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Glucose Regulation

A Pre-College Instructional Guide Employing Dynamic Computer Simulation

Prepared by
the MIT Pre-College Education Project
Under the Supervision of
Dr. Jay Forrester

BY

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Abstract

Curriculum Focus: Homeostasis and blood glucose regulation in both a normally functioning body and a diabetic body.

Grade Level: High school biology or human physiology

Number of Periods: 6 class periods

The following material was developed through a joint effort between members of the Pre-College Education Project at the Massachusetts Institute of Technology and Mr. Tad Sudnick of the Cambridge Rindge and Latin High School in Massachusetts. This packet was used as one piece of a fuller curriculum packet using systems thinking, causal loop diagrams, and a STELLA [II] simulation model to teach the chapter on the endocrine system in Mr. Sudnick's intensive biology class. The chapter covered many of the chemical regulatory systems that the human body sets up to maintain homeostasis. The simulation model that was used represented the structure of the body's blood glucose regulatory system. This packet includes the model descriptions and support materials that were used with the simulation model. These may be combined with the endocrine system packet to have a complete lesson on the endocrine system.

The Pre-College Education Project is a group of student researchers working under the direction of Dr. Jay Forrester in the System Dynamics Group at MIT. The group is dedicated to improving primary and secondary education in the United States by supporting the introduction of systems thinking and learner-directed learning to the educational process.

System Dynamics requires a person to consider both the structure and behavior of complex systems. The goal is to understand the relationship between structure and behavior and to be able to transfer this knowledge across disciplines. STELLA is a software program for the Macintosh computer which offers a language for exlpaining system structure and allows witnessing of the resulting behavior. The student uses STELLA as a tool to understand the link between structure and behavior. STELLA is powerful because it provides the ability to simulate something that occurs in real life. The computer program offers feedback for students to test their mental models of reality and to validate proposed policy implementations.

Learner-directed learning allows the student to take control of and responsibility for his own learning. It is based on the belief that the best way to learn is to participate in a project. Educators can stand in front of students all day long and lecture them on how to hit a tennis ball, change the oil in a car, or run a corporation. However, once students find themselves in the position where they have to complete one of these tasks, often they cannot. This is because the mental model of the system that they have created based on lecturing or reading does not fit reality. Students can create a better mental model by participating in the activity and learning from their mistakes. The computer simulation model of the glucose regulatory system allows them to participate in the regulation of the body's blood glucose level. Participation is the key to the students understanding of the body's attempts to maintain homeostasis.

The students study both the structure and the behavior of the body's blood glucose regulatory system. In homework exercises, they discover the structure that produces homeostatic behavior. Through computer exercises, they discover the dynamic behavior that results from the structure of the system. They also learn what happens when the body is unable to maintain homeostasis and the medical profession must develop methods for replacing normal body functions. By considering the structure and behavior of the diabetic system, students discover why one method of providing insulin to the diabetic is preferred over another.

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1 Systems Thinking Educational Learning Laboratory with Animation

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Purpose of Lesson Plan

This lesson plan can be used in many different ways. Materials to serve the following purposes at several levels of complexity are included in this curriculum packet. The teacher may choose to teach all or only one of the many pieces available. Computer disks with copies of both written material and the STELLA models are included to ease modification.

This glucose lesson plan will ideally be combined with a complete endocrine system curriculum using systems concepts. Supplementary materials to be used in teaching the endocrine system will soon be available at the Creative Learning Exchange.

However this particular lesson plan is taught, the following teaching constructs should be adhered to:

Learner-Directed Learning:

- Allow the student to take charge of his own learning.

When in control of his own learning, the student becomes more interested in the knowledge that he is accumulating. The student is able to learn what he feels is important rather than what the teacher says is important.

Systems Thinking:

- To emphasize the relationship between the structure and the behavior of systems.
- To provide an alternative method of modelling our complex world.

TO TEACH THE FOLLOWING SCIENTIFIC CONCEPTS:

Homeostasis: Blood Glucose Regulation

- Illustrate the structure of a homeostatic system by modeling the negative feedback between blood glucose level and insulin secretion in the human body.

Interruption of Homeostasis: The Diabetic

- Help the student understand the structural deficiencies present within the feedback mechanism of the diabetic and the modern techniques (insulin injection and insulin pumps) used to form an artificial feedback to maintain homeostasis.

TO TEACH THE FOLLOWING LIFELONG SKILLS:

Critical Thinking

- To help the student understand the structural deficiencies present within the feedback mechanism of the diabetic and the modern techniques (insulin injection and insulin pumps) used to form an artificial feedback to maintain homeostasis.

Units of Measure

- To help the student understand the structural deficiencies present within the feedback mechanism of the diabetic and the modern techniques (insulin injection and insulin pumps) used to form an artificial feedback to maintain homeostasis.

Graphical Interpretation

- To help the student understand the structural deficiencies present within the feedback mechanism of the diabetic and the modern techniques (insulin injection and insulin pumps) used to form an artificial feedback to maintain homeostasis.

Working and Learning in Groups (Teamwork and Communication Skills)

- Students should be taught that sometimes their own classmates can be their greatest educational resources.

Model Building

- For the advanced classroom, glucose regulation can provide an opportunity for students to sharpen their skills in formulating and quantifying the structural relationships that govern system behavior.

Research Skills

- To help the student understand the structural deficiencies present within the feedback mechanism of the diabetic and the modern techniques (insulin injection and insulin pumps) used to form an artificial feedback to maintain homeostasis.

Setup

Software: STELLA II
Microsoft Word
Disk w/ Glucose Regulation Models
Disk w/ Sample Exercises and Handouts in Microsoft Word

Hardware: Apple Macintosh Computer w/ One Megabyte RAM
(One for every two or three students)

Required familiarity with the Macintosh:
Students should be familiar with the use of the Macintosh interface and mouse.

Required familiarity with STELLA:
Students should understand stock and flow dynamics, as well as STELLA diagrams. They must also be able to change the values of the parameters and to place stocks and flows on the diagram window.

The model is completely built; however, the students will be asked in one of the exercises to modify the structure to model a diabetic. In one exercise, the students are asked to develop a model of an insulin pump with feedback. Although the structure is exactly like the first model, they may not realize it. For this reason, they may end up rebuilding the whole model from scratch.

HINTS

- **Students should work together at the computers in groups of two or three.**

By working in groups, students will be forced to discuss and support their understanding of the computer model and its behavior. This discussion will add to the learning experience and introduce students to the ideas and methods of their fellow classmates. Our experience is that students' interaction is more effective than teacher lectures.

- **The computers should be arranged so that two or three students can easily fit in front of each monitor.**

This may require some planning. It may require setting up the chairs in advance so that everyone is close to the computer (some students will not take the initiative to move themselves). It might also include turning on only every other computer so that there is plenty of space. It may also include finding some out of the way place for students to store their bags and coats.

- **Devise a system to assure that each student gets a chance to be in control of the computer keyboard and mouse.**

It is too easy, in a learner-directed situation, to have one student seize control of the computer keyboard the entire time. Although the other students see everything that is going on, they might not be able to manipulate the keyboard and mouse unless they get practice first.

- **Make sure students learn how to get to the computer laboratory.**

Several minutes will be lost if the students meet in the regular classroom and walk together over to the computer laboratory. It would be best, if the students could meet directly in the computer laboratory on days that they will be using computers.

- **Do not lecture to the students while they are in front of a computer that is turned on.**

The students will pay attention to the computer rather than the person lecturing them. This is especially true if the computer has a screensaver. The students will continually push the computer keyboard to keep the screensaver from coming on.

Description of LDL Activities

The following learner-directed learning activities could be added to the material that is described in these packets. These activities could take the form of students performing interviews and reporting to the class or of inviting a speaker to come into class and answer students' questions.

Discussion with Doctor about Diabetes

Students may ask a doctor about the causes and the temporary cures that are in use to control diabetes. A look at the various methods of artificial glucose control would be beneficial. The students should learn everything that they can about what a diabetic must go through to control their blood sugar level. They can also learn the symptoms to look for, the effects that the disease has, and current research that is going on to help diabetics. Try to find a doctor or hospital with laboratory facilities. It is best if students can do something hands on or at least see it being done.

Discussion with Diabetic

It might be interesting to have a diabetic come into the school to talk to the students. If possible, two people - one with juvenile diabetes and the other with adult-onset diabetes - could come in. You may even be able to find someone using the different forms of temporary cures (insulin injection, pumps, etc.). They could explain what they go through on a daily basis to maintain a healthy glucose level.

At the conclusion of the lesson plan, time could be set aside for students to build any of the more complicated models that the students were unable to do in class time. If class time is not available, some students should be encouraged to work on individual projects after class or during free periods.

Model Extensions

Students should discuss the model boundaries, simplifications, and assumptions. The students should be asked to reread the section in the biology book or a supplementary packet of information to determine the structural changes needed to eliminate simplifications. For example, if students used model #2 in class, they should read about the second feedback loop that affects glucose regulation. If they used model #3 in class, the students should read about the fact that insulin undergoes an activation delay.

Students should be asked how they think making these changes would effect the behavior of the model. Then, they may also be asked to determine how the model could be modified to expand the model's boundaries to include these complexities. When they have completed the new model, they should write a report comparing the output of the more complicated model to the one originally used in class. The goal for them will be to determine the relationship between the structural changes and the resulting behavior.

Potential Schedule for Implementation

This schedule was designed for a class which has minimal experience with system dynamics and STELLA. Determine the level at which your class is working and modify this schedule to best utilize class time. For example, advanced students could simply be given a reading assignment, homework exercises, computer exercises, a report to write, and free time to work on the project.

Homework: Read in textbook about homeostasis, hormones, insulin, Beta cells, the Islets of Langerhans, the pancreas, and other structures relevant to glucose regulation.

Day 1

Lecture Day #1: Review of causal loops, explanation of homeostasis, introduction to hormones, insulin, and glucose.

Homework #1: Self-discovery of the difference between homeostatic and non-homeostatic loops.

Day 2

Lecture Day #2: Review of stocks and flows, introduce glucose/insulin feedback structure.

Homework #2: Stocks and flows, questions about glucose regulation.

Day 3

Lecture Day #3: Classroom explanation of the model or joint model building effort.

Homework #3: Finish reading about homeostasis and glucose regulation.

Day 4

LDL Activity [1]: Computer Exercise #1.

Homework #4: Option #1: Guided worksheet to come up with questions for speaker on day 5.
Option #2: Read in textbook about diabetes.

Day 5

LDL Activity: Option #1: Diabetics or a doctor comes in to talk and answer questions about diabetes.

Option #2: Class discussion and lecture on diabetes.

Homework #5: Read in book about diabetes.

Day 6

LDL Activity: Computer Exercise #2.

Day 7

Optional: Students modify model to expand model boundaries.

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[1] LDL = Learner-directed Learning

Glucose Regulation Description

The goal of the body's blood glucose regulatory system is to maintain a healthy concentration of blood glucose. The body achieves its goal by secreting insulin from the Beta cells of the Islets of Langerhans in the Pancreas. The secreted insulin maintains the proper level of glucose by fixing itself on various cell receptor sites thereby changing the rate at which the glucose flows into or out of the bloodstream.

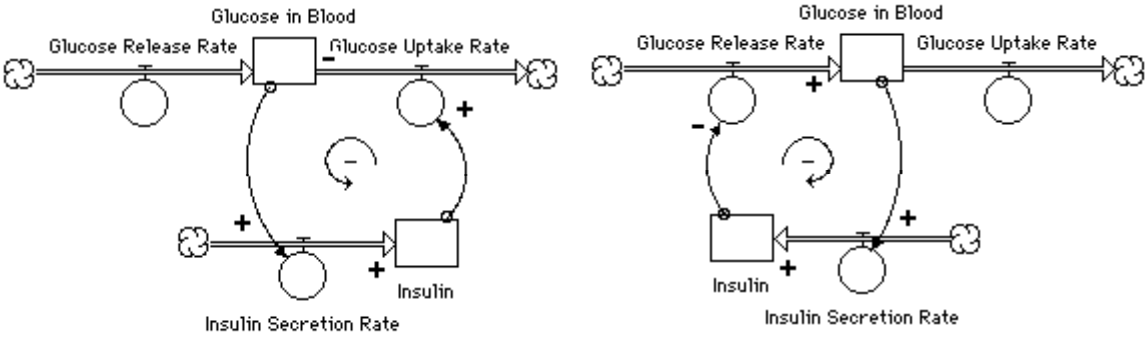
If the glucose concentration in the blood is higher than its desired level, the body tells the Beta cells to secrete extra insulin. This extra insulin elicits two responses from the body:

1) a decrease in the glucose release rate into the blood which is determined by both the rate of glucose digestion and the rate of conversion of glycogen to glucose by the liver, and
2) an increase in the permeability to glucose of the body's cells causing an increase in the glucose uptake rate due to:
    a) diffusion of glucose from the bloodstream to the body's cells to be used as energy,
    b) conversion of glucose to fat, and
    c) conversion of excess glucose to glycogen by the liver and muscles.

The combination of a decreased inflow to the stock of blood glucose and an increased outflow of blood glucose serves to decrease the blood glucose concentration until it reaches the desired level. The body is not able to respond instantaneously to imbalances in the glucose concentration; however, the two negative (homeostatic) feedback loops allow the body to reach homeostasis if given enough time.

The main feedback loops in the system can be seen in Figure 1. Both of the feedback loops are negative. This means that an original increase in the amount of glucose in the blood will cause events in the rest of the system that will feedback to return the level of glucose to its desired level, or goal. This can be explained as goal-seeking or homeostatic behavior.

Figure 1: Negative Feedback Loops in the Glucose Regulatory System of the Human Body.



If **glucose in the blood** increases, the **insulin secretion rate** by the Beta cells will increase causing an increase in the amount of **insulin.** The increase in the amount of **insulin** causes two events:

1) a decrease in the **glucose release rate** which decreases the amount of **glucose in the blood (left diagram)**, and
2) an increase in the **glucose uptake rate**, which decreases the amount of **glucose in the blood. (Right diagram)**

Teaching Notes

A Systems Approach to the Glucose Regulation System

The following teaching notes were developed for use with students who have a minimal familiarity with the computer program STELLA. It is up to the teacher's discretion to determine the necessity of going through the following material.

The teacher should also note that the teaching notes combine material to explain four different models. Teachers who are choosing to use a more simplified model should use discretion in explaining the more complex ideas of the other models. The teacher may wish to simply explain the assumptions that were made and what effect these have on the behavior of the model, or the teacher may choose to withhold this information and ask the students to determine it as described in one of the learner-directed activities.

PLEASE NOTE THAT ANY MATERIAL CONTAINED IN A BOX IS FOR USE ONLY IF THE TEACHER CHOOSES TO USE MODEL #3 OR #4. IF YOU ARE TEACHING WITH MODEL #1 OR #2, PLEASE IGNORE THE BOXED MATERIAL.

Day 1

Objectives:

A. Explanation of curriculum plan to students
B. Explanation of homeostatic feedback loops and polarity of causal connections (same or opposite
C. Explanation of human hormones
D. Description of how insulin effects glucose uptake rate

A. Explanation of Curriculum Plan:

- Explanation of the use of the computer simulation model
- Explanation of the homework assignments
- Explanation of the chosen method of evaluation
- Explanation of working together in groups

B. Examples of Homeostatic Loops:

Stimuli may come from inside or outside the body. An example of an internal stimulus might be hunger pains which an individual will respond to by increasing his rate of eating. An increased eating rate eventually fills the stomach which decreases the hunger pains. Let's use this example

Causal loop diagrams are made up of what we call same and opposite connections.

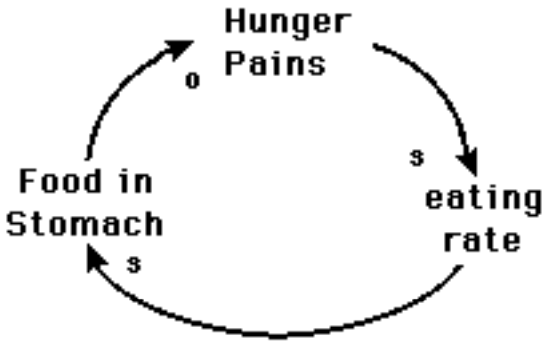
- **Explain same and opposite connections.**[1]

- If an increase in one variable causes an increase in the second, it is a positive or same connection.
- If an increase in one variable causes a decrease in the second, it is a negative or opposite connection.
- Likewise, if a decrease in one variable causes a decrease in the second, it is a same connection (or positive link).
- Also, if a decrease in one variable causes an increase in the second, it is an opposite connection (or negative).

Example #1:

If hunger goes up, eating rate goes up (same connection); as eating rate goes up, food in stomach goes up (same connection); and as food in stomach goes up, hunger pains go down (opposite connection):

(Draw the up and down arrows as you trace around the loop to explain why it is a homeostatic loop)



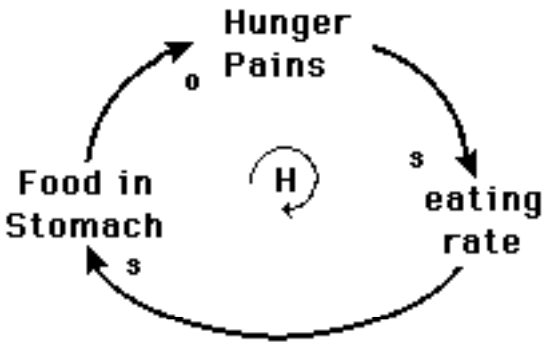
- **Explain why it is a homeostatic loop.**[2]

DO NOT EXPLAIN NON-HOMEOSTATIC LOOPS, THEY WILL FIGURE IT OUT AS HOMEWORK.

- If an original increase in one variable causes an eventual further increase in that same variable due to feedback in a causal loop, the loop is positive or non-homeostatic.
-One easy way to determine whether a loop is homeostatic is to count the number of negatives or opposites around the loop. If the number is zero or even (they cancel), then the loop is non-homeostatic or positive.

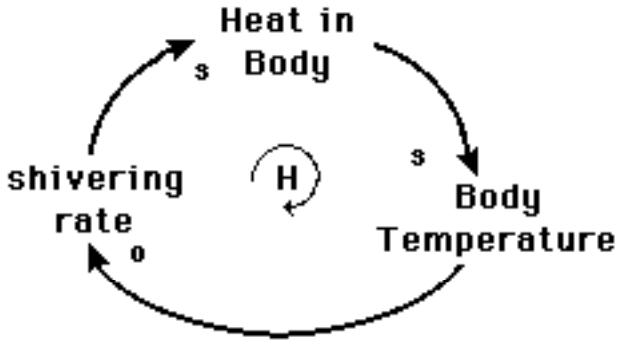
This loop we made with causal connections is a homeostatic loop because what started out as an increase in hunger pains ultimately resulted in a decrease of hunger pains. It is also easily identified as a homeostatic loop because there is an odd number (1) of opposite connections. Let's identify this as a homeostatic loop, by placing a symbol within the causal loop diagram, as shown below.

[1] In causal loop diagramming: same=positive link, opposite = negative link.
[2] A homeostatic loop (or Homey Loop) was the term used to describe a negative feedback loop.



Now that we know how to construct causal connections and homeostatic loops, let's try another example.

Example #2:
If there is a sudden drop in temperature, the body responds by increasing its shivering rate (opposite connection). Since shivering is nothing more than involuntary work by the muscles, shivering increases the heat in the body (same connection) and causes the temperature to rise (same connection):
(Draw the up and down arrows as you trace around the loop to explain why it is a homeostatic loop)



This is also a homeostatic loop because what started out as a body temperature drop ultimately led to an increase in body temperature. Note also, that there is an odd number (1) of opposite connections in this loop.

C. The Endocrine System and Hormones:

The body can respond to external and internal stimuli either chemically or with nervous action. The body's chemical control and self regulation are accomplished through the **endocrine system** which is the topic of this chapter.

The endocrine system is made up of many different **endocrine glands** which secrete substances called **hormones** directly into the blood. Hormones are complex proteins and polypeptides, which are responsible for chemical control within the body.

Today, we are going to look at the hormone called insulin.

D. Insulin's Affect on Glucose:

Glucose in the blood needs to be controlled to maintain it at a healthy level.

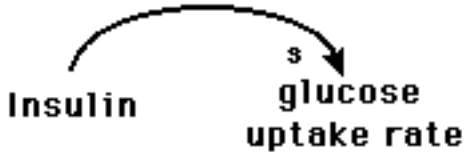
Too much glucose:
- diabetes mellitus
- so much glucose that some leaves through urine
- sufferers are always thirsty and have to urinate frequently

Too little glucose:
- cells starve
- people die

Glucose is regulated by the hormone insulin. Insulin is made by the Beta cells in the Islets of Langerhans of the pancreas.

Insulin causes:
a) conversion of excess glucose to glycogen by liver and muscles.
b) an increase in cell membrane permeability.
c) conversion of glucose to fat.

Notice that the three functions of insulin all contribute to the removal of glucose from the blood stream. In other words, Insulin affects the Glucose Uptake Rate into the cells.



Question -> Is this a "same" or "opposite" relationship?

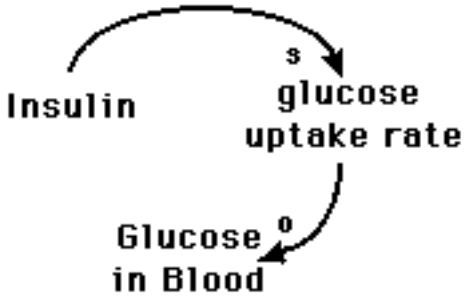
Answer -> Same.

These boxed teacher notes are for Models #3 and #4 only.

Insulin ALSO causes:
a decrease in the conversion of glycogen to glucose by the liver

Question -> Is this a "same" or "opposite" relationship?
Answer -> Opposite.

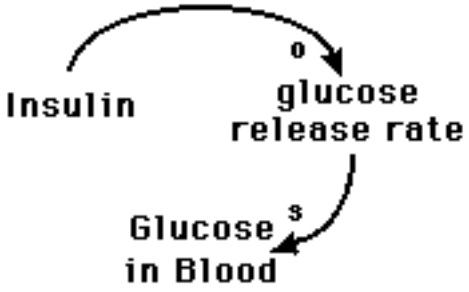
Question -> What does an increase in the glucose uptake rate by the body cells do to the stock of glucose in blood?
Answer -> It causes a decrease in the stock of glucose in blood, because more glucose is flowing out.



Question -> Is this a "same" or "opposite" relationship?
Answer -> Opposite.

These boxed teacher notes are for Models #3 and #4 only.

Question -> What does an decrease in the glucose release rate do to the stock of glucose in blood?
Answer -> It causes a decrease in the stock of glucose in blood, because less glucose is flowing in.



Question -> Is this a "same" or "opposite" relationship?
Answer -> Same.

Summary:

- A same causal connection is one in which a change in one variable causes a change in the same direction in another variable.
- An opposite causal connection is one in which a change in one variable causes a change in the opposite direction in another variable.
- A homeostatic loop is one that maintains a healthy equilibrium level of the stocks in the system.
- In every case, the insulin causes changes that decrease the amount of glucose in the blood.

Homework:

- Homework #1.

Day 2

Objectives:

A. Review stocks as accumulations.
B. Review flow as the rate of change of stock over time.
C. Connecting inflows and outflows to produce homeostasis.
D. Introduce glucose and insulin feedback structure.

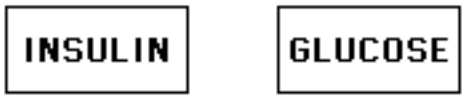
A. Stocks:

A **STOCK** is a generic symbol for anything that accumulates. For example, water accumulates in your bathtub. At any moment, the amount of water in the bathtub reflects the accumulation of what has flowed in from the faucet minus what has flowed out down the drain. The amount of water in the bathtub is the stock of water.

Stocks are represented by rectangles.

Question -> If we were modeling the glucose regulatory system, what would be the stocks?

Answer -> Insulin and Glucose:



B. Flows:

Question -> Can I fill a bathtub in one minute by using a squirt gun?

Answer -> NO.

Question -> Can I fill a bathtub in one minute with a fire hose?

Answer -> Depends on how big the bathtub is.

Question -> True, but which one do you think will fill up the tub faster?

Answer -> The fire hose.

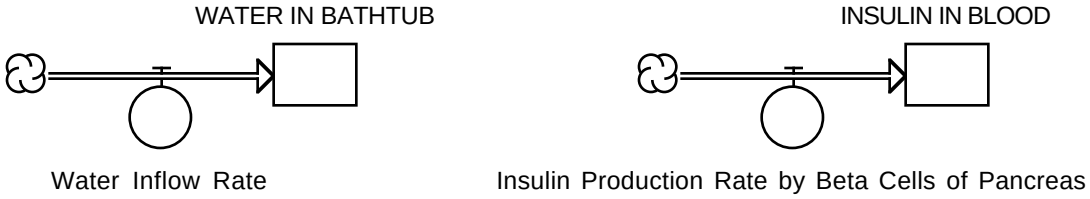
Both the squirt gun and the fire hose are flows into a bathtub stock. However, the flows are different because one fills up a stock faster than another. The concept of time is very important when describing a flow because the definition of a **FLOW** is the change of a stock over time.

Question -> What affects the stock of **INSULIN** in the blood?
Answer -> Insulin secretion rate by the Beta cells of the Islets of Langerhans in the Pancreas. The pancreas controls the **flow** of insulin into the blood just like a faucet controls the flow of water into a bathtub.

Another word for flow is **rate**. Whenever, we talk about flow, it is always described as a certain amount of the stock per time.

