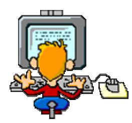
Today's Agenda

- Introduction: Who are we?
- Course Info and Logistics
- Motivation
  - What is Computational Neuroscience?
  - Illustrative Examples
- Neurobiology 101: Neurons and Networks

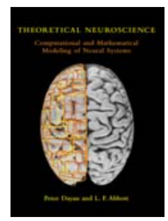
Course Information

- Browse class web page for syllabus and course information:
  - http://www.cs.washington.edu/education/courses/528/05wi
- Lecture slides will be made available on the website
- Add yourself to the mailing list→ see class web page
- Textbook
  - *Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems*
  - By Peter Dayan and Larry Abbott MIT Press, 2001



Peter Dayan

Larry Abbott



Course Topics

- *Descriptive Models of the Brain*
  - How is information about the external world *encoded* in neurons and networks? (Chapters 1 and 2)
  - How can we *decode* neural information? (Chapters 3 and 4)
- *Mechanistic Models of Brain Cells and Circuits*
  - How can we reproduce the behavior of a *single neuron* in a computer simulation? (Chapters 5 and 6)
  - How do we model a *network* of neurons? (Chapter 7)
- *Interpretive Models of the Brain*
  - Why do brain circuits operate the way they do?
  - What are the *computational principles* underlying their operation? (Chapters 7-10)

Course Goals

- **General Goals:**
  1. To be able to quantitatively describe what a given component of a neural system is doing based on experimental data
  2. To be able to simulate on a computer the behavior of neurons and networks in a neural system
  3. To be able to formulate specific computational principles underlying the operation of neural systems
- We would like to enhance *interdisciplinary cross-talk*

  Neuroscience ⟷ Comp. Science and Engineering

  (Experiments, methods, protocols, data, …) (Computational principles, algorithms, simulation software/hardware, …)

Specific Goals

- Learn how to quantify a neuron's response using ideas from statistics and information theory
- Understand neural responses through probabilistic methods such as Bayesian inference and MAP estimation
- Learn to construct and simulate biophysical models of neural membranes, "compartments," and entire neurons
- Explore information processing in networks of neurons
- Learn how networks can adapt themselves based on unsupervised and supervised learning rules

Workload and Grading

- Course grade (out of 4.0) will be based on homeworks and a final group project according to:
  - Homeworks: 70%
  - Final Project: 30%
- No midterm or final
- Homework exercises: Either written or Matlab-based
  - Go over Matlab tutorials on the web
- Group Project: As part of a group of 1-3 persons, investigate a "mini-research" question using methods from this course
  - Each group will submit a report and give a presentation

Okay, enough logistics – let's begin…

What is Computational Neuroscience?

What is Computational Neuroscience?

- "The goal of computational neuroscience is to explain in computational terms how brains generate behaviors" (Sejnowski)
- Computational neuroscience provides tools and methods for "characterizing *what* nervous systems do, determining *how* they function, and understanding *why* they operate in particular ways" (Dayan and Abbott)
  - Descriptive Models (*What*)
  - Mechanistic Models (*How*)
  - Interpretive Models (*Why*)

An Example: Cortical Receptive Fields

- What is the *receptive field* of a brain cell (neuron)?
  - Any ideas?

An Example: Cortical Receptive Fields

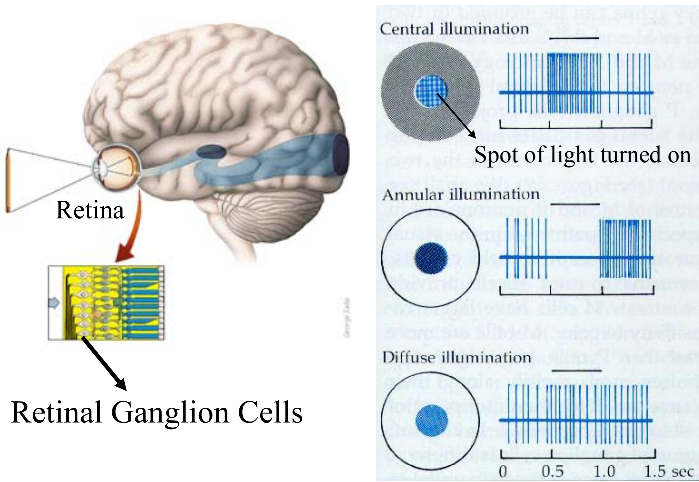
- What is the *receptive field* of a brain cell (neuron)?
- Classical Definition: The region of sensory space that activates a neuron (Hartline, 1938)
  - Example: Region of the retina where a spot of light activates a retinal cell
- Current Definition: Receptive field of a cell = specific properties of a sensory stimulus that generate a strong response from the cell
  - Example: A circular spot of light that turns on at a particular location on the retina

An Example: Cortical Receptive Fields

Let's look at:

I. A *Descriptive Model* of Receptive Fields
II. A *Mechanistic Model* of Receptive Fields
III. An *Interpretive Model* of Receptive Fields

