ORIGIN AND PROPAGATION OF ACTION POTENTIAL AND SYNAPTIC TRANSMISSION.

ZOOA-CC3-6 UNIT-3

DEFINITION

An action potential is defined as a sudden, fast, transitory, and propagating change of the resting membrane potential. Only neurons and muscle cells are capable of generating an action potential; that property is called the excitability.

Action potentials are nerve signals. Neurons generate and conduct these signals along their processes in order to transmit them to the target tissues. Upon stimulation, they will either be stimulated, inhibited, or modulated in some way. Structure and all the types of the neurons with the following study unit.

But what causes the action potential? From an electrical aspect, it is caused by a stimulus with certain value expressed in millivolts [mV]. Not all stimuli can cause an action potential. Adequate stimulus must have a sufficient electrocal value which will reduce the negativity of the nerve cell to the threshold of the action potential. In this manner, there are subthreshold, threshold, and suprathreshold stimuli. Subthreshold stimuli cannot cause an action potential. Threshold stimuli are of enough energy or potential to produce an action potential (nerve impulse). Suprathreshold stimuli also produce an action potential, but their strength is higher than the threshold stimuli.

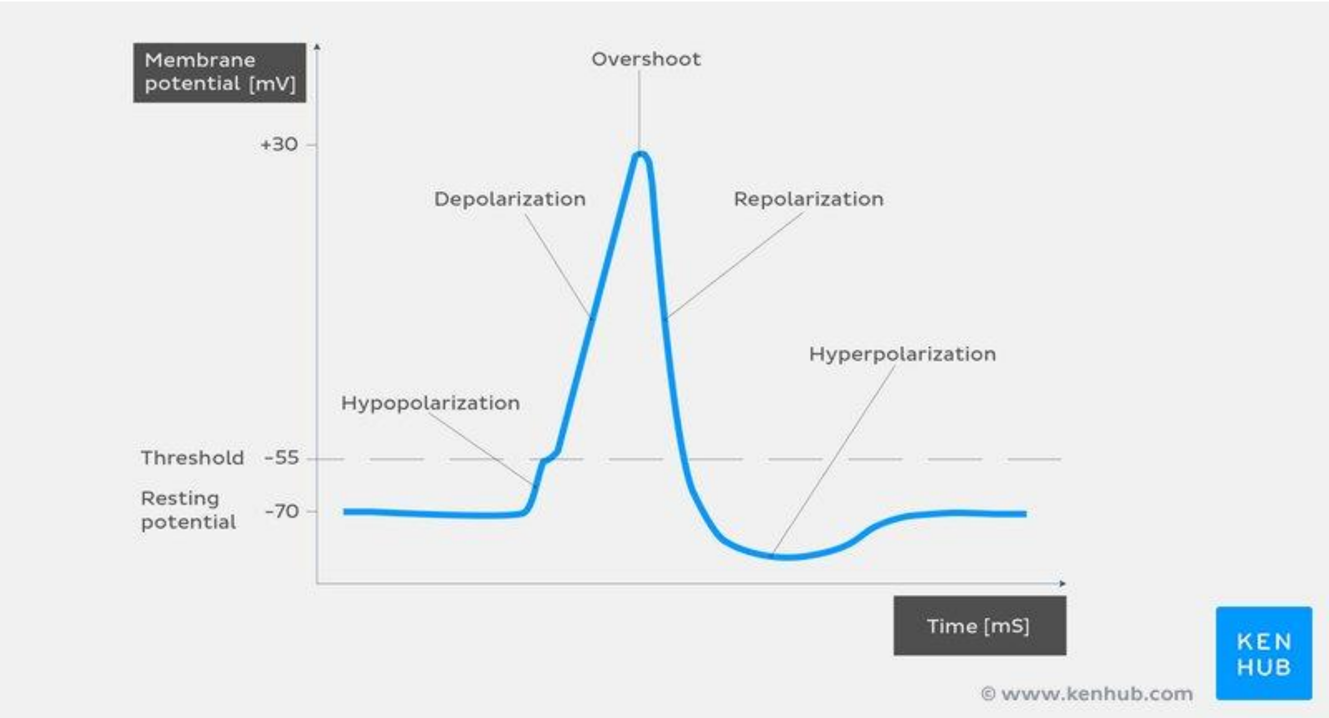
So, an action potential is generated when a stimulus changes the membrane potential to the values of threshold potential. The threshold potential is usually around -50 to -55 mV. It is important to know that the action potential behaves upon the *all-or-none law*. This means that any subthreshold stimulus will cause nothing, while threshold and suprathreshold stimuli produce a full response of the excitable cell.

