Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2025, 2025:139
https://doi.org/10.28919/cmbn/9609
ISSN: 2052-2541

IMPACT OF FOOD INTAKE ON GLUCOSE AND INSULIN REGULATION: AN INTEGRATED MATHEMATICAL MODEL

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Abstract. This study presents a novel and original mathematical model that integrates glucose, insulin, beta cells, and food intake dynamics to explore their interrelationships and impact on glycemic regulation. The model incorporates differential equations representing the changes in glucose levels, insulin secretion, beta cell activity, and dietary intake. By analyzing the stability of equilibrium points, we aim to understand how variations in food intake influence glucose and insulin dynamics. The originality of this model lies in its comprehensive approach to incorporating food intake as a critical factor in glucose homeostasis. The results provide insights into the mechanisms governing glycemic regulation, offering a framework for predicting the effects of dietary changes and improving diabetes management strategies. This model has potential applications in clinical settings, aiding in the personalization of dietary recommendations and therapeutic interventions for individuals with diabetes.

Keywords: mathematical model; glycemic regulation; glucose homeostasis; food intake dynamics; stability analysis; metabolic regulation.

2020 AMS Subject Classification: 92C50.

1. INTRODUCTION

Diabetes, historically associated with economic development and previously considered a disease of wealthier nations, has now become a global public health issue affecting countries

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Received September 21, 2025

worldwide, especially low- and middle-income countries. According to the latest International Diabetes Federation (IDF) report, approximately 80% of the 371 million people living with diabetes are in low- and middle-income countries. Nearly five million deaths are attributed to this disease, and over 471 billion USD was spent on diabetes-related healthcare in 2023 [1]. Due to its chronic nature and severe complications, diabetes requires long-term, costly treatment and care, impacting not only individuals but entire societies and raising equity issues within and across countries [2]. While diabetes prevalence is rising globally, the Middle East and North Africa region has the highest comparative prevalence at 11%. Six of the ten countries with the highest diabetes prevalence (in adults aged 20 to 79) are in this region: Kuwait (21.1%), Lebanon (20.2%), Qatar (20.2%), Saudi Arabia (20%), Bahrain (19.9%), and the United Arab Emirates (19.2%) [1, 3]. As a result, the direct and indirect socioeconomic burden of diabetes is exponentially increasing in this region [4, 5]. In recent decades, numerous mathematical models have been developed to simulate, analyze, and understand the dynamics of glucose and insulin leading to diabetes. Among the pioneers, Bolie (1961) proposed a simple linear model using ordinary differential equations to represent glucose and insulin interactions [6]. The most widely used model is the minimal model, published in the early 1980s by Bergman et al. [7]. Various authors have developed versions and critical extensions of this minimal model, including Derouich and Boutayeb (adding physical activity) [8], De Gaetano and Arino (using delay differential equations) [9], Li et al. (proposing a generalized model) [10], and Roy and Parker (expanding the model to include free fatty acids) [11]. Other research has focused on β-cell dynamics and mechanisms leading to diabetes. Topp et al. developed a model for pathways to diabetes by considering βcell mass alongside insulin and glucose kinetics [12]. Hernandez et al. proposed an extension of Topp's model by adding insulin receptor dynamics on cell surfaces [13]. Using a model similar to Topp's, De Gaetano and colleagues introduced the concept of pancreatic reserve [14]. Gallenberger et al. later developed a model describing glucose and insulin concentration dynamics in relation to the β-cell cycle [15]. Furthermore, diet plays a crucial role in regulating glucose and insulin, also influencing β-cell dynamics essential for insulin production and secretion. The quality and quantity of consumed nutrients can significantly affect blood glucose levels and insulin response, potentially contributing to the

progression toward diabetes. Studies indicate that certain nutrients, such as refined carbohydrates and saturated fats, can worsen insulin resistance, while a diet rich in fiber and unsaturated fats can enhance glycemic regulation. For further details on these models, readers are referred to recent reviews covering various approaches using differential equations, delay differential equations, integro-differential equations, stochastic differential equations, as well as optimal control methods for glycemic control, blood glucose monitoring, and diabetes prevention devices [16, 17, 18, 19, 20, 21, 22]. In this paper, we propose a mathematical model emphasizing the effect of genetic predisposition to diabetes on the dynamics of β-cells, insulin, and glucose, while taking into account the significant influence of food intake on these regulatory mechanisms

2. Materials and Methods

2.1. Impact of Food Intake. Dietary intake plays a central role in the regulation of glucose and insulin and can directly influence metabolic health and susceptibility to type 2 diabetes. Research has shown that diets high in lipids and simple carbohydrates contribute to a metabolic overload that, over time, can lead to insulin resistance and deterioration of pancreatic beta cells, key elements in the pathophysiology of type 2 diabetes [23]. Topp et al. proposed a model to understand how prolonged nutritional overload impacts beta-cell mass, insulin, and glucose, showing that an imbalanced diet accelerates beta-cell failure, making them unable to sustainably compensate for the increased insulin resistance [12]. In particular, unbalanced diets can induce metabolic and inflammatory stress, damaging beta cells and reducing their ability to produce insulin [24]. This nutrient overload activates inflammatory pathways that, combined with genetic predisposition in some individuals, significantly increase the risk of progressing to type 2 diabetes [25]. Moreover, several studies highlight how different macronutrients and dietary patterns—such as high-fat or high-carbohydrate diets—can directly affect insulin sensitivity and glucose metabolism, further supporting the need for balanced nutrition in diabetes prevention and management [26, 27].

2.2. Model Formulation. In this section, we present a mathematical model to describe the interactions between glucose, insulin, beta cells, and food intake using a system of ordinary

differential equations (ODEs). The model captures the dynamics of each variable and their interdependencies, providing a framework for analyzing metabolic regulation.

Regulating blood glucose is a complex and crucial process for maintaining homeostasis within the human body. This regulation involves sophisticated interactions among blood glucose levels, insulin, and dietary intake. Mathematical models play a fundamental role in understanding these interactions and in formulating strategies for diabetes prevention and management [28, 29, 30].

Most mathematical models describing glucose dynamics assume that the concentration of glucose in the blood is governed by a differential equation of the form:

$$\frac{dG(t)}{dt} = a - bG(t) - cI(t)G(t) \text{ [31, 7, 8, 9, 10, 11]}$$

where $G(t)$ represents the glucose concentration at time t, $I(t)$ is the insulin concentration at time t, and a, b, and c are parameters that adjust the rates of glucose increase, decrease, and absorption, respectively. Here, a represents hepatic glucose production (glucose produced by the liver), $bG(t)$ models the glucose decrease independent of insulin, and $cI(t)G(t)$ accounts for glucose absorption based on insulin concentration, capturing the effect of insulin sensitivity.

