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Stability Analysis of Discretized Model of Glucose–Insulin Homeostasis

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Abstract

In this paper, the mathematical model which describes the glucose-insulin homeostasis in healthy rats is considered. The model is discretized by constructing a nonstandard finite difference (NSFD) scheme to obtain the numerical solutions. The equilibrium point of the discretized model is determined and stability analysis of the discretized model is discussed. The effect of time step sizes on 4th order Runge-Kutta method and NSFD method is presented. Also, comparison of NSFD scheme solution, Runge-Kutta-Fehlberg Method (RKF45) solution and analytical solution are presented in graphical form. The effectiveness of the proposed method in the solution and interpretation of the model is observed.

Keywords: Glucose-Insulin homeostasis, nonstandard finite difference scheme, stability analysis.

1. Introduction

In mathematical biology, a lot of studies for patients with diabetes are proposed. The relationship between glucose and insulin has been mathematically modeled, improved and studied. Some of the studies can be listed as follows:

Chen et. al. developed a physiological glucose–insulin dynamic system on diabetics [1]. They aimed to examine dynamic behavior of plasma glucose and insulin on diabetic subject. They constructed a modified delay differential equation system. Dereouich and Boutayeb examined the importance of physical activity on the dynamics of glucose and insulin [2]. Neatpisarnvanit and Boston derived and evaluated two plasma insulin estimators in [3]. They used forward Euler discretization to discrete the continuous model. Finally, they compared the performances of estimator by using computer simulations and clinical data. Li and Kuang [4] generalized the dynamic model on interaction of glucose and insulin to the delay model. They proposed some lemmas, propositions and theorems about the local and global stability of the model. Also, they gave periodic solutions for the discrete delay model. Hussian and Zadeng analyzed the stability of the general glucose-insulin model [5]. They examined the importance of insulin in the disappearance of glucose by doing numerical simulations. Wang et.al [6] proposed a delay model of the insulin therapies. They studied the dynamics of the model. They showed that the numerical results and the findings of the clinical studies agree well.

There are a lot of classical numerical methods for solving these kinds of models such as Euler Method, Runge-Kutta Method etc. But, the studies show that, it is better to prefer nonstandard discretization methods for biological models. Al-Kahby et.al. present the basic stability results of some biological models, shortcomings of some classical discretization methods and the advantage of nonstandard discretization methods [7]. In this study, because of the advantages, we prefer to use NSFD schemes developed by Mickens [8-11]. One of the advantages compared to classical discretization methods is that while classical discretization often produces difference equations which don't share their dynamics, NSFD produce difference equations that share their dynamics. In this discretization method, the critical points are same with the continuous model and the positivity solutions under positive initial conditions are preserved. Since NSFD schemes can preserve all properties of the continuous models for any discretization parameter, the method is successful on dynamical consistency. Also, while NSFD schemes give convergence results for the big step-size,

Celal Bayar University Journal of Science
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the other traditional methods don't. Since there are numerical instabilities in the classical methods, this method provide an advantage of choosing suitable denominator function. One can be referred to [12] for the detailed analysis about determining denominator function. Some studies about NSFD schemes are listed below:

Mickens studied a nonlinear reaction-advection equation which is a partial differential equation [13]. Arenas et. al. analyzed the SIRS model for modelling transmission of respiratory syncytial virus [14]. Khalsaraei and Khodadosti made some applications of NSFD to ordinary and partial differential equations [15]. Their comparisons between the standard methods and NSFD showed that nonstandard schemes perform better. Ongun and Turhan applied NSFD schemes to the HIV infection model which is a nonlinear ordinary differential equation system [16]. They examined stability analysis of the model and gave qualitative results for the fixed points which have biological meanings. Also, Ongun etc. applied NSFD schemes to a fractional-order Brusselator system [17]. They presented the dynamics of the Brusselator model and trajectories by NSFD scheme. A very detailed literature survey is presented by Patidar in [18,19]. Some of the main rules about designing NSFD schemes are summarized and some of the applications of the method in other areas are mentioned.

This study consist of six sections: in Section 2, the model is introduced and discretized through NSFD schemes. In Section 3, Jury Stability test and a theorem about the local asymptotic stability of the model are presented. Equilibrium point of the discrete system is determined, the expression of Jacobian matrix at the equilibrium point and characteristic equation are given. In Section 4, the analytical solution of the linear ordinary differential equation system is given. Section 5 presents the numerical simulations. Considering the optimized values, stability analysis of the problem is given. The effect of time step sizes on the convergence of the 4th order Runge-Kutta method and NSFD scheme is given in tabular form. The graphics for the numerical solutions of the model are presented. Finally, phase portrait of the system is given. The last section concludes the study with a summary.

