Physiology | Lecture 8

Conduction system of the heart pt.2

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Cardiac and Skeletal Muscles

Differences

Skeletal muscle	Cardiac Muscle
• Neurogenic (motor neuron-end plate-acetylcholine)	• Myogenic (action potential originates within the muscle)
• Insulated from each other	• it generates its own electrical impulses and will continue to beat even if physically removed from the body and disconnected from all external nerves and hormones.
• Short action potential	• Gap-junctions
	• Action potential is longer

Cardiac Muscle action potential Vs Skeletal Muscle.

Phase 0: –Depolarization phase (Na+ influx). The same in both

During ion channel opening, each ion moves to drive the membrane toward its specific equilibrium potential: □ seeks +61 mV, □ seeks +120 mV, and □ seeks -90 mV.

Phase 1: partial repolarization, opening of K+ channels. It is called “transient out “I_{to} “ current” (Not in skeletal).

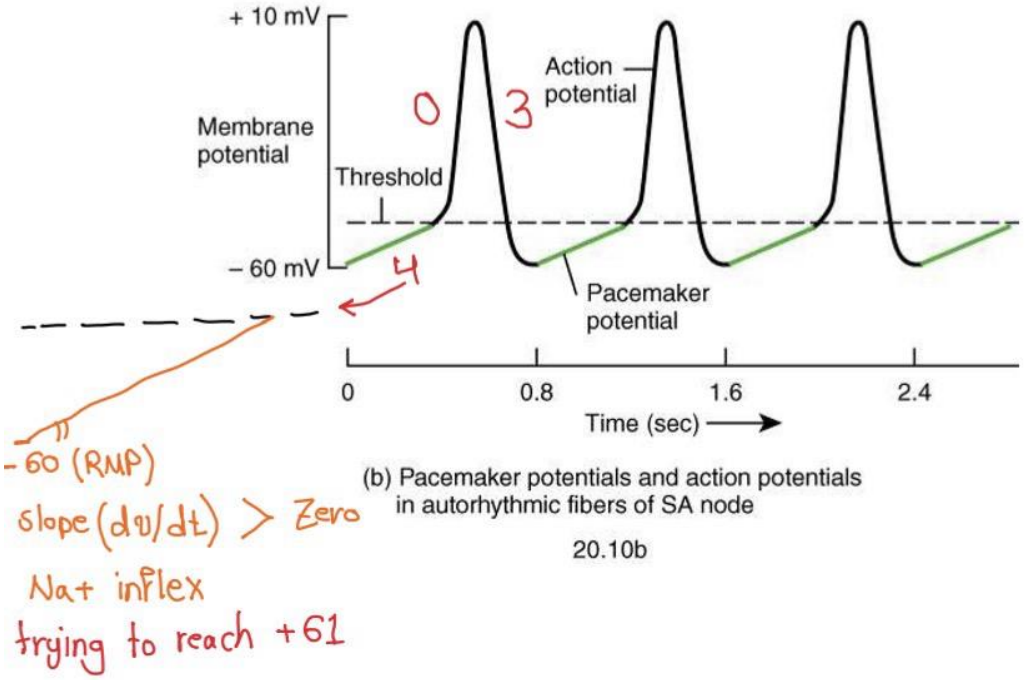
Phase 2 (Plateau Phase): During this phase, the membrane potential remains stable at approximately +10 mV for nearly 250 milliseconds. This stability occurs because the net charge movement across the membrane is zero (□); the influx of positive calcium ions is precisely and perfectly balanced by the efflux of

positive potassium ions. This prolonged plateau is a physiological 'gift' from God that ensures the heart has enough time to contract and relax without the risk of tetanization.

Phase 3: fast repolarization phase (K+) repolarization. The same in both

Phase 4: resting membrane potential.The same in both
No plateau = no phase 1 and 2 as the myocytes

The instability of Phase 4 in the SA node is mathematically defined by a positive slope (□), where the change in voltage over time ensures the membrane reaches the threshold autonomously. Unlike skeletal muscle, which maintains a stable resting potential, the heart's pacemaker cells utilize this inherent instability to dictate the rhythm of contraction without requiring an external neural trigger



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

20.10b

Sodium channels are not identical; they differ in their gating mechanisms and kinetics. Some are voltage-gated, others are ligand-gated, mechanically gated, or thermally gated, meaning they respond to different stimuli and open at different membrane potentials.

