Globally Qualitative Analysis of HIV-I Model With Harmless Nonlinear Infection Rate

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***Abstract* — This paper studies the HIV-I model with nonlinear infection rate. By means of Dulac function, the completely qualitative analysis to this model are obtained. It is found that the nonlinear infection rate is harmless, and cannot affect the final development of the virus infection.**

Keywords - HIV-I model, harmless, equilibria, nonlinear infection rate, Dulac function.

I. INTRODUCTION

In the view of ecology, the process of microbial or parasitic infection in the host body, which is essentially equal to the struggle process of the pathogen populations to survive, evolve and adapt in the host environment [1]. In recent decades, we pay great attention to the research on population dynamics of the host body. The study of the human immunodeficiency virus (HIV) has become a hot spot in recent years, especially. A large number of HIV models have been proposed and studied (see [2-7]).

In the recent papers, the authors tend to choose the standard infection or bilinear infection, and the rich conclusions are given. But in the experimental study of micro parasitic infections, [8-9] observed a clear non-linear relationship between dose and infection rates. In [10] studied the virus dynamics model which infection rate is $\beta V^q T^p$. [11] proposed another non-linear infection rate $\beta(y) = \beta y^p / (1 + by^q)$. The paper [12] studied this non-linear infection rate when $p = 1, q = 1$.

Furthermore, cell-to-cell (healthy $CD4^+$ T-cells infected by infected $CD4^+$ T-cells) spread of HIV-I is thought to be a much more important mode than cell-free viral spread in areas such as the lymph nodes and brain[13-14]. Sato et al.[13] presented that cell-to-cell spread of virus is favored over infections with cell-free virus inocula. There has many virus dynamics models with cell-to-cell spread were studied(see[2,4-5,15]).

In [15] Bonhoeffer, coffin and Nowak proposed the following model of cell-to-cell spread of HIV-I:

$$\begin{cases} \dfrac{dx}{dt} = \lambda - dx - \beta xy, \\ \dfrac{dy}{dt} = \beta xy - ay. \end{cases} \qquad (1)$$

where $x(t)$ represents the concentration of healthy $CD4^+$ T-cells at time t, y represents the concentration of infected $CD4^+$ T-cells. To explain the parameters: λ is the source term for healthy $CD4^+$ T-cells, d and a is the death rate of healthy T-cells, infected T-cells, respectively. β is the rate of infection of T-cells with infected T-cells. It is assumed that all the parameters are positive constants.

In this paper, we consider the non-linear infection rate $\beta(y) = \beta y^p / (1 + by^q)$ based on the model (1) by using the improved method of [11]. We mainly analyze the influence of the non-linear infection rate to the dynamic behavior of the virus when $p = 1, q = 2$. We study the cell-to-cell spread of HIV-I model with a non-linear infection rate as follows:

$$\begin{cases} \dfrac{dx}{dt} = \lambda - \dfrac{\beta xy}{1 + by^2} - dx, \\ \dfrac{dy}{dt} = \dfrac{\beta xy}{1 + by^2} - ay. \end{cases} \qquad (2)$$

where βy measures the infection force of the infected $CD4^+$ T-cells, $1/(1+by^2)$ represents the inhibition effect from the behavioral change of the infected $CD4^+$ T-cells when their number increases. The biological meanings of other parameters are the similar to those appearing parameters in model (1).

II. EQUILIBRIA AND STABILITY ANALYSIS

Firstly, we shall prove the model (2) is dissipative.

Theorem2.1 All solutions of model (2) are positive and ultimately bounded, that is to say, model (2) is dissipative.

Prove. Now, we prove that all solution of model (2) are positive.

Suppose $x(t)$ is not always positive. Let $t_1(t_1 > 0)$ be the first time such that $x(t_1) = 0$. By the first equation of model (2) we have $x'(t_1) = \lambda > 0$, that is to say, $x(t) < 0$ for $t \in (t_1 - \varepsilon, t_1)$ (ε is an arbitrarily small positive constant), which is a contradiction. Thus $x(t)$ is always positive. Moreover the boundary $y = 0$ is a constant solution of model (2), by the uniqueness and continuity of the solution for initial conditions, we have that $y(t) > 0$ for any t. It is obvious that $D = \{(x, y) : x > 0, y > 0\}$ is the positive invariant set of model (2).

