Modeling and Simulation -

Lab Assignment 1

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Objective

Problem 1

Part A:

Write down the differential equation that models Newton's law :

$$\frac{dT}{dt} \propto (T - T_m)$$

$$\frac{dT}{dt} = -k(T - T_m)$$

Part B:

Solve this equation for T as a function of t :

$$\frac{dT}{dt} = -k(T - T_m)$$

Taking Laplace Transformation:

$$sF - T(0) = -k(F) + \frac{kT_m}{s}$$

$$(s+k)F = \frac{kT_m}{s} + T(0)$$

$$F = T_m(\frac{1}{s} - \frac{1}{s+k}) - \frac{T(0)}{k}(1 - \frac{k}{s+k}) + \frac{T(0)}{k}$$

Taking Inverse Laplace Transformation:

$$T(t) = T_m(1 - e^{-kt}) + T(0)e^{-kt}$$

Equation for the Temperature at time t is:

$$T(t) = T_m + (T(0) - T_m)e^{-kt}$$

Part C:

Assuming $T_m = 25°C$, suppose cold water at $6°C$ is placed in a room. After $1h$, the temperature of the water is $20°C$. Determine all the constants in the equation for T :

$T_m = 25°C$

$T(t) = 20°C$

$T(0) = 6°C$

$t = 3600$ seconds

$T(t) = T_m + (T(0) - T_m)e^{-kt}$

$20 = 25 + (6 - 25)e^{-k3600}$

$e^{-k3600} = \frac{-5}{-19}$

$-k3600 = \log(0.263157895)$

$k = 0.000370834\ s^{-1}$

Part D:

How long will it take for the water to warm to $12°C$ in part (c) ? : $T_m = 25°C$

$T(t) = 12°C$

$T(0) = 6°C$

$k = 0.000370834\ s^{-1}$

$T(t) = T_m + (T(0) - T_m)e^{-kt}$

$12 = 25 + (6 - 25)e^{-kt}$

$e^{-tk} = \frac{-13}{-19}$

$t = 1023.1332743s$

Part E:

Implement your model of Newton's law of cooling on the computer using Euler's method. Solve for time step t= 1, 0.5, 0.1, 0.05. What would be a reasonable time step for this model?

Explanation : For dt = 1, we see unexpected behaviour as value of T reaches above 25 C. For dt = 0.5, curve is not smooth as that seen for dt = 0.1 and dt = 0.5. For dt = 0.1 and dt = 0.05 curve almost coincides hence either of the value of dt is suitable. But for dt = 0.1 number of computations are less hence it is preferable.

Code:

```
%Q1(e)
close all;
clear all;
Tm = 25;
k = 0.000370834 * 3600;
dt1 = [1, 0.5, 0.1, 0.05];
total = 6;
set(gca,'fontsize',13)
```

```
hold on
for j = 1 : 4
    dt = dt1(j);
    iter = (total - 1) / dt + 1;
    T = zeros(iter, 1);
    T(1) = 6;
    t = zeros(iter, 1);
    for i = 2 : iter
        T(i) = T(i - 1) - dt * (k * (T(i - 1) - Tm));
        t(i) = t(i - 1) + dt;
    end
    plot(t, T,'lineWidth',1.5)
    hold on
end
legend(strcat('dt=',num2str(1)), strcat('dt=',num2str(0.5)), strcat('dt=',num2str(0.1)),
title('Comparison of different values of dt');
xlabel('Time (in hours)');
ylabel('Temperature (in degree celcius)');
```

