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COMPUTATIONAL METHODS FOR THE FRACTIONAL OPTIMAL CONTROL HIV INFECTION

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Abstract. In this paper two numerical methods are used to study the nonlinear fractional optimal control problem (FOCP) for the human immunodeficiency virus (HIV) model. The objective functional is based on a combination of maximizing benefit relied on uninfected cells count and minimizing the systemic cost of chemotherapy. The state equations are given as a system of fractional order differential equations (FODEs). The fractional derivatives are described in the Caputo sense. The Pontriagyn maximum principle (PMP) is used to obtain a necessary optimality condition for the FOCP. The optimality system is derived and we introduce an iterative optimal control method (IOCM) to solved it numerically, comparisons between IOCM and the generalized Euler method (GEM) are given. Numerical experiment is presented to demonstrate the validity and applicability of the proposed technique. we can conclude that IOCM is preferable because the uninfected cells are increasing using the proposed method than GEM, moreover the infected cells are decreasing in better way than GEM.

1. Introduction

It is well known that the human immunodeficiency virus (HIV) is a retrovirus that infects cells of the immune system, destroying or impairing their function. As the infection progresses, the immune system becomes weaker, and the person becomes more susceptible to infections. The most advanced stage of HIV infection is acquired immunodeficiency syndrome (AIDS) [22]. HIV infection can generally be broken down into four distinct stages: primary infection, clinically asymptomatic stage, symptomatic HIV infection, and progression from HIV to AIDS.

This paper attempts the numerical solution for fractional order model of HIV infection of $CD4^{+}T$ cells. The reason of using FODEs are that, naturally related to systems with memory because the definition of fractional derivative involves an integration which is non local operator (as it is defined on an interval) so fractional derivative is a non local operator. Also FODEs are closely related to fractals which are abundant in biological systems.

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Fractional calculus has been successfully applied to system biology, physics, chemistry and biochemistry, hydrology, medicine, and finance see ([6],[8],[11],[18]). It is also shown that the materials with memory, hereditary effects and dynamical processes including gas diffusion and heat conduction in fractal porous media can be modeled by fractional order models better than integer models [21].

Fractional optimal control problems (FOCPs) are a set of FODEs describing the paths of the control variables that maximize a function of the state and control variables. There are several different ways of defining fractional derivatives, and, consequently, different types of FOCPs. However, the ones in the sense the Riemann-Liouville and the Caputo have been more widely used. In ([3],[4]), the FOCPs are formulated using the definition of fractional derivatives in the sense of Caputo. There are a lot of the numerical methods to solve a FOCPs such as ([2], [5], [20]).

Model Problem: There are several mathematical models have been proposed to describe the in vivo dynamics of T cell and HIV interaction, these models using ordinary differential equations (ODEs) have been developed to investigate the dynamics of HIV infection, see ([9],[12],[15],[16]). We consider the HIV infection model of $CD4^+T$ cells [7]. Let $T(t)$ and $I(t)$ be the concentration (population number per unit volume) of uninfected and infected $CD4^+T$ cells, respectively. Let $V(t)$ be the concentration of free virus particles. We interested in the retention and/or increase of the $CD4^+T$ cell count. This model is characterized by a system of the nonlinear ordinary differential equations.

Let us consider the following optimal control problem:

$$\text{maximize } J(t,u,T) = \int_0^L \left[T(t) - \frac{B}{2}(1-u(t))^2 \right] dt, \tag{1}$$

subject to the constraints:

$$\begin{aligned} \frac{dT}{dt} &= \frac{s}{1+V(t)} - m_1 T(t) + rT(t)\left(1 - \frac{T(t)+I(t)}{T_{max}}\right) - u(t)kV(t)T(t); \\ \frac{dI}{dt} &= u(t)kV(t)T(t) - m_2 I(t); \\ \frac{dV}{dt} &= Nm_2 I(t) - m_3 V(t); \end{aligned} \tag{2}$$

