Cardiac Muscle Physiology

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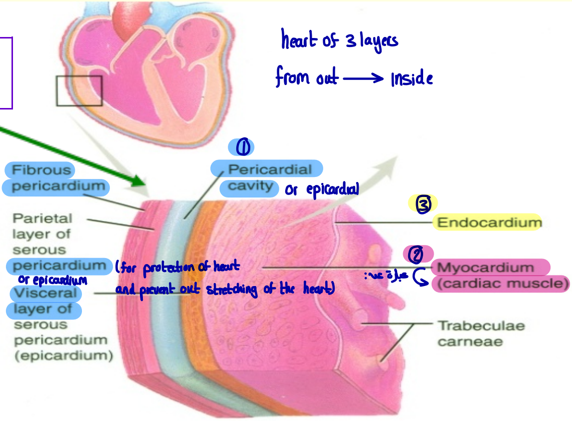
Objectives:

By The end of this lecture students should be able to:

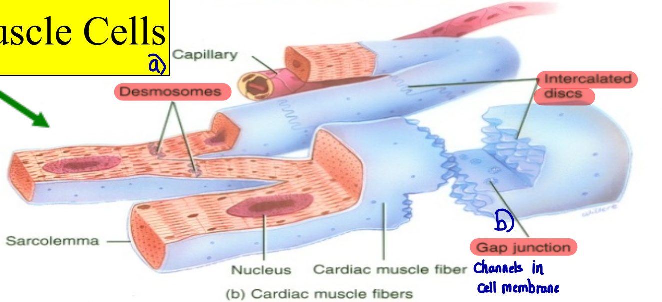
- Distinguish the cardiac muscle cell microstructure
- Describe cardiac muscle action potential
- Point out the functional importance of the action potential
- Outline the intracellular calcium homeostasis

Wall of the heart



(a) Portion of pericardium and heart wall

Cardiac Muscle Cells



(b) Cardiac muscle fibers

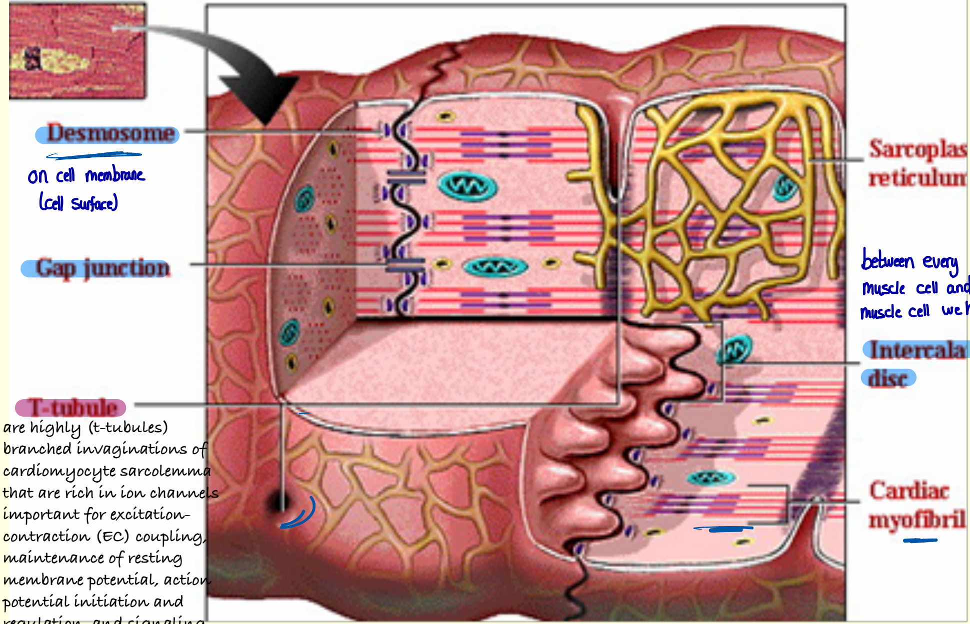
Layers of the Heart Wall

- ① Epicardium (external layer)…prevent the heart from overstretching as we will see later when we discuss Frank-Starling law of the heart.
  - Visceral layer of serous pericardium
  - Smooth, slippery texture to outermost surface
- ② Myocardium
  - 95% of heart is cardiac muscle
- ③ Endocardium (inner layer)
  - Smooth lining for chambers of heart, valves and continuous with lining of large blood vessels

Cardiac Muscle Tissue and the Cardiac Conduction System

- Histology
  - Shorter and less circular than skeletal muscle fibers
  - Branching gives "stair-step" appearance
  - Usually, one centrally located nucleus
  - Ends of fibers connected by intercalated discs
  - Discs contain desmosomes (hold fibers together) and gap junctions (allow action potential conduction from one fiber to the next) → **syncytium** [the atrium بتقبضوا مع بعض / the ventricle بتقبضوا مع بعض] الـ heart بس ينقبض بتقبض كوحدة واحدة
  - Mitochondria are larger and more numerous than skeletal muscle
  - Same arrangement of actin and myosin because of the contraction

MAGNIFIED VIEW OF CARDIAC MUSCLE CELLS



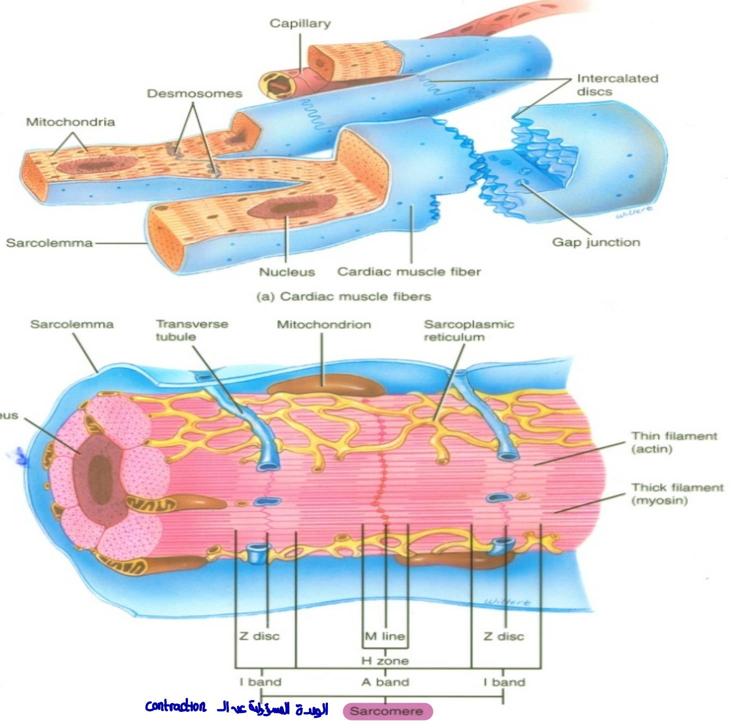
Desmosome: on cell membrane (cell surface)

between every muscle cell and muscle cell we have: Intercalated disc

T-tubule: are highly (t-tubules) branched invaginations of cardiomyocyte sarcolemma that are rich in ion channels important for excitation-contraction (EC) coupling, maintenance of resting membrane potential, action potential initiation and regulation, and signaling transduction

Cardiac muscle, like skeletal muscle, is striated. Unlike skeletal muscle, its fibers are shorter, they branch, and they have only one (usually centrally located) .nucleus

Cardiac muscle cells connect to and communicate with neighboring cells through gap junctions in .intercalated discs



