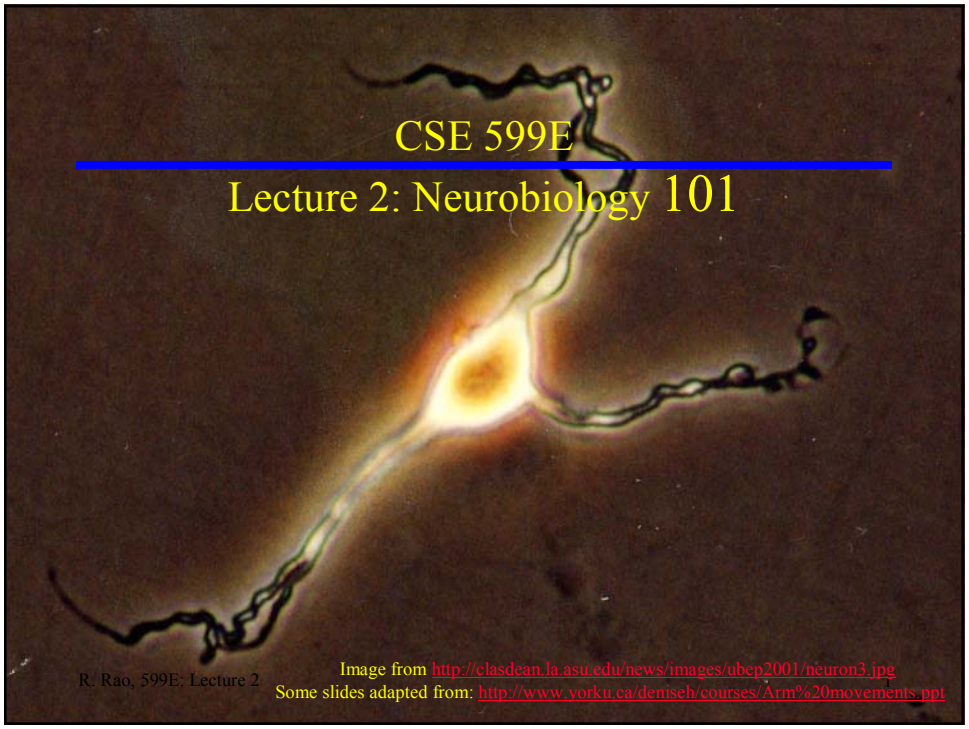


CSE 599E

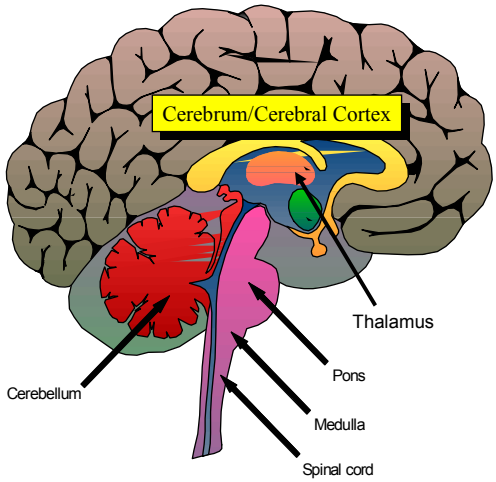
Lecture 2: Neurobiology 101

Image from http://clasdean.la.asu.edu/news/images/ubep2001/neuron3.jpg
Some slides adapted from: http://www.yorku.ca/deniseh/courses/Arm%20movements.ppt

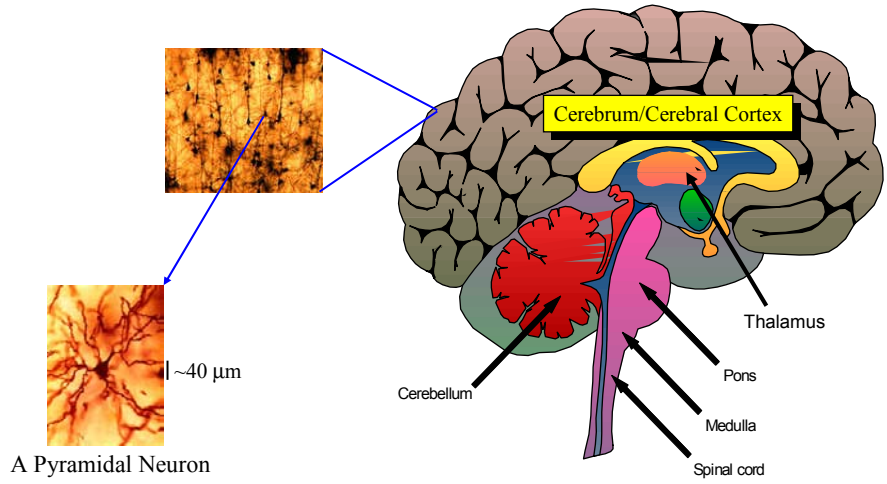
Today's Roadmap

- The neuron doctrine (or dogma)
- Neuronal signaling
  - The electrochemical dance of ions
  - Action Potentials (= spikes)
  - Synapses and Synaptic Plasticity
- Brain organization and anatomy
- Information processing in the brain
  - Focus on: Properties of neurons in the motor cortex and potential applications in BCI

