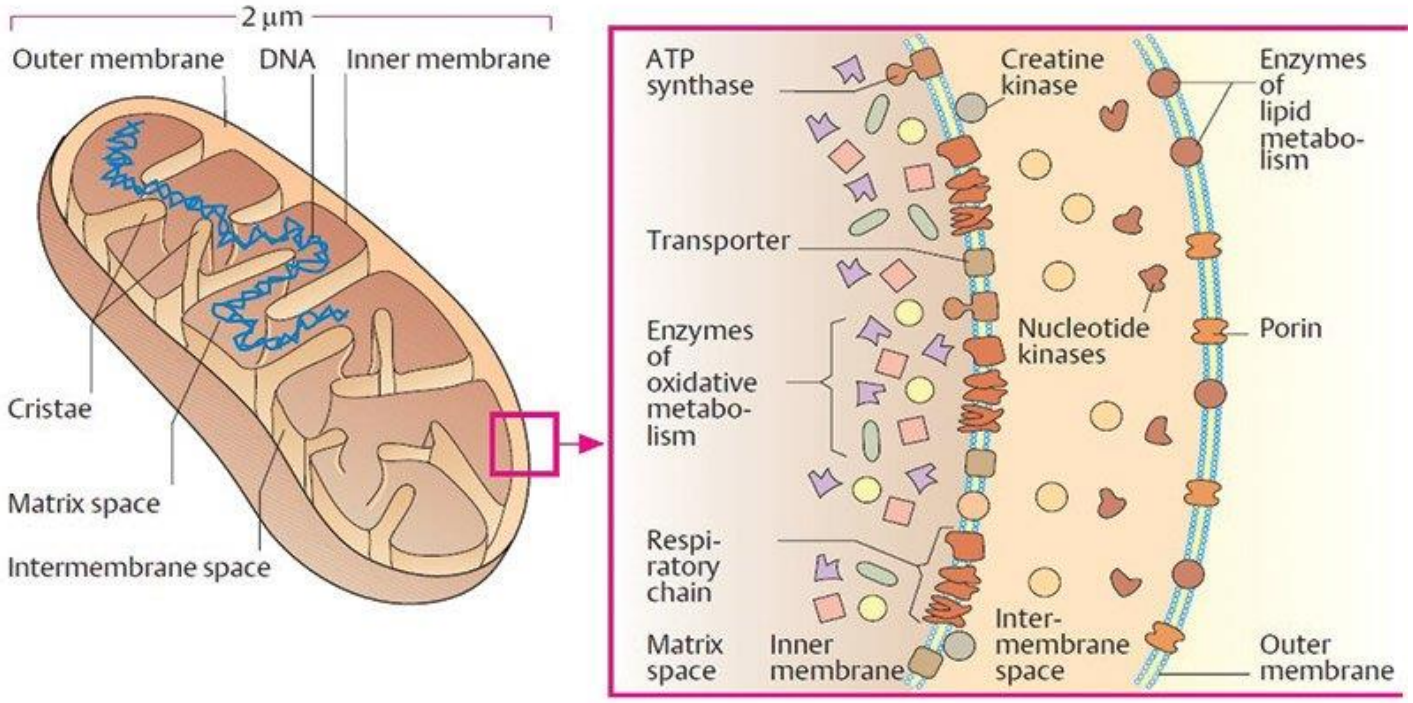


Mitochondrion

- Energy metabolism – **oxidative phosphorylation (ATP synthesis)**

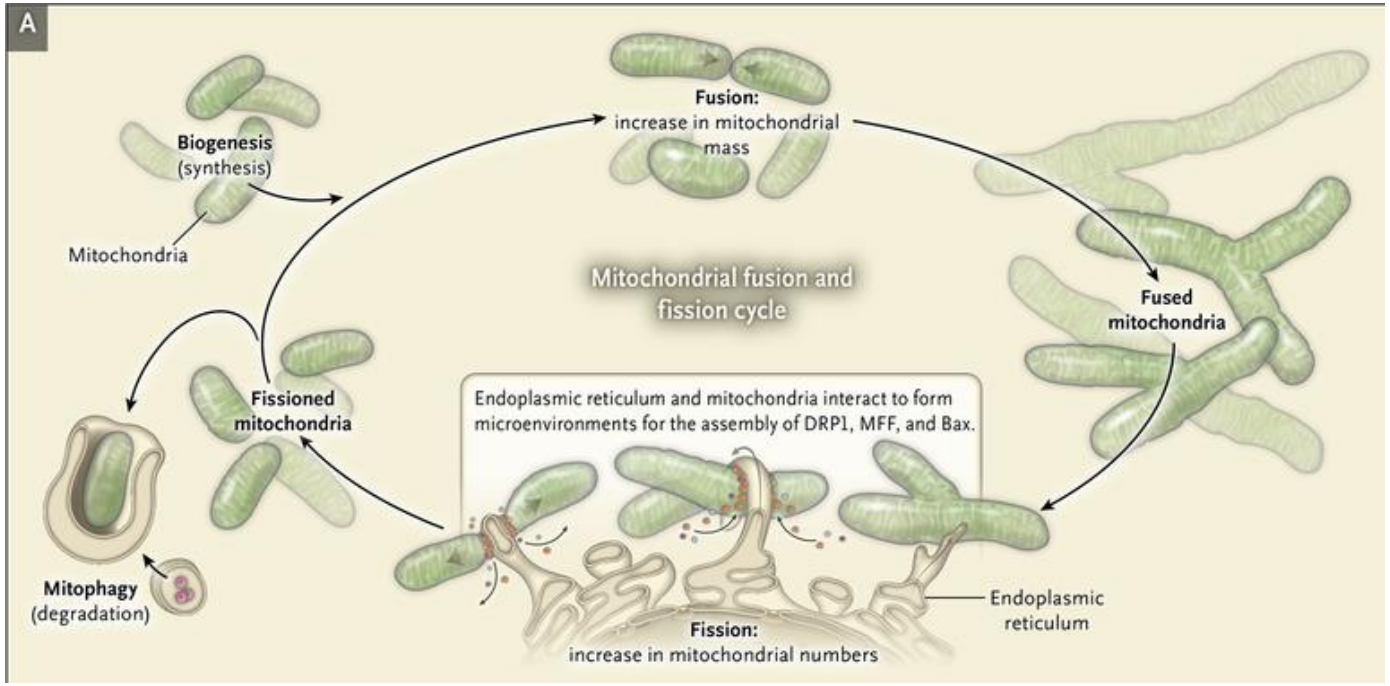
2 biomembranes – 2 compartments

- Outer membrane
- Inner membrane: **cristae**
  - **Respiratory chain proteins**
  - **ATP synthase**
- **Intermembrane space**
  - Cytochrome c: ETC & apoptosis
- **Matrix**
  - **Enzymes of metabolic pathways**



