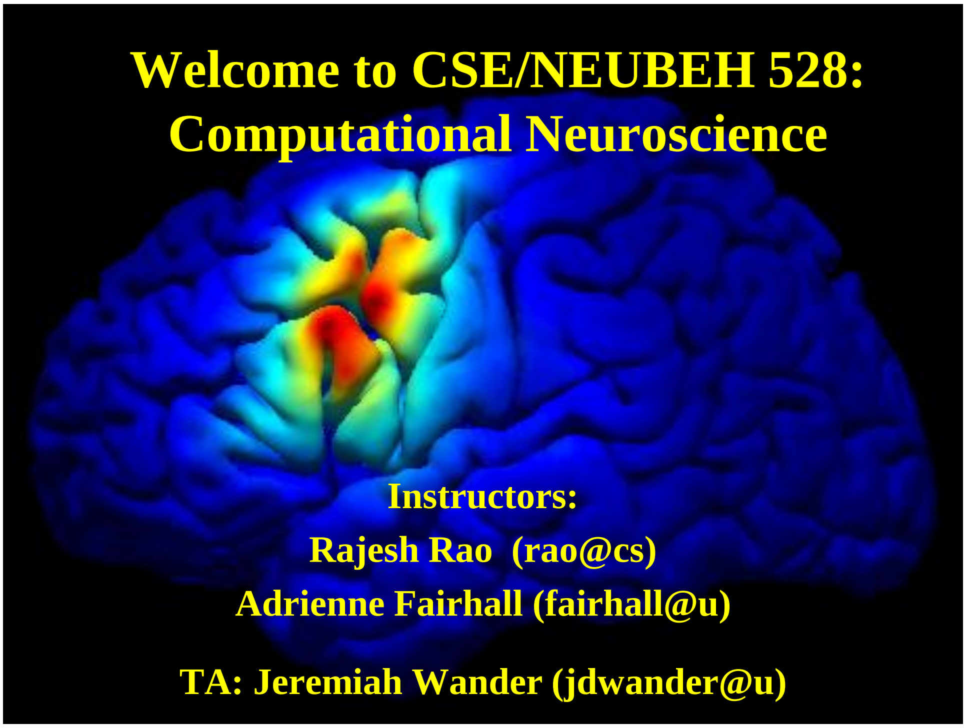
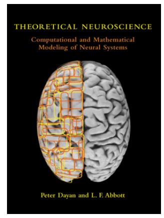



# Today's Agenda

- 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://www.cs.washington.edu/education/courses/528/
- 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

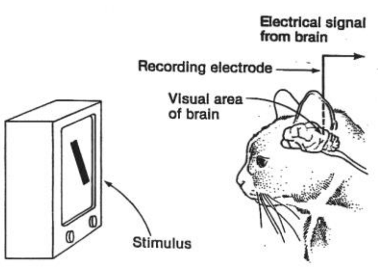
- "The goal of computational neuroscience is to explain in computational terms *how brains generate behaviors*" (Sejnowski)
- Computational neuroscience provides tools and methods for "characterizing *what* nervous systems do, determining *how* they function, and understanding *why* they operate in particular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

## An Example: “Receptive Fields”

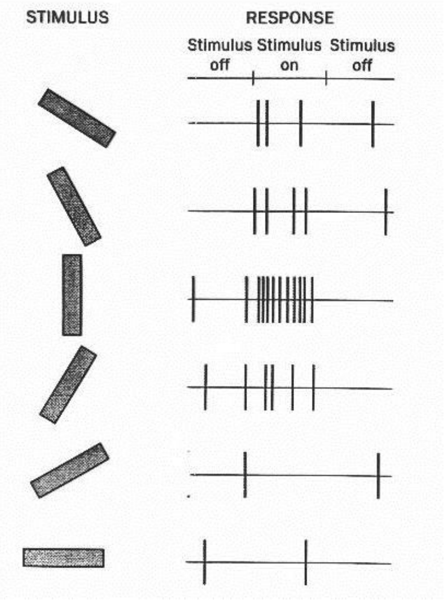
- What is the *receptive field* of a brain cell (neuron)?
  - Any ideas?