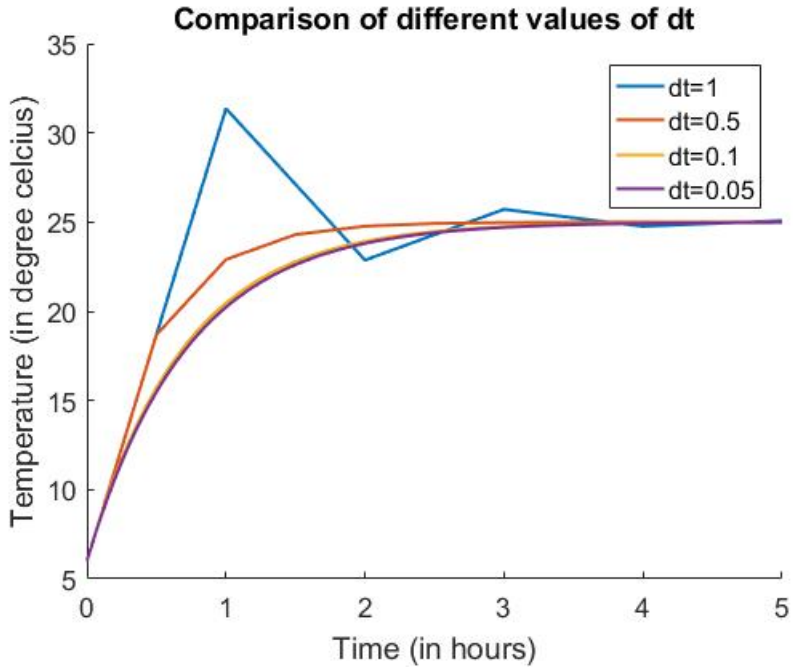

Figure 1

Problem 2

Consider a two compartment model of drug dosage. The two compartments here can be thought of to represent the gastrointestinal tract (GI-tract) and blood stream. The pill or drug that is taken first goes to the GI-tract from where it dissolves in the blood stream and then is finally eliminated. Assuming that the rate of change of the drug in either of the compartments is proportional to the amount present model the following three scenarios.

Part A:

If the drug in the GI-tract immediately dissolves to the blood stream, what would be a reasonable model. Assume that the proportionality constant for drug elimination from the blood stream is k_2 , $k_2 > 0$. Solve analytically. Let's assume that drug amount in the GI-tract is Q_1 and in the blood stream is Q_2. From the problem statement we can observe that,

$$\frac{dQ_1}{dt} = 0$$

$$\frac{dQ_2}{dt} = -k_2 \times Q2$$

Taking Laplace Transform for Q_1:

$$sF - Q_1(0) = 0$$

$$F = \frac{Q_1(0)}{s}$$

Taking Inverse Laplace Transform:

$$Q_1 = Q_1(0)$$

Taking Laplace Transform for Q_2:

$$sF - Q_2(0) = -k_2 \times F$$

$$F = \frac{Q_2(0)}{s + k_2}$$

Taking Inverse Laplace Transform:

$$Q_2 = Q_2(0)e^{-k_2 t}$$

Part B:

Now consider the situation in which the drug enters the GI-tract instantaneously and then slowly diffuses into the blood stream. Let the proportionality constant for this process be k_1. Modify your model appropriately. How will the instantaneous intake be incorporated in your equations. Solve analytically

Let's assume that drug amount in the GI-tract is Q_1 and in the blood stream is Q_2. From the problem statement we can observe that,

$$\frac{dQ_1}{dt} = -k_1 \times Q1$$

$$\frac{dQ_2}{dt} = k_1 \times Q1 - k_2 \times Q2$$

Taking Laplace Transform for Q_1:

$$sF - Q_1(0) = -k_1 \times F$$

$$F = \frac{Q_1(0)}{s + k_1}$$

Taking Inverse Laplace Transform:

$$Q_1 = Q_1(0)e^{-k_1 t}$$

Taking Laplace Transform for Q_2:

$$sF - Q_2(0) = \frac{-k_1 Q_1(0)}{s + k_1} + -k_2 \times F$$

Taking Inverse Laplace Transform:

$$Q_2 = \frac{k_1 Q_1(0)}{k_1 - k_2}\left(e^{-k_2 t} - e^{-k_1 t}\right) + Q_2(0)e^{-k_2 t}$$

Part C:

If we now break the assumption of instantaneous intake of pills but rather assume that it is taken at regular intervals, how would you modify your model.

Let's assume that drug amount in the GI-tract is Q_1 and in the blood stream is Q_2. a is the constant rate at which the drug is consumed by the subject. From the problem statement we can observe that,

$$\frac{dQ_1}{dt} = a - k_1 \times Q1$$

$$\frac{dQ_2}{dt} = k_1 \times Q1 - k_2 \times Q2$$

Taking Laplace Transform for Q_1:

$$sF - Q_1(0) = \frac{a}{s} - k_1 \times F$$

$$F = \frac{a}{k_1}\left(\frac{1}{s} - \frac{1}{s+k_2}\right) + \frac{Q_1(0)}{s+k_1}$$

Taking Inverse Laplace Transform:

$$Q_1 = \frac{a}{k_1}\left(1 - e^{-k_1 t}\right) + Q_1(0)e^{-k_1 t}$$

Taking Laplace Transformation for Q_2:

$$\frac{dQ_2}{dt} = k_1\left(\frac{a}{k_1}\left(1 - e^{-k_1 t}\right) + Q_1(0)e^{-k_1 t}\right) - k_2 Q_2$$

$$sF - Q_2(0) = a\left(\frac{1}{s} - \frac{1}{s+k_1}\right) + \frac{k_1 Q_1(0)}{s+k_1} - k_2 F$$