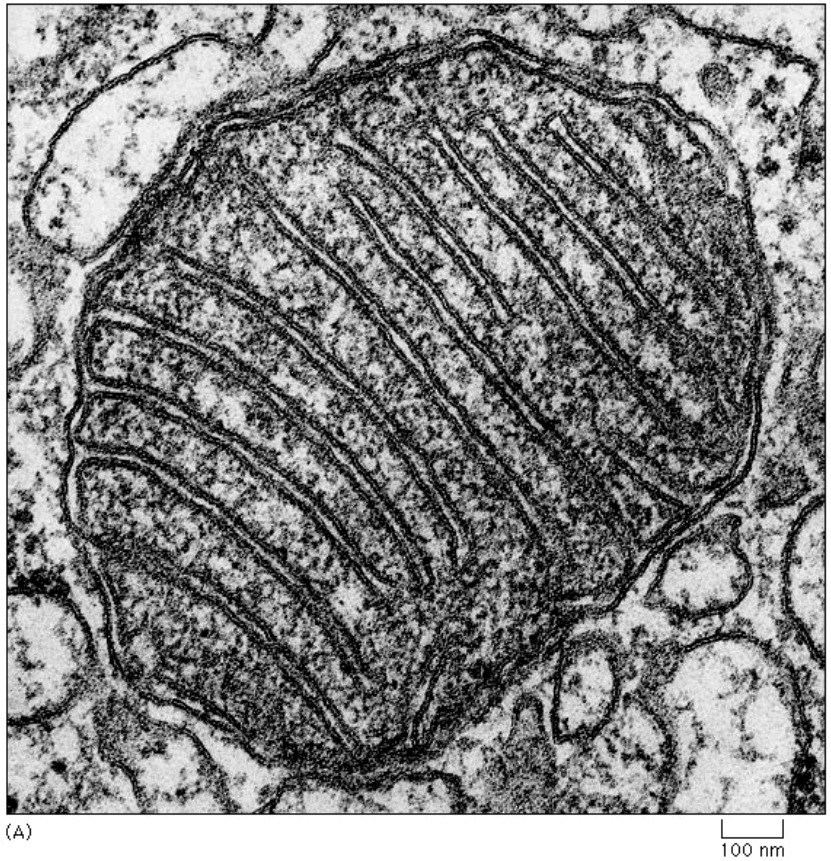
Mitochondria: semiautonomous and dynamic

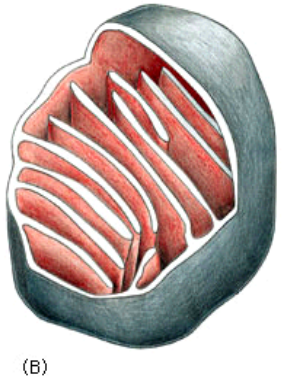
- **Own genome** (circular mtDNA) and protein synthesis apparatus
- **Mitochondrial ribosomes** similar to prokaryotic → endosymbiosis
- **Highly dynamic**
  - Fusion / fission
  - Mitochondrial network / fragmented
  - Associated with microtubules
- **Biogenesis only from pre-existing mitochondria**
  - Autoreplication capacity