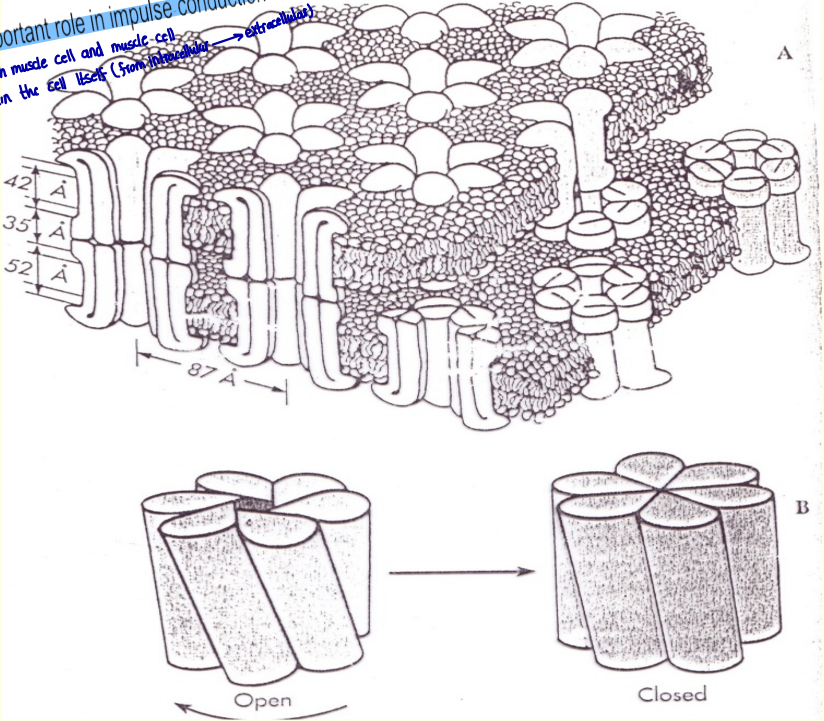
(a) Cardiac muscle fibers

(b) Diagram based on an electron micrograph

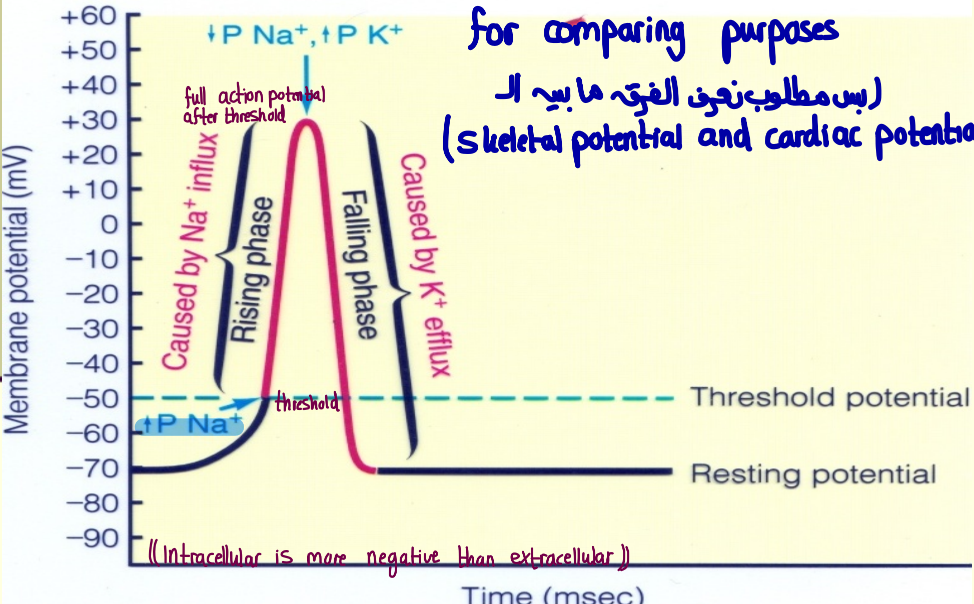
Gap junction channels

play an important role in impulse conduction

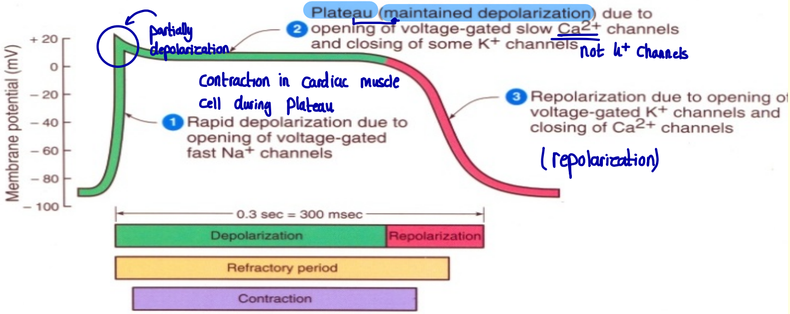
between each muscle cell and muscle cell and within the cell itself (from intracellular ⟶ extracellular)



Permeability Changes and Ionic Fluxes During an Action Potential (skeletal Muscle)



Cardiac muscle potential



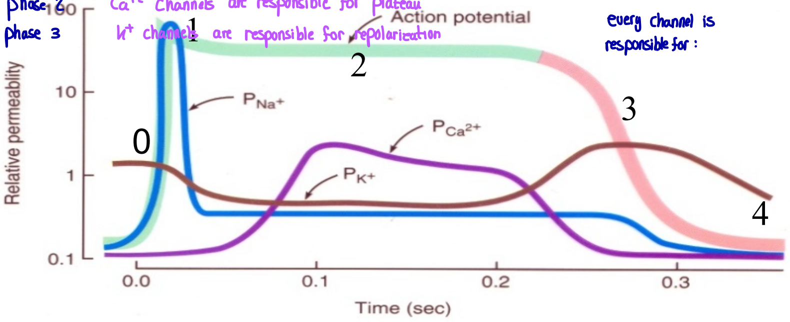
(a) Action potential, refractory period, and contraction

phase 0+1 — Na^+ channels are responsible for depolarization in these phases (0+1)

phase 2 — Ca^{+2} channels are responsible for plateau

phase 3 — K^+ channels are responsible for repolarization

every channel is responsible for :



(b) Membrane permeability (P) changes

The Action Potential in Skeletal and Cardiac Muscle

2 kinds of refractory periods

absolute — relative

In skeletal : short

In cardiac: long

In skeletal muscle: Contraction happens after action potential (قبل ما يخلص ال repolarization بشوي)

In cardiac muscle: the contraction will take place during (plateau)

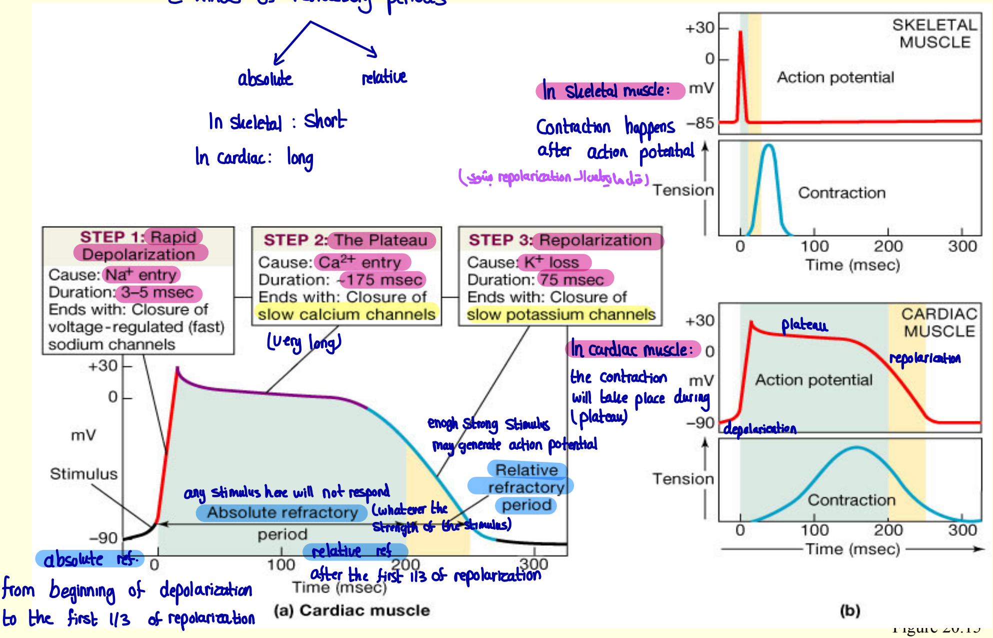
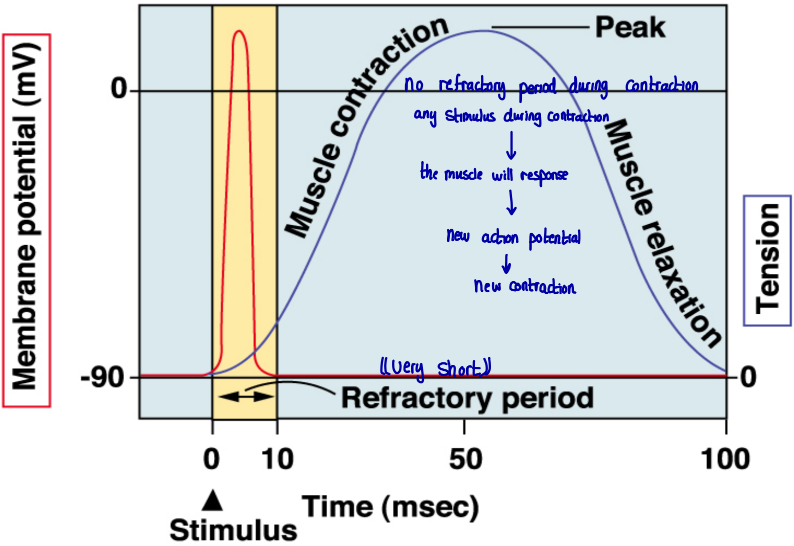
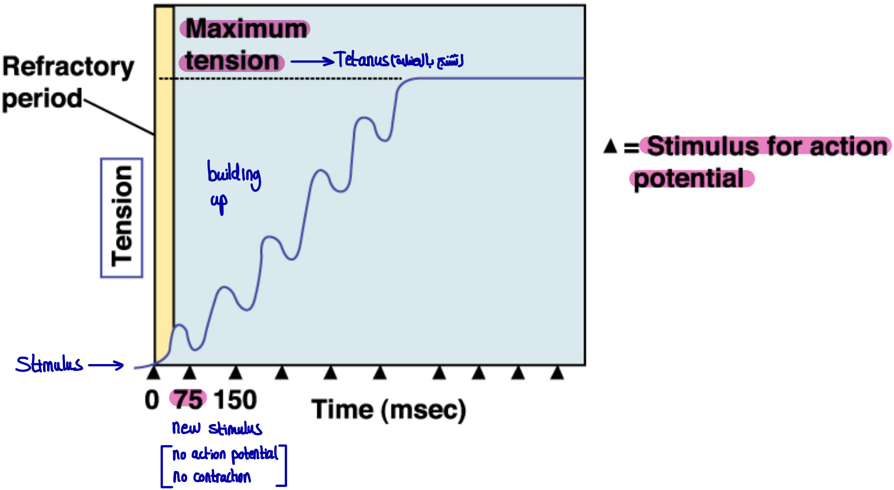


