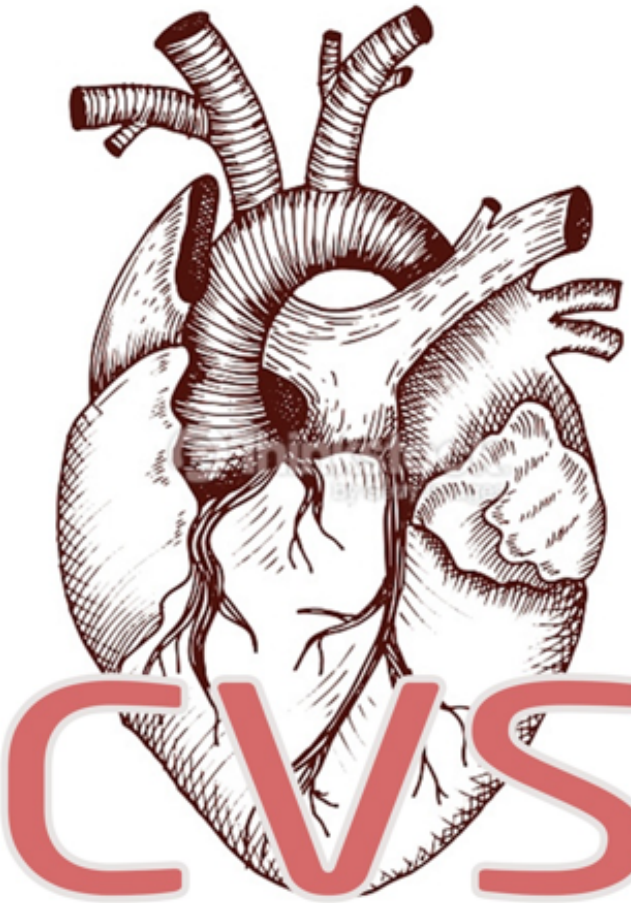

CVS

Physiology

♡ Slide Sheet ♥

Number:	2
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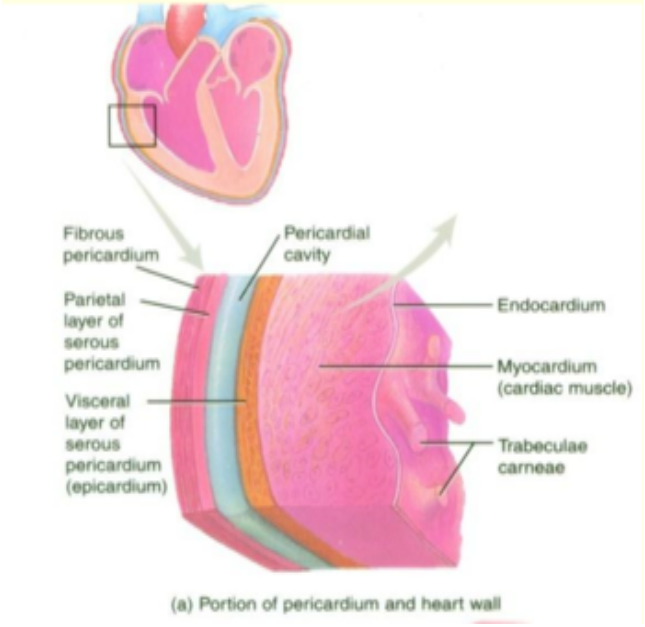
اللهمّ لا سهل إلا ما جعلته سهلا ، وأنت تجعل الحَزن إذا شئت سهلا

Cardiac muscle physiology

By taking a part from the wall of the heart , we will see that it is composed of three layers :



(a) Portion of pericardium and heart wall

1- **Endocardium** : the inner most layer . it is different from any other epithelial layer in our body by which it can secret hormones that affect the blood flow like NO which is an endothelial derived relaxing factor .