$$T(0) = T_0,\ I(0) = I_0,\ V(0) = V_0,\ 0 \le u(t) \le 1; \tag{3}$$

where L is a final time and $B > 0$ is a cost parameter. The variables and parameters are described below in Table 1, for more details see [7]. We introduce fractional-order into the model (2) of HIV infection of the $CD4^+T$ cells. The new system is described by the following set of FODEs of order $\alpha > 0$:

$$\begin{aligned} {}_0^C D_t^\alpha T(t) &= \frac{s}{1+V(t)} - m_1 T(t) + rT(t)\left(1 - \frac{T(t)+I(t)}{T_{max}}\right) - u(t)kV(t)T(t), \\ {}_0^C D_t^\alpha I(t) &= u(t)kV(t)T(t) - m_2 I(t), \\ {}_0^C D_t^\alpha V(t) &= Nm_2 I(t) - m_3 V(t), \end{aligned} \tag{4}$$

where ${}_0^C D_t^\alpha$ is the Caputo fractional derivative.

The remainder of this paper is organized as follows : In Section 2, mathematical preliminaries of the fractional calculus theory which are required for establishing

TABLE 1. Variables and parameters of the proposed model with their values.

Notation	Dependent variables	Values
T	Uninfected $CD4^+T$ cell population	800 mm^3
I	Infected $CD4^+T$ cell population	0.04 mm^3
V	Infectious HIV population	1.5 mm^3
	Parameter and Constants	
s	Source term for uninfected $CD4^+T$	10 mm^3d^{-1}
m_1	Death rate of uninfected $CD4^+T$ cell population	0.02 d^{-1}
m_2	Death rate of infected $CD4^+T$ cell population	0.5 d^{-1}
m_3	Death rate of free virus	$4.4d^{-1}$
k	Rate $CD4^+T$ cells become infected by free virus	0.000024 mm^3d^{-1}
r	Rate of growth for the $CD4^+T$ cell population	0.03 d^{-1}
N	Number of free virus produced by I cells	300
T_{max}	Maximum $CD4^+T$ cell population level	1500 mm^3

the results are given. In Sections 3, the necessary optimality conditions for the fractional order HIV model are derived. In Section 4, IOCM is introduced for solving the propose model. Finally, in Section 5, numerical simulations are given to show the efficiency of proposed method.

2. Definitions and Preliminaries

Definition 2.1. [17] *The left Caputo fractional derivative (LCFD) is defined as follows:*

$$ {}_a^C D_t^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \int_a^t (t-\tau)^{n-\alpha-1} \frac{d^n}{d\tau^n} x(\tau) d\tau, $$

the right Caputo fractional derivative (RCFD) is defined as follows:

$$ {}_t^C D_b^\alpha f(t) = \frac{(-1)^n}{\Gamma(n-\alpha)} \int_t^b (\tau-t)^{n-\alpha-1} \frac{d^n}{d\tau^n} x(\tau) d\tau. $$

Where Γ is the Euler gamma function.

Definition 2.2. [17] *The Grünwald-Letnikov's fractional derivative (GLFD) is defined as:*

$$ D^\alpha f(t) = \lim_{h\to 0} \frac{1}{h^\alpha} \sum_{i=0}^{[\frac{t}{h}]} w_i^{(\alpha)} f(t-ih), $$

where $[a]$ denotes the integer part of a and

$$ w_i^{(\alpha)} = (-1)^i \binom{\alpha}{i} = \frac{\Gamma(\alpha+1)}{i!\Gamma(\alpha-i+1)}, $$

with $\binom{\alpha}{i}$ being the fractional binomial coefficients. It is clear that the coefficients $w_i^{(\alpha)}$ can be evaluated recursively as follows:

$$ w_0^{(\alpha)} = 1, \quad w_i^{(\alpha)} = \left(1 - \frac{\alpha+1}{1}\right) w_{i-1}^{(\alpha)}, \quad i \geq 1. $$

2.1. **Generalized Euler Method.**

GEM is a generalization of the classical Euler's method. The headlines of this method is given as follows, let us consider the following initial value problem

$$D_*^{\alpha} y(t) = f(y(t), t), \quad y(0) = y_0, \quad 0 < \alpha \leq 1, \quad t > 0, \tag{5}$$

where D_*^{α} is the Caputo fractional derivative. Let $[0, a]$ be the interval over which we want to find the solution of the problem (5). The interval $[0, a]$ will be subdivided into k subintervals $[t_j, t_{j+1}]$ of equal width $h = a/k$ by using the nodes $t_j = jh$, for $j = 0, 1, ..., k$.