2. Discretization of the Model

In this section, the model proposed by [20] is considered. The model describing glucose–insulin homeostasis in healthy rats is given as:

$$\begin{aligned}\frac{dI}{dt} &= -k_6 I + k_1 G \\ \frac{dG}{dt} &= -\left(k_2 + k_4\right) I + k_0 D - k_3 + k_4 I_{pi} \\ \frac{dD}{dt} &= -k_a D,\end{aligned} \tag{2.1}$$

where, I, G and D denote to variation of blood insulin concentration, blood glucose concentration and amount of glucose in the intestine, respectively. The parameters in Eq. (2.1) are given in Table 1.

Table 1. The meaning of the parameters in epidemic model (2.1).

Parameters	Meanings
k_0	the rate constant of blood glucose incorporation from diet
k_1	the rate constant of insulin secretion
k_2	the rate constant of insulin-dependent glucose uptake by the tissues
k_3	the rate constant of insulin-independent glucose uptake by the tissues
k_4	the rate constant of liver glucose transfer
k_6	the rate constant of blood insulin clearance
k_a	the rate constant of glucose absorption
I_{pi}	the blood insulin concentration when the liver changes from the uptake to the production of glucose

The discretization has an important role on dynamic behavior of epidemic models; because the data's are collected in discrete-time. Since the classical discretization methods often lead to difference equations which don't share their dynamics, it is more suitable to discretize the models by nonstandard discretization methods. In the light of this information, the model given by Equations (2.1) is discretized by nonstandard finite difference method proposed by Mickens [8,-11]. This discretization method is preferred because of the advantages of choosing denominator function arbitrary by local discretization. Also, NSFD method has advantage on removing numerical instabilities obtained by standard finite difference procedures.

The discretization of the model (2.1) has been done by NSFD scheme in the view of positivity conditions. To satisfy the positivity condition, the discretized procedure for the first equation of Eq. (2.1) is given as $G(t) \to G(n)$ and $I(t) \to I(n+1)$. Later on, the discretized terms $I(t) \to I(n)$ and $D(t) \to D(n+1)$ are applied to the second equation of Eq. (2.1). Finally, by using the $D(t) \to D(n+1)$ discretization for the last equation of Eq. (2.1), the model is rewritten as

$$
\begin{aligned}
I(n+1) &= \frac{I(n)+k_1\phi_1 G(n)}{1+k_6\phi_1},\\
G(n+1) &= G(n)+\phi_2\left[-(k_4+k_2)I(n)\right.\\
&\quad \left.+k_0 D(n)-k_3+k_4 I_{pi}\right],\\
D(n+1) &= \frac{D(n)}{1+k_a\phi_3},
\end{aligned}
\tag{2.2}
$$

where ϕ_i, $i=1,2,3$ are denominator functions and determined as

$$
\begin{aligned}
\phi_1 &= \frac{e^{k_6 h}-1}{k_6},\\
\phi_2 &= h,\\
\phi_3 &= \frac{e^{k_a h}-1}{k_a}.
\end{aligned}
$$

For detailed information of finding denominator functions, one can check the reference [10].

3. Stability Analysis of the Discretized Model

Lemma 3.1 From the positivity of the parameters, the solution of discrete system (2.2) is positive with positive initial conditions under the assumption of

$$\frac{G(n)}{\phi_2} > (k_4+k_2)I(n)-k_0 D(n)+k_3-k_4 I_{pi}.$$

Proof

i) For $k_6>0$, $h>0$ and $\phi_1,\phi_2,\phi_3>0$, it is obvious that $e^{k_6 h}>1$. So, $e^{k_6 h}-1>0$ is obtained. Dividing this expression into the term k_6 leads to $\frac{e^{k_6 h}-1}{k_6}=\phi_1>0$. So, the solution $I(n+1)=\frac{I(n)+k_1\phi_1 G(n)}{1+k_6\phi_1}>0$ is positive.

ii) If $\frac{G(n)}{\phi_2} > (k_4+k_2)I(n)-k_0 D(n)+k_3-k_4 I_{pi}$ then, for $h=\phi_2>0$,

$G(n) > \phi_2\left[(k_4+k_2)I(n)-k_0 D(n)+k_3-k_4 I_{pi}\right]$ is obtained. So the solution

$$G(n+1)=G(n)+\phi_2\left[-(k_4+k_2)I(n)+k_0 D(n)-k_3+k_4 I_{pi}\right]>0$$

is positive.

iii) For $k_a>0$ and $h>0$, it is obvious that $e^{k_a h}>1$. So, $e^{k_a h}-1>0$ is obtained. Dividing this expression into the term k_a leads to $\frac{e^{k_a h}-1}{k_a}=\phi_3>0$. So, the solution $D(n+1)=\frac{D(n)}{1+k_a\phi_3}>0$ is positive.

