physiology

premed 2018 - JU

◉ Sheet ○ Slides

Number

24

Done by:

Omar Bani-ata

Corrected by:

Omar Bani-ata

Doctor

Yanal Shafagoj

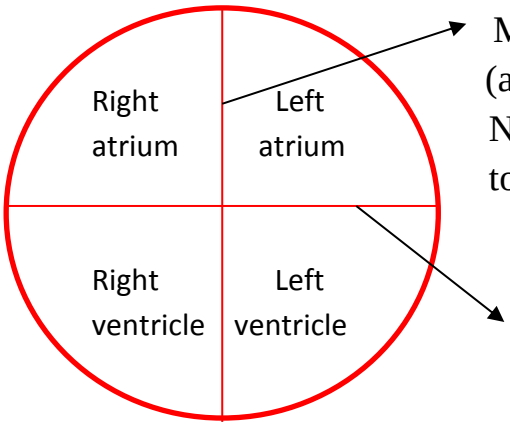
TOPICS of this sheet

LAST LECTURE

✓ We talked about the type of cells which are Excitable (Muscles) & Non-Excitable (Endocrine cells).
✓ Most of our cells are polarized, that means they have RMP (Resting Membrane Potential)
✓ Although our cells have the same distribution of ions across the cell membrane, they have different resting membrane potentials.
✓ The reason for the last point is the **conductance** (permeability) of the membrane to different ions.
✓ Nernst equation: measure the magnitude of equilibrium potential for a single ion.
$E_x = \pm 61 \times \log [C\ in \backslash C\ out]$
✓ Current: Flow of charges per time unit.
✓ If the RMP is -90 mV, and the change in voltage per unit time is zero (equilibrium), there is outward current of K^+ generating positive charge outside (positive current). Also, there is inward Na^+ current and inward Ca^{++} current generating negative charge outside (we record from outside), and therefore their current is negative current.
✓ Types of Na^+ channels: Fast & Slow.
✓ Na^+ leaky channels are found in the SA nodal cells (**self-excitable cells**) which are found in the heart.
✓ Na^+ channel has its fast gate (M gate), and slow gate (H gate).
✓ m gate is called **activation gate**, while h gate is called **deactivation gate.**
✓ There are gap junctions between cardiac muscle cells, they transmit the action potential from one cell to the adjacent cell.
✓ Hyperkalemia: A situation in which the concentration of K^+ increased outside, this causes the membrane potential to become less negative.

PREFACE

- IF we consider roughly that this figure is for heart.



Mechanical isolator.
(as we studied in anatomy)
NO travel of AP from right to left.

Electrical isolator.
(as we will learn)

Before u start:

-Abbreviations

- AP → Action Potential.
- I → Current.
- SA → Sinoatrial.
- AV → Atrioventricular
- H.R. → Heart rate
- RMP → Resting Membrane Potential

- When the left atrium contracts, the pressure in the left atrium is more then it in the left ventricle, then the valve (that is located between the atrium and the ventricle) will open allowing the blood to move to the left ventricle (**Filling phase**).

- The question is how the atrium contracts ???
Atrium contracts when there is electrical stimulation (Impulse), leads to mechanical response (contraction).

- The contraction of the atrium and the ventricle should NOT be at the same time !!!!
  **What will happen to prevent synchronously contraction of both atrium and ventricle?
  There will be a **delay in the impulse transmission in AV nodal cells which located between atrium and ventricle.
- AV Node is the responsible for the communication between atrium and ventricle.