The general formula for GEM when $t_{j+1} = t_j + h$ is

$$y(t_{j+1}) = y(t_j) + \frac{h^{\alpha}}{\Gamma(\alpha + 1)} \ f(t_j, y(t_j)), \tag{6}$$

for $j = 0, 1, ..., k - 1$. It is clear that if $\alpha = 1$, then the GEM (6) reduces to the classical Euler's method, for more details see [13]

2.2. **Fractional Optimal Control Problem Formulation.**

The main point in FOCPs is to find the optimal control $u(t)$ which maximizes the following objective function [1]

$$J(u) = \int_0^1 f(x, u, t) \ dt, \tag{7}$$

subject to the constraint,

$${}_a^C D_t^{\alpha} x = g(x, u, t), \tag{8}$$

and satisfying the initial conditions

$$x(0) = x_0.$$

Here t denotes the time, $x(t)$ and $u(t)$ are a $n \times 1$ state and $m \times 1$ control vectors (not necessarily in same dimension) respectively, f and g are a scalar and a $n \times 1$ vector functions, a ${}_a^C D_t^{\alpha} x$ is LCFD of order α of x, with respect to t. The following expression defines a modified objective function

$$\tilde{J} = \int_0^1 \left[H(x, u, t) - \lambda^{tr} \ {}_a^C D_t^{\alpha} x \right] dt, \tag{9}$$

where $H(x, u, t)$ is the following Hamiltonian

$$H(x, u, \lambda, t) = f(x, u, t) + \lambda^{tr} \ g(x, u, t), \tag{10}$$

and λ^{tr} is the transpose of a $n_x \times 1$ vector of Lagrange multipliers. Here the superscript tr represents the transpose of the vector. From (9) and (10), we can derive [1]:

$$\begin{aligned} {}_t^C D_1^{\alpha} \lambda &= \frac{\partial H}{\partial x}, \\ 0 &= \frac{\partial H}{\partial u}, \\ {}_0^C D_t^{\alpha} x &= \frac{\partial H}{\partial \lambda}, \end{aligned} \tag{11}$$

and it is also required that

$$\lambda(b) = 0. \tag{12}$$

Eqs.(11) and (12) describe the necessary conditions in terms of a Hamiltonian for the FOCP defined above. These conditions result a set of fractional differential equations (FDEs), in terms of the variables state x, control u, and Lagrange multiplier λ , to be solved analytical or numerically or even both.

3. Optimality Condition for the Fractional-Order HIV Model

To obtain the necessary optimality conditions for FOCPs, we define the Hamiltonian function as:

$$\begin{aligned} H(T,I,V,u,\lambda_1,\lambda_2,\lambda_3) = T - \frac{B}{2}(1-u)^2 + \lambda_1\left[\frac{s}{1+V} - m_1T + rT\left(1-\frac{T+I}{T_{max}}\right) - ukVT\right] \\ + \lambda_2\left(ukVT - m_2I\right) + \lambda_3\left(Nm_2I(t) - m_3V(t)\right), \end{aligned}$$

where $\lambda_i(t), \quad i = 1,2,3$ are the Lagrange multipliers, also known as a co-state or adjoint variables.

