Introduction to Neurobiology

BIOL3833

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Module 1: Passive Membrane Properties

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This document includes materials adapted from Nace Golding's lab manual for Neurobiology Laboratory at the University of Texas.

Module 1: Passive Membrane Properties

Introduction to Membrane Biophysics

Additional Reading: Chapter 1 of the Axon CNS guide is **recommended**

Part I: Summary of Neurophysiology Terminology

An important step toward becoming a neurobiologist is to understand the biological membrane from the point of view of a physicist. To this end, we will first review the basic concepts in physics that you probably have encountered already in other classes

1.1. Charge (Q)

All matter is made up of charged particles, and can exist as positive protons (+) or negative electrons (-), in more or less equal numbers. Like charges repel one another, and dissimilar charges attract. The unit of charge that we will commonly deal with is the coulomb (C). How much is a coulomb? The charge on a gram of a monovalent ion such as Na^+ would be 96,500 C.

1.2. Current (I)

Current is the flow of charge past a location per unit time (**dQ/dt**). The unit of current is the **Ampere**, which equals **1 coulomb/sec**. Currents in neurons and muscles are usually on the order of picoamps (pA; 10^{-12} A) or nanoamps (nA; 10^{-9} A). By convention, current moves from positive to negative. Different from electric current used to power light bulbs or computers where current is carried by the movement of elecctrons, biological current is carried by the movement of charged salt ions (e.g. Na^+, Cl^-). In biological systems it is more convenient and conventional to consider electrical current as the movement of positively charged ions.

1.3. Potential difference, or Voltage (V)

A potential difference, or voltage, is the work that must be done to separate two charges (negative vs. positive). A difference in electrical potential creates a force that acts to remove the difference in potential. Voltage is expressed in volts (**V**) or millivolts (**mV**, 1 V = 1,000 mV).

Current and Voltage are intimately related: Voltage is what keeps current flowing in a continuous cycle through a complete circuit.

1.4. Resistance (R) and Conductance (G)

Charge flowing in a medium encounters atoms, which impede their flow, generating heat in the process (that's why computers and electronics get warm as they run). This is resistance. Similarly, ions flowing across ion channels on the membrane are also met with resistance, as they will have to go through the water-filled pore of the protein and interact with charged residues in its lining. The resistance of cells is usually expressed as megaohms (MΩ or 10^6 Ohms) .

One concept used often by electrophysiologists is conductance, which is the inverse of resistance, or G=1/R, and refers to the ease of which ions can move through a medium or membrane. The unit for conductance is siemens; most single channel conductance is in picosiemens (pS). Throughout this course, we will often move quickly between the concepts of resistance and conductance. It is therefore important to become very comfortable in doing so. As conductance increases, resistance decreases and vice-versa. As resistance increases conductance decreases and vice-versa.

1.5 Circuits and the Conservation of Current

Current only flows through a complete circuit – charges move through the circuit in a continuous fashion. One of the central principles governing current in electrical circuits is "Conservation of Current" This principle can be expressed in many ways, for example "Current is neither created nor destroyed". But the best expression of this principle for our purposes is that **the current flowing into any point in a circuit is always equal to the current flowing out of that point**. This is a point that will have important consequences for how we understand the electrical behavior of cell membranes.

1.6. Capacitance (C)

When two conductors (e.g. two metal plates) are in very close proximity to one another but are separated by a nonconductive medium (e.g. air, paper, glass), charges on each side attract one another and impede one another's movement. The conductors thus can be said to store charges. The amount of this charge storage, or capacitance, is proportional to the area of the conductor, and inversely proportional to the distance separating the conductors. The unit capacitance is the farads (F), which equals 1 coulomb of charge a capacitor can store for each volt applied to it. Hence, C=Q/V. The capacitance of biological membranes is usually on the order of picofarads or nanofarads.

1.7. Ohm's Law (V = IR)

This relationship between voltage, current and resistance is absolutely critical for understanding the electrical behavior of neurons and muscle. If you are pondering what your next tattoo should be, consider an inscription of Ohm's law because if you are involved in neurobiology, Ohm's law never goes away and it should never be forgotten.,

Ohms law relates volts, amps, and ohms: 1 V = 1 A * 1 Ω

In neurobiology we work with much smaller units of voltage and current but much higher values of resistance, so a convenient shortcut for neurobiology is to remember this: 1 mV = 1 nA * 1 MΩ

This analogy might help you develop an intuitive understanding of the relationship between voltage, current, and resistance: *Imagine you turn on a faucet, forcing water through a garden hose. In this case, pressure is analogous to voltage (V).*

the flow of water and the resistance it encounters going through the hose is analogous to current (I) and resistance (R) in electricity. For a given hose (i.e. R remains the same), water flow (I) increases if one turns up the faucet to increase the water pressure (V). Similarly, for a given water pressure (V), the amount of water coming out of the hose will decrease if the hose diameter is too small (i.e. R is high) or vice versa.

