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Dynamics of a PDE viral infection model incorporating cell-to-cell transmission

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ABSTRACT

This paper is concerned with the global dynamics of a PDE viral infection model with cell-to-cell transmission and spatial heterogeneity. The basic reproduction number $\Re_0$, which is a threshold value that predicts whether the infection will go to extinction or not, is defined in a variational characterization. In quite a general setting in which every parameter can be spatially heterogeneous, it is shown that if $\Re_0 \leq 1$, then the infection-free steady state is globally asymptotically stable, while if $\Re_0 > 1$, then the system is uniformly persistent and the infection steady state is globally asymptotically stable. The proof is based on the construction of the Lyapunov functions and usage of the Green's first identity. Finally, numerical simulation is performed in order to verify the validity of our theoretical results.

1. Introduction

In recent years, the in-host viral infection models incorporating spatial dispersion have been considered. In these models, it is assumed that only the free virus diffuses while the host cells do not (see e.g. [7,2,25] and the references cited therein). Such hybrid systems of differential equations (that is, systems of two ordinary differential equations (ODEs) for the cells and one parabolic partial differential equation (PDE) for the virus) account for the spatial dispersion of virus due to many factors: i) the interaction between the virus and the immune system is localized according to the type of tissues and also in a given tissue such as lymph nodes [2]; ii) the hepatocytes can not move under normal conditions [25,29,15] and viruses can move freely and their motion follows a Fickian diffusion [26]. In order to be more realistic, these models often incorporate: i) time delays, where the delays take into account the time between infection of a target cell

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and the emission of viral particles [25]; ii) heterogeneous parameters, where all parameters are allowed to be location dependent except the diffusion coefficient [26].

Due to the PDEs formulations, the system should be analyzed under suitable spatial domain equipped with suitable boundary condition. In Wang et al. [25], the densities of uninfected cells, infected cells and free viruses are assumed to be located at x at time t, which are denoted by $u_1(x,t)$, $u_2(x,t)$, $u_3(x,t)$, respectively, and the spatial domain is assumed to be one dimensional, that is, $(x,t) \in (-\infty,\infty) \times (0,\infty)$. Brauner et al. [2] extended the works in [25] to a two-dimensional square domain $(0,l) \times (0,l)$ with periodic boundary conditions, and provided that the recruitment rate to be space dependent. In a recent work, Wang et al. [26] argued that a realistic spatial domain should be bounded but is typically not a square, under suitable types of boundary conditions. They proposed a zero-flux boundary condition in a general bounded domain $\Omega \subset \mathbb{R}^n$ with smooth boundary $\partial\Omega$ (homogeneous Neumann boundary condition). The model studied in [26] takes the following hybrid system of two ODEs and one PDE:

$$\begin{cases} \dfrac{\partial u_1(x,t)}{\partial t} = \lambda(x) - \beta_1(x)u_1(x,t)u_3(x,t) - a(x)u_1(x,t), \\ \dfrac{\partial u_2(x,t)}{\partial t} = \beta_1(x)u_1(x,t)u_3(x,t) - b(x)u_2(x,t), \quad (x,t) \in \Omega \times (0,\infty), \\ \dfrac{\partial u_3(x,t)}{\partial t} = d\Delta u_3(x,t) + k(x)u_2(x,t) - m(x)u_3(x,t), \\ \dfrac{\partial u_3(x,t)}{\partial \nu} = 0, \quad x \in \partial\Omega, \quad t > 0, \\ u_i(x,0) = u_i^0(x) \geq 0, \quad x \in \Omega, \quad i = 1,2,3. \end{cases} \tag{1.1}$$

Here, for each $x \in \Omega$, $\lambda(x)$ denotes the number of newly produced uninfected cells, $a(x)$, $b(x)$ and $m(x)$ denote the death rates of uninfected cells, infected cells and free viruses, respectively. $\beta_1(x)$ is the transmission coefficient for virus-to-cell infection, $k(x)$ is the rate of virus production due to the lysis of infected cells, d is the diffusion coefficient and Δ is Laplacian. By analyzing the model and identifying the basic reproduction number, they only obtained the global dynamics of the model when all model parameters are constants (the spatially homogeneous case), but the global dynamics of heterogeneous parameters case was left as an open problem. Recent studies in [29], a hepatitis B virus infection with delay, diffusion and Holling type-II infection rate was investigated. They proved the global stability of infection-free steady state by comparison arguments when the basic reproductive number is less than unity, and obtained sufficient conditions for the global stability of infection steady state when the basic reproductive number is greater than unity. Chí et al. [4] provided a detailed analysis of similar model but with standard incidence function. By means of an iteration technique, sufficient conditions for the global stability of the infection steady state were obtained. In [15], McCluskey and Yang successfully proved the threshold dynamics of a viral infection model by constructing Lyapunov functions, which contains time delay and a general incidence function.

Recent studies reveal that the high efficiency of infection by large numbers of virions can be vital to a transfer of multiple virions to an uninfected target cell [20,9]. The virus-induced cell-cell fusion observed from experiments is very likely the result of gp120/gp41 proteins, on the surface of infected cells, interacting with CD4 molecules on uninfected cells [14,22]. In this case, viral particles can be transferred from infected target cells to uninfected ones through virological synapses. From these findings, we have no doubt that the direct cell-to-cell infection affects the mechanism(s) of HIV-1 transmission in vivo. We list some extensive literatures for studying the dynamics of cell-to-cell spread of HIV with and without delays [10,30,11].

Motivated by the previous works, to examine the effects of both diffusion and spatial heterogeneity, incorporating cell-to-cell transmission into system (1.1) leads to the following hybrid system of two ODEs coupled with one PDE under the homogeneous Neumann boundary condition: