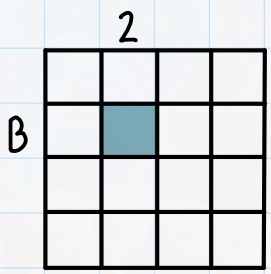
B2.1 Membranes and Membrane Transport

Guiding Questions
How do molecules of lipid and protein assemble into biological membranes?
What determines whether a substance can pass through a biological membrane?

Linking Questions
What processes depend on active transport in biological systems?
What are the roles of cell membranes in the interaction of a cell with its environment?



Theme: Form and Function

Level of Organization: Cells

Written and drawn by:

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NOTEWORTHY SCIENCE

MARIER

https://www.artstation.com/artwork/VgyEbR

SL Learning Content

B2.1.1	Lipid bilayers as the basis of cell membranes	Phospholipids and other amphipathic lipids naturally form continuous sheet-like bilayers in water.
B2.1.2	Lipid bilayers as barriers	Students should understand that the hydrophobic hydrocarbon chains that form the core of a membrane have low permeability to large molecules and hydrophilic particles, including ions and polar molecules, so membranes function as effective barriers between aqueous solutions.
B2.1.3	Simple diffusion across membranes	Use movement of oxygen and carbon dioxide molecules between phospholipids as an example of simple diffusion across membranes.
B2.1.4	Integral and peripheral proteins in membranes	Emphasize that membrane proteins have diverse structures, locations and functions. Integral proteins are embedded in one or both of the lipid layers of a membrane. Peripheral proteins are attached to one or other surface of the bilayer.
B2.1.5	Movement of water molecules across membranes by osmosis and the role of aquaporins	Include an explanation in terms of random movement of particles, impermeability of membranes to solutes and differences in solute concentration.
B2.1.6	Channel proteins for facilitated diffusion	Students should understand how the structure of channel proteins makes membranes selectively permeable by allowing specific ions to diffuse through when channels are open but not when they are closed.
B2.1.7	Pump proteins for active transport	Students should appreciate that pumps use energy from adenosine triphosphate (ATP) to transfer specific particles across membranes and therefore that they can move particles against a concentration gradient.
B2.1.8	Selectivity in membrane permeability	Facilitated diffusion and active transport allow selective permeability in membranes. Permeability by simple diffusion is not selective and depends only on the size and hydrophilic or hydrophobic properties of particles.
B2.1.9	Structure and function of glycoproteins and glycolipids	Limit to carbohydrate structures linked to proteins or lipids in membranes, location of carbohydrates on the extracellular side of membranes, and roles in cell adhesion and cell recognition.
B2.1.10	Fluid mosaic model of membrane structure	Students should be able to draw a two-dimensional representation of the model and include peripheral and integral proteins, glycoproteins, phospholipids and cholesterol. They should also be able to indicate hydrophobic and hydrophilic regions.

HL Learning Content

B2.1.11	Relationships between fatty acid composition of lipid bilayers and their fluidity	Unsaturated fatty acids in lipid bilayers have lower melting points, so membranes are fluid and therefore flexible at temperatures experienced by a cell. Saturated fatty acids have higher melting points and make membranes stronger at higher temperatures. Students should be familiar with an example of adaptations in membrane composition in relation to habitat.
B2.1.12	Cholesterol and membrane fluidity in animal cells	Students should understand the position of cholesterol molecules in membranes and also that cholesterol acts as a modulator (adjustor) of membrane fluidity, stabilizing membranes at higher temperatures and preventing stiffening at lower temperatures.
B2.1.13	Membrane fluidity and the fusion and formation of vesicles	Include the terms “endocytosis” and “exocytosis”, and examples of each process.
B2.1.14	Gated ion channels in neurons	Include nicotinic acetylcholine receptors as an example of a neurotransmitter-gated ion channel and sodium and potassium channels as examples of voltage-gated channels.
B2.1.15	Sodium–potassium pumps as an example of exchange transporters	Include the importance of these pumps in generating membrane potentials.
B2.1.16	Sodium-dependent glucose cotransporters as an example of indirect active transport	Include the importance of these cotransporters in glucose absorption by cells in the small intestine and glucose reabsorption by cells in the nephron.
B2.1.17	Adhesion of cells to form tissues	Include the term “cell-adhesion molecules” (CAMs) and the understanding that different forms of CAM are used for different types of cell–cell junction. Students are not required to have detailed knowledge of the different CAMs or junctions.

