Organizational

- **Instructor contact**
  - mscohen@ucla.edu, 310-980-7453. Suite 17-369 NPI
  - Please include NITP in the subject line of emails
- **Sections and TAs**
  - Kevin McEvoy kmcevoy@ucla.edu
- **Web site** (http://ccn.ucla.edu/wiki/index.php/Principles_of_Neuroimaging_A) *is a Wiki*
  - *Username:* NITP *Password:* 2007Problem Sets
  - Due one week after assignment (usually)
  - Send via email to Kevin and Mark
  - NITP in Subject Line
- **Midterm and Final**

Requirements

- MATLAB

- Signal Processing for Neuroscientists
- Cartoon Guide to Statistics (optional)
- Class List

- Pre-Requisites
  - Basic Statistics
  - Programming
  - Integral Calculus
  - Functional Neuroanatomy

Schedule (http://ccn.ucla.edu/wiki/index.php/Class_Schedule)

Week	Topic
1	Orientation to Neuroimaging, Neurons, Brains
2	Linear Systems
3	Noise
4	Electricity and Electronics
5	Electrophysiology and Stats review
6	Advanced Statistics
7	Real-World Circuits
8	Getting your hands dirty
9	*tbd*
10	*tbd*
11	FINALS

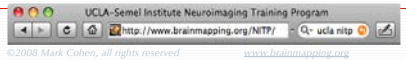
Topics To Be Scheduled:

Spike Measurement and Analysis
Point Spread Functions
Principles of Optical Neuroimaging and Microscopy
Exploratory Data Analysis
Loose ends

the UCLA Neuroimaging Training Program

- NIH-Sponsored Program Promoting Multidisciplinary Training

  Neuroscience, Statistics, Mathematics, Physics, Engineering Computer Sciences
- Five Graduate Fellowships (including non-US nationals)
- Annual Summer Advanced Fellowship
- *Only* Three Such Programs Funded



How to Apply for Training

- NITP Will Prepare a Certificate for students completing the requirements. This does not depend on receipt of a fellowship.
- Pre-requisites:
  - *Integral Calculus*
  - *Basic Statistics*
  - *Electricity and Magnetism*
  - *Computer Programming (any language)*
  - *Functional Neuroanatomy*
- Discuss with Home Department
- Contact Mark Cohen

Neuronal Anatomy and Electrical Activity

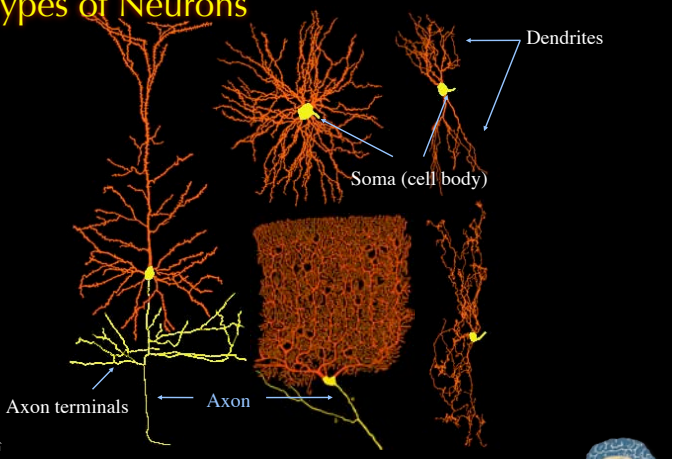
Mark S. Cohen
UCLA Psychiatry, Neurology, Radiology, Psychology,
Biomedical Engineering, Biomedical Physics

Suite 17-369 NPI

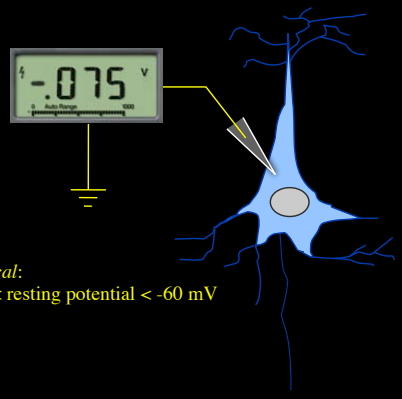
Topics

- anatomy of single neurons
- resting and action potentials
- transmission of signals
- chemical and electrical synapses
- information coding
- BOLD and unit activity
- EEG & SITE
- MR-visible effects

