

Modeling the Cardiovascular System using STELLA[®]

A module for Computational Biology by Karl Romstedt

Description

This module teaches concepts regarding cardiovascular function and modeling. It is intended for a college audience but requires only basic skills in biology, mathematics and programming. The module will include lecture/discussion periods, computer laboratories and hands-on experimentation. It is designed to be a stand-alone unit that can be integrated anywhere into the course on Computational Biology. If it is used after the section on statistics and curve-fitting, however, these concepts can be incorporated into group projects involving physiological experimentation and data collection. Little in the way of explicit prerequisites are required since the intention is to cover the required biology and computational science during the module. Some questions may require using the web or other references for investigation of advanced topics. The central focus will be on a model for blood flow that uses Poiseuille's Law to explain the relationship between blood vessel diameter, blood viscosity and blood pressure.

Goals

To learn the basic physiology of the cardiovascular system.

To apply mathematical principals to the function of the cardiovascular system.

To learn how to make models using STELLA[®] Software.

To model the cardiovascular system using STELLA[®] Software.

To use models to show how pathologies and pharmacological treatments affect the function of the cardiovascular system.

Introduction

Jason is an avid cyclist and he has become quite successful in both local and regional bicycle marathons. His father was a worldwide champion and Jason very much desires to show his father that the son is worthy of his father's praise. Jason's next goal is to win a national championship but he knows that it will be an extremely difficult endeavor with intense competition from worthy opponents. If only he had an edge. Jason has read about a process called "**doping**" that might give him such an edge. Moreover, he fears that his opponents will be using this technique to promote their own chances so Jason

feels that he must follow suit to remain competitive. Doping refers to methods for enhancement of aerobic capabilities by increasing the concentration of red blood cells (RBC's) in the bloodstream. The increased oxygen carrying capacity of the blood enhances any extended athletic endeavor such as a cycling marathon.

Doping may be accomplished by drawing a pint or two of blood from the athlete and then restoring it back to the person's bloodstream a week or so later but within a few days of a competitive event. During the intervening time, the person will naturally regenerate the blood cells they lost so that after the infusion of their stored blood their RBC count will be unnaturally high. Since no drugs are involved, the condition cannot be detected by typical urine tests. It could be detected by centrifuging a sample of blood to measure the **hematocrit** which is the percentage volume of the packed cells compared to the total volume of the blood sample.

An increase in RBC count can also occur naturally during hypoxic conditions such as living in high altitudes. In this situation, the body responds to low oxygen pressure in the atmosphere by increasing the red cell count to provide better oxygen carrying capacity. This can give athletes who live in elevated environments an advantage when competing at sea level or can create a handicap for athletes from lower altitudes when they compete in the mountains. The natural stimulation of **erythrocyte** (red blood cell) production involves a hormone called **erythropoietin** (EPO). Injection of this drug can be yet another way to enhance performance.

There is a potentially lethal drawback to doping. The increase in solid, cellular elements within the blood causes it to become thicker and more viscous. This makes the blood more difficult to pump, especially in the venous system where the pressure that pushes blood back to the heart is low. A further complication is that physiological dehydration may be a consequence of extended and vigorous exertion during a marathon. Loss of water, the blood solvent, results in an increased concentration of erythrocytes so that the blood becomes even more viscous. Can you envision potential consequences of blood doping?

Statement of the Problem

The introductory scenario poses a question that is one of several that will be investigated. This module will utilize STELLA[®] Systems Thinking modeling software to illustrate relationships between blood viscosity, pressure and flow. STELLA[®] is especially well adapted to showing dynamic relationships between flow elements such as are found in the cardiovascular system. A number of questions will be investigated using this modeling tool:

What happens to blood flow through the heart as viscosity increases?

What happens to blood flow if cardiac muscle is damaged by a heart attack?

What happens to blood flow if you have high or low blood pressure?

What happens to blood flow as you reduce the radius of arteries as occurs in arteriosclerosis?

After learning the fundamentals of the cardiovascular system, students will use a prepared STELLA[®] model to answer such questions and then make their own models for further inquiries into questions of their own choosing.

Background Information

This section contains an introduction to the cardiovascular system followed by a brief introduction to STELLA[®] modeling software.

Introduction to the Cardiovascular system

Most human body cells are anchored to a fixed place, so supply of essential nutrients must occur through a delivery system. This is the function of the cardiovascular system. It brings energy molecules (glucose), vitamins and other needed molecules to cells from the digestive system. It also provides oxygen that is absorbed from the lungs in the respiratory system. In addition, as body cells chemically carry out the chemical metabolism, they produce some molecules that they cannot use and which may even be toxic to the cells that make them. The cardiovascular system removes these and transports them to appropriate disposal facilities. These include the urinary system (kidneys, bladder, etc.) for nitrogen-containing compounds and the respiratory system where carbon dioxide waste is exhaled.

The cardiovascular system has other functions in addition to distribution of nutrients and waste removal. Arteries and veins provide conduits for immune cells and antibodies to reach areas of infection. Blood works in concert with the nervous system to deliver cellular messages called hormones to targets throughout the body. The blood also maintains a constant environment with respect to temperature and mineral content of fluids that bathe the cells. Advanced life forms are thought to have evolved in seawater and the inorganic composition of blood may be a reflection of the home of our ancient ancestors. To emerge from the sea onto dry land, life needed to bring some of the sea with it.

The cardiovascular system develops in the embryo as a system of tubes that connect all of the regions of the body to a central pumping station, the heart. The human heart itself has evolved from a contractile tube that now has many specialized structures. In an adult human, there are about 100,000 kilometers of blood vessels! Every living cell in the body is within about a millimeter of the blood stream or fluids that are in contact with the blood supply.

Human circulation can be divided into two main highways. In the **systemic circulation**, blood emerges from the left side of the heart and travels throughout most of the body including the head, chest walls, abdomen and limbs. It then returns to the heart to complete the cycle (hence the term circulation). The other pathway is the **pulmonary circulation** that sends blood from the right side of the heart to the lungs where gas exchange occurs, trading carbon dioxide for oxygen. Since all blood must pass through both these areas, the circulation of any particular sample of blood alternates between the systemic and pulmonary pathways. The complete route includes:

- 1) Left side of heart
- 2) Body (Systemic circulation)
- 3) Return to heart, Right side
- 4) Lungs (Pulmonary circulation)
- 5) Return to Heart, Left side
- 6) Repeat from 1)

The human heart actually contains 4 chambers, 1 pair for each side of the heart. Each pair consists of an **atrium** and **ventricle**. As blood returns to the heart, it flows into an atrium on the appropriate side. The atrium expands to accommodate the blood. When the ventricle is ready, the corresponding atrium contracts and forces blood into the chamber of the ventricle. Subsequently, the ventricle contracts to propel blood from the heart. The atrium has two functions. First, it is a reservoir for returning blood since blood returns in a continuous, uninterrupted flow. It stores the blood momentarily while the ventricle is busy pumping the blood it already contains. The second function of the atrium is to contract at the appropriate time, thus delivering its store of blood into the ventricle. Once primed in this fashion, a ventricle's job is to contract, forcing blood into the systemic or pulmonary pathways.

Since blood alternates in its pathway through the heart, a common misconception is that only one side of the heart will contract at a time. This is true with respect to the viewpoint of a particular segment of the blood which can only be on one side or the other. However, blood is flowing everywhere in both the systemic and pulmonary circulations at the same time. As the heart pumps blood, both atria contract simultaneously. A moment later, both ventricles contract together. Thus, there are only two contractile events for the heart even though there are four chambers. That is why the beating heart has a "lub dup" sound. Each of the two sounds is caused by one-way valves that slam shut following contraction of first the atria and then the ventricles. These valves prevent blood from flowing backwards into the chamber that had just contracted. If a valve is damaged, then a portion of the blood can reverse direction and an abnormal whooshing noise, or heart **murmur** can be heard. The reverse flow of blood is called **regurgitation**.

