TWMS J. App. and Eng. Math. V.11, N.1, 2021, pp. 273-281

SEMI-ANALYTICAL APPROACH FOR SOLVING A MODEL FOR HIV INFECTION OF CD4$^+$ T-CELLS

S. DENİZ, §

Abstract. In this work, a mathematical model for the human immunodeficiency virus (HIV) infection of CD4$^+$ T-cells by using the optimal perturbation iteration method (OPIM) is analyzed. Optimization and classical perturbation techniques are combined to build the new proposed method. The iteration algorithm for systems of nonlinear differential equations for this optimal perturbation iteration technique is constructed for the first time. A test problem has been solved and some plots are given to show the reliability and efficiency of the proposed method. Obtained results exhibit the effectiveness and accuracy of the semi-analytical technique.

Keywords: HIV infection model, optimal perturbation iteration method, semi-analytical solution.

AMS Subject Classification: 81Q15,78A70

1. Introduction

CD4, which means a cluster of differentiation antigen 4, is actually a glyco-protein located in the outer region of immune cells such as T assistant cells, dendritic cells, and macrophages. They were invented in 1970 and were firstly known as leu-3 and T4 before being they are named as CD4 in 1984. CD4+ T assistant cells are blood white cells which are usually known as the main part of the body immune system. They are often referred to as T-helper cells, CD4 cells or T4 cells. The reason for saying "helper cells" is that their main acts is to deliver signals to alternative types of human immune cells, including CD8 terminator cells. After then they demolish the poisonous particle. If those cells become consumed, for instance in untreated the human immunodeficiency virus (HIV) infection, or following immune suppression prior to a transplant, the body can be counted as defenceless to a wide range of contaminations that it would in other way have been able to be forced to be defeated.

Analyzing the mathematical models of some constructive situations enables us to discover the distinct dynamics of these kinds of situations. Many scientists have studied a number of models to see different aspects of HIV infection. By doing so, they can also predict the spread of this deadly ailment. To investigate the model, many different techniques have been used such as variational iteration method [16], Laplace Adomian decomposition method [19], the modified variational iteration method [15], the homotopy analysis method [11], etc. In addition

---

Department of Mathematics, Faculty of Art and Sciences, Manisa Celal Bayar University, 45140, Manisa, Turkey.
e-mail: sinandeniz01@gmail.com; ORCID: https://orcid.org/0000-0002-8884-3680.

§ Manuscript received: February 23, 2019; accepted: May 4, 2019.

Table 1. List of variables-parameters used in this work ([16]).

Parameters-variables	Meaning
H	Uninfected CD4+ T-cell concentration
I	Unhealthy CD4 + T-cells
V	Free HIV virus at time t
s	Source term for healthy CD4+ T- cells
μ_H	Natural death rate
g	Growth rate of healthy CD4 + T-cells
H_{max}	Maximum possibility of presence of number of T-cells
k	Rate at which healthy cells become infected
k'	Rate of infectious cells to become actively infected
K	Number of viral particles
μ_I	Blanket death rates for infected cells
μ_V	Loss rate for virus.
τ	The amount of delay

to those papers, Perelson [17] presented a comprehensive work on the mathematical model of this infection involving a delay term in the differential equation. His team also investigated different dynamics of HIV infection [20]. In [12], the authors also discussed the usefulness of the delay term in ordinary differential equations for population dynamics and studied on the stability analysis for the considered models. In [18], Nowak studied the injurious effects of long incubation period of virus infection and introduced a simple model for this disease.

The motivation of this work is to improve the implementation of the semi-analytic optimal perturbation iteration method (OPIM) to investigate a model for HIV infection of CD4$^+$ T cells:

$$\begin{aligned}
\frac{dH(t)}{dt} &= s-\mu_H H(t)+gH(t)\left(1-\frac{H(t)+I(t)}{H_{max}}\right)-kH(t)V(t)\\
\frac{dI(t)}{dt} &= k'H(t-\tau)V(t-\tau)-\mu_I I(t) \qquad (1)\\
\frac{dV(t)}{dt} &= K\mu_I I(t)-kH(t)V(t)-\mu_V V(t).
\end{aligned}$$

The above equation is the mathematical description of human health related phenomena, particularly about the presence, decrease or increase in HIV. Figure 1 represents flow diagram for the Eq. (1).

