

Research Article

Optimal Control of a Delayed HIV Infection Model via Fourier Series

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We present a delayed optimal control which describes the interaction of the immune system with the human immunodeficiency virus (HIV) and CD4⁺ T-cells. In order to improve the therapies, treatment and the intracellular delays are incorporated into the model. The optimal control in this model represents the efficiency of drug treatment in preventing viral production and new infections. The optimal pair of control and trajectories of this nonlinear delay system with quadratic cost functional is obtained by Fourier series approximation. The method is based on expanding time varying functions in the nonlinear delay system into their Fourier series with unknown coefficients. Using operational matrices for integration, product, and delay, the problem is reduced to a set of nonlinear algebraic equations.

1. Introduction

Delays occur frequently in biological, chemical, electronic, and transportation systems [1]. Many mathematical models have been developed in order to understand the dynamics of HIV infection [2–7]. Moreover, optimal control methods have been applied to the derivation of optimal therapies for this HIV infection [8–14]. All these methods are based on HIV models which ignore the intracellular delay by assuming that the infectious process is instantaneous; that is, as soon as the virus enters an uninfected cell, it starts to produce virus particles; however, this is not reasonable biologically. In this paper, we consider the mathematical model of HIV infection with intracellular delay presented in [15] in order to make the model more tangible and closer to what happens in reality.

Orthogonal functions (OFs) have received considerable attention in dealing with various problems of dynamic systems. Using operational matrices, the technique is based on reduction of these problems to systems of algebraic equations. Special attention has been given to applications of Walsh functions [16], block-pulse functions [17], Laguerre polynomials [18], Legendre polynomials [19], Chebyshev polynomials [20], and Fourier series [21].

In this paper, we apply Fourier series approximation to find the optimal pair of control and trajectories of the nonlinear delayed optimal control system governed by ordinary delay differential equations which describe the interaction of the human immunodeficiency virus (HIV). Operational matrices of integration, product, and delay have the most important role in our method. The paper is organized as follows. Section 2 consists of an introduction to Fourier series approximation and operational and other matrices, being used in Section 4. Section 3 proposes the delayed optimal control model of HIV infection. In Section 4, we utilize the Fourier series approximation to solve our model and results are demonstrated by some figures. Finally, the conclusions are summarized in Section 5.

2. Properties of Fourier Series

A measurable function defined over the interval 0 to L may be expanded into a Fourier series as follows:

$$f(t) = a_0 + \sum_{n=1}^{\infty} \left\{ a_n \cos\left(\frac{2n\pi t}{L}\right) + a_n^* \sin\left(\frac{2n\pi t}{L}\right) \right\}, \quad (1)$$

where the Fourier coefficients a_n and a_n^* are given by

$$a_0 = \frac{1}{L} \int_0^L f(t) dt, \quad (2a)$$

$$a_n = \frac{2}{L} \int_0^L f(t) \cos\left(\frac{2n\pi t}{L}\right) dt, \quad n = 1, 2, 3, \dots, \quad (2b)$$

$$a_n^* = \frac{2}{L} \int_0^L f(t) \sin\left(\frac{2n\pi t}{L}\right) dt, \quad n = 1, 2, 3, \dots \quad (2c)$$

The series in (1) has an infinite number of terms. To obtain an approximate expression for $f(t)$, one can truncate the series up to the $(2r + 1)$ th term as follows:

$$\begin{aligned} f(t) &= a_0 + \sum_{n=1}^r \left\{ a_n \cos\left(\frac{2n\pi t}{L}\right) + a_n^* \sin\left(\frac{2n\pi t}{L}\right) \right\} \\ &= A^T \phi(t), \end{aligned} \quad (3)$$

where the Fourier series coefficient vector A and the Fourier series vector $\phi(t)$ are defined as

$$A = [a_0 \ a_1 \ a_2 \ \dots \ a_r \ a_1^* \ a_2^* \ \dots \ a_r^*]^T, \quad (4)$$

$$\Phi = [\phi_0(t) \ \phi_1(t) \ \dots \ \phi_r(t) \ \phi_1^*(t) \ \dots \ \phi_r^*(t)]^T, \quad (5)$$

where

$$\phi_n(t) = \cos\left(\frac{2n\pi t}{L}\right), \quad n = 0, 1, 2, 3, \dots, r, \quad (6a)$$

$$\phi_n^*(t) = \sin\left(\frac{2n\pi t}{L}\right), \quad n = 1, 2, 3, \dots, r. \quad (6b)$$

