

# Stability Analysis for an HIV Infection Model with Immune Response and Cure Rate

Linli Zhang<sup>1,2\*</sup>, Lin Wang<sup>2</sup>

<sup>1</sup>Hainan University, Danzhou 571737, China;

<sup>2</sup>Haikou University of Economics, Haikou 571127, China

E-mail: [zhanglinli63021@163.com](mailto:zhanglinli63021@163.com)\*, [whu05@qq.com](mailto:whu05@qq.com)<sup>2</sup>

**Abstract.** The dynamics of HIV infection model with immune response and cure rate is investigated. The explicit expression for the basic reproduction number of the model which determines where the virus dies out or not is obtained. With characteristic equation and Hurwitz criterion, the local stability of the equilibriums is analyzed.

## 1. Introduction

The human immuno-deficiency virus (HIV) infection, which can cause acquired immuno-deficiency syndrome(AIDS), has become an important infectious disease in both the developed and the developing nations. It causes mortality of millions of people and expenditure of a huge amount of money in disease control and health care. In recent years, some scholars have achieved many significant results by establishing the mathematical model of HIV pathogenesis which is used to study the HIV virus concentration and the change of CD4<sup>+</sup>T cells concentration in the body [1-7]. The research [8] shows that, for a chemotherapy of HBV infection, under the effect of drugs, the infection of target cells can overflow from the nucleus into uninfected state covalently closed circular DNA (cccDNA). Zhou *et al.* [6], consider a HIV pathological model with the cure rate, and the results show that it will be able to effectively extend the duration of HIV infection if the cure rate is improved in a certain extent. The immune response following viral infection is universal and necessary in controlling or even eliminating the disease [9]. Under the inspiration of these references, we will consider a HIV infection model with immune response and cure rate in this paper as follows:

$$\begin{cases} x'(t) = \lambda - dx - \beta xy + \rho y, \\ y'(t) = \beta xy - ay - pyz - \rho y, \\ z'(t) = cyz - bz. \end{cases} \quad (1)$$

Here  $x(t)$  is the concentration of uninfected cells at time  $t$ ;  $y(t)$  is the concentration of infected cells that produce virus at time  $t$ ;  $z(t)$  is the concentration of antigen-specific CTLs at time  $t$ .  $\lambda$  is the growth rate of new healthy cells.  $a$  and  $d$  are the death rate of infected cells and uninfected cells, respectively.  $\beta$  is the rate constant characterizing infection of the cells.  $p$  is the death rate of infected cells due to the immune system.  $\rho$  is the rate at which infected cells return to healthy cells after treatment. The immune response is supposed to decay exponentially at a rate  $bz$  and get stronger at a rate  $cyz$ . All parameters in the model are positive.

Model (1) needs to be analyzed with the following initial conditions:



$$x(0) > 0, y(0) > 0, z(0) > 0. \quad (2)$$

It can be proved that the solution of system (1) - (2) exists and is positive.

## 2. Equilibrium States

By solving the equations (3), we can obtain the three types of nonnegative equilibrium of model (1).

$$\begin{cases} \lambda - dx - \beta xy + \rho y = 0, \\ \beta xy - ay - pyz - \rho y = 0, \\ cyz - bz = 0. \end{cases} \quad (3)$$

Model (1) always has an infection-free equilibrium, where  $E_0 = (x_0, 0, 0) = \left(\frac{\lambda}{d}, 0, 0\right)$ .

We denote:

$$R_0 = \frac{\lambda\beta}{d(a+\rho)}, \quad R_1 = \frac{c\lambda}{ab} - \frac{cd(a+\rho)}{ab\beta} = \frac{cd(a+\rho)}{ab\beta}(R_0 - 1).$$

$R_0$  and  $R_1$  are defined as the basic reproductive number and the immune reproduction number of model (1), respectively.

When  $R_0 < 1$ , Model (1) has an unique immune-absence equilibrium  $E_1$  besides  $E_0$ , where

$$E_1 = (x_1, y_1, z_1) = \left(\frac{a+\rho}{\beta}, \frac{\lambda\beta - d(a+\rho)}{a\beta}, 0\right).$$

When  $R_1 < 1$ , Model (1) has an unique interior immune-presence equilibrium  $E^*$  besides  $E_0$

and  $E_1$ , where  $E^* = (x^*, y^*, z^*) = \left(\frac{\lambda c + \rho b}{dc + \beta b}, \frac{b}{c}, \frac{cd(a+\rho)(R_0 - 1) - a\beta b}{p(dc + \beta b)}\right)$ .

