Membrane Potentials and Bioelectricity

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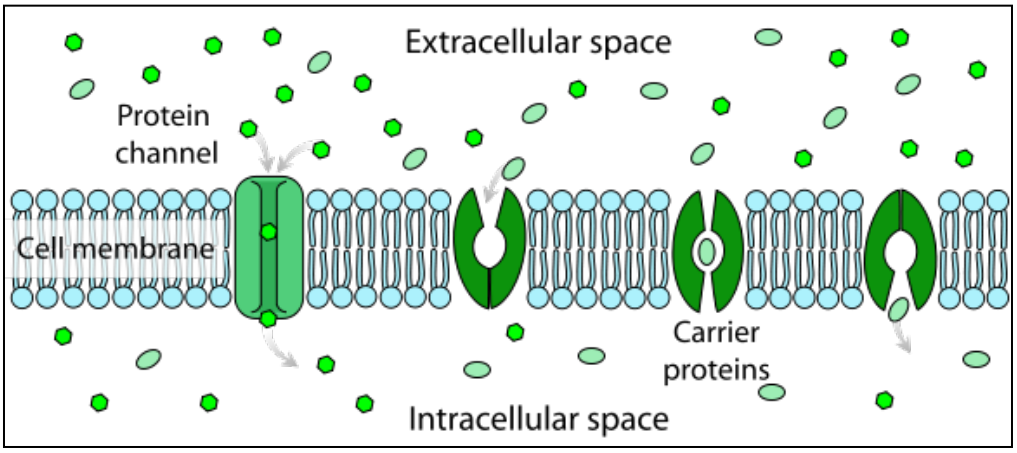
Most, if not all, cells in the human body have a net electric charge to some degree on either side of their cell membranes. This results in an electric potential across the membranes (Cardoso and Sabbatini 1999). A few types of cells, known as excitable cells, use this feature as a part of their primary functions within the body. Nerve and muscle cells are two notable examples of this (*Britannica Encyclopedia Online 2010*). Nerve cells change their membrane potential to receive, transmit, and process information, while muscle cells do this to initiate muscle contractions (Byrne and Schultz 1988, 93). These functions play integral roles in the human body, and as such it is important to understand the mechanisms by which this phenomenon operates.

One of the essential parts of the cell with respect to generating electric potentials is the cell membrane, also called the plasma membrane. This membrane is composed primarily of lipids and proteins. Specifically, the lipids are phospholipids, which consist of a polar, hydrophilic, phosphate group "head" and a non-polar, hydrophobic, fatty acid "tail" (Stein 1980, 2). These phospholipids form a continuous bilayer—with the tails facing inwards and the heads facing outwards—whose primary function is to keep ions and most molecules from passing through it. This function is accomplished because the arrangement of the polar heads and the non-polar tails prevents large, water-soluble molecules, and smaller ions and charged molecules from passing through. In this way, the lipid bilayer has some electrically insulating properties. However, water and small, uncharged molecules can permeate the membrane (Keynes and Aidley 1991, 26). The protein component of the cell membrane varies widely depending on the variety of cell, ranging from just a few types to over one hundred different proteins. These proteins include enzymes, receptors, and transport proteins. (Berne et al. 2004, 5).



Lipid Bilayer with Various Transport Proteins (Villarreal 2007)

The other major cause of the electric potentials is the presence of ions in the cytoplasm and in the extracellular fluid, which are the fluids inside and outside of the cell respectively. While ions are unable to diffuse across the phospholipid bilayer, certain proteins in the cell membrane act as ion channels, allowing ions to diffuse in and out of the cell. Some of these ion channels only allow specific ions to pass through them, while others allow all ions below a certain size to pass. Furthermore, some ion channels are controlled by voltage differences, and others by certain molecules such as neurotransmitters (Berne et al. 2004, 10). Because the membrane is only permeable to certain substances, it is known as being selectively permeable.

The electric potential itself is called a membrane potential because it is measured across the plasma membrane. It is measured relative to the extracellular fluid, which is to say that if the potential is negative, then that means that the inside of the cell membrane is more negative than the outside. (Levitan and Kaczmarek 1991, 34). Electric potentials are caused by the separation of charges and the associated fields of those charges. In membrane potentials, those separated charges come in the form of the ions and charged molecules on either side of the plasma membrane (Stein 1980, 33). To determine how the ions move across cell membrane, it must first be considered how charged particles move across permeable membranes.

