Introduction to Computational Neuroscience  
(Fall 2023)  
The Hodgkin-Huxley Model

\[ \text{K}^+ \text{ channels} \]

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

\[
C \underset{\beta_n}{\overset{\alpha_n}{\rightleftharpoons}} O
\]

where $\alpha_n$ is the closed-to-open transition rate (units of ms$^{-1}$) and $\beta_n$ 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):

\[
\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n.
\]

The rate coefficients both depend on $V$.
- The equilibrium value of $n$ (denoted $n_\infty$) and time constant ($\tau_n$) are both $V$-dependent and satisfy:

\[
n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n} \quad \text{and} \quad \tau_n = \frac{1}{\alpha_n + \beta_n}.
\]

Using these, Eq. 1 can be rewritten as

\[
\frac{dn}{dt} = \frac{n_\infty - n}{\tau_n}.
\]

- 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 $V_1$:

\[
n(t) = n_\infty(V_1) - (n_\infty(V_1) - n_0)\exp(-t/\tau_n(V_1))
\]

where $n_0$ is the value of $n$ at the start of the voltage step.
- It is possible using voltage clamp to find $n_\infty$ and $\tau_n$ from the K$^+$ data. Then the rate coefficients can be obtained using

\[
\alpha_n = \frac{n_\infty}{\tau_n} \quad \text{and} \quad \beta_n = \frac{1 - n_\infty}{\tau_n}.
\]

Fitting the squid giant axon data,

\[
\alpha_n = 0.01 \frac{V + 55}{1 - \exp(-(V + 55)/10)} \quad \text{and} \quad \beta_n = 0.125\exp\left(-\frac{(V + 65)}{80}\right).
\]
• The K⁺ current in the HH model is then

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

**Na⁺ channels**

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

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

and from fitting the squid giant axon data,

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

• Na⁺ channels also inactivate, with inactivation variable \( h \) defined as the fraction of channels not inactivated. Equations are

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

and from fitting the squid giant axon data,

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

• The Na⁺ current in the HH model is then

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

**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

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

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

\[ I_L = \bar{g}_L (V - V_L) \]
• 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

$$C \frac{\partial V}{\partial t} = -I_{\text{Na}} - I_K - I_L + I_e + \frac{d}{4R_a} \frac{\partial^2 V}{\partial x^2}$$

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 $10^\circ$ C. Thus,

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

For the giant axon at $6^\circ$ 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:

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

and there is no effect on the infinity functions.

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

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

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