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SOLUTION OF THE HIV INFECTION MODEL WITH FULL LOGISTIC PROLIFERATION AND VARIABLE SOURCE TERM USING GALERKIN SCHEME

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ABSTRACT

The present study is related to the numerical solution of the human immunodeficiency virus (HIV) infection model with full logistic proliferation and variable source term (depending on the viral load) used for the supply of new $CD4^+$ T-cells from thymus instead of using simple logistic proliferation and constant source term. In simple logistic proliferation term only the healthy or infected $CD4^+$ T-cells proliferation are considered while in full logistic proliferation term both the proliferation of healthy and infected are considered. Consequently, the variable source term is used for the supply of new healthy $CD4^+$ T-cells from thymus, which is a decreasing function depending on the concentration of viral load. Continuous Galerkin-Petrov method, in particular cGP(2)-method has been invoked for finding the approximate solution of the model. For cGP(2)-method, we have two unknowns on each time interval which have to be calculated by solving 2×2 block system. This method is an accurate of order three in the whole time interval and shows the convergence of order four in the discrete time points. We examined the impact of various clinical parameters and study the existence of the infected state. Additionally, the Runge Kutta method of order four briefly RK4-method has also been used to verify and strengthen the results obtained by cGP(2)-method. Obtained results are displayed both graphically and in tabular form. The results obtained in this study confirm the idea that the cGP(2)-method is a powerful technique which can be applied to a large class of linear and nonlinear problems arising in different fields of science and engineering.

KEYWORDS

Human Immunodeficiency Virus, CD4 $^+$ T-cells, Continuous Galerkin-Petrov Method, Runge-Kutta Method.

1. INTRODUCTION

Infectious disease is disorders caused by micro organisms like viruses, bacteria etc. These infectious diseases transfer from human to human, or from other non-living things. It is caused by insects bites, contact with animal or usually acquired by eating or drinking foods contaminated with bacteria. Acquired Immune Deficiency Syndrome (AIDS) is such an infectious disease which is caused by HIV virus. HIV is a viral infection that can be transferred through blood or during pregnancy from mother to child, by sharing needles or from blood transfusions (Bell et al., 2011). AIDS is the most advanced stage of HIV infection. HIV is a small organism which basically targets the $CD4^+$ T-cells which are the most important parts of the immune system. HIV basically creates a needless disturbance on the work of $CD4^+$ T-cells and causes the destruction of $CD4^+$ T-cells and decreases the body's ability to fight against infection. HIV virus can not replicate by itself. It basically depends on a host cell to help in replication. HIV carries copies of its DNA and enters these copies into the host cell's Deoxyribonucleic Acid (DNA).

When the host cell is activated to replicate, then it starts to make copies of the virus. $CD4^+$ T-cells act as the host cell. These cells play an important role in the immune response. Main function of $CD4^+$ T-cells is to boost the command forces, which can obtain by $CD8^+$ T-cells. $CD8^+$ T-cells activate the immune response against viruses. These cells control the virus by bounding the HIV replication and intrude it into target cells. To understand the development of AIDS from HIV infection, it is important to analyze the dynamics of HIV, $CD4^+$ T-cells, and $CD8^+$ T-cells throughout the period of infection (Mccune, 2001). $CD4^+$ T-cells are naturally refilled in the human body, but the infection decreases the number of $CD4^+$ T-cells in the human body. Normally, HIV kills a small fraction of these cells approximately 10^{-4} to 10^{-5} at one time, but the reason in the reduction of $CD4^+$ T-cells count is reasonably unknown during the last stages of AIDS (Anderson et al., 1998). The count of $CD4^+$ T-cells is a primary signal having HIV which is used to measure proliferation rate of HIV infection (Mohri et al., 1998). Since this study is related to $CD4^+$ T-cells so, we will use the term T-cells for to mean $CD4^+$ T-cells throughout the reminder of this article.

To understand and analysed the dynamics T-cells, HIV virus, and interaction of HIV with human immune system, several mathematical

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models have been developed. Some of these mathematical models are widely used to study the mechanism of HIV virus that help to improve the understanding of the disease growth, its function in the host cells, test treatment strategies and the secondary infections such as tuberculosis (Kirschner et al., 1997; Hu et al., 2010). Based on these models, many researchers have studied in optimal drug dose control problems (Kutch and Gurfil, 2002; Anthea et al., 1993). Several studies have found evidence for high level of T-cells which controls HIV reproduction, and found that T-cells may control the presence of virus in the blood (Bonhoeffer et al., 1997). A group researchers analyzed the dynamics of a delayed HIV pathogenesis model (Hu et al., 2010). A study the HIV-I dynamics in vivo and analyzed the virion clearance rate, infected T-cell lifespan, viral generation time and developed a simple model for the interaction between the human immune system and HIV (Perelson and Nelson, 1999). Some researchers explored the HIV-I dynamics at different time scales under anti-retroviral therapy (Garcia et al., 2006).

