International Journal of Innovation and Scientific Research
ISSN 2351-8014 Vol. 16 No. 1 Jun. 2015, pp. 79-85

http://www.ijisr.issr-journals.org/

A Numerical Solution of a Model for HIV Infection $CD4^+$ T-Cell

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ABSTRACT: In this paper, a new Iteration Algorithm is examined to provide an approximate solution of a model for HIV infection of $CD4^+$ T-Cells. This method allows the solution of governing differential equation calculated in the form of an infinite series, with components that can be easily calculated. The reliability and the efficiency of proposed approach is demonstrated in different time intervals by numerical example. All computations have been carried out by computer code written in Mathematica 9.0

KEYWORDS: HIV Infection, $CD4^+$ T-Cell, Perturbation Iteration Algorithm, Infinite Series.

1 INTRODUCTION

HIV / AIDS is a major global health problem of the age. There have been some breakthroughs, some small conquests, but nothing concrete. It is irrefutable fact that millions of dollars being spent every year in the treatment of the disease but no cure is available yet. Approximately, 25 million HIV infected individuals live in sub-Saharan Africa [Center for Disease Control (CDC); http://www.cdc.gov/ HIV]. The progression of the HIV / AIDS disease consists of three stages: the acute stage, characterized by extensive initial virus growth, the chronic or asymptomatic phase, where virus loads are low and the patient appears healthy, and the AIDS phase where there is a sharp increase of virus load and the destruction of the $CD4^+$ T helper cells, leading to the failure of the human body. The fact that the HIV virus debilitates not only the immune system but the HIV -specific responses [5], and its ability to rapidly evolve in vivo, escaping the immune responses of the patient [6], makes the HIV virus one of the most complex viruses to fight and overcome.

Many mathematical models have been proposed for the dynamics of HIV infection. In 1989, a model for the infection of HIV into the human immune system was developed by Perelson [1]. This model of the spread of the virus has three variables: the population sizes of uninfected cells, infected cells, and free virus particles. Perelson et al. [2] extended the model described in [1] and developed a new model by considering four variables:

1. Uninfected cells
2. Latently infected cells
3. Actively infected cells, and
4. Free virus particles.

Their model is described by a system of four ordinary differential equations. It was noted that the model can replicate many of the symptoms of AIDS observed clinically. Culshaw and Ruan [3] reduced the model described in [2] to a system of three ordinary differential equations by assuming that all the infected cells are capable of producing the virus.

The model, as discussed in [3], is

$$\frac{dT}{dt} = s - \alpha T + rT\left(1 - \frac{T+I}{T_{max}}\right) - kVT$$

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$$\frac{dI}{dt} = kVT - \beta I \tag{1}$$

$$\frac{dV}{dt} = N\beta I - \gamma V$$

Table 1. List of variables and parameters (modified from [3]).

Parameters and variables	Meaning
Dependent variables	Uninfected $CD4^+$ T-cell concentration
T	
I	Infected $CD4^+$ T-cell concentration
V	Concentration of HIV RNA
Parameters And constants	Natural death rate of $CD4^+$ T-cell concentration
α	
β	Blanket death rate of infected $CD4^+$ T-cells
γ	Death rate of free virus
k	Rate $CD4^+$ T-cells become infected with virus
r	Growth rate of $CD4^+$ T-cell concentration
N	Number of virion produced by infected $CD4^+$ T-cells
T_{max}	Maximal concentration of $CD4^+$ T-cells
s	Source term for uninfected $CD4^+$ T-cells

Where $T(t)$, $I(t)$ and $V(t)$ represent the concentration of healthy $CD4^+$ T-cells at time t, infected $CD4^+$ T-cells, and free HIV at time t, respectively. Table 1 summarizes the meanings of parameters and variables. Stability and existence aspects of this model were discussed in [3, 4].

