

Pharmacokinetics of Circulating Insulin

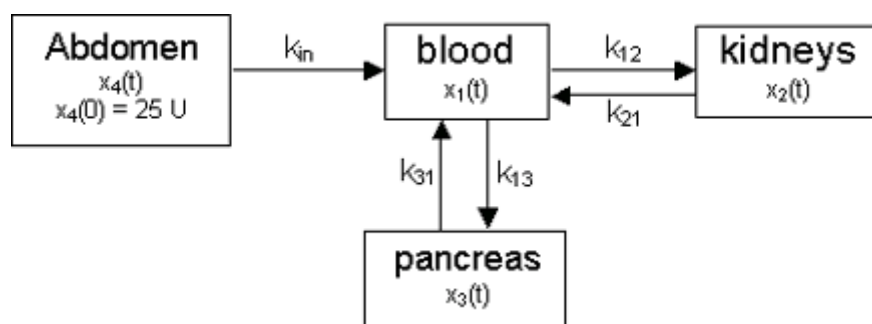
Problem Definition

A significant amount of diabetic patients use daily insulin injections to keep their blood sugar stable. Increasing the amount of insulin in the blood decreases the amount of sugar in the blood. Several methods exist for monitoring blood sugar, however, the inability to achieve a predictable blood sugar over time is a frustrating problem that constantly plagues diabetics.

Problem Analysis

The model shown in the Figure below represents the flux of insulin through specific parts of the body. For analytical purposes, this model does not take into account other factors, such as glucose, that may normally affect the concentration of insulin throughout the body. Using this model, it is your goal to predict the level of insulin in the blood over time after an insulin injection.

The Figure shows the flow of insulin in the body. A patient is first given an insulin injection, usually in the abdomen or upper arm. The insulin then dissolves into the bloodstream. Once in the blood, insulin flows to and from the kidneys, as well as to and from the pancreas.



Let:

- $x_1(t)$ be the concentration of insulin in the blood.
- $x_2(t)$ be the concentration of insulin in the kidneys.
- $x_3(t)$ be the concentration of insulin in the pancreas.
- Let $x_4(t)$ be the concentration of insulin in the abdomen. Initialize $x_4(0) = 25$ Units (U) to be the amount of insulin initially present in the abdomen due to the injection.
- $k_{in} = 2$ U/hr be the flow rate of insulin from the abdomen into the blood.
- $k_{12} = 1$ U/hr be the flow rate of insulin from the blood into the kidneys.
- $k_{21} = 1.5$ U/hr be the flow rate of insulin from the kidneys into the blood.
- $k_{13} = 2$ U/hr be the flow rate of insulin from the blood into the pancreas.
- $k_{31} = 1.75$ U/hr be the flow rate of insulin from the pancreas into the blood.

Objectives

- Using the model, determine the flux equations for this system.
- Solve these equations for the concentration of insulin in each compartment.
- Plot the concentrations of insulin in each compartment for up to 10 hours.
- Given these results, estimate the steady-state level of insulin in the blood and the time at which this level is reached.

Solution

Derive Flux Equations for Each Compartment

The first step in solving this problem is to derive the flux (flow rate) equations for each compartment in the system. This is done by a function that will call the MATLAB Ordinary Differential Equation (ODE) solver.

Rate equations (dx/dt) are constructed by subtracting the flow out from the flow in for each compartment. Also, flow = rate*concentration of the flow source block.

The following is the MATLAB code for the needed function, odefun:

```
function dxdt = odefun(t,x)

% Define flow rate constants given in problem statement
kin=2;
k12=1;
k21=1.5;
k13=2;
k31=1.75;

% Flow equation for insulin in Blood
dxdt(1)=kin*x(4) + k31*x(3) + k21*x(2) - k13*x(1) - k12*x(1);

% Flow equation for insulin in Kidneys
dxdt(2)=k12*x(1) - k21*x(2);

% Flow equation for insulin in Pancreas
dxdt(3)=k13*x(1) - k31*x(3);

% Flow equation for insulin in abdomen
dxdt(4)=-kin*x(4);

% concatenate to column vector because this function must pass column vector to ODE
solver
dxdt=[dxdt(1);dxdt(2);dxdt(3);dxdt(4)];
```

Call ODE Function

The next step is to write the MATLAB code that calls your function 'odefun'. This will call the ODE solver to solve these ODEs for specific parameters. For more information on ODE solvers, see Chapter 14 of the MATLAB User's Guide.

The following MATLAB code initializes the time span over which the solver will solve the ODEs, set the initial conditions for each ODE, and call the ODE solver 'ode45' with these input parameters. Note the following:

- The problem asks that the solutions be plotted for $t=0$ to 10 minutes
- The only initial condition in the problem is $x_4(0)=24U$. Other initial conditions are 0.

```
tspan=[0 10];
```

```
initial_condts=[0;0;0;25]
```

```
%Call to ODE solver 'ode45'.
[t,x]=ode45('odefun',tspan,initial_condts)
```

Next, subplots are created to show the level of insulin in each compartment over the ten-minute time span.

