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Discrete Optimal Control Mathematical Model of Diabetes Population

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Abstract
In this work, nonlinear diabetes controlled model with and without complications in a population is considered. The dynamic behavior of diabetes in a population by including a constant control is studied and investigated. The existence of all its possible fixed points is investigated as well as the conditions of the local stability of the considered model are set. We also find the optimal control strategy in order to reduce the number of people having diabetes with complications over a finite period of time. A numerical simulation is provided and confirmed the theoretical results.

Keywords: Discrete optimal control, Difference equations, Diabetes mathematical model.

نموذج رياضي للسيطرة المثلى المتقطعة لمرضى السكري

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الخلاصة
الهدف من هذا البحث تم فرض نموذج سيطرة مثلى مع وجود مضاعفات اوعدم وجود مضاعفات لمرضى السكري . كذلك تم دراسة السلوك الديناميكي للنموذج الرياضي و تم ايضا ايجاد جميع نقاط الاتزان المحتملة للنموذج المقترح .كذلك تم مناقشة الاستقرار المحلي لجميع النقاط الاتزان لقد تم توسيع النموذج إلى مسألة سيطرة مثلى لغرض تقليل عدد حاملي المرض مع المضاعفات في فترة زمنية محددة. اعطيت امثلة عددية لتأكيد النتائج النظرية..

1-Introduction:

Diabetes is one of the worst chronic diseases that is caused either by the lack of producing enough insulin in the pancreas or by the lack of insulin in the cells. Someone is diagnosed to have diabetes when the level of plasma glucose density is more than 6.1 mmol/L [1]. Many researchers have investigated and developed a large number of mathematical models by using ordinary differential equations, difference equations and fractional-order derivatives. In particular, they have studied the dynamics of diabetes in a population based on the pathogenesis of the disease. See[2-14]. These models provide an important role to model a variety of problems in real life, in particular the diabetes disease .The related research work is done by Boutayeb and Chetouani [2,15,16] , Deronich et. al [3]. They considered and used a system of the ordinary differential equation, while other authors used difference equations or

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fractional-order derivatives to describe their models to study the dynamics of the population of diabetes.

The outline of the paper is as follows. In section two, we consider the nonlinear diabetes model with all interpretations of all its parameters. Further, we discuss the local stability of all fixed points. In section three, we study a discrete optimal control problem for the considered model, and we also characterize the optimal solutions by employing the Pontryagin maximum principle. Numerical simulations are presented in section four. Finally, the conclusions are highlighted in Section five.

2- Formulation of the model:

Boutayeb et. al [3] considered and investigated the following diabetics model :

$$\begin{aligned} \frac{dD}{dt} &= I - \alpha D(t) - \mu D(t) + \gamma C(t), \\ \frac{dC}{dt} &= \alpha D(t) - (\gamma + \mu + v + \delta) C(t). \end{aligned} \tag{1}$$

All parameters are positive constants. The descriptions of all variables and parameters are given in the following table.

Variables and parameters	Description
t	Time
$D(t)$	Density of diabetes people without complication at time t
$C(t)$	Density of diabetes people with complication at time t
I	Incidence of diabetes mellitus which is assumed to be constant
α	Probability of developing a complication
μ	Natural death rate
γ	Rate at which complication are cured
δ	Death rate due to complications
v	Death rate at which patients with complications become severely disabled

System (1) is modified to the following control system

$$\begin{aligned} \frac{dD}{dt} &= I - \alpha(1-u)D - \mu D + \gamma C, \\ \frac{dC}{dt} &= \alpha(1-u)D - (\gamma + \mu + v + \delta)C, \end{aligned} \tag{2}$$

where u is the control variable. In this work, we investigate the system (2) with assumption that the probability of developing complication α is non-constant which is given by $\alpha = \alpha(t) = \beta \frac{C(t)}{N(t)}$, where β is positive constant and $N(t) = D(t) + C(t)$. Here, $N(t)$ is the number of diabetics people. Then, the system (2) can be written as follows:

$$\begin{aligned} \frac{dC}{dt} &= [\beta(1-u) - \theta]C - \beta\frac{C^2}{N}(1-u), \\ \frac{dN}{dt} &= I - (v + \delta)C - \mu N, \end{aligned} \tag{3}$$

where $\theta = \gamma + \mu + v + \delta$ and u is the control variable such that $0 \le u \le 1$. First, we assume u is constant then after, we extend the system (3) to the optimal control problem. The