This may lead to the effects of various parameters upon the viral load in different compartments at different stages after Highly Active Anti-Retroviral Therapy (HAART) in order to identify the most sensitive parameters. Attaullah and Sohaib implemented two numerical schemes namely continuous Galerkin–Petrov (cGP(2)) and Legendre Wavelet Collocation Method (LWCM) for the approximate solution of the mathematical model which describes the behavior of T-cells, infected T-cells and free HIV virus particles after HIV infection (Attaullah and Sohaib, 2020). They presented and analyzed the effect of constant and different variable source terms (depending on the viral load) used for the supply of new T-cells from thymus on the dynamics of T-cells, infected T-cells and free HIV virus. Furthermore, they also solved the model using fourth order Runge Kutta (RK4) method. They highlights the accuracy and efficiency of the proposed schemes with the other traditional schemes. A study the dynamics of giving up smoking model of fractional order and presented the approximate solution of the concerned model utilizing Laplace transformation (Haq et al., 2018).

They compared their results with the results obtained by Runge-Kutta method. A group researcher described the fractional order epidemic model of a vector-born disease with direct transmission in a population which is assumed to have a constant size over the period of the epidemic is consider (Haq et al., 2017). They solved the model numerically using Laplace Adomian decomposition method and compared the obtained results with the results of Runge-kutta method. A group researchers considered fractional order endemic model of non-fatal disease in a community (Shah and Bushnaq, 2017). They implemented Laplace transform coupled with Adomian decomposition method and obtained numerical solution of the proposed model. The solutions obtained by this method are compared with the solutions obtained by the RK4 and homotopy perturbation method for taking classical order derivative of the governing equations. Some researchers established the existence theory of solutions to HIV-1 infection model of T-cells with fractional order derivative (Bushnaq et al., 2017). The corresponding fractional order derivative is considered in Caputo-Fabrizio sense, which possesses more important characteristics in mathematical modeling. They provided the numerical solution and showed the effectiveness of the theoretical results. The study of some reesearchers concerned to the existence and stability of HIV/AIDS infection model with fractional order derivative (Bushnaq et al., 2018).

The corresponding derivative is taken in Caputo-Fabrizio sense, which is a new approach for such type of biological models. With the help of Sumudu transform, some new results are handled. Further for the corresponding results, existence theory and uniqueness for the equilibrium solution are provided via using nonlinear functional analysis and fixed point theory due to Banach. In other study, authors worked on HIV drug therapy and virus load (Bonhoeffer et al., 1997). A group resaerhcers investigated an approximate solution of a model for HIV infection of T-cells using homotopy analysis method (Ghoreishi et al., 2011). Mostly researchers have worked in respect to the pathogenesis of HIV in host using simple logistic proliferation term. A group researcher and other researchers have assumed the HIV model with the growth of T-cells by using a simple logistic proliferation term (Roy and Chatter, 2010; Kirschner, 1996; Leenheer and Smith, 2003; Wang and Ellermeyer, 2006). In literature, researchers suggest that all T-cells (healthy and infected) divide and increase in population and proliferate when these are activated once by antigen (Ghoreishi et al., 2011; Kirschner et al., 1993; Culshaw and Ruan, 2000; Wang and Li, 2006; Wang and Song, 2007; Otunuga, 2018; Gonzalez et al., 2020; Zhang and Liu, 2020; Qesmi and Hammoumi, 2020).

Inspired by their work, we assumed that T-cells (healthy and infected) are governed by a full logistic growth term. Many researchers have considered that the human body produces T-cells in bone marrow and thymus at a constant rate during HIV infection (Roy and Chatterjee, 2010; Ghoreishi et al., 2011; Kirschner et al., 1993; Culshaw and Ruan, 2000; Wang and Li, 2006; Wang and Song, 2007). Since, HIV virus has the ability to infects the thymus, due to this, constant source rate of healthy T-cells becomes decreasing source rate depending on viral load [23, 24], therefore we assumed variable source rate. We have utilized cGP(2)-method for HIV the model and find out the approximate solution (Schieweck, 2010; Matthies and Schieweck, 2011; Hussain et al., 2011; Hussain et al., 2012). This method has an advantages over other traditional methods, e.g., laplace adomian decomposition method, bessel collection method, homotopy analysis method, etc. To validate the solution, we also solved the model by using RK4-method and compared the results of both methods. All the numerical simulations for various sets of parameters are performed using a computer code written in MATLAB ™. Obtained results are displayed both graphically and in tabular form to illustrate the accuracy and effectiveness of the proposed method as compare to the other classical numerical schemes.

