PHSL2101 Summary Notes

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Learning Aims:
- Define the study of physiology
- Describe very generally two examples go single cell function
- Be able to define what is meant by excitable cells and give some examples
- Appreciate single cells use chemical and electrical signalling
- Schematically draw a cell membrane and to identify the functional components of a typical membrane phospholipid and give an example
- Know the terms polar and non-polar and how to relates to membranes and ions
- Relate the basic components of an electrical circuit to a potential different across the cell membrane

Excitable Cells: textbook references — chapters 1,2,4,5,7 & 8

What is is physiology?

The study of body function and its systems - circulatory (cardiovascular), nervous, respiratory, digestive, skeletal, and muscular ect. Physiology gives a basis of how the body normally functions to then understand the bodies limits and disease. We learn the basis principals to then understand how these apply under different systems and circumstances.
All these systems are made up of many different cells, and hence we first learn about cell physiology to then apply to these systems.

Cell physiology: the functions of single cells

Cells are the basic funded uni and come in different and complex shapes and forms. Cells are autonomous units that can function by themselves, where the plasma membrane allows a separation to the extracellular environment.

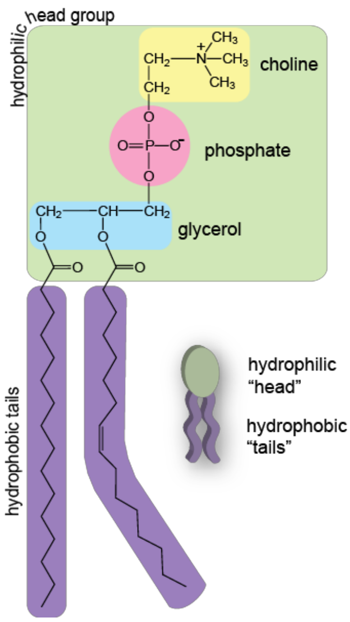
Excitable cells

These are cells with a potential difference (or voltage) across their membrane - such as neurons in the brain. Can also be thought of as cells that:
- Use electrical and/or chemical signalling
- Move substances across their membranes

Hence this includes most cells, such as nerve cells, muscle cells, and epithelial cells.
The clinical implications of these cells involves diseases such as epilepsy, anxiety, depression, and drugs such as sedatives and alcohol.

Cell examples
- Hair cells, which respond to sound by moving, which amplifies sound to send to our auditory cortex where the sound is interpreted. The movement is triggering molecular switches, which allows ion channels to open, allowing ion movement across the membrane, changing the electrical potential in the hair cells. This electrical signal can then be transmitted to brain ect.
- Nerve cells, which responds to stimuli with electrical impulses, called the **action potential**, which is a sudden change in the voltage inside the cell. When a nerve cell is 'resting' it has an internal potential of about -80mV (mili volts) in regards to the voltage outside the cell. When an action potential occurs, it's generally by 100mV, hence changing the internal potential to +20. Hence there are cycles of different electrical patterns in cells depending on stimuli, such as brain cells waking up.
- Muscle Cells, which can move and contract alone, without surrounding connective tissue or tendons. There are three types of muscle cells, cardiac skeletal and smooth muscle. Therefore the muscle cells in our heart move and contract to pump blood via electrical signals. In isolation, cardiac cells can still maintain their intrinsic contraction rhythm, without signals from the brain. Although, once in isolation, the cells cannot change this rhythm under different circumstances, such as when exercising. Also note that different cardiac muscles have different functions throughout the heart, with different action potentials. Smooth muscle isn't under voluntary control like cardiac muscle, and is found in internal organs, such as the intestines to allow for peristalsis.

Review Question:
Which of the following is an example of the function of a single cell?
A. Beating of the heart to pump blood
B. Transition of sound waves into perceived sounds
C. Generation of an action potential in a skeletal muscle cell
D. Waking up in response to neural signals



The cell membrane
The critical component for excitable cells. It separates the intracellular and extracellular environment, allowing cells to function autonomy, hence differentiate and mediate different functions. Apart of this differentiation is the different types of proteins and signalling pathways in the lipid membrane.

The lipid bilayer membrane, which consists of a non-polar tails (hydrophobic) and polar (hydrophilic) heads. Polarity refers to having partial charges which are arranged in an uneven distribution.
The tail is a hydrocarbon chain (CH2), where the straight tail is saturated and the bent tail is unsaturated with a cis-double bond.

The head has a glycerol connector, phosphate group, and can have different head groups, such as choline. If the phosphate group is present, it is a phospholipid, but this can be replaces with other molecules to make sphingolipids, glycolipids, and cholesterol.

