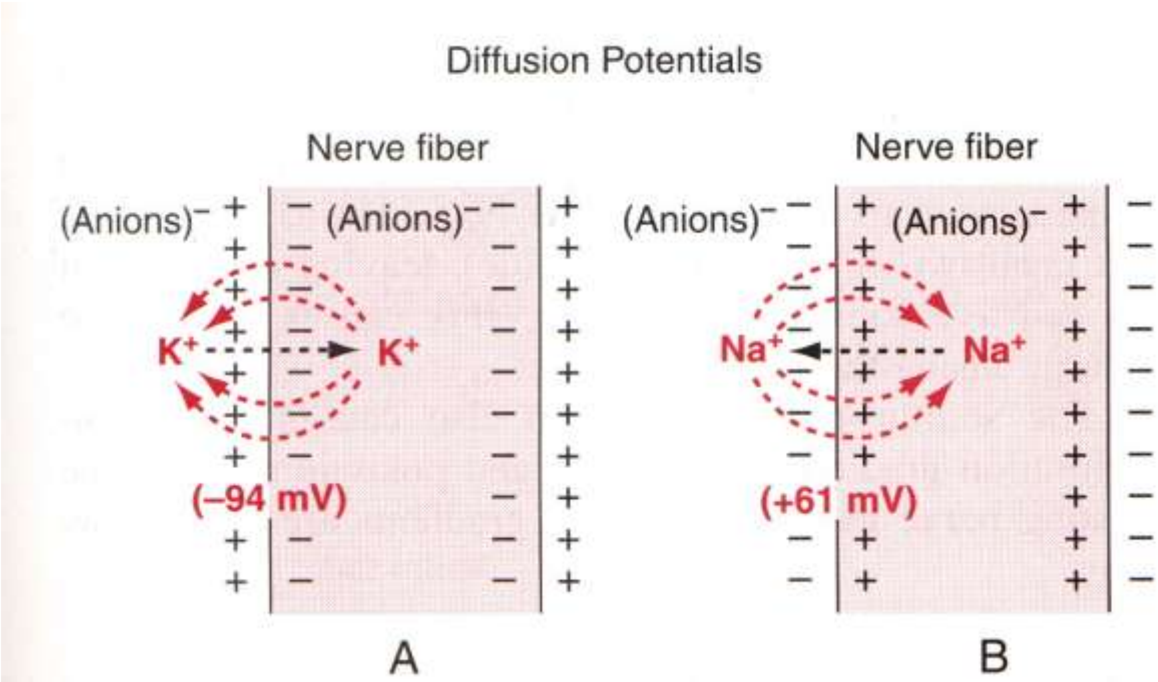
Membrane Potentials and Action Potentials

Basic physics of membrane potentials

- Membrane potentials caused by diffusion



Remember: sodium is pumped out of the cell, potassium is pumped in...

Resting membrane potential of nerves

Active Transport of Sodium and Potassium Ions Through the Membrane

Na (outside)	=	142	mEq/L
Na (inside)	=	14	mEq/L
K (outside)	=	4	mEq/L
K (inside)	=	140	mEq/L

The Goldman-Hodgkin-Katz equation

$$\text{EMF (millivolts)} = -61 \cdot \log \frac{C_{\text{Na}^+{}_i} P_{\text{Na}^+} + C_{\text{K}^-{}_i} P_{\text{K}^+} + C_{\text{Cl}^-{}_o} P_{\text{Cl}^-}}{C_{\text{Na}^+{}_o} P_{\text{Na}^-} + C_{\text{K}^-{}_o} P_{\text{K}^+} + C_{\text{Cl}^-{}_i} P_{\text{Cl}^-}}$$

Sodium-Potassium Pump

Pumps sodium ions out and two potassium into three the cell

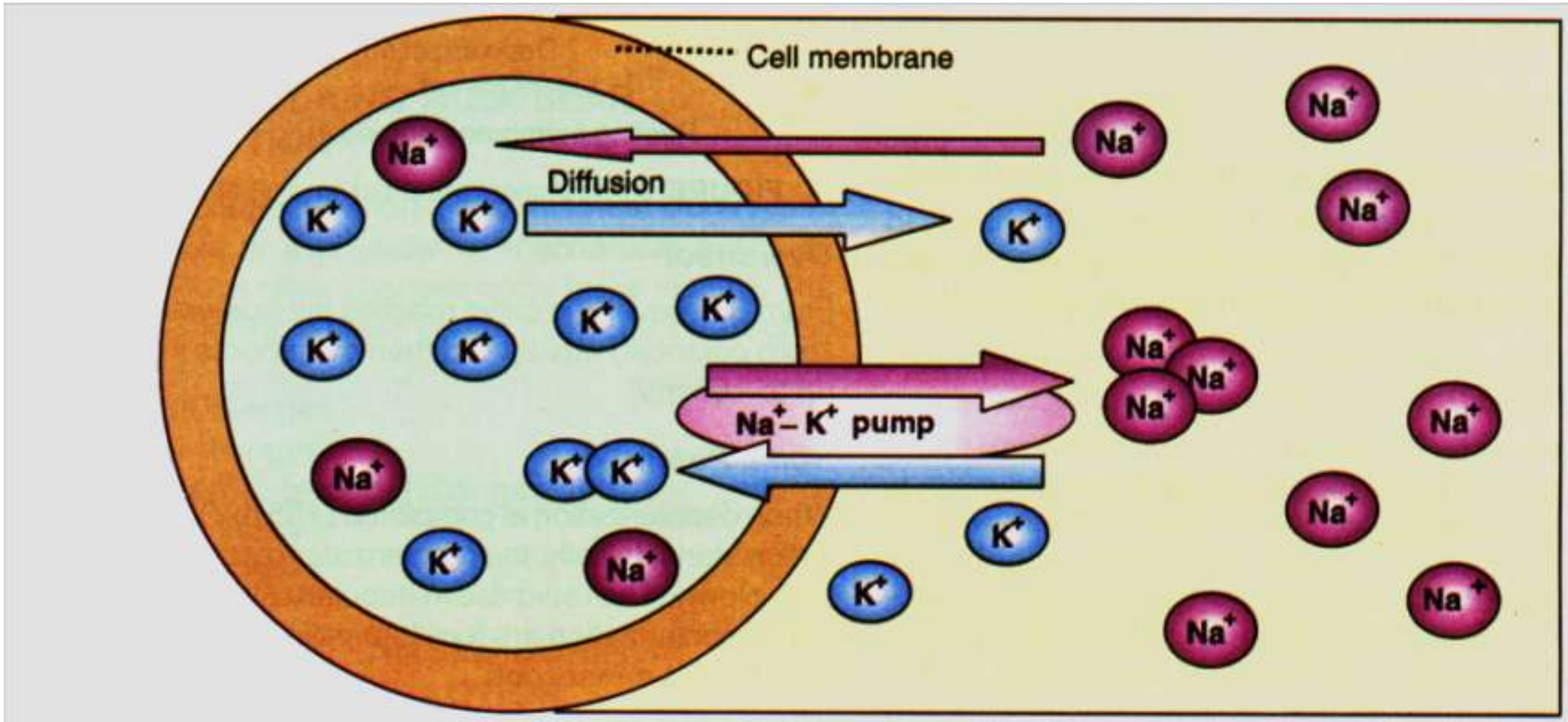


FIGURE 31-2: Development of resting membrane potential by Sodium–potassium (Na^+-K^+) pump and diffusion of ions. Na^+-K^+ pump actively pumps three Na^+ ions out and two K^+ into the cell. However, the diffusion of K^+ out of the cell is many times greater than the diffusion of Na^+ ions inside the cell because many of the K^+ leak channels are opened and many of the Na^+ leak channels are closed

