

Biophysical principles of nerve impulse propagation

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Biophysical Principles of Nerve Impulse Propagation

Resting Potential

The Resting Potential is an electrostatic potential across the plasma membrane of a neuron, that is not conducting an impulse and adds up to -70 to -80 mV. The Resting Potential is crucial as initial state for the propagation of nerve impulses along the plasma membrane of a neuron.

Establishing the Resting Potential

The Electrostatic Potential arises from an uneven distribution of ions across the selective permeable membrane of a neuron. It describes the work that can be performed if the tensions are balanced. Crucial ions are: Sodium Cations (Na^{2+}) that are situated in the extracellular matrix as well as Chloride anions (Cl^-), Potassium Cations (K^+) mostly distributed in intracellular matrix together with negatively charged organic molecules. The distribution of ions also leads to a diffusion potential along the concentration gradient. The negatively charged molecules can not pass the membrane and are therefore enclosed in the intracellular matrix and evoke a negatively charged environment. Chloride Anions can diffuse into the intracellular matrix but are mostly repelled by the organic anions and attracted by the cations outside the cell and are therefore preferential situated in the extracellular matrix. Sodium cations are situated in the extracellular matrix and can only pass the plasma membrane through selective channel transport proteins that are most often closed. Potassium cations pass the plasma membrane by free diffusion through potassium channel proteins. They pass outside the cell until an equilibrium is established between their concentration gradient (diffuse to the extracellular matrix) and the electrostatic potential (diffuse into intracellular matrix, attracted by negatively charged anions). There is a greater number of potassium cations in the intracellular matrix but due to their single positive charge they do not affect the total negative charge. Hence the intracellular matrix carries a negative charge in comparison to the extracellular matrix. This equilibrium is kept by Sodium-Potassium Pumps. These integral membrane proteins pump natrium cations outside the cell and Potassium cations to the intracellular matrix using energy in form of ATP. This is essential because the opening of sodium channels is by probability and mediated by tension. Therefore some sodium cations may diffuse into the intracellular matrix at times.

Impulse Conduction

Action Potential

The action potential is the reversal (depolarization) and reestablishment (re polarization) of the electrostatic potential across the membrane of a neuron as an electrical impulse passes along it (transient negative shift).

Ion Channels

The Conduction of impulses along the plasma membrane of a neuron happens in form of action potentials. Therefore, a conducted impulse is the depolarization of successive membrane regions. To trigger an action potential the ion channels need to be conformed in order for cations to pass the plasma membrane and to provide its depolarization. The ion channels's conformations is mediated by tension. There exists a negative feedback between the conformation of the ion channels and the membrane potential. An increased membrane potential

causes the ion channels to change their conformation (they open) and cations diffuse into the extracellular matrix. This process further increases the membrane potential, therefore even more ion channels change their conformation and depolarization continues. There are two main Types of channels to distinguish that differ in their sensitivity to voltage. Sodium ion channels (Hodkin-Huxley Sodium Channels) are found in neurons. The impulse conduction takes under one millisecond. Calcium ion channels mediate a slower conduction, as the negative shift lasts about 100 milliseconds longer. These are mostly found in membranes of muscle cells (sarcoplasmic reticulum). There also exist cells which exhibit both forms. This paper will focus on the Sodium ion channels only as they are the most well studied.

There are three conformation states for the Sodium Ion Voltage gated channel (Nav). At low membrane potentials, the NAV is deactivated and no sodium ions can diffuse. At the membrane threshold value (-55 mV) the NAV are activated allowing diffusion of Sodium cations. The higher the membrane potential, the higher the probability of NAVs to open. As long as a high a high membrane potential insists, the NAVs are in the inactivated state. At a low membrane potential the NAVs close and are again inaccessible to Sodium cations (deactivated). During one action potential the NAVs change their conformation from deactivated to activated to inactivated to deactivated. A channel in the inactivated state is refractory until again deactivated. this way no action potential can be transmitted and it is ensured that the impulses can only propagate one way. The duration of the inactivated state is called refractory period.

