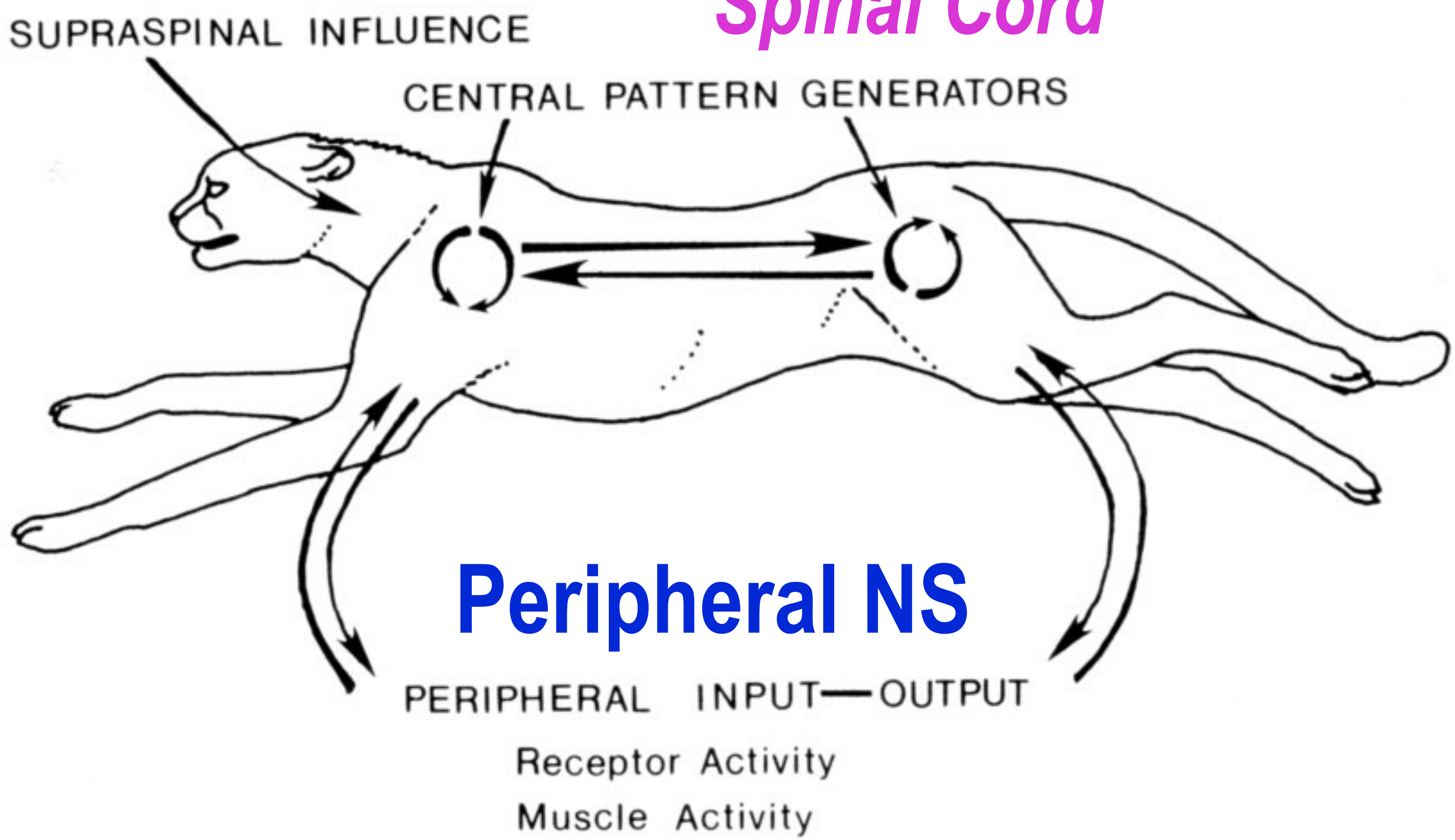
Neurobiology

Neurons and Nervous System Organization

Text: Chapter 6 Membrane Physiology

Road Map

Central NS *Brain Spinal Cord*

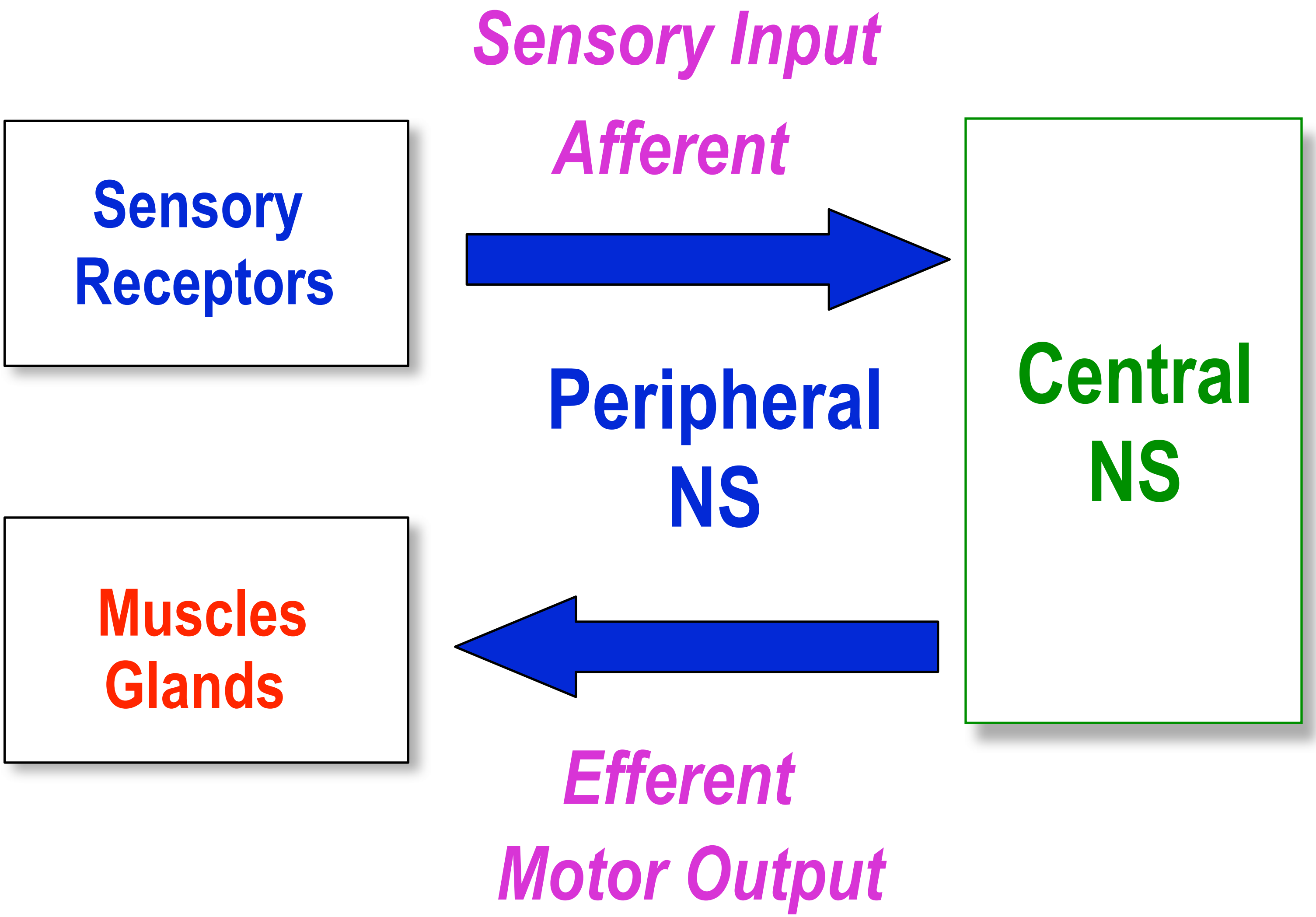


Peripheral NS

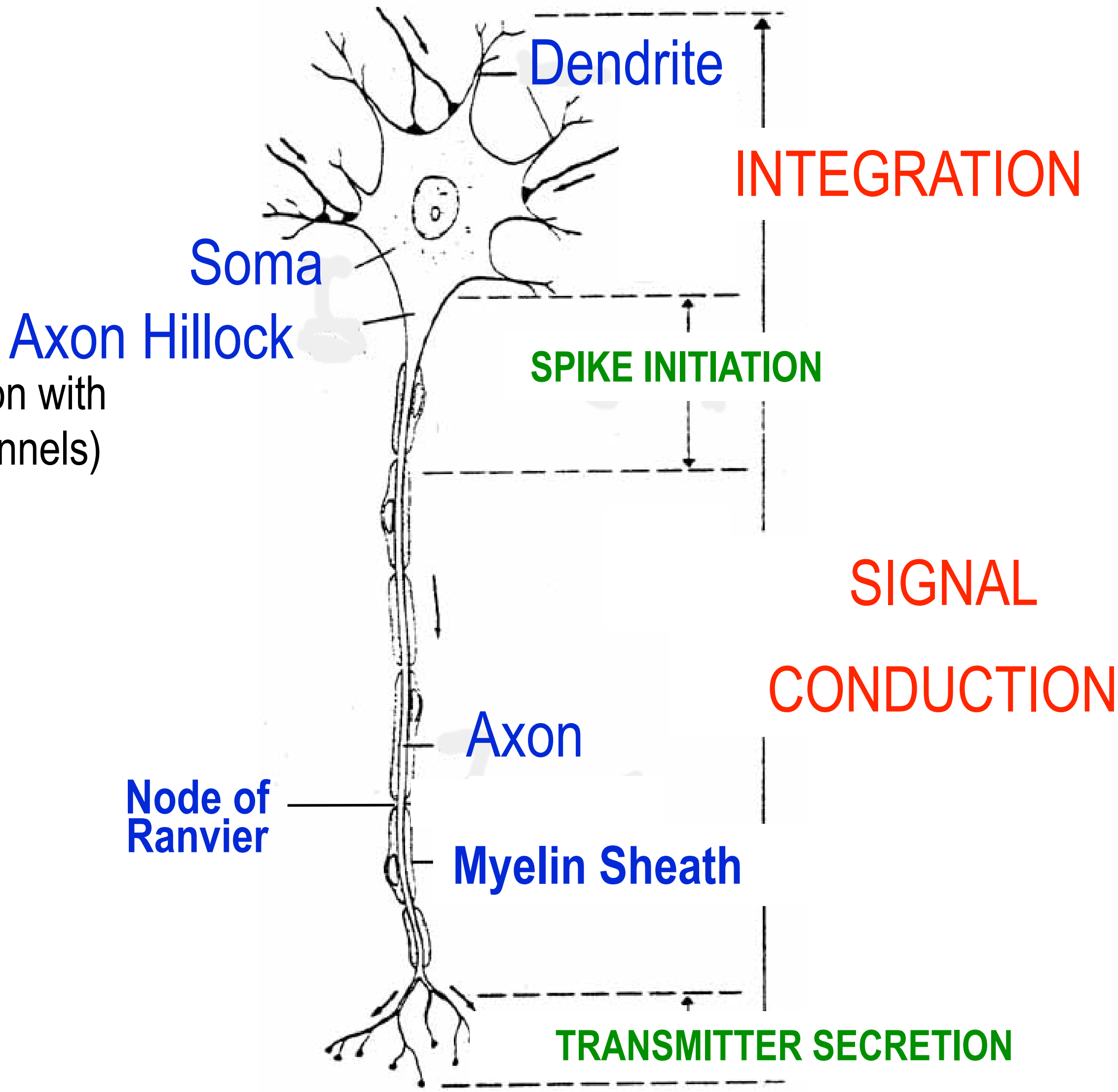
Ascending and Descending Neurons

Neural Control of Motor Output

Road Map

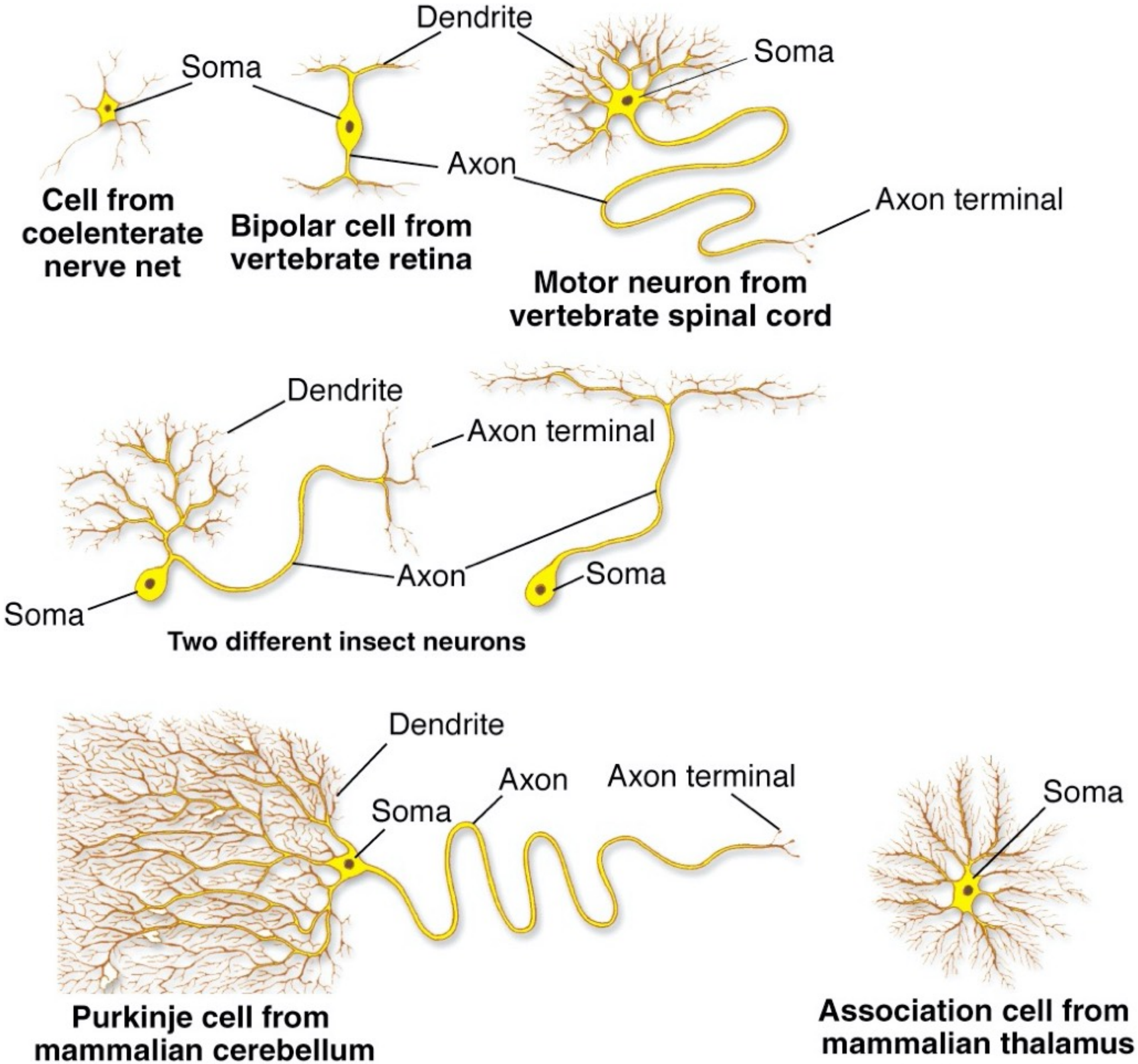

Sensory Input
Afferent
Sensory Receptors
Peripheral NS
Central NS
Muscles Glands
Efferent
Motor Output