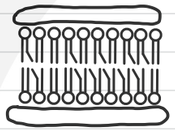
B2.1.1—Lipid bilayers as the basis of cell membranes. B2.1.2—Lipid bilayers as barriers. B2.1.4—Integral and peripheral proteins in membranes. B.2.1.9—Structure and function of glycoproteins and glycolipids. B2.1.10—Fluid mosaic model of membrane structure

Cell membranes are an essential component of all cells: ① allows internal conditions to be different from surroundings ② controls entry and exit of substances ③ allows sensitivity and communication

cell structure A2.2

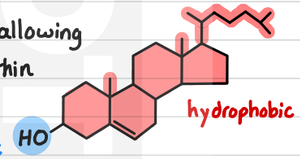
fluid mosaic model: accepted view of the cell membrane structure proposed by Singer and Nicolson (1972): dynamic, flexible structure made primarily of a phospholipid bilayer with proteins and carbohydrates.
↳ "fluid": components can move laterally + "mosaic": non-uniform, made of many different components (lipid, carbohydrate, and protein) in various configurations

※ the previous "protein-lipid sandwich" model by Dauson and Danielli (1935) was falsified using:



↳ immunofluescence where tagged membrane proteins moved laterally ▶ proteins were mobile i.e. fluid
↳ freeze-fracturing where the membrane bilayer was split open showing proteins ▶ integral transmembrane proteins

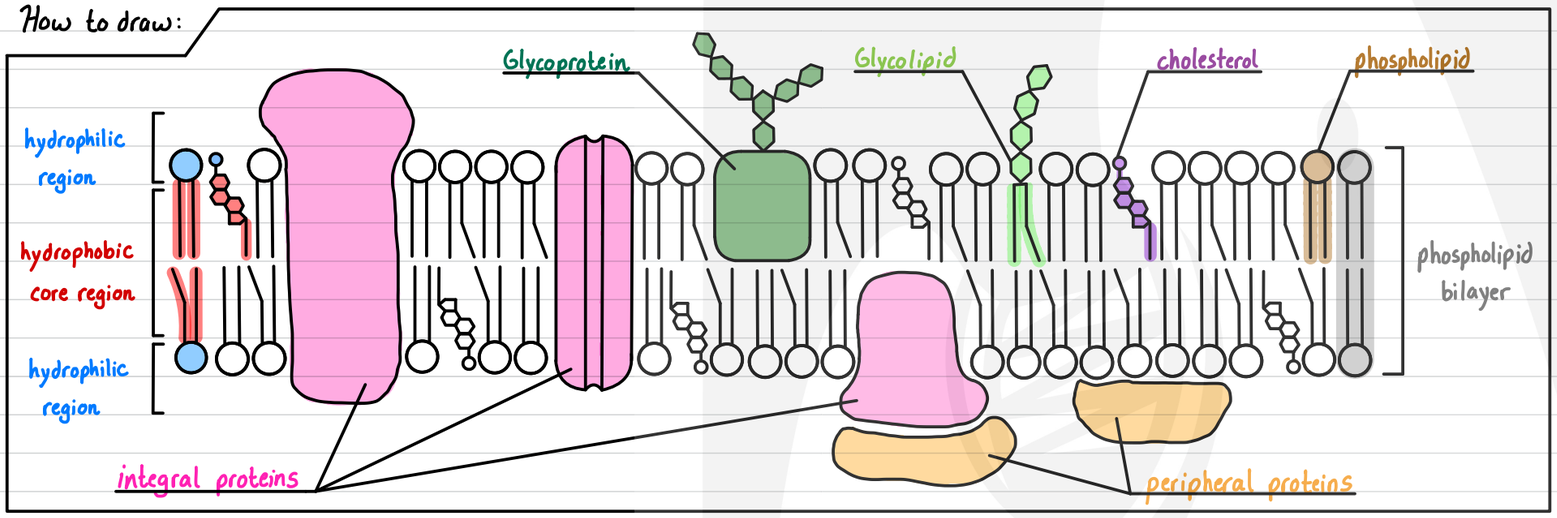
Cholesterol: amphipathic lipid, allowing it to integrate within bilayer



▶ help control membrane fluidity: ensuring they are not too fluid or too stiff

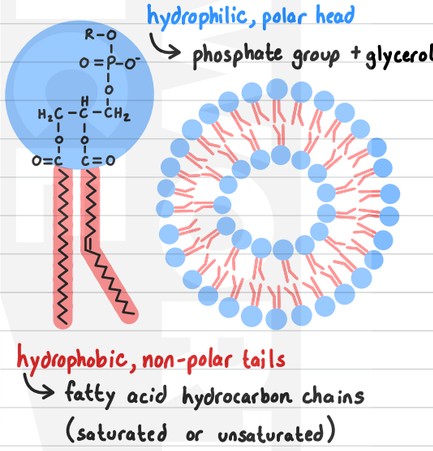
⟶ expanded in HL

How to draw:



Phospholipids are amphipathic and spontaneously form bilayers in solutions

lipids B1.1



↳ **semi-permeable** barrier between aqueous solutions i.e. inside and outside the cell:

✓ hydrophobic molecules - high permeability
ex: non-polar steroids (testosterone)

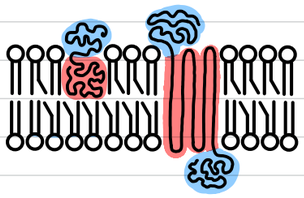
✓ very small non-polar molecules - high permeability
ex: O_2, CO_2

✓ small, uncharged polar molecules - permeable
ex: H_2O, ethanol, urea, glycerol

× large uncharged polar molecules
ex: glucose, sucrose
× charged molecules and ions
ex: amino acids, Na^+, K^+, Cl^-, Ca^{2+}, H^+
} low permeability require transport proteins