In a normal human body, the level of $CD4^+$ T cells in the peripheral blood is regulated at a level between 800 and $1200 mm^3$. $CD4^+$ T cells are also named as T-helper cells or leukocytes. These cells are the most abundantly found white blood cells of the human immune system that fight actively against diseases. HIV wrecks the most heinous damage to these cells, causing their decline and destruction and, thus, decreasing the resistance of the human immune system. The dynamic model has proved valuable in understanding the dynamics of HIV infection.

[4] shows us clearly the practical and industrial exposures of such a model. For the proper numerical derivation of a model for HIV infection of $CD4^+$ T-cells, Ongun [7] have applied the Laplace Adomian Decomposition Method; Merdan has used the Homotopy Perturbation Method [8], moreover, Merdan et al. have practiced the Padé approximate and the amended Variational Iteration Method [9]. Vineet K. Srivastava et al solved dynamical model of HIV infection of $CD4+$ T-cells numerically using the differential transform method (DTM)[10]. Suayip Yuzbası [11] derived the approximate solutions of the HIV infection model of $CD4^+$ T by coming up with and further developing the Bessel collocation method. In this paper, the Perturbation Iteration Algorithm (PIA) is launched and extended for solving most approximately the model for HIV infection of $CD4^+$ T-cells of Culshaw and Ruan as described above.

The residual part of the paper is systematized as follows; in Section 2, the basic idea of the Perturbation Iteration Algorithm (PIA) is illustrated mathematically. The numerical implementation of the method for $CD4^+$ T-cells model and its numerical results, an in-depth comparison between Perturbation Iteration Algorithm (PIA),Euler's, Differential transform and RK4 methods is given in Section 3, while Section 4 rounds up and concludes the discussion.

2 PERTURBATION ITERATION ALGORITHM (PIA)

A new and much improved iteration-perturbation method called the "Perturbation-Iteration Method" has been derived recently by [12]. This new method employs masterfully a combination of perturbation expansions and Taylor series expansions to give rise to an iteration scheme. Authors in [12,13] introduced expansion and correction terms of only first

derivatives in the Taylor Series expansion, i.e. $n=1$, $m=1$ and one correction term in the perturbation. The algorithm is named $\text{PIA}(1,1)$. Consider the following system of first-order differential equations.

$$G_k(\dot{u}_k, u_j, \varepsilon, t) = 0 \; ; \qquad k=1,2,3,.....,K \quad ; \qquad j=1,2,3,....,K \tag{2}$$

where K is a representative of the number of differential equations in the system and the number of dependent variables $K=1$ for a single equation. In the open form, the system of equations is

$$G_1 = G_1(\dot{u}_1, u_1, u_2, u_3, ..., u_K, \varepsilon, t) = 0$$

$$G_2 = G_2(\dot{u}_2, u_1, u_2, u_3, ..., u_K, \varepsilon, t) = 0$$

$$G_3 = G_3(\dot{u}_3, u_1, u_2, u_3, ..., u_K, \varepsilon, t) = 0$$

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$$G_K = G_K(\dot{u}_K, u_1, u_2, u_3, ..., u_K, \varepsilon, t) = 0 \tag{3}$$

Assume an approximate solution of the system

$$u_{k,n+1} = u_{k,n} + \varepsilon u^c_{k,n} \tag{4}$$

with one correction term in the perturbation expansion. The subscript n represents the n^{th} iteration over this approximate solution. The system can be approximated with a Taylor series expansion in the neighborhood of $\varepsilon = 0$ as

$$G_k = \sum_{m=0}^{M} \frac{1}{m!}\left[\left(\frac{d}{d\varepsilon}\right)^m G_k\right]_{\varepsilon=0} \varepsilon^m \quad , \quad k = 1,2,3,...., K \tag{5}$$

where

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

is defined for the $(n+1)^{th}$ iterative equation

$$G_k(\dot{u}_{k,n+1}, u_{j,n+1}, \varepsilon, t) = 0 \tag{7}$$

Substituting (5) into (4), an iteration equation is obtained

$$G_k = \sum_{m=0}^{M} \frac{1}{m!}\left[\left(\dot{u}^c{}_{k,n}\frac{\partial}{\partial \dot{u}_{k,n+1}} + \sum_{j=1}^{K}\left(u^c{}_{j,n}\frac{\partial}{\partial u_{j,n+1}}\right) + \frac{\partial}{\partial \varepsilon}\right)^m G_k\right]_{\varepsilon=0} \times \varepsilon^m = 0 \quad ;$$

