Neural Signaling – Membrane Potentials

The neuron

The nerve cells are called *neurons* which have these major components:

- Cell body (also called soma) containing a nucleus
- Dendrites, tree-branch like fibres which receive neural signals (in the form of impulses of action potentials) through synaptic connections from other neurons.
- Axon a long fibre which carries the impulses generated by the neuron to other neurons through synaptic connections.

../figures/neuron.gif

The cell wall is a lipid bilayer membrane which separetes the intracellular fluid from the extracellular space.

../figures/membrane.gif

Resting Membrane Potential

- **Transmembrane Pumps**

  Enzymes (proteins) located in the neuronal membrane behave like pumps which move sodium ions (Na^+) out of the cell and potassium ions (K^+) into the cell. In the resting state there is a higher concentration of Na^+ in the extracellular fluid and higher concentration of K^+ in the intracellular fluid.

- **Nongated Channels**

  Transmembrane proteins form two types of nongated ion channels, the K^+ channels and the Na^+ channels, through the membrane. Due to the ion concentration gradients, the nongated K^+ channels leak potassium ions out from the neuron, and the nongated Na^+ channels leak sodium ions into the neuron.

- **Resting Potential**

  As there are more K^+ channels than Na^+ channels, there are more out going K^+ ions than in coming Na^+ ions. As the result, an electrical potential difference is created across the membrane. The outside is about 70 mV higher than the inside. If the potential of extracellular space is used as the reference, the membrane potential is negative 70 mV. The neuron with this resting potential difference is said to be polarized.

../figures/channels.gif
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Depolarization and Passive Current

Some other transmembrane ion channels are affected by external influences such as voltage, chemicals (e.g., neurotransmitters), or physical stimulation (e.g., pressure in touch receptors in the skin, or light in photoreceptor in the eye). Voltage-gated channels are closed at the resting membrane potential but open as the membrane is *depolarized*, i.e., intracellular voltage is raised from negative 70 mV to some value closer to zero. These gated ion channels play an essential role in generating action potentials for transmitting neuronal signals through long distances.

../figures/depolarization.gif

When a sensory receptor (such as the photoreceptors in the retina) or synapse is activated by chemical or physical stimuli, ion channels in a localized region open to let ionic current (Na^+, K^+, Cl^-) flow across the membrane. These inward electrical currents raise the intracellular potential and the membrane potential is reduced or depolarized. These currents gradually leak back out of the neuron due to the transmembrane channels to form complete circuits. The membrane depolarization declines with the distance from the site of the receptor or the synapse

$$v(x) = v_{max}(1 - e^{-cx})$$

where x is the distance and c is some constant.

As passive current does not travel far inside the neuron, it is not sufficient for neuronal signal transmission, especially along the long axons to convey the information to the next neuron.

../figures/leakage.gif

Action Potential

- **Phase I – Depolarization**

  When a passive current flows across the membrane following a synaptic or receptor potential, the depolarized membrane potential triggers the voltage-gated Na^+ channels to open. The inward Na^+ ionic currents enhance the depolarization which triggers more Na^+ channels to open to let in more ionic currents. This is a positive feedback loop called the *Hodgkin-Huxley cycle*).

  If the initial depolarization caused by a passive current is not strong enough to reach a threshold (about -48 mV), it will diminish without triggering any significant response from the neuron. But if the depolarized membrane potential passes the threshold, the Na^+ channel currents dominate the process and the membrane potential is highly depolarized to form a positive peak (a spike), the *action potential*, whose amplitude is independent of the initial depolarization. Note that the intensity of the neural signal transmitted in a neuron is not coded by the magnitude of the membrane potential (as all action potentials are of the same intensity), but by the number of action potentials generated per unit time, called the *firing rate*.

- **Phase II – Hyperpolarization**

  With a short delay after the opening of the voltage-gated Na^+ channels, membrane depolarization triggers the voltage-gated K^+ channels to open and the outward K^+ currents lead to a strong repolarization. The membrane potential drops quickly from the positive peak to a negative level even lower than the resting potential (70 mV). This is called *hyperpolarization*, the second phase of the action potential. After a few milliseconds the membrane potential returns to its resting level.