Taking Inverse Laplace Transform:

$$Q_2 = \frac{a}{k_2}\left(1 - e^{-k_2 t}\right) + \left(\frac{k_1 Q_1(0) - a}{k_2 - k_1}\right)\left(e^{-k_1 t} - e^{-k_2 t}\right)$$

Problem 3

Part A:

For part above write a code and obtain the evolution in time of the amount of drug in GI-tract and blood stream. Assume that $k_1 = .386^{-1}$and $k_2 = 0.1386hr^{-1}$. Let the initial intake be 1 units. What is the highest level of the drug in the blood.

Explanation : Highest level of drug achieved in blood stream = 0.7885 units.

Code:

```
%Q3 (a) :
close all;
clear all;
total = 24;
dt = 0.1;
set(gca,'fontsize',13)
hold on
iter = (total - 1) / dt + 1;
Q1 = zeros(iter, 1);
Q2 = zeros(iter, 1);
Q1(1) = 1;
Q2(1) = 0;
k1 = 1.386;
k2 = 0.1386;
t = zeros(iter, 1);
ma = 0;
for i = 2 : iter
    Q1(i) = Q1(i - 1) - dt * k1 * Q1(i - 1);
    Q2(i) = Q2(i - 1) + dt * (k1 * Q1(i - 1) - k2 * Q2(i - 1));
    if ma < Q2(i)
        ma = Q2(i);
    end;
    t(i) = t(i - 1) + dt;
end;
ma
plot(t, Q2,'lineWidth',1.5);
```

```
hold on
plot(t, Q1,'lineWidth',1.5);
legend('For GI Tract', 'For Blood stream');
title('Drug concentration level');
xlabel('Time (in hours)');
ylabel('Drug concentration');
```

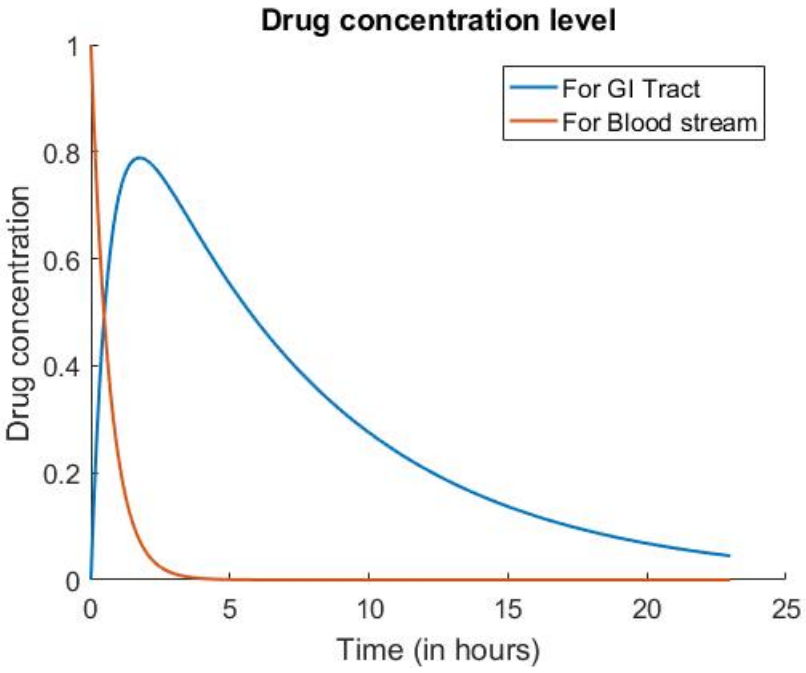

Figure 2

Part B:

Take different values of k2(k2 = 0.01386, 0.06, 0.1386, 0.6386, 1.386 per hour) and study the effect. Comment on the different behaviors observed.

Explanation : For smaller values of k_2 it can be seen that it takes longer time for drug level in blood stream to reduce to zero level. Also the maximum drug level reached in blood stream is higher for lower values of k_2. This is because higher the value of k_2 fast the drug will eliminate

and so the maximum drug level reached is less for same value of k_1. Here the diffusion rate of drug in blood stream will remain same irrespective of value of k_2. The increase in drug level in blood stream phase almost coincides for all values of k_2 till maximum level is reached because the drug is diffused in blood stream at same rate.