The vessels that carry blood as it emerges from the heart are called arteries. The major artery that begins the systemic circulation is the **aorta**. The walls of the aorta are **elastic** so that the sudden filling causes it to expand as the left ventricle contracts. This has a **dampening effect** on changes of blood pressure within the aorta. During contraction, the heart is actively forcing blood through the arteries and the pressure is at its peak at

this time. This maximum pressure is called the **systolic pressure**. Between contractions, the pressure ebbs away to a minimum value referred to as the **diastolic pressure**. During diastole, the elastic aorta is forcibly shrinking, thus applying pressure to minimize the fall in pressure between heartbeats. Blood pressure is reported as systolic/diastolic values which are typically "120 over 80." The units are in millimeters of mercury that can be supported by the pressure. If the aorta were a stiff, inelastic tube without elastic dampening, the range between the systolic and diastolic pressures would be greater. The resulting high systolic blood pressure could cause the rupture of a blood vessel which would deprive a part of the body of its blood supply. In the brain, this causes a type of **stroke**. Arteries tend to lose their elasticity with age and **arteriosclerosis** (hardening of the arteries) is associated a diet high in saturated fats and cholesterol. This may result in high blood pressure and an increased likelihood of a stroke or other disorder.

Beyond the aorta, other vessels that carry blood from the heart are called **arteries**. Unlike the aorta, many arteries are stiff, thick tubes referred to as **conducting arteries**. Their diameter remains constant throughout each heartbeat and their function is to maintain pressure which provides the force needed for the blood to flow to distant body parts. One function of arteries is as **pressure reservoirs** which means that they contain and maintain pressure. The nervous system can change the diameter of blood vessels by signaling smooth muscle in their walls to contract or relax. The muscle is wrapped around the vessels so that contraction reduces their diameter. This is one of several mechanisms by which the body can control blood pressure. Relaxing arterial smooth muscle reduces the pressure and contraction has the opposite effect.

In order to supply all parts of the body, arteries branch into smaller ones and ultimately become very small arteries called **arterioles**. Because of their small diameters, arterioles have the greatest overall resistance to blood flow, so blood that passes them has a greatly reduced pressure. As an analogy, consider an electronic circuit. If you have studied circuits, you know that there is a voltage drop (pressure decrease) downstream of a resistor. Therefore, the electric current (blood flow) is diminished.

Arterioles ultimately empty into **capillaries** which are the smallest blood vessels. Only about 5% of the total blood volume resides here at any one time. They exist in networks (capillary beds) that perfuse body tissues with blood. The thin walls of capillaries (~1 : m) would be unable to contain the pressure found in arteries. However, thin walls allow substances to diffuse easily between the blood and tissue cells. The reduced pressure and flow rate also augment the exchange of materials. Aside from the drop in pressure, another reason for the reduced flow rate is that the total cross sectional area of capillaries is much greater than in other parts of the circulatory system. This is because there are 10-40 billion capillaries. Since the volume of flow is the same in all parts of the system, it must be slower where there is a greater surface to accommodate the flow. This is similar to when a river spreads out in a delta system. The total volume that passes per minute is the same, but the linear speed is slower. The opposite happens when many small, slow-moving streams merge to form a rapidly moving river.

Thus far, we have considered the delivery of blood to the vicinity of cells throughout the body. The blood must return to the heart to complete the circulation. On the return journey, blood travels through conduits called **veins**. The veins connected directly to the capillaries are small ones called **venules**. These merge to make larger veins and so on. Veins typically have a greater diameter than corresponding arteries. Their walls are more flaccid so they do not contain pressure. After passing through arterioles and capillary beds, blood has little pressure anyway. Aside from conducting blood back to the heart, veins function as **volume reservoirs**. That is, they can store excess volume by relaxing and accommodating more blood. If the total volume of blood gets low, the smooth muscle of veins can contract, so that the volume within veins gets smaller. Blood will then be shifted from veins into other parts of the circulatory system.

The low pressure on the venous side of the circulation presents a special problem with regard to blood flow. With low pressure, there is little force to promote the return of venous blood to the heart, a process called **venous return**. So how does blood from the toes manage to defeat gravity and reach the heart? The answer is related to special one-way valves found in veins, but not arteries. These valves resemble pockets attached to the inside of the veins with their open ends facing the same way as normal blood flow. Blood flowing in the correct direction will bypass the opening of the pocket and flatten it as it flows by. When gravity pulls blood in the wrong direction, blood fills the pockets, swelling them until they block the diameter of the vein. Blood that is trapped above a vein is propelled forward by something pressing on the vein and squeezing the contents away from the valve. That something that presses on the vein in this fashion is skeletal muscle. Skeletal muscle is the muscle that is attached to the skeleton and is used to move portions of the body. Therefore, normal body movements participate in pushing venous blood back towards the heart. Soldiers standing at attention for long periods of time on a parade ground sometimes faint. This results from inactivity and a corresponding lack of blood return to the heart. Blood pools in the feet and the heart has less to pump to the brain. The brain starves and malfunctions, creating the fainting condition. Another consequence of inactivity is seen in patients who have been bedridden for long periods of time. Lack of physical activity allows blood to pool in the venous reservoir, stagnate and then clot. This condition is called **deep vein thrombosis** (thrombus = clot).

The human heart pumps about once per second and will do so about 3 billion times during a person's lifetime. Like any other tissue, heart tissue needs to be supplied by blood within a system of capillaries that are in intimate contact with the heart muscle cells. The atria and ventricles allow large volumes of blood to flow through the heart, but this blood does not nourish the cells of the heart. This is the job of the **coronary arteries** that divert a portion of the blood into cardiac capillary beds. Whenever something blocks blood flow in a coronary artery, the heart malfunctions and a heart attack ensues.

The blood itself is an aqueous mixture containing cells and dissolved chemicals. The dissolved substances include minerals, vitamins, sugars, lipids, amino acids and proteins. Most of the cells are red blood cells (**erythrocytes**). These cells contain **hemoglobin**. This protein latches onto oxygen in oxygen-rich regions such as the lungs and then releases it in tissues that are oxygen-poor. Unlike most body cells, erythrocytes do not

contain a nucleus. This may provide more room for hemoglobin or may facilitate the passage of these cells through capillaries which are barely one cell thick in diameter. The cells may have to squeeze through some capillaries, or roll along the inner capillary wall using their cell membrane like a tank tread.

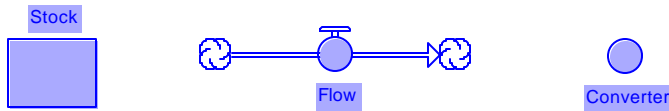
Because of the high concentration of red blood cells (5 billion/ml), they have a profound effect on blood flow dynamics. They add **viscosity** to blood which contributes to the resistance to blood flow. Anything that increases the concentration of cells will increase the viscosity of blood and, in the absence of compensating factors, will decrease the rate of blood flow. One compensating mechanism would be to increase the blood pressure in order to maintain the usual rate of flow. An example of viscosity can be seen when comparing two brands of ketchup. The thicker, more viscous ketchup is more difficult to pour from the bottle.

Because of its viscosity, blood has a high degree of friction along the inner walls of blood vessels. As a result, the blood near the walls of larger vessels flows at a slower rate than blood near the center. Blood in intermediate positions flows at an intermediate speed. This produces a layering of the blood with each layer flowing at a slightly different speed. This is called **laminar flow**, where laminar refers to a system of layers as in a laminated photograph. Remember to visualize this in three dimensions within the cross-sectional area of an artery. From the perspective of looking through an artery, the layers would appear as concentric circles as would be seen on a dart board. Such flow is smooth and quiet. If you press on an artery, the smooth flow is interrupted and results in turbulence that is audible when using a stethoscope. This phenomenon is used in measuring blood pressure. The inflated cuff starts with enough pressure to completely block blood flow. As the pressure in the cuff falls, it reaches a point where the systolic blood pressure within the occluded artery is high enough to counteract that of the cuff. The blood then passes through the vessel in a spurt with each heartbeat. This is audible because the flow is turbulent. As the cuff pressure drops still more, the sound will stop when laminar flow is reinitiated. This occurs when the diastolic blood pressure is sufficient to constantly maintain the artery in a fully uncompressed state despite the cuff pressure. By recording the cuff pressure when sound of blood flow is first heard and then when the sound disappears, we have determined the systolic and diastolic blood pressures, respectively.