2. Mathematical Formulation

This section deals with the model proposed (Roy and Chatterjee, 2010). The model of HIV consisting of three coupled non linear ordinary differential equations that considered three populations, i.e., healthy T-cells, infected T-cells and free virus. Let *T(t)*, *I(t)* and *V(t)* be the concentration of healthy T-cells, infected T-cells and free viruses respectively at time t. The HIV model is as follows (Roy and Chatterjee, 2010):

$$\frac{dT}{dt} = s + \rho T\left(1 - \frac{T}{T_{\max}}\right) - \mu_T T - \kappa TI, \tag{1}$$

$$\frac{dI}{dt} = \kappa TI - \mu_I I - \beta IV, \tag{2}$$

$$\frac{dV}{dt} = \eta I - \mu_V V. \tag{3}$$

Initial conditions are $T(0) = T_0$, $I(0) = I_0$ and $V(0) = V_0$. The parameter 's' represents the constant source term for the supply of new T-cells. It represents the rate at which healthy T-cells are produced from the precursor such as bone marrow and thymus (Wang and Song, 2007). The term $\rho T\left(1 - \frac{T}{T_{\max}}\right)$ in Equation (1) shows the growth rate of the healthy T-cells where the parameter 'ρ' denotes the average specific healthy T-cells growth rate obtained in the absence of population of healthy T-cells. The parameter '$T_{\max}$', represents the maximum level of T-cells in the body, i.e., when the population reaches '$T_{\max}$', it starts to reduce naturally, so that, T-cells never grow larger than '$T_{\max}$' (Hu et al., 2010). The probability that an infected or healthy T-cell will die with respect to time is not known. Therefore, we assume that the natural death rate per T-cell is 'μ_T' for healthy T-cells and 'μ_I' for infected T-cells (Perelson and Nelson, 1999).

The parameter 'κ' represents the constant rate between virus and healthy T-cells. The term 'κTI' of Equation (1) expresses the rate at which free virus V infects T-cell. When T-cell is infected with virus, then it becomes latently infected. Therefore, we assume that when infection occurs by virus and infects the healthy T-cell, then it causes the loss of healthy T-cells at the rate $-\kappa TI$ and the production of infected T-cells at the rate κTI (Perelson and Nelson, 1999). Thus, infection occurs by virus interacting with healthy T-cells causing the loss of healthy T-cells at rate $-\kappa TI$ in Equation (1) and causing the generation of infected T-cells at rate κTI in Equation (2). Then, infected cells are vanished either by having finite

duration of life or by being stimulated to reproduce (Kirschner, 1996). The parameter 'β' denotes the killing rate of infected cells and 'μ_V' represents the clearance rate of free viruses. In Equation (3), the parameter 'η' denotes the rate of reproduction of CD8 molecule, and '$\mu_V V$' accounts for the viral removal from the body (Kirschner et al., 1997). In Table 1 all the parametrical values and the initial conditions are given to explore the numerical results.

Table 1: Explanation of variables, parameters with their values involved in the model.

Variables	Description	Values	References
T_0	Number of healthy T-cells	50 mm^{-3}	(Roy and Chatterjee, 2010)
I_0	Number of infected T-cells	50 mm^{-3}	(Roy and Chatterjee, 2010)
V_0	Number of free Viruses	2 mm^{-3}	(Roy and Chatterjee, 2010)
Parameters			
s	Rate at which healthy T-cells are generated	10.0 $mm^{-3}day^{-1}$	(Kirschner et al., 1997; Perelson and Nelson, 1999; Culshaw and Ruan, 2000)
ρ	Constant rate for growth of T-cells population	0.03 day^{-1}	(Kirschner et al., 1997; Hu et al., 2010; Perelson and Nelson, 1999; Wang and Li, 2006)
$T_{\max}$	Maximum T-cells growth level	1500 $mm^{-3}day^{-1}$	(Kirschner et al., 1977; Hu et al., 2010; Perelson and Nelson, 1999; Wang and Li, 2006)
μ_T	Death rate of healthy T-cells	0.01 day^{-1}	(Perelson and Nelson, 36; Zhou et al., 2008)
κ	Rate at which T-cells infected by free virus	0.002 $mm^{-3}day^{-1}$	(Bonhoeffer and Nowak, 1997)
μ_I	Death rate of virus producing T-cells	0.24 day^{-1}	(Kirschner et al., 1993; Culshaw and Ruan, 2000)
β	Killing rate of virus producing T-cells	0.001 $mm^{-3}day^{-1}$	(Bonhoeffer and Nowak, 1997)
η	Reproduction rate of $CD8^+$ T-cells	0.2 day^{-1}	(Bonhoeffer and Nowak, 1997)
μ_V	Death rate of free viruses	0.02 day^{-1}	(Bonhoeffer and Nowak, 1997)

2.1 Modified Formulation

In this section, we extended the model proposed and many others, considered the HIV infection model with simple logistic proliferation term, i.e., $\rho T(1-\frac{T}{T_{\max}})$ and constant source term for the supply of healthy T-cells, but recently most of the researchers proposed the HIV model with full logistic proliferation term, i.e., $\rho T(1-\frac{T+I}{T_{\max}})$ and the variable source term, i.e., $(\frac{s}{1+V})$ (Roy and Chatterjee, 2010; Kirschner, 1996; Leenheer and Smith, 2003; Wang and Ellermeyer, 2006; Ghoreishi et al., 2011; Wang and Li, 2006; Wang and Song, 2007). Full logistic proliferation term represents the proliferation of both healthy and infected T-cells and the variable source term denotes the generated amount of new healthy T-cells from thymus and we consider source of healthy T-cells to be a decreasing function which depends on the concentration of free virus particles (Kirschner et al., 1997; Connor et al., 1993). The extended model is follows as:

$$\frac{dT}{dt} = \frac{s}{1+V} + \rho T(1-\frac{T+I}{T_{\max}}) - \mu_T T - \kappa TI, \tag{4}$$

$$\frac{dI}{dt} = \kappa TI - \mu_I I - \beta IV, \tag{5}$$

$$\frac{dV}{dt} = \eta I - \mu_V V. \tag{6}$$

where the dependent T(t), I(t) and V(t) represents the population of healthy T-cells, infected T-cells and free virus respectively. The explanation and the values of all parameters are given in Table 1. Disease-free equation points are those steady state solutions where there is no disease. For steady state of Equation (4), when there is no virus, we impose the initial conditions $T(0) = T_0$, $V(0) = 0$, and $I(0) = 0$. In order to understand the dynamical behavior of the Equations (4)–(6), we set right hand side of all equations in the system (4)–(6) equal to zero (Lashari and Zaman, 2012). We write Equation (4) as:

$$F(t) = \frac{s}{1+V} + \rho T(1-\frac{T+I}{T_{\max}}) - \mu_T T - \kappa TI = 0. \tag{7}$$

We have used the corresponding initial conditions and find out the solution by using quadratic formula. Direct calculations shows that the Equation (4) has a disease free point, which is

$$T_0 = \frac{T_{\max}}{2\rho}\left\{(\rho-\mu_T) \pm \sqrt{(\rho-\mu_T)^2 + \frac{4\rho s}{T_{\max}}}\right\}. \tag{8}$$

The Equation (8) has two roots, one positive and other is negative, here, we skip the negative root and considered the positive root that represents physical possible steady state of the system in the absence of virus (Kirschner et al., 1993).

2.2 Continuous Galerkin-Petrov Method

The system of ODEs for HIV model (1)–(3) or (4)–(6) can considered as:

Find $\boldsymbol{u}$: $[0, t_{max}] \to \boldsymbol{V} = \mathbb{R}^d$ *such that*

$$\begin{array}{rcll} d_t\mathbf{u}(t) & = & \mathbf{F}(t,\mathbf{u}(t)) & \text{for} \quad t \in (0, t_{max}), \\ \mathbf{u}(0) & = & \mathbf{u}_0, & \end{array} \tag{9}$$

where $\mathbf{u}(t) = [T(t), I(t), V(t)]$ and $\mathbf{F}$ is the nonlinear right hand side vector valued function. At $t = 0, u_1(0) = T(0) = T_0, u_2(0) = I(0) = I_0$ and $u_3(0) = V(0) = V_0$, where T_0, I_0 and V_0 are the initial conditions given in Table 1.

In order to find the approximate solution of (9), we partitioned the time interval $I := [0, t_{max}]$ into a number of small pieces $I_n := (t_{n-1}, t_n)$, where $n \in \{1, \dots, N\}$ and $0 = t_0 < t_1 < \cdots < t_{N-1} < t_N = t_{max}$.

The symbol $\tau = t_n - t_n$ is used to represent the maximum time step size. For the derivation of the cGP-method, the system of equations in (9) is multiplied with a suitable test functions (see for more details) and integrate over I_n (Schieweck, 2010; Hussain et al., 2011; Matthies and Schieweck, 2011). The discrete solution $\mathbf{u}_\tau|_{I_n}$ can be represent by the polynomial ansatz.

$$\mathbf{u}_\tau|_{I_n}(t) := \sum_{j=0}^{k} \mathbf{U}_n^j \phi_{n,j}(t), \tag{10}$$

where $\mathbf{U}_n^j$ are the members of the function space $\mathbf{V}$ and the basis functions $\phi_{n,j} \in \mathbb{P}_k(I_n)$ can be chosen as Lagrange basis functions w. r. t. the $k+1$ points $t_{n,j} \in I_n$ with the following assumption

$$\phi_{n,j}(t_{n,i}) = \delta_{i,j}, \qquad i, j = 0, \dots, k \tag{11}$$

where $\delta_{i,j}$ is the usual Kronecker delta. We choose the points as $t_{n,0} = t_{n-1}$ and $t_{n,1}, \dots, t_{n,k}$ the $(k+1)$-quadrature points of Gauß-Lobatto formula on each time interval. In this way, the initial condition can be written as:

$$\mathbf{U}_n^0 = \mathbf{u}_\tau|_{I_{n-1}}(t_{n-1}) \quad \text{if} \quad n \geq 2 \qquad \text{or} \qquad \mathbf{U}_n^0 = \mathbf{u}_0 \quad \text{if} \quad n = 1. \tag{12}$$

The basis functions $\phi_{n,j} \in \mathbb{P}_k(I_n)$ of (10) are defined using the reference transformations (Schieweck, 2010; Hussain et al., 2011; Hussain et al., 2012; Matthies et al., 2011). Similarly, the test basis functions $\hat{\psi}_i \in \mathbb{P}_{k-1}(\hat{I})$ are defined with appropriate choice in order to compute the coefficients (Schieweck, 2010; Hussain et al., 2011; Hussain et al., 2012; Matthies et al.,

