Department of Electronic and Telecommunication Engineering
University of Moratuwa

BM2101 – Analysis of Physiological Systems

Assignment 4

Use of MATLAB to investigate compartmental systems

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Contents

1 Part 1

1.1 Question 1

Since the plasma glucose/insulin model could be expressed through,

$$\frac{di}{dt} = -0.8i + 0.2g \dots\dots\dots\dots\dots\dots\dots\dots\dots [1.1]$$

$$\frac{dg}{dt} = -5i - 2g + A(t) \dots\dots\dots\dots\dots\dots\dots\dots [1.2]$$

where i is the deviation in insulin level from normal (in international units/kg), g is the deviation in glucose level from normal (in g/kg) and t is time in hours.

Therefore, for a step input,

$$A(t) = \frac{1\frac{g}{kg}}{h} for\ t > 0 \dots\dots\dots\dots\dots\dots\dots\dots [1.3]$$

As per yp = ax+b,

$$\begin{bmatrix} \frac{di}{dt} \\ \frac{dg}{dt} \end{bmatrix} = \begin{bmatrix} -0.8 & 0.2 \\ -5 & -2 \end{bmatrix} \begin{bmatrix} i \\ g \end{bmatrix} + \begin{bmatrix} 0 \\ u(t) \end{bmatrix} \dots\dots [1.4]$$

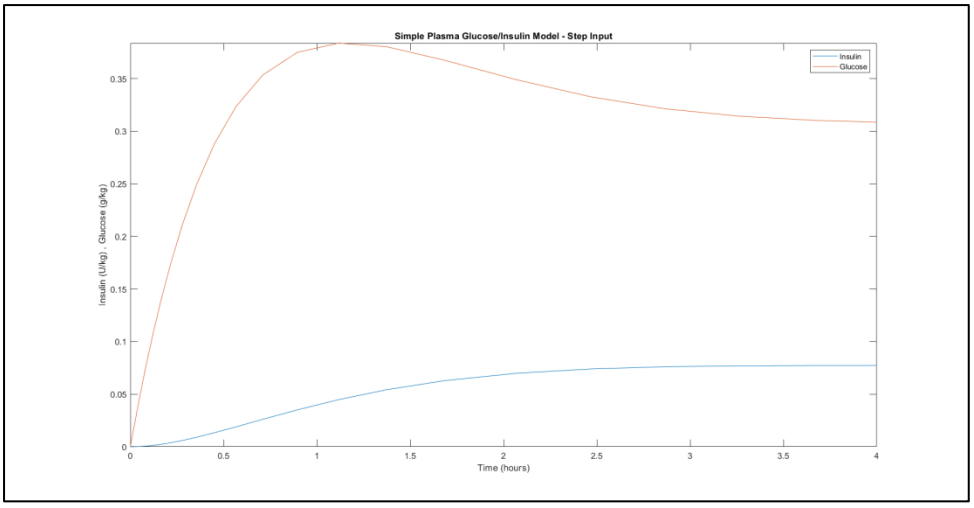

Figure 1: MATLAB implementation of plasma glucose/insulin model for a step input

For a bolus input,

$$x = 1 - sign(t)\ where\ x\ is\ a\ \delta\ function\ at\ t = 0 \dots\dots [1.5]$$

Therefore,

$$\begin{bmatrix} \frac{di}{dt} \\ \frac{dg}{dt} \end{bmatrix} = \begin{bmatrix} -0.8 & 0.2 \\ -5 & -2 \end{bmatrix} \begin{bmatrix} i \\ g \end{bmatrix} + \begin{bmatrix} 0 \\ \delta(t) \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots [1.6]$$

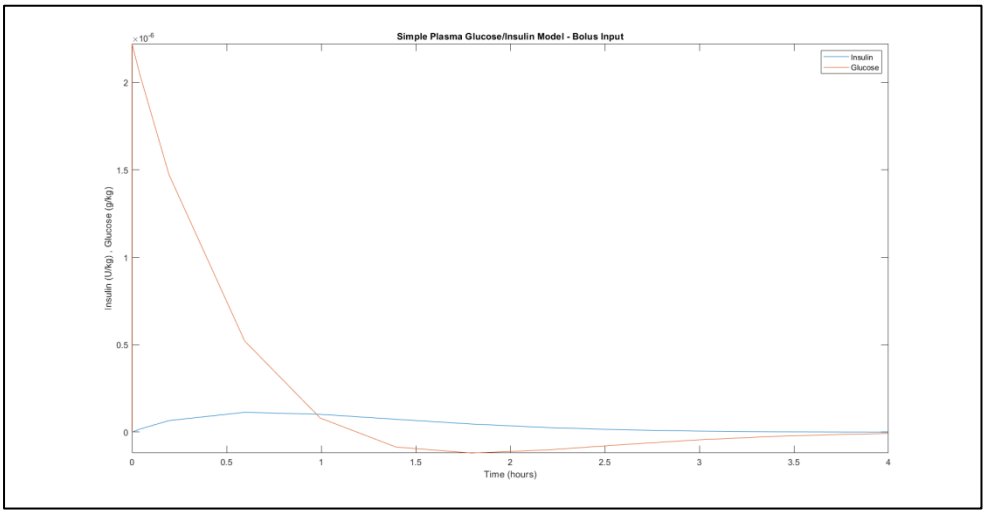

Figure 2: MATLAB implementation of plasma glucose/insulin model for a bolus input

For a diabetic subject (with no specific insulin infusion) in response to a step input,

$$\begin{bmatrix} \frac{di}{dt} \\ \frac{dg}{dt} \end{bmatrix} = \begin{bmatrix} -0.8 & 0.02 \\ -5 & -2 \end{bmatrix} \begin{bmatrix} i \\ g \end{bmatrix} + \begin{bmatrix} 0 \\ u(t) \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots [1.7]$$

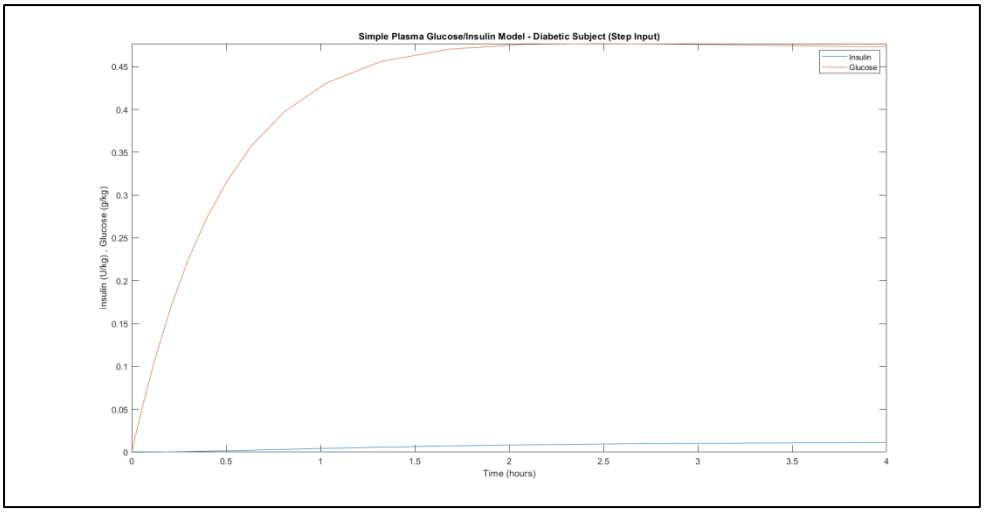

Figure 3: MATLAB implementation of plasma glucose/insulin model for a diabetic subject with no insulin infusion (step input)

For a diabetic subject with an insulin infusion of 100mU/kg/h in response to a step input,

$$\begin{bmatrix} \frac{di}{dt} \\ \frac{dg}{dt} \end{bmatrix} = \begin{bmatrix} -0.8 & 0.02 \\ -5 & -2 \end{bmatrix} \begin{bmatrix} i \\ g \end{bmatrix} + \begin{bmatrix} 0.1 \\ u(t) \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots [1.8]$$

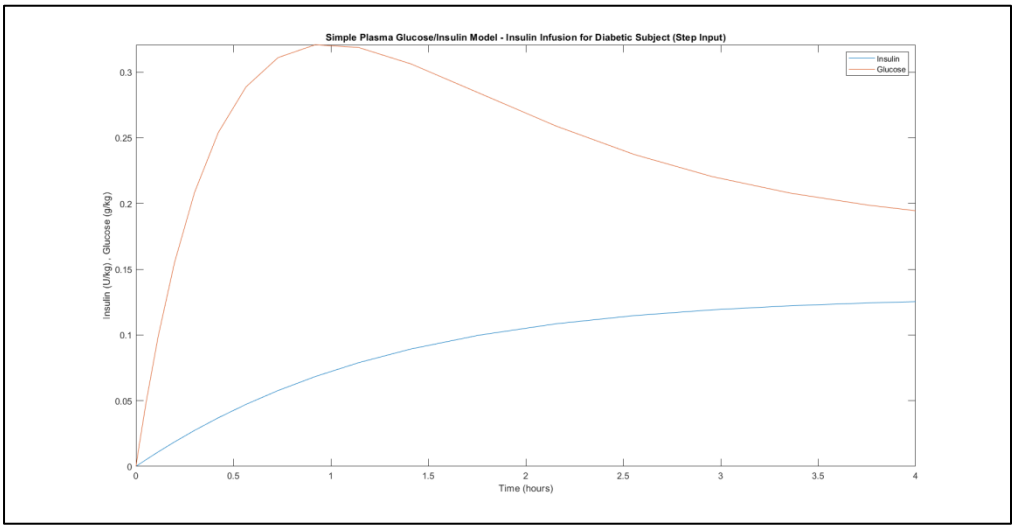

Figure 4: MATLAB implementation of plasma glucose/insulin model for a diabetic subject with insulin infusion (step input)

1.2 Question 2

The general form for

$$\begin{bmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{bmatrix} = \begin{bmatrix} -k_I & 0 & k_3 \\ k_1 & -k_2 & 0 \\ 0 & k_2 & -k_H \end{bmatrix} \begin{bmatrix} I \\ G \\ H \end{bmatrix} + \begin{bmatrix} B_1 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [1.9]$$

The Riggs model for iodine metabolism where the daily iodine intake is sufficient (150µg per day) could be referenced as,

$$\begin{bmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{bmatrix} = \begin{bmatrix} -2.52 & 0 & 0.08 \\ 0.84 & -0.01 & 0 \\ 0 & 0.01 & -0.1 \end{bmatrix} \begin{bmatrix} I \\ G \\ H \end{bmatrix} + \begin{bmatrix} 150 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [1.10]$$

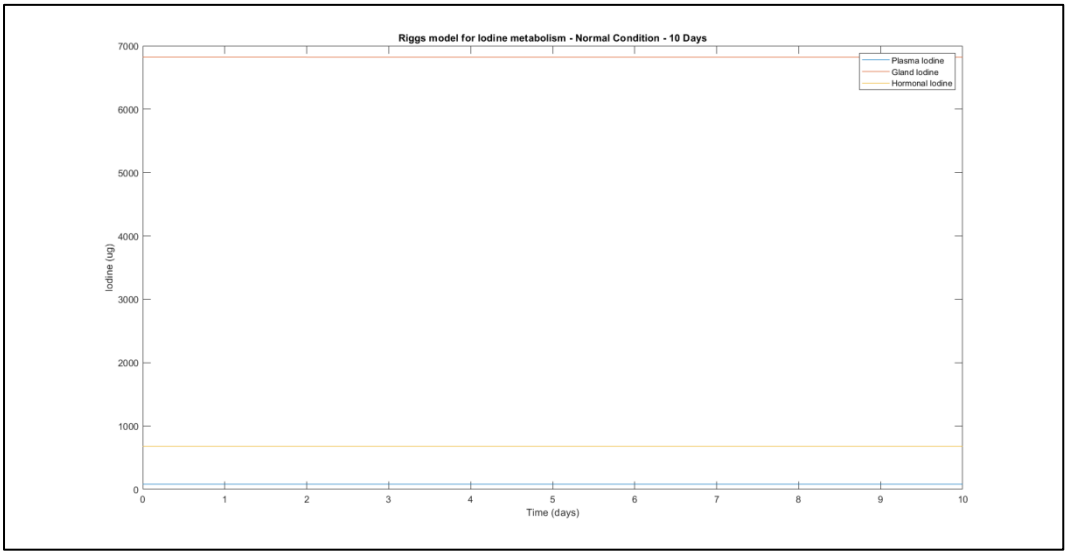

Figure 5: MATLAB implementation of the Riggs model for iodine metabolism for a sufficient daily iodine intake (10 days)

