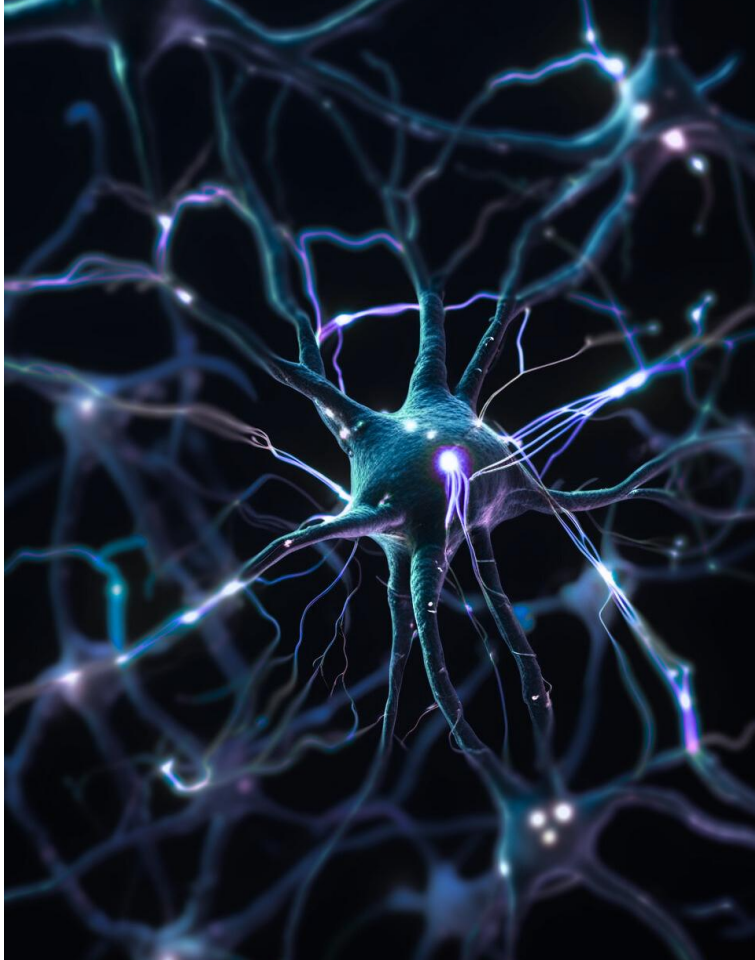
Computational Neuroscience

Session 1: Single Neuron Models (1)