$k=1,2,3,....,K$ (8)

Which is a first-order differential equation and can be solved for the correction term $u^c_{k,n}$. Then, using (4), the $(n+1)^{th}$ iteration solution can be found. Iterations are terminated after a satisfactory approximation is obtained.

Note that for a more general algorithm, n correction terms instead of one can be taken in expansion (4) which would then be $\text{PIA}(n,m)$ algorithm. The algorithm can also be used generally and be applied to a differential equation system having arbitrary order of derivatives. Within the scope of this paper, only a case $n=m=1$ is considered for the sake of simplicity, because more Algebra is involved in constructing iteration solutions for $\text{PIA}(1,2)$ and $\text{PIA}(1,3)$ as compared to $\text{PIA}(1,1)$. We have computed the numerical results by the well-known symbolic software "Mathematica 9.0"

3 NUMERICAL SIMULATION

In order to show the effectiveness of Perturbation Iteration Algorithm for solving the dynamical model of HIV infection of $CD4^+$ T cells, we present the following system of differential equation of HIV model shown in equation (1), we take values of these parameters as.

$\alpha = 0.02$; $k = 0.0027$; $\beta = 0.3$; $\gamma = 2.4$; $N = 10$; $s = 0.1$; $T_{max} = 1500$, $r = 3$

So system of differential equation becomes

$$\frac{dT}{dt} = 0.1 + 2.978T - 0.002T^2 - 0.0027IT$$

$$\frac{dI}{dt} = 0.0027VT - 0.3I \tag{9}$$

$$\frac{dV}{dt} = 3I - 2.4V$$

With initial conditions $T(0) = 0.1$; $I(0) = 0$; $V(0) = 0.1$

The system is solved by using $PIA(1,1)$. The perturbation parameter ε is artificially introduced as

$$G_1 = \dot{T} - 0.1 - 2.978T + 0.0027IT\varepsilon + 0.002T^2\varepsilon = 0$$

$$G_2 = \dot{I} - 0.0027VT\varepsilon + 0.3I = 0 \tag{10}$$

$$G_3 = \dot{V} - 3I\varepsilon + 2.4V = 0$$

For the equation (10) the system (1) with correction terms becomes

$$\dot{T}_n - 0.1 - 2.978T_n + \dot{T}_n^c\varepsilon - 2.978T_n^c\varepsilon + 0.0027V_nT_n\varepsilon + 0.002T_n^2\varepsilon = 0$$

$$\dot{V}_n + 2.4V_n + \dot{V}_n^c\varepsilon + V_n^c 2.4\varepsilon - 3I_n = 0 \tag{11}$$

$$\dot{I}_n + 0.3I_n + \dot{I}_n^c\varepsilon + I_n^c 0.3\varepsilon - 0.0027V_nT_n\varepsilon = 0$$

We take initial guess in this system as

$T_{1,0} = 0.1$; $I_{1,0} = 0$; $V_{1,0} = 0.1$

After substituting initial guess in (11) and with the help of equation (4), the first approximation has been obtained, which is

$$T_{1,1} = 0.1 + 0.13356380120886502\left(e^{2.978t} - 1\right)$$

$$I_{1,1} = 0.00009\left(1 - e^{-0.3t}\right)$$

$$V_{1,1} = 0.1 - 0.1\left(1 - e^{-2.4t}\right)$$

Another Iteration gives more accurate results than the previous one

$$T_{1,2} = 0.1 + 0.13356380120886502\left(e^{2.978t} - 1\right) - 0.0000119807e^{-7.778t}\begin{pmatrix} 0.140647e^{5.378t} + 1.25417e^{7.778t} - 1.25418e^{8.356t} - \\ 1.14064e^{10.756t} + e^{13.734t} - 1.49671te^{10.756t} \end{pmatrix}$$