- **Phase III – Refractory Period**

  During the time following the repolarization phase of the action potential, the voltage-gated Na^+ channels are inactivated and unable to be opened, regardless of how much the membrane is depolarized. This is the *absolute refractory period*, which is followed by a short *relative refractory period* during which action potential can be generated but only with larger-than-normal depolarization. This limited rate of action potential generation determines the neurons' frequency resolution.

../figures/threshold.gif

Neuronal Signaling through Action Potentials

The passive current across the membrane caused by a synaptic or receptor stimulation does not travel far because the depolarization declines with distance, due to the leakage through the transmembrane ion channels. However, if this initial depolarization is strong enough to pass the threshold, an action potential will be triggered (usually initiated at the interface between the cell body and axon) and the inward Na^+ currents produce more passive currents, which travel down the axon to depolarize new pieces of membrane to continue the process. The sequentially triggered action potentials relay the neuronal signal from the synapse or the receptor along the axon to its terminators, where the signal is passed on to other neurons.

../figures/actionpotential.gif

Saltatory Conduction and the Role of Myelination

Myelin is a fatty substance that wraps the axons to increase the membrane resistance (by blocking the leakage through the ion channels). The passive current can flow through a piece myelinated axon without leaking until it reaches the nodes of Ranvier (French histologist) where myelination is interrupted. Here inward Na^2 currents through the voltage-gated Na^+ channels cause another action potential which regenerate the passive current to flow through the next segment of myelinated axon. This process is repeated at every node until the signal arrives at the terminals. The signal travels through the axon at a speed about 120 m/sec.

../figures/actionpotentialtransmission.gif

Synaptic Transmission

An action potential arriving at the axon terminal depolarizes the terminal region and initiates an influx of Ca^{++} ions into the region. As a result, small vesicles containing neurotransmitter fuse with the membrane at the synapse and release this transmitter into the synaptic cleft, the space between the presynaptic and postsynaptic neuronal membranes. Crossing the cleft by diffusion, the transmitter arrives at the postsynaptic membrane and binds and interact with the receptor molecules embedded in the membrane.

../figures/synapse.gif

Excitatory and Inhibitory Stimulation

The chemical interaction of the neurotransmitter and the postsynaptic receptor initiates events that lead to either depolarization (excitation) or hyperpolarization (inhibition) of the postsynaptic cell. If this cell is a neuron, an excitatory postsynaptic potential (EPSP) can lead to the generation of action potentials in this neuron. If this cell is a muscle cell, the EPSP leads to action potentials in the muscle and muscle contraction. If the postsynaptic membrane potential is hyperpolarized, the postsynaptic cell is less likely to generate an action potential and is inhibited.

../figures/transmitter.gif

Neuronal Model

Whether and how much a neuron is excited or inhibited depends on the synaptic stimulations it receives from other neurons. The intensity of each synaptic stimulation is in turn determined by the level of excitation (or inhibition) of the neuron transmitting the signal and the synaptic connectivity between the transmitting and receiving neurons. This process can be modeled mathematically by

$$a_i = \sum_{j=1}^{n} x_j w_{ij}$$

where a_i represents the activation of the ith neuron in a population of n neurons, x_i represents the signal intensity transmitted by the jth neuron ($j = 1, 2, \cdots, n$), and w_{ij} represents the synaptic connectivity from the jth neuron to the ith neuron.

If the activation level a_i is higher than the threshold represented by μ_i, the receiving neuron is excited to generate action potentials that travel along its axon to other neurons down stream. The intensity of this output signal is a function of the activation

$$y_i = \begin{cases} 0 & \text{if } a < \mu_i \\ f(a_i) & \text{if } a > \mu_i \end{cases}$$

../figures/neuronmodel.gif

In some other mathematical models for a single neuron, an sigmoidal function is used as the function $f(a)$:

../figures/sigmoidal.gif