Structure of Neuron

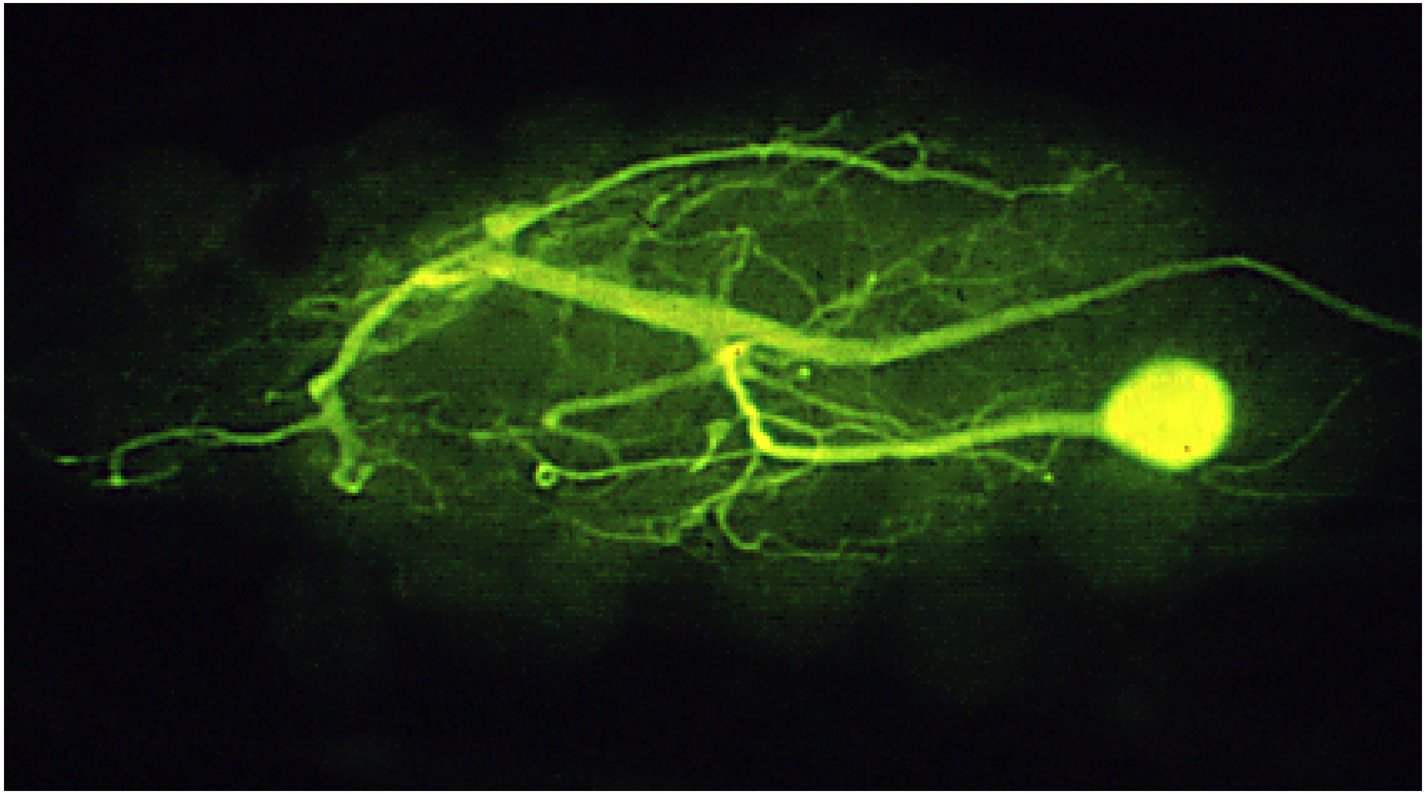


(Region of Axon with
more Na+ channels)

Structure of Neuron



Real Neuron



Functional Characterization

1. Afferent (to carry) - Sensory (skin, sense organs) to brain/spinal cord

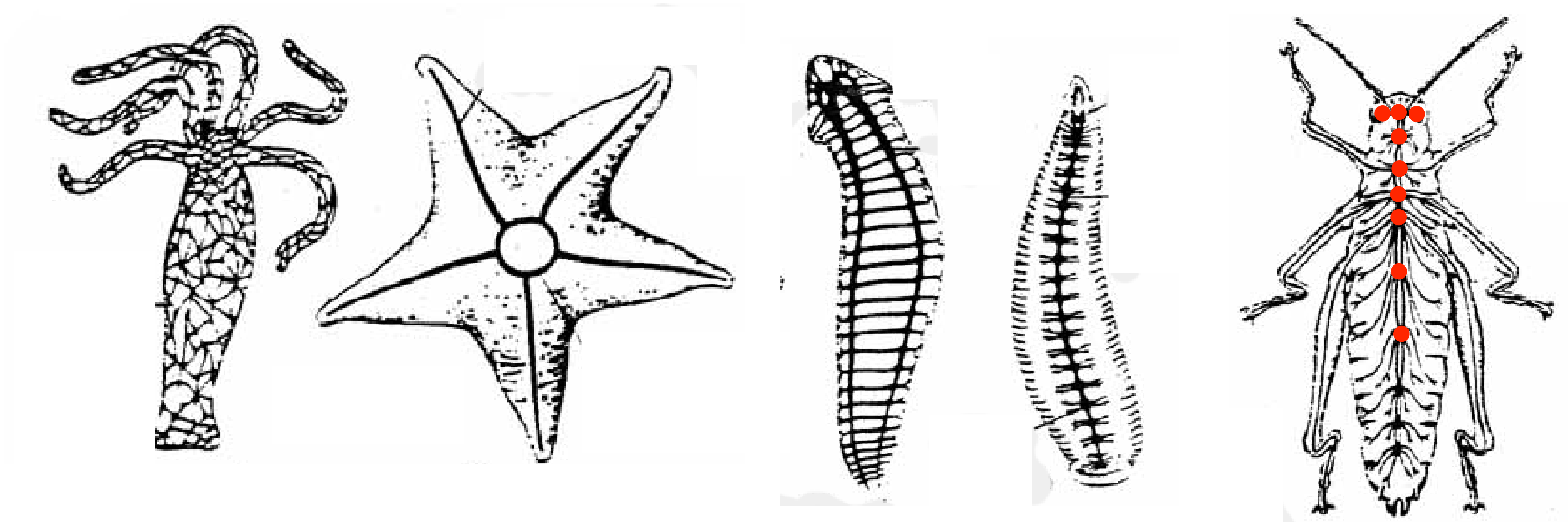
2. Efferent (to carry away) - Motor (brain/spinal cord) to muscles, glands

3. Interneuron - conduction among neurons (in C.N.S.), integrate and store information from other neurons

4. Neurosecretory - receive stimulus and secrete hormones into blood

Structure of Nervous System

Nerve Net | **Ganglia - cluster of nerve cell bodies**

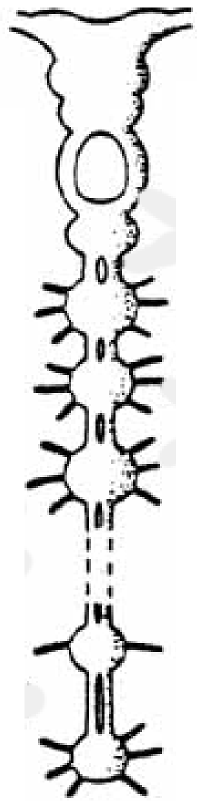


Diffuse | **Directional** | **Repeated in all segments** | **Condensation Specialization**

