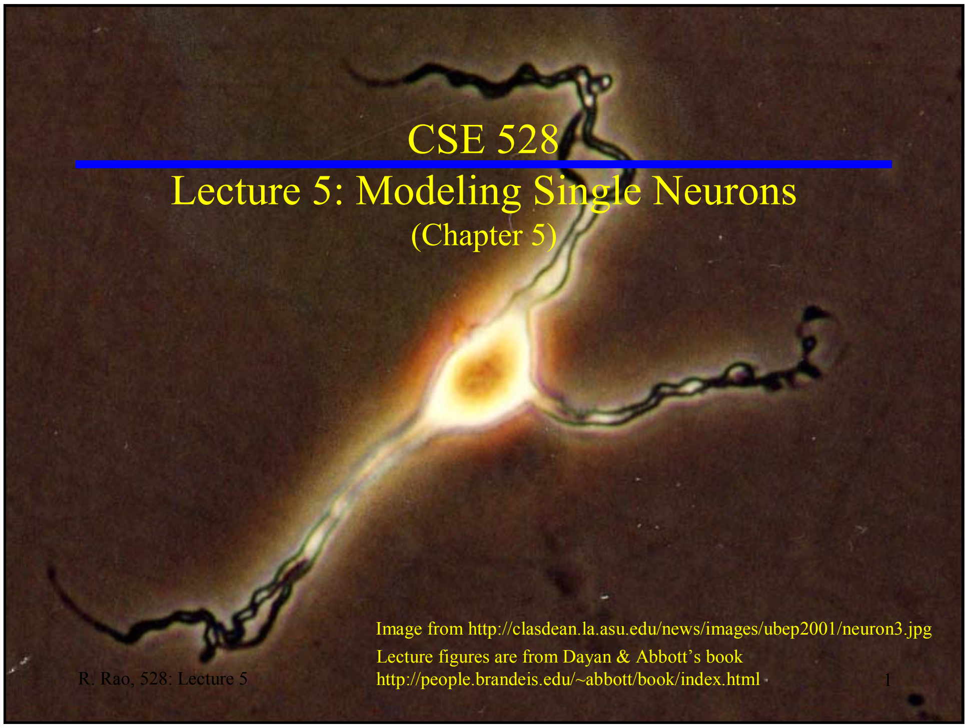
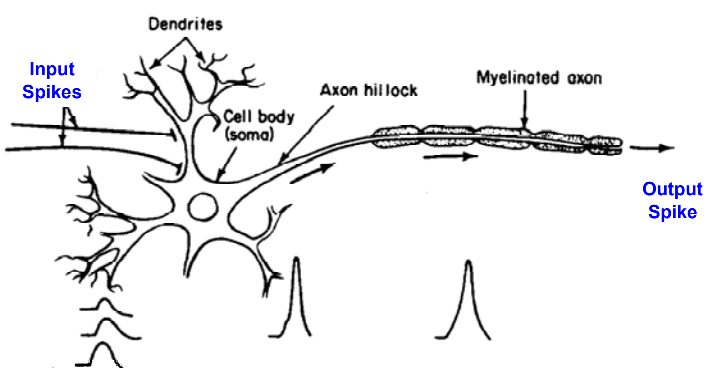


The Problem: Simulating Neurons

Goal: Model the transformation from input to output spikes



Sub-Problems and Solutions

- Model how the membrane potential changes with inputs
  - ➩ Passive "RC" membrane model
- Model the entire neuron as one component
  - ➩ Integrate-and-Fire Model
- Model the effects of inputs from synapses
- Model active membranes
  - ➩ Hodgkin-Huxley model
- Model the structure of neurons
  - ➩ Dendrites, cell body, axon
- Chapters 5 & 6 in text

} Conductance-based Compartmental Models (next class)