The elements of $\Phi(t)$ are orthogonal in the interval $[0, L]$. By integrating both sides of (6a) and (6b) with respect to θ , we obtain

$$\int_0^t \phi_0(\theta) d\theta = t, \quad (7)$$

$$\int_0^t \phi_n(\theta) d\theta = \frac{L}{2n\pi} [\phi_n^*(t) - \phi_n^*(0)], \quad n \geq 1, \quad (8)$$

$$\int_0^t \phi_n^*(\theta) d\theta = \frac{L}{2n\pi} [\phi_n(0) - \phi_n(t)], \quad n \geq 1. \quad (9)$$

Now, we approximate the function t in the (7) by a truncated Fourier series. Consequently, the forward integral of the Fourier series vector $\Phi(t)$ can be represented by

$$\int_0^t \Phi(\theta) d\theta \cong P\Phi(t), \quad (10)$$

where $P_{(2r+1) \times (2r+1)}$ is the Fourier series operational matrix of forward integration and is given as

$$P = L \begin{bmatrix} \frac{1}{2} & 0 & 0 & \dots & 0 & 0 & \frac{-1}{\pi} & \frac{-1}{2\pi} & \dots & \frac{-1}{(r-1)\pi} & \frac{-1}{r\pi} \\ 0 & 0 & 0 & \dots & 0 & 0 & \frac{1}{2\pi} & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & 0 & 0 & 0 & 0 & \dots & \frac{1}{2(r-1)\pi} & 0 \\ 0 & 0 & 0 & \dots & 0 & 0 & 0 & 0 & \dots & 0 & \frac{1}{2r\pi} \\ \frac{1}{2\pi} & \frac{-1}{2\pi} & 0 & \dots & 0 & 0 & 0 & 0 & \dots & 0 & 0 \\ \frac{1}{4\pi} & 0 & \frac{-1}{4\pi} & \dots & 0 & 0 & 0 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \frac{1}{2r\pi} & 0 & 0 & \dots & 0 & \frac{-1}{2r\pi} & 0 & 0 & \dots & 0 & 0 \end{bmatrix}. \quad (11)$$

As a result, we obtain

$$\int_{\tau}^t \Phi(\theta - \tau) d\theta = P\Phi(t - \tau). \quad (12)$$

Moreover,

$$\int_0^{\tau} \Phi(t) dt = \Phi(\tau) - \Phi(0) = Z\Phi(t), \quad (13)$$

where

$$Z = \begin{bmatrix} \tau & 0 & \cdots & 0 & 0 & \cdots & 0 \\ \frac{L}{2\pi} \sin \frac{2\pi\tau}{L} & 0 & \cdots & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \frac{L}{2r\pi} \sin \frac{2r\pi\tau}{L} & 0 & \cdots & 0 & 0 & \cdots & 0 \\ \frac{L}{2\pi} \left(1 - \cos \frac{2\pi\tau}{L}\right) & 0 & \cdots & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \frac{L}{2r\pi} \left(1 - \cos \frac{2r\pi\tau}{L}\right) & 0 & \cdots & 0 & 0 & \cdots & 0 \end{bmatrix}. \quad (14)$$

The delay function $\Phi(t - \tau)$ is the shift of the function $\Phi(t)$ defined in (5) along the time axis by τ . The general expression is given by

$$\Phi(t - \tau) = S_{\tau}\Phi(t), \quad (15)$$

where S_{τ} is the delay operational matrix of Fourier series, which is as follows:

$$S_{\tau} = \begin{bmatrix} 1 & 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ 0 & \cos \frac{2\pi}{L} & 0 & \cdots & 0 & \sin \frac{2\pi}{L} & 0 & \cdots & 0 \\ 0 & 0 & \cos \frac{4\pi}{L} & \cdots & 0 & 0 & \sin \frac{4\pi}{L} & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & -\sin \frac{2\pi}{L} & 0 & \cdots & 0 & \cos \frac{2\pi}{L} & 0 & \cdots & 0 \\ 0 & 0 & -\sin \frac{4\pi}{L} & \cdots & 0 & 0 & \cos \frac{4\pi}{L} & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & \cdots & -\sin \frac{2r\pi}{L} & 0 & 0 & \cdots & \cos \frac{2r\pi}{L} \end{bmatrix}. \quad (16)$$

