# The Cardio-VASCULAR System

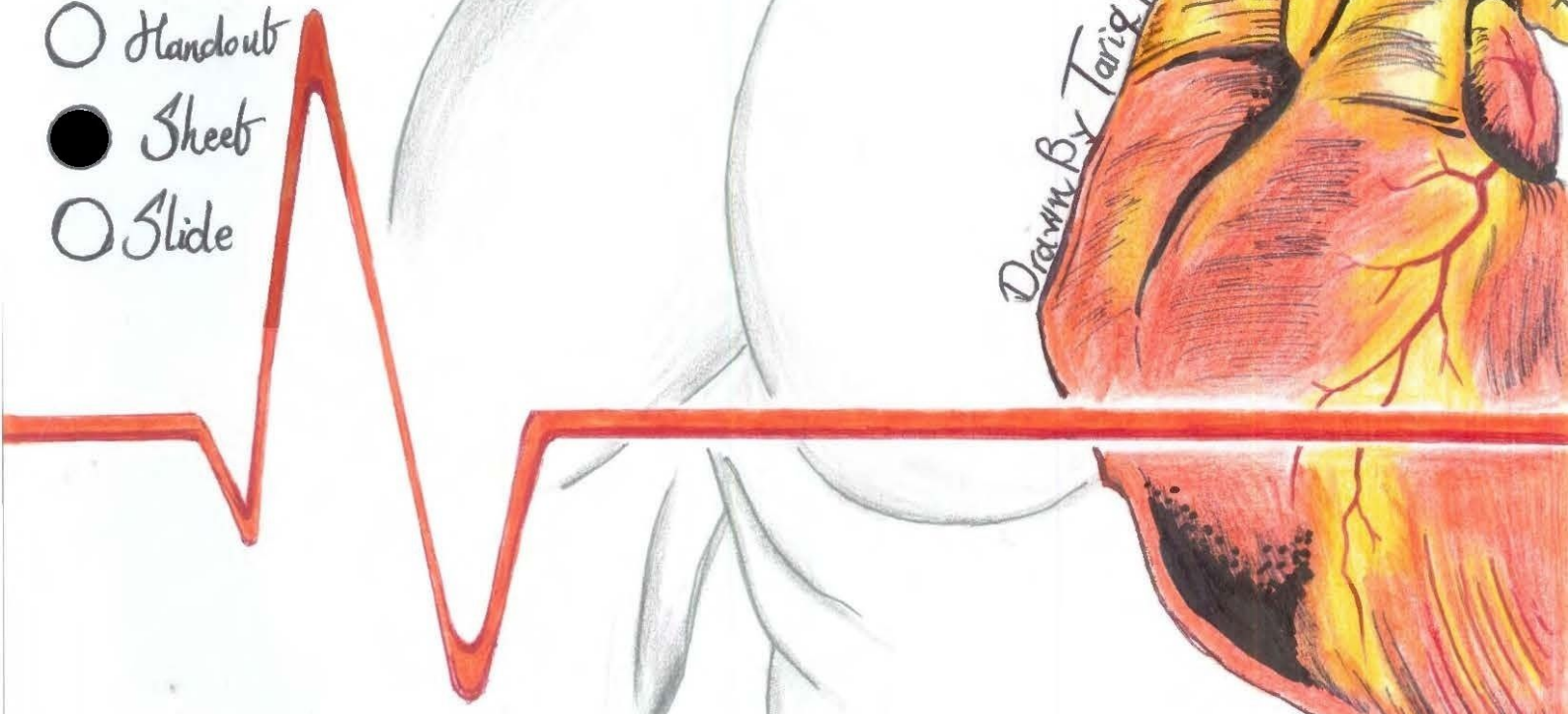
- ○ Anatomy
- ○ Histology
- ○ Pathology
- ○ Pharmacology
- ● Physiology
- ○ Microbiology

Lec #: 3

Dr. Name: Faisal.m

Done By: Ebraheem alabdali

- ○ Handout
- ● Sheet
- ○ Slide



# Length - tension relation & conduction system

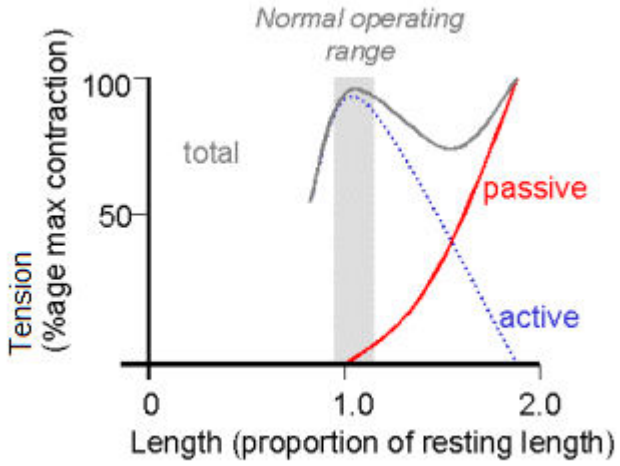
The doctor began the lecture by explaining a couple of points from the previous lecture:

Phospholamban is a SR protein which can be found in two conformations; phosphorylated (active) and dephosphorylated (inactive). Ca-ATPase is also a sarcoplasmic reticulum protein. When Phospholamban is phosphorylated, it stimulates adjacent Ca-ATPase pumps, whereas when dephosphorylated, Phospholamban inhibits Ca-ATPase.

Phospholamban can be phosphorylated by protein kinase A (cAMP-dependant) and Ca/Calmodulin-dependant protein kinase. When the Calcium pump is activated, Calcium will be re-uptaken from the sarcoplasm by the SR faster, going from a sarcoplasmic Calcium concentration of 10*10^-5 to 10*10^-7 (diastole) faster, and shortening the relaxation phase.

## - Length-Tension Relation

- The X axis represent the length of the muscle and the Y axis represent the tension(force of contraction)
- This graph is for skeletal muscles
- Let's define some terms:
  - **Passive tension**: how much the muscle is pulled outward (the tension that's found in the muscle before it contracts)




  - **Active tension**: tension that is actually produced by the contracting muscle (that's what we care about when measuring the contractile force of the muscle)
  - **Total tension**: How much tension develop in the muscle when you stimulated it equals Active and passive tension combined (AT+PT)



Written by Ebraheem Alabdali

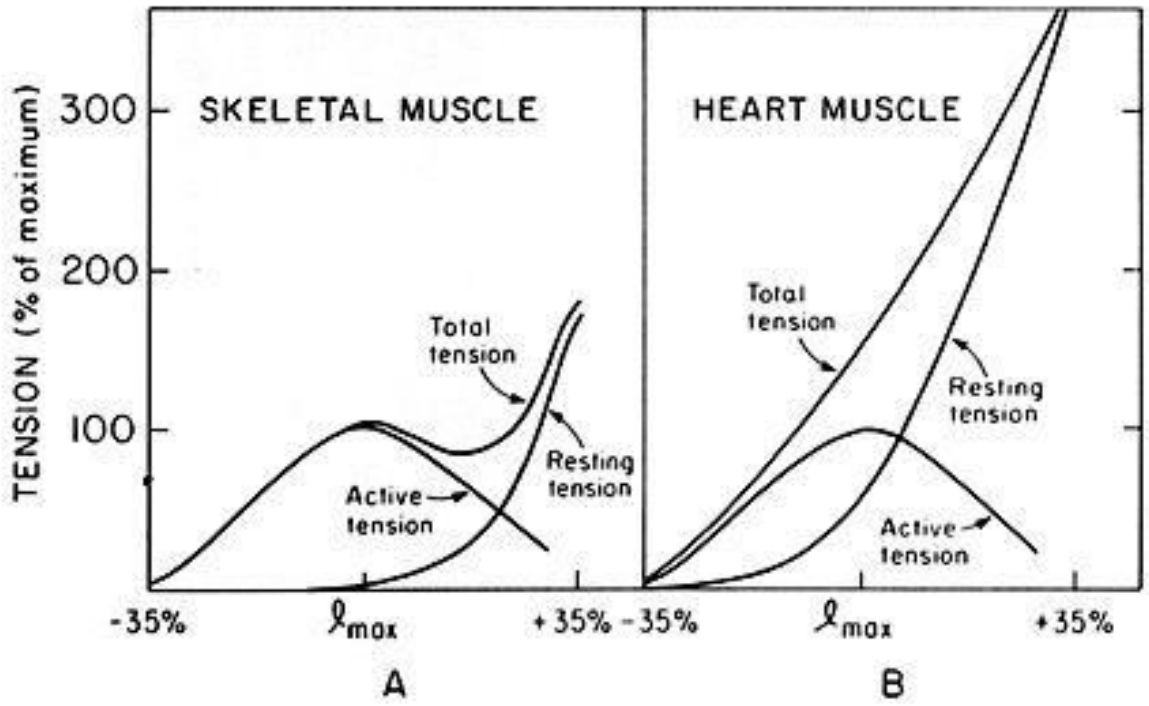
- ✓ The contraction must be inward, so for the muscle to contract it must overcome the passive tension (outward force), and if there's tension (force) left >>> the muscle will contract.