Initiation of an Action Potential

The initial depolarization to evoke the membrane threshold value and trigger an action potential is on the axon hillock of a neuron. The triggering of an action potential is dependent on the depolarization of the plasma membrane of the neuron. This depolarization needs to succeed the threshold value of approximately -55 mV (threshold potential) in order for an action potential to be developed. Incoming Impulses cause a polarization of the neurons plasma membrane. Hereby, multiple impulses are added up in aspects of time of arrival and location on the plasma membrane. Depending on the ion channels (depolarizing/hyper polarization) impulses are inhibitory or promotive and prevent or urge a strong depolarization of the plasma membrane. On the axon hill all impulses/polarizations are added up and if they exceed the threshold membrane potential an action potential is triggered. Generally it can be said that the tension (electrical potential) across the membrane decreases. The action potential is an all or nothing event. If the depolarization on the axon hill does not exceed the threshold membrane potential, no action potential is triggered.

The plasma membrane can be Polarized either by impulses conducted by a synapse (mediated by neurotransmitters) and gap junction from a preceding neuron. There are also neurons with ion channels responding to sensory stimuli. These sensory neurons respond to pressure, temperature, light or sound and can be found in for example on skin, ears, nose, etc..

Phases of an Action Potential

Proceeding from the depolarization reaching the threshold value on the axon hill, the depolarization of the plasma membrane continues with more Sodium Channels opening. Sodium cations stream into the cell following the electrical potential and the concentration gradient, causing the overall tension across the plasma membrane to drop. The intracellular matrix gains an overall positive charge whereas in the extracellular matrix a negative charge prevails. This depolarization continues until a complete charge reversal is established and the tension across the plasma membrane adds up to about +30 mV. This is the peak of the action potential.

Mediated by the positive tension, sodium ion channels close, and potassium ion channels open. Following the now reversed electrical potential, potassium cations diffuse to the extracellular matrix. This process continues until the former charge distribution of charge is established (extracellular matrix: net positive charge, intracellular matrix: net negative charge). This re polarization even exceeds the former negative tension, causing a hyper polarization (tension of more than -70 mV) until the potassium ion channels close.

File:Action Potential
Phases of an Action
Potential

Finally a protein complex called the potassium-sodium pump transports potassium ions inside the cell and sodium ions to the extracellular matrix. This process is a linked transport, transferring two potassium ions for each sodium ions across the plasma membrane. This way the former configuration of ions across the membrane is reestablished, and this part of the axon can be aroused once again. The before mentioned hyper polarization prolongs this process and therefore the refractory time. This is important in ways to grant protection from overexcitement of the axon and prevents the reflux of impulses along the axon. Impulses can only propagate one way.

Equalizing Currents

This only explains the progress of an action potential in one segment on the axon. For an impulse to pass along it, the successive segments need to be excited. This is granted by equalizing currents. Once the segment of an axon is depolarized, its intracellular matrix carries a net positive charge. The successive segment which is still in an unexcited state and therefore displays the electron distribution of the resting potential, hence possesses a negatively charged intracellular matrix. The sodium cations of the excited segment are attracted by the anions in the successive segment. Therefore some sodium cations follow the electrical potential and also their diffusion potential diffuse to the region of the successive segment of the axon and cause its depolarization. And again if the threshold value is reached, the less negative charge causes sodium ion channels to open and a new action potential is triggered. This way an impulse propagates along an axon.

Continuous and Saltatory conduction

The described mechanism above is called continuous conduction of an impulse. It propagates from one segment of a neuron's membrane to the next. However, to accelerate this process, most nerve cells are enclosed by a multilamellar membrane, the so-called myelin sheath (consisting of Schwann cells). This sheath is not entirely enclosed around the axon but regularly leaves uncovered sectors called "nodes of Ranvier". The covered membrane regions do not possess ion channels and thus no connection to the extracellular matrix. In this case these regions cannot develop an action potential. Therefore the equalizing currents alternate between the nodes of Ranvier, from each node to the successive one. As a result the impulses proceed about ten times faster along the axon as a lot less depolarization needs to happen. Also the energy required for the reestablishing of the resting potential is less, therefore the process is also much more energy efficient.

Action potentials that reach the synaptic knobs are transmitted to the next neuron or terminal cell by chemical synapses, or transformed into a hormonal signal.

References

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