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A Multistage Homotopy Perturbation Method for Solving Human T-Cell Lymphotropic Virus I(HTLV-I) Infection of CD4⁺ T-Cells Model

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Abstract: In this article, a multistage homotopy perturbation method is implemented to give approximate and analytical solutions of nonlinear ordinary differential equation systems such as human T-cell lymphotropic virus I (HTLV-I) infection of $CD4^+$ T-cells model. Numerical results are compared to those obtained by the fourth-order Runge-Kutta method. Some plots and tables are presented to show the reliability and simplicity of the method.

Key words: Homotopy perturbation method · Human T-cell lymphotropic virus I (HTLV-I) infection of $CD4^+$ T-cells model · Nonlinear systems

INTRODUCTION

Dynamics of human T-cell lymphotropic virus I (HTLV-I) infection of $CD4^+$ T-cells is examined [1-6] at the study. The components of the basic four-component model are the concentration of healthy $CD4^+$ T-cells at time t, the concentration of latently infected $CD4^+$ T-cells, the concentration of actively infected $CD4^+$ T-cells and the concentration of leukemic cells at time t are denoted respectively by $T(t)$, $T_L(t)$, $T_A(t)$ and $T_M(t)$. These quantities satisfy.

$$\begin{aligned}
\frac{dT}{dt} &= \lambda - \mu_T T - \kappa T_A T \\
\frac{dT_L}{dt} &= \kappa_1 T_A T - (\mu_L + \alpha) T_L \\
\frac{dT_A}{dt} &= \alpha T_L - (\mu_A + \rho) T_A \\
\frac{dT_M}{dt} &= \rho T_A + \beta T_M (1 - T_M / T_{max}) - \mu_M T_M
\end{aligned} \tag{1}$$

With the initial conditions:

$$T(0) = P_1, T_L(0) = P_2, T_A(0) = P_3, T_M(0) = P_4 \tag{2}$$

Where T, T_L, T_A and T_M denote the numbers of uninfected, latent infected, actively infected $CD4^+$ cells, the number of leukemia cells, respectively. The parameters λ, μ_T, κ and κ_1 are the source of $CD4^+$ T-cells from precursors, the natural death rate of $CD4^+$ T-cells, the rate at which uninfected cells are contacted by actively infected cells, the rate of infection of T-cells with virus from actively infected cells, respectively. μ_L, μ_A and μ_M are blanket death terms for latently infected, actively infected and leukemic cells. Additionaly, α and ρ represent the rates at which latently infected and actively infected cells become actively infected and leukemic, respectively. The rate β determines the speed at which the saturation level for leukemia cells is reached. T_{max} is the maximal value that adult T-cell leukemia can reach. The main purpose of this paper is to extend the application of the multi-step homotopy perturbation method, a reliable algorithm based on an adaptation of the standard homotopy perturbation method [7-16], developed in [17-20] to obtain numerical solution of Eqs. (1) subject to the initial conditions (2). Throughout this paper, we set μ_T = 0.66(mm^3 / day) μ_L = 0.06(day), μ_A = 0.05(day), μ_M = 0.005(day), k = 0.5, α = 0.004(day), β = 0.0003(day), ρ = 0.00004 (day), T_{max} = 2200(mm^3). The paper is organized as follows: A brief review of HPM and MsHPM are given in Section 2 and 3, respectively. The application of the proposed numerical scheme to model (1) is illustrated in Section 4. The conclusions are then given in the final Section 5.

