

BME 1532-CELL BIOLOGY

Membrane Structure and Transport

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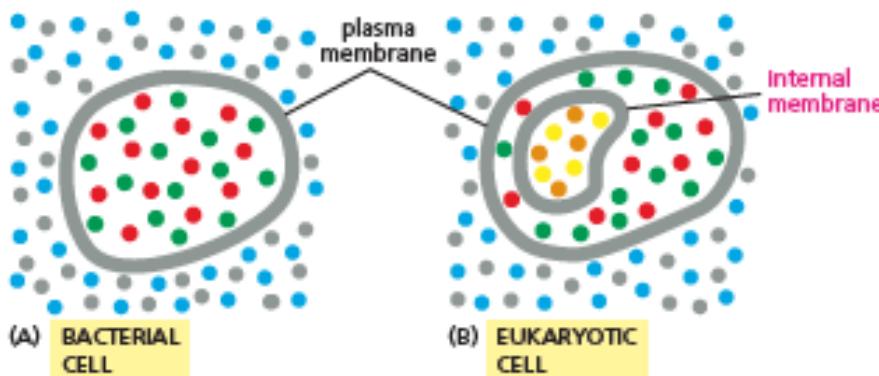
Yıldız Technical University
Biomedical Engineering Department
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- The first cell probably came into being when a membrane formed, enclosing a small volume of aqueous solution and separating it from the rest of the universe.
- Membranes define the external boundaries of cells and regulate the molecular traffic across that boundary; in eukaryotic cells, they divide the internal space into discrete compartments to segregate processes and components.
- They organize complex reaction sequences and are central to both biological energy conservation and cell-to-cell communication.

Prokaryotes have only a single membrane—the plasma membrane—whereas eukaryotic cells also contain internal membranes that enclose intracellular compartments. The internal membranes form various organelles, including the endoplasmic reticulum, Golgi apparatus, and mitochondria. Although these internal membranes are constructed on the same principles as the plasma membrane, there are subtle differences in their composition, especially in their resident proteins.

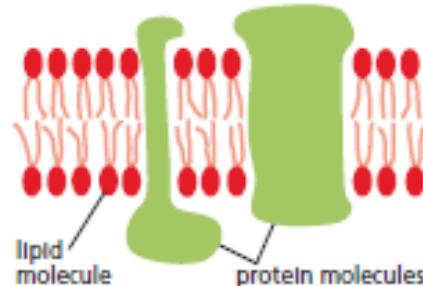


The plasma membrane separates a cell from its surroundings, enabling the molecular composition of a cell to differ from that of its environment.

- (A) In some bacteria, the plasma membrane is the only membrane.
- (B) Eukaryotic cells also have internal membranes that enclose individual organelles. All cell membranes prevent molecules on one side from freely mixing with those on the other, as schematically indicated by the colored dots.

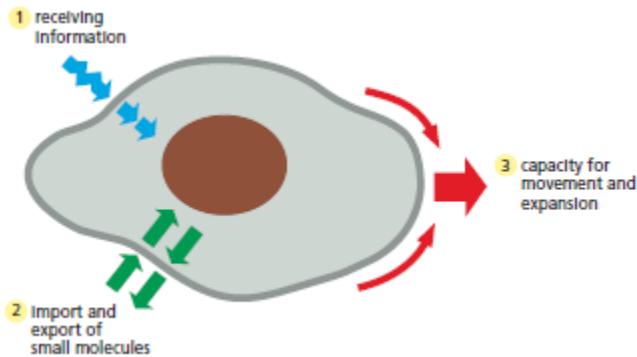
Membrane Functions

- The structure of the plasma membrane is simple: it consists of a two sheets of lipid molecules into which proteins have been inserted.
- Although it serves as a barrier to prevent the contents of the cell from escaping and mixing with the surrounding medium, the plasma membrane does much more than that.
- If a cell is to survive and grow, nutrients must pass inward across the plasma membrane, and waste products must pass out. To facilitate this exchange, the membrane is penetrated by highly selective channels and transporters—proteins that allow specific, small molecules and ions to be imported and exported.
- Other proteins in the membrane act as sensors, or receptors, that enable the cell to receive information about changes in its environment and respond to them in appropriate ways.



Properties of Biological Membranes

- The mechanical properties of the plasma membrane are remarkable. When a cell grows or changes shape, so does its membrane: it enlarges in area by adding new membrane without ever losing its continuity, and it can deform without tearing.
- Membranes are flexible, self-sealing, and selectively permeable to polar solutes.
- Their flexibility permits the shape changes that accompany cell growth and movement.
- With their ability to break and reseal, two membranes can fuse, as in exocytosis, or a single membrane-enclosed compartment can undergo fission to yield two sealed compartments, as in endocytosis or cell division, without creating gross leaks through cellular surfaces.

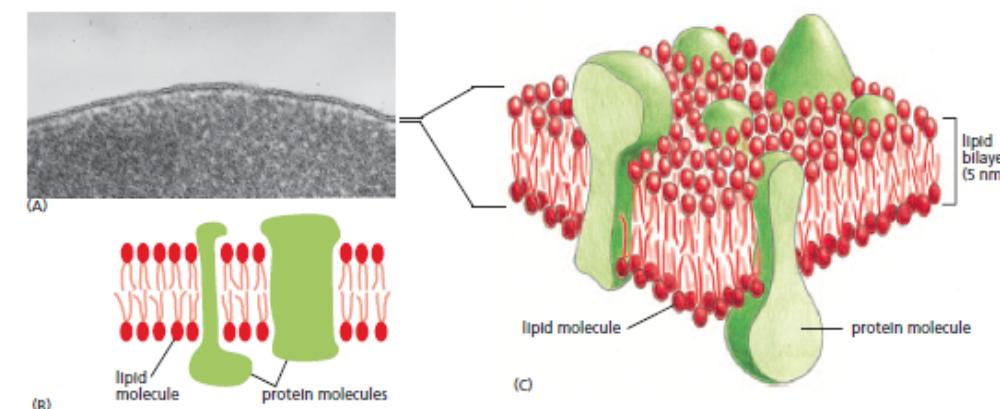


The plasma membrane is involved in cell communication, import and export of molecules, and cell growth and motility.

- (1) Receptor proteins in the plasma membrane enable the cell to receive signals from the environment;
- (2) Transport proteins in the membrane enable the import and export of small molecules;
- (3) The flexibility of the membrane and its capacity for expansion allow the cell to grow, change shape, and move.

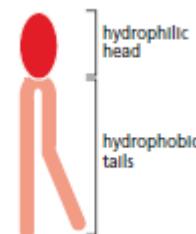
Membrane Structure

- Regardless of their location, all cell membranes are composed of lipids and proteins and share a common general structure.
- The lipids are arranged in two closely apposed sheets, forming a *lipid bilayer*.
- This lipid bilayer serves as a permeability barrier to most water-soluble molecules.
- The proteins embedded within lipid bilayer carry out the other functions of the membrane and give different membranes their individual characteristics.



