CoreModels

Glucose-Insulin Model

A CORE LEARNING GOALS ACTIVITY FOR SCIENCE AND MATHEMATICS

Summary

Students use two prebuilt STELLA® models to investigate the relationship between the amount of glucose in the blood and the amount of insulin secreted by the pancreas. They use the models to simulate blood glucose and insulin responses to different glucose release rates. The activity includes an optional part and extensions about diabetes.

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Contents

Glucose-Insulin Model
Teacher Guide—Explanation

Overview

Students use two prebuilt STELLA® models to investigate the glucose-insulin relationship. The first model has an insulin secretion rate set at the homeostatic level. The second model permits students to "play the part of the pancreas" and control the insulin secretion rate.

Using the first model, students simulate the response to three glucose release rates. They select rates that represent three scenarios—homeostasis, eating simple sugars, and eating pasta. Using the second model, they simulate the response for three more glucose release rates they choose—steady release, moderate then low release, and a glucose-release scenario of their choice. An optional diabetes simulation can be used to conclude the activity. The goal of each part of the activity is for students to understand how the glucose-insulin feedback mechanism achieves and maintains homeostasis.

After students complete Part A, they are familiar with the model. In each scenario of Part B they form a hypothesis about the body's response to that glucose release and predict how the model will behave based on their hypothesis. Throughout the activity they record and analyze the data that the model generates.

Interpreting the models and graphs is the essence of the activity. You may use Appendix G, Generic Graph Questions, and Appendix H, CoreModels Graph Interpretation Guidelines, for students who need help.

The basis for this activity is models and activities developed by Will Glass-Husain of Catalina Foothills School District, Tucson, AZ, with support from the Waters Foundation and found at the Creative Learning Exchange web site. The Maryland Virtual High School version can be found at the MVHS web site.

Activities at a Glance

Part	Title	Estimated Minutes
A	Simulating homeostasis	10
B	Eating simple sugars	20
C	Eating complex carbohydrates	15
D	Playing the part of the pancreas	
Scenario I	Steady glucose release	15
Scenario II	Moderate, then low glucose release	10
Scenario III	Student choice of glucose release rates	20
E	Thinking about glucose and insulin	15
F (optional)	Thinking about diabetes	20
Extension	Appendix E, Diabetes Questions	10
Extension	Appendix F, Simulating Diabetic Response	15

Prior Knowledge

Human physiology. Students should have a basic understanding of the digestive system and the functions of the pancreas. They should know what glucose and insulin are. They should be familiar with the concept of homeostasis.

Food. Students should know the structure and role of simple and complex carbohydrates.

Feedback. Students should know how a feedback loop operates (see Appendix B) and be able to give examples. The glucose-insulin relationship is a negative feedback. You may wish to make sure students understand the difference between positive and negative feedback.

Computer skills. Students with no STELLA® experience can do this activity, but may require an explanation of the application before they start.

Teaching Tips

Homeostasis. A good way to introduce this activity to students with no STELLA® experience is to use Scenario I, Simulating homeostasis, as classroom instruction, guiding the students through each question and reminding them of appropriate values and units of measure.

Information section. The information on glucose, insulin and the pancreas in the box on the model page is reproduced in Appendix A, should you wish to use it as a handout. Experience shows that many students refer repeatedly to this section.

Models and graphs. Appendix C shows the two STELLA® models. Examples of graphs for the different scenarios are in Teacher Guide—Answers. The models' equations are in Appendix D.

Tables. Each model has a table icon where numerical values accumulate during a model run. Students frustrated with seeing values flash by in the numeric displays can use the table to find whatever values they are looking for.

Diabetes. If you use Part D, Thinking about diabetes, or a diabetes extension, you may wish to add class time for students to share their thoughts (sometimes misconceptions) about diabetes, insulin, sugar in the urine and other glucose-insulin problems. You could include such a discussion in your introduction to the activity, or as an introduction to Part D.

Extensions

Feedback. Many systems operate by feedback. A familiar one is the thermostat that controls air temperature in a home by turning the furnace on and off. Students could compare different feedback systems to the glucose-insulin relationship.

Diabetes. Students could develop scenarios to simulate diabetic situations. Some examples are in Appendix E, Diabetes Questions (E-2 can be duplicated as a student worksheet). The student guide for Appendix F, Simulating Diabetic Response to Insulin Release, can also be duplicated.

Biochemistry. Students could draw the chemical formulas for glucose and insulin and diagram the feedback mechanism. Such work could be added to students packets made for diabetes extension questions in appendixes E and F.

Resources. The American Diabetes Association has a web site and offers information sheets.

Glucose-Insulin Model
Teacher Guide—Answers

Glucose is the molecule that the cells of the human body use as an energy source. Cells use glucose to make ATP, which is the primary energy provider in the cell. Maintaining a steady level of glucose in the blood is critical in the human body. If the amount of blood glucose is too much or too little, serious physical problems can occur. In people with diabetes, the body cannot properly control its glucose level. Diabetics must adjust their dietary and exercise styles and often must take medicine.

In this activity you will examine the relationship between glucose and insulin in the human body. You are going to use the STELLA® glucose-insulin models developed for the activity to simulate different types of glucose release into the bloodstream and the insulin secreting response of the pancreas. The models are based on the physiology of glucose metabolism and insulin secretion.

- Double-click Glucose 1.stm to open the first model.
- Read the introduction and scroll around the page to become familiar with its parts. You may wish to read the information section.

The model has three graphs. You will use the small Glucose Release graph to set glucose release rates for the different scenarios in this activity. The two larger graphs record a model's behavior by showing the changing levels of glucose and insulin in the blood for each scenario. The box above each graph is a STELLA® numeric display. It shows the total amount of glucose or insulin in the blood while each simulation progresses. To see all the values for a model run, double-click the Table 1 icon.

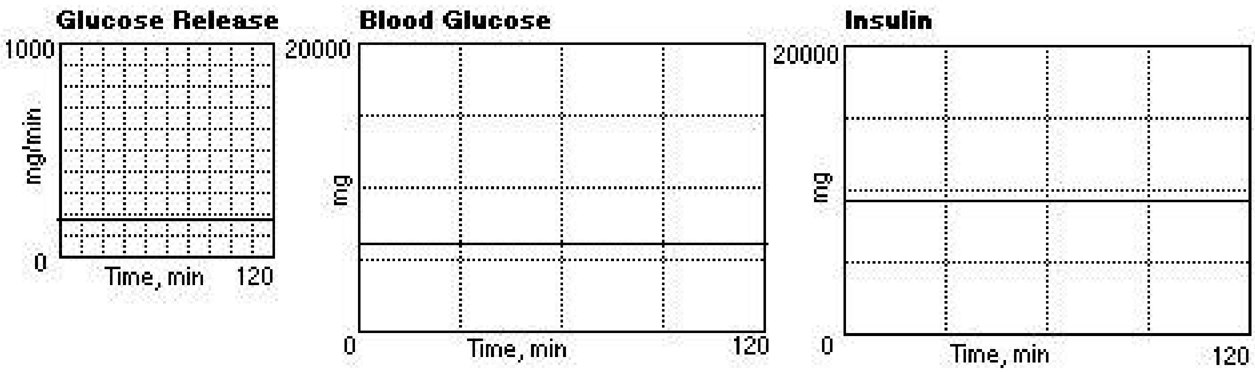
Part A. Analyzing the glucose-insulin model

Scenario I. Simulating homeostasis

Homeostasis is the normal, steady internal environment of the human body. You will run the simulation to see and record the behavior of glucose and insulin at homeostatic levels. The values on the graphs and in the numeric displays indicate the total amount of glucose and of insulin in the blood.

- Double-click the small Glucose Release graph to open it. Check the release rate shown by the STELLA® graphical function (also called the input graph). It should be steady at about 200 mg/min, which is the homeostatic level. If the release rate has not been preset, enter in the Output column 200 for each Input step, or click each vertical time line at the 200 mL level (the rate does not have to be exactly 200 mg/min.).
- Click OK when you have checked or set the rate.
- Under the Run pull-down menu, select Run. You should see lines forming on the two larger graphs in the model.

QUESTION 1. How do the model's graphs look? Use the blank graphs on the next page to record what you see on the model's graphs.



QUESTION 2. What is the homeostatic level of glucose in the blood? HINT: Enlarge the graph for easier reading (click + at lower left), check the numeric display above the graph, or look at the table.

The homeostatic level is about 6000 mg.

QUESTION 3. What is the homeostatic level of insulin in the blood?

The homeostatic level of insulin is about 9000 mg.

QUESTION 4. How do the amounts change in relation to each other?

Neither amount changes, so the relationship stays constant.

