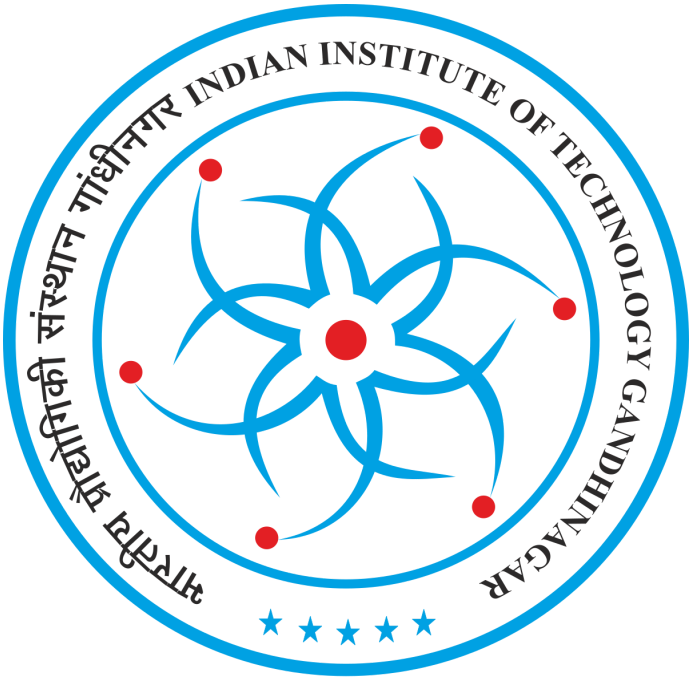
MATHEMATICAL MODELING OF GLUCOSE CONTROL IN DIABETIC PATIENTS



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1 PROBLEM STATEMENT

Our project addresses the need for a comprehensive numerical analysis of glucose control in diabetic patients using the **Bergman minimal model**.

Diabetes is a chronic disease of the endocrine system where the body cannot control blood glucose level. Obesity caused by eating habits and lifestyle, reduces the body's responsiveness to insulin, which causes the condition known as diabetes.

Treatment of diabetes may include exercise, dieting, oral medications, or insulin injections. Most insulin-dependent diabetics follow a management plan that requires frequent testing of blood glucose levels and then injection of a prescribed dose of insulin based on the blood glucose level. However, the downside of this treatment method is that there is no predictive control. If blood glucose levels are falling and insulin is administered, a hypoglycemic episode may occur.[1]

Recent biomedical advancements have resulted in continuous blood glucose monitoring devices as well as insulin pumps (a small wearable electronic device that helps regulate insulin and blood glucose (sugar) levels).[2]

Continuous monitoring allows for finer blood glucose control and can help predict fluctuations in the blood glucose level. Insulin pumps replace the need to administer insulin injections by automatically injecting a prescribed dose, however, it requires blood glucose level input from the patient. In the future, insulin pumps and continuous blood glucose monitors may be integrated forming a closed-loop control system that can replace the body's own faulty control system.
A numerical solution is required for this problem.

We are studying the dynamics of glucose and insulin in the human body. The main challenge of our project is to develop a numerical approach that can efficiently solve the system of Ordinary Differential Equations (ODEs) within the Bergman minimal model.

We aim to:

- Implement numerical methods, such as Runge-Kutta or finite difference schemes, to solve the ODEs governing glucose and insulin dynamics.
- Validate our numerical model against clinical data to ensure its accuracy and reliability.
- Investigate the impact of various parameters on glucose control, such as insulin sensitivity and glucose production.
- Analyze the effectiveness of different diabetic treatment strategies, such as insulin therapy and lifestyle modifications, through simulations.
- Provide insights and recommendations for optimizing glucose control and improving diabetic patient outcomes based on our numerical analysis.

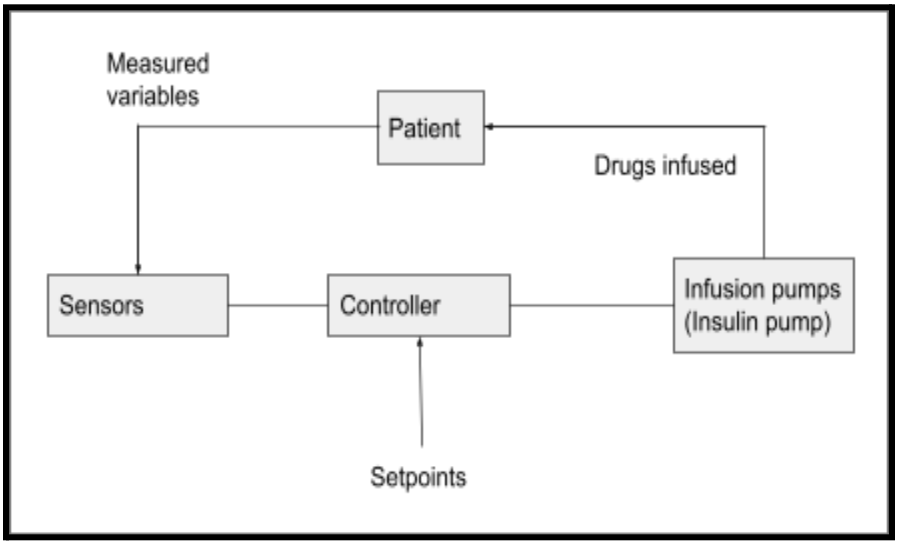

Figure 1: Control schematic of insulin infusion [1]

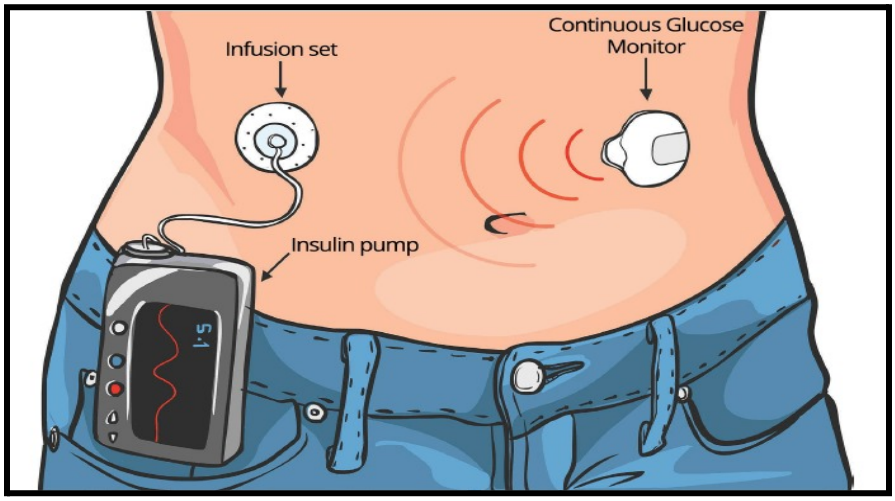

Figure 2: Insulin pump [4]

2 PARAMETERS [3]

In the Bergman 'Minimal Model,' there are several parameters that describe the dynamics of blood glucose and insulin concentrations. These parameters are essential for modeling the glucose-insulin system.

