Journal of mathematics and computer science 11 (2014), 86-92

Contents list available at JMCS

Journal of Mathematics and Computer Science

Journal Homepage: www.tjmcs.com

# Using Fourier series for solving optimal control problem of an HIV infection treatment control model

S. Mosarreza Nouri[1], Mohammad Alizadehjamal[2]

[1]*M.Sc. of Control, Iran*

[2]*Department of Mathematics, Science and Research Branch, Islamic Azad University, Tehran, Iran*

***m_alizadehjamal@mailfa.org***

**Article history:**
**Received April 2014**
**Accepted May 2014**
**Available online June 2014**

***Abstract***

In this paper we introduce a numerical technique based on Fourier series for solving of nonlinear optimal control problems, where this approach is used for solving optimal control problem of an HIV infection treatment control model. In this paper, first by using healthy cells $CD4^{+}T$ (T), infected cells $CD4^{+}T$ (I), viral load (V) and also by using a drug inhibitor of reverse polygraph as a control function, a control model is presented for treatment of HIV infection. A cost function to minimize the cost of drug during the treatment is defined as well. To find the pair of trajectory and control of such nonlinear optimal control problem, we used Fourier series to approximate optimal pair of trajectory and control.

**Keywords:** Fourier Series, approximation theory, HIV infection, optimal control.

## 1. Introduction

Despite remarkable success in medical science, still solution and definitive treatment for HIV has not been found by scientists, and every day is added to statistics victims and patients. The importance of these diseases caused, the other researchers including mathematic scientists, to deal with it, come to the help of medical science scientists. In this regard, various mathematical models to represent the dynamics of immune system cells and the HIV virus, has been presented. Solving optimal control problems related to these models, because of the nonlinear dynamic system, the classic method of solving the optimal control is not possible. Therefore present a simple and efficient method for solving such problems is very important. In recent years approximation functions, such as orthogonal functions and polynomials to solve a variety of mathematical and dynamical systems are used. Orthogonal functions and polynomial series have received considerable attention in dealing with various problems of dynamical systems. Examples are the use of the Fourier series [1]-[3], the Walsh functions [3], the Taylor series [4], the

Legender polynomials[5], the Chebyshev polynomials [6] and the block– pulse functions [7].In this paper we described the optimal control model of HIV will be solved by Fourier series.

## 2. Fourier series

A function $f(t)$ belong to the space $L^2[0,L]$ may be expanded into a Fourier series as follows:

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

where the Fourier coefficients given by

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

$$a_n = \frac{2}{L}\int_0^L f(t)cos\frac{2n\pi t}{L}dt \qquad n = 1,2,3,\ldots \quad (2)$$

$$a^*{}_n = \frac{2}{L}\int_0^L f(t)sin\frac{2n\pi t}{L}dt \qquad n = 1,2,3,\ldots$$

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

$$f(t) \cong a_0 + \sum_{n=1}^{r}\{a_n\varphi_n(t) + a_n^*\varphi_n^*(t)\} = A^T\varphi(t) = \varphi(t)^T A\,. \quad (3)$$

Here, the Fourier series coefficient vector A and the Fourier series vector $\varphi(t)$ are defined as

$$A = [a_0\ \ a_1\ \ a_2\ \ \ldots\ \ a_r\ \ a_1^*\ \ a_2^*\ \ \ldots\ \ a_r^*]^T = [a_0 \vdots \tilde{a}^T \vdots \tilde{a}^{T*}] \quad , \quad (4)$$

$$\varphi(t) = [\varphi_0(t)\ \ \varphi_1(t)\ \ \varphi_2(t)\ \ \ldots\ \ \varphi_r(t)\ \ \varphi_1^*(t)\ \ \varphi_2^*(t)\ \ \ldots\ \ \varphi_r^*(t)]^T \quad (5)$$

with

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

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

The elements of ϕ(t) are orthogonal in the interval (0,L).