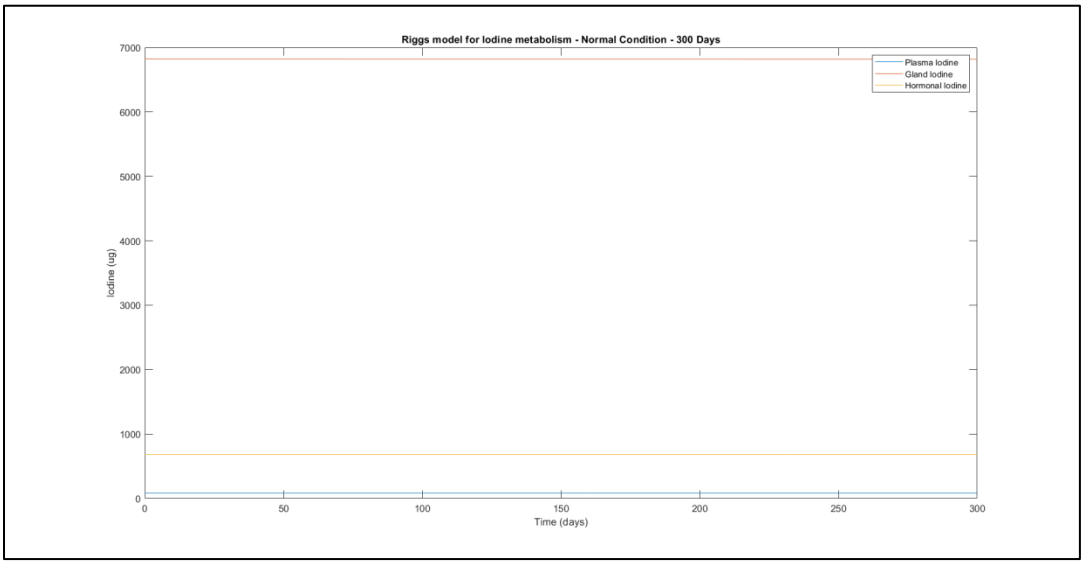

Figure 6: MATLAB implementation of the Riggs model for iodine metabolism for a sufficient daily iodine intake (300 days)

The Riggs model for iodine metabolism where a sudden drop in daily iodine intake is presented (15µg per day) could be referenced as,

$$\begin{bmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{bmatrix} = \begin{bmatrix} -2.52 & 0 & 0.08 \\ 0.84 & -0.01 & 0 \\ 0 & 0.01 & -0.1 \end{bmatrix} \begin{bmatrix} I \\ G \\ H \end{bmatrix} + \begin{bmatrix} 15 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [1.11]$$

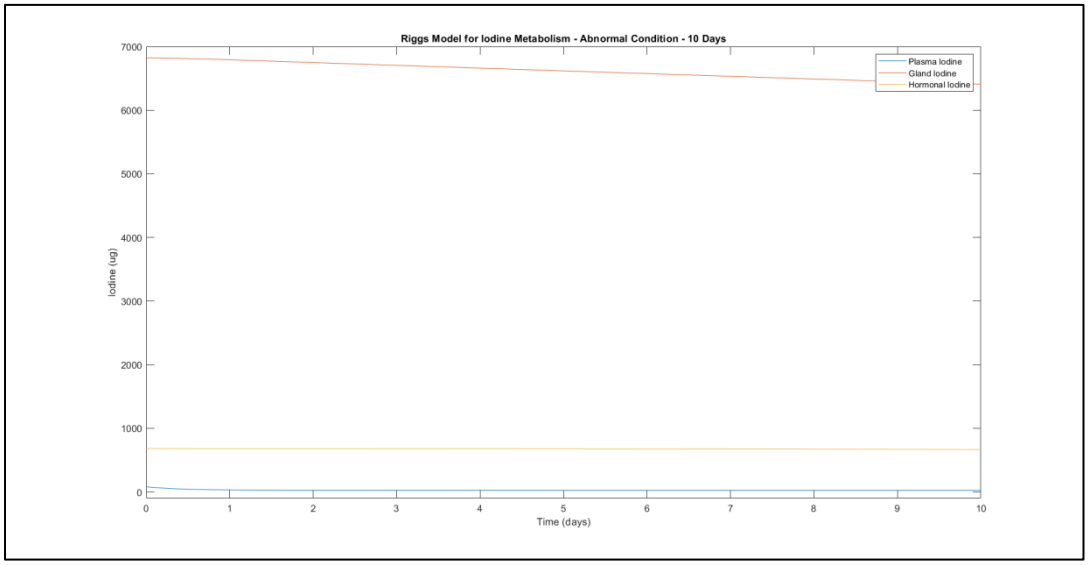

Figure 7: MATLAB implementation of the Riggs model for iodine metabolism for an insufficient daily iodine intake (10 days)

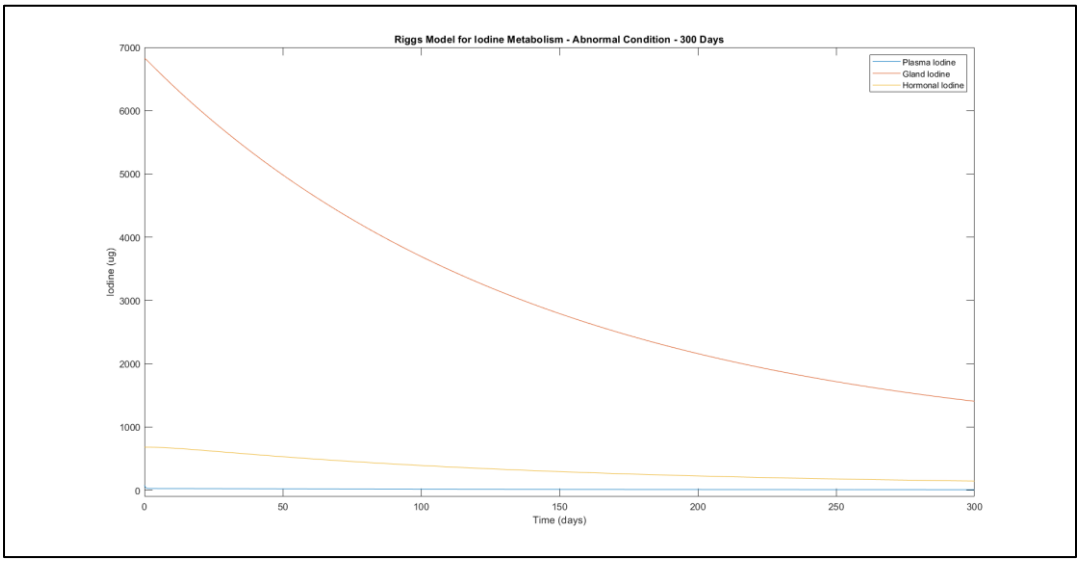

Figure 8: MATLAB implementation of the Riggs model for iodine metabolism for an insufficient daily iodine intake (300 days)

Hypothyroidism is a disorder in the endocrine system in which enough thyroid hormones are not produced by the thyroid gland. This is also called as underactive thyroid, low thyroid or hypothyreosis in several contexts. In worldwide view, the most common reasons for hypothyroidism are the insufficient dietary iodine which leads to iodine deficiency and the autoimmune thyroid diseases such as Hashimoto's thyroiditis where the immune system attacks the thyroid glands and thus, the hormonal output from the thyroid gland is considerably reduced.

The effect of autoimmune diseases to the iodine metabolism could be conveyed through altering corresponding parameters of the general form of [1.9] as necessary (reducing the value of k_2 parameter).

$$\begin{bmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{bmatrix} = \begin{bmatrix} -2.52 & 0 & 0.08 \\ 0.84 & -0.001 & 0 \\ 0 & 0.001 & -0.1 \end{bmatrix} \begin{bmatrix} I \\ G \\ H \end{bmatrix} + \begin{bmatrix} 150 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots [1.12]$$

Therefore,

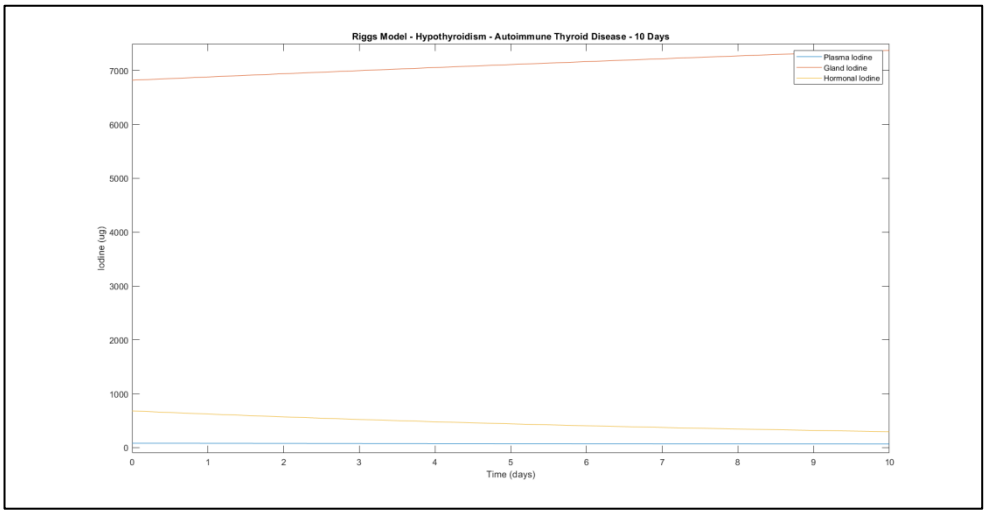

Figure 9: MATLAB implementation of the Riggs model for iodine metabolism where an autoimmune thyroid disease is presented (10 days)

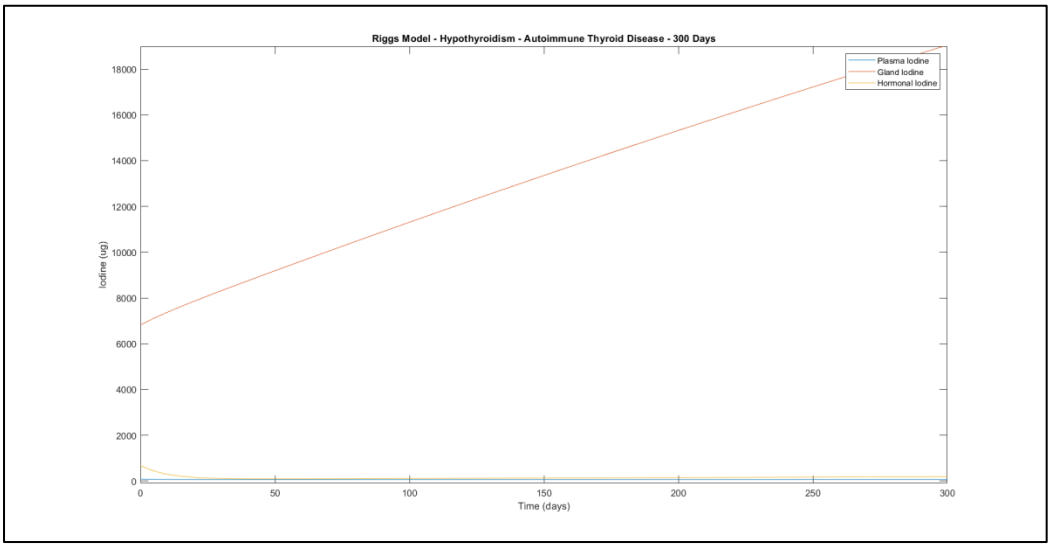

Figure 10: MATLAB implementation of the Riggs model for iodine metabolism where an autoimmune thyroid disease is presented (300 days)

Figure 9 and 10 conveys a reduction in hormonal iodine while an increment of glandular iodine is presented over the specific time periods where an autoimmune thyroid disease is presented.

