PHYSIOLOGY

Lec: 14

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Re-establishing sodium and potassium ionic gradients after action potentials are completed—importance of energy metabolism

- Very small amount of Na enters the cells and very small amount of K leaves the cell during an action potential
- Indeed, 100,000 to 50 million impulses can be transmitted by large nerve fibers before the concentration differences reach the point that action potential conduction ceases.
- Even so, with time, it becomes necessary to re-establish the sodium and potassium membrane concentration differences, which is achieved by action of the Na+-K+ pump in the same way as described previously for the original establishment of the resting potential

الانتقال من عصبون إلى آخر -

Propagation of Action Potential

Opening of Na^+ channels generates local current that depolarizes adjacent membrane, opening more Na^+ channels…

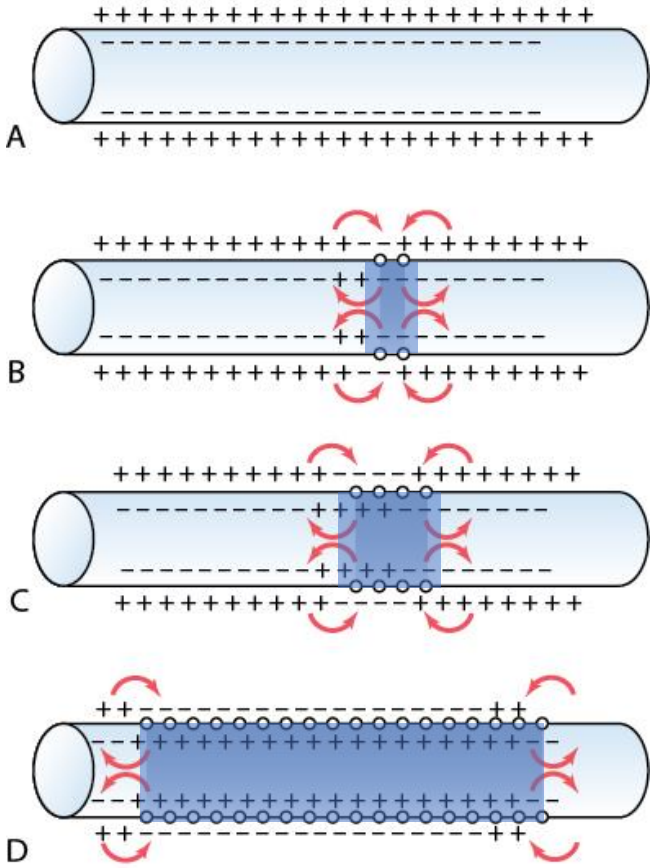
Rest

يوجد تأثير واحد

Stimulated
(local depolarization)

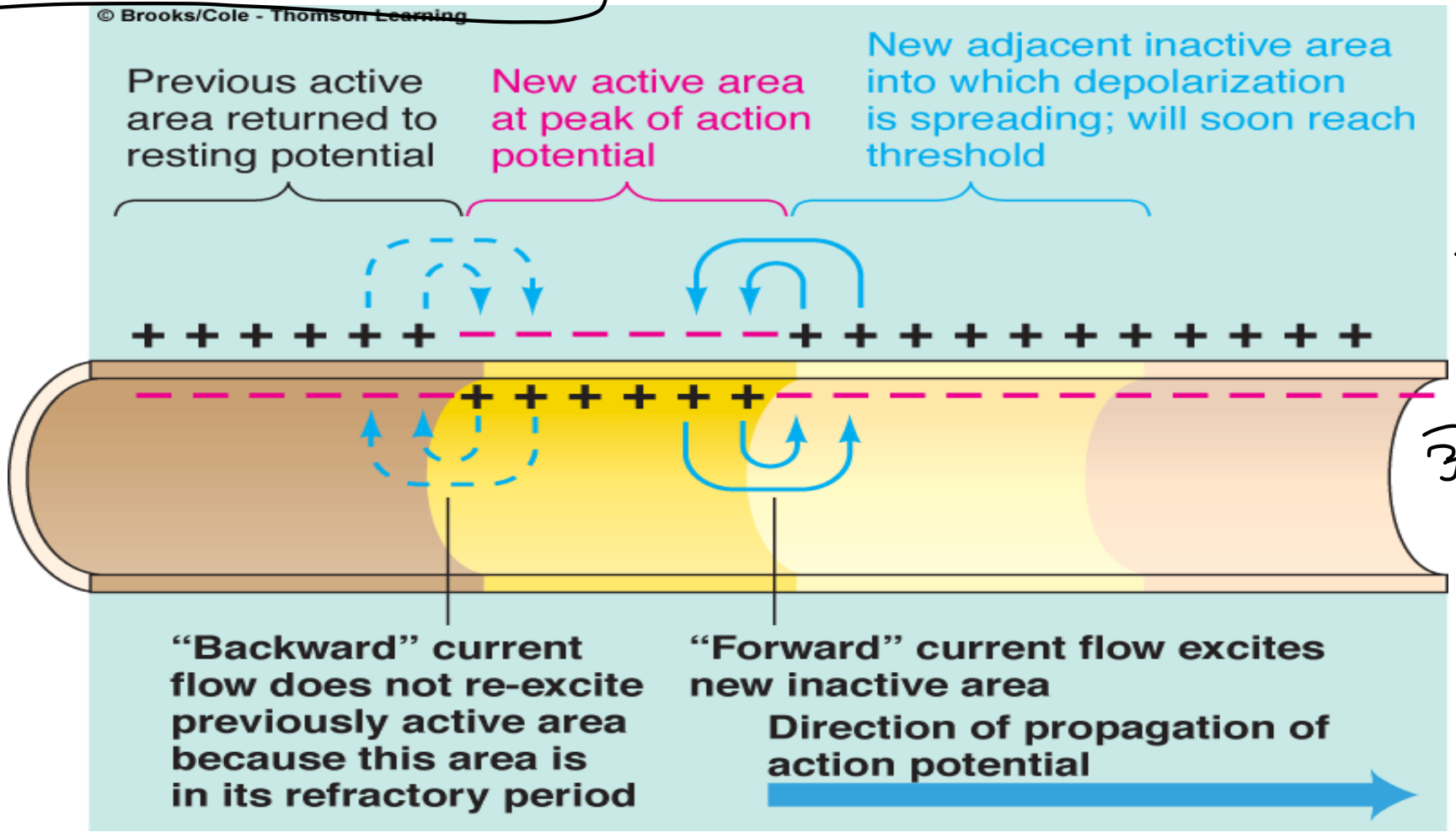
Propagation
(current spread)

يحدث جريان



we need just one action → one stimulation

Action potential propagation in none myelinated nerves



Axons

unmyelinated

- no myelin
- another propagation of the AP
- ال AP بيصير بشكل تخطي عكس النوع الآخر ((Saltatory نقل)) in myelinated

myelinated

- It's covered by lipid called myelin
- It transfers the action potential more quickly than unmyelinated one.
- It's more common in human body
- around the myelin their is a cell called Schwann cell

Signal Transmission

↳ Jumping

Myelination

- **Schwann cells** surround the nerve axon forming a myelin sheath
- Sphingomyelin decreases membrane capacitance and ion flow 5,000-fold
- Sheath is interrupted every 1-3 mm by a **node of Ranvier**