I. Descriptive Model of Receptive Fields

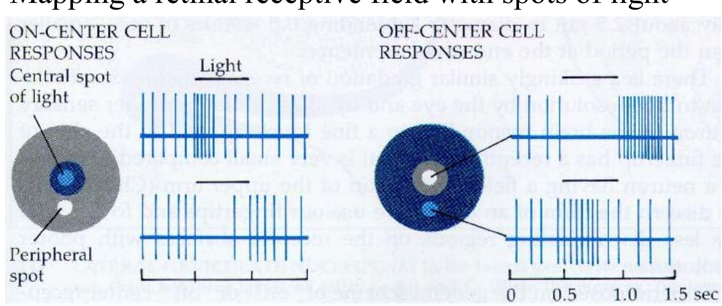


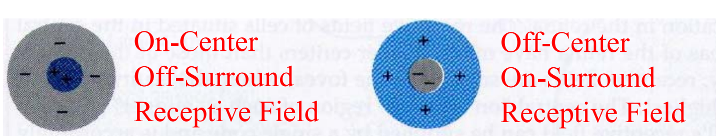
Output responses (spike trains) from a Retinal Ganglion Cell

(From Nicholls et al., 1992)

I. Descriptive Model of Receptive Fields

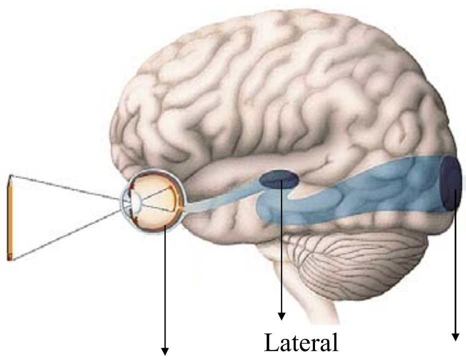
Mapping a retinal receptive field with spots of light

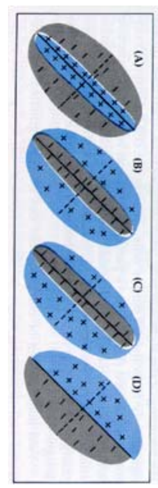




(From Nicholls et al., 1992)

Descriptive Models: Cortical Receptive Fields



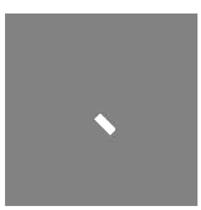


Examples of receptive fields in primary visual cortex (V1)

(From Nicholls et al., 1992)

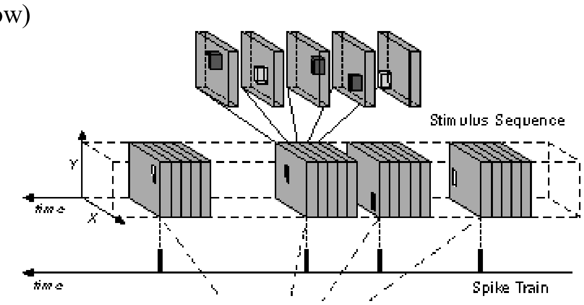
Extracting a *Quantitative* Descriptive Model

- The Reverse Correlation Method
  (Brief intro for now)



Random Bars Sequence (white noise stimulus)

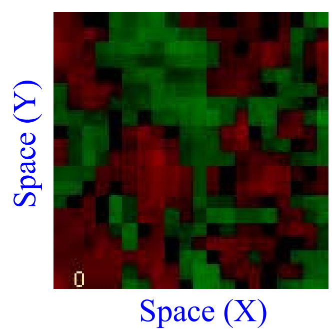
(Copyright, Izumi Ohzawa)



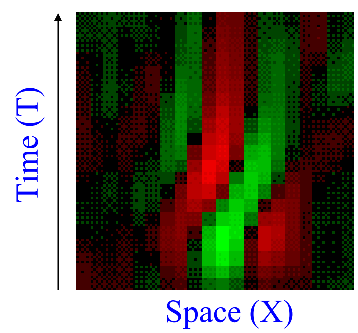
For each output spike, look back in time for the stimulus sequence that caused this spike; compute the average sequence

A Quantitative Model of a V1 Receptive Field

Spatial Receptive Field for T = 0-300 ms



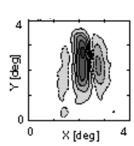
Space-Time Receptive Field

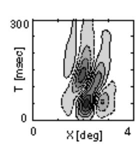


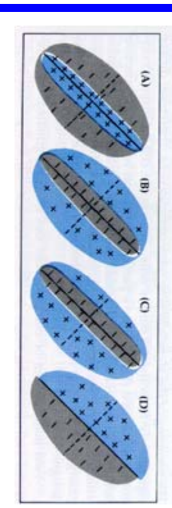
(Copyright 1995, Izumi Ohzawa)

II. Mechanistic Model of Receptive Fields

- The Question: *How* are receptive fields constructed using the neural circuitry of the visual cortex?