The optimal perturbation iteration method has been developed by using the idea of perturbation iteration method (PIM) [5, 9]. Many studies show that approximate PIM solutions can be healed by inserting the convergence control-parameter p to PIM algorithms. One can easily adjust the convergence with the aid of the parameter p. OPIM has been applied to many kinds of differential equations [10, 8, 3, 7, 4, 6].

This study is organized as follows: In the following part, section 2, the optimal perturbation-iteration algorithm is described and also improved for the solution of systems of differential equations for the first time. In section 3, OPIM is implemented to a test problem to get the approximate solutions. Finally, in Section 4, the conclusion of this research paper is given.

2. Optimal Perturbation-Iteration Algorithm

In this part, a perturbation-iteration algorithm is presented by using only one correction term in the straightforward perturbation expansion and a correction term of nth-order derivatives from the Taylor expansion of a function.

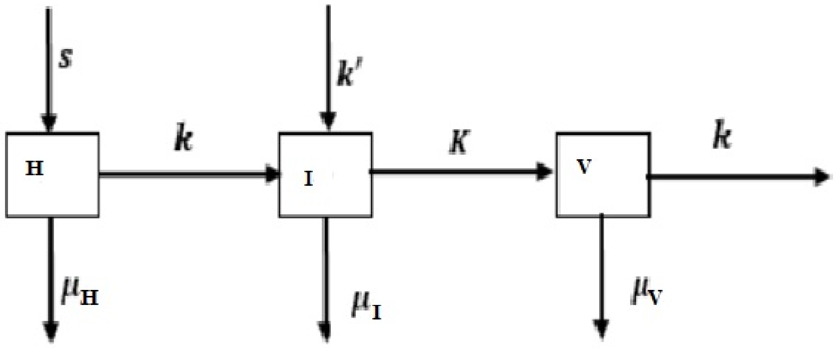

FIGURE 1. Flow diagram for HIV model

Let us look at the following non-linear (or linear) system of differential equations

$$A_k(\dot{x}_k, x_j, \epsilon, t) = 0; k = 1, 2, ..., K; j = 1, 2, ..., K \tag{2}$$

where k denotes the number of differential equations in the system. Obviously, the system of equations can be written as

$$\begin{aligned} A_1 &= A_1(\dot{x}_1, x_1, x_2, x_3, ..., x_K, \epsilon, t) = 0 \\ A_2 &= A_2(\dot{x}_2, x_1, x_2, x_3, ..., x_K, \epsilon, t) = 0 \\ &\vdots \\ A_k &= A_k(\dot{x}_k, x_1, x_2, x_3, ..., x_K, \epsilon, t) = 0. \end{aligned} \tag{3}$$

Let us consider an approximate solution of the system

$$x_{k,n+1} = x_{k,n} + \varepsilon x^c_{k,n} \tag{4}$$

with one correction term in the perturbation expansion. The subscript letter n symbolizes the nth order iteration over the obtained approximate solution. One can approximate to the system with a Taylor series expansion as

$$A_k = \sum_{m=0}^{M} \frac{1}{m!} \left[(\frac{d}{d\varepsilon})^m A_k \right]_{\varepsilon=0} \varepsilon^m; \quad k = 1, 2, ..., K \tag{5}$$

in the neighborhood of $\varepsilon = 0$ where

$$\frac{d}{d\varepsilon} = \frac{\partial \dot{x}_{k,n+1}}{\partial \varepsilon} \frac{\partial}{\partial \dot{x}_{k,n+1}} + \sum_{j=1}^{K} \left(\frac{\partial \dot{x}_{k,n+1}}{\partial \varepsilon} \frac{\partial}{\partial \dot{x}_{k,n+1}} \right) + \frac{\partial}{\partial \varepsilon} \tag{6}$$

is defined for the $(n+1)$th iterative equations

$$A_k(\dot{x}_{k,n+1}, x_{j,n+1}, \epsilon, t) = 0 \tag{7}$$

substituting equation (6) into (5), an iteration algorithm is attained;

