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Research Article

On the Stability Property of the Infection-Free Equilibrium of a Viral Infection Model

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The dynamics of a viral infection model with nonautonomous lytic immune response is studied from the perspective of dying out of the disease. With the help of the theory of exponential dichotomy of linear systems, we give a new proof about the global asymptotic stability of the infection-free equilibrium for the case $R_0 = 1$. The result improves and complements one of the results of Wang et al. (2006).

1. Introduction

Throughout this paper, given a bounded continuous function p defined on R, let p^l and p^u be defined as

$$p^l = \inf_{t\in R} p(t), \qquad p^u = \sup_{t\in R} p(t). \tag{1.1}$$

The aim of this paper is to investigate the stability property of the infection-free equilibrium of the following nonautonomous viral infection model:

$$\begin{aligned} \dot{x}(t) &= \lambda - dx - \beta xy, \\ \dot{y}(t) &= \beta xy - ay - p(t)yz, \\ \dot{z}(t) &= cy - bz, \end{aligned} \tag{1.2}$$

where $x(t)$, $y(t)$, and $z(t)$, represents susceptible host cells, a virus population, and a CTL response, respectively. Susceptible host cells are generated at a rate λ, die at a rate dx, and become infected by virus at a rate βxy. Infected cells die at a rate ay and are killed by the CTL response at a rate $p(t)yz$. The CTL response expands in response to viral antigen derived from infected cells at a rate cy and decay in the absence of antigenic stimulation at a rate bz. We assume that λ, d, β, a, c, and b are all positive constants and $p(t)$ is a continuous, real-valued functions which is bounded above and below by positive constants. For more detail deduction and background of the above model, see Wang et al. [1] and Fan and Wang [2].

We consider (1.2) together with the following initial conditions

$$x(0) > 0, \quad y(0) > 0, \quad z(0) > 0. \tag{1.3}$$

It is not difficult to see that solutions of (1.2)-(1.3) are well defined and positive for all $t \geq 0$.

Recently, Wang et al. [1] proposed and studied the dynamic behaviors of the system (1.2). Obviously, system (1.2) admits one and only one steady state $E_0 = (x^*, 0, 0) = (\lambda/d, 0, 0)$, which represents the infection-free equilibrium. The basic reproductive ratio of the virus is given by $R_0 = \lambda\beta/ad$. It can be expected that disease dies out if $R_0 < 1$ and becomes endemic if $R_0 > 1$. However, it seems not an easy thing to deal with the critical case $R_0 = 1$. In [1], the authors obtained the following interesting result.

Theorem A. *The infection-free equilibrium E_0 is globally asymptotically stable if $R_0 = 1$.*

Indeed, in their proof of Theorem A, by using the variation of constants formula for inhomogeneous linear ordinary differential equations, the solution to the third equality of system (1.2) takes the form

$$z(t) = z(0)e^{-bt} + \frac{\int_0^t cy(s)e^{bs}ds}{e^{bt}}. \tag{1.4}$$

From this equality, they immediately declared that

$$\left| z(t) - \frac{cy(t)}{b} \right| \longrightarrow 0 \quad \text{as } t \longrightarrow +\infty. \tag{1.5}$$

Maybe it is obviously to some scholars that equality (1.4) implies (1.5), however, we found it is not an easy thing for us to understand this deduction. Since (1.4) and (1.5) play crucial role in their prove of Theorem A, it motivated us to propose the following interesting issue.

Is It Possible for Us to Give a Different Proof of Theorem A?

On the other hand, we argue that it is more suitable to consider a general nonautonomous $p(t)$ than that of a periodic function. Thus, it is natural to propose the following question.

Whether the Conclusion of Theorem A Still Holds Under the Assumption That $p(t)$ is a General Positive Nonautonomous Continuous Function?

The aim of this paper is, by applying the theory of exponential dichotomies of linear system [3, 4] and adapting some analysis technique recently developed by Chen et al. [5–8], to give an affirmed answer to above two issues, more precisely, we obtain the following theorem.

Theorem B. *Let $p(t)$ be a positive continuous function bounded above and below by positive constants. Then the infection-free equilibrium E_0 of system* (1.2) *is globally asymptotically stable if* $R_0 = 1$.