The two main factors that determine the movement of charged particles across a membrane are the concentration gradient and the electrical gradient. If a membrane is permeable to a particular type of charged particle, then a particle of that kind will tend to move towards the side of the membrane that has a lower concentration of that species of particle. Likewise, the charged particle will also tend to move towards the side of the membrane that has a lower concentration of the kind of charge on the particle—in other words, the particle will move down its electric potential. As a result of these tendencies, the movement of the particles across the membrane will quickly reach equilibrium such that the movement due to concentration difference and the movement due to electrical difference will equal each other and there will be no net movement (Berne et al. 2004, 22).

In the case of the plasma membrane, the two ions mainly responsible for setting up most cells' membrane potentials are sodium (Na^+) and potassium (K^+). This is because of a special protein known as the sodium-potassium pump. This protein uses ATP from the cell to pump Na^+ out of the cell and simultaneously pump K^+ into the cell (Stein 1980, 27). Of course, this alone would not generate a separation of charge as both Na^+ and K^+ are equally charged. However, most cell membranes are actually significantly more permeable to K^+ than to Na^+. All of this means that as K^+ is pumped into the cell, it quickly diffuses out—down its concentration gradient. Likewise, as Na^+ is pumped out of the cell, it quickly diffuses back in. However, because of the differences in permeability, more K^+ moves out of the cell than Na^+ moves in, thus resulting in more positive charge in the extracellular fluid relative to the cytoplasm. This buildup of charge creates an electric potential across the cell membrane—the membrane potential! Eventually, enough Na^+ and K^+ builds up outside the cell membrane that the combined force from the concentration gradient and the electric gradient equal the force from the Na^+-K^+

pump and, even though there is still a flow of ions, there is no net movement across the membrane. This type of membrane potential is typically known as a "resting potential" because it does not change with time. It is also worth noting that the pump itself is not electrically neutral, which is to say that it pumps three Na^+ out of the cell for every two K^+ that it pumps in. This alone causes a buildup of positive charges outside the cell, and therefore an additional electric potential is created. While the potential created solely by the sodium-potassium pump is not insignificant, the vast majority of the total membrane potential is caused by the difference in the permeability of Na^+ and K^+ (Byrne and Schultz 1988, 74-78).

Interestingly, because the plasma membrane restricts the flow of charge while also separating positive and negative regions, it can be modeled as a resistor and a capacitor in parallel. As such, the equations describing the behavior of RC circuits can be applied with great accuracy in describing the charging or discharging of the membrane potential. Of course, owing to the variability of biological membranes, the time constant in the RC circuit equations differs significantly between different cells, and even between different regions of membrane on the same cell (Levitan and Kaczmarek 1991, 35-37).

While all cells have a membrane potential to some degree, certain types of cells use this feature as a part of their primary function. These cells are called excitable cells. One notable type of excitable cell is the neuron.

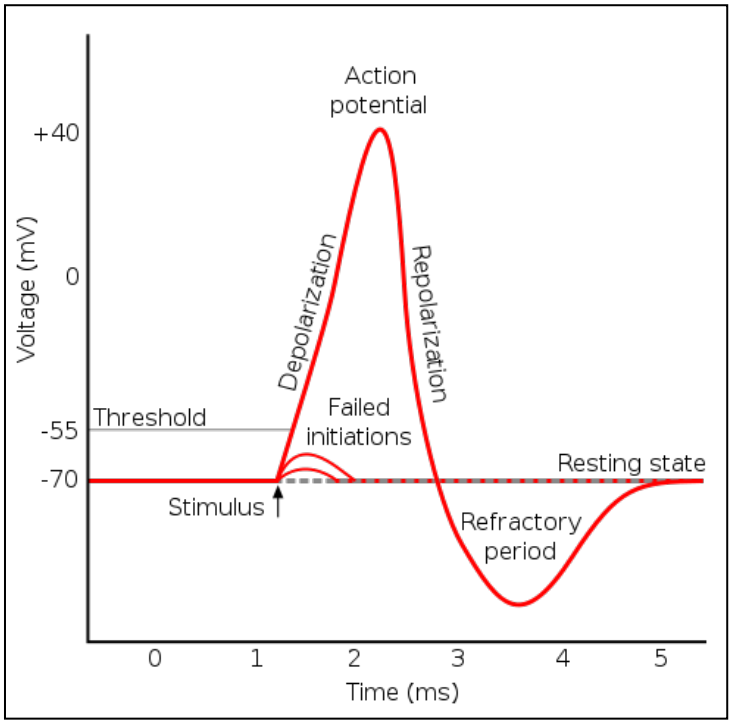
Neurons, also known as nerve cells, are the basic unit of the nervous system. The exact structure of a neuron varies depending on the type and function, however the basic components are a cell body, dendrites, and an axon. The cell body is the part of the neuron where the nucleus and most of the other organelles are contained. Extending off of the cell body are a number of processes known as dendrites, where incoming information is received. One of the processes,

