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,

$$g_{sra} \rightarrow g_{sra} + \Delta g_{sra}.$$  

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.

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:

$$g_i = \text{channel conductance} \times \text{channel density} \times \text{fraction open} \times \text{max conductance} \times \frac{g_i}{\bar{g}_i} \times P_i.$$  

Thus, we get

$$g_i = \bar{g}_i P_i.$$
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 \( K^+ \) currents (that repolarize after a spike) have such persistent conductance.
- \( P_K \) (prob. of \( K^+ \) 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:
  \[
  \frac{dn}{dt} = \alpha_n(V)(1 - n) - \beta_n(V)n,
  \]
  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:

\[
\alpha_n(V) = A_\alpha \exp\left(-qB_\alpha/k_B T\right) = A_\alpha \exp\left(-B_\alpha V/V_T\right)
\]

\[
\beta_n(V) = A_\beta \exp\left(-qB_\beta/k_B T\right) = A_\beta \exp\left(-B_\beta V/V_T\right)
\]

- Plugging the above into:

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

we get

\[
n_\infty(V) = \frac{1}{1 + (A_\beta/A_\alpha) \exp\left((B_\alpha - B_\beta) V/V_T\right)}.
\]

This is basically a sigmoid function: 

\[
g(x) = \frac{1}{1+a \exp(-bx)},
\]

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:

\[
\alpha_n(V) = \frac{0.01(V + 55)}{1 - \exp(-0.1(V + 55))}
\]

and

\[
\beta_n(V) = 0.125 \exp(-0.0125(V + 65))
\]

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

**Transient Voltage-Dependent Conductances**

- \(\text{Na}^+\) channels are transient, i.e., they activate and quickly inactivate. Modeling activation with probability \(m\) and inactivation with probability \((1 - h)\), we get:

\[
P_{\text{Na}} = m^k h,
\]

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**

- Single compartment model:

\[
c_m \frac{dV}{dt} = -i_m + \frac{I_e}{A}
\]

- Hodgkin-Huxley model’s membrane currents:

\[
i_m = \bar{g}_L(V - E_L) + \bar{g}_K n^4 (V - E_K) + \bar{g}_\text{Na} m^3 h (V - E_{\text{Na}}).
\]

- \(\bar{g}_K = g_K P_K\)

- \(\bar{g}_\text{Na} = g_{\text{Na}} P_{\text{Na}}\)
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>
<thead>
<tr>
<th>Table: Neurotransmitters by channel type</th>
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<tbody>
<tr>
<td>Type</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>Ionotropic</td>
</tr>
<tr>
<td>Metabotropic</td>
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</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.

Postsynaptic Conductances

Starting from:

\[ \frac{dP_s}{dt} = \alpha_s (1 - P_s) - \beta_s P_s, \]

- 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):

$$P_s = P_{\text{max}} \exp(-t/\tau_s),$$

where $\tau_s = 1/\beta_s$. (Same as the last eq. in previous page.)

Fast Postsynaptic Conductances: Time evolution

- The differential equation version of $P_s = P_{\text{max}} \exp(-t/\tau_s)$ 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

$$B = \left( \frac{\tau_2}{\tau_1} \right)^{\tau_{\text{rise}}/\tau_1} - \left( \frac{\tau_2}{\tau_1} \right)^{\tau_{\text{rise}}/\tau_2} \right)^{-1},$$

where $\tau_{\text{rise}} = \tau_1 \tau_2 / (\tau_1 - \tau_2)$.

Alpha Function

- Another way to express $P_s$ is:

$$P_s = \frac{P_{\text{max}} t}{\tau_s} \exp(1 - t/\tau_s),$$

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:
  \[ \tau_m \frac{dV}{dt} = E_L - V - r_m g_s P_s (V - E_s) + R_m I_e. \]