Code:

```
%Q3(b):
close all;
clear all;
total = 24;
set(gca,'fontsize',13)
hold on
dt = 0.1;
iter = (total - 1) / dt + 1;
k1 = 1.386;
ks = [0.01386, 0.06, 0.1386, 0.6386, 1.386];
for j = 1 : 5
    k2 = ks(j);
    Q1 = zeros(iter, 1);
    Q2 = zeros(iter, 1);
    Q1(1) = 1;
    Q2(1) = 0;
    t = zeros(iter, 1);
    for i = 2 : iter
        Q1(i) = Q1(i - 1) - dt * k1 * Q1(i - 1);
        Q2(i) = Q2(i - 1) + dt * (k1 * Q1(i - 1) - k2 * Q2(i - 1));
        t(i) = t(i - 1) + dt;
    end;
```

```
    if(j == 1)
        plot(t, Q1)
        hold on
    end;
    plot(t, Q2)
    hold on
end;
legend('GI Tract', strcat('Blood Stream k2=',num2str(ks(1))), strcat('Blood Stream k2=',
title('Drug concentration level for different k');
xlabel('Time (in hours)');
ylabel('Drug concentration');
```

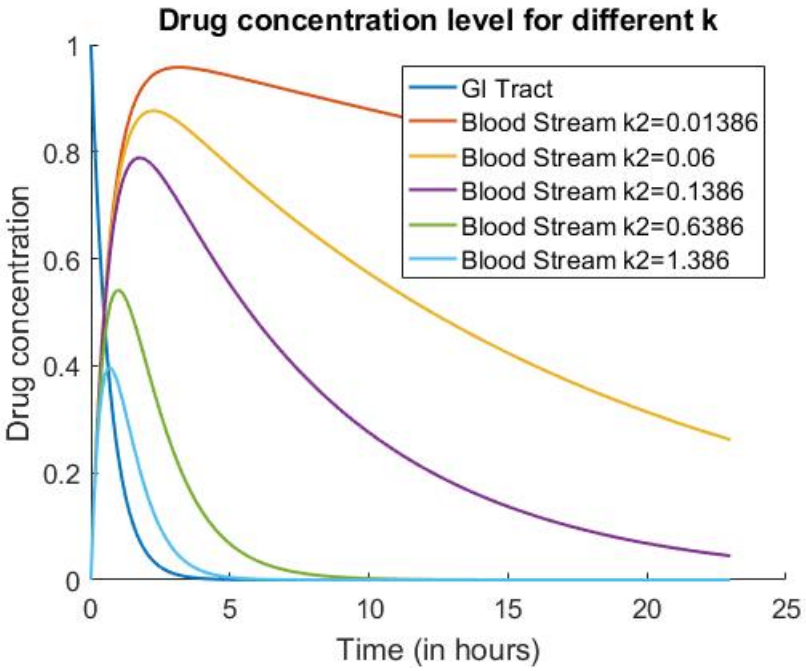

Figure 3

Part C:

Take different values of k1(k1 = 0.06931, 0.11, 0.691, 1.0, 1.5 per hour) and study the effect. Comment on the different behaviors observed.

Explanation : Higher the value of k_1 faster the drug will diffuse in blood stream and so the maximum drug level in blood stream is reached faster. As the difference in value of k_1 and k_2 decreases (here $k_1 > k_2$ always), drug elimination occurs faster and so maximum value reached also decreases for smaller values of k_1. So, as k_1 increases time to reach maximum drug value ans also the maximum drug value reached increases.

Code:

```
%Q3(c):
close all;
clear all;
total = 80;
set(gca,'fontsize',13)
hold on
dt = 0.1;
iter = (total - 1) / dt + 1;
k2 = 0.0231;
ks = [0.06931, 0.11, 0.691, 1.0, 1.5];
Q1 = zeros(2, iter);
Q2 = zeros(2, iter);
for j = 1 : 5
    k1 = ks(j);

    Q1(j,1) = 1;
    Q2(j,1) = 0;
    t = zeros(iter, 1);
```

```
    for i = 2 : iter
        Q1(j,i) = Q1(j,i - 1) - dt * k1 * Q1(j,i - 1);
        Q2(j,i) = Q2(j,i - 1) + dt * (k1 * Q1(j,i - 1) - k2 * Q2(j,i - 1));
        t(i) = t(i - 1) + dt;
    end;
end;
for j = 1 : 5
    plot(t, Q1(j, :));
    hold on;
end;
legend(strcat('k1=',num2str(ks(1))),strcat('k1=',num2str(ks(2))),strcat('k1=',num2str(ks
title('Drug concentration level in GI tract for different k');
xlabel('Time (in hours)');
ylabel('Drug concentration');

figure;
set(gca,'fontsize',13)
hold on
for j = 1 : 5
    plot(t, Q2(j, :));
    hold on;
end;
legend(strcat('k1=',num2str(ks(1))),strcat('k1=',num2str(ks(2))),strcat('k1=',num2str(ks
title('Drug concentration level in Blood stream for different k');
xlabel('Time (in hours)');
ylabel('Drug concentration');
```