Contribution of the potassium diffusion potential = -94 MV

Contribution of Sodium diffusion through the nerve membrane = +61 MV

Contribution of the Na-K pump = -4 MV

The Potassium Nernst Potential

...also called the equilibrium potential

$$E_K = -61 \log \frac{K_i}{K_o}$$

Example: If K_o = 5 mM and K_i = 140 mM

E_K = -61 log(140/4)

E_K = -61 log(35)

E_K = -94 mV

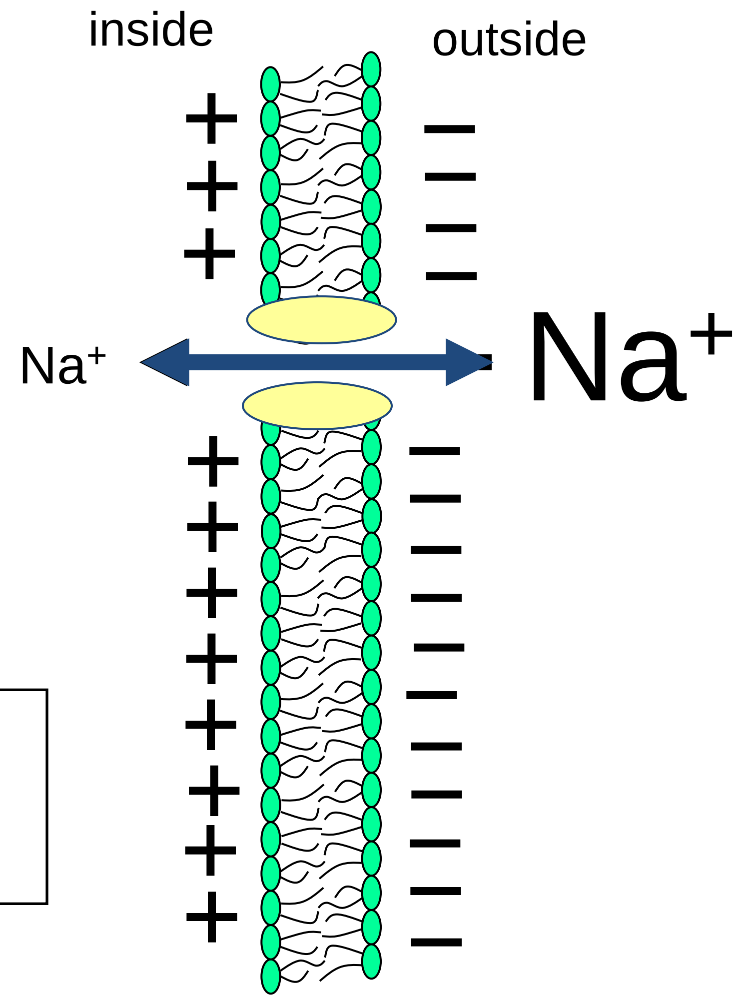
So, if the membrane were permeable only to K+, Vm would be -94 mV

Simplest Case Scenario:

If a membrane were permeable to only Na^+ then…

Na^+ would diffuse down its concentration gradient until potential across the membrane countered diffusion.

The electrical potential that counters net diffusion of Na^+ is called the Na^+ equilibrium potential (E_{Na}).



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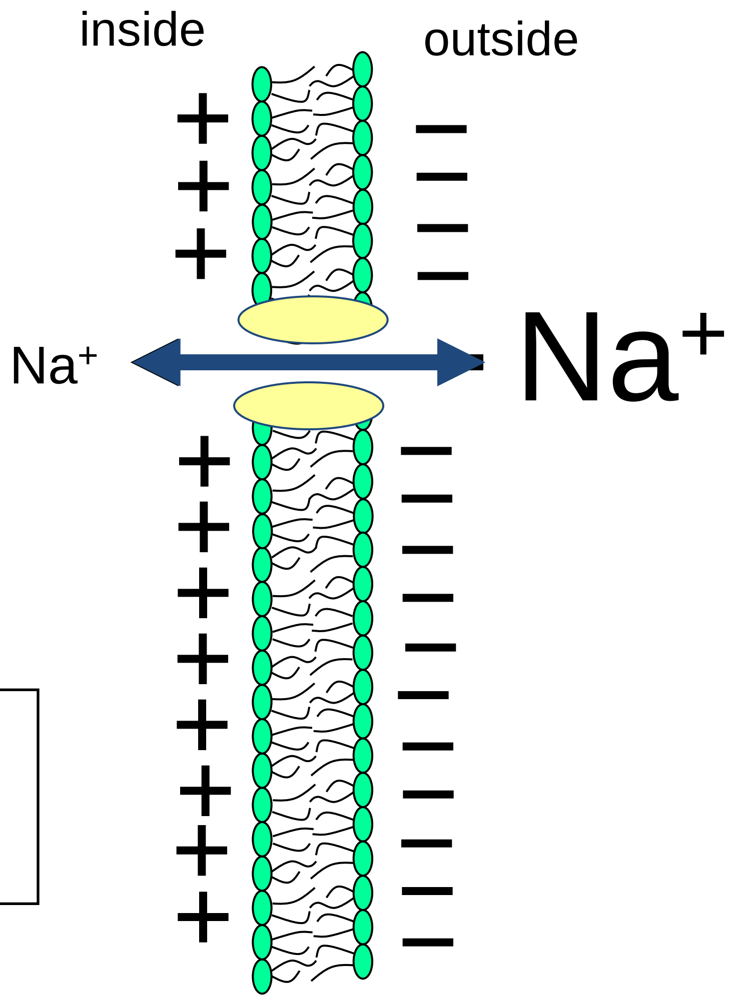

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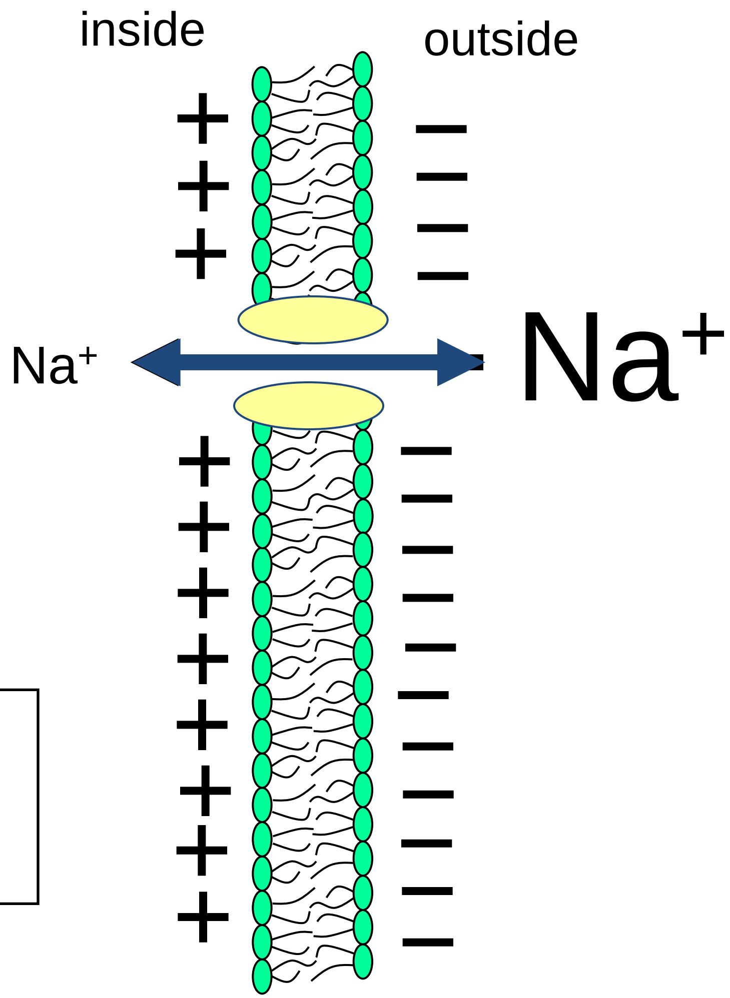