2011). Finally, the cGP(k)-method reads:

$$\sum_{j=0}^{k} \alpha_{i,j}\mathbf{U}_n^j = \frac{\tau_n}{2}\{\mathbf{F}(t_{n,i},\mathbf{U}_n^i) + \beta_i\mathbf{F}(t_{n,0},\mathbf{U}_n^0)\} \quad \forall\, i = 1,2,3,\cdots,k, \tag{13}$$

where $\mathbf{U}_n^0 = \mathbf{U}_{n-1}^k$ for $n > 1$ and $\mathbf{U}_1^0 = u_0$ for $n = 1$, are the initial values and $\alpha_{i,j}$ and β_i are defined are

$$\alpha_{i,j} = \hat{\varphi}_j'(\hat{t}_i) + \beta_i\hat{\varphi}_j'(\hat{t}_0),\ t_{n,u} = \omega_n(\hat{t}_\mu) \text{ and } \beta_i = \hat{w}_0\hat{\psi}_i(\hat{t}_0). \tag{14}$$

Once the above system is solved, the initial condition for the next time interval $\bar{I}_{n+1}$ is set to $\mathbf{U}_{n+1}^0 = \mathbf{U}_n^k$. For $k = 2$, the coefficients $\alpha_{i,j}$ and $\beta_{i,j}$ of the cGP(2)-method are computed as follows.

2.2.1 *The cGP(2) Method*

Three-point Gauß-Lobatto formula (Simpson rule) is used to define the quadratic basis functions with weights $\hat{w}_0 = \hat{w}_2 = 1/3$, $\hat{w}_1 = 4/3$ and $\hat{t}_0 = -1$, $\hat{t}_1 = 0$, $\hat{t}_2 = 1$. Then, we get

$$\alpha_{i,j} = \begin{pmatrix} -\frac{5}{4} & 1 & \frac{1}{4} \\ 2 & -4 & 2 \end{pmatrix}, \quad \beta_i = \begin{pmatrix} \frac{1}{2} \\ -1 \end{pmatrix}, \quad i = 1,2, \quad j = 0,1,2.$$

Thus, the system to be solved for $\mathbf{U}_n^1, \mathbf{U}_n^2 \in \mathbf{V}$ from the known $\mathbf{U}_n^0 = \mathbf{U}_{n-1}^2$ becomes:

$$\alpha_{1,1}\mathbf{U}_n^1 + \alpha_{1,2}\mathbf{U}_n^2 = -\alpha_{1,0}\mathbf{U}_n^0 + \frac{\tau_n}{2}\{\mathbf{F}(t_{n,1},\mathbf{U}_n^1) + \beta_1\mathbf{F}(t_{n,0},\mathbf{U}_n^0)\}, \tag{15}$$

$$\alpha_{2,1}\mathbf{U}_n^1 + \alpha_{2,2}\mathbf{U}_n^2 = -\alpha_{2,0}\mathbf{U}_n^0 + \frac{\tau_n}{2}\{\mathbf{F}(t_{n,2},\mathbf{U}_n^2) + \beta_2\mathbf{F}(t_{n,0},\mathbf{U}_n^0)\}, \tag{16}$$

where $\mathbf{U}_n^0$ represent the initial condition at the current time interval.

2.3 Classical Explicit Runge-Kutta Method

This method is very famous having order four developed by (Kutta, 1901;Butcher, 2008).

2.4 Comparison between the Solutions of cGP(2)-Method and RK4-Method for the Model

In this section, we have solved the extended model for HIV infection by using Runge-Kutta method of order four (RK4-method) and compared the results with those obtained from the cGP(2)-method. We illustrated the preciseness and effectiveness of the cGP(2)-method. All the computations are performed by using a computer code written in MATLAB ™. Tables 2–4 show that the cGP(2)-method solutions for the model are very close to the RK4-method solutions and found a small differences between the values. In Figure 1a–1c, we observed that the results for $T(t), I(t), V(t)$ are overlapping over each other. Finally, we have computed the absolute error between the results of both method. From the comparison, we conclude that the proposed scheme is effective, reliable and shows better performance for obtaining the approximate solution of real world problems.