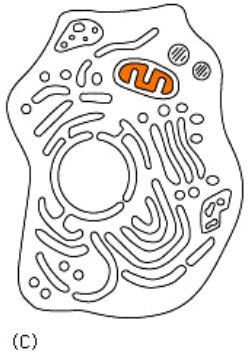


Mitochondria form mitochondrial network

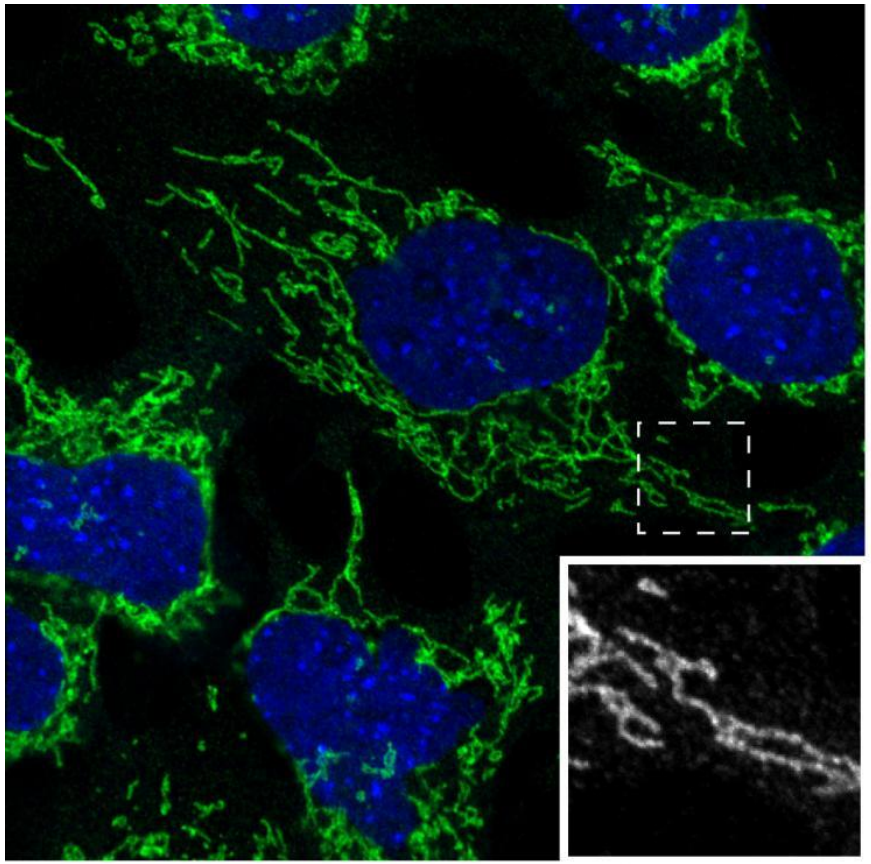
- Mitochondrion



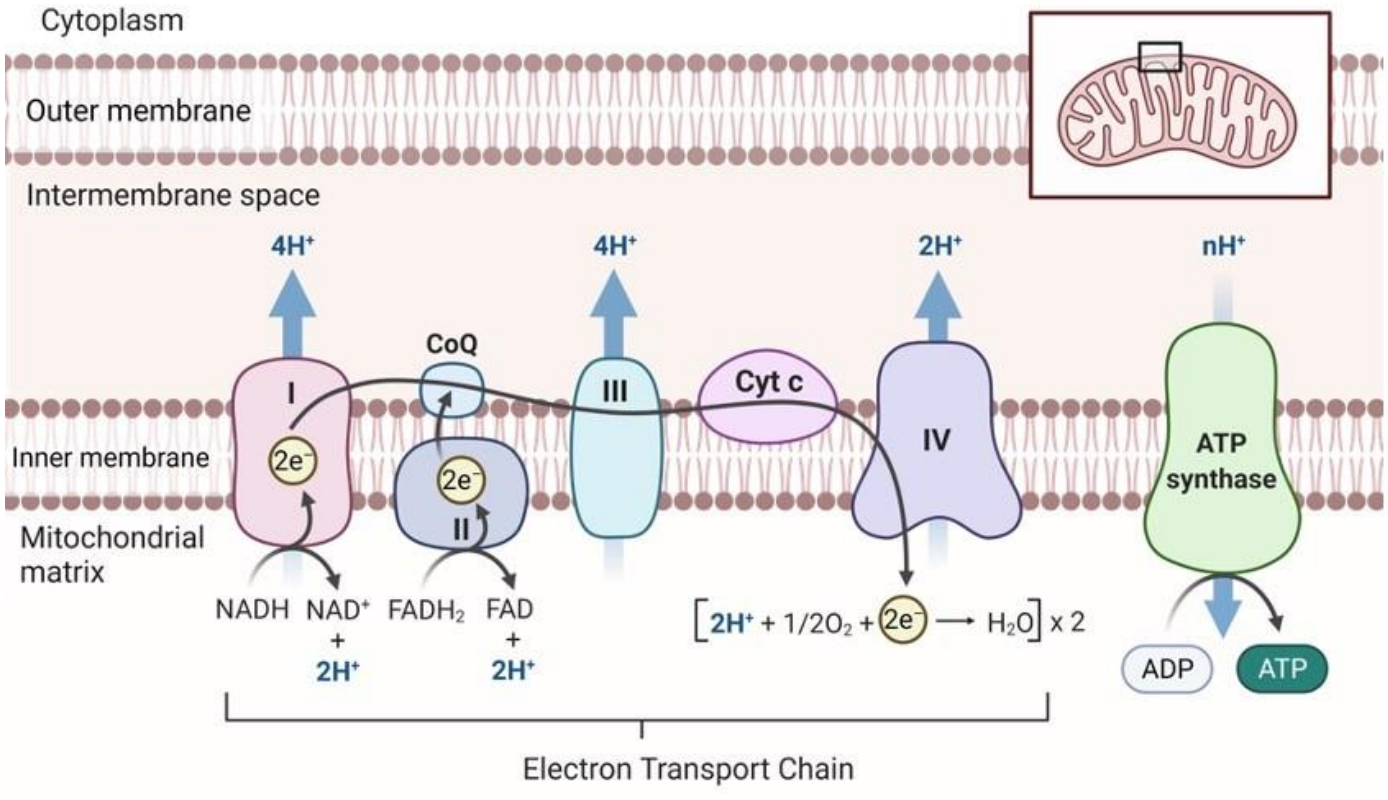




- Mitochondrial network



Cristae: oxidative phosphorylation



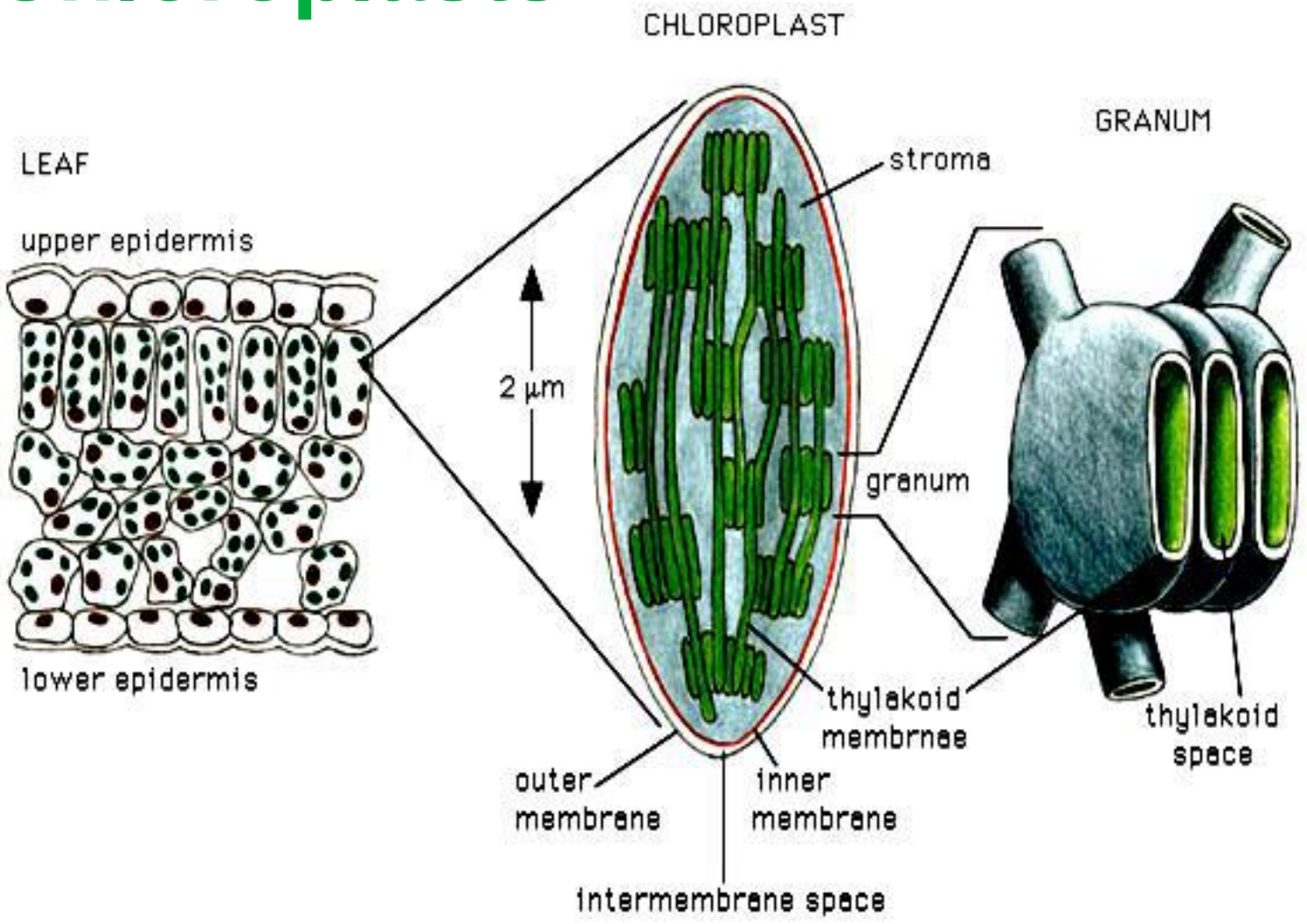
Chloroplasts

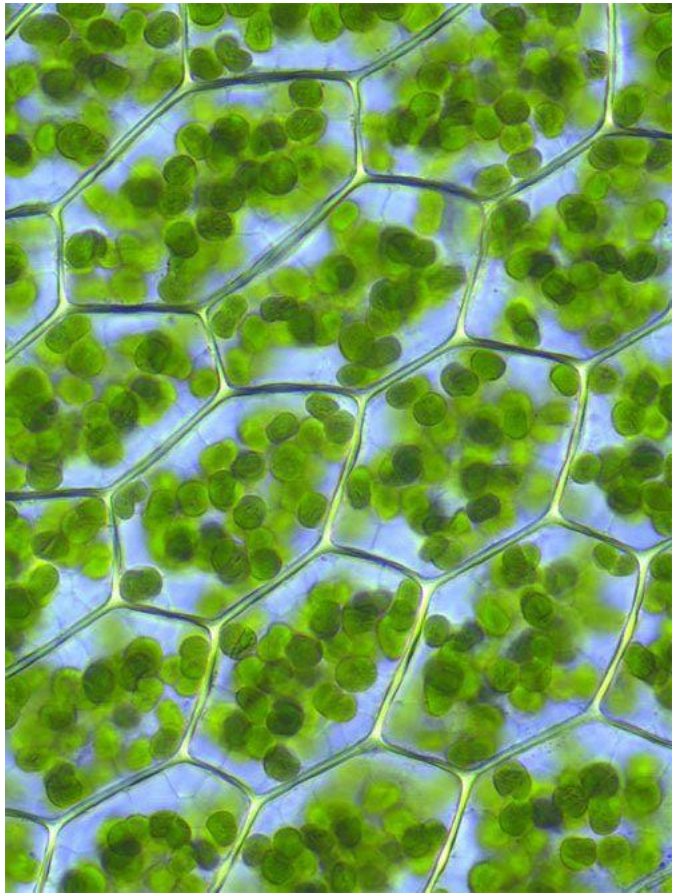
- Energy metabolism: **photosynthesis (ATP synthesis and carbon fixation)**; **only in plant cells**

2 biomembranes – 2 compartments

- Outer membrane **– intermembrane space –** inner membrane **– stroma with thylakoids** containing photosynthetic pigments and enzymes
- **Own genome** (circular cpDNA) and protein synthesis apparatus
- **Chloroplast ribosomes** similar to prokaryotic → endosymbiosis
  - Autoreplication capacity