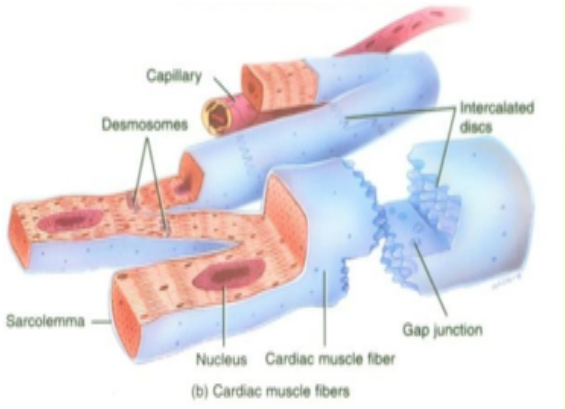
2- **Myocardium** : the most important layer , which is the contractile force of the heart .

3-**pericardium** : it has two layers ; one that is very close to the muscle called **visceral** and the other is away called **parietal .** and in between , there is a space called **pericardial space** or **cavity ,** it contains a proteinous fluid . the amount of this fluid is very little about 50-100 ml , and it is important to protect the heart from any damaging effects of shocks , same as the pleural and cerebrospinal fluids . it might increase in certain diseases , this is called **pericardial effusion** ; and if it is too much it might limit the ventricular filling ! . In other words , when the fluid increases , the filling of the ventricles by blood is becoming less reducing the input of the blood to the heart ;and consequently the cardiac output (ejection) will be less too . if the cardiac output reaches zero , it will lead to death .

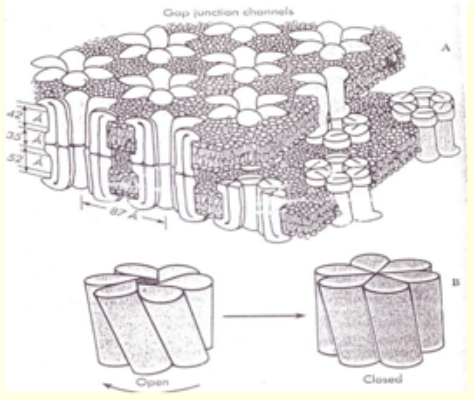
pericardial effusion is also known as **cardiac tamponade .**

The treatment is through the extraction of the fluid by a syringe in the hospital .But if the patient is away from the hospital , you must use any sharp (so we can create a hole in the pericardium) and save his life .Because patients with cardiac tamponade are in a very bad situation, they suffocate and strive for air. Thus, we don't care about infections, but rather the life of the patient. Once relieved, the patient will be able to breathe easily.

The Myocardium



The myocardial cells are different from the skeletal cells . the skeletal cells are spindle in shape going from the origin to the insertion ,they range from 1cm up to 100 cm long . On the other hand , the myocardial cells are very short with rectangular shape and they are interconnected with each other by **intercalated disc.** and in between these discs we have **Gap junctions** .



Gap junctions are hexagonal proteins , and they are voltage gated channels , they open or close according to the change in voltage . Once there is a change in voltage , the channel opens ; and because the cells are interconnected with each other , the adjacent channel will open too, as this change in voltage will spread to all cells . they are called **electrical couplers.**

From Guyton

at each intercalated disc the cell membrane fuse with one another to form permeable "communicating " junctions (gap junctions) that allow rapid diffusion of ions . Therefore , from a functional point of view , ions move with ease in the intracellular fluid along the longitudinal axes of the cardiac muscle fibers so that action potentials travel easily from one cardiac muscle cell to the next , past the intercalated discs . Thus , cardiac muscle is **syncytium** of many heart muscle cells in which the cardiac cells are so interconnected that when one cell becomes excited , the action potential rapidly spreads to all of them .

gap junctions are forming what we call **low electrical resistance area ,** which allows the spreading of action potential to all cells if one cell is excited . They are absent in the skeletal muscle .

