

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

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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

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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:

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

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 n th-order derivatives from the Taylor expansion of a function.

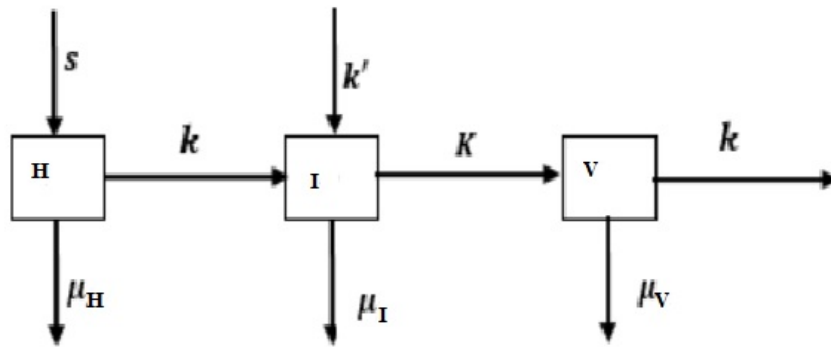


FIGURE 1. Flow diagram for HIV model

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

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

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

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

Let us consider an approximate solution of the system

$$x_{k,n+1} = x_{k,n} + \varepsilon x_{k,n}^c \quad (4)$$

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

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

in the neighborhood of $\varepsilon = 0$ where

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

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

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

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

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

which is a first-order ordinary differential equation and can be solved for the correction terms $x_{k,n}^c$. 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

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

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 m th 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:

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

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

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

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

$$\frac{dJRes_{A_1}}{dp_1} = 0, \quad \frac{dJRes_{A_2}}{dp_2} = 0, \dots, \quad \frac{dJRes_{A_K}}{dp_K} = 0. \quad (12)$$

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

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

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.