Introduction to STELLA[®] Modeling

STELLA[®] is a “systems thinking” modeling system that uses a graphical user interface. The user places interconnected icons on the screen and defines their functions mathematically. The basic icons are **Stocks, Flows, Converters** and **Action Connectors**. The Stocks may be thought of as containers or buckets. The Flows typically move materials to and from Stocks over time. Flow icons look like a pipe with a valve on it. The rate of a flow is defined by a user-specified formula that may use constants and variables. If a calculation within a flow uses a variable that is derived from

another part of the model, then an action connector is needed to link the icons involved. This specifies that the variable is common to both parts of the model.



One way to think of the models is that the Flows specify rates, or derivatives. The user does not enter equations based on calculus, however, since the software automatically includes the effect of time. For instance, putting +1 as the mathematical definition of a Flow will specify that 1 unit will pass through it during every time period. The timing can be specified elsewhere but is not necessary within the user definition of a Flow. Likewise, the stocks are containers and the amount of material in them can change over time. If a Flow is placing material that builds up in a Stock, the effect is that the Stock behaves like an integrator. It's value can be checked at various times as a program runs or the output can automatically go into a table or graph.

STELLA[®] programming can be applied to a wide range of models. The Stocks sound like something you would find in a factory, and models for movement of materials through a factory is one possible application of STELLA[®]. There are even Flow options that allow them to behave as conveyor belts that sometimes are waiting for material be set on them. Models are limited only by one's imagination, however. Some deal with movement of animals from one condition (alive) to another (dead). Chemical reactions may be modeled as well. The pipeline analogy for Flows is particularly applicable to descriptions of blood flow that are investigated in this module.

Within STELLA[®] are many tools that can be invoked for constructing a model. Not all of them are apparent when the program first comes up. It typically starts in a Mapping mode, where icons can be used to show interrelationships. Clicking on the Earth button in the upper left will toggle the software into a mathematics mode, symbolized by the Earth changing to a chi-squared (χ^2). It is this mode that allows portions of your map to interact according to equations you provide. Another level of the authoring program contains a selection of interface icons that allow someone to interact with a model in meaningful ways. There is plenty of help available from within the program if you wish to know more about using a particular tool. There are also a number of tutorials within the Getting Started Guide for demonstrations of specific tools and modeling concepts.

Explanation of the Model

Equations

A number of mathematical relationships have been described for the cardiovascular system. A simple one relates the output of the heart (**Cardiac Output**) to the volume

expelled with each beat (**Stroke Volume**). Over time, this would be influenced by the **heart rate** (HR) such that...

$$CO = SV \times HR$$

This relationship can be further refined by considering that the ventricles only expel about 50% of the blood they contain with each beat. The amount that remains unpumped after an active contraction (systole) of a ventricle is the **End Systolic Volume** (ESV). Likewise, the **End Diastolic Volume** is the volume of blood a ventricle holds just after diastole (relaxation) which is the time just prior to the onset of an active contraction. The actual stroke volume is the difference between EDV and ESV. Substituting this in the above equation for Cardiac Output results in the following equation:

$$CO = (EDV - ESV) \times HR$$

This defines the cardiac output in terms of volume/time, typically milliliters per minute. Another relationship describes the flow of blood as a function of pressure and vascular resistance:

$$\text{Flow rate} = \frac{\Delta P}{R}$$

In the above relationship, ΔP is the blood pressure differential that pushes blood from one point of reference to another. R is the peripheral resistance to the flow of blood. Thus, the flow is directly proportional to the pressure and inversely proportional to the resistance. Some might recognize this as Ohm's law when applied to electrical systems. This law states that $I = E/R$ where I is electron current (amperes) and E is the electromotive force (volts). In this respect, volts is equivalent to pressure.

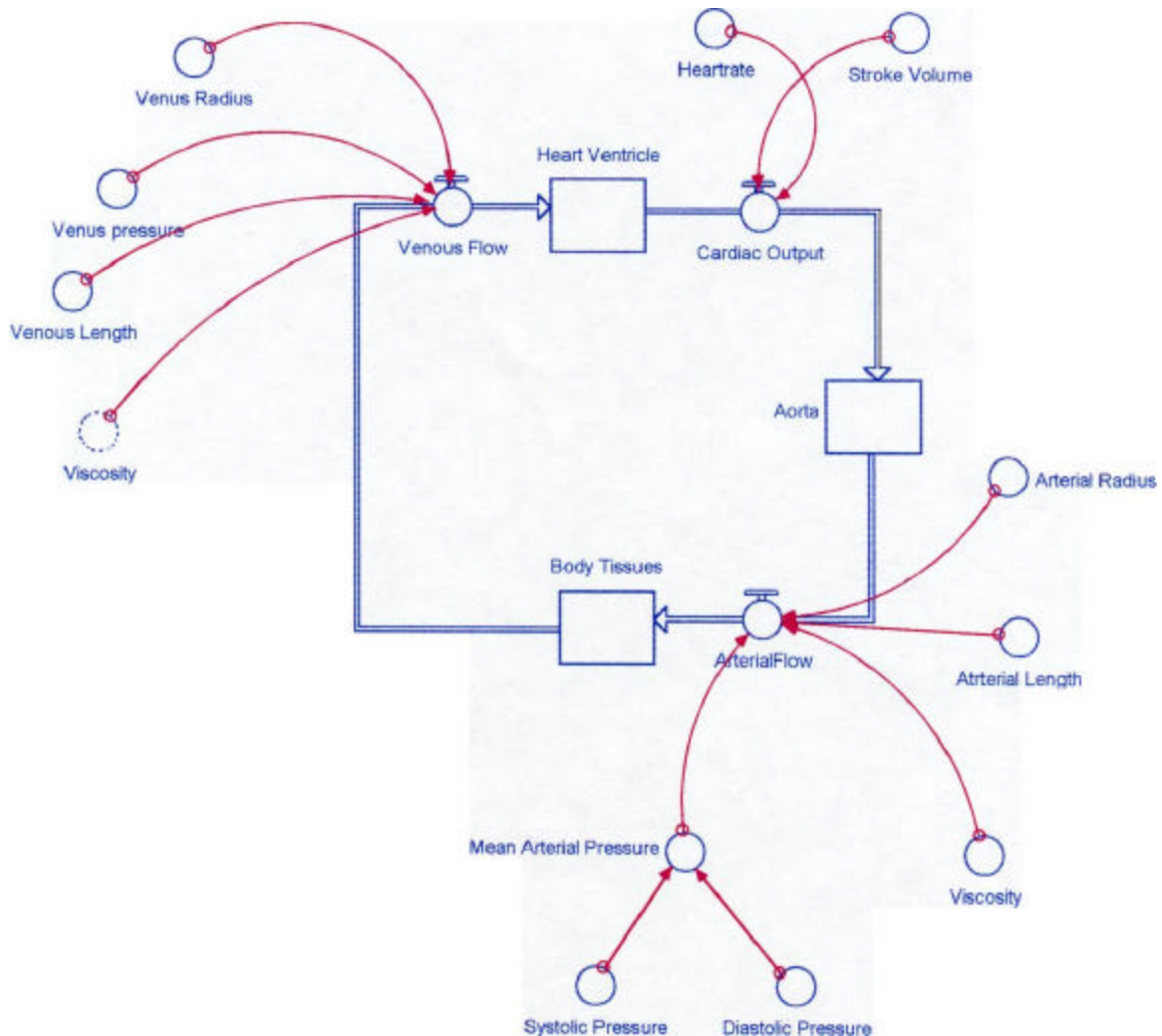
Other factors are known to influence blood flow and these can be approximated according to rules adopted from the flow of fluids in pipes. The relationship between viscosity and other factors for fluid flow within a tube can be modeled using **Poiseuille's Law**:

$$\text{Flow rate} = \frac{\rho \Delta P r^4}{8L\eta}$$

This equation is merely an extension of the previous one for flow rate. However, it no longer has a variable for resistance. Instead, resistance has been broken down into other factors that affect it. The equation now has variables that include the influence of the radius of the tube (r , in cm), length of the tube (L) and the viscosity of the fluid (η). The pressure differential (ΔP) is obtained as the difference ($P_1 - P_2$) between the pressure at the beginning (P_1) and end (P_2) of the tube. An examination of the equation shows that the flow rate (ml/sec) increases with larger diameters or greater pressures, and it decreases with greater distance or fluid viscosity.

