

C2.2 Neural Signalling

Guiding Questions

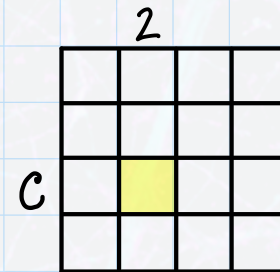
How are electrical signals generated and moved within neurons?

How can neurons interact with other cells?

Linking Questions

In what ways are biological systems regulated?

How is the structure of specialized cells related to function?



Theme: Interactions + Interdependence

Level of Organization: Cells

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SL Learning Outcomes

C2.2.1	Neurons as cells within the nervous system that carry electrical impulses	Students should understand that cytoplasm and a nucleus form the cell body of a neuron, with elongated nerve fibres of varying length projecting from it. An axon is a long single fibre. Dendrites are multiple shorter fibres. Electrical impulses are conducted along these fibres.
C2.2.2	Generation of the resting potential by pumping to establish and maintain concentration gradients of sodium and potassium ions	Students should understand how energy from ATP drives the pumping of sodium and potassium ions in opposite directions across the plasma membrane of neurons. They should understand the concept of a membrane polarization and a membrane potential and also reasons that the resting potential is negative.
C2.2.3	Nerve impulses as action potentials that are propagated along nerve fibres	Students should appreciate that a nerve impulse is electrical because it involves movement of positively charged ions.
C2.2.4	Variation in the speed of nerve impulses	Compare the speed of transmission in giant axons of squid and smaller non-myelinated nerve fibres. Also compare the speed in myelinated and non-myelinated fibres. Application of skills: Students should be able to describe negative and positive correlations and apply correlation coefficients as a mathematical tool to determine the strength of these correlations. Students should also be able to apply the coefficient of determination (R^2) to evaluate the degree to which variation in the independent variable explains the variation in the dependent variable. For example, conduction speed of nerve impulses is negatively correlated with animal size, but positively correlated with axon diameter.
C2.2.5	Synapses as junctions between neurons and between neurons and effector cells	Limit to chemical synapses, not electrical, and these can simply be referred to as synapses. Students should understand that a signal can only pass in one direction across a typical synapse.
C2.2.6	Release of neurotransmitters from a presynaptic membrane	Include uptake of calcium in response to depolarization of a presynaptic membrane and its action as a signalling chemical inside a neuron.
C2.2.7	Generation of an excitatory postsynaptic potential	Include diffusion of neurotransmitters across the synaptic cleft and binding to transmembrane receptors. Use acetylcholine as an example. Students should appreciate that this neurotransmitter exists in many types of synapse including neuromuscular junctions.

HL Learning Outcomes

C2.2.8	Depolarization and repolarization during action potentials	Include the action of voltage-gated sodium and potassium channels and the need for a threshold potential to be reached for sodium channels to open.
C2.2.9	Propagation of an action potential along a nerve fibre/axon as a result of local currents	Students should understand how diffusion of sodium ions both inside and outside an axon can cause the threshold potential to be reached.
C2.2.10	Oscilloscope traces showing resting potentials and action potentials	Application of skills: Students should interpret the oscilloscope trace in relation to cellular events. The number of impulses per second can be measured.
C2.2.11	Saltatory conduction in myelinated fibres to achieve faster impulses	Students should understand that ion pumps and channels are clustered at nodes of Ranvier and that an action potential is propagated from node to node.
C2.2.12	Effects of exogenous chemicals on synaptic transmission	Use neonicotinoids as an example of a pesticide that blocks synaptic transmission, and cocaine as an example of a drug that blocks reuptake of the neurotransmitter.
C2.2.13	Inhibitory neurotransmitters and generation of inhibitory postsynaptic potentials	Students should know that the postsynaptic membrane becomes hyperpolarized.
C2.2.14	Summation of the effects of excitatory and inhibitory neurotransmitters in a postsynaptic neuron	Multiple presynaptic neurons interact with all-or-nothing consequences in terms of postsynaptic depolarization.
C2.2.15	Perception of pain by neurons with free nerve endings in the skin	Students should know that these nerve endings have channels for positively charged ions, which open in response to a stimulus such as high temperature, acid, or certain chemicals such as capsaicin in chilli peppers. Entry of positively charged ions causes the threshold potential to be reached and nerve impulses then pass through the neurons to the brain, where pain is perceived.
C2.2.16	Consciousness as a property that emerges from the interaction of individual neurons in the brain	Emergent properties such as consciousness are another example of the consequences of interaction.

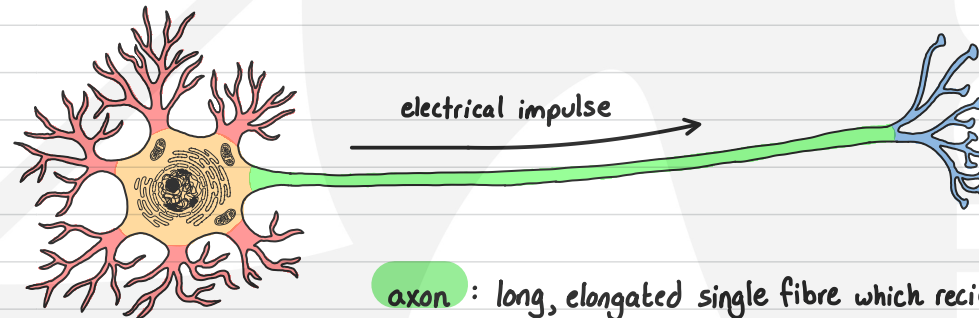
C2.2.1—Neurons as cells within the nervous system that carry electrical impulses. C2.2.2—Generation of the resting potential by pumping to establish and maintain concentration gradients of sodium and potassium ions.

C2.2.3—Nerve impulses as action potentials that are propagated along nerve fibres

neuron: or nerve cell is a specialized cell which is the primary component of the nervous system. It is adapted to receive and transmit signals in the form of electrical impulses (action potential) and chemicals (neurotransmitters)

Dendrites: multiple short fibres projecting from the cell body (soma) which receives electrical impulses and propagates them towards the cell body

cell body (soma): contains nucleus and other organelles



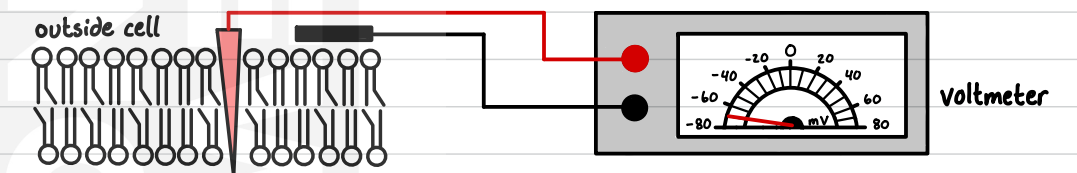
axon terminals: terminating portions of the branches of the axon which transmit electrical impulses from the axon to other cells at junctions (synapses) by using chemical neurotransmitters

axon: long, elongated single fibre which receives electrical impulses from soma and carries it away towards the axon terminals