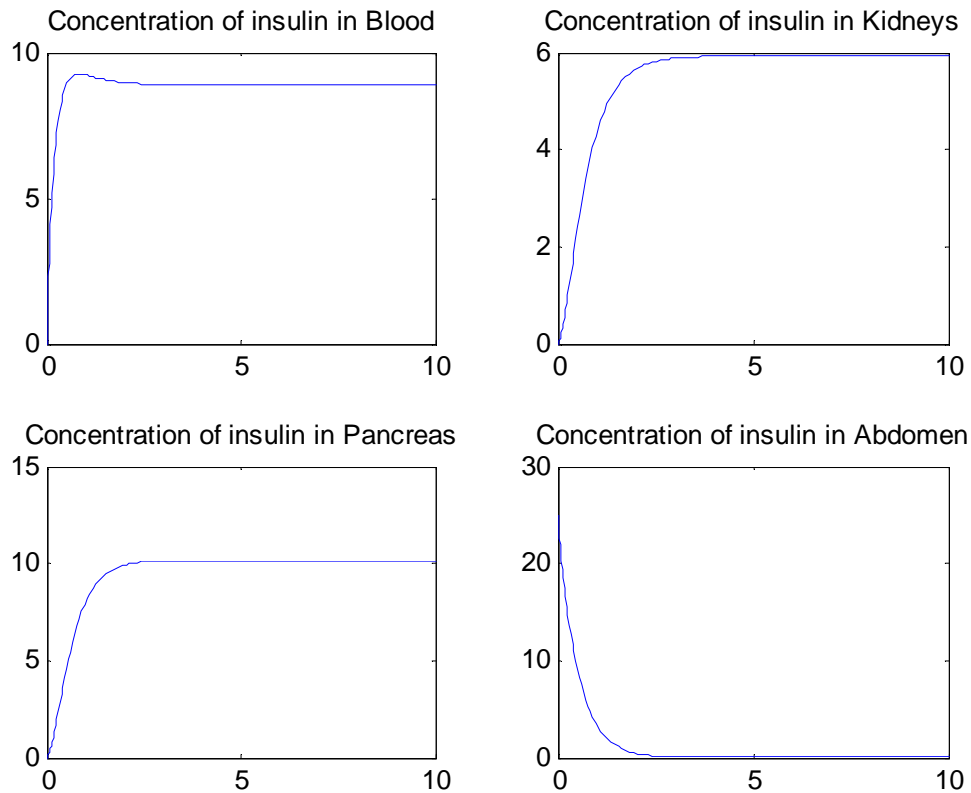
```
subplot(2,2,1)
plot(t,x(:,1))
title('Concentration of insulin in Blood')

subplot(2,2,2)
plot(t,x(:,2))
title('Concentration of insulin in Kidneys')

subplot(2,2,3)
plot(t,x(:,3))
title('Concentration of insulin in Pancreas')

subplot(2,2,4)
plot(t,x(:,4))
title('Concentration of insulin in Abdomen')

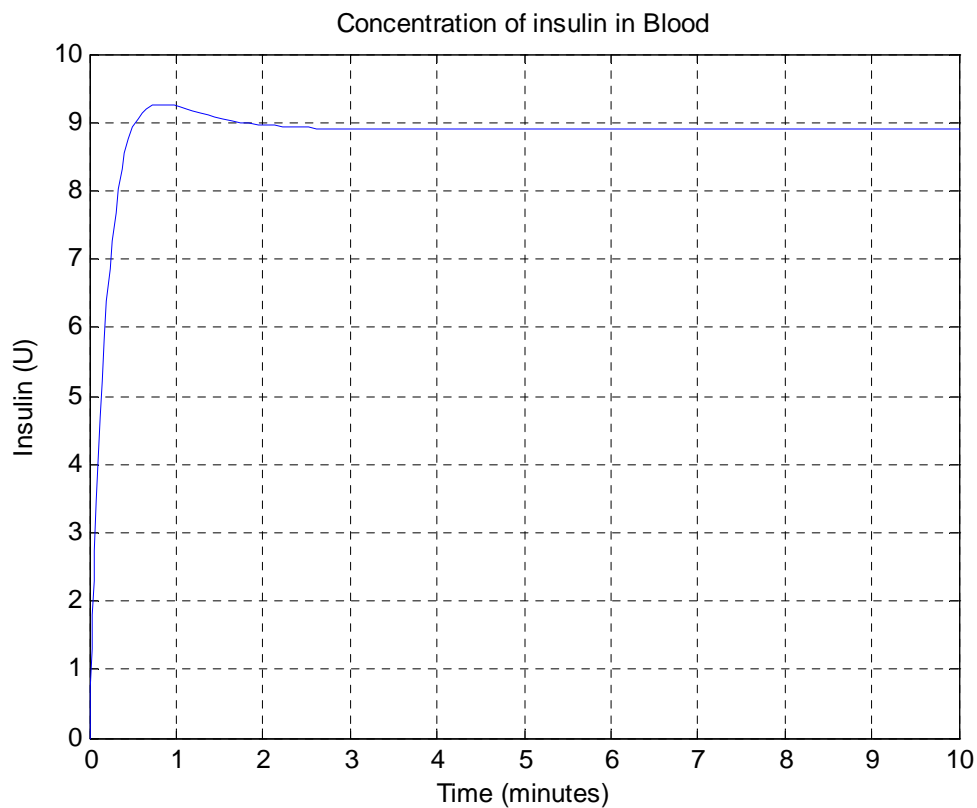
createInferenceFigure
```



Estimate Time to Steady State

Lastly, from the subplot showing the "Concentration of Insulin in the Blood" below we can estimate the time at which the level of insulin reaches its steady-state value. Constructing this plot and overlaying a grid on top of the figure helps to estimate the steady-state value.

```
figure
plot(t,x(:,1))
title('Concentration of insulin in Blood')
xlabel('Time (minutes)')
ylabel('Insulin (U)')
grid on
createInferenceFigure
```



Conclusion

The steady-state of the insulin in the blood is approximately 8.9 U and this level is reached at approximately 2.5 hours post-injection.