Use of Matlab to investigate compartmental systems

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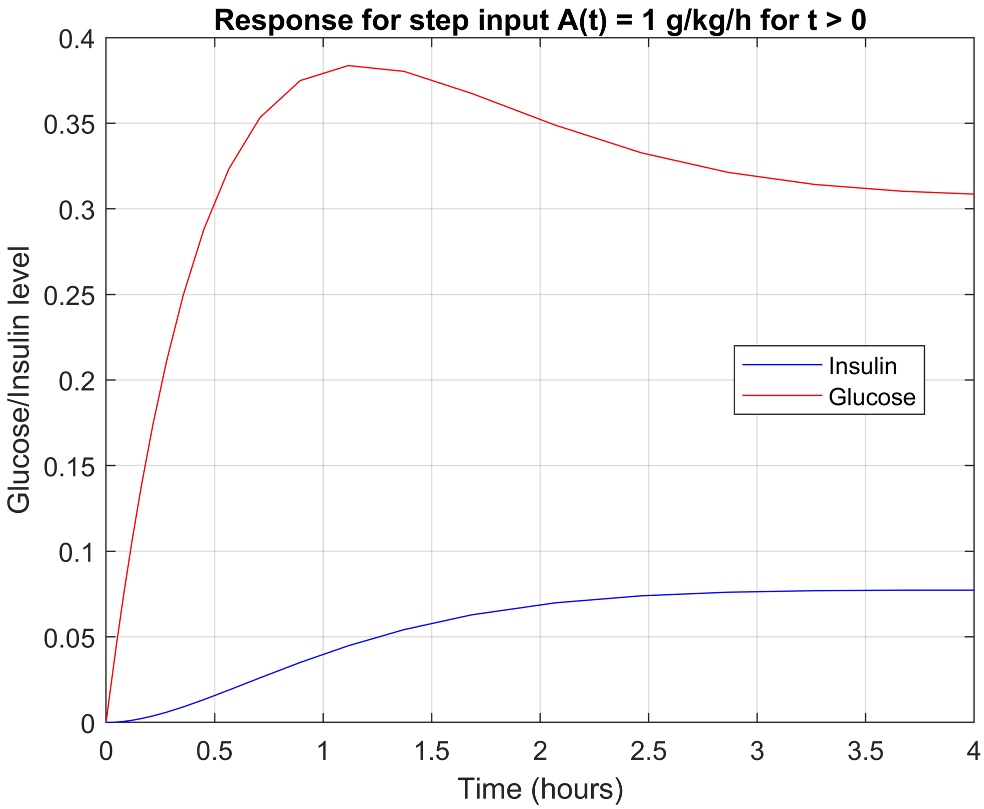
Part 01

Question 01

Response for step input

```
function dydt = Unit_Step(t, y)

A = 1;  % Step input magnitude

dydt = [-0.8, 0.2; -5, -2] * y + [0; 1] * A;

end
```

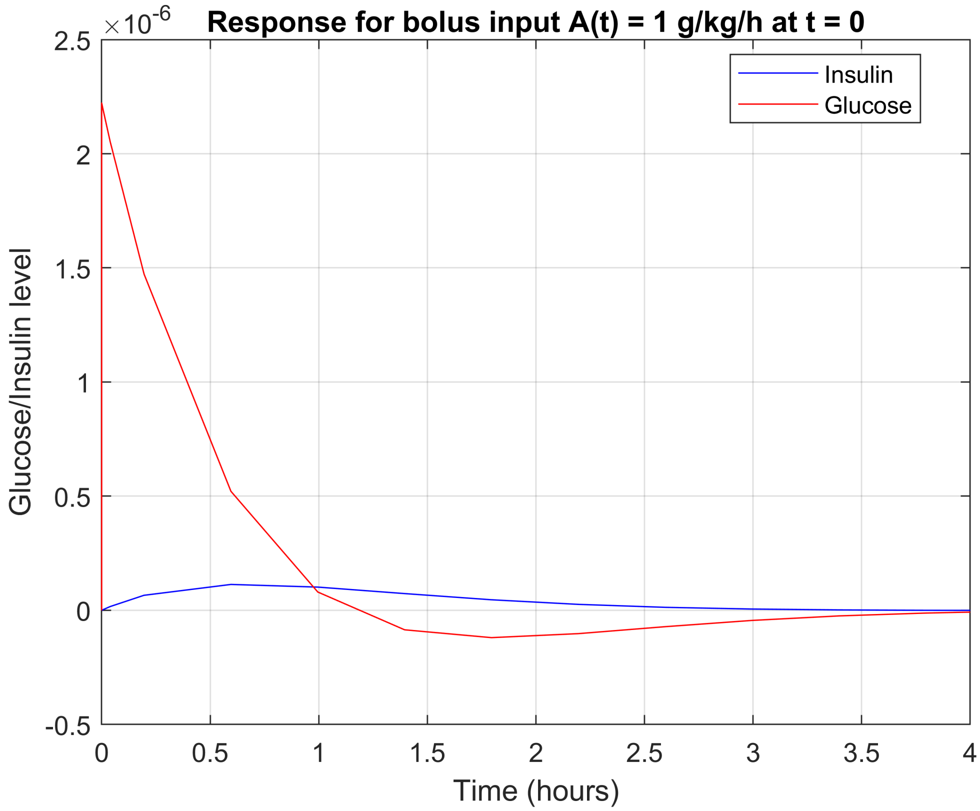
```
% Solve the ODEs for step input
[t, y] = ode23(@Unit_Step, [0, 4], [0, 0]);

% Plot the results for step input
figure;
plot(t, y(:,1), '-b', 'DisplayName', 'Insulin'); % Insulin levels (y(:,1))
hold on;
plot(t, y(:,2), '-r', 'DisplayName', 'Glucose'); % Glucose levels (y(:,2))
legend('Insulin', 'Glucose', 'Location', 'best');
xlabel('Time (hours)');
ylabel('Glucose/Insulin level');
title('Response for step input A(t) = 1 g/kg/h for t > 0');
grid on;
```



Response for bolus input

```
function dydt = Bolus_Input(t, y)

A = 1;  % Magnitude of the bolus input

dydt = [-0.8, 0.2; -5, -2] * y + [0; 1] * (t == 0) * A;

end
```

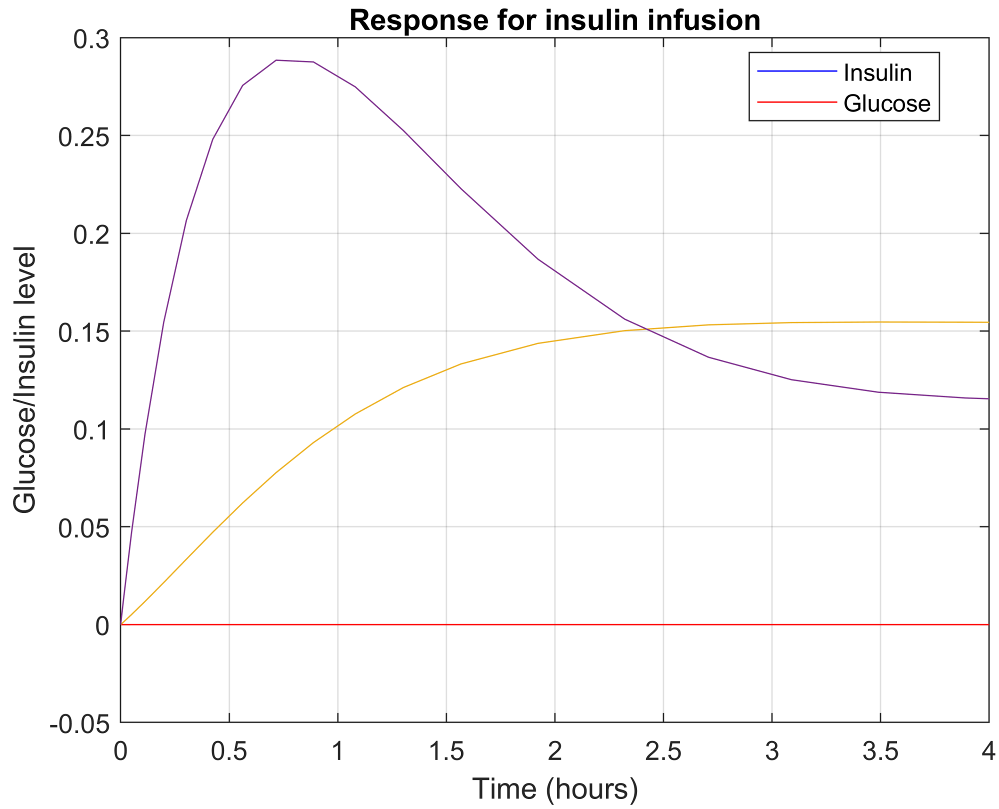
```
% Solve the ODEs for bolus input
[t, y] = ode23(@Bolus_Input, [0, 4], [0, 0]);

% Plot the results for bolus input
figure;
plot(t, y(:,1), '-b', 'DisplayName', 'Insulin'); % Insulin levels (y(:,1))
hold on;
plot(t, y(:,2), '-r', 'DisplayName', 'Glucose'); % Glucose levels (y(:,2))
legend('Insulin', 'Glucose', 'Location', 'best');
xlabel('Time (hours)');
ylabel('Glucose/Insulin level');
title('Response for bolus input A(t) = 1 g/kg/h at t = 0');
grid on;
```



Simulating a diabetic subject with insulin infusion

```
function dydt = insuline_infused_patient(t, y)

A = 1;  % Magnitude of the bolus input

dydt = [-0.8, 0.2; -5, -2] * y + [0.1; 1];

end
```

