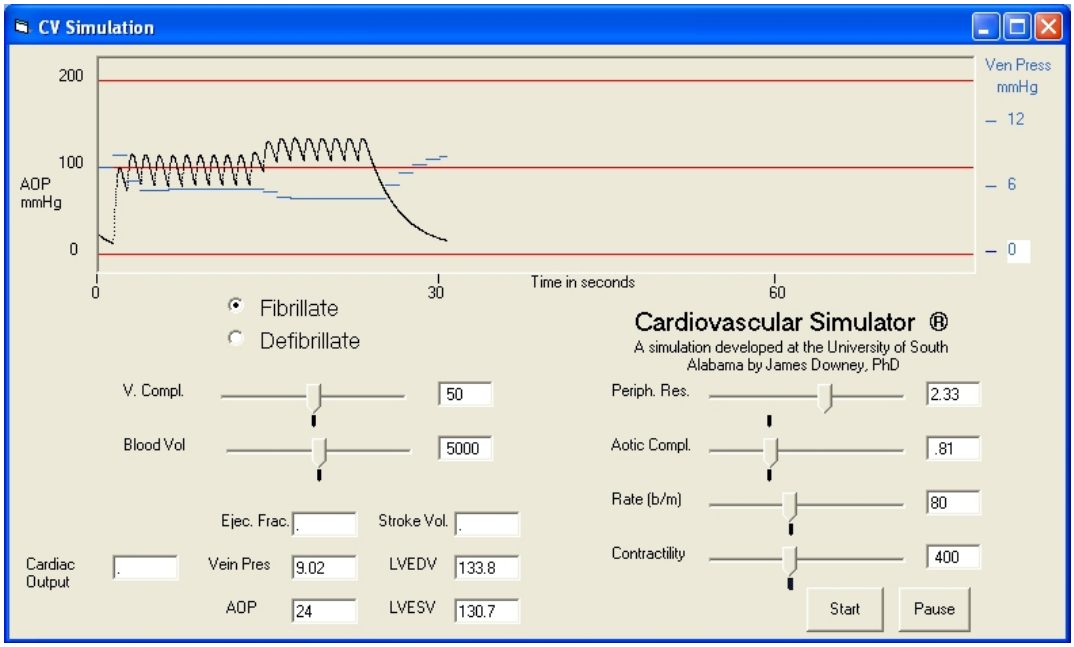
Working with the Cardiovascular Simulator



In the body cardiovascular reflexes control cardiac output by varying the peripheral resistance, the venous compliance, the heart rate and the cardiac contractility. Similarly, the kidney controls blood volume. In this simulation the operator must control these parameters manually. We have also added one more control with which the student can simulate disease states: aortic compliance. We would like you to complete the following exercises which should help you better understand how the cardiovascular system behaves in normal and disease states.

1. **The effect of changing peripheral resistance.** Start the simulation program. You will see a control panel, some text windows and graph window. Click the start button to begin the simulation. The default settings when the program starts provide normal physiological values. The heart is beating at 80 beats per minute and blood pressure is about 110/75. Mean aortic pressure is about 95 mmHg. Fill in column 1 of the table below.

Peripheral resistance	1.333 (Default)	3.0
Mean aortic pressure		
Cardiac output		
LVESV		
LVEDV		
Stroke volume		
Ejection fraction		
Aortic pulse pressure		
Venous pressure		

Now increase peripheral resistance to 3.0 by moving the slider. When a steady state is achieved, again fill in the table. The most obvious effect was on blood pressure which rose as you probably predicted. This was not an isolated effect however. Note that stroke volume, cardiac output and ejection fraction all fell. Some of this was the result of falling venous pressure causing a

reduction of LVEDV which would be expected if more blood were trapped on the arterial side leading to a rise in aortic pressure. But some of the effect was also related to increased aortic pressure against which the heart had to eject. Increase blood volume until venous pressure and LVEDV are restored. Did that restore stroke volume? _____ The high aortic pressure caused the ventricle to stop ejecting at a higher left ventricular end systolic volume. Since stroke volume is the difference between LVEDV and LVESV, it fell. Because all parameters interact, any change in one parameter causes changes in the others. The purpose of this exercise is to show you how to analyze this interactive system.

