

Membrane Potentials

Membrane potentials are described by various ionic concentration configurations outside and inside the membrane of a cell. These potentials are:

1. Resting membrane potential: the membrane potential at rest, steady-state conditions.
2. Action potential: a non-graded potential, much like binary code (on/off).
3. Post-synaptic potentials: graded potentials, that can be summated/subtracted by modulation from presynaptic neurons.

Resting Membrane Potential (RMP)

The human organism is composed of multiple cells, all of them with different components and therefore with different **resting membrane potentials**. Some of these cells are excitable (e. g.: cells; neurons; muscle fibers), generating an action potential when subjected to an external stimulus, causing its membrane depolarization. The **resting membrane potential (RMP)** is due to changes in membrane permeability for potassium, sodium, calcium, and chloride, which results from the movement of these ions across it. Once the membrane is *polarized*, it acquires a voltage, which is the difference of potentials between intra and extracellular spaces.

What is a RMP?

Resting membrane potential is:

- the unequal distribution of ions on the both sides of the cell membrane;
- the *voltage difference* of quiescent cells;
- the membrane potential that would be maintained if there weren't any stimuli or conducting impulses across it;
- determined by the concentrations of ions on both sides of the membrane;
- a *negative value*, which means that there is an excess of negative charge inside of the cell, compared to the outside.
- much depended on intracellular potassium level as the membrane permeability to potassium is about 100 times higher than that to sodium.

Producing and maintaining RMP

RMP is produced and maintained by:

Donnan effect

described as large impermeable negatively charged intracellular molecules attracting positively charged ions (e. g.: Na^+ and K^+) and repelling negative ones (e. g.: Cl^-)

Membrane selectivity

is the difference of permeabilities between different ions

Active transport (Na^+/K^+ ATPase pump)

is the mediated process of moving particles across a biological membrane, against the concentration gradient.

- *Primary active transport* – if it spends energy. This is how the Na^+/K^+ ATPase pump functions.
- *Secondary active transport* – if it involves an electrochemical gradient. This is not involved in maintaining RMP.

Ion affection of resting membrane potential

RMP is created by the distribution of ions and its diffusion across the membrane. Potassium ions are important for **RMP** because of its *active transport*, which increase more its concentration inside the cell. However, the *potassium-selective ion channels* are always open, producing an accumulation of negative charge inside the cell. Its outward movement is due to random molecular motion and continues until enough excess negative charge accumulates inside the cell to form a membrane potential.

Na^+/K^+ ATPase pump affection of the RMP

The **Na^+/K^+ ATPase pump** creates a concentration gradient by moving 3Na^+ out of the cell and 2K^+ into the cell. Na^+ is being pumped out and K^+ pumped in against their concentration gradients. Because this pump is moving ions against their concentration gradients, it *requires energy*.

Ion channels affection of resting membrane potential

The cell membrane contains *protein channels* that allow ions to diffuse passively without direct expenditure of metabolic energy. These channels allow Na^+ and K^+ to move across the cell membrane from a higher concentration toward a lower. As these channels have selectivity for certain ions, there are *potassium-* and *sodium-selective ion channels*. All cell membranes are more permeable to K^+ than to Na^+ because they have more K^+ channels than Na^+ .

The Nernst Equation

It's a mathematical equation applied in physiology, to calculate equilibrium potentials for certain ions.

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$$E_i = \left(\frac{R \cdot T}{F \cdot z}\right) \cdot \ln \frac{[X]_1}{[X]_2}$$**

- **R** = Gas Constant
- **T** = Absolute temperature (K)
- **E** = The potential difference across the membrane
- **F** = Faradays Constant (96,500 coulombs/mole)
- **z** = Valency of ion

The Goldman-Hodgkin-Katz Equation

Is a mathematical equation applied in Physiology, to determine the potential across a cell's membrane, taking in account all the ions that are permeable through it.

$$E_m = 58 \log \left(\frac{P_{Na} \cdot [Na]_{out} + P_K \cdot [K]_{out}}{P_{Na} \cdot [Na]_{in} + P_K \cdot [K]_{in}} \right)$$

- **E** = The potential difference across the membrane
- **P** = Permeability of the membrane to sodium or potassium
- **[]** = Concentration of sodium or potassium inside or outside

Measuring resting potentials

In some cells, the **RPM** is always changing. For such, there is never any **resting potential**, which is only a theoretical concept. Other cells with membrane transport functions that change potential with time, have a resting potential. This can be measured by inserting an electrode into the cell. Transmembrane potentials can also be measured optically with dyes that change their optical properties according to the membrane potential.