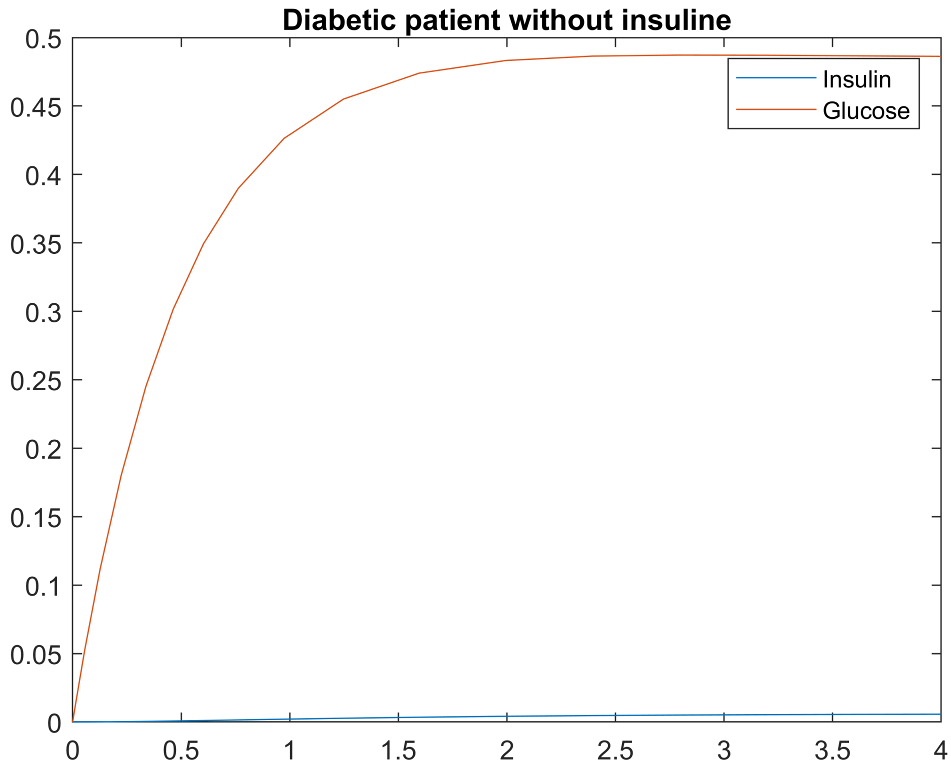
```
[t,y]=ode23(@insuline_infused_patient,[0 4],[0 0]);
plot(t,y);
title('Response for insulin infusion');
legend('Insulin','Glucose');
```



Simulating a diabetic subject without insulin infusion

```
function dydt = diabetic(t, y)

A = 1;  % Magnitude of the bolus input

dydt = [-0.8, 0.01; -5, -2] * y + [0; 1] * A;

end
```

```
[t,y] = ode23( @diabetic, [0, 4], [0, 0]);
plot(t,y);
legend('Insulin','Glucose');
title ('Diabetic patient without insuline');
```

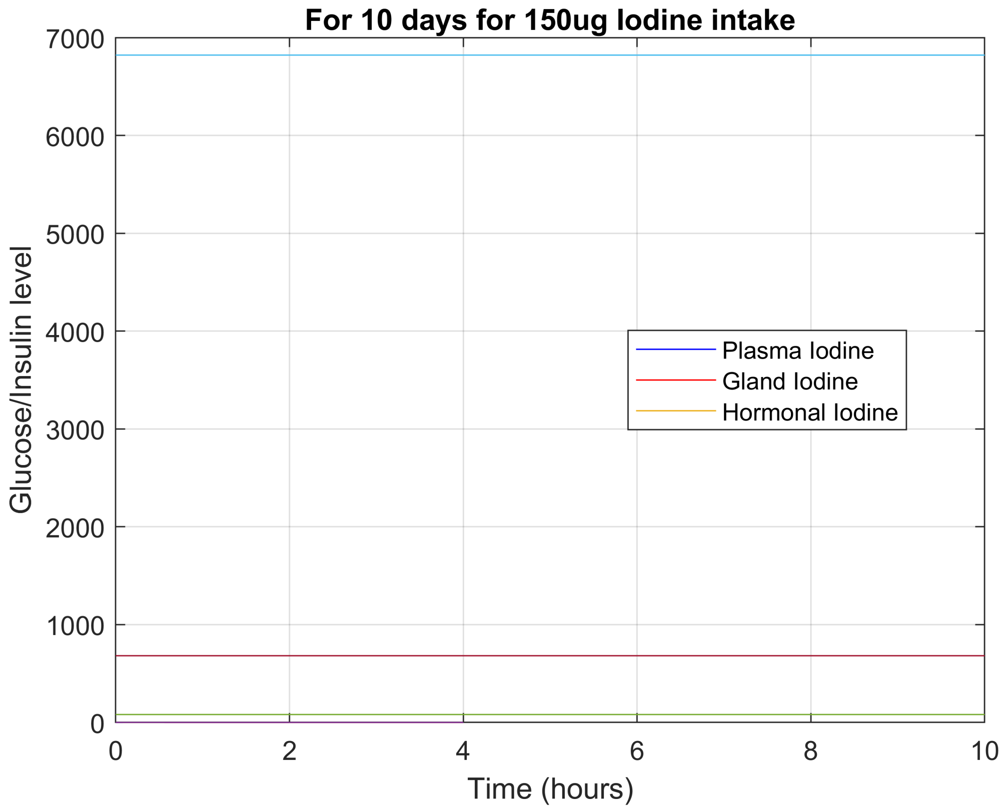


Question 02

Iodine intake 150 μg/day for 10 days

```
function dydt = Riggs_Iodine(t, y)

A = [-2.52, 0, 0.08; 0.84, -0.01, 0; 0, 0.01, -0.1];

B = [150; 0; 0];

dydt = A * y + B;

end
```

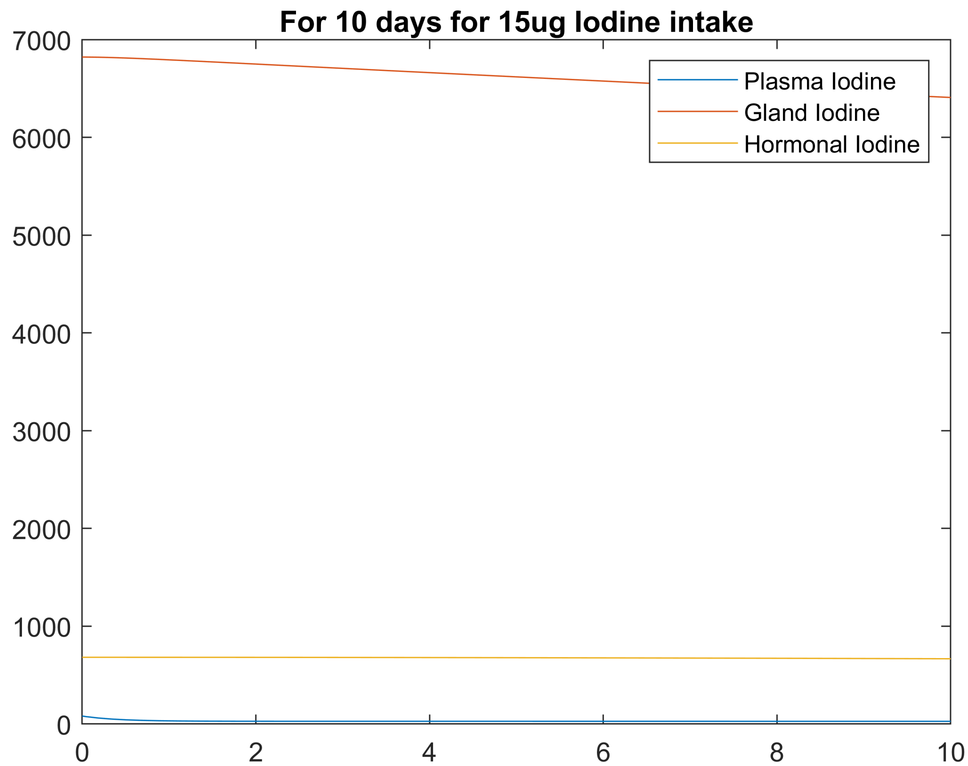
```
[t,y] = ode23(@Riggs_Iodine,[0 10],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('For 10 days for 150ug Iodine intake');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



Iodine intake 15 µg/day for 10 days

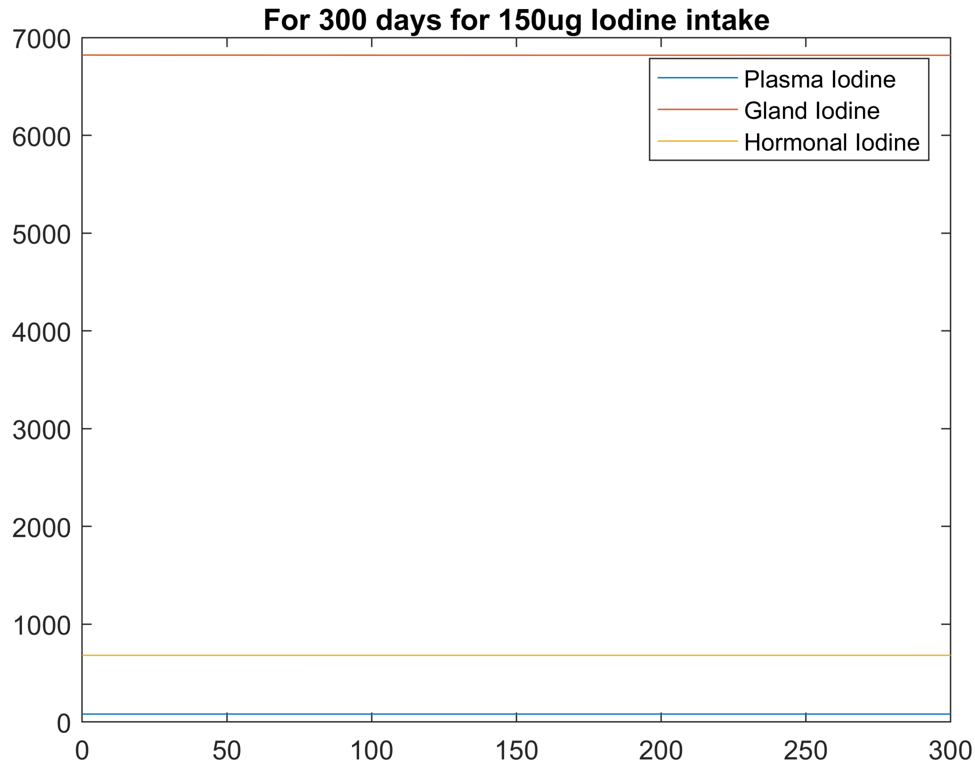
```
function dydt = Riggs_Iodine_15(t, y)

A = [-2.52, 0, 0.08; 0.84, -0.01, 0; 0, 0.01, -0.1];

B = [15; 0; 0];

dydt = A * y + B;

end
```

```
clf;
[t,y] = ode23(@Riggs_Iodine_15,[0 10],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('For 10 days for 15ug Iodine intake');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



