University of Moratuwa
Faculty of Engineering
Department of Electronic & Telecommunication Engineering

Modelling and Analysis of Physiological Systems

Compatmental modelling

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Contents

Part 1

1) Simple plasma glucose(g)/insulin(i) model

1.1) When i,g are initially zero

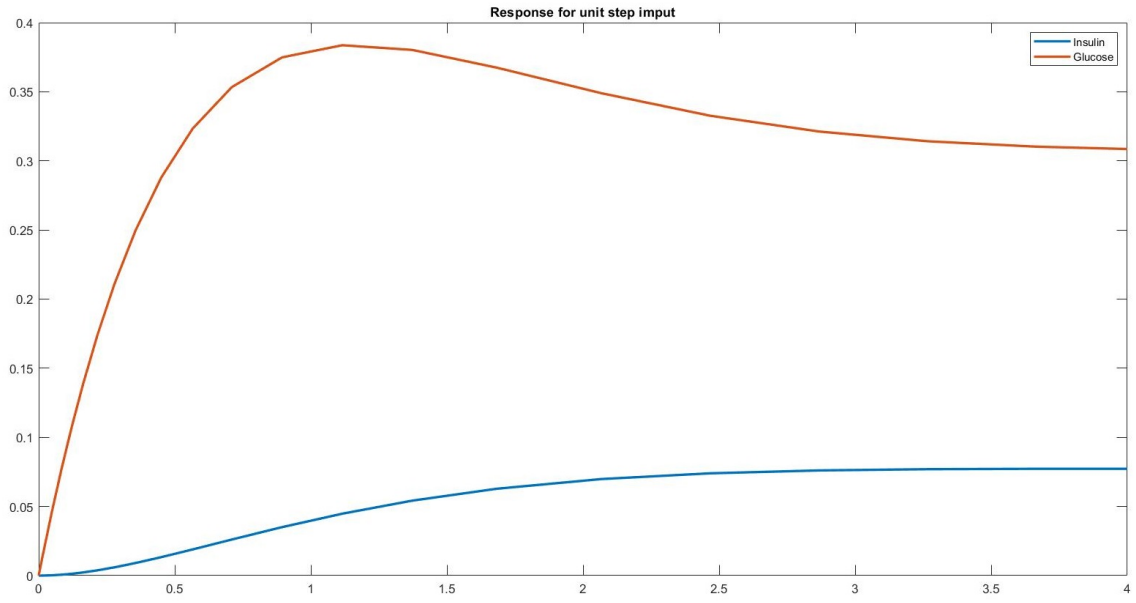

Figure 1

1.2) for a bolus input (x = 1 -$sign(t)$ is a delta function at t = 0

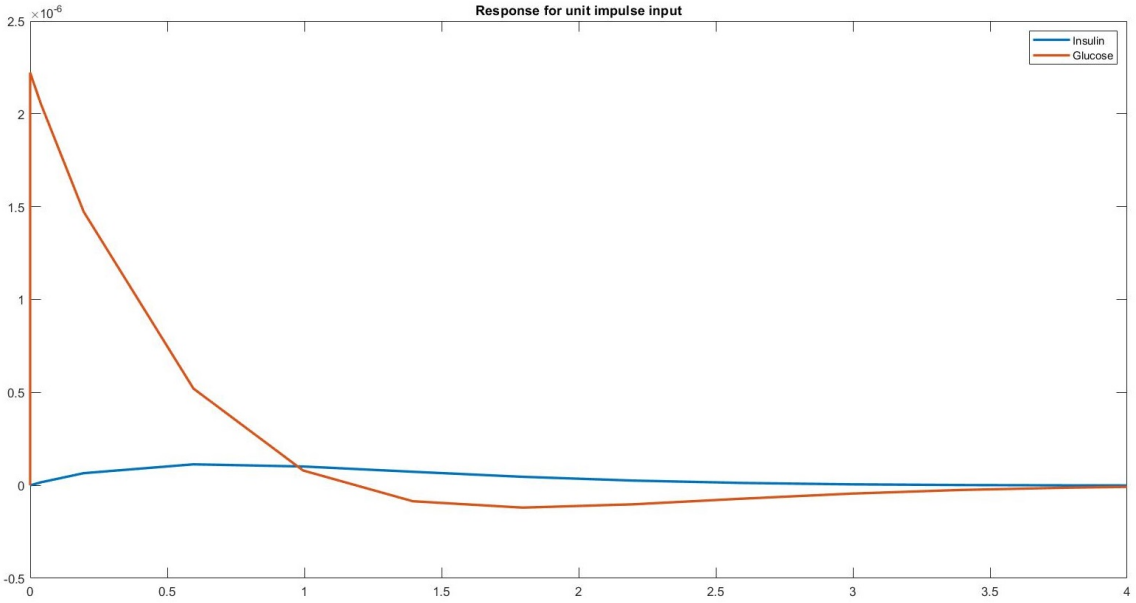

Figure 2

1.3) When the patient is not subjected to the insulin infusion

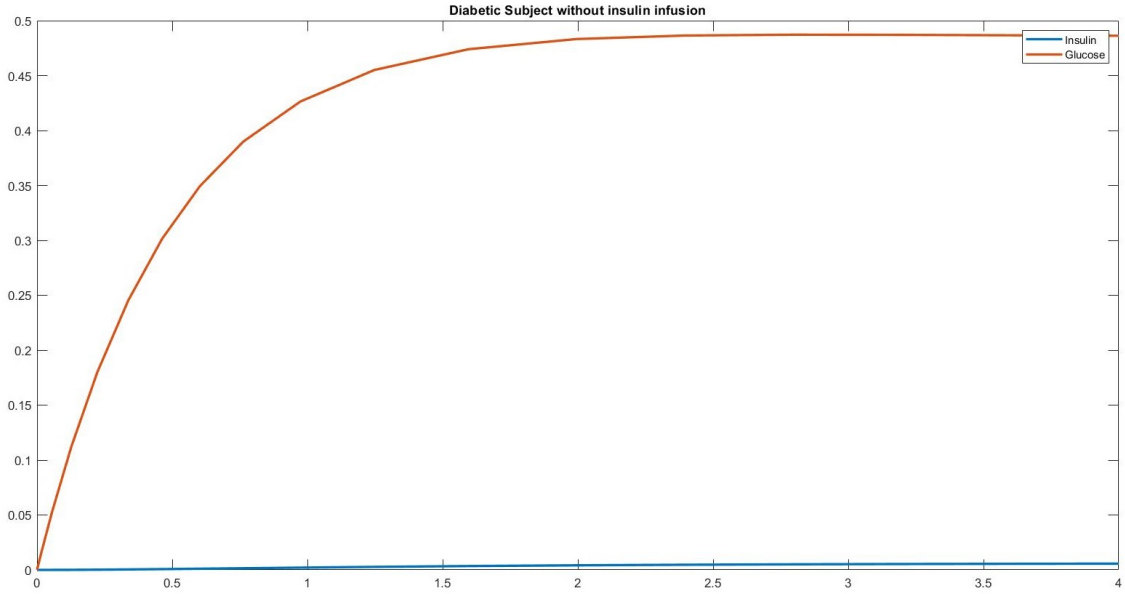

Figure 3: C

1.4) When the patient is subjected to insulin infusion of 100 mU/kg/h

