UNIVERSITY OF MORATUWA
ELECTRONIC AND TELECOMMUNICATION DEPARTMENT

Compatmental modelling

Student name: *K.R.H.M.D.M. Kularatne - 180330K*

Course: *BM2101 - Analysis of Physiological Systems* – Professor: *Dr. Anjula De Silva*
Due date: *March 9th, 2021*

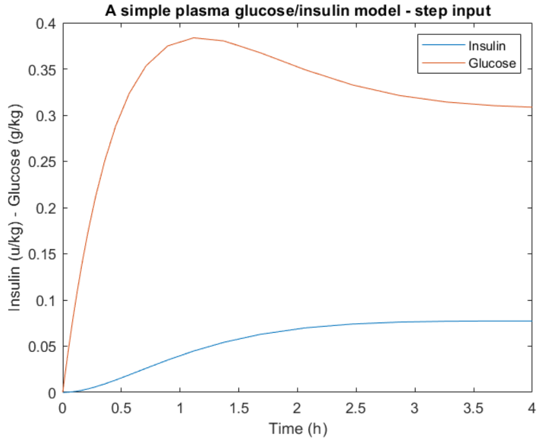
Question 1.1

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

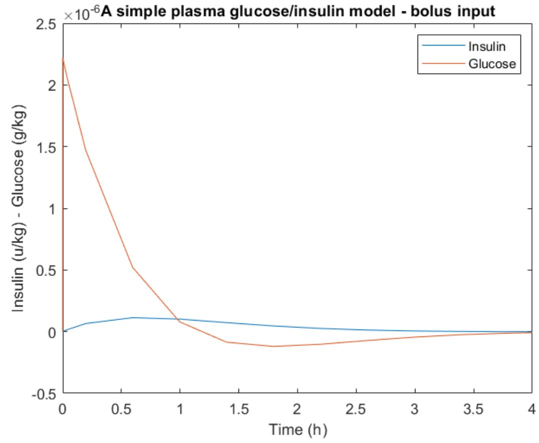
$$\frac{di}{dt} = -0.8i + 0.2g$$
$$\frac{dg}{dt} = -5i - 2g + A(t)$$

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 $y_p = ax + b$ 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 $x = 1 - sign(t)$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).

Solution. The plots are as follows,
Step input Here $A(t)$ = 1

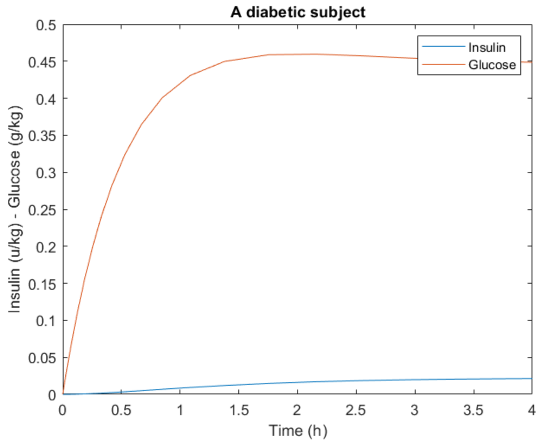


bolus input Here $A(t) = 1 - sign(t)$

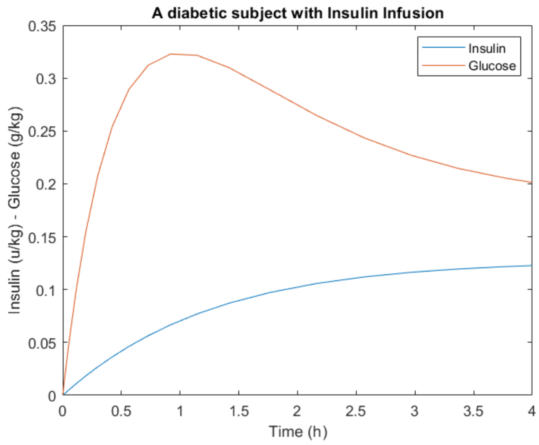


for diabetic patients, High blood sugar level will remain for certain period because insufficient insulin production by the β-cells of the pancreatic islets.

A diabetic subject



A diabetic subject with infuse $100mU/Kg/h$ **insulin**



Question 1.2

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 g to 15 g 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.

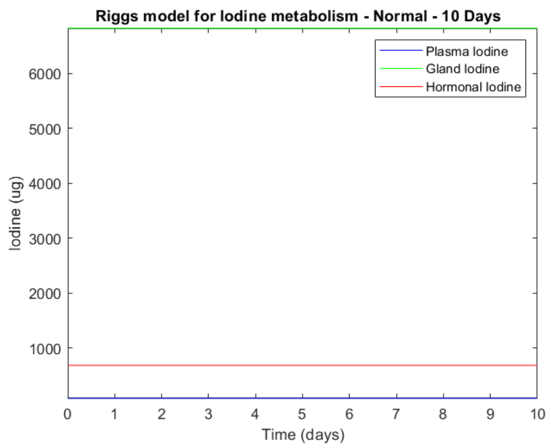
(*a*) Hypothyroidism due to autoimmune thyroid disease