However, as noted by Li et al., the relationship between glucose and insulin, expressed through a mass-action term $cI(t)G(t)$, can be replaced by a more general expression that better reflects the complexity of biological interactions [10]. These more sophisticated models allow for a better capture of the nonlinear dynamics between glucose and insulin.

In this context, we propose a novel approach by modifying the term a to directly include the impact of food intake. Specifically, we replace the hepatic glucose production term with $aF(t)$, where $F(t)$ represents dietary glucose intake. This substitution reflects the idea that dietary intake has a direct and measurable impact on blood glucose concentration. The modified model becomes:

$$\frac{dG(t)}{dt} = aF(t) - bG(t) - cI(t)G(t) \tag{1}$$

where a adjusts the intensity of the impact of dietary intake on blood glucose levels.

This modification allows for a better understanding of how variations in dietary intake influence glucose concentration, providing a more realistic perspective on glucose management in

the context of nutrition. By integrating the term $aF(t)$, the model more accurately reflects the metabolic system's response to changes in dietary intake, while retaining the essential dynamics of insulin and glucose regulation. This approach aims to improve the model's predictions and offer more precise tools for studying diabetes management and preventing metabolic complications.

For the dynamics of insulin, we use the same expression employed in the model by Topp et al. [12], assuming that the net rate of insulin secretion can be modeled by a sigmoid function of glucose, while insulin clearance is modeled as $fI(t)$. Using a Hill function of the form $\frac{G(t)^2}{e+G(t)^2}$ as a sigmoid function reaching half of its maximum saturation at $G = \sqrt{e}$, the dynamics of insulin is given by:

$$\frac{dI(t)}{dt} = \frac{d\beta(t)G(t)^2}{e+G(t)^2} - fI(t) \tag{2}$$

where $\beta(t)$ represents the mass of pancreatic beta-cells (mg), and insulin secretion is assumed to be uniform for all beta-cells, with a maximal rate of d (mU/ml/mg).

Finally, as previously noted, we assume that the dynamics of beta-cell mass for individuals predisposed to type 2 diabetes, as used in the model by Topp et al. [12], is given by the following equation:

$$\frac{d\beta(t)}{dt} = (g + hG(t) - iG(t)^2)\beta(t) \tag{3}$$

where $\beta(t)$ (mg) represents the mass of beta-cells [13].

The novelty of our model lies in incorporating the impact of food intake on glucose dynamics through a direct influence of the food intake variable. The differential equation governing the dynamics of food intake $F(t)$ is expressed as:

$$\frac{dF(t)}{dt} = F_0 + (k_1 - 1)G(t) - k_2 I(t) \tag{4}$$

BIOLOGICAL INTERPRETATION OF THE EQUATION FOR $F(t)$

The equation:

$$\frac{dF(t)}{dt} = F_0 + (k_1 - 1)G(t) - k_2 I(t)$$

describes the dynamics of food intake $F(t)$ as a function of glucose levels $G(t)$ and insulin levels $I(t)$.

- $F(t)$: Represents the food intake, indicating the amount of energy available in the system due to food consumption. This is crucial for meeting the body's energy demands.
- F_0: Refers to a baseline food intake level, representing the minimum energy the body requires to function, even in the absence of other stimuli [32].
- $(k_1-1)G(t)$: Illustrates the influence of glucose on food intake.
  - If $k_1 > 1$: An increase in glucose $G(t)$ signals adequate energy availability, which may lead to a decrease in hunger and food intake. This reflects a normal metabolic response where high glucose levels indicate sufficient energy, reducing the desire to eat [33].
  - If $k_1 < 1$: An increase in $G(t)$ could paradoxically increase appetite. This phenomenon may occur in pathological states, such as insulin resistance, where the body does not effectively respond to elevated glucose levels [34].
- $-k_2 I(t)$: Shows that insulin plays an inhibitory role on food intake. When insulin levels rise (in response to increased glucose), it signals the brain that energy stores are sufficient, reducing the sensation of hunger. Consequently, higher insulin concentrations lead to decreased food intake [35].

This equation highlights the complex interactions between food intake, glucose, and insulin. It underscores the importance of a balanced regulation of these elements to maintain optimal metabolic health and prevent imbalances, such as type 2 diabetes. By incorporating these dynamics, the model provides a framework for understanding how variations in food intake can influence glucose and insulin regulation in the body.

Based on the previous descriptions, our mathematical model is described by the following system of differential equations:

$$
\begin{cases}
\dfrac{dG(t)}{dt} = aF(t) - bG(t)I(t) - cG(t) \\
\dfrac{dI(t)}{dt} = d\beta(t)\dfrac{G(t)^2}{e+G(t)^2} - fI(t) \\
\dfrac{d\beta(t)}{dt} = \left(-g + hG(t) - iG(t)^2\right)\beta(t) \\
\dfrac{dF(t)}{dt} = F_0 + (k_1-1)G(t) - k_2 I(t)
\end{cases} \tag{5}
$$

All the coefficient parameters, thier interpretation and value are recalled in Table 1 [12, 36, 37, 38].

Parameter	Value	Units	Biological Interpretation
a	1.2	mg/dl	Proportionality factor for the effect of food intake on glucose concentration.
c	1.44	d^{-1}	glucose clearance rate independent of insulin
b	0.72	ml/μU d	insulin induced glucose uptake rate
d	43.2	μU/ml d mg	β-cell maximum insulin secretory rate
e	20,000	mg^2/dl^2	gives inflection point of sigmoidal function
f	342	d^{-1}	whole body insulin clearance rate
i	0.2423e-5	dl^2/mg^2 d	determines β-cell glucose tolerance range
g	0.03	d^{-1}	β-cell natural death rate
h	0.84e-3	dl/mg d	determines β-cell glucose tolerance range
F_0	500	calories/time	Baseline rate of change in food intake over time
k_1	1.1	calories/time	Coefficient that regulates how glucose concentration affects the rate of change of food intake
k_2	20	calories/time	Coefficient that regulates how insulin concentration affects the rate of change of food intake.

TABLE 1. Table of parameters with their values, units, and biological interpretation.

