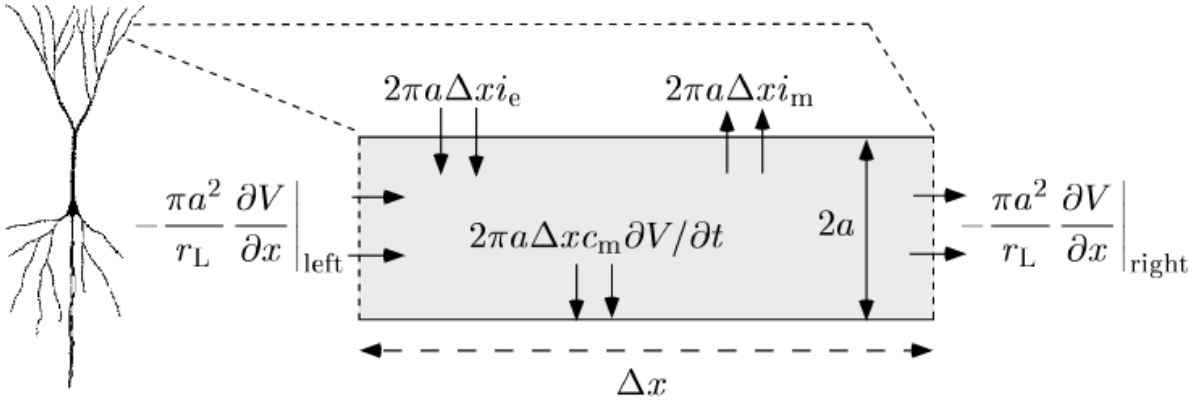
Hodgkin-Huxley Model

Cable Equation Derivation



For a cylindrical segment with radius a, intracellular resistivity r_L, and membrane capacitance per unit area c_m:

Longitudinal resistance:

$$R_L = \frac{r_L \Delta x}{\pi a^2} \tag{1}$$

Longitudinal voltage drop:

$$\Delta V = -I_L R_L = -I_L \frac{r_L \Delta x}{\pi a^2} \tag{2}$$

Longitudinal current:

$$I_L = \frac{-\pi a^2}{r_L} \frac{\Delta V}{\Delta x} \tag{3}$$

Membrane current:

$$i_m = \sum_i g_i (V - E_i) \tag{4}$$

The sum of the Longitudinal current coming in and out of the segment, the membrane current, and external current (i_e) is equal to the total capacitance of the neuron $2\pi a \Delta x c_m$ times the rate of change of the membrane potential $\frac{\partial V}{\partial t}$:

"The longitudinal input current is with respect to the previous segment/neuron, and is assumed to be equal to the longitudinal output current with respect to the next segment/neuron which have the same radius a, specific resistivity r_L, and length Δx."

$$2\pi a \Delta x c_m \frac{\partial V}{\partial t} = -\left(\frac{\pi a^2}{r_L}\frac{\Delta V}{\Delta x}\right)\bar{v}_{\text{in}} + \left(\frac{\pi a^2}{r_L}\frac{\Delta V}{\Delta x}\right)\bar{v}_{\text{out}} - 2\pi a \Delta x (i_m - i_e) \tag{5}$$

Dividing both sides by $2\pi a \Delta x$ and taking the limit as $\Delta x \to 0$ gives the cable equation:

$$c_m \frac{\partial V}{\partial t} = \frac{a}{2r_L}\frac{\partial^2 V}{\partial x^2} - i_m + i_e \tag{6}$$

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Multi-Compartment Approximation

