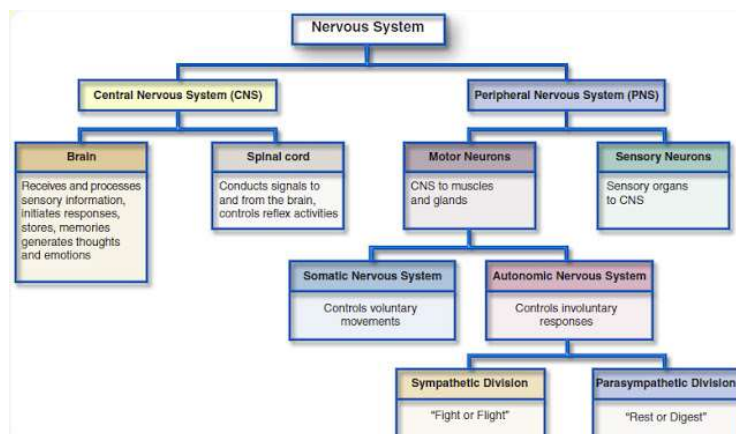


GENERAL PHYSIOLOGY

EXCITABLE TISSUES

- These are cells that respond to stimuli
- Nerves and muscles are the only body's excitable cells specialized to respond to stimuli or exhibit excitability

31-2

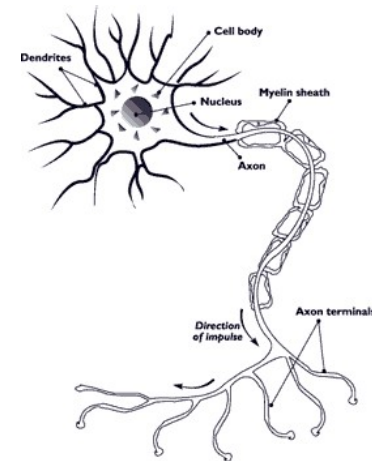


THE NERVE TISSUE

- This is comprised of nerve cells (neurons) specialized for carrying information at high speed from one area of the body to another, or for integrating information from various sources in the body.

Nerve tissue cont'd

- Neurons are able to respond to stimuli such as touch, sound, light, pressure.
- Generate and conduct electrical impulses and communicate with each other and with other types of cell



6

RESTING MEMBRANE POTENTIAL

- Membranes are polarized i.e. exhibit a resting membrane potential.
- This means that there is an unequal distribution of ions on the two sides of the nerve cell membrane.

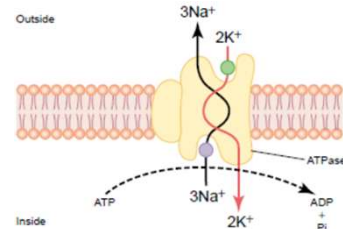
RESTING MEMBRANE POTENTIAL

- The resting membrane potential of large nerve fibres is -90mV.
- The potential inside the fibre is 90mV more negative than the potential in the ECF on the outside of the fiber

Factors that contribute to RMP

1. Na⁺-K⁺ pump

- Pumps 3 Na⁺ from the inside to the outside and 2 K⁺ from the outside to the inside.