Resting membrane potential varies according to types of cells

For example:

- **Skeletal muscle cells:** -95 mV
- **Smooth muscle cells:** -50 mV
- **Astrocytes:** -80/-90 mV
- **Neurons:** -70 mV
- **Erythrocytes:** -12 mV

Action potential (AP)

Action potential is an event in which the membrane potential of the cell quickly rises and falls. The trajectory follows a constant pattern.

Components

Resting potential

Resting potential is largely determined by the difference concentration of K⁺ ions and has a value of -70 to -90 mV, the cell's interior has a negative charge.

Action potential

If we introduce one electrode inside the axon and one to the cytoplasmic surface of the axon, hyperpolarization (in the case of negative internal electrodes) or depolarization (in the case of negative external) occurs.

If we increase the membrane potential to the *threshold potential* (in membrane with *resting membrane potential*, from -70mV to about -55 mV), nerve fiber responds with the emergence of an action potential (sudden opening voltage-gated sodium ion channels, thus allowing ions of sodium to enter through the membrane, causing the inside of the cells to become positive - there is *depolarization*).

If the increment in the membrane potential doesn't reach "threshold potential", the sodium voltage-gated channel will not open. In this case, no action potential is generated.

In the next phase, the membrane again becomes permeable for potassium ions and the potential returns to resting value despite a slight hyperpolarization.

Differences with postsynaptic potential

Parameter	AP	PSP
Characteristic	All or nothing	graded
amplitude	cca 100 mV	1-10 mV
duration	cca 10-40 ms	1-5 ms
Where?	along the axon	postsynaptic membrane (neuronal cell body, dendrites)
spread	without decrement	with decrement

Post-Synaptic Potentials

Ionic Basis of Postsynaptic Excitation

At an excitatory synapse, neurotransmitter opens channels in the postsynaptic membrane that are permeable to cations, principally Na^+ and K^+ . The net ionic current (IEPSP) that gives rise to an EPSP is a sum of the individual currents carried by all the ions that permeate the channel.

EPSP reversal potentials. Reversal potential (Nernst potential) is the membrane potential E_m at which the net ionic current through a channel is zero.

$$I_{\text{EPSP}} = I_{\text{Na}} + I_{\text{K}}$$

$$E_{\text{rev}} = g_{\text{Na}} E_{\text{Na}} + g_{\text{K}} E_{\text{K}} / g_{\text{Na}} + g_{\text{K}}$$

g_{Na} , g_{K} – conductances proportional to the permeability of the channel to Na^+ and K^+

E_{Na} , E_{K} – the Nernst potentials for these ions.

Rearranging

$$\frac{g_{\text{Na}}}{g_{\text{K}}} = \frac{E_{\text{K}} - E_{\text{rev}}}{E_{\text{rev}} - E_{\text{K}}}$$

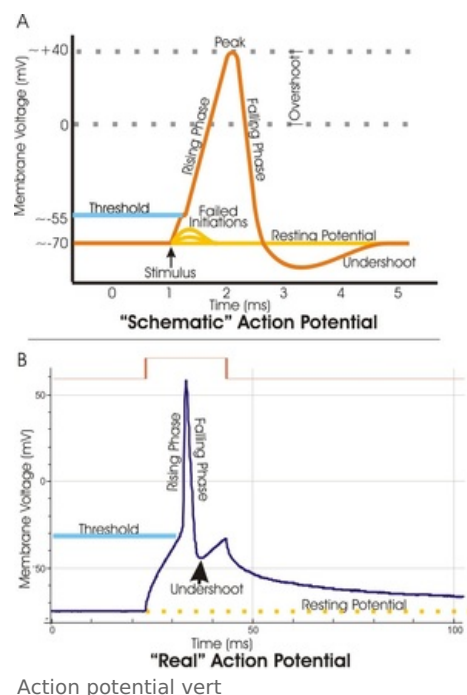
Ionic Basis of Postsynaptic Inhibition

When the resting membrane potential is -65 mV, the direction of IEPSP is outward; an outward Cl^- current represents an influx of the negatively charged Cl^- , which will hyperpolarize the cell. The outward synaptic current will increase as the membrane potential is made less negative (depolarized) and decrease as the potential is made more negative (hyperpolarized).

Another possibility is that the inhibitory synapse channel is permeable to K^+ , with a Nernst potential of -90 mV. An increased permeability to K^+ can bring the membrane potential close to the Nernst potential for K^+ and thus hyperpolarize the cell.

