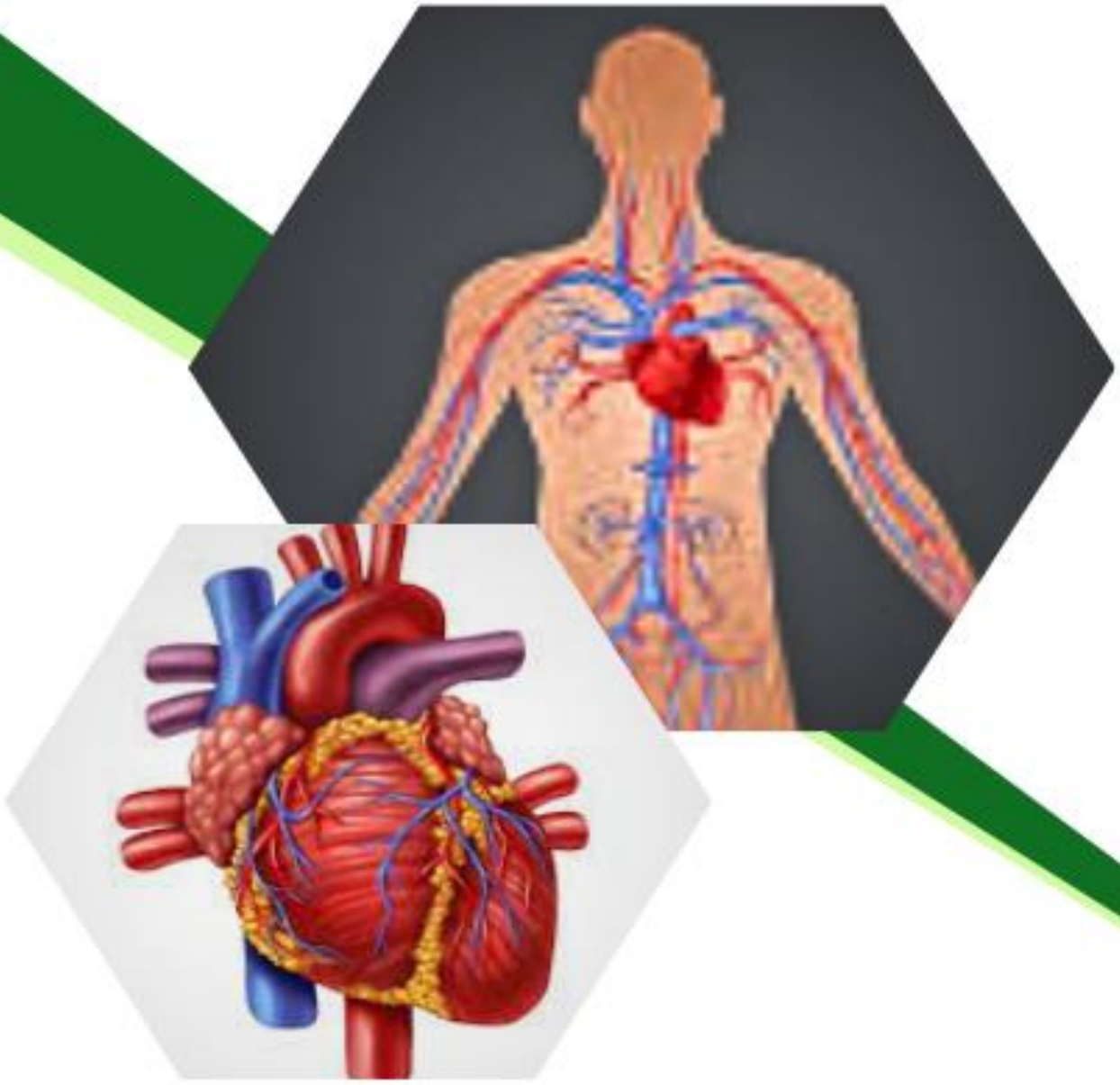
Doctor.021
no.3

CVS
PHYSIOLOGY



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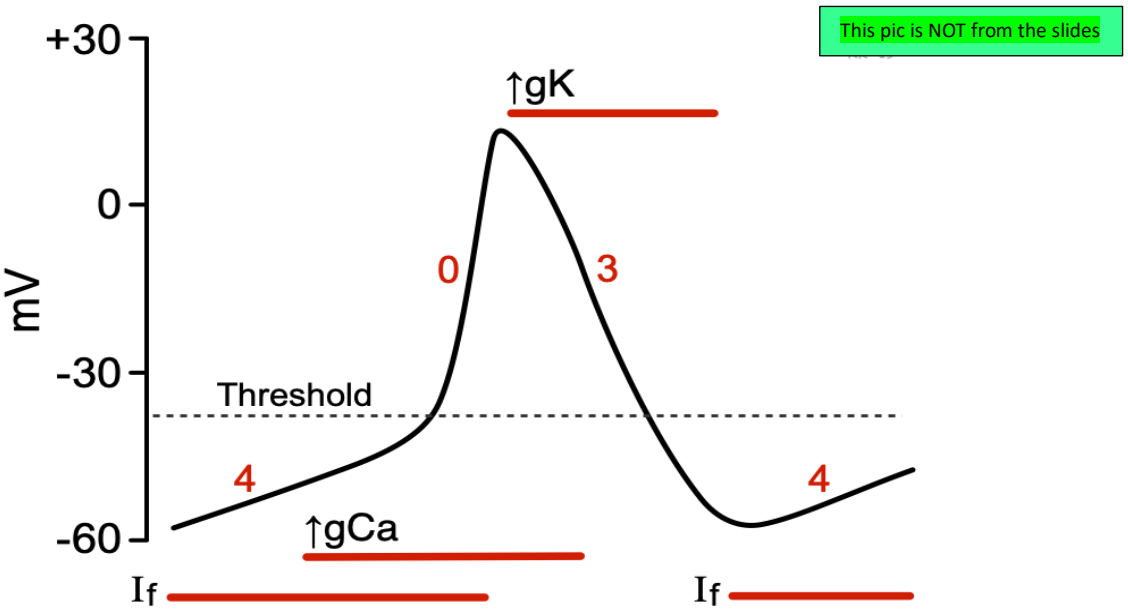
**Italic and green → From google for further explanation.*

SA node action potential (slow response action potential)



Phase 4 :

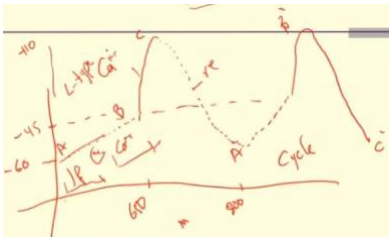
- Also called the diastolic resting state or resting membrane potential.
- During this phase, a slow leakage of current through the slow channels of the cellular membrane leads to spontaneous depolarization, the membrane potential slowly becomes more positive, until it reaches the threshold (around -45mv).
- At -60 mv (resting membrane potential):
  - ✓ we have an ascending wave (resting depolarization wave)
  - ✓ moderate slope (Na+ ions are entering the cells but at a slow rate)
  - ✓ Na+ ions enter the cell (If or funny current), **why?** Because Na+ has an equilibrium potential of +61, so Na+ ions enter the cell until its potential reaches +61. (Remember: driving force = Em-ENA + * gNa+)
  - ✓ These Na + channels will be closed, and ca ++ transient channels will be opened.
  - ✓ fast Na+ channels are closed and inactive (can't be open upon stimulus).
- Between (-50mv and -45mv) transient Ca++ channels (t-type) open and Ca++ enter the cell, they remain open and close when it reaches the threshold (-45 mv).
- This phase takes 650 milliseconds

Phase 0 :

- Is the depolarization phase of the action potential.
