Cardiac muscle is different from other types of muscle in that cardiac muscle contracts spontaneously, without any external stimuli, whereas other muscles require signals from the nervous system in order to contract. The heart’s ability to trigger its own contractions is called *autorhythmicity*. If cardiac muscle cells are isolated, placed into cell culture, and observed under the microscope, the cells can be seen to undergo contractions. No other muscle cells will contract like this unless stimulated in some manner.

Each cardiac cell has its own intrinsic rate of contraction. However, if two cells of different contraction rates are joined together, the two will contract at the rate of the faster cell. In the heart, the cells with the fastest contraction rates join together to form the *sinoatrial node* (SA node)—the “pacemaker” of the heart. Cells in the SA node, called *pacemaker cells*, direct the contraction rate of the entire heart by generating action potentials on a regular basis. These cells (and consequently, heart rate) are under the influence of the *sympathetic nervous system*, which releases the neurotransmitter norepinephrine, and the *parasympathetic nervous system*, which releases the neurotransmitter acetylcholine. Sympathetic neurons cause pacemaker cells to generate action potentials more frequently, and thus increase heart rate. In contrast, parasympathetic neurons have the opposite effect—they cause a decrease in the frequency of action potentials generated by pacemaker cells, and thus decrease heart rate. The heart simultaneously receives both sympathetic and parasympathetic signals in a “push-pull” manner: Increases in one are accompanied by decreases in the other. In healthy adults, resting heart rate is about 70 beats per minute, although this varies depending on factors such as a person’s age, physical fitness, and emotional state.

The heart receives sympathetic input via several nerves extending from the spinal cord, and receives parasympathetic input via a single pair of cranial nerves called *vagus nerves*. Once stimulated by a nerve, cardiac muscle cells depolarize. There are five main phases of depolarization (see Figure 6.1). *Phase 0* is characterized by a rapid upswing in membrane potential. Depolarization causes voltage-gated sodium channels in the cell membrane to open, increasing the flow of sodium ions into the cell and increasing the membrane potential. In *phase 1*, the open sodium channels begin to inactivate, decreasing the flow of sodium ions into the cell and causing the membrane potential to fall slightly. At the same time, however, voltage-gated potassium channels close while voltage-gated calcium channels open.
subsequent decrease in the flow of potassium out of the cell and increase in the flow of calcium into the cell act to depolarize the membrane and curb the fall in membrane potential caused by the inactivation of sodium channels. In phase 2, known as the plateau phase, the membrane remains in a depolarized state. Potassium channels stay closed and calcium channels stay open. This plateau lasts about 0.2 second. The internal potential then gradually falls to more negative values during phase 3, when a second set of potassium channels that began opening in phases 1 and 2 allow significant amounts of potassium to flow out of the cell. The fall in potential causes calcium channels to begin closing, reducing the flow of calcium into the cell and repolarizing the membrane until the resting potential is reached. The period of resting potential until the next depolarization is known as phase 4.

**Figure 6.1** The stages of the cardiac action potential are shown on the top graph. Notice the difference between the cardiac action potential graph and the skeletal muscle action potential graph below it.

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**Activity 1**

**Direct Heart Stimulation**

In Exercise 2, Skeletal Muscle Physiology, we witnessed the phenomenon of summation in skeletal muscles. Recall that summation was the result of the skeletal muscle being stimulated with such frequency that twitches overlapped and resulted in a stronger contraction than a stand-alone twitch. This was possible because skeletal muscle has a relatively short refractory period (a period during which no action potentials can be generated). Unlike skeletal muscle, cardiac muscle has a relatively long refractory period, and is thus incapable of summation. In fact, cardiac muscle is incapable of reacting to any stimulus before about the middle of phase 3, and will not respond to a normal cardiac stimulus before phase 4. The period of time between the beginning of the cardiac action potential and the approximate middle of phase 3 is the **effective refractory period**. The period of time between the effective refractory period and phase 4 is the **relative refractory period**. The refractory period of cardiac muscle is about 250 milliseconds—almost as long as the contraction of the heart. In this activity we will use direct heart stimulation to better understand the refractory period of cardiac muscle.

1. Click on the **Direct Heart Stimulation** electrode and drag it to the electrode holder (the post with the four green squares). Release the electrode; it will click into place, touching the ventricle of the heart.

2. Look at the heartbeat trace. Recall that the smaller rise is atrial contraction and the larger rise is ventricular contraction. Click **Single Stimulus** right at the beginning of ventricular contraction.
FIGURE 6.2 Opening screen of the Electrical Stimulation experiment.