Lemma 3.2 From the positivity of the parameters and Lemma 3.1, if $\frac{G(n)}{I(n)}<\frac{k_6}{k_1}$, the solution of discrete system (2.2) decreases monotonically.

Proof From the third equation of discrete system (2.2), $\frac{D(n+1)}{D(n)}=\frac{1}{1+k_a\phi_3}=\frac{1}{e^{k_a h}}<1$ is obtained. Rewritten the second equation of system (2.2) as, $\frac{G(n+1)}{G(n)}=1+\frac{\phi_2\left[-(k_4+k_2)I(n)+k_0 D(n)-k_3+k_4 I_{pi}\right]}{G(n)}$ and considering the assumption in Lemma 3.1, for $\frac{\phi_2}{G(n)}<\frac{1}{(k_4+k_2)I(n)-k_0 D(n)+k_3-k_4 I_{pi}}$, it is obtained that

$$
\begin{aligned}
\frac{G(n+1)}{G(n)} &= 1+\frac{\phi_2\left[-(k_4+k_2)I(n)+k_0 D(n)-k_3+k_4 I_{pi}\right]}{G(n)}\\
&< 0 < 1.
\end{aligned}
$$

Finally, from the first equation of the system (2.2) and the assumption $\frac{G(n)}{I(n)}<\frac{k_6}{k_1}$,

$$\frac{I(n+1)}{I(n)}=\frac{I(n)+k_1\phi_1 G(n)}{(1+k_6\phi_1)I(n)}<\frac{1}{1+k_6\phi_1}+\frac{k_1\phi_1 k_6}{(1+k_6\phi_1)k_1}=1$$

is obtained.

Locally asymptotic stability of the system depends on the eigenvalues of the Jacobian matrix at the equilibrium points. The eigenvalues are the zeros of the following characteristic polynomial

$$p(\lambda)=\lambda^n+a_1\lambda^{n-1}+a_2\lambda^{n-2}+\ldots+a_n, \tag{3.1}$$

where $a_1, a_2, \ldots, a_n$ are constants.

Theorem 3.1 If the solutions $\lambda_i, i=1,2,\ldots,n$ of Equation (3.1), $p(\lambda)=0$ satisfy $|\lambda_i|<1$, then

i) $p(1)=1+a_1+a_2+\ldots+a_n>0$,

ii) $(-1)^n\, p(-1)=1-a_1+a_2-\ldots+(-1)^n a_n>0$, (alternate in sign),

iii) $|a_n|<1$. [21]

Celal Bayar University Journal of Science
Volume 17, Issue 4, 2021, p 369-377
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Jury Stability Test

Let us consider the characteristic polynomial

$$p(z)=a_0z^n+a_1z^{n-1}+\ldots+a_{n-1}z+a_n,\quad a_0>0.$$

The conditions of stability of the system are:

i) $|a_n|<a_0$,

ii) $p(1)>0$,

iii) $\begin{cases} p(-1)>0, & \text{for n is even} \\ p(-1)<0, & \text{for n is odd} \end{cases}$,

iv) $\left.\begin{array}{l} |b_{n-1}|>|b_0| \\ |c_{n-2}|>|c_0| \\ \vdots \\ |q_2|>|q_0| \end{array}\right\}$ $(n-2)$ constraints ,

where,

$$b_k=\begin{vmatrix} a_n & a_{n-1-k} \\ a_0 & a_{k+1} \end{vmatrix},\quad k=\overline{0,n-1},$$

$$c_k=\begin{vmatrix} b_{n-1} & b_{n-2-k} \\ b_0 & b_{k+1} \end{vmatrix},\quad k=\overline{0,n-2},$$

$$\vdots$$

$$q_k=\begin{vmatrix} p_3 & p_{2-k} \\ p_0 & p_{k+1} \end{vmatrix},\quad k=\overline{0,2}\ [21,22].$$

For the stability analysis of model, equilibrium point of Equations (2.2) are obtained as

$$E^*=\left(I^*,G^*,D^*\right)=\left(\frac{-k_3+k_4I_{pi}}{k_4+k_2},\frac{\left(-k_3+k_4I_{pi}\right)k_6}{\left(k_4+k_2\right)k_1},0\right).$$

Note that, the equilibrium points of continuous model (2.1) and discrete model (2.2) are same.

