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AN APPLICATION OF EXPONENTIAL-POLYNOMIAL SINGLE STEP METHOD FOR SOLVING VIRAL MODEL WITH DELAYED IMMUNE RESPONSE

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Abstract: This paper illustrates an application of the single step method based on polynomial interpolation function for solving viral infection model with delayed immune response. The effect of time delay on the dynamics of viral infection with cytotoxic T-Lymphocytes (CTLs) response is studied. It has been modelled into the system of delay differential equations. This delay system has been solved using single step method that is based on the combination of exponential-polynomial interpolating function. From the numerical simulations, the dynamic behaviour in this model has been observed.

Key words: exponential-polynomial single step method, viral model with immune response, dynamic behaviour, delay differential equations.

2010 Mathematics Subject Classification: 34K, 65L, 68N.

1. Introduction:

Delay differential equations (DDEs) play an import role in various fields of science and engineering. These equations arise very frequently in population dynamics [9], control systems [7], chemical kinetics [4] etc. Recently there has been a growing interest in obtaining the numerical solutions of DDEs. Some of the notable numerical methods are Adomian decomposition method [12], block method [11], Homotopy perturbation method [6], variation iteration method [13] etc.

Several one-step numerical techniques have been developed for the solution of first order ordinary differential equations (ODEs) by means of interpolating functions. In 1988, Van Niekerek [14] have presented a new algorithm which consists of the rational interpolating function for solving ODEs. Kama and Ibijola [8] have developed the new one-step polynomial and exponential interpolating function technique for solving initial value problems (IVPs). In 2017, Abolarin and Akingbade [1] have derived the fourth stage inverse polynomial scheme to IVPs. Fadugba and Falodun [5] have developed the new one-step power series polynomial scheme for IVPs in ODEs.

Recently, many mathematical models have been developed to describe the dynamic behaviour in viral models. Wang et al. [15] have studied the dynamical behaviour in a viral model with retarded immune response. Xueyong and Jingan [17] have discussed the effect of time delay and stability in viral infection model.

In this paper, an application of the single step method based on the combination of exponential and polynomial interpolation function for solving viral infection model with delayed immune response is illustrated. The organization of the paper is as follows: In section 2, the derivation of the exponential-polynomial single step method is given. In section 3, the viral infection model with delayed immune response is described. In section 4, numerical simulations of the dynamical behaviour of the model are given.

2. Exponential – Polynomial Single step Method (EPSM):

Consider the first order DDEs of the following form:

$$y'(t) = f\big(t, y(t), y(t-\tau)\big), \quad t > t_0$$
$$y(t) = \Phi(t), \quad t \le t_0 \qquad (1)$$

where $\Phi(t)$ is the initial function and $\tau = \tau(t, y(t))$.

Let us assume that the analytical solution $y(t)$to the initial value problem (1) can be locally represented in the interval $[t_n, t_{n+1}]$, $n \geq 0$ by the non-linear polynomial interpolating function which consists of both polynomial and exponential function of the form

$$F(t) = a_1 e^{2t} + a_2 t^4 + a_3 t^3 + a_4\, t^2 + a_5\, t + a_6\,, \qquad (2)$$

where $a_1, a_2 a_3, a_4, a_5$ and a_6 are undetermined coefficients. We shall assume y_n is a numerical approximation to the analytical solution $y(t)$ and using mesh points as follows:

$$t_n = t_0 + nh, \qquad n = 0,1,2,\ldots \qquad (3)$$

Consider the following constraints on the interpolating function (2) in order to get the undetermined coefficients.

Firstly, the interpolating function must coincide with the analytical solution at

$t = t_n$and $t = t_{n+1}$.

Hence we required that

$$F(t_n) = a_1 e^{2t_n} + a_2 {t_n}^4 + a_3 {t_n}^3 + +a_4 {t_n}^2 + a_5 t_n + a_6$$

And $F(t_{n+1}) = a_1 e^{2t_{n+1}} + a_2 {t_{n+1}}^4 + a_3 {t_{n+1}}^3 + a_4 {t_{n+1}}^2 + a_5 t_{n+1} + a_6$

Secondly, the derivatives of the interpolating function are required to coincide with the differential equation as its first, second, third and fourth derivatives with respect to *t*at $t = t_n$.