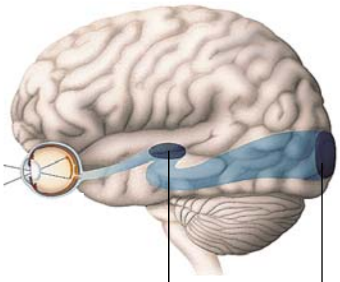


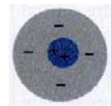


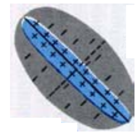


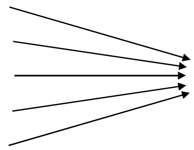
How are these *oriented* receptive fields obtained?

II. Mechanistic Model of Receptive Fields: V1

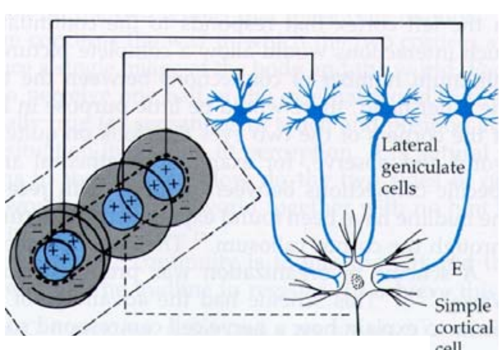








II. Mechanistic Model of Receptive Fields: V1



(From Nicholls et al., 1992)

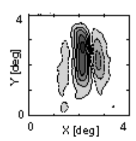
Model suggested by Hubel & Wiesel in the 1960s: V1 RFs are created from converging LGN inputs

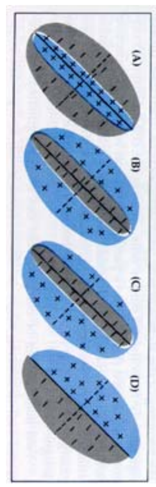
Center-surround LGN RFs are *displaced along preferred orientation* of V1 cell

This simple model is still controversial!

III. Interpretive Model of Receptive Fields

- The Question: *Why* are receptive fields in V1 shaped in this way?





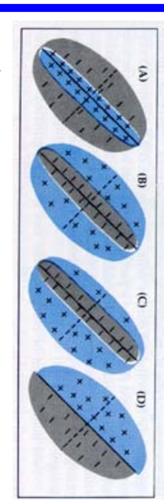
What are the computational advantages of such receptive fields?

III. Interpretive Model of Receptive Fields

- Computational Hypothesis: Suppose the goal is to *represent images as faithfully and efficiently as possible* using neurons with receptive fields $\mathbf{RF}_1$, $\mathbf{RF}_2$, etc.
- Given image $\mathbf{I}$, want to reconstruct $\mathbf{I}$ using neural responses r_1, r_2 etc.:

$$\hat{\mathbf{I}} = \sum_i \mathbf{RF}_i r_i$$

- *Idea*: Find the $\mathbf{RF}_i$ that *minimize* the squared pixelwise errors: $\| \mathbf{I} - \hat{\mathbf{I}} \|^2$ and are as *independent* from each other as possible



$\mathbf{RF}_1$

$\mathbf{RF}_2$

$\mathbf{RF}_3$

$\mathbf{RF}_4$

III. Interpretive Model of Receptive Fields

- Start out with random **RF**$_i$ and run your algorithm on natural images

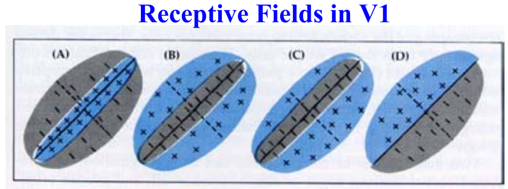
Natural Images

Receptive Fields from Natural Images

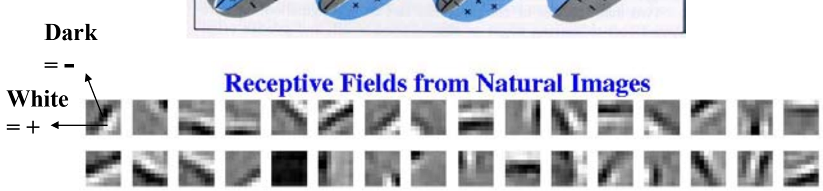
III. Interpretive Model of Receptive Fields

- Conclusion: The receptive fields in V1 may be a consequence of the brain trying to find *faithful and efficient* representations of an animal's natural environment

Receptive Fields in V1



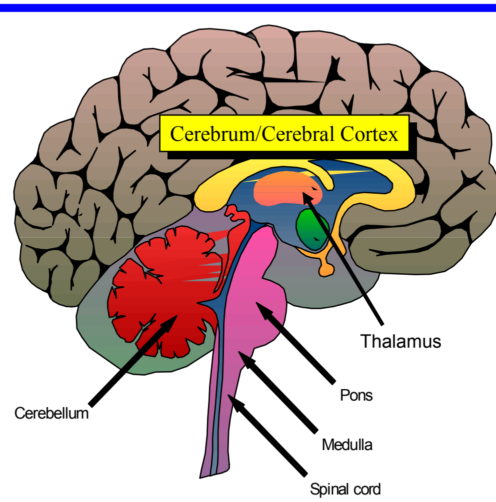
Receptive Fields from Natural Images



We will explore a variety of *Descriptive*, *Mechanistic*, and *Interpretive* models throughout this course