Question -> If **INSULIN** is measured in units of milligrams, what are its flows measured in?
Answer -> flows = milligrams / time unit (let's use minutes as time units)

Stocks are depicted graphically as rectangles. Since flows are the only things that can change stocks, they are depicted as pipes either leading into or out of a stock. For example, we have water in a tub and insulin in the blood:



PLEASE PUT UP TRANSPARENCY #1: Inflow Example

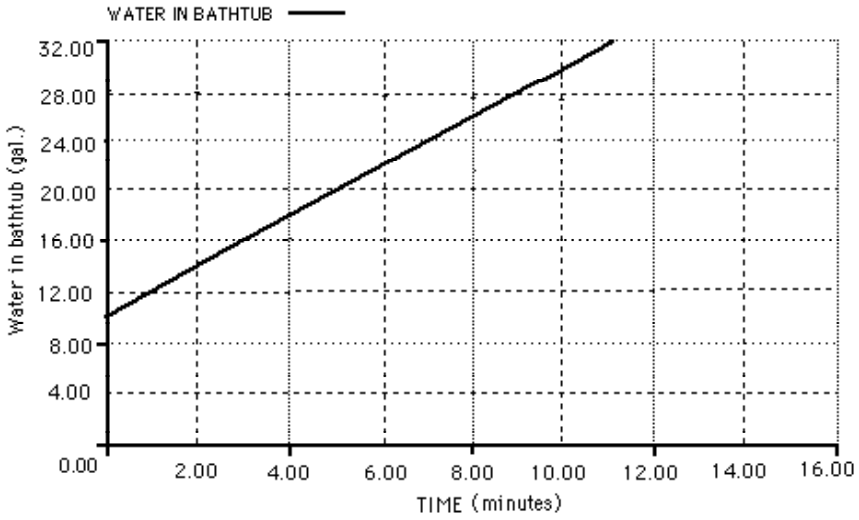
Let's apply our knowledge of stocks and flows to a few problems. Let's say that we start with a bathtub stock of 10 gallons of water. We then turn on a faucet with a flow of 2 gallons per minute.

With the students, graph the system's behavior over time on the transparency:

Question-> After one minute, how much water will be in the stock?
Answer - > 12 gallons.

Question-> After three minutes, how much water will be in the stock?
Answer - > 16 gallons.

Water in bathtub over time



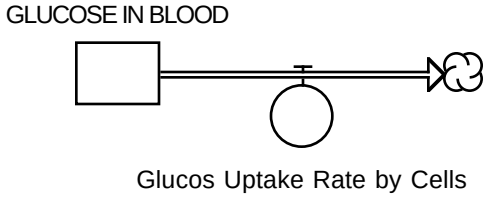
This graph is called linear (comes from the word line). A constant flow produced a linear or steady change in the stock of water over time.

The same graph would be produced for a stock of insulin in the blood that is increased by a constant flow from the pancreas.

Outflow Example:

Just as we can have inflows to stocks, it is possible to have outflows from stocks. In a bathtub, one outflow would be water flowing down the drain. In the case of glucose in the bloodstream, an outflow might be glucose taken up into the cells or the liver.

DRAW THIS ON THE CHALKBOARD.

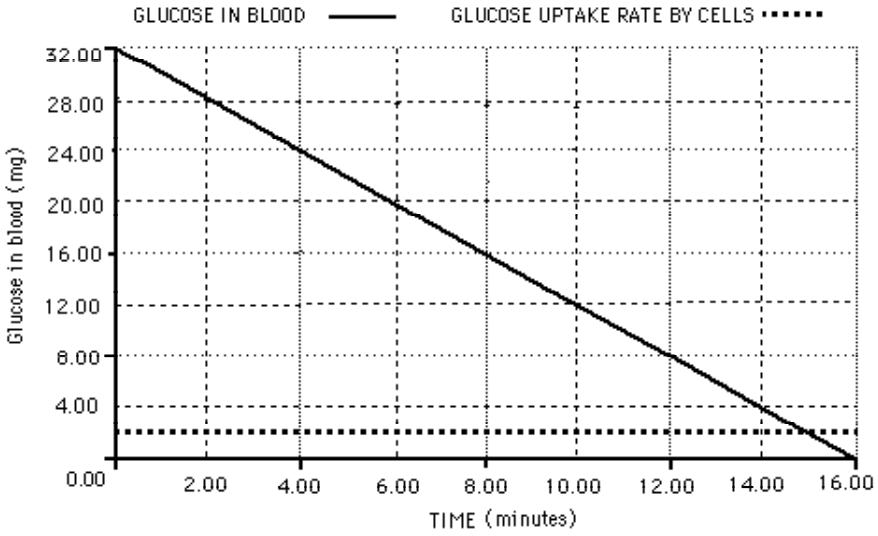


Begin with a stock of Glucose in Blood = 32 milligrams
and a Glucose Uptake Rate = 2 mg/min

PLEASE PUT UP TRANSPARENCY #1: Outflow Example

With the students, graph the system's behavior over time on the transparency:

Glucose in blood over time



C. Connecting Inflows and Outflows to Produce Homeostasis:

Finally, it is possible to connect both an inflow and outflow to the same stock. In fact, every stock has both an inflow and an outflow. Inflows only allow a stock to increase and outflows only allow a stock to decrease. Giving a stock both allows it to increase and to decrease over time.

Let's continue thinking about the glucose in the blood. We said that an example of an outflow from the stock of blood glucose is the glucose uptake rate by the cells.

Question -> What is an example of an inflow into the stock of glucose in the blood?

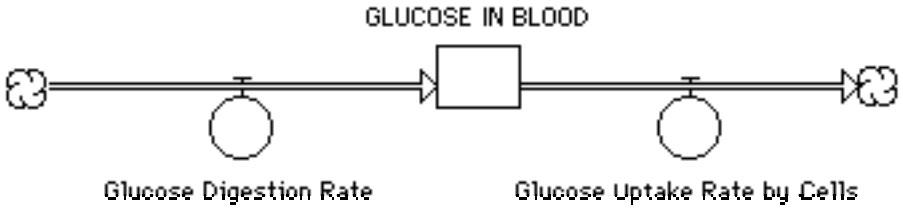
Answer -> digestion or release rate

Question -> If the stock of glucose in the blood is measured in milligrams, what is the inflow measured in?

Answer -> mg/minute

DRAW THIS UP ON THE CHALKBOARD.

Here is how we represent a stock with an inflow and an outflow:



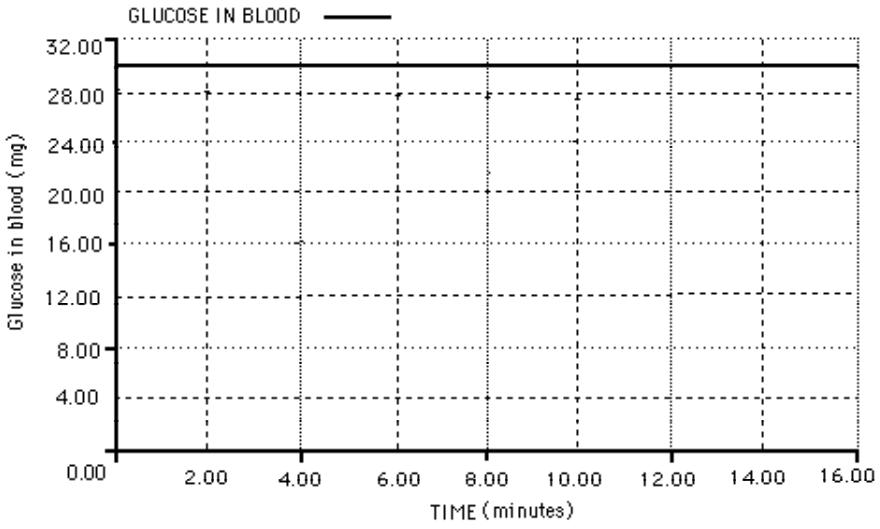
Assume this structure, begin with the following values, and answer the following questions:

Glucose in the Blood = 30 mg
Glucose Release Rate into Blood = 5 mg/min
Glucose Uptake Rate by Cells = 5 mg/min

TRANSPARENCY #2:

Question -> What would a graph of the stock of glucose in the blood look like over time?

Answer -> **Glucose in blood over time**



Notice that the outflow is exactly equal to the inflow of the stock of blood glucose. This produces a stock that is constant throughout time.

This is one of the keys to **homeostasis**. The body wants to keep everything in balance. In the case of glucose in the blood, the body tries to match cell uptake with the release of glucose into the bloodstream so that the stock of glucose in the blood changes as little as possible over time.

D. Glucose and Insulin Feedback Structure:

Yesterday, we mentioned that the stock of glucose in the blood is regulated by the hormone insulin. Insulin controls both the rates of inflow of glucose into the blood and the rate of outflow of glucose from the blood.

Insulin:

For Models #1, 2, 3, and 4:

1) increases the glucose uptake rate by the cells.

For Models #3 & #4 Only:

2) decreases the glucose release rate into the bloodstream.

Question -> What controls the amount of insulin secreted into the bloodstream? How does this mechanism know how much insulin to secrete into the blood?

Answer -> Islets of Langerhans know when to secrete insulin into the blood by constantly sensing the stock of glucose in the blood through the bodies feedback mechanisms. If there is too much glucose, the islet cells will produce more insulin, and if there is too little glucose, the islet cells will decrease the flow of insulin into the stock of insulin in the blood.

Question -> What would the causal connections between Glucose in the Blood and Insulin look like? Let's add them to the structures we have already built.

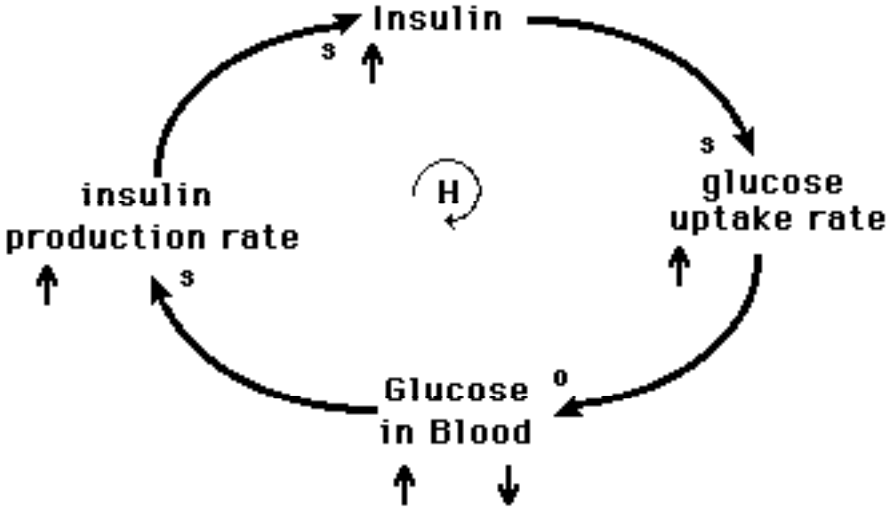
Answer -> Use transparency #3 to go through the loop. First draw the connections. Then starting with an increase (up arrow) at Glucose in Blood, trace the effect around the loop using up and down arrows. As you go label each connection as either same or opposite.

TRANSPARENCY #3:

There is a certain range of healthy amounts of glucose in the blood. If the body starts out with too much (↑) **Glucose in Blood**, the **insulin production rate** will increase (same connection). This increase will cause the stock of **Insulin** to increase (same connection). The increase in **Insulin** causes the permeability of the cell membranes to increase so that the **glucose uptake rate** will increase (same connection). The increased **glucose uptake rate** causes a decrease in the stock of **Glucose in Blood** (opposite connection).

An initial increase in the level of **Glucose in Blood** eventually leads to a decrease in **Glucose in the Blood** to maintain homeostasis.

Feedback Loop #1:



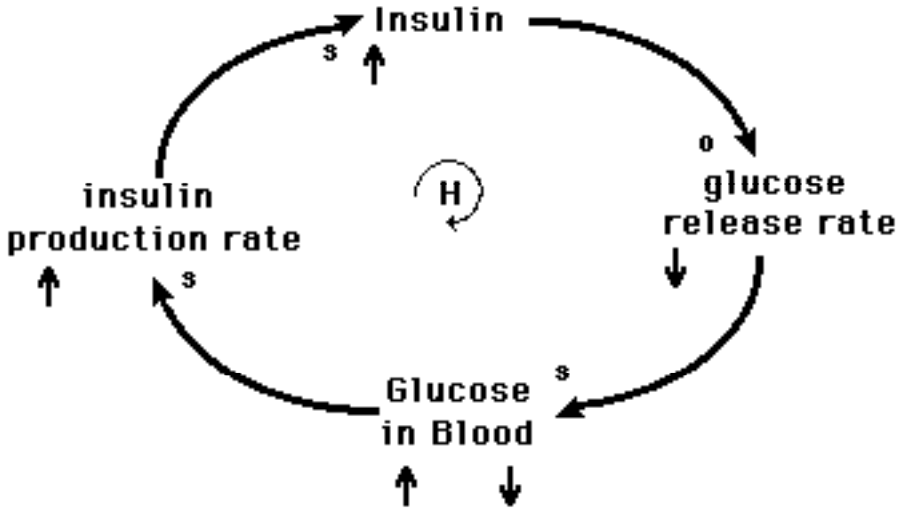
TRANSPARENCY #3:

These boxed teacher notes are for Models #3 and #4 only.

There is a certain range of healthy amounts of glucose in the blood. If the body starts out with too much **Glucose in Blood**, the **insulin production rate** will increase (same connection). This increase will cause the stock of **Insulin** to increase (same connection). The increase in **Insulin** causes a decrease in the **glucose release rate** (opposite connection). The decreased **glucose uptake rate** causes a decrease in the stock of **Glucose in Blood** (same connection).

An initial increase in the level of **Glucose in Blood** eventually led to a decrease in **Glucose in the Blood** to maintain homeostasis.

Feedback Loop #2:

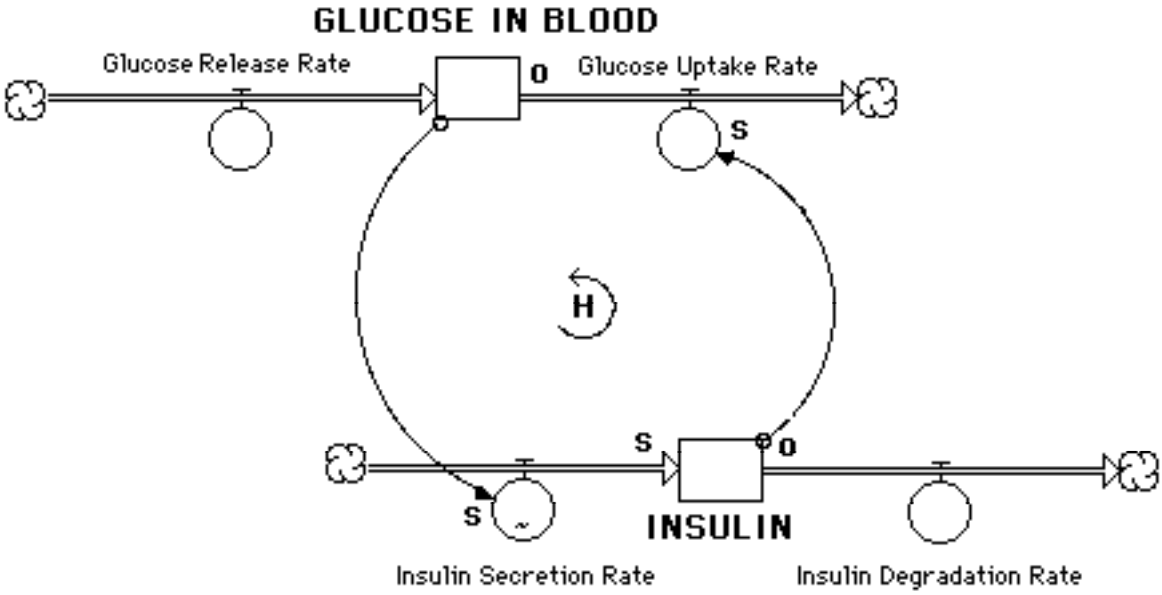


Two different homeostatic loops in the same system are both helping to maintain the stock of glucose in the blood at its healthy level.

TRANSPARENCY #4:

Relate this stock and flow diagram to feedback loop #1 presented in transparency #3.

Feedback Loop #1:



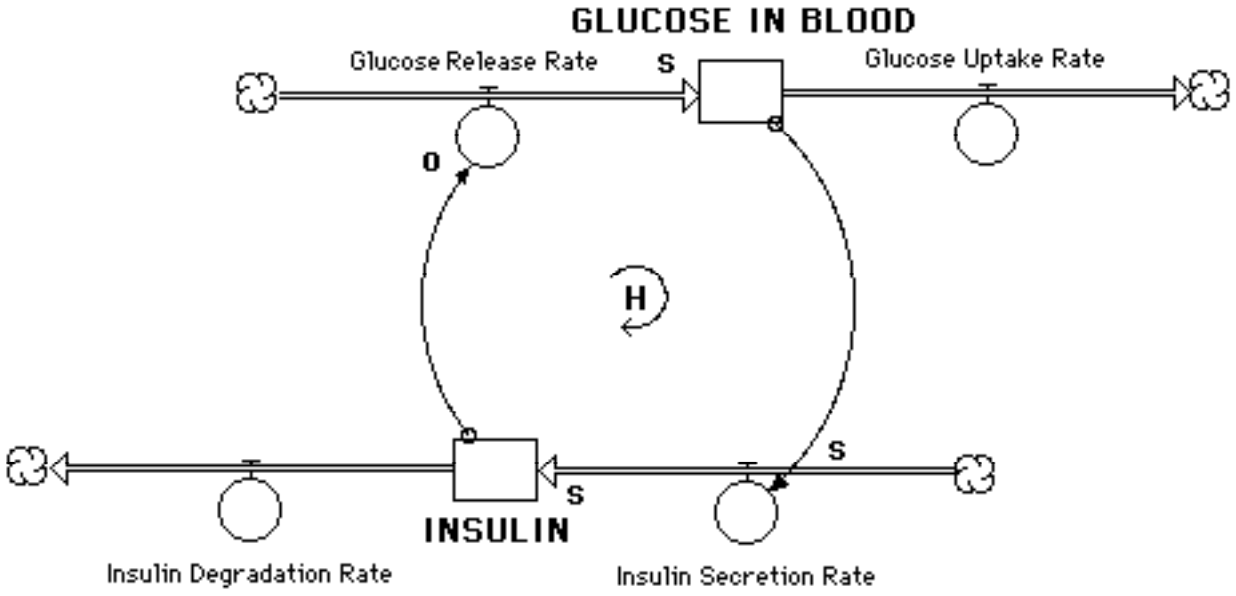
Glucose and insulin operate in the body to produce equilibrium, unchanging levels in the stocks, through a homeostatic feedback process. If a person eats a large meal, thereby increasing the **Glucose Digestion Rate**, the stock of **GLUCOSE IN THE BLOOD** rises. As the **GLUCOSE IN THE BLOOD** increases, the beta cells in the Islets of Langerhans of the pancreas respond by increasing the **Insulin Secretion Rate**. As the **Insulin Secretion Rate** increases, the stock of **INSULIN** in the bloodstream also increases. Insulin acts to both increase cell membrane permeability and cause the liver and muscles to convert glucose in the blood to glycogen. These processes remove glucose from the bloodstream. Thus, as the **INSULIN** stock increases, it acts to increase the **Glucose Uptake Rate** by cells. A greater **Glucose Uptake Rate** acts to decrease the stock of **GLUCOSE IN BLOOD**. What begins as an increase in the stock of **GLUCOSE IN BLOOD** eventually results in a decrease of the **GLUCOSE IN BLOOD** back to its equilibrium value. This process combined with thousands of others contribute to the homeostasis within your body.

TRANSPARENCY #4:

These boxed teacher notes are for Models #3 and #4 only.

Relate this stock and flow diagram to feedback loop #2 presented in transparency #3.

Feedback Loop #2:

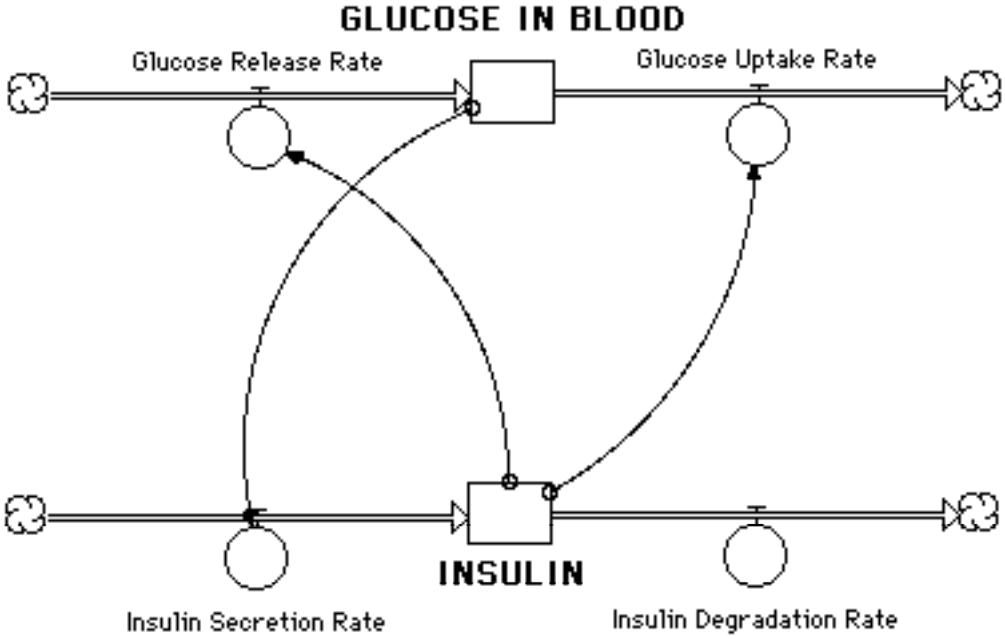


Glucose and insulin operate in the body to produce equilibrium, unchanging levels in the stocks, through a homeostatic feedback process. If a person eats a large meal, thereby increasing the **Glucose Digestion Rate**, the stock of **GLUCOSE IN THE BLOOD** rises. As the **GLUCOSE IN THE BLOOD** increases, the beta cells in the Islets of Langerhans of the pancreas respond by increasing the **Insulin Secretion Rate**. As the **Insulin Secretion Rate** increases, the stock of **INSULIN** in the bloodstream also increases. Insulin decreases the liver's rate of conversion of glycogen to glucose. Thus, as the **INSULIN** stock increases, it acts to decrease the **Glucose Release Rate**. A smaller **Glucose Release Rate** acts to decrease the stock of **GLUCOSE IN BLOOD**. What begins as an increase in the stock of **GLUCOSE IN BLOOD** eventually results in a decrease of the **GLUCOSE IN BLOOD** back to its equilibrium value. This process combined with thousands of others contribute to the homeostasis within your body.

TRANSPARENCY #5:

These boxed teacher notes are for Models #3 and #4 only.

Explain how this stock and flow diagram results from combining the previous two stock and flow diagrams. Trace out the two feedback loops in this diagram.



Feedback Loop #1:

- **Glucose INCREASE eventually causes Insulin INCREASE.**
- **Insulin INCREASE causes Glucose Uptake Rate to INCREASE.**
- **Glucose Uptake Rate INCREASE causes Glucose to DECREASE.**

Feedback Loop #2:

- **Glucose INCREASE eventually causes Insulin INCREASE.**
- **Insulin INCREASE causes Glucose Release Rate to DECREASE.**
- **Glucose Release Rate DECREASE causes Glucose to DECREASE.**

Summary:

- **Glucose in Blood** and **Insulin** are the two stocks in the body's glucose regulatory system.
- The flows of the stock of Glucose in the Blood are **Glucose Release Rate** and **Glucose Uptake Rate** by body cells.
- The flows of the stock of Insulin are **Insulin Secretion Rate** by the Beta cells of the Pancreas and the **Insulin Degradation Rate**.

Homework:

- Homework #2.

Day 3

Things to Accomplish:

A. Review of Day 2.
B. Explain the two smaller feedback loops associated with the outflows.
C. Present more formal STELLA model explanation.
D. Explain the table functions present in the model.

A. Day 2 Review:

Show class transparency #4 and explain again.

B. Two More Negative Feedback Loops:

Show transparency #5 to build up the complete model.

In a stock of population, the death rate or outflow is dependent upon the number of people in the population. If there are more people, more people are going to die. If there are fewer people, fewer people are going to die. *Show example stock and flow diagram.*

In the glucose regulation model, both of the stocks exhibit this same behavior.

Glucose:
If there is more glucose, the probability of the glucose diffusing into the cells is greater given some constant cell membrane permeability. Because of this greater probability, more glucose will be uptaken by the cells. Because this is true, the glucose uptake rate is dependent upon the amount of glucose in the blood.

Question -> What happens if there are fewer glucose molecules in the blood?
Answer -> The probability that they will go through the cell membrane decreases causing the glucose uptake rate to decrease.

In this case, the glucose uptake rate is a function of the stock of glucose. In other words, in STELLA, the information about the stock of glucose must be connected to the flow of glucose into the blood. In STELLA this is done with a **connecter**. It looks like this:

Add arrows.
Insert Picture as example.

Insulin:
If there is more insulin, more of it will degrade in each period of time. This is exactly analogous to the population and death rate. Consider degradation as being the same as dying. In other words, if the stock of insulin is high, the degradation rate will be high.

Question -> What happens to the amount of insulin if the degradation rate increases?

Answer -> It decreases.

In this case, the insulin degradation rate is a function of the amount of insulin. In STELLA, the information about the stock of insulin must be connected to the flow of insulin out of the blood.

Question -> In STELLA, how would we pass the information about the stock of insulin to the degradation rate?

Answer -> With a connector drawn from the amount of insulin to the degradation rate.

Add arrows.

Insert Picture as example.

Exercise to graph behavior.

C. Present more formal STELLA model explanation:

Show transparency #5 to build up the complete model.