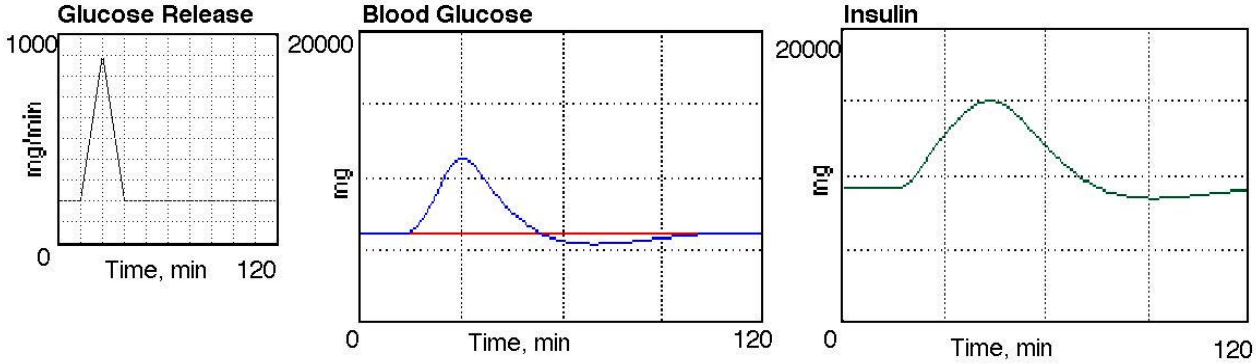
Scenario II. Eating simple sugars

Eating a candy bar will release a surge of glucose into your bloodstream and give you what is often called a “sugar high.” A typical candy bar contains about 30 g (30,000 mg) of simple sugars. A 12-ounce can of regular (not diet) soda contains about 41 g of simple sugars. Simple sugars move rapidly from the digestive system into the bloodstream. The whole candy bar or soda might be absorbed in 20 to 30 minutes.

To simulate eating a candy bar, you are going to change the glucose release input graph to produce a spike of glucose in the blood — a quick rise followed by a quick drop.

- Open the glucose release input graph.
- From your knowledge of the amount of sugar in a candy bar and the speed of absorption, choose a glucose release rate that will make a glucose spike. Click the appropriate time (vertical) lines at the value or values of your chosen rate.
- Click OK when you have set your glucose release rate.
- Run the simulation. You should see lines forming on the blood glucose and insulin graphs.
- To close any message box that may appear, click the small box in its upper left corner. Select Run again to continue the simulation. Or simply select Run again; the message will automatically close.

QUESTION 5. How do the model's graphs look? Use the blank graphs below to record the curves the model has generated. NOTE: The red line in the blood glucose graph marks the homeostatic level of 6000 mg.



QUESTION 6. What glucose release rate or rates did you choose? Which time line or lines did you click?

Answers will vary for glucose rate but it should be at least 400 mg/min, preferably higher. The time lines should be between 12 and 48 minutes.

QUESTION 7. How does the blood level of insulin change as blood glucose increases?

The blood level of insulin increases.

QUESTION 8. How would you describe when the change occurs? How long is the lag interval (the time required for insulin secretion to show a response)?

The increase in amount of insulin is delayed; it starts after the increase in blood glucose. The lag interval is about 10 minutes. Answers may vary as students try to read their graphs. You may wish to suggest that they use the zoom function for a closer view.

QUESTION 9. What might cause the change and lag in insulin secretion?

The increasing amount of glucose signals the pancreas to start secreting more insulin to control the rising blood glucose level. The lag time is how long it takes the beta cells in the pancreas to secrete enough insulin to begin to make a difference in the glucose level.

QUESTION 10. How does the blood level of insulin change as blood glucose decreases?

As blood glucose decreases, the amount of insulin in the blood decreases.

QUESTION 11. What is the lag time?

The lag time is about 10 minutes. Answers may vary.

QUESTION 12. Why does the insulin level decrease?

The insulin level decreases because the high levels of insulin have caused cells to take up glucose, lowering the blood glucose level. The pancreas receives a weaker and weaker signal to secrete insulin, so produces less and less.

QUESTION 13. How long after glucose release starts does the blood glucose level return to normal? That is, how long does the glucose spike last?

Answers will vary depending on the students' glucose release rate choices. The total time is 80-90 minutes: 20-30 minutes to peak, 20 minutes to decline, and 40-50 minutes recovery.

NOTE: The model may have displayed a message when the blood glucose level reached 9600 mg, "Renal Threshold for Glucose — Kidneys can no longer conserve glucose. Glucose begins to spill out into urine." Students who selected a glucose release rate greater than 801 mg/min for 2 or more time lines triggered a second message, "Hyperglycemia — levels of glucose are dangerously high." You may wish to explain these messages now if you didn't explain them during the activity introduction.

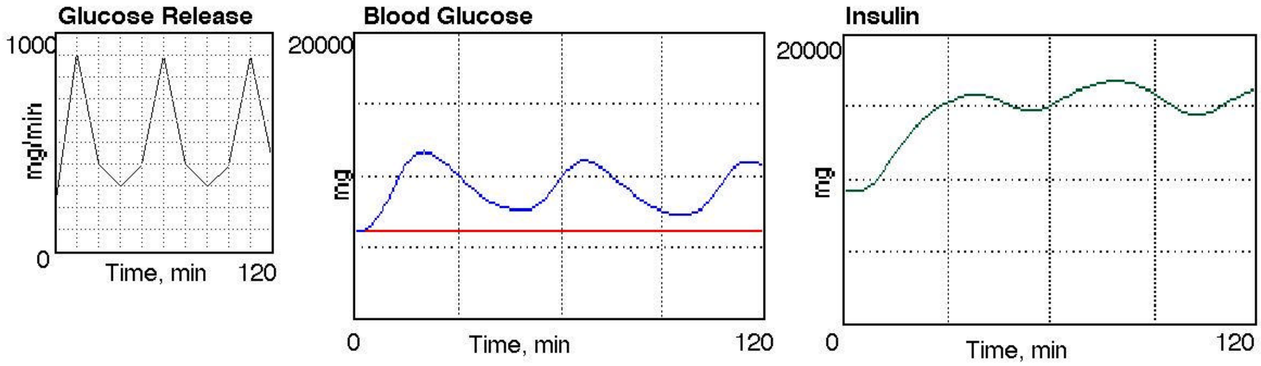
QUESTION 14. At what glucose release rate in the model does the body begin passing excess glucose into the urine? (You may need to choose a higher glucose release rate to observe the alert.)

The body begins passing glucose into the urine at a glucose release rate greater than about 700 mg/min. (The exact number in the model is 688 mg/min.)

QUESTION 15. If you eat 3 candy bars at different times in 2 hours, how do you think your blood glucose and insulin levels would respond?

By eating each bar (simple sugars) at a different time, you get 3 glucose spikes. (The blood glucose level rises rapidly.) The blood glucose and insulin graphs would show three peaks and would take a long time to return to normal, maybe longer than the model run. The closer together in time you eat the candy bars, the more the insulin curve shows just one peak. The insulin level goes up and stays up as each glucose release appears.

QUESTION 16. How do you think the model's graphs will look? Use the blank graphs below to sketch your chosen glucose release rate and your predictions of the shape of the blood glucose and insulin curves.



- Open the glucose release input graph.
- Choose three glucose release rates to represent the 3 candy bars and click 3 time lines at those values. Click OK.
- Run the simulation.

QUESTION 17. How do the model's graphs compare with your predictions?

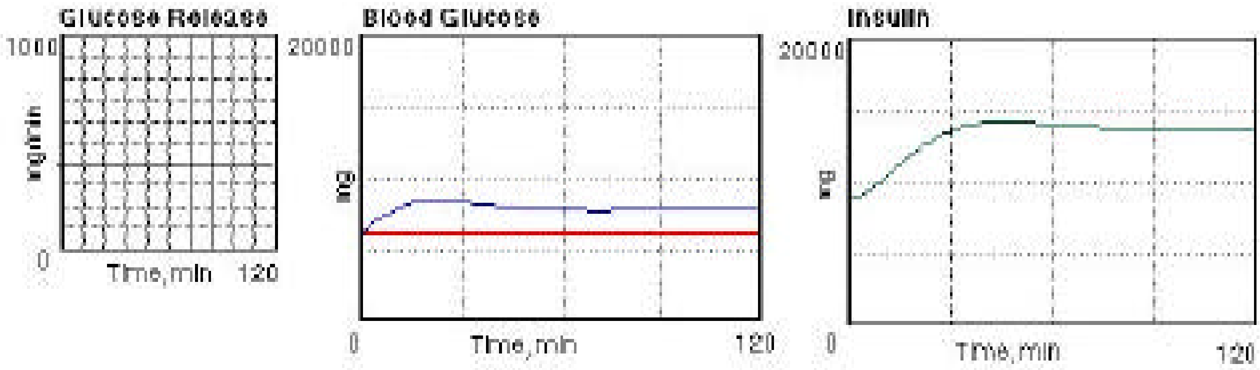
Answers will vary from very short confirmations to longer discussion of differences. Students may sketch the model's graphs to show their results.

Scenario III. Eating complex carbohydrates

Foods like beans, rice, oats and other cereal grains, fleshy fruit, vegetables, whole-grain bread, and pasta contain combinations of sugars and starches. Digestion converts these complex carbohydrates into glucose at a much steadier rate than the rapid absorption of simple sugars. You are going to simulate the body's response to eating pasta.

- Under the Map pull-down menu, choose Restore » All Devices. The blood glucose and insulin graphs will clear and the Glucose Release graph will return to the homeostatic rate. Alternatively, on the small Glucose Release graph click the U (in a box in the lower left corner) to reset glucose release to the homeostatic rate. The U appeared in Scenario II when you entered a new glucose release rate. When you next run the simulation, the old curves will vanish, to be replaced by new curves.
- Open the glucose release input graph.
- Click the time lines to set input values for a moderate glucose release of about 400 mg/min that is maintained for the duration of the model run. Click OK when you have set the values.
- Run the simulation.

