Physiology of Cardiac Muscle

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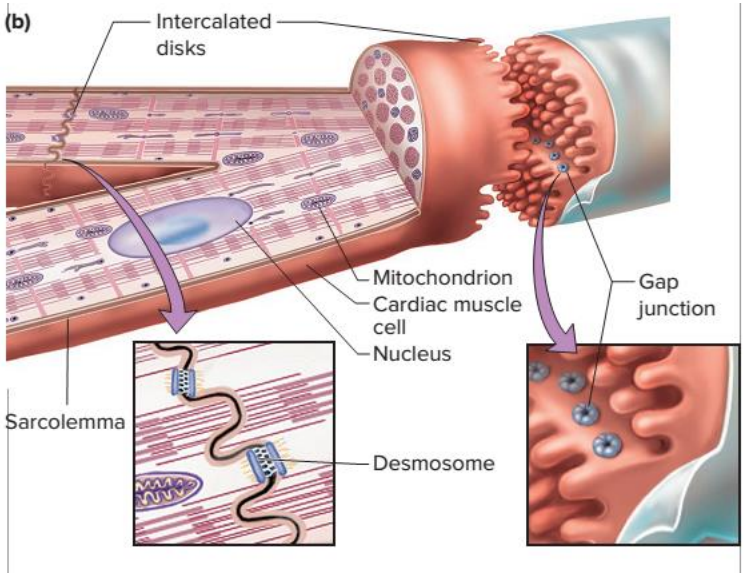
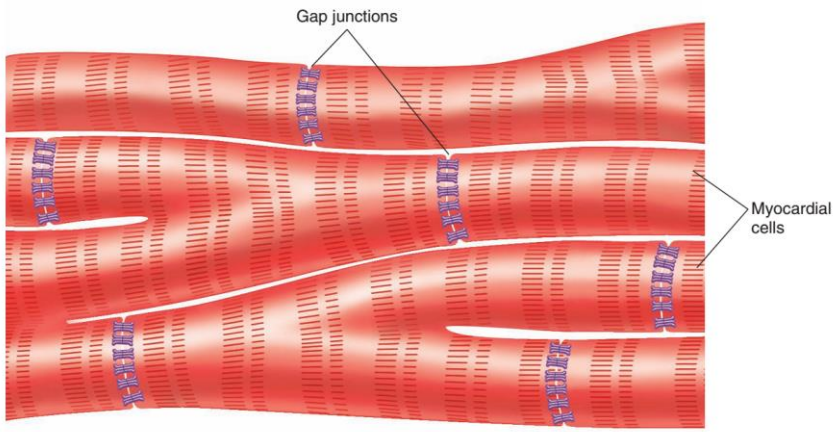
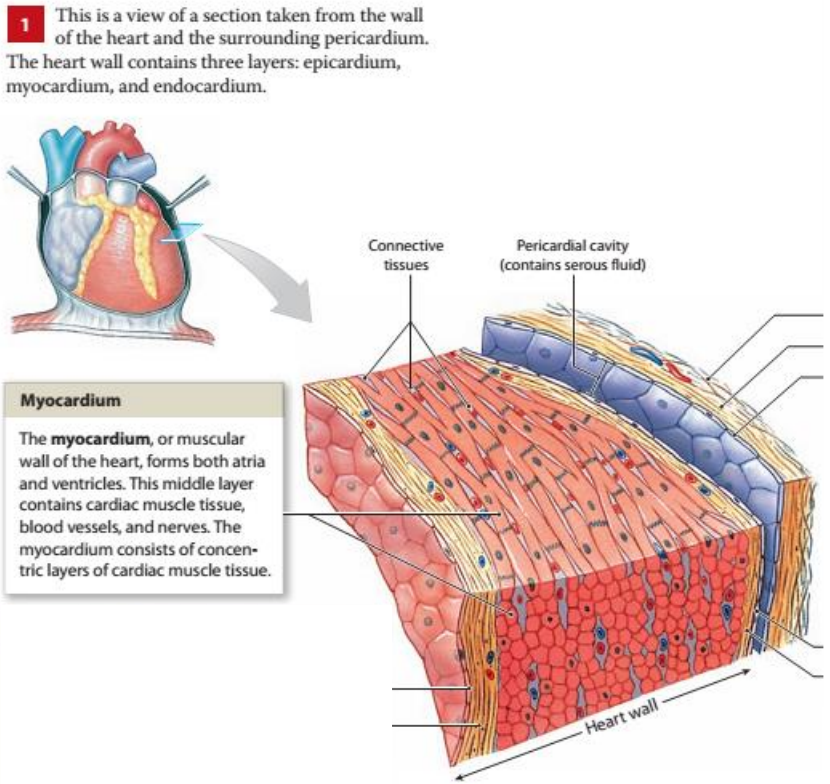
Myocardial Cells

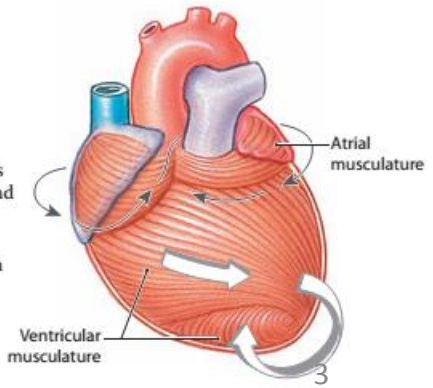
- Similar to skeletal muscle; striated and contains sarcomeres that shorten by sliding of thin and thick filaments
- Short (one nucleus), branched
- Interconnected by gap junctions and desmosomes (intercalated discs)



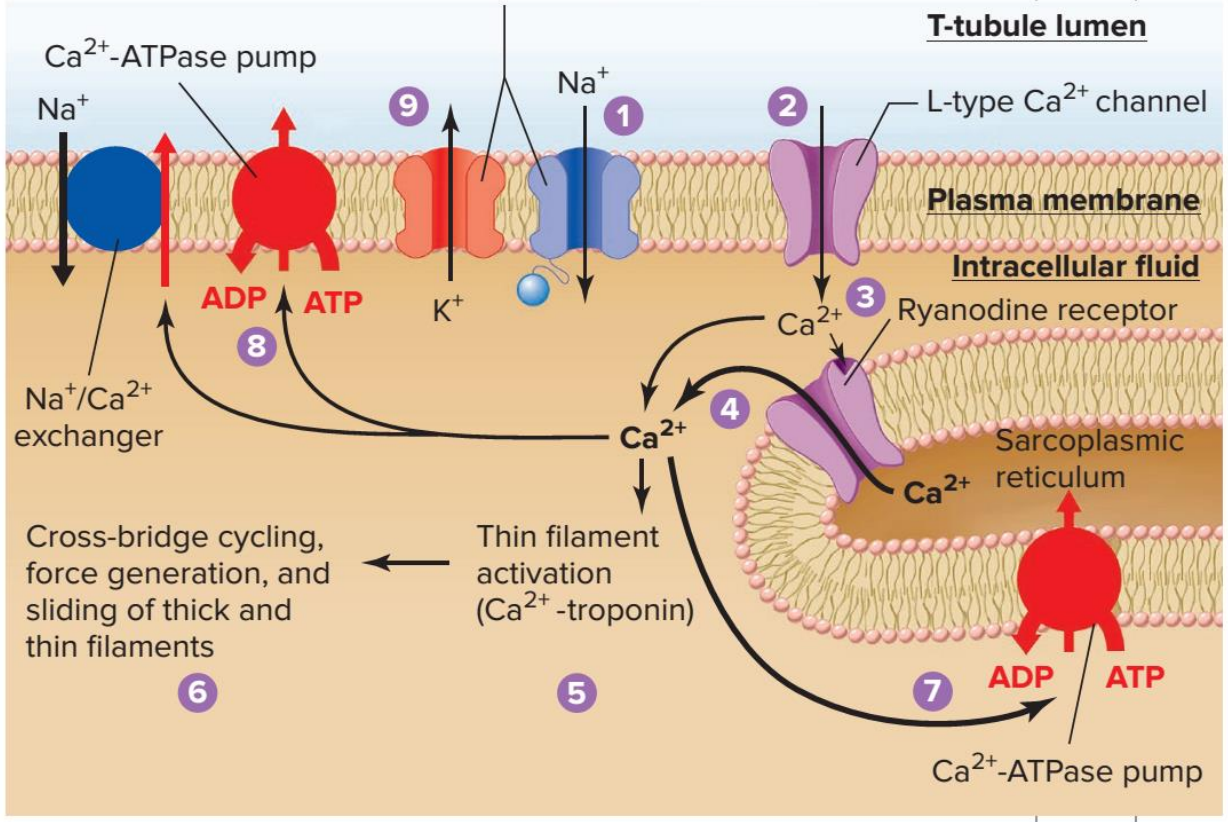


- Myocardial cells are arranged in layers and surround hollow cavities (chambers of the heart)
- When myocardium contracts, it acts like a squeezing fist and exerts pressure on the blood inside
- Single functional unit
  - Electrically joined myocardium
  - Contracts to its full extent each time as all of its cells contribute to the contraction (can be modified by epinephrine and strecthing of the heart chambers)





