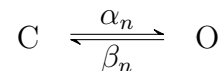


Introduction to Computational Neuroscience (Fall 2023)

The Hodgkin-Huxley Model

K⁺ channels

- The activation of K⁺ channels can be described by “gating particles” that are either closed or open. Each satisfies a first-order kinetic scheme:



where α_n is the closed-to-open transition rate (units of ms⁻¹) and β_n is the open-to-closed transition rate (same units). **The first-order kinetic equation** for K⁺ channel gates comes from applying the **Law of Mass Action** to this kinetic scheme, defining n as the fraction of gates that are open (or the probability that a gate is open):

$$(1) \quad \frac{dn}{dt} = \alpha_n(1 - n) - \beta_n n .$$

The rate coefficients both depend on V .

- The equilibrium value of n (denoted n_∞) and time constant (τ_n) are both V -dependent and satisfy:

$$(2) \quad n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n} \quad \text{and} \quad \tau_n = \frac{1}{\alpha_n + \beta_n} .$$

Using these, Eq. 1 can be rewritten as

$$(3) \quad \frac{dn}{dt} = \frac{n_\infty - n}{\tau_n} .$$

- The first-order kinetic equation Eq. 3 is linear for a fixed value of V and can be solved in response to a voltage step to a value V_1 :

$$(4) \quad n(t) = n_\infty(V_1) - (n_\infty(V_1) - n_0)\exp(-t/\tau_n(V_1))$$

where n_0 is the value of n at the start of the voltage step.

- It is possible using voltage clamp to find n_∞ and τ_n from the K⁺ data. Then the rate coefficients can be obtained using

$$(5) \quad \alpha_n = \frac{n_\infty}{\tau_n} \quad \text{and} \quad \beta_n = \frac{1 - n_\infty}{\tau_n} .$$

Fitting the squid giant axon data,

$$(6) \quad \alpha_n = 0.01 \frac{V + 55}{1 - \exp(-(V + 55)/10)} \quad \text{and} \quad \beta_n = 0.125 \exp\left(\frac{-(V + 65)}{80}\right) .$$

- The K^+ current in the HH model is then

$$(7) \quad I_K = \bar{g}_K n^4 (V - V_K).$$

Na⁺ channels

- The activation properties of Na⁺ channels are similar in form to those of K⁺ channels. This is reflected in the activation variable m .

$$(8) \quad \frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m \quad \text{or} \quad \frac{dm}{dt} = \frac{m_\infty - m}{\tau_m}$$

and from fitting the squid giant axon data,

$$(9) \quad \alpha_m = 0.1 \frac{V + 40}{1 - \exp(-(V + 40)/10)} \quad \text{and} \quad \beta_m = 4 \exp\left(\frac{-(V + 65)}{18}\right).$$

- Na⁺ channels also inactivate, with inactivation variable h defined as the fraction of channels *not inactivated*. Equations are

$$(10) \quad \frac{dh}{dt} = \alpha_h(1 - h) - \beta_h h \quad \text{or} \quad \frac{dh}{dt} = \frac{h_\infty - h}{\tau_h}$$

and from fitting the squid giant axon data,

$$(11) \quad \alpha_h = 0.07 \exp\left(\frac{-(V + 65)}{20}\right) \quad \text{and} \quad \beta_h = \frac{1}{\exp(-(V + 35)/10) + 1}.$$

- The Na⁺ current in the HH model is then

$$(12) \quad I_{Na} = \bar{g}_{Na} m^3 h (V - V_{Na}).$$

The Hodgkin-Huxley model

- This is a 4-dimensional system of coupled ODEs (for the space-clamped system) with two activation variables, an inactivation variable, and the V dynamics given by

$$(13) \quad \frac{dV}{dt} = -(I_{Na} + I_K + I_L - I_e)/C$$

where I_e is the current applied through an electrode and the constant-conductance leak current is

$$(14) \quad I_L = \bar{g}_L (V - V_L)$$

- When space is not clamped, impulses can propagate down an axon in a regenerative manner. These are called **solitons** by physicists, since the amplitude of the wave (the impulse) does not decrease like a water wave does. The HH model is a PDE in this case, with V equation

$$(15) \quad C \frac{\partial V}{\partial t} = -I_{\text{Na}} - I_{\text{K}} - I_{\text{L}} + I_{\text{e}} + \frac{d}{4R_{\text{a}}} \frac{\partial^2 V}{\partial x^2}$$

where d is the axon diameter and R_{a} is the axial resistance.

The effect of temperature

- The rate coefficients increase in a multiplicative manner with an increase in temperature. This effect is captured in an ad hoc way with the Q_{10} , which is the multiplicative speedup factor when temperature is increased by 10° C. Thus,

$$(16) \quad \alpha(V, T_2) = \alpha(V, T_1) Q_{10}^{\frac{T_2 - T_1}{10}} \quad \text{and} \quad \beta(V, T_2) = \beta(V, T_1) Q_{10}^{\frac{T_2 - T_1}{10}}.$$

For the giant axon at 6° C, $Q_{10} \approx 3$.

- In terms of time constants and infinity functions, the effect of temperature is included by making the time constants smaller:

$$(17) \quad \tau(V, T_2) = \tau(V, T_1) / Q_{10}^{\frac{T_2 - T_1}{10}}$$

and there is no effect on the infinity functions.

- The maximum conductance is also increased by an increase in temperature. For ion type x ,

$$(18) \quad \bar{g}_x(T_2) = \bar{g}_x(T_1) Q_{10}^{\frac{T_2 - T_1}{10}}$$

but for conductances the Q_{10} is smaller than for channel rates, $Q_{10} \in [1.2, 1.5]$ for conductances.