The Conduction System of the heart

The heart's function is to eject blood, in order to do that it must contract and in order to contract it must receive impulses. Electrical (Action potential) followed by Mechanical (Contraction and ejection).

- We have two types of cells in our body:

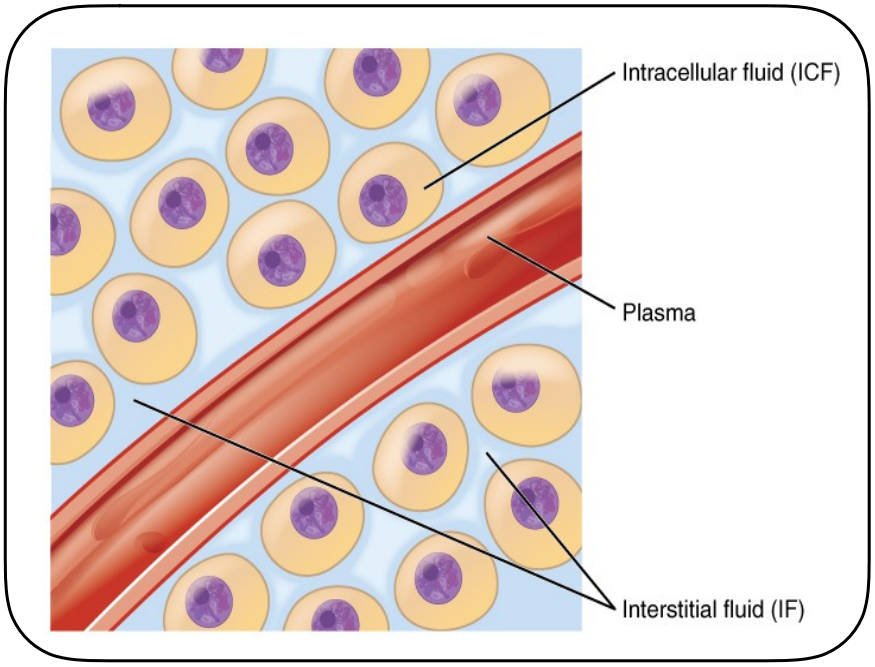
1. Excitable cells: can't perform it's function unless it is excited (Heart cells).
2. Non Excitable cells: can perform its function without excitation (Endocrine cells).

- Excitation: reversal of the membrane potential by introducing positive ions (Na+, Ca+2).

- There are three main fluid Compartments:

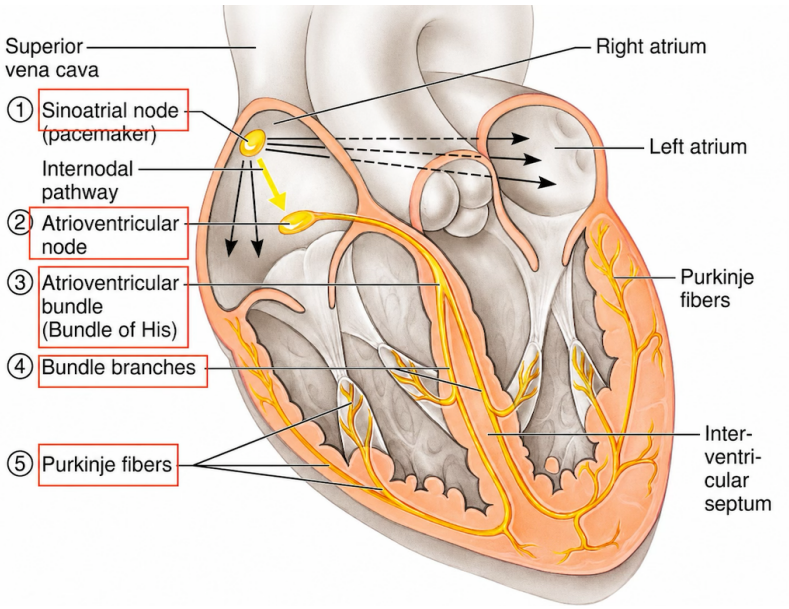
1. Intracellular (inside cells)
2. Interstitial (around cells)
3. Intravascular (the blood plasma)

- Interstitial fluid and plasma are very similar in composition but the plasma contains more proteins.



The Intrinsic Cardiac Conduction System: is an electrical system that can generate and conduct impulses without needing nervous stimulation (they lack actin and myosin) and is considered the conductive system of the heart that controls cardiac contractions. It includes:

1. SA Node
2. AV Node
3. AV bundle (Bundle of his)
4. Right and left bundle branches
5. Purkinje fibers



Intrinsic Cardiac Conduction System.

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

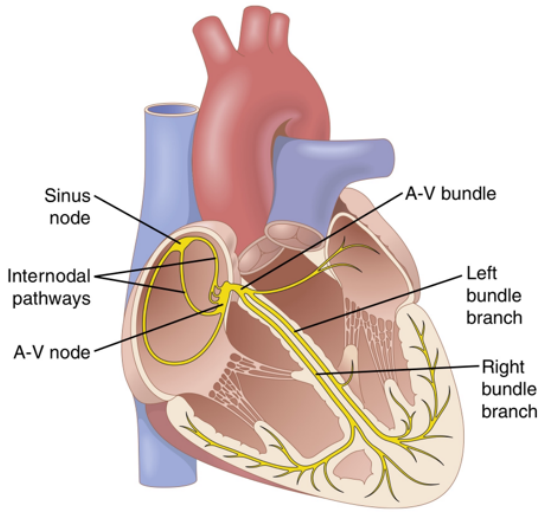
- Approximately 1% of cardiac muscle cells are autorhythmic rather than contractile. The heart contains two main types of cardiac muscle cells:

1. Contractile cells (contract and pump blood, can't start impulses).
2. Autorhythmic cells also called pacemaker cells (start impulses without needing stimulation from nerves) they form the heart's Instrinsic conduction system.

Impulse conduction pathway:

- SA node: generates the normal rhythmical impulses and conduct it to the AV nodal cells, right and left atria (slow speed of conduction).
- AV node: delay the impulses before passing from the atria to the ventricles (slowest speed of conduction).
- The AV bundle: conducts impulses from the atria into the ventricles.
- Purkinje fibers: conduct impulses to all parts of the ventricles (Fastest speed of conduction).
- There are gap junctions (very low electrical resistance) between the contractile cells which resulte in Atrial syncytia and Ventricular syncytia (all or none, you can't excite one cell without exciting the rest). Separated by fibrous ring.