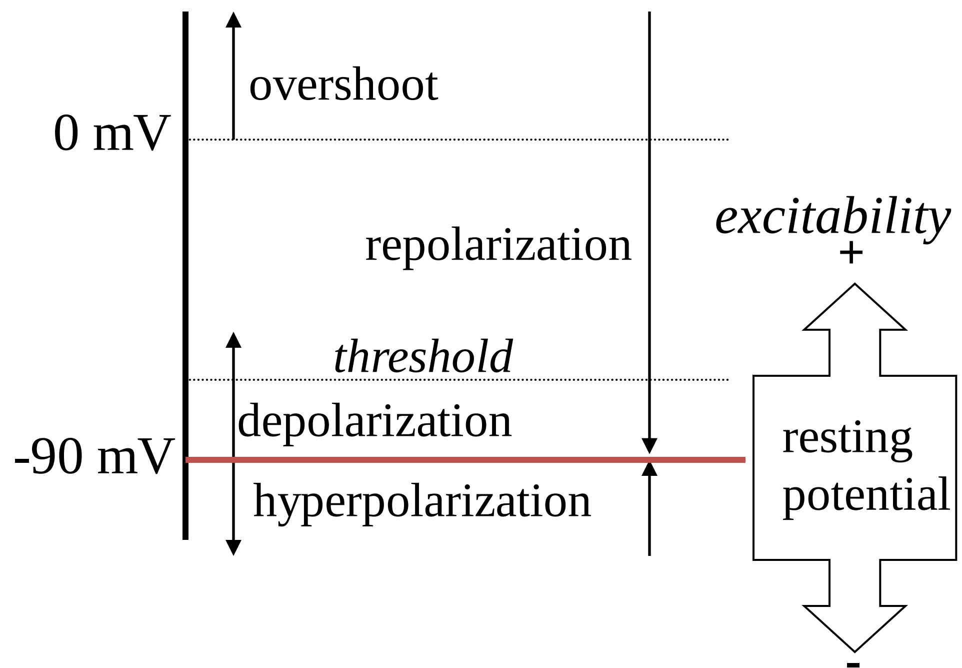
Resting and action potentials

$$V_m = 61.\mathbf{log}\frac{p'_K[K^+]_o + p'_{Na}[Na^+]_o + p'_{Cl}[Cl^-]_i}{p'_K[K^+]_i + p'_{Na}[Na^+]_i + p'_{Cl}[Cl^-]_o}$$

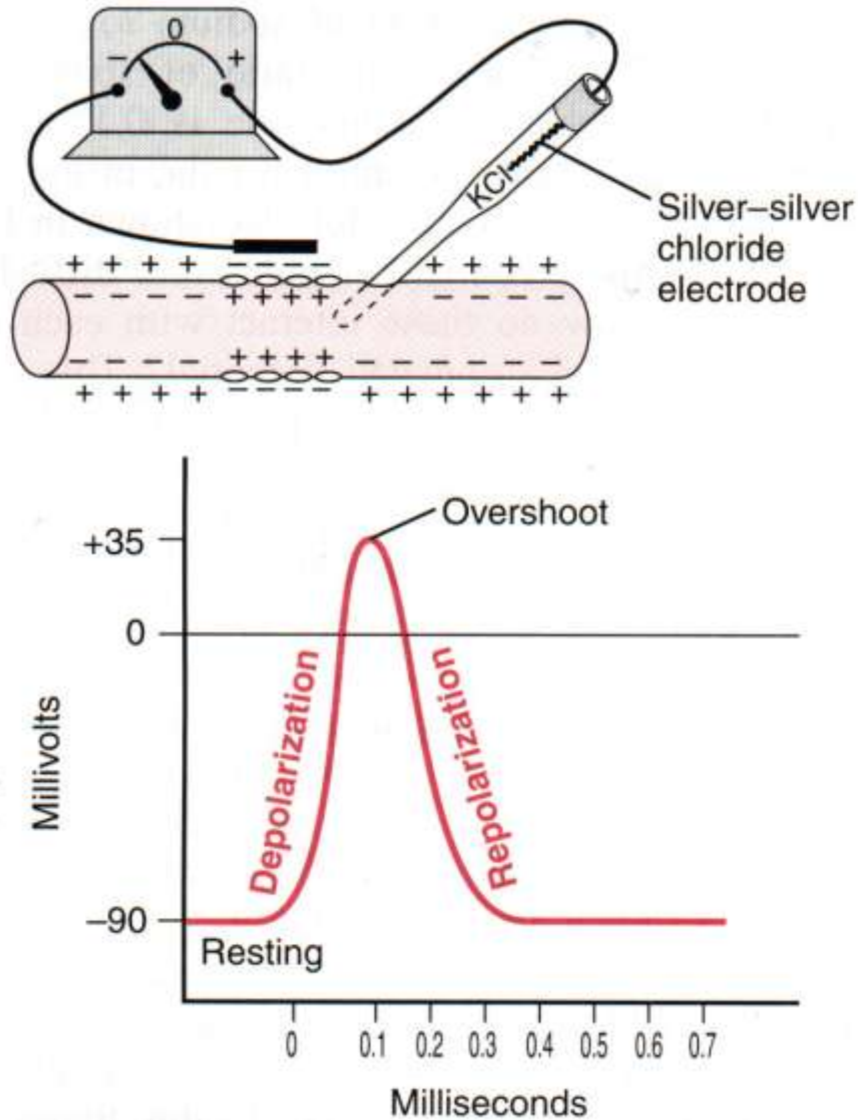
NOTE:
P' = permeability

- Recall also that cell membranes are permeable to other ions (mainly Na^+ & Cl^-).
- The Goldman Constant Field equation can account for other ions

- There are some terms that need to be understood & remembered:
  - excitability
  - depolarization
  - hyperpolarization
  - overshoot
    - means positive to 0 mV
  - repolarization
    - towards resting potential
  - threshold *(for action potential generation)*