Explain insulin degradation time constant and plug it in

Now explain what insulin secretion rate is dependent upon:

answer: glucose surplus

What is glucose surplus?

that it meqans more than a regular amount. Let's call the regular amount the healthy level. Insert healthy level into model and explain how it is derived.

Build in this feature

Explain need for uptake fraction converter. Then go in and explain what it is in the next section.

Show equations all the way through.

D. Explain the table functions present in the model.

Now explain table functions for

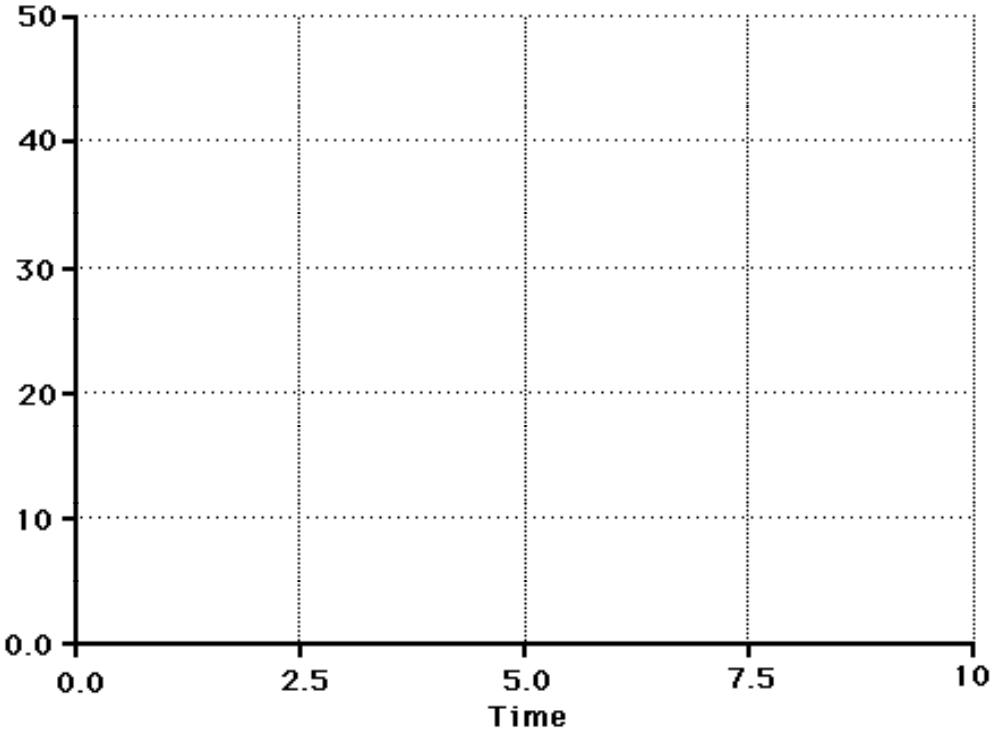
secretion rate transparency #8

uptake fraction transparency #9

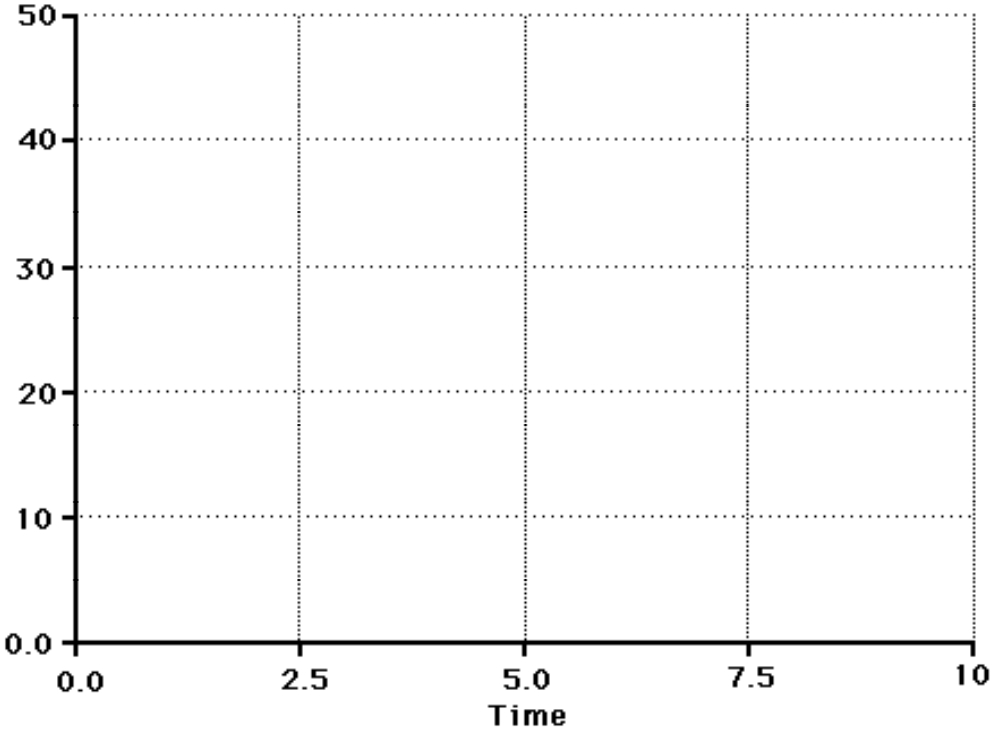
Now show on overhead the whole model we just built. Transparency #10.

TRANSPARENCY #1:

Stock from Inflow Example:

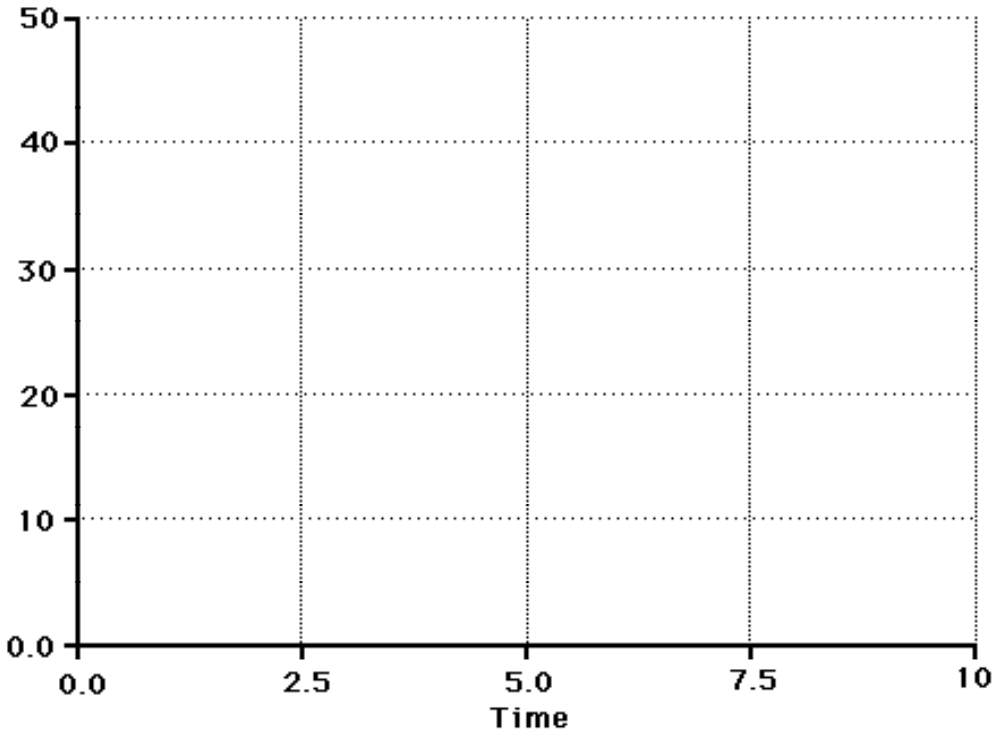


Stock from Outflow Example:



TRANSPARENCY #2:

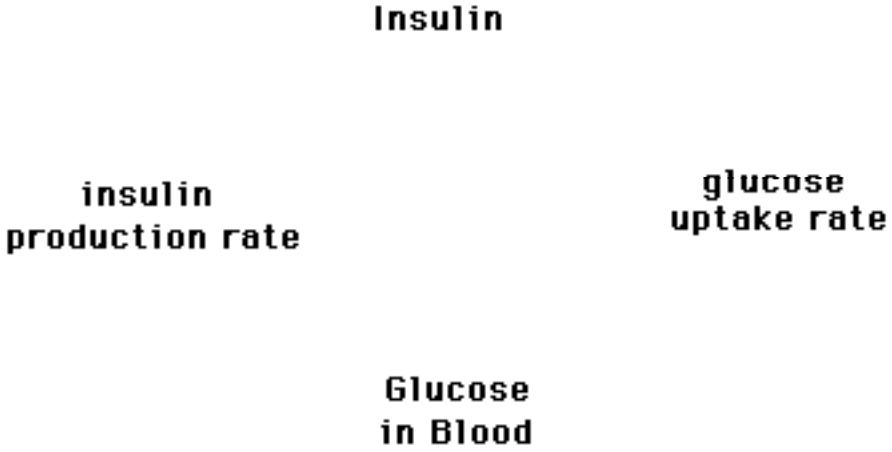
Stock from Homeostatic Example:



TRANSPARENCY #3: FOR MODELS #1 AND #2.

Insulin and Glucose Feedback Loops

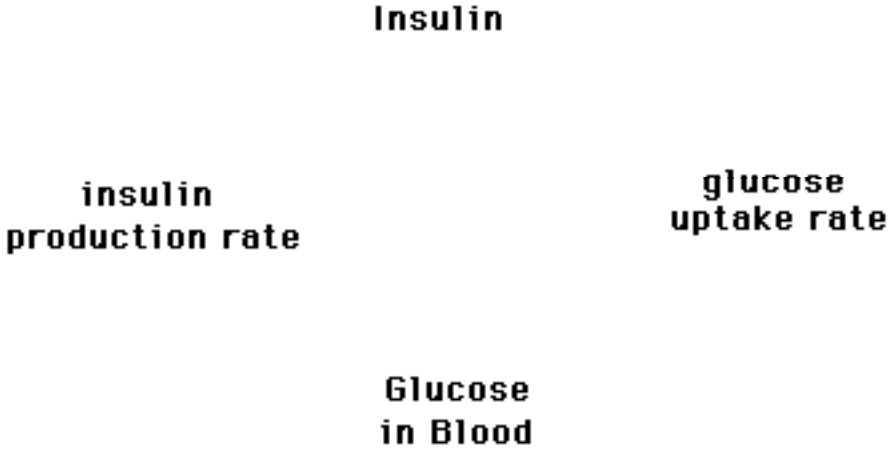
Feedback Loop #1



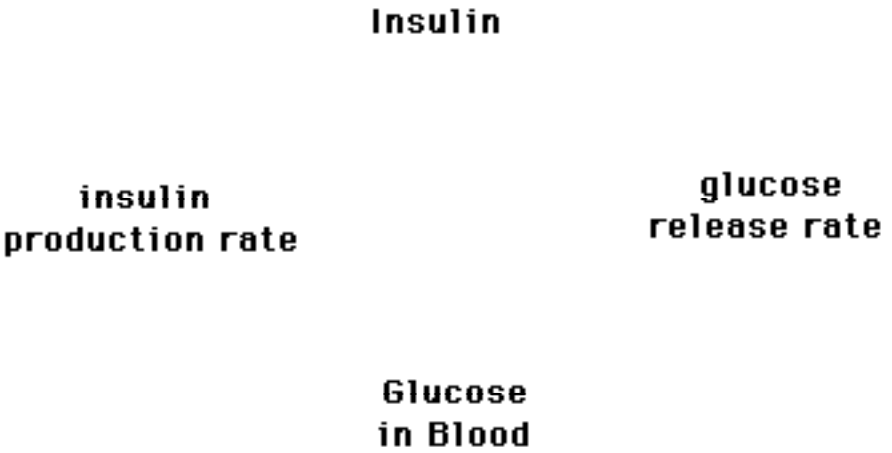
TRANSPARENCY #3: FOR MODELS #3 AND #4.

Insulin and Glucose Feedback Loops

Feedback Loop #1

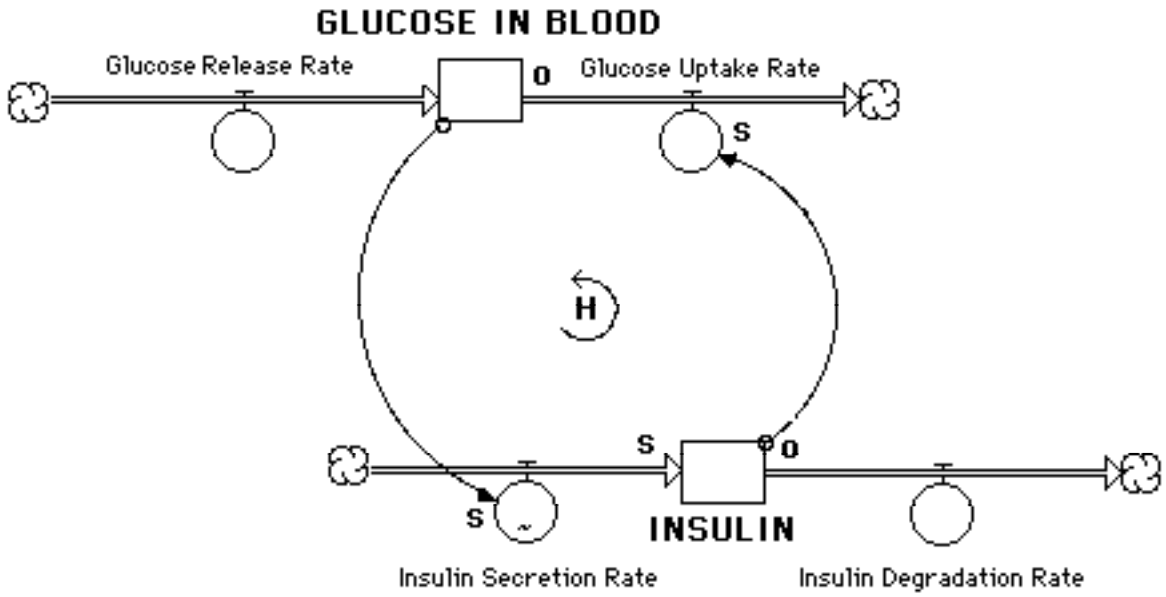


Feedback Loop #2



<u>TRANSPARENCY #4:</u> FOR MODELS #1, 2, 3, AND 4.

Feedback Loop #1:

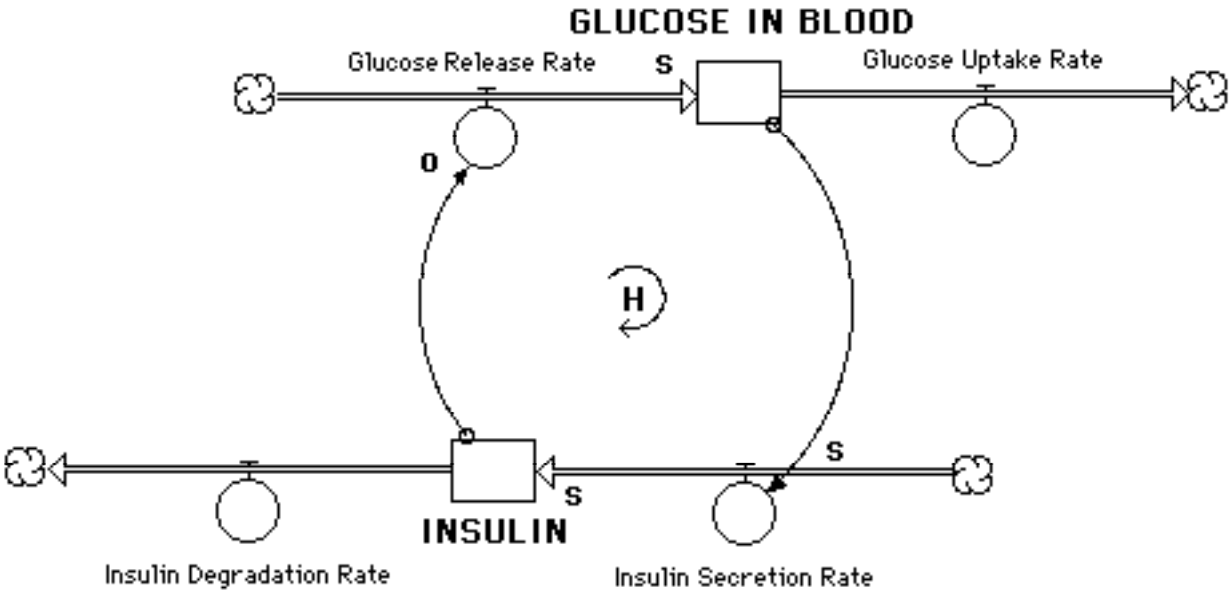


Feedback Loop #1:

- **Glucose INCREASE eventually causes Insulin INCREASE.**
- **Insulin INCREASE causes Glucose Uptake Rate to INCREASE.**
- **Glucose Uptake Rate INCREASE causes Glucose to DECREASE.**

<u>TRANSPARENCY #4B:</u> FOR MODELS #3 AND #4.

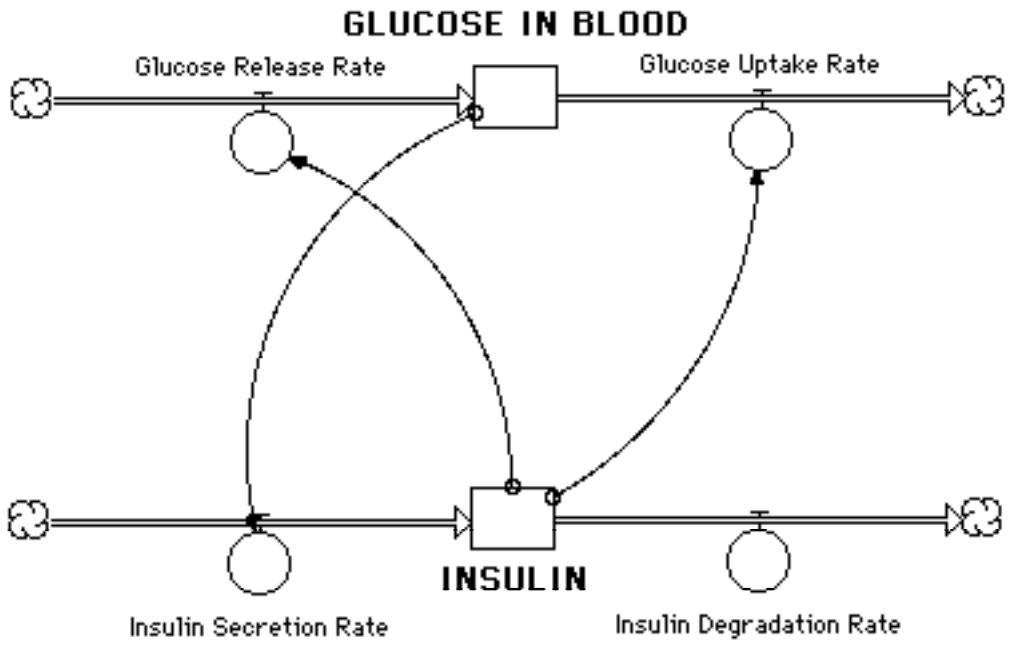
Feedback Loop #2:



Feedback Loop #2:

- **Glucose INCREASE eventually causes Insulin INCREASE.**
- **Insulin INCREASE causes Glucose Release Rate to DECREASE.**
- **Glucose Release Rate DECREASE causes Glucose to DECREASE.**

<u>TRANSPARENCY #4C:</u> FOR MODELS #3 AND #4.



Feedback Loop #1:

- **Glucose INCREASE eventually causes Insulin INCREASE.**
- **Insulin INCREASE causes Glucose Uptake Rate to INCREASE.**
- **Glucose Uptake Rate INCREASE causes Glucose to DECREASE.**

Feedback Loop #2:

- **Glucose INCREASE eventually causes Insulin INCREASE.**
- **Insulin INCREASE causes Glucose Release Rate to DECREASE.**
- **Glucose Release Rate DECREASE causes Glucose to DECREASE.**

Transparency #5:

transparency #4 without the feedback loops to be used to build up the final model before the class.

TRANSPARENCY #6:

Complete Model

Transparency #7:
Equations

TRANSPARENCY #8:
Cell uptake fraction versus Insulin Level for Models 1 and 2

Transparency #8A

Cell uptake fraction vs. insulin level for models 3 and 4

TRANSPARENCY #9:

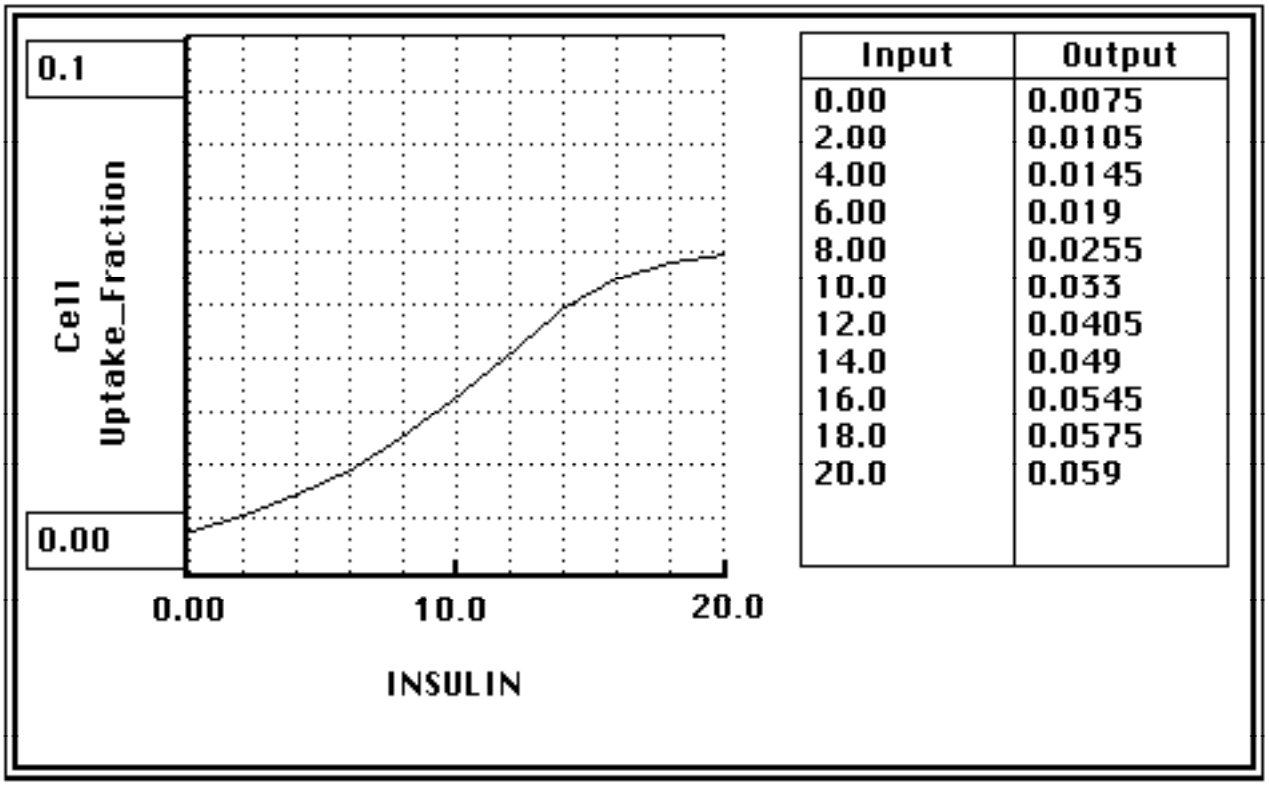
Insulin Secretion Rate versus Glucose Surplus for models 1 and 2

Transparency #9B

Insulin Secretion Rate vs. Glucose Concentration Surplus for models 3 and 4

TRANSPARENCY #8:

Cell Uptake Fraction versus Insulin Level (MODELS #1 and #2 ONLY)



Input	Output
0.00	0.0075
2.00	0.0105
4.00	0.0145
6.00	0.019
8.00	0.0255
10.0	0.033
12.0	0.0405
14.0	0.049
16.0	0.0545
18.0	0.0575
20.0	0.059

Important Points:

- **High Insulin Levels**

  Body Has Too Much Glucose In Blood
  Results in a High Glucose Uptake Rate

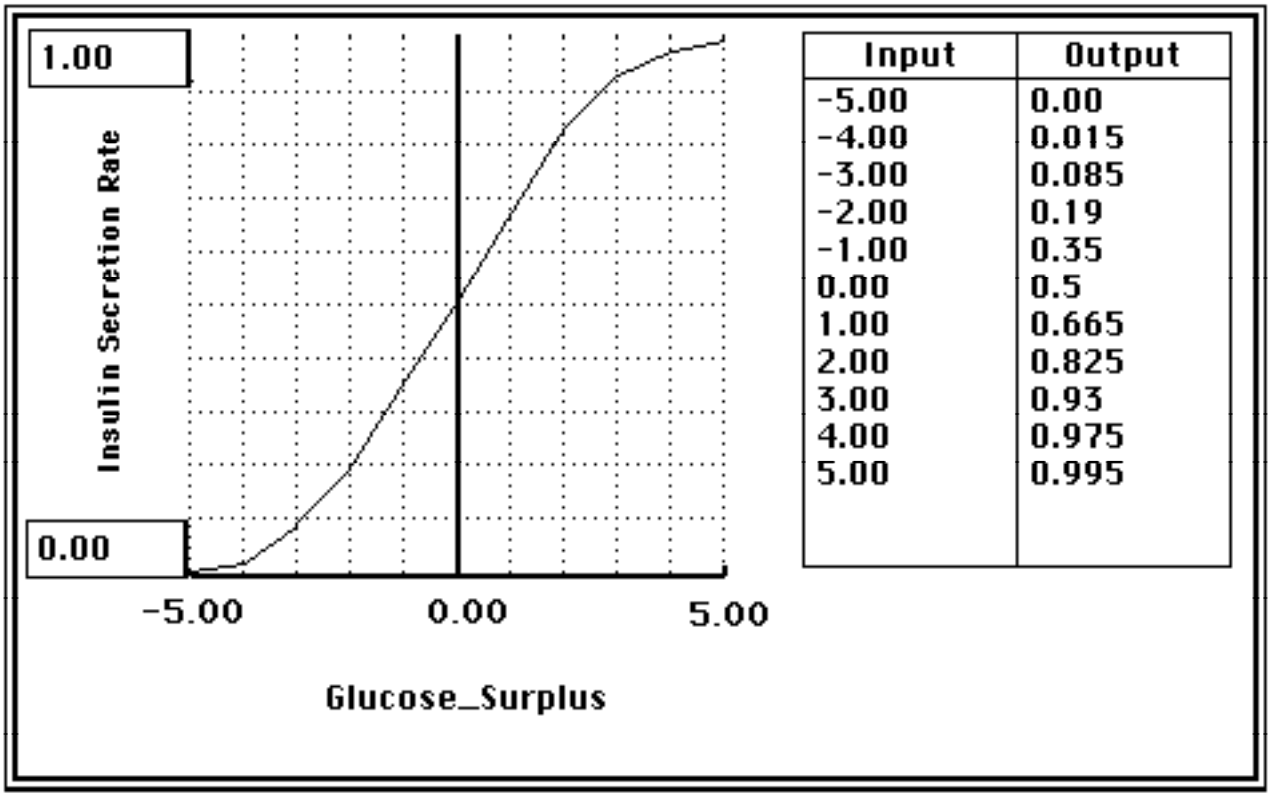
- **Low Insulin Levels**

  Body Needs More Glucose in the Blood
  Results in a Low Glucose Uptake Rate

- **Limits on Production of Insulin Result in S-shaped Growth of Cell Uptake Curve**

TRANSPARENCY #9:

Insulin Secretion Rate versus Glucose Surplus (MODELS #1 and #2 Only)



Input	Output
-5.00	0.00
-4.00	0.015
-3.00	0.085
-2.00	0.19
-1.00	0.35
0.00	0.5
1.00	0.665
2.00	0.825
3.00	0.93
4.00	0.975
5.00	0.995

Important Points:

- Positive Glucose Surplus

Body Has Too Much Glucose In Blood
Results in a High Insulin Secretion Rate

- Negative Glucose Surplus

Same as a Glucose Deficiency
Body Needs More Glucose in the Blood
Results in a Low Insulin Secretion Rate

- Zero Surplus

Point of Homeostasis
Insulin Produced Balances Insulin Degradation

The Endocrine System

Homework #1: Homeostatic vs. Non-Homeostatic Loops

Name_____ Due Date_____ Period_____

1) Draw the causal loop diagrams described by the following sentences. Label the causal connections as either *same* (s) or *opposite* (o). Label the causal loops as *homeostatic* (H) or *non-homeostatic* (NH).

a) If the *CO_2 level* of the blood increases, the *breathing rate* will increase eventually causing the *CO_2 level* of the blood to decrease.

b) The amount of *water in the blood* is controlled by the hormone vasopressin. If there is too little *water in the blood*, the pituitary increases the *vasopressin production rate*. A greater *vasopressin production rate* increases the *vasopressin in the blood*. More *vasopressin in the blood* increases the *rate kidney tubules absorb water* which increases the *water in the blood*.

c) If a person begins to smoke cigarettes, his *dependency on cigarettes* increases. If a person's *dependency on cigarettes* increases, the *amount he smokes* increases.