## 3. The operational matrix of integration

Integration of vector ϕ(t) defined in (5) can be approximated by

$$\int_0^t \phi(t)dt \cong H\phi(t) \quad (7)$$

where H is the $(2r+1)\times(2r+1)$ operational matrix for forward integration and is given as follows[7]:

$$H = L\begin{bmatrix} \frac{1}{2} & 0 & 0 & \dots & 0 & 0 & \frac{-1}{\pi} & \frac{-1}{2\pi} & \dots & \frac{-1}{(r-1)\pi} & \frac{-1}{r\pi} \\ 0 & 0 & 0 & \dots & 0 & 0 & \frac{1}{2\pi} & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & 0 & 0 & 0 & 0 & \dots & \frac{1}{2(r-1)\pi} & 0 \\ 0 & 0 & 0 & \dots & 0 & 0 & 0 & 0 & \dots & 0 & \frac{1}{2r\pi} \\ \frac{1}{2\pi} & \frac{-1}{2\pi} & 0 & \dots & 0 & 0 & 0 & 0 & \dots & 0 & 0 \\ \frac{1}{4\pi} & 0 & \frac{-1}{4\pi} & \dots & 0 & 0 & 0 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \frac{1}{2r\pi} & 0 & 0 & \dots & 0 & \frac{-1}{2r\pi} & 0 & 0 & \dots & 0 & 0 \end{bmatrix}_{(2r+1)\times(2r+1)}$$

If we integrate both sides of (3) from *0* to $t$ and using (7), we obtain

$$\int_0^t f(t')dt' = A^T H\phi(t) = \phi(t)^T H^T A \tag{8}$$

One may express the product of $\varphi\varphi^T$ as follow:

$$\varphi\varphi^T A = \tilde{A}\varphi \tag{9}$$

where $\tilde{A}$ is the product operational matrix for vector $A$ and can be written as:

$$\tilde{A} = \begin{bmatrix} a_0 & a_1 & a_2 & \cdots & a_r & a_1^* & a_2^* & \cdots & a_r^* \\ \frac{1}{2}a_1 & a_0 + \frac{1}{2}a_2 & \frac{1}{2}(a_1 + a_3) & \cdots & \frac{1}{2}a_{r-1} & \frac{1}{2}a_2^* & \frac{1}{2}(a_1^* + a_3^*) & \cdots & \frac{1}{2}a_{r-1}^* \\ \frac{1}{2}a_2 & \frac{1}{2}(a_1 + a_3) & a_0 + \frac{1}{2}a_4 & \cdots & \frac{1}{2}a_{r-2} & \frac{1}{2}(a_3^* - a_1^*) & \frac{1}{2}a_4^* & \cdots & \frac{1}{2}a_{r-2}^* \\ \vdots & \vdots & \vdots & \cdots & \vdots & \vdots & \vdots & \cdots & \vdots \\ \frac{1}{2}a_r & \frac{1}{2}a_{r-1} & \frac{1}{2}a_{r-2} & \cdots & a_0 & -\frac{1}{2}a_{r-1}^* & -\frac{1}{2}a_{r-2}^* & \cdots & 0 \\ \frac{1}{2}a_1^* & \frac{1}{2}a_2^* & \frac{1}{2}(a_3^* - a_1^*) & \cdots & -\frac{1}{2}a_{r-1}^* & a_0 - \frac{1}{2}a_2 & \frac{1}{2}(a_1 - a_3) & \cdots & \frac{1}{2}a_{r-1} \\ \frac{1}{2}a_2^* & \frac{1}{2}(a_3^* + a_1^*) & \frac{1}{2}a_4^* & \cdots & -\frac{1}{2}a_{r-2}^* & \frac{1}{2}(a_1 - a_3) & a_0 - \frac{1}{2}a_4 & \cdots & \frac{1}{2}a_{r-2} \\ \vdots & \vdots & \vdots & \cdots & \vdots & \vdots & \vdots & \cdots & \vdots \\ \frac{1}{2}a_r^* & \frac{1}{2}a_{r-1}^* & \frac{1}{2}a_{r-2}^* & \cdots & 0 & \frac{1}{2}a_{r-1} & \frac{1}{2}a_{r-2} & \cdots & a_0 \end{bmatrix}.$$

## 4. HIV Basic Model

The target cells of HIV infection are lymphocyte helper cells, especially $CD4^+T$ cells. These cells become infected and begin to produce free various. The main fact about HIV infection is reducing the count of $CD4^+T$ cells, which have an essential role in protecting body against deferent pathogens. So it is important to understand the dynamics of $CD4^+T$ cell count as a function of time. In HIV infection basic model, three groups of molecules are considered; Uninfected $CD4^+T$ cells (T), infected $CD4^+T$ cells (I) and viral load (V). Biological descriptions, translation to reactions and corresponding ODE's are presented in Table 1.