- After threshold is achieved at -45mv, Calcium long lasting channels (L-type channels) open, leading to depolarization.
- This phase ends at +10 mv (its amplitude = +10 - -60 =70 mv).

Phase 3 :

- Repolarization occurs as K+ channels open.
- At +10 mv, K+ channels open, and due to electrochemical gradient, K+ ions leave the cell, leading to a drop in the charge (but it doesn't reach -90mv), this is called repolarization.
- Its takes 800 milliseconds (0.8 seconds) from the beginning of phase 4 to the end of phase 3, i.e. from A to À in this figure, this is only one cycle.



- The frequency of action potential generation in the SA node is 75 bmp (beat per minute) in normal conditions (60 sec ÷0.8).
- **What is tachycardia?**
  A heart rate that's faster than normal (~120 bmp in a 0.5s cycle)
  How does it happen?
  In case of sympathetic stimulation, NE binds to Beta-adrenergic receptor type 1 → activation of cAMP → activation of protein kinase A → Ca++ & Na+ channels phosphorylation → entry of Na+ and Ca++ → shorter phase 4 → faster action potential → higher HR.
- NE, E, dopamine and thyroxine are tyrosine derivatives, and they all can produce tachycardia. So Thyrotoxicosis patients have tachycardia, while hypothyroidism patients have bradycardia.

In general, adrenergic stimulation (sympathetic) causes the action potential firing rate to increase and cholinergic stimulation (parasympathetic) causes the action potential firing rate to decrease.

