Article

Time lag analysis of novel arithmetic modeling in breast cancer

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Abstract

In this paper, a mathematical model which considers population dynamics among infected and uninfected cancer tumor cells has been proposed. Delay differential equations have been utilized to demonstrate the framework to consider the periods of the cell cycle. We examine the steadiness of the framework and demonstrate a hypothesis dependent on the contention standard to decide the dependability of a fixed point and show that the solidness may rely upon the delay. We show hypothetically as well as through numerical results that periodic oscillations may arise through Hopf bifurcations. In this paper we study a stochastic model for the conduct of malignancy tumors, depicted by a stochastic differential condition with multiplicative noise term. We study the existence of the solution process, as well as its behavior in the framework of stochastic inclusion problems and long time behavior.

Keywords breast cancer; time lag; stability; hopf-bifurcation; stochasticity.

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1 Introduction

Breast cancer is a frequently occurred cancer among women, which is affecting 2.1 million women each year. It caused approximately 15% of all cancer deaths among women in 2018 (WHO, 2020). Symptoms of breast cancer include breast lump, bloody discharge from the nipple, and changes in the nipple or breast shape or texture. The treatment of cancer depends on type of cancer. For instance, chemotherapy, radiation, hormone therapy, and surgery some options to treat breast cancer (Diaby et al., 2015). The target organ breast cancer is a collection of malignancies in breast epithelial cells. Histological subtypes include ductal (70-80% of diagnosed cases), lobular (10-15% of diagnosed cases) or medular (3-5% of diagnosed cases). About 65% of

breast cancers are either estrogen receptor (ER) or progesterone receptor (PR) positive (Parise, 2014). These hormone receptor-positive cancers tend to have a 5-year survival rate higher than other subtypes (Lehmann, 2011). Other subtypes include HER2-positive breast cancer, characterized by HER2 protein over expression or gene amplification, and triple negative breast cancer (TNBC), lacking expression of ER / PR and HER2 amplification or over expression. Morphomolecular analyzes revealed new ways to classify breast cancers (Sorlie, 2003; Network, 2012). Based on comprehensive genomic classifications, breast cancers were divided into four groups: i) the luminal A subtype, which is ER and/or PR-positive and HER2-negative and has a low proliferative index of Ki67; ii) the luminal B subtype, which is ER and/or PR-positive and may be HER2-positive, has a high Ki67 index and a lower prognosis than the luminal A subtype; iii) the HER2-enriched subtype ; The latter is a high-grade, fast-growing cancer with the worst prognosis compared to all subtypes (Parise, 2014). The triple-negative subtype tends to occur more frequently in younger premenopausal women and is believed to be more prevalent in some high-genetic-risk patients as defined in the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (Criscitiello, 2012; Oncology NCCNCPGi, 2015) specifically in BRCA1 mutation carriers21. These high-genetic patients also have an increased risk of developing ovarian cancer somewhere in their life (Wong-Brown et al., 2015). To investigate the complexities of cancer progression and reaction in breast malignancies, we claim that comprehensive mathematical modelling systems are required from a system biology perspective. Such integrated frameworks could offer innovative contributions to the clinical women's cancer community, as clinical questions cannot always be answered with contemporary clinical and experimental tools. Any breast cancer screening test aims at early detection and decrease in cancer-related mortality. As on date, current non-invasive methods for monitoring and identifying breast cancers in all subtypes of general risk people provide diagnostic techniques such as mammograms and magnetic resonance imaging (MRI) and surgical breast and self-breast examination. Screening imaging techniques may be used to monitor and assess improvements in breast tissue, but not often provide sufficient responsiveness or specificity (Petrucelli et al., 2010).

