

Excitable Cells and Action Potentials

Membrane Potentials

The cell membrane, also referred as plasmalemma, is where most of the processes responsible for the intracellular communication take place. As we know, all living cells have an electrical gradient across their membranes, where it is possible to measure the potential difference of the inside in respect to the outside. This quality of the plasmalemma is used by the CNS (Central Nervous System) as a mean for our body's mechanism of communication, and the language in which this occurs is analogous to binary sequences. The same way a computer interprets any information in terms of 1's and 0's; our body understands impulses (AP) and resting potentials.

Resting Potentials

The basic way, in which neurons are able to use the cell membrane to communicate, lies on the generation of ionic gradients. This occurs by the combined action of energy-consuming ionic pumps as well as semi permeable membranes. It is accepted that the cell membrane is most permeable to K^+ , which allows these positively charged ions to flow down the concentration gradient. This allows an electrical potential difference across the plasmalemma to be created. Since the K is moving out of the cell, a net negative charge is created inside the membrane. A chemical gradient of specific ions is essential for the proper functioning of the neuron. However to create this chemical gradient it is necessary to actively transport different ions across the membrane, which reduces its entropy.

In order for this process to occur, an active Na^+ ion pump must do work breaking down ATP, thus these ion pumps are actually 'ATPases'. These enzymes are also called Na^+,K^+ -dependent ATPase, or ' Na^+/K^+ Pump'. The concentration of Na^+ is smaller on the inside of the cell, which is why the ATP is required, in order to move these ions to the outer side of the membrane. At the same time K^+ ions are being pumped from the outside to the inside of the cell, which also is against its concentration gradient. In general for every ATP molecule used 3 Na^+ ions are pumped out of the cell and 2 K^+ ions are pumped into the cell, this constitutes for about 1/3 of the energy consumption of the body.

In order to fully visualize this potential difference we must also understand that, inside the cell there are proteins being produced, which are large molecules and cannot diffuse across the cellular membrane. These large

molecules have a negative charge, and as they are found in high concentrations inside the cell, they produce a negative charge on the interior side of the membrane, which also causes the Cl^- ions found inside the cell to be repelled to the outside of the cell, where there is a higher concentrations of these molecules.

Now that we covered the elements producing the potential difference, we still don't know how it is created. As mentioned before, during the efflux of the 2 K^+ and the influx of 3 Na^+ , there is an inequality between this 'trade', which is responsible for a -10mV difference on the membrane. We also must understand that as the K^+ ions diffuse across the membrane, down its concentration gradient, a positive charge is built on the outside of the membrane. As this charge builds up, the K^+ ions begin to be repelled due to their charge, which cause a stop on the efflux of K, as the electrochemical equilibrium is reached. Intuitively, the greater concentration gradient of K^+ , the greater the potential difference to oppose it must be. This can be calculated through the Nernst Equation.

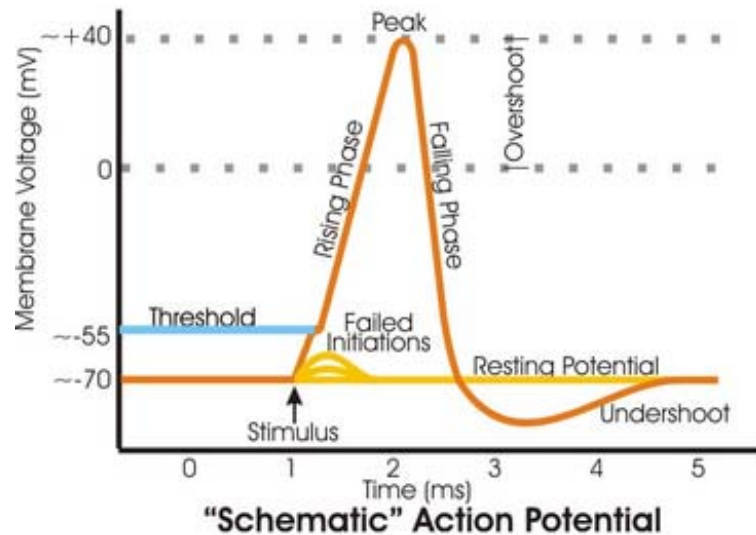
$$E_k = (RT/F) * \ln ([\text{K}^+]_o / [\text{K}^+]_i) \approx -90\text{mV}$$

The potential difference in the membrane is expressed for the inside of the neuron relative to the outside. The value of -90mV is accurate for some cells, for example in the heart, but it is found that in neurons the resting potential is around -70mV , due to a leakage of other ions, for example Cl^- and Na^+ . In this case the Goldman equation is more suited. Now if the properties of the membrane change in such manner that it becomes most permeable to Na^+ ions, there will be a net Na^+ current inward. This influx will happen until electrochemical equilibrium is reached. This equilibrium can be calculated to be about 50mV , notice the positive charge since in this situation the positive ions are coming into the cell, unlike the efflux of K.

