Assignment 4

Use of Matlab to investigate compartmental systems

Submission: Moodle (single compressed file including results/explanations and Matlab files)

Many compartmental systems can be represented by a series of first-order differential equations:

$$\frac{dx_1}{dt} = a_{11}x_1 + a_{12}x_2 + \ldots + a_{1n}x_n + b_1(t)$$

$$\frac{dx_2}{dt} = a_{21}x_1 + a_{22}x_2 + \ \ldots \ + \ a_{2n}x_n + b_2(t)$$

$$\vdots$$

$$\frac{dx_n}{dt} = a_{n1}x_1 + a_{n2}x_2 + \ldots + a_{nn}x_n + b_n(t)$$

An m-file can be generated in which the matrix of coefficients $|a_{ij}|$ and $|b_j|$ are defined in $yp = ax + b$. This can be then solved using a similar command:

```
[t,y] = ODE23('mfilename',[0,20],[10 0 0]')
```

Refer lecture slides for more codes.

Part 1

1. A simple plasma glucose/insulin model can be expressed as:

$$\frac{di}{dt} = -0.8i + 0.2g$$
$$\frac{dg}{dt} = -5i - 2g + A(t)$$

where i is the deviation in insulin level from normal (in international units/kg) and g that for glucose (g/kg). The unit of time is hours. Enter the coefficients in the form $yp = ax + b$. For a step input $A(t) = 1$ g/kg/h for $t > 0$, plot the changes in i and g over a 4 h period given that i and g are zero initially. Modify the equations to model a bolus input ($x = 1 - sign(t)$ is a delta function at $t = 0$). Now simulate a diabetic subject and a diabetic subject with insulin infusion of 100 mU/kg/h (both in response to the previous step input).

2. Set up an m-file to represent the Riggs model for iodine metabolism, then use ode23 to simulate the response to a sudden drop in iodine intake from 150 µg to 15 µg per day (this involves setting $B_n(t)$ to [15 0 0], at [150 0 0] no changes occur since this represents a steady-state). Produce plots for 0-10 days, then 0-300 days.

   Certain thyroid diseases can be simulated by altering some of the parameters. Simulate the following diseases and provide notes and plots.

a. Hypothyroidism due to autoimmune thyroid disease
b. Hypothyroidism due to low Iodine intake
c. Hyperthyroidism due to Grave's disease
d. What are some common causes of goitre and tumors and how can they be simulated in the Riggs' model?

Part 2

1. The Simulink diagram below represents following equations (used to solve numerically in Part 1)

$$\frac{di}{dt} = -0.8i + 0.2g + B(t)$$
$$\frac{dg}{dt} = -5i - 2g + A(t)$$

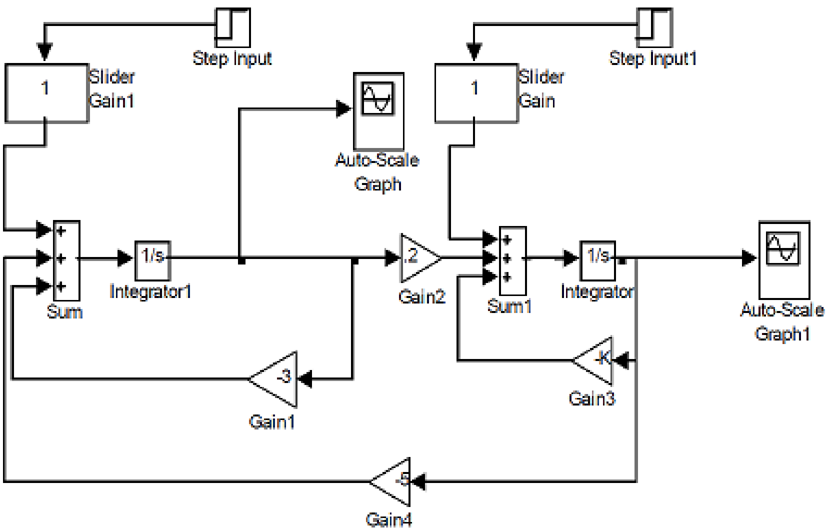
The step input $A(t)$ is set at 1 g/kg/h for $t > 1$, $B(t)$ is presently set at 0 for all time. The slider gain is a quick way of altering the height of the step. Start the simulation and then stop it after a few hrs have elapsed. The plots should look similar to those in part 1.

Now try:

$$\frac{di}{dt} = -0.63i + 0.13g - - - - - - - - (1)$$
$$\frac{dg}{dt} = -5i - 2.5g + A(t)$$

which correspond to an alternative set of coefficients, determined by a different procedure in the original article (Bolie, J Appl Physiol, 16:783). What difference does this make?

Now try $B(t) = 0.1$ U/kg/h in a normal subject and a diabetic subject (change last term in equation (1) to $0.01g$).



2. Using a similar Simulink model to simulate the Riggs iodine model in Part 1.

$$\frac{dI}{dt} = -2.52I + 0.08H + 15$$

$$\frac{dG}{dt} = 0.84I - 0.01G$$

$$\frac{dH}{dt} = 0.01G - 0.1H$$

Part 3

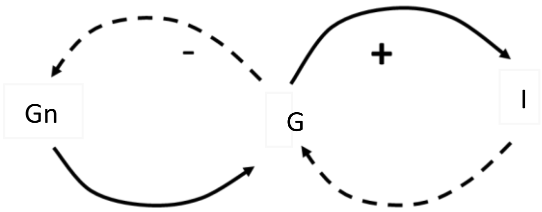
1. Derive the analytical solution for the Bolies' glucose $g(t)$, insulin $i(t)$ model (refer lecture notes). Answer should be explained in terms of the stability curve.

$$\frac{dg(t)}{dt} = -k_4 g(t) - k_6 i(t) + A(t)$$

$$\frac{di(t)}{dt} = k_3 g(t) - k_1 i(t) + B(t)$$

Hint: to find $g(t)$, solve $\frac{d^2g}{dt^2} + (k_1 + k_4)\frac{dg}{dt} + (k_1k_4 + k_3k_6)g = k_1 a + a.\frac{du(t)}{dt}$

2. Bolies' model considers only the reduction of plasma glucose levels with insulin. Expand this model by including the effects of glucagon which helps to increase the plasma glucose levels.



Steps to follow:

- Get inputs from the Anatomy and Physiology lecturer about the functionality of glucagon $gn(t)$.
- Propose a compartmental model by mapping it to a similar compartmental model to that of Bolies'.
- Derive necessary differential equations for $gn(t), g(t)$ and $i(t)$ (if required)
- Provide plots and explanations to validate the proposed model.