BME 444
Glucose Homeostasis 1
April 18, 2024

System Overview

The human body carefully maintains fasting blood glucose concentrations within a range of 80–90 mg/dl of blood. This process is called *glucose homeostasis*. After a meal, blood glucose concentration increases. The increase in glucose is sensed by β-cells in the pancreas (Figure 1) and they begin to secrete insulin in response. Insulin enters the blood where it is distributed throughout the body and signals cells to increase their glucose uptake from the blood. The liver, in particular, absorbs a significant amount of glucose compared to other tissues. The net result is that the blood glucose level falls back to its normal range. As the blood glucose level falls, the β -cells sense less glucose and in response secrete less insulin. Figure 2 shows the effect of meals on blood glucose and blood insulin levels over a 24 hour period.

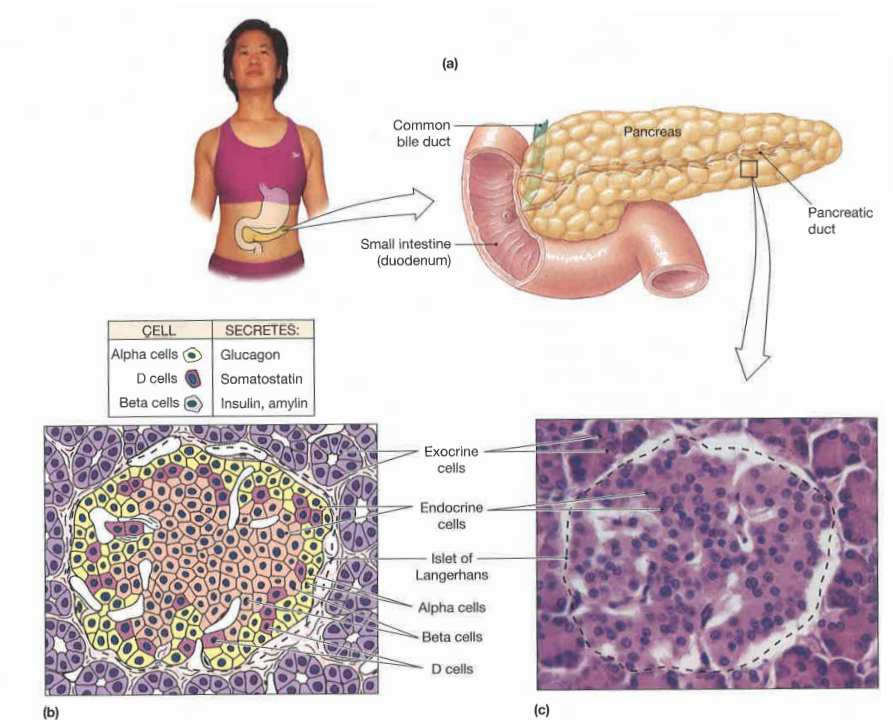


Figure 1. *Overview of pancreas structure. Beta cells comprise the vast majority of cells within the pancreas. (From Moffet, Moffet, and Schauf 1993).*

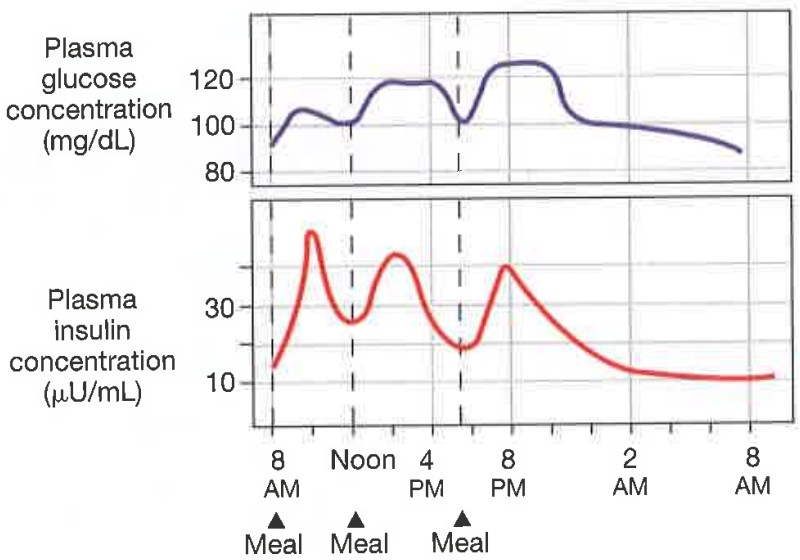


Figure 2. *Blood (plasma) glucose and insulin levels over time. Note how insulin levels lag the glucose levels. (From Moffet, Moffet, and Schauf 1993).*

System Model

Assume we want to model glucose homeostasis and insulin homeostasis as a single compartment model. Since we wish to model two different mass species, we will need two differential equations.

