UNIVERSITY OF MORATUWA, SRI LANKA
Faculty of Engineering
Department of Electronic and Telecommunication Engineering
Semester 4 (Intake 2020)

BM2102 Analysis of physiological systems
Assignment 4
Compartmental Modelling

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Plasma Glucose/ Insulin model

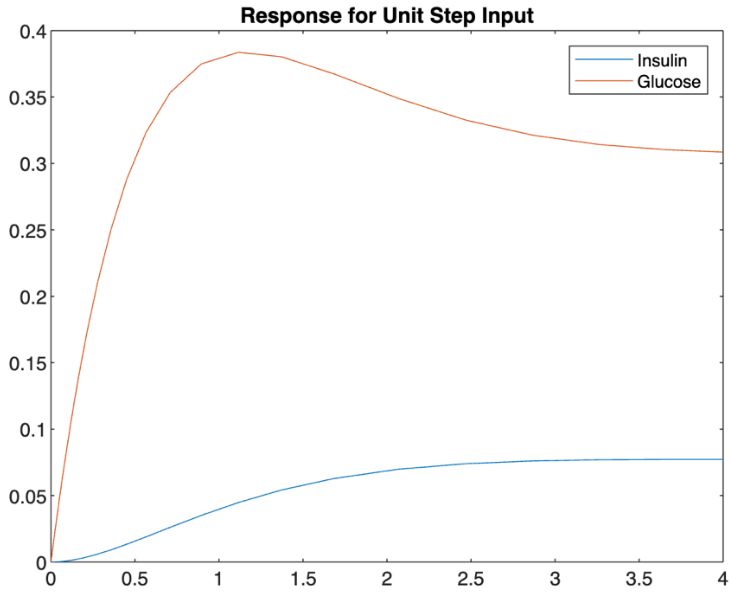
A simple plasma glucose/insulin model can be expressed as:

$$\frac{di}{dt} = -0.8i + 0.2g$$

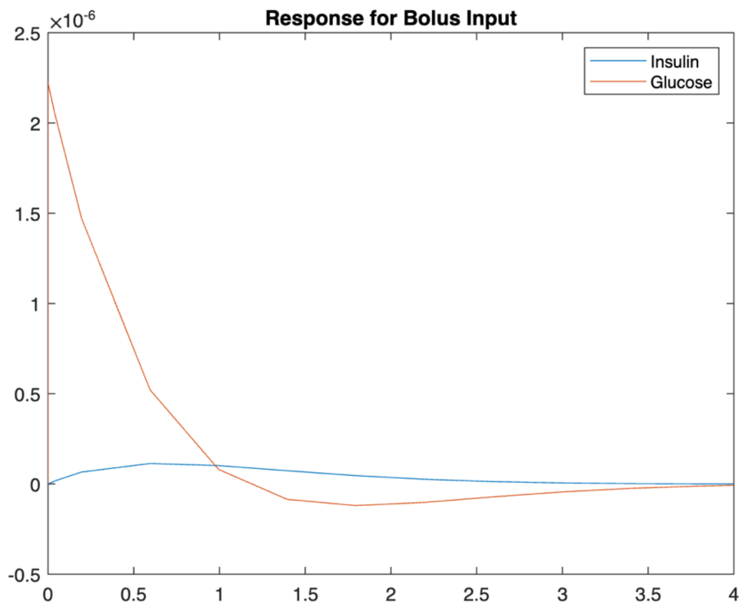
$$\frac{dg}{dt} = -5i - 2g + A(t)$$

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.

