Cell Biology &

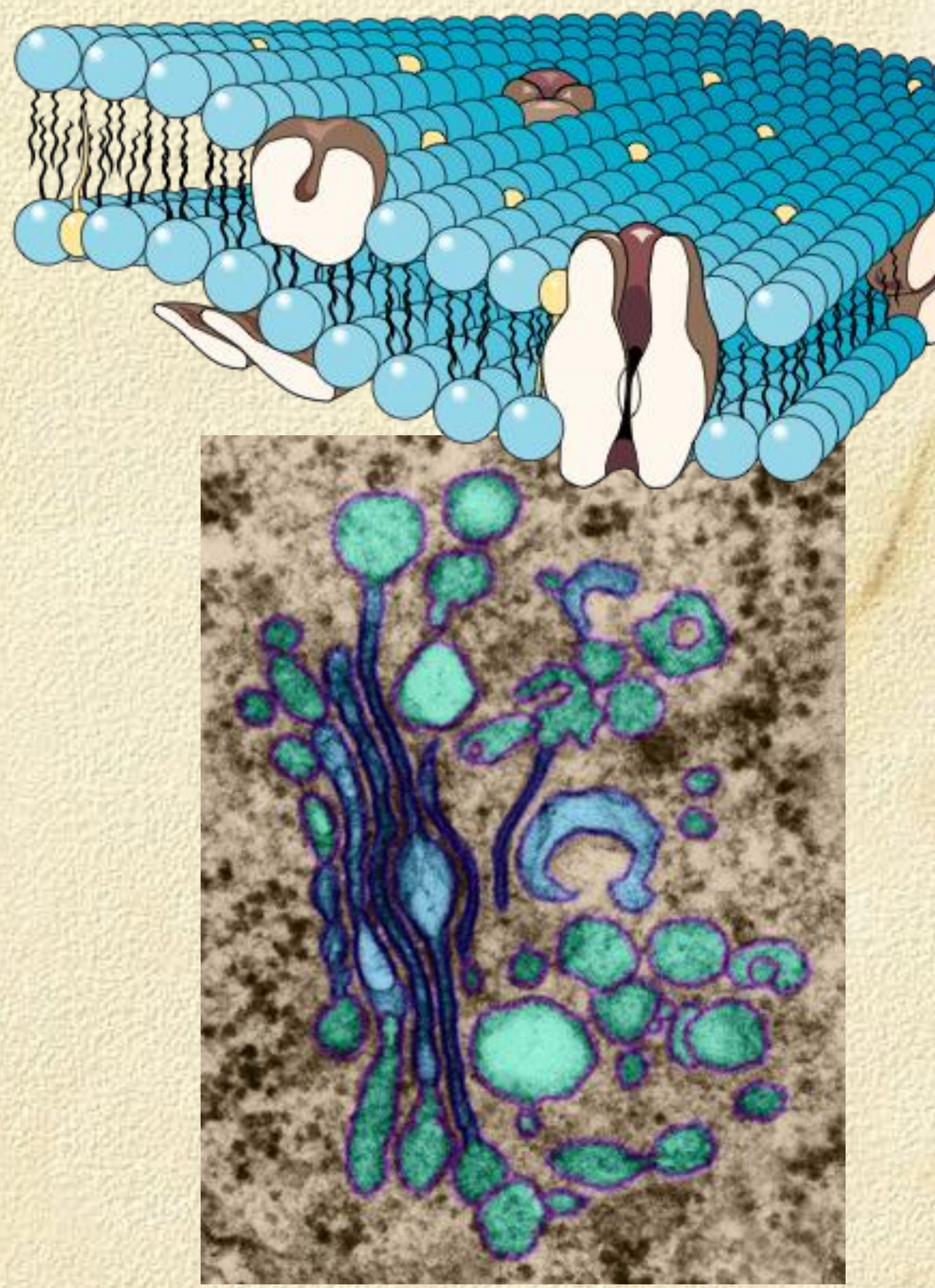
Biochemistry Series:

Set 4

Cell Membranes & Transport

Version: 1.0

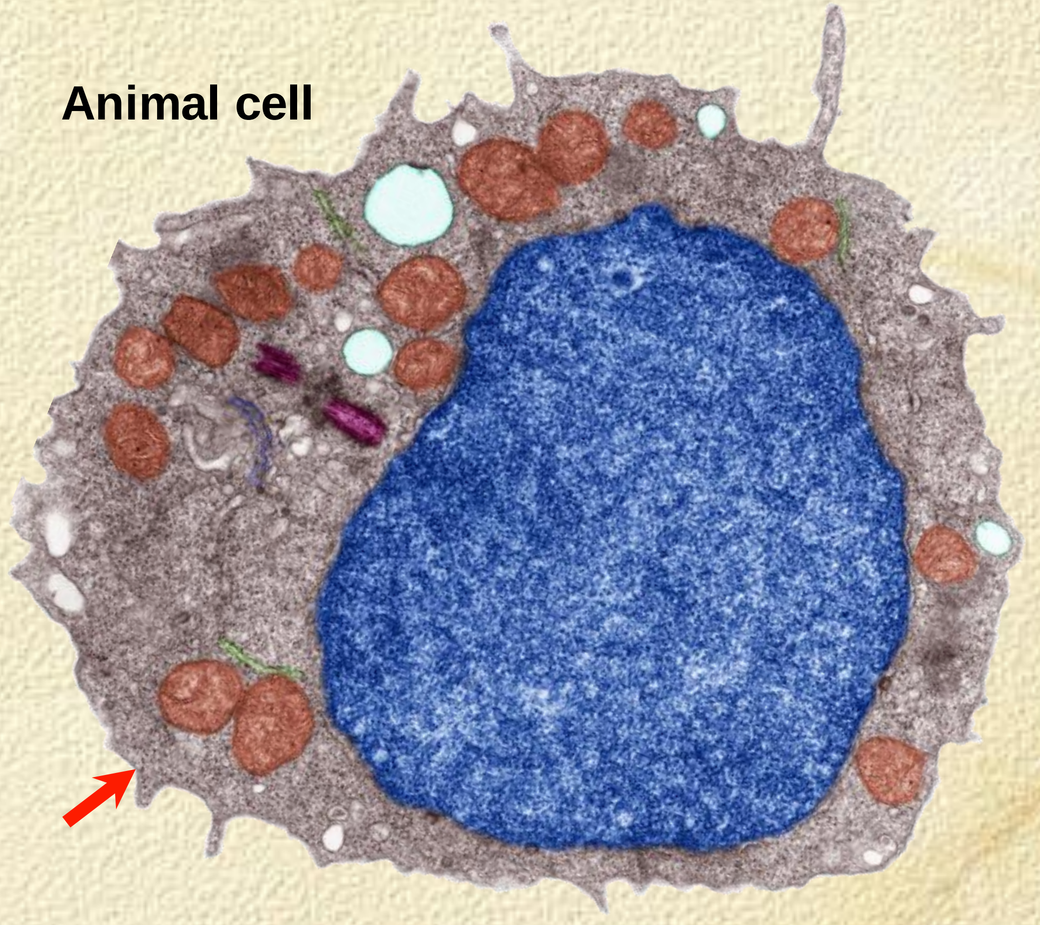
BIOZONE



Cells and Membranes

- The membrane surrounding a cell, called the **plasma membrane**, forms the boundary that separates the living cell from its non-living surroundings.
- Although the plasma membrane (arrowed) is only about 8 nm thick, it:
  - selectively controls the movement of materials into and out of the cell
  - is responsible for cell-cell recognition (e.g. when cells aggregate into tissues
  - is a dynamic structure, with distinct inside and outside faces.

Animal cell

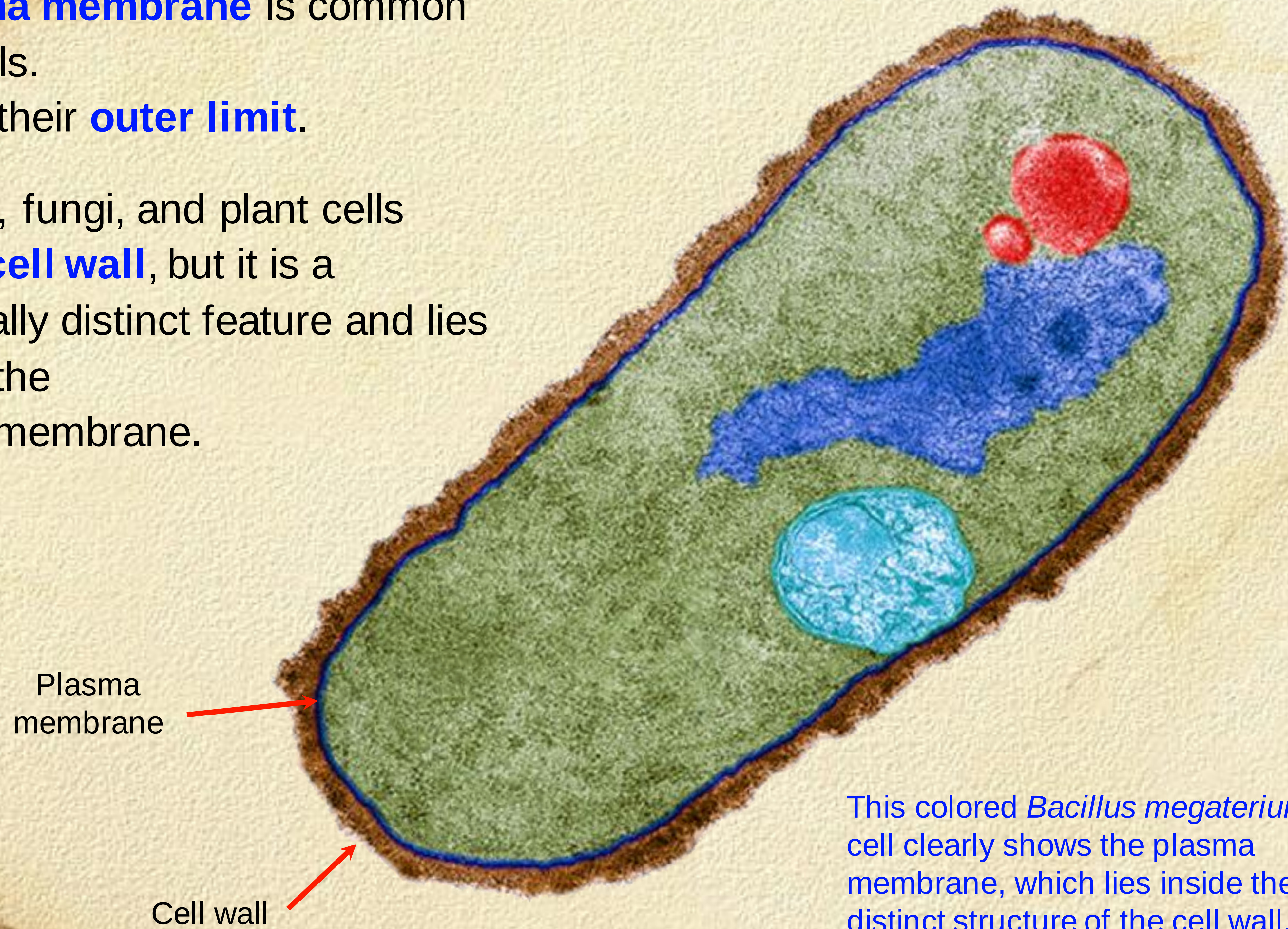


Plant cell

The Plasma Membrane

- A **plasma membrane** is common to all cells.
  It forms their **outer limit**.

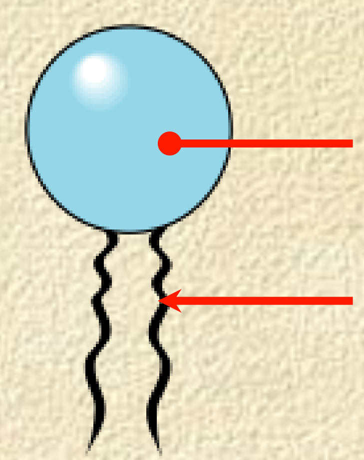
- Bacteria, fungi, and plant cells have a **cell wall**, but it is a structurally distinct feature and lies outside the plasma membrane.



This colored *Bacillus megaterium* cell clearly shows the plasma membrane, which lies inside the distinct structure of the cell wall.

Membrane Structure

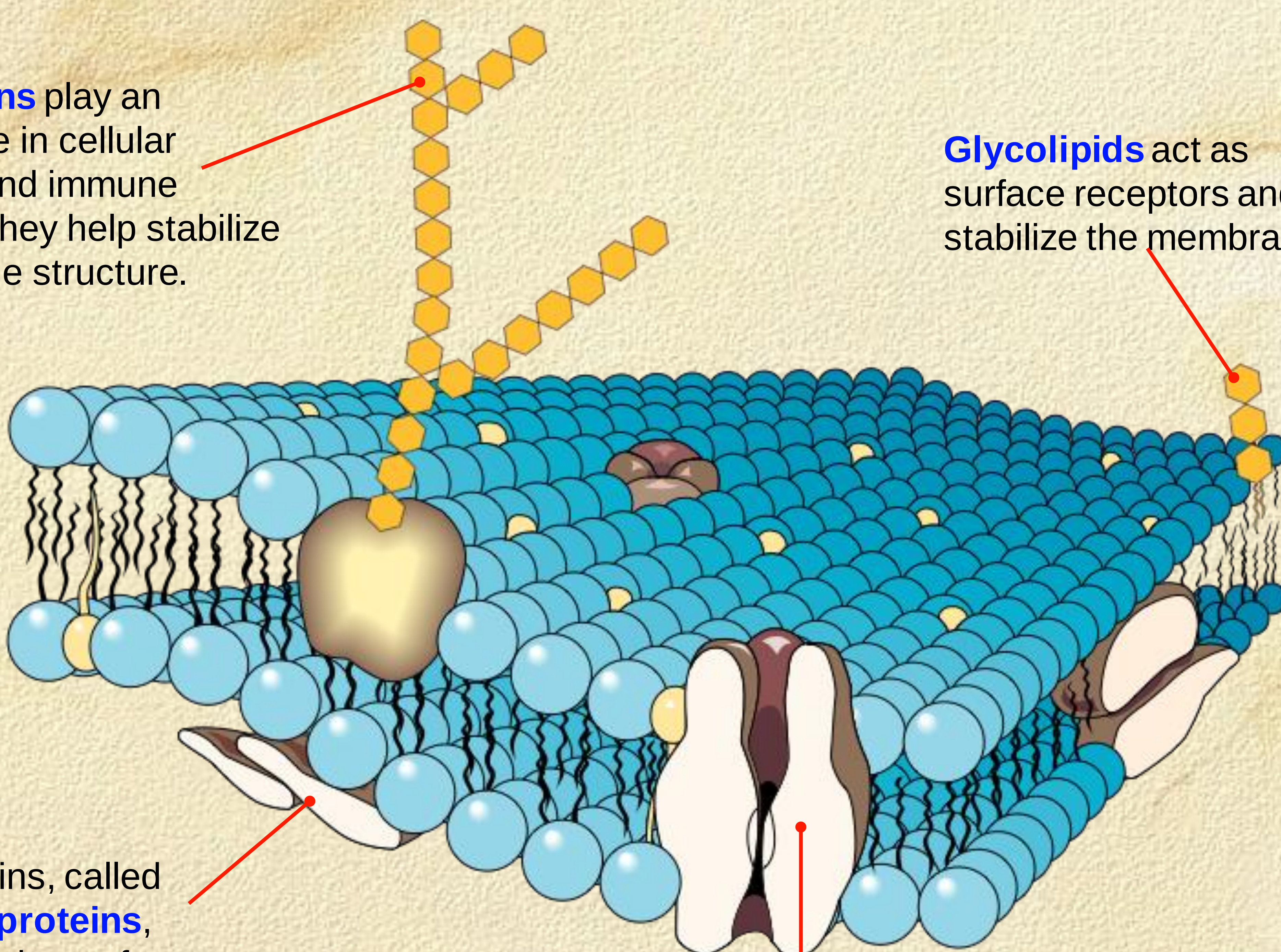
- The currently accepted model for the structure of the **plasma membrane** (and cellular membranes generally) is the **fluid mosaic model**.
  - In this model there is a double layer of **phospholipids** (fats), which are arranged with their **hydrophobic tails** facing inwards.
  - The double layer of lipids is quite **fluid**, with **proteins** floating within it.
  - Glycoproteins, glycolipids, and cholesterol are also an integral part of the membrane structure.



Membrane Structure

Glycoproteins play an important role in cellular recognition and immune responses. They help stabilize the membrane structure.

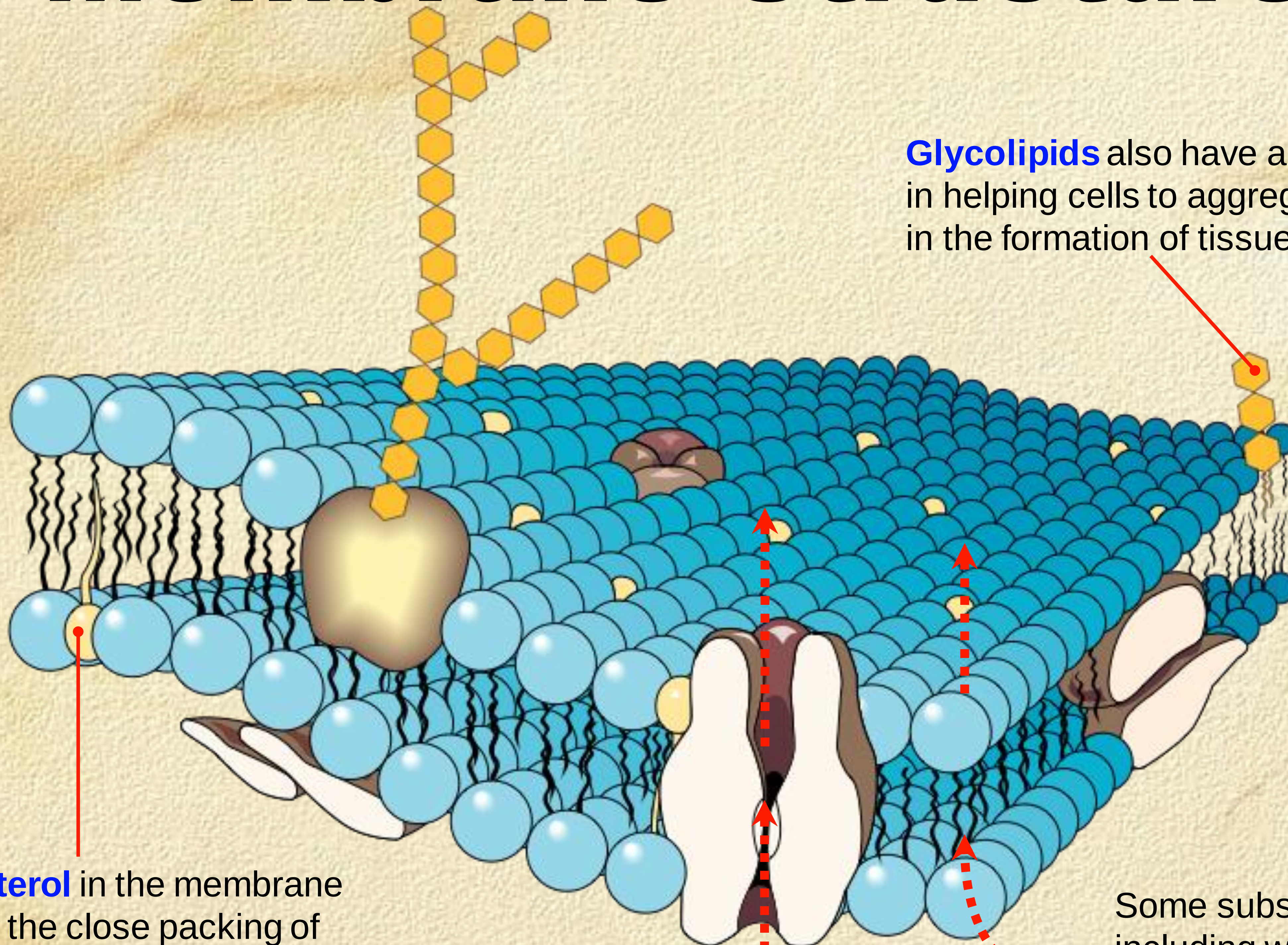
Glycolipids act as surface receptors and stabilize the membrane.



Some proteins, called **peripheral proteins**, are stuck to the surface of the membrane.

Some proteins completely penetrate the phospholipid layer. These proteins may control the movement of specific molecules into and out of the cell.

Membrane Structure



Glycolipids also have a role in helping cells to aggregate in the formation of tissues.

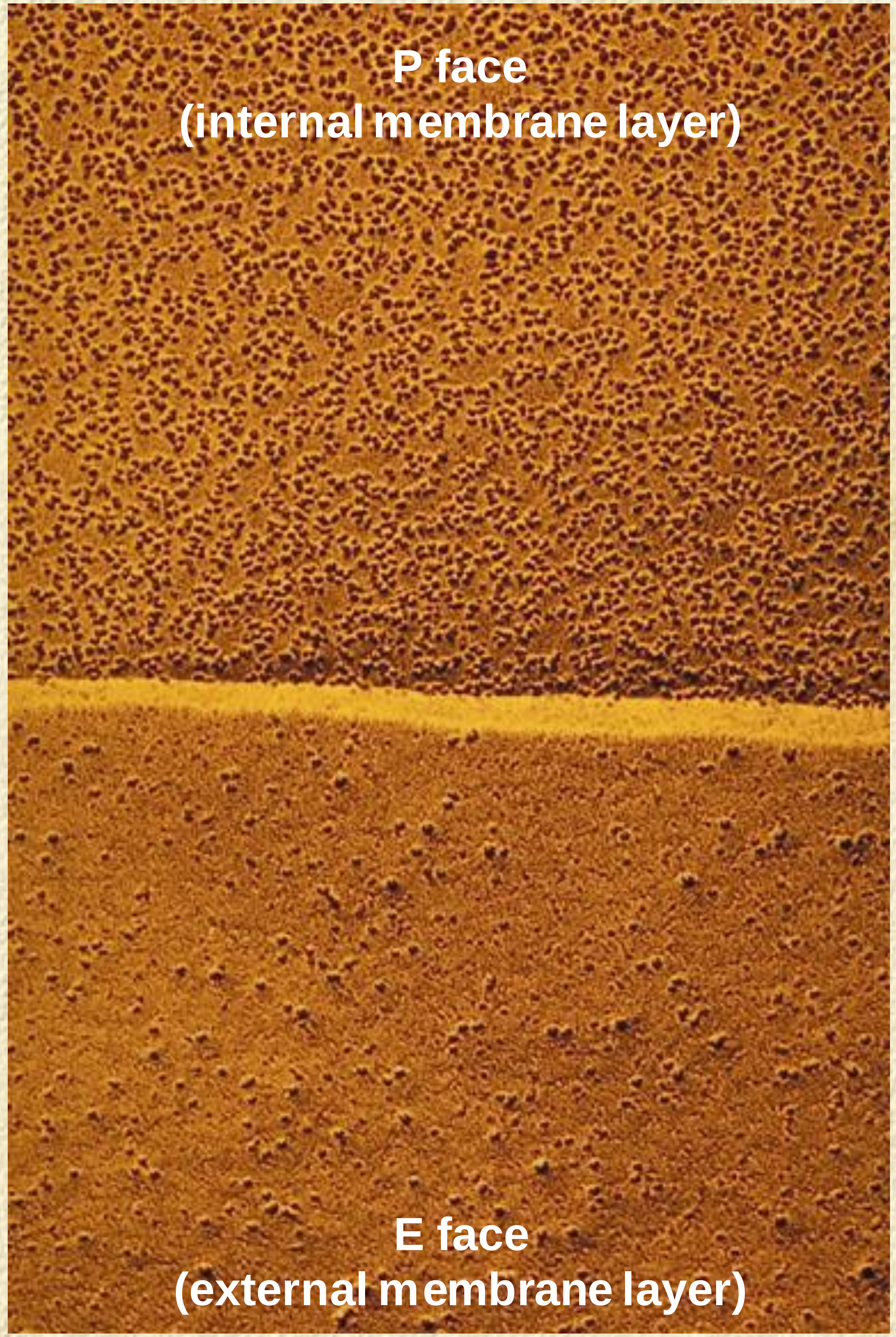
Cholesterol in the membrane disturbs the close packing of the phospholipids and keeps the membrane more fluid.

Some substances, particularly ions and carbohydrates, are transported across the membrane via the proteins.

Some substances, including water, are transported directly through the **phospholipid bilayer**.

Evidence for the Fluid Mosaic Model

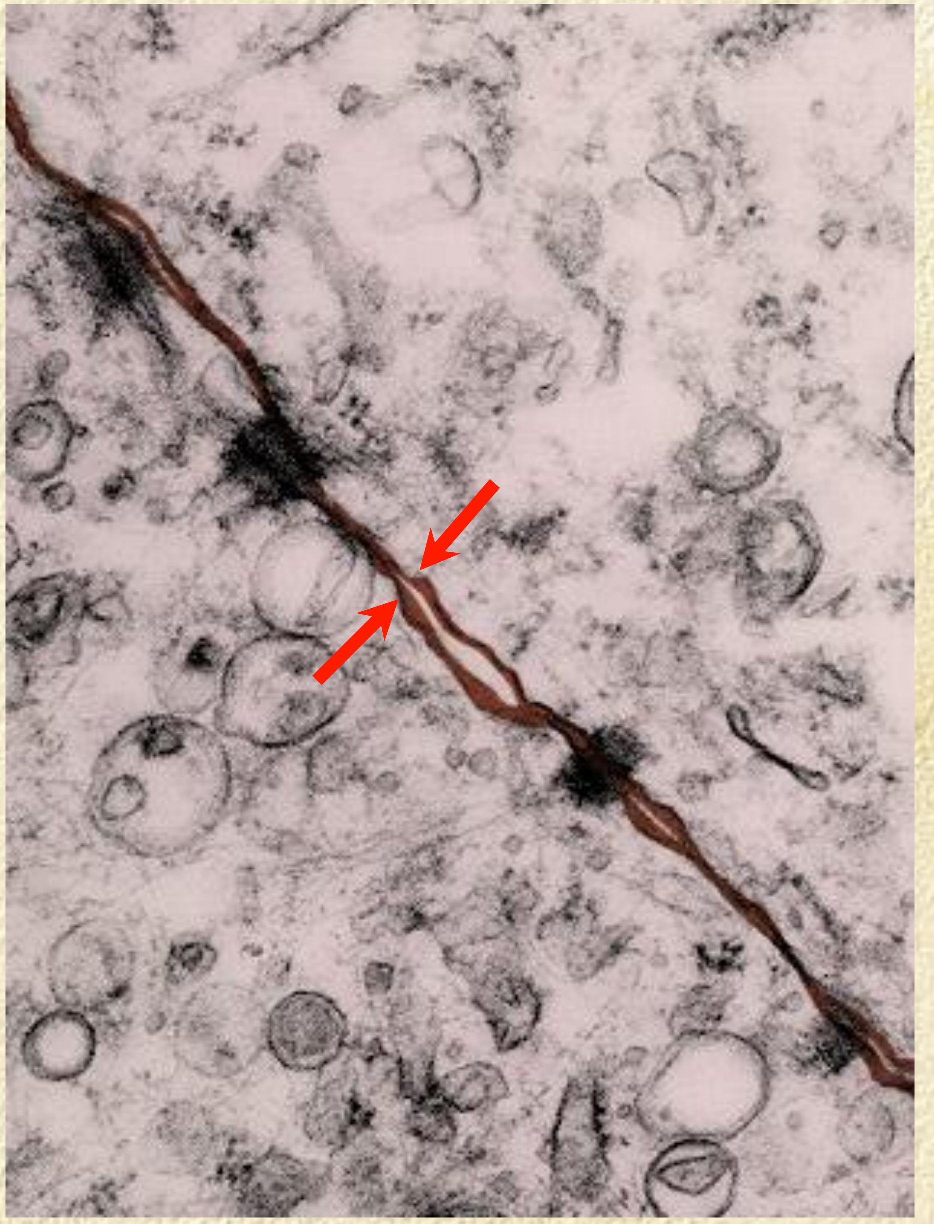
- The invention of **freeze fracture electron microscopy** has played a critical role in determining membrane structure.
- The models revealed **pitted areas** amongst a smooth background.
  - The “pits” were the indentations left by the **embedded proteins** within the phospholipid bilayer of the membrane.
  - This evidence gave support to the fluid mosaic membrane model.



A **freeze fractured erythrocyte** (red blood cell) membrane magnified 120,000 times by SEM.

The Role of Membranes

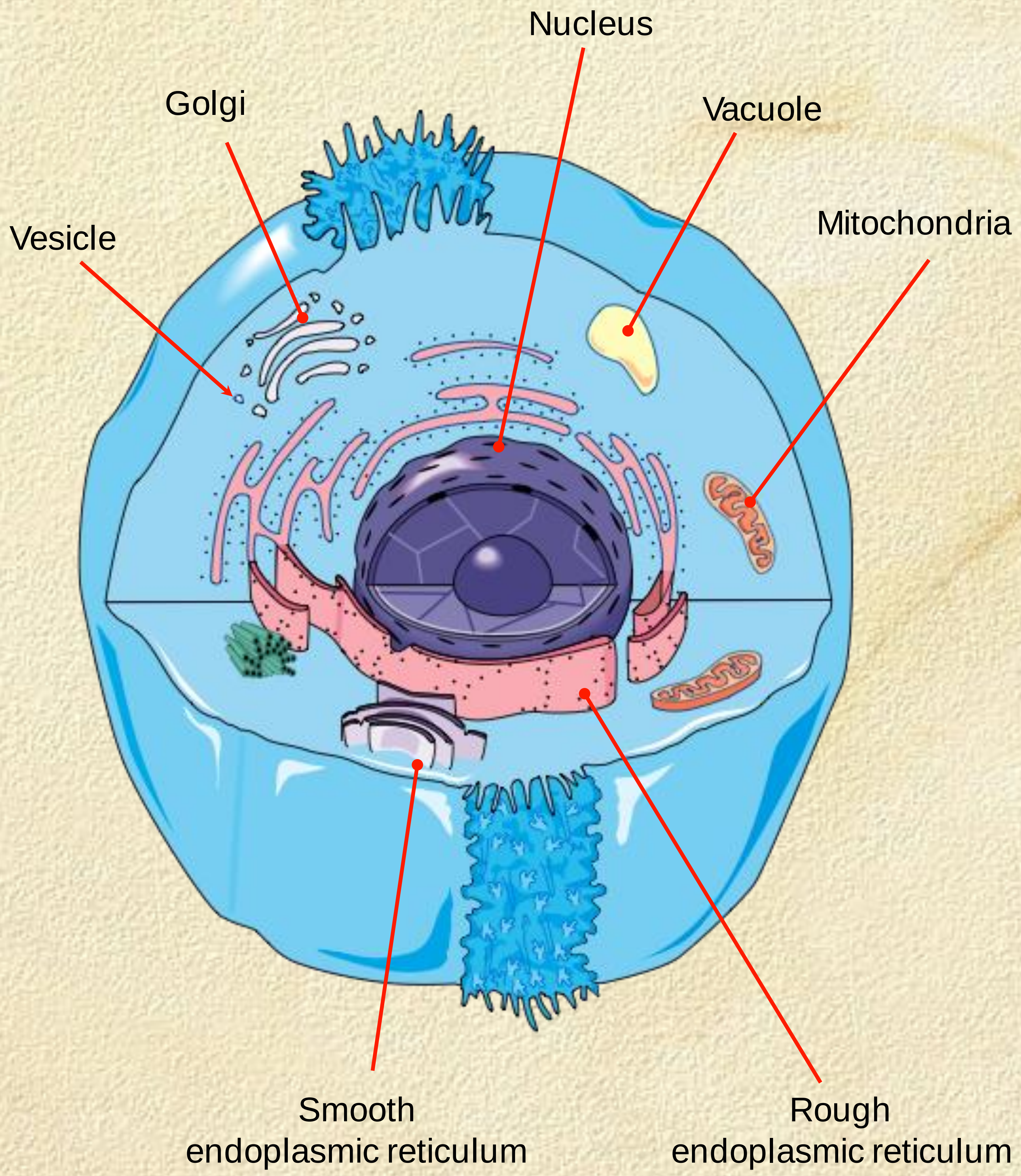
- **Membranes** fulfill a role in **recognition** and **communication** between cells.
  - This allows 'like' cells to form **tissues** and **organs**.
  - It allows the body to **distinguish foreign material** from its own tissue.
- Some membranes are involved in **membrane transport**, where:
  - materials required by the cell are imported into the cell.
  - waste products are removed from the cell.



The plasma membrane surrounds the cell and has an important role in containment, transport, signaling and communication. The image above shows the plasma membranes of two neighboring cells.

