Chaos, Solitons and Fractals 93 (2016) 1–13

Contents lists available at ScienceDirect

Chaos, Solitons and Fractals

Nonlinear Science, and Nonequilibrium and Complex Phenomena

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

Stochastic stability and state shifts for a time-delayed cancer growth system subjected to correlated multiplicative and additive noises☆

Kang Kang Wang[a,b,*], Ya Jun Wang[a], Sheng Hong Li[a,c], Jian Cheng Wu[d]

[a] School of Mathematics and Physics, Jiangsu University of Science and Technology, Zhenjiang 212003, China
[b] Department of Mathematics, Southeast University, Nanjing 210096, China
[c] College of Mathematics, Nanjing Normal University, Nanjing 210097, China
[d] State Key Laboratory of Mechanics and Control of Mechanical Structures, Nanjing University of Aeronautics and Astronautics, Nanjing 210016, China

ARTICLE INFO

Article history:
Received 6 April 2016
Revised 17 September 2016
Accepted 24 September 2016

Keywords:
Multiplicative noise
Addictive noise
Time delay
Cancer growth model
Mean treatment time
System stability

ABSTRACT

In the present paper, we investigate the stationary probability distribution(SPD) and the mean treatment time of a time-delayed cancer growth system induced by cross-correlated intrinsic and extrinsic noises. Our main results show that the resonant-like phenomenon of the mean first-passage time (MFPT) appears in the tumor cell growth model due to the interaction of all kinds of noises and time delay. Due to the existence of the resonant-like peak value, by increasing the intensity of multiplicative noise and time delay, it is possible to restrain effectively the development of the cancer cells and enhance the stability of the system. During the process of controlling the diffusion of the tumor cells, it contributes to inhibiting the development of cancer by increasing the cross-correlated noise strength and weakening the additive noise intensity and time delay. Meanwhile, the proper multiplicative noise intensity is conducive to the process of inhibition. Conversely, in the process of exterminating cancer cells of a large density, it can exert positive effects on eliminating the tumor cells by increasing noises intensities and the value of time delay.

1. Introduction

During the past decades, it is always a hot issue of medical profession in the world to investigate the evolvement of cancer cells. Whereas, so far we still know very little about the mechanisms of its growth and destruction. Up to now, there are some important measures designed for the treatment, such as surgery, chemotherapy and radiotherapy, but all of those traditional treatment methods could not eradicate the cancer, and many patients experience recurrence and die of cancer eventually after all kinds of treatment methods. Recently, a method of adoptive cellular immunotherapy [1,2] has obtained increasing importance to investigate for cancer treatment, integrating with the traditional tools. In order to explore the mechanisms of the cure for the cancer growth, a lot of applied mathematical models reflecting the change rule of tumor growth are proposed [3–7]. Besides, environmental factors often play critical roles in the process of cancer treatment, such as the temperature, radiations, chemical drugs, degree of vascularization of tissues, supply of oxygen and nutrients, and the immunological state of the host. Hence, it should be necessary to take into account the probable impacts of the all types of stochastic disturbances on the treatment process before launching the treatment experiment [8–13]. In the previous work, the effect of the noise in the cancer dynamics has been studied analytically and numerically. Stochastic characteristics in all types of cancer models have been investigated widely, such as the stationary probability distribution [14,15], mean first passage time [15–18], resonant activation [19–23], noise enhanced stability [24–29]. Lately, Zeng et.al [30] investigated the phenomenon of stochastic resonance in a tumor growth model under the presence of immune surveillance with consideration of time delay and cross-correlation between the multiplicative and additive noises. Afterwards, they [31] discussed the phenomenon of stochastic resonance in a vegetation ecological system with time delay, at which the vegetation dynamics is assumed to be disturbed by both intrinsic and extrinsic noises. In Ref [32], Zhong studied that stochastic resonance driven by pure multiplicative noise in a noise-resonant effects in cancer development induced by external fluctuations and periodic treatment. However, few works study the joint action of the correlated noise, due to the interaction of internal and the external noises and time delay which always exists in the developing process of cancer growth.

☆ Project supported by the National Natural Science Foundation of China (Grant No 11072107, 61371114), the Research Fund of State Key Laboratory of Mechanics and Control of Mechanical Structures of Nanjing University of Aeronautics and astronautics, China (Grant No. 0113G01), China Postdoctoral Science Foundation Funded Project (Grant No: 2016M591737) and the Project Fund of Jiangsu University of Science and Technology, China (Grant No. 633051203).

* Corresponding author.
E-mail address: wkk_com@126.com (K.K. Wang).

http://dx.doi.org/10.1016/j.chaos.2016.09.022

Moreover, few works analyze theoretically the characteristics of the steady states and transient properties of cancer growth system subjected to the correlated noises and time delay. In fact, the combination of noises and time delay is ubiquitous in nature and often changes fundamental dynamics of the system. Zeng et al [34,35] studied Schöogl model with time-delayed feedback to investigate the switching behavior of a bistable chemical reaction system in the presence of cross-correlated multiplicative and additive noise sources. They analyze the impact of noise and time delay in the monomer-dimer (MD) surface reaction model by using theoretical analysis. Meanwhile, they [36,37] investigated the noise-and delay- induced regime shifts in an ecological system of vegetation, the transport of an inertial Brownian motor moving in an asymmetric periodic potential, where it is driven by a time periodic and a constant biasing driving force. Also, Zeng et.al [38] discussed the dynamical properties of an anti-tumor cell growth system in the presence of delay and correlated noises. Valenti et.al [42,43] analyzed the dynamics of the FitzHugh–Nagumo (FHN) model in the presence of colored noise and a periodic signal and a spatially extended system of two competing species in the presence of two noise sources. They [44–47] also studied variable randomness of the stochastic process by varying the memory and investigated a mathematical model describing the growth of tumor in the presence of immune response of a host organism. In recent years, some study on the probability density function of the residence times in metastable systems, and on the role of additive and multiplicative noise sources in biological and magnetic systems are made in [48–50].

