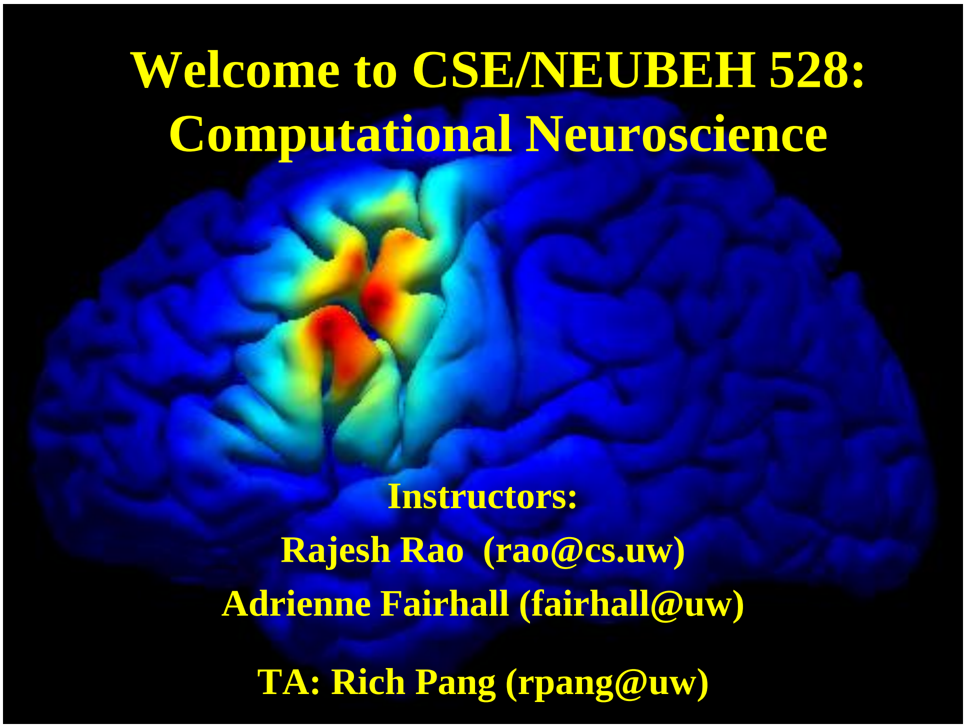
Welcome to CSE/NEUBEH 528: Computational Neuroscience



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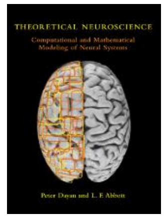
Today's Agenda

- 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://courses.cs.washington.edu/courses/cse528/17wi/
- Lecture slides will be made available on the website
- Textbooks
  - Required:
    Theoretical Neuroscience:
    Computational and Mathematical Modeling
    of Neural Systems by P. Dayan & L. 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: Be able to**
  1. Quantitatively describe what a given component of a neural system is doing based on experimental data
  2. Simulate on a computer the behavior of neurons and networks in a neural system
  3. Formulate computational principles underlying the operation of neural systems

- We would like to enhance *interdisciplinary cross-talk*

Neuroscience ⟷ Computing and Engineering

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

Workload and Grading

- Course grade (out of 4.0) will be based on homeworks and a final group project according to:
  - Homeworks: 70%
  - Final Group Project: 30%
- No midterm or final
- Homework exercises: Either written or Matlab-based
  - Go over Matlab tutorials and homework on class website
- 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

Let's begin…

What is Computational Neuroscience?

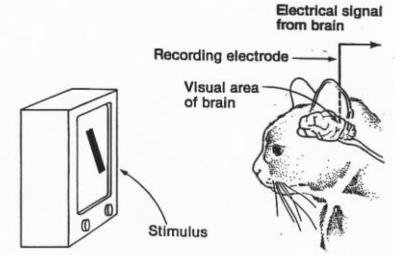
Computational Neuroscience

- "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*)

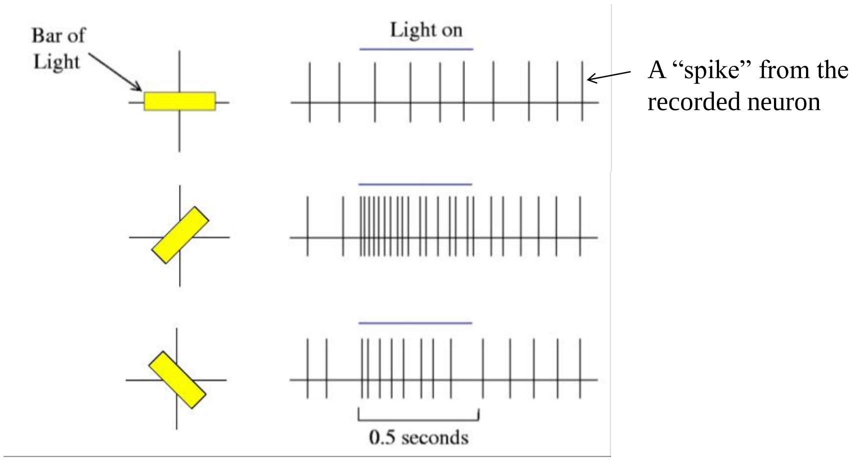
An Example: "Receptive Fields"

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

Recording the Responses of a Neuron in an Intact Brain



(Hubel and Wiesel, c. 1965)



Receptive Field

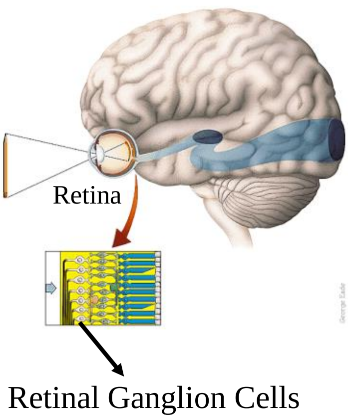
- What is the *receptive field* of a brain cell (neuron)?
- Classical Definition: The region of sensory space that activates a neuron (Hartline, 1938)
  - Example: Region on the retina that activates a visual cortex cell
- Current Definition: *Specific properties* of a sensory stimulus that generate a strong response from the cell
  - Example: A bar of light that turns on at a particular orientation and location on the retina