Membrane Bound Organelles

- Membranes are also found within eukaryotic cells as part of the structure of **membranous organelles**.
- Examples of membrane-bound organelles include:
  - mitochondria
  - nucleus
  - Golgi apparatus
  - endoplasmic reticulum
  - vesicles
  - vacuoles
  - chloroplasts (not shown, this example is of an animal cell)



Membranes Inside Cells

- The membranes of **organelles** have the same basic structure as the plasma membrane surrounding the cell.
- Membrane-bound organelles compartmentalize specific activities within the cell.
- Examples of membrane-bound organelles are shown on the false-color TEM of a plant cell (right):
  - A: vacuole
  - B: mitochondrion
  - C: nucleus
  - D: chloroplast

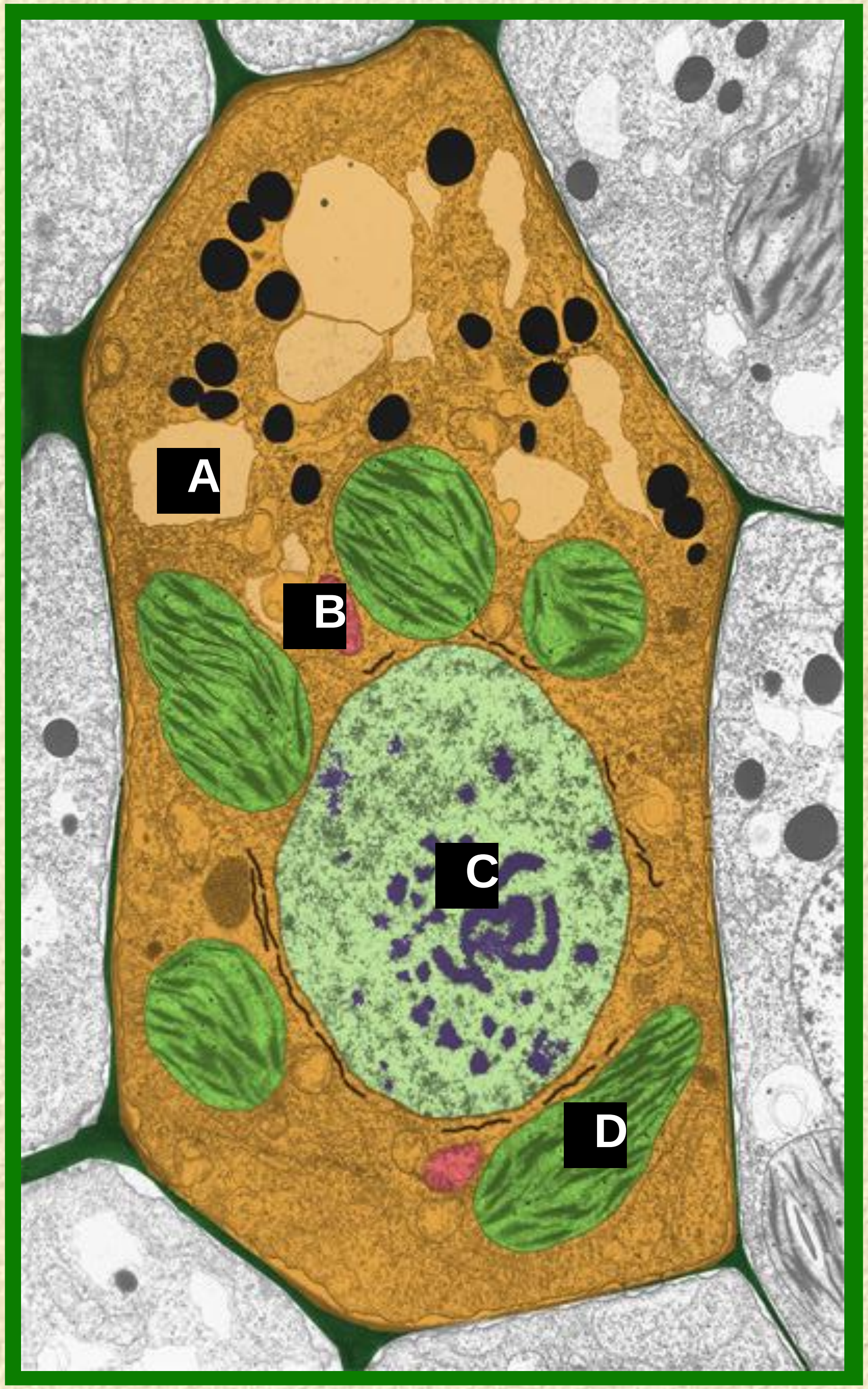
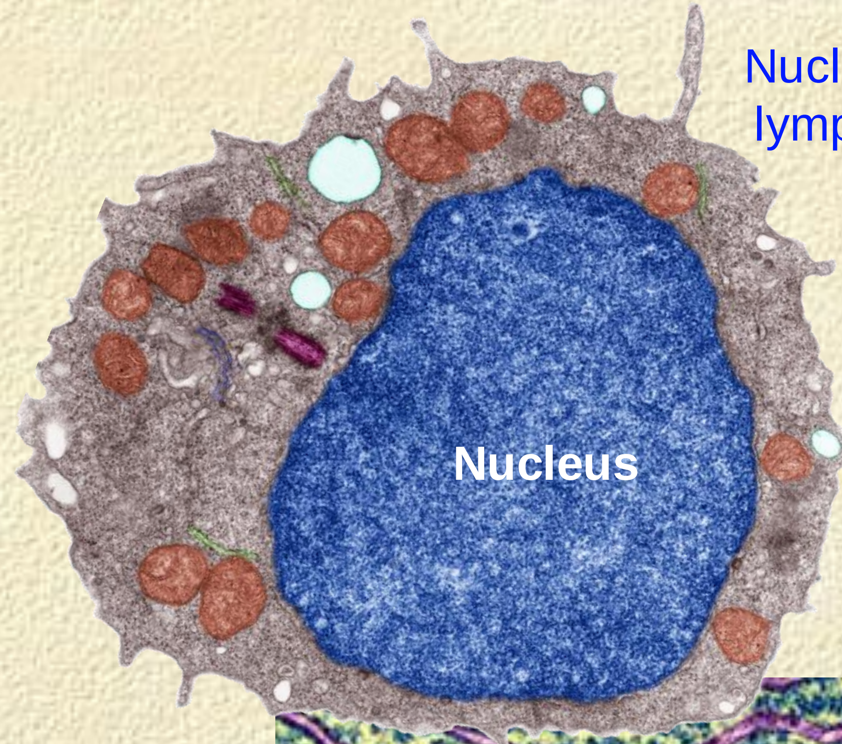


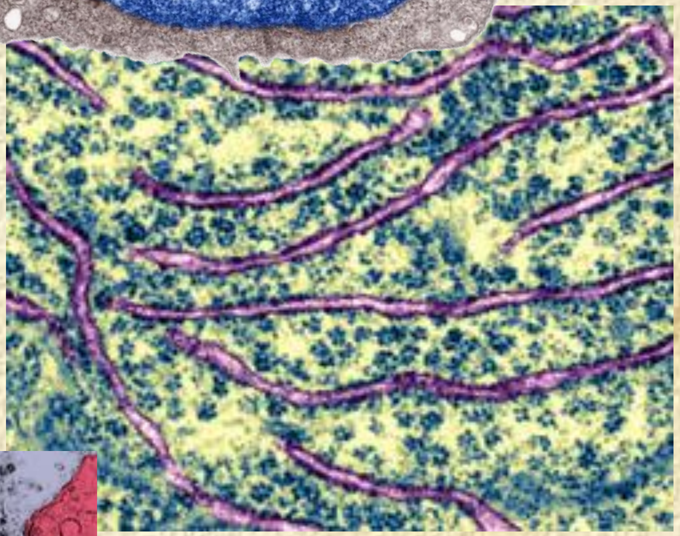
Photo: Brian Finerran

The Functions of Organelles

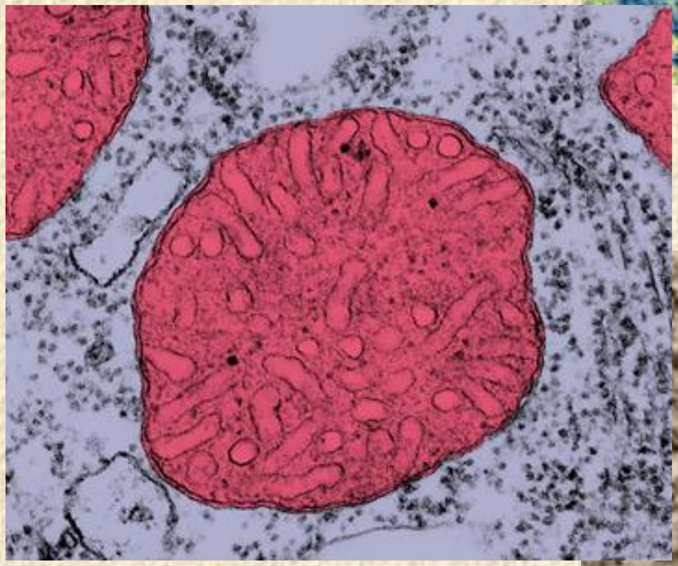
- All cellular **organelles** have specific functions.
- The cell can be compared to a **factory** with an assembly line.
  - Organelles in the cell provide the equivalent of the:
    - control center (**nucleus**)
    - packaging department (**Golgi**)
    - transport system (**endomembrane** systems and vesicles)
    - power supply (**mitochondria**)
    - assembly line (**ribosomes**)
    - repair and maintenance (**lysosomes**)



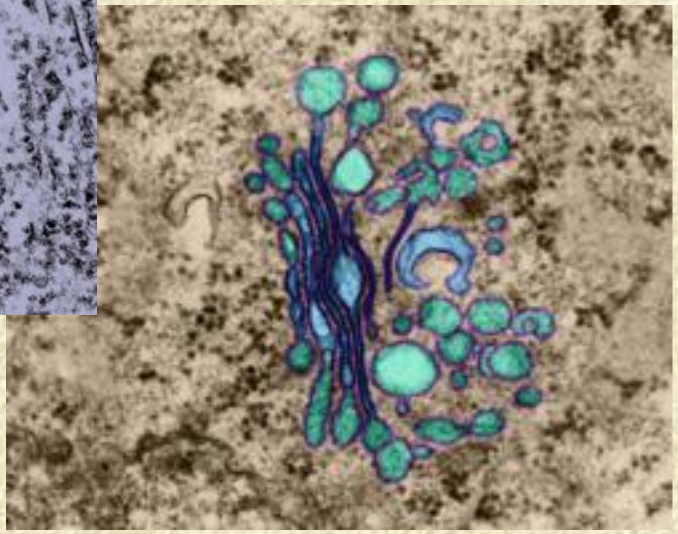
Nucleus of a lymphocyte



Rough endoplasmic reticulum



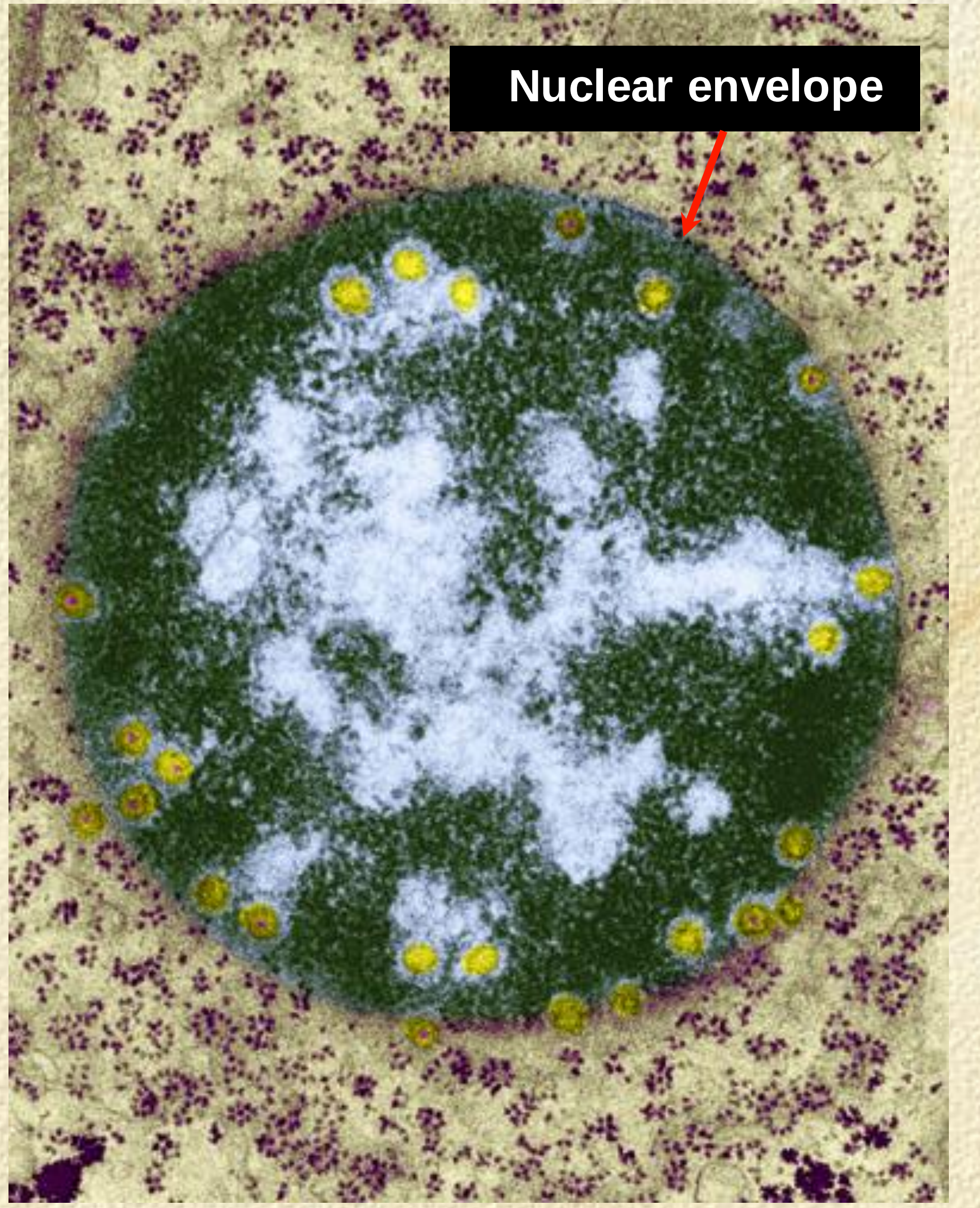
Mitochondrion



Golgi apparatus

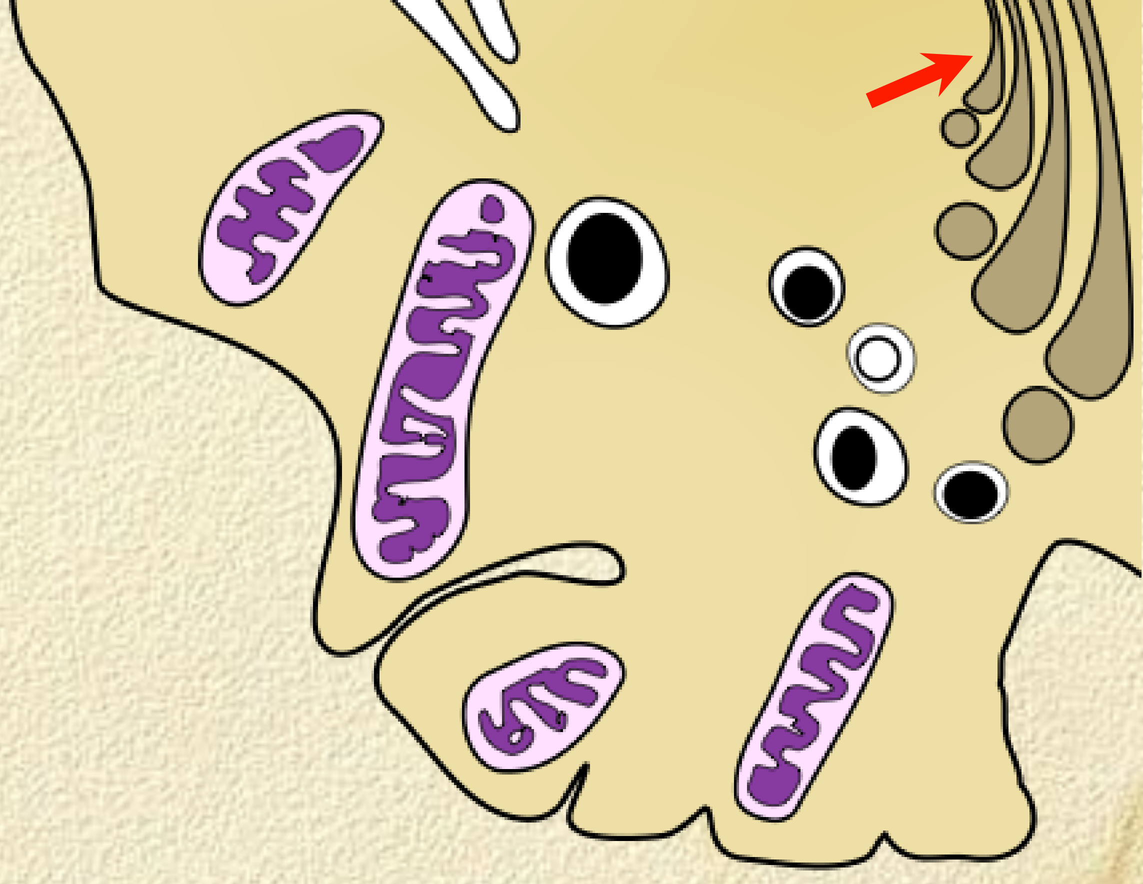
The Control Center

- In eukaryotic cells, the nuclear membrane, or **nuclear envelope**, encloses the nucleus, separating its contents from the cytoplasm.
- The nuclear envelope controls the passage of genetic information to the cytoplasm and may also protect the DNA.
  - It is a double membrane.
  - The two membranes are separated by a space of 20-40 nm.
  - A layer of protein associated with the nuclear side of the envelop helps to maintain the shape of the nucleus.
  - The nuclear envelope is perforated by **nuclear pores** about 100 nm in diameter. The pores regulate the passage of materials into and out of the nucleus.

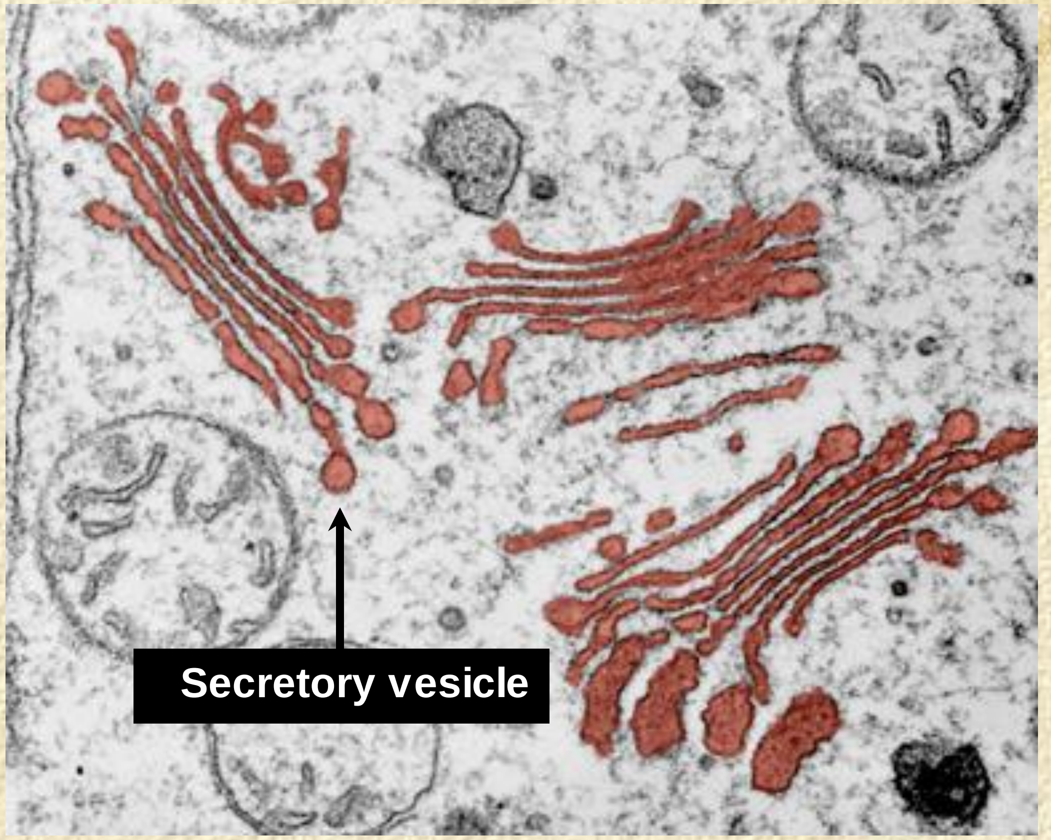


The **nuclear envelope** is a double layered structure perforated by pores.

Packaging and Secretion

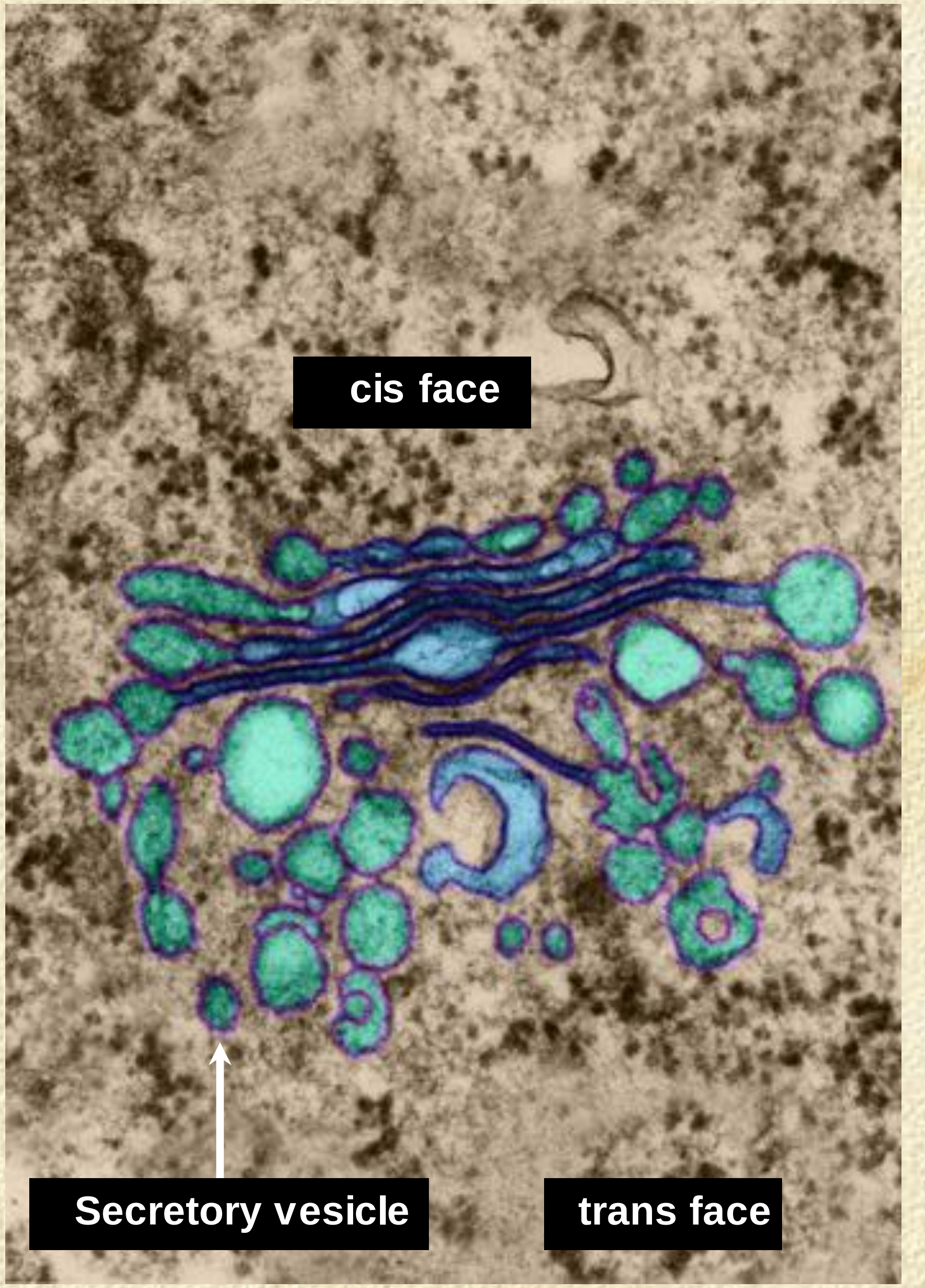


- In eukaryotic cells, the center of manufacturing, storing, sorting and shipping is the **Golgi apparatus** (right).
  - Within the Golgi, the products of the endoplasmic reticulum, e.g. lipids and proteins, are modified, stored, and sent to other cellular destinations.
  - The Golgi apparatus is also the site of **lysosome formation**.
  - Substances leave the Golgi packaged into membrane-bound **vesicles**.
  - The Golgi is most extensive in cells that are specialized for secretion (e.g. antibody secreting cells).



Packaging and Secretion

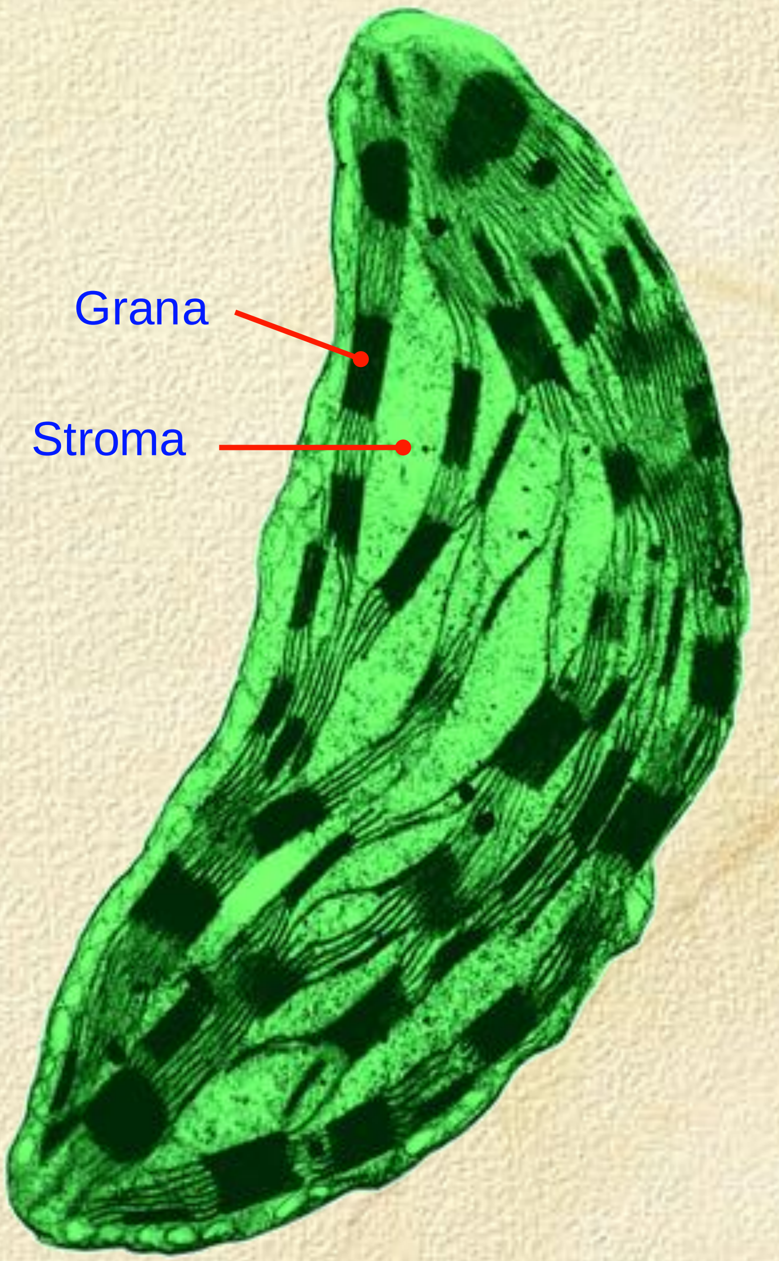
- A Golgi stack has two distinct faces:
  - the ***cis* face** (or forming face) receives vesicles from the ER.
  - the ***trans* face** (or maturing face) ships materials in vesicles, which pinch off from the Golgi and travel to other sites.
- Products of the ER are usually modified as they move from the *cis* to the *trans* face.
  - Products are modified in stages; different cisternae between *cis* and *trans* faces contain different suites of enzymes.
  - Vesicles transfer the products of processing between one cisterna and the next.
  - Before products are shipped, they are tagged with (e.g. with phosphate groups) for transport to different parts of the cell.



The Golgi apparatus comprises stacks of membrane-bound sacs called **cisternae**.

Light Capture and Carbon Fixation

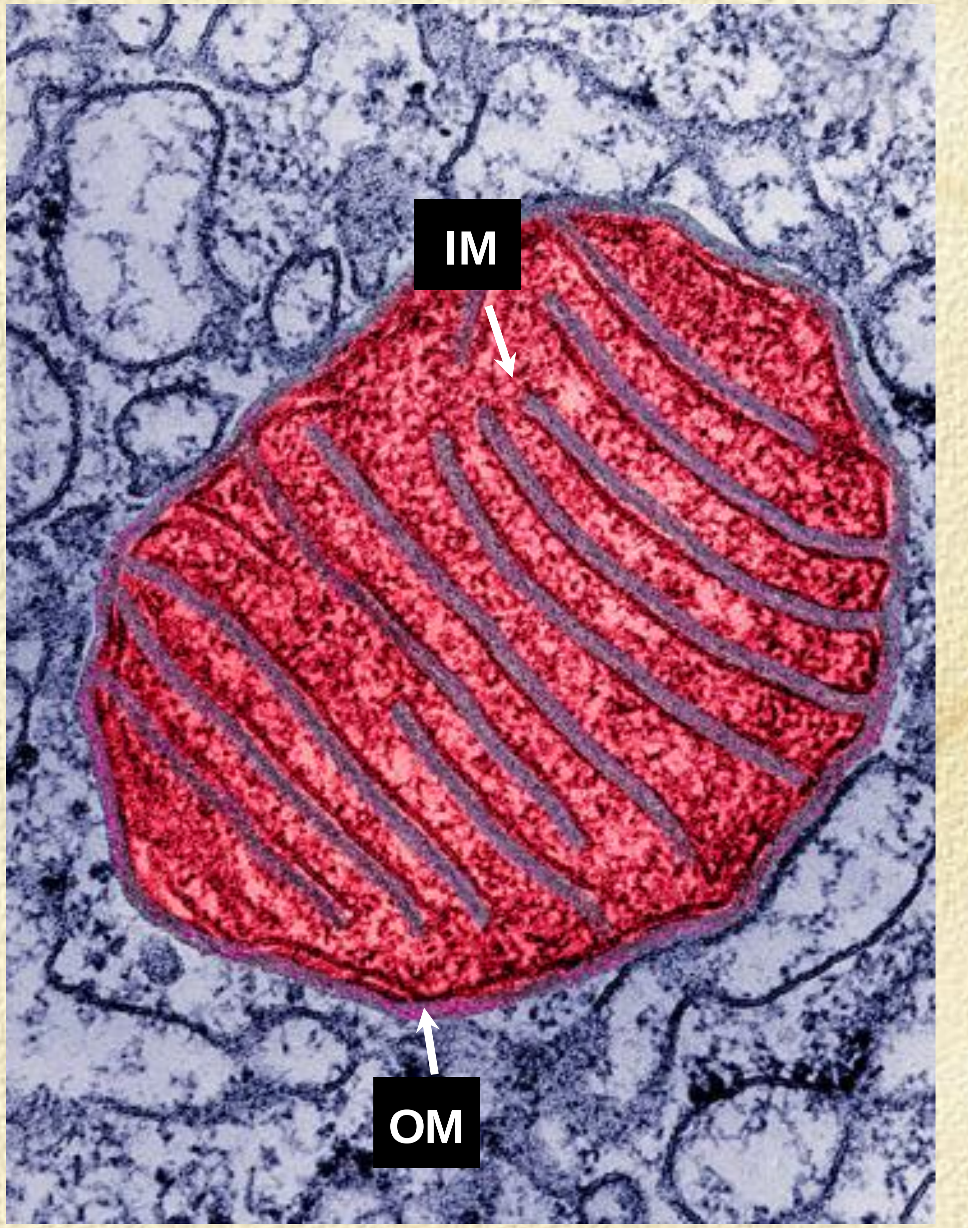
- **Chloroplasts** are membrane-bound organelles found in plants and protists. They are the site of photosynthesis.
- The chloroplast is enclosed by an envelope consisting of two membranes separated by a very narrow intermembrane space.
- Membranes also divide the interior of the chloroplast into compartments:
  - flattened sacs called thylakoids stacked into structures called **grana**.
  - the **stroma** (fluid) outside the thylakoids.
- The light reactions of photosynthesis occur on the thylakoid membranes. The dark reactions occur in the stroma.



Chloroplasts have a double membrane called the **chloroplast envelope**. The outer membrane is permeable to metabolites, and the inner membrane contains many transport proteins.

Energy Production

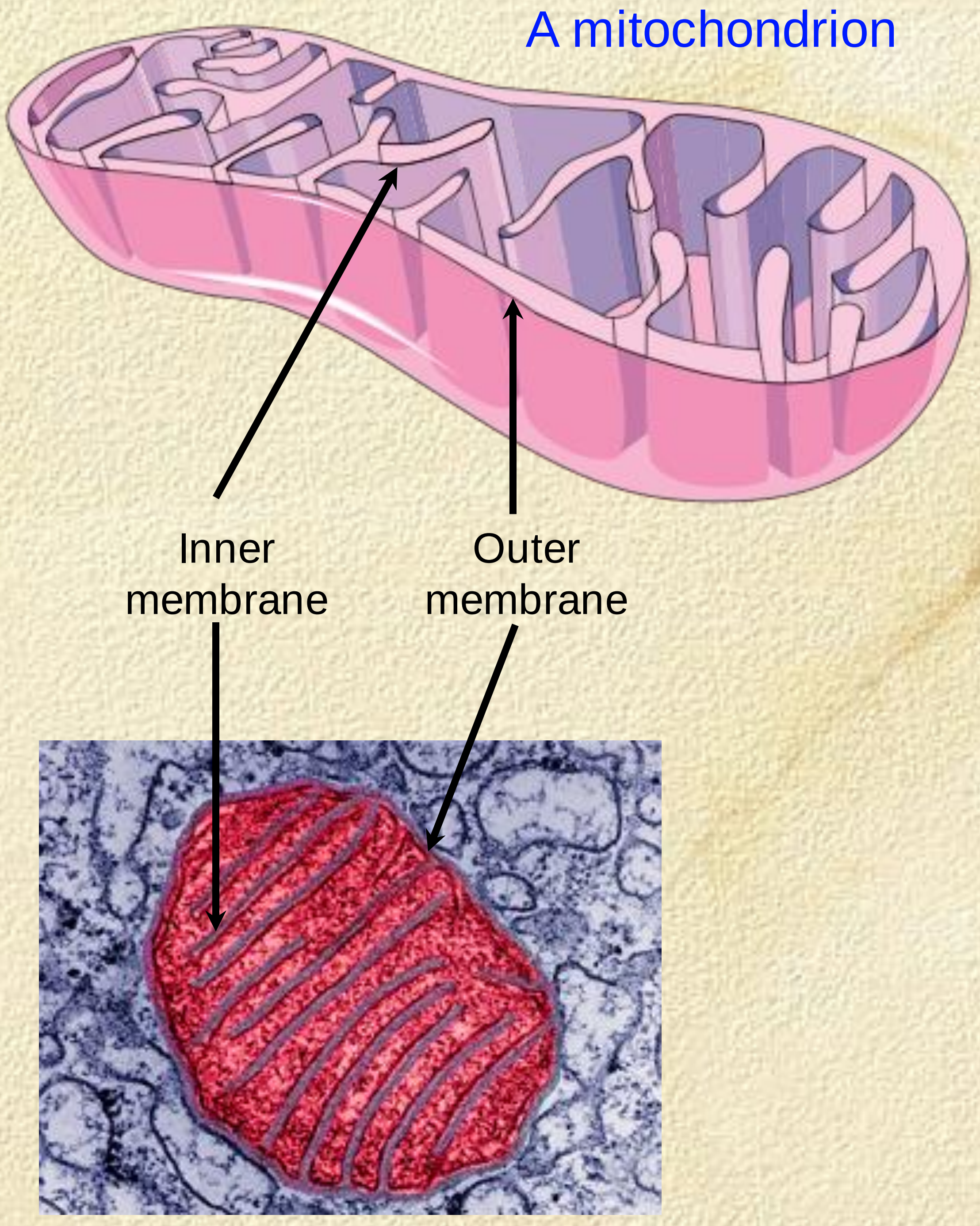
- **Mitochondria**, like chloroplasts, are membrane-bound organelles that convert energy to forms the cell can use.
- The mitochondrion is the site of cellular respiration, in which ATP is generated from the oxidation of fuels such as glucose.
- They are found in almost all eukaryotic cells.
- Like chloroplasts, mitochondria are enclosed by an envelope of two membranes separated by a narrow intermembrane space.
    - the outer membrane is smooth.
    - the inner membrane is convoluted, with infoldings called **cristae**.
    - the membranes divide the mitochondrion into two internal compartments.



Mitochondria have a **double membrane** structure. The outer membrane (**OM**) controls the passage of materials involved in aerobic respiration. Inner membranes (**IM**) provide the attachment sites for the enzymes involved in cellular respiration.

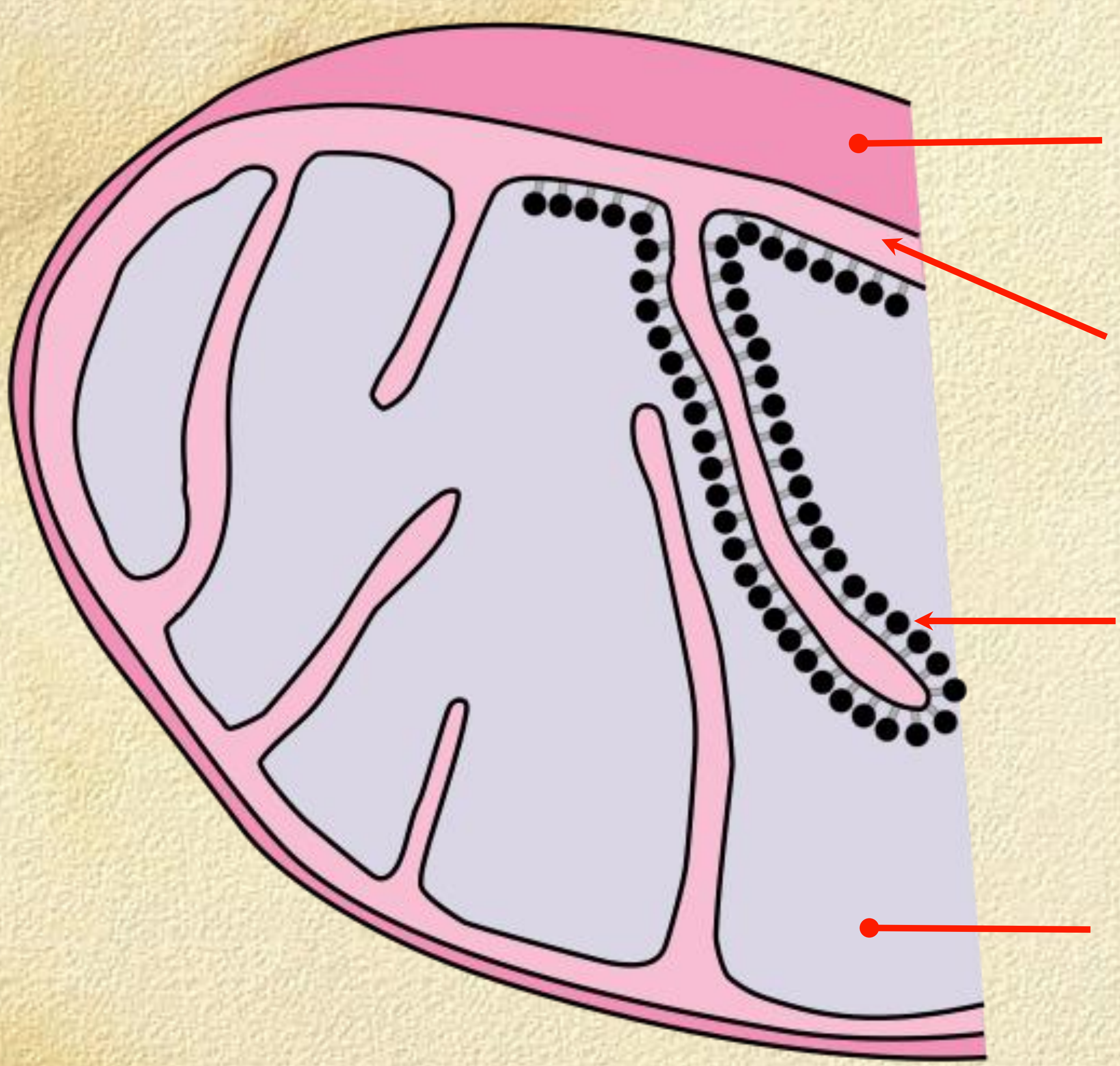
Compartmentation

- Membrane systems form discrete regions within the cells where enzyme reactions are **compartmentalized**.
  - Specific enzymes are often located in particular organelles, and even within particular regions of the organelle.
- The **rate** at which a reaction proceeds is limited by the speed at which substrates can enter the organelle.
- Membranes regulate this passage, just as they regulate movement of materials into and out of the cell itself.
- For example, the rate of ATP production is limited by the rate at which ADP can enter the mitochondrion.



Mitochondrion (false colored) taken by TEM. Magnification x 14,000

Enzymes in Organelles



Amine oxidases and other enzymes on the outer membrane surface.

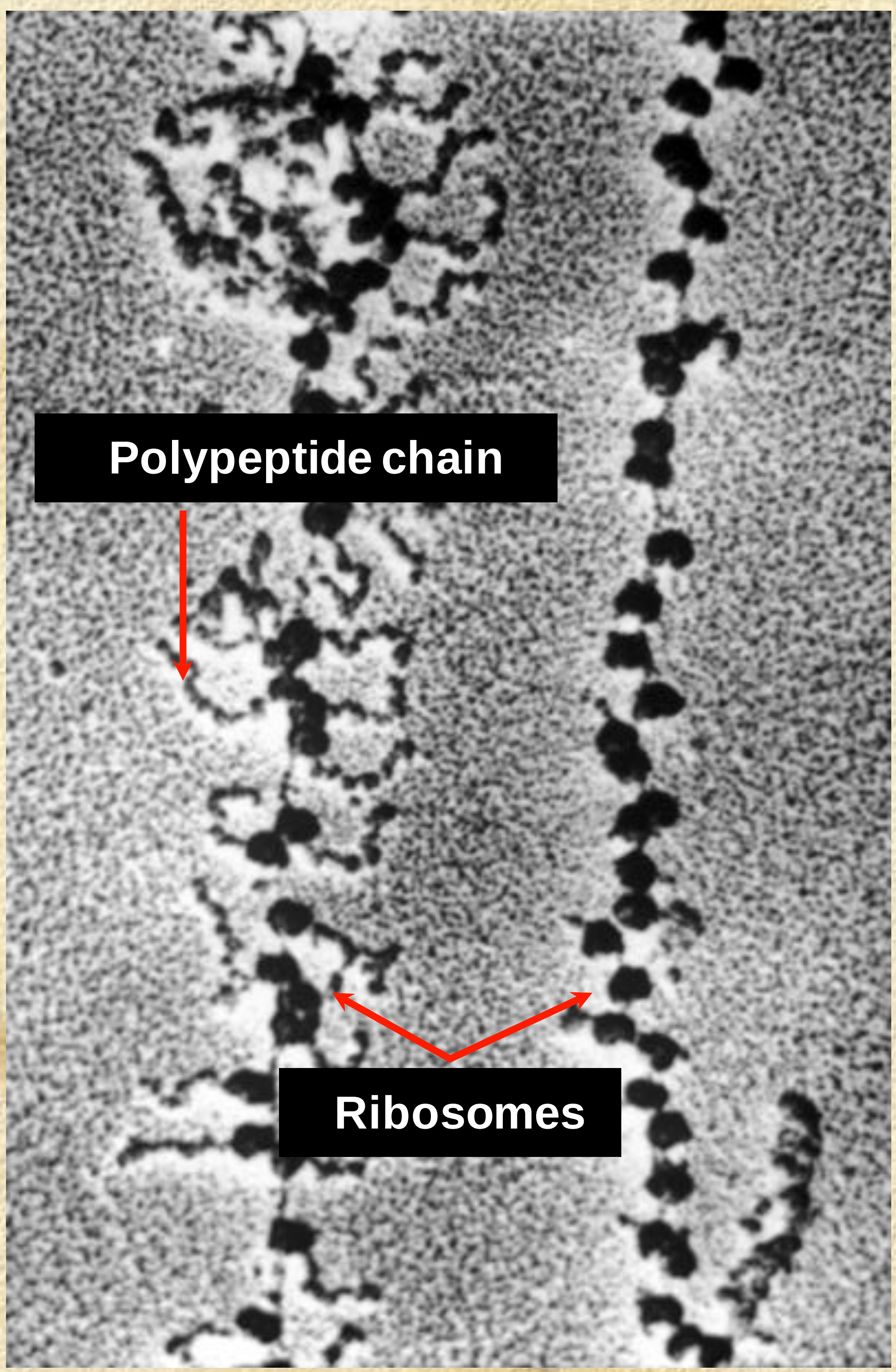
Adenylate kinase and other **phosphorylases** between the membranes.

Respiratory assembly enzymes embedded in the membrane (**ATPase**).

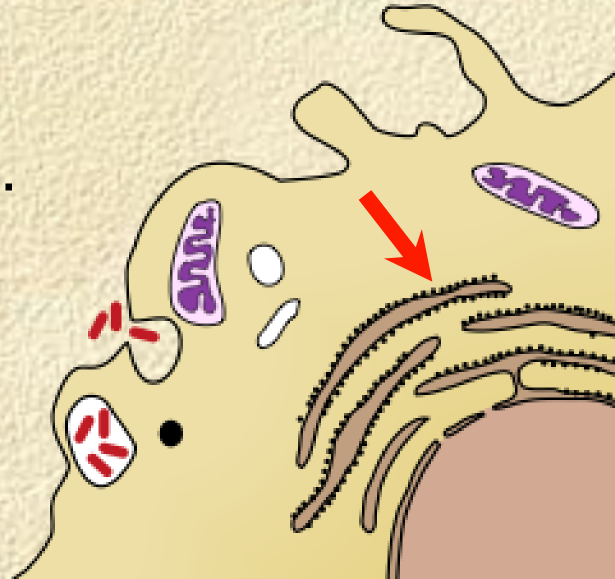
Many soluble enzymes of the Krebs cycle, as well as the enzymes for fatty acid degradation, float in the matrix.

The mitochondrion (cross section above) is an excellent example of how membranes can **compartmentalize** reactions in cellular organelles. Many different enzyme reactions occur in specific regions of the mitochondrion.

Protein Synthesis

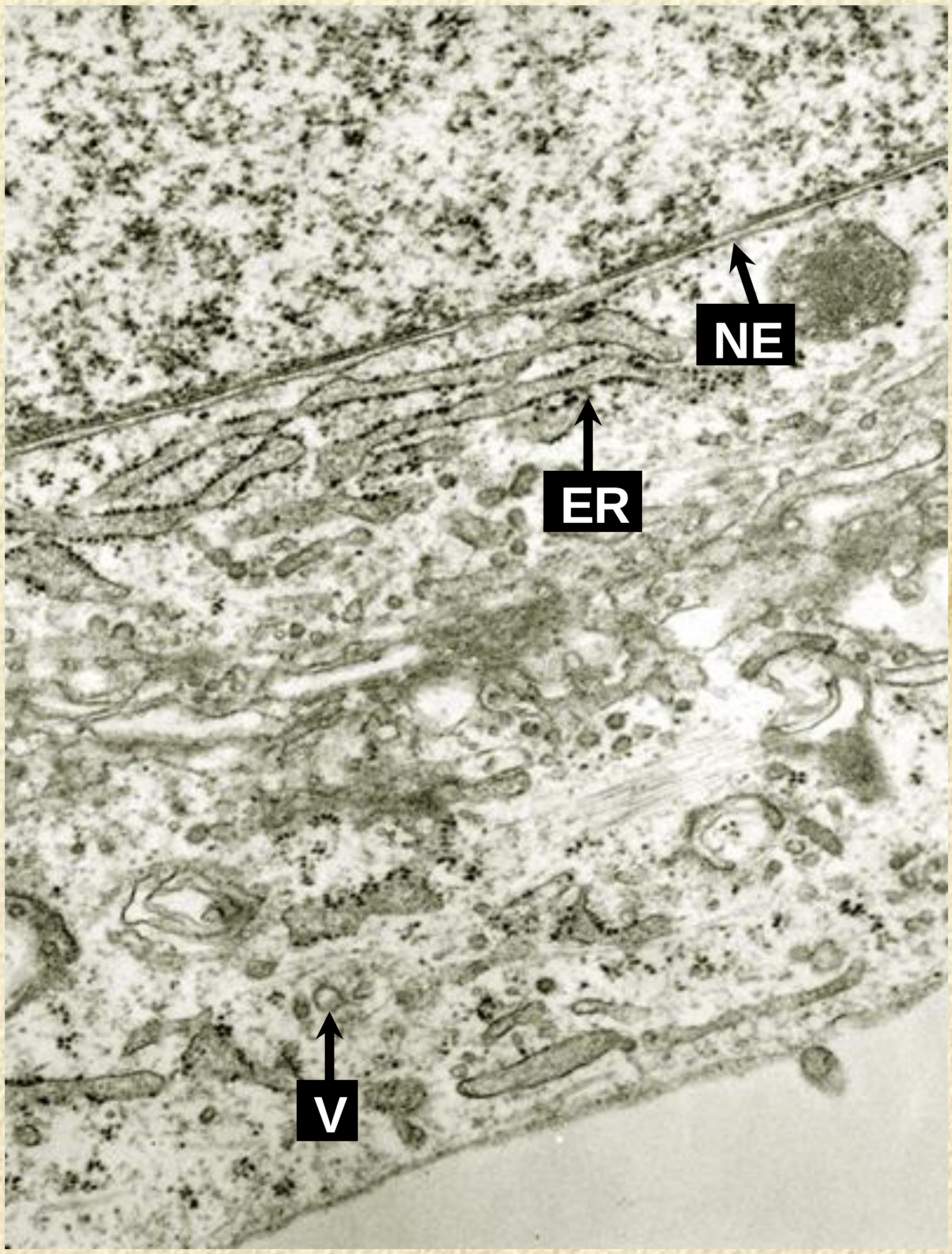


- **Protein synthesis** occurs on **ribosomes**, which can be:
  - bound to the **rough endoplasmic reticulum** (RER) or
  - **free in the cytosol**
- Most protein synthesis occurs at the RER. These proteins are usually **exported** from the cell or incorporated into membranes.
- **Protein modification** can also occur within the ER.
- Proteins produced on free ribosomes stay in the cytosol.



The Endomembrane System

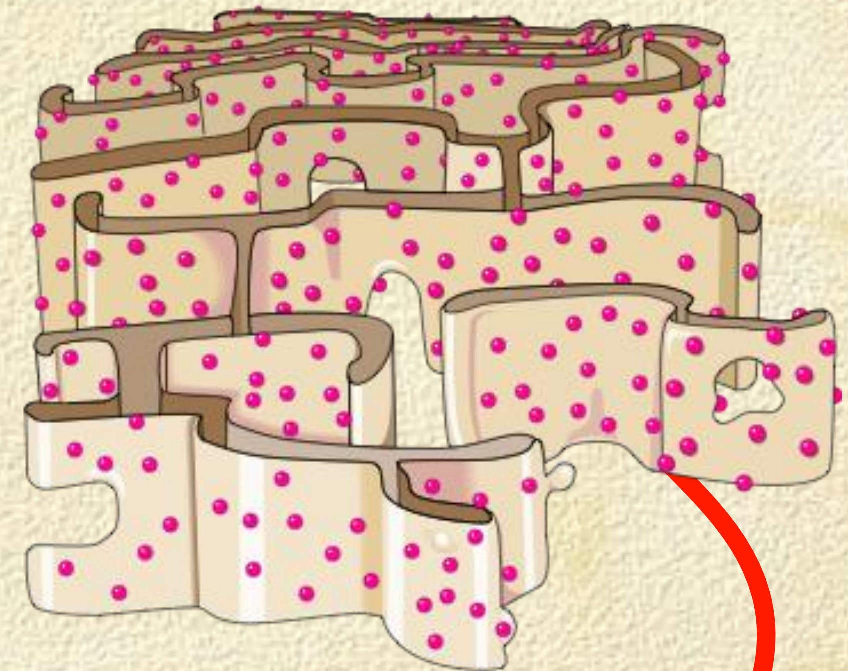
- Many of the different membranes within the cell are part of the endomembrane system.
- These membranes are related by:
  - direct physical continuity
  - by the transfer of membrane segments through the movement of vesicles.
- Although related, the various membranes are structurally and functionally distinct.
- The endomembrane system includes:
  - **nuclear envelope**
  - **endoplasmic reticulum**
  - **Golgi** and **vesicles**
  - **lysosomes**, **peroxisomes**, **vacuoles**
- It does not include mitochondria or chloroplasts.



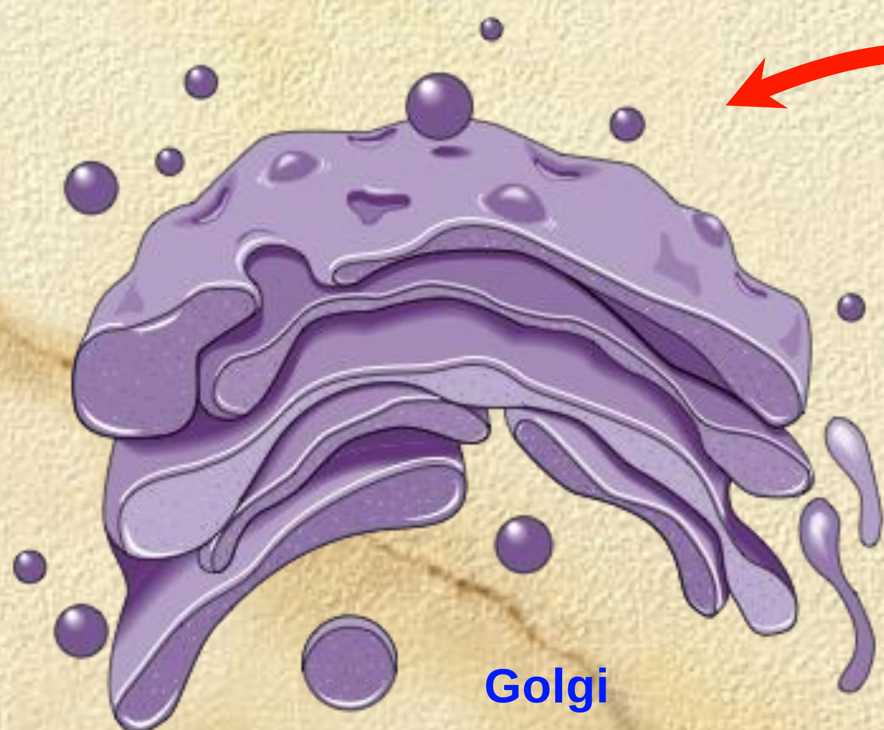
The nuclear envelope (**NE**) is part of the endo-membrane system, which includes vesicles (**V**) and endoplasmic reticulum (**ER**)

Macromolecule Synthesis

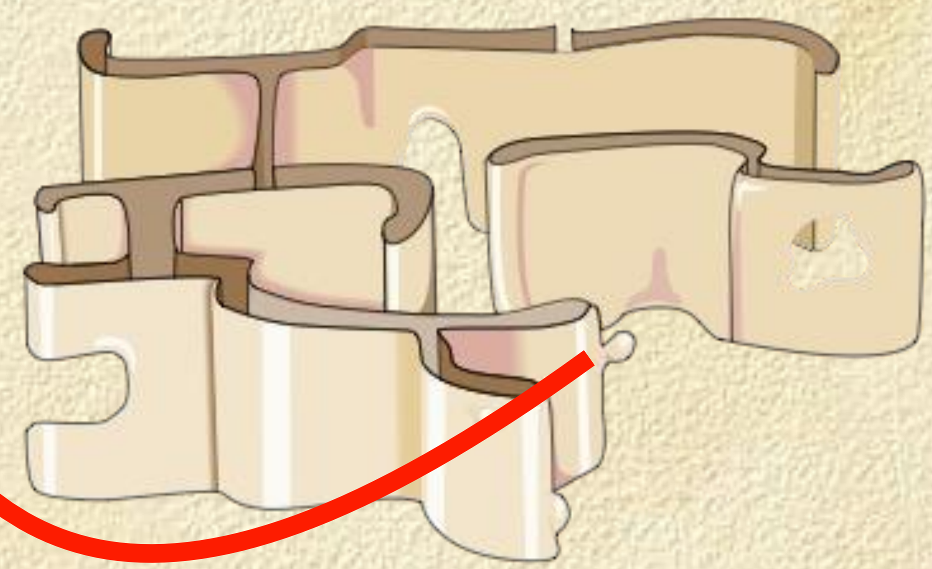
- The endomembrane system is important in the synthesis of **macromolecules**.
- Cells produce a range of macromolecules; **organic polymers** made up of repeating units of smaller molecules.
  - The synthesis, packaging and movement of these molecules inside the cell involves a number of membrane bound organelles (right and below).



Rough endoplasmic reticulum (RER)
(ribosomes attached)

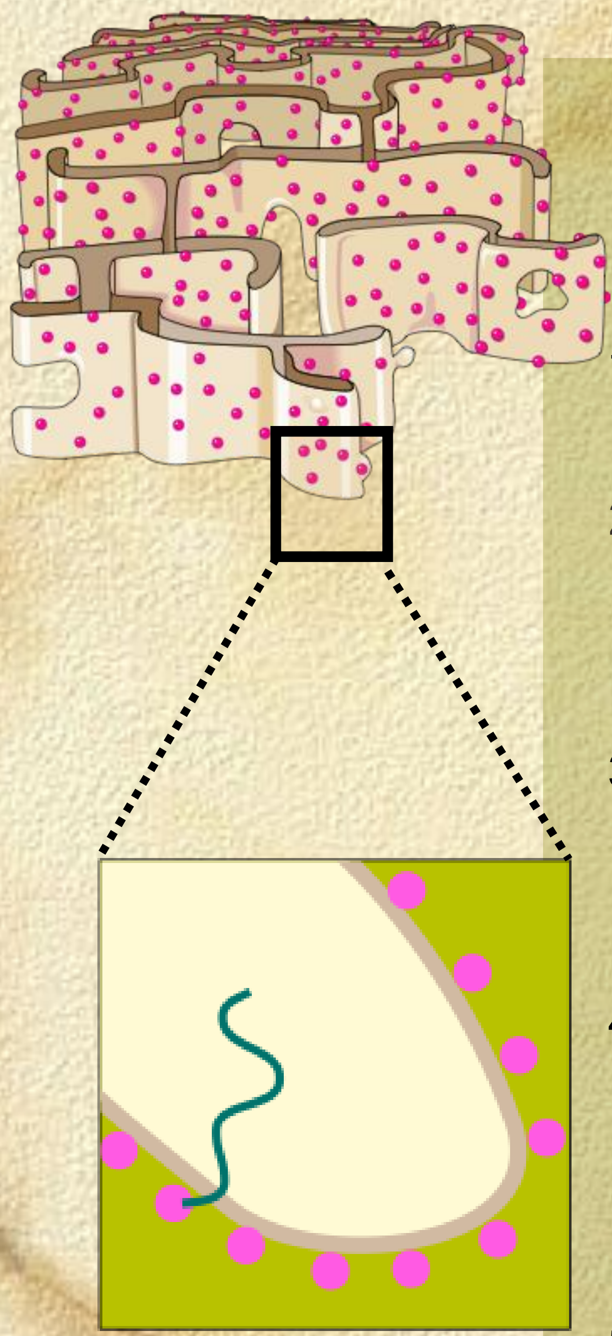


Golgi



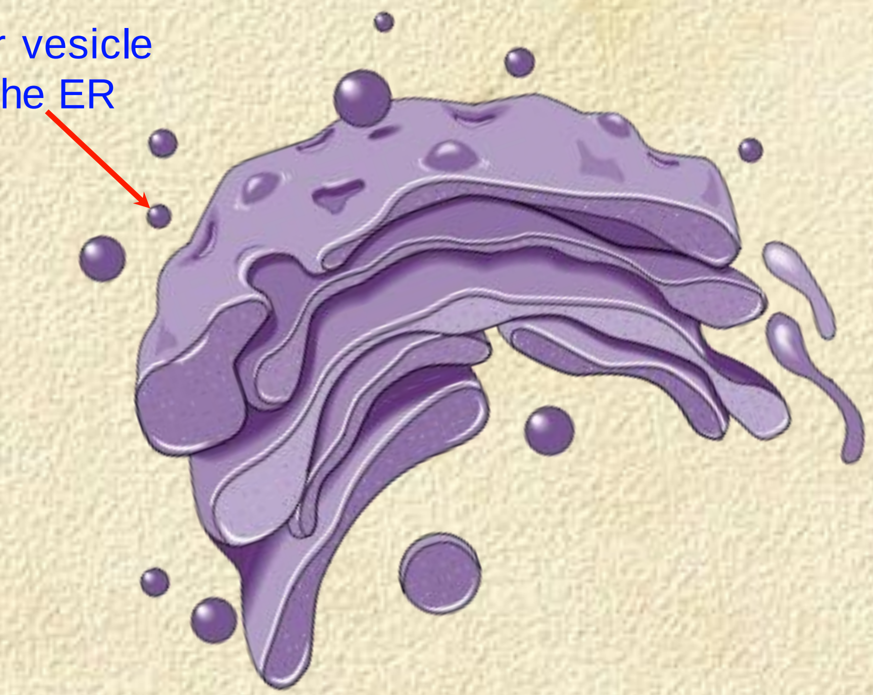
Smooth endoplasmic reticulum (SER)

Macromolecule Synthesis

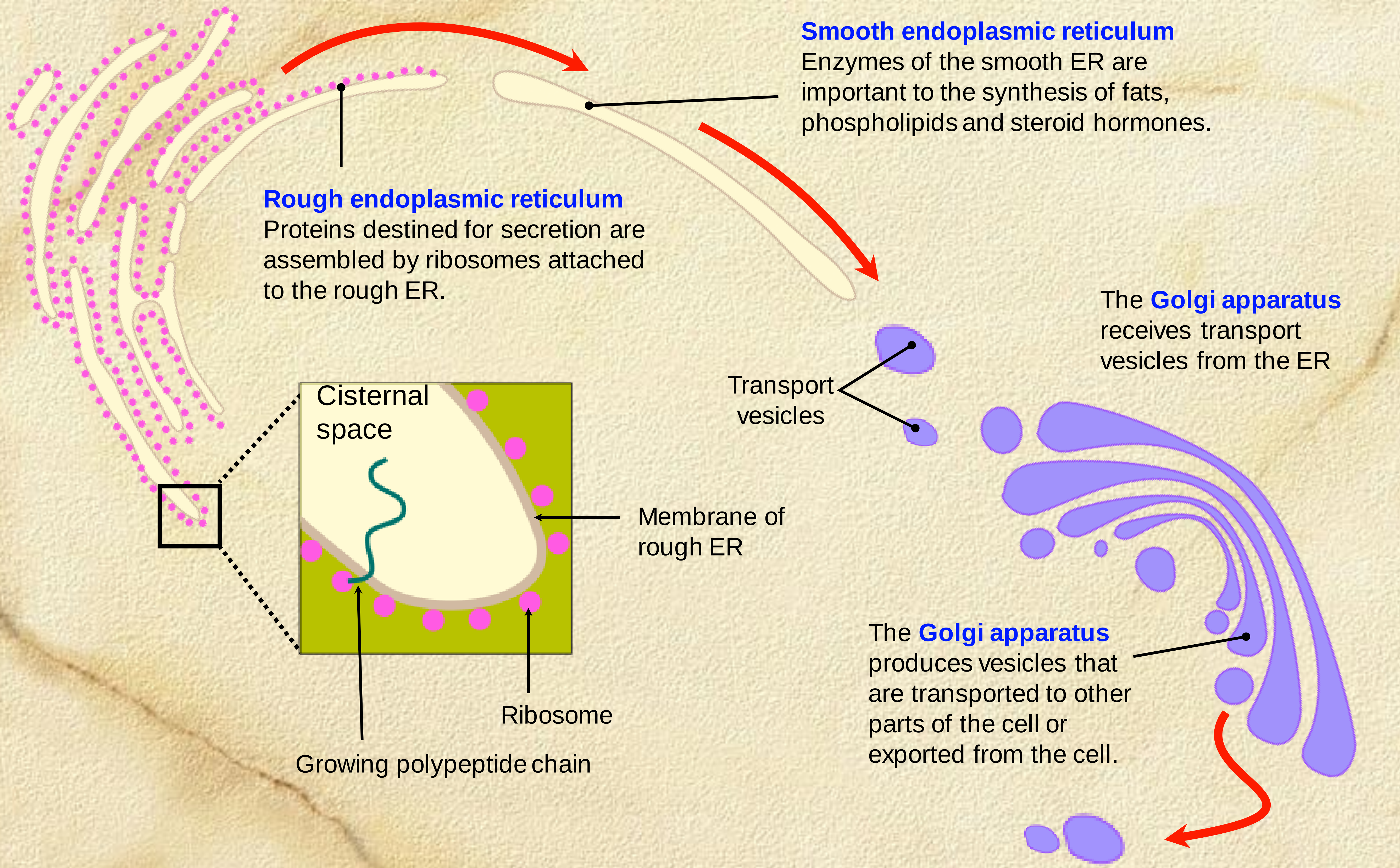


Creating Proteins for Exocytotic Secretion

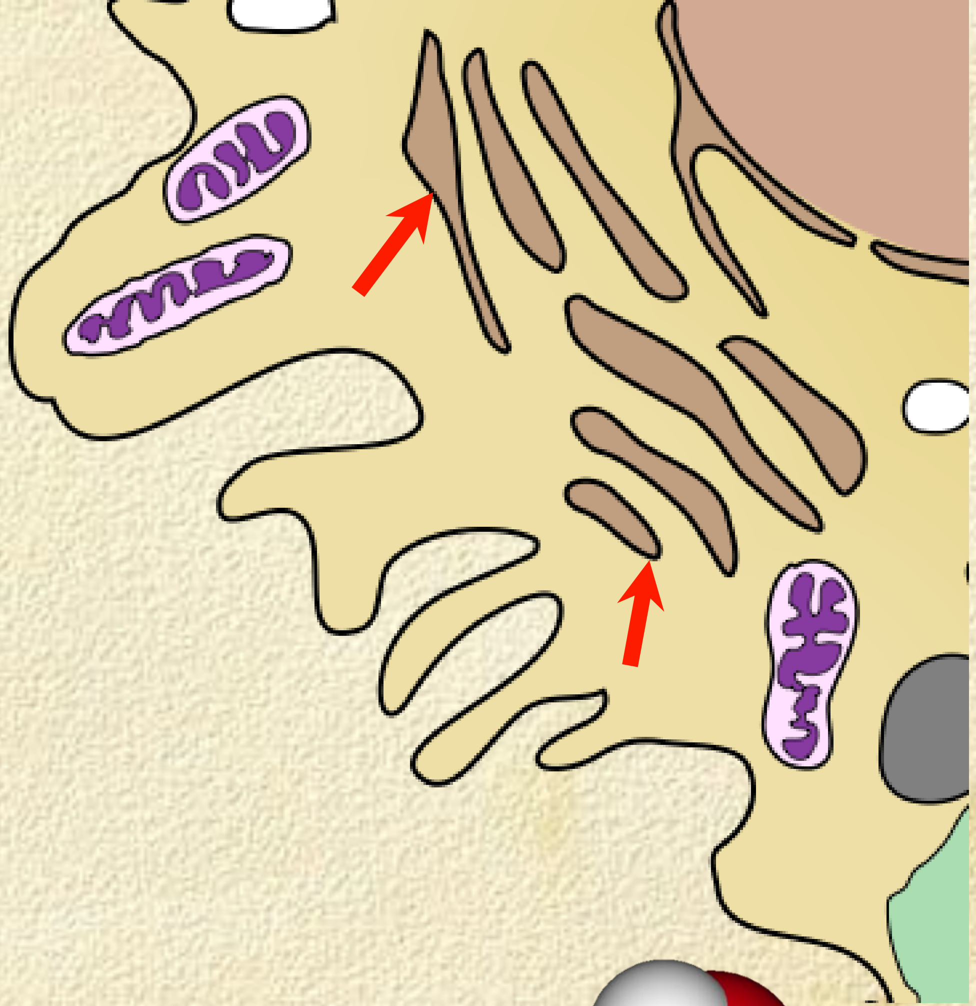
1. A **polypeptide** chain grows from a bound **ribosome**.
2. The chain is threaded through the ER membrane into the **cisternal space**, possibly through a pore.
3. As it enters the cisternal space inside the ER, it folds up into a 3-dimensional shape.
4. Most proteins destined for secretion are **glycoproteins**. The carbohydrate is attached to the protein by enzymes.
5. The ER membrane keeps secretory proteins separate from proteins made by free ribosomes.
6. Proteins destined for secretion leave the ER in **transport vesicles** which bud off from the ER. The chain is threaded through the ER membrane into the cisternal space, possibly through a pore.
7. These vesicles are received by the **Golgi apparatus**, where they are modified, stored and eventually shipped to the cell's surface, for exportation by **exocytosis**.



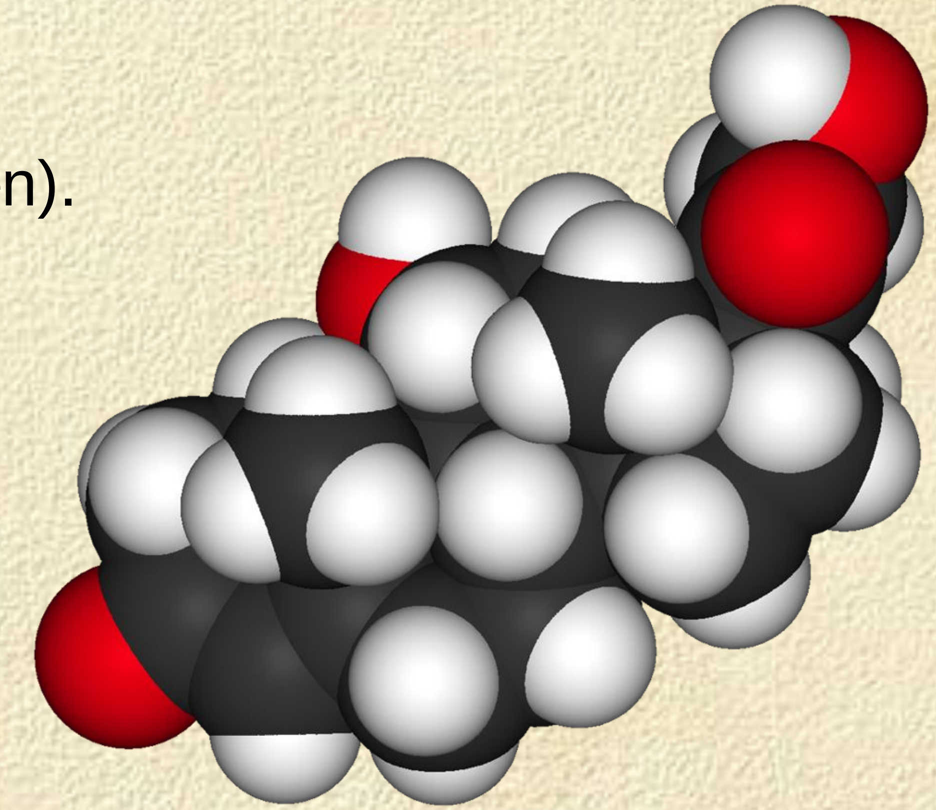
Macromolecule Synthesis



Lipid Synthesis



- The **smooth endoplasmic reticulum** is the site of **lipid synthesis** in the cell.
  - The smooth ER produces fats, phospholipids and steroids.
- Unlike rough ER, smooth ER **lacks ribosomes** (hence its name).
- Important synthesis products include:
  - **Sex hormones** (e.g. testosterone and estrogen).
    - Smooth ER is abundant in cells that secrete these products (testes and ovaries).
  - **Steroid hormones** (e.g. cortisol) produced by the adrenal glands.
    - Cortisol plays an important role in regulating blood pressure and cardiovascular activity.

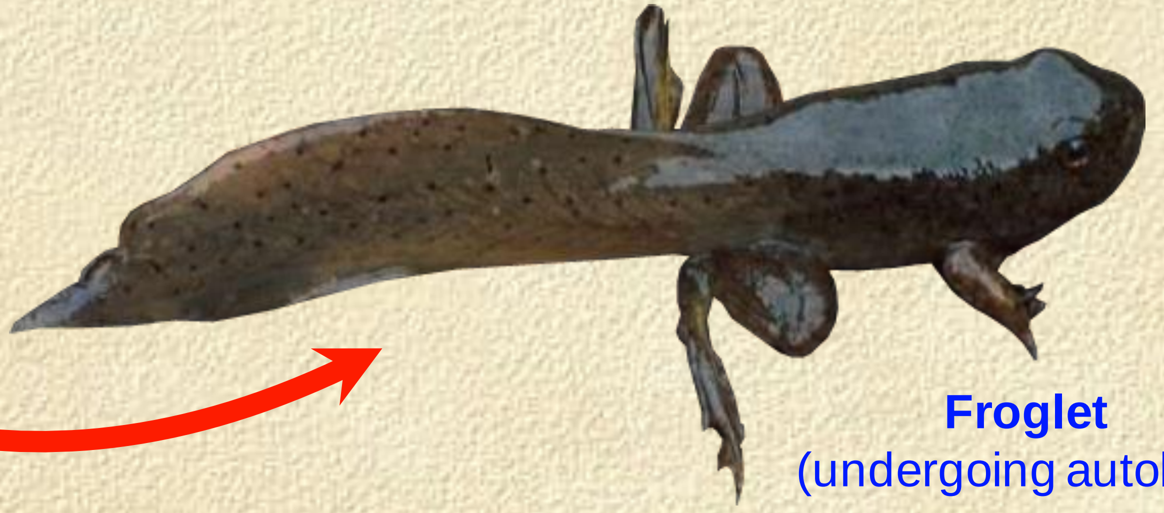


A 3D space filling model of the steroid hormone **cortisol**.

Autolysis

- **Lysosomes** are specialized organelles containing **hydrolytic enzymes** enclosed within a single membrane. They are responsible for:
  - intracellular digestion of macromolecules
  - recycling of cellular components (autophagy)
  - **autolysis**, the enzymatic self digestion of the cell itself
- Autolysis is usually prevented because the enzymes are enclosed within the lysosome membrane.
- Autolysis is important in the development of some organisms. During **metamorphosis** in frogs, lysosomes destroy the cells of the froglet tail resulting in a tail-less adult.

Frog
(autolysis complete)



Froglet
(undergoing autolysis)

Tadpole

Oxidative Reactions

- **Peroxisomes** are specialized lysosomes which rid the body of toxic substances by a series of **oxidative reactions**.
- They are usually roughly spherical and often have a granular or crystalline core.
- Peroxisomes contain **oxidative enzymes** which break down toxic organic molecules (e.g. **alcohol detoxification**).
  - Hydrogen ions from the toxic component are transferred to oxygen atoms forming **hydrogen peroxide (H_2O_2)**.
  - Hydrogen peroxide is toxic, but within the peroxisome it is converted by the enzyme **catalase** into harmless water and oxygen molecules.

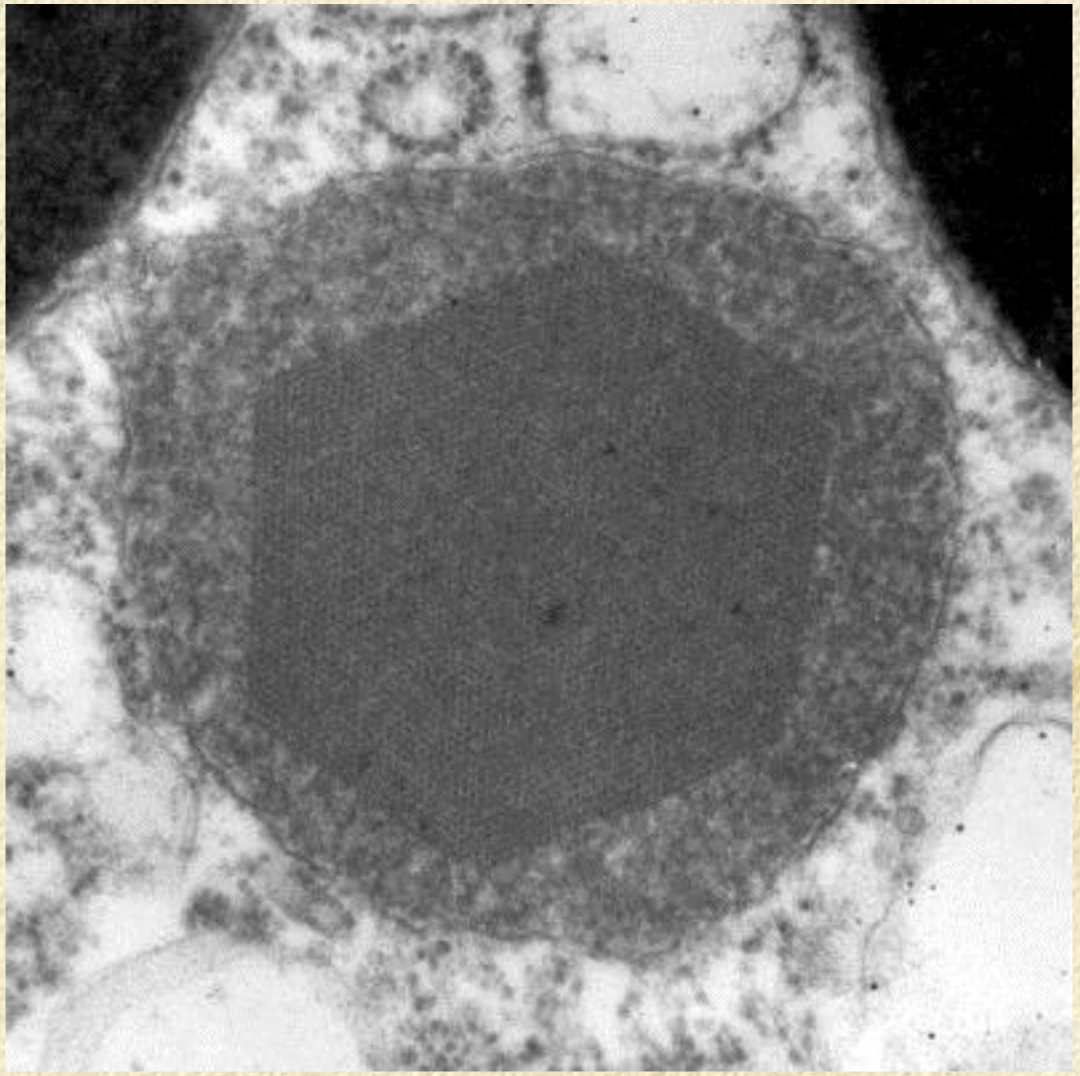
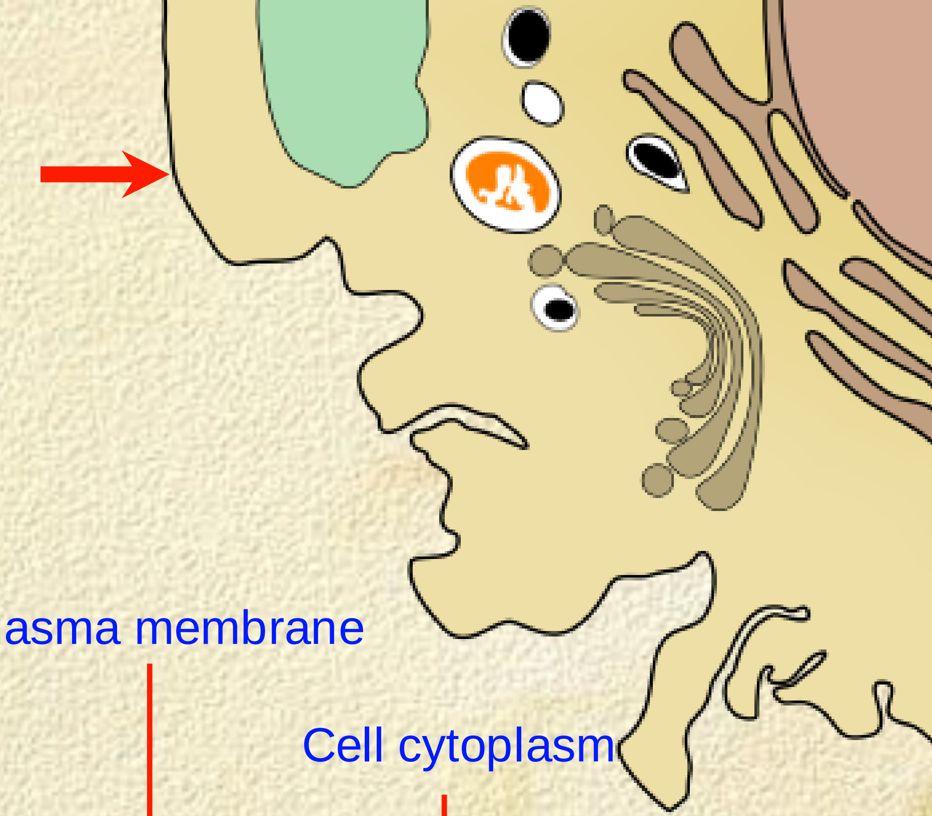


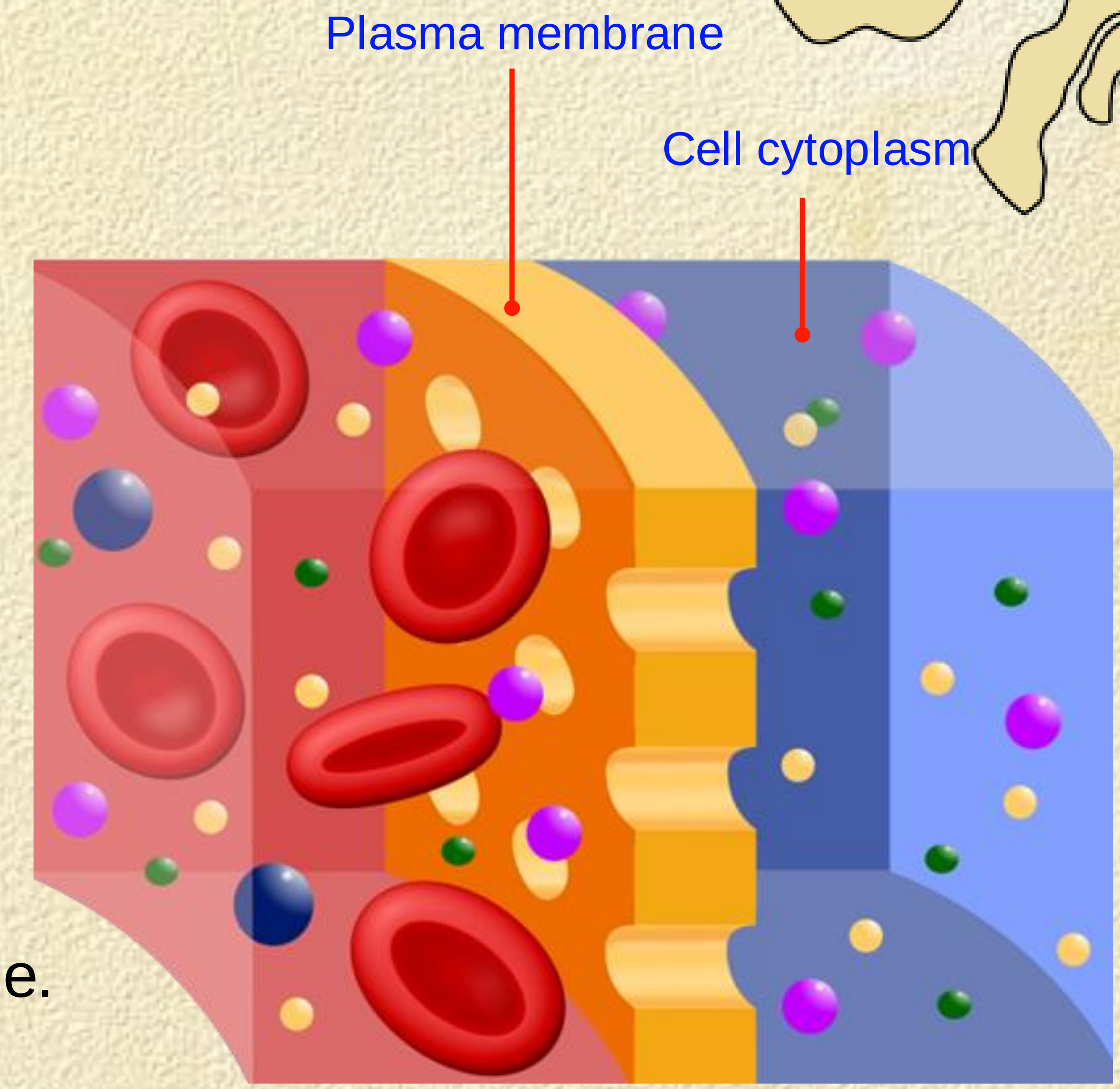
Photo: Alexandre Lobo da Cunha, University of Porto

TEM of a **peroxisome** from the marine snail *Gibulla umbilicalis*. Note the crystalline appearance of the core. This is where the enzymes are thought to be concentrated.

Cell Transport



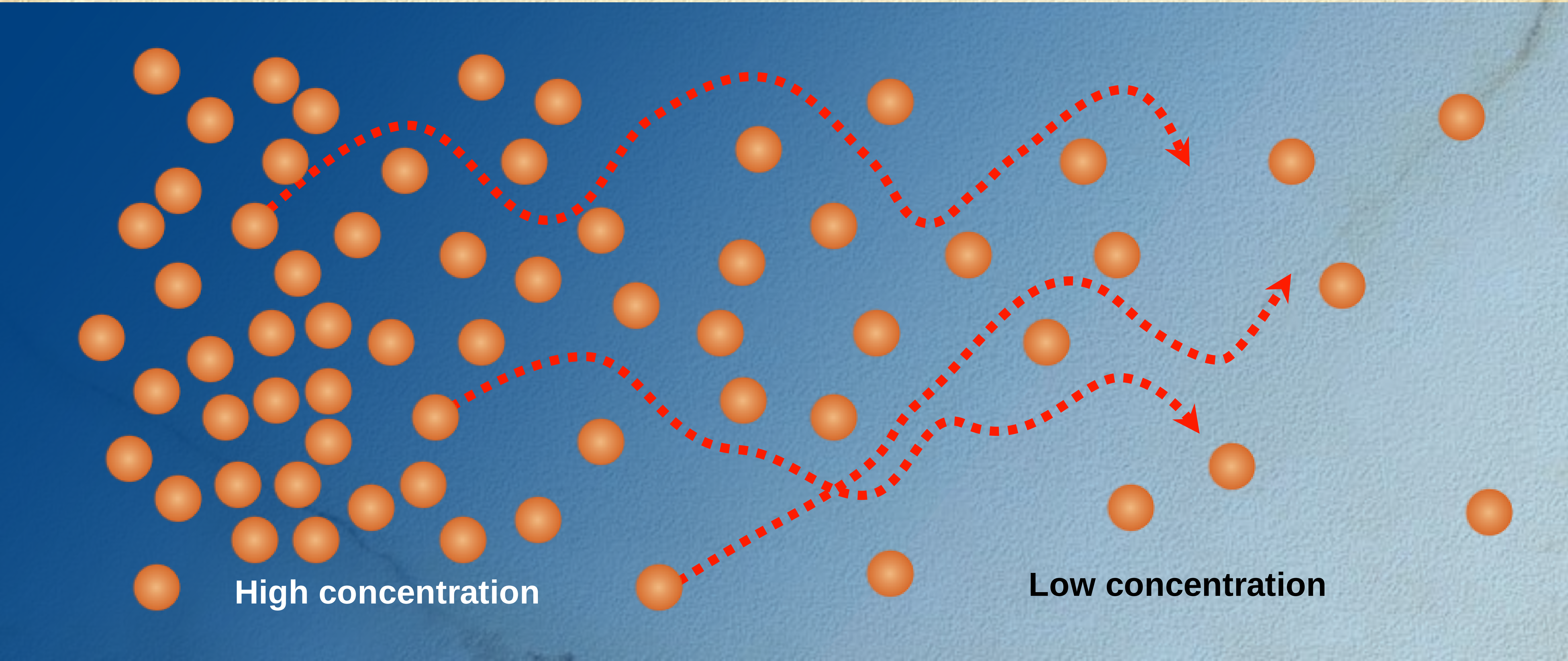
- Substances need to move into and out of the cell. They are moved across the plasma membrane by cellular transport mechanisms. These may be:
  - **passive** (not requiring energy)
    - diffusion and facilitated diffusion
    - osmosis
  - **active** or energy requiring
    - ion pumps
    - cytosis
- The plasma membrane is **partially permeable** to certain molecules.
  - **Channel and carrier proteins** are involved in selective transport of small molecules and ions across the membrane.
  - **Large molecules** (e.g. proteins) are transported by **cytosis** (formation of membrane-bound vesicles or vacuoles).



The plasma membrane is partially permeable, allowing some molecules to pass through, and preventing the passage of others.

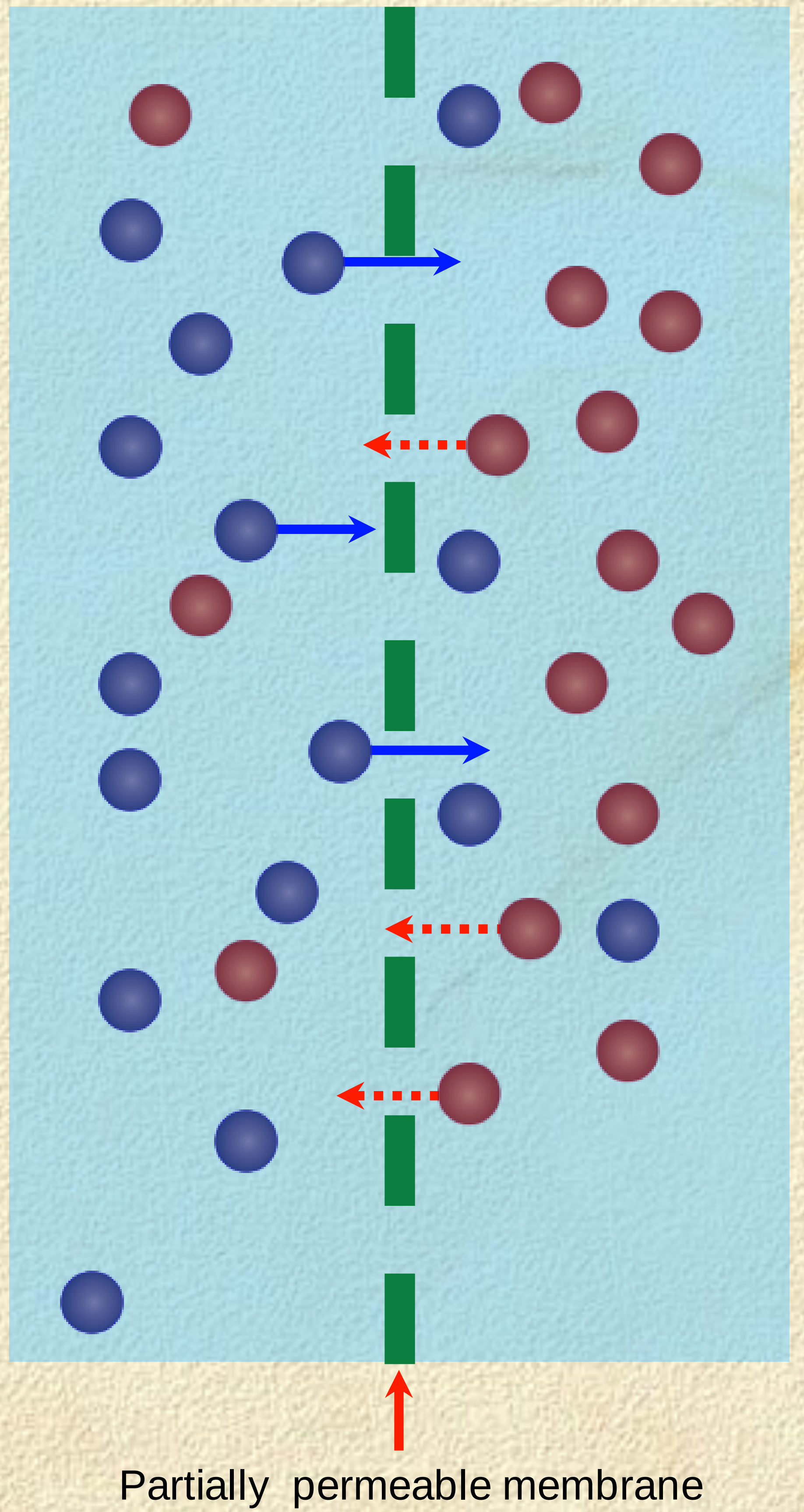
Diffusion

- **Diffusion** is a **passive transport** process. It does not require energy to occur.
- Diffusion describes the movement of molecules from regions of high concentration to areas of low concentration along a **concentration gradient**.
- In biological systems, diffusion often occurs across **partially permeable membranes**.



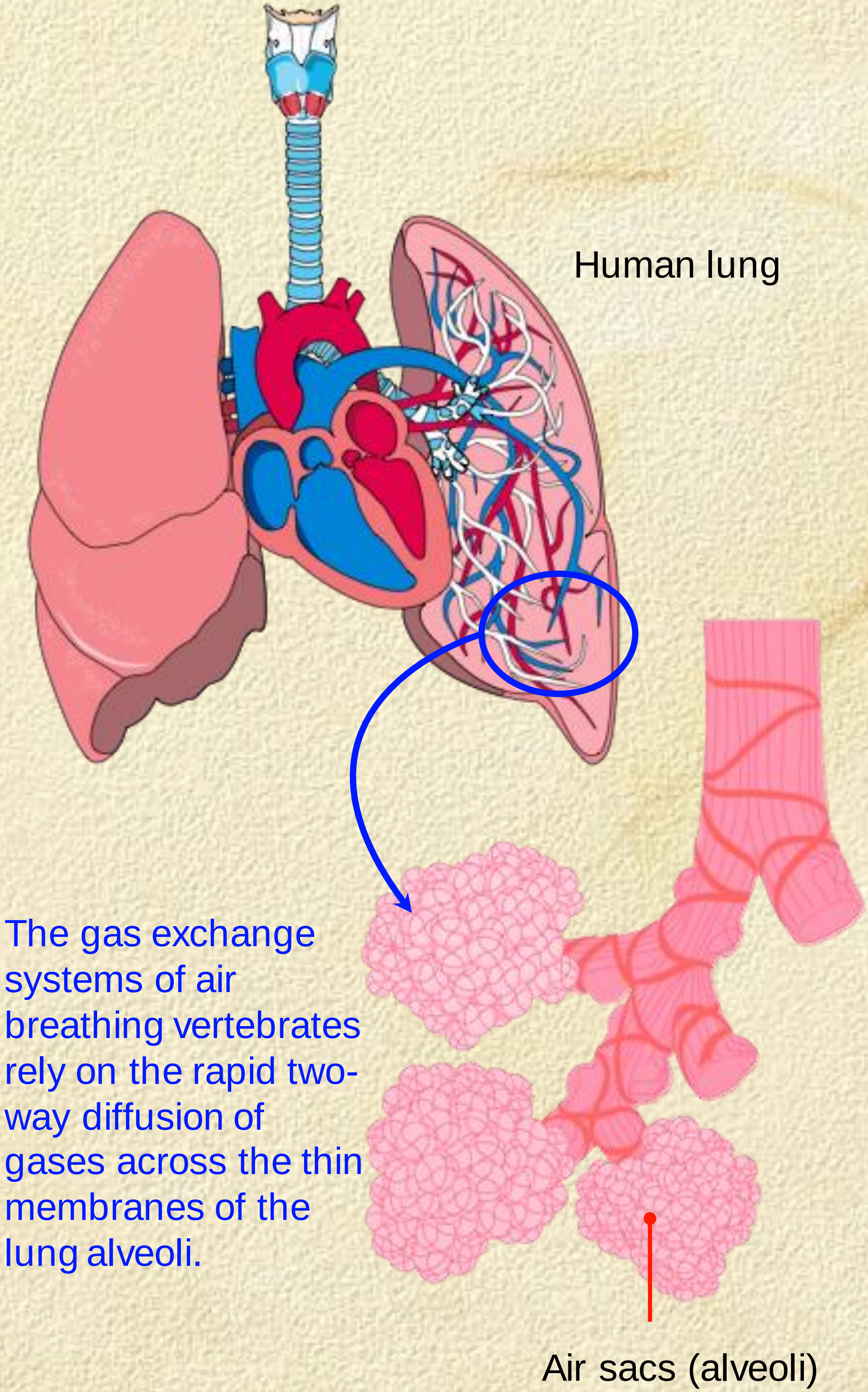
Diffusion Across Membranes

- In any type of diffusion, each type of diffusing molecule (gas, solvent, solute) **moves along its own concentration gradient**.
- An **equilibrium** is reached when the net concentration of molecules on each side of the membrane are equal.
  - At this point, **net movement** stops.
- **Two-way diffusion** across a partially permeable membrane is common in biological systems.
  - For example, at the lung surface, carbon dioxide diffuses out of the blood across the membranes of the capillaries and the lung alveoli, while oxygen diffuses in the opposite direction into the blood.



Factors Affecting Diffusion

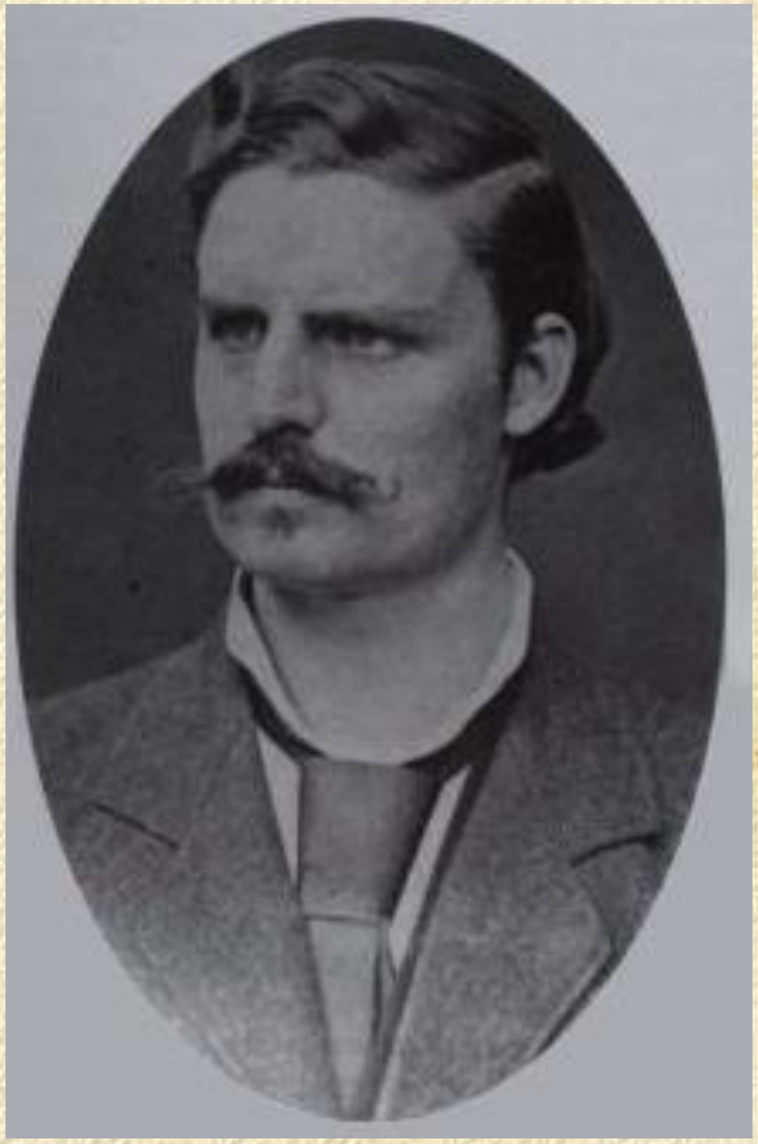
- Four main factors affect the rate of diffusion across a membrane:
  - **Concentration gradient**. Diffusion rates will be higher when there is a greater difference in concentration between two regions.
  - **The diffusion distance**. Diffusion over shorter distances occurs at a greater rate than diffusion over larger distances.
  - **Surface area**. The rate of diffusion is greater when there is a large surface area across which diffusion can occur.
  - **Physical barriers**. Thick barriers slow the rate of diffusion. Pores in a barrier enhance diffusion.



Fick's Law

- The factors governing the rate of diffusion across membranes are described by **Fick's law**.
- Fick's law is expressed as:

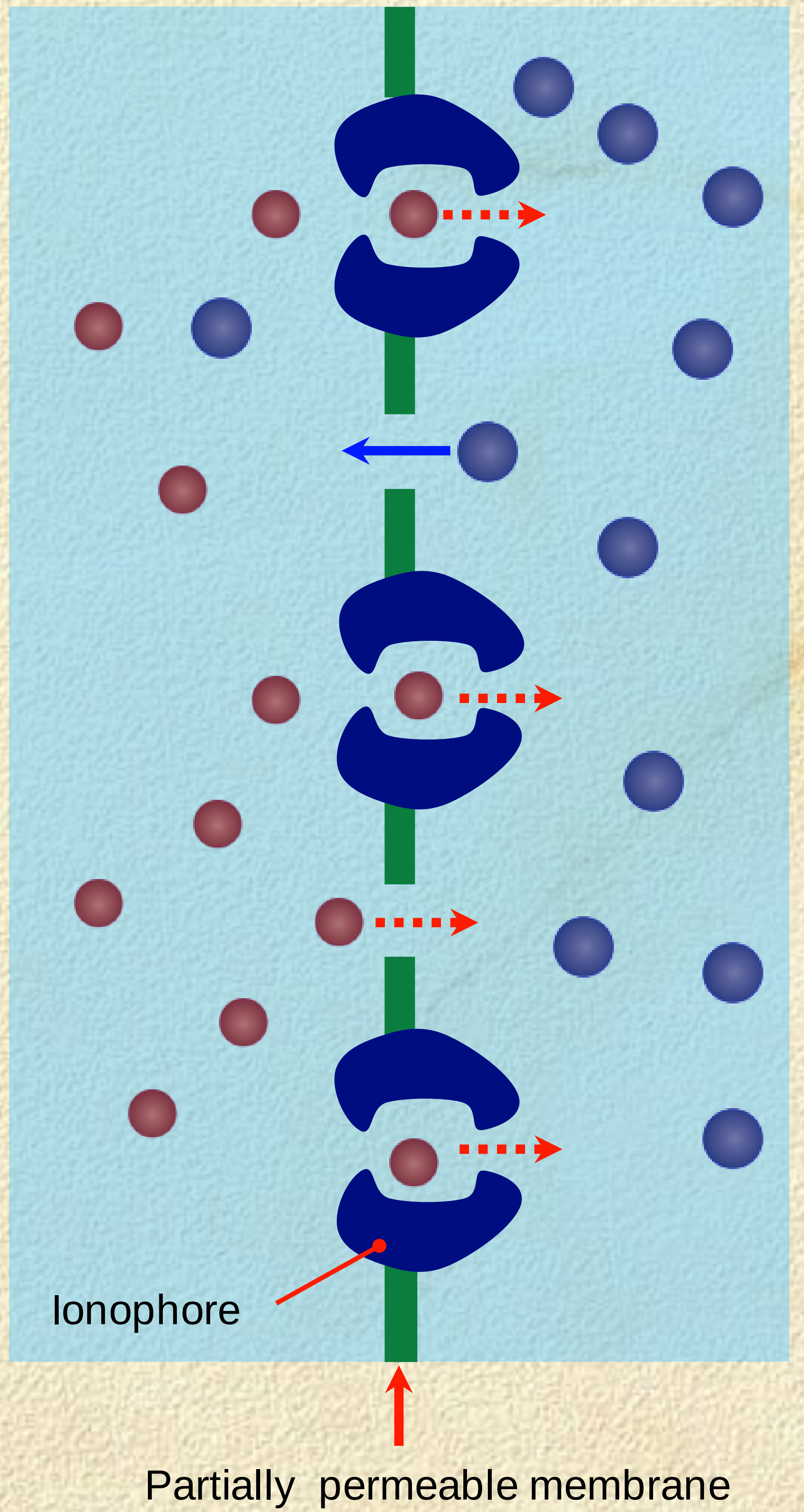
$$\frac{\textbf{Surface area of membrane} \times \textbf{Difference in concentration across the membrane}}{\textbf{Length of the diffusion path (thickness of the membrane)}}$$



Adolf Fick (above) was a German physiologist who proposed the laws that govern gas diffusion across a membrane (**Fick's law**). He is also credited with designing the first contact lens and devising the technique for measuring cardiac output (Fick's principle).

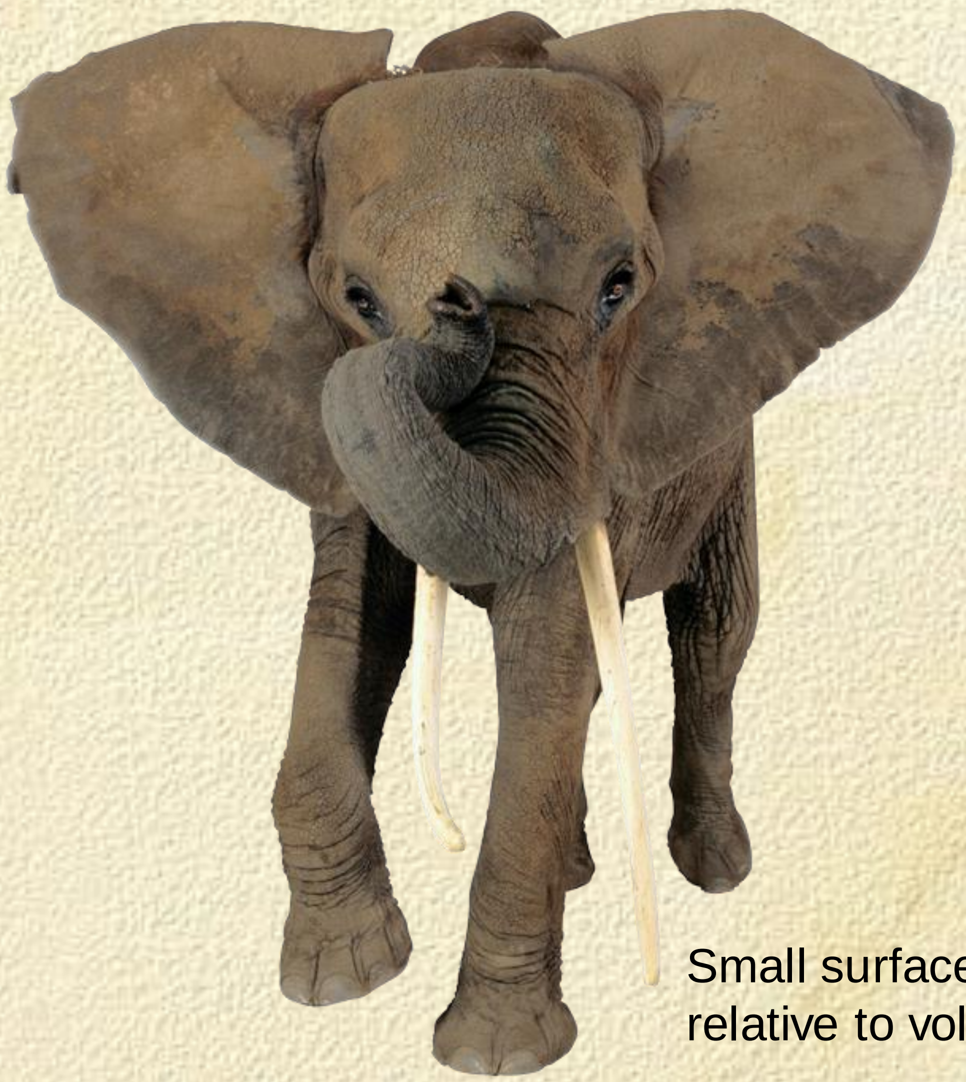
Facilitated Diffusion

- **Facilitated diffusion** occurs when a substance is aided across a membrane by **ionophores**.
  - Ionophores are lipid-soluble molecules that increase the permeability of cellular membranes to specific ions.
  - Ionophores often act as channel formers that introduce a hydrophilic pore in the membrane through which ions may pass.
- Facilitated diffusion **selectively increases** the diffusion rate of specific molecules (e.g. glucose, amino acids).
  - It does not require energy because the molecules are not moving against their concentration gradient.
  - It occurs when a higher diffusion rate is desirable, e.g. transport of glucose into skeletal muscle fibers.



Limitations to Cell Size

- A small organism (such as a unicellular protist) has a large **surface area** relative to its **volume**. For these organisms, **diffusion** is an effective way to transport materials into and out of the cell.
- As an organism becomes larger, its surface area decreases relative to its volume and diffusion ceases to be an effective way to exchange materials with the environment.
- For this reason, there is a physical limit for the size of a cell, with the effectiveness of diffusion being the controlling factor.

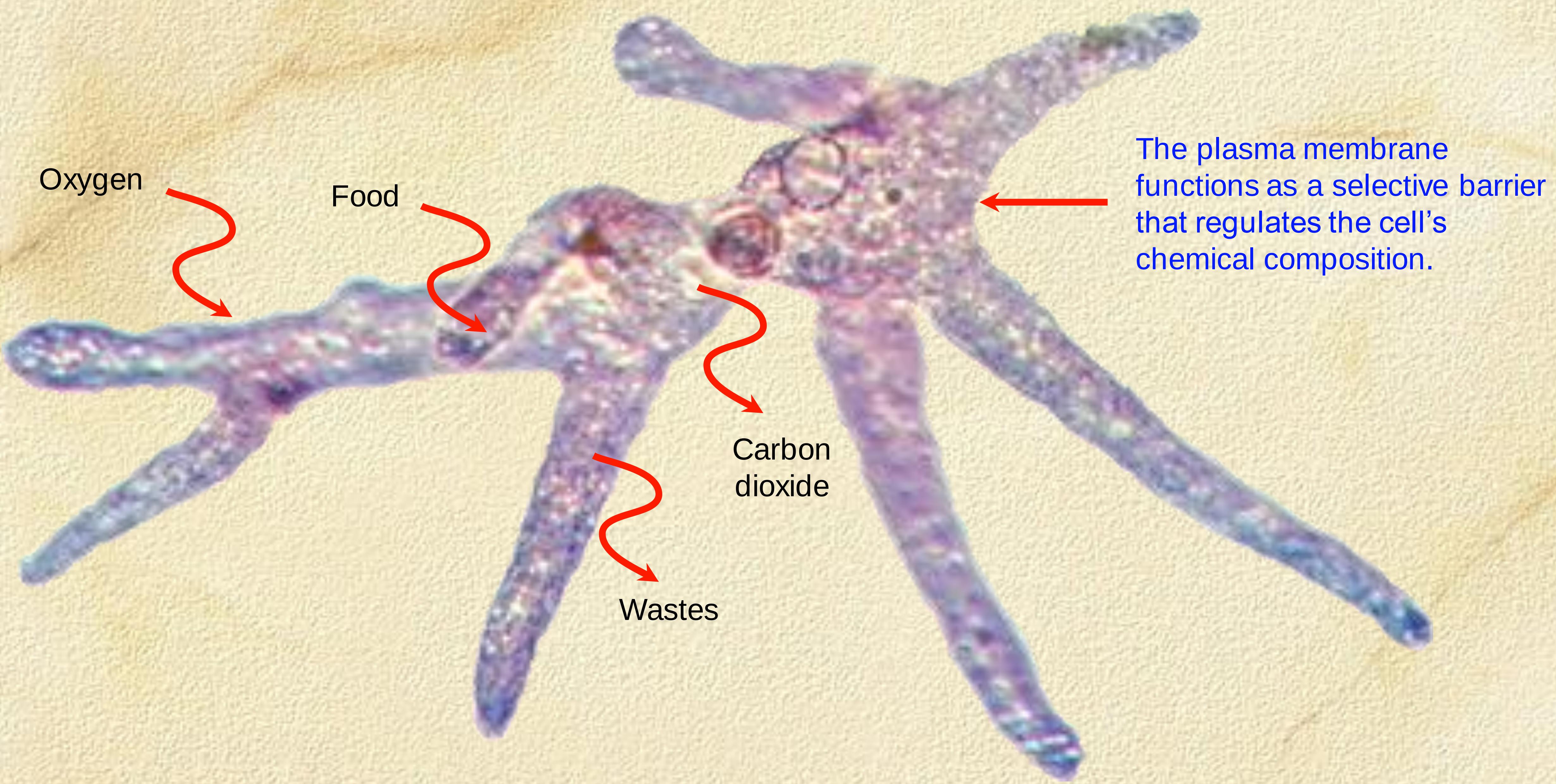


Small surface area relative to volume

Large surface area relative to volume

For small organisms such as the *Amoeba* (left), **diffusion** across the body surface is a viable method of exchanging materials (e.g. gases) with the environment. For large organisms, such as an elephant (above), specialized systems, such as lungs, permit efficient exchanges with the environment.

Limitations to Cell Size

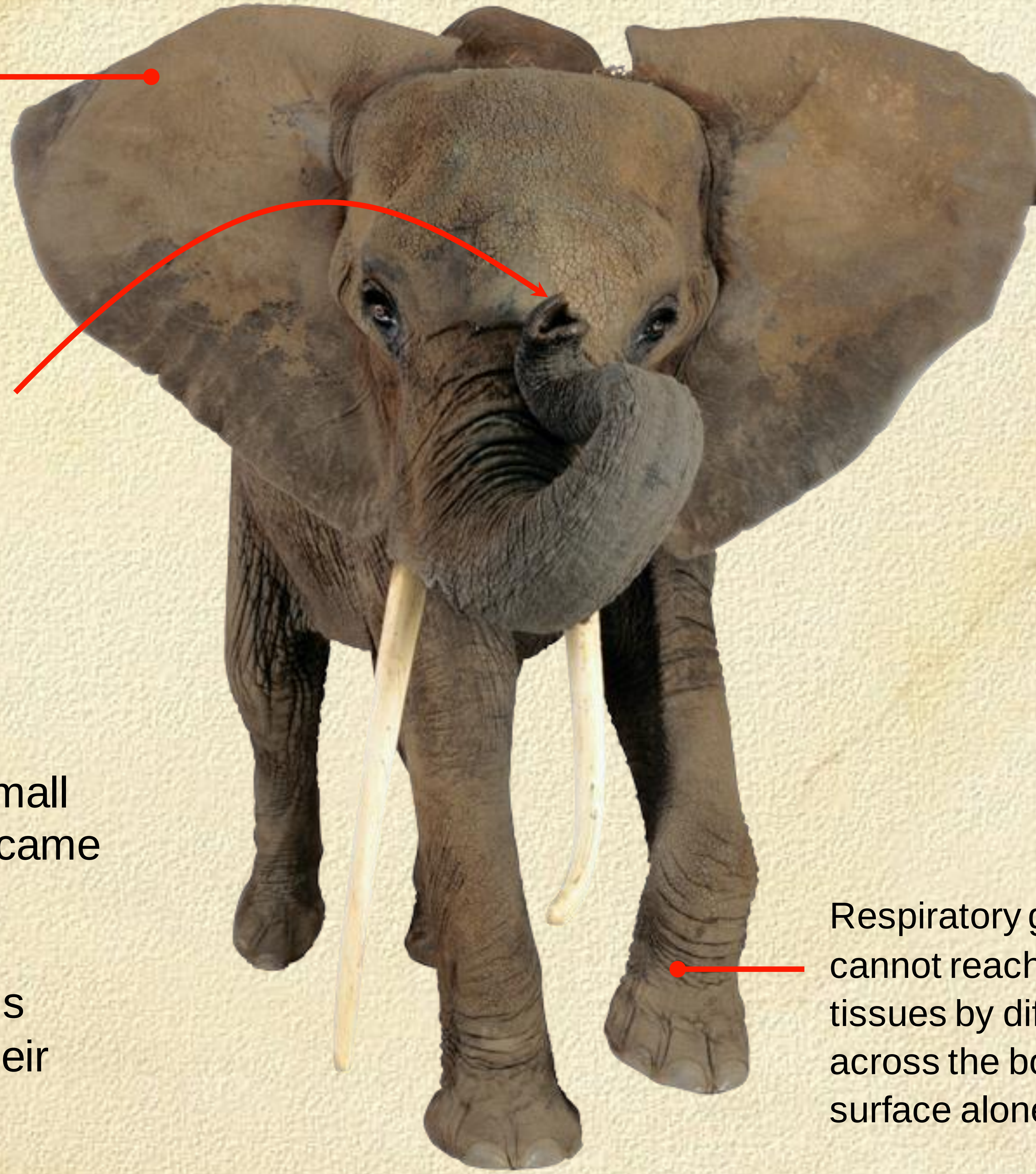


- The small size of single-celled protists such as *Amoeba* (above), provides a **large surface area relative to the cell's volume**.
- This is adequate for materials to be moved directly into and out of the cell by diffusion or active transport across the plasma membrane.

Limitations to Cell Size

The surface area of an elephant is increased, for radiating body heat, by large flat ears.

Specialized exchange surfaces (e.g. lungs, capillary beds, gut villi, and skin) provide a high surface area across which exchanges with the environment can be made. Complex organ systems link exchange surfaces to move materials efficiently through the body between these exchange surfaces.



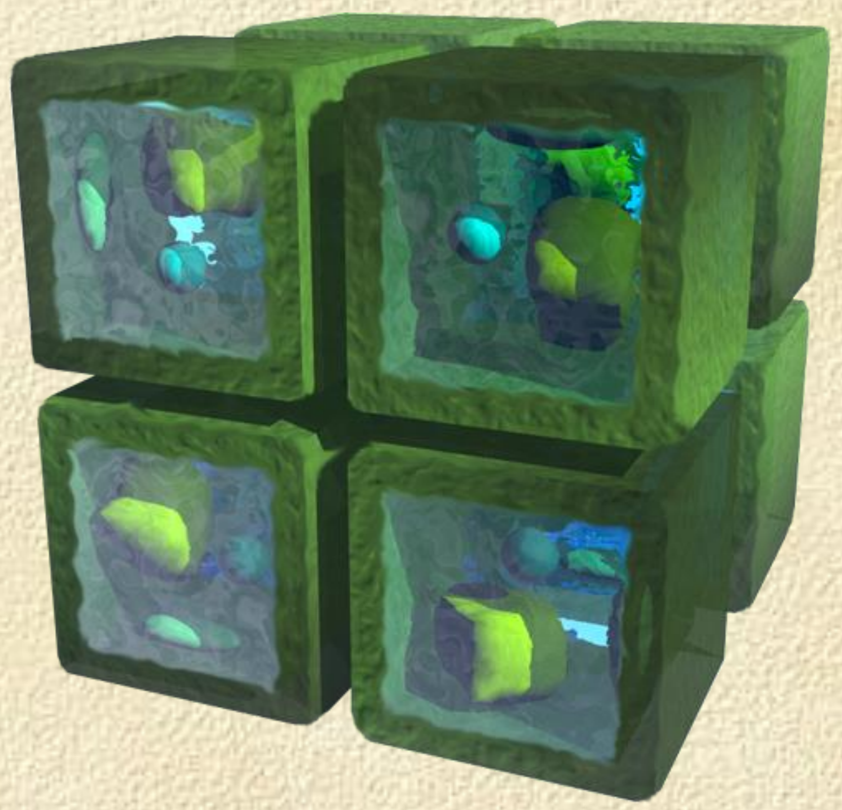
Multicellular organisms

To overcome the problems of small cell size, plants and animals became multicellular. They have a small surface area compared to their volume but have evolved various adaptive features to increase their effective surface area.

Respiratory gases cannot reach body tissues by diffusion across the body surface alone.

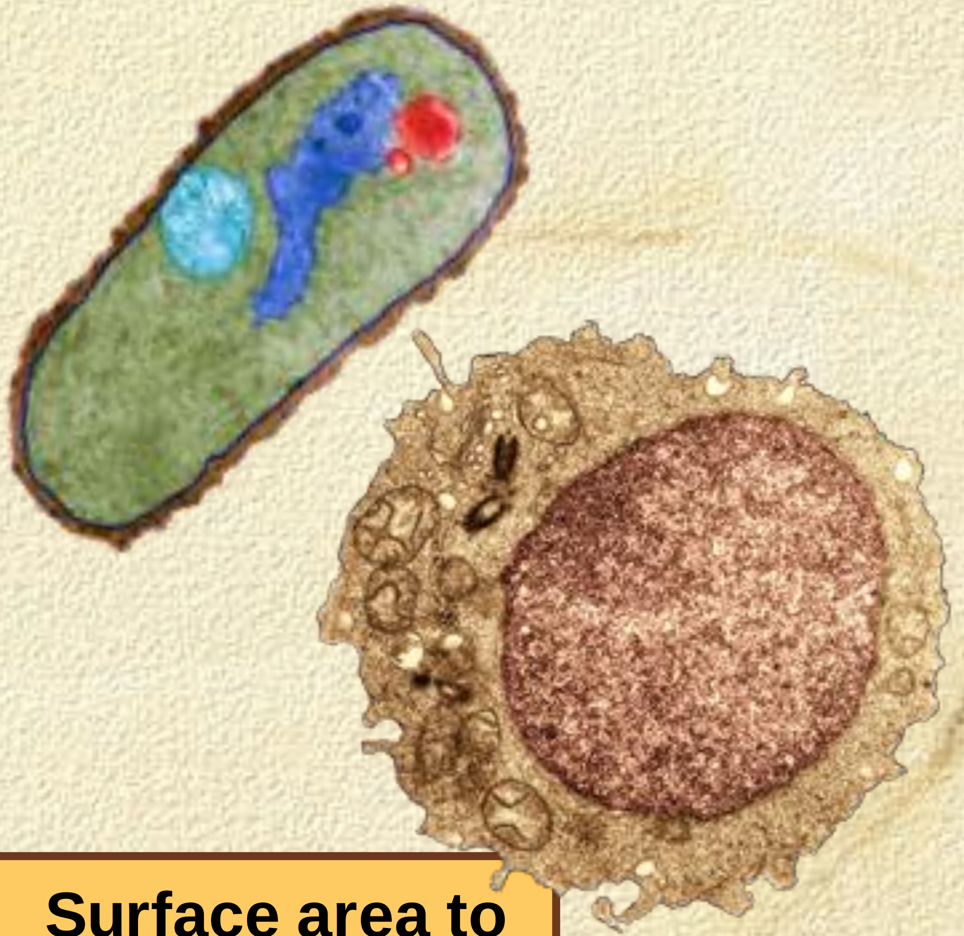
Limitations to Cell Size

- The eight small cells (below right) and the single large cell (above right) have the **same total volume**, but their surface areas are different.
- The small cells together have twice the total surface area of the large cell, because there are more exposed (inner) surfaces.
- Real organisms have complex shapes, but the same principles apply. The **surface-area volume relationship** has important implications for processes involving **transport** into and out of cells across membranes.



Limitations to Cell Size

- As cell size increases:
  - its volume increases at a faster rate than the surface area.
  - there is less surface area, so the surface area to volume ratio decreases (see table below).
  - large cells will have difficulties in exchanging materials at rates adequate to meet demands. Cell size is limited by diffusion capability.



Cube size	Surface area	Volume (h x w x d)	Surface area to volume ratio
2 cm cube	2 x 2 x 6 = 24 cm^2	2 x 2 x 2 = 8 cm^2	24 to 8 = 3:1
3 cm cube	3 x 3 x 6 = 54 cm^2	3 x 3 x 3 = 27 cm^2	54 to 27 = 2:1
4 cm cube	4 x 4 x 6 = 96 cm^2	4 x 4 x 4 =64 cm^2	96 to 64 = 1.5:1
5 cm cube	5 x 5 x 6 = 150 cm^2	5 x 5 x 5 = 125 cm^2	150 to 125 = 1.2:1

Osmosis

- **Osmosis** is defined as the net movement of water molecules across a partially permeable membrane from a region of higher to lower concentration (of water molecules).
- Usually, water movements are expressed in terms of water and solute potential:
  - **Water molecules always move towards regions of more negative water potential** (=higher concentration of solute molecules).
- Osmosis provides the primary means by which water is transported into and out of cells. The net direction of water movement in cells can be predicted on the basis of the water potential of the solutions involved.
- Osmosis is affected by the same factors as diffusion.

A plant's root system covers a large area, allowing it to draw water and nutrients up from the soil. Water is drawn into the root system by osmosis.

What is Water Potential?

- The **water potential** (Ψ) of a solution describes the tendency for water molecules to enter or leave a solution by osmosis.
  - Pure water has the highest Ψ, set at zero.
  - Dissolving any solute into pure water lowers the water potential (makes it more negative).
  - Water always diffuses from regions of less negative to more negative water potential.
- Water potential is determined by two components:
  - the solute potential, Ψs (of the cell sap)
  - the pressure potential, Ψp.
  - This is expressed as a simple equation:

$$\Psi Cell = \Psi s + \Psi p$$

Dialysis tubing is a partially permeable cellulose or cellophane tubing used to demonstrate osmosis. The tubing (filled with a solution) simulates a plasma membrane. By placing it into containers of varying osmotic solutions, the principles of osmosis can be explored.

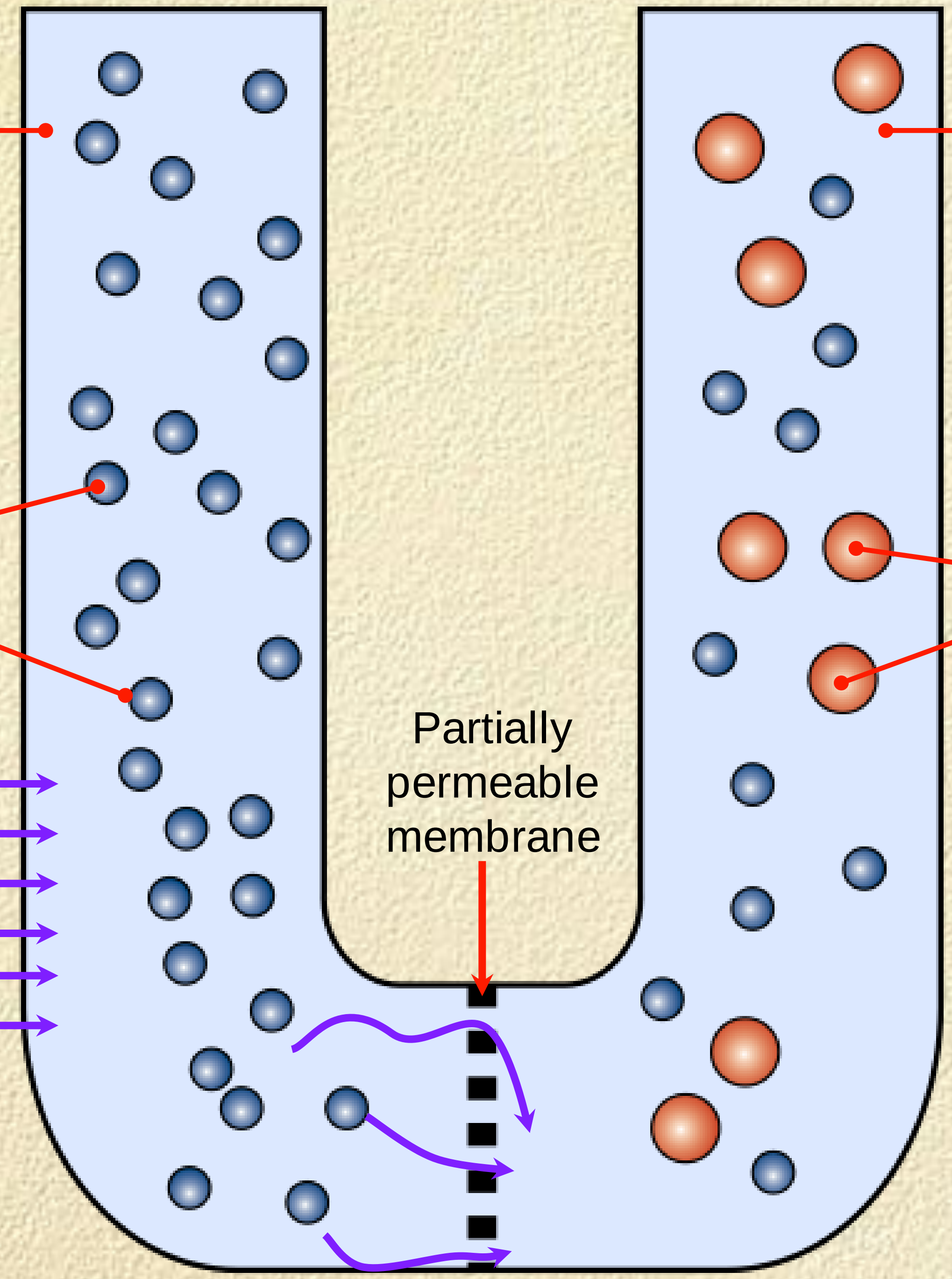
Osmosis & Water Potential

Less negative ψs
Less negative ψ
Hypotonic

Loses water by osmosis

More negative ψs
More negative ψ
Hypertonic

Gains water by osmosis



Water molecules

Solute molecules cannot pass through the partially permeable membrane

Pressure potential (ψp)

The hydrostatic pressure to which water is subjected (e.g. by a rigid plant cell wall). It is usually positive. It is sometimes called turgor or wall pressure.

Solute potential (ψs)

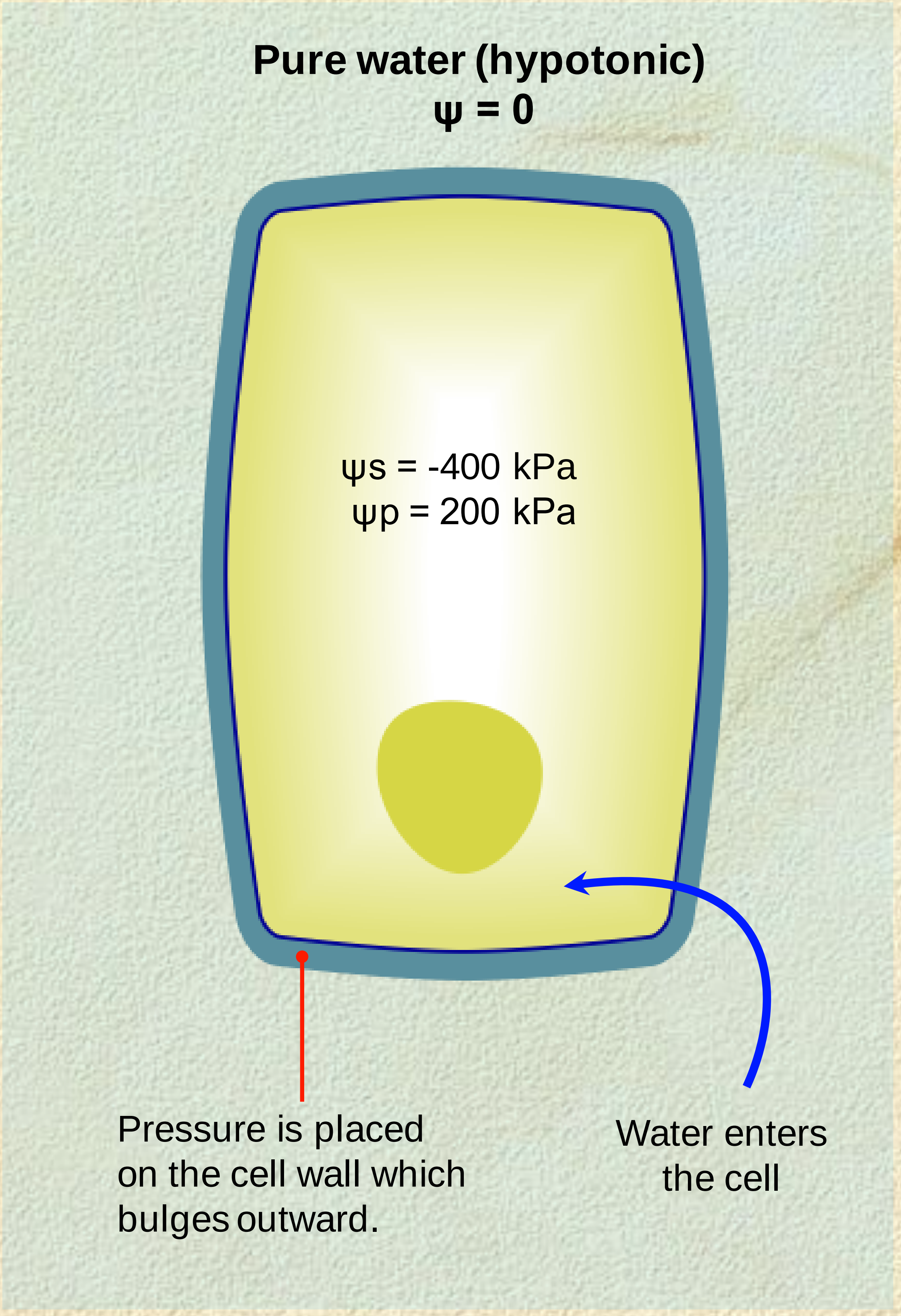
ψs measures the reduction in water potential due to the presence of solutes. It is **negative**. It is sometimes referred to as the osmotic potential or osmotic pressure.

There is a net movement of water molecules towards the more negative ψ until water concentrations equalize.

Turgor in Plant Cells

- If a plant cell is placed in a **hypotonic** solution, water enters the cell causing it to swell. The rigid cell wall prevents cell rupture.
- The cell contents press against the cell wall creating a wall pressure (Ψp) which rises progressively until it offsets Ψs. Water uptake stops when the $\Psi cell = 0$.
- Cells in this state are termed **turgid**.

