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A numerical method for delayed partial differential equations describing infectious diseases

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ABSTRACT

In this paper, we propose a numerical method for delayed partial differential equations that describe the dynamics of viral infections such as the human immunodeficiency virus (HIV) and the hepatitis B virus (HBV). We first prove that the proposed numerical method preserves the positivity and boundedness of solutions in order to ensure the well-posedness of the problem. By constructing appropriate discrete Lyapunov functionals, we show that the proposed method also preserves the global stability of equilibria of the corresponding continuous system with no restriction on the space and time step sizes. Moreover, the discrete model and main results presented in Qin et al. (2014) are extended and generalized.

1. Introduction

Infectious diseases caused by viruses such as HIV, HBV, Ebola and more recently Zika virus, represent a major global health problem. According to the World Health Organization (WHO), about 240 million people worldwide live with chronic HBV infection, and more than 780 000 people die every year due to complications of hepatitis B, including cirrhosis and liver cancer [1]. To better understand the dynamics of these infections, many mathematical models have been proposed by using ordinary differential equations (ODEs), delay differential equations (DDEs) as well as partial differential equations (PDEs). In this paper, we consider the generalized HBV infection model that was investigated in our recent work [2]. This model is described by the following system of PDEs,

$$\begin{cases} \dfrac{\partial T}{\partial t} &= \lambda - dT(x,t) - f\big(T(x,t), I(x,t), V(x,t)\big)V(x,t), \\ \dfrac{\partial I}{\partial t} &= f\big(T(x,t-\tau_1), I(x,t-\tau_1), V(x,t-\tau_1)\big)V(x,t-\tau_1)e^{-\alpha_1\tau_1} - aI(x,t), \\ \dfrac{\partial V}{\partial t} &= d_V\triangle V + kI(x,t-\tau_2)e^{-\alpha_2\tau_2} - \mu V(x,t), \end{cases} \tag{1}$$

where $T(x,t)$, $I(x,t)$ and $V(x,t)$ denote the densities of uninfected cells, infected cells and free virus at position x and time t, respectively. λ is the recruitment rate of uninfected cells; k is the production rate of free virus by infected cells; d, a and μ are the death rates of uninfected cells, infected cells and free virus, respectively. The first delay τ_1 represents the time

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needed for infected cells to produce virions after viral entry and the factor $e^{-\alpha_1\tau_1}$ accounts for the probability of surviving from time $t-\tau_1$ to time t, where α_1 is the death rate for infected but not yet virus-producing cells. The second delay τ_2 denotes the time necessary for the newly produced virions to become mature and then infectious particles. The probability of survival of immature virions is given by $e^{-\alpha_2\tau_2}$ and the average life time of an immature virus is given by $\frac{1}{\alpha_2}$. Finally, d_V is the diffusion coefficient and $\triangle$ is the Laplacian operator. All the parameters given in system (1) are positive constants and the general incidence function $f(T,I,V)$ is continuously differentiable in the interior of $\mathbb{R}^3_+$ and satisfies the three fundamental hypotheses given in [3] and used in [4–9], that are:

(H_1) $f(0,I,V)=0$, for all $I\geq 0$ and $V\geq 0$,
(H_2) $f(T,I,V)$ is a strictly monotone increasing function with respect to T, for any fixed $I\geq 0$ and $V\geq 0$,
(H_3) $f(T,I,V)$ is a monotone decreasing function with respect to I and V, i.e., $\frac{\partial f}{\partial I}(T,I,V)\leq 0$ and $\frac{\partial f}{\partial V}(T,I,V)\leq 0$ for all $T\geq 0, I\geq 0$ and $V\geq 0$.

From the biological point of view, the three hypotheses are reasonable and consistent with the reality. For more details on the biological significance of these three hypotheses, we refer the reader to the works [10,11]. Furthermore, the general incidence function $f(T,I,V)$ includes several types of incidence rate existing in the literature such as the mass action or so-called bilinear incidence when $f(T,I,V)=\beta T$, the standard incidence function was used in [12,13] when $f(T,I,V)=\frac{\beta T}{T+I}$, the saturation incidence when $f(T,I,V)=\frac{\beta T}{1+\alpha V}$, the incidence function was used in [14,15] when $f(T,I,V)=\frac{\beta T}{T+V}$, Beddington–DeAngelis response when $f(T,I,V)=\frac{\beta T}{1+\alpha_1 T+\alpha_2 V}$, Crowley–Martin response when $f(T,I,V)=\frac{\beta T}{1+\alpha_1 T+\alpha_2 V+\alpha_1\alpha_2 TV}$ and Hattaf–Yousfi response (see Section 4 in [16]) when $f(T,I,V)=\frac{\beta T}{\alpha_0+\alpha_1 T+\alpha_2 V+\alpha_3 TV}$, where $\alpha,\alpha_0,\alpha_1,\alpha_2,\alpha_3\geq 0$ are the saturation factors measuring the psychological or inhibitory effect and $\beta>0$ is the infection coefficient. In addition, system (1) is the generalization of all diffusive viral infection models presented in [17–23].

