BME331: Physiological Control Systems

Lab 1

Introduction:

The objective of this lab is to familiarize you with the process of modeling and simulating the behavior of a physiological control system. You will learn to use Simulink, a key tool in the study of control systems in general. We will focus here on modeling the system responsible for the regulation of glucose and insulin in the blood. You will implement an existing model in Simulink, use it to examine the response of the system to different inputs, and lastly experiment with making changes to the model. The lab is to be done in groups of 3.

Pre-lab tasks [10 marks]

Simulink is a graphical extension to MATLAB for the modeling and simulation of systems. You will be using Simulink in every lab in this course.

In preparation for the lab exercise, you should familiarize yourself with the basics of the Simulink software beforehand. A number of tutorials can be found online, and there is extensive help documentation within Matlab/Simulink itself. Here are tutorials of an appropriate level:

http://ctms.engin.umich.edu/CTMS/index.php?aux=Basics_Simulink

https://www.mathworks.com/videos/getting-started-with-simulink-part-1-building-and-simulating-a-simple-simulink-model-1508442030520.html

Work through the tutorials before the lab sessions, so that you are ready to start building and working with the model right away.

You will be expected to have read through the lab document beforehand, so that you know what needs to be done and can manage your time accordingly.

After reading through the lab document and familiarizing yourself with Simulink, provide brief (1-2 sentences) answers to the following questions. Your answers must be submitted via Quercus by the beginning of your first lab session. Each member of your group should submit their pre-lab individually.

1. Explain the difference between sources and sinks in Simulink.

2. Explain why the threshold operators are needed in the model shown in Figure 1.

3. Explain the difference between Type I and Type II diabetes.

4. At the level of the cell membrane, how can insulin help to promote the uptake of glucose into the cell?

5. On a copy of Figure 1, circle and label the portions of the system that correspond to each of the terms in Equation (6).

Background:

The model used in this lab is described in the Khoo textbook[1]. Its governing equations are reproduced here. First, let *x* be the plasma glucose concentration and *y* be the plasma insulin concentration (both in units of mg ml^{-1}). Let Q_L be the input flow rate (in mg h^{-1}) of glucose into the blood, through absorption from the gastrointestinal tract or through production from the liver. Glucose is eliminated from the blood in three major ways:

1. The kidneys excrete glucose when x exceeds a threshold θ, at a rate proportional to x – θ, as follows:

$$Renal\ loss\ rate = \begin{cases} \mu(x - \theta), & x > \theta \\ 0, & x \le \theta \end{cases} \tag{1}$$

2. Glucose moves from the blood into most cells through facilitated diffusion, at a rate proportional to the glucose concentration, following:

$$Tissue\ utilization\ rate\ (insulin - independent) = \lambda x \tag{2}$$

3. In certain types of cells, insulin helps to stimulate the facilitated diffusion process by promoting insertion of glucose carrier proteins into the cell membrane. The rate of glucose uptake is then proportional to both *x* and *y*:

$$Tissue\ utilization\ rate\ (insulin - dependent) = \nu xy \tag{3}$$

The rates μ, λ, and ν are constants.

As for insulin, it is produced by the pancreas at a rate dependent on the plasma glucose level, as long as the glucose level is above a certain level:

$$Insulin\ production\ rate = \begin{cases} 0, & x \le \phi \\ \beta(x - \phi), & x > \phi \end{cases} \tag{4}$$

Conversely, insulin is destroyed by the enzyme insulinase at a rate proportional to the insulin concentration:

$$Insulin\ destruction\ rate = \alpha y \tag{5}$$

Based on the equations above, we can see that the dynamics of plasma glucose concentration are governed by:

$$
\begin{aligned}
C_G \frac{dx}{dt} &= U(t) + Q_L - \lambda x - \nu x y, && x \le \theta \\
C_G \frac{dx}{dt} &= U(t) + Q_L - \lambda x - \nu x y - \mu(x - \theta), && x > \theta
\end{aligned} \tag{6}
$$

Here, C_G is the glucose capacitance in the extracellular space, and U(t) represents the time course of glucose being infused into the bloodstream, for instance as part of a glucose tolerance test.