Is an action potential different depending on whether it's caused by threshold or suprathreshold potential? The answer is no. The length and amplitude of an action potential are always the same. However, increasing the stimulus strength causes an increase in the frequency of an action potential. An action potential propagates along the nerve fiber without decreasing or weakening of amplitude and length. In addition, after one action potential is generated, neurons become refractory to stimuli for a certain period of time in which they cannot generate another action potential.

PHASES

From the aspect of ions, an action potential is caused by temporary changes in membrane permeability for diffusible ions. These changes cause ion channels to open and the ions to decrease their concentration gradients. The value of threshold potential depends on the membrane permeability, intra- and extracellular concentration of ions, and the properties of the cell membrane.

An action potential has several phases; hypopolarization, depolarization, overshoot, repolarization and hyperpolarization.

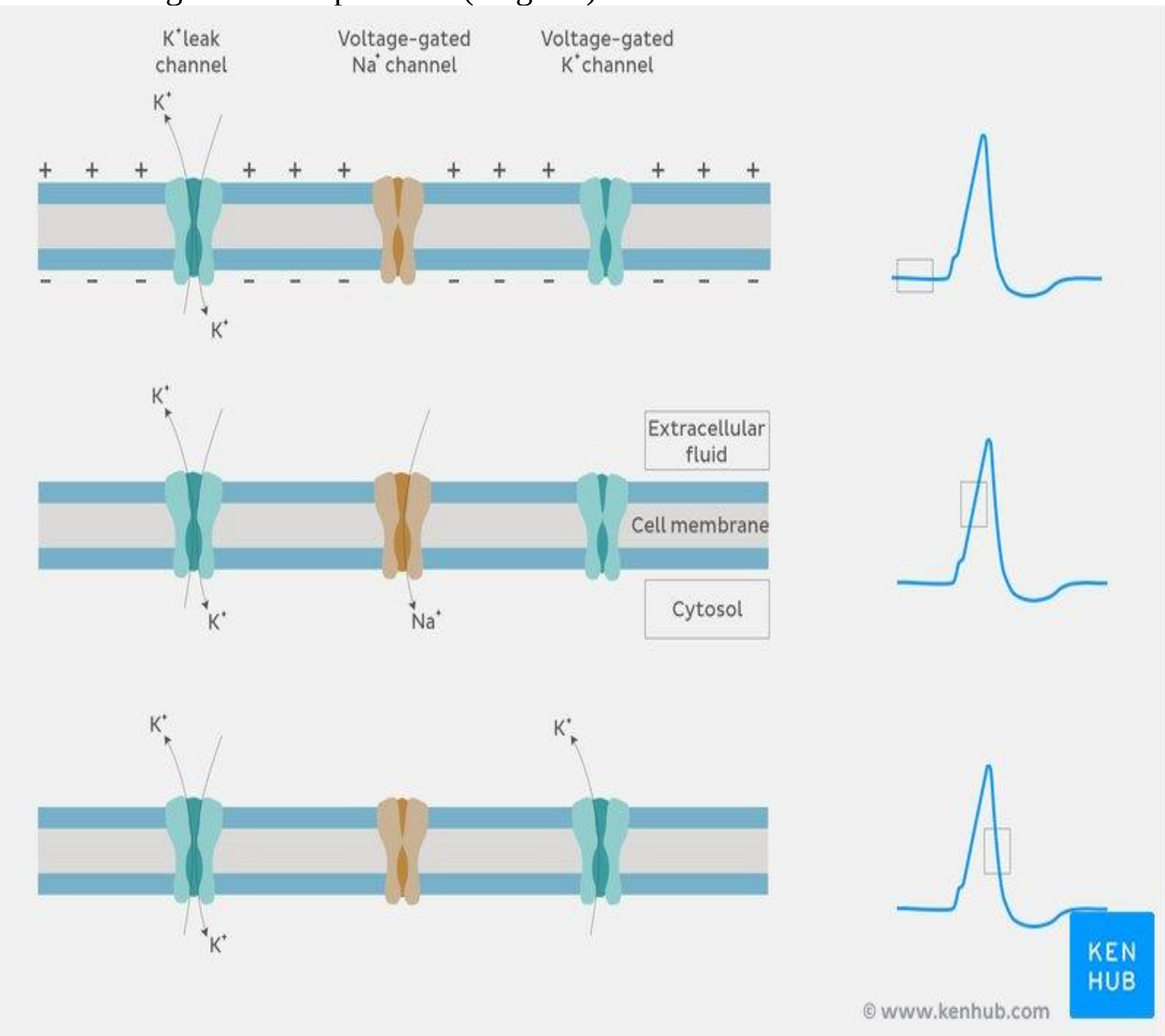


Action potential curve and phases (diagram)

Hypo polarization is the initial increase of the membrane potential to the value of the threshold potential. The threshold potential opens voltage-gated sodium channels and causes a large influx of sodium ions. This phase is called the depolarization. During depolarization, the inside of the cell becomes more and more electropositive, until the potential gets closer the electrochemical equilibrium for sodium of +61 mV. This phase of extreme positivity is the overshoot phase.

After the overshoot, the sodium permeability suddenly decreases due to the closing of its channels. The overshoot value of the cell potential opens voltage-gated potassium channels, which causes a large potassium efflux, decreasing the cell's electro positivity. This phase is the repolarization phase, whose purpose is to restore the resting membrane potential. Repolarization always leads first to hyperpolarization, a state in which the membrane potential is more negative than the default membrane potential. But soon after that, the membrane establishes again the values of membrane potential.

Ions exchange in action potential (diagram)