Membrane potential: the potential difference (voltage) between the interior and exterior of a cell due to an imbalance of charges. Represents the energy (J) per charge (C) required to move a cation from outside to inside of a cell

Resting potential: the potential difference across the membrane of a neuron when it is not being stimulated (i.e. at rest)

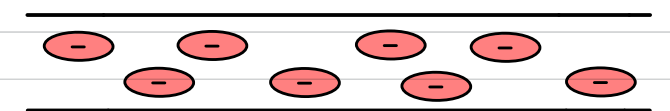
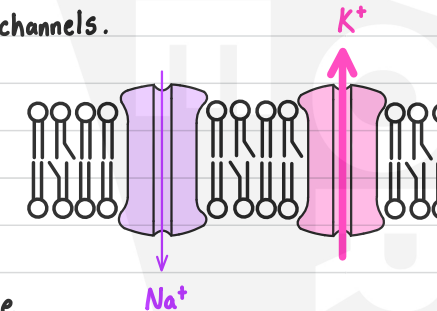
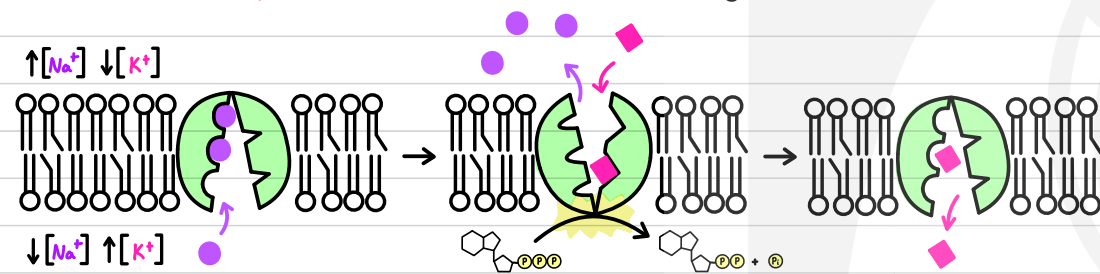
Typically it is around -70mV (i.e. the inside potential is 70mV less than the outside) and thus is polarized → how?



- Sodium-potassium pump** uses ATP to actively pump 3 sodium ions out of the cell and 2 potassium ions into the cell, creating a charge imbalance

- Na^+ and K^+ ions diffuse across the membrane down their concentration gradients through specific ion 'leak' channels. However, membrane is 50x more permeable to K^+ than Na^+
- ∴ rate of K^+ diffusion out is much greater than rate of Na^+ diffusion in, leading to imbalance

- Within the cell there are many negatively-charged molecules (organic anions) such as proteins further contributing to the relatively more negative interior



Nerve impulses: are action potentials (rapid, brief change in membrane voltage) which propagate along nerve fibres. ✖ These are electrical in nature as they involve the flow of charges, in this case cations: Na^+

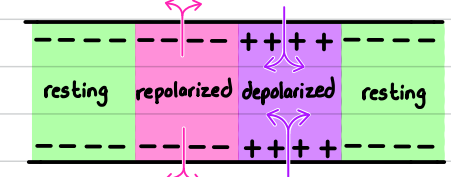
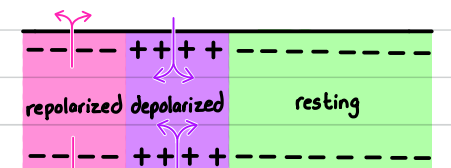
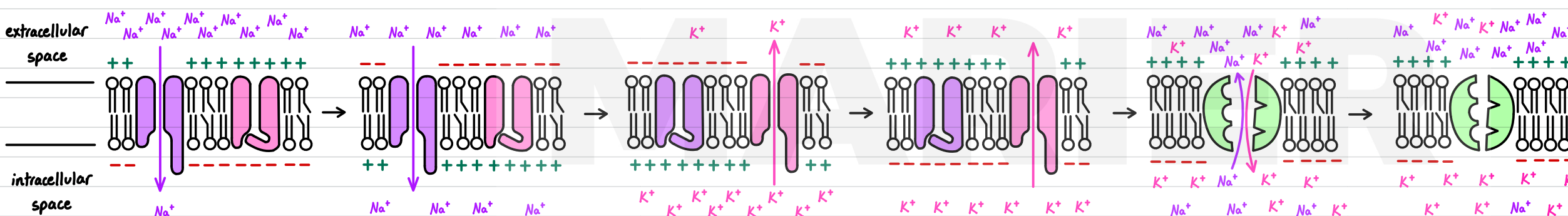
an action potential involves 3 major steps which occur sequentially as a unidirectional wave along nerve fibres: (expanded upon in HL)

- Depolarization**: change in membrane potential from negative to positive. Caused by the rapid diffusion of Na^+ into the cell via opened gated sodium channels

- Repolarization**: change in membrane potential from positive to negative. Caused by the rapid diffusion of K^+ out of the cell via opened gated potassium channels

- Resetting resting potential**: through the use of the sodium-potassium pump, $[\text{Na}^+]$ and $[\text{K}^+]$ and resting potential are re-established

An action potential in one part of the neuron triggers one in the adjacent section



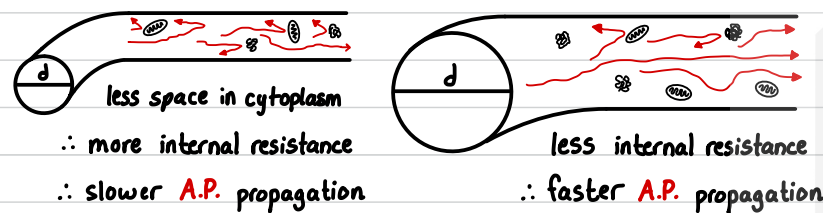
C2.2.4—Variation in the speed of nerve impulses. C2.2.5—Synapses as junctions between neurons and between neurons and effector cells. C2.2.6—Release of neurotransmitters from a presynaptic membrane.