An Example: Cortical Receptive Fields

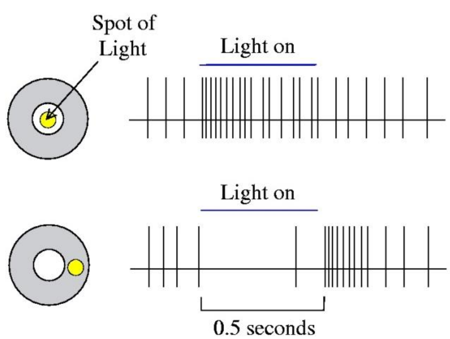
Let's look at:

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

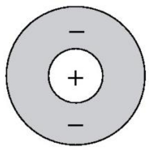


Receptive Fields in the Retina

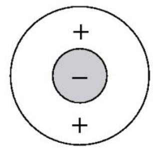


I. Descriptive Model of Receptive Fields

Center-Surround Receptive Fields in the Retina

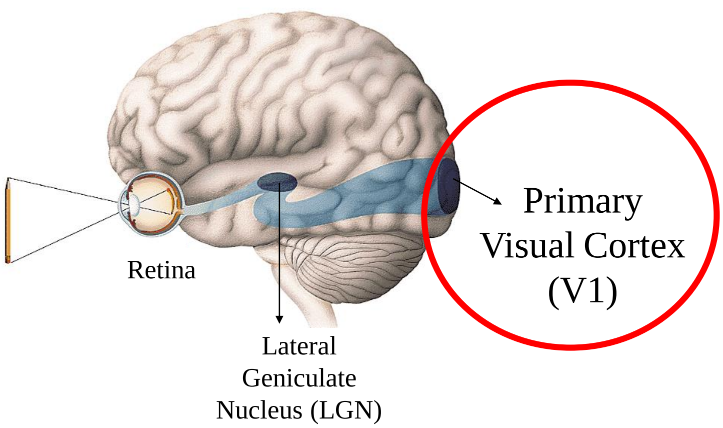


On-Center
Off-Surround
Receptive Field



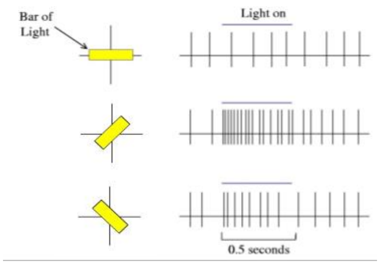
Off-Center
On-Surround
Receptive Field

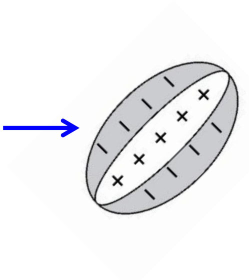
Descriptive Models: Cortical Receptive Fields



Descriptive Models: Cortical Receptive Fields

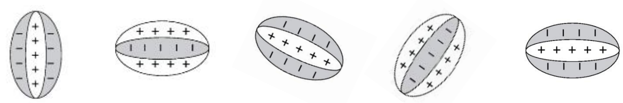
Orientation Preference



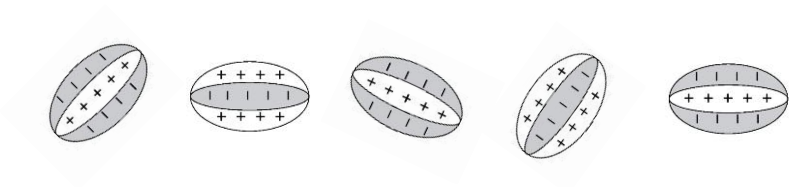


Oriented receptive field of a neuron in primary visual cortex (V1)

Other examples of oriented receptive fields

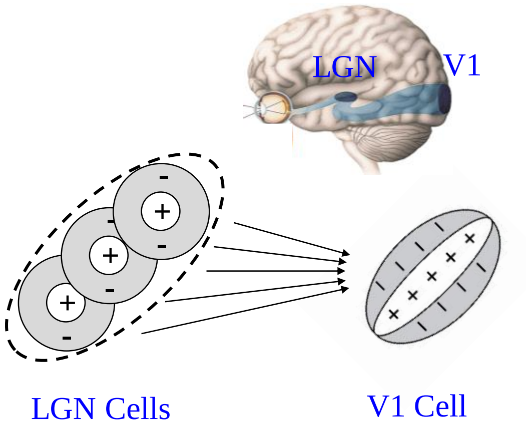


We will learn later how to quantify these using reverse correlation



How are these *oriented* receptive fields obtained from *center-surround* receptive fields?

II. Mechanistic Model of Receptive Fields: V1



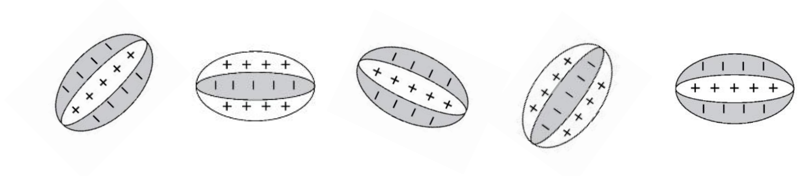
Model suggested by Hubel & Wiesel in the 1960s: V1 RFs are created from converging LGN inputs

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?

