DEPARTMENT OF ELECTRONIC AND TELECOMMUNICATION ENGINEERING
UNIVERSITY OF MORATUWA

MUDALIGE DINETH NAVODYA

170401V

BM 2101 - ANALYSIS OF PHYSIOLOGICAL SYSTEMS

Use of MATLAB to investigate compartmental systems

This is submitted as a partial fulfillment for the module
BM 2101 - Analysis of Physiological Systems

—

February 3, 2020

Contents

List of Figures

1 Part 1

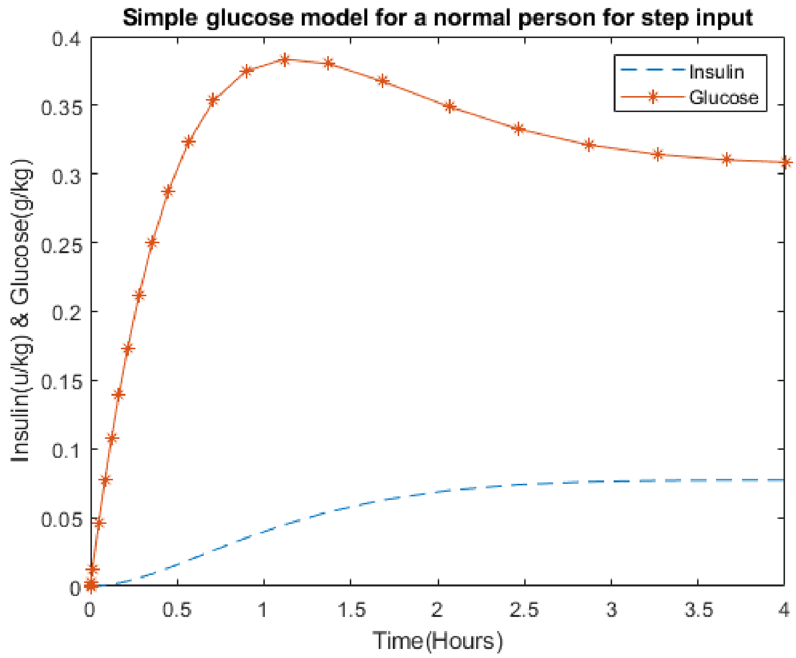

Figure 1: Simple glucose model for unit step input

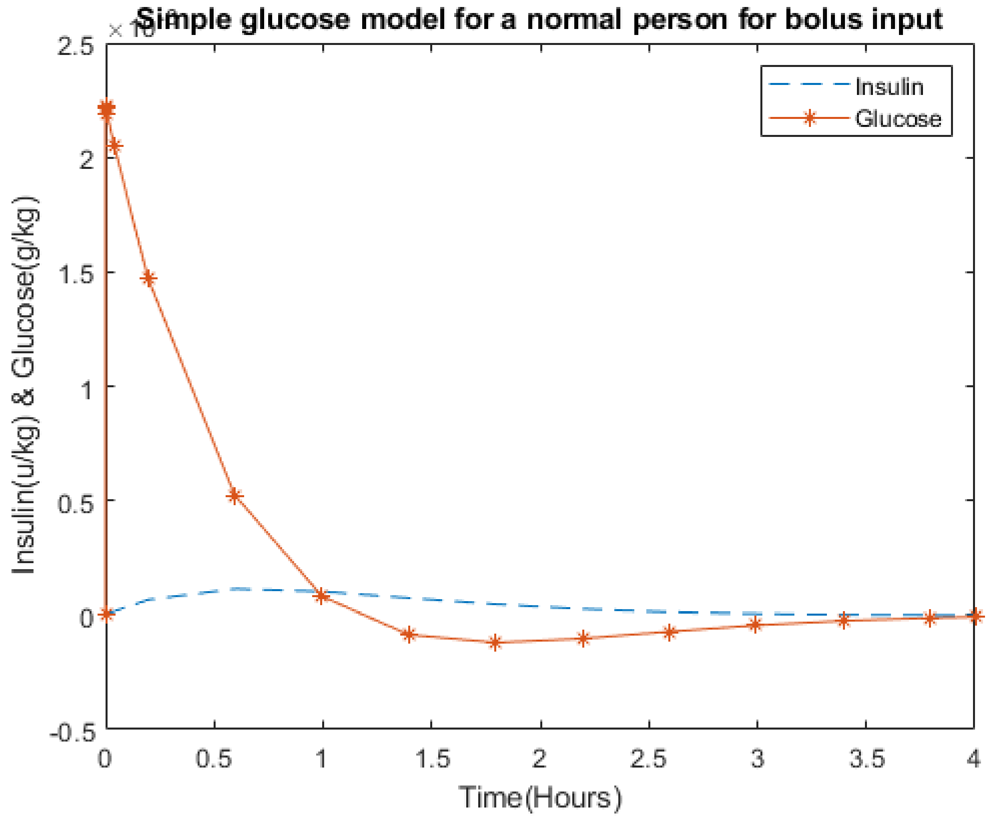

Figure 2: Simple glucose model for a bolus input

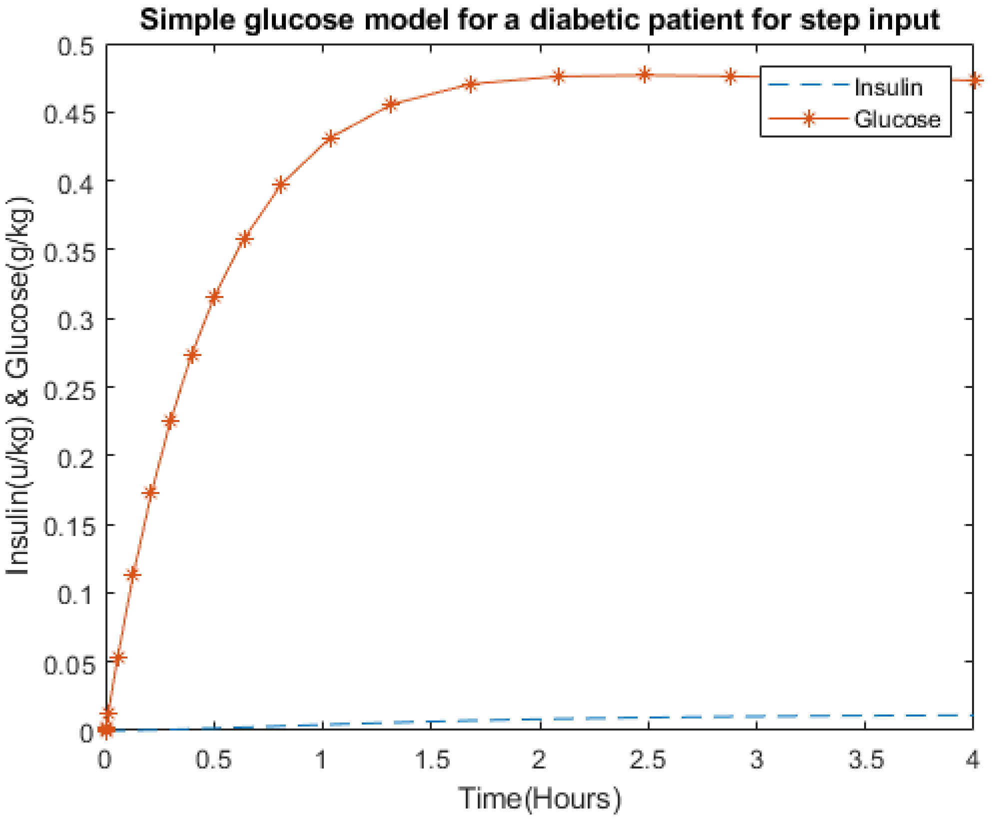

Figure 3: Simple glucose model for a diabetic patient

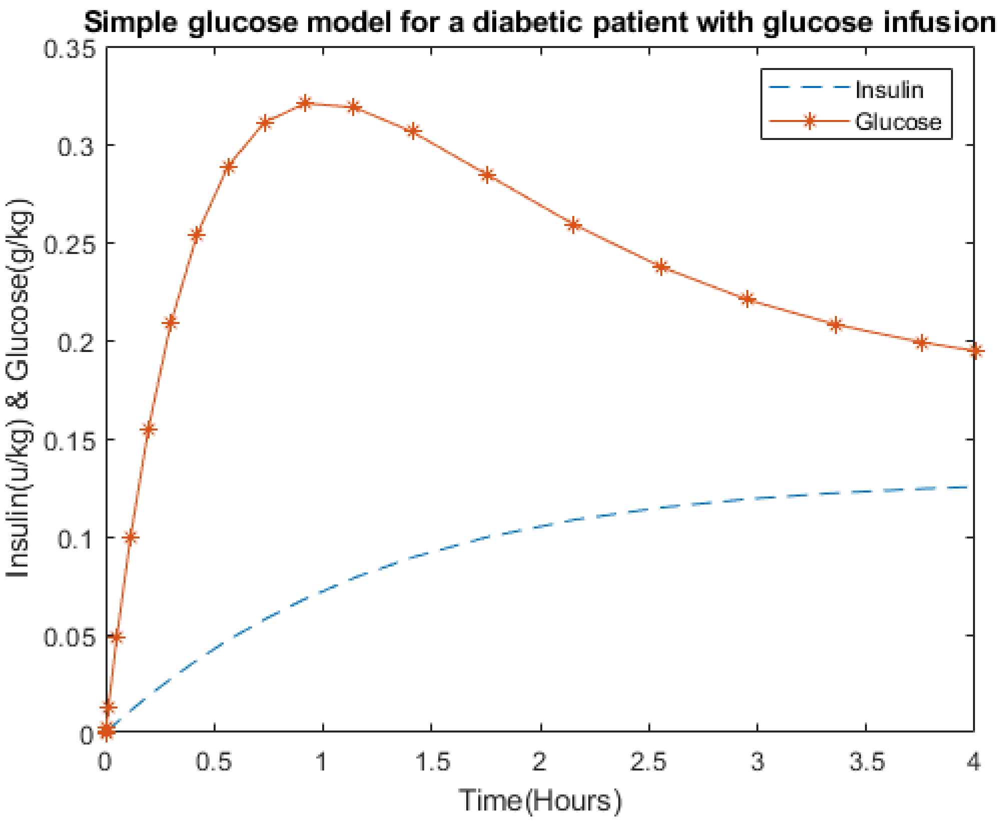

Figure 4: Simple glucose model for a diabetic patient with glucose infusion

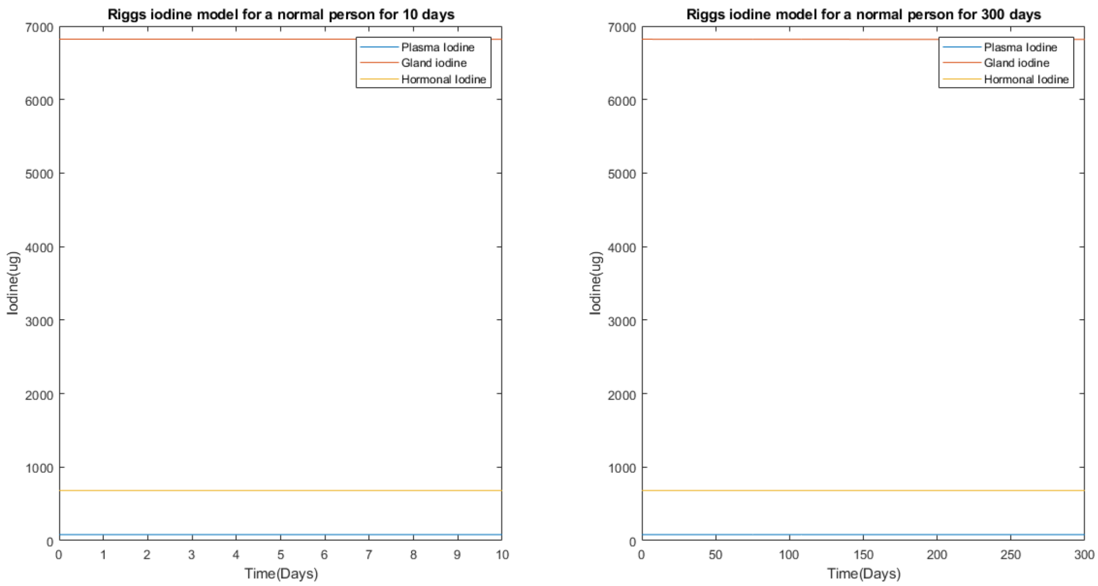

Figure 5: Riggs iodine model for a normal patient

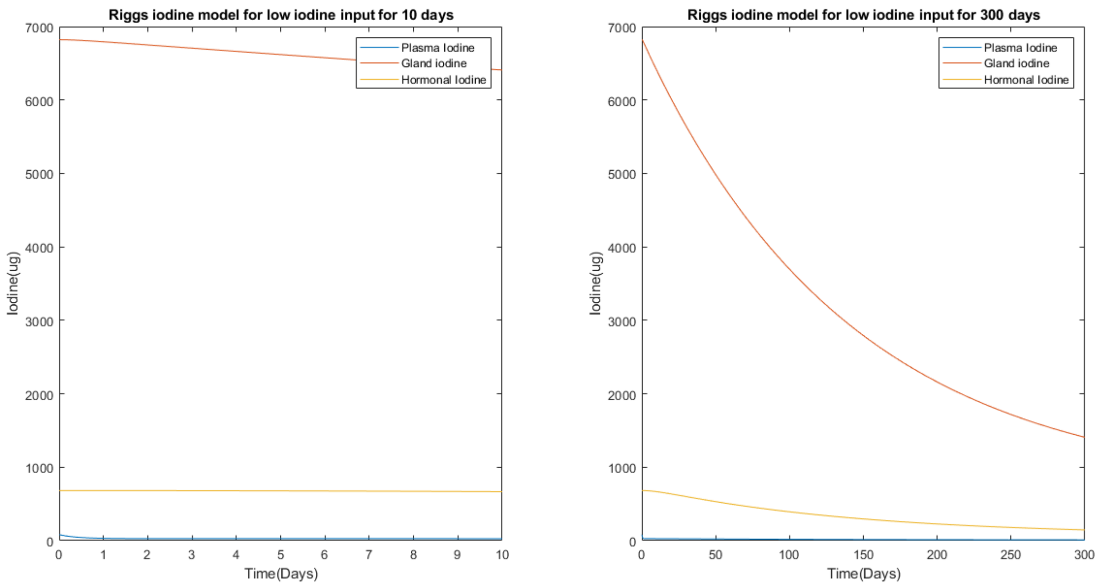

Figure 6: Riggs iodine model for a low iodine patient

$$\dot{\mathbf{y}} = \mathbf{A}.\mathbf{y} + \mathbf{B}$$