The subject of our exploration:
Our (3-pound) Universe

Our 3-pound Universe

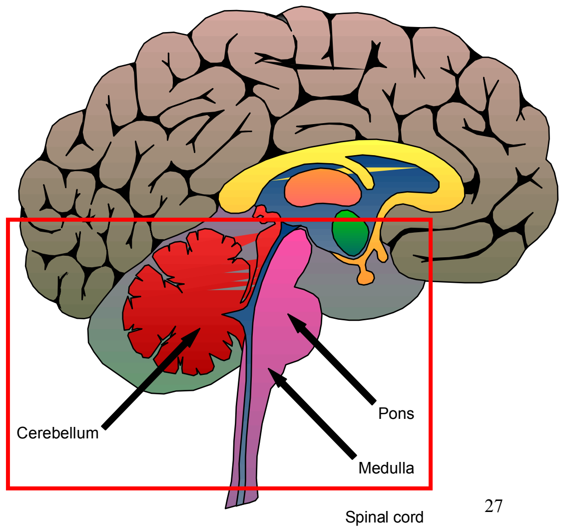


Major Brain Regions: Brain Stem & Cerebellum

Medulla
Breathing, muscle tone and blood pressure

Pons
Connects brainstem with cerebellum & involved in sleep and arousal

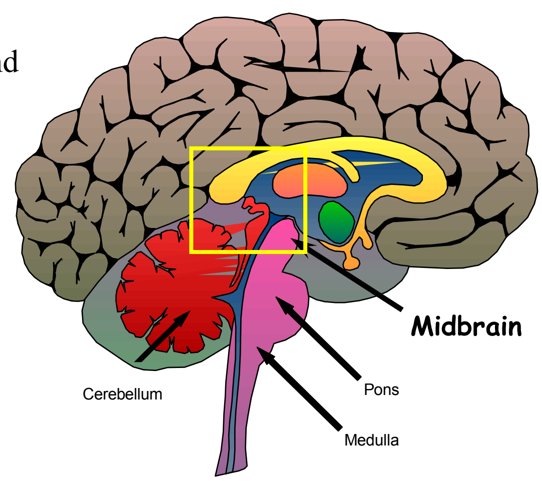
Cerebellum
Coordination of voluntary movements and sense of equilibrium



Major Brain Regions: Midbrain & Retic. Formation

Midbrain
Eye movements, visual and auditory reflexes

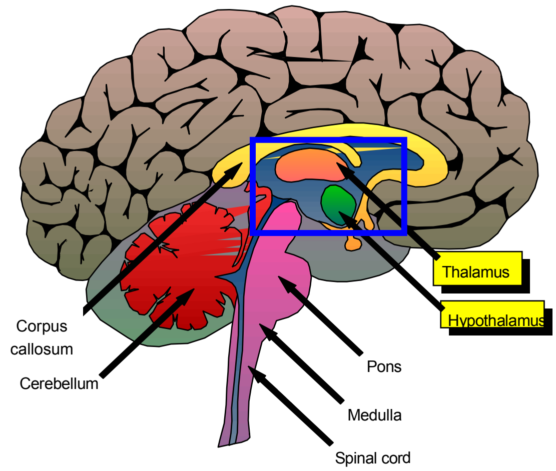
Reticular Formation
Modulates muscle reflexes, breathing & pain perception. Also regulates sleep, wakefulness & arousal



Major Brain Regions: Thalamus & Hypothalamus

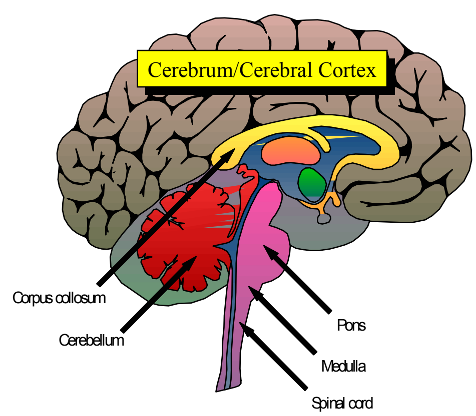
Thalamus
"Relay station" for all sensory info (except smell) to the cortex

