Tools of computational neuroscience : Models of neurons

Readings:
D&A Chapter 5.
Izhikevich, 2004, ‘which model to use for cortical spiking neurons’

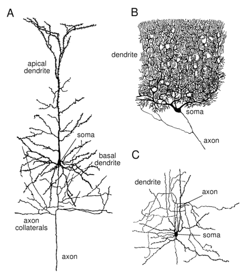
Types of models: descriptive vs explanatory

• Until now, descriptive/phenomenological models of statistics of responses (spike count). short hand for describing neural data. (what)
[question: knowing the statistics of the response, how can we relate the responses with behavior?]

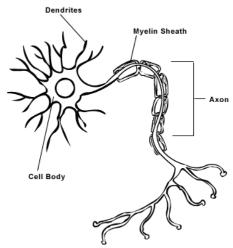
• explanatory -- mechanistic models / dynamical systems -- circuits
[questions: what are the mechanisms & circuits involved? what is the influence of some part of the circuit (e.g. inhibition/neuromodulator/dynamic synapses) on global behaviour? (e.g. gain modulation/oscillations/ variability)]
Identify the building blocks of brain function. (how)

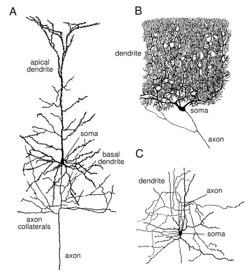
• Multiple level of abstraction are possible/ Neurons and Networks.

Models of neurons -
How do neurons get activated?



Neurons



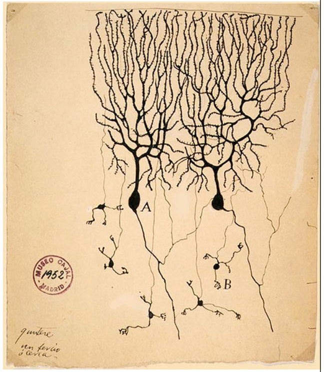


- neuron = cell, diverse morphologies
- **Dendrites**: receive inputs from other cells, mediated via synapses.
- **Soma** (cell body): integrates signals from dendrites. 4-100 micrometers.
- Action potential: All-or-nothing event generated if signals in soma exceed threshold.
- **Axon**: transfers signal to other neurons.
- **Synapse**: contact between pre- and postsynaptic cell.
  - Efficacy of transmission can vary over time.
  - Excitatory or inhibitory.
  - Chemical or electrical.

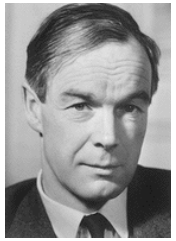
10^16 synapses in young children (decreasing with age -- 1-5x10^15)

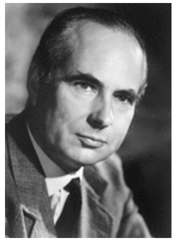
A bit of history

- 1791-1797: Galvani describes electrical activity in nerves
- 1848 Emil du Bois Reymond discovered the action potential
- Ramon y Cajal (Nobel prize 1906) established that nervous tissue is made up of discrete cells
- In 1902 and 1912, Bernstein advanced the hypothesis that the action potential resulted from a change in the permeability of the axonal membrane to ions.



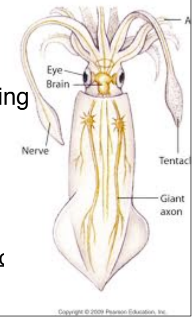
Hodgkin & Huxley (1952)





- Cambridge (1935-1952)
- experimental measurements theory of the action potential

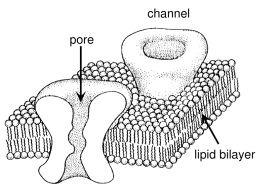
- Used the giant axon of the squid which enabled them to record ionic currents
- voltage clamp technique: to measure ionic currents across membrane by holding potential constant.