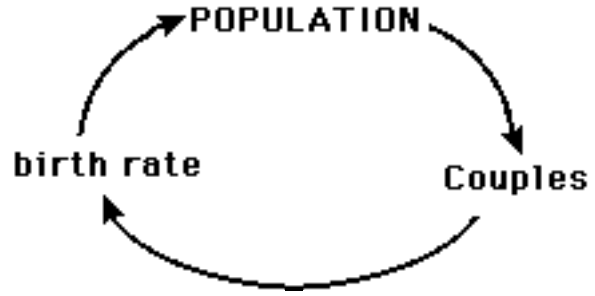
d) An increase in the amount of *heat* in a system will cause a greater *chemical reaction rate*. Chemical reactions release energy in the form of heat. A greater *chemical reaction rate* will increase the *heat production rate* which will increase the amount of *heat*.

e) If the amount of *swelling and pain* increase, the amount of *aspirin* taken by an individual increases. If *aspirin* increases, *prostaglandin production* decreases. If *prostaglandin production* increases, the amount of *prostaglandin* increases. If the amount of *prostaglandin* increases, *swelling and pain* increase.

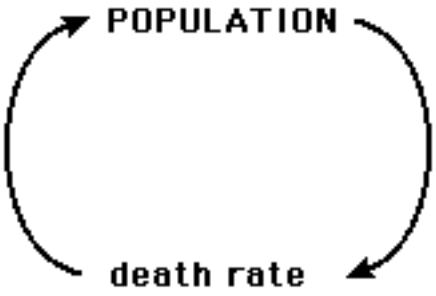
f) If the amount of *glucose in the blood* increases, the *insulin secretion rate* will increase. If the *insulin secretion rate* increases, more *insulin* will be produced. If more *insulin* is produced, the *cell membrane permeability* will increase. If the *cell membrane permeability* increases, the *rate at which glucose leaves the blood* will increase. If this *rate* increases, the amount of *glucose in the blood* will decrease.

2) Describe in a sentence or two the systems which are governed by the following causal loop diagrams. Label the causal connections as either *same* (s) or *opposite* (o). Label the causal loops as *homeostatic* (H) or *non-homeostatic* (NH), and describe the behavior of the non-homeostatic loops.

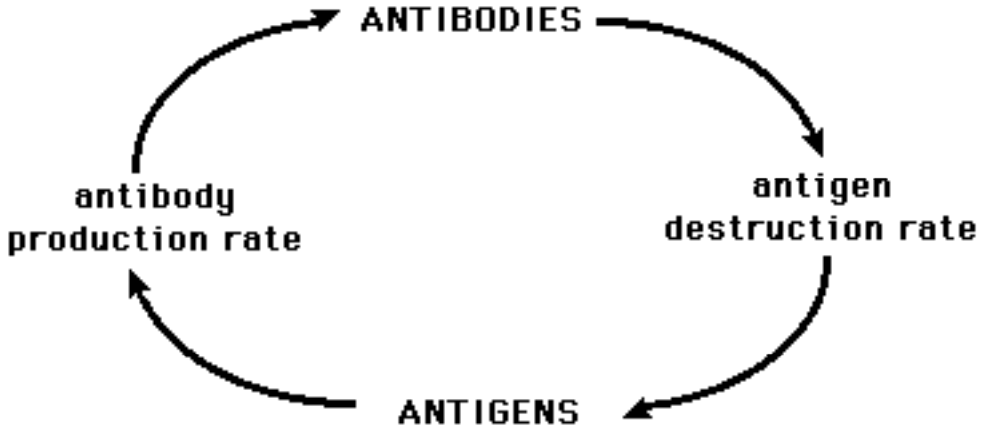
a)



b)



c)



The Endocrine System

Homework #2: Thyroxine Stock and Flow Example

Name_____Due Date_____ Period_____

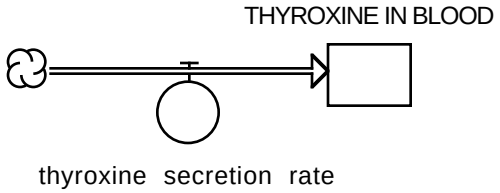
1) Label each of the following variables as either a *stock* or a *flow*. Label the units which might be used to measure each variable. Draw and label the stock and flow diagrams associated with each set of variables.

Hint: all units associated with time will be measured in years or minutes.

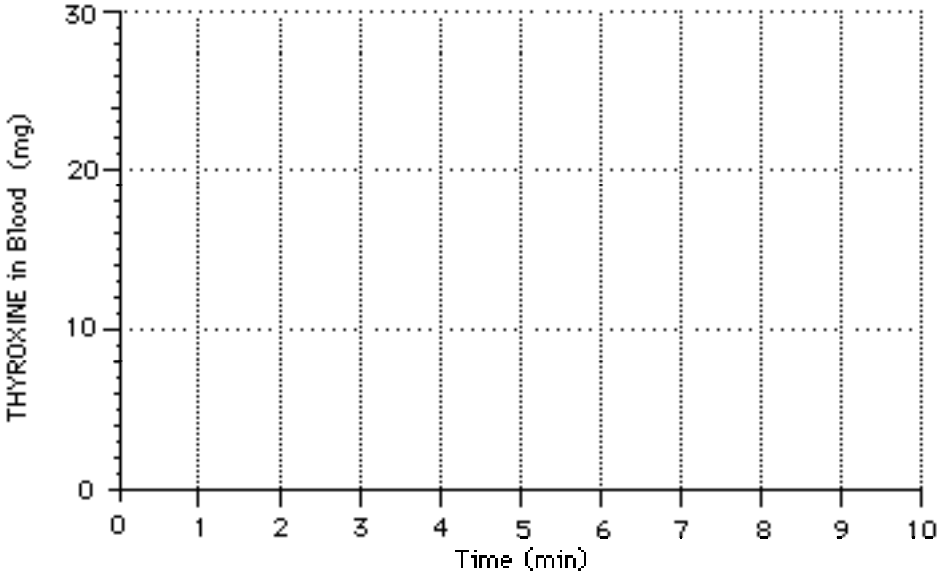
	Stock or Flow	Units	Stock and Flow Diagram
a) TSH in blood			
TSH decrease rate			
TSH increase rate			
b) Thyroxine uptake			
Thyroxine in blood			
Thyroxine secretion			
c) RF uptake			
RF secretion			
Releasing Factor in blood			

d) Combine thyroxine, TSH, and releasing factor (RF) and their secretion rates into either a single causal loop diagram or a stock and flow diagram showing causal links. Label the links as same or opposite and label the loop as homeostatic or non-homeostatic. (*Hint: Read section 29.6, page 558 of Oram, 1983*)

2) The following STELLA diagram represents the secretion of thyroxine into the bloodstream. Answer the following questions regarding this structure.



a) There is initially a stock of 10 milligrams (mg) of thyroxine in the blood. Assume that there is no way for the thyroxine to exit the bloodstream and that the thyroid gland constantly secretes 2 milligrams per minute (mg/min). On the graph below plot a graph of thyroxine in the blood versus time for a ten minute period.



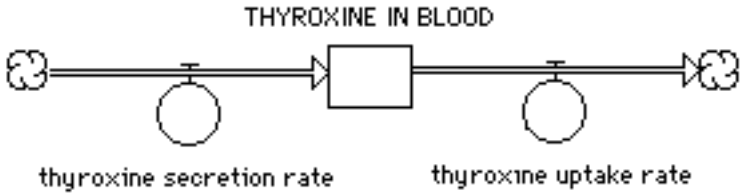
b) Do you think that this structure correctly represents what is happening to thyroxine in the bloodstream?_____
Why or why not?_____
_____

3) It is unrealistic to assume that thyroxine will continue to build up in the bloodstream forever. In reality, thyroxine in the blood is taken up by the cells of the body.

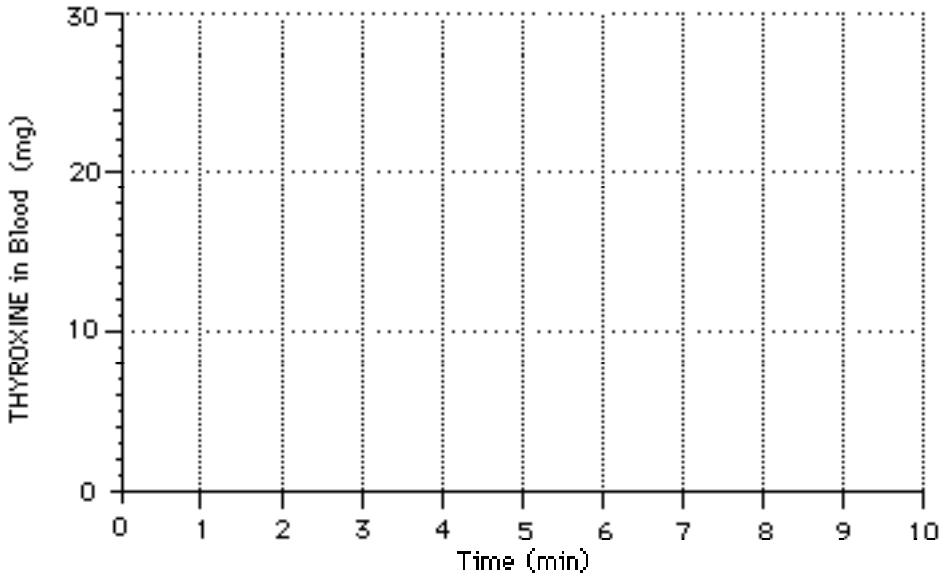
a) What is thyroxine responsible for controlling in the body?

b) Does thyroxine increase or decrease the rate of what it controls in the body? Is this a same (s) or opposite (o) relationship?

c) Just as the thyroxine secretion rate of the thyroid gland was the **inflow** into the stock of thyroxine in the blood, the thyroxine cell uptake rate is the **outflow** from the stock of thyroxine in the blood.

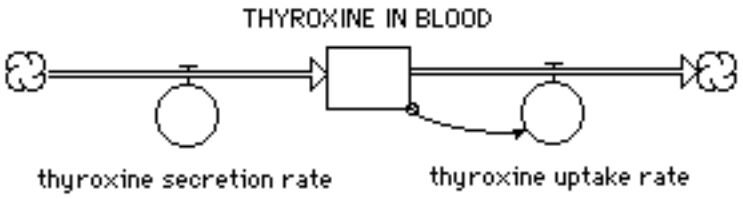


There is initially a stock of 10 milligrams of thyroxine in the blood. The thyroid gland constantly secretes 2 milligrams per minute (mg/min). The thyroxine uptake rate by the cells is 3 milligrams per minute. Plot a graph of thyroxine in the blood versus time for a ten minute period.



d) If we continued to graph the stock of thyroxine in the blood in problem 3, how much thyroxine would be in the blood after 20 minutes? Is this possible? Why or why not?

4) It does not make sense to have a negative stock of thyroxine in the blood. The smallest amount possible is zero. One way to make sure that the stock of thyroxine never goes negative is to make the outflow (thyroxine uptake rate) dependent upon how much thyroxine is present within the bloodstream. This can be done by saying that the thyroxine uptake rate is 20% of the thyroxine in the blood each minute.



a) What is 20 % of 10 milligrams of thyroxine? _____

b) Your answer from part (a) is the outflow (thyroxine uptake rate). Subtracting this number from the inflow (thyroxine secretion rate) will give you the change in the stock (thyroxine in blood) each minute.

change in stock = inflow - outflow

If the inflow is 2 mg/min, what is the change in the stock (thyroxine in blood) each minute?

_____mg/min

c) We begin with 10 mg of thyroxine. If the thyroxine secretion rate is 2 milligrams of thyroxine each minute and the thyroxine uptake rate is the value which you computed in part (b), how much thyroxine is in the blood after the first minute?

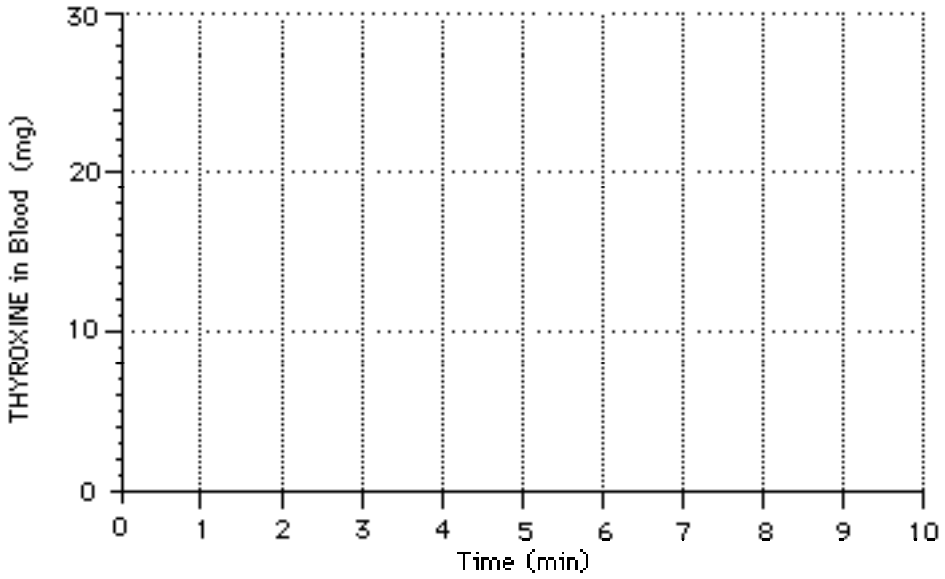
_____mg

d) How much thyroxine is in the blood after the second minute? _____mg

e) There is initially a stock of 10 milligrams of thyroxine in the blood, and the thyroid gland constantly secretes 2 milligrams per minute. The thyroxine uptake rate is defined as 20 percent of the thyroxine in the blood each minute.

Initial Value of THYROXINE IN BLOOD = 10 mg
thyroxine uptake rate (mg/min) =THYROXINE IN BLOOD * 0.20
thyroxine secretion rate = 2 mg/min

Plot a graph of thyroxine in the blood versus time for a ten minute period.



f) Homeostasis is defined as the state of equilibrium produced by a balance of functions and chemical compositions within the body OR as the act of trying to reach an equilibrium level. Does the graph above appear to display behavior which one might call homeostatic? Why or why not? (put answer on back of paper if you run out of space)

Explanation of Model Boundaries

The following pages detail four distinct glucose regulation models. Each model surpasses the level of complexity of the one previous to it. Pick the level of complexity that you would like your class to use and teach for that particular model. No matter what model you use, be sure to point out its simplifications.

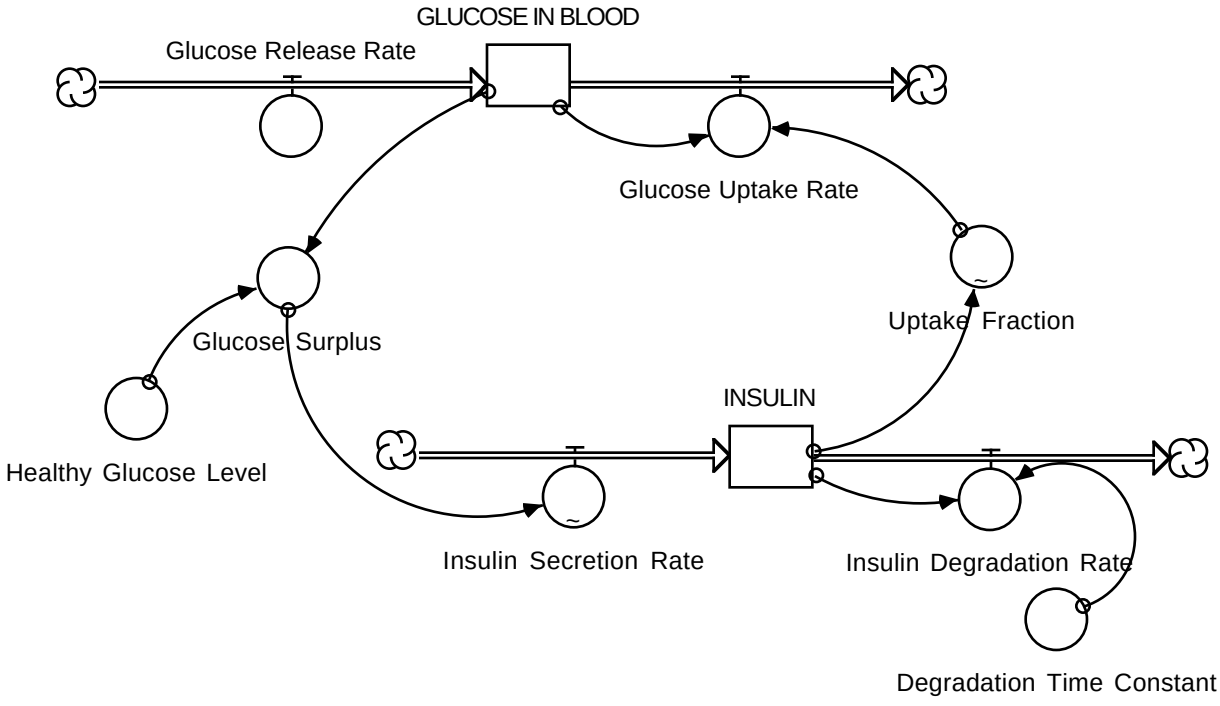
Model #1: Single Feedback System (No Concentration)
Model #2: Single Feedback System (Concentration)
Model #3: Double Feedback System
Model #4: Double Feedback System with Insulin Activation Delay

Glucose Regulation Model #1:

Single Feedback System (No Concentration)

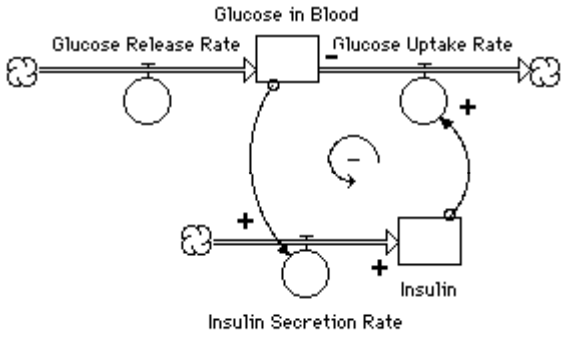
Assumptions:

a) This person has 6 liters of blood, an average healthy glucose level of 6,000 milligrams, and an average healthy insulin level of 9000 units.
b) An increase in the amount of insulin simply increases the flow of glucose from the bloodstream into the cells and does NOT decrease the flow of glucose into the bloodstream,
c) There is no activation time that must take place before secreted insulin becomes effective,
d) The insulin secretion rate is affected only by the amount of glucose in the blood and NOT also by the rate at which the blood glucose level is increasing,
e) We may consider simply the amount of glucose in the blood rather than the concentration of glucose in the blood.



Model #1 Explanation:

In this model, there is only one negative (homeostatic) feedback loop which is working to regulate the body's blood glucose level:



Because of this feedback loop, if the **Glucose in Blood** rises above its normal level, the **Insulin Secretion Rate** will increase causing the level of **Insulin** to increase. Increased **Insulin** has the effect of increasing the **Glucose Uptake Rate** which causes the **Glucose In Blood** to decrease back to its normal value.

Glucose Regulation Model # 2:

Simple Single Feedback Loop

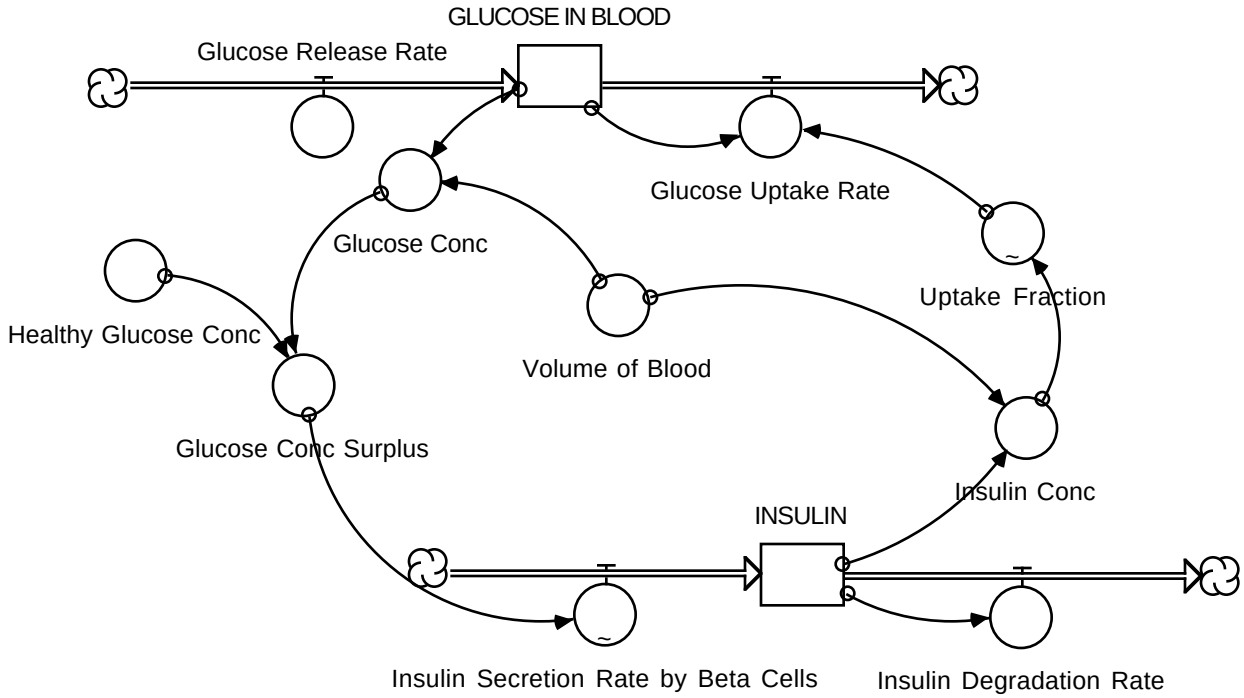
Assumptions:

a) This person has 6 liters of blood, an average healthy glucose level of 6,000 milligrams, and an average healthy insulin level of 9000 units.

b) An increase in the amount of insulin simply increases the flow of glucose from the bloodstream into the cells and does NOT decrease the flow of glucose into the bloodstream,

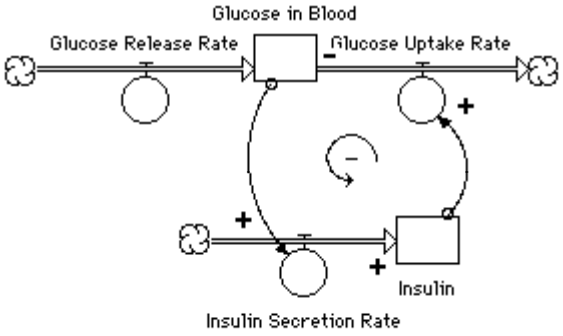
c) There is no activation time that must take place before secreted insulin becomes effective,

d) The insulin secretion rate is affected only by the amount of glucose in the blood and NOT also by the rate at which the blood glucose level is increasing,



Model #2 Explanation:

In this model, there is only one negative (homeostatic) feedback loop which is working to regulate the body's blood glucose level:



However, in this case, the effects are caused not by a surplus level, but rather a surplus concentration. In other words if the **Glucose in Blood** rises above its normal level, the **Glucose Concentration Surplus** will increase causing the **Insulin Secretion Rate** to increase. The increase in the **Insulin Secretion Rate** will cause the level of **Insulin** to increase, causing an increase in the **Insulin Concentration**. Increased **Insulin Concentration** has the effect of increasing the **Glucose Uptake Rate** which causes the **Glucose In Blood** to decrease bringing the **Glucose Concentration Surplus** back down to zero.