We denote the i[th] total derivatives of *F* and *f* with respect to *t* as$F^{(i)}$ and $f^{(i)}$ and assume that

$$F^{(1)}(t_n) = f_n$$
$$F^{(2)}(t_n) = f_n^{(1)}$$
$$F^{(3)}(t_n) = f_n^{(2)}$$
$$F^{(4)}(t_n) = f_n^{(3)}$$
$$F^{(5)}(t_n) = f_n^{(4)}$$

Now $f_n = 2a_1 e^{2t_n} + 4a_2 t_n^3 + 3a_3 t_n^2 + 2a_4 t_n + a_5$ (4)

$f_n^{(1)} = 4a_1 e^{2t_n} + 12a_2 t_n^2 + 6a_3 t_n + 2a_4$ (5)

$f_n^{(2)} = 8a_1 e^{2t_n} + 24a_2 t_n + 6a_3$ (6)

$f_n^{(3)} = 16a_1 e^{2t_n} + 24a_2$ (7)

$f_n^{(4)} = 32a_1 e^{2t_n}$ (8)

Solving the simultaneous equations (4) - (8), we get the values of a_1, a_2, a_3, a_4 and a_5 as follows:

$$a_1 = \frac{f_n^{(4)}}{32e^{2t_n}} \qquad (9)$$

$$a_2 = \frac{1}{24}\left[f_n^{(3)} - \frac{f_n^{(4)}}{2}\right] \qquad (10)$$

$$a_3 = \frac{1}{6}\left[\left(f_n^{(2)} - \frac{f_n^{(4)}}{4}\right) - \left(f_n^{(3)} - \frac{f_n^{(4)}}{2}\right) t_n\right] \qquad (11)$$

$$a_4 = \frac{1}{2}\left[\left(f_n^{(1)} - \frac{f_n^{(4)}}{8}\right) - \left(f_n^{(2)} - \frac{f_n^{(4)}}{4}\right)t_n - \left(\frac{f_n^{(4)}}{4} - \frac{f_n^{(3)}}{2}\right){t_n}^2\right] \quad (12)$$

$$a_5 = \left[\left(f_n - \frac{f_n^{(4)}}{16}\right) - \left(f_n^{(1)} - \frac{f_n^{(4)}}{8}\right)t_n - \left(\frac{f_n^{(4)}}{8} - \frac{f_n^{(2)}}{2}\right){t_n}^2 - \left(\frac{f_n^{(3)}}{6} - \frac{f_n^{(4)}}{12}\right){t_n}^3\right] \quad . \quad (13)$$

Since $F(t_{n+1}) = y(t_{n+1})$ and $F(t_n) = y(t_n)$ implies that

$$y(t_{n+1}) = y_{n+1} \text{and} y(t_n) = y_n$$

Thus we have $F(t_{n+1}) - F(t_n) = y_{n+1} - y_n$. Hence

$$y_{n+1} - y_n = a_1(e^{2t_{n+1}} - e^{2t_n}) + a_2({t_{n+1}}^4 - {t_n}^4) + a_3({t_{n+1}}^3 - {t_n}^3) + a_4({t_{n+1}}^2 - {t_n}^2) + a_5(t_{n+1} - t_n) \quad . \quad (14)$$

Setting $t_0 = 0$ in (3), we get $t_n = nh$ and $t_{n+1} = (n+1)h$.

From these, we have:

$$t_{n+1} - t_n = nh \quad (15)$$

$${t_{n+1}}^2 - {t_n}^2 = (2n+1)h^2 \quad (16)$$

$${t_{n+1}}^3 - {t_{n+1}}^3 = (3n^2 + 3n + 1)h^3 \quad (17)$$

$${t_{n+1}}^4 - {t_{n+1}}^4 = (4n^3 + 6n^2 + 4n + 1)h^4 \quad (18)$$

Using (15) – (18) in (14), we get

$$y_{n+1} = y_n + a_1(e^{2t_{n+1}} - e^{2t_n}) + a_2h^4(1 + 4n + 6n^2 + 4n^3) + a_3h^3(1 + 3n + 3n^2) + a_4h^2(1 + 2n) + a_5h \quad (19)$$

Eqn. (19) gives the solution of (1) by this Exponential – Polynomial single step method.