After reviewing the roles of ions, the threshold potential define more precisely as the value of the membrane potential at which the voltage-gated sodium channels open. In excitable tissues, the threshold potential is around 10 to 15 mV less than the resting membrane potential.

REFRACTORY PERIOD

The refractory period is the time after an action potential is generated, during which the excitable cell cannot produce another action potential. There are two sub phases of this period, absolute and relative refractoriness.

Absolute refractoriness overlaps the depolarization and around 2/3 of repolarization phase. A new action potential cannot be generated during depolarization because all the voltage-gated sodium channels are already opened or being opened at their maximum speed. During early repolarization, a new action potential is impossible since the sodium channels are inactive and need the resting potential to be in a closed state, from which they can be in an open state once again. Absolute refractoriness ends when enough sodium channels recover from their inactive state.

Relative refractoriness is the period when the generation of a new action potential is possible, but only upon a suprathreshold stimulus. This period overlaps the final 1/3 of repolarization.

PROPAGATION OF ACTION POTENTIAL

An action potential is generated in the body of the neuron and propagated through its axon. Propagation doesn't decrease or affect the quality of the action potential in any way, so that the target tissue gets the same impulse no matter how far they are from neuronal body.

The action potential generates at one spot of the cell membrane. It propagates along the membrane with every next part of the membrane being sequentially depolarized. This means that the action potential doesn’t move but rather causes a new action potential of the adjacent segment of the neuronal membrane.

We need to emphasize that the action potential always propagates forward, never backwards. This is due to the refractoriness of the parts of the membrane that were already depolarized, so that the only possible direction of propagation is forward. Because of this, an action potential always propagates from the neuronal body, through the axon to the target tissue.