Features of the Intrinsic Cardiac Conduction System:



Sinus node and the Purkinje system of the heart, showing also the atrioventricular (A-V) node, atrial internodal pathways, and ventricular bundle branches.

1. Atria contract before ventricles
   the A-V node in which impulses from the atria are delayed before passing into the ventricles which allows filling of the ventricles before they pump blood through the lungs and peripheral circulation.
2. Ventricles contract almost simultaneously
   Due to rapid conduction of the A-V bundle which conducts impulses from the atria into the ventricles and Purkinje fibers which conduct the impulses to all parts of the ventricles, this is essential for the most effective pressure generation and pumping in the ventricular chambers.

- The rapid conduction of the Purkinje system normally permits the cardiac impulse to arrive at almost all portions of the ventricles within a narrow span of time, exciting the first ventricular muscle fiber only very short period of time ahead of excitation of the last ventricular muscle fiber. This timing causes all portions of the ventricular muscle in both ventricles to begin contracting at almost the same time and then to continue contracting for about another 0.3 second.
- Effective pumping by the two ventricular chambers requires this synchronous type of contraction. If the cardiac impulse should travel through the ventricles slowly, much of the ventricular mass would contract before contraction of the remainder, in which case the overall pumping effect would be greatly depressed. Indeed, in some types of cardiac disfunction, slow transmission does occur, and the pumping effectiveness of the ventricles is decreased. Implantable cardiac resynchronization devices are types of pacemakers using electrical wires or leads that can be inserted into the cardiac chambers to restore appropriate timing between the atria and both ventricles to improve pumping effectiveness in patients with enlarged and weakened hearts.

- Atrial contraction is not essential for life but without vetricular contraction we will die.

- Any cardiac muscle cell (pacemaker or contractile) has three main types of membrane ion channels that play important roles in causing the voltage changes of the action potential:

1. Fast sodium channels.
2. Calcium channels ("slow" calcium channels).
3. Potassium channels.

- The importance of each channel differs between contractile and pacemaker cells.

Action Potential of Contractile Cardiac Muscle Cell and Pacemaker Potential

- **Phases of action potential of cardiac ventricular muscle cell:**

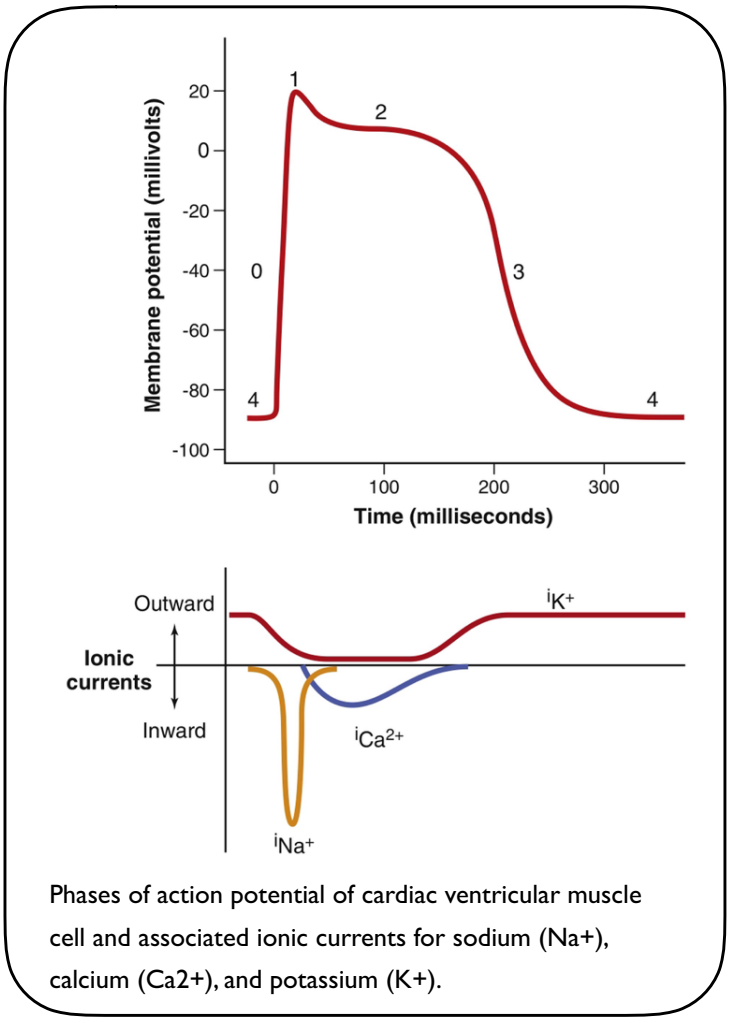
Phase 0 (Depolarization): Fast Sodium Channels Open.

Phase 1 (Initial Repolarization): Fast Sodium Channels Close.

Phase 2 (Plateau): Calcium Channels Open and Fast Potassium Channels Close.

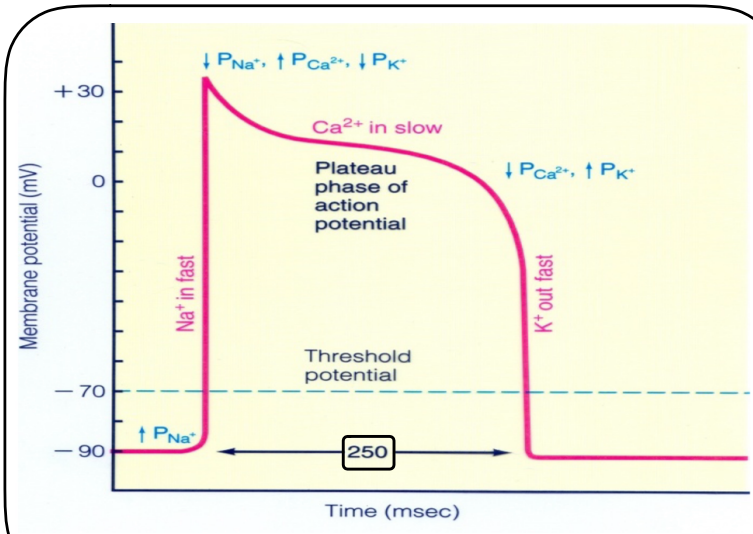
Phase 3 (Rapid Repolarization): Calcium Channels Close and Slow Potassium Channels Open.