Euler method is applied to the system (3) with the step size m to get the following non-linear discrete-time system

$$C_{t+1} = C_t + m\left[[\beta(1-u)-\theta]C_t - \beta(1-u)\frac{C_t^2}{N_t}\right], \qquad (4)$$
$$N_{t+1} = N_t + m[I-(v+\delta)C_t - \mu N_t],$$

the fixed points of the system (4) arise when we solve the following algebraic equations.

$$C = C + m[[\beta(1-u)-\theta]C - \beta(1-u)\frac{C^2}{N}]$$
$$N = N + m[I-(v+\delta)C - \mu N\ ]$$

So that the system (4) has two fixed points, namely;

$$I_1 = \left(0, \frac{I}{\mu}\right), \qquad I_2 = (C^*, N^*),$$

where $C^* = \frac{kI}{k(v+\delta)+\mu\beta(1-u)}$, $and\ \ N^* = \frac{\beta(1-u)I}{k(v+\delta)+\mu\beta(1-u)}$, $with\ k = \beta(1-u) - \ \theta$ and $k > 0$.

Definition 1:[17] A fixed point x^* of a discrete-time system $\vec{x}_{t+1} = f(\vec{x}_t)$ is called locally stable if all eigenvalues of Jacobain matrix J of the system lie into the unit circle. Otherwise, the fixed point is said to be unstable. The stability behavior of fixed points of system (4) is determined by the value of the eigenvalues of Jacobian matrix of system (4). Therefore, the Jacobian matrix J associated with system (4) at a given point (C,N) is given as follows:

$$J(\mathrm{C},\mathrm{N}) = \begin{bmatrix} 1 + m[\beta(1-u)-\theta] - 2\frac{\beta(1-u)mC}{N} & \frac{m\beta(1-u)C^2}{N^2} \\ -m(v+\delta) & 1-m\mu \end{bmatrix}.$$

Therefore, the characteristic polynomial of J is $f(\lambda) = \lambda^2 + a_0\lambda + a_1$ where $a_0 = -2 + m\mu - mk_1 + m\theta + \frac{2k_{1mC}}{N}$ and $a_1 = 1 + mk_1 - m\theta - 2k_1\frac{mC}{N} - m\mu - m^2\mu k_1 + m^2\theta\mu + 2m^2\frac{k_1\mu C}{N} + m^2(v+\delta)\frac{k_1C^2}{N^2}$ with $k_1 = \beta(1-u)$.

The next theorem discusses the behavior of the fixed point I_1.

Theorem 1:

If $k_1 \in \left(\theta - \frac{2}{m}, \theta\right)$ $and\ \mu < \frac{2}{m}$, then the fixed point $I_1 = \left(0, \frac{I}{\mu}\right)$ is locally stable point.

Proof: It is clear that

$$\mathrm{J}_{\mathrm{I}_1} = \begin{bmatrix} 1+\mathrm{m}(\mathrm{k}_1-\theta) & 0 \\ -\mathrm{m}(\mathrm{v}+\delta) & 1-\mathrm{m}\mu \end{bmatrix}.$$

Therefore, the eigenvalues of $J_{I_1}$are $\lambda_1 = 1 + m(k_1-\theta)$ $and\ \lambda_2 = 1 - m\mu$ so that if $k_1 \in \left(\theta - \frac{2}{m}, \theta\right)$, then $\theta - \frac{2}{m} < k_1 < \theta$, $and\ \ m\theta - 2 < mk_1 < m\theta\ \ hence -1 < 1 + m(k_1-\theta) < 1$ there fore $|\lambda_1| < 1$.