3. Formulation of Viral Model with Delayed Immune Response:

Many mathematical models have been developed to explain the epidemic and viral dynamics. These viral models can give insights in the dynamics of viral load in biology and play an important role for a better understanding of diseases. Viral reproduction involves host cells and uses the cells machinery for synthesizing new components of the virus. Nowak et al. [10] and Bonhoeffer et al. [3] proposed the ODE viral model as follows.

$$\frac{dx}{dt} = \lambda - dx - \beta xy$$

$$\frac{dy}{dt} = \beta xy - ay$$

$$\frac{dv}{dt} = ky - uv \quad (20)$$

This model consists of three variables: the populations of uninfected cells $x(t)$, infected cells that produce virus $y(t)$and free virus particles $v(t)$. Uninfected cells are generated at a constant rate λ and dieat the rate *dx*. They become infected cells at the rate βxy. The death rate of infected cells is *ay*. The production rate of new virus from infected cells is *ky* and the death rate is *uv*.

According to Bartholdy et al. [2] and Wodarz et al. [16], the amount of free virus is simply proportional to the population of infected cells. Hence, the population of infected cells $y(t)$ can be considered as an amount of virus load $v(t)$. Thus (20) is simplified to:

$$\frac{dx}{dt} = \lambda - dx - \beta xy$$

$$\frac{dy}{dt} = \beta xy - ay \quad (21)$$

In many viral infections, CTLs play a significant role in antiviral defence by attacking infected cells. If $z(t)$is the number of CTLs, then (21) can be modified to

$$\frac{dx}{dt} = \lambda - dx - \beta xy$$

$$\frac{dy}{dt} = \beta xy - ay - pyz$$

$$\frac{dz}{dt} = f(y,z) - bz \quad (22)$$

Here $f(y,z)$ denotes the rate of immune response due to virus activation. The infected cells are killed by the CTL response at a rate *pyz*. The CTL response decays at rate *bz*. If we assume that the production of CTLs depends only on the number of infected cells, then $f(y,z) = cy$.

In the models of immune response, time delays cannot be ignored. Antigenic stimulation generating CTLs may need a period of time τ, i.e., the CTL response at time t may depend on the number of antigens at a previous time $t-\tau$. In this paper, we consider the model by incorporating a time delay of the immune response as follows:

$$\frac{dx}{dt} = \lambda - dx - \beta xy$$
$$\frac{dy}{dt} = \beta xy - ay - pyz$$
$$\frac{dz}{dt} = cy(t-\tau) - bz \qquad (23)$$

The CTL response is activated at a rate proportional to the population of infected cells at a previous time$cy(t-\tau)$, and also decays exponentially at a rate proportional to its current strength bz. Moreover,τ is the time delay of CTL response.

4. Numerical Simulations:

The basic reproductive ratio (R_0) is the average number of newly infected cells generated from one infected cell at the beginning of the infectious process. For the system (23), this ratio is given by $R_0 = \lambda\beta/ad$. The detailed stability analysis of this model is discussed in [12]. In order to find the complex dynamic behaviour of system (23) and to verify the stability switches, we do numerical calculations using different time delays τ and birth rates of susceptible cells λ.

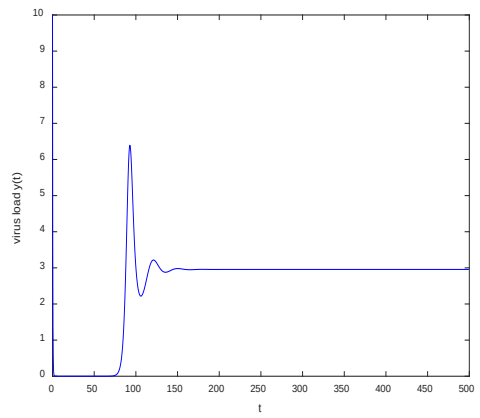
Consider$a = 5$, $b = 0.3$, $c = 0.2$,$d = 0.1$, $\beta = 0.002$, $p = 0.05 < \frac{ab\beta}{cd}$. The initial conditions are taken as x(θ) = 1000 , y(θ) = 10 and z(θ) = 10 where θ∈(-τ,0].If $\lambda = 270$, then $R_0 = 1.8 > 1$. From Fig. 1(a) and 1(b), it is noted that, the time delay cannot affect the dynamic behaviour if the birth rate of the infected cells$\lambda = 270$.

