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ORIGINAL ARTICLE

An Approximate Solution for Glucose Model via Parameterization Method in Optimal Control Problems

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KEYWORDS

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ABSTRACT: Glucose tolerance test is advised to detection of pre-diabetics and mild diabetics in the medical practice. Several mathematical models such as glucose model, were proposed for mimicking the blood glucose-insulin interaction. To predict accurate insulin requirement for each glucose concentration, we need to solve optimal control problems. In this model, constraints are linear and nonlinear forms of cost function. Although ordinary methods can be used in glucose model, but non-negative natures of medical variables made them difficult to use. To finding a new approximate solution of glucose model, parameterization method with non-negative coefficients in polynomial was used. In this state parameterization method, we use polynomials that ensure that the control variable is non-negative in this model. And increases the time for the model solution to be non-negative compared to conventional methods. The simplicity, lower requirement for mathematical calculations and more compatibility with variables are positive aspects of our parameterization method.

INTRODUCTION

Blood glucose, the main energy source of body, is crucial to maintaining health. Impairment in the blood glucose regulation for a long time, leads to the major health problems such as diabetes mellitus. Diabetes mellitus is a metabolic disease characterized by high levels of sugar and keto acids in the blood. This disease is one of the main causes of death in the worldwide and especially widespread among young adults. Diabetes mellitus will occur when pancreas produces little insulin or in conditions such as insulin resistance.

Optimal control problems (OCPs) are contain an optimization problem with dynamic systems, initial and boundary conditions. Optimal control (OC) has applied by many branches of sciences such as engineering, biology, pharmacology and medicine [1–3]. For example, OC is used to modeling important phenomena such as glucose regulation in the blood [2, 4 and 5]. A control problem consists of a cost function which contains function of state and control variables. In OCP, differential equations or partial differential equations were used to minimize the cost function. Both direct and indirect methods can be used for solving of an optimal control problem (OCP). In indirect method, OCP is converted into another form of problem. Such as differential equations or partial differential equations.

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On the other words, in the direct method, parameterization and linearization directly is used for solving main problem. In this method state and control or state-control are considered as a series of simple and known function of G. Then, all constrains with along initial and boundary conditions must be satisfied and finally, optimization parameters of the cost function will be obtained [6–9]. It is important to mention that although both methods are used to solve OCP, but it is possible that state or control variables are not satisfied conditions and monotonicity of physical problems for state and control variables is not considered.

Glucose tolerance test (GTT) is advised to detection of pre-diabetics and mild diabetics in the medical practice [2]. Several mathematical models were proposed for mimicking the blood glucose-insulin interaction in the body. Ackerman proposed accurate model to detect pre-diabetics and mild diabetics by GTT [4]. Also solutions for glucose model is accurate, but it is may be negative in some control values. This model considers the concentration of blood glucose as g function and net hormonal insulin concentration as h function. It was shown that

$$\begin{cases} g'(t) = c_1 g(t) + c_2 h(t) \\ h'(t) = c_3 g(t) + c_4 h(t) \end{cases}$$

Where $c_1, c_2, c_3 < 0$ and $c_4 \geq 0$. The prime sign indicates the derivative of the function relative to t.

Eisen verified $g = x_1$ and $h = x_2$ variables and improved glucose model for better prediction of blood glucose levels [10]. For decreasing cost of the treatment, he tried to find best insulin level, $u(t)$, to minimize the difference between x_1 and desired constant glucose level, l. So, optimal control obtains as the following form:

$$\text{Min} \quad J = \int_0^T (A(x_1(t) - l)^2 + u^2(t))dt$$

$$\text{subject to} \begin{cases} x'_1(t) = -a x_1(t) - b x_2(t) \\ x'_2(t) = -c x_2(t) + u(t) \end{cases} \quad (1)$$

with the initial conditions

$$x_1(0) = \alpha, \quad x_2(0) = 0.$$

where $a, b, c > 0$ and $A \geq 0$.