3. EQUILIBRIUM POINTS

Proposition 1. *The mode* (1) *admits 3 equilibrium point follow:*

$P_1(G_1, I_1, \beta_1, F_1)$, $P_2(G_2, I_2, \beta_2, F_2)$ $P_3(G_3, I_3, \beta_3, F_3)$

where

$$G_1 = \frac{F_0}{1-k_1}; I_1 = 0; \beta = 0; F_1 = \frac{cF_0}{(1-k_1)a},$$

and

$$G_2 = \frac{-h+\sqrt{h^2-4ig}}{-2i}; I_2 = \frac{F_0+(k_1-1)G_2}{k_2}$$

$$F_2 = \frac{bG_2I_2+cG_2}{a}, \beta_2 = \frac{fI_2(e+G_2^2)}{dG_2^2}$$

$$G_3 = \frac{-h-\sqrt{h^2-4ig}}{-2i}; I_3 = \frac{F_0+(k_1-1)G_3}{k_2}$$

$$F_3 = \frac{bG_3I_3+cG_3}{a}; \beta_3 = \frac{fI_3(e+G_3^2)}{dG_3^2}$$

The condition $h^2 \geq 4ig$ must be met.

Regarding the equilibrium point P_1, its existence is shown under the following conditions: $k_1 < 1$ for P_1 and $k_1 > 1$ for P_2, P_3

Equation 3 gives:

$$\beta(t) = 0 \text{ or } -g + hG(t) - iG(t)^2 = 0$$

thus,

$$\beta = 0 \text{ or } \triangle = h^2 - 4ig$$

which implies

$$\beta = 0 \text{ or } \triangle = h^2 - 4ig > 0$$

under the condition $h^2 \geq 4ig$; this leads to

$$\beta = 0 \text{ or } G_1 = \frac{h - \sqrt{h^2 - 4ig}}{2i} \text{ or } G_2 = \frac{h + \sqrt{h^2 - 4ig}}{2i}$$

Thus, the system (5) admits the following three equilibrium points:
$P_1(G_1, I_1, \beta_1, F_1)$, $P_2(G_2, I_2, \beta_2, F_2)$ $P_3(G_3, I_3, \beta_3, F_3)$

4. Stability Analysis

To analyze the stability of the equilibrium points, we compute the Jacobian matrix of the system. The Jacobian matrix J is given by:

$$J = \begin{pmatrix} -bI - c & -bG & 0 & a \\ \frac{2ed\beta G}{(e+G^2)^2} & -f & d\frac{G^2}{e+G^2} & 0 \\ (h - 2iG)\beta & 0 & -g + hG - iG^2 & 0 \\ k_1 - 1 & -k_2 & 0 & 0 \end{pmatrix}$$

We evaluate this matrix at the equilibrium points and analyze its eigenvalues to determine the stability of each point.

- $P_1(G_1,0,0,F_1)$

$$J=\begin{pmatrix} -c & -bG_1 & 0 & a \\ 0 & -f & \frac{dG_2}{e+G^2} & 0 \\ 0 & 0 & -g+hG-iG^2 & 0 \\ k_1-1 & -k_2 & 0 & 0 \end{pmatrix}$$

Characteristic Polynom is :

$$P_1(\lambda)=(-f-\lambda)(-g+hG_1-iG_1^2-\lambda)(\lambda^2+\lambda c+(1-k_1))$$

$$\lambda_1=-f$$

$$\lambda_2=-g+hG_1-iG_1^2.$$

$-g+hH_1-iG_1^2$ is negatif because G_1 is greatest from two racines G_2 and G_3.

So ; $\lambda_1<0$, $\lambda_2<0$

We have : $\lambda^2+\lambda c+(1-k_1)=0$ $c>0$ and $1-k_1>0$

- $P_2(G_2,I_2,\beta_2,F_2)$ and $P_3(G_2,I_2,\beta_3,F_3)$

The characteristic polynom is:

$$P(\lambda)=\lambda^4+A_1\lambda^3+B_1\lambda^2+C_1\lambda+D_1 \tag{6}$$

Where : $A_1=f+bI$

$$B_1=\frac{1}{(e+G^2)^2}(2ed\beta G^2b+fce^2+2fceG^2+fcG^4+fbIe^2+2fbIeG^2+fbIg^4)$$

$$C_1=\beta_1(h-2iG)\frac{db}{(e+G^2)}+a(k_1-1)$$

$$D_1=aC\beta(h-2iG)K_2+\alpha f(k_1-1)$$

Stability $P_2(G_2,I_2,\beta_2,F_2)$

Characteristic polynom (6) give :

$A_1>0$, $B_1>0$, $C_1<0$ and $D_1<0$

$G_2 = \frac{h+\sqrt{h^2-4ig}}{2i} \Longrightarrow h - 2iG_2 = -\sqrt{h^2-4ig} < 0$

$\Longrightarrow C_1 < 0$ also $D_1 < 0$

According Routh-Hurwitw P_2 is not stable

stability $P_3(G_3, I_3, \beta_3, F_3)$

P_3 is stable for the value of parameters in Table 1 for each value of a

$$J(P_3) = \begin{pmatrix} -bI_3 - c & -cG_3 & 0 & a \\ \frac{2edG_3}{(e+G_3^2)2} & -f & \frac{dG_3^2}{e+G_3^2} & 0 \\ (h-2iG_3)\beta & 0 & 0 & 0 \\ k_1 - 1 & -k_2 & 0 & 0 \end{pmatrix}$$

$$J = \begin{pmatrix} -19,8 & 72 & 0 & a \\ 146 & -432 & 11,4 & 0 \\ 0,8 & 0 & 0 & 0 \\ 0,1 & -20 & 0 & 0 \end{pmatrix}$$

The power iteration method is used to calculate the eigenvalue with the largest magnitude.

```
#include <stdio.h>
#include <stdlib.h>
#include <math.h>

// Size of the matrix
#define N 4

```

```
// Function to normalize a vector
void normalize(double *v) {
    double norm = 0.0;
    for (int i = 0; i < N; i++) {
        norm += v[i] * v[i];
    }
    norm = sqrt(norm);
    for (int i = 0; i < N; i++) {
        v[i] /= norm;
    }
}

// Function to multiply a matrix by a vector
void matrix_vector_mult(double matrix[N][N], double *vector,
   double *result) {
    for (int i = 0; i < N; i++) {
        result[i] = 0.0;
        for (int j = 0; j < N; j++) {
            result[i] += matrix[i][j] * vector[j];
        }
    }
}

int main() {
    // Define constants
    double amin = 0.2;
    double amax = 4.4;
    double step = 0.2;  // Step size for incrementing a
    double v_old[N] = {1, 0, 0, 0};  // Initial vector
```

```
    double v_new[N];
    double yk[N];

    for (double a = amin; a <= amax; a += step) {
        // Define the matrix J with the current value of a
        double J[N][N] = {
            {-19.8, 72, 0, a},
            {146, -432, 11.4, 0},
            {0.8, 0, 0, 0},
            {0.1, -20, 0, 0}
        };

        // Normalize the initial vector
        normalize(v_old);

        int k = 0;
        double lambda = 0.0;

        // Perform 11 iterations of the power method
        for (k = 0; k < 11; k++) {
            // Compute yk = J * v_old
            matrix_vector_mult(J, v_old, yk);

            // Compute the approximate eigenvalue
            lambda = 0.0;
            for (int i = 0; i < N; i++) {
                lambda += yk[i] * v_old[i];
            }