Unit Step Input

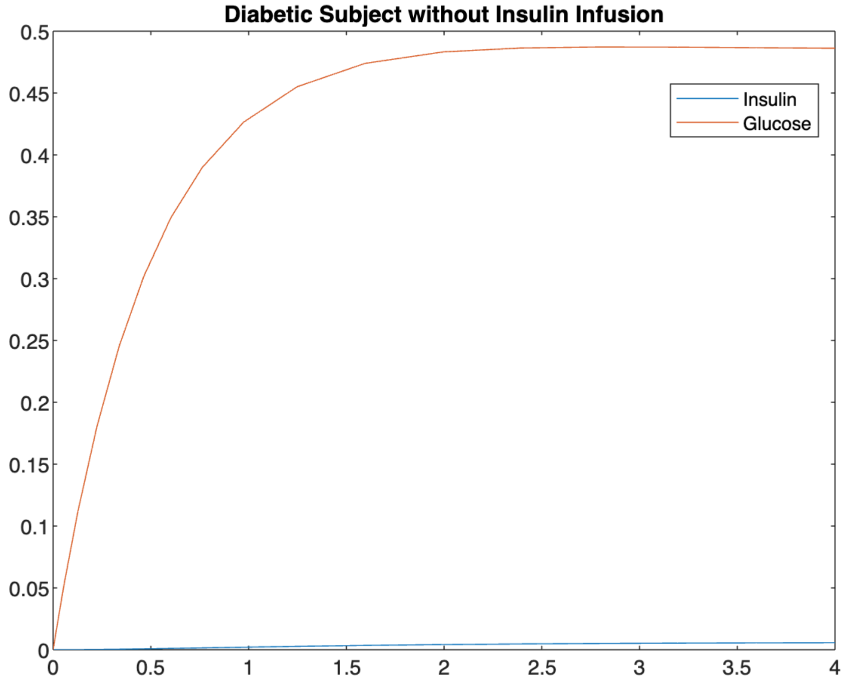


Bolus Input

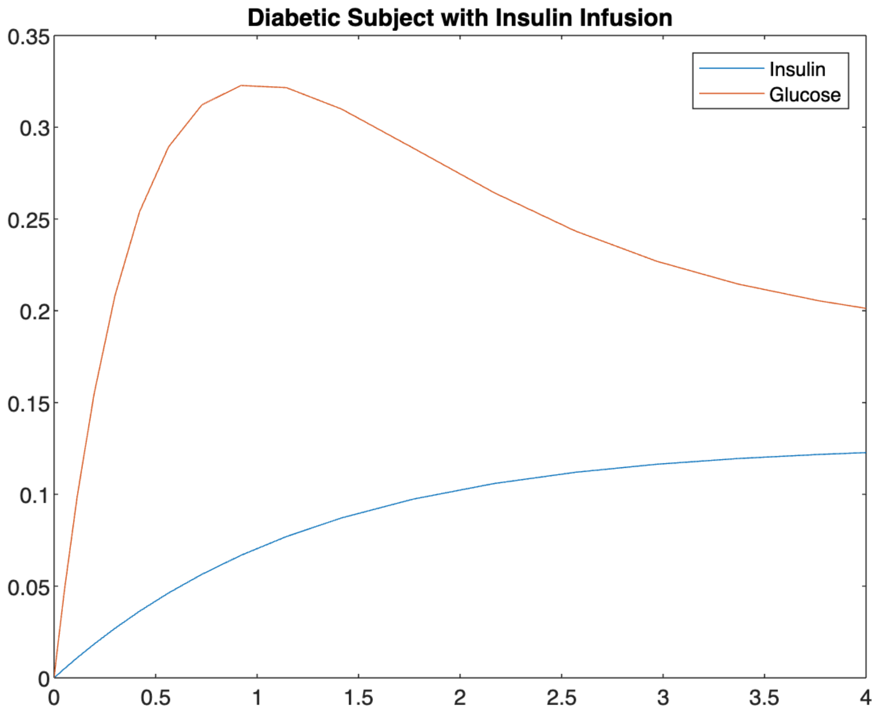


Diabetic subject without insulin infusion

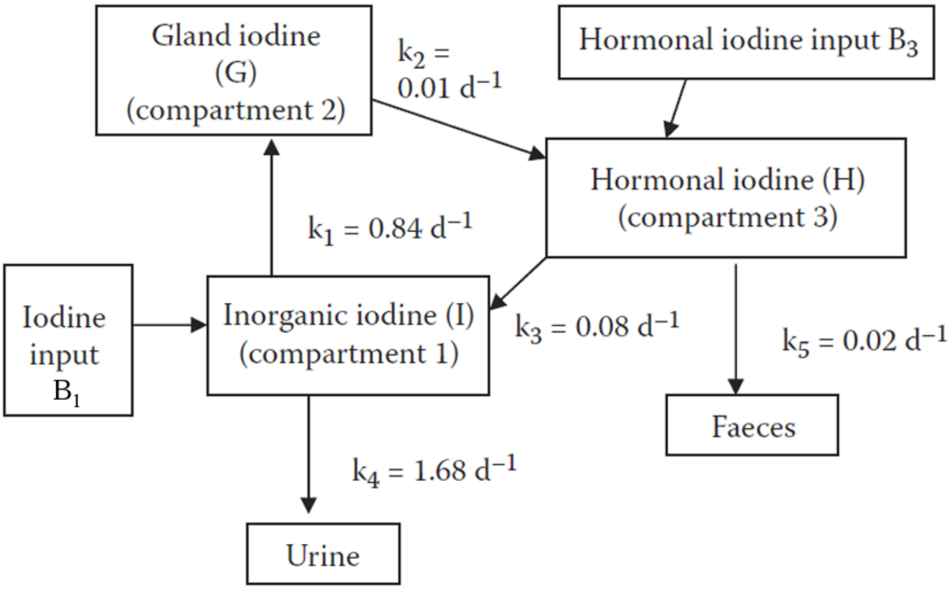
For a diabetic subject transfer rate from glucose to insulin reduces to $0.01h^{-1}$ ($0.2h^{-1}$ for a healthy person),



Diabetic subject with insulin infusion of 100 mU/kg/h



Riggs model for iodine metabolism



Control Theory and Physiological Feedback Mechanisms, Riggs (1970)