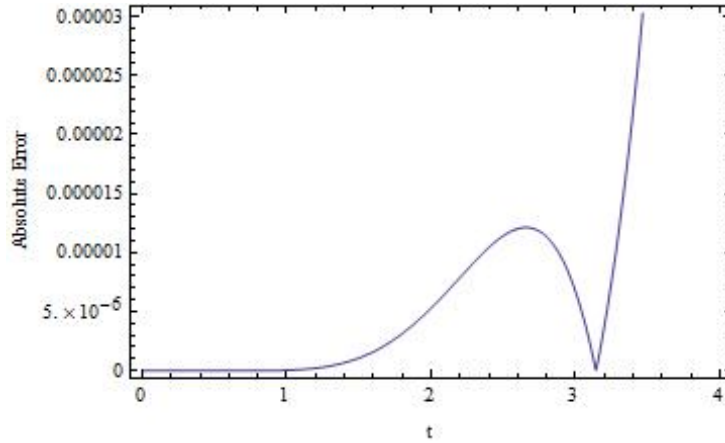


FIGURE 2. Absolute error for fourth order OPIM solution of $H(t)$

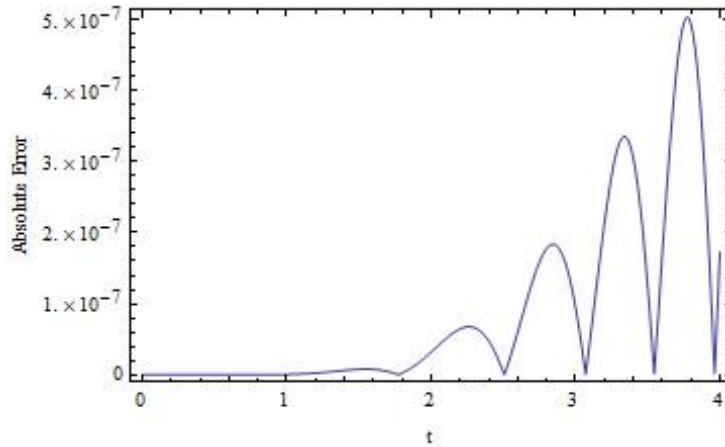


FIGURE 3. Absolute error for fourth order OPIM solution of $I(t)$

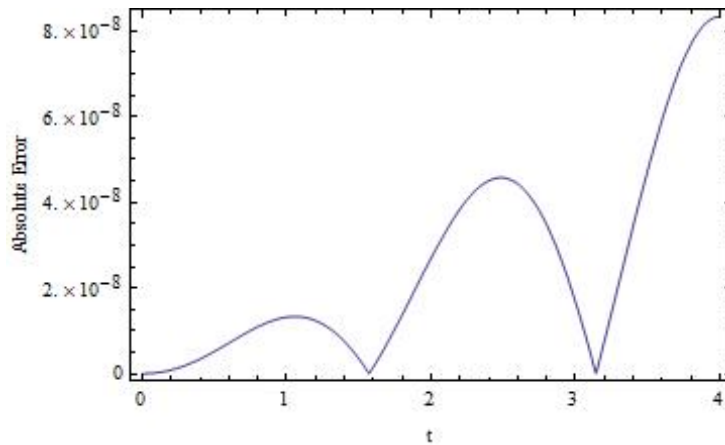
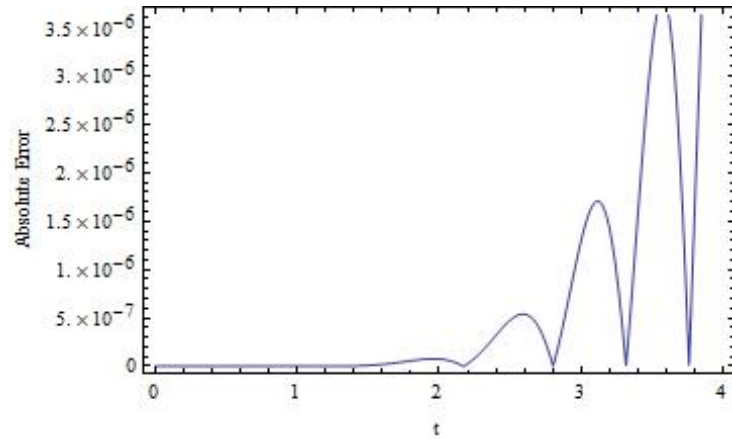
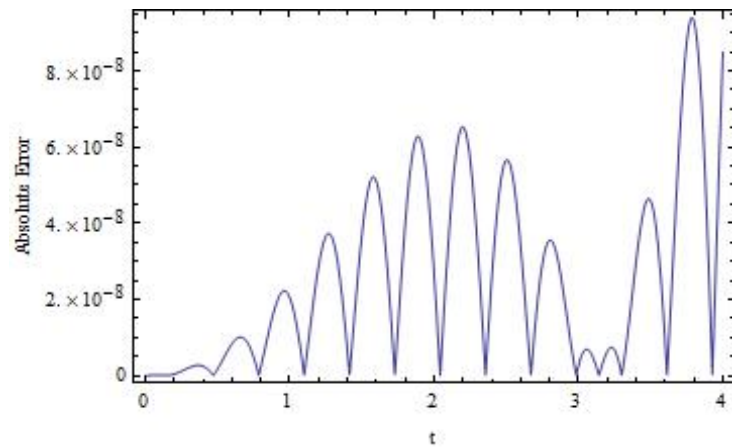
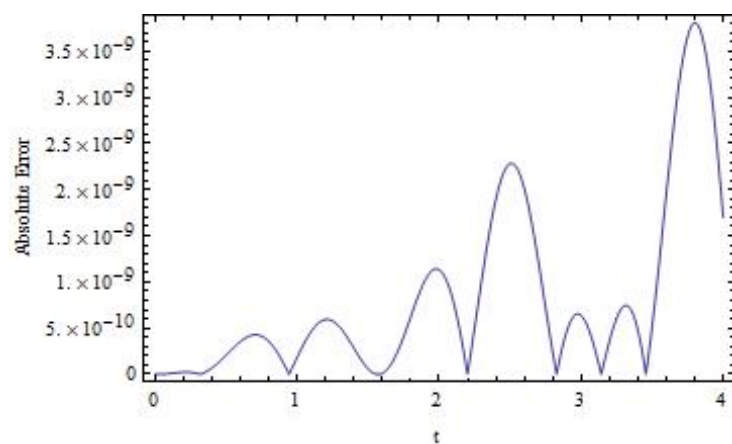


FIGURE 4. Absolute error for fourth order OPIM solution of $V(t)$

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.

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