$$A_k = \sum_{m=0}^{M} \frac{1}{m!} \left[\left(\dot{x}^c_{k,n} \frac{\partial}{\partial \dot{x}_{k,n+1}} + \sum_{j=1}^{K} \left(\dot{x}^c_{j,n} \frac{\partial}{\partial \dot{x}_{j,n+1}} \right) + \frac{\partial}{\partial \varepsilon} \right)^m H_k \right]_{\varepsilon=0} \varepsilon^m = 0 \tag{8}$$

which is a first-order ordinary differential equation and can be solved for the correction terms $x^c_{k,n}$ Then, using Eq.(3), the $(n+1)$th iteration solution can be found. Iterations are stopped after a satisfactory approximate solution is obtained.

In order to improve the approximate PIM solutions, a new approach to perturbation iteration algorithms is proposed. Based on the idea of homotopy analysis method (HAM) [1, 21, 23], a convergence-control parameter p is furnished into Eq. (4) and then establish new components, described by

$$\begin{aligned} x_{k,1}(t;p) &= x_{k,0} + p_0 x^c_{k,0} \\ x_{k,2}(t;p) &= x_{k,1} + p_1 x^c_{k,1} \\ &\vdots \\ x_{k,m+1}(t;p) &= x_{k,n} + p_m x^c_{k,m}. \end{aligned} \tag{9}$$

It is evident that when the convergence parameters p_m are all equal to one, (9) is converted to the classical PIM. As observed in [1, 21], the region of validity of these parameters p_m can be determined by drawing constant level curves for some arbitrary values of the solution. This can be done by selecting a non-zero value of the mth order approximate solution, mapping it out against the parameter p and tracking the interval of p for which only a small change in the value is sought. Although this approach enables us to estimate a value for p, it is not a sufficient method to find the optimum value. To get a better and optimum value, the similar strategy mentioned by Marinca et al [14, 2] is used. To achieve this, the approximate solution x_m is inserted into the Eq.(2). Correspondingly, the general problem results in the following residual:

$$\begin{aligned} Res_{A_1} &= A_1(\dot{x}_{1,m}, x_{1,m}, x_{2,m}, ..., x_{K,m}, p_0, \epsilon, t) = 0 \\ Res_{A_2} &= A_2(\dot{x}_2, x_{1,m}, x_{2,m}, ..., x_{K,m}, p_1, \epsilon, t) = 0 \\ &\vdots \\ Res_{A_k} &= A_k(\dot{x}_k, x_{1,m}, x_{2,m}, ..., x_{K,m}, p_{m-1}\epsilon, t) = 0. \end{aligned} \tag{10}$$

Apparently, when $Res(t;p_m) = 0$ then the approximation $x_m(t;p)$ will be the desired exact solution.In fact, one cannot encounter with this case for especially nonlinear equations, but one can perform some calculation for the functional

$$\begin{aligned} JRes_{A_1}(p_1) &= \textstyle\int_\Omega (Res_{A_1})^2(t;p_0)dt \\ JRes_{A_2}(p_2) &= \textstyle\int_\Omega (Res_{A_2})^2(t;p_1)dt \\ &\vdots \\ JRes_{A_k}(p_K) &= \textstyle\int_\Omega (Res_{A_k})^2(t;p_{K-1})dt \end{aligned} \tag{11}$$

where Ω is the domain that one wishes to obtain the solution of the problem. Therefore, the convergence-control parameters p can be optimally identified from the condition

$$\frac{dJRes_{A_1}}{dp_1} = 0, \quad \frac{dJRes_{A_2}}{dp_2} = 0, \cdots, \frac{dJRes_{A_K}}{dp_K} = 0. \tag{12}$$

Both of these techniques have their drawbacks. Therefore, firstly the level curves are used to determine the valid region of p, then use the residual to find its optimum value around this region. All of these processes are called the optimal perturbation iteration method (OPIM) since one can obtain the optimal convergence control parameter in this manner.