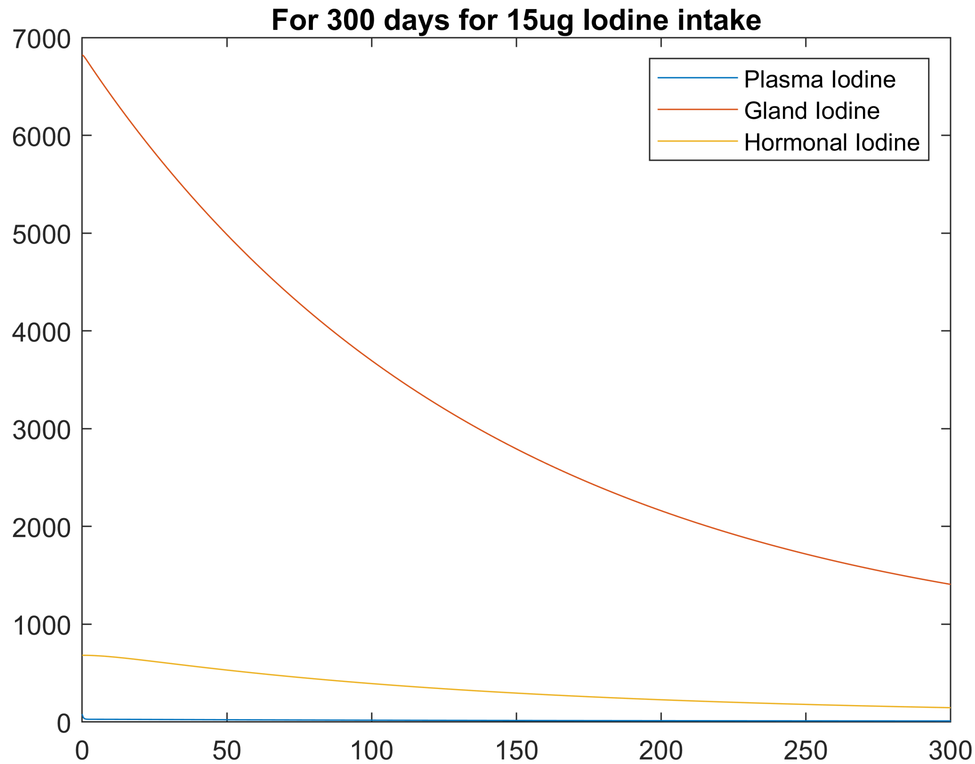
Iodine intake 150 μg/day for 300 days

```
[t,y] = ode23(@Riggs_Iodine,[0 300],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('For 300 days for 150ug Iodine intake');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



Iodine intake 15 μg/day for 300 days

```
clf;
[t,y] = ode23(@Riggs_Iodine_15,[0 300],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('For 300 days for 15ug Iodine intake');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



Part a

In this disease, the cells responsible for producing thyroid hormones gradually die, leading to a decline in hormone production despite normal iodine intake. This condition can be modeled using the Riggs model by reducing the k2 parameter. In the simulation, the k2 value was decreased from 0.01 to 0.005. The k2 parameter represents the rate of thyroid hormone degradation. By lowering the k2 value, the degradation of thyroid hormone is slowed down, allowing more hormone to remain available in the body, even as the hormone-producing cells deteriorate.

function dydt = Riggs_Iodine_a(t, y)

A = [-2.52, 0, 0.08; 0.84, -0.005, 0; 0, 0.005, -0.1];

B = [15; 0; 0];

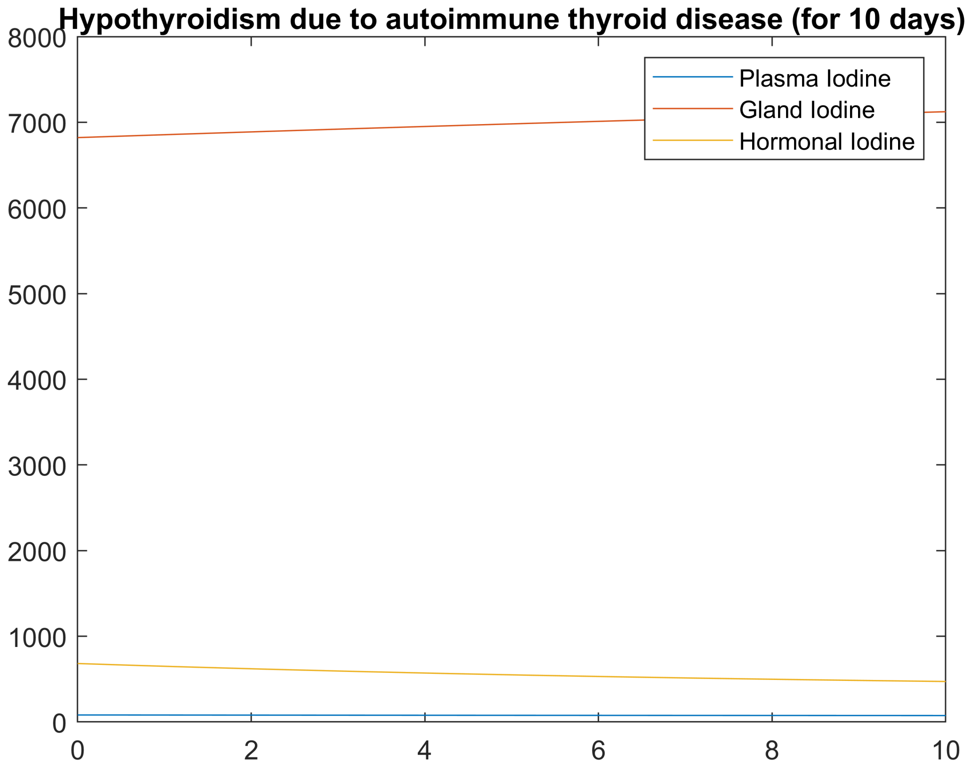
dydt = A * y + B;

end

<u>Hypothyroidism due to autoimmune thyroid disease (for 10 days)</u>

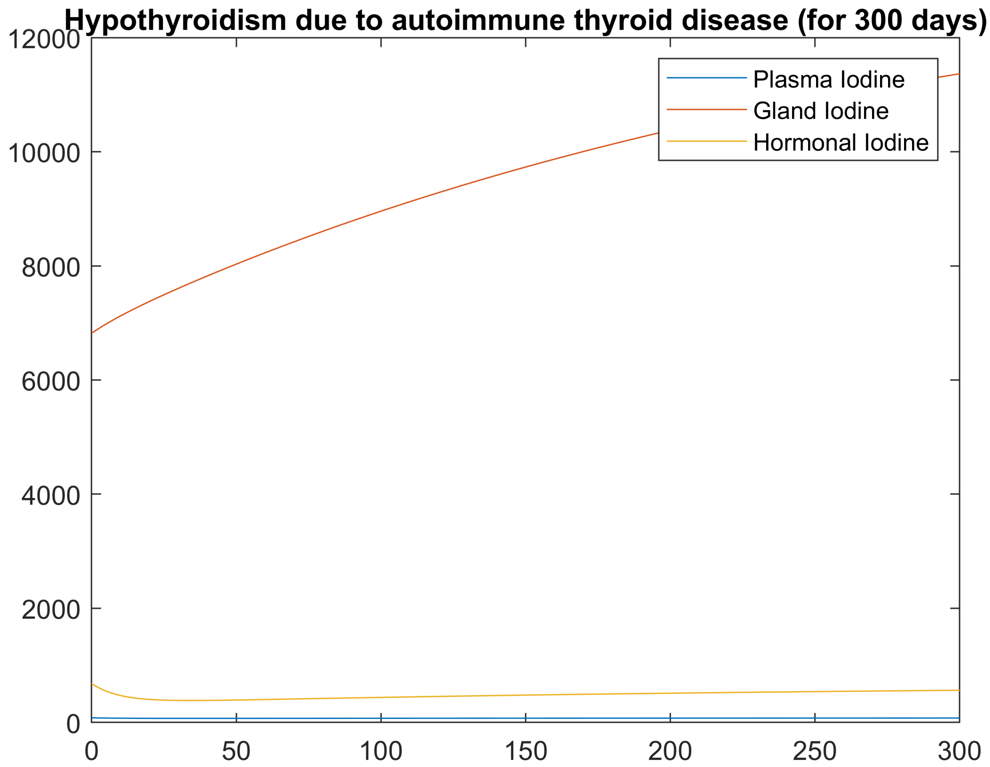
```
[t,y] = ode23(@Riggs_Iodine_a,[0 10],[81.2 6821 682]);
plot(t,y);
```

```
ylim([0 8000]);
title('Hypothyroidism due to autoimmune thyroid disease (for 10 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



Hypothyroidism due to autoimmune thyroid disease (for 300 days)

```
[t,y] = ode23(@Riggs_Iodine_a,[0 300],[81.2 6821 682]);
plot(t,y);
ylim([0 12000]);
title('Hypothyroidism due to autoimmune thyroid disease (for 300 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



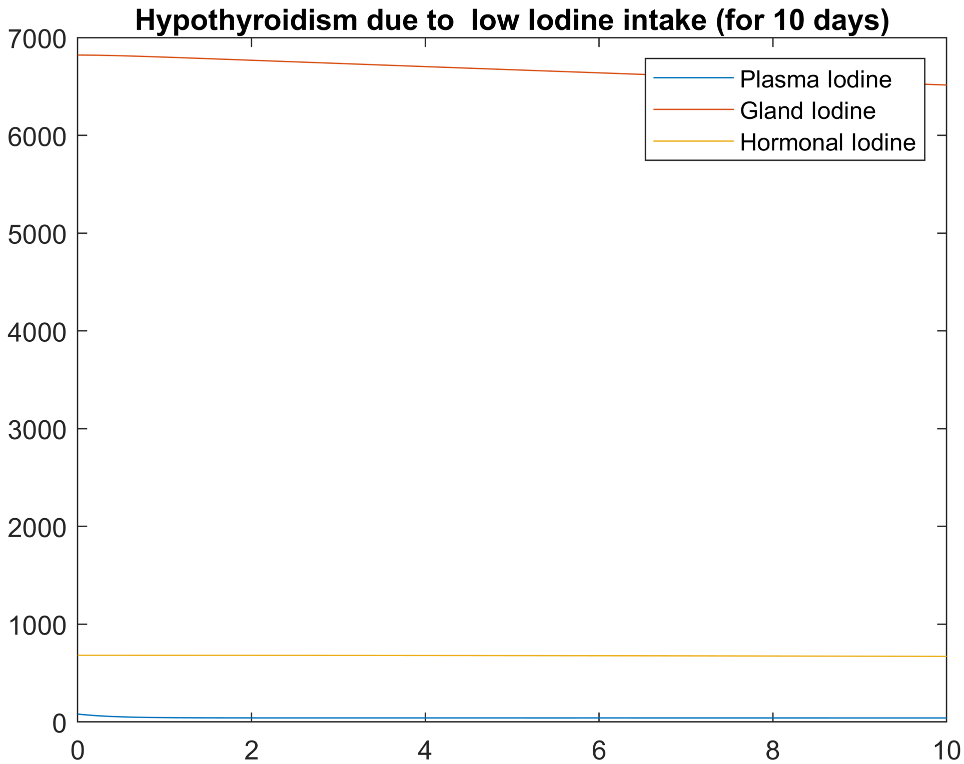
Part b

This disease, caused by iodine deficiency in the diet, can be modeled using the Riggs model by decreasing the input B1(t). In the simulation, the value of B1(t) was reduced from 150 to 50, representing a significant drop in iodine intake.

```
function dydt = Riggs_Iodine_b(t, y)

A = [-2.52, 0, 0.08; 0.84, -0.01, 0; 0, 0.01, -0.1];

B = [50; 0; 0];

dydt = A * y + B;

end
```

