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On the numerical solution of the model for HIV infection of CD4$^+$ T cells

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ABSTRACT

In this article, a variational iteration method (VIM) is performed to give approximate and analytical solutions of nonlinear ordinary differential equation systems such as a model for HIV infection of CD4$^+$ T cells. A modified VIM (MVIM), based on the use of Padé approximants is proposed. Some plots are presented to show the reliability and simplicity of the methods.

1. Introduction

Dynamics of a model for HIV infection of CD4$^+$ T cells is examined [1] at the study. The components of the basic three-component model are the concentration of susceptible CD4$^+$ T cells, CD4$^+$ T cells infected by the HIV viruses and free HIV virus particles in the blood are denoted, respectively, by $T(t)$, $I(t)$ and $V(t)$. CD4$^+$ T cells are also named as leukocytes or T helper cells. These with order cells in human immunity systems fight against diseases. HIV use cells in order to propagate. The number of CD4$^+$ T cells in a healthy person is $\frac{800}{1200}$ mm^3. These quantities satisfy

$$\begin{aligned}
\frac{\mathrm{d}T}{\mathrm{d}t} &= q - \alpha T + \gamma T\left(1 - \frac{T+1}{T_{max}}\right) - kVT \\
\frac{\mathrm{d}I}{\mathrm{d}t} &= kVT - \beta I \\
\frac{\mathrm{d}V}{\mathrm{d}t} &= N\beta I - \gamma V
\end{aligned} \tag{1}$$

with the initial conditions: $T(0) = r_1, I(0) = r_2$ and $V(0) = r_3$. Throughout this paper, we set $q = 0.1, \alpha = 0.02, \beta = 0.3, r = 3, \gamma = 2.4, k = 0.0027, N = 10, T_{max} = 1500$. The logistic growth of the healthy CD4$^+$ T cells is now described by $(1 - \frac{T+I}{T_{max}})$, and proliferation of infected CD4$^+$ T cells is neglected. The term KVT describes the incidence of HIV infection of healthy CD4$^+$ T cells, where $k > 0$ is the infection rate. Each infected CD4$^+$ T cell is assumed to produce N virus particles during its lifetime, including any of its daughter cells. The body is believed to produce CD4$^+$ T cells from precursors in the bone marrow and thymus at a constant rate q. When stimulated by antigen or mitogen, T cells multiply through mitosis with a rate r. T_{max} is the maximum level of CD4$^+$ T cell concentration in the body [2–5].

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The motivation of this paper is to extend the application of the analytic variational iteration method [6–9] to solve a model for HIV infection of $CD4^{+}$ T cells (1). The variational iteration method (VIM) was first proposed by the Chinese mathematician He [8]. The first connection between series solution methods such as an Adomian decomposition method and Padé approximants was established in [10]. The transmission and dynamics of HTLV-I feature several biological characteristics that are of interest to epidemiologists, mathematicians, and biologists; see, for example [11–14], etc. Like HIV, HTLV-I targets $CD4^{+}$ T cells, the most abundant white cells in the immune system, decreasing the body's ability to fight infection. Several approximate analytical methods have proposed to solve this system. Some commonly used techniques are the homotopy perturbation method [15–17] and the Adomian decomposition method [18]. We will use Laplace transform and Padé approximant to deal with the truncated series.

2. Padé approximation

A rational approximation to $f(x)$ on $[a, b]$ is the quotient of two polynomials $P_N(x)$ and $Q_M(x)$ of degrees N and M, respectively. We use the notation $R_{N,M}(x)$ to denote this quotient. The $R_{N,M}(x)$ Padé approximations to a function $f(x)$ are given by [10]

$$R_{N,M}(x) = \frac{P_N(x)}{Q_M(x)} \quad \text{for } a \le x \le b. \tag{2}$$

The method of Padé requires that $f(x)$ and its derivative be continuous at $x = 0$. The polynomials used in (2) are

$$P_N(x) = p_o + p_1 x + p_2 x^2 + \cdots + p_N(x) \tag{3}$$

$$Q_M(x) = q_o + q_1 x + q_2 x^2 + \cdots + q_M(x). \tag{4}$$

The polynomials in (2) and (3) are constructed so that $f(x)$ and $R_{N,M}(x)$ agree at $x = 0$ and their derivatives up to $N + M$ agree at $x = 0$. In the case $Q_0(x) = 1$, the approximation is just the Maclaurin expansion for $f(x)$. For a fixed value of $N + M$ the error is smallest when $P_N(x)$ and $Q_M(x)$ have the same degree or when $P_N(x)$ has degree one higher than $Q_M(x)$.