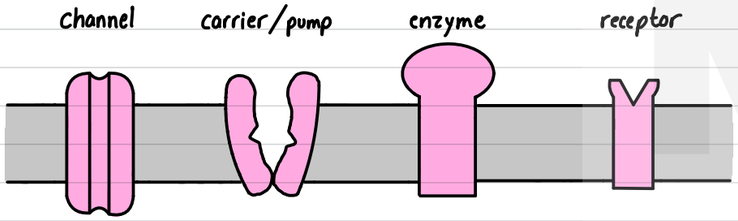
Integral proteins: proteins permanently embedded in the membrane

↳ monotopic (one side) ↳ transmembrane (both sides)



Integral membrane proteins are amphipathic; having hydrophilic regions and hydrophobic regions allowing them to integrate within the phospholipid bilayer

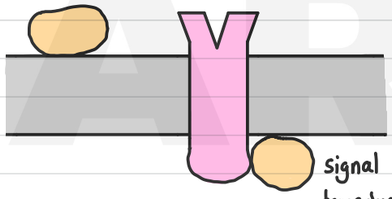
ex: channel carrier/pump enzyme receptor



Peripheral proteins: proteins attached (often temporarily) to the surface of the membrane or on an integral protein

Peripheral proteins are hydrophilic allowing them to interact on the surface of the bilayer

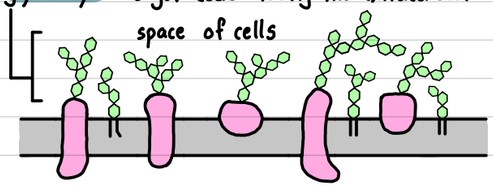
ex: transporter



Glycoprotein: polypeptide bound to a carbohydrate

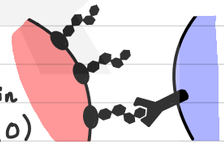
Glycolipid: lipid bound to a short carbohydrate chain

↳ **glycocalyx** "sugar coat" facing the extracellular space of cells

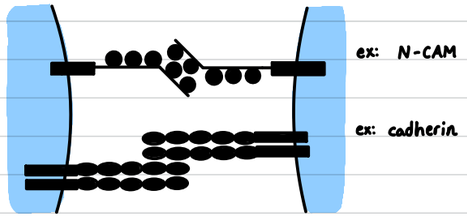


▶ cell recognition lipids B1.1
unique shape of glycoproteins and glycolipids act as antigen or surface markers, allowing cells to recognize self from non-self through binding

ex: red blood cells have glycoprotein antigens (A, B, O)



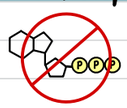
▶ cell adhesion ⟶ expanded in HL
glycocalyxes of adjacent cells fuse, holding cells and tissues together



B2.1.3—Simple diffusion across membranes. B2.1.5—Movement of water molecules across membranes by osmosis and the role of aquaporins. B2.1.6—Channel proteins for facilitated diffusion. B2.1.7—Pump proteins for active transport. B2.1.8—Selectivity in membrane permeability

Many of the processes of life (such as metabolism, homeostasis, nutrition, excretion) require transport of materials in and out of cells. This can occur both passively or actively

Passive transport: net movement of particles from an area of high concentration to low concentration without the use of ATP

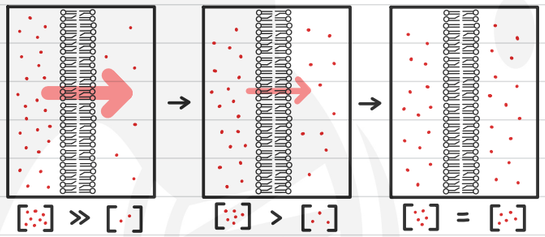


- particles are constantly in random motion (due to kinetic energy) and move independent of each other but as there are more particles in areas of high concentration that can randomly move to areas of low concentration than the other way around, a net movement from high to low concentration will occur passively.
- rate can be increased by increasing concencentration gradient and membrane surface area and decreasing distance needed to move

↳ **Simple diffusion**: passive net movement of particles from an area of high concentration to low concentration in fluids (gas or liquid)

- small / non-polar molecules can diffuse easily across membranes
  - small → able to pass in between phospholipid molecules
  - non-polar → able to pass through hydrophobic core easily

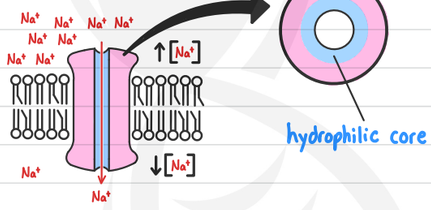
  ex: O_2, CO_2, steroids (testosterone and oestradiol)



※ not selective: only depends on size and water-affinity

↳ **Facilitated diffusion**: passive net movement of particles from an area of high concentration to low concentration using membrane proteins (such as channel or carrier proteins)

- **Channel proteins**: integral membrane proteins which have a hydrophilic pore allowing a passage for charged (Na^+, K^+, Cl^-, Ca^{2+}) or polar molecules (glucose, water) to cross the membrane's hydrophobic core easily