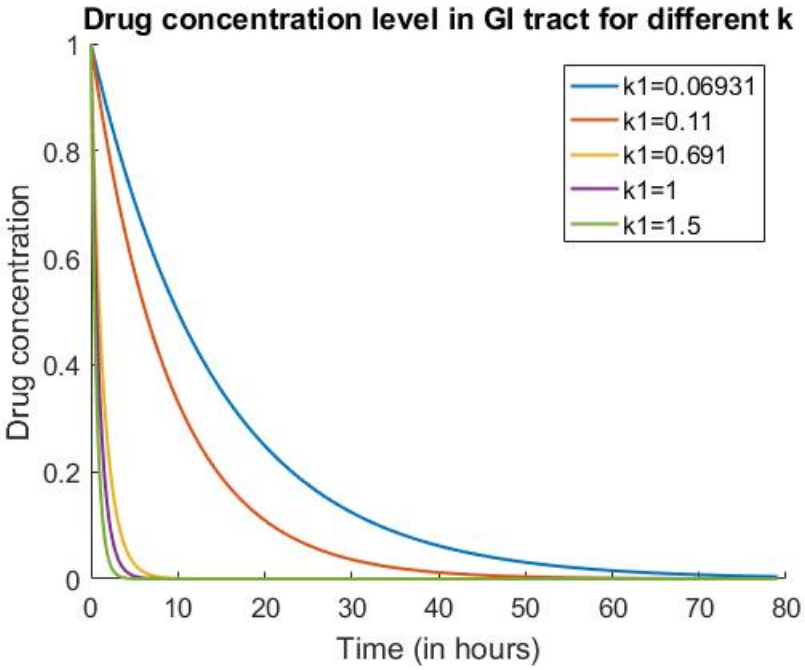

Figure 4

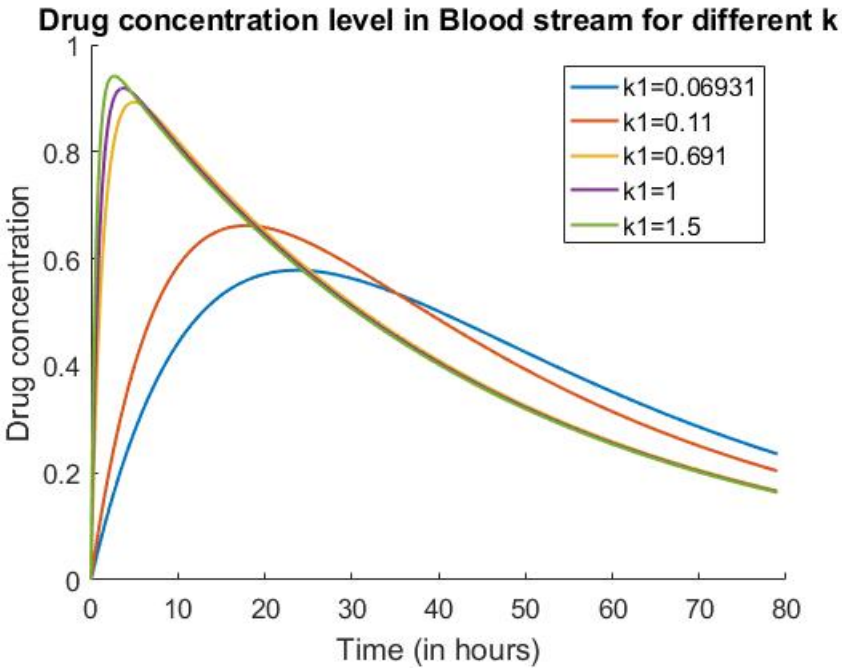

Figure 5

Part D:

Part (1c) is for regular dosage. First have a constant supply of 3 units of the drug at all times. Analyze the behavior for 24 hours. Assume that at t = 0 there is no drug in the GI-tract or blood stream. Initial conditions are the same as in part(a).