Now, if $\mu < \frac{2}{m}$ then $-1 < 1 - m\mu < 1$ $\ and\ |\lambda_2| < 1$. Therefore, $I_1 = (0, \frac{I}{\mu})$ is stable point.

Lemma 2: [17] Let $f(\lambda) = \lambda^2 + a_0\lambda + a_1$ such that f (1) > 0, and λ_1, λ_2 are the roots of f, then $|\lambda_i| < 1\ for\ i = 1{,}2,$ if and only if$f(-1) > 0\ and\ a_1 < 1$.

The following theorem gives the behavior of the unique interior fixed point $I_2 = (C^*, N^*)$.

Theorem 3:
If $\mu \in (z_1, z_2)$ *and* $mk < 1$, then the unique positive fixed point $I_2 = (C^*, N^*)$ is locally stable point, where $z_1 = \frac{k - m(v+\delta)\frac{k^2}{k_1}}{mk-1}$ *and* $z_2 = \frac{2mk - 4 - m^2(v+\delta)\frac{k^2}{k_1}}{m^2k - 2m}$.

Proof: Since $-\mu k_1 + \theta\mu + 2\mu k > 0$, then $-\mu k_1 + \theta\mu + 2\mu k + (v+\delta)\frac{k^2}{k_1} > 0$, *so that* $-\mu k_1 + \theta\mu + 2k_1\mu\frac{k}{k_1} + (v+\delta)\frac{k^2 k_1}{k_1^2} > 0$. It is clear that $\frac{C^*}{N^*} = \frac{k}{k_1}$. Therefore, we have $-m^2\mu k_1 + m^2\theta\mu + 2m^2 k_1 \mu\frac{C^*}{N^*} + m^2(v+\delta)k_1\frac{{C^*}^2}{{N^*}^2} > 0$.
This gives that $1 + a_0 + a_1 > 0$. Therefore, $f(1)$ is always greater than 1.
Now, we have to prove that $f(-1) > 0$. Let $\mu < z_2$ *and* $mk < 1$, *then* $\mu < \frac{2mk - 4 - m^2(v+\delta)\frac{k^2}{k_1}}{m^2k - 2m}$. *This gives* $(m^2k - 2m)\mu > 2mk - 4 - m^2\frac{(v+\delta)k^2}{k_1}$, *since* $mk < 1$ *and* $4 - 2m\mu - 2mk + m^2(v+\delta)\frac{k^2}{k_1} > 0$.
Therefore, $1 - a_0 + a_1 > 0$ and $f(-1) > 0$.
Finally, we assume that $\mu > z_1$, so that $\mu > \frac{k - m(v+\delta)\frac{k^2}{k_1}}{mk-1}$, *and* $\mu(mk - 1) < k - m\frac{(v+\delta)k^2}{k_1}$.
Hence, $-k - \mu + mk\mu + m(v+\delta)\frac{k^2}{k_1} < 0$. This gives $a_1 < 1$. By Lemma 2 the result is obtained.

3. The optimal control approach:

In this section, we use the discrete optimal control theory to reduce the number of people that having diabetes with complications. Therefore, we find the optimal control u_t that minimizes the following objective function $J_{(u_t)} = \sum_{t=1}^{T-1} cC_t + au_t^2$, subject to following state equations:

$C_{t+1} = C_t + m\{[\beta(1-u_t) - \theta]C_t - \beta(1-u_t)\frac{C_t^2}{N_t}],$

$N_{t+1} = N_t + m[I - (v+\delta)C_t - \mu N_t],$

where u_t is the control variable such that $0 \le u_t \le 1$ and the parameters c *and* a are positive constants. According to Pontryagin's maximum principle, we define the Hamiltonian function as follows:

$$H_t = cC_t + au_t^2 + \lambda_{1,t+1}\left[C_t + m(\beta(1-u_t) - \theta)C_t - m\beta(1-u_t)\frac{C_t^2}{N_t}\right] + \lambda_{2,t+1}[N_t + m(I - (v+\delta)C_t - \mu N_t)].$$

where $\lambda_{1,t}$ *and* $\lambda_{2,t}$ are the adjoint variables such that

$$\lambda_{1,t} = \frac{dH_t}{dC_t} = c + \lambda_{1,t+1}[1 + m(\beta(1-u_t) - \theta) - \frac{2\beta(1-u_t)C_t}{N_t}] - \lambda_{2,t+1}m(v+\delta),$$

$$\lambda_{2,t} = \frac{dH_t}{dN_t} = \lambda_{1,t+1}(m\beta(1-u_t)\frac{C_t^2}{N_t^2}) + \lambda_{2,t+1}[1 - \mu m].$$