## 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

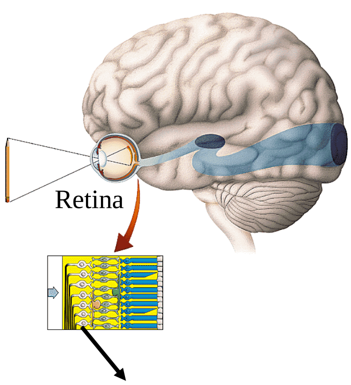
# An Example: Cortical Receptive Fields

Let's look at:

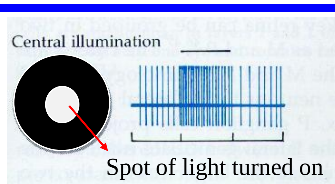
I. A *Descriptive Model* of Receptive Fields
II. A *Mechanistic Model* of Receptive Fields
III. An *Interpretive Model* of Receptive Fields



# I. Descriptive Model of Receptive Fields



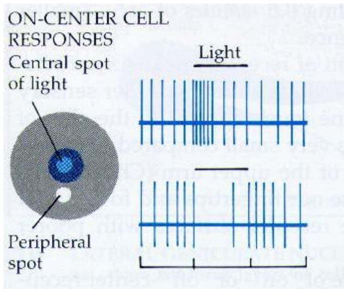

Retinal Ganglion Cells

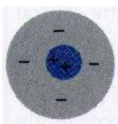



Output responses (spike trains) from a Retinal Ganglion Cell

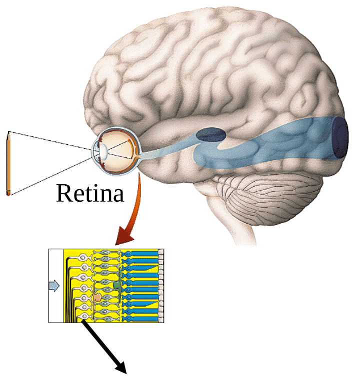
# I. Descriptive Model of Receptive Fields

Mapping a retinal receptive field with spots of light



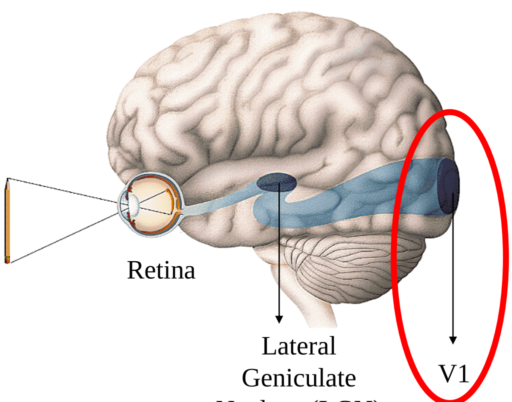



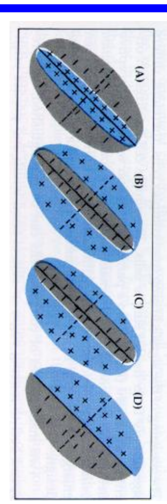
On-Center
Off-Surround
Receptive Field






# Descriptive Models: Cortical Receptive Fields



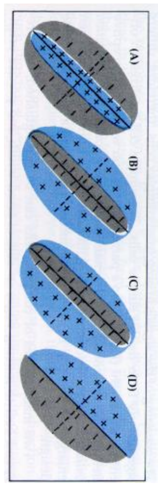



Examples of receptive fields in primary visual cortex (V1)

(From Nicholls et al., 1992)

# II. Mechanistic Model of Receptive Fields

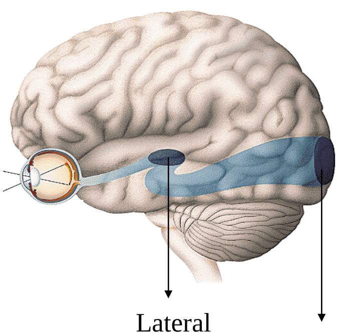
- The Question: *How* are receptive fields constructed using the neural circuitry of the visual cortex?

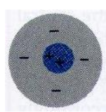


How are these *oriented* receptive fields obtained?



# II. Mechanistic Model of Receptive Fields: V1

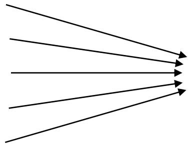


LGN RF

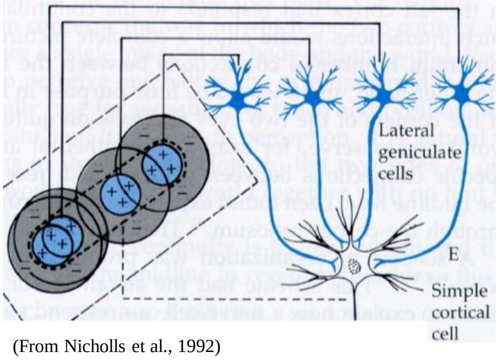
V1 RF

LGN Cells



V1 Cell

# 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

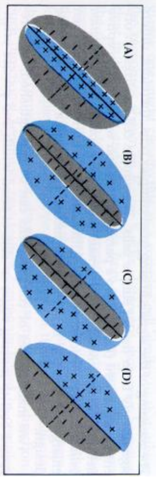
Center-surround LGN RFs are *displaced along preferred orientation* of V1 cell

This simple model is still controversial!