Our 3-pound Universe

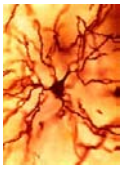


Enter…the neuron ("brain cell")

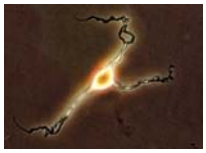


A Pyramidal Neuron

The Neuron Doctrine/Dogma

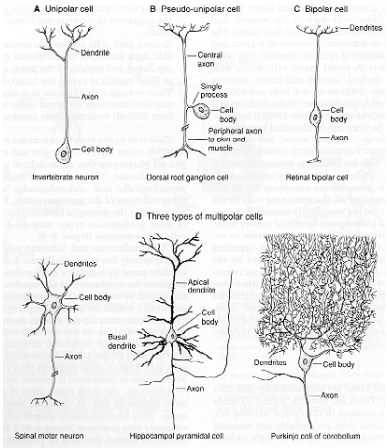


Cerebral Cortex Neuron



Neuron from the Thalamus

Neuron from the Cerebellum



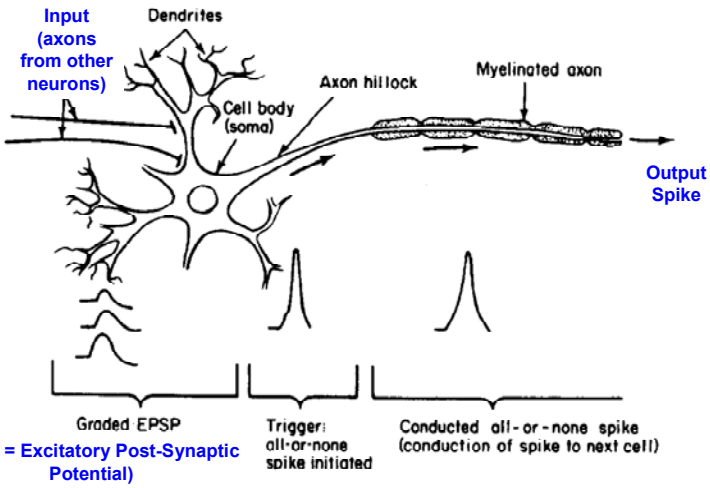
From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pg. 21

Neuron Doctrine:

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

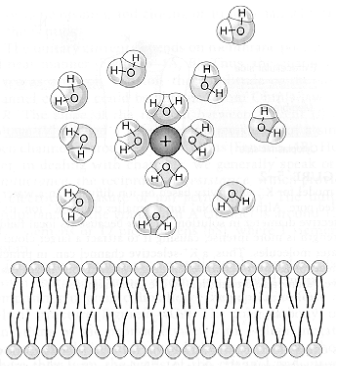
First suggested in 1891 by Waldeyer

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

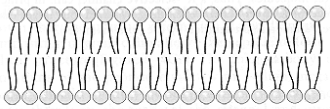
The Electrical Personality of a Neuron

- 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



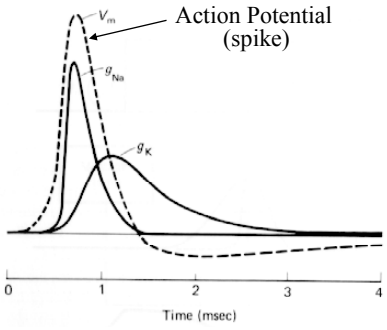
-70 mV Inside

$[K^+]$, $[A^-]$

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

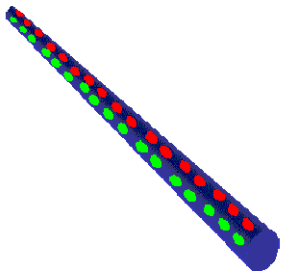
The Output of a Neuron: Action Potentials

- 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



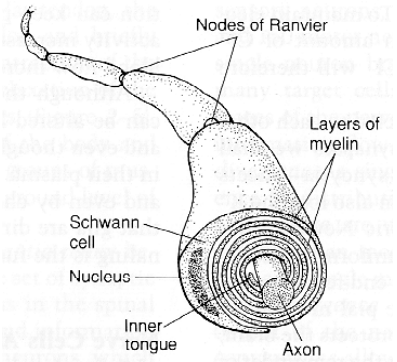
From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pg. 110

Propagation of a Spike along an Axon



Active Wiring: Myelination of axons

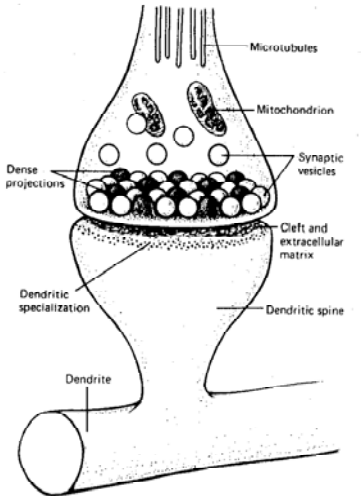
- Myelin due to Schwann cells (glia) wrap axons and enable *long-range spike communication*
  - "Active wire" allows lossless signal propagation, unlike electric signals in a copper wire
  - Speeds up spike propagation by conducting only at non-myelinated areas ("nodes of Ranvier")