Phase 4 (Resting Membrane Potential): Averages about −90 millivolts.



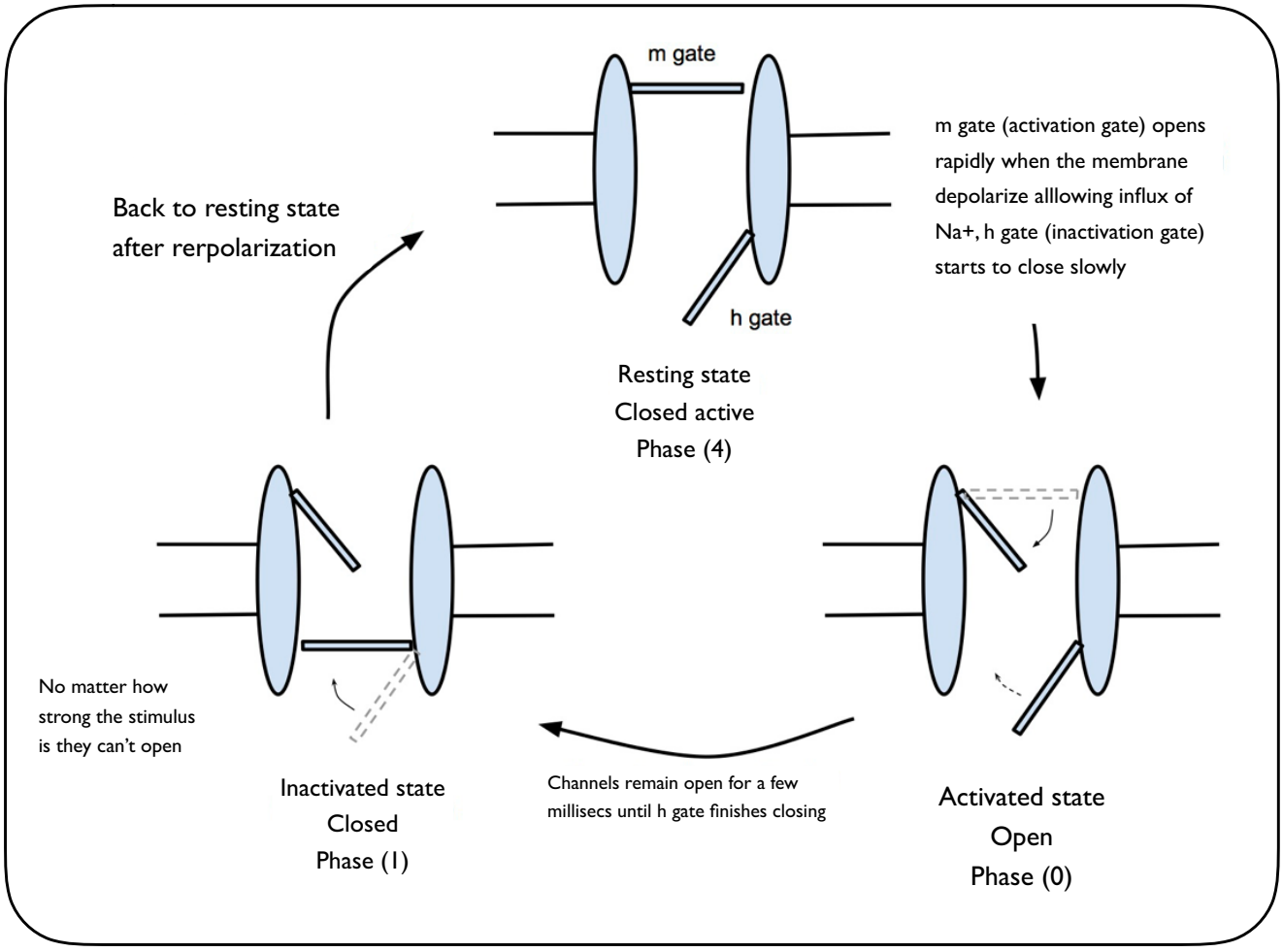
Phases of action potential of cardiac ventricular muscle cell and associated ionic currents for sodium (Na+), calcium (Ca2+), and potassium (K+).

- cardiac ventricular muscle cell depends on the Na+ fast channels, when they open they undergo positive feedback and reach the peak very fast because of rapid influx of positive sodium ions which causes depolarization(phase 0).At the peak of depolarization the fast Na+ channels close(phase 1).Then, the plateau of the ventricular action potential is caused primarily by slower opening of the slow calcium channels, which lasts for about 0.3 second(phase 2).Finally, opening of potassium channels allows for the diffusion of large amounts of positive potassium ions in the outward direction through the fiber membrane(phase 3)and returns the membrane potential to its resting level.the resting membrane potential of the ventricular muscle fiber is -90 millivolts and it's stable with respect to time which means that it's not autorhythmic and need an external stimulus to initiate an action potential (phase 4).



Fast Response Action Potential of Contractile Cardiac Muscle Cell

Fast Na+ channels



Tetanus

Defenition

- Refers to sustained contraction because the muscle doesn't have time to relax between stimuli.
- Tetanization is impossible in ventricles, if the ventricles could go into tetanus the heart would not relax, no enough blood to fill the ventricles which leads to death.

Protective features against Tetanus:

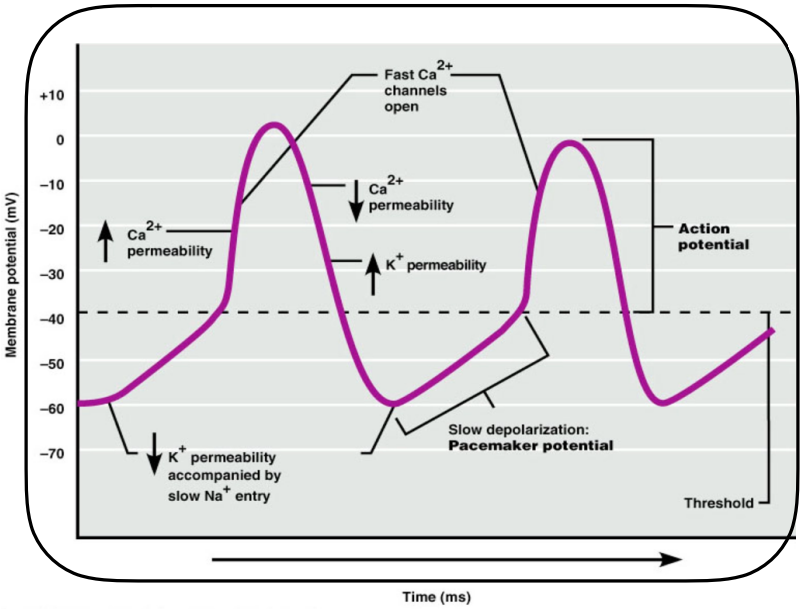
- Very long action potential especially the plateau phase (250ms). At the plateau phase
  Ca+2 influx = K+ efflux
  This balance keeps the membrane potential for a long time.
- No Summation, Each contraction finishes before the next one can begin so no overlaping of contractions.