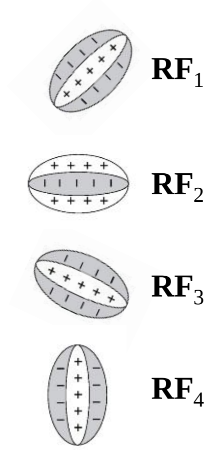
III. Interpretive Model of Receptive Fields

- Efficient Coding 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 $\mathbf{I}$, we can reconstruct $\mathbf{I}$ using neural responses $r_1, r_2 \ldots$:

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

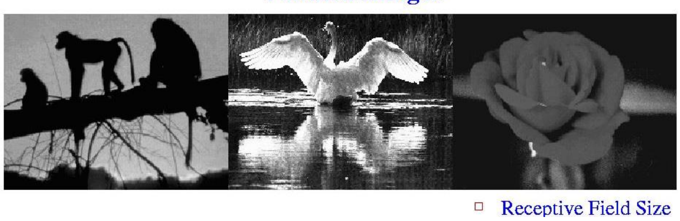
- *Idea*: What are the $\mathbf{RF}_i$ that *minimize* the total squared pixelwise errors between $\mathbf{I}$ and $\hat{\mathbf{I}}$ and are as *independent* as possible?



III. Interpretive Model of Receptive Fields

- Start out with random $\mathbf{RF}_i$ and run your efficient coding algorithm on natural image patches

Natural Images

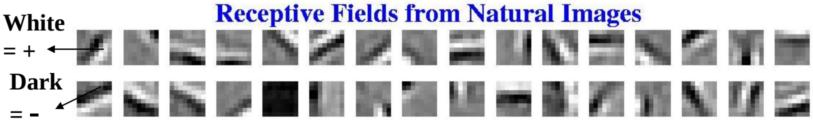


Sparse coding ICA Predictive coding

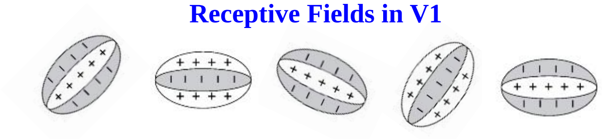
(Olshausen & Field, 1996; Bell & Sejnowski, 1997; Rao & Ballard, 1999)

III. Interpretive Model of Receptive Fields

Receptive Fields from Natural Images



Receptive Fields in V1

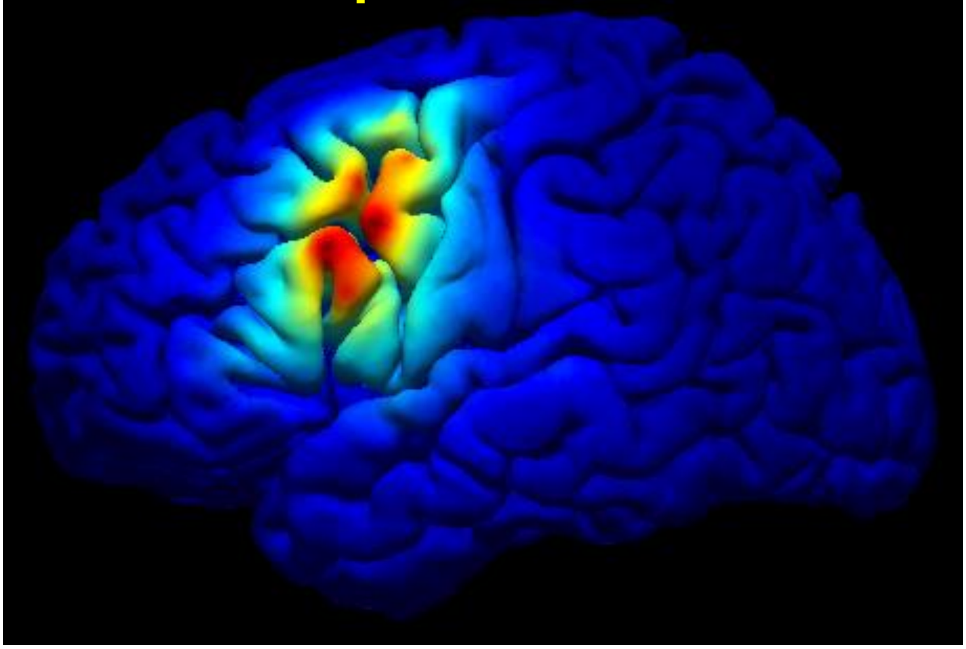


Conclusion: The brain may be trying to find *faithful and efficient* representations of an animal's natural environment

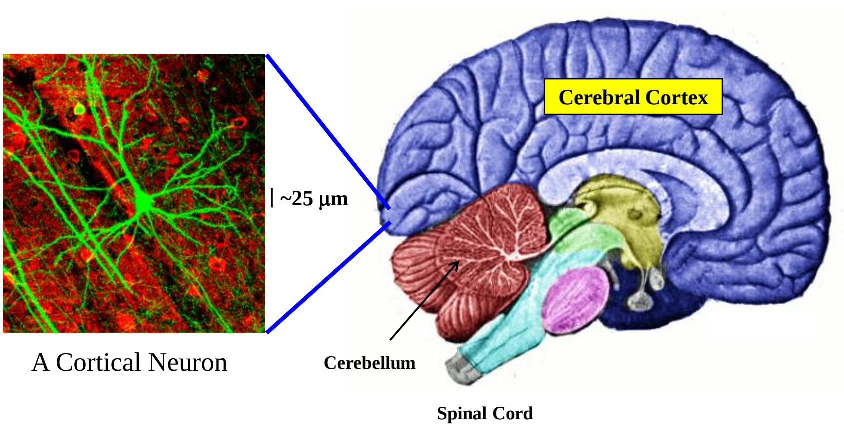
We will explore a variety of *Descriptive*, *Mechanistic*, and *Interpretive* models throughout this course

Neuroscience Review Slides:
Neurons, synapses, brain regions
(see also class web resources)

Our 3-pound universe



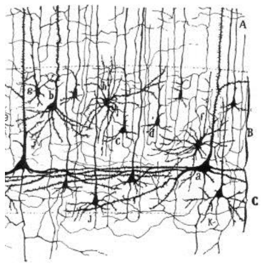
Enter…the Neuron (Brain Cell)