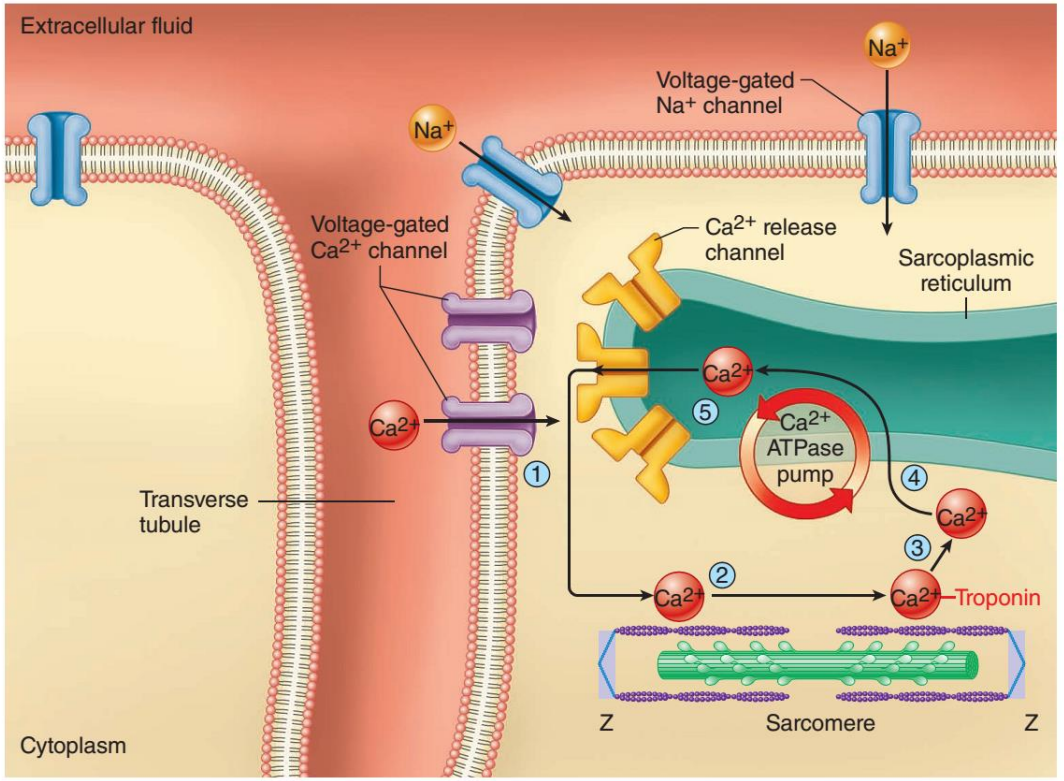
Excitation-Contraction Coupling



1. The membrane is depolarized by Na^+ entry as an action potential begins.
2. Depolarization opens L-type Ca^{2+} channels in the T-tubules.
3. A small amount of "trigger" Ca^{2+} enters the cytosol, contributing to cell depolarization. That trigger Ca^{2+} binds to, and opens, ryanodine receptor Ca^{2+} channels in the sarcoplasmic reticulum membrane.
4. Ca^{2+} flows into the cytosol, increasing the Ca^{2+} concentration.
5. Binding of Ca^{2+} to troponin exposes cross-bridge binding sites on thin filaments.
6. Cross-bridge cycling causes force generation and sliding of thick and thin filaments.
7. Ca^{2+}-ATPase pumps return Ca^{2+} to the sarcoplasmic reticulum.
8. Ca^{2+}-ATPase pumps and Na^+/Ca^{2+} exchangers remove Ca^{2+} from the cell.
9. The membrane is repolarized when K^+ exits to end the action potential.