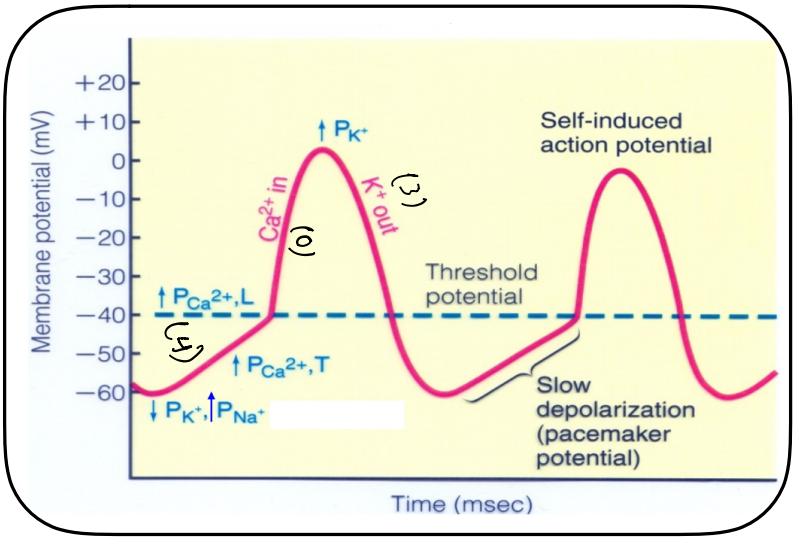
SA node

The fibers of SA node have almost no contractile muscle filaments. However, the sinus nodal fibers connect directly with the atrial muscle fibers, so that any action potential that begins in the sinus node spreads immediately into the atrial muscle wall.
the sinus node ordinarily controls the beat rate of the entire heart. They are capable of self-excitation which can cause autorhythmical discharge and contraction. This capability is especially true of the heart's specialized conducting system.

Leakiness causes Self-Excitation

Leakiness of Sinus Nodal Fibers to Sodium and Calcium Causes Self-Excitation. Because of the high Na+ ion concentration in the extracellular fluid outside the nodal fiber, as well as a moderate number of already open sodium channels, Na+ ions from outside the fibers tend to leak to the inside through inward, "funny" currents. Therefore, between heartbeats, the Na+ influx causes a slow rise in the resting membrane potential in the positive direction. Thus, the resting potential gradually rises and becomes less negative between each two heartbeats. When the potential reaches a threshold voltage of about –40 millivolts, the slow calcium channels become activated, thus causing the action potential. Therefore, basically, the inherent leakiness of the sinus nodal fibers to Na+ and Ca+2 ions causes their self-excitation.



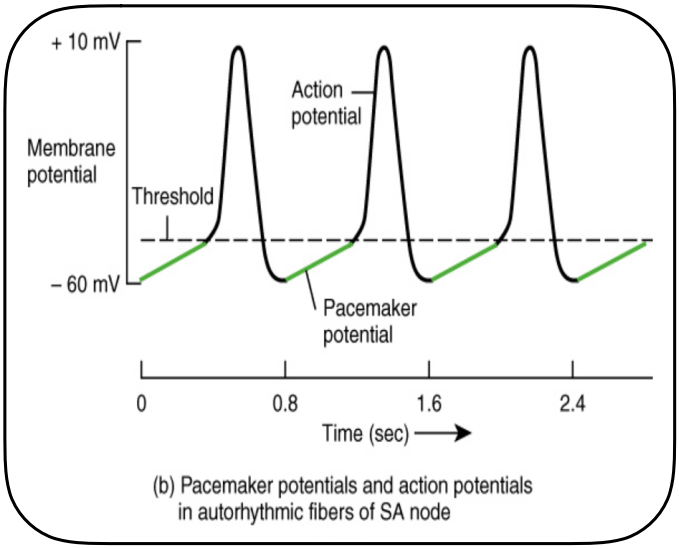


Why does this leakiness to Na+ and Ca+2 ions not cause the sinus nodal fibers to remain depolarized all the time?

Two events occur during the course of the action potential to prevent such a constant state of depolarization. First, the slow calcium channels become inactivated (they close) within about 100 to 150 milliseconds after opening. Second, at about the same time, greatly increased numbers of potassium channels open. Therefore, influx of positive calcium and sodium ions through the slow calcium channels ceases, while at the same time large quantities of positive potassium ions diffuse out of the fiber. Both these effects reduce the intracellular potential back to its negative resting level and therefore terminate the action potential. Furthermore, the potassium channels remain open for another few tenths of a second, temporarily continuing movement of positive charges out of the cell, with resultant excess negativity inside the fiber; this process is called hyperpolarization. The hyperpolarization state initially carries the resting membrane potential down to about –60 millivolts at the termination of the action potential.

Why is this new state of hyperpolarization not maintained forever?

The reason is that during the next few tenths of a second after the action potential is over, progressively more and more potassium channels close. The inward-leaking sodium ("funny" current) and calcium ions once again overbalance the outward flux of potassium ions, which causes the resting potential to drift upward once more, finally reaching the threshold level for discharge at a potential of about –40 millivolts. Then, the entire process begins again: self-excitation to cause the action potential, recovery from the action potential, hyperpolarization after the action potential is over, drift of the resting potential to threshold, and finally re-excitation to elicit another cycle. This process continues throughout a person's life.