So that the optimal control solution is given by

$\frac{dH_t}{du_t}|_{u_t = u_t^*} = 2au_t^* - \lambda_{1\,t+1}\beta m C_t + \lambda_{1\,t+1}\beta m\frac{C_t^2}{N_t} = 0.$

Therefore, the characteristic optimal strategy solution is given by:

$$u_t^* = min\{ u_{Max},\ Max\left\{0, \frac{\left[m\beta\lambda_{1\ t+1}\left(C_t - \frac{C_t^2}{N_t}\right)\right]}{2a}\right\}\},\ t = 0,1,2,\dots,T-1.$$

We apply an iterative method to compute the optimal strategy for more details, see [18-22].

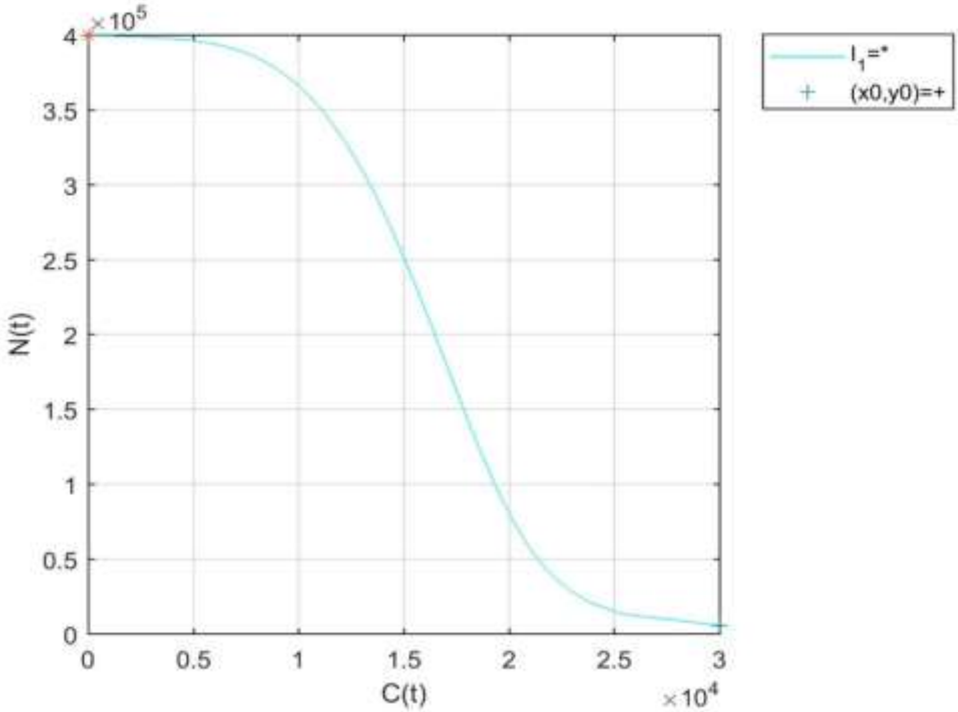
4-Numerical analysis

In order to verify theoretical outcomes in our proposed model, we use the MATLAB program and the following parametric values:

1-To show the local stability for the point $I_1 = \left(0, \frac{I}{\mu}\right)$, the values in Table 1 are used. Figure 1 illustrates the stability of point I_1.

Table 1:The values of parameters

Parameter	Value
m	0.1
I	80000
u	0.7
μ	0.2
γ	0.07
v	0.05
δ	0.02
β	1
$C(0)$	30000
$N(0)$	6.e+03



The local stability of $I_1 = \left(0, \frac{I}{\mu}\right)$.

