·基础理论研究 ·

Dynamics of a Viral Model with Linear Infection Rate

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Abstract: This paper considers the classical mathematical model with a class of the linear infection rate. Boundedness of solutions, nature of equilibria, permanence, and stability are analyzed.

Key words: stability analysis; permanence; HIV

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0 Introduction

Over the past decade, a number of models (see [1～7]) have been developed to describe the immune system, its interaction with HIV, and the decline in $CD4^+$ T cells. These models consider the dynamics of the $CD4^+$ T cell and virus populations. In this paper, we introduce a population of uninfected target cells, T, and productively infected cells, I, the virus concentration, V. Although the population dynamics of target cells ($CD4^+$ T cells) is not completely understood. Nevertheless, a reasonable model for this population of cells is

$$\dot{T} = s - dT + aT(1 - T/T_{max}), \tag{1}$$

where T is the number of target cells, s represents the rate at which new T cells are created from sources within the body, such as the thymus, a is the maximum proliferation rate of target cells, T_{max} is the T population density at which proliferation shuts off, d is death rate of the T cells. If the oppulation ever reaches T_{max} it should decrease, thus we impose the constraint $dT_{max} > s$. Equation (1) has a single stable steady state given by

$$\hat{T} = \frac{T_{max}}{2a}[a - d + \sqrt{(a-d)^2 + 4as/T_{max}}]. \tag{2}$$

In the presence of virus, T cells become infected. The simplest and most common method of modelling infection is to augment (1) with a "mass-action" term in which the rate of infection is given by βTV, with β being the infection rate constant. This type of term is sensible, since virus must meet T cells to infect them and the probability of virus encountering a T cell at low concentrations (when V and T motions can be regarded as independent) can be assumed to be proportional to the product of their concentrations, which is called linear infection rate. Thus, in what follows, the classical models assume that infection occurs by virus, V, interacting with uninfected T cells, T, causing the loss of uninfected T cells at rate $-\beta TV$ and the generation of infected T cells at rate βTV.

We investigate the viral model with linear infection rate in the following. The model can be written as

$$\begin{aligned} \dot{T} &= s - dT + aT(1 - T/T_{max}) - \beta TV, \\ \dot{I} &= \beta TV - \delta I, \\ \dot{V} &= pI - cV. \end{aligned} \tag{3}$$

where T is the number of target cells, I is the number of infected cells, V is the viral load of the virions, s represents the rate at which new T cells are created from sources within the body, a is the maximum proliferation rate of target cells, T_{max} is the T population density at which proliferation shuts off, d is death rate of the T cells, β is the infection rate constant, δ is the loss rate constant of infection cells, p is the reproductive rate of the infected cell, and p/δ is the total number of virions produced by a productively infected cell during its lifetime, c is the clearence rate constant of free virions.

1 Stability analysis and permanence

System (3) always has non-negative equilibria $E_1(\hat{T}, 0, 0)$, $E_2(\bar{T}, \bar{I}, \bar{V})$, where

$$\hat{T} = \frac{T_{max}}{2a}[a - d + \sqrt{(a-d)^2 + 4as/T_{mzx}}],$$

$$\bar{T} = \frac{c\delta}{p\beta},\quad \bar{I} = [s - d\bar{T} + a\bar{T}(1 - \bar{T}/T_{max})]/\delta,$$

$$\bar{V} = p[s - d\bar{T} + a\bar{T}(1 - \bar{T}/T_{max})]/(\delta c).$$

Let

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$$R_0 = \frac{\hat{T}}{\bar{T}} = \frac{p\beta T_{max}}{2ac\delta}[a - d + \sqrt{(a-d)^2 + \frac{4as}{T_{max}}}].$$

which is called the basic reproductive ratio of system (3). We can see that R_0 is a bifurcation parameter.

The Jacobian matrix of $E_1(\hat{T}, 0, 0)$ is

$$J(E_1) = \begin{pmatrix} a - d - \frac{2a\hat{T}}{T_{max}} & 0 & -\beta\hat{T} \\ 0 & -\delta & \beta\hat{T} \\ 0 & p & -c \end{pmatrix},$$

Its characteristic equation is

$$(\lambda + \sqrt{(a-d)^2 + 4as/T_{max}})[\lambda^2 + (\delta + c)\lambda + \delta c - p\beta\hat{T}] = 0. \quad (4)$$

Thus, $E_1(\hat{T}, 0, 0)$ is locally asymptotically stable for $\hat{T} < \bar{T}$, and is a saddle point with $\dim W^u(E_1) = 1$, $\dim W^s(E_1) = 2$, for $\hat{T} > \bar{T}$.