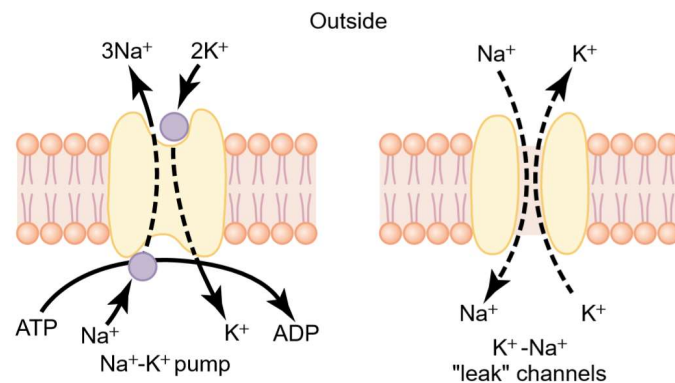


- ### 2. Proteins have a negative charge & can not leave the cell to the outside

Factors that contribute to RMP cont'd

3. Sodium and Potassium leak channels.

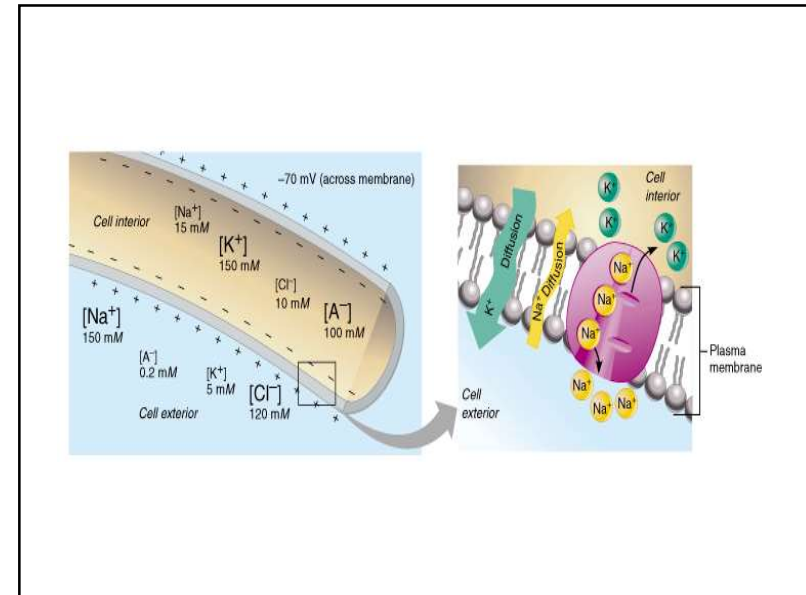
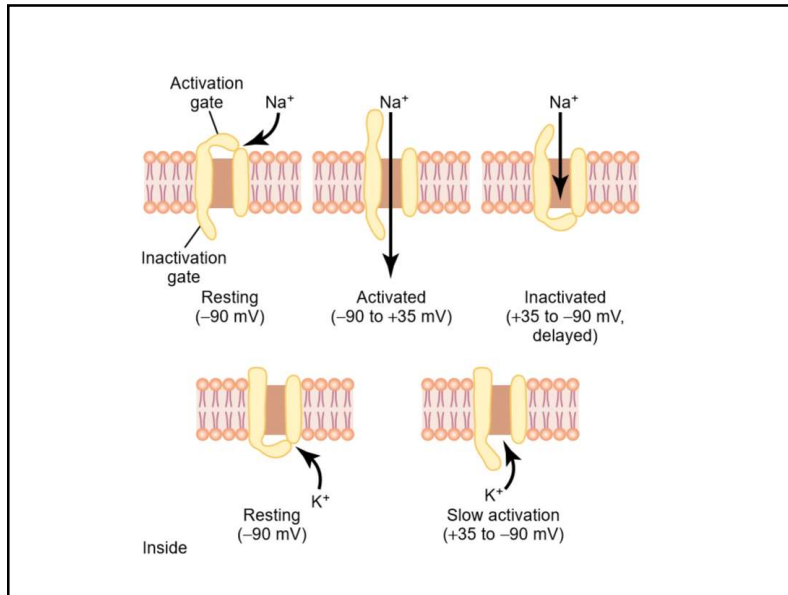
- These channels are far more permeable to potassium than to sodium, normally about 100 times as permeable



Factors that contribute to RMP

4. Sodium and Potassium voltage gated channels

- Both sodium and potassium voltage gated channels are closed



Nernst potential

Relation of the Diffusion Potential to the Concentration Difference—The Nernst Potential. The diffusion potential level across a membrane that exactly opposes the net diffusion of a particular ion through the membrane is called the *Nernst potential* for that ion, a term that was introduced in Chapter 4. The magnitude of this Nernst potential is determined by the *ratio* of the concentrations of that specific ion on the two sides of the membrane. The greater this ratio, the greater the tendency for the ion to diffuse in one direction, and therefore the greater the Nernst potential required to prevent additional net diffusion. The following equation, called the *Nernst equation*, can be used to calculate the Nernst potential for any univalent ion at normal body temperature of 98.6°F (37°C):

$$\text{EMF (millivolts)} = \pm 61 \log \frac{\text{Concentration inside}}{\text{Concentration outside}}$$

where EMF is electromotive force.

ACTION POTENTIAL

- An action potential is a rapid change in membrane potential that occurs when a nerve/muscle cell membrane is stimulated.

