



# Lecture 1: Introduction & endoplasmic reticulum

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Second year, First semester, 2026-2027

# Instructors



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# Course outline (1)



Focus on  
functions  
and  
diseases

- Introduction and biomembranes
- Endoplasmic reticulum and protein sorting
- Golgi apparatus and vesicular transport
- Mitochondria and mitochondrial diseases
- Peroxisomes
- The nucleus
- Cytoskeletal networks
- The extracellular network
- Cell signaling, proliferation, differentiation, and death
- The biology of cancer

# Course outline (2)



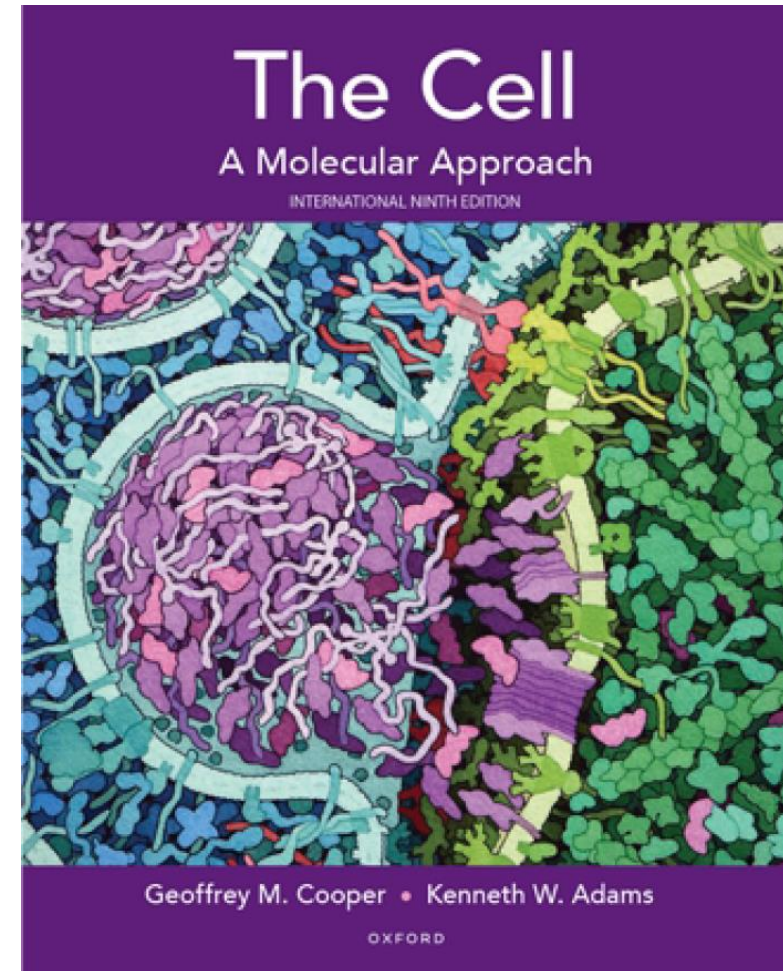
Focus on  
processes and  
techniques

- Overview of nucleic acids and gel electrophoresis
- The concept and utilization of the (de/re)naturation concepts
  - Dot blotting and Southern blotting
- Restriction endonucleases, recombinant DNA technology
- The central dogma of molecular biology and DNA replication
- PCR and DNA sequencing
- The human genome
- Transcription, mechanisms of regulation, and epigenetics
  - Coding and non-coding RNAs
- RNA detection and quantification and luciferase reporter assay
- Translation and mechanisms of regulation
- Yeast two-hybrid system
- DNA mutations
- DNA repair and CRISPR-Cas9

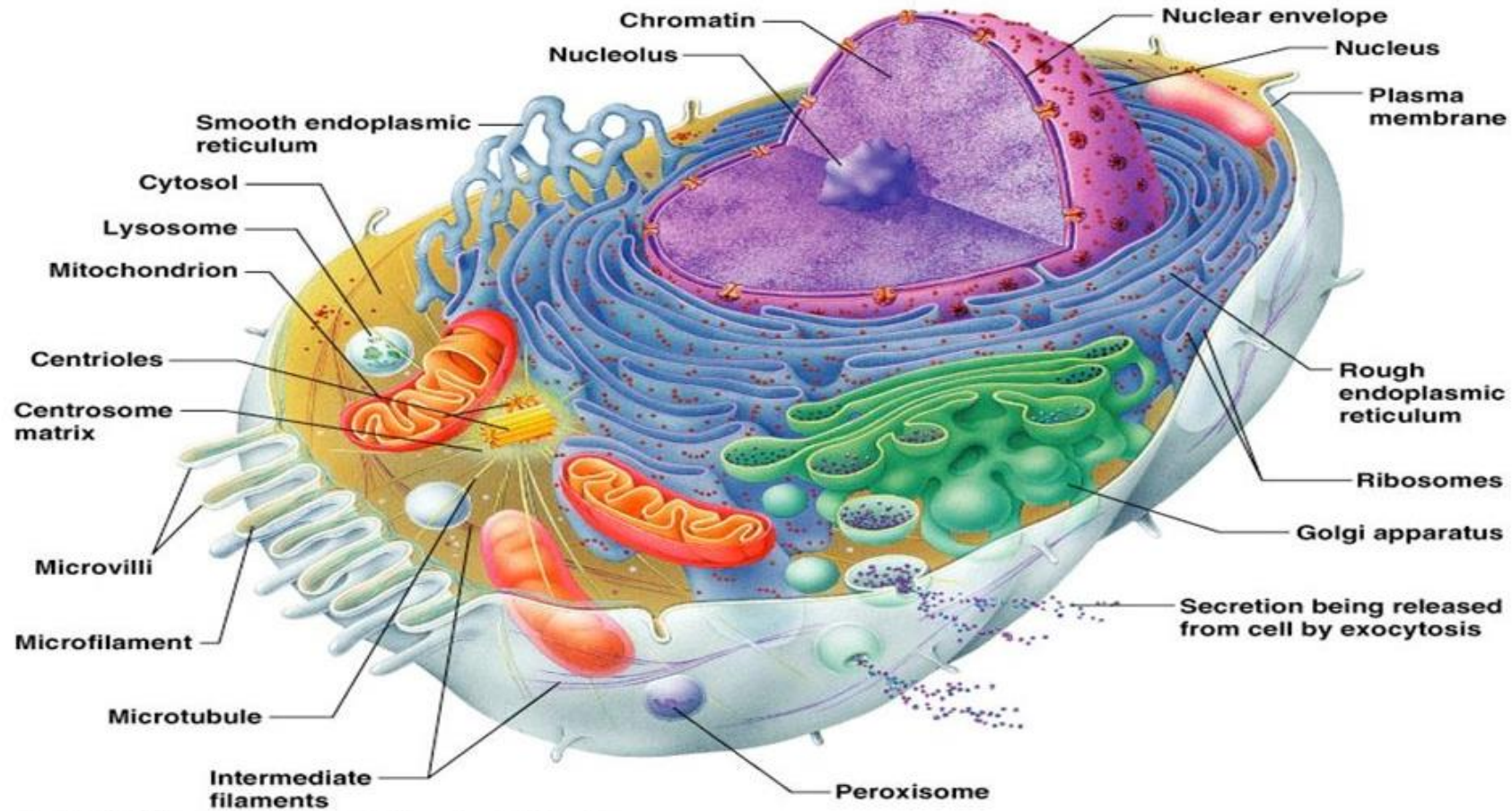
# The textbook



- **The Cell: A Molecular Approach**, [Geoffrey M. Cooper](#) and Kenneth W. Adams, 9th edition, Sinauer Associates, 2023.



# The cell

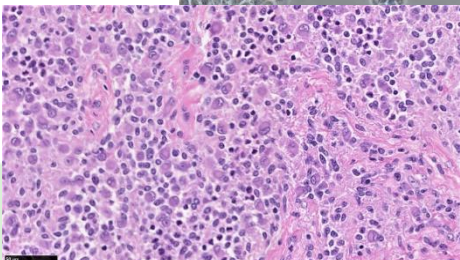
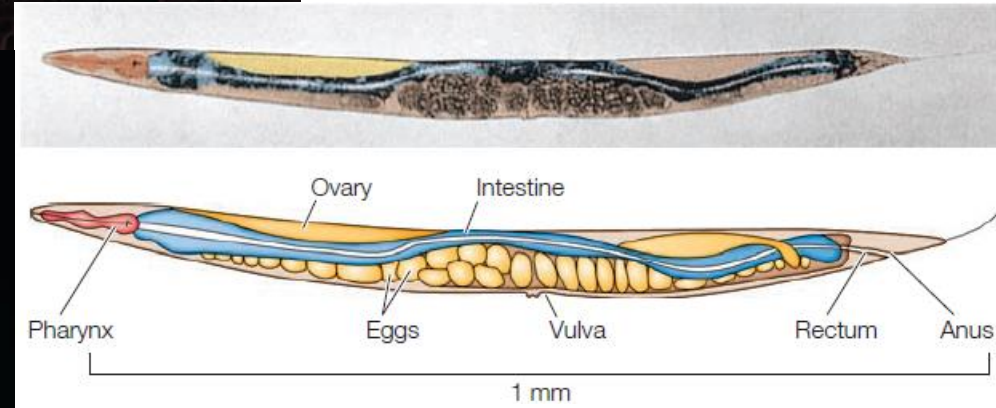
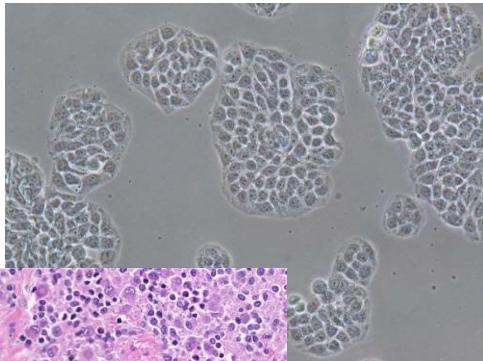
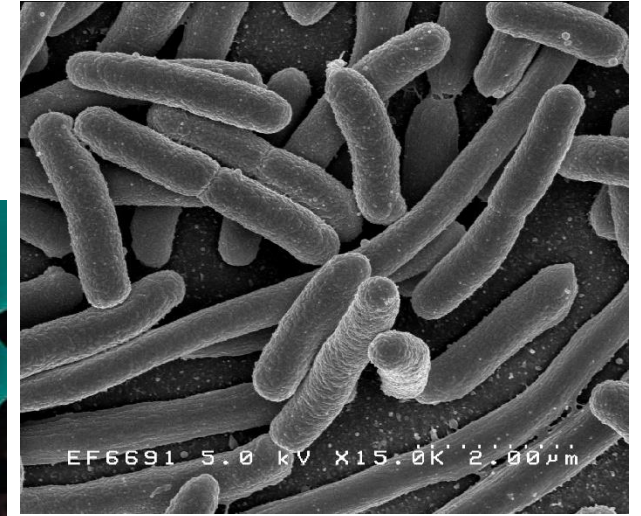
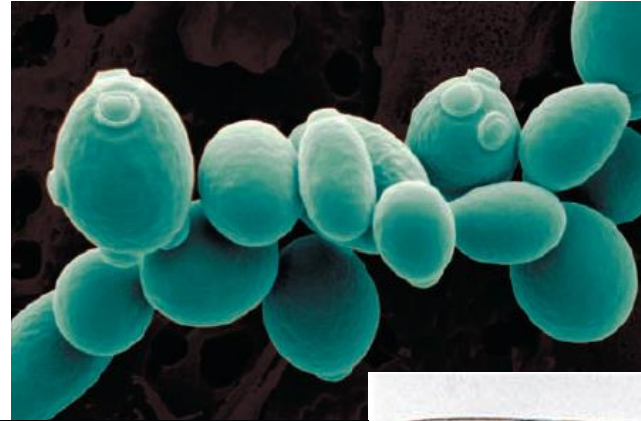


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# What organisms do we use to study cells?