3. Test Problem

In this section, the system (1) by using OPIM algorithms is solved. To start the iterations, the initial conditions will be taken as $H(-\tau) = H_0(t) = H(0) = 900$, $I_0(t) = I(0) = 0$, $V(-\tau) = V_0(t) = V(0) = 0.005$. With these values, one can follow the procedure for OPIM mentioned in Section 2 to solve the following system:

$$\begin{aligned}
\frac{dH(t)}{dt} &= 18-0.05H(t)+0.05H(t)\left(1-\frac{H(t)+I(t)}{120}\right)-0.0028H(t)V(t)\\
\frac{dI(t)}{dt} &= 0.0029H(t-\tau)V(t-\tau)-0.27I(t)\\
\frac{dV(t)}{dt} &= 600I(t)-0.0028H(t)V(t)-3.5V(t).
\end{aligned}\tag{13}$$

Perturbation parameter ε can be embedded to the above system

$$\begin{aligned}
A_1 &= \frac{dH(t)}{dt}-\left(18-0.05H(t)+0.05\varepsilon H(t)\left(1-\frac{H(t)+I(t)}{120}\right)-0.0028\varepsilon H(t)V(t)\right)\\
A_2 &= \frac{dI(t)}{dt}-\left(0.0029\varepsilon H(t-\tau)V(t-\tau)-0.27I(t)\right)\\
A_3 &= \frac{dV(t)}{dt}-\left(600I(t)-0.0028\varepsilon H(t)V(t)-3.5V(t)\right)
\end{aligned}\tag{14}$$

Correspondingly, the Eq. (8) turns into

$$\begin{aligned}
\dot{H}_k+\varepsilon\dot{H}_k^{\,c}+18-0.05\dot{H}_k+0.05\varepsilon\dot{H}_k\left(1-\frac{\dot{H}_k+\dot{I}_k}{120}\right)&\\
-0.0028\varepsilon\dot{H}_k\dot{V}_k &= 0\\
\dot{I}_k+\varepsilon\dot{I}_k^{\,c}+0.0029\varepsilon\dot{H}_k(t-\tau)\dot{V}_k(t-\tau)-0.27\dot{I}_k &= 0\\
\dot{V}_k+\varepsilon\dot{V}_k^{\,c}+600\dot{I}_k-0.0028\varepsilon\dot{H}_k\dot{V}_k-3.5\dot{V}_k &= 0.
\end{aligned}\tag{15}$$

One can continue the process till fifth - order approximation and can obtain the following residual functions as:

$$\begin{aligned}
Res_{H_5} &= \dot{H}_5-18+0.05\dot{H}_5-0.05\dot{H}_5\left(1-\frac{\dot{H}_5+\dot{I}_5}{120}\right)+0.0028\varepsilon\dot{H}_5\dot{V}_5\\
Res_{I_5} &= \dot{I}_5-\left(0.0029\dot{H}_5(t-\tau)\dot{V}_5(t-\tau)-0.27\dot{I}_5\right)\\
Res_{V_5} &= \dot{V}_5-\left(600\dot{I}_5-0.0028\dot{H}_5\dot{V}_5-3.5\dot{V}_5\right)
\end{aligned}\tag{16}$$

Unknown parameters p_0, p_1, p_2 can be obtained by using the idea described in Section 2 as

$$\frac{dJRes_{H_5}}{dp_0}=0,\quad \frac{dJRes_{I_5}}{dp_1}=0,\quad \frac{dJRes_{V_5}}{dp_2}=0.\tag{17}$$

Graphics of absolute residual errors obtained by optimal perturbation iteration method for each group are displayed in Figures 2-7 for fourth and fifth order approximate solutions respectively. For this problem, the optimal values of $p_0 = 0.996121$, $p_1 = 0.070589$ and $p_2 = 0.200365$ are obtained by minimizing the residual error for fifth - order approximation. One can easily get the approximate OPIM results by substituting these parameters in their places.