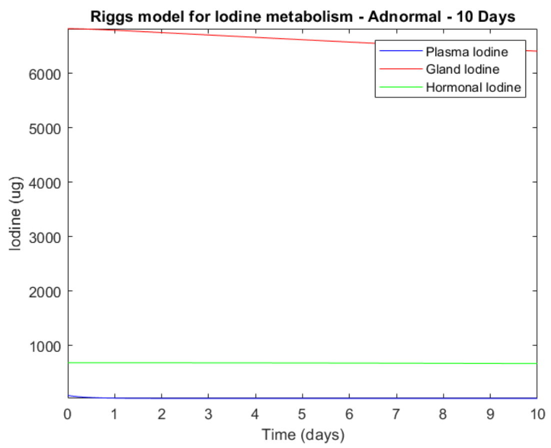
(*b*) Hypothyroidism due to low Iodine intake

(*c*) Hyperthyroidism due to Grave's disease

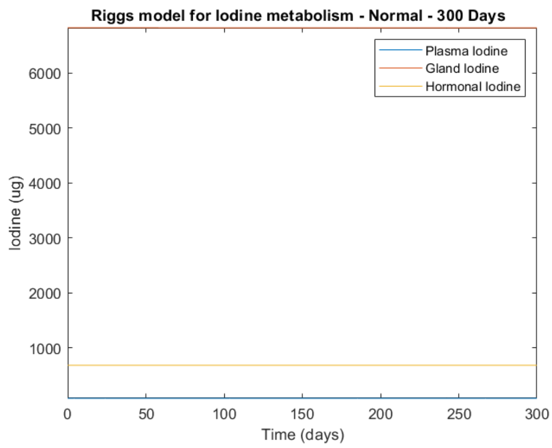
(*d*) What are some common causes of goitre and tumors and how can they be simulated in the Riggs' model?

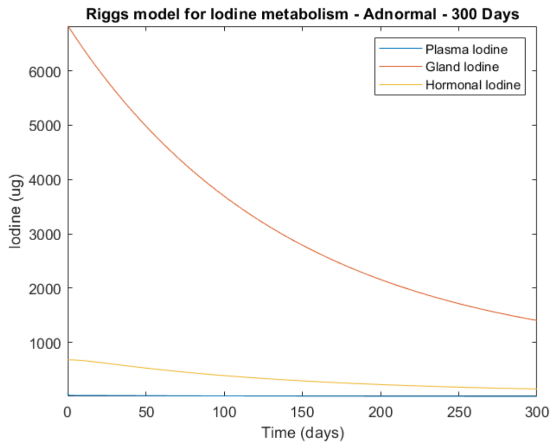
Answer. Riggs model for Iodine metabolism - Normal vs Adnormal through 10 days.



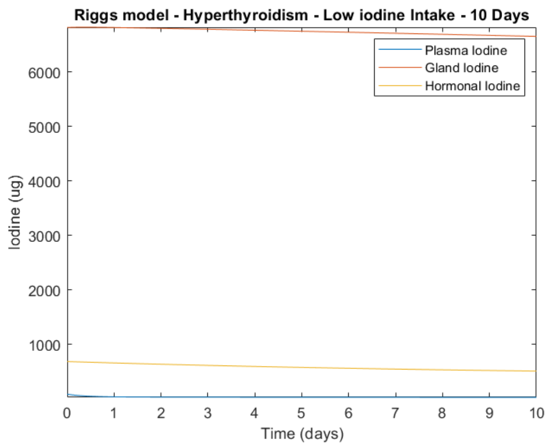


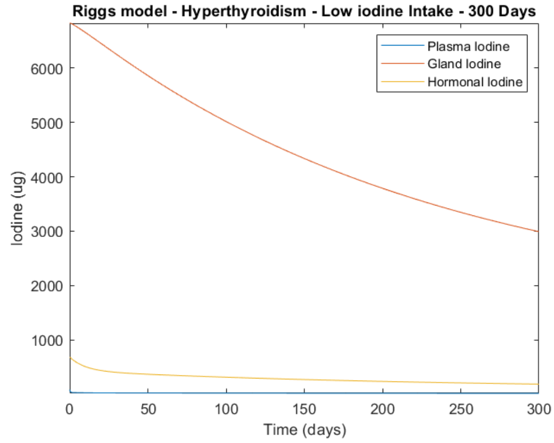
Riggs model for Iodine metabolism - Normal vs Adnormal through 300 days.