Glucose Regulation Model # 3:

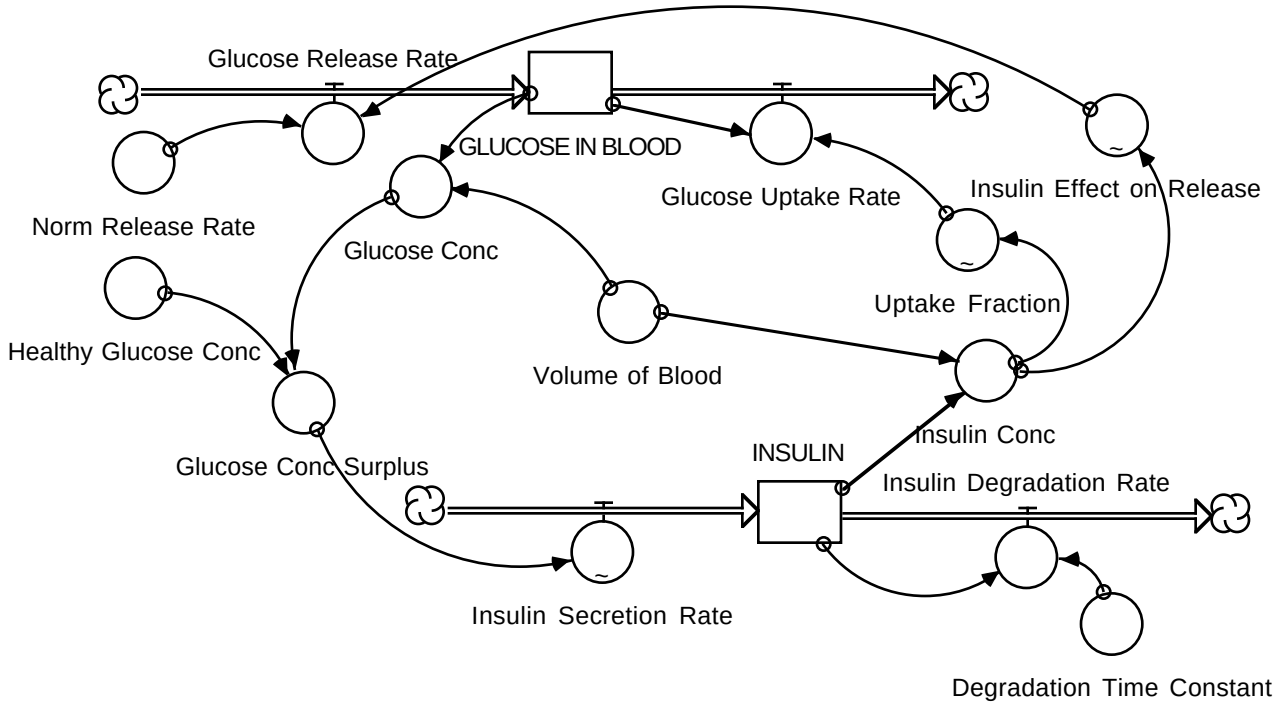
Double Feedback Loop

Assumptions:

a) This person has 6 liters of blood, an average healthy glucose level of 6,000 milligrams, and an average healthy insulin level of 9000 units.

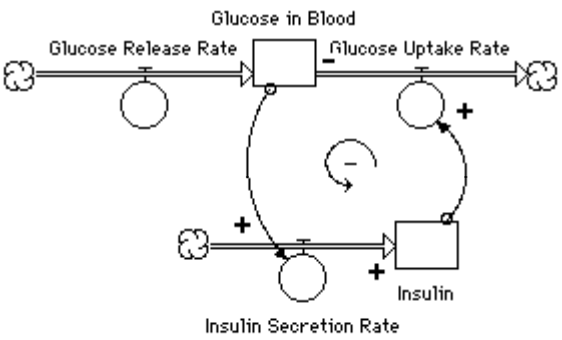
b) There is no activation time that must take place before secreted insulin becomes effective,

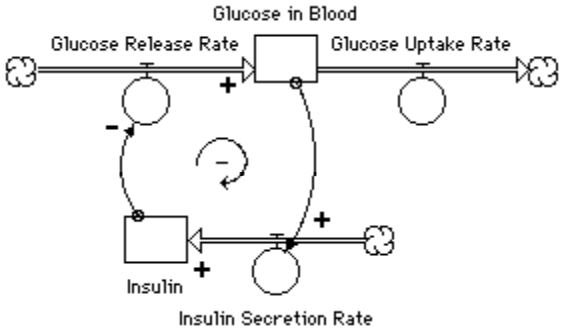
c) The insulin secretion rate is affected only by the amount of glucose in the blood and NOT also by the rate at which the blood glucose level is increasing,



Model #3 Explanation:

In this model, there are two negative (homeostatic) feedback loops which are working together to regulate the body's blood glucose level:





However, in this case, the effects are caused not by a surplus level, but rather a surplus concentration. In other words if the **Glucose in Blood** rises above its normal level, the **Glucose Concentration Surplus** will increase causing the **Insulin Secretion Rate** to increase. The increase in the **Insulin Secretion Rate** will cause the level of **Insulin** to increase, an increase in the **Insulin Concentration**. Increased **Insulin Concentration** causes two different events to happen:

1) an increase in the **Glucose Uptake Rate** which causes the **Glucose In Blood** to decrease bringing the **Glucose Concentration Surplus** back down to zero and
2) a decrease in the **Glucose Release Rate** which slows down the growth of **Glucose in the Blood**.

The combination of both of these, allows the glucose regulatory system to regain homeostasis at a greater rate than if only the single feedback loop were present in the body.

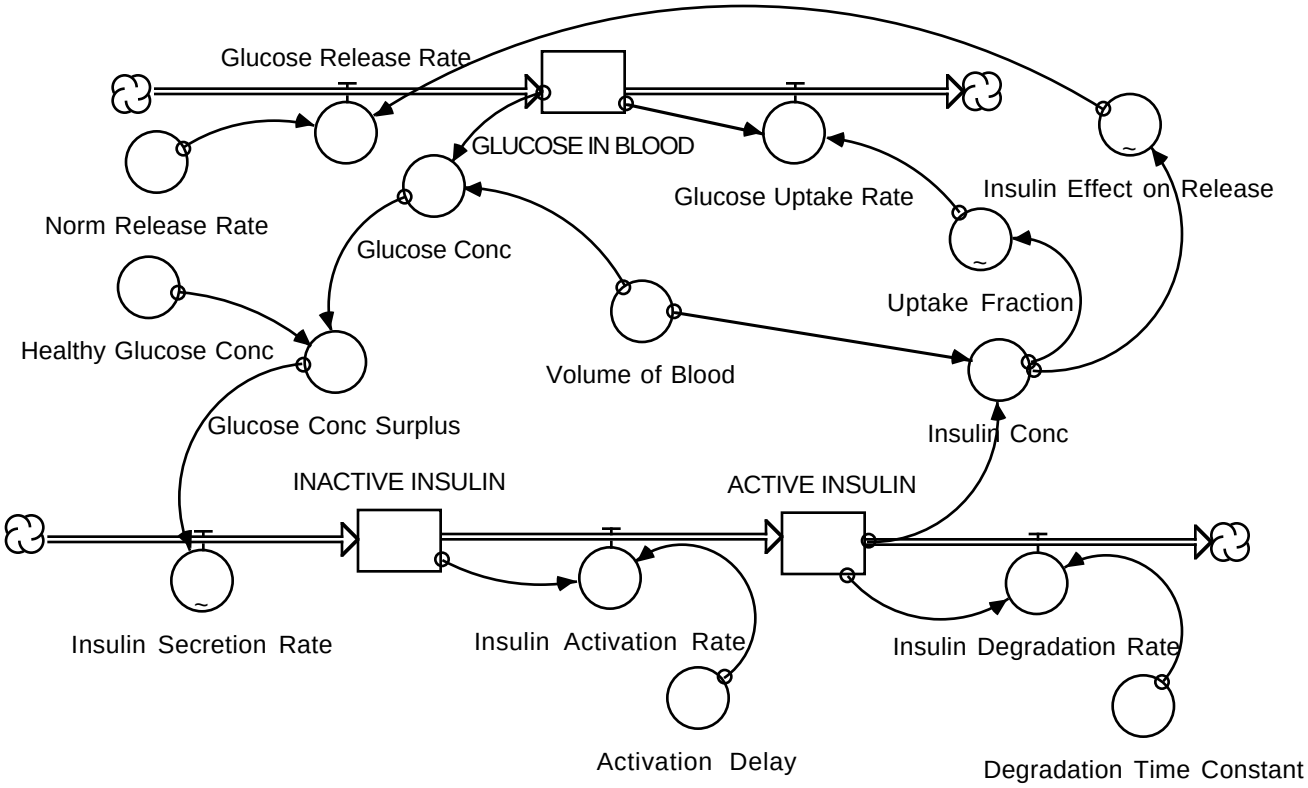
Glucose Regulation Model #4:

Double Feedback Loop w/ Activation Time

Assumptions:

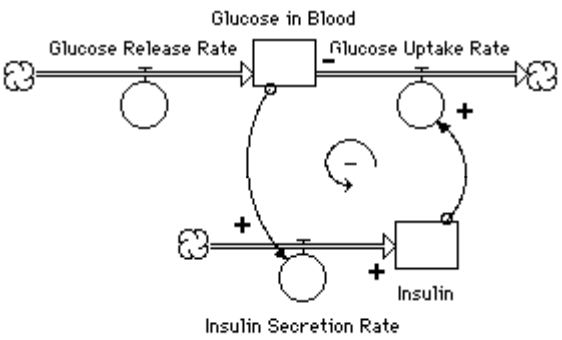
a) This person has 6 liters of blood, an average healthy glucose level of 6,000 milligrams, and an average healthy insulin level of 9000 units.

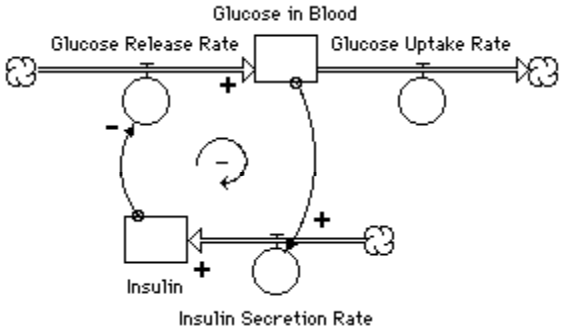
b) The insulin secretion rate is affected only by the amount of glucose in the blood and NOT also by the rate at which the blood glucose level is increasing,



Model #4 Explanation:

In this model, there are two negative (homeostatic) feedback loops which are working together to regulate the body's blood glucose level:





However, in this case, the effects are caused not by a surplus level, but rather a surplus concentration. In other words if the **Glucose in Blood** rises above its normal level, the **Glucose Concentration Surplus** will increase causing the **Insulin Secretion Rate** to increase. The increase in the **Insulin Secretion Rate** will cause the level of **Insulin** to increase, an increase in the **Insulin Concentration**. Increased **Insulin Concentration** causes two different events to happen:

1) an increase in the **Glucose Uptake Rate** which causes the **Glucose In Blood** to decrease bringing the **Glucose Concentration Surplus** back down to zero and
2) a decrease in the **Glucose Release Rate** which slows down the growth of **Glucose in the Blood**.

The combination of both of these, allows the glucose regulatory system to regain homeostasis at a greater rate than if only the single feedback loop were present in the body.

One major difference in this model is that secreted insulin does not become effective immediately. It has to wait approximately 18 minutes before it becomes active. This delay causes several events to happen which change the behavior of the system.

Equations for Glucose Regulation Model #1

STOCK

GLUCOSE_IN_BLOOD(t)= GLUCOSE_IN_BLOOD(t - dt) + (Glucose_Release_Rate - Glucose_Uptake_Rate) * dt
INITIAL GLUCOSE_IN_BLOOD = 6,000 milligrams

DOCUMENT: This is the amount of glucose that is present in the bloodstream. 70-120 mg of glucose/dL of blood is normal for a person who has been fasting. An average person has approximately 6 liters (60 dL) of blood. Assuming a healthy glucose level of 100 mg/dL, the person being modeled will begin with a normal blood sugar level of 6000 mg.
UNITS: milligrams (mg)

INFLOWS:

Glucose_Release_Rate = 198 milligrams/minute

DOCUMENT: This is the amount of glucose that is released into the bloodstream each minute. Glucose is released into the bloodstream by digestion of food or by the breakdown of fat in the liver.
UNITS: milligrams/minute (mg/min)

OUTFLOWS:

Glucose_Uptake_Rate = GLUCOSE_IN_BLOOD*Uptake_Fraction

DOCUMENT: The glucose uptake rate is affected by three processes:
1) conversion of excess glucose to glycogen by the liver & muscles,
2) uptake by cells due to cell wall permeability changes, and
3) conversion of glucose to fat.
UNITS: milligrams/minute (mg/min)

STOCK

INSULIN(t)=INSULIN(t-dt)+(Insulin_Secretion_Rate-Insulin_Degradation_Rate) * dt
INITIAL INSULIN = 9000 units (mg)

DOCUMENT: Insulin is the hormone that is secreted by the Beta cells of the Islets of Langerhans in the Pancreas. Insulin causes an increase in the cell membrane permeability so that glucose may pass from the bloodstream into the cells.
UNITS: units

INFLOWS:

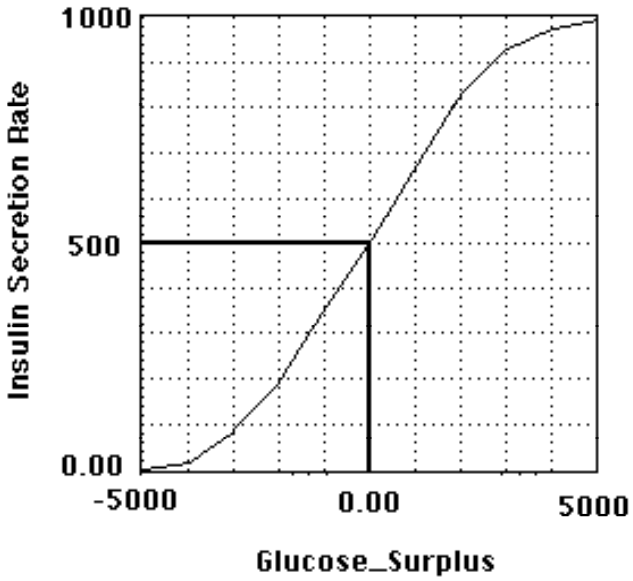
Insulin_Secretion_Rate = GRAPH(Glucose_Surplus)

DOCUMENT: The insulin secretion rate is defined as a graphical function based on the surplus of glucose in the blood. If the glucose surplus equals zero (the body is at the healthy level), the insulin secretion rate is equal to 500 units/min (the amount necessary to maintain the equilibrium amount of insulin.

If the glucose surplus is positive, the body will tell Beta cells to produce more insulin. This explains the increasing secretion rate as the glucose surplus increases. However, once the surplus reaches a certain high level, the B cells can no longer produce as much insulin. This explains the decreasing slope as the glucose surplus gets very high.

If the glucose surplus is negative, the body does not have enough blood glucose. If this is the case, it would be expected that the body would try to conserve the glucose by slowing down its rate of flow into the body cells. The body does this by decreasing its insulin secretion rate. The decreasing slope of the curve as very low glucose surpluses are reached can be explained by the fact that the body has lower limits to the amount of insulin that it can produce. In this case this lower limit is assumed to be zero. It is possible that the actual lower limit is some number greater than zero.

UNITS: units/minute



Input	Output
-5000	0.00
-4000	15.0
-3000	85.0
-2000	190
-1000	350
0.00	500
1000	665
2000	825
3000	930
4000	975
5000	995

OUTFLOWS:

Insulin_Degradation_Rate = INSULIN/Degradation_Time_Constant

DOCUMENT: The insulin degradation rate is dependent upon the amount of insulin and the degradation time constant. Every minute 1/18 (the degradation time constant) of the insulin degrades. Therefore, if there is a high amount of insulin, the degradation rate will be higher than if there is a low amount of insulin.

UNITS: units/minute

Converter

○ **Degradation_Time_Constant** = 18 minutes

DOCUMENT: The degradation time constant is a measure of the length of time that it takes one milligram of insulin to decay. Therefore, one eighteenth of the total amount of insulin degrades every minute.
UNITS: minutes

Converter

○ **Glucose_Surplus** = GLUCOSE_IN_BLOOD-Healthy_Glucose_Level

DOCUMENT: The glucose surplus is the difference between the actual glucose level and the healthy glucose level. The value will be positive (a surplus) if the actual level is higher than the healthy level. If there is a glucose surplus, properly functioning Beta cells of the Islets of Langerhans in the Pancreas will secrete insulin. The value will be negative (a deficit) if the actual level is lower than the healthy value. If there is a glucose deficit, the body will try to conserve blood glucose by secreting less insulin.
UNITS: milligrams (mg)

Converter

○ **Healthy_Glucose_Level** = 6000 milligrams(mg)
DOCUMENT: 70-120 milligrams of glucose/deciliter of blood is a normal glucose concentration for a person who has been fasting. Assuming the person being modeled has a healthy glucose concentration of 100 mg/dL and a volume of blood equal to 60 dL (6 L), his healthy glucose level is 6000 mg.
UNITS: milligrams (mg)

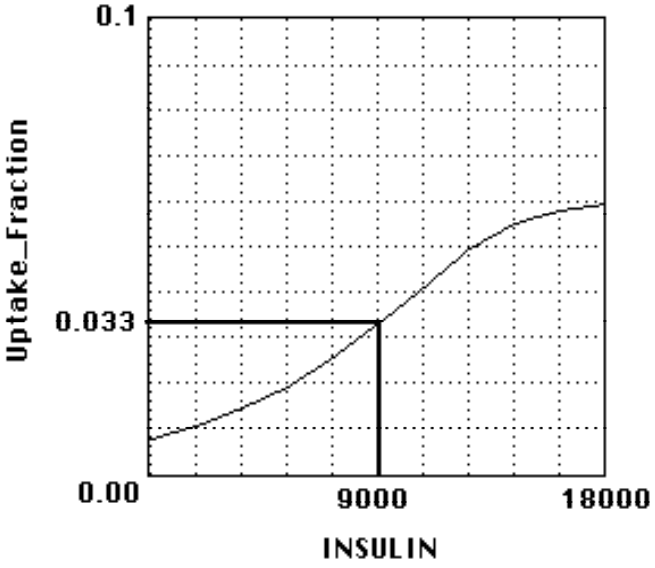
Converter

○ **Uptake_Fraction** = GRAPH(INSULIN)

DOCUMENT: The glucose uptake fraction is the percentage of the total amount of glucose that will be taken up by the cells each minute. It is a graphical function dependent upon the amount of insulin. If insulin is at its normal level of 9000 units, the cells will uptake 3.3% of the available blood glucose.

If insulin is higher than the normal level, the cells will take up a larger fraction of the glucose. The fraction taken up will increase until the insulin level gets too high and the cells are unable to take in as much glucose as the insulin would like to allow. At some point the fraction levels off because the cells can no longer take in a greater fraction of the glucose.

If the insulin is lower than the normal level, the cells will be able take up only a smaller fraction of the available glucose. As insulin decreases, the fraction of glucose taken up decreases at a slower rate because the cells, which need the sugar for energy, will continue to take up as much as they possibly can given the available insulin.
UNITS: dimensionless



Input	Output
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

Equations for Glucose Regulation Model #2

NOTE: EQUATIONS AND DOCUMENTATION THAT HAVE CHANGED FROM THE PREVIOUS MODEL ARE WRITTEN ENTIRELY IN BOLD LETTERS FOR EASE IN PICKING OUT.

STOCK

GLUCOSE_IN_BLOOD(t) = GLUCOSE_IN_BLOOD(t - dt) + (Glucose_Release_Rate - Glucose_Uptake_Rate) * dt

INITIAL GLUCOSE_IN_BLOOD = 6,000 milligrams (mg)

DOCUMENT: This is the amount of glucose that is present in the bloodstream. 70-120 mg/dL of glucose is normal for a person who has been fasting. An average person has approximately 6 liters (60 dL) of blood. Assuming a healthy glucose level of 100 mg/dL, the person being modeled will begin with a normal blood sugar level of 6000 mg.
UNITS: milligrams (mg)

INFLOWS:

Glucose_Release_Rate = 198 milligrams/minute (mg/min)

DOCUMENT: This is the amount of glucose that is released into the bloodstream each hour. Glucose is released into the bloodstream by the digestion of food or by the breakdown of fat in the liver.
UNITS: milligrams/minute (mg/min)

OUTFLOWS:

Glucose_Uptake_Rate = GLUCOSE_IN_BLOOD*Uptake_Fraction

DOCUMENT: The glucose uptake rate is affected by three processes:
1) conversion of excess glucose to glycogen by the liver & muscles,
2) uptake by cells due to cell wall permeability changes, and
3) conversion of glucose to fat.
UNITS: milligrams/minute (mg/min)

STOCK

INSULIN(t)=INSULIN(t-dt)+(Insulin_Secretion_Rate) - (Insulin_Degradation_Rate) * dt

INITIAL INSULIN = 9,000 units

DOCUMENT: Insulin is the hormone that is secreted by the Beta cells of the Islets of Langerhans in the Pancreas. Insulin causes an increase in the cell membrane permeability so that glucose may pass from the bloodstream into the cells.
UNITS: units

INFLOWS:

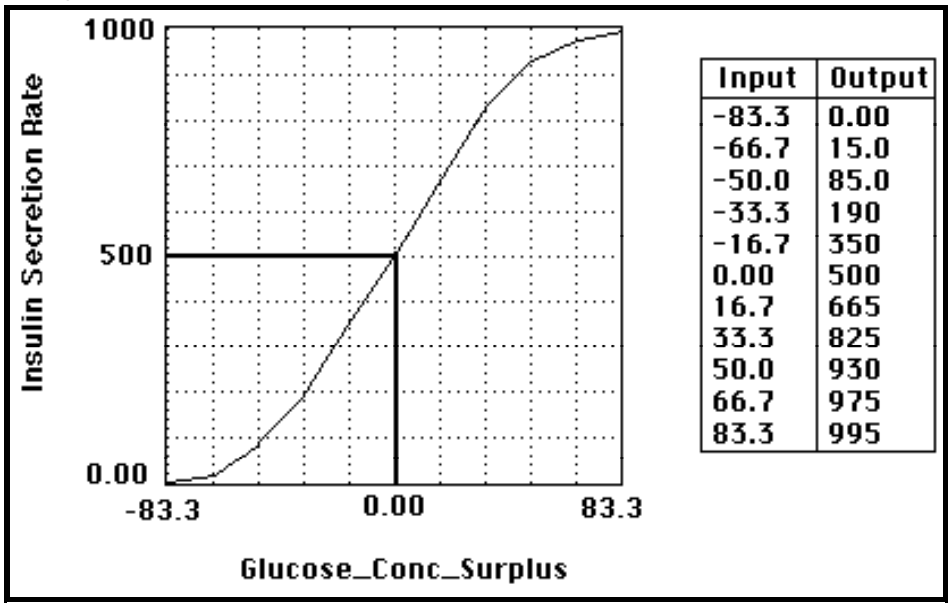
Insulin_Secretion_Rate = GRAPH(Glucose_Conc_Surplus)

DOCUMENT:The insulin secretion rate is defined as a graphical function based on the surplus of glucose in the blood. If the glucose surplus equals zero (the body is at the healthy level), the insulin secretion rate is equal to 500 units/min (the amount necessary to maintain the equilibrium amount of insulin.

If the glucose surplus is positive, the body will tell Beta cells to produce more insulin. This explains the increasing secretion rate as the glucose surplus increases. However, once the surplus reaches a certain high level, the B cells can no longer produce as much insulin. This explains the decreasing slope as the glucose surplus gets very high.

If the glucose surplus is negative, the body does not have enough blood glucose. If this is the case, it would be expected that the body would try to conserve the glucose by slowing down its rate of flow into the body cells. The body does this by decreasing its insulin secretion rate. The decreasing slope of the curve as very low glucose surpluses are reached can be explained by the fact that the body has lower limits to the amount of insulin that it can produce. In this case this lower limit is assumed to be zero. It is possible that the actual lower limit is some number greater than zero.