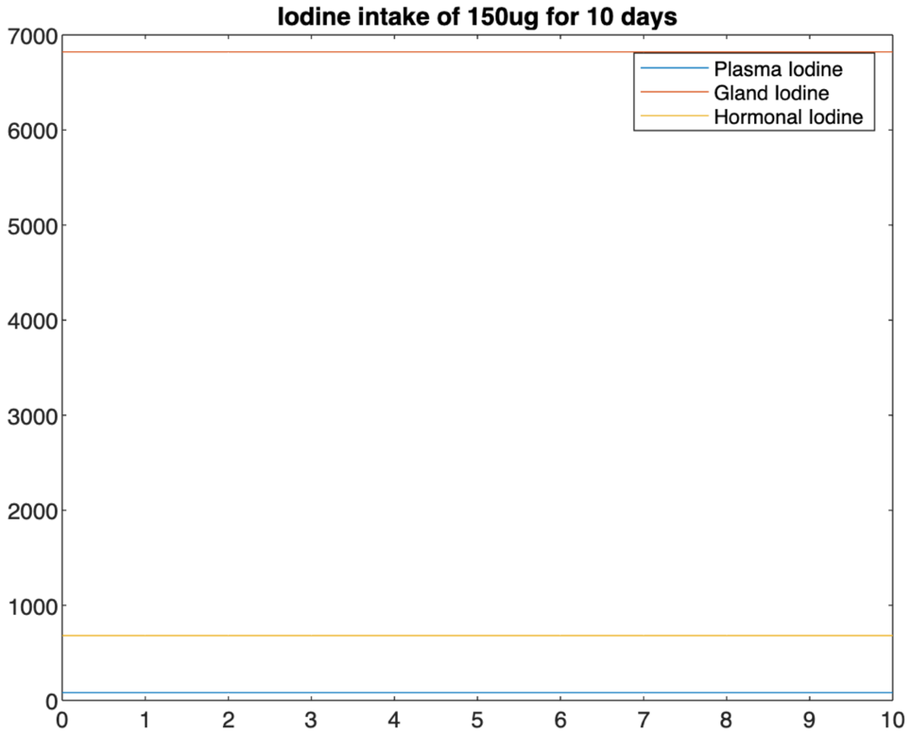
By Mass Conservation Law,

$$\frac{dI}{dt} = -(k_1 + k_4)I + k_3 H + B_1(t)$$

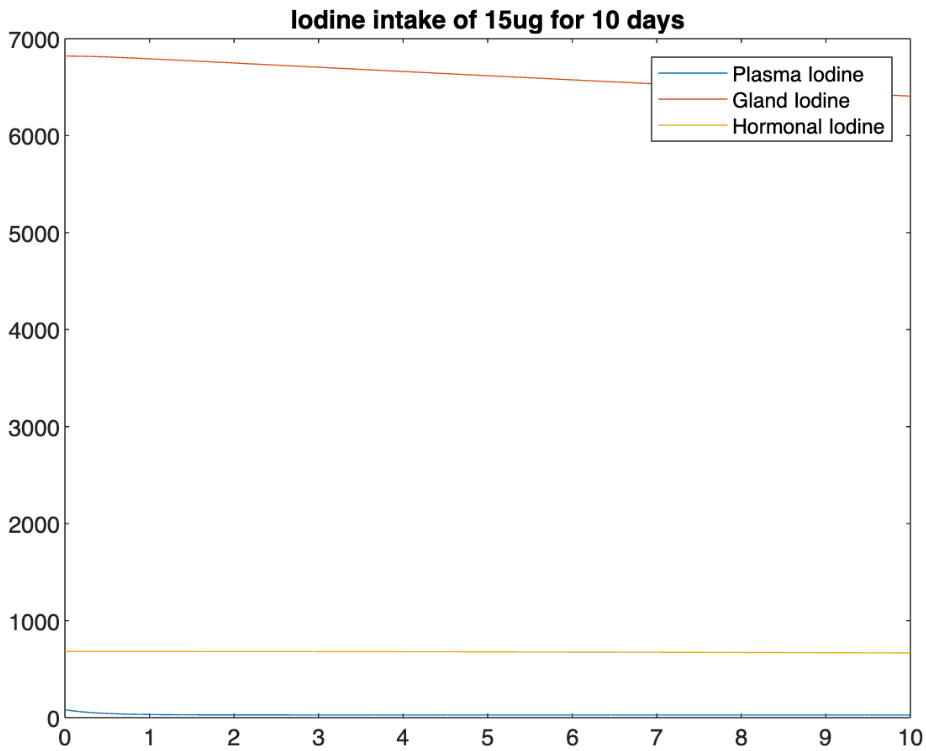
$$\frac{dG}{dt} = k_1 I - k_2 G$$

$$\frac{dH}{dt} = k_2 G - (k_3 + k_5)H + B_3(t)$$

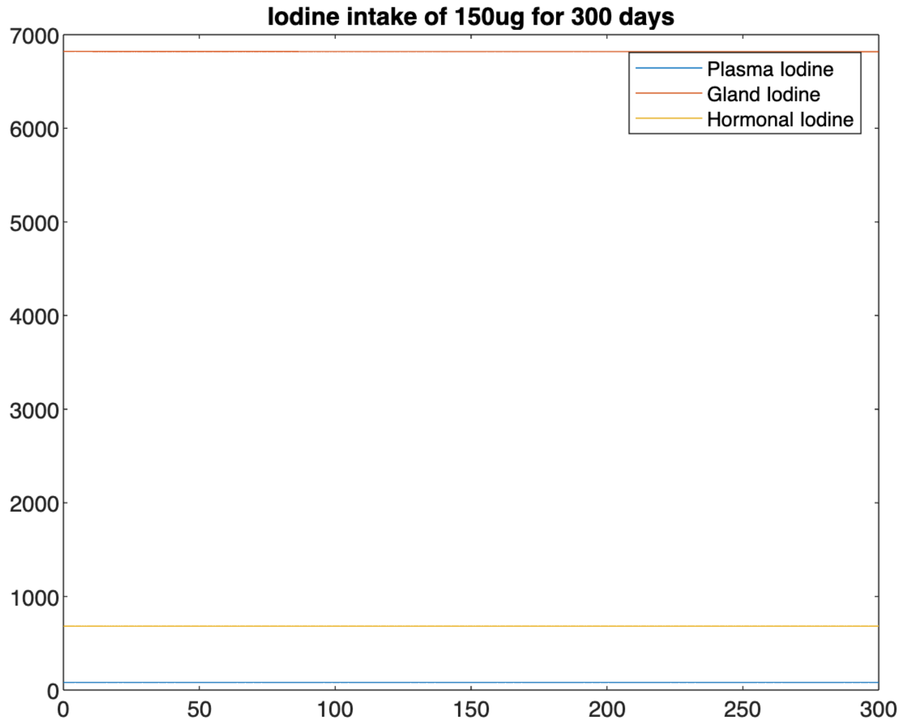
Iodine intake of 150ug for 10 days



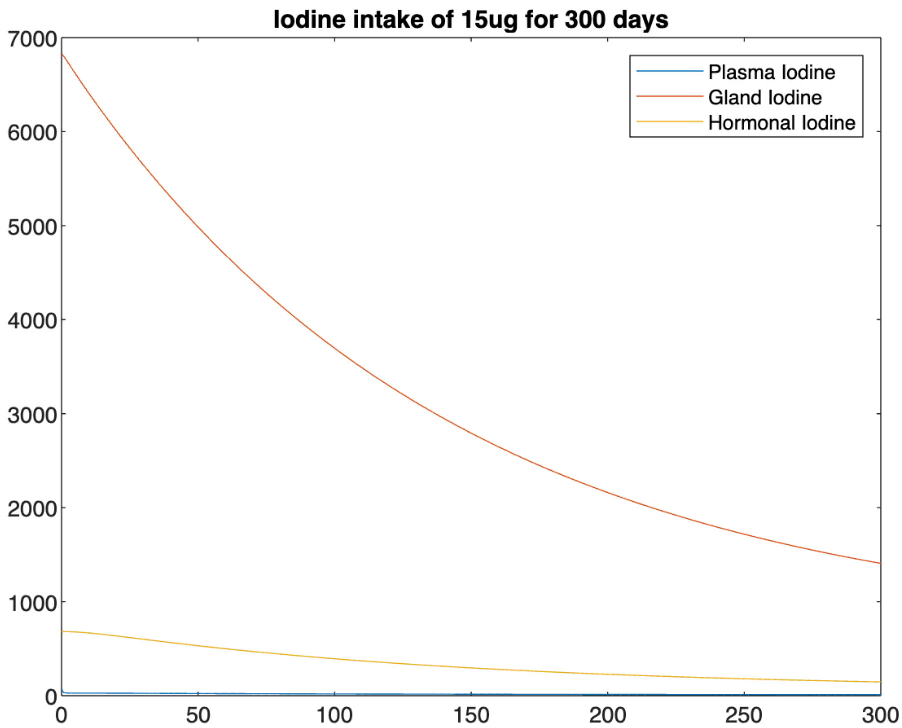
Iodine intake of 15ug for 10 days



Iodine intake of 150ug for 300 days



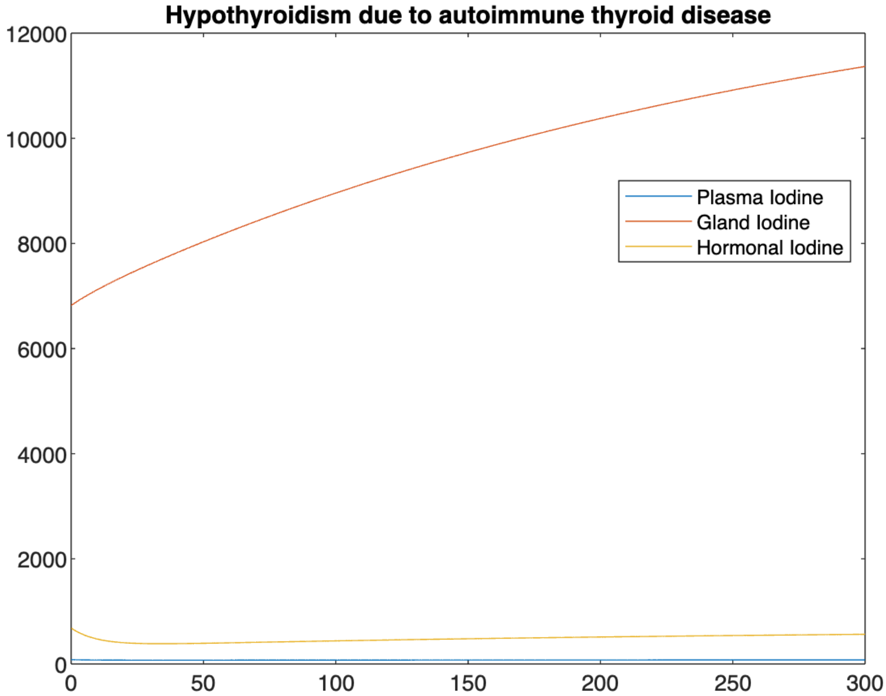
Iodine intake of 15ug for 300 days



Thyroid diseases

Hypothyroidism due to autoimmune thyroid disease

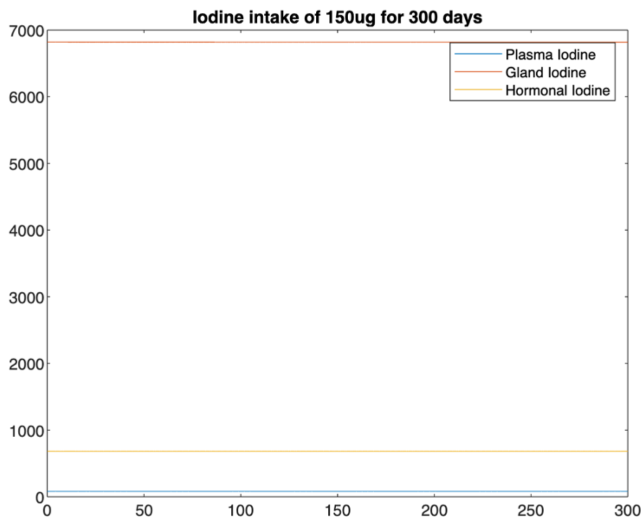
Hashimoto's disease or autoimmune thyroiditis is an autoimmune thyroid disease which causes hypothyroidism. In Hashimoto's disease, immune-system cells lead to the death of the thyroid's hormone-producing cells. The disease usually results in a decline in hormone production. This could be modelled using the Rigg's model by reducing the transfer rate k_2 (which is the transfer rate from thyroid gland to hormones).
Reducing k_2 from $0.01d^{-1}$ to $0.005d^{-1}$,

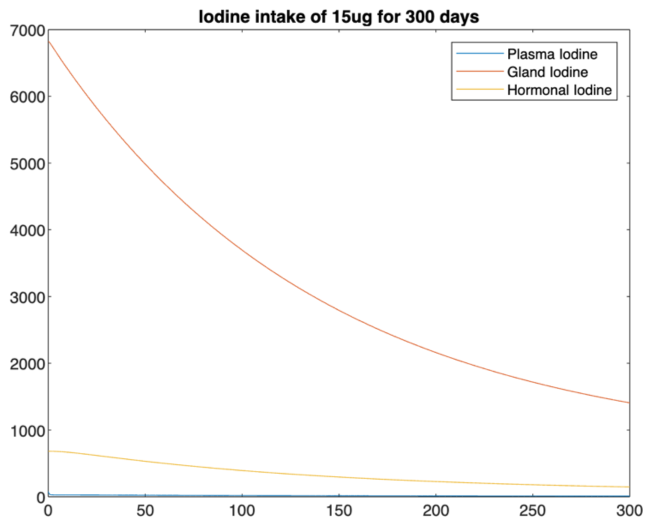


Although the Gland Iodine level increases, Plasma and Hormonal iodine levels decrease due to this autoimmune disease.

Hypothyroidism due to low Iodine intake

This low iodine intake can be simulated by reducing the Iodine Input, $B_1(t)$. The comparison is between 150ug of iodine intake per day and 15ug of iodine intake per day (for 300 days).