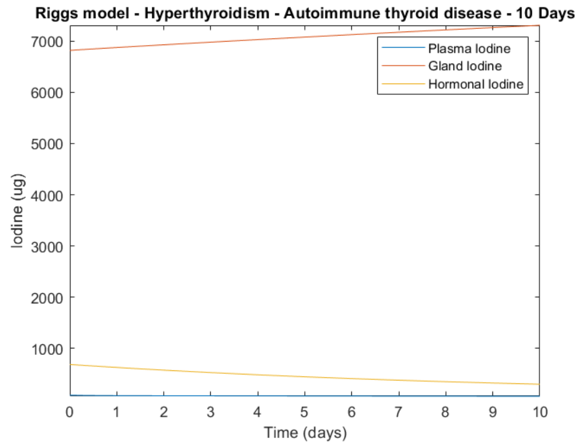


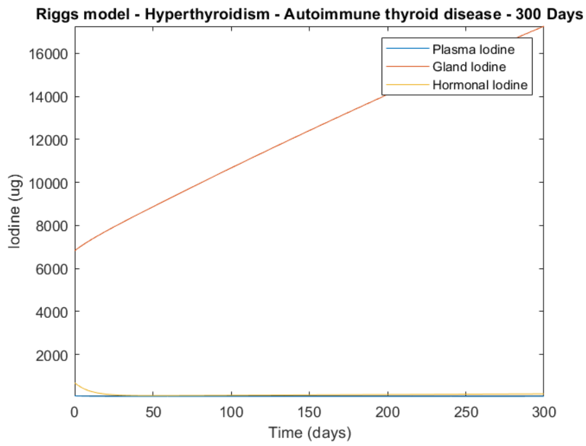
(*a*) Hypothyroidism due to autoimmune thyroid disease
A decreased production of the thyroid hormone is known as hypothyroidism. Hashimoto's disease is the main reason for this. In this disease, there is an immune response of body against the thyroid gland, which causes decreased function of the thyroid. This is modelled by decreasing k_2 parameter.



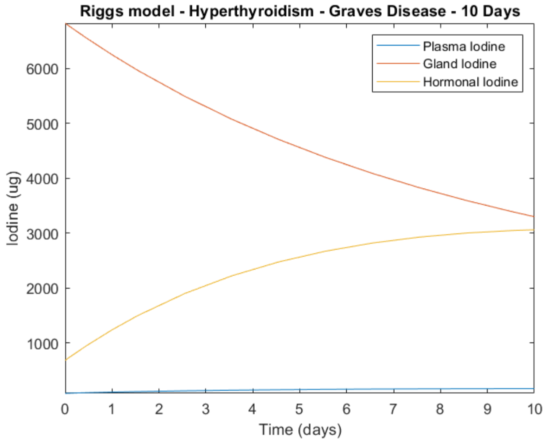


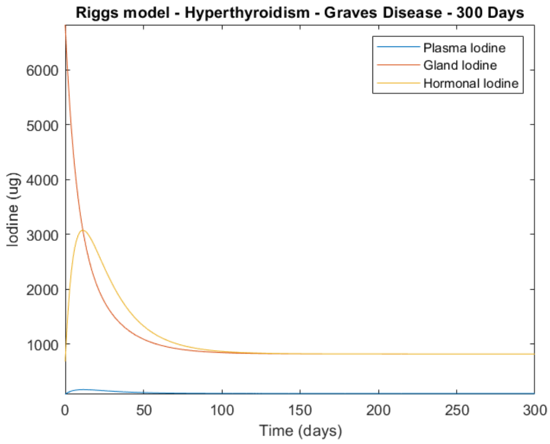
(*b*) Hypothyroidism due to low Iodine intake
A decreased production of the thyroid hormone is known as hypothyroidism. Low iodine intake is another reason for above condition. This is modelled by decreasing the intake of iodine.





(*c*) Hyperthyroidism due to Grave's disease
An excessive production of thyroid hormone is called hyperthyroidism. Graves disease is the main autoimmune disease cause for hyperthyroidism. Here, the body produces antibodies to stimulate the thyroid gland which produces thyroid hormone in excess. This is modelled by increasing the k_2 parameter.

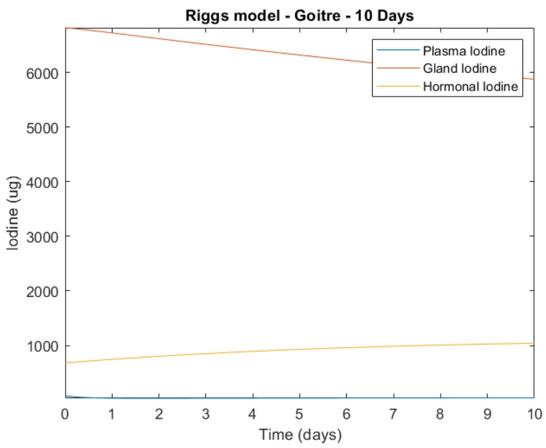


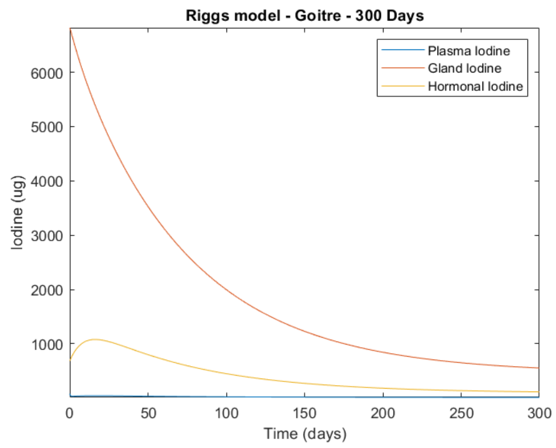


(*d*) What are some common causes of goitre and tumors and how can they be simulated in the Riggs' model?
Goitre is an enlarged thyroid gland due to underacting or overactive thyroid. The neck region becomes swollen. This means that they make too much or too little thyroid hormone. This too can be due to excess or low iodine input as mentioned earlier or Graves disease. Some common causes of goitre and tumours are iodine de