# III. Interpretive Model of Receptive Fields

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

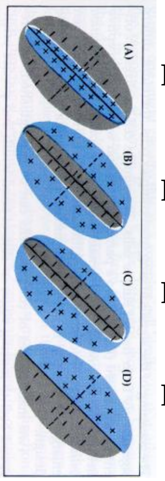



What are the computational advantages of such receptive fields?

## 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 $r_1, r_2 \ldots$:

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



$\mathbf{RF}_1$

$\mathbf{RF}_2$

$\mathbf{RF}_3$

$\mathbf{RF}_4$



## III. Interpretive Model of Receptive Fields

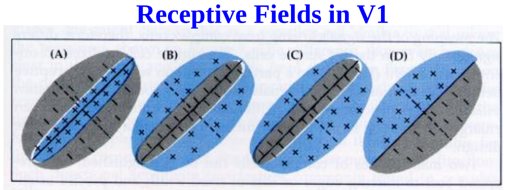
- Start out with random $\mathbf{RF}_i$ and run your algorithm on natural images

**Natural Images**

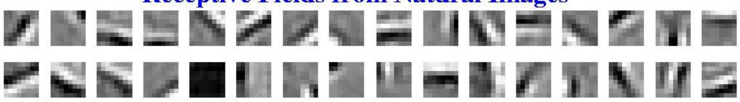
# III. Interpretive Model of Receptive Fields

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

**Receptive Fields in V1**




**Receptive Fields from Natural Images**





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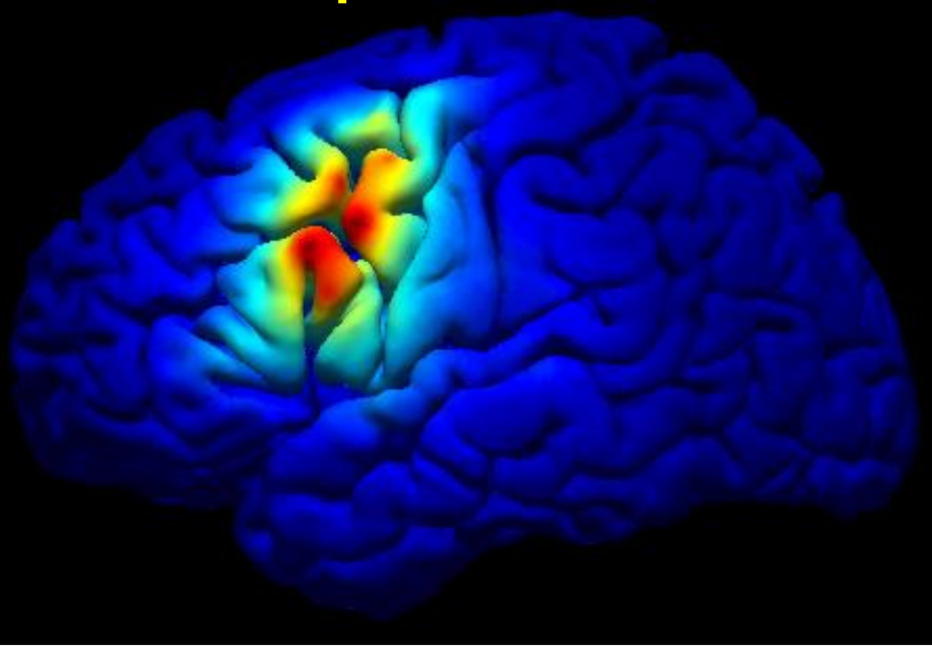
We will explore a variety of *Descriptive*, *Mechanistic*, and *Interpretive* models throughout this course

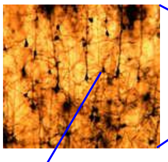
Neurobiology 101:
Brain regions, neurons, and synapses