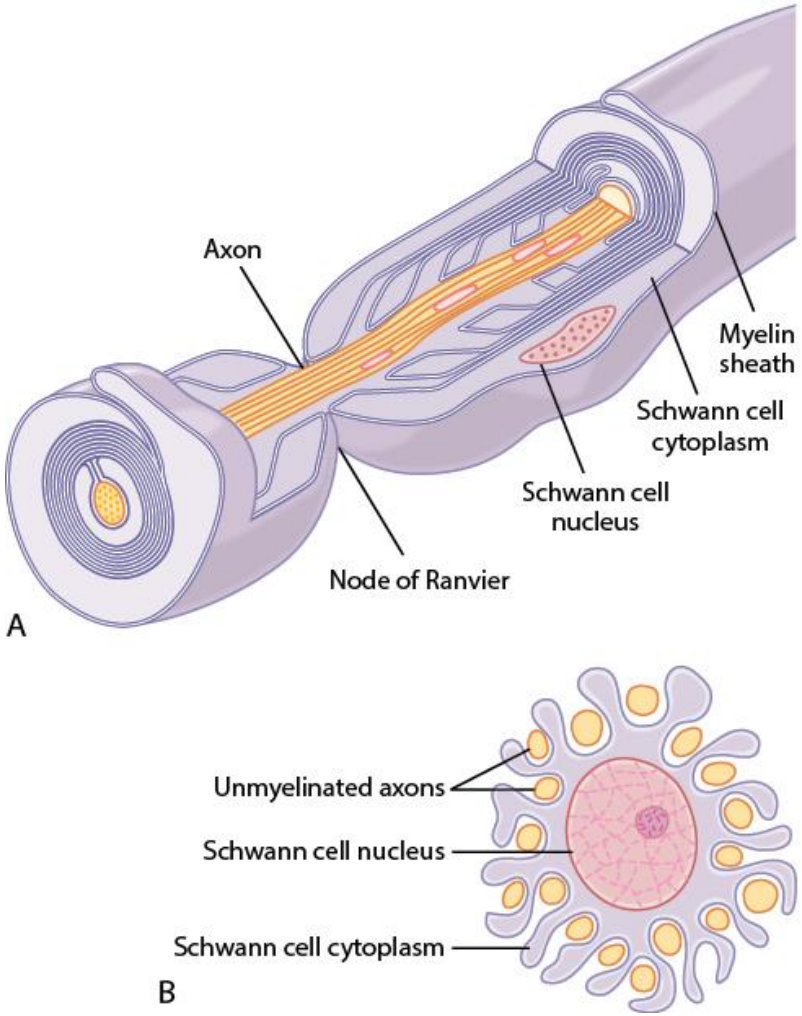


Figure 5-16

Saltatory Conduction

- AP's only occur at the node *(Na channels are concentrated here!)*
- Increased velocity
- Energy conservation

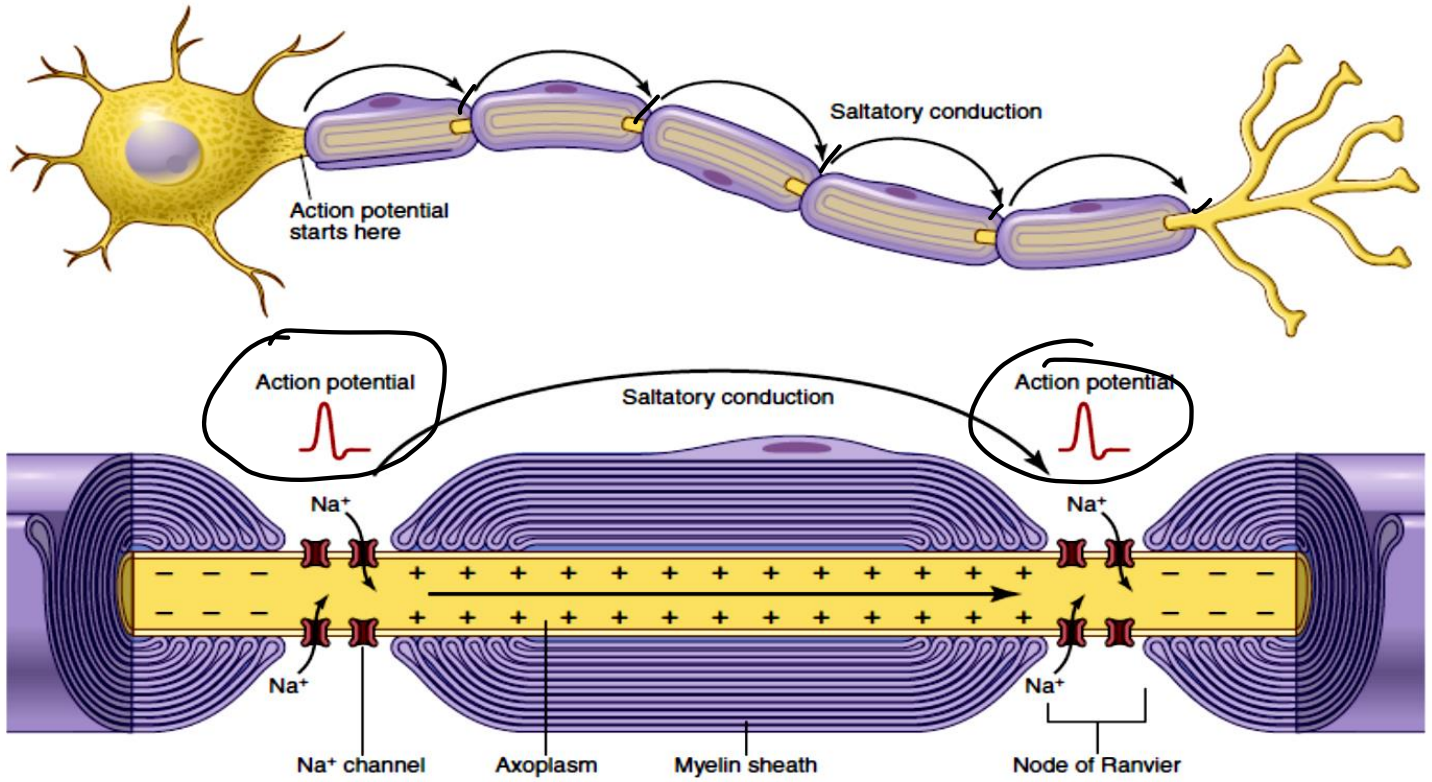
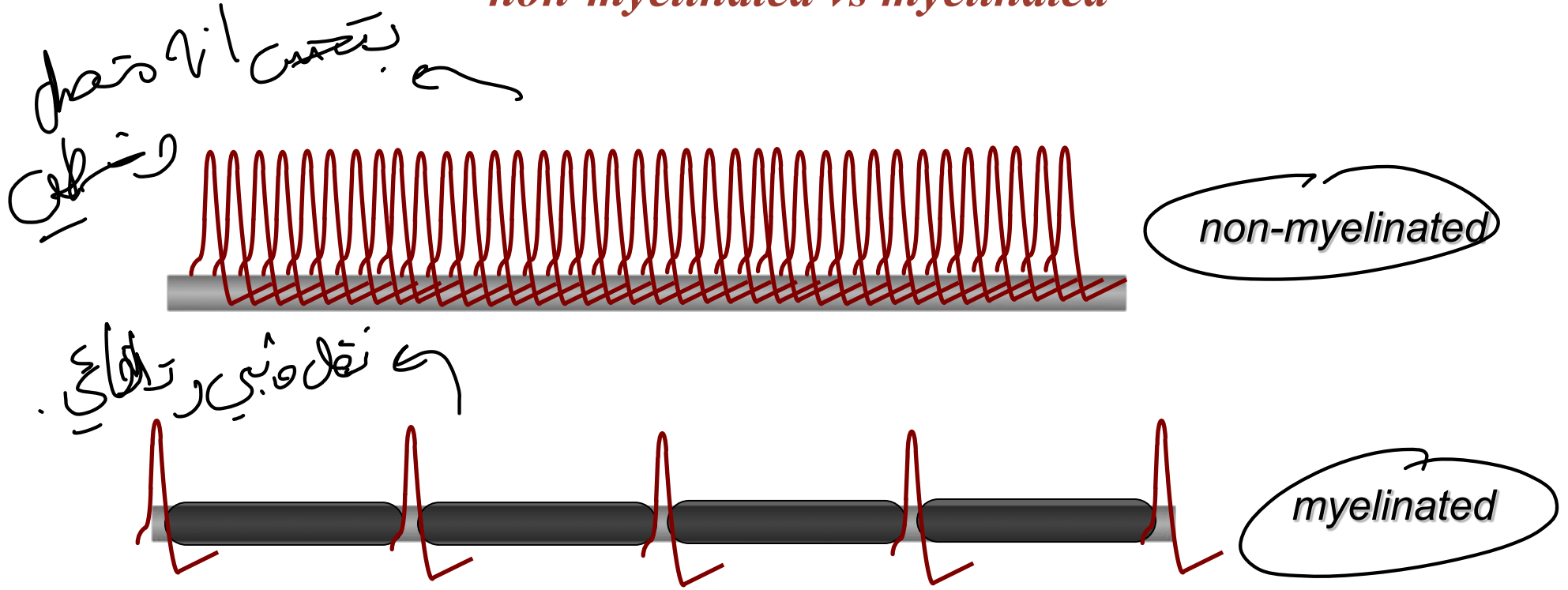