- Parasympathetic:
  - ✓ Decreases If
  - ✓ Decreases Ca++
  - ✓ Increases K+

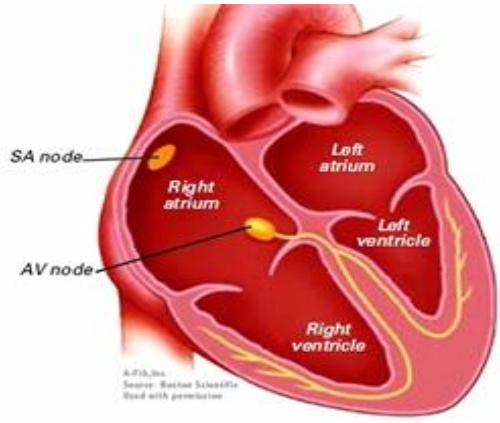
- Sympathetic:
  - ✓ Increases If
  - ✓ Increases Ca++
  - ✓ Decreases K+

- When you increase potassium current (outward K+), it makes the membrane potential more negative, and it becomes difficult to reach the threshold. This is how Ach (Acetylcholine) works, it extends phase 4 causing bradycardia.
- We call any drug that increases heart rate (tachycardia) a **positive chronotropic drug**
- Any drug that decreases heart rate (bradycardia) a **negative chronotropic drug**

QUICK REVISION

The heart has 3 electrically important areas:

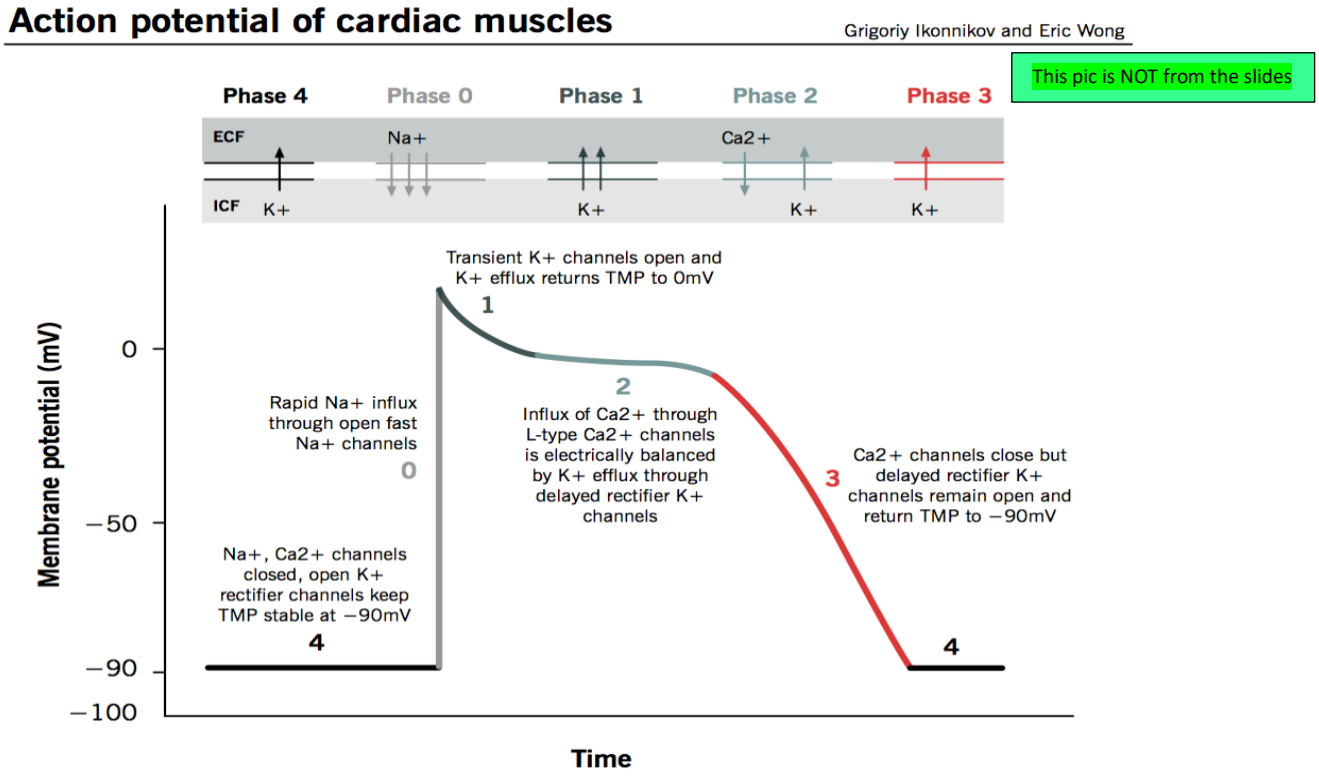
The SA node, The AV node and the ventricle.