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

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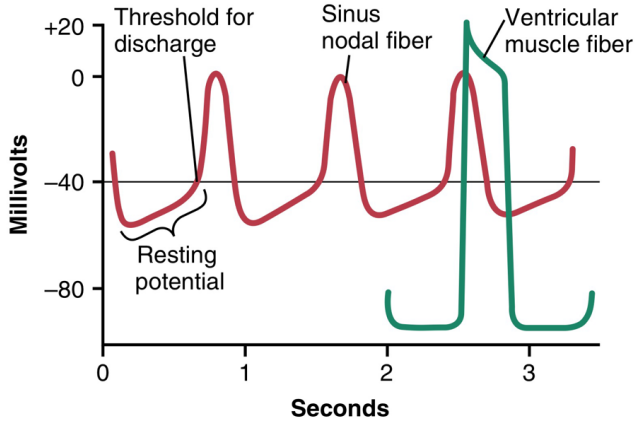
Comparison between the SA node fibers and the Ventricular muscle fiber

- ## The resting membrane potential:

The resting membrane potential of the sinus nodal fiber between discharges is about –60 millivolts, in comparison with –90 millivolts for the ventricular muscle fiber. The cause of this lower negativity is that the cell membranes of the sinus fibers are naturally leaky to sodium and calcium ions, and positive charges of the entering sodium and calcium ions neutralize some of the intracellular negativity.



Rhythmical discharge of sinus nodal fiber. Also, the sinus nodal action potential is compared with that of a ventricular muscle fiber.

- ## The function of channels:

There is a difference in the function of these channels in the sinus nodal fiber because the resting potential is much less negative in the nodal fiber instead of the ventricular muscle fiber. At this level of –60 mv, the fast sodium channels mainly have already become inactivated, or blocked. This is because any time the membrane potential remains less negative than about –60 millivolts for more than a few milliseconds, the inactivation (h) gates become closed and remain so. Therefore, only the slow calcium channels can open (can become activated) and thereby cause the action potential. As a result, the nodal action potential is slower to develop than the action potential of the ventricular muscle. Also, after the action potential does occur, return of the potential to its negative state occurs slowly as well, rather than the abrupt return that occurs for the ventricular fiber.

Ion	SA node	Ventricular Muscle
Na+	Minor role	Rapid depolarization
Ca+2	Main depolarizing ion	Plateau + contraction
K+	Repolarization	Repolarization

Phase	SA node	Ventricular muscle
4	Slow depolarization (Unstable)	Stable
0	Ca+2 influx	Rapid Na+ influx
1	Absent	Brief K+ efflux
2	Absent	Plateau (Ca+2 in balances K+ out)
3	K+ efflux	K+ efflux

Ischemia

- resulting from inadequate coronary blood flow. The effect is often a bizarre heart rhythm or an abnormal sequence of contraction of the heart chambers, and the pumping effectiveness of the heart can be affected severely(O_2 delivery decreases), even to the extent of causing death.

- The duration of normal cardiac cycle is 0.8s which result in 70-80 beats per minute.
- For ventricles there is two phases the systole (contraction) phase lasts for 0.3s and the diastole (relaxation) phase lasts for 0.5s.
- Very short diastole can reduce coronary blood flow and may contribute to ischemia.

Ischemia, infection in the SA node and Sick Sinus Syndrome lead to ectopic pacemakers.

THE SINUS NODE IS THE NORMAL PACEMAKER OF THE HEART

- In discussing the transmission of the cardiac impulse through the heart, we have noted that the impulse normally arises in the sinus node. In some abnormal conditions, this is not the case. Other parts of the heart can also exhibit intrinsic rhythmical excitation in the same way as the sinus nodal fibers; this is particularly true of the AV nodal and Purkinje fibers.
  The AV nodal fibers, when not stimulated from some outside source, discharge at an intrinsic rhythmical rate (Action potential) of 40 to 60 times per minute, and the Purkinje fibers discharge at a rate of 15 to 40 times per minute. These rates are in contrast to the normal rate of the sinus node of 70 to 80 times per minute.

Why then does the sinus node rather than the AV node or the Purkinje fibers control the heart's rhythmicity?

The answer derives from the fact that the action potential rate of the sinus node is considerably faster than the natural self-excitatory action potential rate of either the AV node or the Purkinje fibers. Each time the sinus node discharges, it's impulse is conducted into both the AV node and Purkinje fibers, also discharging their excitable membranes. However, the sinus node discharges again before either the AV node or Purkinje fibers can reach their own thresholds for self-excitation. Therefore, the new impulse from the sinus node discharges both the AV node and Purkinje fibers before self-excitation can occur in either of these sites. Intrinsic rate of subsequent parts is suppressed by "Overdrive suppression".
Thus, the sinus node controls the beat of the heart because its rate of rhythmical discharge is faster than that of any other part of the heart. Therefore, the sinus node is almost always the pacemaker of the normal heart.

Abnormal Pacemakers—Ectopic Pacemaker

- A pacemaker elsewhere than the sinus node is called an ectopic pacemaker. An ectopic pacemaker causes an abnormal sequence of contraction of the different parts of the heart and can cause significant weakening of heart pumping.

- Can occur in two cases:

1. A portion of the heart with a more rapid discharge than the sinus node.
2. transmission from sinus node to AV node is blocked (AV block).

- parts of the heart develops a rhythmical discharge rate that is more rapid than that of the sinus node. This could occur in:

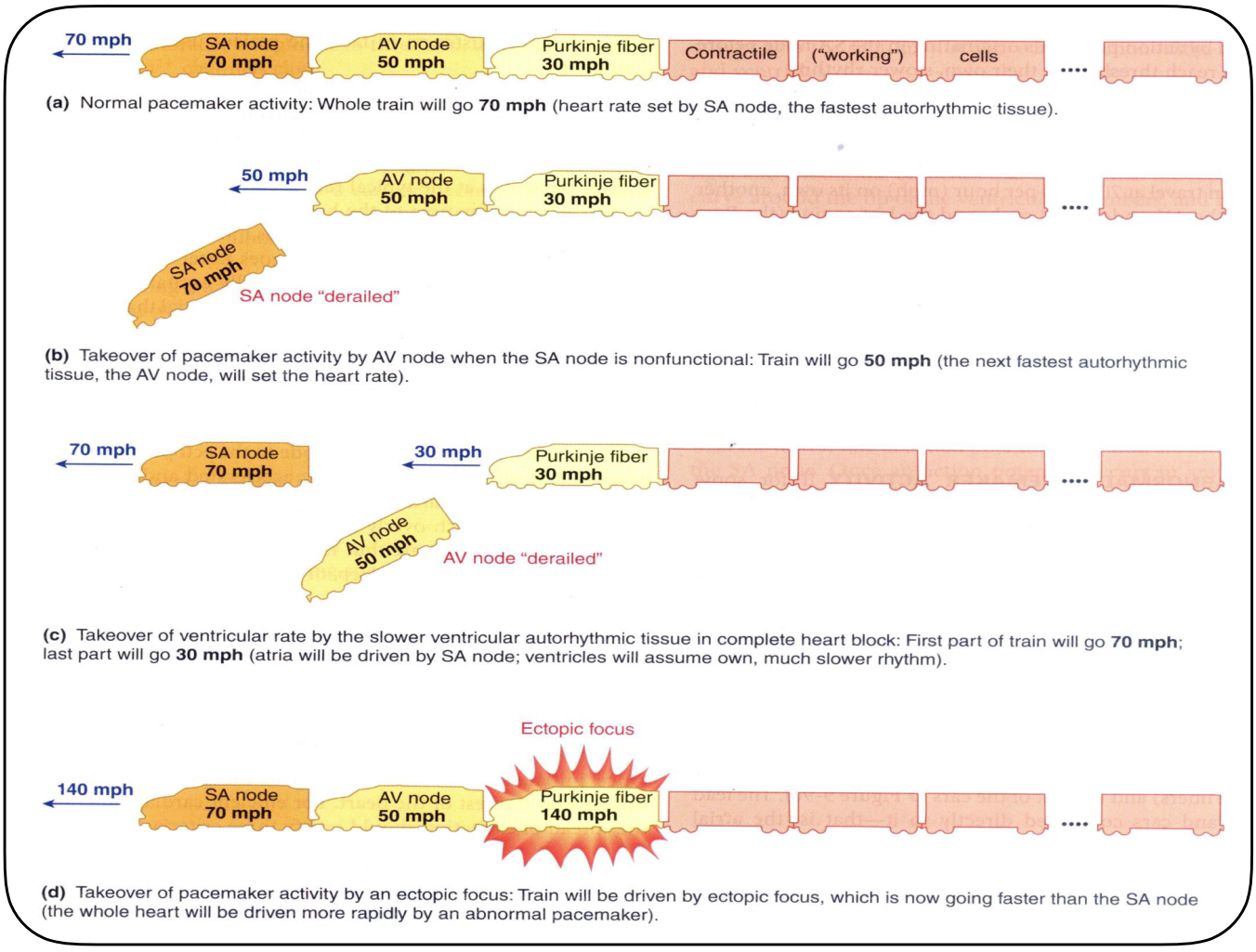
1. AV node (latent)
2. Purkinje fibers (latent)
3. Under rare conditions, a place in the atrial or ventricular muscle (ectopic)

- Blockage of transmission of the cardiac impulse from the sinus node to the other parts of the heart:

  The new pacemaker then usually occurs at the AV node or in the penetrating portion of the AV bundle on the way to the ventricles.

  When AV block occurs that is, when the cardiac impulse fails to pass from the atria into the ventricles through the AV nodal and bundle system, the atria continue to beat at the normal rate of rhythm of the sinus node while a new pacemaker usually develops in the Purkinje system of the ventricles and drives the ventricular muscle at a new rate, somewhere between 15 and 40 beats per minute.

  After sudden AV bundle block, the Purkinje system does not begin to emit its intrinsic rhythmical impulses until 5 to 20 seconds later because, before the blockage, the Purkinje fibers had been "overdriven" by the rapid sinus impulses and, consequently, are in a suppressed state. During these 5 to 20 seconds, the ventricles fail to pump blood, and the person faints after the first 4 to 5 seconds because of lack of blood flow to the brain. If the delay period is too long, it can lead to death.



- You need to understand something here, we have two conditions:

1. The SA node is functioning perfectly but another part of the conduction system developed a faster rate of discharge than the SA node, we call this Ectopic pacemaker.
2. The SA node is not functioning, in this case, other latent pacemakers take over as a protective mechanism and it is called Escape Rhythm. The AV node is usually the first backup pacemaker and can maintain life with a slower rhythm. If impulses fail to originate from or pass through the AV node (blockage), the Purkinje fibers take over, producing a very slow ventricular rhythm that is usually insufficient long-term, so an artificial pacemaker may be needed.

Situation	Escape Rythm	Ectopic pacemaker
SA node status	Failed	Normal
New pacemaker	AV / Purkinje	Cells that developed higher discharge rate
Rate (Than normal)	Slower (Bradycardia)	Faster (Tachycardia)

The normal heart rate is 60-100 bpm

<60 bpm Bradycardia

>100 bpm tachycardia

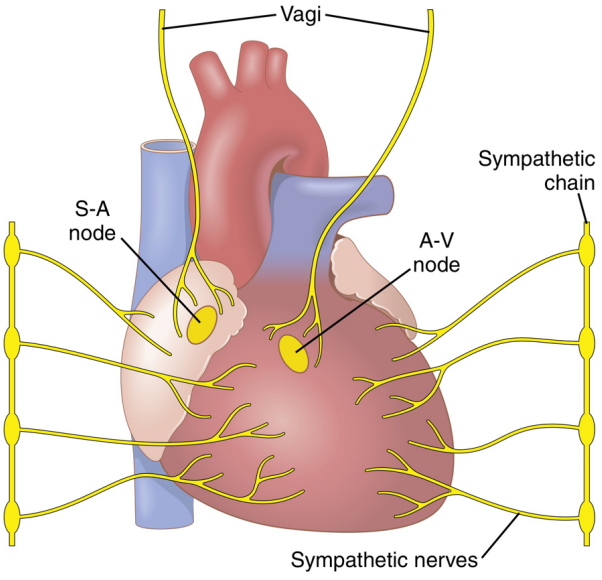
The SA node is the pacemaker of the heart because:

1. It has the highest slope of phase (4)
2. It's more leaky to Na+ at rest than any other cell in the heart
3. It's membrane property

Pay attention to the slopes of phase (4) cuz the doctor mentions them a lot in his questions in the exam :)

Extrinsic Innervation of the Heart

- **SYMPATHETIC AND PARASYMPATHETIC NERVES CONTROL HEART RHYTHMICITY AND IMPULSE CONDUCTION BY THE CARDIAC NERVES**



Cardiac sympathetic and parasympathetic nerves. (The vagus nerves to the heart are parasympathetic nerves.)

