Frog Cardiovascular Physiology: Computer Simulation

**OBJECTIVES**

1. To list the properties of cardiac muscle as automaticity and rhythmicity, and to define each.
2. To explain the statement, “Cardiac muscle has an intrinsic ability to beat.”
3. To compare the relative length of the refractory period of cardiac muscle with that of skeletal muscle, and to explain why it is not possible to tetanize cardiac muscle.
4. To define extrasystole, and to explain at what point in the cardiac cycle (and on an ECG tracing) an extrasystole can be induced.
5. To describe the effect of the following on heart rate: vagal stimulation, cold, heat, pilocarpine, atropine, epinephrine, digitalis, and potassium, sodium, and calcium ions.
6. To define vagal escape and discuss its value.
7. To define ectopic pacemaker.

In this exercise, you will conduct the cardiac investigations just mentioned.

**Special Electrical Properties of Cardiac Muscle: Automaticity and Rhythmicity**

Cardiac muscle differs from skeletal muscle both functionally and in its fine structure. Skeletal muscle must be electrically stimulated to contract. In contrast, heart muscle can and does depolarize spontaneously in the absence of external stimulation. This property, called **automaticity**, is due to plasma membranes that have reduced permeability to potassium ions but still allow sodium ions to slowly leak into the cells. This leakage causes the muscle cells to slowly depolarize until the action potential threshold is reached and fast calcium channels open, allowing Ca\(^{2+}\) entry from the extracellular fluid. Shortly thereafter, contraction occurs.

The spontaneous depolarization-repolarization events occur in a regular and continuous manner in cardiac muscle, a property referred to as **rhythmicity**.

In the following experiment, you will observe these properties of cardiac muscle in a computer simulation. Additionally, your instructor may demonstrate this procedure using a real frog.
**Nervous Stimulation of the Heart**

Both the parasympathetic and sympathetic nervous systems innervate the heart. Stimulation of the sympathetic nervous system increases the rate and force of contraction of the heart. Stimulation of the parasympathetic nervous system (vagal nerves) decreases the depolarization rhythm of the sinoatrial node and slows transmission of excitation through the atrio-ventricular node. If vagal stimulation is excessive, the heart will stop beating. After a short time, the ventricles will begin to beat again. This is referred to as **vagal escape** and may be the result of sympathetic reflexes or initiation of a rhythm by the Purkinje fibers.

**Baseline Frog Heart Activity**

The heart’s effectiveness as a pump is dependent both on intrinsic (within the heart) and extrinsic (external to the heart) controls. In the first experimental series, Activities 1–3, you will investigate some of these factors.

The nodal system, in which the “pacemaker” imposes its depolarization rate on the rest of the heart, is one intrinsic factor that influences the heart’s pumping action. If its impulses fail to reach the ventricles (as in heart block), the ventricles continue to beat but at their own inherent rate, which is much slower than that usually imposed on them. Although heart contraction does not depend on nerve impulses, its rate can be modified by extrinsic impulses reaching it through the autonomic nerves. Cardiac activity is also modified by various chemicals, hormones, ions, and metabolites. The effects of several of these chemical factors are examined in the next experimental series, Activities 4–9.

The frog heart has two atria and a single, incompletely divided ventricle. The pacemaker is located in the sinus venosus, an enlarged region between the venae cavae and the right atrium. The sinoatrial (SA) node of mammals may have evolved from the sinus venosus.

Choose Exercise 34B: Frog Cardiovascular Physiology from the drop-down menu and click GO. Then click Electrical Stimulation. The opening screen will appear in a few seconds (Figure 34B.1). When the program starts, you will see a tracing of the frog’s heartbeat on the oscilloscope display in the upper right part of the screen. Because the simulation automatically adjusts itself to your computer’s speed, you may not see the heart tracing appear in real time. If you want to increase the speed of the tracing (at the expense of tracing quality), click the Tools menu, choose Modify Display, and then select Increase Speed.

![FIGURE 34B.1 Opening screen of the Electrical Stimulation experiment.](image-url)
To familiarize yourself with the equipment, choose Balloons On/Off from the Help menu. This feature allows you to scroll around the screen and view equipment labels. You can turn off this feature by returning to the Help menu and selecting Balloons On/Off.