Healthy turgor in *Coleus*



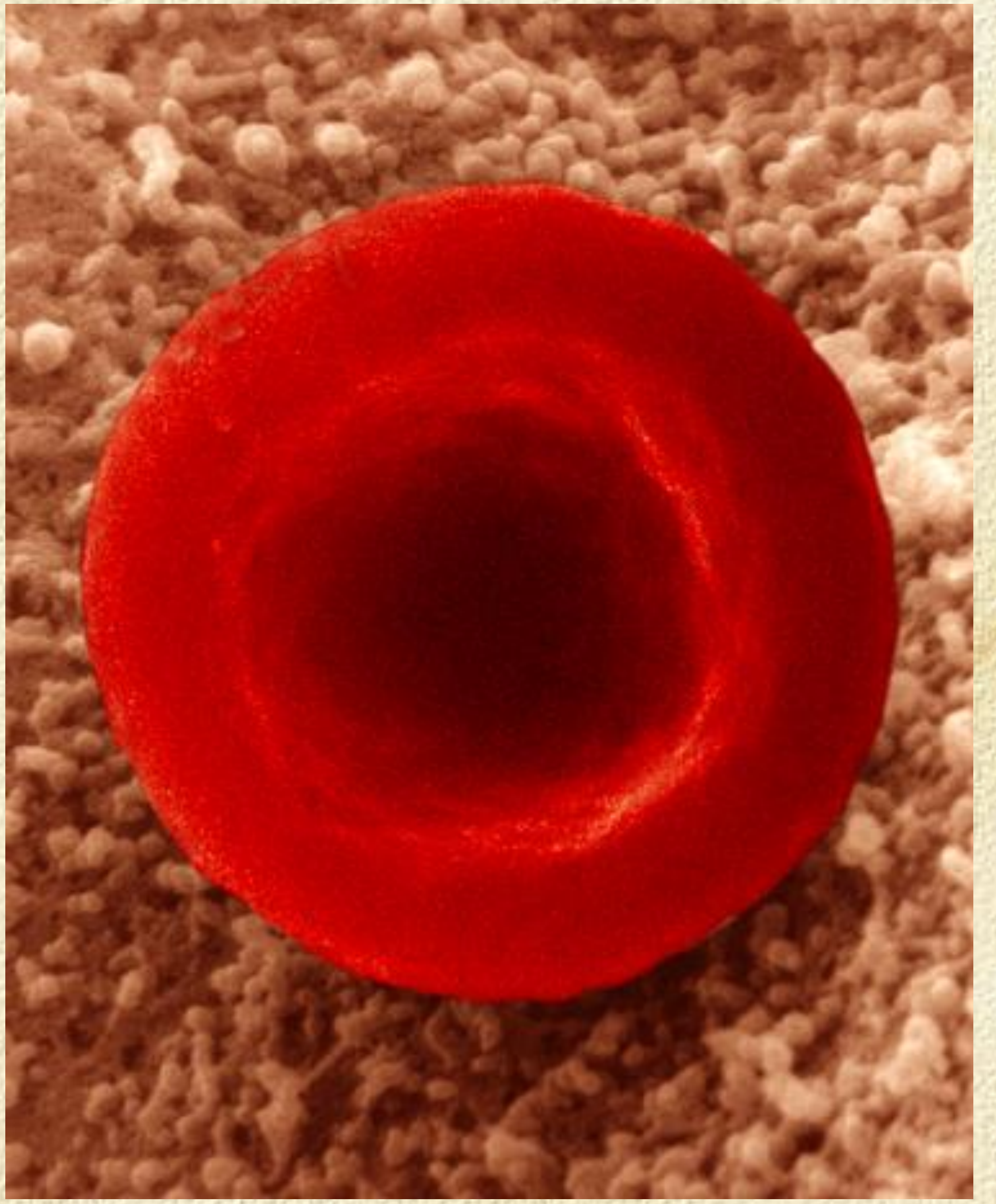
Plasmoylsis in Plant Cells

- If a plant cell is placed in a **hypertonic** solution, the plant cell loses water to the environment.
- The membrane shrinks away from the cell wall, the vacuole collapses, and the cell becomes **flaccid** (Ψp = 0).
- This state is called **plasmolysis.**
- Full plasmolysis is irreversible; the cell cannot recover by taking up water.

Wilting in *Coleus* induced by water loss from the cells.

Cellular Environments

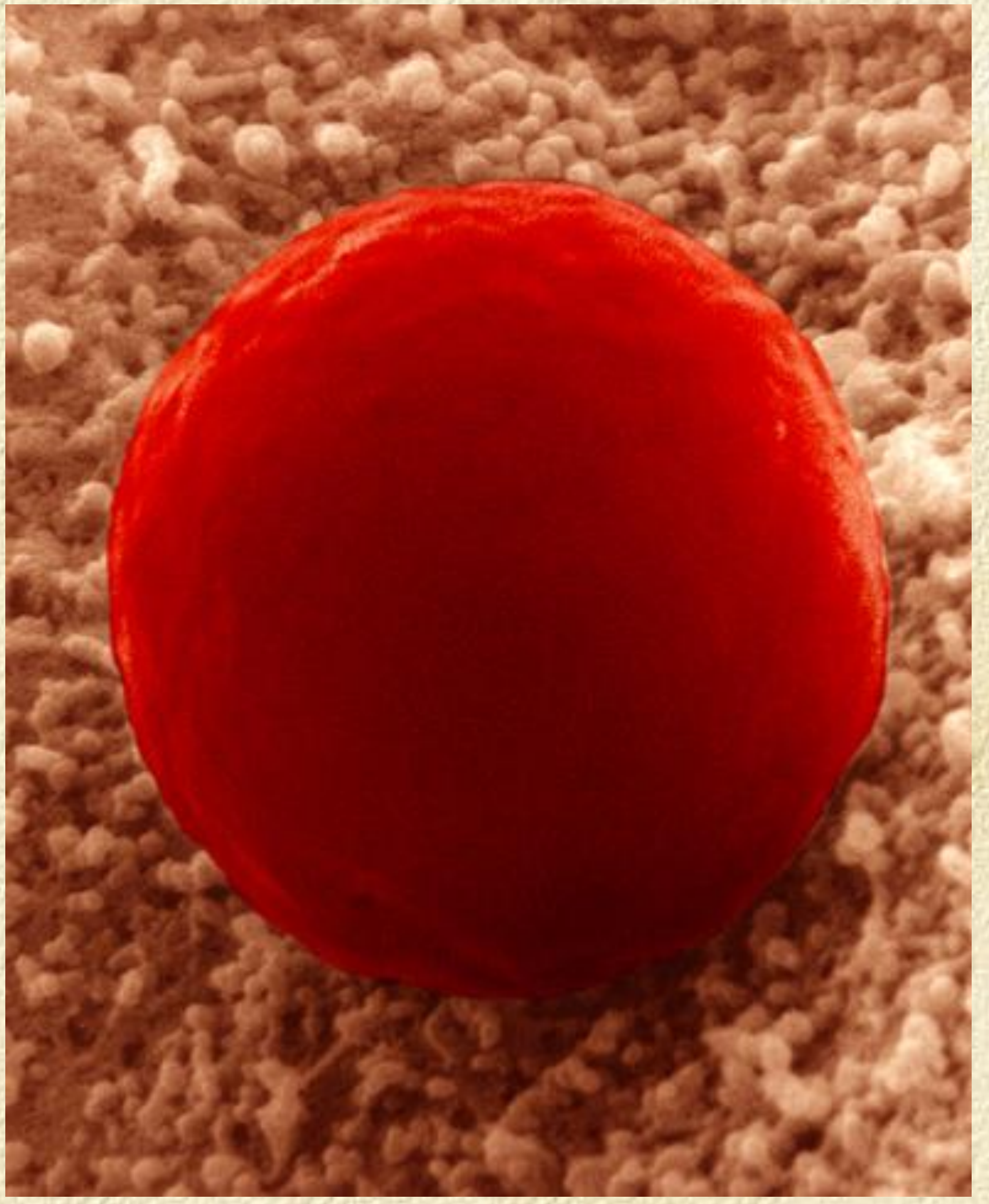
- Animal cells lack the cell wall that, in plants, contributes to pressure potential (Ψp).
- Without a rigid cell wall, animals cells may change shape depending upon the conditions of the cellular environment.
- Biologists often refer to these conditions as:
  - **Isotonic**
  - **Hypotonic**
  - **Hypertonic**
- When the extracellular environment has the same water potential (osmotic environment) as a cell, it is referred to as **isotonic**.
- Under these conditions, an animal cell maintains its **normal shape** and form.



In an **isotonic environment**, cells, such as the red blood cell above, maintain their **normal shape** as there is **no net water movement** across the plasma membrane.

Hypotonic Environment

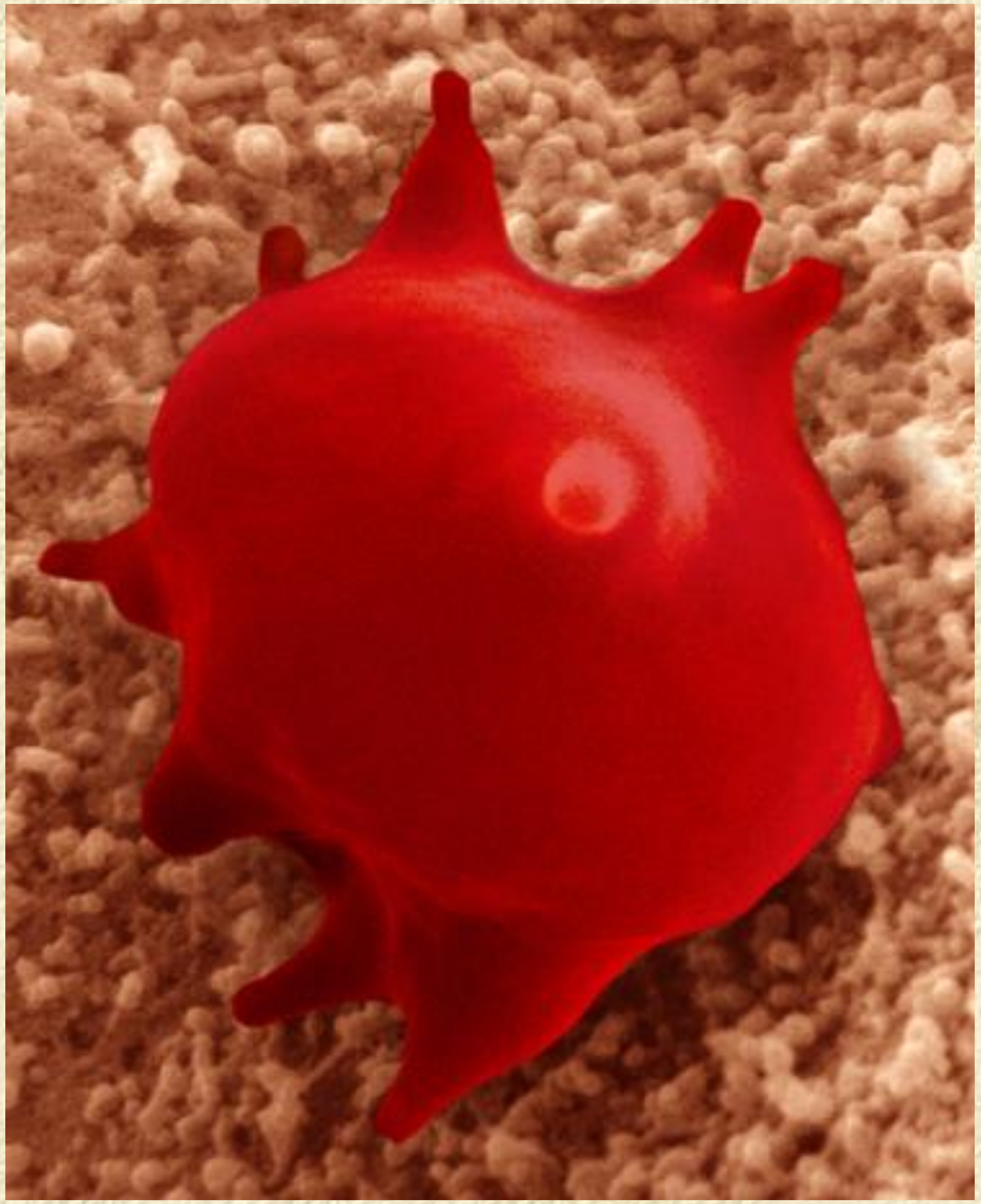
- When the water potential of the extracellular environment is less negative (lower solute concentration) than that of the cell, it is termed **hypotonic**.
- In a **hypotonic environment**, water will enter the cell because the cell cytoplasm has a higher solute concentration.
- In an animal cell (with no cell wall), this will eventually cause **cell lysis** (the cell will burst open).
- In cells surrounded by a **cell wall** (e.g. plant cells), the cell wall provides rigidity and a wall pressure to counteract the influx of water and prevent cell rupture.



In a **hypotonic environment**, cells **swell** because of a **net gain** of water across the plasma membrane. This red blood cell will eventually **burst** because its membrane cannot withstand the internal pressure.

Hypertonic Environment

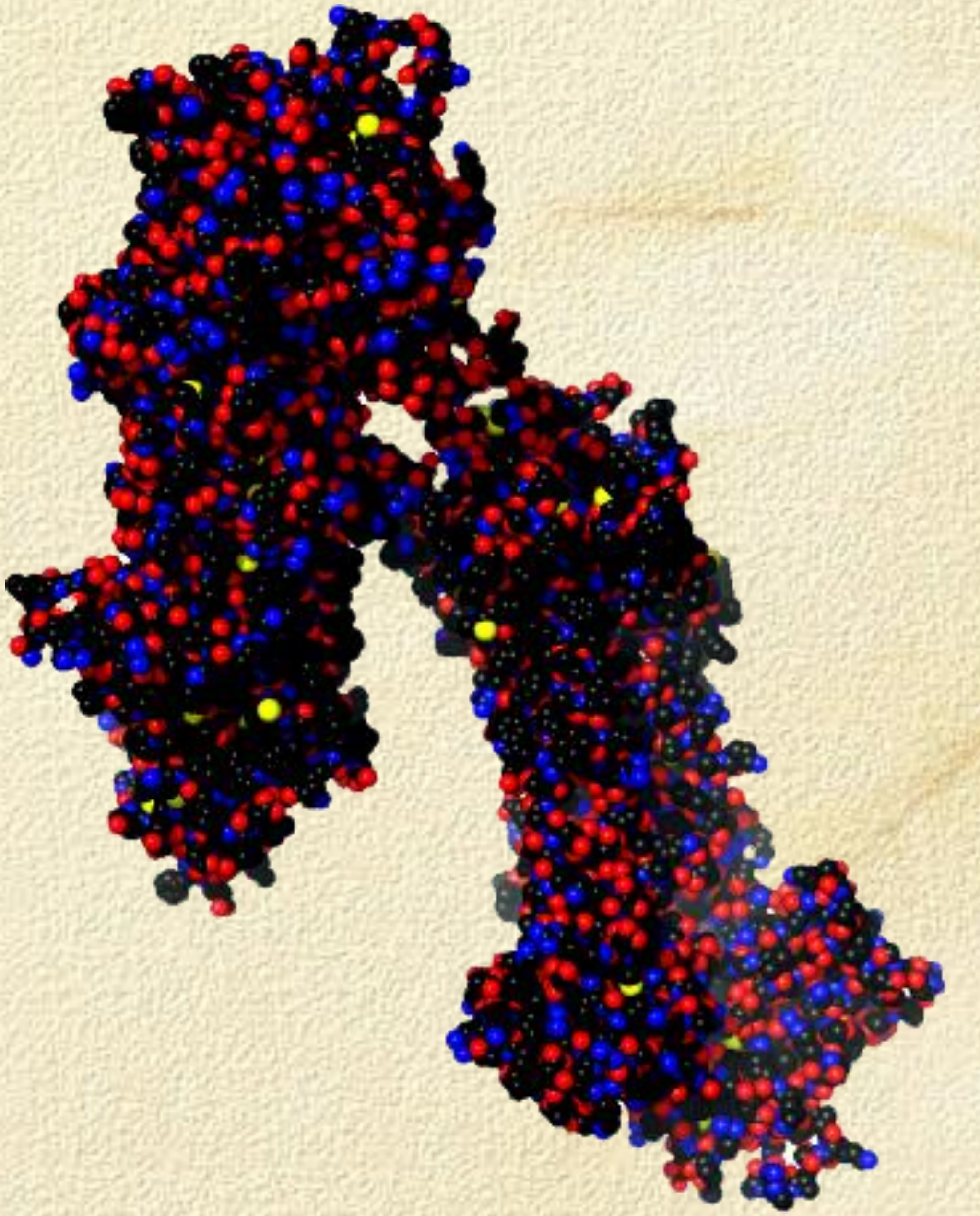
- When the water potential of the extracellular environment is more negative (higher solute concentration) than that of the cell,
  it is termed **hypertonic**.
- In a **hypertonic environment**, the cell will lose water because the cellular environment has a higher solute concentration.
  - The term for this process in animal cells is **crenation** (*alt.* crenulation).
  - In plant cells, the process is termed **plasmolysis**.
  - A cell can lose its ability to function if it becomes too severely dehydrated.



In a **hypertonic environment**, cells **shrink** because of a **net loss** of water across the plasma membrane. This red blood cell has lost its normal shape and form and is termed crenate.

Active Transport Processes

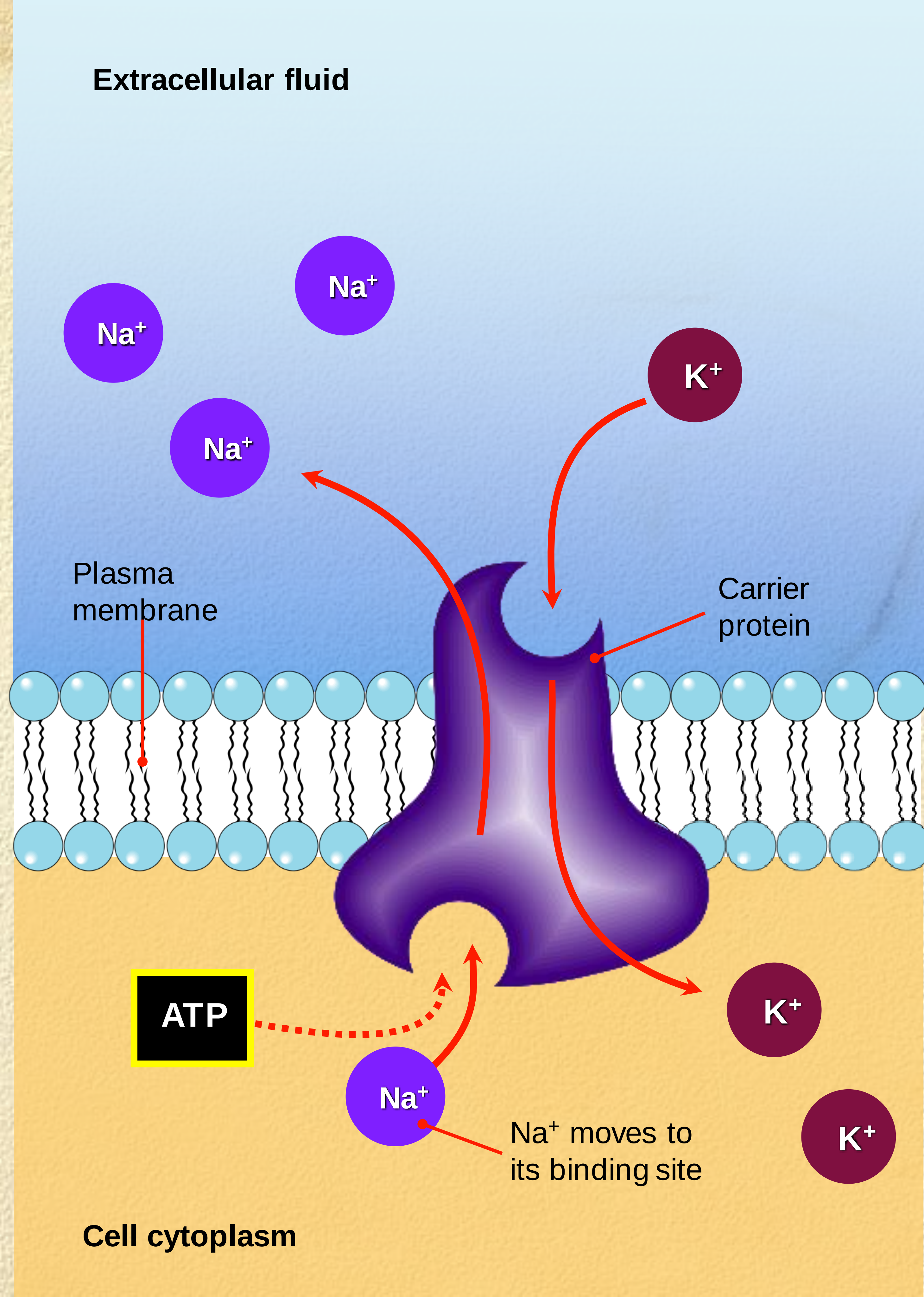
- **Active transport** processes require **energy expenditure** because materials must be moved **against their concentration gradient**.
- Active transport is performed by specific **carrier proteins** in the membrane.
- Transport proteins harness the energy of **ATP** to pump molecules from a low concentration to a high concentration (the reverse of diffusion).
  - When ATP transfers a phosphate group to the carrier protein, the protein changes its shape so that the bound molecule can move across the membrane.



Space filling model of rabbit calcium ATPase. Calcium ATPase is a membrane transport protein which transfers calcium after a muscle has contracted.

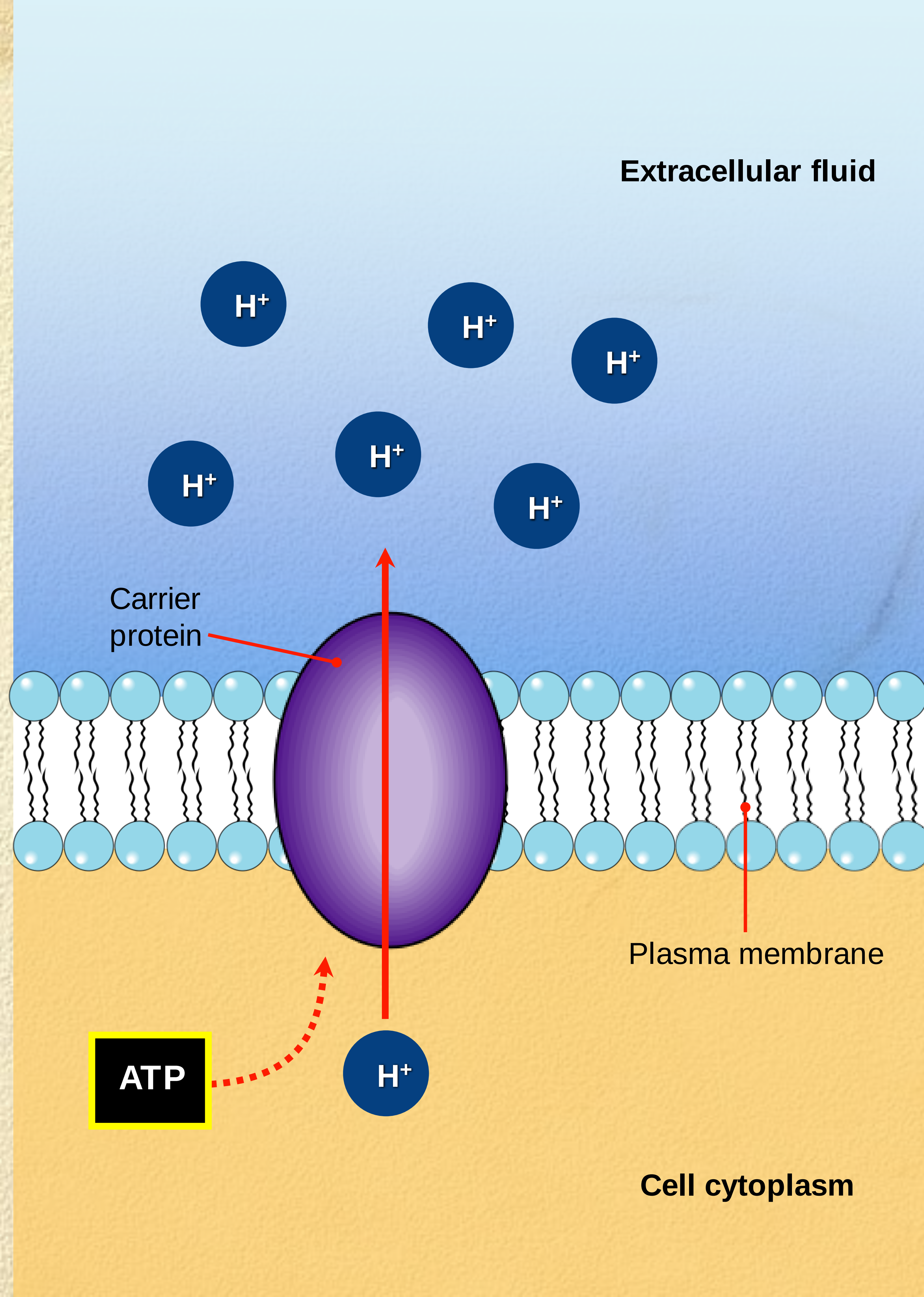
Sodium-Potassium Pumps

- The **sodium-potassium pump** is a protein in the membrane that exchanges sodium ions (Na^+) for potassium ions (K^+) across the membrane.
- ATP is used as the energy source for the exchange.
- The unequal balance of Na^+ and K^+ across the membrane creates large gradients in ion concentration, which can be used to drive other active transport mechanisms.



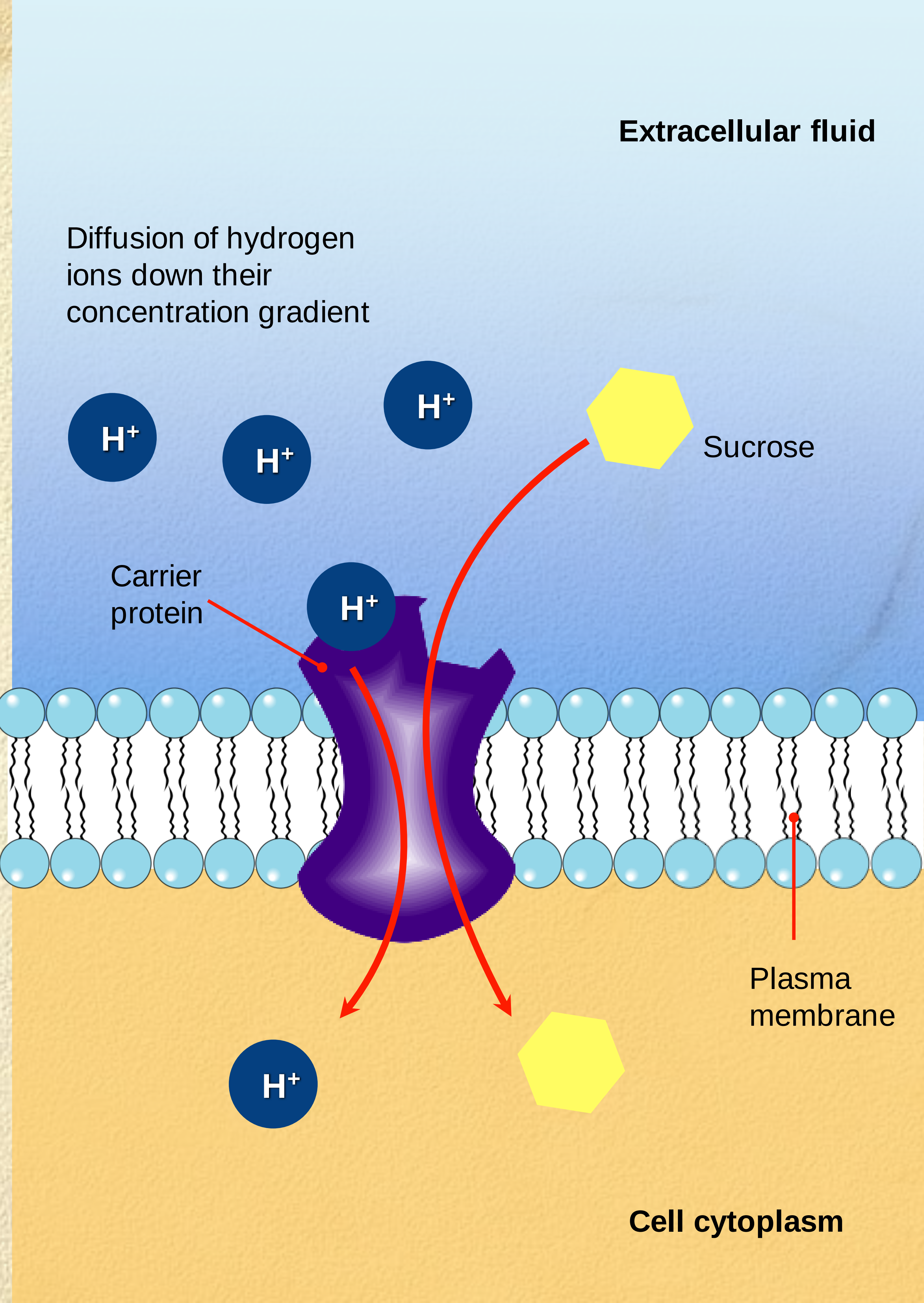
Proton Pumps

- **Proton pumps** use the energy from ATP to move **hydrogen ions** (H^+) from inside the cell to the outside.
- This creates a large difference in the proton concentration either side of the membrane, leaving the inside of the plasma membrane negatively charged.
- The **potential difference** created can be coupled to transport other molecules across the membrane.



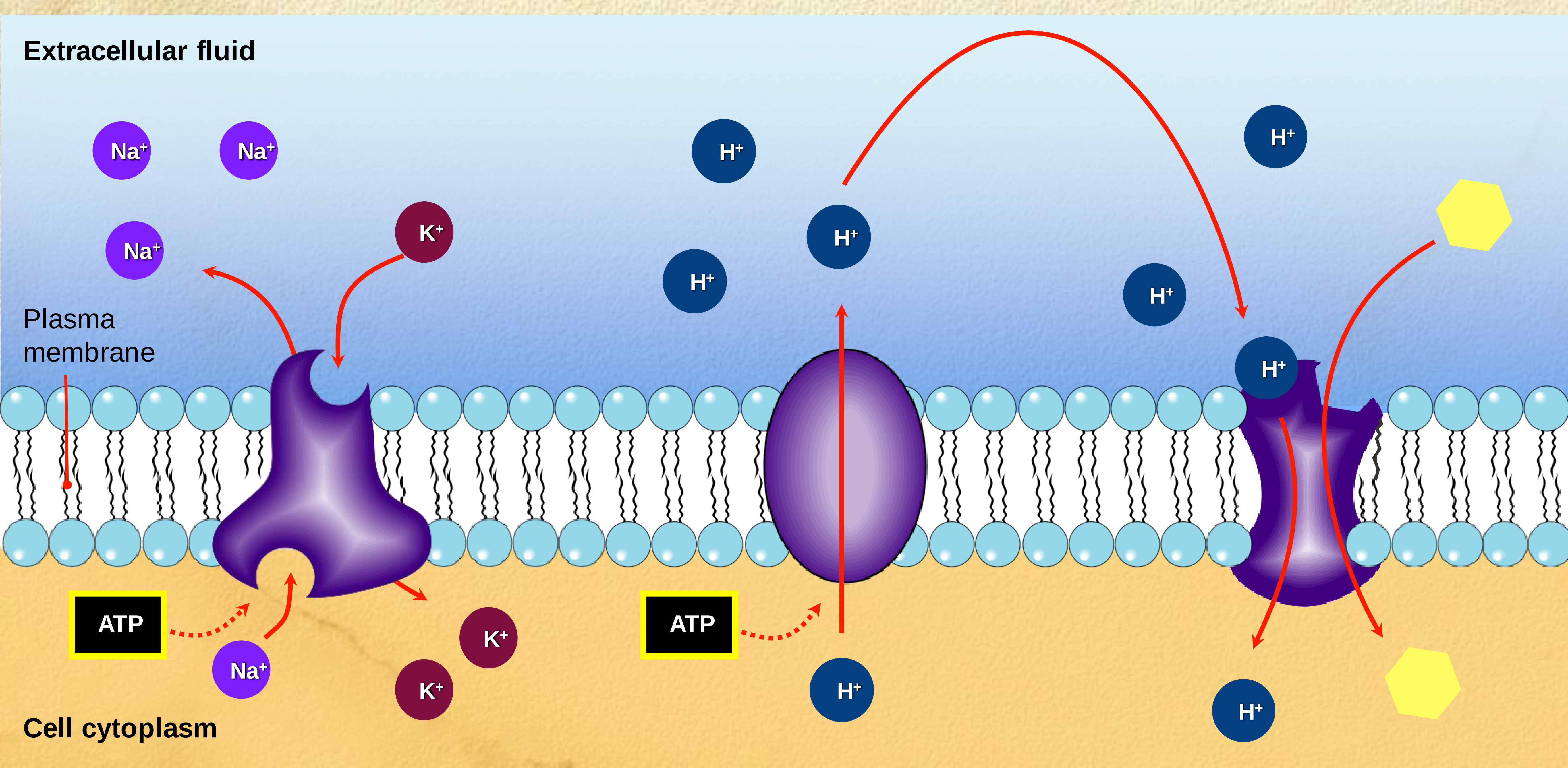
Coupled Transport

- **Coupled transport** is also called **co-transport**.
  - Plant cells use the hydrogen gradient created by proton pumps to actively transport nutrients into the cell.
  - For example, the return of H^+ is coupled to the transport of sucrose into the phloem cells. The sucrose rides with the H^+ as it diffuses down the concentration gradient maintained by the proton pump.