Types of Neurons

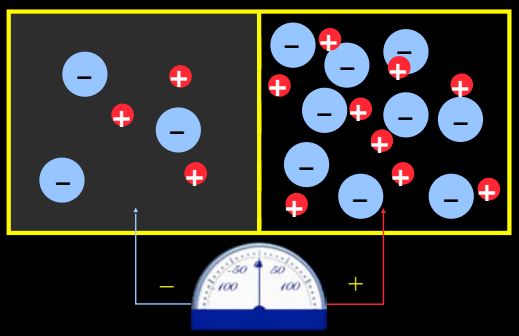


Resting Potential

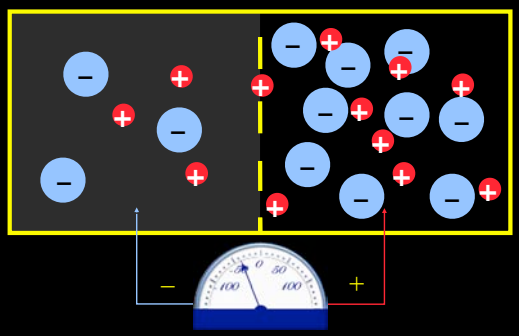


Typical:
-90 < resting potential < -60 mV

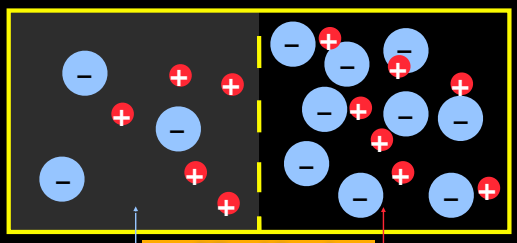
Development of the Membrane Potential



Development of the Membrane Potential



Development of the Membrane Potential



$$E = \frac{RT}{F} \ln \frac{[C_{inside}]}{[C_{outside}]}$$

Nernst Potential: $\approx 27\text{mV} \ln \frac{[C_{inside}]}{[C_{outside}]}$

Observed Ion Concentrations

Nernst Potential @37°C

[Na+] 460 mM → [Na+] 50 mM

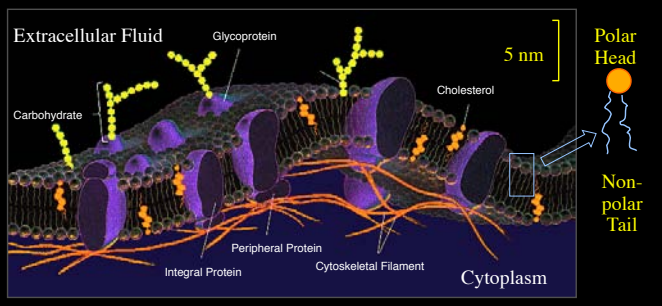
+60 mV

$$E = \frac{RT}{F} \ln \left(\frac{p_A[\mathrm{A}]_{out}\, p_B[B]_{out}\, p_y[x]_{in}\, p_y[y]_{in}}{p_A[\mathrm{A}]_{in}\, p_B[\mathrm{B}]_{in}\, p_x[x]_{out}\, p_y[y]_{out}} \right)$$

A,B are cations

x,y are anions

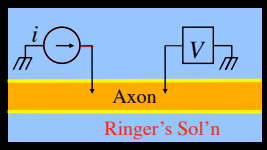
Structure of the Cell Membrane

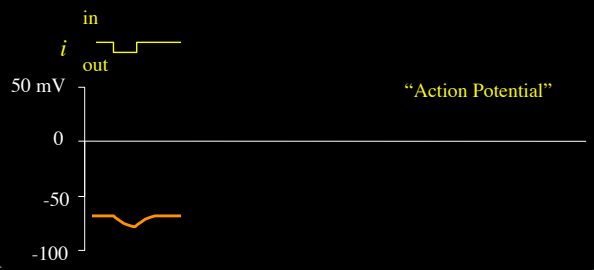


Note: E-field is >10 MV/m!

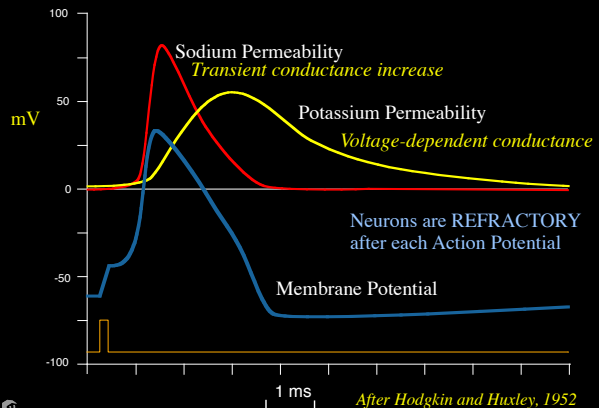
Taken from *Human Biology* by Daniel Chiras

Electrical Behavior of Neurons





Current and Voltage

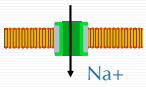


Sodium Leakage with Action Potentials

Cell Volume = 9 x 10^{-13} liters, about half of which is liquid.

At 40 mM Sodium:

= 4.0 x 10^{-14} Moles Sodium/cell

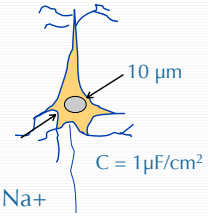


With Each Action Potential:

ΔV = 0.13 Volt

Q = CV = 1.3 x 10^{-7} Coulombs /cm^2

= 1.4 x 10^{-12} Moles/cm^2

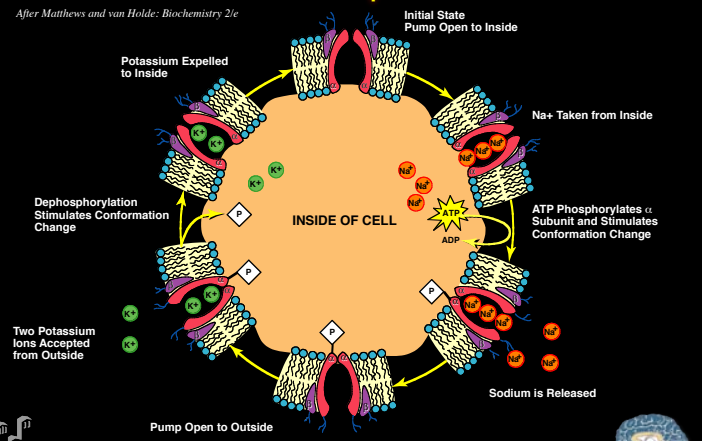


Surface Area = 2.8 x 10^{-5} cm^2

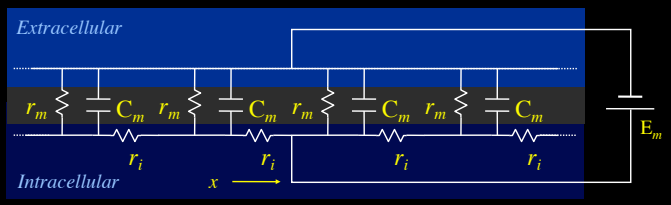
Each AP passes 3.7 x 10^{-17} Moles of Na+

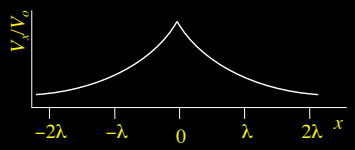
[Na+] is increased by 0.1% with each Action Potential!