$$\dot{\mathbf{y}} = \begin{vmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{vmatrix} \quad \mathbf{A} = \begin{vmatrix} -k_I & 0 & k_3 \\ k_1 & -k_2 & 0 \\ 0 & k_2 & -k_H \end{vmatrix} \quad \mathbf{y} = \begin{vmatrix} I \\ G \\ H \end{vmatrix} \quad \mathbf{B} = \begin{vmatrix} B_1 \\ 0 \\ 0 \end{vmatrix} \tag{1}$$

1. Hypothyroidism due to autoimmune thyroid disease

   In the autoimmune thyroid disease, the immune system attacks the thyroid. It damages the thyroid gland and the amount of gland iodine reduces. Therefore, in modelling I reduced the k_2 parameter in the equation 1.

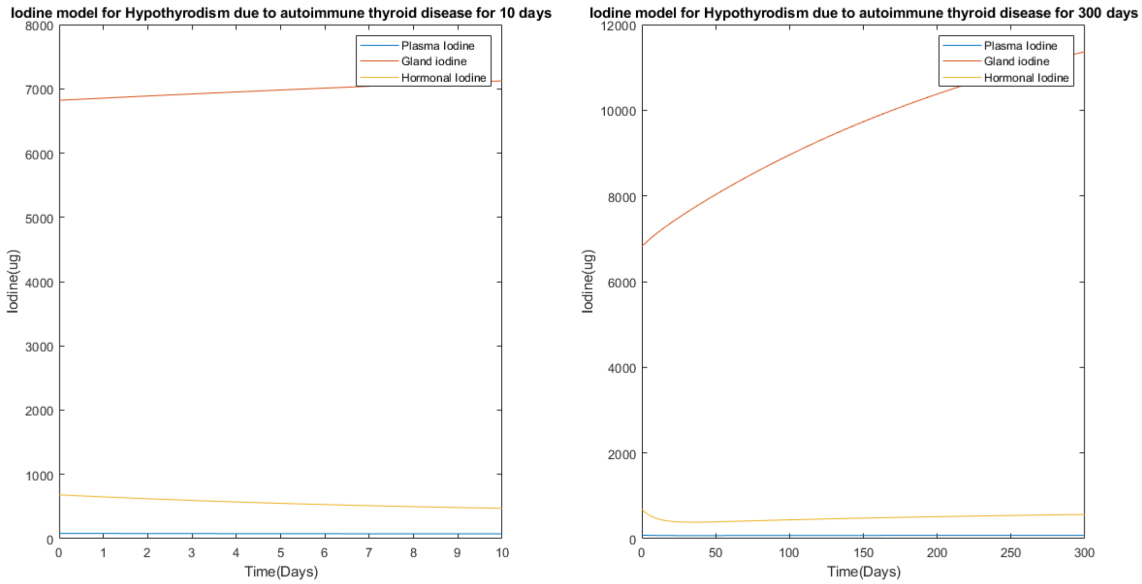

Figure 7: Riggs iodine model for hypothyroidism due to autoimmune thyroid disease

2. Hypothyroidism due to low iodine intake Here the B1 constant in equation 1 is reduced. Therefore, in the modelling, I reduced the initial value to 10µg.

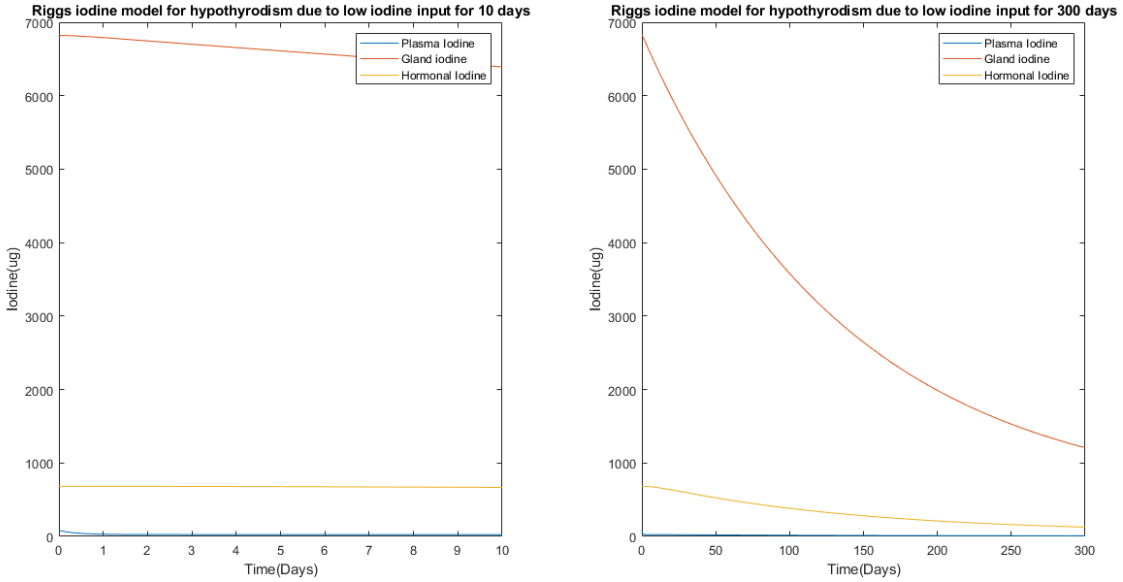

Figure 8: Riggs iodine model for hypothyroidism due to low iodine input

3. Hyperthyroidism due to Grave's disease

   Grave's disease[1] is a condition that increases the iodine production by the thyroid gland. In modelling, I increased the k2 parameter in equation 1 10 times.

