Introduction to Computational Neuroscience (Fall 2023)

The Hodgkin-Huxley Model

$\boxed{\text{K}^+ \text{ channels}}$

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

$$\mathrm{C} \underset{\beta_n}{\overset{\alpha_n}{\rightleftharpoons}} \mathrm{O}$$

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):

$$\frac{dn}{dt} = \alpha_\mathrm{n}(1-n) - \beta_\mathrm{n} n \quad . \tag{1}$$

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:

$$n_\infty = \frac{\alpha_\mathrm{n}}{\alpha_\mathrm{n} + \beta_\mathrm{n}} \quad \text{and} \quad \tau_\mathrm{n} = \frac{1}{\alpha_\mathrm{n} + \beta_\mathrm{n}}. \tag{2}$$

Using these, Eq. 1 can be rewritten as

$$\frac{dn}{dt} = \frac{n_\infty - n}{\tau_\mathrm{n}}. \tag{3}$$

- 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:

$$n(t) = n_\infty(V_1) - (n_\infty(V_1) - n_0)\exp(-t/\tau_\mathrm{n}(V_1)) \tag{4}$$

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

$$\alpha_\mathrm{n} = \frac{n_\infty}{\tau_\mathrm{n}} \quad \text{and} \quad \beta_\mathrm{n} = \frac{1 - n_\infty}{\tau_\mathrm{n}}. \tag{5}$$

Fitting the squid giant axon data,

$$\alpha_\mathrm{n} = 0.01\frac{V + 55}{1 - \exp(-(V+55)/10)} \quad \text{and} \quad \beta_\mathrm{n} = 0.125\exp\left(\frac{-(V+65)}{80}\right). \tag{6}$$

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

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

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

and from fitting the squid giant axon data,

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

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

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

and from fitting the squid giant axon data,

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

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

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

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

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

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

- 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

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

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,

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

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:

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

and there is no effect on the infinity functions.
- The maximum conductance is also increased by an increase in temperature. For ion type x,

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

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