Online, you can find a much more detailed and a very effective presentation of Ohms law which includes some very useful shortcuts for using Ohms law in calculations (hint – calculations you might have to perform during a quiz or exam).

Part II. Principles of Membrane Biophysics

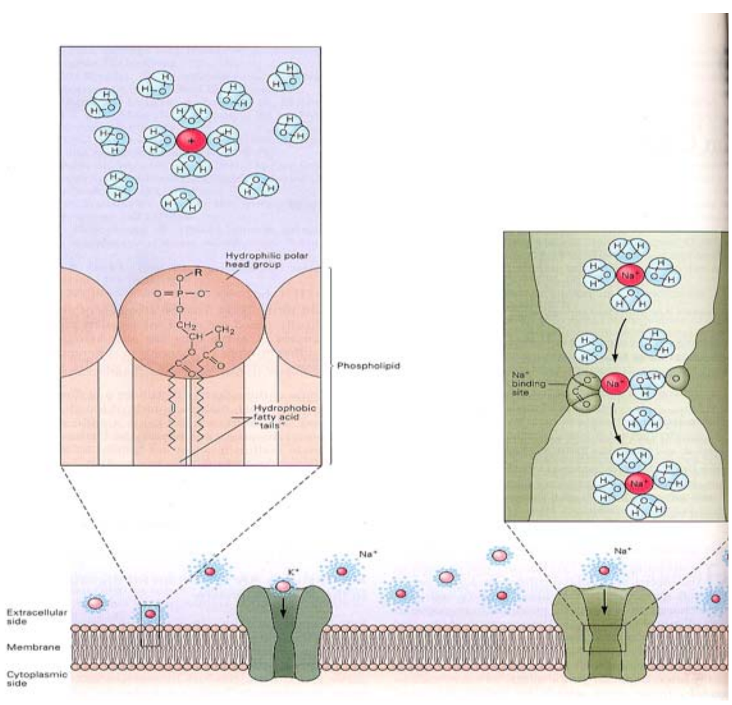
2.1. The Physics of Biological Membranes

Biological membranes consist of a phospholipid bilayer, with the charged polar heads of the phospholipids facing the internal and external ionic environments, and the hydrophobic fatty acids facing the interior. In electrophysiologists' eyes, biological membranes have many similarities to the physical property described earlier. In other words, a membrane contains resistors, capacitors, batteries, and pathways for current to flow.

Membrane Resistance

Membranes possess ion channel proteins, most of which selectively allow charged ions to pass through their water-filled pores.

Ions exist in solution surrounded by water. This is called a sphere of hydration. Charged ions exchange water molecules with charged residues in the channel pore, allowing them to pass through. Membrane resistance is usually determined by the number of ion channels and the state (open or closed) of these channels.



The flow of charged ions through membrane channels represents transmembrane current flow. The resistance of this current flow across the membrane results in a transmembrane voltage change. The relationship between current, resistance, and voltage is reflected by **Ohm's Law:**

Ohm's Law: $V = I * R$ **Equation 1**

Membrane Capacitance

Membranes also act as capacitors, as they are able to store charge on their surfaces. This is because there are two conductors (the intracellular and extracellular aqueous environments) that are separated by an extremely thin insulator (the fatty acids of the bilayer). The thickness of the membrane is only about 6-7 nm. The capacitance of the membrane is described by:

Membrane capacitance: $C = Q / V$ **Equation 2**

This equation states that the membrane capacitance is equal to the amount of charge that can be stored on a membrane for a given transmembrane voltage change.

Rearranging, **$Q = CV$** **Equation 3**

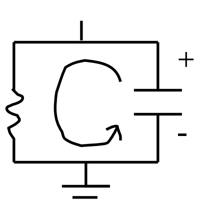
Now differentiate the equation: **$dQ/dt = C * dV/dt$** **Equation 4**

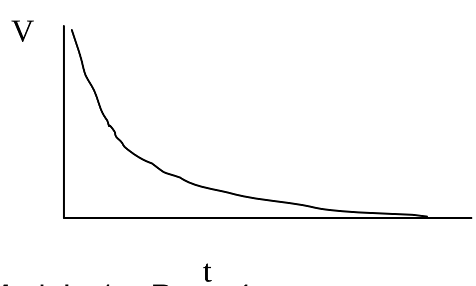
Since dQ/dt is current (I, the flow of charge past a point per unit time), this equation states that current onto and off the membrane (for storage) is proportional to the ***change*** in membrane voltage. In other words, there is no capacitive current when the voltage is stable (e.g. at the resting potential).

Time Constant (τ)

The change in membrane voltage would occur instantaneously if resistance to current flow did not exist. This can be appreciated using Ohm's law. Using Ohm's Law, the maximum current (I) equals V/R. When R is 0, the current is infinitely large such that a capacitor can be charged or discharged with a rapid rate. When R is large, the current flow reduces, taking a long time to change the voltage cross the capacitor.