- The parasympathetic nerves (the vagi) are distributed mainly to the S-A and A-V nodes and the muscle of the two atria, and very little directly to the ventricular muscle.
- The sympathetic nerves from the cardiac plexus, conversely, are distributed to all parts of the heart (atria, ventricle and all parts of the conduction system).

- **Parasympathetic (Vagal) Stimulation:**

In normal resting conditions the parasympathetic nervous system dominates extrinsic control.

- Slows the Cardiac Rhythm and Conduction. Stimulation of the parasympathetic nerves to the heart (the vagi) causes acetylcholine to be released at the vagal endings. This neurotransmitter has two major effects on the heart:

1. It decreases the rate of the sinus nodal discharge.
2. It decreases the rate of conduction, as well as the level of excitability of the heart, especially the atria and the AV node.
3. It decreases the force of atrial contraction slightly, but has little effect on ventricular contraction.

- Types of vagal stimulation:

1. Weak to moderate vagal stimulation: slows the rate of heart pumping, often to as little as one-half normal.
2. Strong stimulation: completely stops the rhythmical excitation by the sinus node or completely block transmission of the cardiac impulse from the atria into the ventricles through the A-V node.

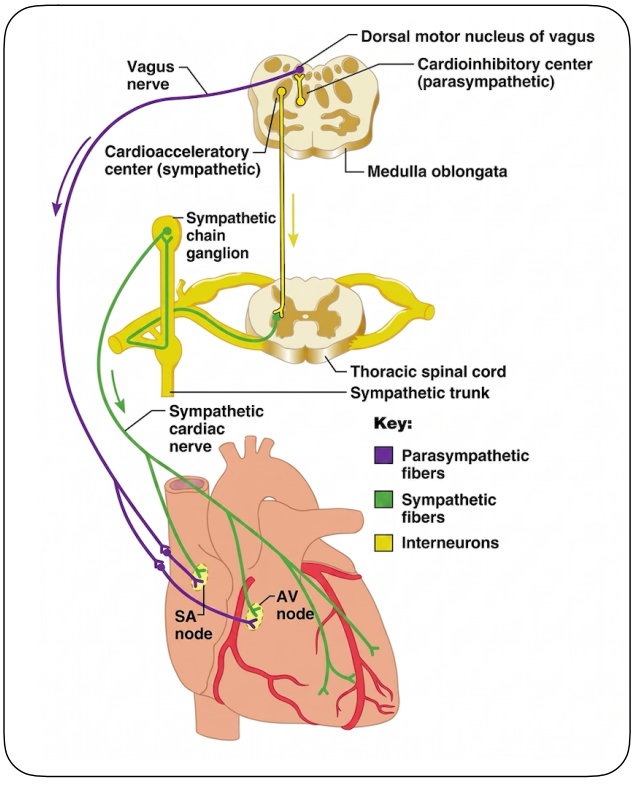
- During strong parasympathetic (vagal) stimulation, rhythmic excitatory impulses from the SA node may fail to reach the ventricles because conduction through the AV node is suppressed. The ventricles may stop beating for 5–20 seconds. After that, a pacemaker within the Purkinje system or ventricles develops its own spontaneous rhythm, producing ventricular contractions at about 15–40 beats per minute. This is called ventricular escape (protective emergency mechanism).

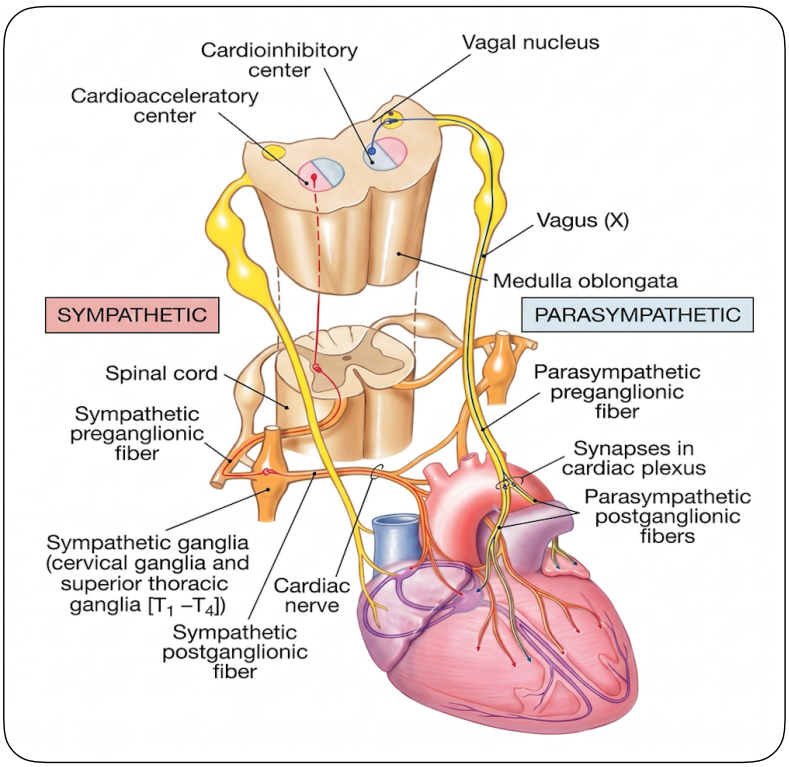
- Effect on ions:
  Increase the permeability of the cardiac cells to K+ and decrease its permeability to Na+ and Ca+2.

- **Mechanism of the Vagal Effects**

The acetylcholine released at the vagal nerve endings greatly increases the permeability of the fiber membranes to potassium ions, which allows rapid leakage of potassium out of the conductive fibers. This process causes increased negativity inside the fibers, an effect called hyperpolarization, which makes this excitable tissue much less excitable. In the sinus node, the state of hyperpolarization makes the resting membrane potential of the sinus nodal fibers considerably more negative than usual that is, −65 to−75 millivolts rather than the normal level of −55 to −60 millivolts. Therefore, the initial rise of the sinus nodal membrane potential caused by inward sodium and calcium leakage requires much longer to reach the threshold potential for excitation. This requirement greatly slows the rate of rhythmicity of these nodal fibers. If the vagal stimulation is strong enough, it is possible to stop the rhythmical self-excitation of this node entirely.

In the AV node, vagal stimulation causes hyperpolarization of the nodal fibers, making the resting membrane potential more negative than normal. Because of this, the incoming impulse requires more time and stronger depolarization to reach threshold. As a result, conduction through the AV node slows. Weak vagal stimulation delays conduction, while strong vagal stimulation may block conduction completely.