Notice that the constant coefficient of Q_M is $q_0 - 1$. This is permissible, because it can be noted that 0 and $R_{N,M}(x)$ are not changed when both $P_N(x)$ and $Q_M(x)$ are divided by the same constant. Hence the rational function $R_{N,M}(x)$ has $N + M + 1$ unknown coefficients. Assume that $f(x)$ is analytic and has the Maclaurin expansion

$$f(x) = a_0 + a_1 x + a_2 x^2 + \cdots + a_k x^k + \cdots. \tag{5}$$

And from the difference $f(x)Q_M(x) - P_N(x) = Z(x)$:

$$\left[\sum_{i=0}^{\infty} a_i x^i\right]\left[\sum_{i=0}^{M} q_i x^i\right] - \left[\sum_{i=0}^{N} p_i x^i\right] = \left[\sum_{i=N+M+1}^{\infty} c_i x^i\right]. \tag{6}$$

The lower index $j = N + M + 1$ in the summation on the right side of (6) is chosen because the first $N + M$ derivatives of $f(x)$ and $R_{N,M}(x)$ should agree at $x = 0$.

When the left side of (6) is multiplied out and the coefficients of the powers of x^i are set equal to zero for $k = 0, 1, 2, \ldots, N + M$, the result is a system of $N + M + 1$ linear equations:

$$\begin{aligned} &a_0 - p_0 = 0 \\ &q_1 a_0 + a_1 - p_1 = 0 \\ &q_2 a_0 + q_1 a_1 + a_2 - p_2 = 0 \\ &q_3 a_0 + q_2 a_1 + q_1 a_2 + a_2 - p_3 = 0 \\ &q_M a_{N-M} \mid q_{M-1} a_{N-M-1} \mid a_N - p_N = 0 \end{aligned} \tag{7}$$

and

$$\begin{aligned} &q_M a_{N-M+1} + q_{M-1} a_{N-M+2} + \cdots + q_1 a_N + a_{N+2} = 0 \\ &q_M a_{N-M+2} + q_{M-1} a_{N-M+3} + \cdots + q_1 a_{N+1} + a_{N+3} = 0 \\ &\vdots \\ &q_M a_N + q_{M-1} a_{N+1} + \cdots + q_1 a_{N+M+1} + a_{N+M} = 0. \end{aligned} \tag{8}$$

Notice that in each equation the sum of the subscripts on the factors of each product is the same, and this sum increases consecutively from 0 to $N + M$. The M equations in (8) involve only the unknowns $q_1, q_2, \ldots, q_M$ and must be solved first. Then the equations in (7) are used successively to find $p_1, p_2, \ldots, p_N$ [10].

3. Variational iteration method

According to the variational iteration method [4], we consider the following differential equation:

$$Lu + N(u) = g(t) \tag{9}$$

where L is a linear operator, N is a nonlinear operator, and $g(t)$ is an inhomogeneous term. Then, we can construct a correct functional as follows:

$$u_{n+1}(t) = u_n(t) + \int_0^t \lambda\{Lu_n(s) + N\tilde{u}_n(s) - g(s)\}\mathrm{d}s \tag{10}$$

where λ is a general Lagrangian multiplier [2–5], which can be identified optimally via variational theory. The second term on the right is called the correction and $\tilde{u}_n$ is considered as a restricted variation, i.e., $\delta\tilde{u}_n = 0$.

4. Applications

In this section, we will apply the variational iteration method to nonlinear ordinary differential systems (1).