- Escherichia coli (E. coli)
- Yeast (*Saccharomyces cerevisiae*)
- *Caenorhabditis elegans*
- *Drosophila melanogaster*
- Mice
- Cultured cells and tissues



# Nobel prize 2026



Karl Deisseroth

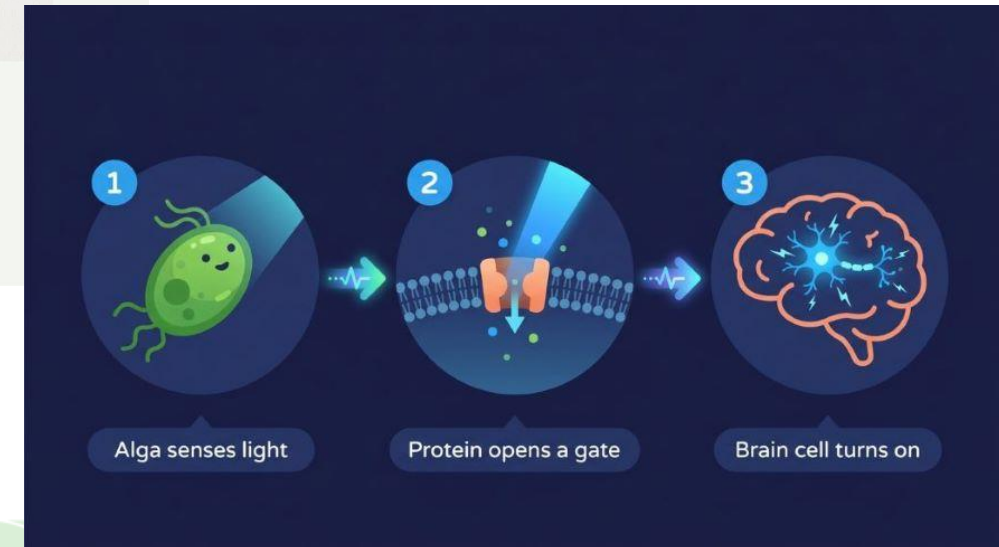


Peter Hegemann



Georg Nagel

## Nobel Prize Winners in Physiology or Medicine 2026 Announced



## Nucleus

### Nuclear envelope:

membrane enclosing the nucleus. Protein-lined pores allow material to move in and out.

**Chromatin:** DNA plus associated proteins.

### Nucleolus:

condensed region where ribosomes are formed.

**Peroxisome:**  
metabolizes waste

## Endoplasmic reticulum

**Rough:** associated with ribosomes; makes secretory and membrane proteins.

**Smooth:** makes lipids.

## Cytoskeleton

**Microtubules:** form the mitotic spindle and maintain cell shape.

**Centrosome:** microtubule-organizing center.

**Intermediate filaments:** fibrous proteins that hold organelles in place.

### Microfilaments:

fibrous proteins; form the cellular cortex.

**Plasma membrane**

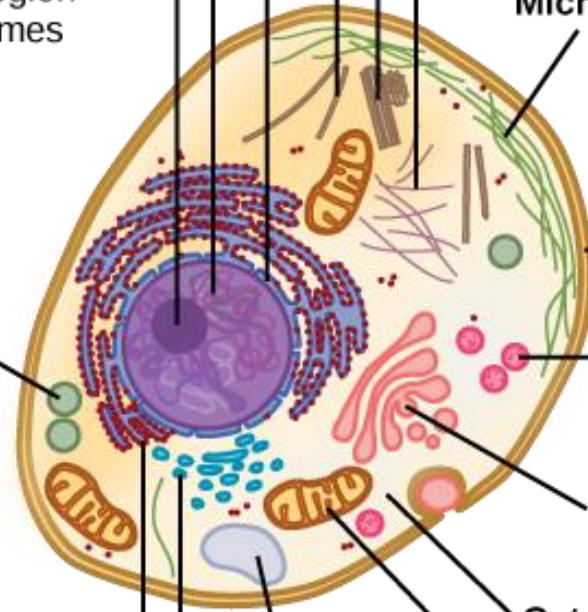
**Lysosome:**  
digests food and waste materials.

**Golgi apparatus:**  
modifies proteins.

## Cytoplasm

**Mitochondria:**  
produce energy.

**Vacuole**



# Organelles



**TABLE 4-2** *Organelles*

| Organelle                       | Function                                                                                                                          |
|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| Mitochondrion                   | transfers energy from organic compounds to ATP                                                                                    |
| Ribosome                        | organizes the synthesis of proteins                                                                                               |
| Endoplasmic reticulum (ER)      | prepares proteins for export (rough ER); synthesizes steroids, regulates calcium levels, breaks down toxic substances (smooth ER) |
| Golgi apparatus                 | processes and packages substances produced by the cell                                                                            |
| Lysosome                        | digests molecules, old organelles, and foreign substances                                                                         |
| Microfilaments and microtubules | contribute to the support, movement, and division of cells                                                                        |
| Cilia and flagella              | propel cells through the environment; move materials over the cell surface                                                        |
| Nucleus                         | stores hereditary information in DNA; synthesizes RNA and ribosomes                                                               |

# Major molecular components of cells

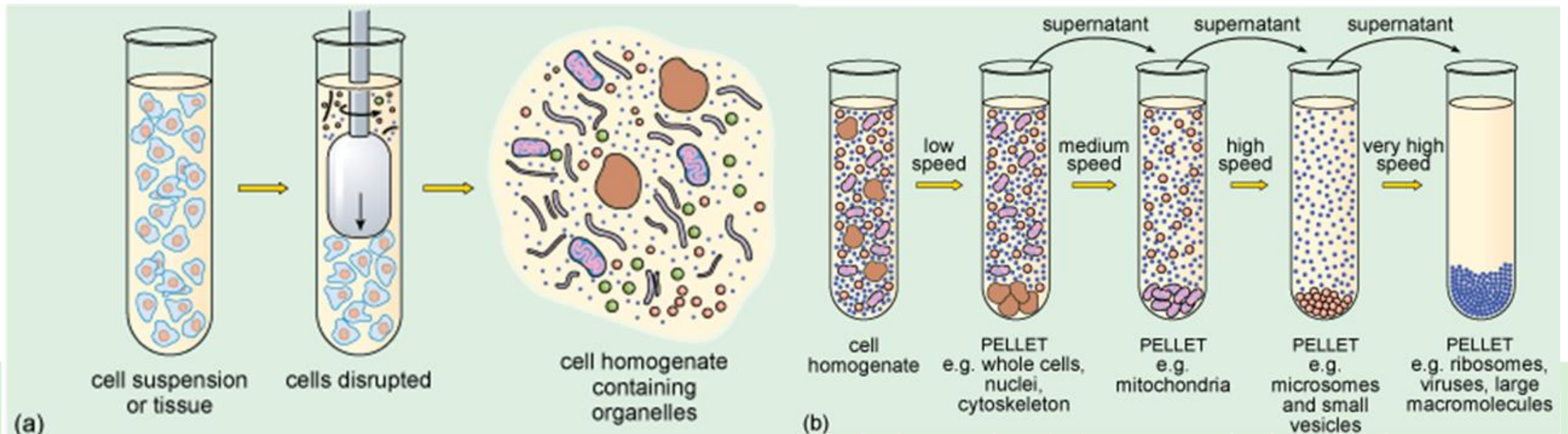
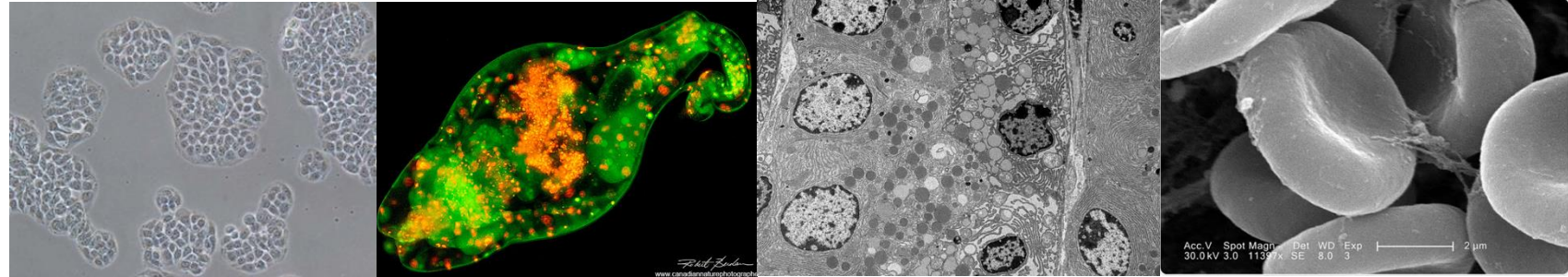


- Nucleic acids
- Carbohydrates
- Proteins
- Lipids (50% of mass of plasma membranes, 30% of mitochondrial membranes)
- Molecules function by interacting with each non-covalently.

# How do we study cell components?

## Cell and protein detection

- Microscopy
  - Light, fluorescence (immunofluorescence), electron, scanning electron
- Cell fractionation



<https://www.facebook.com/reel/792265814706206>



# Biochemical composition of plasma membranes



| Membrane                             | Protein (%) | Lipid (%) | Carbohydrate (%) | Weight fraction of protein | Ratio of protein to lipid |
|--------------------------------------|-------------|-----------|------------------|----------------------------|---------------------------|
| Plasma membranes                     |             |           |                  |                            |                           |
| → Myelin                             | 18          | <u>79</u> | 3                | 0.18                       | <u>0.23</u>               |
| Blood platelets                      | 33—42       | 51—58     | 7.5              | 0.4                        | 0.7                       |
| Mouse liver cells                    | 46          | 54        | 2—4              | 0.46                       | 0.85                      |
| → Human erythrocytes                 | <u>49</u>   | 43        | 8                | 0.49                       | <u>1.1</u>                |
| Amoeba                               | 54          | 42        | 4                | 0.54                       | 1.3                       |
| Rat liver cells                      | 58          | 42        | (5—10)*          | 0.58                       | 1.4                       |
| HeLa cells                           | 60          | 40        | 2.4              | 0.6                        | 1.5                       |
| Nuclear envelope of rat liver cells  | 59          | 35        | 2.9              | 0.59                       | 1.6                       |
| Retinal rods, bovine                 | 51          | 49        | 4                | 0.51                       | 1.0                       |
| → Mitochondrial outer membrane       | <u>52</u>   | 48        | (2—4)*           | 0.52                       | <u>1.1</u>                |
| Sarcoplasmic reticulum               | 67          | 33        | —                | 0.67                       | 2.0                       |
| Chloroplast lamellae, spinach        | 70          | 30        | (6)*             | 0.7                        | 2.3                       |
| → Mitochondrial inner membrane       | <u>76</u>   | 24        | (1—2)*           | 0.76                       | 3.2                       |
| Gram-positive bacteria               | 75          | 25        | (10)*            | 0.75                       | 3.0                       |
| <i>Halobacterium</i> purple membrane | 75          | 25        |                  | 0.75                       | 3.0                       |

# Lipid composition of organelles



Table 1: Head group composition of the membranes of some mammalian liver cells, erythrocytes , and nerve cells in weight percent. Adapted from Jamieson and Robinson (1977). Abbreviations: PC = phosphatidylcholines, PE = phosphatidylethanolamines, PS = phosphatidylserines, PI = phosphatidylinositols, SM = sphingomyelin, CL = cardiolipin.