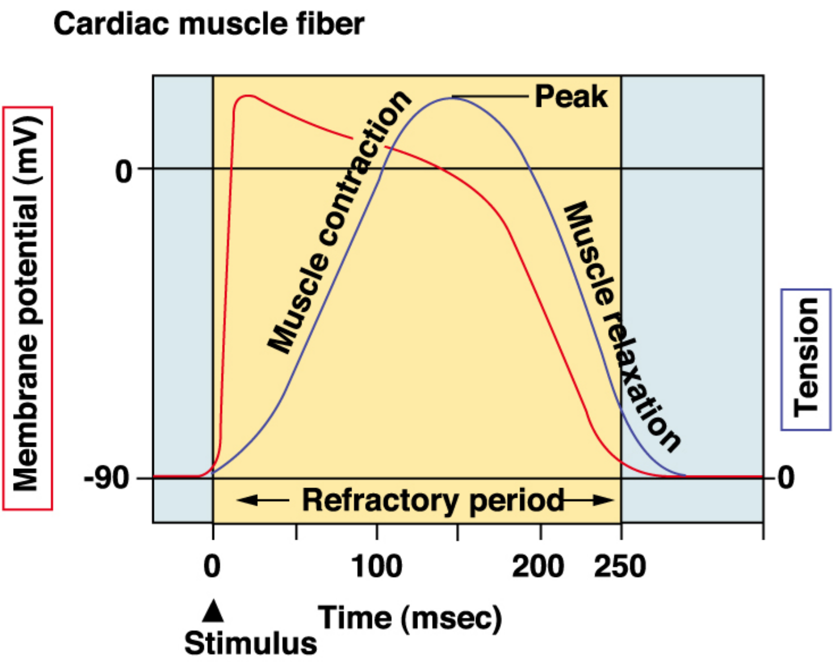
Figure 20.15

Skeletal muscle fast-twitch fiber



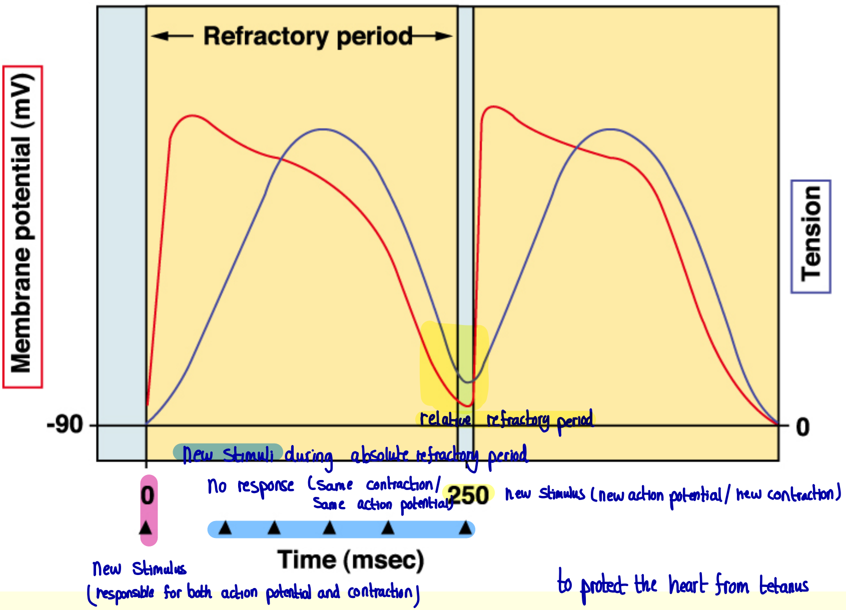
Tetanus in a skeletal muscle.
Action potentials not shown.





Cardiac muscle fiber
Membrane potential (mV)
0
-90
Peak
Muscle contraction
Muscle relaxation
Tension
0
Refractory period
0
100
200
250
Stimulus
Time (msec)

Long refractory period in a cardiac muscle prevents tetanus.



to protect the heart from tetanus

Cardiac and Skeletal Muscles

Differences

Skeletal muscle

- Neurogenic neuromuscular Junction (motor neuron-end plate-acetylcholine)
- Insulated from each other
- Short action potential

Contraction after action potential

tetanus is possible

Cardiac Muscle

- Myogenic (action potential originates within the muscle)
- Gap-junctions and Intercalated disc
- Action potential is longer

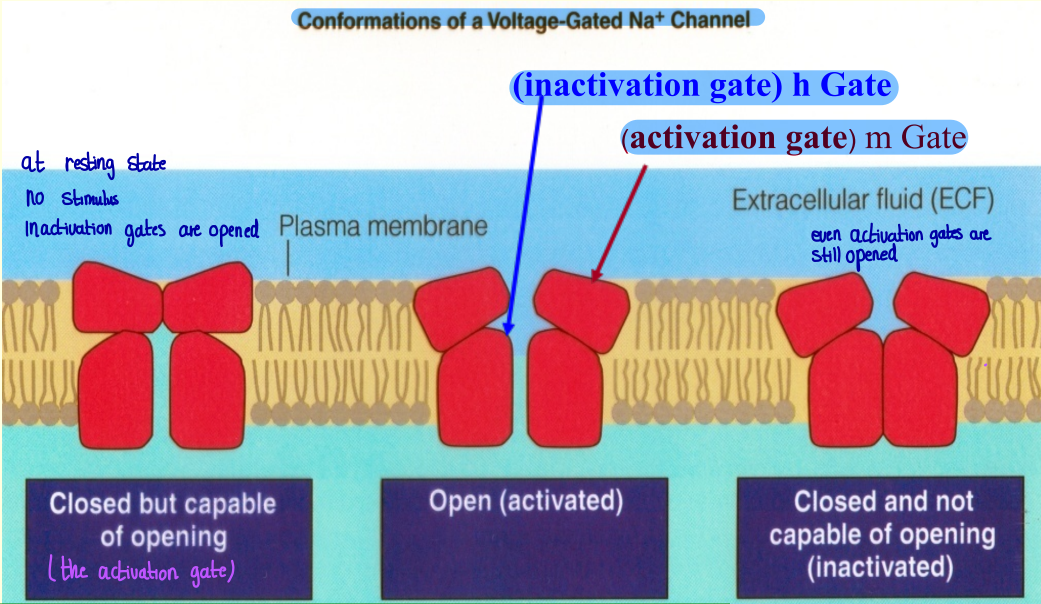
refractory period longer

Contraction during action potential

no possible tetanus

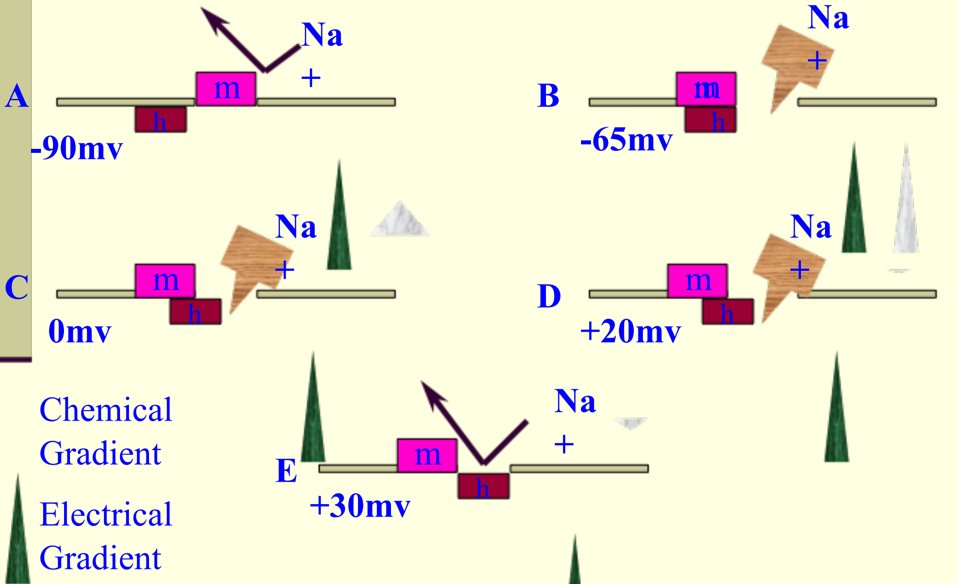
Functional importance of Cardiac action potential

- The decrease in conductance (permeability) of potassium at phase 0 and 1 of the cardiac action potential contributes to the maintenance of depolarization in phase 2 (plateau)
- The long absolute refractory period prevent the occurrence of tetanus (maintained contraction without a period of relaxation) in the cardiac muscle.
- Skeletal muscle action potential is short that allows tetanus to occur