As described earlier, the crucial root cause for hypothyroidism is the insufficient dietary iodine intake; this progressively leads to the condition: iodine deficiency over the time. The reduction of the parameter B_1 of the general form of [1.9] leads to represent this phenomenon.

$$\begin{bmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{bmatrix} = \begin{bmatrix} -2.52 & 0 & 0.08 \\ 0.84 & -0.01 & 0 \\ 0 & 0.01 & -0.1 \end{bmatrix} \begin{bmatrix} I \\ G \\ H \end{bmatrix} + \begin{bmatrix} 15 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [1.13]$$

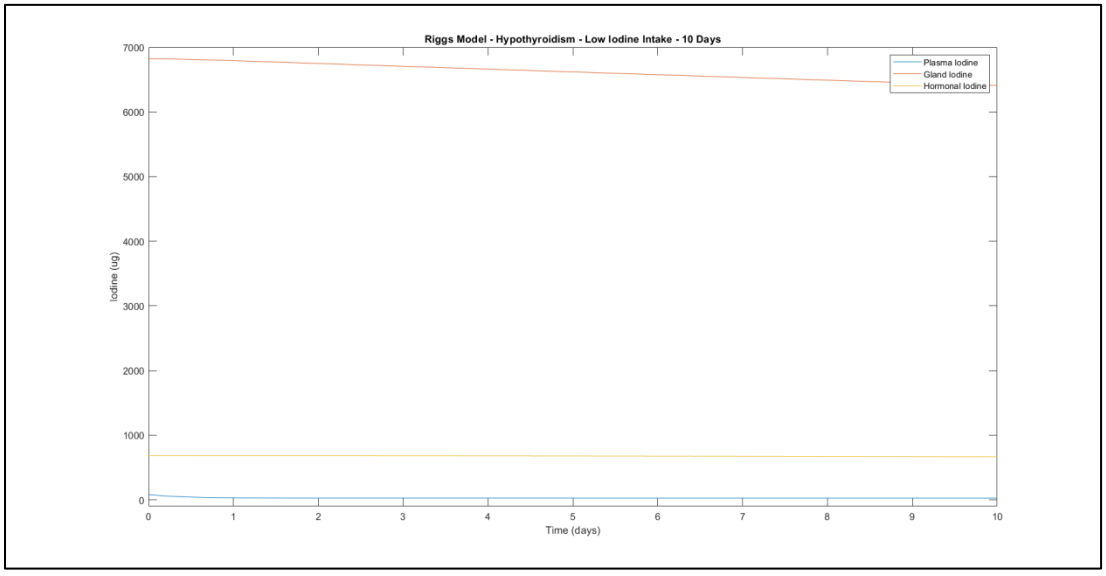

Figure 11: MATLAB implementation of the Riggs model for iodine metabolism where a low iodine intake is presented for 10 days

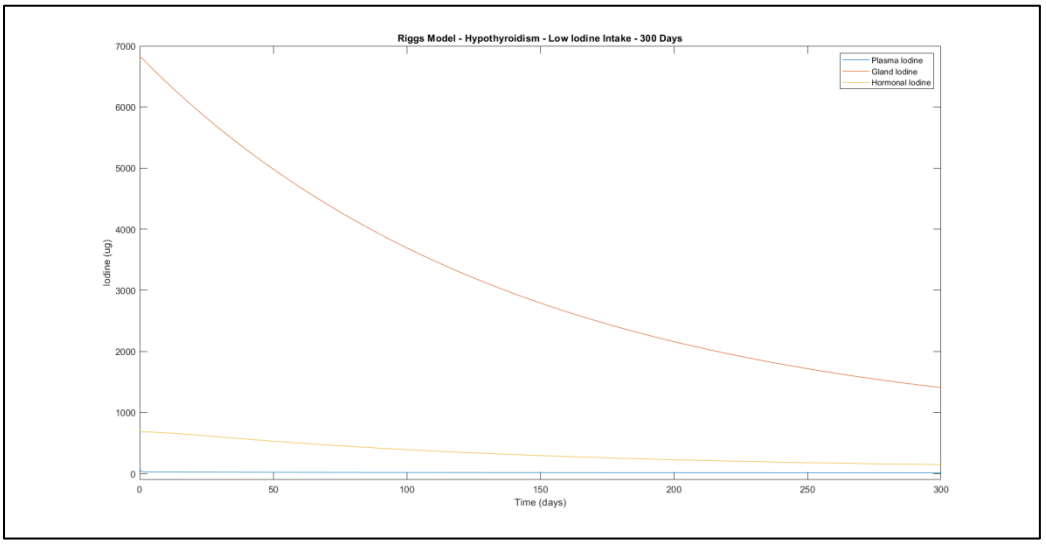

Figure 12: MATLAB implementation of the Riggs model for iodine metabolism where a low iodine intake is presented for 300 days

Figure 11 and 12 conveys a reduction in hormonal iodine as well as a reduction of glandular iodine is presented over the specific time periods where an iodine deficiency is presented.

Hyperthyroidism (which is also known as overactive thyroid or hyperthyreosis) is the condition that occurs due to comparatively excessive thyroid hormone production by the thyroid gland, at which several obvious consequences such as increase of metabolism in the body, unintentional weight loss and rapid/irregular heartbeat may occur. A common cause for hyperthyroidism is the Grave's disease in which the immune system attacks the thyroid gland to produce excessive thyroid hormones.
The Riggs model for this condition would be,

$$\begin{bmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{bmatrix} = \begin{bmatrix} -2.52 & 0 & 0.08 \\ 0.84 & -0.1 & 0 \\ 0 & 0.1 & -0.1 \end{bmatrix} \begin{bmatrix} I \\ G \\ H \end{bmatrix} + \begin{bmatrix} 150 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots [1.14]$$

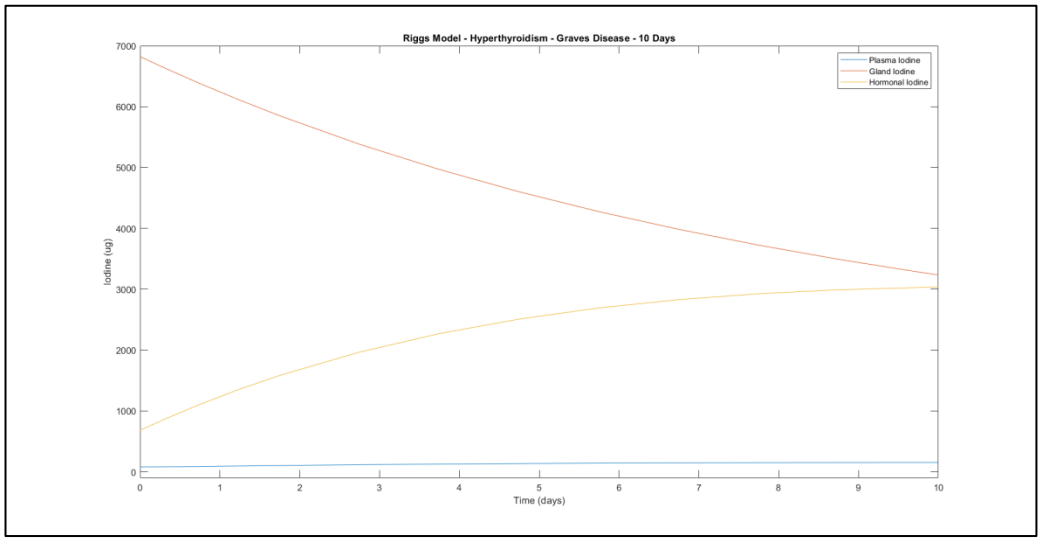

Figure 13: MATLAB implementation of the Riggs model for iodine metabolism where hyperthyroidism is occurred due to Grave's disease (10 days)

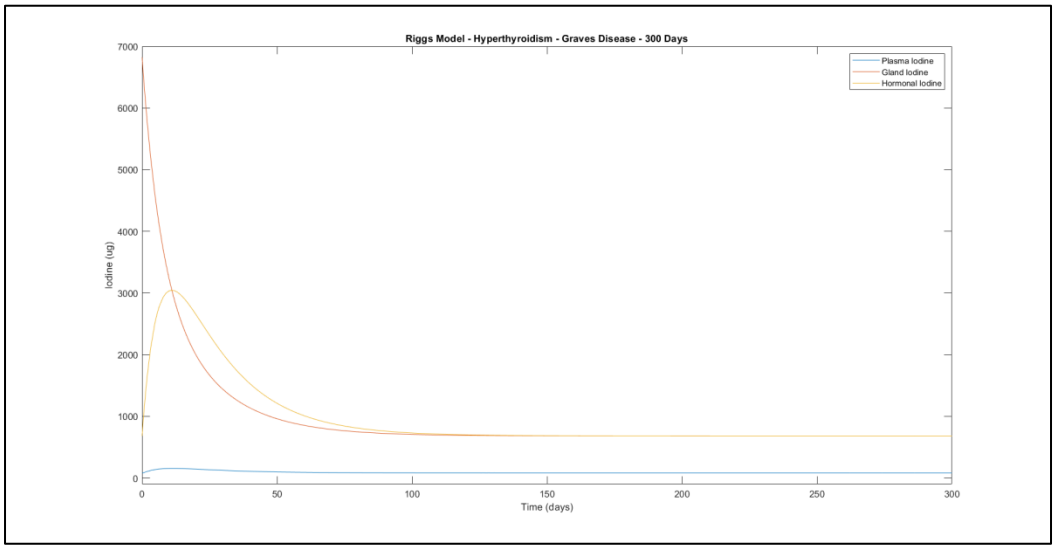

Figure 14: MATLAB implementation of the Riggs model for iodine metabolism where hyperthyroidism is occurred due to Grave's disease (300 days)

Thyroid tumors could be divided as benign and malignant which could either be cancerous or non-cancerous. Non-cancerous tumors include the thyroid adenomas which are small nodules that start in the cell layer that lines the inner surface of the thyroid gland. These nodules are capable of secreting thyroid hormones and thus, may lead to hyperthyroidism as well. Cancerous tumors may result from a radiation undergone to the head, neck or chest and is presented via a considerable growth in nodules or non-functioning nodules.

Hence, these tumors could be modeled via low iodine intake and hyperthyroidism whereas the parameters of [1.9] are changed as relevantly.

$$\begin{bmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{bmatrix} = \begin{bmatrix} -2.52 & 0 & 0.08 \\ 0.84 & -0.05 & 0 \\ 0 & 0.05 & -0.1 \end{bmatrix} \begin{bmatrix} I \\ G \\ H \end{bmatrix} + \begin{bmatrix} 15 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots [1.15]$$

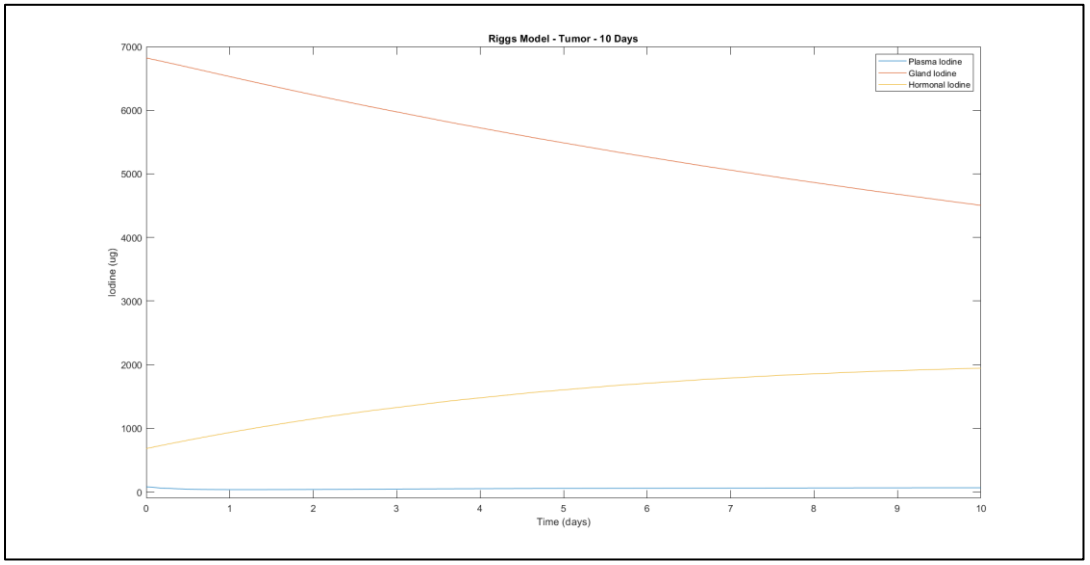

Figure 15: MATLAB implementation of the Riggs model for iodine metabolism where a tumor is presented (10 days)

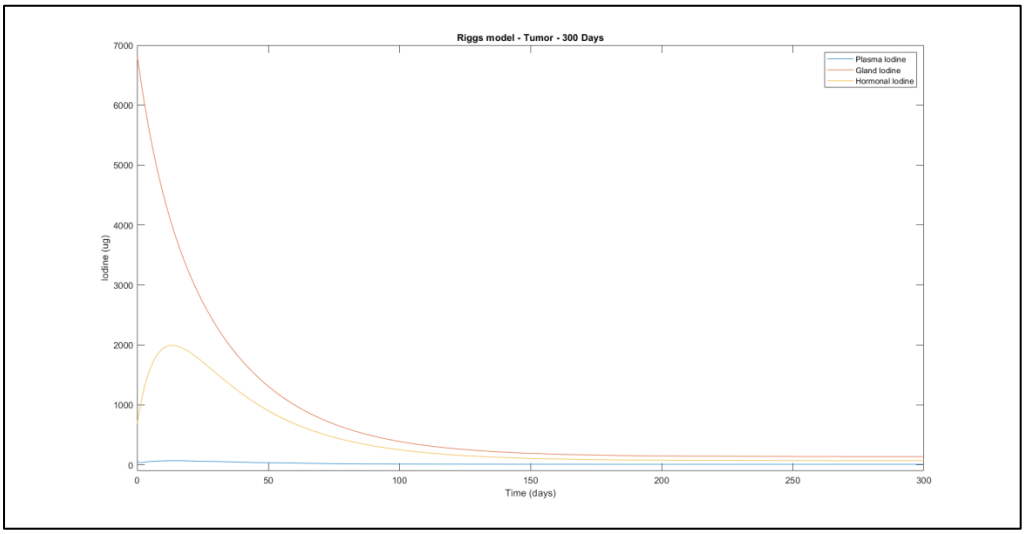

Figure 16: MATLAB implementation of the Riggs model for iodine metabolism where a tumor is presented (300 days)

A goiter is eccentrically identified as an abnormal enlargement of the thyroid gland and iodine deficiency is identified to be the most common reason for goiter. In the condition of goiter, the thyroid gland progressively enlarges since it attempts to satisfy the demand for thyroid hormone production within the body. The most common reason for the goiter is the iodine deficiency where low dietary iodine is critical.