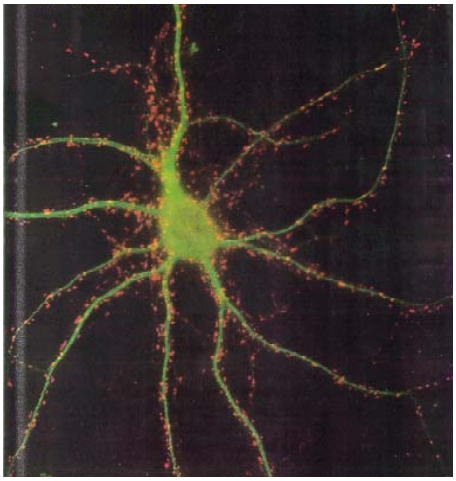
From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pgs. 23 & 44

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



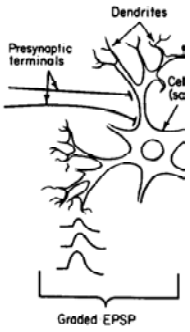
Distribution of synapses on a real neuron…



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

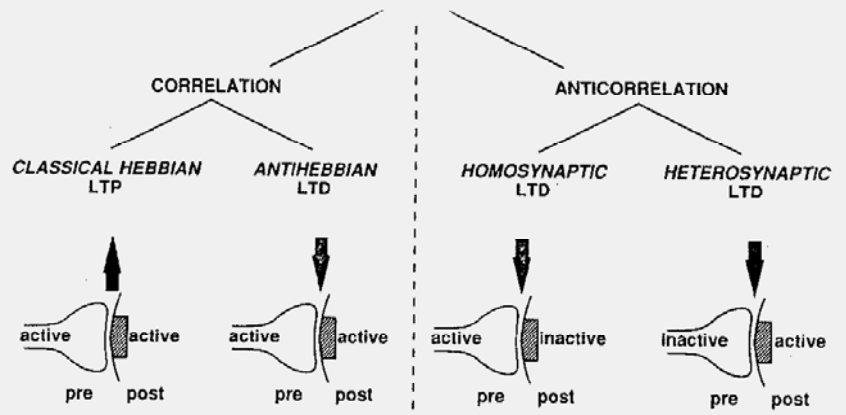
LTP observed as an increase in size of EPSP for the same presynaptic input



Types of Synaptic Plasticity

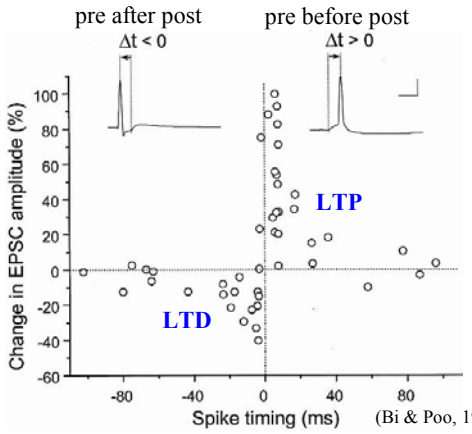
- Hebbian LTP: synaptic strength increases after prolonged pairing of presynaptic and postsynaptic spiking (correlated firing of two connected neurons).
- Long Term Depression (LTD): Reduction in synaptic strength that lasts for several hours or more
- Spike-Timing Dependent Plasticity: LTP/LTD depends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

Types of Synaptic Plasticity



Spike-Timing Dependent Plasticity

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



(Bi & Poo, 1998)

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 and behavior?

Not as much

Next: Brain organization and information processing in networks of neurons

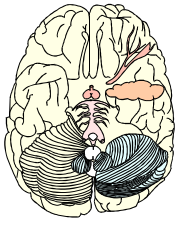
Organization of the Nervous System

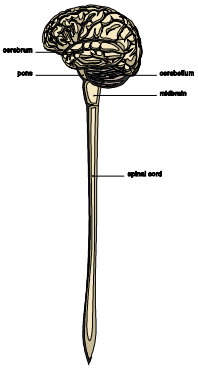
Central Nervous System

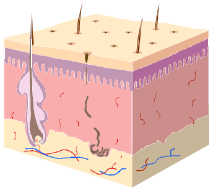
Brain Spinal Cord

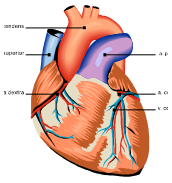
Peripheral Nervous System

Somatic Autonomic



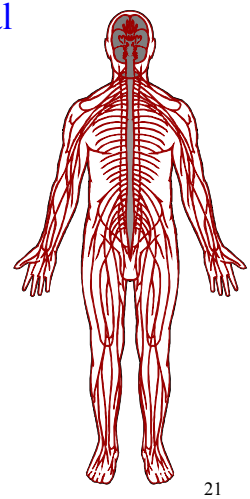






Skeletal/Somatic Nervous System

Nerves that connect to voluntary skeletal muscles and to sensory receptors



Afferent Nerve Fibers
Axons that carry info away from the periphery to the CNS

Efferent Nerve Fibers
Axons that carry info from the CNS outward to the periphery

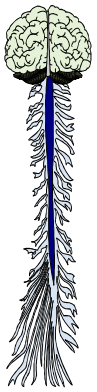
Autonomic and Central Nervous System

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 the brain activate spinal motor neurons
- Ascending sensory axons transmit sensory feedback information from muscles and skin back to brain