Human breast cancer growth trend is clinically significant, and it is primarily for predicting the length of silent growth pre-diagnosis and planning an optimum post-surgery chemotherapeutic plan. Breast cancer growth trends theoretical research has been the topic of significant discussion and contention among mathematical oncologists over two decades (Diaby et al., 2015; Petrucelli, 2010). For a more comprehensive recent review and theoretical comparison of the various mathematical formulations used to model tumour growth dynamics (Ribba, 2014). Unlike Speer et al. (1984), Norton et al. (1988) demonstrated in 1988 that the deterministic Gompertz equation was the best fit for clinical breast cancer sizes and post-therapy regression rates. Norton developed a conceptual survival curve fitting the classic Gompertzian rise, model to the percentage of surviving patients per year after diagnosis In comparison to the stochastic existence of the analogous parameter used by Speer et al. The likelihood distribution feature of the rise decay parameter was calculated lognormal and based on the current number of tumor cells. While Norton's proposed model fits clinical data on untreated breast cancer, it is unclear whether Gompertzian Kinetics (or variant) also refers to disease development before or after treatment. Spratt et al. (1993) measured uncontrolled development levels in breast cancer before detection in 1993-97. They used data from mammographic breast cancer tumor measurements and conducted a minimum square regression analysis to prove that a generalized logistic equation was the best fit for the observed data. The mathematical analysis conducted excluded data from patients whose tumors were clinically detected between two consecutive mammogram screenings or whose tumors showed no size change during clinical observation. Using their growth model, Spratt et al. (1993) generated probability distributed tumor duplication functions at mammographic detection and increased untreated tumor size after 1-2 years of detection. Whereas the analysis quantitatively underlines the substantial

natural variation in growth levels in untreated human breast cancer, whether histological and morph molecular features affect simulation outcomes remains unknown from this method. Moreover, the reported mathematical results might have been selectively biased towards reflecting the progression of slower growing tumors, as these tumors are more representative of clinical cases amenable to detection via regular mammographic screening. In a different attempt to model the natural history of breast cancer, Koscielny et al. (1985) considered two growth patterns, exponential and Gompertzian, in 1985 to assess the timing of initiation of distant metastases using observed data in breast cancer patients. Koscielny et al. (1983) reported that the mean metastasis development period is around 3.8 years with all growth rates, and that a 30% decrease in metastasis occurrence is expected if primary tumors are handled 12 months sooner. In order to assess the time at which metastases are initiated, Koscielny et al. assume a linear relationship between doubling times of primary breast tumors and of their metastases. The validity of such a limiting assumption, however, is empirically questionable as, to the best of our knowledge; no deterministic relationship has been established in any published in vitro or in vivo investigations. Here, we recapitulate scientifically established breast cancer development and care information. Whenever possible, we compare and contrast the two malignancies to highlight areas where clinically inspired and validated mathematical modeling could contribute substantially.

We show how current paradigms in the mathematical oncology community focusing on the two malignancies do not make comprehensive use of existing clinical data or reflect substantially, and we highlight the modeling areas in the most critical need for clinical data integration. They stress that any statistical analysis of women's cancers will be directed specifically at solving clinically related problems.

Cancer is turning into the leading cause of death across our planet but with all of our details on how to expand, complementary treatment strategies continue to be a mystery. The growth is caused by the abnormal growth of the traditional tissue that attacks parts of our body. The reaction begins when the cell growth area is known by our immune cells. Mathematical modeling can be a powerful tool that has the potential to raise an understanding of birth defects (Adam et al., 1997; Araujo et al., 2004; Khajanchi, 2018; Kuznetsov et al., 1994; Preziosi, 2003; Starkov et al., 2016).

Mathematical models provide realistic representations and sizes of complex biological systems, as well as the clarification of organisms by their effects can provide insight into the shape predictions of the plant under different conditions. At the beginning of the nineteenth century, the concept of using a mathematical model of tumor-immune interactive dynamics began to be developed, after which a series of mathematical models were developed to report the overlap between the competitive anti-disease program by several authors (Kirschner et al., 1998; Kuznetsov et al., 1994; Rejniak et al., 2011; Villasana et al., 2003). Many authors like Delaware Boer et al. (1985), Goldstein et al. (2004) and Kronic et al. (2008) have used mathematical models to explain against the immune response to tumor growth. Several authors (Kuznetsov et al., 1994; Sarkar et al., 2005; El-Gohary, 2008) have used the idea of dealing with prey in the gastrointestinal tract wherever immune cells play a role and other cells in the mammary gland.

