Cellular and Molecular Biology of the Neuron

Resting Membrane Potential;
Action Potential;
Synaptic Interaction

Basic Concepts

- **Volt**
  - *A charge difference between two points in space*

Basic Concepts

- **Ions – charged particles**
- **Anions – Negatively charged particles**
- **Cations – Positively charged particles**

Basic Concepts
Forces that determine ionic movement

- **Electrostatic forces**
  - Opposite charges attract, Identical charges repel
- **Concentration forces**
  - Diffusion – movement of ions through semipermeable membrane
  - Osmosis – movement of water from region of high concentration to low
- **Hydrostatic Forces**
  - Gravity forces upon osmosis

The combination of these forces leads to dynamic equilibrium in the cellular environment

Basic Concepts
The selective permeability of membranes

- Neuronal membranes
- Hydrophobic lipid bilayer
  - Two fatty layers separated by protein
- Gated ion channels
- Nongated ion channels

Forces
that determine the movement of ions

- Diffusion
- Osmosis
- Electrostatic Forces
- Hydrostatic Forces

Selective Permeability of Membranes

- Some ions permitted to cross more easily than others
- Neuronal membranes contain ion channels
  - Protein tubes that span the membrane
  - Some stay open all the time (nongated)
  - Some open on the occasion of an action potential, causing a change in the permeability of the membrane (gated)

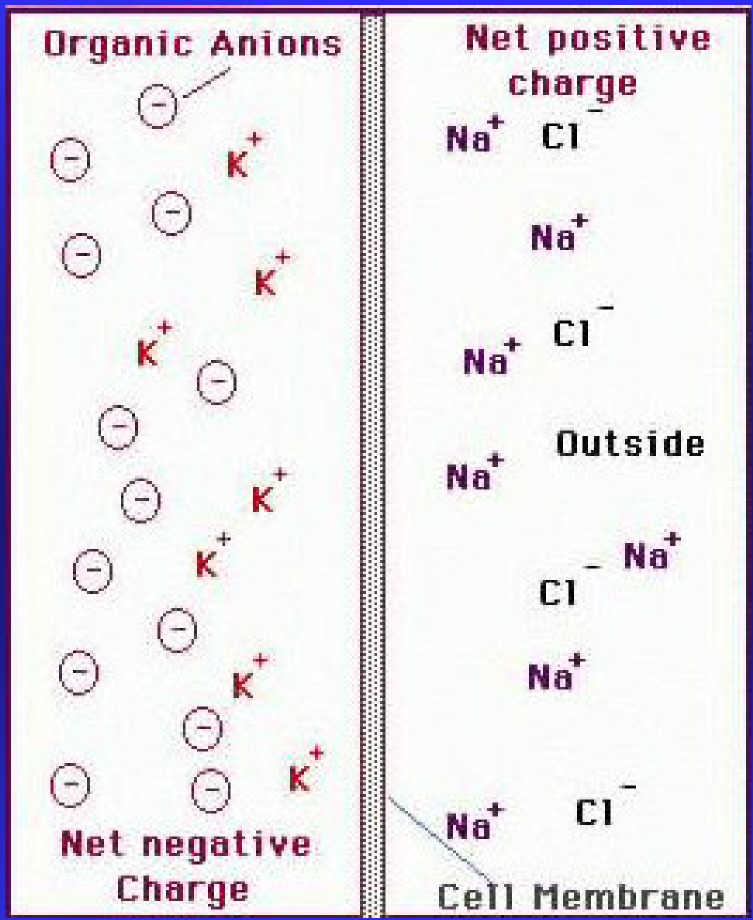
Membrane Resting Potential

- The electrochemical state of the neuron at rest

- Cell’s ability to fire an action potential is due to the cell’s ability to maintain the cellular resting potential at approximately
  –70 mV (-.07 volt)

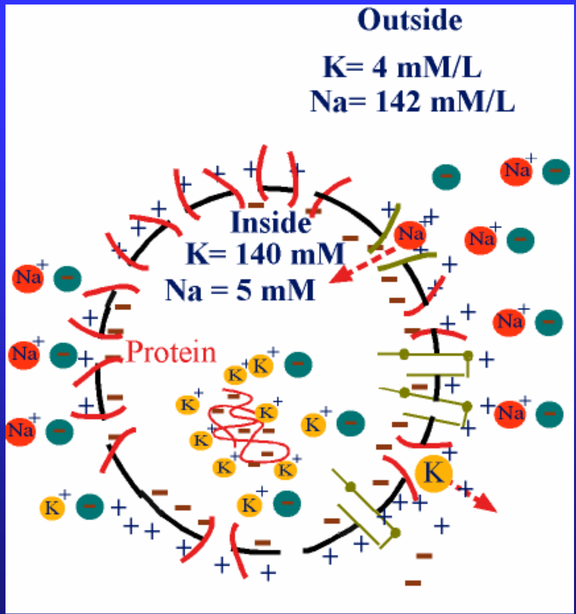
- The basic signaling properties of neurons are determined by changes in the resting potential