Nerve Action potential

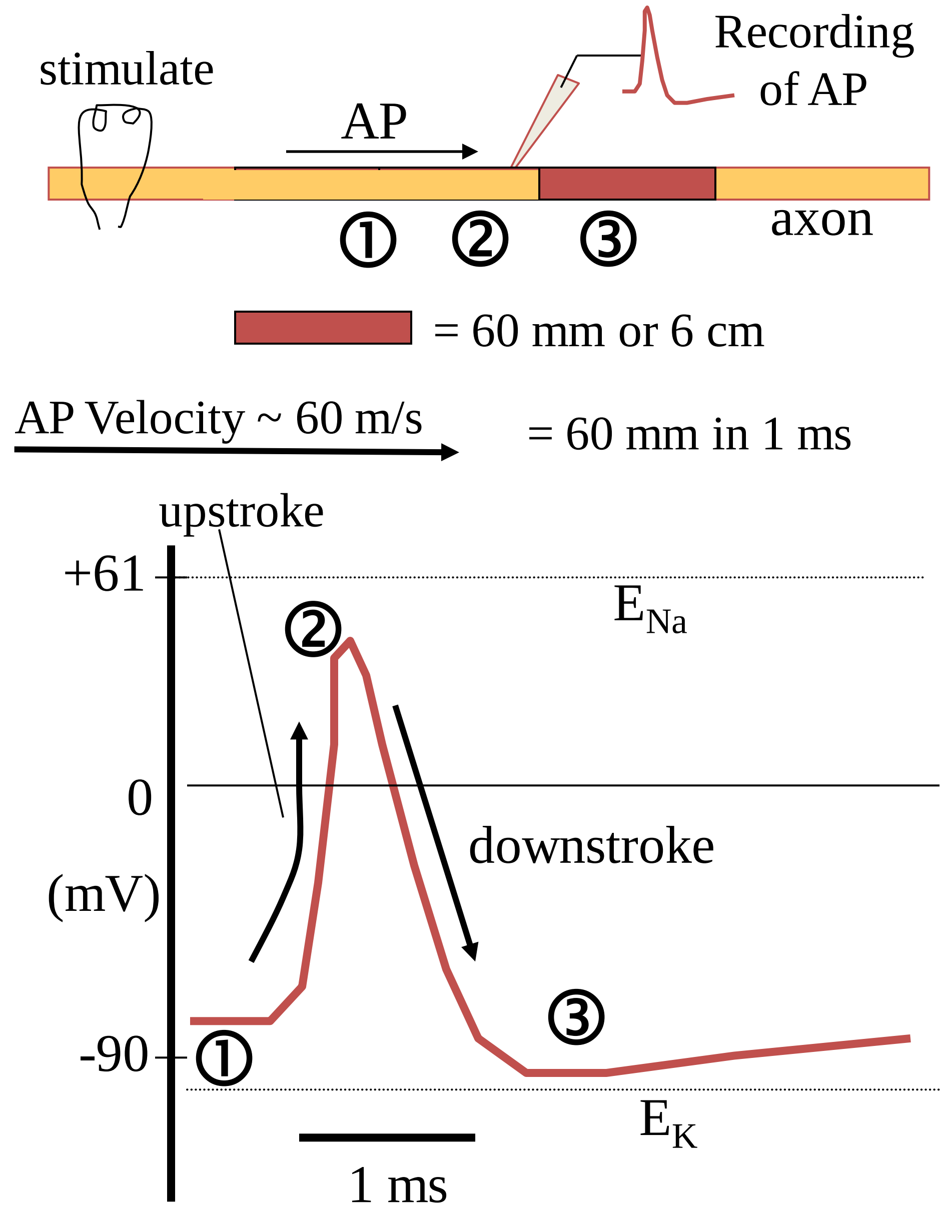


The action potential (AP)

- An action potential is:
  - A regenerating depolarization of membrane potential that ***propagates*** along an ***excitable*** membrane.

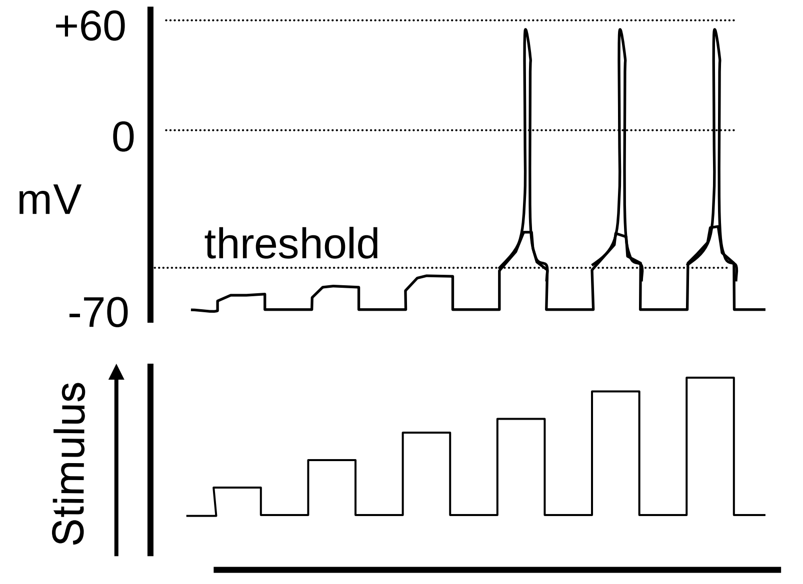
*[**propagates** = conducted without decrement (an 'active' membrane event)]*
*[**excitable** = capable of generating action potentials]*

- Action potentials:
  - ➢ are all-or-none events
    - ❑ need to reach threshold
  - ➢ have constant amplitude
    - ❑ do not summate
  - ➢ are initiated by depolarization
  - ➢ involve changes in permeability
  - ➢ rely on voltage-gated ion channels