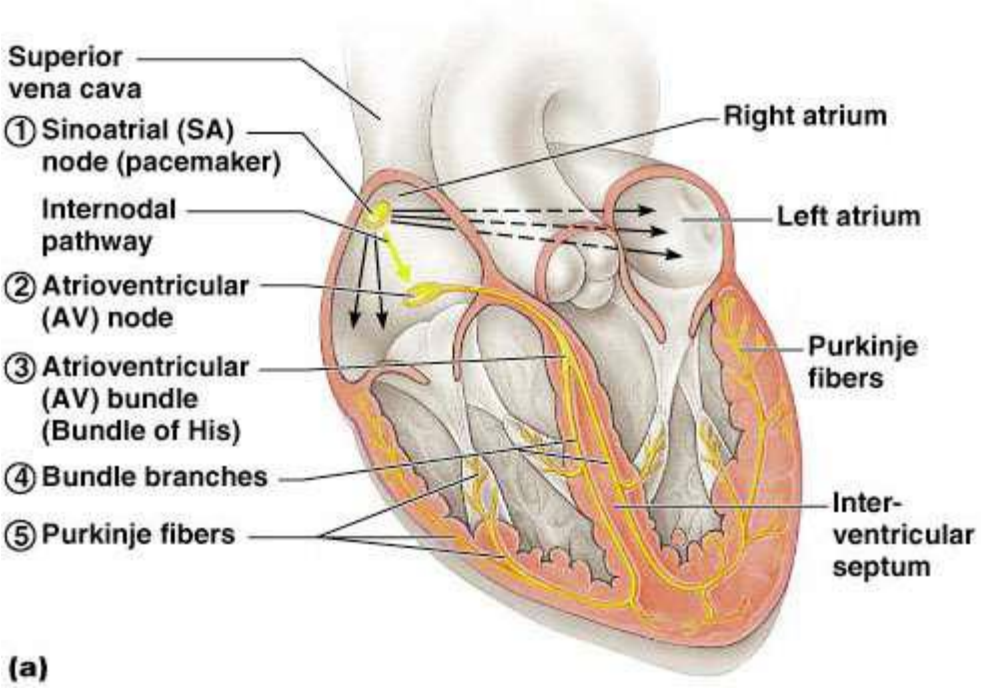
- The impulse transmission in the heart:

SA Nodal cells → AV Nodal cells → Bundle of His → Left & Right branches → Purkinje fibers

Ventricular cells
Not Muscle cells

-NOTE: Bundle of His is also called "AV bundle".

- The figure in the next page represents the plane above.



**We will study each one in details.

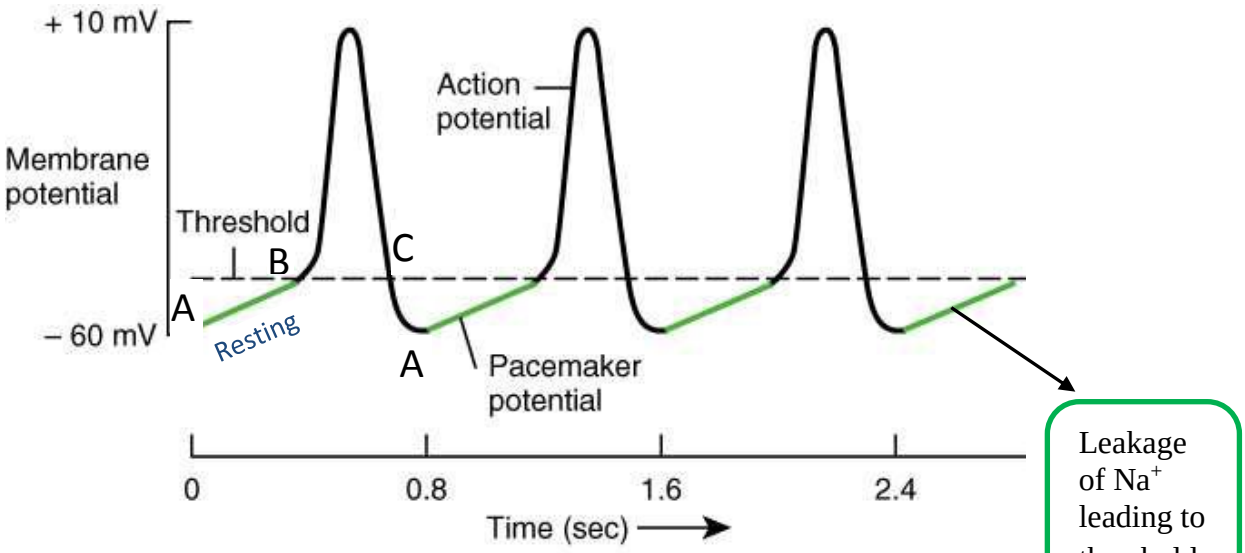
◙ All the cells mentioned (1-5) are **NOT contractile** cells. Instead, they are **conduction** cells.

