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Research Article

An exponential Galerkin method for solutions of HIV infection model of CD4⁺ T-cells

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ABSTRACT

In this study, we consider a nonlinear first order model about the infection of CD4⁺ T-cells by HIV. In order to solve it numerically, we present a new method based on exponential polynomials reminiscent of the Galerkin method. Considering the approximate solutions in the form of exponential polynomials, we first substitute these approximate solutions in the original model. Some relations are thus obtained, which we express in terms of matrices. Taking inner product of a set of exponential functions with these matrix expressions then yields a nonlinear system of algebraic equations. The solution of these equations gives the approximate solutions of the model. Additionally, the technique of residual correction, which aims to reduce the error of the approximate solution by estimating this error, is discussed in some detail. The method and the residual correction technique are illustrated with an example. The results are also compared with numerous existing methods from the literature.

1. Introduction

Infection with Human Immunodeficiency Virus (HIV) is known to result in the suppression of the immune system due to depletion of CD4⁺ T-cells (known commonly as T-helper cells or T4-cells), cells which play a central role in the human immune system (Perelson, 1989). Most of the immunological abnormalities that accompany HIV infection can be attributed to the decline in these cells (Lane and Fauci, 1985). Since T4-cells have such a central role in immune regulation, their depletion can have a disastrous effect on the functioning of the immune system. In fact, the extent of the decline in the number of T4-cells in peripheral blood is used as an indicator of the disease stage (Perelson et al., 1993; Redfield et al., 1986).

After the progress of Acquired Human Immunodeficiency Syndrome (AIDS) in an infected individual was explored to be in a close relationship with the number of T4-cells in peripheral blood, the necessity to describe this relationship quantitatively was soon realized. In the last three decades, the field of mathematical biology saw the emergence of numerous models on this subject. One of the first, and arguably the most famous, of such models was proposed by Perelson (1989) in 1989. This model consisted of a system of three first order differential equations on three unknown functions; namely, the population of healthy T4-cells, the population of infected T4-cells and the concentration of free HIV in bloodstream. Perelson et al. (1993) extended this model to four unknown functions by recognition of the fact that not all infected T4-cells are capable of producing a virus. Later on, by ignoring this differentiation, Culshaw and Ruan (2000) considered this model in terms of three unknown functions. After some simplifications, this model can be described by the following:

$$\begin{aligned} \frac{dT}{dt} &= s - \alpha T + rT\left(1 - \frac{T+I}{T_{\max}}\right) - kVT, \\ \frac{dI}{dt} &= kVT - \beta I, \\ \frac{dV}{dt} &= N\beta I - \gamma V. \end{aligned} \tag{1}$$

Here, the system is considered in the time interval $0 \le t \le a$ and with the initial conditions $T(0) = T_0, I(0) = I_0, V(0) = V_0$.

The above first order nonlinear ordinary differential equation system will be our main interest throughout this paper. Here $T(t)$ represents the concentration of healthy T4-cells at time t, $I(t)$ represents the concentration of infected T4-cells at time t, and $V(t)$ represents the concentration of free HIV at time t. The explanation of the related parameters is as follows: s represents the source of T4-cells from the precursors, α is the natural death rate of T4-cells, r is their growth rate, and T_{max} is their carrying capacity. k is the

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rate of infection of T4-cells with free virus present in the environment and hence is a plus term for infected T4-cells. β is the overall death rate for infected T4-cells, with the assumption that N virus particles are released by each dying (infected) T4-cell. Lastly, γ is the death rate of viruses.

Since the model (1) is known to possess no exact solutions as of today, numerical methods have been called for. To name a few, it has been approximately solved by homotopy perturbation method (Merdan, 2007), a modified version of variational iteration algorithm (Merdan et al., 2011), perturbation-iteration algorithm (Khalid et al., 2015), an improved version of the Bessel collocation method (Yüzbaşı, 2012a), the differential transform method (Srivastava et al., 2014), and Laplace Adomian decomposition method (Ongun, 2011). Apart from numerical solutions, users interested in its global dynamics can refer to (Wang and Li, 2006). In this paper, we will use the scheme presented in the next section to find approximate solutions of the model (1) in terms of exponential polynomials. Namely, we will seek solutions expressed as a linear combination of the functions 1, e^{-t}, e^{-2t}, …, e^{-Nt}. Recently, such an approach was employed in (Yüzbaşı, 2015) with the addition of collocation points.

The remaining of the paper is designed as follows: In Section 2, the numerical method to be used is presented. The subject of Section 3 is a technique which aims to obtain better solutions using an already obtained solution. Section 3.2 contains a note on how the Taylor truncation error can be used to derive an upper bound for the error of the present scheme. In Section 4, we apply the method to an example problem and compare our results with other results from the literature. Finally, Section 5 contains comments regarding the results of this paper.

2. Method of solution

In this section, we describe the numerical scheme that we will use to obtain approximate solutions of the system (1). Since this scheme should be programmable in computer, matrix counterparts of expressions will be provided whenever possible as it is particularly easier to work with matrices in most computer algebra systems.