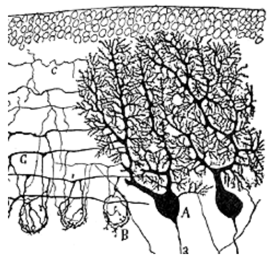
A Cortical Neuron

Image Source: Wikimedia Commons

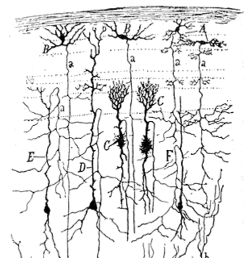
The Neuronal Zoo



Visual Cortex



Cerebellum



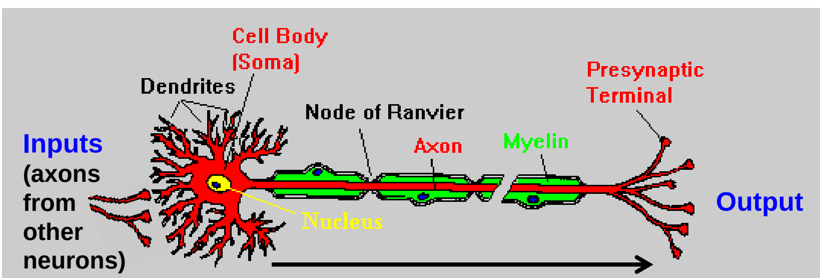
Optic Tectum

(Drawings by Ramón y Cajal, c. 1900)

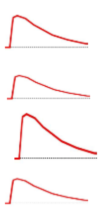
Neuron Doctrine:

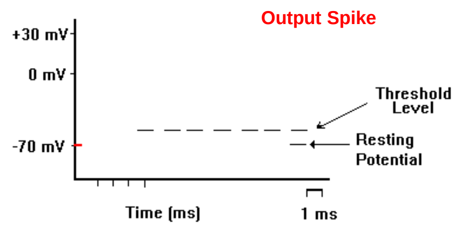
- The neuron is the fundamental structural & functional unit of the brain
- Neurons are discrete cells and not continuous with other cells
- Information flows from the dendrites to the axon via the cell body

The Idealized Neuron



EPSP = Excitatory Post-Synaptic Potential

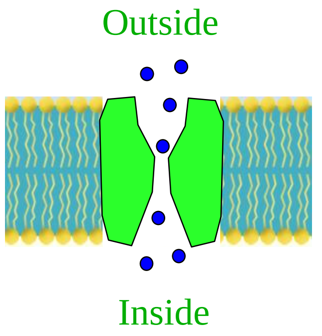




Images by Eric Chudler, UW

What is a Neuron?

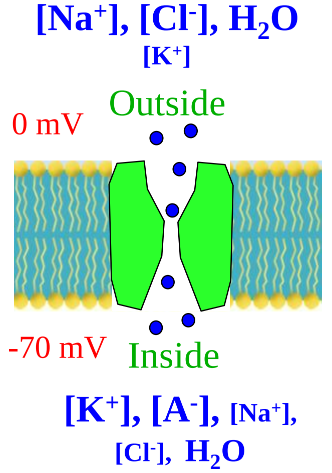
- A "leaky bag of charged liquid"
- Contents of the neuron enclosed within a *cell membrane*
- Cell membrane is a *lipid* bilayer
  - Bilayer is impermeable to charged ion species such as Na^+, Cl^-, and K^+
  - Ionic channels embedded in membrane allow ions to flow in or out



Adapted from Wikipedia

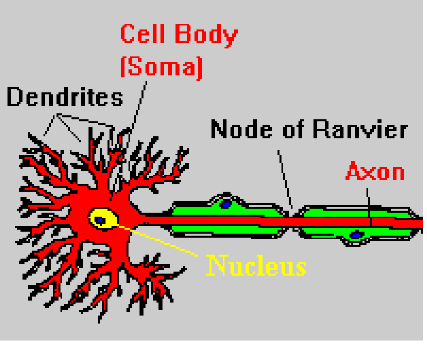
The Electrical Personality of a Neuron

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



Influencing a Neuron’s Electrical Personality

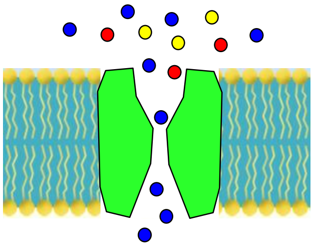
How can the electrical potential be changed in local regions of a neuron?



Ionic Channels: The Gatekeepers

- Ionic channels in membranes are proteins that are *selective* and allow only specific ions to pass through
  - E.g. Pass Na^+ but not K^+ or Cl^-
- 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

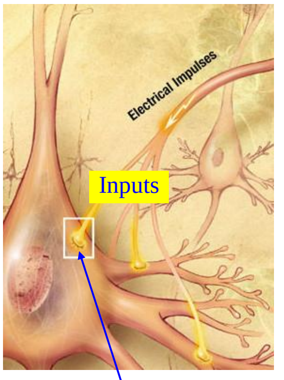
Outside



Inside

Gated Channels allow Neuronal Signaling

- Inputs from other neurons → chemically-gated channels (at "synapses") open → Changes in local membrane potential
- This in turn causes opening/closing of voltage-gated channels in dendrites, body, and axon, resulting in depolarization (positive change in voltage) or hyperpolarization (negative change in voltage)
- Strong enough depolarization causes a spike or "action potential"



Synapse (Junction between neurons)

Image Source: Wikimedia Commons

The Output of a Neuron: Action Potential (Spike)

Voltage-gated channels cause action potentials (spikes)

1. Strong depolarization opens Na^+ channels, causing rapid *Na^+ influx* and more channels to open, until they inactivate
2. *K^+ outflux* restores membrane potential