Sodium Potassium Pump



Cable Properties



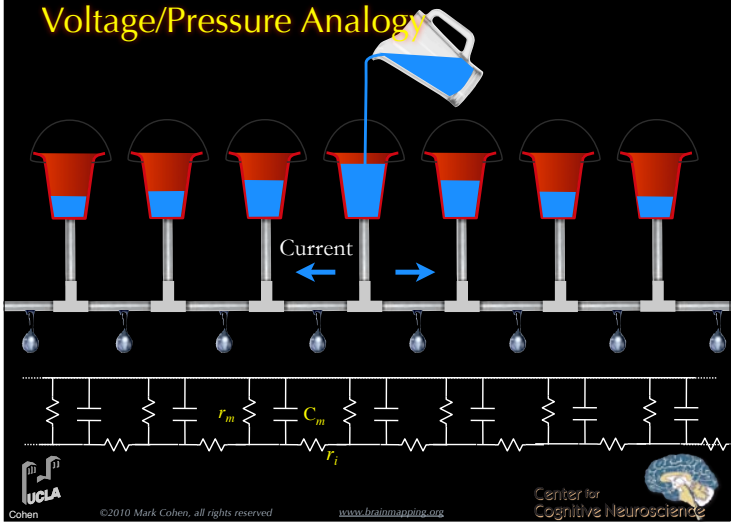


$$\frac{V_x}{V_0} = e^{-x/\lambda}$$

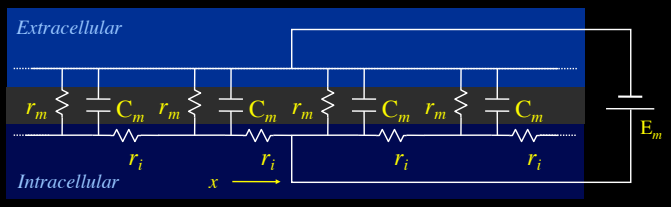
$$\lambda = \sqrt{r_m / r_i}$$

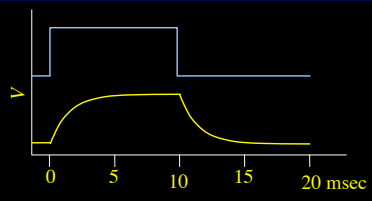
For vertebrate neurons:
$\mu m < \lambda <$ mm

Voltage/Pressure Analogy



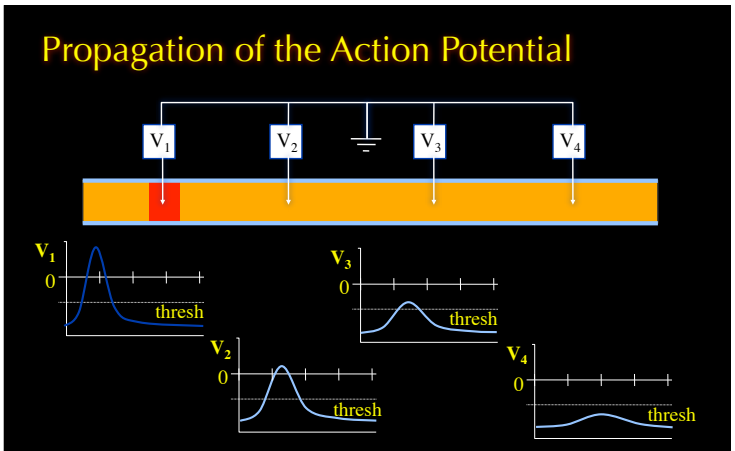
Cable Properties





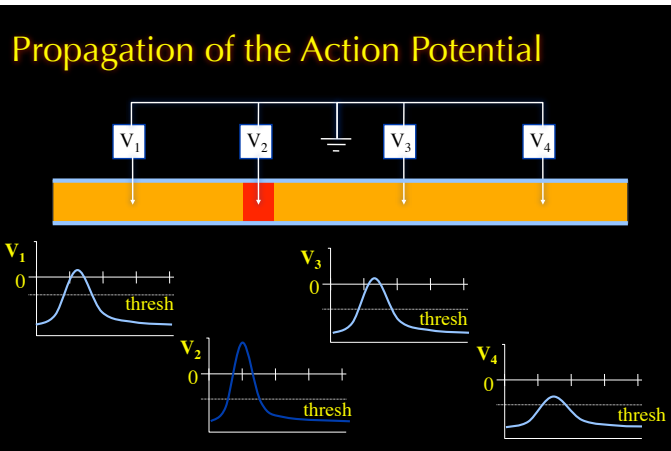
For vertebrate neurons:
0.5 msec < τ < 5 msec

