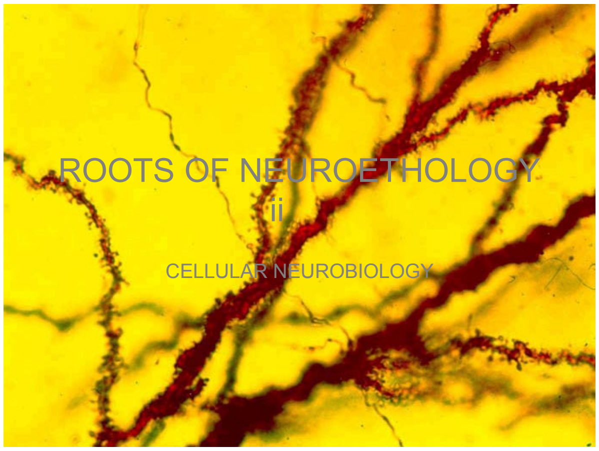


Discussion Sections Friday

BIO NB 424 Section One
Carl D. Hopkins
Morrison Room, Fridays 11:15-12:05

Asare, Mariette
Correa, Stephanie
Eldridge, Matt
Ho, Catherine
Hough, Lauren
Krainman, Jennifer
Lehr, Tiffany
Morse, Alix
Orloski, Joseph
Pilz, Kevin
Ramsey, Caitlin
Sinha, Smrita
Svenson, Gavin
Valotta, Jamye
Wiltrout, Charles

BIO NB 424 Section Two
Bruce A. Carlson
W358, Fridays 11:15-12:05

Armstrong, Caren
Bhatia, Sonica
Costello, Jen
Gilley, David
Hood, Chris
Khan, Tanvir
Lee, Jonathan
Liem, Agnes
Norris, Sarah
Paulk, Angelique
Pons, Maureen
Riley, Melissa
Steinberg, Emily
Tarantino, Marissa
Verma, Archana
Wu, Osmond

Discussion Friday

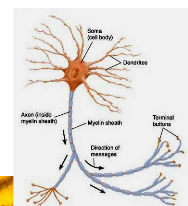
What is NEUROETHOLOGY?
Article by Graham HOYLE (see Web Site)

What is the goal of neuroethology?
Is it distinct from general neuroscience?
What is the legacy of Ethology? Is it a help or hinderance?

What do you see as unique about the discipline?
Do you agree with Hoyle's recommendations?

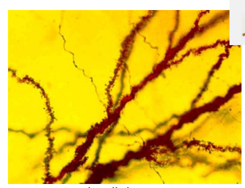
ANALYSIS LEVEL

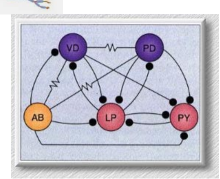

molecular



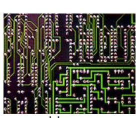
cellular

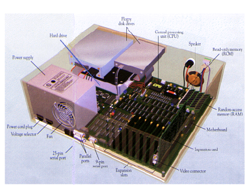

whole animal

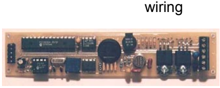

subcellular

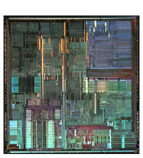


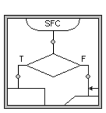
circuits


wiring


layout


components


inside components



software


whole machine

NEURON

Unit of structure.

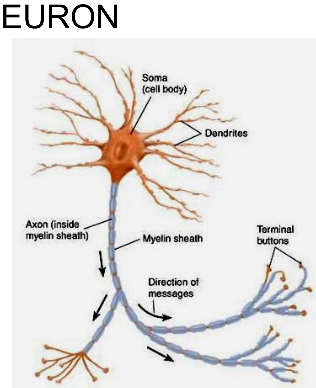
Independent metabolic unit.

Controlled in large part by events in cell nucleus.

Cell has a 'life history' (development), including birth, maturation, cell death.

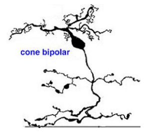
A focus for studies of:

- electrical activity
- intracellular chemical composition.
- polarization (directionality)
- connectivity (wiring)

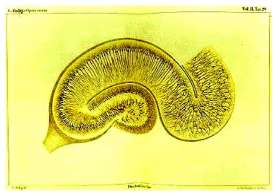


Neuron Doctrine

Nervous system is composed of cells (not universally accepted until 1900's).



Alternative: reticular theory (a network of interconnected cells – multinucleated) (Golgi)



Problems for Neuron theory in 1835-1880

- Could not see membranes between adjacent cells
- Could not resolve the pale and branching network of dendrites
- Could not imagine how axon cylinder could be related to a cell body.