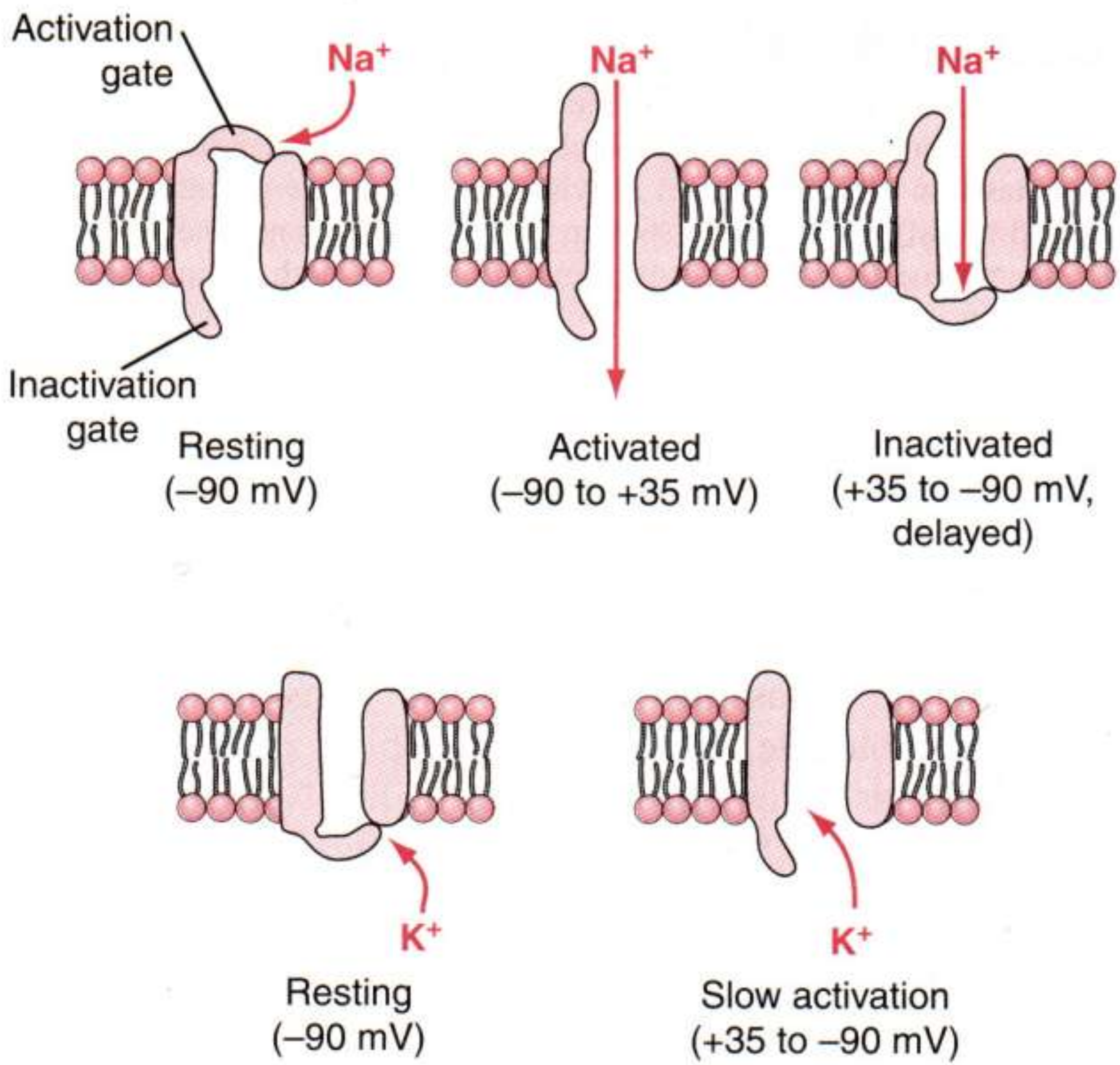
Properties of action potentials

- Action potentials:
  - are all-or-none events
    - threshold voltage (usually 15 mV positive to resting potential)
  - are initiated by depolarization
    - action potentials can be induced in nerve and muscle by extrinsic (percutaneous) stimulation
  - have constant amplitude
    - APs do not summate - information is coded by frequency not amplitude.
  - have constant conduction velocity
    - True for given fiber. Fibers with large diameter conduct faster than small fibers.



- Polarization Stage. = -90 mv (Resting Stage)
- Depolarization Stage.= +35 mv Action Stage
- Repolarization Stage.= 0 → -90 mv
- Hyperpolarization Stage.= -100 mv

Activation of the Sodium and Potassium Channels

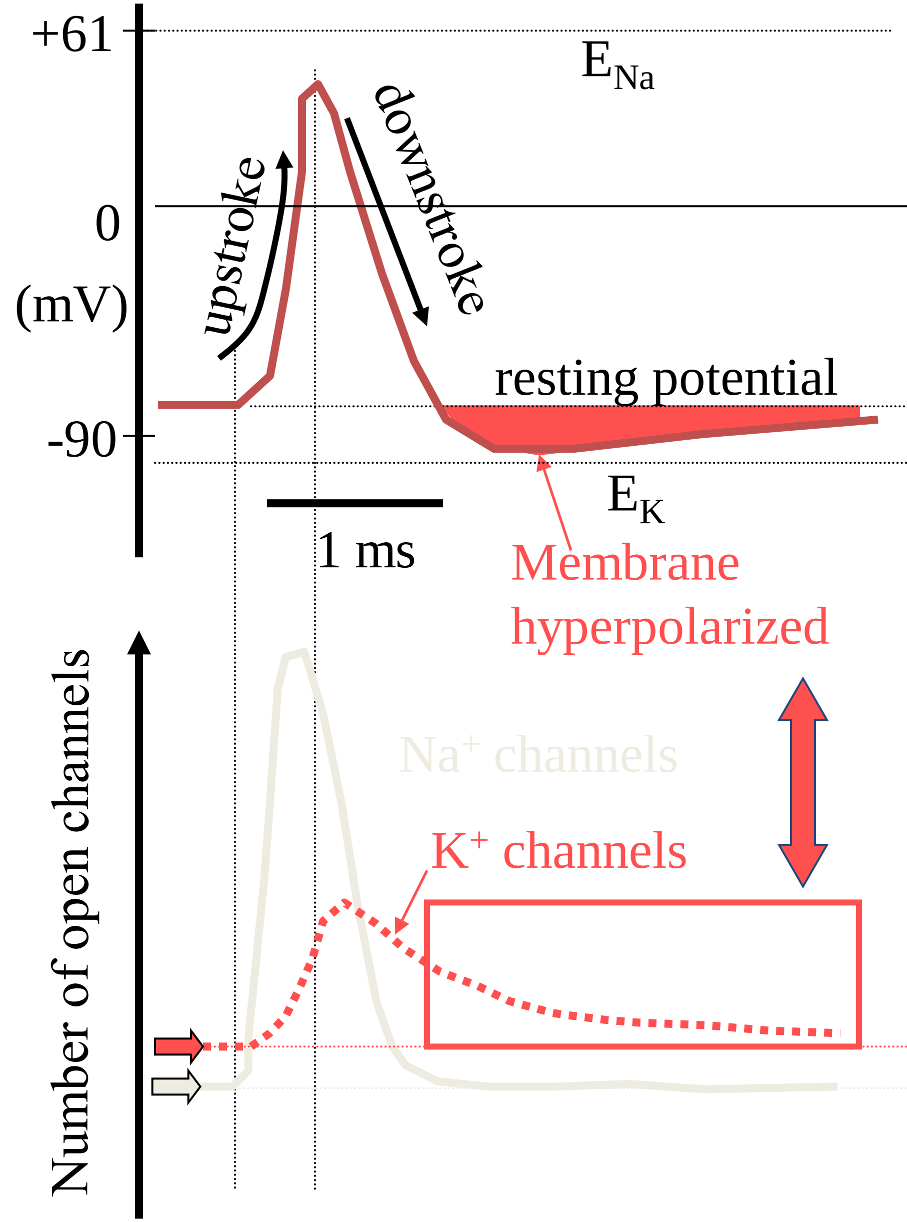


Channels & local potentials

- The ionic basis of the action potential
  - membrane permeability
  - ion channels
    - types of channels
      - voltage-dependent channels
      - receptor operated (ligand-gated) channels.
- Properties of ion channels
      - selectivity (refers to which ions can cross the channel)
      - gating (the process of opening and closing)
      - voltage dependence (activation, deactivation, inactivation)
- Action potentials
  - extracellularly recorded action potentials
- Synaptic transmission & graded membrane potentials
    - electrotonic conduction (conduction of subthreshold) passive impulses
    - excitatory & inhibitory *(defined by effect on post-synaptic cell)*
      - summation (temporal and spatial)