STELLA® Model

We will now set up a model that uses the above relationships to describe a simple blood circulation using a single-chambered heart. Begin by running the STELLA® research program. Once in the program, look near the upper left and toggle the Earth (mapping) icon to the chi-squared (math) symbol. Use the accompanying figure to construct your model according to the described specification.



1. Begin by placing 3 Stocks on the screen, one for the *Heart Ventricle*, one for the *Aorta* and one for *Body Tissues*. This is done by clicking once on the Stock tool (a box) near the upper left and then clicking once more on the desired location of the Stock. Click on the Stock names to rename them.
2. Connect a Flow between the *Heart Ventricle* and the *Aorta*. Click on the Flow tool (an arrow with a valve) and your cursor will change to a Flow. Then

click on the *Heart Ventricle* and drag the flow to the *Aorta* while holding the mouse button down. Press the Shift key when you want to turn a corner as you position the Flow. Name this Flow, *Cardiac Output*.

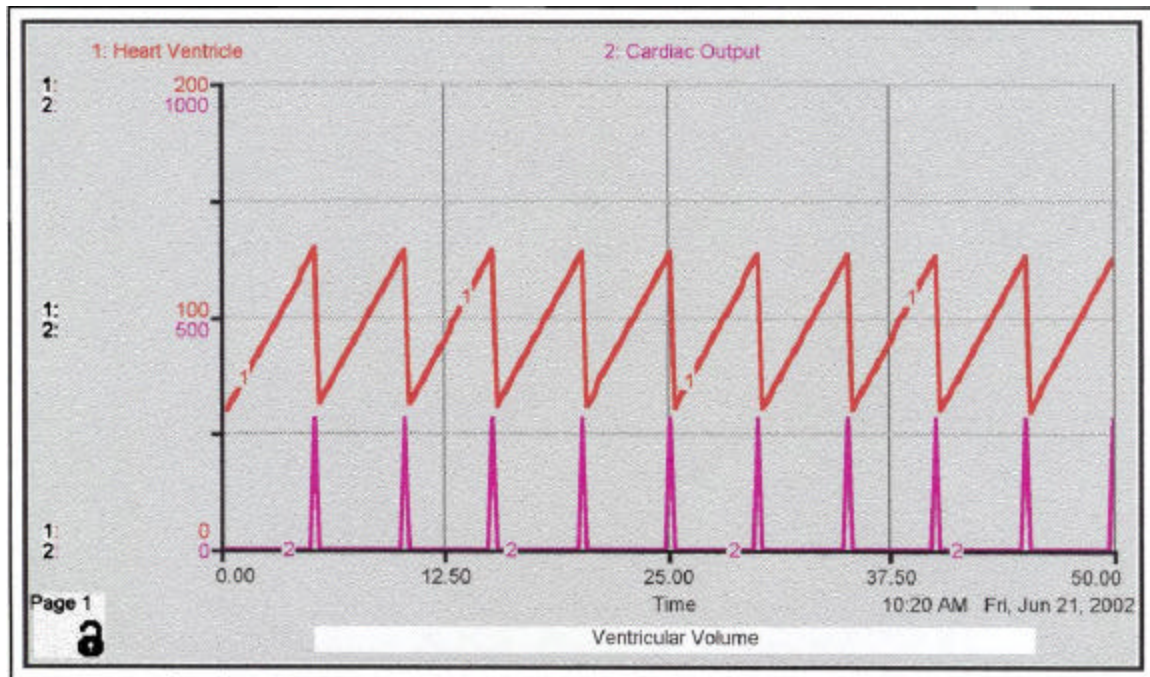
3. Connect a Flow between the *Aorta* and *Body Tissues*. Name this Flow, *Arterial Flow*.
4. Connect another between the *Body tissues* and the *Heart Ventricle* to complete the circuit. Name this Flow, *Venous Flow*.
5. Double-click the *Heart Ventricle* and give it an initial value of 60 in the large white box. This corresponds to 60 ml which is a typical end systolic volume. Immediately after a heart beat.
6. Place an initial value of 100 in the *Aorta*. This value was chosen arbitrarily and is not tracked by the model.
7. Give the *Body Tissues* an initial value of 5000, which corresponds to the total volume in milliliters that a typical person has.
8. Cardiac output was defined previously in terms of stroke volume and heart rate. These could be put directly into *Cardiac Output*, but we will put them each in their own converter icon to make it easier to experiment with changing them. Place a Converter icon (circle or octagon) for *Stroke Volume* near the Flow for *Cardiac output*. Label it and set it equal to 70 which is the typical stroke volume in milliliters. Finally, use the Action Connector tool to draw an arrow from the converter to the *Cardiac Output*. This allows the Flow to use the value from the converter. No element of this STELLA[®] model may access values from another unless they are linked by a Flow or an Action Connector.
9. Make a Converter labeled *Heart Rate* and then connect it to *Cardiac Output*. Set it equal to 5. Rather than defining a heart rate in human terms, this value means that the heart will pump once after every 5 clock cycles when we run the model.
10. We will now put a pumping function into our *Cardiac Output* Flow. Double click it to open it. Then scroll down the “Built-ins” Box near the middle right and select “PULSE.” The syntax for this function is PULSE(<volume>[,<first pulse>,<interval>]). You can look up information on using this or any other built-in or tool from within the help menu. The precise function we want is PULSE(Stroke_Volume,Heartrate,Heartrate). Do not type Stroke_Volume or Heartrate. Rather, put your cursor where they should go and then click on them in the left window which supplies these via action connectors placed during the previous steps. This Flow will now pump out a volume of blood (70) every 5th clock cycle and then passively accumulate inflowing blood between pulses.

11. Make a converter for *Arterial Radius* and connect it to *Arterial Flow*. Set it equal to 6.2. This value was chosen empirically to balance the initial blood flow between compartments.
12. Make a converter for *Arterial Length* and connect it to *Arterial Flow*. Set it equal to 1000.
13. Make a converter for *Viscosity* and connect it to *Arterial Flow*. Set it equal to 4 since “blood is thicker than water.” The viscosity of water would be 1.
14. Make a converter for *Mean Arterial Pressure* and connect it to *Arterial Flow*. Do not define its value.
15. Make a converter for *Diastolic Pressure* and connect it to *Mean Arterial Pressure*. Set it equal to 80 which is normal diastolic pressure.
16. Make a converter for *Systolic Pressure* and connect it to *Mean Arterial Pressure*. Set it equal to 120 which is normal systolic pressure.
17. We are now ready to incorporate Systolic and Diastolic pressures into a single value, *Mean Arterial Pressure*. The formula for this is $\text{Diastolic_Pressure} + (\text{Systolic_Pressure} - \text{Diastolic_Pressure})/3$. Place this formula in the converter for mean pressure. Remember to click on the variables to insert them into the equation. Note: do not put spaces in the equations. Some are included here to facilitate formatting on the page.
18. Now define the *Arterial Flow* icon in terms of Poiseuille’s equation:
 $(\text{Mean_Arterial_Pressure} * \text{PI} * \text{Arterial_Radius}^4) / (8 * \text{Arterial_Length} * \text{Viscosity})$.
19. We will now begin working on converters that contain variables or constants for the *Venous Flow* icon. We will consider the viscosity of blood to remain unchanged, so we can connect the same *Viscosity* converter to the *Venous Flow* as well as the *Arterial Flow*. However, this would be a bit messy, so we will make a copy of the *Viscosity* converter to use near the venous side. Use the ghost tool to make a copy. Click on the ghost found to the right side of the toolbar. Click on *Viscosity* and then click on the new location for the ghosted icon. Finally, connect the ghost to *Venous Flow* using an action connector. A ghost is not a mere copy of the original. It is actually the same icon with two images. Any change in one will appear in the other.
20. Make a converter for *Venous Length*, set it equal to 10 and link it to *Venous Flow* with an action connector. The value 10 was chosen as much smaller than that for Arteries (1000) since the arterial value was considered to

represent both arteries and capillaries through which blood must pass in order to reach tissues.