- **Sympathetic Stimulation:**

- Increases the Cardiac Rhythm and Conduction. Sympathetic stimulation causes essentially the opposite effects on the heart as those caused by vagal stimulation, as follows.

1. It increases the rate of sinus nodal discharge.
2. It increases the rate of conduction, as well as the level of excitability in all portions of the heart.
3. It increases greatly the force of contraction of all the cardiac musculature, both atrial and ventricular.

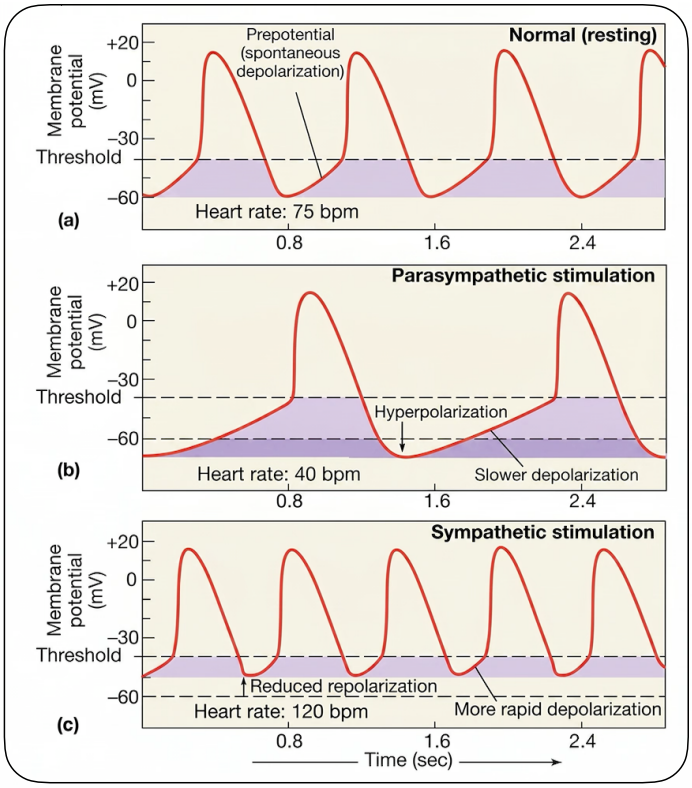
- Sympathetic stimulation increases the overall activity of the heart. Maximal stimulation can almost triple the heartbeat frequency and can increase the strength of heart contraction as much as twofold.
- Effect on ions:
  Increase the permeability of the cardiac cells to Na+ and Ca+2
- **Mechanism of the Sympathetic Effect**

Stimulation of the sympathetic nerves releases norepinephrine at the sympathetic nerve endings. Norepinephrine, in turn, stimulates receptors, which mediate the effects on heart rate. The precise mechanism is somewhat unclear, but is thought to increase the permeability of the fiber membrane to sodium and calcium ions. In the sinus node, an increase of sodium-calcium permeability causes a more positive resting potential. It also causes an increased rate of upward drift of the diastolic membrane potential toward the threshold level for self-excitation, thus accelerating self-excitation and, therefore, increasing the heart rate.
In the A-V node and A-V bundles, increased sodium-calcium permeability makes it easier for the action potential to excite each succeeding portion of the conducting fiber bundles, thereby decreasing the conduction time from the atria to the ventricles.
The increase in permeability to calcium ions -along with other factors- is responsible for the increase in contractile strength of the cardiac muscle under the influence of sympathetic stimulation. This is because calcium ions play a powerful role in exciting the contractile process of the myofibrils.

Approximate heart rates in different conditions:

(Notice the relations between the numbers)

Condition	Heart rate
Intrinsic (SA node)	100 bpm
Resting (Parasympathetic)	75 bpm
Strong Parasympathetic	45 or lower
Sympathetic	>100 bpm



Parasympathetic Effects on Heart Rate

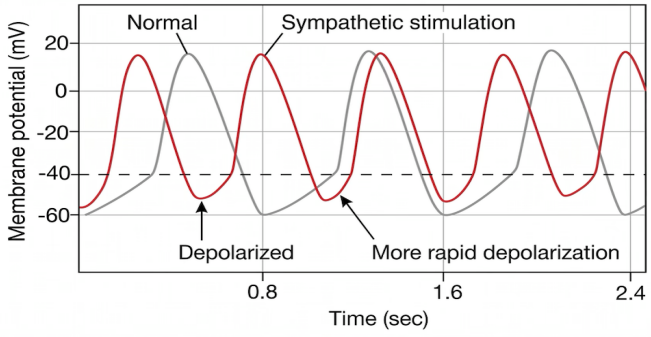
Parasympathetic (vagal) nerves, which release acetylcholine at their endings, innervate S-A node and A-V junctional fibers proximal to A-V node. Causes hyperpolarization because of increased K+ permeability in response to acetylcholine.

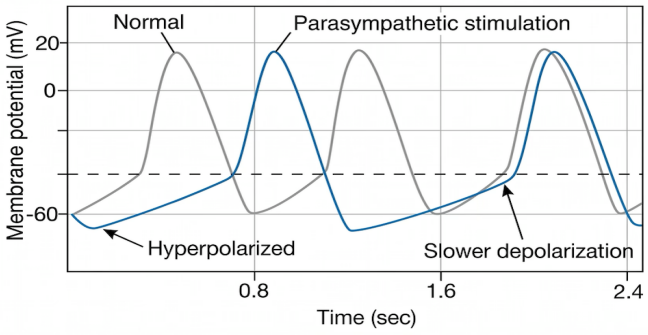
This causes decreased transmission of impulses maybe temporarily stopping heart rate. Decreases the slope of dV/dt of phase (4)

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), increases the slope of dV/dt of phase (4)

- Autonomic neurotransmitters affect ion flow to change rate
- Sympathetic – increases heart rate by Ca+2 & (If) channel (net Na+) flow
- Parasympathetic – decreases rate by K+ efflux & Ca+2 influx





- What part of the graph is not changed by autonomic influences?

Autonomic influences mainly affect Phase 4 depolarization, while the threshold potential and action potential peak remain relatively unchanged.

- Chronotropic means Heart rate
- Inotropic means Contraction force
- Dromotropic means Conduction velocity
- Bathmotropic means Excitability

Positive ⟶ Stronger

Negative ⟶ Weaker