Applied Mathematics and Computation 293 (2017) 630–641

Contents lists available at ScienceDirect

Applied Mathematics and Computation

journal homepage: www.elsevier.com/locate/amc

Periodic solution of a stochastic HBV infection model with logistic hepatocyte growth

Falan Xie[a], Meijing Shan[b], Xinze Lian[c], Weiming Wang[a,d,*]

[a] College of Mathematics and Information Science, Wenzhou University, Wenzhou 325035, PR China
[b] Institute of Information Science and Technology, East China University of Political Science and Law, Shanghai 201620, PR China
[c] Oujiang College, Wenzhou University, Wenzhou 325035, PR China
[d] School of Mathematical Science, Huaiyin Normal University, Huaian 223300, PR China

ARTICLE INFO

Keywords:
Hepatitis B virus
White noise
Periodic solution
Persistence in mean

ABSTRACT

In this paper, we present a stochastic hepatitis B virus (HBV) infection model with logistic hepatocyte growth. We show that the stochastic differential equation (SDE) HBV model has at least one periodic solution induced by the white noise, and a unique stationary distribution which is stable. One of the most interesting findings is that random perturbations may be beneficial to format the periodic solution to the SDE HBV model.

1. Introduction

Hepatitis B virus (HBV) is one of the major disease in the world. The World Health Organization (WHO) has reported in 2015 that there are an estimated 240 million chronically infected persons worldwide [1]. Infection with HBV represents a dynamic process with a spectrum of clinical outcomes ranging from acute infection followed by virus clearance to chronic persistence of the virus [2]. Between 20% and 30% of those who become chronically infected will develop these complications, and an estimated 0.65 million people will die annually [3].

The study of HBV infection treatment may benefit from the use of mathematical modeling. Several models have been introduced for understanding HBV dynamics [2–5]. Among those models, Nowak et al. [4] formulated a basic virus infection model which is widely used in the studies of virus infection dynamics:

$$\begin{cases} \dot{x} = \lambda - dx - \beta vx, \\ \dot{y} = \beta xv - ay, \\ \dot{v} = ky - rv, \end{cases} \tag{1}$$

where x, y and v are numbers (densities) of healthy hepatocytes, infected hepatocytes and viral particles (virions) at time t, respectively. Healthy hepatocytes are assumed to be produced at the constant λ, die at the rate of dx and become infected at the rate of βxv, where β is a rate constant describing the infection process. Infected hepatocytes are thus produced at the rate of βxv and die at the rate of ay, and virus are produced by infected hepatocytes at a rate ky and removed at a rate rv.

* Corresponding author at: College of Mathematics and Information Science, Wenzhou University, Wenzhou 325035, PR China. Tel.: +86 13957755621.
E-mail addresses: xiefalan2015@163.com (F. Xie), shanmeijing@ecupl.edu.cn (M. Shan), xinzelian@163.com (X. Lian), weimingwang2003@163.com (W. Wang).

http://dx.doi.org/10.1016/j.amc.2016.06.028
0096-3003/

Based on the results of [4], and after considering the ability of regeneration of the hepatocytes possess, Li et al. [5] established an HBV infection model with logistic hepatocyte growth as follows:

$$\begin{cases} \dot{x} = r_1 x\left(1 - \dfrac{x+y}{K}\right) - \beta x v, \\ \dot{y} = \beta x v - a_1 y, \\ \dot{v} = k_1 y - r v, \end{cases} \tag{2}$$

and they determined the extinction and the persistence of HBV infection by the basic reproduction number.

Although persistent HBV infection is associated with ineffective CTL responses, the onset of chronic infections is considered to be multifactorial with the potential contributing factors including mutational variations of HBV, alterations in the innate- and B-cell responses [6]. In fact, the parameters for growth depend on the state and nature of the virus, the condition of the immune system, and the environment in which the interaction takes place the body. The environment of the body is determined by the overall health of the individual. This overall health affects the condition and readiness of the immune system [7]. The variations can affect either the replication of the virus or its elimination kinetics. One way to explore their impact on the dynamics of HBV infection could be the extension of the deterministic description of the virus-CTL interaction to include the stochastic forcing either in an additive or multiplicative way. The resulting stochastic models can offer a more realistic representation for studying the long-term kinetics of HBV-immune system interaction [2].

To incorporate the effect of mutational variations, here, based on the model of Li et al. [5], we formulate a stochastic model by introducing the multiplicative noise terms into the growth equations of both the healthy and infected hepatocytes. Following [8–16], in this paper, we assume that the infectious rate β will fluctuate around some average value due to continuous fluctuation in the environment. And we introduce randomness into the deterministic model (2) by perturbing β to $\beta + \sigma\zeta(t)$, and obtain the following stochastic differential equations:

$$\begin{cases} \dot{x} = r_1 x\left(1 - \dfrac{x+y}{K}\right) - (\beta + \sigma\zeta(t))xv, \\ \dot{y} = (\beta + \sigma\zeta(t))xv - a_1 y, \\ \dot{v} = k_1 y - r v, \end{cases} \tag{3}$$

where $\zeta(t)$ is a Gaussian white noise and characterized by:

$$\langle \zeta(t) \rangle = 0, \qquad \langle \zeta(t)\zeta(t') \rangle = \delta(t - t'),$$

here $\langle \cdot \rangle$ denotes ensemble average and $\delta(\cdot)$ is the Dirac-δ function. σ denotes the intensity of environmental forcing. Now we can rewrite model (3) into the form of stochastic differential equations as follows:

$$\begin{cases} dx = \left(r_1 x\left(1 - \dfrac{x+y}{K}\right) - \beta x v\right)dt - \sigma x v dB(t), \\ dy = \left(\beta x v - a_1 y\right)dt + \sigma x v dB(t), \\ dv = \left(k_1 y - r v\right)dt, \end{cases} \tag{4}$$

where $B(t)$ is the standard one-dimensional independent Wiener process defined over the complete probability space $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\geq 0}, \mathcal{P})$, the relations between the white noise terms and Wiener process are defined by $dB(t) = \zeta(t)dt$.

On the other hand, as one of organismic physiological systems, human immune system has a very high degree of complexity. The HBV system can be modulated by circadian rhythms and some other behaviors such as periodically taking some drugs [17,18]. In view of this, we assume that the coefficients $r_1(t), K(t), \beta(t), a_1(t), k_1(t), r(t)$ and $\sigma(t)$ in the SDE model (5) are all positive T-periodic (T is a positive constant) continuous functions.

Based on the discussions above, in this paper, we will focus on the existence of nontrivial positive periodic solution in the following SDE HBV model with periodic immune response:

$$\begin{cases} dx = \left(r_1(t)x\left(1 - \dfrac{x+y}{K(t)}\right) - \beta(t)xv\right)dt - \sigma(t)xv dB(t), \\ dy = \left(\beta(t)xv - a_1(t)y\right)dt + \sigma(t)xv dB(t), \\ dv = \left(k_1(t)y - r(t)v\right)dt. \end{cases} \tag{5}$$

The rest of this article is organized as follows: in Section 2, we present some definitions and known results. In Section 3, we prove that the SDE HBV model (5) has a globally positive solution. In Section 4, we present sufficient conditions for the existence of a positive periodic solution of model (5). In Section 5, we provide some numerical results to support our analytical results. In the last section, Section 6, we provide a brief discussion and summary of main results.