Theorem 3.1. [10] *Given an optimal control u and solutions of the corresponding state system (4), there exist costate variables $\lambda_i, \quad i = 1,2,3$ satisfying*

(i) *co-state equations:*

$$\begin{aligned} \dot{\lambda_1} &= -\frac{\partial H}{\partial T} = -1 + \lambda_1\left(m_1 - r + \frac{2rT + rI}{T_{max}}\right) - (\lambda_2 - \lambda_1)kuV, \\ \dot{\lambda_2} &= -\frac{\partial H}{\partial I} = \frac{\lambda_1 rT}{T_{max}} + \lambda_2 m_2 - \lambda_3 N m_2, \\ \dot{\lambda_3} &= -\frac{\partial H}{\partial V} = \frac{s\lambda_1}{(1+V)^2} - (\lambda_2 - \lambda_1)(kuT) + \lambda_3 m_3, \end{aligned} \tag{13}$$

(ii) *optimality conditions:*
$H(T,I,V,\lambda_1,\lambda_2,\lambda_3,u) = \max_{0\le u\le 1} H(T,I,V,\lambda_1,\lambda_2,\lambda_3,u^*)$, *which implies that*

$$u = \min\left\{\left(\frac{(\lambda_2-\lambda_1)kVT + B}{B}\right)^+, 1\right\}, \tag{14}$$

where the stationarity condition is $\frac{\partial H}{\partial u} = 0$ *and*

$$\left(\frac{(\lambda_2-\lambda_1)kVT+B}{B}\right)^+ = \begin{cases} \frac{(\lambda_2-\lambda_1)kVT+B}{B}, & if \quad \frac{(\lambda_2-\lambda_1)kVT+B}{B} \ge 0 \\ 0, & if \quad \frac{(\lambda_2-\lambda_1)kVT+B}{B} < 0 \end{cases};$$

(iii) *transversality conditions :*

$$\lambda_i(t_f) = 0, i = 1,2,3. \tag{15}$$

4. A Numerical Scheme for the Fractional-Order HIV Model

The aim of this section is to solve FODEs (4) it must first be discretized. In this part we use Grünwald-Letnikov's method (definition 2.2) to discretization the fractional derivative ${}_a^C D_t^\alpha f(t)$. So by some simple calculations, system (4) is discretized

as follows:

$$
\begin{aligned}
T_j &= \frac{\frac{s}{1+V_j} - \sum_{i=1}^{j} w_i^{\alpha} T_{j-i}}{w_0^{\alpha} + m_1 - r\left(1 - \frac{T_j + I_j}{T_{max}}\right) + k u_j V_j} \\
I_j &= \frac{k u_j V_j T_j - \sum_{i=1}^{j} w_i^{\alpha} I_{j-i}}{w_0^{\alpha} + m_2} \\
V_j &= \frac{N m_2 I_j - \sum_{i=1}^{j} w_i^{\alpha} V_{j-i}}{w_0^{\alpha} + m_3}
\end{aligned}
\tag{16}
$$

4.1. **IOCM Algorithm.**

In the following we presented IOCM algorithm to solving the optimization problem (1) :

Step 0: *Choose a starting point* (T_0, I_0, V_0); *set* $j = 0$.

Step 1: *Compute* $u(j)$ *according to the formula*

$$u(j) = \min\left\{\left(\frac{(\lambda_2(j) - \lambda_1(j))kV(j)T(j) + B}{B}\right)^{+}, 1\right\},$$

where $(a)^{+}$ *is defined as*

$$(a)^{+} = \begin{cases} a, & if \quad a > 0 \\ 0, & if \quad a \leq 0 \ ; \end{cases}$$

by solving the co-state system (13) with transversality conditions $\lambda_i(t_f) = 0,\ i = 1, 2, 3$.

Step 2: *Plugging the value of* $u(j)$ *into the system (16) and solve it with the same starting point to obtain the new starting point* (T_j, I_j, V_j).

Step 3: *The stopping criterion is as follows:*
if $\mid u(j) - u(j+1) \mid < \epsilon$ *then* ***stop***
else $j = j + 1$; *go to* ***Step 1***. *Where* ϵ *is a small positive integer.*

5. Numerical Experiment

The following, IOCM is used to obtain the approximate solutions for systems (4) and (13) as explained in the fourth section. Using the initial condition and parameters in Table 1.