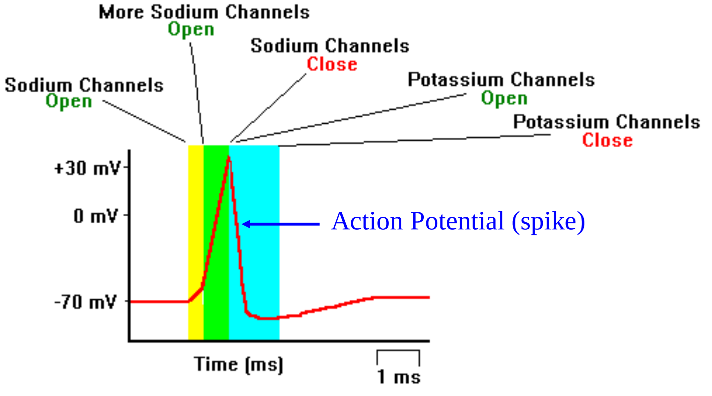
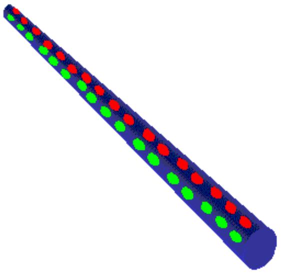


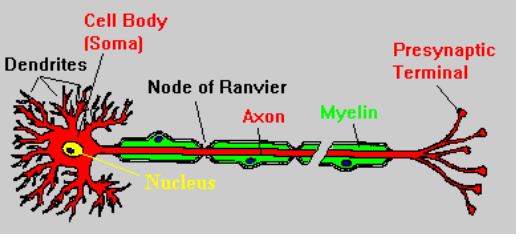
Image by Eric Chudler, UW

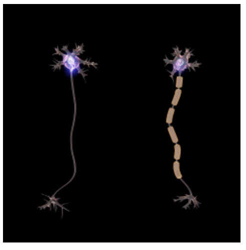
Propagation of a Spike along an Axon



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

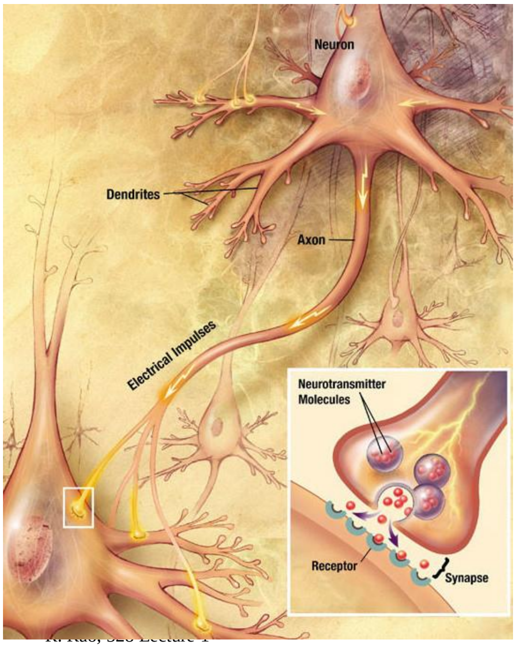
Active Wiring: Myelination of Axons





- Myelin due to oligodendrocytes (glial cells) wrap axons and enable *fast long-range spike communication*
  - Action potential "hops" from one non-myelinated region (node of Ranvier) to the next (*saltatory conduction*)
  - "Active wire" allows lossless signal propagation

Image Source: Wikimedia Commons



What happens to the spike (action potential) when it reaches the end of an axon?

Enter…
the Synapse

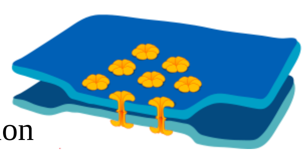
Image Source: Wikimedia Commons

What is a Synapse?

- A Synapse is a "connection" or junction between two neurons
  - Electrical synapses use *gap junctions*
  - Chemical synapses use *neurotransmitters*