Homotopy Perturbation Method: To illustrate the homotopy perturbation method (HPM) for solving non-linear differential equations, He [7, 8] considered the following non-linear differential equation:

$$A(u) = f(r), \; r \in \Omega \tag{3}$$

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Subject to the boundary condition

$$B\left(u,\frac{\partial u}{\partial n}\right)=0, r\in G \quad (4)$$

Where A is a general differential operator, B is a boundary operator, $f(r)$ is a known analytic function, Γ is the boundary of the domain Ω and $\frac{\partial}{\partial n}$ denotes differentiation along the normal vector drawn outwards from Ω. The operator A can generally be divided into two parts M and N. Therefore, (3) can be rewritten as follows:

$$M(u) + N(u) = f(r),\ r \in \Omega \quad (5)$$

He [7, 8] constructed a homotopy $v(r,p)$: $\Omega \times [0,1] \to \mathbb{R}$ which satisfies

$$H(v,p) = (1-p)\,[M(v) - M(u_0)] + p[A(v) - f(r)] = 0 \quad (6)$$

Which is equivalent to

$$H(v,p) = M(v) - M(u_0) + pM(v_0) + p[N(v) - f(r)] = 0 \quad (7)$$

Where $p \in [0,1]$ is an embedding parameter and u_0 is an initial approximation of (3). Obviously, we have

$$H(v,0) = M(v) - M(u_0) = 0,\ H(v,1) = A(v) - f(r) = 0. \quad (8)$$

The changing process of p from zero to unity is just that of $H(v,p)$ from $M(v) - M(u_0)$ to $A(v) - f(r)$. In topology, this is called deformation and is called homotopic. According to the homotopy perturbation method, the parameter p is used as a small parameter and the solution of Eq. (6) can be expressed as a series in p in the form.

$$v = v_0 + pv_1 + p^2v_2 + p^3v_3 + \ldots \quad (9)$$

When $p \to 1$ Eq. (6) corresponds to the original one, Eqs. (7) and (8) become the approximate solution of Eq. (3), i.e.,

$$u=\lim_{p\to 1} v = v_0 + v_1 + v_2 + v_3 + \ldots \quad (10)$$

The convergence of the series in Eq. (10) is discussed by He in [7, 8].

Multistage Homotopy Perturbation Method: For large t, HPM is not good result to approximate solution of some differential equation. To guarantee validity of approximation solution for large t, the studies at [17-20], a new approach called the MSHPM is mentioned. According to this approach, the solution from $[t_0, t)$ to be reproduced by subdividing this interval into $[t_0, t)$, $[t_1,t_2),\ldots,[t_{j-1},t_j = t)$ and a recursive formula of (11) to be applied on each subinterval [17-20]:

The initial approximation in each interval is taken from the solution in the previous interval,

$$u_{i,0}(t) = u_i(t^*) = c_i^* \quad (11)$$

Where t_i^* is the left-end point of each subinterval and c_i^* is denoted as the initial approximations for $i = 1,2,\ldots,m$. By knowing the first initial conditions, one would be able to by appling the inverse linear operator for all unknowns $u_{i,n}(t),(i = 1,2,\ldots,m;\ n = 0,1,\ldots)$ as follow:

$$L^{-1}(.)=\int_{t^*}^{t}(.)\,dt. \quad (12)$$

In order to carry out the iteration in every subinterval of equal length $\Delta t, [t_0,t), [t_1,t_2),\ldots,[t_{j-1},t_j = t)$ we need to know the values of the following:

$$u_{i,0}^*(t)=u_i\left(t^*\right)=c_i^*, i=1,2,\ldots,m. \quad (13)$$

This information is typically not directly attainable, but through the initial value $t^* = t_0$, we could derive all the initial approximations. This is done by taking the previous initial approximation from the n-th-iterate of the preceding subinterval given by (13), i.e.

$$u_{i,0}^*(t)\cong u_{i,n}\left(t^*\right), i=1,2,\ldots,m \text{ and } t^*\in\left(t_0,t_1\right). \quad (14)$$

Applications

HPM Solution: In this section, we will apply the homotopy perturbation method to nonlinear ordinary differential systems (1).