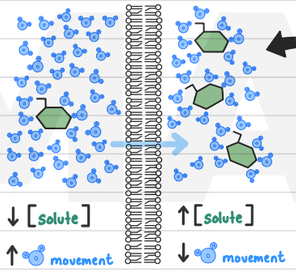


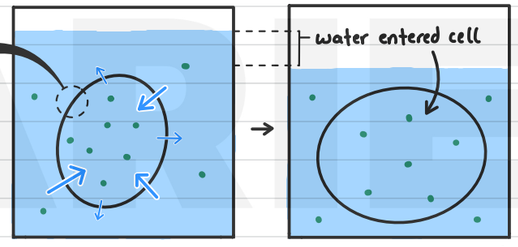
※ channels are selectively permeable: shape/size/charge of pore ensures specificity ex: Na^+ channels only allow Na^+ some (like voltage-gated ion channels) can be open or closed, allowing control

↳ **Osmosis**: passive net movement of water from an area of low solute concentration to high solute concentration across a semi-permeable membrane

water potential D2.3

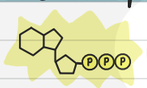
- membranes allow the passage of water but restrict the movement of larger or charged solutes, thus causing water to move more
- when water is interacting with and dissolving solutes its movement is restricted ▶ water in a dilute solution is more free and likely to move to a more concentrated solution
- equilibrium when overall solute concentration is equal on both sides



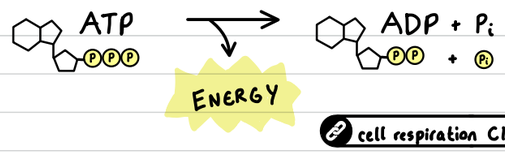


cell is more concentrated ∴ takes in water (net)

Active transport: movement of particles from an area of low concentration to high concentration using ATP



- particles in an area of low concentration are less likely to move to an area of high concentration then the other way around, thus for this to occur reliably an external energy input is required
- ATP is the cell's 'energy currency' storing potential energy from cellular respiration. When hydrolyzed it releases this energy to power metabolic processes

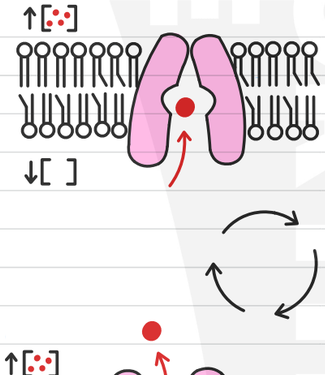


cell respiration C1.2

- **Pump proteins**: transmembrane proteins which use chemical energy - ATP in order to transport particles across membranes against their concentration gradient ex: sodium-potassium pump

※ Pump proteins allow selective permeability: only transport specific ions or molecules in one direction

neural signaling C2.2



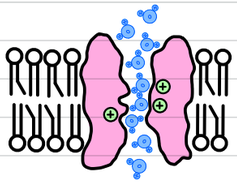
1 Pump protein in its stable conformation is open to one side of membrane. It has high affinity to particle (•) and binds to it.

2 ATP is hydrolyzed to ADP, releasing energy. Energy causes a conformational change to a more unstable form, causing it to be open to the other side of the membrane

3 Pump is open to other side and has low affinity for particle, releasing it against its concentration gradient. Pump reverts back to its original, stable conformation - ready for reuse

Aquaporins: channel proteins which selectively allow passage of water

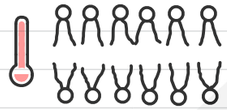
- greatly increases permeability to water and osmotic rate
- located in collecting ducts in kidneys and plant roots for water absorption



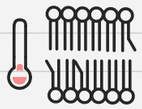
Aquaporin has a very narrow pore which is positively charged only allowing water through (excluding H^+)

HL B2.1.11—Relationships between fatty acid composition of lipid bilayers and their fluidity. B2.1.12—Cholesterol and membrane fluidity in animal cells. B2.1.13—Membrane fluidity and the fusion and formation of vesicles. B2.1.17—Adhesion of cells to form tissues

Temperature impacts membrane <u>fluidity</u> i.e. the degree of random movement of the components, namely phospholipids which can move laterally, rotate and even switch positions



more movement
greater fluidity
greater permeability

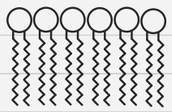


less movement
lower fluidity
lower permeability

Impact of phospholipid fatty acid composition on membrane fluidity

↳ the fatty acid composition of phospholipids can be saturated (no double bonds) or unsaturated (≥1 double bond) lipids B1.1

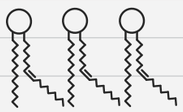
fatty acid tails → saturated
pack very tightly - high density
∴ high intermolecular forces
∴ high melting point



less fluid / more viscous
less permeable
less flexible

stronger
too solid

fatty acid tails → unsaturated
pack loosely - lower density
∴ low intermolecular forces
∴ low melting point



more fluid / less viscous
more permeable
more flexible

too fluid
fluid

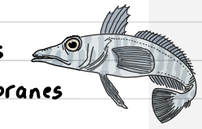
↳ General trend: the relative percentage composition of saturated and unsaturated fats differ depending on surrounding temperature

higher percentage of saturated fatty acids

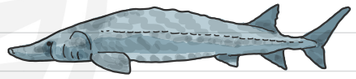
higher percentage of unsaturated fatty acids