Hypothalamus
Regulates basic needs fighting, fleeing, feeding, and mating

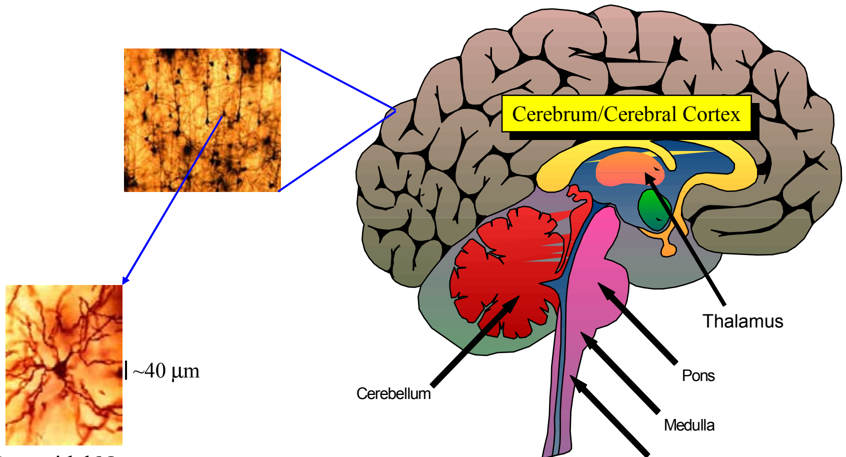


Major Brain Regions: Cerebral Hemispheres

- Consists of: Cerebral cortex, basal ganglia, hippocampus, and amygdala
- Involved in perception and motor control, cognitive functions, emotion, memory, and learning

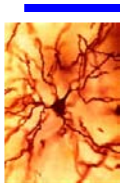


Enter…the neuron ("brain cell")



A Pyramidal Neuron

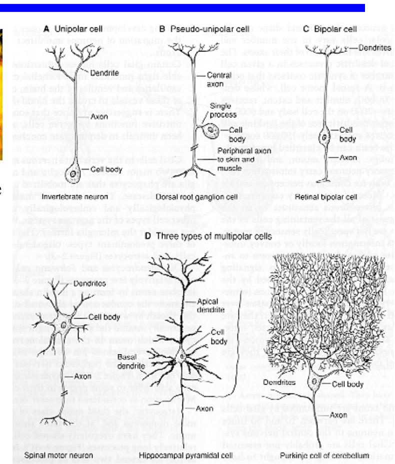
The Neuron Doctrine/Dogma



Cerebral Cortex Neuron

Neuron from the Thalamus

Neuron from the Cerebellum



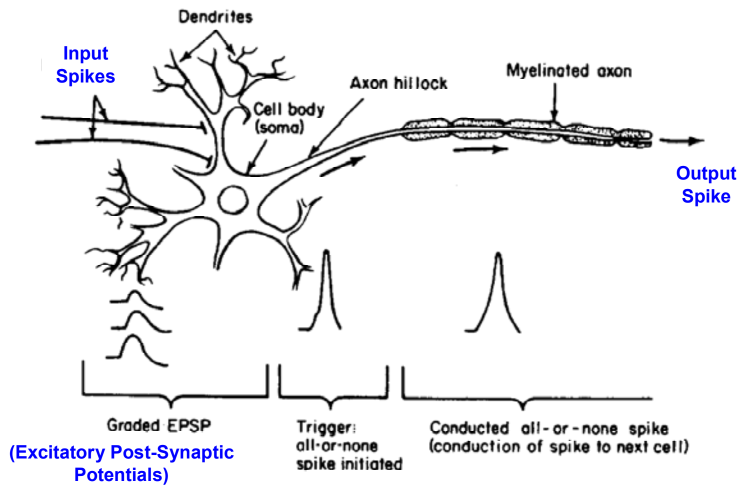
From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pg. 21

Neuron Doctrine:

"The neuron is the appropriate basis for understanding the computational and functional properties of the brain"

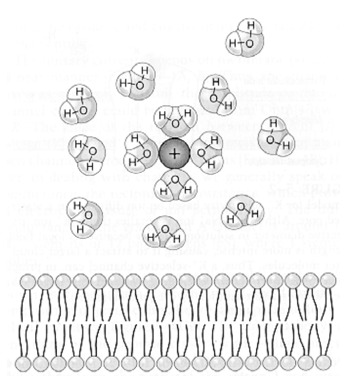
First suggested in 1891 by Waldeyer

The Idealized Neuron



What is a Neuron?

- A "leaky bag of charged liquid"
- Contents of the neuron enclosed within a *cell membrane*
- Cell membrane is a *lipid* bilayer
  - Bilayer is impermeable to charged ion species such as Na^+, Cl^-, K^+, and Ca^{2+}



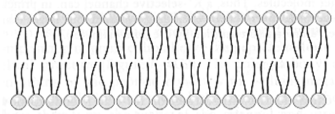
From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pg. 67

The Electrical Personality of a Neuron

- Each neuron maintains a *potential difference* across its membrane
  - Inside is –70 to –80 mV relative to outside
  - $[Na^+]$, $[Cl^-]$ and $[Ca^{2+}]$ higher outside; $[K^+]$ and organic anions $[A^-]$ higher inside
  - *Ionic pump* maintains -70 mV difference by expelling Na^+ out and allowing K^+ ions in

