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Review Article

Membrane Bioelectric Properties: a Biophysical approaches to cell physiology- A study revision

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ABSTRACT
The contributions of Biophysics scientists measuring aspects of the membrane electricity have been so well thought of that multiple prizes have been given out in this field. The field has generated quantitative findings based on the Goldman field equation and the Nernst equation that provide understanding into the importance of sodium and potassium in cell signaling. The graded and action potentials that bring information in the interior the cell and all over the body are central in the considerations of the brain and the activities of muscle. This work covers the biophysics essential of these process.
Key-words: Biophysics; Bioelectrogenesis; Biomembrane; Ion Channels;

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MEMBRANE ELECTRIC POTENTIAL

The membrane potential is due of diffusible and non-diffusible ions across the membrane. The principal charged substance that can never diffuse across a membrane is protein, which has a net negative charge and a great molecular mass [1]. Start with equal concentrations of anions and cations on both sides of a cell membrane, with diffusible cation C^+ in equal concentrations on the both sides of a membrane. The anions on the outside consist only of a diffusible anion $[A^-]_o$ while that inside has both protein and $[A^-]_I$, with $[A^-]_o$ greater than $[A^-]_i$. The anion will diffuse into the cell down its concentration gradient, with the cation following into the cell down its electrical gradient [2]. This will result in an osmotic gradient across the membrane with (Eqn.1)

$$C_i^+ + A_i^- + \text{Protein}^- > C_o^+ + A_o^-$$

This results in the Gibbs-Donnan equilibrium [3], in which the ratios of the diffusible cations and anions are equal across the membrane, yielding the relation (Eqn.2)

$$C_i^+ \cdot A_i^- = C_o^+ \cdot A_o^-$$

This creates an osmotic gradient [4], and water would enter the cell until the osmotic pressure either stabilities the interior ion flux or the cell membrane ruptures. The process reaches equilibrium when the osmotic pressure balances the inward ionic movements [5]. Because protein is non-diffusible, the diffusible ions will distribute themselves according their concentrations and electrical gradients and permeability across the membrane. For cells, the concentrations gradients are produced by the Na-K ATPase Mg dependent plump [6], which transfers Na^+ out of the cell and K^+ into the cell. The diffusible anion across membranes is always Cl^-. Chloride is not actively pumped, but diffuses down its concentration gradient until there is equilibrium between its concentration and electrical gradients. In all cells, potassium is more permeable than any other cation, including sodium, sometimes by more than

100-fold [7]. The net effect is that the concentrations of potassium increase inside a cell because of the action of the Na-K ATPase Mg dependent pump. It will have a concentration gradient from inside to out which will be balanced by an electrical gradient from outside to in [8]. If potassium were the only diffusible cation, then it would reach equilibrium just as chloride does. There is some diffusion of sodium across the membrane. The membrane potential therefore is a product of the concentration gradients and permeability of potassium and sodium [3, 9]. The membrane potential, concentration gradients, and permeability can all be measured independently. The measurements with the experiments of Hodgkin and Huxley (1939; 1952), the Goldman field equation (1941), the patch clamp technology of Neher and coworkers (1978) were solid contributions to the chemical measurements in membrane [10-12].

The membrane potential can be measured using a glass pipette microelectrode that penetrates the cell membrane without injury it (Figure 1).

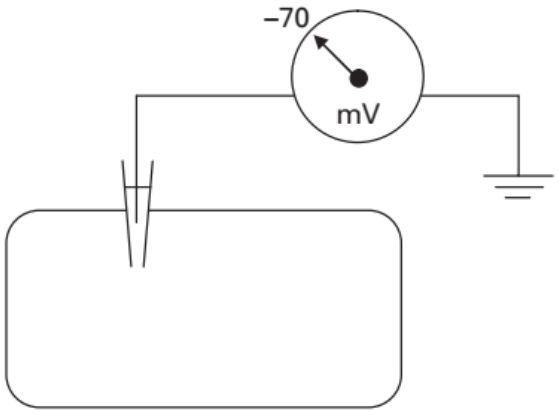

Figure 1: Microelectrode recording of the cell membrane potential. The electrode has a small diameter compared with the cell, minimizing chemical exchange between the cell and the electrode.

These pipettes have a very small diameter. While this produces a relatively small signal, a small diameter minimizes the change in the cell contents, as well as minimizing the leak of current around the pipette. Membrane potentials are always in the millivolt range (Table 1). Many neurons have a resting membrane potential of -70mV [13]. It would be difficult to find a cell of scientific interest that has not had its membrane potential measured.