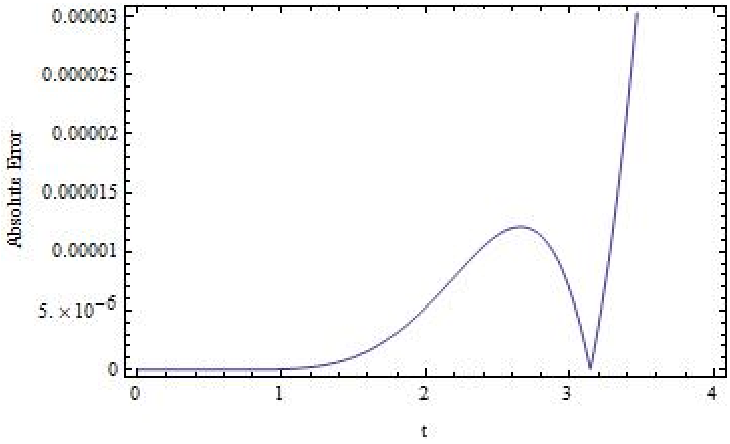

Figure 2. Absolute error for fourth order OPIM solution of $H(t)$

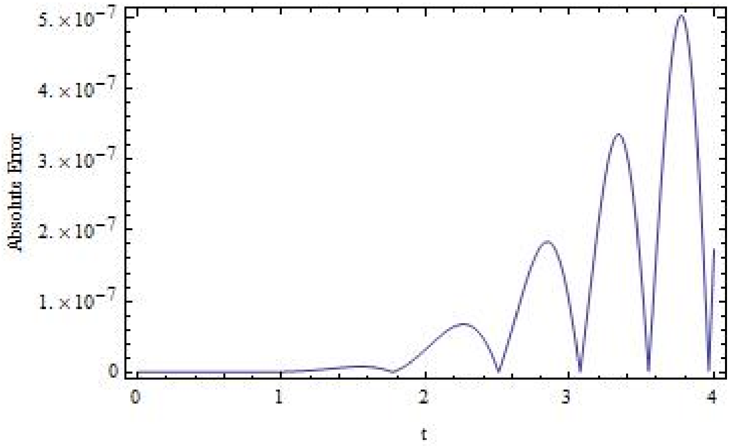

Figure 3. Absolute error for fourth order OPIM solution of $I(t)$

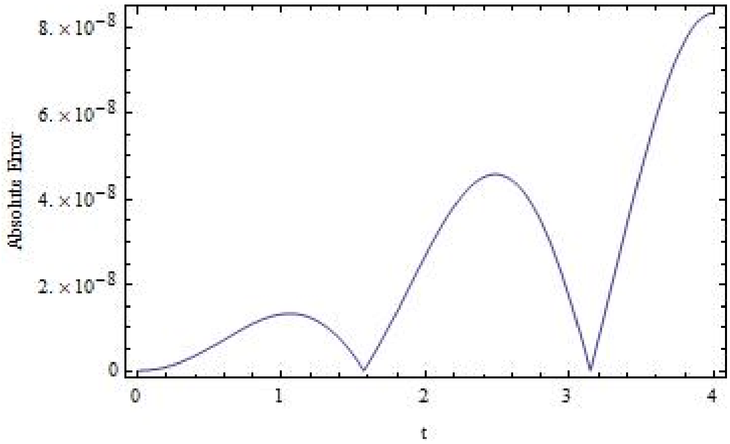

Figure 4. Absolute error for fourth order OPIM solution of $V(t)$

4. Conclusions

In this research paper, the approximate solutions of the mathematical model of HIV infections is analyzed. Newly developed optimal perturbation iteration method has been improved to solve the system of differential equations. Applying this technique to the model for HIV infection of CD4$^+$ T-cells reveals that this method is powerful and effective to get the approximate solutions