The parameters are:

- $G(t)$: Blood glucose concentration(mg/dL)
- $X(t)$: The effect of active insulin i.e. $(1/min)$
- $I(t)$: Blood insulin concentration (mU/L)
- $I_2(t)$: Active insulin concentration (mU/L)
- G_b: Basal blood glucose concentration (mg/dL)
- I_b: Basal blood insulin concentration (mU/L)
- V_G : Volume of the glucose compartment (dL)
- p_1: Glucose clearance rate $(1/min)$
- p_2: Rate of clearance of active insulin $(1/min)$
- p_3: Increase in uptake ability caused by insulin. (L/$(min)^2$ mU))
- p_4: decay rate of blood insulin $(1/min)$
- p_5: The target glucose level (mg/dL)
- p_6: Rate of pancreatic release after glucose bolus $(m\ U\ dL/L\ mg\ min)$
- V_{I_2} : Volume of the remote pool (L)
- Q_{G1} : flow (dL/min)
- Q_{G2} : flow (dL/min)
- $Q_{I_1 1}$: flow (L/min)
- $Q_{I_2 2}$: flow (L/min)
- w_1 : effect factor $[dl^2/(min \cdot mU)]$
- w_2 : effect factor $[dl^2/(min \cdot mU)]$

3 MATHEMATICAL MODEL [3]

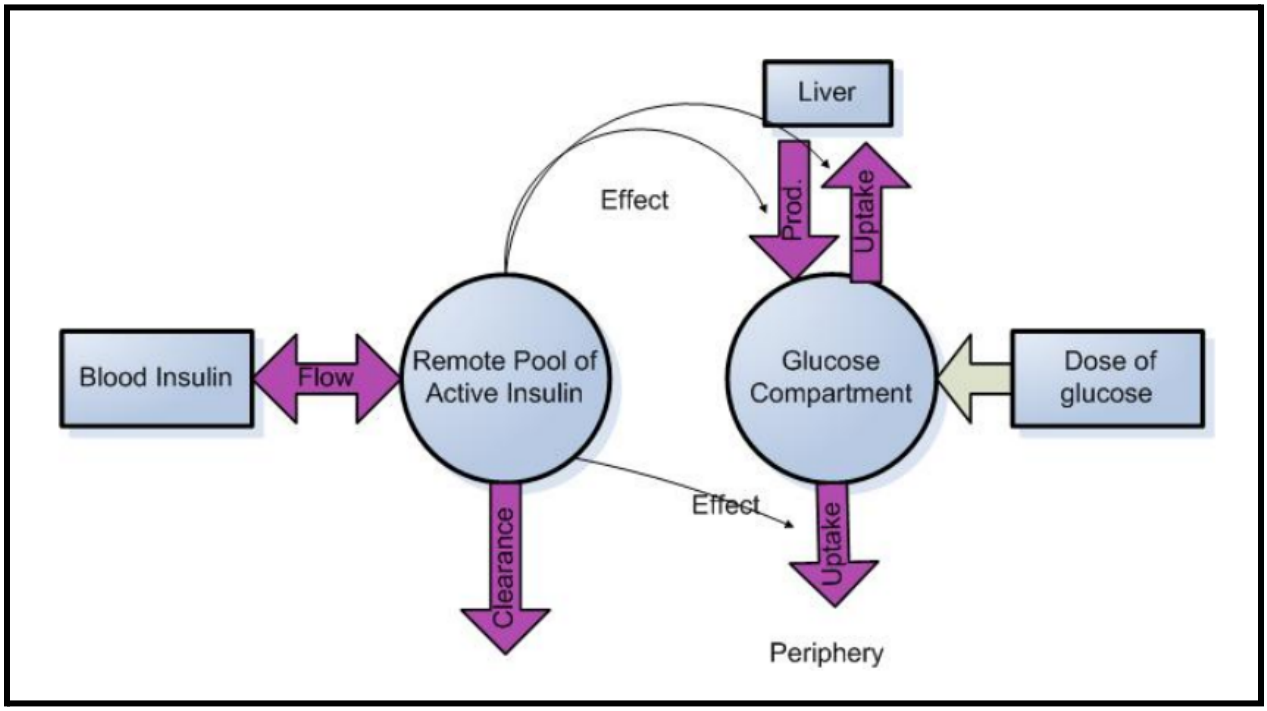

Figure 3: Graphical representation of the minimal glucose model[3]

Let's start with the rule of mass balances:

$$accumulated = V_G \cdot G(t_0 + \Delta t) - V_G \cdot G(t_0)$$

This equation represents the net change in glucose concentration over a small time interval (Δt).

Glucose A compartment is responsible for maintaining a baseline glucose concentration (G_b) through the movement of glucose in and out. The major elements involved in this process are the uptake of glucose by peripheral tissues (upt_p), the uptake of glucose by the liver (upt_l), and glucose production by the liver. The equilibrium between the liver's production and uptake is termed Net Hepatic Glucose Balance($NHGB$), which can be augmented by insulin. The levels of $NHGB$ and uptake by peripheral tissues are denoted as

$$upt_p = (Q_{G1} \cdot G(t) \cdot \Delta t + G(t) \cdot k \cdot w_1 \cdot I_2(t) \cdot \Delta t) + upt_{gluinsid}$$

$$NHGB = prod_{gluinsid} - (Q_{G2} \cdot G(t) \cdot \Delta t + G(t) \cdot k \cdot w_2 \cdot I_2(t) \cdot \Delta t)$$

Here, k is a constant, and $prod_{gluinsid}$ and $upt_{gluinsid}$ represent glucose and insulin-independent production and uptake, respectively.