Golgi Method

Revolutionary 'Black Reaction' Method

Harden tissue with potassium dichromate.

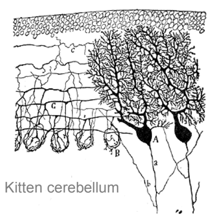
Stain with silver nitrate

Few neurons stain, but when they do, the entire cell stains black.

Technique developed by Golgi, but Golgi was anti-neuron doctrine (favored reticular theory)

Golgi method improved by intensification reaction methods of Cajal.

Cajal' Contribution



Kitten cerebellum

Basket endings convincing proof of separate cells.

Axons criss-cross, but never connect.

Each element autonomous (a cell).

Calaj's Neuron Doctrine

- Neurons are morphological units.
- Neurons make intimate contacts (contiguous but not continuous).
- Cell bodies and dendrites are conductors, just like axons.
- Dynamic polarization
- When there are axon collaterals, they act together.
- Axons arise in development by neurite outgrowth

Summarized in Nobel speech (1906) - shared with Golgi.

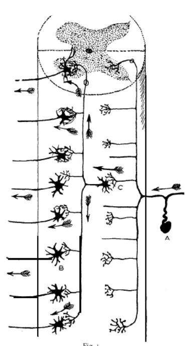
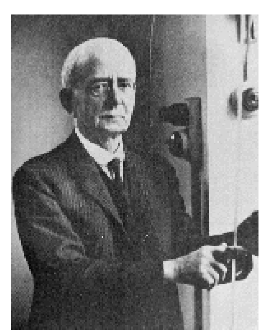


Fig. 1

A physiologist contributes

- Unidirectional flow of information
- Synaptic delay.
- Coordination of the action of many synapses.
- Excitatory and Inhibitory actions.
- Only the excitatory action propagates



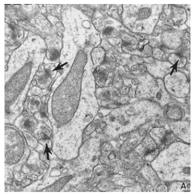
Sir Charles Sherrington

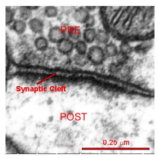
Electron Microscopy Clinches The Neuron Doctrine

First electron microscope is developed in Germany in 1930's

Palade and Porter develop ways to fix tissues in 1950's

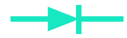
Palay and Palade, and also DeRobertis and Bennett show existence of distinct membranes, and synaptic regions (including extra-cellular space in synaptic cleft) (1954-9).





The Neuron By Analogy

Neuron as a wire.

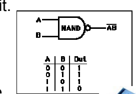
Neuron as a rectifier. 

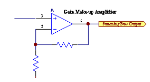
Neuron as transducer.

Neuron as a connector. 

Neuron as an summing circuit.

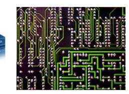
Neuron logic.





Neuron as a memory storage device.

Neuron in a circuit.



Neuron as a Wire

Neuron Shape: long axon makes long distance, highly specific contact possible.

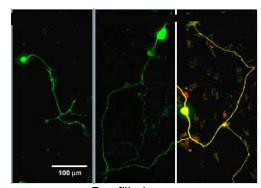
Neuron electrical properties:
- signals travel within a neuron (insulation)
- travel at high speed (propagatoin)
- use electric signals (=action potentials)

Branching: permit elaborate connections
- divergence
- convergence

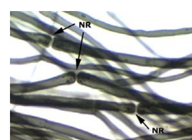
Neuron Shape

Axon serves as information conduit.
- -- long distances
- -- efficiently packaged

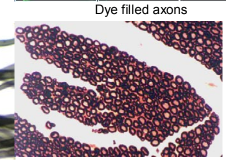
Consider a scale model of motor neuron (soma = 100 microns; axon = 1 m)



Dye filled axons

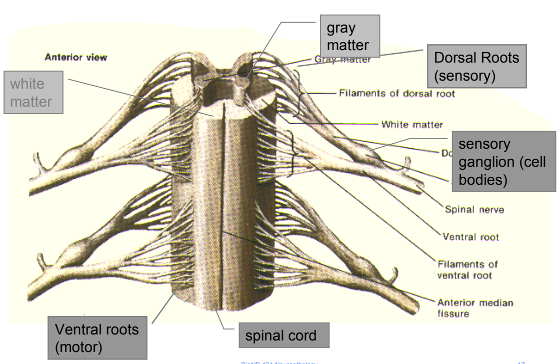


Axons, longitudinal view



Axons, cross section

Axon bundles make up nerve



Nerve Cells Communicate with Targets Using Electric Signals

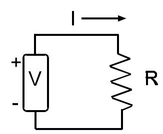
1) Resting neurons are electrically polarized.
   - resting potential

2) Action potentials: transient events caused by opening of ion channels in membrane. Propagates down axon.