- We can measure the passive tension and the total tension, but we can't measure the active tension but we can calculate it

**Active tension = Total tension – passive tension**

- Note that active tension falls away linearly with increasing length

- So the **maximum contraction( maximum active tension)** will happen when the muscle is at **optimum length**
  - But when we stretch the muscle too much (passive tension is too much) the contraction force will decrease
  - And when under-stretching the muscle, the contraction force (active tension) will decrease



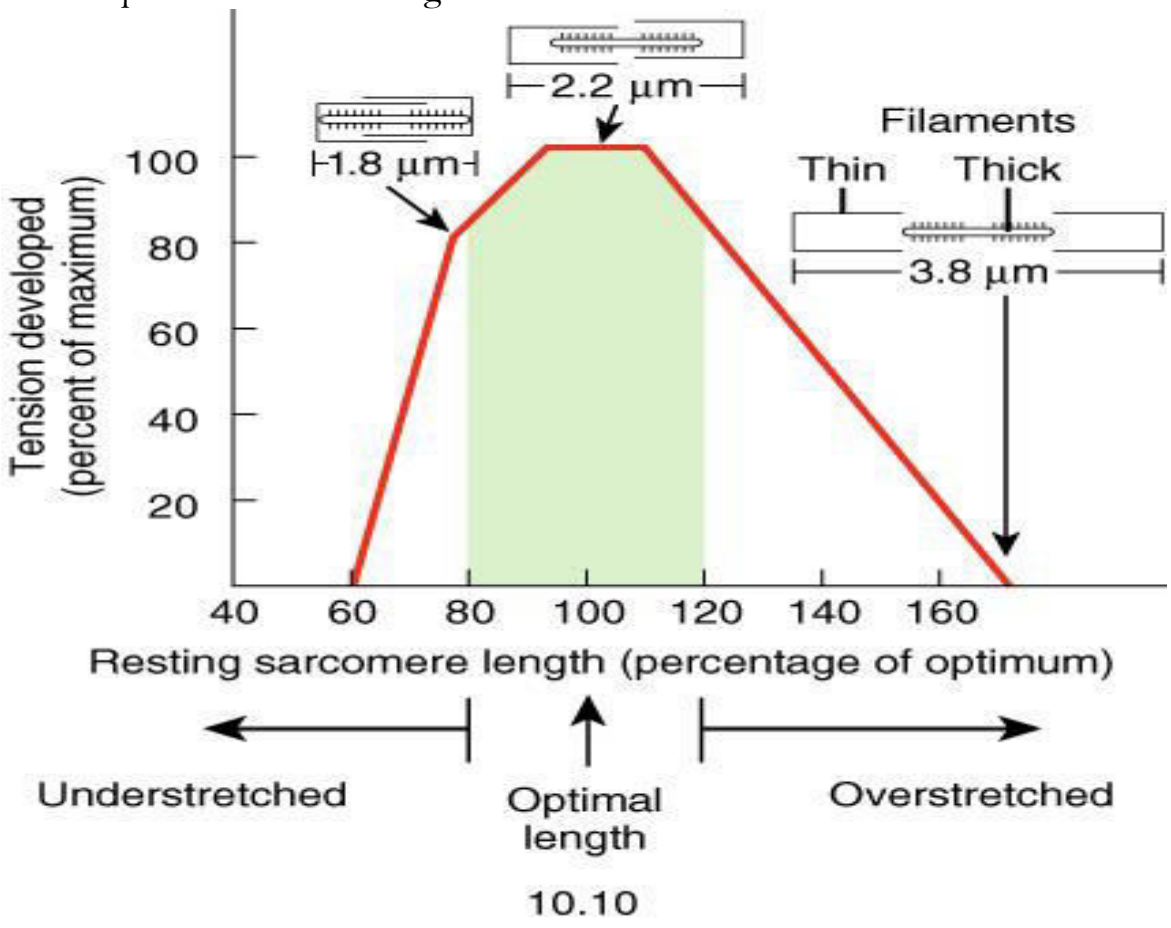

  - The difference between the cardiac and skeletal is explained by the skeletal muscle having **elastic** elements

- At the level of the **sarcomere**: Picture in the next page

- Notice when there's overstretching: the actin and myosin are far from each other (not enough myosin heads available for interaction with action filaments)
- When there's under-stretching: there's too much overlapping (myosin heads at the ends not available)
- In the optimum level: there's perfect matching between myosin and actin

✓ The line represent the active tension which can reach to zero if the muscle is over or under stretched

✓ The total tension when the muscle is over stretched is high (TT = passive + active), because although active tension = zero, the passive tension is high

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❖ In the cardiac muscle this is defined by **Frank-starling law**

➢ **Within physiological limits, an increase in the resting length of the heart muscle (passive tension), increases tension {force} of contraction (Active tension).**

- Physiologic limits that's mean until we reached the optimum length of the fiber (sarcomere) which is around 2 micrometer.