QUESTION 18. How do the model's graphs look? Use the blank graphs below to record the curves that the model generates.



QUESTION 19. How does this blood glucose graph differ from the same graph generated by eating a candy bar (question 5)?

The pasta blood glucose curve stays steady throughout the model run. It also rises higher than the candy-bar curve at a 400 mg/min spike.

QUESTION 20. What might cause the difference?

Because pasta is a complex carbohydrate, it takes longer to digest than a candy bar, so glucose release is slower and lasts longer.

QUESTION 21. How is the insulin graph different from the same graph generated by eating a candy bar (question 5)?

The differences are the same as for the blood glucose graph.

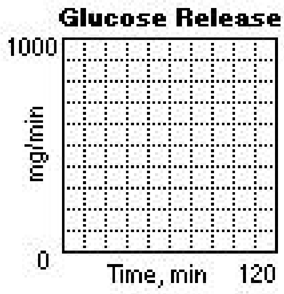
QUESTION 22. What might cause the difference?

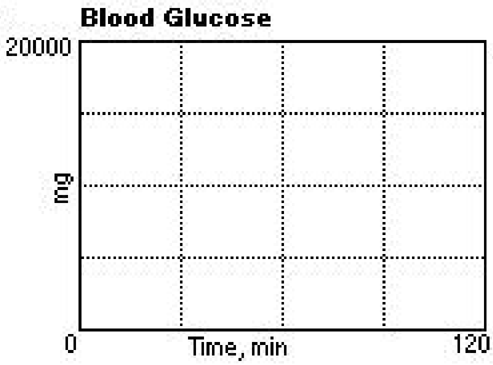
In response to a steady glucose release, the pancreas secretes a steady amount of insulin until the blood glucose level returns to normal.

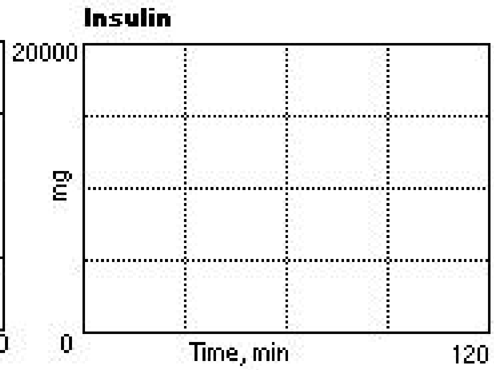
QUESTION 23. Why do the blood glucose and insulin graphs have a similar shape in a particular simulation?

The shape of the insulin curve will mimic the shape of the blood glucose curve in a particular model run because the blood glucose level directly affects the insulin level.

QUESTION 24. How do you think the graphs would look if you extended the model run longer than 120 minutes? Use the blank graphs below to sketch your chosen glucose release rate and your prediction of the shape of the blood glucose and insulin curves. At the lower right corner of each graph, write the number of minutes you would extend the model run.







QUESTION 25. What body responses are you showing in your predictions?

> **Digesting complex carbohydrates takes longer than absorbing simple sugars. In another hour (180 minutes) the body probably has finished work on the pasta meal, unless you stuffed yourself. Then you might need to extend the run by 2 hours. NOTE: The prediction graphs should show blood glucose and insulin levels returning to normal (6000 and 9000 mg, respectively), with the glucose return slightly before the insulin return.**

Part B. Playing the Part of the Pancreas

The human pancreas secretes chemicals to break down almost all food molecules, buffers against stomach acid, and hormones including insulin. After you eat, glucose enters your bloodstream faster than your cells can use it. Your blood glucose level rises, stimulating the beta cells in the pancreas to secrete insulin. Insulin targets mainly liver, fat and muscle cells to use glucose or store excess as glycogen.

In this part of the activity, you will be simulating pancreatic action by controlling the insulin secretion rate for three glucose-release scenarios. For each scenario, you will make a hypothesis about how the pancreas should respond to a particular change in glucose release rate. From your hypothesis, you will try to predict the blood glucose and insulin levels from the insulin secretion rate you have chosen. Each prediction has two parts—the insulin secretion rate you think will work for the scenario, and the response of blood glucose and insulin levels to that rate.

You will be using a second version of the glucose-insulin prebuilt model. It is similar to Glucose 1, but has a STELLA® slider in the lower right of the model box. The slider lets you change the value of the insulin secretion rate, a value that in Glucose 1 was controlled by the model. In Glucose 2, you will control the insulin secretion rate to keep the blood glucose level within a healthy range. To change the insulin secretion rate, move the slider bar with the computer mouse click-and-drag technique, or click in the value box and type a different value.

QUESTION 26. What is a healthy blood glucose range for human adults? (HINT: Read the model's information section.)

A healthy blood glucose range for adult humans is 70 to 120 mg/dL. Multiply by 60 dL of blood to get a total glucose range of 4200 to 7200 mg.

Scenario IV. Simulating steady glucose release

You will be setting glucose release at a steady, moderate rate and maintaining it for the duration of the model run. (The values are like those in Part C, Eating pasta.)

- Double-click Glucose 2.stm to open the model.
- Open the glucose release input graph.
- Click the time lines or enter values in the Output column to set the glucose release level at 400 mg/min for the length of the model run. Click OK.

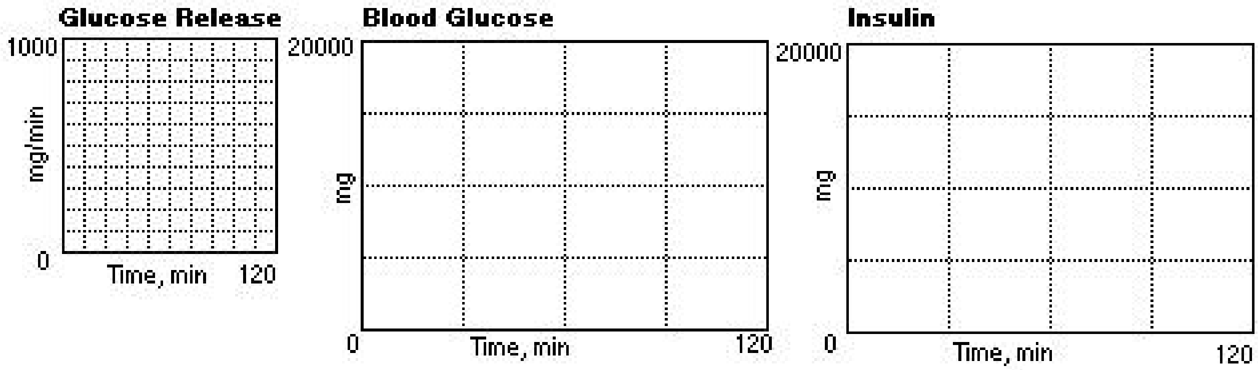
QUESTION 27. What is your hypothesis about how the pancreas will respond to an increased glucose release rate?

Answers will vary. All should say that insulin secretion must increase to counter the blood glucose increase, that insulin secretion suffers a time lag, and that the insulin rate has to remain steady because the glucose release rate is steady. A sample answer: My hypothesis is that the pancreas will increase insulin secretion as soon as it receives glucose signals. Because the glucose release rate will remain steady through the simulation, the insulin secretion rate will remain steady.

QUESTION 28. How will you, playing the part of the pancreas, change the insulin secretion rate to keep the blood glucose level in a healthy range? This is the first part of your prediction about how the system being modeled should behave as you manipulate the insulin secretion rate slider. (NOTE: The replacement of degraded insulin is included in the amount secreted at the homeostatic level.)

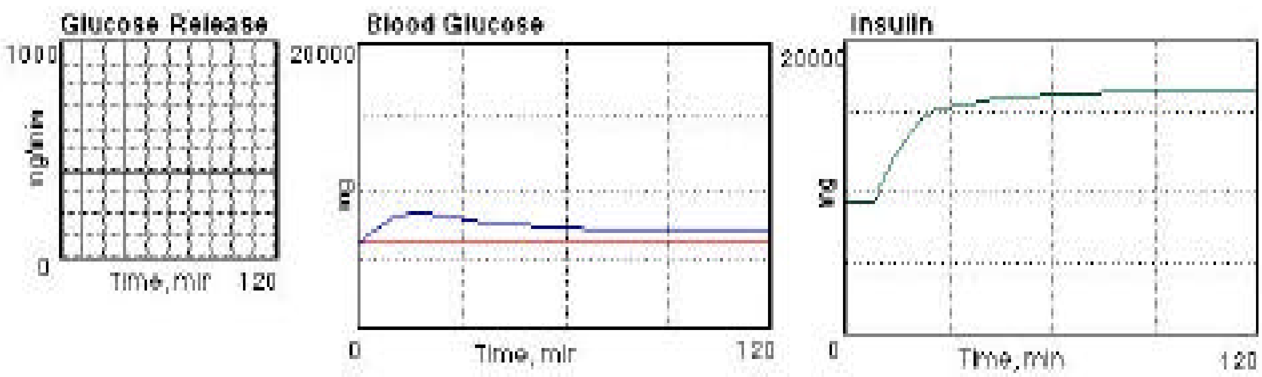
Answers will vary. A sample answer might include the following items: I, as the pancreas, need to increase my insulin secretion rate to take care the glucose release of 400 mg/min. (I don't have to worry about replacing degraded insulin.) From simulating homeostasis, I know that at 200 mg/min glucose release, the blood glucose level is 6000 mg and the insulin level is 9000 mg, which is 1.5 times the blood glucose level. I figure I have to add at least 1.5 times the homeostatic insulin secretion rate, which would be 250 units/min. But because of the lag time, a lot of glucose will have arrived before I can secrete anything, so I have to start by secreting much more insulin. I will increase my secretion rate by 400 to 500 units/min. I know that the pancreas takes time to start secreting more insulin, so I will start the increase about 10 min after the glucose level starts to rise; the amount of time for me to move the slider after starting a run seems to correspond to the insulin lag time.

