Hodgkin-Huxley Model of Action Potentials

Differential Equations
Math 210
Neuron

**Dendrites**
Collect electrical signals

**Cell body**
Contains nucleus and organelles

**Axon**
Passes electrical signals on to dendrites of another cell or to an effector cell
Electrochemical Equilibrium
Action Potential

- Axon membrane potential difference
  \[ V = V_{in} - V_{out} \]
- When the axon is excited, \( V \) spikes because sodium \( \text{Na}^+ \) and potassium \( \text{K}^+ \) ions flow through the membrane
Modeling the dynamics of an action potential

- Alan Lloyd Hodgkin and Andrew Huxley
  - Proposed model in 1952
  - Explains ionic mechanisms underlying the initiation and propagation of action potential in the squid giant axon
  - Received the 1963 Nobel Prize in Physiology or Medicine
Circuit model for axon membrane

\[ q(t) = \text{the charge carried by particles in circuit at time } t \]
\[ I(t) = \text{the current (rate of flow of charge in the circuit)} = \frac{dq}{dt} \]
\[ V(t) = \text{the voltage difference in the electrical potential at time } t \]
\[ R = \text{resistance (property of a material that impedes flow of charge particles)} \]
\[ g(V) = \text{conductance} = \frac{1}{R} \]
\[ C = \text{capacitance (property of an element that physically separates charge)} \]

**Conductors** or **resistors** represent the ion channels.
**Capacitors** represent the ability of the membrane to store charge.
Physical relationships in a circuit

- **Ohm’s law**: the voltage drop across a resistor is proportional to the current through the resistor; \( R \) (or \( 1/g \)) is the factor of proportionality

\[
V(t) = I(t)R = \frac{I(t)}{g}
\]

- **Faraday’s law**: the voltage drop across a capacitor is proportional to the electric charge; \( 1/C \) is the factor of proportionality

\[
V(t) = \frac{q(t)}{C}
\]
For elements in parallel, the total current is equal to the sum of currents in each branch; the voltage across each branch is then the same.

\[ I(t) = I_1(t) + I_2(t) + I_3(t) \]

Differentiate Faraday’s Law \( V(t) = \frac{q(t)}{C} \) leads to

\[ \frac{dV}{dt} = \frac{1}{C} \frac{dq}{dt} = \frac{I(t)}{C} = \frac{1}{C} (I_1(t) + I_2(t) + I_3(t)) \]
Hodgkin-Huxley Model

\[
\frac{dV}{dt} = -\frac{1}{C} \left( I_{Na}(t) + I_K(t) + I_L(t) \right)
\]

- \( I_{Na} = g_{Na}(V - E_{Na}) \)
- \( I_K = g_K(V - E_K) \)
- \( I_L = g_L(V - E_L) \)

- \( g_L \) is constant
- \( g_{Na} \) and \( g_K \) are voltage-dependent
Ion channel gates

"n" gates

Membrane

Ion channel
Voltage dependency of gate position

\[ n \rightarrow \alpha_n \rightarrow n - 1 \rightarrow \beta_n \]

- \( n \) (proportion in the open state)
- \( \alpha_n \) and \( \beta_n \) are transition rate constants (voltage-dependent)
- \( \alpha_n \) = the # of times per second that a gate which is in the shut state opens
- \( \beta_n \) = the # of times per second that a gate which is in the open state shuts

Fraction of gates opening per second = \( \alpha_n(1 - n) \)
Fraction of gates shutting per second = \( \beta_n n \)

The rate at which \( n \) changes:

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

Equilibrium:

\[
n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n}
\]

What is the behavior of \( n \)?
Gating variable

\[ \frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n, \quad n(0) = n_0 \]

- Solve initial value problem by separation of variables:

\[
n(t) = \frac{\alpha_n}{\alpha_n + \beta_n} - \left( \frac{\alpha_n}{\alpha_n + \beta_n} - n_0 \right) e^{-(\alpha_n + \beta_n)t} \\
= n_\infty - (n_\infty - n_0) e^{-t/\tau}, \quad \text{where } \tau_n = \frac{1}{\alpha_n + \beta_n}
\]

- If \( \alpha_n \) or \( \beta_n \) is large \( \rightarrow \) time constant is short \( \rightarrow \) \( n \) approaches \( n_\infty \) rapidly
- If \( \alpha_n \) or \( \beta_n \) is small \( \rightarrow \) time constant is long \( \rightarrow \) \( n \) approaches \( n_\infty \) slowly

*time constant*
Gating Variables

- $K^+$ channel is controlled by 4 $n$ activation gates:

\[
\frac{dn}{dt} = \frac{1}{\tau_n} (n_{\infty} - n) \quad \Rightarrow \quad g_K = n^4 g_K
\]

- $Na^+$ channel is controlled by 3 $m$ activation gates and 1 $h$ inactivation gate:

\[
\frac{dm}{dt} = \frac{1}{\tau_m} (m_{\infty} - m)
\]

\[
\frac{dh}{dt} = \frac{1}{\tau_h} (h_{\infty} - h)
\]

- **Activation gate**: open probability increases with depolarization
- **Inactivation gate**: open probability decreases with depolarization
Steady state values
Time constants
Voltage step scenario

Given the voltage step above:

- Sketch $n$ as a function of time. What does $n^4$ look like?
- Sketch $m$ and $h$ on the same graph as functions of time. What does $m^3h$ look like?
How does the Hodgkin-Huxley model predict action potentials?

**Positive Feedback**
(results in *upstroke* of $V$)
- Depolarization
- Fast $\uparrow$ in $m$
- $\text{Na}^+$ inflow
- $\uparrow g_{\text{Na}}$

**Negative Feedback**
(this and leak current repolarizes)
- Depolarization
- Slow $\uparrow$ in $n$
- Repolarization
- $\uparrow g_K$
- $\text{K}^+$ outflow