- Skeletal muscle usually works at its optimum level so if you increase the passive tension the force of contraction will decrease

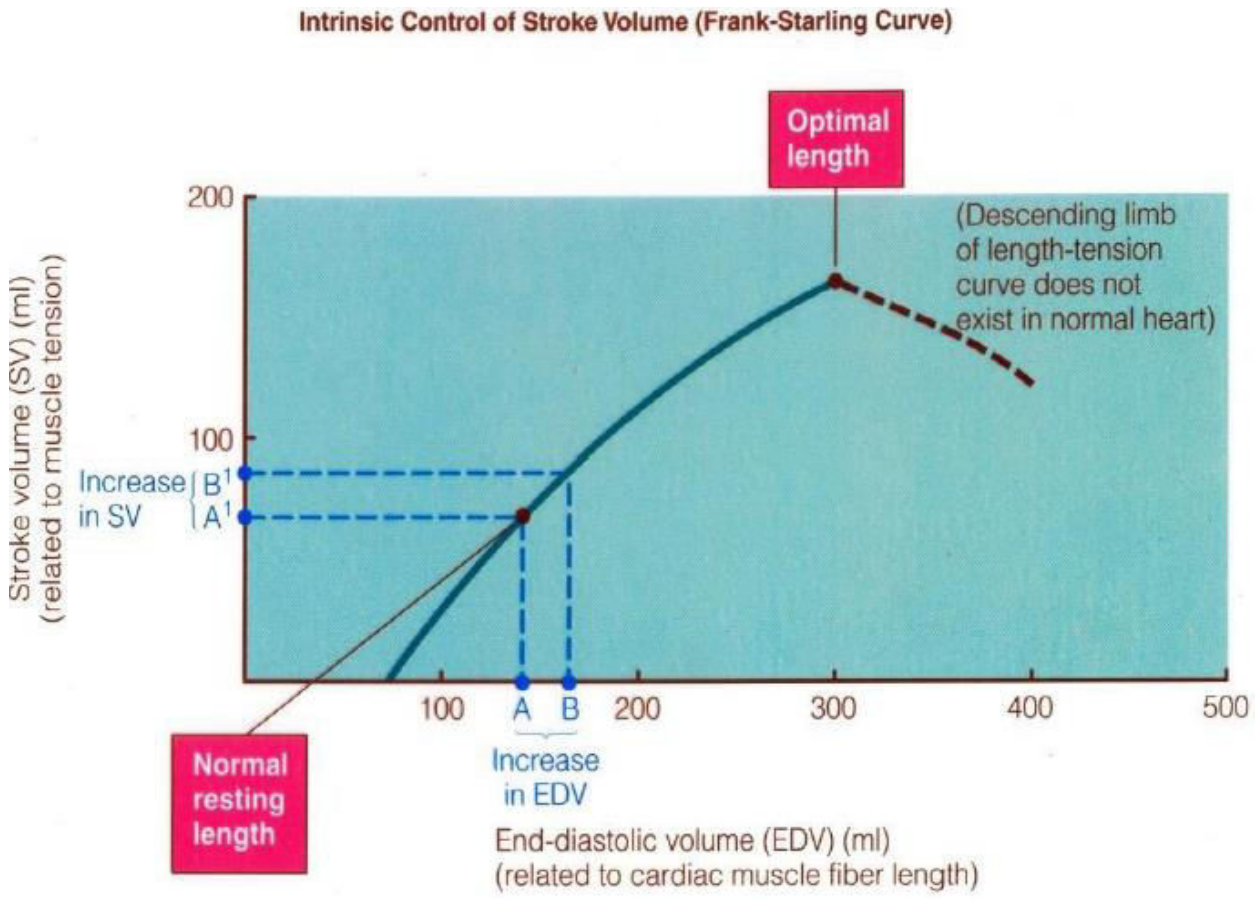
- But for the cardiac muscle, it work at less than its optimum levels so if you increase the length of the cardiac muscle you will increase the force of contraction

- **How you will increase the length of the cardiac muscle?**

  **<u>By increasing the volume of the blood in the heart</u>**

- In the ventricle for example: When you increase the volume before the muscle contracts you are increasing the length of the muscle
  - ✓ this volume is called **end diastolic volume (EDV)**