The heart is composed of two syncytia :

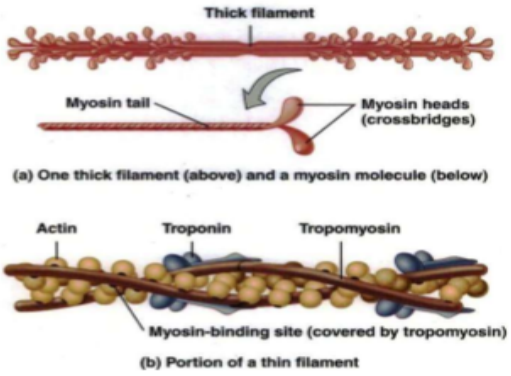
ventricular syncytium : since the interventricular septum between the two ventricles is composed of muscles, all cells of the two ventricles are interconnected with each other forming a syncytium , so they can function as a one unit .

atrial syncytium : in which all cells of the two atriums are interconnected with each other forming a syncytium .

remember that following an action potential is a mechanical response of contraction , and the importance of this syncytium is when there is an action potential in one cell, the action potential spreads to all cells through low resistance gap junctions , that's why all cells almost contract at the same time "**simultaneous contraction** " forming a force inside the heart . As the heart is a hollow organ and the cells are overlapping in all direction, when cells contract together the force is directed toward the center of the heart causing an increase in the pressure and pumping of the blood .

if there is no simultaneous contraction (every cell is contracted by its self ;one cell is contracted and the other is relaxed) , not enough force is formed ! this is called **Ventricular fibrillation** which is lethal . in this case we do **EC shock** to cause **defibrillation .** in contrast , the skeletal muscle does not have a syncytium .

as the skeletal muscle , the cardiac muscle is also striated . This striation is due to the overlapping between the contractile proteins . So we have a thick area (dark area) and thin area (light area) due to the sequence of thick filaments and thin filaments. The thick filaments consist of one protein called **myosin** , but the thin filaments consist of three proteins . the thick and thin filaments are interdigitate(like two clasped hands) , and when the thin filaments slide over the thick filaments , contraction occurs.



In cardiac muscle :