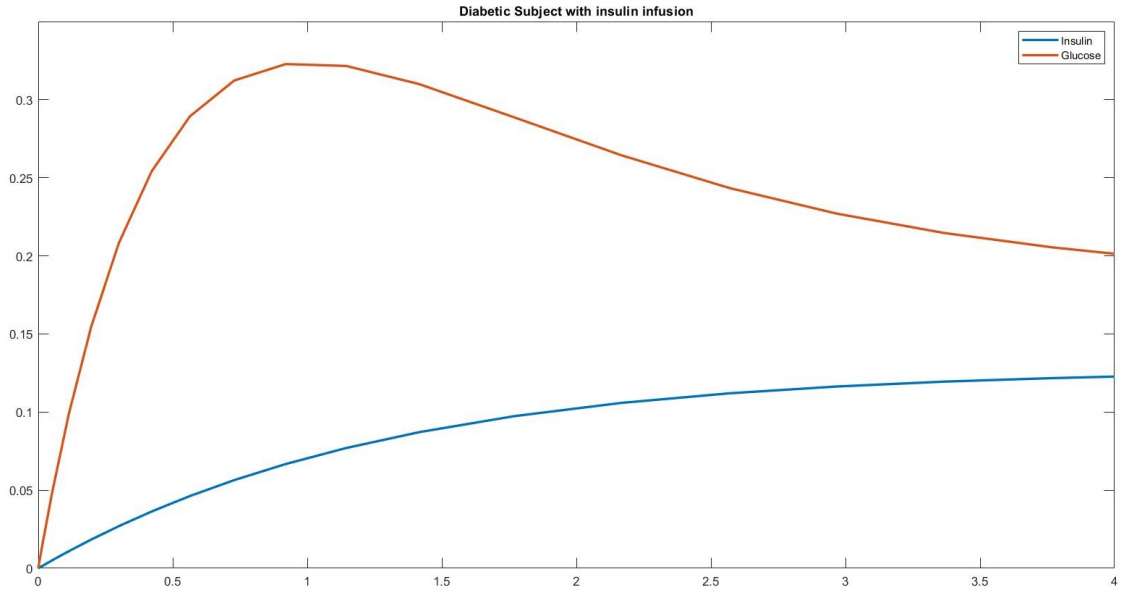

Figure 4

2) Riggs model for iodine metabolism

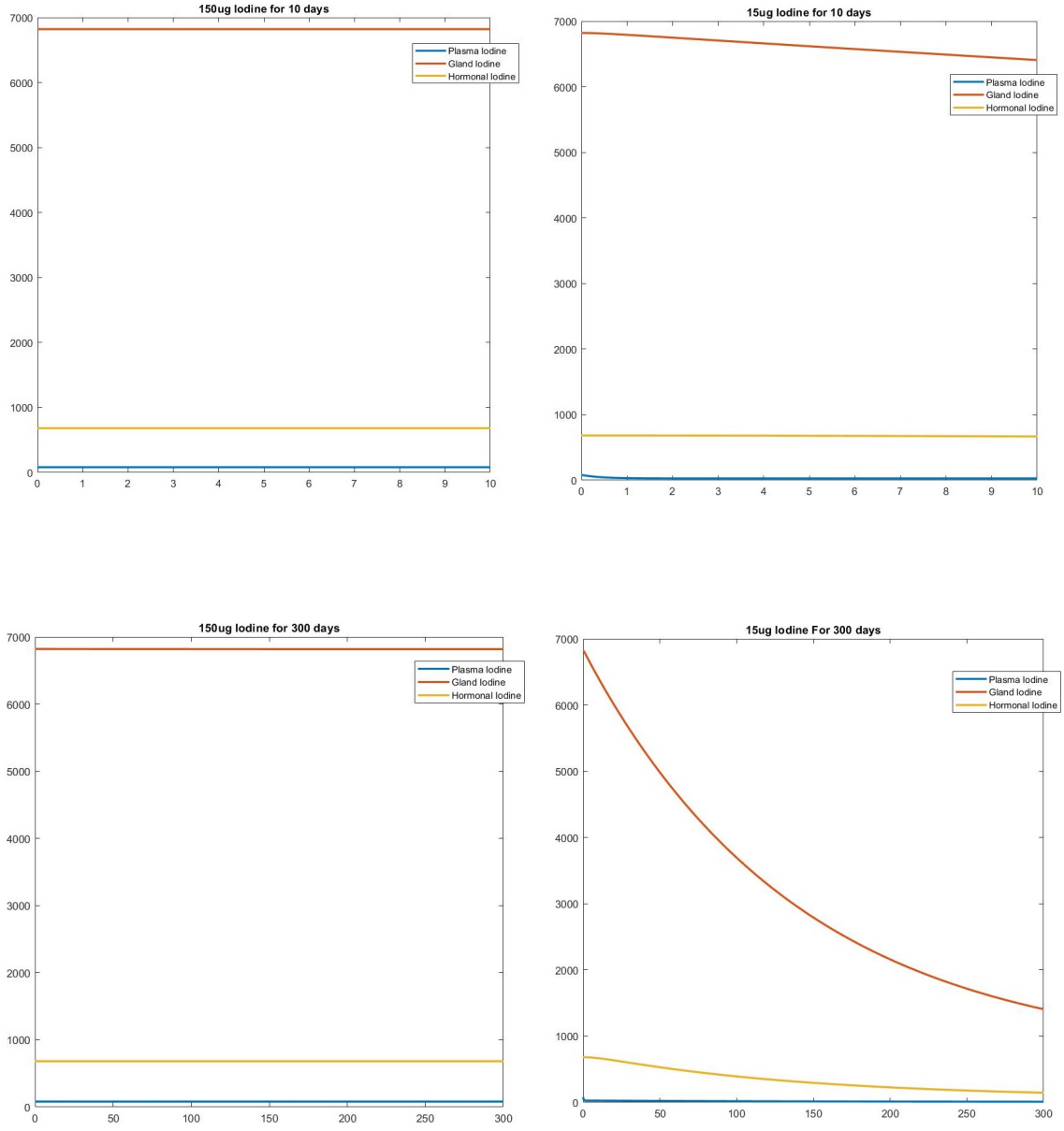

Figure 5

We can simulate thyroid diseases by altering some parameters,

a) Hypothyroidism due to autoimmune thyroid disease

Autoimmune thyroid disease make our own autoimmune system attack the thyroid gland. So the gland will not be able to produce the required amount of thyroid hormone. We can model this by reducing K_2 coefficient. As you can see although gland iodine increases, hormonal and plasma iodine decreases.

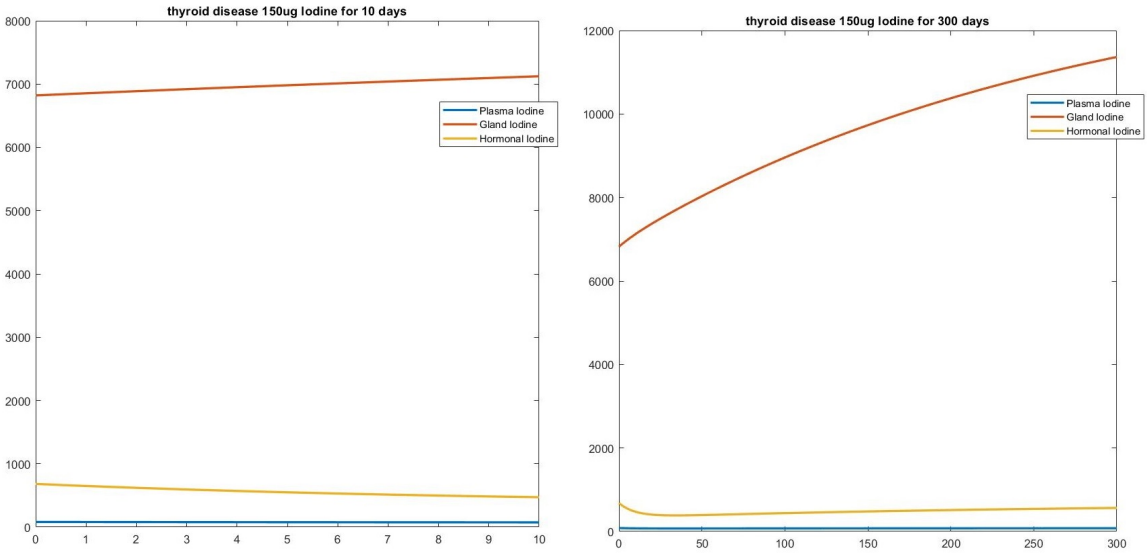

Figure 6

b) Hypothyroidism due to low Iodine intake

This is already been modeled in the first parts of the question.

