Single-Compartment Neural Models

BENG/BGGN 260 Neurodynamics

University of California, San Diego

Week 2

B. Hille, Ion Channels of Excitable Membranes, Sinauer, 2001, Ch. 2 and 3, pp. 25-92.

C. Koch, Biophysics of Computation, Oxford Univ. Press, 1999, Ch. 6 through 8, pp. 142-211.


E.M. Izhikevich, Dynamical Systems in Neuroscience, MIT Press, 2007, Ch. 2, pp. 32-49.

Channel Gate Dynamics

The opening rate of the channel gate is given by:

\[
\alpha_n(V_m) 
\]

The closing rate is:

\[
\beta_n(V_m) 
\]

These rate constants are used to describe the fraction of gates closed ("particles") and the fraction of gates open ("particles").

The differential equation for the fraction of gates open is:

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

The steady-state fraction of gates open is:

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

The time constant is:

\[
\tau_n = \frac{1}{\alpha_n + \beta_n}
\]
Voltage Gated Ion Channels

n: slow K⁺ activation; m: fast Na⁺ activation; h: slow Na⁺ inactivation

Figure 5.8 Gating of membrane channels. In both figures, the interior of the neuron is to the right of the membrane, and the extracellular medium is to the left. (A) A cartoon of gating of a persistent conductance. A gate is opened and closed by a sensor that responds to the membrane potential. The channel also has a region that selectively allows ions of a particular type to pass through the channel, for example, K⁺ ions for a potassium channel. (B) A cartoon of the gating of a transient conductance. The activation gate is coupled to a voltage sensor (denoted by a circled +) and acts like the gate in A. A second gate, denoted by the ball, can block that channel once it is open. The top figure shows the channel in a deactivated (and deinactivated) state. The middle panel shows an activated channel, and the bottom panel shows an inactivated channel. Only the middle panel corresponds to an open, ion-conducting state. (A from Hille, 1992; B from Kandel et al., 1991.)

Dayan & Abbot 2001, pg. 169
4 “particles” (gates) model: channel active probability = $n_4$ with:

\[
\begin{align*}
\frac{dn_0}{dt} &= -4\alpha_n n_0 + \beta_n n_1 \\
\frac{dn_1}{dt} &= 4\alpha_n n_0 - (3\alpha_n + \beta_n) n_1 + 2\beta_n n_2 \\
\frac{dn_2}{dt} &= 3\alpha_n n_1 - (2\alpha_n + 2\beta_n) n_2 + 3\beta_n n_3 \\
\frac{dn_3}{dt} &= 2\alpha_n n_2 - (\alpha_n + 3\beta_n) n_3 + 4\beta_n n_4 \\
\frac{dn_4}{dt} &= \alpha_n n_3 - 4\beta_n n_4
\end{align*}
\]
K+ Channel Gate Dynamics: Reduced Model

\[ 4\alpha_n \quad \Rightarrow \quad \frac{3\alpha_n}{2\beta_n} \quad \Rightarrow \quad \frac{2\alpha_n}{3\beta_n} \quad \Rightarrow \quad \frac{\alpha_n}{4\beta_n} \]

- Reduced (equivalent) model: channel active probability = \( n^4 \) with:

\[
\begin{align*}
\frac{dn}{dt} &= \alpha_n (1 - n) - \beta_n n \\
\end{align*}
\]

\[
\begin{align*}
n_0 &= (1 - n)^4 \\
n_1 &= 4n(1 - n)^3 \\
n_2 &= 6n^2(1 - n)^2 \\
n_3 &= 4n^3(1 - n) \\
n_4 &= n^4
\end{align*}
\]
-4 “particles” (gates) model: channel active probability $= s_{31}$

<table>
<thead>
<tr>
<th>State</th>
<th>Equation</th>
<th>Diagram</th>
</tr>
</thead>
<tbody>
<tr>
<td>$s_{01}$</td>
<td>$(1 - m)^3 h$</td>
<td><img src="image" alt="s01 Diagram" /></td>
</tr>
<tr>
<td>$s_{11}$</td>
<td>$3m(1 - m)^2 h$</td>
<td><img src="image" alt="s11 Diagram" /></td>
</tr>
<tr>
<td>$s_{21}$</td>
<td>$3m^2 (1 - m) h$</td>
<td><img src="image" alt="s21 Diagram" /></td>
</tr>
<tr>
<td>$s_{31}$</td>
<td>$m^3 h$</td>
<td><img src="image" alt="s31 Diagram" /></td>
</tr>
</tbody>
</table>

$Koch, \ Ch. 8.2, \ pg. \ 200-202$
Na⁺ Channel Gate Dynamics: Reduced Model

\[
\begin{align*}
s_{01} &= (1 - m)^3 h \\
s_{11} &= 3m (1 - m)^2 h \\
s_{21} &= 3m^2 (1 - m) h \\
s_{31} &= m^3 h
\end{align*}
\]

