Review Paper

International Physiology
Vol. 5 No. 2, July - December 2017
DOI: https://dx.doi.org/10.21088/ip.2347.1506.5217.17

Role of Resting Membrane Potential in the Regulation of Cellular Functions

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Abstract

The membrane potential of a cell in non excited state is called Resting Membrane Potential (RMP). RMP of large nerve fiber is –90 mV. It allows a cell to function as a battery, providing power to operate a variety of "molecular devices" embedded in the membrane. In electrically excitable cells, it is used for transmitting signals between different parts of a cell. Membrane potential is contributed by the electrical force from mutual attraction between particles with opposite charges and repulsion between the particles with same charges. Diffusion also contributes to membrane potential by the tendency of particles to redistribute from regions of high concentration to low due to thermal energy. The diffusion potential across the membrane that exactly opposes the net diffusion of a particular ion through the membrane is called the Nernst potential for that ion. Factors responsible for generation of RMP are Na^+- K^+ pump and leakage of K^+. Membrane potential can be measured by patch clamp methods and voltage sensitive fluorescent dyes. Bioelectric properties can serve as markers for cell characterization, control cell mitotic activity and also cell cycle progression and differentiation.

Keywords: Resting Membrane Potential; Nernst Potential; Na^+- K^+ Pump; Bioelectric Properties.

Introduction

The membrane potential of a cell in non excited state is called Resting Membrane Potential (RMP). RMP of large nerve fiber is - 90 mV [1]. It allows a cell to function as a battery, providing power to operate a variety of "molecular devices" embedded in the membrane. In electrically excitable cells, it is used for transmitting signals between different parts of a cell [2]. Membrane potential is contributed by the electrical force from mutual attraction between particles with opposite charges and repulsion between the particles with same charges. Diffusion also contributes to membrane potential by tendency of particles to redistribute from regions of high concentration to low due to thermal energy [3].

Basic Physics of Membrane Potentials

The generation of membrane potential involves establishment of a diffusion potential across a nerve fiber membrane. It is established by diffusion of potassium ions from inside the cell to outside through a membrane that is selectively permeable only to potassium and also by the diffusion of sodium ions from outside to inside when the nerve fiber membrane is permeable only to sodium ions [1].

Nernst Equation describes the relation of diffusion potential to the ion concentration difference across the membrane. The diffusion potential across the membrane that exactly opposes the net diffusion of a particular ion through the membrane is called the *Nernst potential for that ion.* It is determined by the *ratio of the concentrations of that* specific ion on the two sides of the membrane. *Nernst equation* used to calculate the Nernst potential for any univalent ion at the normal body temperature of 98.6°F (37°C):

$$\text{EMF(mv)} = \pm \frac{61}{z} \times log \frac{concentration \quad inside}{concentration \quad outside}$$

Where *EMF is electromotive force and z is the electrical* charge of the ion [1].

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Received on: October 16, 2017 **Accepted on:** October 30, 2017

Goldman-Hodgkin-Katz Equation

Goldman-Hodgkin-Katz equation is used to calculate the diffusion potential when the membrane is permeable to several different ions. The diffusion potential that develops depends on three factors: The polarity of the electrical charge of each ion, the permeability of the membrane (P) to each ion and the concentrations (C) of the respective ions on the inside (I) and outside (O) of the membrane [1].

The Goldman equation infers that sodium, potassium, and chloride ions are the most important ions involved in the development of membrane potentials in nerve and muscle fibres. Also the concentration gradient of each of these ions across the membrane helps determine the voltage of the membrane potential. Further, the quantitative importance of each of the ions in determining the voltage is proportional to the membrane permeability for that particular ion and a positive ion concentration gradient from *inside the membrane to the outside causes electro-negativity* inside the membrane [1].

Measurement of Membrane Potential

Small pipette filled with an electrolyte solution is impaled through the cell membrane to the interior of the fibre. Another electrode, called the "indifferent electrode", is then placed in the extracellular fluid. The potential difference between the inside and outside of the fibre is measured using an appropriate voltmeter. The other methods of measuring membrane potential in small cells is by Patch clamp method and Voltage-sensitive fluorescent dyes. The advantages of these methods are, they are easy to use and simultaneous monitoring of many cells can be done [4,5].

Factors Responsible for Generation of RMP

The RMP of neuron is due to Na^+- K^+ pump and also due to leakage of K^+ through membrane. Na^+- K^+ pump is an electrogenic pump – more positive charges are pumped to the outside than to the inside (3 Na^+ outside and 2K^+ inside). Na^+-K^+ pump causes concentration gradient of Na^+(outside): 142mEq/L, Na^+(inside): 14mEq/L, K^+(outside): 4mEq/L, K^+ (inside): 140mEq/L. The ratios of these two respective ions from the inside to the outside are: Na^+ inside/Na^+ outside = 0.1 and K^+ inside /K^+ outside = 35.0 [1].

Leakage of potassium through the nerve cell membrane through *Potassium channel, or Potassium [K⁺] "leak" channel located in the* nerve membrane. The potassium can leak even in a resting cell state, these K+ leak channels may also leak sodium ions slightly but are 100 times more permeable to potassium than to sodium [1].

Origin of the Normal Resting Membrane Potential

Normal resting membrane potential is attained by the contribution of potassium and sodium diffusion potential. The ratio of potassium ions inside to outside is 35: 1. The Nernst potential corresponding to this ratio is -94 mV (the logarithm of 35 is 1.54, and this multiplied by -61 mV is -94 mV). Therefore, if potassium ions were the only factor causing the resting potential, the resting potential inside the fibre would be equal to -94 mV. The ratio of sodium ions from inside to outside the membrane is 0.1, which gives a calculated Nernst potential for the inside of the membrane of +61 mV.