Thus, the goiter could be modeled via iodine deficiency and hypothyroidism whereas the parameters of [1.9] are changed as relevantly.

$$\begin{bmatrix} \frac{dI}{dt} \\ \frac{dG}{dt} \\ \frac{dH}{dt} \end{bmatrix} = \begin{bmatrix} -2.52 & 0 & 0.08 \\ 0.84 & -0.005 & 0 \\ 0 & 0.005 & -0.1 \end{bmatrix} \begin{bmatrix} I \\ G \\ H \end{bmatrix} + \begin{bmatrix} 15 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots\dots\dots\dots\dots [1.16]$$

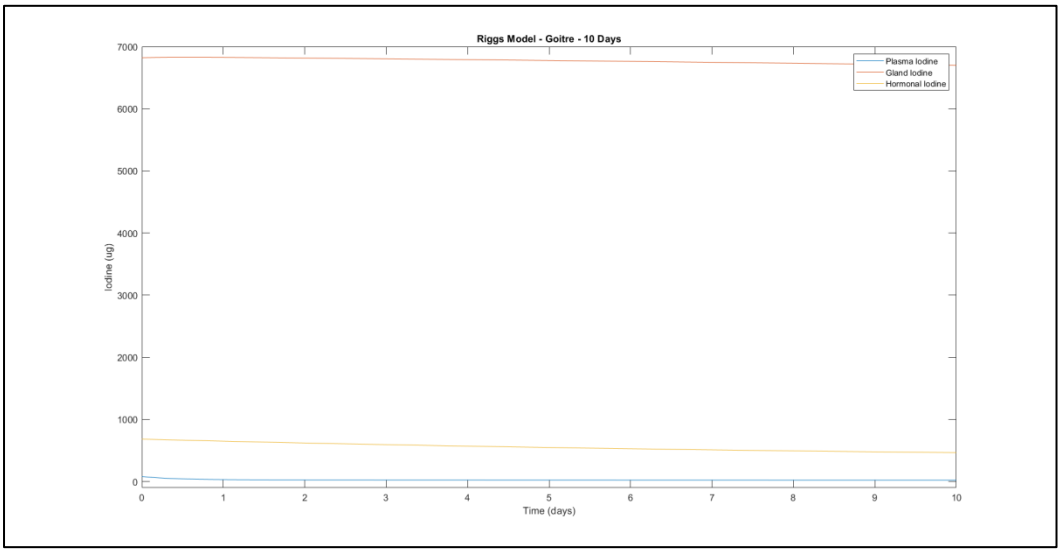

Figure 17: MATLAB implementation of the Riggs model for iodine metabolism where a goiter is presented (10 days)

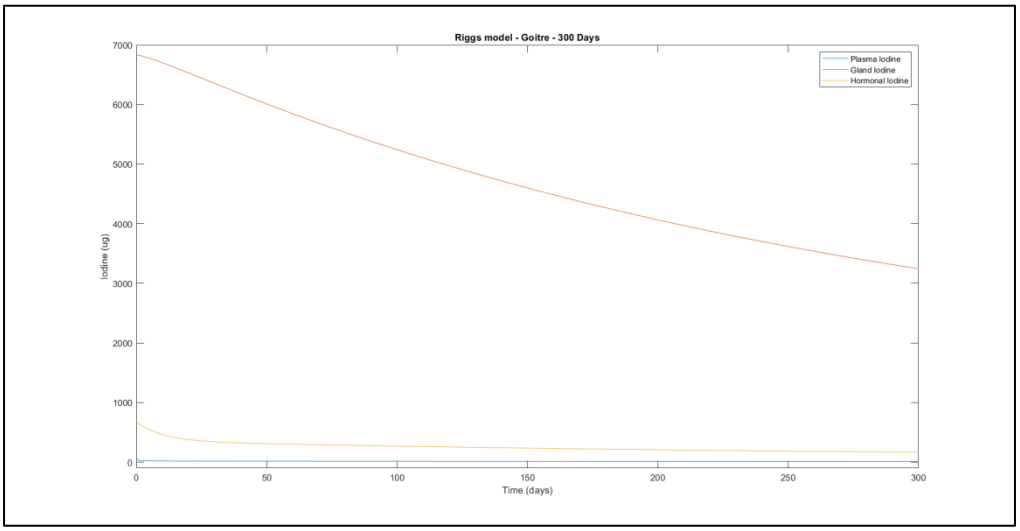

Figure 18: MATLAB implementation of the Riggs model for iodine metabolism where a goiter is presented (300 days)

2 Part 2

2.1 Question 1

As per the following equations,

$$\frac{di}{dt} = -0.8i + 0.2g + B(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.1]$$

$$\frac{dg}{dt} = -5i - 2g + A(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.2]$$

$$A(t) = 1\frac{\frac{g}{kg}}{h} for\ t > 1 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.3]$$

$$B(t) = 0 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.4]$$

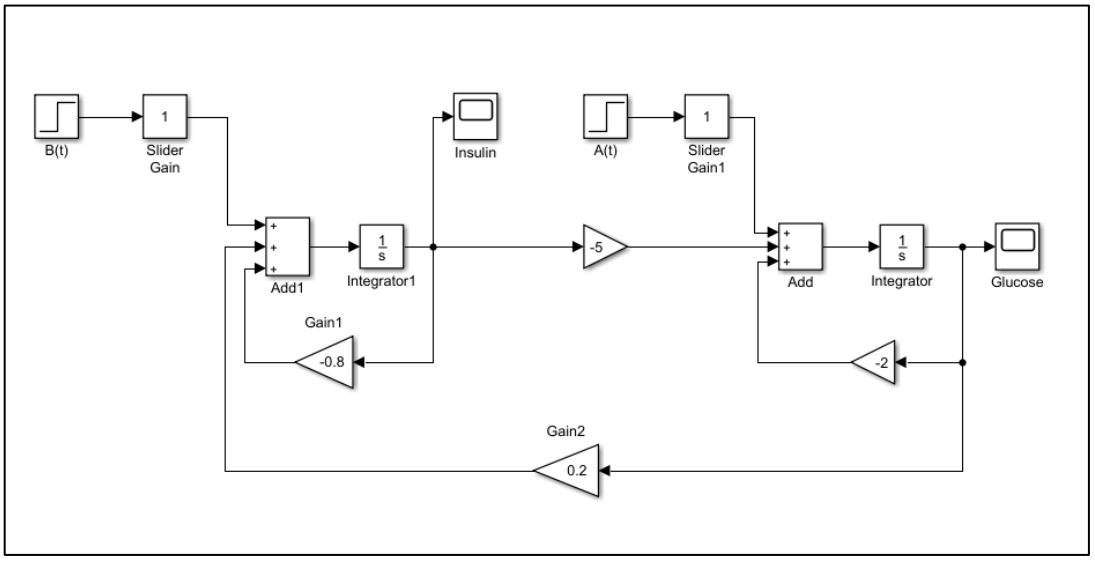

Figure 19: Simulink implementation of the glucose/insulin model for step inputs

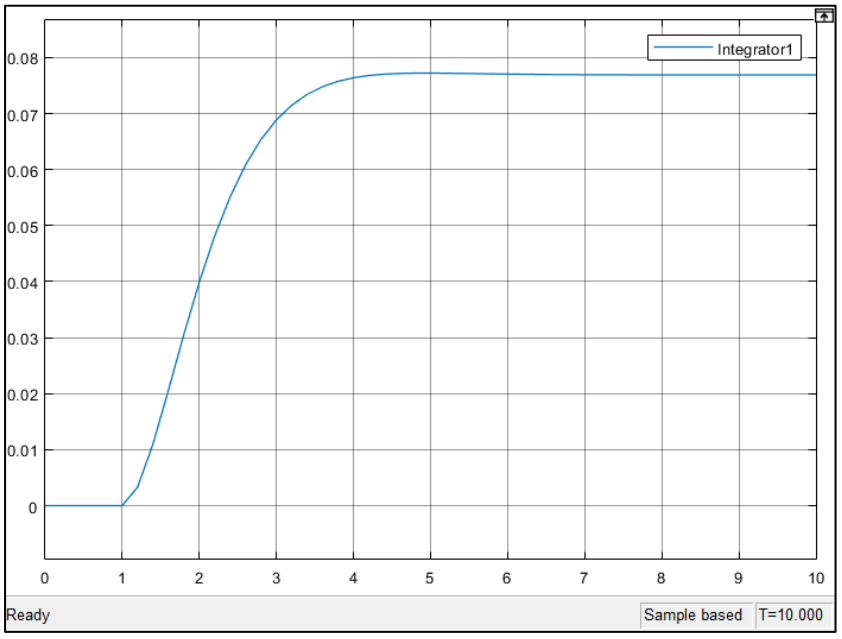

Figure 20: Simulink plot for the diagram in Figure 19 for insulin

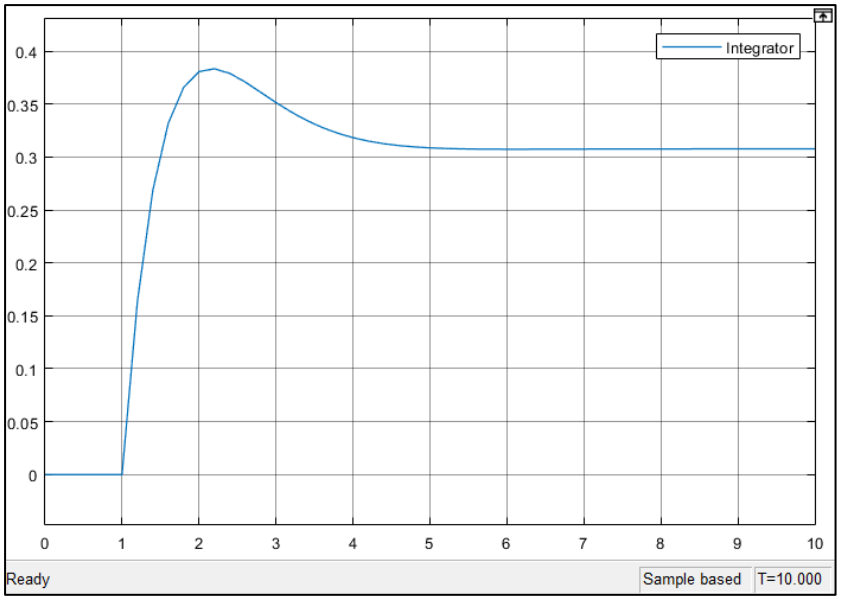

Figure 21: Simulink plot for the diagram in Figure 19 for glucose

For an alternative set of coefficients,

$$\frac{di}{dt} = -0.63i + 0.13g + B(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots [2.5]$$

$$\frac{dg}{dt} = -5i - 2.5g + A(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.6]$$

$$A(t) = 1\frac{\frac{g}{kg}}{h} for\ t > 1 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.7]$$

$$B(t) = 0 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.8]$$

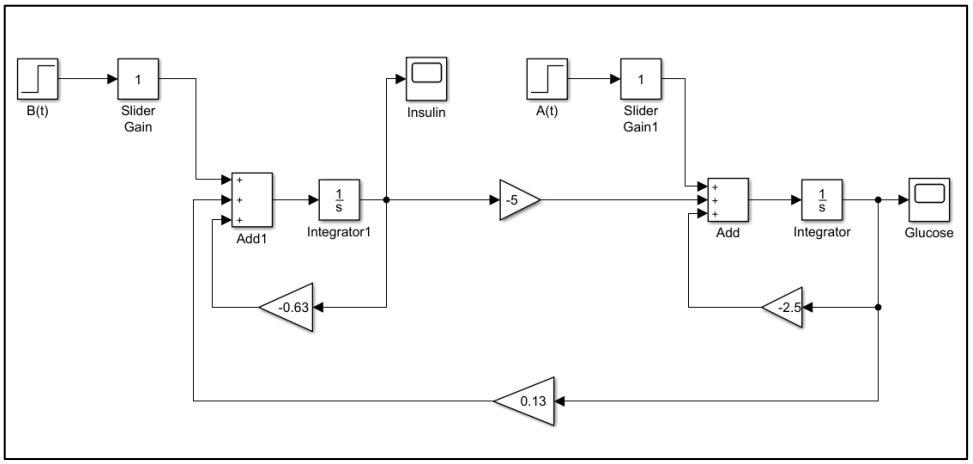

Figure 22: Simulink implementation of the glucose/insulin model (for a different set of coefficients)