- 3 Sympathetic branches:
  1) To the SA node, increases heartrate (+ve chronotropic)
  2) To the AV node, increases conduction velocity (+ve dromotropic effect)
  3) To ventricles, increases Ca++ entry (increases contractility) (+ve inotropic)

- Parasympathetic (vagus nerve)
  1) To the SA node, decreases heartrate (-ve chronotropic)
  2) To the AV node, decreases conduction velocity (-ve dromotropic effect)
  3) No parasympathetic effect on ventricles by the vagus nerve (even though there are muscarinic receptors on them, so injecting the patient with acetylcholine causes -ve inotropic effect).

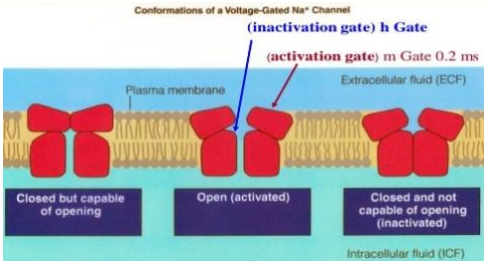
Ventricular myocyte action potential(fast response action potential)



- Note that phases 1 & 2 are present here in fast response, unlike slow response.
- Resting membrane potential = -90mv
- At **-90mv**, **fast sodium channels are closed but active**
  Meaning that once the ventricle is stimulated, sodium channels will open leading to huge amounts of sodium entering the cell. Phase 4
- This will lead to depolarization (voltage will reach +30mv in no time) (extremely high slope, almost a right angle). phase 0
- After it reaches +30 mv, Na+ channels close.
- Transient K+ channels open leading to K+ efflux phase 1
- Ca++ & Na+ influx, and K+ efflux occur simultaneously, leading to an action potential of +10 mv for 250 milliseconds (plateau). phase 2. In this phase the entry of calcium is balanced by the exit of potassium (1 Ca++ enters: 2 K+ leave)
- At phase 3, Ca++ channels are closed, more K+ channels are opened, causing the membrane potential to go back to -90mv.

❖ Few important notes that you should keep in mind:

- **During plateau phases (phase 2), fast Na+ channels are closed and inactive**.

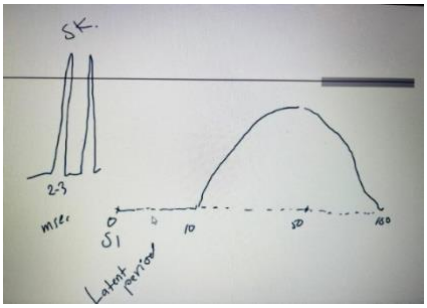


- At this phase, the M gate or the activation gate is not blocking ions entry, whereas the H gate or the inactivation gate is blocking the channel. Giving a second stimulus at this phase won't generate action potential because the H gate will only move if the membrane potential go back to -90mv.
- During phase 0, the conduction occurs very fast and the slope (dv/dt) is almost infinity, so once the first cell is depolarised the action potential will be conducted to the adjacent cells in no time.
- If phase 0 consumed time, the contraction of the first cell would end before the action potential reaches the last cell.
- In phase 4:
  - ✓ Voltage is stable with respect to time
  - ✓ Slope=0
  - ✓ Positive ion influx (Ca++ and Na+)= positive ion efflux (K+).
- Ventricular cells are not autorhythmic (they cannot bring themselves to the threshold)
- They reach the threshold upon external stimulus (SA node, AV node, AV bundle, Purkinje fibers)
- As you know, the heart is divided into 2 parts: upper atria and lower ventricles
- Muscles of the atria and those of the ventricles are arranged to form an atrial and ventricular syncytium. syncytium is an arrangement of muscle fibers in which the fibers fuse to form an interconnected mass of fibers. So, you can't stimulate an atrium and leave the other, nor can you stimulate a ventricle and leave the other. Due to the presence of gap junctions between their cells, they work as all or none.
- A fibrous ring is present between the atria and the ventricles. It works as an electrical insulator. So you can't depolarize a cell in the ventricle by stimulating a cell in the atrium.
- The only normal electrical connection between atria and ventricles is through the AV node and AV bundle.