According to Steil et al., the basal glucose concentration G_b is determined by the difference between glucose and insulin-independent production and uptake:

$$prod_{gluinsid} - upt_{gluinsid} = Q_{G1} \cdot G_b \cdot \Delta t + Q_{G2} \cdot G_b \cdot \Delta t$$

This difference gives the threshold G_b for glucose concentration.

By inserting this term into the mass balance equation, you get:

$$accumulated = V_G \cdot G(t_0 + \Delta t) - V_G \cdot G(t_0) \Leftrightarrow NHGB - upt_p$$
$$= (Q_{G1} \cdot G_b \cdot \Delta t + Q_{G2} \cdot G_b \cdot \Delta t) + (Q_{G2} \cdot G(t) \cdot \Delta t + G(t) \cdot w_2 \cdot I_2(t) \cdot \Delta t)$$
$$+ (Q_{G1} \cdot G(t) \cdot \Delta t + G(t) \cdot k \cdot w_1 \cdot I_2(t) \cdot \Delta t)$$

Dividing by Δt and V_G, we derive the following term:

$$\frac{G(t_0+\Delta t)}{\Delta t} = \frac{Q_{G1}}{V_G} \cdot G_b + \frac{Q_{G2}}{V_G} \cdot G_b - (\frac{Q_{G1}}{V_G} \cdot G(t) + \frac{w_1}{V_G} \cdot G(t) \cdot I_2(t) + \frac{Q_{G2}}{V_G} \cdot G(t)$$
$$+ \frac{w_2}{V_G} \cdot G(t) \cdot I_2(t))$$

By defining the constants $k_1 = \frac{Q_{G1}}{V_G}$, $k_4 = \frac{w_1}{V_G}$, $k_5 = \frac{Q_{G2}}{V_G}$, $and\ k_6 = \frac{w_2}{V_G}$, we get the following differential equation:

$$\frac{dG(t)}{dt} = k_1 \cdot G_b + k_5 \cdot G_b - (k_1 \cdot G(t) + k_4 \cdot G(t) \cdot I_2(t)$$

The calculation presented here fails to consider the lag in the alteration of $I_2(t)$ caused by the transportation of insulin through capillaries. Consequently, a formula accounting for the delay is introduced. $I_2(t)$ denotes active insulin present in a distant reservoir with inflow and outflow mechanisms. During periods when the concentration of insulin in blood, $I(t)$, crosses its baseline quantity Ib, the insulin cascades into the remote reservoir. On the flip side, it flows out when $I(t)$ goes below the baseline quantity. This state of equilibrium is referenced as balanceins. Additionally, a clearance, representing another means of elimination, varies in proportion to the level of I2(t). These components are described as:

$$accumulated = V_{I2} \cdot I_2(t_0 + \Delta t) - V_{I2} \cdot I_2(t_0)$$

Dividing by Δt and V_{I2} , then taking the limit $\Delta t \to 0$ we get the following:

$$\frac{dI_2(t)}{dt} = -\frac{Q_{I_2 2}}{V_{I2}} \cdot I_2 + \frac{Q_{I_2 1}}{V_{I2}} (I_t - I_b)$$

Define constants $k_3 = \frac{Q_{I_2 2}}{V_{I2}}$ and $k_2 = \frac{Q_{I_2 1}}{V_{I2}}$, resulting in:

$$\frac{dI_2(t)}{dt} = -k_3 \cdot I_2 + k_2 \cdot (I_t - I_b)$$

$\frac{dI_2(t)}{dt}$ describes the delay in the change of $I_2(t)$, but instead of that we introduce

$$X(t) = (k_4 + k_6) \cdot I_2(t)$$

Also, introducing the constants:

$$p_1 = k_1 + k_5$$

$$p_2 = k_3$$

$$p_3 = k_2 \cdot (k_4 + k_6)$$

Now we got,

$$\frac{dG(t)}{dt} = -p_1 \cdot G(t) + p_1 \cdot G_b$$

$$\frac{dX(t)}{dt} = -p_2 \cdot X(t) + p_3 \cdot (I(t) - I_b)$$

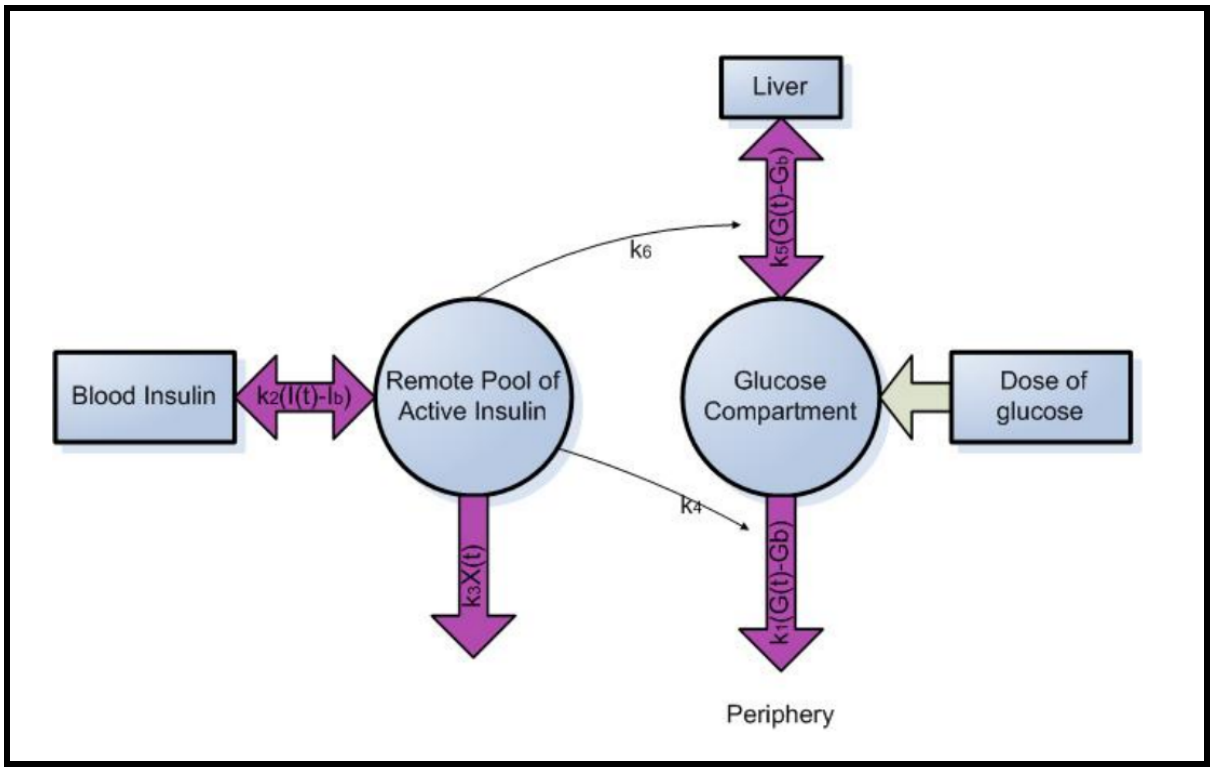

Figure 4: The minimal model describing glucose kinetics[3]