Also, we have (see [21])

$$D = \int_0^L \Phi(t) \Phi^T(t) dt = L \begin{bmatrix} 1 & & & \\ \frac{1}{2} & & & \\ & \frac{1}{2} & & 0 \\ 0 & & \frac{1}{2} & \ddots \\ & & & \frac{1}{2} \end{bmatrix}, \quad (17)$$

$$W = \int_0^L \Phi(t) dt = L \begin{bmatrix} 1 \\ 0 \\ \vdots \\ 0 \end{bmatrix}. \quad (18)$$

Using (3) and (10) leads to

$$\int_0^t f(\theta) d\theta \cong \int_0^t A^T \Phi(\theta) d\theta \cong A^T P\Phi(t). \quad (19)$$

We can get

$$\Phi(t) \Phi^T(t) A = \tilde{A}\Phi(t), \quad (20)$$

where \tilde{A} is the product operational matrix for the vector A (see [22]).

As a result,

$$\Phi(t - \tau) \Phi^T(t - \tau) A = \tilde{A}\Phi(t - \tau). \quad (21)$$

3. HIV Delayed Optimal Control Problem

Using time delay dynamic systems, many physical systems are best modeled as follows:

$$\begin{aligned} \frac{dx(t)}{dt} &= F(t, x(t), u(t), x_1(t - \tau_1), \dots, x_p(t - \tau_p), \\ &u_1(t - \eta_1), \dots, u_m(t - \eta_m)), \quad t \in [t_0, t_f], \end{aligned} \quad (22a)$$

$$x(t) = \Phi(t), \quad t \leq t_0, \quad (22b)$$

$$u(t) = \Psi(t), \quad t \leq t_0, \quad (22c)$$

where the state $x(t)$ is a p vector function, $u(t)$ is an m vector control function, τ_i and η_j ($i = 1, 2, \dots, p$, $j = 1, 2, \dots, m$) are nonnegative constant time delays, and the vector functions $\Phi(t)$ and $\Psi(t)$ are defined appropriately and given (see [23–26]).

In some systems of this type, it is desirable to select the optimal pair $(x^*(\cdot), u^*(t))$ which satisfies (22a), (22b), and (22c) and minimizes performance criterion modeled by a cost function of the form

$$I = G(x(t_f), t_f) + \int_{t_0}^{t_f} g(t, x(t), u(t)) dt. \quad (23)$$

The following model is a delayed control system of HIV infection of CD4⁺ T-cells (for more details, see [15]):

$$\dot{T} = s - \mu_T T(t) + rT(t) \left(1 - \frac{T(t) + I(t)}{T_{\max}}\right) \quad (24a)$$

$$- K_1 V(t) T(t),$$

$$\dot{I} = K_2 V(t - 1) T(t - 1) - \mu_I I(t), \quad (24b)$$

$$\dot{V} = N_1 \mu_b I(t) u(t) - K_1 V(t) T(t) - \mu_V V(t), \quad (24c)$$

$$T(t) = 120, \quad t \in [-1, 0], \quad (24d)$$

$$I(t) = 25, \quad t \in [-1, 0], \quad (24e)$$

$$V(t) = 2000, \quad t \in [-1, 0], \quad (24f)$$

$$u(t) = 0, \quad t \in [-1, 0], \quad (24g)$$

$$0 \leq u(t) \leq 1, \quad t \in [t_0, t_f], \quad (24h)$$

where control function $u(t)$ is showing the effect of drugs on HIV virus production. For the delayed control model (24a), (24b), (24c), (24d), (24e), (24f), (24g), and (24h), we consider the objective functional to be defined as

$$J(T, u) = \int_{t_0}^{t_f} \left(T - \frac{1}{2} B(1 - u(t))^2\right) dt, \quad (25)$$

where B , the weight of current costs of treatment, is assumed to be 100. Our goal is to maximize the objective functional (25) subject to the delayed control system (24a), (24b), (24c), (24d), (24e), (24f), (24g), and (24h), that is, to maximize

the total count of CD4⁺ T-cells and to minimize the costs of treatment. The treatment interval is assumed to be $I = [t_0, t_f] = [0, 300]$, which shows the duration on treatment in terms of days.