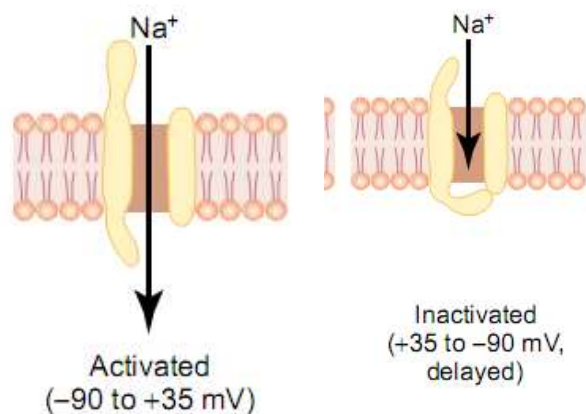
Action Potential cont'd

- The membrane potential goes from the resting potential (-90 mV) to some positive value (about +35 mV) in a very short period of time.

Action potential cont'd

- The stimulus causes the Na⁺ channels to open, Na⁺ then diffuses rapidly into the nerve cell.
- Na⁺ influx causes the membrane potential to become positive
- The inside of the membrane is now positive relative to the outside

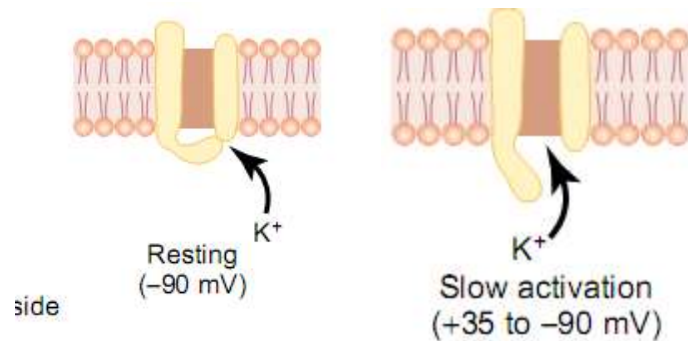
Action potential cont'd



Action potential cont'd

- The Na⁺ channels open only briefly, and then close again.
- The K⁺ channels then open, and K⁺ diffuse out.
- As these positive ions go out, the inside of the membrane once again becomes negative with respect to the outside

Action potential cont'd



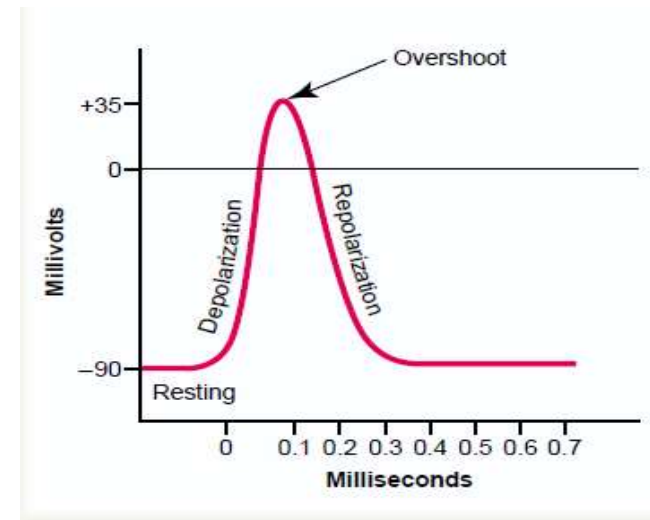
Action potential cont'd

- The successive stages of the action potential are as follows

1. Resting stage
2. Depolarisation
3. Repolarisation
4. Hyperpolarisation

Resting Stage

- This is the resting membrane potential before the action potential begins.
- The membrane is said to be “polarized” during this stage because of the -90 mV negative membrane potential that is present.



Depolarisation

- When a nerve is adequately stimulated, Na^+ - channels are triggered to open allowing Na^+ ions to diffuse rapidly into the cell reducing the negative RMP rises to a less value and producing a local depolarization

Depolarisation cont'd

- When the local depolarisation surpasses a limit called the threshold potential (-55mV)
- Additional Na^+ - channels are activated to open and more Na^+ ions rush into the cell
- This shifts the membrane potential towards 0mV