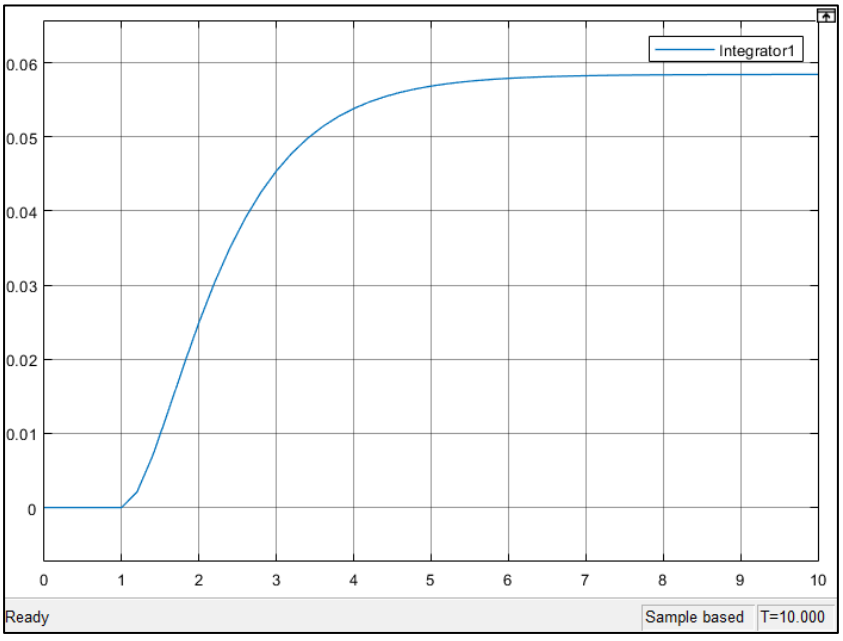

Figure 23: Simulink plot for the diagram in Figure 22 for insulin

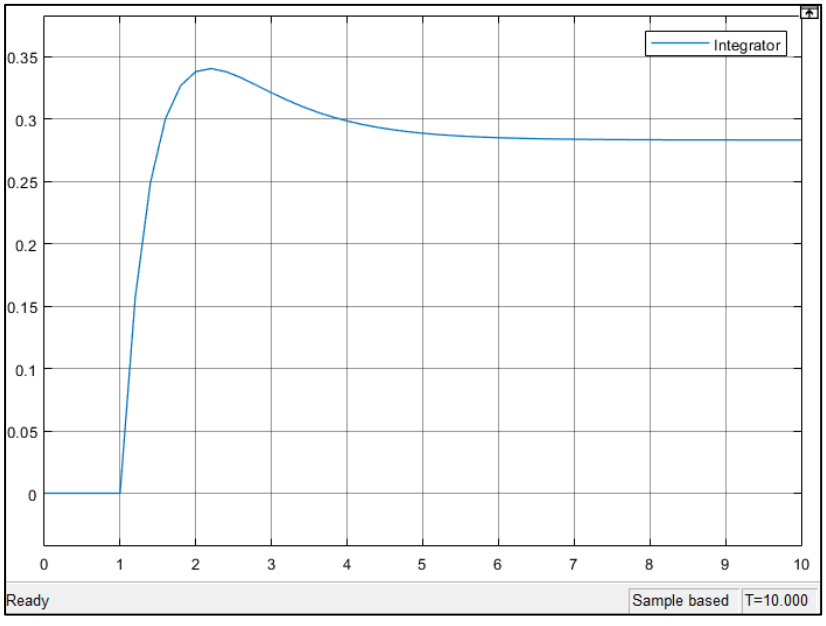

Figure 24: Simulink plot for the diagram in Figure 22 for glucose

The comparison of graphs in Figure 16 with Figure 18 and Figure 17 with Figure 19 suggest that there exists an obvious difference in the steady state values of each insulin and glucose levels when the coefficients are changed. Further, the rate of change of insulin and that of glucose have also been changed due to the executed coefficient deviation.

When B(t) is changed to 0.1U/kg/h, for a non-diabetic normal subject,

$$\frac{di}{dt} = -0.63i + 0.13g + B(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.5]$$

$$\frac{dg}{dt} = -5i - 2.5g + A(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.6]$$

$$A(t) = 1\frac{\frac{g}{kg}}{h} for\ t > 1 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.7]$$

$$B(t) = \frac{\frac{0.1U}{kg}}{h} for\ t > 0 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.9]$$

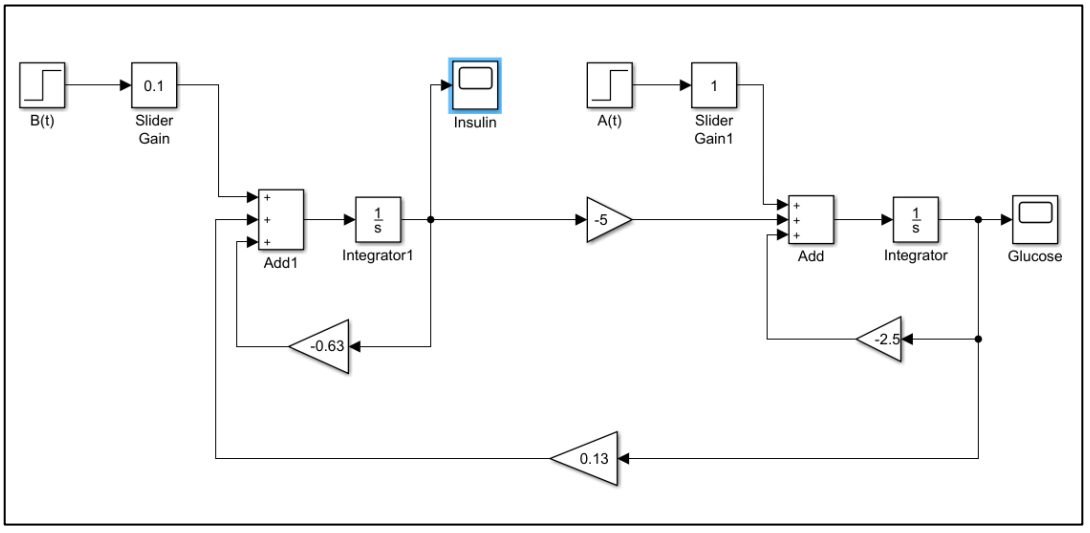

Figure 25: Simulink implementation of the glucose/insulin model for B(t) = 0.1U/kg/h for a normal subject

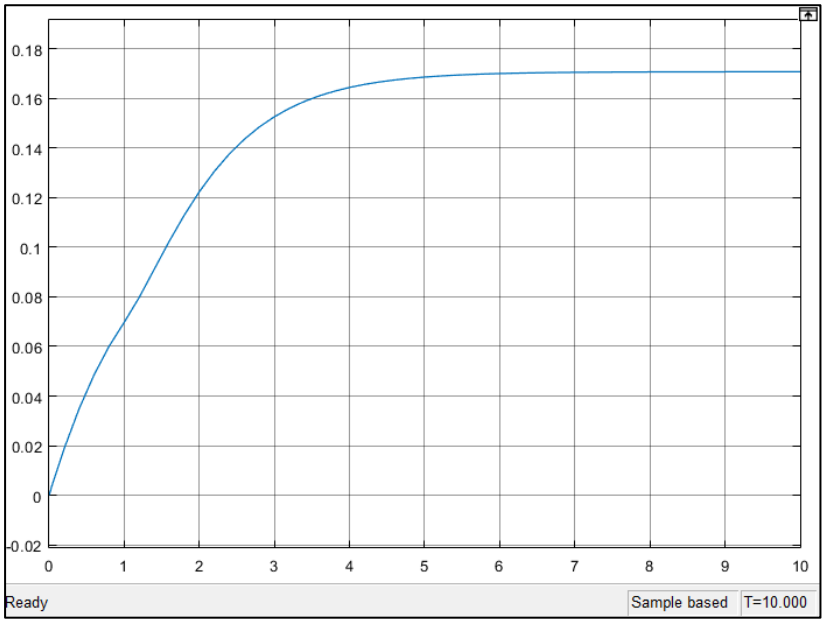

Figure 26: Simulink plot for the diagram in Figure 25 for insulin

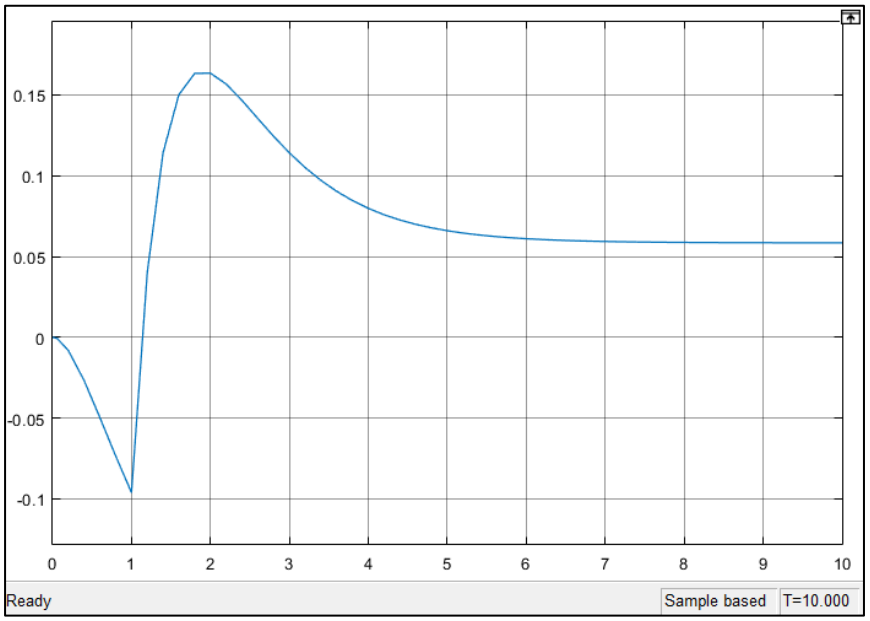

Figure 27: Simulink plot for the diagram in Figure 25 for glucose

When B(t) is changed to 0.1U/kg/h, for a diabetic subject,

$$\frac{di}{dt} = -0.63i + 0.01g + B(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.10]$$

$$\frac{dg}{dt} = -5i - 2.5g + A(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.6]$$

$$A(t) = 1\frac{\frac{g}{kg}}{h} for\ t > 1 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.7]$$

$$B(t) = \frac{\frac{0.1U}{kg}}{h} for\ t > 0 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [2.9]$$

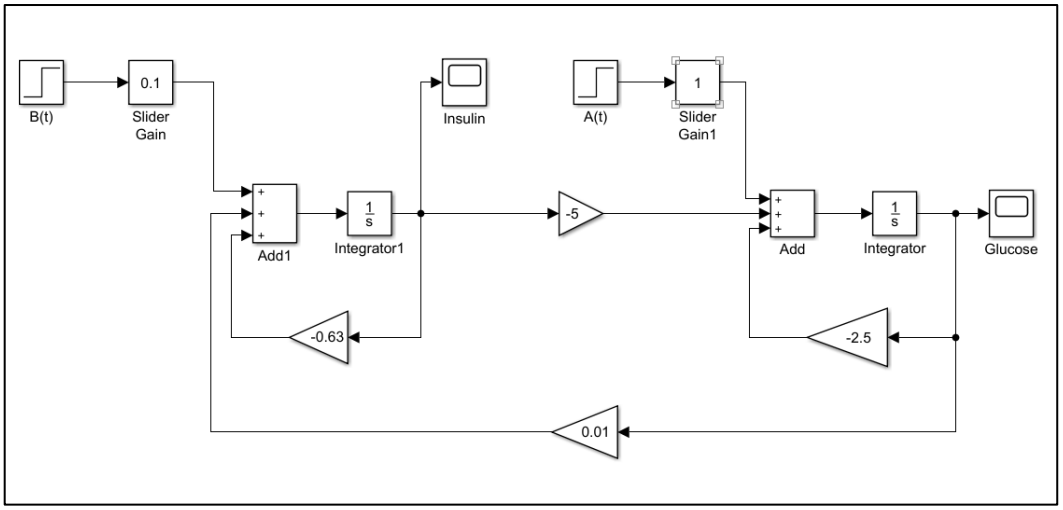

Figure 28: Simulink implementation of the glucose/insulin model for B(t) = 0.1U/kg/h for a diabetic subject