Nervous Impulses

The Na^+ influx mentioned above, happens due to **Voltage-Gated Na^+ channels**, which are essential for the production of electrical impulses on the neurolemma. These channels are opened by, depolarizing the membrane from its resting level, near -70mV , to a *threshold potential* of about -50mV . This explains the name, these channels need a specific electric field in order to change their shapes and open. Upon the opening of a channel, permeable only to Na^+ ions, the membrane increases its conductance, which generates an **action potential**. Voltage-Gated Na^+ channels are found in high density within

excitable membranes. When an AP is created, the channel stay open for a very small fraction of time, when the membrane potential surges towards 50mV, never actually achieving this value. When the V-G Na⁺ channels become inactivated, the main current present is a K⁺ leakage and the resting potential is restored, where positive ions are diffusing out of the cell.



After the inactivation of the Na⁺ channels, they will remain inactivated until the membrane potential drops below 'threshold'. That time is called the **Refractory Period**. There are two kinds of R.P. The *absolute refractory period*, which is the case where none of the Na⁺ pores, can re-open until the membrane is re-polarized, in order to resume their resting configuration. This can last around 1ms. The *relative refractory period* in the other hand corresponds to the opening of some of the Na⁺ channels. Basically a second action potential cannot be triggered during the absolute RF, no matter how strong the depolarizing current is applied because the Na⁺ channels are all inactivated (depolarization block). After this period we have the relative refractory period, where a second impulse can be generated, provided a stronger than normal depolarizing current, which is used to open the relatively dispersed population of available channels. Generally this lasts between 2-5 ms.

Another phenomenon worth knowing is the After-Hyperpolarization or "undershoot". In some membrane locations, voltage-gated K⁺ channels can be found, which are opened by depolarization of the membrane to its threshold point. This increases the permeability of K⁺ ions, allowing them to flow down the concentration gradient more easily. Unlike the Na⁺ channels, these channels are much slower and the permeability is much smaller, this is partly

because there are far less of these channels in the neurolemma. Invertebrate axons have prominent K^+ currents but mammalian myelinated axons have effectively none. The purpose of these channels is to accelerate the repolarization of the membrane. In fact, when this happens, there is a period of afterhyperpolarization after the depolarizing spike, which takes the membrane potential lower than the resting potential (-70mV).

Impulse Transmission

When an AP is created, it propagates from its origin across the rest of the cell, depolarizing all adjacent regions of the membrane. When this AP moves across the membrane, it opens Na^+ channels on its path. This causes the signal to be regenerated in the membrane. Most cells in the body are not considered excitable, meaning that they cannot generate action potentials, since they lack Na^+ channels.

Axons are long projections of neurons, in which electrical impulses are created and also can travel away from the neuron's cell body (soma). Axons can be compared to electric cables due to their capability to transmit impulses. Neurons with long axons and muscle cells generate propagating AP. Even though axons have these properties, it differs from man-made cables because they aren't very good conductors. Protein channels on the membrane do allow ion species to cross the membrane with a lot of resistance in special conditions, so it is unlike copper wires in the sense that membranes are not completely insulated. Another difference is that in the membrane signals that arrive are smoothed during the transmission for this same reason. But this loss of signal is compensated by a boost on the signal along the axon, which continually regenerates the action potential.

Membrane capacitance and membrane resistance are two major factors determining axonal cable properties. The conduction speed of an AP depends on the membrane length constant λ . This constant represents the distance traveled before a potential difference drops to 37% of its original amplitude. The longer the signal can travel, the faster impulse conduction can occur. λ is increased by increasing the axon diameter or by increasing the resistance across the membrane.

Out of these two ways to increase λ , the most feasible is the change in membrane resistance (R_m). Increasing the diameter of axons would depend on a spatial availability and also nutritional support. However, in order to increase R_m , there is an addition of the *myelin sheath* on the outside of the axolemma. Specialized glial cells wrap around successive section of the axon forming *myelin sheath*. These are nothing more than piles of membrane

stacked tightly around the axon; this substance is composed of white colored phospholipids. A small space is left between successive glial cells (Schwann cells in the PNS and oligodendrocytes in the CNS), these are called **Nodes of Ranvier**. These nodes are very important since they are necessary openings for the ionic fluxes generating a new spike to boost the decrementing voltage of a prior impulse. This happens because these nodes have a high density of Na^+ channels but no voltage-gated K^+ channels. An AP that is generated, will travel along the axon, through several nodes before it actually gets regenerated. This leaping mode of transmission is termed saltatory conduction.

However, not all axons are myelinated. In unmyelinated axons, Na^+ and K^+ voltage-gated channels are intermixed and in some cases one glial cell wraps around many axons in bundles. This form of axons are the majority, even though they have slower conduction velocities, due to smaller diameter and lower R_m .

- Leonardo Sileniek