usually much larger than the others, is the axon, along which outgoing information is transmitted. While the cell body is vital for the survival and growth of the neuron, it is relatively unimportant in terms of signal transmission (Keynes and Aidley 1991, 2-3).

Like all cells, neurons have a resting potential. In neurons, this potential is about -70 mV. However, because neurons are excitable cells, they also exhibition the quality of being able to alter their membrane potentials. Changes in membrane potential are either depolarizing or hyperpolarizing. A change from -70 mV to -20 mV is depolarizing because the potential difference is decreased. Conversely, a change form -70 mV to -90 mV is hyperpolarizing because the potential difference is increased (Levitan and Kaczmarek 1991, 34).

When a neuron is subjected to either a depolarizing or hyperpolarizing current, caused by some external stimulus, the resulting potential spreads over a small area of the neuron, with the change in potential diminishing as it moves farther from its point of creation. If this changed potential is below a certain level, then it is known as subthreshold. However, when a neuron's membrane potential is depolarized to a specific level called the threshold, then an event known as an action potential occurs. The action potential is an almost instantaneous complete depolarization of the membrane potential. In fact, the action potential does not just depolarize the membrane; it goes on to reverse the membrane potential. The threshold for most neurons is around -55 mV. When this level is reached, an action potential occurs and the membrane potential jumps to around +50 mV. Then, just as quickly as it depolarized and reversed potential, the neuron repolarizes to its resting potential of -70 mV. In actuality, the neuron overshoots -70 mV and is hyperpolarized for some time before it levels out at its resting potential. During the action potential there is a period of time known as the absolute refractory period, in which no amount of stimulus can cause another action potential to occur. There is also a relative refractory

period during which another action potential can occur, but only if the stimulus is particularly large. Action potentials are so-called "all-or-nothing" events, which is to say that they either happen completely or they do not happen at all (Cardoso, de Mello, and Sabbatini 2000).



Schematic of an Action Potential (Iberri 2007)

The actual mechanisms by which action potentials occur involve a complex sequence of events at the molecular level. In short, when the membrane potential reaches the threshold—due to an accumulation of individual subthreshold potentials or otherwise—certain membrane proteins known as voltage-gated ion channels open. The first channels to open only allow sodium to pass through, and so the membrane becomes more permeable to Na^+. Thus, the excess Na^+ in the extracellular fluid quickly diffuses down its concentration gradient into the cell, causing the inside of the membrane to become more positively charged than the outside, resulting in the aforementioned +50 mV membrane potential. Once this maximum voltage is attained the Na^+ voltage-gates inactivate—which is different from their original state of being

closed in that they cannot be opened again for some time—and simultaneously other voltage-gates open that only allow K^+ through. As such, K^+ quickly diffuses out of the cell, compensating for the Na^+ that rushed into cell. The K^+ outflow actually overcompensates, which causes the temporary hyperpolarization. The K^+ voltage-gates quickly close, and the original resting potential is restored by the Na^+-K^+ pumps. The absolute refractory period corresponds to the times at which the Na^+ voltage-gates are all inactive, while the relative refractory period occurs when only some of the Na^+ voltage-gates are so. (Berne et al. 2004, 32-37).

The primary function of neurons is to transmit information encoded as a series of action potentials. To accomplish this, action potentials must be able to propagate along the neuron, or more specifically, along the axon. In reality, if a stimulus does manage to excite the dendrites and/or the cell body of a neuron to threshold, then the resulting action potential will seem to travel with a discrete width along the entire length of the axon. Not only that, but the action potential travels along the axon without decreasing in magnitude—it is therefore said to be "conducted." This phenomenon can be explained by taking into account the fact that when an action potential is elicited somewhere on the neuron, a significant amount of positive charge is brought to the inside of the cell membrane at the site of the action potential. This positive charge—in the form of ions—will spread out a bit along the inside of the membrane. When this happens, the areas neighboring the site of the action potential become somewhat depolarized, assuming that they were originally at resting potential. In fact, they become depolarized enough to reach the threshold level. This of course causes new action potentials to occur adjacent to the original one. In this way, once an action potential occurs somewhere on the neuron, it is conducted along the entire cell, travelling all the way down the axon (Byrne and Schultz 1988, 144-146).