21. Make a converter for *Venous Pressure*, set it equal to 10 and link it to *Venous Flow* with an action connector. Note that blood pressure within veins is much lower than that found in arteries, as is discussed in the background information. The true value for human venous pressure averages 17 mm of mercury but varies over a wide range. Ten was chosen as representative value. This is much lower than 63 which is found in the *Mean Arterial Pressure* converter and is derived from a normal blood pressure of 120/80.
22. Make a converter for *Venous Radius*, set it equal to 3.45 and link it to *Venous Flow* with an action connector. The value 3.45 was chosen by trial-and error to balance the model in its initial state.
23. Now define *Venous Flow* in terms of Poiseuille's equation:
$$(Venus_pressure * PI * Venus_Radius^4) / (8 * Venous_Length * Viscosity)$$
24. We will now make a graphing window for displaying output from the model. Click on the graph pad icon and place it near your model. Double click it to access options for the graph. Check Time Series (the default selection) along the top.
25. On the left of the options box is a list of variables that you are allowed to plot. Select the *Heart Ventricle Stock* and then press >> to move it over to the list of items selected for plotting.
26. Likewise, select the *Cardiac Output Flow* to plot.
27. Enter "Ventricular Volume" for the title.
28. Select "Show Numbers on Plots" and "Show Grid" both of which should already be checked by default. Also check "Thick Lines."
29. Specify that the display range should be from 0 to 50.
30. At the top of the screen, pull down the Run menu and select "Run specs..." to set the last few parameters of the model. Change the "Length of simulation:" to be from 0 to 50.
31. In "Sim Speed:" put 0.2. This is the interval in seconds between each clock tick for the model. Since we previously set the heart to beat after every 5 clock cycles, the resulting heart rate will be 1 beat per second or 60 times a minute. This is slightly slower than a typical heart rate of 70 beats per minute.
32. Other options for "Run Specs..." will remain in their default condition.

33. It is now time to test the model. Have the graph open so that you can see the output. Pull down the Run menu and click on “Run.” It should appear as in the next figure.
34. If the model runs as expected, save it and keep this as your basic model. If you make any modifications, save it under a different name.



As is shown in the above figure, you should see two events being plotted over the course of the simulation. The purple line on the bottom illustrates cardiac output. Every 5 clock cycles, this value jumps up and corresponds to a single heart (ventricular) contraction. The value plotted is the amount of blood being ejected from the heart into the bloodstream. Cardiac output rapidly subsides after each pulse as an indication that the heart is now relaxed and not pumping blood.

The red line shows the amount of blood in the heart and how that is changing over time. Initially, the heart has a normal volume of about 60 ml. This would be immediately after a heartbeat that is not shown on the graph and this starting value would be the end systolic volume. Remember from the background information that systole refers to active contraction and diastole refers to the relaxed periods between contractions. The model shows that the amount of blood in the heart gradually increases as the venous system returns blood to the heart. Its maximal amount, just prior to the next contraction is the end diastolic volume. After this is reached, the heart contracts to pump blood into the aorta and the amount of blood in the heart drops again to the end systolic volume. The model runs through a total of 10 of these cycles.

Solution Implementation

The model is designed to demonstrate a simple circulatory system with a one-chambered heart. As we will see, the volumes displayed during the heart cycle can change if we alter the parameters found within the model. This allows us to make changes that mimic pathological or drug-induced conditions and to see how the output from the model is affected.

Effect of Viscosity

In the introduction, we considered the possibility of increasing an athlete's red blood cell count to allow their blood to carry more oxygen to enhance their performance. This could be done by receiving an infusion of one's own blood or by taking the hormone erythropoietin. Let's examine this process using the model we have created. Double click on the *Viscosity Converter* and change the viscosity from 4 to 5. Open the graph and run the model. Watch as the data is plotted in real time. You will see that the volume of blood in the heart gradually diminishes. Answer the following questions:

1. Examine the first few cycles closely. Is the purple graph for cardiac output affected?
2. What aspect of the blood circulation is changed? Explain why.
3. The Cardiac Output does change later in the simulation. Why?
4. What would you expect if you changed the viscosity to 8. Try it. How is the output different from before? Was your prediction correct?
5. What would you expect to happen if you changed the blood viscosity to a lower value than it was originally? This could happen if a person has a chronic loss of blood cells as in chronic bleeding due to colon cancer. Try it using a viscosity of 3.

Effect of Stroke Volume

Lets consider another scenario where we use the model to investigate the effect of damaged heart muscle. This usually results from blockage of the coronary arteries that supply the heart tissue. The blood involved is not the same as the much larger amount that passes through the heart chambers and is destined to circulate throughout the rest of the body. If the coronary arteries are blocked, a bypass operation can attempt to reroute the flow of blood into the heart tissue by using unneeded veins from the legs. Prolonged lack of circulation through the heart tissue can result in necrosis (death) of cardiac cells

and this can lead to a malfunction of the heart's pumping activity. Such a malfunction is called a heart attack or **myocardial infarction**. To simulate a damaged heart, we can lower the stroke volume. As cardiac muscle cells die, the overall strength of contraction of the heart will diminish and less blood can be forced out with each contraction.

1. Reset the viscosity to 4 and confirm that normal heart cycles are seen.
2. Change the *Stroke Volume* from 70 to 50. Predict the outcome and then run the model to test your hypothesis. The result is an example of **congestive heart failure**

Effect of Venous Pressure

Venous pressure is barely adequate to push blood back to the heart against the influence of gravity. As is discussed elsewhere, skeletal muscle contraction is harnessed to press blood past a series of one-way valves in the veins. If a person is perfectly still, like a soldier standing at attention, blood circulation can become abnormal and fainting may occur.

1. Reset the stroke volume to 70 and confirm that the model is working normally.
2. Change *Venous Pressure* from 10 to 8. Predict the outcome and then run the model to test your hypothesis.
3. Change it again to 2 and view the results.
4. When normal people stand for long periods, how do they keep venous return flowing normally?
5. If you had to stand at attention for a prolonged time interval, how could you prevent the effects seen in the model.

Arterial Effects

Thus far, the model is good at representing events that involve changing venous parameters or cardiac output. As it stands, however, it fails to show effects that might occur when changing the characteristics of arterial flow. In part, this is because the desired output in the heart is found at the end of the venous system. The representative artery is more remote from the output and is buffered by both the venous system and the large volume of blood in the *Body Tissues* Stock. The input to the *Arterial Flow* is also buffered by the volume of blood in the *Aorta* Stock. The aortic volume falls during the simulation but does not reach a critical level where it might be affecting the supply of blood into the *Arterial Flow*. You can check the final value for this or any icon by

resting the cursor on the icon after running a simulation. With a few adjustments, the model can show effects due to changes on the arterial side of the circulation.