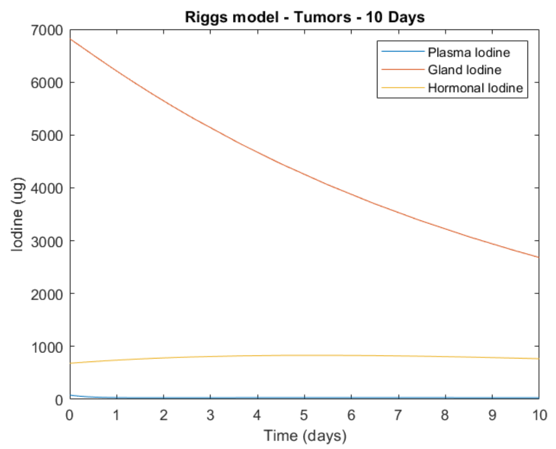
ciency and above mentioned thyroid diseases. odine de

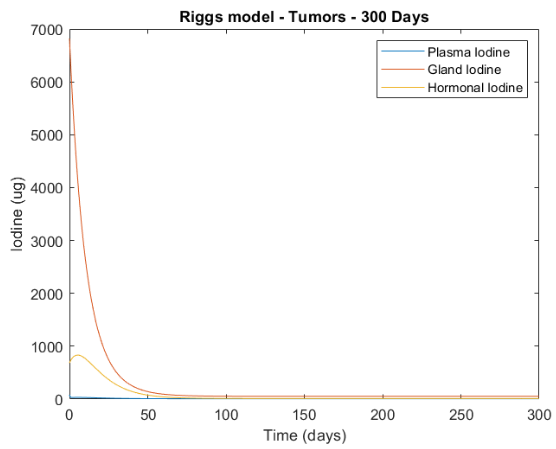
ciency can be modelled in Riggs model by low intake of iodine. This will cause for enlargement of thyroid gland of the patient.





Tumors in the thyroid gland can also cause hypothyroidism, hyperthyroidism and goiter. However, less iodine input to the body is a major reason for the tumor.





Question 2.1

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

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

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

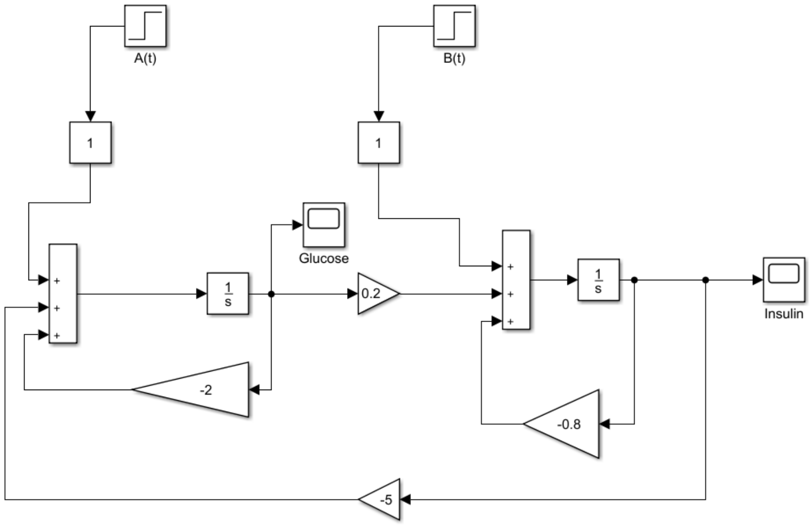
The step input $A(t)$ is set at 1 g/kg/h for $t > 1$, $B(t)$ is presently set at 0 for all time. The slider gain is a quick way of altering the height of the step. Start the simulation and then stop it after a few hrs have elapsed. The plots should look similar to those in part 1.
Now try :

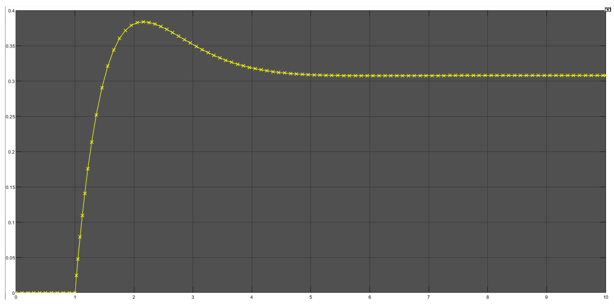
$$\frac{di}{dt} = -0.63i + 0.13g$$

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

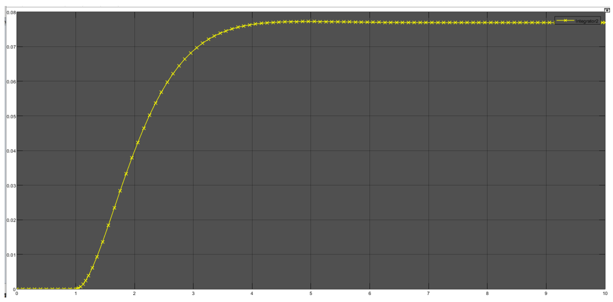
which correspond to an alternative set of coefficients, determined by a different procedure in the original article (Bolie, J Appl Physiol, 16:783). What difference does this make?
Now try:
$B(t)$ = 0.1 U/kg/h in a normal subject and a diabetic subject (change last term in equation (1) to $0.01g$.

