MEMBRANE POTENTIAL

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Resting Membrane Potential

- Electrical potentials, of the order of a few millivolts (mV) to over 100 mV, commonly occur across cell membranes.
- The resting membrane potential (Em) remains constant for many types of cells but alters dramatically for excitable (irritable) cells, such as sensory, nerve, and muscle.
- Essentially three mechanisms contribute to these potentials:
- (1) the electrogenic ion pump,
- (2) the Donnan equilibrium, and
- (3) diffusion potentials.

- The electrogenic Na^+ -K^+ pump exchanges 3 Na^+ for 2K^+ per ATP hydrolyzed.
- There is thus a net transfer of 1 + charge, and this contributes to the normal membrane potential.
- However, it is not the immediate cause of normal membrane potential, as is apparent when the Na^+ -K^+ pump is poisoned by specific blockers, such as ouabain.
- There is a little or no effect of ouabain on Em (although the Em ultimately declines to 0 as the Na^+ and K^+ concentration gradients dissipates)

- A Donnan equilibrium contributes a small membrane potential because the intracellular fluid has a higher protein (Pr^-) concentration than the extracellular fluid.
- The Donnan potential is generally not responsible for the resting Em.
- The third and most important mechanism contributes to the Em is the existence of marked diffusion potentials for various ions across the membrane; these occur because there are large ionic concentration differences for ions that are permeable across the membrane.

Diffusion Potentials

- There are three important aspects to the electrical contribution of ions to the membrane potentials;
- (1) ion mobility,
- (2) selectively ion permeability, and
- (3) ion concentration gradients.
- **Ion Mobility.**

All ions are not equally mobile in solution. Ions experience frictional forces when in motion, and these frictional forces retard their movement. The magnitude of the frictional force depends on the size of the ion, and so mobility (*u*).

- **Ionic Permeability.**
- The electrical properties of cell membrane depend on the selective (and often changing) permeabilities of the membrane to different ions. There are many specific ion channels, or pores, that make the cell membrane highly but selectively permeable to ions.
- For example, there are Na^+ channels, K^+ channels, Ca^2 channels, Cl^- channels, etc. These channels are usually very selective.
- The Na^+ channel is quite specific for Na^+; it is considerably less permeable to similar ions such as K^+, Rb^+, and Cs^+ .
- The K^+ and relatively impermeable to Na^+ and Li^+. The selective permeability of channels is not just due to molecular weight and size, but also hydrate radius.

- **Ionic Concentration Differences.**
- In general, the intercellular fluid has a lower Na and Cl^- concentration and a higher K^+ concentration than the extra-cellular fluid.
- Ion gradients are summarized for frog and insect muscle in table 6-4. The intracellular K^+ concentrations are about 10 to 60 X higher than extracellular concentrations.

Excitable Cell Membranes

- All cell membranes have an electrical potential because there is an ionic concentration gradient across membrane.
- The membrane potential is stable in some cells but often transiently increases, forming an action potential in excitable cells (primarily sensory, nerve, and muscle cells).

Action Potentials

- The cell membrane is essentially an electrical circuit with a capacitance and parallel resistances for the flow of each ion, e.g., K^+, Na^+, and CL^-.
- The most important are, as we shall see, Na+ and K^+, and their resistances are variable. In assertion, each ionic resistance is in series with the equilibrium potential of each ion.
- For example, there is no current flow due to potassium ions if $E_m = E_k$; the E_m for no K current flow is not 0 mV!

- The resting membrane potential is approximately equal to the potassium equilibrium potential.
- Let us now consider what happens if K is not the most permeable ion. If CL- becomes the most permeable ion, then the rather uninteresting effects is very similar to the resting E_m towards the E_{cl}, which is very similar to the most very different (about + 65 mV) from the resting E_m, E_k, and $E_{cl.}$ Thus, increasing Na^+ conductance (g_{na}) by 1000 X would dramatically shift the E_m towards o mV and positive mV values (i.e. , towards E_{Na}) is **depolarization**.
- If the g_{Na} returns to normal, then the E_m returns to resting E_m; this is **repolarization.** The membranes potential becomes even more negative than resting E_m (moves towards E_k) if the K^+ conductance is increased; this is **hyperpolarization**.
- This rather simplistic analysis of depolarization and hyper polarization in response t increase in g_{Na} and g_k conductance is actually quite similar to the events during an action is actually quite similar to the events during and action potential.