Table 2: Difference between the results of cGP(2) and RK4 method for *T(t)*.

t_i	cGP(2)-Method	RK4-Method	$\| cGP(2) - RK4 \|$
0.0	50.000000000000000	50.000000000000000	0.000000000000000E-000
0.1	49.630067343055948	49.630067342311833	0.074411588002476E-008
0.2	49.279971528595631	49.279971527134457	0.146117429267179E-008
0.3	48.949272098558801	48.949272096408222	0.215057838204302E-008
0.4	48.637537080231205	48.637537077419310	0.281189471706966E-008
0.5	48.344343055338200	48.344343051893397	0.344480355352061E-008
0.6	48.069275203421036	48.069275199371901	0.404913436113929E-008
0.7	47.811927321677778	47.811927317052927	0.462485161278892E-008
0.8	47.571901823335374	47.571901818163383	0.517199083560627E-008
0.9	47.348809716505215	47.348809710814507	0.569070834899321E-008
1.0	47.142270565361706	47.142270559180453	0.618125284290727E-008

Table 3: Difference between the results of cGP(2) and RK4 method for *I(t)*.

t_i	cGP(2)-Method	RK4-Method	$\| cGP(2) - RK4 \|$
0.0	50.000000000000000	50.000000000000000	0.000000000000000E-000
0.1	49.290735743520315	49.290735743216572	0.030374280868273E-008
0.2	48.583273721133715	48.583273720557500	0.057621463156465E-008
0.3	47.878091707318433	47.878091706499710	0.081872286727958E-008
0.4	47.175643347543620	47.175643346511052	0.103256780903394E-008
0.5	46.476358601841703	46.476358600622675	0.121902843375210E-008
0.6	45.780644221620769	45.780644220241363	0.137940503464051E-008
0.7	45.088884255636934	45.088884254121943	0.151499079947826E-008
0.8	44.401440581267330	44.401440579640287	0.162704338890762E-008
0.9	43.718653457443814	43.718653455726994	0.171682046357091E-008
1.0	43.040842095825035	43.040842094039476	0.178555836782834E-008

Table 4: Difference between the results of cGP(2) and RK4 method for *V(t)*.

t_i	cGP(2)-Method	RK4-Method	$\| cGP(2) - RK4 \|$
0.0	2.000000000000000	2.000000000000000	0.000000000000000E-000
0.1	2.987914157758028	2.987914158513685	0.075565731449956E-008
0.2	3.959700546934367	3.959700548415517	0.148115031350926E-008
0.3	4.915432214578426	4.915432216754915	0.217648832290251E-008
0.4	5.855191365894124	5.855191368735907	0.284178369724941E-008
0.5	6.779068868217863	6.779068871695105	0.347724249394332E-008
0.6	7.687163765189299	7.687163769272456	0.408315781186275E-008
0.7	8.579582801717525	8.579582806377427	0.465990268594396E-008
0.8	9.456439960264792	9.456439965472715	0.520792298175365E-008
0.9	10.317856008893918	10.317856014621645	0.572772762552631E-008
1.0	11.163958061454098	11.163958067673986	0.621988860416423E-008

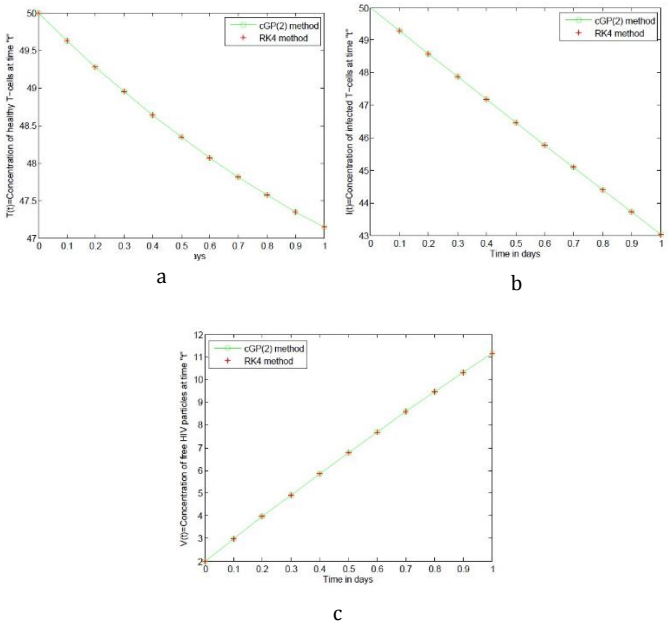


Figure 1: Graphical comparison between the solutions of cGP(2)-method and RK4-method for $T(t), I(t)$ and $V(t)$

3. Numerical Simulations and Discussions

In this section, we apply the cGP(2)-method for HIV model (4)–(6) and find out the numerical solutions of the extended HIV model. The initial values of the dependent variables, different parameter values and their explanations are given in Table 1. In order to see the effects of some parameters, we vary some of the parameters values and keep all other parameters values fixed. Figure 2a–2c represents the outputs for different values of 'μ_T'. The Figure 2a depicts that when the death rate of healthy T-cells 'μ_T' increases, the capability of healthy T-cells to fight against viruses reduces which causes the progression of AIDS. As a result, viruses make more copies during the initial stage. We also observe that during initial 100 days approximately, the concentration of healthy T-cells increases but after one week approximately, due to the death of healthy T-cells, the concentration of healthy T-cells decreases again and touches the lowest level which signify that healthy T-cells are attacked by viruses.