Answer. **Bolies**$_{M}odel_{1}$



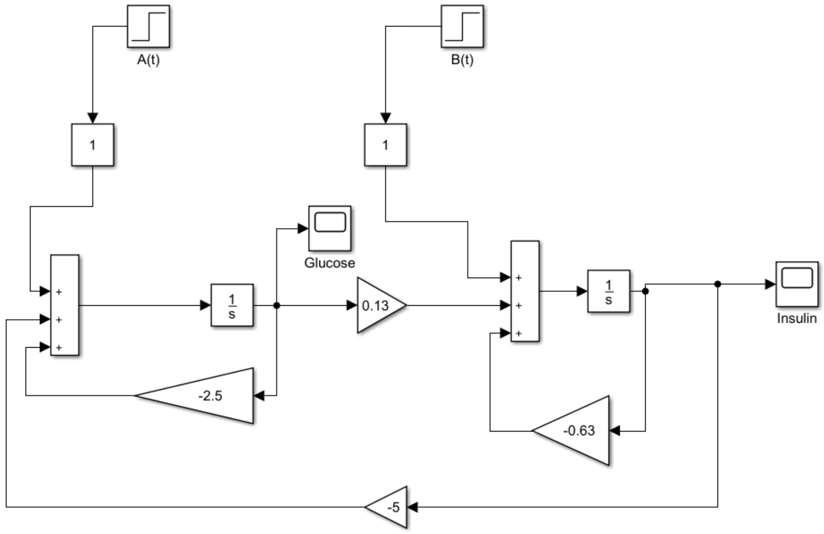


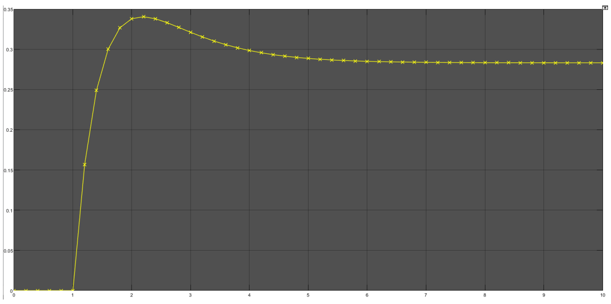
Glucose level

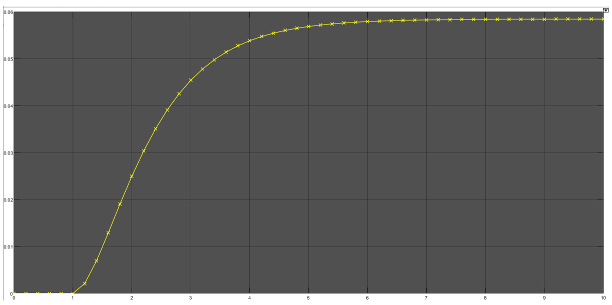


Iodine level

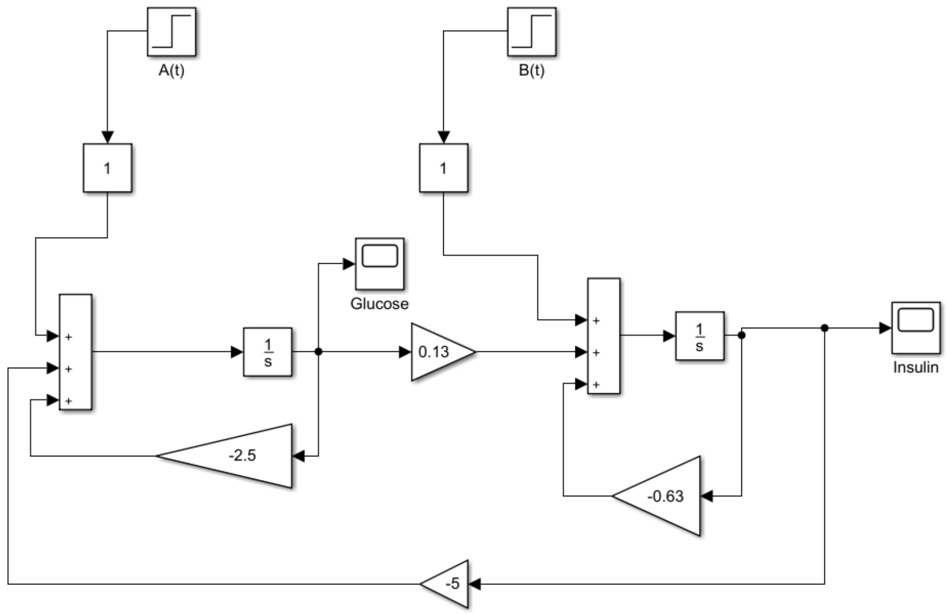
Bolies$_{M}odel_{2}$

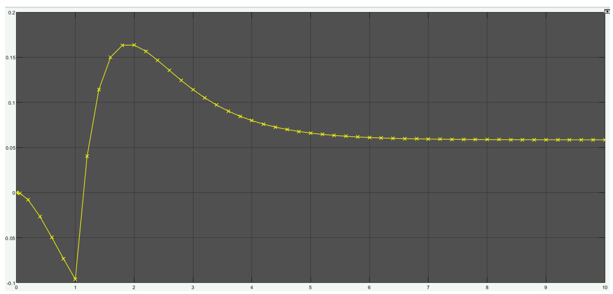



Glucose level

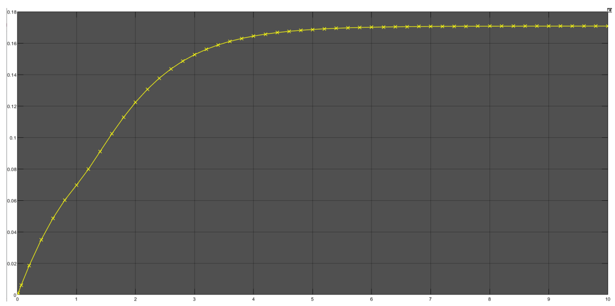

Iodine level

Normal Subject



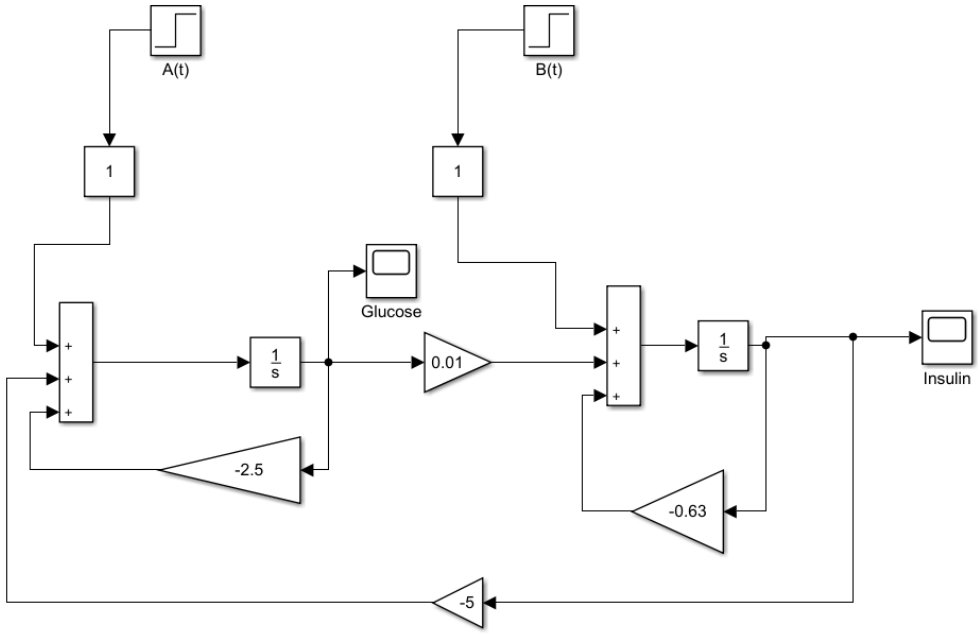


Glucose level

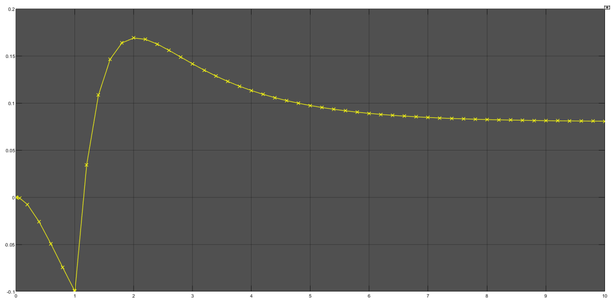


Iodine level

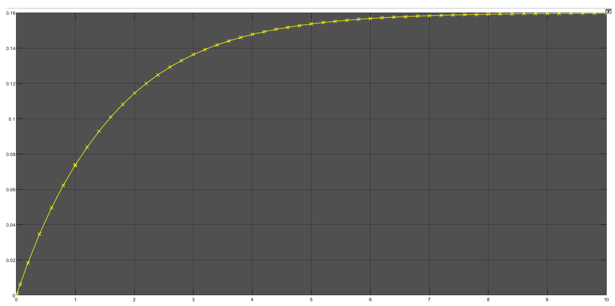
Diabetoc Subject



Iodine level



Glucose level



Iodine level

Question 2.2

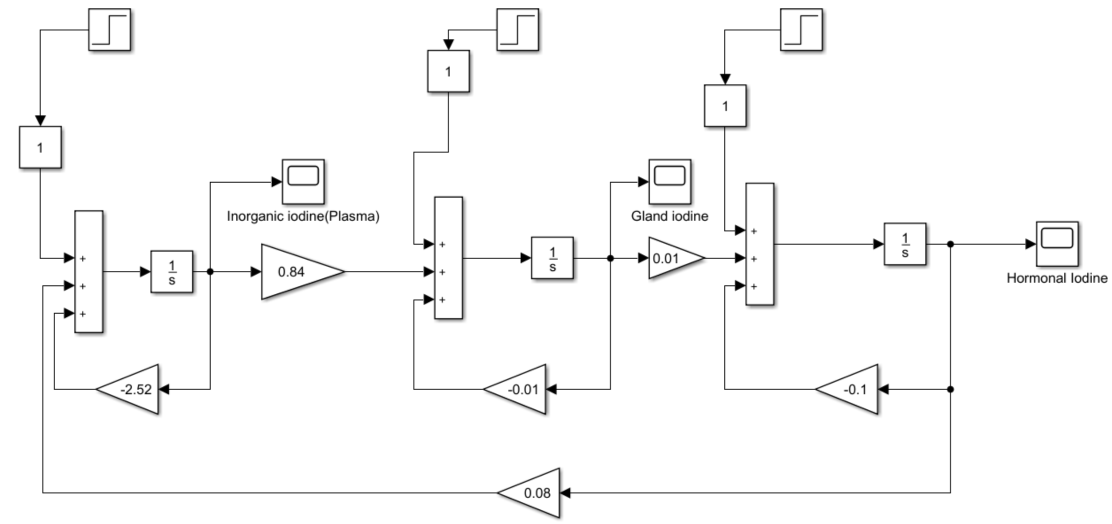
Using a similar Simulink model to simulate the Riggs iodine model in Part 1.