Figure 5-17 Saltatory conduction along a myelinated axon. The flow of electrical current from node to node is illustrated by the arrows.

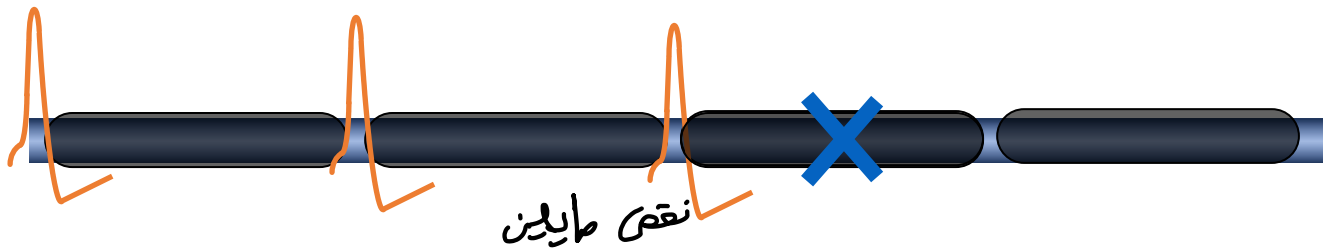
Conduction velocity

- non-myelinated vs myelinated -



Multiple Sclerosis

العطل الوبيي



- *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.

تنميل

 http://www.emedicine.com/pmr/topic82.htm

Effects of Drugs and Toxin on Action Potential

- **Tetrodotoxin** (TTX), a poison found in the internal organs of puffer fish, selectively blocks nerve Na channels at nanomolar concentrations.
- **Local anesthetics such as *lidocaine*** or ***benzocaine*** also block NaV channels.
- **Tetraethyl ammonium (TEA) ions** and 4-aminopyridine are among the KV channel blockers.
- There are also compounds that activate NaV channels, such as veratridine, pyrethroid insecticides.

Functions of action potentials

- **Deliver sensory information to CNS**
  - APs in sensory nerves are blocked by local anesthetics. This usually produces analgesia without paralysis. **WHY?** LAs are more effective against small diameter neurons with a large surface area to volume ratio. **Hence**, small C-fibers that conduct pain sensations are affected more than a-motorneurons.
- **Information encoding**
  - The frequency of APs encodes information (amplitude of AP is constant).
- **Rapid transmission over distance (nerve cell APs)**
  - The speed of transmission depends on fiber size and whether it is myelinated. Information of lesser importance is carried by slowly conducting unmyelinated fibers.
- **In non-nervous tissues, APs initiate various cellular responses**
  - muscle contraction
  - secretion (eg. Epinephrine from chromaffin cells of medulla)

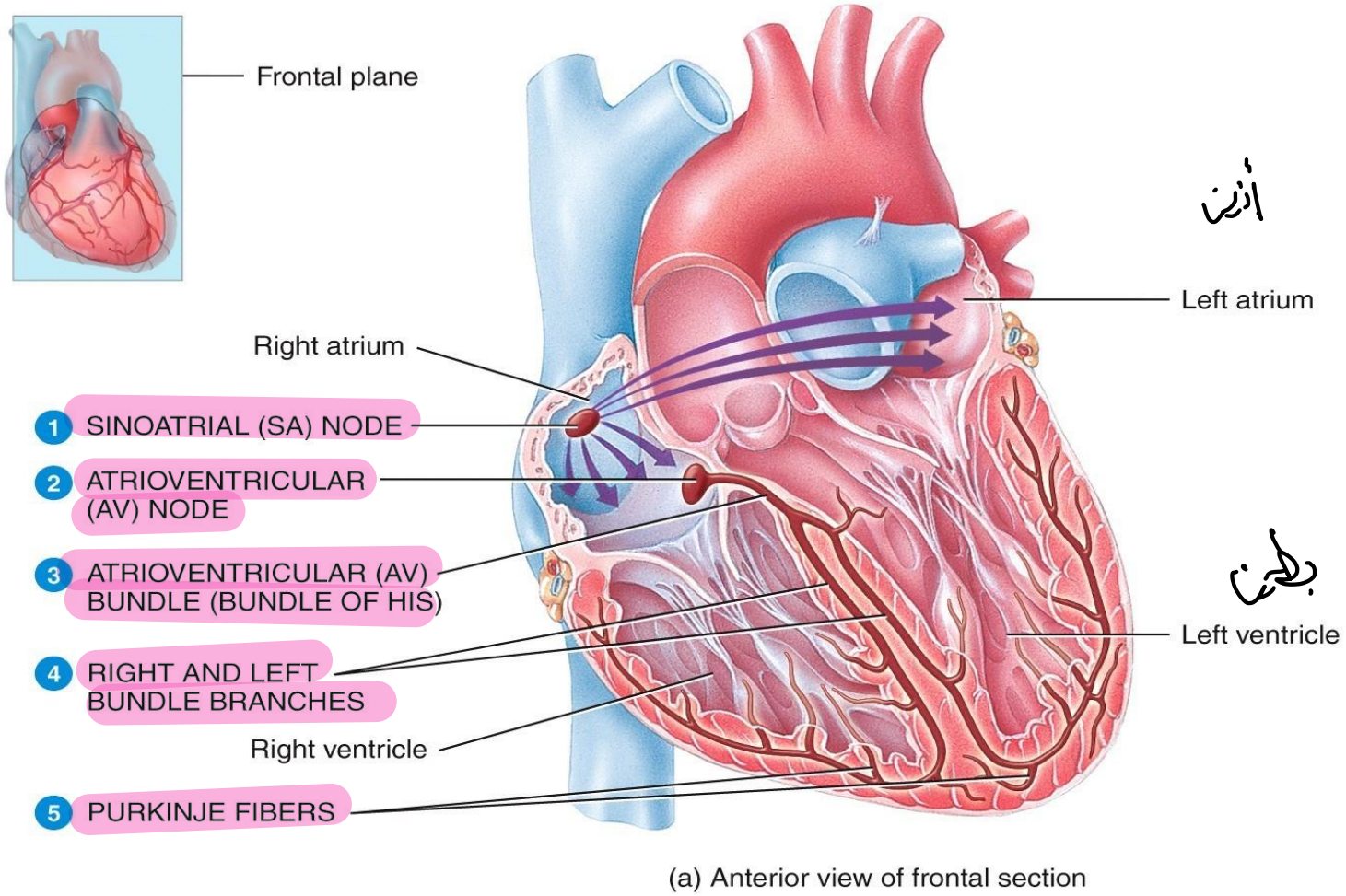
Electrical Properties of Cardiac Cells and Cardiac Cell Action Potential