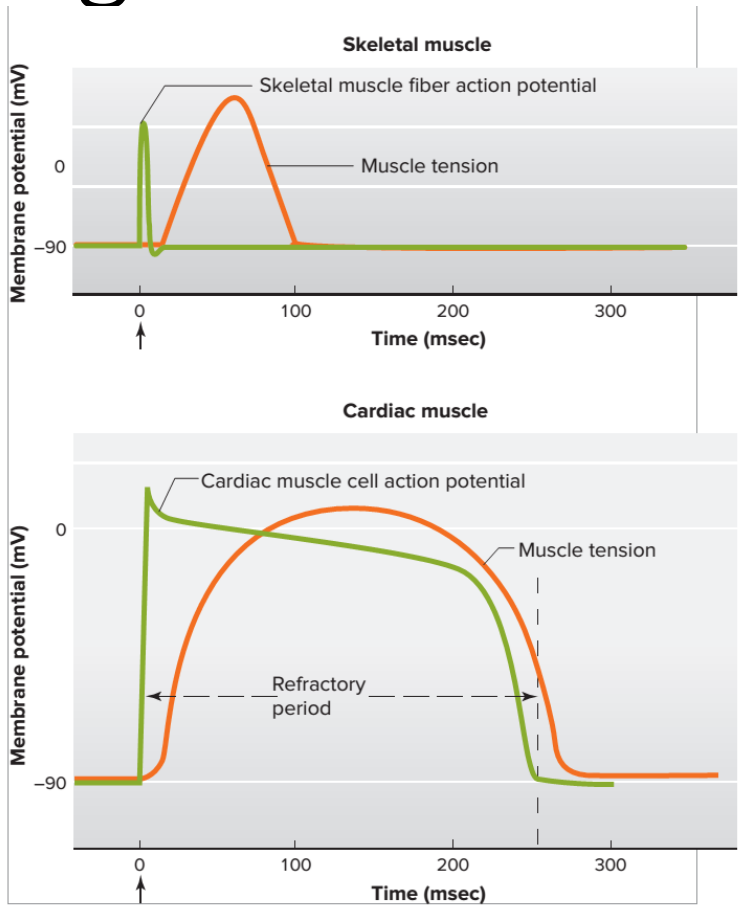
Calcium-induced calcium release

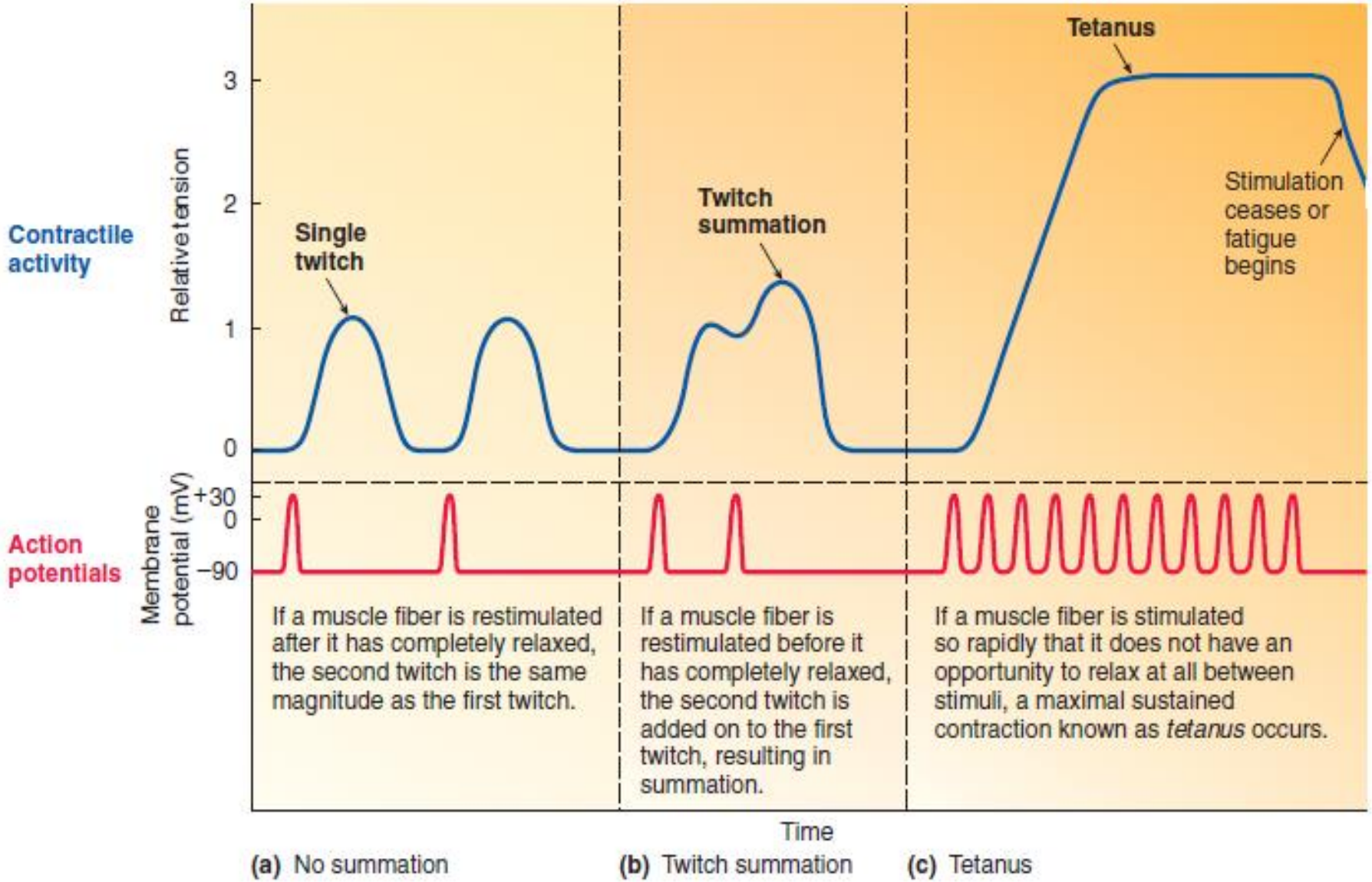
- Depolarization opens voltage gated Ca^{2+} channels on the membrane
- Ca^{2+} enters the cytoplasm and interacts with Ca^{2+} release channels on the SR
- Source of internal Ca^{2+} is *extracellular fluid* and sarcoplasmic reticulum
- Ca^{2+} pumped back to SR and *extracellular fluid* by Ca^{2+} -ATPase pump