According to homotopy perturbation method, we derive a correct functional as follows:

$$\begin{aligned}
&v_1' - x_0' + p\left(x_0' - \lambda + \mu_T v_1 + \kappa v_1 v_3\right) = 0,\\
&v_2' - y_0' + p\left(y_0' - \kappa_1 v_1 v_3 + (\mu_L + \alpha)v_2\right) = 0,\\
&v_3' - z_0' + p\left(z_0' - \alpha v_2 + (\mu_A + \rho)v_3\right) = 0,\\
&v_4' - r_0' + p\left(r_0' - \rho v_3 - \beta v_4(1 - \frac{v_4}{T_{max}} + \mu_M v_4\right) = 0.
\end{aligned} \quad (15)$$

The initial approximations are as follows:

$$\begin{aligned}
v_{10}(t) &= x_0(t) = T(0) = P_1,\\
v_{20}(t) &= y_0(t) = T_L(0) = P_2,\\
v_{30}(t) &= z_0(t) = T_A(0) = P_3,\\
v_{40}(t) &= r_0(t) = T_M(0) = P_4,
\end{aligned} \quad (16)$$

and

$$v_1 = \sum_{j=0}^{\infty} v_{1j} p^j,$$
$$v_2 = \sum_{j=0}^{\infty} v_{2j} p^j,$$
$$v_3 = \sum_{j=0}^{\infty} v_{3j} p^j,$$
$$v_4 = \sum_{j=0}^{\infty} v_{4j} p^j. \tag{17}$$

Where $v_{i,j}$, i,j = 1,2,3.... are functions yet to be determined. Substituting Eqs.(16) and (17) into Eq. (15) and arranging the coefficients of "p" powers, we have.

$$\begin{aligned}
&\left(v'_{1,1} - \lambda + \mu_T P_1 + kP_1P_3\right)p + \left(v'_{1,2} + \mu_T v_{1,1} + \kappa\left(P_1 v_{3,1} + P_3 v_{1,1}\right)\right)p^2 \\
&+\left(v'_{1,3} + \mu_T v_{1,2} + \kappa\left(P_1 v_{3,2} + P_3 v_{1,2} + v_{1,1}v_{3,1}\right)\right)p^3 + ... = 0, \\
&\left(v'_{2,1} - \kappa P_1P_3 + (\mu_L + \alpha)P_2\right)p + \left(v'_{2,2} - \kappa\left(P_1 v_{3,1} + P_3 v_{1,1}\right) + (\mu_L + \alpha)v_{2,1}\right)p^2 \\
&+\left(v'_{2,3} - \kappa\left(P_1 v_{3,2} + P_3 v_{1,2} + v_{1,1}v_{3,1}\right) + (\mu_L + \alpha)v_{2,2}\right)p^3 + ... = 0, \\
&\left(v'_{3,1} - \alpha P_2 + (\mu_A + \rho)P_3\right)p + \left(v'_{3,2} - \alpha v_{2,1} + (\mu_A + \rho)v_{3,1}\right)p^2 \\
&+\left(v'_{3,3} - \alpha v_{2,2} + (\mu_A + \rho)v_{3,2}\right)p^3 + ... = 0, \\
&\left(v'_{4,1} - \rho P_3 + (\mu_M - \beta)P_4 + \frac{\beta}{T_{Max}}P_4^2\right)p + \left(v'_{4,2} - \rho v_{3,1} + (\mu_M - \beta)v_{4,1} + \frac{\beta}{T_{Max}}2P_4v_{4,1}\right)p^2 \\
&+\left(v'_{4,3} - ?v_{3,2} + (\mu_M - \beta)v_{4,2} + \frac{\beta}{T_{Max}}\left(v_{4,1}^2 + 2P_4v_{4,2}\right)\right)p^3 + ... = 0.
\end{aligned} \tag{18}$$

In order to obtain the unknowns $v_{i,j}$ i,j = 1,2,3,... we must construct and solve the following system which includes nine equations with nine unknowns, considering the initial conditions $v_{i,j}(0)$ i,j = 1,2,3,...