Membrane Resting Potential

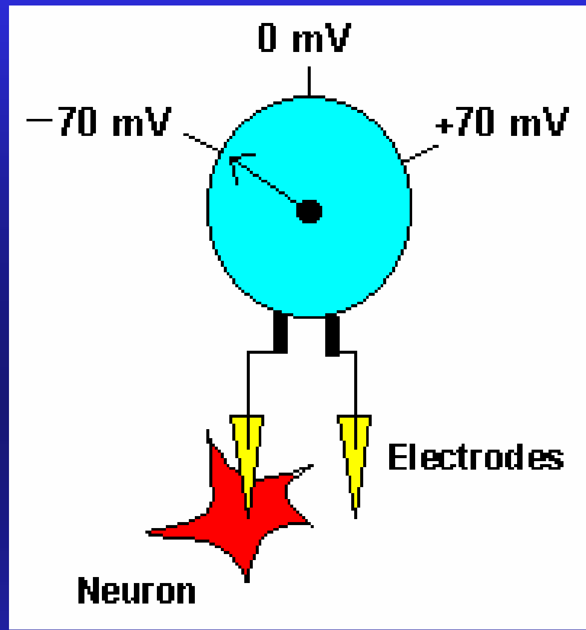


- Every neuron has a separation of electrical charge across its cell membrane.
- The membrane potential results from a separation of positive and negative charges across the cell membrane.

Membrane Resting Potential

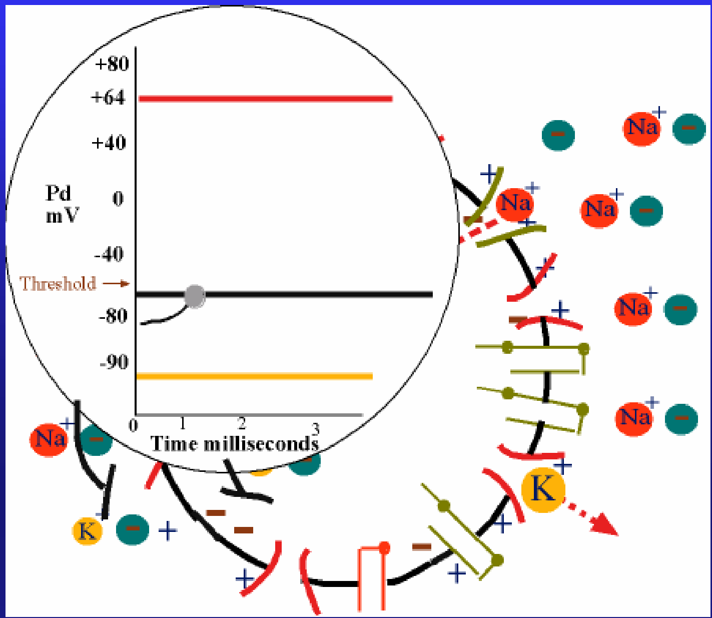


- excess of positive charges outside and negative charges inside the membrane
- maintained because the lipid bilayer acts as a barrier to the diffusion of ions



- gives rise to an electrical potential difference, which ranges from about 60 to 70 mV.

Membrane Resting Potential

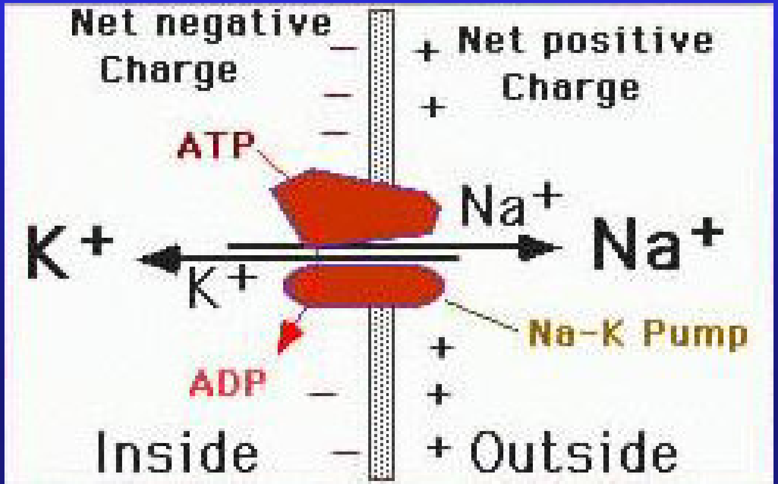


- The charge separation across the membrane, and therefore the resting membrane potential, is disturbed whenever there is a net flux of ions into or out of the cell.

- A reduction of the charge separation is called *depolarization*;

- An increase in charge separation is called hyperpolarization

Ion Channels



- A class of integral proteins that span the cell membrane
- Permit Transient current flow
- Facilitate Depolarization, Hyperpolarization

Ion Channels

- Two Types of Ion Channels
- Gated
- Non-Gated

Ion Channels

- **Recognize and select among specific ions**

- **The distribution of ionic species across the membrane depends on the particular distribution of ion channels in the cell membrane.**

