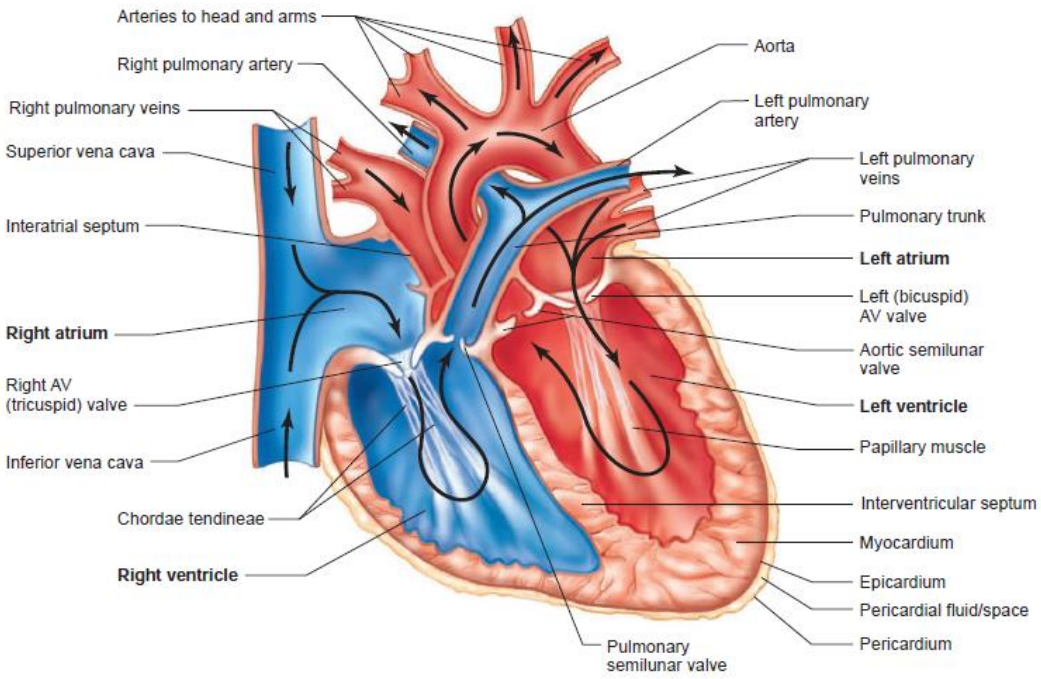
Cardiac Muscle

2nd year Students

Anatomy of the Heart

The heart is a muscular organ enclosed in a protective fibrous sac, the **pericardium,** and located in the chest. A fibrous layer is also closely affixed to the heart and is called the **epicardium.** The extremely narrow space between the pericardium and the epicardium is filled with a watery fluid that serves as a lubricant as the heart moves within the sac.

The wall of the heart, the **myocardium,** is composed primarily of cardiac muscle cells. The inner surface of the cardiac chambers, as well as the inner wall of all blood vessels, is lined by a thin layer of cells known as **endothelial cells,** or **endothelium.**