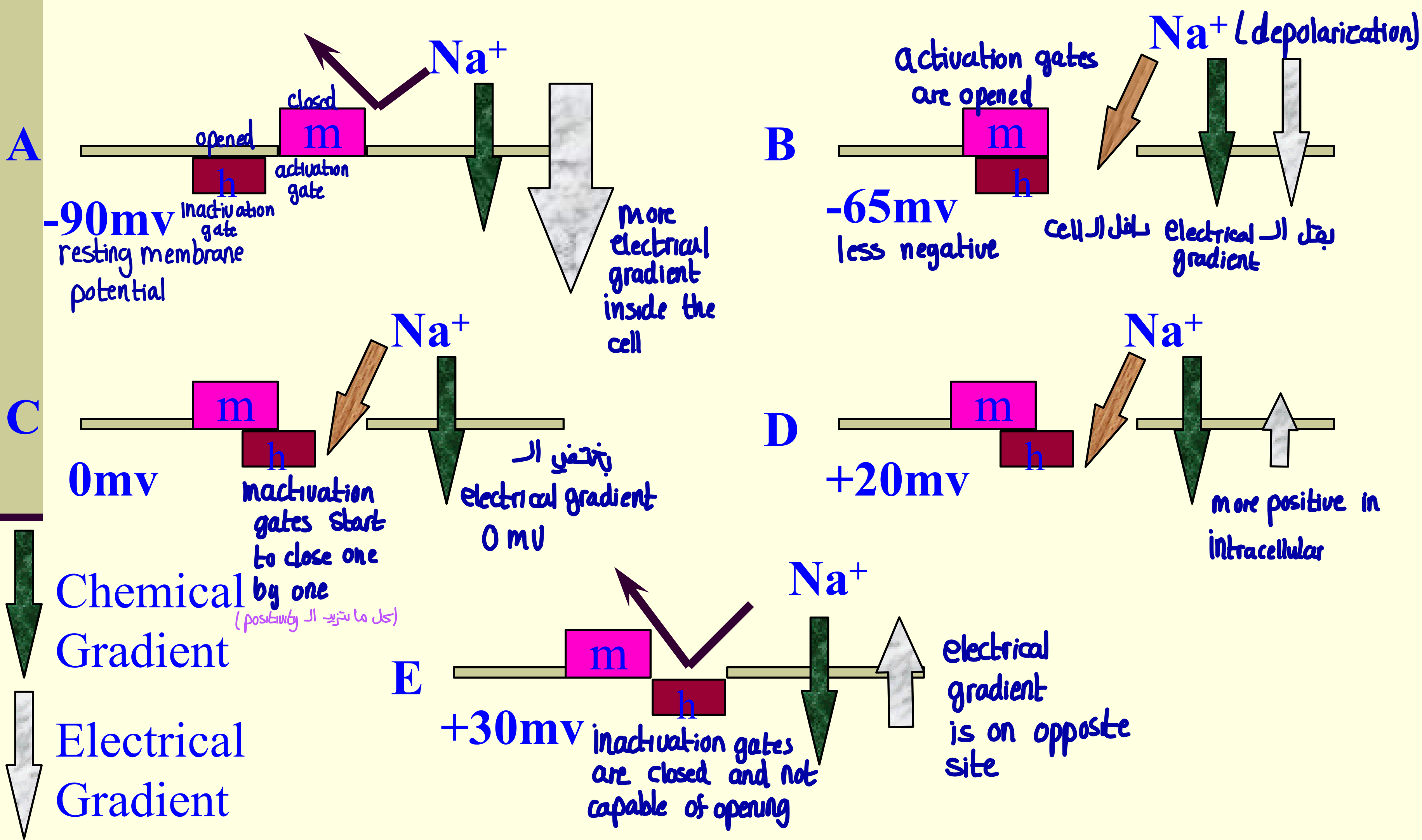


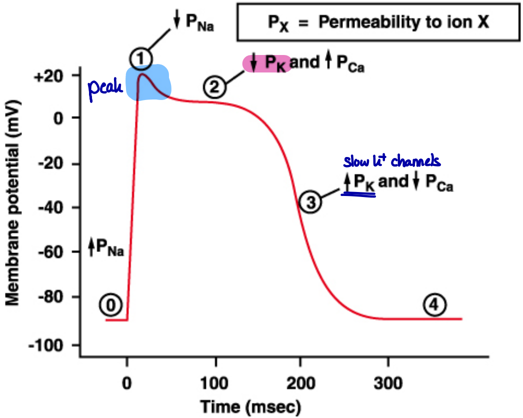
Activation gates open when the membrane potential becomes less negative and the inactivation gates close when the potential becomes less negative. The activation gate is fast but the inactivation is slow responding

PHASE 0 OF THE FAST FIBER ACTION POTENTIAL



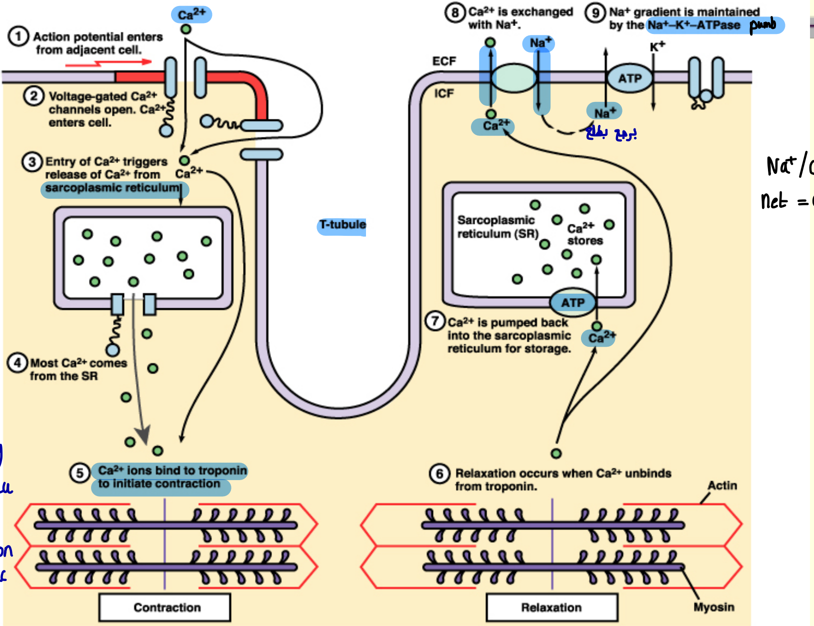
PHASE 0 OF THE FAST FIBER ACTION POTENTIAL





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

The importance of calcium influx through the slow voltage gated calcium channels

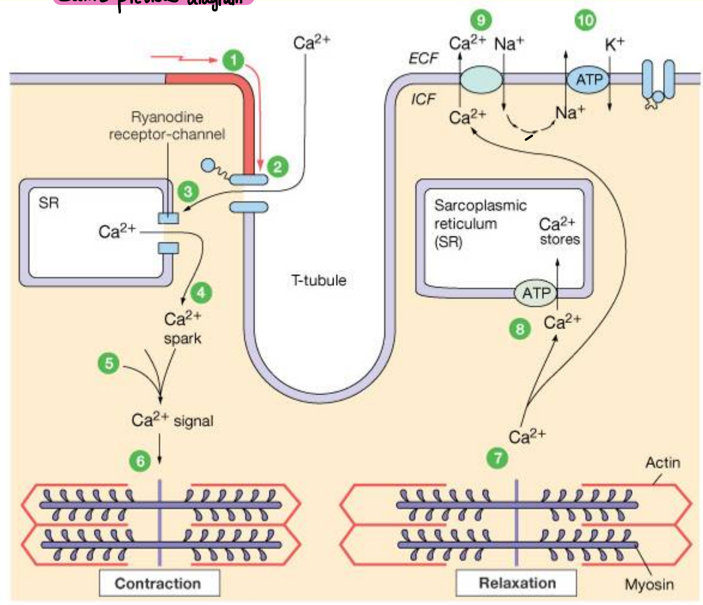


Na^+/Ca^{+2}
net = 0

during plateau
↓
contraction of cardiac muscle

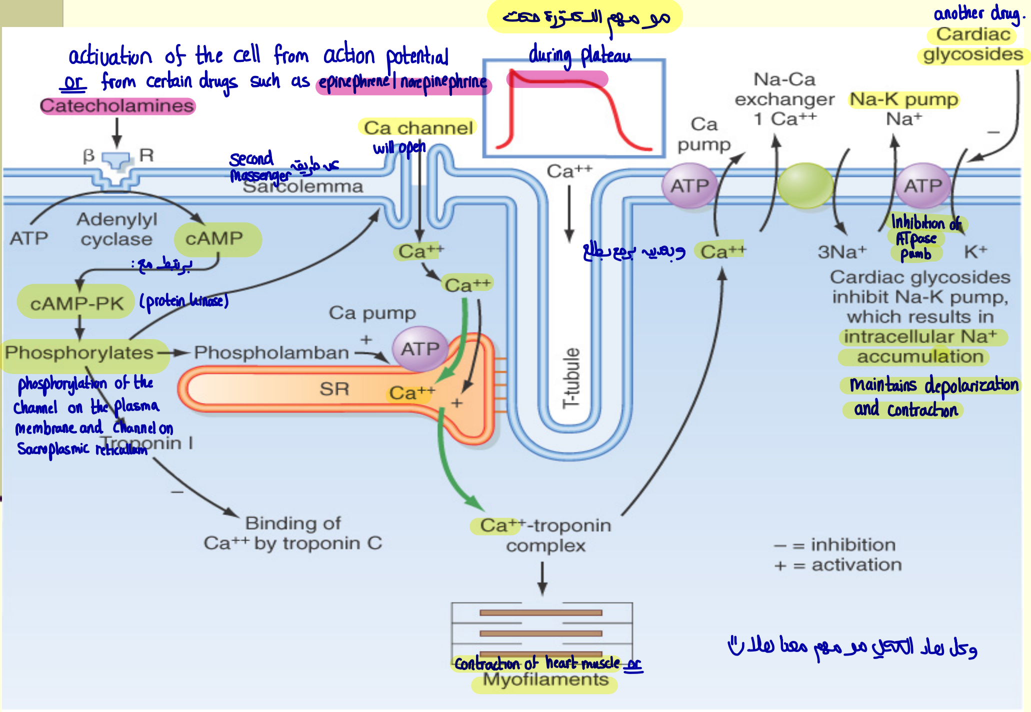
Mechanism of Cardiac Muscle Excitation, Contraction & Relaxation