$$I_{1,2} = 0.00009\left(1 - e^{-0.0t}\right) - 0.00009e^{-2.4t}\left(-0.0479483 - 0.495683e^{2.1t} + e^{2.4t} - 0.456368e^{2.978t}\right)$$

$$V_{1,2} = 0.1 - 0.1\left(1 - e^{-2.4t}\right) + 0.0001125e^{-2.4t}\left(0.142857 - 1.14286e^{2.1t} + e^{2.4t}\right)$$

Table 2. Comparison between PIA(1,1) and other methods for concentration of Uninfected T-cells.

t	RK4	PIA	DTM	Euler
0.0	0.1000000000000000	0.1000000000000000	0.1000000000	0.1000000000
0.2	0.2087297222454430	0.2087295073948490	0.2116480000	0.2066396850
0.4	0.4059409955447710	0.4059404993468250	0.4226850000	0.3455020000
0.6	0.7635801781341750	0.7635790156330420	0.8179400000	0.6050020000
0.8	1.4119574363577000	1.4119543417994200	1.5462110000	1.0420600000
1.0	2.5867778755778800	2.5867690583329300	2.8540530000	1.7779900000

Table 3. Concentration of HIV RNA i.e. V(t) from DTM, Euler, RK4 and PIA(1,1)

t	RK4	PIA	DTM	Euler
0.0	0.1000000000000000	0.1000000000000000	0.10000000000	0.10000000000
0.2	0.0618798121706440	0.0618796999022359	0.06188000000	0.05776100000
0.4	0.0382948730759080	0.0382939096056007	0.03830900000	0.03336600000
0.6	0.0237045402752520	0.0237016917514381	0.02392000000	0.01927900000
0.8	0.0146803506585660	0.0146744145285035	0.01621200000	0.01114500000
1.0	0.0091008270878710	0.0090905052391029	0.01605000000	0.00645000000

To demonstrate the effectiveness of the proposed algorithm the perturbation-iteration algorithm, differential transform method, Euler's method and RK4 are applied to the HIV model of $CD4^+$ T-cells. The solution obtained by PIA is compared with above mentioned methods (as shown in table 2, 3 and 4). It can be deduced that second approximation of perturbation iteration algorithm are in good agreement with the RK4 method while solutions obtained by other methods are less accurate.

Table 4. Concentration of Infected T-cell i.e. I(t) from RK4, PIA(1,1) and other methods.

t	RK4	PIA	DTM	Euler
0.0	0.0000000000000000	0.0000000000000000	0.000000000000	0.000000000000
0.2	0.0000060315204770	0.0000060315204441	0.000006914977	0.000059531387
0.4	0.0000131530315000	0.0000131530687549	0.000002218815	0.000001288463
0.6	0.0000212106240460	0.0000212101256473	0.000005722250	0.000002061344
0.8	0.0000301518386990	0.0000301480518052	0.000121495184	0.000002906056
1.0	0.0000399942614780	0.0000399785098805	0.000207581862	0.000003821604

