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Dynamics of a stochastic cell-to-cell HIV-1 model with distributed delay

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HIGHLIGHTS

- A stochastic cell-to-cell HIV-1 model with distributed delay is proposed and investigated.
- We establish sufficient conditions for extinction of the disease.
- We establish sufficient conditions for the existence of an ergodic stationary distribution.
- The stationary distribution implies that the disease can be persistent in the mean.

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ABSTRACT

In this paper, we consider a stochastic cell-to-cell HIV-1 model with distributed delay. Firstly, we show that there is a global positive solution of this model before exploring its long-time behavior. Then sufficient conditions for extinction of the disease are established. Moreover, we obtain sufficient conditions for the existence of an ergodic stationary distribution of the model by constructing a suitable stochastic Lyapunov function. The stationary distribution implies that the disease is persistent in the mean. Finally, we provide some numerical examples to illustrate theoretical results.

1. Introduction

Human immunodeficiency virus-1 (HIV-1) continues to be a major global public health issue and priority. Many scientists have made great effort against HIV-1, and they are still going on. Mathematics and biological researchers also contribute to this by revealing its transmission and dynamics. Recently, many mathematical models have been formulated to describe the immunological response to infection with HIV-1. Most of these models focus on cell-free viral spread in a compartment such as the bloodstream, see for example, Callaway and Perelson [1], Spouge, Shrager and Dimitrov [2], Kirschner, Lenhart and Serbin [3], Kirschner and Webb [4–6], McLean and Kirkwood [7], McLean and Nowak [8], Müller et al. [9], Nowak and

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Bangham [10], Nowak and May [11,12], Perelson, Kirschner and De Boer [13], Perelson [14], Perelson and Nelson [15], Wodarz et al. [16], etc. Some most advances in areas of modeling cell-to-cell transmission and of modeling physical processes with distributed time delay [17–20]. And these models have been used to explain different phenomena. This is because HIV-1 mathematical models can provide insights into the dynamics of viral load in vivo and can play an important role in the development of a better understanding of HIV/AIDS and drug therapies. Especially, by assuming that infection is spread directly from infected cells to healthy cells and neglecting the effects of free virus, Culshaw et al. [17] considered a two-dimensional model of cell-to-cell spread of HIV-1 in tissue cultures

$$\begin{cases} \dfrac{dC(t)}{dt} = r_C C(t)\left(1 - \dfrac{C(t)+I(t)}{C_M}\right) - \kappa_I C(t)I(t), \\ \dfrac{dI(t)}{dt} = \kappa_I' \displaystyle\int_{-\infty}^{t} C(u)I(u)F(t-u)du - \mu_I I(t), \end{cases} \tag{1.1}$$

where $C(t)$ and $I(t)$ denote the concentration of healthy cells and infected cells at time t, respectively and all of the parameters are positive constants. r_C is the effective reproductive rate of healthy cells (the term is the total reproductive rate for healthy cells r minus the death rate for healthy cells μ_C), and so $r_C C(t)$ denotes the number of effective reproductive cells per unit time, C_M is the effective carrying capacity of system (1.1), κ_I denotes the infection of healthy cells by the infected cells in a well-fixed system, $\frac{\kappa_I'}{\kappa_I}$ is the fraction of cells surviving the incubation period, μ_I is the death rate of the infected cells. It is assumed that the cells, which are productively infectious at time t, were infected u time units ago, where u is distributed according to a probability distribution $F(u)$, called the delay kernel.

