RESTING POTENTIAL

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1. Core Definition

The **Resting Potential** (V_{rest}) represents the steady-state electrical charge difference measured across the plasma membrane of an electrically excitable cell when that cell is in a quiescent state, meaning it is not actively propagating an electrical impulse such as an action potential. This potential is a form of stored electrical energy, resulting from a precise and sustained imbalance in the distribution of charged ions between the intracellular (cytosolic) fluid and the extracellular environment.

This fundamental potential difference is crucial because it establishes the baseline condition from which all electrical signaling originates. For most neurons and muscle cells, the interior of the cell is negatively charged relative to the exterior, typically registering potentials ranging from -60 to -75 millivolts (mV). It is important to recognize that the term "resting" does not imply inactivity; rather, it describes a dynamically maintained equilibrium state where the passive leakage of ions is constantly offset by active transport mechanisms.

While the physical process applies to all electrically excitable tissues--including neurons, cardiac myocytes, and skeletal muscle fibers--the precise magnitude of the resting potential is cell-type specific. As indicated in foundational physiological texts, the potential for a neuron is distinct from that found in glial cells or muscle cells due to differences in ion channel density and ionic permeabilities, reflecting the varied functional roles these cells perform within the body.

2. Ionic Basis and Mechanism

The generation of the resting potential relies overwhelmingly on the unequal concentration gradients of three major ions: potassium (K^+), sodium (Na^+), and chloride (Cl^-). The steepness of these concentration gradients is essential, with potassium being heavily concentrated inside the cell, while sodium and chloride are highly concentrated in the extracellular space. These gradients are initially established and continuously maintained by energy-intensive membrane pumps.

The single most dominant factor determining the magnitude of the resting potential is the selective permeability of the cell membrane to potassium ions. The membrane contains numerous non-gated potassium channels, often referred to as K^+ leak channels, which allow K^+ ions to exit the cell relatively freely down their steep concentration gradient. As positively charged potassium ions leave the cell interior, they leave behind negatively charged, impermeant molecules, such as large proteins and organic phosphates, causing the inside of the cell to

become negative.

This accumulating negative charge creates an opposing electrical gradient that begins to pull K^+ ions back into the cell, counteracting the outward chemical (concentration) gradient. The resting potential is achieved when the net movement of potassium ions stops; the electrical force exactly balances the chemical force, a condition known as the equilibrium potential for potassium (E_K). Because the membrane is slightly permeable to Na^+ ions, the V_{rest} is typically measured a few millivolts less negative than the pure E_K, reflecting a minor persistent inward leak of sodium.

3. Key Characteristics and Voltage Parameters

A key characteristic of the resting potential is its stability and predictability, which is critical for reliable neural function. In a typical mammalian neuron, the potential stabilizes around -70 mV. This precise voltage is not arbitrary; it is the weighted average of the equilibrium potentials for all permeable ions, with the weighting determined by the relative membrane permeability of each ion, as described by the Goldman-Hodgkin-Katz equation.

The magnitude of the resting potential is tightly regulated because any deviation significantly affects the excitability of the cell. A shift toward a less negative value (e.g., from -70 mV to -60 mV) is termed **depolarization**, which increases the likelihood of firing an action potential. Conversely, a shift toward a more negative value (e.g., from -70 mV to -80 mV) is called **hyperpolarization**, which suppresses excitability.

Variations exist not only across different cell lines but also within the same cell type under different physiological conditions. Glial cells, which typically have high K^+ conductance but lack significant sodium channels, often possess a resting potential closer to the theoretical E_K, sometimes reaching -90 mV. Furthermore, the V_{rest} can transiently change in response to neurotransmitters that open ligand-gated channels, preparing the cell for or inhibiting subsequent electrical activity.

4. Maintenance and Role of the Sodium-Potassium Pump

While the passive diffusion of potassium primarily sets the voltage of the resting potential, the long-term integrity of the ionic gradients absolutely depends upon the active expenditure of energy via the **sodium-potassium pump** (Na^+/K^+ ATPase). This vital enzyme-pump complex acts continuously to reverse the passive leaks of Na^+ into and K^+ out of the cell, thus preventing the eventual collapse of the concentration gradients.

The Na^+/K^+ ATPase is an electrogenic pump, meaning it moves unequal numbers of charge across the membrane. Specifically, for every molecule of ATP hydrolyzed, the pump transports

three Na^+ ions out of the cell and two K^+ ions into the cell. This 3:2 stoichiometry results in a net transfer of one positive charge out of the cell during each cycle.

This continuous net efflux of positive charge contributes a small but measurable component to the resting potential, typically adding 5 to 10 mV of negativity. However, the pump's primary and most critical role is not voltage generation, but rather gradient maintenance. By sustaining the high internal K^+ and high external Na^+ concentrations, the pump ensures that the system remains ready for signaling events, preventing the dissipation of the electrochemical potential energy necessary for generating action potentials.

5. Significance in Excitability and Signal Transmission

The negative resting potential is the essential prerequisite for generating the rapid, regenerative electrical signals known as action potentials. It provides the necessary baseline potential energy that enables voltage-gated ion channels to function correctly. Specifically, the negative V_{rest} keeps voltage-gated sodium channels--the channels responsible for the rising phase of the action potential--in their closed but receptive conformation.

When an excitatory stimulus depolarizes the cell to the **threshold potential** (typically around -55 mV), the voltage change is sufficient to induce a conformational shift in these sodium channels, causing them to open rapidly. The substantial inward rush of Na^+ (driven by both concentration and electrical gradients) constitutes the action potential, allowing the fast transmission of information over long distances.

If the resting potential were significantly depolarized (e.g., chronically resting at -40 mV), the voltage-gated sodium channels would enter an inactivated, non-conductive state. In this condition, known as depolarization block, the cell becomes paradoxically inexcitable, unable to respond to further stimuli because the channels cannot transition back to the closed, ready-to-open state. Thus, the stability and magnitude of the resting potential define the fundamental excitability of a nerve or muscle cell.

6. Clinical Relevance and Pathophysiology

Disruptions to the ionic basis of the resting potential are frequent causes of physiological distress and disease, particularly involving the cardiovascular and nervous systems. Because the resting potential is so heavily dependent on the extracellular concentration of potassium, conditions that alter plasma K^+ levels have immediate and dramatic effects on cell excitability.

Hyperkalemia (abnormally high K^+ concentration in the blood) decreases the concentration gradient across the membrane, making the equilibrium potential for potassium (E_K) less negative. This shifts the resting potential closer to the threshold, causing chronic depolarization

and leading to hyperexcitability, often resulting in dangerous cardiac arrhythmias. Conversely, **hypokalemia** (abnormally low K^+ concentration) makes the E_K more negative, leading to hyperpolarization and reducing cell excitability, which can cause muscle weakness and paralysis.

Furthermore, genetic defects affecting the structure or function of specific ion channels, known as **channelopathies**, can directly destabilize V_{rest}. For example, mutations in K^+ leak channels can lead to continuous depolarization or hyperpolarization, contributing to conditions like familial hemiplegic migraine or specific forms of epilepsy, highlighting the resting potential's sensitivity as an indicator of cellular health.

7. Further Reading

Wikipedia: Resting Potential
Wikipedia: Action Potential
Wikipedia: Sodium-Potassium Pump
Neuroscience Online: Resting Membrane Potential