Propagation of the Action Potential

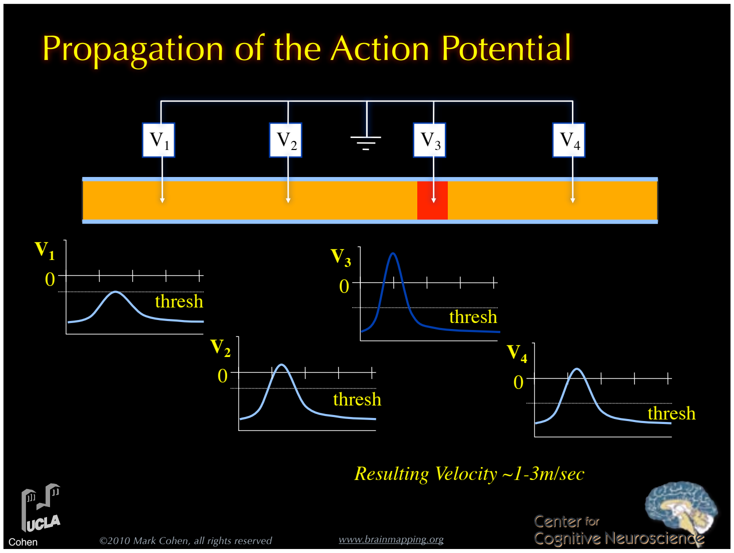


Resulting Velocity ~1-3m/sec

Propagation of the Action Potential



Resulting Velocity ~1-3m/sec


Propagation of the Action Potential
V1
V2
V3
V4
0
thresh
Resulting Velocity ~1-3m/sec
UCLA
Cohen
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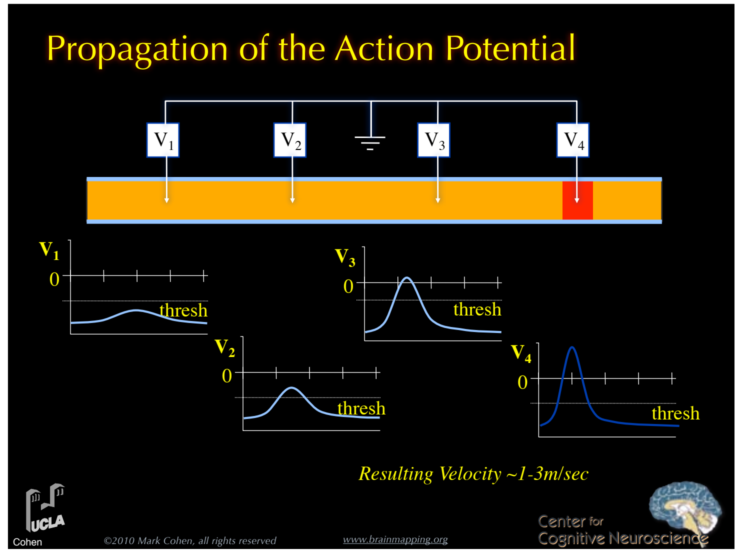
www.brainmapping.org
Center for Cognitive Neuroscience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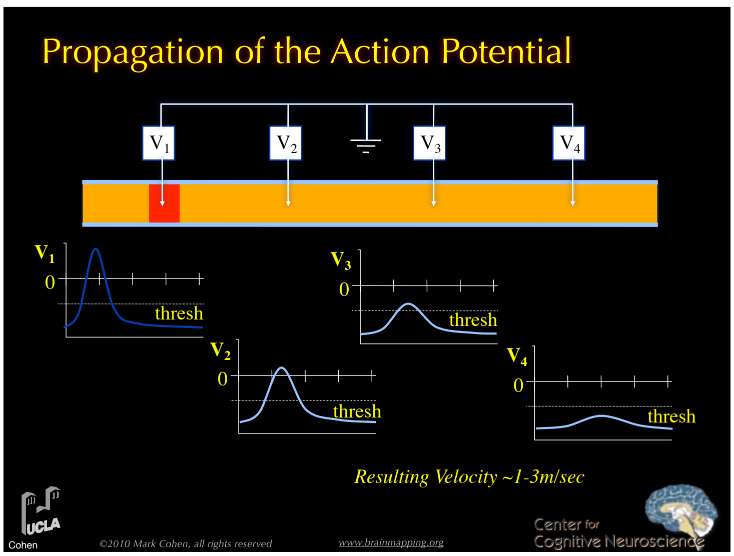
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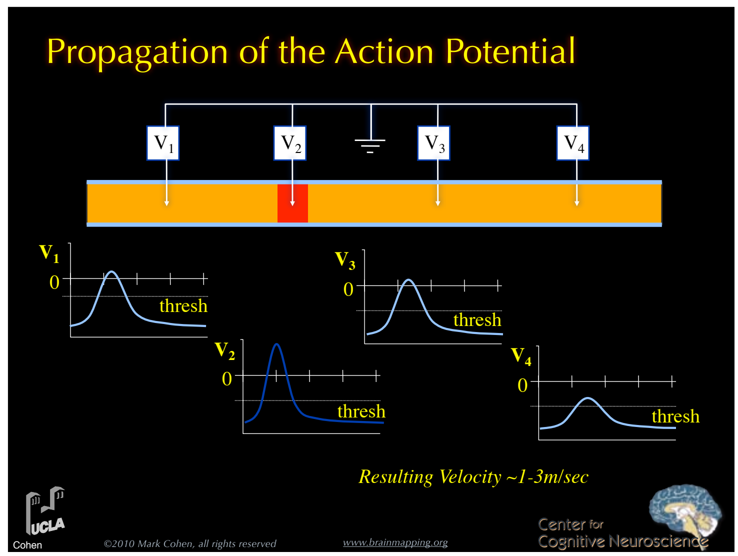
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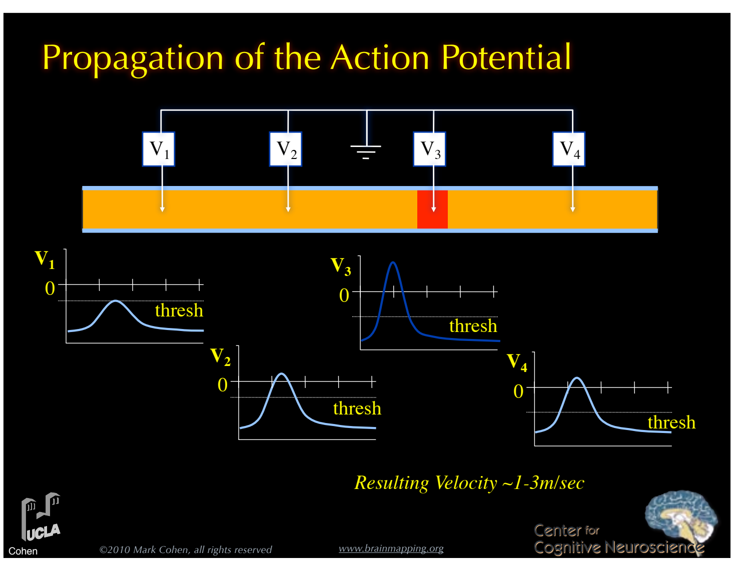
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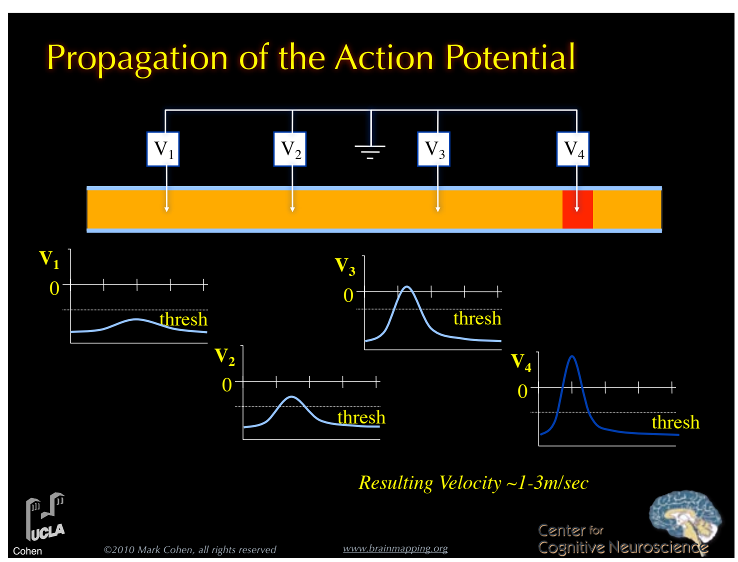
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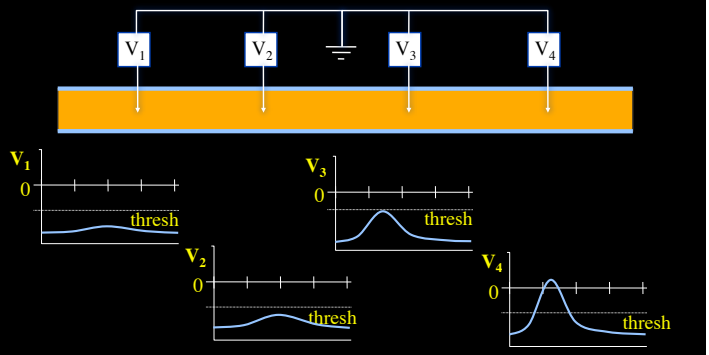
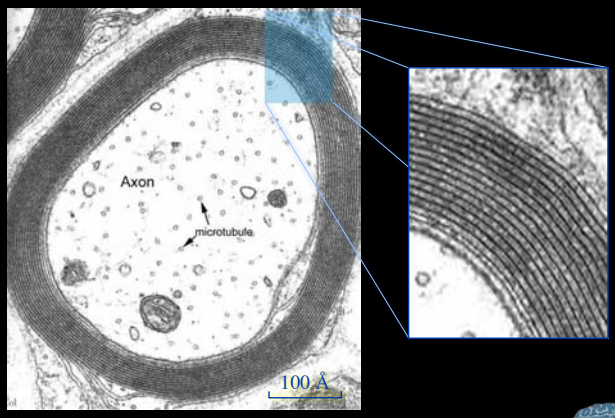
Propagation of the Action Potential