The AP - membrane permeability

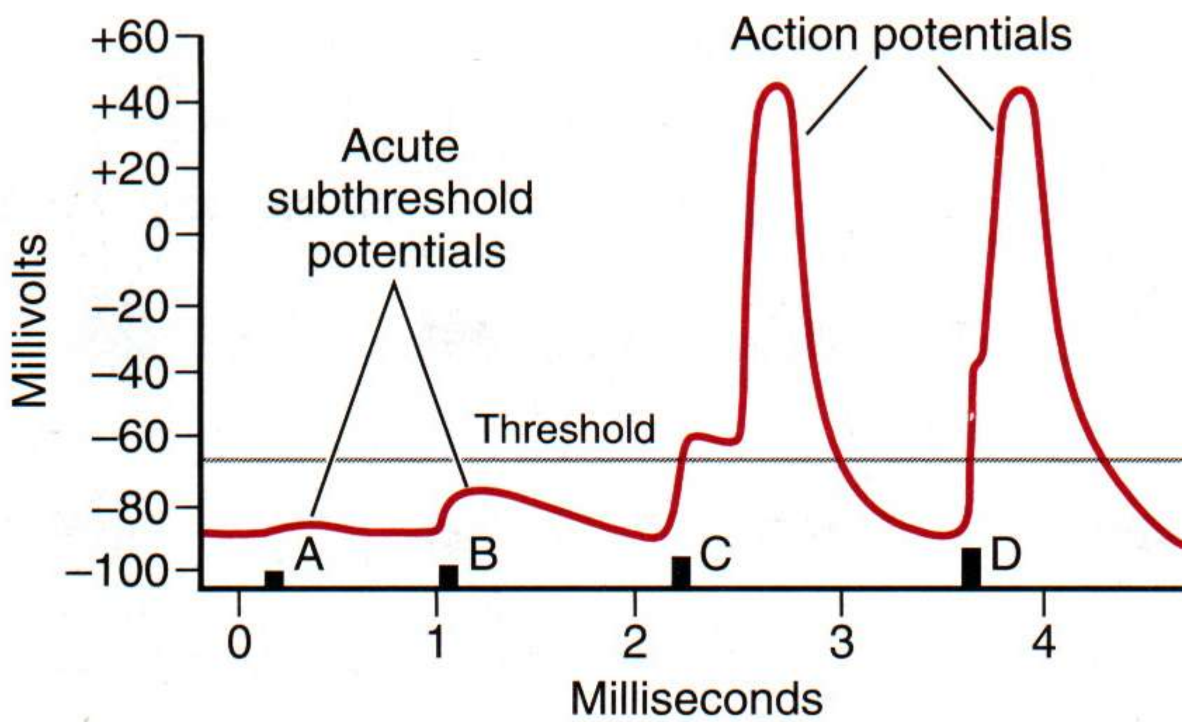
- During the upstroke of an action potential:
  - Na permeability increases
    - due to opening of Na^+ channels
      - memb. potential approaches E_{Na}
- During the downstroke of an action potential:
  - Na permeability decreases
    - due to inactivation of Na^+ channels
  - K permeability increases
    - due to opening of K^+ channels
      - mem. potential approaches E_K
- After hyperpolarization of membrane following an action potential:
  - not always seen!
  - There is increased K^+ conductance
    - due to delayed closure of K^+ channels



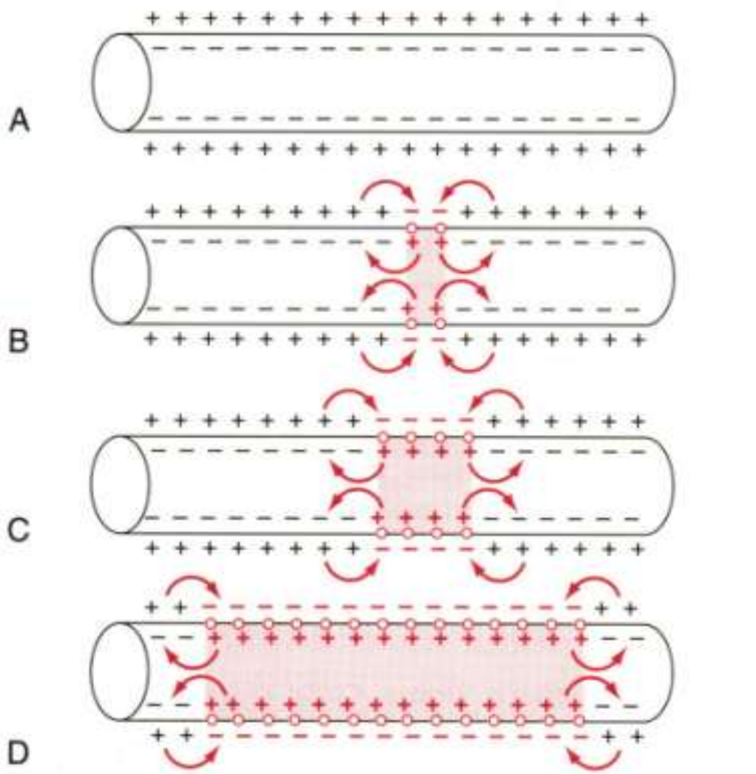
Roles of Other Ions During the Action Potential

Calcium Ions (keep the resting membrane potential)

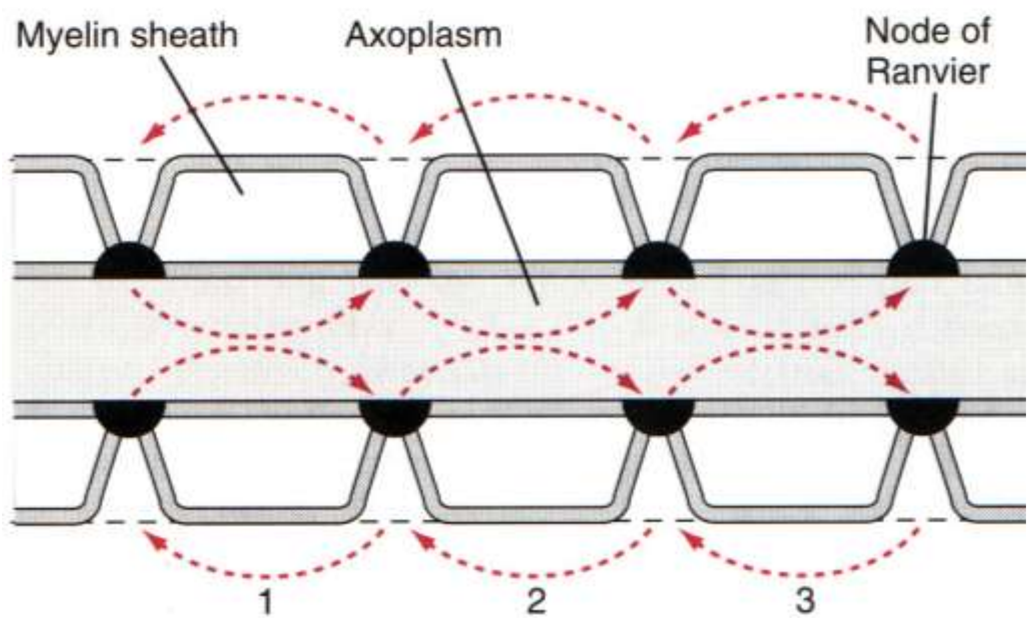
Threshold for the initiation of the Action Potential



Propagation of the Action Potential



Propagation of action potentials in both directions along a conductive fiber.