4. Solving the Delayed Optimal Control Model of the HIV Infection Using Fourier Series

According to Section 2, each function of $T(\cdot)$, $I(\cdot)$, $V(\cdot)$, and $U(\cdot)$ in the interval I can be approximated by a Fourier series. So,

$$\begin{aligned} T(t) &= \widehat{T}^T \Phi(t) = \Phi^T(t) \widehat{T}, \\ I(t) &= \widehat{I}^T \Phi(t) = \Phi^T(t) \widehat{I}, \\ V(t) &= \widehat{V}^T \Phi(t) = \Phi^T(t) \widehat{V}, \\ u(t) &= \widehat{U}^T \Phi(t) = \Phi^T(t) \widehat{U}, \end{aligned} \quad (26)$$

where \widehat{T} , \widehat{I} , \widehat{V} , and \widehat{U} are, respectively, the Fourier series coefficient vectors (all are unknown) of $T(t)$, $I(t)$, $V(t)$, and $u(t)$. For time delay functions $T(t - 1)$ and $V(t - 1)$, we have

$$\begin{aligned} 0 \leq t \leq 1 &\implies -1 \leq t - 1 \leq 0, \\ T(t - 1) &= 120, \quad 0 \leq t \leq 1, \\ V(t - 1) &= 2000, \quad 0 \leq t \leq 1. \end{aligned} \quad (27)$$

Therefore, for the interval I , we have

$$T(t - 1) = \begin{cases} 120, & 0 \leq t \leq 1, \\ \widehat{T}^T \Phi(t - 1) & 1 \leq t \leq 300, \end{cases} \quad (28a)$$

$$V(t - 1) = \begin{cases} 2000, & 0 \leq t \leq 1, \\ \widehat{V}^T \Phi(t - 1), & 1 \leq t \leq 300. \end{cases} \quad (28b)$$

By using (17), (18), and (26), one can rewrite (25) as follows:

$$\begin{aligned} J(T, u_2) &= \int_0^{300} \left[\widehat{T}^T \Phi(t) - 50 \right. \\ &\quad \left. \times (A^T \Phi(t) + \widehat{U}^T \Phi(t) \Phi^T(t) \widehat{U} - 2\widehat{U}^T \Phi(t)) \right] dt \\ &= \widehat{T}^T W - 50 (A^T W + \widehat{U}^T D \widehat{U} - 2\widehat{U}^T W), \end{aligned} \quad (29)$$

where $A^T \Phi(t)$ is Fourier series of 1, while $A = [1, 0, \dots, 0, 0, \dots, 0]^T$.

By integrating both sides of (24a) from 0 to t and using (26), (20), and (10), we obtain

$$\begin{aligned}
\int_0^t \dot{T}(\theta) d\theta &= T(t) - T(0) = \hat{T}^T \Phi(t) - T_0^T \Phi(t), \\
\int_0^t \left[s - \mu_T T + rT \left(1 - \frac{T+I}{T_{\max}} \right) - K_1 VT \right] d\theta \\
&= \int_0^t \left[S^T \Phi(\theta) - \mu_T \hat{T}^T \Phi(\theta) + r \hat{T}^T \Phi(\theta) - \frac{r}{T_{\max}} \right. \\
&\quad \times \left(\hat{T}^T \Phi(\theta) \Phi^T(\theta) \hat{T} + \hat{T}^T \Phi(\theta) \Phi^T(\theta) \hat{I} \right) \\
&\quad \left. - K_1 \hat{V}^T \Phi(\theta) \Phi^T(\theta) \hat{T} \right] d\theta \quad (30) \\
&= S^T P \Phi(t) + (r - \mu_T) \hat{T}^T P \Phi(t) \\
&\quad - \frac{r}{T_{\max}} \left(\hat{T}^T \tilde{T} P \Phi(t) + \hat{T}^T \tilde{I} P \Phi(t) \right) \\
&\quad - K_1 \hat{V}^T \tilde{T} P \Phi(t),
\end{aligned}$$

where S and T_0 are the Fourier series coefficient vectors of s and $T(0)$, respectively; that is, $S = [s, 0, \dots, 0, 0, \dots, 0]^T$, $T_0 = [120, 0, \dots, 0, 0, \dots, 0]^T$.