$$\begin{aligned}
&v'_{1,1} - \lambda + \mu_T P_1 + kP_1P_3 = 0, \\
&v'_{1,2} + \mu_T v_{1,1} + k\left(P_1 v_{3,1} + P_3 v_{1,1}\right) = 0, \\
&v'_{1,3} + \mu_T v_{1,2} + k\left(P_1 v_{3,2} + P_3 v_{1,2} + v_{1,1}v_{3,1}\right) = 0, \\
&v'_{2,1} - kP_1P_3 + (\mu_L + \alpha)P_2 = 0, \\
&v'_{2,2} - k\left(P_1 v_{3,1} + P_3 v_{1,1}\right) + (\mu_L + \alpha)v_{2,1} = 0, \\
&v'_{2,3} - k\left(P_1 v_{3,2} + P_3 v_{1,2} + v_{1,1}v_{3,1}\right) + (\mu_L + \alpha)v_{2,2} = 0, \\
&v'_{3,1} - \alpha P_2 + (\mu_A + \rho)P_3 = 0, \\
&v'_{3,2} - \alpha v_{2,1} + (\mu_A + \rho)v_{3,1} = 0, \\
&v'_{3,3} - \alpha v_{2,2} + (\mu_A + \rho)v_{3,2} = 0, \\
&v'_{4,1} - \rho P_3 + (\mu_M - \beta)P_4 + P_4^2\beta/T_{max} = 0, \\
&v'_{4,2} - \rho v_{3,1} + (\mu M - \beta)v_{41} + 2P_4v_{41}\beta/T_{\max} = 0, \\
&v'_{4,3} - \rho v_{3,2} + (\mu_M - \beta)v_{4,2} + \beta/T_{\max}\left(v_{4,1}^2 + 2P_4v_{4,2}\right) = 0.
\end{aligned} \tag{19}$$

From Eq. (19), if the 3- terms approximations are sufficient, we will obtain:

$$\begin{aligned} T(t) &= \lim_{p\to 1} v_1(t) = \sum_{k=0}^{3} v_{1,k}(t), \\ T_L(t) &= \lim_{p\to 1} v_2(t) = \sum_{k=0}^{3} v_{2,k}(t), \\ T_A(t) &= \lim_{p\to 1} v_3(t) = \sum_{k=0}^{3} v_{3,k}(t), \\ T_M(t) &= \lim_{p\to 1} v_4(t) = \sum_{k=0}^{3} v_{4,k}(t). \end{aligned} \tag{20}$$

Hence the 2-term approximate series solutions of HPM are

$$T = P_1 + \lambda t - \mu_T P_1 t - \kappa P_1 P_3 t$$

$$+\frac{1}{2}\begin{pmatrix} \left(-\mu_T\left(\lambda - \mu_T P_1 - \kappa P_1 P_3\right) - \kappa\left(\lambda - \mu_T P_1 - \kappa P_1 P_3\right)\right) P_3 \\ -\kappa P_1\left(\alpha P_2 - \left(\mu_A + \rho\right) P_3\right) \end{pmatrix} t^2 + \ldots,$$

$$T_L = P_2 + \kappa P_1 P_3 t - \left(\mu_L + \alpha\right) P_2 t$$

$$+\frac{1}{2}\begin{pmatrix} \kappa\left(\lambda - \mu_T P_1 - k_2 P_1 P_3\right) P_3 + \kappa P_1\left(\alpha P_2 - \left(\mu_A + \rho\right) P_3\right) \\ -\left(\mu_L + \alpha\right)\left(\kappa P_1 P_3 - \left(\mu_L + \alpha\right) P_2\right) \end{pmatrix} t^2 + \ldots,$$

$$T_A = P_3 + \alpha P_2 t - \left(\mu_A + \rho\right) P_3 t$$

$$+\frac{1}{2}\left(\alpha\left(\kappa P_1 P_3 - \left(\mu_L + \alpha\right) P_2\right) - \left(\mu_A + \rho\right)\left(\alpha P_2 - \left(\mu_A + \rho\right) P_3\right)\right) t^2 + \ldots,$$