We will prove Theorem B in the next section and give a numeric simulation in Section 3. We end this paper by a briefly discussion. For more works on viral infection model, one could refer to [1–6, 9–17] and the references cited therein. For the works about the stability of differential equations, one could refer to [7, 8, 18, 19] and the references cited therein.

2. Proof of Theorem B

Now we state several lemmas which will be useful in proving of our main result.

Lemma 2.1 (see [13]). *If $a > 0$, $b > 0$ and $\dot{x} \geq x(b - ax)$, when $t \geq t_0$ and $x(t_0) > 0$, one has*

$$\liminf_{t \to +\infty} x(t) \geq \frac{b}{a}. \tag{2.1}$$

If $a > 0$, $b > 0$ and $\dot{x} \leq x(b - ax)$, when $t \geq t_0$ and $x(t_0) > 0$, one has

$$\limsup_{t \to +\infty} x(t) \leq \frac{b}{a}. \tag{2.2}$$

Lemma 2.2. *Let b be a positive constant and let $c(t)$ is a nonnegative continuous bounded function, then system*

$$\dot{x}(t) = -bx + c(t) \tag{2.3}$$

admits a unique bounded solution $x^*(t)$, which is globally attractive.

Proof. Since b is a positive constant, it follows that system

$$\dot{x}(t) = -bx \tag{2.4}$$

admits the exponential dichotomies. From He [3, page 59] or Lin [4, page 55] we know that (2.3) admits a unique bounded solution

$$x^*(t) = \int_{-\infty}^{t} e^{-b(t-s)} c(s) ds. \tag{2.5}$$

Let $x(t)$ be any solution of system (2.3), and $u(t) = x(t) - x^*(t)$. Then

$$\begin{aligned}\dot{x}(t) &= -bx(t) + c(t),\\ \dot{x}^*(t) &= -bx^*(t) + c(t).\end{aligned} \tag{2.6}$$

It follows that u satisfies

$$\dot{u}(t) = -bu(t). \tag{2.7}$$

Thus,

$$u(t) = u(0)e^{-bt} \longrightarrow 0 \quad \text{as } t \longrightarrow +\infty, \tag{2.8}$$

that is,

$$\lim_{t\to+\infty}(x(t) - x^*(t)) = 0. \tag{2.9}$$

This ends the proof of Lemma 2.3. □

Lemma 2.3 (see [1]). *All solutions of system* (1.2) *are positive for* $t > 0$ *and there exists* $M > 0$, *such that all the solutions satisfy* $x(t)$, $y(t)$, $z(t) < M$ *for all large* t.

Lemma 2.4 (see [1]). *Let* $x^\infty = \limsup_{t\to+\infty} x(t)$. *Then* $x^\infty \le x^* := \lambda/d$.

Proof of Theorem B. Let $(x(t), y(t), z(t))^T$ be any positive solution of system (1.2), from Lemma 2.4 it follows that $y(t)$ is bounded for all $t > 0$. From the third equation of system (1.2) we have

$$\dot{z}(t) = cy(t) - bz(t). \tag{2.10}$$

It follows from Lemma 2.3 that system (2.10) admits a unique bounded solution

$$z^*(t) = \int_{-\infty}^{t} e^{-b(t-s)}cy(s)ds, \tag{2.11}$$

also,

$$|z(t) - z^*(t)| \longrightarrow 0 \quad \text{as } t \longrightarrow +\infty, \tag{2.12}$$

For arbitrarily small positive constant ε (without loss of generality, we may assume that $2(b+(\beta+p^u)\varepsilon)\ \varepsilon<1$), it follows from (2.12) and Lemma 2.2 that there exists a $T_1>0$ such that for all $t>T_1$

$$\begin{aligned} z(t) &> z^*(t)-\varepsilon, \\ x(t) &< x^*+\varepsilon. \end{aligned} \tag{2.13}$$

Substituting (2.13) to the second equation of system (1.2) leads to

$$\dot{y}=\beta xy-ay-p(t)yz\le\left(\beta(x^*+\varepsilon)-a-p(t)(z^*-\varepsilon)\right)y. \tag{2.14}$$

