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.

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 Na+/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).
Models of neurons

- One extreme: detailed description of the morphology of the neuron -- multi-compartmental models. Based on cable (differential) equations to solve \( V_m(x,t) \), simulations with softwares like NEURON.
- Integrate and fire neurons (family). Spike generation replaced by stereotyped form.

This course

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:

\[
C_m \frac{dV}{dt} = \frac{dQ}{dt} = -i_m
\]

\( V \)

\( i_m \)

here, by convention \( i_m \) is positive outwards

This is the basic equation used to model neurons.

\[
C_m \frac{dV}{dt} = - \sum I_{ion} + I_{ext}(t)
\]

Point neurons (2)

\[
C_m \frac{dV}{dt} = - \sum I_{ion} + I_{ext}(t)
\]

- 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 \( g \) and equilibrium or reversal potential \( E \). \( E \) 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 \( E \) will tend to move \( V_m \) towards \( E \), \( E_Na \sim -70 \text{ to } -90 \text{ mV} \), \( E_K \sim -50 \text{ mV} \), \( E_Cl \sim -60 \text{ mV} \) to -65mV.

Hodgkin-Huxley Model (in a nutshell)

- 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 are 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

\[
\begin{align*}
\frac{dn}{dt} &= a_n(V)(1-n) - b_n(V)n \\
\frac{dm}{dt} &= a_m(V)(1-m) - b_m(V)m \\
\frac{dh}{dt} &= a_h(V)(1-h) - b_h(V)h
\end{align*}
\]

- \( a_n(V) = \) opening rate
- \( b_n(V) = \) closing rate
- \( a_m(V) = \) opening rate
- \( b_m(V) = \) closing rate
- \( a_h(V) = \) opening rate
- \( b_h(V) = \) closing rate

\[
\begin{align*}
a_n &= (0.01(V+55))/(1-\exp(-0.1(V+55))) \\
a_m &= (0.1(V+40))/(1-\exp(-0.1(V+40))) \\
a_h &= 0.07\exp(-0.05(V+65)) \\
b_n &= 0.125\exp(-0.0125(V+65)) \\
b_m &= 4.00\exp(-0.0556(V+65)) \\
b_h &= 1.0/(1+\exp(-0.1(V+35)))
\end{align*}
\]

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 \( R_m C_m = \tau_m \)

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

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.

![Integrate and fire neuron example](image)

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 \( E_L = V_{reset} = -65 \text{ mV}; V_{th} = -50 \text{ mV}; t_m = 10 \text{ ms}; \) and \( R_m = 10 \text{ M}\Omega. \)

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 refactoriness and spike rate adaptation (and more)
  - conductance-based IAF: these phenomena + inputs are modeled using added conductances.

![Spike rate adaptation](image)
Integrate and fire neurons (4): adding spike rate adaptation

- Spike rate adaptation can be modeled as an hyperpolarizing K+ current
  \[ \tau_m \frac{dV}{dt} = E_L - V - \tau_m g_{sra}(t)(V - E_K) + R_m I_e \]
- 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 \( \tau_{sra} \)
  \[ \tau_{sra} \frac{dg_{sra}(t)}{dt} = -g_{sra}(t) \]

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
  \[ \tau_m \frac{dV}{dt} = E_L - V - \tau_m \sum_{s} P_s(V - E_s) + R_m I_e \]
- Each time a presynaptic spike occurs (+ synaptic delay), \( P_s \) is modified.
  For example, \( P_s \) can be modeled using an alpha-function:
  \[ P_s(t) = \frac{P_{max}}{\tau_s} \exp(1 - \frac{t}{\tau}) \]
- A variety of models can be used for \( P_s \) depending on dynamics that we want to
  account for (slow/fast synapses)
- \( E_s = 0 \) for excitatory synapses, \( E_s = -70–90 \) 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.

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.

- Regular spiking (RS)
- Intrinsically bursting (IB)
- Chattering (CH)
- Fast spiking (FS)
- Low-threshold spiking (LTS)

- Thalamo-cortical (TC)
- Resonator (RZ)

\[
v(t) = 0.04v(t)^2 + 5v(t) + 140 - u(t) + I(t)
\]

\[
u'(t) = a(bv(t) - u(t))
\]

If \(v(t) = 30\) mV,
then \(v = c, u = u + d\)

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).