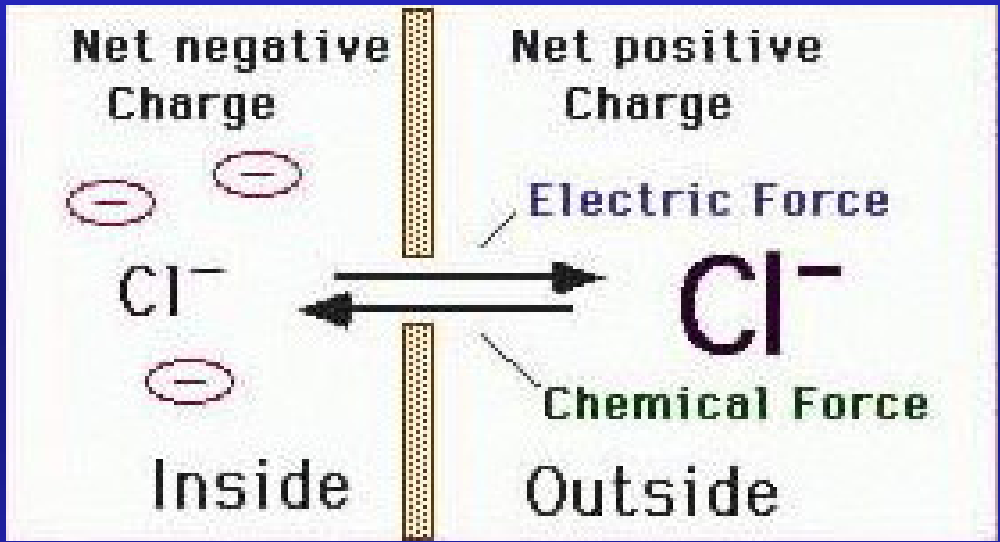
- ***Ionic species are not distributed equally on the two sides of a nerve membrane***

Resting Membrane Potential

- Na+ and Cl- are more concentrated outside the cell

- K+ and organic anions (organic acids and proteins) are more concentrated inside. The overall effect of this ionic distribution is the resting potential

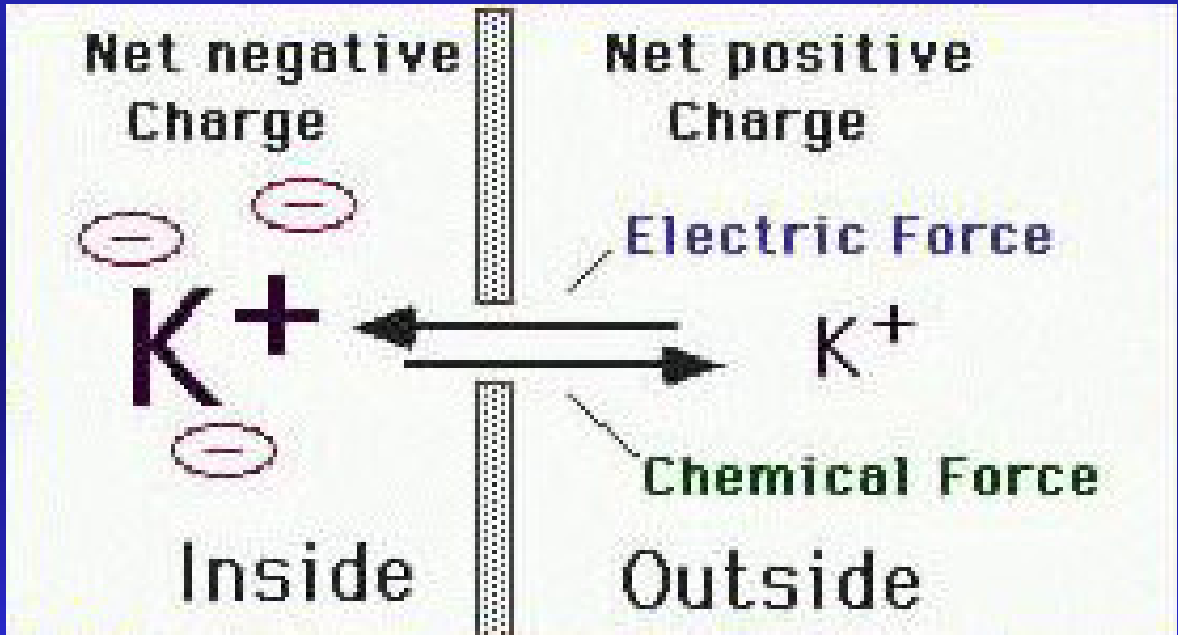
Resting Membrane Potential



- Chloride ions, concentrated outside the cell tend to move inward down their concentration gradient through nongated chloride channels
- But the relative excess of negative charge inside the membrane tend to push chloride ions back out of the cell

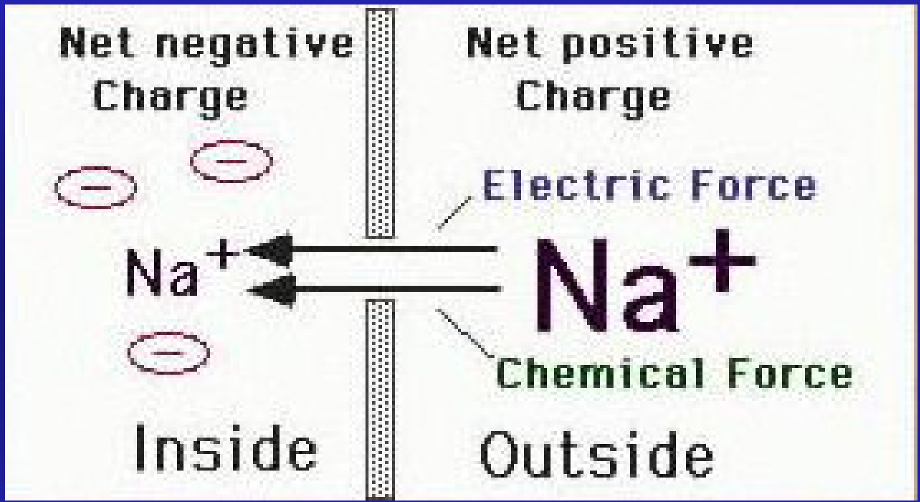
- Two forces acting on a given ionic species
- Chemical forces tend to drive ions down their concentration gradients