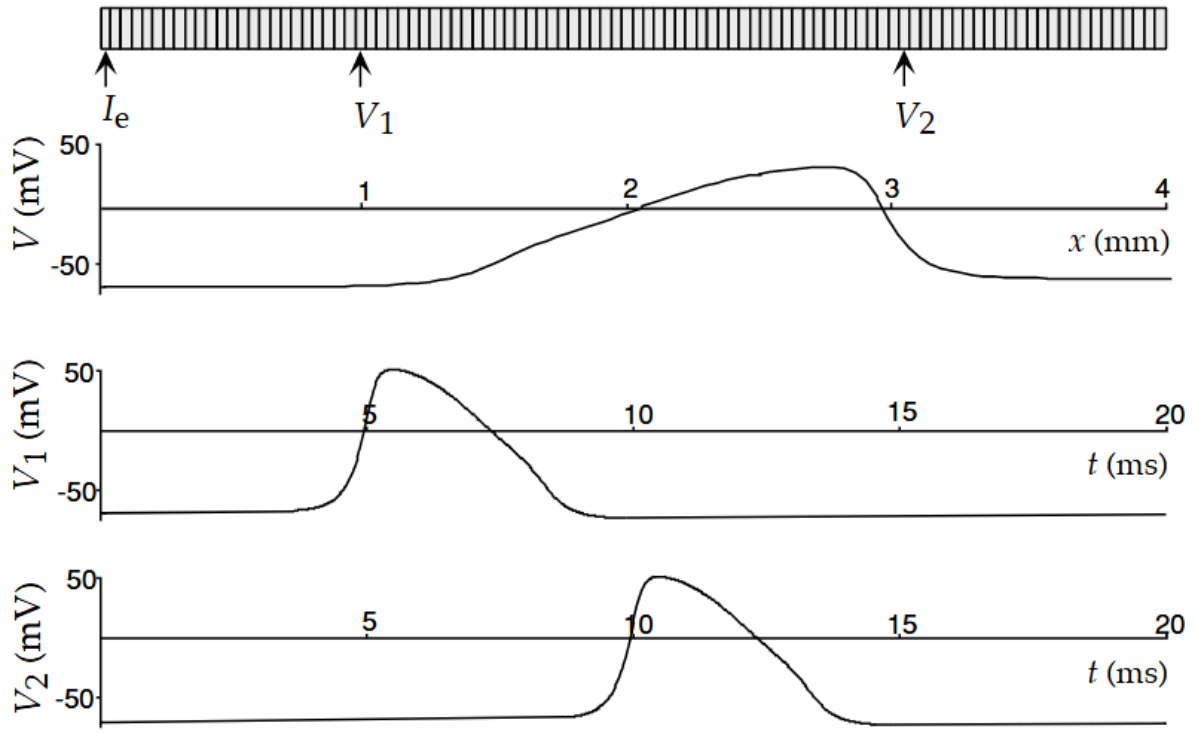

Figure 1: Figure 6.17 Propagation of an action potential along a multi-compartment model axon

The neuron is divided into discrete compartments indexed by μ. Each has membrane potential V_μ and membrane area A_μ. For a cable without branching:

The longitudinal resistance between compartments μ and μ':

$$R_L^{(\mu,\mu')} = \frac{r_L L_\mu}{2\pi a_\mu^2} + \frac{r_L L_{\mu'}}{2\pi a_{\mu'}^2} \tag{7}$$

The conductance between compartments μ and μ' is the reciprocal of the resistance divided by the area of compartment μ, $A_\mu = 2\pi a_\mu^2 L_\mu$:

$$g_{\mu,\mu'} = \frac{1}{R_L^{(\mu,\mu')} A_\mu} = \frac{a_\mu a_{\mu'}^2}{r_L L_\mu (L_\mu a_{\mu'}^2 + L_{\mu'} a_\mu^2)} \tag{8}$$

Letting the length of each compartment be denoted by L_μ, the equation for compartment μ is:

$$c_m \frac{dV_\mu}{dt} = -i_m^\mu + i_e^\mu + g_{\mu,\mu+1}(V_{\mu+1} - V_\mu) + g_{\mu,\mu-1}(V_{\mu-1} - V_\mu) \tag{9}$$

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Synaptic Transmission

As with a voltage-dependent conductance, a synaptic conductance can be written as the product of a maximal conductance and an open channel probability, $g_s = \bar{g_s} P$, where P can be expressed as the joint probability of transmitter binding and channel opening, $P = P_{\text{rel}} P_s$.

$$c_m \frac{dV}{dt} = -i_m + i_e - \bar{g_s} P (V - E_s) \tag{10}$$

where E_s is the synaptic reversal potential, which is typically around 0 mV for excitatory synapses and around −70 mV for inhibitory synapses.

The synaptic open channel probability P has complex dynamics, but can be simplified to a exponentially decaying function that has a discrete jump after a presynaptic spike time.

or in the multi-compartment model for compartment μ:

$$c_m \frac{dV_\mu}{dt} = -i_m^\mu + i_e^\mu - \bar{g_s} P(V_\mu - E_s) + g_{\mu,\mu+1}(V_{\mu+1} - V_\mu) + g_{\mu,\mu-1}(V_{\mu-1} - V_\mu) \tag{11}$$