Utilizing insulin levels as input, the primary use for the Glucose Minimal Model is interpreting data from the Intravenous Glucose Tolerance Test (IVGTT). Deriving two key parameters, Insulin Sensitivity and Glucose Effectiveness (SG), is accomplished by employing parameter estimation techniques - such as weighted nonlinear least squares.

Glucose Effectiveness (S_G) represents the rate at which glucose is taken up independently of insulin. In this model, $S_G = p_1$, where is p_1 defined as the combination of two uptake rates: k1 and k5. These rates depend on $G(t)$, but not on $X(t)$.

To find an expression for insulin sensitivity, we need to maintain $X(t)$ at a steady state.

$$\frac{dX(t)}{dt} = -p_2 \cdot X(t) + p_3 \cdot (I(t) - I_b)$$

$$\Leftrightarrow X(t) = \frac{p_3}{p_2} \cdot (I(t) - I_b)$$

Now we can write $\frac{dG(t)}{dt}$ as

$$\frac{dG}{dt} = -(p_1 + X) \cdot G + p_1 \cdot G_b$$

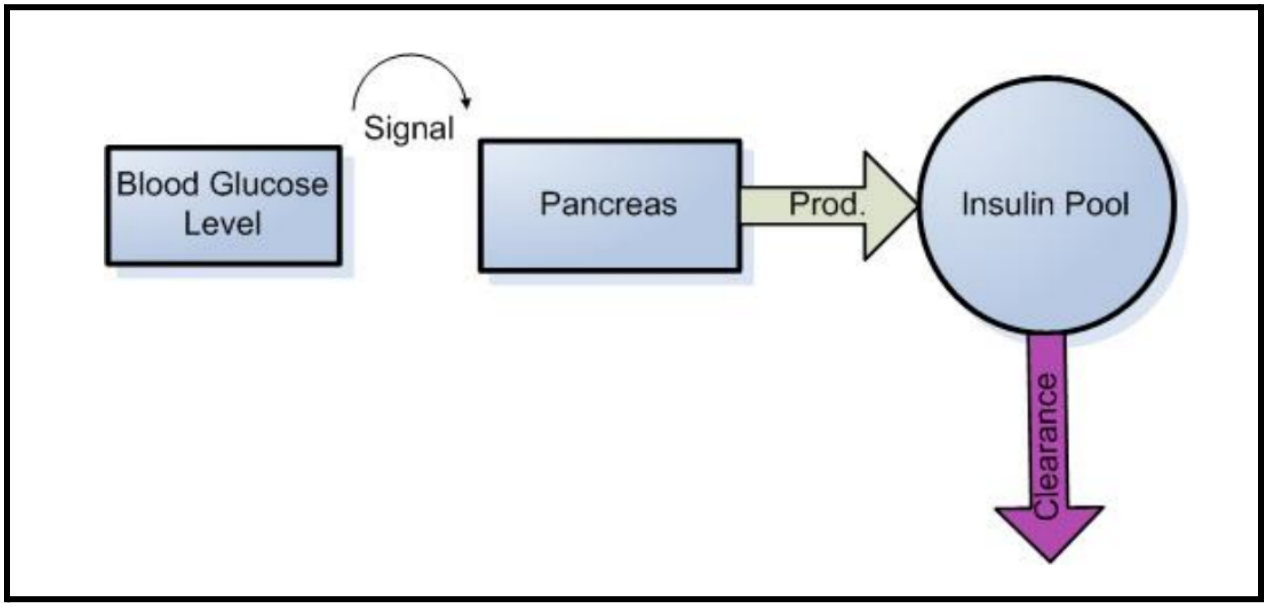

Figure 5: Graphical representation of the insulin minimal model[3]

We begin the insulin model by considering the accumulated part of the equation, which represents the difference between the initial and final blood insulin mass.

$$accumulation = V_I \cdot I(t_0 + \Delta t) - V_I \cdot I(t_0)$$

The equation above accounts for the net change in insulin for the small amount of time(Δt).

The pancreas is the primary source of insulin. Insulin is continuously produced and cleared to maintain the basal insulin concentration (I_b). The amount of insulin in the blood affects both how much is produced and how much is cleared. Clearance of insulin increases above basal (I_b), and synthesis of insulin increases below basal (I_b). In addition, the pancreas releases more insulin at a set rate in response to high glucose levels.

$$Pancreas(t) = (G(t) - p_5)^+ \cdot t$$

where $(\dots)^+$ will be 0 if $(\dots) < 0$.

This $(G(t) - p_5)^+$ determines the extent of insulin production.

Although the above-mentioned pancreatic function responds to the Intravenous Glucose Tolerance Test (IVGTT), it is unable to account for the first insulin surge seen during an IVGTT.

Insulin concentration, at its original value (I_0), is used to indicate this first peak. However, the second insulin peak is described by pancreatic function. The pancreas function is multiplied by "t", indicating that the pancreas reaction is proportional to both the degree of hyperglycemia attained and the amount of time since the glucose stimulus. We get the following equation by using the basal production/clearance term and the pancreas function as the 'in-out' component in the rule of mass balances.

Equations:

$$accumulated = in - out + generated - consumed$$

$$\Rightarrow accumulated = Pancreas(t) + (Prodbasal - clearance)$$

$$\Rightarrow V_I \cdot I(t_0 + \Delta t) - V_I \cdot I(t_0) = Q_{I2} \cdot (G(t) - p_5)^+ \cdot t \cdot \Delta t - (Q_{I1} \cdot (I(t) - I_b)\Delta t)$$

The equation describes the change of insulin accumulation over time in response to glucose and basal insulin production/clearance.