```

```
            // Compute v_new = yk normalized
            for (int i = 0; i < N; i++) {
                v_new[i] = yk[i];
            }
            normalize(v_new);

            // Update v_old for the next iteration
            for (int i = 0; i < N; i++) {
                v_old[i] = v_new[i];
            }
        }

        // Print the eigenvalue for the current value of a
        printf("For a = %.2f, the largest eigenvalue after 11
           iterations is approximately: %lf\n", a, lambda);
    }

    return 0;
}
```

LISTING 1. C Code for Calculating Eigenvalues

```
input
For a = 0.20, the largest eigenvalue after 9 iterations is approximately: -456.093509
For a = 0.40, the largest eigenvalue after 9 iterations is approximately: -456.096292
For a = 0.60, the largest eigenvalue after 9 iterations is approximately: -456.099075
For a = 0.80, the largest eigenvalue after 9 iterations is approximately: -456.101858
For a = 1.00, the largest eigenvalue after 9 iterations is approximately: -456.104641
For a = 1.20, the largest eigenvalue after 9 iterations is approximately: -456.107424
For a = 1.40, the largest eigenvalue after 9 iterations is approximately: -456.110207
For a = 1.60, the largest eigenvalue after 9 iterations is approximately: -456.112989
For a = 1.80, the largest eigenvalue after 9 iterations is approximately: -456.115772
For a = 2.00, the largest eigenvalue after 9 iterations is approximately: -456.118555
For a = 2.20, the largest eigenvalue after 9 iterations is approximately: -456.121337
For a = 2.40, the largest eigenvalue after 9 iterations is approximately: -456.124120
For a = 2.60, the largest eigenvalue after 9 iterations is approximately: -456.126902
For a = 2.80, the largest eigenvalue after 9 iterations is approximately: -456.129684
For a = 3.00, the largest eigenvalue after 9 iterations is approximately: -456.132466
For a = 3.20, the largest eigenvalue after 9 iterations is approximately: -456.135249
For a = 3.40, the largest eigenvalue after 9 iterations is approximately: -456.138031
For a = 3.60, the largest eigenvalue after 9 iterations is approximately: -456.140813
For a = 3.80, the largest eigenvalue after 9 iterations is approximately: -456.143595
For a = 4.00, the largest eigenvalue after 9 iterations is approximately: -456.146377
```

LISTING 2: Compilation Result Of a C Program

The other eigenvalues are easily calculated by solving the cubic polynomial in λ

$\lambda_2 = -25,6924; \lambda_3 = -0,0919; \lambda_4 = -0,0556.$

Point P_3 is stable for any values of the parameters a since $\lambda_1, \lambda_2, \lambda_3 < 0$.

5. Classification and Interpretation of Equilibrium Points

$P_1(G_1, I_1, \beta_1, F_1)$**:**

In this section, we present the results of the numerical simulation of the model and analyze the equilibrium point obtained.

The equilibrium point of the system is characterized by the following values:

- Glucose concentration: $G = 555$ mg/dL
- Insulin concentration: $I = 0\ \mu U/mL$
- Beta cell mass: $\beta = 0$
- Food intake: $F = 666$ calories per day

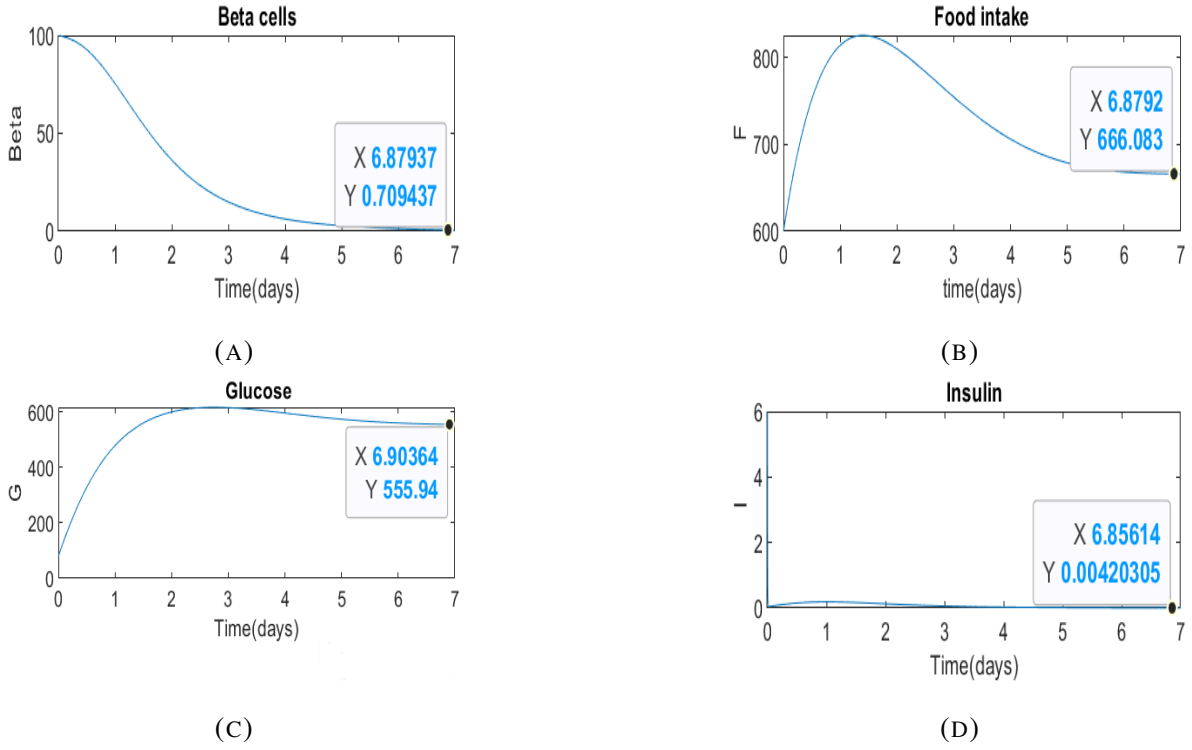

FIGURE 1. Evolution of β-cells, Food intake, Glucose, and Insulin

This equilibrium point represents a highly pathological state in the context of glucose metabolism. The glucose concentration of $G = 555$ mg/dL indicates severe hyperglycemia, which is a dangerous condition typically associated with uncontrolled diabetes.