Resting Membrane Potential



- The same mechanisms operate on potassium…

Resting Membrane Potential

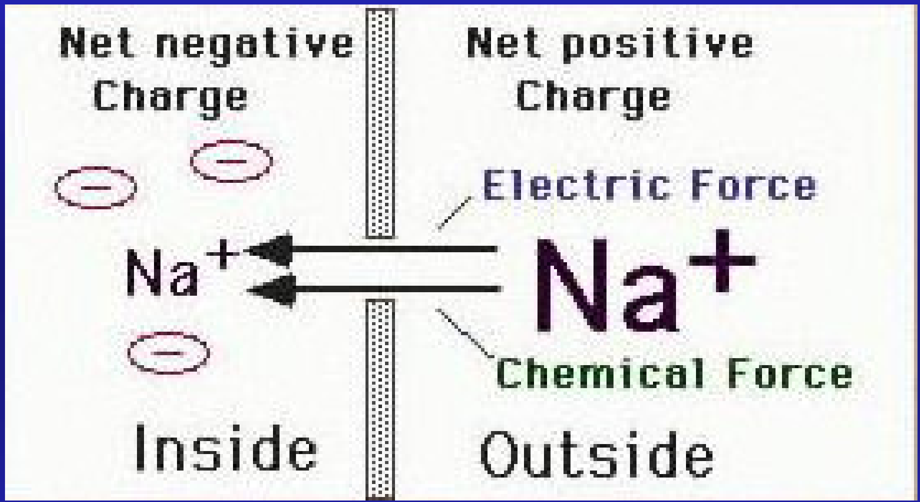


Na is more concentrated outside than inside and therefore tends to flow into the cell down its concentration gradient

Na is driven into the cell by the electrical potential difference across the membrane.

- ***But what about sodium?***
- **Electrostatic and Chemical forces act together on Na ions to drive them into the cell**

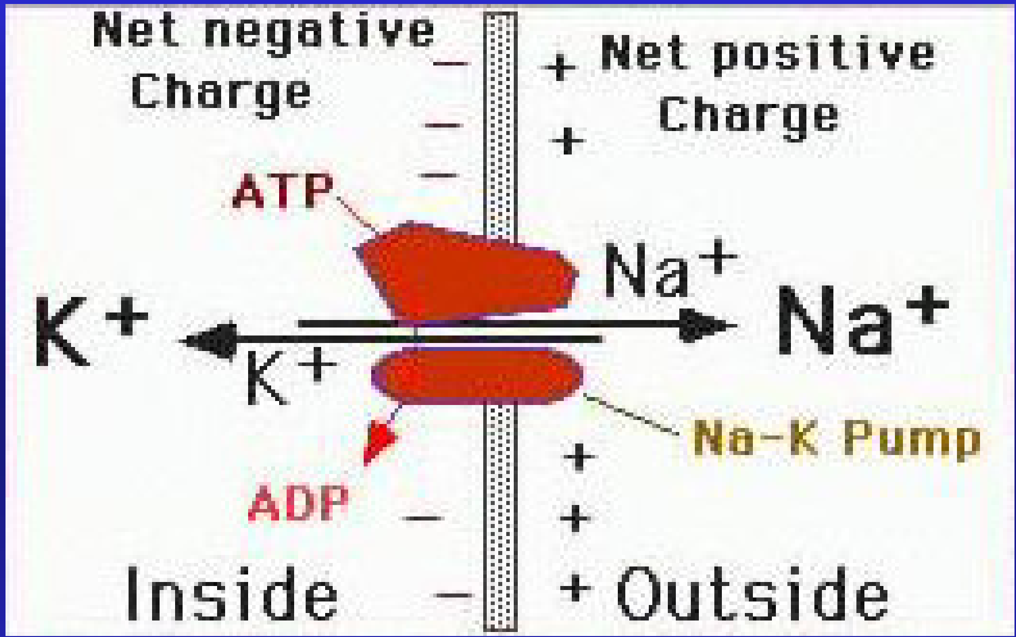
Resting Membrane Potential



•Electrostatic and Chemical forces act together on Na ions to drive them into the cell

- this process cannot be allowed to continue unopposed
- Otherwise, the K pool would be depleted, intracellular Na would increase, and the ionic gradients would gradually run down, reducing the resting membrane potential.