Summated potential can be derived from Goldman equation. If the membrane is highly permeable to potassium but only slightly permeable to sodium, the diffusion of potassium contributes far more to the membrane potential than does the diffusion of sodium. Using this value in the Goldman equation gives a potential inside the membrane of -86 mV, which is near the potassium potential [1].

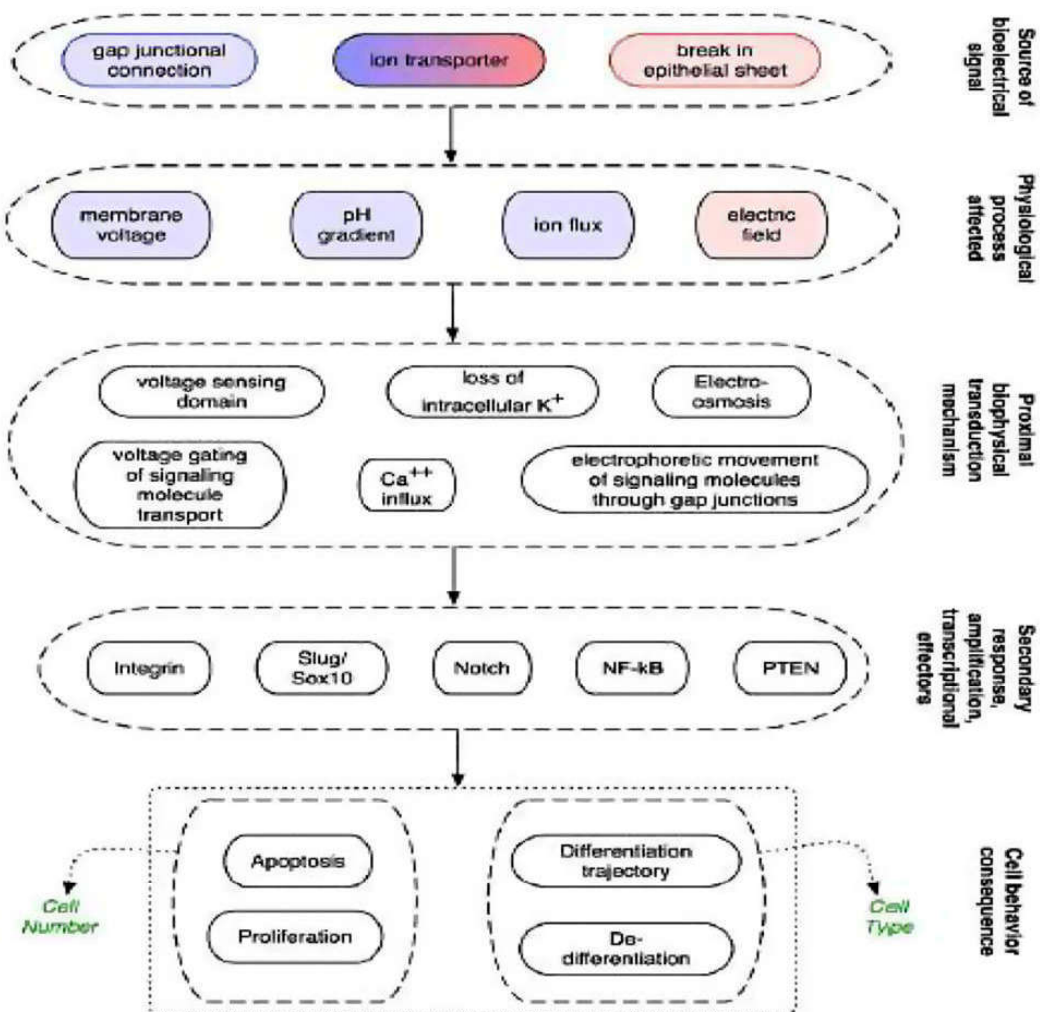
Na^+-K^+ pump also contributes to origin of RMP. Pumping of three sodium ions to the outside occurs for two potassium ions pumped to the inside of the membrane. Loss of positive charges from inside the membrane creates an additional degree of negativity of -4 mV inside [1].

Probable Systemic Effects of Resetting of RMP [6,7]

Cell/ Tissue/ System	RMP towards depolarization	RMP towards hyperpolarization
Nerve & Muscle	Shortened reaction time, Flickering, Fasciculation, Twitching	Increased reaction time, Flaccidity
Cardiovascular Conducting cells/ tissue myocytes	↑HR , Arrhythmias ↑ force of contraction	↓HR, Heart block ↓ force of contraction

Respiratory- Smooth muscles	Bronchospasm	Bronchodilation
GIT smooth muscles	Motility increases leading to diarrhoea.	Motility decreases leading to constipation.
Reproductive system		
Female	↑ Contractility- Cervical, Vaginal , Uterine- Sperm transport Fallopian tubes- Ovum transport	↓Contractility- Cervical, Vaginal , Uterine- ↓Sperm transport Fallopian tubes- ↓Ovum transport
Ova	↑ fertilization capacity	↓ fertilization capacity
Male	Early ejaculation	Delayed ejaculation/ Anejaculation
Sperm cell	↓ fertilization capacity	↑ fertilization capacity
CNS	Anxiety, Tremors, Seizures, Exaggerated reflexes, Rigidity, Spasticity	Depression, Decreased reflexes, Flaccidity
Cell proliferation & differentiation	↑	↓

Bioelectric Signal Causes Cell Proliferation and Differentiation [4]



Conclusion

The above stated studies conclude that every cell of body has its own resting membrane potential and react differently to resetting of RMP and the bioelectric properties can serve as markers for cell characterization, control of cellular mitotic activity and also cell cycle progression and differentiation.

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