Table 1: Ion concentrations, equilibrium potentials, membrane potential and relative potassium/sodium permeability in skeletal muscle, neurons and red blood cells

	Skeletal muscle	Neuron	Red blood cell	Interstitial fluid
Na^+ mM	12	15	19	150
K^+ mM	155	150	136	5
Cl^- mM	3.8	9	78	120
V_{Na} mV	67.5	61.5	55.2	
V_K mV	−91.7	−90.8	−88.2	
V_{Cl} mV	−92.2	−69.2	−11.5	
V_m mV	−90	−70	−7 to −14	
P_K/P_{Na}	450	25.2	1.65	

Membrane characteristics can be measured using electrodes that set the voltage across the membrane and measure the change in current, a voltage clamp, or set the current across the membrane and measure the change in voltage, a current clamp [12]. These methods are used to determine how ion channels operate when the cell is activated by neurotransmitters or other molecules. Surface recording of cells in the central nervous system, called single unit recording, is used to map neural pathways in the brain. The fiber had a membrane potential of -89mV [14]. The equilibrium potential for Na+ is approximately +60 mV. The patch has a 60 GΩ seal. When the voltage is negative to the equilibrium potential, the inward current increases in a voltage dependent manner. Channels exhibit virtual square-wave behavior. Jumping from closed non-conducting state at the top of each recording to the open conducting state at the bottom of each recording [15]. The more negative the potential, the greater the current carried by the channel, and the deeper the well when it is open.

GOLDMAN AND NERNST EQUATIONS

The membrane potential is a consequence of the concentration difference of the ions across the membranes and the permeability of those ions [11]. If the concentrations of the ions are very small compared with other ions of similar permeability, the small concentration ions will not significantly contribute to the membrane potential. Similarly, if an ion has a very small permeability compared with other ions of similar concentrations, their contribution to the membrane potential will be much smaller. In mammalian systems potassium, sodium and chloride have sufficient concentrations and permeability to be included in calculations of the membrane potential [16].

Ion differences across a membrane are a consequence of the ATPase-dependent ion pump generation of the concentration gradients and the dissipation of the electrical and concentration gradients through ion channels. The membrane potential requires differences in ionic concentrations across the membrane, differences generated by the activity of ion ATPase's and other ion transport systems that move ions across the membrane against their energy gradient [8].

The movement of an ion through ion channels across the membrane, described by Goldman, is a consequence of two forces: diffusion down a concentration gradient and migration down an electrical gradient. Diffusion movement is measured using the Fick equation [17], and electrical movement is measured using the electrical form of the Stokes equation. The total flux J_i of an ion across the membrane is (Eqn.3)

$$J_{\mathrm{i}} = -D_{\mathrm{i}}\left(\frac{\mathrm{d}C_i}{\mathrm{d}l} - \frac{V_{\mathrm{m}} z_{\mathrm{i}} F C_{\mathrm{i}}}{RTL}\right)$$

where D_i is the diffusion constant of the ion, C_i is the local concentration of the ion, dC_i is the concentration gradient, L is the width of the membrane, dl is the change in distance over which a concentration change occurs, V_m is the membrane potential, z_i is the valence of the ion, and F is Faraday's constant. This equation can be rearranged to separate the variables dC_i and dl (from 0 to L across the membrane) and integrated to yield (Eqn.4)

$$J_{\mathrm{i}} = \beta z_{\mathrm{i}} P_{\mathrm{i}} \frac{C_{\mathrm{out}} - C_{\mathrm{in}} e^{\beta z_{\mathrm{i}}}}{1 - e^{\beta z_{\mathrm{i}}}}$$

Where (Eqn.5)

$$\beta = \frac{V_{\mathrm{m}} F}{RT}$$

and P_i is the ionic permeability (Eqn.6)

$$P_{\mathrm{i}} = \frac{D_{\mathrm{i}}}{L}.$$

In the steady state, the membrane potential will not be changing [18]. Thus, the net flux, the sum of the inward and outward fluxes, will be zero for the combination of all the relevant ions (Eqn.7):

$$J_{\mathrm{net}} = \sum_{\mathrm{i}} J_{\mathrm{i}} = 0$$

which Goldman solved for monovalent ions, yielding (Eqn.8)

$$\frac{V_{\mathrm{m}}F}{RT} = \ln \frac{\sum\limits_{\mathrm{cat}} P_{\mathrm{cat}} C^{+}_{\mathrm{out}} + \sum\limits_{\mathrm{an}} P_{\mathrm{an}} A^{-}_{\mathrm{in}}}{\sum\limits_{\mathrm{cat}} P_{\mathrm{cat}} C^{+}_{\mathrm{in}} + \sum\limits_{\mathrm{an}} P_{\mathrm{an}} A^{-}_{\mathrm{out}}}$$