Suppose we take $\lambda = 1000$, then $R_0 = 4.0 > 1$. From Fig. 1(c) - 1(g), it is noted that, the time delay can affect the dynamic behaviour if the birth rate of the infected cells $\lambda = 1000$. Also there appears stability switch and chaotic pattern as time delay increases.

Numerical simulation by EPSM is compared with the numerical simulation presented by Wang et al. [12] in Fig. 1(a)-1(g).

Fig. 1(a)($\tau = 0.5$)

Numerical Simulation by EPSM



Numerical Simulation in Wang et al. [12]

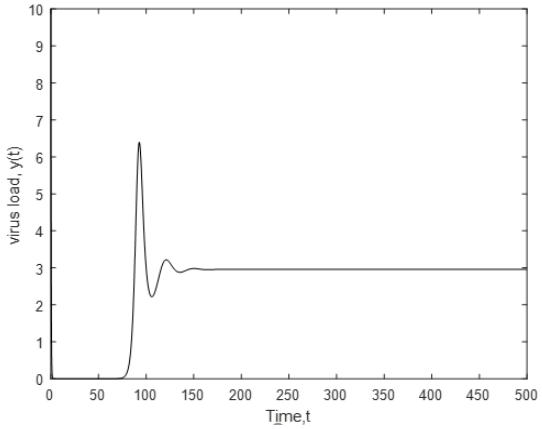


Fig. 1(b)($\tau = 11.5$)

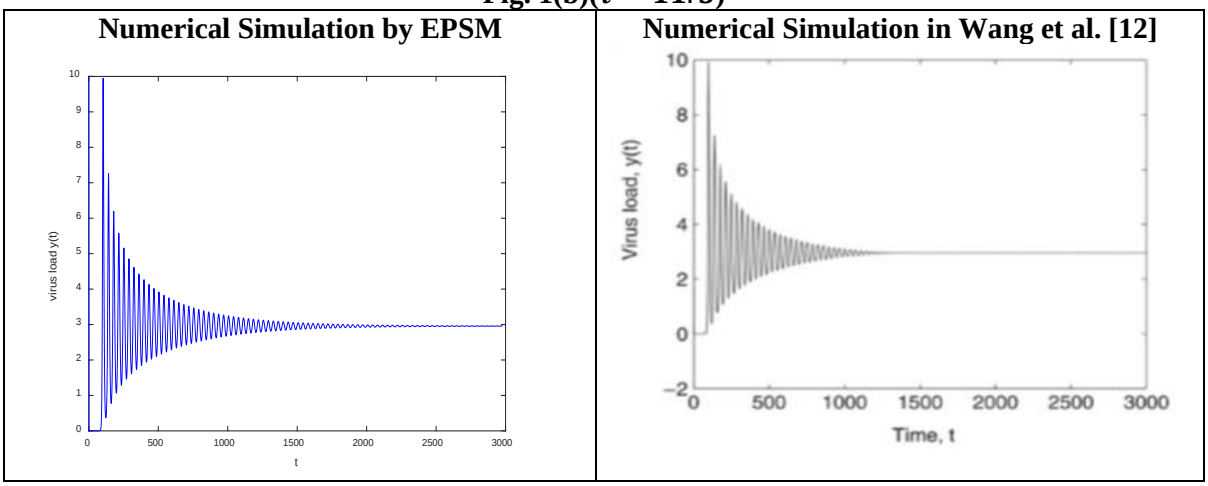


Fig. 1(c)($\tau = 0.05$)