1. Change the initial value of the *Aorta* Stock to 10.
2. Likewise, change the initial value of the *Body Tissues* Stock to 10. These two changes remove the buffering effects of these containers and make the system more responsive to changes in the arterial parameters.
3. Open the graph and run the model. After the first heart cycle, the display reaches a new equilibrium which is the baseline for our next few experiments. Note that the maximal ventricular volume is about 70 after equilibrium is reached.
4. First we will try the effects of **hypertension** (high blood pressure). Pressure greater than 140/90 is considered high. Change the systolic pressure to 160 and the diastolic to 100. Open the graph and run the simulation. Is there a change? Is it a significant change? How could this relate to the fact that high blood pressure begins as an asymptomatic disease.
5. Now we will try low blood pressure which is anything lower than 100/60. Set the systolic and diastolic pressures to 90 and 50. Open the graph and then run the simulation. How is venous return affected? Low blood pressure can result from an injury that results in the loss of significant blood volume.
6. Reset the blood pressure to normal (120/80) and run to simulation to confirm that it shows the typical baseline.
7. Our final run will simulate **arteriosclerosis** in which arteries harden as they are infiltrated by saturated fatty deposits. The deposits calcify to become hardened **plaques**. The open space within the artery (**lumen**) is gradually **occluded** (blocked) by the encroaching plaques. This is most dangerous in **coronary arteries** that supply the heart tissue. It can result in insufficient blood flow to support normal heart function and a heart attack can ensue. Change the arterial radius from 6.2 to 3. What happens?

Assessment of the Model

While the model presented here does illustrate principles of cardiovascular dynamics, there are many simplifications employed. Some are inherent to the architecture of the model. First of all, the model heart has only one chamber in contrast to the human heart which has four. The model circulation has only one major circuit as opposed to the human cardiovascular system which contains both systemic and pulmonary circulations. Moreover, the model does not reflect the many branches and the wide range of vessel types through which blood must travel.

On a functional level, blood vessels do not behave as solid tubing. Some arteries such as the aorta in particular, have an elastic nature so that they do not contain pressure passively. Rather, they react to pressure, accommodating a pressure surge by stretching and then contributing pressure to the system by collapsing forcibly to their relaxed states between pulses. These fluctuations are avoided by the model since mean arterial pressure is used instead of the dynamic cycle of pressure that follows from true cardiac activity. The normal cycle of heart contractions and pressure can be felt when taking someone's pulse.

The heart also has an elastic nature and the systolic propulsion of blood from the heart does not occur as fast as is implied by the model. It begins rapidly as the ventricle contracts but then the rate of emptying gradually slows towards the end of the contraction. Ventricular filling also has a shape more complex than that of the ramp depicted by the model. It begins rapidly when the valve opens between the ventricle and its associated atrium. The rate then tapers off until atrial contraction becomes important as it actively pushes blood into the ventricle. This adds a second wave of ventricular filling on top of the passive filling that was already in progress but slowing.

A major deficiency of the model is that it treats the components of the cardiovascular system as inert and nonreactive. The natural system is full of checks and balances that actively respond to compensate for changing conditions. Some of this is inherent to heart tissue. Heart cells contain **actin** and **myosin**, proteins that produce a contractile force by sliding past one another. As heart muscle is stretched, a greater overlap between these molecules causes the heart muscle to contract more strongly. This is the **Frank-Starling law of the heart**. The result is that stretching of the heart due to increased blood volume causes stronger contractions that increase the stroke volume—thus ejecting the extra blood. There is a limit to this compensation, however, and congestive heart failure does occur if sufficient cardiac tissue is damaged.

The brain also has centers that contribute to compensatory mechanisms through the **autonomic nervous system**. This is a self-governing part of the nervous system over which we have no conscious control. It has two branches, the **sympathetic** and **parasympathetic nervous systems** which can stimulate or relax heart activity, respectively. The sympathetic nervous system does this in part by releasing adrenalin which speeds up heart rate and causes the heart to contract more vigorously with each beat. The sympathetic nervous system also controls smooth muscle within blood vessels so as to alter vessel diameter and modulate blood pressure. In an emergency, such as low blood volume due to traumatic body damage and bleeding, the sympathetic nervous system would diminish the diameter of blood vessels and increase the heart rate in an attempt to compensate for falling blood pressure and reduced venous return.

The sometimes arbitrary initial values used within the converters of the model represent another source of inaccuracy. When known, real human values were typically used. Some of the values are not easily found, however, or were not available when the model was constructed. In some cases such as arterial radius, determination of an appropriate value is difficult because only a single artery is used in the model but it represents many

arteries with different characteristics. The distribution of blood in the model is another example of where the model does not reflect reality. Percentages should be heart (7), pulmonary vessels (9), systemic arteries and arterioles (15), capillaries (5) and veins (64). The pulmonary component is absent from the model.

Some experimentation was required when selecting initial values so as to balance the system. The desired output was to show a stable series of cycles over the period that the model runs. Finding starting values that did not have a destabilizing effect was given priority over using real values when known. The model is not entirely stable which can be demonstrated by running it with the initial conditions for longer than 50 clock cycles. If you change it to 150 clock cycles under "Run Specs...", you will see that the ventricular volume is gradually decreasing. This might be fixed in part by finding more precise starting values using more significant digits. However, a better approach to stability would be to build in negative feedback loops that automatically compensate to bring critical values back to normal. This is the approach that the human body uses. In other words, the model would become more stable if it were changed from a passive model to a reactive model.

Conceptual Questions

Introduction

1. Heart disease is the leading of death in the U.S. The only exception was in the Autumn of 1918. What happened? (Note: the answer is not contained within the module).
2. What is "doping." What are 2 ways to artificially achieve this effect?
3. How can doping be detected?
4. What natural conditions might lead to an increase in hematocrit?
5. What consequences could result from an abnormally high red blood cell concentration?
6. Erythropoietin is made by the kidney. What would be some consequences of a kidney tumor within tissues that release this hormone?
7. Polycythemia is another term for an abnormally high red blood cell count. This can occur from anoxia due to chronic mountain sickness. Explain.

Background Information, Cardiovascular

8. What is the primary function of the cardiovascular system?

9. What other body systems interact with the cardiovascular system?
10. What are the two main circulatory pathways?
11. Diagram the pathway of blood through the heart.
12. What is the function of each chamber of the human heart.
13. Why does the heart make a "lub, dup" sound?
14. What is regurgitation in the heart and how could it be detected?
15. List the types of blood vessels, in order, through which blood passes on its journey away from and returning to the heart.
16. What are diastole and systole?
17. Why is blood pressure reported as two values, e.g., 120 over 80?
18. What is a stroke? What factors could lead to it?
19. What effect does the aorta have on blood pressure? How does it accomplish this?
20. What types of blood vessels are pressure reservoirs? What does that mean?
21. What types of blood vessels are volume reservoirs? What does that mean?
22. Why is there a big pressure drop in arterioles?
23. What factors slow blood in capillaries? Why is this advantageous?
24. How does blood move through veins despite the low blood pressure there?
25. What are coronary arteries? Why are they needed?
26. Why is blood red?
27. What is the major factor in viscosity of blood?
28. Describe laminar flow of blood.
29. How is laminar flow related to taking a blood pressure measurement?
30. Describe how to determine a person's blood pressure.

Background Information, STELLA®

31. What are the four basic icons used in our STELLA® model? Describe the function of each.
32. How are flows and stocks related to calculus in their implementation?
33. Provide some examples of ways to use STELLA®.
34. What is the significance of O^2 when programming a STELLA® model?