C2.2.7—Generation of an excitatory postsynaptic potential

the velocity (ms^{-1}) nerve impulses travel along axons can vary by 2 major factors:

- **axon cross-sectional diameter**: the larger the axon diameter, the faster the transmission speed

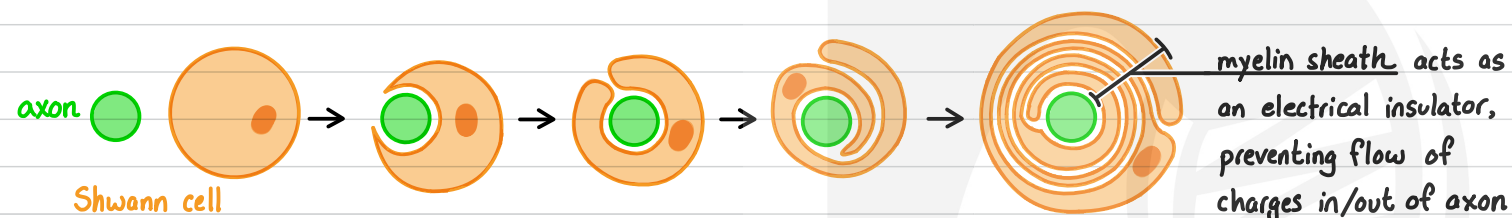
→ larger cross-sectional axon area (πa^2) the greater the number of paths for the charge to flow through the cytoplasm and thus the lower its membrane resistance $\therefore$ faster **action potential (A.P.)** propagation



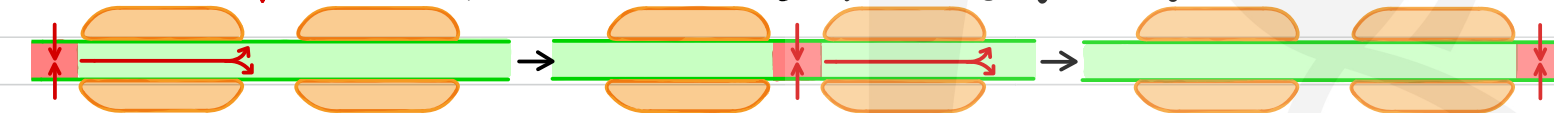
ex: squid have giant axons (diameters up to 1.5mm compared to typical 0.5mm) which controls part of their water jet-propulsion system allowing very fast reaction and escape response

- **myelination**: presence of myelin on axons greatly increases the transmission speed

→ in some axons (such as long motor neurons), Schwann cells surround the axon, forming a fatty myelin sheath



→ in myelinated axons only the gaps between the sheaths (Nodes of Ranvier) undergo depolarization and repolarization thus **action potentials** 'jump' from node to node, greatly increasing signal propagation → expanded in HL

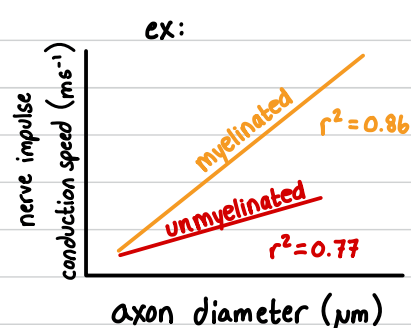


Correlation: statistical test for degree of association between two variables. Can be positive or negative

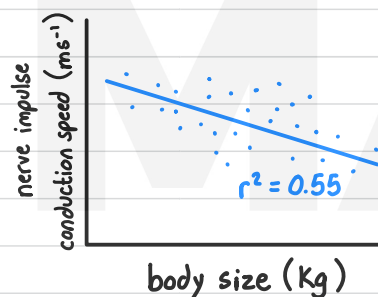
correlation coefficient (r) expresses strength (>0.5 or <-0.5 = strong) and direction (+ or -) of a linear correlation.

coefficient of determination (r^2) indicates what percentage of the variation in the dependent variable (y) is explained by the variation in the independent variable (x) i.e. how close each data point fits a regression line. ✗ correlation does not equal causation

transport B3.2



positive correlation between impulse conduction speed and axon diameter. For myelinated axons, 86% of the variation in speed is predicted by variation in axon diameter.

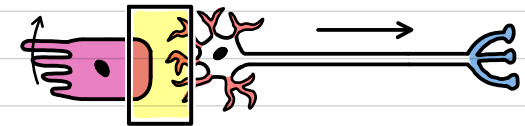


negative correlation between conduction speed and body size. larger organisms tend to have more complex neural pathways with more synapses, adding delay

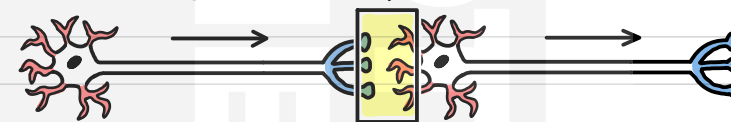
Synapse: junction between a neuron and another cell, where signals are transmitted between cells. 3 main types:

- **Sensory cell to neuron**: signals sent from pre-synaptic

sensory cell to post-synaptic dendrite ex: hair cell in ear

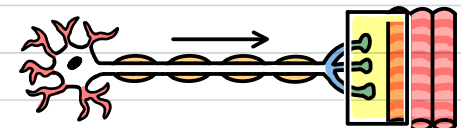


- **neuron to neuron**: signals sent from pre-synaptic axon terminal to post-synaptic dendrite



these are common in the brain and spinal cord

- **neuron to effector cell**: signals sent from pre-synaptic axon terminal to gland or muscle cell ex: neuromuscular junction

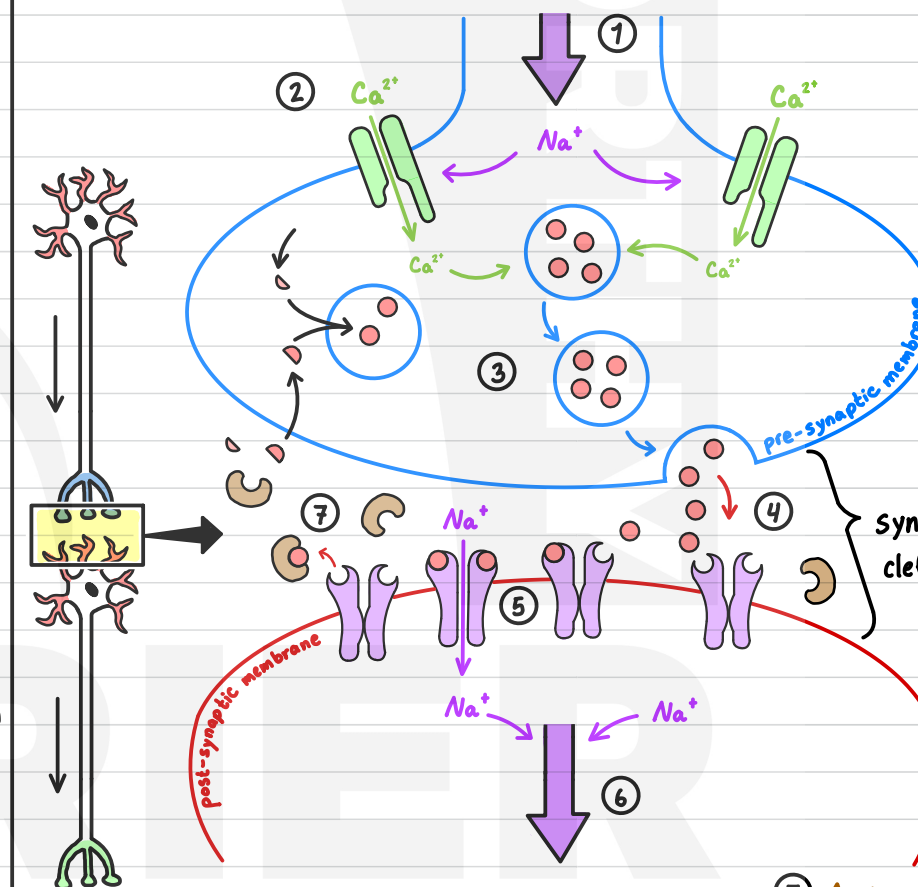


✗ chemical signals can only be sent across a typical synapse in one direction (axon → dendrite) as chemicals sent (neurotransmitters) are made and stored in axon terminals and neurotransmitter receptors only present on dendrites

