

Model Neurons: Neuroelectronics

(Part II)

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

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

Instructor: Yoonsuck Choe; CPSC 644 Cortical Networks

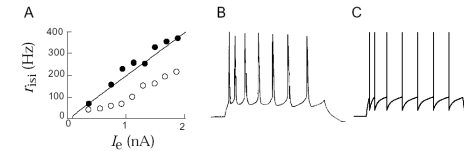
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Refractory Period

- 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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Spike Rate Adaptation



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

$$\tau_m \frac{dV}{dt} = E_L - V - r_m g_{sra} (V - E_K) + R_m I_e, \text{ where}$$

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

In addition, when a spike occurs,

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

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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:

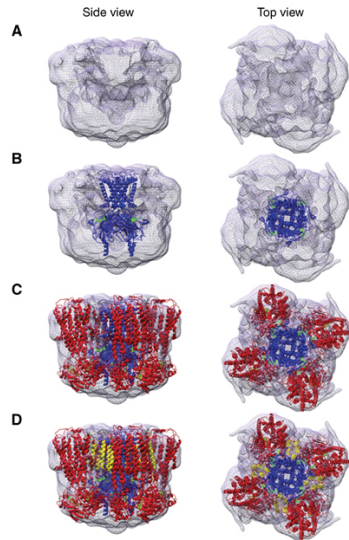
$$g_i = \underbrace{\text{channel conductance} \times \text{channel density}}_{\text{max conductance } \bar{g}_i} \times \underbrace{\text{fraction open}}_{P_i}$$

Thus, we get

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

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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 α helices.
- The structure of the subunits changes depending on different electrochemical conditions.

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

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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 $k = 4$.

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Persistent Conductance: Subunit activation n

- The subunit activation probability n is time-varying:

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

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 value of n is:

$$\alpha_n(V)(1 - n) - \beta_n(V)n = 0,$$

and solving for n , we get:

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}.$$

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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:

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

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Persistent Conductance: Subunit activation n

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

$$\alpha_n(V) = A_\alpha \exp(-qB_\alpha/k_bT) = A_\alpha \exp(-B_\alpha V/V_T)$$

$$\beta_n(V) = A_\beta \exp(-qB_\beta/k_bT) = A_\beta \exp(-B_\beta V/V_T)$$

- Plugging the above into:

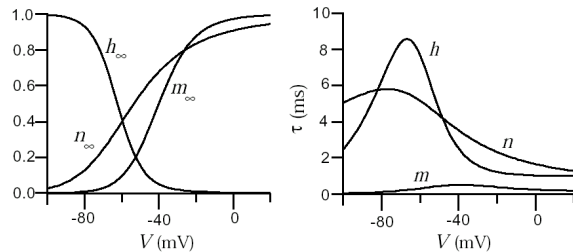
$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}, \text{ we get}$$

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

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 ($B_\beta > 0$).

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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:

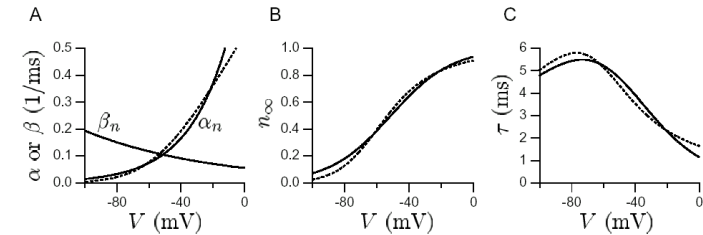
$$P_{\text{Na}} = m^k h,$$

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 .

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Comparison of Energy-Requirement-Based vs. HH



- Hodgkin and Huxley empirically estimated α_n and β_n as:

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

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

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

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The Hodgkin-Huxley Model

- Single compartment model:

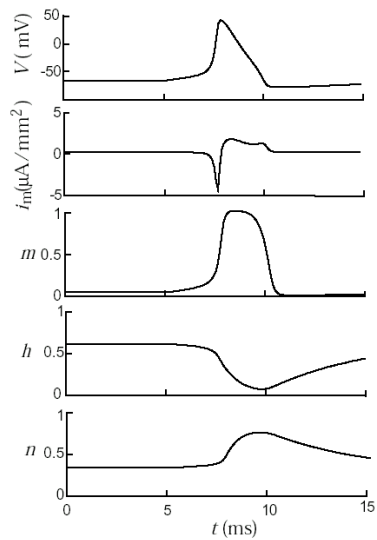
$$c_m \frac{dV}{dt} = -i_m + \frac{I_e}{A}$$

- Hodgkin-Huxley model's membrane currents:

$$i_m = \bar{g}_L(V - E_L) + \underbrace{\bar{g}_K n^4}_{g_K = \bar{g}_K P_K} (V - E_K) + \underbrace{\bar{g}_{\text{Na}} m^3 h}_{g_{\text{Na}} = \bar{g}_{\text{Na}} P_{\text{Na}}} (V - E_{\text{Na}}).$$

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The Hodgkin-Huxley Model: Simulation



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

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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_{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.

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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

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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:

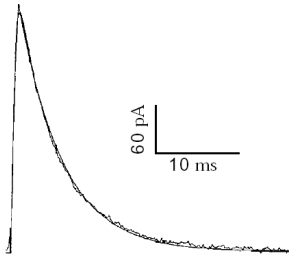
$$P_s(t) = 1 + (P_s(0) - 1) \exp(-\alpha_s t) \text{ for } 0 \leq t \leq T.$$

- After $t = T$, $\alpha_s \ll \beta_s$, so we can ignore the first term. Integrating the rest:

$$P_s(t) = P_s(T) \exp(-\beta_s(t - T)) \text{ for } t \geq T.$$

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Postsynaptic Conductances: Data vs. Fit



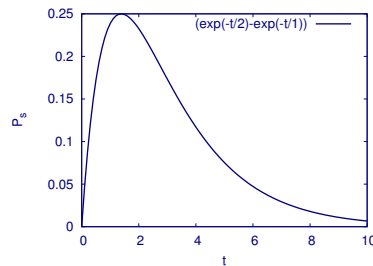
- The rising phase dominated by α_s is very rapid.
- The falling phase dominated by β_s is relatively slower.
- For such fast rising PSPs, P_s can be modulated with only β_s (instantaneous rise):

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

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

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Slow Postsynaptic Conductances



- Typically modeled as:

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

where $\tau_1 > \tau_2$, and

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

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

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Fast Postsynaptic Conductances: Time evolution

- The differential equation version of

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

is simply

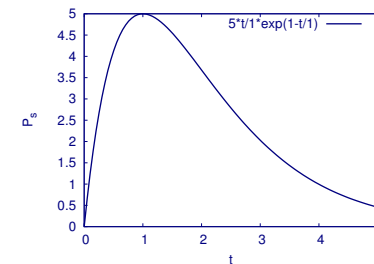
$$\tau_s \frac{dP_s}{dt} = -P_s,$$

and after each presynaptic action potential,

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

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Alpha Function



- Another way to express P_s is:

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

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:

$$\tau_m \frac{dV}{dt} = E_L - V - r_m \bar{g}_s P_s (V - E_s) + R_m I_e.$$