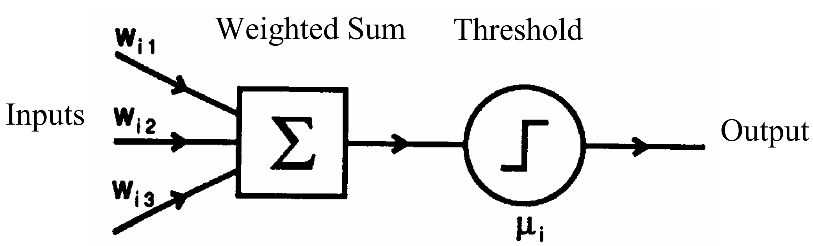
Today's Agenda

- Single Neuron Models
  1. Just the bare essentials: Connectionist Model
  2. Modeling membranes: The RC model
  3. Keeping it simple: 1-Compartment Model
  4. Producing spikes: Integrate-and-Fire Model
  5. Modeling inputs: Synapse models
  6. Example applications
- Next time: Active membranes and multi-compartment models
  1. Modeling spike generation: Hodgkin-Huxley Model
  2. Modeling it all (almost): Multi-Compartment Models

Connectionist Model of a Neuron

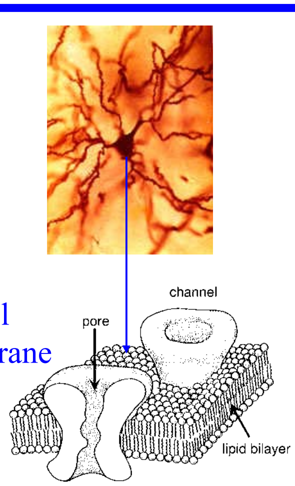
- Attributes of artificial neuron:
  - m binary inputs and 1 output (0 or 1)
  - Synaptic weights w_{ij}
  - Threshold μ_i

$$out_i = \begin{cases} 1 & \text{if } \sum_j w_{ij} in_j \geq \mu_i \\ 0 & \text{otherwise} \end{cases}$$



A Closer Look at a Neuron

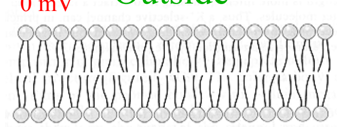
Cell Membrane



$[Na^+]$, $[Cl^-]$, $[Ca^{2+}]$

$[K^+]$, $[A^-]$

0 mV Outside



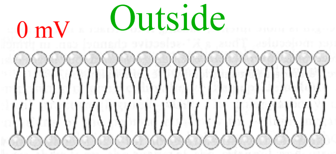
-70 mV Inside

$[K^+]$, $[A^-]$

$[Na^+]$, $[Cl^-]$, $[Ca^{2+}]$

Equilibrium Potential of Ions (Nernst Equation)

$[Na^+]$, $[Cl^-]$, $[Ca^{2+}]$
$[K^+]$, $[A^-]$



$[K^+]$, $[A^-]$
$[Na^+]$, $[Cl^-]$, $[Ca^{2+}]$

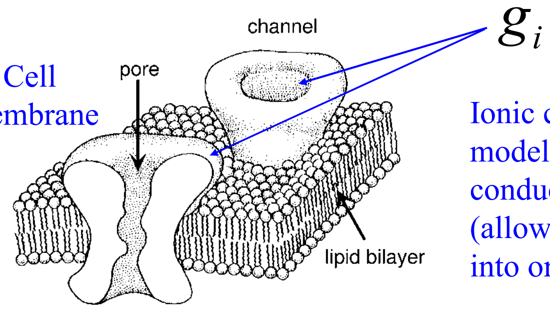
E = Membrane potential at which current flow due to diffusion of ions is balanced by electric forces

$$E = \frac{RT}{zF} \ln\left(\frac{[outside]}{[inside]}\right)$$

(T = temp, R & F = constants, z = valence of ion)
e.g. E_{Na} = 50 mV, E_K = -80 mV

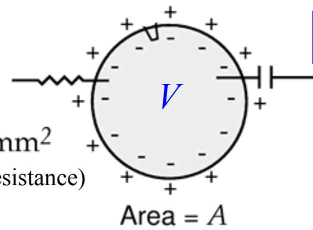
Ionic Channels = Conductances

Cell Membrane



Ionic channels are modeled as conductances g_i (allow current to flow into or out of cell)

Modeling Neural Membranes



$Q = C_m V$

$R_m = r_m / A$

$r_m \approx 1 \text{ M}\Omega \text{ mm}^2$

(specific membrane resistance)