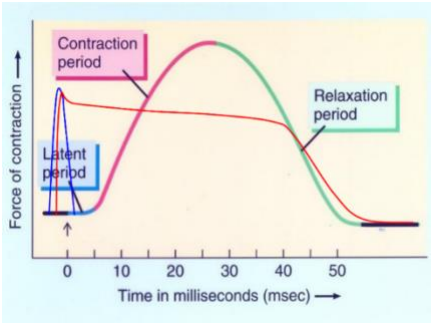
- Imagine if a patient came to you with abnormal connection between the atrium and the ventricle (other than the normal AV node and AV bundle), what you should do? You should perform cardiac ablation.

comparison between skeletal & cardiac cells

Cardiac Muscle action potential Vs. Skeletal Muscle:



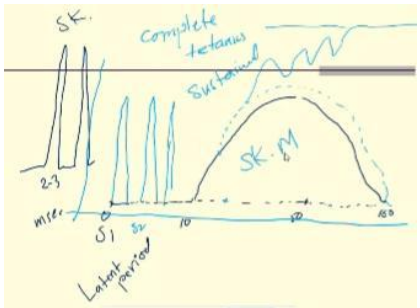
- Phase 0 –Depolarization phase (Na+ Influx)
- Phase 1 partial repolarization (Not in Skeletal)
- Phase 2 Plateau (depolarization not in Skeletal) slow calcium channels
- Phase 3 fast repolarization phase (K+ efflux
- Phase 4 resting membrane potential



- Skeletal muscle action potential takes 2-3 milliseconds, so after 2-3 milliseconds you can stimulate the fiber and you get a new action potential.
- So in skeletal muscle (for example the gastrocnemius muscle), we give stimulus after 10 seconds(latent period), contraction follows that and it takes 40 milliseconds, then relaxation period takes 50 milliseconds.

Latent period: The time between the activation of a motor neuron until the muscle contraction (sliding) occurs (the time required by the action potential to move from the sarcolemma through T-tables and the SR, the release of Ca ++ from the SR or the calcium induced calcium release, the binding of Ca ++ with troponin c which is bound to troponin T, the moving of tropomyosin, the binding of myosin heads and the sliding of the of the fibers).

- So this muscle's twitch duration = 100 milliseconds (intermediate)
- Eyelid muscle for example takes from 10-20 milliseconds (very fast)



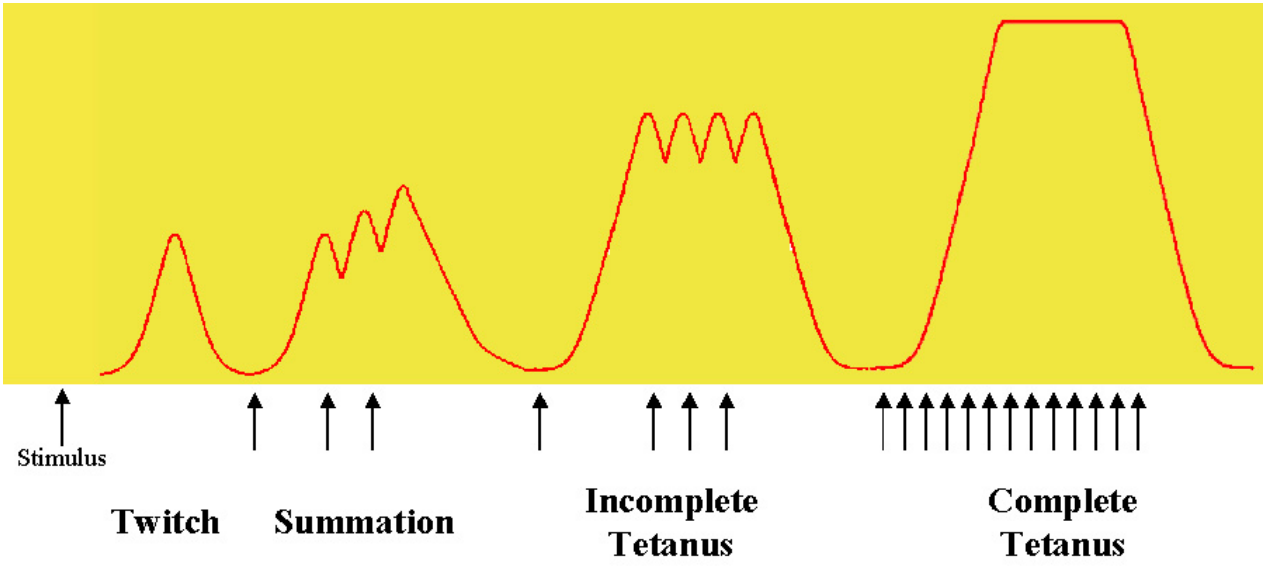
- In this picture, the dr explained what happens when multiple stimuli that cause contraction act on a muscle that is already contracted. Here, we use summation.
- Stimulation of the smooth muscles while contraction is still on process will lead to the

initiation of the second contraction before finishing the first, causing summation of contractions.