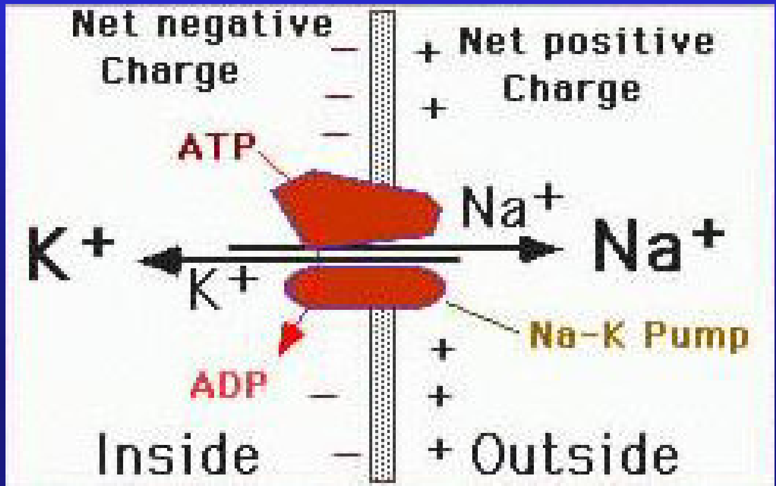
The Sodium-Potassium Pump



extrudes Na from the cell while taking in K

- Dissipation of ionic gradients is ultimately prevented by Na-K pumps

The Sodium-Potassium Pump



The energy necessary for this process is obtained from the hydrolysis of ATP (an energy carrying molecule)

- Because the pump moves Na and K against their net electrochemical gradients, energy is required to drive these actively transported fluxes.
- Chloride pumps also that actively transport chloride ions toward the outside assure that the extra- to intracellular Cl concentration is greater than what would result from passive diffusion alone.

Graded Potentials

- The response of the cell to stimulation
- Characteristic of the Dendrites and Cell Body
- Can take on different gradations,
- Decremental conduction
  - The further they must travel the weaker they become
- May be excitatory or inhibitory

Graded Potentials

- Sum at Axon Hillock
- Spatial summation – if two potentials arrive at the axon hillock at the same moment they are summed spatially across the cell body

Graded Potentials

- Sum at Axon Hillock
- Temporal summation – if two potentials arrive at the axon hillock at the close enough in time to be summed across the cell body

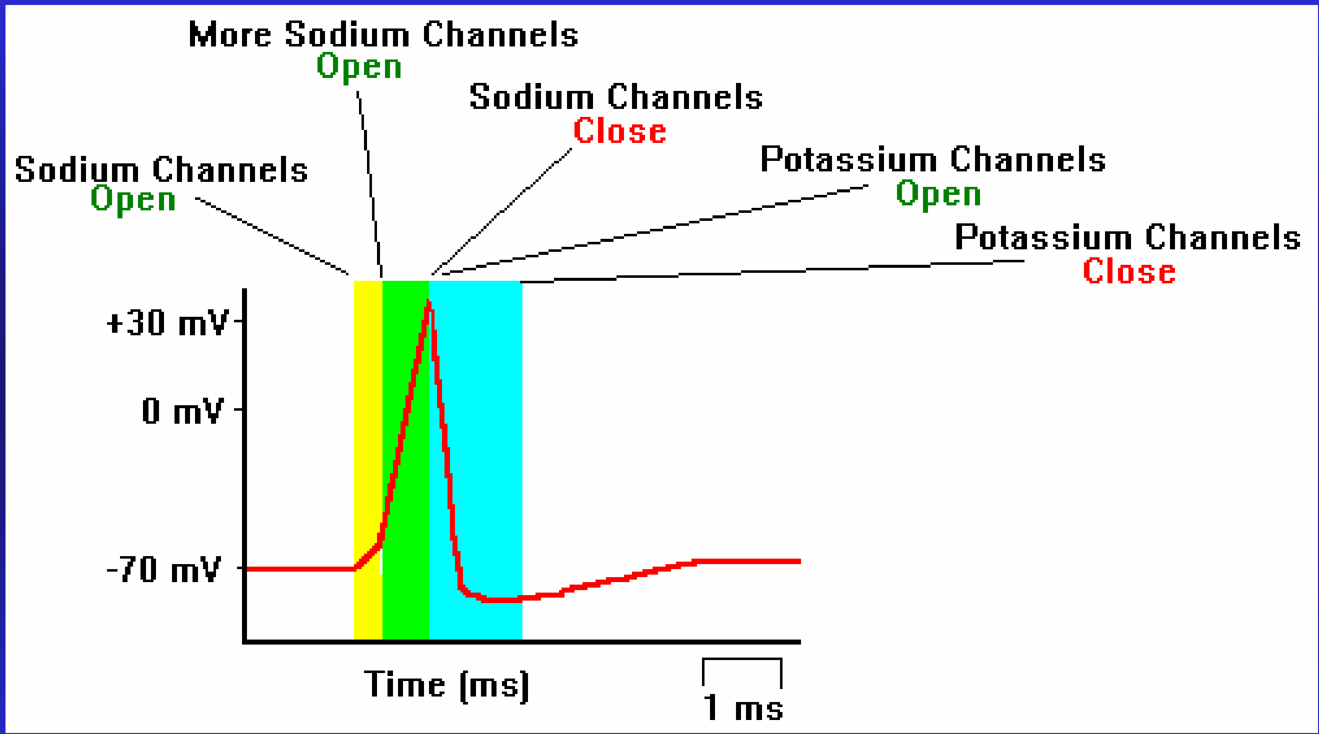
Graded Potentials

- Sum at Axon Hillock
- If enough excitatory (depolarizing) potentials sum at the axon hillock,
- That is, if the depolarizing sums to about
- –50 mV, a brief change in the membrane permeability occurs …

