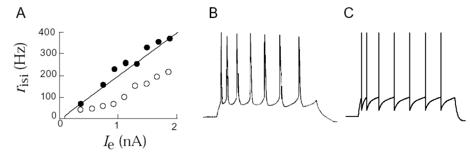
Model Neurons: Neuroelectronics (Part II)

Dayan and Abbott (2001) Chapter 5 and Appendix A.4.

- Spike rate adaptaion.
- Voltage-dependent conductances.
- Hodgkin-Huxley model.
- Synaptic coductances.

Instructor: Yoonsuck Choe; CPSC 644 Cortical Networks

Spike Rate Adaptation



- Gradual slowing of firing is called spike rate adaptaion.
- Can be modeled as a K^{+} conductance.

$$\tau_{\mathrm{m}} \frac{dV}{dt} = E_{\mathrm{L}} - V - r_{\mathrm{m}} g_{\mathrm{sra}} (V - E_{\mathrm{K}}) + R_{\mathrm{m}} I_{\mathrm{e}}, \text{ where}$$

$$\tau_{\mathrm{sra}} \frac{dg_{\mathrm{sra}}}{dt} = -g_{\mathrm{sra}}.$$

In addition, when a spike occurrs,

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

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

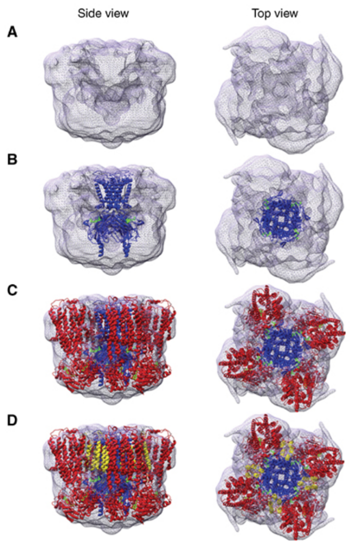
- Single channel opening/closing is stochastic.
- Probability of channel opening/closing depends on
  - Membrane potential, presence/absence of neurotransmitters, Ca^{2+} concentration, etc.
- Conductance per unit area g_i is determined by:

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

Thus, we get

$$g_i = \bar{g}_i P_i.$$

Ion Channel Structure



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

Mikhailov et al. (2005) *The EMBO Journal* 24:4166–4175

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:

$$P_{\mathrm{K}} = n^k,$$

with $k = 4$.

Persistent Conductance: Subunit activation n

- The subunit activation probability n is time-varying:

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n, \qquad (1)$$

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 $dn/dt = 0$, 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 n

- Dividing

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n,$$

with $\alpha_n(V) + \beta_n(V)$, we get:

$$\frac{1}{\alpha_n(V)+\beta_n(V)}\frac{dn}{dt} = n_\infty(V) - n.$$

Let $\tau_n(V) = 1/(\alpha_n(V)+\beta_n(V))$, we finally arrive at:

$$\tau_n(V)\frac{dn}{dt} = n_\infty(V) - n.$$

Persistent Conductance: Subunit activation n

- Based on energy requirement argument for moving a charge, we get:

$$\alpha_n(V) = A_\alpha \exp(-qB_\alpha/k_\mathrm{b}T) = A_\alpha \exp(-B_\alpha V/V_T)$$

$$\beta_n(V) = A_\beta \exp(-qB_\beta/k_\mathrm{b}T) = A_\beta \exp(-B_\beta V/V_T)$$

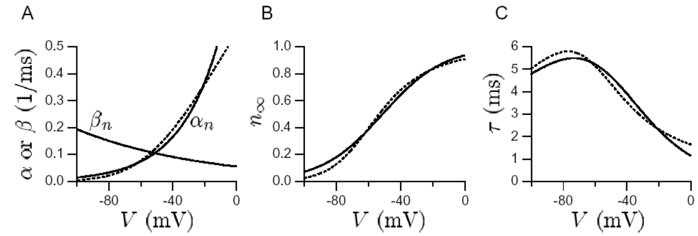
- Plugging the above into:

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}, \text{ we get}$$

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

This is basically a sigmoid function: $g(x) = \frac{1}{1+a\,\exp(-bx)}$, 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



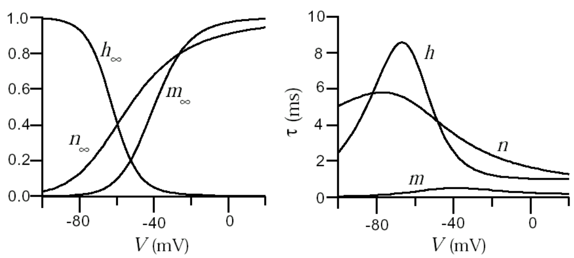
- Hodgkin and Huxley empirically estimated α_n and β_n as:

$$\alpha_n(V) = \frac{0.01(V+55)}{1 - \exp(-.1(V+55))} \quad \text{and}$$

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

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

Transient Voltage-Dependent Conductances



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

$$P_\mathrm{Na} = m^k h,$$

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

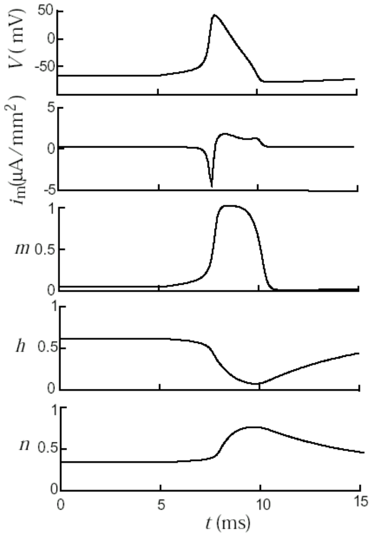
- Single compartment model:

$$c_\mathrm{m}\frac{dV}{dt} = -i_\mathrm{m} + \frac{I_\mathrm{e}}{A}$$

- Hodgkin-Huxley model's membrane currents:

$$i_\mathrm{m} = \bar{g}_\mathrm{L}(V - E_\mathrm{L}) + \underbrace{\bar{g}_\mathrm{K} n^4}_{g_\mathrm{K} = \bar{g}_\mathrm{K} P_\mathrm{K}}(V - E_\mathrm{K}) + \underbrace{\bar{g}_\mathrm{Na} m^3 h}_{g_\mathrm{Na} = \bar{g}_\mathrm{Na} P_\mathrm{Na}}(V - E_\mathrm{Na}).$$

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: Neurotransmitters by channel type

Type	Excitatory	Inhibitory
Ionotropic	AMPA	$GABA_{A}$
Metabotropic	NMDA	$GABA_{B}$

Postsynaptic Conductances

- Postsynaptic conductance:

$$g_{s} = \bar{g}_{s} P, \text{ where}$$

$$P = P_{s} P_{rel},$$

where P_{s} is the synaptic open probability and P_{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 α_{s} is modulated by neurotransmitter concentration, and close rate β_{s} is a constant.

Postsynaptic Conductances

Starting from:

$$\frac{dP_{s}}{dt} = \alpha_{s}(1 - P_{s}) - \beta_{s} P_{s},$$

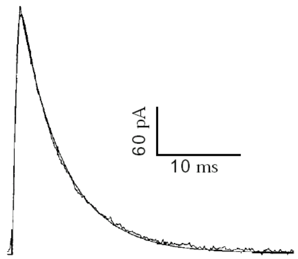
- Neurotransmitter concentration is usually modeled as a step function, between $t = 0$ to $t = T$.
  - During this, $\alpha_{s} >> \beta_{s}$, so we can ignore the second term in the equation above. Integrating the rest:

$$P_{s}(t) = 1 + (P_{s}(0) - 1)\exp(-\alpha_{s} t) \text{ for } 0 \leq t \leq T.$$

  - After $t = T$, $\alpha_{s} << \beta_{s}$, 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 α_{s} is very rapid.
- The falling phase dominated by β_{s} is relatively slower.
- For such fast rising PSPs, P_{s} can be modulated with only β_{s} (instantaneous rise):

$$P_{\mathrm{s}} = P_{\max} \exp(-t/\tau_{\mathrm{s}}),$$

where $\tau_{\mathrm{s}} = 1/\beta_{\mathrm{s}}$. (Same as the last eq. in previous page.)

Fast Postsynaptic Conductances: Time evolution

- The differential equation version of

$$P_{\mathrm{s}} = P_{\max} \exp(-t/\tau_{\mathrm{s}})$$

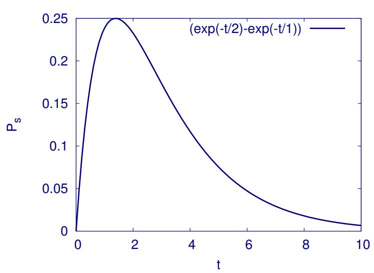
is simply

$$\tau_s \frac{dP_{\mathrm{s}}}{dt} = -P_{\mathrm{s}},$$

and after each presynaptic action potential,

$$P_{\mathrm{s}} \rightarrow P_{\mathrm{s}} + P_{\max}(1 - P_{\mathrm{s}}).$$

Slow Postsynaptic Conductances



- Typically modeled as:

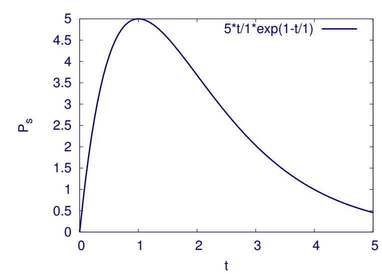
$$P_{\mathrm{s}} = P_{\max} B(\exp(-t/\tau_1) - \exp(-t/\tau_2)),$$

where $\tau_1 > \tau_2$, and

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

where $\tau_{\mathrm{rise}} = \tau_1 \tau_2 / (\tau_1 - \tau 2)$.

Alpha Function



- Another way to express P_{s} is:

$$P_{\mathrm{s}} = \frac{P_{\max} t}{\tau_{\mathrm{s}}} \exp(1 - t/\tau_s),$$

which is called the “alpha function”.

Synapses on INF Neurons

- The original INF without synaptic conductance is:

$$\tau_{\mathrm{m}} \frac{dV}{dt} = E_{\mathrm{L}} - V + R_{\mathrm{m}} I_{\mathrm{e}}.$$

- Synaptic conductances can be added to the INF model as follows:

$$\tau_{\mathrm{m}} \frac{dV}{dt} = E_{\mathrm{L}} - V - r_{\mathrm{m}} \bar{g}_{\mathrm{s}} P_{\mathrm{s}} (V - E_{\mathrm{s}}) + R_{\mathrm{m}} I_{\mathrm{e}}.$$