So,

$$\begin{aligned}
&\hat{T}^T \Phi(t) - T_0^T \Phi(t) \\
&= S^T P \Phi(t) + (r - \mu_T) \hat{T}^T P \Phi(t) \\
&\quad - \frac{r}{T_{\max}} \left(\hat{T}^T \tilde{T} P \Phi(t) + \hat{T}^T \tilde{I} P \Phi(t) \right) \\
&\quad - K_1 \hat{V}^T \tilde{T} P \Phi(t). \quad (31)
\end{aligned}$$

Similarly, for (24b), we have

$$\begin{aligned}
\int_0^t \dot{I}(\theta) d\theta &= I(t) - I(0) \\
&= \tilde{I}^T \Phi(t) - I_0^T \Phi(t), \quad (32)
\end{aligned}$$

by using (28a) and (28b) for the right-hand side of (24b), one can obtain

$$\begin{aligned}
&\int_0^t [K_2 V(\theta - 1) T(\theta - 1) - \mu_I I(\theta)] d\theta \\
&= \int_0^1 [K_2 V(\theta - 1) T(\theta - 1)] d\theta \\
&\quad + \int_1^t [K_2 V(\theta - 1) T(\theta - 1)] d\theta - \int_0^t \mu_I I(\theta) d\theta
\end{aligned}$$

$$\begin{aligned}
&= \int_0^1 (K_2 \times 2000 \times 120) d\theta \\
&\quad + \int_1^t K_2 \hat{V}^T \phi(\theta - 1) \Phi^T(\theta - 1) \hat{T} d\theta \\
&\quad - \int_0^t \mu_I \tilde{I}^T \Phi(\theta) d\theta \\
&= M_1 + M_2 - M_3, \quad (33)
\end{aligned}$$

where $M_1 = \int_0^1 (K_2 \times 2000 \times 120) d\theta$, $M_2 = \int_1^t K_2 \hat{V}^T \phi(\theta - 1) \Phi^T(\theta - 1) \hat{T} d\theta$, and $M_3 = \int_0^t \mu_I \tilde{I}^T \Phi(\theta) d\theta$.

To compute M_1 , we consider $b = K_2 \times 2000 \times 120$, which is approximated by Fourier series as

$$b = B^T \Phi(t), \quad (34)$$

where B is the Fourier series coefficient vector of b in the interval I and $B = [b, 0, \dots, 0, 0, \dots, 0]^T$.

By using (13) and (34), we have

$$M_1 = \int_0^1 B^T \Phi(\theta) d\theta = B^T \int_0^1 \Phi(\theta) d\theta = B^T Z \Phi(t). \quad (35)$$

To find M_2 , one can use (12), (21), and (15). Hence,

$$\begin{aligned}
M_2 &= \int_1^t K_2 \hat{V}^T \phi(\theta - 1) \Phi^T(\theta - 1) \hat{T} d\theta \\
&= K_2 \hat{V}^T \tilde{T} \int_1^t \Phi(\theta - 1) d\theta \\
&\cong K_2 \hat{V}^T \tilde{T} P \Phi(t - 1) \cong K_2 \hat{V}^T \tilde{T} P S_1 \Phi(t). \quad (36)
\end{aligned}$$

Similarly,

$$M_3 = \int_0^t \mu_I \tilde{I}^T \Phi(\theta) d\theta = \mu_I \tilde{I}^T P \Phi(t). \quad (37)$$