## 3. Local Stability

Next, with characteristic equation and Hurwitz criterion, we analyze the local stability of model (1).

**Theorem 1** Consider model (1)

- (i) If  $R_0 < 1$ , the infection-free equilibrium  $E_0$  is locally asymptotically stable;
- (ii) If  $R_0 > 1$  and  $R_1 < 1$ , the immune-absence equilibrium  $E_1$  is locally asymptotically stable;
- (iii) If  $R_1 > 1$  and  $\beta b - c\rho > 0$ , the immune-present equilibrium  $E^*$  is locally asymptotically stable.

**Proof.** (i) The Jacobian matrix of model (1) at  $E_0$  is obtained as follows:

$$J(E_0) = \begin{pmatrix} -d & -\beta x_0 + \rho & 0 \\ 0 & \beta x_0 - a - \rho & 0 \\ 0 & 0 & -b \end{pmatrix}.$$

The characteristic equation of  $J(E_0)$  takes the form:

$$\begin{vmatrix} -d-r & -\beta x_0 + \rho & 0 \\ 0 & \beta x_0 - a - \rho - r & 0 \\ 0 & 0 & -b-r \end{vmatrix} = 0. \quad (4)$$

By solving the third order determinant, equation (4) can be simplified as follows:

$$(r+d)(r+b)(r+a+\rho-\beta x_0) = 0. \quad (5)$$

The equation (5) has three roots:  $r_1 = -d, r_2 = -b, r_3 = (a+\rho)(R_0 - 1)$ . When  $R_0 < 1$ , that is  $r_3 < 0$ , equation (5) has three negative real roots, hence  $E_0$  is locally asymptotically stable. When  $R_0 > 1$ , that is  $r_3 > 0$ , equation (5) has a positive real root, thus  $E_0$  is unstable.

(ii) The Jacobian matrix of model (1) at  $E_1$  is obtained as follows:

$$J(E_1) = \begin{pmatrix} -d - \beta y_1 & -\beta x_1 + \rho & 0 \\ \beta y_1 & 0 & 0 \\ 0 & 0 & cy_1 - b \end{pmatrix}.$$

The characteristic equation of  $J(E_1)$  takes the form:

$$\begin{vmatrix} -d - \beta y_1 - r & -\beta x_1 + \rho & 0 \\ \beta y_1 & -r & 0 \\ 0 & 0 & cy_1 - b - r \end{vmatrix} = 0. \quad (6)$$

By solving the third order determinant, equation (6) can be simplified as follows:

$$(b + r - cy_1)[r^2 + (d + \beta y_1)r - \beta y_1(\rho - \beta x_1)] = 0. \quad (7)$$

The equation (7) a characteristic root:  $r_1 = cy_1 - b = b(R_1 - 1)$ . When  $R_1 < 1$ , that is  $r_1 < 0$ . The rest of the characteristic roots satisfy the equation (8):

$$r^2 + (d + \beta y_1)r - \beta y_1(\rho - \beta x_1) = 0. \quad (8)$$

Because  $x_1 = \frac{a + \rho}{\beta}$ , the equation (8) is simplified as follows:

$$r^2 + (d + \beta y_1)r + \beta y_1 a = 0. \quad (9)$$

All coefficients of quadratic equation (9) are positive, and hence its roots have negative real parts. That is  $R_1 < 1$  ensures that all eigenvalues have negative real parts of equation (7) and hence the immune-absence equilibrium  $E_1$  is locally asymptotically stable if  $R_0 > 1$  and  $R_1 < 1$ .

(iii) The Jacobian matrix of model (1) at  $E^*$  is obtained as follows:

$$J(E^*) = \begin{pmatrix} -d - \beta y^* & -\beta x^* + \rho & 0 \\ \beta y^* & 0 & -py^* \\ 0 & cz^* & 0 \end{pmatrix}.$$

The characteristic equation of  $J(E^*)$  takes the form:

$$\begin{vmatrix} -d - \beta y^* - r & -\beta x^* + \rho & 0 \\ \beta y^* & -r & -py^* \\ 0 & cz^* & -r \end{vmatrix} = 0. \quad (10)$$

By solving the third order determinant, the equation (10) can be simplified as follows:

$$r^3 + a_2 r^2 + a_1 r + a_0 = 0, \quad (11)$$

where

$$a_2 = d + \beta y^* > 0,$$

$$a_0 = cpy^* z^* (d + \beta y^*) > 0,$$

$$a_1 = cz^* py^* + \beta^2 y^* y^* - \rho \beta y^* = cz^* py^* + \beta y^* (\beta y^* - \rho) = cz^* py^* + \beta y^* \left( \beta \frac{b}{c} - \rho \right),$$

$$a_2 a_1 - a_0 = (d + \beta y^*) (\beta y^* - \rho) \beta y^* = (d + \beta y^*) \left( \beta \frac{b}{c} - \rho \right) \beta y^*.$$