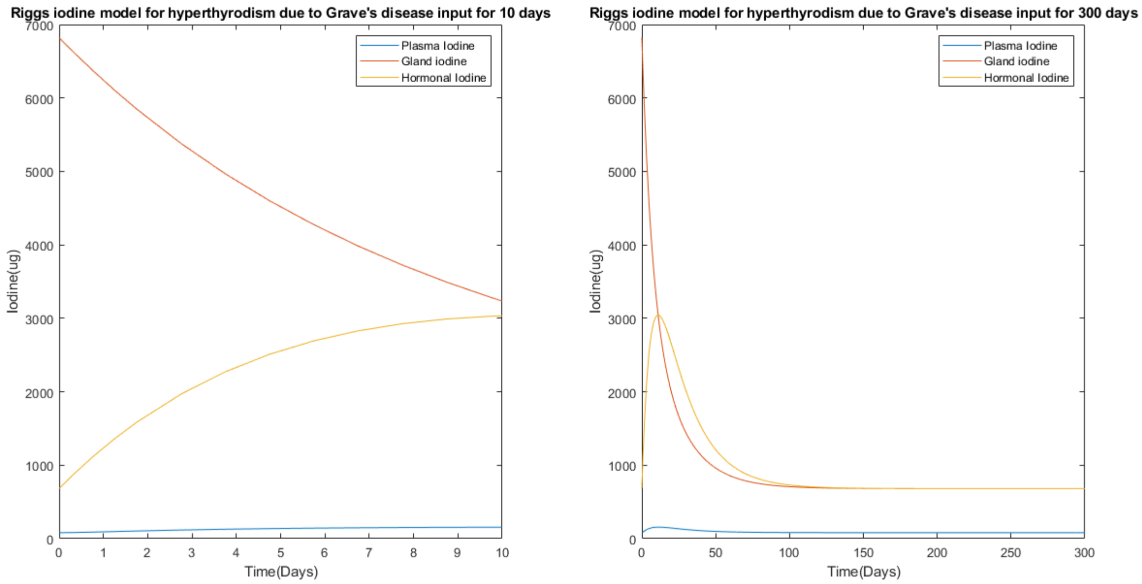

Figure 9: Riggs iodine model for hyperthyroidism due to Grave's disease

4. What are some common causes of goitre and tumours and how can they be simulated in the Riggs' model?

   Goitre is the enlargement of the thyroid gland normally due to iodine deficiency. It will result in hyperthyroidism[2]. Goitre can be modelled increasing k_2 and decreasing B_1.

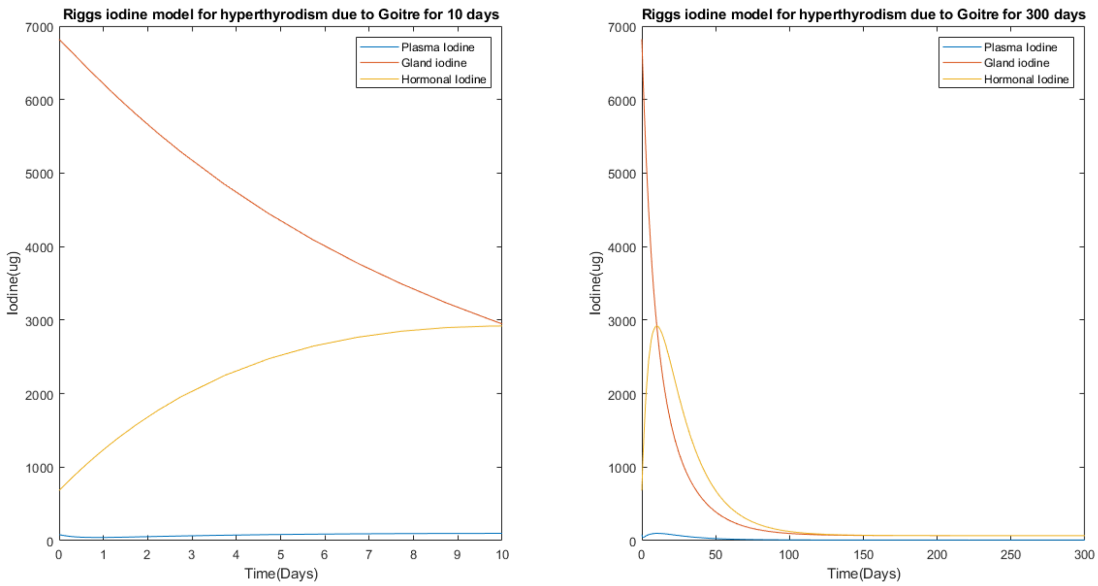

Figure 10: Riggs iodine model for hyperthyroidism due to Goitre

   Tumours are divided into two types as benign and malignant. The most common type is benign.It increases the formation of iodine by the thyroid gland which may lead to hyperthyroidism. To model this the k_2 parameter in the equation1 will increase. The graph will be similar to the Figure9.

2 Part II

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

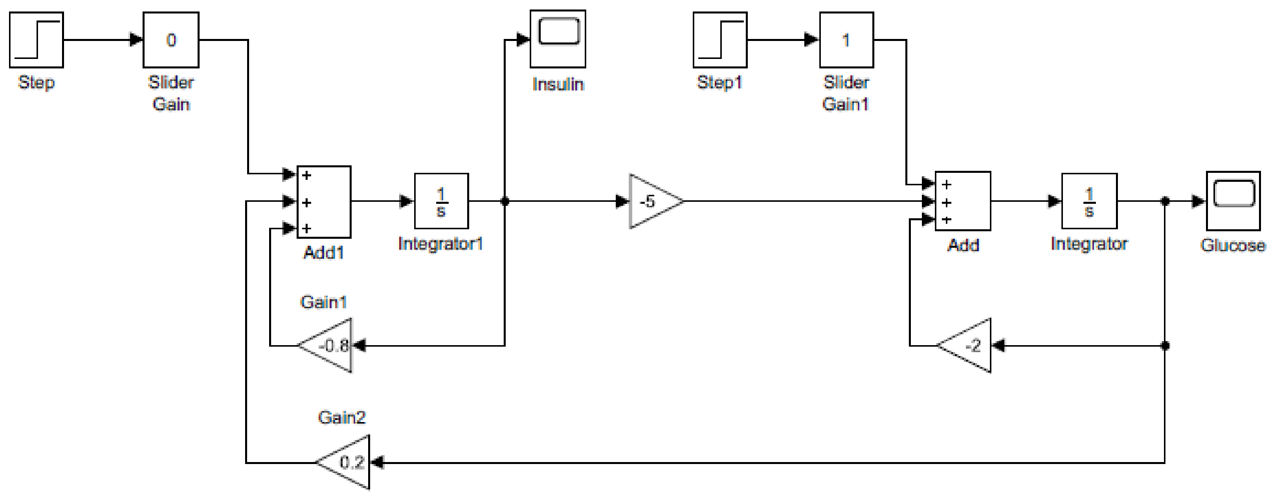

Figure 11: Simulink model for equation2

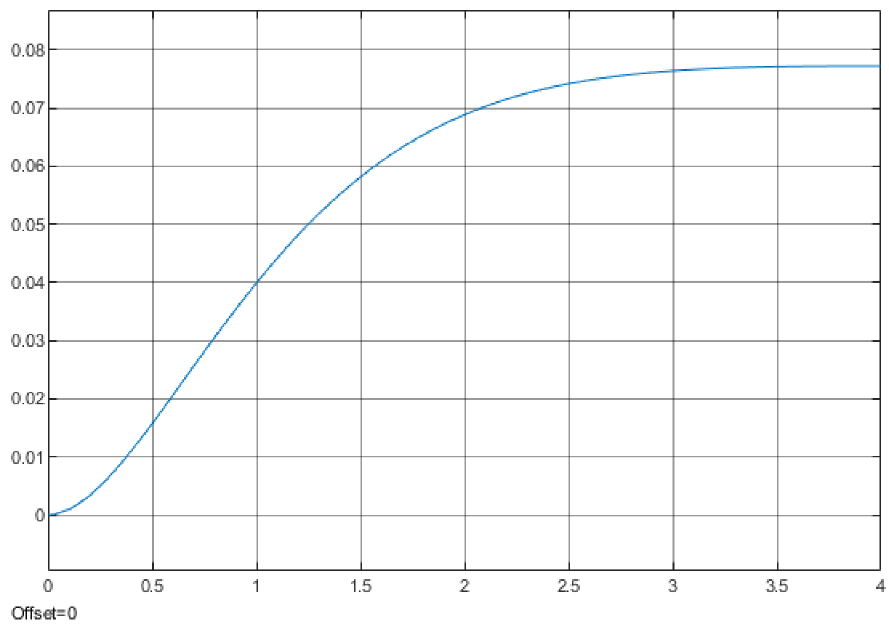

Figure 12: Insulin graph for the Simulink model in Figure11

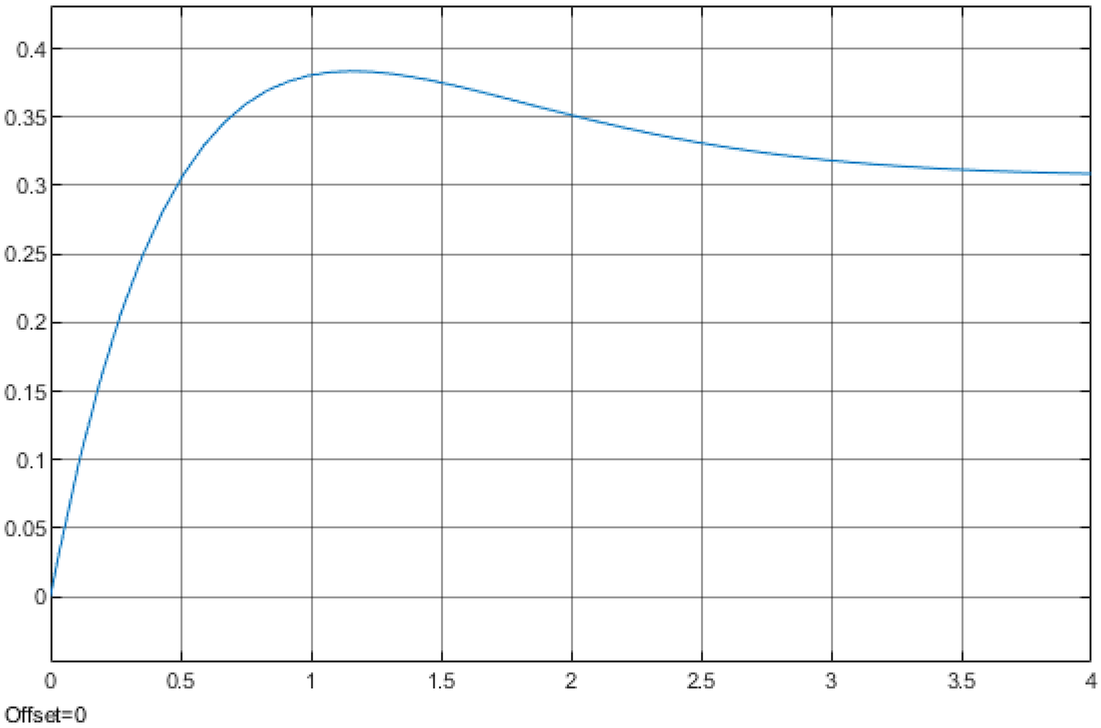

Figure 13: Glucose graph for the Simulink model in Figure11

$$\begin{aligned} \frac{di}{dt} &= -0.63i + 0.13g \\ \frac{dg}{dt} &= -5i - 2.5g + A(t) \end{aligned} \tag{3}$$