Chloroplasts



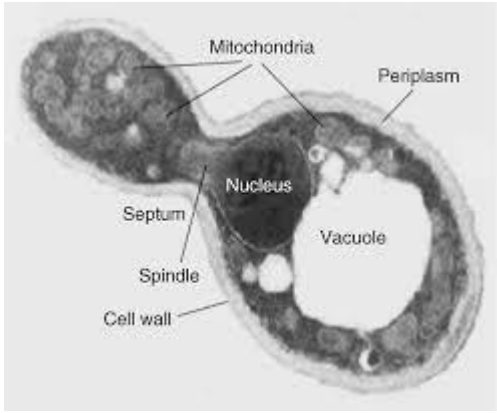


Lysosomes

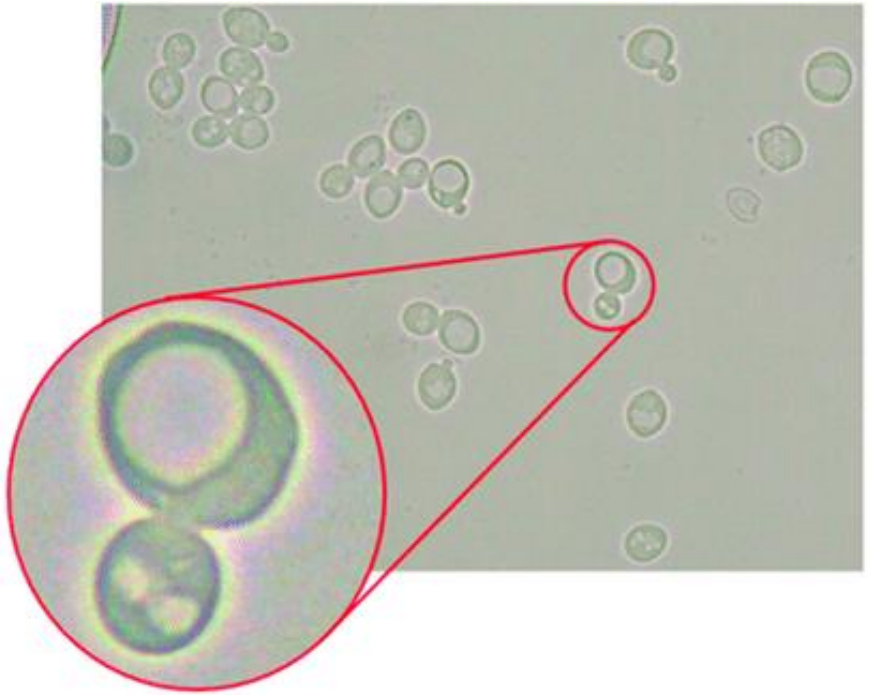
- Catabolism: **degradation of molecules and organelles**
- **Acidic interior**: ~50 different pH-sensitive hydrolases, pH ~4.5–5.0
- Highly glycosylated membrane proteins – protection against degradation by hydrolases
- **Primary** (newly formed) vs. **secondary** (fusion of the primary lysosome with an endosome/phagosome)
- **Extracellular digestion** – release of lysosomal enzymes outside the cell (e.g., bone resorption; crucial balance)

Vacuoles

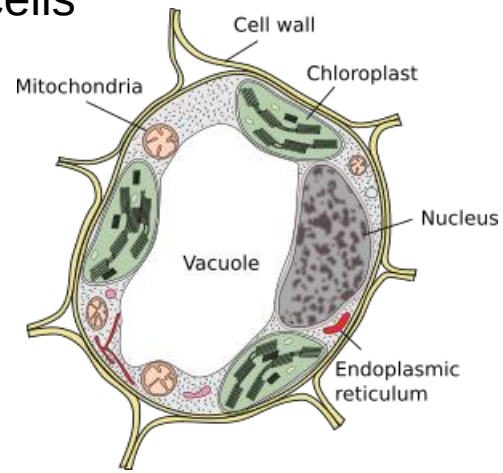
- Functional analogy of lysosomes, in plant and fungal cells
- Catabolism: **degradation of molecules**
- **Storage of water – regulation of turgor**