Explanation : Maximum drug level = $\frac{a}{k_1}$ (a = 3, k_1 = 1.386 here) is reached in GI-tract and remains same forever as constant supply is given continuously. Similarly some maximum value in blood stream is reached after some time which remains constant forever. Here if value of k_2 increases maximum value reached is less and it takes less time to reach that value as drug elimination rate increases.

Code:

```
%Q3(d):
close all;
clear all;
set(gca,'fontsize',13)
hold on

total = 100;
dt = 0.1;
iter = (total - 1) / dt + 1;
Q1 = zeros(iter, 1);
Q2 = zeros(iter, 1);
Q1(1) = 0;
Q2(1) = 0;
k1 = 1.386;
k2 = 0.1386;
t = zeros(iter, 1);
for i = 2 : iter
```

```
    Q1(i) = Q1(i - 1) - dt * k1 * Q1(i - 1) + 3 * dt;
    Q2(i) = Q2(i - 1) + dt * (k1 * Q1(i - 1) - k2 * Q2(i - 1));
    t(i) = t(i - 1) + dt;
end;
plot(t, Q1,'lineWidth',1.5);
hold on
plot(t, Q2,'lineWidth',1.5);
legend('GI Tract', 'Blood stream');
title('Drug concentration level where inflow is constant');
xlabel('Time (in hours)');
ylabel('Drug concentration');
```

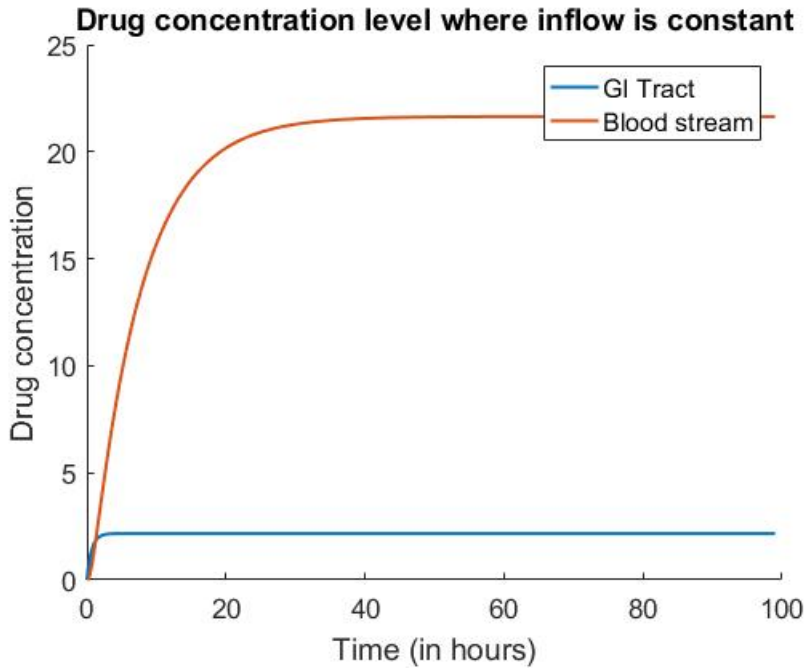

Figure 6

Part E:

Now modify your code for repeated dosage. Assume that the drug is administered for 1/2 hour every 6 hours. Assume that during the administration phase this intake is a constant at 6 units. Take k1= 0.6931 and k2 = 0.0231 per hour. How does the amounts in GI-tract and blood stream change over a period of 24 hours?

Explanation : For 1 / 2 hours the value of drug increases at constant rate and reaches its maximum value in GI-tract. Then it shows the same behaviour as we saw in problem (a) for 6 hours and process repeats. The increase in drug level in blood stream is also same as seen in problem (a) for every 6 hours. Here it keeps on increasing.