3) Slow potentials: originate in sensory receptors, and at synapse. Local, do not propagate.

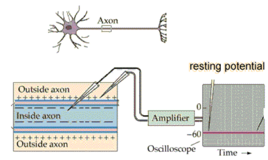
Voltage and Current

- Voltage, (V, = “Potential”): potential energy of position for a charged particle (electrons, ions).
- Current, (I): the amount of flow of charged particles (by convention, current is flow of + charges).
- Resistance (R): measure of resistance to current flow for a given voltage.
- Ohm’s Law: V = I R
- Analogy with water flow: pressure (voltage), resistance (electrical resistance), current (current).



Nerve cell at rest has a voltage across its membrane

The Resting Potential
(a baseline voltage)
At rest, cells are “polarized”
- Inside -70 millivolts compared to outside.
- Due to
  (a) ionic concentration gradients across membranes (mainly Potassium ions, but also Chloride, Calcium), and
  (b) selective permeability of membrane.
- Requires energy to maintain. Ion gradients are maintained by ATP-based ion pumps.

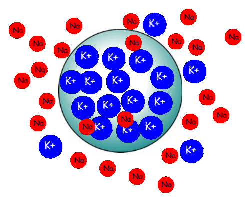


Origin of Resting Potential

Inside: K^+, Na^+

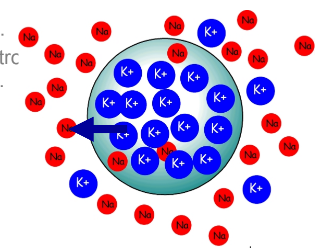
Outside: K^+, Na^+

Neutrality



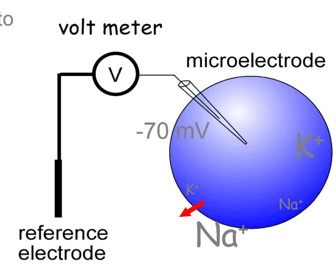
At rest, Membrane Permeable to K

- 1) K^+ diffuses out.
- 2) + charge accumulates outside.
- 3) Equilibrium: electrc chemical equilibrium.
- 4) Resting Voltage



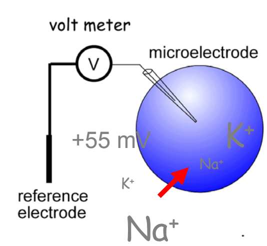
Membrane Potentials: Case 1

- Membrane is permeable only to Potassium



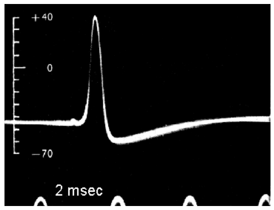
Membrane Potentials: Case 2

- Membrane is permeable only to SODIUM



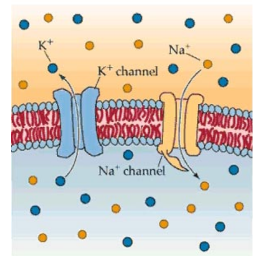
Action Potentials

The Action Potential (spike):
- Transient (1 millisecond duration)
- "de-polarization"
- peak voltage = +55 mV inside (mainly due to influx of Na^+ ions)
- All or None (threshold)
- propagates along axon



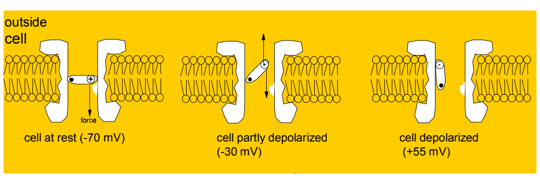
Membranes are Permeable to Ions because of ION CHANNELS

- Made from Protein
- Trans-membrane pores
- Selective
- Allow ions to diffuse through membrane



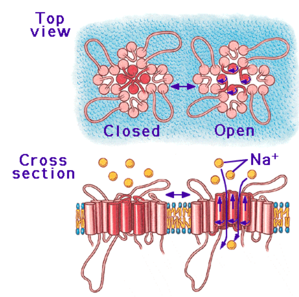
Some Ion Channels in Nerve Membranes are Voltage-Dependent

- Ion selective AND Voltage dependent (opening controlled by voltage)
  - opening regulated by voltage across membrane
  - Model: "gate" in ion pore is charged, thus opening regulated by membrane voltage.