Same previous diagram

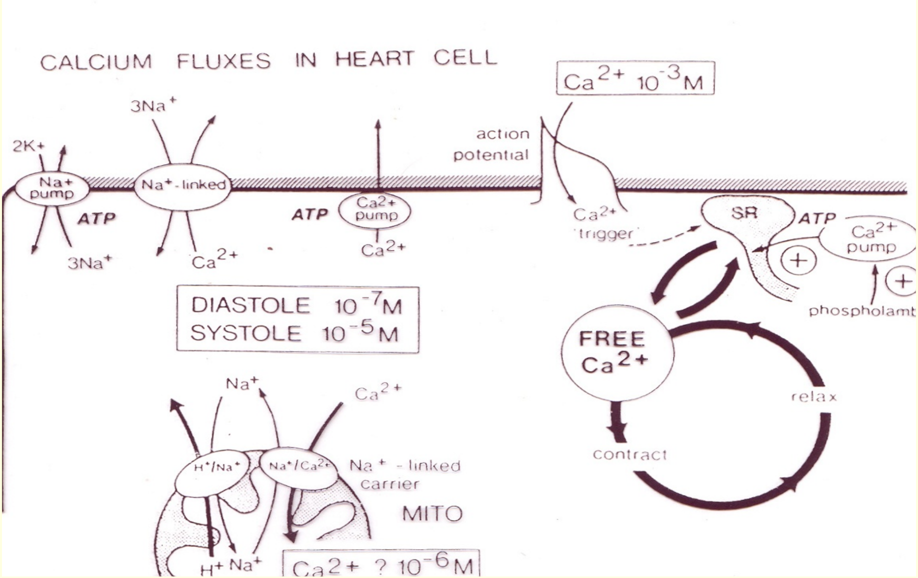


1. Action potential enters from adjacent cell.
2. Voltage-gated Ca^{2+} channels open. Ca^{2+} enters cell.
3. Ca^{2+} induces Ca^{2+} release through ryanodine receptor-channels (RyR).
4. Local release causes Ca^{2+} spark.
5. Summed Ca^{2+} sparks create a Ca^{2+} signal.
6. Ca^{2+} ions bind to troponin to initiate contraction.
7. Relaxation occurs when Ca^{2+} unbinds from troponin.
8. Ca^{2+} is pumped back into the sarcoplasmic reticulum for storage.
9. Ca^{2+} is exchanged with Na^+.
10. Na^+ gradient is maintained by the Na^+-K^+-ATPase.

Intracellular Calcium Homeostasis…1



Intracellular Calcium Homeostasis…2



Cardiac Muscle action potential Vs. Skeletal Muscle (summary)

- Phase 0 –Depolarization phase (Na+ opening influx) Skeletal and cardiac muscle
- Phase 1 partial repolarization (Not in skeletal) before the plateau in the cardiac (after the peak)
- Phase 2 Plateau (~ depolarization not in skeletal) in cardiac muscle slow calcium channels
- Phase 3 fast repolarization phase (K+ repolarization()
- Phase 4 resting membrane potential

both in skeletal and cardiac

Note: action potential in skeletal in general is shorter than the action potential of cardiac

Thank You

Conduction System of the Heart

before the action potential get to the contractile fibers how doesn't generate and how it propagate

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Objectives

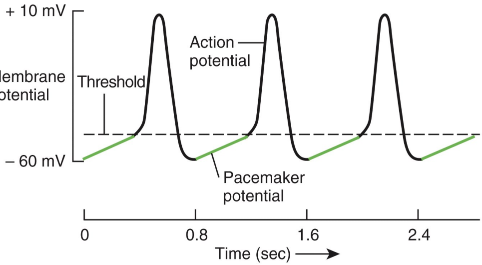
- List the parts that comprise the conduction system
- Explain the mechanism of slow response action potential (pacemaker potential)
- Point out the regulation of the conduction system potential by Autonomic Nerves

Autorhythmicity (the heart is pumping by itself from a conduction)

It is pumping without going back to CNS

- During embryonic development, about 1% of all of the muscle cells of the heart form a network or pathway called the **cardiac conduction system.** before the action potential arrives to contractile fibers (atrium and ventricle)
- This specialized group of **myocytes** is unusual in that they have the ability to spontaneously depolarize.

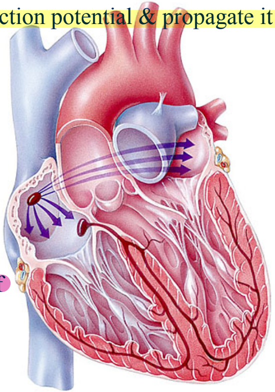
responsible for generating and conduction of action potential in the heart muscle itself



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

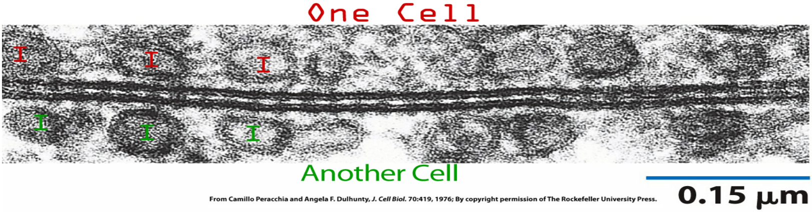
Autorhythmicity

- The rhythmical electrical activity they produce is called **autorhythmicity**. (conduction system that makes the action potential & propagate it)
- It does not rely on the central nervous system to sustain a lifelong heartbeat.
  - How did they know? Simple massage of the heart
    ↓ chest compression during (CPR)
  - During open heart surgery the heart will start pumping by itself



Autorhythmicity

- Autorhythmic cells spontaneously depolarize at a given rate, some groups faster, some groups slower.
- Once a group of autorhythmic cells reaches threshold and starts an action potential (AP), all of the cells in that area of the heart also depolarize.



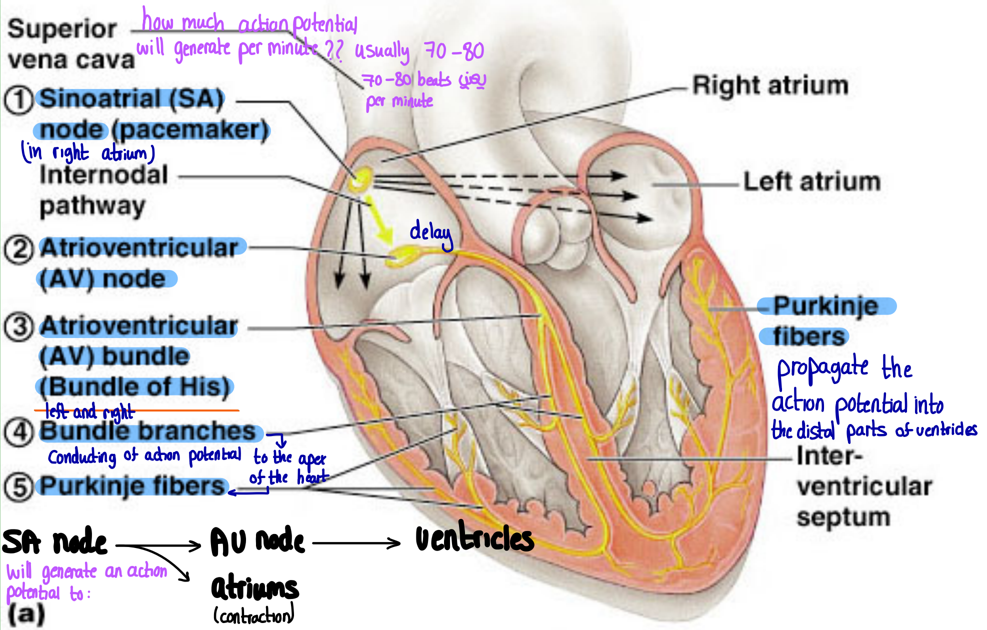
Membrane of two cells clearly seen. The spread of ions through gap junctions of the Intercalated discs (I) allows the AP to pass from cell to cell

and desmosome

Autorhythmic Fibers

- Specialized cardiac muscle fibers
- Self-excitable
- Repeatedly generate action potentials that trigger heart contractions
- 2 important functions
  - Act as pacemaker (generator of action potential)
  - Form conduction system (for the propagation of the action)

Conducting System of Heart



Intrinsic Cardiac Conduction System

Approximately 1% of cardiac muscle cells are autorhythmic rather than contractile