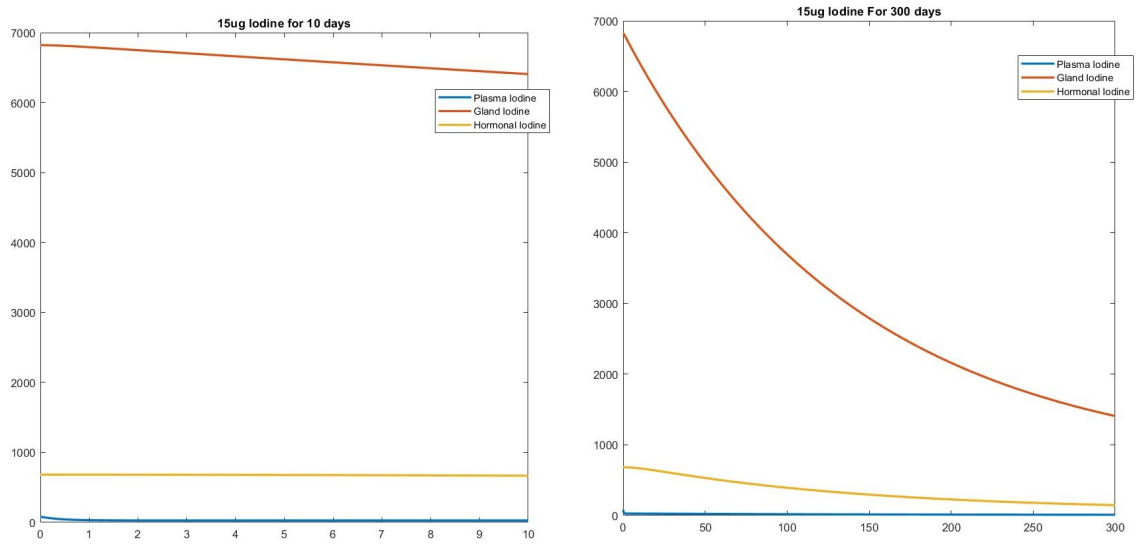

Figure 7

c) Hypothyroidism due to Grave's disease

When the Thyroid hormone is over produced. Modelled by reducing K2 to 0.005 from 0.01

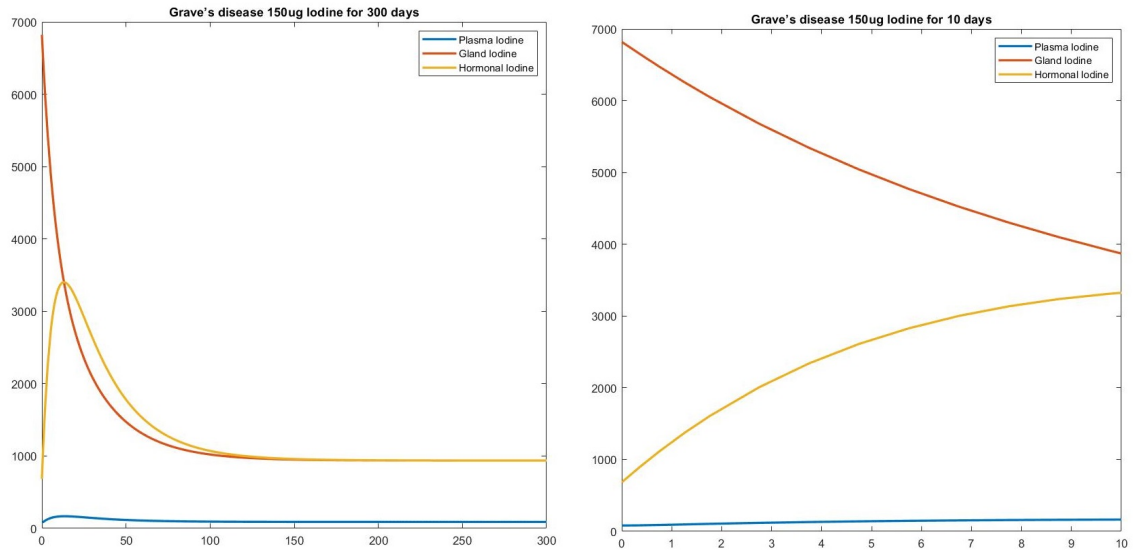

Figure 8

d) Common causes of goitre and tumors and how can they be simulated in the Riggs' model?

A goitre is a lump or swelling at the front of the neck caused by a swollen thyroid. goitre is not cancerous. Lack of iodine intake causes this disease. Iodine intake has been reduced to 50ug per day.
Usual Causes are,

- Iodine deficiency: In areas where iodine intake is insufficient, the thyroid gland may enlarge in an attempt to produce more thyroid hormones. This condition is known as endemic goitre.
- autoimmune thyroid disease(Hashimoto's thyroiditis): It is an autoimmune disorder where the body's immune system mistakenly attacks the thyroid gland, leading to its inflammation and enlargement.
- Graves' disease: This autoimmune condition causes the thyroid gland to produce excessive amounts of thyroid hormones, leading to goitre formation.
- Multinodular goitre: It occurs when multiple nodules develop within the thyroid gland, causing enlargement.

Thyroid tumors refer to abnormal growths or masses that develop in the thyroid gland. These tumors can be benign (noncancerous) or malignant (cancerous).

- Benign Thyroid Nodules: These are noncancerous growths that can develop within the thyroid gland. They are relatively common and often do not cause any symptoms or health problems. However, large nodules may cause compression symptoms or produce excessive thyroid hormones, resulting in hyperthyroidism.
- Thyroid Cancer: Thyroid cancer occurs when cells in the thyroid gland grow and divide uncontrollably. There are different types of thyroid cancer, including papillary, follicular, medullary, and anaplastic thyroid cancer. Symptoms may include a lump in the neck, hoarseness, difficulty swallowing, or swollen lymph nodes. Treatment for thyroid cancer typically involves

surgery, radioactive iodine therapy, external beam radiation, or targeted therapy, depending on the type and stage of cancer.