It is also important to note that the traveling action potentials, called nerve impulses, are conducted in one direction down the axon, and then stop when they reach the end. Obviously, this is important because the information needs to flow in one direction down the axon, not "bounce" around on it, disrupting any new incoming information. This feature is accomplished because as an action potentials travels down the axon, the area of the membrane that it just came from cannot be brought back to threshold because it is still in its absolute refractory period (Levitan and Kaczmarek 1991, 43-44). Because of this attribute, the action potential does not truly spread out over the neuron, but rather travels along it.

Many neurons have the quality of being myelinated. This means that sections of the axon are wrapped in a thick lipid sheath, which is actually the curled-up membrane of a glial cell—the exact type of glial cell varies based on the type of neuron. The regions of myelinated axon are separated by small regions of non-myelination called nodes of Ranvier (Keynes and Aidley 1991, 6-9). These sheaths are somewhat analogous to insulation on a wire in that, on a myelinated axon the impulse will "jump" from one node of Ranvier to another, thus greatly increasing the rate of transmission (Keynes and Aidley 1991, 21).

Given that action potentials have an all-or-nothing quality, information cannot be specified by the strength, or amplitude, of the nerve impulse. It is instead encoded in the frequency of the impulses (Levitan and Kaczmarek 1991, 41). For example, if light of constant intensity is hitting a person's retina, the receptor cells there will transmit a constant stream of action potentials. However, if the light intensity is increased and again held constant, the receptors will send out impulses that are spaced closer together, which is to say that they will have a higher frequency. This is because the stronger the stimulus, the sooner another action potential can be generated while the membrane is in the relative refractory period. Therefore, the

brain determines light intensity from the frequency of the impulses that it receives on the optic nerve.

Up till now, only the transmission of information on a single neuron has been discussed. Of course, neurons have to spread said information on to other neurons in order for the nervous system to function. This is accomplished at places called synapses. Synapses are points where the synaptic bulbs—which branch off of the end an axon—of one neuron meet the synaptic end-plates—which cover the dendrites and cell body—of another neuron. The synaptic bulbs and end-plates of most synapses are separated by a gap of approximately 50 nanometers, called the synaptic cleft. Because of the gap, most synaptic transmissions are not electrical events, but rather chemical ones. In short, when a nerve impulse reaches a synaptic bulb, also called an axon terminal, chemicals known as neurotransmitters are released into the synaptic cleft. The neurotransmitters then act as stimuli on the end-plates of the post-synaptic neuron, causing local depolarizing potentials. If there is enough stimulus, an action potential is initiated, which then travels down the axon of the neuron until it reaches another synapse, and the cycle repeats itself (Keynes and Aidley 1991, 89-94). Depending on the type and function of a neuron, it may synapse with multiple other neurons, and may require multiple incoming impulses from the other neurons to initiate a single impulse in itself. Or vice versa, a single neuron could initiate simultaneous impulses in multiple other neurons. Additionally, some neurotransmitters can actually inhibit impulses from being initiated in the post-synaptic neurons (Berne et al. 2004, 50-51). All of these different possibilities explain why neural circuitry is so very complicated.

Another type of excitable tissue is muscle. Skeletal muscle cells, commonly known as muscle fibers, are excited in much the same way that neurons are, with action potentials being initiated and then conducted across their surfaces. Neurons meet muscle fibers at special

synapses called neuromuscular junctions. When a nerve impulse reaches the synaptic bulb of the neuron, neurotransmitters are released. These neurotransmitters initiate an action potential on the muscle fiber, which spreads very quickly over the surface of the cell. This in turn causes a series of chemical reactions that lead to the contraction of the entire muscle fiber (Berne et al. 2004, 44-45). This is why muscles contract in response to an electric shock. The shock initiates an action potential, which then causes muscle contraction.

As is apparent, electric potentials play a vitally important role in the human body. They provide a means by which information can be rapidly detected, transmitted, and processed. Membrane potentials allow people to sense the world around them and to react to their environment. Given that the brain operates via nerve impulses, electric potentials make possible the very existence of human consciousness itself. For these reasons, a detailed knowledge of the features of membrane potentials and the mechanisms by which they function allows science to advance its understanding of both how the human body works and what it means to be human.

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