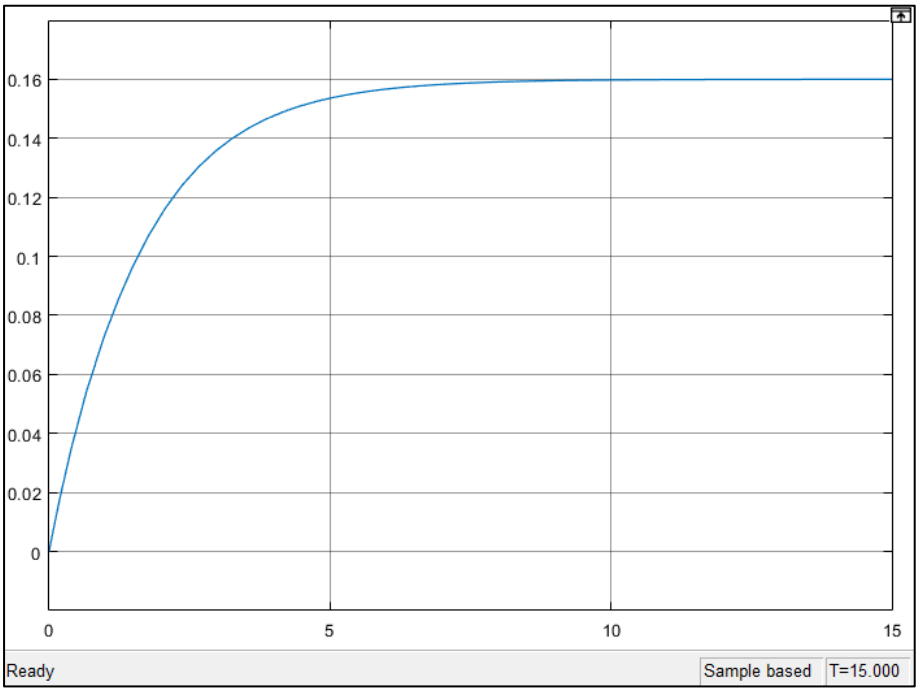

Figure 29: Simulink plot for the diagram in Figure 28 for insulin

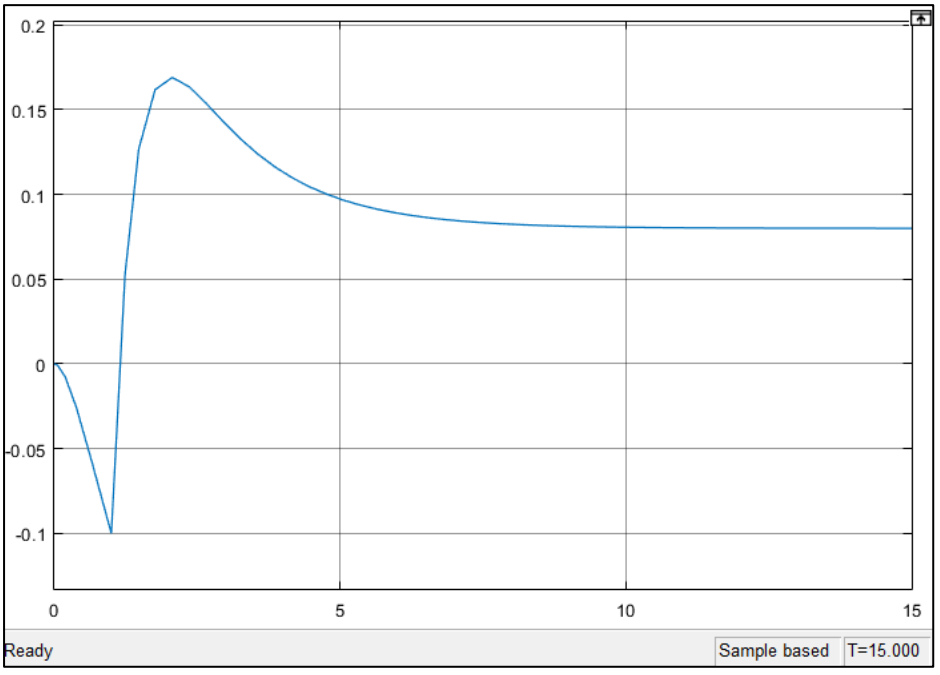

Figure 30: Simulink plot for the diagram in Figure 28 for glucose

2.2 Question 2

For the purpose of Simulink simulation of the Riggs iodine model via the following equations,

$$\frac{dI}{dt} = -2.52I + 0.08H + A(t) \dots\dots\dots\dots\dots\dots\dots [2.11]$$

$$\frac{dG}{dt} = 0.84I - 0.01G + B(t) \dots\dots\dots\dots\dots\dots\dots [2.12]$$

$$\frac{dH}{dt} = 0.01G - 0.1H + C(t) \dots\dots\dots\dots\dots\dots\dots [2.13]$$

Where,

$$A(t) = 15\frac{\mu g}{d} for\ t > 0 \ldots\ldots\ldots\ldots\ldots\ldots [2.14]$$

$$B(t) = 0 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots [2.15]$$

$$C(t) = 0 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots [2.16]$$

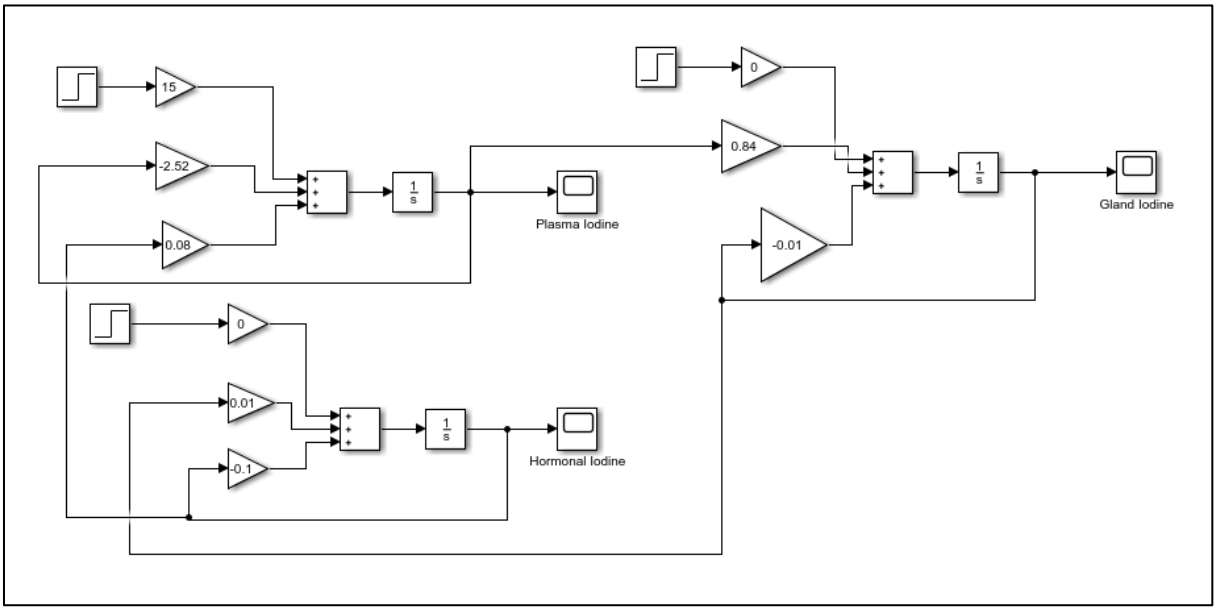

Figure 31: Simulink implementation of the Riggs iodine model

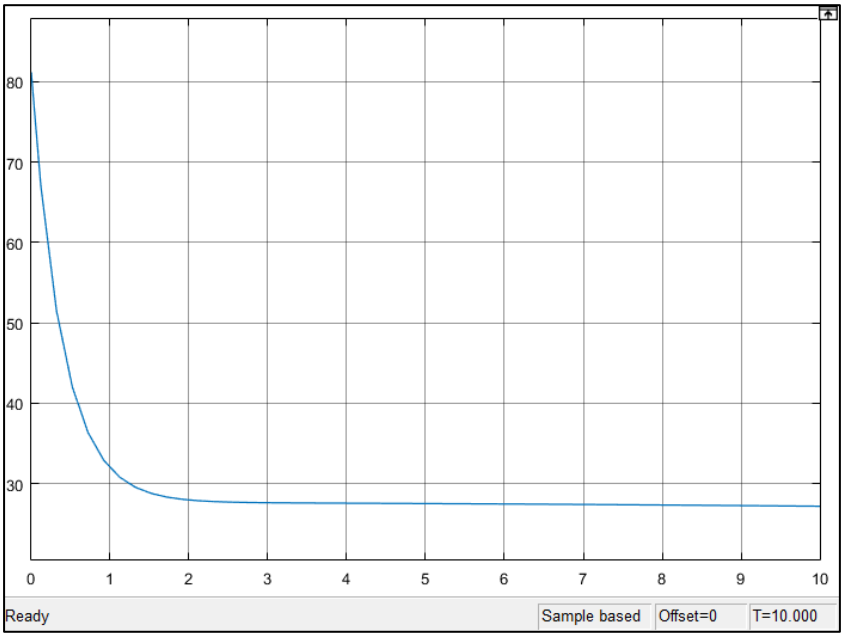

Figure 32: Simulink plot for the diagram in Figure 31 for plasma iodine (10 days)

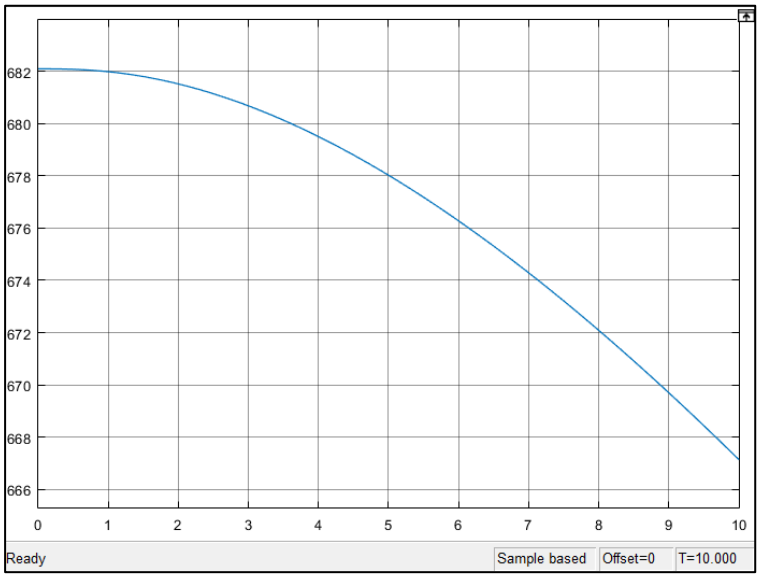

Figure 33: Simulink plot for the diagram in Figure 31 for hormonal iodine (10 days)

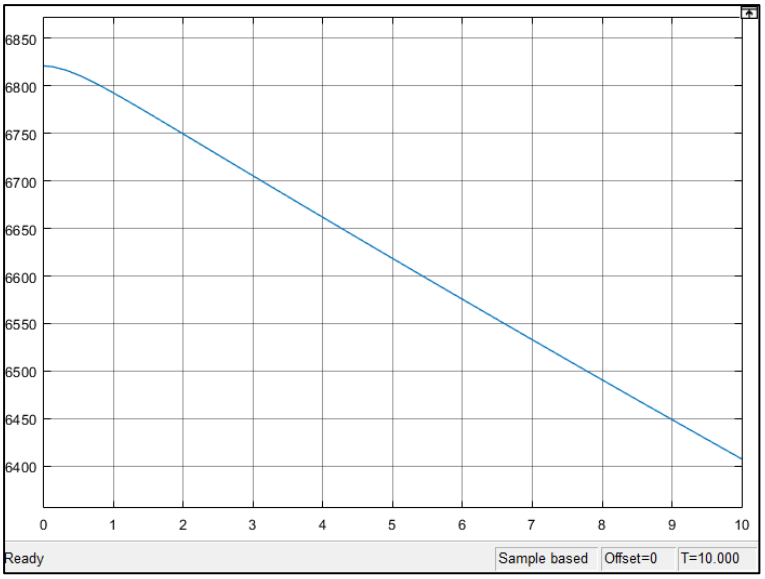

Figure 34: Simulink plot for the diagram in Figure 31 for glandular iodine (10 days)