Cardiac Muscle Action Potential Excitation–Contraction Coupling

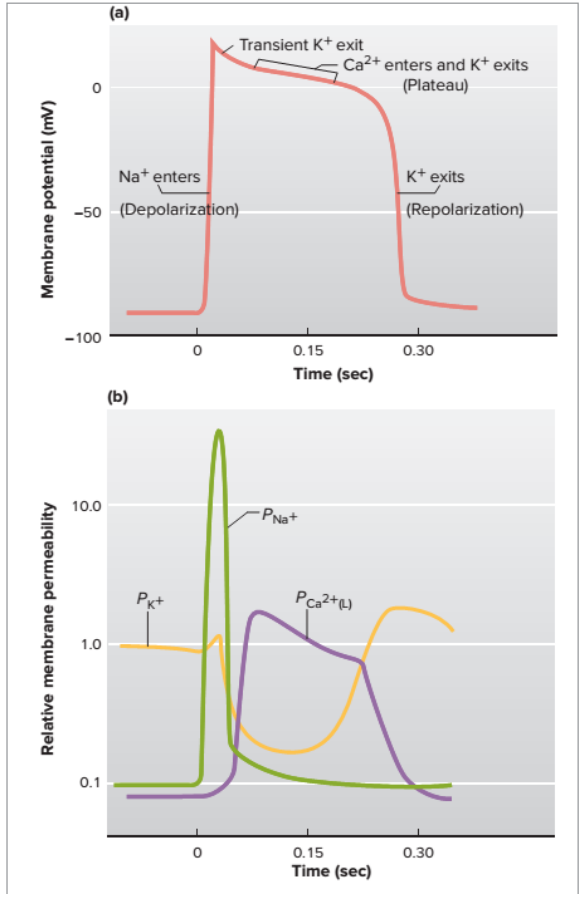
- Action potential and twitch are both prolonged
  - Plasma membrane remains refractory to additional stimuli as long as it is depolarized → cannot undergo tetanic contractions
    - Oscillating pump (alternate between being relaxed—and filling with blood—and contracting to eject blood)




Contractile activity
Relative tension
3
2
1
0
Single twitch
Twitch summation
Tetanus
Stimulation ceases or fatigue begins
Action potentials
Membrane potential (mV)
+30
0
−90
If a muscle fiber is restimulated after it has completely relaxed, the second twitch is the same magnitude as the first twitch.
If a muscle fiber is restimulated before it has completely relaxed, the second twitch is added on to the first twitch, resulting in summation.
If a muscle fiber is stimulated so rapidly that it does not have an opportunity to relax at all between stimuli, a maximal sustained contraction known as tetanus occurs.
Time
(a) No summation
(b) Twitch summation
(c) Tetanus