The Jacobian matrix is determined as

$$J\left(I(n),G(n),D(n)\right)=\begin{bmatrix} \frac{1}{1+k_6\phi_1} & \frac{k_1\phi_1}{1+k_6\phi_1} & 0 \\ \phi_2\left(-k_4+k_2\right) & 1 & \phi_2k_0 \\ 0 & 0 & \frac{1}{1+\phi_3k_a} \end{bmatrix}.$$

The value of Jacobian matrix at the equilibrium point and obtained characteristic polynomial are given below:

$$J\left(I^*,G^*,D^*\right)=\begin{bmatrix} \frac{1}{1+k_6\phi_1} & \frac{k_1\phi_1}{1+k_6\phi_1} & 0 \\ \phi_2\left(-k_4+k_2\right) & 1 & \phi_2k_0 \\ 0 & 0 & \frac{1}{1+\phi_3k_a} \end{bmatrix},$$

$$p(\lambda)=\lambda^3-\frac{3+2k_6\phi_1+2\phi_3k_a+k_ak_6\phi_1\phi_3}{\left(1+k_a\phi_3\right)\left(1+k_6\phi_1\right)}\lambda^2$$
$$-\frac{\left(1+k_a\phi_3\right)\phi_1\phi_2k_1\left(k_2-k_4\right)-3-k_6\phi_1-k_a\phi_3}{\left(1+k_a\phi_3\right)\left(1+k_6\phi_1\right)}\lambda \quad \textbf{(3.2)}$$
$$+\frac{k_1\phi_1\phi_2\left(-k_4+k_2\right)-1}{\left(1+k_a\phi_3\right)\left(1+k_6\phi_1\right)},$$

where the eigenvalues are

$$\lambda_1=\frac{1}{1+\phi_3k_a},$$

$$\lambda_2=\frac{2+k_6\phi_1+\sqrt{k_6^2\phi_1^2-4k_1\phi_1\phi_2\left(k_4-k_2\right)\left(1+k_6\phi_1\right)}}{2\left(1+k_6\phi_1\right)},$$

$$\lambda_3=\frac{-2-k_6\phi_1+\sqrt{k_6^2\phi_1^2-4k_1\phi_1\phi_2\left(k_4-k_2\right)\left(1+k_6\phi_1\right)}}{2\left(1+k_6\phi_1\right)}.$$

Now, let us analyze the stability of the model at the equilibrium point.

Theorem 3.2 The system is locally asymptotically stable at the equilibrium point E^*, if the following conditions are satisfied

i) $\left|\frac{-k_1k_4\phi_1\phi_2+k_1k_2\phi_1\phi_2-1}{\left(1+k_a\phi_3\right)\left(1+k_6\phi_1\right)}\right|<1.$

ii) $\frac{k_1k_a\left(k_4-k_2\right)\phi_1\phi_2\phi_3}{\left(1+k_a\phi_3\right)\left(1+k_6\phi_1\right)}>0.$

iii) $\frac{k_1k_a\phi_1\phi_2\phi_3\left(k_2-k_4\right)-2\left[3+2\left(k_6\phi_1+k_a\phi_3\right)+k_6k_a\phi_1\phi_3\right]}{\left(1+k_a\phi_3\right)\left(1+k_6\phi_1\right)}<0.$

$$\left|\left\{\left(k_1\phi_1\phi_2\left(k_2-k_4\right)-\left(1+k_6\phi_1\right)\left(1+k_a\phi_3\right)-1\right)\left(k_1\phi_1\phi_2\left(k_2\right.\right.\right.\right.$$
$$\left.\left.\left.\left.-k_4\right)+k_6\phi_1\left(1+k_a\phi_3\right)+k_a\phi_3\right)\right\}/\left\{\left(1+k_a\phi_3\right)^2\left(1+k_6\phi_1\right)^2\right\}\right|$$

iv) $>\left|\left(\left(k_4-k_2\right)\phi_1\phi_2k_1\left(\phi_1k_6\left(1-\phi_3k_a\right)+2-k_a^2\phi_3^2\right)-k_a\phi_3\left(2\right.\right.$
$$\left.+k_a\phi_3\right)+k_a^2k_6\phi_1^2\phi_3^2k_1\left(-k_4+k_2\phi_2\right)-k_6\phi_1\left(2+k_6\phi_1\right)$$
$$\left.+\phi_1\phi_3k_ak_6\left(-k_6\phi_1+k_a\phi_3-4\right)\right)/\left(\left(1+k_a\phi_3\right)^2\left(1+k_6\phi_1\right)^2\right)\Big|.$$