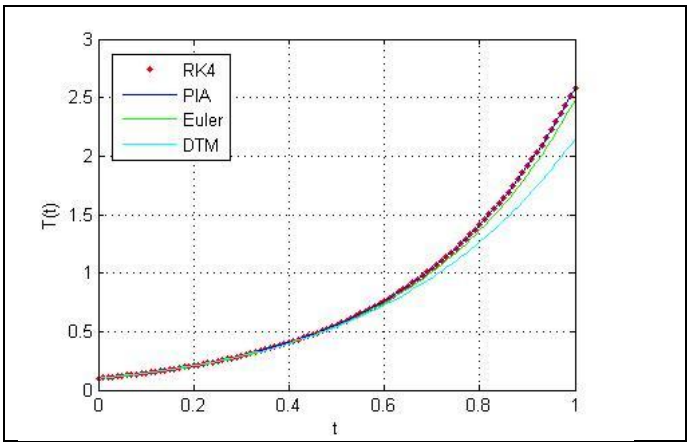

Fig. 1. Graphical comparison of uninfected T-cell (T) concentration

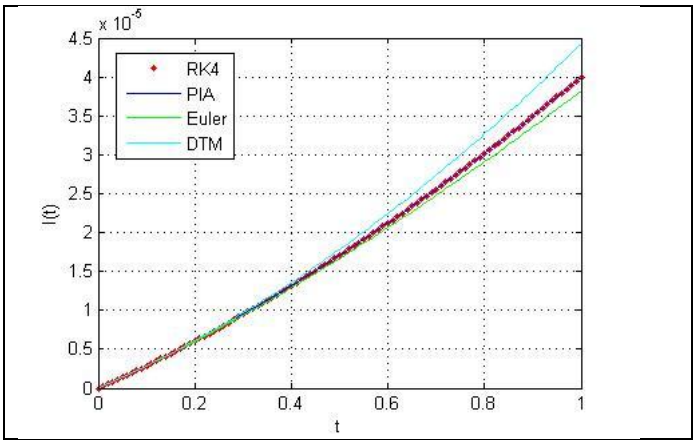

Fig. 2. Infected T-cell (I) concentration.

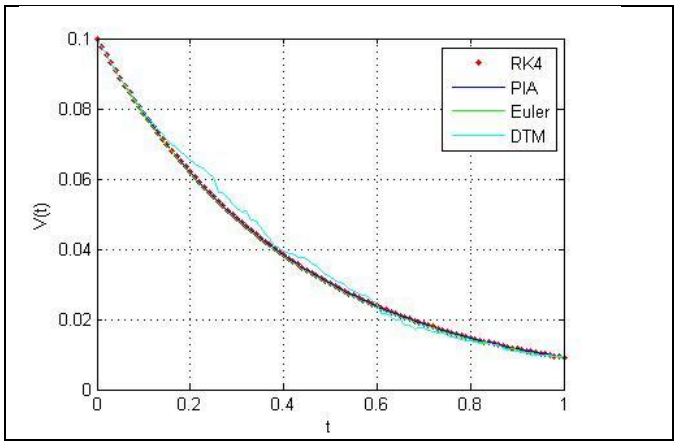

Fig. 3. Graphical comparison of Concentration of V(t).

Figure 1 ,2 and 3 show that the approximate solutions obtained by perturbation iteration algorithm for the HIV infection model of CD+4 T-cells are very close to the Runge-Kutta approximation solution.

4 CONCLUDING REMARKS

In this study, we developed the Perturbation Iteration Algorithm (PIA) and successfully applied it for solving a model for HIV infection of $CD4^+$ T-cells. The solutions obtained by the Perturbation Iteration Algorithm (PIA) seem to match well when compared with those obtained by Euler's, Differential transform and RK4 methods. Additionally, this method, which is a simple and powerful mathematical tool, can be easily employed to solve nonlinear problems which may arise in systems of nonlinear differential equations and, also, in dynamical systems. We have shown that the proposed algorithm is very accurate and efficient method compared with other methods for the HIV infection model of $CD4^+$ T-cells. A significant advantage of the method is that the approximate solutions can be calculated effortlessly with computer programs in lesser amount of time. The computations associated with the example have been performed on a computer with the aid of a computer code written in Mathematica 9.0.

ACKNOWLEDGMENT

The authors thank the anonymous referees for their valuable suggestions and helpful comments and Ms Wishaal Khalid for her help in proofreading.The authors are thankful to Federal Urdu University for research grant.

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