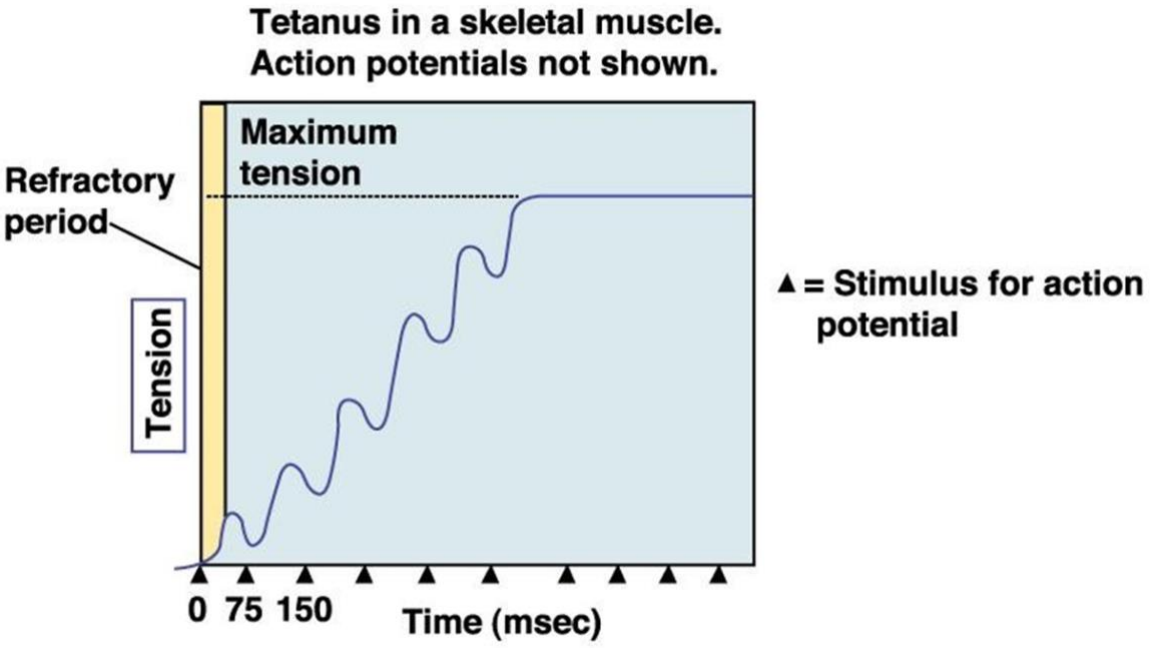
- Continuous stimulation will lead to sustained contraction which is called tetanus.

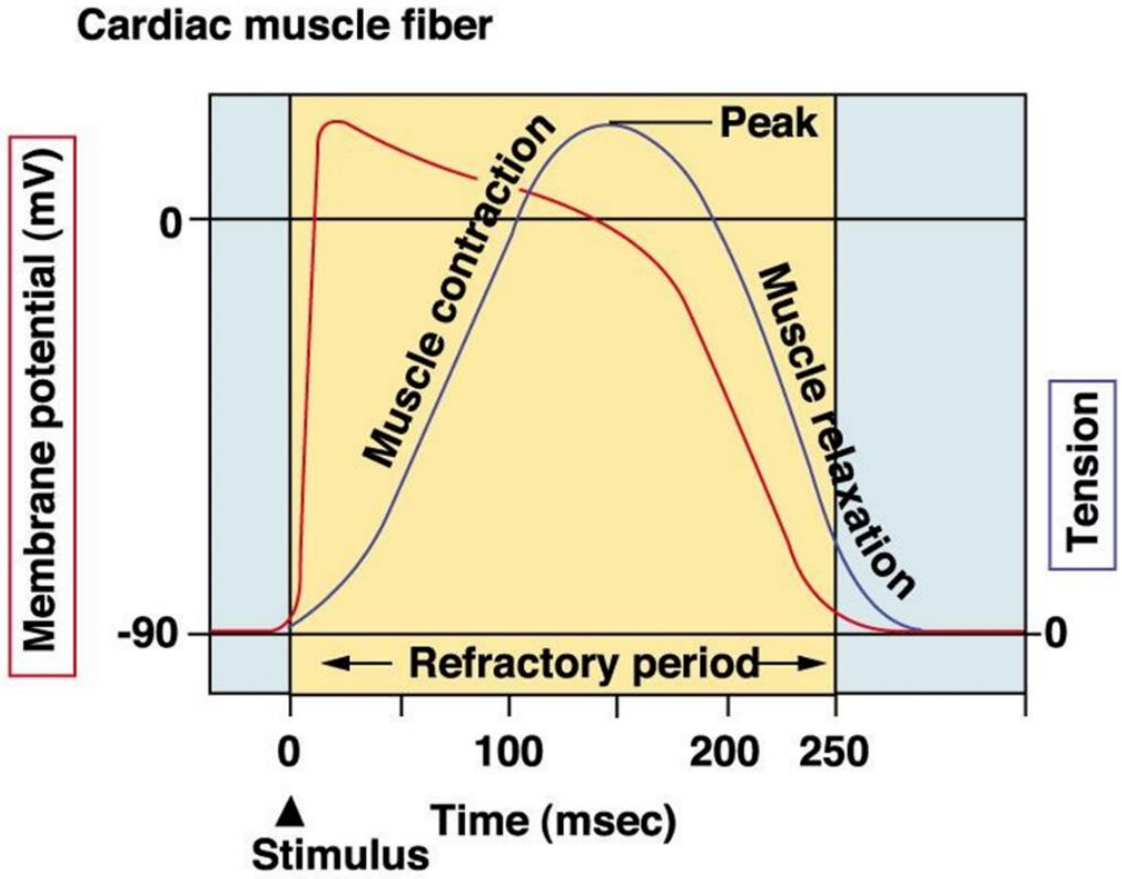
Summation occurs as successive stimuli are added together to produce a stronger muscle contraction.

