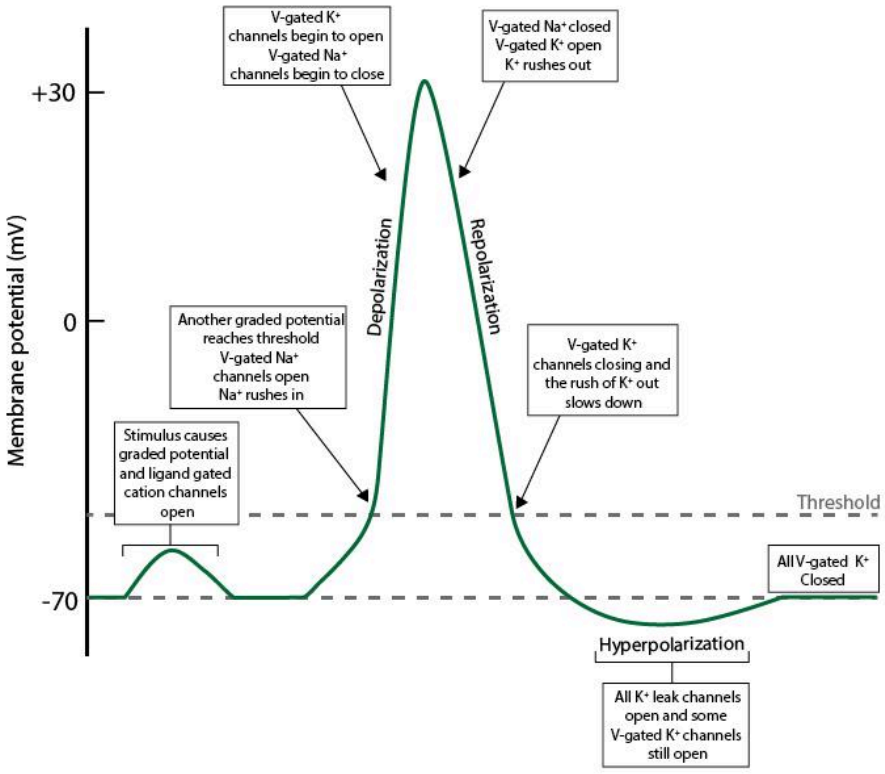
1.2.1

Action Potentials in Cardiac Contractile Muscle Cells

Like skeletal muscle, the signal that triggers contraction of cardiac muscle is an action potential. Action potentials are highly ordered changes in membrane potentials due to the movement of ions across the membranes through voltage-gated ion channels.