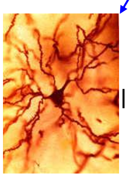


# Our 3-pound universe

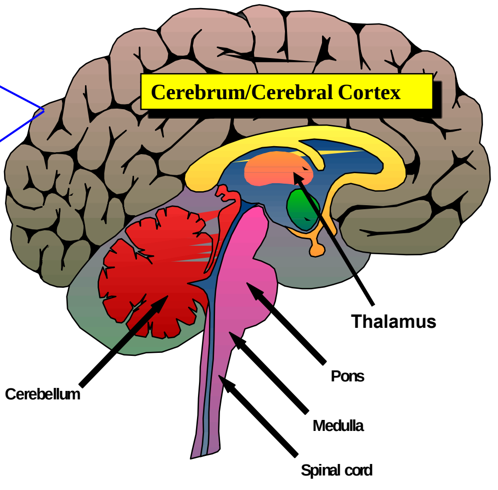


# Enter…the neuron ("brain cell")



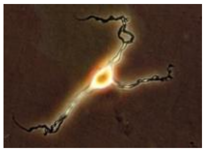



A Pyramidal Cortical Neuron



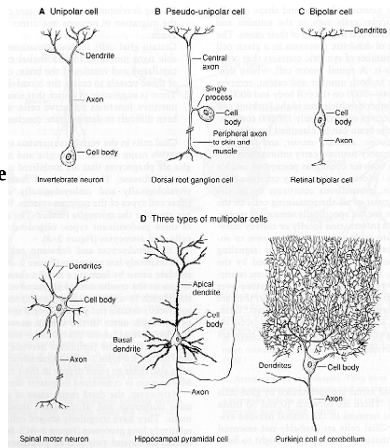
# The Neuronal Zoo

**Neuron from Cerebral Cortex**



**Neuron from the Thalamus**

**Neuron from the Cerebellum**

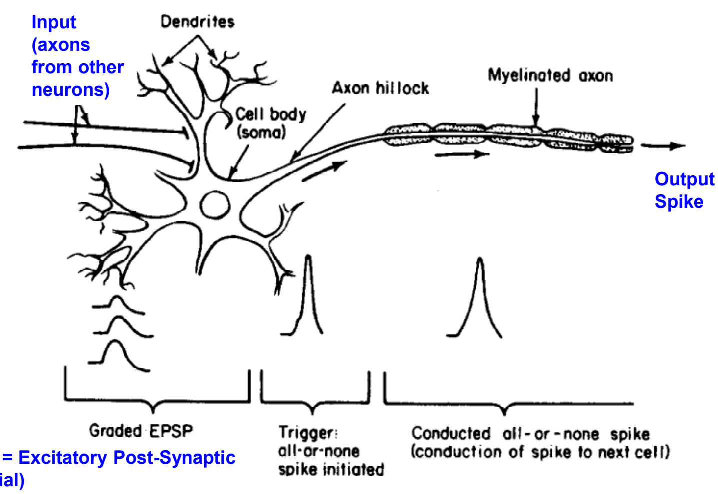



From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pg. 21

**Neuron Doctrine**:
"The neuron is the appropriate basis for understanding the computational and functional properties of the brain"
First suggested in 1891 by Waldeyer



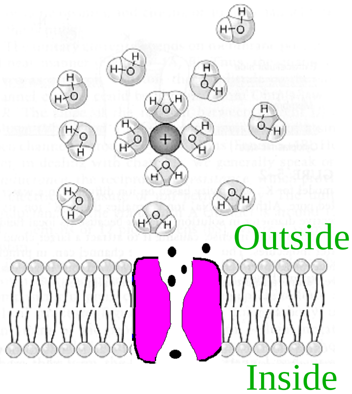
# The Idealized Neuron




(EPSP = Excitatory Post-Synaptic Potential)

## 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 $Ca^{2+}$
  - Ionic channels embedded in membrane allow ions to flow in or out

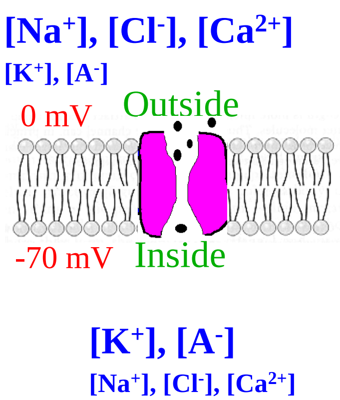



**From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pg. 67**



## 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



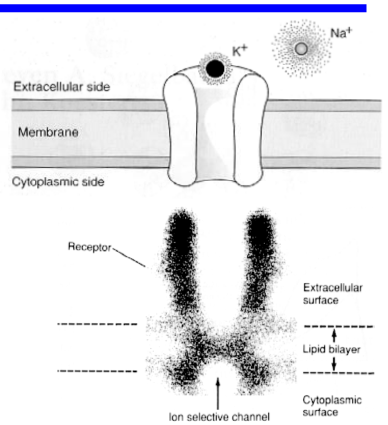
## Influencing a Neuron's Electrical Personality

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



## Ionic Channels: The Gatekeepers

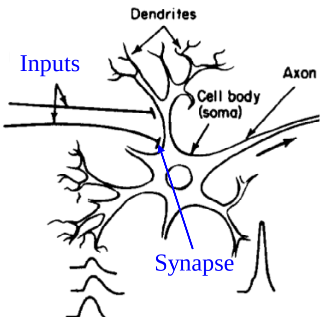
- Proteins in membranes act as channels that allow specific ions to pass through.
  - E.g. Pass $K^+$ but not $Cl^-$ or $Na^+$
- These "ionic channels" are *gated*
  - Voltage-gated: Probability of opening depends on membrane voltage
  - Chemically-gated: Binding to a chemical causes channel to open
  - 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