Similarly, for insulin:

$$
\begin{aligned}
C_I \frac{dy}{dt} &= -\alpha y, && x \le \phi \\
C_I \frac{dy}{dt} &= -\alpha y + \beta(x - \phi), && x > \phi
\end{aligned} \tag{7}
$$

where C_I is the insulin capacitance of the extracellular space.

Experimental Procedures:

1. *Model creation in Simulink*

Figure 1 is taken from the textbook by Khoo [1], and shows an implementation of the mathematical model described in the previous section. Your first task is to re-create this model in Simulink. Figures 2, 3 and 4 provide the parameters not visible in Figure 1. The objective at this stage is to practice using the Simulink interface that you familiarized yourselves with during the pre-lab, and to become comfortable with how the different components of the model are interconnected.

⇨ Once you are done, take a screenshot of your model, similarly to a) and b) in Figure 1.

2. *Use of the model to simulate system behavior*

a) Change the run time to 20s, and leave all other parameters at the default values shown in Figures 2-4 (corresponding to an impulse-like glucose infusion every 5 hours). Run the simulation and observe the outputs using the scope blocks.

⇨ Record screenshots of the insulin and glucose responses. Rename the corresponding input and output variables (u, x, and y) in the Matlab workspace to u_2a, x_2a, and y_2a and save them for later analysis.

b) In the Glucose Infusion block, change the input period to 100 and the input pulse width to 0.25. Run the simulation again and observe the outputs using the scope blocks.

⇨ Record screenshots of the insulin and glucose responses. Rename the corresponding input and output variables (u, x, and y) in the Matlab workspace to u_2b, x_2b, and y_2b and save them for later analysis.

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[1] M.C.K. Khoo, Physiological Control Systems: Analysis, Simulation, and Estimation, IEEE Engineering in Medicine and Biology Society, Wiley & Sons, ISBN 0-7803-3408-6.