The delay in characterization has long been used in characterizing the cancer model (Forys et al., 2011; Miękisz et al., 2011; Piotrowska et al., 2011; Piotrowska et al., 2011). Byrne (1997) looks at the impact of your delay on the growth potential of a vascular tumor by introducing a time-delayed problem in cell growth. In this study the variability of the sound of the points entered due to the time delay and the possibility of the emergence of conflict resolution solutions. Recently, Forys and Kolev (2002) suggested and studied the role of time delay in the dynamic growth of tumors. They are studying the delay model according to the law of accountability and the mass conservation law. The related (Yafia, 2006) stimulates the interaction between the expanding lesion and the quiescent cells with a single delay.

2 Formulation of Mathematical Model

The model contains two types of tumor cells x and y that respectively are the size of uninfected tumor cells and infected tumor cells by the virus. In this model r is growth rate of tumor in a logistic fashion, d is death rate. The maximum size or space that tumor is allowed to occupy is given by its carrying capacity k. Parameter β is spread rate of virus in tumor cells (this parameter can be viewed as summarizing the replication rate of the virus). Death rate of infected tumor cells by virus represents by a; moreover, s shows growth rate in a logistic fashion. Based on these assumption model is given the following form

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

$$\frac{dy}{dt} = \beta x(t-\tau)\, y(t-\tau) + sy\left(1-\frac{x+y}{k}\right) - \alpha y$$

where τ has the usual meaning for discrete time delay.

3 Stability Analysis with Time Delay

Generally for the system (1) four equilibrium points are exist, that are $E_0(0,0), E_1\left(\frac{k(r-d)}{r},0\right), E_2\left(0,\frac{k(s-\alpha)}{s}\right)$ and $E^*\left(\frac{k}{r}\left(r-\frac{ry^*}{k}-d-\beta y^*\right), \frac{r\alpha - sd + k\beta d - k\beta r}{\beta(s-k\beta-r)}\right)$.

In this paper we considered only positive equilibrium E^* because biologically at this point both infected and uninfected tumor cell are exist and spread of the virus is stable for the two tumor cells.

The Jacobian matrix of the system (1) is given by

$$J = \begin{bmatrix} \frac{-rx}{k} & \frac{-rx}{k} - \beta x \\ \beta e^{-\lambda\tau} y - \frac{sy}{k} & \beta e^{-\lambda\tau} x + s - \alpha - \frac{sx}{k} - \frac{2sy}{k} \end{bmatrix} \tag{2}$$

The characteristic equation of (2) is given by

$$D(\lambda,\tau) = \lambda^2 + P_1\lambda + P_2 + e^{-\lambda\tau}(Q_1\lambda + Q_2) = 0 \tag{3}$$

where

$$P_1 = \frac{x^*}{k}(r+s) + \frac{2sy^*}{k} + \alpha - s \qquad P_2 = \frac{rx^*}{k}(\alpha - s) + \frac{rs}{k^2}(x^{*2} + x^*y^*) - \frac{\beta s}{k}x^*y^*$$

$$Q_1 = -\beta x^* \qquad Q_2 = \frac{r\beta}{k}(x^*y^* - x^{*2}) + \beta^2 x^* y^*$$

Here we can define $\lambda = 0$ is a root of equation (3) if and only if $P_2 = 0$.

3.1 Non-existence of delay induced instability

Based on the following conditions (Gopalaswamy, 1992) we can discuss the asymptotical stability of the system (1) when $\tau \geq 0$.

(i) The real parts of all the roots of $D(\lambda,\tau)=0$ are negative.