Membrane proteins
Proteins imbedded in the phospholipid bilayer, which have many functions, including cell signalling for communication. Transport proteins help generate membrane potential, bring glucose in for energy, or carry metabolic waste out of the cell.
They come in many sizes and shapes, some more complex than others, with multiple peptides or being tethered to the membrane rather than embedded.

Cell membrane properties
The bi-lipid layer and the imbedded proteins work together to give the membrane important features:
- Essentially water and solute impermeant
- Hydrophobic/non-polar substances can cross
- Excellent electrical insulation (-100mV / 10nm = 10-5V /cm) - Hence allows separation of electrical charges (different internal and external charge)
- Behaves as a capacitor which effects the voltage response of the cell to stimulation (current injection)
- A capacitor is the combination of two conductors or charged plates (internal and external) separated by an insulating material (the lipid)

Another cell: epithelial cells, which function is to transport from one compartment to another.

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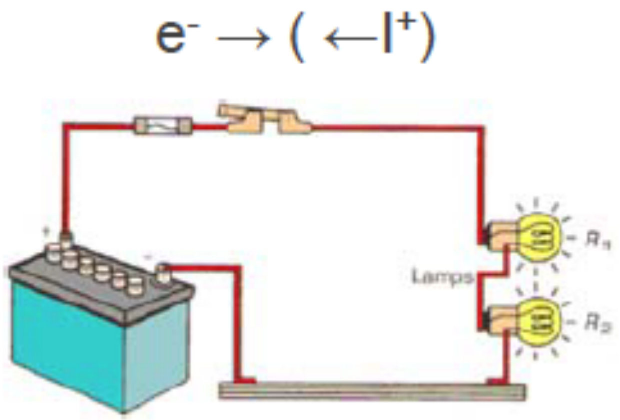
Cell membrane signalling protein example: Photoreceptor cells in our retina, which respond to photons of light. Light activities the photoreceptor cells as it passes through the retina, and acts on a protein called rhodopsin, which is in the membrane of photoreceptor cells. This eventually leads to signals being send to the visual cortex which allows the response to light. Each photoreceptor cell can have up to 100 million rhodopsin proteins.

Excitable Cells
Excitable cells are polarised - they have a different voltage/potential inside the cell with respect to the outside. This involves moving charged ions and other solutes (substances dissolved in solution) across their cell membrane.

Biological energy

In an electrical circuit, the battery provides the driving force. The circuit is complete when the switch is closed, and the current (movement of charge) is carried by electrons flowing in a conductor (wire). The current flows through a resistor (light bulb) to cause a response. Current doesn't pass through an object with high resistance well, and is hence a bad conductor.



Glossary of Electrical Terms

Charge (Q or q) : property of matter, negative or positive. Measured in Columbus (C). A single e- has a charge of 10-19.

Voltage (V) : the electrical force exerted on charged substance (once charge has been separated, giving potential energy)

Current (I): the flow of charge, measured in amperes (A)

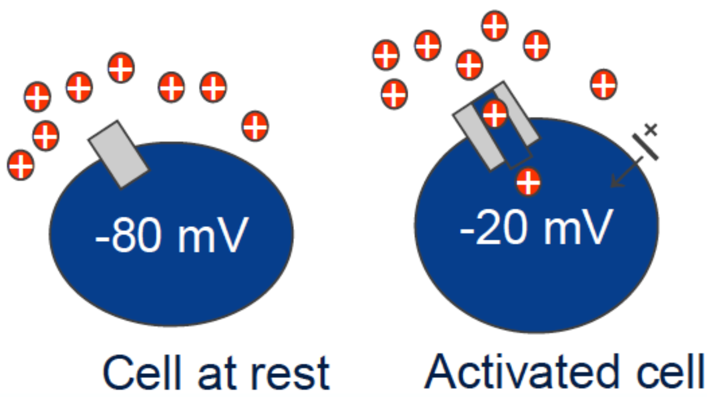
Resistance : measure of how easily charge can move given a potential difference (R+V/I, Ohm's Law)

Capacitance (C) : ability to store separated charge - two conductors separated by an insulator (C = Q/V). Units in Farads (1F - C/V)

In excitable cells, the electrochemical potential provides the driving force, the switch is an ion channel and the current is carried by **ions** (a cation in adjacent figure) to results in a response (depolarization).
The inside of a cell will have a negative potential, and the outside a positive.

Ions in solution

An Experiment with Copper Sulphate ($CuSO_4$), a salt where copper atoms are blue.
This compound will dissolve in water, due to partial charges (dipoles) on a water molecule. Hence ions in solutions are surrounded by stabilised water molecules, making the compound hydrated.
The polar water molecule will start to break up the ionic bonds of CuSO4, and surround the cation and anion. These ions are now free to move independently, such as moving across the cell membrane.