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

0 mV Outside



-70 mV Inside

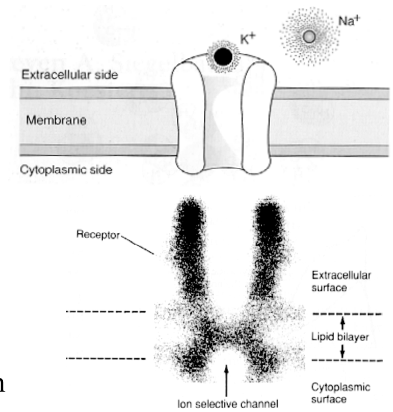
$[K^+]$, $[A^-]$
$[Na^+]$, $[Cl^-]$, $[Ca^{2+}]$

Influencing a Neuron's Electrical Personality

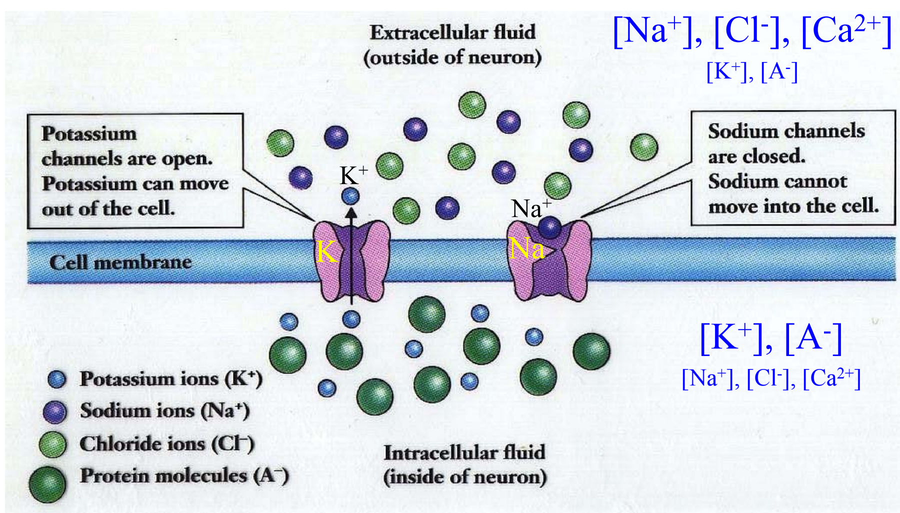
How can the electrical potential difference be changed in local regions of a neuron?

Membrane Proteins: The Gatekeepers

- Proteins in membranes act as pores or channels that are ion-specific. E.g. Pass K^+ but not Cl^- or Na^+
- Ionic channels are *gated*
  - Voltage-gated: Probability of opening depends on membrane voltage
  - Chemically-gated: Binding to a chemical causes channel to open
  - Mechanically-gated: Sensitive to pressure or stretch

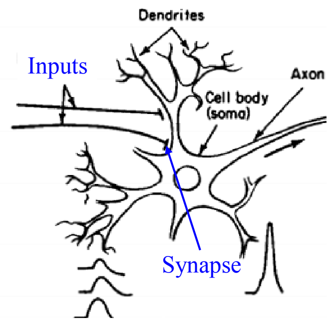


From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pgs. 68 & 137



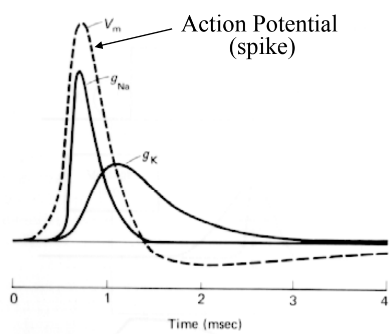
Gated Channels allow Neuronal Signaling

- Inputs from other neurons → chemically-gated channels (at "synapses") → Changes in local membrane potential
- Potentials are integrated spatially and temporally in dendrites and cell body of the neuron
- Cause opening/closing of voltage-gated channels in dendrites, body, and axon → causes depolarization (positive change in voltage) or hyperpolarization (negative change)

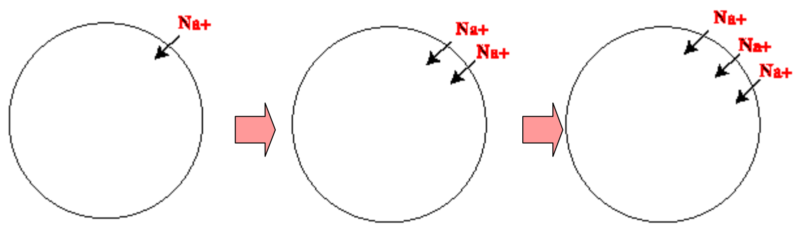


The Output of a Neuron: Action Potentials

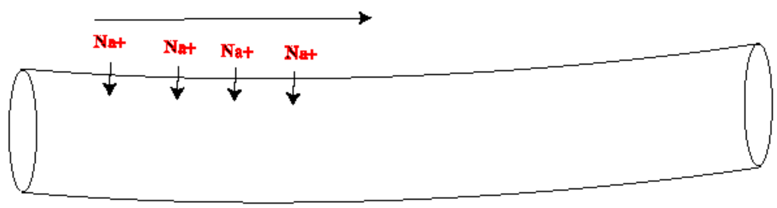
- Voltage-gated channels cause action potentials (spikes)
  1. Rapid Na^+ influx causes rising edge
  2. Na^+ channels deactivate
  3. K^+ outflux restores membrane potential
- Positive feedback causes spike
  - Na^+ influx increases membrane potential, causing *more* Na^+ influx



