A Study of Verhulst's Model with Gaussian Correlated Noise

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Abstract**—** The Verhulst's differential equation is used to analyze cancer cell population in the existence of correlated white noise. We discuss the steady state properties of tumor cell growth and discuss the effect of correlated noise. We have obtained steady state probability function for tumor cell population from Fokker-Planck equation. The study reveals that as degree of correlation of the noise increases tumor cells died out.

Keywords: Verhulst differential equation, Stationary probability density function, Gaussin correlation noise

I. Introduction:

Tumor cell growth can be modeled by a single deterministic differential equation. Stochastic noise functions characterize total effect of many different factors that affect the tumor cell population. The exact value of stochastic variable can not be found but the probability density function is known and can be used to estimate the probability density function of the tumor cell population. The deterministic differential equation with stochastic noise is called Langevin equation. The solution of Langevin equation is called Fokker-panck equation. **[1]** have presented results of the stationary probability distribution and mean first passage time for a bistable potential, obtained with a particular family of interpolating functions. **[2]** studied a tumor cell logistic growth model in the presence of correlated additive and multiplicative noise**. [3]** explored that the multiplicative noise induces a phase transition of the tumor growth from a uni - stable state to a bi-stable state**. [4]** have studied the effects of noise color on the phase diagram and the steady state probability distribution when the noise correlation time is varied.**[5]** have used logistic growth model to describe the bacterial growth in the presence of Gaussian colored noise. **[6]** studied the effect of noise in an avascular tumor growth model. **[7]** investigated a time delayed tumor cell growth model with correlated noise. **[8]** presented some analytical results on such delayed stochastic systems from both dynamical and probabilistic perspectives.

In this paper, we study verhulst's model before correlated additive and multiplicative noise and demonstrate how noise correlation can enthusiastically cause tumor cell annihilation.

II. Mathematical Formulation:

The Verhulst's tumor growth model has been used in many cases as a basic model of both cell growth and more particularly, tumor cell growth. Here, we only consider tumor cell growth. The verhulst differential equation is shown,

$$\frac{dx}{dt} = rx\left(1-\frac{x}{k}\right) \tag{1}$$

Where x is the tumor mass, r is the growth, and k is the carrying capacity of environment. We consider effects due to some external factors such as temperature, drugs, radiotherapy and chemotherapy etc. These factors can influence the tumor mass directly as well as tumor growth rate. In other words, the fluctuation of these factors affects the parameter r generating multiplicative noise, at the same time, some factors, such as drugs and radiotherapy restrains the tumor cell, giving rise to a negative additive noise. As a result, we obtain

$$\frac{dx}{dt} = rx\left(1-\frac{x}{k}\right) + x\delta(t) - \mu(t) \tag{2}$$

Where $\delta(t)$ and $\mu(t)$ are Gaussian multiplicative and additive noises respectively with the following properties:

$$\langle\delta(t)\rangle = \langle\mu(t)\rangle = 0 \tag{3}$$

$$\langle\delta(t)\delta(t')\rangle = 2D\eta(t-t') \tag{4}$$

$$\langle\mu(t)\mu(t')\rangle = 2\beta\eta(t-t') \tag{5}$$

$$\langle\delta(t)\mu(t')\rangle = 2\omega\sqrt{D\beta}\,\delta(t-t') \tag{6}$$

Where β and D are the intensity of the additive and multiplicative noises respectively. and ω denotes the degree of correlation between $\delta(t)$ and $\mu(t)$ with $0 \le \omega \le 1$.

Since the cell number x cannot be negative, we can derive the Fokker-Planck equation for the evolution of steady probability distribution function (SPDF) corresponding to eqn. (2) under the constraint $x \ge 0$. The equations are

$$\frac{\partial P(x,t)}{\partial t} = -\frac{\partial A(x)P(x,t)}{\partial x} + \frac{\partial^2 B(x)P(x,t)}{\partial x^2} \tag{7}$$

Where $P(x,t)$ is the probability density and

$$A(x) = rx\left(1-\frac{x}{k}\right) + Dx - \omega\sqrt{D\beta} \tag{8}$$

$$B(x) = Dx^2 - 2\omega\sqrt{D\beta}\,x + \beta \qquad (9)$$

The stationary probability distribution of equation is given as

$$P_{st}(x) = \frac{N}{B(x)} \exp\left[\int_0^x \frac{A(x_1)}{B(x_1)} dx\right] \qquad (10)$$

Where N is the normalizing constant.

The extrema of $P_{st}(x)$ follow a universal equation $A(x) - \frac{dB(x)}{dx} = 0$.

$$(D - r)x + \frac{rx^2}{k} - \omega\sqrt{D\beta} \qquad (11)$$

If $\omega = 0$, the end term of eqn. (11) will be zero and we will obtain extrema of SPDF for only multiplicative noise process. For zero correlation, additive noise has no effect on the position of extrema of SPDF which are $x = 0$ and $x = \frac{k}{r}(r - D)$.