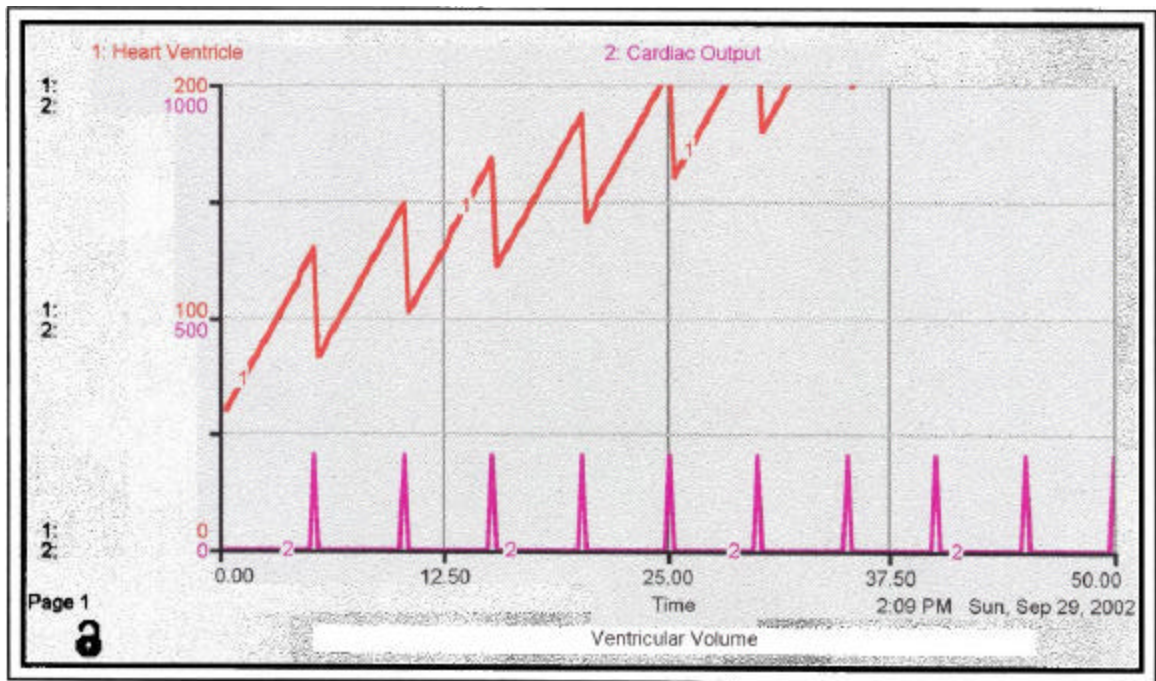
Explanation of the Model

35. What are SV and CO and what is their mathematical relationship?
36. What are EDV and ESV? Show how they can be used to define SV.
37. Compare Ohm's Law to factors influencing blood flow.
38. Explain Poiseuille's Law.
39. What are the stocks and flows used in the presented model? How are they interrelated?
40. How much blood does a typical person have?
41. What is a typical human ESV? What does this mean?
42. What is a typical SV? Using the last question, calculate a typical EDV.
43. Explain the STELLA® PULSE function syntax.
44. What formula approximates the average arterial pressure?
45. What is a ghost in STELLA®?

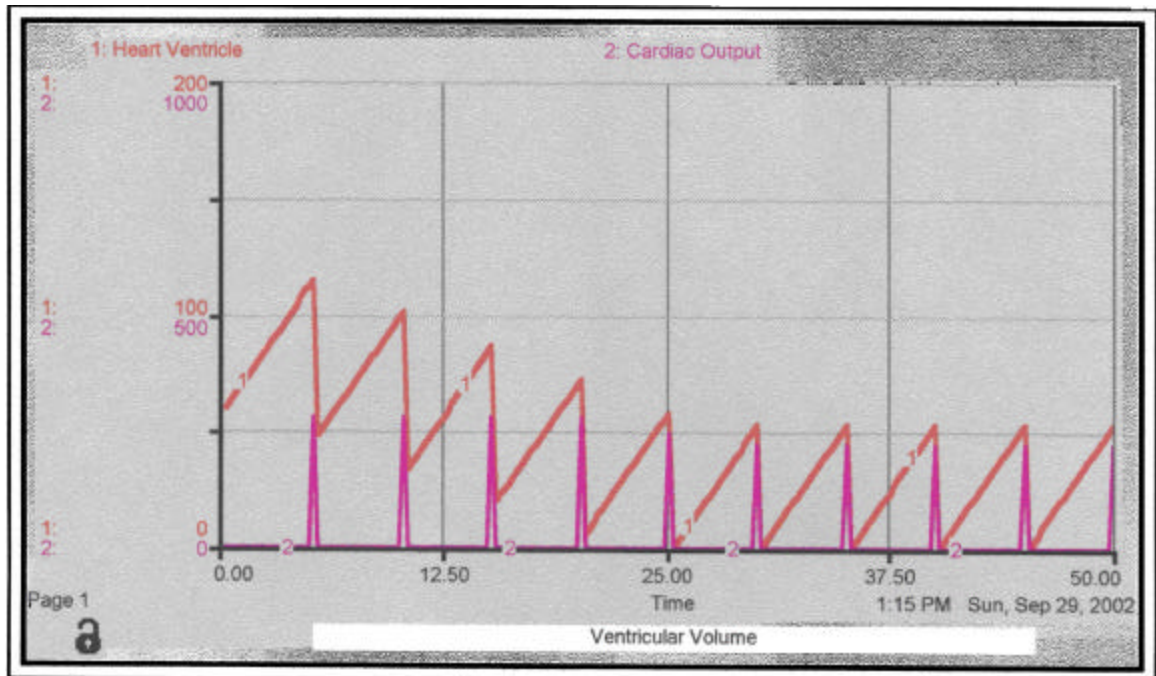
Implementation of the model

46. What is the effect of changing blood viscosity?
47. How are the experiments with viscosity related to blood doping?
48. What is a myocardial infarction?

49. How was a myocardial infarction simulated in the model? Describe the change output from the model.
50. What is congestive heart failure?
51. What happens to blood flow if you stand perfectly still?
52. How could you stand in place yet prevent the changes you described in the previous question?
53. Examine the following output and explain what factors might have caused the change from normal.



54. Examine the following output and explain what factors might have caused the change from normal.



55. The next few questions assume you have tuned the model for showing arterial effects. What is the effect of hypertension?
56. What is the effect of hypotension?
57. How does arteriosclerosis and narrowing of the arteries affect the model?

Assessment of the Model

58. How are arteries different from tubes?
59. What is the Frank-Starling Law of the heart? How would it influence the results found when using the model to show congestive heart failure from reduced stroke volume?
60. How does the autonomic nervous system influence the cardiovascular system in ways that are not demonstrated by the model?
61. How does adrenaline influence blood pressure?
62. What is the true distribution of blood volumes in different compartments throughout the body?
63. The model is not 100% stable if run for an extended time period. How does the body accomplish stability in the face of many changing influences?

Problems and Projects

Activities for learning STELLA[®]

1. Run the STELLA[®] getting Started guide. Look at STELLA[®] : How it works
2. Run the STELLA[®] getting Started guide: An overview of the STELLA[®] Environment
3. Run the STELLA[®] getting Started guide: An Overview of the STELLA[®] Language
4. Run the STELLA[®] Applications & Models: Pollution Dynamics
5. Run the STELLA[®] Applications & Models: Simple Predator Prey Dynamics
6. Run the STELLA[®] Applications & Models: Simple Samples, Science & Research, Pharmacokinetics

Activities for Investigating Cardiovascular Physiology

7. Use a stethoscope and listen to your heart. Explain the sounds you hear.
8. Take the pulse of a fellow student and compare to the normal heart rate of 70 beats per minute. Have the subject run in place for 1 minute and then do the pulse again. Suggest reasons why it changes?
9. Take some actual blood pressure measurements using an arm cuff. How do they change after running in place for 1 minute? Why?
10. Determine venous pressure from your fellow students. An approximate pressure can be found as follows: First, the subject should stand with their arms to the side. Note the veins on the back of the hand should be distended with blood. Have the person gradually raise their arm to the side until you observe that the blood drains from the veins. Record the height of the hand in millimeters in comparison to the position of the right atrium of the heart. The venous pressure can be estimated by converting the specific gravity of blood (1.056) to that of mercury (13.6) using the following formula:

$$P_v = \frac{1.056 \times mm}{13.6}$$

11. If equipment is available, obtain an ECG of your heart. Using information not found in this module, explain the meaning of the output.