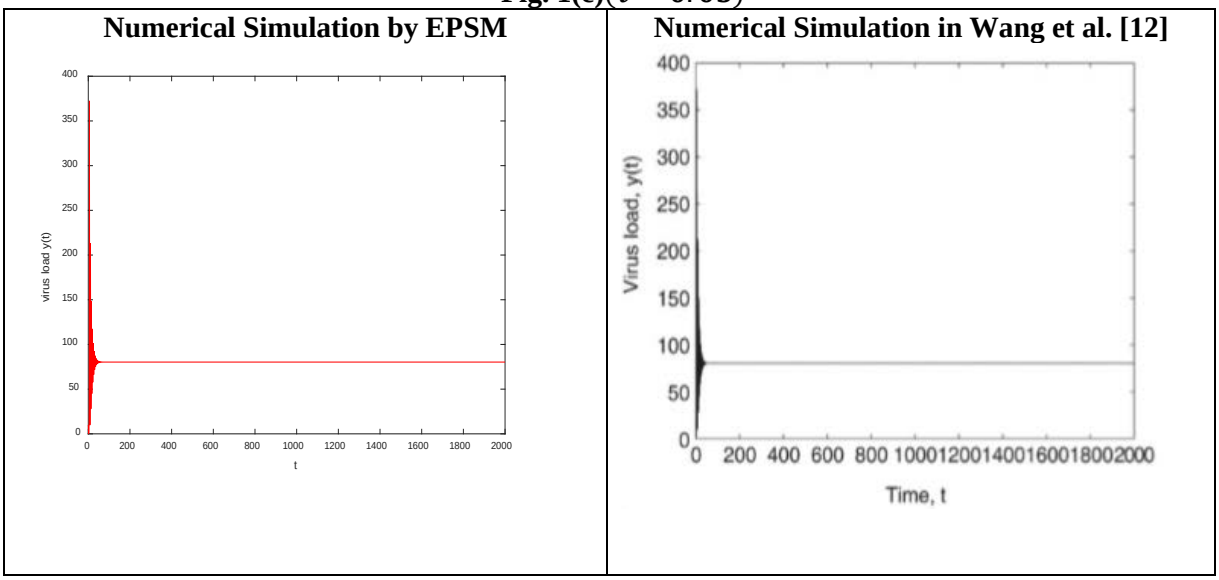
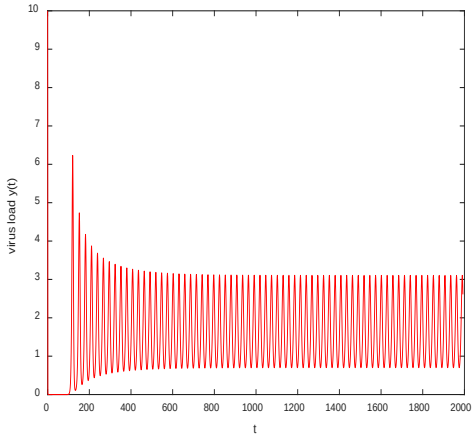


Fig. 1(d)($\tau = 2.5$)

Numerical Simulation by EPSM



Numerical Simulation in Wang et al. [12]

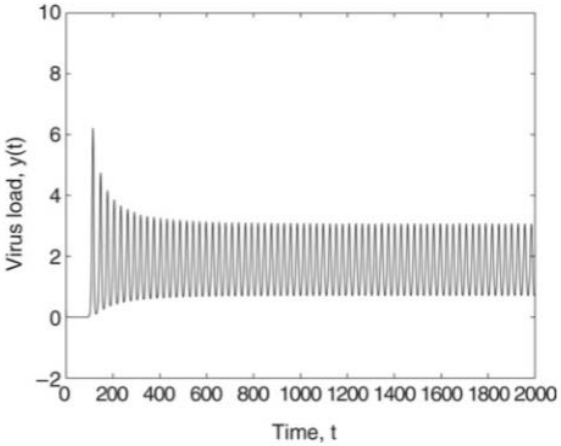
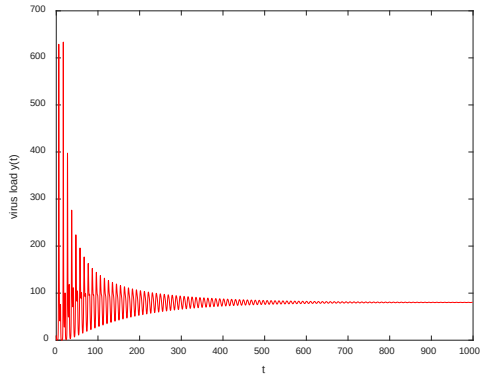


Fig. 1(e)($\tau = 4.5$)

Numerical Simulation by EPSM



Numerical Simulation in Wang et al. [12]