QUESTION 29. How do you think the blood glucose and insulin graphs will look after you change the insulin secretion rate? This is the second part of your prediction of the system's behavior at the insulin secretion rate you have chosen. Use the blank graphs below to sketch the glucose release rate and the curves you predict the model will generate.



- Run the simulation. Remember to control the insulin secretion rate as you have planned, to bring the blood glucose level as close to normal (the red line) as possible.

QUESTION 30. How did the model behave? Use the blank graphs below to record the curves you see on the model's graphs.



QUESTION 31. What does the shape of the blood glucose curve tell you about the amount of glucose in the blood?

Answers will vary. The shape of the blood glucose curve is similar to that generated by eating pasta. As the minutes pass, the curve rises slowly from normal, reaches a gentle peak in about 20 minutes, declines slightly, then stays approximately steady to the end of the model run. The shape shows a constant glucose release.

QUESTION 32. What does the shape of the insulin curve tell you about the amount of insulin in the bloodstream?

Answers will vary. The shape of the insulin curve is also similar to the pasta curve. The curve starts rising about 10 minutes after the blood glucose curve starts rising. It reaches its highest point in about 60 minutes, then stays at that level. The insulin secretion rate stays steady because the glucose release rate is steady and moderate.

QUESTION 33. How can you tell how successful you were at maintaining a healthy level of blood glucose?

> **Answers will vary. Students may say simply that the blood glucose curve got close to the red line. Others may offer detailed descriptions and numbers from the simulation. For example: If the blood glucose level returns to 7200 mg or lower, I was successful. If I brought the blue blood glucose curve very close to the red normal line, I was successful. Adding 400 units/min insulin brings the glucose level down from about 7500 to about 6900. More insulin, even much more, than this rate doesn't lower the steady blood glucose level very much. I tried lower rates, but they didn't lower the blood glucose level enough. Adding about 300 units/min insulin allows the glucose to stay at around 7500 mg. This level is above the healthy range.**

Scenario V. Simulating moderate, then low glucose release

For this scenario, you will be simulating a drop on the body's glucose release rate. You need a moderate glucose release of 400 mg/min for a short time, followed by very low glucose release of 100 mg/min for the rest of the model run.

- Open the glucose release input graph.
- Click the time lines to enter starting values of 400 mg/min for a short time, then 100 mg/min for the duration of the model run. Click OK.

QUESTION 34. What is your hypothesis about how the pancreas should respond in this scenario?

> **My hypothesis that the pancreas should increase, then decrease insulin secretion.**

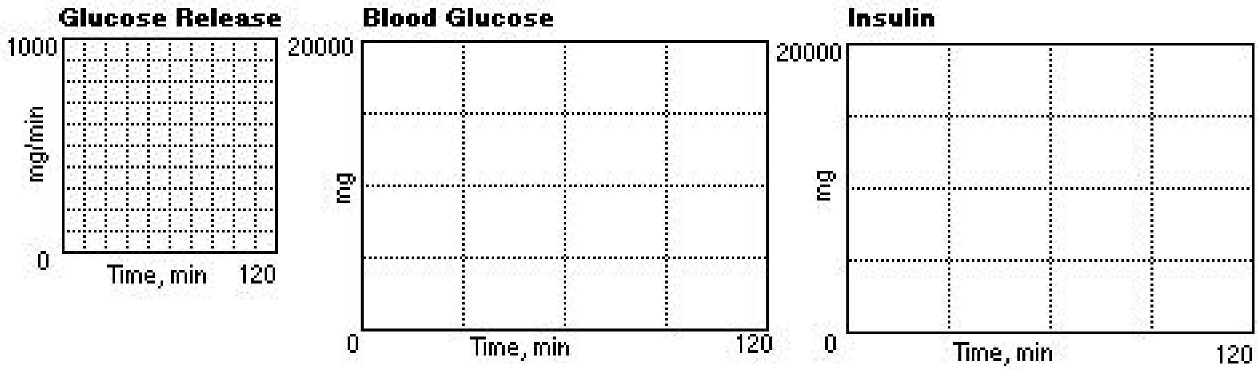
QUESTION 35. What insulin secretion rate do you predict will keep the blood glucose level in a healthy range?

> **Answers will vary. An example: As the pancreas, I must increase insulin secretion to meet the initial 400 mg/min glucose release. I'll try 900 units/min as in Scenario IV, but only for 10 minutes. Then I must decrease insulin secretion a lot because the 100 mg/min glucose release is below the homeostatic level. I'll try 200 units/min for the duration of the run.**

QUESTION 36. What changes in blood glucose and insulin levels do you predict will occur when you change the insulin secretion rate?

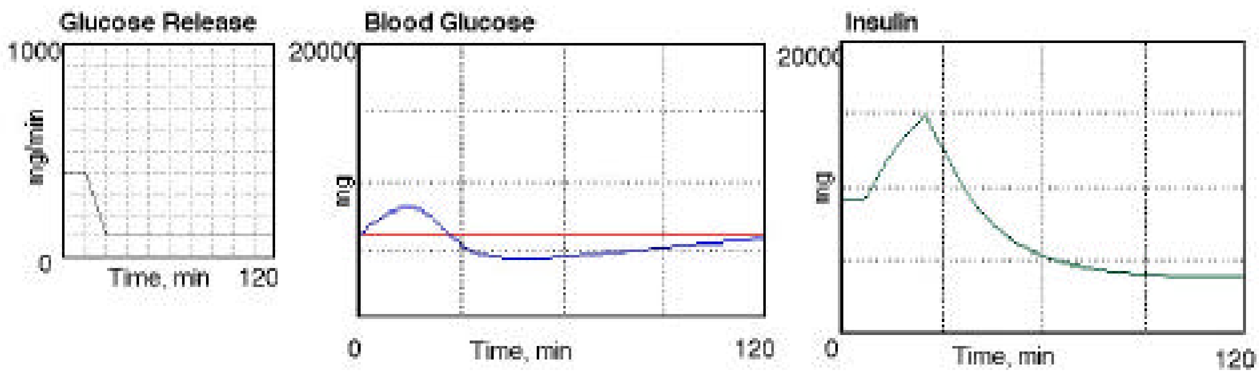
> **Answers will vary. An answer might include descriptions of the initial, middle, and final shapes of the two curves or might have a table or list of blood glucose and insulin values as the curves change. A student may predict that the blood glucose level will return to the normal range but insulin will not, or vice versa.**

QUESTION 37. How do you think the blood glucose and insulin graphs will look after you change the insulin secretion rate? This is part of your prediction of the system's behavior at the insulin secretion rate you have chosen. Use the blank graphs below to sketch the glucose release rate for Scenario V and the curves you predict the model will generate.



- Run the simulation. Remember to control the insulin secretion rate as you have planned, to bring the blood glucose level as close to normal (the red line) as possible.

QUESTION 38. How did the model behave? Use the blank graphs below to record the curves you see on the model's graphs.



QUESTION 39. What does the shape of the blood glucose curve tell you about the amount of glucose in the blood?

Answers will vary. One answer might say, The blood glucose curve is sort of S-shaped. It rises for about 20 minutes, as the 400 mg/min of glucose comes in for 20 min. When the glucose release rate drops to 100 mg/min, the blood glucose curve starts downward. In another 20 minutes it goes below the red line and continues downward slowly for 20 more minutes until it slowly heads up. Another answer might say, The blood glucose curve rises from 6000 to about 9000 mg in about 20 minutes and declines to below 6000 in about 20 minutes. In 20 minutes more it is at a minimum of about 5000 mg, then begins to rise slowly, to the end of the simulation.

QUESTION 40. What does the shape of the insulin curve tell you about the amount of insulin in circulation?

Answers will vary. Possible details: The insulin curve starts rising because the pancreas is secreting more insulin for the 400 mg/min glucose release. The curve starts up about 10 minutes after the blood glucose curve starts rising because of the lag time. The curve reaches its highest point in about 20 minutes, then declines because the insulin secretion rate responds to the sudden drop in glucose release, reaching about 2/3 of the homeostatic level at the end of the simulation.

QUESTION 41. What evidence tells you how successful you were at maintaining a healthy level of blood glucose?

Answers will vary. Students may say simply that the blood glucose curve got close to the red line. Others may offer detailed descriptions and numbers from the simulation.

Scenario VI. Simulating your choice of glucose release rate

Now, you will create your own scenario, using glucose release rates that you choose. You will need to explain the scenario you have decided to test, state your hypothesis about how the pancreas should respond, and predict the blood glucose and insulin levels that will result.

QUESTION 42. What pattern of glucose release are you going to try?