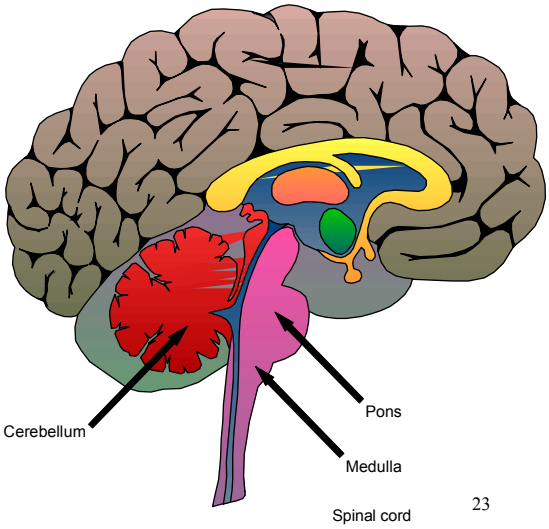


Major Brain Regions: Brain Stem

Medulla
Breathing, muscle tone and blood pressure

Pons
Connects brainstem with cerebellum & involved in sleep and arousal

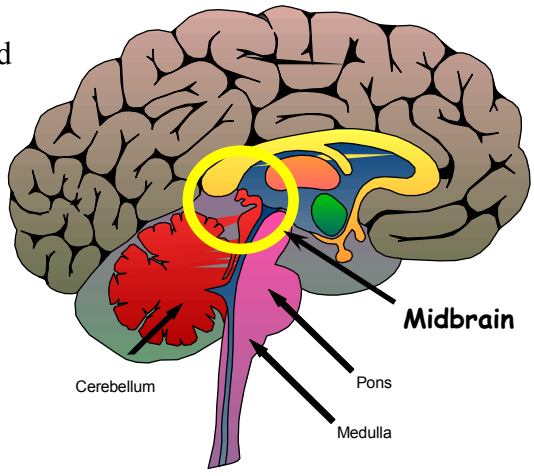
Cerebellum
Coordination of volunt movements and sense of equilibrium



Major Brain Regions: Brain Stem

Midbrain
Eye movements, visual and auditory reflexes

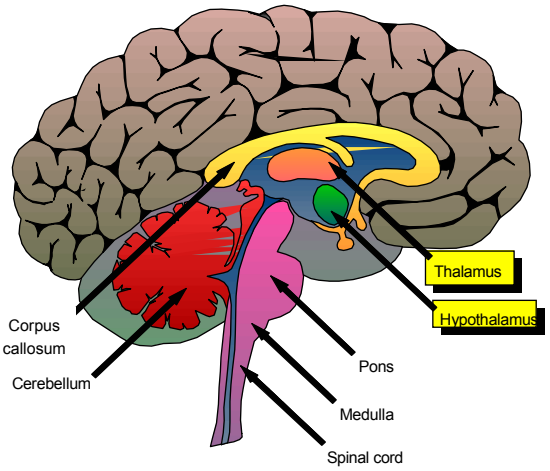
Reticular Formation
Modulates muscle reflexes, breathing & pain perception. Also regulates sleep, wakefulness & arousal



Major Brain Regions: Diencephalon

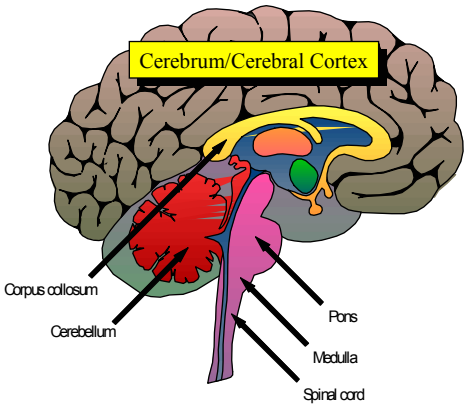
Thalamus
"Relay station" for all sensory info (except smell) to the cortex

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



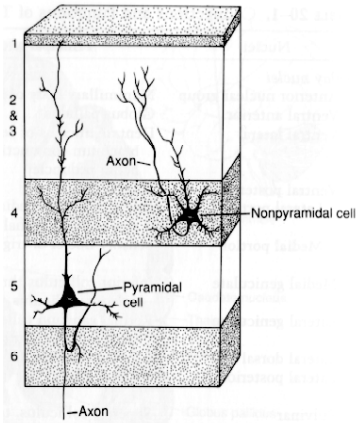
Major Brain Regions: Cerebral Hemispheres

- 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 + 270 billion Glial cells
- Each nerve cell makes about 10,000 synapses: approximately 300 trillion connections in total



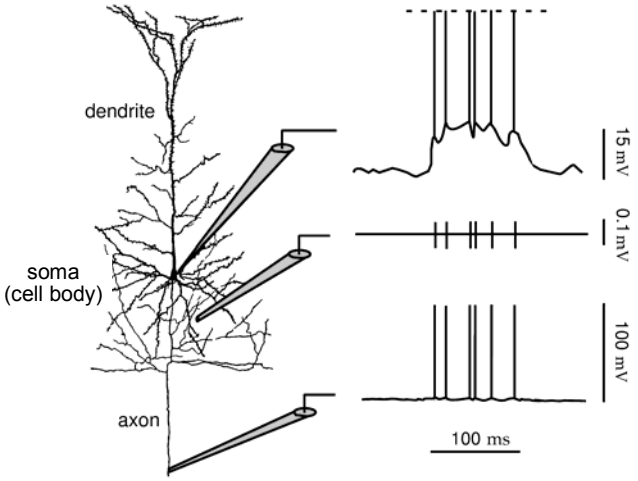
From Kandel, Schwartz, Jessel, Principles of Neural Science, 3rd edn., 1991, pgs.