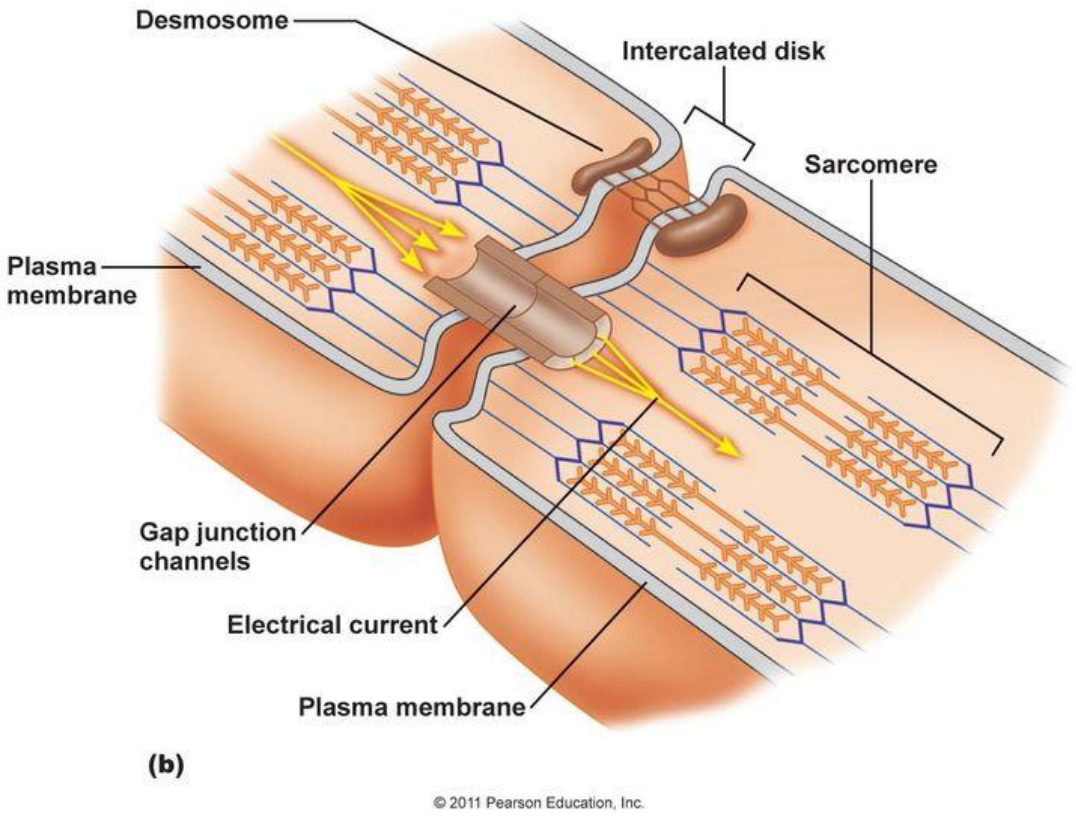
Cardiac Muscle

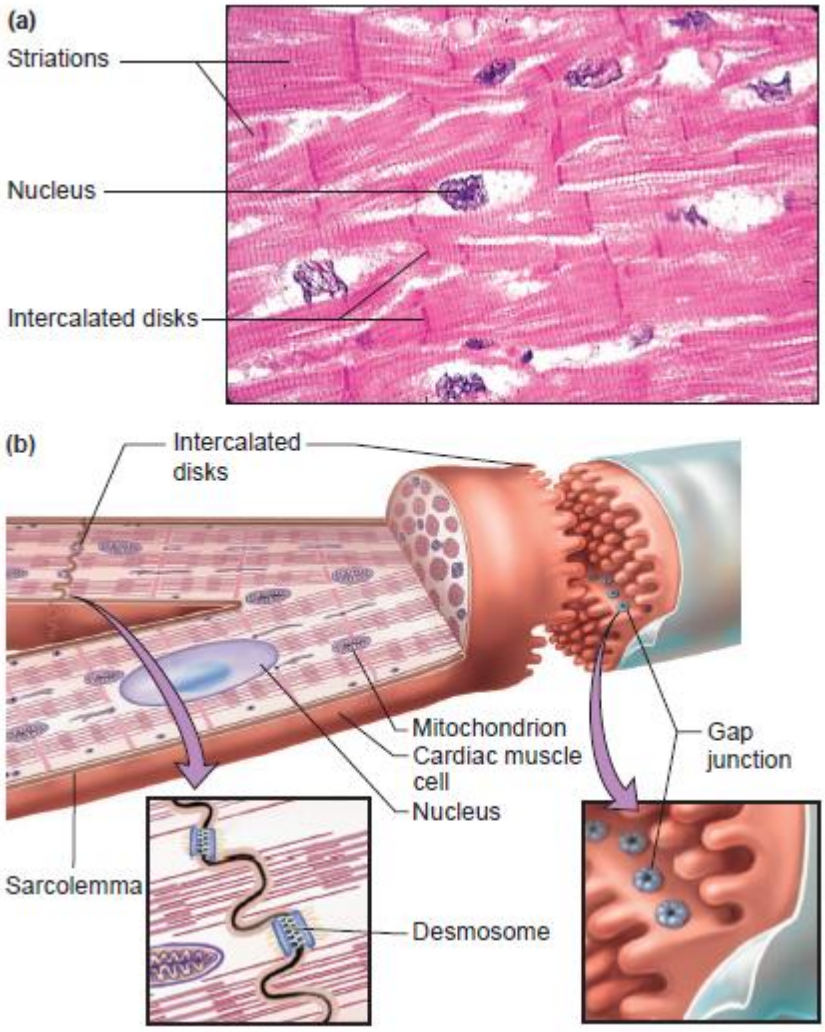
Cellular Structure of Cardiac Muscle

The third general type of muscle, cardiac muscle, is found only in the heart. Cardiac muscle combines properties of both skeletal and smooth

muscle. Like skeletal muscle, it has a striated appearancedue to regularly repeating sarcomeres composed of myosin-containing thick filaments interdigitating with thin filaments that contain actin. Troponin and tropomyosin are also present in the thin filament, and they have the same functions as in skeletal muscle. Cellular membranes include a T-tubule system and associated Ca^{++} -loaded sarcoplasmicreticulum.

