You were recently hired by a pharmaceutical company to evaluate the efficacy of a new drug to treat diabetes. You have a population of up to 20 asymptomatic subjects, 20 subjects with Type I diabetes, and 20 subjects with Type II diabetes for each of the experiments you would like to run.

In these experiments, you may probe the glucose metabolism process using infusions of either glucose or insulin. To remain within safe limits, the glucose injection rate ($\dot{G}_{\text{in}}$) should be limited to less than 5000 mg/hr, and the insulin injection rate ($\dot{I}_{\text{in}}$) to less than 500 mU/hr; mU is a standard measure of insulin.

To a first approximation, the steady state response of glucose and insulin can be modeled by the following coupled equations, which have been adapted from Khoo (1999). The first represents the rate of change of glucose in the blood stream, and the second the rate of change of insulin.

$$\dot{G}_{\text{in}} = \beta_0 + \beta_1 G_{blood} + \beta_2 G_{blood} I_{blood}$$
$$\dot{I}_{\text{in}} = \gamma_0 + \gamma_1 G_{blood} + \gamma_2 I_{blood}$$

In these equations, G_{blood} is the concentration of glucose in the blood, and I_{blood} is the concentration of insulin in the blood. Both are measured response variables. The remaining parameters are constants to be estimated from experimental data.

For Type I diabetes, the main effect is that pancreas does not produce sufficient insulin. This might be seen in the model as a reduction in the γ_1 parameter, which represents the rate of insulin production in response to an increase in glucose. For Type II diabetes, the main effect is not a reduction of insulin production, but rather a reduction in the ability of insulin to stimulate glucose uptake. This might be seen in the β_2 parameter, which represents the insulin-dependent rate of glucose uptake by the body.

Experimental data can be "collected" using the following function:

```
[glucoseOut,insulinOut] = CollectDrugData(glucoseIn,insulinIn,Subj,Drug)
```

All inputs and outputs for these functions are scalars. Additional details can be found in the Appendix. Before running, they must be placed in the same folder as ***Glucose_Insulin_Dynamics.slx***, the Simulink model used for all simulations.

NOTE: While the measured infusion rates can be considered noise-free, there is known to be substantial noise on the measures of glucose and insulin in the blood stream. This should be considered in your analysis

Reference

M. C. K. Khoo, *Physiological Control Systems*. Wiley-IEEE Press, 1999.

*This activity has been modified with permission from Eric Perreault, PhD.

BME 407 Homework #2

Complete the following tasks. All responses should be quantitative. Use statistics and figures as needed. Be thorough but parsimonious in your responses.

1. Develop a regression analysis to compare the three populations of subjects in the absence of any administered drug (set drug=0 in your simulation). Consider each equation in the glucose metabolism model as a separate model.
    a. Design an appropriate set of inputs (insulin and glucose injection rates) for estimating your model parameters. Succinctly describe your rationale. Assume that only a single measurement can be obtained from each subject. Each measurement corresponds to the model output for the specified inputs.
    b. Simulate your data using the designed inputs in MATLAB (see Appendix A). The data set should contain 60 points, one for each of the 20 subjects in each of the 3 groups.
    c. Create the appropriate models in Python using the above simulated data. How well does each model describe the data for each subject group? Respond at the level of the whole model -- not individual parameters. Save that for part e.
    d. Do your models or the simulated data violate any assumptions of the regression analysis you have performed? Explain.
    e. Which model parameters are significant? Can you justify removing any parameters from your model? Simply reading off the ANOVA tables is sufficient for this assignment. (Please be prepared for using regularization on the test though.)
    f. Describe which parameters differ between subject populations. Is this as expected based on the physiological processes attributed to each parameter?

2. Briefly describe if the linear regression analysis you performed was appropriate for this problem. Justify your answer, carefully considering the noise in your measurements and how it influenced your results.

Appendix

Usage notes for simulation file

CollectDrugData

CollectDrugData Runs the Glucose_Insulin_Dynamics model.

```
[glucoseOut,insulinOut] = CollectDrugData(glucoseIn,insulinIn,Subj,Drug)

INPUTS:
glucoseIn - glucose infusion rate (mg/hr)
insulinIn - insulin infusion rate (mU/hr)
Subj - 0: Asymptomatic
1: Type I diabetes
2: Type II diabetes
Drug - 0: no drug
1-8: Test drug coded by group number

OUTPUTS:
glucoseOut - steady-state glucose concentration in the blood (mg/mL)
insulinOut - steady-state insulin concentration in the blood (mU/mL)
```

Additional simulation tips

1. The simulation file (CollectDrugData.p) will return a measurement (steady-state glucose and insulin levels) from a single patient for the specified conditions (injection rates, subject group, drug administered). The patient can be considered to have been selected randomly from the population of all possible patients in the specified group. Each time a simulation is run with the same parameters, it will return a different result. This is designed to represent the typical variability seen across a population of subjects.
2. There is no way to simulate a repeated experiment on the same subject. Hence, your simulated data set should include only 60 points, one for each of the 20 subjects in each group.
3. The "subject" input parameter for the simulations refers to the group from which the subject was chosen, not a specific subject.