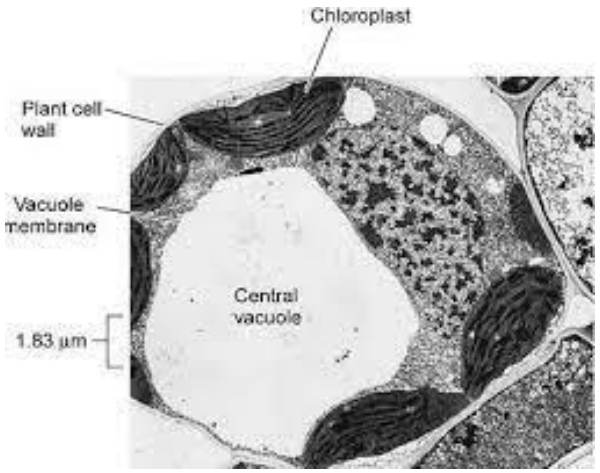


yeast cells



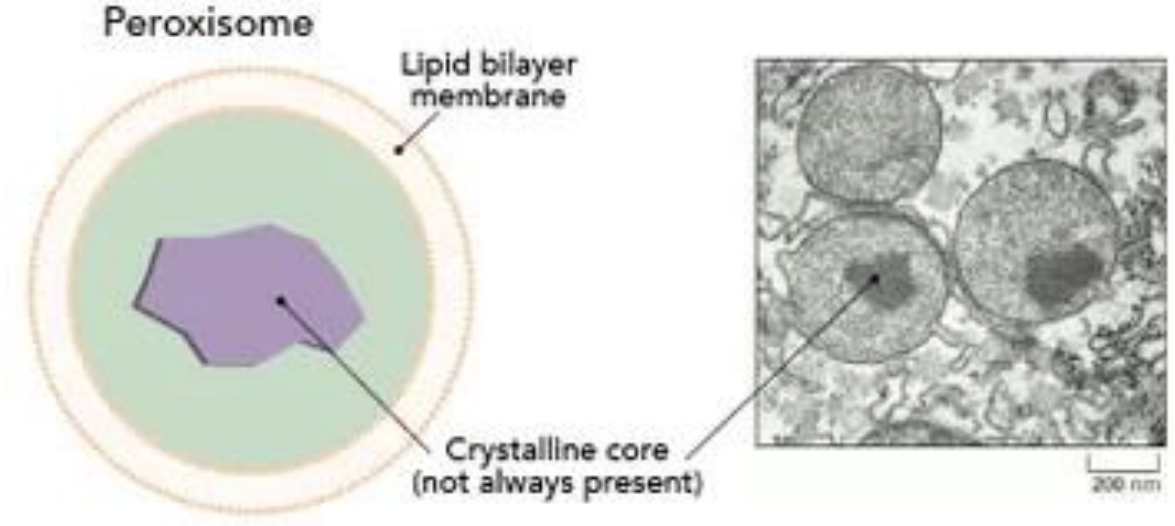
plant cells

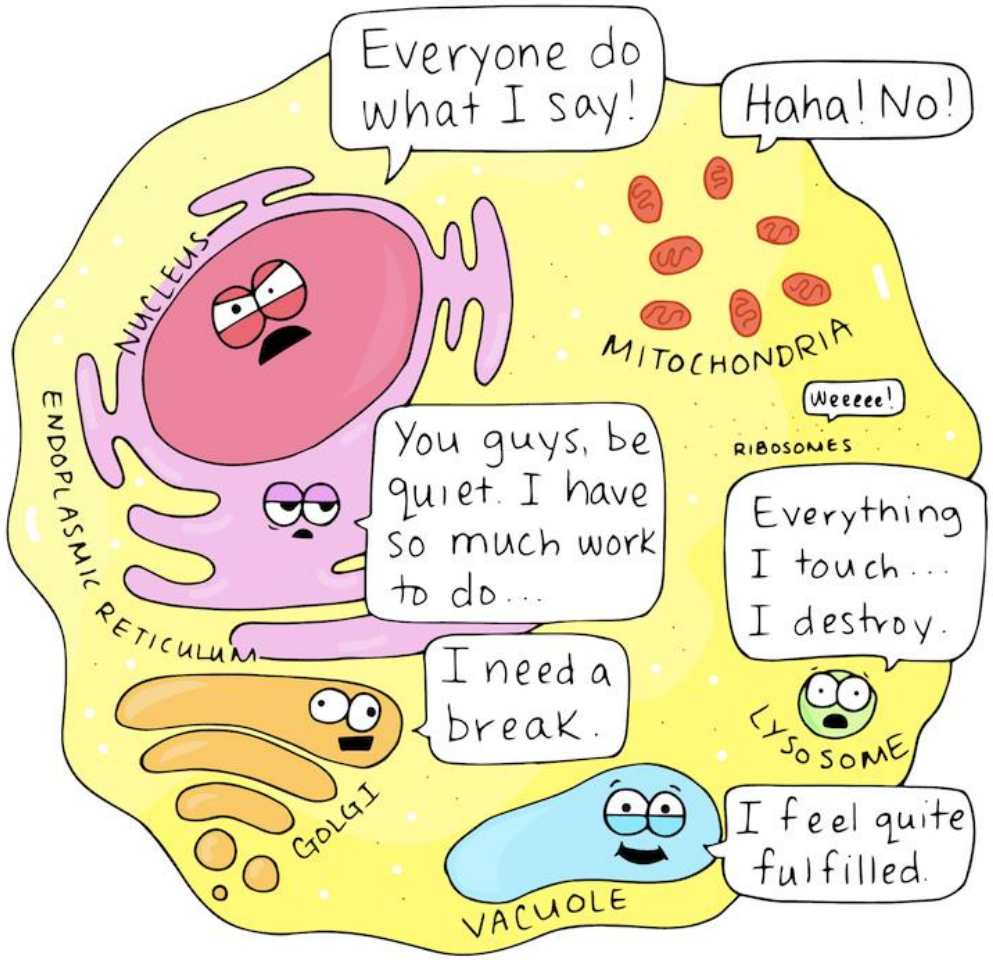




Peroxisomes, glyoxysomes

- Catabolism: **long fatty acid oxidation, oxidation of toxic molecules**
- **Detoxification of reactive oxygen species** (H_2O_2, superoxide)
- Derived from ER, membrane growth and division
- Contain **oxidases, catalase** ($2H_2O_2 \rightarrow 2H_2O + O_2$), luciferase (in fireflies)
- **Glyoxysomes:** specialized peroxisomes in plant cells (e.g., seeds that contain fats and oils) and fungal cells





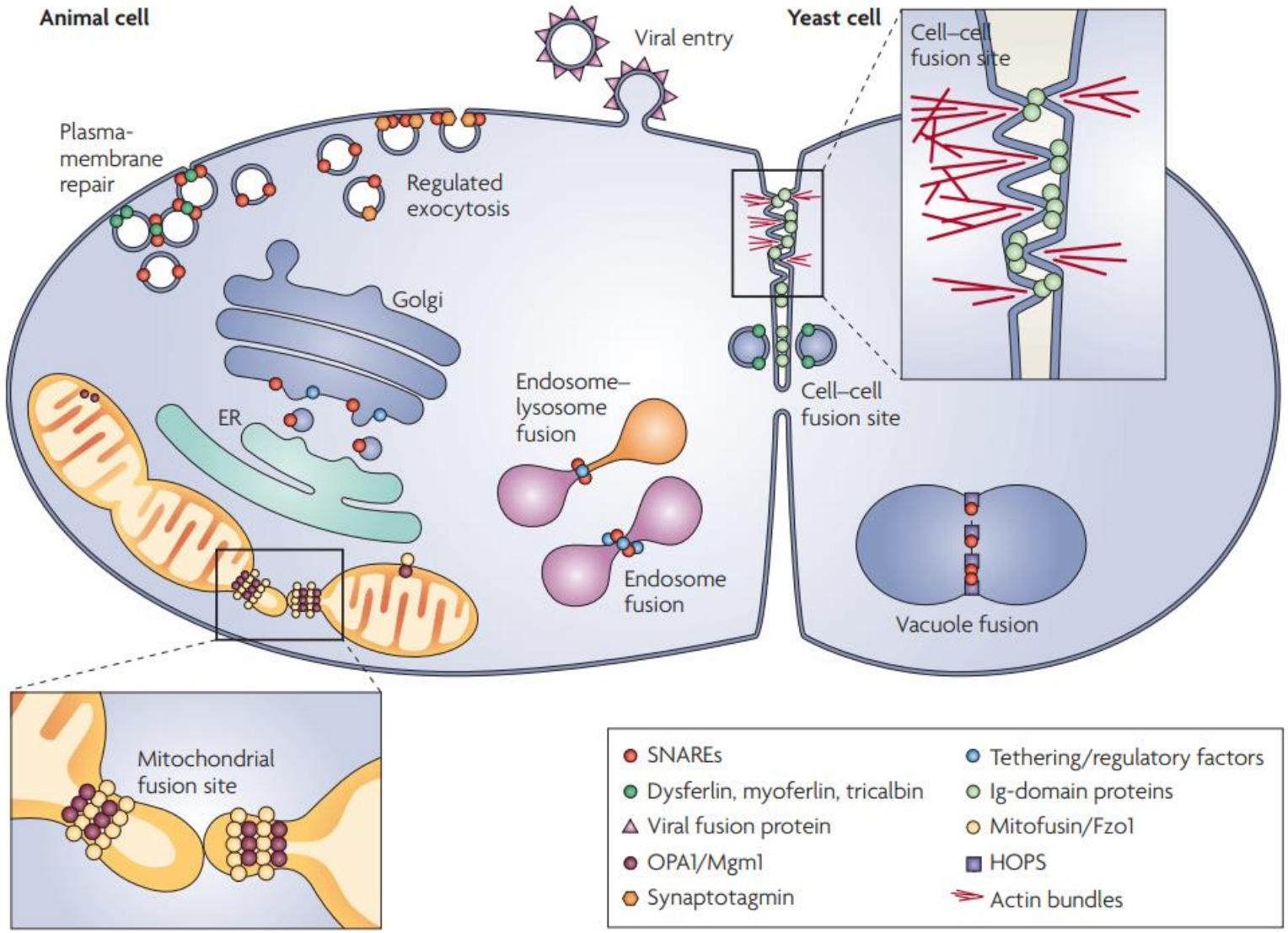
If organelles could talk.

