The Action Potential

Introduction

- The action potential conveys information over distances in the nervous system.
- The frequency and pattern of action potentials makes the code used by neurons to transfer information.
- Action potentials are rapid reversals of the membrane potential from negative to positive and back to negative (all relative to the extracellular fluid).

Properties of the Action Potential

Elecrical characteristics

- The membrane potential at rest is about –65 mV.
- During the rising phase of the action potential, the membrane potential rapidly changes to about +40 mV.
- During the falling phase of the action potential, the membrane potential rapidly changes to about –75 mV.
- During restoration the membrane potential returns to about –65 mV.

Generation of an Action Potential

- Based on an example in a sensory nerve.
- Stimulation opens Na^+ permeable channels.
- Entry of Na^+ depolarizes the membrane – called a generator potential.
- If the depolarization reaches a critical level the membrane will generate an action potential.

Generation of Multiple Action Potentials

- The rate of action potential generation depends on the magnitude and duration of the generator potential (or other source of depolarization).

Ion Conductance and Ion Movement

- When the membrane is depolarized there is a transient increase in the Na^+ conductance.
- The increase in Na^+ conductance allows the entry of Na^+ which depolarizes the neuron
- The Na^+ conductance is very brief.
- Recovery of the negative membrane potential is aided by a transient increase in K+ conductance.
- The increase in K+ conductance allows the exit of K+ which repolarizes the neurons.

The Ion Pumps and Channels

- The high concentration of Na^+ in the extracellular fluid and the high concentration of K^+ in the intracellular fluid are maintained largely by transmembrane proteins called Na^+/K^+ pumps.
- The resting membrane is about forty (40) times more permeable to K^+ than to Na^+, due to the presence of transmembrane proteins called Na^+ channels and K^+ channels.

Voltage Gated Na^+ Channels

- The voltage gated sodium channel is a transmembrane protein that forms a pore that is highly selective to Na^+ ions.
    - The pore is opened and closed by changes in the electrical potential of the membrane

Structure of Na^+ Channels

- Na^+ Channels are composed of a single long polypeptide divided into four domains, each with six transmembrane alpha helix segments.
- The four domains clump together to form a pore.
- The pore is closed at the resting membrane potential (–65 mV).
- When the membrane is depolarized, the domains twist and open the pore.

Properties of Na^+ Channels

- Changing the membrane potential from –65 mV to –40 mV causes the Na^+ channels to open.
    - They open with a very short delay.
    - They stay open for about 1 msec and then close (inactivate).
    - They cannot be opened again by depolarization until the membrane potential returns to a negative value near the resting membrane potential.
- There are several different Na^+ channels genes in the human genome.
    - A single amino acid mutation of one causes generalized epilepsy with febrile seizures.

Effects of Toxins and Local Anesthetics on the Na^+ Channels

- Tetrodotoxin (TTX), from the ovaries of the puffer fish, blocks the Na^+ channel pore by binding to the channels and prevents action potentials.
- Saxitoxin, from dinoflagellates often consumed by shellfish, blocks Na^+ channels.
- Lidocaine, and other similar local anesthetics, bind to the inside of the Na^+ channel pore, and interfere with movement of Na^+.

Voltage Gated K^+ Channels

- The voltage gated potassium channels are transmembrane proteins that form pores that are highly selective to K^+ ions.
    - The pore is opened and closed by changes in the electrical potential of the membrane

Properties of K^+ Channels

- Changing the membrane potential from –65 mV to –40 mV causes the Na^+ channels to open.
    - They open with a delay of about 1 msec.
    - They stay open as long as the membrane is depolarized.

Synthesis

- Upon stimulation voltage gated Na^+ channels open and Na^+ rushes into the cell.
- The membrane potential goes positive (toward the equilibrium potential for Na^+).
- Voltage gated Na^+ channels close (inactivate), Voltage gated K^+ channels open (delayed in response to depolarization), and K^+ rushes out of the cell.
- The membrane potential goes negative (toward the equilibrium potential for K^+) until the voltage gated K^+ channels close.
- Na^+ channels remain inactive until the membrane potential goes sufficiently negative.
- The Na^+/K^+ pumps are working quietly in the background.

Conduction of the Action Potential

- The conduction of the action potential represents the sequential opening and closing of voltage gated Na^+ channels and voltage gated K^+ channels from one end of the excitable membrane to the other.
    - The influx of Na^+ depolarizes the segment of the membrane immediately ahead of the action potential until that segment reaches threshold.
- Voltage gated Na^+ channels usually are found in axons of neurons and not in dendrites or the cell body.