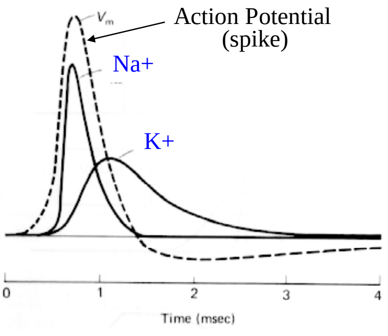
- Inputs from other neurons → chemically-gated channels (at "synapses") → Changes in local membrane potential
- This causes opening/closing of voltage-gated channels in dendrites, body, and axon, resulting in depolarization (positive change in voltage) or hyperpolarization (negative change)





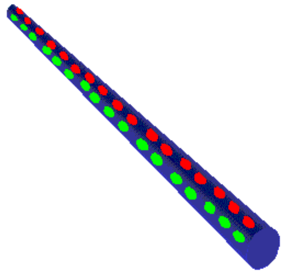

## The Output of a Neuron: Action Potentials

- Voltage-gated channels cause action potentials (spikes)
  1. Strong depolarization causes rapid *$Na^+$ influx* until channels inactivate
  2. *$K^+$ outflux* restores membrane potential
- Positive feedback causes spike
  - $Na^+$ influx *increases* membrane potential, causing *more* $Na^+$ influx until inactivation




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

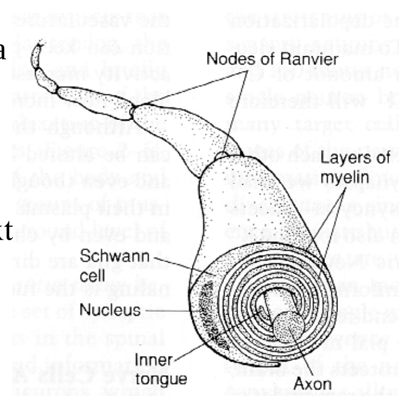
# Propagation of a Spike along an Axon



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

# Active Wiring: Myelination of axons

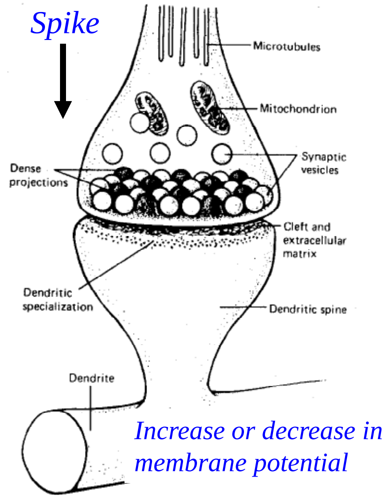
- Myelin due to Schwann cells (aka glia) wrap axons and enables *long-range spike communication*
  - Action potential "hops" from one non-myelinated region ("node of Ranvier") to the next
  - "Active wire" allows lossless signal propagation, unlike electric signals in a copper wire




**From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pgs. 23 & 44**

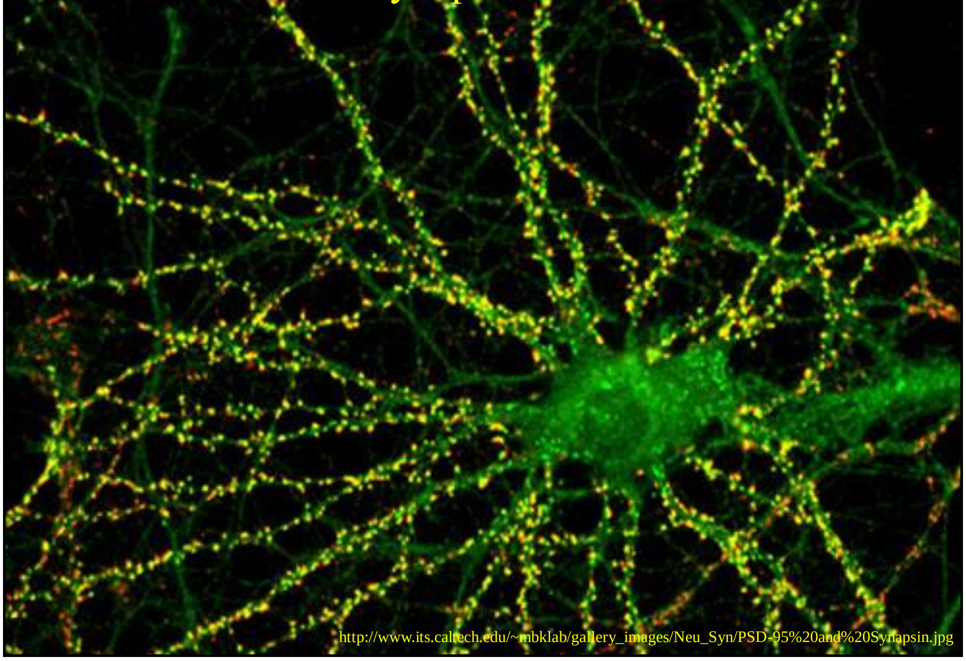
## Communication between Neurons: Synapses