The absence of insulin ($I = 0$) suggests that the body is unable to facilitate the uptake of glucose from the bloodstream into the cells, leading to the accumulation of glucose in the blood. Additionally, the lack of functioning beta cells ($\beta = 0$) implies that the pancreas is no longer able to produce insulin, a scenario consistent with advanced Type 1 diabetes or severe pancreatic dysfunction.

Despite the relatively low caloric intake of $F = 666$ calories per day, the glucose levels remain dangerously elevated. This highlights the critical role of insulin in maintaining normal glucose levels. Even a small amount of food intake can lead to severe hyperglycemia in the absence of insulin.

Biologically, this equilibrium point indicates a situation where the body's ability to regulate blood sugar levels is completely compromised due to the absence of insulin and beta cell function. It underscores the severity of insulin deficiency and illustrates the necessity of external interventions, such as insulin therapy, to manage glucose levels effectively in such pathological conditions.

$P_2(G_2, I_2, \beta_2, F_2)$

At the equilibrium point with glucose (G) at 100 mg/dL, insulin (I) at 24 µU/mL, beta cells (β) at 753, and a food intake (F) of 1400 calories, the following insights are observed:

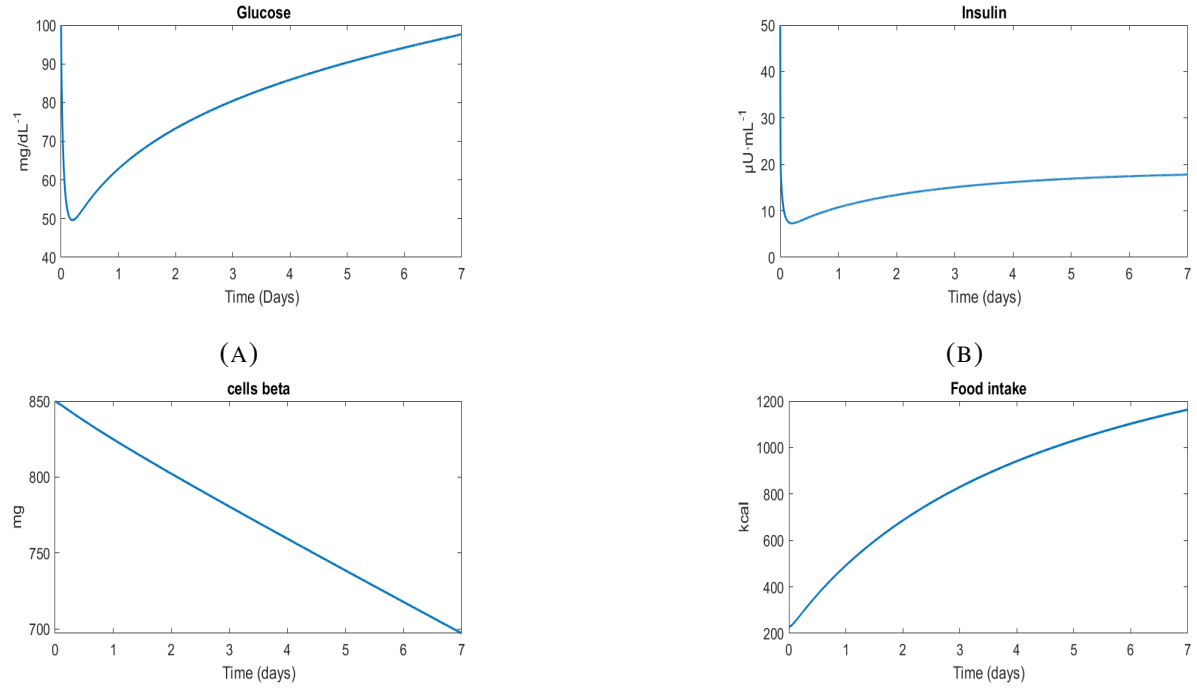

FIGURE 2. Variation in Glucose, Insulin, β-cells, and Food intake in 7 Days

- **Glucose Levels**: The glucose level of 100 mg/dL is within the normal range, suggesting that glucose regulation is currently well-managed.
- **Insulin Levels**: An insulin level of 24 µU/mL is elevated, which could indicate that the body is producing more insulin to maintain glucose levels within the normal range. This may suggest an increased demand for insulin, potentially due to insulin resistance.

- **Beta Cell** : A high number of beta cells ($\beta = 753$) suggests that the pancreas has a substantial capacity to produce insulin. This indicates that, despite the elevated insulin level, the beta cells are not significantly impaired.
- **Caloric Intake**: An intake of 1400 calories is relatively high. Although this caloric intake is not necessarily excessive, it could influence glucose and insulin dynamics, especially if the body requires increased insulin production to manage the glucose effectively.

With a normal glucose level, elevated insulin levels, a high number of beta cells, and a relatively high caloric intake, the system appears to be managing glucose well but with an increased insulin output. The elevated insulin levels might indicate a compensatory response to dietary intake or insulin resistance. Monitoring both glucose and insulin dynamics, alongside managing caloric intake, is important for maintaining metabolic balance.

$P_3(G_3, I_3, \beta_3, F_3)$**:**

At the equilibrium point with glucose (G) at 250 mg/dL, insulin (I) at 16 μU/mL, beta cells (β) at 154, and a food intake (F) of 975 calories, the following insights are observed:

- **Glucose Levels**: The glucose level of 250 mg/dL indicates significant disruption in glucose regulation. This elevated level suggests hyperglycemia, a condition commonly associated with prediabetes or type 2 diabetes.
- **Insulin Levels**: With an insulin level of 16 μU/mL considered normal, insulin production itself does not appear to be the primary issue. The focus should be on the effectiveness of insulin in regulating blood glucose.
- **Beta Cell**: A reduced number of beta cells ($\beta = 154$) may hinder the pancreas's ability to produce sufficient insulin. This reduction in beta cell function can contribute to elevated glucose levels and potential insulin resistance.
- **Caloric Intake**: An intake of 975 calories is within a normal range, suggesting that caloric consumption is not excessively high. Therefore, the primary challenges likely lie in glucose regulation and beta cell function rather than in dietary intake.

The elevated glucose level, along with normal insulin levels and a reduced number of beta cells, indicates a disruption in glucose regulation. While the primary factors involve metabolic processes, it is important to acknowledge that other factors, such as stress, could also impact glucose regulation and beta cell function. Addressing both metabolic factors and potential external influences like stress is crucial for improving overall metabolic control.

6. SIMULATION

6.1. Impact of Metabolic Factors on Glucose Regulation.

1ST SCENARIO $a = 0,2$

- **Glucose Concentration ($G = 62\ mg/dL$)**

  Significance: A glucose level of 62 mg/dL is considered hypoglycemic, indicating insufficient glucose concentration in the blood to meet the body's energy needs. Symptoms may include fatigue, trembling, palpitations, or even loss of consciousness if glucose levels remain low.