- *Tetanic contraction: is the result of repeated stimuli at such short intervals that the muscle fiber (or muscle) doesn't have time to fully relax before it is called upon to contract again.*
- *Complete tetanus: If the stimulus frequency is so high that the relaxation phase disappears completely, contractions become continuous.*



- Skeletal muscle is borne to tetanisation, because the action potential duration is short (2-3 milliseconds) and then you can re-stimulate.
- While in the heart, its different. The refractory period of cardiac muscle (250 milliseconds which covers the entire contraction) is dramatically longer than that of skeletal muscle (2-3 milliseconds).
- This prevents tetanus from occurring and ensures that each contraction is followed by enough time to allow the heart chamber to be refilled with blood before the next contraction so that effective ejection (the main function of the heart) can occur.
- Note that there is no summation in cardiac action potentials and contractions.
- If the ventricles tetanized → no enough time for filling → no enough blood is ejected → death.


Tetanus in a skeletal muscle.
Action potentials not shown.
Maximum tension
Refractory period
Tension
▲ = Stimulus for action potential
0 75 150
Time (msec)

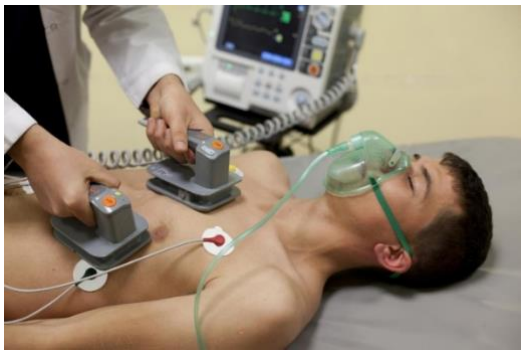

Cardiac muscle fiber
Membrane potential (mV)
0
-90
Peak
Muscle contraction
Muscle relaxation
Tension
0
Refractory period
0
100
200
250
Stimulus
Time (msec)

Ventricular fibrillation

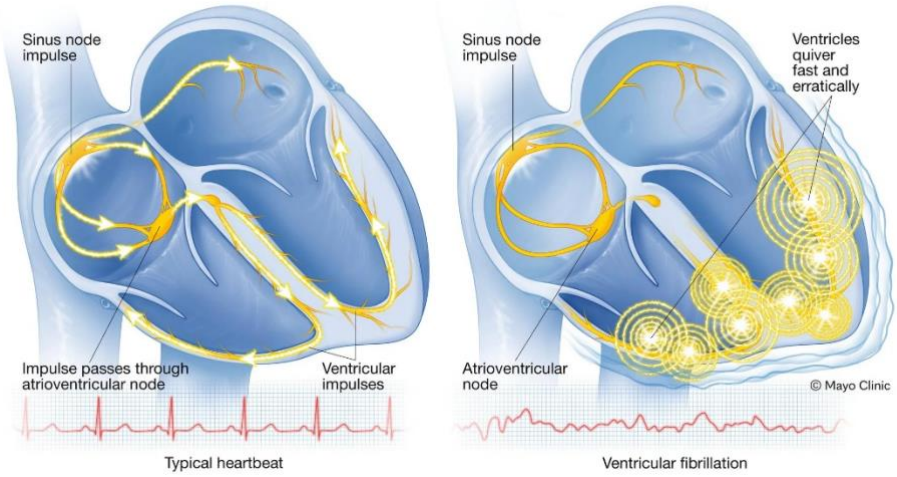
What happens in ventricular fibrillation?