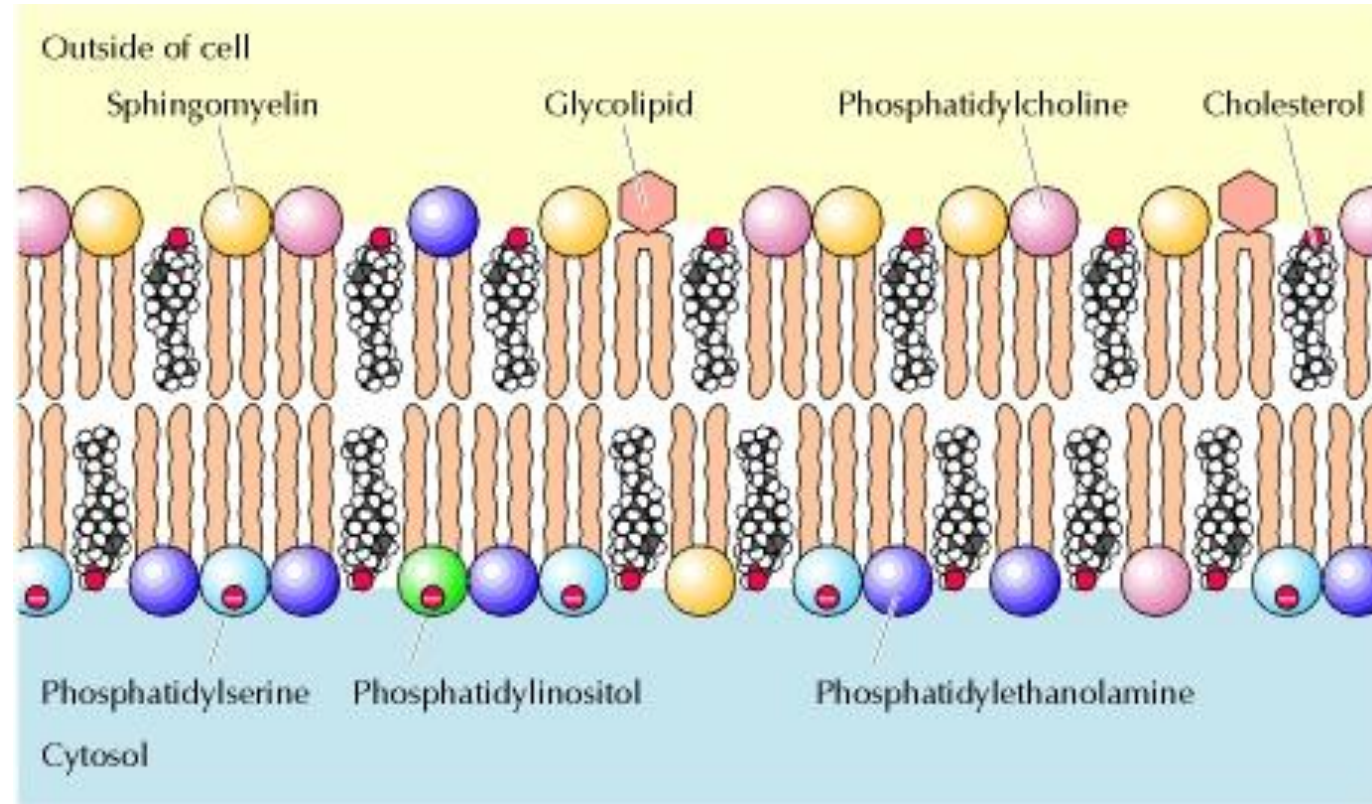
| Membrane            | PC | PE | PS | PI       | SM | CL        | Glycolipid | Cholesterol | Others |
|---------------------|----|----|----|----------|----|-----------|------------|-------------|--------|
| Erythrocyte (human) | 20 | 18 | 7  | 3        | 18 | –         | 3          | 20          | 11     |
| Plasma (rat liver)  | 18 | 12 | 7  | 3        | 12 | –         | 8          | 19          | 21     |
| ER                  | 48 | 19 | 4  | 8        | 5  | –         | tr         | 6           | 10     |
| Golgi               | 25 | 9  | 3  | 5        | 7  | –         | 0          | 8           | 43     |
| Lysosome            | 23 | 13 | –  | 6        | 23 | ≈ 5       | –          | 14          | 16     |
| Nuclear membrane    | 44 | 17 | 4  | 6        | 3  | 1         | tr         | 10          | 15     |
| Mitochondria        | 38 | 29 | 0  | 3        | 0  | <u>14</u> | tr         | <u>3</u>    | 13     |
| Neurons             | 48 | 21 | 5  | <u>7</u> | 4  | –         | 3          | 11          | 1      |
| Myelin              | 11 | 17 | 9  | 1        | 8  | –         | <u>20</u>  | <u>28</u>   | 6      |

**Cholesterol is an essential component of animal plasma membranes. It is not present in bacteria and plant cells, but the latter cells contain sterols.**

# Composition and properties of plasma membranes

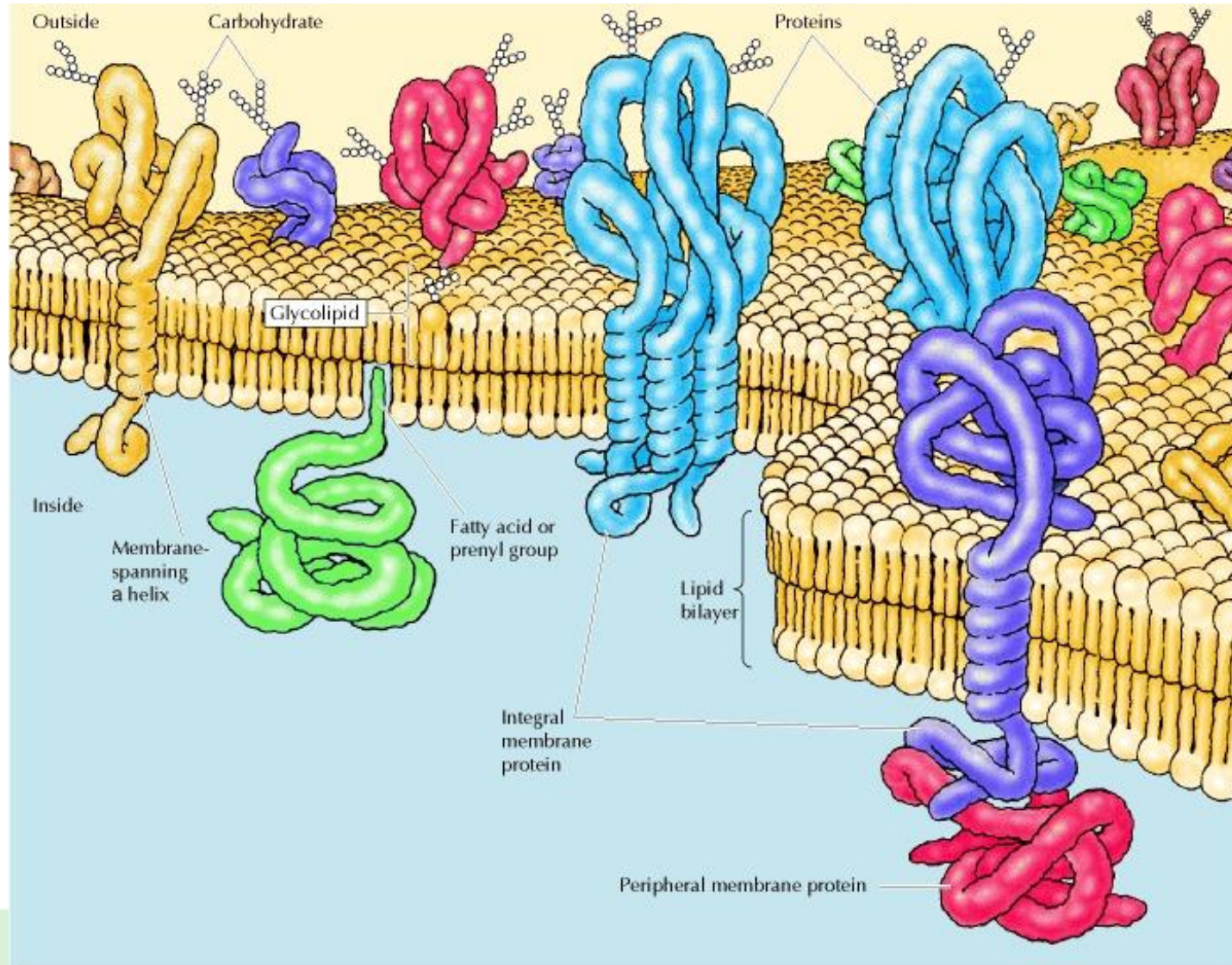


- The phospholipids are asymmetrically distributed between the two halves of the membrane bilayer.
  - The outer leaflet: @choline, sphingomyelin
  - The inner leaflet: @ethanolamine, @serine, @inositol (minor)
    - @inositol has a role in cell signaling.
  - Glycolipids are found exclusively on the outer membrane.



@ = Phosphatidyl...

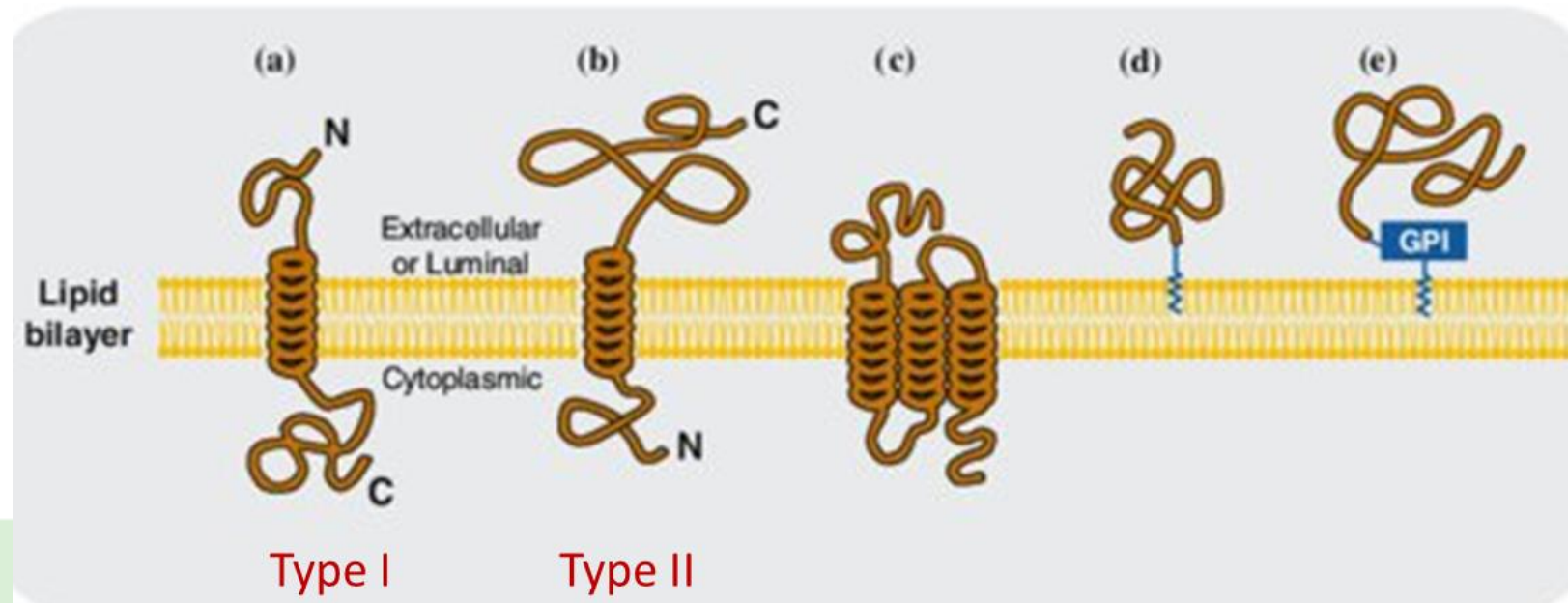
# Membrane proteins



# Types of membrane proteins



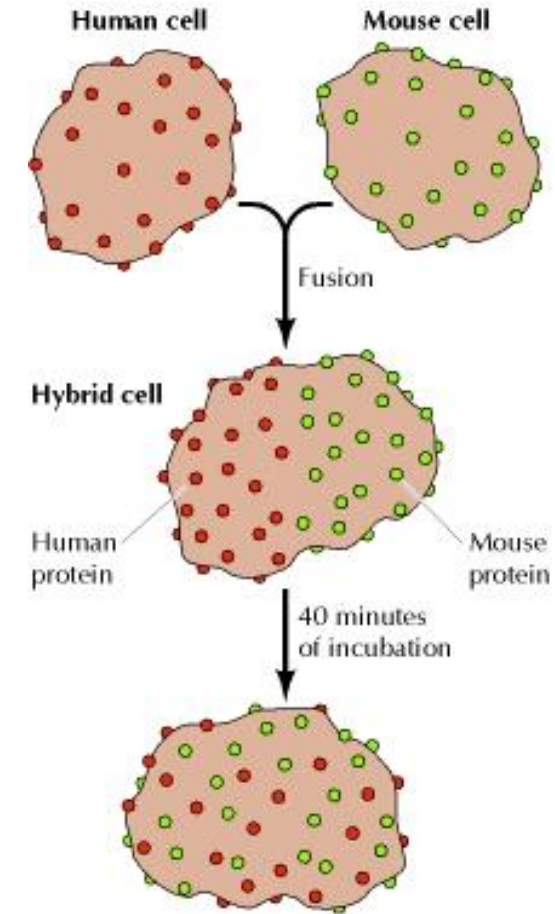
- Peripheral membrane proteins are indirectly and loosely associated with membranes through protein-protein interactions, mainly ionic bonds.
- Integral membrane proteins have some of their **helical** parts inserted into the lipid bilayer.
  - Single-pass (type I or II) or multi-pass proteins.
- Lipid-anchored membrane proteins (myristoylation, palmitoylation , glycosyl-phosphatidylinositol)