Lenhart [2] showed that when $a = b = c = 1$, $\alpha = 0.75, l = 0.5,$ and $A = 2$, this problem is ill-condition. For example, it is impossible in $T = 1$ because there is a serious contradiction. In this point, x_1 and u (hormonal concentration and insulin level) *will be* negative. To find a better solution, in this work, we apply parameterization method by nonnegative coefficient polynomials. In this method coefficients are non-negative and approximate solution is found.

This paper is organized as follows. In Section 2, OCP is introduced and we use parameterization method. In Section 3, we represent an algorithm for solving OCP in the form (1). In Section 4, this algorithm is used for solving Glucose OCP and finally the conclusion is made in Section 5

Problem statement

We consider OCP in the form of:

$$\text{Min} \quad J = \int_{t_0}^{T} f(x, u, x', u', x'', u'', \ldots)dt$$

$$\text{subject to} \quad u = H(t, x, x', x'', x''', \ldots)$$

with the initial conditions

$$x(t_0) = \alpha, \quad \beta_1 x'(t_0) + \beta_2 x(t_0) = \beta_0.$$

Where $\beta_0, \beta_1, \beta_2, \alpha, t_0$ and T are constants, x and u are state and control variables respectively. Both x and u are real-valued functions with continuous derivations that introduce to segment $I = [t_0, T]$. Both H and f are vectorvalued function that continuous derivative respect to all its arguments.

The proposed state parameterization method

In the state parameterization method, state variable is written by expanding to $t^i, i = 0,1,2,...,n$ [6, 7] or known polynomials such as Boubaker polynomials [9], Chebyshev polynomials [8] and so on. We approximate state variable in the form

$$x(t) = \sum_{i=0}^{n} a_i t^i.$$

By putting initial conditions and constrains, control value will obtain in a polynomial form of t , such as a function of parameter a_i for $i = 0,1,2,...,n$ as

$$u = u(a_0, a_1, a_2, ..., a_n).$$

Because control variable is a polynomial, so we can write

$$u(t) = \sum_{i=0}^{n} b_i t^i.$$

In several problems such as glucose model, state control or state-control parameters must be non-negative functions. For $u(t) \geq 0$ we put $b_i \geq 0$ for $i = 0,1,2,...,n$. It means that for finding $a_i, i = 0,1,2,...,n,$ cost function must be optimized with $(n+1)$ in the new conditions. After substitution in cost function, OCP converts to a nonlinear optimization problem with parameters

$$a = a(a_0, a_1, a_2, ..., a_n).$$

For obtaining of $a_i, i = 0,1,2,...,n$, new optimization problem must be solved. Based on above statements, we present following algorithm in several Steps.

Algorithm

Step 1: Choose $\varepsilon > 0$.

Step 2: Put $n = 1$.

Step 3: Put $x_n(t) = \sum_{i=0}^{n} a_i t^i$.

Step 4: The control variable is obtained by substituting $x_n(t)$ in constrains and initial conditions.

Step 5: For optimization cost function, after adding $(n+1)$ constrains $b_i \geq 0, i = 0,1,2,...,n,$ J_n value will obtain.

Step 6: If $n = 1$ then put $n = n+1$ and go to Step 3.

Step 7: If $|J_n - J_{n-1}| \leq \varepsilon$ then stop Algorithm; Otherwise, put $n = n+1$ and go to Step 3.

Computation results

In OCP (1), if we put $A = 2, l = 0.5, a = b = c = 1.$ $t_0 = 0$, and $\alpha = 0.75$, then we will have:

$$\text{Min} \quad J = \int_0^T (2(x_1(t) - 0.5)^2 + u^2(t))dt$$

$$\text{subject to} \begin{cases} x_1'(t) = -x_1(t) - x_2(t) \\ x_2'(t) = -x_2(t) + u(t) \end{cases} \quad (2)$$

Another form of the first constraint is

$$x_2(t) = -x_1'(t) - x_1(t)$$

where by putting initial condition in it

$$x_1'(0) + x_1(0) = 0.$$

will obtain.