Beatrice the Biologist

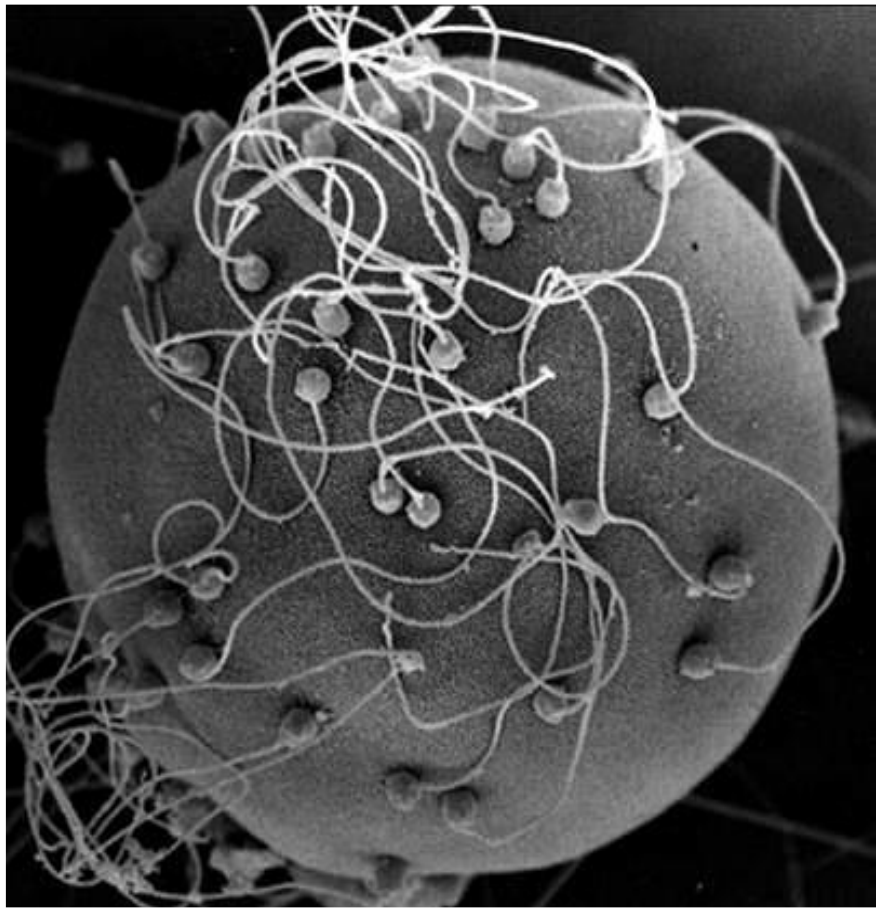
Membrane fusion and vesicular transport

A fundamental process in life

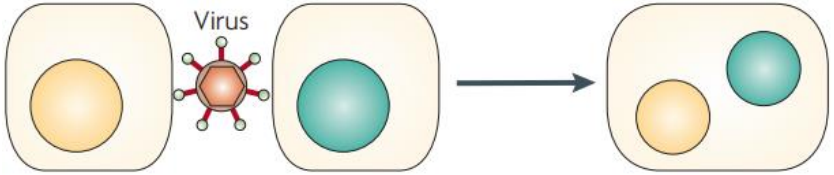
Examples of membrane fusion



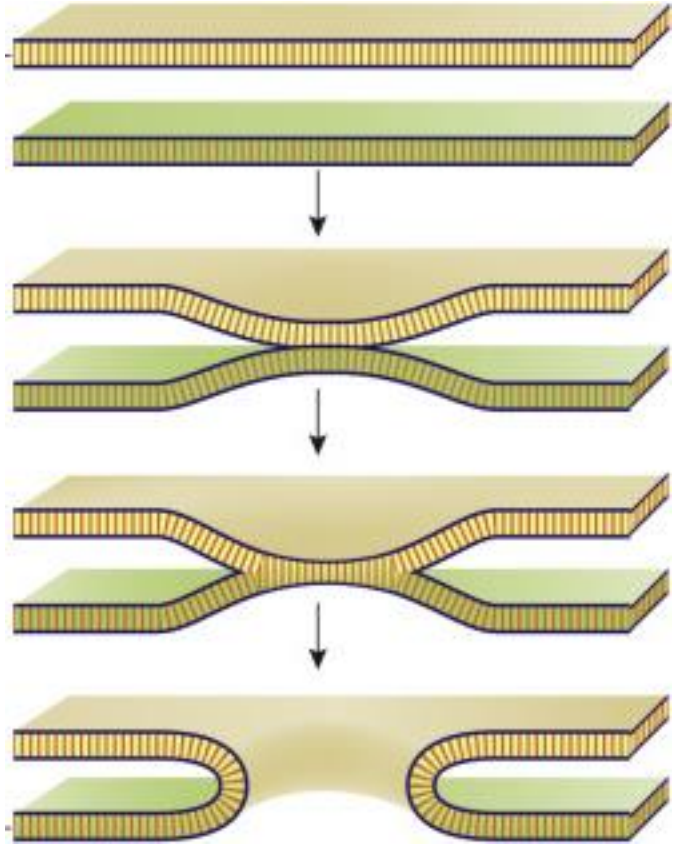
Cell-cell fusion

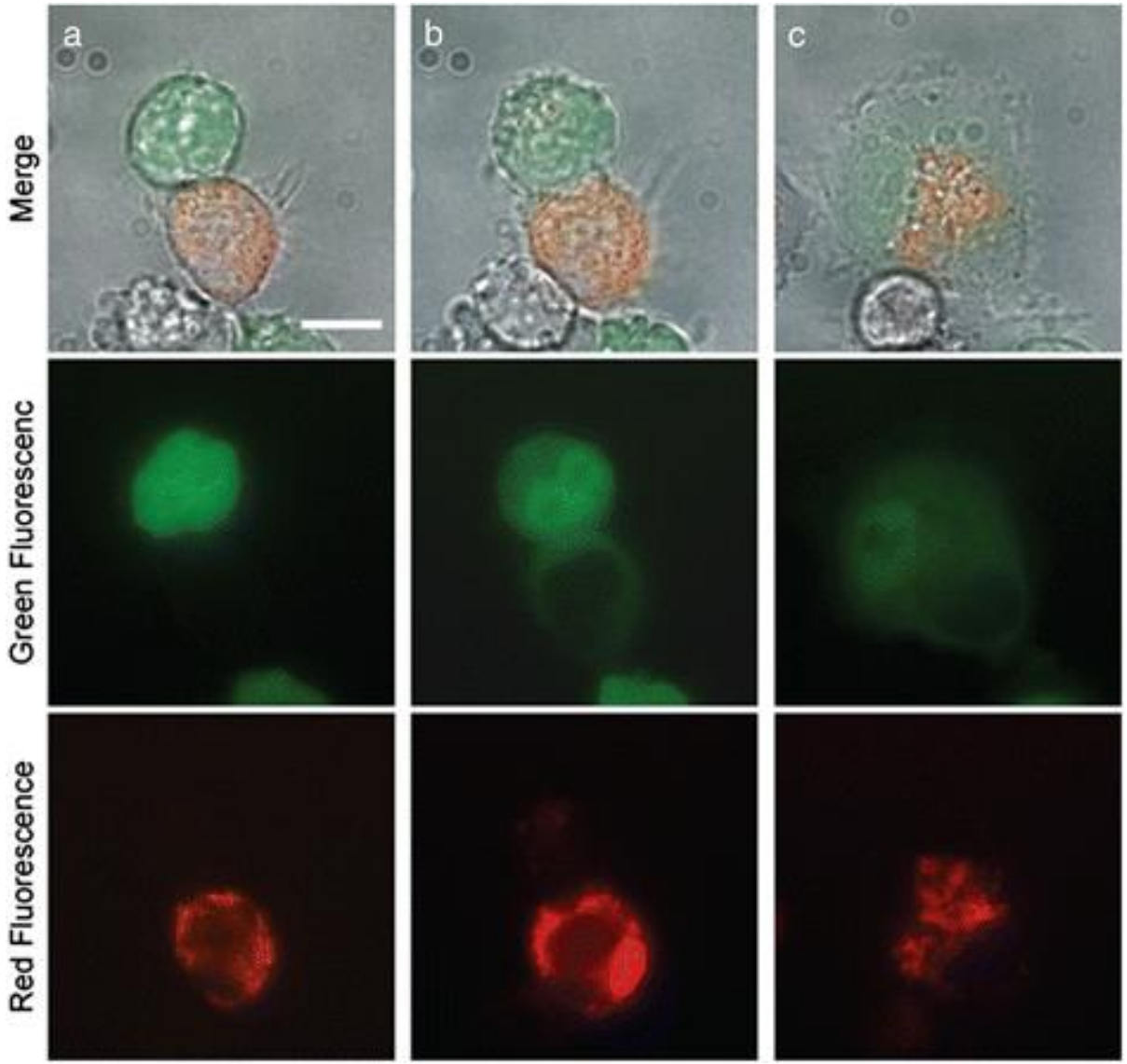


- **Natural fusion**
  - Fertilization
  - Formation of syncytium
  - Yeast mating: fusion of haploid cells
- **Induced fusion – use of fusogens:**
  - **Electric field (electroporation)**