# Protein mobility



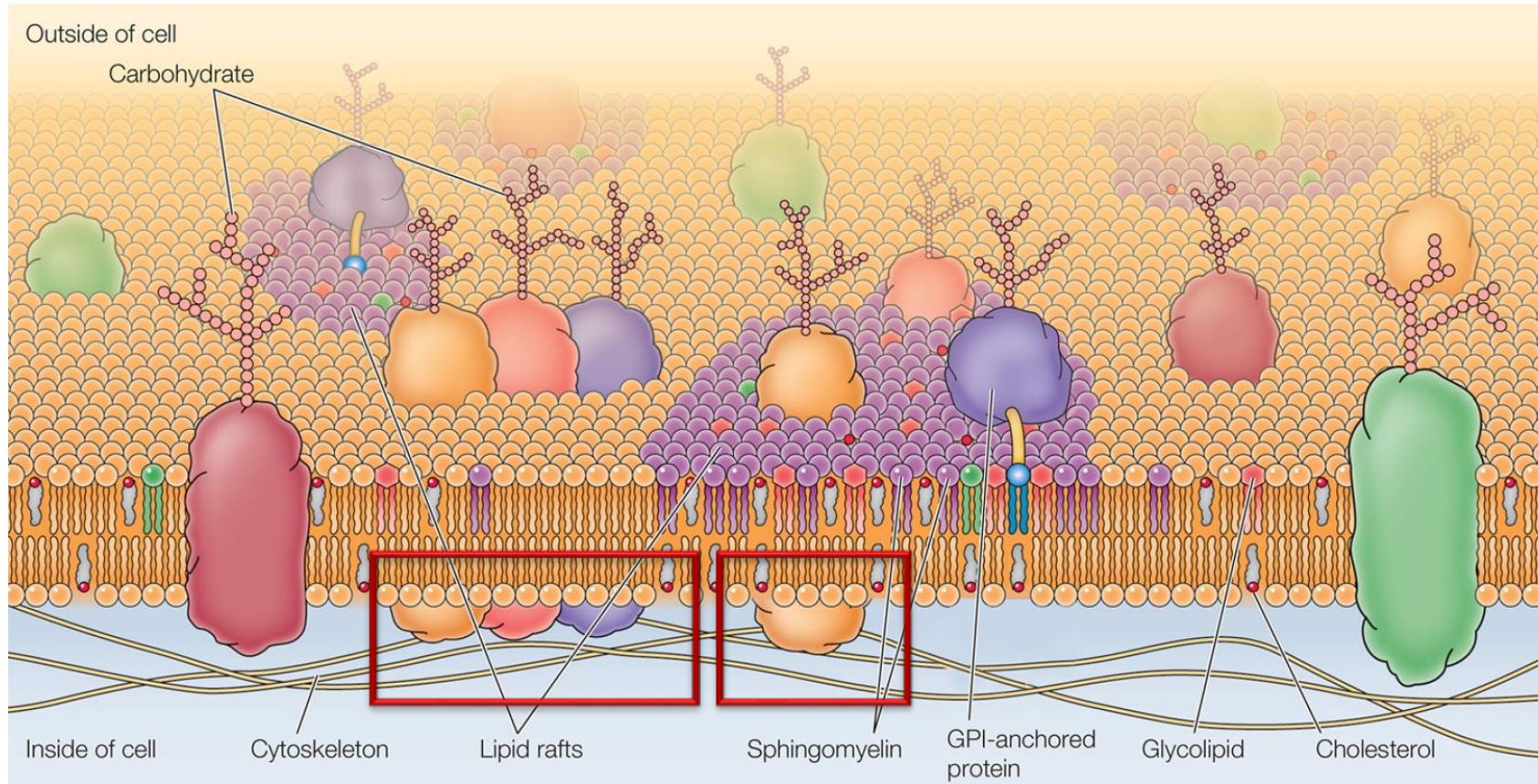
- Proteins and lipids are able to diffuse laterally through the membrane.
- BUT, in specialized epithelial cells, the mobility of membrane proteins by three mechanisms.



# Mechanism 1

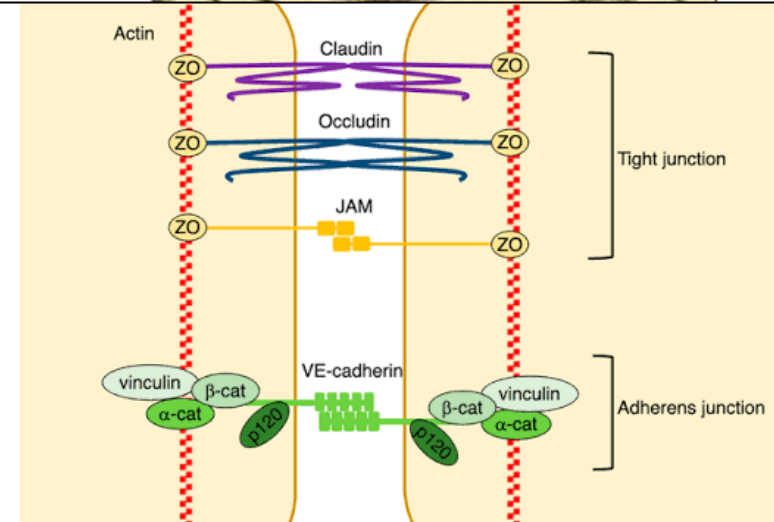
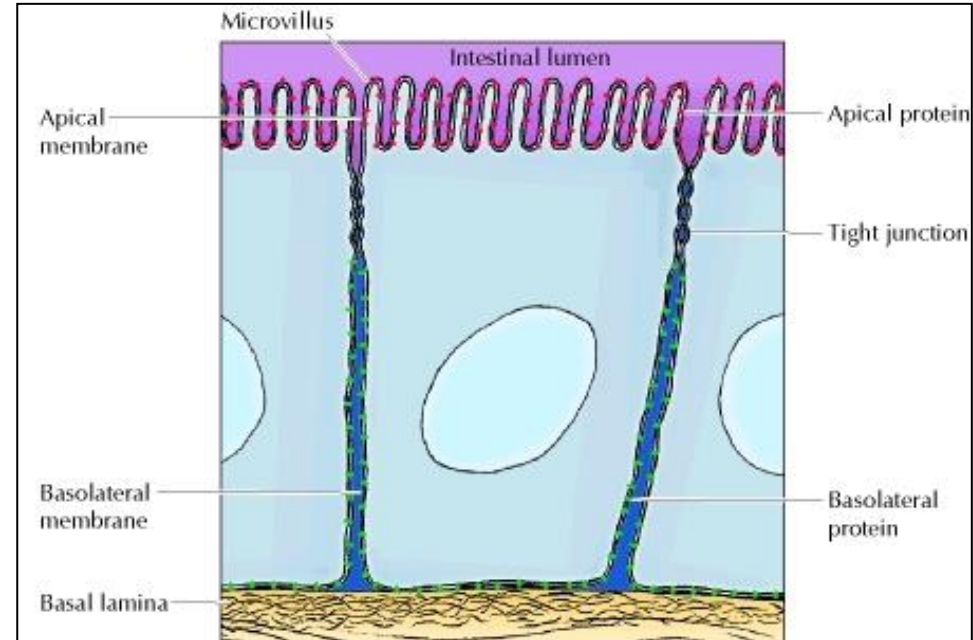


## ● Membrane protein association with the cytoskeleton



# Mechanism 2

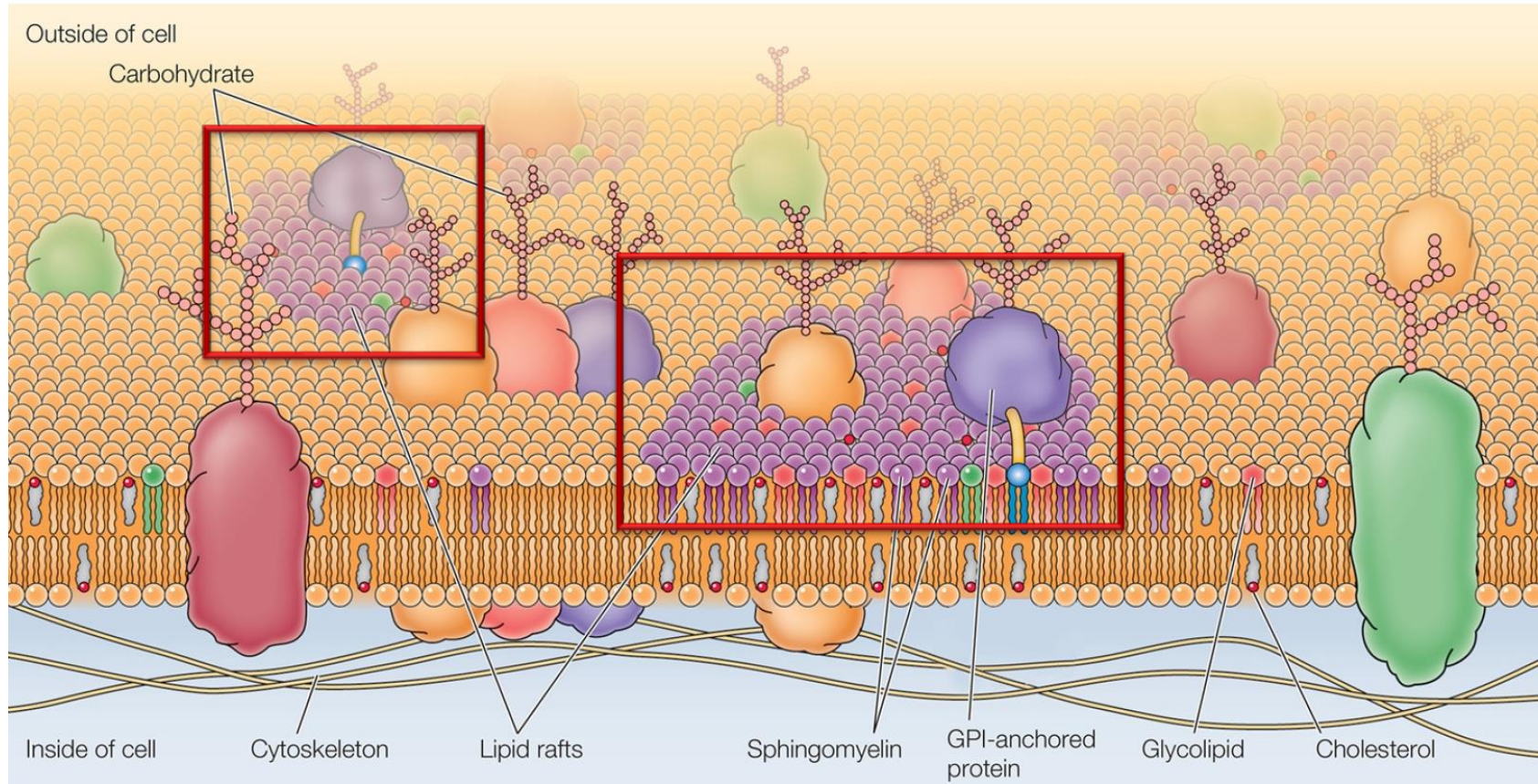
- Specific membrane domains can be created by **tight junctions**.
- Specialized seals between adjacent cells that prevent fluid leakage and control the movement of molecules between tissue compartments.
- Tight junctions divide the plasma membrane into apical and basolateral surface.
- The proteins are also names as apical and basolateral.