Did you see any change in the trace?

Why/why not?

3. Click Single Stimulus again, this time near the peak of ventricular contraction.

Did you see any change in the trace?

Why/why not?

4. Click Single Stimulus again, this time during the “fall” of ventricular contraction. If you do not see any change in the trace, try clicking Single Stimulus twice in quick succession until you do see a change.

Describe the change you see in the trace. How does it differ from the baseline trace?

What part of the trace shows the refractory period?

5. Next, click on Multiple Stimulus (note that the button changes to Stop Stimulus). This will administer repeated stimuli (20 per second) to the heart. After a few seconds, click Stop Stimulus to stop the stimulations.

What effect do the repeated stimuli have on the heartbeat trace? Describe the trace.

What part of the trace shows the refractory period?
3. Observe the effects of stimulation on the heartbeat. Allow the trace to cross the length of the monitor five times before you click Stop Stimulus. Describe the effect of the vagus nerve stimulation on the heartbeat.

Soon after you applied the stimuli, did the heart rate increase or decrease?

Why?

How do the sympathetic and parasympathetic nervous systems work together to regulate heart rate?

Complete the following: As heart rate decreases, cardiac output __________. As heart rate increases, cardiac output __________.

Research has shown that in the absence of neural or hormonal influences, the SA node generates action potentials at a frequency of approximately 100 beats per minute. Yet, the average resting heart rate is 70 beats per minute. What does this tell you about the parasympathetic nervous system in relation to the sympathetic nervous system and hormones?

Modifiers of Heart Rate

Next we will observe the effects of various drugs, hormones, and ions on heart rate. Click Experiment at the top of the screen and then select Modifiers of Heart Rate. You will see the opening screen shown in Figure 6.4. Notice the seven dropper bottles resting on a shelf above the monitor. You will be administering drops of each bottle’s contents onto the frog heart and observing the effects. You will also be keeping a record of your data by clicking the Record Data button on the data collection box at the bottom of the screen. You may print your recorded data at any time by clicking Tools at the top of the screen and then selecting Print Data.
ACTIVITY 3
Effect of Epinephrine

Epinephrine is a hormone secreted by the adrenal glands. It travels through the bloodstream to the heart, on which it has a significant effect. Epinephrine is an important mediator of rapid fuel mobilization, or increasing metabolic rate.

1. Click the top of the dropper bottle labeled Epinephrine and drag the dropper over to the top of the frog heart and release the mouse button. You will see drops of epinephrine released onto the heart.

2. Observe the heart rate trace and watch the status window on the lower right corner of the heart rate monitor.

3. Wait until the status window reads Heart Rate Stable, then click Record Data.

4. Click the 23°C (room temperature) Ringers solution button to bathe the heart and flush out the epinephrine. Wait until the status window reads Heart Rate Normal before proceeding to the next activity.

What was the effect of epinephrine on heart rate?

Does this effect mimic the effect of the sympathetic nervous system or that of the parasympathetic nervous system?

What is the heart rate when the status window reads Heart Rate Stable?

ACTIVITY 4
Effect of Pilocarpine

Pilocarpine is a cholinergic drug—that is, a drug that inhibits, mimics, or enhances the action of acetylcholine in the body.

1. Click the top of the dropper bottle labeled Pilocarpine and drag the dropper over to the top of the frog heart and release the mouse button. You will see drops of pilocarpine released onto the heart.
2. Observe the heart rate trace and watch the status window on the lower right corner of the heart rate monitor.

3. Wait until the status window reads Heart Rate Stable, then click Record Data.

4. Click the 23°C (room temperature) Ringers solution button to bathe the heart and flush out the pilocarpine. Wait until the status window reads Heart Rate Normal before proceeding to the next activity.

What was the effect of pilocarpine on heart rate?

What is the heart rate when the status window reads Heart Rate Stable? __________ 

**ACTIVITY 5**

**Effect of Atropine**

Atropine is another cholinergic drug, although its effects are quite different from that of pilocarpine.

1. Click the top of the dropper bottle labeled Atropine and drag the dropper over to the top of the frog heart and release the mouse button. You will see drops of atropine released onto the heart.

2. Observe the heart rate trace and watch the status window on the lower right corner of the heart rate monitor.

3. Wait until the status window reads Heart Rate Stable, then click Record Data.

4. Click the 23°C (room temperature) Ringers solution button to bathe the heart and flush out the atropine. Wait until the status window reads Heart Rate Normal before proceeding to the next activity.