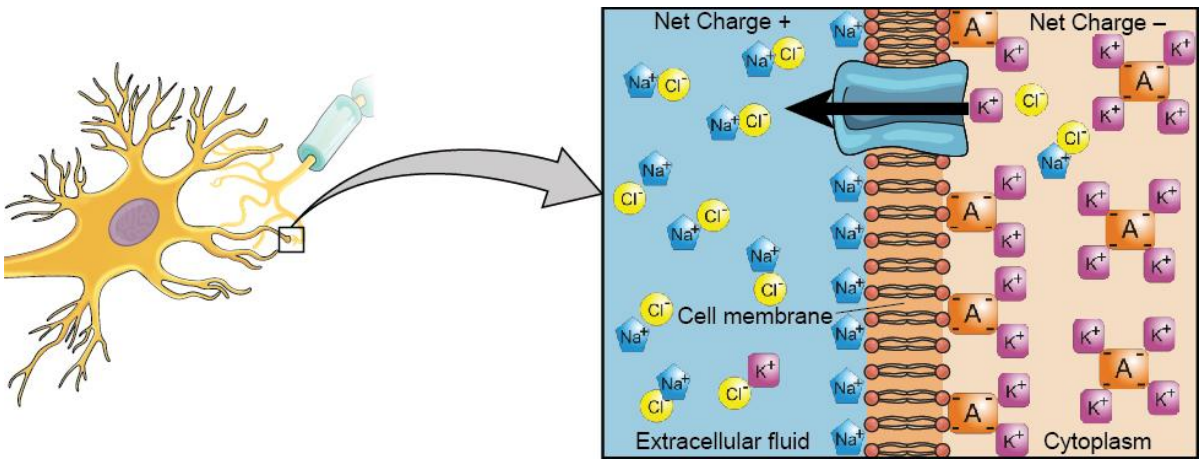
Instructor: Ashkan Damavandi

August 2, 2025



Neuron’s Membrane

There are only 10^{11} or so neurons in the human brain, much fewer than the number of non-neural cells such as glia. Neurons are unique in the sense that only they can transmit electrical signals over long distances. The neuron is the fundamental information processing unit of the nervous system. Central to its function is the neuronal membrane, a sophisticated structure that separates the cell's interior from the extracellular environment. From a physics perspective, the membrane is not merely a passive container but a dynamic electrical interface. Its properties give rise to ionic currents, potential differences, and regenerative electrical pulses known as action potentials. Understanding the membrane's biophysical characteristics is the first step in modeling the neuron as a computational device.



Neuron's Membrane Structure and Properties

The neuronal membrane is primarily a phospholipid bilayer roughly 3-5 nm thick, separating two conductive solutions: the intracellular cytoplasm and the extracellular fluid. The polar (hydrophilic) heads of the phospholipids face the aqueous exterior and interior of the cell, while the hydrophobic tails form the interior of the bilayer. This lipid bilayer alone is an excellent electrical insulator; its resistance to ion flow is extremely high. However, real neuronal membranes also contain a mosaic of proteins embedded in the lipid. These proteins (which can constitute anywhere from ~20% up to ~80% of the membrane's dry weight, depending on cell type) include ion channels, transporters, and receptors. They provide pathways for ions and thus dramatically lower the effective membrane resistance compared to pure lipid. In other words, the lipid part of the membrane acts as an electrical insulator (analogous to a parallel-plate capacitor), but the membrane proteins (especially ion channels) introduce conductive pathways that allow current to flow.

C_m (Membrane Capacitance): By separating ionic charges across its thin insulating layer, the lipid bilayer acts as a capacitor (positive charges on one side attract negative charges on the other, but they cannot cross directly). This property allows the membrane to store charge. The specific membrane capacitance is remarkably consistent across all neurons, approximately 1 µF/cm² (a 1 cm² patch of membrane can store about 1 µC of charge per 1 V of potential difference). The consequence of this capacitance is that the membrane voltage can't change instantaneously in response to a current input; the capacitance must charge or discharge. Just like a parallel-plate capacitor, the relation is:

$$Q = C_m \cdot V$$

So, a certain charge Q must flow to change the voltage by V. A higher capacitance means more charge is needed to achieve the same change in voltage. Thus, the membrane capacitance tends to soak up fast, transient currents, smoothing rapid voltage changes. High-frequency electrical inputs are attenuated by the capacitive effect, acting as a low-pass filter.
Quantitatively, the time constant τ of a membrane (the time it takes voltage to change ~63% toward a new value in response to a current step) is:

$$\tau_m = R_m C_m$$

R_m (Membrane Resistance): Embedded within the lipid bilayer are various protein structures, most importantly ion channels. These channels provide specific pathways for ions to cross the membrane. Collectively, these open channels create a path for current flow, giving the membrane a specific resistance (R_m in Ω·cm²), or its inverse, specific conductance ($G_m = 1/R_m$, in S/cm²). Unlike the nearly perfect insulator of the lipid itself, the channels allow for controlled current leakage. A high R_m means few channels are open (less leak), while a low R_m means many conductive channels (more ionic "leak"). Ohm's law applies:

$$V = I \cdot R_m \quad \text{or} \quad I = G_m \cdot V$$

The current through open ion channels is proportional to the driving force (voltage difference) and the conductance. In fact, for a given ion species, we can write:

$$I_{\text{ion}} = G_{\text{ion}} (V - E_{\text{ion}})$$

Where E_{ion} is that ion's equilibrium or Nernst potential. This equation is a form of Ohm's law, with $(V - E_{\text{ion}})$ as the voltage difference driving the current. The sign of the current (inward vs. outward) depends on whether V is above or below E_{ion}. A pure lipid bilayer contributes essentially no conductance ($G \approx 0, R \approx \infty$), whereas ion channels provide G_{ion} values that can sum to a total membrane conductance G_m.