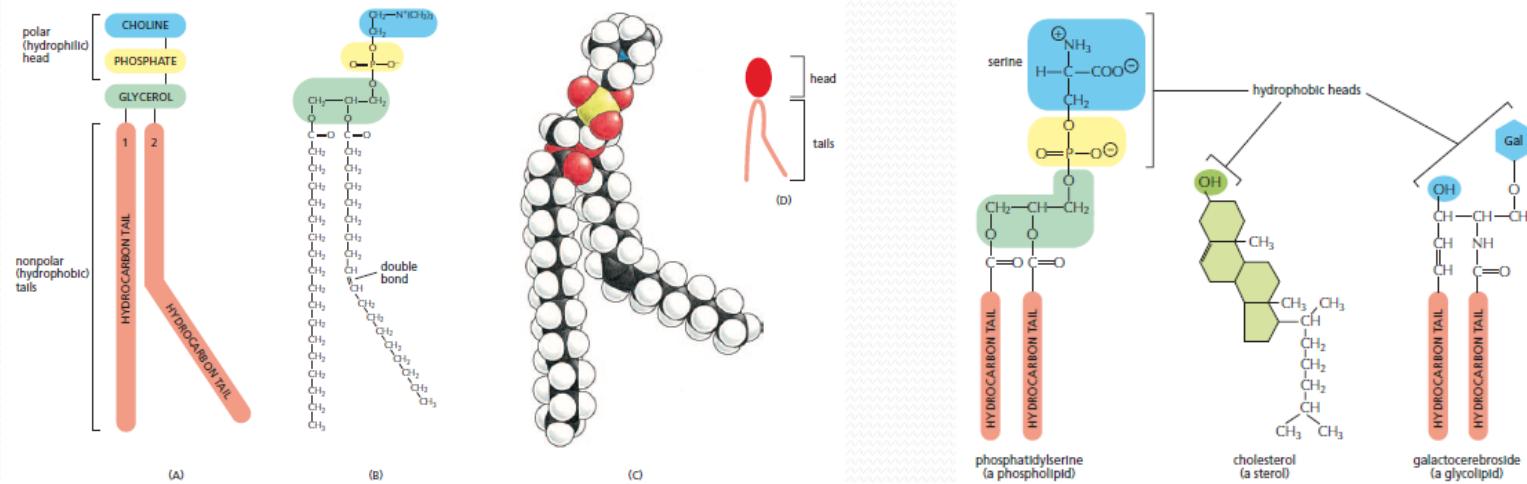
Membrane Lipids

- The lipids in cell membranes combine two very different properties in a single molecule: each lipid has a hydrophilic (“water-loving”) head and a hydrophobic (“water-fearing”) tail.
- The most abundant lipids in cell membranes are the phospholipids, which have a phosphate-containing, hydrophilic head linked to a pair of hydrophobic tails.
- Molecules with both hydrophilic and hydrophobic parts are termed amphipathic. Having both hydrophilic and hydrophobic parts plays a crucial part in driving these lipid molecules to assemble into bilayers in an aqueous environment.



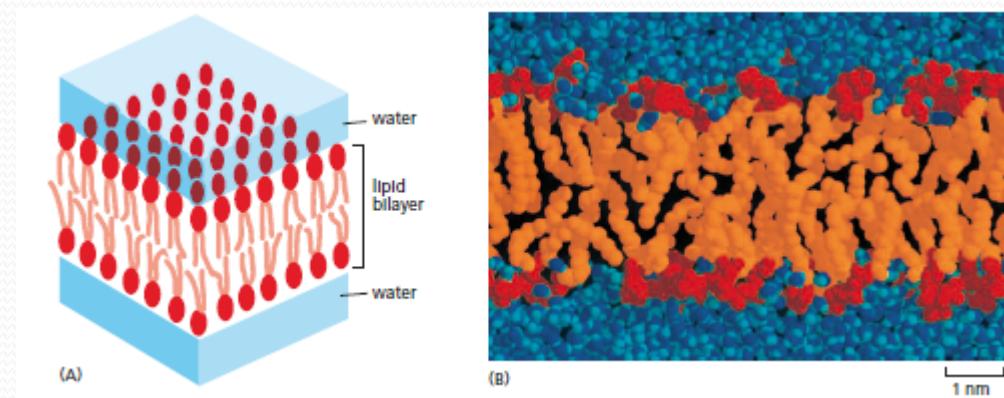
Membrane Lipids

- Phosphatidylcholine, for example, is the most common phospholipid in cell membranes and it has the small molecule choline attached to a phosphate group as its hydrophilic head.
- Other types of lipids (such as phosphotidylserine and cholesterol) and glycolipids also have hydrophilic head linked to a pair of hydrophobic tails.



Formation of Lipid Bilayer

- Amphipathic molecules, such as phospholipids are subject to two conflicting forces: the hydrophilic head is attracted to water, while the hydrophobic tails escape from water and aggregate with other hydrophobic molecules.
- This conflict is beautifully resolved by the formation of a lipid bilayer—an arrangement that satisfies all parties.
- The hydrophilic heads face water on both surfaces of the bilayer; but the hydrophobic tails are all shielded from the water, as they lie next to one another in the interior, like the filling in a sandwich.

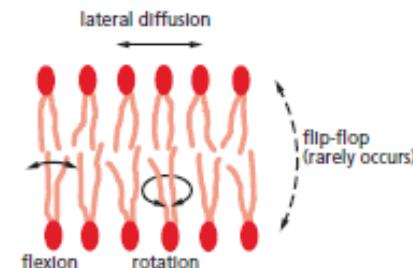


Membrane Fluidity

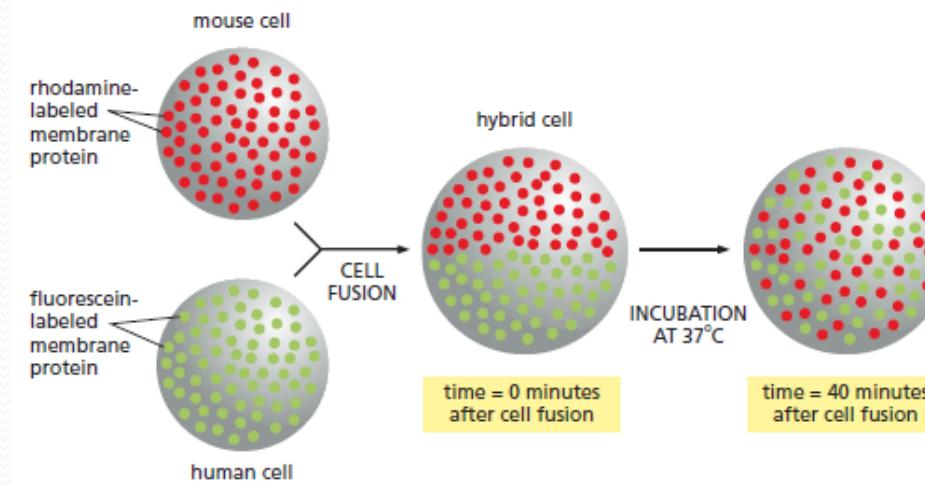
- The aqueous environment inside and outside a cell prevents membrane lipids from escaping from the bilayer, but nothing stops these molecules from moving about and changing places with one another within the plane of the bilayer.
- The membrane therefore behaves as a two-dimensional fluid, a fact that is crucial for membrane function and integrity.
- The structure of biological membranes is best described via the **fluid mosaic model**.
- The lipid bilayer is also flexible—that is, it is able to bend. Like fluidity, flexibility is important for membrane function, for example when vesicles are formed from it.

Membrane Fluidity

- The lipids in a bilayer are in constant motion giving lipid bilayers many of the properties of fluids.
- The membrane mosaic is fluid because most of the interactions among its components are noncovalent, leaving individual lipid and protein molecules free to move laterally in the plane of the membrane.
- The rapid movement of lipids within the plane of one monolayer is an example of two-dimensional lateral diffusion.
- In contrast, transverse diffusion (or flip-flop) is the passage of lipids from one monolayer of the bilayer to the other. Flip-flop is seen very rarely.
- Lipid molecules also flex their hydrocarbon tails and rotate rapidly about their long axis.

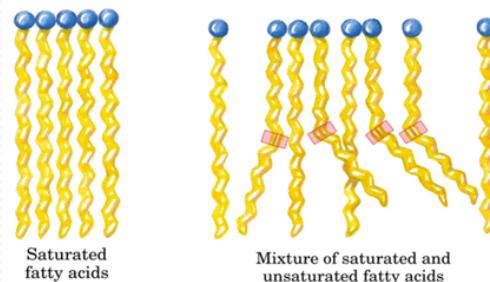


- Because a membrane is a two-dimensional fluid, many of its proteins, like its lipids, can move freely within the plane of the lipid bilayer.
- This lateral diffusion was initially demonstrated by experimentally fusing a mouse cell with a human cell to form a double-sized hybrid cell and then monitoring the distribution of certain mouse and human plasma membrane proteins.
- At first, the mouse and human proteins are confined to their own halves of the newly formed hybrid cell, but within half an hour or so the two sets of proteins become evenly mixed over the entire cell surface.