- So the end diastolic volume is proportional to passive tension (or end diastolic pressure)



- In this picture:
  - **End diastolic volume(EDV):** is the amount of blood present in the ventricle prior to contraction, and represents the length (passive tension)
  - **Stroke volume(SV):** represent the force of contraction (active tension)
  - Whenever you **increase the EDV there is increase in the stroke volume (that will increase the Cardiac output CO=SV*Heart rate)**
  - This is true until we reach the optimum length(volume) after that any increase in length(volume) >>> the stroke volume decreases
    - ✓ And this is heart failure which means the heart fails to pump the blood it receives (its' input 300ml … output 200ml)

# – Conduction system

- If we place skeletal muscle in a solution that contains Ca+ no contraction will occur ( because it needs external stimulation by neurons)
- If we placed the heart in a solution that contains Ca+ it will keep on contracting
  - Before the contraction happens, an electrical event (action potential) has to occur
  - This indicates that there must be an **intrinsic** source of action potential in the heart since when we transport the heart outside the body in this solution, there are no neural connections.
- The calcium will enter through Ca+ channel and cause calcium induced calcium release and contraction will occur
- The solution is called ringer's solution

❖ From that, we conclude that the heart has an **intrinsic** system responsible for Action Potentials called: ***The conduction system of the heart.***

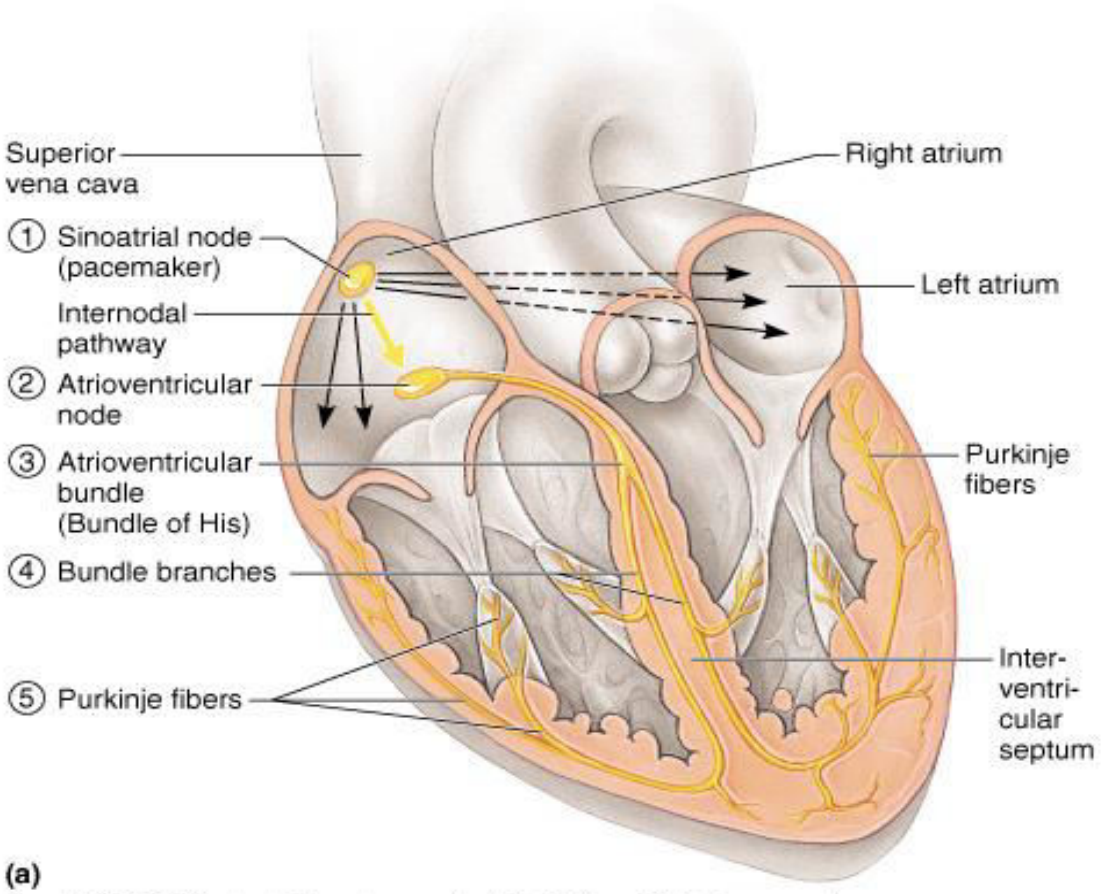
- It consists of a group modified cardiac cells (not nerves)