Celal Bayar University Journal of Science
Volume 17, Issue 4, 2021, p 369-377
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Proof Considering Jury stability test [21,22] and the coefficients of characteristic polynomial (3.2) obtained as

$$a_1 = -\frac{3+2k_6\phi_1+2\phi_3k_a+k_ak_6\phi_1\phi_3}{(1+k_a\phi_3)(1+k_6\phi_1)},$$
$$a_2 = -\frac{(1+k_a\phi_3)\phi_1\phi_2k_1(k_2-k_4)-3-k_6\phi_1-k_a\phi_3}{(1+k_a\phi_3)(1+k_6\phi_1)} \quad \text{and}$$
$$a_3 = \frac{k_1\phi_1\phi_2(-k_4+k_2)-1}{(1+k_a\phi_3)(1+k_6\phi_1)},$$

it is obvious that, if the conditions (i-iv) are satisfied, the equilibrium point is locally asymptotically stable.

In addition, as is known, the order of convergence in Mickens' method generally matches the order of the differential equation [23]. Also, in the view of [23,24], it can be easily seen that the order of convergence for NSFD schemes we proposed is one.

4. The Analytical Solution of the System

In this section, to compare the results obtained by the NSFD schemes, the analytical solution of the system of ordinary differential equations is presented under the initial conditions $I(0)=I_0>0$, $G(0)=G_0>0$, $D(0)=D_0>0$. The model (2.1) is solved by elimination method. In the view of the elimination method, the system is converted to the following differential equations,

$$\begin{aligned}
\left[\mathrm{D}^2+k_6\mathrm{D}+k_1(k_2+k_4)\right]I(t) &= k_0k_1c^*e^{-k_at} \\
&\quad +(-k_3+k_4I_{pi})k_1, \\
\left[\mathrm{D}^2+k_6\mathrm{D}+k_1(k_2+k_4)\right]G(t) &= k_0c^*(k_6-k_a)e^{-k_at} \\
&\quad +(-k_3+k_4I_{pi})k_6, \\
(\mathrm{D}+k_a)D(\mathrm{t}) &= 0,
\end{aligned} \quad \textbf{(4.1)}$$

where D is the derivation operator and c^* is the arbitrary parameter obtained from the solution of the third equation of Eq. (4.1). The characteristic equation of the first and second equations of Eq. (4.1) is obtained for the homogeneous solution as

$$m_{1,2} = \frac{-k_6 \mp \sqrt{k_6^2-4k_1(k_2+k_4)}}{2}.$$

For the different cases of characteristic equation, the homogeneous solutions are obtained. Later, private solutions are obtained by using the method of undetermined coefficients. So, we can summarize the solution of system (2.1) as follows:

i) If $k_6^2-4k_1(k_2+k_4)>0$, $\frac{-k_6 \mp \sqrt{k_6^2-4k_1(k_2+k_4)}}{2} \neq -k_a$ and $\frac{-k_6 \mp \sqrt{k_6^2-4k_1(k_2+k_4)}}{2} \neq 0$, then

$$I(t) = c_1e^{m_1t}+c_2e^{m_2t}+\frac{k_0k_1c_3}{k_a^2-k_ak_6+k_1(k_2+k_4)}e^{-k_at} + \frac{-k_3+k_4I_{pi}}{k_2+k_4},$$

$$G(t) = \frac{c_1(m_1+k_6)}{k_1}e^{m_1t}+\frac{c_2(m_2+k_6)}{k_1}e^{m_2t} + \frac{k_0c_3(k_6-k_a)}{k_a^2-k_ak_6+k_1(k_2+k_4)}e^{-k_at}+\frac{k_6(-k_3+k_4I_{pi})}{k_1(k_2+k_4)},$$

$$D(t) = c_3e^{-k_at},$$

where, the coefficients c_1, c_2, c_3 are obtained from initial conditions as,

$$c_1 = \frac{1}{m_1-m_2}\left\{k_1G_0-\frac{k_0k_1D_0(k_6-k_a)}{k_a^2-k_ak_6+k_1(k_2+k_4)} - \frac{k_6(-k_3+k_4I_{pi})}{k_2+k_4}-(m_2+k_6)\left[I_0 - \frac{k_0k_1D_0}{k_a^2-k_ak_6+k_1(k_2+k_4)}-\frac{-k_3+k_4I_{pi}}{k_2+k_4}\right]\right\},$$