◙ Although Purkinje cells have actin and myosin filaments, they are NOT contractile cells.

◙ Remember that in 2nd step, the cells will delay the transmission.

SA Node as a Pacemaker

- SA nodal cells are the smallest cells with 3 µm in diameter.
- They do NOT have actin and myosin.
- They have **Na^+ leaky channels** → **Self-excitable** → Bring themselves to threshold.
- Na^+ leaks **inside** because $[Na^+]_o$ = 140 mM ,,,,,, while $[Na^+]_i$ = 14 mM



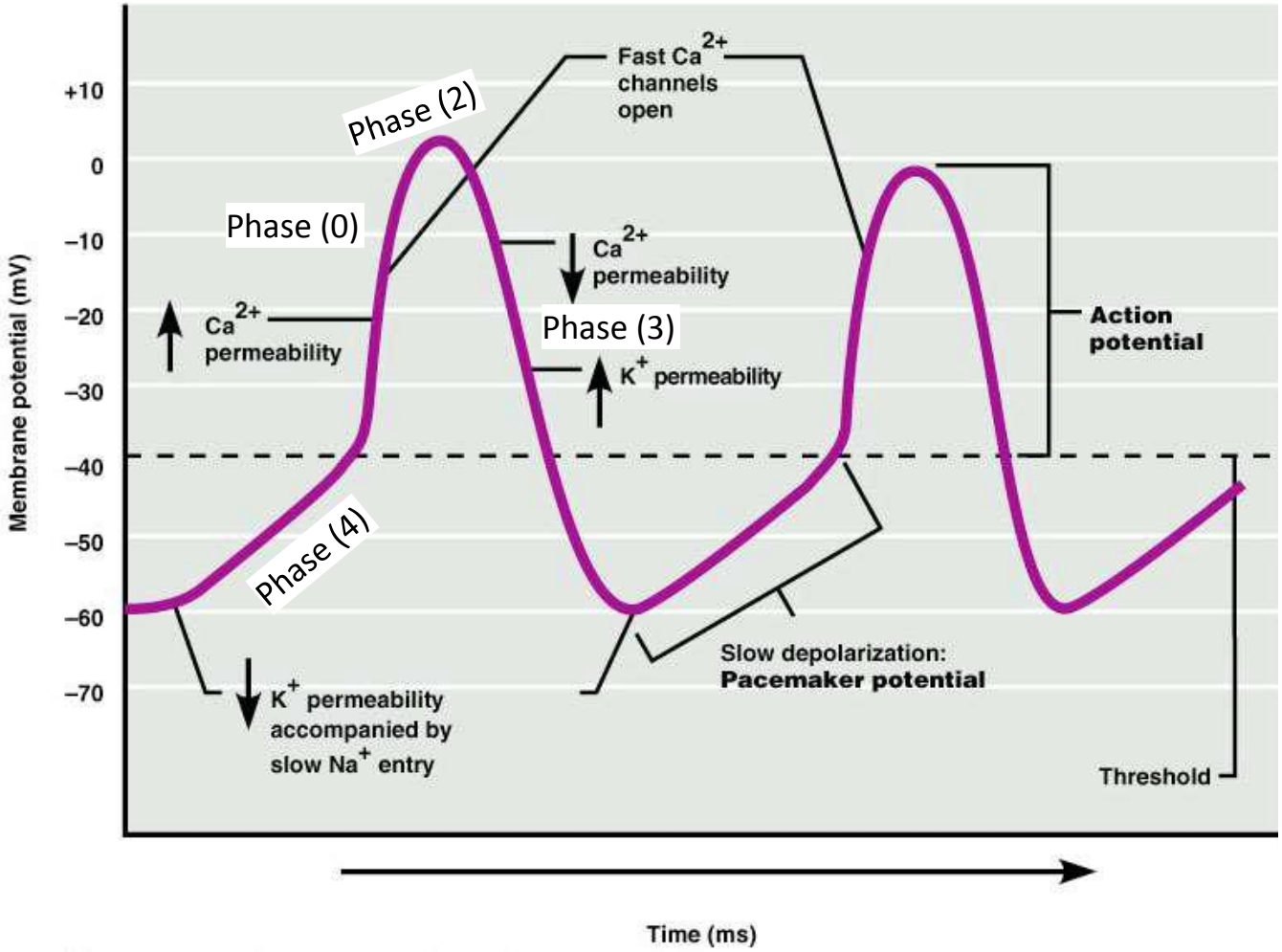
(b) Pacemaker potentials and action potentials in autorhythmic fibers of SA node