As viral particles cannot move outside of the liver and state variables represent the densities of hepatocytes (liver cells) and virus, we have considered system (1) with Neumann boundary conditions given by

$$\frac{\partial V}{\partial \nu}=0,\quad on\ \partial\Omega\times(0,+\infty), \tag{2}$$

and initial conditions

$$\begin{aligned} &T(x,s)=\phi_1(x,s)\geq 0,\qquad I(x,s)=\phi_2(x,s)\geq 0,\\ &V(x,s)=\phi_3(x,s)\geq 0,\qquad (x,s)\in\bar{\Omega}\times[-\tau,0], \end{aligned} \tag{3}$$

where $\tau=\max(\tau_1,\tau_2)$, Ω is a bounded domain in $\mathbb{R}^n$ with smooth boundary $\partial\Omega$, and $\frac{\partial v}{\partial \nu}$ denotes the outward normal derivative on $\partial\Omega$. We have proved the existence, positivity and boundedness of solutions to ensure the well-posedness of the problem. Further, we have investigated of the global stability of equilibria in terms of the basic reproduction number R_0 which is given by

$$R_0=\frac{k}{au}f\left(\frac{\lambda}{d},0,0\right)e^{-\alpha_1\tau_1-\alpha_2\tau_2}.$$

System (1) includes three PDEs which cannot be solved explicitly. Also, statistical and clinical data on infectious diseases are collected and analyzed at discrete times. For these reasons, we will discretize system (1) by using 'mixed' Euler method that is a mixture of both forward and backward Euler methods. Recently, this numerical method is used for viral infection models governed by ODEs in [24,25] and for delayed viral infection models governed by DDEs in [10]. The choice of the discretization scheme is motivated by the work of Hattaf et al. [26]. Note that the authors Qin et al. [27] in their recent paper discretized system (1) in the case without delays ($\tau_1=\tau_2=0$) the incidence rate is bilinear ($f(T,I,V)=\beta T$). They proved the positivity of approximate solutions by using the theory of M-matrices. Further, they established the global stability of equilibria. But they not investigated the boundedness of solutions. In this study, we will prove that the delayed discrete model obtained by the mixed Euler method maintains essential dynamical properties, such as positivity, boundedness and global behaviors of solutions with no restriction on the space and time step sizes.

The organization of the rest of this paper is as follows. In the next section, we introduce the numerical method to discretize system (1), and establish some preliminary results. In Section 3, we investigate the global dynamics of the delayed discrete model derived from the discretization scheme by constructing appropriate discrete Lyapunov functionals. In Section 4, we give an application and present some numerical simulations. The paper ends with a brief conclusion in Section 5.

2. Numerical method and preliminaries

In the following, we consider our model (1) in the spatial domain $\Omega=[x_{\min},x_{\max}]$ where $x_{\min},x_{\max}\in\mathbb{R}$. Let Δt be the time step size and $\Delta x=(x_{\max}-x_{\min})/N$ be the space step size with N is a positive integer. Assume that there exist two integers $(m_1,m_2)\in\mathbb{N}^2$ with $\tau_1=m_1\Delta t$ and $\tau_2=m_2\Delta t$. The space and time grid points are $x_n=x_{\min}+n\Delta x$ for $n\in\{0,1,\ldots,N\}$ and $t_m=m\Delta t$ for $m\in\mathbb{N}$. The solution of system (1) at the discretized spatio-temporal point (x_n,t_m) is $\big(T(x_n,t_m),I(x_n,t_m),V(x_n,t_m)\big)$. Hence, we denote the approximations of $T(x_n,t_m)$, $I(x_n,t_m)$ and $V(x_n,t_m)$ by T_n^m, I_n^m and V_n^m,

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