When we divide the equation by V_I and Δt where $\Delta t \to 0$, we get the following equation:

$$\frac{dI}{dt} = p_6 \cdot (G - p_5)^+ t - p_4 \cdot (I - I_b)$$

Where $p_6 = \frac{Q_{I2}}{V_I}$ and $p_4 = \frac{Q_{I1}}{V_I}$

4 ASSUMPTIONS

The assumptions taken into consideration are:

- The insulin secretion by the pancreas occurs in two phases: a rapid first-phase release and a slower second-phase release.
- The relationship between insulin and glucose uptake is more complex, but a linear approximation is used to simplify the modeling process.
- All insulin is treated as a single compartment in the body.
- There is no delay between when insulin is released and when it starts to act on glucose uptake.
- The parameters describing insulin sensitivity and glucose effectiveness are constant over the measurement period.
- The system is in a steady-state condition, which simplifies the mathematical analysis.
- The glucose production by the liver is constant and does not change in response to insulin or other factors.
- All tissues have the same insulin sensitivity and glucose effectiveness.

5 GOVERNING EQUATIONS

We use the Bergman minimal model to describe the dynamic interplay of glucose, insulin, and their regulatory processes in context to our study in the numerical analysis of glucose control in diabetic patients.

The model comprises three key differential equations:

- **Glucose Rate Equation ($\frac{dG}{dt}$):**

  The rate of change of glucose concentration (dG/dt) characterizes the dynamics of blood glucose levels. It considers glucose production, glucose uptake, and their regulation. This equation describes the rate of change in glucose concentration as influenced by insulin concentration (X) and glucose basal production (Gb).

$$\frac{dG}{dt} = -(p_1 + X) \cdot G + p_1 \cdot G_b \qquad (1)\ [3]$$

- **Dynamic Insulin Sensitivity Equation ($\frac{dX}{dt}$):**

  The rate of change of dynamic insulin sensitivity (dX/dt) represents the patient's insulin sensitivity over time. This equation quantifies how insulin sensitivity is influenced by insulin concentration and other parameters. It accounts for the rate of insulin uptake (p2) and its effect on glucose uptake (p3).

$$\frac{dX}{dt} = -p_2 \cdot X + p_3 \cdot (I - I_b) \qquad (2)\ [3]$$

- **Insulin Concentration Equation ($\frac{dI}{dt}$):**

  The rate of change of insulin concentration (dI/dt) accounts for the dynamics of insulin secretion and its effects on glucose regulation. Depending on the current glucose levels relative to a threshold (p5), insulin concentration can either decrease or increase. If glucose levels are below the threshold, insulin concentration decreases due to insulin clearance (p4). Conversely, if glucose levels exceed the threshold, insulin concentration increases with a rate constant (p6) proportional to the deviation of glucose from the threshold.

$$\frac{dI}{dt} = p_6 \cdot (G - p_5)^+ t - p_4 \cdot (I - I_b) \qquad (3)\ [3]$$

where $(\ldots)^+$ will be 0 if $(\ldots) < 0$.

6 INITIAL CONDITIONS

$$G(0) = G_0$$
$$X(0) = X_0$$
$$I(0) = I_0$$

The initial conditions taken into consideration are:

X_0 = 0 [assuming no initial glucose effectiveness]

G_0 = 291.2 mg/dL [starting glucose concentration at the basal level in a diabetic patient]

I_0 = 0 [assuming no insulin concentration at the basal level]

7 NUMERICAL SOLUTIONS[5]

We will use the **Runge-Kutta method** to solve our system of three first-order differential equations. The Runge-Kutta method is an iterative numerical technique for solving ordinary differential equations. The accuracy of your solution depends on the choice of step size and the convergence of the Runge-Kutta method.

Runge-Kutta (RK) methods offer a means to achieve an accuracy comparable to a Taylor series approach while avoiding the need to compute higher-order derivatives. These methods come in various forms but can all be expressed using a generalized equation.

$$y_{i+1} = y_i + \phi(x_i, y_i, h) \cdot h$$

where $\phi(x_i, y_i, h)$ is called an increment function, which can be interpreted as a representative slope over the interval. Its general form can be written as

$$\phi = a_1 \cdot k_1 + a_2 \cdot k_2 + \ldots + a_n \cdot k_n$$

where the a's are constants and the k's are

$$k_1 = f(x_i, y_i)$$

$$k_2 = f(x_i + p_1 \cdot h, y_i + q_{11} \cdot h \cdot k_1)$$

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$$k_n = f(x_i + p_{n-1} \cdot h, y_i + q_{n-1,1} \cdot h \cdot k_1 + q_{n-1,2} \cdot h \cdot k_2 + \ldots + q_{n-1,n-1} \cdot h \cdot k_{n-1})$$

where the p's and q's are constants. Notice that the k's are recurrence relationships. That is, k_1 appears in the equation for k_2, which appears in the equation for k_3, and so forth. Because each k is a functional evaluation, this recurrence makes RK methods efficient for computer calculations.

We will use the fourth-order Runge-Kutta method.

$$y_{i+1} = y_i + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4) \cdot h$$

where

$$k_1 = f(x_i,\ y_i)$$

$$k_2 = f(x_i + \tfrac{1}{2}h,\ y_i + \tfrac{1}{2}h \cdot k_1)$$

$$k_3 = f(x_i + \tfrac{1}{2}h,\ y_i + \tfrac{1}{2}h \cdot k_2)$$

$$k_1 = f(x_i + h,\ y_i + h \cdot k_3)$$

By this above method we will proceed with these equations:

$$\frac{dG}{dt} = -(p_1 + X) \cdot G + p_1 \cdot G_b$$

$$\frac{dX}{dt} = -p_2 \cdot X + p_3 \cdot (I - I_b)$$

$$\frac{dI}{dt} = p_6 \cdot (G - p_5)^+ t - p_4 \cdot (I - I_b)$$

From initial conditions,

$$G(0) = 291.2\ mg/dL$$

$$X(0) = 0$$

$$I(0) = 364.8\ mU/L$$

Let the step size (h) = 0.01

Now, let's calculate the intermediate values at each time step using the RK4 method. We'll start with the values at t = 0:

Calculate k_1 values for each variable:

$$k_1(G) = -(p_1 + X_0) \cdot G_0 + p_1 \cdot G_b$$

$$k_1(X) = -p_2 \cdot X_0 + p_3(I_0 - I_b)$$

$$k_1(I) = p_6 \cdot (G_0 - p_6)^+ t - p_4 \cdot (I_0 - I_b)$$

Calculate intermediate values (at t = 0.01/2 = 0.005):

$$G_1 = G_0 + \tfrac{h}{2}k_1(G)$$

$$X_1 = X_0 + \frac{h}{2}k_1(X)$$

$$I_1 = I_0 + \frac{h}{2}k_1(I)$$

Calculate k_2 values for each variable at t = 0.005:

$$k_2(G) = \; -(p_1 + X_1) \cdot G_1 + p_1 \cdot G_b$$

$$k_2(X) = \; -p_2 \cdot X_1 + p_3(I_1 - I_b)$$

$$k_2(I) = \; p_6 \cdot (G_1 - p_6)^+ t - p_4 \cdot (I_1 - I_b)$$

Calculate intermediate values (at t = 0.01/2 = 0.005):

$$G_2 = G_0 + \frac{h}{2}k_2(G)$$

$$X_2 = X_0 + \frac{h}{2}k_2(X)$$

$$I_2 = I_0 + \frac{h}{2}k_2(I)$$

Calculate k_3 values for each variable at t = 0.005:

$$k_3(G) = -(p_1 + X_2) \cdot G_2 + p_1 \cdot G_b$$

$$k_3(X) = -p_2 \cdot X_2 + p_3(I_2 - I_b)$$

$$k_3(I) = \; p_6 \cdot (G_2 - p_6)^+ t - p_4 \cdot (I_2 - I_b)$$

Calculate intermediate values (at t = 0.01):

$$G_3 = G_0 + k_3(G)$$

$$X_3 = X_0 + k_3(X)$$

$$I_3 = I_0 + k_3(I)$$

Calculate k_4 values for each variable at t = 0.01:

$$k_4(G) = -(p_1 + X_3) \cdot G_3 + p_1 \cdot G_b$$

$$k_4(X) = -p_2 \cdot X_3 + p_3(I_3 - I_b)$$

$$k_4(I) = p_6 \cdot (G_3 - p_6)^+ t - p_4 \cdot (I_3 - I_b)$$

Now, you can use these k values to calculate the updated values for $G,\ X,\ and\ I$ at t = 0.01 using the RK4 formula:

$$G(0.01) = G(0) + \frac{h}{6}[k_1(G) + 2k_2(G) + 2k_3(G) + k_4(G)]$$

$$X(0.01) = X(0) + \frac{h}{6}[k_1(X) + 2k_2(X) + 2k_3(X) + k_4(X)]$$

$$I(0.01) = I(0) + \frac{h}{6}[k_1(I) + 2k_2(I) + 2k_3(I) + k_4(I)]$$

Repeat these steps for subsequent time points (t = 0.02, 0.03, ...) to obtain the numerical solution for G, X, and I as you advance in time.

8 ALGORITHMS USED

- **Import libraries like Numpy and Matplotlib.**
  Numpy is imported as np for numerical computations.
  Matplotlib.pyplot is imported as plt for plotting graphs.

- **Define the differential equations.**
  Our three governing equations, dGdt, dXdt, and dIdt are defined.
  They represent the rate of change of variables $G, X, and\ I$ over time, respectively.

- **Set the initial conditions.**
  The initial values of $G, X, and\ I$ as well as parameters are defined.
  G0 = 291.2 (mg/dL)
  X0 = 0.0 (1/min)
  I0 = 364.8 (mU/L)
  p1 = 0.0317 (1/min)
  p2 = 0.0123 (1/min)
  p3 = 0.492*1e-5 (L/$(min)^2$ mU))
  p4 = 0.2659 (1/min)
  p5 = 79.0353 (mg/dL)
  p6 = 0.0039 (mUdL/ L mg min)
  Gb = 60.0 (mg/dL)
  Ib = 7.0 (mU/L)

- **Set time parameters.**
  t_start = 0 min
  t_end = 200 min
  h = 0.01 min
  Here, t_start, t_end define the time intervals over which the equations will be solved.
  h is the step size used for numerical integration.

- **Initialize the arrays to store the required information.**
  The arrays t_values, G_values, X_values, and I_values are initialized.
  t_values → store the time steps
  G_values → store the G values
  X_values → store the X values
  I_values → store the I values

- **Perform the Runge-Kutta Method**

A while loop is used to iteratively solve the differential equations over the specified time interval.
Inside the loop, the fourth-order Runge-Kutta method is applied for each time step:
k1_G, k1_X, and k1_I are calculated based on the initial values of G, X, and I and the differential equations.
k2_G, k2_X, and k2_I are calculated using the updated values from halfway through the time step.
k3_G, k3_X, and k3_I are similarly calculated using k2 values.
k4_G, k4_X, and k4_I are calculated using the final k3 values.
The new values of G, X, and I are updated using a weighted average of these k values.
The time, t, is incremented by the step size h.
The updated values are appended to the result arrays.