According to the variational iteration method, we derive a correct functional as follows:

$$\begin{aligned}
T_{n+1}(t) &= T_n(t) + \int_0^t \lambda\left\{T_n'(\xi) - q + \alpha\tilde{T}_n - r\tilde{T}_n\left(1 - \frac{\tilde{T}_n + \tilde{I}_n}{T_{max}}\right) + k\tilde{T}_n\tilde{V}_n\right\}\mathrm{d}\xi \\
I_{n+1}(t) &= T_n(t) + \int_0^t \lambda\{I_n'(\xi) - k\tilde{T}_n\tilde{V}_n + \beta\tilde{I}_n\}\mathrm{d}\xi \\
V_{n+1}(t) &= V_n(t) + \int_0^t \lambda\{V_n'(\xi) - N\beta\tilde{I}_n + \gamma\tilde{V}_n\}\mathrm{d}\xi
\end{aligned} \tag{11}$$

where λ_1, λ_2 and λ_3 are general Lagrange multipliers, $\tilde{T}_n(\xi), \tilde{I}_n(\xi)$ and $\tilde{V}_n(\xi)$ denote restricted variations, i.e. $\delta\tilde{T}_n(\xi) = \delta\tilde{I}_n(\xi) = \delta\tilde{V}_n(\xi) = 0$.

Making the above correction functional stationary, we can obtain following stationary conditions:

$$\begin{aligned}
&\lambda_1'(\xi) = 0, \\
&1 + \lambda_1(\xi)\,|_{\xi=t} = 0, \\
&\lambda_2'(\xi) = 0, \\
&1 + \lambda_2(\xi)\,|_{\xi=t} = 0, \\
&\lambda_3'(\xi) = 0, \\
&1 + \lambda_3(\xi)\,|_{\xi=t} = 0.
\end{aligned} \tag{12}$$

The Lagrange multipliers, therefore, can be identified as

$$\lambda_1 = \lambda_2 = \lambda_3 = -1. \tag{13}$$

Substituting Eq. (13) into the correction functional equation (11) results in the following iteration formula:

$$\begin{aligned}
T_{n+1}(t) &= T_n(t) - \int_0^t \left\{T_n'(\xi) - q + \alpha\tilde{T}_n - r\tilde{T}_n\left(1 - \frac{\tilde{T}_n + \tilde{I}_n}{T_{max}}\right) + k\tilde{T}_n\tilde{V}_n\right\}\mathrm{d}\xi \\
I_{n+1}(t) &= I_n(t) - \int_0^t \{I_n'(\xi) - k\tilde{T}_n\tilde{V}_n + \beta\tilde{I}_n\}\mathrm{d}\xi \\
V_{n+1}(t) &= V_n(t) \int_0^t \{V_n'(\xi) - N\beta\tilde{I}_n + \gamma\tilde{V}_n\}\mathrm{d}\xi.
\end{aligned} \tag{14}$$

We start with initial approximations $T_0(t) = N_1, I_0(t) = N_2, V_0(t) = N_3$. By the above iteration formula, we can obtain a few first terms being calculated:

$$\begin{aligned}
T_1(t) &= N_1 \\
I_1(t) &= N_2 \\
V_1(t) &= N_3
\end{aligned} \tag{15}$$

$$\begin{aligned}
T_2(t) &= N_1 \\
I_2(t) &= N_2 \\
V_2(t) &= N_3 \\
&\vdots
\end{aligned} \tag{16}$$

Continuing in this manner, we can find the rest of components. The first n terms approximation to the solutions are considered

$$\begin{aligned} T(t) &\approx T_n \\ I(t) &\approx I_n \\ V(t) &\approx V_n. \end{aligned} \tag{17}$$

This was done with the standard parameter values given above and initial values $N_1 = 0.05$, $N_2 = 0.1$, $N_3 = 0.5$ for the three-component model.