$$c_2 = \frac{1}{m_2-m_1}\left\{-(m_1+k_6)\left[I_0-\frac{k_0k_1D_0}{k_a^2-k_ak_6+k_1(k_2+k_4)} - \frac{-k_3+k_4I_{pi}}{k_2+k_4}\right]+k_1G_0-\frac{k_0k_1D_0(k_6-k_a)}{k_a^2-k_ak_6+k_1(k_2+k_4)} - \frac{k_6(-k_3+k_4I_{pi})}{k_2+k_4}\right]\right\},$$

$$c_3 = D_0.$$

ii) If $k_6^2-4k_1(k_2+k_4)=0$, $\frac{k_6}{2} \neq k_a$ and $k_6=0$, then

Celal Bayar University Journal of Science
Volume 17, Issue 4, 2021, p 369-377
Doi: 10.18466/cbayarfbe.838451

$$I(t)=(c_1+c_2t)e^{-\frac{k_6}{2}t}+\frac{k_0k_1c_3}{k_a^2-k_ak_6+k_1(k_2+k_4)}e^{-k_at}+\frac{-k_3+k_4I_{pi}}{k_2+k_4},$$

$$G(t)=\left(\frac{k_6c_1+c_2}{k_1}+\frac{k_6c_2}{2k_1}t\right)e^{-k_6t}+\frac{k_0c_3(k_6-k_a)}{k_a^2-k_ak_6+k_1(k_2+k_4)}e^{-k_at}+\frac{k_6(-k_3+k_4I_{pi})}{k_1(k_2+k_4)},$$

$$D(t)=c_3e^{-k_at},$$

where, the coefficients c_1,c_2,c_3 are obtained from initial conditions as,

$$c_1=-\frac{k_0k_1D_0}{k_a^2-k_ak_6+k_1(k_2+k_4)}-\frac{-k_3+k_4I_{pi}}{k_2+k_4}+I_0,$$

$$c_2=k_1\left\{G_0-\frac{k_6(-k_3+k_4I_{pi})}{k_1(k_2+k_4)}-\frac{k_0D_0(k_6-k_a)}{k_a^2-k_ak_6+k_1(k_2+k_4)}+\frac{k_0k_6D_0k_1}{k_a^2-k_ak_6+k_1(k_2+k_4)}+\frac{k_6(-k_3+k_4I_{pi})}{k_2+k_4}\right\},$$

$$c_3=D_0.$$

iii) If $k_6^2-4k_1(k_2+k_4)<0$,

$$I(t)=(c_1\cos(bt)+c_2\sin(bt))e^{-\frac{k_6}{2}t}+\frac{k_0k_1c_3}{k_a^2-k_ak_6+k_1(k_2+k_4)}e^{-k_at}+\frac{-k_3+k_4I_{pi}}{k_2+k_4},$$

$$G(t)=\left(\left(c_2b+\frac{k_6c_1}{2}\right)\frac{1}{k_1}\cos(bt)+\frac{1}{k_1}\left(-c_1b+\frac{k_6c_2}{2}\right)\sin(bt)\right)e^{-k_6t}+\frac{k_0c_3(k_6-k_a)}{k_a^2-k_ak_6+k_1(k_2+k_4)}e^{-k_at}+\frac{k_6(-k_3+k_4I_{pi})}{k_1(k_2+k_4)},$$

$$D(t)=c_3e^{-k_at},$$

where, the coefficients c_1,c_2,c_3 are obtained from initial conditions as,

$$c_1=-\frac{k_0k_1D_0}{k_a^2-k_ak_6+k_1(k_2+k_4)}-\frac{-k_3+k_4I_{pi}}{k_2+k_4}+I_0,$$

$$c_2=\frac{1}{b}\left\{k_1\left[G_0-\frac{k_6(-k_3+k_4I_{pi})}{k_1(k_2+k_4)}-\frac{k_0D_0(k_6-k_a)}{k_a^2-k_ak_6+k_1(k_2+k_4)}\right]-\frac{k_6}{2}\left[-\frac{k_0D_0k_1}{k_a^2-k_ak_6+k_1(k_2+k_4)}-\frac{-k_3+k_4I_{pi}}{k_2+k_4}+I_0\right]\right\},$$

$$c_3=D_0.$$

5. Results and Discussion

In this study, since discrete-time dynamic systems have advantages over continuous-time dynamic systems, we convert a continuous time dynamic system to a discrete-time dynamic system. One of them is that the data in real life are collected in discrete time. Also discrete-time dynamic systems present more complicated dynamical behaviors.

