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Stability and Hopf bifurcation for a virus infection model with delayed humoral immunity response

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ABSTRACT

In this paper, we investigate the dynamical behavior of a virus infection model with delayed humoral immunity. By using suitable Lyapunov functional and the LaSalle's invariance principle, we establish the global stabilities of the two boundary equilibria. If $R_0 < 1$, the uninfected equilibrium E_0 is globally asymptotically stable; if $R_1 < 1 < R_0$, the infected equilibrium without immunity E_1 is globally asymptotically stable. When $R_1 > 1$, we obtain the sufficient conditions to the local stability of the infected equilibrium with immunity E_2. The time delay can change the stability of E_2 and lead to the existence of Hopf bifurcations. The stabilities of bifurcating periodic solutions is also studied. We check our theorems with numerical simulations in the end.

1. Introduction

Many virus infection models have been studied recently (see [1–3,5–21]). As we all know that immunity response plays an important role in protecting us from virus infections. A specific immunity is composed of humoral immunity and cellular immunity, which is mainly expressed by B cells and T cells separately. Models with cellular immunity have been analyzed by many researchers (see [10,11,16,19–21]). But the humoral immunity is more effective than cellular in some infection processes (see [3]). Shifei Wang (see [17]) discussed a model with humoral immunity

$$\begin{cases} T'(t) = \lambda - \beta TV - dT, \\ I'(t) = \beta TV - aI, \\ V'(t) = kI - uV - qBV, \\ B'(t) = gBV - cB, \end{cases}$$

where $T(t)$, $I(t)$, $V(t)$ and $B(t)$ denote the concentration of the uninfected cells, the infected cells, the virus and the B cells at time t, respectively. Constants d, a, u and c represent, respectively, the death rate of the uninfected cells, the infected cells, the virus and the B cells. Constant β is the infection rate of the uninfected cells. Constants λ, k and g are birth rate of the uninfected cells, the virus and the B cells, respectively. Constant q is removed rate of virus.

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In the end of [17], they discussed the following delay model

$$\begin{cases} T'(t) = \lambda - \beta T V - dT, \\ I'(t) = \beta T(t-\tau_1)V(t-\tau_1) - aI, \\ V'(t) = kI(t-\tau_2) - uV - qBV, \\ B'(t) = gBV - cB. \end{cases}$$

The intracellular delay, τ_1, represents the time between viral entry into a cell and the production of new virus particles. τ_2 represents the maturation time of the newly produced viruses. Their theorems show that the two delays cannot change the stabilities of the three equilibria. So we discuss a new delay in the following model

$$\begin{cases} T'(t) = \lambda - \beta T(t)V(t) - dT(t), \\ I'(t) = \beta T(t)V(t) - aI(t), \\ V'(t) = kI(t) - uV(t) - qB(t)V(t), \\ B'(t) = gB(t-\tau)V(t-\tau) - cB(t), \end{cases} \tag{1.1}$$

where τ represents the time that antigenic stimulation needs for generating immunity response [15]. The initial conditions for system (1.1) take the form

$$\big(T(0), I(0), V_0(\theta), B_0(\theta)\big) \in R_+ \times R_+ \times C^+ \times C^+,$$

where $C^+ = C([-\tau, 0], R_+)$ which is the Banach space of continuous functions mapping the interval $[-\tau, 0]$ into R_+ with the topology of uniform convergence.

This paper is organized as follows. In the next section, we discuss the global asymptotic stabilities of the two boundary equilibria, the infection-free equilibrium and the infected equilibrium without B cells response. In Section 3, we analyze the local stability of the positive equilibrium and the existence of Hopf bifurcations. The orbital asymptotic stabilities of the bifurcating periodic solutions are studied in Section 4. In Section 5, we present the numerical simulations to illustrate our result. The conclusions of our paper are given in Section 6.

2. Global stabilities of two boundary equilibria

Considering the existence of the three equilibria, we have the following theorem.

Theorem 2.1. *(See [9].) The infection-free equilibrium of system (1.1) is $E_0 = (T_0, 0, 0, 0)$ where $T_0 = \frac{\lambda}{d}$. If and only if $R_0 > 1$, where*

$$R_0 = \frac{\lambda k \beta}{aud},$$

there exists the other boundary equilibrium without B cells response $E_1 = (T_1, I_1, V_1, 0)$, where

$$T_1 = \frac{au}{\beta k}, \qquad I_1 = \frac{u}{k}V_1 \quad \text{and} \quad V_1 = \frac{\lambda k}{au} - \frac{d}{\beta}.$$

If and only if

$$R_1 = \frac{k\beta\lambda}{au(d + \beta\frac{c}{g})} > 1,$$

there exists an infected equilibrium $E_2 = (T_2, I_2, V_2, B_2)$, where

$$V_2 = \frac{c}{g}, \qquad T_2 = \frac{\lambda}{\beta V_2 + d}, \qquad I_2 = \frac{\beta c}{ag}T_2 \quad \text{and} \quad B_2 = \frac{k\beta}{aq}T_2 - \frac{u}{q}.$$

Next we investigate the global stabilities of two boundary equilibria.

Theorem 2.2. *If $R_0 < 1$, the infection-free equilibrium E_0 of system (1.1) is globally asymptotically stable. If $R_0 > 1$, E_0 is unstable.*

Proof. Consider a Lyapunov functional

$$L_0(t) = T(t) - T_0 - T_0 \ln \frac{T(t)}{T_0} + I(t) + \frac{a}{k}V(t) + \frac{aq}{gk}B(t) + \frac{aq}{k}\int_{t-\tau}^{t} B(\theta)V(\theta)\,\mathrm{d}\theta.$$