- Cardiac action potentials differ sharply from those of skeletal muscle or nerve in three important ways that promote synchronous rhythmic excitation of the heart
- They can be self-generating
- They can be conducted directly from cell to cell via gap junctions
- They have long durations.
- Slower conduction velocity

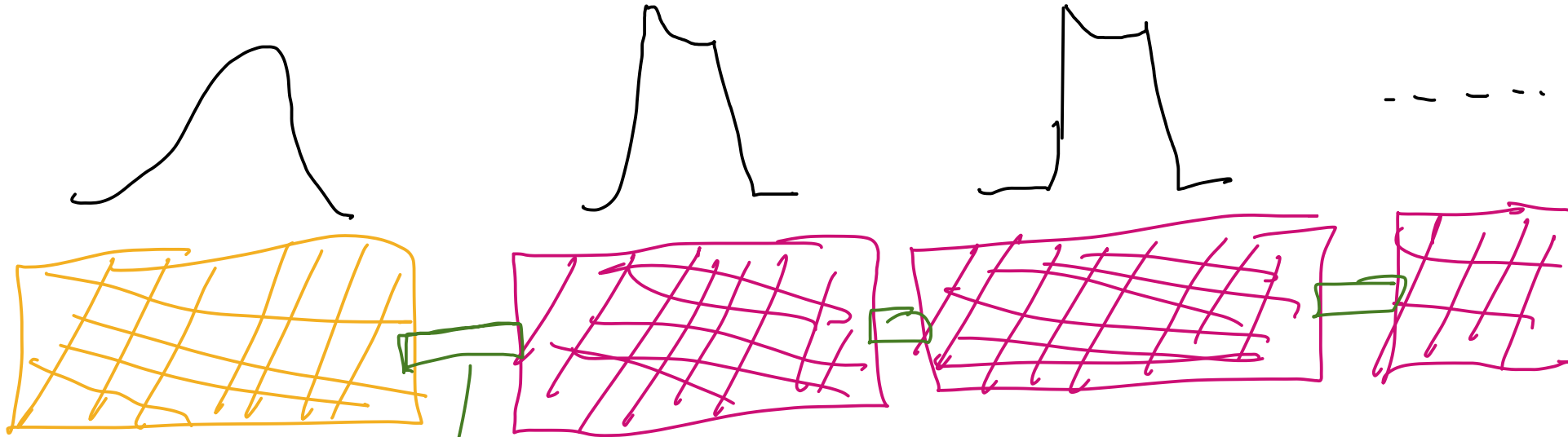
Types of Cardiac Muscle Cell

1. Contractile cells (Atrial and Ventricular)
   - 99% of cardiac muscle cells
   - Contract during the cardiac cycle and pump blood
2. Autorhythmic cells: Pacemaker cells
   - Exhibits spontaneous depolarization
   - Do not contract. Known as (conductive system of the heart).
   - Specialized for initiating and conducting action potentials responsible for contraction of atria and ventricle.