(ii) For all real L and any $\tau \geq 0$, $D(iL,\tau)\neq 0$ where $i=\sqrt{-1}$

If $D(\lambda,\tau)=0$, then from (3) $D(\lambda,\tau)=\lambda^2+P_1\lambda+P_2+(Q_1\lambda+Q_2)=0$ (4)

If $(P_1+Q_1)>0$ and $(P_2+Q_2)>0$ i.e., $x^*>k, x^*<\frac{a}{\beta}$ and $r>s$ then the system (1) is asymptotically stable.

Hence system (1) is asymptotically stable at positive equilibrium if $x^*>k, x^*<\frac{a}{\beta}$ and $r>s$

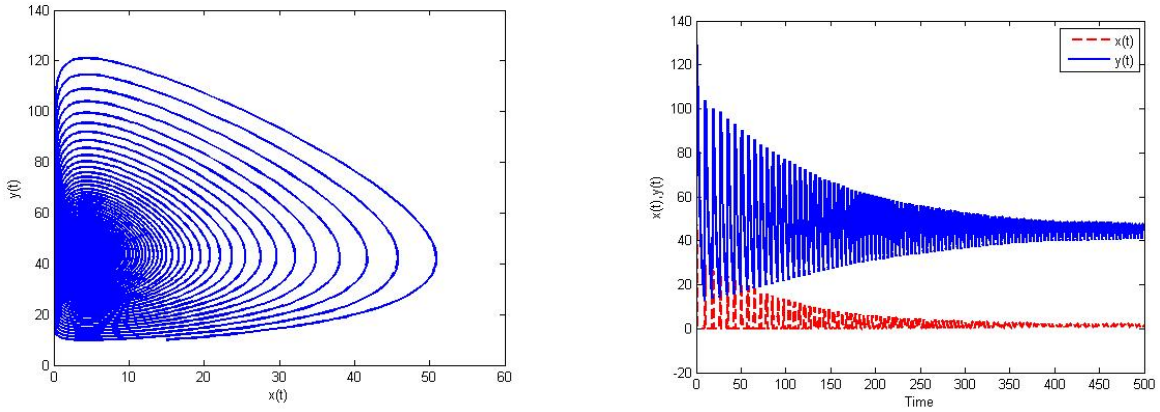

Fig. 1 The following figure shows the positive equilibrium is asymptotically stable for the parameter values as $r=10; k=1000; d=0.676; \beta=0.2; s=0.03; \alpha=0.3;$

For $L=0, D(0,\tau)=P_2\neq 0$

For $L\neq 0$

$$D(iL,\tau)=-L^2+iP_1L+P_2+e^{-iL\tau}(Q_1iL+Q_2)$$

Now Let $D(iL,\tau)=0$ and separating the real and imaginary parts

$$\begin{aligned} Q_1L\sin L\tau+Q_2\cos L\tau &= L^2-P_2 \\ Q_1L\cos L\tau-Q_2\sin L\tau &= -P_1L \end{aligned} \quad (5)$$

Squaring and adding the above two equations

$$L^4+M_1L^2+M_2=0 \quad (6)$$

Where $M_1=P_1^2-2P_2-Q_1^2, M_2=P_2^2-Q_2^2$

Therefore, if $M_1>0$, and $M_2>0$ then the positive equilibrium is asymptotically stable for all $\tau\geq 0$ (These

are sufficient conditions).

3.2 Length of delay to preserve stability

Here, we consider the equilibrium E * is asymptotically stable in the absence of delay. By continuity and for sufficiently small $\tau > 0$, all eigen values of (3) have negative real part provided one can guarantee that no eigen value with positive real part bifurcates from infinity (which could happen since it is a retarded system). To discuss the stability we applied Nyquist criterion (Fredman et al., 1986). To do this, we consider the system (1) and the space of real valued continuous function defined on (τ, ∞) satisfying the initial conditions. Then (1) can be written as

$$\frac{du}{dt} = A_1' u(t) + A_2'' v(t)$$
$$\frac{dv}{dt} = B_1' u(t) + B_2'' v(t) + B_3''' u(t-\tau) + B_4^{iv} v(t-\tau) \quad (7)$$