Resulting Velocity ~1-3m/sec

Myelin Sheath



Nodes of Ranvier

Saltatory Conduction

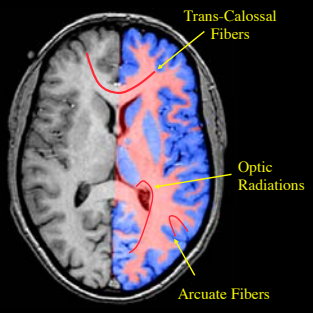
Internode:
- High Membrane Resistance
- Long Spatial Constant
- Short Time Constant

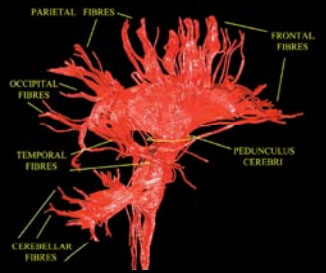
Efficient Electrotonic Conduction

Node:
- Low Membrane Resistance
- High Membrane Current Flow
- Fires Action Potential

Action Potential Regeneration

White and Gray Matter

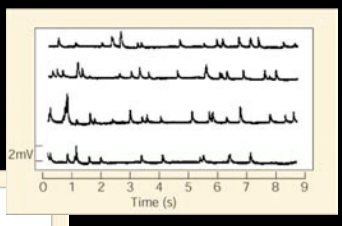


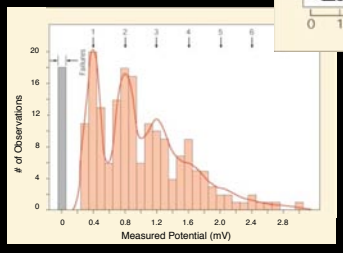


After: Catani, et al., NeuroImage 17:77, 2002

EPSP's: *Excitatory Post-Synaptic Potentials*

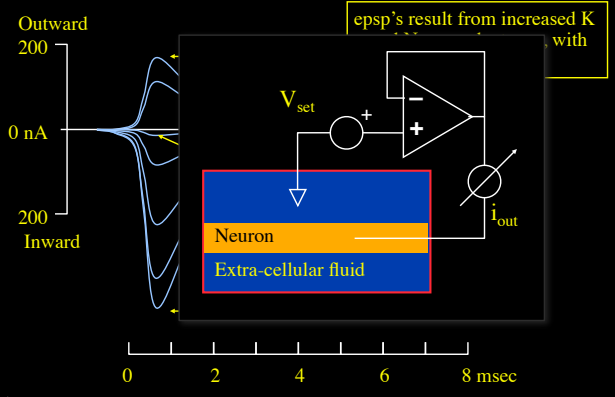
Muscle end plate potentials
Recorded in low Ca^{2+} / high Mg^{2+}
Boyd & Martin, 1956