With supposing $x_1(t) = x(t)$, OCP (2) is converts to the following form:

$$\text{Min} \quad J = \int_0^T (2(x(t) - 0.5)^2 + u^2(t))dt$$

$$\text{subject to } u(t) = -x''(t) - 2x'(t) - x(t) \quad (3)$$

with the initial conditions

$$x(0) = 0.75, \quad x'(0) + x(0) = 0.$$

As previously mentioned, in ordinary methods x or u values may be negative. Therefore, we try to use another algorithm (3.1). Based on this algorithm, where $n = 9, T = 1$, and with considering

$$x(t) = \sum_{i=0}^{9} a_i t^i \quad (4)$$

control values will have an expansion to form polynomial such as

$$u(t) = \sum_{i=0}^{9} b_i t^i \quad (5)$$

So, with substituting in the constraint and initial conditions and coefficients of control, value will be as following form:

$$\begin{aligned} b_0 &= 0.75 - 2a_2, \\ b_1 &= -4a_2 - 6a_3 + 0.75, \\ b_2 &= -a_2 - 6a_3 - 12a_4, \\ b_3 &= -a_3 - 8a_4 - 20a_5, \\ b_4 &= -a_4 - 10a_5 - 30a_6, \\ b_5 &= -a_5 - 12a_6 - 42a_7, \\ b_6 &= -a_6 - 14a_7 - 56a_9, \\ b_7 &= -a_7 - 16a_8 - 72a_9, \\ b_9 &= -a_8 - 18a_9, \\ b_9 &= -a_9. \end{aligned}$$

If we put these values in the cost function, object function will be a function of a_i for $i = 0,1,2,...,9$, In this case, problem optimizes with non-negative constrain for b_i and parameters will obtain such as following form:

$$\begin{aligned} a_0 &= 0.75, \\ a_1 &= -0.75, \\ a_2 &= 0.375, \\ a_3 &= -0.125, \\ a_4 &= 0.03125, \\ a_5 &= -0.00625, \\ a_6 &= 0.0010416666666667, \\ a_7 &= -0.000148809523809528, \\ a_8 &= 0.0000186011904761915, \\ a_9 &= -0.00000206679894179910 \end{aligned}$$

The value of cost function will be $J = 0.0381930784823$.

In Figures 1-3, state and control variables, and constrain error is shown.

For $T = 1$ cost functional for several n is obtained and in Table 1 is shown.