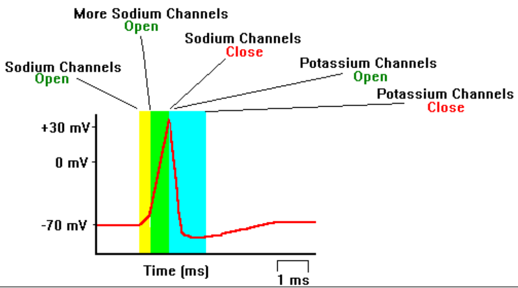


http://www.youtube.com/watch?v=k48jXzFGMc

Membrane potential and action potential

- Ions channels across the membrane, allowing ions to move in and out, with selective permeability (mainly Na+, K+, Ca2+,Cl-)
- Vm: difference in potential between interior and exterior of the neuron.
- at rest, Vm~-70 mV (more Na+ outside, more K+ inside, due to N+/K+ pump)
- Following activation of (Glutamatergic) synapses, depolarization occurs.
- if depolarization > threshold, neuron generates an action potential (spike) (fast 100 mv depolarization that propagates along the axon, over long distances).





Point neurons (1)

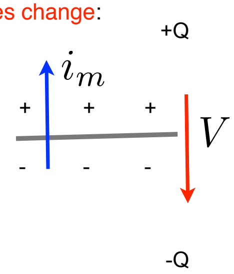
- We describe the membrane potential by a single variable V.
- membrane capacitance: Due to excess of negative charges inside the neuron, positive charges outside the neuron, membrane acts like a capacitor
- V and the amount of charges Q are related by the standard equation for capacitor: $$Q = C_m V$$
- From this we can determine how V changes when charges change:

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

here, by convention i_m is positive outwards

This is the basic equation used to model neurons.

$$C_m \frac{dV}{dt} = -\sum_{ion} I_{ion} + I_{ext}(t)$$



Point neurons (2)

$$C_m \frac{dV}{dt} = -\sum_{ion} I_{ion} + I_{ext}(t)$$

- The ion movements are due to channels that are open all the time (leakage), or that open at specific times, dependent on V, e.g. to generate action potential, or following synaptic events.

- Each current can be described in terms of a conductance g_i and equilibrium or reversal potential E_i. E_i describes the value of potential at which the current would stop, because the forces driving the ions (diffusion and electric forces) would cancel.

$$I_i = g_i(V - E_i)$$

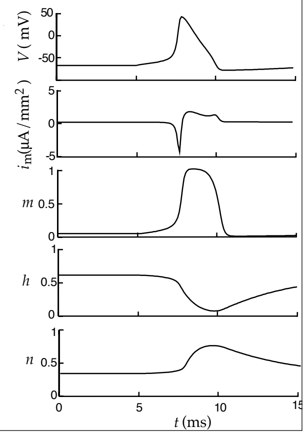
A conductance with reversal potential E_i will tend to move Vm towards E_i

E_{K+}~-70--90 mV, E_{Na+}~50mV, E_{cl-}~-60mV--65mV.

Hodgkin-Huxley Model (in a nutshell)

$$C_m \frac{dV}{dt} = -\sum_{ion} I_{ion} + I_{ext}(t)$$

$$\overline{g}_L(V - E_L) + \overline{g}_K n^4 (V - E_K) + \overline{g}_{Na} m^3 h (V - E_{Na})$$



- describe ionic movements involved in generation of action potential.
- n,m,h are the gating variables describing the dynamics of the K+, and Na+ channels.

m: opening of Na+ (activation)

h: closing of Na+ (inactivation)

n: opening of K+ (activation)

- They depend on V and their evolution (V,t) is described by other differential equations.

Hodgkin-Huxley Model (in a nutshell)

