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Nonstandard finite difference scheme for a diffusive within-host virus dynamics model with both virus-to-cell and cell-to-cell transmissions☆

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ABSTRACT

In this paper, we first propose a diffusive within-host virus dynamics model with both virus-to-cell and cell-to-cell transmissions. Then, we consider the discretization of the model by using nonstandard finite difference scheme. It is then followed by the investigation of the global stability of the equilibria of the discrete model. Our study shows that if the basic reproduction number $\mathcal{R}_0 \leq 1$, then the infection-free equilibrium is globally asymptotically stable; however if $\mathcal{R}_0 > 1$, then the infection equilibrium is globally asymptotically stable. Numerical simulations are presented to illustrate our theoretical results.

1. Introduction

The classical model for within-host virus dynamics is a system of three ordinary differential equations [1,2], where the key assumption is that cells and viruses are well mixed. Recent study shows that the interaction between pathogens and the immune response actually tends to be local within the body of infected hosts [3]. Hence, there is a need to study the effect of spatial structure on virus dynamics. To this end, Wang and Wang [4] considered the following model taking into account the random mobility of viruses

$$\begin{cases} \dfrac{\partial T}{\partial t} = B - d_1 T(x,t) - \beta_1 T(x,t) V(x,t), \\ \dfrac{\partial I}{\partial t} = \beta_1 T(x,t) V(x,t) - d_2 I(x,t), \\ \dfrac{\partial V}{\partial t} = d \triangle V(x,t) + \gamma I(x,t) - d_3 V(x,t), \end{cases} \tag{1.1}$$

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 at time t, respectively. B is the recruitment rate of the uninfected cells. β_1 is the virus-to-cell infection rate. d_1, d_2 and d_3 are death rates

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of uninfected cells, infected cells and free viruses, respectively. γ is the recruitment rate for free viruses. d is the diffusion coefficient and Δ is the Laplacian operator. Then they investigated the existence of traveling wave solution when $x \in \mathbf{R}$.

Since then, the study of dynamical behavior of virus dynamics with spatial structure has attracted much attention, for example Brauner et al. [5], Stancevic et al. [6], Hattaf and Yousfi [7,8], McCluskey and Yang [9], Wang et al. [10], Wang and Wang [11], Xu and Ma [12], Zhang and Xu [13]. Many of these studies only focus on virus-to-cell spread in the bloodstream even though some studies reveal that cell-to-cell transmission is vital to spread of virus in vivo such as Bangham [14], Culshaw et al. [15], Dimitrov et al. [16], Gummuluru et al. [17], Sigal et al. [18]. Motivated by this fact, some researchers have constructed ODE and DDE models to investigate the dynamics of within-host virus dynamics models to take both virus-to-cell and cell-to-cell transmissions into account, for instance, Lai and Zou [19,20], Li and Wang [21], Pourbashash et al. [22], Yang et al. [23]. To the best of our knowledge, there is barely any work studying the diffusive within-host virus dynamics model with both virus-to-cell and cell-to-cell transmissions. Therefore, in this paper, we propose the following model

$$\begin{cases} \dfrac{\partial T}{\partial t} = B - d_1 T(x,t) - \beta_1 T(x,t)V(x,t) - \beta_2 T(x,t)I(x,t), \\ \dfrac{\partial I}{\partial t} = \beta_1 T(x,t)V(x,t) + \beta_2 T(x,t)I(x,t) - d_2 I(x,t), \\ \dfrac{\partial V}{\partial t} = d\triangle V(x,t) + \gamma I(x,t) - d_3 V(x,t), \end{cases} \tag{1.2}$$

where $\beta_2 \geq 0$ is the cell-to-cell infection rate. When $\beta_2 = 0$, system (1.2) reduces to system (1.1).

In general, system of PDEs cannot be solved explicitly. Thus, people seek numerical ones instead. However, the problem of proper selection of the discrete scheme so that the global stability of equilibria of the corresponding continuous models can be preserved remains open [24]. Mickens made an attempt in this regard, by proposing a robust nonstandard finite difference (NSFD) scheme [25], which has been widely employed in the study of different epidemic models, for example, Arenas et al. [26], Ding et al. [27], Hattaf and Yousfi [28,29], Jódar et al. [30], Liu et al. [31], Muroya et al. [32]. More recently, Qin et al. [33] used the NSFD scheme to discretize system (1.1) and found that the discrete model has the same dynamics as the original system.

The purpose of this paper is to study the dynamics of the discretized system of (1.2), by using the NSFD scheme. We first give some basic results about the system in Section 2. Then, using the theory of M-matrix, we prove, in Section 3, that the solution of discrete model is positive for given initial values and any spatial and time step sizes. In Section 4, by constructing discrete Lyapunov functions, we show that the global stability of the discretized model depends only on the basic reproduction number, $\mathcal{R}_0$. It is then followed by numerical simulations, in Section 5, and a brief conclusion in Section 6.

2. Local stability of equilibria of system (2.1)

For the convenience of discussion, introduce

$$\overline{T} = \frac{d_1 T}{B}, \quad \overline{I} = \frac{d_1 I}{B}, \quad \overline{V} = \frac{\beta_1 V}{d_1}, \quad \overline{t} = d_1 t,$$
$$\rho_0 = \frac{\beta_2 B}{d_1^2}, \quad \rho_1 = \frac{d_2}{d_1}, \quad \rho_2 = \frac{\beta_1 \gamma B}{d_1^3}, \quad \rho_3 = \frac{d_3}{d_1}, \quad \overline{D} = \frac{d}{d_1}.$$

And then after dropping the overhead bars for simplicity of notations, one obtains

$$\begin{cases} \dfrac{\partial T}{\partial t} = 1 - T(x,t) - T(x,t)V(x,t) - \rho_0 T(x,t)I(x,t), \\ \dfrac{\partial I}{\partial t} = T(x,t)V(x,t) + \rho_0 T(x,t)I(x,t) - \rho_1 I(x,t), \\ \dfrac{\partial V}{\partial t} = D\triangle V(x,t) + \rho_2 I(x,t) - \rho_3 V(x,t). \end{cases} \tag{2.1}$$

Now, we assume that system (2.1) is subject to initial value condition

$$T(x,0) = \phi(x) \geq 0, \quad I(x,0) = \varphi(x) \geq 0, \quad V(x,0) = \psi(x) \geq 0, \quad x \in \overline{\Omega},$$

and Neumann boundary condition

$$\frac{\partial V}{\partial \vec{n}} = 0, \quad t > 0, \quad x \in \partial\Omega,$$

where Ω is a connected, bounded domain in $\mathbb{R}^n$ with smooth boundary $\partial\Omega$, $\frac{\partial}{\partial \vec{n}}$ is an outward normal vector of $\partial\Omega$.

It is easy to see that system (2.1) always has an infection-free equilibrium $E_0(1, 0, 0)$. And if

$$\mathcal{R}_0 = \frac{\rho_2 + \rho_0\rho_3}{\rho_1\rho_3},$$