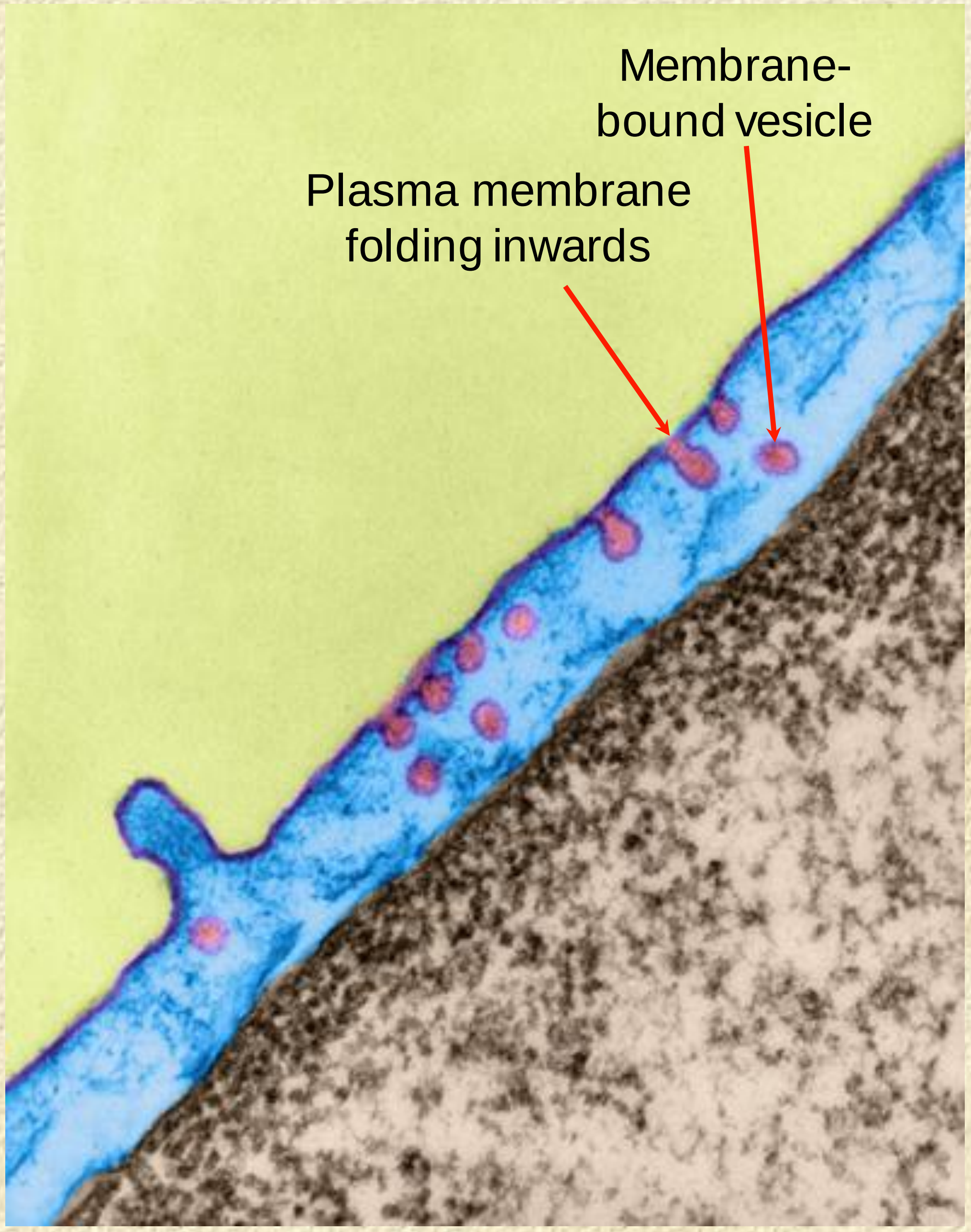
Summary-Membrane Pumps

- Membrane pumps are proteins,which require energy (often as ATP) to transport molecules across the cell membrane.
- The activity of pumps may be coupled, e.g. the accumulation of H^+ from the proton pump is used to drive the transport of sucrose against its concentration gradient.



Active Transport: Cytosis

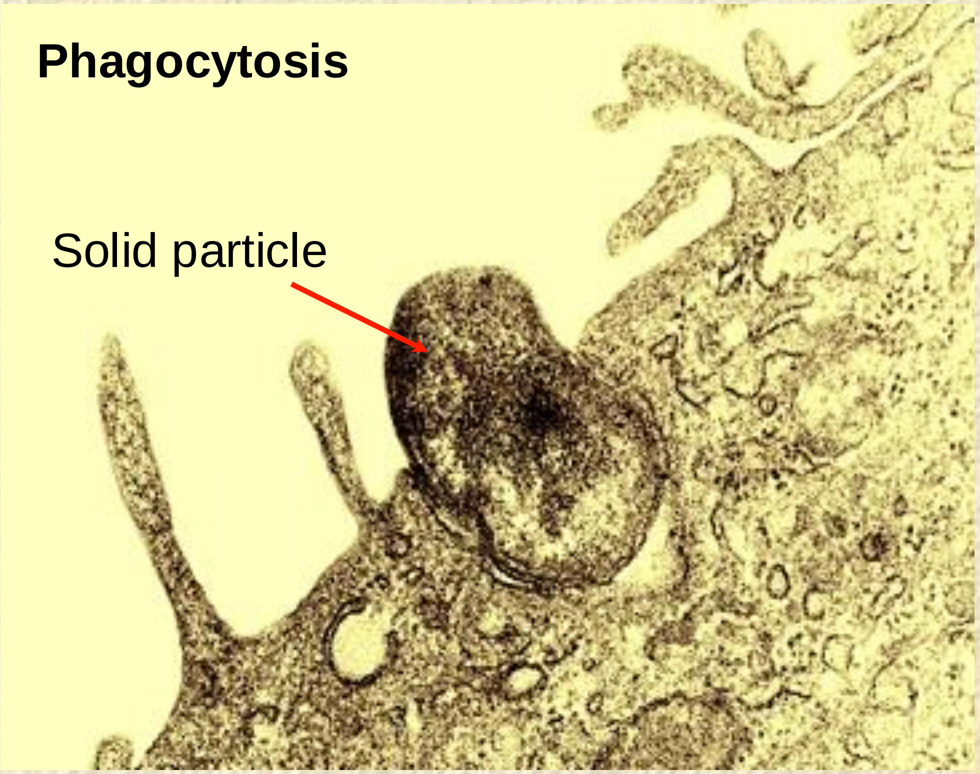
- **Cytosis** is a form of **active transport** involving the formation of membrane-bound vesicles or vacuoles.
- Regions of the plasma membrane become infolded (invagination) or outfolded (evaginated) to transport substances across the membrane.
- Cells are able to do this because of the mobile nature of the membrane.
- Most cells carry out various forms of cytosis, including:
  - **endocytosis**
  - **exocytotosis**



This cell is carrying out a form of **endocytosis** called pinocytosis in which the plasma membrane forms **invaginations** to enclose liquids and bring them into the cell.

Endocytosis

- **Endocytosis** describes the incorporation of substances from outside the cell into the cell as a membrane-bound vesicle or vacuole.
- During endocytosis the plasma membrane **invaginates** (folds in) around the molecules to be transported into the cell.
- There are three forms of endocytosis:
  - **phagocytosis**: the engulfment of solid particles.
  - **pinocytosis**: the engulfment of liquid particles.
  - **receptor mediated**: engulfment of specific particles according to membrane receptors.



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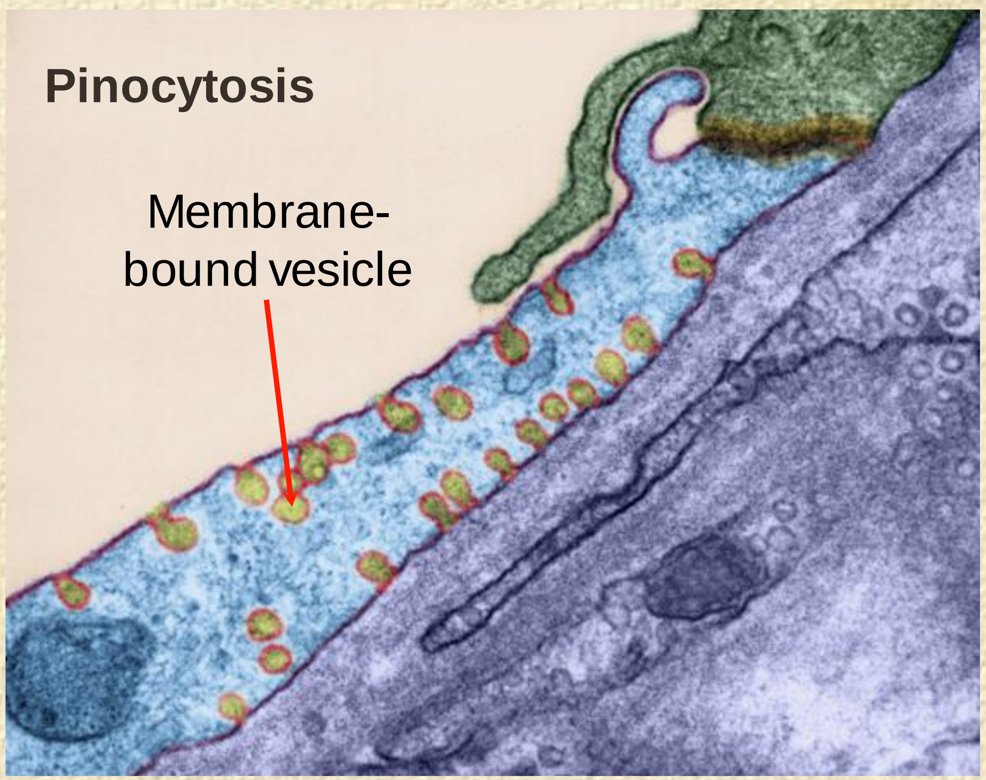
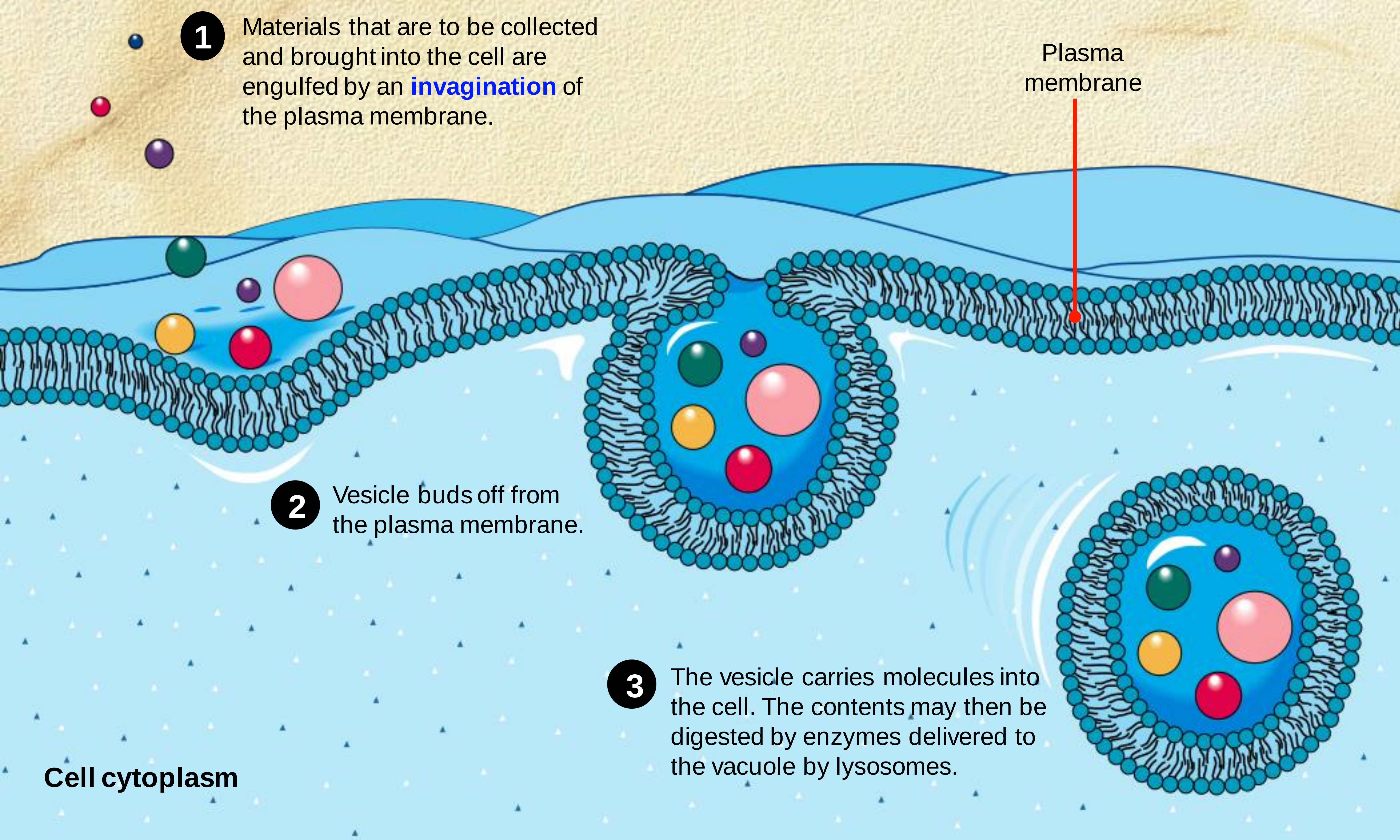
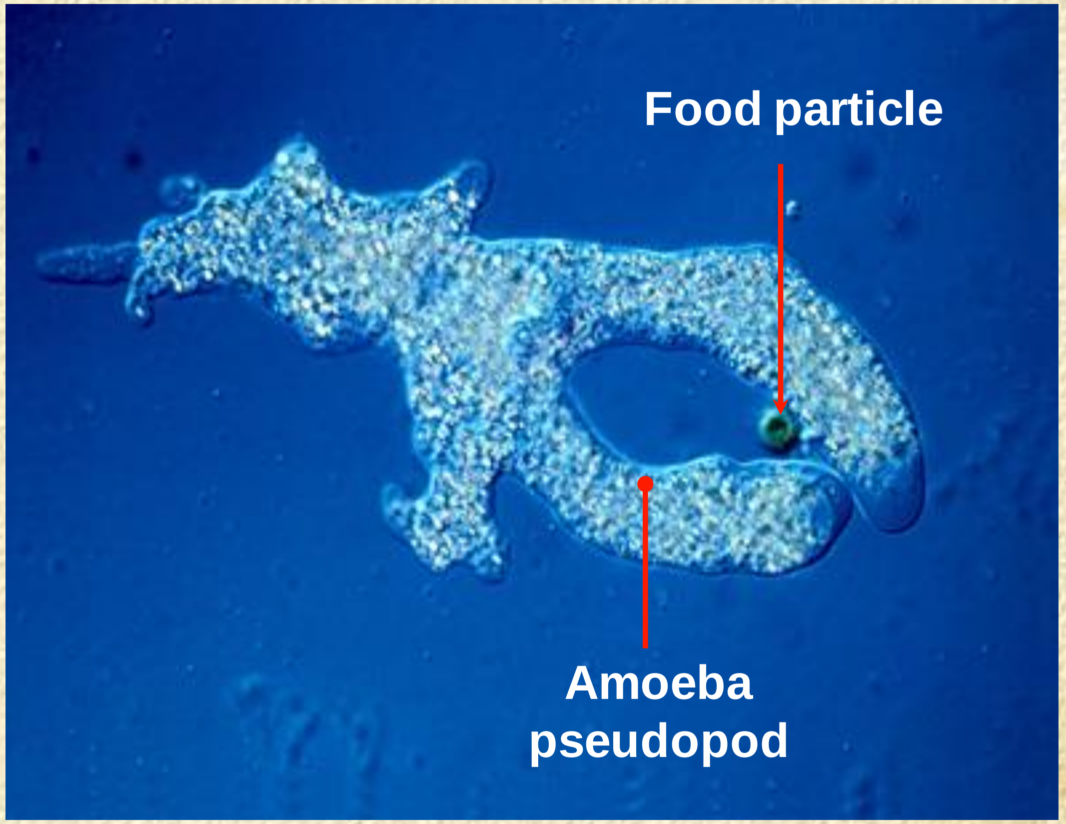


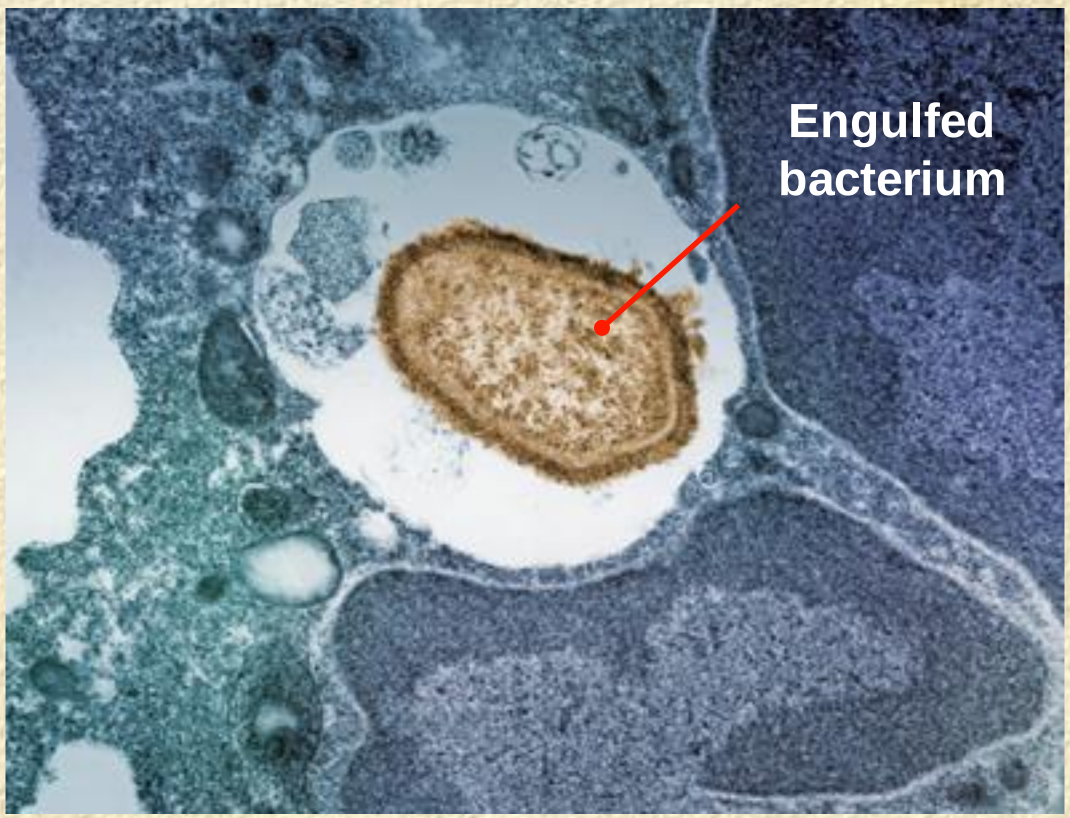
Endocytosis



Endocytosis: Phagocytosis

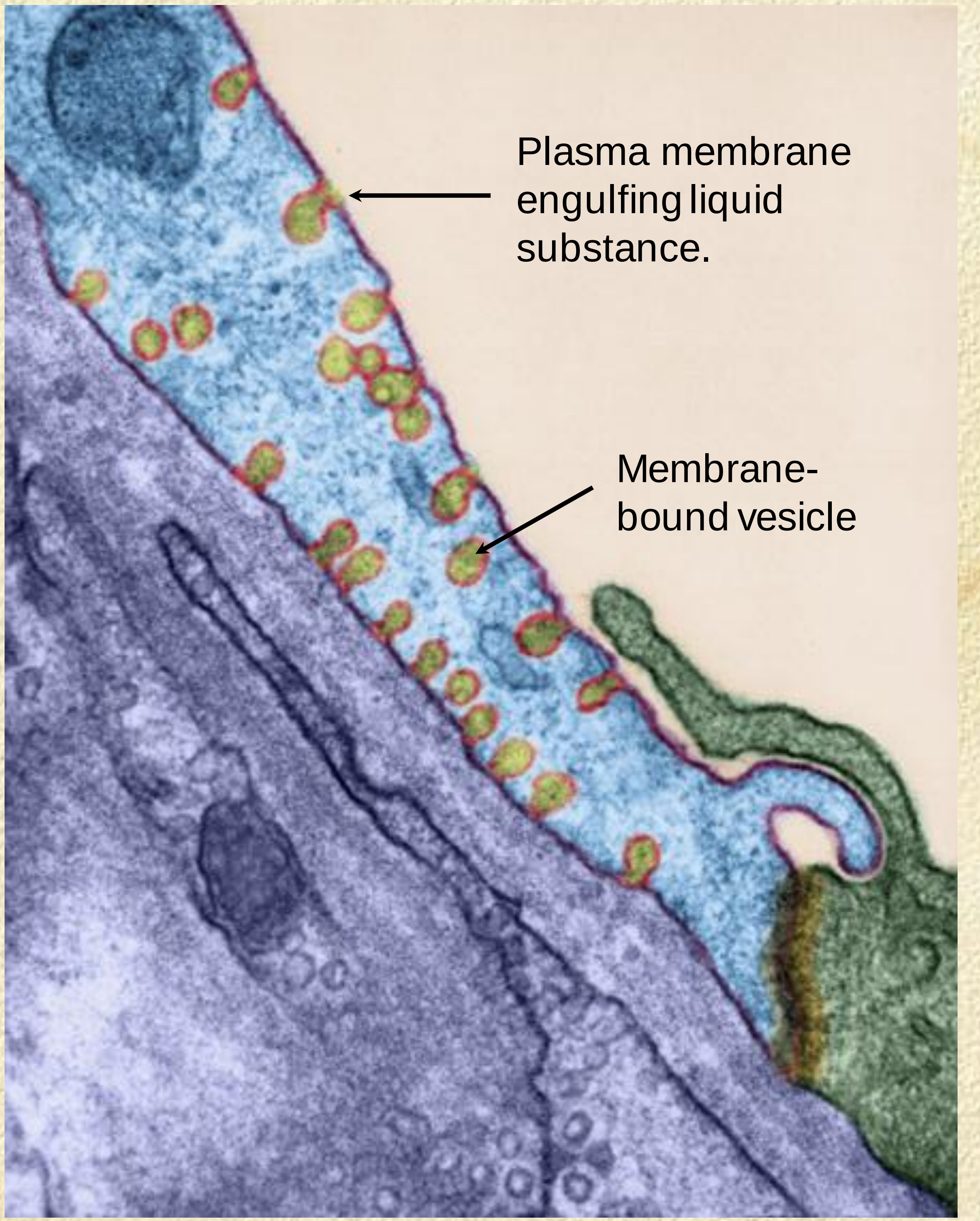
- **Phagocytosis** (literally cell eating) describes the engulfment and transport of **solid particles** into the cell.
  - The particles are contained within a membrane enclosed sac (a **vacuole**).
  - Digestion of the particles occur when the vacuole fuses with a lysosome containing digestive enzymes.
- **Amoebae** use phagocytosis to capture and ingest their food (top right).
- In humans, **white blood cells**, such as neutrophils and macrophages, use phagocytosis to clean up cell debris and foreign material such as bacteria.
  - The macrophage (right) has engulfed a *Staphylococcus* bacterium.





Endocytosis: Pinocytosis

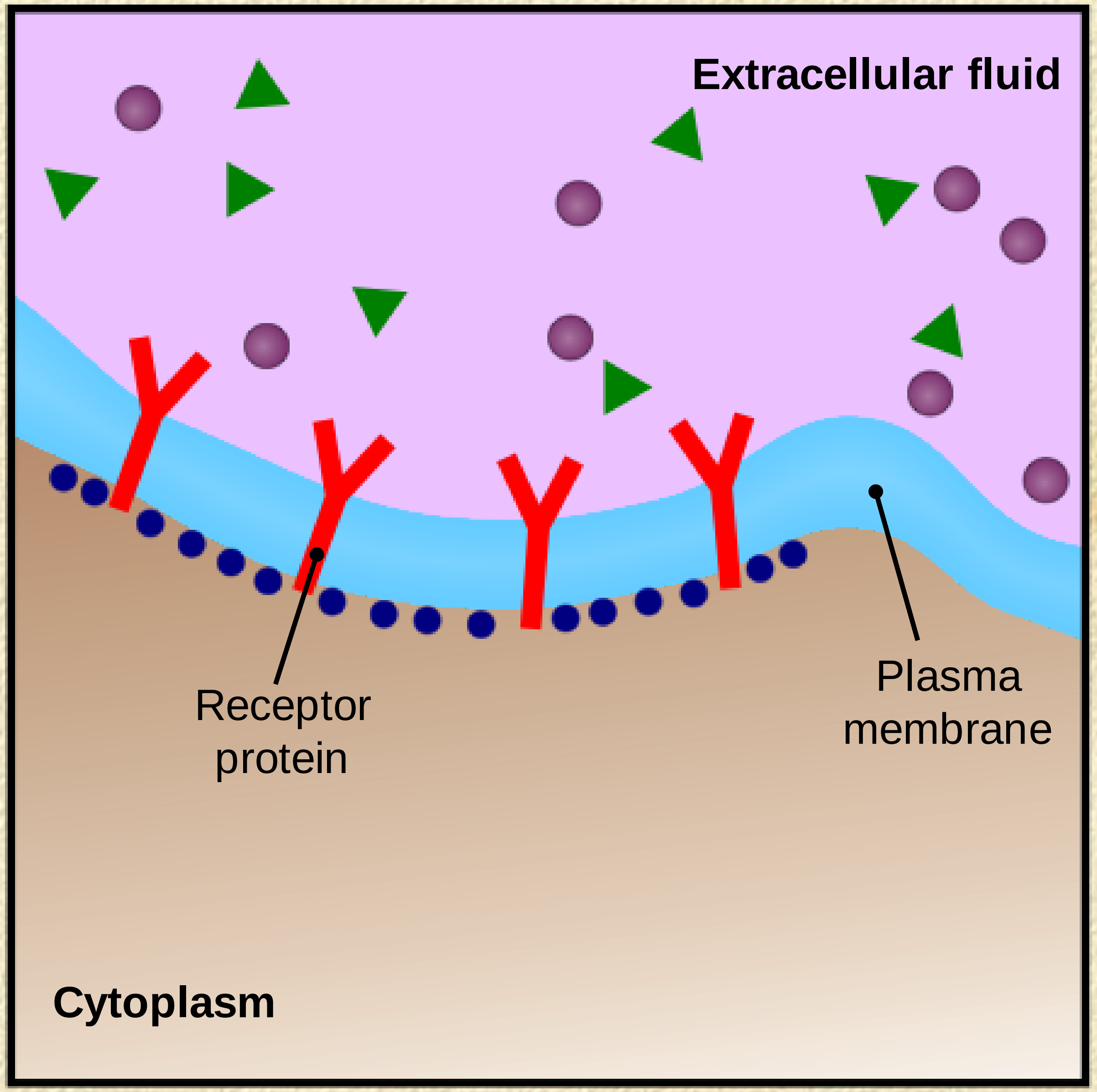
- **Pinocytosis** describes the engulfment of **liquids** or fine liquid suspensions into the cell.
  - Invaginations of the plasma membrane enclose the liquid droplets within small vesicles.
  - The fluid within the vesicle is transferred to the cytosol.
- Pinocytosis is a **non-specific** form of endocytosis.
  - Whatever solutes are suspended within the watery medium are also taken into the cell.



Pinocytosis by a capillary endothelial cell. TEM (X12,880)

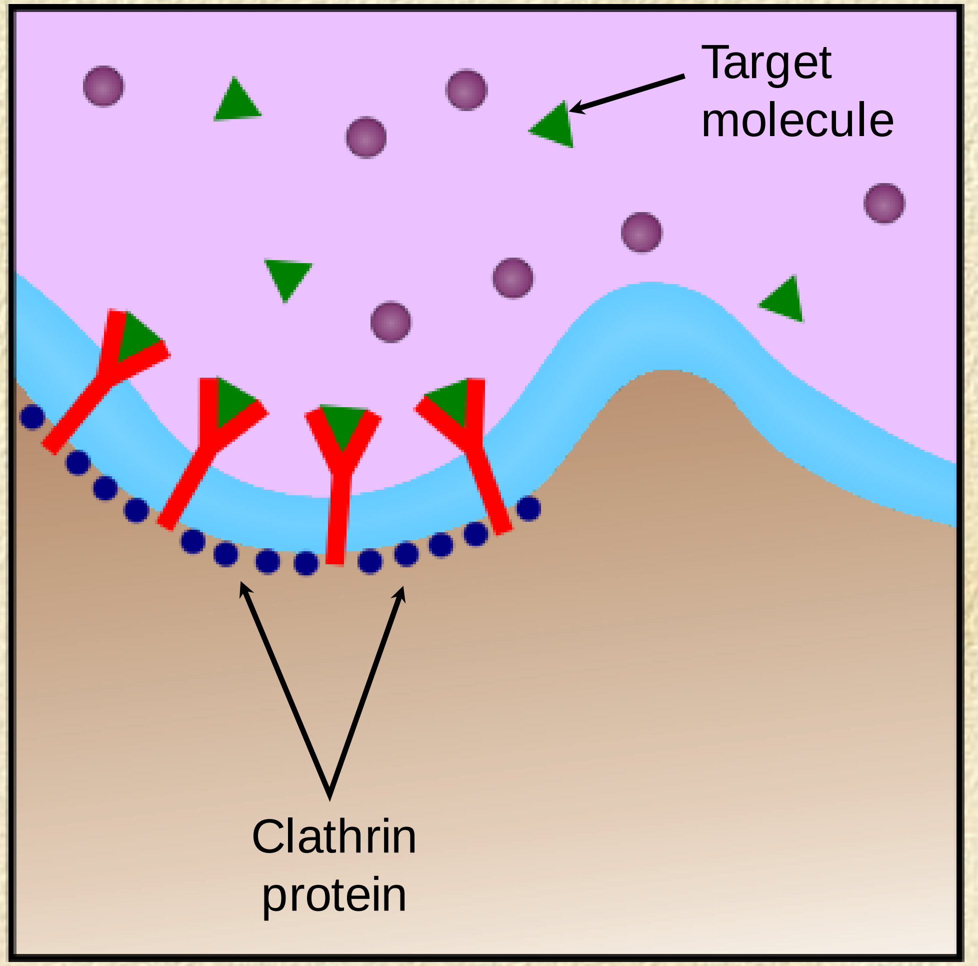
Receptor-Mediated Endocytosis

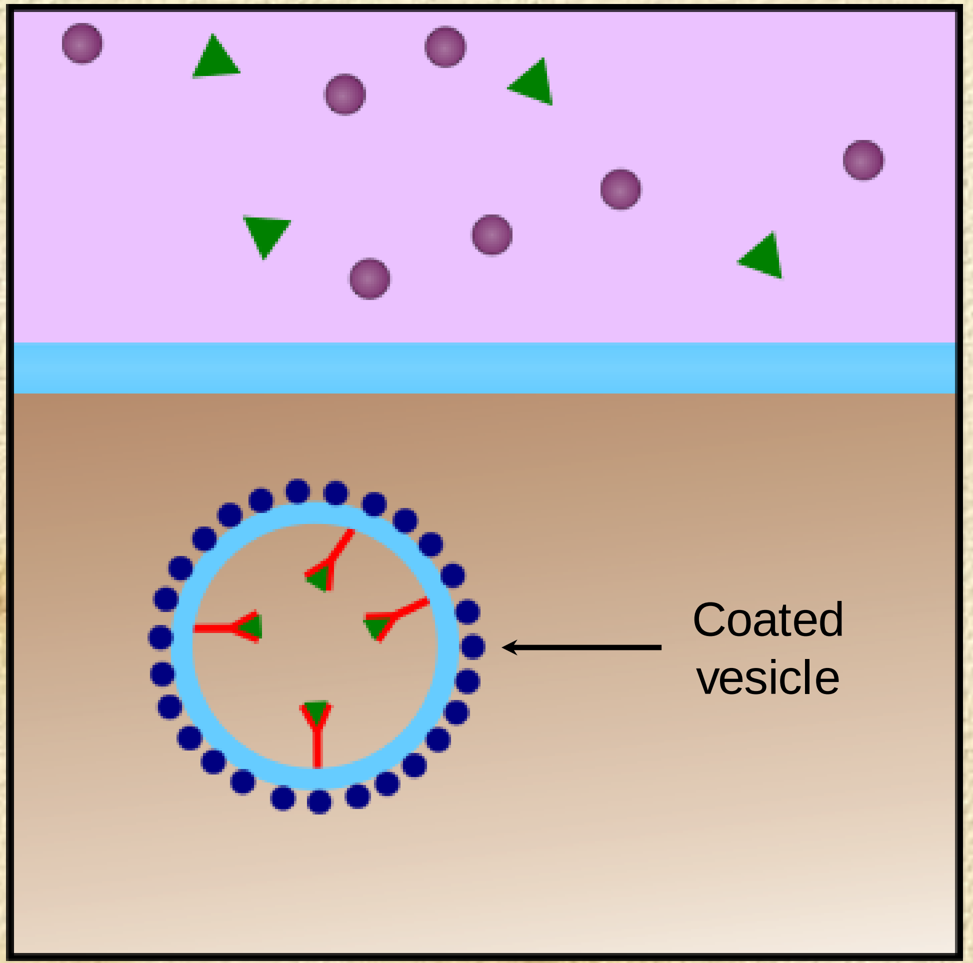
- Unlike the other forms of endocytosis, **receptor mediated endocytosis** involves the engulfment and transport of **specific molecules** into the cell.
- The cell membrane has regions of **receptor proteins** exposed to the extracellular environment.
- The receptor proteins occur in clusters (called **coated pits**) and have binding sites that will only bind specific molecules.



Receptor-Mediated Endocytosis

The cytoplasmic side of the coated pit is lined with a special protein called **clathrin protein**, which provides membrane stability (right).