## ❖ Structures of the conduction system

1. **SA node**: located in the posterior wall of the right atrium.
2. **AV node**: located between the atria and the ventricles, it in the fibrous septum that separates the atrium from the ventricle.
3. **AV bundle**: (bundle of His) branch in the interventricular septum to left and right
4. **Right and left bundle branches**:
5. **Purkinje fibers**: The bundle branches end as Purkinje fibers, they run sub-endocardialy, and supply 2 thirds of the ventricular muscles

❖ They differ in their ability to produce impulses *at **different rates***:

1. **SA node:** is able to produce impulses at the rate of **70-80** impulse/min.
2. **AV node:** is able to produce impulses at the rate of **40-60** impulse/min.
3. **Purkinje fibers:** are able to produce **15-40** impulse/min.



- Since the **SA node** has the highest rate of impulse production, it's the **pacemaker** of the heart (sets the rate{speed} for the whole heart)

  - ✓ We can think of it as a train that consists of three carts, each having its own motor and speed, the first cart has the highest spend and the last one is the slowest, if all carts work normally; the speed of the train is the speed of the fastest one, which is the SA node. If the SA node is destroyed or damaged the heart rate will follow the AV node's rate.

- IF Anything other than the SA node work as a pacemaker then it's called **ectopic pacemaker** (ectopic = abnormal place).

- The **autonomic nervous system with** its branches; sympathetic and parasympathetic, supply all parts of the heart:

  1. **Sympathetic:** Atria, SA node and AV node, AV bundle and ventricles (**all heart**). It affects all parts of the heart atria and ventricles.

     - ✓ From the cardiac plexus

  2. **Parasympathetic:** Atria, SA node and AV node. Very little or no supply to the ventricles, it doesn't affect the ventricular function (only affects electrical parts and contractile parts of the atria)

     - ✓ From vagus (10th cranial) nerve.

- The cardiac muscles are of two types:

a) **Cardiac muscle proper** or the contractile muscle fibers.

b) **Auto rhythmic cells;** the cells that produce the impulses, they constitute about 1% of the total cardiac muscle fibers, they are very important, (they form the structures of the conduction system).

- The sequence in which the impulse is conducted:

**SA >>> AV >>> Bundle >>> Branches >>> Purkinje fibers**

- **Pathway of Heartbeat**
  1. Begins in the **sinoatrial (S-A) node**
     - Internodal pathway to atrioventricular (A-V) node??

- ✓ Some people believe that there are internodal pathway between the SA node and the AV node are the ones to transmit the impulses between them.
- ✓ Others, including the doctor, believe that the impulse from the SA node reaches the AV node through the atrial muscles and not through internodal fibers.

2. Impulse delayed **in A-V node(allows atria to contract before ventricles)**

   • Most delay is in A-V node
   Delay AV node---0.09 sec.
   Delay AV bundle--0.04 sec.

3. **A-V bundle** takes impulse into ventricles

   - Normally one-way conduction through the bundles, Only conducting path between atria and ventricles is A-V node - A-V bundle
   - Because of the absolute refractory period

4. **Left and right bundles of Purkinje fibers** take impulses to all parts of ventricles

   - Transmission time between A-V bundles and last of ventricular fibers is 0.06 second (QRS time)

- ✓ **AV Block/Heart Block:** Even if the SA node is intact but the AV node is destroyed, In other words: there is NO connection between the SA node and the purkinje fibers, so the ventricles will work at the rate of purkinje fibers. In this case the rate will be between 15-40 impulse/min.

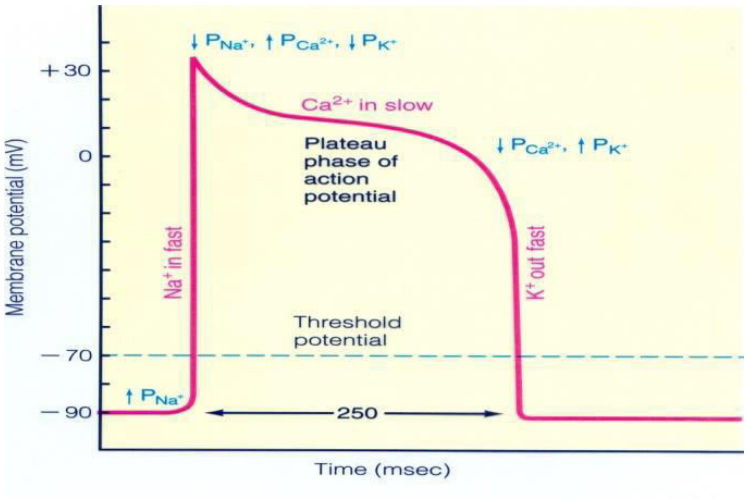
- In the conduction system component: There is a difference between the **intrinsic rate** (how much AP they can make per min) and their **conduction speed** (how much the impulse need to pass through them)
- Atrial and ventricular muscles conduction speed 0.3-0.5 m/s
- AV node 0.05 m/s the slowest