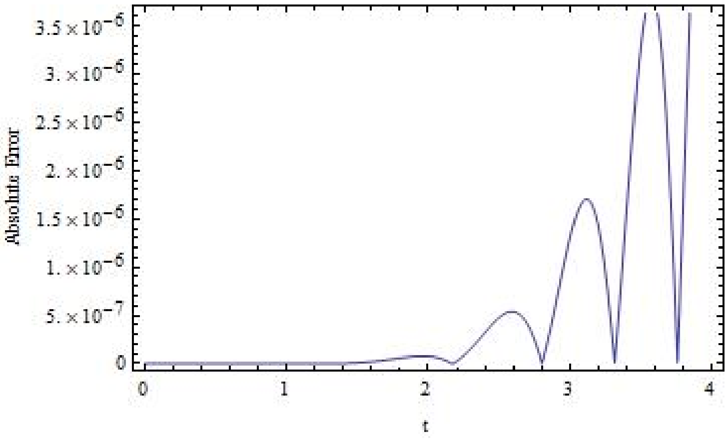

Figure 5. Absolute error for fifth order OPIM solution of $H(t)$

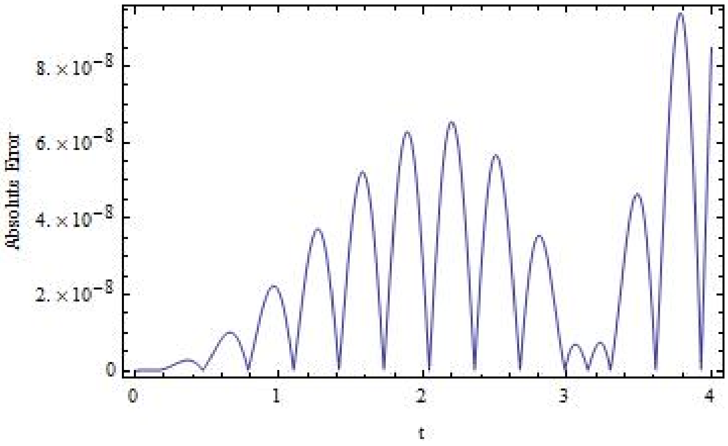

Figure 6. Absolute error for fifth order OPIM solution of $I(t)$

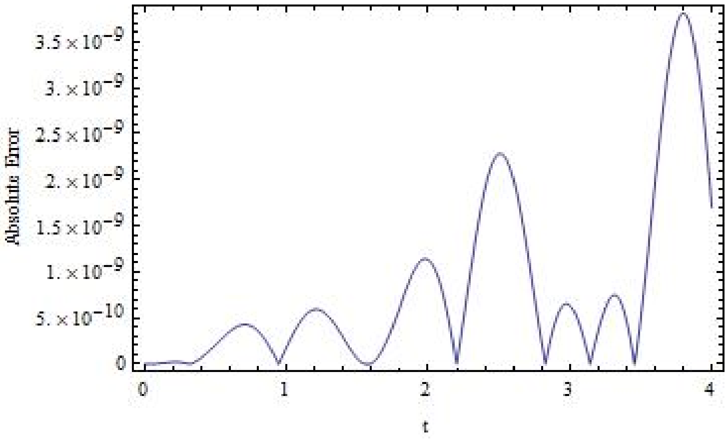

Figure 7. Absolute error for fifth order OPIM solution of $V(t)$

of these types of problems. Graphics for absolute residual errors also support this claim. Finally, one can conclude that OPIM provide a simple and easy way to control and adjust the convergence region and it is also applicable to the nonlinear biological systems.

REFERENCES

[1] Abbasbandy, S. and Zakaria, F. S., (2008), Soliton solutions for the fifth-order KdV equation with the homotopy analysis method. Nonlinear Dynamics, 51(1-2), 83-87.

[2] Ali, J., Islam, S., Islam, S. and Zaman, G., (2010), The solution of multipoint boundary value problems by the optimal homotopy asymptotic method. Computers & Mathematics with Applications, 59(6), 2000-2006.

[3] Bildik, N. and Deniz, S., (2017), A new efficient method for solving delay differential equations and a comparison with other methods. The European Physical Journal Plus, 132(1), 51.

[4] Bildik, N. and Deniz, S., (2017), A Practical Method for Analytical Evaluation of Approximate Solutions of Fisher's Equations. In ITM Web of Conferences (Vol. 13, p. 01001). EDP Sciences.

[5] Bildik, N. and Deniz, S., (2018), Comparative study between optimal homotopy asymptotic method and perturbation-iteration technique for different types of nonlinear equations. Iranian Journal of Science and Technology, Transactions A: Science, 42(2), 647-654.

[6] Bildik, N. and Deniz, S., (2018), New analytic approximate solutions to the generalized regularized long wave equations. Bulletin of the Korean Mathematical Society, 55(3), 749-762.

[7] Bildik, N. and Deniz, S., (2018), Solving the burgers' and regularized long wave equations using the new perturbation iteration technique. Numerical Methods for Partial Differential Equations, 34(5), 1489-1501.