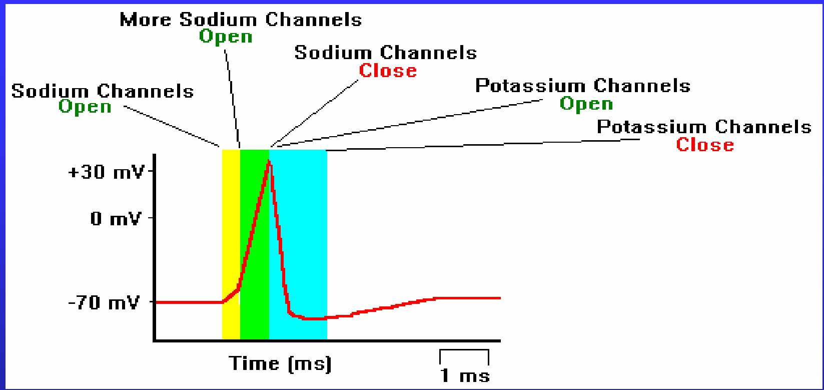
Action Potential

- This change or "overshoot" is called the "Action Potential"
- The basic unit of conduction in the nervous system
- Characteristic of axons
- Non-decremental conduction –
  - "all-or-none law"

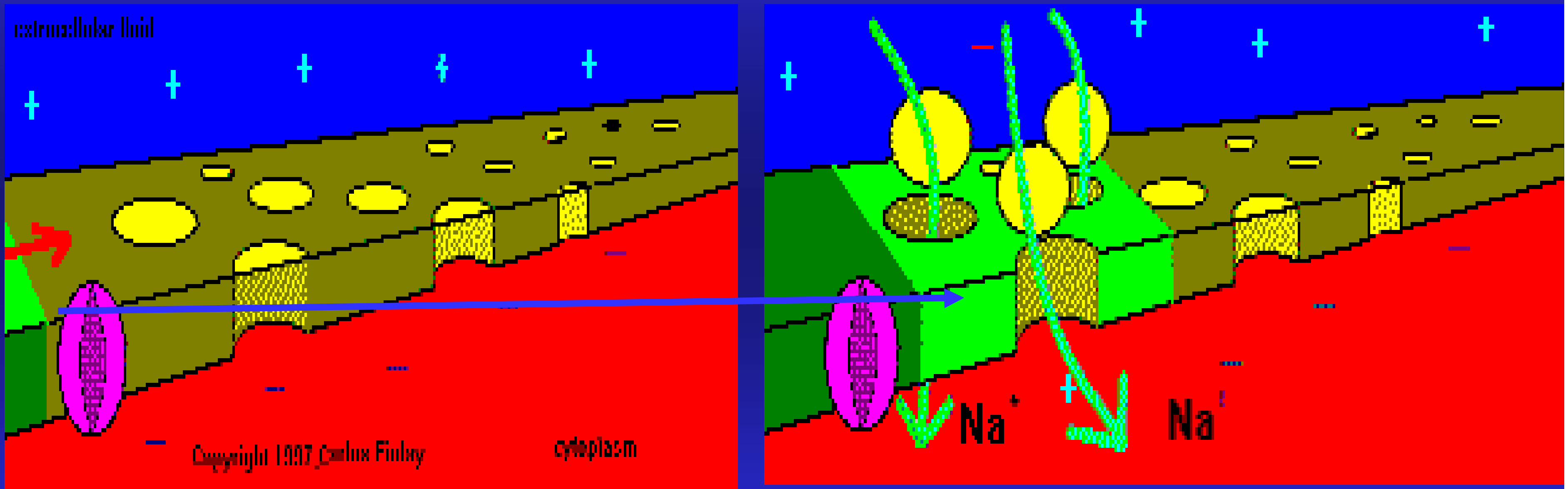
Action Potential Sequence



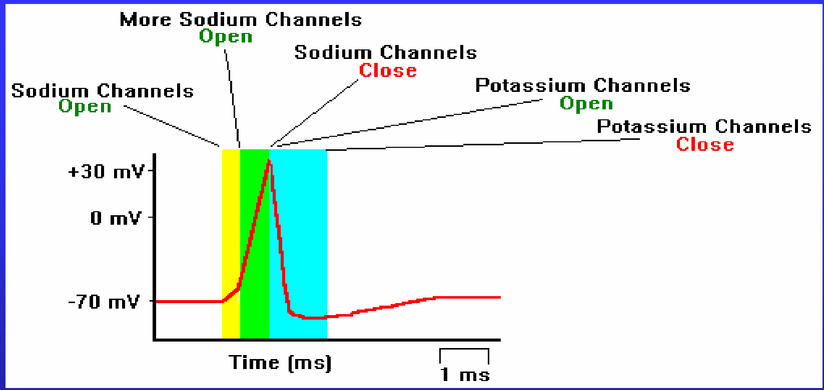
- Involves the action of voltage-gated channels
- Exchanges of ions in and out of the cell