Excitatory synapse: an action potential in a pre-synaptic cell increases likelihood of an action potential in a post-synaptic cell

→ uses excitatory neurotransmitters such as **Acetylcholine** in **cholinergic synapses** (shown below) other examples of this include neuromuscular junctions

muscle B3.3

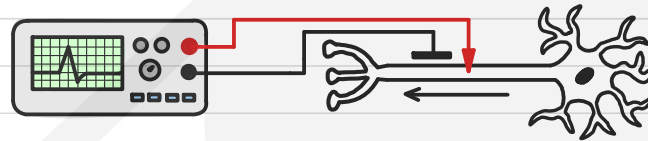


- ① action potential arrives at axon terminal, depolarizing the membrane
- ② voltage-gated Ca^{2+} channels open, causing Ca^{2+} to diffuse into axon terminal
- ③ Ca^{2+} acts as signal and triggers synaptic vesicles to fuse with pre-synaptic membrane
- ④ **Acetylcholine (ACh)** released via exocytosis and diffuses across synaptic cleft
- ⑤ **ACh** binds to **ACh transmembrane receptors**, causing them to open, allowing Na^+ to diffuse into post-synaptic cell
- ⑥ post-synaptic membrane depolarizes, causing a new **action potential** to be propagated
- ⑦ **Acetylcholinesterase** breaks down **ACh**, where **choline** is then taken back into pre-synaptic cell to be recycled into **ACh**

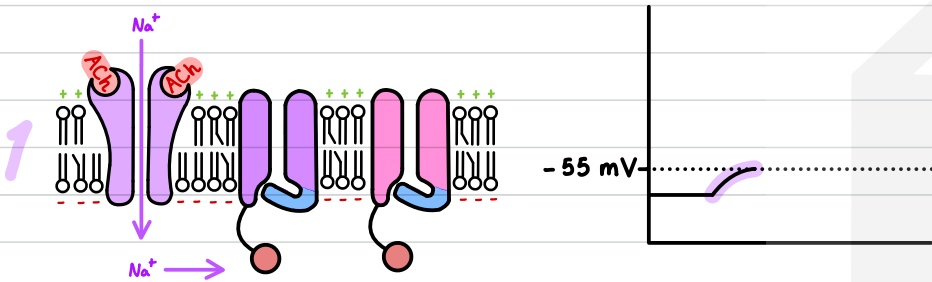
C2.2.8—Depolarization and repolarization during action potentials. C2.2.9—Propagation of an action potential along a nerve fibre/axon as a result of local currents. C2.2.10—Oscilloscope traces showing resting potentials and action potentials. C2.2.11—Saltatory conduction in myelinated fibres to achieve faster impulses

HL

The change in neuron membrane potential during action potential propagation can be measured and visualized with an oscilloscope, producing a trace (mV over time)

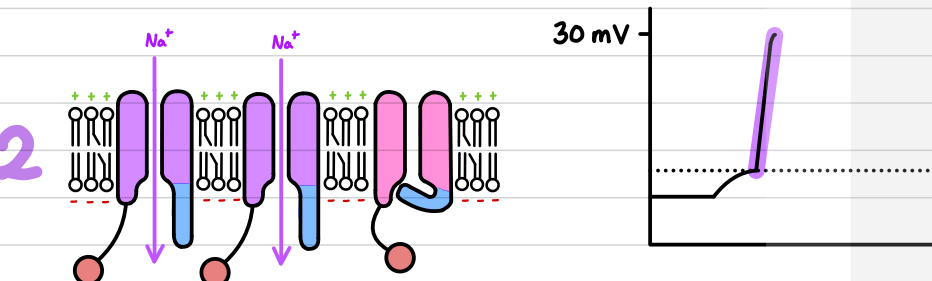


action potentials are generated on a "all or nothing" principle meaning that unless the membrane potential rises to the **threshold potential**, depolarization will not occur and resting potential is re-established



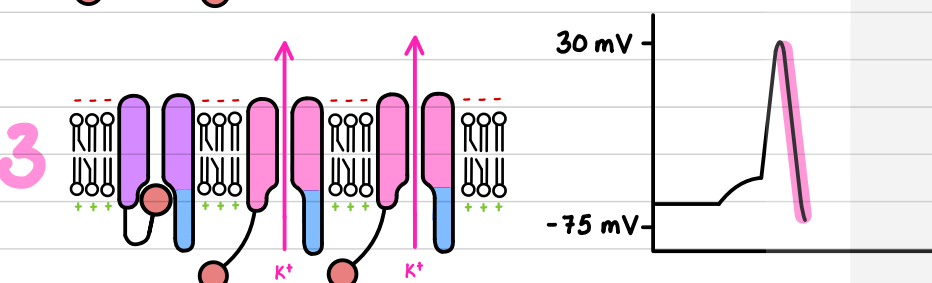
Excitatory post-synaptic potential (EPSP)

Initially, binding of excitatory neurotransmitters to dendrites cause an influx of Na^+ into cell and along with diffusion of Na^+ from an adjacent sections, the membrane potential rises. If it rises sufficiently, threshold potential ($\sim -55\text{mV}$) is reached



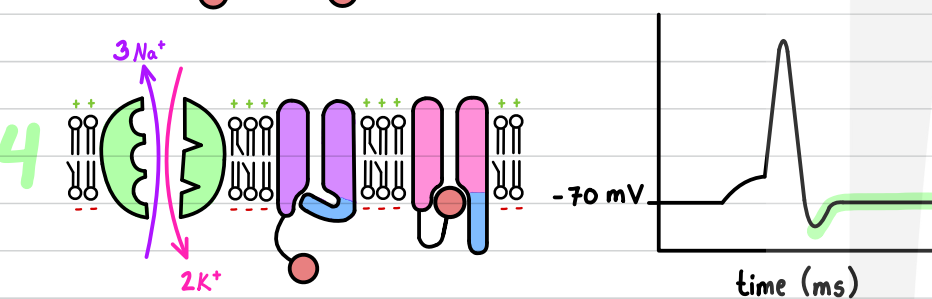
Depolarization

Once threshold potential is reached, **voltage-gated sodium channels** open, causing Na^+ to rapidly diffuse into the cell. Membrane potential depolarizes quickly and becomes positive