We can see that R_0 is a bifurcation parameter. When $R_0 < 1$, the uninfected steady state E_1 is stable and the infected steady state E_2 does not exist (unphysical). When $R_0 > 1$, E_1 becomes unstable and E_2 exists. Thus, the basic reproductive number R_0 determines the dynamical properties of system (3) over a long period of time.

Standard and simple arguments show that solutions of the system (3) always exist, stay positive and boundedness.

The Jacobian matrix of $E_2(\bar{T}, \bar{I}, \bar{V})$ is

$$J(E_2) = \begin{pmatrix} a - d - \frac{2a\bar{T}}{T_{max}} - \beta\bar{V} & 0 & -\beta\bar{T} \\ \beta\bar{V} & -\delta & \beta\bar{T} \\ 0 & p & -c \end{pmatrix},$$

Its characteristic equation is

$$\lambda^3 + b_1\lambda^2 + b_2\lambda + b_3 = 0, \quad (5)$$

here

$$b_1 = \delta + c + d - a + \frac{2a\bar{T}}{T_{max}} + \beta\bar{V} = \delta + c + M,$$

$$b_2 = (\delta + c)(d - a + \frac{2a\bar{T}}{T_{max}} + \beta\bar{V}) = (\delta + c)M,$$

$$b_3 = \delta c\beta\bar{V} > 0, M = d - a + \frac{2a\bar{T}}{T_{max}} + \beta\bar{V}.$$

If $M > 0$, then $b_1 > 0$, $b_2 > 0$, we have

$$b_1 b_2 - b_3 = (\delta + c)^2 M + (\delta + c)M^2 - \delta c\beta\bar{V}.$$

By Routh-Hurwits Criterion, we know that

Theorem 1 If

(i) $R_0 > 1$,

(ii) $a < d$,

(iii) $b_1 b_2 - b_3 = (\delta + c)^2 M + (\delta + c)M^2 - \delta c\beta\bar{V} > 0$.

Then the positive equilibrium $E_2(\bar{T}, \bar{I}, \bar{V})$ is locally asymptotically stable.

It is to see that solution of the system (3) always exist and stay positive. Indeed, as is obvious for system (3), we have

$$\lim_{t\to\infty}\sup T(t) \le \hat{T} = \frac{T_{max}}{2a}[a - d + \sqrt{(a-d)^2 + 4as/T_{max}}].$$

Then there is a $t_1 > 0$ such that for any sufficiently small $\varepsilon > 0$, we have

$$T(t) \le \hat{T} + \varepsilon, \text{ for } t > t_1. \quad (6)$$

Theorem 2 There is an $M_1 > 0$ such that for any positive solution $(T(t), I(t), V(t))$ of system (3),

$$I(t) < M_1, V(t) < M_1, \text{ for all large } t.$$

Proof Set $V_1(t) = T(t) + I(t)$. Calculating the derivative of $V_1(t)$ along the solutions of system (3), we find

$$\dot{V}_1(t) = s - dT(t) + aT(t)(1 - T(t)/T_{max}) - \delta I(t) = -dT(t) - \delta I(t) + aT(t) - aT^2(t)/T_{max} + s \le -hV_1(t) + M_0,$$

here $h = \min(d, \delta)$, $M_0 = (T_{max}a^2 + 4as)/4a$. Recall that $T(t) \le \hat{T} + \varepsilon$, for all $t > t_1$. Then there exists an M_2, depending only on the parameters of system (3), such that $V_1(t) < M_2$, for $t > t_1$. Then $I(t)$ has an ultimately above bound. It follows from the third equation of Eq. (3) that $V(t)$ has an ultimately above bound, say, their maximum is an M_1. ▭

Define

$$\Omega = \{(T, I, V): 0 \le T \le \hat{T}, 0 \le I \le M_1, 0 \le V \le M_1\}.$$

Theorem 3 Under the assumption $R_0 < 1$, the local stability of $E_1(\hat{T}, 0, 0)$ implies its global stability in Ω.

