2. Neurons

Typical Neuron

Dendritic Trees of Some Neurons
A. inferior olivary nucleus
B. granule cell of cerebellar cortex
C. small cell of reticular formation
D. small gelatinous cell of spinal trigeminal nucleus
E. ovoid cell, nucleus of tractus solitarius
F. large cell of reticular formation
G. spindle-shaped cell, substantia gelatinosa of spinal cord
H. large cell of spinal trigeminal nucleus
I. potassium of lenticular nucleus
J. double pyramidal cell, Ammon’s horn of hippocampal cortex
K. thalamic nucleus
L. globus pallidus of lenticular nucleus

Synapses
video by Hybrid Medical Animation

Chemical Synapse
1. Action potential arrives at synapse
2. Opens Ca ion channels and Ca^{++} ions enter cell
3. Vesicles move to membrane, release neurotransmitter
4. Transmitter crosses cleft, causes postsynaptic voltage change
2. Neurons

Typical Receptor

Synapse with Receptors

Fig. 3 Activity-dependent modulation of pre-, post-, and trans-synaptic components.

Fig. 4 Local regulation of the synaptic proteome.

Fig. 3: A 3D model of synaptic architecture.

- A section through the synaptic bouton, indicating 60 proteins.
- High-zoom view of the active zone area.
- High-zoom view of one vesicle within the vesicle cluster.
- High-zoom view of a section of the plasma membrane in the vicinity of the active zone. Clusters of synaptotagmin (yellow) and SNAP-25 (red) are visible, as well as a recently fused synaptic vesicle (top). The graphical legend indicates the different proteins (right). Displayed synaptic vesicles have a diameter of 42 nm.
Overall Strategy

- Neurons are electrical systems, can be described using basic electrical equations.
- Use these equations to simulate on a computer.
- Need a fair bit of math to get a full working model (more here than most chapters), but you only really need to understand conceptually.

Membrane Potential: Channels

- Na-K pump ⇒ intracellular negative
- Na⁺, K⁺, Cl⁻ diffusing through their channels
- create potentials across channels
Membrane Potential: Channels & Equivalent Circuit

- Open channels define resistance to ion flow
- Membrane acts like insulator
- Ion pump charges membrane capacitance

Neurophysiology of Membrane

- Na-K pump pumps Na⁺ out of the neuron and pumps a lesser amount of K⁺ into the neuron
- Creates negative resting potential (~70 mV)
- Na⁺ wants in (can't, due to closed channels)
- Cl⁻ is in balance (diffusion pushes in, electrical pushes out)
- K⁺ is in balance (diffusion pushes out, electrical pushes in)

Ions Summary

- Excitatory synaptic input boosts the membrane potential by allowing Na⁺ ions to enter the neuron (depolarization)
- Inhibitory synaptic input serves to counteract this increase in membrane potential by allowing Cl⁻ ions to enter the neuron
- The leak current (K⁺ flowing out of the neuron through open channels) acts as a drag on the membrane potential. Functionally speaking, it makes it harder for excitatory input to increase the membrane potential.

Input Signals

- Excitatory
  - about 85% of inputs
  - AMPA channels, opened by glutamate
- Inhibitory
  - about 15% of inputs
  - GABA channels, opened by GABA
- Leakage
  - potassium channels
- Synaptic efficacy (weight) is net effect of:
  - presynaptic neuron to produce neurotransmitter
  - postsynaptic channels to bind it

Membrane Potential (Variables)

- $g_e =$ excitatory conductance
- $E_e =$ excitatory potential (~0 mV)
- $g_i =$ inhibitory conductance
- $E_i =$ inhibitory potential (~70 mV)
- $g_l =$ leakage conductance
- $E_l =$ leakage potential
- $V_m =$ membrane potential
- $\theta =$ threshold
2. Neurons

The Tug-of-War

How strongly each guy pulls: \( I = g(E - V_m) \)
- \( g \) = how many input channels are open
- \( E \) = driving potential (pull down for inhibition, up for excitation)
- \( V_m \) = the “flag” - reflects net balance between two sides

Relative Balance

Equations

\[ I_{net} = I_i + I_e = g_i (E_i - V_m) + g_e (E_e - V_m) + g (E_l - V_m) \]
\[ V_m(t) = V_m(t-1) + \Delta t_{net} I_{net} \]
\[ V_m(t) = V_m(t-1) + \Delta t_{net} [g_i (E_i - V_m) + g_e (E_e - V_m) + g (E_l - V_m)] \]

Equilibrium

\[ V_m = \frac{g_i}{g_i + g_e + g_l} E_i + \frac{g_e}{g_i + g_e + g_l} E_e + \frac{g_l}{g_i + g_e + g_l} E_l \]

This is just the balance of forces

Generating Output

- If \( V_m \) gets over threshold, neuron fires a spike
- Spike resets membrane potential back to rest
- Has to climb back up to threshold to spike again

Input Conductances and Weights

- Just add them up (and take the average)
  \[ g_i(t) = \frac{1}{n} \sum_{i=1}^{n} f_i w_i \]
- Key concept is weight: how much unit listens to given input
- Weights determine what the neuron detects
- Everything you know is encoded in your weights
2. Neurons

Action Potential Generation

Frequency Coding

Slow Potential Neuron

Dendritic computation in pyramidal cells.