Code:

```
%Q3(e):
close all;
clear all;
total = 24;
dt = 0.05;
set(gca,'fontsize',13)
hold on

iter = (total - 1) / dt + 1;
Q1 = zeros(iter, 1);
Q2 = zeros(iter, 1);
Q1(1) = 6 * dt;
Q2(1) = 0;
k1 = 0.6931;
k2 = 0.0231;
t = zeros(iter, 1);
ti = -1;
```

```
for i = 2 : iter
    add = 0;
    t(i) = t(i - 1) + dt;
    if mod(t(i), 6) >= 0 && mod(t(i), 6) <= 0.5
        add = 6 * dt;
    end;
    Q1(i) = Q1(i - 1) - dt * k1 * Q1(i - 1) + add;
    Q2(i) = Q2(i - 1) + dt * (k1 * Q1(i - 1) - k2 * Q2(i - 1));
end;
plot(t, Q1,'lineWidth',1.5);;
hold on
plot(t, Q2,'lineWidth',1.5);;
legend('GI Tract', 'Blood stream');
title('repeated dosage (Administration)');
xlabel('Time (in hours)');
ylabel('Drug concentration');
```

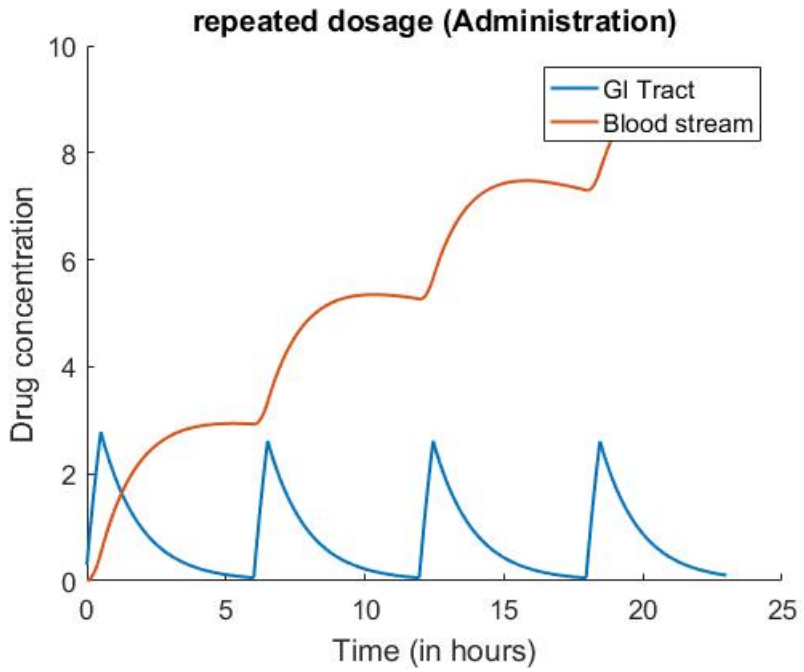

Figure 7

Part F:

Assuming that the maximum therapeutic limit is at 20 units in the blood stream what is the time duration after which the drug will have adverse effect?

Explanation :Maximum therapeutic limit of 20 units is reached at 103.4 hours. After which drug will have adverse effect.

Code:

```
%Q3(f):
close all;
clear all;
total = 200;
dt = 0.05;
iter = (total - 1) / dt + 1;
Q1 = zeros(iter, 1);
```

```
Q2 = zeros(iter, 1);
Q1(1) = 6 * dt;
Q2(1) = 0;
k1 = 0.6931;
k2 = 0.0231;
t = zeros(iter, 1);
set(gca,'fontsize',13)
hold on

ti = -1;
for i = 2 : iter
    add = 0;
    t(i) = t(i - 1) + dt;
    if mod(t(i), 6) >= 0 && mod(t(i), 6) <= 0.5
        add = 6 * dt;
    end;
    Q1(i) = Q1(i - 1) - dt * k1 * Q1(i - 1) + add;
    Q2(i) = Q2(i - 1) + dt * (k1 * Q1(i - 1) - k2 * Q2(i - 1));
    if(Q2(i) >= 20 && ti == -1)
        ti = t(i);
    end;
end;
ti
plot(t, Q1,'lineWidth',1.5);
hold on
plot(t, Q2,'lineWidth',1.5);
legend('GI Tract', 'Blood stream');
```

```
title('repeated dosage (Administration)');
xlabel('Time (in hours)');
ylabel('Drug concentration');
```