20.10b

**About the last figure:

- From A → B >>> 650 msec = 0.65 sec.
- From B → A >>> 150 msec = 0.15 sec.
- So, from A → A >>> 800 msec = **0.8 sec.**
- A → A >>> is a cycle **(One Heart beat)**.
- Normal heart beat (in the presence of SA node) = **75 bpm** (beats per minute).
- SA nodal cells are **<u>Autorhythmic</u>** cells.
- Avg heart rate in the presence of SA Node = 60-100 bpm.

Now, look to the figure below and pay attention to the **phases** and the **permeability of each ion in different phases**.



** Note that there is Not phase (1) !!!!!!!

- Although SA nodal cells are autorhythmic cells, they can be affected by nervous system and endocrine system:

♠ Sympathetic >>> Norepinephrine.

♥ Parasympathetic >>> Acetylcholine (Ach).

*** For details ,,,, see the next page.

♫ We have studied in ANS that sympathetic ANS increases the heart rate, but the question is HOW ??

Norepinephrine makes the SA nodal cells more leakage to Na^+, then it will reach threshold faster, which increases the AP rate. Look at the next example for more explanation.

♪ If you are in fight and flight situation, your sympathetic nervous system will secrete norepinephrine, which leads to increase the leakage of sodium ions in SA nodal cells, and therefore depolarization will be faster to reach the threshold. So, the duration of A⟶B phase (in the last page) will decrease and reach for example 350 msec = 0.35 sec.

● Therefore, 0.35 + 0.15 (B⟶A) = 0.5 sec …… that means 120 bpm ,,, it was 75 bpm !!!!

♫ Also, when we are at rest, parasympathetic nervous system will secrete Ach, which in turn decrease sodium current (permeability).

∫ Normal heart rate (HR) >>> 60-100
- **HR >100 : Tachycardia**.
- **HR <60 : Bradycardia**.

SA Node is called Pacemaker because it's the structure that determines the Pace (rhythm) of the heart (Heart Rate).

-The question that is going on in your mind is:

◙ *What if SA Node can't function because of infection, inflammation, destruction…etc ??*

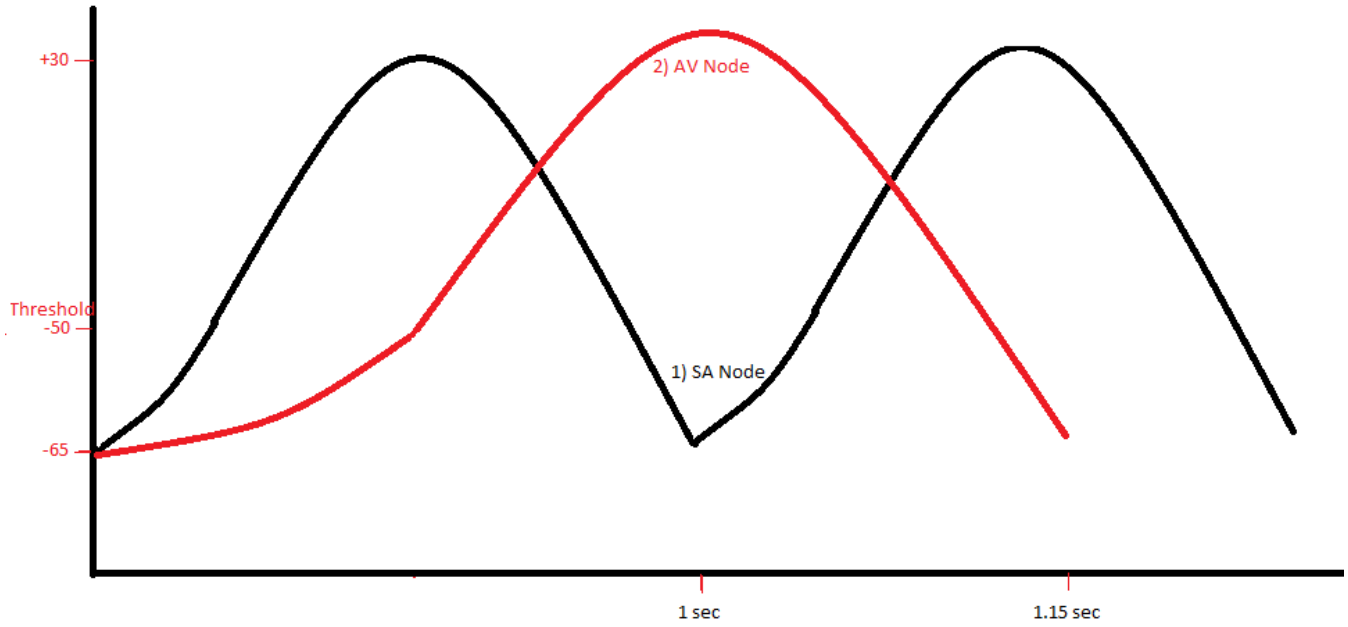
-You can answer this question after studying the following topic. ☺