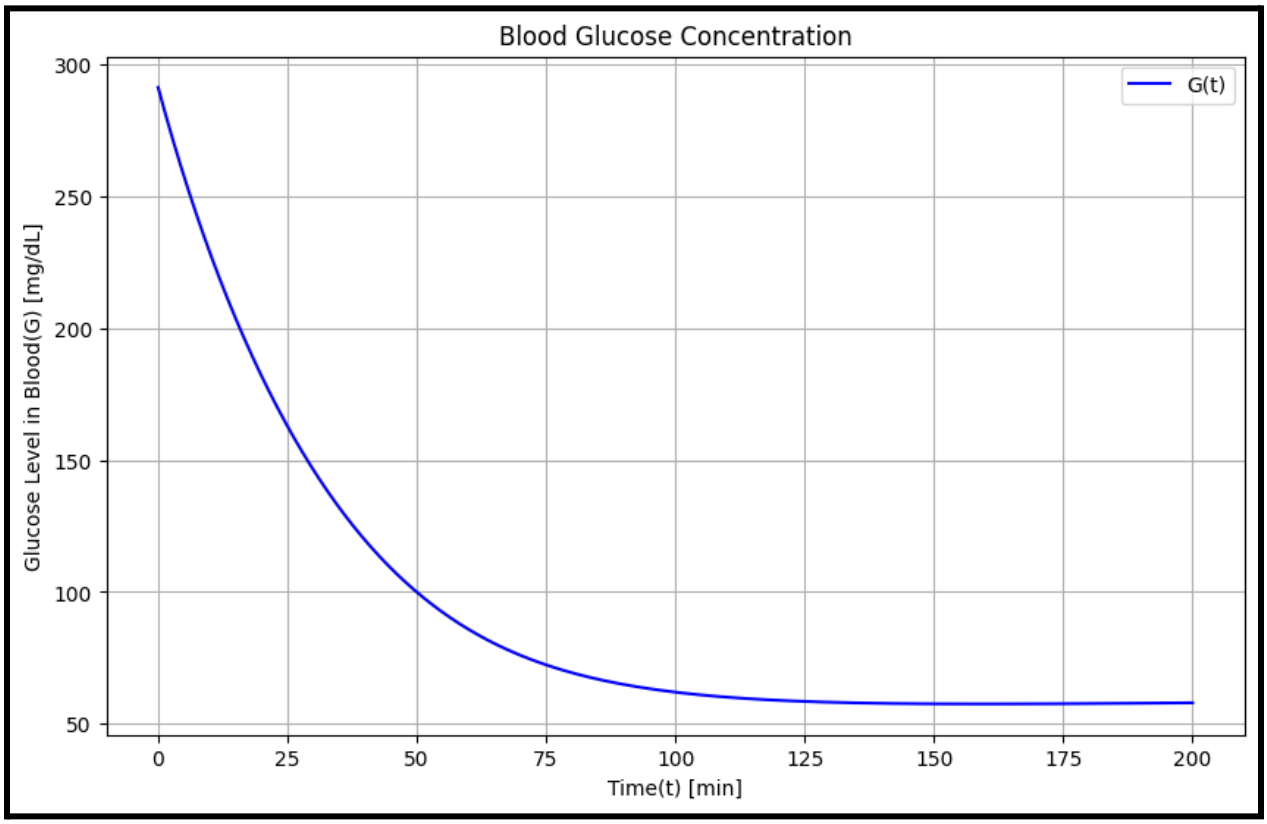
- **Plot the results**
  Plot the results using Matplotlib.
  The code uses Matplotlib to create a plot showing how the values of $G(t),\ X(t)\ and\ I(t)$ change over time.

9 RESULTS AND DISCUSSIONS

9.1 GRAPH INTERPRETATION

The obtained graphs after solving the differential equations of the **Bergman minimal model** using Runge Kutta method are below.

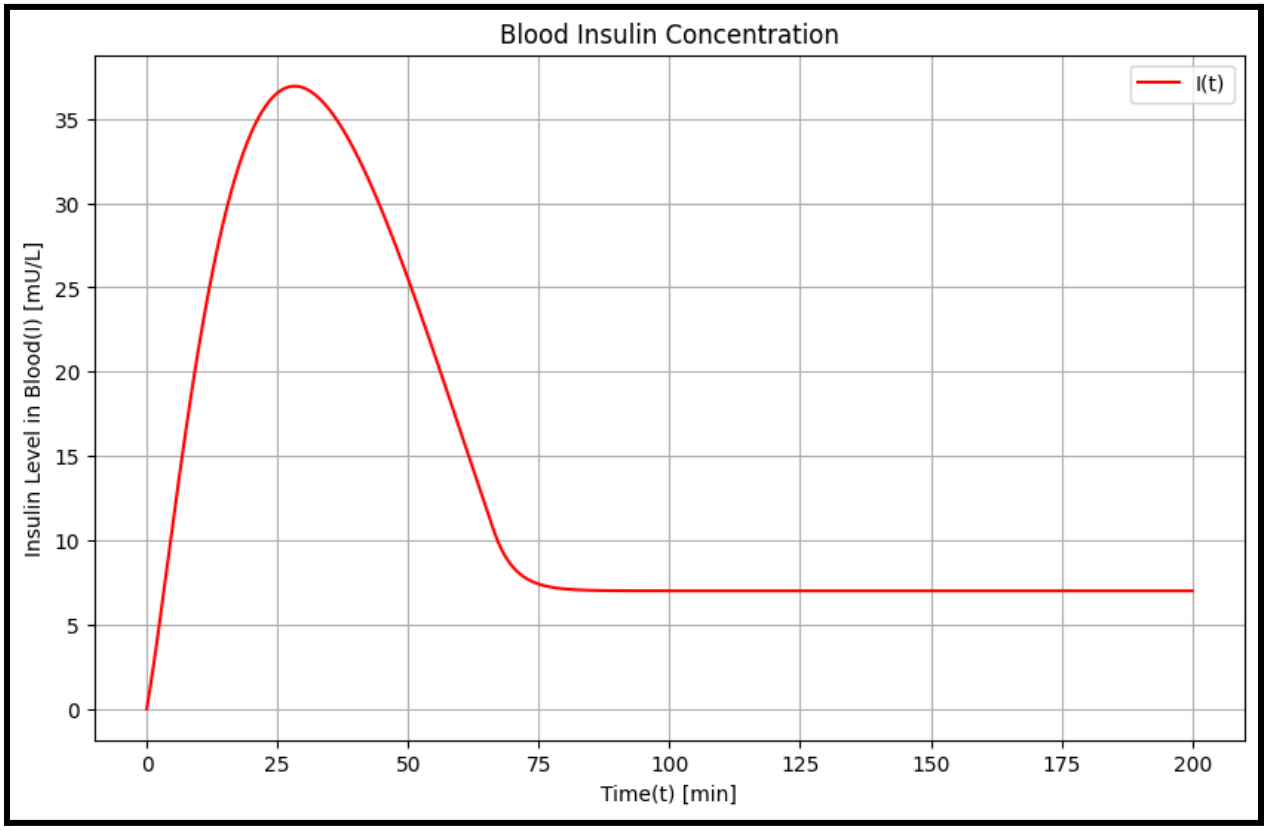
The **first graph** represents the change in glucose level with respect to time. Initially, at time t=0, the blood glucose level is maximum in the diabetic patient. And we can notice from the below graph, the glucose in the blood decreases with respect to time. This decrease is due to the insulin which is infused into the fatty tissue inside the patient. The maximum value of glucose beyond which insulin has to be pumped can be initialized in the closed system monitor program.