- Reduced (equivalent) model: channel active probability = \( m^3 h \) with:

**FAST ACTIVATION**

\[
\begin{bmatrix}
1 - m & \alpha_m \\
\beta_m & \bullet
\end{bmatrix}
\]

**SLOW INACTIVATION**

\[
\begin{bmatrix}
1 - h & \alpha_h \\
\beta_h & \triangle
\end{bmatrix}
\]

\[
\begin{cases}
\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m \\
\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h
\end{cases}
\]
HH Activation and Inactivation Functions

- **n**: slow $K^+$ activation
- **m**: fast $Na^+$ activation
- **h**: slow $Na^+$ inactivation

**Figure 2.13**

Steady-state (in)activation functions (left) and voltage-dependent time constants (right) in the Hodgkin-Huxley model.

Izhikevich 2007, pg. 39
Na+ and K+ Conductance Dynamics

Fig. 6.4 K+ and Na+ Conductances During a Voltage Step

Experimentally recorded (circles) and theoretically calculated (smooth curves) changes in $G_{Na}$ and $G_{K}$ in the squid giant axon at 6.3°C during depolarizing voltage steps away from the resting potential (which here, as throughout this chapter, is set to zero). For large voltage changes, $G_{Na}$ briefly increases before it decays back to zero (due to inactivation), while $G_{K}$ remains activated. Reprinted by permission from Hodgkin (1958).

$n$: slow K+ activation; $m$: fast Na+ activation; $h$: slow Na+ inactivation

Koch 1999, pg. 149
Hodgkin-Huxley Model *

Squid axon:

\[
C_m \frac{dV_m}{dt} = I_{\text{ext}} - \left( -\bar{g}_K n^4 (V_m - E_K) - \bar{g}_{Na} m^3 h (V_m - E_{Na}) - g_L (V_m - E_L) \right)
\]
\[
C_m = 1 \mu F/cm^2
\]
\[
E_K = -12 \text{ mV} \quad \bar{g}_K = 36 \text{ mS/cm}^2
\]
\[
E_{Na} = 120 \text{ mV} \quad \bar{g}_{Na} = 120 \text{ mS/cm}^2
\]
\[
E_L = 10.6 \text{ mV} \quad g_L = 0.3 \text{ mS/cm}^2
\]

\[
\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n = \frac{n_{\infty} - n}{\tau_n}; \quad \alpha_n (V_m) = \frac{10 - V_m}{100(e^{1 - V_m/10} - 1)}; \quad \beta_n (V_m) = \frac{1}{8} e^{-V_m/80}
\]
\[
\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m = \frac{m_{\infty} - m}{\tau_m}; \quad \alpha_m (V_m) = \frac{25 - V_m}{100(e^{2.5 - V_m/10} - 1)}; \quad \beta_m (V_m) = 4e^{-V_m/18}
\]
\[
\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h = \frac{h_{\infty} - h}{\tau_h}; \quad \alpha_h (V_m) = \frac{7}{100} e^{-V_m/20}; \quad \beta_h (V_m) = \frac{1}{1 + e^{3 - V_m/10}}
\]

\(\alpha_x\) and \(\beta_x\) in units \(1/\text{ms}\); \(V_m\) in units \(\text{mV}\)

* \(V_m\) slightly shifted by 65\text{mV} so that \(E_{\text{rest}} \equiv 0\text{mV}\)
Hodgkin-Huxley Dynamics

Figure 2.15
Action potential in the Hodgkin-Huxley model.

Izhikevich 2007, pg. 40
From Hodgkin-Huxley to FitzHugh-Nagumo

**Fig. 7.1 Reducing the Hodgkin-Huxley Model to the FitzHugh-Nagumo System**

Evolution of the space-clamped Hodgkin-Huxley and the FitzHugh-Nagumo equations in response to a current step of amplitude 0.18 nA in A and B and of amplitude I=0.35 in C and D. **(A)** Membrane potential $V(t)$ and sodium activation $m(t)$ (see also Fig. 6.8). Sodium activation closely follows the dynamics of the membrane potential. **(B)** Sodium inactivation $1-h$ and potassium activation $n$ of the Hodgkin-Huxley system. **(C)** “Excitability” $V(t)$ of the two-dimensional FitzHugh-Nagumo equations (Eqs. 7.1) with constant parameters has a very similar time course to $V$ and $m$ of the squid axon (notice the different scaling). **(D)** The “accommodation” variable $W$ shows modulations similar to $1-h$ and $n$ of the Hodgkin-Huxley equations.