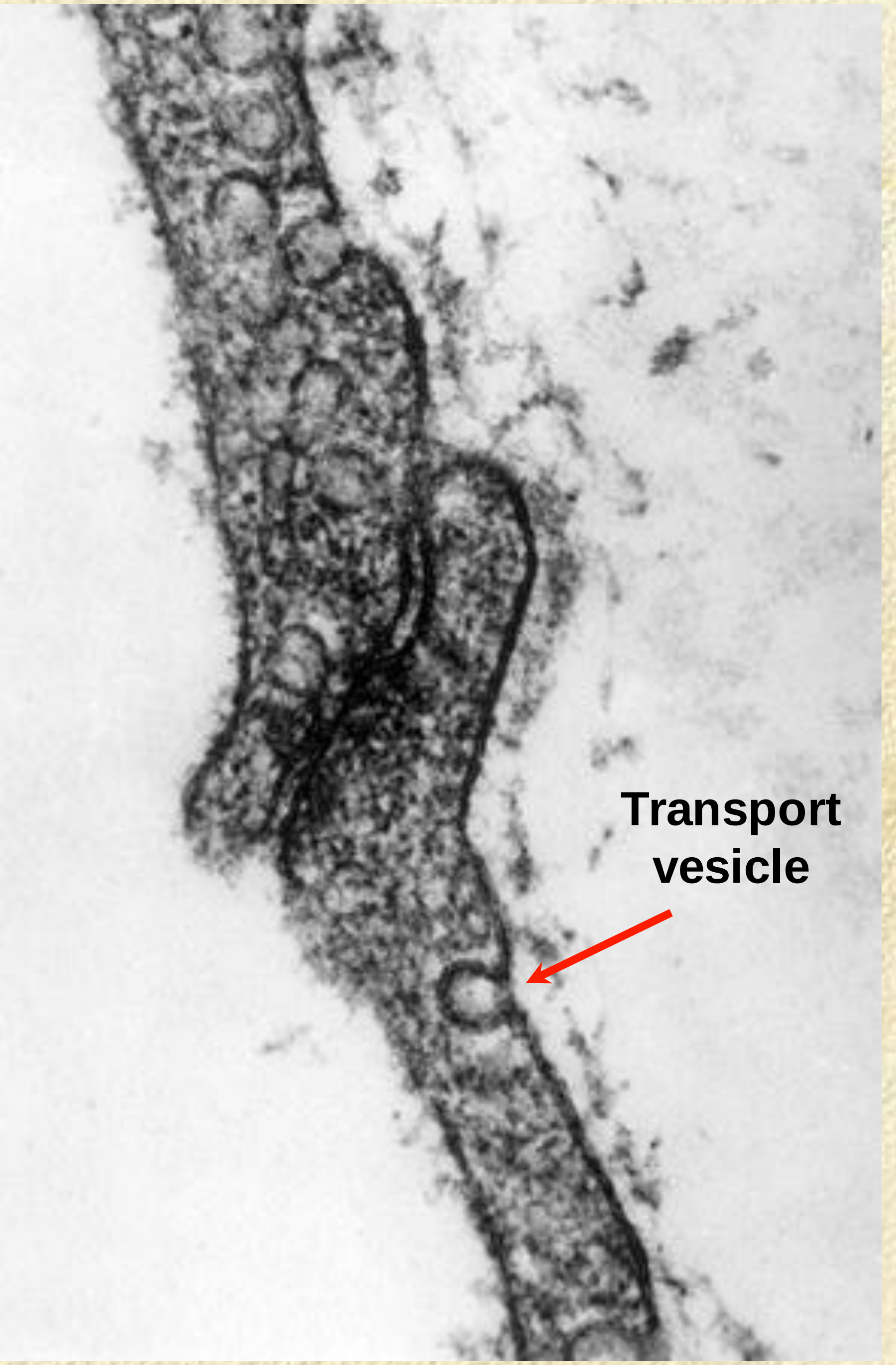




When the target molecule (**ligand**) binds to the receptor protein (left), a **coated vesicle** forms around it, allowing the molecule to be imported into the cell.

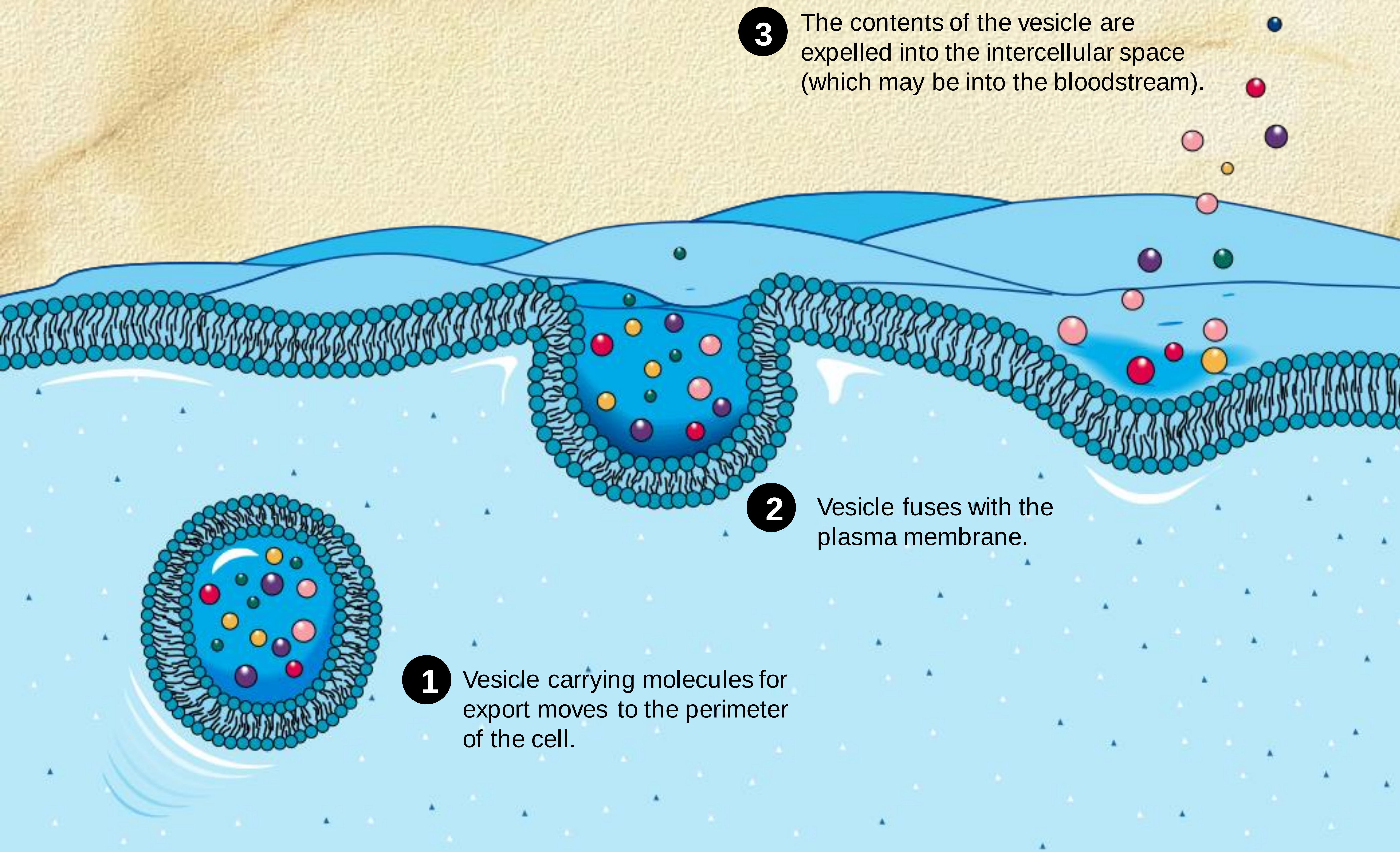
Exocytosis

- **Exocytosis** releases substances from the inside of the cell to outside of the cell.
- Exocytosis occurs by fusion of a vesicle membrane with the plasma membrane. The vesicle contents are then released to the outside of the cell.
- In multicellular organisms, various types of cells are specialized to manufacture and export products from the cell to elsewhere in the body or outside it.



Cross section through the plasma membrane of cardiac muscle showing the presence of **transport vesicles**. TEM X 162,000

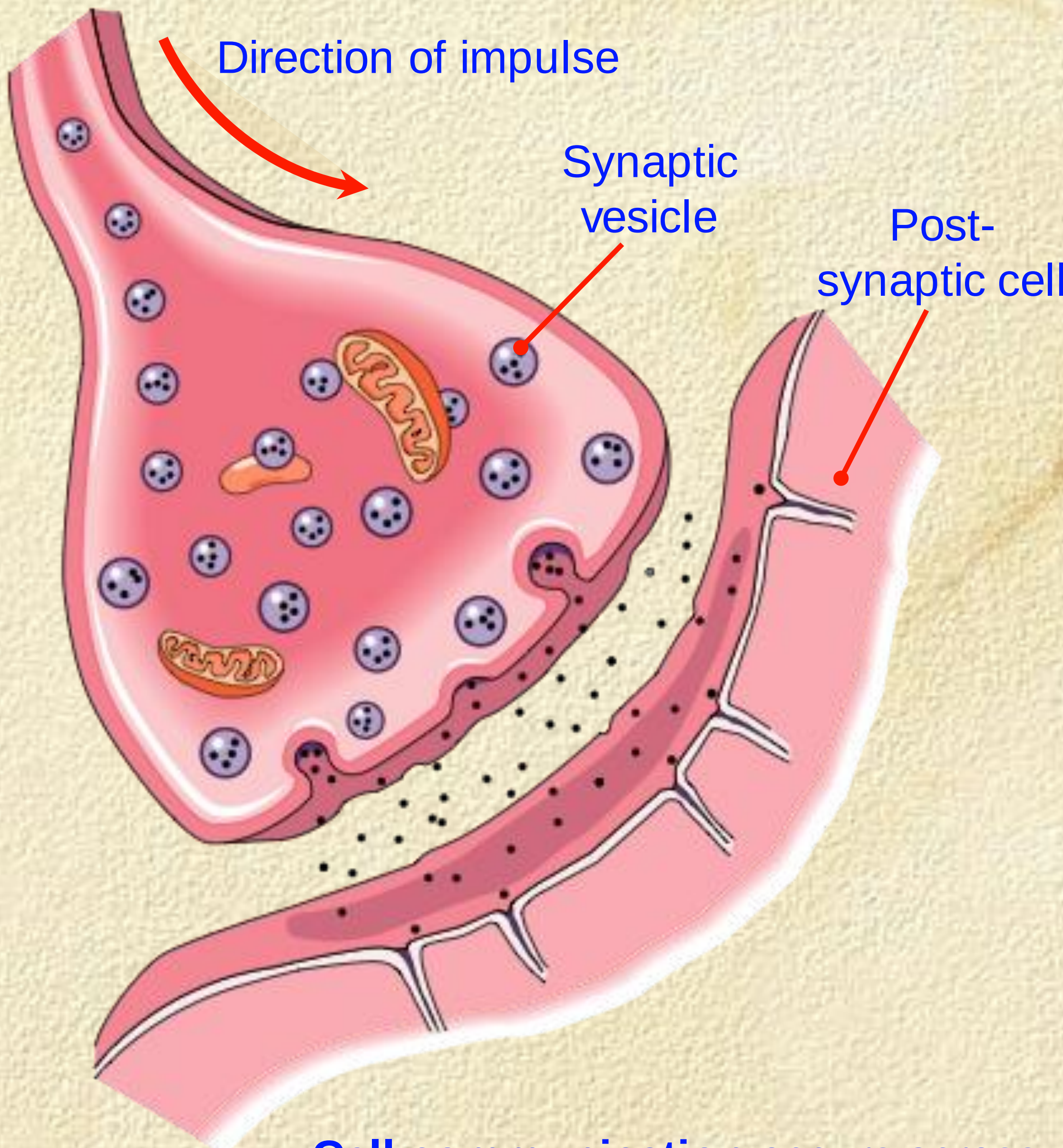
Exocytosis



3 The contents of the vesicle are expelled into the intercellular space (which may be into the bloodstream).
2 Vesicle fuses with the plasma membrane.
1 Vesicle carrying molecules for export moves to the perimeter of the cell.

Cell Communication and Recognition

- Cells have a means of communication and recognition which allows them to:
  - **form tissues** with cells of the same or a related type.
  - **detect foreign cells** and launch an immune response.
- Special **signaling proteins** in the plasma membrane act as:
  - **receptor molecules** for hormones and neurotransmitters
  - **identity markers**
- Signaling proteins are often **glycoproteins**.



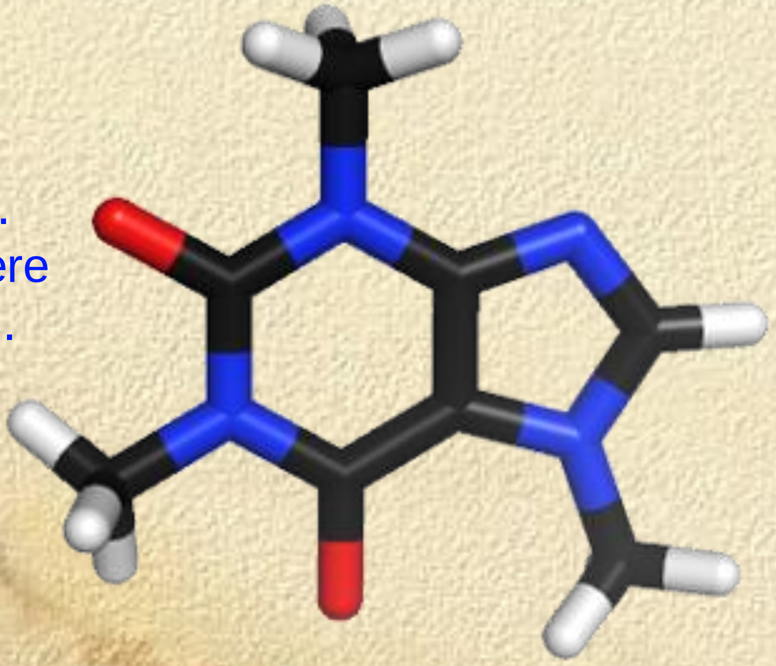
Cell communication occurs across **synapses**. Electrical impulses result in neurotransmitter transfer between cells. The neurotransmitter produces a response in the post-synaptic cell.

Cell Signaling

- Cells use **signaling molecules** (chemical messengers) to:
  - gather information about the environment
  - respond to changes in their environment
  - **communicate** with other cells
- The signaling and response process is called the **signal transduction pathway**.
  - It often involves a number of enzymes and molecules in a **signal cascade** that results in a large response in the target cell.

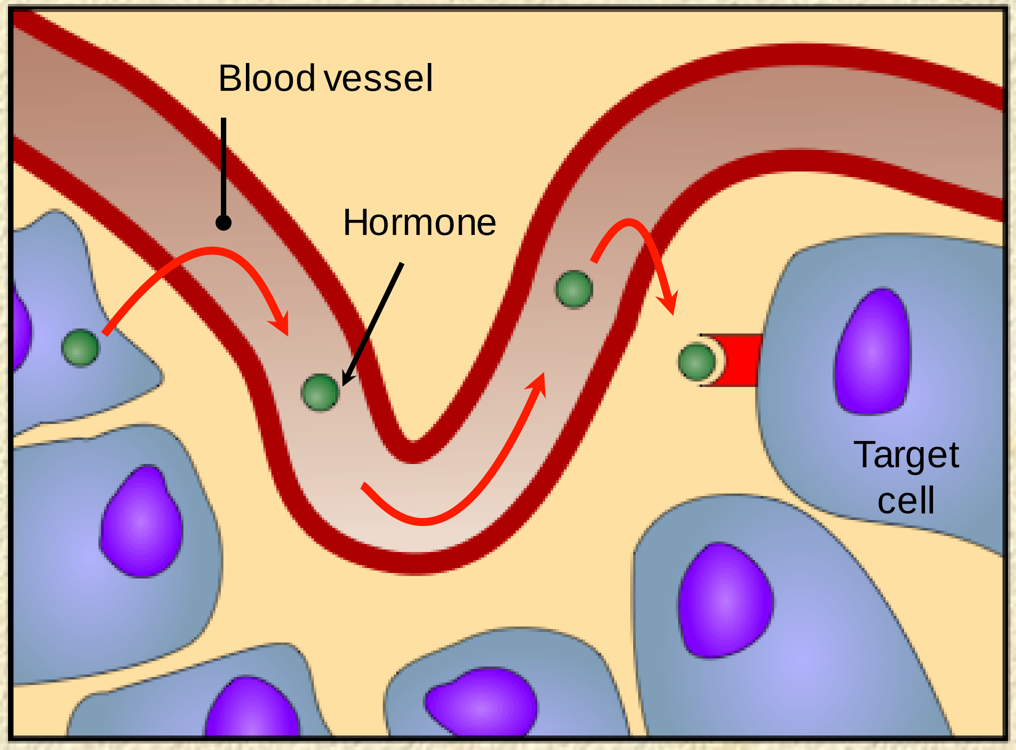
The **caffeine** contained in this cup of coffee acts as a **chemical signal**, stimulating the central nervous system. It will temporarily reduce physical fatigue and increase mental alertness in the user.

Caffeine is a metabolic stimulant. It is represented here as a 3D stick model.

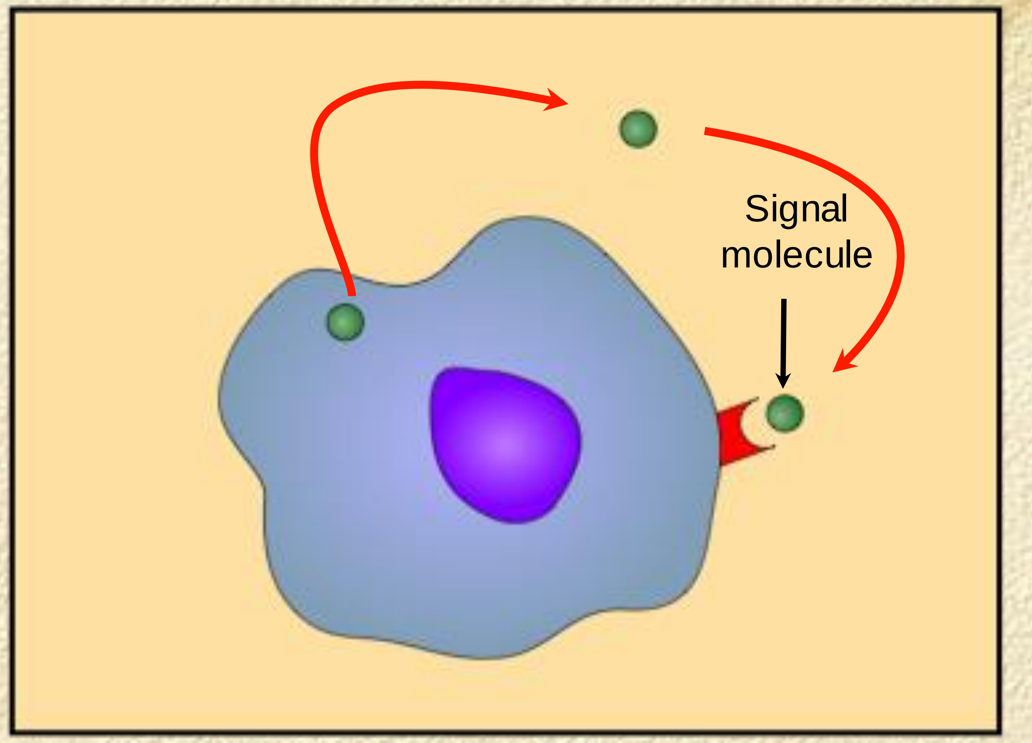


Types of Cell Signaling

- There are three main pathways by which cell signaling occurs:
  - the **endocrine** pathway
  - the **paracrine** pathway
  - the **autocrine** pathway
- Cell signaling pathways are categorized primarily on the distance over which the signal molecule is transmitted.
  - In the **endocrine pathway** (top right), the signals are hormones, released by endocrine glands. They travel via the circulatory system to target cells and tissues.
  - The **autocrine pathway** involves a cell producing, and reacting to, its own signal. This pathway is seen in the T cell response to infection (below right).



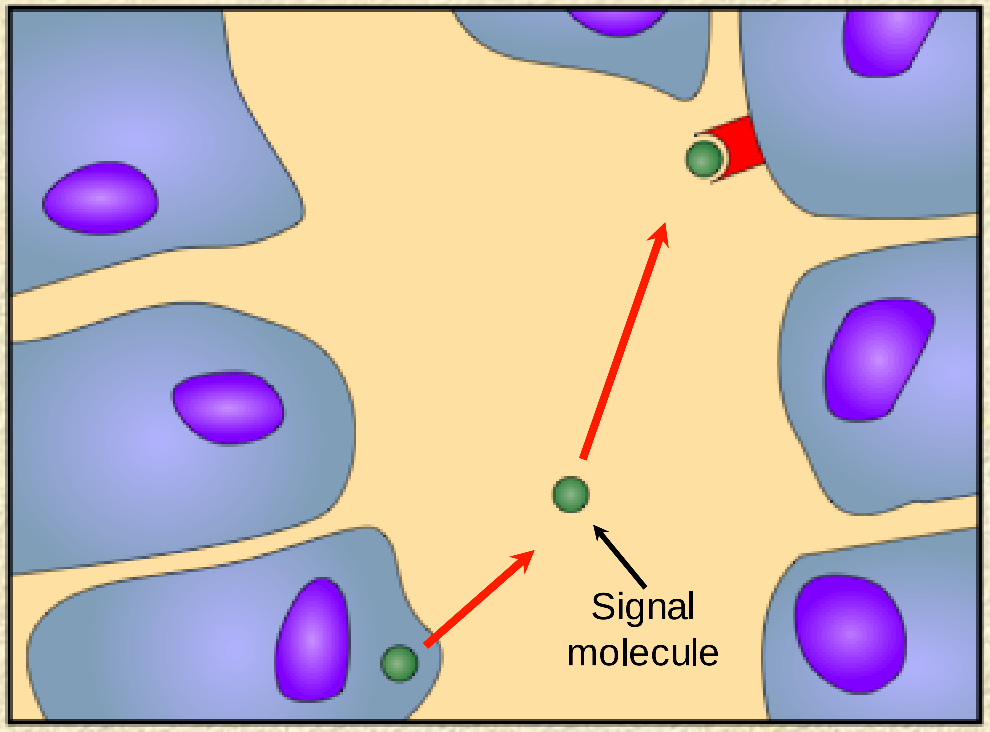
Endocrine signaling involved hormones carried in the blood, e.g. sex hormones, growth factors and neurohormones such as dopamine.



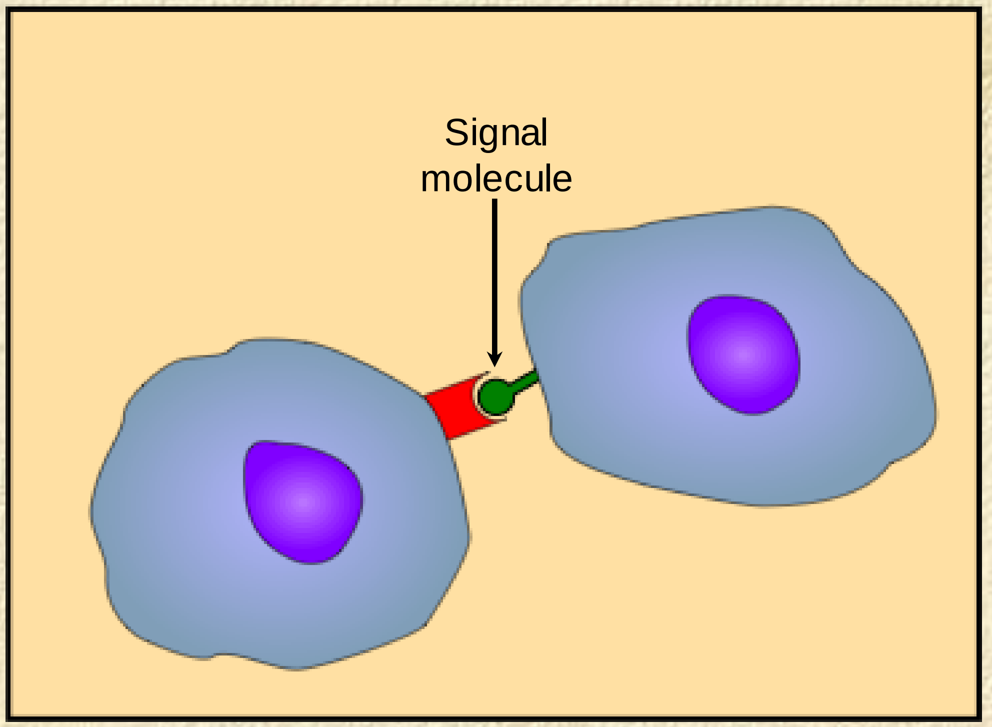
In vertebrates, T cells produce a growth factor when they encounter a foreign antibody. They respond to the growth factor by proliferating.

Paracrine Signaling

- In the **paracrine pathway**, a signal released from a cell acts on target cells within its immediate vicinity.
  - The production and transmission of **neurotransmitters**, which are used to transfer signals between a cell and a neuron, is an example of a common paracrine signaling pathway.
- **Direct cell to cell** signaling is a form of paracrine signaling:
  - The chemical message is transferred directly between neighboring cells. This form of signal transduction is important during embryonic development.



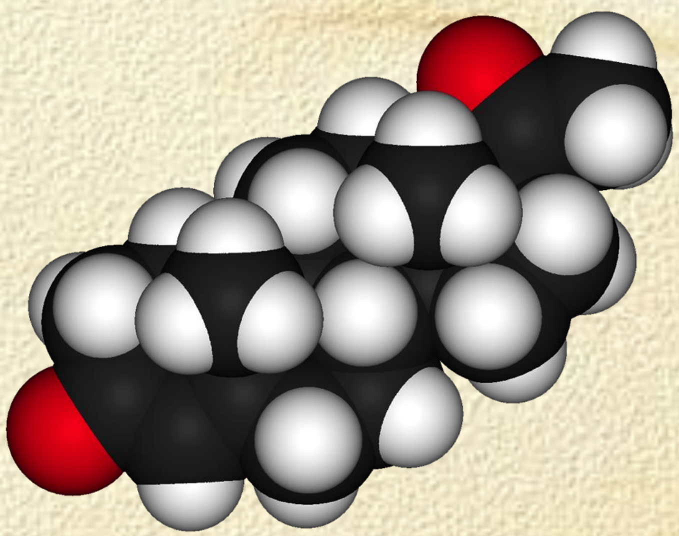
In **paracrine** signaling, a signal released from a cell and acts upon target cells within its immediate vicinity.

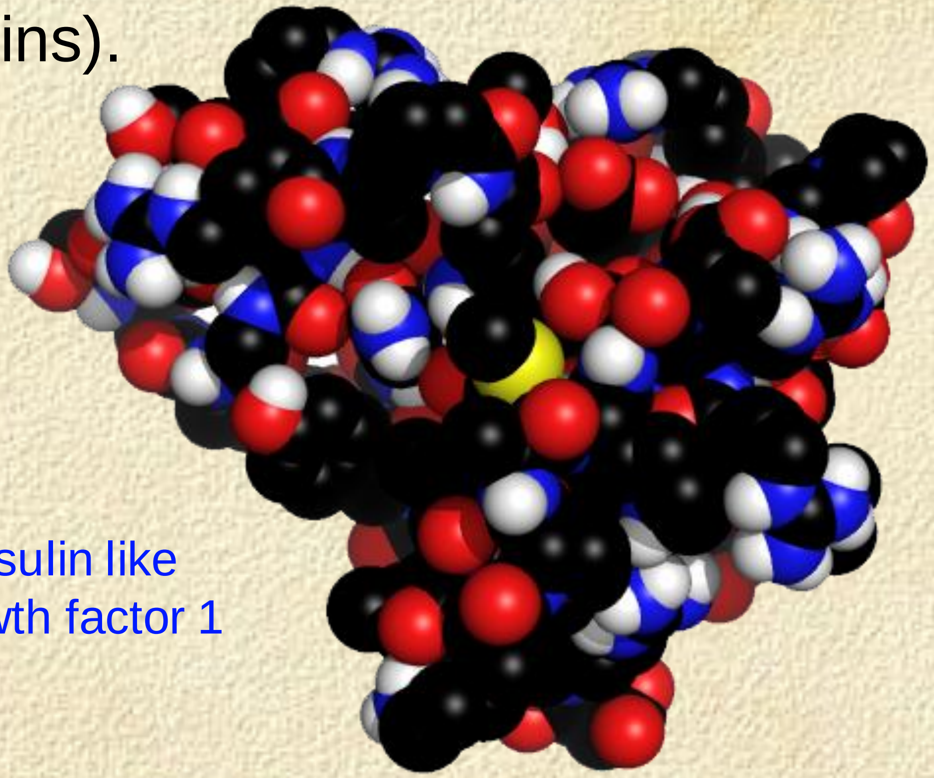


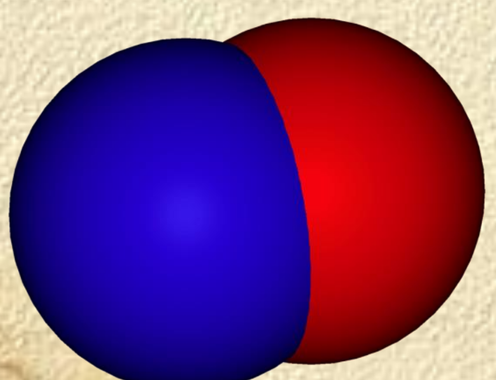
Direct **cell to cell signaling** involves a signal molecule being transferred directly between neighboring cells.

Types of Cell Signaling Molecules

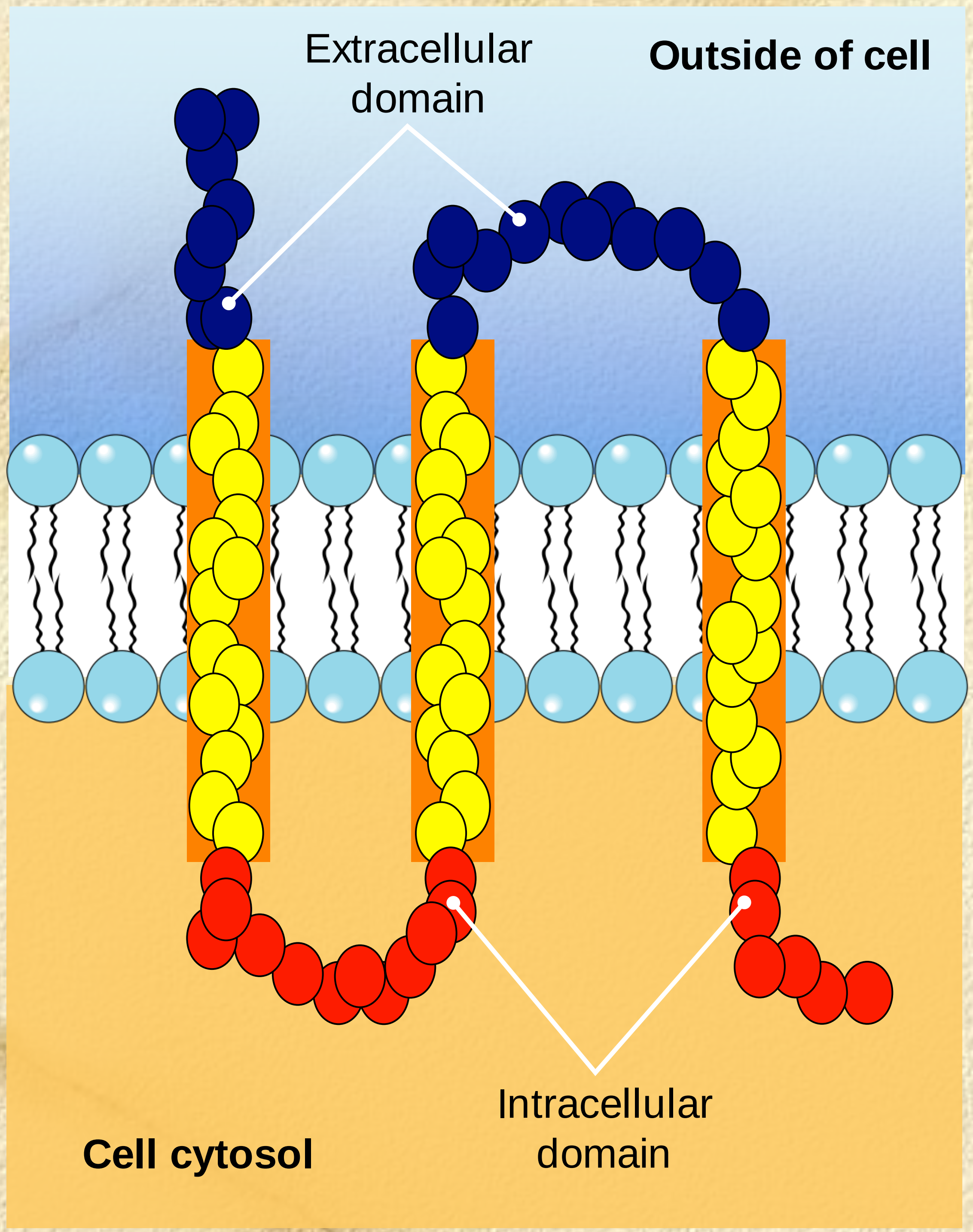
- Cell signals (**ligands**) are a varied group of chemical messengers. They fall into six broad groups:
  - **Steroid hormones** (e.g. progesterone).
  - Simple gases (e.g. nitric oxide).
  - **Neurotransmitters** (e.g. adrenalin).
  - **Peptide hormones** and **growth factors** (e.g. insulin).
  - **Eicosanoids**, a class of lipids (e.g. prostaglandins).
  - **Plant hormones** (e.g. auxins).


Progesterone


Insulin like growth factor 1


Nitric oxide

Types of Signal Receptors



Transmembrane receptors (above) have an **extracellular domain** located outside the cell, and an **intracellular domain** within the cell cytosol.

- The binding sites of cell receptors are very specific; they will only bind certain **signal molecules** (**ligands**).
- This prevents them from reacting to every signal encountered by the cell.
- Cell receptors fall into two major categories:
  - **Transmembrane receptors**: these span the cell membrane and bind the ligands that cannot cross the plasma membrane, and include:
    - ion channels.
    - protein kinases.
    - G-protein linked receptors.
  - **Cytoplasmic receptors**: these are located within the cell cytoplasm. They bind the ligands that can cross the plasma membrane.