Noting that $R_0=1$, which implies that $\beta x^*-a=0$, thus, above inequality leads to

$$\begin{aligned} \dot{y}(t) &\le \left((\beta+p(t))\varepsilon-cp(t)\int_{-\infty}^{t}e^{-b(t-s)}y(s)ds\right)y(t) \\ &\le \left((\beta+p^u)\varepsilon-cp^l\int_0^{\infty}e^{-bs}y(t-s)ds\right)y(t) \\ &\le \left((\beta+p^u)\varepsilon-cp^l\int_0^{t}e^{-bs}y(t-s)ds\right)y(t). \end{aligned} \tag{2.15}$$

It follows from (2.15) that

$$\dot{y}(t)\le(\beta+p^u)\varepsilon y(t). \tag{2.16}$$

For $t-s\ge 0$, integrating (2.16) on $[t-s,t]$, we derive

$$y(t-s)\ge y(t)e^{-(\beta+p^u)\varepsilon s}. \tag{2.17}$$

Substituting (2.17) into (2.15) leads to

$$\begin{aligned} \dot{y}(t) &\le \left((\beta+p^u)\varepsilon-cp^l\int_0^{t}e^{-bs}y(t)e^{-(\beta+p^u)\varepsilon s}ds\right)y(t) \\ &= \left((\beta+p^u)\varepsilon-cp^l\int_0^{t}e^{-(b+(\beta+p^u)\varepsilon)s}ds\,y(t)\right)y(t). \end{aligned} \tag{2.18}$$

Noting that

$$\int_0^{t}e^{-(b+(\beta+p^u)\varepsilon)s}ds\longrightarrow\int_0^{\infty}e^{-(b+(\beta+p^u)\varepsilon)s}ds=\frac{1}{b+(\beta+p^u)\varepsilon}\quad\text{as } t\longrightarrow+\infty. \tag{2.19}$$

It follows from (2.19) that for above $\varepsilon > 0$, there exists an enough large $T_1 > 0$ such that for all $t > T_1$,

$$\int_0^t e^{-(b+(\beta+p^u)\varepsilon)s} ds \geq \frac{1}{b + (\beta + p^u)\varepsilon} - \varepsilon \geq \frac{1}{2(b + (\beta + p^u)\varepsilon)}. \tag{2.20}$$

Substituting (2.20) into (2.18), for $t \geq T_1$, one has

$$\dot{y}(t) \leq \left((\beta + p^u)\varepsilon - \frac{cp^l}{2(b + (\beta + p^u)\varepsilon)} y(t) \right) y(t). \tag{2.21}$$

Applying Lemma 2.1 to (2.18), it immediately follows that

$$\limsup_{t \to +\infty} y(t) \leq \frac{2\left[b + (\beta + p^u)\varepsilon\right](\beta + p^u)\varepsilon}{cp^l}. \tag{2.22}$$

Since $y(t) > 0$ for all $t > 0$, it follows that

$$0 \leq \liminf_{t \to +\infty} y(t) \leq \limsup_{t \to +\infty} y(t) \leq \frac{2\left[b + (\beta + p^u)\varepsilon\right](\beta + p^u)\varepsilon}{cp^l}. \tag{2.23}$$

Since ε is arbitrarily small positive constant, setting $\varepsilon \to 0$ in (2.23) leads to

$$\lim_{t \to +\infty} y(t) = 0. \tag{2.24}$$

The rest of the proof is similarly to the proof of Theorem 2.2 in [1] and we omit the detail here. □