Koch 1999, pg. 174
FitzHugh-Nagumo Model

Simplification of Hodgkin-Huxley, reduced to 2 dimensions:

**Excitability**: \( \frac{d}{dt} V = V - \frac{V^3}{3} - W + I_{ext} \).

models fast dynamics of \( V_m \) and \( m \) activation

**Accommodation**: \( \frac{d}{dt} W = \phi (V + \alpha - \beta W) \).

models slow dynamics of \( n \) and \( 1 - h \) inactivation

\( \phi = 0.08 \quad \alpha = 0.7 \quad \beta = 0.8 \)

Facilitates theoretical analysis of stability & dynamics, at the expense of accuracy.
Barnacle muscle fibers:

\[ C_m \frac{dV_m}{dt} = I_{\text{ext}} - \bar{g}_K w (V_m - E_K) - \frac{I_K}{I_K} - \bar{g}_C m_\infty (V_m - E_Ca) - g_L (V_m - E_{\text{rest}}) \]

\[ C_m = 1 \mu F/cm^2 \]

\[ I_K = 2.0 \text{ mS/cm}^2 \]  \[ E_K = -70\text{ mV} \]  \[ \bar{g}_K = 2.0 \text{ mS/cm}^2 \]

\[ I_Ca = 1.1 \text{ mS/cm}^2 \]  \[ E_{Ca} = 100\text{ mV} \]  \[ \bar{g}_{Ca} = 1.1 \text{ mS/cm}^2 \]

\[ g_L = 0.5 \text{ mS/cm}^2 \]  \[ E_{\text{rest}} = -50\text{ mV} \]

\[ \tau_w (V_m) \frac{dw}{dt} = w_\infty (V_m) - w; \]

\[ w_\infty (V_m) = \frac{1}{2} \left( 1 + \tanh \frac{V_m}{30} \right) \]

\[ m_\infty (V_m) = \frac{1}{2} \left( 1 + \tanh \frac{V_m + 1}{15} \right) \]

The simplifying assumption \( \tau_m \ll \tau_w \) leads to a 2-D dynamical model, like Fitzhugh-Nagumo.
(A) Random opening and closing of a handful of fast sodium channels in a mouse muscle cell. The membrane potential was stepped from $-80$ to $-40$ mV; the first trial reveals the simultaneous opening of two Na$^+$ channels, while on all other trials, only a single channel was open. (B) Averaging over 352 such trials leads to a smoothly varying current in accordance with the $m^3h$ model of Hodgkin and Huxley. Experiment carried out at 15°C. Reprinted by permission from Patlak and Ortiz (1986).
Individual Channels and Stochastic Conductance

**Fig. 8.7 Simulated Life History of Individual Sodium Channels**

The membrane potential in a simulated membrane patch containing a variable number of Na$^+$ channels was stepped from $V_0 = 0$ to $V_1 = 50$ mV at 5 msec (arrow). The normalized conductance associated with the eight-state Markov model shown in Fig. 8.5 was evaluated numerically for several trial runs (see Strassberg and DeFelice, 1993). As the number of channels is increased from 6 to 600, the graded and deterministic nature of the (normalized) sodium conductance emerges from the binary and stochastic single-channel behavior. The top trace shows the conductance computed using the continuous time-course (approximating $(1 - e^{-t/\tau_m})^3 e^{-t/\tau_h}$) formalism of Hodgkin and Huxley (1952). This figure should be compared against the experimentally recorded sodium current through a few channels in Fig. 8.6B. Reprinted in modified form by permission from Strassberg and DeFelice (1993).

Computed membrane potential (relative to $V_{\text{rest}}$ indicated by horizontal lines) in different size patches of squid axon membrane populated by a constant density of Na+ and K+ channels. The space-clamped membrane is responding to a current injection of 100 $\text{pA}/\mu\text{m}^2$. The transitions of each all-or-none channel are described by its own probabilistic Markov model (the eight-state model in Fig. 8.5 for the Na+ channel and the simplest possible five-state linear model for the K+ channel). For patches containing dozens or fewer channels it becomes impossible to define action potentials unambiguously, since the opening of one or two channels can rapidly depolarize the membrane (not shown). As the membrane potential acts on 1000 or more binary and stochastic channels, the response becomes quite predictable, and merges into the behavior expected by a numerical integration of the Hodgkin-Huxley equations for continuous and deterministic currents (top trace). The density is set to 60 Na+ channels and 18 K+ channels per square micrometer, each with a single channel conductance $\gamma$ of 20 pS. All other values are as specified in the standard Hodgkin-Huxley model. Reprinted in modified form by permission from Strassberg and DeFelice (1993).

- Shot noise in action potentials due to stochastic individual channels
- Spontaneous, Poisson distributed action potentials even without input (Fig. 8.9, pg. 208)

Koch 1999, pg. 207