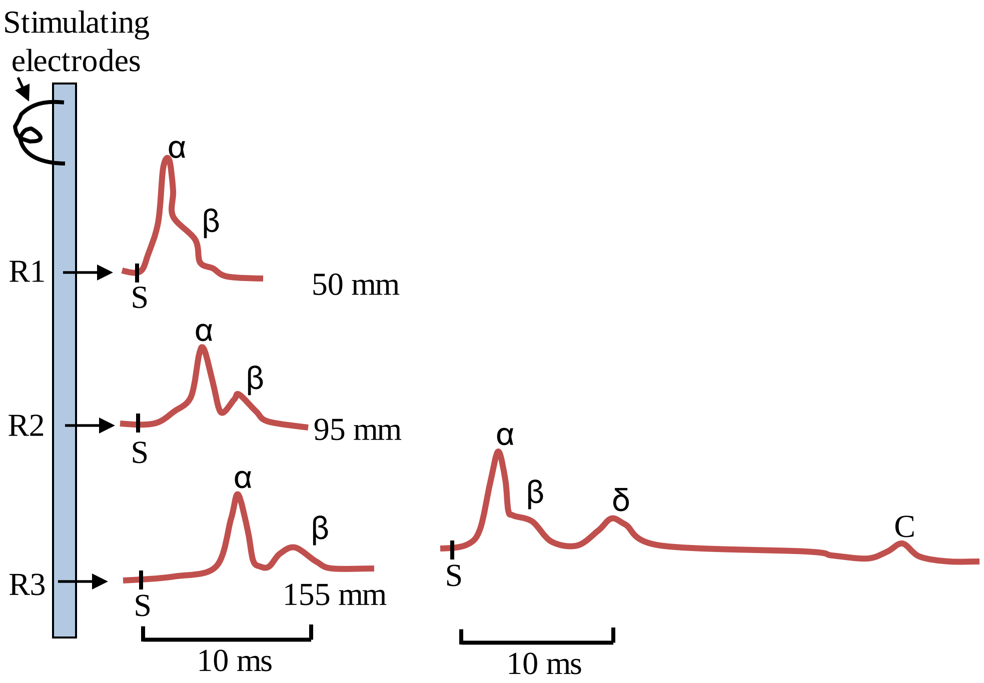


Saltatory conduction along a myelinated axon.

- **Direction of propagation**
- **All-or-Nothing principle**

Conduction velocity of AP

- Compound action potentials are recorded from nerve trunks
  - measured percutaneously from nerves that are close to surface (eg. ulnar nerve)
  - passage of action potentials in all axons of nerves is seen as a small (mV) voltage signal on body surface
  - as recordings are made further from the site of stimulation the waveform develops into several discrete peaks

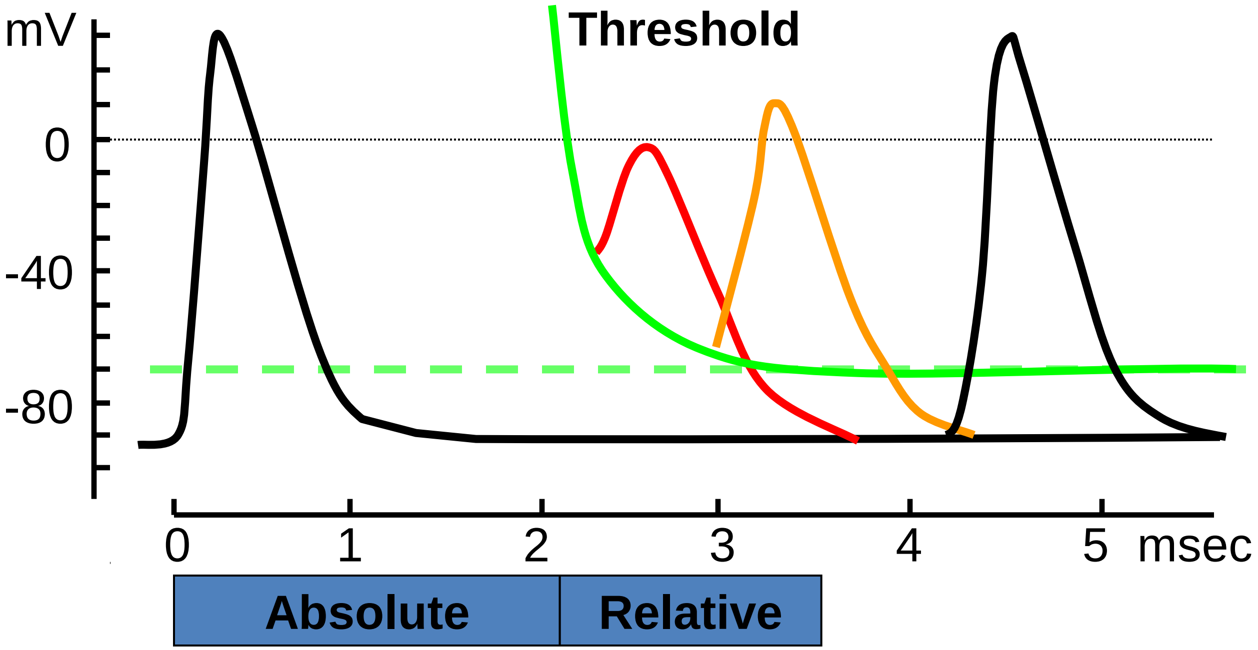


- The first signal to arrive at a distant recording site has travelled the fastest
  - Thus, each peak represents a set of axons with similar conduction velocity
    - velocity is calculated from the distance between R1 and R3 and the time taken to traverse that distance - distance/time = velocity (ranges from 0.5 to ~100 m/s)

Functions of action potentials

- Information delivery to CNS
  - Transfers all sensory input to CNS. Block APs in sensory nerves by local anesthetics. This usually produces analgesia without paralysis. WHY? Because local anesthetics are more effective against small diameter (large surface area to volume ratio). C fibers more than a-motor neurons.
- Information encoding
  - The frequency of APs encodes information (recall amplitude cannot change).
- Rapid transmission over distance (nerve cell APs)
  - Note: speed of transmission depends on fiber size and whether it is myelinated.
  - In non-nervous tissue APs are the initiators of a range of cellular responses.
  - Muscle contraction
  - Secretion (eg. epinephrine from chromaffin cells of medulla)