Repolarization

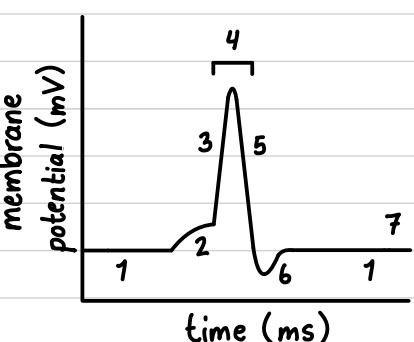
voltage-gated Na^+ channels are inactivated and close **voltage-gated potassium channels** open, causing K^+ to diffuse out of the cell. Membrane potential repolarizes and becomes negative beyond resting potential



Resetting resting potential

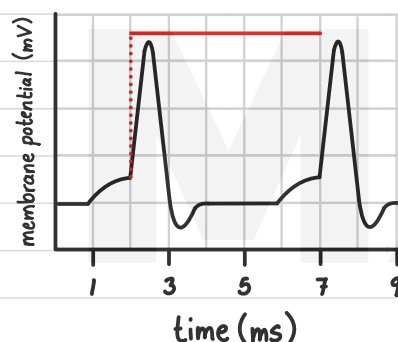
voltage-gated potassium channels are slower to close causing **hyperpolarization**. Resting potential and sodium and potassium concentration gradients are re-established actively, using the **sodium-potassium pump**. Cell ready for new impulse once resting potential re-established.

Reading oscilloscope traces



- ① resting potential
- ② EPSP
- ③ depolarization
- ④ action potential
- ⑤ repolarization
- ⑥ hyperpolarization
- ⑦ threshold potential

Calculating impulse rate



How many action potentials are propagated

a) per second?

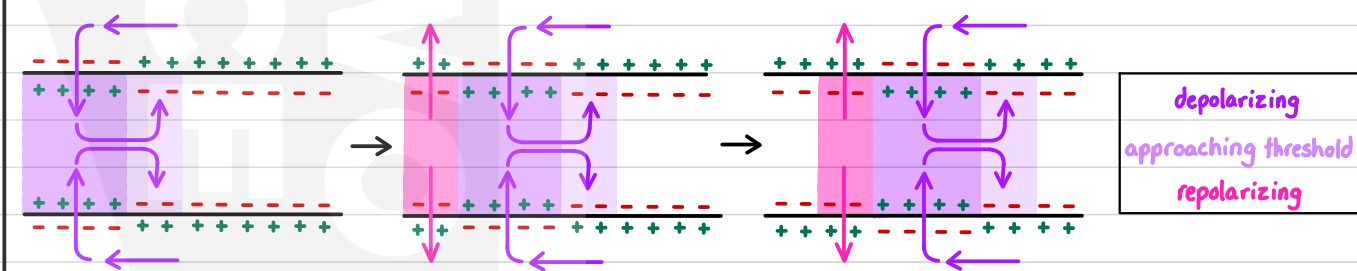
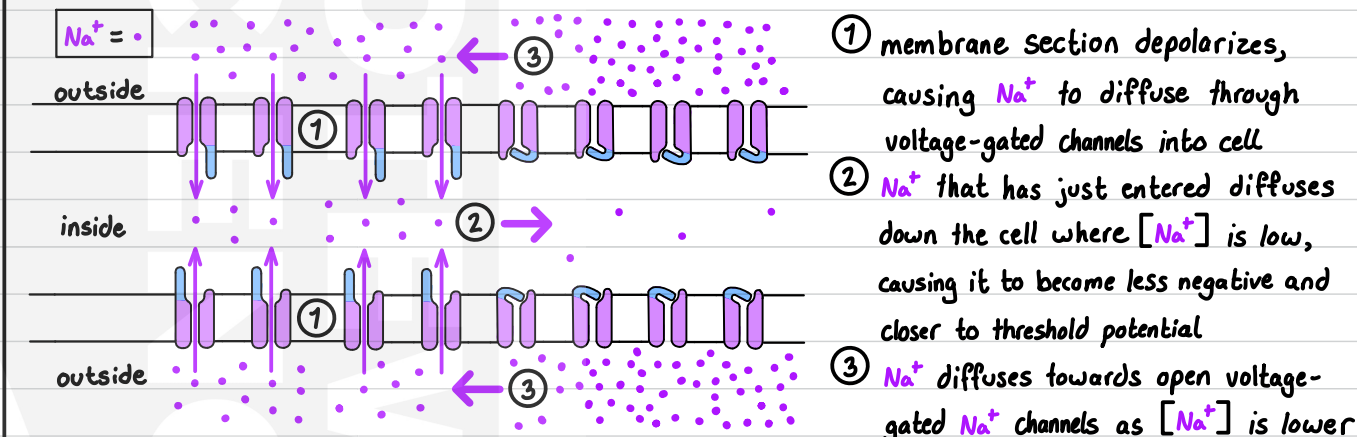
$$\frac{2}{5\text{ms}} \times \frac{1000\text{ms}}{1\text{s}} = 400 \text{ impulses/s}$$

b) per minute?

$$\frac{400}{1\text{s}} \times \frac{60\text{s}}{1\text{min}} = 24000 \text{ impulses/min}$$

Action potentials are propagated along nerve fibres by one part of the fibre depolarizing which in turn causes the adjacent section to depolarize in a wave-like fashion.

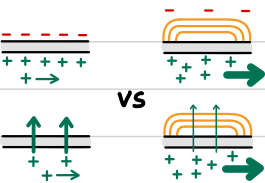
occurs as a result of **local currents** of **sodium** both inside and outside nerve fibre



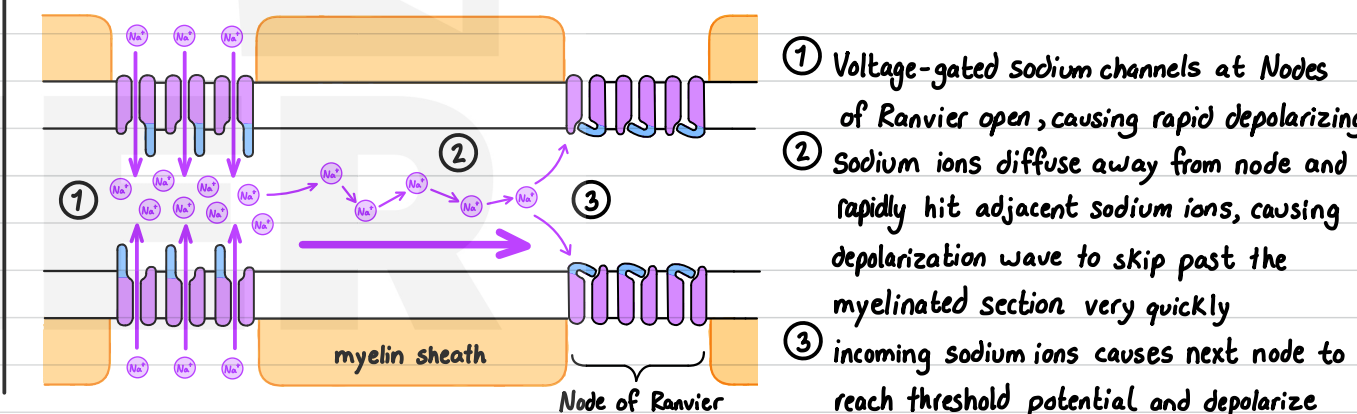
Saltatory conduction: propagation of action potentials down a myelinated neuron, 'jumping' from one Node of Ranvier (unmyelinated node) to the next, increasing transmission speed

depolarization cannot occur through myelin sheaths as it acts as an electrical insulator:

- myelin reduces membrane capacitance $\rightarrow$ less Na^+ along membrane surface
 - myelin increases membrane resistance $\rightarrow$ less Na^+ ions leak out
- $\therefore$ more free Na^+ to depolarize other sections $\rightarrow$ faster ion travel



voltage-gated ion channels and sodium-potassium pumps only at **Nodes of Ranvier** as only these sections generate action potentials, thus increasing impulse speeds and reducing ATP use

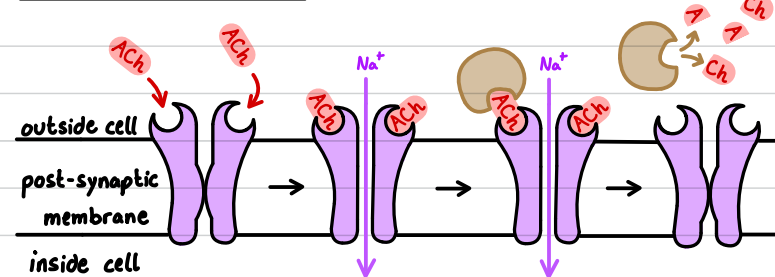


Exogenous chemical : chemical originating from an outside source that enters the body of an organism (through absorption, inhalation, ingestion and/or intravenously)

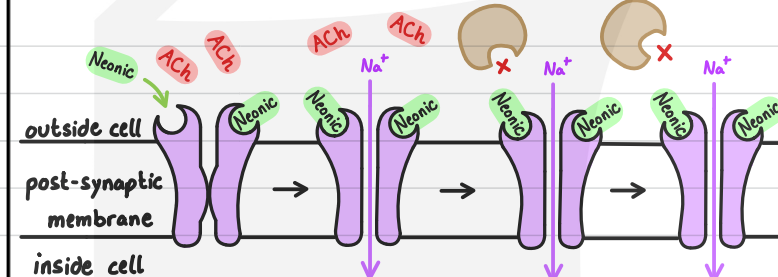
→ these chemicals can alter synaptic transmission (and thus action potential propagation) by either blocking it or promoting it. This can occur via various mechanisms.

→ **Neonicotinoids** : insecticide chemically similar to nicotine which blocks neurotransmission by binding irreversibly to nicotinic acetylcholine receptors, causing overstimulation leading to paralysis and death

Without neonicotinoids



With neonicotinoids



Acetylcholine binds to **ACh receptors**, allowing **Na⁺** influx and generation of action potential in the post-synaptic cell.

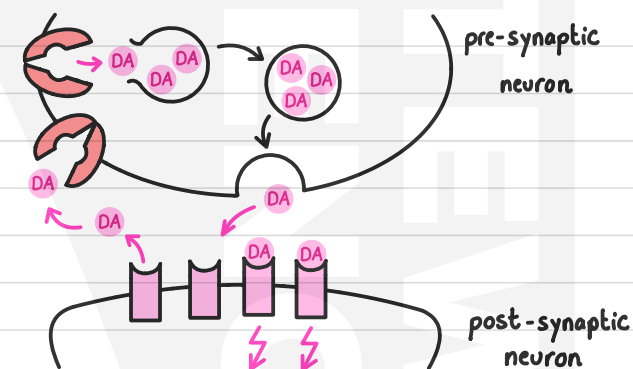
Acetylcholinesterase breaks down **ACh** into **acetate** and **choline**, closing the receptor and halting transmission.

neonicotinoids bind to **ACh receptors** instead of **Acetylcholine**. Similarly, this causes an **Na⁺** influx. However, unlike **ACh**, **Acetylcholinesterase** cannot break down **neonicotinoids**, thus **receptors** are blocked and remain open. This leads to an overabundance of **Na⁺**, causing overstimulation and paralysis

✗ neonicotinoids bind more strongly to ACh receptors in insects but not in mammals making them safe to use for crops. However they are non-selective and kill many non-target insects such as bees, which have large ecological importance

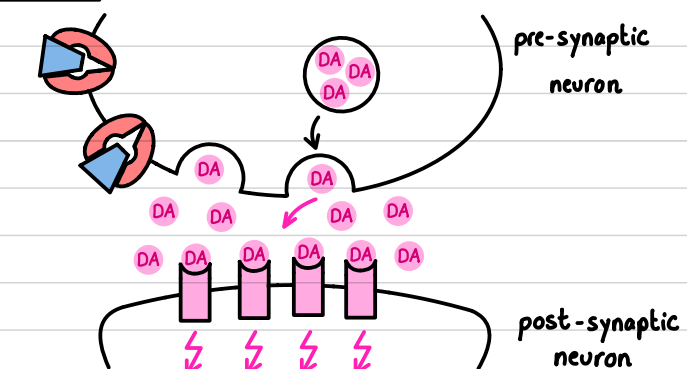
→ **Cocaine** : stimulant drug made from the leaves of the coca plant. As a powder it can be snorted or dissolved and injected. promotes synaptic transmission of dopamine by blocking its re-uptake into the pre-synaptic neuron

Without cocaine



Dopamine binds to **dopamine receptor**, initiating a response. **Dopamine** is pumped back into pre-synaptic neuron via **Dopamine transporter** to halt the signal and to be reused

With cocaine

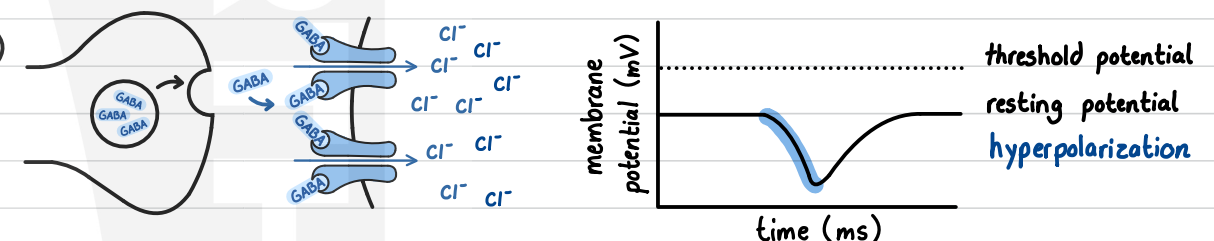


Cocaine binds to **dopamine transporter**, blocking it. As a result, **dopamine** builds up in synaptic cleft and binds to **dopamine receptors** longer, causing a prolonged, stronger signal