# Mechanism 3



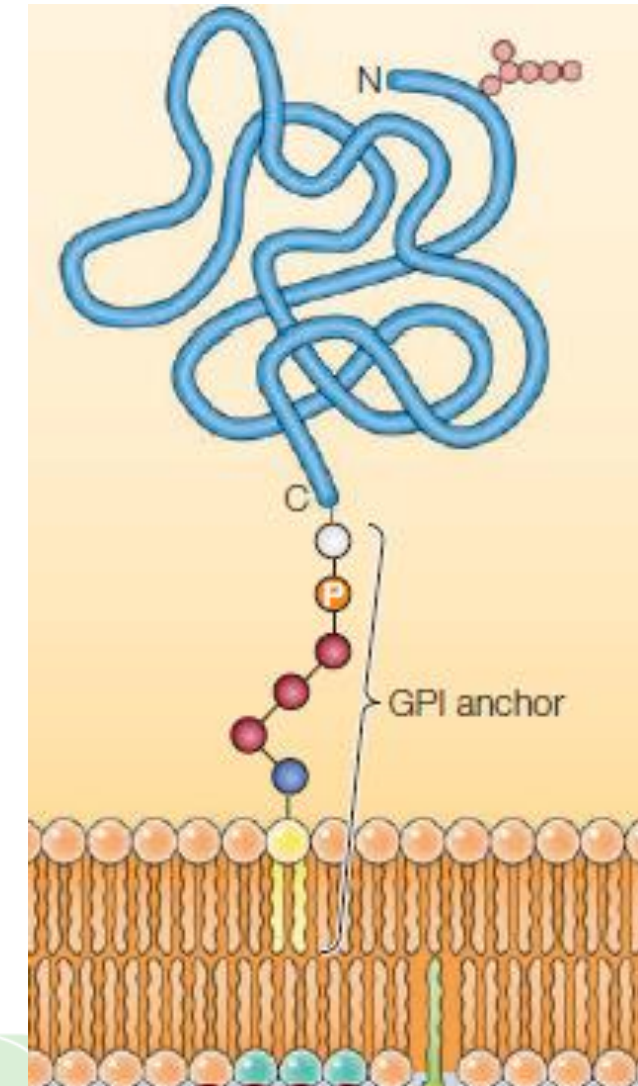
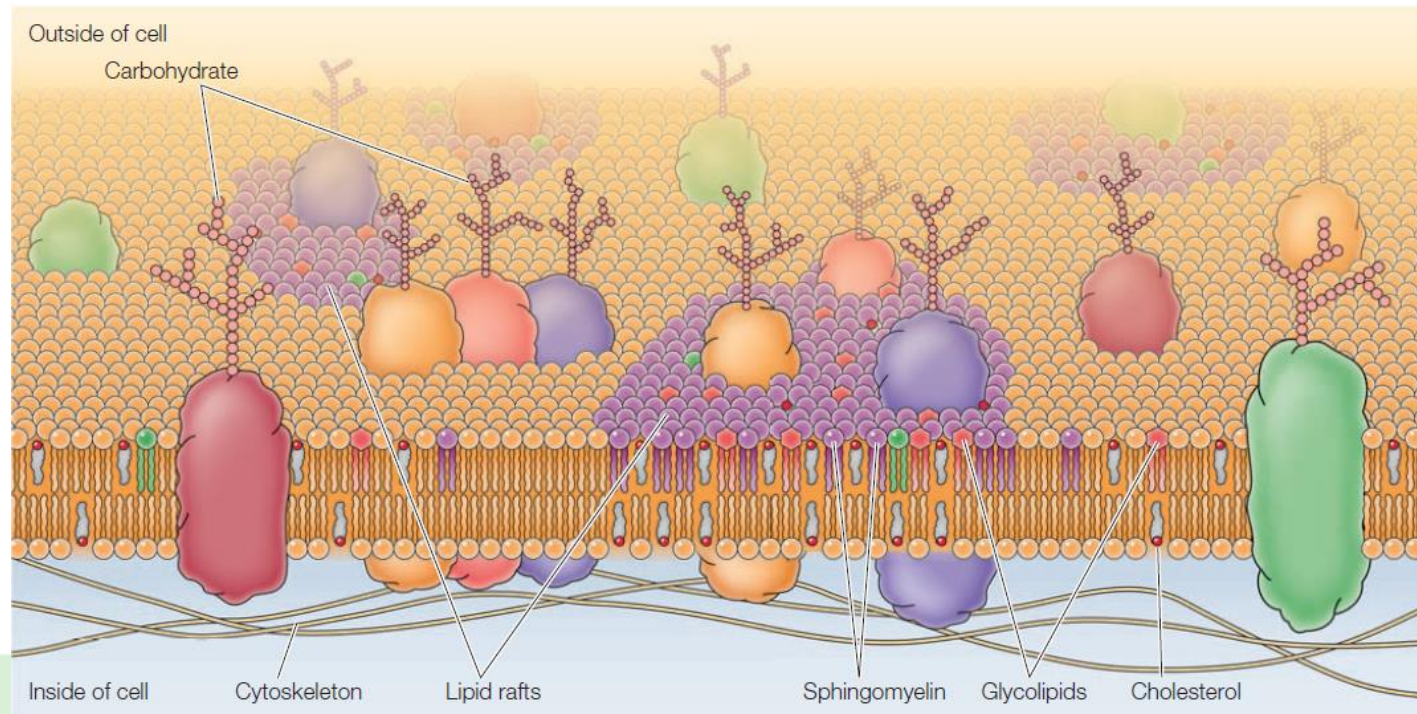
- Specific lipid composition of the membrane (e.g. lipid rafts)



# Lipid rafts



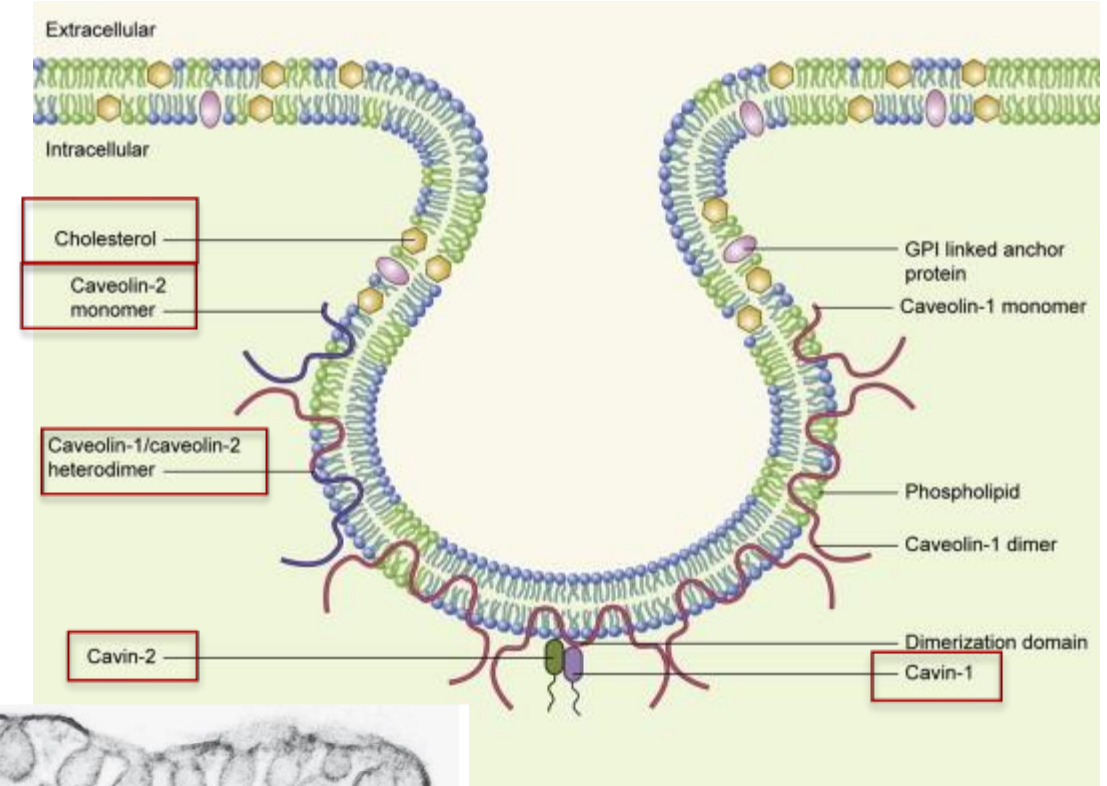
- Specialized membrane regions with clusters of cholesterol and the sphingolipids (sphingomyelin and glycolipids).
- Rafts are enriched in glycosylphosphatidylinositol (GPI)-anchored proteins, and proteins involved in signal transduction and intracellular vesicular trafficking (transport).



# Caveolae

(Latin for “little caves”)

- They are a subset of lipid rafts that **require cholesterol** for their formation.
- They are formed the membrane protein **caveolin**, which interacts with cholesterol and **the cytoplasmic protein cavin**.
- They are important for several cellular activities, including endocytosis, cell signaling, regulation of lipid transport, and protection of the plasma membrane against mechanical stress.



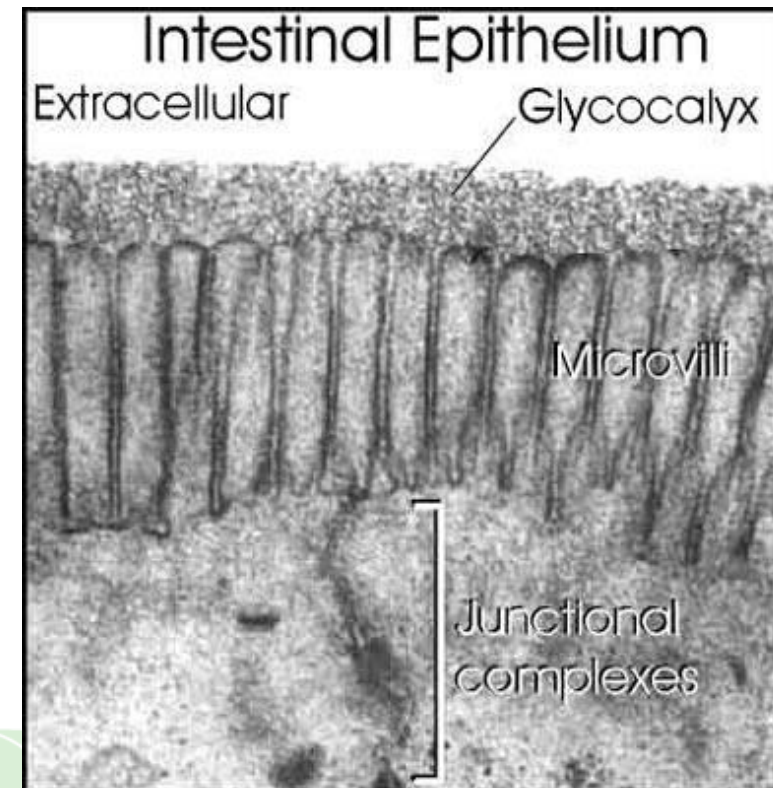
# Glycocalyx



- The surface of the cell can be covered by a carbohydrate coat, known as the **glycocalyx**, formed by the oligosaccharides of glycolipids and glycoproteins.

## Functions:

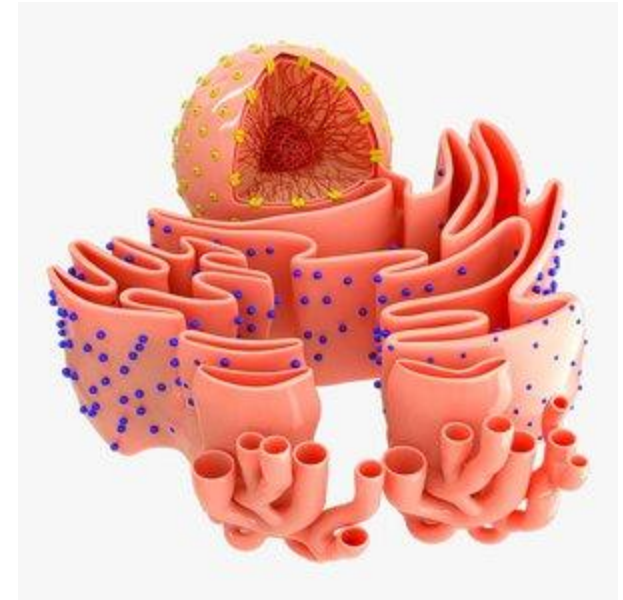
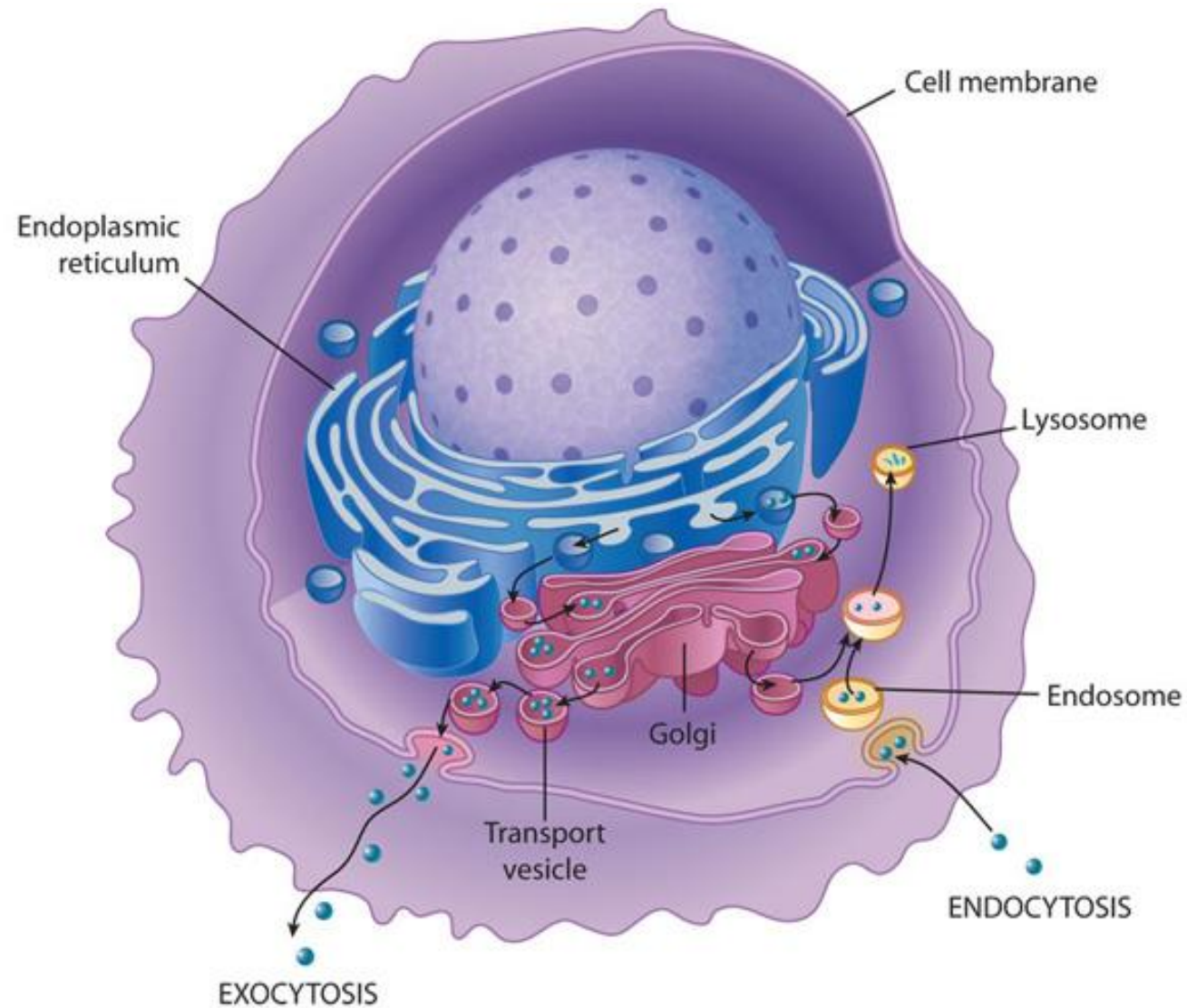
- Cell-cell interactions such as immune cells
- Protection of cell surface from ionic and mechanical stress
- Formation of a barrier for microorganisms