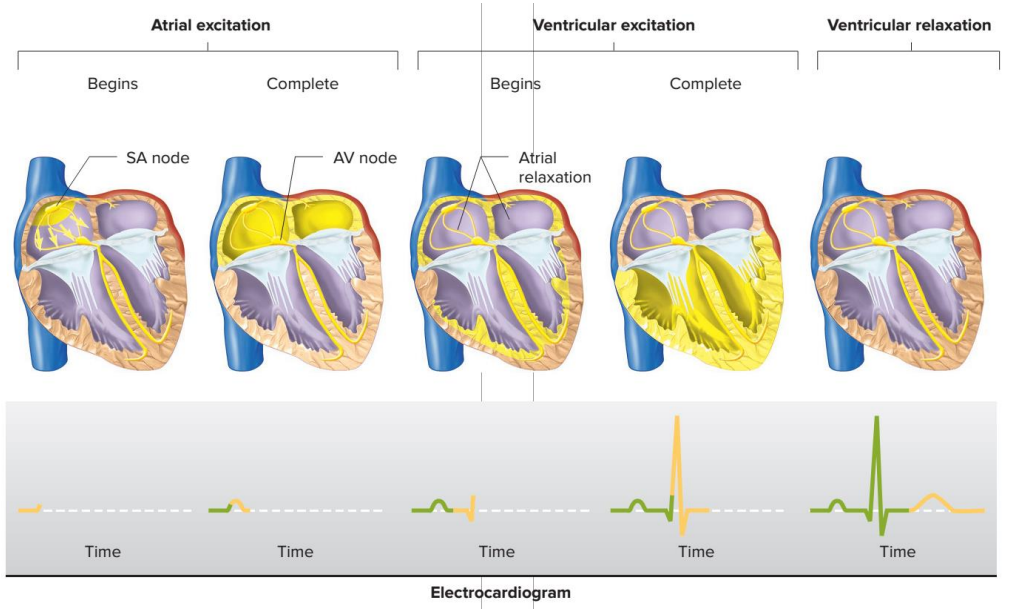
Myocardial Cell Action Potentials

- Plateau phase
  - K^+ permeability declines below the resting value due to the closure of the K^+ channels that were open in the resting state
  - A large increase in the cell membrane permeability to Ca^{2+}
    - Voltage gated Ca^{2+} channels in the plasma membrane, L-type Ca^{2+} channels, stay open for a long time (L = Long lasting)
    - Balance between influx of Ca^{2+} and efflux of K^+
- Repolarization
  - Inactivation of L-type Ca^{2+} channels
  - Opening of another subtype of K^+ channels (slowly responsive to depolarization like in neurons)



Sinoatrial Node Cells

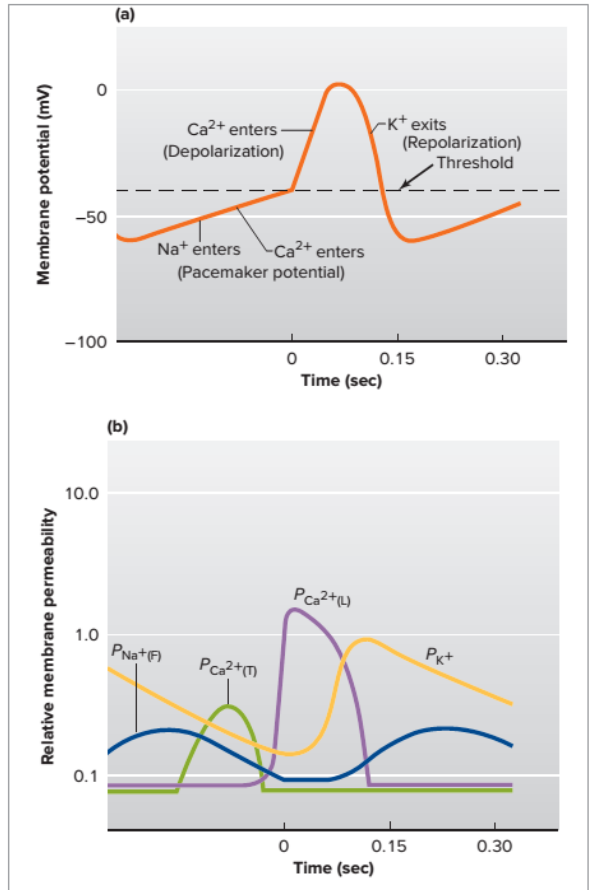
- Initial depolarization arises in a small group of conducting-system cells called the sinoatrial (SA) node
- Pacemaker for the entire heart
- The action potential initiated in the SA node spreads throughout the myocardium, passing from cell to cell by way of gap junctions



Nodal Cell Action Potential

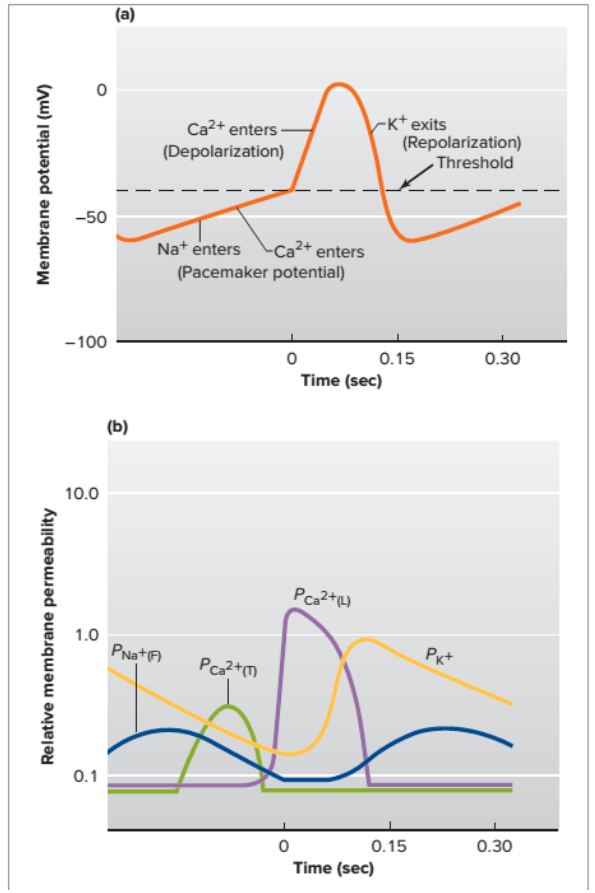
- Pacemaker potential
  - not a steady resting potential but, a gradual slow depolarization that brings the membrane potential to threshold, at which point an action potential occurs