Conduction system of the heart and spread of electrical activity



(a) Anterior view of frontal section

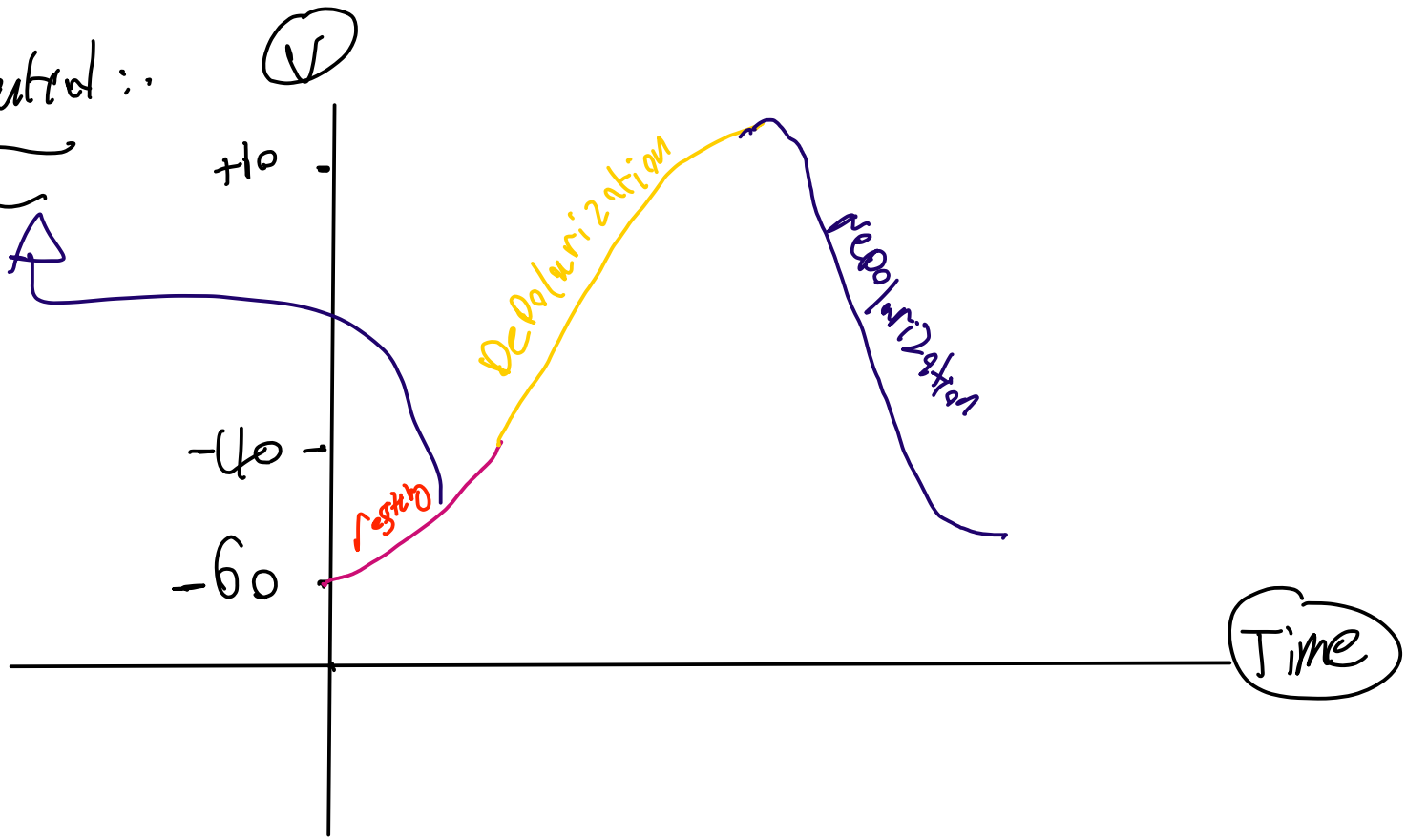


Gap Junctions

The ions will be transported through the Gap-J

⇒ * That will make diff types of action Potential :-

1. Pacemaker Potential :-



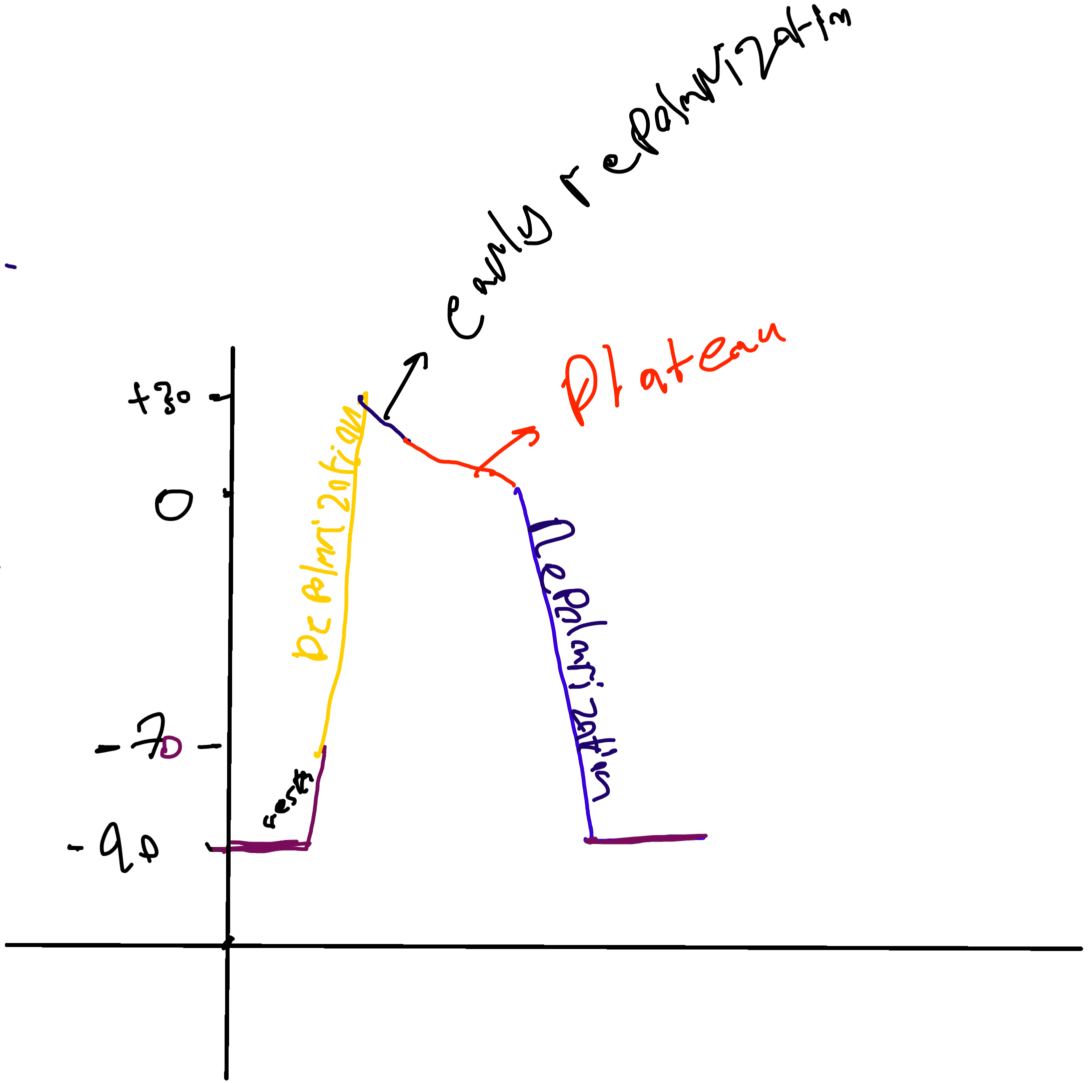
Conducted Potential :-