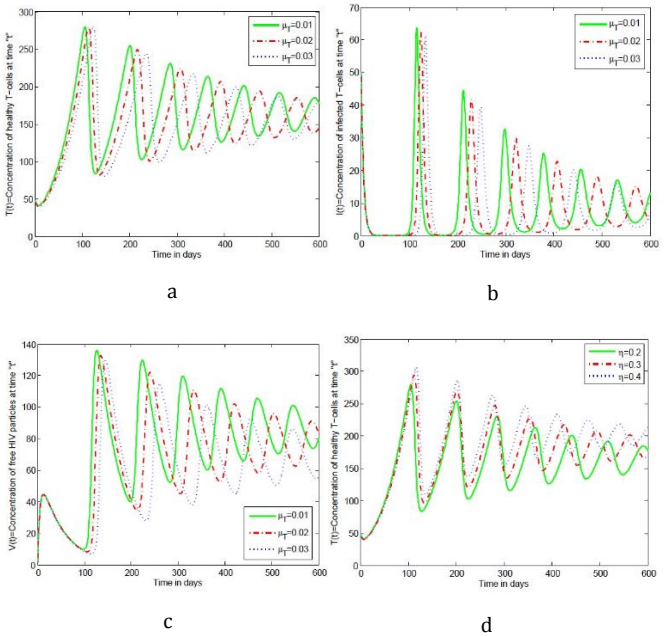
The production rate of healthy T-cells starts to oscillate by increasing the rate of 'μ_T'. The oscillation in the concentration of healthy T-cells shows the fight between the immune cells and viruses and gradually, their level declines. Similarly, from the observation of Figure 2b, due to the death of healthy T-cells, the production rate of infected T-cells reaches to top level at the beginning, but after some weeks, it comes on bottom level due to the healthy T-cells response. Death of healthy T-cells causes the replication of viruses and after 100 days approximately, the infected T-cells increases. During some days, its wavelength starts decreasing with time and touches the lowest level and the production of infected T-cells starts to oscillate. Figure 2c represents the concentration of free HIV virus particles which indicates a very clear impact of 'μ_T'. HIV viruses gain command from the infected T-cells, so their number would be high.

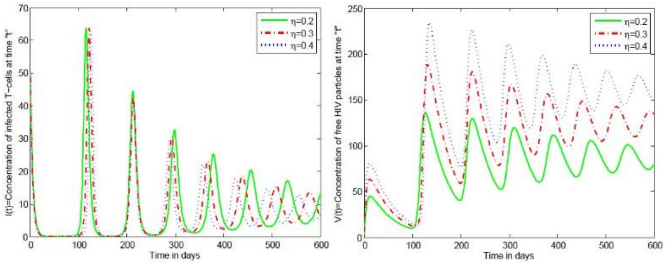
As immune cells going to be decreased with the passage of time, so the quantity of free viruses rises. Therefore, the number of free viruses and infected T-cells increases while the concentration of healthy T-cells become smaller by increasing 'μ_T'. The viruses attack on immune cells and convert the healthy T-cells into infected T-cells. Human body has the ability to recognize these viruses and fight off against. CD8 $^+$ T-cells are responsible to fight against HIV viruses. To study the functions of CD8 $^+$ T-cells, we numerically integrate 'η' which represents the rate at which CD8 $^+$ T-cells reproduce. These cells are responsible to detect the viruses and fight off against. Figure 2d–2f illustrates typical solutions for different values of 'η'. Figure 2d–2f demonstrates that if the potential of CD8 $^+$ T-cells increases, it causes the increment in immunity response of healthy T-cells and growth rate of healthy T-cells.

Initially the total number of healthy T-cells increases. Meanwhile, viruses continue to attack on immune cells. For this reason, after 150 days approximately, the T-cells count decreases with time and touches the lowest level and at the same time, due to the production of healthy T-cells, immunity level rises which kills the infected T-cells. As a result of the reduction of infected T-cells, number of CD8 $^+$ T-cells again increases and this starts to oscillate. These results depict that high production rate of T-cells is possible due increment in CD8 $^+$ T-cells and to reduce the virus concentration. If the long-term changes in the CD8 $^+$ T-cells response is sufficiently small, then the CD8 $^+$ T-cells response cannot be responsible for the reduction in virus load. Biologically, it suggests that the proliferation of CD8 $^+$ T-cells increases the possibility of the reduction of HIV infection. Figure 3a–3c depicts the behavior of $T(t)$, $I(t)$ and $V(t)$ for different values of 'β' which represents the Killing rate of virus producing T-cells.

We observed from the Figure 3a–3b that if the death rate of infected T-cells increases then the viral load decreases due to the increment in the level of antibodies against HIV. Due to the death of infected T-cells, the number of viruses decay and the healthy T-cells population increases. We also observe that the early peak in $V(t)$ corresponds to primary infection. Primary infection is followed by a long period during which the viral load changes little. Ultimately, the viral load increases and goes to the top level which is the sign of full blown AIDS appear. But due to the death of infected T-cells, its level reduces and comes to the lowest position after 100 days approximately. This oscillation continues and free viruses decreases gradually. This observation suggests that high level of 'β' would reduce the infection and decreases the production of free viruses. This may be a signal to therapists that they should find such a medicine which lower the viral production and these drugs may aid in suppressing the disease.