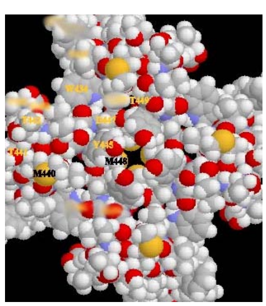
The Sodium Channel

- Membrane bound protein.
- Selective for Na^+ ions.
- Pore: intersection of several sub-units
- Normally closed (at -70 mV)
- Opens when membrane voltage is *depolarized*
- When open: Na influx →depolarization
- POSITIVE FEEDBACK
- Channel opens transiently (eventually closes)



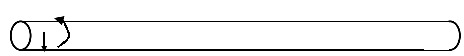
Potassium Channels

- One of many different K^+ channels.
- Voltage gated: closed at -70 mV, opens slowly with depolarization.
- Remains open if depolarized
- K^+ flows out of cell
- Repolarization of cell membrane.



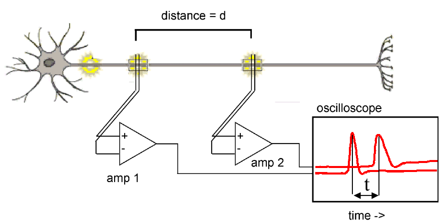
How the action potential propagates

- Inward Na^+
- Depolarizing return current: opens new Na^+ channels
- Bi-directional, but membrane refractory period prevents re-stimulation of membrane behind a.p.



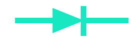
- Speed (dependent on axon diameter)
  - unmyelinated 0.1 to 1 m/s
  - myelinated: 10-40 m/s

Propagation Velocity



- Measuring velocity with two electrodes
- velocity = distance / time
- myelinated nerve: 10 to 100 m/sec

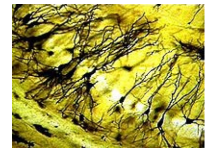
Neuron as Rectifiers



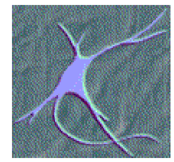
Input to neuron is in the dendrites.

Output is along the axon.

Although the axon is capable of carrying an actionpotential in either direction, the cell is polarized, Why?



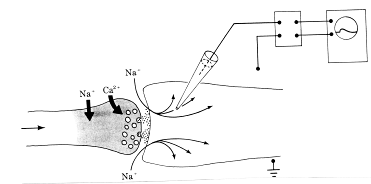
Sherrington: one way transmission at the synapse.



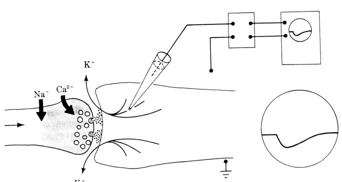
SYNAPSES

Excitatory Influx of cations (+ charge)

cause membrane depolarization



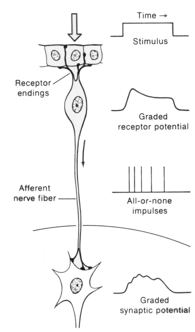
Inhibitory: Eflux of Cations, cause hyperpolarization.



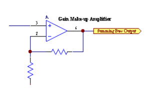
Transducers

How do signals get started in neurons?

- sensory cells: convert energy (chemical, movement, sound, light) into electrical depolarization.
- synapses: excitatory, inhibitory.



Summation

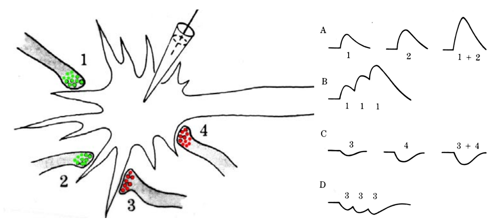


Synapses: synaptic potentials sum on the post-synaptic cell, providing for:

-- spatial summation: inputs from different places.

-- temporal summation: integrated inputs from same cell.

-- subtraction: through inhibitory synapses



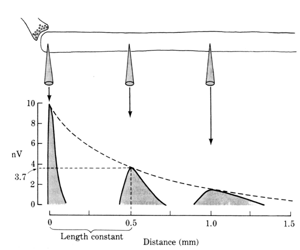
Fine Tuning the Neuron as Integrator (summing network)

Excitatory synapse generates a depolarizing potential.

Membrane voltage decreases exponentially with distance.

Rise time increases with distance.

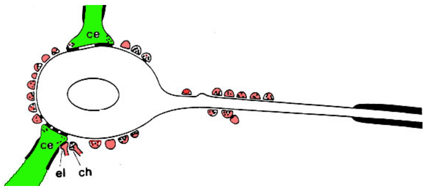
Consider a synapse on a dendrite.