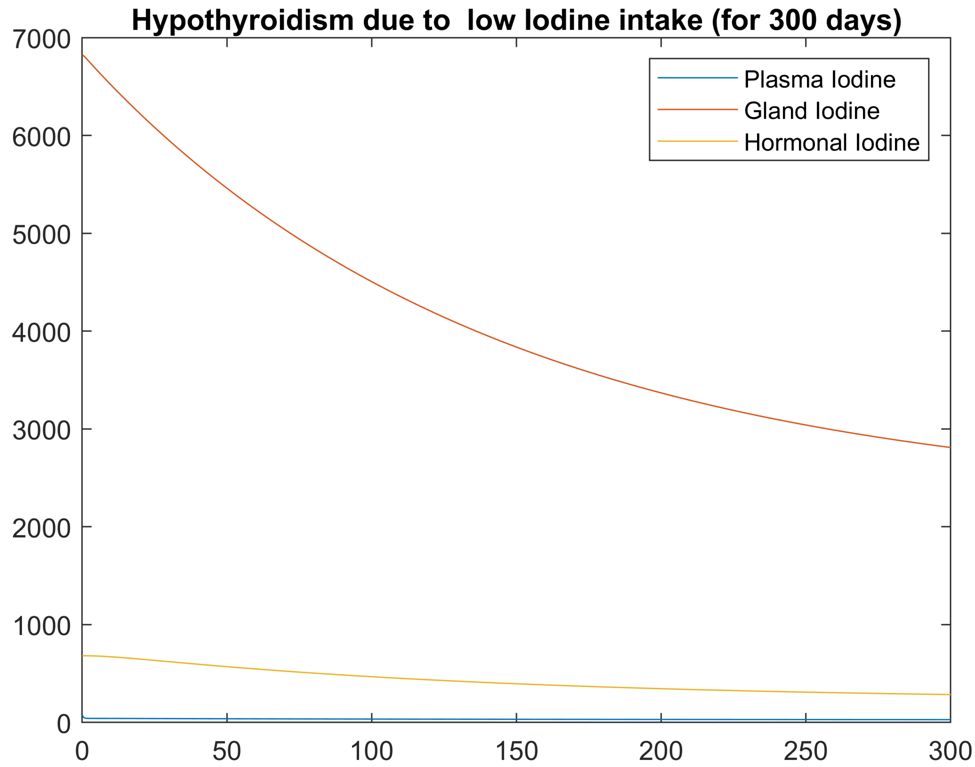
<u>Hypothyroidism due to low Iodine intake (for 10 days)</u>

```
[t,y] = ode23(@Riggs_Iodine_b,[0 10],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('Hypothyroidism due to  low Iodine intake (for 10 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



Hypothyroidism due to low Iodine intake (for 300 days)

```
[t,y] = ode23(@Riggs_Iodine_b,[0 300],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('Hypothyroidism due to  low Iodine intake (for 300 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



Part c

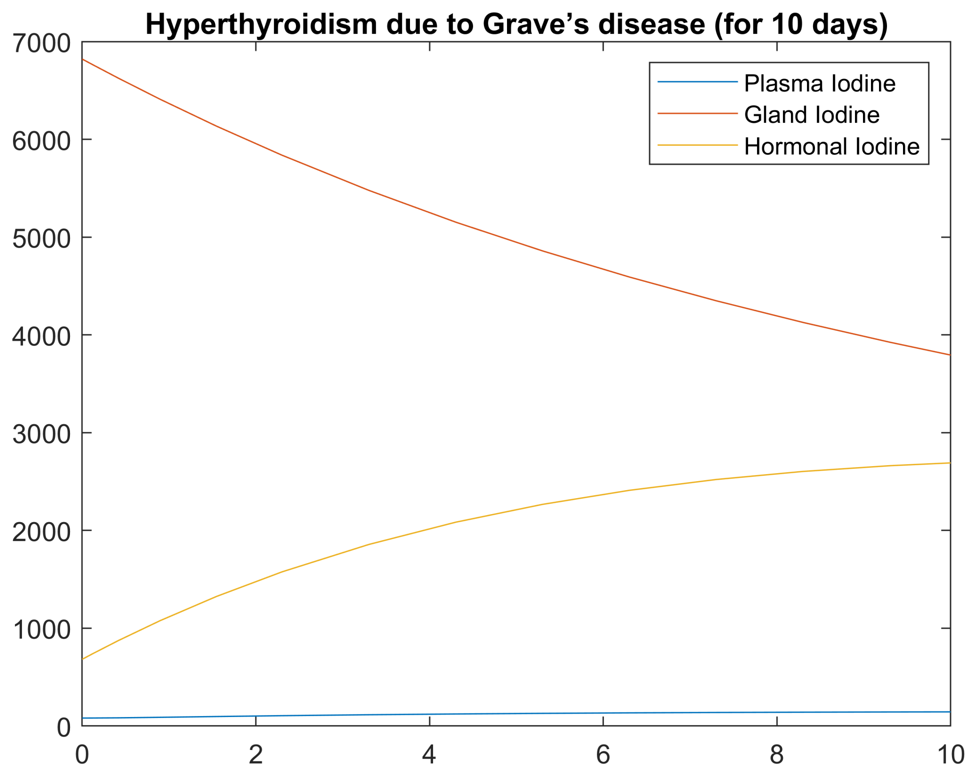
Graves' disease is a condition where the thyroid gland produces an excessive amount of thyroid hormone, leading to symptoms such as weight loss, rapid heart rate, and irregular heartbeat. The Riggs model can be utilized to simulate the effects of Graves' disease. In this simulation, the k2 parameter was increased from 0.01 to 0.08, representing an accelerated rate of thyroid hormone degradation. This adjustment results in a reduced availability of thyroid hormone in the body, which can help mitigate the symptoms associated with Graves' disease.

```
function dydt = Riggs_Iodine_c(t, y)

A = [-2.52, 0, 0.08; 0.84, -0.08, 0; 0, 0.08, -0.1];

B = [150; 0; 0];

dydt = A * y + B;

end
```

<u>Hyperthyroidism due to Grave's disease (for 10 days)</u>

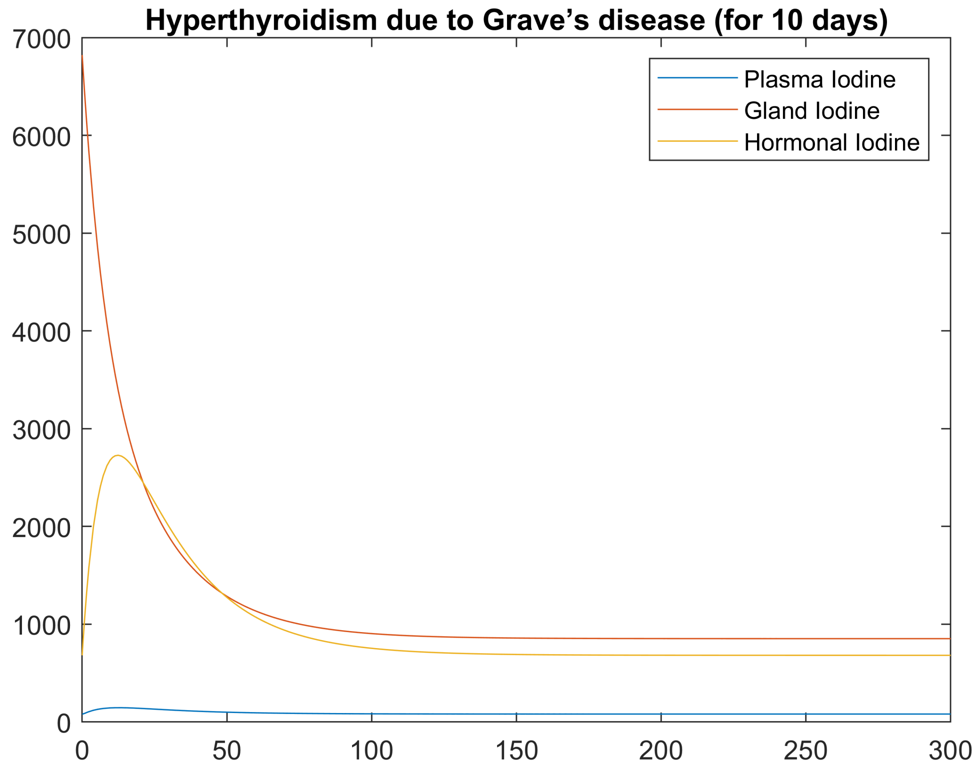
```
[t,y] = ode23(@Riggs_Iodine_c,[0 10],[81.2 6821 682]);
plot(t,y);
```

```
ylim([0 7000]);
title('Hyperthyroidism due to Grave's disease (for 10 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



<u>Hyperthyroidism due to Grave's disease (for 300 days)</u>

```
[t,y] = ode23(@Riggs_Iodine_c,[0 300],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('Hyperthyroidism due to Grave's disease (for 300 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



Part d

Common Causes of Goitre and Tumors

Goitre is an enlargement of the thyroid gland and can be classified into several types based on its etiology:

- Iodine Deficiency: This is the most common cause of goitre globally, leading to an increase in thyroid-stimulating hormone (TSH) due to low levels of thyroid hormones (T3 and T4). In iodine-deficient regions, the prevalence of goitre can be high.
- Autoimmune Disorders: Conditions like Graves' disease and Hashimoto's thyroiditis can lead to goitre formation. In Graves' disease, the thyroid is overstimulated, while in Hashimoto's, it may become inflamed and enlarged due to autoimmune attack.
- Nodular Growths: The presence of nodules within the thyroid can lead to a nodular goitre. These nodules can be benign (such as adenomas) or malignant (thyroid cancer).
- Goitrogens: Certain foods and substances (like soy and cruciferous vegetables) can inhibit thyroid hormone production, contributing to goitre development, especially in individuals with low iodine intake.