70-80/min

(SA node)Action potential or beats

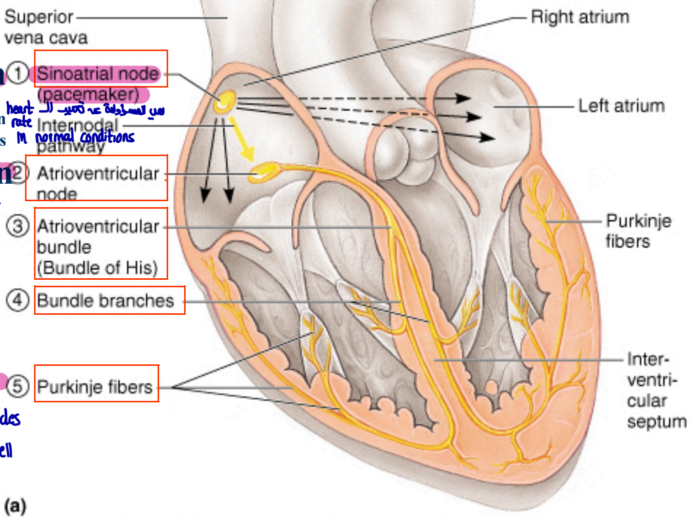
هي المسؤولة عن تحديد الـ heart rate in normal conditions

40-60/min

If SA node wasn't functioning

15-40/min

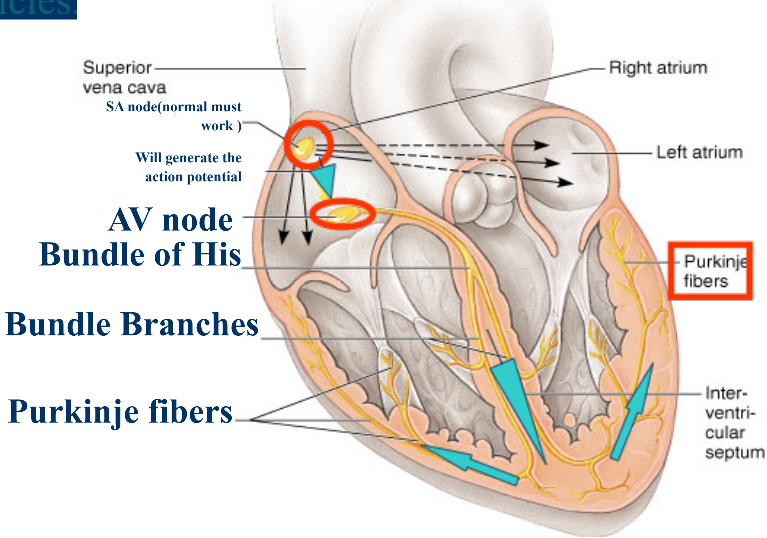
If both SA/AV nodes weren't functioning well



Approximately 1% of the cardiac muscle cells are autorhythmic rather than contractile. * These specialized cardiac cells don't contract but are specialized to initiate and conduct impulses through the heart to coordinate its activity. * These constitute the intrinsic cardiac conduction system.
These autorhythmic cells constitute the following components of the :intrinsic conduction system
the sinoatrial (SA) node, just inferior to the entrance of the superior vena * ,cava into the right atrium
the atrioventricular node (AV) node, located just above the tricuspid valve * ,in the lower part of the right atrium
the atrioventricular bundle (bundle of HIS), located in the lower part of * the interatrial septum and which extends into the interventricular septum where it splits into right and left bundle branches * which continue toward the apex of the heart and the purkinje fibers * which branch off of the bundle branches to complete the pathway into the apex of the heart and turn upward to carry conduction impulses to the papillary muscles and the .rest of the myocardium
Although all of these are autorhythmic, they have different rates of depolarization. * For instance, the SA node * depolarizes at a rate of 75/ min. * The AV node depolarizes at a rate of 40 to 60 beats per minute, * while the rest have an intrinsic rate of around 30 depolarizations/ minute. * Because the SA node has the fastest rate, it serves as the pacemaker for the * .heart

Intrinsic Conduction System

Function: initiate & distribute impulses so heart depolarizes & contracts in orderly manner from atria to ventricles.



As indicated previously, the function of the intrinsic conduction system is to initiate and distribute impulses, so the heart depolarizes and contracts in an orderly manner from atria to ventricles. * As you must be able to identify the parts of the conduction system and trace the path of depolarization from the .SA node to the Purkinje fibers, we will review this

Since the SA node * has the highest rate of depolarization (75/min) , it starts the process by sending a wave of depolarization * .through the myocardium of the atria

When this reaches the AV node * it depolarizes * and causes the Bundle of His * to depolarize.The depolarization travels into the septum through the bundle branches * * and from the bundle branches into the Purkinje fibers * * which cause depolarization .of the ventricular myocardium

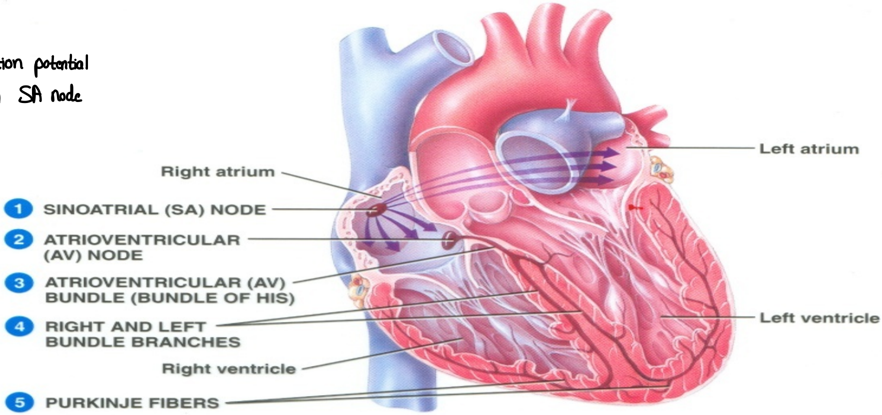
When the cardiac muscle cells of the myocardium, including the papillary muscles, the ventricles contract forcing blood out of the * .ventricles

Sinus Node

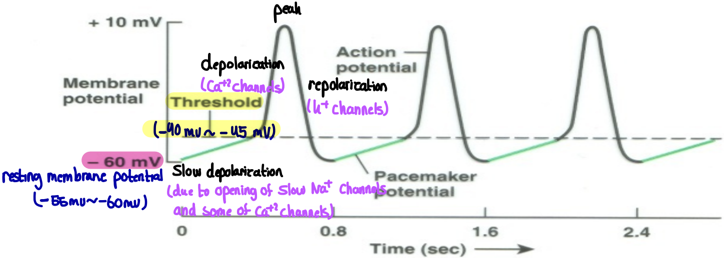
action potential in SA node it will open Na channels

- Specialized cardiac muscle connected to atrial muscle.
- Acts as pacemaker because membrane leaks Na+ and membrane potential is -55 to -60mV
- When membrane potential reaches -40 mV, slow Ca++ channels open causing action potential.
- After 100-150 msec Ca++ channels close and K+channels open more thus returning membrane potential to -55mV.

action potential in SA node



(a) Anterior view of frontal section

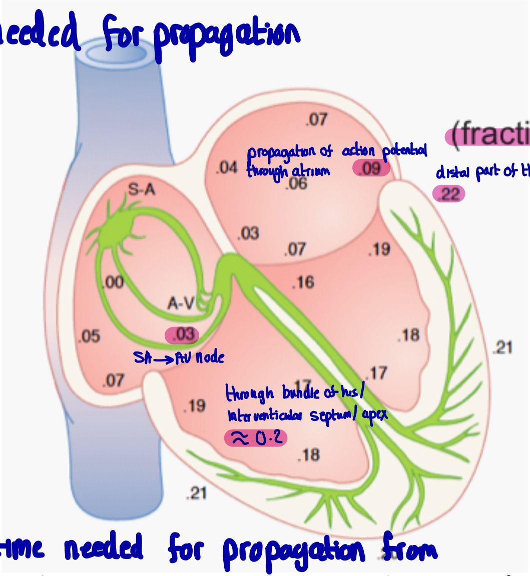


(b) Pacemaker potentials and action potentials in autorhythmic fibers of SA node

resting membrane potential= -55 (1
-60 mV
Before threshod Slow (2
depolarization Na^+ leaky channels &
slow Ca channels & Threshold(-40 –
–45mV)slow Na & some Ca channels
after threshold Ca channels are
responsible for the depolarization (L
type)
The Ca will close
The K+ will open repolarization

Transmission of electrical impulse

The time needed for propagation



(fraction of second)

distal part of the ventricle

Propagation of action through artia

the time needed for propagation from SA node ——> آخر نقطة for the action potential (distal part of the ventricle)

Conduction System

- ① Begins in sinoatrial (SA) node in right atrial wall
- Propagates through atria via gap junctions In both atrium (SA node action potential)
- ② Atria will contract

2. ③ Reaches atrioventricular (AV) node in interatrial septum
3. ④ Enters atrioventricular (AV) bundle (Bundle of His)

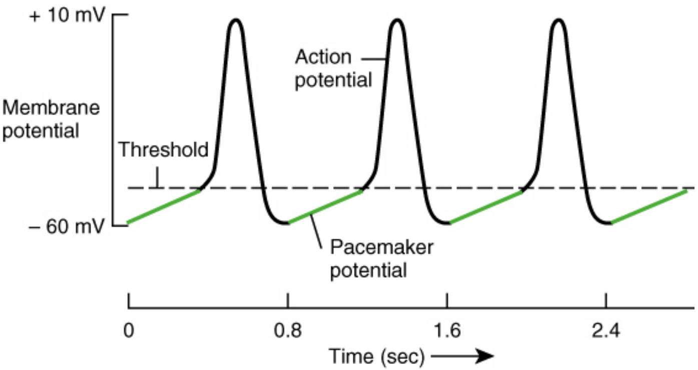
- AV node is the only site where action potentials can conduct from atria to ventricles due to fibrous skeleton

4. ⑤ Enters right and left bundle branches which extends through interventricular septum toward apex
5. ⑥ Finally, large diameter Purkinje fibers conduct action potential to remainder of ventricular myocardium

- ⑦ Finally, ventricles contract.