Repolarization

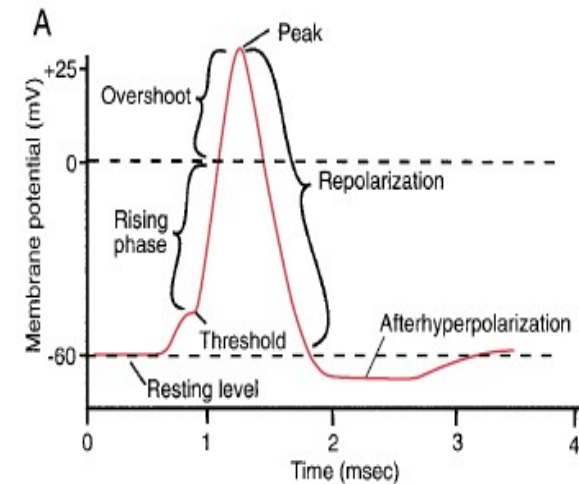
- Once the peak of the neuron's AP is reached ($+35\text{mV}$) the MP begins to move back towards the RMP (-90mV) in a process called **repolarization**
- The rise of the MP from -90mV towards 0mV also opens the voltage sensitive K^+ ion channels
- However they just open at the same time the sodium channels are beginning to close

Repolarization cont'd

- The decrease in Na^+ entry and simultaneous increase in K^+ exit from the cell, combine to speed up the repolarization process that leads to full recovery of RMP

Repolarization cont'd

- The K^+ channels open more than they normally do during repolarization and their return to the closed state is slow
- Thus too many K^+ ions may rush out of the cell, this causes a brief period of hyperpolarisation before the RMP is restored by the action of Na – K pump

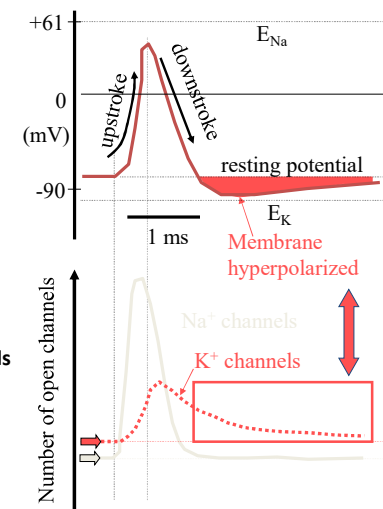


All or non law

- Application of a threshold stimulus either produces a full response or not at all.
- Further increase in the intensity of a stimulus produces no increment or other changes in action potential.
- The action potential fails to occur if the stimulus is sub-threshold, it produces only local changes with no propagation

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- During the upstroke of an action potential:
 - ☐ Na permeability increases
 - due to opening of Na^+ channels
- During the downstroke of an action potential:
 - ☐ Na permeability decreases
 - due to inactivation of Na^+ channels
 - ☐ K^+ permeability increases
 - due to opening of K^+ channels

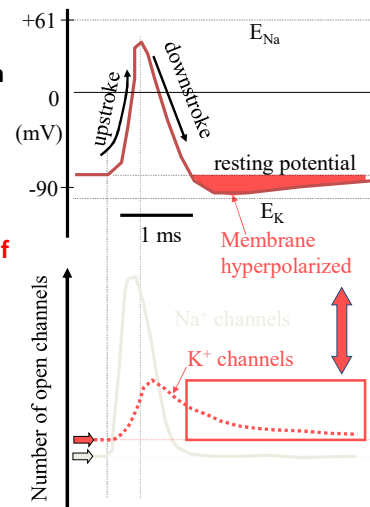


- After hyperpolarization of membrane following an action potential:

❑ not always seen!