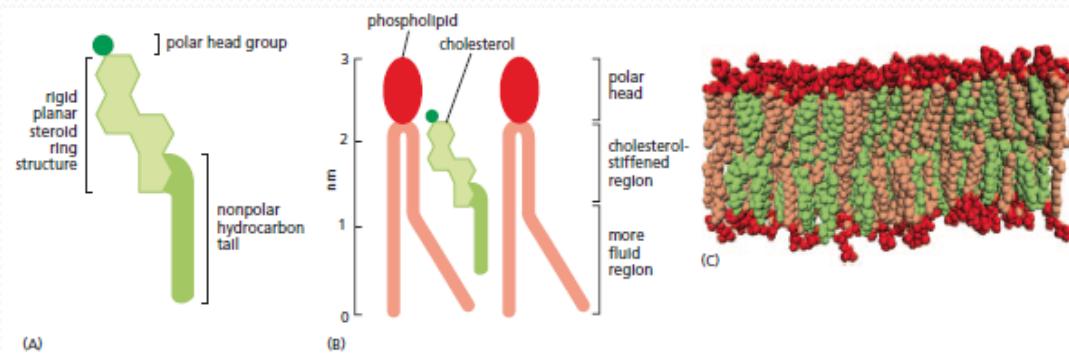
Membrane Fluidity

- The fluidity of a cell membrane—the ease with which its lipid molecules move within the plane of the bilayer—is important for membrane function and has to be maintained within certain limits.
- Just how fluid a lipid bilayer is at a given temperature depends on its phospholipid composition and, in particular, on the nature of the hydrocarbon tails: the closer and more regular the packing of the tails, the more viscous and less fluid the bilayer will be.
- Two major properties of hydrocarbon tails affect how tightly they pack in the bilayer: their length and the number of double bonds they contain.
- A shorter chain length reduces the tendency of the hydrocarbon tails to interact with one another and therefore increases the fluidity of the bilayer.
- Each double bond in an unsaturated tail creates a small kink in the tail, which makes it more difficult for the tails to pack against one another.



Cholesterol decreases the membrane fluidity

- In bacterial and yeast cells, which have to adapt to varying temperatures, both the lengths and the unsaturation of the hydrocarbon tails in the bilayer are constantly adjusted to maintain the membrane at a relatively constant fluidity: at higher temperatures, for example, the cell makes membrane lipids with tails that are longer and that contain fewer double bonds.
- In animal cells, membrane fluidity is modulated by the inclusion of the sterol cholesterol. This molecule is present in especially large amounts in the plasma membrane, where it constitutes approximately 20% of the lipids in the membrane by weight.
- Because cholesterol molecules are short and rigid, they fill the spaces between neighboring phospholipid molecules left by the kinks in their unsaturated hydrocarbon tails.
- In this way, cholesterol tends to stiffen the bilayer, making it less flexible, as well as less permeable.

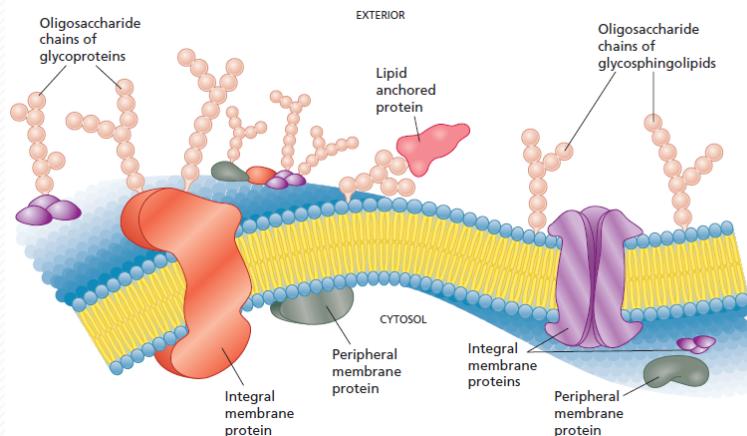


Importance of Membrane Fluidity

- For all cells, membrane fluidity is important for many reasons. It enables many membrane proteins to diffuse rapidly in the plane of the bilayer and to interact with one another, as is crucial, for example, in cell signaling.
- It permits membrane lipids and proteins to diffuse from sites where they are inserted into the bilayer after their synthesis to other regions of the cell.
- It ensures that membrane molecules are distributed evenly between daughter cells when a cell divides.
- Under appropriate conditions, it allows membranes to fuse with one another and mix their molecules.
- If biological membranes were not fluid, it is hard to imagine how cells could live, grow, and reproduce.

Membranes are asymmetric

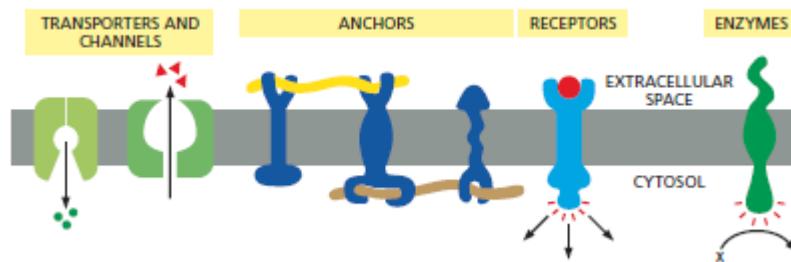
- Phospholipids form a bilayer in which the nonpolar regions of the lipid molecules in each layer face the core of the bilayer and their polar head groups face outward, interacting with the aqueous phase on either side.
- Proteins are embedded in this bilayer sheet, held by hydrophobic interactions between the membrane lipids and hydrophobic domains in the proteins.
- Some proteins protrude from only one side of the membrane; others have domains exposed on both sides.
- Both the lipid composition and the orientation of proteins in the bilayer is asymmetric, giving the membrane “**sidedness**”: The lipid composition and the protein domains exposed on one side of the bilayer may differ from those exposed on the other side, reflecting **functional asymmetry**.



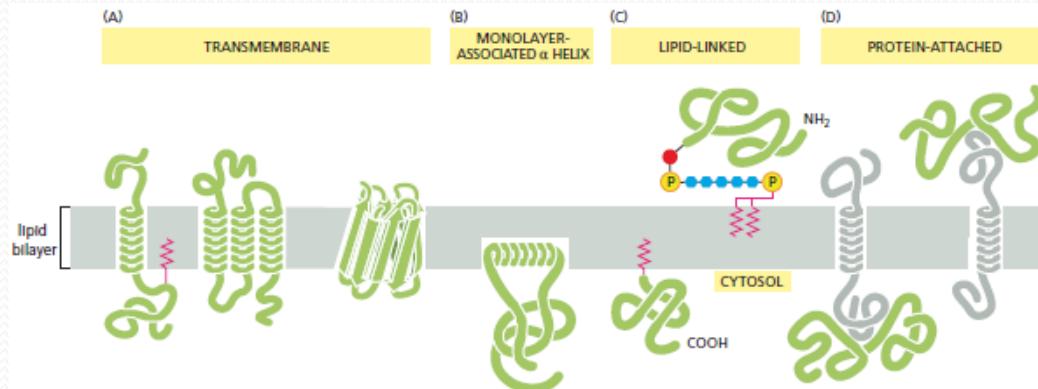
- This asymmetry is preserved as membranes bud from one organelle and fuse with another—or with the plasma membrane. This means that all cell membranes have distinct “inside” and “outside” faces: the cytosolic monolayer always faces the cytosol, while the noncytosolic monolayer is exposed to either the cell exterior—in the case of the plasma membrane—or to the interior space (*lumen*) of an organelle.
- This conservation of orientation applies not only to the phospholipids that make up the membrane, but to any proteins that might be inserted in the membrane.
- For membrane proteins, this positioning is very important, as their orientation within the lipid bilayer is often crucial for their function.