1. progressive reduction in K^+ permeability (The K^+ channels that opened during the repolarization phase of the previous action potential gradually close due to the membrane's return to negative potentials)
2. voltage-gated ion channels, open when the membrane potential is at negative values (F (funny) channels: nonspecific cation channels, conduct mainly an inward, depolarizing Na^+ current,)
3. T-type Ca^{2+} channels (T = transient) (opens only briefly but contributes inward Ca^{2+} current and an important final depolarizing boost to the pacemaker potential)



Nodal Cell Action Potential

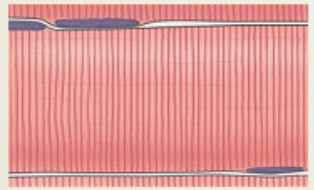
- The depolarizing phase is caused by Ca^{2+} influx through L-type Ca^{2+} channels.
  - action potentials propagate more slowly along nodal-cell membranes than in other cardiac cells
- L-type channels close and K^+ channels open, repolarizes to pacemaker potential
- Automaticity of SA node
- The inherent rate of the SA node—the rate exhibited in the absence of any neural or hormonal input to the node—is approximately 100 depolarizations per minute. But changes with external factors



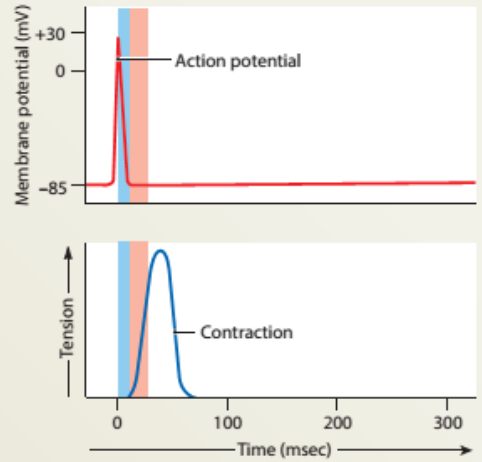
Cardiac muscle cell contractions last longer than skeletal muscle fiber contractions primarily due to differences in membrane permeability

Muscle Cell Contractions

Skeletal Muscle



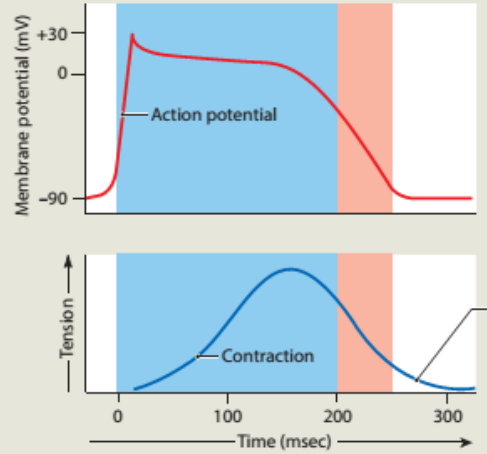
1 In a skeletal muscle fiber, the action potential is relatively brief and ends as the related twitch contraction begins. The twitch contraction is short and ends as the sarcoplasmic reticulum reclaims the Ca^{2+} it released. Note that the refractory period ends before peak tension develops. As a result, twitches can summate and tetanus can occur.



KEY
- Absolute refractory period
- Relative refractory period

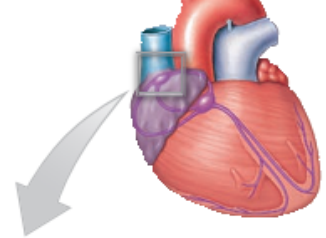
Cardiac Muscle

2 In a cardiac muscle cell, the action potential is prolonged because calcium ions continue to enter the cell for an extended period. As a result, the period of active muscle cell contraction is also extended. Note that the refractory period continues until relaxation is well under way. Thus, summation cannot occur, and tetanic contractions do not occur in normal cardiac muscle tissue. This feature is vital: A heart in tetany could not pump blood.



With a single twitch lasting 250 msec or longer, a normal cardiac muscle cell could reach 300–400 contractions per minute under maximum stimulation. The normal heart rate never gets that high because the stimulus for contraction cannot spread that quickly through the heart muscle.