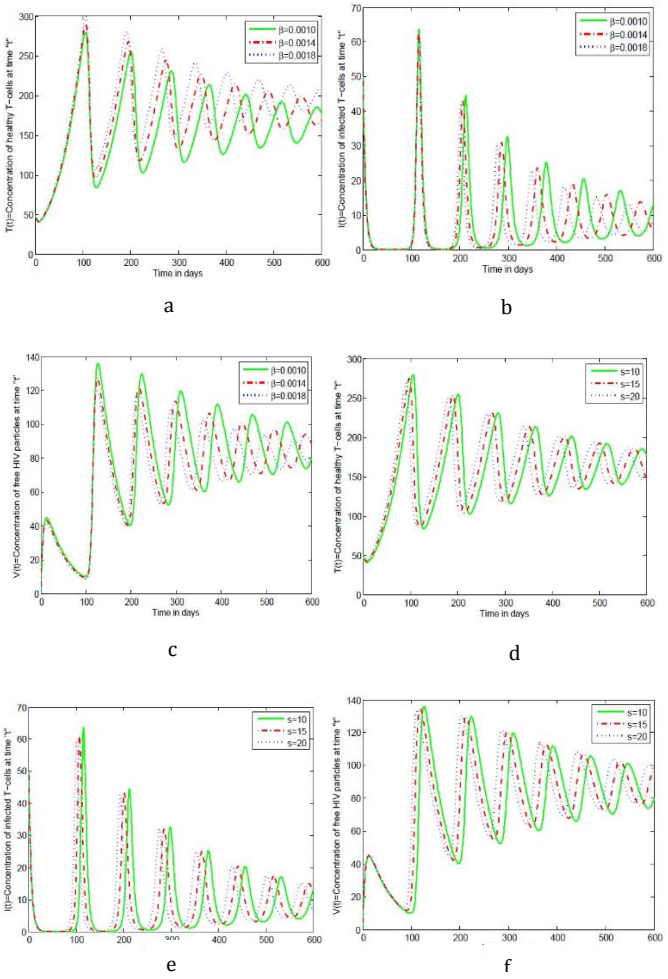
Now, we illustrate the typical solutions of *T(t)*, *I(t)* and *V(t)* for different values of '*s*' in Figure 3e–2f, where '*s*' denotes the rate of generation of new healthy T-cells from thymus. These results (Figure 2e–2f) depicts that large value of '*s*' has a role to block the evolution of the virus in the body and maintain balance between the virus and the defense system of human's body. It could be seen that the viral load decreases during initial 100 days approximately and the healthy T-cells population raises. The biological implications of these results are that for large value of 's', the infection around a disease remains relatively high but after some period viral load goes to low level. In this case, there is a higher healthy T-cells concentration and a lower viral load. However, for small values of '*s*', infection converges to the chronic disease steady state and the virus persist. It means that human body can lower the infection due to the increment in the supply of healthy T-cells.





e f

Figure 2: Numerical simulations of the model variables *T(t)*, *I(t)* and *V(t)* for different values of 'μ_T' and 'η'.



a b

c d

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Figure 3: Graphical representation of *T(t)*, *I(t)* and *V(t)* for different values of 'μ_I' and 's'.

4. Conclusion

In this manuscript, we have studied the two forms of HIV infection model. In first form, growth of healthy T-cells is considered while source term for the generation of new healthy T-cells from thymus is taken constant. In the 2nd form, we modified the model by considering the growth of both healthy T-cells and infected T-cells briefly full logistic proliferation of T-cells and the source of healthy T-cells as a decreasing function depending on the concentration of free viruses briefly variable source term. We have applied the cGP(2)-method to solve the ordinary differential equations of both these models of HIV and studied the impact of different parameters involved in the model on the population dynamics of healthy T-cells, infected T-cells and free viruses.

We have varied the values of different clinical parameters and observed their behavior e.g., the concentration of healthy T-cells increases while the population of infected T-cells and free virus are decreases with an increase in the death rate of healthy T-cells μ_T, and the oscillation of dynamical change in concentration becoming more gradual. Reproduction number η has $CD8^+$ T-cells has increasing effect on the population dynamics of healthy and infected T-cells while decreasing effect on the population dynamics of free Virus particles. The concentration of infected T-cells and virus decreases and the concentration of healthy T-cells increases with the increase in the killing rate of virus β. We observed a slightly change in the concentration of healthy/infected T-cells and virus by increasing the rate of generation of healthy T-cells.

Biologically, it implies that some parameter values can cause the cell and virus population to fluctuate. In general, these process can be helpful to clinicians, as a range for possible parameter values can be suggested. Moreover, we have solved the HIV model with variable source term and full logistic proliferation term by using RK4-method and compared the Numerical results obtained by both methods. We computed the absolute errors between the results of healthy T-cells, infected T-cells and free HIV virus. Comparison clearly expose that the cGP(2)-method and RK4-method provides the results of the model in a reasonably good agreement with each other. We concluded that the proposed method is effective and reliable for obtaining the numerical solution of the real world problems.

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