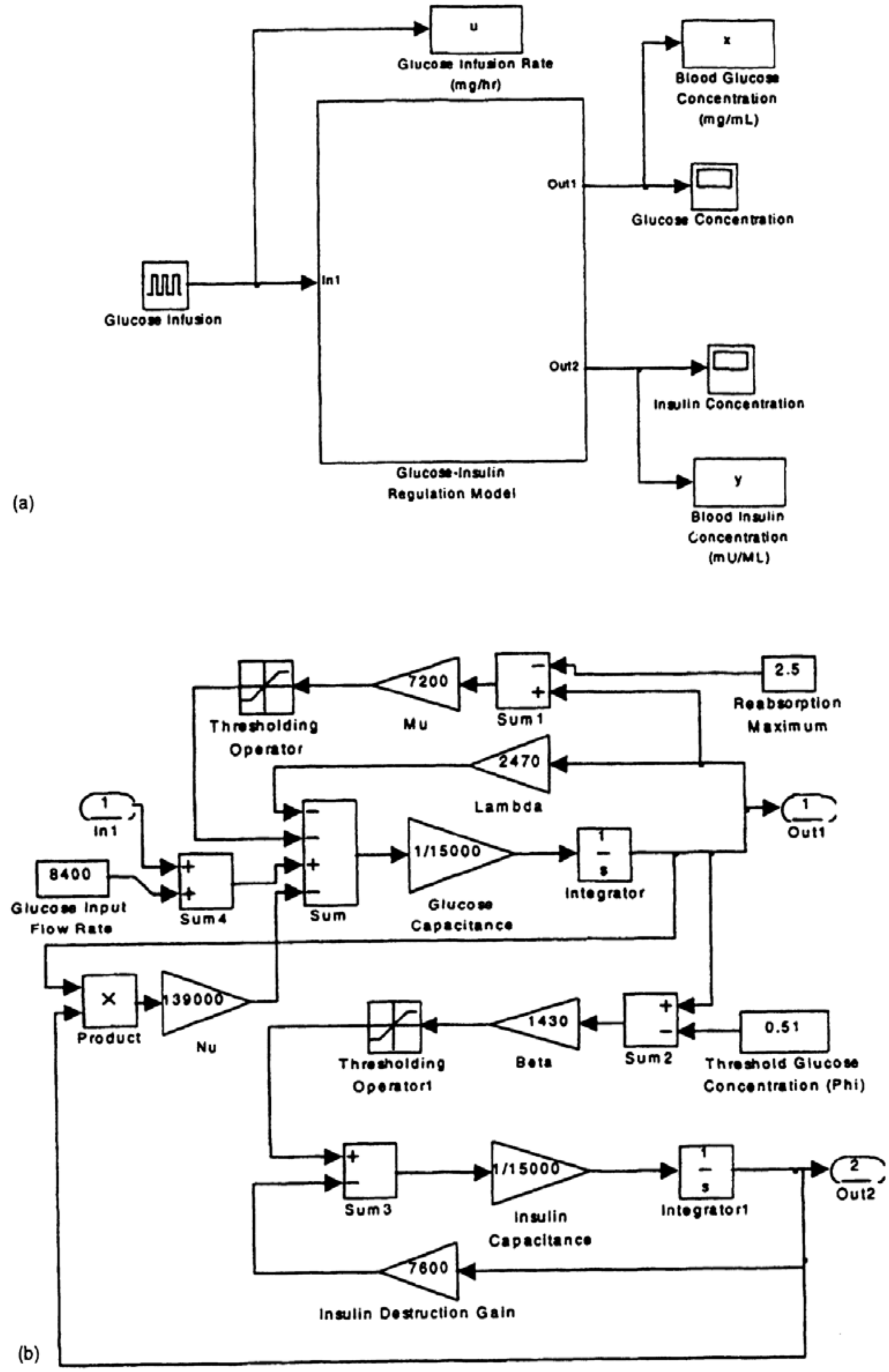

Figure 5.16 SIMULINK model of blood glucose–insulin regulation. (a) The input to and outputs from the model. (b) Details of the dynamic structure.

Figure 1: The glucose-insulin Simulink model

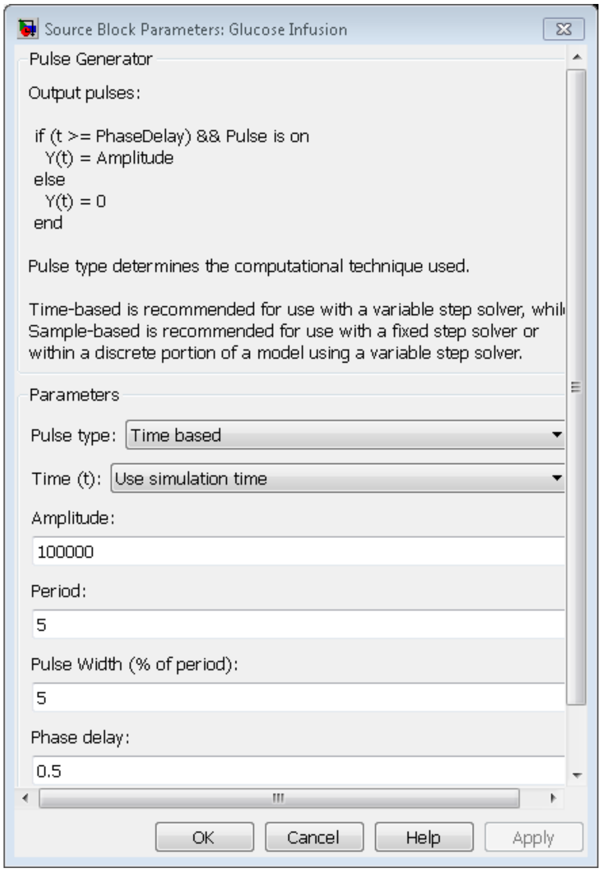

Figure 2: Parameters for the glucose infusion block

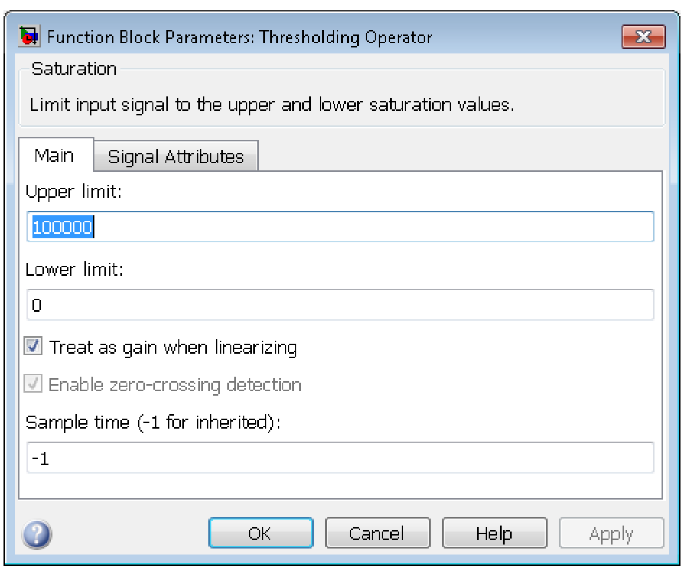

Figure 3: Parameters for the two thresholding blocks (both are the same)