Next, let $N(t) = x(t) + y(t)$, we have

$$N'(t) = (x(t) + y(t))' = \lambda - dx - ay \le \lambda - Ay$$

where $A = \min\{a, d\}$. It is easy to obtain that $\lim_{t\to\infty} N(t) \le \overline{N}$ ($\overline{N} = \frac{\lambda}{A}$). According to the non-negativity of the solution, all solutions of mode (2) are ultimately bounded. Thus model (2) is dissipative. □

Secondly, we begin to investigate the existence of equilibria of model (2) and their stability.

Let $R_0 = \frac{\beta\lambda}{ad}$, then R_0 is the basic reproductive number of model (2), which describes the average number of newly infected $CD4^+$ T-cells generated from one infected $CD4^+$ T-cells.

Let $x'(t) = 0,\ y'(t) = 0$, we have

$$\begin{cases} P(x, y) = \lambda - \dfrac{\beta xy}{1 + by^2} - dx = 0, \\ Q(x, y) = \dfrac{\beta xy}{1 + by^2} - ay = 0. \end{cases}$$

By the calculation, we can obtain the infected-free equilibrium $E_0 = (x_0, 0)$ and the positive equilibrium $E_1 = (x_1, y_1)$ of model (2), where $x_0 = \lambda/d$, $x_1 = a(1 + by_1^2)/\beta$, and

$$y_1 = \frac{-\beta a + \sqrt{(\beta a)^2 + 4adb(\lambda\beta - da)}}{2dab} (R_0 > 1).$$

Theorem2.2 Model (2) always exists the infected-free equilibrium E_0. When $R_0 > 1$, model (2) also has a unique positive equilibrium E_1.

Theorem 2.3 The infected-free equilibrium E_0 is globally asymptotically stable when $R_0 < 1$. The positive equilibrium E_1 is globally asymptotically stable when $R_0 > 1$.

Prove. Now, we study the stability of equilibria. The Jacobian matrix of model (2) is given by:

$$J(E) = \begin{pmatrix} -\dfrac{\beta y}{1 + by^2} - d & -\dfrac{\beta x - \beta bxy^2}{(1 + by^2)^2} \\ \dfrac{\beta y}{1 + by^2} & \dfrac{\beta x - \beta bxy^2}{(1 + by^2)^2} - a \end{pmatrix}$$

By simple computation, the Jacobian matrix of model (2) at E_0 is:

$$J(E_0) = \begin{pmatrix} -d & -\beta\dfrac{\lambda}{d} \\ 0 & \beta\dfrac{\lambda}{d} - a \end{pmatrix}$$

Then we get the characteristic equation at E_0 : $\Delta(U) = (U + d)(U - \beta\frac{\lambda}{d} + a)$. By the Routh-Hurwitz criterion, the infected-free equilibrium E_0 is locally stable if and only if $R_0 < 1(\beta\lambda < ad)$, E_0 is unstable when $R_0 > 1(\beta\lambda > ad)$.

Because $\frac{1}{1 + by_1^2} = \frac{a}{\beta x_1}$, we have the following conclusions by the calculation

$$\begin{aligned} trJ(E_1) &= -d - \frac{\beta y_1}{1 + by_1^2} + \frac{\beta x_1 - \beta bx_1 y_1^2}{(1 + by_1^2)^2} - a \\ &= -d - \frac{\beta y_1}{1 + by_1^2} - \frac{2\beta bx_1 y_1^2}{(1 + by_1^2)^2} < 0 \end{aligned}$$