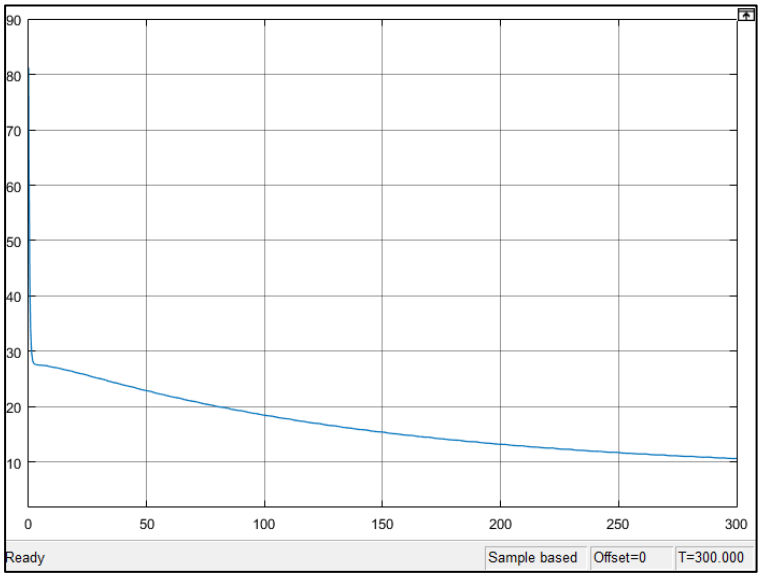

Figure 35: Simulink plot for the diagram in Figure 31 for plasma iodine (300 days)

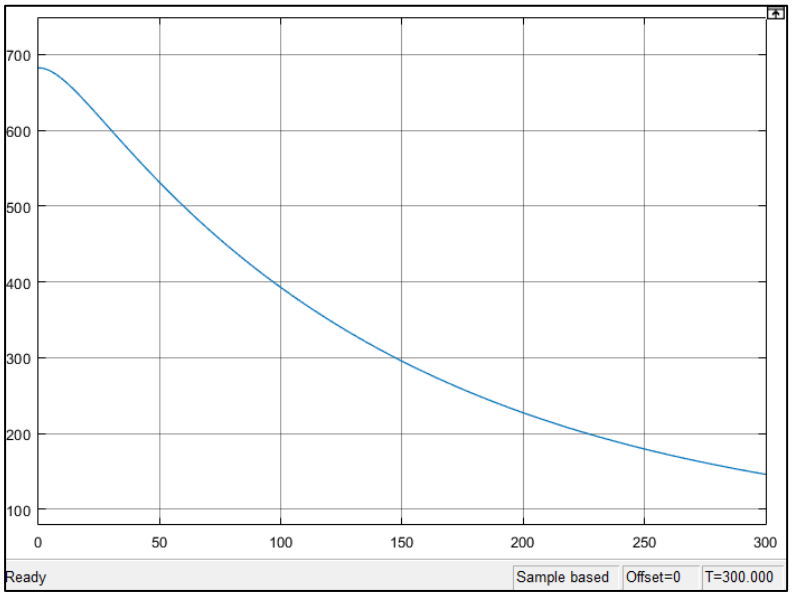

Figure 36: Simulink plot for the diagram in Figure 31 for hormonal iodine (300 days)

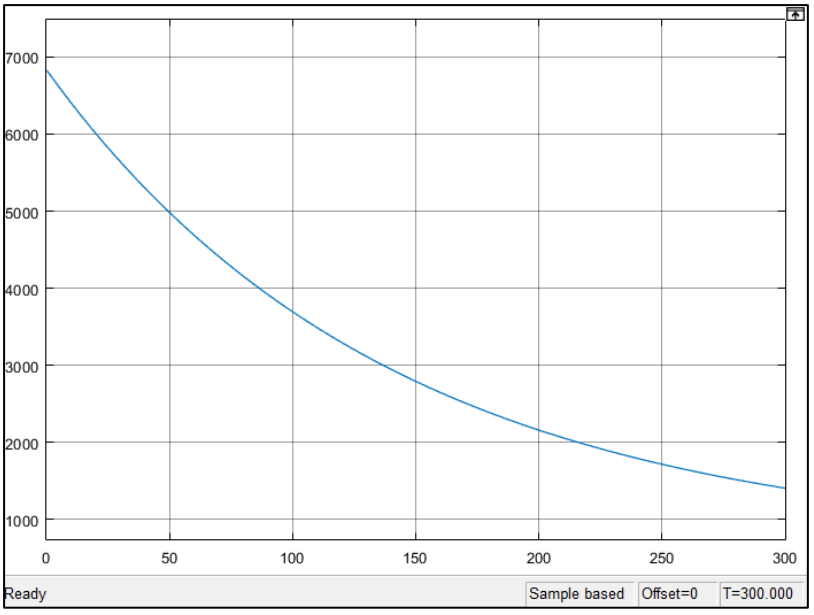

Figure 37: Simulink plot for the diagram in Figure 31 for glandular iodine (300 days)

3 Part 3

3.1 Question 1

As per Bolies' plasma-glucose model,

$$\frac{d^2g}{dt^2} + (k_1 + k_4)\frac{dg}{dt} + (k_1k_4 + k_3k_6)g = k_1a + a\frac{du}{dt} \dots\dots\dots\dots\dots [3.1]$$

By substituting the typical values for each constant,

$$k_1 = 0.8h^{-1}\ ;\ k_3 = 0.2\ IU/h/g\ ;\ k_4 = 2h^{-1}\ ;k_6 = 5\ g/h/IU\ ;a = 1\ g/l/h$$

$$\frac{d^2g}{dt^2} + (2.8)\frac{dg}{dt} + (2.6)g = 0.8 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [3.2]$$

For a step function,

$$\frac{du}{dt} = 0 \; for \; t > 0$$

Therefore, the solution for [3.2] 2nd order ODE could be assumed as,

$$g(t) = g_c(t) + g_p(t) \; \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots [3.3]$$

For complementary solution, via [3.2],

$$\frac{d^2g}{dt^2} + (2.8)\frac{dg}{dt} + (2.6)g = 0 \; \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots [3.4]$$

Hence, the characteristic equation is,

$$m^2 + 2.8m + 2.6 = 0 \; \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots [3.5]$$

Which gives,

$$m = -1.4 \pm j0.8 \; \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots [3.6]$$

Therefore, the complementary solution is,

$$g_c(t) = [C_1 \, cos(0.8t) + C_2 \, sin(0.8t)] \, e^{-1.4t} \; \ldots\ldots [3.7]$$

For the particular solution,

$$\frac{d^2g}{dt^2} + (2.8)\frac{dg}{dt} + (2.6)g = 0.8 \; \ldots\ldots\ldots\ldots\ldots\ldots [3.8]$$

Assume,

$$g_p(t) = G$$

$$0 + 0 + (2.6)G = 0.8$$

$$G = g_p(t) = \frac{4}{13} \; \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots [3.9]$$

Therefore, from [3.3], [3.7] and [3.9];

$$g(t) = [C_1 \, cos(0.8t) + C_2 \, sin(0.8t)] \, e^{-1.4t} + \frac{4}{13} \; \ldots\ldots\ldots\ldots\ldots [3.10]$$

From [3.10],

$$g'(t) = [(-0.8)C_1 \, sin(0.8t) + (0.8)C_2 \, cos(0.8t)] \, e^{-1.4t} + (-1.4)e^{-1.4t}[C_1 \, cos(0.8t) + C_2 \, sin(0.8t)]$$

Applying the boundary conditions,

$$g(0) = 0 \; ; \; g'(0) = 1$$

$$g(0) = 0 = C_1 + \frac{4}{13}$$

$$g'(0) = 1 = (0.8)C_2 - (1.4)C_1$$

$$C_1 = -\frac{4}{13}$$

$$C_2 = \frac{37}{52}$$

Therefore, [3.10] becomes,

$$g(t) = \left[-\frac{4}{13}cos(0.8t) + \frac{37}{52}sin(0.8t)\right] e^{-1.4t} + \frac{4}{13} \; \ldots\ldots\ldots\ldots\ldots [3.11]$$

Since, as per the Bolies' model,

$$g'(t) = -2g(t) - 5i(t) + 1$$

$$i(t) = 0.2(-g'(t) - 2g(t) + 1) \; \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots [3.12]$$

From [3.11] and [3.12],

$$i(t) = \left[-\frac{1}{13}cos(0.8t) - \frac{7}{52}sin(0.8t)\right]e^{-1.4t} + \frac{1}{13} \dots\dots\dots\dots\dots\dots\dots\dots [3.13]$$

Therefore, the stability curves are as follows:

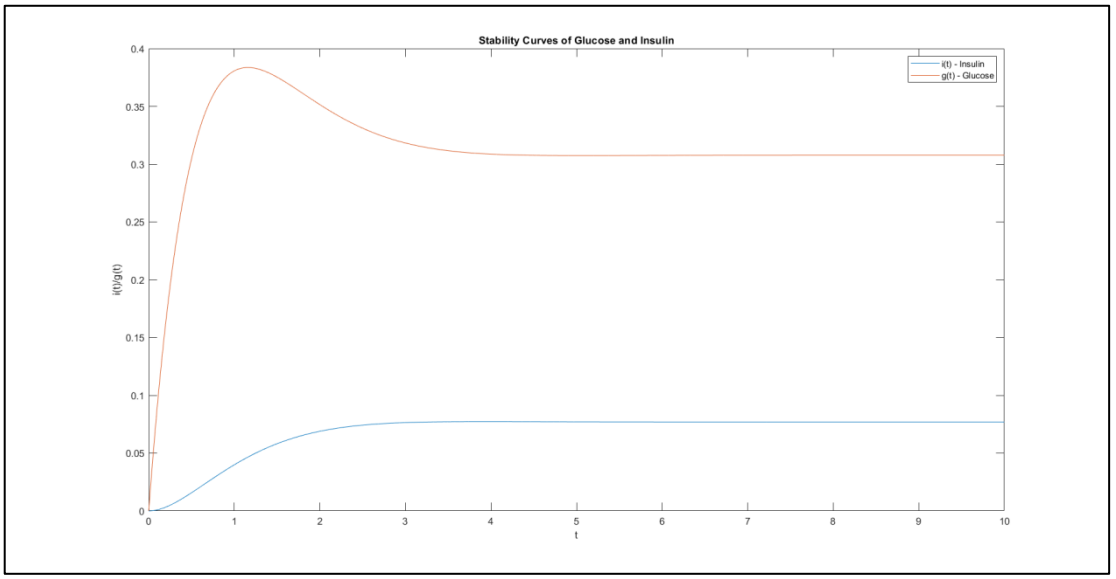

Figure 38: Stability curves for insulin and glucose as per the Bolies' plasma-glucose model

3.2 Question 2

Since glucagon (from alpha islet cells of the pancreas) is responsible for maintaining blood glucose level when it is comparatively low (by converting the stored glycogen in liver into glucose), the compartment model of glucose/glucagon is mostly similar to the bolies' glucose/insulin model except that glucagon stimulates the release of glucose to plasma whereas insulin stimulates absorption of glucose by cells from plasma.