$C_m = c_m A$

$c_m \approx 10 \text{ nF/mm}^2$

(specific membrane capacitance)

$$c_m \frac{dV}{dt} = \frac{dQ}{dt} = -i_m$$

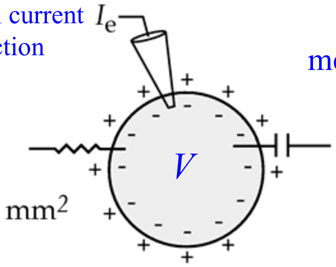
Membrane Current due to Ions
("Leak Current")

$$i_m = \sum_i g_i (V - E_i) = \bar{g}_L (V - E_L) = \frac{(V - E_L)}{r_m}$$

Leak conductance

Summary of 1-Compartment Membrane Model

External current I_e injection



$\tau_m = r_m c_m =$ membrane time constant

$R_m = r_m / A$

$r_m \approx 1 \text{ M}\Omega \text{ mm}^2$

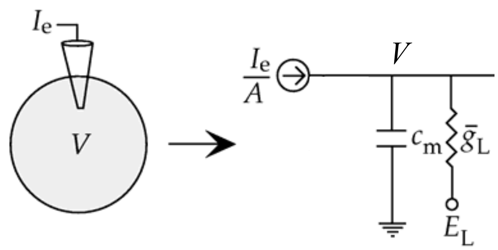
$C_m = c_m A$

$c_m \approx 10 \text{ nF/mm}^2$

$$c_m \frac{dV}{dt} = -\frac{(V - E_L)}{r_m} + \frac{I_e}{A}, \text{ or equivalently}$$

$$\tau_m \frac{dV}{dt} = -(V - E_L) + I_e R_m$$

Producing Spikes: Integrate-and-Fire Model



$$\tau_m \frac{dV}{dt} = -(V - E_L) + I_e R_m$$

If V > $V_{threshold}$ → Spike

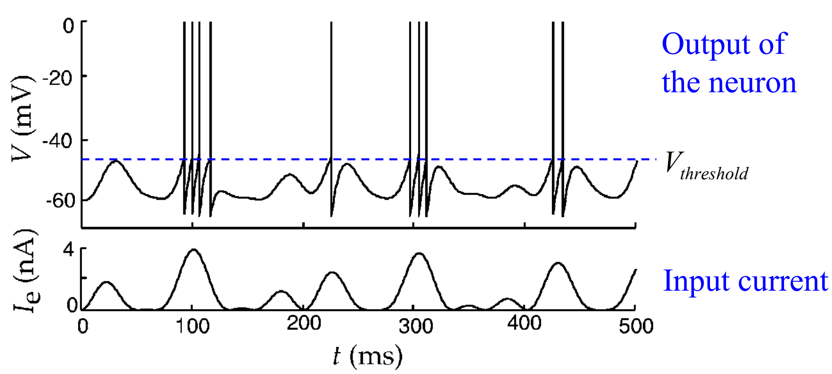
Then reset: V = V_{reset}

$E_L \approx -70$ mV (resting potential)

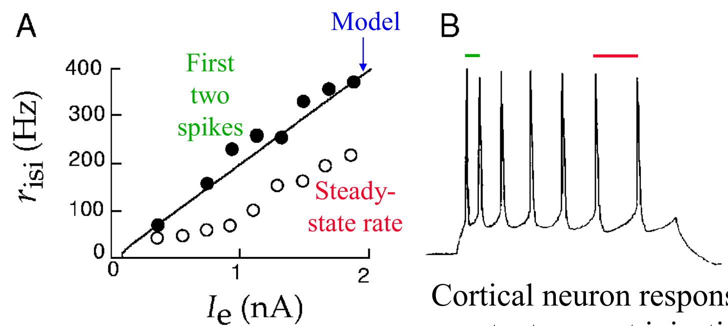
$V_{threshold} \approx -50$ mV

$V_{reset} \approx E_L$

The Integrate-and-Fire Model in Action



Comparison of I & F Model to Data



Cortical neuron response to constant current injection

Real neuron exhibits spike-rate adaptation and refractoriness

Making the I & F model more realistic

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

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

Spike-rate adaptation

If $V > V_{threshold}$ →
Spike and set $g_{sra} = g_{sra} + \Delta g_{sra}$
Reset: $V = V_{reset}$