- [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



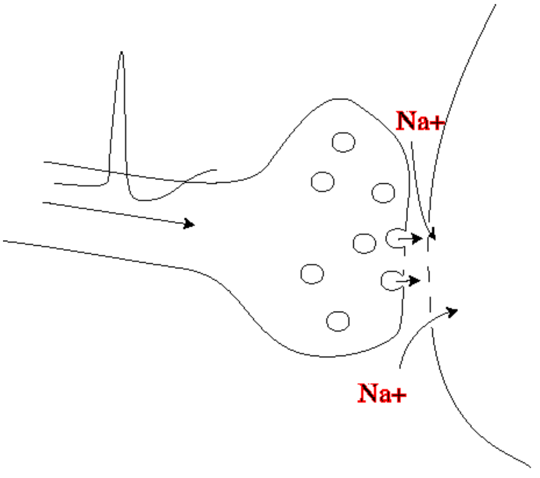



## Distribution of synapses on a real neuron…



http://www.its.caltech.edu/~mbklab/gallery_images/Neu_Syn/PSD-95%20and%20Synapsin.jpg

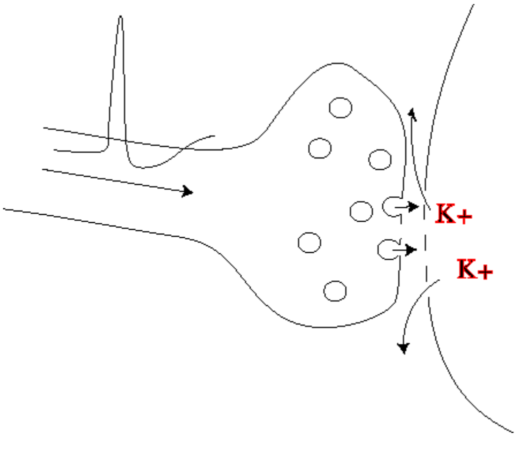
## An **Excitatory** Synapse




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



## An **Inhibitory** Synapse



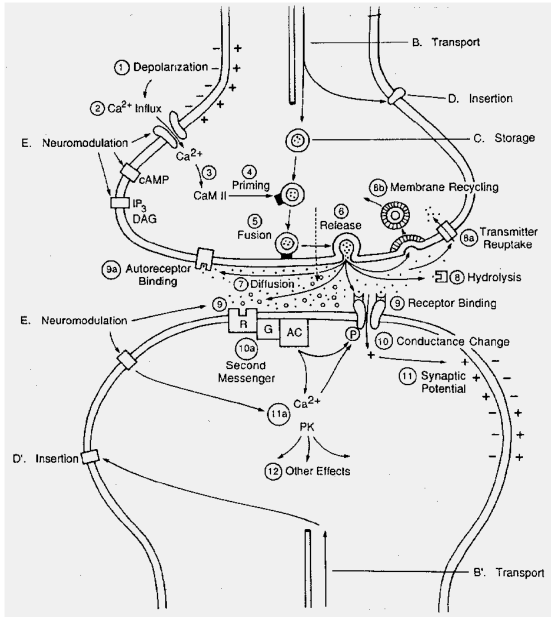

Input spike →
Neurotransmitter release →
Binds to K channels →
K+ leaves cell →
Hyperpolarization due to IPSP (inhibitory postsynaptic potential)

# 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

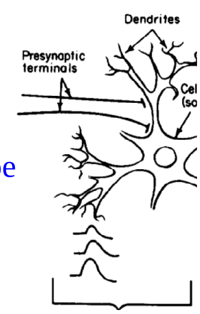





# Synaptic plasticity: Adapting the connections

- 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 or slope of EPSP for the same presynaptic input