Latent Pacemakers

●**AV Node** is also leaky to Na^+, but **less leaky** than SA Node → then it takes longer to reach the threshold.
→When SA node is destroyed, AV Node must play its role and become the Pacemaker of the heart.

♠ **When AV Node is the pacemaker then it is called "*Latent Pacemaker*"**

** Latent means hidden.



- You can observe from the figure above that AV Nodal cells need more time to reach threshold than SA Nodal cells do.

- But in the presence of SA Node, action potential is transmitted from SA to AV Node, then **AV Node can NOT express itself as a pacemaker because of the presence of SA Node (Overdriving-Suppression).**

- We said that when AV Node becomes the pacemaker it will take longer to reach threshold, so what is the heart rate now ?? H.R. >>> 40 -60 ,,,,, it was 60-100 !!!!

● Dear doctor ,,, take a look at the title at the top of this page. What did u find ?

Yes, it is latent pacemaker**s**, not only one. What are they ?

Let us travel to the next page to know them,,,

💣 *What if AV Node is destructed (complete AV Block) ??*

● If AV Node is damaged, there will be NO connection between left atrium and left ventricle (Dissociation), so **Purkinje cells** & **bundle of His** will become "**Latent Pacemaker**" → They are leaky to Na+, but **less leaky** than AV Node.

→ So, Atrium will beat as normal (70-80 bpm) because of the presence of SA Node. On the other hand, Ventricle will beat around 20-40 bpm which is Not enough. **(How do we solve this issue**)?

Ans: The medical solution is an **external artificial pacemaker**, connected by wires to the ventricle, and gives impulse every 0.8 second→ Normal Heart Rate is recovered.

● **Inside ventricle**
- → AV bundle cells. (Bundle of His)
- → Left & Right branches of bundle of His.
- → Purkinje cells.

Remember

***Cells next to this box are NOT able to contractile.**
***These cells are leaky to Na^+ but less than SA & AV Node.**
***They are called latent pacemakers**

- Before we switch to a new topic, you have to know two terms:

1) Diastole (relaxation): when the ventricles are relaxed and expanded while refilling with blood returning from the circulatory system (after contraction).

2) Systole: represents the contraction (pumping) (ejection) of ventricles, happens right after Diastole.

☯ SA : Pacemaker.
☯ AV : Latent Pacemaker.
☯ Bundle of His : Latent Pacemaker.
☯ Purkinje : Latent Pacemaker.
☯ **Ventricular cells (Muscle cells):** they aren't leaky to Na+ and suppressed by SA Node then AV Node. Therefore, they will never become the Pacemaker.(**What if all of the mentioned above are ruined??)**

Ans: Ventricular cells must be the Pacemaker and called "**ectopic pacemaker**".
➔ Ectopic pacemaker is life threatening. **WHY?**

1. Normal duration of Systole (contraction) is 0.3 sec, Diastole (filling) is 0.5 sec, and our heart pump 5L/min of blood.
2. When Ventricular cells function: they generate abnormal electrical impulses.

3. Chambers contract in a rapid and unsynchronized way (filling duration is significantly reduced ➔ 0.1 sec for example).