$$\frac{dI}{dt} = -2.52I + 0.05H + 15$$

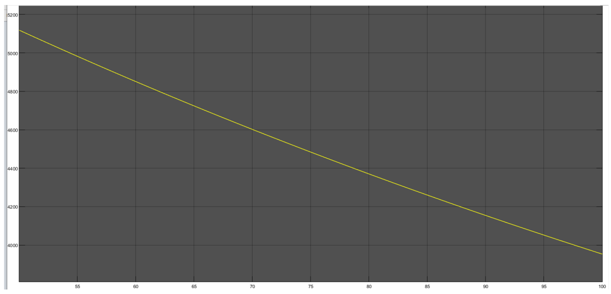
$$\frac{dG}{dt} = 0.84I - 0.01G$$

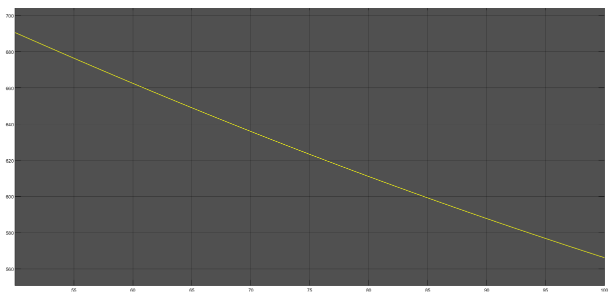
$$\frac{dH}{dt} = 0.01G - 0.1H$$

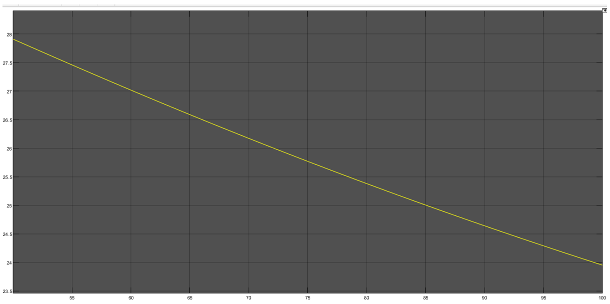
Answer.



A diabetic subject with infuse $100mU/Kg/h$ **insulin**


plasma iodine level


Gland Iodine level



Homonial Iodine level

Question 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.

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

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

Answer. lets consider,

$$\frac{d^2 g}{dt^2} + (k_1 + k_4)\frac{dg}{dt} + (k_1 k_4 + k_3 k_6) g = k_1 a + a\frac{du}{dt}$$

when t = 0,

$$\frac{du}{dt} = 0$$

so,

$$\frac{d^2 g}{dt^2} + (k_1 + k_4)\frac{dg}{dt} + (k_1 k_4 + k_3 k_6) g = k_1 a$$

by substituting the relevant coeffients,

$$k_1 = 0.8 k_1 + k_4 = 2.8 k_1 + k_4 + k_3 + k_6 = 2.6 a = 1$$

then,

$$\frac{d^2 g}{dt^2} + 2.8\frac{dg}{dt} + 2.6 g = 0.8$$

lets take g_h as the particular solution,

$$\frac{d^2 g}{dt^2} + 2.8\frac{dg}{dt} + 2.6 g = 0$$

we can assume the solution,

$$g_h = e^{Dt}$$

which,

$$D^2 + 2.8D + 2.6 = 0$$

then we get,

$$D = -1.4 \pm 0.8j$$

Since we have two complex conjugate roots, then the general solution is,

$$g_h = c_1 . e^{(-1.4+0.8j)t} + c_2 . e^{(-1.4-0.8j)t}$$

for the non homogenous part $g(t) = 0.8$,assume a solution of the form: $g_p = a_0$. So,