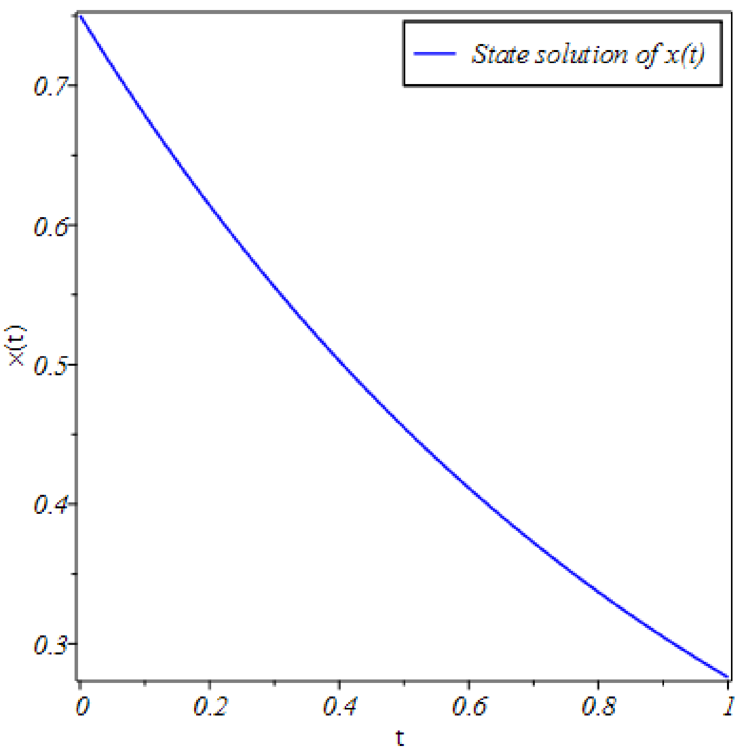

Figure 1. State function for Glucose model

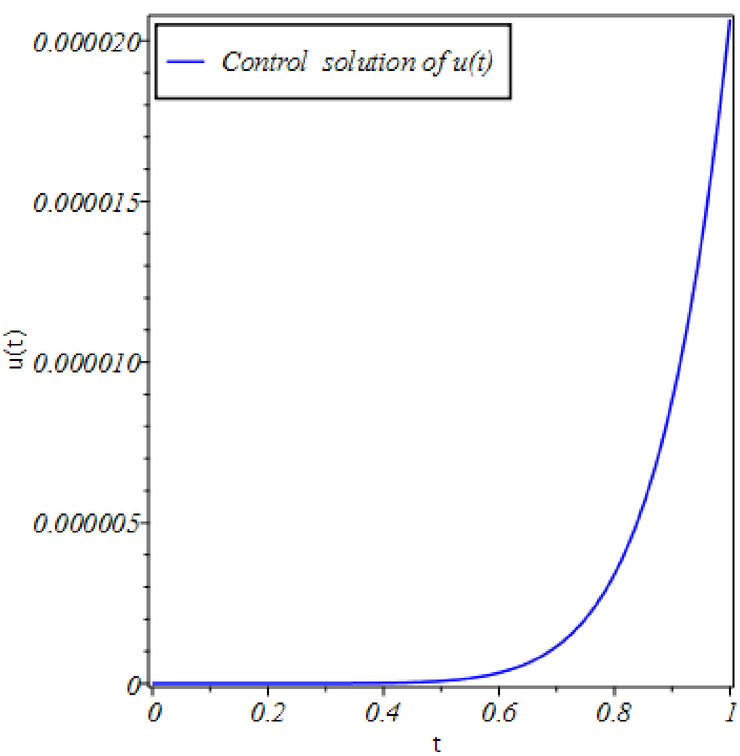

Figure 2. Control function for Glucose model

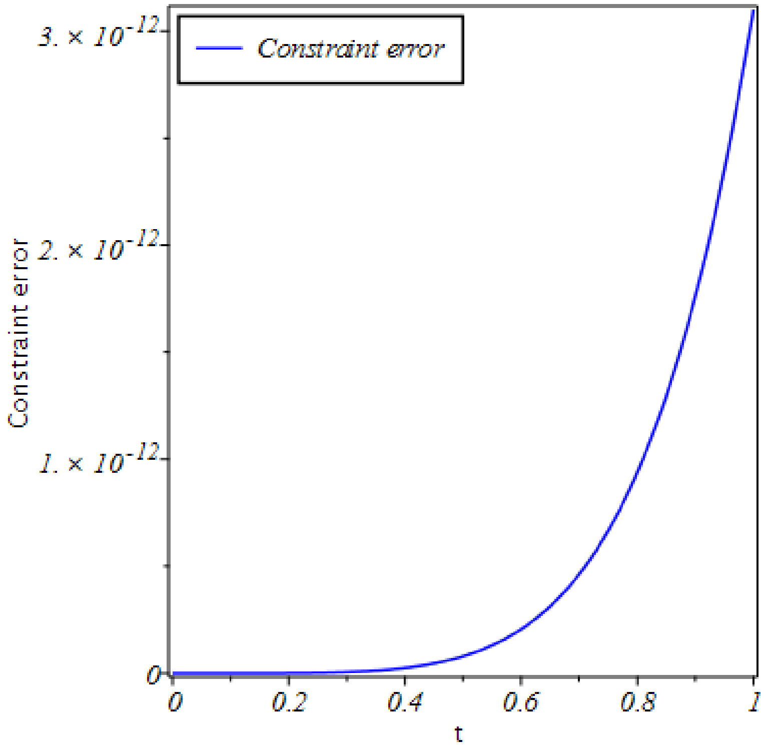

Figure 3. Constraint error $\left|x''(t)+2x'(t)+x(t)+u(t)\right|$ for Glucose model

Table 1. Cost functional for several of n in Glucose model

n	**Cost function**
1	1.437500000
2	1.43749999998125
3	0.08794642855625
4	0.06243489581885
5	0.03844195299755
6	0.0384415299755
7	0.03819462508368
8	0.03819462508368
9	0.03819307874823
10	0.03819307874823
11	0.03819306501308

It is clear that when algorithm 3.1 is repeated 10 times, the cost function with error 10^{-8} and high accuracy will obtain.

On the other hand, the approximation was examined in form (4)-(5) for the Glucose model without using the non-negative constraints $b_i \geq 0$ for $i = 0,1,2,...,n$. In Figure 4 the control variable is plotted. It is clear that the solution is not acceptable.