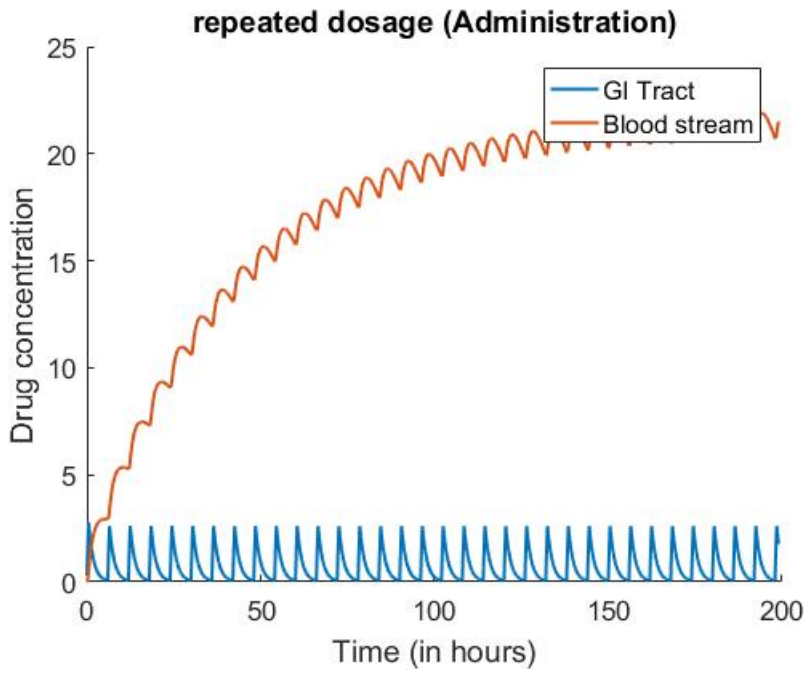

Figure 8

Part G:

Now assume that the drug is taken every 8 hours. Assume all other conditions to be the same as in part (f) determine if the drug will have an adverse effect or not.

Explanation : Drug will not have adverse effect as the maximum value reached is 16.81 units.

Code:

```
%Q3(g) :
close all;
clear all;
total = 500;
set(gca,'fontsize',13)
```

```
hold on


dt = 0.05;
iter = (total - 1) / dt + 1;
Q1 = zeros(iter, 1);
Q2 = zeros(iter, 1);
Q1(1) = 6 * dt;
Q2(1) = 0;
k1 = 0.6931;
k2 = 0.0231;
t = zeros(iter, 1);
ti = -1;
for i = 2 : iter
    add = 0;
    t(i) = t(i - 1) + dt;
    if mod(t(i), 8) >= 0 && mod(t(i), 8) <= 0.5
        add = 6 * dt;
    end;
    Q1(i) = Q1(i - 1) - dt * k1 * Q1(i - 1) + add;
    Q2(i) = Q2(i - 1) + dt * (k1 * Q1(i - 1) - k2 * Q2(i - 1));
    if(Q2(i) >= 20 && ti == -1)
        ti = t(i);
    end;
end;
ti
plot(t, Q1,'lineWidth',1.5);
hold on
```

```
plot(t, Q2,'lineWidth',1.5);
legend('GI Tract', 'Blood stream');
title('repeated dosage (Administration)');
xlabel('Time (in hours)');
ylabel('Drug concentration');
```

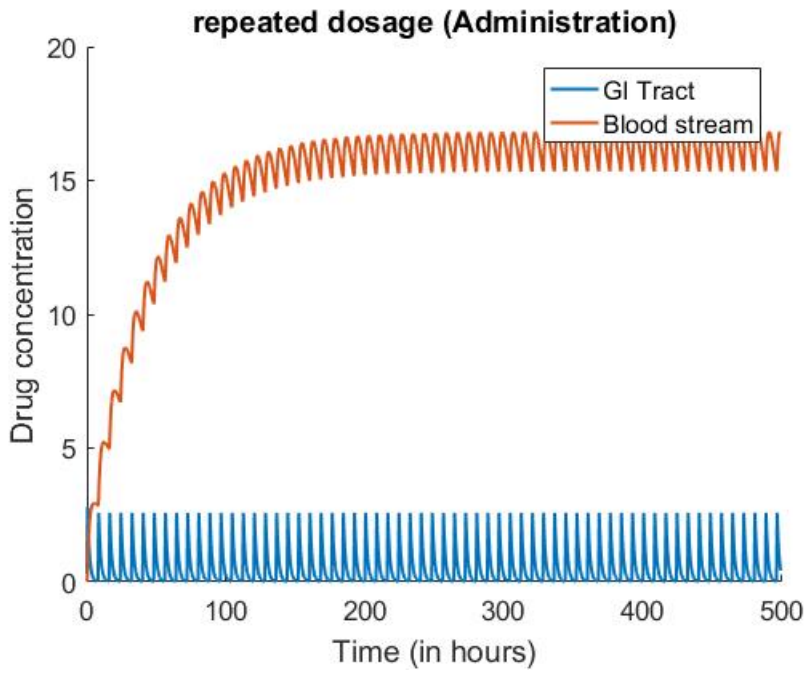

Figure 9

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