We will seek solutions to the system (1) in the form of polynomials in exponential functions having nonpositive powers. More explicitly, we start by assuming

$$T_N(t)=\sum_{k=0}^{N}s_k e^{-kt},\quad I_N(t)=\sum_{k=0}^{N}u_k e^{-kt},\quad V_N(t)=\sum_{k=0}^{N}v_k e^{-kt}$$

are the approximate populations of healthy T4-cells, infected T4-cells and free virus particles at time t, respectively. Our aim is to obtain the unknown coefficients s_k, u_k and v_k and hence the approximate solutions T_N, U_N and V_N. We first note that the above equations can be expressed in terms of matrices by collecting the unknown coefficients and variables inside separate vectors. Thus, we can write

$$T_N(t)=\mathbf{EX}_N(t)\mathbf{S},\quad U_N(t)=\mathbf{EX}_N(t)\mathbf{U},\quad V_N(t)=\mathbf{EX}_N(t)\mathbf{V},$$

where

$$\mathbf{S}=[\,s_0\quad s_1\quad s_2\quad\dots\quad s_N\,]^T,$$
$$\mathbf{U}=[\,u_0\quad u_1\quad u_2\quad\dots\quad u_N\,]^T,$$
$$\mathbf{V}=[\,v_0\quad v_1\quad v_2\quad\dots\quad v_N\,]^T,$$
$$\mathbf{EX}_N(t)=[\,1\quad e^{-t}\quad e^{-2t}\quad\dots\quad e^{-Nt}\,].$$

The derivatives can also be expressed in terms of matrices with the help of the $(N+1)\times(N+1)$ square matrix $\mathbf{M}$ with entries $\mathbf{M}_{i,i}=1-i$ for $i=1,2,\dots,N+1$ and $\mathbf{M}_{i,j}=0$ otherwise. More explicitly, if $\mathbf{M}$ is the matrix given by

$$\mathbf{M}=\begin{bmatrix}0&0&0&\dots&0\\0&-1&0&\dots&0\\0&0&-2&\dots&0\\\vdots&\vdots&\vdots&\ddots&\vdots\\0&0&0&\dots&-N\end{bmatrix},$$

then we have the following for the derivatives in (1):

$$\frac{dT_N}{dt}=\mathbf{EX}_N(t)\mathbf{MS},\quad \frac{dI_N}{dt}=\mathbf{EX}_N(t)\mathbf{MU},\quad \frac{dV_N}{dt}=\mathbf{EX}_N(t)\mathbf{MV}.$$

Next step is to take care of the nonlinearities present in the equations related to $T(t)$ and $I(t)$ in the system (1). We do this by defining a companion matrix associated with the coefficient vectors $\mathbf{S}$ which we defined previously. The companion matrix in question is the $(2N+1)\times(N+1)$ matrix S with entries defined according to the following rule: $S_{ij}=s_{i-j}$ if $j\le i\le j+N$ and $S_{ij}=0$ otherwise. More explicitly, S is given by

$$S=\begin{bmatrix}s_0&0&0&\dots&0\\s_1&s_0&0&\dots&0\\s_2&s_1&s_0&\dots&0\\\vdots&\vdots&\vdots&\ddots&\vdots\\s_N&s_{N-1}&s_{N-2}&\dots&s_0\\0&s_N&s_{N-1}&\dots&s_1\\0&0&s_N&\dots&s_2\\\vdots&\vdots&\vdots&\ddots&\vdots\\0&0&0&\dots&s_N\end{bmatrix}.$$

Then, the matrix counterparts of the nonlinear terms in (1) are given by the following:

$$T_N^2(t)=\mathbf{EX}_{2N}(t)S\mathbf{S},\quad T_N(t)I_N(t)=\mathbf{EX}_{2N}(t)S\mathbf{U},$$
$$T_N(t)V_N(t)=\mathbf{EX}_{2N}(t)S\mathbf{V}.$$

Next step is to substitute the matrix expressions that we have obtained so far in the system (1). Doing this, we arrive at the following expressions:

$$\begin{aligned}&\mathbf{EX}_N(t)\mathbf{MS}+(\alpha-r)\mathbf{EX}_N(t)\mathbf{S}+\frac{r}{T_{\max}}\mathbf{EX}_{2N}(t)S(\mathbf{S}+\mathbf{U})\\&\quad+k\mathbf{EX}_{2N}(t)S\mathbf{V}=s,\\&\mathbf{EX}_N(t)\mathbf{MU}-k\mathbf{EX}_{2N}(t)S\mathbf{V}+\beta\mathbf{EX}_N(t)\mathbf{U}=0,\\&\mathbf{EX}_N(t)\mathbf{MV}-N\beta\mathbf{EX}_N(t)\mathbf{U}+\gamma\mathbf{EX}_N(t)\mathbf{V}=0.\end{aligned}\tag{2}$$

Now is the time to apply the central idea of our numerical method. Namely, we apply inner product to the above equations with the elements of the set

$$\mathbf{\Phi}=\{1,e^{-t},e^{-2t},\dots,e^{-Nt}\},$$

where the inner product is defined by

$$\langle f,g\rangle=\int_0^a f(t)g(t)dt.$$