Funny channels (If) are unique voltage-gated channels found in pacemaker cells (SA node). They open at hyperpolarized potentials (around −60 mV) and allow mainly Na^+ influx, generating a slow spontaneous depolarization (phase 4). This gradual depolarization is then followed by the opening of Ca^{2+} channels, which complete the depolarization process.

Conduction system composed of:

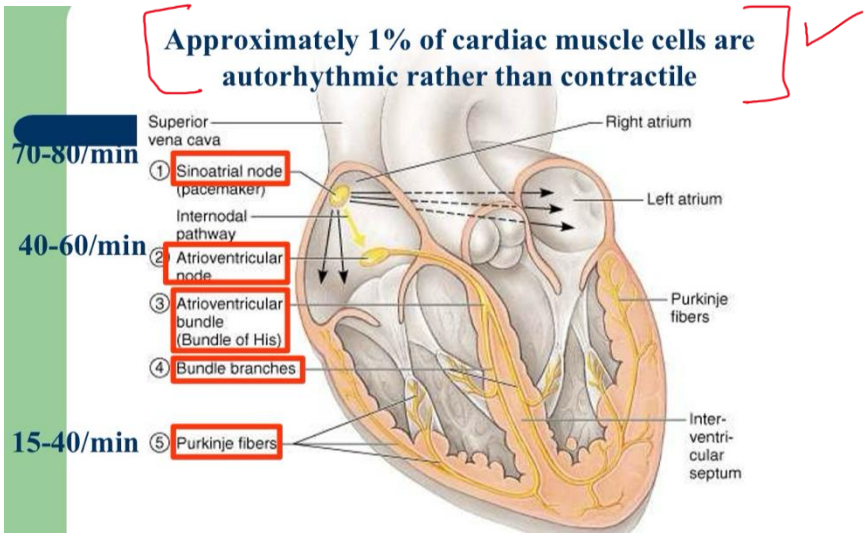
A-Sinoatrial (SA node) pacemaker

B-Atrioventricular node (AV)

C-Atrioventricular bundle (bundle of his)

D-Bundle branches

E-Purkinje Fibers.



The anatomical distribution of the cardiac conduction system involves specialized auto-rhythmic cells, which are approximately **1%** of the total cardiac muscle mass. As illustrated in the figure, each has a different discharge rate: the SA node (70–80 bpm), the AV node (40–60 bpm), and the Purkinje fibers (15–40 bpm). This hierarchy ensures that the fastest part, the SA node, typically functions as the dominant pacemaker.

the Sympathetic nervous system reaches all three areas (SA node, AV node, and Ventricles). However, the Parasympathetic nervous system only reaches the SA and AV nodes and does not innervate the Ventricles.

Each of these parts can spontaneously generate APs at a given rate (they are Self-excitable) but the fastest of them is the SA node.

If the primary pacemaker fails, latent pacemakers drive the heart at lower survival rates: SA Node: ~75 bpm, AV Node: ~50 bpm, and Purkinje Fibers: ~30 bpm.

SA node is **the pacemaker** of the heart (it determines heart rate), because it is more leaky to Na+ more than any other cells in the heart. And it reaches the threshold earlier.

- the term "threshold" refers to the membrane potential at which **fast** voltage-gated Ca^{2+} channels open, leading to the upstroke (depolarization).