❑ There is increased K^+ conductance

➤ due to delayed closure of K^+ channels

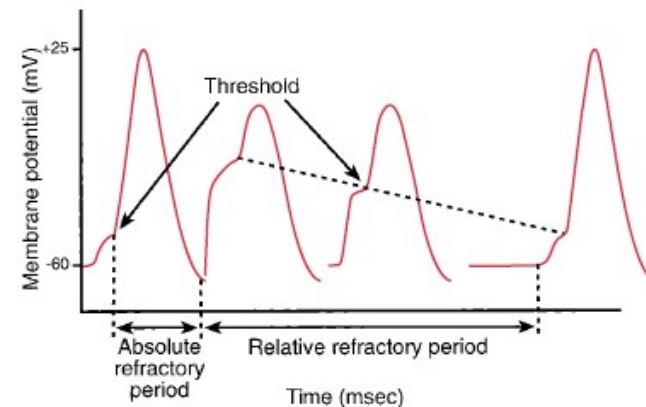


Absolute Refractory periods

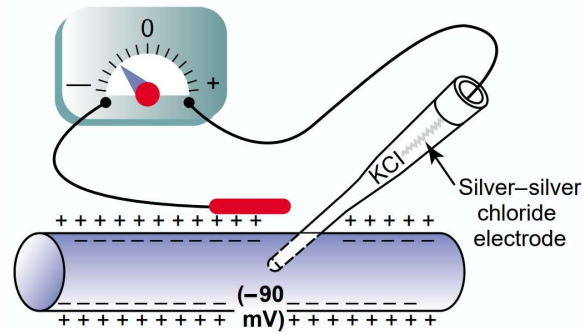
- During an action potential, a second stimulus will not produce a second action potential
- Corresponds to the period when the voltage gated sodium channels are still open

Relative refractory periods

- Another action potential can be produced, but only if the stimulus is greater than the threshold stimulus.
- Corresponds to the period when the potassium channels are open



Measuring the Membrane Potential

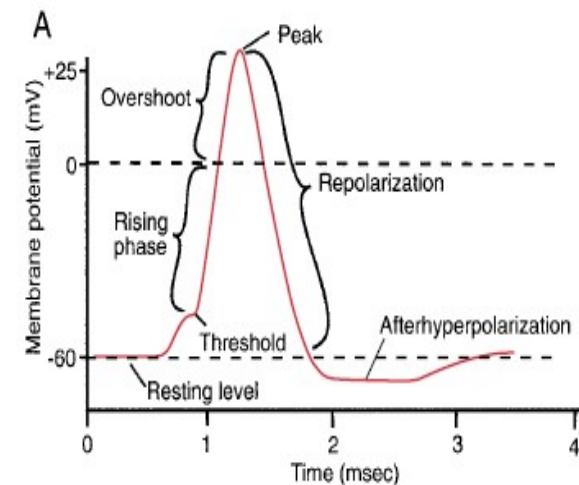


Measuring the MP cont'd

- A small pipette filled with an electrolyte solution is impaled through the cell membrane to the interior of the fiber.
- Then another indifferent electrode is placed in the extracellular fluid
- The potential difference between the inside and outside of the fiber is measured using a voltmeter.

Measuring the MP cont'd

- For recording rapid changes in the MP during transmission of nerve impulses, the microelectrode is connected to an oscilloscope

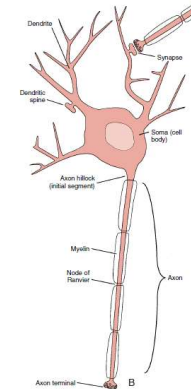


Impulse conduction

- An impulse is simply the movement of *action potentials* along a nerve cell.
- In unmyelinated axons, voltage-gated sodium and potassium channels are distributed uniformly along the length of the axonal membrane.

Propagation of an impulse cont'd

- An action potential is generated when the axon hillock is depolarized by the passive spread of synaptic potentials along the somatic and dendritic membrane

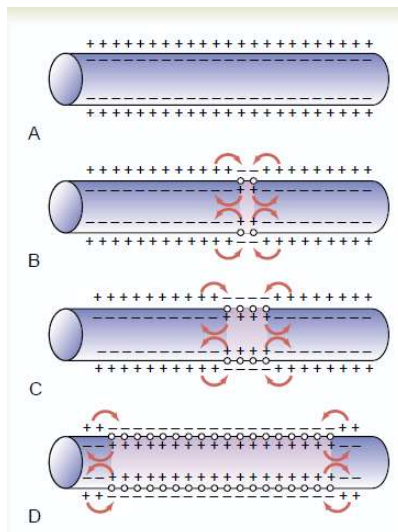


Propagation of an impulse cont'd

- The entry of sodium ions into the axon hillock causes the adjacent region of the axon to depolarize as the ions that entered the cell, during the peak of the action potential, flow away from the sink.