  - **Chemical** (e.g., polyethylenglycol, aka PEG)
  - **Viruses** (e.g., Sendai virus)

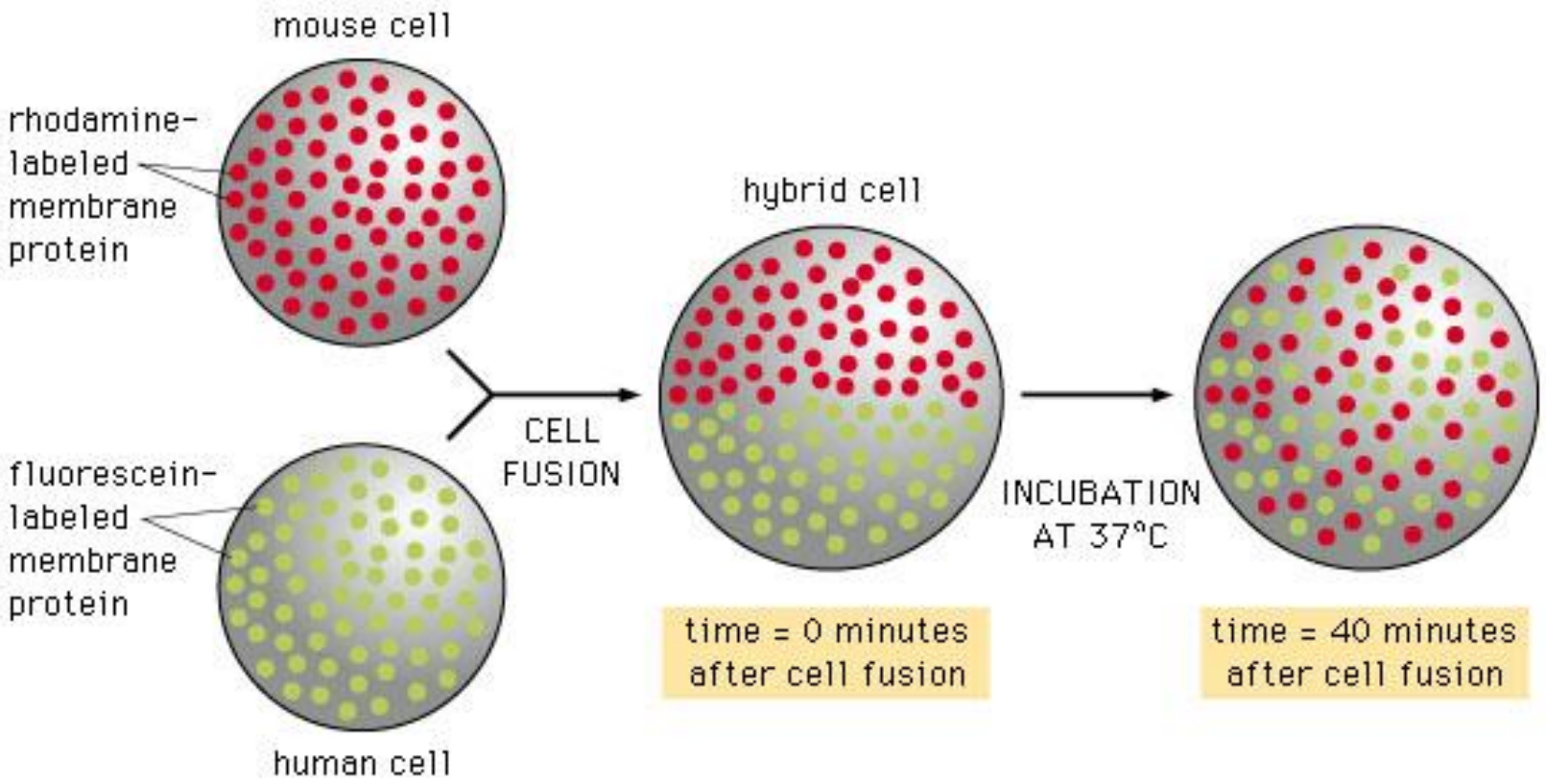


Fusion process





Cell-cell fusion as an evidence of membrane fluidity



- 1970, **Frye-Eddidin experiment**
- Lateral diffusion of proteins

Essential roles of membrane fusion

- **Formation of membrane-bound vesicles and their trafficking between organelles: cargo transport, secretion, uptake**
- **Organelle dynamics** (e.g., mitochondria)