- Purkinji fibers has the fastest speed of conduction (wide diameter , less resistance, faster conduction):
  - many gap junctions at intercalated disks
  - This is to make sure that the impulses are conducted through to all parts of the ventricles at the same time, and this ensures that all the cells of the ventricles will contract as one unit and makes them an effective pump.
  - This is called **synchronous conduction**
  - This is essential for the normal function of the heart.
  - ✓ If conduction is not synchronous : ventricular fibrillation = death

❖ **How does the conductive system intrinsically produce impulses (intrinsically active)?**

- **What is the mechanism?**

- This diagram represents the AP of the **<u>contractile muscle proper</u>** <u>(not the conduction system)</u>




- We said the conducting system cells(**autorhythmic cardiac cells)** are **specialized cardiac cells**; there specialization in terms of:

A. Anatomy:
- They are rounded, except the Purkinje fibers.
- They lack/ very little contractile muscle fibers -unable to contract.

B. Function:
- They are leaky to Na+. Not through voltage gated channels, instead, the membrane contains leaky Na+ Channels.

**SO:**

- During phase 4 for **<u>contractile muscle proper</u>**: membrane potential returns to -90.

- **BUT** in **autorhythmic cardiac cells;** <u>since these cells are Leaky to Na+:</u>

- There is Na influx during **Phase 4**, and the resting membrane potential will never reach -90
- It will be less negative: -60 or -65.
- During Phase 4, the membrane potential is depolarizing: therefore it is called the ***slow*** **depolarization phase.** As Na+ enters until the threshold is reached slowly.

- This gives enough time for the *slow inactivation gate*s to *close before the fast activation gates open.* Therefore, Sodium will not enter.

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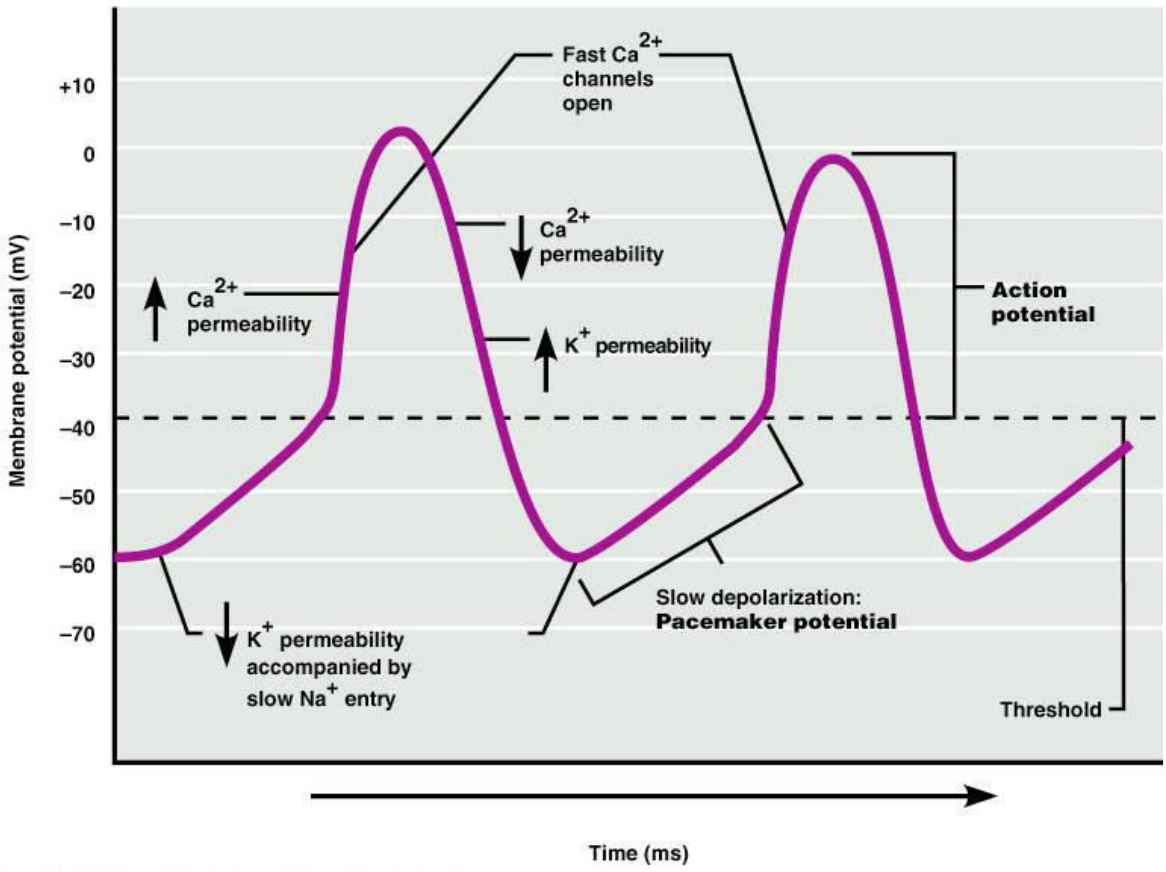
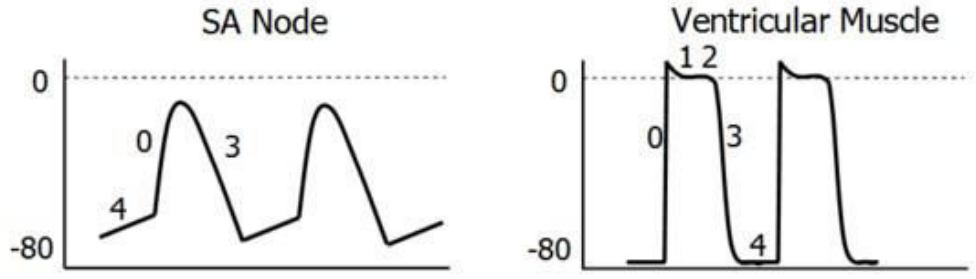



