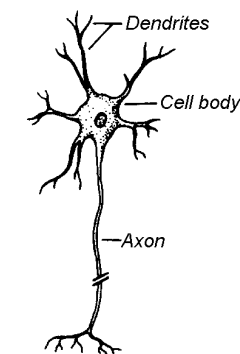
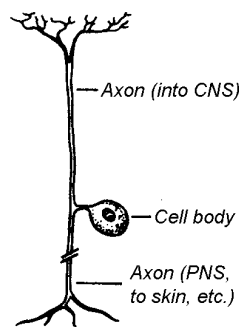


## INTRODUCTION

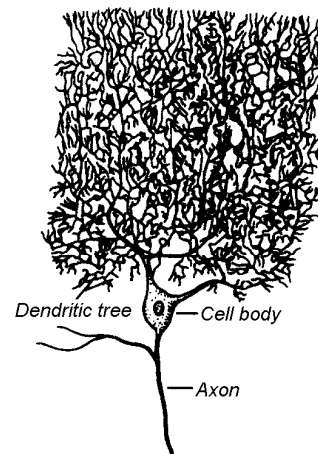
- A. Excitable Tissue: able to generate Action Potentials (APs) (e.g. neurons, muscle cells)
- B. Neurons (nerve cells)
  - a. components
    - 1) soma (cell body): metabolic center (vital, always present, contains cell nucleus): information integration
    - 2) dendrites (branches from the soma): receive information, generally but not always present
    - 3) axons (one or two generally long branches from the soma): transmit information



Spinal motor (efferent) neuron



Dorsal root ganglion sensory (afferent) neuron



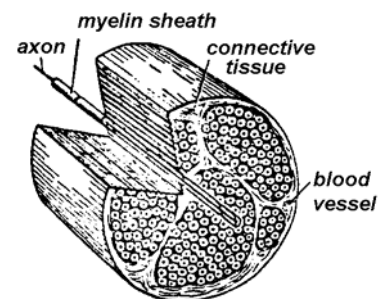
Purkinje neuron of the cerebellum

- b. organization

- 1) Central Nervous System (CNS): neurons of the brain and spinal cord
- 2) Peripheral Nervous System (PNS): neurons outside the brain and spinal cord

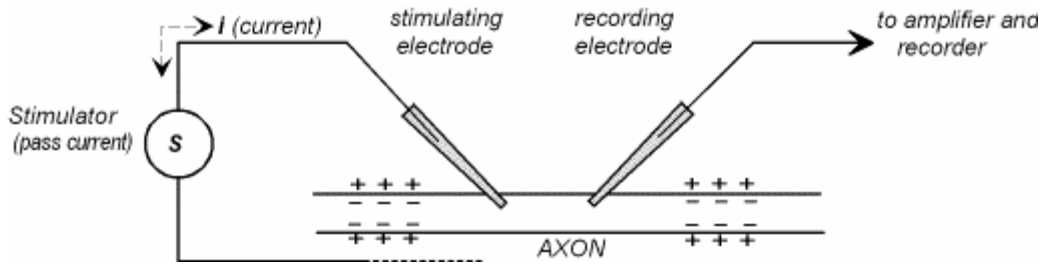
Note: Sometimes the neurons within the alimentary tract are considered a separate division, the enteric nervous system

- 3) axon groups: axons running together in the PNS are termed nerves; axon groups running together and of similar function are in the CNS generally called tracts, although other terms are frequently used (column, lemniscus, etc.)
- 4) a group of somas of similar function in the PNS is called a ganglion; in the CNS, it is generally called nucleus