These can be modelled similarly as shown below by reducing the intake 50ug per day

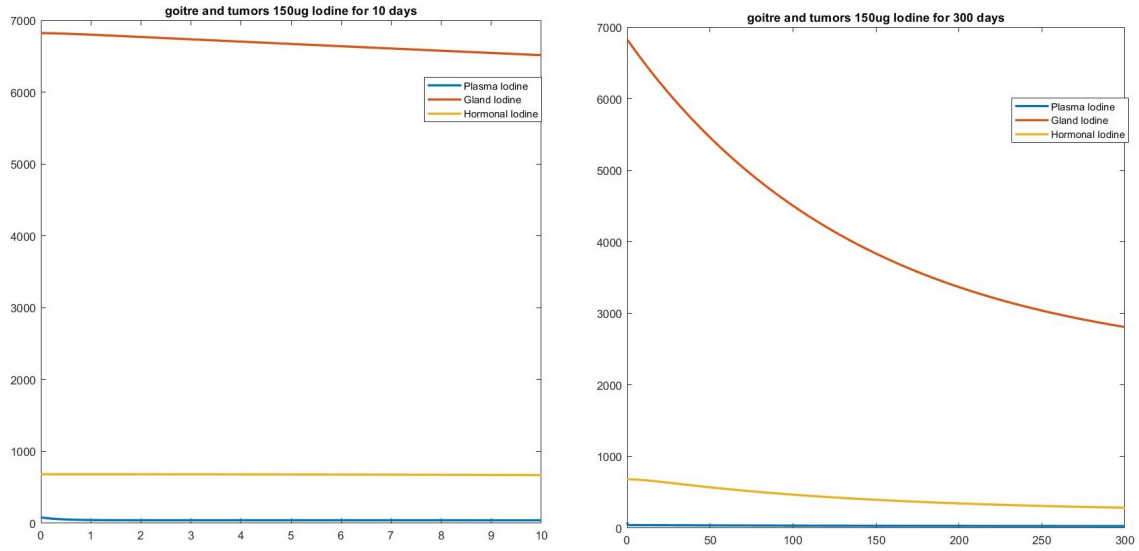

Figure 9

Part 2

1) Simulink diagrams for glucose(g)/insulin(i) model

Bolus input - multiSIM

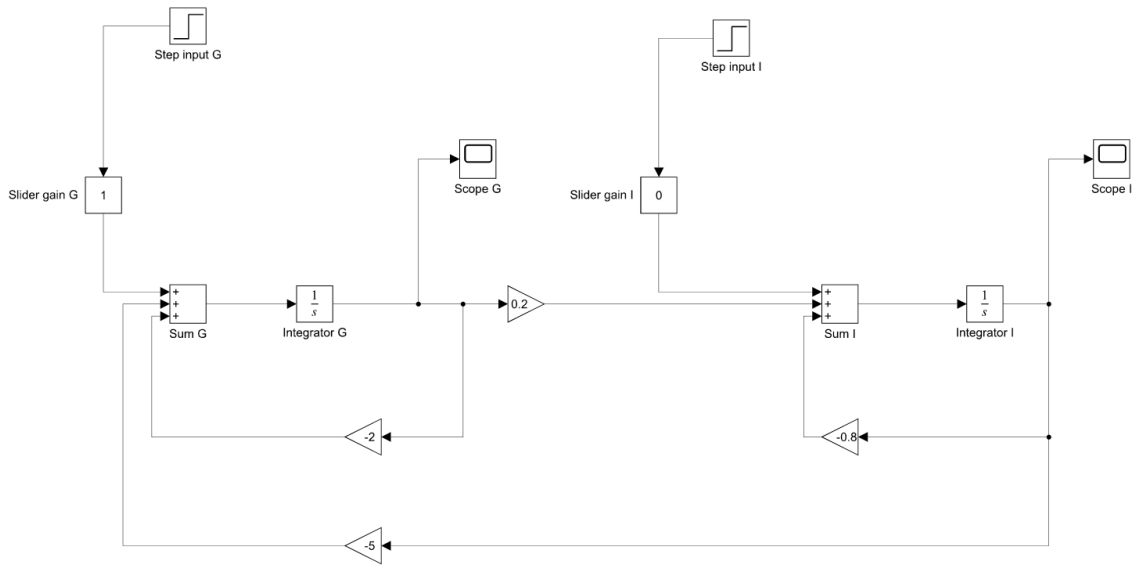

Figure 10

Glucose:

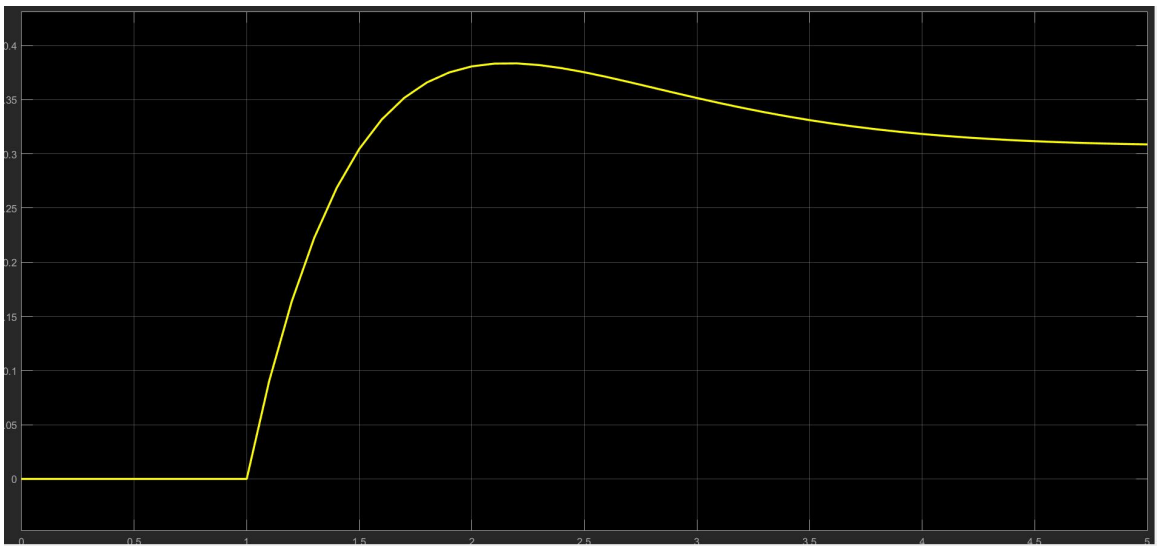

Figure 11

Insuline:

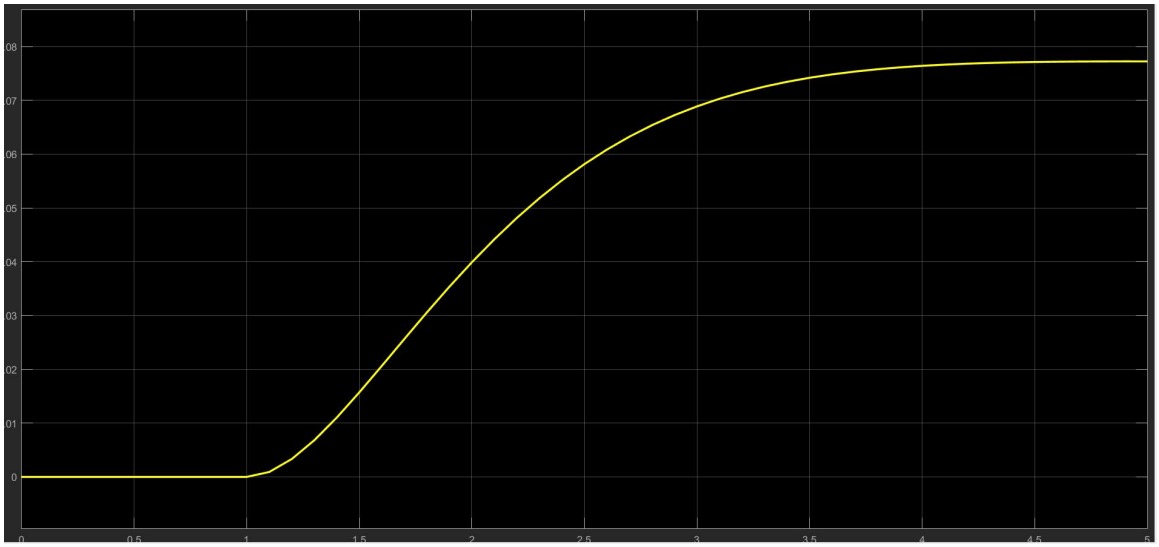

Figure 12

Apart from the delay, shape of the graphs match with the earlier ones.