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

Don't know fully yet!

Current knowledge based on: electrophysiological, imaging, molecular, psychophysical, anatomical and lesion (brain damage) studies

Recording the Output of a Neuron

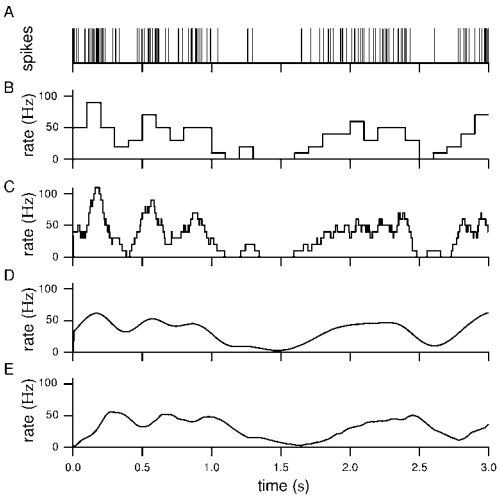


Intracellular Recording at the Soma

Extracellular Recording near the Soma

Intracellular Recording at the Axon

Computing the Firing Rate of a Neuron



Extracellular spike train

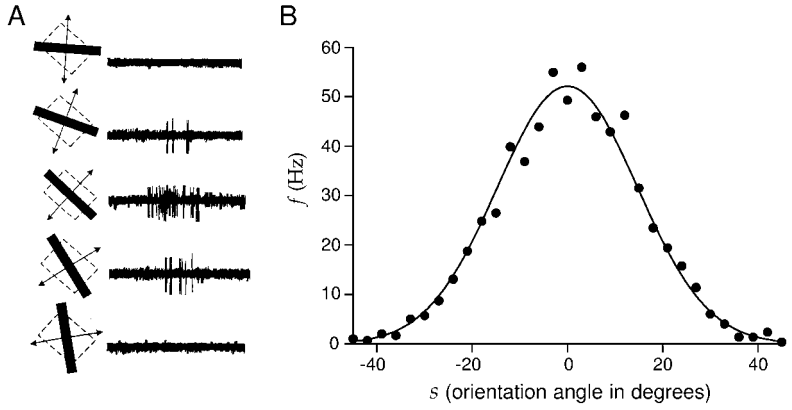
Rectangular Window (100 ms)

Sliding Window (100 ms)

Gaussian Window (σ = 100 ms)

Causal Window ($1/\alpha$ = 100 ms)

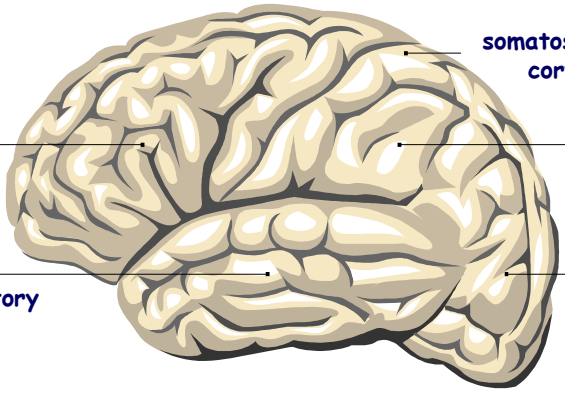
Tuning Curve of a Visual Cortical Neuron



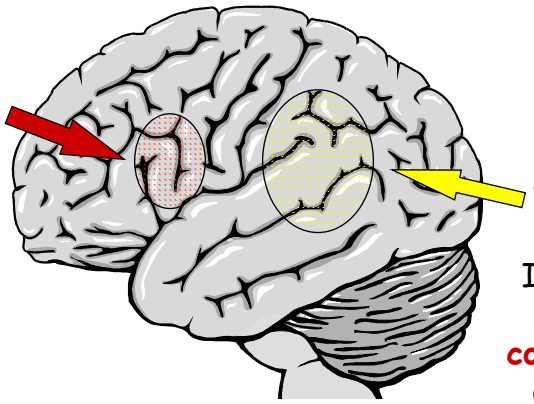
Spike trains as a function of bar orientation

Gaussian Tuning Curve

Specialization of Function in Cerebral Cortex



The Brain is specialized by Region: Language



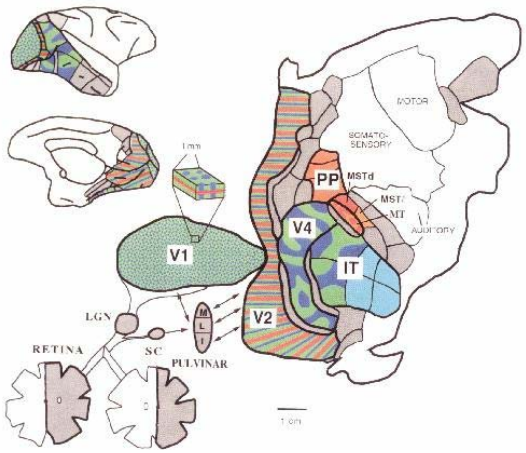
Specialization is based on Connectivity

- A Hypothesis: Cortical areas perform the same computation
  - Specialization arises from differences in local connectivity, numbers of neurons, and input-output connectivity to/from areas
- Complex behavior arises from the interaction of multiple brain regions
  - Example: Damage to Broca's area
    - Person can understand language
    - Person can say words or sing
    - Person can't speak or write grammatically

