Model Neurons: Neuroelectronics
(Part II)


- Spike rate adaptation.
- Voltage-dependent conductances.
- Hodgkin-Huxley model.
- Synaptic conductances.

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Spike Rate Adaptation

- Gradual slowing of firing is called spike rate adaptation.
- Can be modeled as a $K^+$ conductance.

\[
\tau_m \frac{dV}{dt} = E_L - V - \tau_m g_{sra}(V - E_K) + R_m I_e, \text{ where} \\
\tau_{sra} \frac{dg_{sra}}{dt} = -g_{sra}.
\]

In addition, when a spike occurs,

\[
g_{sra} \rightarrow g_{sra} + \Delta g_{sra}.
\]

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Refractory Period

- During the refractory period immediately following firing, it is very hard (relative refractory period) or impossible to fire no matter what the input is (absolute refractory period).
- Refractory periods can be modeled as SRA conductance in the previous page, or $V_{th}$ can be momentarily increased and decayed.

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Voltage-Dependent Conductances

- Single channel opening/closing is stochastic.
- Probability of channel opening/closing depends on
  - Membrane potential, presence/absence of neurotransmitters, $Ca^{2+}$ concentration, etc.
- Conductance per unit area $g_i$ is determined by:

\[
g_i = \left[ \frac{\text{channel conductance} \times \text{channel density} \times \text{fraction open}}{\text{max conductance} g_i P_i} \right]
\]

Thus, we get

\[
g_i = \bar{g}_i P_i.
\]

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**Ion Channel Structure**

- Ion channels consist of several subunits.
- The vertical columns surrounding the pore correspond to one subunit.
- One subunit consists of several $\alpha$ helices.
- The structure of the subunits change depending on different electrochemical conditions.

**Persistent Voltage-Dependent Conductances**

- Channels activate (opening the gate) and deactivate (closing the gate).
- Delayed rectifier $\text{K}^+$ currents (that repolarize after a spike) have such persistent conductance.
- $P_K$ (prob. of $\text{K}^+$ channels opening) increases with high membrane potential and decreases with low membrane potential.
- This probability depends on structural changes in four identical subunits, each with probability $n$. So, we get:
  \[ P_K = n^k, \]
  with $k = 4$.

**Persistent Conductance: Subunit activation $n$**

- The subunit activation probability $n$ is time-varying:
  \[
  \frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n, \tag{1}
  \]
  where $\alpha_n(V)$ and $\beta_n(V)$ are the voltage-dependent opening/closing rate. To open, the subunit needs to be in a closed state thus $1 - n$ is multiplied, and similarly in order to close $n$ is multiplied.
- Letting $\frac{dn}{dt} = 0$, the steady state valued of $n$ is:
  \[
  \alpha_n(V)(1 - n) - \beta_n(V)n = 0,
  \]
  and solving for $n$, we get:
  \[
  n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}.
  \]
Persistent Conductance: Subunit activation

- Based on energy requirement argument for moving a charge, we get:
  \[ \alpha_n(V) = A_\alpha \exp(-qB_\alpha/k_BT) = A_\alpha \exp(-B_\alpha V/V_T) \]
  \[ \beta_n(V) = A_\beta \exp(-qB_\beta/k_BT) = A_\beta \exp(-B_\beta V/V_T) \]

- Plugging the above into:
  \[ n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)} , \]
  we get
  \[ n_\infty(V) = \frac{1}{1 + (A_\beta/A_\alpha) \exp((B_\alpha - B_\beta) V/V_T)} . \]

This is basically a sigmoid function: \( g(x) = \frac{1}{1 + a \exp(-b x)} \), since \( \alpha_n(V) \) is an increasing function \( (B_\alpha < 0) \) and \( \beta_n(V) \) is a decreasing function \( (B_\beta > 0) \).

Comparison of Energy-Requirement-Based vs. HH

- Hodgkin and Huxley empirically estimated \( \alpha_n \) and \( \beta_n \) as:
  \[ \alpha_n(V) = \frac{0.01(V + 55)}{1 - \exp(-0.1(V + 55))} \]
  \[ \beta_n(V) = 0.125 \exp(-0.0125(V + 65)) \]

- There is a close fit between HH and the energy-based derivation in the previous pages.

The Hodgkin-Huxley Model

- Single compartment model:
  \[ c_m \frac{dV}{dt} = -i_m + I_e / A \]

- Hodgkin-Huxley model's membrane currents:
  \[ i_m = g_L(V-E_L) + g_K n^4 (V-E_K) + g_Na m^3 h (V-E_{Na}) . \]

Transient Voltage-Dependent Conductances

- Na\(^+\) channels are transient, i.e., they activate and quickly inactivate. Modeling activation with probability \( m \) and inactivation with probability \( (1 - h) \), we get:
  \[ P_{Na} = m^k h , \]
  where \( k = 3 \) is a parameter.