A few first approximations for $T(t)$, $I(t)$ and $V(t)$ are calculated and presented below:

$$T(t) \approx T_n \tag{18}$$
$$I(t) \approx I_n$$
$$V(t) \approx V_n$$

$$T_1(t) = 0.1 + 0.397953t \tag{19}$$
$$I_1(t) = 0.27e^{-4}t$$
$$V(t) = 0.1 - 0.24t$$

$$T_2(t) = 0.1 + 0.397953t + 0.592849053t^2 - 0.1962704196e^{-4}t^2 \tag{20}$$
$$I_2(t) = 0.27e^{-4}t + 0.17273655e^{-4}t^2 - 0.85957848e^{-4}t^3$$
$$V_2(t) = 0.1 - 0.24t + 0.2880405t^2$$

$$\begin{aligned} T_3(t) \;=\; & 0.1 + 0.397953t + 0.592849053t^2 - 0.1962704196e^{-4}t^3 - 0.2318834562e^{-3}t^4 \\ & - 0.2327875585e^{-3}t^5 + 0.2728806044e^{-7}t^6 - 0.5920911616e^{-12}t^7 \end{aligned} \tag{21}$$
$$\begin{aligned} I_3(t) \;=\; & 0.27e^{-4}t + 0.17273655e^{-4}t^2 - 0.85957848e^{-4}t^3 - 0.1222309057e^{-4}t^4 \\ & + 0.9221539400e^{-4}t^5 - 0.2544022341e^{-5}t^6 \end{aligned}$$
$$V_3(t) = 0.1 - 0.24t + 0.2880405t^2 - 0.2304151263t^3 - 0.6446838600e^{-4}t^4$$

$$\begin{aligned} T_4(t) \;=\; & 0.1 + 0.397953t + 0.592849053t^2 - 0.1962704196e^{-4}t^3 - 0.2318834562e^{-3}t^4 \\ & - 0.2327875585e^{-3}t^5 + 0.2728806044e^{-7}t^6 - 0.5920911616e^{-12}t^7 \\ & + 0.4674292582e^{-28}t^{15} + 0.4401106523e^{-23}t^{14} - 0.1378891999e^{-18}t^{13} \\ & + 0.1599285430e^{-14}t^{12} - 0.5946938932e^{-11}t^{11} - 0.2636484877e^{-10}t^{10} \\ & + 0.3272726240e^{-7}t^9 + 0.1427969646e^{-6}t^8 \end{aligned} \tag{22}$$
$$\begin{aligned} I_4(t) \;=\; & 0.27e^{-4}t + 0.17273655e^{-4}t^2 - 0.85957848e^{-4}t^3 - 0.1222309057e^{-4}t^4 \\ & + 0.9221539400e^{-4}t^5 - 0.2544022341e^{-8}t^6 + 0.8588511349e^{-20}t^{12} \\ & - 0.3983212932e^{-15}t^{11} + 0.2354315149e^{-11}t^{10} + 0.1609817522e^{-7}t^9 \\ & - 0.1740929189e^{-7}t^8 - 0.5234087602e^{-4}t^7 \end{aligned}$$
$$\begin{aligned} V_4(t) \;=\; & 0.1 - 0.24t + 0.2880405t^2 - 0.2304151263t^3 - 0.6446838600e^{-4}t^4 \\ & - 0.1090295289e^{-8}t^7 + 0.4610769700e^{-4}t^6 + 0.2361097094e^{-4}t^5. \end{aligned}$$

For large t, VIM is not a good result to approximate solutions of some differential equations of this system. To guarantee the validity of approximation solution for large t, the series solutions are obtained from VIM applied Pade approximation and Laplace transformation. This approach is called the modified variational iteration method (MVIM).

First, Laplace transformation is applied to the series solutions in (22) and then $\frac{1}{t}$ is written in place of s in the equation obtained. Then, Padé approximant [3/3] is applied and $\frac{1}{s}$ is written in place of t. Finally, by using the inverse Laplace transformation, we obtain the modified approximate solution

$$\begin{aligned} T(t) &= -0.3352759138e^{-1}e^{-0.9307708506e-3t} + 0.1335507819e^{2.980494283t} - 0.2319051141e - 4e^{5.413786559t}, \\ I(t) &= 0.4346123862e^{-5}e^{-2.395968046t} - 0.448969638e^{-4}e^{-0.3062539727t} + .4055084553e^{-4}e^{0.5835463689t}, \\ V(t) &= 0.9999780863e^{-1}e^{-2.400133231t} + 0.21913700e^{-5}e^{3.679664095t}. \end{aligned} \tag{23}$$

These results obtained by VIM, MVIM and the fourth-order Runge–Kutta method for $T(t)$, $I(t)$ and $V(t)$ are presented below. In Fig. 1, the local changes of $T(t)$, $I(t)$ and $V(t)$ variables are given. It is observed that, $T(t)$, the concentration of susceptible $CD4^+$ T cells increases speedily, $I(t)$, the number of $CD4^+$ T cells infected by the HIV viruses increases quite slowly and $V(t)$, the number of free HIV virus particles in the blood decreases in a very short time after the onset of infection.