* وطبعاً لما يصير stimulation

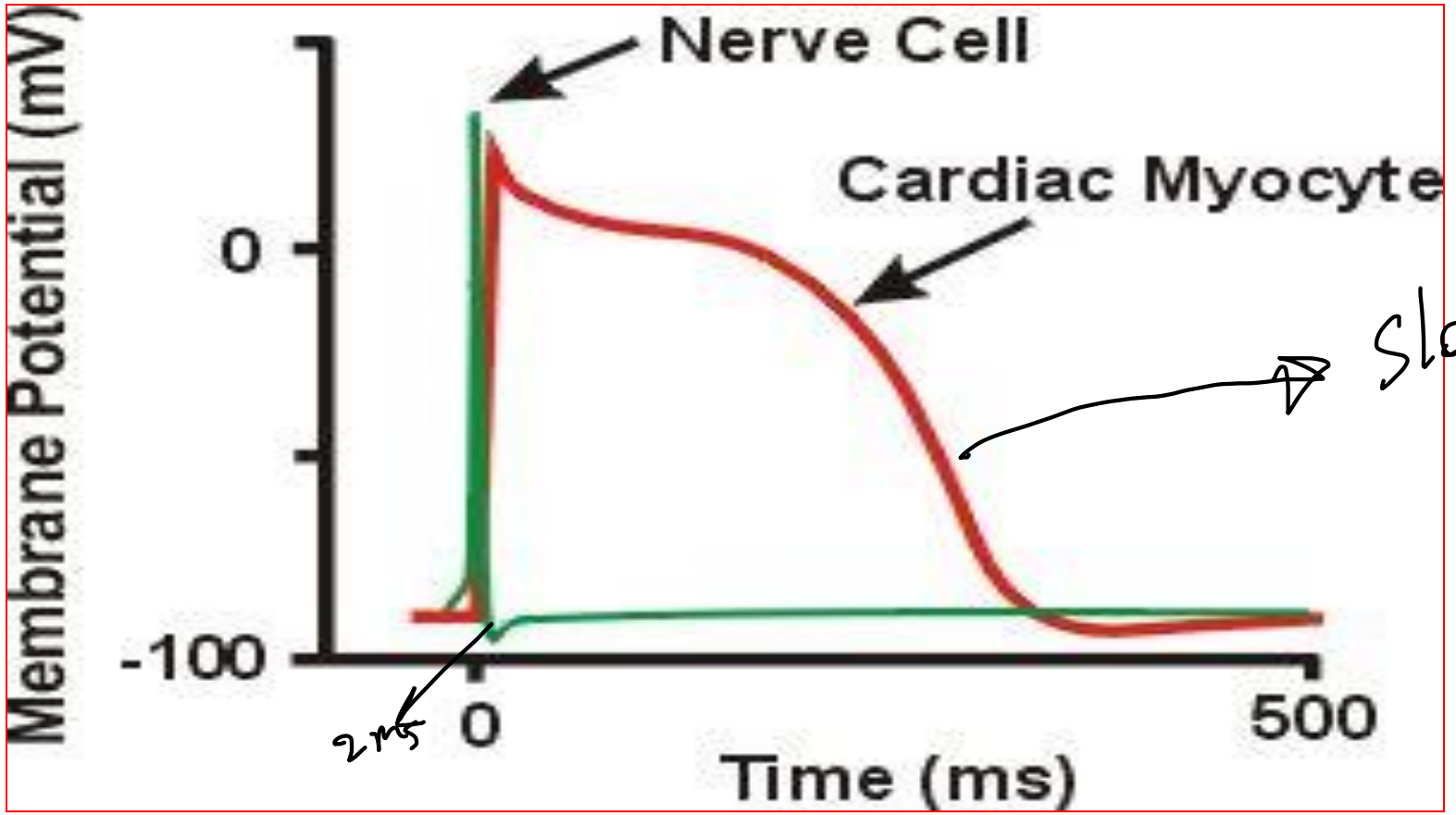
تاني مرة بتنتقل الايونات من

خلال الاشي بجار

* gap junctions



Action potential in nerve cells and cardiac cells

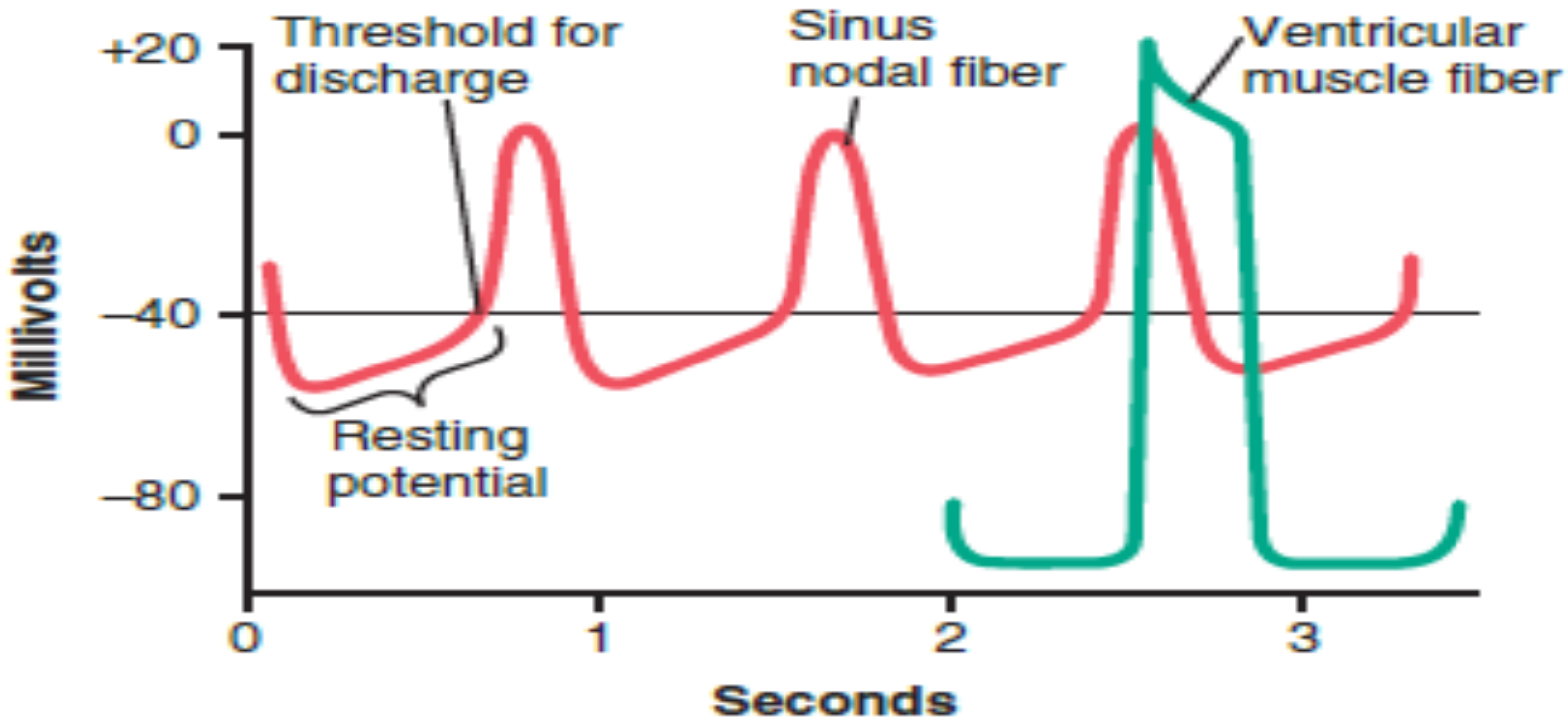


Cardiac Muscles AP

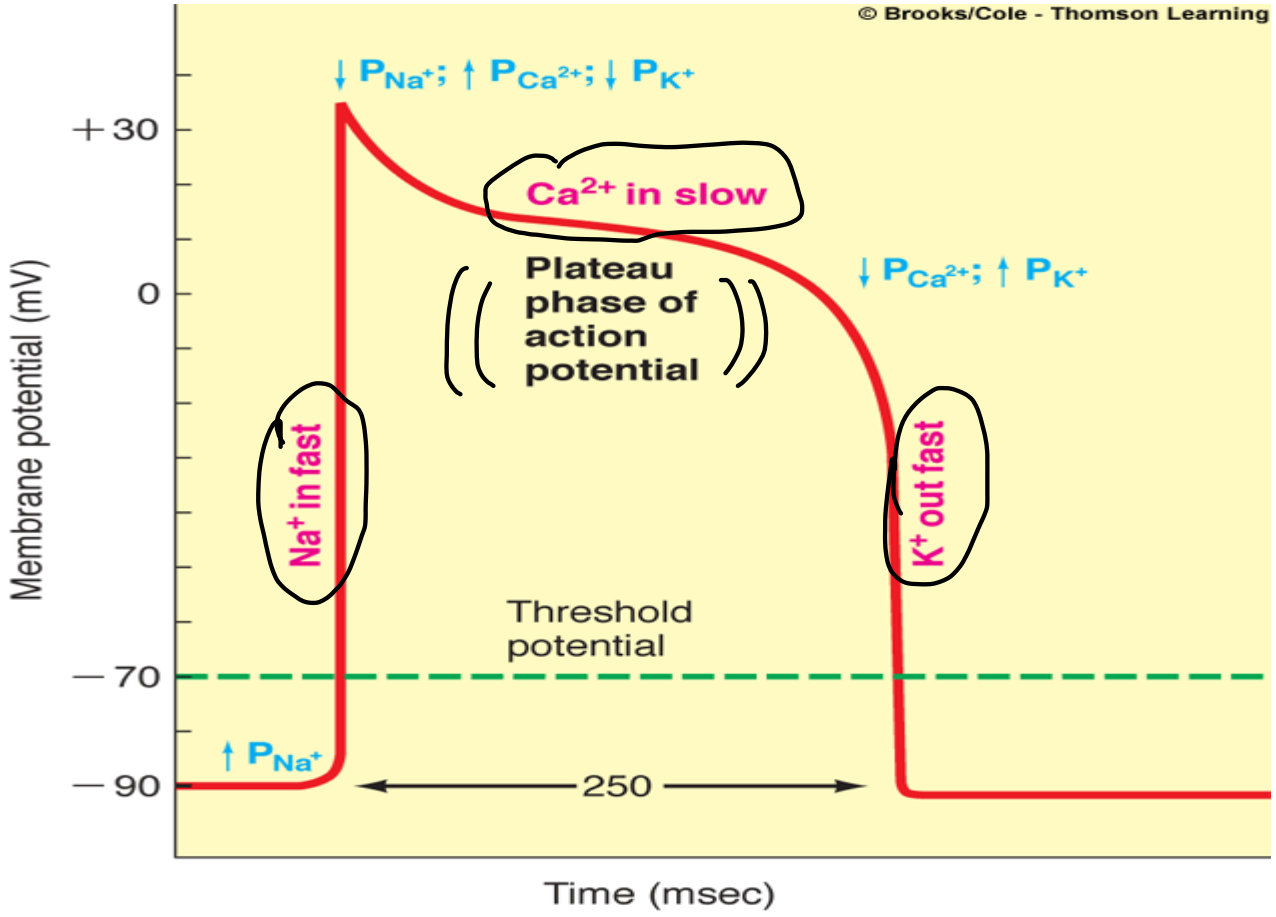
There are two cardiac action potentials produced by myocytes,