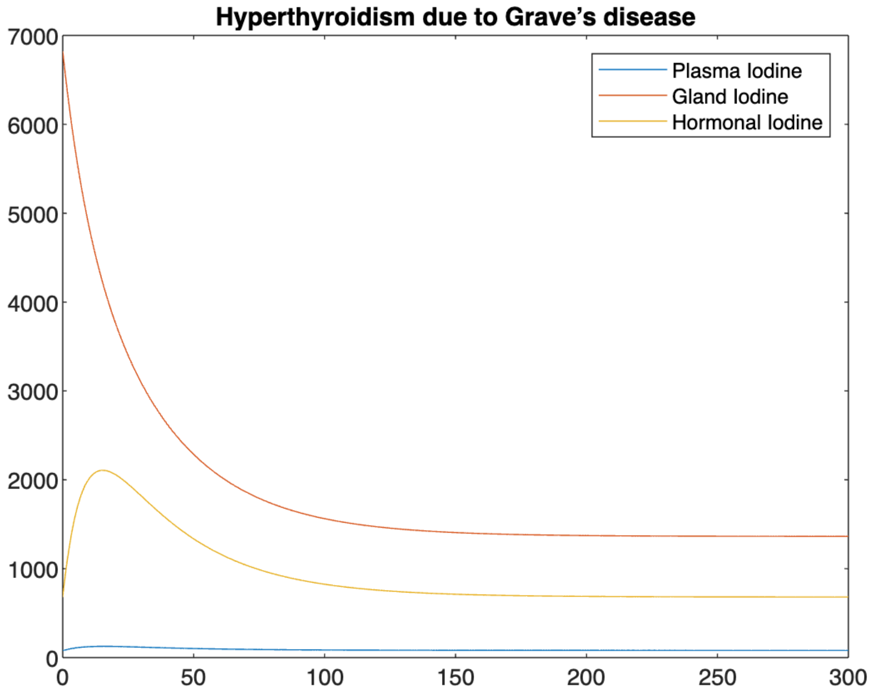




Due to the reduction of Iodine intake all three iodine levels, Plasma iodine level, Gland iodine level and Hormonal iodine level decrease.

Hyperthyroidism due to Grave's disease

Grave's disease is an autoimmune thyroid disease which causes hyperthyroidism. The disease usually results in an overproduction of thyroid hormones. This could be modelled using the Rigg's model by increasing the transfer rate k_2 (which is the transfer rate from thyroid gland to hormones).
Increasing k_2 from $0.01d^{-1}$ to $0.05d^{-1}$,



Goitre and Tumors

A goitre is the swelling of the thyroid gland, which can either be a temporary issue that resolves on its own or a sign of another thyroid-related condition that needs medical treatments.
There can be several causes for Goiters and Tumors,

1. Iodine Deficiency
One of the most common causes of goitre worldwide is a lack of dietary iodine. Iodine is essential for the production of thyroid hormones, and when there is a deficiency, the thyroid gland may enlarge to compensate.
This can be simulated in the Rigg's model by lowering iodine intake $B_1(t)$.

2. Hashimoto's Thyroiditis
In this autoimmune disorder, the immune system attacks the thyroid gland, leading to inflammation and, in some cases, goitre. Over time, it can also result in an underactive thyroid (hypothyroidism).
This condition can be simulated by reducing the transfer rate k_2 (which is the transfer rate from thyroid gland to hormones) in Rigg's model.

3. Graves' Disease
This autoimmune condition, causes the thyroid gland to produce excessive amounts of thyroid hormones. This overactivity of the thyroid gland can lead to goitre. This could be modelled using the Rigg's model by increasing the transfer rate k_2.

4. Thyroid Nodules
Thyroid nodules are lumps or abnormal growths within the thyroid gland. Most nodules are noncancerous (benign) and do not cause symptoms. However, certain nodules can grow large and cause goitre or produce excessive thyroid hormone. This too can be modelled by increasing the transfer rate k_2 of the Rigg's model.

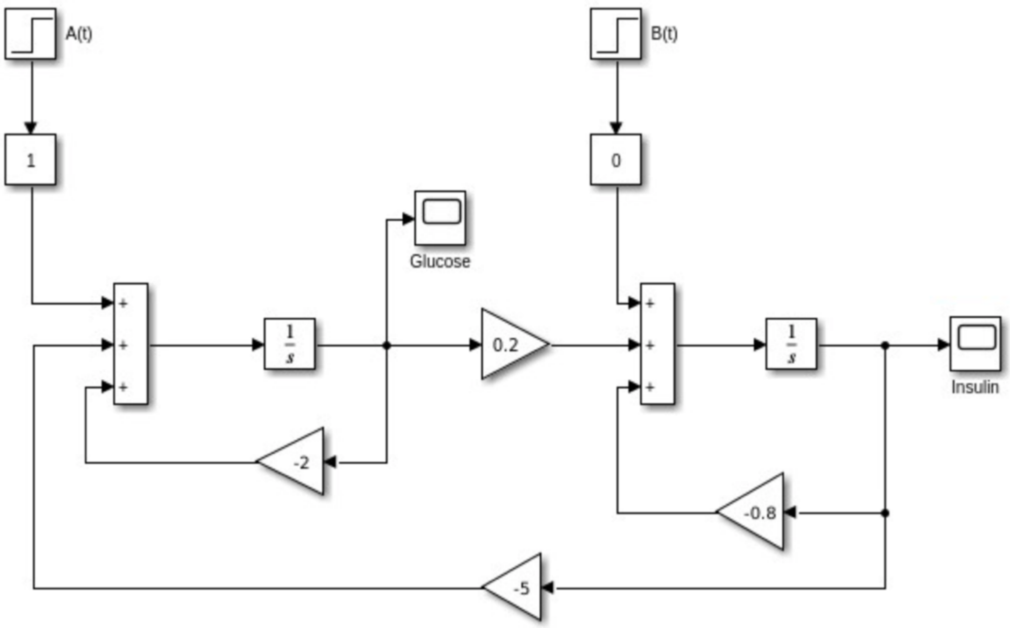
5. Thyroid Cancer: Although less common than benign nodules, thyroid cancer can also cause goitre. Different types of thyroid cancer can develop within the thyroid gland, and they may require specific treatments.

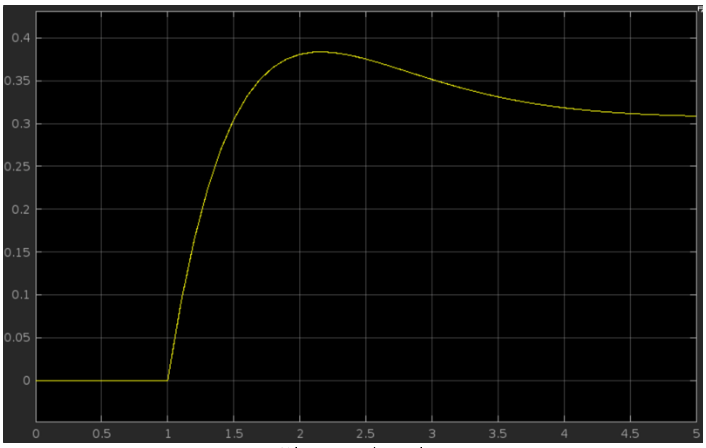
Simulink Results for Plasma Glucose/Insulin Model