From the obtained results in the presented tables and figures, it is clear that the primary stage of the infection with the HIV virus, a dramatically decrease in the level of the $CD4^{+}T$ cells occurs because of the death of such infected cells. On the other hand, the number of uninfected cells increase. The number of the free HIV virus particles are decrease with time as shown in figures above. This assumes that the growth of healthy cells slows down during the course of HIV infection. The concentration of uninfected $CD4^{+}T$ cells T, infected $CD4^{+}T$ cells I and free virus particles V in the blood have been obtained, therefor when, $\alpha = 1$ the solution of the fractional model (4), reduce to standard solution.

6. Conclusions

In this paper the fractional optimal control problems for HIV infection is presented and a set of necessary optimality conditions are derived. The methods GEM and IOCM are applied to solve the model problem numerically. Numerical experiment is given to demonstrate the validity and applicability of the presented technique. It is found that IOCM is preferable because the uninfected cells are increasing using the proposed method than GEM, moreover the infected cells are decreasing in better way than GEM.

References

[1] O.P. Agrawal,*A Formulation and Numerical Scheme for Fractional Optimal Control Problems*, Journal of Vibration and Control, 14 (2008) 1291-1299.

[2] O.P.Agrawal, D.Baleanu,*A Hamiltonian Formulation and a Direct Numerical Scheme for Fractional Optimal Control Problems*, Journal of Vibration and Control, 13 (2007) 1269-1281.

[3] O.P. Agrawal, *A Quadratic Numerical Scheme for Fractional Optimal Control Problems*, ASME Journal of Dynamic Systems, Measurement, and Control, 130 (2008) 011010-1 - 011010-6.

[4] O.P. Agrawal, *Fractional Optimal Control of a Distributed System Using Eigenfunctions*, ASME Journal of Computational and Nonlinear Dynamics, 3 (2008) 021204-1 - 021204-6.

[5] D.Baleanu, O.Defterli, O.P.Agrawal, *A Central Difference Numerical Scheme for Fractional Optimal Control Problems*, Journal of Vibration and Control, 15 (2009) 583-597.

[6] D. Baleanu, K. Diethelm, E. Scalas, and J. J. Trujillo, *Fractional Calculus Models and Numerical Methods. Series on Complexity, Nonlinearity and Chaos*, World Scientific Publishing Co. Pte. Ltd., Hackensack, NJ, USA, 2012.

[7] S.Butler, D. Kirschner and S. Lenhart, *Optimal Control of the Chemotherapy Affecting the Infectivity of HIV*, Advances in Mathematical Population Dynamics-Molecules, Cells and Man(1997), Editors: O. Arino, D. Axelrod, and M. Kimmel, World Scientific Press, Singapore, 557-569.

[8] L. Debnath, *Recent Applications of Fractional Calculus to Science and Engineering*, International Journal of Mathematics and Mathematical Sciences, 54 (2003), 3413?3442.

[9] P. De Leenheer, H.L. Smith, *Virus Dynamics: a Global Analysis*, SIAM J. Appl. Math., 63 (2003) 1313-1327.

[10] K. R. Fister, S. Lenhart and J. S. McNally, *Optimizing Chemotherapy in an HIV Model*, Electronic Journal of Differential Equations, 1998 (1998), 1-12.

[11] E. R. Hilfer, *Applications of Fractional Calculus in Physics*, World Scientific, River Edge, NJ, USA, 2000.

[12] P. W. Nelson, A. S. Perelson, *Mathematical Analysis of Delay Differential Equation Models of HIV-1 Infection*, Math.Biosci., 179 (2002), 73-94.

[13] Z. Odibat and S. Momani, *An Algorithm for the Numerical Solution of Differential Equations of Fractional Order*, J. Appl. Math. Inform., 26 (2008), 15-27.

[14] Z. Odibat and N. Shawagfeh, *Generalized Taylor?s formula*, Appl. Math. Comput., 186 (2007), 286-293.

[15] A. S. Perelson, P. W. Nelson, *Mathematical Analysis of HIV-I Dynamics in Vivo*, SIAM Rev., 41 (1999), 3-44.