UNITS: units/minute



Input	Output
-83.3	0.00
-66.7	15.0
-50.0	85.0
-33.3	190
-16.7	350
0.00	500
16.7	665
33.3	825
50.0	930
66.7	975
83.3	995

OUTFLOWS:

Insulin_Degradation_Rate = INSULIN/Degradation Time Constant

DOCUMENT: The insulin degradation rate is dependent upon the amount of insulin and the degradation time constant. Every minute 1/18 (the degradation time constant) of the insulin degrades. Therefore, if there is a high amount of insulin, the degradation rate will be higher than if there is a low amount of insulin.

UNITS: units/minute

Converter

Degradation_Time_Constant = 18 minutes

DOCUMENT: The degradation time constant is a measure of the length of time that it takes one milligram of insulin to decay. Therefore, one eighteenth of the total amount of insulin degrades every minute.
UNITS: minutes (min)

Converter **Glucose_Conc = GLUCOSE_IN_BLOOD/Volume_of_Blood**

DOCUMENT: The concentration of glucose in the blood is equal to the amount of glucose in the blood divided by the volume of blood in the body. If the glucose concentration is higher than it normally should be, the B cells of the Islets of Langerhans secrete insulin.
UNITS: milligrams/deciliter (mg/dL)

Converter **Glucose_Conc_Surplus = Glucose_Conc-Healthy_Glucose_Conc**

DOCUMENT: The glucose concentration surplus is the difference between the actual glucose concentration and the healthy glucose concentration. The value will be positive (a surplus) if the actual concentration is higher than the healthy concentration. If there is a surplus glucose concentration, the B cells of the Islets of Langerhans will secrete insulin. The value will be negative (a deficit) if the actual level is lower than the healthy value. If there is a glucose deficit, the body will try to conserve blood glucose by secreting less insulin.
UNITS: milligrams/deciliter (mg/dL)

Converter **Healthy_Glucose_Conc = 100 milligrams/deciliter (mg/dL)**

DOCUMENT: 70-120 milligrams of glucose/deciliter of blood is a normal glucose concentration for a person who has been fasting. We will assume that this person's healthy glucose concentration is 100 mg/dL.
UNITS: milligrams/deciliter (mg/dL)

Converter **Insulin_Conc = INSULIN/Volume_of_Blood**

DOCUMENT: The concentration of insulin in the blood is equal to the amount of insulin divided by the volume of blood. For this person it is assumed that a normal insulin concentration would be equal to 175 units/dL.
UNITS: units/deciliter (units/dL)

Converter **Volume_of_Blood = 60 deciliters (dL)**

DOCUMENT: This is an assumed number for the volume of blood in an average human body. A normal person has 6 liters (60 dL) of blood in his body.
UNITS: deciliters (dL)

Converter

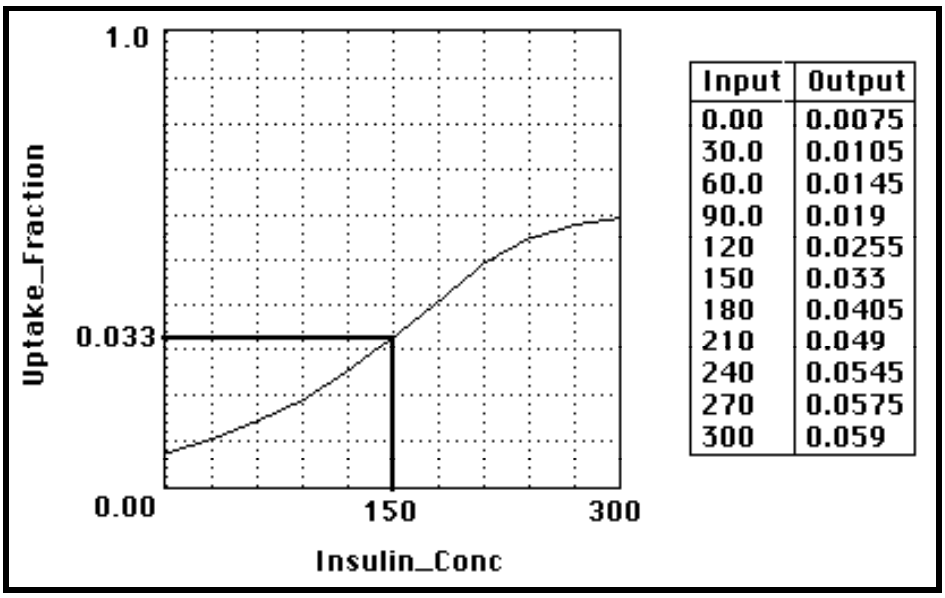
Uptake_Fraction = GRAPH(Insulin_Conc)

DOCUMENT: The glucose uptake fraction is the percentage of the total amount of glucose that will be taken up by the cells each minute. It is a graphical function dependent upon the amount of insulin. If insulin is at its normal level of 9000 units, the cells will uptake 3.3% of the available blood glucose.

If insulin is higher than the normal level, the cells will take up a larger fraction of the glucose until the insulin level gets too high and the cells are unable to take in as much glucose as the insulin would like to allow. At some point the fraction levels off because the cells can no longer take in a greater fraction of the glucose. This maximum uptake fraction is dependent upon the properties of the cell membrane.

If the insulin is lower than the normal level, the cells will be able take up only a smaller fraction of the available glucose. As insulin decreases, the fraction of glucose taken up decreases at a slower rate because the cells, which need the sugar for energy, will continue to take up as much as they possibly can given the available insulin.

UNITS: dimensionless (if the values are multiplied by 100 they will be a percent (%))



Input	Output
0.00	0.0075
30.0	0.0105
60.0	0.0145
90.0	0.019
120	0.0255
150	0.033
180	0.0405
210	0.049
240	0.0545
270	0.0575
300	0.059

Equations for Glucose Regulation Model #3

NOTE: EQUATIONS AND DOCUMENTATION THAT HAVE CHANGED FROM THE PREVIOUS MODEL ARE WRITTEN ENTIRELY IN BOLD LETTERS FOR EASE IN PICKING OUT.

STOCK

GLUCOSE_IN_BLOOD(t)=GLUCOSE_IN_BLOOD(t-dt)+(Glucose_Release_Rate-Glucose_Uptake_Rate) * dt

INITIAL GLUCOSE_IN_BLOOD = 6,000 milligrams (mg)

DOCUMENT: This is the amount of glucose that is present in the bloodstream. 70-120 mg/dL of glucose is normal for a person who has been fasting. An average person has approximately 6 liters (60 dL). Assuming a healthy glucose level of 100 mg/dL, the person being modeled will begin with a normal blood sugar level of 6000 mg.
UNITS: milligrams (mg)

INFLOWS:

Glucose_Release_Rate=Norm_Release_Rate*Insulin_Effect_on_Release

DOCUMENT: This is the amount of glucose that is released into the bloodstream each hour. Glucose is released into the bloodstream by the digestion of food, or by the breakdown of fat in the liver.
UNITS: milligrams/minute (mg/min)

OUTFLOWS:

Glucose_Uptake_Rate = GLUCOSE_IN_BLOOD*Uptake_Fraction

DOCUMENT: The glucose uptake rate is affected by three processes:
1) conversion of excess glucose to glycogen by the liver & muscles,
2) uptake by cells due to cell wall permeability changes, and
3) conversion of glucose to fat.

UNITS: milligrams/minute (mg/min)

STOCK

INSULIN(t)=INSULIN(t-dt)+(Insulin_Secretion_Rate-Insulin_Degradation_Rate) * dt

INITIAL INSULIN = 9,000 units

DOCUMENT: Insulin is the hormone that is secreted by the Beta Cells of the Islets of Langerhans in the Pancreas. Insulin causes an increase in the cell membrane permeability so that glucose may pass from the bloodstream into the cells.
UNITS: units

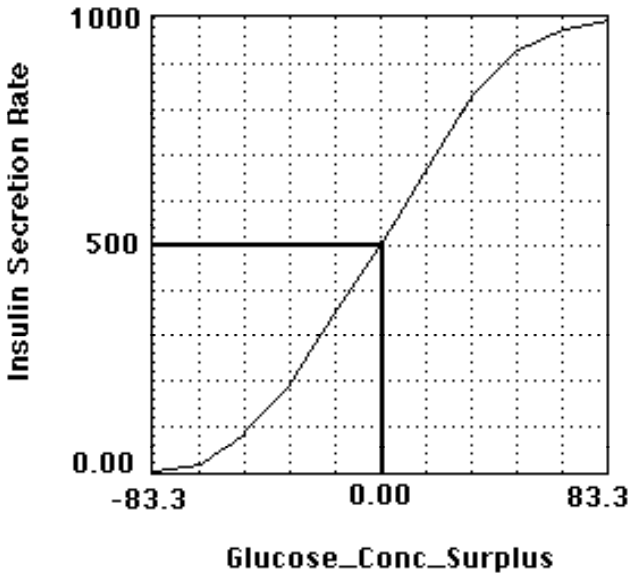
INFLOWS:

Insulin_Secretion_Rate = GRAPH(Glucose_Conc_Surplus)

DOCUMENT:The insulin secretion rate is defined as a graphical function based on the surplus of glucose in the blood. If the glucose surplus equals zero (the body is at the healthy level), the insulin secretion rate is equal to 500 units/min (the amount necessary to maintain the equilibrium amount of insulin.

If the glucose surplus is positive, the body will tell the Beta cells to produce more insulin. This explains the increasing secretion rate as the glucose surplus increases. However, once the surplus reaches a certain high level, the B cells can no longer produce as much insulin. This explains the decreasing slope as the glucose surplus gets very high.

If the glucose surplus is negative, the body does not have enough blood glucose. If this is the case, it would be expected that the body would try to conserve the glucose by slowing down its rate of flow into the body cells. The body does this by decreasing its insulin secretion rate. The decreasing slope of the curve as very low glucose surpluses are reached can be explained by the fact that the body has lower limits to the amount of insulin that it can produce. In this case this lower limit is assumed to be zero. It is possible that the actual lower limit is some number greater than zero.
UNITS: units/minute (units/min)



Input	Output
-83.3	0.00
-66.7	15.0
-50.0	85.0
-33.3	190
-16.7	350
0.00	500
16.7	665
33.3	825
50.0	930
66.7	975
83.3	995

OUTFLOWS:

Insulin_Degradation_Rate = INSULIN/Degradation Time Constant

DOCUMENT: The insulin degradation rate is dependent upon the amount of insulin and the degradation time constant. Every minute 1/18 (the degradation time constant) of the insulin degrades. Therefore, if there is a high amount of insulin, the degradation rate will be higher than if there is a low amount of insulin.
UNITS: units/minute

Converter

Degradation_Time_Constant = 18 minutes

DOCUMENT: The degradation time constant is a measure of the length of time that it takes one milligram of insulin to decay. Therefore, one eighteenth of the total amount of insulin degrades every minute.
UNITS: minutes (min)

Converter

Glucose_Conc = GLUCOSE_IN_BLOOD/Volume_of_Blood

DOCUMENT: The concentration of glucose in the blood is equal to the amount of glucose in the blood divided by the volume of blood in the body. If the glucose concentration is higher than it normally should be, the B cells of the Islets of Langerhans secrete insulin.
UNITS: milligrams/deciliter (mg/dL)

Converter

Glucose_Conc_Surplus = Glucose_Conc-Healthy_Glucose_Conc

DOCUMENT: The glucose concentration surplus is the difference between the actual glucose concentration and the healthy glucose concentration. The value will be positive (a surplus) if the actual concentration is higher than the healthy concentration. If there is a surplus glucose concentration, the B cells of the Islets of Langerhans will secrete insulin. The value will be negative (a deficit) if the actual level is lower than the healthy value. If there is a glucose deficit, the body will try to conserve blood glucose by secreting less insulin.
UNITS: milligrams/deciliter (mg/dL)

Converter

Healthy_Glucose_Conc = 100 milligrams/deciliter (mg/dL)

DOCUMENT: 70-120 milligrams of glucose/deciliter of blood is a normal glucose concentration for a person who has been fasting. We will assume that this person's healthy glucose concentration is 100 mg/dL.
UNITS: milligrams/deciliter (mg/dL)

Converter

Insulin_Conc = INSULIN/Volume_of_Blood

DOCUMENT: The concentration of insulin in the blood is equal to the amount of insulin divided by the volume of blood. For this person it is assumed that a normal insulin concentration would be equal to 175 units/dL.
UNITS: units/deciliter

Converter

Norm_Release_Rate = 198 milligrams/minute (mg/min)

DOCUMENT: 198 milligrams is the amount of glucose that will normally be released into the bloodstream each minute. This value changes as the amount and type of food eaten by the person changes.
UNITS: milligrams/minute (mg/min)

Converter

○ **Volume_of_Blood** = 60 deciliters (dL)

DOCUMENT: This is an assumed number for the volume of blood in an average human body. A normal person has 6 liters (60 dL) of blood in his body.
UNITS: deciliters (dL)

Converter

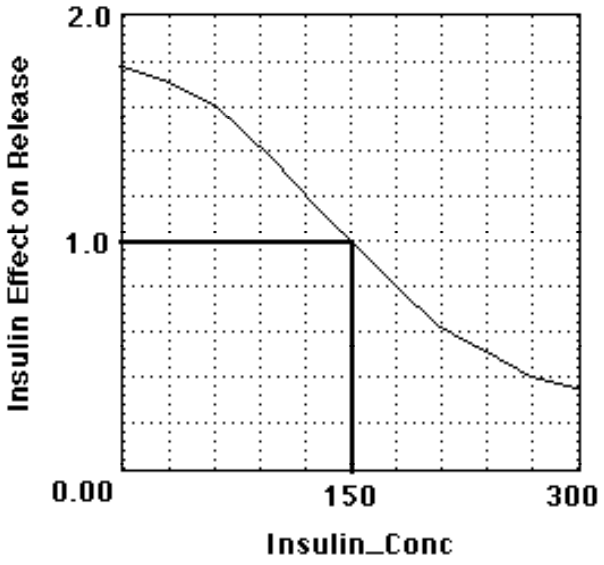
○ Insulin_Effect_on_Release = GRAPH(Insulin Conc)

DOCUMENT: The effect that insulin has on the release of glucose into the bloodstream is a function of the amount of insulin. The insulin effects the liver's rate of transformation of glycogen to glucose.

At a normal insulin concentration of 150 units/dL, there is no effect on the release of glucose into the bloodstream. The normal glucose release amount of 198 mg/min is multiplied by 1.0 to give a glucose release rate of 198 mg/min.

If the insulin concentration is greater than normal, the extra insulin will cause a decrease in the amount of glucose that is released into the blood stream.

If the insulin concentration is less than normal, the lack of insulin will allow the release of more than the normal amount of glucose into the bloodstream.
UNITS: percent (%)



Input	Output
0.00	1.78
30.0	1.71
60.0	1.61
90.0	1.42
120	1.20
150	1.00
180	0.8
210	0.62
240	0.51
270	0.4
300	0.35

Converter

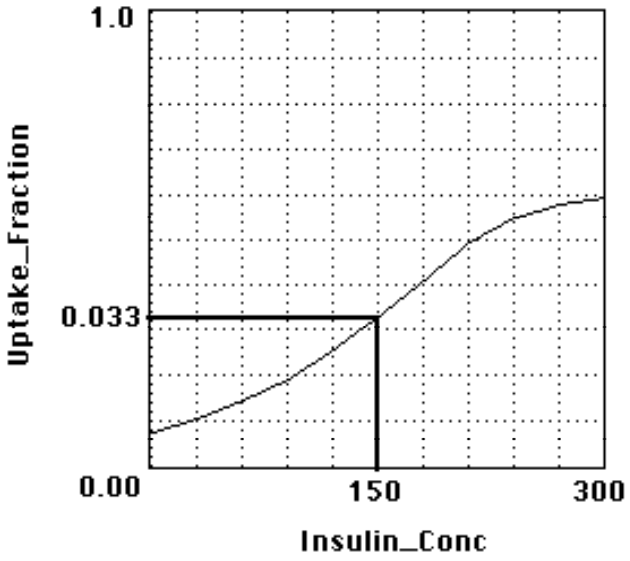
○ **Uptake_Fraction** = GRAPH(Insulin_Conc)

DOCUMENT: The glucose uptake fraction is the percentage of the total amount of glucose that will be taken up by the cells each minute. It is a graphical function dependent upon the amount of insulin. If insulin is at its normal level of 9000 units, the cells will uptake 3.3% of the available blood glucose.

If insulin is higher than the normal level, the cells will take up a larger fraction of the glucose until the insulin level gets too high and the cells are unable to take in as much glucose as the insulin would like to allow. At some point the fraction levels off because the cells can no longer take in a greater fraction of the glucose. This maximum uptake fraction is dependent upon the properties of the cell membrane.

If the insulin is lower than the normal level, the cells will be able take up only a smaller fraction of the available glucose. As insulin decreases, the fraction of glucose taken up decreases at a slower rate because the cells, which need the sugar for energy, will continue to take up as much as they possibly can given the available insulin.

UNITS: dimensionless (if the values are multiplied by 100 they will be a percent (%))



Input	Output
0.00	0.0075
30.0	0.0105
60.0	0.0145
90.0	0.019
120	0.0255
150	0.033
180	0.0405
210	0.049
240	0.0545
270	0.0575
300	0.059

Equations for Glucose Regulation Model #4

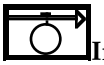
NOTE: EQUATIONS AND DOCUMENTATION THAT HAVE CHANGED FROM THE PREVIOUS MODEL ARE WRITTEN ENTIRELY IN BOLD LETTERS FOR EASE IN PICKING OUT.

ACTIVE_INSULIN(t)=ACTIVE_INSULIN(t-dt)+(Insulin_Activation_Rate-Insulin_Degradation_Rate) * dt

INITIAL ACTIVE_INSULIN = 9000 units

DOCUMENT: Insulin is the hormone that is secreted by the Beta Cells of the Islets of Langerhans in the Pancreas. After the insulin becomes active it is able to cause an increase in the cell membrane permeability so that glucose may pass from the bloodstream into the cells.
UNITS: units

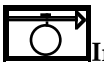
INFLOWS:



Insulin_Activation_Rate = INACTIVE_INSULIN/Activation_Delay

DOCUMENT: The insulin activation rate is the amount of inactive insulin that becomes active each minute. Because the activation delay is 18 minutes, one eighteenth of the current amount of inactive insulin will become active each minute.
UNITS: units/minute

OUTFLOWS:



Insulin_Degradation_Rate=
ACTIVE_INSULIN/Degradation_Time_Constant

DOCUMENT: The insulin degradation rate is dependent upon the amount of insulin and the degradation time constant. Every minute 1/18 (the degradation time constant) of the insulin degrades. Therefore, if there is a high amount of insulin, the degradation rate will be higher than if there is a low amount of insulin.
UNITS: units/minute

GLUCOSE_IN_BLOOD(t)=GLUCOSE_IN_BLOOD(t-dt)+(Glucose_Release_Rate-Glucose_Uptake_Rate) * dt
INITIAL GLUCOSE_IN_BLOOD = 6000 milligrams (mg)

DOCUMENT: This is the amount of glucose that is present in the bloodstream. 70-120 mg/dL of glucose is normal for a person who has been fasting. An average person has approximately 6 liters (60 dL). Assuming a healthy glucose level of 100 mg/dL, the person being modeled will begin with a normal blood sugar level of 6000 mg.
UNITS: milligrams (mg)

INFLOWS:

Glucose_Release_Rate=
Norm_Release_Rate*Insulin_Effect_on_Release

DOCUMENT: This is the amount of glucose that is released into the bloodstream each hour. Glucose is released into the bloodstream by the digestion of food or by the breakdown of fat in the liver.
UNITS: milligrams/minute (mg/min)

OUTFLOWS:

Glucose_Uptake_Rate = GLUCOSE_IN_BLOOD*Uptake_Fraction

DOCUMENT: The glucose uptake rate is affected by three processes:
1) conversion of excess glucose to glycogen by the liver & muscles,
2) uptake by cells due to cell wall permeability changes, and
3) conversion of glucose to fat.
UNITS: milligrams/minute (mg/min)

INACTIVE_INSULIN(t)=INACTIVE_INSULIN(t-dt)+(Insulin_Secretion_Rate-Insulin_Activation_Rate) * dt
INITIAL INACTIVE_INSULIN = 9000 units

DOCUMENT: Insulin is the hormone that is secreted by the Beta Cells of the Islets of Langerhans in the Pancreas. When insulin is first secreted, it is inactive for 18 minutes. Inactive insulin does NOT cause the increase in the cell membrane permeability that active insulin does.
UNITS: units

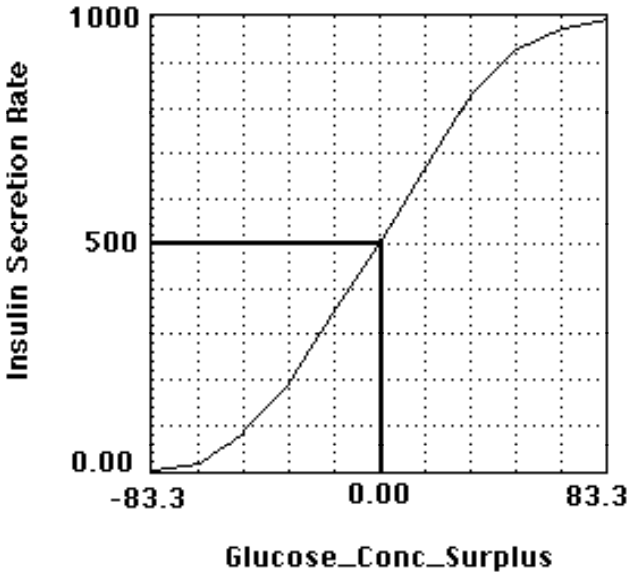
INFLOWS:

Insulin_Secretion_Rate = GRAPH(Glucose_Conc_Surplus)

DOCUMENT: The insulin secretion rate is defined as a graphical function based on the surplus of glucose in the blood. If the glucose surplus equals zero (the body is at the healthy level), the insulin secretion rate is equal to 500 units/min (the amount necessary to maintain the equilibrium amount of insulin.

If the glucose surplus is positive, the body will tell Beta cells to produce more insulin. This explains the increasing secretion rate as the glucose surplus increases. However, once the surplus reaches a certain high level, the B cells can no longer produce as much insulin. This explains the decreasing slope as the glucose surplus gets very high.

If the glucose surplus is negative, the body does not have enough blood glucose. If this is the case, it would be expected that the body would try to conserve the glucose by slowing down its rate of flow into the body cells. The body does this by decreasing its insulin secretion rate. The decreasing slope of the curve as very low glucose surpluses are reached can be explained by the fact that the body has lower limits to the amount of insulin that it can produce. In this case this lower limit is assumed to be zero. It is possible that the actual lower limit is some number greater than zero.
UNITS: units/minute



Input	Output
-83.3	0.00
-66.7	15.0
-50.0	85.0
-33.3	190
-16.7	350
0.00	500
16.7	665
33.3	825
50.0	930
66.7	975
83.3	995

OUTFLOWS:

Insulin_Activation_Rate = INACTIVE_INSULIN/Activation_Delay

DOCUMENT: The insulin activation rate is the amount of inactive insulin that becomes active each minute. Because the activation delay is 18 minutes, one eighteenth of the current amount of inactive insulin will become active each minute.
UNITS: units/minute

Converter

Activation_Delay = 18 minutes

DOCUMENT: When insulin is first secreted by the Beta cells of the Islets of Langerhans in the Pancreas, it is inactive(it has no effect on the uptake of glucose from the bloodstream). It takes 18 minutes for the newly secreted inactive insulin to become active. Therefore, every minute one eighteenth of the inactive insulin will become active.
UNITS: minutes (min)

Converter

Degradation_Time_Constant = 18 minutes

DOCUMENT: The degradation time constant is a measure of the length of time that it takes one milligram of insulin to decay. Therefore, one eighteenth of the total amount of insulin degrades every minute.
UNITS: minutes (min)

Converter

Glucose_Conc = GLUCOSE_IN_BLOOD/Volume_of_Blood

DOCUMENT: The concentration of glucose in the blood is equal to the amount of glucose in the blood divided by the volume of blood in the body. If the glucose concentration is higher than it normally should be, the B cells of the Islets of Langerhans secrete insulin. The value will be negative (a deficit) if the actual level is lower than the healthy value. If there is a glucose deficit, the body will try to conserve blood glucose by secreting less insulin.

UNITS: milligrams/deciliter (mg/dL)

Converter

Glucose_Conc_Surplus = Glucose_Conc-Healthy_Glucose_Conc

DOCUMENT: The glucose concentration surplus is the difference between the actual glucose concentration and the healthy glucose concentration. The value will be positive (a surplus) if the actual concentration is higher than the healthy concentration. If there is a surplus glucose concentration, the B cells of the Islets of Langerhans will secrete insulin.
UNITS: milligrams/deciliter (mg/dL)

Converter

Healthy_Glucose_Conc = 100 milligrams/deciliter (mg/dL)

DOCUMENT: 70-120 milligrams/deciliter of glucose is normal for a person who has been fasting. We will assume that this person's healthy glucose concentration is 100 mg/dL.
UNITS: milligrams/deciliter (mg/dL)

Converter

Insulin_Conc = ACTIVE_INSULIN/Volume_of_Blood

DOCUMENT: The concentration of insulin in the blood is equal to the amount of insulin divided by the volume of blood. For this person it is assumed that a normal insulin concentration would be equal to 175 units/dL.
UNITS: units/deciliter

Converter

Norm_Release_Rate = 198 milligrams

DOCUMENT: 198 milligrams is the amount of glucose that will normally be released into the bloodstream each minute. This value changes as the amount and type of food eaten by the person changes.
UNITS: milligrams/minute (mg/min)

Converter

Volume_of_Blood = 60 deciliters

DOCUMENT: This is an assumed number for the volume of blood in an average human body. A normal person has 6 liters (60 dL) of blood in his body.
UNITS: deciliters (dL)

Converter

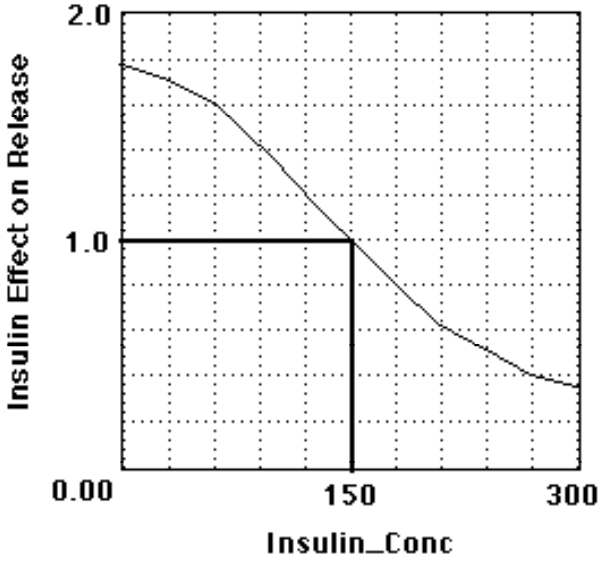
○ **Insulin_Effect_on_Release** = GRAPH(Insulin_Conc)

DOCUMENT: The effect that insulin has on the release of glucose into the bloodstream is a function of the amount of insulin. The insulin effects the liver's rate of transformation of glycogen to glucose.