$$2.6 a_0 = 0.8 g_p = a_0 = \frac{4}{13}$$

so now we can write,

$$g = c_1.e^{(-1.4+0.8j)t} + c_2.e^{(-1.4-0.8j)t} + \frac{4}{13}$$

we can simplify this as,

$$g = e^{-1.4t}(c_1 cos(0.8t) + c_2 sin(0.8t) + \frac{4}{13}$$

lets substitute the boundary value conditions to find the constants. $g(0) = 0$ and $g'(0) = 1$, and we get $c_1 = -\frac{4}{13}$ and $c_2 = \frac{37}{52}$

so we can write,

$$g = -\frac{4}{13}e^{(-1.4t}cos(0.8t) + \frac{37}{52}e^{(-1.4t}sin(0.8t) + \frac{4}{13}$$

the we can find out the $i(t)$. since,

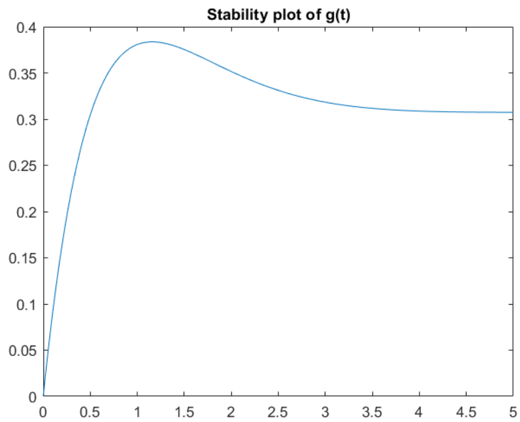
$$\frac{dg}{dt} = -2g(t) - 5i(t) + 1$$

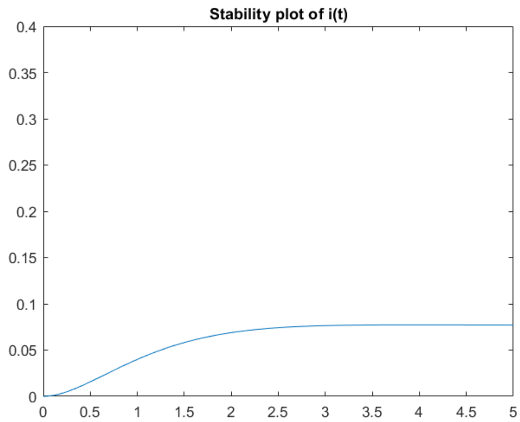
we can substitute the solved $g(t)$ function to above equation and substitute the initial conditions to the equation.$i(0) = 0$ and $i'(0) = 0$

now we get,

$$i = -\frac{1}{13}e^{(-1.4t}cos(0.8t) - \frac{7}{52}e^{(-1.4t}sin(0.8t) + \frac{1}{13}$$

with these equation we can plot the graphs and find out the stablility of $g(t)$ and $i(t)$.





Question 3.2

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:

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

Answer. so we can write,

$$\frac{dG}{dt} = k_5 - k_4 G(t) - k_6 I(t) + k_1 0 G_n(t) + A(t)$$

$$\frac{dG_n}{dt} = k_8 - k_7 G_n(t) + k_9 G(t) + P(t)$$

$$\frac{dI}{dt} = k_2 - k_I(t) + k_3 G(t) + B(t)$$

when we considering the equilibirum state,

$$\frac{dG}{dt} = \frac{dG_n}{dt} = \frac{dI}{dt} = 0$$

so ,

$$k_5 = k_4 G_0 + k_6 I_0 - k_{10} G_{n0}$$

$$k_2 = k_1 I_0 + k_3 G_0$$

$$k_8 = k_7 G_{n0} + k_9 G_0$$

now subsitute,

$$i = I - I_0$$

$$g = G - G_0$$

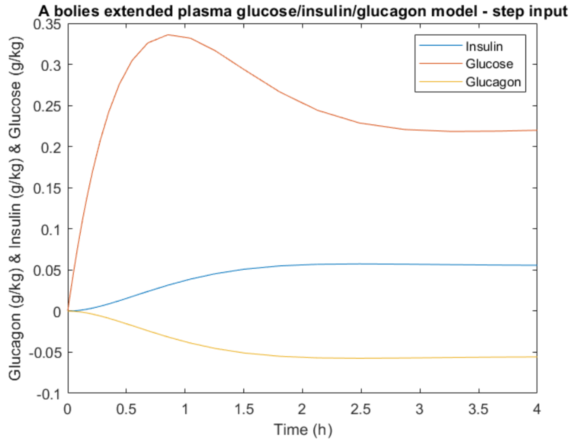
$$g_n = G_n - G_{n0}$$

so,

$$\frac{dg}{dt} = -k_4 g(t) - k_6 g(t) + k_1 0 g_n(t) + A(t) where A(t) = a.u(t)$$

$$\frac{dg_n}{dt} = -k_7 g_n(t) + k_9 g(t) + P(t) where P(t) = 0$$

$$\frac{di}{dt} = -k_i(t) + k_3 g(t) + B(t) where B(t) = 0$$



here we initially taken the blood glucose level as 500 mg/l which is much here than the normal value. we can see the stabilization here very clearly.