$$T_M = P_4 + \rho P_3 t + \beta P_4 t - \beta P_4^2 t / T_{\max} - \mu_M P_4 t$$

$$+\frac{1}{2}\begin{pmatrix} \rho\left(\alpha P_2 - \left(\mu_A + \rho\right) P_3\right) + \beta\left(\rho P_3 + \beta P_4 - \beta P_4^{\,2} / \left(T_{\max} - \mu_M P_4\right)\right) \\ -2\beta P_4 / T_{\max}\left(\rho P_3 + \beta P_4 - \beta P_4^2 / T_{\max} - \mu_M P_4\right) - \mu_M\left(\rho P_3 + \beta P_4 - \beta P_4^{\,2} / \left(T_{\max} - \mu_M P_4\right)\right) \end{pmatrix} t^2 + \ldots \tag{21}$$

MsHPM Solution: According to MsHPM, we choose the initial approximations as

$$\begin{aligned} v_{10}(t) &= x_0(t) = T\left(t^*\right) = P_1^*, \\ v_{20}(t) &= y_0(t) = T_L\left(t^*\right) = P_2^*, \\ v_{30}(t) &= z_0(t) = T_A\left(t^*\right) = P_3^*, \\ v_{40}(t) &= r_0(t) = T_M\left(t^*\right) = P_4^*. \end{aligned} \tag{22}$$

Carrying out the steps involved in MsHPM gives,

$$
\begin{aligned}
T &= P_1^* + \lambda\left(t-t^*\right) - \mu_T P_1^*\left(t-t^*\right) - \kappa P_1^* P_3^*\left(t-t^*\right) \\
&+\frac{1}{2}\begin{pmatrix} \left(-\mu_T\left(\lambda-\mu_T P_1^* - \kappa P_1^* P_3^*\right) - \kappa\left(\lambda-\mu_T P_1^* - \kappa P_1^* P_3^*\right)\right)P_3^* \\ -\kappa P_1^*\left(\alpha P_2^* - \left(\mu_A+\rho\right)P_3^*\right) \end{pmatrix}\left(t-t^*\right)^2+\ldots, \\
T_L &= P_2^* + \kappa P_1^* P_3^*\left(t-t^*\right) - \left(\mu_L+\alpha\right)P_2^*\left(t-t^*\right) \\
&+\frac{1}{2}\begin{pmatrix} \kappa\left(\lambda-\mu_T P_1^* - k_2 P_1^* P_3^*\right)P_3^* + \kappa P_1^*\left(\alpha P_2^* - \left(\mu_A+\rho\right)P_3^*\right) \\ -\left(\mu_L+\alpha\right)\left(\kappa P_1^* P_3^* - \left(\mu_L+\alpha\right)P_2^*\right) \end{pmatrix}\left(t-t^*\right)^2+\ldots, \\
T_A &= P_3^* + \alpha P_2^*\left(t-t^*\right) - \left(\mu_A+\rho\right)P_3^*\left(t-t^*\right) \\
&+\frac{1}{2}\left(\alpha\left(\kappa P_1^* P_3^* - \left(\mu_L+\alpha\right)P_2^*\right) - \left(\mu_A+\rho\right)\left(\alpha P_2^* - \left(\mu_A+\rho\right)P_3^*\right)\right)\left(t-t^*\right)^2+\ldots, \\
T_M &= P_4^* + \rho P_3^*\left(t-t^*\right) + \beta P_4^*\left(t-t^*\right) - \beta P_4^{*2}\left(t-t^*\right)\Big/T_{\max} - \mu_M P_4^*\left(t-t^*\right) \\
&+\frac{1}{2}\begin{pmatrix} \rho\left(\alpha P_2^* - \left(\mu_A+\rho\right)P_3^*\right) + \beta\left(\rho P_3^* + \beta P_4^* - \beta P_4^{*2}\Big/\left(T_{\max} - \mu_M P_4^*\right)\right) \\ -2\beta P_4^*\Big/T_{\max}\left(\rho P_3^* + \beta P_4^* - \beta P_4^{*2}/T_{\max} - \mu_M P_4^*\right) - \mu_M\left(\rho P_3^* + \beta P_4^* - \beta P_4^{*2}\Big/\left(T_{\max} - \mu_M P_4^*\right)\right) \end{pmatrix}\left(t-t^*\right)^2+\ldots
\end{aligned}
\tag{23}
$$