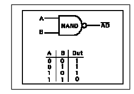
Neuron as Connector

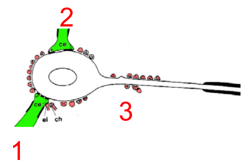
Some neurons serve to relay signals from one cell to another.'

Signal is relayed from input to the output



Neuron Logic



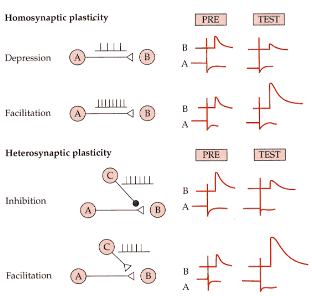


AND logic
- Output spike only if 1 + 2 are active at same time.

OR logic
- Output spike if either 1 or 2 are active

NOT logic
- Output spike if 1 OR 2, but NOT 3

Neuron Memory



Synapses retain a memory of recent events.

Depression: recent activity leads to decrease in response.

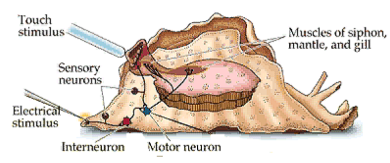
Facilitation: recent activity leads to increase.

Pre-synaptic inhibition.

Pre-synaptic facilitation.

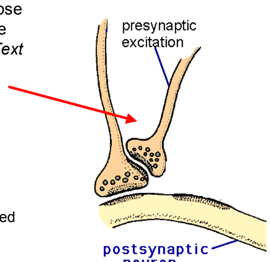
Changing the Strength of a Synapse

- Fatigue
  - depletion of synaptic transmitter
- Habituation
  - decrease in amount of transmitter released, but not due to fatigue
- Sensitization
  - increase in amount of transmitter released

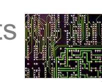


Changing the Strength of Synapses

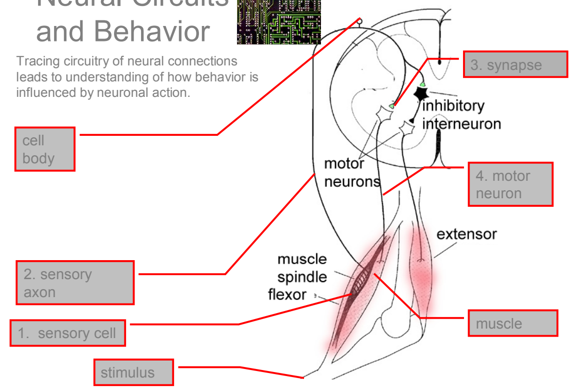
- Pre-synaptic excitation
  - a synapse on a synapse (primes synapse to be stronger). *Aplysia*, *Text* p. 303
- Hebbian Learning
  - NMDA receptor for glutamate: synapse is made stronger if activated when cell already depolarized



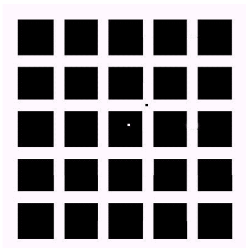
Neural Circuits and Behavior

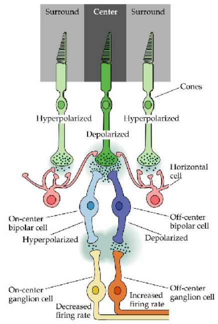


Tracing circuitry of neural connections leads to understanding of how behavior is influenced by neuronal action.



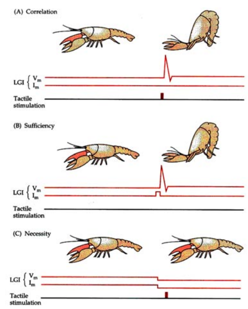
Neural Circuits and Behavior





Perception correlates with characteristics of neural circuit.

Neuronal Activity is both Necessary and Sufficient

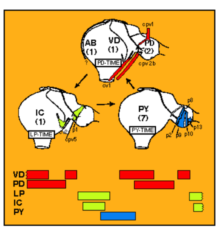


A) Correlation between behavior and activity of a particular neuron (LGI)

B) Sufficient: artificial stimulation of the neuron causes both a spike, and the behavior.

C) Necessary: if the neuron spike is blocked, the natural behavior is blocked, even though stimulus is OK.

Complex Behavior, Complex Circuits



The PYLORIC muscles and patterns of contraction.

Stomatogastric Ganglion of Lobster.

A restricted neural network (30 cells).

Controls muscles of gastric mill and the <u>pylorus</u> (movements involved in griding of food and of digestion).