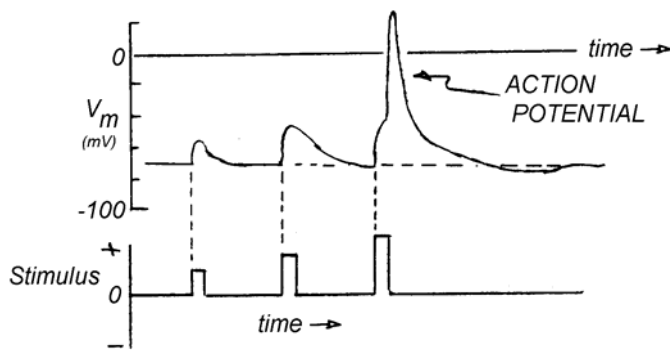


PHENOMENON OF EXCITABILITY

A. Response to brief Electrical Stimulus (Pulse)



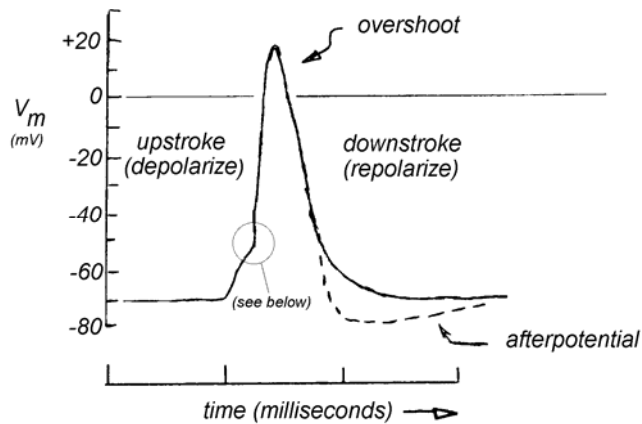
1. Effect of brief depolarization (inside less negative)



Weak stimulus: Brief depolarization followed return to resting potential; due to ion movement, particularly  $K^+$  and  $Cl^-$

Stronger stimulus: Action potential; due to regenerative  $Na^+$  influx

B. Properties of the Action Potential (AP)

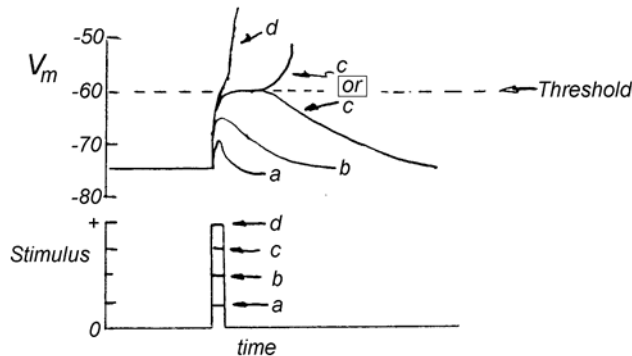


PHENOMENON OF EXCITABILITY

B. Properties of the Action Potential (AP) – continued

1. shape ("spike")

- a. brief membrane depolarization
- b. overshoots zero (membrane positive), usually
- c. duration about 1 msec ( millisecond, 0.001 second)
- d. may or may not undershoot resting potential (after potential) when AP is complete, but eventually returns to resting level



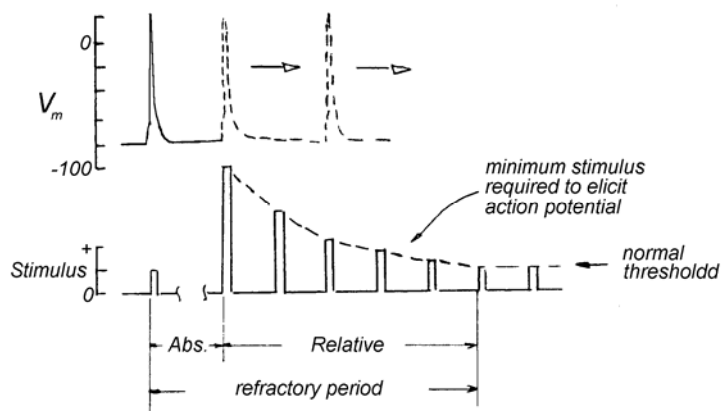
2. Threshold: minimum depolarization required to generate an action potential

3. All-or-None law

An action potential is an "event" that either occurs or does not occur. Once generated, it is independent of the initial stimulus

4. Refractory period

Immediately following an action potential, there is a period of reduced excitability; the reduced excitability dissipates with time and eventually, complete excitability is recovered