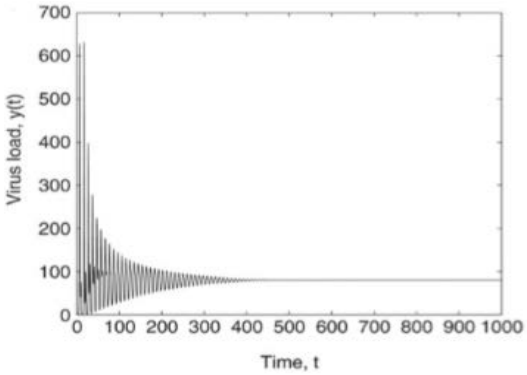
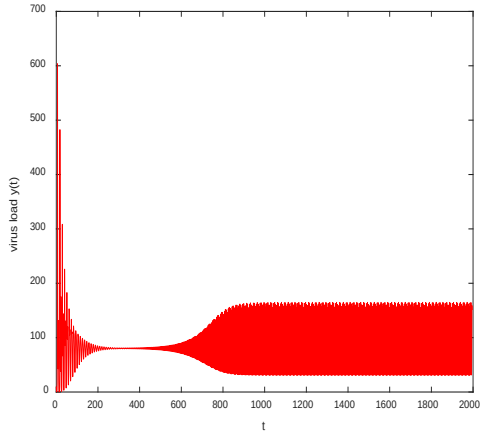


Fig. 1(f)($\tau = 5.0$)

Numerical Simulation by EPSM



Numerical Simulation in Wang et al. [12]

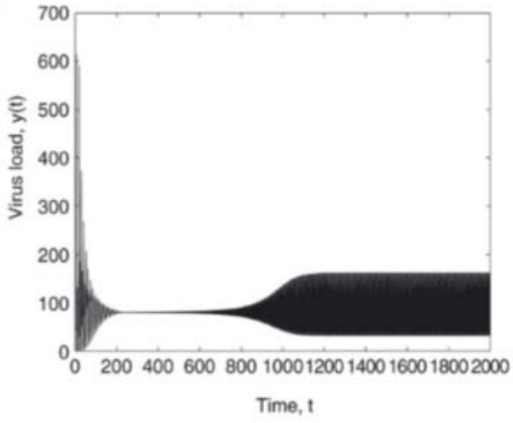
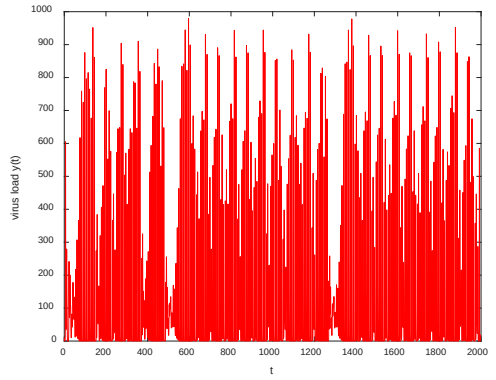
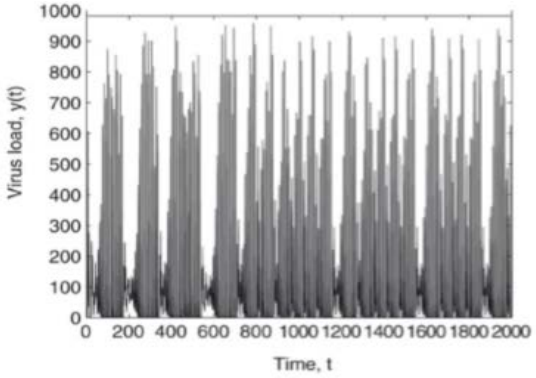


Fig. 1(g)($\tau = 8.5$)

Numerical Simulation by EPSM	Numerical Simulation in Wang et al. [12]
	

5. Conclusion:

In this paper, we have solved a viral infection model with delayed immune response by using polynomial-exponential single-step method. The effect of time delay on the dynamics of viral infection with cytotoxic T-Lymphocytes (CTLs) response is studied. From the results, we can see the time delay τ plays an important role in preventing the virus.

The numerical simulations (Fig. 1(a) and 1(b)) reveal that the dynamic behaviour is not affected by the time delay when the birth rate of infected cells or the basic reproductive ratio of the virus is below a certain threshold. However, when the birth rate of infected cells is increased to $\lambda = 1000$ ($R_0 = 4.0$), the numerical simulations (Fig. 1(c) - 1(g)) reveal that the dynamic behaviour of system (23) is affected by the time delay.

Hence, it is concluded that the proposed single step method is very much applicable in solving the real-world problems like viral infection model and similar realistic problem existing in various fields of science and engineering.

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