Refractory Periods

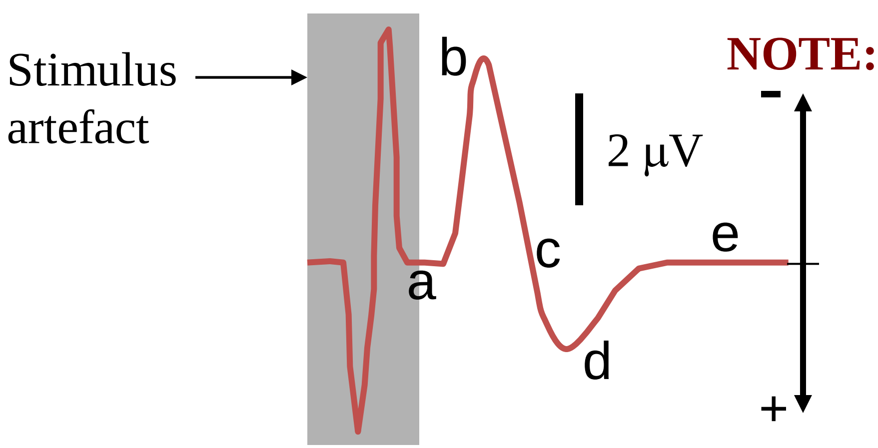


ARP - due to voltage inactivation of Na channels

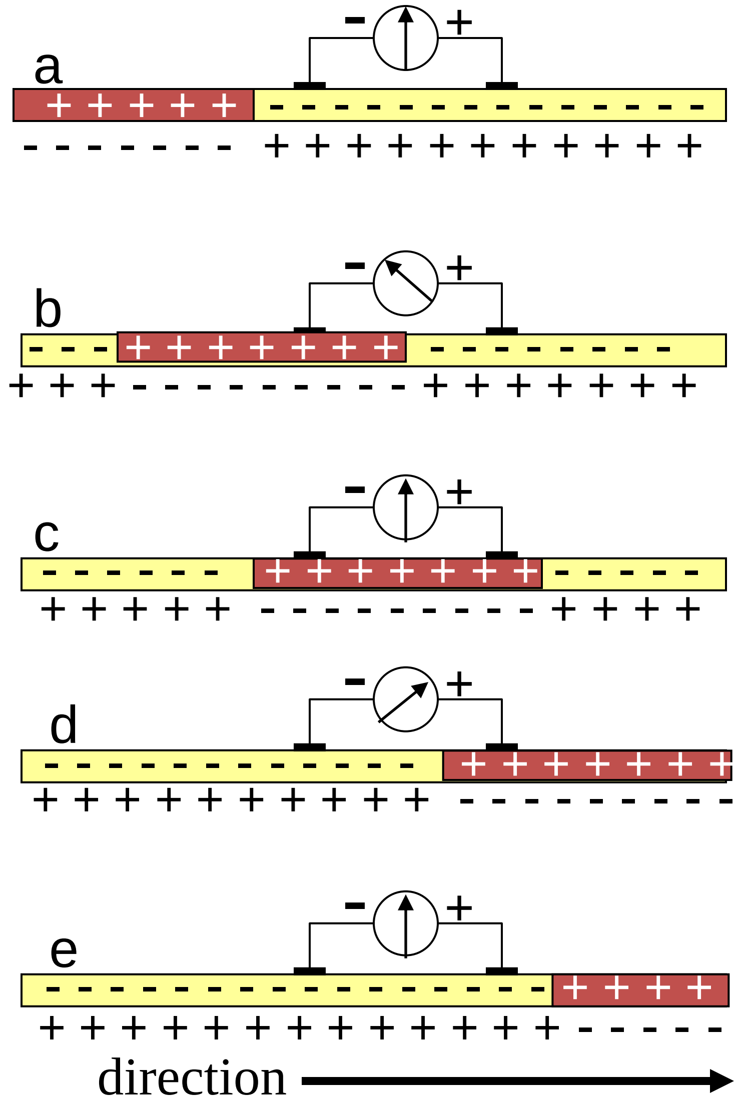
Refractory periods limit maximum frequency of APs

Extracellularly recorded APs

- Most text books show intracellularly recorded action potentials
  - such recording are usually not made in clinical practice
    - extracellular recordings are made
  - a so-called ‘bi-polar’ action potential is seen

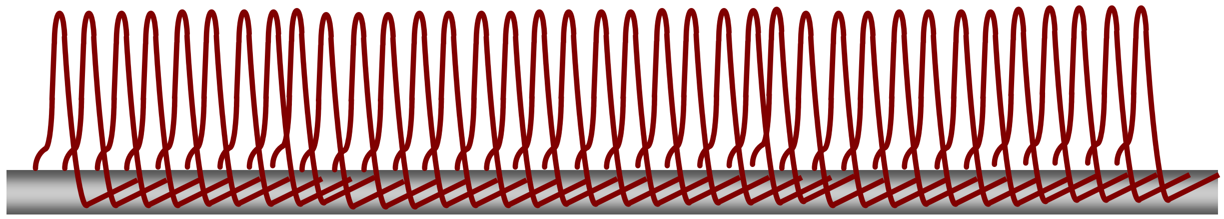


- Why does the action potential look like this?

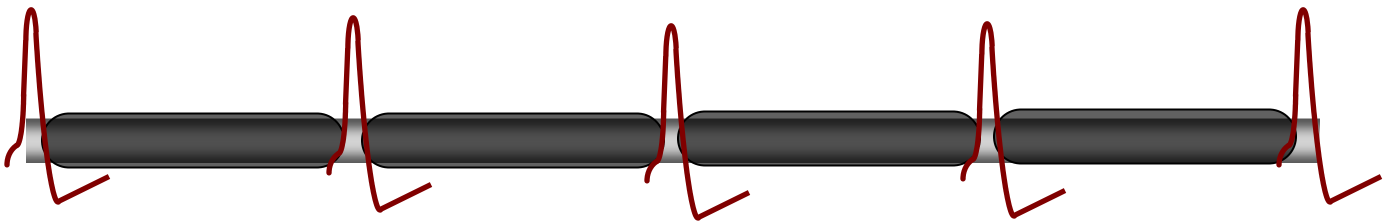


Conduction velocity

- non-myelinated vs myelinated -

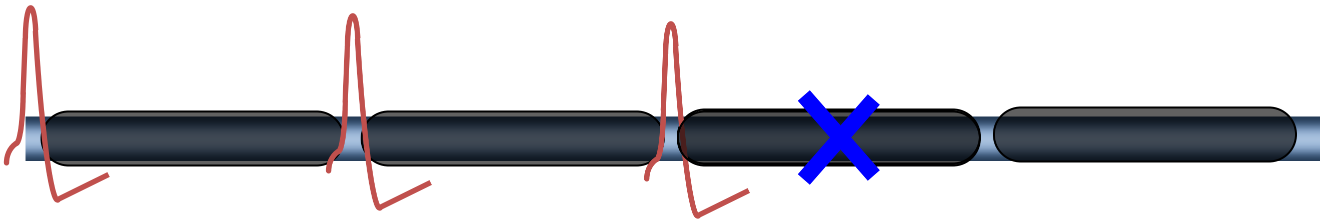


non-myelinated



myelinated

Multiple Sclerosis



- *MS is an immune-mediated inflammatory demyelinating disease of the CNS -*

- *About 1 person per 1000 in US is thought to have the disease - The female-to-male ratio is 2:1 - whites of northern European descent have the highest incidence*

Patients have a difficult time describing their symptoms. Patients may present with paresthesias of a hand that resolves, followed in a couple of months by weakness in a leg or visual disturbances. Patients frequently do not bring these complaints to their doctors because they resolve. Eventually, the resolution of the neurologic deficits is incomplete or their occurrence is too frequent, and the diagnostic dilemma begins.

Refractory period

After action potential ,during which a new stimulus can't be elicited

Because the Na+ and/or Ca++ become inactive

1/2500 second → maximum 2500 impulse/sec

Inhibition of excitability

Stabilizers

Ca++ reduce membrane permeability to Na+

Local Anesthetics

Procaine & tetracaine

Make Na+ channel much hard to open → reduce membrane excitability

$$\text{Safety factor} = \frac{\text{action potential strength}}{\text{excitability threshold}}$$

If safety factor < 1.0 impulses fail to pass along the anesthetized nerves