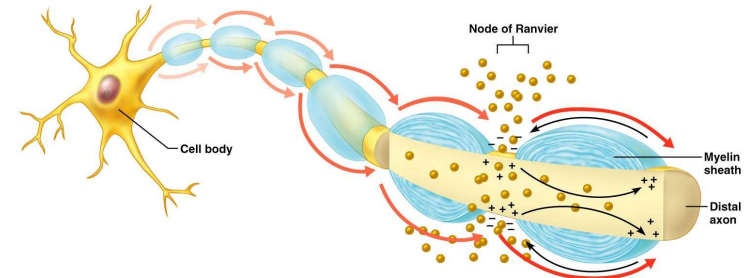
Propagation of an impulse cont'd

- This local spread of the current depolarizes the adjacent region to threshold and causes an action potential in that region.
- By sequentially depolarizing adjacent segments of the axon, the action potential moves along the length of the axon



SALTATORY CONDUCTION

- In myelinated axons all voltage gated sodium channels are concentrated between the nodes of Ranvier



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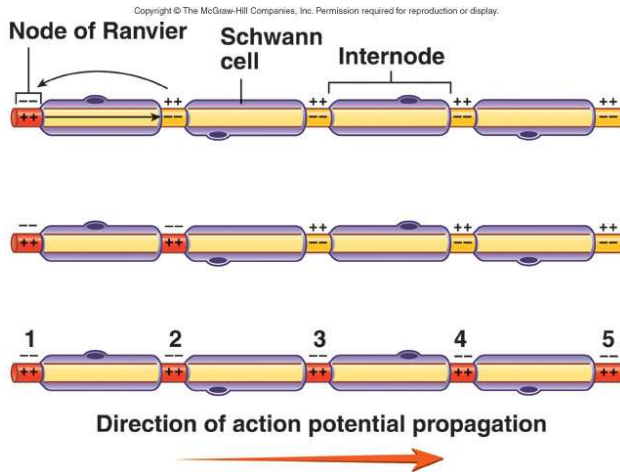
Saltatory conduction cont'd

- When an AP is initiated at the axon hillock, the influx of Na^+ causes the adjacent node of ranvier to depolarize
- This, in turn, causes depolarization of the next node of Ranvier and the eventual initiation of an action potential

Saltatory conduction cont'd

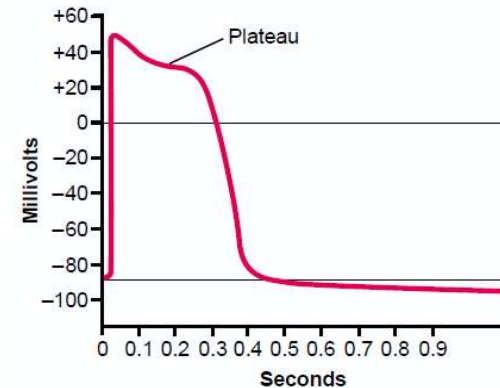
- Action potentials are successively generated at neighbouring nodes of ranvier
- **Therefore, the action potential in a myelinated axon appears to jump from one node to the next**

Saltatory Conduction: Action Potential Propagation in a Myelinated Axon



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Plateau in Some Action Potentials



Action Potentials cont'd

- The usual voltage-activated sodium channels (fast channels)
- Voltage-activated calcium-sodium channels which are slow to open (slow channels)
- Opening of fast channels causes the spike portion of the action potential

Action Potentials cont'd

- The slow calcium-sodium channels allows calcium ions to enter the fiber, which is largely responsible for the plateau portion of the action potential
- The voltage-gated potassium channels are slower than usual to open, often not opening very much until the end of the plateau

RHYTHMICITY OF SOME EXCITABLE TISSUES

- Repetitive self-induced discharges occur normally in
 1. The rhythmical beat of the heart
 2. Rhythmical peristalsis of the intestines (smooth muscles)
 3. Neuronal events in the rhythmical control of breathing.

Repetitive Discharge cont'd

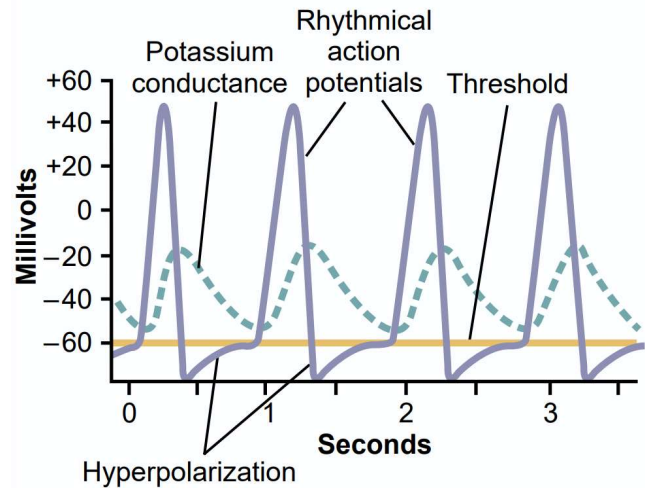
- For spontaneous rhythmicity to occur the membrane in its natural state must be permeable enough to sodium ions or to calcium.
- The SAN of the heart has a RMP of only -60 to -70mV not enough to keep the Na^+ and Ca^{++} channels totally closed.