Alternatively,

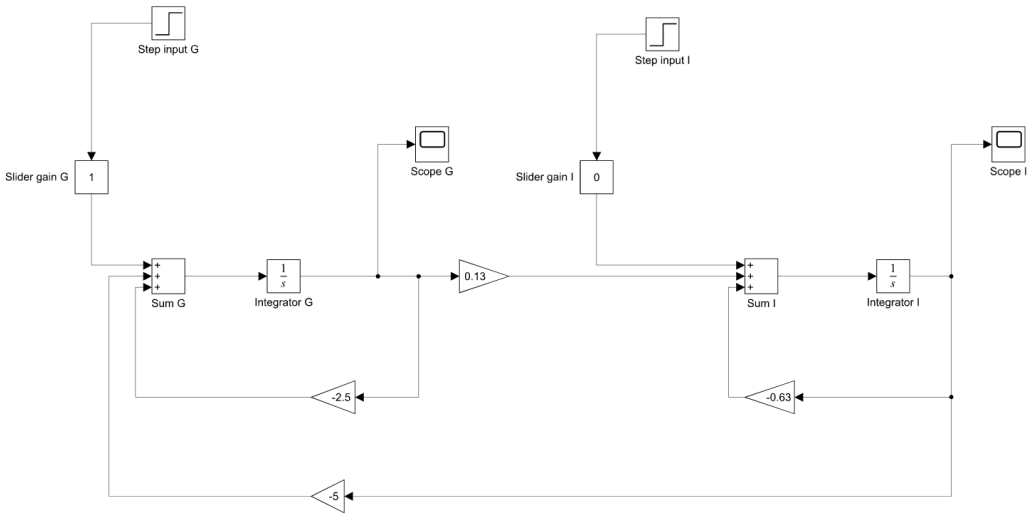

Figure 13

Glucose:

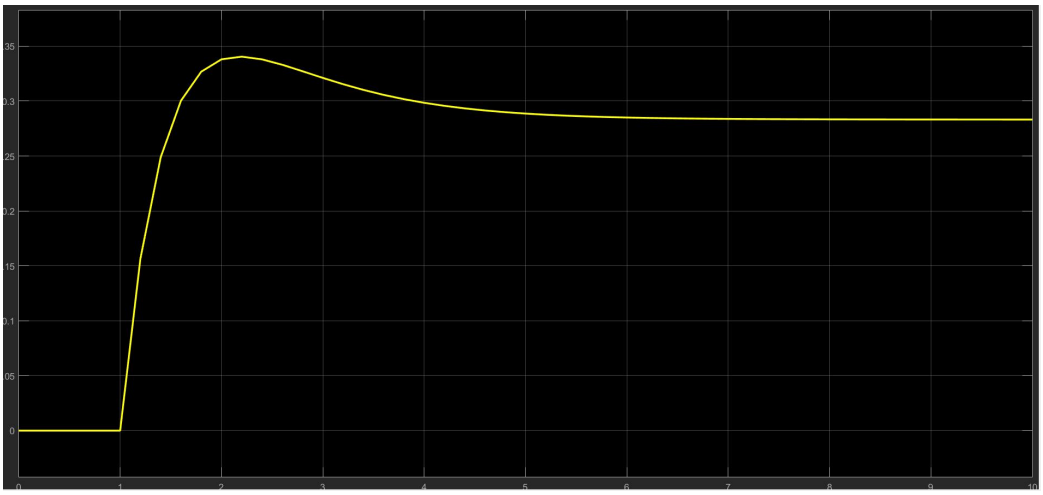

Figure 14

Insuline:

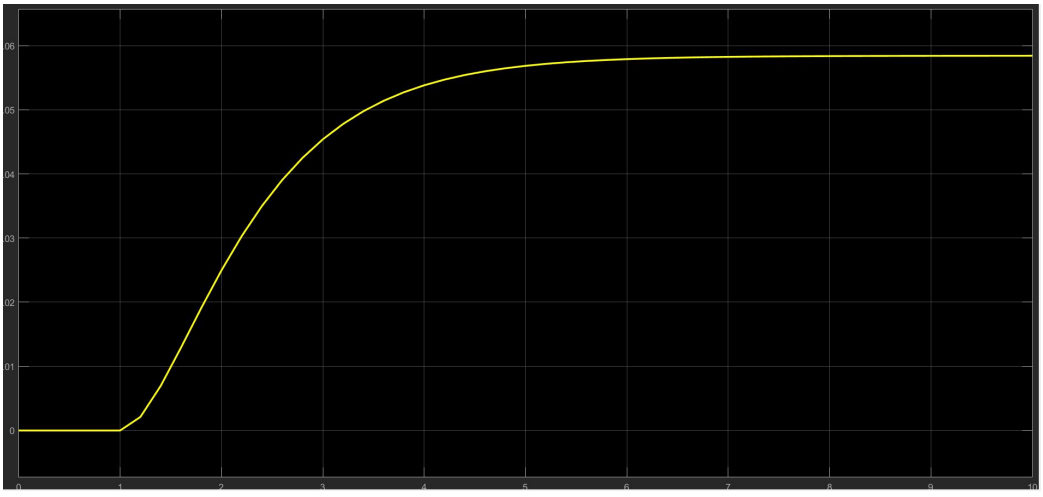

Figure 15

Diabetic patient can be simulated by changing k3 to 0.13 from 0.2(normal subject.)

Normal patient

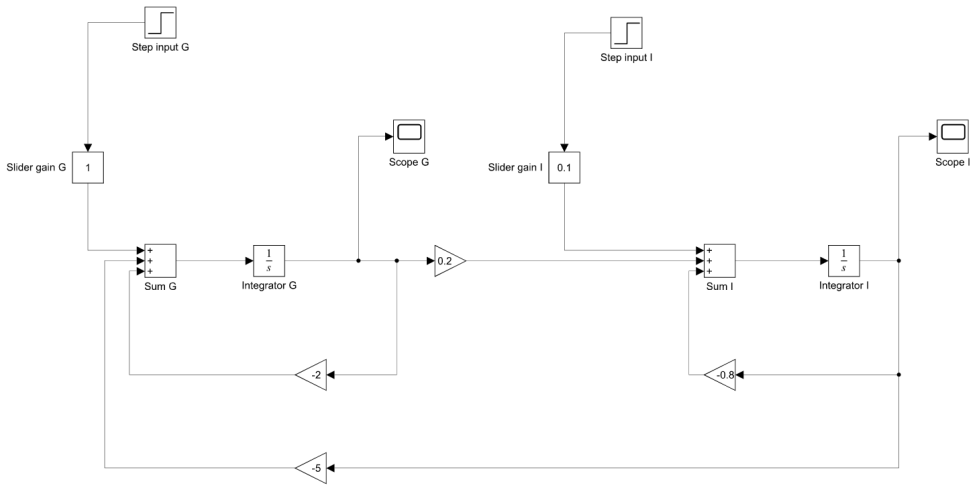

Figure 16

Glucose:

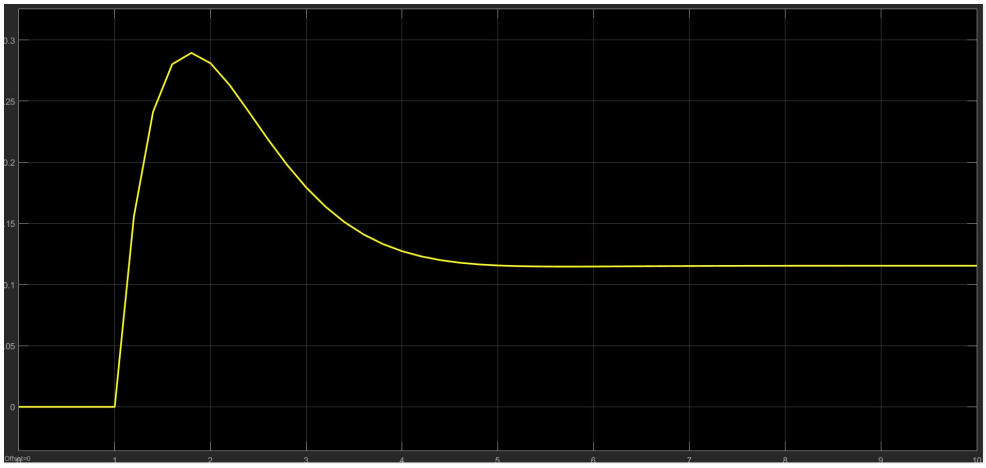

Figure 17

Insuline:

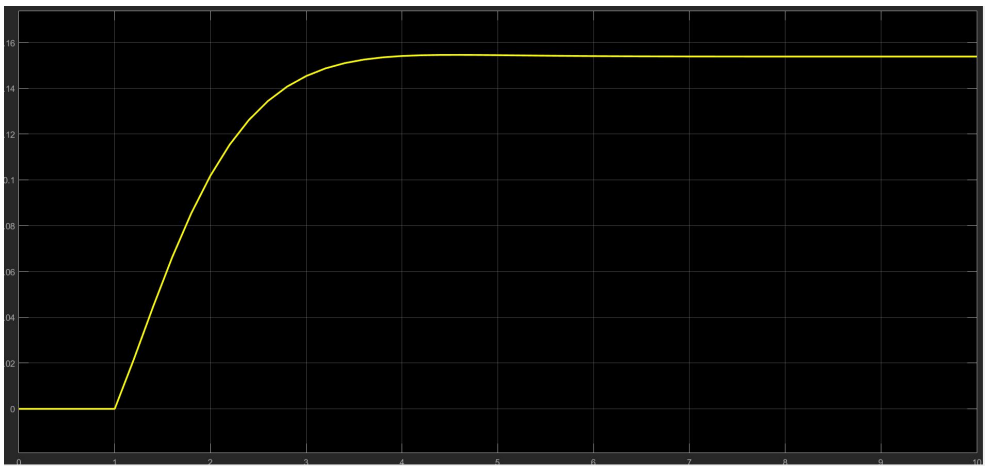

Figure 18

Diabetic patient

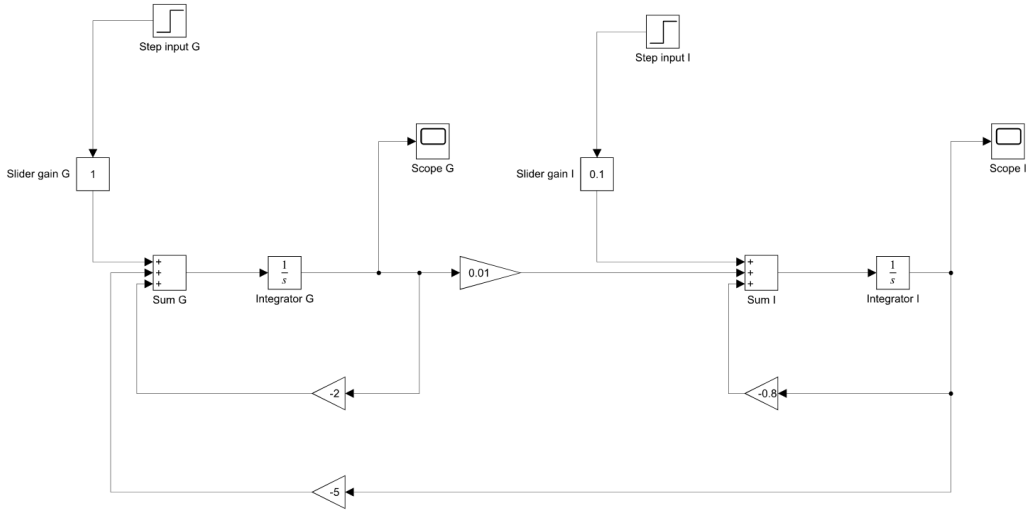

Figure 19

Glucose:

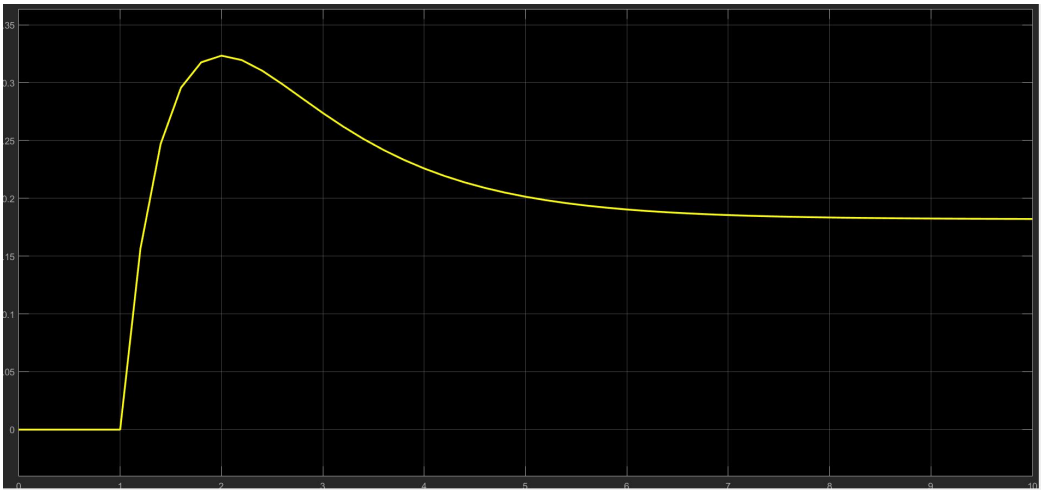

Figure 20

Insuline:

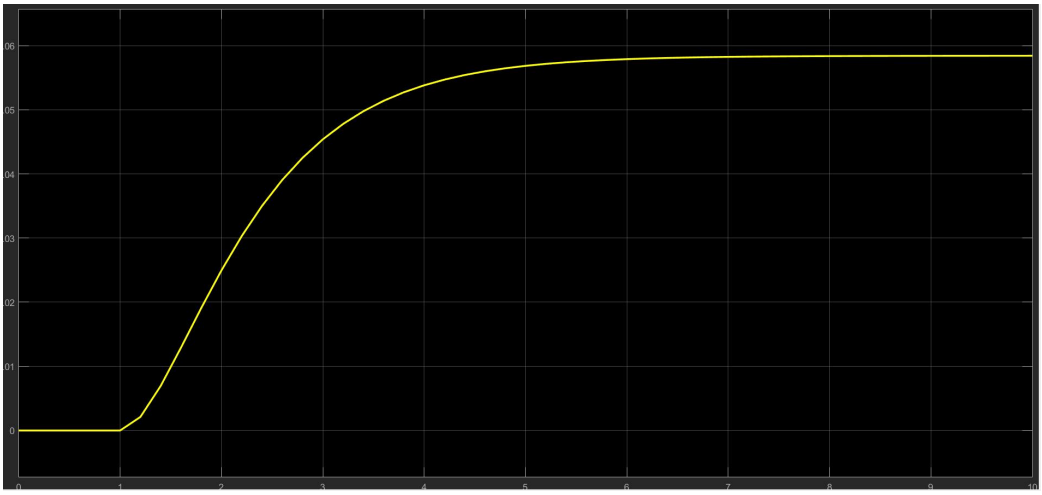

Figure 21

We can see the high glucose level in diabetic patient.