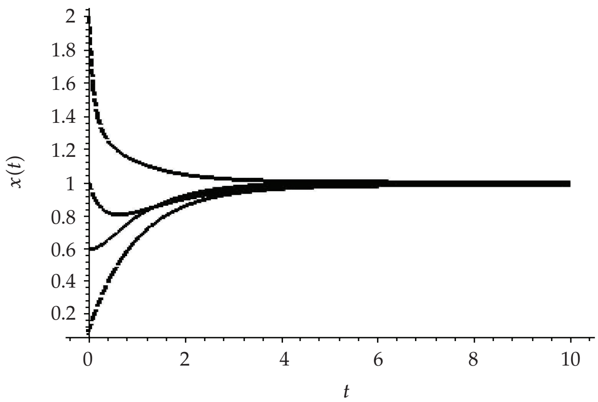

Figure 1: Dynamic behaviors of the first component $x(t)$ of the solution $(x(t), y(t), z(t))^T$ to system (3.1) with the initial condition $(0.1, 0.1, 0.1)^T$, $(1, 1, 1)^T$, $(2, 3, 4)^T$, and $(0.6, 1, 2)^T$, respectively.

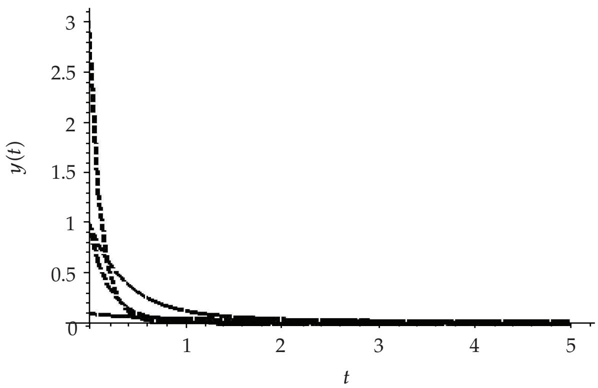

Figure 2: Dynamic behaviors of the second component $y(t)$ of the solution $(x(t), y(t), z(t))^T$ to system (3.1) with the initial condition $(0.1, 0.1, 0.1)^T$, $(1, 1, 1)^T$, $(2, 3, 4)^T$, and $(0.6, 1, 2)^T$, respectively.

3. An Example

Consider the following viral infection model:

$$\dot{x} = 1 - x - xy,$$
$$\dot{y} = xy - y - \left(3^{-t} + 1 + \frac{\cos\left(\sqrt{3}t\right)}{3} + \frac{\sin(t)}{3}\right)yz, \tag{3.1}$$
$$\dot{z} = \frac{1}{2}y - \frac{1}{3}z.$$

In this case, corresponding to system (1.2), $\lambda = a = d = \beta = 1$, $c = 1/2$, $b = 1/3$, $p(t) = 1 + \cos(\sqrt{3}t)/3 + \sin(t)/3$. Obviously, $R_0 = \lambda\beta/ad = 1$. Thus, as a consequence of Theorem B, the infection-free equilibrium E_0 is globally asymptotically stable. Numeric simulations (Figures 1, 2, and 3) support this conclusion. We mention here that since $p(t)$

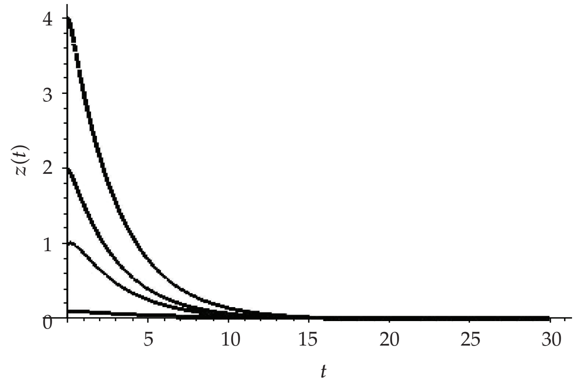

Figure 3: Dynamic behaviors of the third component $z(t)$ of the solution $(x(t), y(t), z(t))^T$ to system (3.1) with the initial condition $(0.1, 0.1, 0.1)^T$, $(1, 1, 1)^T$, $(2, 3, 4)^T$, and $(0.6, 1, 2)^T$, respectively.

is general nonautonomous continuous function, Theorem A could not be applied to system (3.1).

4. Conclusion

In this paper, we revisit the model proposed by Wang et al. [1]. By applying the theory of exponential dichotomy of linear systems and the differential inequality theory, we show that for general nonautonomous positive continuous coefficient $p(t)$, $R_0 = 1$ is enough to ensure the global asymptotic stability of the infection-free equilibrium.

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