Nerve Cords

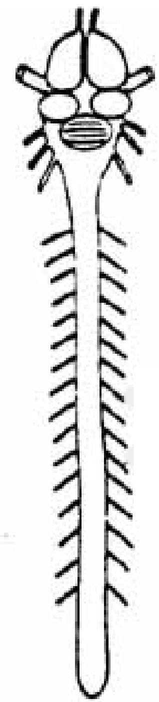
Invertebrate

Ventral



Vertebrate

Dorsal



Segmentation

Condensation

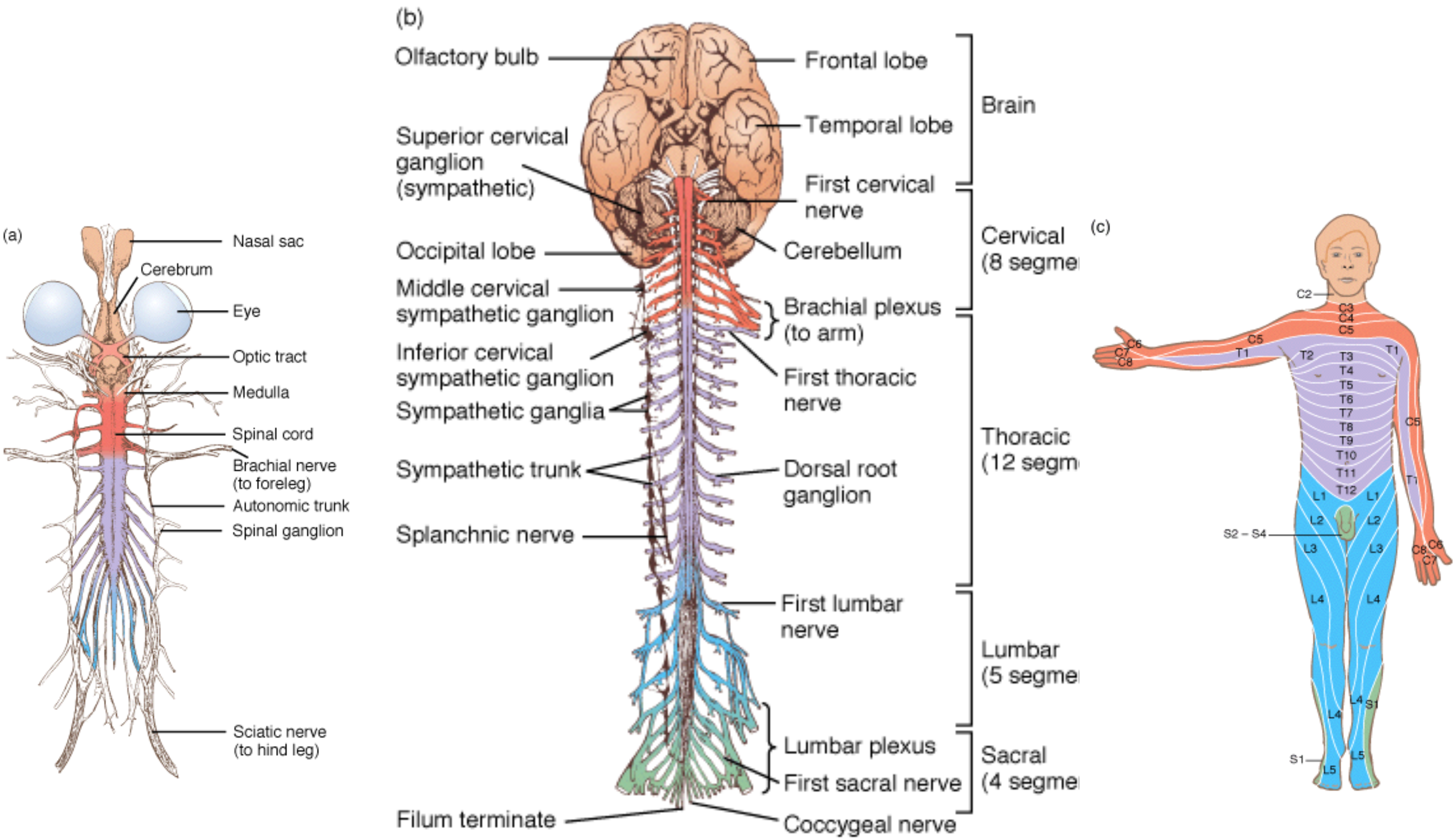
Specialization

Remarkable

Similarities

X-section

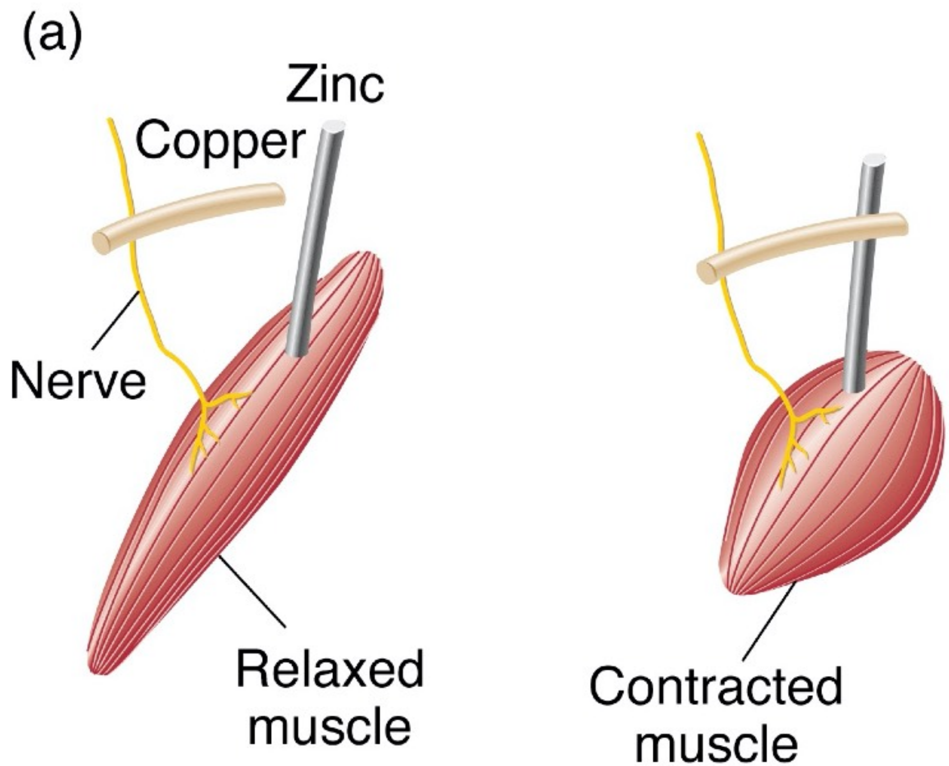
Segmentation, Specialization



Animal Electricity

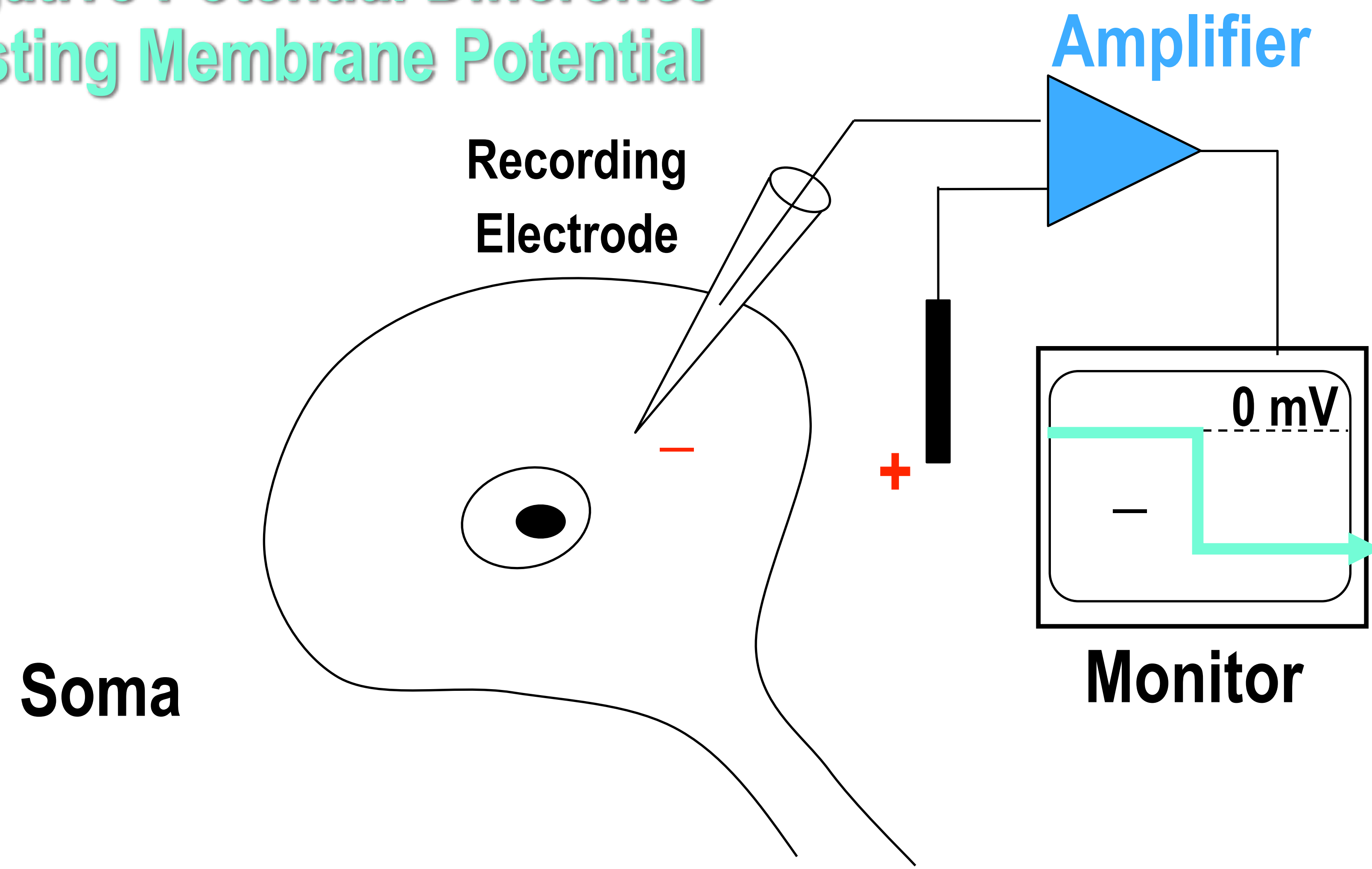
1791 Galvani hypothesized “electric fluid” passed from muscle to wires to nerves and back to muscle.

1792 Volta proposed an electrolytic effect which lead to the first “wet-cell” battery.

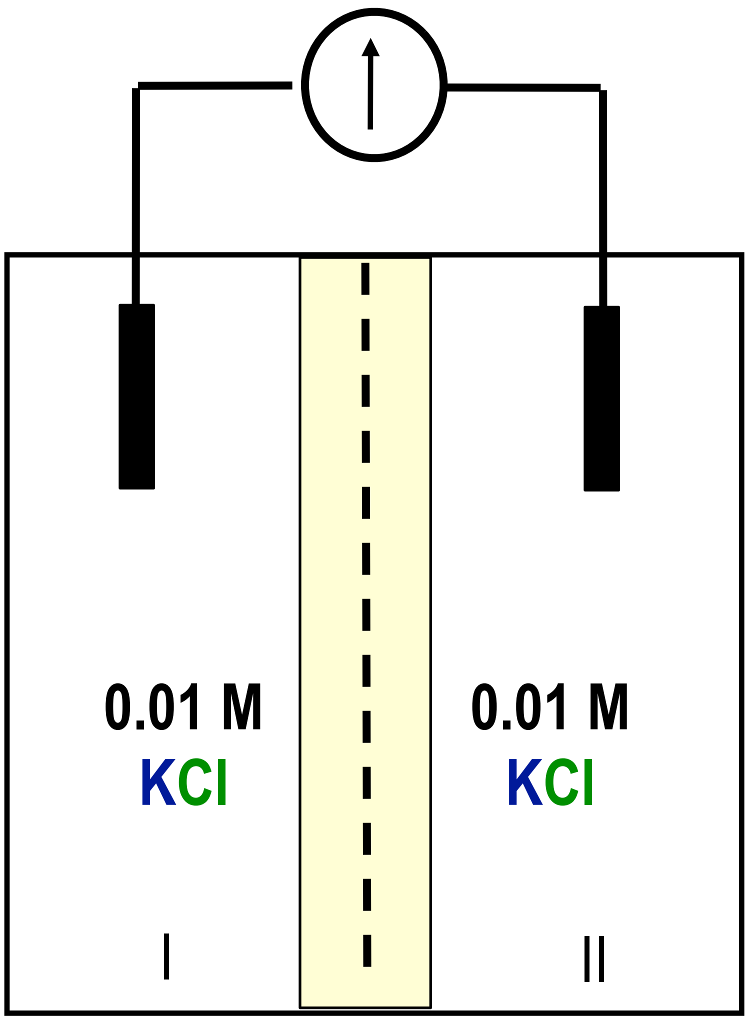


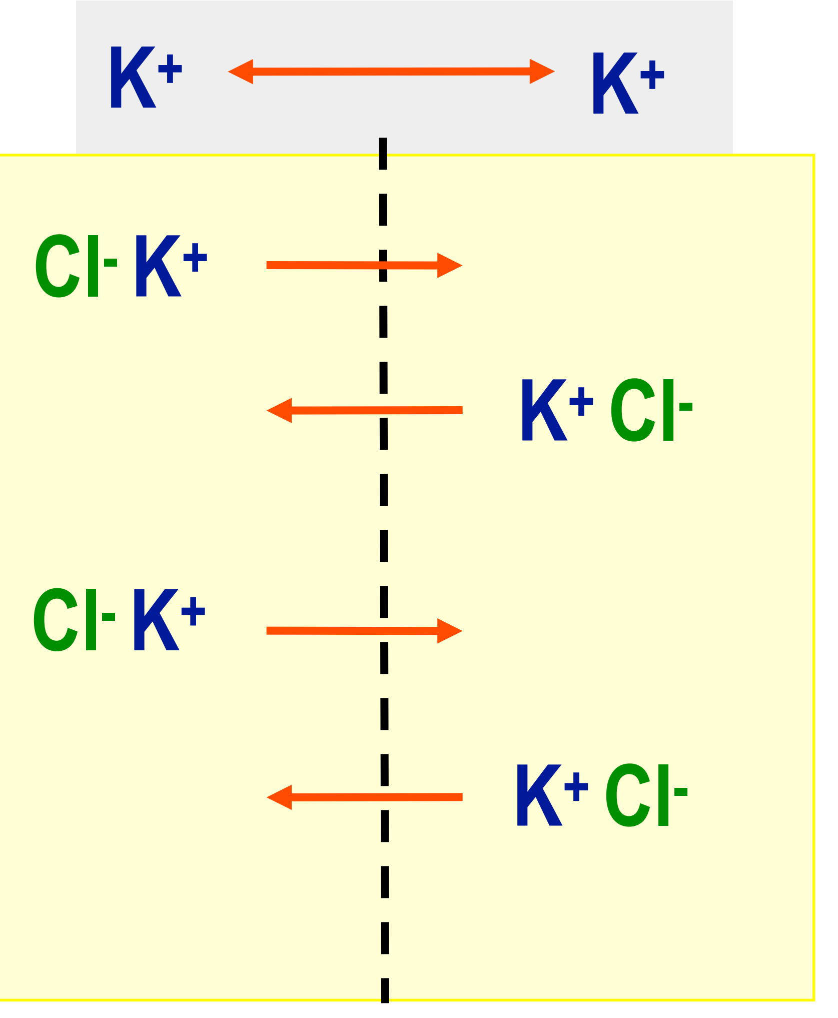
Excitable Cells

Negative Potential Difference
Resting Membrane Potential



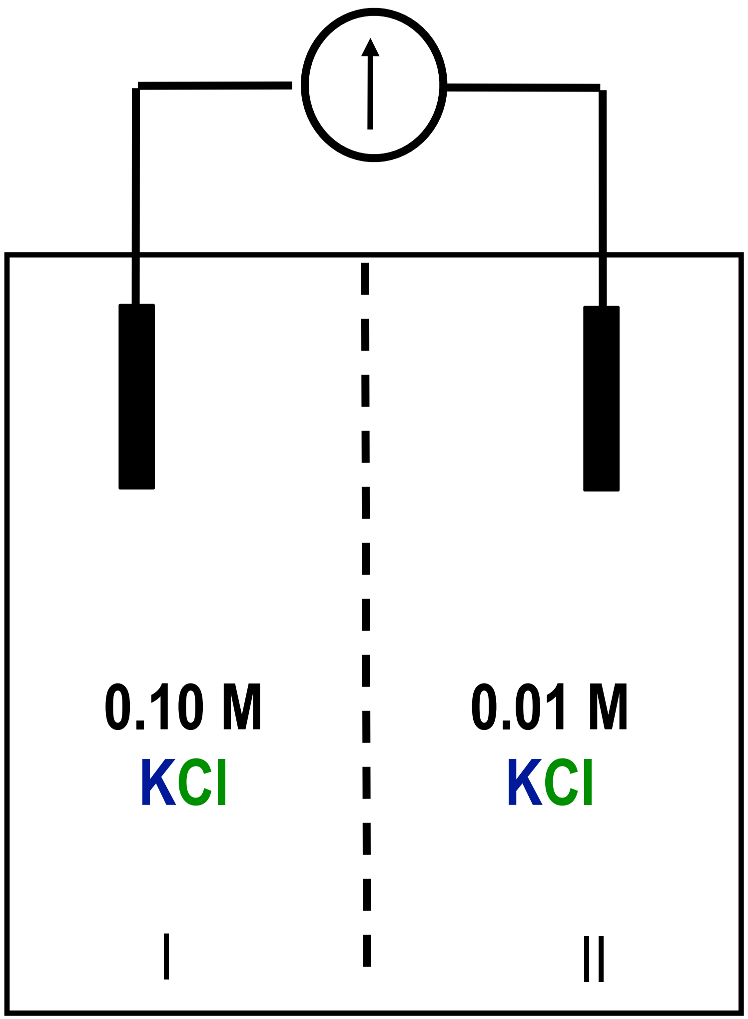
Equilibrium Potential

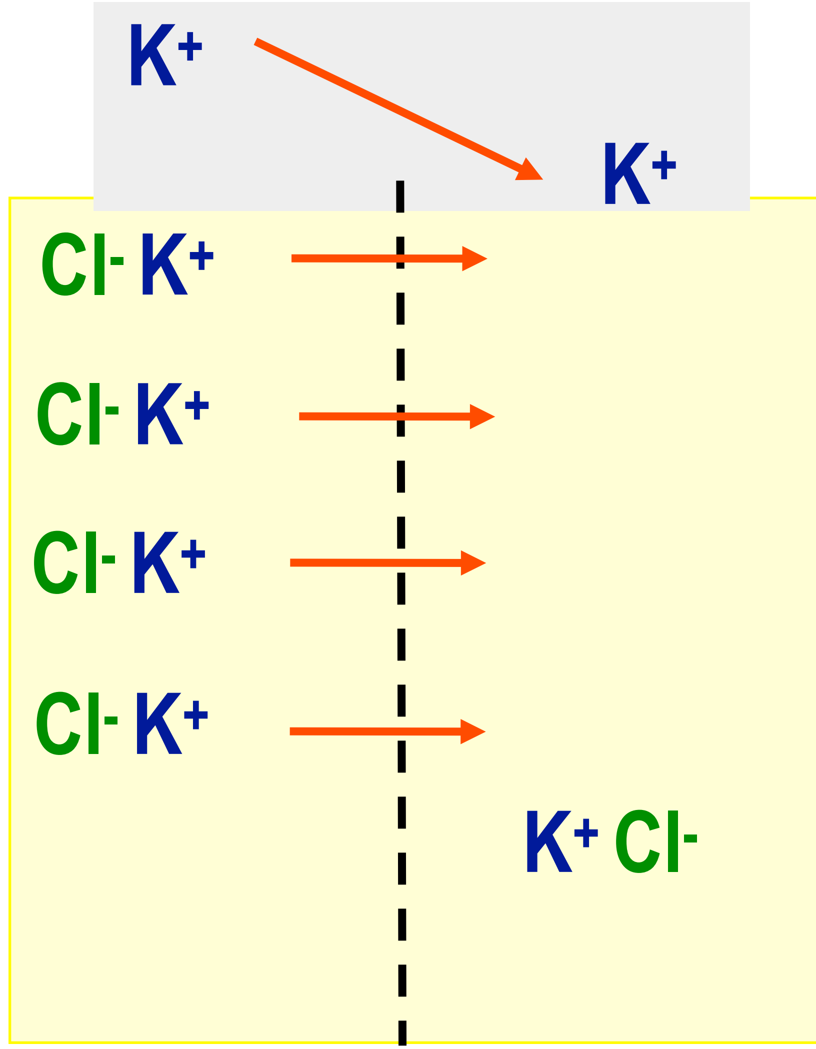




Permeable to K^+ only!