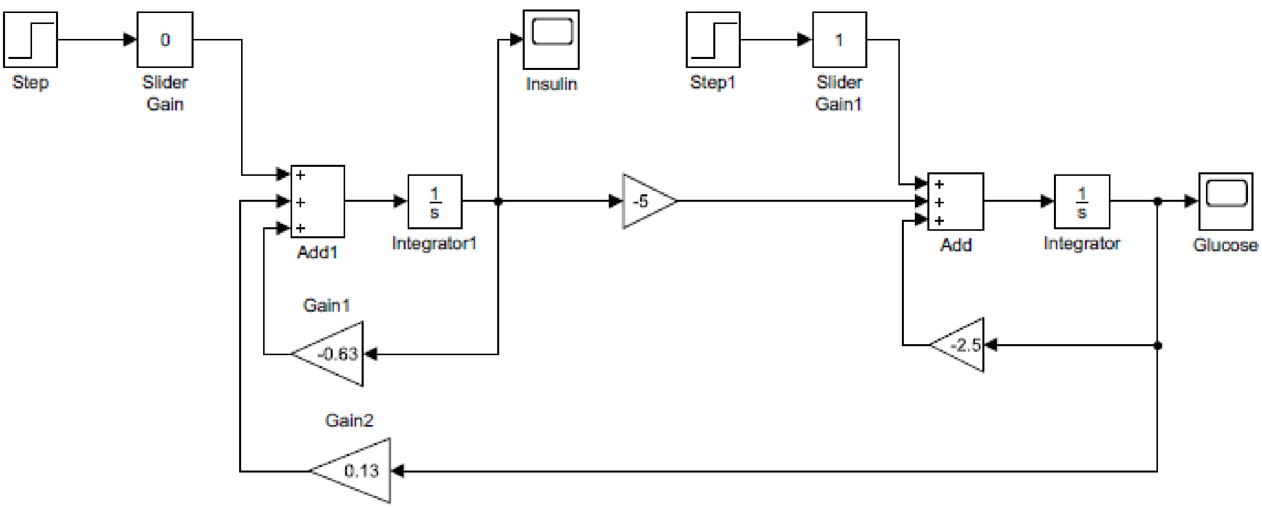

Figure 14: Simulink model for equation3

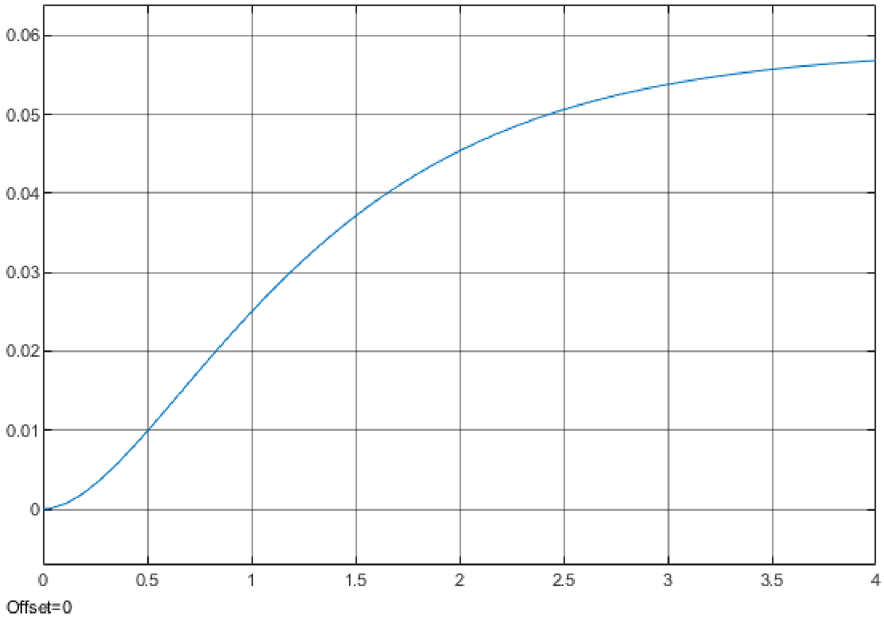

Figure 15: Insulin graph for the Simulink model in Figure14

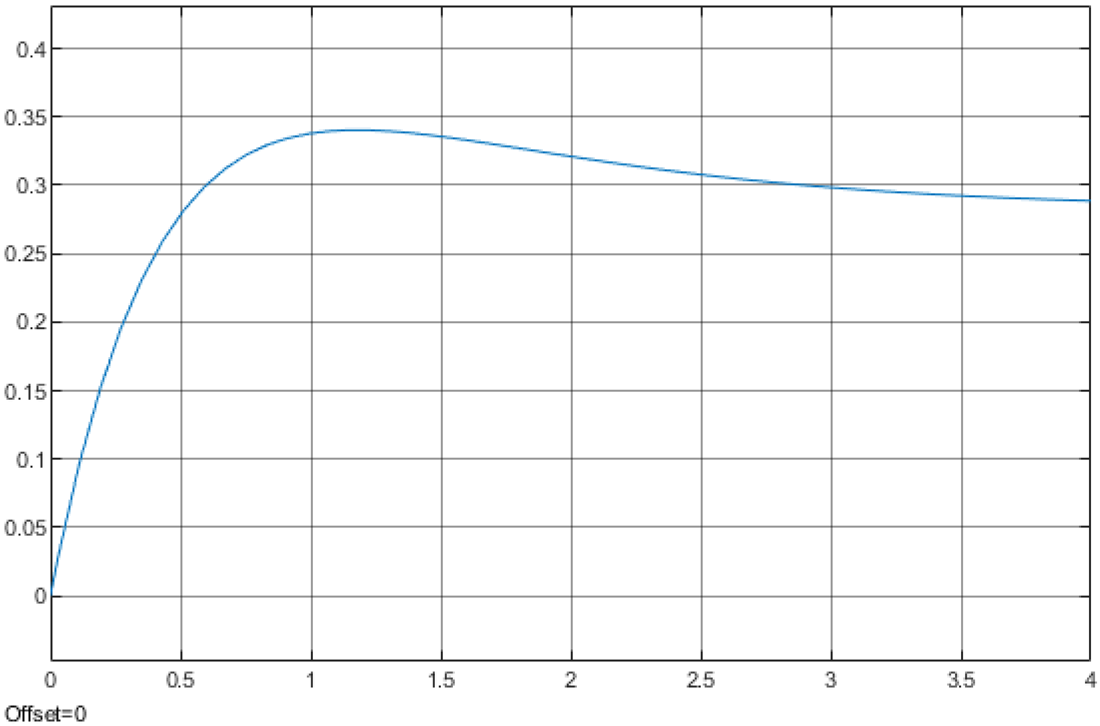

Figure 16: Glucose graph for the Simulink model in Figure14

When considering the two Simulink models shown by Figure[11] and Figure[14], there are differences in the graphs due to the change of the coefficients.In the Figure[13], the glucose level has a peak around 0.375 and the steady value is above 0.3 but the glucose level in the Figure[16] has a peak of about 0.325 and the steady value is below 0.3. In the Figure[12], the insulin level has a peak value of about 0.075 and it becomes stable after 3 hours but in the Figure[15], the insulin level has a peak value of about 0.055 and it becomes stable after 4 hours.

$$\begin{aligned} \frac{di}{dt} &= -0.63i + 0.13g + 0.1 \\ \frac{dg}{dt} &= -5i - 2.5g + A(t) \end{aligned} \tag{4}$$

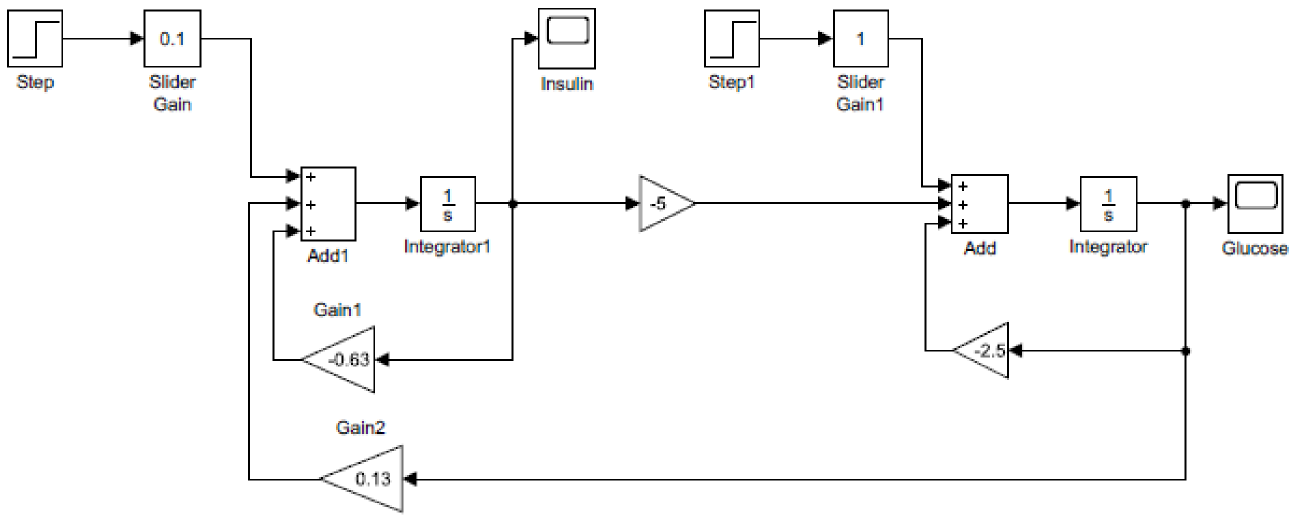

Figure 17: Simulink model for equation4

$$\begin{aligned} \frac{di}{dt} &= -0.63i + 0.01g + 0.1 \\ \frac{dg}{dt} &= -5i - 0.01g + A(t) \end{aligned} \tag{5}$$