[8] Deniz, S. and Bildik, N., (2017), A new analytical technique for solving Lane-Emden type equations arising in astrophysics. Bulletin of the Belgian Mathematical Society-Simon Stevin, 24(2), 305-320.

[9] Deniz, S. and Bildik, N., (2018), Optimal perturbation iteration method for Bratu-type problems. Journal of King Saud University-Science, 30(1), 91-99.

[10] Deniz, S., (2017), Optimal perturbation iteration method for solving nonlinear heat transfer equations. Journal of Heat Transfer, 139(7), 074503.

[11] Ghoreishi, M., Ismail, A. M. and Alomari, A. K., (2011), Application of the homotopy analysis method for solving a model for HIV infection of CD4+ T-cells. Mathematical and Computer Modelling, 54(11-12), 3007-3015.

[12] Gopalsamy, K., (2013), Stability and oscillations in delay differential equations of population dynamics (Vol. 74). Springer Science & Business Media.

[13] Iqbal, S., Idrees, M., Siddiqui, A. M. and Ansari, A. R., (2010), Some solutions of the linear and nonlinear Klein–Gordon equations using the optimal homotopy asymptotic method. Applied Mathematics and Computation, 216(10), 2898-2909. (2010): 2898-2909.

[14] Iqbal, S. and Javed, A., (2011), Application of optimal homotopy asymptotic method for the analytic solution of singular Lane–Emden type equation. Applied Mathematics and Computation, 217(19), 7753-7761.

[15] Merdan, M., Gökdoğan, A. and Yildirim, A., (2011), On the numerical solution of the model for HIV infection of CD4+ T cells. Computers & Mathematics with Applications, 62(1), 118-123.

[16] Nazir, A., Ahmed, N., Khan, U. and Mohyud-Din, S. T., (2018), Analytical approach to study a mathematical model of CD4+ T-cells. International Journal of Biomathematics, 11 (03), 1-12.

[17] Nelson, P. W. and Perelson, A. S., (2002), Mathematical analysis of delay differential equation models of HIV-1 infection. Mathematical biosciences, 179(1), 73-94.

[18] Nowak, M. A. and May, R. M., (1991), Mathematical biology of HIV infections: antigenic variation and diversity threshold. Mathematical Biosciences, 106(1), 1-21.

[19] Ongun, M. Y., (2011), The Laplace Adomian Decomposition Method for solving a model for HIV infection of CD4+ T cells. Mathematical and Computer Modelling, 53(5-6), 597-603.

[20] Perelson, A. S., Kirschner, D. E. and De Boer, R., (1993), Dynamics of HIV infection of CD4+ T cells. Mathematical biosciences, 114(1), 81-125.

[21] Rashidi, M. M., Domairry, G. and Dinarvand, S., (2009), Approximate solutions for the Burger and regularized long wave equations by means of the homotopy analysis method. Communications in Nonlinear Science and Numerical Simulation, 14(3), 708-717.

[22] Shah, R. A., Islam, S., Siddiqui, A. M. and Haroon, T. , (2011), Optimal homotopy asymptotic method solution of unsteady second grade fluid in wire coating analysis. Journal of the Korean Society for Industrial and Applied Mathematics, 15(3), 201-222.

[23] Tari, H., Ganji, D. D. and Rostamian, M., (2007), Approximate solutions of $K(2,2)$, KdV and modified KdV equations by variational iteration method, homotopy perturbation method and homotopy analysis method. International Journal of Nonlinear Sciences and Numerical Simulation, 8(2), 203-210.

Sinan DENİZ has been a research assistant of Mathematics at Manisa Celal Bayar University since September 2012. He received his BsC degree in “Mathematics” from Fatih University, Istanbul, Turkey. He completed his master study in Applied Mathematics at Manisa Celal Bayar University in 2014 and his PhD in 2018 at Manisa Celal Bayar University with a dissertation about optimization of analytical approximate solutions of ODEs and PDEs. His main research interests are: Nonlinear Ordinary and Partial Differential Equations, Asymptotic and Computational Methods for ODEs and PDEs, Semi-Analytical and Numerical Methods, Mathematical Modeling