In the present paper, based on the stochastic cancer development model, the characteristics of stationary probability distribution for the system and the mean treatment time caused by the impact of the additive noise, multiplicative noise, the cross-correlated noise between them and the time delay are explored. The paper aims to contributing to a comprehensive and systematic understanding of the behavior of the tumor cells caused by the influences of the additive and multiplicative noises with the time delay. In Section 2, we introduce the stochastic cancer growth system. In Sections 3 and 4, the steady state properties for the generalized potential function and the SPDF of the cancer growth system are discussed in detail. In Section 5, the expressions for the mean treatment time between two stable states of the system are derived, and the effects of the noises and time delay on the MFPT of the stochastic system are analyzed numerically. A detailed conclusion and some description are given in the final section.

2. A stochastic cancer growth model including noise terms and time delay

In the light of the derivation of Lefever and Garay [8,9], we can put forward the deterministic dynamical equation of the cancer growth model as follows:

$$\frac{dx(t)}{dt} = (1-\theta x)x - \beta\frac{x}{1+x}, \tag{1}$$

where x stands for the number of tumor cells, θ and β represent the influence coefficients which control the varying of number of tumor cells. $\theta > 0$, $\beta > 0$. In fact, the status of tumor cells are always disturbed by all types of internal or external factors. Hence, we can rewrite the coefficient β as $\beta+\xi(t)$, where $\xi(t)$ indicates the fluctuation of many external factors, such as temperature, drugs, radiotherapy on the stochastic system. Meanwhile, taking into account some factors such as interaction between organs and the nervous system fluctuation, hormonal change and time delay that the drugs and radiotherapy need to militate in the human body, we have reason to introduce an additive noise $\eta(t)$ and a time delay term τinto the tumor cell model in order to describe

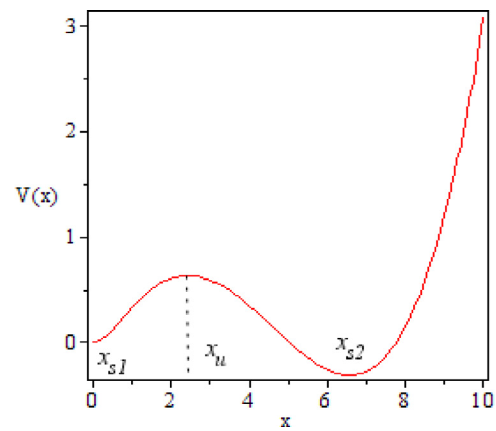

Fig. 1. The bistable potential $V(x)$. The parameter values of the potential $V(x)$ are $\theta=0.1$, $\beta=2.6$. The two stable states are $x_{s1}=0$, and $x_{s2}\approx 6.56155$, and one unstable state is $x_u\approx 2.43847$.

the effects of all external factors on the development of cancer cells:

$$\frac{dx(t)}{dt} = x(t-\tau)(1-\theta x(t-\tau)) - [\beta+\xi(t)]\frac{x(t)}{1+x(t)} + \eta(t), \tag{2}$$

in which $\xi(t)$ and $\eta(t)$ denote Gaussian white noises, whose statistical properties are defined as follows:

$$\langle\xi(t)\rangle = \langle\eta(t)\rangle = 0,$$

$$\langle\xi(t)\xi(t')\rangle = 2Q\delta(t-t'),$$

$$\langle\eta(t)\eta(t')\rangle = 2M\delta(t-t'),$$

$$\langle\xi(t)\eta(t')\rangle = \langle\eta(t)\xi(t')\rangle = 2\lambda\sqrt{QM}\delta(t-t'), \tag{3}$$

where both of Q and $M$are the intensities of the multiplicative noise and the additive noise respectively. On the other hand, because all kinds of external fluctuations from drugs, radiotherapy and so on can interact with the intrinsic impact from human organs and the nervous system, a cross-correlated noise can be produced naturally by the external noise and the internal one. Here, we denote by λ the strength of the cross-correlated noise. $-1 < \lambda < 0$ represents the negative correlation strength between the two noises; $0 < \lambda < 1$denotes the positive one between the two noises. The deterministic potential function corresponding to Eq. (1) can be written as follows:

$$V(x) = \frac{\theta}{3}x^3 - \frac{1}{2}x^2 + \beta x - \beta\ln(1+x). \tag{4}$$

Its figure in the interval [0,10] is plotted in Fig 1.

Without counting the impact of noise terms and time delay, the fixed points of Eq. (1) are totally dependent on θ and β: (1) For $\theta > 1$ and $0 < \beta < 1$, a stable point $x_s=0$ and an unstable point $x_u = \frac{1-\theta+\sqrt{(1+\theta)^2-4\beta\theta}}{2\theta}$;

(2) For $0 < \theta < 1$ and $0 < \beta < (1+\theta)^2/4\theta$, two stable point $x_{s1}=0$,

$x_{s2} = \frac{1-\theta+\sqrt{(1+\theta)^2-4\beta\theta}}{2\theta}$and an unstable point $x_u = \frac{1-\theta-\sqrt{(1+\theta)^2-4\beta\theta}}{2\theta}$;

(3) For $0 < \theta < 1$ and $\beta=(1+\theta)^2/4\theta$, a stable point $x_s=0$ and an unstable point $x_u = (1-\theta)/2\theta$. In the following section, we will