Like smooth muscle cells, individual cardiac muscle cells are relatively small (100 mm long and 20 mm in diameter) and generally contain a single nucleus. Adjacent cells are joined end to end at structures called **intercalated disks,**within which are desmosomes (also known as a **macula adherens)** which is a cell structure specialized for cell-to-cell adhesionthat hold the cells together and to which the myofibrils are attached.

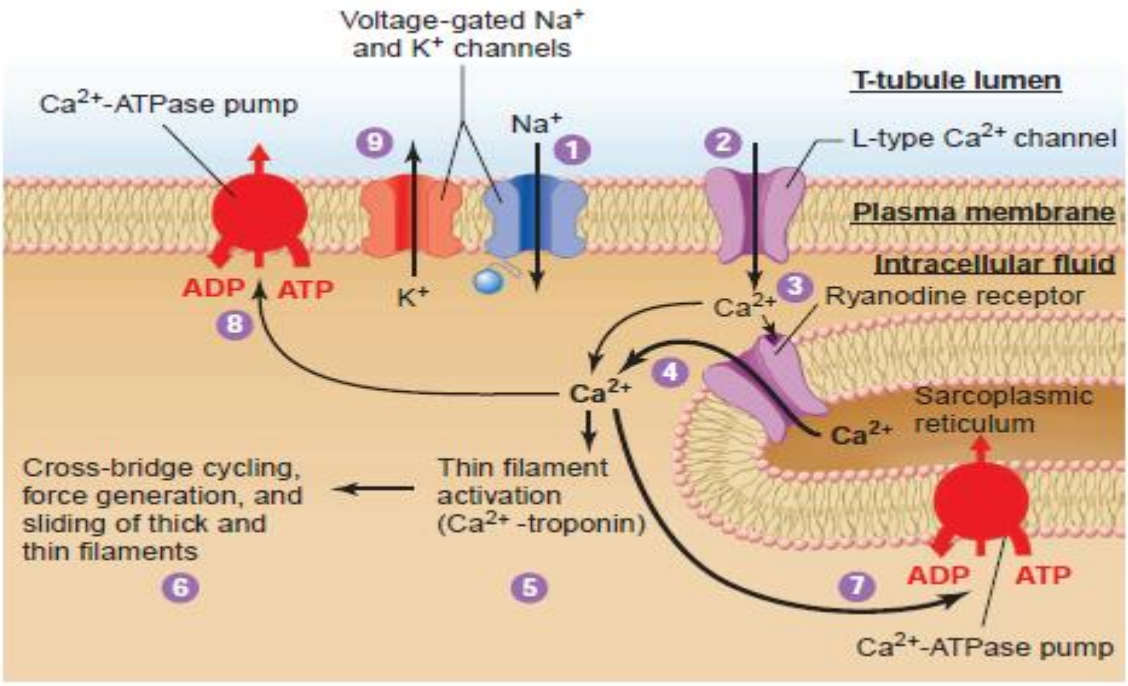




Also found within the intercalated disks are gap junctions similar to those found in single-unit smooth muscle. Cardiac muscle cells also are arranged in layers and surround hollow cavities—in this case, the blood-filled chambers of the heart. When muscle in the walls of cardiac chambers contracts, it acts like a squeezing fist and exerts pressure on the blood inside.