Ventricular fibrillation

When the ventricle fibrillates the heart stops pumping blood. You can simulate this by clicking the "fibrillate" button. Notice that arterial pressure falls and venous pressure rises until they are equal. This is the mean systemic filling pressure (MSFP). While the heart is stopped, increase the peripheral resistance. What happened to MSFP?_____ Now decrease venous compliance. What was the effect on MSFP?_____ You can restart the heart by clicking "defibrillate".

The effect of increasing blood volume

Figure 4 shows the venous function curves in blue. Notice that venous pressure falls as cardiac output increases. That is because there is less blood in the veins and more in the arteries at high cardiac outputs. The red line shows a ventricular function curve superimposed on the figure. This curve plots cardiac output as a function of the heart's venous pressure. The venous and cardiac curves present two equations based on venous pressure they can be solved simultaneously. Their unique solution is where the lines cross. That crossing is the resulting venous pressure and cardiac output. Three blood volumes are shown. The graph predicts that increasing blood volume (hypervolemia) will increase venous pressure and cardiac output. Conversely, lowering blood volume (hypovolemia) will decrease the two parameters.

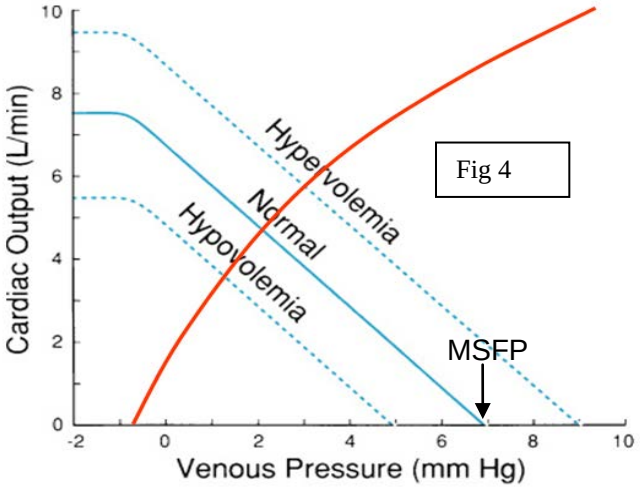


Fig 4

Start the simulation with the default parameters and fill in column 1 of the table below. Now increase blood volume to 6200 ml and fill in the next column. Did cardiac output go up? _____ Did venous pressure go up? _____

Blood Volume	5000	6200	3500
Mean aortic pressure			
Cardiac output			
LVESV			
LVEDV			
Stroke volume			
Ejection fraction			
Aortic pulse pressure			
Venous pressure			

Hemorrhagic shock

Shock is a condition in which the cardiac output is inadequate to meet the needs of the body. Patients suffering blood loss experience hemorrhagic shock. This can be simulated by reducing blood volume to 3500. Fill in the third column of the table. Note that both venous pressure and cardiac output fell. The low venous pressure resulted in a small LVEDV. That in turn gave the ventricle less blood to eject so stroke volume decreased and cardiac output is simply the product of stroke volume and heart rate. Note that small changes in venous pressure cause big changes in cardiac output. What happened to cardiac output?_____ See if you can restore cardiac output by giving a vasoconstrictor drug. These drugs constrict both arteries and veins. Increase peripheral resistance to 3 and decrease venous compliance to 34. What was the effect on blood pressure? _____ Did it restore cardiac output?_____ It is easy to restore blood pressure with a vasoconstrictor drug and mistakenly think the patient is OK. In fact you may have worsened the shock condition by further reducing cardiac output! Unfortunately blood pressure is easily measured in the ER but cardiac output is not. One of the clues that cardiac output is inadequate is the patient's pulse pressure. Pulse pressure is determined by stroke volume divided by aortic compliance. Changing either parameter changes pulse pressure. What happened to pulse pressure as compared to that with the normal settings?_____ Compare this pulse pressure with that in the aortic aneurism and the hardening of the arteries exercises below. Why does blood loss make the cardiac output so low? _____ What would be the best treatment for this patient?_____