4. The ventricles "**fibrillate**" rather than beat.

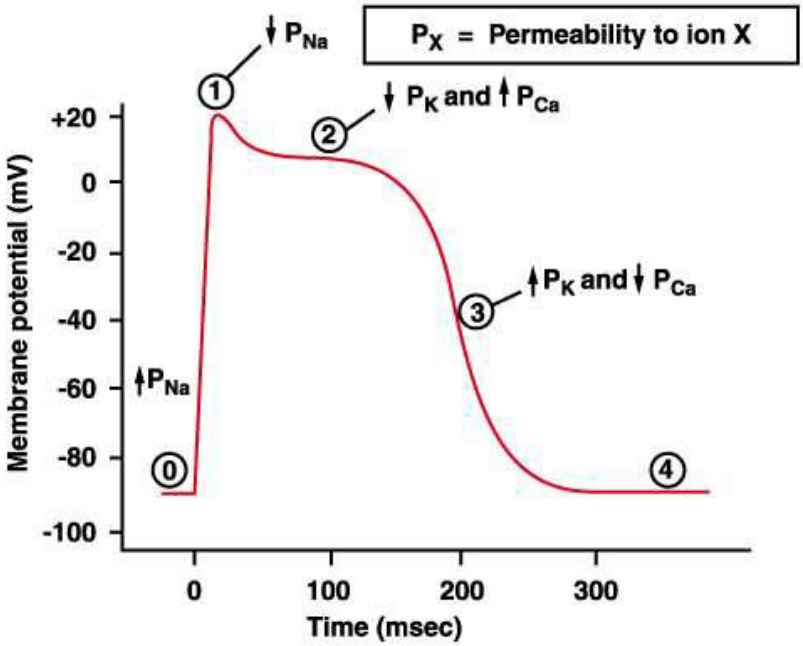
5. No cardiac output (The heart pumps little or no blood, for ex: 0.5-1L/min).

❀This causes "**Ventricular fibrillation**" which leads to **DEATH!**

NOTE: Action Potentials in SA, AV, Atrial cells are ***slow*** response action potential(RMP = -65) see the figure in page 6 ,
While in Ventricle (Muscle cells), it's ***fast*** action potential (RMP = -90) the next topic

Stimulation of ventricular cells

FAST Response AP



Phase	Membrane channels
0	Na^+ channels open
1	Na^+ channels close
2	Ca^{2+} channels open; fast K^+ channels close
3	Ca^{2+} channels close; slow K^+ channels open
4	Resting potential

●NOTES : the last figure :

➔ In phase (4): dv / dt = Zero ,,,, that means $I_{Na+} + I_{K+} + I_{Ca++} + I_{Cl-}$ = Zero ,,,, and that means NO change in membrane potential (RMP) ✓