✗ As dopamine is associated with the reward pathway, stimulating feelings of pleasure, cocaine enhances and prolongs these feelings making it highly addictive. Additionally, prolonged use causes a tolerance to develop, requiring higher and higher doses

Inhibitory neurotransmitters : reduces likelihood of an action potential in a post-synaptic cell by generating inhibitory post-synaptic potential (IPSP)

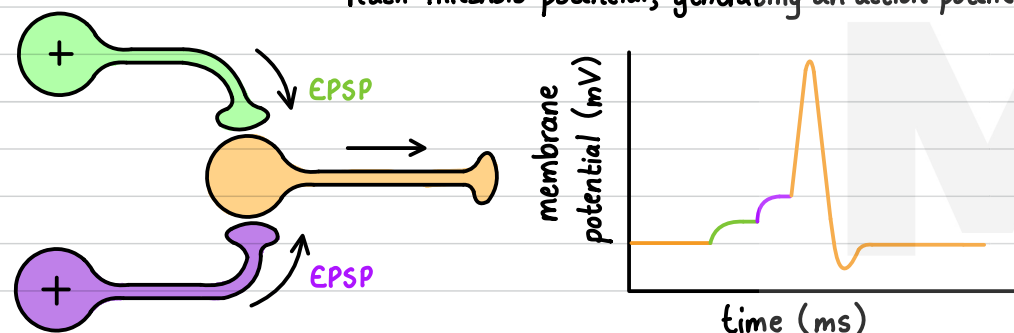
→ when these neurotransmitters (such as GABA) bind to receptors on the post-synaptic membrane, they induce an influx of chloride ions, causing the membrane potential to decrease below rest (hyperpolarization) and making it harder to depolarize as it's further from threshold



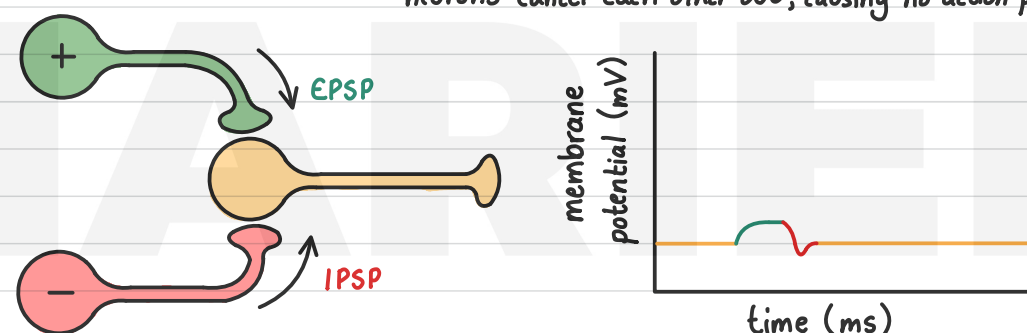
More than one presynaptic neuron can form a synapse with the same post-synaptic neuron (this is especially common in the brain where one may synapse with thousands)

Summation can also occur from a single pre-synaptic neuron

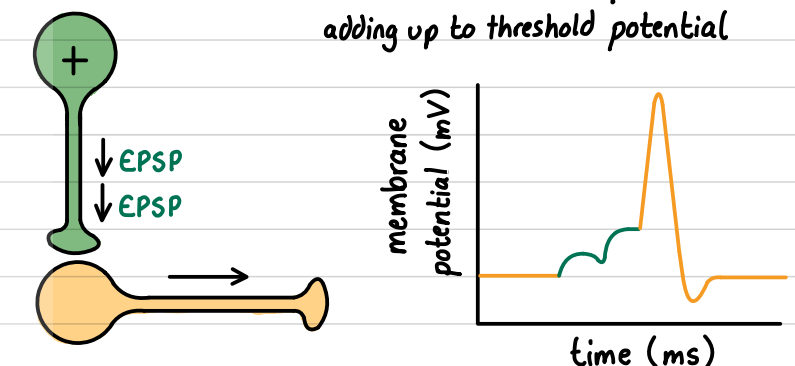
→ **Spatial Summation** : Excitatory Post Synaptic Potentials from multiple pre-synaptic neurons have a cumulative effect to reach threshold potential, generating an action potential



→ **EPSP-IPSP Summation** : Excitatory Post Synaptic Potentials and Inhibitory Post Synaptic Potentials from multiple pre-synaptic neurons cancel each other out, causing no action potential



→ **Temporal Summation** : multiple Excitatory Post Synaptic Potentials are sent in quick succession, adding up to threshold potential



Pain is a feeling of distress often caused by an intense, damaging stimulus. Can be:



mechanical



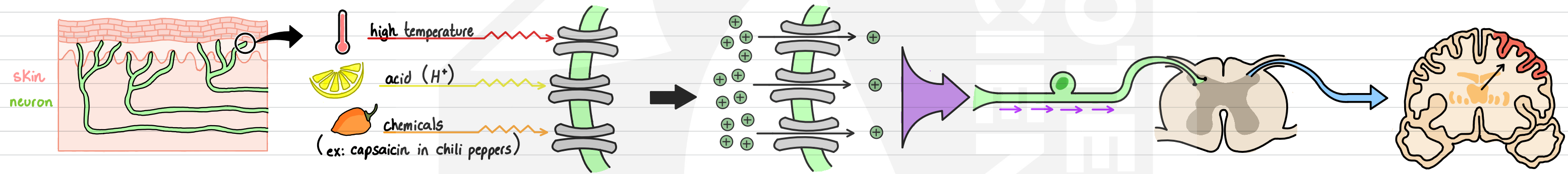
thermal



chemical

→ This sensation exists to motivate the organism to withdraw from the stimulus to prevent further damage and to avoid the same stimulus in the future to prevent future potential harm  integration of body systems C3.1

→ A painful stimulus is detected by sensory neurons called **nociceptors**. Many of these neurons have free nerve endings which branch in the skin for sensation and which then send signals to central nervous system

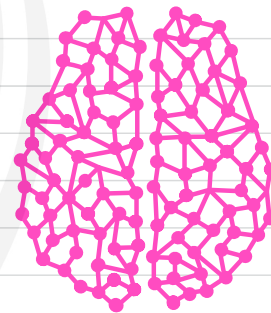


- ① **nociceptors** have **free nerve endings** within the **skin** and detect stimuli
- ② high temperature / acid / capsaicin activates Transient Receptor Potential (TRP) channel on **nociceptor membrane**
- ③ TRP channel open and allow **cations** to diffuse into the **nociceptor** causing it to approach threshold potential
- ④ nociceptor depolarizes and an **action potential** is propagated along towards **spinal cord**
- ⑤ **nociceptor** synapses with another **neuron** which propagates impulse towards the **brain**
- ⑥ impulse reaches **thalamus** and then the **somatosensory cortex** where pain is processed

The brain is composed of over 100 billion (10^{11}) neurons which form over 100 trillion (10^{14}) synapses!