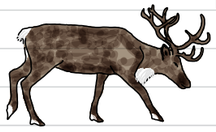
↳ Adaptation examples:

Fish living in Antarctic waters (such as C.hamatus) have membranes rich in unsaturated fatty acids



The temperate freshwater fish A.fulvescens increases its membrane unsaturated content when lake temperatures decrease

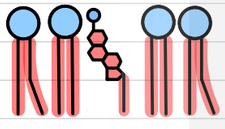




The caribou R.tarandus has different membrane fatty acid composition in different tissues, as a trend: the further away tissues are from the body core, the more unsaturated fatty acids (hooves > upper leg > body)

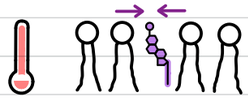
Impact of cholesterol on membrane fluidity

↳ cholesterol embeds itself in the plasma membrane as its amphipathic - OH 'head' is polar, body is non-polar

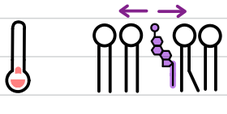


※ cholesterol is present in animal but not plant membranes

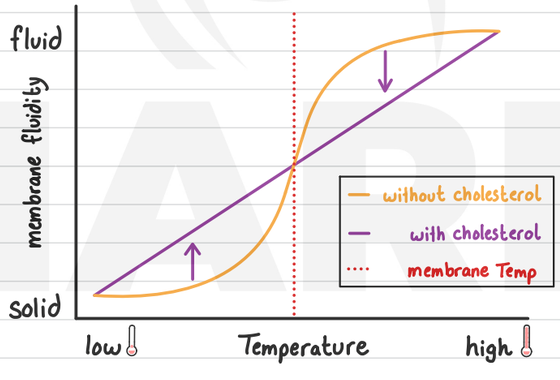
↳ cholesterol acts as a membrane fluidity <u>modulator</u>:



Cholesterol decreases fluidity by constraining phospholipid movement - stabilizing membrane



Cholesterol increases fluidity by disrupting phospholipid tight packing - preventing stiffening

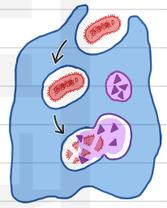


The fluidity of the membrane allows for phospholipid bilayers to change shape and fuse, and thus the formation (endocytosis) and fusion (exocytosis) of vesicles

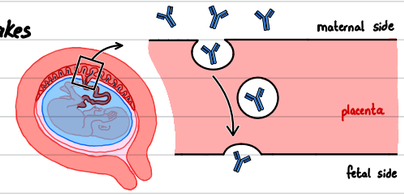
Endocytosis: the formation of a vesicle from the invagination and pinching off of a piece of the plasma membrane - bringing <u>extracellular content</u> within the cell
Process requires ATP
fluids (pinocytosis) ↔ solids (phagocytosis)

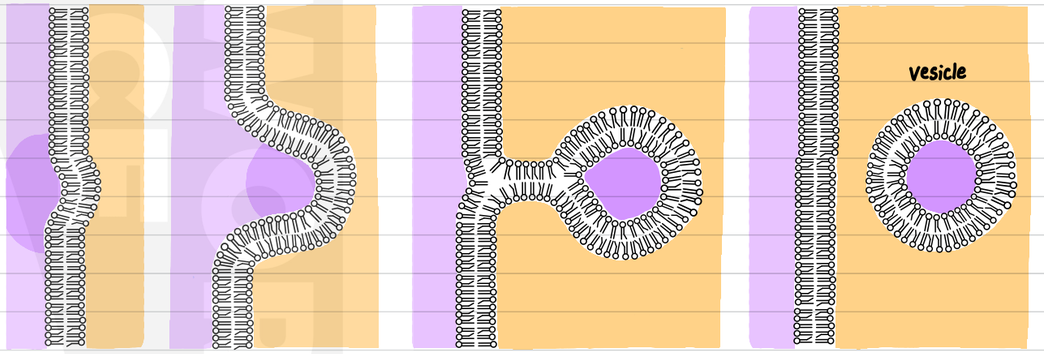
ex:

Phagocytic white blood cells and paramecia engulf and destroy pathogens / food particles using phagocytosis



Developing fetus takes in antibodies into its blood stream from the mother via the placenta

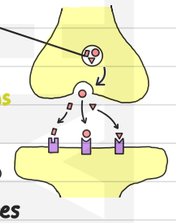




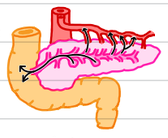
Exocytosis: the fusion of vesicle a with the plasma membrane - discharging vesicle contents into the extracellular space (i.e. outside the cell). Process requires ATP

ex:

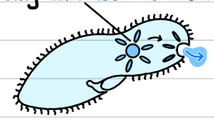
Neurotransmitters (such as Acetylcholine) are released by neurons during Synaptic transmission in order to propagate nerve impulses



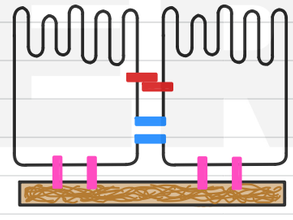
Pancreas secretes digestive enzymes (such as lipase) into the duodenum and hormones (such as insulin) into the blood stream for signaling



Paramecia osmoregulate by loading and expelling excess water using contractile vacuoles



cell-adhesion molecules (CAMs): cell-surface proteins/glycoproteins which link cells with other cells forming junctions - providing structure and tissue formation



↳ seal cells together, creating a barrier
↳ act as a bridge, allowing communication and material exchange
↳ connect cells to extracellular matrix, providing anchorage

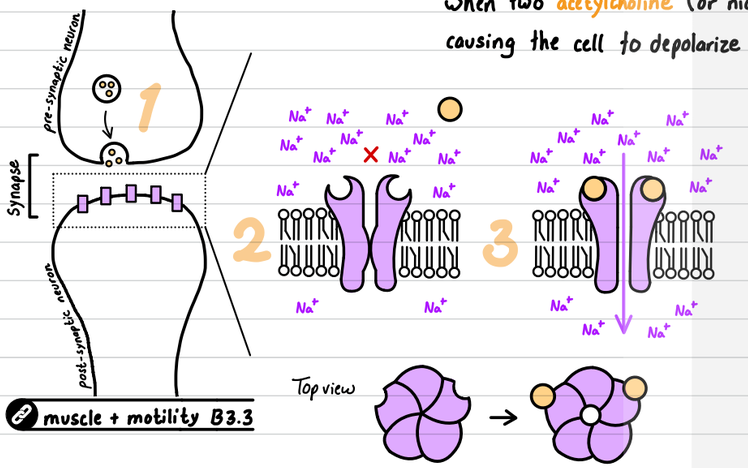
HL B2.1.14—Gated ion channels in neurons. B2.1.15—Sodium–potassium pumps as an example of exchange transporters. B2.1.16—Sodium-dependent glucose cotransporters as an example of indirect active transport

Channel proteins allow for facilitated diffusion, transporting specific materials that otherwise would only diffuse slowly or not at all across a phospholipid bilayer (such as ions). While they do not control direction of flow (always a net flow high to low concentration) they can be opened or closed reversibly to control transport

Neurotransmitter-gated ion channel: Transmembrane protein channels which allow the diffusion of a specific ion 'Gated' as they open or close in response to binding of a neurotransmitter

※ neurotransmitters are signalling molecules which are secreted by a neuron at synapses to cause an effect
ex: Acetylcholine, Glutamate, GABA, Dopamine, Serotonin, Epinephrine

↳ **Nicotinic acetylcholine receptors**: gated ion channel allowing diffusion of sodium (Na^+) into the cell when two acetylcholine (or nicotine) molecules bind to the receptor, causing the cell to depolarize and an action potential to be propagated



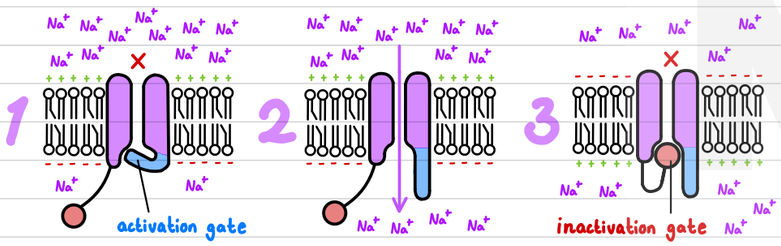
1 Acetylcholine is secreted from the pre-synaptic neuron into the synaptic cleft and diffuses across
2 Before binding, receptor is closed, preventing Na^+ from diffusing
3 Two Acetylcholine molecules bind to the receptor, inducing a conformational change, opening a pore and allowing Na^+ to diffuse through

muscle + motility B3.3

Voltage-gated ion channel: Transmembrane protein channels which allow the diffusion of a specific ion 'Gated' as they open or close in response to a specific membrane potential (voltage)

※ potential difference or voltage is the amount of electric potential energy between two points (V or JC^{-1})
membrane potential is the difference in electric potential (V) between the inside and outside of the cell
↳ inside of the cell ~ -70mV compared to the outside → generated by the sodium-potassium pump