General Properties of Post-Synaptic Potentials

- Postsynaptic potentials (like end-plate and receptor potentials) are a graded potential change. The amplitude of the postsynaptic potential increases with the amount of neurotransmitter released. In other words, it increases with the number of receptors bound by neurotransmitter, given that these receptors will lead to **depolarization** of the cell, leading to influx of Ca^{2+} which will eventually cause the exocytosis of the neurotransmitter in the following synaptic cleft.
- Since post-synaptic potentials are graded, individual potential changes can summate. The summation of postsynaptic potentials can be either temporal or spatial:
 - Temporal summation** arises when the same input is stimulated repetitively, such that the second synaptic potential arrives before the postsynaptic cell has recovered from the first synaptic potential. There is a margin of 15 ms since the onset of the action potential, during which the second post-synaptic potential can be superimposed and add on the first one before it fades out to -65 mV (resting). This gives rise to a staircase increase in the postsynaptic potential change.
 - During **spatial summation** the second synaptic potential is provided by a second input simultaneously, which makes synaptic contact in close proximity to the first input. If the two inputs have the same sign (both excitatory or both inhibitory) the postsynaptic response evoked by stimulating will be larger than if either input is stimulated alone.
 - Single excitatory PSPs are not greater than 0.5-1 mV.
 - In both excitatory and inhibitory PSPs, the ion conductivity change (peak) lasts for 1-2 ms, and then it takes



up to 15 ms for restoration of the resting potential, because this is the time it takes for the excess positive/negative charges to leak out/in from/to the cell.

- The threshold for excitation averages around -45mV. To reach this threshold we need +20mV summated EPSP. Spatial and Temporal summation of single PSPs (40-80 EPSPs) from the dendrites and soma can yield such value.
- However, even if this value (+20 mV) is reached and the soma potential > -45 mV (threshold), the action potential cannot be elicited. This threshold applies only for the *axon hillock*, where there is the maximal density of Na⁺-VGCs. For an action potential to be elicited from the soma, the summated EPSP must be between +30 mV and 40 mV instead.

The importance of summation is evident when the spinal motor-neuron model is considered: Each motoneuron carries about 20,000 individual synaptic boutons, which represent about 6000 separate inputs (each input forms more than one synapse). In the real situation, neurons are under a constant influence of both inhibitory and excitatory synaptic inputs. At any moment the membrane potential of the neurons reflects the sum of all these inputs. A decrease in the level of the tonic excitatory input will hyperpolarize the cell, as well as an increase in the inhibitory input. Similarly an increase in the tonic excitatory input will depolarize the cell, which may be achieved also by a decrease in the power of the tonic inhibitory input.

Facilitation of Neurons

Facilitation of neurons means getting closer to the threshold. Often, the summated postsynaptic potential is excitatory but has not risen high enough to reach the threshold for firing by the postsynaptic neuron. When this happens, the neuron is said to be facilitated. That is, its membrane potential is nearer the threshold for firing than normal, but not yet at the firing level. Consequently, another excitatory signal entering the neuron from some other source can then excite the neuron very easily. Diffuse signals in the nervous system often do facilitate large groups of neurons so that they can respond quickly and easily to signals arriving from other sources.

Excitatory State

The “excitatory state” of a neuron is defined as the summated degree of excitatory drive to the neuron. If there is a higher degree of excitation than inhibition of the neuron at any given instant, then it is said that there is an excitatory state. Conversely, if there is more inhibition than excitation, then it is said that there is an inhibitory state. When the excitatory state of a neuron rises above the threshold for excitation, the neuron will fire repetitively as long as the excitatory state remains at that level.

Some neurons in the central nervous system fire continuously because even the normal excitatory state is above the threshold level. Their frequency of firing can usually be increased still more by further increasing their excitatory state. The frequency can be decreased, or firing can even be stopped, by superimposing an inhibitory state on the neuron. This is similar to carrier-wave type modulation on continuous firing rates.

Thus, different neurons respond differently, have different thresholds for excitation, and have widely differing maximum frequencies of discharge.

Presynaptic inhibition

Presynaptic inhibition is caused by release of an inhibitory substance onto the outsides of the presynaptic nerve fibrils before their own endings terminate on the postsynaptic neuron. In most instances, the inhibitory transmitter substance is GABA (γ-aminobutyric acid). This has a specific effect of opening anion channels, allowing large numbers of chloride ions to diffuse into the terminal fibril. The negative charges of these ions inhibit synaptic transmission because they cancel much of the excitatory effect of the positively charged sodium ions that also enter the terminal fibrils when an action potential arrives. Presynaptic inhibition occurs in many of the sensory pathways in the nervous system. In fact, adjacent sensory nerve fibers often mutually inhibit one another, which minimizes the sideways spread and mixing of signals in sensory tracts. It is the basis of Lateral Inhibition.

Links

Related articles

- Heart Autorhythmicity

Sources

- POKORNY, Jaroslav. *Ion Channels, Membrane Potentials and their Propagation* [lecture for subject Physiology, specialization Physiology, 1. LF UK Charles University in Prague]. Prague. 2010.

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- DESPOPOULOS, Agamnenon – SILBERNAGL, Stefan. *Color Atlas of Physiology*. 5. edition. Thieme, 2003. ISBN 3135450058.

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