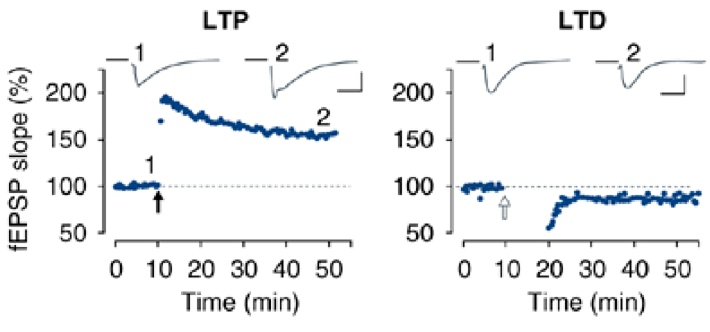

**EPSP**

# Types of Synaptic Plasticity

- Long Term Potentiation (LTP): Increase in synaptic strength that lasts for several hours or more
- Long Term Depression (LTD): Reduction in synaptic strength that lasts for several hours or more



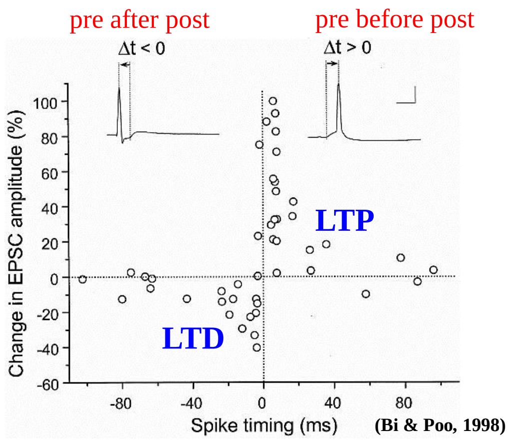
# Example of measured synaptic plasticity




(From: http://www.nature.com/npp/journal/v33/n1/fig_tab/1301559f1.html)

# Spike-Timing Dependent Plasticity

- Amount of LTP/LTD depends on relative timing of pre & postsynaptic spikes



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We seem to know a lot about channels, single 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

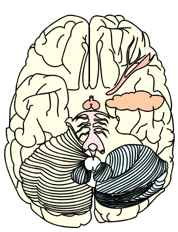


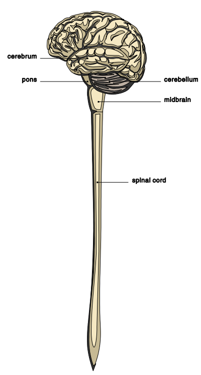
## Organization of the Nervous System

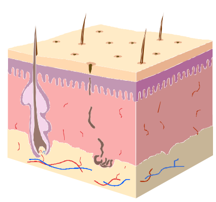
**Central Nervous System**

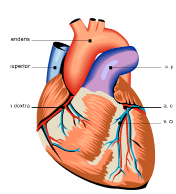
**Peripheral Nervous System**

**Brain** **Spinal Cord** **Somatic** **Autonomic**



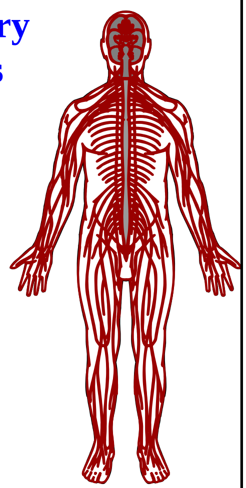




## Somatic Nervous System

**These are nerves that connect to voluntary skeletal muscles and to sensory receptors**



**Afferent Nerve Fibers (incoming)**

Axons that carry info away from the periphery to the CNS

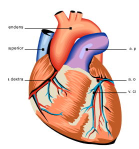
**Efferent Nerve Fibers (outgoing)**

Axons that carry info from the CNS outward to the periphery



## Autonomic and Central Nervous System

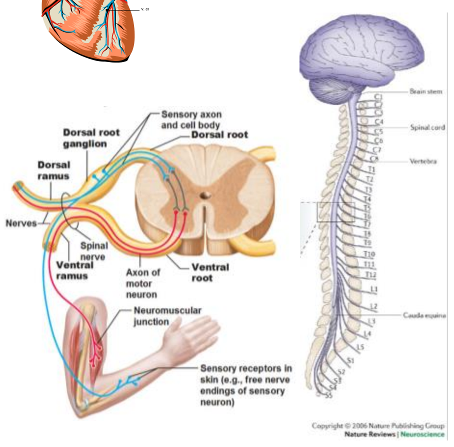
**Autonomic**: Nerves that connect to the heart, blood vessels, smooth muscles, and glands