Membrane Proteins

- Although the lipid bilayer provides the basic structure of all cell membranes and serves as a permeability barrier to the hydrophilic molecules on either side of it, most membrane functions are carried out by membrane proteins.
- Membrane proteins serve many functions:
 - Some transport particular nutrients, metabolites, and ions across the lipid bilayer.
 - Others anchor the membrane to macromolecules on either side.
 - Still others function as receptors that detect chemical signals in the cell's environment and relay them into the cell interior, or work as enzymes to catalyze specific reactions at the membrane.



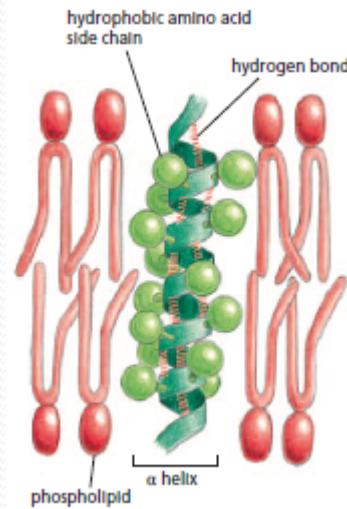
- Proteins can be associated with the lipid bilayer of a cell membrane in any of the ways below:
 - Many membrane proteins extend through the bilayer, with part of their mass on either side. Like their lipid neighbors, these *transmembrane proteins* are amphipathic, having both hydrophobic and hydrophilic regions. Their hydrophobic regions lie in the interior of the bilayer, nestled against the hydrophobic tails of the lipid molecules. Their hydrophilic regions are exposed to the aqueous environment on either side of the membrane.
 - Other membrane proteins are located almost entirely in the cytosol and are associated with the cytosolic half of the lipid bilayer by an amphipathic α helix exposed on the surface of the protein.
 - Some proteins lie entirely outside the bilayer, on one side or the other, attached to the membrane only by one or more covalently attached lipid groups.
 - Yet other proteins are bound indirectly to one or the other face of the membrane, held in place only by their interactions with other membrane proteins.



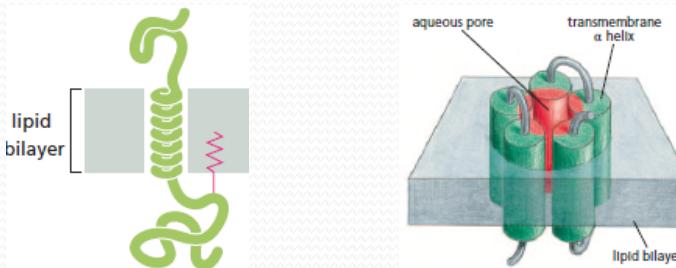
Membrane Proteins

- Proteins that are directly attached to the lipid bilayer—whether they are transmembrane or associated with the lipid monolayer, are known as *integral membrane proteins*.
- Proteins that are anchored to the lipid bilayer by lipid molecules are called *lipid anchored membrane proteins*.
- The remaining membrane proteins are known as *peripheral membrane proteins*.

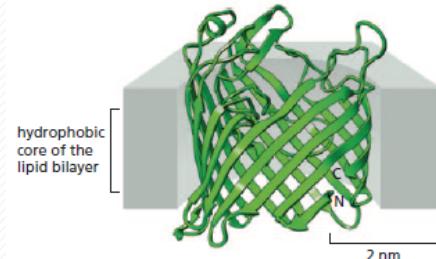
- All membrane proteins have a unique orientation in the lipid bilayer, which is essential for their function.
- For a transmembrane receptor protein, for example, the part of the protein that receives a signal from the environment must be on the outside of the cell, whereas the part that passes along the signal must be in the cytosol.
- The portions of a transmembrane protein located on either side of the lipid bilayer are connected by specialized membrane-spanning segments of the polypeptide chain.
- These segments, which run through the hydrophobic environment of the interior of the lipid bilayer, are composed largely of amino acids with hydrophobic side chains.
- Because these side chains cannot form favorable interactions with water molecules, they prefer to interact with the hydrophobic tails of the lipid molecules, where no water is present.
- In contrast to the hydrophobic side chains, however, the peptide bonds that join the successive amino acids in a protein are normally polar, making the polypeptide backbone hydrophilic .
- Because water is absent from the interior of the bilayer, atoms forming the backbone are driven to form hydrogen bonds with one another. Hydrogen-bonding is maximized if the polypeptide chain forms a regular α helix, and so the great majority of the membrane-spanning segments of polypeptide chains traverse the bilayer as α helices. In these membrane-spanning α helices, the hydrophobic side chains are exposed on the outside of the helix, where they contact the hydrophobic lipid tails, while atoms in the polypeptide backbone form hydrogen bonds with one another on the inside of the helix.



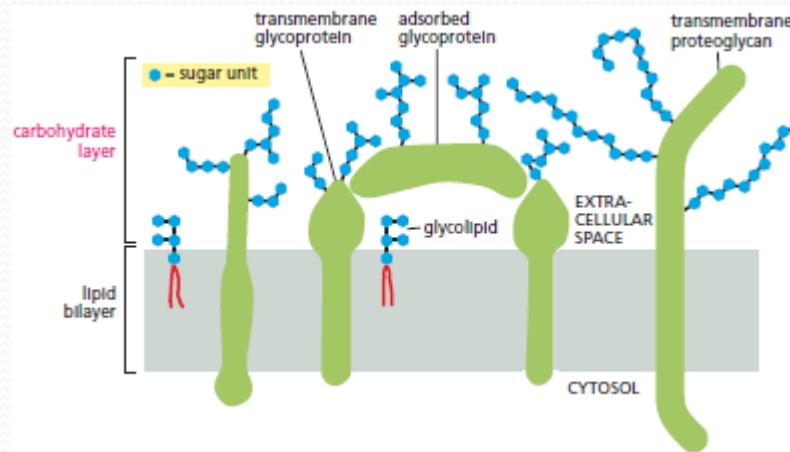
- In many transmembrane proteins, the polypeptide chain crosses the membrane only once. Many of these *single-pass* transmembrane proteins are receptors for extracellular signals.
- Other transmembrane proteins function as channels, forming aqueous pores across the lipid bilayer to allow small, water-soluble molecules to cross the membrane. Such channels cannot be formed by proteins with a single transmembrane α helix. Instead, they usually consist of a series of α helices that cross the bilayer a number of times.
- In many of these *multipass* transmembrane proteins, one or more of the membrane-spanning regions are amphipathic—formed from α helices that contain both hydrophobic and hydrophilic amino acid side chains. These amino acids tend to be arranged so that the hydrophobic side chains fall on one side of the helix, while the hydrophilic side chains are concentrated on the other side.
- In the hydrophobic environment of the lipid bilayer, α helices of this sort pack side by side in a ring, with the hydrophobic side chains exposed to the lipids of the membrane and the hydrophilic side chains forming the lining of a hydrophilic pore through the lipid bilayer.



- Although the α helix is by far the most common form in which a polypeptide chain crosses a lipid bilayer, the polypeptide chain of some transmembrane proteins crosses the lipid bilayer as a β sheet that is rolled into a cylinder structure called a β barrel.
- As expected, the amino acid side chains that face the inside of the barrel, and therefore line the aqueous channel, are mostly hydrophilic, while those on the outside of the barrel, which contact the hydrophobic core of the lipid bilayer, are exclusively hydrophobic.