Leaky Integrate-and-Fire (LIF) Model: For a patch of membrane with membrane resistance R_m and capacitance C_m, the differential equation is:

$$C_m \frac{dV}{dt} = -\frac{1}{R_m}(V - E_{\text{rest}}) + I_{\text{inj}}(t)$$

Where $I_{\text{inj}}(t)$ is an injected current and E_{rest} is the resting potential (the steady-state solution). Solving this yields an exponential charging or discharging with time constant τ. In many neurons, time constants can range from sub-millisecond (for very leaky, small cells) up to tens of ms for larger or less leaky cells. This equation states that the capacitive current

(charging the membrane) is equal to the sum of the ionic "leak" current through the resistor and the externally injected current. Rearranging this gives the standard form for the Leaky Integrate-and-Fire (LIF) model:

$$\tau_m \frac{dV_m}{dt} = -(V_m - V_{\text{rest}}) + R_m I_{\text{inj}}(t)$$

Here, $\tau_m = R_m C_m$ is the **membrane time constant**. Using the typical values above, τ_m would be approximately 0.85 ms, representing the characteristic time for the membrane potential to charge or discharge.

Ion Channels: Neurons possess a remarkable diversity of ionic channels, with dozens of different types possible. These channels vary in their density across different parts of the neuron and can be exquisitely sensitive to changes in voltage (voltage-gated channels) or depend on the binding of neurotransmitters (ligand-gated channels). Examples of specific ion currents and the channels that mediate them include:

• Transient Sodium Current ($I_{Na,t}$): Rapidly activates and inactivates, crucial for action potential generation, found in axons and cell bodies.
• Persistent Sodium Current ($I_{Na,p}$): A non-inactivating sodium current, smaller in amplitude, that can enhance excitation and maintain moderate depolarization, making it easier for a cell to fire.
• A-type Potassium Current (I_A): A transient potassium current (mA-current) that can shape repetitive firing and influence the refractory period.
• H-current (I_h): A hyperpolarization-activated current, often mediating subthreshold oscillations.
• Inwardly Rectifying Potassium Current (I_{Kir}): Activated by hyperpolarization and turned off by depolarization, it influences the resting potential and can contribute to bistability.

Membrane Potential and Ionic Gradients

The electrical potential across the membrane arises from the differential distribution of ions (high extracellular Na^+, high intracellular K^+). This creates two opposing forces: a chemical force (diffusion) and an electrical force (drift).

Nernst Potential: For a single ion species, the equilibrium potential (E_{ion}) or Nernst Potential, is the potential at which these two forces are perfectly balanced. The Nernst equation quantifies this:

$$E_{\text{ion}} = \frac{RT}{zF} \ln\left(\frac{[\text{Ion}]_{\text{out}}}{[\text{Ion}]_{\text{in}}}\right)$$

Where R is the gas constant, T is temperature, z is ion valence, and F is Faraday's constant. In a typical mammalian neuron, these potentials are approximately:

- $E_K \approx -90mV$
- $E_{Na} \approx +60mV$
- $E_{Cl} \approx -54mV$
- $E_{Ca} \approx +120mV$

Goldman-Hodgkin-Katz (GHK) Equation: Since the membrane is permeable to multiple ions, the resting potential is better described by the GHK equation, which weights each ion's Nernst potential by its relative permeability (P):

$$V_m = \frac{RT}{F} \ln\left(\frac{P_K[\text{K}^+]_{\text{out}} + P_{Na}[\text{Na}^+]_{\text{out}} + P_{Cl}[\text{Cl}^-]_{\text{in}}}{P_K[\text{K}^+]_{\text{in}} + P_{Na}[\text{Na}^+]_{\text{in}} + P_{Cl}[\text{Cl}^-]_{\text{out}}}\right)$$

At rest, the permeability to potassium (P_K) is much higher than to sodium (P_{Na}), which is why V_{rest} (typically -30 to -90 mV) is close to E_K. The ionic current for a given species follows Ohm's Law, driven by the difference between the membrane potential and the ion's equilibrium potential ($I_{\text{ion}} = G_{\text{ion}}\,(V - E_{\text{ion}})$), where G_{ion} is the dynamically controlled conductance. Inward currents (e.g., Na^+, Ca^{2+}) cause depolarization (making V_m more positive), while outward currents (e.g., K^+, or inward Cl^-) cause hyperpolarization (making V_m more negative).

Dynamic Control of Membrane Permeability

The membrane's conductance is not static; it is dynamically regulated by the opening and closing of a diverse zoo of ion channels.