  Implication: This hypoglycemia may result from excessive calorie intake without adequate carbohydrate consumption, increased glucose utilization by cells, or an inappropriate insulin response [39, 40].

- **Insulin Concentration ($I = 10$ µU/mL)**

  Significance: An insulin level of 10 µU/mL is generally considered normal. However, in the context of hypoglycemia, it may indicate that insulin is produced sufficiently to regulate glucose but that this regulation is not effective.

  Implication: This could suggest insulin resistance, where the body produces insulin, but the cells do not respond adequately, allowing glucose levels to remain low despite caloric intake [41, 42].

- **Beta Cell Mass ($\beta = 671$)**

  Significance: A high beta cell mass indicates that the pancreas is capable of producing insulin. In this case, the mass is sufficient to respond to an increase in glucose levels.

  Implication: However, the presence of hypoglycemia despite adequate beta cell mass

may indicate a failure in insulin release in response to elevated glucose levels or a dysregulation in insulin signaling [43].

- **Food Intake ($F = 3369$ calories)**

  Significance: A caloric intake of 3369 calories is high and suggests significant food consumption, which may indicate overeating or high carbohydrate intake.

  Implication: Despite this high caloric intake, the low glucose level may signal ineffective metabolism. The body may not be able to efficiently convert these calories into available glucose, potentially due to insulin resistance or an inability of cells to uptake glucose [44, 45].

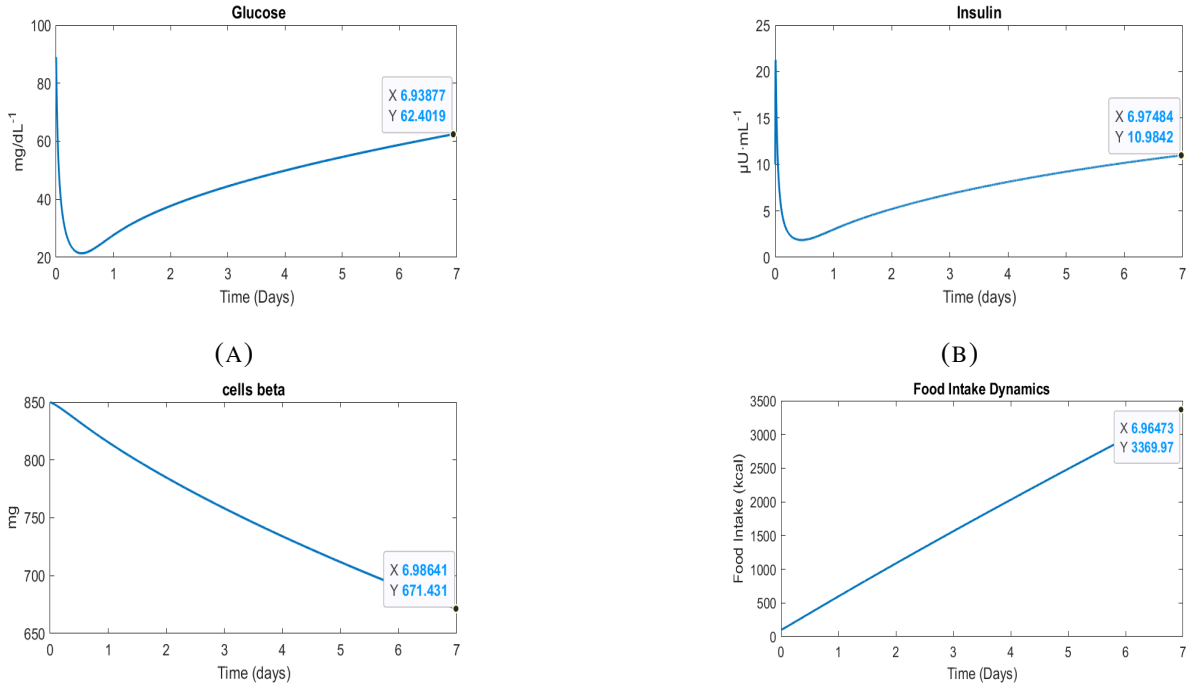

FIGURE 3. Simulation Results using the parameter values given in Table for $a = 0,2$

The combination of these values suggests a situation where, despite a high caloric intake, glucose regulation is compromised. The low glucose level may indicate hypoglycemia due to ineffective glucose absorption or insulin resistance. Insulin is produced in adequate amounts,

but its ability to manage glucose levels appears impaired. This may be characteristic of metabolic disorders such as prediabetes or other insulin-related disorders, where the body fails to utilize available energy efficiently, leading to dysregulation of blood glucose levels [46].

2ND SCENARIO $a = 4.2$

- **Glucose Concentration** ($G = 233$ **mg/dL**)

  Significance: A glucose level of 233 mg/dL is indicative of hyperglycemia, which suggests that the concentration of glucose in the blood is significantly elevated, potentially leading to symptoms such as increased thirst, frequent urination, fatigue, and blurred vision.

  Implication: This hyperglycemia may result from inadequate insulin response, insulin resistance, or excessive carbohydrate intake, indicating that the body's ability to regulate glucose is impaired [47].
- **Insulin Concentration** ($I = 46$ **µU/mL**)

  Significance: An insulin level of 46 µU/mL is elevated compared to normal levels, suggesting that the body is producing more insulin to compensate for the high glucose levels.

  Implication: This could indicate insulin resistance, where the body produces more insulin but is less effective at utilizing it to lower glucose levels, contributing to hyperglycemia [39, 48].

- **Beta Cell Mass** ($\beta = 616$) *Significance:* A beta cell mass of 616 indicates that the pancreas has a reasonable capacity for insulin production.

  Implication: However, despite having a sufficient beta cell mass, the presence of hyperglycemia and elevated insulin levels may suggest that the beta cells are overstimulated or that there is a dysfunction in insulin secretion or action.
- **Food Intake** ($F = 1938$ **calories**) *Significance:* A caloric intake of 1938 calories is moderate, but depending on the individual's energy requirements, it may be contributing to the elevated glucose levels if the intake includes a high proportion of carbohydrates.

Implication: The interaction between food intake and glucose regulation suggests that despite a moderate caloric intake, if it is high in sugars or refined carbohydrates, it could exacerbate hyperglycemia and contribute to insulin resistance.