Proof From the last two equations of Eq. (3), for $t > t_1$, we have

$$\dot{I} \le \beta\hat{T}V - \delta I, \quad \dot{V} = pI - cV. \quad (7)$$

Consider the following equations

$$\begin{cases} \dot{u}_1(t) = \beta\hat{T}u_2(t) - \delta u_1(t), \\ \dot{u}_2(t) = pu_1(t) - cu_2(t). \end{cases} \quad (8)$$

Since $R_0 < 1$, then $p\beta\hat{T} < \delta c$. Obviously, for any solution of (8) with nonnegative initial values we $\lim_{t\to+\infty} u_i(t) = 0$, $i = 1, 2$. Let $0 < I(0) \le u_1(0)$, $0 < V(0) \le u_2(0)$. If $(u_1(t), u_2(t))$ is a solution of system (8) with initial value $(u_1(0), u_2(0))$, then by the comparison theorem we have $I(t) \le u_1(t)$, $V(t) \le u_2(t)$ for all $t > t_1$, and $\lim_{t\to+\infty} I(t) = 0$, $\lim_{t\to+\infty} V(t) = 0$.

For an $\varepsilon \in (0, 1)$ sufficiently small, there exists $t_2 = t_2(\varepsilon)$ such that for $t > t_2$,

$$s - \beta\hat{T}\varepsilon + (a - d)T - aT^2/T_{max} \le \dot{T} \le s + (a - d)T - aT^2/T_{max}.$$

Thus $\lim_{t\to+\infty} T(t) = \hat{T}$. ▭

Theorem 4 System (3) is permanent provided $R_0 > 1$.

Proof We begin by showing weakly persistence of system (3). If it is not weakly persistence, it follows from the proof of Theore 3 that there is a positive orbit $(T(t), I(t), V(t))$ of (3) such that

$$\lim_{t\to+\infty} T(t) = \hat{T}, \lim_{t\to+\infty} I(t) = 0, \lim_{t\to+\infty} V(t) = 0.$$

Since $R_0 > 1$, then $\hat{T} > \frac{\delta c}{p\beta}$, we can choose $\varepsilon > 0$ small enough such that

$$\hat{T} - \varepsilon > \frac{\delta c}{p\beta}, \tag{9}$$

Then choose $t_0 > 0$ large enough such that if $t \geq t_0$, we get

$$\dot{I}(t) \geq \beta(\hat{T} - \varepsilon) V(t) - \delta I(t),$$
$$\dot{V} = pI(t) - cV(t). \tag{10}$$

Considering the matrix A_ε defined by

$$\begin{pmatrix} -\delta & \beta(\hat{T} - \varepsilon) \\ p & -c \end{pmatrix}.$$

Since A_ε admits positive off-diagonal element, Perron-Frobenius Theorem implies that there is positive eigenvector $v = (v_1, v_2)$ for the maximum eigenvalue α_1 of A_ε. Moreover, by (9), we see that the maximum eigenvalue α_1 is positive.

We consider that

$$\dot{u}_1 = \beta(\hat{T} - \varepsilon) u_2 - \delta u_1,$$
$$\dot{u}_2 = pu_1 - cu_2. \tag{11}$$

Let $u(t) = (u_1(t), u_2(t))$ be a solution of system (12) through (lv_1, lv_2) at $t = t_0$, where $l > 0$ satisfies $lv_1 < I(t_0)$, $lv_2 < V(t_0)$. Since the semiflow of (12) is monotone and $A_\varepsilon v > 0$, it follows that $u_i(t)$ is strictly increasing and $u_i(t) \to +\infty$, as $t \to +\infty$, contradicting the eventual boundedness of positive solution of (3). Thus, no positive orbit of (3) tends to $(\hat{T}, 0, 0)$ at $t \to +\infty$. This shows that system (3) is weekly persistent. Then an application of the techniques of paper [8] concludes the permanence of (3). ▭

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一类具有线性感染率的病毒模型的动力学性质

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摘 要: 考虑了一类带有线性感染率的病毒模型, 分析了解的有界性, 平衡点的性质, 系统的持续生存性及稳定性.

关键词: 稳定性分析; 持续生存; HIV

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