2) Riggs iodine model using SIMULINK

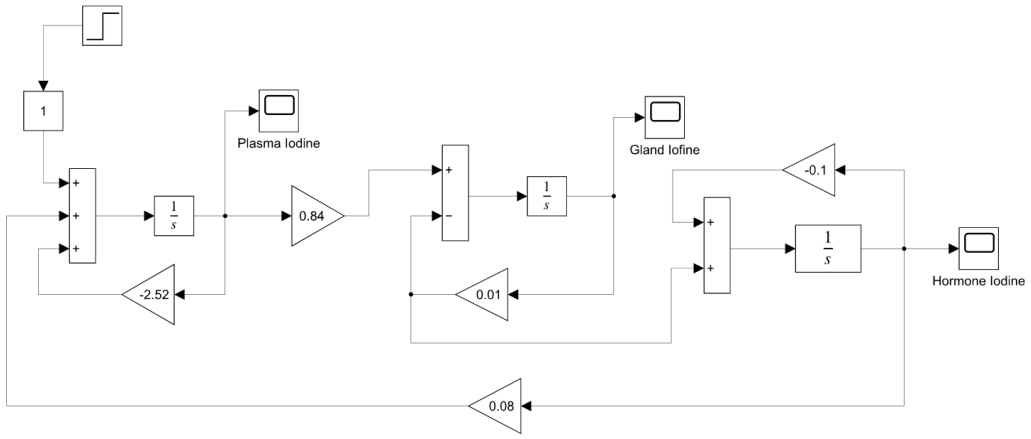

Figure 22

Plasma Iodine:

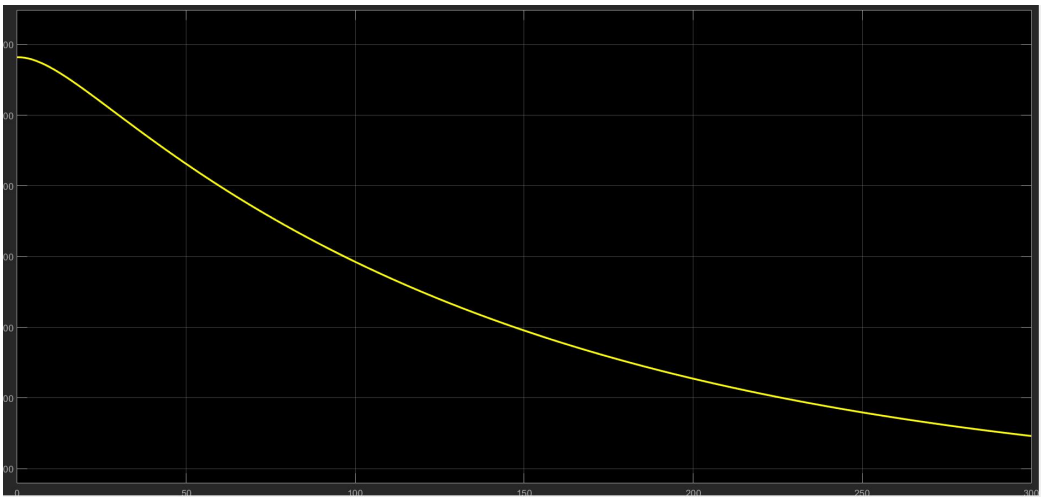

Figure 23

Gland Iodine:

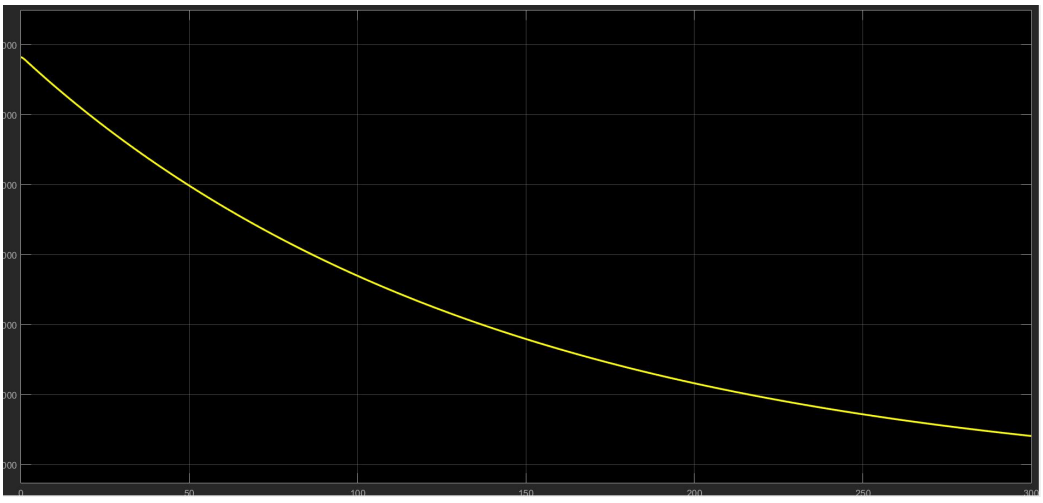

Figure 24

Hormone Iodine:

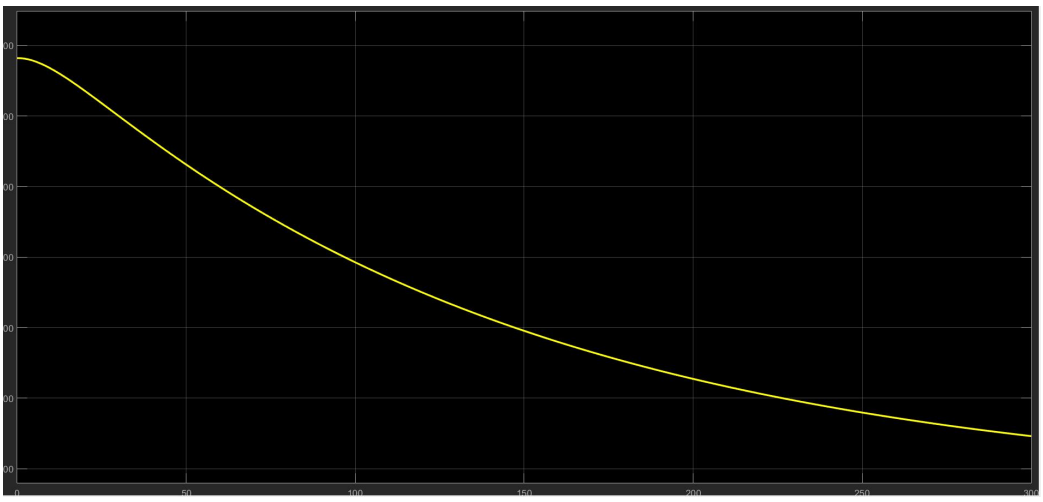

Figure 25

Part 3

1) Bolies' glucose g(t), insulin i(t) model

$$\frac{di}{dt} = -k_1 i + k_3 g$$

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

With Typical values, $K_1 = 0.8h^{-1}$; $K_3 = 1IUh^{-1}g^{-1}$, $K_6 = 5gh^{-1}IU^{-1}$, a = $1gl^{-1}h^{-1}$