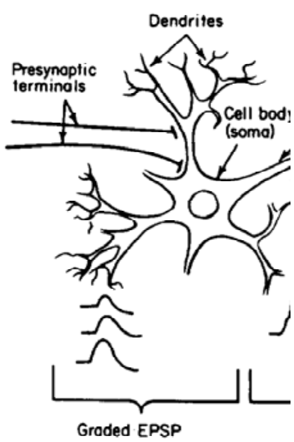
(can also add refractoriness similarly)

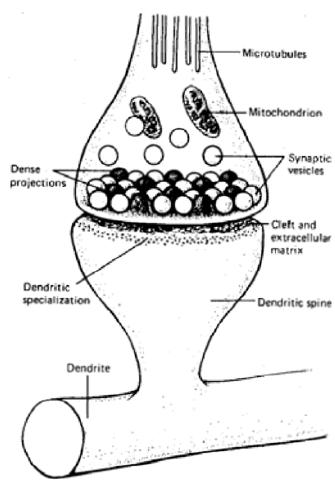
I & F Model with Spike-Rate Adaptation

Cortical Neuron

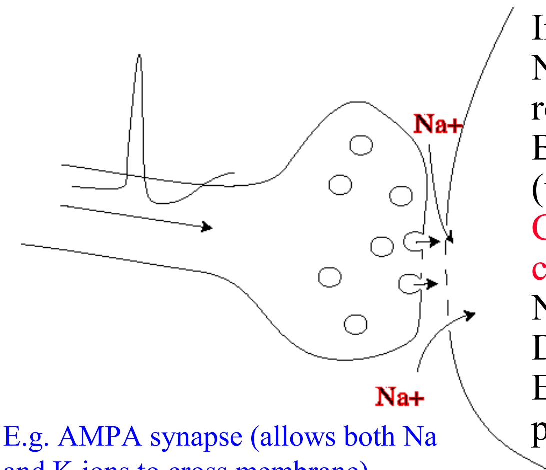
Integrate-and-Fire Model
with Spike-Rate Adaptation

Synapses: Modeling the Inputs to a Neuron





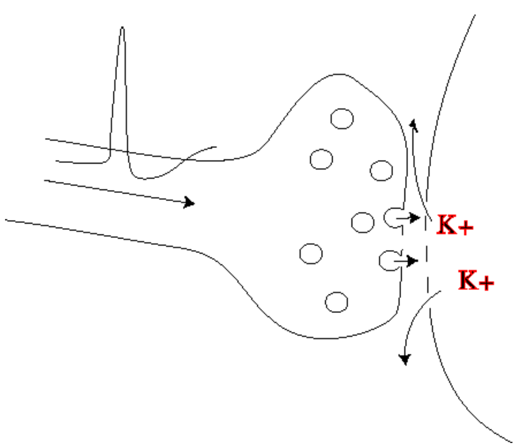
Example of An Excitatory Synapse



E.g. AMPA synapse (allows both Na and K ions to cross membrane)

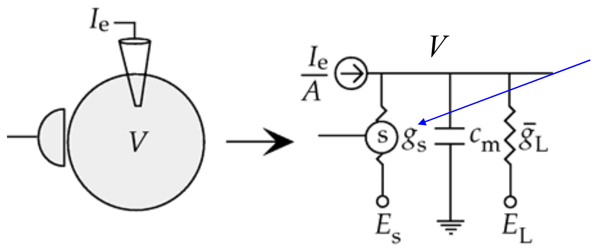
Input spike → Neurotransmitter release → Binds to Na channels (which open) → Change in synaptic conductance→ Na+ influx → Depolarization due to EPSP (excitatory postsynaptic potential)

Example of An Inhibitory Synapse



Input spike → Neurotransmitter release → Binds to K channels → Change in synaptic conductance → K+ leaves cell → Hyperpolarization due to IPSP (inhibitory postsynaptic potential)

Modeling a Synaptic Input to a Neuron



Synaptic conductance

$$\tau_m \frac{dV}{dt} = -(V - E_L) - r_m g_s (V - E_s) + I_e R_m$$

$$g_s = g_{s,\max} P_{rel} P_s$$

P_s: Probability of postsynaptic channel opening (= fraction of channels opened)