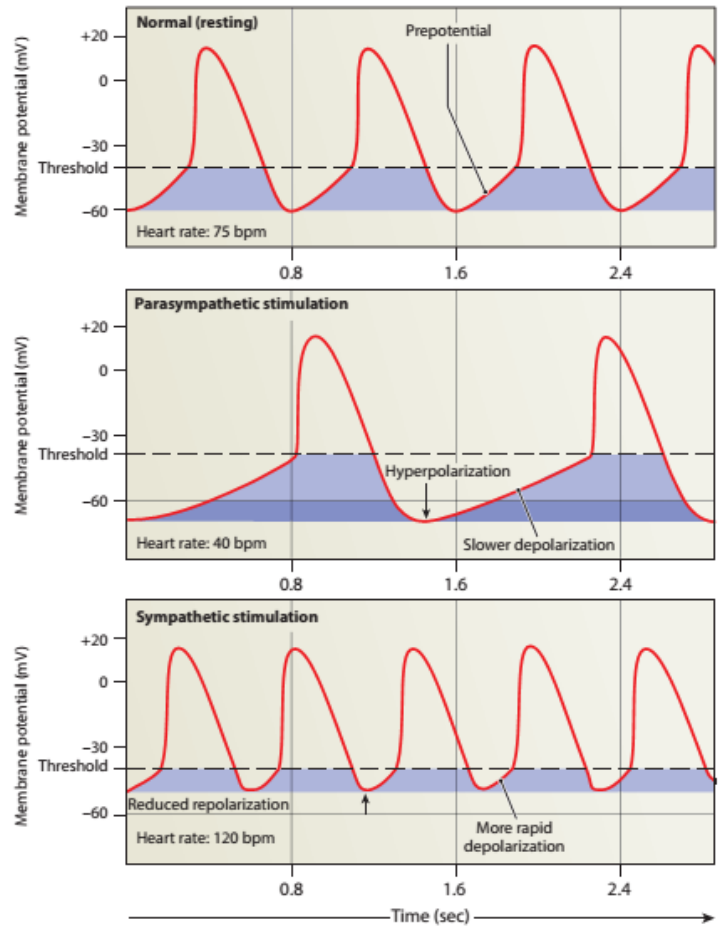
The intrinsic heart rate can be altered by autonomic activity



1 Cells of the SA and AV nodes cannot maintain a stable resting potential. After each repolarization, the membrane gradually drifts toward threshold. This gradual spontaneous depolarization is called a **prepotential** or **pacemaker potential**. The rate of spontaneous depolarization is fastest at the SA node, which without neural or hormonal stimulation generates action potentials at a rate of 80–100 per minute. Because the SA node reaches threshold first, it establishes the heart rate—the impulse generated by the SA node brings the AV nodal cells to threshold before the prepotential of the AV nodal cells can do so.

2 Any factor that changes the rate of spontaneous depolarization or the duration of repolarization will alter the heart rate by changing the time required to reach threshold. Acetylcholine released by parasympathetic neurons opens chemically gated K^+ channels in the plasma membrane, thereby slowing the rate of spontaneous depolarization and also slightly extending the duration of repolarization. The result is a decline in heart rate.

3 Norepinephrine (NE) released by sympathetic neurons binds to beta-1 receptors, leading to the opening of ion channels that increase the rate of depolarization and shorten the period of repolarization. Because the nodal cells reach threshold more quickly, the heart rate increases.



4 Every person has a characteristic resting heart rate that varies with age, general health, and physical conditioning. However, there is a normal range of heart rates. The American Heart Association considers 60–100 bpm to be the normal range of resting heart rates.

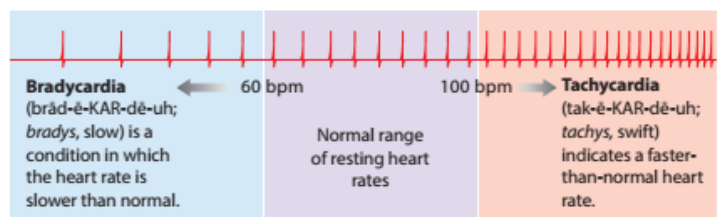


Table 12.8 | Comparison of Skeletal, Cardiac, and Smooth Muscle

Skeletal Muscle	Cardiac Muscle	Smooth Muscle
Striated; actin and myosin arranged in sarcomeres	Striated; actin and myosin arranged in sarcomeres	Not striated; more actin than myosin; actin inserts into dense bodies and cell membrane
Well-developed sarcoplasmic reticulum and transverse tubules	Moderately developed sarcoplasmic reticulum and transverse tubules	Poorly developed sarcoplasmic reticulum; no transverse tubules
Contains troponin in the thin filaments	Contains troponin in the thin filaments	Contains calmodulin, a protein that, when bound to Ca^{2+}, activates the enzyme myosin light-chain kinase
Ca^{2+} released into cytoplasm from sarcoplasmic reticulum	Ca^{2+} enters cytoplasm from sarcoplasmic reticulum and extracellular fluid	Ca^{2+} enters cytoplasm from extracellular fluid, sarcoplasmic reticulum, and perhaps mitochondria
Cannot contract without nerve stimulation; denervation results in muscle atrophy	Can contract without nerve stimulation; action potentials originate in pacemaker cells of heart	Maintains tone in absence of nerve stimulation; visceral smooth muscle produces pacemaker potentials; denervation results in hypersensitivity to stimulation
Muscle fibers stimulated independently; no gap junctions	Gap junctions present as intercalated discs	Gap junctions present in most smooth muscles