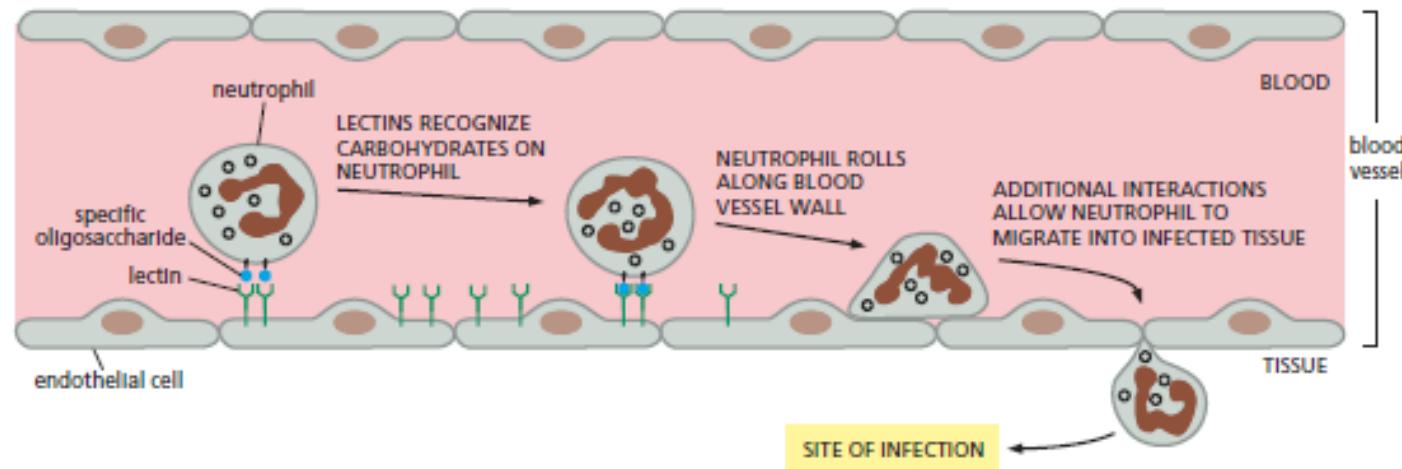


- Most of the proteins in the plasma membrane have short chains of sugars, called oligosaccharides, linked to them; they are called *glycoproteins*.
- Other membrane proteins, the *proteoglycans*, contain one or more long polysaccharide chains. All of the carbohydrate on the glycoproteins, proteoglycans, and glycolipids is located on the outside of the plasma membrane, where it forms a sugar coating called the *carbohydrate layer* or *glycocalyx*.



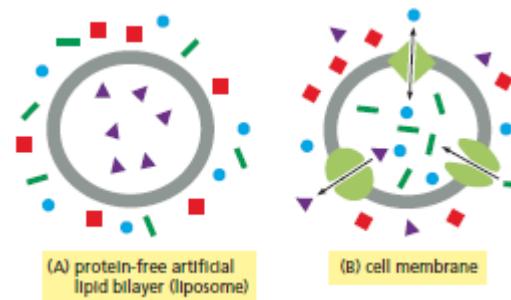
- This layer of carbohydrate helps protect the cell surface from mechanical damage. As the oligosaccharides and polysaccharides adsorb water, they also give the cell a slimy surface, which helps motile cells such as white blood cells squeeze through narrow spaces and prevents blood cells from sticking to one another or to the walls of blood vessels.
- Cell-surface carbohydrates do more than just protect and lubricate the cell, however. They have an important role in cell-cell recognition and adhesion.
- Just as many proteins will recognize a particular site on another protein, proteins called *lectins* are specialized to bind to particular oligosaccharide side chains.
- The carbohydrate layer on the surface of cells in a multicellular organism serves as a kind of distinctive clothing, like a police officer's uniform. It is characteristic of each cell type and is recognized by other cell types that interact with it.
- Specific oligosaccharides in the carbohydrate layer are involved, for example, in the recognition of an egg by a sperm.

- Similarly, in the early stages of a bacterial infection, the carbohydrate on the surface of white blood cells called neutrophils is recognized by a lectin on the cells lining the blood vessels at the site of infection; this recognition causes the neutrophils to adhere to the blood vessel wall and then migrate from the bloodstream into the infected tissue, where they help destroy the invading bacteria.



Transport Across Cell Membranes

- To survive and grow, cells must be able to exchange molecules with their environment. They must import nutrients such as sugars and amino acids and eliminate metabolic waste products. They must also regulate the concentrations of a variety of inorganic ions in their cytosol and organelles.
- A few molecules, such as CO₂ and O₂, can simply diffuse across the lipid bilayer of the plasma membrane. But the vast majority cannot. Instead, their transfer depends on specialized membrane transport proteins that span the lipid bilayer, providing private passageways across the membrane for select substances.

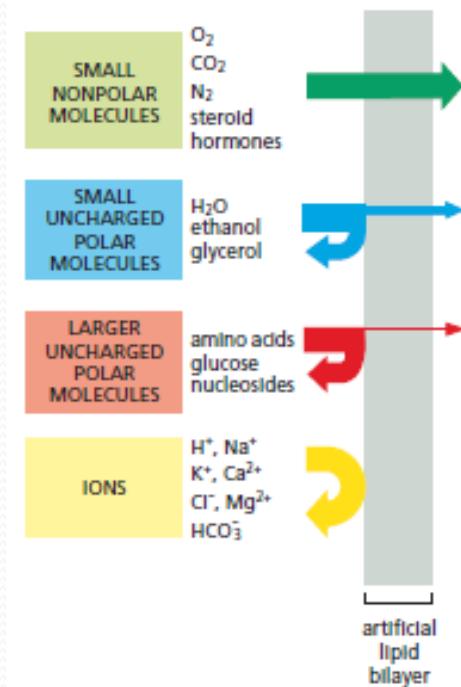


Principles of Transmembrane Transport

- The hydrophobic interior of the lipid bilayer creates a barrier to the passage of most hydrophilic molecules, including all ions.
- These molecules are as reluctant to enter a fatty environment as hydrophobic molecules are reluctant to enter water.
- But cells and organelles must also allow the passage of many hydrophilic, water-soluble molecules, such as inorganic ions, sugars, amino acids, nucleotides, and other cell metabolites.
- These molecules cross lipid bilayers far too slowly by ***simple diffusion***, so their passage across cell membranes must be accelerated by specialized membrane transport proteins—a process called ***facilitated transport***.

Principles of Transmembrane Transport

1. *Small nonpolar molecules*, such as molecular oxygen (O_2) and carbon dioxide (CO_2), dissolve readily in lipid bilayers and therefore rapidly diffuse across them; indeed, cells depend on this permeability to gases for the cell respiration.
2. *Uncharged polar molecules* (molecules with an uneven distribution of electric charge) also diffuse readily across a bilayer if they are small enough. Water (H_2O .) and ethanol, for example, cross at a measureable rate, while glycerol crosses less rapidly.
3. Larger uncharged polar molecules such as glucose cross hardly at all.
4. In contrast, lipid bilayers are highly impermeable to all *charged molecules*, including all inorganic ions, no matter how small. These molecules' charges and their strong electrical attraction to water molecules inhibit their entry into the inner, hydrocarbon phase of the bilayer.

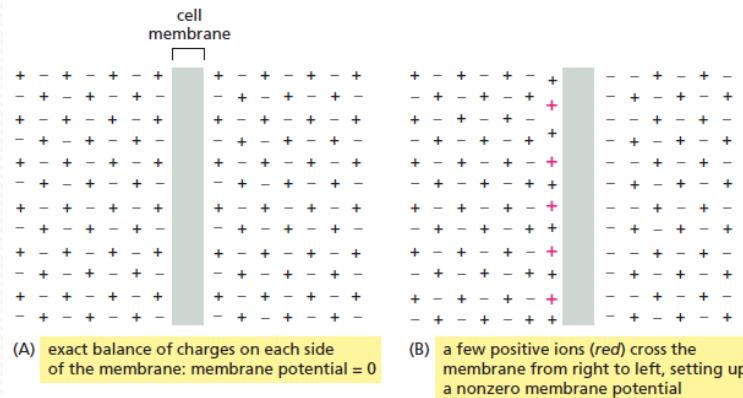


Note that many of the organic molecules that a cell uses as nutrients (shaded in red) are too large and polar to pass through the lipid bilayer.