The rate of discharge at a given time is defined as -dQ/dt (negative because the charge is decreasing with time), which is essentially the same as the magnitude of the current. Hence, equation 4 becomes





$$dV/dt = -(1/C) * dQ/(dt)$$

$$dV/dt = -V/ (R*C) \qquad \textbf{Equation 5}$$

Where V is the initial voltage and decreases as the capacitor is discharged. This equation states that the speed of the voltage change from the capacitor is proportional to the voltage remaining. Thus, as voltage decreases, the rate also decreases. **RC is the time constant or tau.**

This effect is analogous to water draining from a bathtub. The amount of water the bathtub "stores" is analogous to capacitance. The pressure on the water to flow through the drain pipe is analogous to voltage, and the size of the drain pipe determines the resistance to water flow. When the bathtub is full, there is a lot of driving force on the water to flow through the pipe, and so the flow of water out of the bathtub is initially fast. However, as the water nears the bottom, there is not much driving force pushing the water out, and so this water drains out more slowly. Of course, the pipe size also influences the draining rate. A larger pipe (i.e. smaller R) will drain faster than a smaller pipe.

This example shows how membrane resistance and capacitance are BOTH involved in regulating how fast membrane voltage changes can occur. If resistance is high (a narrow pipe in the bathtub example), a given amount of current takes longer to pass through. If membrane capacitance is high (there is a lot of water stored in the bathtub), it also takes longer for the larger amount of current to "drain" away, so to speak.

Functionally, the membrane time constant reflects how fast a neuron or muscle can respond to a synaptic signal. The more open channels (low R), the faster the response.

The equation 5 is a first-order differential equation whose solution is:

$$V(t) = V e^{(-t/RC)}$$

The membrane time constant, or tau is the time it takes for voltage to fall to 1/e, or 36% of the initial voltage (or ~63% of the final voltage).

$$\boxed{\tau = RC}$$

When a capacitor is charged through a resistor (e.g. during a step depolarization), the equation is:

$$V(t) = I R + C*dV/dt R$$

the solution: $$V(t) = I * R (1 - e^{(-t/RC)})$$

Here, tau refers to the time required to reach 63% of the final voltage.

A time constant is the time it takes for any exponential process to reach 63% of its final value. In the case of biological membranes, the exponential process is a change in membrane voltage. The membrane time constant, or tau, is directly proportional to the membrane resistance and the membrane capacitance (per unit area). That is, $\tau = R_m C_m$. Larger cells will have larger C_m *because* C_m *is a direct function of membrane surface area. Since* C_m *is largely constant for a particular cell, any changes in the membrane time constant thus reflect the number and type of ion channels expressed in the neuron (which determines* R_m*).*

<u>The Pathway for Current Flow Across the Membrane</u>

Movement of charged ions across the membrane carries the membrane current. Ions are charged particles that will not flow easily across the membrane lipid bilayer. Rather, ions pass through the membrane through specific ion channels. Therefore, ion channels are the 'metal wire' of a circuit so to speak.

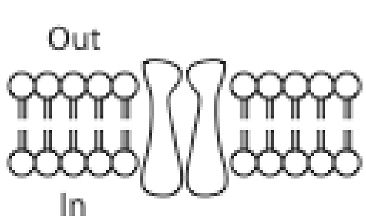
2.2. Biological Membrane as Electrical Equivalent Circuits

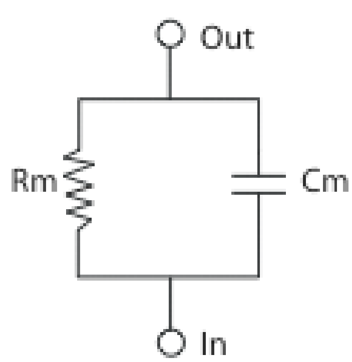
One can view the membrane as the following electrical equivalent circuit.

Features:

- Ion channel proteins possess transmembrane pores that conduct ions across the membrane. This introduces membrane resistance (Rm), which is the inverse of conductance. The value of the resistor is thus proportional to the number of channels that are open.
- The phospholipids bilayer stores electrical charge, giving rise to the property of membrane capacitance (Cm).
- The behavior of a biological membrane may be simulated closely by the behavior of a simple RC electrical circuit with solid-state components.

Biological Membrane | **Electrical Circuit**





2.3 Internal resistance and membrane resistance determine the cable pro[illegible]s of cylindrical components such as axons and dendrites

As electrical charge moves through neural processes such as axons and dendrites, passive properties also determine how far and how fast voltage changes occur along the membrane**.**

The take-home messages

- Biological membranes possess 2 primary “passive” electrical properties: resistance and capacitance. Together these determine the rate at which passive voltage changes can occur. Resistance independently determines the magnitude of the membrane voltage change in response to a given input current.

- It follows that membrane resistance and capacitance determine the window over which synaptic potentials can sum with one another in neurons and muscles. Passive membrane properties help determine the speed at which neurons signal within their networks, and how closely changes in a neuron’s membrane potential track changes in the inputs it receives.