In Fig. 2, $T - I$, $T - V$, $I - V$ and $T - I - V$ phase portraits obtained using 5-term MVIM solutions are given.

In Tables 1–3, the results of LADM–Pade [18], VIM, MVIM and the fourth-order Runge–Kutta method are shown. The results obtained from LADM–Pade and VIM slightly diverge from those for the fourth-order Runge–Kutta, but the results obtained from MVIM are in good agreement.

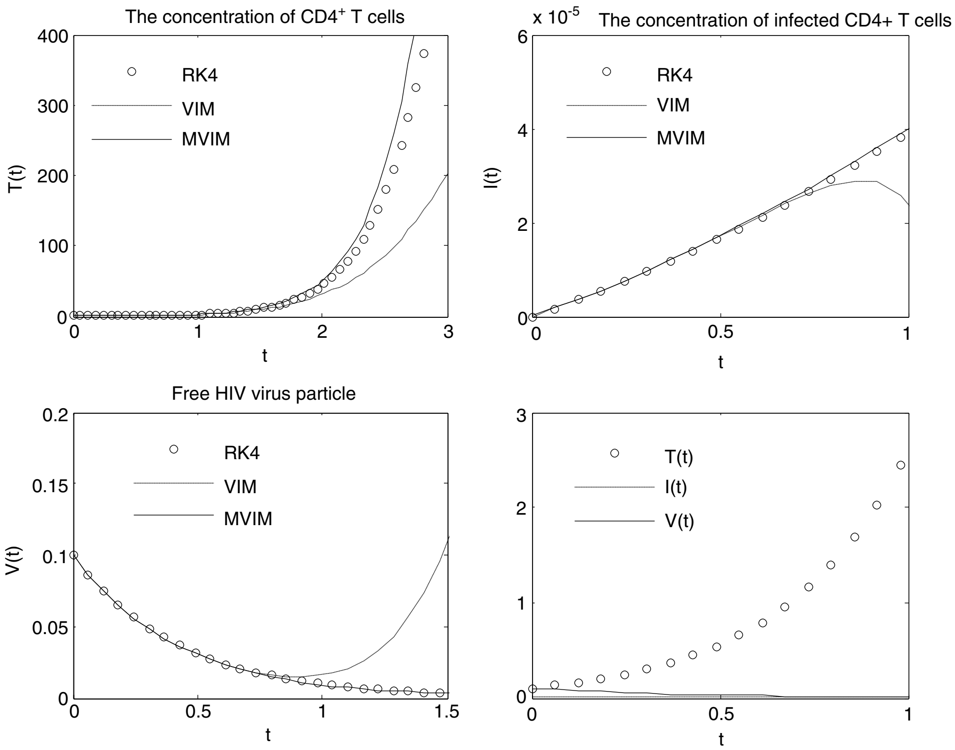

Fig. 1. Plots of approximations obtained from RK4, VIM and MVIM for a model for HIV infection of $CD4^+$ T cells.