Finally, by considering M_1 , M_2 , and M_3 , we have

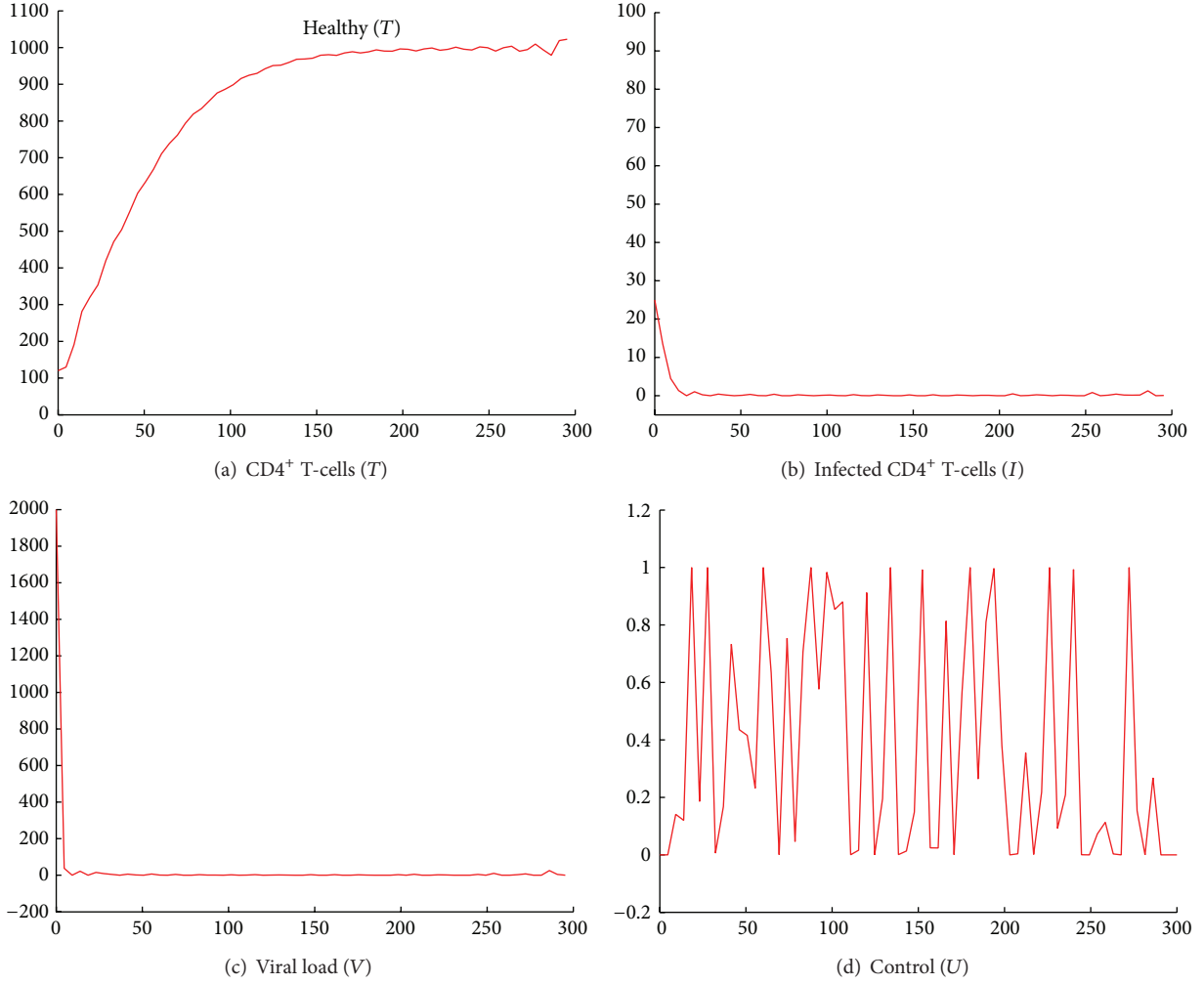
$$\begin{aligned}
&\int_0^t [K_2 V(\theta - 1) T(\theta - 1) - \mu_I I(\theta)] d\theta \\
&= B^T Z \Phi(t) + K_2 \hat{V}^T \tilde{T} P S_1 \Phi(t) - \mu_I \tilde{I}^T P \Phi(t). \quad (38)
\end{aligned}$$

Now, we equalize (32) and (38); from the two sides of (24b),

$$\begin{aligned}
\tilde{I}^T \Phi(t) - I_0^T \Phi(t) &= B^T Z \Phi(t) + K_2 \hat{V}^T \tilde{T} P S_1 \Phi(t) \\
&\quad - \mu_I \tilde{I}^T P \Phi(t). \quad (39)
\end{aligned}$$

Similarly, by integrating (24c) from 0 to t , we obtain

$$\begin{aligned}
\hat{V}^T \Phi(t) - V_0^T \Phi(t) &= N_1 \mu_b \hat{U}^T \tilde{I} P \Phi(t) - K_1 \hat{V}^T \tilde{T} P \Phi(t) \\
&\quad - \mu_V \hat{V}^T P \Phi(t). \quad (40)
\end{aligned}$$

FIGURE 1: The suboptimal $T(t)$, $I(t)$, $V(t)$, and $u(t)$.