Neuron A

Gap junction



Neuron B

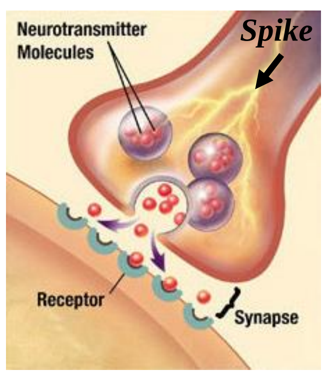
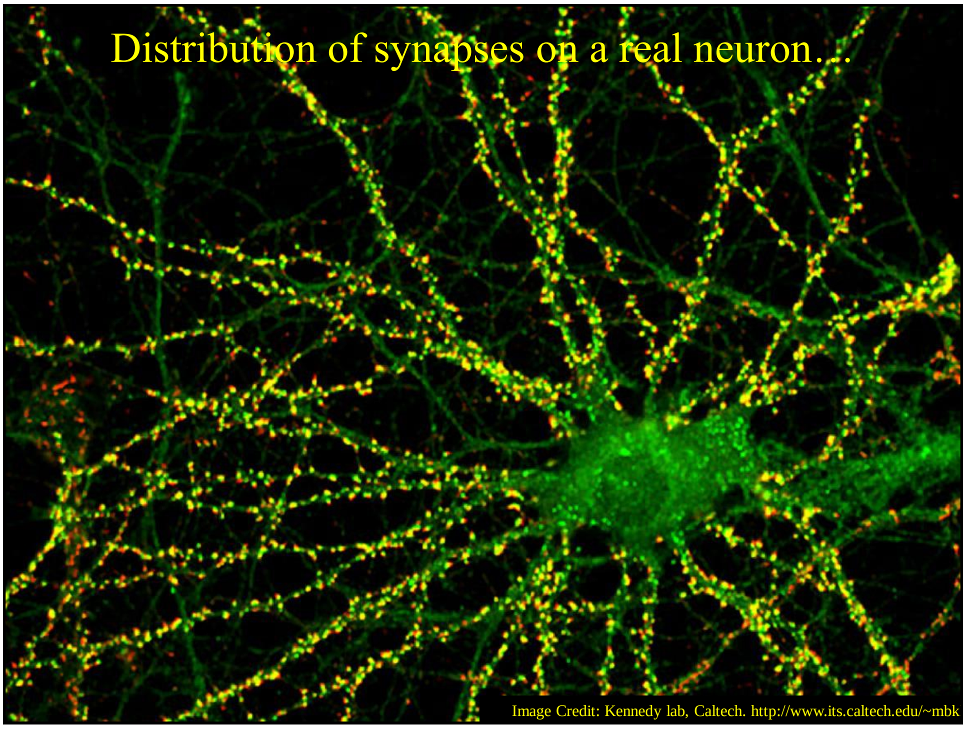
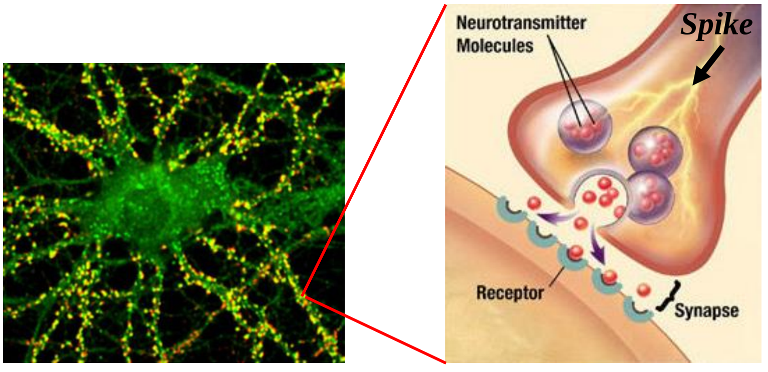


Image Source: Wikimedia Commons



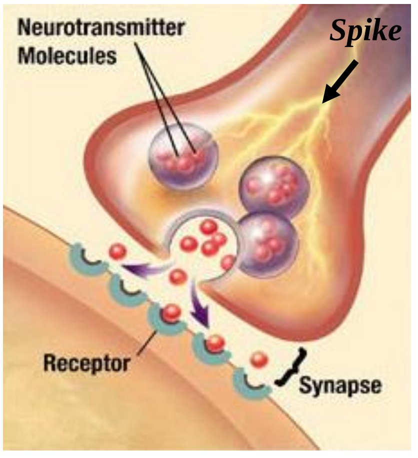
Synapses can be Excitatory or Inhibitory



Increase or decrease postsynaptic membrane potential

Image Source: Wikimedia Commons

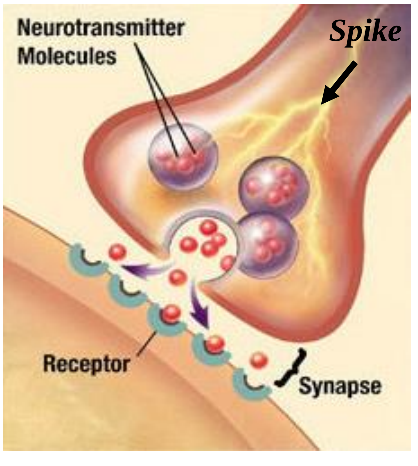
An **Excitatory** Synapse



Input spike → Neurotransmitter release (e.g., Glutamate) → Binds to ion channel receptors → Ion channels open → Na+ influx → Depolarization due to EPSP (excitatory postsynaptic potential)

Image Source: Wikimedia Commons

An **Inhibitory** Synapse

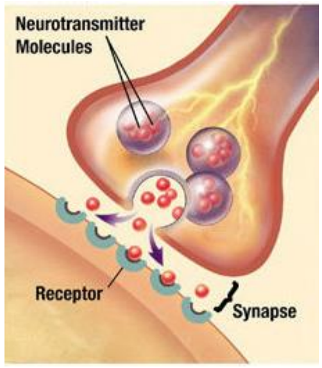


Input spike → Neurotransmitter release (e.g., GABA) → Binds to ion channel receptors → Ion channels open → Cl- influx→ Hyperpolarization due to IPSP (inhibitory postsynaptic potential)

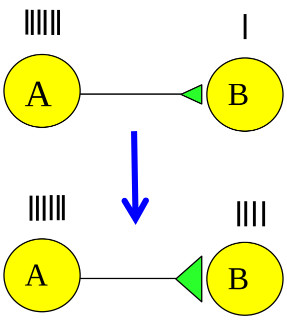
Image Source: Wikimedia Commons

The Synapse Doctrine

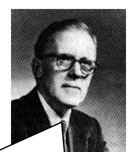
Synapses are the basis for memory and learning



How do Brains Learn? Synaptic Plasticity



Hebbian Plasticity



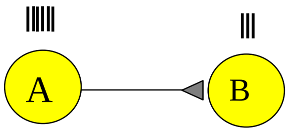
If neuron A repeatedly takes part in firing neuron B, then the synapse from A to B is strengthened

"Neurons that fire together wire together!"