The first differential equation is a mass balance for glucose (GLU). There is one input for GLU. It can enter the system through absorption from gastrointestinal tract, intravenous infusion, or supply from the liver. There are two outputs for GLU: (1) passive diffusion into the liver and tissue (controlled by GLU concentration) and (2) facilitated diffusion into the tissues (controlled by insulin (INS) concentration), which can be 20x larger that the passive diffusion rate. Note that "controlled by" means "multiplied by". Assume the coefficient δ is the rate constant for passive diffusion and the coefficient γ is the rate constant for facilitated diffusion.

The second differential equation is a mass balance for INS. There are two inputs for INS: (1) intravenous infusion (injection), and (2) production in the pancreas due to the beta-cells of the islets of Langerhans. Output is by inactivation (consumption) by blood insulinase activity. Assume the coefficient α is the rate constant for consumption and β is the rate constant for secretion from the pancreas.

Lesson 19 Student Exercises - Due by Apr 20

1. Write the mass balance equations for glucose and insulin. Use *g* for glucose mass and *i* for insulin mass.

$$\frac{dGLU}{dt} = ? \qquad \text{and} \qquad \frac{dINS}{dt} = ?$$

2. Convert the equations from (1) into LaPlace notation and enter them into MATLAB. Use solve() to find expressions for GLU and INS. Use the function collect() to simplify the expressions once you have solved for them. Rearrange the equations to get something that looks like the equations shown below.

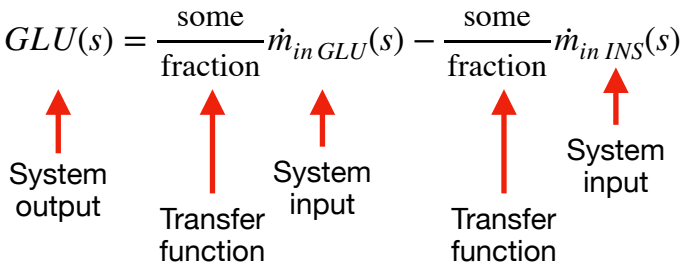
$$GLU(s) = \frac{\text{some}}{\text{fraction}}\dot{m}_{in\,GLU}(s) - \frac{\text{some}}{\text{fraction}}\dot{m}_{in\,INS}(s)$$

and

$$INS(s) = \frac{\text{some}}{\text{fraction}}\dot{m}_{in\,GLU}(s) + \frac{\text{some}}{\text{fraction}}\dot{m}_{in\,INS}(s)$$

3. From visual inspection of the transfer functions from #2, what is the order of each system?

4. Build a model containing the equations from #2 in Simulink. To get you started, consider visualizing the first equation like this:



Use a total simulation time of 24 (hrs). Use the variable solver ode15s. Enter the following values for the coefficients into your model:

$\alpha = 0.916\,\text{hr}^{-1}$
$\beta = 0.198$ unit/hr/gm
$\gamma = 3.23$ gm/hr/unit
$\delta = 0.304$ gm/hr/gm

Use SCOPE blocks to plot *GLU* and *INS*. Assume $\dot{m}_{in\,GLU}$ is a step input with a value of 100 gm/hr and $\dot{m}_{in\,INS} = 0$. What type of system does each response suggest? Why?

5. Plot *GLU* and *INS* if $\dot{m}_{in\,INS}$ is an insulin step input with a value of 100 gm/hr and $\dot{m}_{in\,GLU} = 0$. What type of system does each response suggest? Why?

6. What is the %OS for #4 and #5? NOTE: you cannot directly calculate ζ using the formulas we used in class because the transfer function has the term $(s+a)$ in the numerator. Instead, write the output of each to the workspace and find the maximum and then calculate the %OS.

7. Assume the glucose transfer function is $T_{GLU}(s) = \dfrac{GLU(s)}{\dot{m}_{inGLU}}$ when $\dot{m}_{inINS} = 0$. Assume $T_{INS}(s) = \dfrac{INS(s)}{\dot{m}_{inINS}}$ when $\dot{m}_{inGLU} = 0$. Are $T_{GLU}(s)$ and $T_{INS}(s)$ stable? Prove your answer.

8. Determine the steady-state error for $T_{GLU}(s)$ and $T_{INS}(s)$. For $T_{GLU}(s)$ SSE, assume $\dot{m}_{inINS} = 0$ and $\dot{m}_{inGLU}$ is a step input of amplitude 100 gm/hr. For $T_{INS}(s)$ SSE, assume $\dot{m}_{inGLU} = 0$ and $\dot{m}_{inINS}$ is a step input of amplitude 100 gm/hr.