Equilibrium Potential

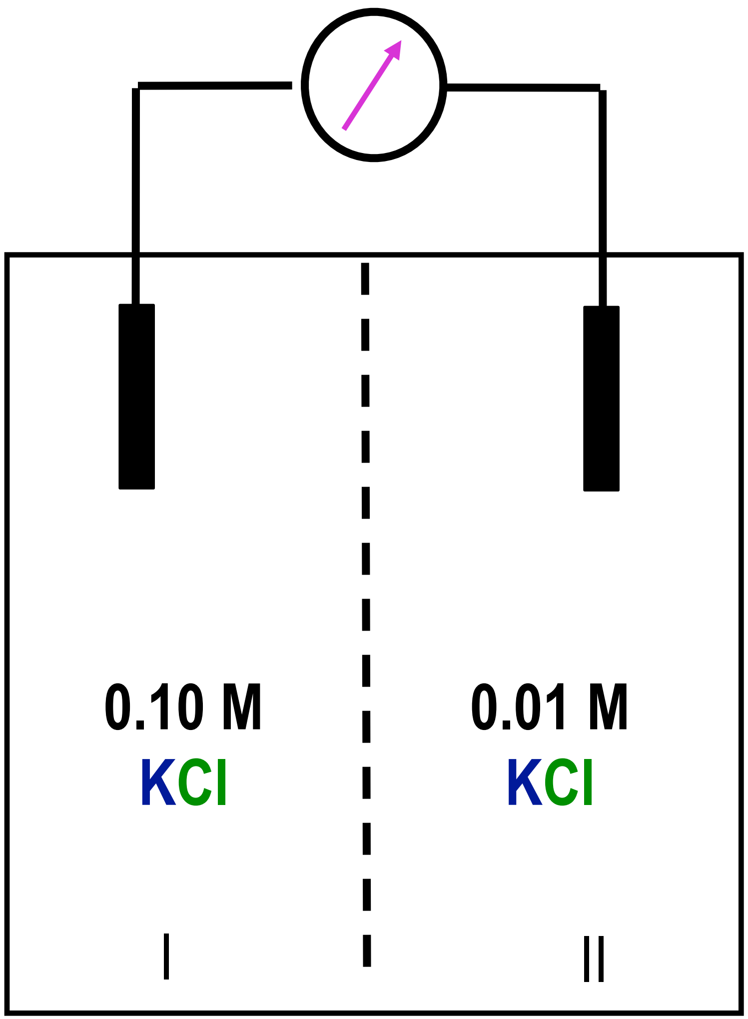


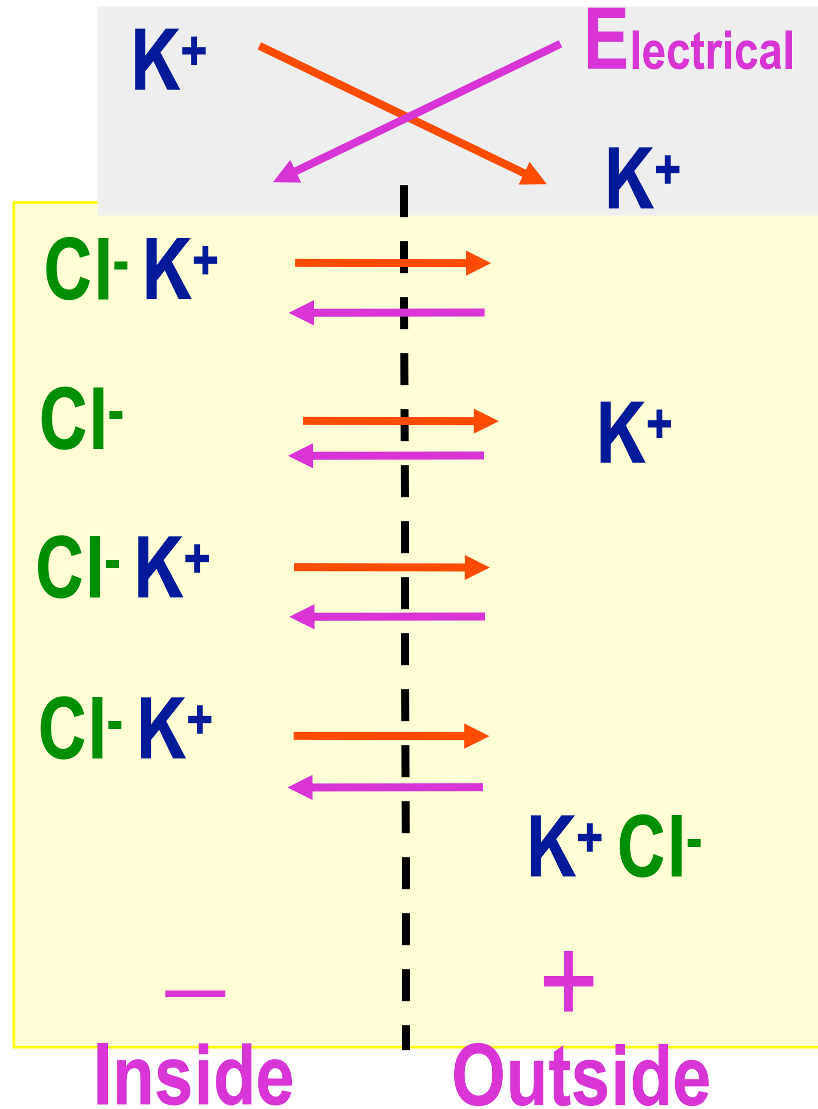


Initially electrically neutral

Equilibrium Potential

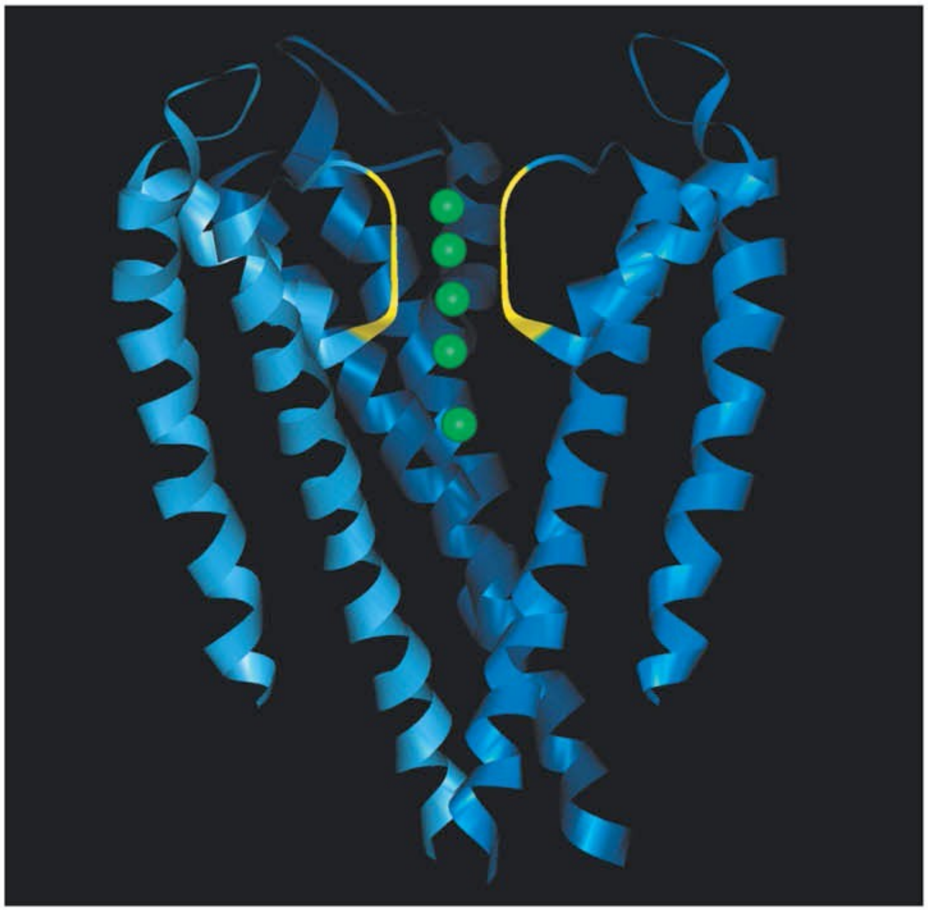
Chemical Work = Electrical Work

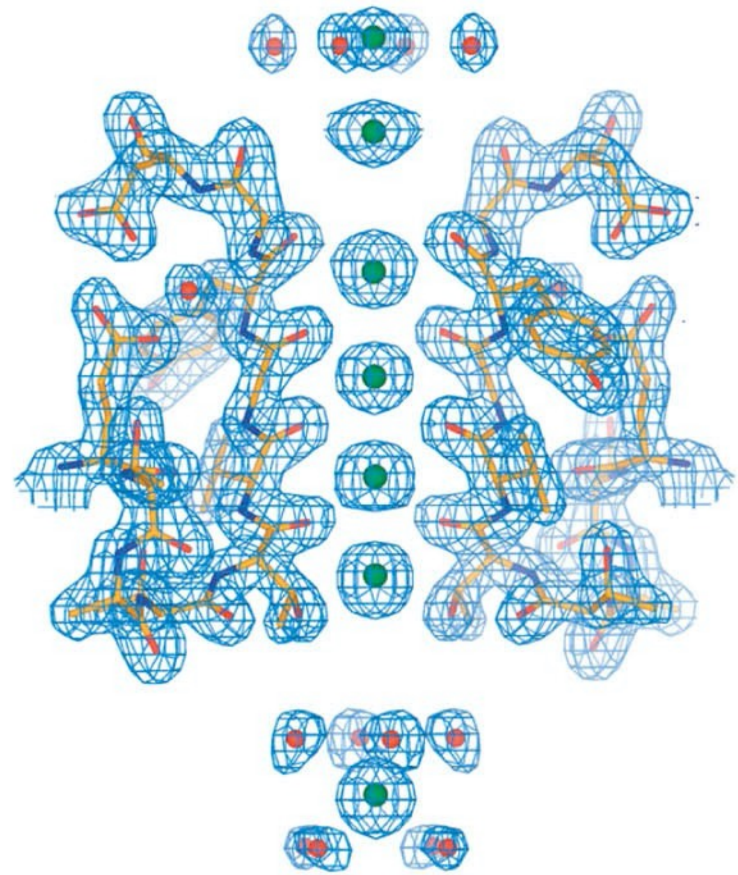




K Channel Function

Selective permeability partially establishes membrane potential





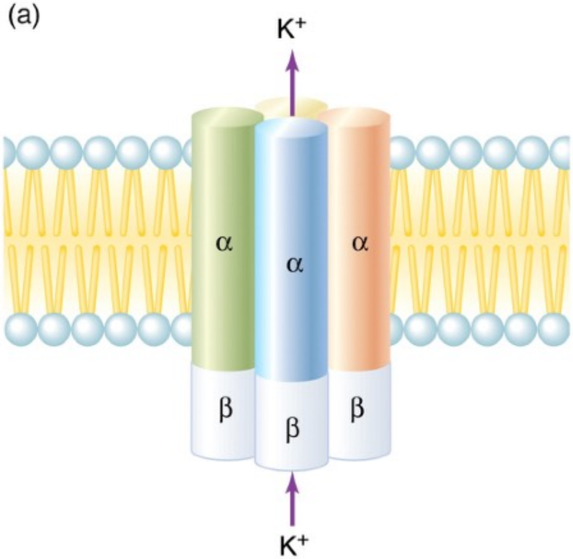
K+ leak (always open)

Important Players:

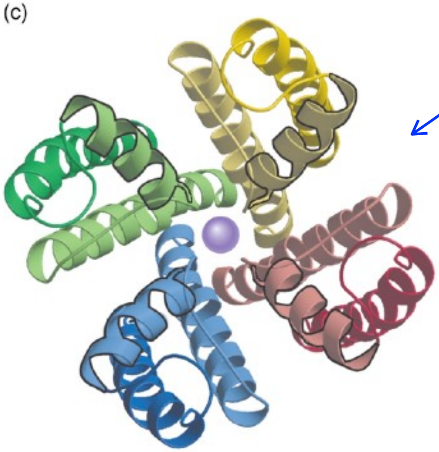
- voltage-gated Na+
- voltage-gated K+
- **K+ leak (always open)**

Potassium Channel

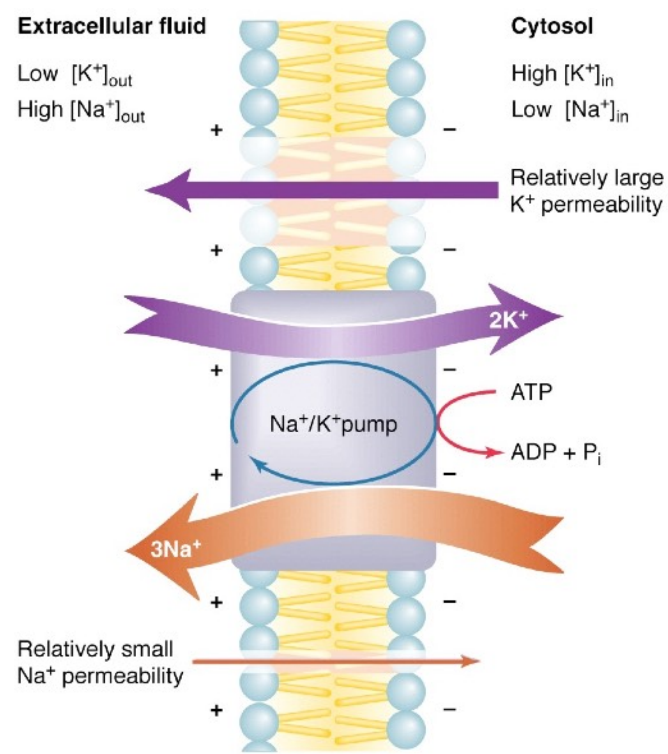
(a)



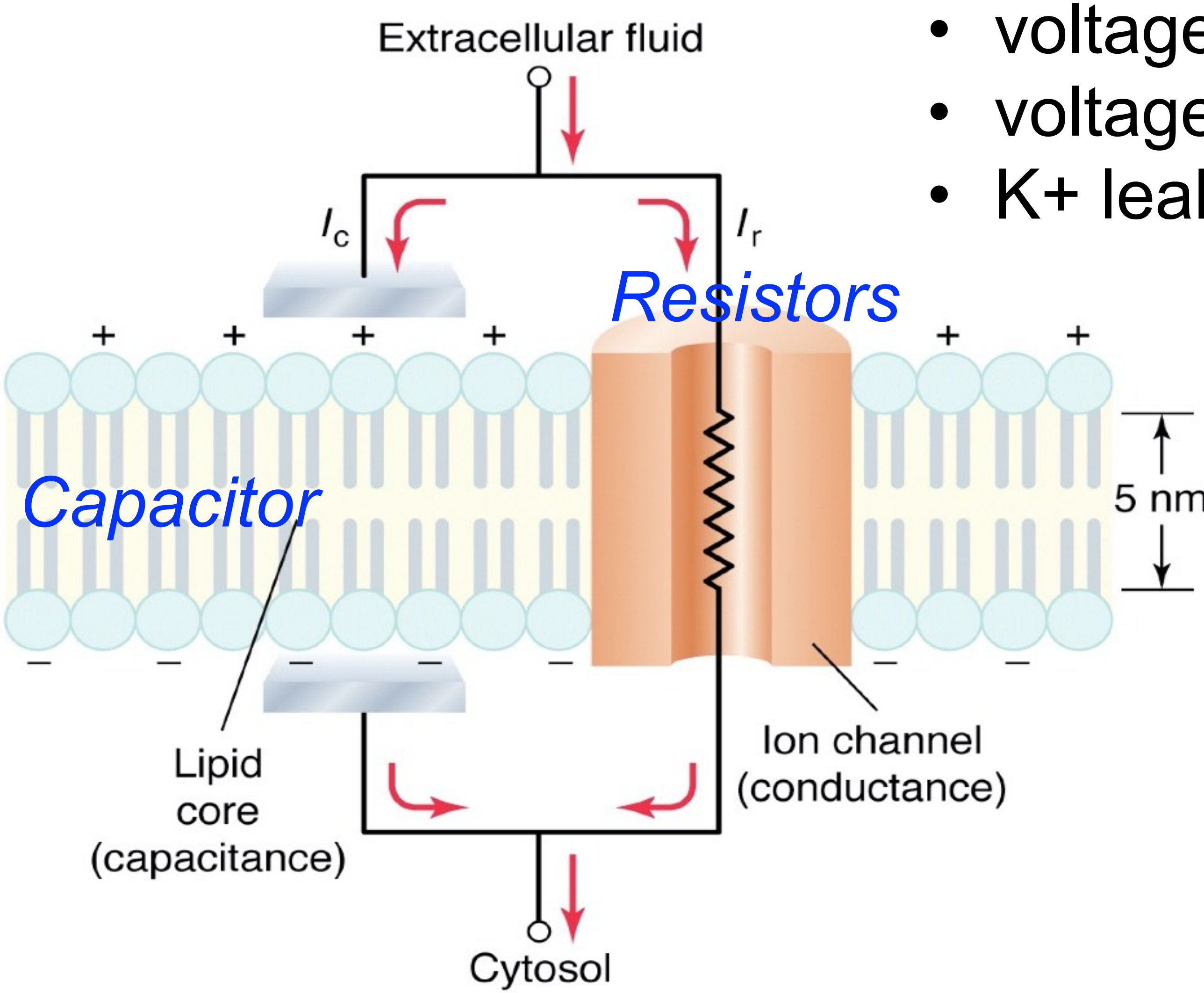
(c)