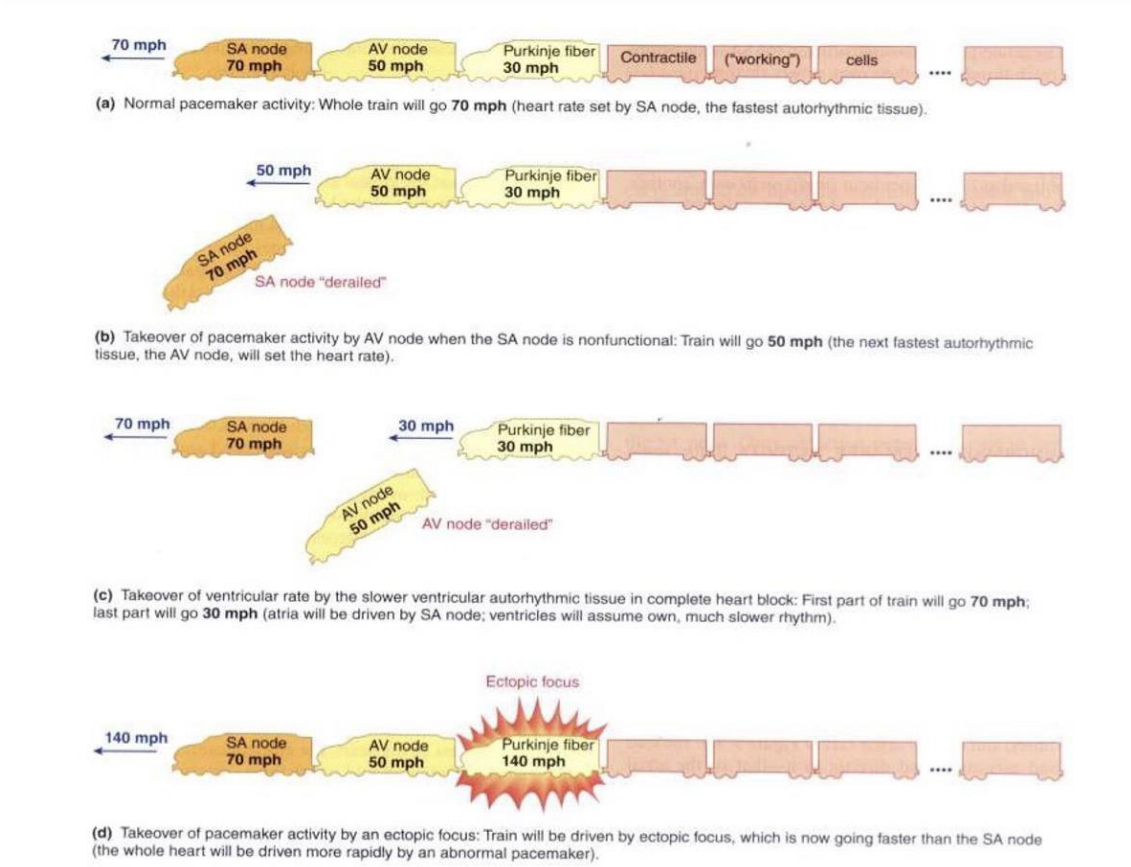
Phase 4 slope of AV < SA node, so it takes longer time to reach thresholds. (Please, look at the note in the last page to clarify this point)

In the SA node, the I_f (funny) channels open at -60 mV and close at -50 mV. Subsequently, 'slow inward' Calcium channels open at -45 mV to continue depolarization toward the threshold.

There is a conducting pathway from SA to AV node and both atria (From SA to left atrium through interatrial bundles. From SA to right atrium through three internodal pathways) which have very high conduction velocity to AV before it reaches threshold by itself.

AV node can not express itself, reach threshold or become pacemaker by itself, because it is over driven (suppressed by cell which has higher rate). The latent pacemakers undergo overdrive suppression. The tissue is suppressed because it is driven by other tissues. Tissue is suppressed if they are stimulated at high frequency (this include SA if receives electrical stimulus).

The nervous system and pharmacological agents regulate the heart through three distinct mechanisms: Chronotropic Effect (regulation of rate/time), Dromotropic Effect (regulation of conduction velocity), and Inotropic Effect (regulation of the force of contraction).



Think of the heart's rhythm as a **train with multiple engines**. The fastest engine always sets the speed for the entire train—a rule known as **"overdrive suppression."**

- **Normal Pace (a):** The **SA node** is the lead engine, running at **70 mph** and keeping the whole heart on track.
- **Backup Engine (b):** If the SA node fails, the **AV node** takes over. However, it is a slower engine, running at only **50 mph**.
- **Complete Block (c):** If the connection breaks, the heart splits. The top part (atria) stays with the fast engine, but the bottom part (ventricles) is forced to use its own very slow rhythm of **30 mph**.
- **The "Rebel" Engine (d):** An **ectopic focus** is like a rogue engine that suddenly fires at **140 mph**. Because it is the fastest, it forces the entire heart to follow its dangerously rapid pace

If we have sss (sick sinus syndrome), then the AV node will lead the heart so HR (heart rate) will be slower, almost 50 beat per minute, and we can survive with this.