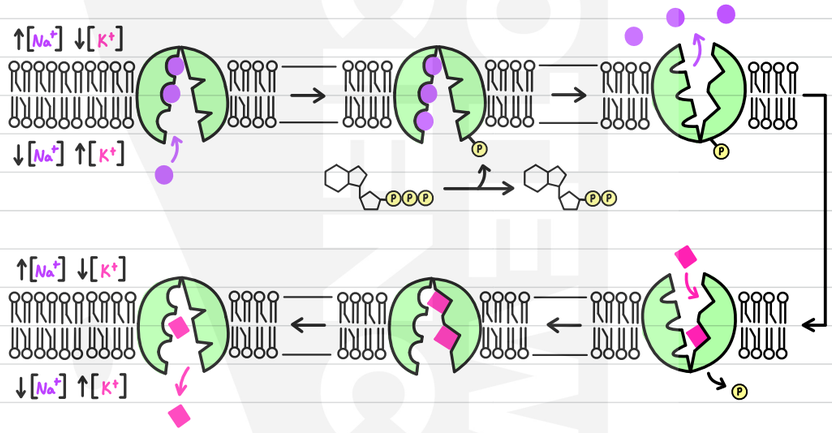
↳ **voltage-gated sodium channel**: gated ion channel allowing diffusion of sodium (Na^+) into the cell when there is an increase in membrane potential (-70mV to -55mV) causing the cell to depolarize (negative to positive)



1 activation gate closes channel, blocking Na^+ diffusion (-70mV)
2 activation gate opens, allowing Na^+ to diffuse into cell (-55mV)
3 inactivate gate rapidly closes channel, halting Na^+ diffusion (30mV)

Exchange transporters (antiporter): Transmembrane protein which transports different substances in opposite directions across the membrane against their respective gradients, thus 'exchanging' them

↳ **Sodium-Potassium pump** (Na^+/K^+-ATPase): exchange transporter moving 3 Na^+ and 2 K^+ against their respective concentration gradients across the membrane using ATP

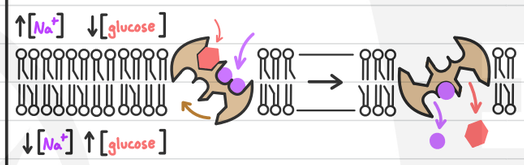


1 Pump binds 3 Na^+ from cytoplasm of cell with high affinity
2 ATP is hydrolyzed to ADP, binding phosphate to (phosphorylating) pump
3 Phosphorylation causes a change in pump conformation, reducing its affinity for Na^+, releasing 3 Na^+ outside cell
4 New pump shape binds 2 K^+ from outside cell with high affinity
5 Binding K^+ triggers release of phosphate, causing pump to revert to original conformation and release 2 K^+ into cell
Pump ready for reuse.

※ as the pump undergoes unequal exchange of cations (lose 3, take in 2) it maintains a relative negative membrane potential (-70mV)

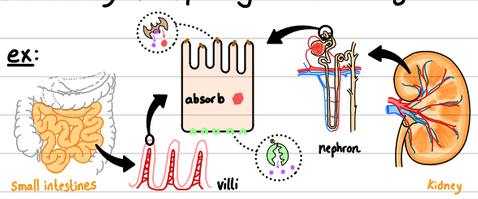
Indirect active transport: uses the energy produced by the movement of one substance down its concentration gradient to transport another against its concentration gradient. Direct ATP use not required

↳ **Sodium-glucose cotransporter** (symporter): cotransporter protein which transports glucose against its concentration gradient into the cell using the energy from simultaneously transporting Na^+ down its gradient



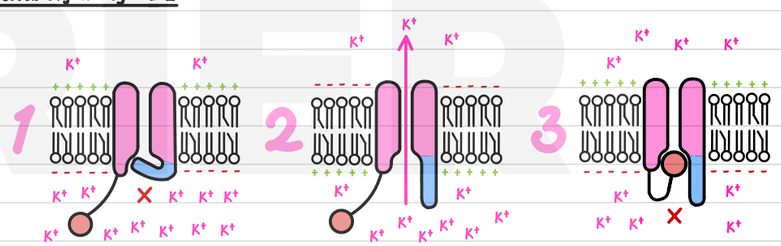
Na^+ moves down its gradient binding onto cotransporter. This energy is used to bind and move glucose into cell

ex:



↳ **voltage-gated potassium channel**: gated ion channel allowing diffusion of potassium (K^+) out of the cell when the membrane potential has flipped (-70mV to 30mV) causing the cell to repolorize (positive to negative)

neural signalling C2.2

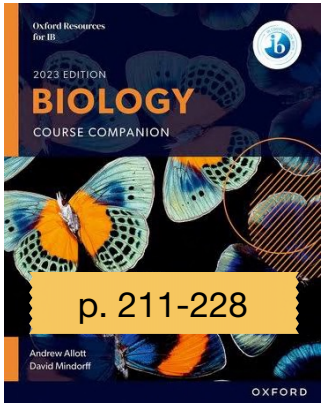


1 activation gate closes channel, blocking K^+ diffusion (-70mV)
2 activation gate opens, allowing K^+ to diffuse out of cell (30mV)
3 inactivate gate rapidly closes channel, halting K^+ diffusion (-70mV)