[16] A. S. Perelson, D. E. Kirschner and R. de Boer, *Dynamics of HIV Infection of $CD4^+T$ Cells*, Math. Biosci., 114 (1993), 81-125.

[17] I. Podlubny, *Fractional Differential Equations*, Academic Press, New York, 1999.

[18] F. A. Rihan, *Numerical Modeling of Fractional Order Biological Systems*, Abstract and Applied Analysis, 2013, (2013), 11 pages.

[19] N. H. Sweilam, T. M. Al-Ajami, and R. H. W. Hoppe, *Numerical Solution of Some Types of Fractional Optimal Control Problems*, The Scientific World Journal, 2013 (2013), 9 pages.

[20] C. Tricaud, Y. Chen, *An Approximate Method for Numerically Solving Fractional Order Optimal Control Problems of General Form*, Computers and Mathematics with Applications, 59 (2010), 1644-1655.

[21] M. Zamani, M. Karimi-Ghartemani and N. Sadati, *FOPID Controller Design for Robust Performance Using Particle Swarm Optimization*, J. Fract. Calc. Appl.Anal., 10 (2007), 169-188.
[22] `http://www.who.int/topics/hiv_aids/en/`.

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TABLE 2. Comparisons between GEM and IOCM after 20 days from infection, where (T_0, I_0, V_0)=(800, 0.04, 1.5)and $\alpha = 1$.

	GEM				IOCM - Algorithm			
$t(days)$	T	I	V	u	T	I	V	u
0	800.00	0.0400	1.5000	0.0010	800.00	0.0400	1.5000	0.0000
5	809.53	0.0029	0.1105	0.0010	884.96	0.0002	0.0080	0.6955
10	831.37	0.0002	0.0081	0.8050	941.04	0.0004	0.0123	0.6830
15	852.45	0.00006	0.0006	0.9927	967.84	0.0009	0.0292	0.7088
20	871.27	0.00002	0.0001	0.9990	965.75	0.0094	0.3169	1.0000

TABLE 3. Comparisons between GEM and IOCM after 20 days from infection, where (T_0, I_0, V_0)=(800, 0.04, 1.5)and $\alpha = 0.98$.

	GEM				IOCM - Algorithm			
$t(days)$	T	I	V	u	T	I	V	u
0	800.00	0.0400	1.5000	0.0010	800.00	0.0400	1.5000	0.0000
5	810.36	0.0026	0.0985	0.0010	842.05	0.0003	0.0087	0.6840
10	833.20	0.0002	0.0065	0.8433	906.02	0.0003	0.0118	0.7060
15	854.93	0.00001	0.0005	0.9945	942.20	0.0008	0.0279	0.7256
20	874.18	0.000001	0.00003	0.9990	947.13	0.0113	0.3759	1.0000

TABLE 4. Comparisons between GEM and IOCM after 20 days from infection, where (T_0, I_0, V_0)=(800, 0.04, 1.5)and $\alpha = 0.95$.

	GEM				IOCM - Algorithm			
$t(days)$	T	I	V	u	T	I	V	u
0	800.00	0.0400	1.5000	0.0010	800.00	0.0400	1.5000	0.0000
5	811.69	0.0021	0.0821	0.0010	778.24	0.0003	0.0096	0.6722
10	836.05	0.0001	0.0046	0.8889	849.64	0.0003	0.0110	0.7409
15	858.73	0.00007	0.0003	0.9963	897.43	0.0007	0.0250	0.7629
20	878.62	0.00004	0.00001	0.9990	916.43	0.0083	0.2758	1.0000