Excitation–Contraction Coupling in Cardiac Muscle

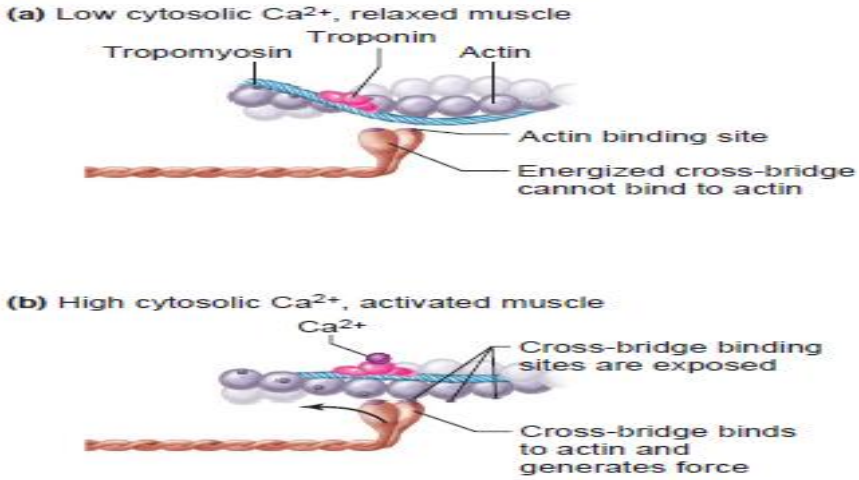
As in skeletal muscle, contraction of cardiac muscle cells occurs in response to a membrane action potential that propagates through the T-tubules, but the mechanisms linking that excitation to the generation of force exhibit features of both skeletal and smooth muscles.