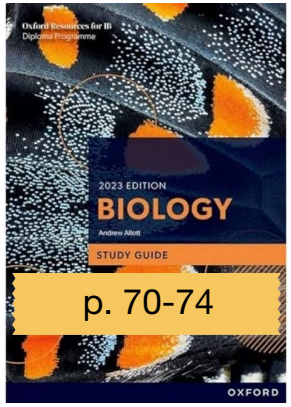
Resource Links

each resource is hyperlinked

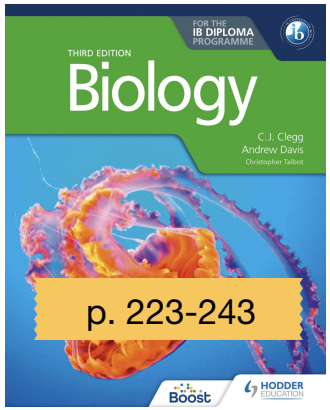
Textbooks



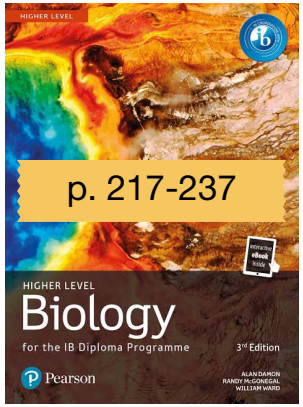
p. 211-228



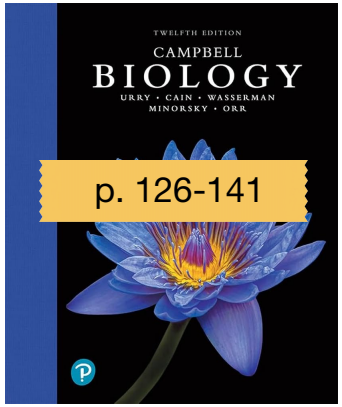
p. 70-74



p. 223-243

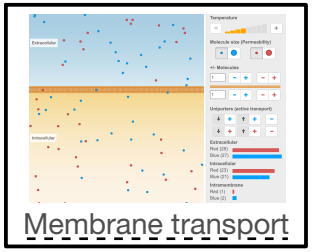


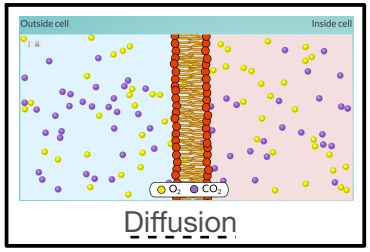
p. 217-237



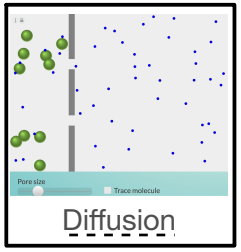
p. 126-141

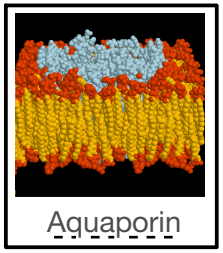
Simulators / Interactives


Membrane transport



Diffusion


Diffusion


Aquaporin

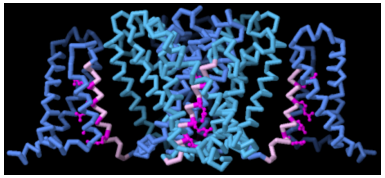
Articles

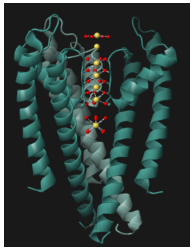
Benga G. (2012). The first discovered water channel protein, later called aquaporin 1: molecular characteristics, functions and medical implications. Molecular aspects of medicine, 33(5-6), 518–534. https://doi.org/10.1016/j.mam.2012.06.001

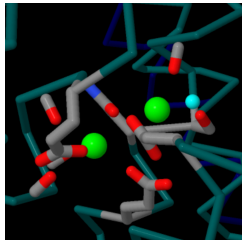
Ernst, R., Ejsing, C. S., & Antonny, B. (2016). Homeoviscous Adaptation and the Regulation of Membrane Lipids. Journal of molecular biology, 428(24 Pt A), 4776–4791. https://doi.org/10.1016/j.jmb.2016.08.013

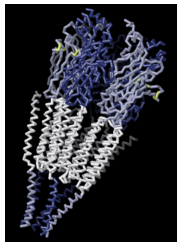
Janiszewska, M., Primi, M. C., & Izard, T. (2020). Cell adhesion in cancer: Beyond the migration of single cells. The Journal of biological chemistry, 295(8), 2495–2505. https://doi.org/10.1074/jbc.REV119.007759

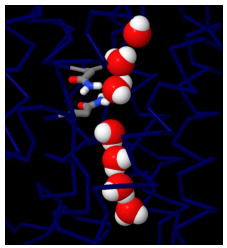
3D models

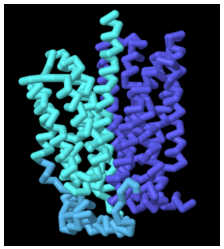

Voltage-gated Sodium channel

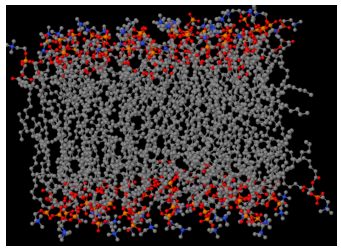

Potassium channel


Sodium-Potassium Pump


Acetylcholine Receptor


Aquaporin


Glucose transporters


Phospholipid bilayer