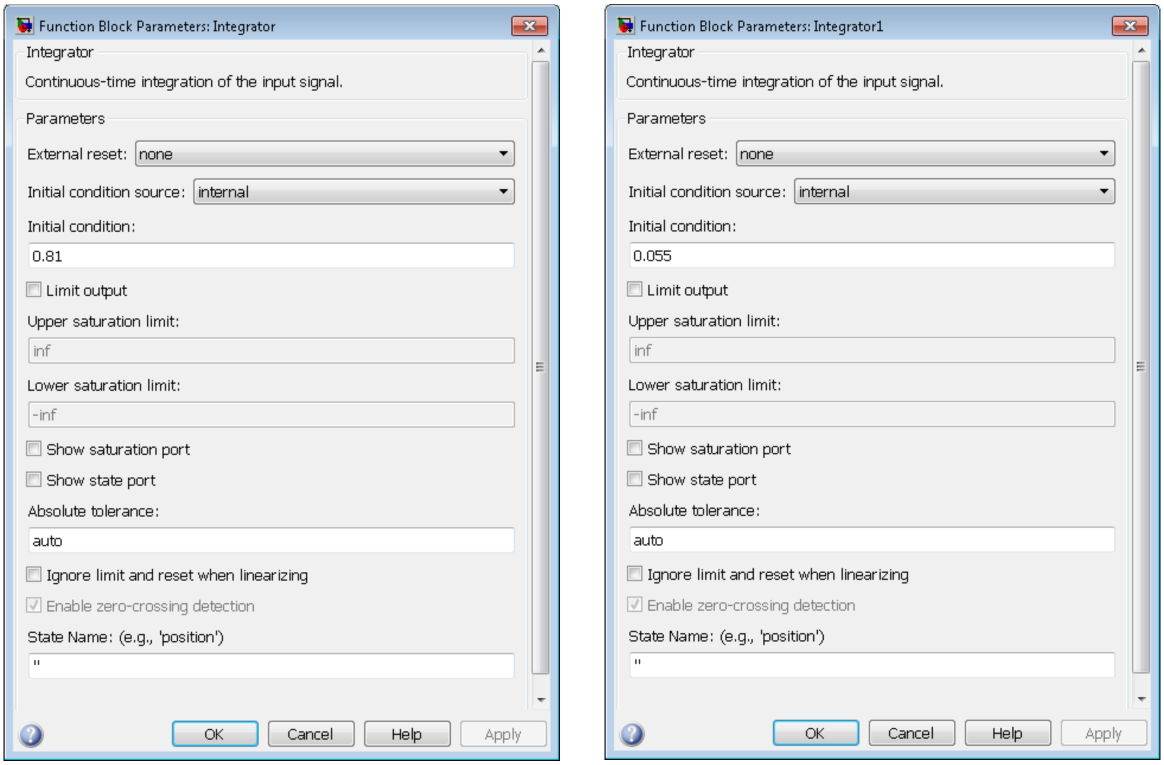

Figure 4: Parameters for the two integrator blocks

<u>For the following sections, restore the parameters of the Glucose Infusion block to their original values (Fig. 2).</u>

3. *Use the model to understand system disruptions*

   a) Type I diabetes is characterized by an inability of the islet cells in the pancreas to produce sufficient insulin. This can be implemented in the model by reducing the sensitivity of insulin production to the glucose concentration. Identify the appropriate Simulink block parameter, and simulate the system's behavior when this parameter is set to a fraction of its default value, in increments of 20% (i.e., simulate the response if the parameter is set to 0%, 20%, 40%, …, 100% of its default value). Note that all of these simulations can be conducted simultaneously by providing a vector of values instead of a single value in the appropriate Simulink block. This way, you can visualize all of the resulting curves simultaneously on one graph.