- If the depolarization does not reach threshold (is subthreshold), then an action potential will not be initiated; the E_m will return to the normal resting value. An action potential is “all-or-none”; it either occurs or it doesn’t.
- There is (normally) no such thing as a “small” action potential or a “big” action potential.
- The inability of a membrane to support a second action potential during, or soon after, a previous action potential. This period when a membrane cannot be stimulated to support an action potential is call the absolute refractory period.

Properties of Action Potentials

- There are number of general properties of action potentials, such as threshold, shape and frequency. That merit further discussion.
- The properties of membranes, enzymes and protein channels are also influenced by the physical environment; two important physical parameters of the environment that can dramatically influence the electrical characteristics of membranes are temperature and pressure.

Threshold

- A depolarization must reach a certain, critical level before the feedback cycle between depolarization and increase in gNa becomes positive. This critical depolarization level is the threshold.
- A threshold depolarization fails to reach threshold and does not elicit an action potential. A suprathreshold depolarization exceeds threshold and will elicit an action potential. In general, a faster rate depolarization will cause a more rapid attainment of threshold and action potential initiation.

All-or-Non Response

- Normally, all action potentials of a given neutron are exactly equivalent in shape, i.e., have the same duration and amplitude.
- The effect of membrane depolarization is “All-or-non”; there is an action potential if Em reaches threshold (“all”), but no action potential if threshold is not reached (“none”).

Latency

- The latency is the time period between the onset of the stimulus current and the peak of the ensuing action potential.
- Latency decreases with increasing current strength because the depolarization to threshold occurs faster.

Strength – duration relationship

- A stimulating current must be of al least a minimal value to depolarization a cell membrane to threshold , but both the strength and the duration of nthe stimulus determine whether threshold is reached.
- Rheobase
- chronaxie

Accommodation

- A constant depolarizing or hyperpolarization current can modify the kinetics of sodium and potassium channels and alter the kinetics.

Refractory period

- It is not possible to elicit a second action potential for a brief period after an action potential .
- This short period is called the absolute refractory period.

Axonal propagation

- Excitable cell membranes not only sustain an action potential, but also allow its spread , or propagation.
- The passive electrical spread is similar to the conduction of electricity through wires, resistors and capacitors ; it is electrotonic spread.
- The extent of passive electrotonic spread is determined by the values of the membrane resistances and capacitances.

- An action potential travelling in the correct direction, from neuron soma to axon terminus, is describe as **orthodromic**, whereas an action potential traveling in the abnormal direction is **antidromic.**

Synaptic Transmission

- Action potentials are transmitted from one cell to another. There are essentially two different mechanism for transfer of electrical information from one cell (the presynaptic cell) to the next(the postsynaptic cell):
- (1) electrical synapses
- (2) chemical synapses

Electrical synapses

- Electrical synapses have a very specific anatomical organization and specialized membrane properties to electronically transmit an action potential from the presynaptic membrane to the postsynaptic membrane without so much attenuation that the postsynaptic cell fails to be depolarized to threshold .
- The presynaptic membrane at an electrical synapse is closely apposed to the postsynaptic membrane to form a **gap junction.**
- These gap junction are composed of numerous connexons that allow direct movement of ions and small molecules from the presynaptic cell into the postsynaptic cell.
- Preferential current flow in one direction is rectification

Chemical synapses

- Chemical synapses connect sensory cells to neurons, neurons to other neurons, and neurons to effector cells.
- They have a more complex structure than the simple gap junctions of electrical synapses.
- The neuromuscular junction is the typical example of a chemical synapse between a presynaptic neuron membrane and a postsynaptic muscle cell membrane.
- The synaptic portion of the muscle cell membrane is the **end plate.**

The basic sequence of events during chemical synaptic transmission.

- Transmitter release
- Receptor binding
- End plate potentials
- Synaptic delay
- neurotransmitters

Neurotransmitters

- Identification of a substance as a neurotransmitter is often difficult.
- Criteria for identification as a neurotransmitter:
- 1) Released from presynaptic terminal during action potential transmission
- 2) elicit the normal postsynaptic depolarization
- 3)the effect of the substance must be blocked by the same agent that block synaptic transmission .
- Four categories
- Acetylcholine
- Biogenic amines
- Amino acids
- Peptides

Synaptic Agonists and Antagonists

- Modification of any of the sequential process of synaptic transmission can block or potentiate transmission. Chemicals agents or drugs that have the same effect as a neurotransmitter are agonists (or mimetics), whereas chemicals that reduce or prevent synaptic transmission are antagonists.