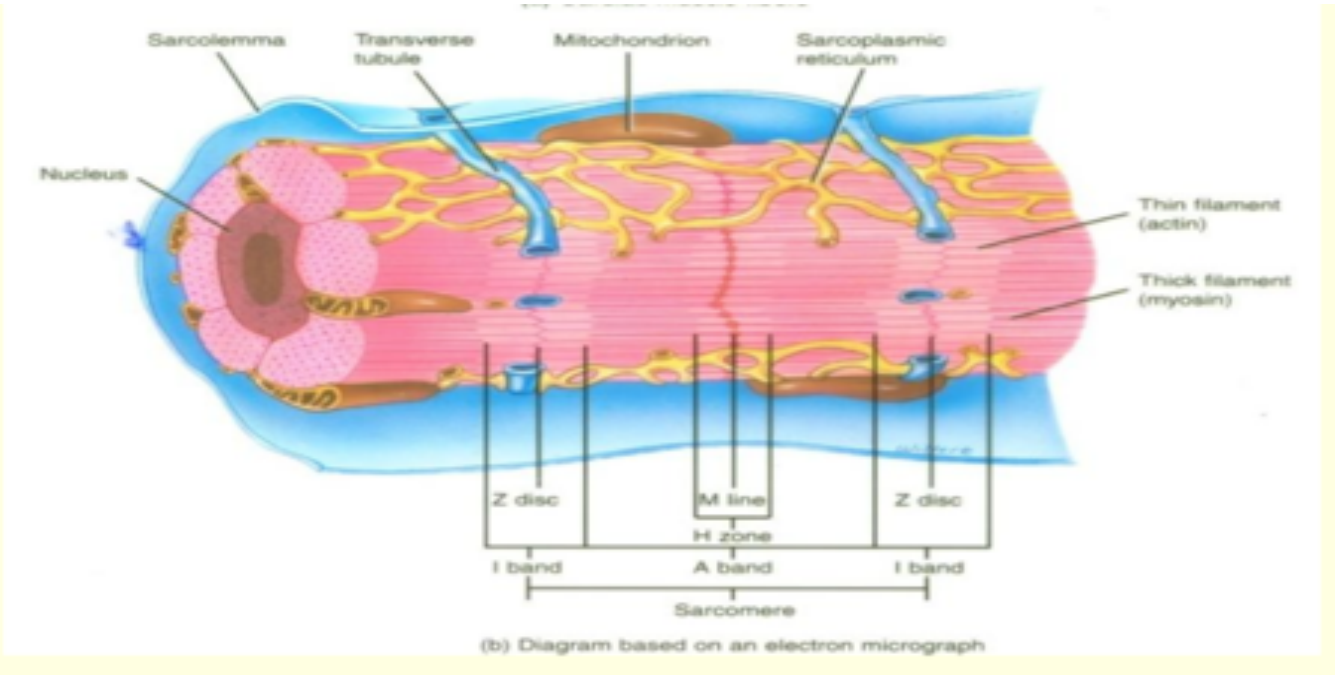
Sarcolemma = plasma membrane ,

sarcoplasmic reticulum =smooth endoplasmic reticulum ,

sarcoplasm = cytoplasm

the distance between two Z lines is called **sarcomere ,** and the sliding will shorten the sarcomere resulting in contraction . one sarcomere is shortened by 0.1 μm. (total shortening is equal to 0.1 multiplied by the number of sarcomeres in one cell which reaches hundreds).

Inside the cardiac muscle we find :



* **sarcomere** between two **Z lines** , it contains thick filaments called **A band ,** and thin filaments called **I band** . thick filaments consist of one protein called **myosin** . thin filament appears as a double helix and composed of actin, tropomyosin and troponin C .

During relaxation, tropomyosin blocks myosin binding sites on actin, when calcium is released calcium ions bind to troponin which displaces tropomyosin which exposes myosin binding sites on actin and allow the binding of myosin and actin . as the sliding over occurs , the actin and myosin complex moves inward (this is called **power stroke**), resulting in the shortening of the sarcomere and muscle contraction . to end the contraction state and reestablish the relaxation state, calcium must be returned to its storage sites. That's why calcium is called **excitation – contraction coup**ler .

*** transverse tubules (T tubules) ,** that are formed by the invagination of the sarcolemma . the T tubule of the cardiac muscle occurs at the Z line ; consequently , we have one T tubule per one sarcomere . on the other hand the T tubule of the skeletal muscle occurs at the I band , so we will end up with 2 T tubules per one sarcomere . in the cardiac it is shorter an wider , but in the skeletal is slender and longer.

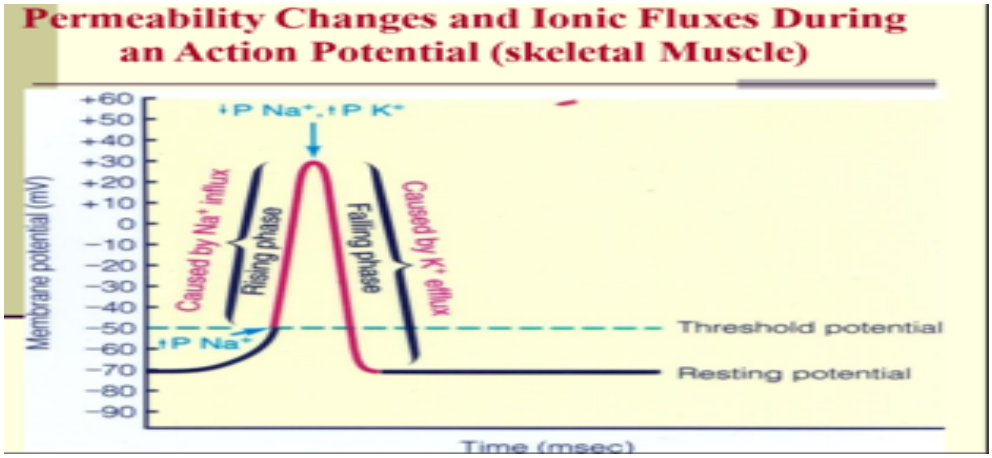
*number of **mitochondria is** much higher than the skeletal muscle , because higher energy is needed in the cardiac muscle . but it contains less nuclei .