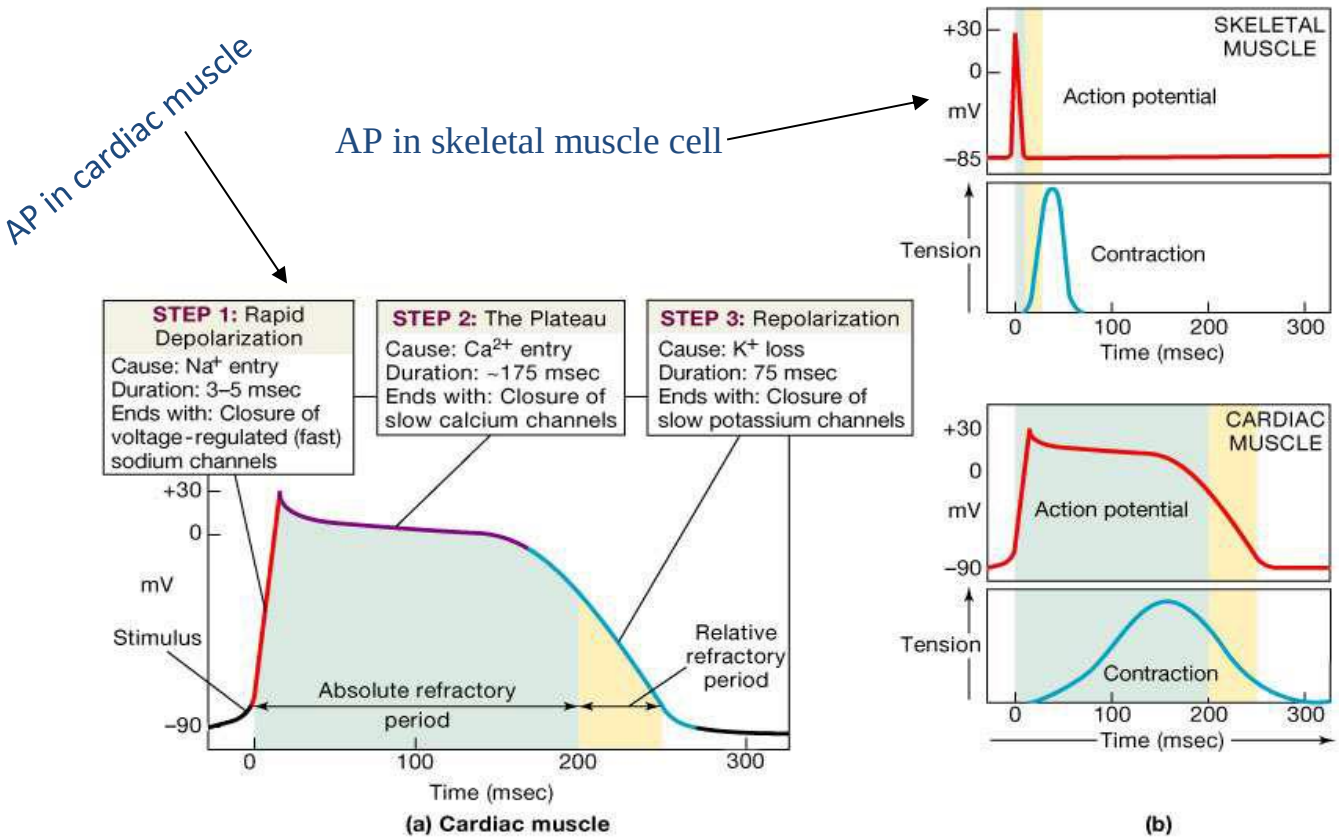
➔ In phase (2) is called **<u>Plateau</u>** (200 msec) : Ca^{++} enters and K^{+} exits. Also, Na^{+} channels are closed inactive. (Refractory period) ➔ we can NOT re-stimulate the cardiac muscle cells.

Wait,, Wait,, Wait,, did u take a break ??
If u don't ,,, please take ,,,, we are about to finish and I need you to pay attention.

NOW, can you remember where are we know ? I will tell you.

♋ SA Nodal cells brought themselves to threshold ➔ they transmit AP to AV Nodal cells and then to bundle of His to reach the two branches and after that to Purkinje cells, ➔ **Purkinje cells stimulate ventricular muscle cells to contract** which the last figure represents. ☺

Overview of the difference between
AP in skeletal & cardiac Muscle cells



Tetanization

■ Cardiac muscle differs markedly from skeletal muscle in the number of ways that are essential for its function. Cardiac muscle cells are connected with each other via low-resistance regions. **This permits excitation of one cell to be easily transmitted to its neighboring cells (the concept of Syncytium=cells together)**.

■ The cardiac muscle action potential is considerably longer than that of skeletal muscle, and the calcium must enter the cell during the action potential for the subsequent contraction to occur. Due to the long action potential, cardiac muscle cannot be ***tetanized.***

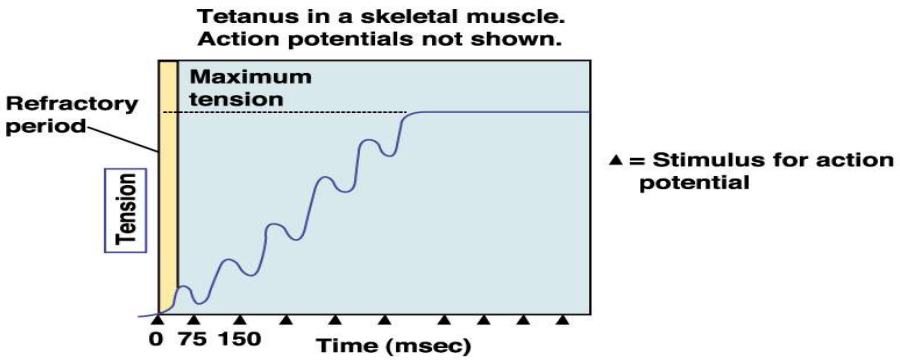
Tetanization: sustained muscle contraction when the motor nerve that innervates a muscle emits action potentials at a very high rate.