Repetitive Discharge cont'd

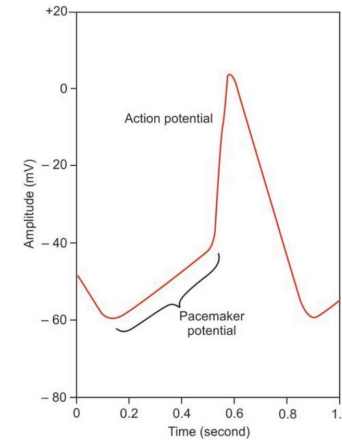
- Therefore
 1. Some sodium and calcium ions flow inward
 2. This increases the membrane voltage in the positive direction, which further increases membrane permeability
 3. Still more ions flow inward
 4. The permeability increases more, and so on, until an action potential is generated.

Repetitive Discharge cont'd

- Then, at the end of the action potential, the membrane repolarizes.
- After another delay of milliseconds or seconds, spontaneous excitability causes depolarization again, and a new action potential occurs spontaneously
- This cycle continues over and over and causes self-induced rhythmical excitation of the excitable tissue



Electrical Activity in Pacemaker cont'd



Inhibition of Excitability

- Membrane stabilizing factors, can decrease excitability of a nerve membrane
- For instance, a high ECF Calcium ion concentration decreases membrane permeability to sodium ions and simultaneously reduces excitability.
- Therefore, calcium ions are said to be a “stabilizer.”

Local Anesthetics

- Some stabilisers such as procaine and tetracaine are used as local anesthetics
- These act directly on the activation gates of the sodium channels, making it much more difficult for these gates to open, thereby reducing membrane excitability

SYNAPSE

- The location or junction between 2 neurons where the transmission of information occurs
- There are two major types of synapses:
 1. Chemical synapse
 2. Electrical synapse

ELECTRICAL SYNAPSE

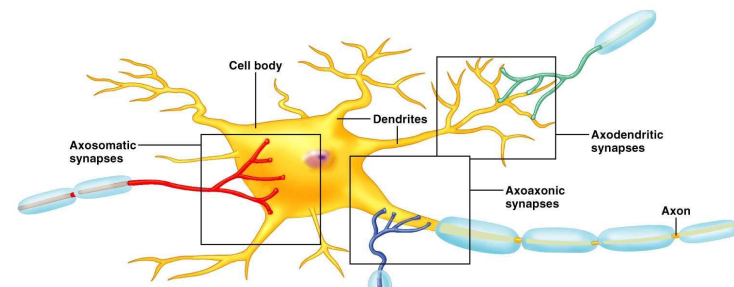
- Electrical synapses are characterized by direct open fluid channels that conduct electricity from one cell to the next

Examples

- Gap junctions in smooth muscle and cardiac muscle cell fiber

CHEMICAL SYNAPSES

- Specialized for release and reception of chemical neurotransmitters
- Contains 3 parts
 1. **Axon Terminal**- filled with vesicles containing neurotransmitter
 2. **Synaptic Cleft**- space between the neurons
 3. **Neurotransmitter Receptor Region**- located on the post synaptic neuron



(a)

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AP transfer across a synapse

1. When an action potential depolarizes the presynaptic membrane
2. Calcium channels open and allow large numbers of calcium ions to flow into the terminal.

AP transfer across a synapse cont'd

3. The calcium ions stimulate vesicles to release their neurotransmitter into the cleft
4. The neurotransmitter molecules diffuse across the cleft and fit into receptor sites in the postsynaptic membrane.

AP transfer across a synapse cont'd

5. If the neurotransmitter is excitatory e.g. acetylcholine and noradrenaline
 - It causes slight depolarization by the opening of sodium channels in the postsynaptic membrane and the influx of sodium ions from ECF.