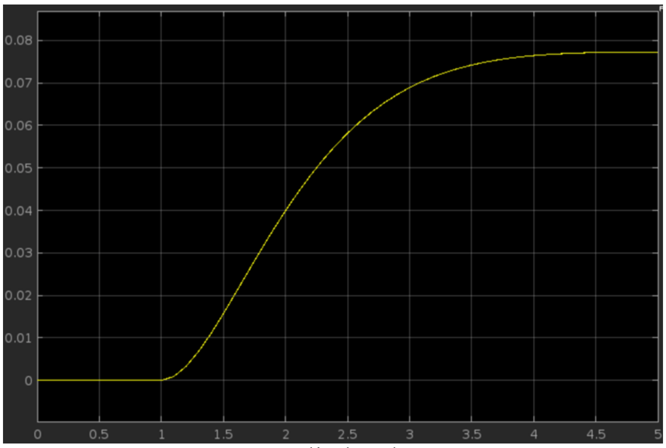
<u>Plasma Glucose/Insulin model</u>

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

with $A(t)$ set at 1 g/kg/h for t>1



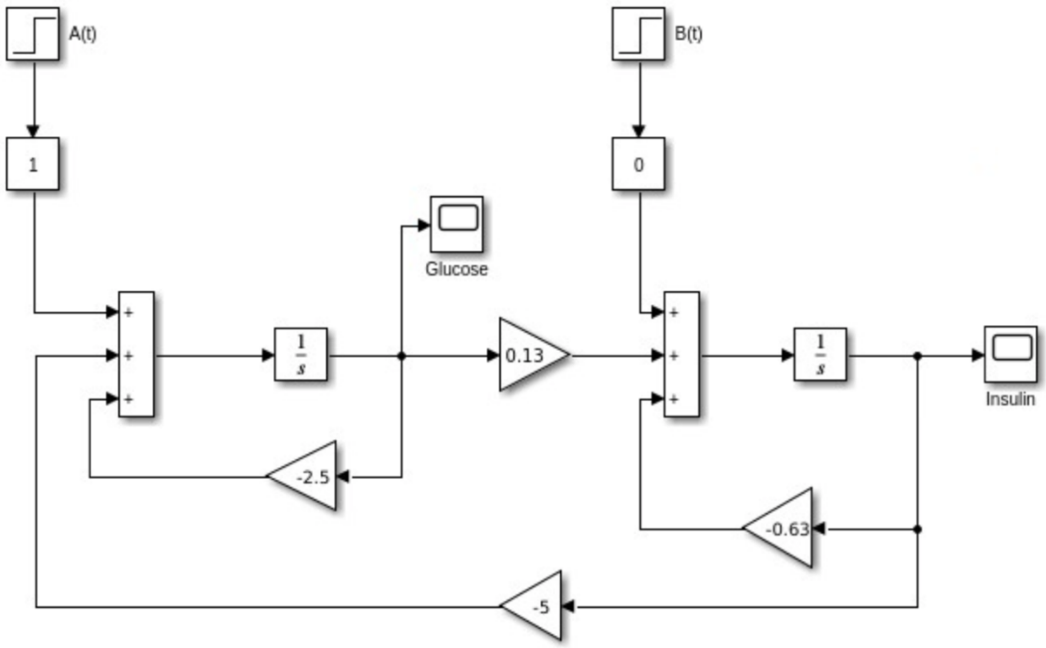

Glucose level

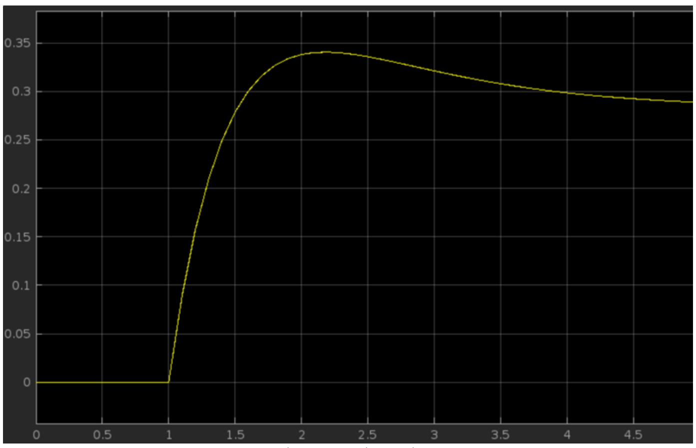

Insulin level

The Simulink plots are similar to those obtained in Part(1).

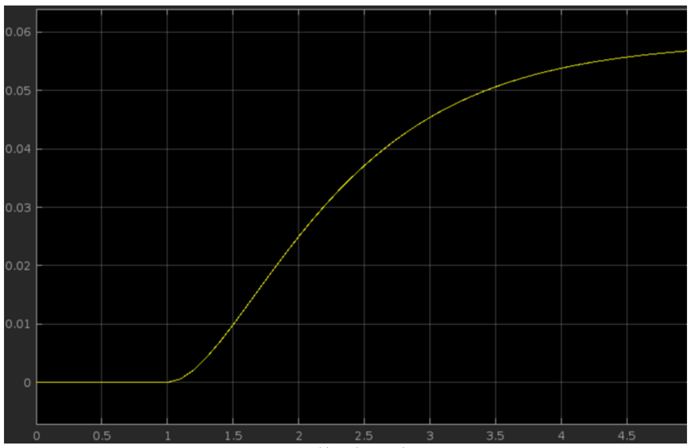
$$\frac{di}{dt} = -0.63i + 0.13g$$
$$\frac{dg}{dt} = -5i - 2.5g + A(t)$$

with $A(t)$ set at 1 g/kg/h for t>1





Glucose level



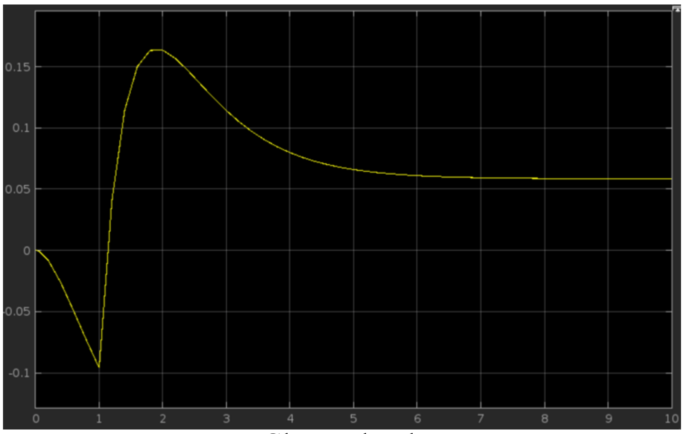
Insulin level

Although the variations are similar for both Insulin and Glucose levels in the two cases, the values are lower for both levels in the second scenario compared to the first.

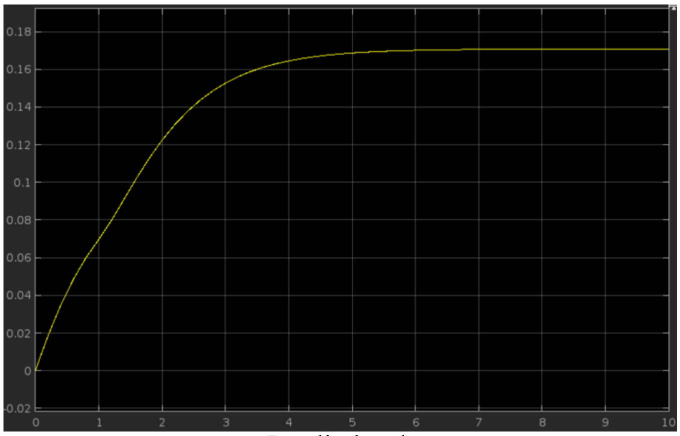
In a Normal subject,

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

with $A(t)$ = 1 g/kg/h for t>1 and $B(t)$ = 0.1 U/kg/h for t>0
Note : As no time value for when B(t) is injected is given in the assignment, it is assumed that B(t) is given from t > 0.



Glucose level



Insulin level

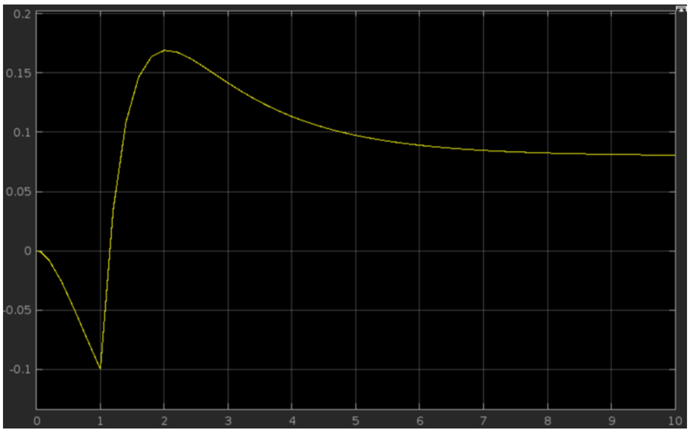
The spike at the beginning of the glucose level curve is because no glucose is infused until t = 1 although there's an insulin infusion from t > 0 (Glucose level decreases due to the insulin infusion from t > 0 and starts to rise from t = 1 due to the glucose infusion).