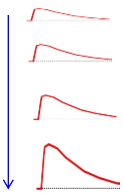
Image Source: Wikimedia Commons

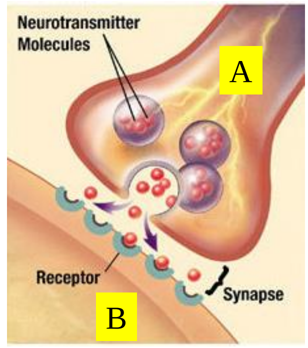
Long Term Potentiation (LTP)

LTP = Experimentally observed *increase* in synaptic strength that lasts for hours or days



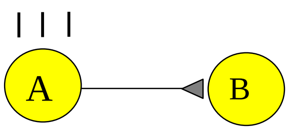
Increase in EPSP size for same input over time



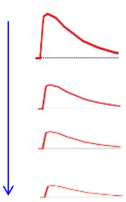


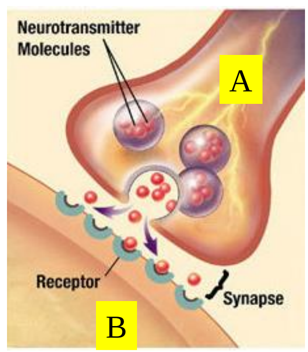
Long Term Depression (LTD)

LTD = Experimentally observed *decrease* in synaptic strength that lasts for hours or days



Decrease in EPSP size for same input over time

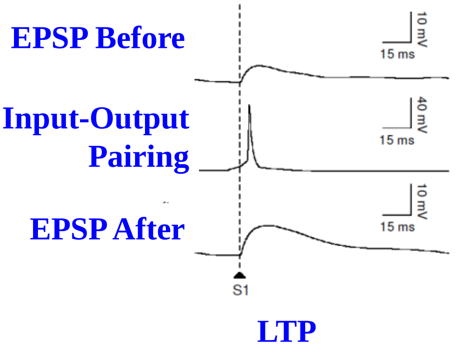




Synaptic Plasticity depends on Spike Timing!

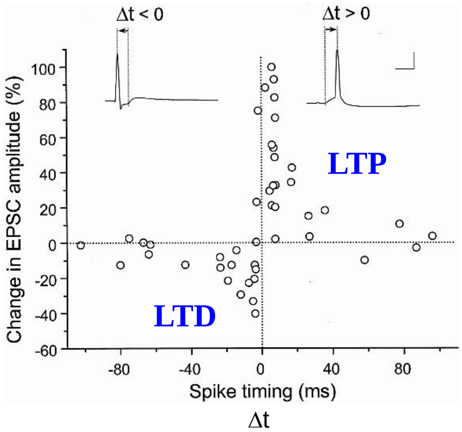
LTP/LTD depends on relative timing of input and output spikes

Input Spike before Output Spike



Spike-Timing Dependent Plasticity (STDP)

Input after Output Input before Output



(Bi & Poo, 1998)

We seem to know a lot about channels, neurons, and synapses…

What do we know about how networks of neurons give rise to perception, behavior, and consciousness?

Not as much

Next: Brain organization and information processing in networks of neurons

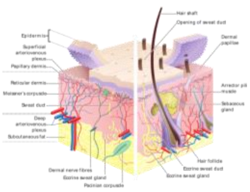
Organization and Function of the Nervous System

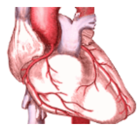
Peripheral Nervous System (PNS)

Somatic | **Autonomic**

Central Nervous System (CNS)

Brain | **Spinal Cord**





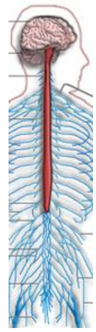
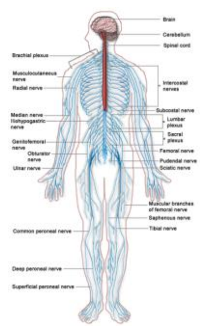


Image Source: Wikimedia Commons

Peripheral Nervous System (PNS)

Somatic: Nerves connecting to voluntary skeletal muscles and sensory receptors

- ***Afferent* Nerve Fibers (incoming)**: Axons that carry info away from the periphery to the CNS
- ***Efferent* Nerve Fibers (outgoing)**: Axons that carry info from the CNS outward to the periphery



Autonomic: Nerves that connect to the heart, blood vessels, smooth muscles, and glands

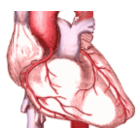
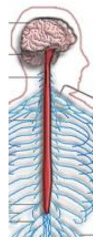


Image Source: Wikimedia Commons

Central Nervous System (CNS)

CNS = Spinal Cord + Brain



Spinal Cord

- Local feedback loops control reflexes ("reflex arcs")
- Descending motor control signals from the brain activate spinal motor neurons
- Ascending sensory axons convey sensory information from muscles and skin back to the brain

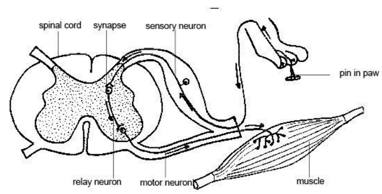
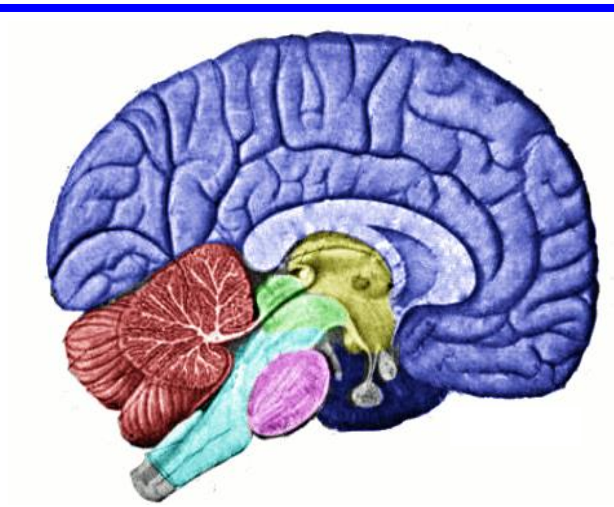


Image Source: Wikimedia Commons

CNS = Spinal Cord + **Brain**



Major Brain Regions: The Hindbrain

Medulla Oblongata
Controls breathing, muscle tone and blood pressure

Pons
Connected to the cerebellum & involved in sleep and arousal

Cerebellum
Coordination and timing of voluntary movements, sense of equilibrium, language, attention,…