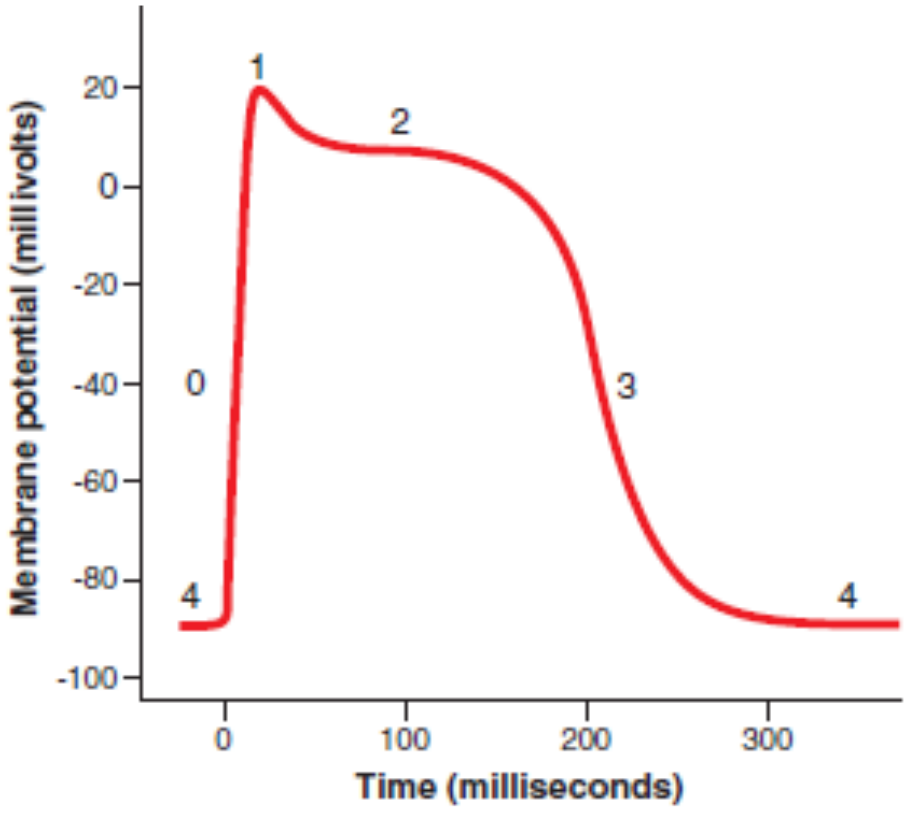
1- Fast AP: is characterized by containing a plateau phase. Usually seen in the normal contractile cardiomyocytes.

2- The Slow AP: As seen in the conductive system (for example SA node and Av node cells



Cardiac action potentials Ventricular and Purkinje system (Intracellular recording)
Phases of action potentials and its ionic basis of action potential





Cardiac Action Potentials of Ventricular Cells

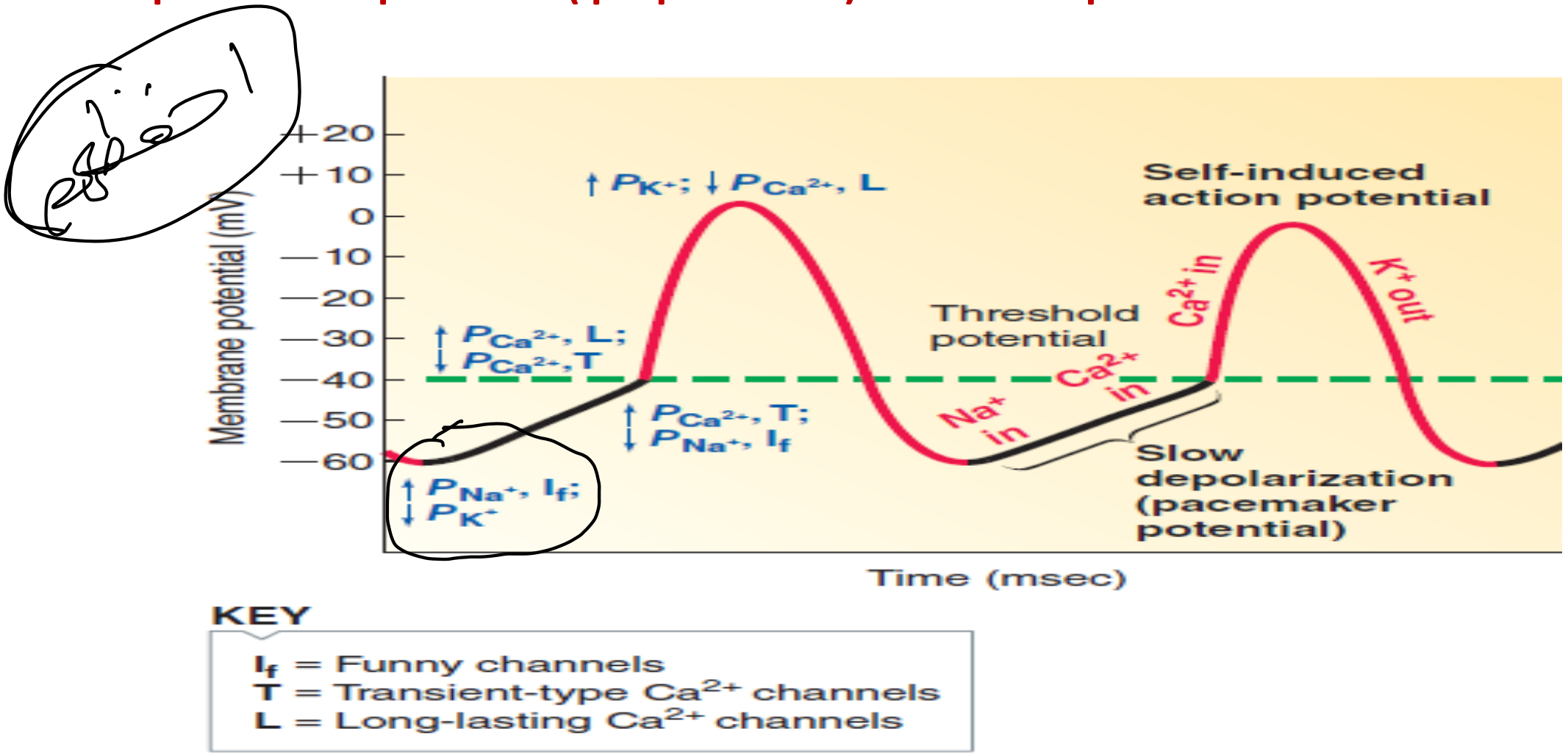
- *Phase 0 (depolarization)*

When the cardiac cell is stimulated and depolarizes, the membrane potential becomes more positive. Voltage gated sodium channels (fast sodium channels) open and permit sodium to rapidly flow into the cell and depolarize it. The membrane potential reaches about +20 millivolts before the sodium channels close

- *Phase 1 (initial repolarization)fast sodium channels close*.
  - The fast sodium channels close, the cell begins to repolarize, and potassium ions leave the cell through the activation fast potassium channels.
- *Phase 2 (plateau)*

  Due to the opening or activation of *L-type calcium channels (slow calcium channels),* which are also called *calcium-sodium channels open and fast potassium channels close*.
- *Phase 3 (rapid repolarization)*
  - *calcium channels close and slow potassium channels open*. The closure of calcium ion channels and increased potassium ion permeability, permitting potassium ions to rapidly exit the cell, ends the plateau and returns the cell membrane potential to its resting level.
- *Phase 4 : (resting membrane potential) averages about −90 millivolts*.