AP transfer across a synapse cont'd

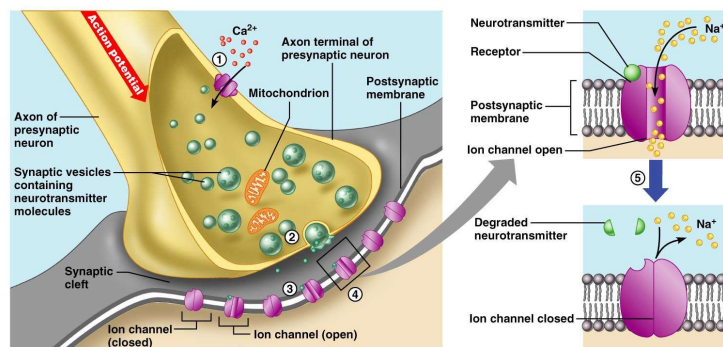
- This slight depolarization is called excitatory postsynaptic potential (EPSP).
6. EPSP in turn causes development of action potential in the initial segment of the axon of the postsynaptic neuron.

AP transfer across a synapse cont'd

- If the neurotransmitter is inhibitory e.g. **gamma aminobutyric acid (GABA)** and **dopamine**.
- It causes opening of potassium channels in the postsynaptic membrane and efflux of potassium ions.

AP transfer across a synapse cont'd

- This leads to hyperpolarization, which is called the inhibitory postsynaptic potential (IPSP).
- **When IPSP is developed, the action potential is not generated in the postsynaptic neuron.**



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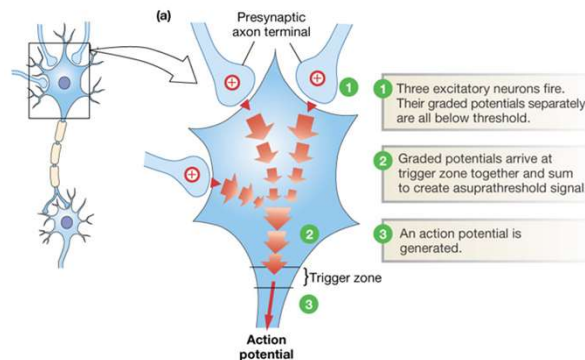
Termination of Neurotransmitter Effects

- Degradation by enzymes at the post synaptic membrane
- Reuptake of the neurotransmitter at the presynaptic terminal
- Diffusion away from the synapse

Some Special xtics of Synaptic Transmission

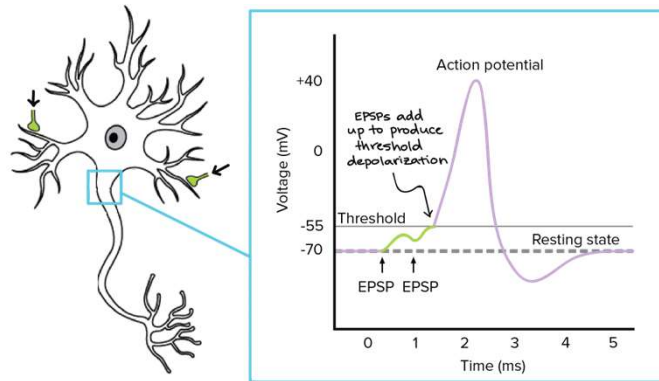
Spatial Summation

- Excitation of a single presynaptic terminal on the surface of a neuron almost never excites the neuron
- Because insufficient neurotransmitter is released by a single terminal to cause an EPSP
- Many presynaptic terminals are usually stimulated at the same time.



Temporal Summation

- Successive discharges from a single presynaptic terminal, if they occur rapidly enough, can add to one another and increase the postsynaptic potential to a greater level



Fatigue of Synaptic Transmission

- When an excitatory synapse is stimulated rapidly
- The number of discharges by the postsynaptic neuron is at first great, but becomes less in succeeding milliseconds
- Due to exhaustion partial exhaustion of the stores of transmitter substance

Synaptic Delay

- Time consumed during transmission of a neuronal signal from a presynaptic neuron to a postsynaptic neuron
1. Discharge of the transmitter substance by the presynaptic terminal
 2. Diffusion of the transmitter to the postsynaptic neuronal membrane

Synaptic Delay cont'd

3. Action of the transmitter on the membrane receptor
4. Action of the receptor to increase the membrane permeability
5. Inward diffusion of sodium to raise the excitatory postsynaptic potential to a high enough level to elicit an action potential