Answers should state the chosen glucose release values and how long each will operate.

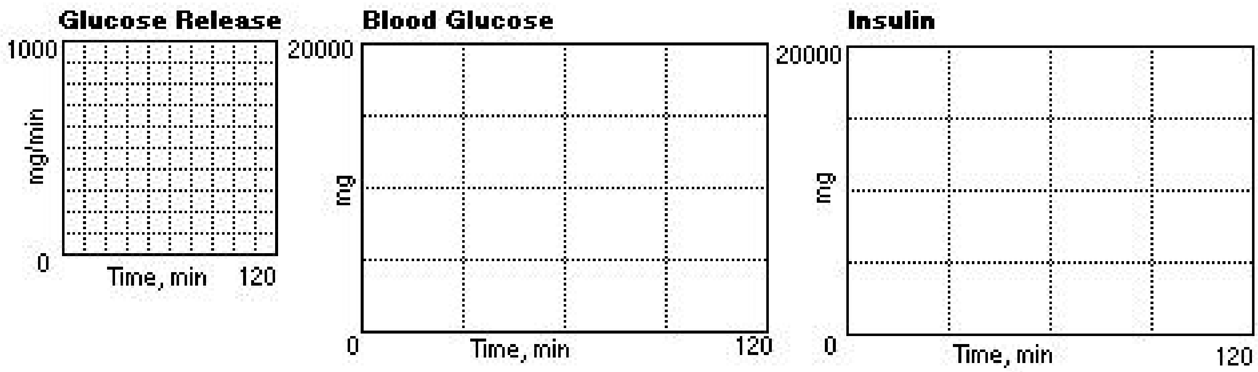
QUESTION 43. What does this pattern represent?

Answers will vary but should be more or less realistic.

QUESTION 44. What is your hypothesis about how the pancreas should respond?

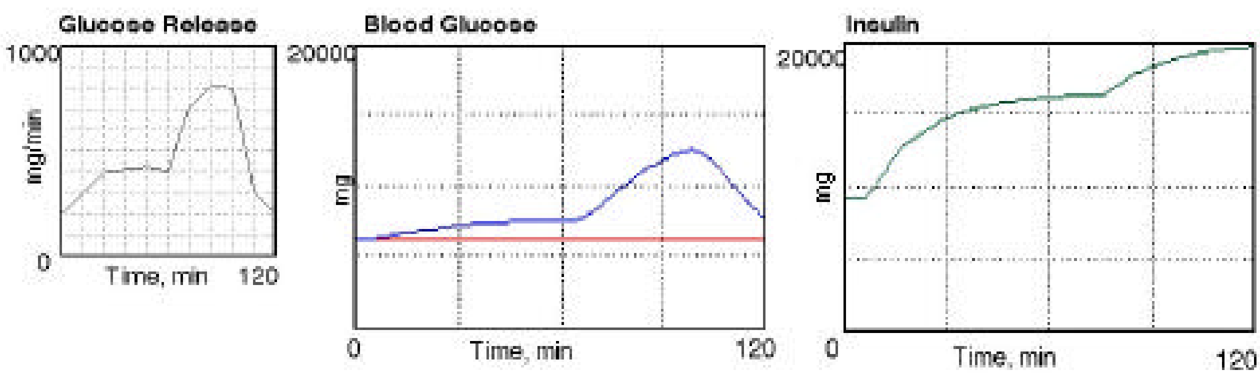
Answers will vary but should indicate increasing or decreasing insulin secretion for increased or decreased glucose release, with appropriate lag times.

QUESTION 45. How should the glucose release, blood glucose and insulin graphs look in your scenario? Use the blank graphs below to sketch your prediction.



- Set your glucose release rate.
- Run the simulation.

QUESTION 46. Using your scenario, how did the model behave? Use the blank graphs below to record the model-generated curves. **Example: A meal with a large, sweet dessert.**



QUESTION 47. What evidence can you use to tell if the behavior of the model supports your hypothesis?

Answers will vary, but should show that the student understands (1) that insulin secretion rises as glucose release does and lags in initial response by about 10 minutes and (2) that subsequent insulin secretion depends on the size of the glucose release and its duration.

Part C. Thinking about glucose and insulin

The normal relationship between glucose release and insulin secretion is a feedback mechanism governed by chemical signals carried in the bloodstream. The STELLA® models you have been using to simulate glucose-release scenarios are based on the physiology of the average, healthy human. Individual healthy humans are not necessarily average.

QUESTION 48. What similarities in the glucose-insulin relationship would you expect all healthy humans to share?

I would expect all healthy humans to show insulin secretion increase about 10 minutes after a glucose release. As the insulin reacts with body cells to permit

glucose intake, the blood glucose level decreases, signaling the pancreas to reduce insulin secretion, permitting a return to homeostasis.

QUESTION 49. What differences in healthy humans do you think would make differences in how their bodies respond to glucose release?

Humans differ in body weight, metabolism rate, genetic makeup, and environment (food intake and amount of exercise, for example). All these factors could influence an individual's response to glucose release.

QUESTION 50. How does the glucose-insulin feedback mechanism keep the healthy human body in homeostasis in spite of glucose fluctuations?

When glucose is released into the bloodstream, blood glucose level increases. The increase send a chemical signal to the pancreas to secrete more insulin to keep the blood glucose level normal. As the blood glucose level decreases, the chemical signal decreases, so insulin secretion decreases.

When the blood glucose level is lower than the homeostatic level, such as between meals, the pancreas secretes a lower level of insulin until it signals storage cells to turn glycogen to glucose so that the glucose level can rise to a healthy level.

In a healthy human, the feedback mechanism is able to maintain homeostasis and keep the blood glucose level within a narrow range.

Part D. Thinking about diabetes

In people with diabetes, the body can't control the blood glucose level. The glucose-insulin feedback mechanism does not work. In Type I diabetes, the beta cells secrete little or no insulin. Type I is often called juvenile diabetes because it occurs most often in young people. In Type II diabetes, the pancreas secretes insulin at healthy rates but the body's cells do not take in glucose because they do not respond well when insulin tries to help them take in glucose. Type II is often called adult-onset diabetes or insulin-resistant diabetes.

A glucose tolerance test is often used to diagnose diabetes. The test gauges the body's ability to use glucose. The person taking the test fasts for 8 to 12 hours, then drinks a solution containing 75 g of glucose. During the next 3 hours, 4 blood samples are taken at equal time intervals. For a healthy person, the blood glucose concentration should be less than 195 mg/dL after 1 hour, less than 160 mg/dL after 1.5 hours, and less than 140 mg/dL after 2 hours.

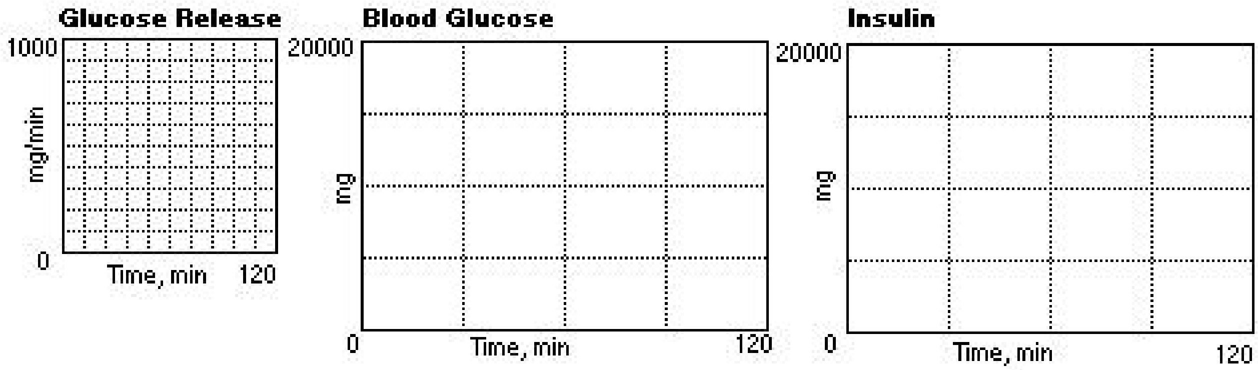
Glucose conditions after a glucose tolerance test are in the table below.

Condition	Glucose concentration	Amount of blood	Total blood glucose
Normal blood glucose	80 110 mg/dL	60 dL	4800 6600 mg
Hypoglycemia	<40 mg/dL	60 dL	<2400 mg
Renal threshold	160 180 mg/dL	60 dL	9600 10,800 mg
Hyperglycemia	>210 mg/dL	60 dL	>12,600 mg

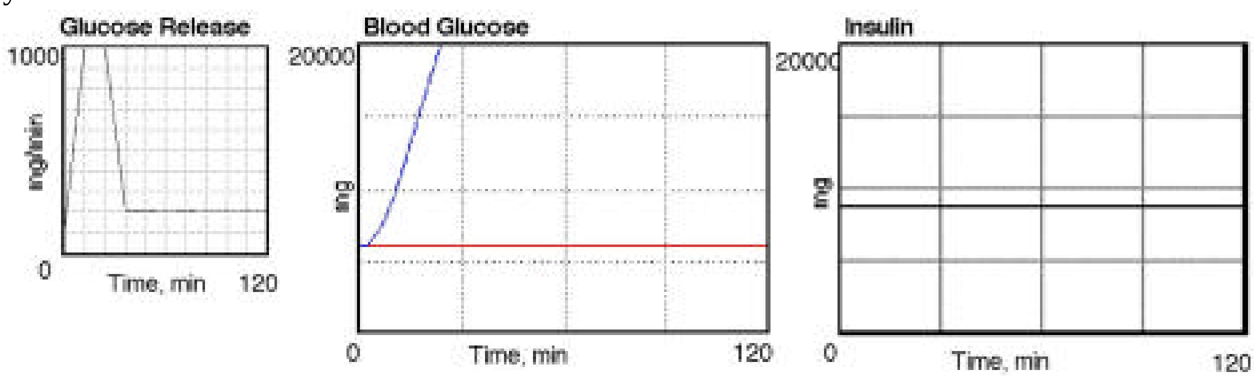
QUESTION 51. Which part of this activity would the glucose tolerance test resemble?

