1.3.6

Propagation of an Action Potential

The ultimate goal of the action potential is to spread along the membrane inducing changes in voltage-gated proteins. This process allows ions to follow their gradients and generate electrical current. In order to understand this spreading phenomenon (commonly referred to as propagation), it is important to understand three concepts: membrane conductance, capacitance, and resistance.

In cell membranes, conductance is the unit of measurement used to describe the movement of ions across the cell membrane through channel proteins. The movement is often described as permeability. Different kinds of ions vary in their permeabilities, mainly due to the number of channel proteins available to a given ion and the driving force for the ion. Capacitance is the unit of measurement used to describe how much charge is separated (positives from negatives) and stored on both the intracellular and extracellular membrane surfaces. A key word is separate. Charges are difficult to separate because placing “like” charges together takes force or energy to break their bond, since they repel each other. The force or energy (voltage) that is generated by electrochemical gradients establishes the resting membrane potential. The resting membrane potential is measured in volts and represents the potential energy available to return the separated charges to each other if conductance (open channels) allows. Mathematically, capacitance represents the ratio of charge on the surface of the membrane per volt in the membrane potential. It is expressed as:

Equation 1:  \( C = \frac{Q}{V} \)

Q represents the amount of charge separated, and V represents the voltage difference between the membrane surfaces. In cells’ membranes at rest, the extracellular surface has a positive charge (+Q) and the intracellular surface has a negative charge (-Q). One way to look at this is by observing the resting membrane potential, if it is negative 70 mV then there is 70 mV of potential energy available for use. This energy will help move positive charge back into the cell and join negative charge on the inside of the cell. Capacitance exists in cells because the cell membrane is able to act as a capacitor. A capacitor is essentially an electrically charged sandwich with each piece of bread storing charge at its surface and in its center (distance between the two pieces of bread) which will act as an insulator (ie., no polarity, no attraction to charge). In the case of cell membranes, the capacitor sandwich is the result of the phospholipids’ tail (center), the separated cations and anions associated with the phosphate heads (pieces of bread). It is important to understand that the distance between the two phospholipid bilayers in all cell membranes is essentially the same distance because the center of the membrane is a highly conserved ratio of hydrocarbons and proteins.

As stated, “like” charges are difficult to arrange together because of repulsion forces. However, any polar molecules in the center of a membrane (center of the sandwich) can alter these repulsion forces by contributing an attractive force towards the center. This newly added attractive force can
“absorb” some of the charges, making the repulsive force weaker. This results in the same 70mV of RMP potential energy occurring as well as more charges on the surfaces of the membranes and higher capacitance. This is explained by the equation:

**Equation 2: \( C = \varepsilon \times (A/d) \)**

The Greek symbol \( \varepsilon \) represents what is called the permittivity of the center portion of the capacitor. A technical definition of permittivity can be complex so we will take some liberties in the definition and try to ignore our cringing physicist friends. Thus, for our purposes, it is best to think of permittivity as the amount of polar molecules found within the center portion of the membrane. The *more polar a membrane, the higher the capacitance, and the more charge separation we find per volt*. The variable \( d \) represents the distance between charge separations (the distance between the external and internal surface of the “slices of bread”). As stated above, in most cell membranes this value never changes, however, in the case of an insulated axon (myelination), the distance of charge separation \( d \) can increase substantially. Also, myelin layers have very little protein, so the overall polarity of the “center” of our sandwich decreases \( \varepsilon \) decreases). The variable \( A \) is a unit of area available for charge separation. If \( A \) is bigger, the charges can spread out more and experience less charge repulsion, resulting in more charge separation per volt (increased capacitance).

**Resistance** is the unit of measurement used to describe the ability of something to oppose electrical current of electrical fields. In the case of cell membranes, resistance is used to describe the behavior of ions in terms of their “leakiness” or conductance across the membrane \( R_m \) and once inside the membrane, how far their charge can influence other “down-stream” voltage-gated proteins (sphere of influence). If we were actual physicists we would probably start pontificating about electrical fields at this point, but since we lack pocket protectors for our pens we will instead try to stay more simple and use the term “sphere of influence”. The distance the sphere of influence can travel is determined by how much intracellular resistance it encounters \( R_i \). For a membrane to depolarize and trigger an action potential that propagates, the values of \( R_m \) and \( R_i \) are essential.

