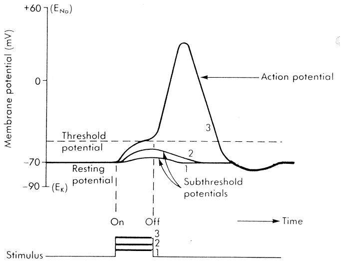
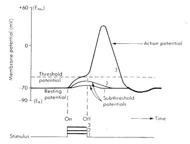
Action potentials



Events in an action potential

- a stimulus causes depolarisation of membrane potential.
- if stimulus is of sufficient strength, the depolarisation will be large enough to reach threshold .
- this results in a very rapid +ve going potential (upstroke) which lasts 0.2 - 0.5ms.
- membrane potential heads towards E_{Na} (overshoot).
- membrane potential then returns towards resting potential (repolarisation).
- small after - hyperpolarisation.
- duration is approximately 1-3 ms
- all-or-none response.

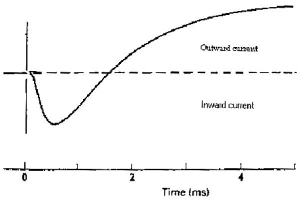


Sodium Theory of Action Potential

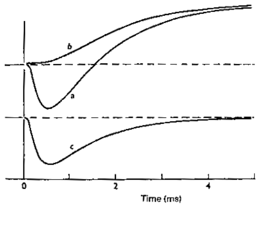
- Hodgkin and Katz (1949) proposed that the action potential was due to a rapid and specific increase in the permeability of the membrane to Na^+ (ie gNa becomes temporarily much greater than gK, so that E_m moves towards ENa)

- the rising phase of the action potential is due to inward movement of Na^+, the falling phase to outward movement of K^+
- voltage clamp experiments make it possible to move the membrane potential (either depolarisation or hyperpolarisation) by passing current into the fibre → any desired potential can be generated and the membrane clamped at that level → the amount of current injected to set the membrane potential at a desired value is equal and opposite to the current flowing across the membrane due to ions

- using squid giant axon, in normal sea water there was a transient inward current followed by a delayed outward current that is maintained for as long as the membrane potential is clamped



- Hodgkin and Huxley removed 90% of Na^+ from external solution (E_{Na} is correspondingly reduced - the membrane potential clamped at -9mV corresponds to E_{Na} and sodium can make no further contribution) →current can then only be carried by K^+



$a = I_{Na} + I_K$
$b = I_K$
$c = I_{Na}$

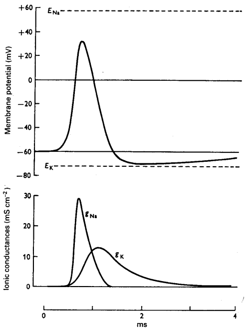
- I_{Na} and I_K can be determined as a function of time and membrane potential

- g_{Na} and g_K can be determined

$$I_{Na} = g_{Na}\,(E_m - E_{Na})$$

$$I_K = g_K\,(E_m - E_K)$$

- both g_{Na} and g_K are increased by depolarising the membrane



- initially g_K is small but g_{Na} is much smaller, so resting potential closer to E_K.

- when membrane depolarised, g_{Na} increases, so small number of sodium ions cross membrane, flowing down their electrochemical gradient - results in further depolarisation and further increase in g_{Na}, so more Na^+ cross membrane.

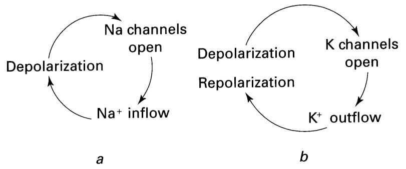
- membrane potential races towards sodium equilibrium potential (E_{Na}).

-sodium conductance is then inactivated

- g_K increases but at a slower rate → membrane potential brought rapidly back to resting level (repolarisation).

- g_K is still higher than usual so membrane potential passes resting level and moves closer to E_K.

- as g_K declines, membrane potential moves back to its resting level.



Na channels open

Depolarization

Na^+ inflow

a

Depolarization

K channels open

Repolarization

K^+ outflow

b

- increase (and decrease in case of sodium inactivation) is due to Na^+ and K^+ gating mechanisms that are voltage dependent.

- 3 independent processes.

1. Na^+ channels normally closed (~0.12% open at -90 mV) but swing open rapidly when the inside becomes more positive → Na activation (m gate).

2. Na^+ channels normally open (50% open at 90 mV) but swing closed slowly when the inside becomes more positive →Na inactivation (h gate).

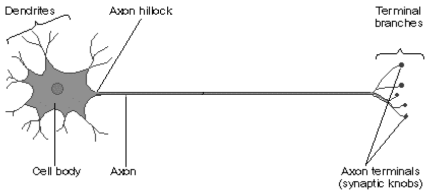
3. K^+ channels normally closed (1% open at -90 mV) but swing open slowly when the inside becomes more positive (n gate).

Refractory periods

- absolute refractory period -after an action potential has been initiated it is impossible to initiate another action potential → corresponds to the time to recover from sodium inactivation - also gK is still high during this period.