Changing contractility

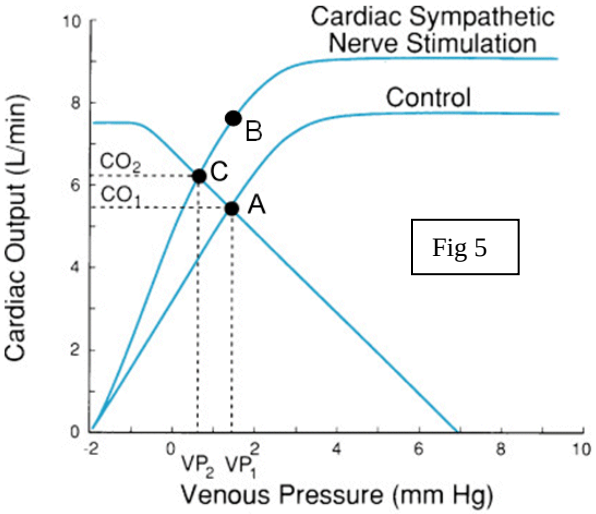


Fig 5

Figure 5 shows the graphic analysis for a change in contractility. Both the ventricular and peripheral venous function curves are drawn. Under control conditions the heart is at point A. Increasing contractility by stimulating sympathetic nerves causes the heart to contact more forcefully at any given length. This shifts the ventricular function curve up and to the left. Therefore at any filling pressure the stimulated heart will pump a greater stroke volume and thus a greater cardiac output (point B). The increased cardiac output will blunt the response, however, because the venous pressure will fall (see Fig. 1). The net result (point C) is still an increased cardiac output, but with a decreased venous pressure.

Fill in column one of the table below using the default parameters and then increase contractility with the slider to 700. Notice the transient response of stroke volume. For several beats stroke volume is quite high, but as venous pressure falls it decreases to a more modest value. When the values stabilize fill in the table. At steady-state was stroke volume increased? _____ What happened to venous pressure?_____. Now drop contractility to 200. Note the changes and at steady-state fill in column 3 of the Table.

Contractility	400	700	200	200 + Blood volume = 6500
Mean aortic pressure				
Cardiac output				
LVESV				
LVEDV				
Stroke volume				
Ejection fraction				
Aortic pulse pressure				
Venous pressure				

The cardinal sign of heart failure is elevated venous pressure. Part of that increase is caused by the immediate increase in venous pressure that accompanies a reduced cardiac output as demonstrated above. The kidneys will detect the reduced cardiac output and they will retain fluid in an attempt to restore cardiac output by increasing blood volume. In the simulation increase blood volume to 6500 while keeping contractility at 200 and fill in the last column of the table. What happened to cardiac output?_____. What happened to venous pressure?_____ This is an example of compensated heart failure. Resting cardiac output and blood pressure are near normal values, but venous pressure is elevated (an important clinical sign). The patient's exercise tolerance would be reduced.

Spinal Shock

In spinal shock peripheral resistance is abnormally low. You can simulate that by reducing peripheral resistance. Return all controls to their default values as indicated by the marks and fill in column 1 of the table below. After a steady state is achieved lower the peripheral resistance to 0.333 and increase venous compliance to 90. When the simulation has settled fill in the second column of the table. Note that all parameters except aortic pressure went up because it is now very easy to pump blood around the system. Because aortic pressure (and thus arterial volume) is low, venous pressure is high so the ventricle has a high LVEDV. We typically use the word "shock" to describe a condition in which cardiac output is inadequate. Spinal shock is a special case. While the cardiac output may be high, flow is actually bypassing vital organs like the brain and heart whose vessels would not be dilated by the loss of sympathetic tone from the injured spinal nerves. Their flows would have actually fallen because of the low aortic perfusion pressure. Peripheral resistance returns to normal after a week or two in these patients.