The normal heart rate ranges from 60 to 100 beats per minute (bpm). A heart rate above 100 bpm is defined as Tachycardia, while a rate below 60 bpm is defined as Bradycardia. Similarly, in respiratory terms, fast breathing (>20 breaths/min) is known as Tachypnea and slow breathing is termed Bradypnea.

If we cut AV bundle (complete AV block), we disconnected any communication between atrium and ventricles, so it become complete AV block, so the atrium will give 75 beats alone, while the ventricles be the pacemaker (30 bpm).

But 30 not enough to sustain cardiac output. This condition .necessitate the implantation of artificial pacemaker

Q = HR * SV, (SV volume blood ejected per beat)

Note: AV bundle, bundle branches, and Purkinje fibers, they are all leaky to Na+ but less leaky than SA and AV nodes. Thus, they take longer time to reach threshold, with AV node they are called latent pacemaker (hidden), they are suppressed by SA node.

We have two syncytia electrically separated by fibrous ring, the first one between the atrium (atrial syncytium), while the second one between the ventricles (ventricles syncytium). Both are **Functional Syncytia**

There are gap junctions (some sort of electrical synapses or **electrical windows**) which once you stimulate one cell the others will be stimulated in no time, they act as one cell.

Between atrium and ventricle there is no communication, they are separated by electrical insulator (fibers ring).

The only way both syncytia can communicate is via AV bundle.

This pathway incorporates a critical delay of 0.12 seconds within the AV node, resulting in a total time of 0.16 seconds before the impulse reaches the ventricles. This delay is physiologically essential to provide the atria sufficient time to contract and empty their blood volume into the ventricles. Without this AV delay, the atria and ventricles would contract simultaneously; the much higher ventricular pressure (120 mmHg) would close the valves prematurely, forcing blood to flow retrograde back into the venous system instead of being ejected into the arteries.

There is no syncytium at the fibers in skeletal muscle, they act as separated "motor units" or motor unit as room lights; when you press a button, you turn 5 lights at once, another button will do another 5 lights, …etc. In contrast, the heart where there is all or non, they all contact at the same time as one unit(in heart).

Ventricular cells have a different resting membrane potential compared to other cardiac cells. In ventricular cells, the resting membrane potential is about **-90 mV**, while in cells like the SA node it is around -60 mV. This means ventricular cells are more negatively charged at rest.

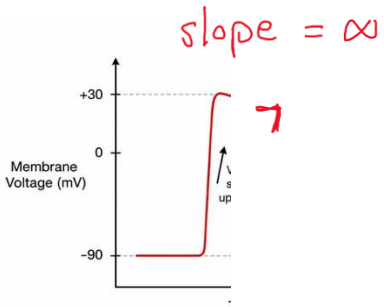
At -90 mV, the **fast** voltage-gated sodium channels are in the closed but activatable state. The m gate (**activation gate)** is closed, while the h gate (**inactivation gate)** is open. When a stimulus arrives, the ***m gate*** *opens very quickly*, in about **0.2 milliseconds**, allowing sodium ions to enter the cell.

This sodium entry happens because of the electrochemical gradient: sodium concentration is higher outside the cell, and the inside of the cell is negatively charged, which strongly attracts sodium ions.

As sodium enters, it causes further depolarization, which opens more sodium channels. This creates **a positive feedback mechanism**, where sodium entry leads to more channel opening and even more sodium entry, causing a rapid rise in membrane potential.