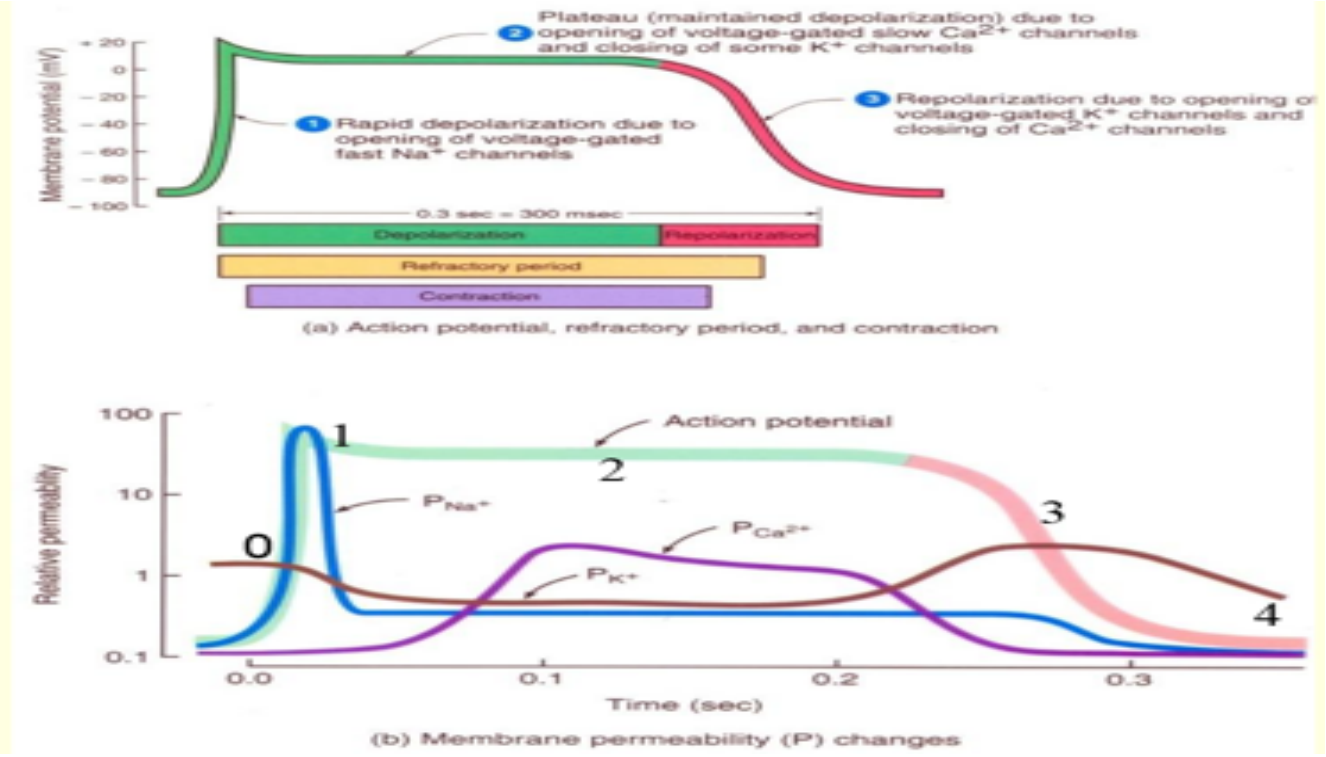
* **sarcoplasmic reticulum** where the calcium is stored . the cardiac muscle sarcoplasmic reticulum is less developed than the skeletal muscle , which means that this source of calcium is not enough for contraction , that's why we have another source **extracellular calcium .**

Action potential

**** skeletal muscle action potential :**

Resting membrane potential is equal to -70 . when a stimulus reaches the threshold, **depolarization** occurs due to the opening of fast voltage gated Na+channels (NA+ influx) , then after the opening of fast voltage gated K+ channels (K+ efflux) , **repolarization** takes place to return the membrane back again to the resting state **.** it is very short (usually 1-2 msec , maximum 10 msec)





**** cardiac muscle action potential**

Resting membrane potential is equal to -90 . 5 phases take place because of the change of membrane permeability (conductance) of ions .