From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pg. 110

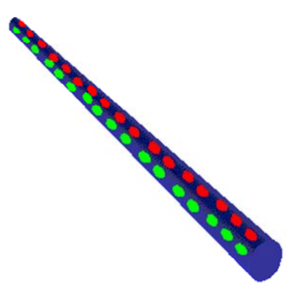


An increase in permeability at one location of the membrane can spread to neighboring locations



Axons have very large concentrations of voltage-gated Na+ channels, causing the excitation to actively travel forward.

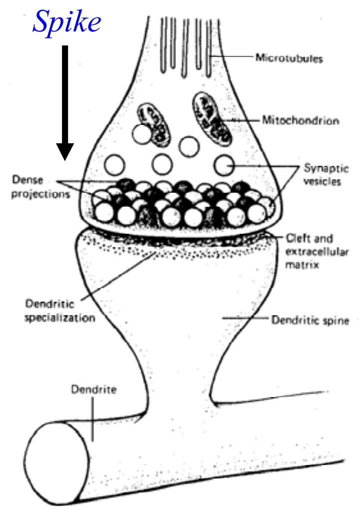
Propagation of a Spike along an Axon



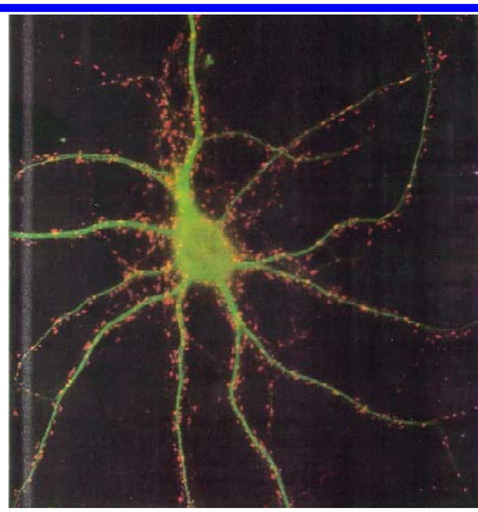
 From: http://psych.hanover.edu/Krantz/neural/actpotanim.html

Communication between Neurons: Synapses

- Synapses are the "connections" between neurons
  - Electrical synapses (gap junctions)
  - Chemical synapses (use neurotransmitters)
- Synapses can be excitatory or inhibitory
- Synapse Doctrine: Synapses are the basis for memory and learning

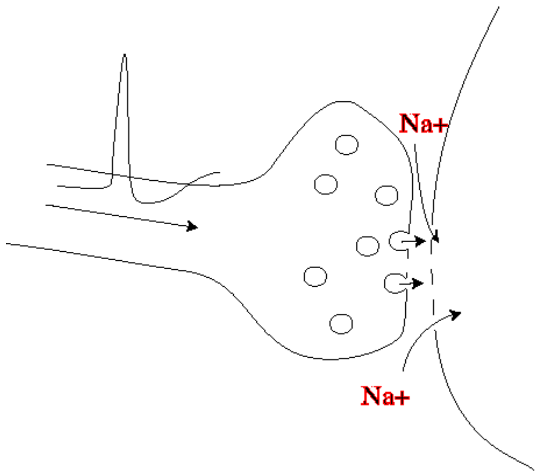


Distribution of synapses on a real neuron…



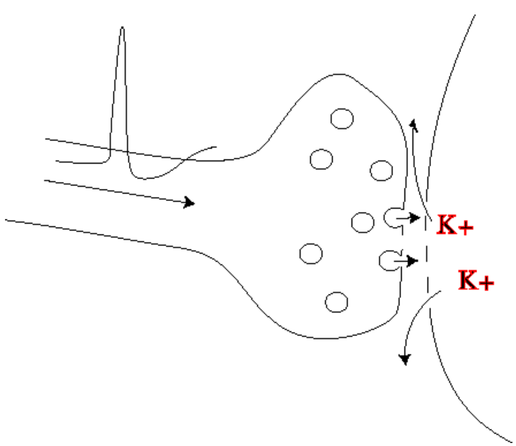
(From Cell/Neuron journal special supplement, 1993)