synapse

Appendix A — Conductance-based neuron models

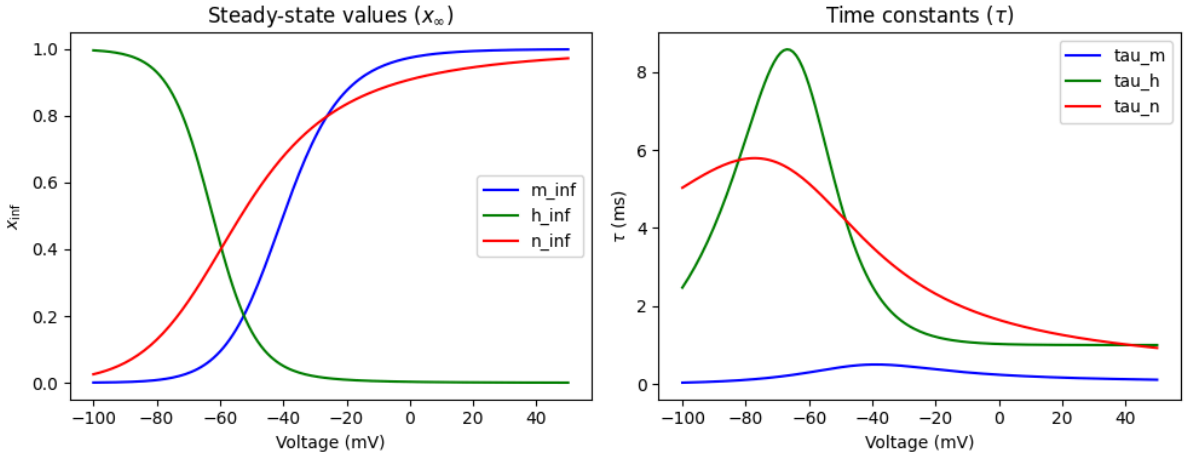

Figure 2: Gating Time Constants and Steady-State Values

Hodgkin–Huxley membrane current can be expressed as a sum of a leakage current, a delayed-rectifier K^+ current, and a transient Na^+ current:

$$i_m = g_L(V - E_L) + g_K, n^4(V - E_K) + g_{Na}, m^3 h(V - E_{Na}). \tag{12}$$

where m, h, n are dynamic gating variables between 0 and 1.

For any gate $z \in m, h, n$:

$$\frac{dz}{dt} = \alpha_z(V)(1 - z) - \beta_z(V)z \quad \Rightarrow \quad \tau_z(V)\frac{dz}{dt} = z_\infty(V) - z, \tag{13}$$

where

$$\tau_z = 1/(\alpha_z + \beta_z) \tag{14}$$

and

$$z_\infty = \frac{\alpha_z}{(\alpha_z + \beta_z)} \tag{15}$$

Numerical integration:

Over small Δt, integrate V and then each gate with the same stable update:

$$\tau_z \frac{dz}{dt} = z_\infty - z \quad \Rightarrow \quad z(t + \Delta t) = z_\infty + (z(t) - z_\infty)e^{-\Delta t/\tau_z}. \tag{16}$$

Appendix B - Synaptic open probability $P_s(t)$ and postsynaptic conductance

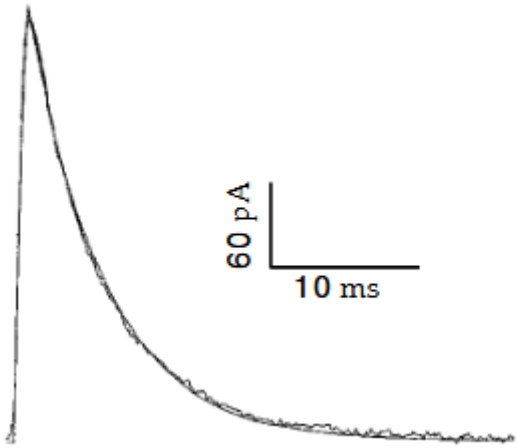

Figure 3: Figure 5.14 A fit of the model discussed in the text to the average EPSC (excitatory postsynaptic current)

If k transmitter molecules bind to open a receptor:

$$\frac{dP_s}{dt} = \alpha_s(1 - P_s) - \beta_s P_s, \quad \alpha_s \propto [\text{transmitter}]^k. \tag{17}$$

““Here, β_s determines the closing rate of the channel and is usually assumed to be a constant. The opening rate, α_s, on the other hand, depends on the concentration of transmitter available for binding to the receptor. If the concentration of transmitter at the site of the synaptic channel is [transmitter], the probability of finding k transmitter molecules within binding range of the channel is proportional to [transmitter]k, and α_s is some constant of proportionality times this factor... As a simple model of transmitter release, we assume that the transmitter concentration in the synaptic cleft rises extremely rapidly after vesicle release, remains at a high value for a period of duration T, and then falls rapidly to 0. Thus, the transmitter concentration is modeled as a square pulse.””