⇨ Record screenshots of the insulin and glucose responses, each of which should have 6 curves. Rename the corresponding input and output variables (u, x, and y) in the Matlab workspace to u_3a, x_3a, and y_3a and save them for later analysis.

⇨ Save the modified model with the filename "glucose_type1"

b) Type II diabetes is characterized by reduction in the ability of insulin to promote glucose update, rather than by a deficit in insulin production. This can be implemented in the model by reducing the insulin-dependent tissue utilization rate. Identify the appropriate model parameter, and simulate the system's behavior when this parameter is set to a fraction of its default value, in increments of 20% (i.e., simulate the response if the parameter is set to 0%, 20%, 40%, …, 100% of its default value). Don't forget to first undo the changes that you made in section 3a. Note that all of these simulations can be conducted simultaneously by providing a vector of values instead of a single value in the appropriate Simulink block. This way, you can visualize all of the resulting curves simultaneously on one graph.

⇨ Record screenshots of the insulin and glucose responses, each of which should have 6 curves. Rename the corresponding input and output variables (u, x, and y) in the Matlab workspace to u_3b, x_3b, and y_3b and save them for later analysis.

⇨ Save the modified model with the filename "glucose_type2"

4. *Modify the model to simulate treatment effects and investigate system properties.*

a) Some of the recommendations for managing diabetes include:

- Insulin injections.
- Managing your diet to limit glucose intake.
- Physical exercise, which requires fuel and promotes the (insulin-independent) uptake of blood glucose.

Propose three modifications of the model or its parameters, each of which models one of the strategies above. In each case, simulate the new behavior in both the type I and type II diabetes models developed above.

⇨ Record screenshots of each modified Simulink model.

⇨ Record screenshots of the insulin and glucose responses, each of which should have 6 curves, for each management strategy and each type of diabetes (6 models total). Rename the corresponding input and output variables (u, x, and y) in the Matlab workspace to u_4a_typeX_modY, x_4a_typeX_modY, and y_4a_typeX_modY and save them for later analysis ($X \in \{1,2\}$ and $Y \in \{1,2,3\}$).

⇨ Save the modified models with the filenames "glucose_typeX_modY"

b) The original model that you created in Section 1 includes three pathways by which glucose is removed from the blood (renal loss rate and insulin-dependent or -independent tissue utilization rates). Using modifications to this model (without diabetes) and appropriate graphical displays, describe how glucose concentrations would be affected if each of these pathways was impaired.

- ⇨ Record screenshots of each modified Simulink model.
- ⇨ Record screenshots of the insulin and glucose responses in each case. Rename the corresponding input and output variables (u, x, and y) in the Matlab workspace to u_4b_modX, x_4b_modX, and y_4b_modX and save them for later analysis (X ∈ {1,2,3}).
- ⇨ Save the modified models with the filenames "glucose_orig_modX"

<u>Report:</u>

- Your team must prepare a lab report showing the outputs that you recorded, as specified in each of the sections above. For each section, you should include the screenshots, as well as Matlab plots where useful to emphasize the key aspects of your results.
    - In describing the results of section 4, precisely describe your modifications, and include plots comparing the outputs with and without your modifications.
    - In sections 3 and 4, describe your modifications to the model by making reference to the equation in the Background section.
- In addition, include a Discussion section in which you will address the following questions (create a separate sub-section for each question):
    - Using the results from section 2b, identify an aspect of the control of glucose that is not captured by this model. What modifications to the model would be required to address these issue? If these modifications were made, how would you expect the output in section 2b to be different?
    - Based on your simulations in section 4a, state whether each of the management strategies proposed (insulin injections, diet, and exercise) are appropriate for each type of diabetes (type I and type II). Justify your answers.
    - Based on the results of your analysis in section 4b, comment on the impact of each of the three glucose removal pathways on glucose concentrations. Which pathway has the most influence? Comment on the implications of these results for diabetes.

<u>Marking scheme</u>

Pre-lab: 5% (individual mark – pass/fail; all questions must be answered)
Experimental results (sections 1-3): 30%
Model modifications and analysis (section 4): 25%
Discussion questions: 30%
Clarity, organization, and language: 10%

Your lab report is due <u>on the dates indicated in the course syllabus</u>. Submit the report via Quercus no later than 5pm on the due date.