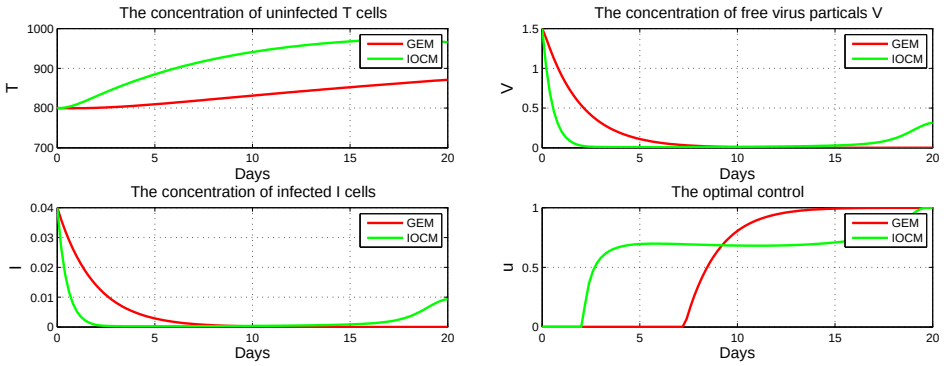

FIGURE 1. The concentration of uninfected $CD4^+T$ cells $T(t)$, infected $CD4^+T$ cells $I(t)$, free infectious virus particles $V(t)$ in the blood and the optimal control u with $0 \leq u \leq 1$. Here we initiate treatment after 20 days from infection, $\alpha = 1$.

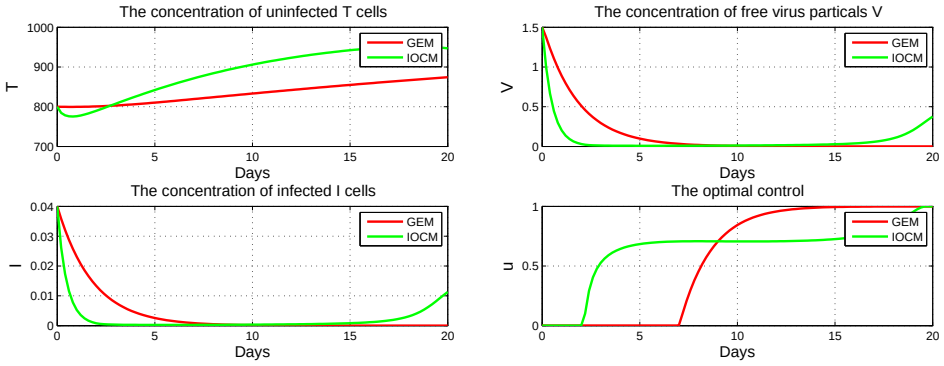

FIGURE 2. The concentration of uninfected $CD4^+T$ cells $T(t)$, infected $CD4^+T$ cells $I(t)$, free infectious virus particles $V(t)$ in the blood and the optimal control u with $0 \leq u \leq 1$. Here we initiate treatment after 20 days from infection, $\alpha = 98$.

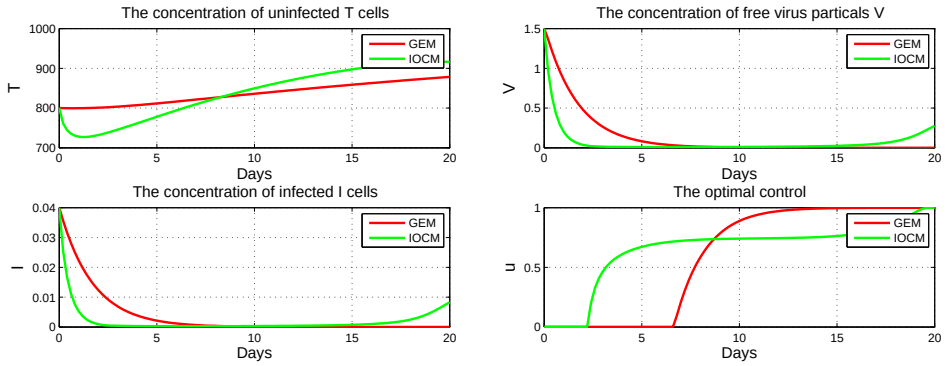

FIGURE 3. The concentration of uninfected $CD4^+T$ cells $T(t)$, infected $CD4^+T$ cells $I(t)$, free infectious virus particles $V(t)$ in the blood and the optimal control u with $0 \leq u \leq 1$. Here we initiate treatment after 20 days from infection, $\alpha = 95$.