2- To show the local stability for the point $I_2 = (C^*, N^*)$, we used the parameters of values in Table 2. Figure 2 shows that the point $I_2 = (C^*, N^*)$ is local stable point.

Table 2: The values of parameters for the point I_2

parameter	Value
m	0.1
I	60000
u	0.4
μ	0.02
γ	0.08
v	0.05
δ	0.01
β	1
$C(0)$	6.8750e+03
$N(0)$	9.3750e+06

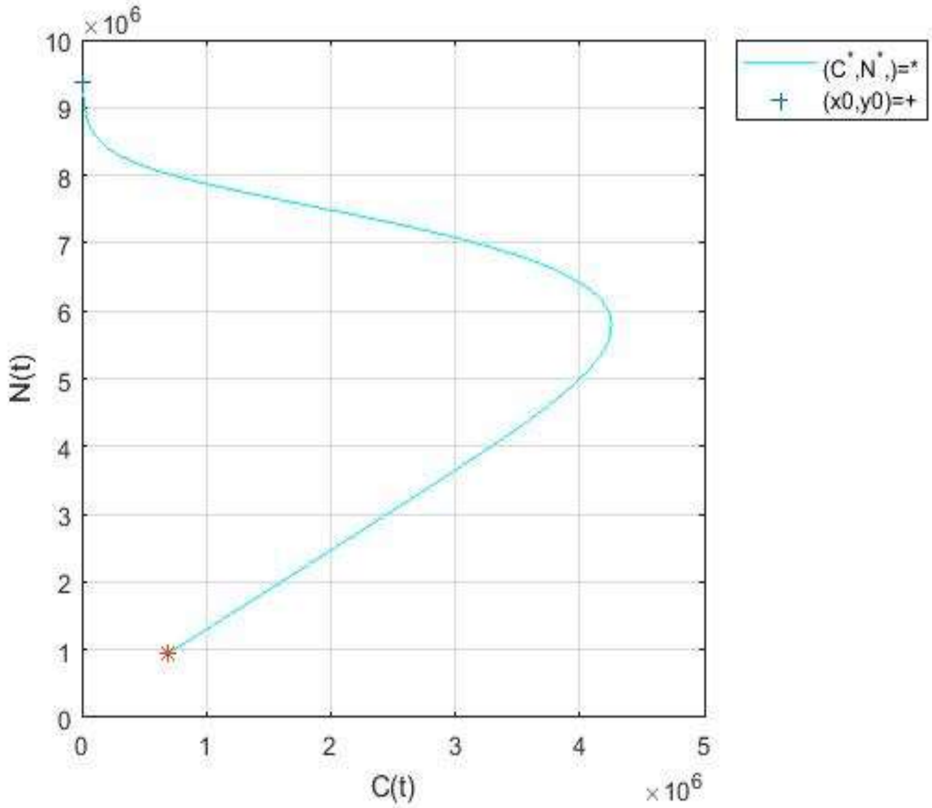


Figure 2: The local stability for the point $I_2 = (C^*, N^*)$.

3-To solve the optimal control problem, we use an iterative method that is described in [10,19,20]. Figure 3 shows the growth of the density of the population having diabetics without complications after applying the control strategy. The solid line indicates the size of the population without complications after applying the control, while the dotted line indicates the size of the population without complications without the control effect**.** Figure 4 shows the decreasing size of the population with complications after applying the control strategy. In Figure 5, the control as a function of time is plotted.