- Because cell membranes are impermeable to inorganic ions, living cells are able to maintain internal ion concentrations that are very different from the concentrations of ions in the media that surrounds them.
- These differences in ion concentration are crucial for a cell's survival and function.
- Among the most important inorganic ions for cells are Na^+ , K^+ , Ca^{2+} , Cl^- , and H^+ (protons). The movement of these ions across cell membranes plays an essential part in many biological processes, but is perhaps most striking in the production of ATP by all cells, and in communication by nerve cells.
- Na^+ is the most plentiful positively charged ion (cation) outside the cell, whereas K^+ is the most abundant inside .
- For a cell to avoid being torn apart by electrical forces, the quantity of positive charge inside the cell must be balanced by an almost exactly equal quantity of negative charge, and the same is true for the charge in the surrounding fluid.
- The high concentration of Na^+ outside the cell is electrically balanced chiefly by extracellular Cl^- , whereas the high concentration of K^+ inside is balanced by a variety of negatively charged organic and inorganic ions (anions) including nucleic acids, proteins, and many cell metabolites.
- Although the electrical charges inside and outside the cell are generally kept in balance, tiny excesses of positive or negative charge, concentrated in the neighborhood of the plasma membrane, do occur.

Membrane Potential

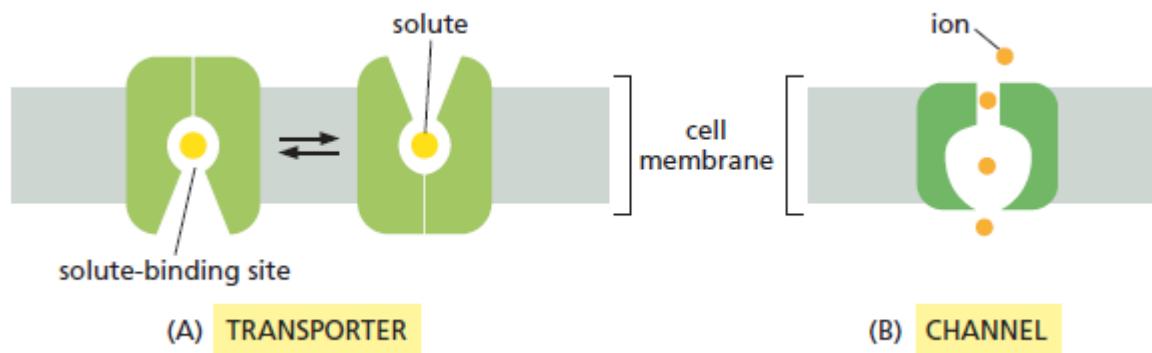
- Such electrical imbalances generate a voltage difference across the membrane called the membrane potential.
- When a cell is “unstimulated,” the exchange of anions and cations across the membrane will be precisely balanced. In such steady-state conditions, the voltage difference across the cell membrane—called the *resting membrane potential*—holds steady. But it is not zero. In animal cells, for example, the resting membrane potential can be anywhere between -20 and -200 millivolts (mV), depending on the organism and cell type.
- The value is expressed as a negative number because the interior of the cell is more negatively charged than the exterior.
- This membrane potential allows cells to power the transport of certain metabolites and provides those cells that are excitable with a means to communicate with their neighbors.
- It is the activity of membrane transport proteins embedded in the bilayer that enables cells to establish and maintain their membrane potential.



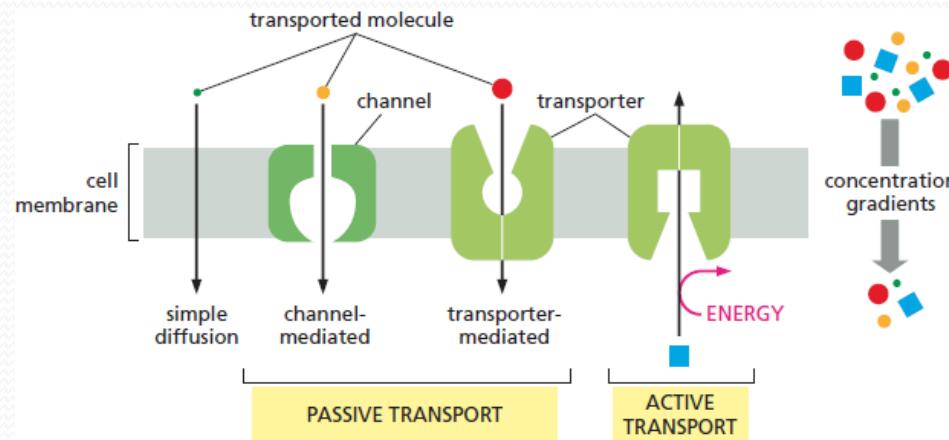
Transport Proteins

- Membrane transport proteins occur in many forms and are present in all cell membranes.
- Each type of cell membrane has its own characteristic set of transport proteins, which determines exactly which solutes can pass into and out of the cell or an organelle.
- There are two main classes of membrane transport proteins: *transporters* and *channels*. These proteins differ in the way they discriminate between solutes, transporting some but not others.

- **Channels** discriminate mainly on the basis of size and electric charge: when the channel is open, any ion or molecule that is small enough and carries the appropriate charge can pass through.
- A **transporter**, on the other hand, transfers only those molecules or ions that fit into specific binding sites on the protein.
- Transporters bind their solutes with great specificity, in the same way an enzyme binds its substrate, and it is this requirement for specific binding that gives transporters their selectivity.



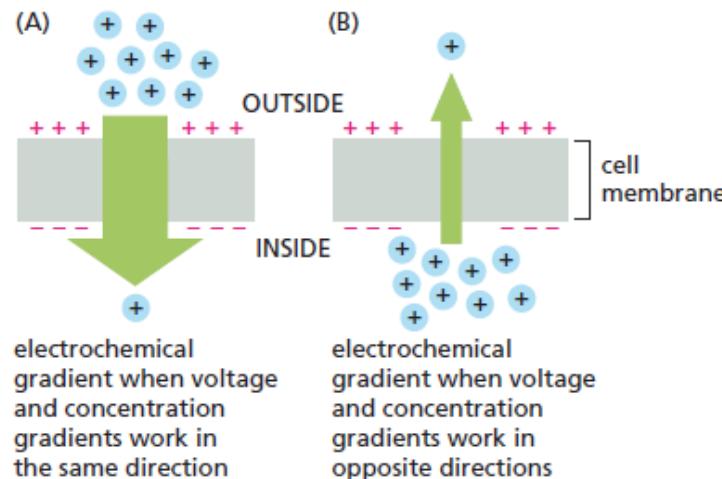
- Transporters and channels allow small hydrophilic molecules to cross the cell membrane depending on the relative concentrations of the solute on either side of the membrane.
- Molecules will spontaneously flow “downhill” from a region of high concentration to a region of low concentration in a process called ***passive transport***.
- All channels and many transporters act as conduits for such passive transport.
- To move a solute against its concentration gradient, a membrane transport protein must do work: it has to drive the flow “uphill” by coupling it to some other process that provides an input of energy.
- The movement of a solute against its concentration gradient in this way is termed ***active transport***, and it is carried out by special types of transporters called *pumps*, which harness an energy source to power the transport process.