What was the effect of atropine on heart rate?

What is the heart rate when the status window reads Heart Rate Stable? __________ 

Circle the correct boldfaced term: Atropine inhibits / mimics / enhances the action of acetylcholine on heart rate.

If you were to administer drops of pilocarpine to the heart and then administer atropine immediately afterward, what effect would you expect to see on the heart rate?

**ACTIVITY 6**

**Effect of Digitalis**

Digitalis (also known as digoxin and digitoxin) is a drug that interferes with the normal conduction pathway in the heart by blocking the conduction of the atrial impulses to the ventricles.

1. Click the top of the dropper bottle labeled Digitalis and drag the dropper over to the top of the frog heart and release the mouse button. You will see drops of digitalis released onto the heart.

2. Observe the heart rate trace and watch the status window on the lower right corner of the heart rate monitor.

3. Wait until the status window reads Heart Rate Stable, then click Record Data.

4. Click the 23°C (room temperature) Ringers solution button to bathe the heart and flush out the digitalis. Wait until the status window reads Heart Rate Normal before proceeding to the next activity.

What was the effect of digitalis on heart rate?

What is the heart rate when the status window reads Heart Rate Stable?

Atrial fibrillation is a condition characterized by the atria of the heart undergoing extremely fast rates of contraction. Why might digitalis be used on a patient with such a condition?

**ACTIVITY 7**

**Effect of Temperature**

The frog is a poikilothermic animal; its internal body temperature changes depending on the temperature of its external environment. In contrast, humans are homeothermic. Our bodies remain at the same temperature (around 37°C) unless we are sick.

1. The frog heart is currently being bathed in room temperature Ringers solution. Click the 5° Ringers solution button to observe the effects of lowering the temperature.

2. Observe the heart rate trace and watch the status window on the lower right corner of the heart rate monitor.

3. Wait until the status window reads Heart Rate Stable, then click Record Data.

4. Click the 23° Ringers solution button to bathe the heart and return it to room temperature. Wait until the status window reads Heart Rate Normal before proceeding.

5. Now click on the 32° Ringers solution button to observe the effects of raising the temperature.

6. Observe the heart rate trace and watch the status window on the lower right corner of the heart rate monitor.

7. Wait until the status window reads Heart Rate Stable, then click Record Data.
8. Click the 23° Ringers solution button to bathe the heart and return it to room temperature. Wait until the status window reads *Heart Rate Normal* before continuing to the next activity.

What was the effect of temperature on the frog’s heart rate?

________________________________________________
________________________________________________
______________________________________________

**ACTIVITY 8**

**Effects of Ions**

A large amount of potassium is present inside the cardiac muscle cell. Sodium and calcium are present in larger quantities outside the cell. The resting cell membrane favors the conduction of potassium over both sodium and calcium. This means that the resting membrane potential of cardiac cells is determined mainly by the ratio of extracellular and intracellular concentrations of potassium. You may wish to review the section on the five phases of cardiac action potential at the beginning of this lab on pp. 77–78 before proceeding with this activity, in which you will be examining the effects of calcium, sodium, and potassium ions on the frog heart rate.

1. Click the top of the dropper bottle labeled Calcium Ions and drag the dropper over to the top of the frog heart and release the mouse button. You will see drops of calcium ions released onto the heart.

2. Observe the heart rate trace and watch the status window on the lower right corner of the heart rate monitor.

3. Wait until the status window reads *Heart Rate Stable*, then click *Record Data*.

4. Click the 23°C (room temperature) Ringers solution button to bathe the heart and flush out the calcium. Wait until the status window reads *Heart Rate Normal* before proceeding.

5. Repeat steps 1–4 with Sodium Ions and then Potassium Ions.

What was the effect of calcium ions on heart rate?

Why?
________________________________________________
________________________________________________
________________________________________________

Where in a heart cell is calcium normally found?
________________________________________________

What was the effect of sodium ions on heart rate?

Why?
________________________________________________
________________________________________________
________________________________________________

Where in a heart cell is sodium normally found?
________________________________________________

What was the effect of potassium ions on heart rate?

Why?
________________________________________________
________________________________________________
________________________________________________

Where in a heart cell is potassium normally found?
________________________________________________

Remember, you may print your recorded data at any time by clicking **Tools** at the top of the screen and then clicking **Print Data**.

**Histology Review Supplement**

For a review of cardiovascular tissue, go to Exercise H: Histology Atlas & Review on the PhysioEx website to print out the Cardiovascular Tissue Review worksheet.