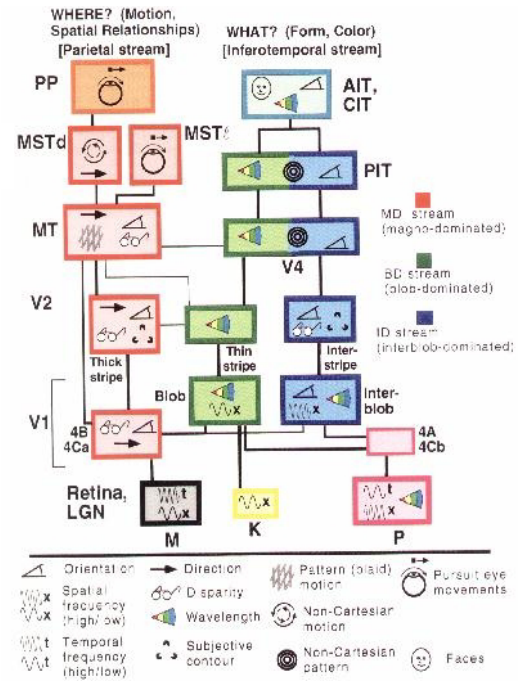
The brain tackles complexity hierarchically

- Example: Motor system
  - Reflexive responses are handled by the spinal cord
  - Control of Movement is handled by the cerebellum
  - Activity is scheduled by the cortex
- Example: Speech learning by children
  - Babies learn sounds (phonemes), then letters
  - Toddlers learn words, then sentences
  - Children learn grammar
  - Teenagers learn composition (one hopes!)

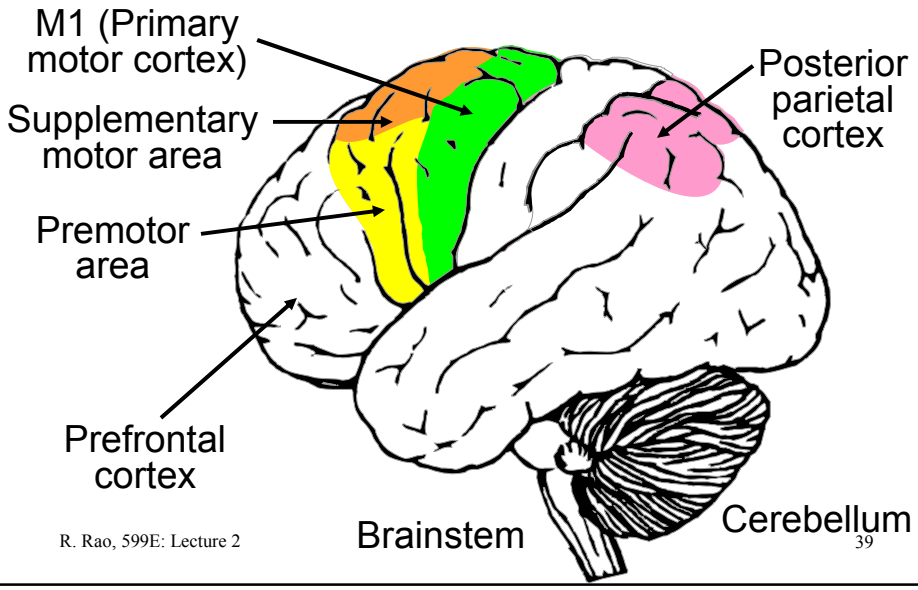
Hierarchical Organization of Visual Cortex