Project: STELLA[®] Model

Each student is expected to make a STELLA[®] model. Students are encouraged to come up with their own ideas but must obtain approval from the instructor prior to making their model. The model could be anything, but preference should be given to physiological models. The student might be expected to learn more specific physiology than that covered in the module if it is needed for their model. A list of potential ideas is found below.

12. Reconstruct the above module to incorporate negative feedback that keeps the model balanced indefinitely if run for longer periods. The module should simulate natural balancing mechanisms such as the Starling-Law of the Heart, or the influence of the autonomic nervous system. Be prepared to discuss and demonstrate disease states that could interfere with the feedback loops.
13. Make a 2-chambered heart model that contains both an atrium and a ventricle. Such a model would need simulated valves after each chamber. Since valves in the real heart are controlled by pressure differentials on either side, the pressure in each compartment would be an important factor to track in this model.
14. Make a 4-chambered heart model.
15. Make a model that contains both systemic and pulmonary circulations which intersect in a single heart. Find out what pulmonary edema is and use your model to show how that is created.
16. The following formula is used to predict turbulent flow in tubes. The higher the Reynolds number (Re) the greater the likelihood that the flow will shift from laminar to turbulent flow. Make a model that demonstrates the contribution of each variable. Q is the flow rate (ml/sec), r = radius (cm), η = viscosity and D = density.

$$R_e = \frac{2Qr}{\eta D}$$

Solutions

1. Heart disease is the leading of death in the U.S. The only exception was in the Autumn of 1918. What happened?

A flu pandemic killed over half a million in the U.S. Between 25 and 50 million are thought to have died worldwide. The flu still kills over 20 thousand in the U.S. every year. The following link is a good place for more information:

<http://www.detnews.com/history/flu/flu.htm>

Suggestions for Instructors

Commercial software is available for learning the physiology of the cardiovascular system in an interactive way. The ADAM Interactive Physiology CD series from Benjamin Cummings is an example. This could be helpful for introducing students to the physiology prior to having them explore the STELLA[®] model.

Glossary of Terms

Action Connectors A STELLA[®] icon that connects variables between sections of a model.

Actin A contractile protein found in cells. Actin and myosin slide past each other to cause contraction of muscle tissues.

Aorta The major artery emerging from the heart that carries blood into the systemic circulation.

Artery Any blood vessel that carries blood away from the heart.

Arteriole A small artery that carries blood into a capillary bed.

Arteriosclerosis A process of hardening of the arteries, usually associated with a diet high in cholesterol and saturated fats.

Atrium A heart chamber that venous blood collects in while a ventricle is contracting. The atrium contracts to fill the ventricle prior to the next ventricular contraction.

Autonomic nervous system A branch of the nervous system that controls internal organs without conscious input.

Capillaries The smallest blood vessels. Capillaries occur in extensive networks within tissues where materials are exchanged between the tissue and blood.

Cardiac Output The volume of blood (milliliters) pumped by a ventricle per minute.

Conducting arteries Non-elastic arteries that contain pressure needed to propel blood long distances.

Congestive heart failure A condition where heart chambers swell with blood because the heart cannot pump it out as fast as it arrives in the heart.

Converter A STELLA[®] icon that can be used to convert or set values used by other parts of a model.

Coronary arteries Arteries that carry blood into heart tissue to maintain the heart in a healthy condition.

Deep vein thrombosis Blood clots that can occur in large veins if venous blood flow is abnormally slow and stagnant. Sometimes associated with prolonged inactivity of bedridden patient. If usually occurs in a leg vein and a major danger is that a blood clot (thrombus) could break off and travel through the circulation until it blocks a narrow artery.

Diastolic pressure The blood pressure that occurs between heartbeats, during diastole, as the pressure from the last pulse subsides to its lowest level.

Doping Abnormally increasing the concentration of red blood cells, usually to enhance athletic ability.

End Diastolic Volume (EDV) The amount of blood that has accumulated in a ventricle at the end of a relaxation period (diastole). It is the amount available to be pumped when the ventricle contracts.

End Systolic Volume (ESV) The volume of blood remaining in a ventricle at the end of a contraction (systole).

Erythrocyte A red blood cell.

Erythropoietin (EPO) A hormone that stimulates red blood cell production in the bone marrow.

Flows STELLA[®] icons that move materials from one place in a model to another. They can also sort items from one class or condition into another.

Frank-Starling law of the heart Describes the positive relationship between the volume of blood in the heart and the strength of contraction. Within limits, the heart will contract with more force if it contains more blood.

Heart rate Beats per minute.

Hematocrit The percentage of packed red blood cells in a sample compared to the total volume of the sample after centrifugation.

Hemoglobin An iron-containing protein in red blood cells that carries oxygen in the blood. It is responsible for the red color of blood.

Hypertension High blood pressure.

Laminar flow Layered, nonturbulent flow of blood within an artery. Blood nearest the walls has more friction and moves slower than blood closer to the center of the artery.

Lumen The open space within a hollow organ such as a blood vessel or the intestines.

Murmur An abnormal heart noise.

Myocardial infarction A malfunction of the heart, typically leading to a heart attack.

Myosin A contractile protein found in cells. Actin and myosin slide past each other to cause contraction of muscle tissues.

Occlusion A blockage of blood flow within a blood vessel. It can lead to a stroke or heart attack if it occurs in the brain or coronary arteries, respectively.

Parasympathetic nervous systems The branch of the autonomic nervous system that promotes resting and digesting.

Poiseuille's Law A mathematical relationship that describes effect of pressure, length, diameter and viscosity on the flow of fluids within a tube.

Plaque A hardened area within the wall of a blood vessel. Associated with arteriosclerosis.

Polycythemia Abnormally high concentration of red blood cells.

Pressure reservoir A function of conducting arteries, to maintain (not dissipate) pressure needed for blood flow.

Pulmonary circulation The circulatory pathway that passes through the lungs.

Regurgitation A condition where a portion of blood flows in the wrong direction due to a faulty valve in the heart.

Stocks STELLA[®] icons that contain materials. They can behave like integrators.

Stroke A condition of reduced blood flow to the brain. It can occur if an artery bursts or is blocked.

Stroke Volume The amount of blood that can be ejected by a ventricle with each heartbeat.

Sympathetic nervous systems The branch of the autonomic nervous system that tunes the body for action as in an emergency. It is responsible for the release of adrenalin.

Systemic circulation The pathway of blood to all parts of the body except for the lungs which is through the pulmonary circulation.

Systolic pressure The maximum arterial pressure that occurs while the heart is actively forcing blood into the aorta. It is felt as a pulse.

Veins Blood vessels that bring blood back to the heart.

Venous return The return of blood to the heart, into the atria.

Ventricle A chamber of the heart that pumps blood into either the systemic or pulmonary circulations.

Venules Small veins that collect blood from capillary beds as blood begins its return trip to the heart.

Viscosity The thickness of a fluid. Blood is thicker than water. Molasses is thicker than either blood or water. Viscosity affects the speed at which a fluid can flow.

Volume reservoirs A function of veins. They contain 64% of all blood and can shift blood into other parts of the circulation if needed.

References

Randall, David and Augustine, George. Animal Physiology, 3rd Ed. W. H. Freeman and Co., New York. ISBN 0-716-71828-6, 1988.

Richmond, Barry, STELLA[®] Software: An Introduction to Systems Thinking. High Performance Systems, Inc., Hanover, NH. ISBN 0-9704921-1-1, 2001.

Sherwood, Lauralee, Human Physiology from Cells to Systems, 2nd Ed. West Publishing Co., New York. ISBN 0-314-01225-7, 1993.

Not used at this time...

Empirical Data

Provide sample data, plots or methods for obtaining data.

Use your model to determine how much the lumen of a stenotic artery must be occluded before appreciable loss of blood flow occurs (70-80% of cross-sectional surface area needed in reality). What does this say about atherosclerosis being a silent disease?

Low viscosity from chronic blood loss, as could occur in colon cancer—kidney malfunction of Antidiuretic hormone (ADH = vasopressin). Ingesting massive amounts of water?