**Table 1.** HIV basic model interactions.

| Biological description | Translation to reactions | Reaction rate | Translation to ODE |
|---|---|---|---|
| | $0 \rightarrow T$ | s | $\dot{T} = s$ |

| | | | |
|---|---|---|---|
| $CD4^+T$ cells production | | | |
| $CD4^+T$ cells natural death | T → 0 | d | $\dot{T} = -dT$ |
| $CD4^+T$ cells become infected by virus | T+V → I +V | β | $\dot{T} = -\beta TV \quad \dot{I} = \beta TV$ |
| Infected $CD4^+T$ cells death | I → 0 | μ | $\dot{I} = -\mu I$ |
| Virus replication in infected $CD4^+T$ | I → I +V | k | $\dot{V} = kI$ |
| Virus natural death | V → 0 | c | $\dot{V} = -cV$ |

Now, according to Table 1, the complete ODE model, which is sum of contributions from all reactions, is as flollows:

$$\begin{aligned} \dot{T} &= s - dT - \beta TV \\ \dot{I} &= \beta TV - \mu I \\ \dot{V} &= kI - cV \end{aligned} \qquad (11)$$

Where the following estimated parameters are as model (1) [9]:
$s = 7, d = 0.007, \beta = 0.00000042163, \mu = 0.0999, c = 0.2, k = 90.67$

## 5. HIV infection treatment control model

There are three convenient groups of drugs for AIDS retroviral therapy; reverse transcriptase, protease, and Integrate enzyme inhibitors. In this section, we study the role of reverse transcriptase inhibitors. The main action of this kind of drugs is preventing to produce viral load with infection Lymphocyte cells. This action is equivalent to the reaction $I \to I + V$ [9]. So we control the third equation to prevent of produce viral load with infection lymphocyte cells. This control function is called u(t), where $0 \le u(t) \le 1$. The most drug efficiency is in the case $u(t) \equiv 1$ which means viral load is not produce by infection cells. At the other side, $u(t) \equiv 0$ is the case which the drug does not change the disease progression. By above argument, the control system is as follows [5]:

$$\begin{aligned} \dot{T} &= s - dT - \beta TV \\ \dot{I} &= \beta TV - \mu I \\ \dot{V} &= kI(1-u) - cV \end{aligned} \qquad (12)$$

## 6. Solving HIV infection treatment control model

Using [10] consider the objective functional to be defined as:

$$J(T, I, V, u) = \int_{t_0}^{t_f} [T(t) - \frac{1}{2}\alpha u^2(t)]dt$$

Where $\alpha = 110$. Our goal is maximizing the objective functional J subject to the control system (12); that is, maximizing the total count of $CD4^+T$ cells and minimizing the costs of treatment by

applying some RTI drugs. The solution of this optimal control problem should be calculated by numerical methods. We have used a special discretization method, based on Fourier series. For detailed explanation of this method, see [10]. So optimal control problem in $[0,1000]$ interval days, given by:

$$\max J = \int_0^{1000} \left[T(t) - \frac{1}{2} \propto u^2(t)\right] dt$$
$$\text{s.t. } \dot{T} = s - dT - \beta TV$$
$$\dot{I} = \beta TV - \mu I$$
$$\dot{V} = kI(1-u) - cV$$
$$T(t), I(t), V(t) \geq 0, 0 \leq u(t) \leq 1, \forall t \in [0,1000]$$
$$T(0) = 363,\ I(0) = 57,\ V(0) = 28860 \qquad (13)$$

In this problem using of drug after 129 days of entry the HIV virus into the body has been considered. Therefore, the initial value of problem to the solution of AVK discrete optimization technique for model-based HIV infection has been calculated at 129 days [9]. Constraints optimal control problem are as a nonlinear differential equations.The approximate solutions for control function u(t) and state functions T(t), I(t) and V(t) are respectively as:

$$u(t) = U^T\varphi(t),\ U = [u_0\ u_1\ u_2\ \dots\ u_r\ u_1^*\ u_2^*\ \dots\ u_r^*]^T;$$
$$T(t) = T^T\varphi(t),\ T = [t_0\ t_1\ t_2\ \dots\ t_r\ t_1^*\ t_2^*\ \dots\ t_r^*]^T;$$
$$I(t) = I^T\varphi(t),\ I = [i_0\ i_1\ i_2\ \dots\ i_r\ i_1^*\ i_2^*\ \dots\ i_r^*]^T;$$
$$V(t) = V^T\varphi(t),\ V = [v_0\ v_1\ v_2\ \dots\ v_r\ v_1^*\ v_2^*\ \dots\ v_r^*]^T. \qquad (14)$$