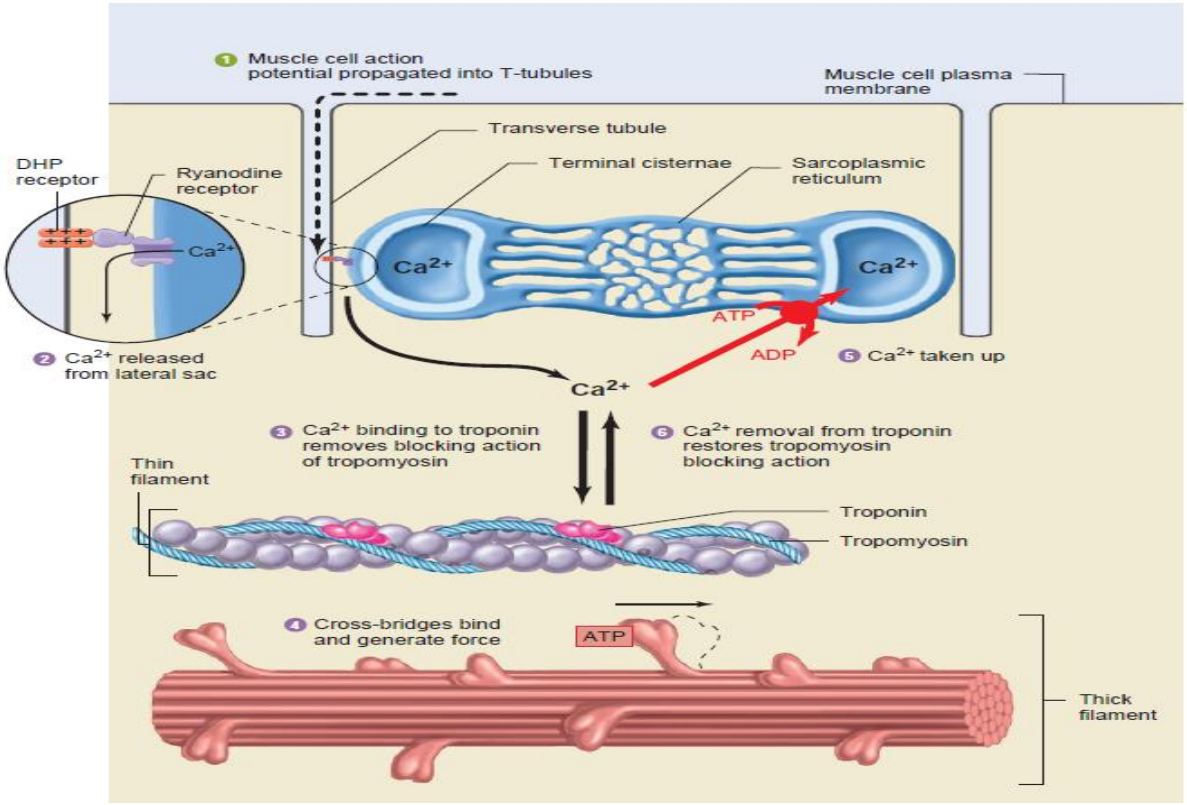


1- The membrane is depolarized by Na+ entry as an action potential begins.
2- Depolarization opens L-type Ca2+ channels in the T-tubules.
3- A small amount of "trigger" Ca2+ enters the cytosol,contributing to cell depolarization. That trigger Ca2+ binds to,and opens, ryanodine receptor Ca2+ channels in the sarcoplasmic reticulum membrane.
4- Ca2+ flows into the cytosol, raising the Ca2+ concentration.
5- Binding of Ca2+ to troponin exposes cross-bridge bindingsites on thin filaments.
6- Cross-bridge cycling causes force generation and slidingof thick and thin filaments.
7- Ca2+-ATPase pumps return Ca2+ to the sarcoplasmicreticulum.
8- Ca2+-ATPase pumps (and also Na+/Ca2+ exchangers)remove Ca2+ from the cell.
9- The membrane is repolarized when K+ exits to end the actionpotential.

Depolarization during cardiac muscle cell action potentials is in part due to an influx of Ca++ through specialized voltage-gated channels. These Ca++ channels are known as **L-type Ca++ channels** (named for their Long-lasting current)

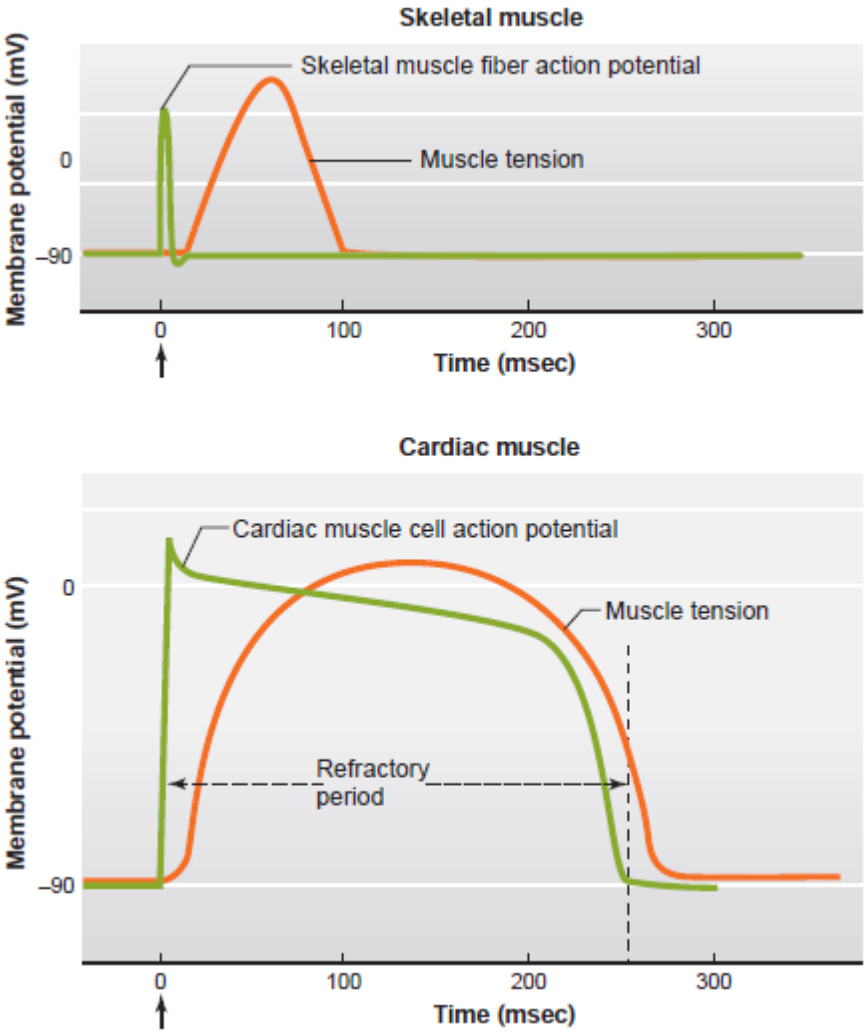
Not only does this entering Ca++participate in depolarization of the plasma membrane and cause a small increase in cytosolicCa++concentration, but it also serves as a trigger for the release of a much larger amount of Ca++from the sarcoplasmic reticulum.





However, hormones and neurotransmitters of the autonomic nervous system modulate the amount of Ca++released during excitation–contraction coupling, enabling the strength of cardiac muscle contractions

to be varied. Cardiac muscle contractions are thus graded in a manner similar to that of smooth muscle contractions. The prolonged duration of L-type Ca++channel current underlies an important feature of this muscle type—cardiac muscle cannot undergo tetanic contractions. in cardiac muscle the action potential and twitch are both prolonged due to the long-lasting Ca++ current.