The oscilloscope display shows the ventricular contraction rate in the Heart Rate window. The heart activity window to the right of the Heart Rate display provides the following messages:

- Heart Rate Normal—displayed when the heart is beating under resting conditions.
- Heart Rate Changing—displayed when the heart rate is increasing or decreasing.
- Heart Rate Stable—displayed when the heart rate is steady, but higher or lower than normal. For example, if you applied a chemical that increased heart rate to a stable but higher-than-normal rate, you would see this message.

The electrical stimulator is below the oscilloscope display. In the experiment, clicking Single Stimulus delivers a single electrical shock to the frog heart. Clicking Multiple Stimulus delivers repeated electrical shocks at the rate indicated in the Stimuli/sec window just below the Multiple Stimulus button. When the Multiple Stimulus button is clicked, it changes to a Stop Stimulus button that allows you to stop electrical stimulation as desired. Clicking the (+) or (−) buttons next to the Stimuli/sec window adjusts the stimulus rate. The voltage delivered when Single Stimulus or Multiple Stimulus is clicked is displayed in the Voltage window just below the Single Stimulus button. The simulation automatically adjusts the voltage for the experiment. The postlike apparatus extending upward from the electrical stimulator is the electrode holder into which you will drag-and-drop electrodes from the supply cabinet in the bottom left corner of the screen.

The left side of the screen contains the apparatus that sustains the frog heart. The heart has been lifted away from the body of the frog by a hook passed through the apex of the heart. Although the frog cannot be seen because it is in the dissection tray, its heart has not been removed from its circulatory system. A thin string connects the hook in the heart to the force transducer at the top of the support bracket. As the heart contracts, the string exerts tension on the force transducer, which converts the contraction into the oscilloscope tracing. The slender white strand extending from the heart toward the right side of the dissection tray is the vagus nerve. In the simulation, room-temperature (23°C) frog Ringer’s solution continuously drips onto the heart to keep it moist and responsive so that a regular heart beat is maintained.

The two electrodes you will use during the experiment are located in the supply cabinet beneath the dissection tray. The Direct Heart Stimulation electrode is used to stimulate the ventricular muscle directly. The Vagus Nerve Stimulation electrode is used to stimulate the vagus nerve. To position either electrode, click and drag the electrode to the two-pronged plug in the electrode holder and then release the mouse button.

**ACTIVITY 1**

**Recording Baseline Frog Heart Activity**

1. Before beginning to stimulate the frog heart experimentally, watch several heartbeats. Be sure you can distinguish atrial and ventricular contraction (Figure 34b.2a).

2. Record the number of ventricular contractions per minute displayed in the Heart Rate window under the oscilloscope.

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___________________ bpm (beats per minute)  
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**ACTIVITY 2**

**Investigating the Refractory Period of Cardiac Muscle**

In Exercise 16b you saw that repeated rapid stimuli could cause skeletal muscle to remain in a contracted state. In other words, the muscle could be tetanized. This was possible because of the relatively short refractory period of skeletal muscle. In this experiment you will investigate the refractory period of cardiac muscle and its response to stimulation.

1. Click and hold the mouse button on the Direct Heart Stimulation electrode, and drag it to the electrode holder.

2. Release the mouse button to lock the electrode in place. The electrode will touch the ventricular muscle tissue.

3. Deliver single shocks in succession by clicking Single Stimulus rapidly. You may need to practice to acquire the correct technique.

Watch for extrasystoles, which are extra beats that show up riding on the ventricular contraction peak. Also note the compensatory pause, which allows the heart to get back on schedule after an extrasystole (Figure 34b.2b).

**FIGURE 34b.2** Recording of contractile activity of a frog heart. (a) Normal heartbeat. (b) Induction of an extrasystole.
On the basis of the recording, during which portion of the cardiac cycle was it possible to induce an extrasystole? Use Figures 34B.2a and b to help you decide.

4. Attempt to tetanize the heart by clicking Multiple Stimulus. Electrical shocks will be delivered to the muscle at a rate of 20 stimuli/sec. What is the result?

Considering the function of the heart, why is it important that the heart muscle cannot be tetanized?