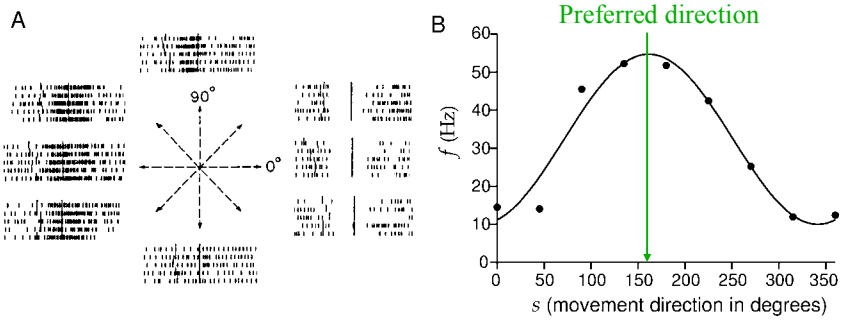
The Visual Processing Hierarchy



The Motor Hierarchy



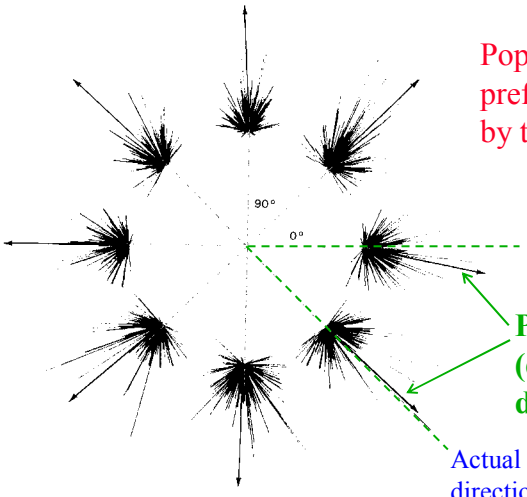
Tuning Curve of a Neuron in M1



Spike trains as a function of hand reaching direction

Cosine Tuning Curve

Movement Direction can be Predicted from a Population of M1 Neurons' Firing Rates



Population vector = sum of preferred directions weighted by their firing rates

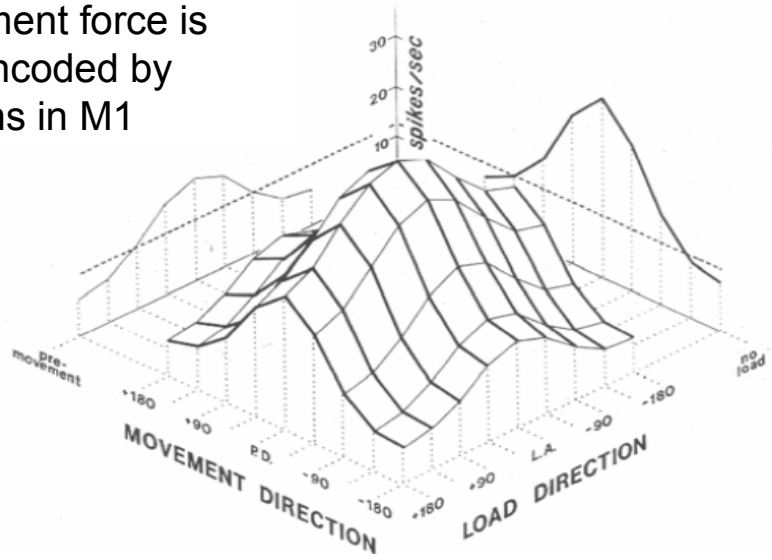
Actual arm movement direction

Population vectors (decoded movement direction)

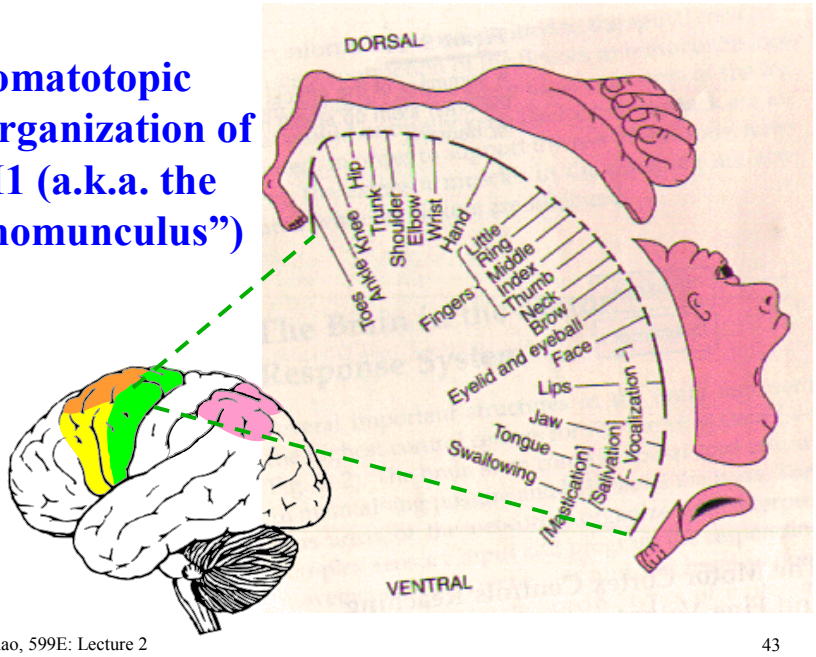
Actual arm movement direction

Simultaneous Encoding of Direction and Force

Movement force is also encoded by neurons in M1

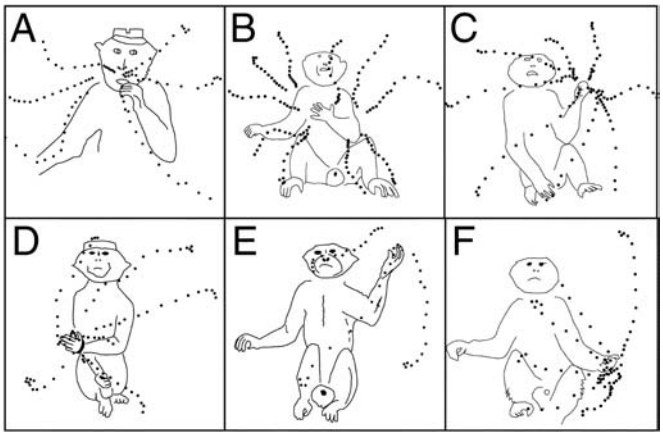


Somatotopic Organization of M1 (a.k.a. the "homunculus")