As insulin is given to the normal subject, when compared to the previous two plots, the glucose level is lower due to the insulin infusion and insulin level is lower as well.

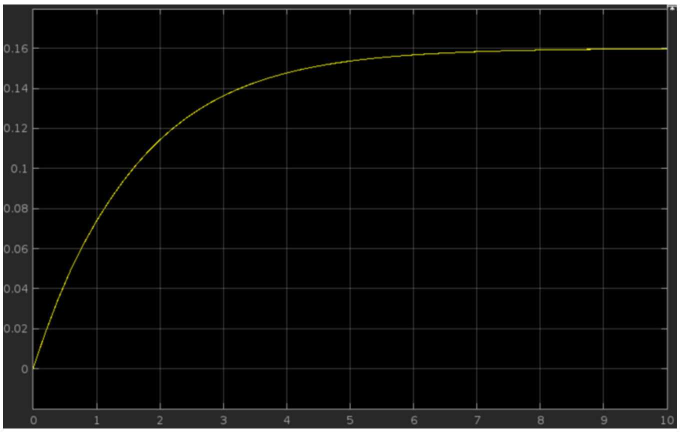
In a Diabetic subject,

$$\frac{di}{dt} = -0.63i + 0.01g + B(t)$$
$$\frac{dg}{dt} = -5i - 2.5g + A(t)$$

with $A(t)$ = 1 g/kg/h for t>1 and $B(t)$ = 0.1 U/kg/h for t>0



Glucose level



Insulin level

By comparing the two scenarios, Glucose level (at steady state) of a Diabetic subject is higher than that of a Normal subject while Insulin level (at steady state) is lower in a Diabetic subject compared to a Normal subject.