Tumors in the thyroid can be benign (adenomas) or malignant (thyroid carcinoma). The risk factors for thyroid tumors include:

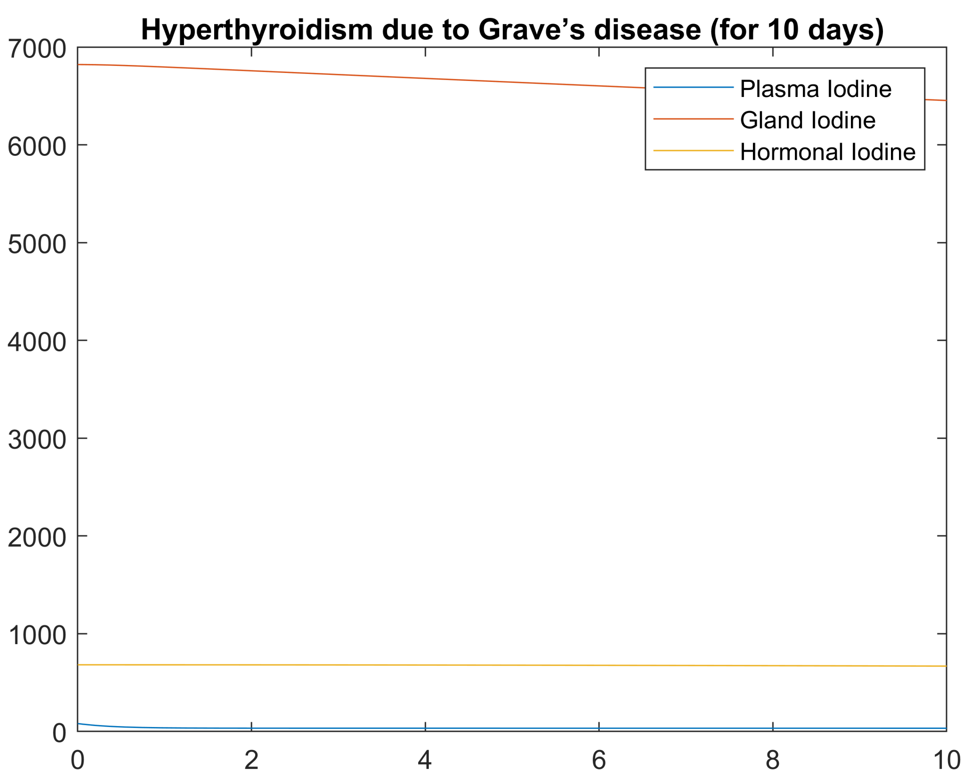
- Family History: Genetic predisposition can increase the risk of developing thyroid cancer.

- Radiation Exposure: Previous exposure to radiation, particularly in childhood, is a known risk factor for thyroid cancer.
- Age and Gender: Thyroid cancer is more common in women and typically occurs in individuals over 40.

<u>Goitre</u>

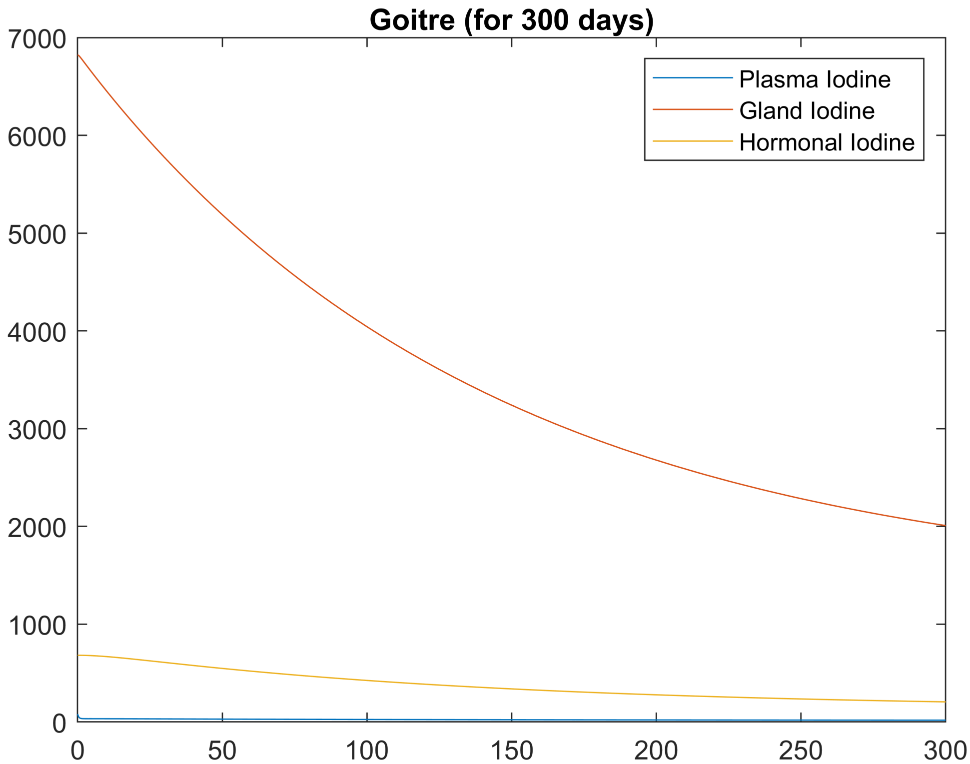
```
function dydt = Riggs_Iodine_d_Goitre(t, y)

A = [-2.52, 0, 0.08; 0.84, -0.01, 0; 0, 0.01, -0.1];

B = [30; 0; 0];

dydt = A * y + B;

end
```

```
[t,y] = ode23(@Riggs_Iodine_d_Goitre,[0 10],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('Goitre (for 10 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```




```
[t,y] = ode23(@Riggs_Iodine_d,[0 300],[81.2 6821 682]);
```

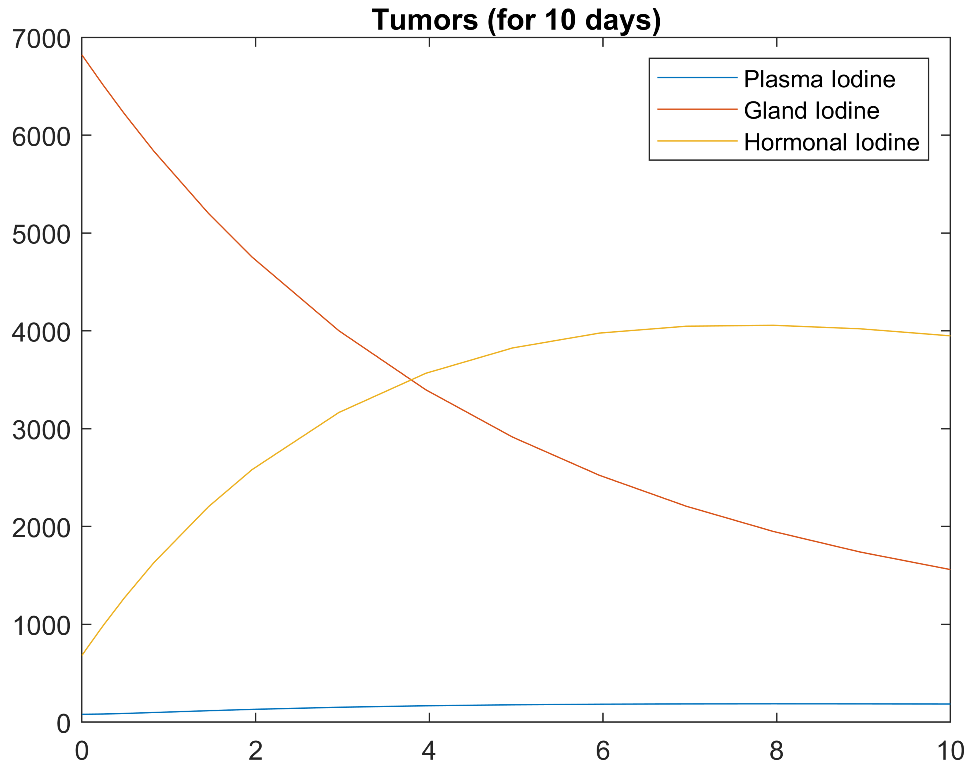
```
plot(t,y);
ylim([0 7000]);
title('Goitre (for 300 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



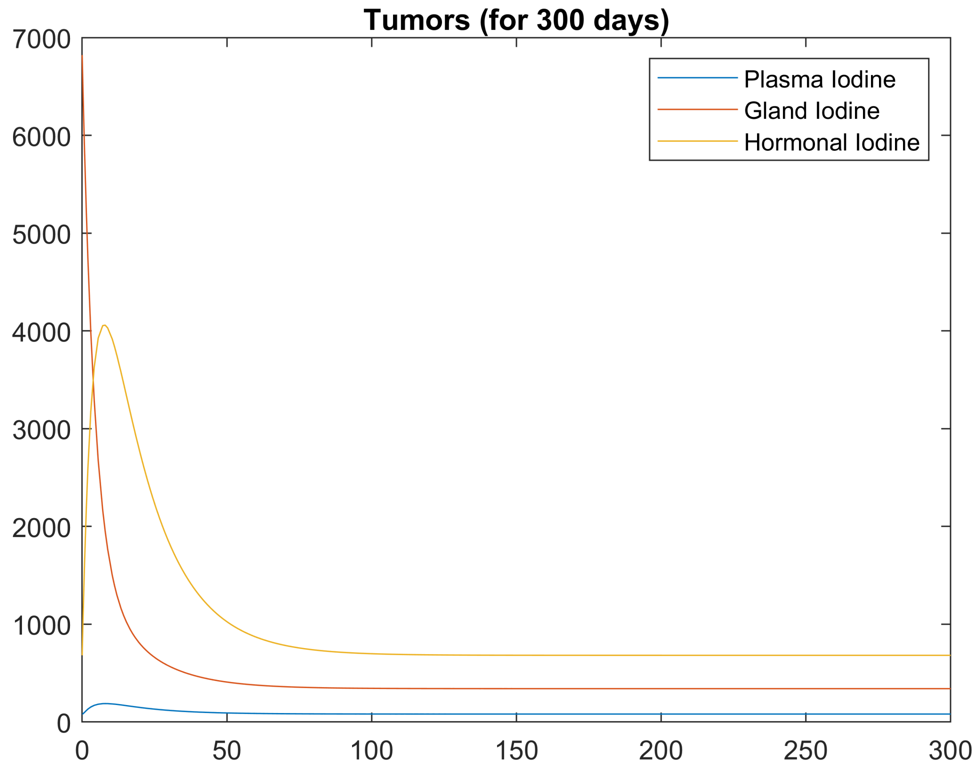
Tumors

```
function dydt = Riggs_Iodine_tumor(t, y)

A = [-2.52, 0, 0.08; 0.84, -0.2, 0; 0, 0.2, -0.1];

B = [150; 0; 0];

dydt = A * y + B;

end
```

```
[t,y] = ode23(@Riggs_Iodine_tumor,[0 10],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('Tumors (for 10 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```



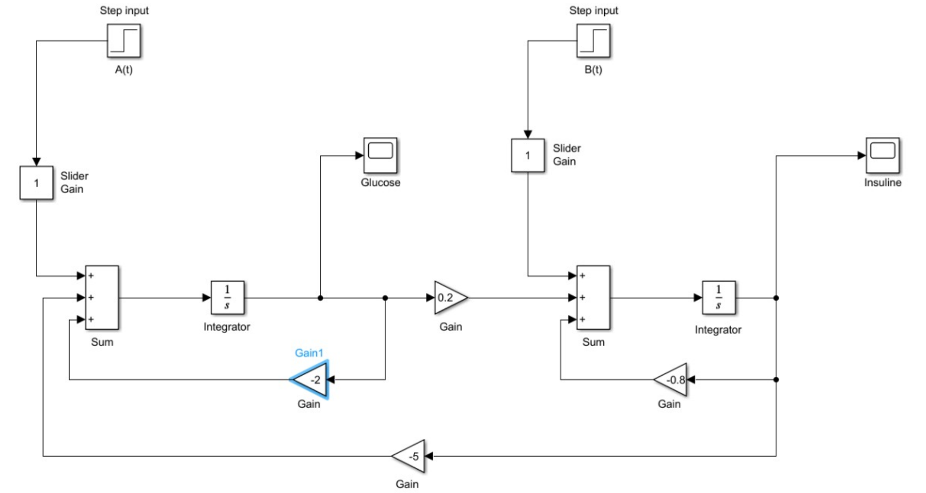