The test would resemble Part B, Eating simple sugar.

QUESTION 52. How do you think the blood glucose and insulin curves will look for a person with Type I diabetes who takes the glucose tolerance test? Use the blank graphs below to sketch your estimates.



QUESTION 53. How do you think the blood glucose and insulin curves will look for a person with Type II diabetes who takes the glucose tolerance test? Use the blank graphs below to sketch your estimates.



QUESTION 54. Based on your estimates about the behavior of the glucose-insulin system for Type I diabetes (question 52), how might you adjust glucose release and insulin secretion in the Glucose 2 model to simulate Type I diabetes?

Answers will vary. Sample: I will select a steady glucose release, about 400 mg/min, as in eating pasta. Because Type I diabetes is caused by little or no insulin secretion in the pancreas, I can simulate Type I diabetes with Glucose 2 by setting the insulin secretion slider to zero.

QUESTION 55. Based on your estimates about the behavior of the glucose-insulin system for Type II diabetes (question 53), how might you adjust the Glucose 2 model to simulate Type II diabetes?

Answers will vary from "Can't do it" to "Difficult but do-able". To simulate Type II diabetes using Glucose 2, set glucose release to a moderate level, such as 400 mg/min, and guide the insulin secretion slider in a Type II diabetes pattern—appropriate lag time, appropriate response to the set glucose release, then decreasing insulin secretion as cells refuse to respond to it, allowing blood glucose to increase.

Appendix A

INFORMATION: Glucose, Insulin, and the Role of the Pancreas

GLUCOSE. *Glucose*, a simple sugar, is the main energy source for most organisms. The human body makes glucose from food and transports it to cells via the bloodstream. Glucose is measured in milligrams per deciliter of blood. The average healthy human has about 60 dL (6 L) of blood and a between-meals blood glucose level of about 100 mg/dL or 6000 mg circulating in the blood. (The range for a person who has been fasting is 70 to 120 mg/dL.)

The amount of glucose in your blood varies with your food intake and your liver's breakdown of fat to make glucose. *Glucose release* is measured in mg/min.

PANCREAS. Your *pancreas* regulates your blood glucose level by secreting the hormone *insulin* in response to an increasing glucose level. The pancreas secretes insulin in groups of beta cells called islets of Langerhans, after the German scientist who first described them.

As insulin circulates in the blood, your body's cells draw glucose from the blood. Your glucose level decreases, so the pancreas secretes less insulin. This mutual relationship between glucose and insulin is an example of *feedback*, and works much as a home thermostat controls room temperature.

INSULIN. Insulin helps cells take in glucose by making the cell membrane more permeable to the sugar. The normal insulin secretion rate is about 500 units/min, the amount necessary to maintain equilibrium between insulin and glucose. This equilibrium is essential to *homeostasis*, the normal stable condition of the human body's internal environment. Insulin level is measured in units (1 unit = 1 mg) and *insulin secretion rate* in units/min.

GLUCOSE USE. Cells use glucose to fuel their energy requirements. Glucose not needed for energy is converted to glycogen in your liver and muscles. These cells change glycogen back to glucose when the body needs it. The body stores excess glucose as fat. *Glucose use rate* is measured in mg/min.

INSULIN BREAKDOWN. Insulin degrades soon after secretion. Every minute 1/18 of the insulin in the blood degrades. At higher insulin levels, more insulin is degrading than at lower levels, that is, the degradation rate is faster at higher insulin levels.

MODEL. This model simulates the body's reaction to eating food: how much and what kind of food, how long ago, how fast digestion proceeds, and how soon your pancreas reacts. The insulin secretion rate is defined as a graphical function based on the surplus of glucose in the blood.

If your glucose level is normal (homeostatic), no excess glucose exists. The surplus is zero and insulin secretion rate is about 500 units/min, maintaining homeostasis.

If the surplus is positive, the insulin secretion rate increases until it reaches a limiting level that the beta cells cannot maintain. The rate begins to decline despite a high glucose level.

If the surplus is negative (a glucose level lower than homeostatic), the insulin secretion rate decreases as the body conserves glucose by slowing down the rate at which cells take it in. Beta cells also have a lower limit on insulin production. In the model this limit is set at zero, though in reality the beta cells are always making some insulin.

Appendix B
Feedback Loops

Stable conditions

To maintain stable conditions—also called steady state or equilibrium conditions, many systems require some sort of feedback mechanism. Feedback is a return to a system's input of part of the system's output. For example, in the human body, the systems for maintaining temperature, blood glucose level, and blood pressure operate by feedback. A house thermostat controls a feedback system.

In the basic STELLA® glucose-insulin model, the amount of glucose and insulin in the blood have relatively constant values as long as conditions in the body do not change, that is, as long as homeostasis is maintained.

Changing conditions

Natural systems tend toward equilibrium, but do not necessarily maintain constant values in their reservoirs and fluxes. Conditions change. Blood glucose concentration rises after you eat and falls when digestion is finished. In healthy humans insulin secretion rises and falls in concert with blood glucose concentration as the body recovers homeostasis. Computer models use feedback loops to simulate natural changes.

Feedback loops

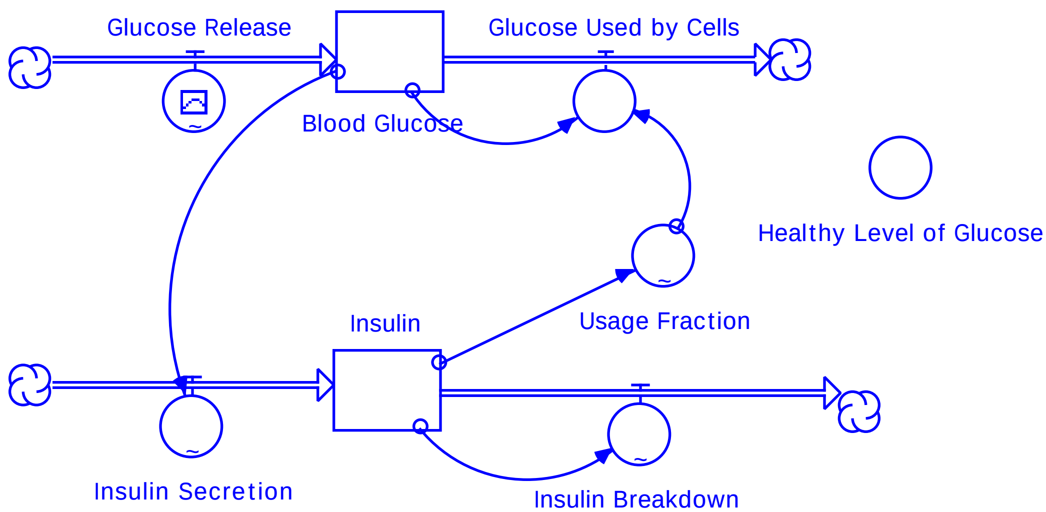
STELLA® models handle changing conditions with feedback loops. Connectors from stocks to flows permit flows to change as the associated stocks change. The nature of the association is entered for the flow instead of a constant value. In the glucose-insulin model, for example, a connector links the blood glucose stock to the insulin secretion flow. The flow value is entered not as a constant, but as an expression permitting it to change as the blood glucose stock's value changes.

For as realistic a simulation as possible, stocks with changing values need to be linked to the appropriate flows to set up feedback loops. In the glucose-insulin model, the glucose release system and the insulin secretion system are linked together so that each system determines the response of the other. The stock of one system is linked to the appropriate flow of the other.

Appendix C
Glucose-Insulin STELLA® Models

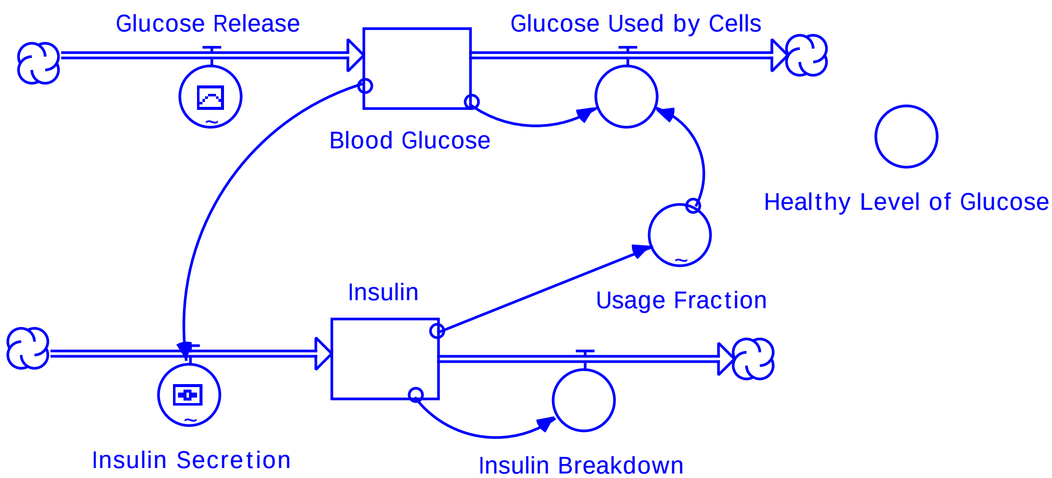
Glucose 1

Insulin Secretion rate is controlled by its relationship to the Blood Glucose level.