- n,m, and h are also described using differential equations

$dn/dt=a_n(V)(1-n)-b_n(V)n$ $a_n(V)$ = opening rate $b_n(V)$ = closing rate

$dm/dt=a_m(V)(1-m)-b_m(V)m$ $a_m(V)$ = opening rate $b_m(V)$ = closing rate

$dh/dt=a_h(V)(1-h)-b_h(V)h$ $a_h(V)$ = opening rate $b_h(V)$ = closing rate

$a_n=(0.01(V+55))/(1-\exp(-0.1(V+55)))$ $b_n=0.125\exp(-0.0125(V+65))$

$a_m=(0.1(V+40))/(1-\exp(-0.1(V+40)))$ $b_m=4.00\exp(-0.0556(V+65))$

$a_h=0.07\exp(-0.05(V+65))$ $b_h=1.0/(1+\exp(-0.1(V+35)))$

HH : Conclusion

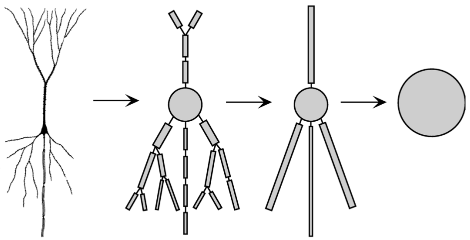
- The Hodgkin Huxley model : one of the most influential models of computational neuroscience
- In terms of models 3 success: (1) good model system (2) introduction of computers (3) right level of details for describing phenomenon --> link microscopic ion channels to macroscopic currents and AP.
- Led to many predictions and experiments, e.g. gating charge movements, that Na+ and K+ channels were separate molecular identities with different pore sizes, other dynamics.
- most biophysical models of spiking neurons still based on H-H equations.

Models of neurons

simplify

- One extreme: detailed description of the morphology of the neuron -- multi-compartmental models. Based on cable (differential) equations to solve Vm(x,t), simulations with softwares like NEURON.
- Hodgkin-Huxley neuron: model of spike generation using differential equations to model dynamics of K+ and Na+
- Integrate and fire neurons (family). spike generation replaced by stereotyped form.
- rate model.

this course



Integrate and fire neurons (1)

1. Only describe ion movements due to channels that are open all the time (leakage)= passive properties.

$$C_m \frac{dV}{dt} = -g_l(V - E_L) + I_{ext}(t)$$

Can be also written, using $R_m C_m = \tau_m$

$$\tau_m \frac{dV}{dt} = -V + E_L + R_m * I_{ext}(t)$$

E_L= resting potential; R_m=1\g$_l$ = membrane resistance; tau$_m$= membrane time constant;

2. When $V>V_{thres}$ (e.g. -55 mV) an action potential is triggered (V set to V_{spike} (e.g. 50 mV)) and V reset to V_{reset} e.g. -75 mV.

Integrate and fire neurons (2)

Example.

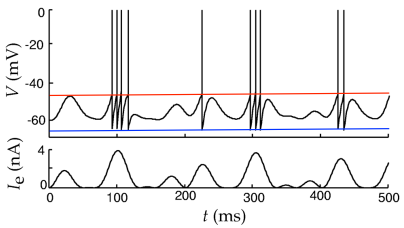
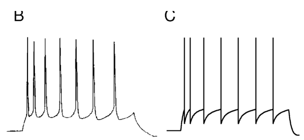


Figure 5.5: A passive integrate-and-fire model driven by a time-varying electrode current. The upper trace is the membrane potential and the bottom trace the driving current. The action potentials in this figure are simply pasted onto the membrane potential trajectory whenever it reaches the threshold value. The parameters of the model are $E_L = V_{reset} = -65$ mV, $V_{th} = -50$ mV, $\tau_m = 10$ ms, and $R_m = 10$ MΩ.

Integrate and fire neurons (3)

- The firing rate of an integrate and fire neuron in response to a constant injected current can be computed analytically (cf D&A).

- Integrate and fire neurons = a family of models.
 Inputs can be modeled as a current, or conductances (better model of synapses).
- Can be modified to account for a repertoire of dynamics e.g. can include a model of refractoriness and spike rate adaptation (and more)
- conductance-based IAF: these phenomena + inputs are modelled using added conductances.



spike rate adaptation

Integrate and fire neurons (4): adding spike rate adaptation

- spike rate adaptation can be modeled as an hyperpolarizing K+ current

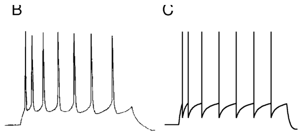
$$\tau_m \frac{dV}{dt} = E_L - V - \boxed{r_m g_{sra}(t)(V - E_K)} + R_m I_e$$

- when neuron spikes, g_{sra} is increased by a given amount:

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

- the conductance relaxes to 0 exponentially with time constant τ_{sra}

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



spike rate adaptation

Conductances triggered by spiking are used to model refractory period, bursting...
Synaptic input can be modeled similarly (but triggered by presynaptic spike)

Integrate and fire neurons (5): adding synaptic input

- Synaptic inputs are modeled as depolarizing or hyperpolarizing conductances

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

- Each time a presynaptic spike occurs (+ synaptic delay), P_s is modified.