Pacemaker Activity Of Cardiac Autorhythmic Cells
pacemaker potential (prepotential) and action potential of SA node cells



KEY

I_f = Funny channels
T = Transient-type Ca^{2+} channels
L = Long-lasting Ca^{2+} channels

Pacemaker Electrical Activity of Sinoatrial Node (pacemaker potential and action potential)

- **Pacemaker potential**
- The first half of the pacemaker potential is the result of simultaneous opening of unique funny channels, which permits inward Na current, and closure of K channels, which reduces outward K current.
- The second half of the pacemaker potential is the result of opening of T-type Ca ions channels.
- **Action potential**
- Once threshold is reached, the rising phase of the action potential is the result of opening of L-type Ca ions channels, whereas the falling phase is the result of opening voltage gated of K channels

Pacemaker Potential and Action Potential of SA Node Cells Summary

- After hyperpolarization of SA node cells that is caused by activation of K channels , a different channel open that can pass both K and Na is activated
- Because this channel is activated following hyperpolarization, it is referred to as an “h” channel; however, because of its unusual (funny) activation, it has been of this has also been given a nick name (funny channel , f channel)
- As the depolarizing current moves through the h channels increases, the membrane begins to depolarize, forming the first part of the prepotential. Then Transit Ca channels (T Channels are activated
- and completes the prepotential, and the cell reaches the threshold
- At this point L type Ca channels are opened and cause the second depolarization phase of action potential
- Finally, the L type Ca channels close and Voltage gated K channels are activated causing repolarization and slight hyperpolarization

Action Potential in SA and AV node

- The action potentials in the SA and AV nodes are largely due to Ca 2+ , with no contribution by Na + influx. Consequently, there is no sharp, rapid depolarizing spike before the plateau, as there is in other parts of the conduction system and the atrial and ventricular fibers.
- In addition, prepotentials are normally prominent only in the SA and AV nodes.
- However, “latent pacemakers” are present in other portions of the conduction system that can take over when the SA and AV nodes are depressed or conduction from them is blocked.
- Atrial and ventricular muscle fibers do not have prepotentials, and they discharge spontaneously only when injured or abnormal

Thank you for your attention

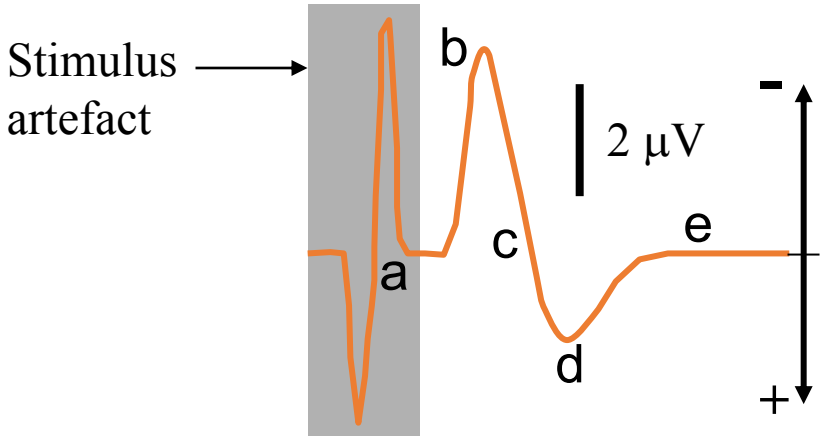
Extra reading for action potential in a nerve truck : Optional reading

- The following two slides are related to recording of electrical activity of nerve truck It gives useful information on conduction velocity of action potentials and more

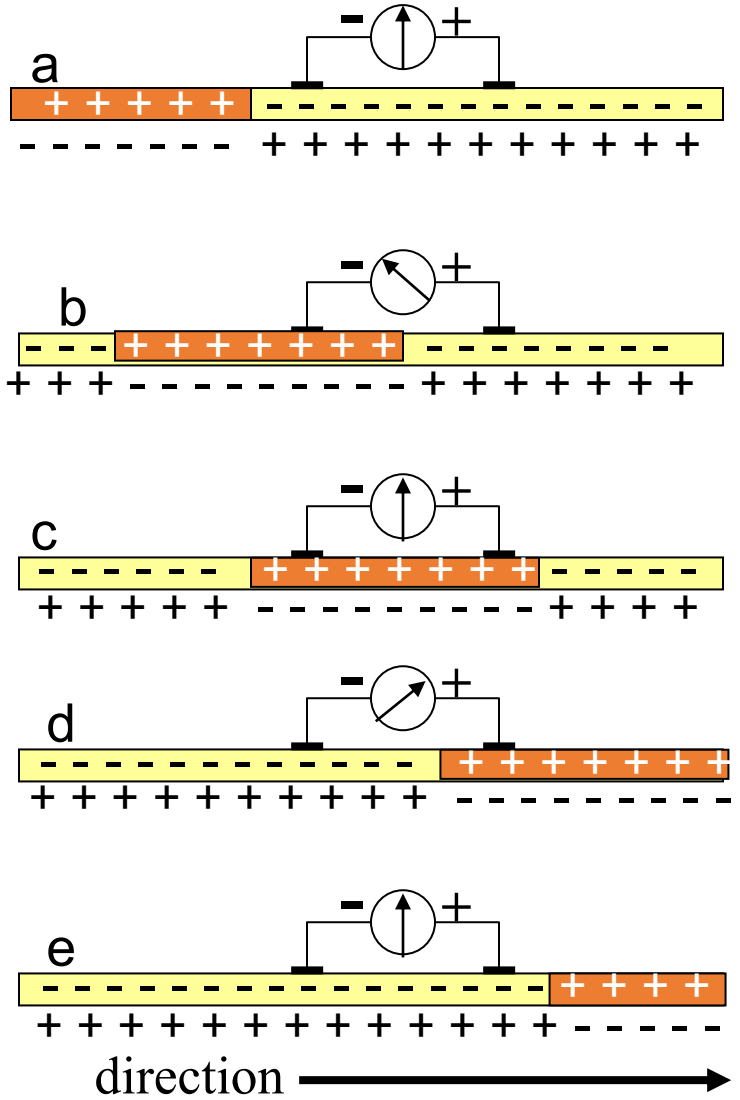
That is the method used in neurology to assess the conduction of sensory and motor fibers

Extracellularly recorded APs

- Most text books show intracellularly recorded action potentials
  - Such recordings are usually not made in clinical practice. Extracellular recordings are made in clinical practice.
  - A so-called '***bi-polar***' action potential is shown

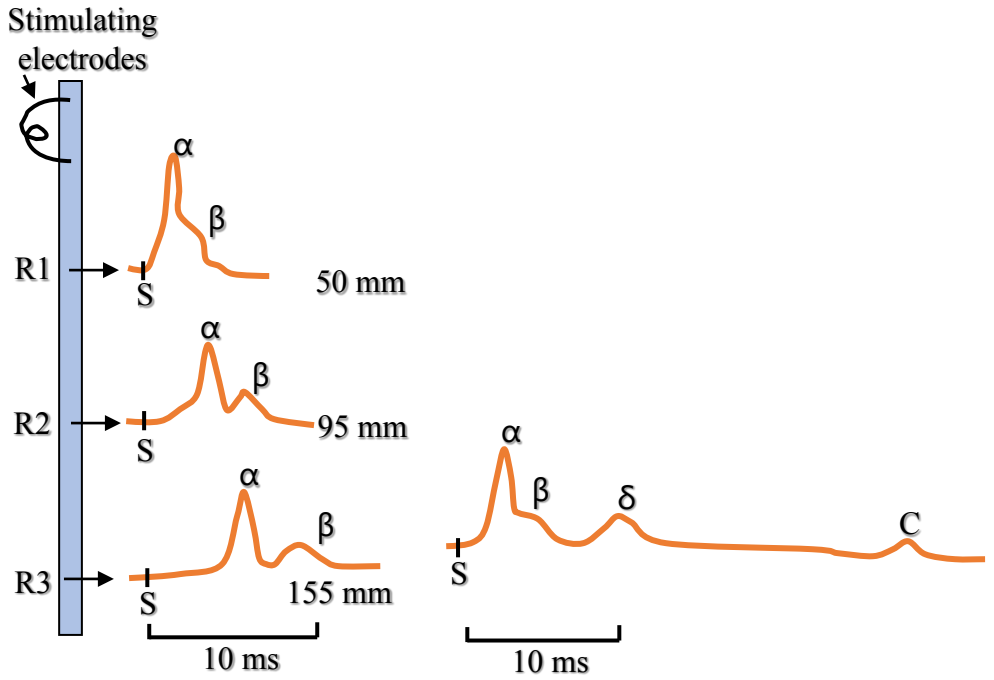


- ***Why does the bi-polar action potential look like this?***



Conduction velocity of AP

- Compound action potentials are recorded from ***nerve trunks***
  - measured percutaneously from nerves that are close to surface (e.g., 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)