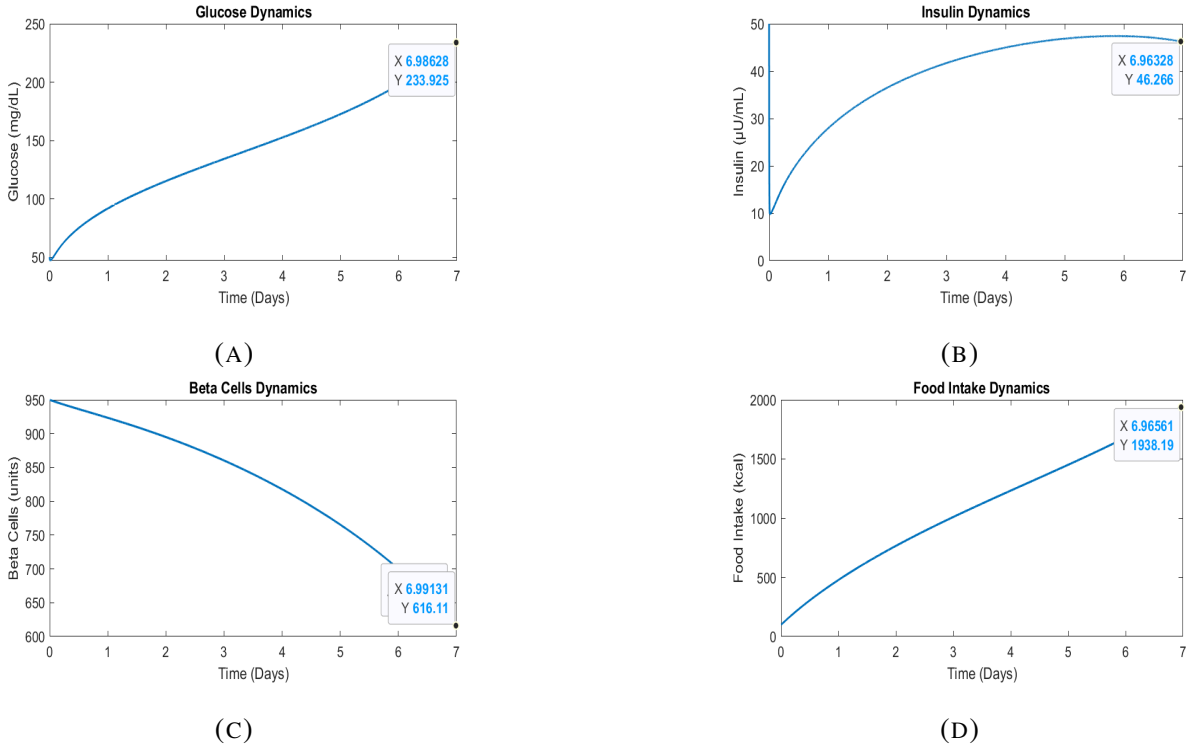

FIGURE 4. Simulation Results using the parameter values given in Table for $a = 4, 2$

6.2. Importance of F_0 in Understanding Food Intake Impact on Glucose Regulation. The parameter F_0, representing the baseline level of food intake, plays a crucial role in understanding glucose regulation within the model. By setting F_0 to different values, one can assess how variations in baseline food intake influence the equilibrium and dynamics of glucose and insulin levels. This adjustment allows for the exploration of how steady-state food intake impacts the overall system behavior, providing insights into the sensitivity of glucose regulation to changes in dietary intake. Variations in F_0 help reveal the extent to which food intake affects glucose control and insulin response, which is essential for developing effective dietary guidelines and

managing metabolic conditions such as diabetes. Analyzing the effects of different F_0 values also contributes to validating the model and ensuring its accuracy in simulating real-world physiological responses[45].

1ST SCINARIO $F_0 = 120$:

- **Low glucose** ($G = 53\ mg/dL$):

  A glucose level of 53 mg/dL is below the normal range, indicating hypoglycemia. This suggests that the body is consuming or utilizing glucose too quickly, or that there isn't enough glucose available from food intake [49].
- **Low insulin** ($I = 8\ \mu U/mL$):

  An insulin level of 8 μU/mL is on the lower end of the normal range. This indicates that the pancreas is not producing much insulin, possibly due to the low glucose levels [49, 50].
- **Beta cells** ($\beta = 681$):

  The number of beta cells remains relatively high, suggesting that the pancreas still has the capacity to produce insulin.
- **Food intake** ($F = 337$):

  A caloric intake of 337 calories is quite low, indicating insufficient food consumption. This could explain the low glucose levels [50].

With a low baseline food intake ($F_0 = 120$), the body exhibits low glucose and insulin levels, which may lead to hypoglycemia. The low food intake limits the availability of glucose in the system, leading to insufficient insulin production despite the relatively healthy number of beta cells [47, 49].

2ND SCENARIO $F_0 = 600$

When $F_0 = 800$ calories, the results obtained for the model's variables are:

- **Elevated glucose** ($G = 139\ mg/dL$):

  A blood glucose level of 139 mg/dL is higher than the normal fasting range. This suggests partial or ineffective glucose regulation in the bloodstream. Such a glucose