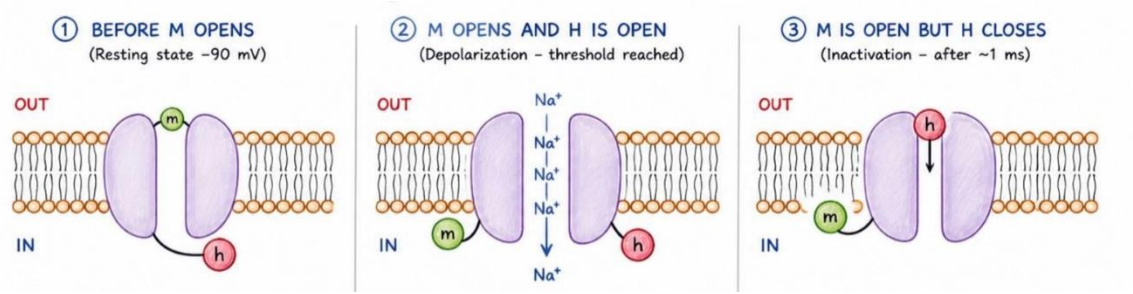
During this phase, the membrane potential rises **quickly** toward positive values, reaching about +30 mV. On *a voltage-time graph*, this produces a **very steep slope, which is often considered almost vertical (very high dV/dt, or "infinite slope" in theory)**. This means the change in voltage happens in a very short time, giving the impression that sodium entry takes "no time" to depolarize the cell. This is why the membrane potential rises sharply toward positive values during phase 0.

It does not reach +61 mV (the theoretical equilibrium potential for sodium) ***because the h gate closes after about 1 millisecond. This inactivation of the channel stops sodium entry before full equilibrium is reached.***



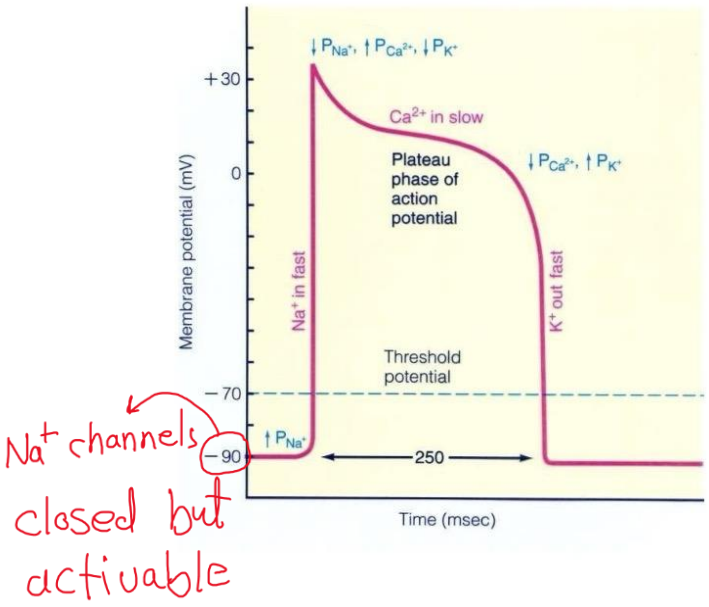
The h gate is slower than the m gate, and this difference in timing is important. The m gate opens very fast (about 0.2 ms), while the h gate closes more slowly (about 1 ms). This brief time window allows sodium to enter the cell before the channel becomes inactivated.

After the h gate closes, the sodium channel becomes **inactivated and cannot be reopened immediately**, even if the stimulus continues. This is what stops further sodium influx and limits the peak voltage.



In **SA node** cells, the membrane potential is about -60 mV, which is less negative than ventricular cells, so most fast sodium channels are already in the inactivated state because the h gate is closed at this less negative level, making the channels closed and not available to open, therefore fast sodium current cannot produce a strong rapid depolarization and cannot generate a steep upstroke, so **SA node cells require a slower depolarization mechanism using calcium (Ca^{2+}) influx**

The graph (the picture below) shows the action potential of ventricular **contractile** muscle cells -cardiac myocyte- (about 99% of heart cells), not the pacemaker/**conducting** system cells (about 1%), which have a different type of electrical activity.



Ventricle cells should not become pacemakers, the conductive pathway in the heart act as nervous system in heart, which have two function **excitation and conduction but not contraction.**
(same function of nervous system).

We call ventricular cell fast response action potential FRAP, while SA node slow response action potential SRAP (the depolarization slow that mean take along time to reach the peak).

Reach the peak to get complete depolarized in order to be able to depolarize your neighbouring cell, so we need two things, depolarized itself and electrical stimulation to contract in no time.

We don't want one part of the heart to contract while other part is relaxing, we need to contract as one unit, otherwise its inefficient contraction (it will not give you anything).