**CNS** = **Brain + Spinal Cord**

**Spinal Cord**:

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

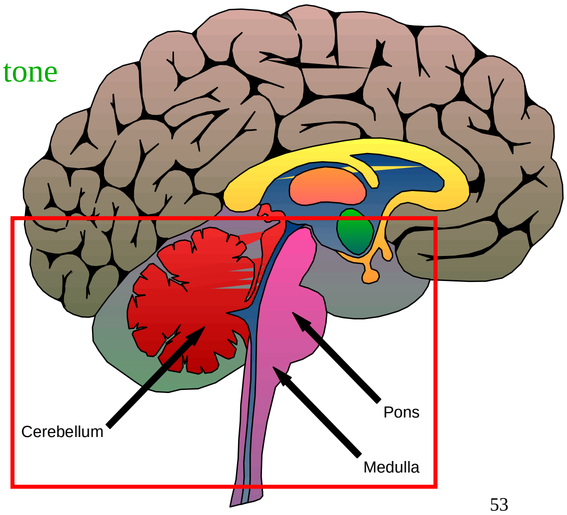


# Major Brain Regions: Brain Stem & Cerebellum

Medulla
Controls breathing, muscle tone and blood pressure

Pons
Connected to the cerebellum & involved in sleep and arousal

Cerebellum
Coordination of voluntary movements and sense of equilibrium

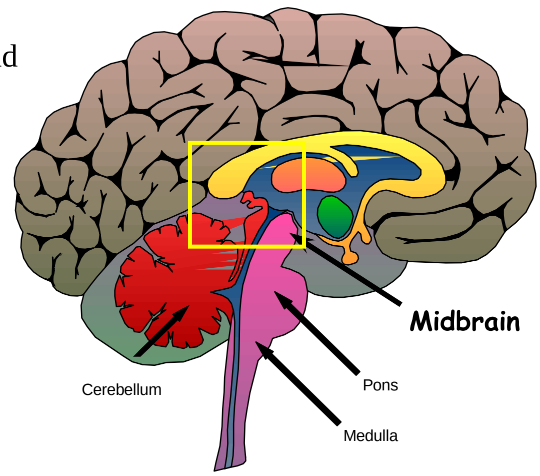





# Major Brain Regions: Midbrain & Retic. Formation

Midbrain
Eye movements, visual and auditory reflexes

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



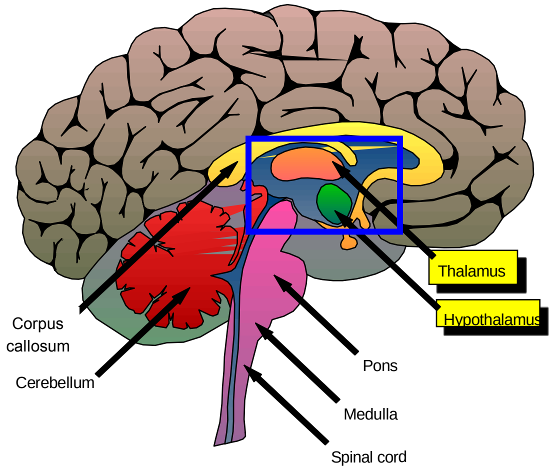
## Major Brain Regions: Thalamus & Hypothalamus

Thalamus

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

Hypothalamus

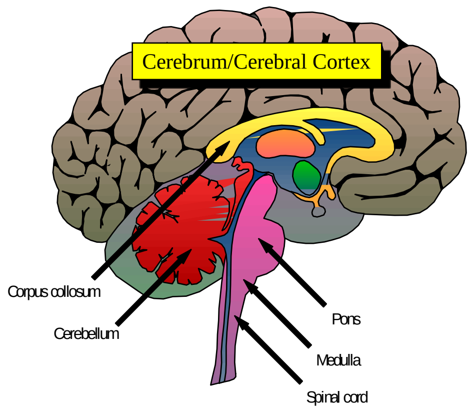
Regulates basic needs fighting, fleeing, feeding, and mating





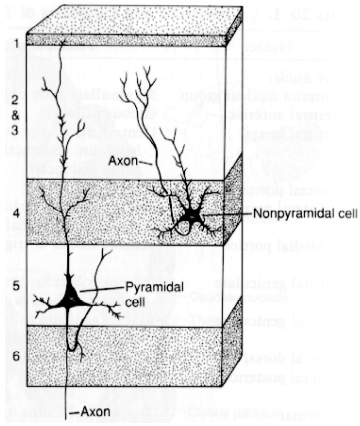

## Major Brain Regions: Cerebral Hemispheres

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



## Cerebral Cortex: A Layered Sheet of Neurons

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




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



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

Don't know fully yet!

But inching closer based on electrophysiological, imaging, molecular, psychophysical, anatomical and 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)

## 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

- Descriptive Models
  - **Neural Encoding**
- Things to do:
  - Visit course website http://www.cs.washington.edu/education/courses/528/
  - Matlab practice: Homework 0 and tutorials online
  - Read Chapter 1 in Dayan & Abbott textbook