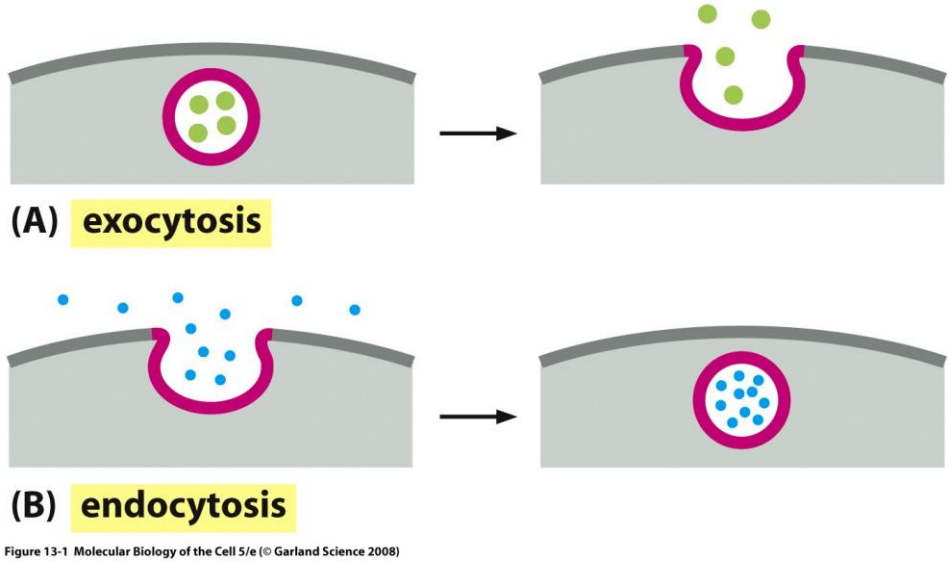
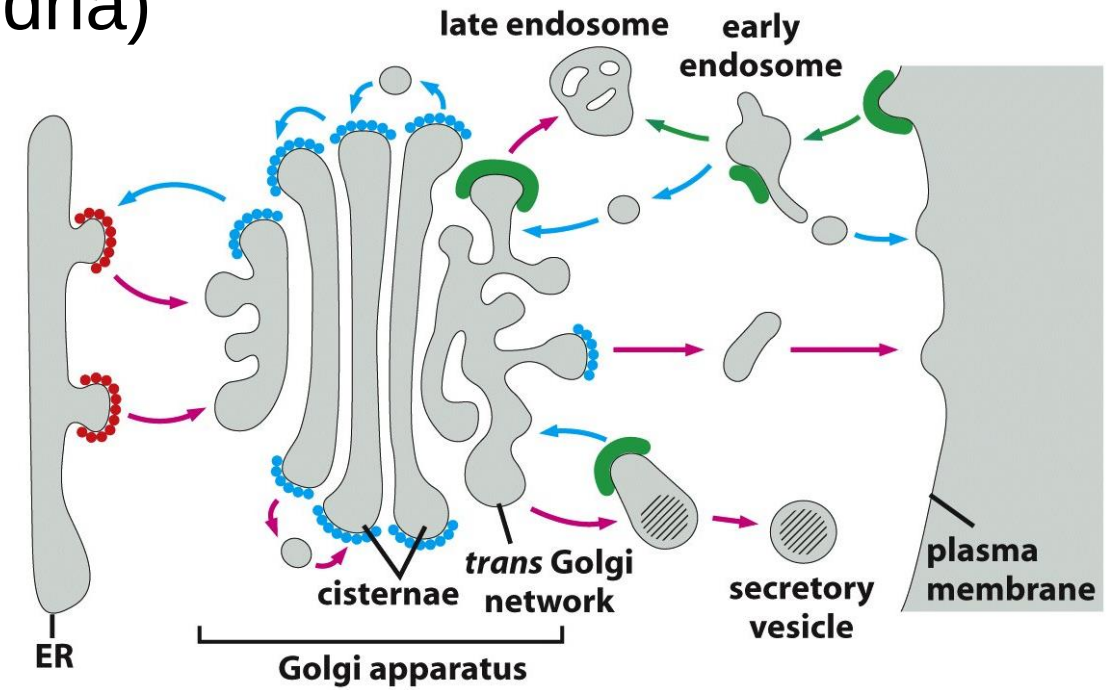
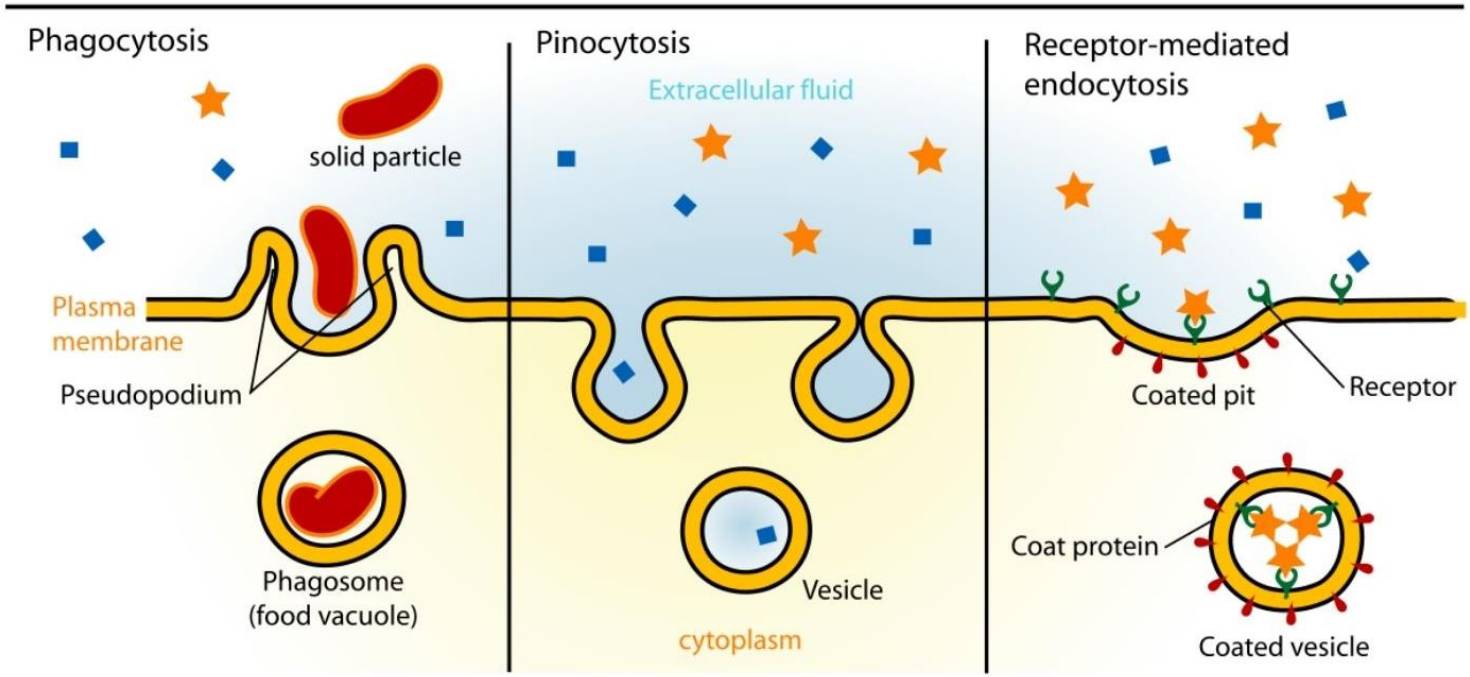


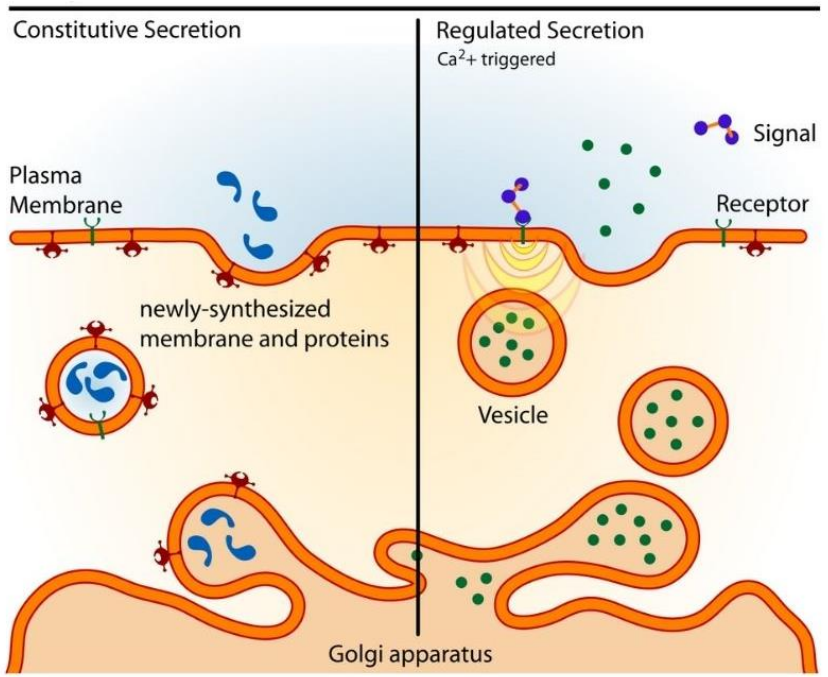
Figure 13-1 Molecular Biology of the Cell 5/e (© Garland Science 2008)



Endocytosis



Exocytosis



Membrane fusion in action

Watch video of amoeba phagocytosing other protists