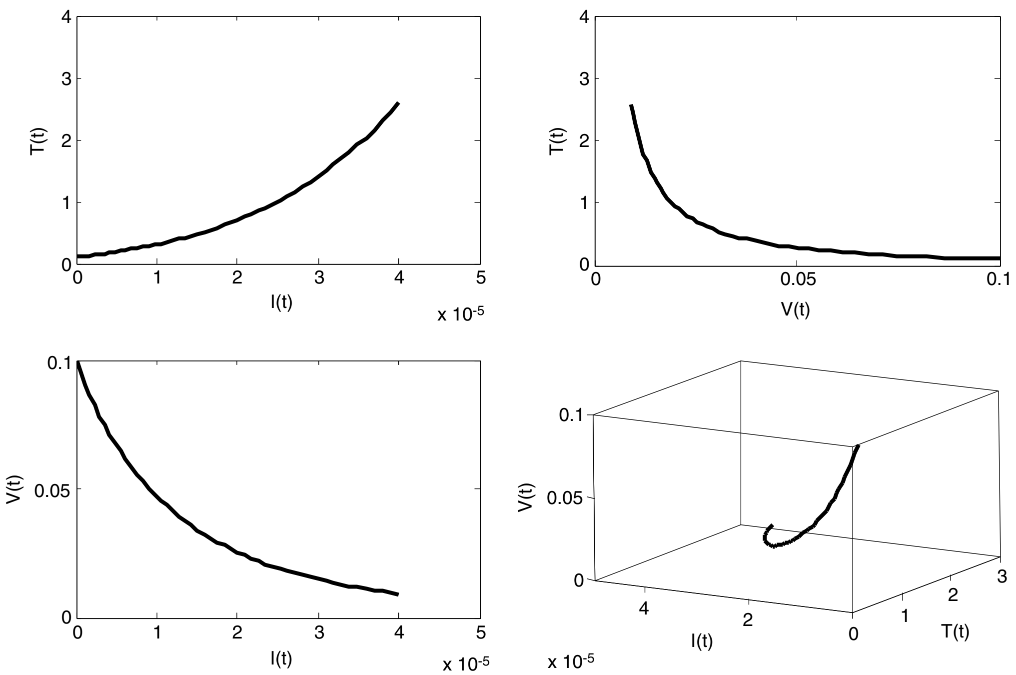

Fig. 2. Phase portraits using 5-term MVIM.

5. Conclusions

In this paper, variational iteration method was used for finding approximate analytical solutions of nonlinear ordinary differential equation systems such as a model for HIV infection of $CD4^+T$ cells. We demonstrated the accuracy and efficiency

Table 1
Numerical comparison for $T(t)$.

t	LADM–Pade [18]	VIM	MVIM	Runge–Kutta
0	0.1	0.1	0.1000000000	0.1
0.2	0.2088072731	0.2088073214	0.2088080868	0.2088080833
0.4	0.4061052625	0.4061346587	0.4062407949	0.4062405393
0.6	0.7611467713	0.7624530350	0.7644287245	0.7644238890
0.8	1.3773198590	1.3978805880	1.4140941730	1.4140468310
1.0	2.3291697610	2.5067466690	2.5919210760	2.5915948020

Table 2
Numerical comparison for $I(t)$.

t	LADM–Pade [18]	VIM	MVIM	Runge–Kutta
0	0.0	0	0.1e−13	0
0.2	0.603270728e−5	0.60326343661e−5	0.60327016510e−5	0.6032702150e−5
0.4	0.131591617e−4	0.1314878543e−4	0.13158301670e−4	0.1315834073e−4
0.6	0.212683688e−4	0.2101417193e−4	0.21223310013e−4	0.2122378506e−4
0.8	0.300691867e−4	0.2795130456e−4	0.30174509323e−4	0.3017741955e−4
1.0	0.398736542e−4	0.2431562317e−4	0.40025404050e−4	0.4003781468e−4

Table 3
Numerical comparison for $V(t)$.

t	LADM–Pade [18]	VIM	MVIM	Runge–Kutta
0	0.1	0.1	0.1000000000	0.1
0.2	0.06187996025	0.06187995314	0.06187990876	0.06187984331
0.4	0.03831324883	0.03830820126	0.03829595768	0.03829488788
0.6	0.02439174349	0.02392029257	0.02371029480	0.02370455014
0.8	0.009967218934	0.01621704553	0.01470041902	0.01468036377
1.0	0.003305076447	0.01608418711	0.009157238735	0.009100845043

of these methods by solving some ordinary differential equation systems. This method solves the problem without any need for discretization of the variables. We use Laplace transformation and Padé approximant to obtain an analytic solution and to improve the accuracy of variational iteration method. The obtained solutions from The VIM, MVIM and RK4 are shown graphically.

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