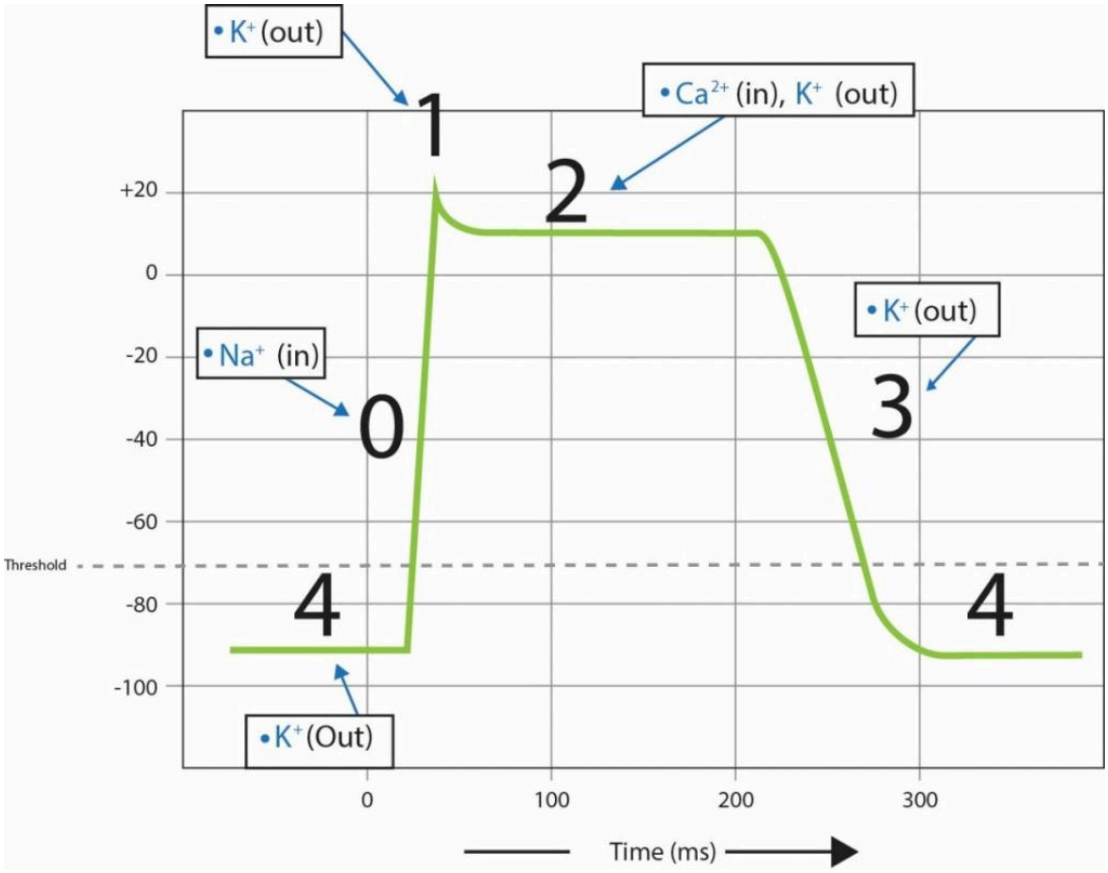


Action Potential in Skeletal Muscle.
Image created by BYU-Idaho student, Kaylynn Lloyd 2013

Recall that the major phases of the action potential for skeletal muscle cells and axons, are depolarization, repolarization, and hyperpolarization. The **o**pening of voltage-gated Na^+ channels and rapid movement of Na^+ into the cell, which causes the membrane potential to become more positive, is the depolarization phase. At the peak of the depolarization phase the inactivation gates on the sodium channels close, preventing further sodium entry. At roughly the same time that the inactivation gates close, the voltage-gated K^+ channels finish opening and K^+ rapidly diffuses out of the cell causing the membrane potential to again become negative, the **repolarization phase.** The relatively slow closing of the voltage-gated K^+ channels results in **hyperpolarization** (potential below the normal resting membrane

potential) and then once they close the resting potential is again restored via leak K^+ channels. All of this takes place in 1-2 milliseconds.

Action potentials in cardiac muscle are significantly different from those in axons and skeletal muscle. The most significant difference is the **plateau phase** (phase 2) that prolongs the action potential to as long as 300 milliseconds. Another difference is that in addition to Na^+ and K^+, $Ca2^+$ plays a significant role in cardiac muscle action potentials. Note in Fig 4 that there are 5 phases in cardiac muscle action potentials (phase 0, 1, 2, 3, and 4). Let's walk through these phases and describe what is happening in each.



Action Potential of Cardiac Myocytes or Cardiac Muscle Cells.
Drawn by BYU-Idaho student Fall 2013

Phase 4: **Resting membrane potential** (RMP). Note that unlike the -70 to -80 mV RMP that we are familiar with in axons and skeletal muscle, in cardiac muscle, the RMP is around -90 mV. This low resting membrane potential is due to a special group of K+ channels that open when the membrane *repolarizes* and close when the membrane *depolarizes.* Because this is essentially the lower limit for the RMP, we do not observe a hyperpolarization at the end of repolarization.

Phase 0: The **depolarization phase.** This phase is due to the opening of voltage-gated Na^+ channels and the influx of Na^+. These are the same channels found in axons and skeletal muscle and, hence, have both activation and inactivation gates. Note that when the membrane depolarizes the K^+ channels mentioned in phase 4 *close.*

Phase 1: **Rapid repolarization.** At the end of the depolarization phase the inactivation gates on the Na^+ close, stopping the influx of Na^+. At the same time, a small number of K^+ channels open and the membrane begins to repolarize.

Phase 2: **Plateau.** This is the phase that distinguishes the cardiac muscle action potential from other excitable tissues and is the result of the opening of **voltage-gated Ca^{2+} channels.** With the opening of these channels, Ca^{2+} enters the cell. Additional K^+ channels also open at about the same time. During the plateau, the influx of Ca^{2+} essentially negates

the effect of the efflux of K^+. Because of the movement of these two ions, K^+ out and Ca^{2+} in, the membrane potential remains fairly constant and does not repolarize. In addition to prolonging the action potential, the Ca^{2+} that is entering the cell plays a critical role in triggering muscle contraction (more on this later).

Phase 3: **Repolarization.** During the plateau phase more and more K^+ channels open and toward the end of the plateau phase the K^+ efflux becomes greater than the Ca^{2+} influx and the membrane begins to repolarize. As the membrane becomes more negative the Ca^{2+} channels close and the membrane quickly returns to the RMP. As RMP is reached, the K^+ channels close (with the exception of those mentioned in phase 4 which open as the membrane repolarizes) and the membrane is ready to respond again. This process is regulated by the ratio of Ca^{2+} to K^+ permeability. There are at least 4 different types of voltage-gated K^+ channels involved in the process, each with slightly different properties.

The prolonged nature of the action potential in cardiac muscle has at least 2 important outcomes. First, it prevents the membrane from being restimulated until the muscle has had time to contract and then relax. Stated another way, the absolute refractory period for cardiac muscle cells is much longer, preventing the muscle from being restimulated until it has time to totally relax. Recall that in skeletal muscle if the frequency of action potentials is high enough the muscle will enter a state of tetany in which the muscle remains continually contracted. If this happened in the heart, blood flow would stop, since refilling of the chambers requires that the heart relax. Second, contraction of cardiac muscle requires the contribution of extracellular Ca^{2+}. All during the plateau phase Ca^{2+} is entering the cell from the extracellular fluid, contributing to total intracellular calcium concentration.