What will happen when paraffin oil is added to the solution of dissolved $CuSO_4$, and then stirred?
A. It will turn blue. Why?
B. It will remain clear. Why?
C. It will explode. Why?

The oil will remain clear, and float on top of the dark blue layer of dissolved CuSO4. Hence, the compound cannot dissolve in non-polar compounds, such as oil or the plasma membrane.

How can substances cross the cell membrane?

1. Passive Diffusion
   a. Simple diffusion
   b. Facilitated diffusion
2. Active Diffusion
3. Via incorporation into lipid vesicle, eg exo and endocytosis

Diffusion

Where substances move passively from a high concentration to a high concentration, due to **Brownian** (random thermal) motions.

- A high concentration of a substance in the centre of a container, will diffuse out to evenly fill the container.
- Individual molecules will smash into each other, and these collisions help push the molecules around to spread out.
- Adding a force of gravity will push movement downwards
- Declining the temperature will slow down movement.
- The larger the space, the lower the concentration will be, and given a gap to diffuse out of, diffusion will be quicker given a smaller gap.
- Will be rapid across small distances (e.g., within or across a single cell), but too slow for signalling over long distances (e.g., from brain to muscle, from adrenal gland to heart - hence electrical and hormone communication).

Fick's general law of Diffusion

Fick's Law is that the rate of diffusion is directly proportional to the concentration gradient and the area available for diffusion. It is also indirectly proportional to the thickness of the gap in which a substance can diffuse.

J = DA (dC/dx)

Where:

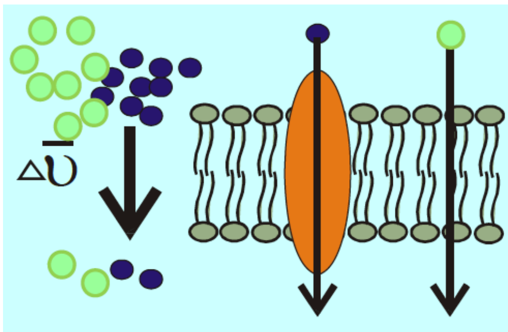
A = the area of the interface

dC/dx = solute concentration gradient across the interface (width = x)

D = the diffusion coefficient (how well a substance diffuses, for example a neurotransmitter across a synapse)

= a proportionality constant that varies directly with the speed of random motion (depends on molecule properties such as size)

The Partition coefficient (K) in J = DKA (dC/dx) refers to how well a substance dissolves in lipids (such as the membrane bilayer). Some ions might have a low partition coefficient, but a high rate of diffusion, due to the aid of facilitated diffusion.



Passive Diffusion across the membrane

1. Simple Diffusion
    - Lipid soluble (hydrophobic substances)
    - Through the membrane
    - Eg gases, steroids, hydrophobic drugs
2. Facilitated Diffusion
    - Water soluble (hydophyllic substances)
    - Via a protein (carrier or channel)
    - Eg ions, glucose, amino acids

Carrier mediated diffusion has a binding site, which causes a change in the shape of the protein, moving the substance through to the other side of the membrane. This binding point can be shaped so specifically, that only the L glucose molecule can pass through, and D glucose can not. The only difference between these molecules is the different position of one of the carbon groups (but still has the same formula).

Hence, **Occluded access** (to close or block).

These proteins look ribbon like, made of one or more often many polypeptides put together.

Facilitated diffusion is dependant on:

1. Specificity
2. Competition
3. Saturation

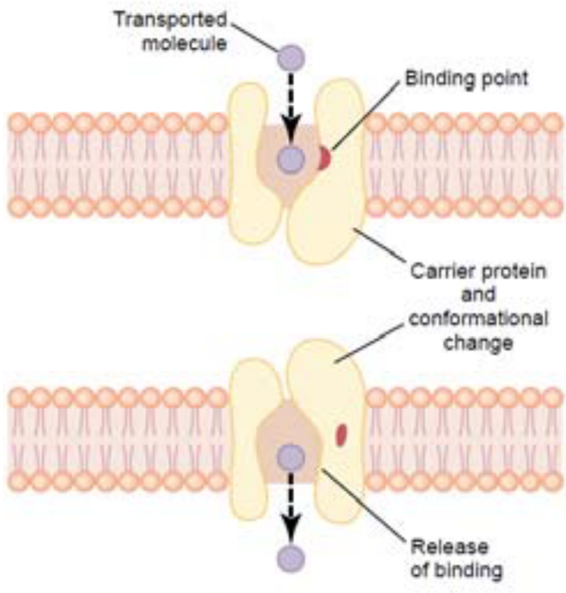


Figure 4–7

Postulated mechanism for facilitated diffusion.