To carry out the iterations in very subinterval of equal length, we take the values of the following,

$$
\begin{aligned}
P_1^* &= T(t^*) \cong \varphi_{T3}(t^*), \\
P_2^* &= T_L(t^*) \cong \varphi_{T_L 3}(t^*), \\
P_3^* &= T_A\left(t^*\right) \cong \varphi_{T_A 3}(t^*), \\
P_4^* &= T_M\left(t^*\right) \cong \varphi_{T_M 3}\left(t^*\right).
\end{aligned}
\tag{24}
$$

Where $\varphi_{T3}\left(t\right) = \sum_{k=0}^{3} v_{1,k}, \varphi_{T_L 3}\left(t\right) = \sum_{k=0}^{3} v_{2,k}, \varphi_{T_A 3}\left(t\right) = \sum_{k=0}^{3} v_{3,k}, and\, \varphi_{T_M 3}\left(t\right) = \sum_{k=0}^{3} v_{4,k}$.

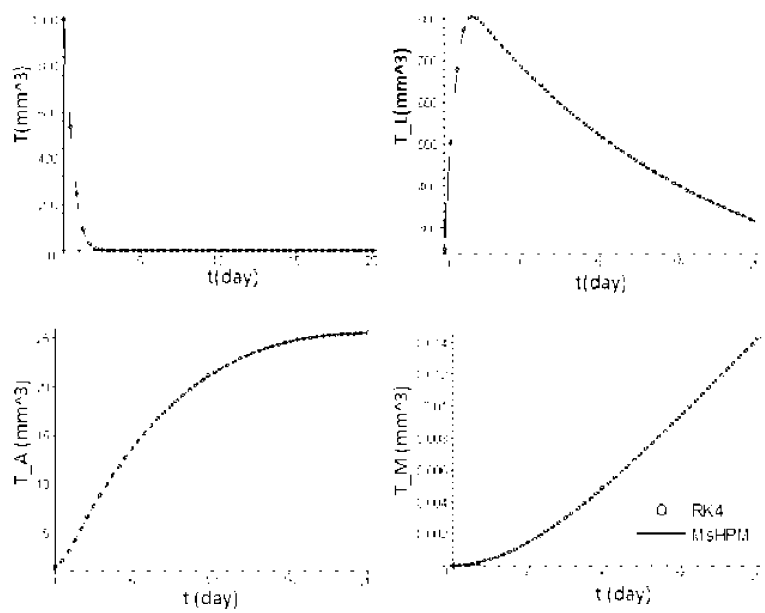

Fig. 1: Comparison of $T(t)$, $T_L(t)$,$T_A(t)$.$T_M(t)$ for 3-term MsHPM with dt = 0.01 and RK4 with h = 0.001

Here, based on initial conditions $T(0)$ 1000 / mm^3, $T_L(0) = 250 / mm^3$,$T_A(0) = 1.5 / mm^3$ for the four-component model are $T_M(0) = 0$ given solutions obtained from MsHPM and RK4 in follow:

Figure 1 show the solutions for $T(t)$, $T_L(t)$, $T_A(t)$,$T_M(t)$ respectively by the 3-term MsHPM and RK4 on time step $dt = 0.01$.