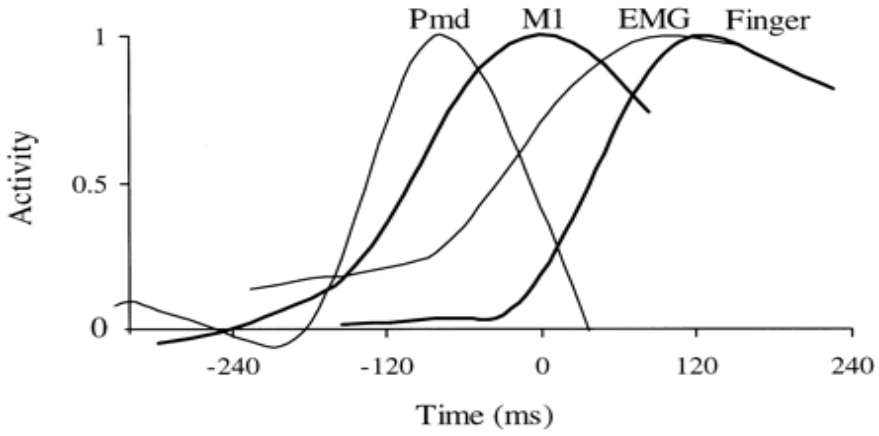


Electrically stimulating M1 elicits primitive movements

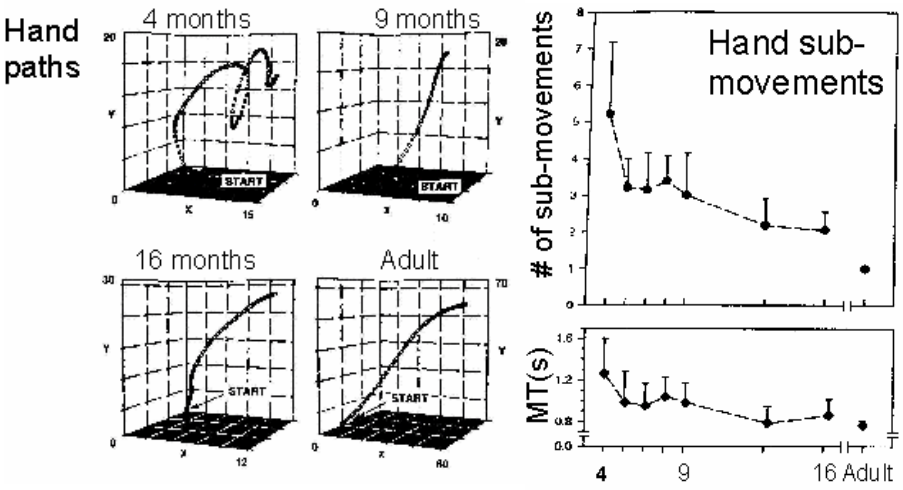
Electrically stimulating *Premotor Area* elicits more complex movements



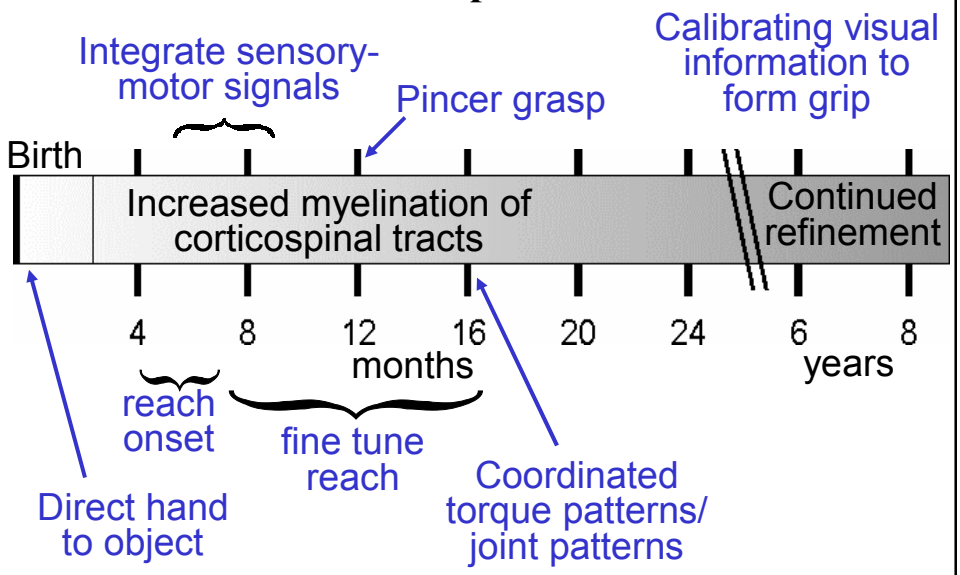
Activity in Motor Hierarchy during Reaching



Development of Movements: From Infant to Adult



Motor Development Timeline



Last Slide: 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 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)?

Summary and Conclusions

- 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) – recent results support Bayesian computational models
- Population coding in Motor Cortex allows decoding of movement direction, force, etc.
  - Useful for BCI (as we shall see)…

Next Class:
Guest Lecture by Eb Fetz on
Volitional Control of Neural Activity and its Application to BCI