Action potenial of pacemaker

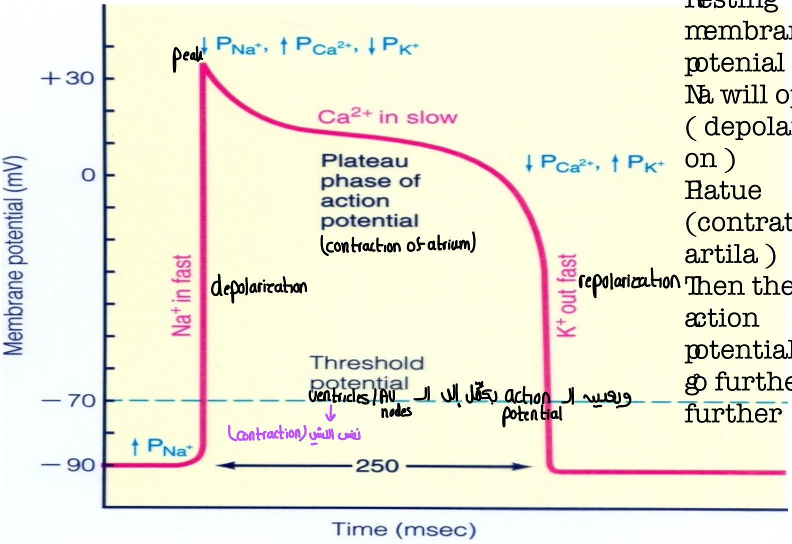
(SA nodes)



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

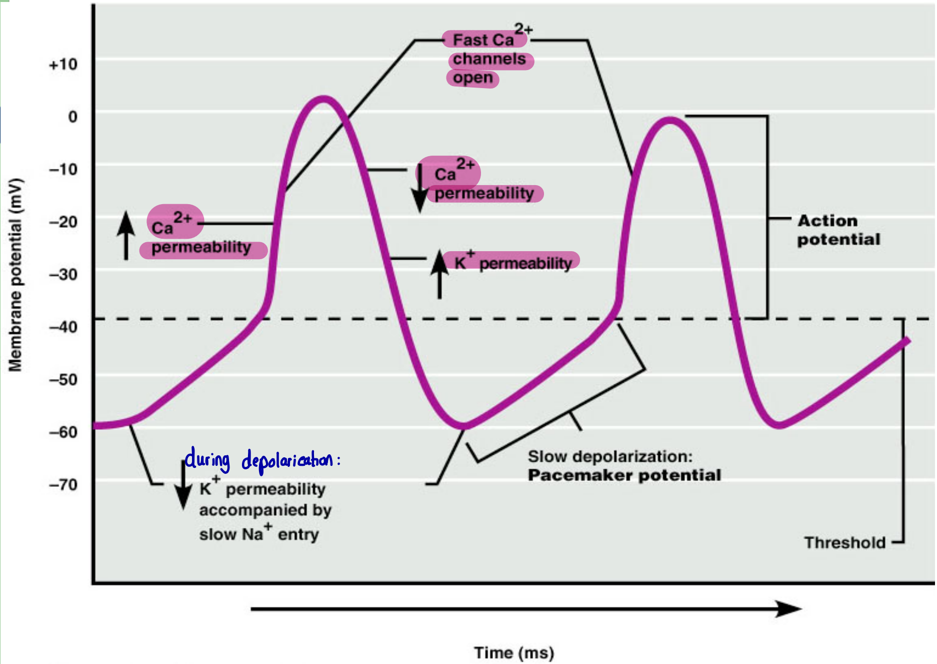
20.10b

Fast Response Action Potential of Contractile Cardiac Muscle Cell



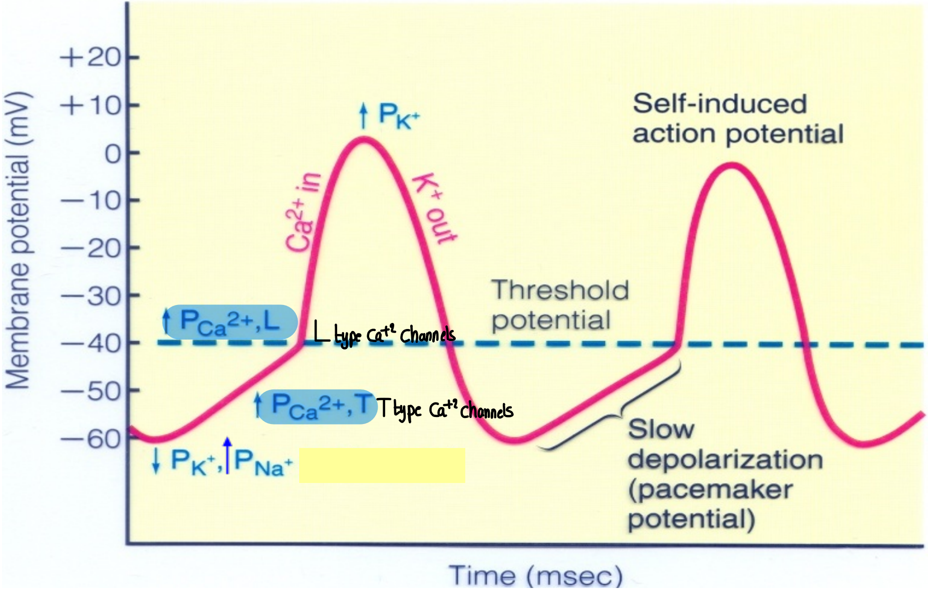
Resting membrane potenial the Na will open (depolarization)
Platue (contration of artila)
Then the action potential will go further & further

Pacemaker and Action Potentials of the Heart



:slow depolarization of the heart is due to
HCN (cyclic nucleotide gated channels) channels are sometimes referred to as pacemaker channels because they help to generate rhythmic activity within groups of heart and brain cells. HCN channels are activated by membrane hyperpolarization, are permeable to Na^+ and K^+, and are constitutively open at voltages near the resting membrane potential
HCN = heart rating control
During depolarization k^+ permeability will decrease

Slow Response Action Potential (Pacemaker Potential) important



L-type channels are found in all cardiac cells and T-type are expressed in Purkinje cells, pacemaker and atrial cells. Both these types of channels contribute to atrioventricular conduction as well as pacemaker activity

SA nodes / AV nodes / any type of cell can be pacemaker

Intrinsic rate and speed of conduction of the components of the system

Or beats

- SA node 60-80 action potential /min (***Pacemaker***) normal
- AV node 40-60 action potential /min
- Purkinje 15-40 action potential /min

↑ heart rate

↓ conduction speed of these fibers

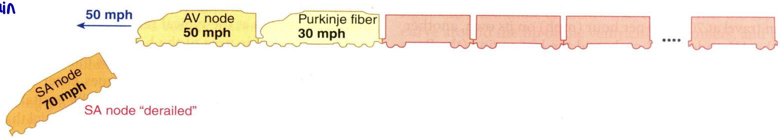
Conduction Speed

- SA node: slow speed of conduction
- Ventricular and Atrial muscle: Moderate speed
- AV node: slowest speed of conduction
- Purkinje fibers: Fastest speed of conduction
- ***Ectopic Pacemaker- Abnormal site of pacemaker***

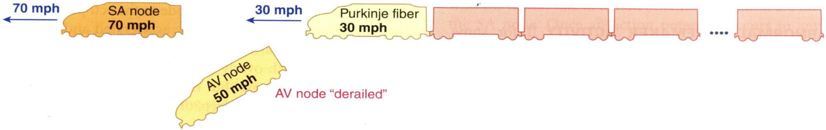
Highest heart rate will
have the slowest
.conduction speed
The fibers are slowest
the more the heart rate

(a) Normal pacemaker activity: Whole train will go **70 mph** (heart rate set by SA node, the fastest autorhythmic tissue).

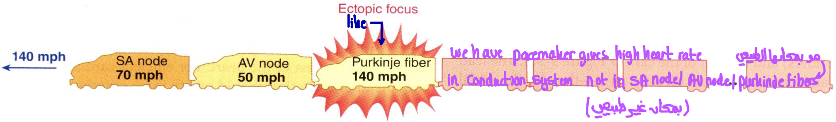
example: like a train



(b) Takeover of pacemaker activity by AV node when the SA node is nonfunctional: Train will go **50 mph** (the next fastest autorhythmic tissue, the AV node, will set the heart rate).



(c) Takeover of ventricular rate by the slower ventricular autorhythmic tissue in complete heart block: First part of train will go **70 mph**; last part will go **30 mph** (atria will be driven by SA node; ventricles will assume own, much slower rhythm).