Peripheral resistance	1.333	0.333 & 90
Mean aortic pressure		
Cardiac output		
LVESV		
LVEDV		
Stroke volume		
Ejection fraction		
Aortic pulse pressure		
Venous pressure		

Third-degree (complete) heart block.
Restart the simulation with default parameters and fill in the table below. In third- degree heart block conduction through the AV node is blocked and the ventricles beat at their own intrinsic rate which is very slow. You can simulate this by moving the rate slider to the left to 32 beats/min. When the system reaches steady state, fill in the second column. These people with complete heart block have extremely low exercise tolerance and often may faint. Can you restore a normal mean aortic pressure by increasing blood volume and contractility?_____. What would be the logical treatment for this patient? _____.

Rate	80	32
Mean aortic pressure		
Cardiac output		
LVESV		
LVEDV		
Stroke volume		
Ejection fraction		
Aortic pulse pressure		
Venous pressure		

Supraventricular tachycardia.
In some individuals disease in the atria causes the atria to beat very rapidly. When that happens the ventricles will try to do the same. Set the simulation to normal parameters and fill in the first column. Then increase the heart rate to 96. What happened to cardiac output? _____ We would have expected a 20% increase in cardiac output since rate increased by 20%. How much did the cardiac output increase (in percentage)?_____ Why didn't it increase by 20%? _____

Now increase the heart rate to 176 and fill in the last column. What happened to cardiac output?_____ Clearly stroke volume fell faster than the increase in rate so that their product decreased. Did stroke volume decrease because venous pressure was low? _____ Why do you think stroke volume decreased so dramatically? _____

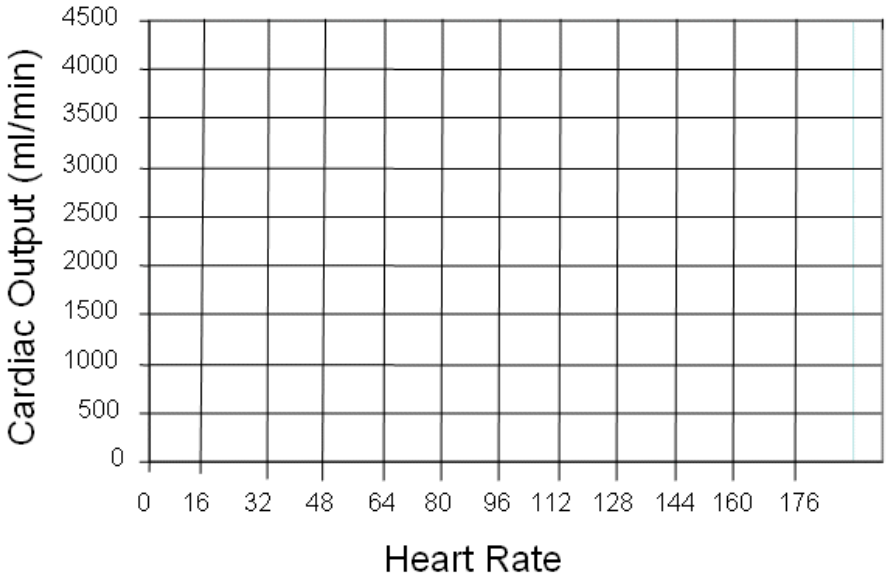
Rate	80	96	176
Mean aortic pressure			
Cardiac output			
LVESV			
LVEDV			
Stroke volume			
Ejection fraction			
Aortic pulse pressure			
Venous pressure			

Below is a grid on which you can plot cardiac output against heart rate. Plot all 10 points on the graph and be sure to include a point at 0, 0. Draw a line from the 80 b/m point and the origin (0,

0). That is what would be expected if cardiac output was proportional to heart rate. Did your points fall on that line?_____ If not, why didn't they? _____
_____

Notice that the curve falls into three regions. Below 60 b/m (bradycardia) and above 130 b/m (tachycardia) cardiac output falls off dramatically. In the normal range (60-100 b/m) cardiac output is relatively independent of heart rate.