```
[t,y] = ode23(@Riggs_Iodine_tumor,[0 300],[81.2 6821 682]);
plot(t,y);
ylim([0 7000]);
title('Tumors (for 300 days)');
legend ('Plasma Iodine','Gland Iodine','Hormonal Iodine');
```

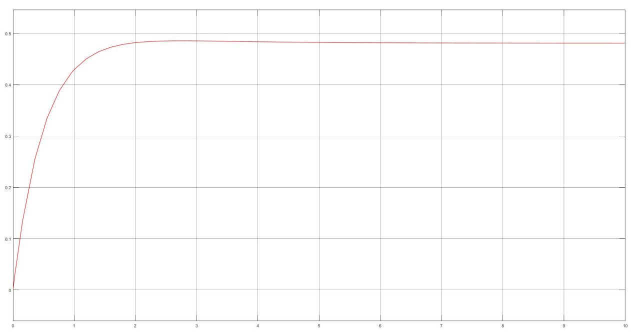

Tumors (for 300 days)
Plasma Iodine
Gland Iodine
Hormonal Iodine
7000
6000
5000
4000
3000
2000
1000
0
0
50
100
150
200
250
300

Part 2

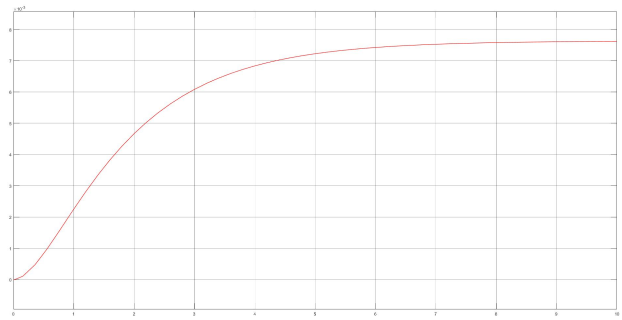
Model 1

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





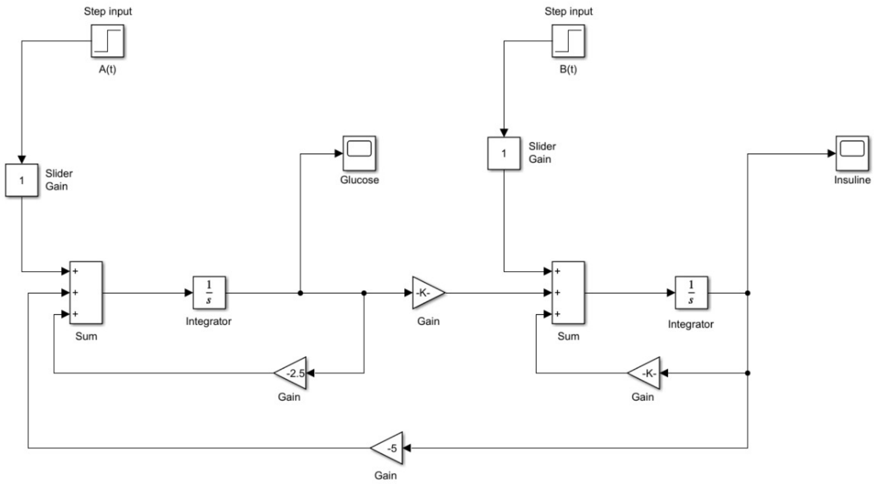
(a) Glucose

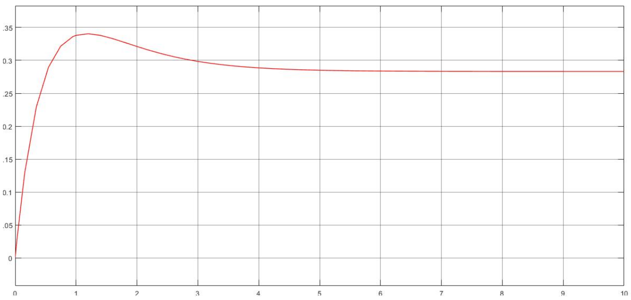


(b) Insuline

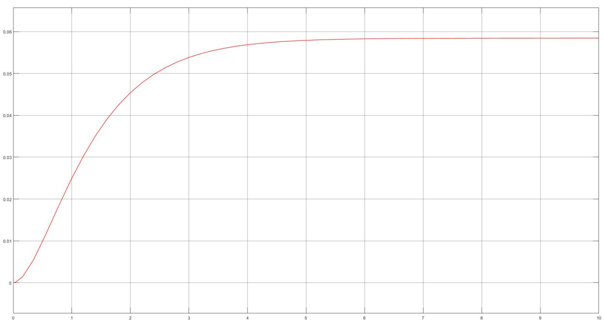
Model 2

$$\frac{di}{dt} = -0.63i + 0.13g$$
$$\frac{dg}{dt} = 5i - 2.59g + A(t)$$





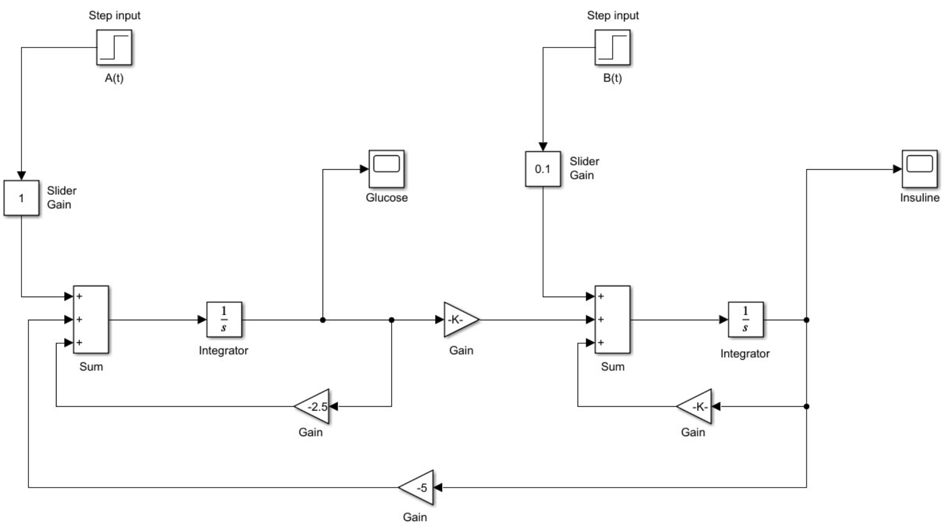
(a) Glucose

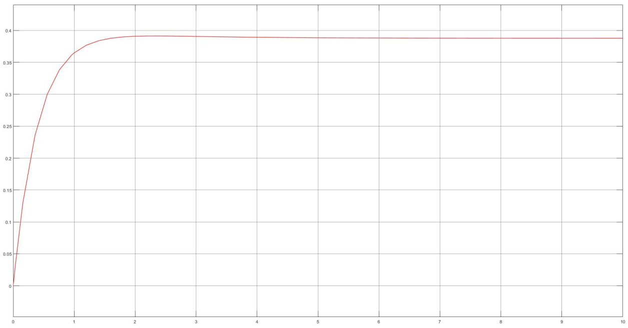


(b) Insuline

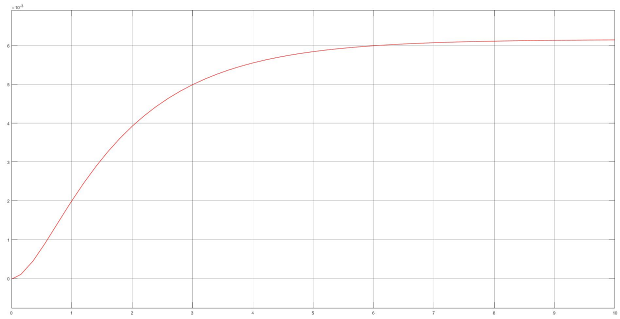
$$B(t) = 0.1\,\mu\text{g/kg/h}$$

Normal Patient



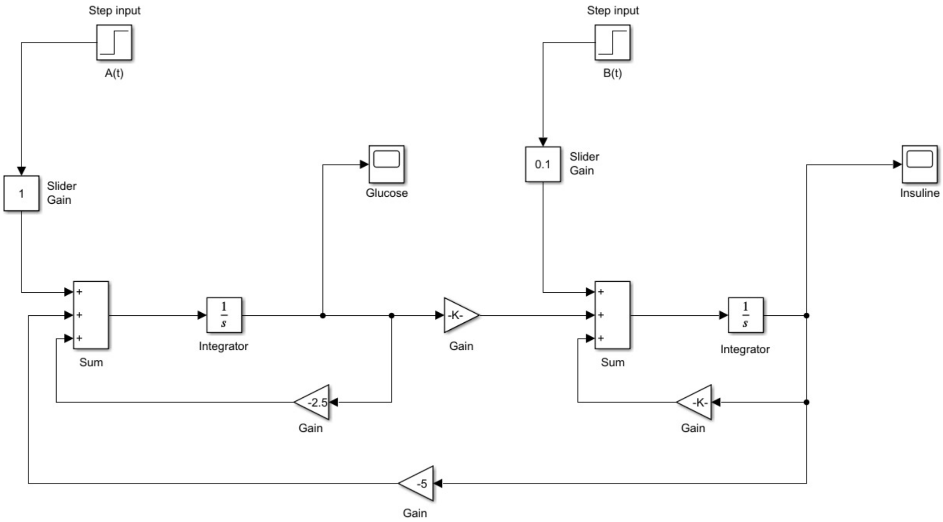


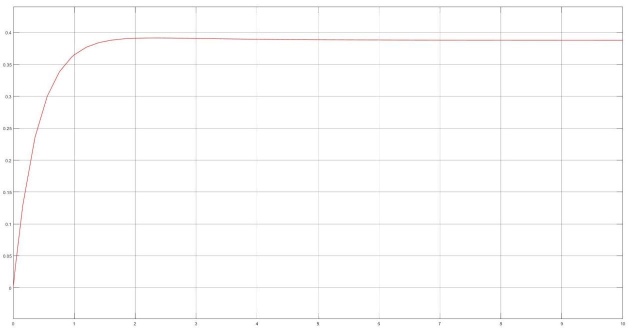
(a) Glucose



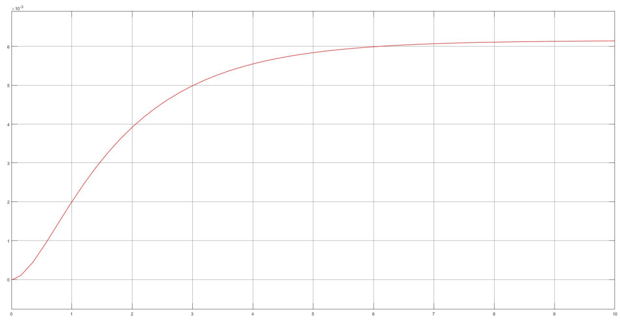
(b) Insuline

Diabetic Patient



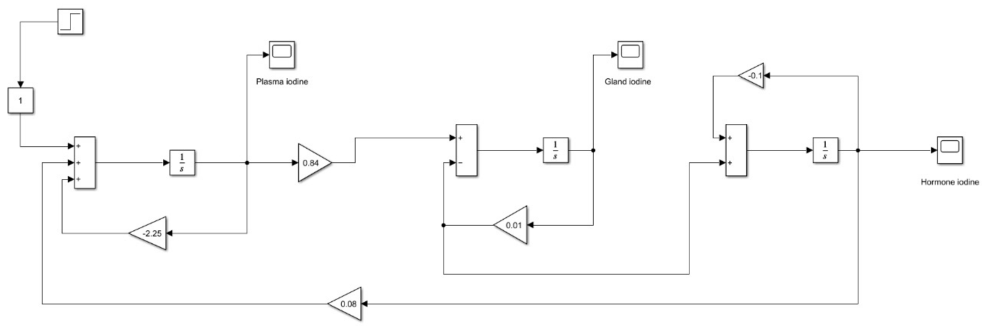


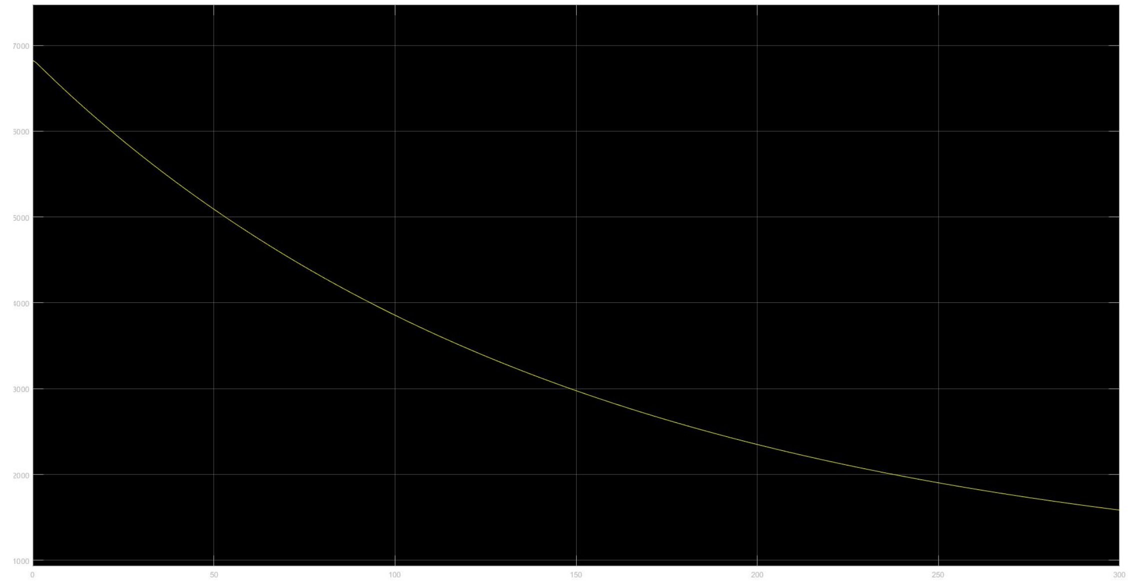
(a) Glucose



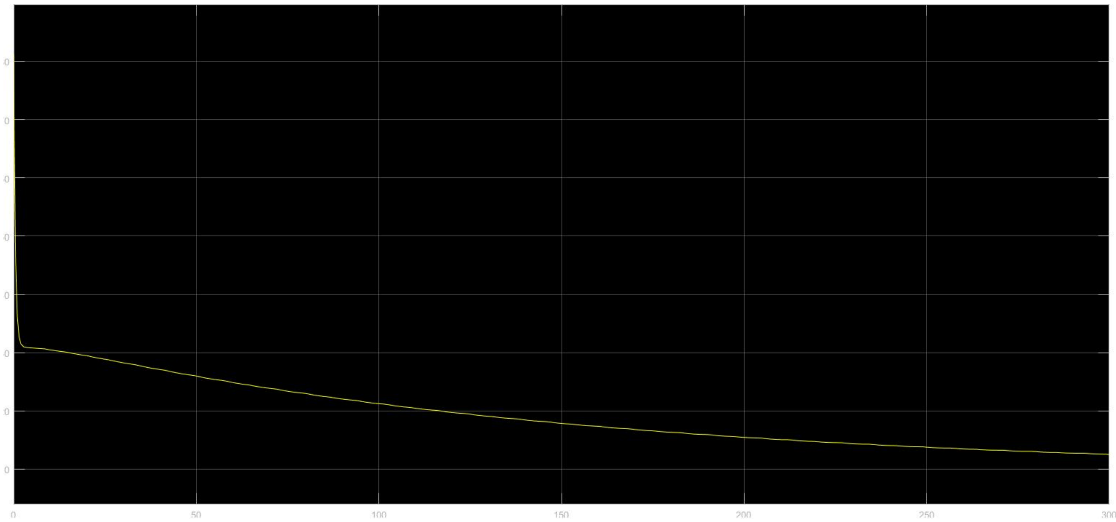
(b) Insuline

Riggs Iodine Model

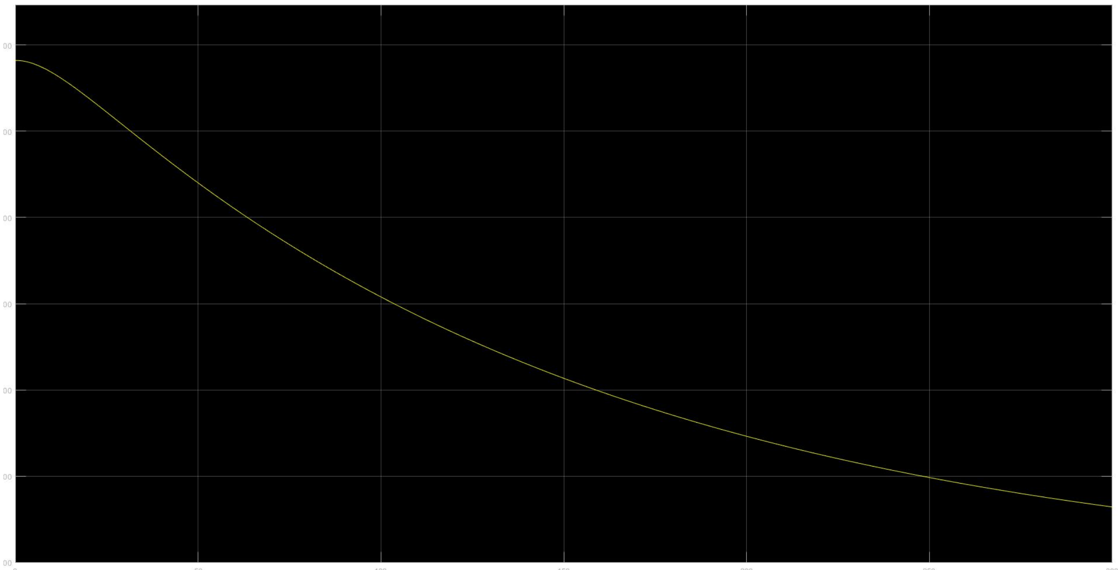




(a) Gland Iodine



(b) Plasma Iodine



(c) Hormone Iodine

Figure 5: Vertically arranged images of Gland, Plasma, and Hormone Iodine

Part 3

$$g'(t) = -k_4 g(t) - k_6 i(t) + A(t) \quad -①$$

$$i'(t) = k_3 g(t) - k_1 i(t) + B(t) \quad -②$$

from ①,