- relative refractory period -- period in which it is possible to initiate a second action potential but the stimulus needs to be stronger to reach threshold → corresponds to the return of potassium conductance to normal.

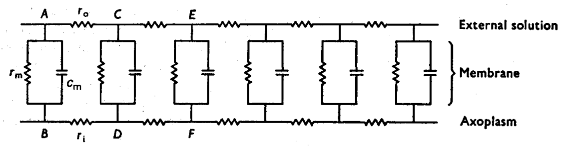
Action potential propagation in axons



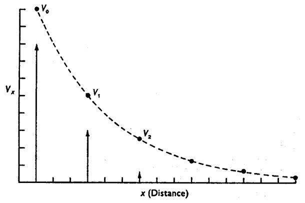
- propagation of an action potential along an axon depends on the electrical excitability of the nerve membrane and also on the cable structure of the axon.

- when a region of membrane is shifted away from its resting potential an electrical gradient is set up between that region and distant regions.

- membrane can be represented as an electrical circuit



- if a constant current is passed across the membrane so as to set up a potential difference (V_o), then voltage falls of exponentially with distance from the point at which current was applied.



- the distance over which the potential decreases to 37% of its maximum value is termed a space constant (λ) (sometimes termed length constant)

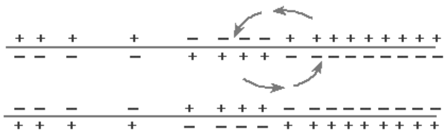
$$\lambda^2 = \frac{r_m}{r_o + r_i}$$

- if r_o considered much less than r_i

$$\lambda = \sqrt{\frac{r_m}{r_i}} \quad \infty \quad \sqrt{d}$$

- the higher r_m and the lower r_i, the further the signal spreads (i.e. larger λ - core becomes a better conductor and membrane a better insulator).

- current flows in local circuits in the axon due to the cable structure of the nerve (local circuit theory).



- action potential conducted along the axon as a wave of depolarisation as the local currents depolarise the membrane ahead of it.

- if the diameter and membrane properties of the axon are uniform, both the amplitude and conduction velocity of the action potential will be constant and behave in an all-or-none fashion.

- conduction of the action potential along the axon will be speeded up by an increase in λ, as the resting membrane will be triggered further ahead of the advancing impulse ($\lambda = \sqrt{d}$, therefore large axons conduct faster than smaller ones).

$$\text{conduction velocity Ø} = \frac{\lambda}{\tau}$$

τ = time constant

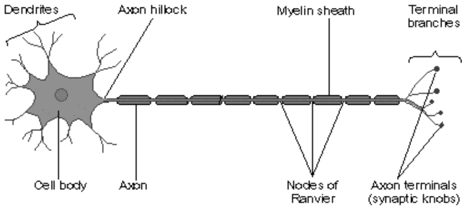
- If τ (the time for membrane to become depolarised) remains constant (depends on membrane capacitance, time for Na^+ to move through membrane i.e. sodium current density)

$\text{Ø} = \lambda \infty \sqrt{d}$ in unmyelinated fibres

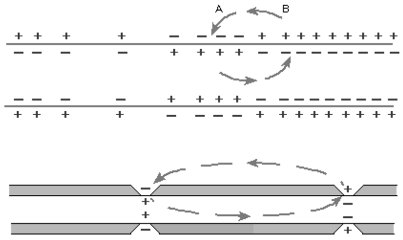
i.e. dependent on r_i (as d ↑, r_i ↓).

Myelinated axons

- most peripheral nerves in the mammal are surrounded by myelin (formed from Schwann cells).



- conduction along a myelinated axon is termed saltatory conduction, with action potentials occurring only at nodes.



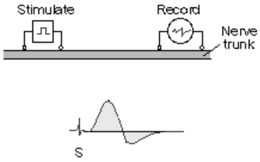
- the myelin sheath has the effect of increasing r_m between nodes. (i.e. insulating the axon).

- has the effect of increasing λ without increasing τ

$$\lambda = \frac{r_m + r_{my}}{r_i}$$

- for myelinated axons Ø ∞ d

Extracellularly recorded action potentials



- the potential across the active membrane is reversed making the outside -ve with respect to the inside.

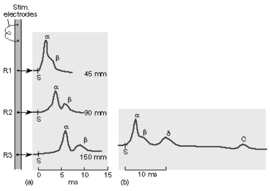
- biphasic action potential.

- conduction velocity Ø = $\Delta l / \Delta t$

Compound action potential

- whole nerve trunk contains fibres of different diameter, spike durations and conduction velocities.

- if stimulate a nerve strongly enough to excite all fibres in it, extracellular recording contains several waves because of dispersion of the conducted action potentials with distance.



- there are three main groups of waves--> A,B and C.

- the A group is further subdivided into four groups --> α, β, γ, δ

- wide distribution in conduction velocity due to variation in fibre diameter (large fibres conduct faster than small fibres, Aα fibres are the largest, Aß the second largest etc.)

- with weak stimulus only Aα excited, if slightly stronger, Aα and Aß excited and so on until all fibres in the nerve are excited.