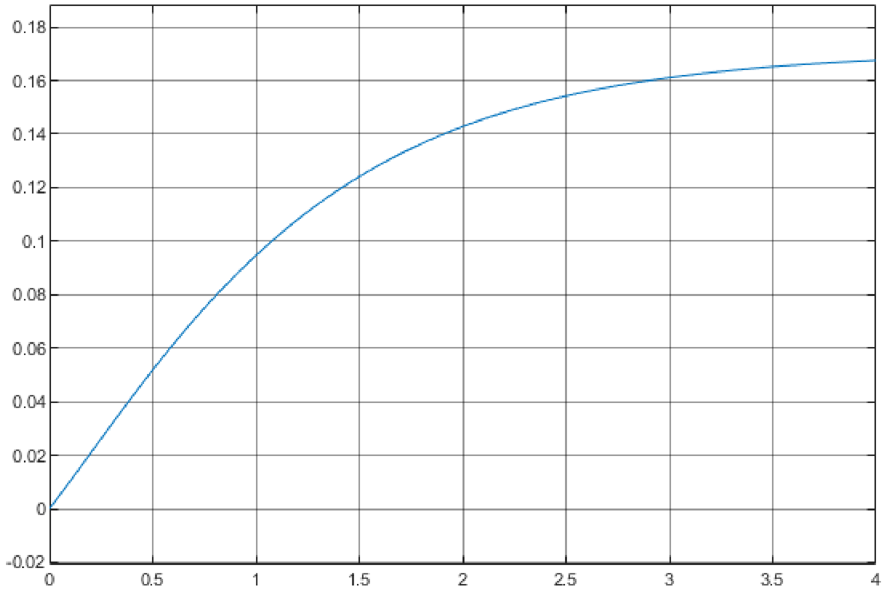

Figure 18: Insulin graph for the Simulink model in Figure17

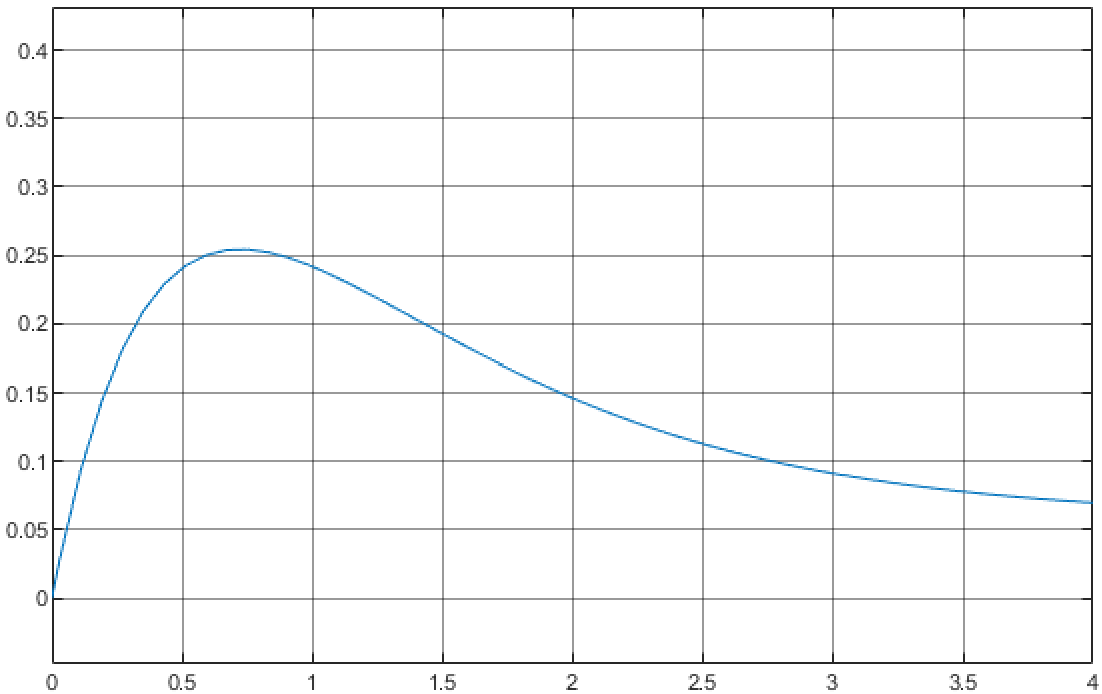

Figure 19: Glucose graph for the Simulink model in Figure17

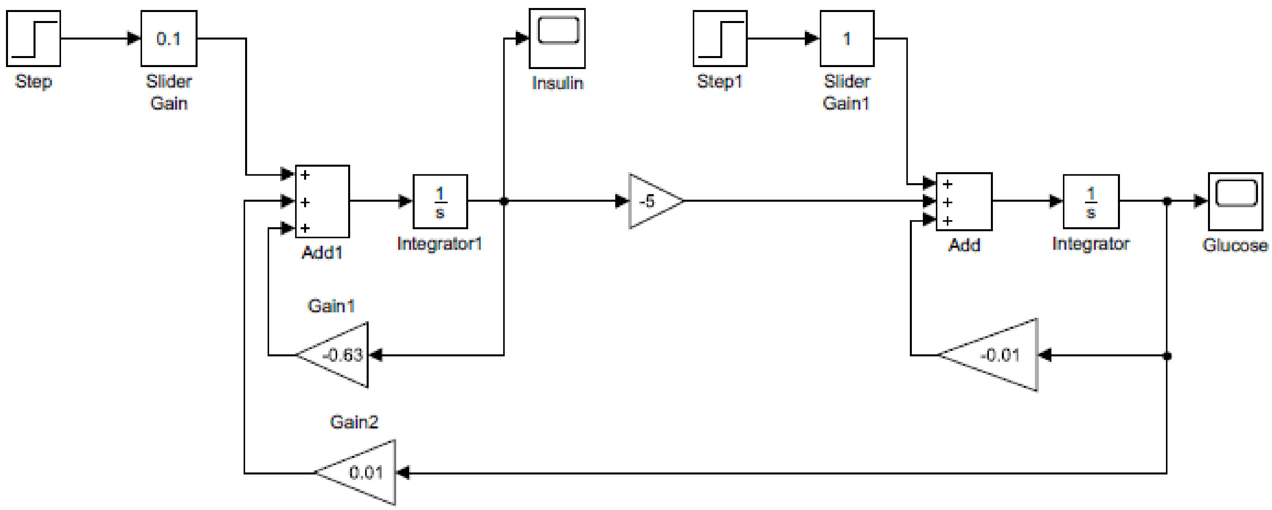

Figure 20: Simulink model for equation5

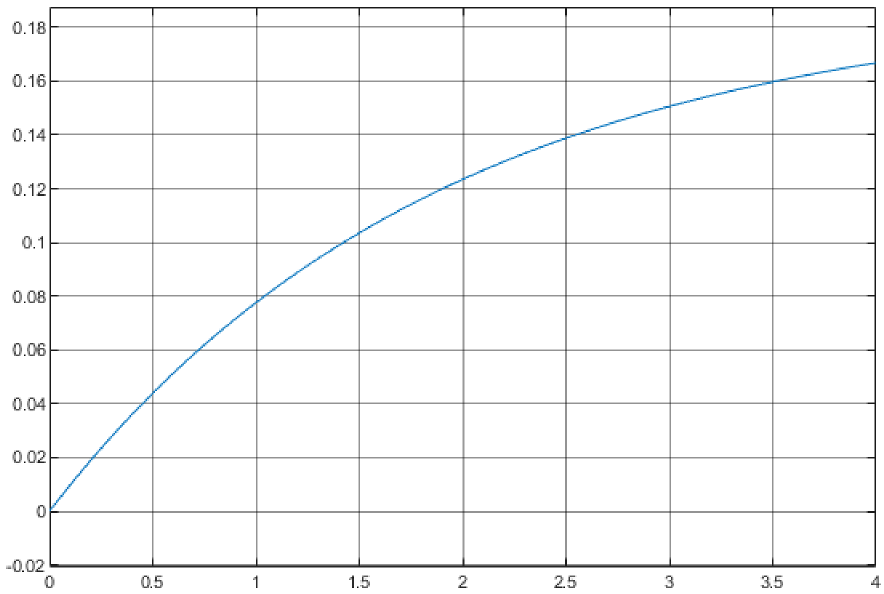

Figure 21: Insulin graph for the Simulink model in Figure20

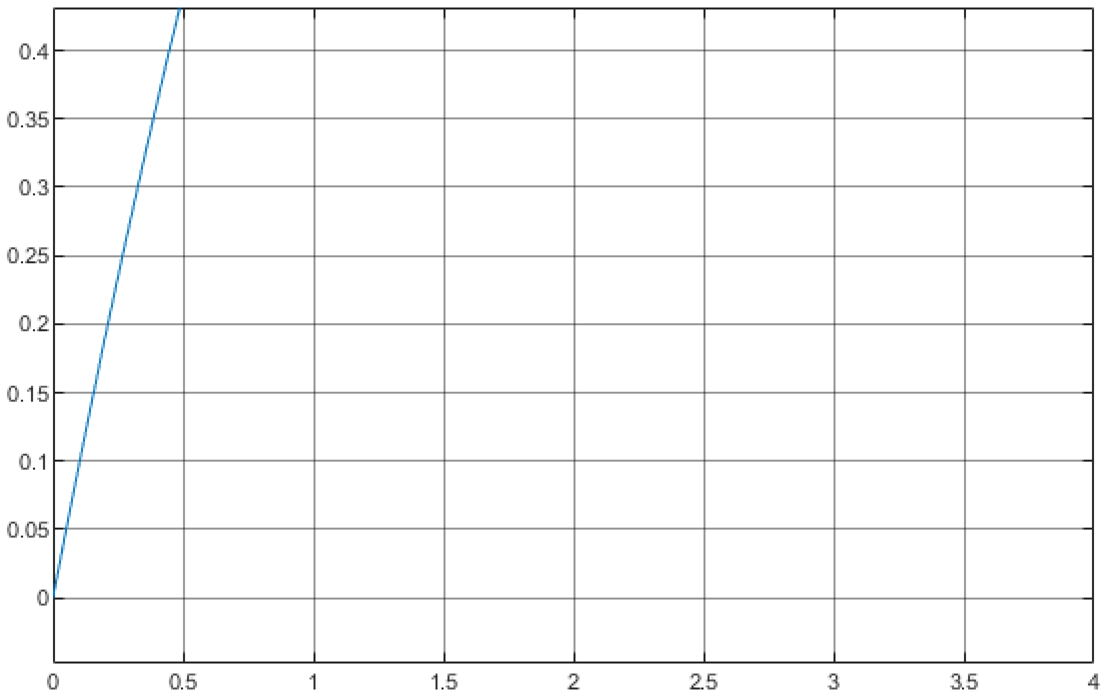

Figure 22: Glucose graph for the Simulink model in Figure20

$$\begin{aligned}\frac{dI}{dt} &= -2.52I + 0.08H + 15 \\ \frac{dG}{dt} &= 0.84I - 0.01G \\ \frac{dH}{dt} &= 0.01G - 0.1H\end{aligned} \tag{6}$$