# *Protein sorting (endoplasmic reticulum)*

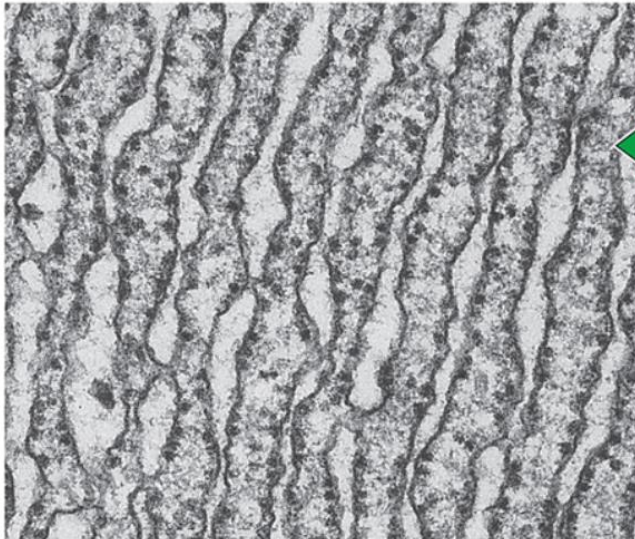
# An overview



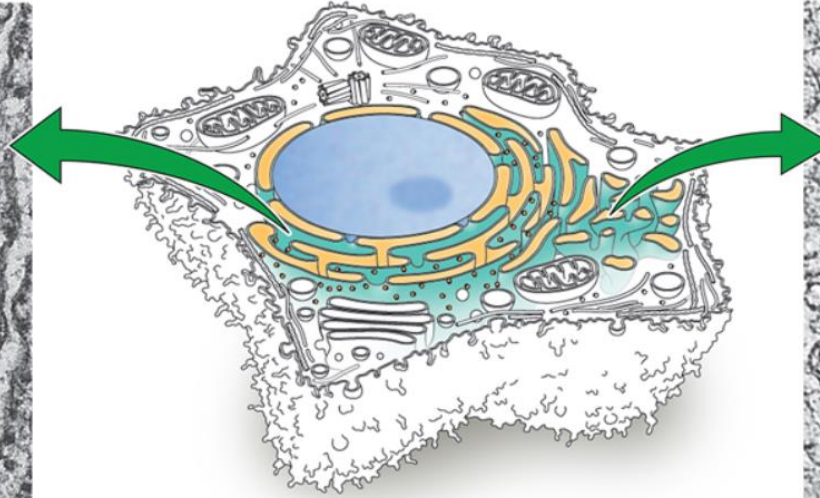
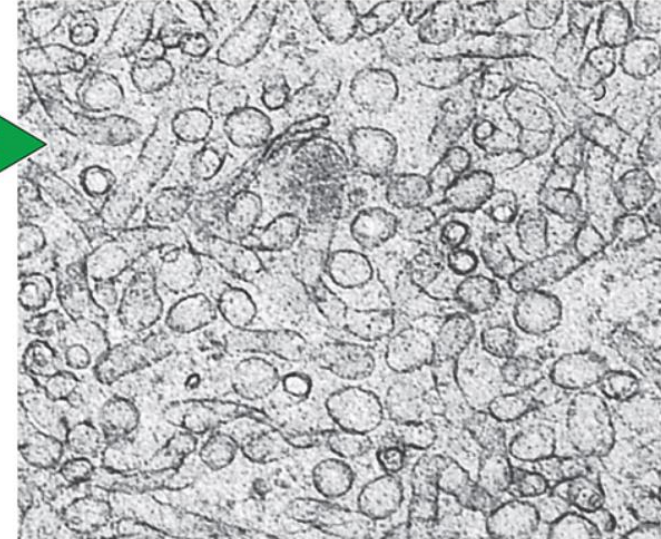
# Endoplasmic reticulum (ER)

- It is a network of membrane-enclosed tubules and sacs (cisternae) that extends from the nuclear membrane throughout the cytoplasm.
- It is the largest organelle of most eukaryotic cells.
- Rough ER: covered by ribosomes on its outer surface and functions in protein processing.
- Smooth ER: lipid metabolism
- Transitional ER: exit of vesicles to Golgi apparatus

(A) Rough endoplasmic reticulum

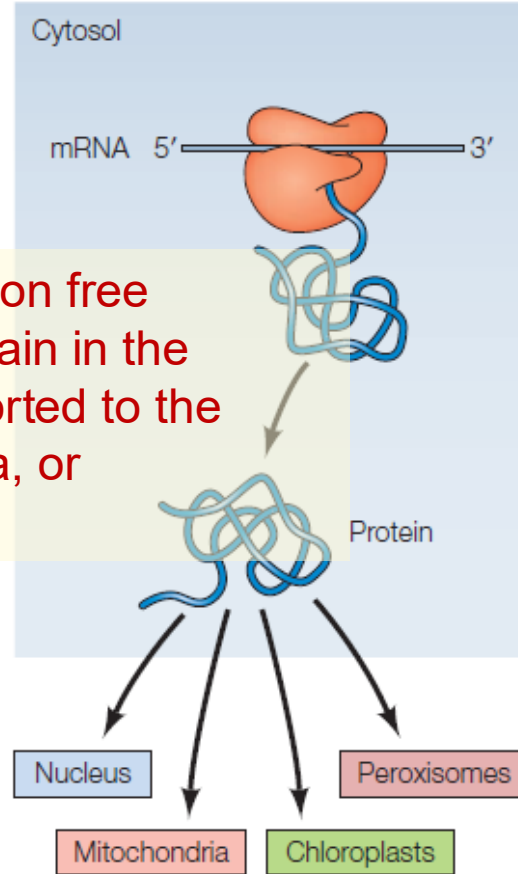


(B) Smooth endoplasmic reticulum



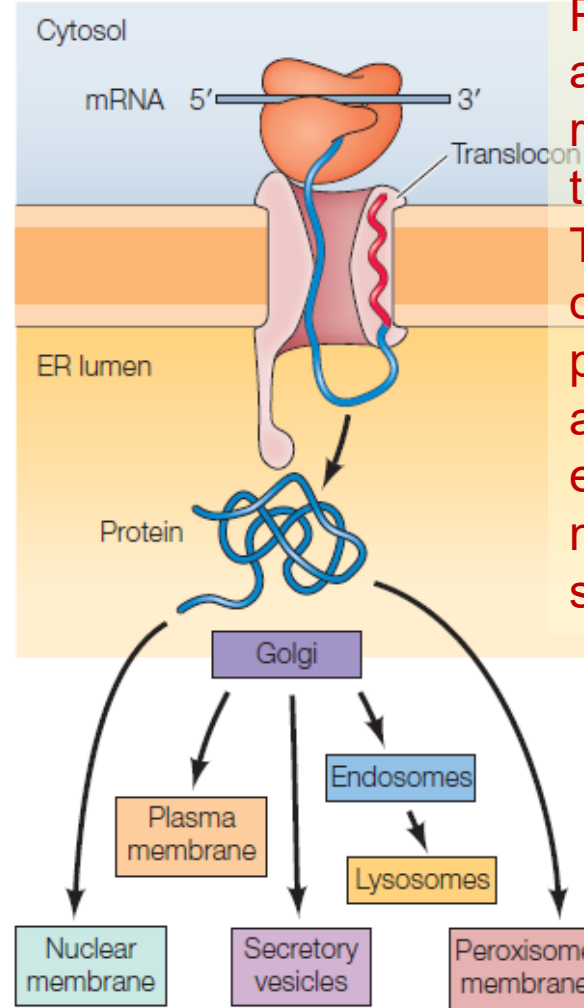
# Protein sorting

Free ribosomes in cytosol



Proteins synthesized on free ribosomes either remain in the cytosol or are transported to the nucleus, mitochondria, or peroxisomes.

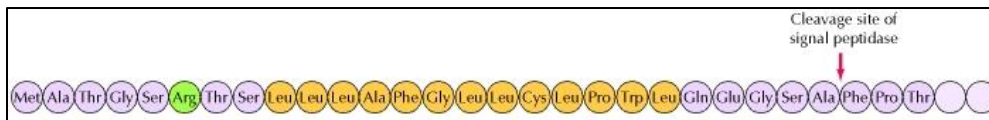
Membrane-bound ribosomes



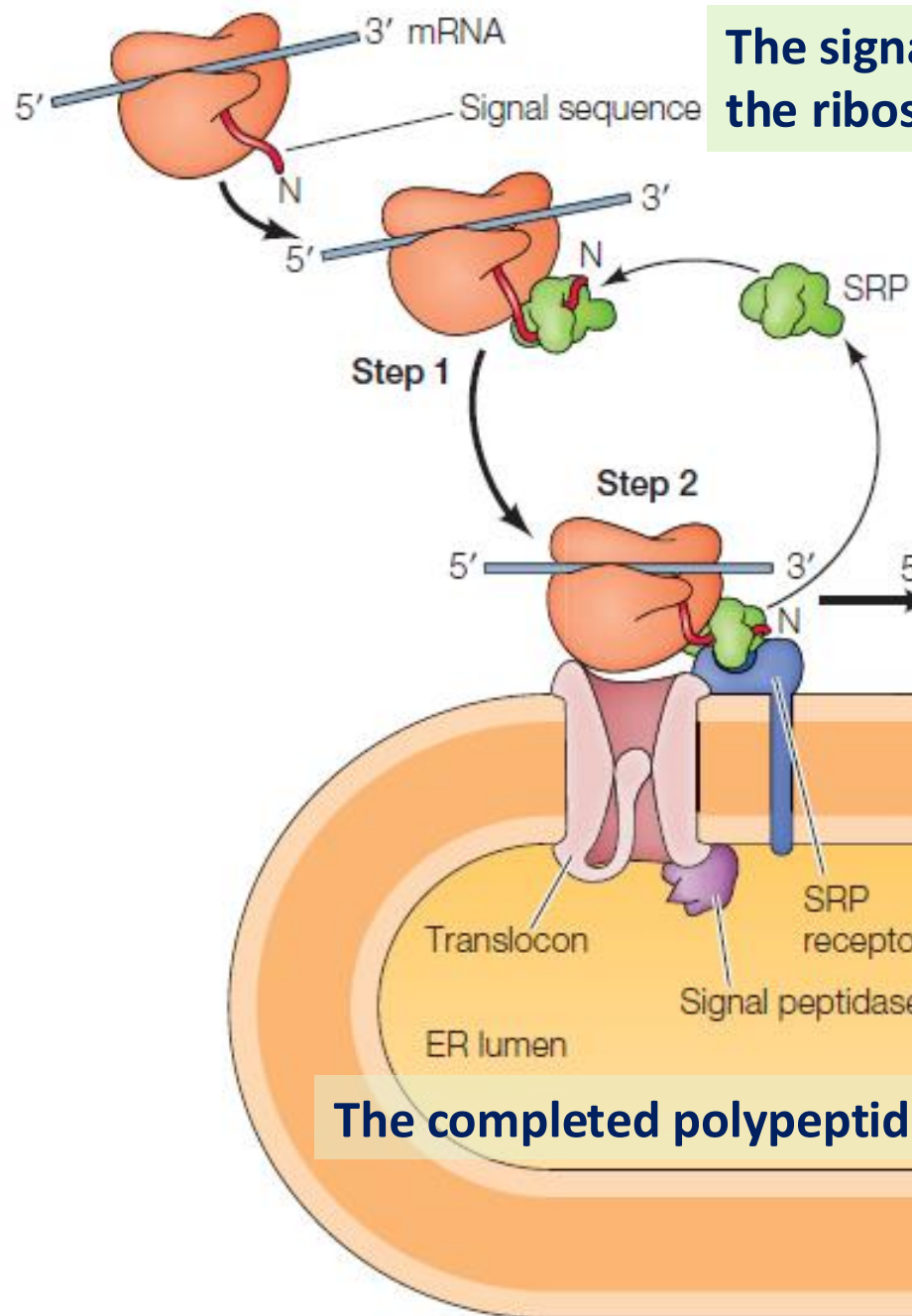
Proteins containing **signal sequences** are synthesized on membrane-bound ribosomes and translocated directly into the ER.