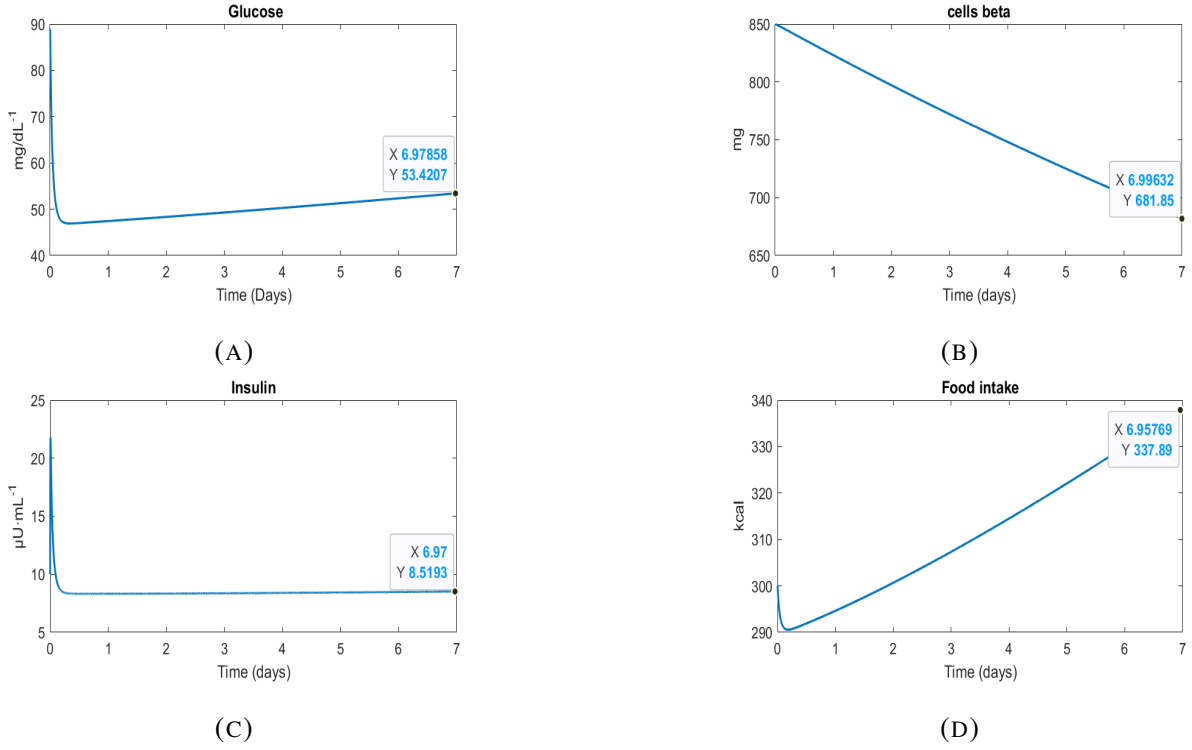

FIGURE 5. Simulation Results using the parameter values given in Table for $F_0 = 120$

level could indicate insulin resistance, where glucose is not efficiently utilized by cells despite the presence of higher insulin levels [44, 47].

- **Insulin** ($I = 33\ \mu U/mL$):

  An insulin level of 33 μU/mL is relatively high, indicating that the pancreas is producing a significant amount of insulin to manage elevated blood glucose. This could reflect a state of insulin resistance, where the body requires more insulin to keep blood sugar levels controlled, but with limited effectiveness [51, 52].

- **Beta cells** ($\beta = 699$):

  The number of beta cells is fairly high in this case. This could indicate that the pancreas is in a compensatory mode, producing more insulin to offset the excess glucose. However, prolonged stress on beta cells at this level might lead to their exhaustion, which increases the risk of developing diabetes over time.

- **Food intake** ($F = 3062$):

  A caloric intake of 3062 calories after setting $F_0 = 800$ indicates significant food consumption. This could suggest excessive caloric intake, which is consistent with the elevated levels of glucose and insulin. This large intake of calories could be contributing to the increase in both glucose and insulin levels, driving metabolic risk [49].

In this scenario, increasing the base food intake ($F_0 = 800$) leads to elevated glucose and insulin levels, reflecting a situation of metabolic dysregulation. Although the beta cells are still capable of producing insulin to compensate, this situation might not be sustainable. Over time, beta cell exhaustion could result, leading to an inability to effectively regulate glucose, which could further promote the development of type 2 diabetes.

This analysis can be included in your thesis to illustrate how an increase in food intake impacts glucose and insulin regulation, and to discuss the potential link to metabolic disorders.

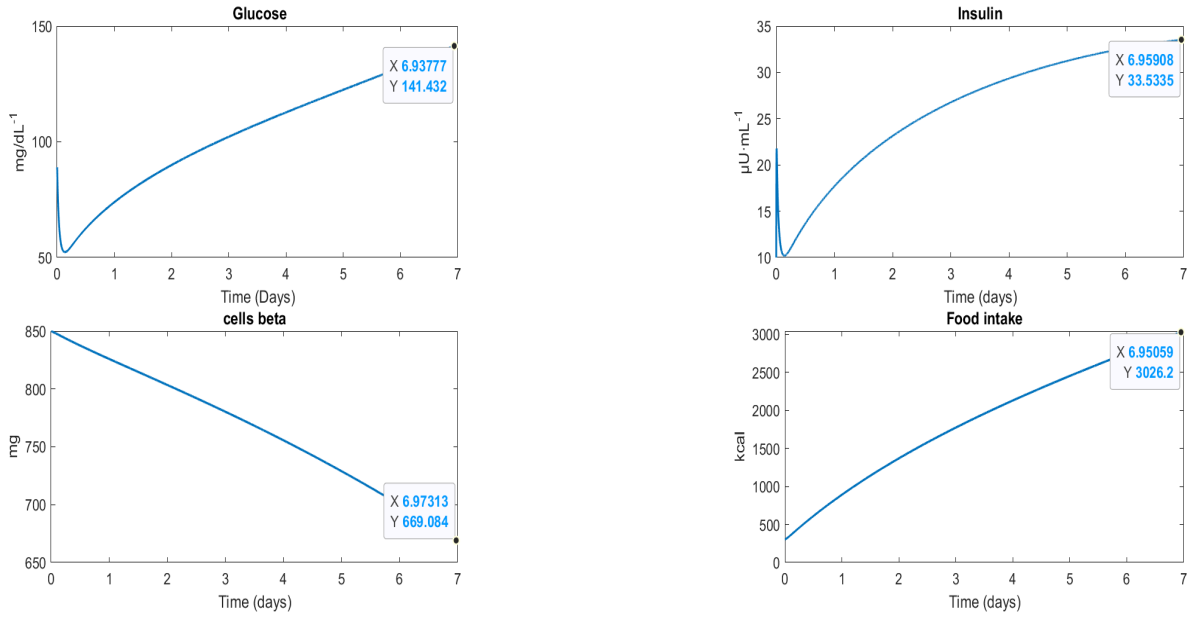

FIGURE 6. Simulation Results using the parameter values given in Table for $F_0 = 800$

CONCLUSION

Our mathematical model highlights the crucial importance of managing food intake for glucose regulation and the prevention of type 2 diabetes. The simulations demonstrate that high food intake can lead to increased blood glucose levels, requiring greater insulin production and raising the risk of hyperglycemia. Conversely, balanced caloric intake helps maintain healthy glucose levels, as indicated by our model results.

Obesity and stress are significant risk factors for type 2 diabetes, disrupting hormonal and metabolic balance, which can lead to insulin resistance and glucose imbalances. *For example*, excessive alcohol consumption can also have a substantial impact on glucose regulation. Previous studies have shown that alcohol can cause significant fluctuations in blood glucose levels, with episodes of hypoglycemia followed by glucose spikes. This complicates glucose management and can increase the risk of developing type 2 diabetes, emphasizing the importance of moderating alcohol intake to maintain optimal glucose balance.

Moreover, regular physical activity and effective stress management are essential for preventing type 2 diabetes. Physical exercise improves insulin sensitivity and helps stabilize glucose levels, while effective stress management techniques can mitigate the negative effects of stress on metabolism.

In conclusion, our model confirms that an integrated approach is necessary for effective glucose regulation and the prevention of type 2 diabetes. This approach includes balanced nutrition, moderate alcohol consumption, weight management, regular physical activity, and stress management. These factors should be considered together in a comprehensive strategy to optimize metabolic health and prevent long-term glycemic disorders.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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