The high conduction velocity ensures all cells reach peak depolarization nearly simultaneously, allowing the ventricle to contract as a single mass unit for effective blood ejection

Phase zero in ventricle the slope is extremely high, it reaches depolarization very fast, fast Na+ channel work (have m gate and h gate), which works by positive feedback after stimulation, each Na+ leads more and more to influx. This happens very

rapidly as the m gate opens.

Sodium channels exhibit diverse kinetics and activation triggers; while some are strictly voltage-gated, others may respond to physical stimuli such as temperature and pressure, or chemical substances. The I_f (funny) channels, specifically, are voltage-gated but characterized by their unique activation at hyperpolarized levels around -60 mV.

The ventricular potential peaks at +30 mV (instead of +61 mV) because the h-gate (inactivation gate) is slow; it closes as the membrane becomes 'less negative' (around - to -60 mV), halting □ influx before the maximum equilibrium is reached

(FRAP) Phase 4 stable with respect to time dv/dt is almost zero (slope). As we say to the ventricle: if you need depolarization, I will give you the order because you cannot reach threshold by yourself (cannot leak Na+ as SA/AV nodes), because if you do that, I will die. So, Na+ channels are completely close. Stimulated by only an external stimulus (Purkinje cells).

-90 mV we need it to change the state of Na+ channels from closed inactive (as it is in -60 mV) to closed active, this cell in ventricle once it stimulated it will utilize the fast Na+ channels they will bring the AP to the peak in no time.

Imagine that we force the SA node resting potential to increase (more negative) from -60 mV to -90 mV as in ventricular cells, by injecting it with Cl-, fast Na+ channels (channels responsible of driving the AP to the peak in no time) will open as it's stimulated.

Ectopic pacemaker: structures that can take the role of the normal pacemaker (SA node).

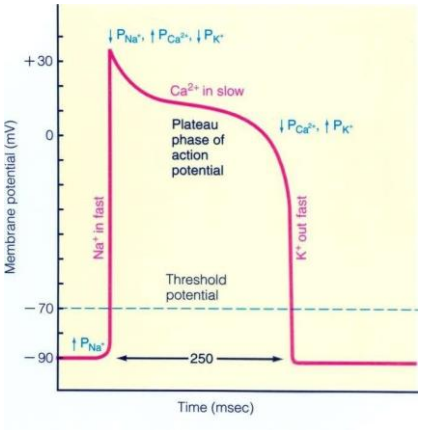
In case the ventricles start to be pacemaker, which causes extreme increase in the HR, so you lose the diastolic activity (ventricular fibrillation; deal with it by suppress it with a DC shock, or defibrillation=10,000 V)
If there is no transmission of action potentials from SA node to AV node, then there will be 2 pacemakers in the heart, one is the SA node, and another one (ectopic) for the ventricles as the electricity cannot reach them.

Function of heart is ejection (systole; 0.3 sec), to do that you must fill (diastole; 0.5 sec), if you want filling that means you need to relax if you not give it the chance to relax it will not fill (death).
The order is: relax, fill, contract, empty.

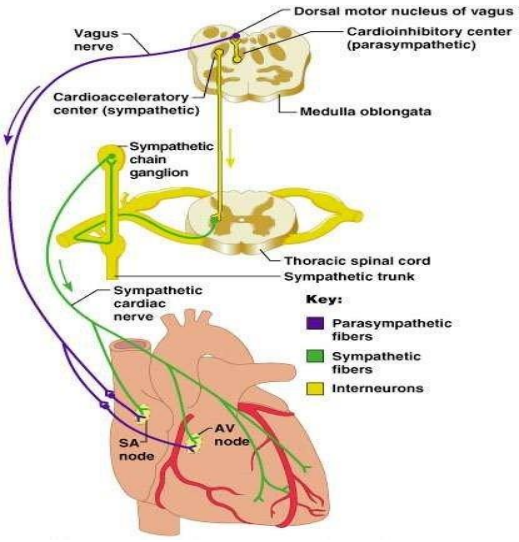
When multiple electrical stimuli are applied to a skeletal muscle at a sufficiently high frequency, twitches merge into higher force contractions, a process referred to as summation. Tetanus is the rigidity of muscle because of maximum summation. Tetanus is sustained contraction without relaxation. Due to the long action potential, cardiac muscle cannot be tetanized.