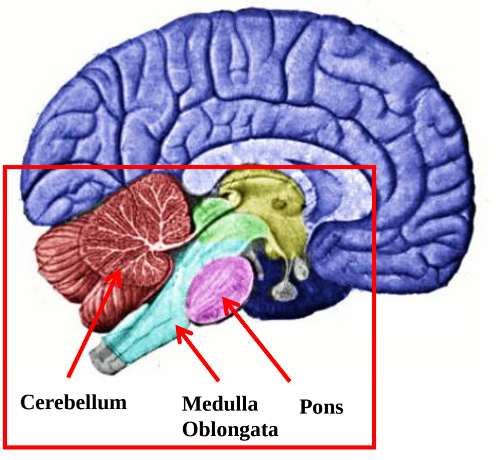
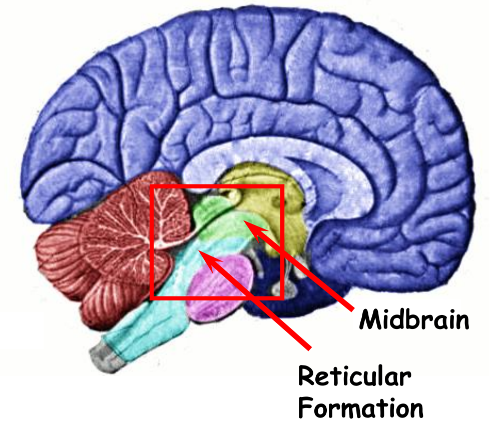


Image Source: Wikimedia Commons

Major Brain Regions: Midbrain & Retic. Formation

Midbrain
Eye movements, visual and auditory reflexes

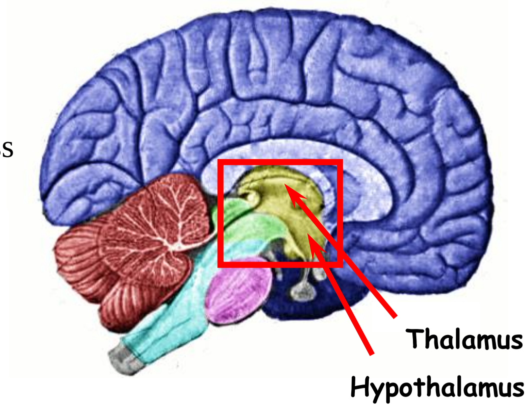
Reticular Formation
Modulates muscle reflexes, breathing & pain perception. Also regulates sleep, wakefulness & arousal



Major Brain Regions: Thalamus & Hypothalamus

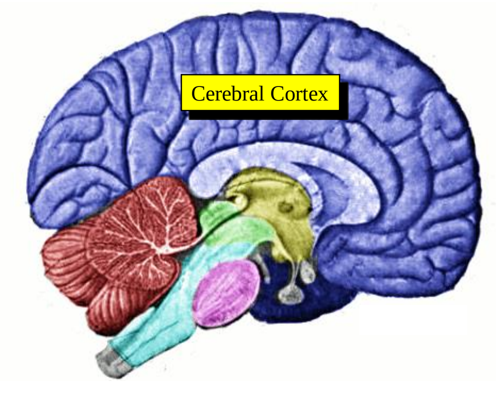
Thalamus
"Relay station" for all sensory info (except smell) to the cortex, regulates sleep/wakefulness

Hypothalamus
Regulates basic needs
Fighting, Fleeing, Feeding, and Mating



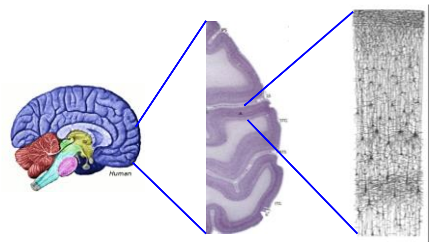
Major Brain Regions: The Cerebrum

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



Cerebral Cortex: A Layered Sheet of Neurons

- ✦ Cerebral Cortex: Convoluted surface of cerebrum, about 1/8th of an inch thick
  - Approximately 30 billion neurons
  - Each neuron makes about 10,000 synapses, approximately 300 trillion connections in total



- ✦ Six layers of neurons
  - Relatively uniform in structure
  - Is there a common computational principle operating across cortex?

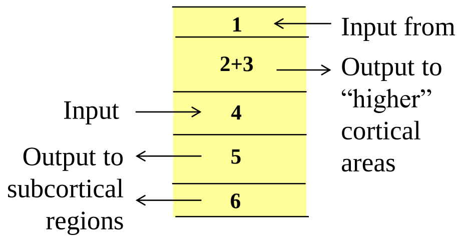


Image Source: Wikimedia Commons

How do all of these brain regions interact to produce cognition and behavior?

Don't know fully yet!

But inching closer based on:

- electrophysiological,
- optogenetic,
- molecular,
- functional imaging,
- psychophysical,
- anatomical,
- connectomic,
- lesion (brain damage) studies…

Neural versus 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 are approaching a 100ps clock (10 GHz)
- Computing paradigm:
  - Brain: Massively parallel computation & adaptive connectivity
  - Digital Computers: sequential information processing via CPUs with fixed connectivity
- Capabilities:
  - Digital computers excel in math & symbol processing…
  - Brains: Better at solving ill-posed problems (speech, vision)
  - Deep neural networks: Best of both worlds?

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 getting closer)
- We can understand neuronal computation by understanding the underlying primitives through:
  - Descriptive models
  - Mechanistic models
  - Interpretive models

Next Class

- Mathematical Foundations of Comp Neurosci.
  - **Lecture by our TA Rich Pang**
- Things to do:
  - Visit course website http://www.cs.washington.edu/education/courses/528/17wi
  - Matlab practice: Homework 0 and tutorials online
  - Read Chapter 1 in Dayan & Abbott textbook