At a normal insulin concentration of 150 units/dL, there is no effect on the release of glucose into the bloodstream. The normal glucose release amount of 198 mg/min is multiplied by 1.0 to give a glucose release rate of 198 mg/min.

If the insulin concentration is greater than normal, the extra insulin will cause a decrease in the amount of glucose that is released into the blood stream.

If the insulin concentration is less than normal, the lack of insulin will allow the release of more than the normal amount of glucose into the bloodstream.
UNITS: percent (%)



Input	Output
0.00	1.78
30.0	1.71
60.0	1.61
90.0	1.42
120	1.20
150	1.00
180	0.8
210	0.62
240	0.51
270	0.4
300	0.35

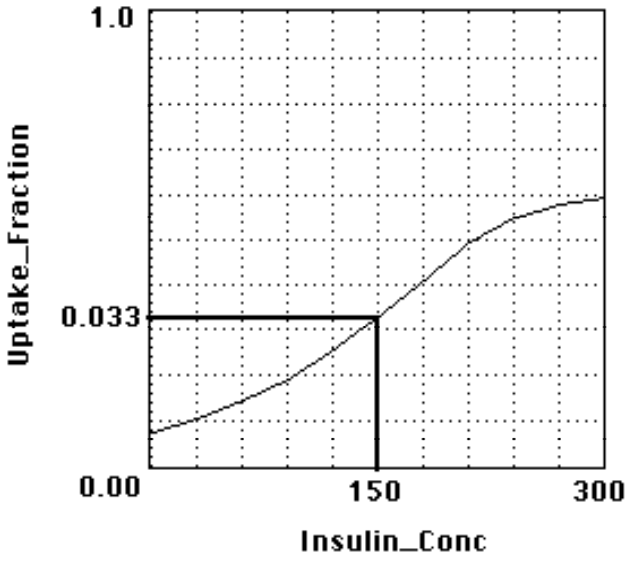
Converter

○ **Uptake_Fraction** = GRAPH(Insulin_Conc)

DOCUMENT: The glucose uptake fraction is the percentage of the total amount of glucose that will be taken up by the cells each minute. It is a graphical function dependent upon the amount of insulin. If insulin is at its normal level of 9000 units, the cells will uptake 3.3% of the available blood glucose.

If insulin is higher than the normal level, the cells will take up a larger fraction of the glucose until the insulin level gets too high and the cells are unable to take in as much glucose as the insulin would like to allow. At some point the fraction levels off because the cells can no longer take in a greater fraction of the glucose. This maximum uptake fraction is dependent upon the properties of the cell membrane.

If the insulin is lower than the normal level, the cells will be able take up only a smaller fraction of the available glucose. As insulin decreases, the fraction of glucose taken up decreases at a slower rate because the cells, which need the sugar for energy, will continue to take up as much as they possibly can given the available insulin.
UNITS: dimensionless (if the values are multiplied by 100 they will be a percent (%))



Input	Output
0.00	0.0075
30.0	0.0105
60.0	0.0145
90.0	0.019
120	0.0255
150	0.033
180	0.0405
210	0.049
240	0.0545
270	0.0575
300	0.059

The Endocrine System

Computer Exercises #1: Glucose Regulation

Name:_____Due Date:_____ Period:_____

Problem #1: Homeostasis

1a) A healthy glucose level in the blood for a normal person is 6,000 milligrams (mg). The amount of insulin in the blood necessary to regulate this healthy level of glucose is 9,000 units.

The model is currently set so:

GLUCOSE IN BLOOD = 6,000 milligrams (mg)

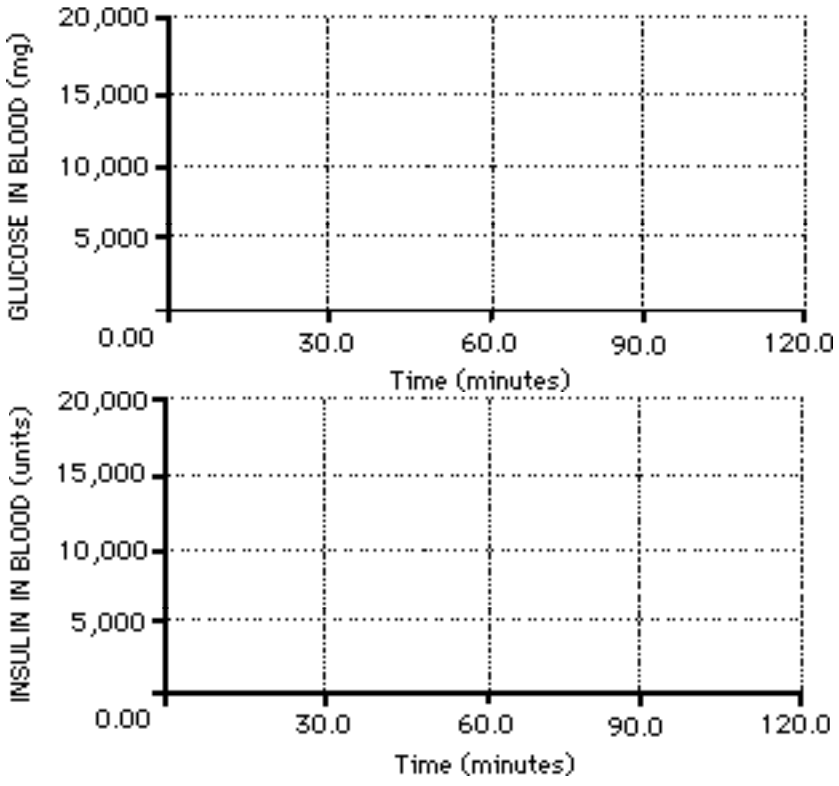
INSULIN = 9,000 units

Assume that there is a steady flow of glucose into the blood because the person is eating carbohydrates (rather than sugar) at necessary intervals. Because of the steady inflow which maintains the healthy level of glucose, the glucose and insulin levels will remain in its **homeostatic state (or equilibrium)**. To verify this, examine the computer generated behavior of insulin and glucose over time.

STEP 1: Select *Graph Pad* from under the *Windows* menu.

STEP 2: Select *Run* from under the *Run* menu.

Copy the computer generated graphs of insulin and glucose on the axes below:



1b) Explain the meaning of homeostasis (note that this is different than the homeostatic state explained above).

Homeostasis is_____

_____

_____

1c) Explain how these graphs represent homeostasis.

_____

_____

_____

_____

1d) Explain what would happen if the person switched from eating carbohydrates to eating sugar, such as in a candy bar.

_____

_____

_____

_____

Problem # 2: Glucose Surplus

2a) Suppose that a person has just eaten 4 candy bars causing the amount of glucose to jump from 6,000 to 12,000 mg. To implement this change in the model, the initial value of glucose must be changed from 6,000 to 12,000 mg:

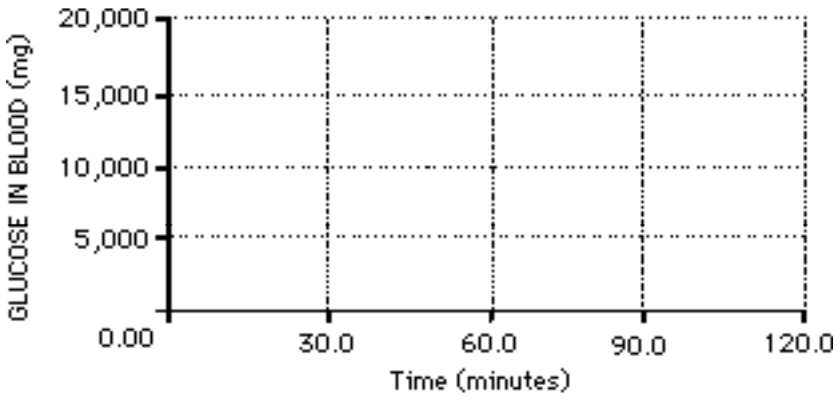
STEP 1: Double-click on the stock labeled *GLUCOSE IN BLOOD*.
STEP 2: Type *12000* on the keypad.
STEP 3: Click the *OK* button.

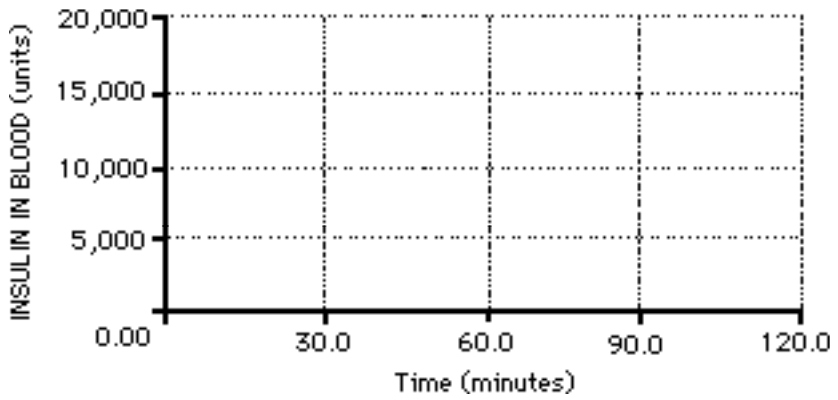
DO NOT RUN THE MODEL UNTIL YOU HAVE SKETCHED HOW YOU BELIEVE INSULIN AND GLUCOSE WILL BEHAVE. MAKE SURE THAT YOU DISCUSS WITH YOUR PARTNER HOW YOU BELIEVE INSULIN AND GLUCOSE WILL BEHAVE OVER TIME.

Now that we have said that the glucose begins at 12,000 mg, how do you think the system will behave over time?

Sketch your prediction of the graphs of insulin and glucose over time on the axes below:

Remember, the initial values are:
GLUCOSE IN BLOOD = 12,000 mg
INSULIN = 9,000 units

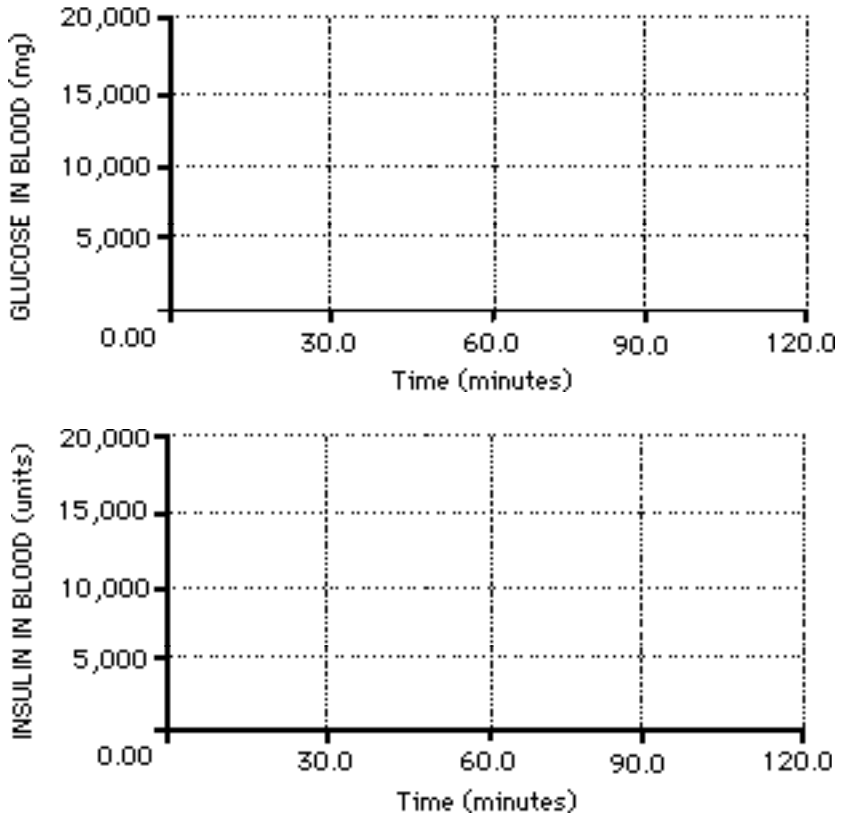




2b) Once you have completed your graphs, simulate the model:

STEP 1: Select *Graph Pad* from under the*Windows* menu.
STEP 2: Select *Run* from under the *Run* menu.

Copy the computer generated graph showing how insulin and glucose change over time:



2c) How close was your intuition to the computer generated results? Explain in a paragraph why insulin and glucose behaved as they did over time. *You may find it useful to refer to a causal loop or stock and flow diagram for this explanation.*
How Close?_____

_____

Explanation:_____

_____

_____

_____

_____

2d) Next, select *Table* from the Windows menu and record the final values of the stocks of GLUCOSE IN BLOOD and INSULIN. How do these numbers compare with the initial values of glucose and insulin which kept the model in homeostasis? Explain why these numbers are similar.

Final GLUCOSE IN BLOOD = _____ **Final INSULIN = _____**
Healthy GLUCOSE IN BLOOD = _____ **Healthy INSULIN = _____**

Explanation:_____
_____
_____

Problem #3: Increased Glucose Release Rate

Once you have completed Problem #2, return GLUCOSE IN BLOOD to its normal value by selecting **Revert** under the File menu and then selecting **do not save** when prompted by the program. If you are using an early version of STELLA, the **Revert** command may not be available to you. In that case, use the following steps:

STEP 1: Double-click on the stock labeled *GLUCOSE*.
STEP 2: Type *6000* on the keypad.
STEP 3: Click the *OK* button.

3a) Now assume the person decides to replace his carbohydrates with a candy bar's sugar. According to your answer in exercise 1d, which variable in the model will change?_____

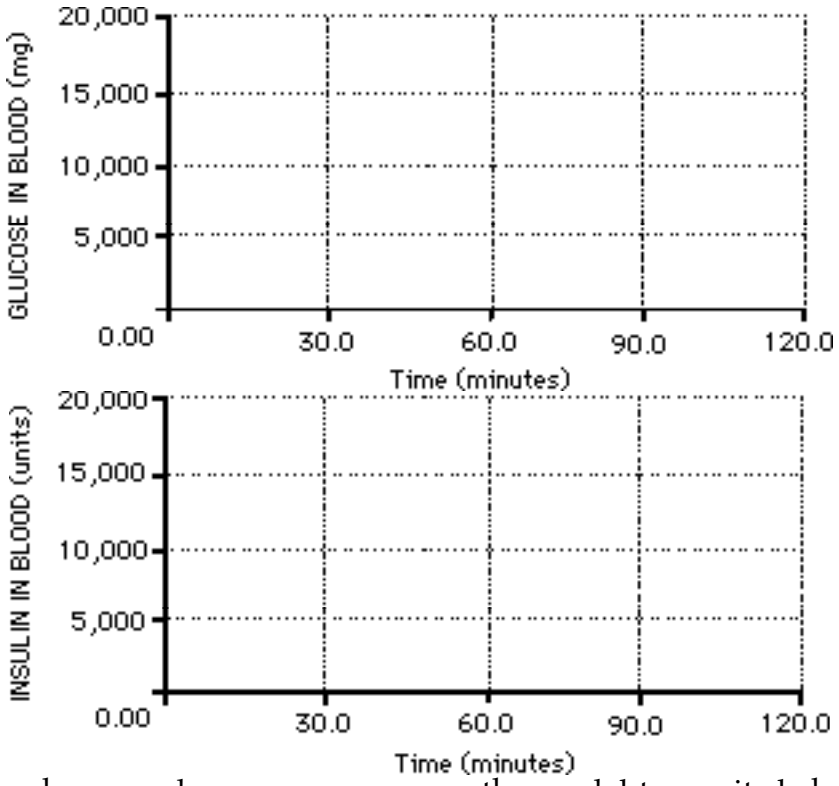
3b) Sugar is broken down much more quickly for release into the bloodstream. This is why it is possible to experience a brief sugar "high". Before a short race, athletes will often eat pure sugar or jello powder for quick energy.

In this case the change from eating carbohydrates to eating sugar will cause an increase in the rate at which glucose is released into the bloodstream. Modify the model so that there is an additional 1,000 mg/min of glucose flowing into the stock of GLUCOSE IN BLOOD:

STEP 1: Double-click on the flow labeled *Glucose Release Rate* if using models 1 or 2. For models 4 and 5, double–click on *Normal Release Rate*.
STEP 2: Type *1198* on the keypad.
STEP 3: Click the *OK* button.

3c) Sketch your prediction of the graphs of insulin and glucose over time on the axes below:

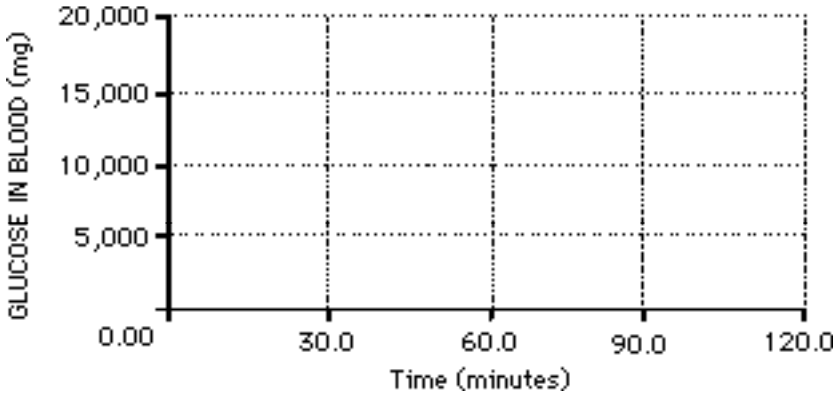
Remember, the initial values are:
GLUCOSE IN BLOOD = 6,000 mg
Glucose Release Rate = 1198 mg/minute
INSULIN = 9,000 units

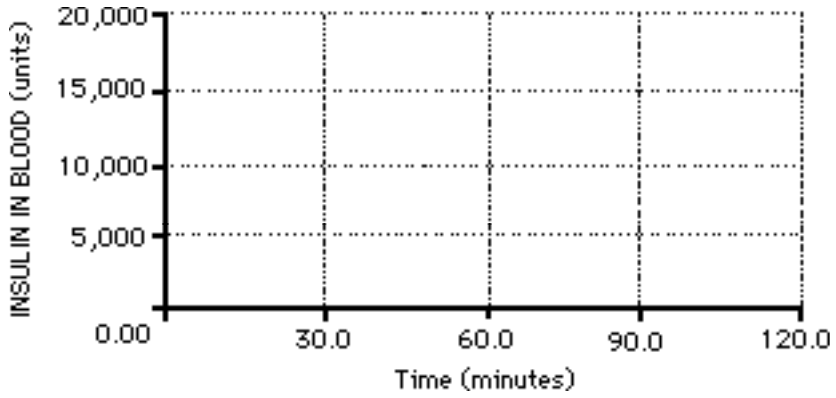


3d) Once you have made your guesses, run the model to see its behavior:

STEP 1: Select *Graph Pad* from under the *Windows* menu.
STEP 2: Select *Run* from under the *Run* menu.

Copy the computer generated graph showing how insulin and glucose change over time:





3b) Explain why the stocks of GLUCOSE and INSULIN exhibited this behavior through time. *You may find it useful to refer to causal loop or stock and flow diagrams in your explanation.*

Explanation:_____

_____

_____

_____

_____

_____

_____

3c) Did the graphs created from this simulation remind you of those in a prior simulation?_____
If so, of which simulation does it remind you? _____

Explain why the graphs of these two simulation would be similar in their behavior over time.

Explanation:_____

_____

_____

_____

_____

3d) Next, select *Table* from the *Windows* menu and record the final values of the stocks of GLUCOSE IN THE BLOOD and INSULIN. How do these numbers compare with the initial values of glucose and insulin which kept the model in homeostasis? Explain why these numbers are so similar.

FinalGLUCOSE IN BLOOD = _____Final INSULIN = _____ _
Healthy GLUCOSE IN BLOOD = _____Healthy INSULIN = _____

Explanation:_____

_____

_____

_____

_____

Problem #4: Deficit of Glucose

Once you have completed Problem #3, return GLUCOSE IN BLOOD to its normal value by selecting **Revert** under the File menu and then selecting **do not save** when prompted by the program. If you are using an early version of STELLA, the **Revert** command may not be available to you. In that case, use the following steps:

STEP 1: Double-click on the stock labeled *Glucose Release Rate* if using models 1 or 2. For models 4 and 5, double–click on *Normal Release Rate.*

STEP 2: Type *198* on the keypad.

STEP 3: Click the *OK* button.

4a) Now, assume that the GLUCOSE IN BLOOD starts out below the healthy level at an amount equal to 4,000 mg. From your understanding of the glucose regulatory system, explain what you think will happen and why. *Use causal loop or stock and flow digrams to back up your answer.*

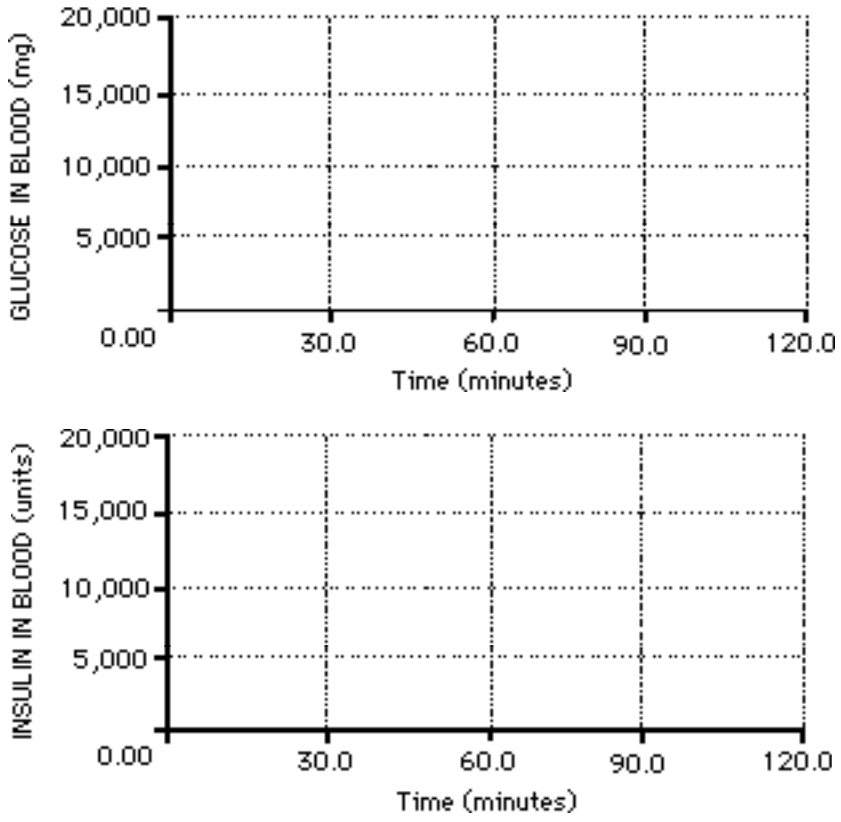
4b) Input the change in the STELLA diagram:

STEP 1: Double-click on the flow labeled *Glucose In Blood*.
STEP 2: Type *4000* on the keypad.
STEP 3: Click the *OK* button.

Once you have made your guesses, run the model to see its behavior:

STEP 1: Select *Graph Pad* from under the *Windows* menu.
STEP 2: Select *Run* from under the *Run* menu.

Copy the computer generated graph showing how insulin and glucose change over time:



4c) If your answer to 4a was incorrect, explain why the coputer generated graphs are correct.

Problem #5: Surplus of Insulin

Once you have completed Problem #4, return GLUCOSE IN BLOOD to its normal value by selecting **Revert** under the File menu and then selecting **do not save** when prompted by the program. If you are using an early version of STELLA, the **Revert** command may not be available to you. In that case, use the following steps:

STEP 1: Double-click on the stock labeled *GLUCOSE IN BLOOD*.
STEP 2: Type *6000* on the keypad.
STEP 3: Click the *OK* button.

5a) Now let's conduct another experiment where we change the initial amount of insulin from 9,000 units to 15,000 units:

STEP 1: Double-click on the stock labeled *INSULIN*.
STEP 2: Type *15000* on the keypad.
STEP 3: Click the *OK* button.