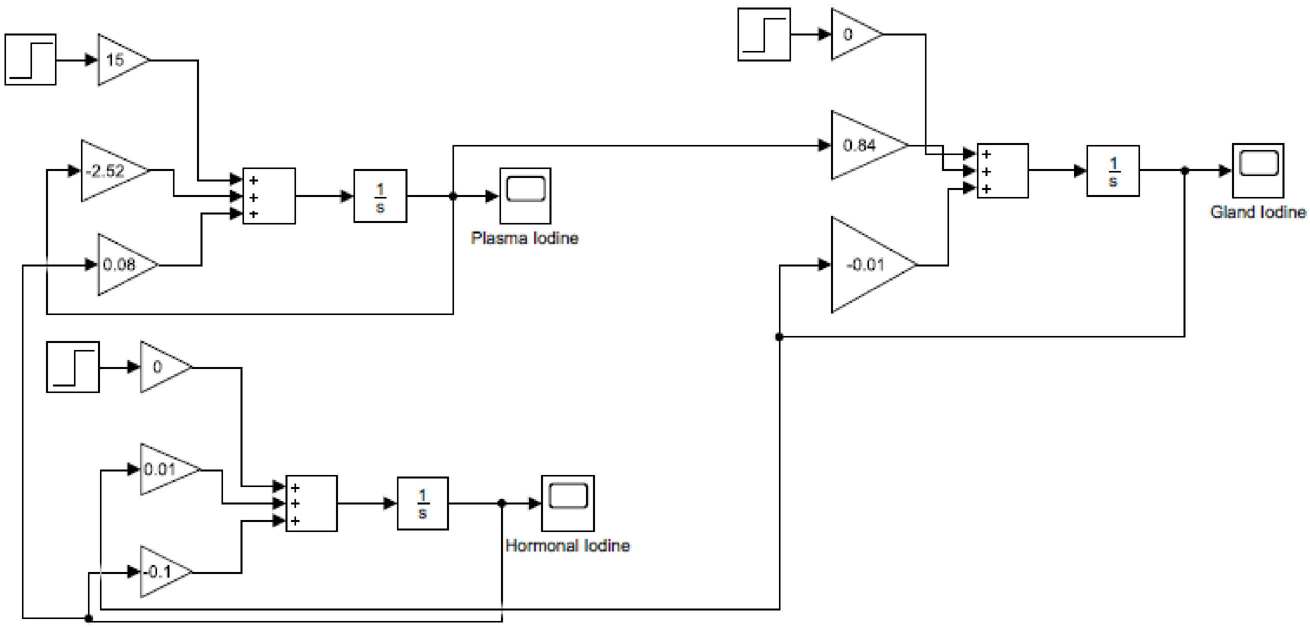

Figure 23: Simulink model for Riggs' iodine model equation6

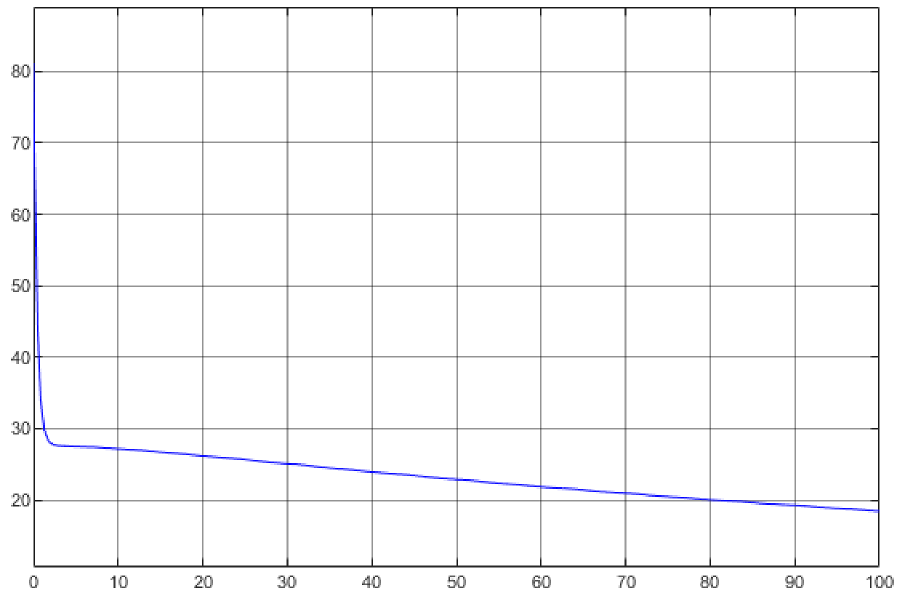

Figure 24: Plasma iodine graph for the Simulink model in Figure23

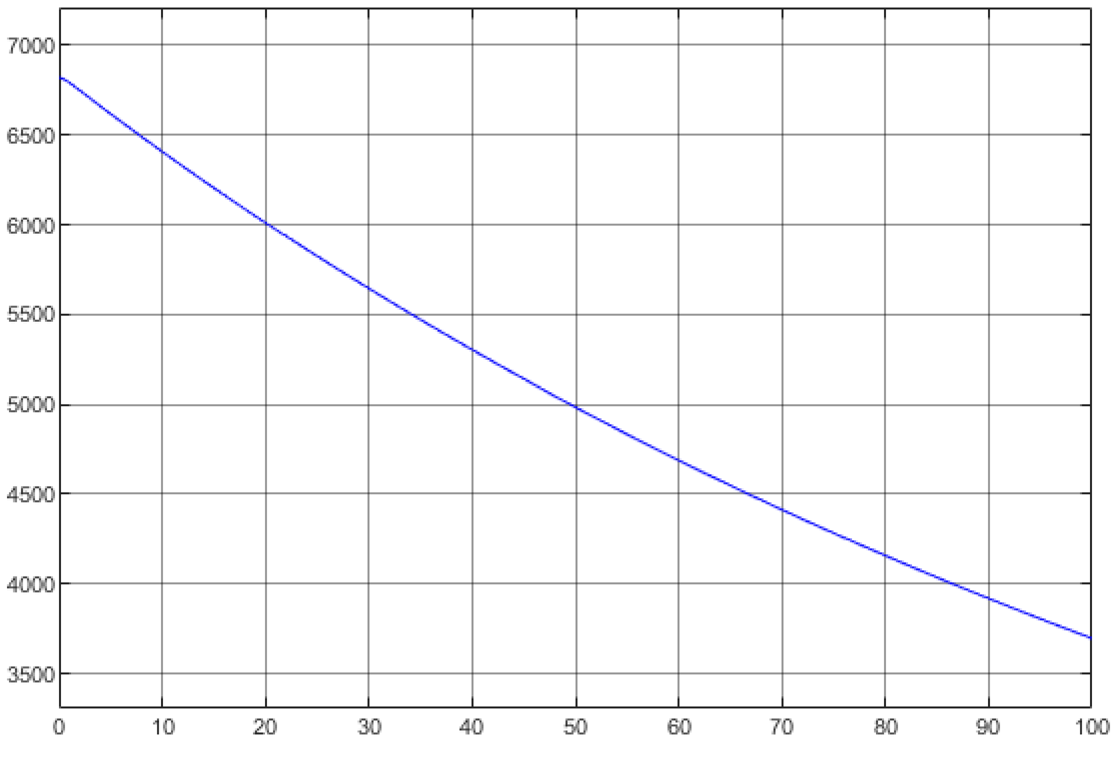

Figure 25: Gland Iodine graph for the Simulink model in Figure23

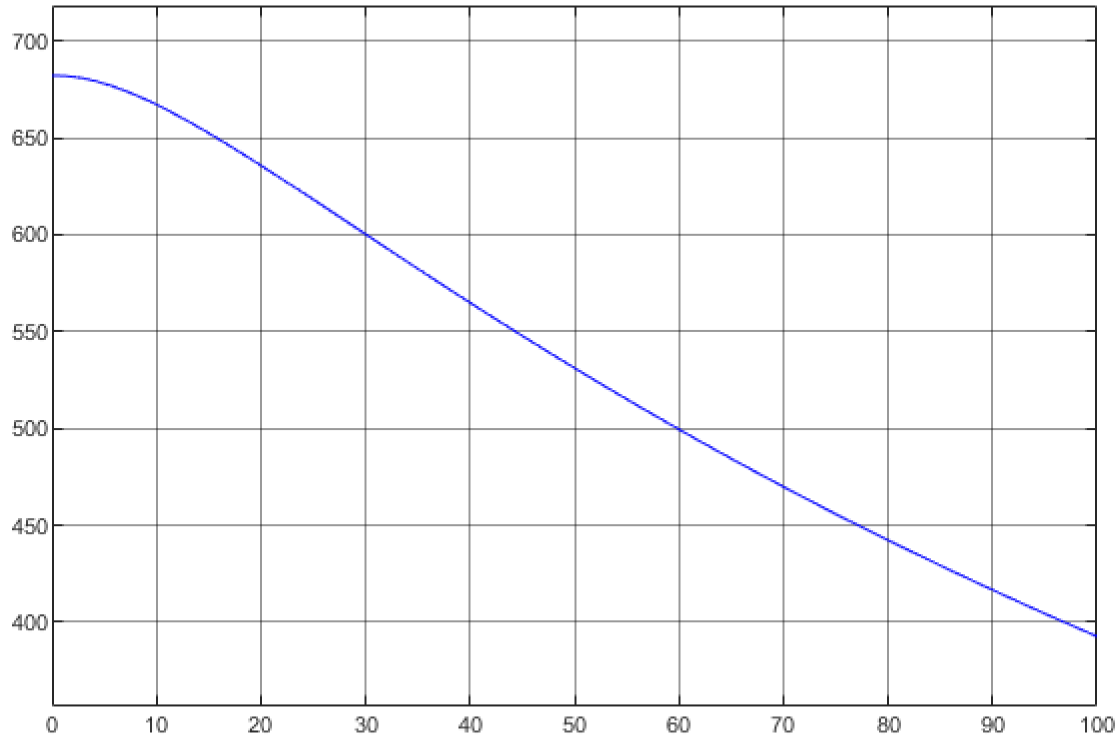

Figure 26: Hormonal Iodine graph for the Simulink model in Figure23

3 Part III

1.

$$\frac{dg}{dt} = -k_4 g(t) - k_6 i(t) + A(t) \quad (7)$$

$$\frac{di}{dt} = k_3 g(t) - k_1 i(t) + B(t) \quad (8)$$

From the Glucose tolerance test, the following constants and functions can be found.