In this section, first, we analyze the stability of the discretized model. Then, we approached the problem by 4-th order Runge-Kutta method and NSFD scheme to observe the convergence of the methods. The numerical solution of the epidemic model is also obtained by RKF45 method. The effectiveness of the numerical methods is compared in Fig. 1-3 with obtained analytical solutions. Finally, the graphics for different glucose intake are presented. Maple package programme is used in all calculations.

The numerical calculations are carried out for the parameters:

$$k_0=0.01,\ k_1=0.7,\ k_2=0.0005,\ k_3=1,\ k_4=0.05,\ k_6=0.5$$
$$k_a=0.15,\ I_{pi}=800,\ \ h=0.01.$$

These parameters are chosen approximately from the optimized parameters in [20].

Now, let us analyze the stability of the problem. By considering Jury stability test,

i) Since $|a_0|=1$ and $|a_3|=0.99352$, $|a_3|<a_0$.

ii) $p(1)=a_0+a_1+a_2+a_3=0.5x10^{-8}>0$.

iii) $p(-1)=-a_0+a_1-a_2+a_3=-5.98702<0$.

iv) Since $|b_0|=0.01290894300$ and $|b_2|=0.01290900830$, $|b_2|>|b_0|$.

So from the conditions (i- iv), the equilibrium point is locally asymptotically stable.

Table 2. Effect of time step sizes on the numerical methods

h	**4-th order Runge-Kutta method**	**NSFD scheme**
0.001	Convergence	Convergence
0.01	Convergence	Convergence
0.1	Convergence	Convergence
0.5	Convergence	Convergence
1	Convergence	Convergence
5	Convergence	Convergence
10	Divergence	Convergence
100	Divergence	Divergence

Table 2 present the effect of time step size on 4-th order Runge-Kutta method and NSFD scheme. As is seen from Table 2, the nonstandard discretization is more effective than the classical method for bigger step-size.

Also, since the model is a system of linear ordinary differential equation, the comparisons of analytical and numerical solutions are done. The results obtained by NSFD scheme, RKF45 method and analytical solution are presented in Figures 1-3.

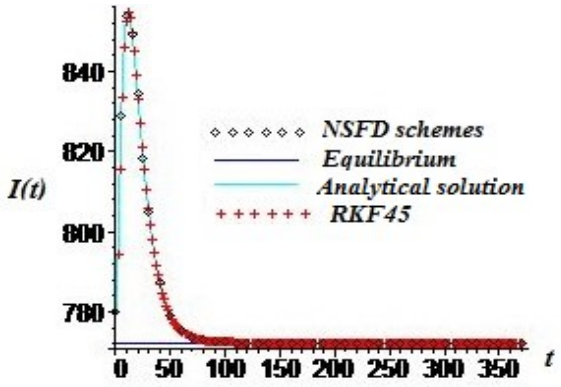

Figure 1. Numerical comparison for I(t).

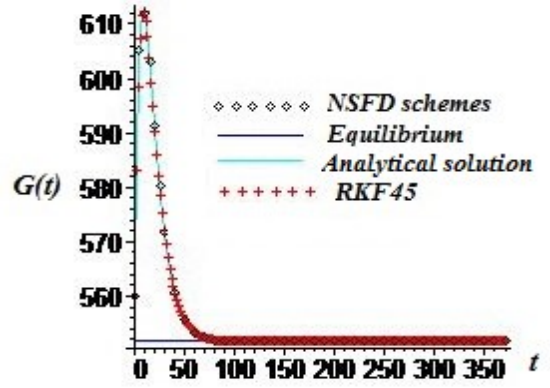

Figure 2. Numerical comparison for $G(t)$.

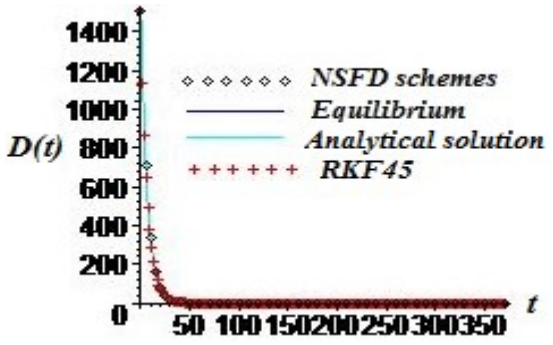

Figure 3. Numerical comparison for $D(t)$.

Clearly, these figures show us the stability of the model and effectiveness of the NSFD scheme. Figures 4-6 present the variation of blood insulin concentration, blood glucose concentration and amount of glucose in the intestine on time for different amount of glucose intake (D_0). So, when the glucose intake increases, levels of blood insulin and blood glucose increase too.