Eliminating $\Phi(t)$ from (31), (39), and (40) results in the following equations:

$$\begin{aligned}
 & \hat{T}^T - T_0^T - S^T P - (r - \mu_T) \hat{T}^T P \\
 & + \frac{r}{T_{\max}} (\hat{T}^T \tilde{T} P + \hat{T}^T \tilde{I} P) + K_1 \hat{V}^T \tilde{T} P = 0, \\
 & \hat{I}^T - I_0^T - B^T Z - K_2 \hat{V}^T \tilde{T} P S_1 + \mu_I \hat{I}^T P = 0, \\
 & \hat{V}^T - V_0^T - N_1 \mu_b \hat{U}^T \tilde{I} P + K_1 \hat{V}^T \tilde{T} P + \mu_V \hat{V}^T P = 0.
 \end{aligned} \tag{41}$$

To apply the constraint $0 \leq u(t) \leq 1$, in (24h), one can first discretize the time interval into $(M + 1)$ grid points as follows:

$$t_j = t_0 + hj, \quad j = 0, 1, 2, \dots, M, \tag{42}$$

where $h = ((t_f - t_0)/M)$. Thus, $0 \leq u(t) \leq 1$ can be rewritten as

$$0 \leq \hat{U}^T \Phi(t_j) \leq 1, \quad j = 0, 1, 2, \dots, M. \tag{43}$$

Similarly, for $T(t)$, $I(t)$, and $V(t) \geq 0$, we have

$$\begin{aligned}
 & \hat{T}^T \Phi(t_j) \geq 0, \quad \hat{I}^T \Phi(t_j) \geq 0, \quad \hat{V}^T \Phi(t_j) \geq 0, \\
 & j = 0, 1, 2, \dots, M.
 \end{aligned} \tag{44}$$

Finally, the optimal control problem now is reduced to

$$\begin{aligned}
 & \text{Max } J(\hat{T}, \hat{U}) = \hat{T}^T W - 50 (A^T W + \hat{U}^T D \hat{U} - 2 \hat{U}^T W) \\
 & \text{s.t. } \hat{T}^T - T_0^T - S^T P - (r - \mu_T) \hat{T}^T P \\
 & + \frac{r}{T_{\max}} (\hat{T}^T \tilde{T} P + \hat{T}^T \tilde{I} P) + K_1 \hat{V}^T \tilde{T} P = 0, \\
 & \hat{I}^T - I_0^T - B^T Z - K_2 \hat{V}^T \tilde{T} P S_1 + \mu_I \hat{I}^T P = 0, \\
 & \hat{V}^T - V_0^T - N_1 \mu_b \hat{U}^T \tilde{I} P + K_1 \hat{V}^T \tilde{T} P + \mu_V \hat{V}^T P = 0, \\
 & 0 \leq \hat{U}^T \Phi(t_j) \leq 1, \quad j = 0, 1, 2, \dots, M.
 \end{aligned} \tag{45}$$

Now, one can use various toolboxes like Matlab software to solve the above problem. The parameters of viral spread in

TABLE I: Parameters for viral spread in model (24a)–(24h).

Parameters	Values	
μ_T	Natural death rate of CD4 T-cells	0.02
μ_I	Blanket death rate of infected CD4 T-cells	0.26
μ_b	Lytic death rate for infected cells	0.24
μ_V	Death rate of free virus	2.4
K_1	Rate by which CD4 T-cells become infected with virus	2.4×10^{-5}
K_2	Rate by which infected cells become active	2×10^{-5}
r	Growth rate of CD4 T-cell population	0.03
N_1	Number of virions produced by infected CD4 T-cells	1000
T_{\max}	Maximal population level of CD4 T-cells	1500
s	Source term for uninfected CD4 T-cells	10

model (24a), (24b), (24c), (24d), (24e), (24f), (24g), and (24h) are presented in Table I.

The results of this optimization problem for $r = 45$ and $M = 65$ are depicted in Figure 1. As can be seen, utilizing the treatment increases the CD4⁺ T-cells (T) (Figure 1(a)) and decreases the infected CD4⁺ T-cells (I) (Figure 1(b)) and viral load (V) (Figure 1(c)).

5. Conclusion

In this paper, we consider a delayed mathematical model describing HIV infection of CD4⁺ T-cells during therapy.

Our objective is to minimize the cost of treatment and to maximize the uninfected CD4⁺ T-cells. We use Fourier series approximation in order to solve the so-called mathematical model. By applying operational matrices for integration, product, and delay, the nonlinear optimal control model is reduced to a set of nonlinear algebraic equations. Since the set of sines and cosines is orthogonal, the operational matrices contain many zero elements. Hence, it makes the method computationally easy and attractive. The results show the efficiency of the method.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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