An Excitatory Synapse



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

An Inhibitory Synapse



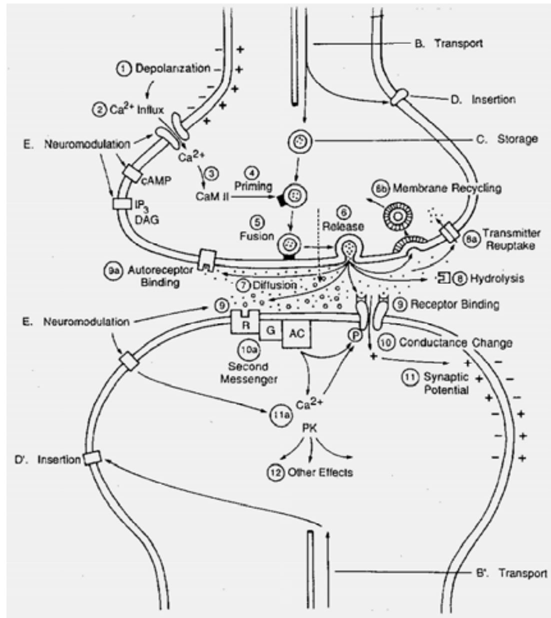
Input spike → Neurotransmitter release → Binds to K channels → K+ leaves cell → Hyperpolarization due to IPSP (inhibitory postsynaptic potential)

Down in the Synaptic Engine Room

A reductionist's dream! (or nightmare?)

Note: Even this is a simplification!

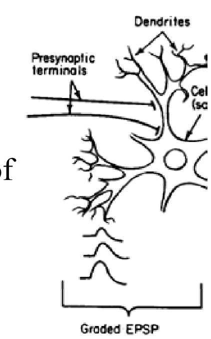
From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991



Synaptic plasticity: Adapting the connections

- Long Term Potentiation (LTP): Increase in synaptic strength that lasts for several hours or more
  - ➩ Measured as an increase in the excitatory postsynaptic potential (EPSP) caused by presynaptic spikes

LTP observed as an increase in size of EPSP for the same presynaptic input

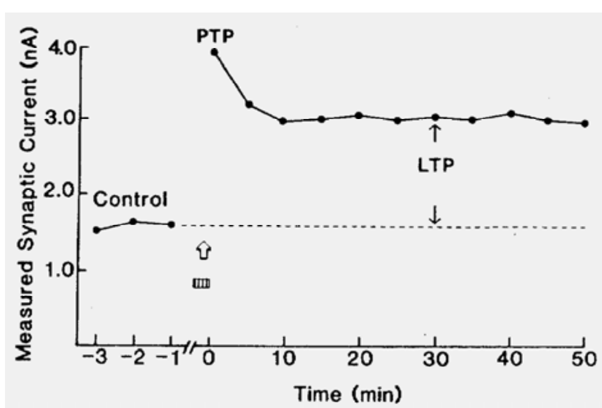


Types of Synaptic Plasticity

- Hebbian LTP: synaptic strength increases after prolonged pairing of presynaptic and postsynaptic spiking (*correlated firing of two connected neurons*).
- Long Term Depression (LTD): Reduction in synaptic strength that lasts for several hours or more
- Spike-Timing Dependent Plasticity: LTP/LTD depends on relative timing of pre/postsynaptic spiking

Example of measured synaptic plasticity

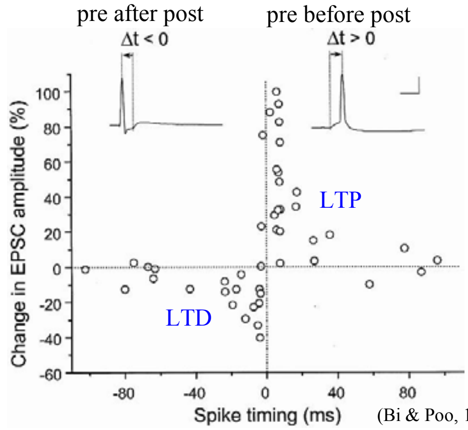
Hebbian LTP



Spike-Timing Dependent Plasticity

- Amount of increase or decrease in synaptic strength (LTP/LTD) depends on relative timing of pre & postsynaptic spikes

pre after post   pre before post



(Bi & Poo, 1998)

Comparing Neural and Digital Computing

- Device count:
  - Human Brain: 10^{11} neurons (each neuron ~ 10^4 connections)
  - Silicon Chip: 10^{10} transistors with sparse connectivity
- Device speed:
  - Biology has 100μs temporal resolution
  - Digital circuits will have a 100ps clock (10 GHz)
- Computing paradigm:
  - Brain: Massively parallel computation & adaptive connectivity
  - Digital Computers: sequential information processing via CPU with fixed connectivity
- Capabilities:
  - Digital computers excel in math & symbol processing…
  - Brains: Better at solving ill-posed problems (speech, vision)?

Conclusions and Summary

- Structure and organization of the brain suggests computational analogies
  - Information storage: Physical/chemical structure of neurons and synapses
  - Information transmission: Electrical and chemical signaling
  - Primary computing elements: Neurons
  - Computational basis: Currently unknown (but inching closer)
- We can understand neuronal computation by discerning the underlying primitives
  - Building descriptive models based on neural data
  - Simulating mechanistic models of neurons and networks
  - Formulating interpretive models of brain function

Next Class: Neural Encoding

- Things to do:
  - Visit course website
  - Sign up for mailing list (instructions on website)
  - Start reading Chapter 1