Change in Glucose level with time

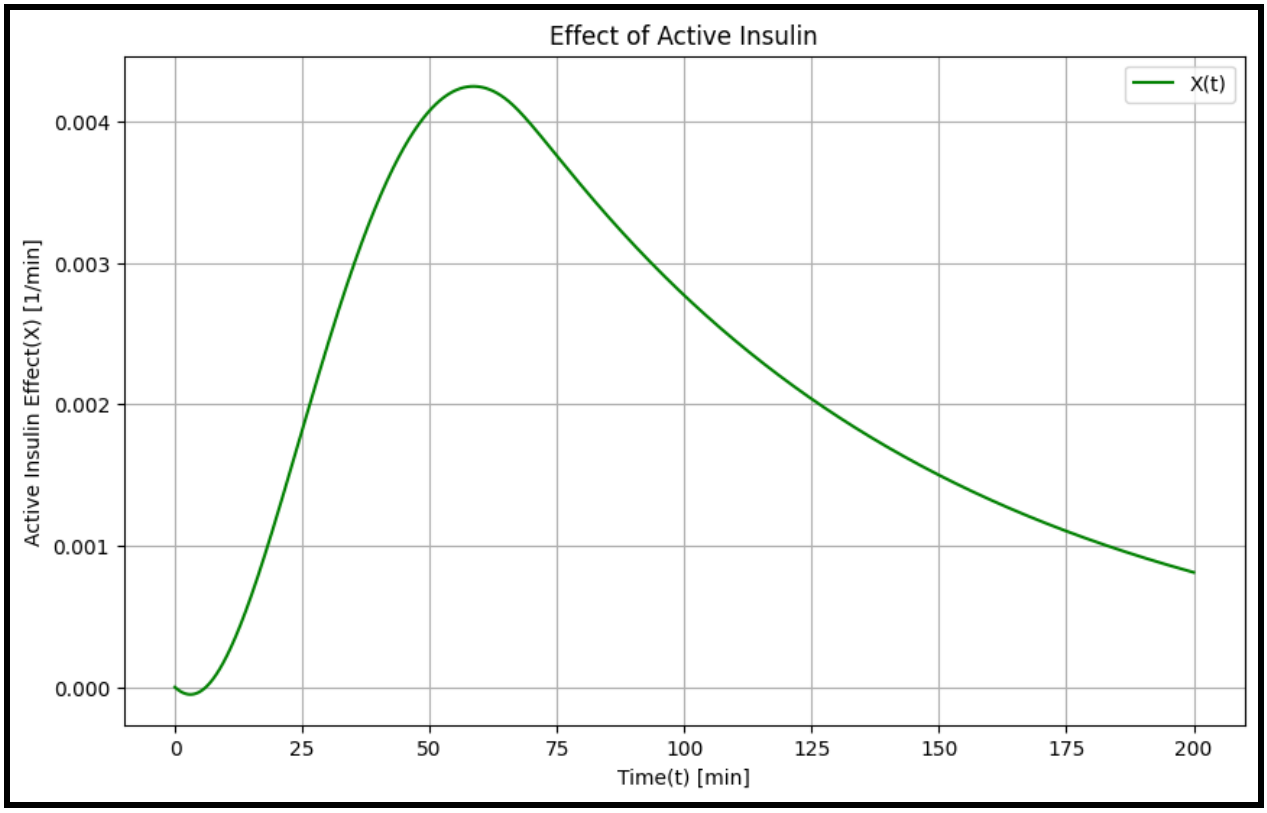
The **second graph** represents the Insulin level concentration in the blood with respect to time. So initially at time t=0, the insulin concentration in the blood is 0 according to our initial conditions. As we are continuously monitoring the blood glucose level, we can set a threshold concentration level, beyond which a bolus of insulin should be infused into the fatty tissue from the insulin pump. This leads to sudden increase or hike in the concentration of insulin in the blood.

Now as the insulin concentration in the blood increases, the effect of insulin actively involved in the disappearance of the blood glucose also increases but with a time lag.
As the blood glucose concentration decreases, the insulin pumped in also reduces later and the insulin concentration in the blood also reduces. After some time, when glucose level becomes normal , the insulin concentration also becomes constant with time.



Change in Insulin level with time

The **third graph** represents the change in active insulin effect with respect to time.
Active insulin effect refers to the amount of insulin that is currently active in the body and actively lowering blood glucose levels.
Initially at time t=0, according to our initial conditions, there will be a time lag for the active insulin to act on the high level glucose. Therefore at t=0, the active insulin effect is also negligible.
Now as we are continuously monitoring the blood glucose level, when the sensor senses a higher glucose level, it lets the insulin pump infuse insulin into the fatty tissue. Due to which the insulin concentration that is acting upon the glucose rises.
With time as the active insulin effect attains a peak, the glucose level almost tends to the normal level.
Now as the glucose level decreases, the active insulin effect also reduces since the insulin concentration in the blood will also drop.



Change inActive insulin level with time

9.2 FINAL INTERPRETATION OF ALL THREE GRAPHS :

The continuous glucose monitor when it senses a higher blood glucose level, triggers the insulin pump to infuse insulin into the bloodstream. Hence the insulin concentration in the blood increases suddenly. This also leads to the active insulin effect to increase with a certain lag. The glucose level decreases with the increase in the active insulin effect. Eventually, the insulin concentration reduces leading to the active insulin effect also decreasing. At time t tending to infinity, the glucose level becomes constant and normal, leading to constant insulin concentration level in the blood. This leads to the active insulin effect to also decrease gradually. This process repeats whenever needed by the diabetic patient.

9.3 CONCLUSION :

Hence using the Bergman minimal model differential equations, we successfully interpreted the actual implication of the insulin pump working in a closed system for the maintenance of normal blood glucose level in diabetic patients.

10 ACKNOWLEDGEMENTS

We would like to express our heartfelt gratitude towards **Prof. Akshaa Vatwani** and **Prof. Dilip Srinivas Sundaram** for providing an opportunity to learn the various methods of numerical analysis to solve the differential equations. This assignment helped us to integrate the theoretical knowledge with the real-time practical applications.

We would like to express our heartfelt gratitude towards **Prof. Umashankar Singh** for guiding us with our topic and helping us.

We got the experience to solve the large scale problems using the conventional methods of numerical analysis.

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Code:

Solution_code