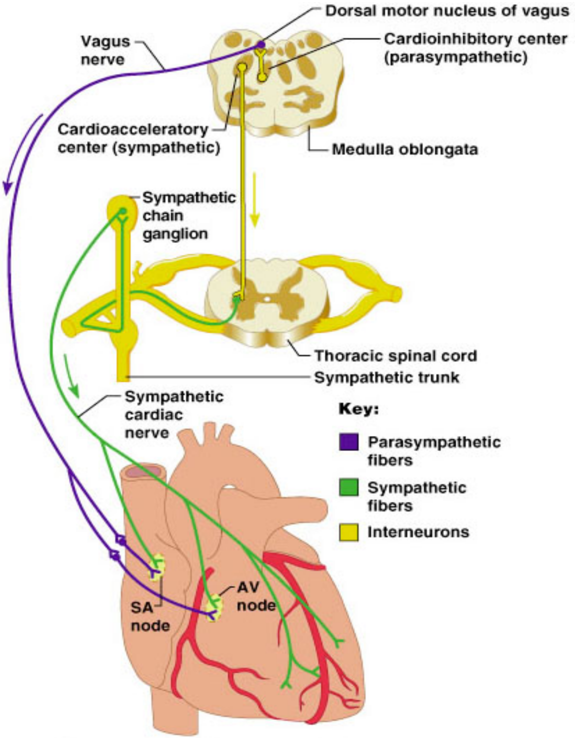


(d) Takeover of pacemaker activity by an ectopic focus: Train will be driven by ectopic focus, which is now going faster than the SA node (the whole heart will be driven more rapidly by an abnormal pacemaker).

Extrinsic Innervation of the Heart

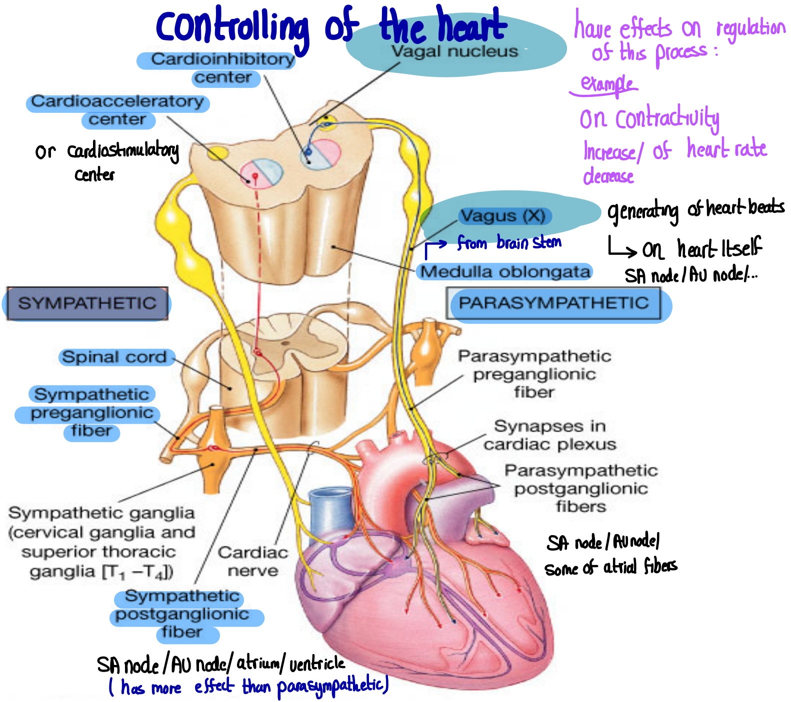
Conduction system = parts
The heart rate that might
occur from each part of the
heart
Action potential of pacemaker
&how it differs from the
contractile fibers

automatic generation of the heart will control the heart beating the autonomic nerve system will only regulate it Sympathetic & parasympathetic

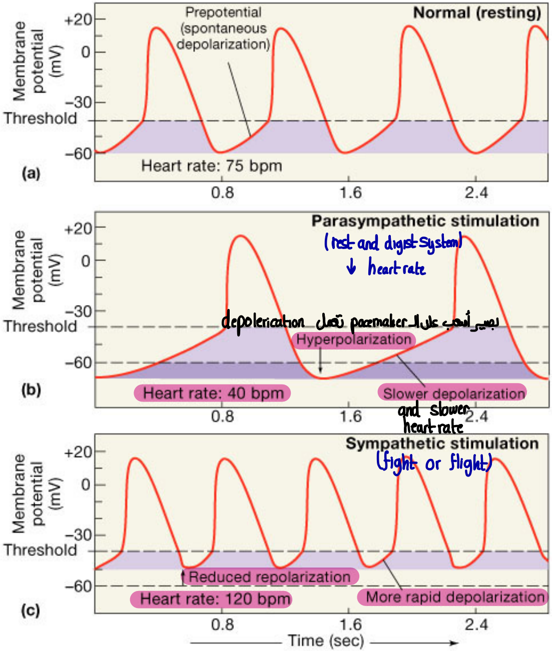


Autonomic Innervation of the Heart

Sympathetic effect is more than the parasympathetic = most of the heat artilas ventricals sa node & av node = upper part node sa & av node & somefibers of the artia



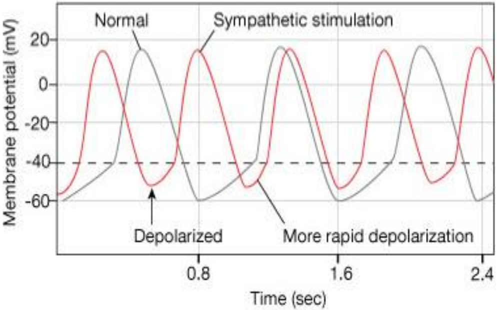
Pacemaker Function

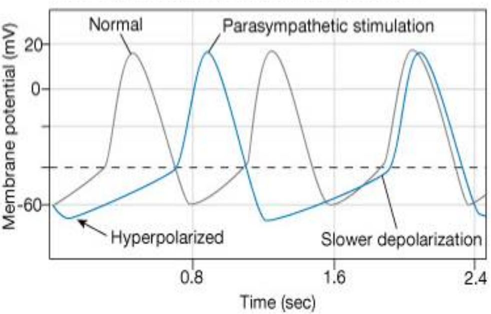


Symbathetic = over riding
Action potential
Slow depolartzation – depolarzation – repolarization 75 beat per min
.
Parasympathic = rest system – lowering the heart beats – over stimulation = slower depolarization & hyper polarization (k+ will get out of the cell more) more negative resting membrane potentail it is harder on the pacemaker to make depolarization – decreasing the heart rate
.
The opposite will happen in sympathetic
Resting membrane will be less negative – rapid depolarization increasing the heart rate & reduce the time of action . Increase the conductivity (more heart rate)

Autonomic neurotransmitters affect ion flow to change rate

- **Sympathetic** – increases heart rate by ↑ Ca^{+2} & If channel (net Na^{+}) flow
  Influx ↑ Funny channels
- **Parasympathetic** – decreases rate by ↑ K^{+} efflux & ↓ Ca^{+2} influx





If channels: "funny" because it has effects opposite to those of most other heart currents. If is a mixed Na+–K+ inward current activated by hyperpolarization and modulated by the autonomic .nervous system

Funny' (f) channels are activated by intracellular cyclic adenosine monophosphate (cAMP) concentrations according to a mechanism mediating regulation of heart rate by the autonomic nervous system, as well as by voltage hyperpolarisation

Regulation of the heart beat

- Sympathetic from the cardiac plexus supplies all parts of the heart (atria, ventricle and all parts of the conduction system)
- Parasympathetic from Vagus nerves supply mainly the atria, SA and AV nodes, very little supply to ventricles
- Sympathetic: increase the permeability of the cardiac cells to Na+ and Ca++ i.e Positive Chronotropic and positive Inotropic action

  ↑ heart rate

  ↑ contractility ~ قوة ال contraction
- Parasympathetic: Increase the permeability of the cardiac cells to K+ and decrease its permeability to Na+ and Ca++

Sinus Node is Cardiac Pacemaker

- Normal rate of discharge in sinus node is 70-80/min.; A-V node - 40-60/min.; Purkinje fibers - 15-40/min.
- Sinus node is pacemaker because of its faster discharge rate
- Intrinsic rate of subsequent parts is suppressed by “Overdrive suppression”

Ectopic Pacemaker

- This is a portion of the heart with a more rapid discharge than the sinus node.
- Also occurs when transmission from sinus node to A-V node is blocked (A-V block).

Parasympathetic Effects on Heart Rate

- Parasympathetic (vagal) nerves, which release acetylcholine at their endings, innervate S-A node and A-V junctional fibers proximal to A-V node.
- Causes hyperpolarization because of increased K+ permeability in response to acetylcholine.
- This causes decreased transmission of impulses maybe temporarily stopping heart rate.

hyperpolarization of parasympathetic → heart rate might stop working

Sympathetic Effects on Heart Rate

- Releases norepinephrine at sympathetic ending
- Causes increased sinus node discharge (***Chronotropic effect***)
- Increases rate of conduction of impulse (***Dromotropic effect***)
- Increases force of contraction in atria and ventricles (***Inotropic effect***)

Most important to know the conduction system the
Action potentail
channels
To know each part of the heart how it is realted to the conduction syhstem
How autonomic nervous system will affect (sympathetic & para sympathertic)
Last slide is important

Thank You