Rigg's model for Iodine metabolism

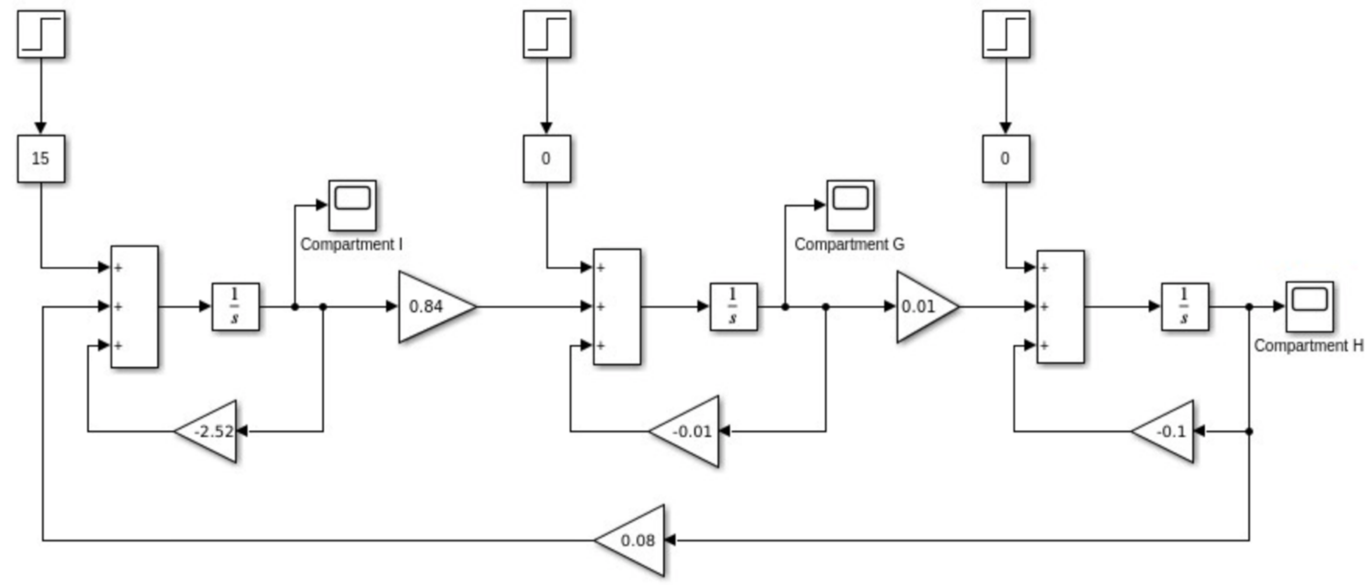
For low Iodine intake condition,

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

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

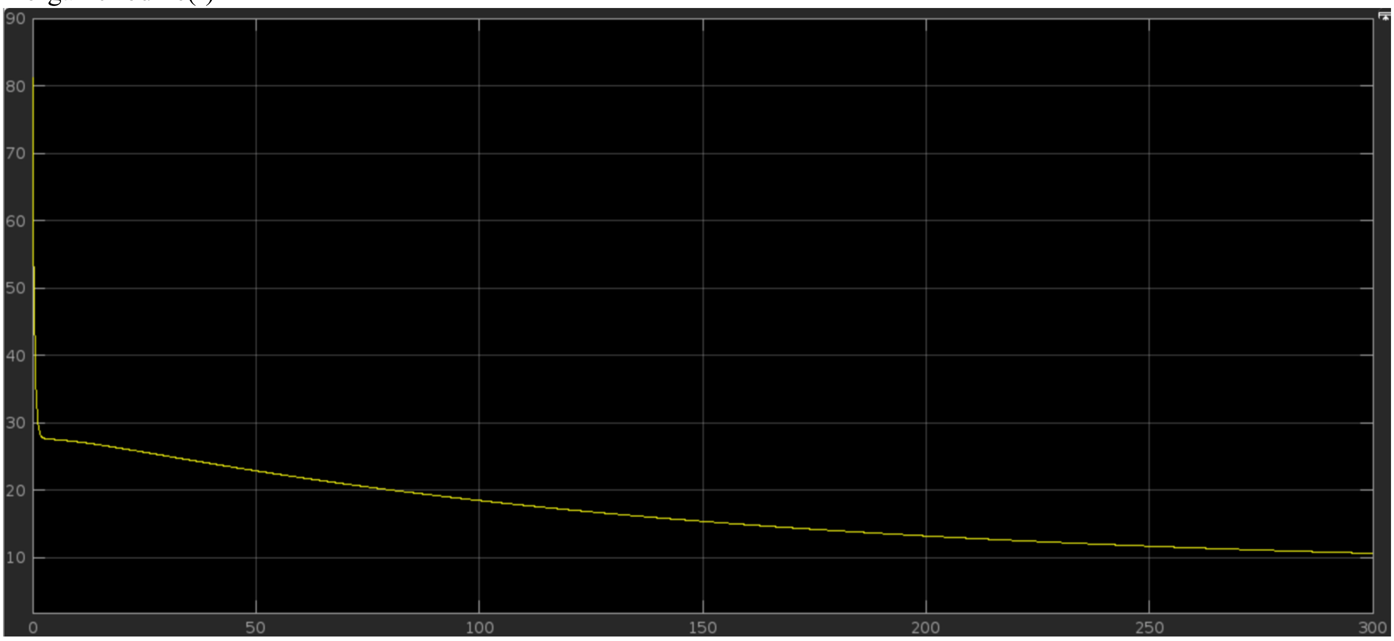
$$\frac{dH}{dt} = 0.01G - 0.1H$$

Simulink Diagram for Rigg's model for Iodine metabolism

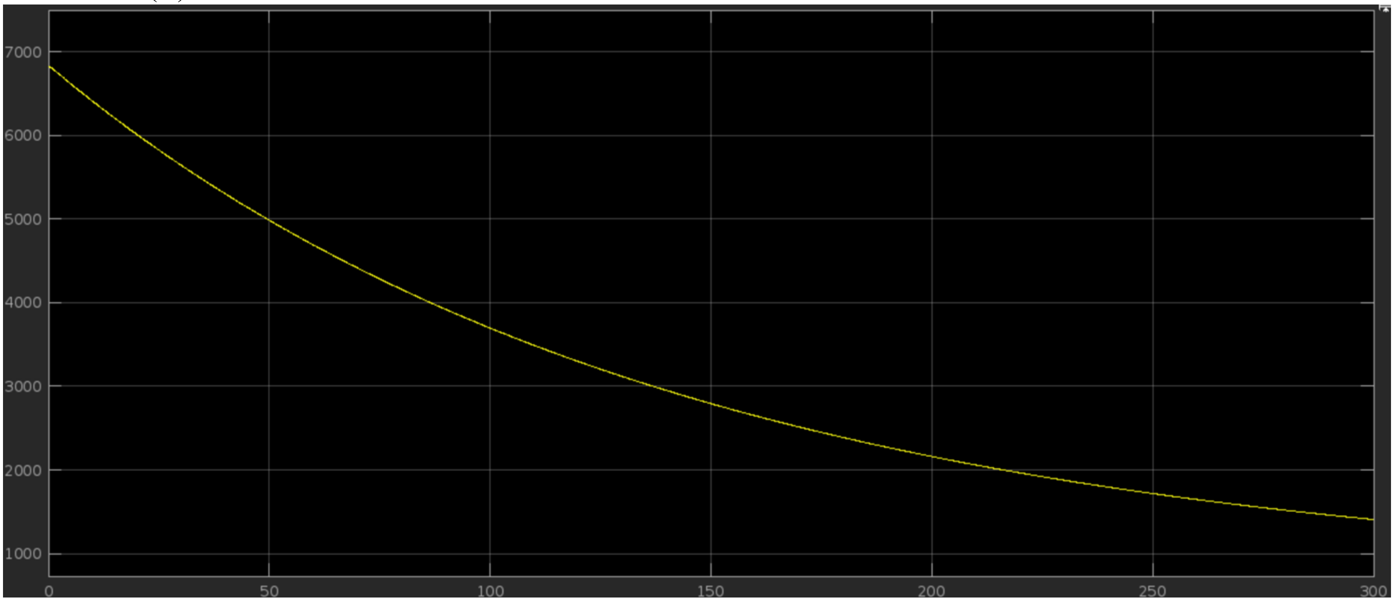


Simulink Results for Rigg's model for Iodine metabolism

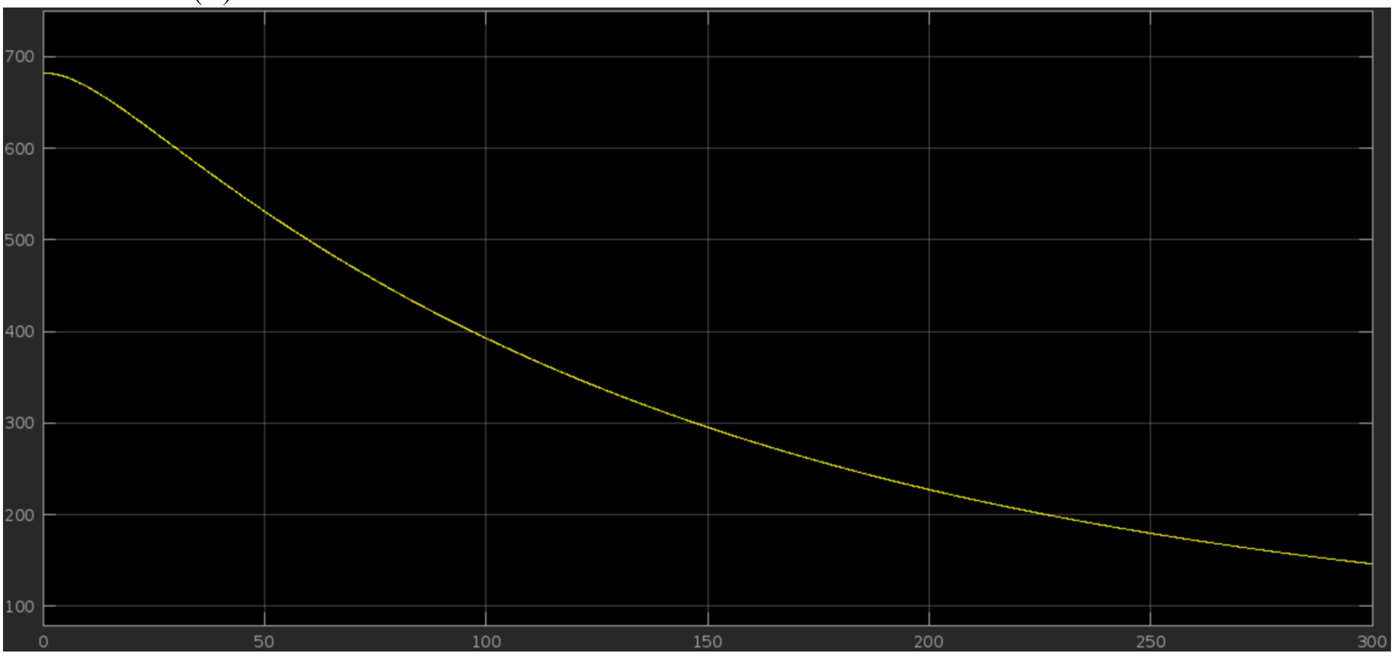
Inorganic Iodine(I)



Gland Iodine(G)



Hormonal Iodine(H)



The Simulink results obtained are similar to the plots obtained in Part (1).

Bolies' Plasma-Glucose model

$$\frac{di}{dt} = -k_1 i + k_3 g$$
$$\frac{dg}{dt} = -k_6 i - k_4 g + a.u(t)$$

Typical values,

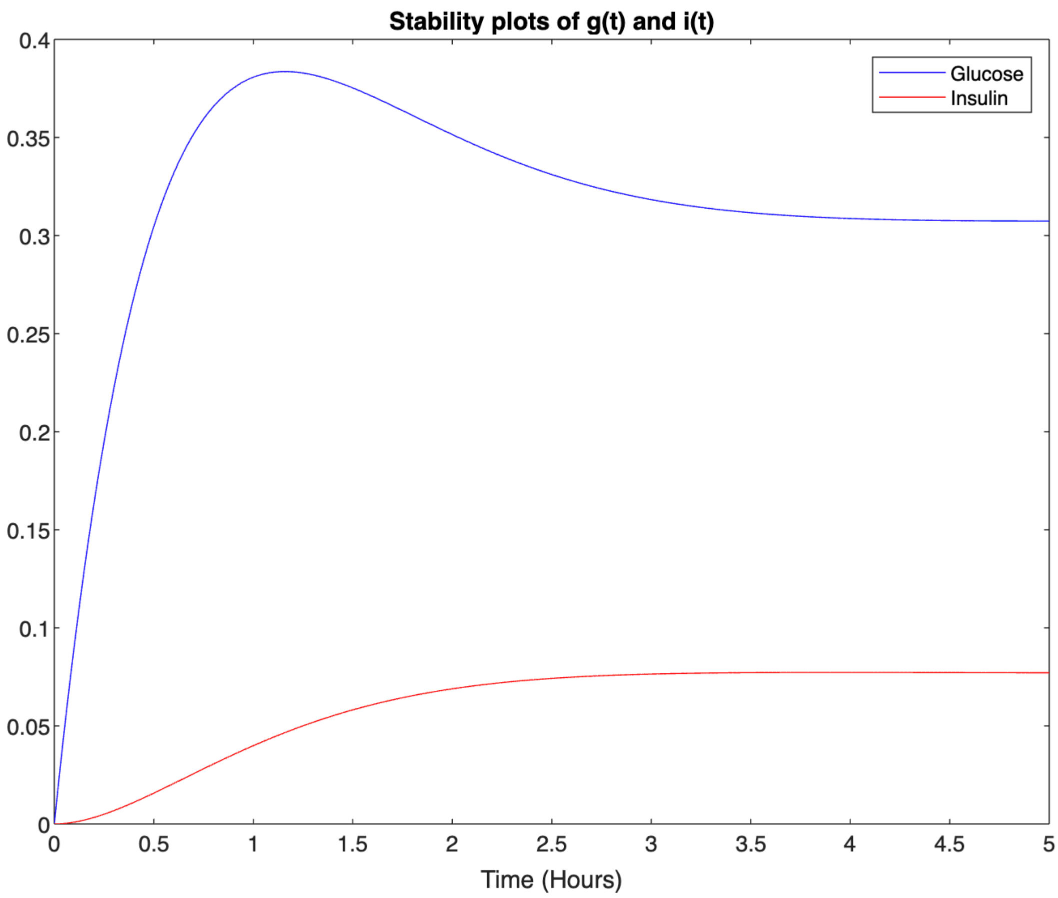
$k_1 = 0.8\, h^{-1}\,; k_3 = IUh^{-1}g^{-1}\,; k_4 = 2h^{-1}\,; k_6 = 5gh^{-1}IU^{-1}\,; a = 1gl^{-1}h^{-1}$

By solving the two differential equations,

$$g(t) = e^{-1.4t}\left(-\frac{4}{13}cos0.8t + \frac{37}{52}sin0.8t\right) + \frac{4}{13}$$

$$i(t) = e^{-1.4t}\left(-\frac{1}{13}cos0.8t - \frac{7}{52}sin0.8t\right) + \frac{1}{13}$$

Derivations are attached as appendix.