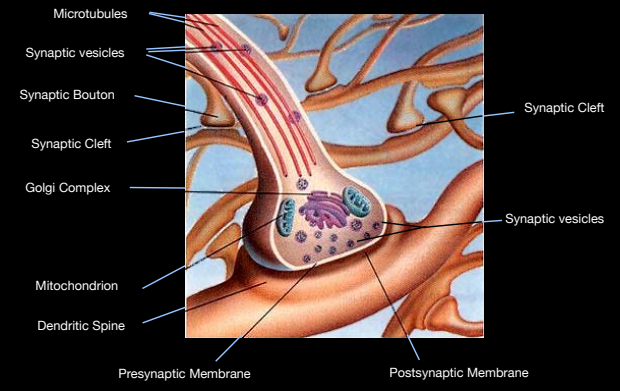
Amplitudes are *quantized* and display a Poisson distribution

Reversal Potential



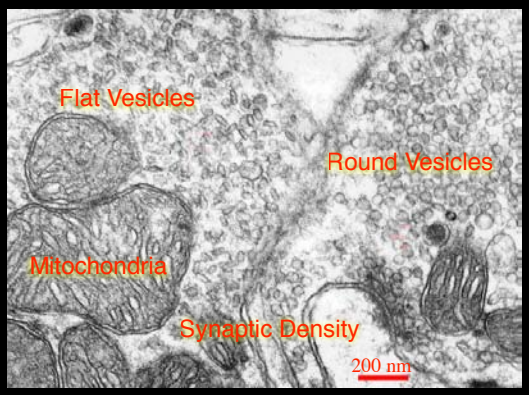
After Magleby and Stevens, 1972

Neural Synapse



From: http://www.driesen.com/synapse.htm

Synapses by EM

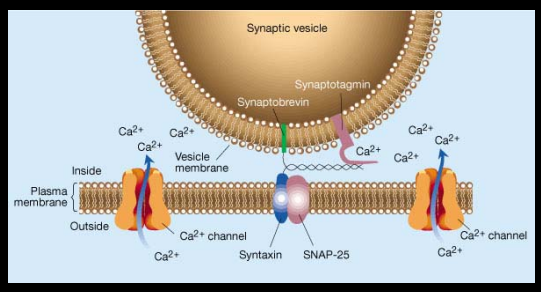


Atlas of Ultrastructural Neurocytology
http://synapses.mcg.edu/atlas/1_6_1.stm

Synaptic Mechanism (movie)

Delay from Presynaptic Action Potential to Post-synaptic Voltage Change is ≈ 0.5 msec

Synaptic Vesicles



Exocytosis of Transmitter requires Ca^{2+}

From: Matthews, G. *Neurobiology: Molecules, Cells and Systems* 2nd edn

Neurotransmitters

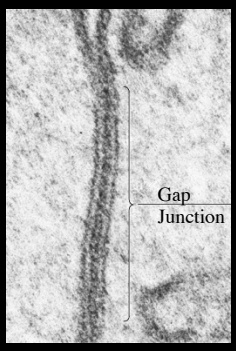
Small Molecules:
- Acetylcholine
- Serotonin
- Histamine
- Epinephrine
- Norepinephrine
- Dopamine
- Adenosine
- ATP
- Nitric Oxide

Amino Acids
- Aspartate
- Gamma-aminobutyric Acid
- Glutamate
- Glycine

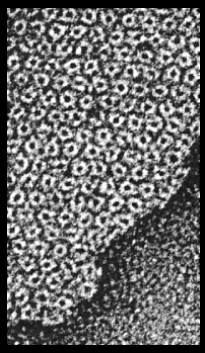
Peptides
- Angiotensin II
- Bradykinin
- Beta-endorphin
- Bombesin
- Calcitonin
- Cholecystokinin
- Enkephalin
- Dynorphin
- Insulin
- Galanin
- Gastrin
- Glucagon
- GRH
- GHRH
- Motilin
- Neurotensin
- Neuropeptide Y
- Substance P
- Secretin
- Somatostatin
- Vasopressin
- Oxytocin
- Prolactin
- Thyrotropin
- THRH
- Luteinizing Hormone
- Vasoactive Intestinal Peptide

…and many others

Electrical Synapses

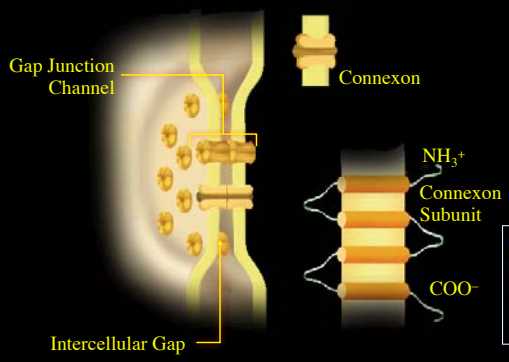


50 nm



50 nm

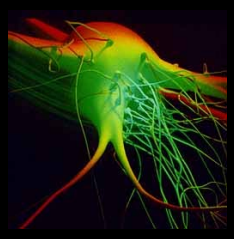
Gap Junction Microstructure

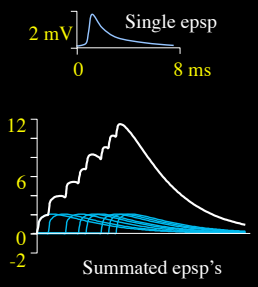


Gap Junctions have no synaptic delay, and may act as simple resistance or as electrical *rectifiers*