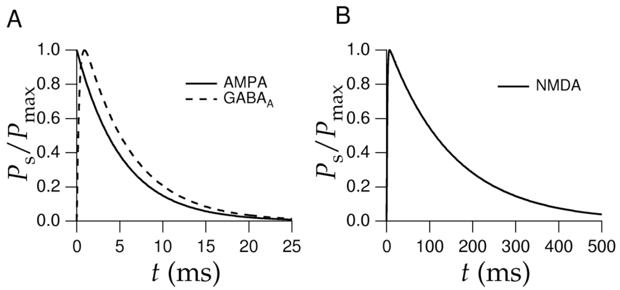
For example, Ps can be modeled using an alpha-function:

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

- a variety of models can be used for Ps depending on dynamics that we want to account for (slow/fast synapses)
- Es=0 for excitatory synapses, Es=-70--90 mV for inhibitory synapses.

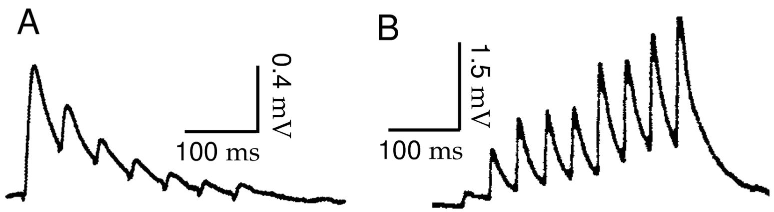
Synaptic input

- Different synapses have different dynamics.
- Excitatory synapses: AMPA is fast, NMDA slow.
- Inhibitory synapses: GABAa are fast, GABAb slower.



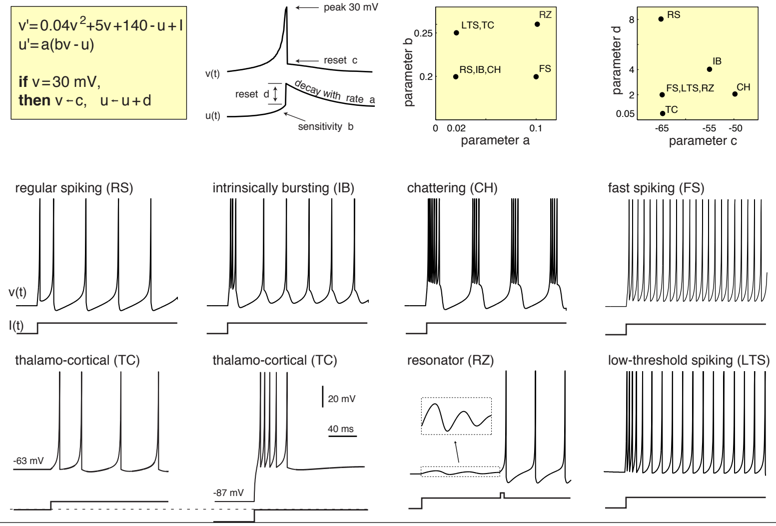
Synaptic input

- The amplitude of synaptic EPSPs and IPSPs may vary depending on spiking history: synaptic facilitation and depression.
- They can also vary on a longer time scale : learning. (LTP, LTD)



Izhikevich neuron (2003,2004)

- A recent and popular alternative to the integrate and fire.



On Numerical Integration

- Sometimes the differential equations can be solved analytically
- Usually though, they are solved numerically
- The simplest method is known as Euler's method: a system

$$\frac{dy}{dt} = f(y)$$

can be simulated by choosing the initial condition y(0) and repeatedly performing the Euler integration step:

$$y(t+dt) = y(t) + dt\, f(y)$$

Higher order and adaptive methods, such as Runge-Kutta are commonly used (check 'numerical recipes', matlab ode23, ode45, and Hansel et al 1998 for an evaluation of such methods with IAF neurons).