Where P_{cat} and P_{an} are the permeability of cation and anions, and C+ and A- are the concentrations of cations and anions on the inside of the cell. The equation can be rearranged to solve for V_m and applied to the ions sodium, potassium and chloride (Eqn.9)

$$V_{\mathrm{m}} = \frac{RT}{F} \ln \left(\frac{P_{\mathrm{Na}}[\mathrm{Na}]_{\mathrm{out}} + P_{\mathrm{K}}[\mathrm{K}]_{\mathrm{out}} + P_{\mathrm{Cl}}[\mathrm{Cl}]_{\mathrm{in}}}{P_{\mathrm{Na}}[\mathrm{Na}]_{\mathrm{in}} + P_{\mathrm{K}}[\mathrm{K}]_{\mathrm{in}} + P_{\mathrm{Cl}}[\mathrm{Cl}]_{\mathrm{out}}} \right).$$

The membrane potential can be measured using a microelectrode. The conductance C_i of a channel and duty cycle f_i (the fraction of time the channel is open) for a single channel can be measured using a patch clamp [12, 15]. The permeability of an ion across the cell membrane will be (Eqn.10)

$$P_{\mathrm{i}} = \sum_{\mathrm{l}}^{n_{\mathrm{i}}} c_{\mathrm{i}} f_{\mathrm{i}}$$

Where n_i is the number of ion channels, each with its own conductance and duty cycle. If an ion only traveled through a single type of channel, its permeability would simplify to (Eqn.11)

$$P_{\mathrm{i}} = n_{\mathrm{i}} c_{\mathrm{i}} f_{\mathrm{i}}.$$

On membrane structure the near-field gold-nanoparticle method demonstrated how to visualize individual proteins on the membrane surface [19-22]. Every element of the Goldman equation is now subject to experimental measurement. The Nernst equation is a reduced form of the Goldman equation applied to a single ion. The Nernst equation assumes the ion is at equilibrium, which is not true in a cell where the membrane potential is in a steady-state balance between the ion pumps and the ion channels [23]. The utility of the Nernst equation lies in its identification of the equilibrium potential, mentioned in describing the patch-clamp recordings [24].

The equilibrium potential is the theoretical potential at which an ion will be at equilibrium with its concentration gradient, balancing the electrical and chemical forces. The Nernst equation for a cation potential V_i at 37 ºC is (Eqn.12)

$$\begin{aligned} V_{\mathrm{i}} &= \frac{RT}{F} \ln \left(\frac{P_{\mathrm{i}} C_{\mathrm{out}}}{P_{\mathrm{i}} C_{\mathrm{in}}} \right) = 2.303 \frac{RT}{F} \log \left(\frac{P_{\mathrm{i}} C_{\mathrm{out}}}{P_{\mathrm{i}} C_{\mathrm{in}}} \right) = 2.303 \frac{RT}{F} \log \left(\frac{C_{\mathrm{out}}}{C_{\mathrm{in}}} \right) \\ &= 61.5\,\mathrm{mV} \left(\frac{C_{\mathrm{out}}}{C_{\mathrm{in}}} \right). \end{aligned}$$

Study shows the ion concentrations for skeletal muscle and neurons, for red blood cells, and for those of interstitial fluid. The interstitial fluid concentrations are the outside ion concentrations in the Goldman and Nernst equations. The ion potentials predicted by the Nernst equation show a positive intracellular value for sodium in the range of +60 mV. This is the theoretical membrane potential that would exactly counter the sodium concentration gradients across the membrane: the concentrations driving sodium into the cell would be countered by the electrical gradient driving sodium out of the cell. For potassium, the equilibrium potential is near -90 mV: the outward potassium concentration gradient would be balanced by an inward electrical gradient. The chloride gradient is variable, and tracks with the membrane potential Vm. This indicates that chloride is at equilibrium across the cell membrane. This also

means that chloride does not contribute to the cell membrane potential, as chloride ions will simply follow the potential generated by the other ion systems. Because of this, the Goldman equation can be rewritten as (Eqn.13)

$$V_{\mathrm{m}} = \frac{RT}{F} \ln \left(\frac{[\mathrm{Na}]_{\mathrm{out}} + (P_{\mathrm{K}}/P_{\mathrm{Na}})[\mathrm{K}]_{\mathrm{out}}}{[\mathrm{Na}]_{\mathrm{in}} + (P_{\mathrm{K}}/P_{\mathrm{Na}})[\mathrm{K}]_{\mathrm{in}}} \right)$$

In this form, all the components of equation are known except the P_K/P_{Na} ratio. Since the concentrations of sodium and potassium are similar in the three different cells, most of the difference in permeability must reside in the number of open channels, their conductance and their duty cycle. The large differences in the ratio make this a fruitful research field, as significant differences in channel behavior must occur [25].

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