The speed of propagation largely depends on the thickness of the axon and whether it’s myelinated or not. The larger the diameter, the higher the speed of propagation. The propagation is also faster if an axon is myelinated. Myelin increases the propagation speed because it increases the thickness of the fibre. In addition, myelin enables saltatory conduction of the action potential, since only the Ranvier nodes depolarize, and myelin nodes are jumped over. In unmyelinated fibres, every part of the axonal membrane needs to undergo depolarization, making the propagation significantly slower.

SYNAPSE

A synapse is a junction between the nerve cell and its target tissue. In humans, synapses are chemical, meaning that the nerve impulse is transmitted from the axon ending to the target tissue by the chemical substances called neurotransmitters (ligands). If a neurotransmitter stimulates the target cell to an action, then it is an excitatory neurotransmitter. On the other hand, if it inhibits the target cell, it is an inhibitory neurotransmitter.

SYNAPTIC TRANSMISSION

Neurons essentially communicate with each other through synapses. When signals have traveled through neurons to the endpoint, they cannot simply continue onto the next neuron. It must trigger the release of neurotransmitters which then carry the signals across the synapse in order to reach the next neuron. Terminal buttons belong to the presynaptic endings of the neuron and have vessels containing neurotransmitters. These are responsible for transmitting signals to other neurons.