Phase 0 : rapid depolarization due to the opening of fast voltage gated Na+ channels (Na+ influx) . (high increase in conductance of Na+) and (decrease in permeability for K+ , which is not found in the skeletal , normally at resting state the permeability for K+ is hundreds time more than Na+ , it decreases during this phase which is very important)

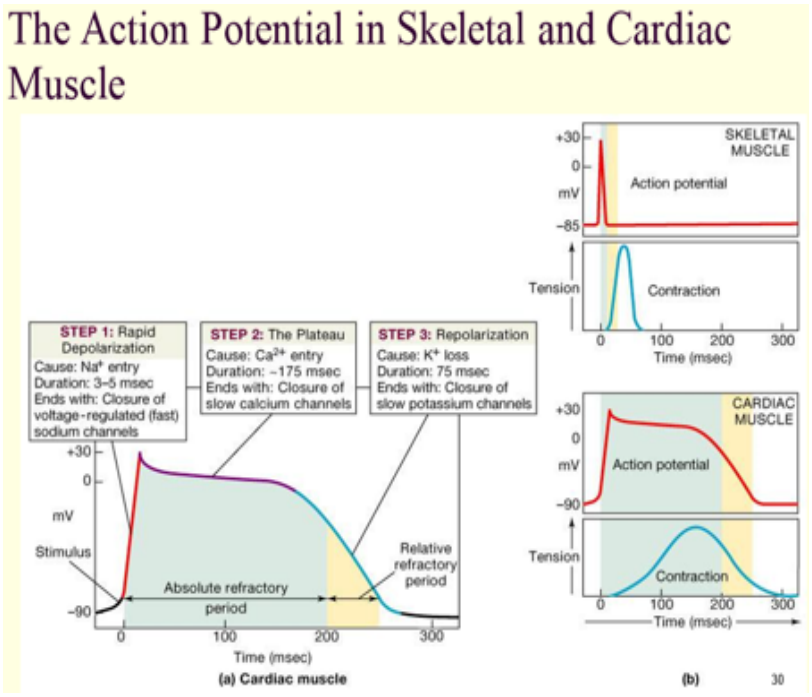
Phase 1 : partial repolarization phase due to the opening of transient k+ channels , and/or CL- channels .(decrease in conductance of K+)

Phase 2 : plateau (maintained depolarization) due to the opening of **slow** voltage gated Ca^{+2} channels (calcium influx) ,and closing of some K+ channels . (increase permeability for Ca^{+2} and decrease permeability for K+ , this is important for the maintenance of plateau)

NOTE: in cardiac muscle there are two sources of calcium : extracellular and endoplasmic . the influx of the extracellular Ca^{+2} during the plateau phase is essential to trigger the release of Ca^{+2} from the SR , this is called **calcium induced calcium release** .

In contrast , action potential of the skeletal muscle causes electrostatic discharge which leads to calcium release.

So calcium release in skeletal muscle is due to electrostatic discharge , and in the cardiac muscle is due to calcium induced calcium release .



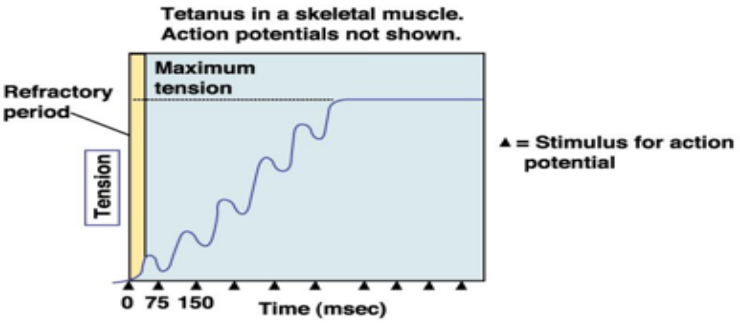
Phase 3 : repolarization due to the opening of voltage gated K+ channels , and closing of Ca^{+2} channels .(increase in K+ permeability , and decrease in calcium permeability) .