Selectivity and Gating: Channels are highly selective for specific ions. Their state (open/closed) is controlled by gating mechanisms. Voltage-gated channels are fundamental to action potentials, while ligand-gated channels are the basis of synaptic communication. Other channels respond to intracellular messengers like Ca^{2+}.

Diversity of Channels: Beyond the primary Na^+ and K^+ channels for action potentials, neurons express many others that shape their firing patterns, such as:

- Persistent Sodium Current ($I_{Na,p}$): A non-inactivating sodium current that can enhance excitation.
- A-type Potassium Current (I_A): A transient potassium current that can delay the onset of firing.
- H-current (I_h): A hyperpolarization-activated current that can mediate subthreshold oscillations.

Synapses as Modulators of Permeability: Synapses act to transiently change the postsynaptic membrane's conductance. The resulting synaptic current is:

$$I_{\text{syn}} = G_{\text{syn}}(t)\left(V_m - E_{\text{syn}}\right)$$

Where E_{syn} is the synaptic reversal potential. The time course of the synaptic conductance, $G_{syn}(t)$, can be modeled by functions like the alpha function, which describes a rapid rise and slower exponential decay:

$$G_{\text{syn}}(t) = G_{\max}\frac{t}{\tau_{\text{syn}}}e^{\left(1-t/\tau_{\text{syn}}\right)}$$

The fact that synapses are conductance changes has profound nonlinear consequences. An increase in synaptic conductance lowers the total membrane resistance, which in turn decreases the membrane time constant (τ_m). This means a neuron under heavy synaptic bombardment becomes "leakier" and responds faster to inputs.

Signal Propagation in Spatially Extended Neurons

Passive Propagation and the Cable Equation: For spatially extended neurons, the Cable Equation describes how voltage evolves in time and space:

$$\tau_m \frac{\partial V}{\partial t} = \lambda^2 \frac{\partial^2 V}{\partial x^2} - (V - V_{\text{rest}})$$

The length constant (λ) is a key parameter describing the spatial scale of voltage decay:

$$\lambda = \sqrt{\frac{r \cdot R_m}{2 \cdot R_a}}$$

Where r is the neurite's radius, R_m is the specific membrane resistance (in Ω·cm^2), and R_a is the specific axial resistance (in Ω·cm).

Electronic Distance: Electrotonic distance is the electrical distance between two points, quantifying signal attenuation. It is not fixed; it depends on morphology and, crucially, on membrane resistance (R_m). Background synaptic activity lowers the effective R_m, making the membrane "leakier" and dynamically shrinking the neuron's electrotonic length. This dynamic modulation of the cell's electroanatomy is a key feature of in-vivo computation. Dendritic spines further complicate this, acting as electrically coupled but biochemically isolated compartments whose geometry can modulate synaptic weight.

Spike, and The Hodgkin-Huxley Model

The action potential (or spike) is a regenerative, all-or-none event initiated when V_m crosses a threshold.

The Hodgkin-Huxley Formalism: The **Hodgkin-Huxley model** provides a detailed biophysical description. The total current is the sum of capacitive and ionic components:

$$C_m \frac{dV_m}{dt} = -I_{\text{ion}} + I_{\text{inj}}$$

The ionic current is composed of multiple components, each with its own voltage- and time-dependent conductance:

$$I_{\text{ion}} = G_{\text{Na}}(V,t)(V_m - E_{\text{Na}}) + G_{\text{K}}(V,t)(V_m - E_{\text{K}}) + G_L(V_m - E_L)$$

The conductances are functions of gating variables (e.g., m, h, n), each representing a population of channel subunits. For example, the sodium and potassium conductances are:

$$g_{\text{Na}} = \overline{g_{\text{Na}}} m^3 h \qquad g_{\text{K}} = \overline{g_{\text{K}}} n^4$$

Where $\bar{g}$ are the maximal conductances. The gating variables each follow their own first-order kinetics:

$$\frac{dx}{dt} = \alpha_x(V)(1-x) - \beta_x(V)x, \quad \text{for } x \in \{m,h,n\}$$

Where $\alpha(V)$ and $\beta(V)$are strongly voltage-dependent rate constants for channel opening and closing, respectively.

For the Next Session…

Excitability and Bifurcations

The Role of Calcium as a Second Messenger

Stochasticity and Noise

Functional and Systems-Level Models: The Volterra Series

.

.

.