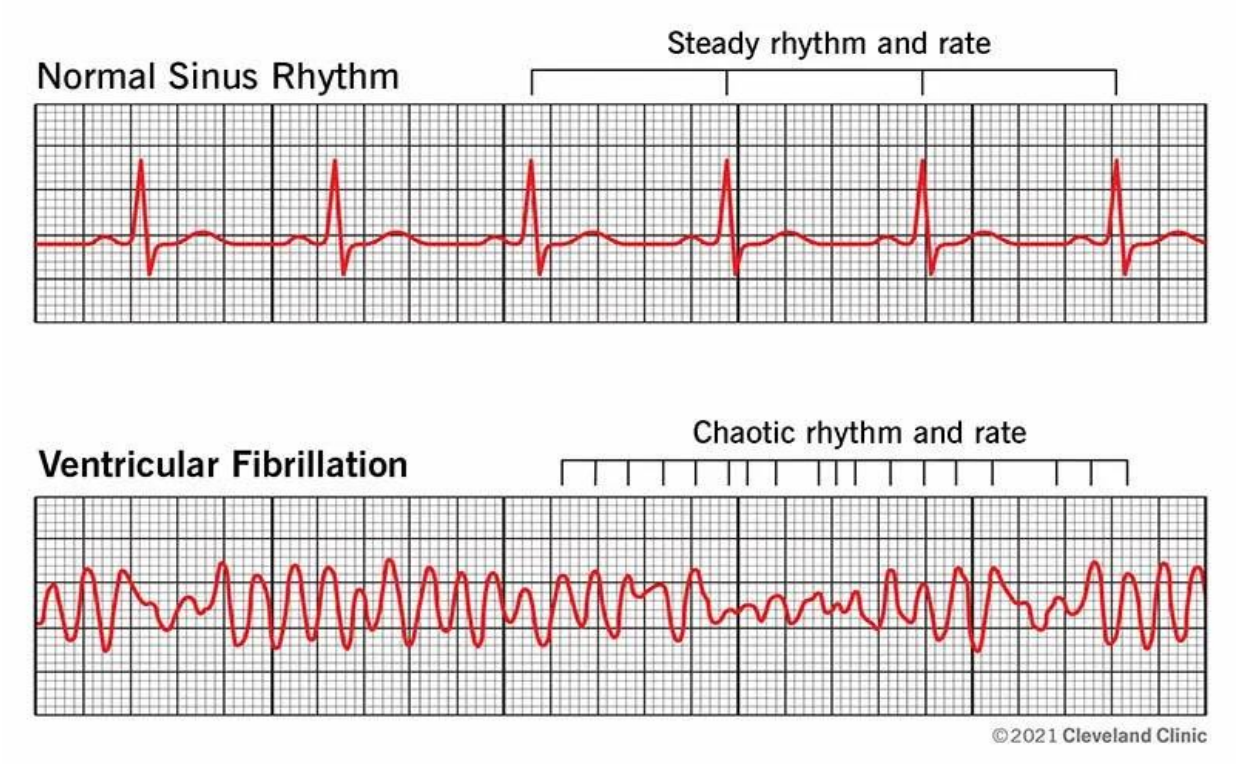
Ventricular fibrillation is a type of irregular heart rhythm (arrhythmia). During ventricular fibrillation, the lower heart chambers contract in a very rapid and uncoordinated manner. As a result, the heart doesn't pump blood to the rest of the body.

- In other words, when the ventricular rate is extremely high, this causes continuous contraction, no relaxation, no time for filling, no ejection, so it means death.
- It occurs when the ventricular cells start to produce their action potential on their own, increasing the heart rate to very high levels.
- The ventricular cells will be called ectopic base -maker.
- It usually occurs in cases of ischemic heart diseases like MI (myocardial infarction), ischemic foci may become pacemakers, that's why any MI patient needs to be rushed to the hospital
- If he has ventricular fibrillation, we give him a DC shock (10000 volt) with very high voltage to silence the SA node, the AV node and the ischemic foci (overdrive suppression) for about 30 seconds, until the recovery time is over and ischemic foci are silenced so that the SA node can take the lead again.



- Otherwise, if the patient gets ventricular fibrillation in his house or in the street it is very hard to help him (unless he came to the hospital within two hours).





Good Luck
V2

The changes are highlighted