In contrast to tachycardias generated by an ectopic focus as in the above example, tachycardia resulting from sympathetic stimulation is well tolerated because adrenergic stimulation of the myocytes causes more rapid ejection and a shortening of the action potential which gives a longer diastolic time for filling between beats.



Hypertension.
Hypertension or "high blood pressure" is a common ailment among adults in this country. There are many forms, but it is usually caused by a combination of increased blood volume and peripheral resistance. You can simulate it by increasing the peripheral resistance to 2.0 and the blood volume to 5600. What is the new mean aortic pressure?_____ A common treatment for hypertension is reduction of blood volume with a diuretic, e.g., furosemide. Can you return mean aortic pressure to 100 by reducing blood volume?_____ What blood volume was required?_____

Another commonly used anti-hypertensive drug is a beta-blocker such as propranolol that blocks beta-adrenergic receptors. It reduces the heart's contractility. Return blood volume to 5600 and see if you can correct the hypertension by reducing contractility. Did reducing contractility reduce the pressure?_____

A third class of anti-hypertensive drug is the calcium channel antagonist such as diltiazem. Both vascular smooth muscle and cardiac muscle are stimulated by calcium entry into the cell. Partial block of calcium channels reduces that entry and depresses their contraction. Those drugs reduce contractility in the heart and dilate both the veins which increases venous compliance and

the arterioles which increases peripheral resistance. Imagine how powerful these drugs can be by affecting all 3 parameters.

Aortic aneurysm

An aneurysm is a dilated section of a large artery. Aneurysms of the aorta can be quite large and can rupture causing sudden death. These aneurysms can greatly increase the compliance of the aorta. Start the simulation with the default parameters and fill in the table below. Increase the aortic compliance to 2.56 and fill in the second column. What is the effect on pulse pressure?_____ Did anything else change by much? _____.

Now return the compliance to normal and increase the rate to 128 beats/min and peripheral resistance to 2. Fill in the third column of the table. What was the effect on pulse pressure? _____ Why was pulse pressure reduced this time?_____

Intervention	normal	Aortic compl. 2.56	Rate 128 Resist. 2
Mean aortic pressure			
Cardiac output			
LVESV			
LVEDV			
Stroke volume			
Ejection fraction			
Aortic pulse pressure			
Venous pressure			

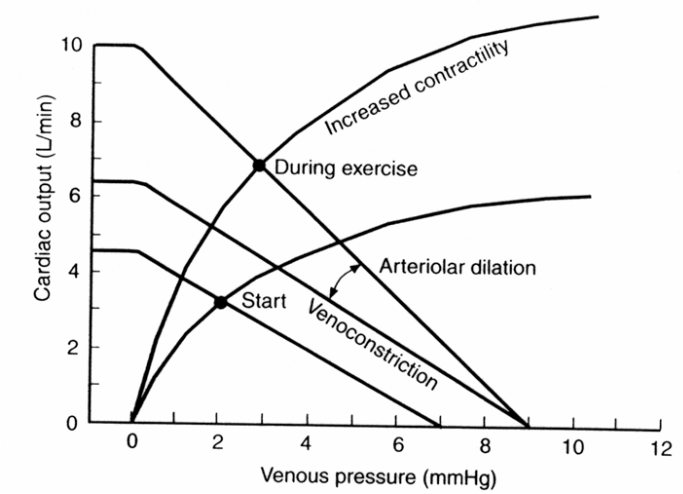
Pulse pressure is determined by stroke volume divided by aortic compliance. Mean aortic pressure is strictly the product of cardiac output and peripheral resistance. Changes in peripheral resistance should not affect pulse pressure. Starting from the default parameters increase peripheral resistance to 2.666. What happened to pulse pressure?_____ The pulse pressure was affected by the decrease in stroke volume caused by the increased afterload and decreased venous pressure. We can restore stroke volume to its original value by increasing blood volume to 5600 ml and contractility to 700. Is the pulse pressure restored to its starting value?_____