$$g''(t) = -k_4 g'(t) - k_6 i'(t) + \frac{d}{dt} A(t)$$

by $A(t) = a u(t)$

$$g''(t) = -k_4 g'(t) - k_3 i'(t) + \frac{d}{dt} a u(t)$$

from ②, by $B(t) = 0$

$$g''(t) = -k_4 g'(t) - k_6 [k_3 g(t) - k_1 i(t)] + \frac{d}{dt} a u(t)$$

from ①,

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

By substituting,

$$g'(t) = -k_4 g'(t) - k_3 k_6 g(t) + k_1 [-g'(t) - k_4 g(t) + a u(t)] + \frac{d}{dt} a u(t)$$

$$g''(t) + (k_1 + k_4) g'(t) + (k_1 k_4 + k_3 k_6) g(t) = k_1 a + a \frac{d}{dt} u(t)$$

Typical values,

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

$$g''(t) + 2.8 g'(t) + 2.6 g(t) = 0.8 + u'(t)$$

for $t > 0$; $\frac{d}{dt} u(t) = 0$

$$g''(t) + 2.8 g'(t) + 2.6 g(t) = 0.8$$

$$g(t) = g_c(t) + g_p(t)$$

$g_c(t) \Rightarrow$

$$g''(t) + 2.8g'(t) + 2.6g(t) = 0$$

by $g(t) = e^{mt}$

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

$$m = -1.4 \pm 0.8i$$

$$g_c(t) = c_1 e^{(-1.4+0.8i)t} + c_2 e^{(-1.4-0.8i)t}$$

$$g_c(t) = e^{-1.4t}\left[b_1 \cos(0.8t) + b_2 \sin(0.8t)\right]$$

To find $g_p(t)$, guess $g_p(t) = k$

$$0 + 0 + 2.6k = 0.8$$

$$k = 4/13$$

$$\Rightarrow g_p(t) = 4/13$$

$$g(t) = e^{-1.4t}\left[b_1 \cos(0.8t) + b_2 \sin(0.8t)\right] + 4/13$$

$g(0) = 0 \qquad \frac{dg(0)}{dt} = 1$

$$b_1 = -4/13$$

$$g'(0) = 0.8b_2 - 1.4b_1 = 1$$

$$b_2 = 37/52$$

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

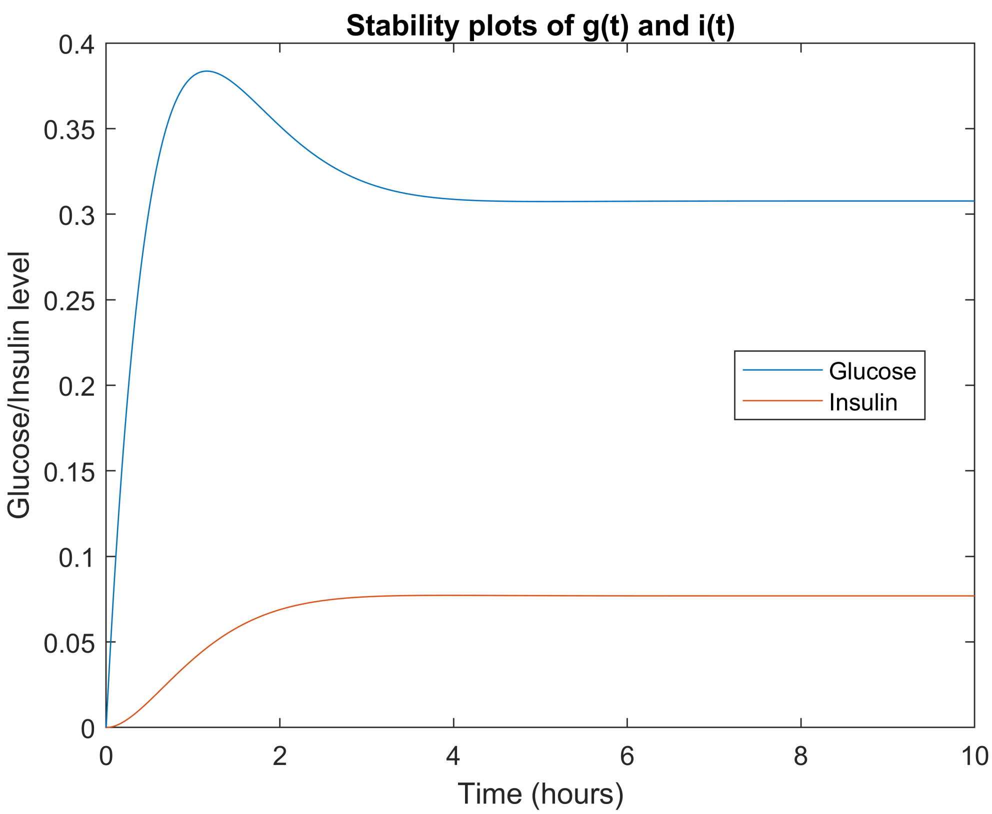
from ①

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

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

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