P_{rel}: Probability of transmitter release given an input spike

Basic Synapse Model

- Assume $P_{rel} = 1$ (for now)
- Model the effect of a single spike input on P_s
- Kinetic Model: closed $\xrightarrow{\alpha_s}$ open

  open $\xrightarrow{\beta_s}$ closed

$$\frac{dP_s}{dt} = \alpha_s (1 - P_s) - \beta_s P_s$$

α_s: Opening rate

$(1 - P_s)$: Fraction of channels closed

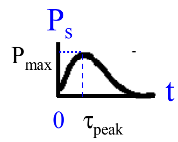
β_s: Closing rate

P_s: Fraction of channels open

Simplified Synapse Models

- "Alpha Function" model:

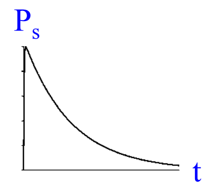
$$P_s(t) = \text{const} \cdot \frac{t}{\tau_{peak}} e^{-\frac{t}{\tau_{peak}}}$$



  - const = eP_{max} so that $P_s(\tau_{peak}) = P_{max}$
  - Why Alpha? People used $\alpha = 1/\tau_{peak}$

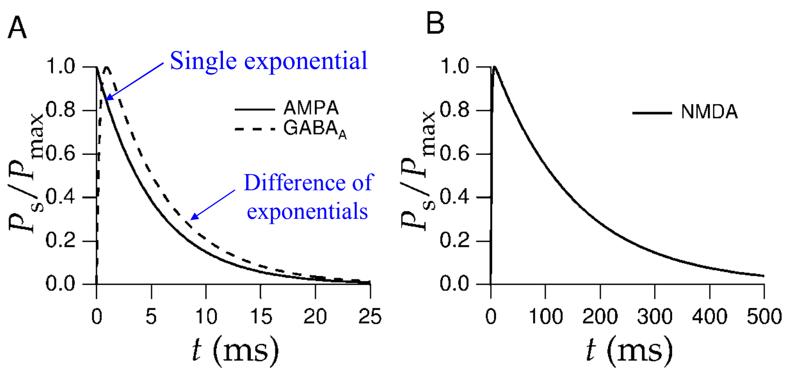
- Difference of Exponentials Model:

$$P_s(t) = \text{const} \cdot P_{\max} (e^{-\frac{t}{\tau_1}} - e^{-\frac{t}{\tau_2}})$$



  - const chosen to make peak of $P_s = P_{max}$

Comparison of Synapse Models to Data



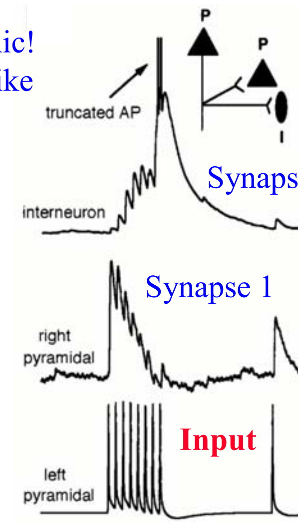
Difference of exponentials model was fit to biological data

What if there are multiple input spikes?

- Biological synapses are dynamic!
- Linear summation of single spike inputs not correct

Short-Term Facilitation

Short-Term Depression

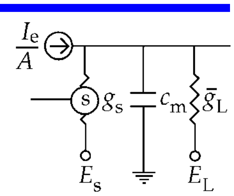


(Markram & Tsodyks, 1998)

Modeling Dynamic Synapses

- Recall definition of synaptic conductance:

$$g_s = g_{s,\max} P_{rel} P_s$$



- Idea: Specify how P_{rel} changes as a function of consecutive input spikes

$$\tau_P \frac{dP_{rel}}{dt} = P_0 - P_{rel}$$

Between input spikes, P_{rel} decays exponentially back to P_0

If Input Spike:

$$P_{rel} \rightarrow f_D P_{rel}$$

Depression: Decrement P_{rel}

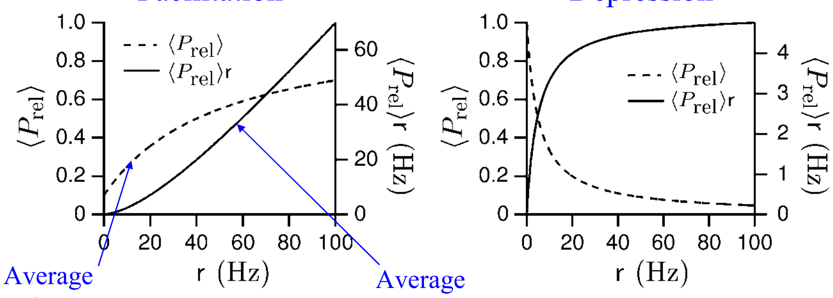
$$P_{rel} \rightarrow P_{rel} + f_F(1 - P_{rel})$$