Sodium Potassium Pump



Membrane Resistance and Capacitance

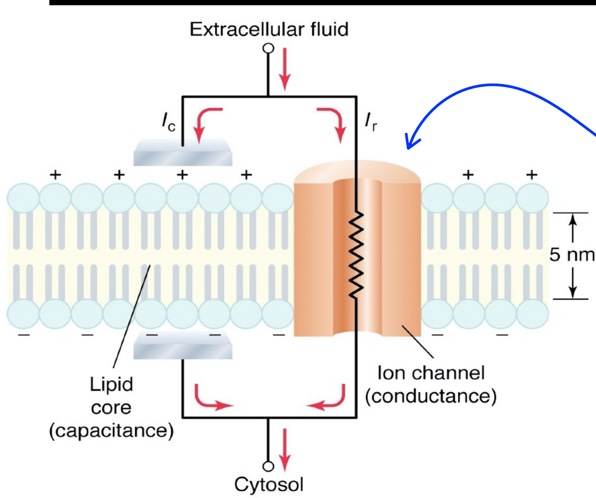


Important Players:

- voltage-gated Na+
- voltage-gated K+
- K+ leak (always open)

Neurons are Electrical Circuits

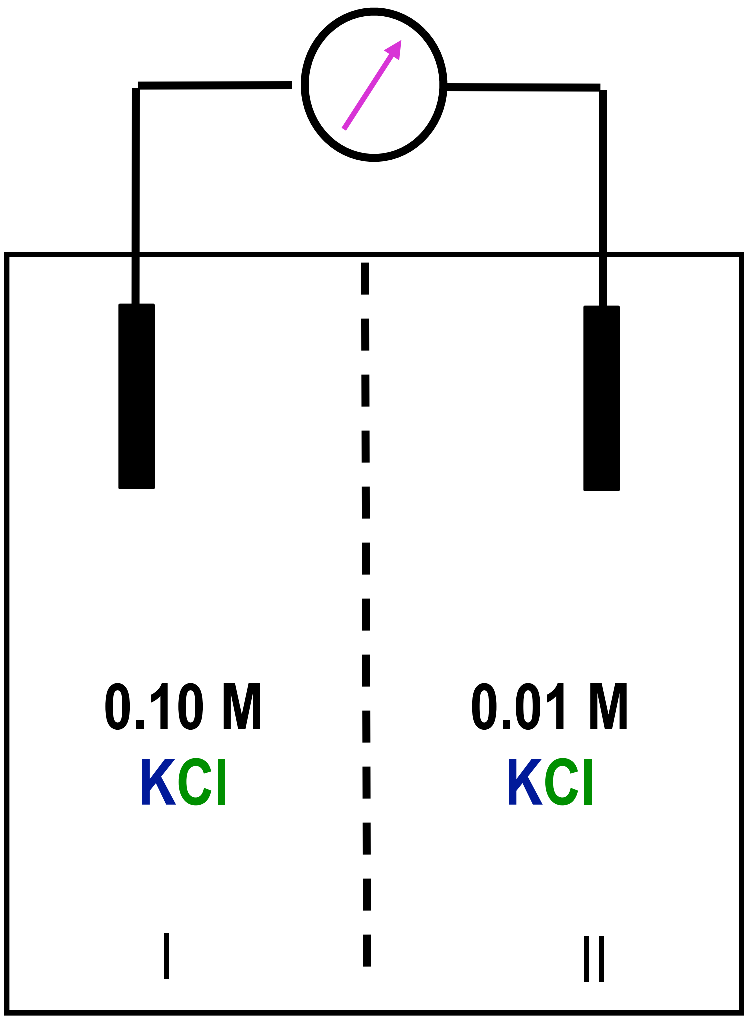
	Electrical Circuits	Neurons
Electrical Potential	Voltage, the difference in charge between electrodes	Membrane Potential: The difference in charge across a membrane due to ionic content and concentration
Resistance	Any barrier or bottleneck to electron flow	Lipid bilayer is a barrier to ion flow, so movement of ions across membrane is *controlled by the number and type of ion channels present*
Capacitance	Amount of charge stored per unit voltage (C=Q/V)	Lipid bilayer is a capacitor because it stores charge

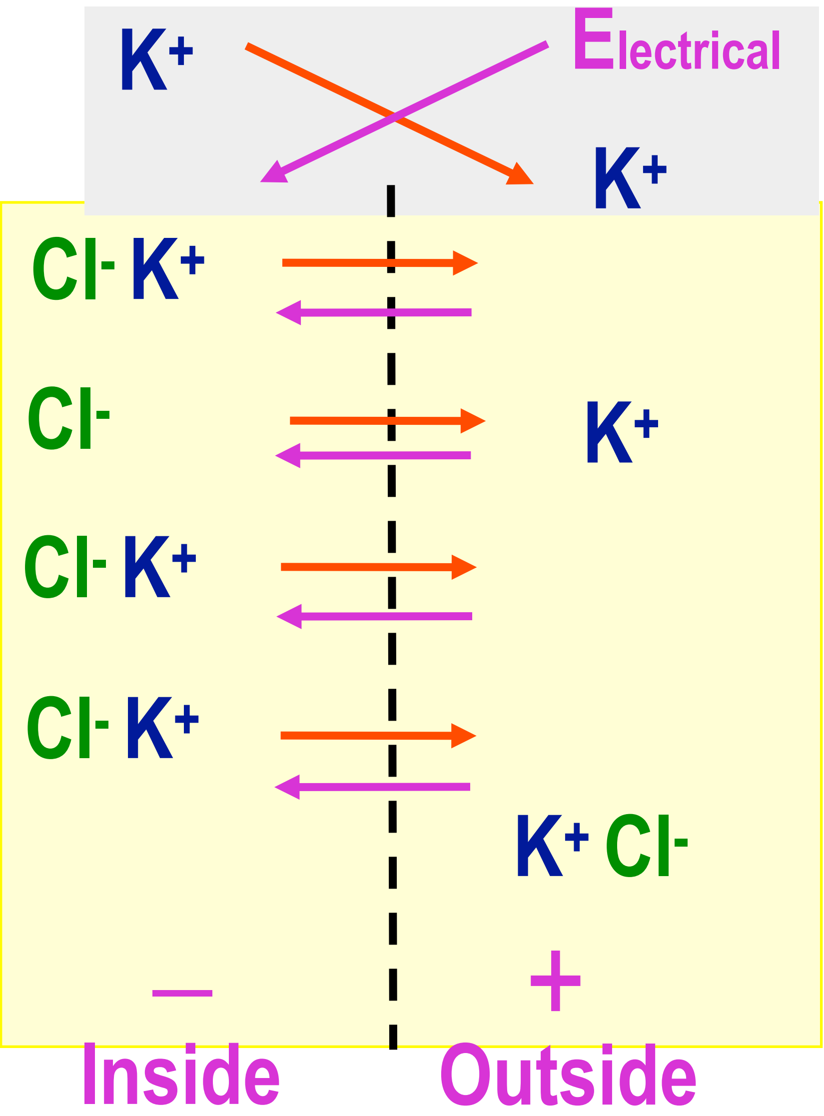


- Ion channels may be always open, or only open sometimes: voltage-gated, ligand-gated

Equilibrium Potential

Chemical Work = Electrical Work





Nernst Equation

used for finding the electric potential of a cell membrane with respect to one type of ion.
Or, how much electric work can the stored chemical energy across cell membrane do?

Chemical Work = Electrical Work

Chemical Work

$$W = RT \ln [X]_I/[X]_{II}$$

Electrical Work

$$W = E_x F z$$

At Equilibrium

$$E_x F z = RT \ln [X]_I/[X]_{II}$$

Equilibrium Potential (voltage difference if permeable)

$$E_x = RT/(Fz) \ln [X]_I/[X]_{II}$$

W = work

R = gas constant

T = absolute temperature

X = given ion

E = potential difference

F = Faraday's constant (charge per mole of electrons)

z = valence (# charges per molecule)

Resting Potentials

Animal	Cell	V_m (mV)
Squid	Giant axon	-60
Earthworm	Giant fiber	-70
Cockroach	Giant fiber	-90
Snail	Ganglion	-60 to -70
Puffer fish	Brain cell	-50 to -80
Frog	Sciatic	-60 to -80
Rabbit	Sympathetic	-65 to 82
Cat	Motor neuron	-55 to -80

Goldman Equation

Used to determine the potential across a cell's membrane taking into account all of the ions that are permeant through that membrane.

What determines (drives) resting membrane potential?

Must consider permeability (P)

$$V_m \propto \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o}$$

$$P_K >> P_{Na} > P_{Cl}$$

Goldman Equation

What determines (drives) resting membrane potential?

Must consider permeability (P)

$$V_m = E_K \propto \frac{P_K[K^+]_o}{P_K[K^+]_i}$$

$$P_K >> P_{Na} > P_{Cl}$$

***Hypothesis*:**

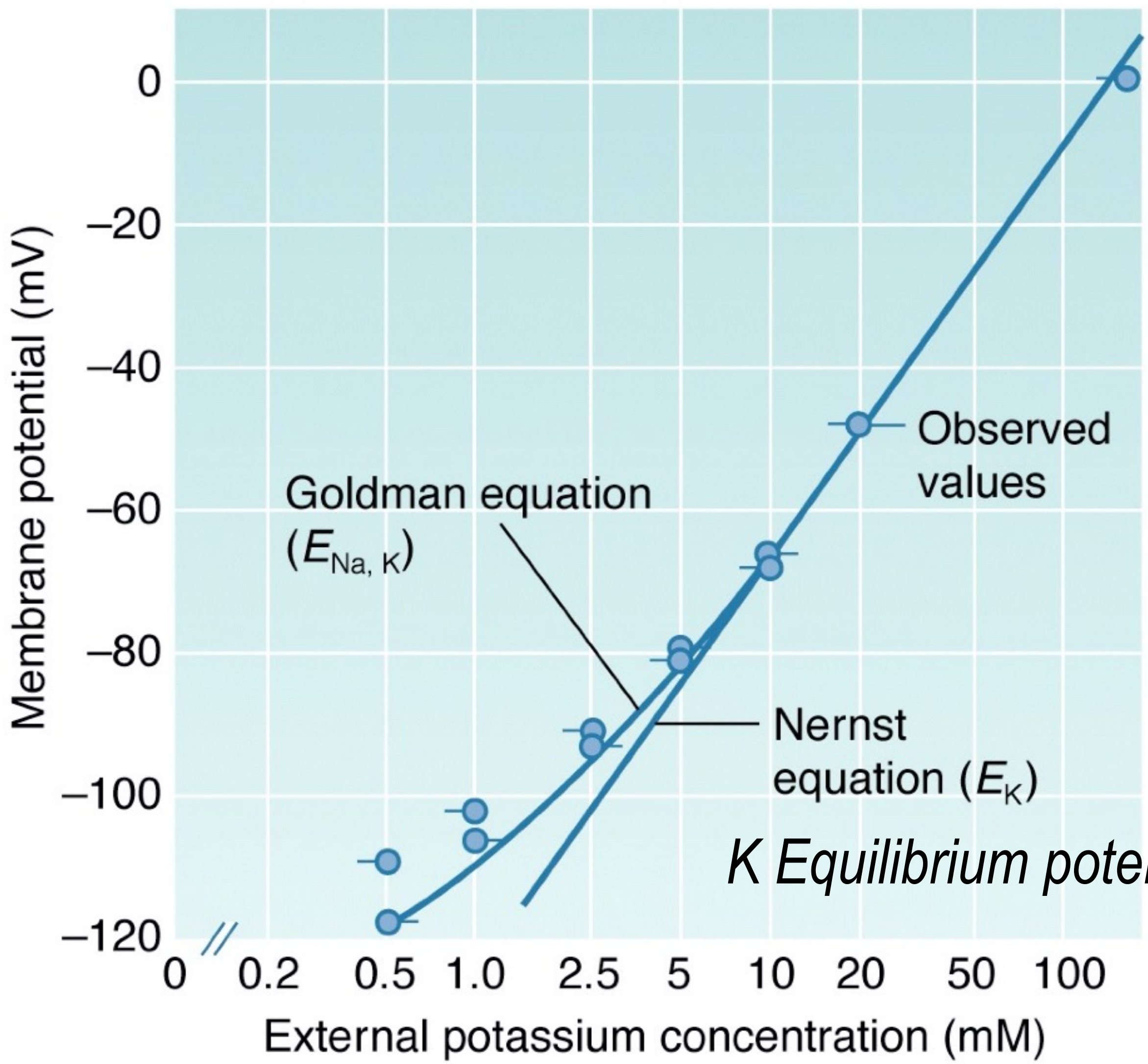
Resting membrane potential determined by K equilibrium potential

Ionic Concentration

Major ions in mammalian excitable tissue

	$[\ ]_i$ mM	$[\ ]_o$ mM	E_x mV	
K^+	155	4	-98	Accept hypothesis!
Na^+	12	145	+67	Positive value
Cl^-	4	123	-90	Low permeability