Sustained contraction without relaxes very painful in skeletal muscle , there are brown to tetanisation (means pain), because the AP is so short, and you can restimulate the muscle after 2ms. It is not life-threating in the lower limbs

Tetanisation for the heart means death because the sustained contraction of the heart means there is no diastolic activity. The presence of phase 2 (plateau phase) prevents the tetanisation.



Extrinsic Innervation of the Heart:



In the medulla oblongata in CNS near

to the neck. Sympathetic ANS branch

in: SA node, AV node, ventricle.

It releases of norepinephrine: increase funny current (If+) and calcium current (Ica++), increase slope for phase 4 so it reaches the threshold faster, so you shrink the cardiac cycle duration (decrease the duration), so it increases the HR (Tachycardia). This is called ***Positive Chronotropic effect.***

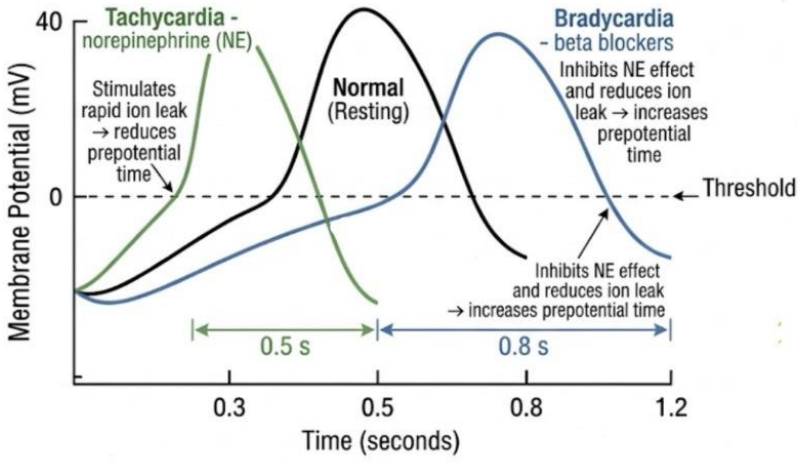
Positive Chronotropic effect (increased rate of sinoatrial node or SA node discharge = increased heart rate).

Positive Dromotropic effect (increase conduction velocity through the AV node).

Positive Inotropic effect: by increasing calcium current (Ica++), thus, increasing the contractility or the force of contraction in the ventricle. Acting especially on the phase 2. Increasing stroke volume

If the factors decreased instead, we call it negative (chronotropic/dromotropic/inotropic) effect.

Some medicines antagonize تعكس the effect of ***noropendipine***. It causes bradycardia. This **bradycardia** slows the rate of the heart, causing **negative chronotropic effect. Beta blockers** are an example of these medicines which cause bradycardia. They are famous. Most of older adults whose age is more than sixty use these medicines for cardiovascular diseases.



Calculations and Concepts

Term	Time for One Beat (seconds)	Calculation (Beats per Minute, bpm)	Physiological State
Normal (Normal)	0.8 s	$\frac{60}{0.8}$ = 75 bpm	Typical Resting State
Tachycardia (Accelerated HR)	0.5 s	$\frac{60}{0.5}$ = 120 bpm	Due to Nore-pinephrine (NE)
Bradycardia (Slowed HR)	1.2 s	$\frac{60}{1.2}$ = 50 bpm	Due to Beta Blockers

(Term) المصطلح	(bpm) معدل ضربات القلب
Normal (طبيعي)	60 - 100
Tachycardia (تسارع)	أكبر من 100
Bradycardia (تباطؤ)	أقل من 60

$$\text{Heart Rate} = \frac{60}{\text{Time for One Beat}}$$

The **sympathetic nervous** system increases heart activity: it produces a positive chronotropic effect at the SA node (increases heart rate), a positive dromotropic effect at the heart AV node (increases conduction velocity), and a positive inotropic effect in the ventricles (increases the force of contraction).