$$\begin{aligned} \det J(E_1) &= (-\frac{\beta y_1}{1 + by_1^2} - d)(\frac{\beta x_1 - \beta bx_1 y_1^2}{(1 + by_1^2)^2} - a) \\ &\quad + \frac{\beta x_1 - \beta bx_1 y_1^2}{(1 + by_1^2)^2} \cdot \frac{\beta y_1}{1 + by_1^2} \\ &= -da\frac{1 - by_1^2}{1 + by_1^2} + da - a\frac{\beta y_1(1 - by_1^2)}{(1 + by_1^2)^2} + a\frac{\beta y_1}{1 + by_1^2} \\ &\quad + a\frac{\beta y_1(1 - by_1^2)}{(1 + by_1^2)^2} \\ &= da\frac{2by_1^2}{1 + by_1^2} + a\frac{\beta y_1}{1 + by_1^2} > 0 \end{aligned}$$

Then the positive equilibrium $E_1 = (x_1, y_1)$ is locally stable when $R_0 > 1(\beta\lambda > ad)$.

Next, we construct the function $f(x, y) = 1/y$. It is obtained that

$$\frac{\partial(f(x,y)P(x,y))}{\partial x}+\frac{\partial(f(x,y)Q(x,y))}{\partial y}$$
$$=-\frac{d}{y}-\frac{\beta}{1+by^2}-\frac{2b\beta xy}{(1+by^2)^2}<0$$

where $P(x,y)=\lambda-\frac{\beta xy}{1+by^2}-dx,\ Q(x,y)=\frac{\beta xy}{1+by^2}-ay$.

Using the Dulac criterion, the model (2) has no closed orbits in the positive invariant set D. Thus we can obtain the following conclusions by the Poincare-Bendixson theorem. (i) when $R_0<1$, the model (2) exists the unique equilibrium E_0 and E_0 is globally asymptotically stable. (ii) when $R_0>1$, positive equilibrium E_1 appear and E_1 is globally asymptotically stable. □

III. CONCLUSION

Comparing the dynamical behavior of the model (1) and model (2), we found that the basic reproductive number R_0 is the same, the number of the equilibria and their stability is also the same. By the calculation, we have the positive equilibrium of the model (1) $P_1=(\frac{a}{\beta},\frac{\beta\lambda-da}{\beta a})$.

Because(E_1 exists if and only if $R_0>1$)

$$\frac{4}{\beta^2}d^2b^2(\lambda\beta-da)^2>0$$
$$\Rightarrow\frac{4}{\beta^2}(d^2b^2\lambda\beta-d^3b^2a)(\lambda\beta-da)>0$$
$$\Rightarrow\frac{4}{\beta}d^2b^2\lambda(\lambda\beta-da)-\frac{4}{\beta^2}d^3b^2a(\lambda\beta-da)>0$$
$$\Rightarrow 4d^2b^2\lambda^2+\frac{4d^4b^2a^2}{\beta^2}-8\frac{d^3b^2\lambda a}{\beta}>0$$
$$\Rightarrow 4d^2b^2\lambda^2+\frac{4d^4b^2a^2}{\beta^2}-8\frac{d^3b^2\lambda a}{\beta}+(\beta a)^2-4d^2a^2b$$
$$+4adb\beta\lambda>(\beta a)^2-4d^2a^2b+4adb\beta\lambda$$
$$\Rightarrow(2db\lambda-\frac{2d^2ba}{\beta}+\beta a)^2>(\beta a)^2-4dab(da-\beta\lambda)$$
$$\Rightarrow 2db\lambda-\frac{2d^2ba}{\beta}+\beta a>\sqrt{(\beta a)^2-4dab(da-\beta\lambda)}$$

Thus $\frac{-\beta a+\sqrt{(\beta a)^2+4adb(\lambda\beta-da)}}{2dab}<\frac{\beta\lambda-da}{\beta a}$. We also found that the infected $CD4^+$ T-cells(viral load) in the host will be reduced when introducing the non-linear infection rate $\beta(y)=\beta y/1+by^2$. Therefore, the non-linear infection rate $\beta(y)=\beta y/1+by^2$ will not only affect the dynamics of viral infection, but also reduce the viral load in the host body, is a kind of harmless non-linear infection rate.

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