$k_1 = 0.8, k_3 = 0.2, k_4 = 2, k_6 = 5$

$A(t) = u(t), B(t) = 0$

Substituting these values in the equation[7] and equation[8];

$$\frac{dg}{dt} = -2g(t) - 5i(t) + u(t) \quad (9)$$

$$\frac{di}{dt} = 0.2g(t) - 0.8i(t) \quad (10)$$

As $g(t) = G(t) - G(0)$, when $t = 0$ $g(0) = 0$. As the same,$i(0) = 0$;

Obtaining the Laplace transform of the equation[9];

$sG(s) - g(0) = -2G(s) - 2I(s) + \frac{1}{s}$

By substituting the initial values;

$$sG(s) = -2G(s) - 2I(s) + \frac{1}{s} \quad (11)$$

Following the same procedure with equation[8];

$$sI(s) = 0.2G(s) - 0.8I(s) \quad (12)$$

From equation[12];

$$I(s) = \frac{0.2}{(s+0.8)}G(s) \quad (13)$$

By substituting equation[13] in equation[11];

$$G(s) = \frac{s+0.8}{s(s^2+2.8s+2)} \quad (14)$$

Obtaining the partial fractions of the equation[14];

$\frac{s+0.8}{s(s^2+2.8s+2)} = \frac{C}{s} + \frac{Ds+E}{s^2+2.8s+2}$

$s + 0.8 = C(s^2 + 2.8s + 2) + s(Ds + E)$

Equating the coefficients;

s^2;
$C + D = 0$

s;
$2.8C + E = 1$

Constant term;
$2C = 0.8$

By solving these equations, the constants can be found.

$C = 0.4, D = -0.4, E = 1 - 2.8D = -0.12$

By substituting these values in equation[14];

$G(s) = \frac{0.4}{s} - \frac{0.4s+0.12}{s^2+2.8s+2}$

Rearranging the terms in the above expression;

$G(s) = \frac{0.4}{s} - 0.4\frac{(s+1.4)}{(s+1.4)^2+(0.2)^2} + \frac{0.44}{(s+1.4)^2+(0.2)^2}$

Finding the inverse Laplace transform;

$$g(t) = 2.2e^{-1.4t}sin(0.2t) - 0.4e^{-1.4t}cos(0.2t) + 0.4u(t) \tag{15}$$

By substituting equation[14] in equation[13];

$I(s) = \frac{0.2}{s(s^2+2.8s+2)}$
Obtaining the partial fractions of the equation[14];

$\frac{0.2}{s(s^2+2.8s+2)} = \frac{F}{s} + \frac{Hs+J}{s^2+2.8s+2}$

$0.2 = F(s^2 + 2.8s + 2) + s(Hs + J)$

Equating the coefficients;

s^2;
$F + H = 0$

s;
$2.8F + J = 0$

Constant term;
$2F = 0.2$

By solving these equations, the constants can be found.

$F = 0.1, H = -0.1, J = -0.28$

By substituting these values in equation[14];

$I(s) = \frac{0.1}{s} - \frac{0.1s+0.28}{s^2+2.8s+2}$

Rearranging the terms in the above expression;

$I(s) = \frac{0.1}{s} - 0.1\frac{(s+1.4)}{(s+1.4)^2+(0.2)^2} - 0.7\frac{0.2}{(s+1.4)^2+(0.2)^2}$

Finding the inverse Laplace transform;

$$i(t) = -0.7e^{-1.4t}sin(0.2t) - 0.1e^{-1.4t}cos(0.2t) + 0.1u(t) \tag{16}$$

To verify the analytically obtained functions [15] and [16], the listing[4] is used. It generates Figure[27] which verifies the Boiles' plasma glucose model.

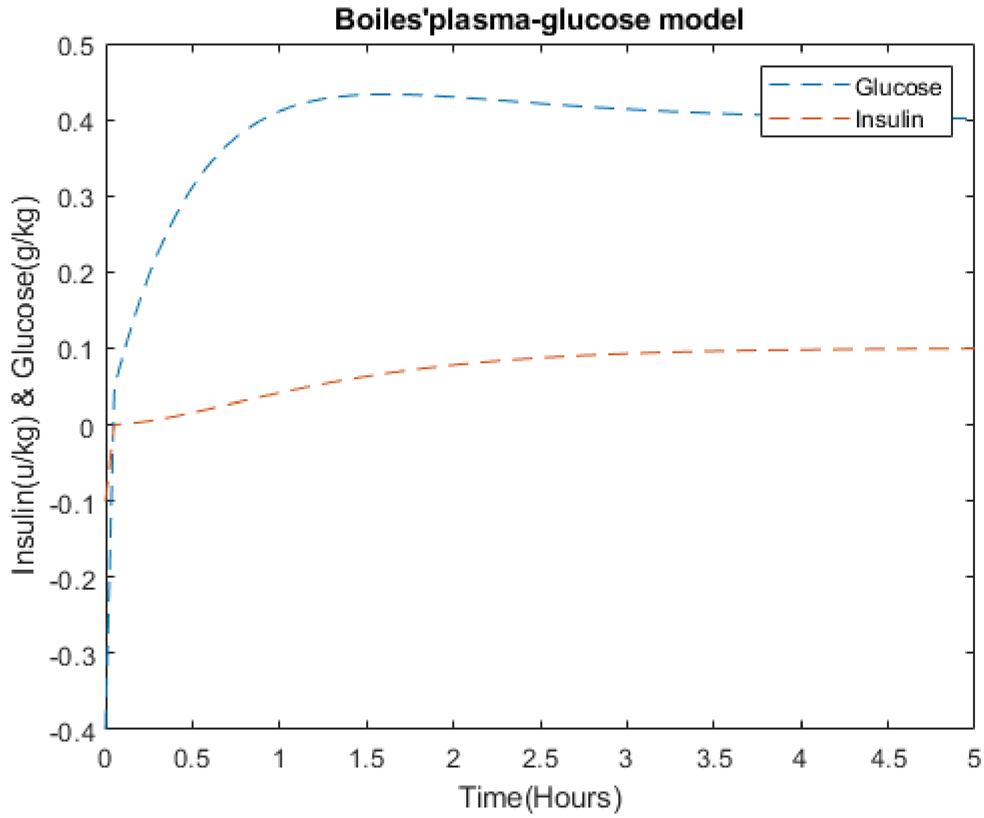

Figure 27: Verification of the Boiles' plasma glucose model

2. Expansion of the Boiles' plasma glucose model considering the effect of glucagon

   When the blood glucose level decreases, glucagon breaks down to form glucose. This process happens in the liver and skeletal muscles and it is called glycogenolysis. When the blood glucose level increases, the opposite process happens and it is called glycogenesis. Glucagon is formed in the pancreas.Therefore, assuming a similar compartmental model as glucose for glucagon;

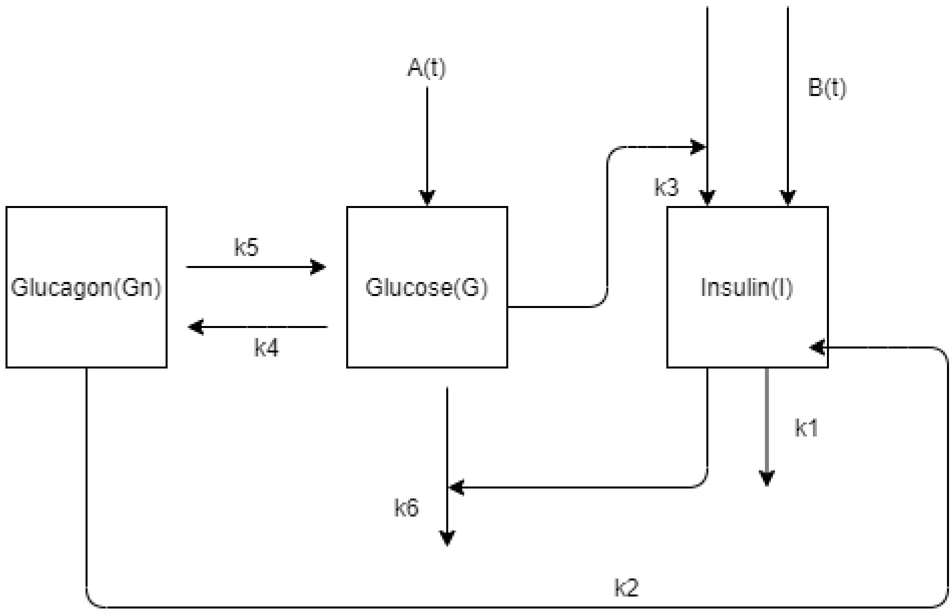

Figure 28: Plasma glucose model with Glucagon

Based on the model shown in Figure[28];

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

$\frac{dI}{dt} = k_3 G(t) - k_1 I(t) + k_2 Gn(t) + B(t)$

$\frac{dGn}{dt} = -(k_5 + k_2)Gn(t) + k_4 G(t)$

In the equilibrium;

$\frac{dG}{dt} = 0, \frac{dI}{dt} = 0, \frac{dGn}{dt} = 0$

Using the above equilibrium conditions, the following can be assumed.