➔ In skeletal muscles, action potential occurs every 2 millisecond. Tetanization in skeletal muscles is a sustained contraction without relaxation **(Summation)**

➔ **Summation:** If a skeletal muscle is stimulated and a second stimulus is applied before relaxation is completed, a second contraction which develops a greater tension is fused to the first one. If the stimulus is repeated at a sufficiently high rate, the muscle will not relax between each stimulus but rather will remain in a contracted state.

✓ In Cardiac Muscle, in order to stimulate it again: membrane potential must go back to -90mV. So, when the 2nd stimulus arrives, the muscle is already relaxed →There is **no Summation** of contraction in Cardiac Muscle. Therefore, **no Tetanization** will be presented **in the heart** ➔ And this is **the importance of Plateau.**

➔If Tetanization occurs in the heart, there will be **no relaxation, no filling** ➔**DEATH**.



SUMMARY

♣ SA nodal cells are self-excitable due to Na+ leak channels (it's the site where Action Potential is born).

♣ How does Action Potential arise in the heart?

1. **SA nodal cells** make the Action Potential.
2. This Action Potential is carried to 3 structures: Left Atrium, Right Atrium and **AV Nodal cells** (AtrioVentricular Node).
3. AV Node is a collection of cells that receive this impulse from SA Node and take it down through bundle of fibers (called **Bundle of His**).
4. Bundle of His then **branches left and right**, and goes down to the Apex.
5. Impulse is carried then by **Purkinje cells** to reach **Ventricular Muscle fibers.**

♣ SA Nodal cells are the most leaky to Na^+, SA Node is the pacemaker of the heart.

♣ AV Nodal Cells, Bundle of His, the two branches and the Purkinje cells all are leaky to Na^+ but less than SA Nodal cells >> therefore they are called "Latent Pacemaker"

♣ Ventricular Muscle cells are NOT leaky to Na^+, and if they become pacemaker, they are called "Ectopic pacemaker".

♣ Fast response resting membrane potential = -90mV, while slow response resting membrane potential = -65mV.

♣ **Plateau**: phase (2) in contraction of ventricular muscle cells. >> Ca^{++} channels open \ K^+ channels still open too \ Fast Na+ channels are closed and inactive (refractory period). \ the importance of this phase is to prevent tetanization.

♣ **Tetanization:** is a sustained muscle contraction evoked when the motor nerve that innervates a skeletal muscle emits action potentials at a very high rate. During this state, a motor unit has been maximally stimulated by its motor neuron and remains that way for some time. This occurs when a muscle's motor unit is stimulated by multiple impulses at a sufficiently high frequency. Each stimulus causes a twitch.

QUIZ

Q1 : What do you think will happen if there is an earthquake in your area (about SA Node)

a) Increase the leakage of Na^+.
b) Increase the leakage of K^+.
c) Decrease the leakage of Na^+.
d) Decrease the leakage of K^+.
e) At least, two of the above are correct.

Q2 : Why the SA Node is the pacemaker of the heart ??

a) Because it is leaky to Na^+.
b) Because it is leaky to K^+.
c) Because it is connected to lot of neurons.
d) Because it is autorhythmic.
e) Because it is the most leaky to Na^+.

Q3 : About the heart rate (in the presence of SA Node), which of the following is always true ?? (Pay Attention please) ☺

a) AV Nodal cells determine HR.
b) SA Nodal cells determine HR.
c) It depends on latent pacemakers.
d) HR depends on SANS & PANS.
e) b + d.
f) None of the above.

Q4 : Which of the following is true about SA Node ? (Past Paper Q)

a) Called latent pacemaker.
b) Found in the lungs.
c) Its cells are naturally permeable to Na^+.
d) It is stimulated by CNS.
e) It transmits AP to Purkinje fibers.

THE END