BME 444
Glucose Homeostasis 2

**Modeling Type 1 Diabetes**

Type 1 (insulin-dependent) diabetes is characterized by dysfunctional beta cells that cannot produce sufficient insulin to control blood glucose levels. This disorder typically appears during childhood and is also known as juvenile-onset diabetes. If an adult develops Type 1 diabetes it is known as ketone-prone diabetes. Type 1 diabetics must carefully monitor their blood sugar levels and be prepared to ingest a high sugar snack if blood glucose levels fall too low, or inject insulin if blood sugar levels are too high.

We can use the model that you developed above to explore how Type 1 diabetes changes the response to a glucose input.

1. Determine which parameter (greek letter) in your model is best suited to model a lack of insulin secretion in response to glucose.

   $\beta$

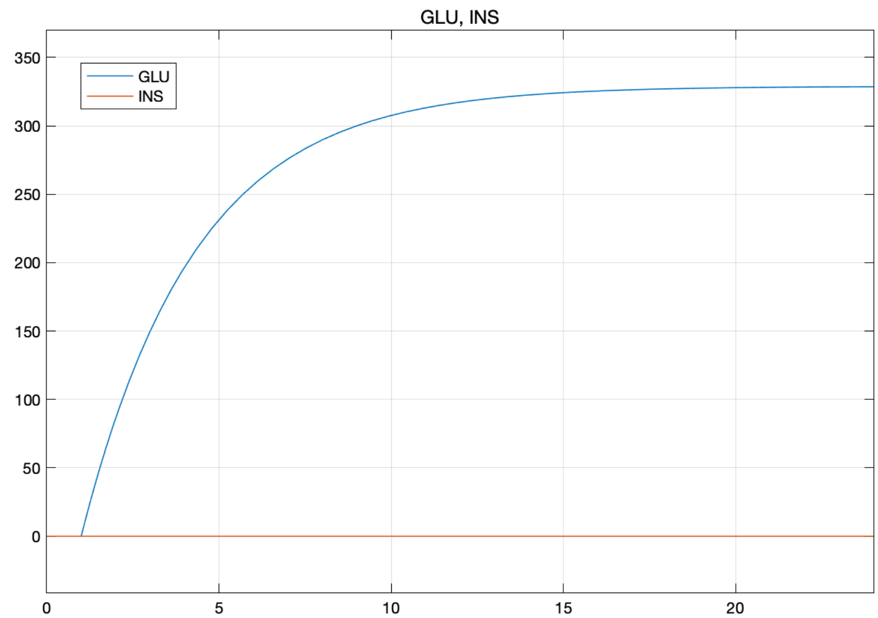
2. Adjust this parameter to 0% of the value you used in Lesson 19 and generate new equations for GLU and INS.

$$GLU = \frac{s + 0.916}{s^2 + s1.22 + 0.278}\dot{m}_{inGLU} - \frac{3.23}{s^2 + s1.22 + 0.278}\dot{m}_{inINS}$$

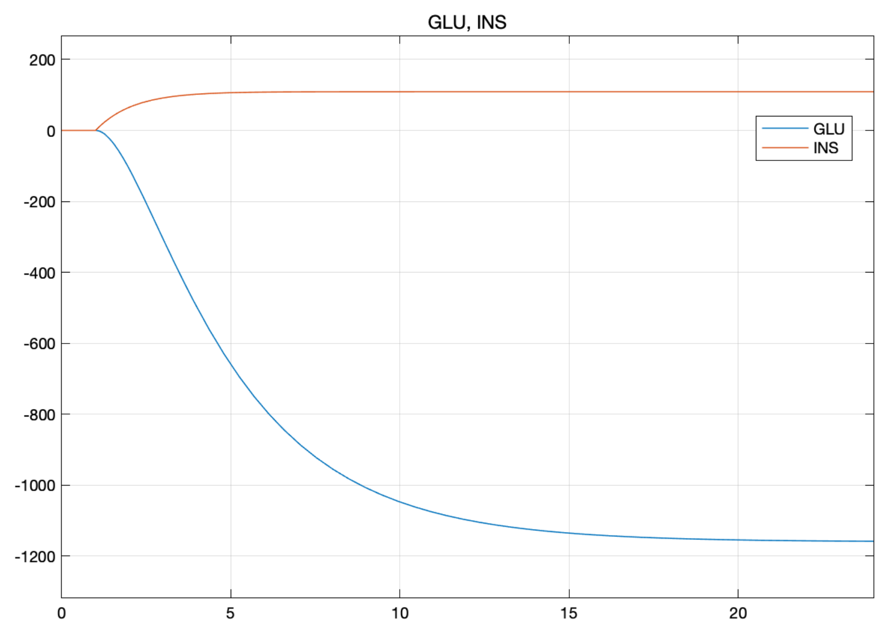
   and

$$INS = \frac{s + 0.304}{s^2 + s1.22 + 0.278}\dot{m}_{inINS}$$

3. Plot the transient glucose and insulin response if $\dot{m}_{in\,GLU}$ is a step input with a value of 100 gm/hr and $\dot{m}_{in\,INS} = 0$.