$k_5 = 4, k_2 = -1, Gn_0 = 0.156$

By substituting the following values in the above equations;

$\frac{dG}{dt} = -2G(t) - 5I(t) + 4Gn(t) + u(t)$

$\frac{dI}{dt} = 0.2G(t) - 0.8I(t) - Gn(t)$

$\frac{dGn}{dt} = 2G(t) - 3Gn(t)$

The above equations are solved as shown in Listing[5] to obtain Figure[29].
The Figure[29] accounts for the effect of glucagon in the plasma glucose model.With the decrease of the insulin

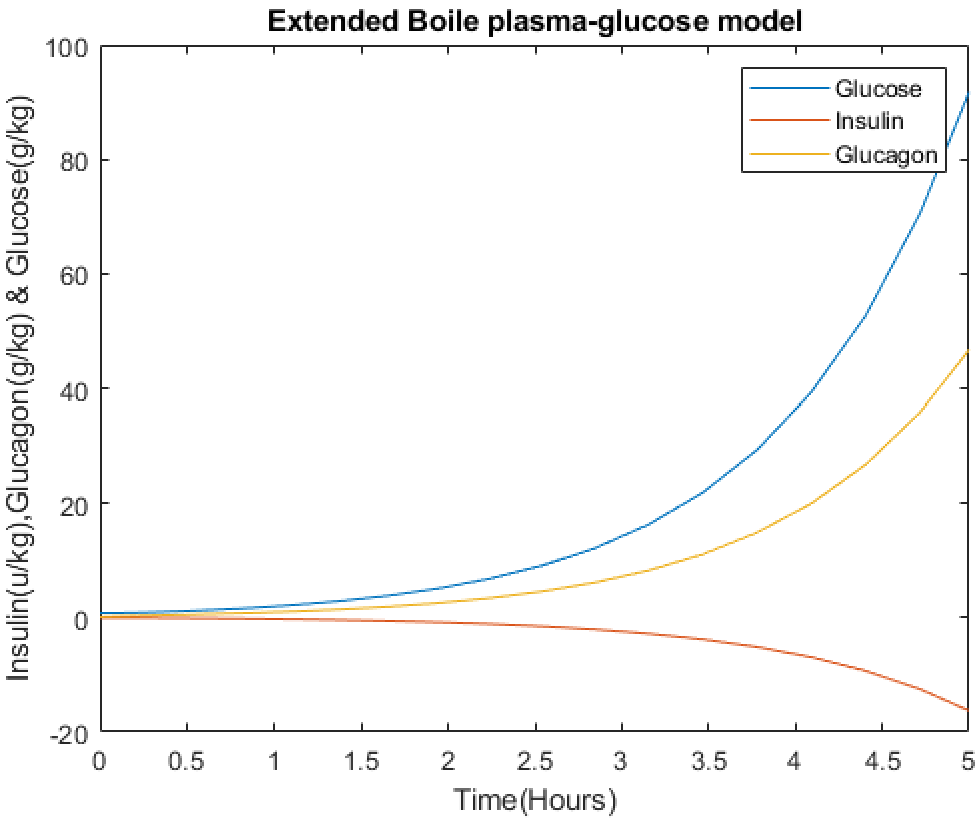

Figure 29: Graph of the extended plasma glucose model

level, the glucose level increases. With the increase of the glucose level, the glucagon level increases.

References

[1] Wikipedia, *Graves' disease — Wikipedia, the free encyclopedia*, http://en.wikipedia.org/w/index.php?title=Graves'%20disease&oldid=937967156, [Online; accessed 01-February-2020], 2020.

[2] A. Waugh and A. Grant, *Ross & Wilson Anatomy and Physiology in Health and Illness E-Book*. Elsevier Health Sciences, 2018, ISBN: 9780702072840. [Online]. Available: https://books.google.lk/books?id=9w5kDwAAQBAJ.

A MATLAB codes

Listing 1: Main code

```
close all;
clear all;
clc;
question1;
question2;
```

Listing 2: The Matlab code for question 1

```
%Question 1
tspan = [0 4];
I0 = 0;
G0 = 0;
%For a normal person
%For a step input
[t,y1] = ode23(@(t,y) [-0.8 0.2;-5 -2]*y+[0 1]', tspan, [I0 G0]);
figure;
plot(t,y1(:,1),'--',t,y1(:,2),'-*');
xlabel('Time(Hours)');
ylabel('Insulin(u/kg) & Glucose(g/kg)');
title('Simple glucose model for a normal person for step input');
legend('Insulin', 'Glucose');
%For a delta function
[t,y2] = ode23(@(t,y) [-0.8 0.2;-5 -2]*y+[0 1-sign(t)]', tspan, [I0 G0]);
figure;
plot(t,y2(:,1),'--',t,y2(:,2),'*-');
xlabel('Time(Hours)');
ylabel('Insulin(u/kg) & Glucose(g/kg)');
title('Simple glucose model for a normal person for bolus input');
legend('Insulin', 'Glucose');
%For a diabetic patient
%For a step input
[t,y3] = ode23(@(t,y) [-0.8 0.02;-5 -2]*y+[0 1]', tspan, [I0 G0]);
figure;
plot(t,y3(:,1),'--',t,y3(:,2),'-*');
xlabel('Time(Hours)');
ylabel('Insulin(u/kg) & Glucose(g/kg)');
title('Simple glucose model for a diabetic patient for step input');
legend('Insulin', 'Glucose');
%For a step input with glucose infusion
[t,y3] = ode23(@(t,y) [-0.8 0.02;-5 -2]*y+[0.1 1]', tspan, [I0 G0]);
figure;
plot(t,y3(:,1),'--',t,y3(:,2),'-*');
xlabel('Time(Hours)');
ylabel('Insulin(u/kg) & Glucose(g/kg)');
title('Simple glucose model for a diabetic patient with glucose infusion');
legend('Insulin', 'Glucose');
```

Listing 3: The Matlab code for question 2

```
tspan1 = [0 10];
tspan2 = [0 300];
I0 = 81.2;
G0 = 6821;
H0 = 682.1;
%Normal iodine input
[t1,y1] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.01 0;0 0.01 -0.1]*y+[150 0 0]', tspan1, [I0
    G0 H0]);
[t2,y2] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.01 0;0 0.01 -0.1]*y+[150 0 0]', tspan2, [I0
    G0 H0]);
figure;
subplot(1,2,1);
plot(t1,y1);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title('Riggs iodine model for a normal person for 10 days');
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
subplot(1,2,2);
plot(t2,y2);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title('Riggs iodine model for a normal person for 300 days');
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
%Low iodine input
[t3,y3] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.01 0;0 0.01 -0.1]*y+[15 0 0]', tspan1, [I0
    G0 H0]);
[t4,y4] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.01 0;0 0.01 -0.1]*y+[15 0 0]', tspan2, [I0
    G0 H0]);
figure;
subplot(1,2,1);
plot(t3,y3);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title('Riggs iodine model for low iodine input for 10 days');
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
subplot(1,2,2);
plot(t4,y4);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title('Riggs iodine model for low iodine input for 300 days');
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
%Hypothyrodism due to autoimmune thyroid disease,k2 is reduced 2 times
[t5,y5] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.005 0;0 0.005 -0.1]*y+[150 0 0]', tspan1, [
    I0 G0 H0]);
[t6,y6] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.005 0;0 0.005 -0.1]*y+[150 0 0]', tspan2, [
    I0 G0 H0]);
figure;
subplot(1,2,1);
plot(t5,y5);
xlabel('Time(Days)');
```

```
ylabel('Iodine(ug)');
title('Iodine model for Hypothyrodism due to autoimmune thyroid disease for 10 days');
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
subplot(1,2,2);
plot(t6,y6);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title('Iodine model for Hypothyrodism due to autoimmune thyroid disease for 300 days');
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
%Hypothyrodism due to low iodine intake, B1 is reduced to 10ug
[t7,y7] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.01 0;0 0.01 -0.1]*y+[10 0 0]', tspan1, [I0
    G0 H0]);
[t8,y8] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.01 0;0 0.01 -0.1]*y+[10 0 0]', tspan2, [I0
    G0 H0]);
figure;
subplot(1,2,1);
plot(t7,y7);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title('Riggs iodine model for hypothyrodism due to low iodine input for 10 days');
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
subplot(1,2,2);
plot(t8,y8);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title('Riggs iodine model for hypothyrodism due to low iodine input for 300 days');
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
%Hyperthyrodism due to Goitre,k2 is increased 10 fold B_1 reduced 10 fold
[t11,y11] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.1 0;0 0.1 -0.1]*y+[15 0 0]', tspan1, [I0
    G0 H0]);
[t12,y12] = ode23(@(t,y) [-2.52 0 0.08;0.84 -0.1 0;0 0.1 -0.1]*y+[15 0 0]', tspan2, [I0
    G0 H0]);
figure;
subplot(1,2,1);
plot(t11,y11);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title(Riggs iodine model for hyperthyrodism due to Goitre for 10 days);
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
subplot(1,2,2);
plot(t12,y12);
xlabel('Time(Days)');
ylabel('Iodine(ug)');
title(Riggs iodine model for hyperthyrodism due to Goitre for 300 days);
legend('Plasma Iodine', 'Gland iodine','Hormonal Iodine');
```

Listing 4: The Matlab code for the functions 15,16

```
t=linspace(0,5);
g = 0.4.*sign(t)+2.2.*exp(-1.4*t).*sin(0.2.*t)-0.4.*exp(-1.4.*t).*cos(0.2.*t);
I = 0.1.*sign(t)-0.7.*exp(-1.4*t).*sin(0.2.*t)-0.1.*exp(-1.4.*t).*cos(0.2.*t);
figure;
plot(t,g,-,t,I,-);
xlabel('Time(Hours)');
ylabel('Insulin(u/kg) & Glucose(g/kg)');
title(Boiles'plasma-glucose model);
legend('Glucose','Insulin');
```

Listing 5: The Matlab code for the extended Boiles'model in Figure28

```
tspan = [0 5];
I0 = 0.005;
G0 = 0.8;
Gn0 =0.156;
[t,y] = ode23(@(t,y) [-2 -5 4;0.2 -0.8 -1;2 0 -3]*y+[sign(t) 0 0]', tspan, [G0 I0 Gn0]);
figure;
plot(t,y);
xlabel('Time(Hours)');
ylabel('Insulin(u/kg),Glucagon(g/kg) & Glucose(g/kg)');
title('Extended Boile plasma-glucose model');
legend('Glucose', 'Insulin','Glucagon');
```