Taking the weak kernel function $F(u) = \alpha e^{-\alpha u}$ ($\alpha > 0$) and letting

$$X(t) = \int_{-\infty}^{t} \alpha e^{-\alpha(t-u)} C(u)I(u)du,$$

system (1.1) is equivalent to the following system

$$\begin{cases} \dfrac{dC(t)}{dt} = r_C C(t)\left(1 - \dfrac{C(t)+I(t)}{C_M}\right) - \kappa_I C(t)I(t), \\ \dfrac{dI(t)}{dt} = \kappa_I' X(t) - \mu_I I(t), \\ \dfrac{dX(t)}{dt} = \alpha C(t)I(t) - \alpha X(t). \end{cases} \tag{1.2}$$

There are three equilibria in system (1.2): the trivial equilibrium $E_0 = (0, 0, 0)$, the healthy equilibrium $E_1 = (C_M, 0, 0)$, and the infected equilibrium $\overline{E} = (\overline{C}, \overline{I}, \overline{X})$ provided $\kappa_I' > \frac{\mu_I}{C_M}$, where $\overline{C} = \frac{\mu_I}{\kappa_I'}$, $\overline{I} = \frac{r_C(\kappa_I' C_M - \mu_I)}{\kappa_I'(\kappa_I C_M + r_C)}$, $\overline{X} = \frac{\mu_I}{\kappa_I'}\overline{I}$. When $C_M < \frac{\mu_I}{\kappa_I}$, the healthy cells predominate and infected cells die exponentially. In this case E_0, $\overline{E}$ are unstable, E_1 is asymptotically stable. When $\frac{\mu_I}{\kappa_I'} < C_M < \frac{r_C}{C_M}$, E_0 remains unstable and E_1 is also unstable. In this situation, healthy cells and infected cells co-exist. Furthermore, if $a_1(\alpha) > 0$, $a_3(\alpha) > 0$ and $a_1(\alpha)a_2(\alpha) - a_3(\alpha) > 0$, then the positive steady state $\overline{E}$ is asymptotically stable, where $a_1(\alpha) = \frac{r_C}{C_M}\overline{C} + \mu_I + \alpha$, $a_2(\alpha) = \alpha(\frac{r_C}{C_M}\overline{C}) + \frac{\mu_I r_C}{C_M}\overline{C}$, $a_3(\alpha) = \alpha(\kappa_I' + \frac{r_C}{C_M})\mu_I\overline{I}$ [17].

On the other hand, in the real world, epidemic models are inevitably subject to the environmental noise, which is an important component in an ecosystem (see e.g. [21,22]). Hence the deterministic models have some limitations in predicting the future dynamics of the system accurately. When modeling biological phenomena such as HIV dynamics, different cells and infective virus particles reacting in the same environment can often give different results. Lately, by incorporating the effects of a fluctuating environment, many authors have studied epidemic models with parameter perturbations (see e.g. [23–31]). For example, Ji and Jiang [23] considered a stochastic HIV-1 infection model with cell-mediated immune response. They established a sufficient condition for the stochastic asymptotic stability in the large of the infection-free equilibrium and gave the conditions for the solution fluctuating around the two infection equilibria (one without CTLs being activated and the other with). Sánchez-Taltavull et al. [24] presented a stochastic model of the dynamics of the HIV-1 infection and studied the effect of the rate of latently infected cell activation on the average extinction time of the infection. Liu [30] analyzed a model of cell-to-cell HIV-1 infection to $CD4^+$ T cells perturbed by stochastic perturbations. He studied the asymptotic behavior of the solution and he also investigated the existence of ergodic stationary distribution.

There are different approaches to introduce random perturbations into the model, both from a mathematical and biological perspective. In this paper, we assume that the environmental noise is proportional to the variables $C(t)$ and $I(t)$. For convenience in mathematics, we also assume that the environmental noise is proportional to $X(t)$ (see Remark 4.1). Then the stochastic version corresponding to system (1.2) takes the following form

$$\begin{cases} dC(t) = \left[r_C C(t)\left(1 - \dfrac{C(t)+I(t)}{C_M}\right) - \kappa_I C(t)I(t)\right]dt + \sigma_1 C(t)dB_1(t), \\ dI(t) = [\kappa_I' X(t) - \mu_I I(t)]dt + \sigma_2 I(t)dB_2(t), \\ dX(t) = [\alpha C(t)I(t) - \alpha X(t)]dt + \sigma_3 X(t)dB_3(t), \end{cases} \tag{1.3}$$