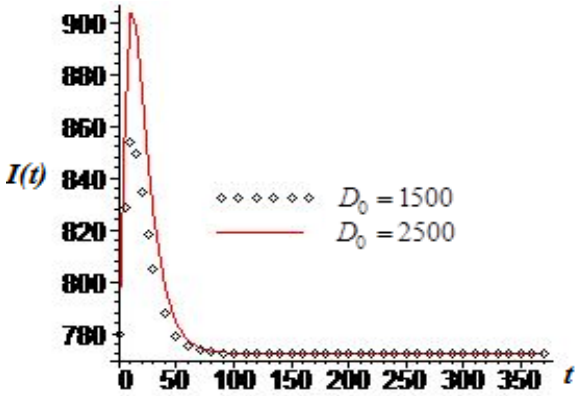

Figure 4. I(t) for different glucose intake (mg).

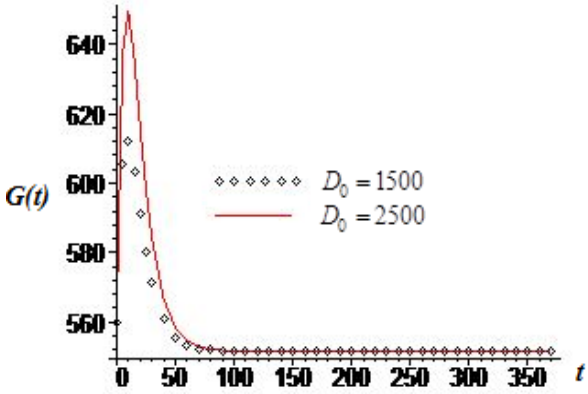

Figure 5. $G(t)$ for different glucose intake (mg).

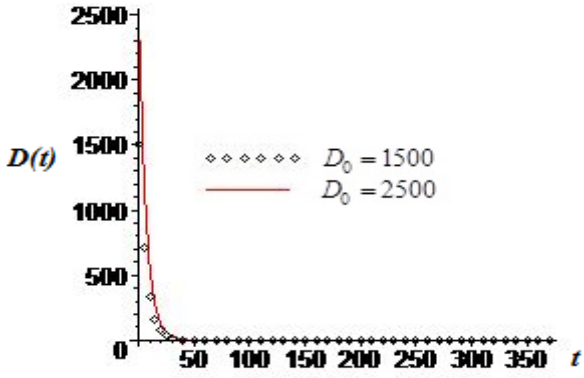

Figure 6. $D(t)$ for different glucose intake (mg).

Finally, the phase portrait of the system is generated by Figure 7.

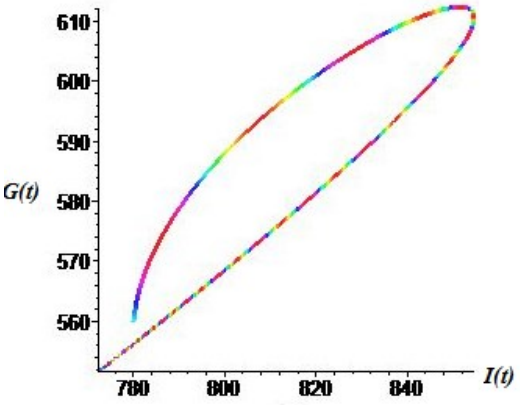

Figure 7. Phase portrait of the system.

6. Conclusion

In this study, a model of glucose–insulin homeostasis in healthy rats is handled. The system is discretized by NSFD schemes. It is seen that the solutions are positive for all positive initial values. The stability analysis of the model is done and it is concluded that equilibrium point is locally asymptotically stable. Convergence is achieved for larger step-size than fourth-order Runge-Kutta method. Since the considered biological model is a system of linear ordinary differential equation, it gives a chance to compare the approximate values with analytical values. So, the effectiveness of the results obtained by NSFD schemes can be seen from figures. Also, biologically, the effect of the glucose intake on blood insulin concentration, blood glucose concentration and glucose in the intestine can be seen from figures. This study shows the effectiveness of the NSFD scheme in many aspects like stability, positivity, preservation of critical points and convenience.

Author's Contributions

İlkem Turhan ÇETİNKAYA: Drafted and wrote the manuscript, performed numerical calculations.
Mehmet KOCABIYIK: Assisted in numerical calculations and helped in manuscript preparation.
Mevlüde YAKIT ONGUN: Supervised the manuscript and performed the result interpretation.

Ethics

There are no ethical issues after the publication of this manuscript.

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