The threshold for the Na channels is the same as that of the Ca channels, therefore, when the threshold is reached, the slow Ca2+ channels open>>>Ca2+ influx

– Rapid depolarization. This is **Phase 0**. (There is influx of Ca2+ but there is no Na+; because the Na+ channels are closed.)

- There is no phase 1 and no plateau.



- Phase 3 is due to the efflux of K+

- **Phase 4:** slow depolarization phase (Na+ leakage), **Phase 0**: due to Ca2+ influx, **Phase 3**: K+ efflux

– This kind of response (phases 4, 0, 3) is called **the slow response action potential** or pacemaker potential.

– The impulse is automatic, as long as Na keeps leaking inside there will be an AP, and it is rhythmic.

- This action potential is autorythmic, produced by the SA node

- The (SA, AV, purkinji) differ in their rates of producing impulses, and this is due to the differences in their leakiness to Sodium:

–The SA node is **more leaky** *to Na*+ than the AV node, and both of them are **more leaky to** *Na*+ than the purkinje.

–At Phase 4/ slow depolarization: the angle of this depolarization is the **slope**. The steeper the slope >>>the higher the heart rate & the less steep the slope >>>the lower the heart rate.

- The slope for the SA node is higher than the AV node which is **higher** than the slope for the Purkinje fibers.

– How can we increase the slope >>> when I give a drug that increases Na+ leakiness

❖ Speeds of conduction
- SA node: Slow
- Ventricular and Atrial muscle: Moderate
- AV node: Slowest
- Purkinje fibers: Fastest

## – Extrinsic Innervation of the Heart

- **Inotropic = contractility**
- **Chronotropic = heart rate**
- **Dromotropic = speed of conduction**

- **Sympathetic**:
  - Release both **Epinephrine and Norepinephrine**>>>increase the permeability of cardiac cells to Na+ and Ca2+ and decreases the permeability to K+.
  - By increasing Ca permeability, it increases the intracellular Ca2+ >>>increase the contractility/ the force of contraction **+ve Inotropic effect.**
  - **+ve Chronotropic Effect**.
  - **+ve Dromotropic Effect**

- **Parasympathetic**: release **Ach**>>> increases the permeability of cells to K+ and decreases it to Na+ and Ca2+.
  - **-ve chronotropic**
  - **-ve dromotropic Effect**
  - **No effect on inotropic** (doesn't supply the ventricles )

❖ **Normal: 75 bpm**

❖ **parasympathetic**
- **resting potential more -ve (effect on K+)**
- **slope slow (Na+, Ca+ effect)**
- **rate 40bpm**

❖ **sympathetic**
- **slope is higher**
- **HR 120 bpm**

✓ **What's not affected is the maximum potential because AP is All or None.**