- \( m, h, m_\infty(V), h_\infty(V), \tau_m(V), \) and \( \tau_h(V) \) are defined similar to corresponding terms for \( n \).
The Hodgkin-Huxley Model: Simulation

- m: Na\(^+\) activation probability (depolarization)
- h: Na\(^+\) non-inactivating probability (transient)
- n: K\(^+\) activation probability (delayed rectifier)

Synaptic Conductances

- Action potential reaching axon terminal opens voltage-gated Ca\(^{2+}\) channels, triggering transmitter release.
- Transmitters bind and open postsynaptic ion channels.
  - Direct opening of ion channels: ionotropic
  - Indirect modulation plus ion channel opening: metabotropic

Table: Neurotransmitters by channel type

<table>
<thead>
<tr>
<th>Type</th>
<th>Excitatory</th>
<th>Inhibitory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ionotropic</td>
<td>AMPA</td>
<td>GABA(_A)</td>
</tr>
<tr>
<td>Metabotropic</td>
<td>NMDA</td>
<td>GABA(_B)</td>
</tr>
</tbody>
</table>

Postsynaptic Conductances

- Postsynaptic conductance:
  \[ g_s = \bar{g}_s P, \text{ where } P = P_s P_{\text{rel}}, \]
  where \( P_s \) is the synaptic open probability and \( P_{\text{rel}} \) the transmitter release probability.

- Time-evolution is similar to voltage-dependent channels:
  \[ \frac{dP_s}{dt} = \alpha_s (1 - P_s) - \beta_s P_s, \]
  where open rate \( \alpha_s \) is modulated by neurotransmitter concentration, and close rate \( \beta_s \) is a constant.

Starting from:

- Neurotransmitter concentration is usually modeled as a step function, between \( t = 0 \) to \( t = T \).
  - During this, \( \alpha_s \gg \beta_s \), so we can ignore the second term in the equation above. Integrating the rest:
    \[ P_s(t) = 1 + (P_s(0) - 1) \exp(-\alpha_s t) \text{ for } 0 \leq t \leq T. \]

  - After \( t = T \), \( \alpha_s \ll \beta_s \), so we can ignore the first term. Integrating the rest:
    \[ P_s(t) = P_s(T) \exp(-\beta_s (t - T)) \text{ for } t \geq T. \]
**Postsynaptic Conductances: Data vs. Fit**

- The rising phase dominated by $\alpha_s$ is very rapid.
- The falling phase dominated by $\beta_s$ is relatively slower.
- For such fast rising PSPs, $P_s$ can be modulated with only $\beta_s$ (instantaneous rise):
  \[
  P_s = P_{\text{max}} \exp\left(-\frac{t}{\tau_s}\right),
  \]
  where $\tau_s = \frac{1}{\beta_s}$. (Same as the last eq. in previous page.)

**Fast Postsynaptic Conductances: Time evolution**

- The differential equation version of
  \[
  P_s = P_{\text{max}} \exp\left(-\frac{t}{\tau_s}\right)
  \]
  is simply
  \[
  \tau_s \frac{dP_s}{dt} = -P_s,
  \]
  and after each presynaptic action potential,
  \[
  P_s \rightarrow P_s + P_{\text{max}}(1 - P_s).
  \]

**Slow Postsynaptic Conductances**

- Typically modeled as:
  \[
  P_s = P_{\text{max}} B(\exp(-t/\tau_1) - \exp(-t/\tau_2)),
  \]
  where $\tau_1 > \tau_2$, and
  \[
  B = \left(\left(\frac{\tau_2}{\tau_1}\right)^{\text{rise}/\tau_1} - \left(\frac{\tau_2}{\tau_1}\right)^{\text{rise}/\tau_2}\right)^{-1},
  \]
  where $\tau_{\text{rise}} = \tau_1 \tau_2/(\tau_1 - \tau_2)$.

**Alpha Function**

- Another way to express $P_s$ is:
  \[
  P_s = \frac{P_{\text{max}} t}{\tau_s} \exp\left(1 - \frac{t}{\tau_s}\right),
  \]
  which is called the “alpha function”.

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Synapses on INF Neurons

- The original INF without synaptic conductance is:
  \[ \tau_m \frac{dV}{dt} = E_L - V + R_m I_e. \]

- Synaptic conductances can be added to the INF model as follows:
  \[ \tau_m \frac{dV}{dt} = E_L - V - \tau_m \bar{g}_s P_s (V - E_s) + R_m I_e. \]