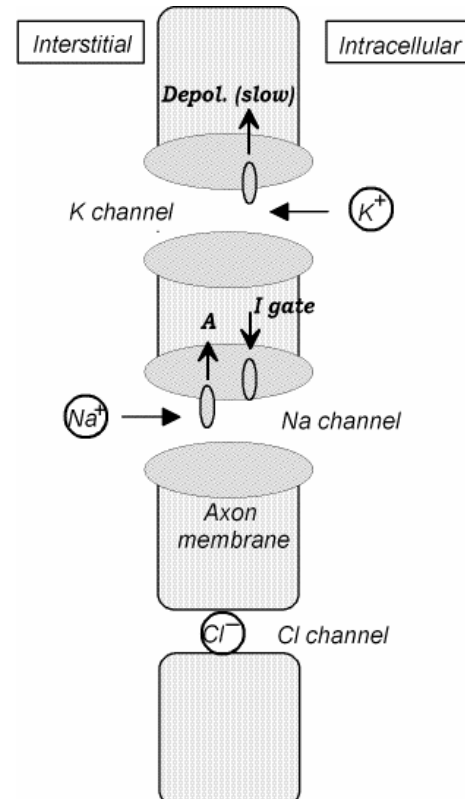


- a. absolute refractory period: interval following an AP during which no further APs can be generated (order of 1 msec)
- b. relative refractory period: interval following the absolute refractory period during which a 2nd AP can be generated only by a higher than normal stimulus (order of several msec); period of increased threshold

IONIC BASIS OF THE ACTION POTENTIAL

A. Mechanism of passive movement of Na<sup>+</sup> and K<sup>+</sup>

1. via ion specific channels, with separate channels for Na<sup>+</sup> and K<sup>+</sup> and Cl<sup>-</sup>
2. permeability ("P") of Na<sup>+</sup> and K<sup>+</sup> channels controlled by one or more gates in the respective channel
  - a. Na<sup>+</sup> channel has two gates, an Activation gate (A) and an Inactivation gate (I)
  - b. Na<sup>+</sup> Activation gate is mainly closed at the membrane resting potential but opens rapidly upon membrane depolarization
  - c. Na<sup>+</sup> Inactivation gate is normally open at the membrane resting potential but closes with delay upon membrane depolarization; reopens slowly following repolarization
  - d. K<sup>+</sup> channel involved in the action potential gate opens with delay upon depolarization; returns slowly to its resting level following repolarization



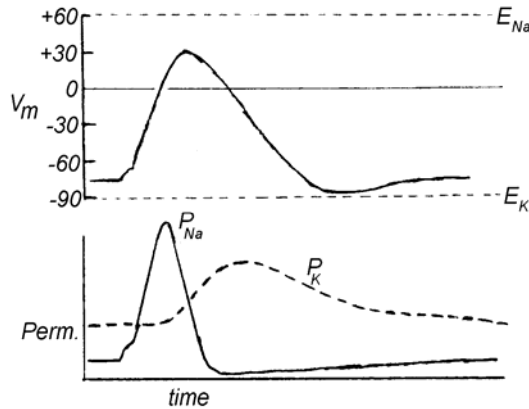
3. Summary

	<b>P<sub>Na</sub></b>	<b>P<sub>K</sub></b>
DEPOLARIZATION: Immediate	Opening of Na channel A gate, leading to large (600x) increase of P-Na	No (or small) change
DEPOLARIZATION Next	Closing of Na channel I gate, leading to decrease of P-Na below its normal resting level	Opening of K channel gate, leading to P-K increase (10x)
REPOLARIZATION Eventual	Return of P-Na gates to their resting state	Return of P-K to its resting level (decrease)

IONIC BASIS OF THE ACTION POTENTIAL (continued)

B. Permeability Changes During Action Potential

1. Changes on initial depolarization (upstroke of AP)

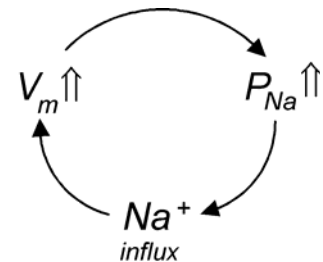


2. Hodgkin cycle

If depolarization proceeds until the  $P_{Na}$  increase causes

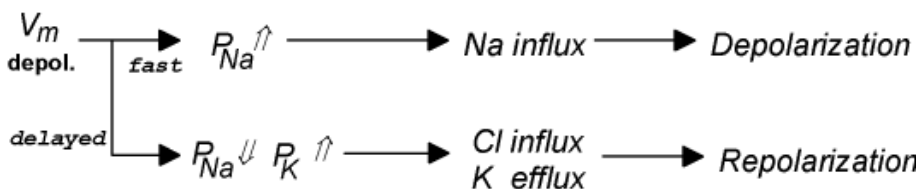
$$Na \text{ influx} > K \text{ efflux} + Cl \text{ influx} \quad (\text{threshold exceeded})$$

then depolarization becomes regenerative: Hodgkin Cycle (example of regenerative behavior or positive feedback)