Glucose 2

Insulin Secretion rate is controlled by the student using the Secretion Rate slider.



Appendix D
Glucose 1 and Glucose 2 Model Equations

Blood_Glucose(t) = Blood_Glucose(t - dt) + (Glucose_Release - Glucose_used_by_cells) * dt

INIT Blood_Glucose = 6000 {mg}

INFLOWS:

Glucose_Release = GRAPH(time)

(0.00, 198), (12.0, 198), (24.0, 198), (36.0, 198), (48.0, 198), (60.0, 198), (72.0, 198), (84.0, 198), (96.0, 198), (108, 198), (120, 198)

OUTFLOWS:

Glucose_used_by_cells = Blood_Glucose*Usage_Fraction

Insulin(t) = Insulin(t - dt) + (Insulin_Secretion - Insulin_Breakdown) * dt

INIT Insulin = 9000 {units}

INFLOWS:

Insulin_Secretion = GRAPH(Blood_Glucose)

(1000, 0.00), (2000, 15.0), (3000, 85.0), (4000, 190), (5000, 350), (6000, 500), (7000, 665), (8000, 825), (9000, 930), (10000, 975), (11000, 995)

OUTFLOWS:

Insulin_Breakdown = Insulin/18

Healthy_Level_of_Glucose = 6000 {mg}

Usage_Fraction = GRAPH(Insulin)

(0.00, 0.0075), (1800, 0.0105), (3600, 0.0145), (5400, 0.019), (7200, 0.0255), (9000, 0.033), (10800, 0.0405), (12600, 0.049), (14400, 0.0545), (16200, 0.0575), (18000, 0.059)

Appendix E-1
Diabetes Questions: Teacher Guide

A diabetic who hasn't taken enough insulin or whose cells are resistant to insulin is, essentially, starving because glucose can't get into the body's cells. A diabetic who takes too much insulin causes too much glucose to enter the cells (Type 1) or too much insulin to accumulate in the blood (Type 2). Either condition can lead to life-threatening physical consequences including diabetic coma. Controlling diabetes require attention to the body's response to varying blood glucose levels to maintain homeostasis.

What changes in life style would you undertake if you were diagnosed with Type 1 or Type 2 diabetes?

Exercise more, use more glucose.
Eat no simple sugar. Cut out candy bars and regular soda.
Eat complex carbohydrates, like fruit, vegetables, pasta and food made with whole grains.
Eat a variety of food so digestion takes more time.
Eat small amounts of food a frequent intervals, for a steady supply of glucose.

A diabetic measured a blood glucose concentration of 220 mg/dL. If one unit of rapid release insulin is required to reduce the concentration by 3 mg/dL, how many unit of insulin would this person need to inject to bring the concentration to a healthy level of 90 mg/dL?

The blood glucose concentration must be reduced by 220 – 90 mg/dL, or 130 mg/dL. Students use proportional thinking. 1 unit insulin:3 mg glucose = N units insulin:130 mg glucose. N = 43.34 units of insulin.

Using STELLA® software and following the example of the models in this activity, construct a glucose-insulin model adjusted for your body weight and blood volume. Run your model for simple sugar and complex carbohydrate scenarios and compare your results to results from this activity, which are for the average person. Prepare a packet of your findings by printing your model, your graphs, and your equations. List your packet contents in the space below.

Work produced for this extension may vary in detail. Students unfamiliar with STELLA® may need help building the model. Student data packets should all be similar.

Appendix E-2
Diabetes Questions: Student Guide

A diabetic who hasn't taken enough insulin or whose cells are resistant to insulin is, essentially, starving because glucose can't get into the body's cells. A diabetic who takes too much insulin causes too much glucose to enter the cells (Type 1) or too much insulin to accumulate in the blood (Type 2). Either condition can lead to life-threatening physical consequences including diabetic coma. Controlling diabetes require attention to the body's response to varying blood glucose levels to maintain homeostasis.

What changes in life style would you undertake if you were diagnosed with Type 1 or Type 2 diabetes?

A diabetic measured a blood glucose concentration of 220 mg/dL. If one unit of rapid release insulin is required to reduce the concentration by 3 mg/dL, how many unit of insulin would this person need to inject to bring the concentration to a healthy level of 90 mg/dL?

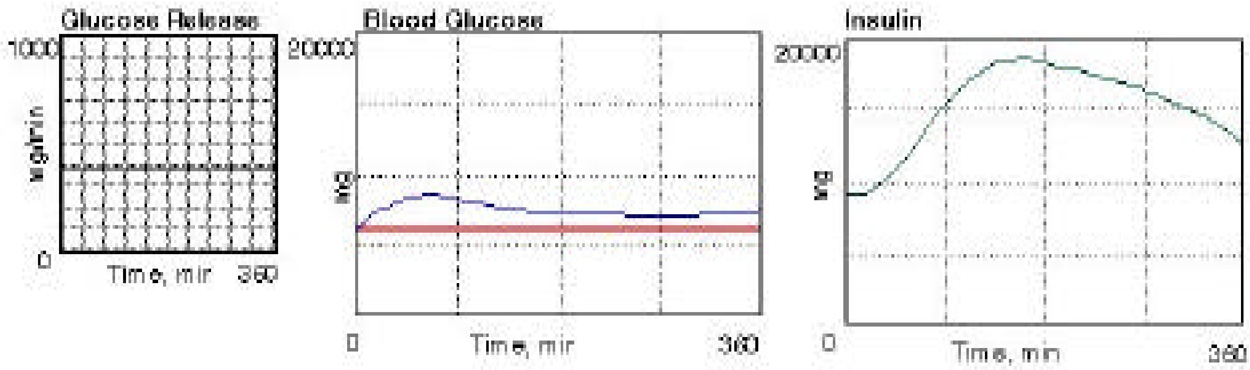
Using STELLA® software and following the example of the models in this activity, construct a glucose-insulin model adjusted for your body weight and blood volume. Run your model for simple sugar and complex carbohydrate scenarios and compare your results to results from this activity, which are for the average person. Prepare a packet of your findings by printing your model, your graphs, and your equations. List your packet contents in the space below.

Appendix F-1
Simulating Diabetic Response to Insulin Release: Teacher Guide

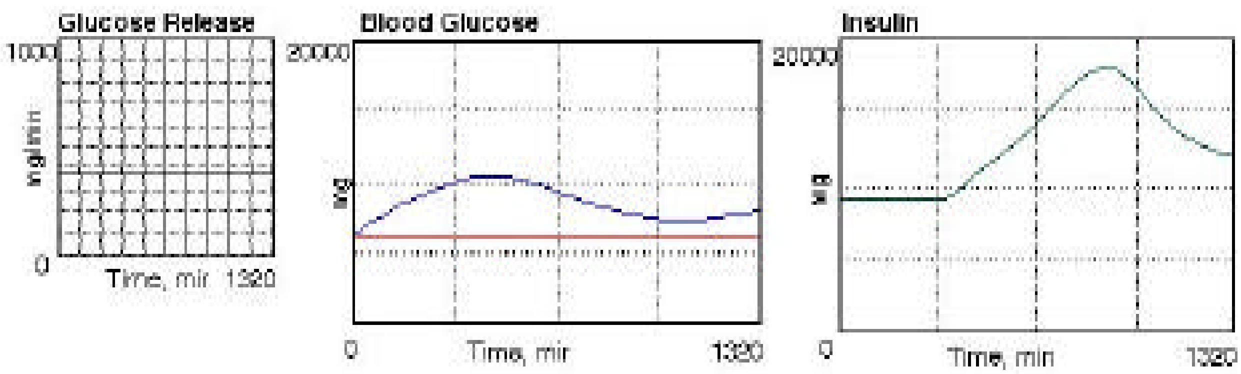
Insulin preparations for diabetics have different release rates—rapid, intermediate, and slow. Using Glucose 2, adjust the duration of model run and the insulin secretion slider to reflect the rates in the table and record your observations on the blank graphs below.