When  $\beta b - c\rho$  is greater than zero, it ensures that  $a_2 a_1 - a_0$  is greater than zero. By the Routh-Hurwitz theorem, all roots of the equation (11) have negative real part, and the immune-present equilibrium  $E^*$  is locally asymptotically stable if  $R_1 > 1$  and  $\beta b - c\rho > 0$ .

#### 4. Conclusion

In this paper, the dynamics of HIV infection model with immune response and cure rate is investigated. The explicit expression for the basic reproduction number of the model which determines where the virus dies out or not is obtained. The sufficient condition of local asymptotic stability of equilibrium is obtained by using the characteristic equation and Hurwitz criterion. The infection-free equilibrium  $E_0$  of model (1) is locally asymptotically stable when  $R_0 < 1$ ; the immune-absence equilibrium  $E_1$  of model (1) is locally asymptotically stable when  $R_0 > 1$  and  $R_1 < 1$ ; the immune-present equilibrium  $E^*$  of model (1) is locally asymptotically stable when  $R_1 > 1$  and  $\beta b - c\rho > 0$ .

The concentration of CD4<sup>+</sup>T cell is an important indicator of HIV infection progression. Because  $x^*$  is a monotone increasing function of cure rate  $\rho$ . Therefore, increasing the cure rate  $\rho$  will further improve the concentration of CD4<sup>+</sup>T cells in the equilibrium point of the disease, thereby prolonging the duration of HIV infection and thus effectively controlling the effect of HIV infection.

In this paper, the immune reproduction number  $R_1$  is the monotone decreasing function of cure rate  $\rho$ , which means the increase of cure rate reduces the production of immune cells in the body. The mechanism is: the cure rate is to vaccinate measures can be considered in this study. Because vaccination is to replace the function of immune cells, the infection to the stimulation of immune becomes smaller. Thus, vaccination can reduce the generation of immune cells in the body.

#### Acknowledgments

This reserach is supported by Hainan Provincial Natural Science Foundation of China (117174; 118MS084)

#### References

- [1] L. Wang, M.Y. Li. Mathematical analysis of the global dynamic of a model for HIV infection of CD4<sup>+</sup>T cells[J]. Mathematical Biosciences, 2006, 200(1): 44-57.
- [2] R.L. Fan, Y.P. Dong, G. Huang, et al. Apoptosis in virus infection dynamics models [J]. Journal of Biological Dynamics, 2014, 8(1): 20-41
- [3] A.S. Perelson, A.U. Neumann, M. Markowitz, et al. HIV-1 dynamics in vivo: Virion clearance rate, infected cell life-span, and viral generation time [J]. Science, 1996, 271(5255): 1582-1586.
- [4] X.D. Liu, H. Wang, Z.X. Hu, et al. Stability of an HIV Pathogenesis Model with Delay and Cure Rate [J]. Journal of Biomathematics, 2011, 26(1): 108-116.
- [5] X.Y. Song, A.U. Neumann. Global stability and periodic solution of the viral dynamics [J]. Journal If Mathematical Analysis and Applications, 2007, 329[1]: 281-396.
- [6] X.Y. Zhou, X.Y. Song, X.Y. Shi. A differential equation model of HIV infection of CD4<sup>+</sup> T-cells with cure rate [J]. Journal of Mathematical Analysis and Applications, 2008, 342(2): 1342-1355.
- [7] A.V.M. Herz, S. Bonhoer, R.M. Anderson, et al. Viral dynamics in vivo: limitations on estimates of intracellular delay and virus decay [J]. Proceedings of the National Academy of Sciences of the United States of America, 1996, 93(14): 7247-7251.
- [8] S. Lewinb, T. Waltersa, S. Locarnini. Hepatitis B treatment: rational combination chemotherapy based on viral kinetic and animal model studies [J]. Antiviral Research, 2002, 55(3): 381-396.
- [9] G. Huang, H. Yokoi, Y. Takeuchi, T. Kajiwara and T. Sasaki. Impact of intracellular delay, immune activation delay and nonlinear incidence on viral dynamics [J]. Japan Journal of

Industrial and Applied Mathematics, 2011, 28(1): 383-411.