Variations in Spiking Behavior

Computational Formulation
Membrane Potential

Currents: $I_x = g_x (E_x - V_m)$, $x = e, i, l$
Net current: $I_{net} = I_e + I_i + I_l$

Change in membrane potential: $V_m = C^{-1} I_{net}$ ($C^{-1}$ is rate constant)

$V_m = C^{-1} [g_x (E_x - V_m) + g_i (E_i - V_m) + g_l (E_l - V_l)]$

Equilibrium $V_m = \frac{g_x E_x + g_i E_i + g_l E_l}{g_x + g_i + g_l}$

Relative vs. Absolute Conductances

- Previously, $g_x$ was absolute conductance (measured in nanosiemens)
- More convenient to represent as product $\bar{g}_x g_x(t)$
  - where $\bar{g}_x$ is the absolute maximum conductance (all channels open)
  - and $g_x(t)$ is the relative conductance at a given time, $0 \leq g_x(t) \leq 1$

Discrete Spiking

if $V_m > \theta$ then
  $y := 1$;
  $V_m := V_m - \theta$;
else $y := 0$;

Rate Code Approximation

- Brain likes spikes, but rates are more convenient
  - Instantaneous and steady – smaller, faster models
  - But definitely lose several important things
  - Solution: do it both ways, and see the differences

- Goal: equation that makes good approximation of actual spiking rate for same sets of inputs

Rate Code Approximation

- Rate-coded (simulated) neurons:
  - short-time avg spike frequency $y$
  - avg behavior of minicolumn (~100 neurons) with similar inputs and output behavior
- Rate not predicted well by $V_m$
- Predicted better by $g_e$ relative to a threshold value $g_e^\theta$

Minicolumn

- Up to ~100 neurons
  - 75–80% pyramidal
  - 20–25% interneurons
  - 20–50µ diameter
- Length: 0.8 (mouse) to 3mm (human)
  - 6×10^6 synapses
  - 75–90% synapses outside minicolumn
- Interacts with 1.2×10^5 other minicolumns
- Mutually excitable
  - Also called microcolumn
2. Neurons

Rate Code Approximation

- \( g_\theta \) is the conductance when \( V_m = \theta \)
- Rate is a nonlinear function of relative conductance
- What is \( f \)?

\[ g_\theta = \frac{E_r g_r + E_i g_i + g_n g_i}{g_r^2 + g_i + g_n} \]

\[ g_\theta \approx \frac{g_r (E_r - \theta) + g_i (E_i - \theta)}{\theta - E_r} \]

\[ y = f (g_r - g_r^\theta) \]

Activation Function

- Desired properties:
  - threshold (~0 below threshold)
  - saturation
  - smooth

- Smooth by convolution with Gaussian to account for noise
- Activity update:

\[ y_{\text{act}} = y + C (y - y_i) \]

Gaussian Smoothing

X-over-X-plus-1 has a very sharp threshold
Smooth by convolve with noise (like “blurring” or “smoothing”):

\[ g^* (z) = \int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi\sigma}} e^{-\frac{1}{2}(z-x)^2} g(z-x) \, dz \]

Approximating Continuous Dynamics

- \( V_m \) changes gradually when input changes
- Firing rate \( y(t) \) should also change gradually (subject to a time constant)
- Discrete-time update equation:

\[ y(t) = y(t-1) + dt \frac{1}{\tau} (g^* (y(t) - y(t-1))) \]

Supplementary:
Mathematics of Action Potentials
2. Neurons

Neural Impulse Propagation

\[
\begin{align*}
\frac{dV}{dt} &= \left(1 - g_{Na}(h) - g_{K}(m^3) - g_{L} - g_{Cl}\right) (V - V_n) \\
\frac{dh}{dt} &= \alpha_h(V)(1 - h) - \beta_h(V)h \\
\frac{dm}{dt} &= \alpha_m(V)(1 - m) - \beta_m(V)m \\
\frac{dV}{dt} &= 0.01(V + 65) + 0.3(V - V_m) \\
\frac{dh}{dt} &= 0.07(V^2 - 15) \\
\frac{dm}{dt} &= 0.07(V^2 - 20) \\
\end{align*}
\]

Hodgkin-Huxley equations

FitzHugh-Nagumo Model

- A simplified model of action potential generation in neurons
- The neuronal membrane is an excitable medium
- \( B \) is the input bias:
  \[
  \dot{u} = u - \frac{u^3}{3} - v + B \\
  \dot{v} = \frac{1}{\tau}(v - u - B)
  \]

Nullclines

Elevated Thresholds During Recovery

Local Linearization

Fixed Points & Eigenvalues

- stable fixed point: real parts of eigenvalues are negative
- unstable fixed point: real parts of eigenvalues are positive
- saddle point: one positive real & one negative real eigenvalue
2. Neurons

Poincaré-Bendixson Theorem

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]

NetLogo Simulation of Excitable Medium in 2D Phase Space

(EM-Phase-Plane.nlogo)

Type II Model

- Soft threshold with critical regime
- Bias can destabilize fixed point

Type I Model

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]

stable manifold

Type I Model (Elevated Bias)

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]

Type I Model (Elevated Bias 2)

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]
Type I vs. Type II

- Continuous vs. threshold behavior of frequency
- Slow-spiking vs. fast-spiking neurons

fig. <Gerstner & Kistler>