Facilitation: Increment P_{rel}

Effects of Synaptic Facilitation & Depression

Facilitation

Depression



Average release probability

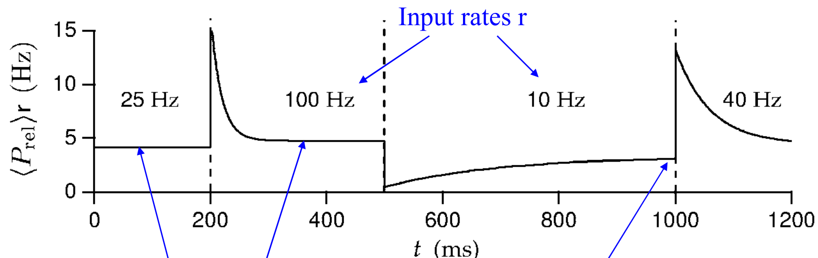
Input Rate

Average transmission rate

Input Rate

Consequences of Synaptic Depression

Input rates r



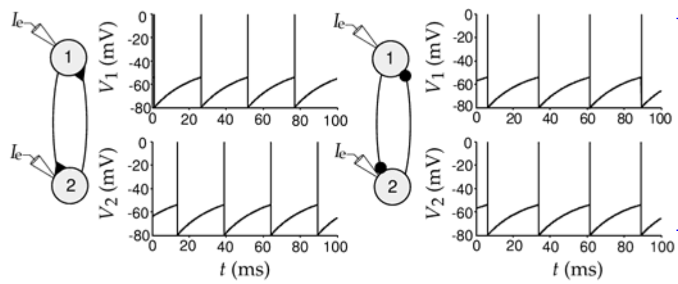
Steady-state transmission rates are similar for different rates

Transient inputs are amplified relative to steady-state inputs

Change in transmission rate ∝ Δr/r
(see text for derivation)

Putting it all together: Network Examples

Excitatory synapses (E_s = 0 mV) Inhibitory synapses (E_s = -80 mV)



Synchrony! (for inhibitory synapses)

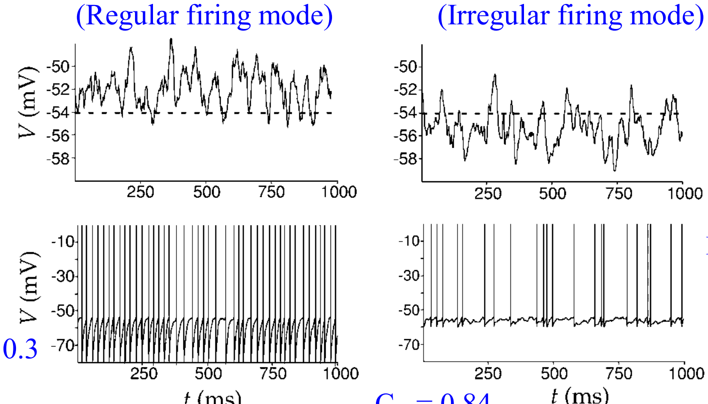
Each neuron: $$\tau_m \frac{dV}{dt} = -(V - E_L) - r_m g_{s,\max} P_s (V - E_s) + I_e R_m$$

Synapses: Alpha function model for P_s

Explaining the Spiking Behavior of Cortical Neurons

- I & F Neuron with 1000 excitatory and 200 inhibitory Poisson inputs

More excitation than inhibition (Regular firing mode) Balanced excitation and inhibition (Irregular firing mode)



$C_V = 0.3$

$C_V = 0.84$

Resembles cortical spiking

Next Class: Compartmental Models

- Things to do:
  - Finish Chapter 5 and Start Chapter 6
  - Matlab homework exercise #2 on web