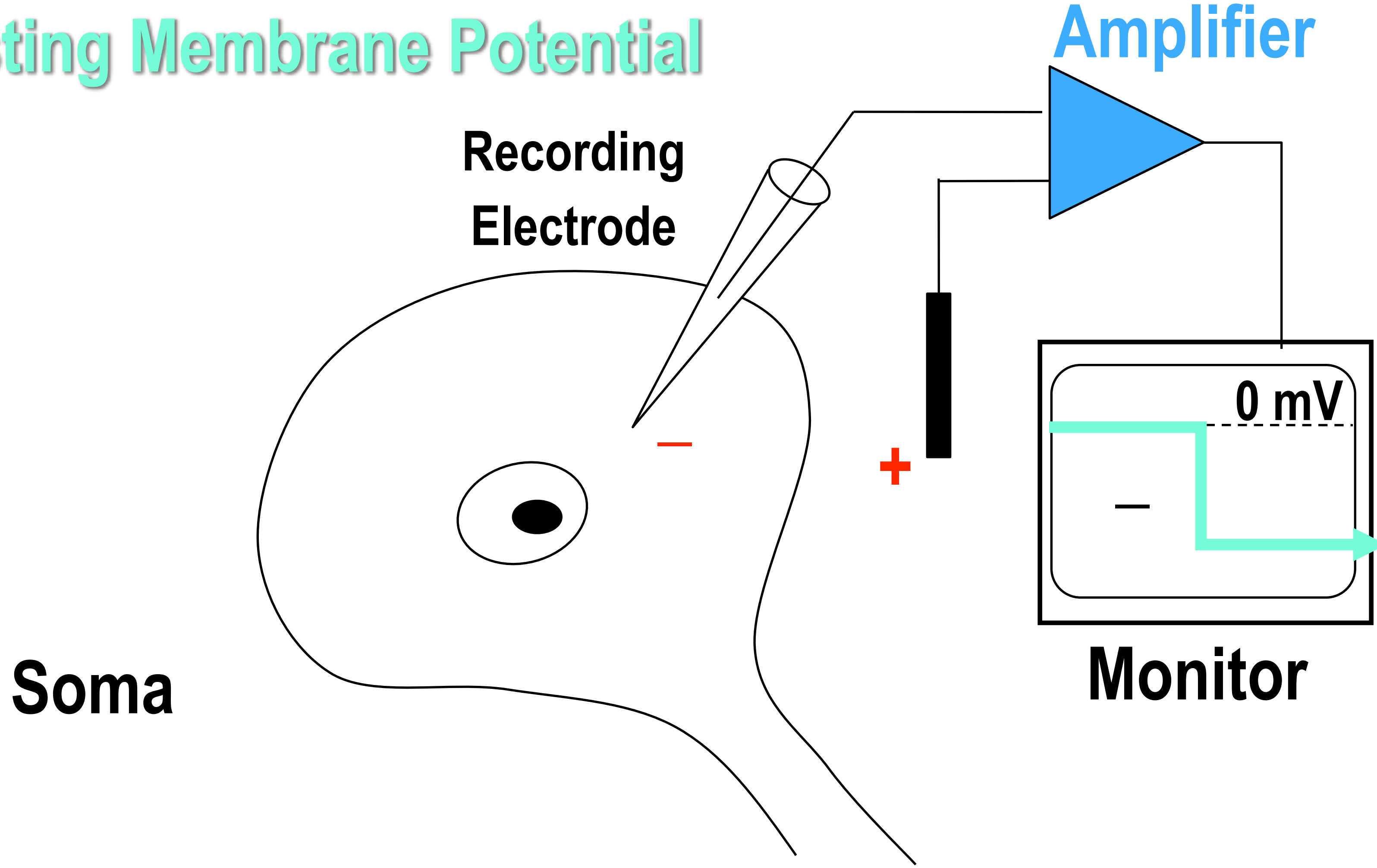
K Determines Membrane V_m



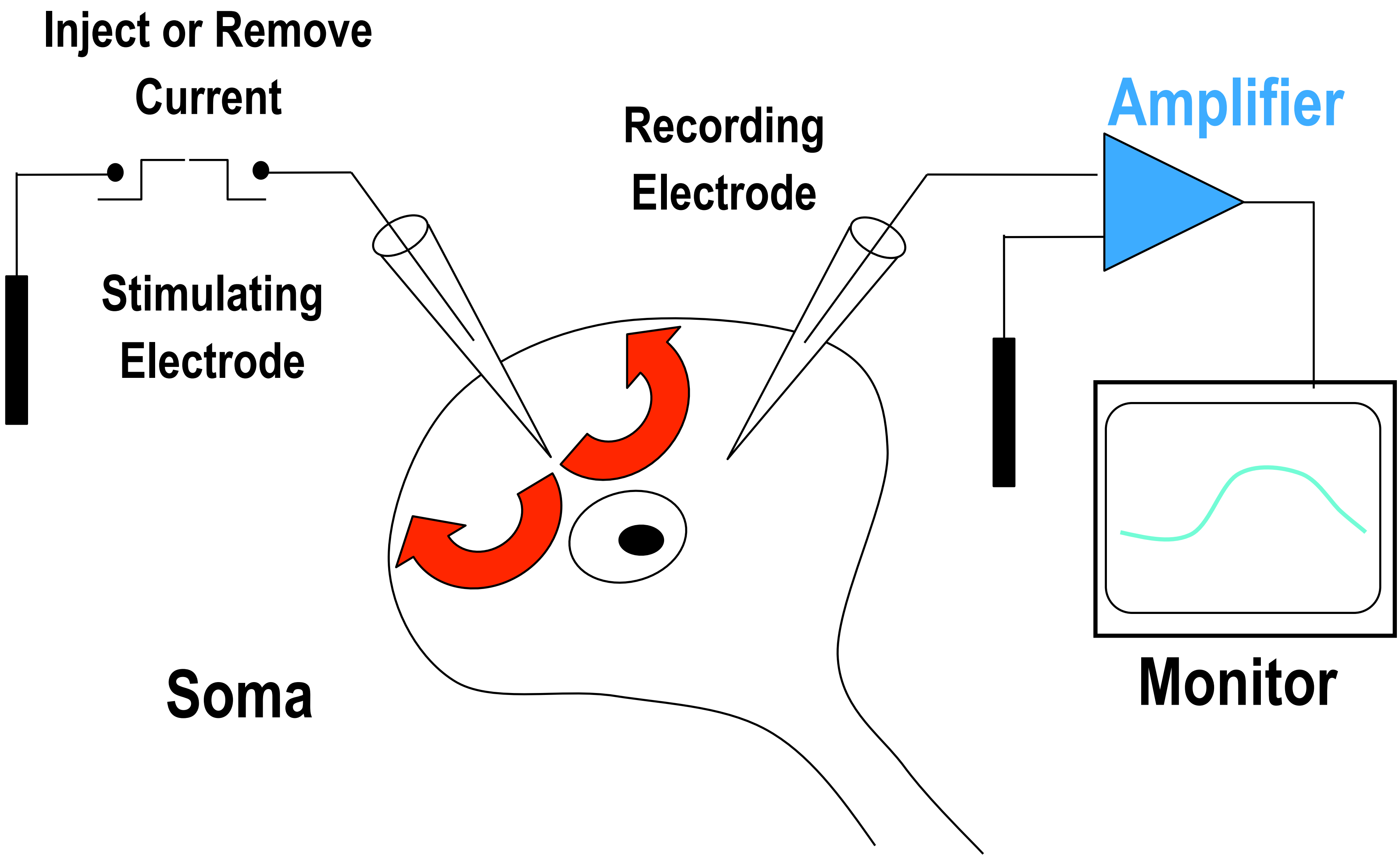
K Equilibrium potential

Excitable Cells

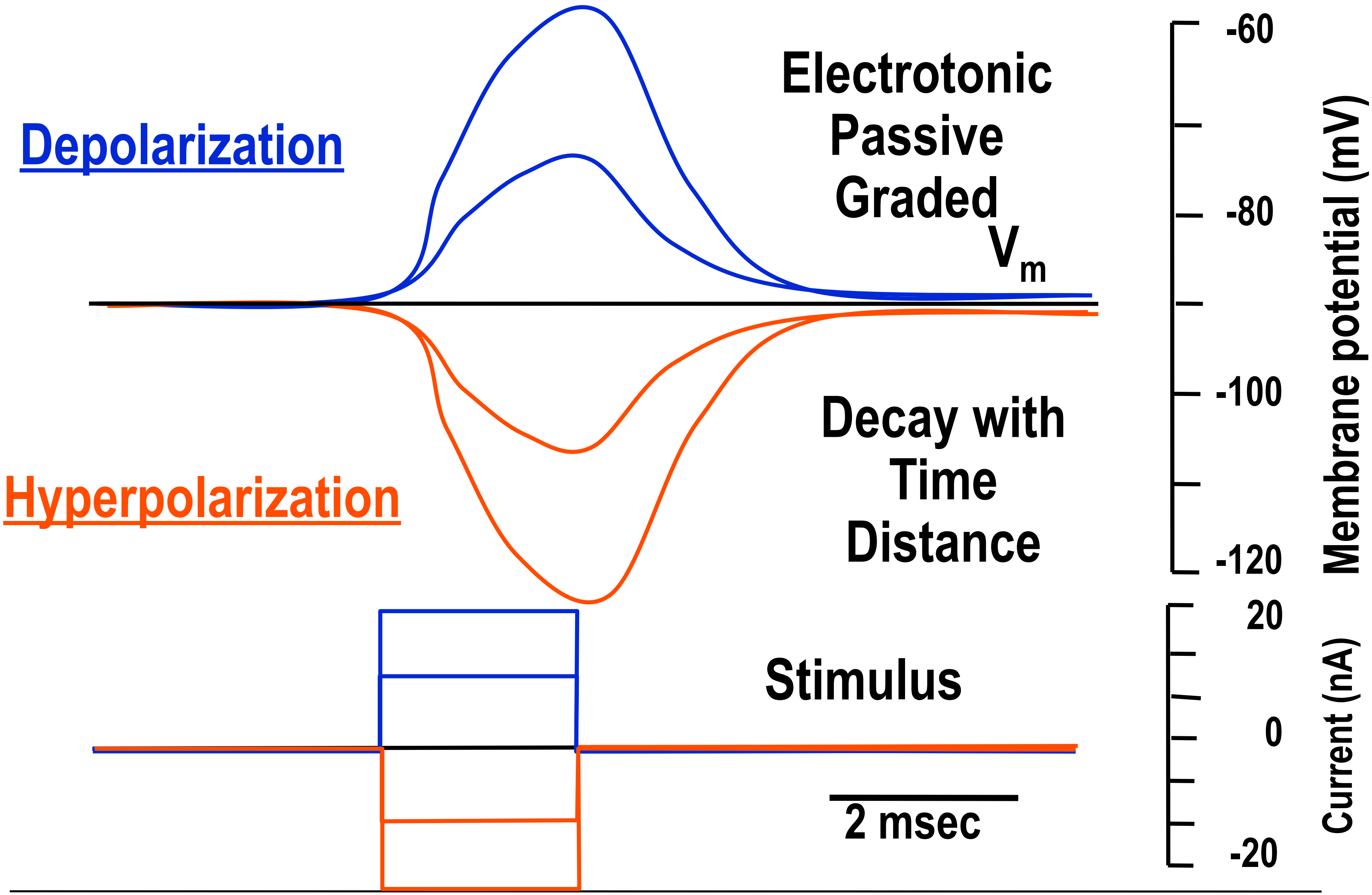
Negative Potential Difference
Resting Membrane Potential



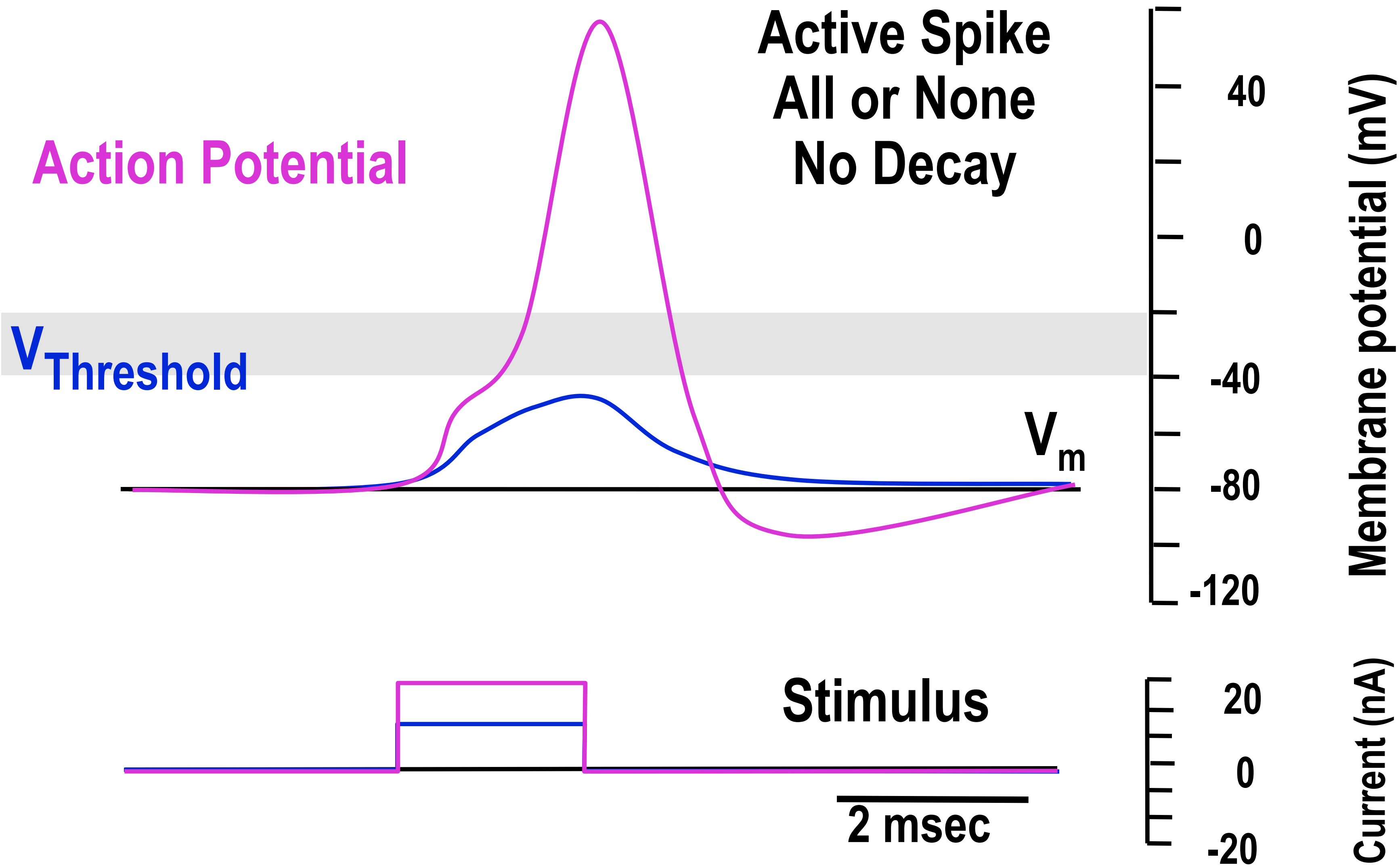
Excitable Cells



Electrotonic Potentials



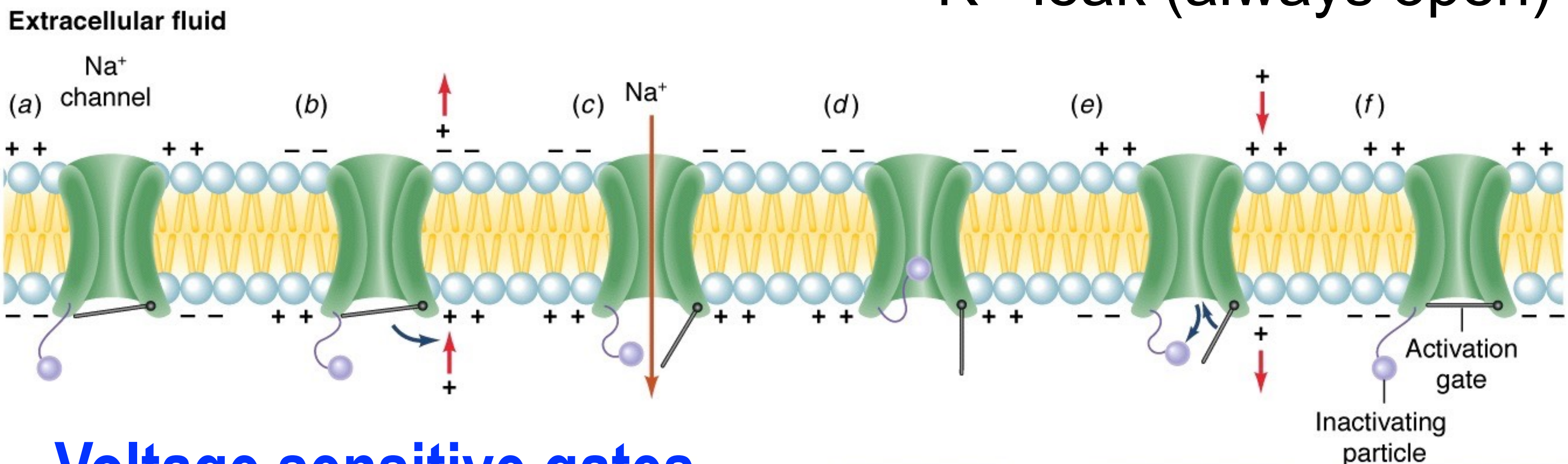
Action Potentials



Voltage-Gated Channels

Important Players:

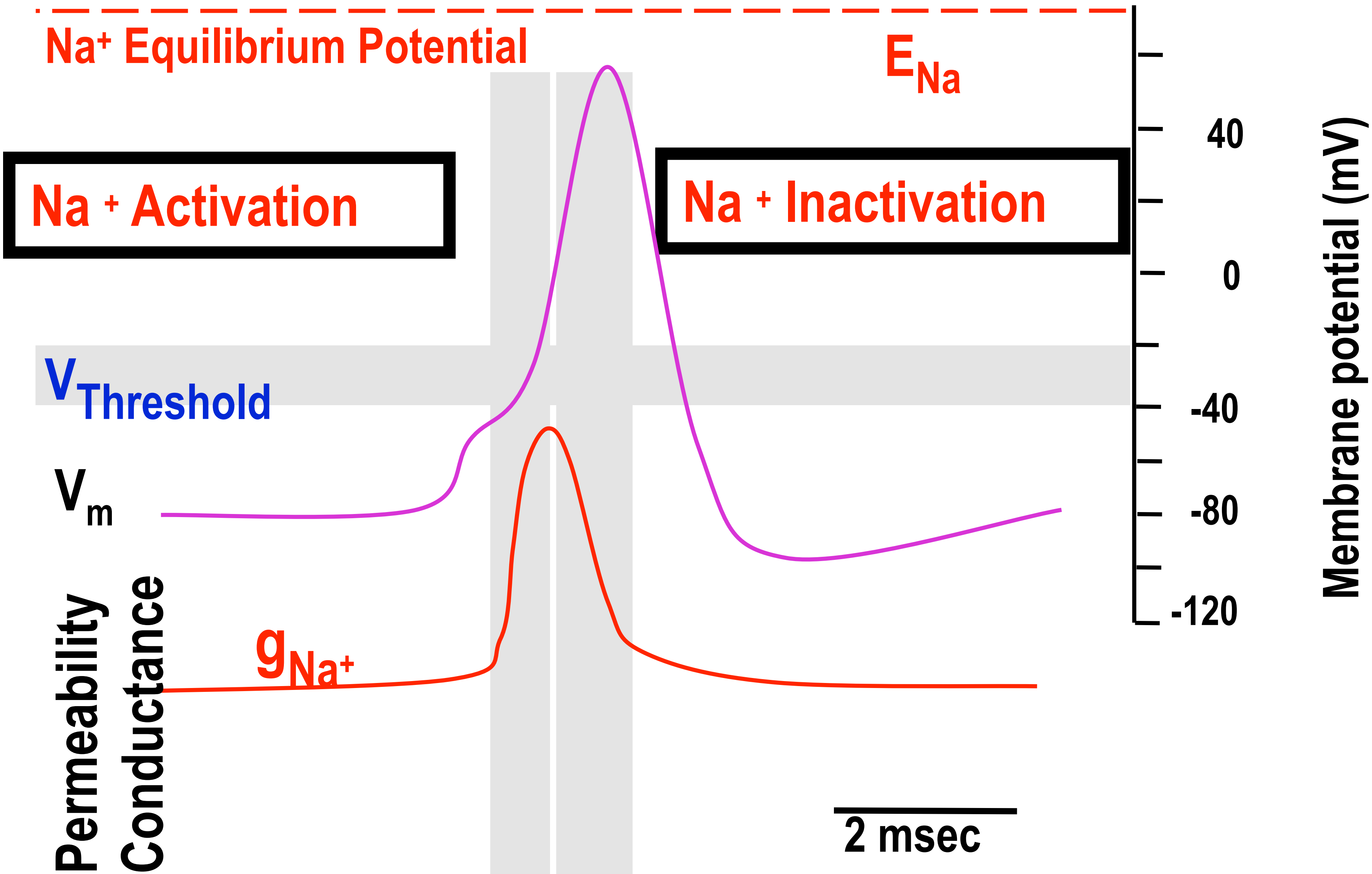
- **voltage-gated Na+**
- **voltage-gated K+**
- K+ leak (always open)



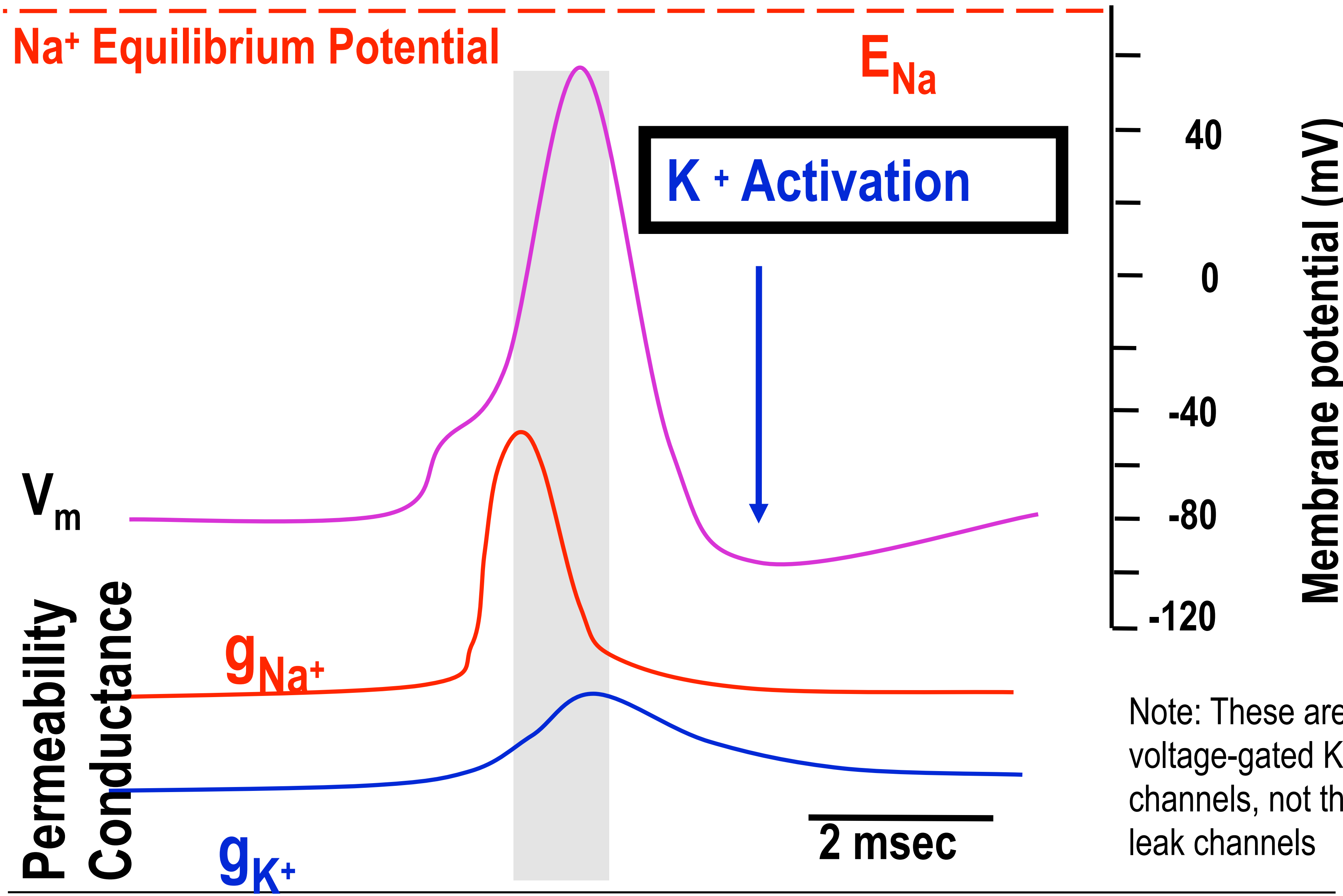
Voltage sensitive gates

1. Activation gate opens
2. Inactivating particle blocks channel
3. Activation gate closes

Action Potentials



Action Potentials



Note: These are voltage-gated K+ channels, not the leak channels

Hodgkin Cycle

1/R = g
g_{Na} = conductance of Na^+
conductance ~ permeability
I = current
V = voltage
E_{Na} = chemical potential for Na^+ (from Ion concentration gradient across membrane)
emf_{Na} = (V_m - E_{Na}), the driving force for Na^+ to cross the membrane -- it can cross when channels are open

Ohm's Law

$$I = \Delta V / R$$

$$I = g_{Na} (V_m - E_{Na})$$

Opening of Na^+ channels in membrane

Increased membrane Na^+ permeability

Increased flow of Na^+ into cell

Depolarization

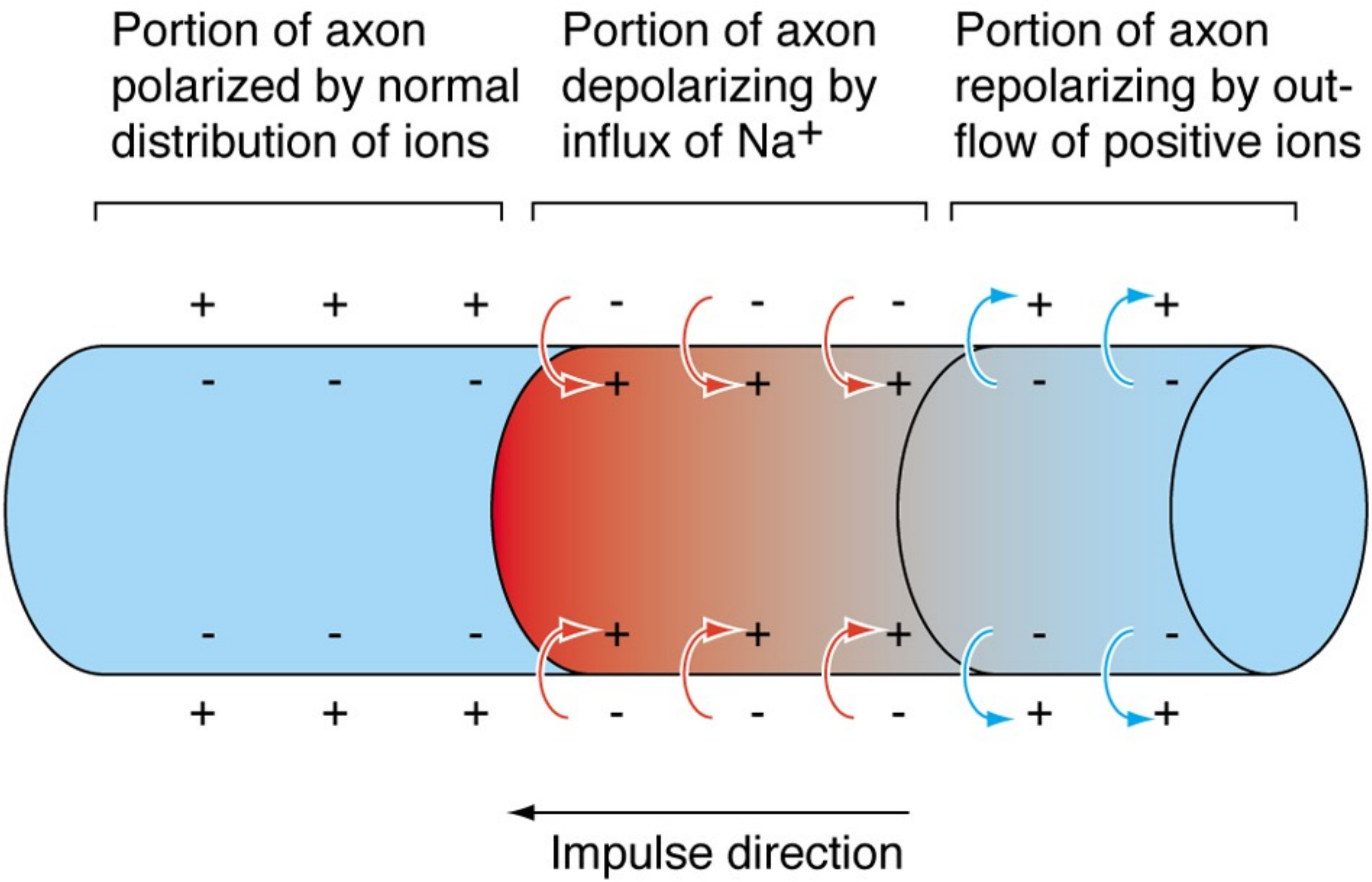
V_m moves toward E_{Na}

Positive Feedback Cycle

Action Potential

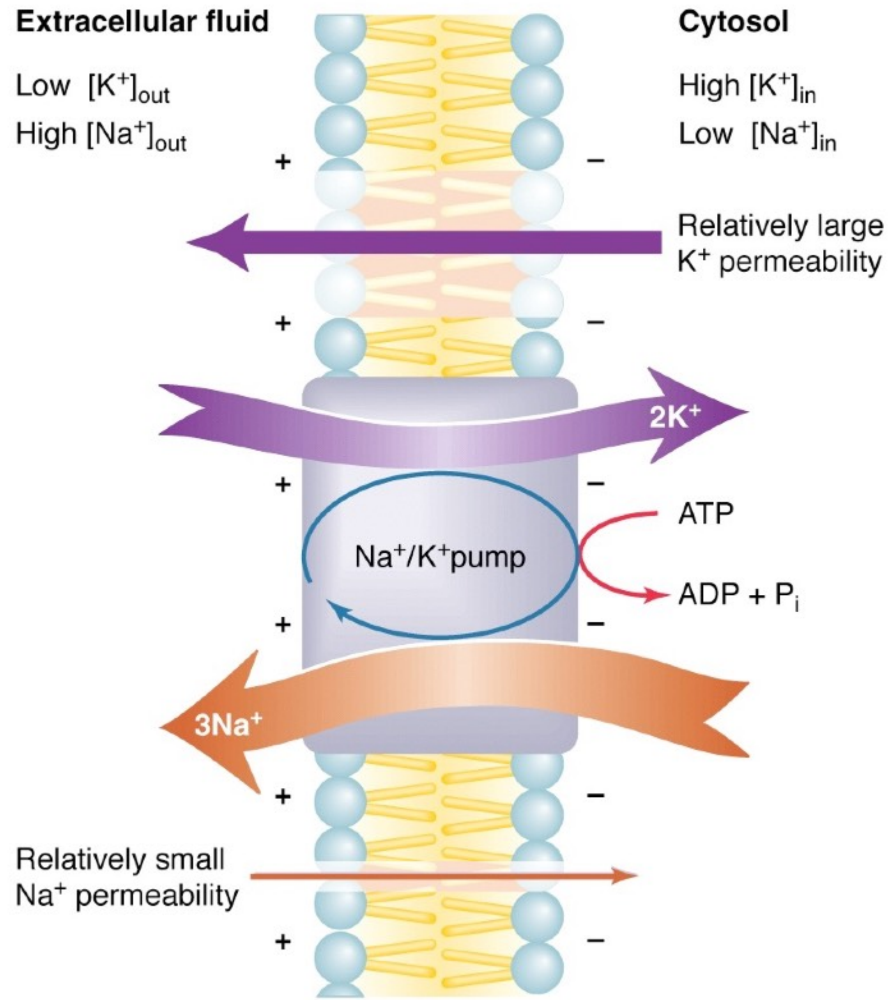
- Axon membrane is polarized: [Na+] high on outside, low on inside
- Na+ ion channels are gated and voltage sensitive:
- Traveling action potential (high voltage) opens neighboring Na+ channels
- Na+ rushes in
- [Na+] gradient provides the chemical potential energy that is transferred to electrical current
- Action potential travels towards chemical gradient -- difference in [Na+] across membrane
- Action potential (high Vm) opens neighboring voltage-sensitive Na+ ion channels.
- It doesn't go backwards because it takes a while to reset the chemical potential of the membrane -- it has to travel towards the "unused" [Na+]