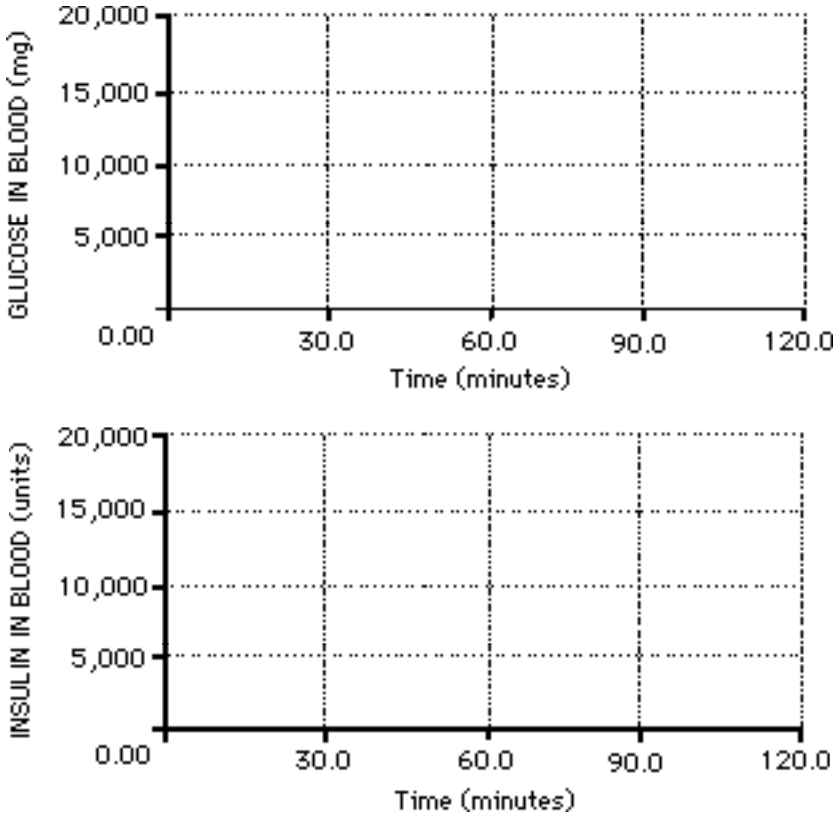
DO NOT RUN THE MODEL UNTIL YOU HAVE DESCRIBED HOW YOU BELIEVE INSULIN AND GLUCOSE WILL BEHAVE OVER TIME.

5b) How do you think the amount of insulin and glucose will behave over time given an initial insulin level of 15,000 units? WHY? *Use causal loop and STELLA diagrams to help explain your answer.*

5c) Once you have completed your explanation, simulate the model:

STEP 1: Select *Graph Pad* from under the*Windows* menu.
STEP 2: Select *Run* from under the *Run* menu.

Copy the computer generated graph showing how insulin and glucose change over time:



5d) How close was your intuition to the computer generated results? Explain in a paragraph why insulin and glucose behaved as they did over time. *You may find it useful to refer to a causal loop or stock an flow diagram for this explanation.*
How Close? _____

_____

Explanation:_____

_____

_____

_____

_____

_____

The Endocrine System

Computer Exercises #2: Diabetes

Name:_____Due Date:_____ Period:_____

Problem #1: Modeling a Diabetic

1a) There are two different forms of diabetes. The first is juvenile, while the second is adult-onset.[1] In juvenile diabetes the Beta cells of the pancreas are destroyed making the body unable to produce a sufficient amount of insulin. In other words, the Insulin Secretion Rate is lower than what would normally be expected.

Change the structure of the STELLA diagram to model a diabetic. Let's assume that the body is unable to produce any insulin because all of the Beta cells have been instantaneously destroyed(this is why the insulin level still begins at the normal level):

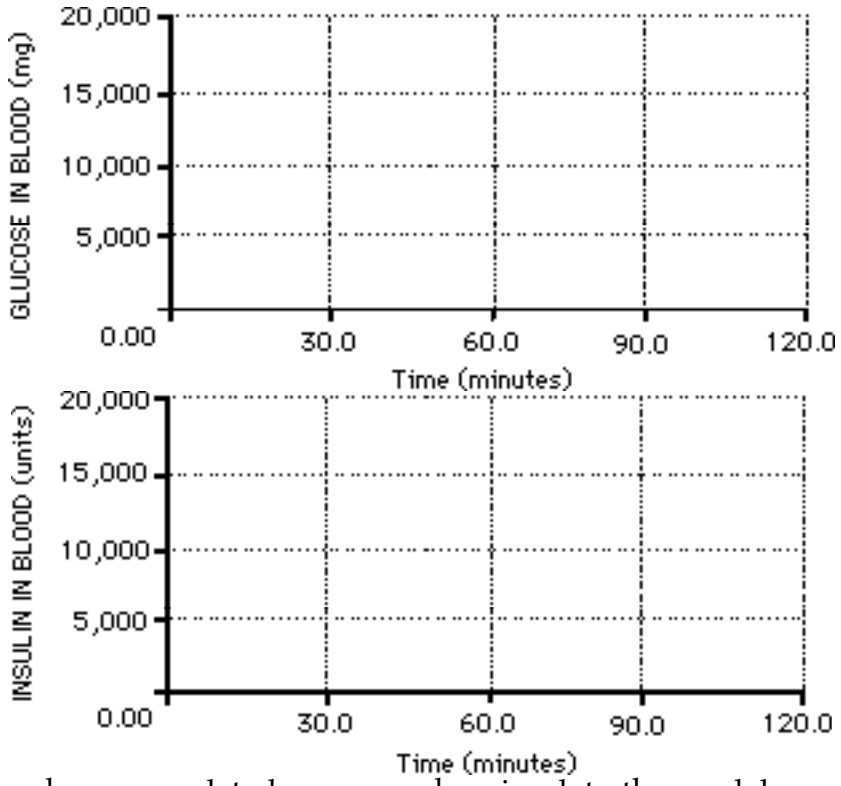
STEP 1: Double-click on the flow labeled *Insulin Secretion Rate*.
STEP 2: Click the *Delete Graph* button.
STEP 3: Type *0** (the required parameter: either *glucose surplus or glucose concentration surplus*) into the keyboard.
STEP 4: Click the *OK* button.

[1] Oram, Hummer, and Smoot. Biology: Living Systems.

On the following axes, graph how you think the glucose and insulin will now behave over time:

Remember, the initial values are:

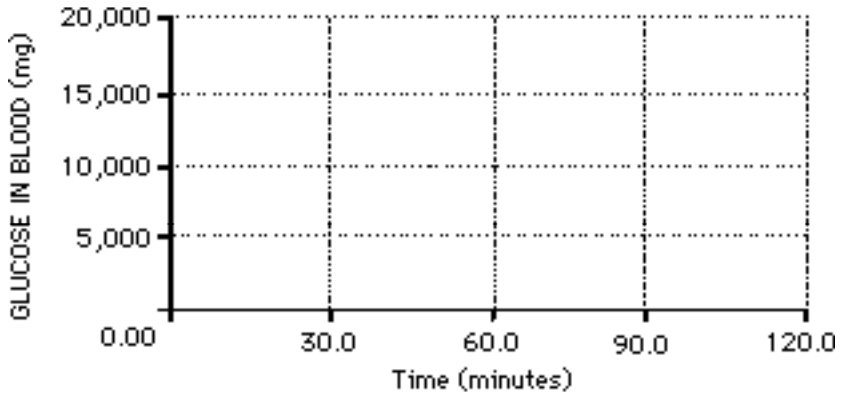
GLUCOSE IN BLOOD = 6,000 mg
INSULIN IN BLOOD = 9,000 units

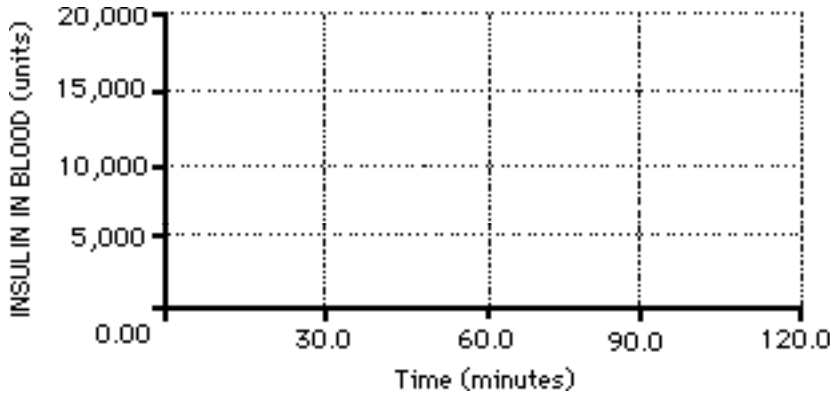


1b) Once you have completed your graphs, simulate the model:

STEP 1: Select *Graph Pad* from under the *Windows* menu.
STEP 2: Select *Run* from under the *Run* menu.

Copy the computer generated graphs of insulin and glucose on the axes below:





1c) How close was your intuition to the computer generated results? Discuss with your partner why insulin and glucose behaved as they did over time and write your explanation below.

How Close? _____

_____

Explanation: _____

_____

_____

_____

_____

_____

1d) Once you have completed Problem 1c, return the Insulin Secretion Rate to its normal value by selecting **Revert** under the File menu and then selecting **do not save** when prompted by the program. If you are using an early version of STELLA, the **Revert** command may not be available to you. In that case, use the following steps:

STEP 1: Select *Close* under the *File* menu.
STEP 2: When the prompt appears, click the *Don't Save* button..
STEP 3: Select *Open* under the *File* Menu.
STEP 4: Click on the *Glucose Regulation* STELLA *model*.

In the case of adult-onset diabetes, which model parameter do you think will be affected?_____

Change the parameter to model adult-onset diabetes:

STEP 1: Double-click on *Glucose Uptake Rate*.
STEP 2: Type *GLUCOSE IN BLOOD * Uptake Rate * 0*.
STEP 3: Click the *OK* button.

1e) Describe what you expect to be the behavior of insulin and glucose in the blood over time.

1f) Once you have completed your graphs, simulate the model:

STEP 1: Select *Graph Pad* from under the *Windows* menu.
STEP 2: Select *Run* from under the *Run* menu.

If the behavior that you guessed was different than the computer generated behavior, explain why the computer generated behavior is correct.

Problem #2: Modeling Insulin Injections

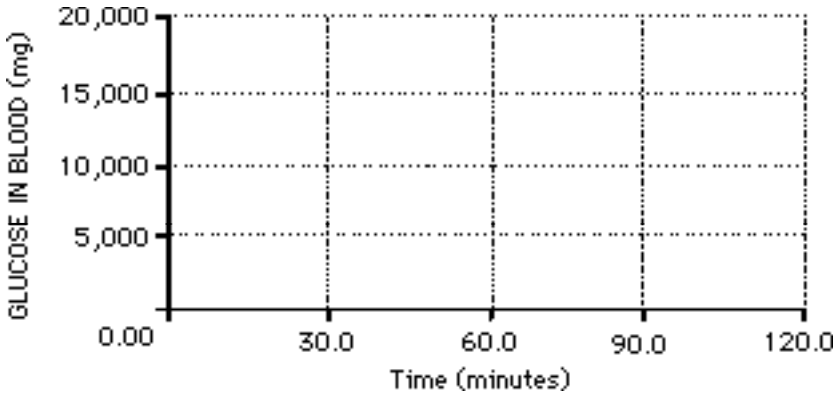
Once you have completed Problem #1, return the Glucose Uptake Rate to its normal value by selecting **Revert** under the File menu and then selecting **do not save** when prompted by the program. If you are using an early version of STELLA, the **Revert** command may not be available to you. In that case, use the following steps:

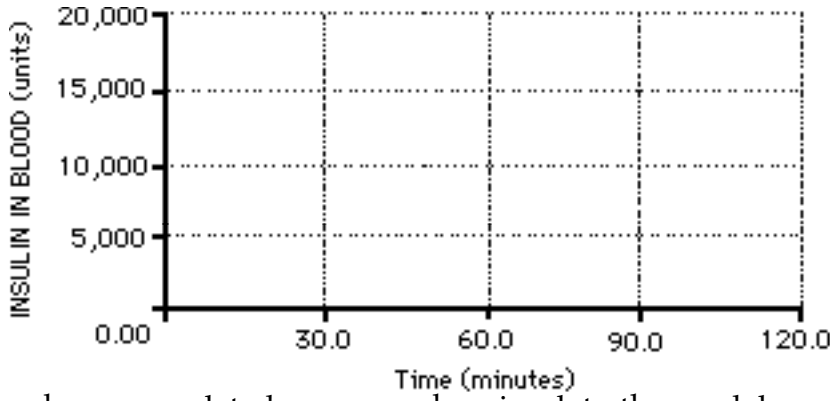
STEP 1: Double-click on *Glucose Uptake Rate*.
STEP 2: Type *GLUCOSE IN BLOOD * Uptake Rate* on the keyboard.
STEP 3: Click *OK* button.

2a) A person with youth-onset diabetes needs to add to his supply of insulin in order to survive. One way to do this is through insulin injections. Since an insulin injection puts insulin directly into the blood, it can be modeled as a flow. If you have any questions, raise your hand so that a teacher can help you.

STEP 1: Double-click on the flow labeled *Insulin Secretion Rate*.
STEP 2: Click the *Delete Graph* button.
STEP 3: Type *0** (the required parameter: either *glucose surplus or glucose concentration surplus*) into the keyboard.
STEP 4: Click the *OK* button - this cuts off the normal insulin secretion.
STEP 5: Click once on the *flow* icon to the left of the STELLA diagram.
STEP 6: Place the arrow one inch below the INSULIN stock.
STEP 7: Click and hold the mouse button.
STEP 8: Drag the mouse until the INSULIN stock darkens.
STEP 9: Release the button.
STEP 10: Type *Insulin Injections*.
STEP 11: Double-click on the new flow labeled *Insulin Injections*.
STEP 12: Type *pulse (12000,30,30)* .
- this tells the computer to inject 12,000 units of insulin every 30 minutes
STEP 13: Click the *OK* button.

Now, the only flow of insulin into the blood comes from injections.
Sketch your prediction of the behavior of insulin and glucose over time on the axes below:
Remember, the initial values are:
GLUCOSE IN BLOOD = 6,000 mg
INSULIN = 9,000 mg

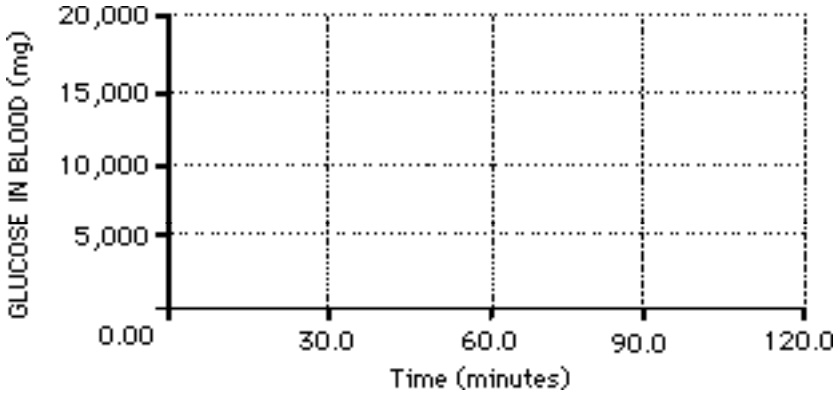


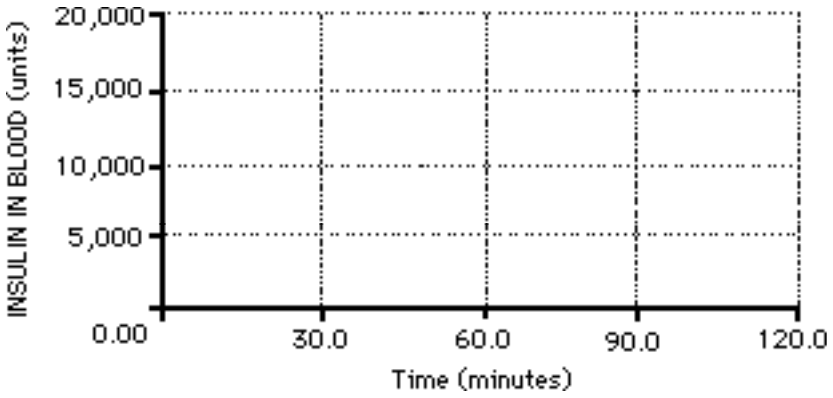


2b) Once you have completed your graphs, simulate the model:

STEP 1: Select *Graph Pad* from under the *Windows* menu.
STEP 2: Select *Run* from under the *Run* menu.

Copy the computer generated graph showing how insulin and glucose change over time:




INSULIN IN BLOOD (units)
20,000
15,000
10,000
5,000
0.00
30.0
60.0
90.0
120.0
Time (minutes)

2c) How close was your intuition to the computer generated results? Explain in a paragraph why insulin and glucose behaved as they did over time. *You may find it useful to refer to a causal loop or stock and flow diagram for this explanation.*

2d) What difficulties do you think occur with the use of injections?

2e) What are some possible ways that these difficulties might be prevented?

2f) Do you think adding insulin would help a person who has adult-onset diabetes?____
Why or why not?_____

Problem #3: Modeling Insulin Pumps

3a) Insulin injections help the body regulate glucose, but they do not keep the body in homeostasis. Devices known as insulin pumps help to maintain the body's blood glucose at levels closer to equilibrium (homeostasis). Insulin pumps constantly release insulin into the blood at a certain rate, rather than making one large injection every thirty minutes.

To model an insulin pump:

STEP 1: Click once on the flow labeled *Insulin Injections*.
STEP 2: Type *Insulin Pump Rate* to rename the flow.
STEP 3: Double-click on the new flow labeled *Insulin Pump Rate*..
STEP 4: Type any number between 0 and 1000.
-The number you typed above will be the number of units of insulin per minute which is secreted into the blood.
STEP 5: Click the *OK* button.

Simulate the model and observe the results on the graph pad:

STEP 1: Select *Graph Pad* from the *Windows* menu.
STEP 2: Select *Run* from the *Run* menu.

3b) Record the value typed in for the Insulin Pump Rate. When you ran the model, was the system in homeostasis? If not, was it because the Insulin Pump Rate was too high or too low? Go back and change the insulin pump rate until you find a value which keeps the body in homeostasis.

TRY #1: Insulin Pump Rate = _____
Is the body in homeostasis?_____
If not, is the Insulin Pump Rate too high or too low?_____

TRY #2: Insulin Pump Rate = _____
Is the body in homeostasis?_____
If not, is the Insulin Pump Rate too high or too low?_____

TRY #3: Insulin Pump Rate = _____
Is the body in homeostasis?_____
If not, is the Insulin Pump Rate too high or too low?_____

TRY #4: Insulin Pump Rate = _____
Is the body in homeostasis?_____
If not, is the Insulin Pump Rate too high or too low?_____

Keep Trying!!!

Homeostasis was achieved when the Insulin Pump Rate = _____.

3c) What if the level of glucose in the blood was changing all the time as it would in a normal human body? Would the value that achieved homeostasis in this case still maintain homeostasis?_____

3d) Test your answer by going into the model and changing the initial stock of glucose to 8,000 mg:

STEP 1: Double-click on the stock labeled *GLUCOSE IN BLOOD*.
STEP 2: Type *8000* on the keypad.
STEP 3: Click the *OK* button.
STEP 4: Select *Graph Pad* from under the *Windows* menu.
STEP 5: Select *Run* from under the *Run* menu.

Is the system still in homeostasis?_____

3e) Explain why the system does not remain in homeostasis.

_____

_____

_____

_____

3f) What changes can be made in the method of administering insulin to ensure that the diabetic will be able to maintain his blood glucose level at equilibrium?

_____

_____

_____

_____

_____

Problem # 4: Improved Insulin Pump

How might this model be modified in order to show the structure of this new method of administration? You may draw the complete structure below. *Consider the first model that you used as well as the model of the insulin pump.*

_____
_____
_____
_____
_____
_____
_____

If you have extra time at the end of class or during a free period, you may try to build the model you developed above on the computer.

Suggested Evaluation

The evaluation could consist of either an in class test or a written take home paper describing their experience on the computer and what they learned in it. An oral presentation of some aspect of the lesson would also be beneficial.

Test Questions:

1) Explain the difference between feedback and homeostasis. Decsribe the relationship between them.

Answer -> Homeostasis is the internal equilibrium that is maintained by the body's regulatory system. It is homeostasis which keeps the body's chemicals at their healthy levels. Feedback is the process necessary for the body to be able to regulate its systems. Infomation about the stock to be controlled must feedback to the hormone that is used to regulate the level. For example, when the glucose level gets too high, information about the surplus goes to the Pancreas where the Islets of Langerhans are notified of the surplus. The Beta Cells of the Pancreas then secrete the necessary insulin to bring the system back to equilibrium. If the feedback had not been there, the Beta cells would not have known to secrete the insulin.

2) Explain the three methods for controlling the blood glucose level in a diabetic. Which method is preferred and why? Why are the other two methods less desirable?

Answer -> Insulin injections involve injecting set amount of insulin at given intervals. The problem here is that the insulin is very high to begin with, but drops quickly, causing oscillations in the blood glucose level. This is not ideal for homeostasis.

One answer to the insulin injections is the insulin pump. The insulin pump pumps insulin into the bloodstream at a steady rate. This solves the problem of insulin injections by smoothing out the level of blood glucose. However, it is not ideal because it does not respond to the changing amount of glucose in the blood. At sometimes the level might be higher than the pump is set to respond to.

The third method involves an insulin pump with some form of feedback to tell it how much insulin to pump in. This is most like the body's own glucose regulatory system and would be the best substitute for normally functioning Beta cells.

3) Describe the two main feedback mechanisms that are crucial in maintaining the body's healthy blood glucose level.

Answer -> The two feedback mechanisms involve the effects that the increased level ofinsulin caused by an increase in the blood glucose level has on th eflows into the stock of glucose in the blood. Increased insulin causes a decrease in the glucose release rate into the blood and an increase

4) What is the difference between a homeostatic and non-homeostatic loop? Give one example of each.

5) If the human body is unable to produce enough insulin, what will happen to the body's cells?

6) In what way is the body's temperature regulation system similar to that of its glucose regulation system? You may use causal loop diagrams to help explein your answer.

Glucose Regulation Curriculum Evaluation

Tad Sudnick used this curriculum packet in his intensive biology class in May of 1991. The following statements were made by him after using the computer simulation model to illustrate the body's glucose regulatory system.

What was the biggest area in which you hoped to improve your class/teaching before the endocrine chapter?

I wanted to improve my teaching by offering more variety in teaching methods to appeal to various students' learning styles.

What, if anything, do you feel that the use of system dynamics helped in adding to this improvement?

Some students who were not performing well before were really "turned on" to the content because of system dynamics.

Relate any(all) singular incidents that made you glad you were using system dynamics in the classroom.

The day we went down on the computers was the best! What was great about it was that the students were in control of their learning--not me! All the students were enjoying the freedom of "playing" with the system and seeing how changes they made in the system affected glucose and insulin levels in the run. I heard many enthusiastic comments between students, like "Now we get to do some injections!" as if they were actually working on a real patient. One student also said things like, "When are we going back to the computers?" and "I like systems dynamics" a lot. This showed in his homeworks where he communicated using causal connections.

Relate all singular incidents that caused you to doubt your decision to introduce systems thinking.

Monday morning many students said they didn't understand all the stocks and flow stuff, but I later realized they were just being reluctant to change and wimpy about digging in and understanding it. By Thursday I was sure that nearly all the students understood and saw the value of stock and flow diagrams.

Overall, what was your impression of the effects of lectures using causal diagrams?

I think that using causal diagrams in the lectures constantly reminded the students about the incredible sensitivity to and need for homeostatic conditions. Causal diagrams help drive home the fact that human internal operations are in dynamic equilibrium.

What were your impressions of the computer simulation?

It was the high point of the unit. The students were empowered learners and were involved in great dialogues. Students discussed and conferred with each other about what might be the result of changing one parameter. Students to student dialogue is often a much more effective learning tool than teacher to student dialogue. It's real nice to see students having a discussion about science instead of simply asking each other "what did you get on question #4?"

Which aspects of this chapter and the teaching method disappointed you?

The only thing that was disappointing was my time constraints. I think the content of the chapter was all relevant and important and I waspleased with the teaching methods used to deliver the content. I guess I only wish I had hopped onto the computer simulations earlier in the chapter.

What changes would you make if you were to use system dynamics again in the future?

I would start my teaching year using system dynamics so that it will become a learning tool throughout the year.

What sorts of things would you like to teach in the future using system dynamics and computer simulation?

-Food chains, Food Webs
-Risk Assessment, Benefit Analysis on issues like hazardous waste disposal
-Fish Banks simulations
-Photosynthetic and respiration rates affected by reactant availability
-Human systems

Any additional comments, suggestions, complaints?

When I saw the students discussing with each other how they formulated their guesses at what the graphical run would look like and getting excited about the resulting run whether their hypothesis was right or wrong, I fully understood what learner-directed learning really means. When students learn this way they become intrinsically motivated to learn and gain more responsibility and control on their learning process. That's the way it should be.

Sources, Resources, and Suggested Reading

Sources

Oram, Raymond F., Hummer Jr., Paul J., and Smoot, Robert C., *Biology: Living Systems.* Columbus: Charles E. Merrill Publishing Co., 1983.

Richmond, Barry, et al. *STELLA II User's Guide*, Hanover, NH: High Performance Systems, Inc., 1990.

Resources and Suggested Reading

Professional endocrinologists and doctors may be good sources of information on glucose regulation and diabetes. In the Boston Metropolitan Directory, they are listed by specialty (i.e. diabetes and endocrinology).

MIT Medical Department

Certified Diabetic Educators

American Diabetes Association

"Diabetes." *Sciquest*, October, 1980.

O'Malley, Bert W., and Schrader, William T., "The Receptors of Steroid Hormones." *Scientific American*, February, 1976.

Nourse, Alan E., *Hormones.* New York: Franklin Watts, Inc., 1979.

Silverstein, Alvin, and Silverstein, Virginia, *The Sugar Disease: Diabetes.* New York: J.B. Lippincott, 1980.