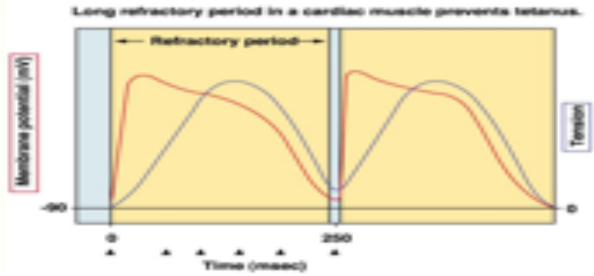
Phase 4 : back to the resting stage .

-Another difference between cardiac muscle action potential and skeletal muscle action potential is the absolute refractory periods which is much longer in cardiac muscle and extends from the beginning of the action potential till half-way of repolarization leaving the cardiac muscle membrane (sarcolemma) unresponsive to any stimulus. This is very crucial to life since this will protect cardiac muscle from tetanization which may occur in skeletal muscle when stimulated repeatedly. The whole skeletal muscle action potential occurs in the latent period before the contraction starts. Thus, you can induce other action potentials before the relaxation of the muscle (and even before the contraction of it) which results in repeated contractions of the skeletal muscle to an extent when the high frequency of action potentials will result in complete contraction with no relaxation.

This mean that If there's another action potential in the latent period, this will induce repeated contractions without giving a chance for the muscle to relax which results in the summation of mechanical contractions and you might reach a stage when the muscle stays contracted and tetanization occurs.

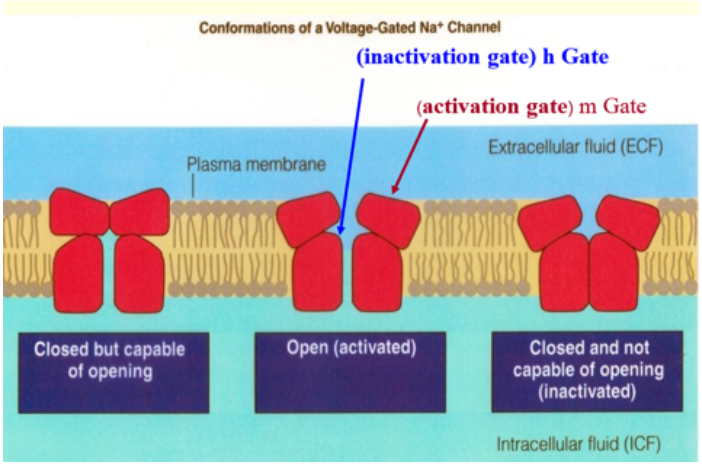
- While in cardiac muscle, thankfully, the long absolute refractory period in which the sarcolemma is unresponsive to any stimuli that gives the muscle the enough time to relax before responding to another stimulus and contract again. So tetanization won't occur.





fast voltage gated Na+ channels

- they have two gates :



****intracellular gate (inactivation gate , h gate) :** it's opened during rest state , and closed when the membrane potential becomes less negative .(**slow gate)**

****extracellular gate (activation gate , m gate) :** it's closed during rest state , and opened when the membrane potential becomes less negative .(**fast gate)**

Both have the same voltage threshold , but they differ in the time , the extra is fast and the intra is slow .

- During depolarization, when membrane potential becomes less negative => M gate (Activation gate) opens very fast and consequently H gate (Inactivation)starts to close at a lower speed. This difference in timing gives Na+ ions a small window of time to escape down their electrochemical gradient (influx of Na+). So, we will have depolarization until we reach the overshot and by that time the H gate will be closed and no more Na+ influx occurs.

Relaxation occurs when calcium is pumped back to its storage site by three mechanisms :

1- Ca++ ATPase in the SR by active transport (Ca++ uptake).

2- Ca^{+2}-Na+ exchanger in the SL by secondary active transport (exchange 3 sodium for one calcium) and it is called an electrogenic pump because it generates different positive charges exchange (3 positive charges of sodium exchanged for 2 positive charge calcium) .

3- Ca++ pumps in the SL by active transport .

*Resting calcium level is 10^{-7} while the contraction level is 10^{-5}

إذا الشّعب، يوماً أراد الحياة فلابدّ أن يستجيب القدر !