Electrochemical Gradient

- For an uncharged molecule, the direction of passive transport is determined solely by its concentration gradient.
- But for electrically charged molecules, whether inorganic ions or small organic molecules, an additional force comes into play: membrane potential.
- The membrane potential exerts a force on any molecule that carries an electric charge. The cytosolic side of the plasma membrane is usually at a negative potential relative to the extracellular side, so the membrane potential tends to pull positively charged solutes into the cell and drive negatively charged ones out.
- At the same time, a charged solute will also tend to move down its concentration gradient.
- The net force driving a charged solute across a cell membrane is therefore a composite of two forces, one due to the concentration gradient and the other due to the membrane potential.
- This net driving force, called the solute's electrochemical gradient, determines the direction that each solute will flow across the membrane by passive transport.

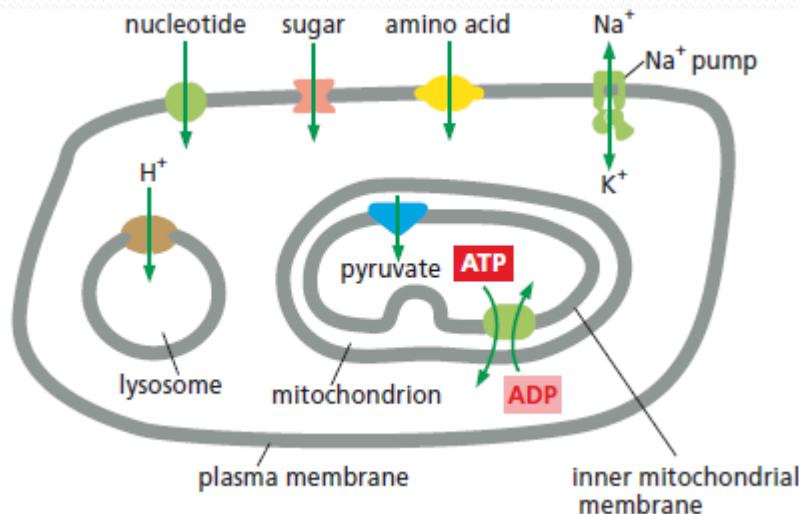
- For some ions, the voltage and concentration gradients work in the same direction, creating a relatively steep electrochemical gradient.
- This is the case for Na^+ , which is positively charged and at a higher concentration outside cells than inside. Na^+ therefore tends to enter cells if given an opportunity.
- If, however, the voltage and concentration gradients have opposing effects, the resulting electrochemical gradient can be small.
- This is the case for K^+ , which is present at a much higher concentration inside cells than outside.
- Because of its small electrochemical gradient across the resting plasma membrane, there is little net movement of K^+ across the membrane even when K^+ channels are open.



Transporters

- Transporters are responsible for the movement of most small, water-soluble, organic molecules and some inorganic ions across cell membranes.
- Each transporter is highly selective, often transferring just one type of molecule.
- They can be either ***passive transporters*** that direct the molecules along their electrochemical gradient or ***pumps*** that direct the molecules against the electrochemical gradient.

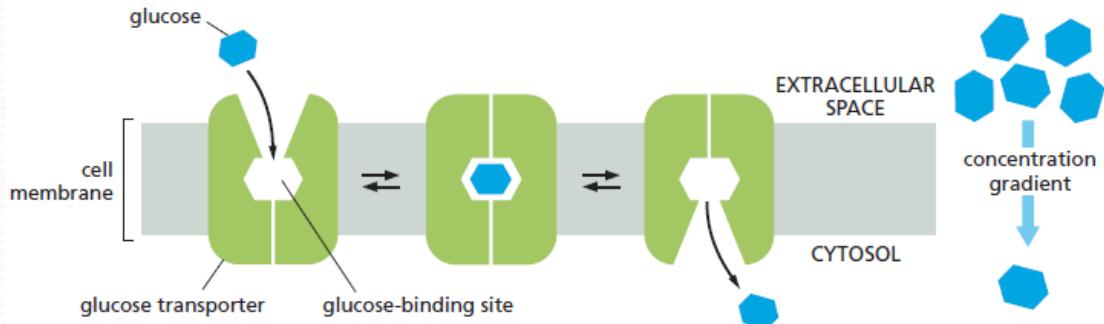
- To guide and propel the complex traffic of solutes into and out of the cell, and between the cytosol and the different membrane-enclosed organelles, each cell membrane contains a characteristic set of different transporters appropriate to that particular membrane.
- For example, the plasma membrane contains transporters that import nutrients such as sugars, amino acids, and nucleotides; the lysosome membrane contains an H⁺ transporter that imports H⁺ to acidify the lysosome interior and other transporters that move digestion products out of the lysosome into the cytosol; the inner membrane of mitochondria contains transporters for importing the pyruvate that mitochondria use as fuel for generating ATP, as well as transporters for exporting ATP once it is synthesized.



Passive Transporters

- An important example of a transporter that mediates passive transport is the *glucose transporter* in the plasma membrane of many mammalian cell types.
- Because glucose is uncharged, the chemical component of its electrochemical gradient is zero. Thus the direction in which it is transported is determined by its concentration gradient alone.
- The net flow of glucose can thus go either way, inward towards the cytoplasm or outwards towards the outside according to the direction of the glucose concentration gradient across the plasma membrane.
- Although passive transporters of this type play no part in determining the direction of transport, they are highly selective. For example, the binding sites in the glucose transporter bind only D-glucose and not its mirror image, L-glucose, which the cell cannot use for glycolysis.

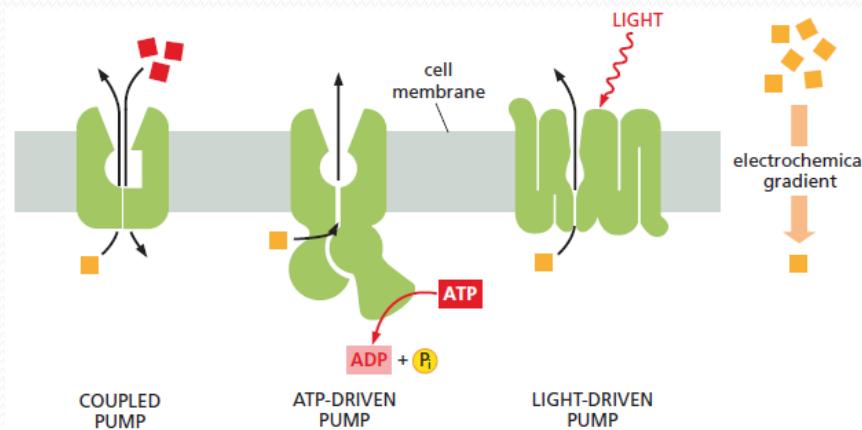
- When glucose is plentiful outside cells, as it is after a meal, the sugar binds to the transporter's externally displayed binding sites; when the protein switches conformation—spontaneously and at random—it carries the bound sugar inward and releases it into the cytosol, where the glucose concentration is low.
- Conversely, when blood glucose levels are low as they are when you are hungry—the hormone glucagon stimulates liver cells to produce large amounts of glucose by the breakdown of glycogen. As a result, the glucose concentration is higher inside liver cells than outside. This glucose binds to the internally displayed binding sites on the transporter. When the protein switches conformation in the opposite direction, the glucose is transported out of the cells, where it is made available for others to import.