When channels are opened and ions start flowing, based on their driving force across the membrane, a current is generated and can be referred to as the **capacitative current**. Capacitors can only gain or lose charge because this movement of charge is what causes current. At the resting membrane potential the cell membrane capacitor is maximally charged, and when additional ion channels are opened (i.e Na+ voltage-gated channels), the capacitor discharges, and the current moves toward zero (less charge separation). This loss of voltage is exponential, increasing more rapidly with each passing millisecond. To describe this exponential loss in current across time, physicists use a unit measurement called the **time constant**. The technical definition of the value of the time constant is the time required for the voltage of the capacitor to fall to 37% of its initial value. Conceptually, we might look at the time constant value as being dependent upon both resistance of the membrane \( R_m \) and the membrane capacitance \( C_m \):

**Equation 3: Time Constant = \( R_m \times C_m \)**

In other words, the time constant is directly proportional to the \( R_m \) and to the \( C_m \). If membrane resistance is increased, the time constant will also increase (by taking longer to depolarize the membrane). Also, if capacitance of the membrane increases, the time constant will also increase. Because there are more charges separated now, it will take longer to depolarize the membrane. Stated another way: As the time constant increases the cell depolarizes slower and the longer it takes to propagate an action potential.
Once an action potential is generated, the next obstacle is propagating it down the membrane. Since action potentials are the result of cations crossing the membrane and influencing protein conformations, how the sphere of influence is distributed once it crosses the membrane will determine the distance the action potential will propagate. There are three possible ways that a cationic charge (sphere of influence) can be affected once it crosses the membrane:

1. The sphere of influence could be neutralized (causing it to have less effect) by anionic charges on the inner surface of the membrane, as well as the anionic charges on polar molecules found in the cytoplasm; this is referred to as internal resistance ($R_i$).
2. The cations may flow back through the membrane, essentially leaking back out and taking their charge with them, thereby diminishing the positive charge; this is referred to as membrane resistance ($R_m$).
3. Whatever is left of a positive charge sphere of influence after losing some to $R_i$ and $R_m$ is able to influence down-stream proteins and to add to the propagation of the depolarizing effect.

As mentioned above, membrane voltage changes can occur as a function of time (the time constant). However, voltage changes can also occur as a function of space. To describe the effect of the charge and its distribution in space we use the unit of measurement called the length constant. For example, a graded membrane potential (what we have been calling a positive charge “sphere of influence”) will decay as it travels away from its site of origin. Importantly, the distance that this influence can go and maintain strength depends on the ratio of the membrane resistance to the internal resistance according to the following equation:

**Equation 4:** $\text{Length Constant} = (R_m/R_i)^{1/2}$

When the ratio of $R_m$ to $R_i$ is high the effect of the charge is large and travels for a longer distance which is equivalent to a larger length constant. The time constant and length constant are most evident when talking about the axon of neurons, especially in reference to the effect of myelin.

Myelin decreases the effect of polarity (decreased $C$) and increases $d$ (equation 2), thereby decreasing capacitance. Because capacitance is inversely correlated with the distance between the charged membranes, myelin reduces the amount of stored charge thereby reducing the time constant (equation 3). Less capacitance means fewer charges are required to move in order to depolarize or decrease the membrane potential toward zero. Decreased capacitance also means there are fewer charges separated. This means $R$, decreases as there are fewer anions on the inner surface of the membrane to diminish the cation “sphere of influence” that develops at the point of depolarization. Myelin also increases membrane resistance, which reduces leakiness. This has the overall effect of increasing the length constant. Thus, myelin allows the membrane to depolarize quicker and to spread out further. It is important to recognize that myelin does not cover the whole axon; instead, it covers it in sections, leaving gaps of unmyelinated membranes called nodes. In the node, since it is bare membrane, capacitance stays the same, but $R_m$ is low because conductance is high (having lots of channels). The nodes act to regenerate the action potential and myelinated sections act to increase the effect of the sphere of influence. This “jumping” of action potential depolarization events from node to node is called **saltatory conduction.** The end result is increased speed of action potential...
propagation with a loss of action potential strength.

The image above shows myelin on a peripheral nerve axon.

The myelin is made up of individual Schwann cells. The myelin covers the axon in a way that "insulates" the axon from depolarization waves. In this way, depolarization will occur only at the nodes of Ranvier (or areas of bare axon between individual myelin segments). When a nerve axon is organized in this way with myelin, action potential propagation can travel much faster (nearly 10 times faster than unmyelinated axons). It might be helpful to think of action potential propagation in terms of speed.