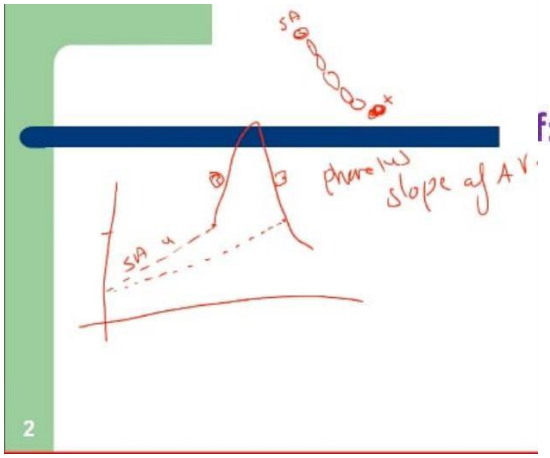
Parasympathetic ANS branch in: SA node, AV node only.

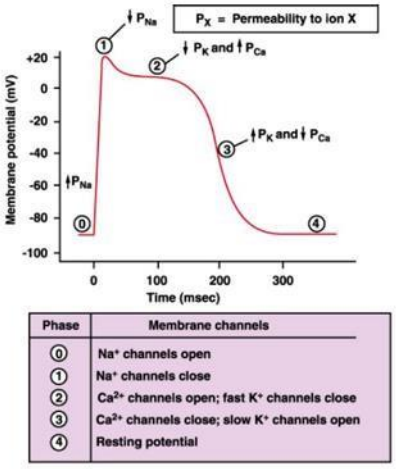
By Vagus (cranial tenth; X) nerve.

The **parasympathetic nervous** system decrease heart activity: it produces a negative chronotropic effect at the SA node (decrease heart rate), a negtive dromotropic effect at the heart AV node (decrease conduction velocity).

It releases of acetylcholine: decrease increase funny current (If+) and calcium current (Ica++) and increase K+ outflux, so decrease HR (with no effect on contractility) = negative chronotropic and dromotropic (by decreasing conduction velocity through the AV node effects.
HR if it is low or high both will be very bad.

VERY IMPORTANT NOTE: Please be careful that when we said: "Phase 4 slope of AV < SA node, so it takes longer time to reach threshold", we meant the phase 4 of the SA/AV node action potential (the first picture below), not the cardiac muscle (ventricular) potential (the second picture below).



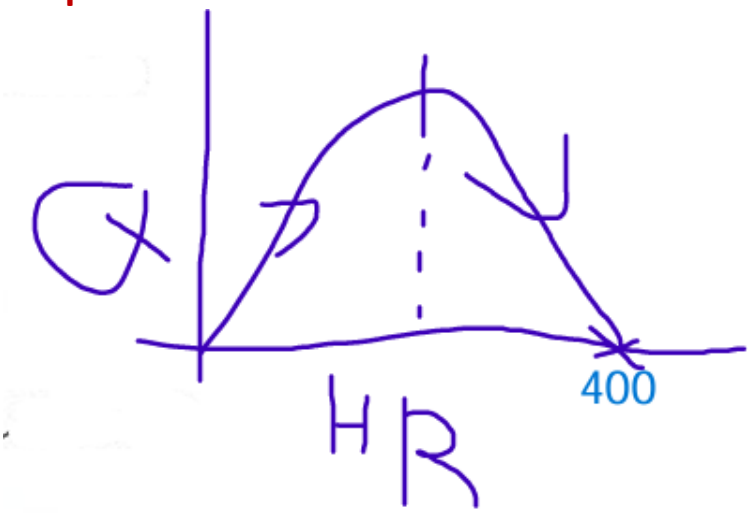


During plateau at +10 mV, where the h gate (the inactivation gate) is the one that closes the Na+ channels. That means these channels will remain close even if a strong stimulus is applied, thus, cannot start a second AP. It is a refractory period. This is why it prevents heart tetanization.

Tetanization doesn't happen in the heart because the action potential duration is prolonged and because of the existence of phase 2 (plateau face).

Note that the negative relationship between HR and stroke volume. That makes the ventricular fibrillation very dangerous (which increases the HR as we said).

Considering what was said above, the relationship between the heart rate (HR) and cardiac output (Q) follows the bell-shaped curve below:



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

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

Additional Resources

رسالة من الفريق العلمي:

Dr. Yanal's recorded lecture 2 and the ppt of the lecture.

For any feedback, click the code.

Versions	Slide #	Before	After
V0 → V1			
V1 → V2			