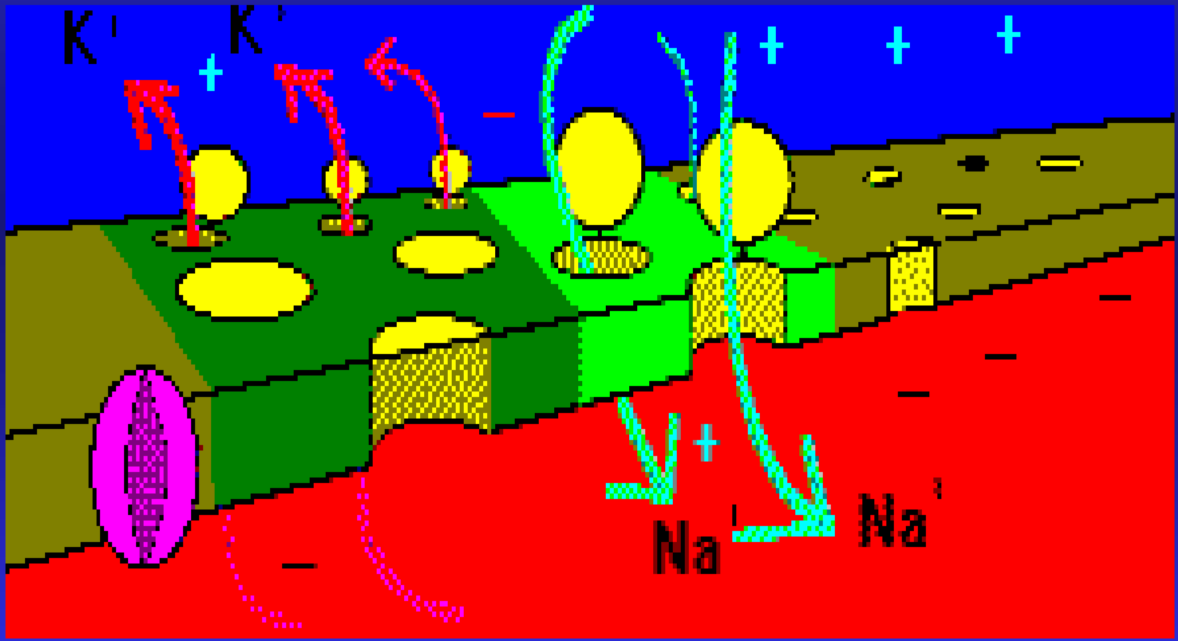
Action Potential Sequence



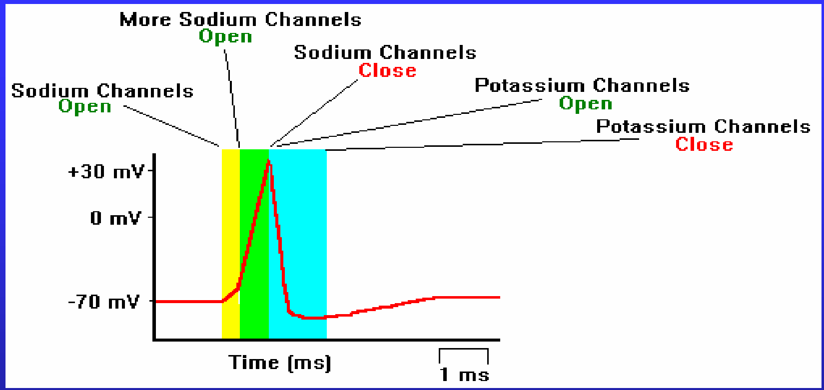
- Voltage-gated Na+ Channels open and Na+ rushes into the cell



Action Potential Sequence



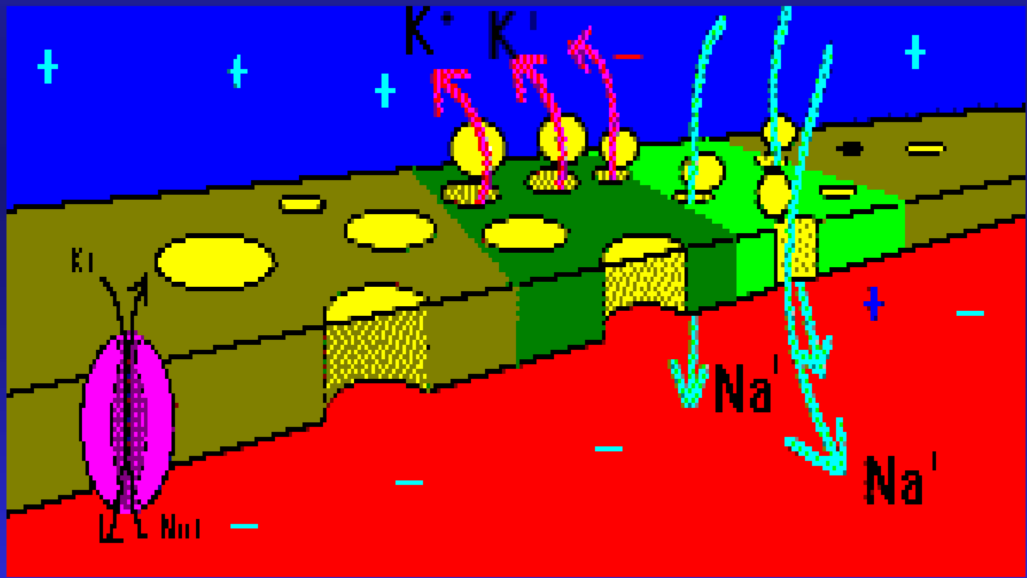
- At about +40 mV, Sodium channels close, but now, voltage-gated potassium channels open, causing an outflow of potassium, down its electrochemical gradient