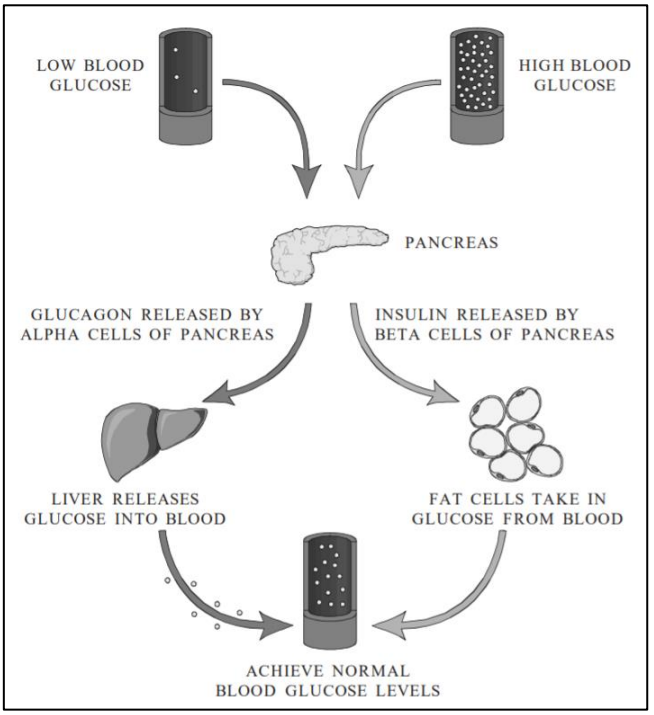

Figure 39: Simplified physiology behind the glucose homeostasis of human body

Since the Bolies' plasma-glucose model is as follows,

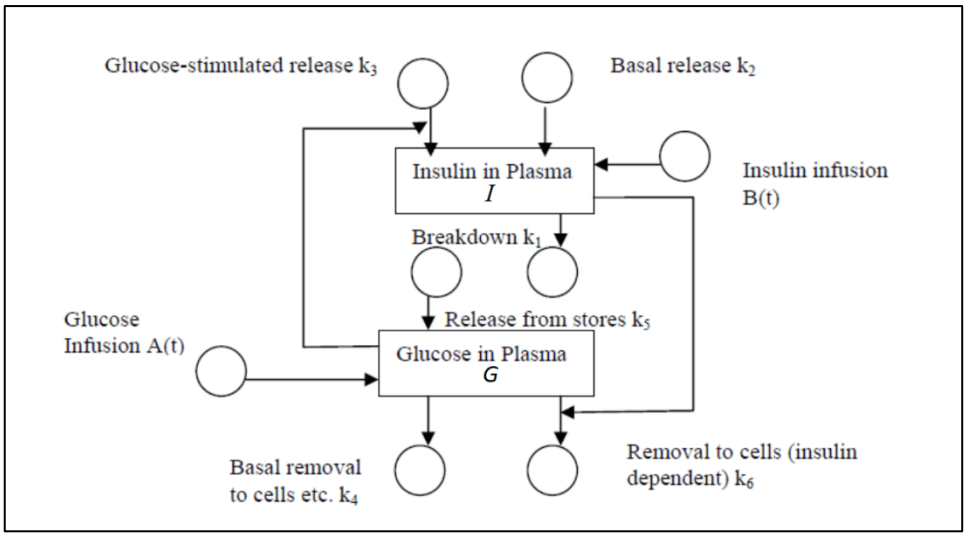

Figure 40: The Bolies' plasma-glucose model with insulin monitoring

It is evident to propose a glucose-glucagon compartment model as follows as per the above argument,

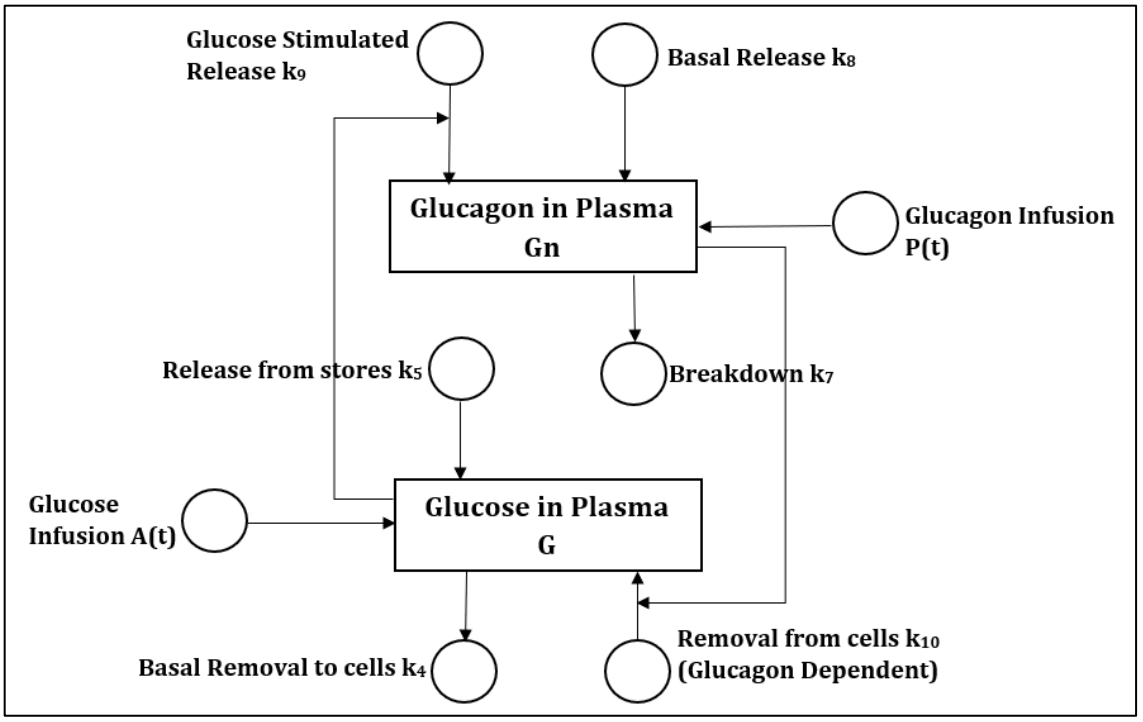

Figure 41: Proposed compartmental model for plasma glucose-plasma glucagon physiology

Thus, it is possible to combine the above two models in Figure 40 and 41 to develop a combined glucose-glucagon-insulin model for glucose homeostasis in human body.

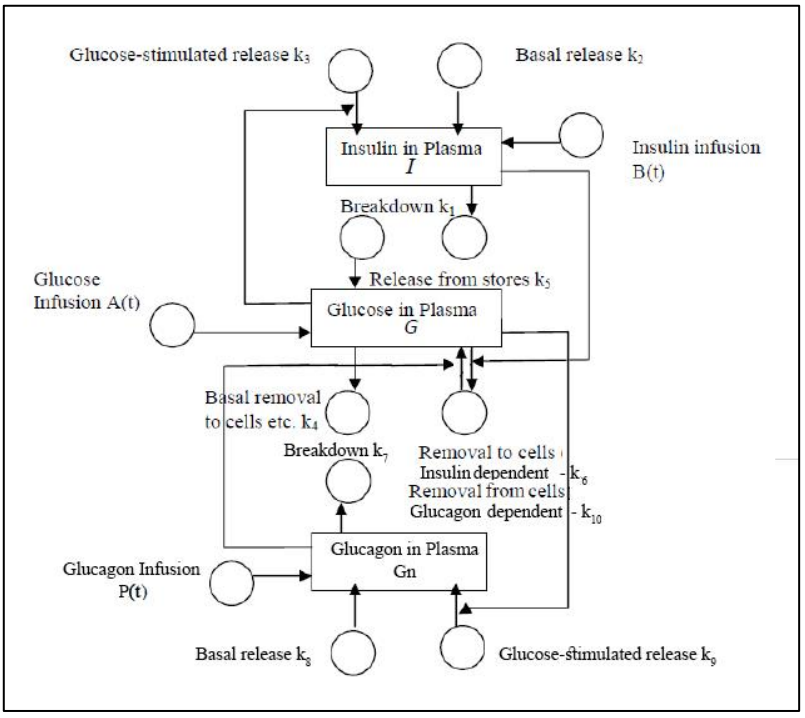

Figure 42: Combined compartmental model for plasma glucose-glucagon-insulin homeostasis

For the glucose in plasma,

$$\frac{dG}{dt} = A(t) + k_5 + k_{10}G_n(t) - k_4G(t) - k_6I(t) \dots\dots\dots\dots\dots\dots\dots [3.14]$$

For the glucagon in plasma,

$$\frac{dG_n}{dt} = P(t) + k_8 + k_9G(t) - k_7G_n(t) \dots\dots\dots\dots\dots\dots\dots\dots [3.15]$$

For the insulin in plasma,

$$\frac{dI}{dt} = B(t) + k_2 + k_3G(t) - k_1I(t) \dots\dots\dots\dots\dots\dots\dots\dots [3.16]$$

By considering a dynamic equilibrium state,

$$\frac{dG}{dt} = \frac{dG_n}{dt} = \frac{dI}{dt} = 0 \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots [3.17]$$

Hence,

$$k_5 = k_4G_0 + k_6I_0 - k_{10}G_{n0}$$
$$k_2 = -k_3G_0 + k_1I_0$$
$$k_8 = -k_9G_0 + k_7G_{n0}$$

But,

$$i = I - I_0$$
$$g = G - G_0$$
$$g_n = G_n - G_{n0}$$

Therefore, from [3.15], [3.16] and [3.17],

$$\frac{dg}{dt} = A(t) + k_{10}g_n(t) - k_4g(t) - k_6i(t) \dots\dots\dots\dots\dots\dots\dots [3.18]$$

$$\frac{dg_n}{dt} = P(t) + k_9g(t) - k_7g_n(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots [3.19]$$

$$\frac{di}{dt} = B(t) + k_3g(t) - k_1i(t) \dots\dots\dots\dots\dots\dots\dots\dots\dots [3.20]$$

By assuming a step input,

$$A(t) = a.u(t), P(t) = 0 \; and \; B(t) = 0 \dots\dots\dots\dots [3.21]$$

It is reasonable to assume $k_1 = k_7, k_3 = k_9 \; and \; k_4 = k_{10}$ since of the strong similarity between the glucose-insulin and glucose-glucagon models. Therefore, substituting typical values,

$k_1, k_7 = 0.8h^{-1}$; $k_3, k_9 = 0.2\; IU/h/g$; $k_4, k_{10} = 2h^{-1}$; $k_6 = 5\; g/h/IU$; $a = 1\; g/l/h$

From [3.18], [3.19] and [3.20],

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

$$\frac{dg_n}{dt} = -0.2g(t) - 0.8g_n(t)$$

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

$$\begin{bmatrix} \frac{dg}{dt} \\ \frac{dg_n}{dt} \\ \frac{di}{dt} \end{bmatrix} = \begin{bmatrix} -2 & 2 & -5 \\ -0.2 & -0.8 & 0 \\ 0.2 & 0 & -0.8 \end{bmatrix} \begin{bmatrix} g \\ g_n \\ i \end{bmatrix} + \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} \dots\dots\dots\dots\dots [3.22]$$

The following plot conveys the MATLAB implementation of [3.22].

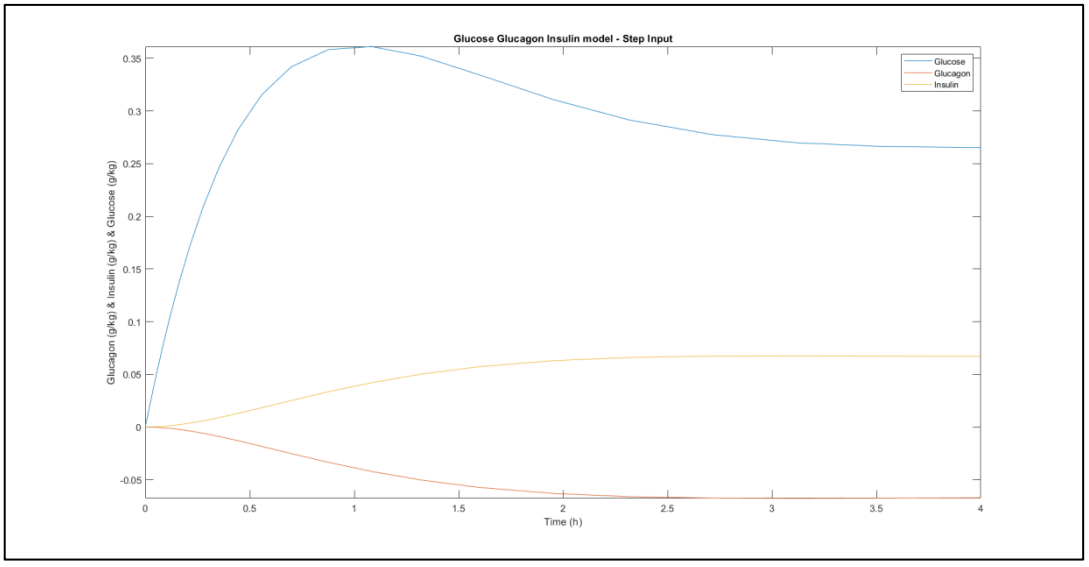

Figure 43: MATLAB implementation of the proposed glucose-glucagon-insulin model

As it is conveyed through Figure 43, since A(t) is considered as a unit step function as in [3.21], the plasma glucose level is increasing with time. This phenomenon results to increase the plasma insulin level in order to maintain the plsma glucose level at equilibrium as the graph presents. As the plasma glucose level is higher than its equilibrium state, level of glucagon gradually decreases in order to ensure that the stored glucose will not be added to the plasma. After a considerable time period, the plasma glucose level stabilizes into an equilibrium while both insulin and glucagon level stabilize in different levels of equilibrium which are not at the initial value of each component.

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