These proteins may stay within the ER or transported to nuclear membranes, peroxisomal membranes, or the Golgi apparatus and, from there, to endosomes, lysosomes, the plasma membrane, or outside the cell via secretory vesicles.

*In cell biology, a lumen is a membrane-defined space that is found inside several organelles, cellular components, or structures*



**Signal sequence:** a short sequence of amino acids of the polypeptide at the amino terminus. It is then cleaved from the polypeptide chain during its transfer into the ER lumen.



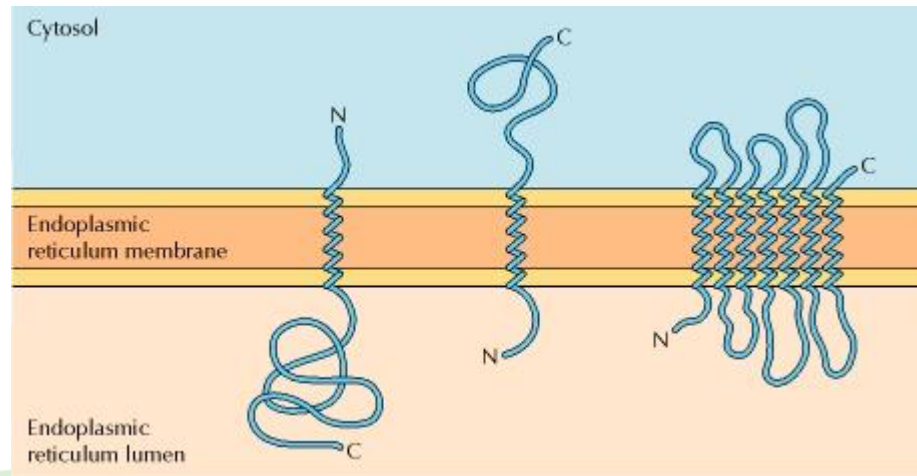
The signal sequence is recognized as the protein is synthesized and the ribosome is transported to the surface of the RER

Translation resumes on the surface of RER, the peptide simultaneously translocates into the ER through the **translocon**, and the signal peptide is cleaved by **signal peptidase**.

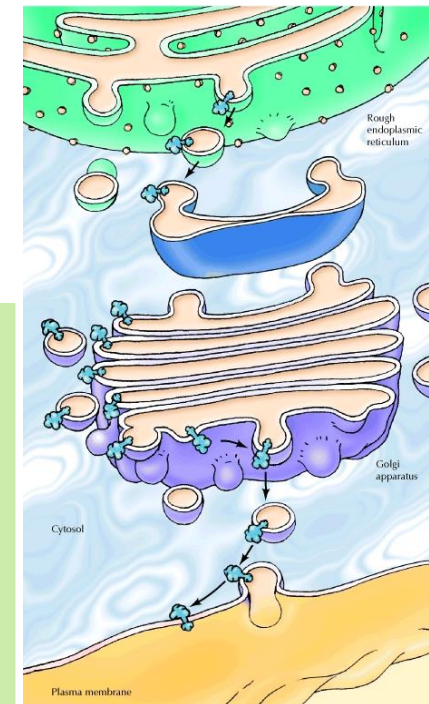
The completed polypeptide chain is released within the ER lumen

# Pathways of protein sorting

- Secretory, ER, Golgi apparatus, and lysosomal proteins are released into the lumen of the ER.
- Membranous proteins are initially inserted into the ER membrane.
- Considerations
  - Single vs. multiple membrane-spanning region
  - Orientation of N- and C-termini

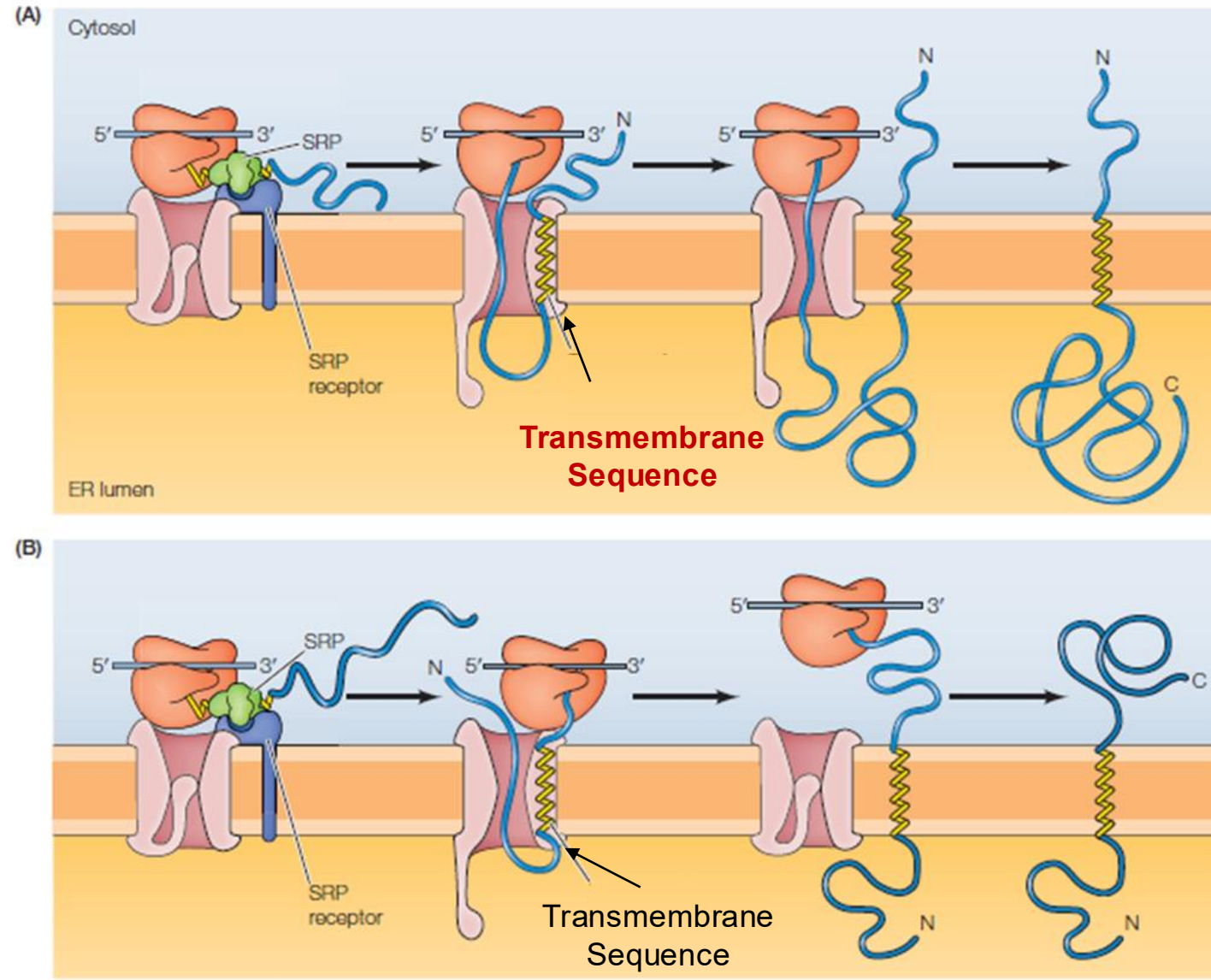


**The lumens of the ER and Golgi apparatus are topologically equivalent to the exterior of the cell.**

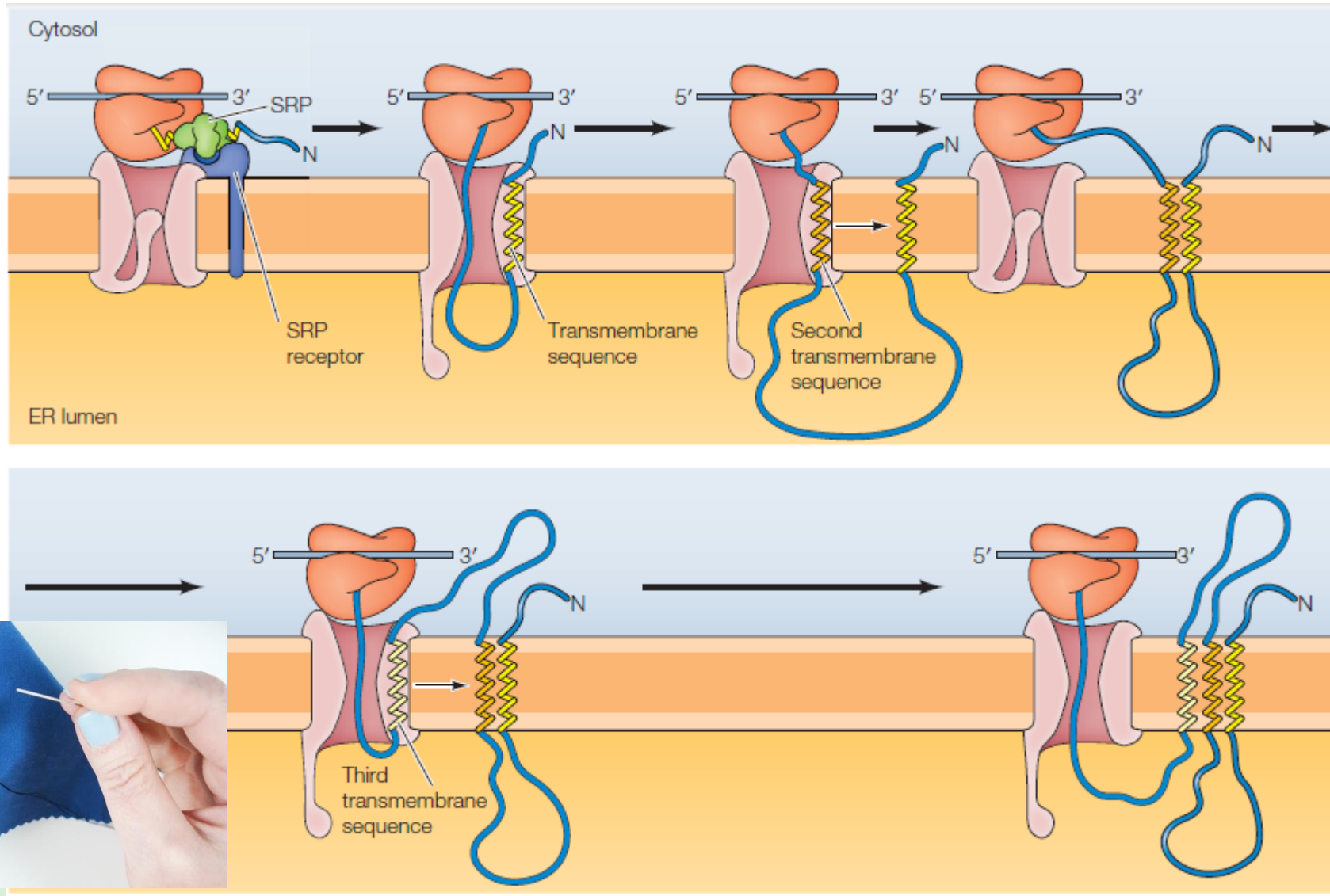


# Insertion of membrane proteins via internal transmembrane sequences

- Translocation of the polypeptide chain stops when the translocon recognizes a transmembrane sequence allowing the protein to become anchored in the ER membrane.
- The direction of the internal transmembrane sequence determines the direction of insertion and orientation of the protein ends.