Action Potential Sequence

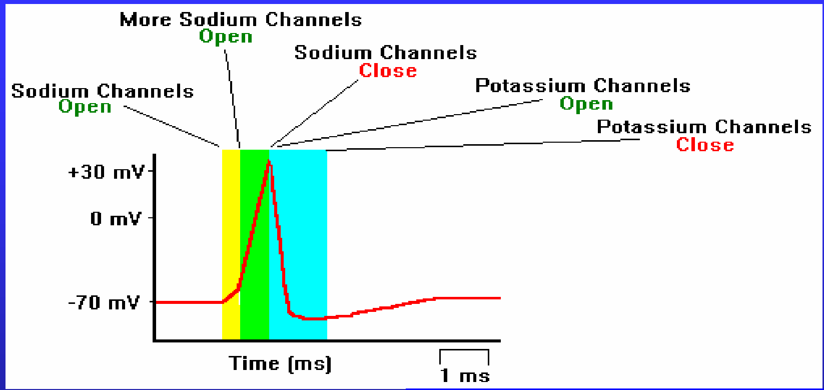
- The voltage-gated K+ channels close, so much Potassium accumulates outside the cell that repolarization occurs

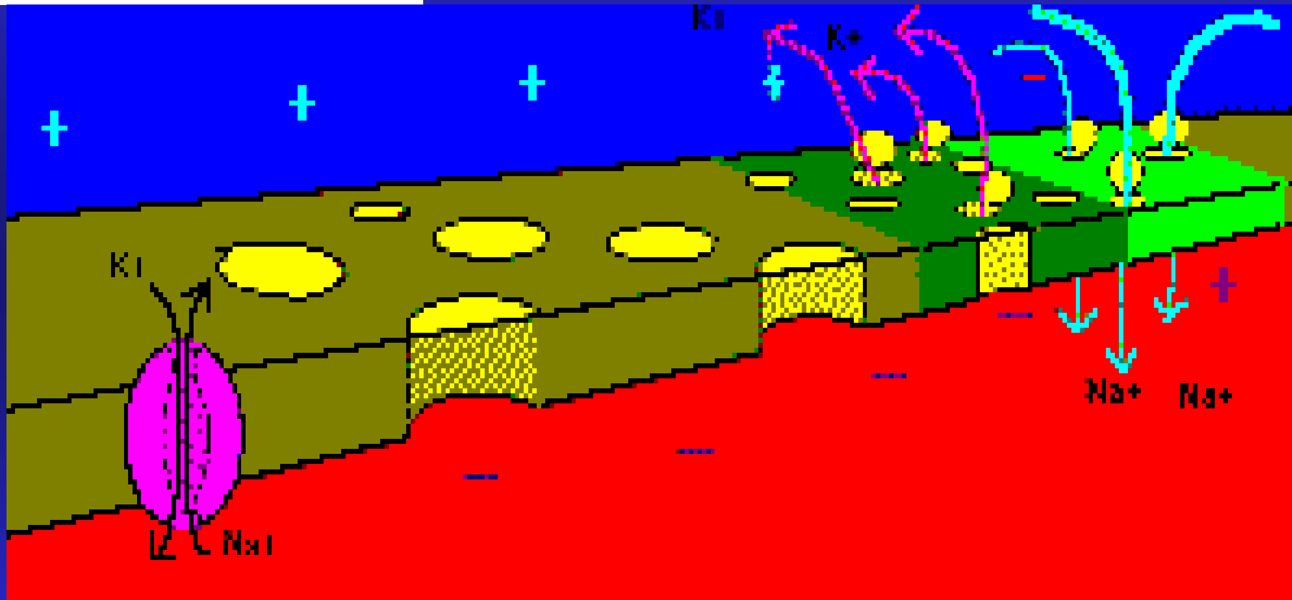
so much so that there is an undershoot at the end of the AP sequence



equilibrium potential of the cell is restored

Action Potential Sequence





- The Sodium – Potassium Pump is left to clean up the mess…

Refractory Period

- Two types
- Absolute
  - When Na+ channels close, at peak of AP, they do not reopen for a time
- Relative
  - Membrane hyperpolarized
  - Some Na+ channels still refractory

Propagation of the Action Potential

- Action Potential spreads down the axon in a chain reaction
- Unidirectional
  - it does not spread into the cell body and dendrite due to absence of voltage-gated channels there
  - Refraction prevents spread back across axon

Propagation of the Action Potential

- Speed of propagation varies with the axon diameter
- Faster with larger axons
- In large axons of mammals
  - 5m/second 2υm axons
  - 20m/second in 20υm axons

Propagation of the Action Potential

- Speed of propagation also assisted by the myelin sheath
  - Provides resistance to AP
- Regular gaps in the myelin sheath (1mm intervals)
  - "Nodes of Ranvier"
  - Increase conduction speed up to 15 times