III. Numerical Results:

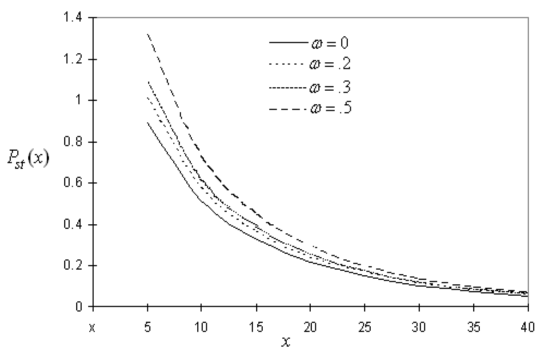

Fig1: $P_{st}(x)$ **(Probability density) Vs** x **(no. of cells)**
$r = .5$, $D = .9$, $\beta = 3$, $k = 10$, $N = 5$, $\omega = 0, .2, .3, .5$

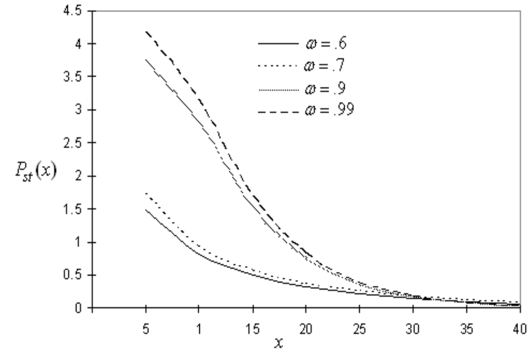

Fig2. $P_{st}(x)$ **(Probability density) Vs** x **(no. of cells)**
$r = .5$, $D = .9$, $\beta = 3$, $k = 10$, $N = 5$, $\omega = .6, .7, .9, .99$

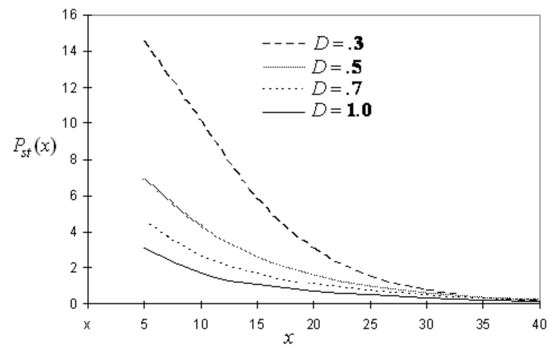

Fig3: $P_{st}(x)$ **(Probability density) Vs** x **(no. of cells)**

$r = .5$, $\beta = .5$, $\omega = 0$, $k = 10$, $N = 5$, $D = .3, .5, .7, 1$

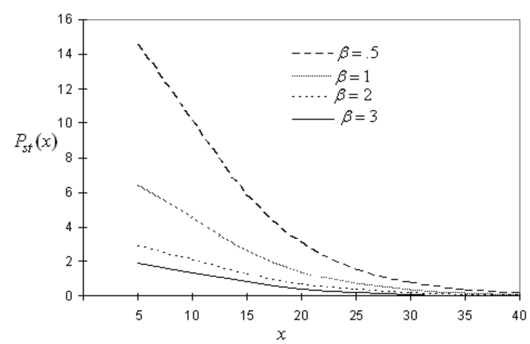

Fig.4: $P_{st}(x)$ **(Probability density) Vs** x **(no. of cells)**
$r = .5$, $D = .9$, $\omega = 0$, $k = 10$, $N = 5$, $\beta = .5, 1, 2, 3$

Fig. (1) And (2) illustrate the effect of the correlation parameter ω on the steady state probability distribution (SPD). As ω increases $P_{st}(x)$ increases for small x and decreases for large x. Since x denotes tumor cell population, it is apparent that increasing ω can cause disappearance of tumor cell population.

Fig. (3) and (4) display the effect of the strength of noise $\delta(t)$ and $\mu(t)$ on the SPDF. A different curve is represented when ω and β are fixed and we change the multiplicative noise intensity D (See Fig. 3). As D is increased, the maximum of SPD moves from a large value of x to small values of x, showing that the multiplicative noise is drift term, which denotes that the multiplicative noise can push the system cell towards disappearance. In other words, severe fluctuation of the growth rate may cause tumor death. When the degree of correlation noises and the strength of multiplicative noises are fixed, as the additive noise intensity β is increased, the maximum value on small value of x increases and the maximum value on large value of x decreases (See Fig. 4). The position of the extrema of the SPDF is weakly affected by the strength β of additive noise.

IV. CONCLUSION:

We have studied the possessions of ecological fluctuations on tumor cell growth and its steady state properties. For large values of ω the distribution of cell population is pointed at $x=0$, which denotes the high annihilation rate. The additive noise is a diffusive aspect, even as the multiplicative noise gives drift feature in the process. It is seen that ecological intensive fluctuations may cause tumor cell extinction.

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