Action Potential

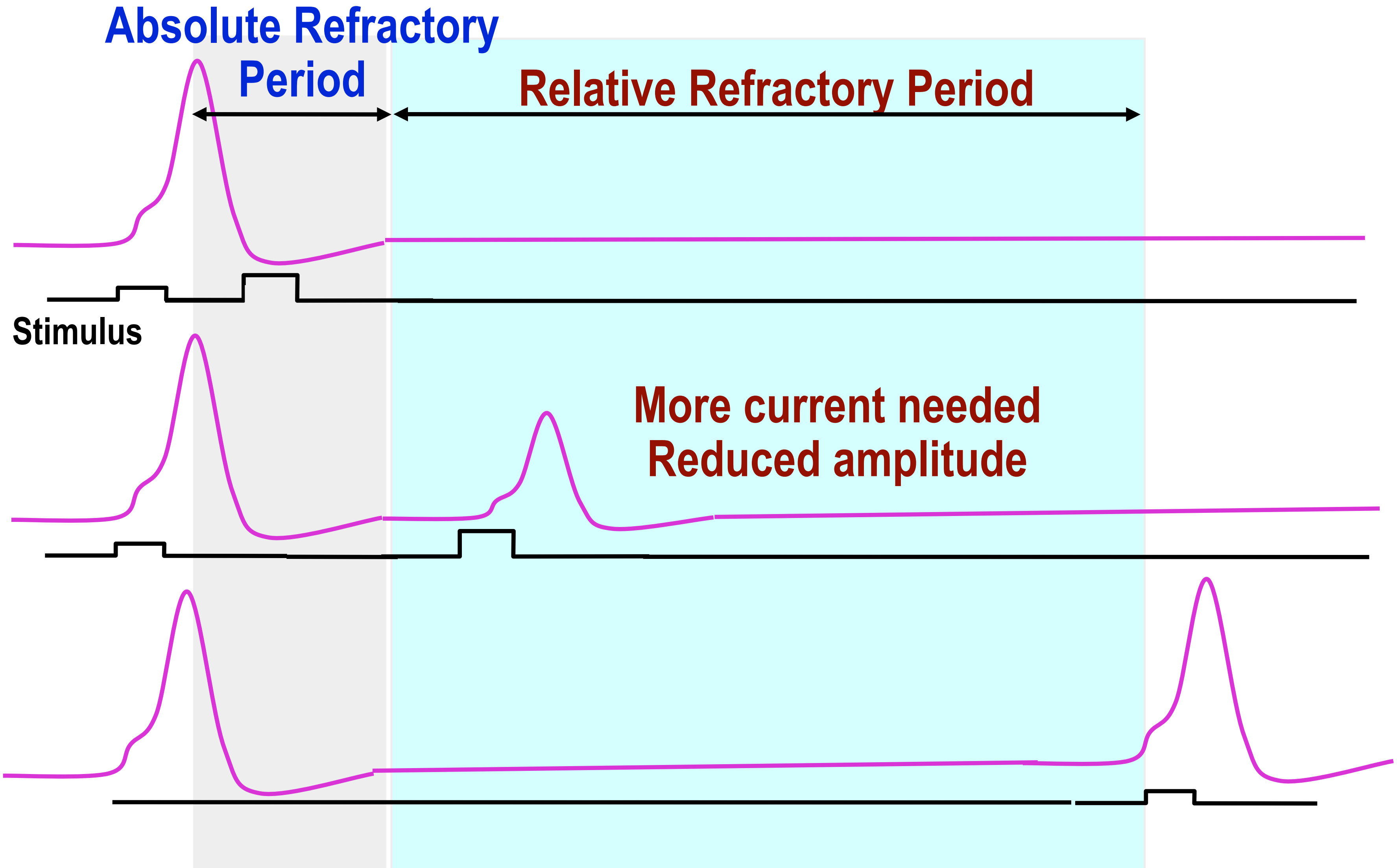


Na^+/ K^+ Pump

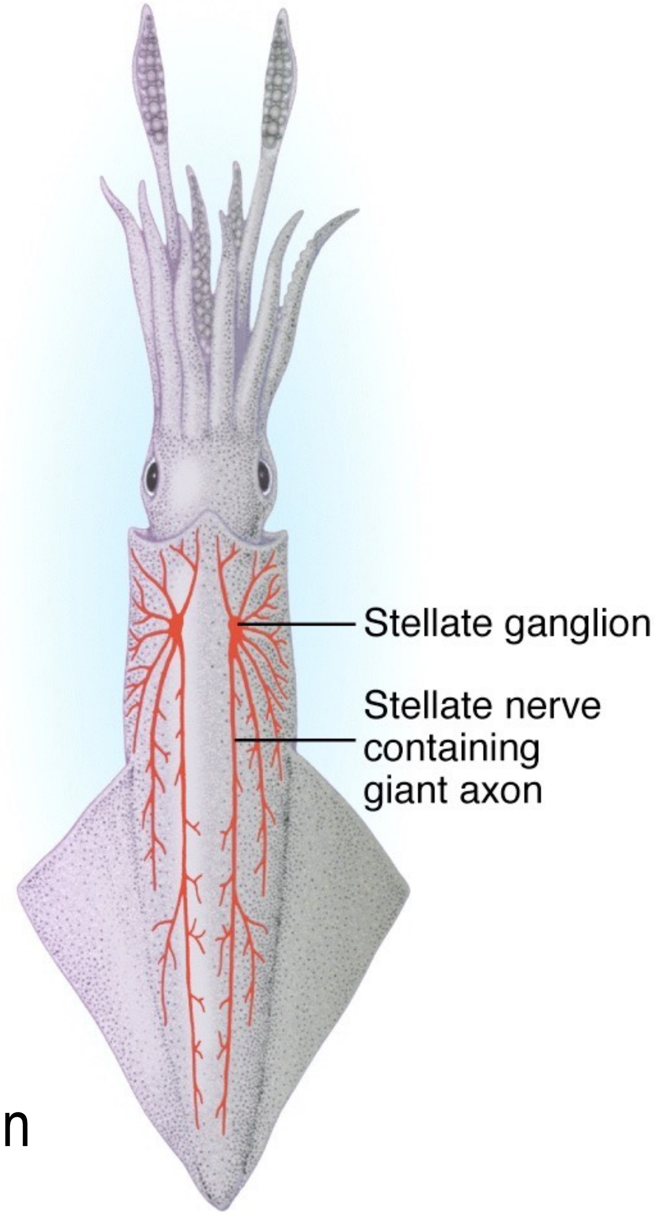
Why doesn't it all run down? Concentrations become equal?



Refractory Periods



Giant Axons in Squid



Allowed first studies of signal propagation

Voltage Clamping

- First applied to Squid Giant Axon
- Allows experimenter to change Vm abruptly to any preselected value and hold it there (employs feedback circuit).
- Since Vm constant, measuring the ion current allows us to determine the emf electromotive force -- i.e., ($Vm - E_{Na}$)

Ohm's Law

$$I = \Delta V / R$$

$$I = g_{Na} (V_m - E_{Na})$$

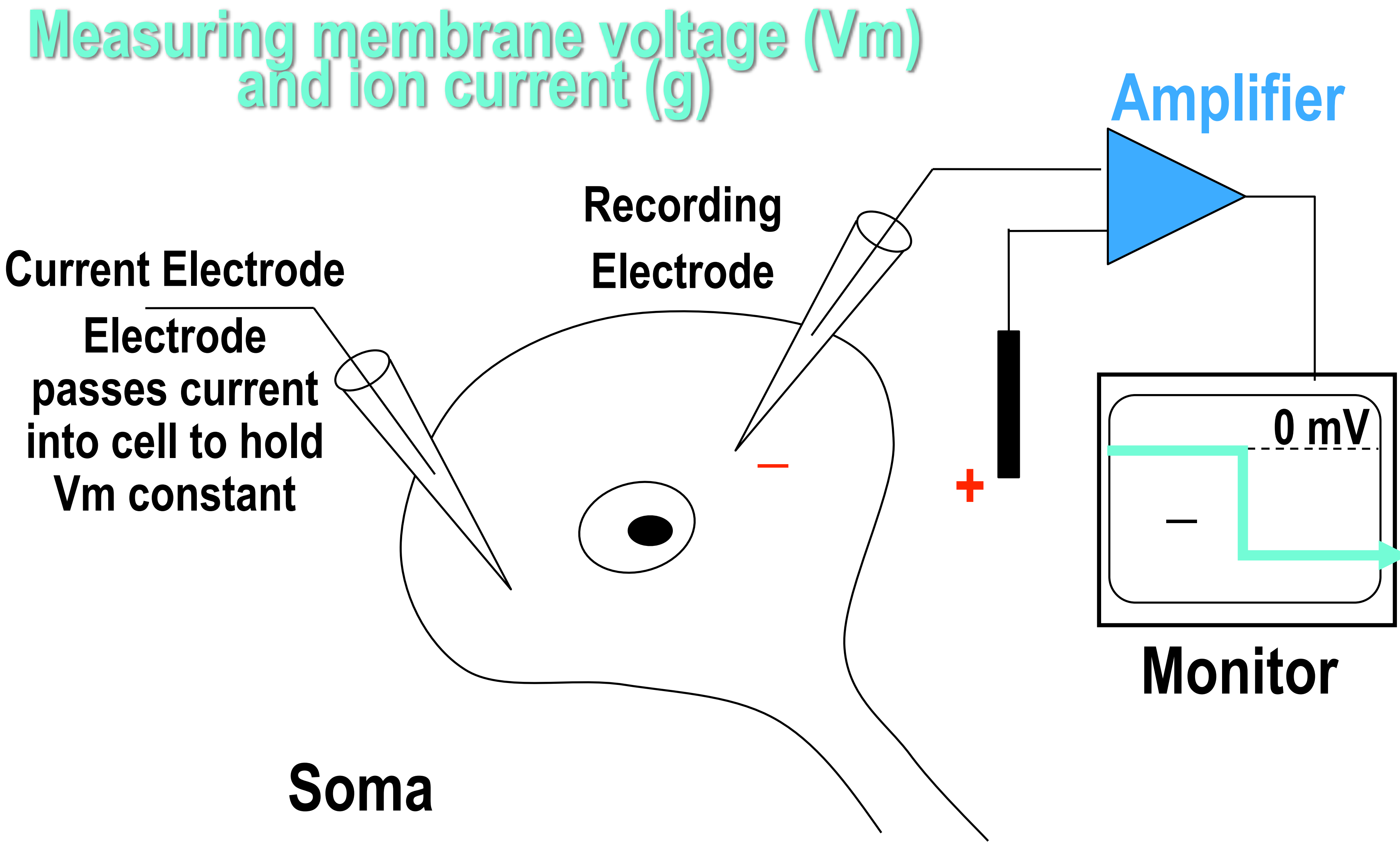
$1/R = g$

g is conductance

conductance ~ permeability

- Can apply Ohm's law to calculate changes in membrane conductances during the Action Potential. When g_{Na} goes up, I goes up.

Voltage Clamping



Voltage Clamping

Experiments of Hodgkin & Huxley:

• Led to the hypothesis that a sudden depolarization causes a large number of Na+ channels to open transiently.

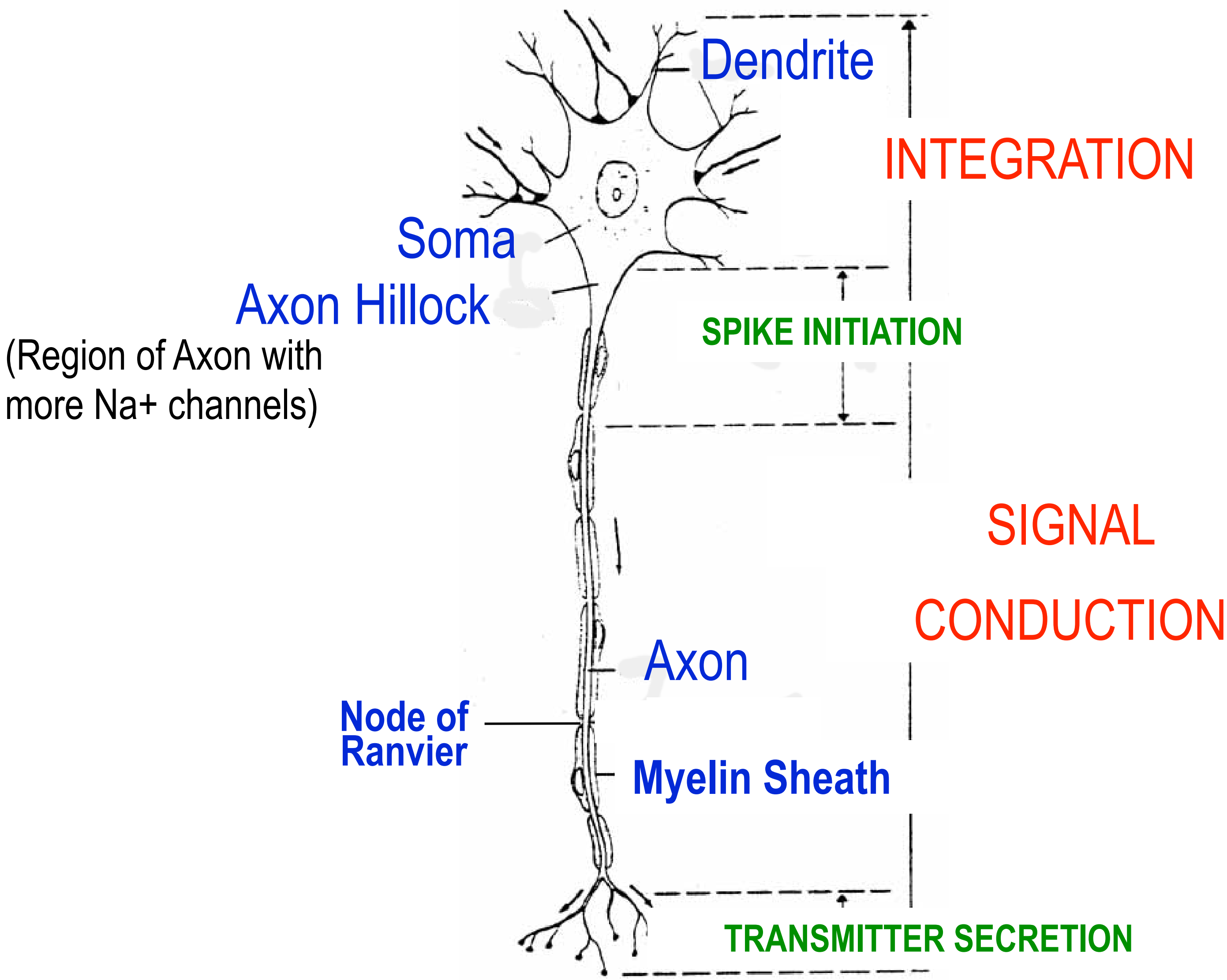
• Producing an increase in Na+ conductance across membrane

• Allows Na+ to flow into axon.

• High Na+ in extracellular environment drives Na+ into axon.

• Rising conductance (g_{Na}) causes current (I_{Na}) to rise.

Structure of Neuron



Changes in Membrane Potential

- **Graded:**
  - Amount of voltage change is proportional to current applied
  - **Depolarization**
    - Two sides of membrane become more equally charged
  - **Hyperpolarization**
    - Two sides of membrane become less equally charged
  - Sub-threshold -- does not elicit all-or-none response
- **All-or-none:**
  - Membrane potential change above a threshold elicits a massive depolarization (**action potential**)