4. Plot the transient glucose and insulin response if $\dot{m}_{in\,INS}$ is an insulin step input with a value of 100 gm/hr and $\dot{m}_{in\,GLU} = 0$.




5. How do glucose and insulin respond to a glucose step input compared to a non-diabetic? How do glucose and insulin respond to an insulin step input compared to a non-diabetic? Do the responses to a glucose step input make sense to you? Remember that the glucose

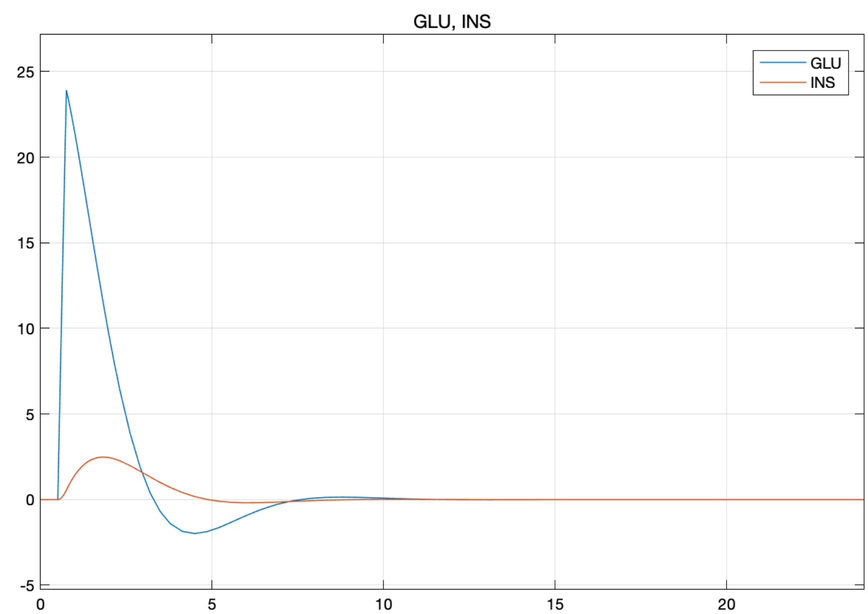
homeostasis system is a regulator, and glucose levels closer to the input step magnitude are better.

GLU step
The diabetic has a much higher steady-state value, no overshoot, and 0 insulin response

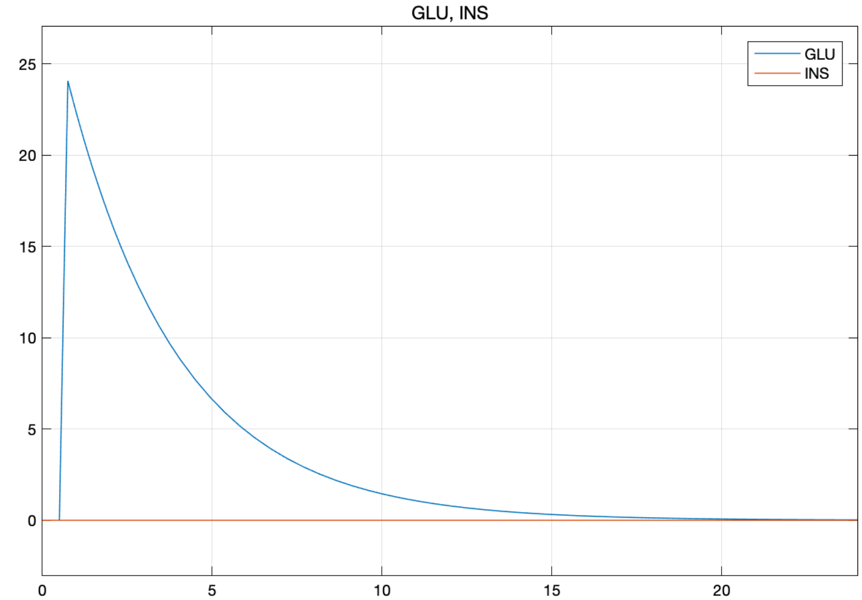
INS step
The diabetic has a lower glucose level and higher steady-state insulin value; responses appear to be first-order (or crit/over damped second order)

The GLU step response makes sense because there is no INS to metabolize the GLU step input; The INS step response makes sense too because there is no GLU input term to help boost the steady-state level of the INS response

6. Plot the transient glucose and insulin response of a normal patient and the Type 1 diabetic to the glucose tolerance test. How does each respond?