Glucose Transporter

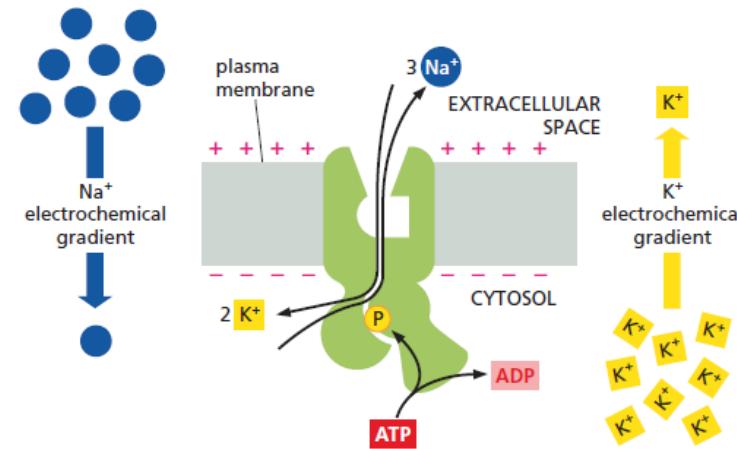
Pumps

- Cells cannot rely solely on passive transport. An active transport of solutes against their electrochemical gradient is essential to maintain the appropriate intracellular ionic composition of cells and to import solutes that are at a lower concentration outside the cell than inside.
- For these purposes, cells depend on transmembrane pumps, which can carry out active transport in three main ways : (i) *ATP-driven pumps* hydrolyze ATP to drive uphill transport. (ii) *Coupled pumps* link the uphill transport of one solute across a membrane to the downhill transport of another. (iii) *Light-driven pumps*, which are found mainly in bacterial cells, use energy derived from sunlight to drive uphill transport.



- In the plasma membrane of an animal cell, an ATP-driven Na^+ pump transports Na^+ out of the cell against its electrochemical gradient; this Na^+ can then flow back into the cell, down its electrochemical gradient.
- As the ion flows back in through various Na^+ -coupled pumps, the influx of Na^+ provides the energy for the active transport of many other substances into the cell against their electrochemical gradients.
- Thus, the ATP-driven Na^+ pump plays such a central part in the energy economy of animal cells.
- This pump uses the energy derived from ATP hydrolysis to transport Na^+ out of the cell as it carries K^+ in.
- The pump is therefore also known as the Na^+-K^+ ATPase or the Na^+-K^+ pump.

Na^+-K^+ Pump



Na⁺ Gradient Across the Plasma Membrane

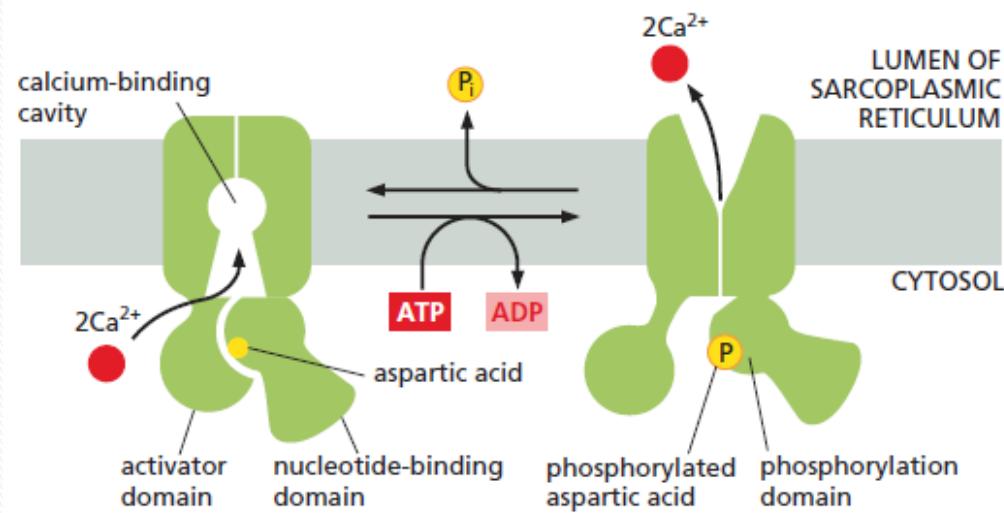
- The Na⁺ pump continuously expel the Na⁺ that is constantly entering the cell through other transporters and ion channels in the plasma membrane.
- In this way, the pump keeps the Na⁺ concentration in the cytosol about 10–30 times lower than in the extracellular fluid and the K⁺ concentration about 10–30 times higher.
- The steep concentration gradient of Na⁺ across the plasma membrane acts together with the membrane potential to create a large Na⁺ electrochemical gradient, which tends to pull Na⁺ back into the cell. This high concentration of Na⁺ outside the cell, on the uphill side of its electrochemical gradient represents a very large store of energy.

Ca²⁺ Gradient Across the Plasma Membrane

- Ca²⁺, like Na⁺, is also kept at a low concentration in the cytosol compared with its concentration in the extracellular fluid.
- The movement of Ca²⁺ across cell membranes is crucial, because Ca²⁺ can bind tightly to a variety of proteins in the cell, altering their activities.
- An influx of Ca²⁺ into the cytosol through Ca²⁺ channels, for example, is used by different cells as an intracellular signal to trigger various cell processes, such as muscle contraction, fertilization, and nerve cell communication.
- Eukaryotic cells in general maintain a very low concentration of free Ca²⁺ in their cytosol in the face of a very much higher extracellular Ca²⁺ concentration.
- This huge concentration difference is achieved mainly by means of ATP-driven Ca²⁺ pumps in both the plasma membrane and the endoplasmic reticulum membrane, which actively pump Ca²⁺ out of the cytosol.

- Ca^{2+} pumps are ATPases that work in much the same way as the Na^{+} pump. The main difference is that Ca^{2+} pumps return to their original conformation without a requirement for binding and transporting a second ion.

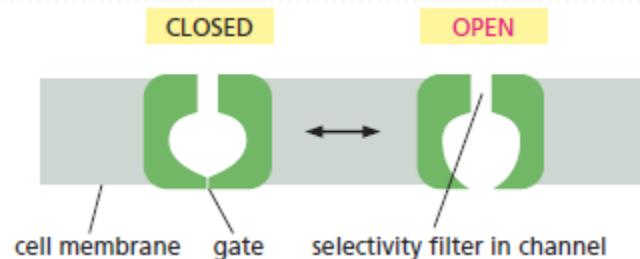
Ca^{2+} Pumps



Channels

- In principle, the simplest way to allow a small water-soluble molecule to cross from one side of a membrane to the other is to create a hydrophilic channel through which the molecule can pass.
- Channel proteins, or channels, perform this function in cell membranes, forming transmembrane pores that allow the passive movement of small water-soluble molecules into or out of the cell or organelle.
- Most of the channels in the plasma membrane form narrow, highly selective pores.
- The bulk of a cell's channels facilitate the passage of select inorganic ions.

- Two important properties distinguish ion channels from simple holes in the membrane.
 - First, they show *ion selectivity*, permitting some inorganic ions to pass but not others. Ion selectivity depends on the diameter and shape of the ion channel and on the distribution of the charged amino acids that line it.
 - Second, ion channels are not continuously open. Instead, ion channels open only briefly and then close again. Most ion channels are *gated*: a specific stimulus triggers them to switch between a closed and an open state by a change in their conformation.
- By the active transport by pumps, the concentrations of most ions are far from equilibrium across a cell membrane.
- When an ion channel opens, therefore, ions usually flow through it, moving rapidly down their electrochemical gradients. This rapid shift of ions changes the membrane potential.
- It is the rapid opening and closing of ion channels, which occurs within milliseconds, that matters most for this type of cell signaling.



Ion Channels and Nerve Cell Signaling

- The fundamental task of a nerve cell, or neuron, is to receive, integrate, and transmit signals. Neurons carry signals inward from sense organs, such as eyes and ears, to the *central nervous system*—the brain and spinal cord.
- In the central nervous system, neurons signal from one to another through networks of enormous complexity, allowing the brain and spinal cord to analyze, interpret, and respond to the signals coming in from the sense organs.
- No matter what the meaning of the signal a neuron carries—whether it is visual information from the eye, a motor command to a muscle, or one step in a complex network of neural processing in the brain—the form of the signal is always the same: **it consists of changes in the electrical potential across the neuron's plasma membrane which is provided by Na⁺ channels.**