RELEASE RATE	ONSET	PEAK	DURATION
Rapid	15 30 min	2 4 hr	6 8 hr
Intermediate	1 3 hr	6 12 hr	18 26 hr
Slow	4 8 hr	14 24 hr	28 36 hr

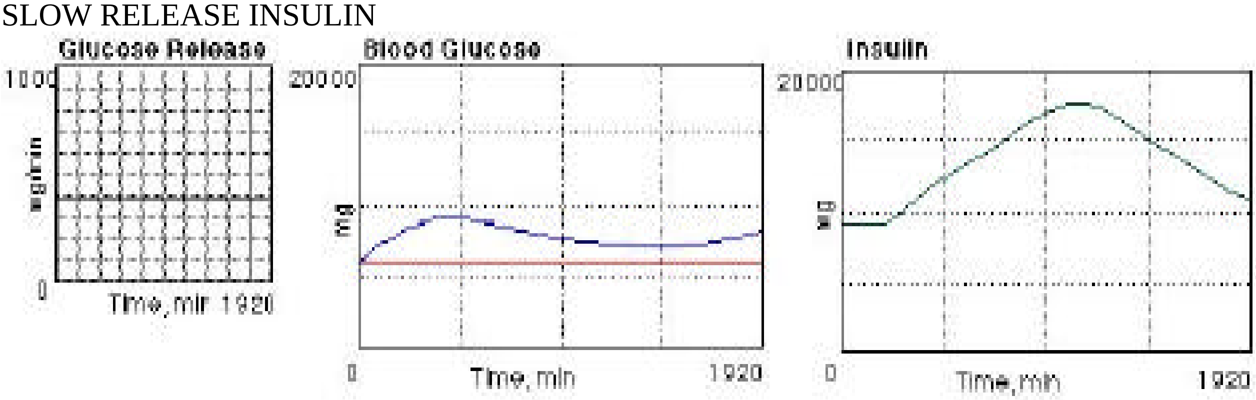
RAPID RELEASE INSULIN



INTERMEDIATE RELEASE INSULIN



SLOW RELEASE INSULIN



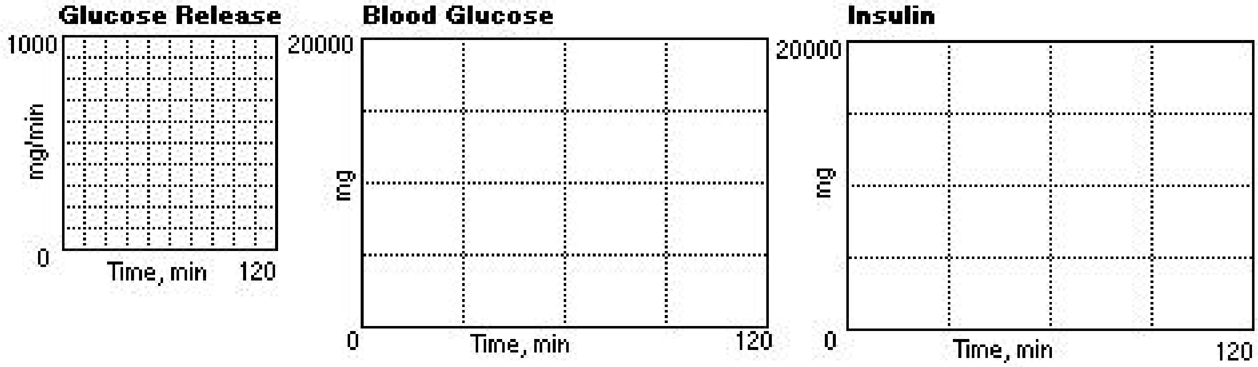
Appendix F-2

Simulating Diabetic Response to Insulin Release: Student Guide

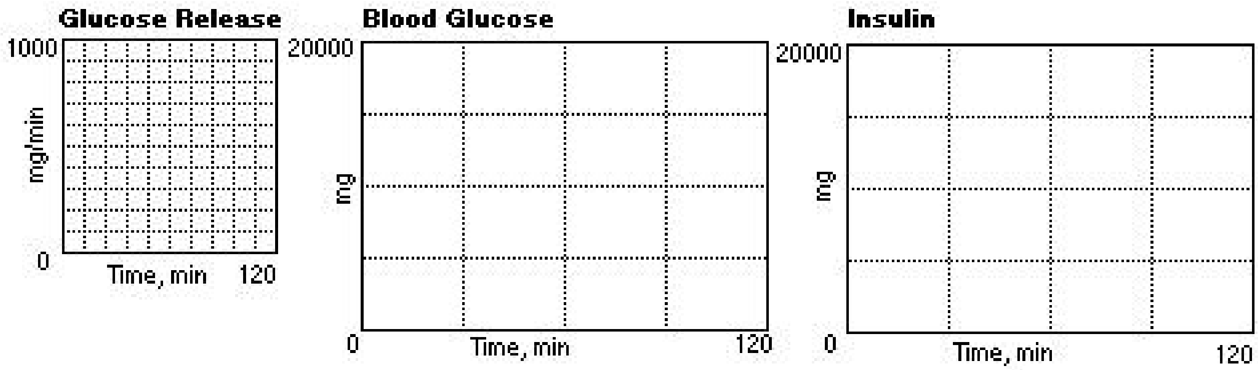
Insulin preparations for diabetics have different release rates—rapid, intermediate, and slow. Using Glucose 2, adjust the duration of model run and the insulin secretion slider to reflect the rates in the table and record your observations on the blank graphs below.

RELEASE RATE	ONSET	PEAK	DURATION
Rapid	15 30 min	2 4 hr	6 8 hr
Intermediate	1 3 hr	6 12 hr	18 26 hr
Slow	4 8 hr	14 24 hr	28 36 hr

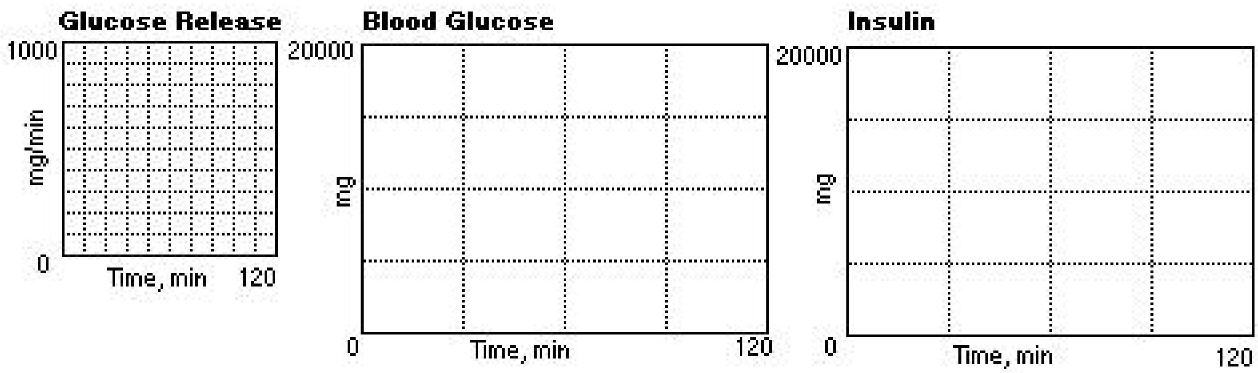
RAPID RELEASE INSULIN



INTERMEDIATE RELEASE INSULIN



SLOW RELEASE INSULIN



Appendix G
Generic Graph Questions

LEVEL I

A. Identify the independent (control) variable.

B. Identify the dependent variable(s).

C. What are the units for each variable?

D. What is the appropriate scale for each axis?

E. What is a meaningful title for the graph?

F. What type of graph—bar, scatter, line—is appropriate for these data?

LEVEL II

G. Describe in words how the dependent variable changes with respect to the independent variable.

H. What type of relationship do the variables have? Is it direct, inverse, linear, exponential, or some other type?

I. What are the units for the slope of the line or curve?

J. What physical phenomenon is represented by the slope units?

K. Describe in words how the slope of the line or curve changes as the graph is read from left to right.

LEVEL III

L. What is the numerical value of the slope of the curve at various points on the horizontal axis?

M. How do changes in the slope relate to the actual events (the physical phenomena) that we are representing with the graph?

LEVEL IV

N. What are the units for the area under the curve?

O. What physical phenomenon is represented by the area units?

P. What is the numerical value of the area under the curve at various points on the horizontal axis?

Q. How do changes in the area relate to the actual events (the physical phenomena) that we are representing with the graph?

LEVEL V

R. What is a best-fit graph? When should it be used?

S. When is it appropriate to interpolate or extrapolate from the data? How do you interpolate? How do you extrapolate?

T. What is a correlation factor (r-factor)? When is it used?

Appendix H
CoreModels Graph Interpretation Guidelines

VERBAL DESCRIPTION

Reading the graph from left to right, you are describing the behavior of the dependent variable in enough detail that the reader could sketch the basic shape of the curve from your description.

Example 1

The dependent variable is increasing at a constant rate and has a y-intercept of __.

Example 2

The dependent variable is increasing at an ever-increasing rate and has a y-intercept of __.

MATHEMATICAL DESCRIPTION

If you have adequate information, you may be able to identify the type of mathematical function represented by the curve.

Example 1

Linear

Example 2

Unknown—could be exponential or a power (polynomial) function

CONTEXTUAL DESCRIPTION

You are applying your verbal description to the physical event being depicted, including appropriate units and terminology for both the line or curve and its slope.

Example 1

The object starts at a zero reference point and moves at a constant velocity measured in m/s for 12 seconds. The velocity is the slope of the line representing the position of the object.

Example 2

The deer population starts at 100 deer and increases exponentially for 50 years. The slope of the curve represents the growth in the deer population per year.