5. Click Stop Stimulus to stop the electrical stimulation.

**ACTIVITY 3**

**Examining the Effect of Vagus Nerve Stimulation**

The vagus nerve carries parasympathetic impulses to the heart, which modify heart activity.

1. Click the Direct Heart Stimulation electrode to return it to the supply cabinet.
2. Click and drag the Vagus Nerve Stimulation electrode to the electrode holder.
3. Release the mouse button to lock the electrode in place. The vagus nerve will automatically be draped over the electrode contacts.
4. Adjust the stimulator to 50 stimuli/sec by clicking the (+) or (−) buttons.
5. Click Multiple Stimulus. Allow the vagal stimulation to continue until the heart stops momentarily and then begins to beat again (vagal escape), and then click Stop Stimulus.

What is the effect of vagal stimulation on heart rate?

The phenomenon of vagal escape demonstrates that many factors are involved in heart regulation and that any deleterious factor (in this case, excessive vagal stimulation) will be overcome, if possible, by other physiological mechanisms such as activation of the sympathetic division of the autonomic nervous system (ANS).

**Assessing Physical and Chemical Modifiers of Heart Rate**

Now that you have observed normal frog heart activity, you will have an opportunity to investigate the effects of various modifying factors on heart activity. After removing the agent in each activity, allow the heart to return to its normal rate before continuing with the testing.

Choose **Modifiers of Heart Rate** from the **Experiment** menu. The opening screen will appear in a few seconds (Figure 34B.3). The appearance and functionality of the oscilloscope display is the same as it was in the Electrical Stimulation experiment. The solutions shelf above the oscilloscope display contains the chemicals you’ll use to modify heart rate in the experiment. You can choose the temperature of the Ringer’s solution dispensed by clicking the appropriate button in the Ringer’s dispenser at the left part of the screen. The doors to the supply cabinet are closed during this experiment because the electrical stimulator is not used.

When you click **Record Data** in the data control unit below the oscilloscope, your data is stored in the computer’s memory and is displayed in the data grid at the bottom of the screen; data displayed include the solution used and the resulting heart rate. If you are not satisfied with a trial, you can click Delete Line. Click Clear Table if you wish to repeat the entire experiment.

**ACTIVITY 4**

**Assessing the Effect of Temperature**

Predict what effect a decrease in temperature will have on heart rate and write your prediction below.

1. Click the 5°C Ringer’s button to bathe the frog heart in cold Ringer’s solution. Watch the recording for a change in cardiac activity.
2. When the heart activity window displays the message Heart Rate Stable, click Record Data to retain your data in the data grid.

What change occurred with the cold (5°C) Ringer’s solution? Compare to the baseline value recorded in Activity 1.

Did this change match your prediction? _________________

3. Now click the 23°C Ringer’s button to flood the heart with fresh room-temperature Ringer’s solution.
4. After you see the message Heart Rate Normal in the heart activity window, click the 32°C Ringer’s button.
5. When the heart activity window displays the message Heart Rate Stable, click Record Data to retain your data.
What change occurred with the warm (32°C) Ringer’s solution?

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Record the heart rate at the two temperatures below.

__________ bpm at 5°C; ______________ bpm at 32°C

What can you say about the effect of temperature on heart rate?

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6. Click the 23°C Ringer’s button to flush the heart with fresh Ringer’s solution. Watch the heart activity window for the message Heart Rate Normal before beginning the next test.

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**ACTIVITY 5**

Assessing the Effect of Pilocarpine

1. Click and hold the mouse on the pilocarpine dropper cap.
2. Drag the dropper cap to a point about an inch above the heart, and release the mouse.
3. Pilocarpine solution will be dispensed onto the heart, and the dropper cap will automatically return to the pilocarpine bottle.
4. Watch the heart activity window for the message Heart Rate Stable, indicating that the heart rate has stabilized under the effects of pilocarpine.
5. After the heart rate stabilizes, record the heart rate in the space provided below, and click Record Data to retain your data in the grid.

__________ bpm
What happened when the heart was bathed in the pilocarpine solution?

Pilocarpine simulates the effect of parasympathetic nerve (hence, vagal) stimulation by enhancing acetylcholine release; such drugs are called parasympathomimetic drugs.

**ACTIVITY 6**

**Assessing the Effect of Atropine**

1. Drag-and-drop the atropine dropper cap to a point about an inch above the heart.
2. Atropine solution will automatically drip onto the heart, and the dropper cap will return to its position in the atropine bottle.
3. Watch the heart activity window for the message Heart Rate Stable.
4. After the heart rate stabilizes, record the heart rate in the space below, and click **Record Data** to retain your data in the grid.

__________ bpm

What is the effect of atropine on the heart?

Atropine is a drug that blocks the effect of the neurotransmitter acetylcholine, liberated by the parasympathetic nerve endings. Do your results accurately reflect this effect of atropine?

Are pilocarpine and atropine agonists or antagonists with respect to each other in their effects on heart activity?

**ACTIVITY 7**

**Assessing the Effect of Epinephrine**

1. Drag-and-drop the epinephrine dropper cap to a point about an inch above the heart.
2. Epinephrine solution will be dispensed onto the heart, and the dropper cap will return to the epinephrine bottle.
3. Watch the heart activity window for the message Heart Rate Stable.
4. After the heart rate stabilizes, record the heart rate in the space provided below, and click **Record Data** to retain your data in the grid.

__________ bpm

What happened when the heart was bathed in the epinephrine solution?

Which division of the autonomic nervous system does its effect imitate?

**ACTIVITY 8**

**Assessing the Effect of Digitalis**

1. Drag-and-drop the digitalis dropper cap to a point about an inch above the heart.
2. Digitalis solution will automatically drip onto the heart, and then the dropper will return to the digitalis bottle.
3. Watch the heart activity window to the right of the Heart Rate window for the message Heart Rate Stable.
4. After the heart rate stabilizes, record the heart rate in the space provided below, and click **Record Data** to retain your data in the grid.

__________ bpm

What is the effect of digitalis on the heart?

Digitalis (also known as digoxin and digitoxin) is a drug commonly prescribed for heart patients with congestive heart failure. It slows heart rate and strengthens the force of contraction of the heart, providing more time for venous return and decreasing the workload on the weakened heart. These effects are thought to be due to inhibition of the sodium-potassium pump and enhancement of Ca^{2+} entry into myocardiial fibers.
ACTIVITY 9

Assessing the Effect of Various Ions

To test the effect of various ions on the heart, apply the desired solution using the following method.

1. Drag-and-drop the calcium ions dropper cap to a point about an inch above the heart.
2. Calcium ions will automatically be dripped onto the heart, and the dropper cap will return to the calcium ions bottle.
3. Watch the heart activity window for the message Heart Rate Stable.
4. When you see Heart Rate Stable on the screen, record the heart rate in the space provided below step 6, and click Record Data to retain your data in the grid.
5. Click the 23°C Ringer’s button to flush the heart with fresh Ringer’s solution. Watch the heart activity window for the message Heart Rate Normal, which means that the heart is ready for the next test.
6. Repeat steps 1 through 5 for sodium ions and then potassium ions.

Effect of Ca\(^{2+}\):
Does the heart rate stabilize and remain stable?

Describe your observations of the rhythm of the heartbeat.

Effect of Na\(^{+}\):
Does the heart rate stabilize and remain stable?

Describe your observations of the rhythm of the heartbeat.

Effect of K\(^{+}\):
Describe what happened to the recording.

Describe your observations of the rhythm of the heartbeat.

Potassium ion concentration is normally higher within cells than in the extracellular fluid. Hyperkalemia decreases the resting potential of plasma membranes, thus decreasing the force of heart contraction. In some cases, the conduction rate of the heart is so depressed that ectopic pacemakers (pacemakers appearing erratically and at abnormal sites in the heart muscle) appear in the ventricle, and fibrillation may occur.

Was there any evidence of premature beats in the recording of potassium ion effects?

Was arrhythmia produced with any of the ions tested?

If so, which?

7. Click Tools → Print Data to print your recorded data for this experiment.

Histology Review Supplement

For a review of cardiovascular tissue, go to Exercise 68: Histology Atlas and Review on myA&P to print out the Cardiovascular Tissue Review worksheet.