Because the plasma membrane remains refractory to additional stimuli as long as it is depolarized, It is not possible to initiate multiple cardiac action potentials during the time frame of a single twitch. This is critical for the heart's function as an oscillating pump, because it must alternate

between being relaxed—and filling with blood—and contracting to eject blood.

Every heart cell contracts with every beat of the heart. Beating about once every second, cardiac muscle cells may contract almost 3 billion times in an average life span without resting! Remarkably, despite this enormous workload, the human heart has a limited ability to replace its muscle cells. Recent experiments suggest that only about 1% of heart muscle cells are replaced per year.

A final question to consider is: What initiates action potentials in cardiac muscle?

Certain specialized cardiac muscle cells exhibit pacemaker potentials that generate action potentials spontaneously. Because cardiac cells are linked via gap junctions, when an action potential is initiated by a pacemaker cell, it propagates rapidly throughout the entire heart. A single heartbeat corresponds to the initiation and conduction of a single action potential.

Innervation

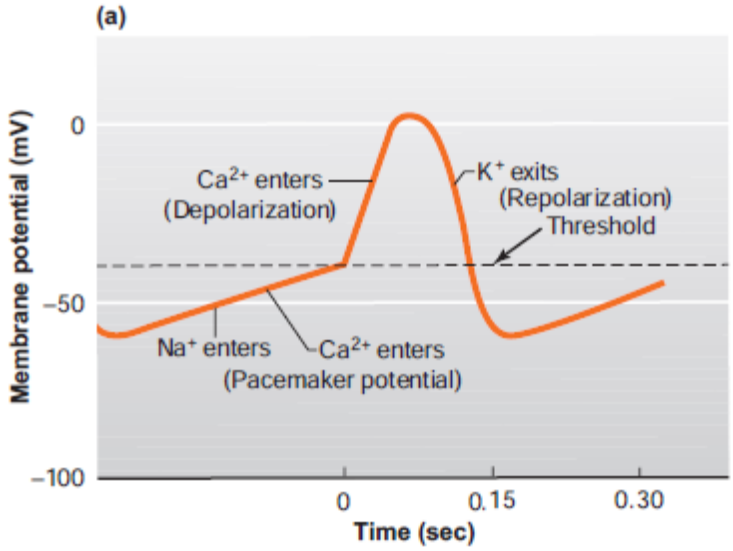
The heart receives a rich supply of sympathetic and parasympatheticnerve fibers, the latter contained in the vagus nerves. The sympathetic postganglionic fibers innervate the entire heart and release norepinephrine, whereas the parasympathetic fibers terminate mainly on cells found in the atria and release primarily acetylcholine.

The receptors for norepinephrine on cardiac muscle are mainly B-adrenergic. The hormone epinephrine, from the adrenal medulla, binds to

the same receptors as norepinephrine and exerts the same actions on the heart.The receptors for acetylcholine are of the muscarinic type.

The flow of positive calcium ions into the cell just balances the flow of positive potassium ions out of the cell and keeps the membrane depolarized at the plateau value. Ultimately, repolarization does occur due to the eventual inactivation of the L-type Ca++ channels and the opening of another subtype of K channels. These K channels are similar to the ones described in neurons and skeletal muscle; they open in response to depolarization (but after a delay) and close once the K current has repolarized the membrane to negative values.

In contrast, there are extremely important differences between action potentials of cardiac muscle cells and those in nodal cells of the conducting system.



Three ion channel mechanism, contribute to the pacemaker potential.

First is a progressive reduction in K permeability. **Second**, pacemaker cells have a unique set of channels that, unlike most voltage-gated channels**.** The third pacemaker channel is a type of Ca++ channel. These channels are called **T-type Ca++ channels** (T transient). Although SA

node and AV node action potentials are basically similar in shape, the pacemaker currents of SA node cells bring them to threshold more rapidly than AV node cells, which is why SA node cells normally initiate action potentials and determine the pace of the heart.

Once the pacemaker mechanisms have brought a nodal cell to threshold, an action potential occurs. The depolarizing phase is caused not by Na but rather by Ca++influx through L-type Ca++ channels. These Ca++currents depolarize the membrane more slowly than voltage-gated Na channels, and one result is that action potentials propagate more slowly along nodal-cell membranes than in other cardiac cells. This explains the slow transmission of cardiac excitation through the AV node.