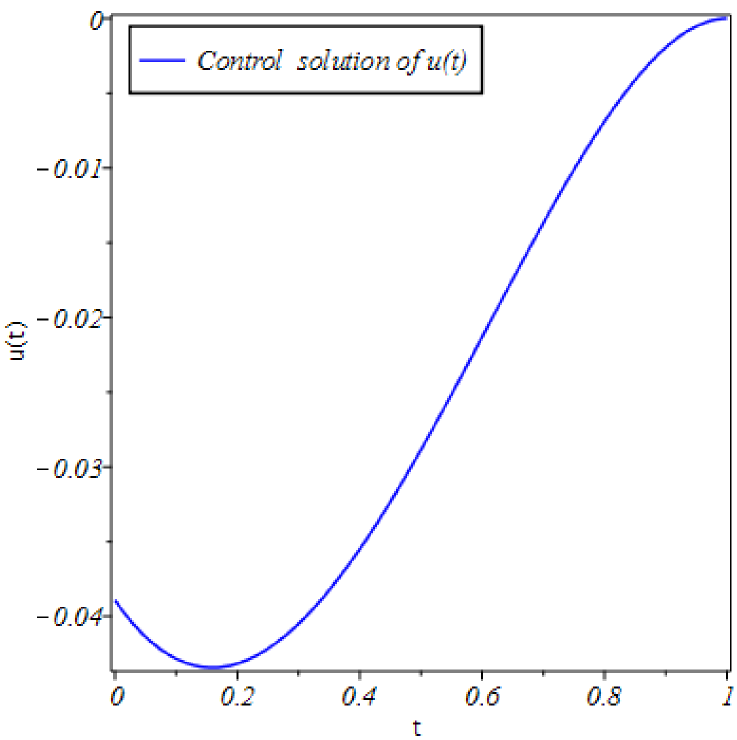

Figure 4. Control function for Glucose model using the power series

In [2] with $T = 0.5$, the control variable becomes negative while in the proposed method with $T = 1$, the control variable is non-negative.

CONCLUSIONS

In this paper, new solution of OCP related to GTT is represented. GTT is widely used in medical filed. In proposing solution, we obtained a series of polynomials with non-negative coefficients for control value by using of parameterization state variable. This approximation for solution, belong to region feasible that related to physical phenomena. The simplicity, lower requirement for mathematical calculations and more compatibility with variables are positive aspects of our parameterization method.

In this work, Maple software is used for calculations.

Conflict of interests

The authors declare that they have no conflict of interest.

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