Normal




Type 1 diabetic

The non-diabetic GLU level returns to 0 faster than the T1D

7. Are the Type 1 glucose and insulin transfer functions stable? How do you know?

   Look at roots of equations; same denominator and both stable

8. Determine the steady-state error for $T_{GLU}(s)$ and $T_{INS}(s)$ for a Type 1 diabetic. For $T_{GLU}(s)$ SSE, assume $\dot{m}_{in\ INS} = 0$ and $\dot{m}_{in\ GLU}$ is a step input of amplitude 100 gm/hr. For $T_{INS}(s)$ SSE, assume $\dot{m}_{in\ GLU} = 0$ and $\dot{m}_{in\ INS}$ is a step input of amplitude 100 gm/hr. How does the steady-state error of a Type 1 diabetic compare to a healthy person?

   SSE for $T_{GLU}(s)$ = -228.9

   SSE for $T_{INS}(s)$ = -9.170

   WRT to a non-diabetic, the GLU SSE is far worse than for a non-diabetic (0.218); INS SSE is worse too, considering that 100 is the desired output; non-diabetic INS is 66.88 for comparison

**Modeling Type 2 Diabetes**

Type 2 (non-insulin-dependent) diabetes is characterized by a lack of tissue response to insulin. The pancreas senses blood glucose normally and produces insulin, but the tissues do not respond to increased insulin levels with increased glucose uptake. This type of diabetes usually occurs in adults and is sometimes known as *adult onset diabetes*.

We can use the model that you developed above to explore how Type 2 diabetes changes the response to a glucose input.

1. Determine which parameter (greek letter) in your model is best suited to model Type 2 Diabetes.

   $\gamma$

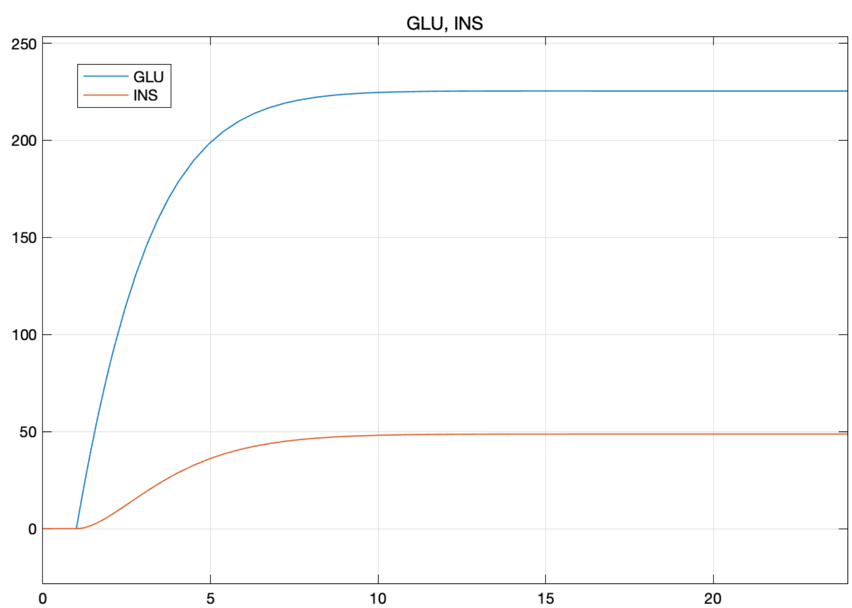
2. Adjust this parameter to 20% of the value you used in Lesson 19 and generate a new transfer function.

$$GLU = \frac{s + 0.916}{s^2 + s1.22 + 0.406}\dot{m}_{inGLU} - \frac{0.646}{s^2 + s1.22 + 0.406}\dot{m}_{inINS}$$