```
t = 0:0.01:10;
g_t = (exp((-1.4).*t)).*(-(4/13)*cos((0.8).*t) + (37/52)*sin((0.8).*t)) + 4/13;
i_t = (exp((-1.4).*t)).*(-(1/13)*cos((0.8).*t) - (7/52)*sin((0.8).*t)) + 1/13;
plot(t,g_t,t,i_t);
legend('Glucose','Insulin',"Location","best")
xlabel ('Time (hours)');
ylabel ('Glucose/Insulin level');
title('Stability plots of g(t) and i(t)');
```



Glucagon is a hormone produced by the pancreatic alpha cells that functions in opposition to insulin, which is produced by the pancreatic beta cells. While insulin facilitates the conversion of glucose into glycogen for storage in the liver, glucagon reverses this process by converting glycogen back into glucose.

The Bolies model is a straightforward model used to simulate the effects of insulin on blood glucose levels. This model can be expanded to incorporate the effects of glucagon by introducing an additional component: the glucagon compartment. This compartment would connect to the liver compartment, with the rate of glucagon transfer between these compartments being determined by the glucagon secretion rate and the glucagon degradation rate.

According to the bolies' plasma - glucose model

* Glucose

- Increased by
  - release from stores (assume constant : k_5)
  - Infusion or ingestion (time varient : $A(t)$)

- Decreased by
  - basal removal to cells : k_4
  - insulin - dependent removal to cells : $k_6 I$

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

* Insulin

- Increased by
  - basal pancreatic release - k_2
  - glucose - stimulated release - $k_3 G$
  - Insulin infusion or injection : $B(t)$

- Decresed by
  - breakdown : $k_1 I$

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

The same way we can obtain a differential equation for glucogen.

* Glucogen

- Increased by
  - Basal pancreatic release : k_8
  - Glucose - stimulated release : $k_4 G$
  - Infusion or injection : $c(t)$

- Decreased by
  - Breakdown : $k_7 G_n$

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

Here, when glucogen involves, the glucose level increases because of it.

$$\frac{d}{dt} G(t) = k_5 + A(t) - k_4 G(t) - k_6 I(t) + k_{10} G_n(t)$$

where $k_{10} G_n(t)$ is removed from cells (Glucogen dependent)

$$\frac{d}{dt} G(t) = k_5 + A(t) - k_4 G(t) - k_6 I(t) + k_{10} G_n(t) \quad \text{— } ①$$

$$\frac{dI(t)}{dt} = k_2 + k_3 G(t) + B(t) - k_1 I(t) \quad \text{— } ②$$

$$\frac{dG_n(t)}{dt} = k_8 + c(t) + k_9 G(t) - k_7 G_n(t) \quad \text{— } ③$$

Considering equilibrium

① = ② = ③ = 0

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

$$k_2 = k_1 I_0 - k_3 G_0$$

$$k_8 = k_7 G_n - k_9 G_0$$

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

As $g = G - G_0 \Rightarrow \frac{dg}{dt} = \frac{dG}{dt}$ since G_0 is a constant.

$$\frac{dg(t)}{dt} = k_4 G_0 + k_6 I_0 - k_{10} G_{n0} + k_{10} G_n(t) - k_4 G(t) - k_6 I(t) + A(t)$$

$$= -k_4 g(t) - k_6 i(t) + k_{10} g_n(t) + a u(t)$$

$$- A(t) = a \cdot u(t)$$

Similarly,

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

$$\frac{d g_n(t)}{dt} = k_9 g(t) - k_7 g_n(t)$$

$$- B(t) = 0, \quad C(t) = 0$$

Initial conditions,

$$g(0) = i(0) = g_n(0) = 0$$

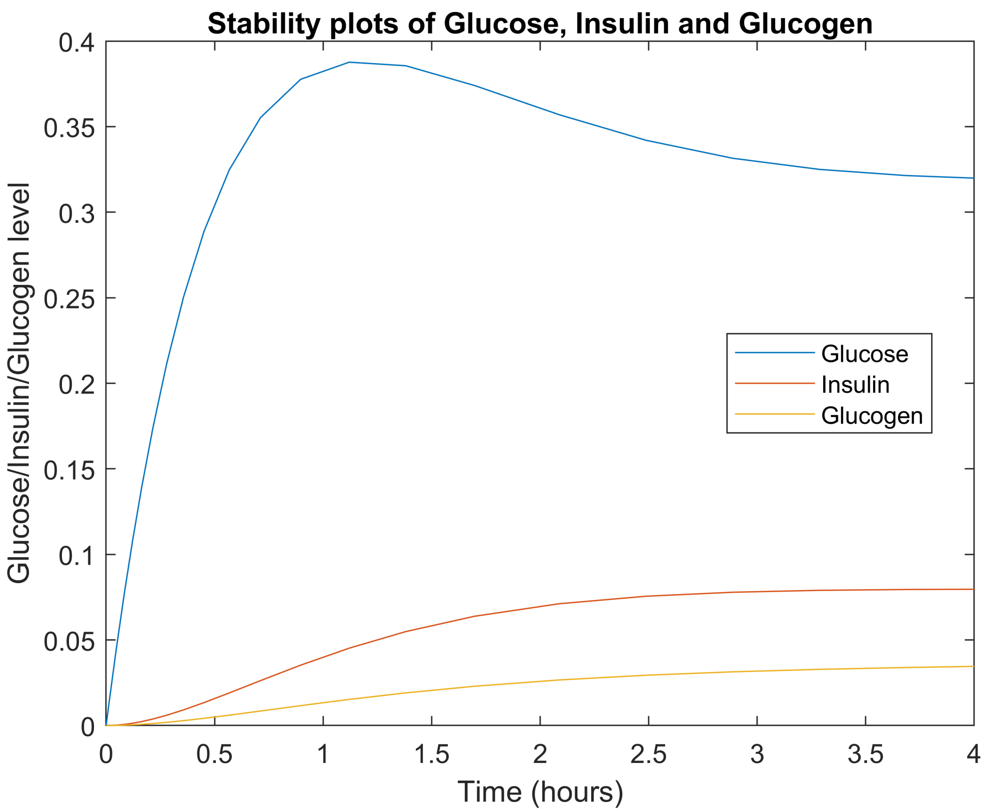
$$\frac{dg(t)}{dt} = -k_4 g(t) - k_6 i(t) + k_{10} g_n(t) + a u(t)$$

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

$$\frac{d g_n(t)}{dt} = k_9 g(t) - k_7 g_n(t)$$

$$\begin{pmatrix} g'(t) \\ i'(t) \\ g_n'(t) \end{pmatrix} = \begin{pmatrix} -k_4 & -k_6 & k_{10} \\ k_3 & -k_1 & 0 \\ k_9 & 0 & -k_7 \end{pmatrix} \begin{pmatrix} g(t) \\ i(t) \\ g_n(t) \end{pmatrix} + \begin{pmatrix} a u(t) \\ 0 \\ 0 \end{pmatrix}$$

```
[t,y] = ode23('G_I_Gn_model',[0 4],[0 0 0]);
plot(t,y)
legend('Glucose','Insulin','Glucogen','Location','best')
xlabel('Time (hours)');
ylabel('Glucose/Insulin/Glucogen level');
title('Stability plots of Glucose, Insulin and Glucogen')
```



The graph illustrates a sharp rise in insulin levels following a significant glucose intake. The peak in insulin occurs shortly after the glucose level reaches its maximum, reflecting the time needed for pancreatic cells to detect the glucose increase and secrete insulin in response.

When glucagon is present, the glucose level remains higher at the endpoint compared to when glucagon is absent. This is because glucagon counteracts insulin's effects. While insulin lowers blood sugar by promoting glucose uptake by cells and encouraging the liver to store glucose as glycogen, glucagon raises blood sugar by stimulating the liver to break down glycogen into glucose.

In the presence of glucagon, the pancreas compensates for the glucose drop by secreting more insulin, which helps prevent blood sugar levels from falling too low. However, the presence of glucagon also results in a higher glucose level at the endpoint compared to when glucagon is absent.