Table 3: The values of parameters for the optimal control

parameter	value
$\boldsymbol{m}$	0.1
$\boldsymbol{I}$	600000
$\boldsymbol{\mu}$	0.2
$\boldsymbol{\gamma}$	0.1
$\boldsymbol{v}$	0.1
$\boldsymbol{\delta}$	0.1
$\boldsymbol{\beta}$	1
$\boldsymbol{a}$	10000
$\boldsymbol{c}$	0.001
$\boldsymbol{C(0)}$	48000
$\boldsymbol{D(0) = N(0) - C(0)}$	552000

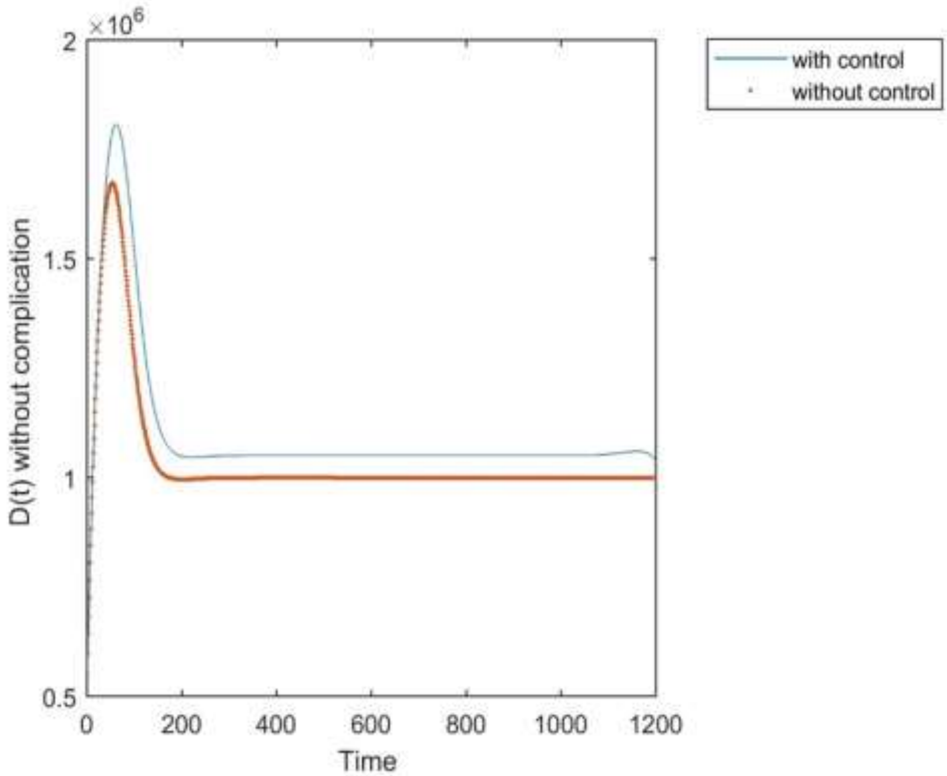


Figure 3: The size of the people having diabetes with complications.