Table 1: Numerical comparison of T for RK4 with $h = 0.001$ and 3-term MsHPM with $dt = 0.01$

t	RK4	MsHPM	|RK4-MsHPM|
0	1000.	1000	0.
2	8.682267410	8.682266400	0.1011 e-5
4	0.956397209	0.956397150	0.5920 e-7
6	0.713837906	0.713837897	0.9400 e-8
8	0.598531209	0.598531200	0.8600 e-8
10	0.533915509	0.533915504	0.4800 e-8
12	0.495080674	0.495080669	0.5100 e-8
14	0.471374381	0.471374379	0.1800 e-8
16	0.457466762	0.457466755	0.6500 e-8
18	0.450396379	0.450396373	0.5700 e-8
20	0.448388749	0.448388739	0.1020 e-8

Table 2: Numerical comparison of T_L for RK4 with $h = 0.001$ and 3-term MsHPM with $dt = 0.01$

t	RK4	MsHPM	|RK4-MsHPM|
0	250.	250.	0.
2	803.3744157	803.3744124	0.33000 e-5
4	722.5191776	722.5191826	0.49000 e-5
6	646.1901762	646.1901799	0.37000 e-5
8	579.1198287	579.1198306	0.19000 e-5
10	520.1674099	520.1674121	0.21000 e-5
12	468.3360672	468.3360667	0.50000 e-6
14	422.7557620	422.7557618	0.20000 e-6
16	382.6653946	382.6653977	0.31000 e-5
18	347.3980294	347.3980334	0.39000 e-5
20	316.3685950	316.3685940	0.11000 e-5

Table 3: Numerical comparison of T_A for RK4 with $h = 0.001$ and 3-term MsHPM with $dt = 0.01$

t	RK4	MsHPM	|RK4-MsHPM|
0	1.5	1.5	0.
2	6.416966379	6.416966388	0.8000 e-8
4	11.61881117	11.61881122	0.4000 e-7
6	15.71097903	15.71097905	0.1000 e-7
8	18.86895765	18.86895790	0.2400 e-6
10	21.24769074	21.24769100	0.2600 e-6
12	22.97924481	22.97924504	0.2200 e-6
14	24.17602333	24.17602348	0.1400 e-6
16	24.93353355	24.93353392	0.3600 e-6
18	25.33276597	25.33276630	0.3200 e-6
20	25.44224472	25.44224528	0.5500 e-6

Table 4: Numerical comparison of T_M for RK4 with $h = 0.001$ and 3-term MsHPM with $dt = 0.01$

t	RK4	MsHPM	|RK4-MsHPM|
0	0.	0.	0.
2	0.0002911773	0.0002911773	0.2911 e-15
4	0.0010147120	0.0010147120	0.1014 e-13
6	0.0021003093	0.0021003093	0.2100 e-13
8	0.0034632272	0.0034632272	0.3463 e-12
10	0.0050328279	0.0050328279	0.5032 e-13
12	0.0067505369	0.0067505369	0.6750 e-12
14	0.0085680395	0.0085680396	0.8568 e-12
16	0.0104457326	0.0104457327	0.1044 e-11
18	0.0123513950	0.0123513951	0.1235 e-11
20	0.0142590459	0.0142590457	0.1425 e-10

Tables 1-4 exhibits a numerical comparison of the results obtained with RK4 and with the MsHPM. It is to be noted that the results obtained the MsHPM agree very vell with RK4 solutions.

CONCLUSIONS

In this paper, multistage homotopy perturbation method was used for finding the solutions of nonlinear ordinary differential equation systems such as human T-cell lymphotropic virus I (HTLV-I) infection of CD4$^+$ T-cells model. We demonstrated the accuracy and efficiency of these methods by solving some ordinary differential equation systems. Comparison between the multistage Homotopy perturbation solution and classical Runge-Kutta solution was discussed and plotted. Higher accuracy solution was obtained via this algorithm.

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