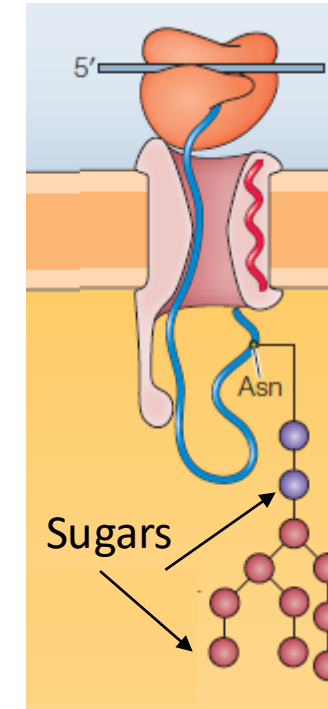
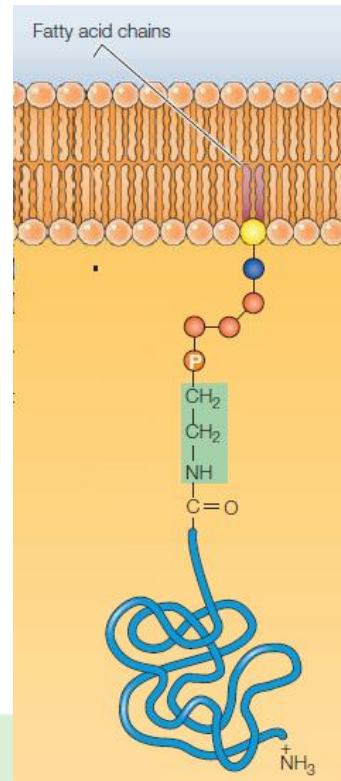
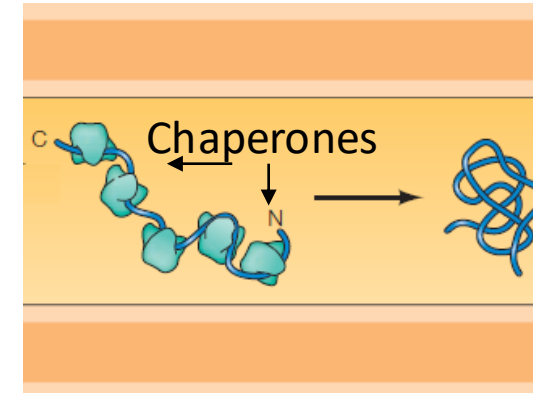


# Multi-transmembrane domain proteins have multiple transmembrane sequences



# Once inside the ER, proteins are

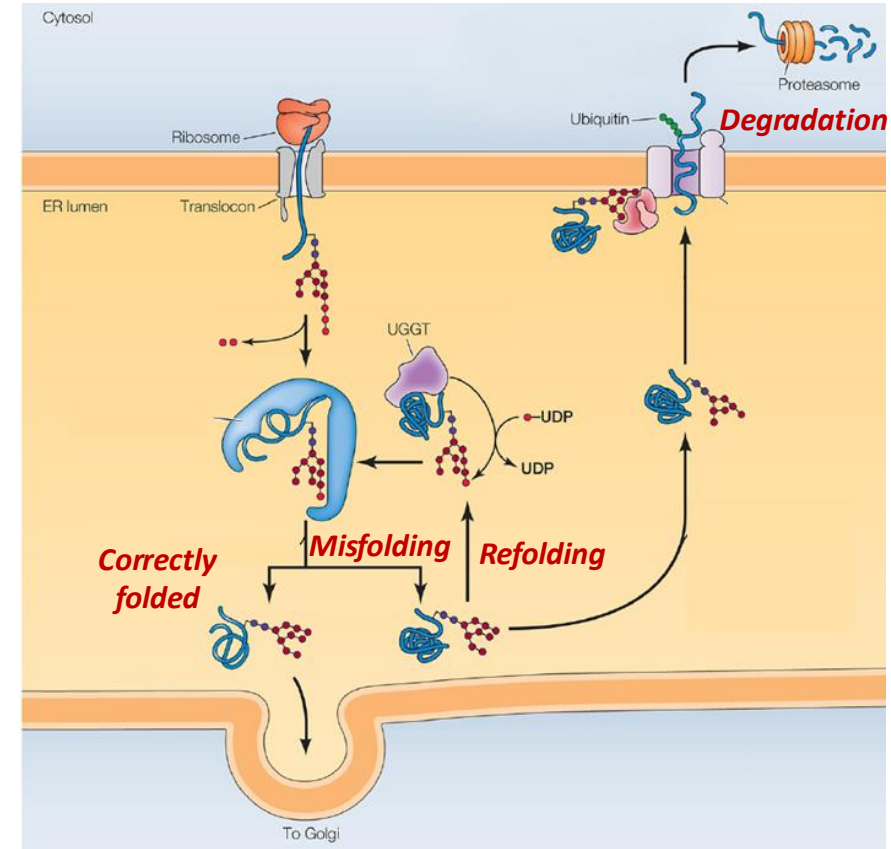
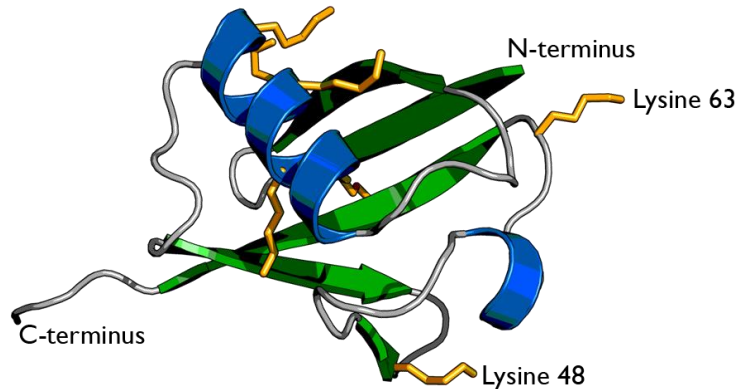
- Folded (with the help of chaperones)
- Complexed (quaternary structure)
- Modified by disulfide bonds formed by **protein disulfide isomerase**
- Glycosylated
- Anchored by lipids



# Protein folding and ER-associated degradation (ERAD)

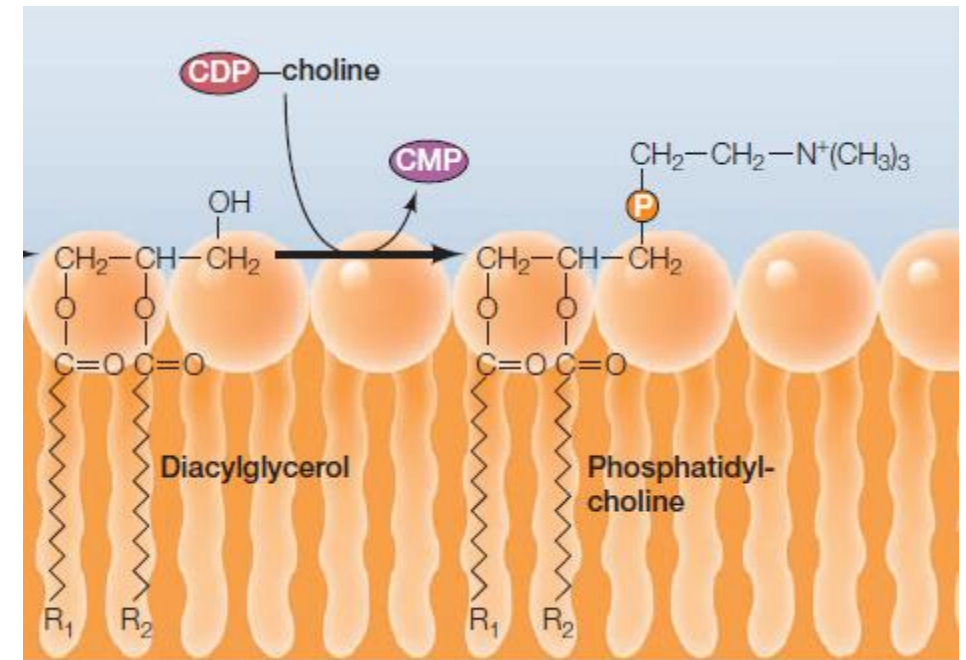


- If correctly folded, proteins move on.
- If misfolded, proteins are refolded, and, if it does not work, sent to the cytosol, ubiquitylated (addition of small proteins called ubiquitins), and degraded in the proteasome.



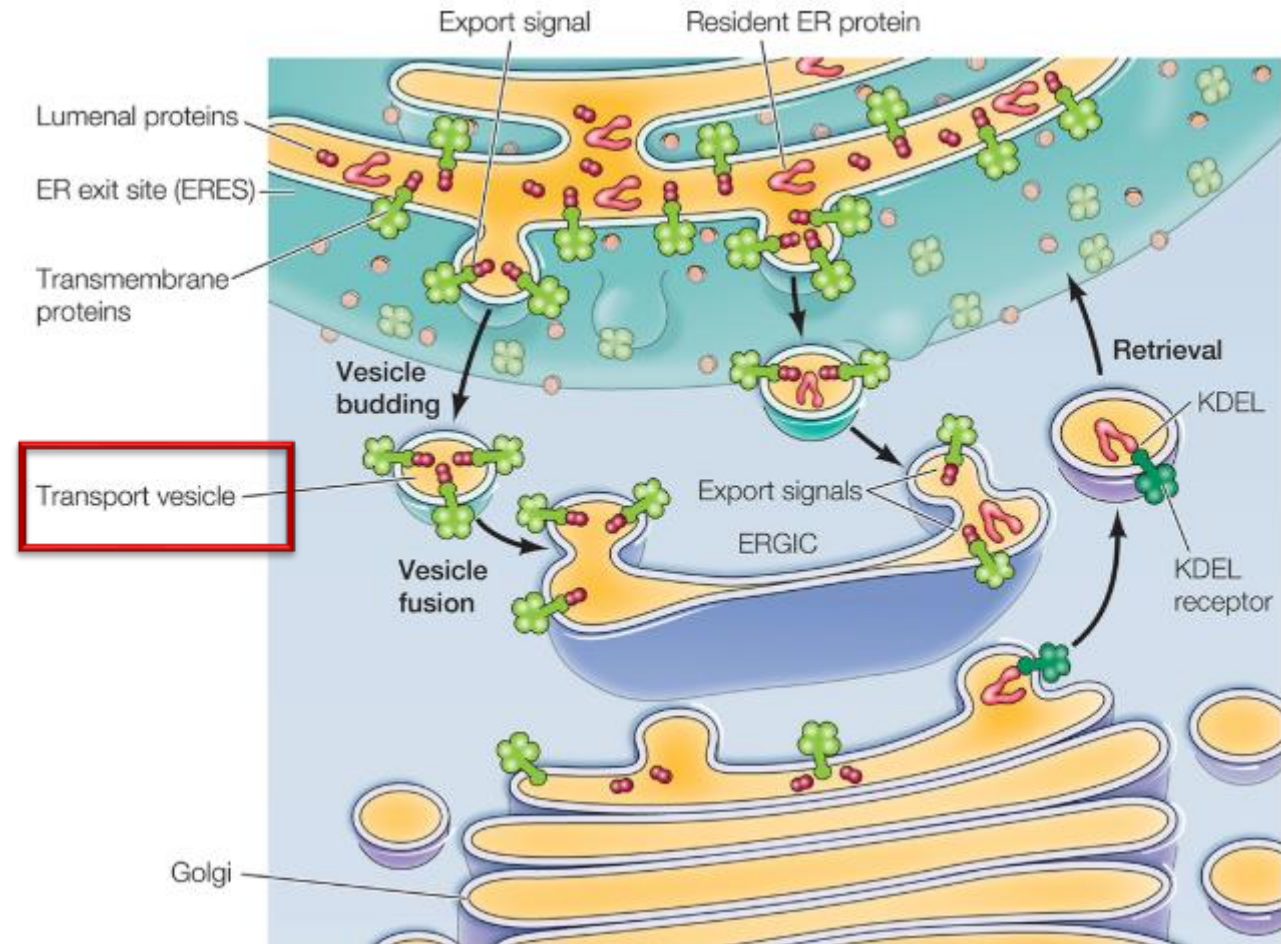
# Synthesis of phospholipids in ER

- The smooth ER is the major site of synthesis of:
  - Membrane glycerophospholipids, which are then transported from the SER to other membranes.
  - Ceramides (The precursor of sphingolipids)
    - Ceramide is converted to either glycolipids or sphingomyelin in the Golgi apparatus.
  - Steroids.
    - Large amounts of smooth ER are found in steroid-producing cells, such as those in the testis and ovary.
- SER is abundant in the liver, which contains enzymes that metabolize various lipid-soluble compounds.



# ER-Golgi intermediate compartment (ERGIC)

- Proteins and lipids are carried from the ER to the Golgi in transport vesicles, which fuse with the ER–Golgi intermediate compartment (ERGIC), and are then carried to the Golgi.



# Retention of ER protein

- Many proteins with **KDEL** sequence (Lys-Asp-Glu-Leu) at C-terminus are retained in the ER lumen.
- If the sequence is deleted, the protein is transported to the Golgi and secreted from the cell.
- Addition of the sequence to a protein causes this protein to be retained in the ER.