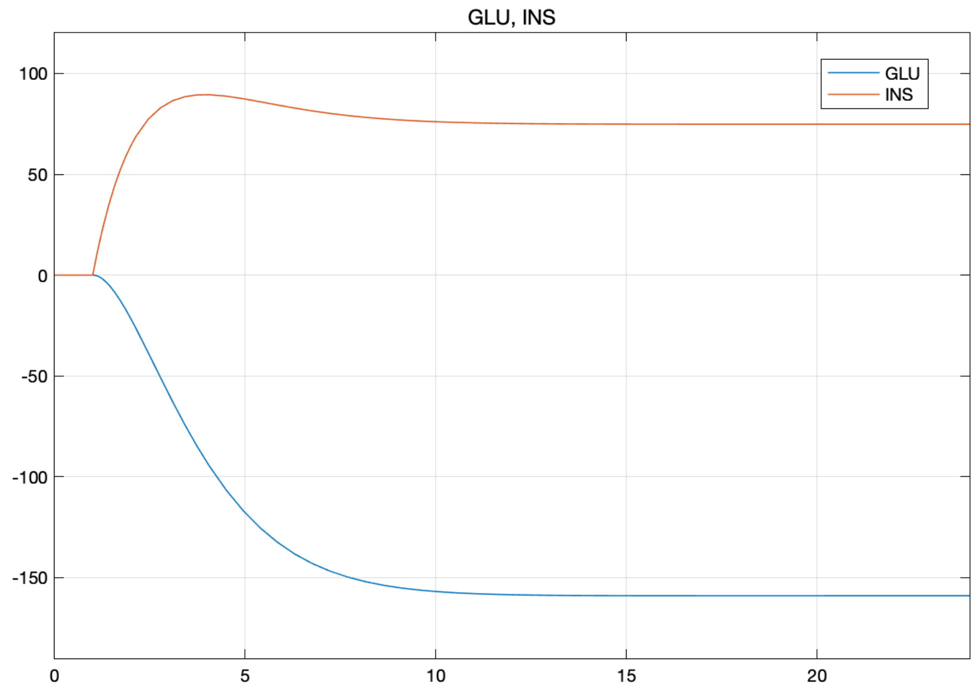
   and

$$INS = \frac{0.198}{s^2 + s1.22 + 0.406}\dot{m}_{inGLU} + \frac{s + 0.304}{s^2 + s1.22 + 0.406}\dot{m}_{inINS}$$

3. Plot the transient glucose and insulin response if $\dot{m}_{in\,GLU}$ is a step input with a value of 100 gm/hr and $\dot{m}_{in\,INS} = 0$.



4. Plot the transient glucose and insulin response if $\dot{m}_{in\,INS}$ is an insulin step input with a value of 100 gm/hr and $\dot{m}_{in\,GLU} = 0$.



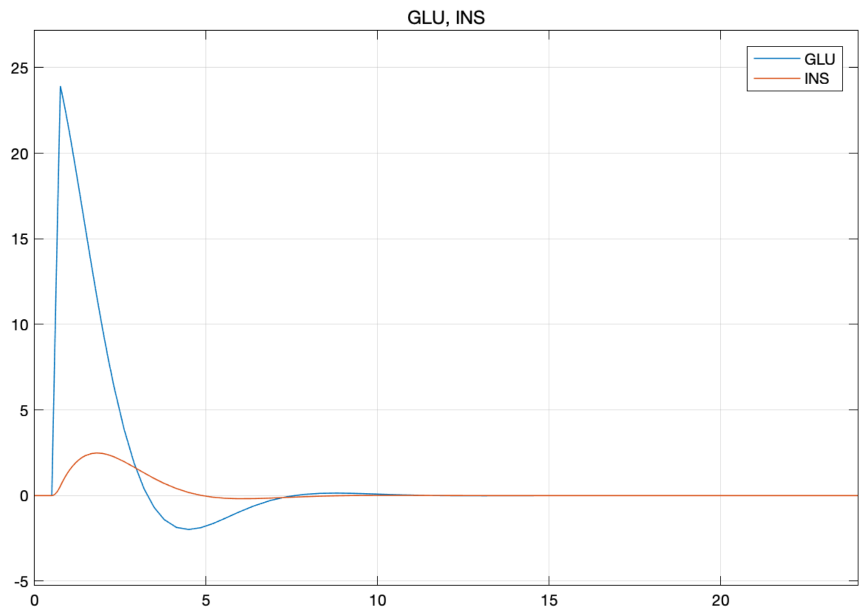

5. How does glucose and insulin respond to a glucose step input compared to a non-diabetic? How does glucose and insulin respond to an insulin step input compared to a non-diabetic? Do the responses to a glucose step input make sense to you? Remember that the glucose homeostasis system is a regulator, and glucose levels closer to the input step magnitude are better.