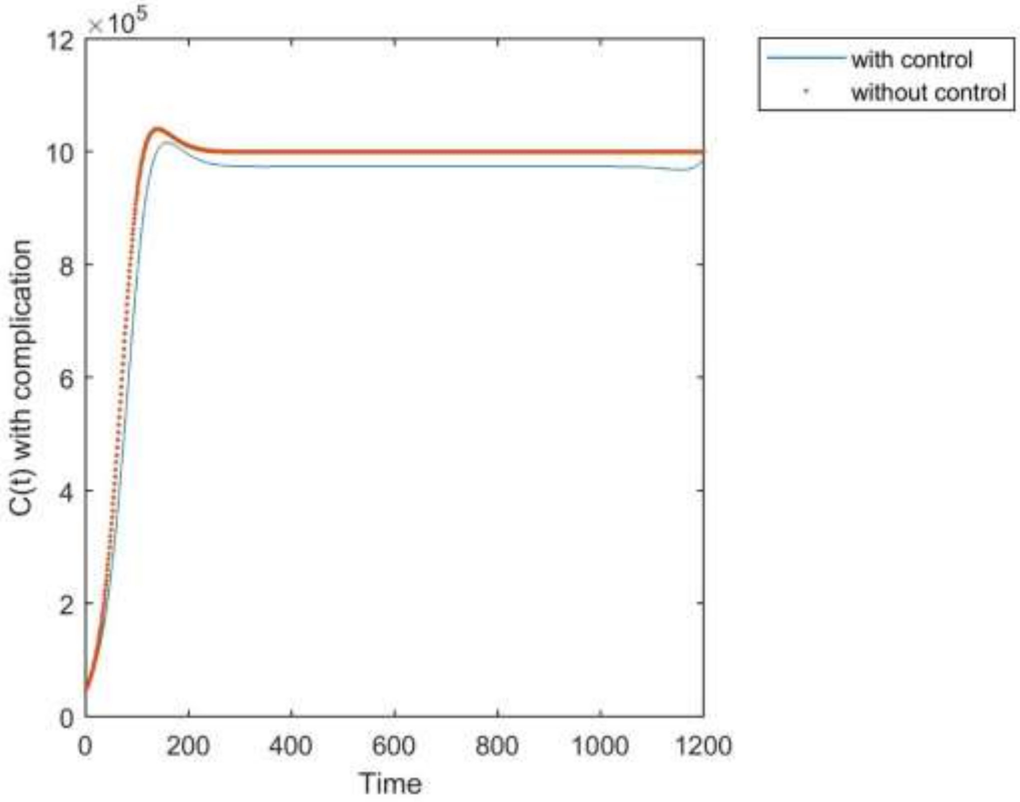


Figure 4: The size of the people having diabetes with complications. The solid line indicates the population with complications after applying the control, while the dot line indicates the population with complication without applying the control**.**

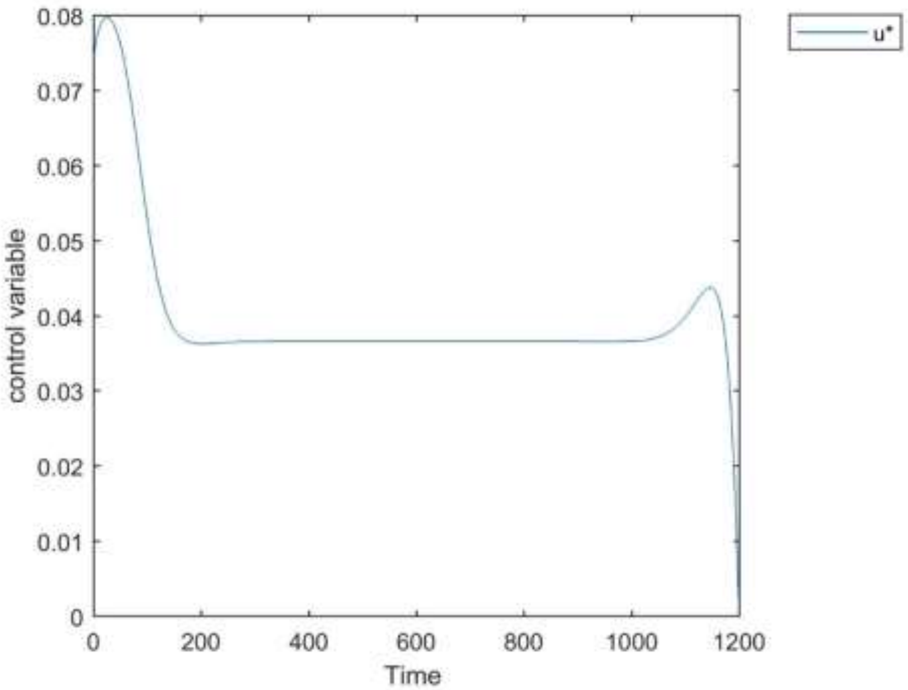


Figure 5: The control is plotted as a function of time**.**

5-Conclusions

In this paper, the nonlinear controlled discrete model of diabetes has been considered. In this system, the population is divided into two parts, namely populations having diabetes with complications and populations having diabetes without complications. It is found that the model has two fixed points. The behavior of the system with constant control has been studied and investigated. Then after the system is extended to an optimal control problem to reduce and decrease the number of the population having diabetics with complications. In figures 3, one can see the size of populations having diabetes without complications is reduced after applying the optimal control strategy, while the opposite can be seen in Figure 4. The discrete-time optimal control is applied to achieve the characterizations of the optimal control solutions. The numerical simulation is given to confirm the theoretical outcomes.

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