Modified from: http://aids.hallym.ac.kr

SpatioTemporal Summation of psp's



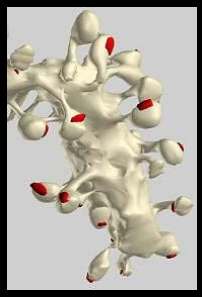


http://www.oseplus.de/Images/jpg/Synapse1.jpg

Integration of Inputs

Electrotonic properties of cells can result in spatial information zones within cells

Dendritic Spines



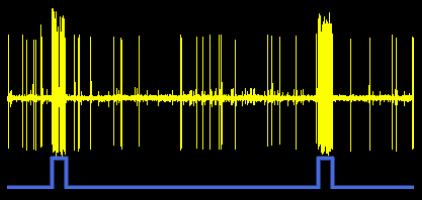
1 μm

Atlas of Ultrastructural Neurocytology

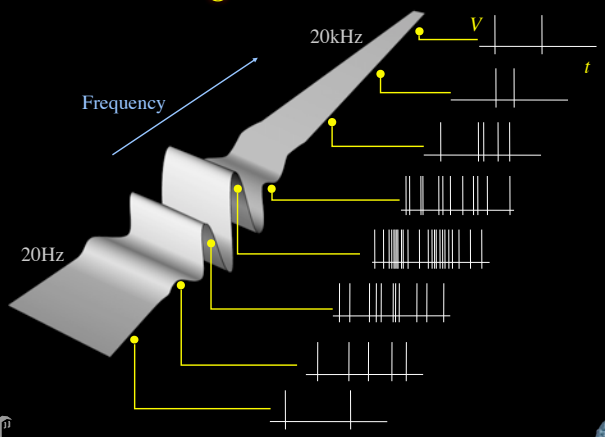
How Do Neurons Encode

Action Potentials are Identical!

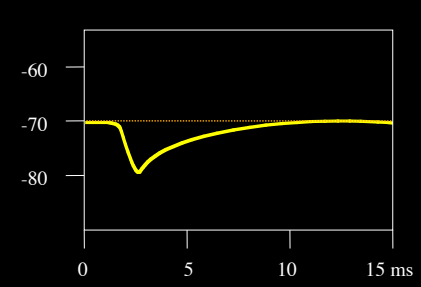
1. Firing Rate: Ranges up to 1000 spikes/ second



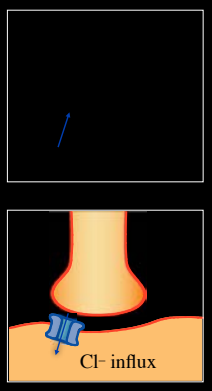
Place Encoding - Basilar Membrane



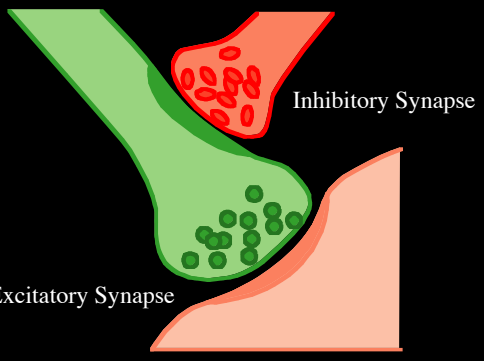
Inhibition



Reversal potential of Cl^- is near the resting potential. Therefore, its inhibition may be silent.



Pre-Synaptic Inhibition

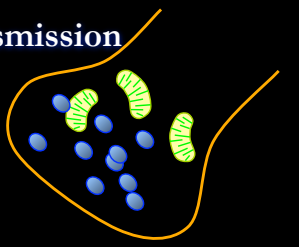


How does BOLD relate to neural firing?

Energy Demands in Transmission

Pre-synaptic:

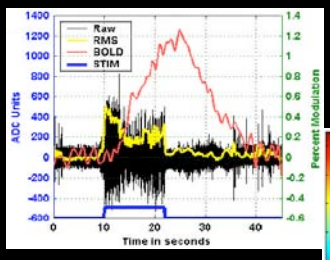
- *Transmitter Synthesis*
- *Exocytosis*
- *Transmitter re-uptake*



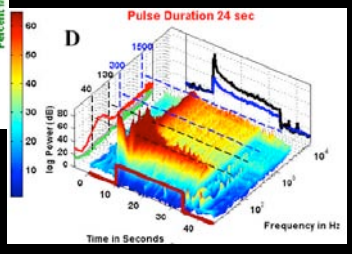
Post-Synaptic

- *Maintenance of membrane potential after ion leakage*
- *Excitatory: Removal of Sodium (Na/K pump)*
- *Inhibitory: ???*