GLU step
The diabetic has a higher steady-state value, no overshoot, and insulin is higher than with T1 diabetic. INS also higher than non-diabetic; responses appear to be first-order (or crit/over damped second order)

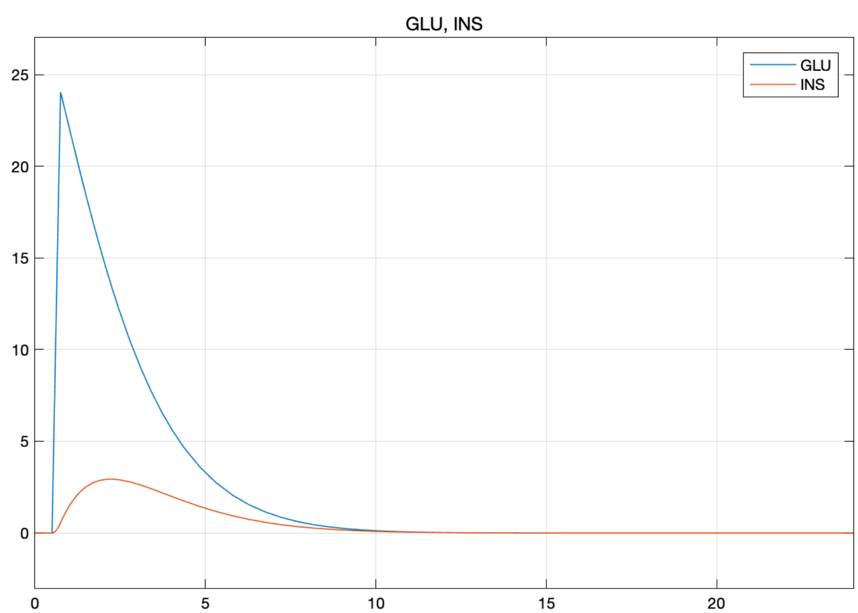
INS step
The glucose level does not go as negative on a T2 diabetic than non-diabetic; (~-160 vs -350); The INS response is higher for the T2 diabetic than non-diabetic (~75 vs ~30); diabetic has a lower glucose level and higher steady-state insulin value; INS response appears to be second order while GLU looks like first-order (or crit/over damped second order)

The GLU step response makes sense because the T2 diabetic can still take up GLU from the blood, so we expect a higher level than non-diabetic but lower level than T1 diabetic; The INS step response makes sense too because not as much GLU is taken up from the blood, so we don't expect a value as negative for a non-diabetic

6. The glucose tolerance test is a common test for diabetes. Use the same pulse input for $\dot{m}_{in\,GLU}$ that you used in the Type 1 diabetic exercise and plot the transient glucose and insulin response of a normal patient and the Type 2 diabetic. How does each respond to the glucose tolerance test?




Normal




Type 2 diabetic

The INS responses appear similar. The GLU responses reach steady-state at almost the same time; There is no negative relative dip on GLU levels for the Type I diabetic, compared a non-diabetic.

7. Are the Type 2 glucose and insulin transfer functions stable? How do you know?

   Yes. Roots() shows that the denominator has roots in the left-hand side of the complex plane.

8. Determine the steady-state error for $T_{GLU}(s)$ and $T_{INS}(s)$ for a Type 2 diabetic. For $T_{GLU}(s)$ SSE, assume $\dot{m}_{in\,INS} = 0$ and $\dot{m}_{in\,GLU}$ is a step input of amplitude 100 gm/hr. For $T_{INS}(s)$ SSE, assume $\dot{m}_{in\,GLU} = 0$ and $\dot{m}_{in\,INS}$ is a step input of amplitude 100 gm/hr. How does the steady-state error of a Type 2 diabetic compare to a healthy person?

   SSE for $T_{GLU}(s)$ = -125.4

   SSE for $T_{INS}(s)$ = 25.19

   WRT to a non-diabetic, the GLU SSE is far worse than for a non-diabetic (0.218) but not as bad as a Type I diabetic (-228.9); INS SSE is worse than a non-diabetic (66.88) but not as bad as a Type I diabetic (-9.170)

9. Just from looking at glucose time responses, is it possible to tell a difference between a Type 1 diabetic and Type 2 diabetic? Why or why not?

   The step responses appear to be more different than the tolerance test results. In other words, the step responses might be a more appropriate test for distinguishing b/w T1 and T2 diabetes.