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The properties of the anti-tumor model with coupling non-Gaussian noise and Gaussian colored noise

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HIGHLIGHTS

- The non-Gaussian noise has a dual role in the development of tumor.
- A minimum of the mean value can be obtained by choosing proper parameters.
- The cross-correlated degree can slow down the transition of tumors.
- The correlation time can enhance the stability of the disease state.

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ABSTRACT

The anti-tumor model with correlation between multiplicative non-Gaussian noise and additive Gaussian-colored noise has been investigated in this paper. The behaviors of the stationary probability distribution demonstrate that the multiplicative non-Gaussian noise plays a dual role in the development of tumor and an appropriate additive Gaussian colored noise can lead to a minimum of the mean value of tumor cell population. The mean first passage time is calculated to quantify the effects of noises on the transition time of tumors between the stable states. An increase in both the non-Gaussian noise intensity and the departure from the Gaussian noise can accelerate the transition from the disease state to the healthy state. On the contrary, an increase in cross-correlated degree will slow down the transition. Moreover, the correlation time can enhance the stability of the disease state.

1. Introduction

The interaction of immune system with tumors is extremely complicated which has been a challenge in medicine, biology and physics [1–4]. On one hand, the immune system functions as an important defense against cancer. On the other hand, the immune system can also facilitate tumor progression. Accordingly, it is necessary to investigate the tumor growth under immune surveillance for developing the efficient strategies against cancer.

In recent years, much effort has been devoted to investigating the mathematical modeling of immune response to tumor cells and a series of intriguing and significant findings have been brought to light [5–15]. In 2006, Zhong et al. investigated the anti-tumor model modulated by a seasonal external field, observing the phenomenon of stochastic resonance induced by pure multiplicative noise [6]. In 2010, the critical phenomenon and the re-entrance phenomenon induced by the time delay have been observed in the anti-tumor model with Gaussian white noise [13]. Further, Guo and his collaborators have studied transitions and stochastic resonance induced by bounded noises and two time delays [14,15]. In 2014, the rich dynamical behaviors of the tumor and immune system interaction model with three delays have been studied [12]. Beyond that, the

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phenomenon of noise enhanced stability (NES) has been widespread concerned and researched [5,10,16,17]. More recently, Yang also investigated the effects of periodic force on the stability of the metastable state in logistic system [18]. Currently, although tumor growth has been widely studied, the fluctuations in these studies are mostly Gaussian noise. In fact, the non-Gaussian noise could be more related to biological systems and the experimental results for one kind of crayfish and rat skin offer compelling indications that the noise sources in these sensory systems could be non-Gaussian [19,20]. Accordingly, it is essential to investigate the effects of non-Gaussian noise on tumor development to provide valuable suggestions for tumor therapy [21–24].

Inspiredly, this paper deals with the tumor and immune system interaction model under immune surveillance driven by cross-correlated multiplicative non-Gaussian noise and additive Gaussian colored noise, investigating the complicated effects of the immune system and the correlated noises on the tumor development and progression.

The rest of this paper is arranged as follows: In Section 2, the stationary probability distribution (SPD) function of the tumor growth model will be derived. Then we will provide some analysis of effects of the multiplicative non-Gaussian noise and additive Gaussian colored noise on the stationary properties and transient properties of tumor growth in Section 3. In Section 4, a brief conclusion ends the paper.

2. Tumor growth model and its SPD

The grow law of tumor evolution can be approximated by an insect outbreak model [25,26]. Despite the model fails to take into account every process of the anti-tumor system, it captures the essence of the interactions between the tumor cells and the immune system and is validated by the experimental and clinical evidences [9,27,28]. In the past decades, the researchers have widely applied the classical model to study the tumor development, finding many significant and valuable results [6,7,9,21].

Given the above facts, we still adopt the insect outbreak model to describe the tumor growth under immune surveillance which reads

$$\frac{\mathrm{d}x}{\mathrm{d}t} = rx - \frac{r}{K}x^2 - \frac{\beta x^2}{1+x^2} = rx - mx^2 - \phi\left(x\right), \tag{1}$$

with $m = r/K$ and $\phi\left(x\right) = \beta x^2/\left(1+x^2\right)$. In Eq. (1), x is the population of tumor cells, the parameter r is the linear birth rate of tumor cells. The quantity m is termed the decay rate which is inversely proportional to the carrying capacity K depending on the resources of the biological environment for tumor cells such as oxygen, and glucose [9]. The ability of immune cells to recognize and attack tumor cells is represented by the function $\phi\left(x\right)$, where β designates the immune coefficient.

The potential corresponding to Eq. (1) is

$$U\left(x\right) = \frac{1}{3}mx^3 - \frac{1}{2}rx^2 + \beta x - \beta \arctan\left(x\right). \tag{2}$$

For $r = 1$, $K = 10$ and $\beta = 2$, Eq. (2) has an unstable state $x_u = 2$ and two stable states $x_- \approx 0.6834$, $x_+ \approx 7.3166$. From the biological point of view, we noted that x_- means the healthy state, where a minority of tumor cells is present and x_+ represents the disease state, where the population of tumor cells stays at a high level. x_u corresponds to sub-healthy state and will move to x_+ or x_- at any small perturbation.

The tumor cell evolution is further influenced by coupling internal noise and external noise. The internal noise should be generated by gene mutations within the tumor system as a kind of self-organization. In contrast, the external noise is thought to be originated from the extracellular matrix embedding the tumor. In the biological or physical context, multiplicative noise denoted by $\eta\left(t\right)$ is equated with the internal noise which will influence the birth rate of tumor cells. So the birth rate r in Eq. (1) should be rewritten as $r - \eta\left(t\right)$. Furthermore, the system is influenced by the additive noise denoted by $\xi\left(t\right)$ which can be identified as external noise caused by environment fluctuation. Thus the stochastic tumor growth model driven by coupling multiplicative noise and additive noise can be given by

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \left(r - \eta\left(t\right)\right)x - mx^2 - \phi\left(x\right) + \xi\left(t\right), \tag{3}$$

where $\eta\left(t\right)$ is a multiplicative non-Gaussian noise which is introduced to mimic the stochastic disturbances of the birth rate and is given by

$$\frac{\mathrm{d}\eta}{\mathrm{d}t} = -\frac{1}{\tau_1}\frac{\mathrm{d}}{\mathrm{d}\eta}V_q\left(\eta\right) + \frac{1}{\tau_1}\varepsilon\left(t\right), \tag{4}$$

where $\varepsilon\left(t\right)$ is a Gaussian white noise and its statistical properties are given by

$$\begin{aligned} &\left\langle \varepsilon\left(t\right)\right\rangle = 0, \\ &\left\langle \varepsilon\left(t\right)\varepsilon\left(s\right)\right\rangle = 2D_1\delta\left(t-s\right). \end{aligned} \tag{5}$$