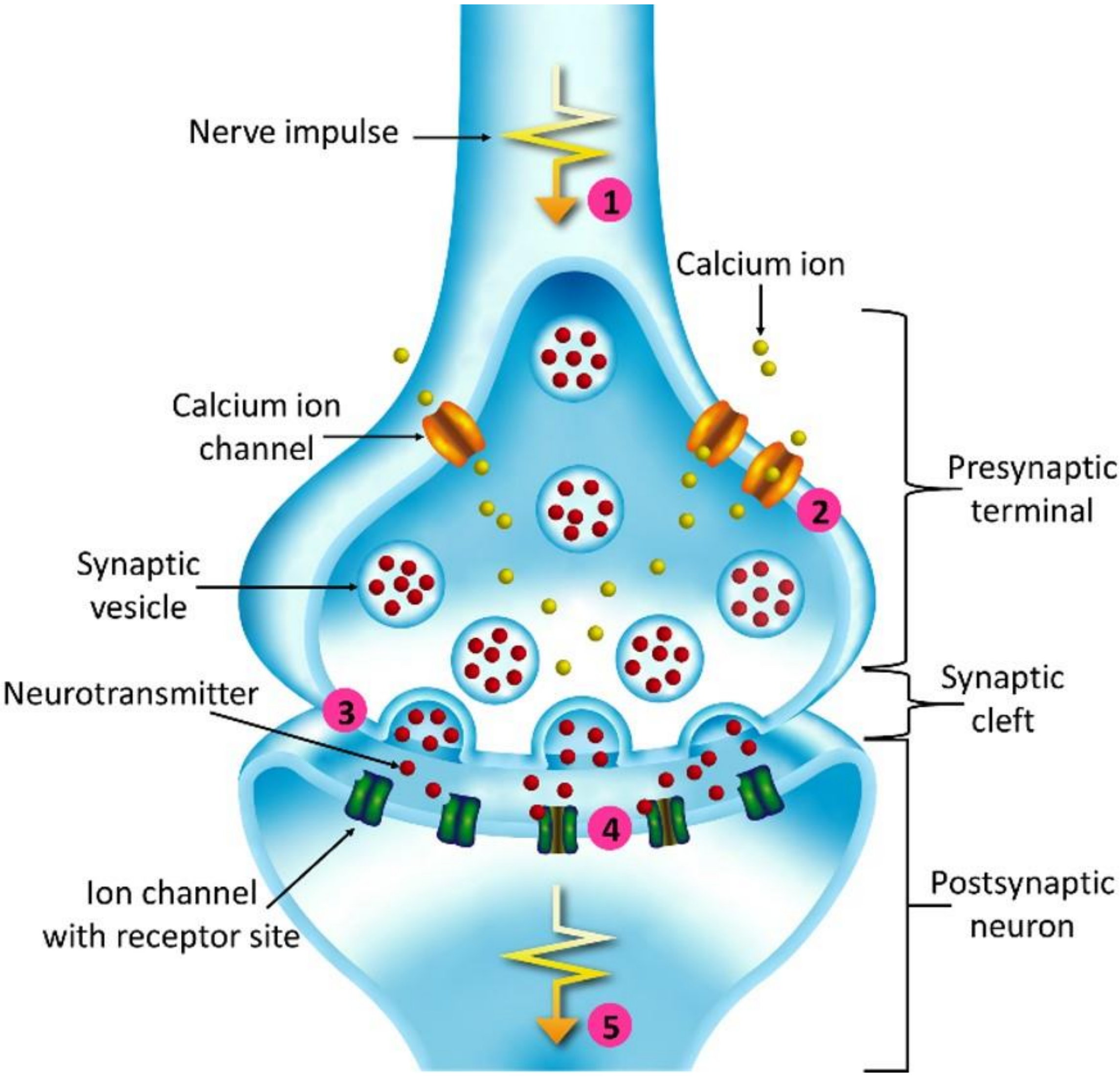


Fig- synaptic transmission through synaptic cleft

When a nerve impulse has triggered the release of these neurotransmitters from the terminal buttons, these chemicals are then released into the synaptic cleft and are then taken up by receptors on the next cell. The neuron that then receives the neurotransmitters is the postsynaptic neuron. Neurons receive messages from many terminal buttons and in turn, terminal buttons form synapses with many other neurons. Synapses can be either chemical or electrical and are essential to the functioning of neural activity. The most commonly found synapses in humans are chemical synapses. This occurs due to electrical activity in the presynaptic neurons triggering the release of neurotransmitters. The neurotransmitters disperse across the synaptic cleft to then bind themselves to specialized receptors of postsynaptic neurons. Once this occurs, the neurotransmitter then either excite or inhibits the postsynaptic neuron. Exciting the postsynaptic neuron leads to a firing of action potential (electrical impulses), whereas inhibiting the postsynaptic neuron prevents the transmission of a signal. Inside the presynaptic neuron are synaptic vesicles, which are covered in membrane and contain neurotransmitters. When an action potential arrives at the presynaptic terminal, it activates voltage-gated calcium channels (Ca^{2} +) in the neuron's membrane. Ca^{2} + are highly concentrated on the outside of the neuron and will rush into the neuron when activated. The Ca^{2} + permits the synaptic vesicles to fuse with the presynaptic terminal's membrane, enabling it to release neurotransmitters into the synaptic cleft. The transmitter molecules then will diffuse across the synaptic cleft and will bind to the receptors of the postsynaptic neuron. When these receptors are activated, this leads to either the opening or closing of ion channels, which are membrane proteins that provide a passageway through which charged ions can cross. Depending on the ions involved, this may either be depolarising- making the inside of the cell more positive, or depolarising- which makes the inside of the cell more negative.

Electrical synapses are different from chemical synapses as there is a direct physical connection between the presynaptic and the postsynaptic neuron. This connection takes the form of something called a gap junction, which is essentially a channel which allows ions to flow directly from the presynaptic cell to the postsynaptic cell. Gap junctions contain paired channels in the membranes of the pre and postsynaptic neurons, forming pores. These pores are larger than those of the voltage-gated ion channels in chemical synapses, meaning that a variety of substances can diffuse between the neurons. Electrical synapses transmit signals much quicker than chemical synapses, almost instantaneously, compared with chemical synapses taking several milliseconds. Despite being a lot faster to transmit signals, electrical synapses' signal strength is diminished over time, whereas chemical synapses do not lose their signal strength. Also, whilst chemical synapses can be excitatory or inhibitory, electrical synapses can only be excitatory.