3. Subsequent event (down stroke of AP)

$P_K \uparrow$  and  $P_{Na} \downarrow$  causes  $V_m$  to decrease, approaching  $E_K$



4. Final event (refractory period)

Following repolarization, several msec are required for Na A and I gates to return to their resting levels and for  $P_K$  to return to its resting level; until this occurs, the membrane is absolutely or relatively refractory

C. Role of Active Transport

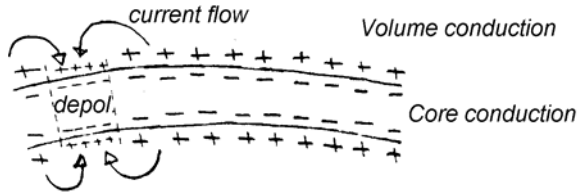
1. Establishes original  $Na^+$  and  $K^+$  concentration gradients (energy source)
2. Not directly involved in the action potential
3. Eventually restores intracellular concentrations of  $Na^+$  and  $K^+$  after the action potential is over (minutes)

Note: In the peripheral nervous system, only small amounts of Na and K move across the membrane for each action potential, so the normal concentrations of  $Na^+$  and  $K^+$  are sufficient to sustain a number of action potentials without additional active transport. But without active transport, nerve axons eventually will lose their ability to generate action potentials because of reduced concentration gradients.

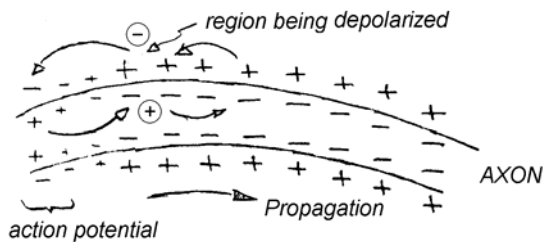
## ACTION POTENTIAL PROPAGATION

### A. Unmyelinated Axon Action Potential Conduction

1. Region undergoing an AP acts to depolarize surrounding regions



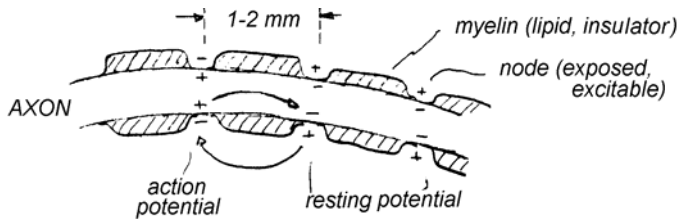
2. Adjacent regions reach threshold first, generating APs in the adjacent regions
3. New site of activity (adjacent region) depolarizes the excitable membrane adjacent to it



4. Sequence continues until AP has propagated along the whole axon

### B. Myelinated Axon Action Potential Conduction (Saltatory Conduction)

1. Functional anatomy: myelinated segments separated by nodes (Nodes of Ranvier)



note that the density of Na channels at the nodes is higher than the density on the remainder of the axon, so the nodes have a lower threshold for excitation

2. Consequences of myelination
  - a. myelin prevents current flow through the underlying axon membrane; thus current is confined to the nodes
  - b. AP propagation jumps from node to node ("saltatory" conduction)
  - c. conduction velocity is increased (compared to an unmyelinated axon of the same diameter)

## ACTION POTENTIAL PROPAGATION (continued)

### C. Conduction Velocity

#### 1. Determining Factors

- a. axon diameter: radius  $\uparrow \Rightarrow$  velocity  $\uparrow$

the larger the fiber diameter, the lower the core electrical resistance

- b. myelination

increases conduction velocity, since membrane capacitance is decreased and distance of passive spread is increased

#### 2. Velocity values

- a. unmyelinated axons

relatively slow, order of 1 meter/sec, because small and unmyelinated

- b. myelinated axons

relatively fast, range of 10-120 meters/sec, because larger (up to 20  $\mu\text{m}$ ) and myelinated

## ALTERATIONS IN AP PROPAGATION

### A. Local Anesthetics; e.g. lidocaine, procaine (Novocain)

Action: block regenerative Na channels and thus prevent generation or propagation of action potentials

### B. Interstitial Potassium Ion Concentration

Action: alters the resting potential and thus the amount of depolarization necessary to reach threshold; e.g. reduced excitability of hypokalemia

### C. Demyelination Diseases

1. Examples: CNS – Multiple Sclerosis; PNS – Guillian-Barre syndrome
2. Consequence: initially slow conduction, eventually block conduction altogether