While the transmitter concentration in the cleft is nonzero, α_s is so much larger than β_s that we can ignore the term involving β_s in the above equation. Under this assumption

$$P_s(t) = 1 + (P_s(0) - 1)\exp(-\alpha_s t) \quad \text{for} \quad 0 \le t \le T \tag{18}$$

The open probability takes its maximum value at time $t = T$ and then, for $t \ge T$, decays exponentially at a rate determined by the constant β_s, and α_s is 0 after because transmitter concentration rapidly falls after T

$$P_s(t) = P_s(T)\exp(-\beta_s(t - T)) \quad \text{for} \quad t \ge T. \tag{19}$$

If $P_s(0) = 0$, as it will if there is no synaptic release immediately before the release at t = 0, the first equation simplifies to $P_s(t) = 1 - \exp(-\alpha_s t)$ for $0 \le t \le T$, and this reaches a maximum value $P_{\max} = 1 - \exp(-\alpha_s T)$. In terms of this parameter the synaptic open probability at time T in the general case can be written as

$$P_s(T) = P_s(0) + P_{\max}(1 - P_s(0)) \tag{20}$$

The figure shows a fit to a recorded postsynaptic current using this formalism. In this case, β_s was set to $0.19ms^{-1}$. The transmitter concentration was modeled as a square pulse of duration T = 1 ms

during which $\alpha_s = 0.93ms^{-1}$. Inverting these values, we find that the time constant determining the rapid rise seen in the figure is 0.9 ms, while the fall of the current is an exponential with a time constant of 5.26 ms.

Spike Trains

Assuming a fast synapse, the rise of the conductance following a presynaptic action potential is so rapid that it can be approximated as instantaneous. Between spikes, P_s decays exponentially, and after each spike, P_s jumps by an amount proportional to the distance from its maximum value:

$$\tau_s \frac{dP_s}{dt} = -P_s, \qquad P_s \to P_s + P_{\max}(1 - P_s). \tag{21}$$

Appendix C — Transmitter release probability $P_{\text{rel}}(t)$ and short-term plasticity

P_{rel} denotes the average release probability across one or many independent sites. It is described using a simple nonmechanistic model that has similarities to the model of P_s. For both facilitation and depression, the release probability after a long period of presynaptic silence is $P_{\text{rel}} = P_0$.

$$\tau_P \frac{dP_{\text{rel}}}{dt} = P_0 - P_{\text{rel}} \tag{22}$$

Spike-triggered updates.

- Facilitation: $P_{\text{rel}} \to P_{\text{rel}} + f_F(1 - P_{\text{rel}}), (0 \le f_F \le 1)$
- Depression: $P_{\text{rel}} \to f_D P_{\text{rel}}, (0 \le f_D \le 1)$.

Analysis for Poisson Spike Trains

Assume presynaptic spikes form a Poisson process with rate r. Between spikes, P_{rel} relaxes exponentially to P_0:

$$\tau_P \frac{dP_{\text{rel}}}{dt} = P_0 - P_{\text{rel}} \tag{23}$$

The general solution is

$$P_{\text{rel}}(t) = P_0 + [P_{\text{rel}}(t_0) - P_0]e^{-(t-t_0)/\tau_P}. \tag{24}$$

Facilitation

Spike rule. After a spike,

$$P_{\text{rel}} \to P_{\text{rel}} + f_F(1 - P_{\text{rel}}) \tag{25}$$

One ISI. Let two spikes be separated by τ. If P_{rel} equals its mean $\langle P_{\text{rel}} \rangle$ just *before* the first spike, then just *after* that spike it is $\langle P_{\text{rel}} \rangle + f_F(1 - \langle P_{\text{rel}} \rangle)$. During the interval τ it decays towards it's resting value P_0, and just before the next spike it is

$$P_0 + (\langle P_{\text{rel}} \rangle + f_F(1 - \langle P_{\text{rel}} \rangle) - P_0)e^{-\tau/\tau_P} \tag{26}$$

Average decay factor over Poisson ISIs.

For a Poisson process with mean firing rate r, the ISI distribution is exponential:

$$p(\tau) = re^{-r\tau}, \quad \tau \ge 0. \tag{27}$$

This gives the probability density for the time gap between spikes.

The expected decay factor over a random interval τ is

$$\langle e^{-\tau/\tau_P}\rangle = \int_0^\infty e^{-\tau/\tau_P} p(\tau) d\tau = r\int_0^\infty e^{-r\tau-\tau/\tau_P} d\tau = \frac{r}{r+1/\tau_P} = \frac{r\tau_P}{1+r\tau_P}. \tag{28}$$

Consistency equation. For steady state,

$$\langle P_{\text{rel}}\rangle = P_0 + (\langle P_{\text{rel}}\rangle + f_F(1-\langle P_{\text{rel}}\rangle) - P_0)\frac{r\tau_P}{1+r\tau_P} \tag{29}$$

Solve.

$$\langle P_{\text{rel}}\rangle = \frac{P_0 + f_F r\tau_P}{1+rf_F\tau_P} \tag{30}$$

Behavior. Low r: $\langle P_{\text{rel}}\rangle \approx P_0$. High r: $\langle P_{\text{rel}}\rangle \to 1$. Transmission rate equals $r\langle P_{\text{rel}}\rangle$, so it grows $\approx P_0 r$ at low r and $\approx r$ at high r.