Hardening of the arteries (arteriosclerosis)

As we age we have a gradual loss of arterial compliance. This causes pulse pressure to increase in the elderly. To simulate this, start the simulator with the default parameters and then decrease aortic compliance to 0.36. What was the effect on pulse pressure?_____ Did the change in compliance greatly change mean aortic pressure?_____

Exercise

During exercise multiple changes occur to increase cardiac output as shown in the graph below. The veins are constricted due to sympathetic stimulation. At the same time the arterioles of the exercising muscle are widely dilated by an active hyperemia which reduces the overall peripheral resistance. Finally, the heart rate increases along with contractility because of stimulation of cardiac sympathetic nerves. In the figure below the adjustments during exercise essentially doubled the cardiac output.



We can simulate the exercise state. Set the simulator to the default parameters and start it. What is the new cardiac output?_____ Now decrease venous compliance to 10 and decrease peripheral resistance to 0.666. Increase contractility to 700 and heart rate to 96. What is the cardiac output now?

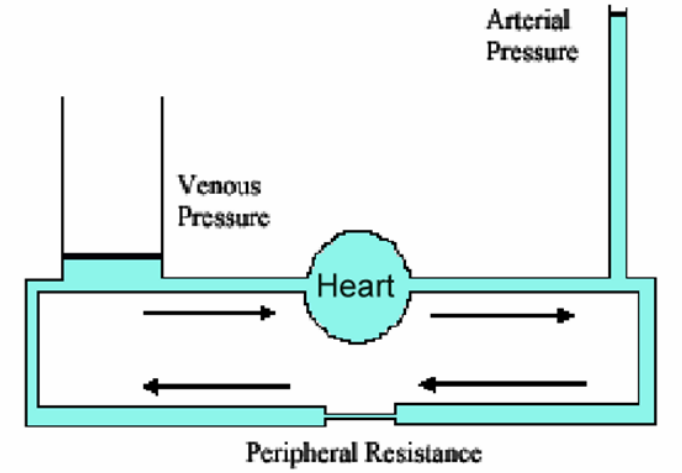
_____

How it works

The peripheral Circulation

The model simulates the cardiovascular system of a 70 kg individual. All cardiovascular reflexes have been deactivated and in their place are controls that allow the operator to adjust the system's control points manually. The cardiovascular system is modeled as shown in figure 1. There are two compartments: the arterial and the venous. The arterial compartment has low compliance and is illustrated as a tall, thin tube. Adding a small volume of fluid to the arterial compartment causes a large increase in height and thus pressure as shown. The venous compartment is represented by a wide reservoir such that pressure rises little when a large volume is added to it. In the simulation the venous compliance is about 100 times the arterial compliance.

