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Global stability of a diffusive virus dynamics model with general incidence function and time delay

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ABSTRACT

In this paper, we propose a model of virus dynamics that includes diffusion, time delay and a general incidence function. By constructing Liapunov functionals, we show that the model has threshold dynamics: if the basic reproduction number $\mathcal{R}_0 \leq 1$, then the infection-free equilibrium is globally asymptotically stable; whereas if $\mathcal{R}_0 > 1$, then there exists an infection equilibrium which is globally asymptotically stable. We pay particular attention to demonstrating that solutions are sufficiently bounded away from 0 that the Liapunov functionals are well-defined. Some applications are listed. Our results improve and generalize some known results.

1. Introduction

Mathematical models have been developed to explore mechanisms and dynamical behaviours of the in-host viral infection process. A basic virus dynamics model consists of the following simple three dimensional system (see [1,2]):

$$\begin{cases} \dot{x}(t) = \lambda - dx(t) - \beta x(t)v(t), \\ \dot{y}(t) = \beta x(t)v(t) - \delta y(t), \\ \dot{v}(t) = ky(t) - \mu v(t). \end{cases} \tag{1.1}$$

The uninfected cell population is denoted by x, infected cells by y and free virus particles by v. The uninfected cells are produced at a constant rate λ and are infected by free virions at a rate βxv. Parameters d, δ and μ represent the death rates of uninfected cells, infected cells and free virus, respectively. The free virions are produced from the infected cells at a rate ky.

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By constructing Liapunov functions, Korobeinikov [3] established the global stability of system (1.1), which uses mass action incidence. Other more complicated incidence functions have been proposed. Regoes et al. [4] proposed a virus dynamics model with the incidence function $x(v/\kappa)^p/(1+(v/\kappa)^p)$ where $\kappa > 0$ and $p > 1$. Song and Neumann [5] proposed an incidence function $xv^p/(1+\alpha v^q)$ where p, q, $\alpha > 0$. Li and Ma [6] considered a delayed HIV-1 infection model with Holling type-II incidence $\beta xv/(1+\alpha v)$. Using a Liapunov functional, they discussed global stability of the infection-free equilibrium. They conjectured that the infection equilibrium of the model is globally stable.

McCluskey [7–9] developed a class of Liapunov functionals to study the global dynamics of delay epidemiological models. Motivated by the works of McCluskey, Nakata [10] investigated the global dynamics of an in-host virus model with Beddington–DeAngelis incidence $\beta xv/(1+ax+bv)$ and with a fixed delay upon infection before becoming infectious, providing an affirmative answer for a conjecture by Li and Ma [6]. For more details about virus dynamics models with Beddington–DeAngelis incidence function, we refer to [11–16].

Recently, virus models with general nonlinear incidence functions have attracted significant attention. Korobeinikov [17] studied an ordinary differential equation model with general nonlinear incidence. Li and Shu [18] considered a model with general nonlinear incidence and distributed delay, while Huang et al. [19] considered a similar model with discrete delay. Hattaf et al. [20] considered a model with general incidence function and two delays.

A key assumption in system (1.1) is that cells and viruses are well mixed. Wang and Wang [21] included a spatial component, adding Fickian diffusion for the virus while assuming that the movement of cells is slow enough that it can be ignored. They obtained the following model:

$$\begin{cases} \dfrac{\partial u}{\partial t} = \lambda - du(x,t) - \beta u(x,t)v(x,t), \\ \dfrac{\partial w}{\partial t} = \beta u(x,t)v(x,t) - \delta w(x,t), \\ \dfrac{\partial v}{\partial t} = D\triangle v(x,t) + kw(x,t) - \mu v(x,t), \end{cases} \tag{1.2}$$

where $u(x,t)$, $w(x,t)$ and $v(x,t)$ represent the densities of uninfected cells, infected cells and free virus at position x at time t, respectively. $\triangle$ is the Laplacian operator and D is the diffusion coefficient.

Then, based on system (1.2), Xu and Ma [22] studied a delayed HBV model with diffusion and Holling type-II incidence. Using comparison arguments, they proved that the uninfected steady state is globally asymptotically stable when the basic reproduction is less than unity and established sufficient conditions for the global stability of the infected steady state. Using Liapunov functionals, Hattaf and Yousfi [23] investigated the global stability of some diffusion equations in biology, including a delayed in-host model with diffusion and Beddington–DeAngelis incidence. More recently, Zhang and Xu [24] provided a detailed analysis of the same model applied to HBV with homogeneous Neumann boundary conditions.

In several previous works involving Liapunov functionals, there has not been proper attention paid to the fact that the Liapunov functional for the interior equilibrium may not be defined when the state variables are zero or close to zero. This stems from the fact that the functional often includes a logarithm (or some other function that is unbounded near zero). Typically, some type of uniform persistence result is needed in order to show that the limit sets are sufficiently bounded away from zero that the integrals involved in the functionals are well-defined. In this paper, we carefully address this issue.

Motivated by the works of [23,22,24], we study the following model:

$$\begin{cases} \dfrac{\partial u}{\partial t} = \lambda - du(x,t) - f(u(x,t),v(x,t)), \\ \dfrac{\partial w}{\partial t} = \mathrm{e}^{-m\tau} f(u(x,t-\tau),v(x,t-\tau)) - \delta w(x,t), \\ \dfrac{\partial v}{\partial t} = D\triangle v(x,t) + kw(x,t) - \mu v(x,t), \end{cases} \tag{1.3}$$