Integrating (12) from *0* to $t$ and using (7)-(9) and by equality the coefficients of the entries vector $\varphi(t)$ we find:

$$T^T - T_0 - sM + dT^T H + \beta T^T \tilde{V} H = 0$$
$$I^T - I_0 - \beta T^T \tilde{V} H + \mu I^T H = 0$$
$$V^T - V_0 - kI^T + kI^T \tilde{U} H + cV^T H = 0 \qquad (15)$$

Where

$T_0 = [363\ 0\ \dots\ 0\ 0\ \dots\ 0]^T$, $I_0 = [57\ 0\ \dots\ 0\ 0\ \dots\ 0]^T$, $V_0 = [28860\ 0\ \dots\ 0\ 0\ \dots\ 0]^T$ and $M = [\frac{1}{2}\ 0\ 0\ \dots\ 0\ \frac{-1}{\pi}\ \frac{-1}{2\pi}\ \dots\ \frac{-1}{r\pi}]^T$ are *(2r+1)×1* matrices.

Now for performance index we have:

$$\max\ J = T^T H\varphi(1000) - \frac{1}{2}\alpha U^T D U \qquad (16)$$

where

$$D = \int_0^{1000} [\varphi(t)\varphi^T(t)]dt = 1000 \begin{bmatrix} 1 & 0 & 0 & \dots & 0 \\ 0 & 0.5 & 0 & \cdots & 0 \\ 0 & 0 & 0.5 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & 0.5 \end{bmatrix}.$$

Now the optimal control problem (13) reduce to maximizing (16), subject to (15). Using the Lagrange multiplier technique, the optimization problem turns into a set of nonlinear algebraic equations which can solved using Newton's iterative method to obtain the variable $u_i$, $u_j^*, t_j$, $t_j^*, i_i$, $i_j^*, v_i, v_j^*$ and $J$, for $i = 0, 1, 2, \dots, r$ and $j = 1, 2, \dots$, r. With solving of this nonlinear programming problem by Mathematica software for $r = 5$,the funtions T(t), I(t), V(t) and u(t) are obtained.

By plotting these functions, we have these diagrams:

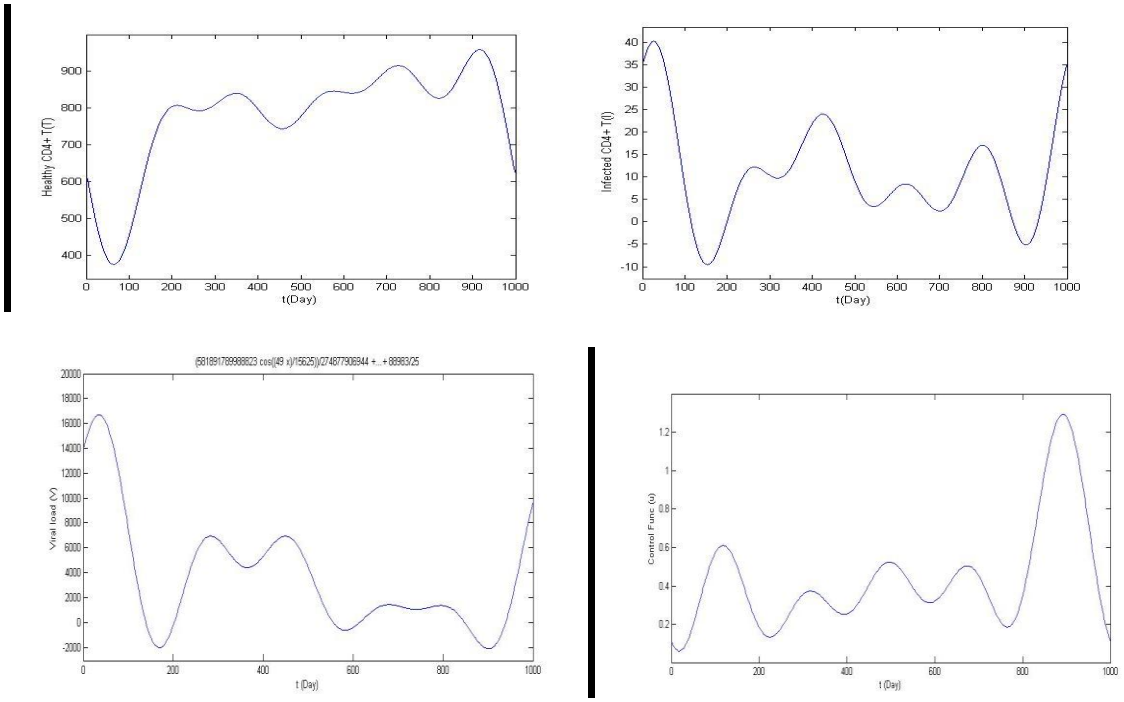


**Figure. 1** Solution of the optimal control problem with control

According to Figure 1, it is seen that after taking the drug, the number of uninfected cells $CD4^+T$ (T) is increasing, however these cells rate of increasing after 200 days because of approaching normal human body decreases. The number of infected cells (I) and viral load (V) is reduced and finally, an average dose for the drug during treatment recommended.

To fix the drug dose, we can use the average value of function u(t) in the $[a, b]$ intervals. So, the drug dose would be according to following table:

**Table 2**

| Days | Drug dose |
|---|---|
| 0-200 | 0.354 |
| 200-800 | 0.341 |
| 800-1000 | 0.823 |

## 7. Conclusions

According to, the dynamic of most real systems in nature are nonlinear and optimal control problems related to them in classical form are often extremely complex and difficult, method used in this paper is effective and efficient method, because it makes these problems to nonlinear algebraic problems solving. In this paper, the problem of minimizing the cost of treatment with drug in a model controlling HIV infection is solved with using Fourier serier and a mean value for drug use during treatment is recommended. Figures obtained from the solution of the problem show drug effects during treatment as well as.

## 8. References

[1] M. Ebrahimi, M.A. Samavat, M. A. Vali, and A. A. Gharavisi, “Application of Fourier series direct method of the optimal control of singular system”, ICGST-ACSE Jornal, Vol. 7, Issue 2, 2007.

[2] S. M. Nouri and M. H. Farhi,"Optimal control of nonlinear systems via Fourier series",in Proc. 5th Iranian Con. on Applied Mathematics, Sep. 2013, pp. 736-739.

[3] W. L. Chen, and Y. P. Shih, "Parameter estimation of bilinear systems via Walsh functions," *Journal of the Franklin Institute*, vol. 305, pp. 249-257, 1978.

[4] M. Gulsu, and M. Sezer, "A Taylor polynomial approach for solving differential-difference equations," *Journal of Computational and Applied Mathematics*, vol. 186, pp. 349-364, 2006.

[5] M. Alizadehjamal, M. H. Farahi, and S. A. Mahdipour, " Using shifted Legendre polynomials for solving optimal control problem of an HIV infection treatment control model", The Journal of Mathematics and Computer Science (JMCS), vol. 8, pp. 251-257, 2014.

[6] H. Jaddu, and E. Shimomura, "Solution of nonlinear optimal control problem using Chebyshev polynomials," *Proceeding of 2nd Asian Control Conference,* pp. 417-420, 1997.

[7] K. Maleknejad, M. Shahrezaee, and H. Khatami, "Numerical solution of integral equations system of the second kind by block-pulse functions," Applied Mathematics and Computation, vol. 166, pp. 15-24, 2005.

[8] M. Razzaghi, “Optimal control of linear Time-Varying systems via Fourier series”, *Journal of Optimization Theory and Applications*, Vol 65, No. 2 , 1990.

[9] S. P. Banks, "Mathematical theories of nonlinear systems,"*Prentice Hall*, Hertfordshire, 1988.

[10] M. Shirazian, and M. H. Farahi, "Optimal control strategy for a fully determined HIV model,"Intelligent control and automation, pp. 15-19, 2010.