Fig 1

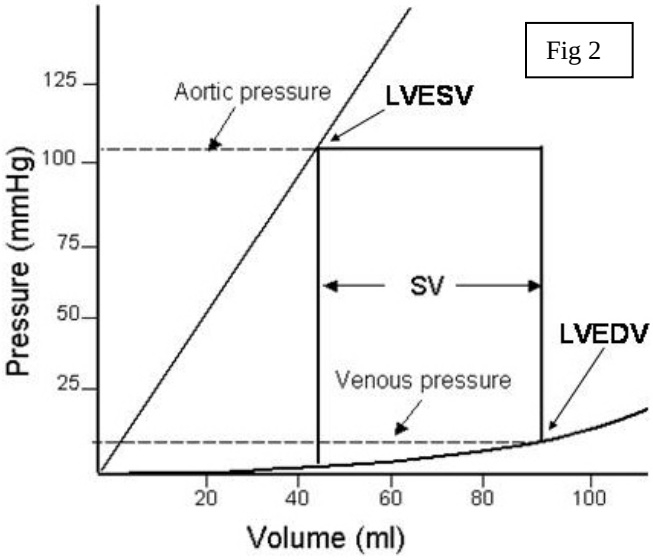


Note that blood flows from the arterial compartment to the venous compartment across the peripheral resistance. Peripheral blood flow is given by Ohm's law as the ratio of the difference between arterial and venous pressure to peripheral resistance. At the same time flow enters the aorta as the cardiac output. Arterial volume is the running integral of inflow minus outflow. At a steady state the cardiac output must equal the peripheral flow. If cardiac output exceeds peripheral flow, blood will accumulate on the arterial side. That will raise arterial pressure and lower venous pressure and increase peripheral flow until a new steady state is achieved.

What makes the model interesting is that the cardiac output is a function of the venous pressure that fills the ventricle. The more the ventricle is filled during diastole, the more blood is pumped during systole. As will be shown below, the heart's stroke volume is determined by 3 factors: filling pressure, aortic pressure and the contractility of the heart. In the simulation the heart's filling pressure is taken from the venous pressure. The following equations were used to calculate the variables for the peripheral circulation:

Cardiac output = a function of ($P_{arterial}$, contractility, P_{venous})
$Volume_{arterial} = \int$ (Cardiac Output – Peripheral flow) dt
$P_{arterial} = Volume_{arterial} / Compliance_{arterial}$
$Volume_{venous}$ = Total Blood volume - $Volume_{arterial}$
$P_{venous} = Volume_{venous} / Compliance_{venous}$
Peripheral flow = ($P_{arterial} – P_{venous}$) / peripheral resistance

The model solves these equations 100 time per second. Notice that moving blood into the arterial compartment reduces venous volume and thus venous pressure. This gives stability to the system and actually tends to buffer any change in cardiac output as will be seen in the exercises.



The heart generates the cardiac output
Figure 2 shows the heart's static mechanics in the pressure-volume curve. The ejection loop is drawn between two curves. The upper curve is for systole when the heart muscle has contracted and the lower curve is for diastole when the heart is relaxed. Notice that the left ventricular end-diastolic volume (LVEDV) is determined by the intersection of venous pressure and the diastolic curve. The left ventricular end systolic volume (LVESV) is determined by the intersection of aortic pressure and the systolic curve. The difference between the two volumes is the stroke volume, the volume of blood pumped by one beat.
The curve in figure 2 shows what happens at the beginning and end of systole but says nothing about what happens in between. Figure 3 shows a force-velocity curve for the ventricle. Notice that the velocity of shortening is determined by both the length of the muscle and the load it is contracting against, in this case ventricular pressure. The curved line on the graph shows ventricular pressure which during ejection is the same as aortic pressure. The intersection of this ventricular/aortic pressure curve with each of the family of force-velocity curves determines the velocity of ejection at that point in time. As the heart ejects blood, the sarcomeres in the muscle shorten and that slows the velocity of ejection. At the onset of systole ejection is very fast, but it then slows as the fibers shorten. It will stop when the muscle fibers are so short that their velocity of shortening against the aortic pressure becomes zero. That point is at LVESV. The simulation calculates ventricular volume with each iteration and determines a pressure-velocity line for that volume. The aortic pressure at that moment determines the rate of ejection for that iteration. Other features in the heart model are reduced filling times at heart rates above 90 beats/min and pericardial restraint that keeps the LVEDV from exceeding 160 ml.