Logothetis Results



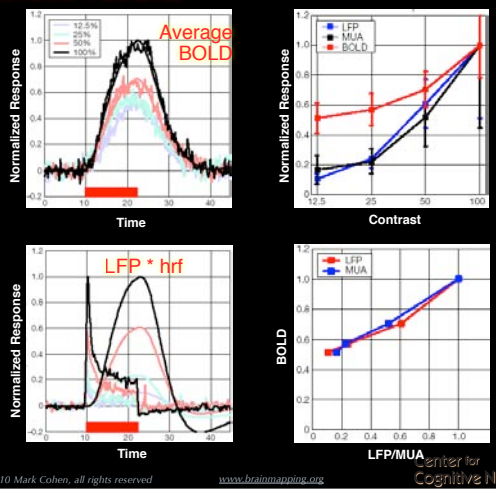
LFP = 40-130 Hz
MUA = 300-1500 Hz



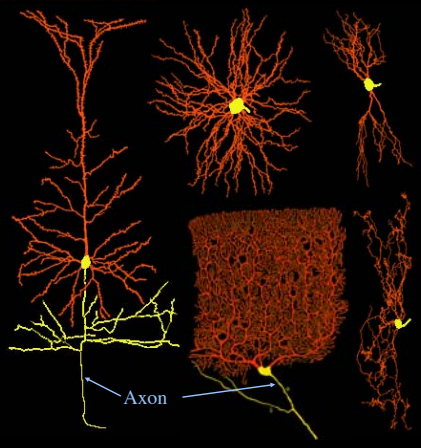
Pre On Post Stim

Logothetis, et al., Nature 412:152, 2001

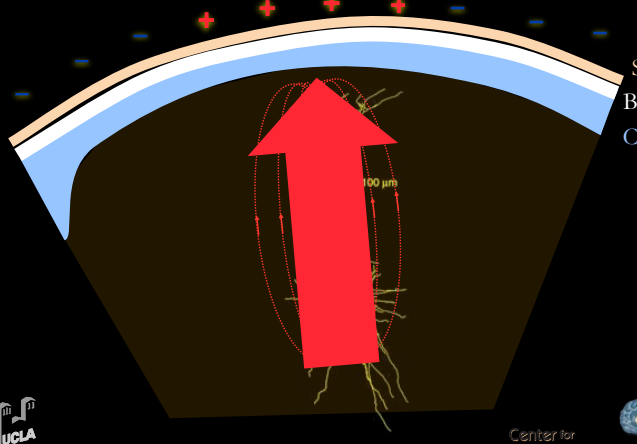
Logothetis results



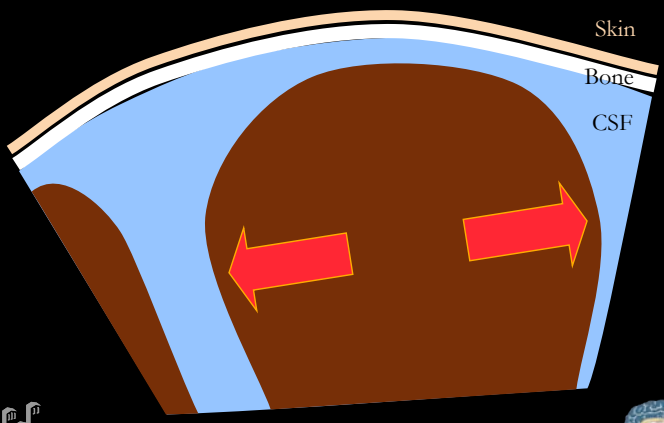
Types of Neurons



Presumed Origin of the EEG



Many Neurons are Not "Seen" by EEG



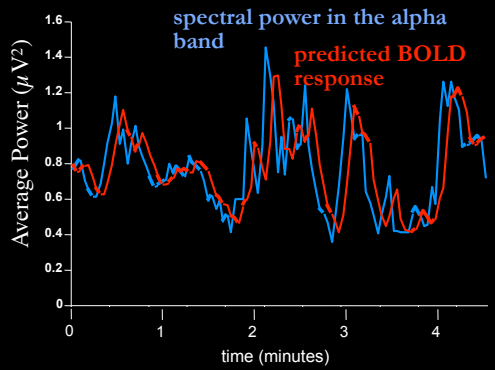
General Limitations in EEG Localization

- Deeper Sources Show Weaker Signals
- Magnitude Depends on Dipole Orientation
- Magnitude Depends on Temporal Synchrony
- Magnitude Depends on Spatial Coherence
- Conductivity of Body Tissues (CSF, scalp) Blur the Scalp Potentials

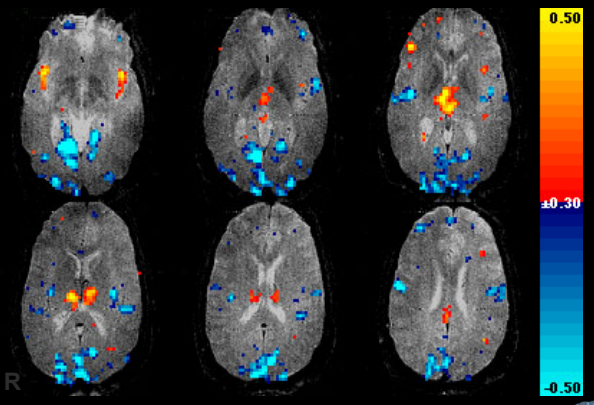
➡ **SITE = *S*imultaneous *I*maging *for* *T*omographic *E*lectrophysiology**

EEG at Rest

Alpha Mapping



SITE of Resting Alpha



Goldman (2002) NeuroReport 13(18):2487

EEG-fMRI Issues

- Scalp Potentials are Proportional to the **Derivative** of the Voltage, whereas fMRI is Proportional to the **Integral** of the Firing
- The Action Potential, *per se*, Is Probably **Invisible** to BOLD
- The Rhythmic Structures in the EEG May Depend More on **Synchronous** Firing than on **High Firing Rate**
- The BOLD Signal is Likely Associated with the *Post*-Synaptic Neurons

MR-Lucent Neurophysiology

Energetic Demands ..... *(BOLD, ASL)*

Transmitter Synthesis, Exocytosis, Metabolism

Na+/K+ Pump

[Na+] ..... *Imaging*

Glucose Metabolism ..... *Spectroscopy*

Extracellular Currents (?) ..... *Phase Disturbance*

Anisotropic Diffusion ..... *DTI, etc…*

Neural Constituents (NAA) ..... *Spectroscopy*

Thanks.

The Neural Membrane

Observed Capacitance: $1\ \mu F/cm^2$

Since: $$C \approx \frac{1.1k}{4\pi d \times 10^{-12}}$$

If k (the dielectric constant) is about 6, then $d \approx 5 \times 10^{-7}$cm = 50 Å.

If P.D. ≈ 0.1 Volt, then the E field is 2×10^7 V/m !

Anatomy of a single neuron