→ with so many connections and interactions, features and properties begin to emerge which are not predicted by only studying neurons, i.e. emergent properties

→ **emergent properties**: property which a system has but which individual members lack due to their interactions i.e. 'the whole is greater than the sum of its parts'



→ **Consciousness** while difficult to properly define can be described as the state of being aware of and responsive to one's surroundings and of one's self

→ consciousness is an emergent property of the many interactions in the brain as no single neuron has this, yet it exists in a human as an organism as a result of their interactions

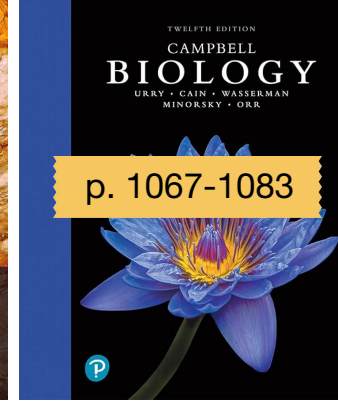
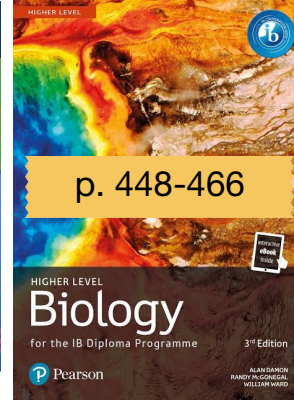
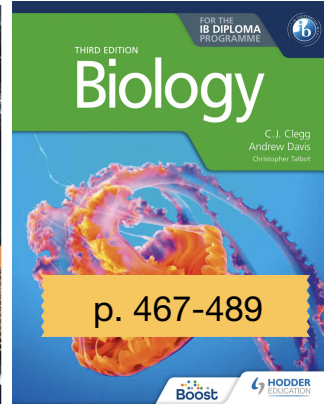
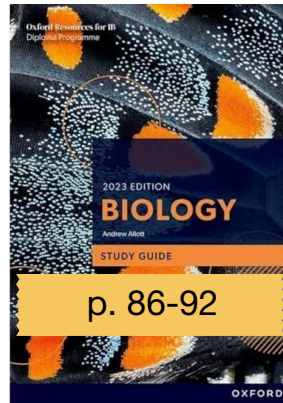
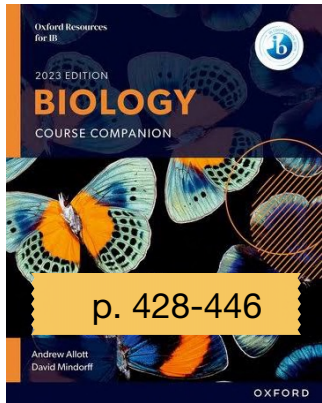
MARIER

Resource Links

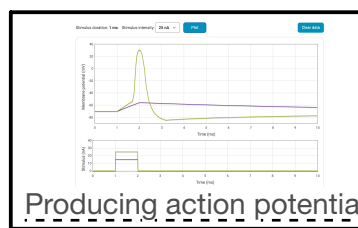
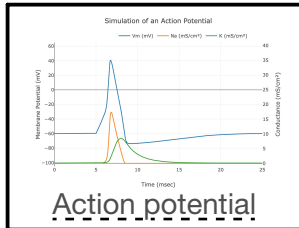
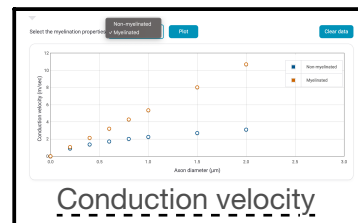
each resource is hyperlinked



Textbooks



Simulators / Interactives



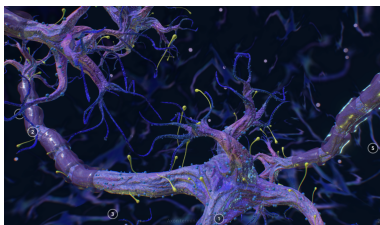
Articles

Hladik, M. L., Main, A. R., & Goulson, D. (2018). Environmental Risks and Challenges Associated with Neonicotinoid Insecticides. *Environmental Science & Technology*, 52(6), 3329–3335. <https://doi.org/10.1021/acs.est.7b06388>

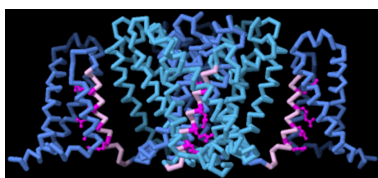
Tononi, G., & Koch, C. (2015). Consciousness: here, there and everywhere? *Philosophical Transactions of the Royal Society B Biological Sciences*, 370(1668), 20140167. <https://doi.org/10.1098/rstb.2014.0167>

Zalc, B. (2006). The acquisition of Myelin: a success story. *Novartis Foundation Symposium*, 15–25. <https://doi.org/10.1002/9780470032244.ch3>

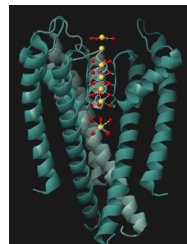
3D models



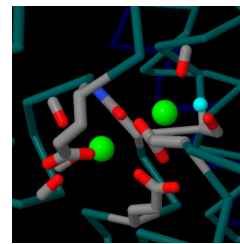
Neurons



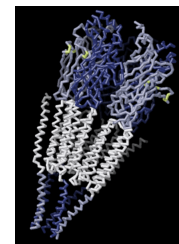
Voltage-gated Sodium channel



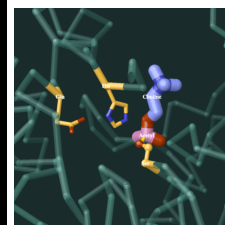
Potassium channel



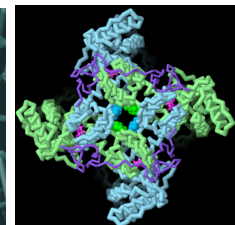
Sodium-Potassium Pump



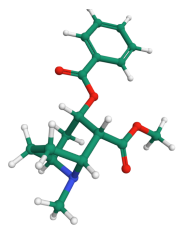
Acetylcholine Receptor



Acetylcholin-esterase



TRPV channel



Cocaine