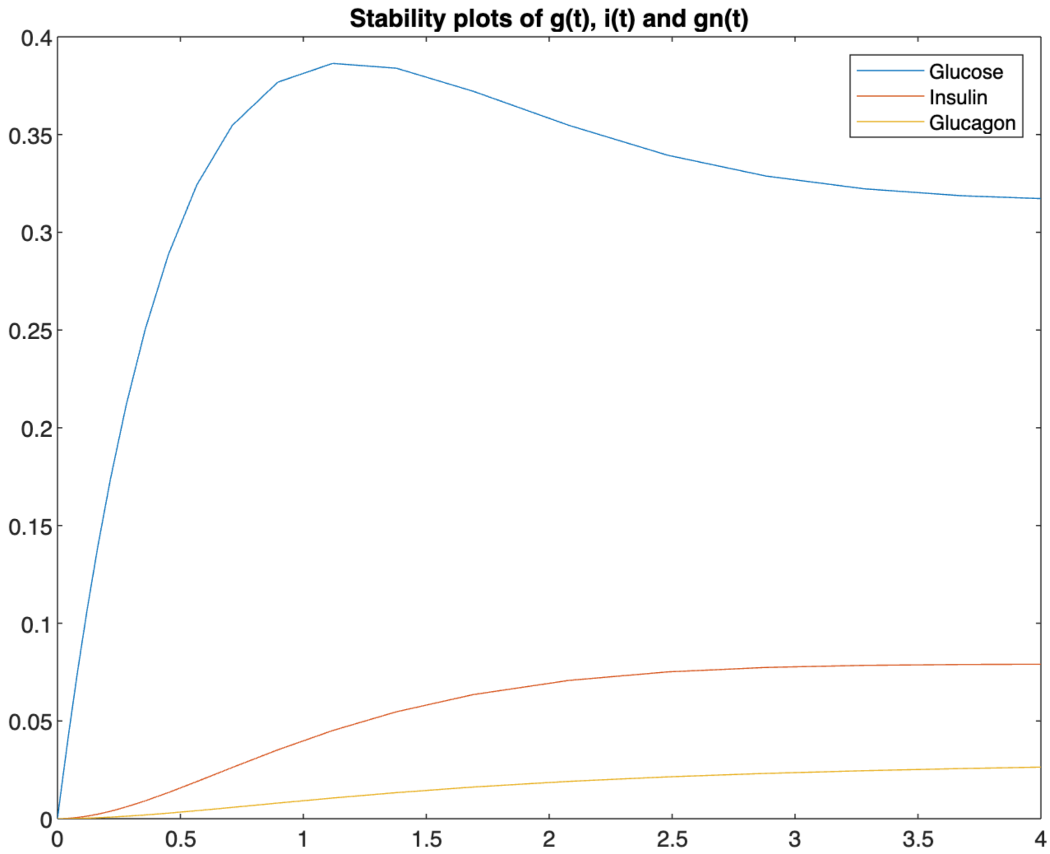
Expanding Bolies' Plasma-Glucose model including the effects of Glucagon

Insulin produced by the pancreatic beta cells, breakdown glucose into glycogen and stores it in the liver. Glucagon which does the opposite of this is produced by pancreatic alpha cells and it converts the glycogen stored in the liver, back into glucose.

The above Bolies' Plasma-Glucose model can be extended as follows.

```
function yp = extendedBolies(t,y);
%Typical values of the bolies' model
k1 = 0.8; k3 = 0.2; k4 = 2; k6 = 5; a = 1;
%Introduced variables for glucagon
k7 = 0.4; k9 = 0.04; k10 = 1;
yp = [-k4 -k6 k10; k3 -k1 0; k9 0 -k7] * y + [a 0 0]';
end
```

```
[t,y] = ode23('extendedBolies',[0 4],[0 0 0]);
plot(t,y)
title('Stability plots of g(t), i(t) and gn(t)');
legend ('Glucose','Insulin','Glucagon');
```



According to the graph, there is a sudden increment in the Glucose level due to the initial injection of glucose of $a = 1gl^{-1}h^{-1}$. Due to the response time delay taking for the pancreatic beta cells to identify the increase in plasma glucose level, the insulin level reaches its peak slightly later than the peak of glucose level.

When insulin reduces the glucose amount, the reduction is detected by the pancreatic alpha cells, producing glucagon to increase the plasma glucose level by breaking down the stored glycogen into glucose. Hence the steady state glucose level is slightly higher than the scenario when effect of glucagon was not considered (first case). Also, the glucagon and insulin levels also show increments over time compared to the first case.

Appendix

Derivations of Bolies' Plasma-Glucose Model

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

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

Typical values :

$k_1 = 0.8\, h^{-1}$

$k_3 = 0.2\ IU/h/g$

$k_4 = 2 h^{-1}$

$k_6 = 5\ g/h/IU$

$a = 1\ g/l/h$

Solution :

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

$$\frac{d^2 g}{dt^2} + (2.8)\frac{dg}{dt} + (1.6 + 1)\, g = 0.8 + \frac{du(t)}{dt}$$

$$\frac{d^2 g}{dt^2} + 2.8\frac{dg}{dt} + 2.6 g = 0.8 \qquad (t > 0)$$

Natural response,

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

$$r_1 = -1.4 + 0.8i$$

$$r_2 = -1.4 - 0.8i$$

$$g(t) = k_1 e^{(-1.4+0.8i)t} + k_2 e^{(-1.4-0.8i)t}$$

$$g(t) = e^{-1.4t}\{A \cos 0.8t + B \sin 0.8t\}$$

Forced response

$$g(t) = C$$

$$0 + 0 + 2.6C = 0.8$$

$$C = \frac{4}{13}$$

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

Assuming zero initial conditions

$$g(0) = 1 \quad (A + 0) + \frac{4}{13} = 0$$

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

$$\dot{g}(t) = -k_4 g(t) - k_6 i(t) + A(t)$$

$$\dot{g}(t) = -2g(t) - 5i(t) + 1$$

Assuming zero initial conditions,

$$\dot{g}(0^+) = 0 + 0 + 1$$

$$\dot{g}(0^+) = 1$$

$$\dot{g}(t) = e^{-1.4t}\{(-1.4A + 0.8B)\cos 0.8t + (-1.4B - 0.8A)\sin 0.8t\}$$

$$1 = 1\{-1.4A + 0.8B + 0\}$$

$$1 = -1.4\left(\frac{-4}{13}\right) + 0.8B$$

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

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

$$\dot{g}(t) = -2g(t) - 5i(t) + 1$$

$$e^{-1.4t}\left\{\cos 0.8t - \frac{39}{52}\sin 0.8t\right\} = e^{-1.4t}\left\{\frac{8}{13}\cos 0.8t - \frac{74}{52}\sin 0.8t\right\} - \frac{8}{13} - 5i(t) + 1$$

$$5\,i(t) = e^{-1.4t}\left\{\frac{-5}{13}\cos 0.8t - \frac{35}{52}\sin 0.8t\right\} + \frac{5}{13}$$

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