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

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

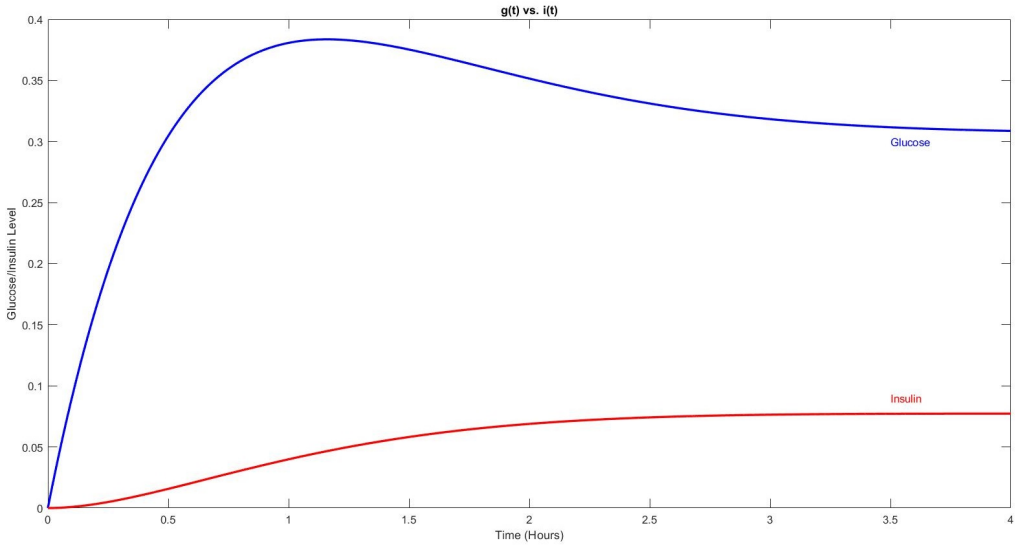

Figure 26

2) Bolies model on reduction of plasma glucose levels with insulin

Factors affecting Bolies' Plasma-Glucose model,

- Glucose
  - Increased when,
    - Infusion (A(t))
    - release from stones (K_5)
    - glucogen dependent increment (K_10)
  - Decreased when,
    - Basal removal cell (K_4)
    - insuline dependent drop (K_6)

$$\frac{dG(t)}{dt} = K_5 + K_{10}G_n(t) - K_4G(t) - K_6I(t) + A(t) \tag{1}$$

- Insulin
  - Increased when,
    - Infusion (B(t))
    - Basal pancreatic release (K_2)
    - glucose simulated release (K_3)
  - Decreased when,
    - breakdown of insuline(K_1)

$$[h]\frac{dI(t)}{dt} = K_2 + K_3G(t) - K_1I(t) + B(t) \tag{2}$$

- Glucogen
  - Increased when,
    - other Inputs (C(t))
    - Basal release (K_8)
    - glucose simulated release (K_9)
  - Decreased when,
    - glucogen breakdown (K_7)

$$\frac{dG_n(t)}{dt} = K_8 + K_9G(t) - K_7G_n(t) + C(t) \tag{3}$$

At equilibrium all rates become 0;
Then,

$$K_5 = K_4G_0 + K_6I_0 - K_{10}G_{n0} \tag{4}$$

$$K_2 = -K_3G_0 + K_1I_0 \tag{5}$$

$$K_8 = -K_9G_0 + K_7G_{n0} \tag{6}$$

Also set A(t) = a.u(t) , B(t) = 0 , C(t) = 0
As g = G-G_0;

$$\frac{dg}{dt} = \frac{dG}{dt}$$

Similarly;

$$\frac{di}{dt} = \frac{dI}{dt}$$
$$\frac{dg_n}{dt} = \frac{dG_n}{dt}$$

Now from above equations,

Equation 1 - 4

$$\frac{dg}{dt} = K_4 g(t) + -K_6 i(t) + K_{10} g_n(t) + +A(t)$$

Equation 2 - 5

$$\frac{di}{dt} = \mathrm{K}_3 g(t) + -K_1 i(t) + 0 + B(t)$$

Equation 3 - 6

$$\frac{dgn}{dt} = \mathrm{K}_9 g(t) + 0 + -K_7 g_n(t) + C(t)$$

Now from these three equations,

$$\begin{bmatrix} \frac{dg}{dt} \\ \frac{di}{dt} \\ \frac{dgn}{dt} \end{bmatrix} = \begin{bmatrix} -k_4 & -k_6 & k_{10} \\ k_3 & -k_1 & 0 \\ k_9 & 0 & -k_7 \end{bmatrix} * \begin{bmatrix} g(t) \\ i(t) \\ g_n(t) \end{bmatrix} + \begin{bmatrix} A(t) \\ B(t) \\ C(t) \end{bmatrix}$$

$$\begin{bmatrix} \frac{dg}{dt} \\ \frac{di}{dt} \\ \frac{dgn}{dt} \end{bmatrix} = \begin{bmatrix} -k_4 & -k_6 & k_{10} \\ k_3 & -k_1 & 0 \\ k_9 & 0 & -k_7 \end{bmatrix} * \begin{bmatrix} g(t) \\ i(t) \\ g_n(t) \end{bmatrix} + \begin{bmatrix} a.u(t) \\ 0 \\ 0 \end{bmatrix}$$

Now we can easily solve the equation as the matrix take the form $Q' = A*Q+f(t)$.

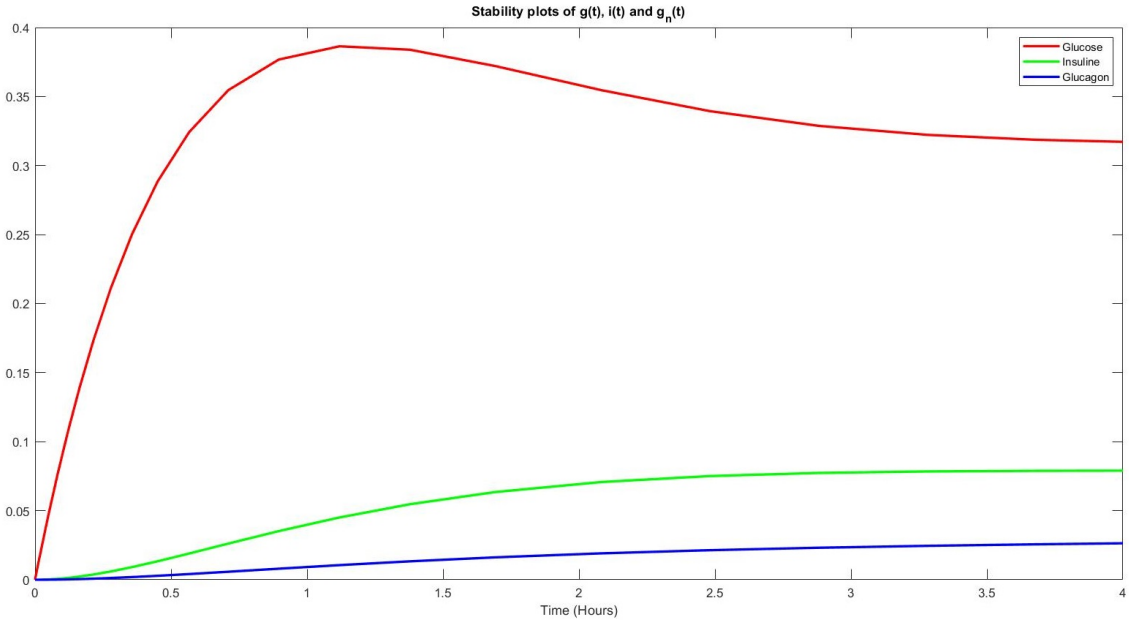
Stability plots of g(t), i(t) and g_n(t)
Glucose
Insuline
Glucagon
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.5
1
1.5
2
2.5
3
3.5
4
Time (Hours)

Figure 27