Where $A_1' = \frac{-2rx^*}{k} - \frac{ry^*}{k} - \beta y^* + r - d$; $A_2'' = \frac{-rx^*}{k} - \beta x^*$; $B_1' = -\frac{sy^*}{k}$;

$B_2'' = -\frac{2sy^*}{k} + s - \alpha - \frac{sx^*}{k}$; $B_3''' = \beta y^*; B_4^{iv} = \beta x^*$;

Let $\bar{u}(S), \bar{v}(S)$ are the Laplace transformation of $u(t), v(t)$ respectively. Taking the Laplace transformation of the system (7), we have

$$(s - A_1')\bar{u}(S) = A_2'' v(S) + u(0)$$
$$(s - B_2')\bar{v}(S) = B_1'\bar{u}(S) + B_3'''\bar{u}(S)e^{-St} + B_3''' e^{-St} K_1(S) + B_4^{iv} e^{-St}\bar{v}(S) + B_4^{iv} e^{-St} K_2(S) + v(0) \quad (8)$$

Where $K_1(S) = \int_{-\tau}^{0} e^{-St} u(t)dt; K_2(S) = \int_{-\tau}^{0} e^{-St} v(t)dt$

The inverse Laplace transform of $\bar{u}(S)$ will have terms which exponentially increase with time, if $\bar{u}(S)$ has poles with positive real parts. As E* to be locally asymptotically stable, it is necessary and sufficient that all poles of $\bar{u}(S)$ have negative real parts. We shall employ the Nyquist criterion which states that if s is the arc length of a curve encircling the right half place, the curve $\bar{u}(S)$ will encircle the origin a number of times equal to the difference between the number of poles of $\bar{u}(S)$ in the right half plane.

Let $F(S) = S^2 + P_1 S + P_2 + e^{-S\tau}(Q_1 S + Q_2)$ (from 4), then the condition for local asymptotic stability of E* is given by Freedman et al. (1989).

$$\mathrm{Im}\, F(iv_0) > 0 \text{ and } \mathrm{Re}\, F(iv_0) = 0 \quad (9)$$

Here v_0 is the smallest root of the above equation.

Therefore,

$$P_1 v_0 > Q_2 \sin v_0\tau - Q_1 v_0 \cos v_0\tau$$

$$v_0^2 - P_2 = Q_2 \cos v_0\tau + Q_1 v_0 \sin v_0\tau$$

Now to find the length of the delay we have to consider the following conditions

$$P_1 v > Q_2 \sin v\tau - Q_1 v \cos v\tau \quad (10)$$

$$v^2 - P_2 = Q_2 \cos v\tau + Q_1 v \sin v\tau \quad (11)$$

Therefore, E^* is stable if (11) is satisfied and $v = v_0$ is the I positive root of (10). Next we have to find the upper bound v_+ of v_0 and also it is free from τ.

Maximizing right hand side of (11) with the conditions $|\sin v\tau| \le 1, |\cos v\tau| \le 1$ then

$$v^2 - P_2 \le Q_2 + Q_1 v \quad (12)$$

and the positive solution is given by $v_+ = \dfrac{Q_1 + \sqrt{Q_1^2 + 4(P_2 + Q_2)}}{2}$

To find τ we have to take inequality (10) and rearranging terms in (10) by $|\sin v\tau| \le v\tau$

and $|1 - \cos v\tau| \le \dfrac{1}{2}\tau^2 v^2$, we obtain $-\dfrac{Q_1}{2}\tau^2 v^2 - Q_2\tau + (P_1 - Q_1) > 0 \quad (13)$

Thus (10) satisfies if $A_0\tau^2 + B_0\tau + C_0 > 0$, where $A_0 = -\dfrac{Q_1}{2}v^2; B_0 = -Q_2; C_0 = P_1 - Q_1$

Thus from Nyquist criterion exist in $0 \le \tau \le \tau_+$ and $\tau_+ = \dfrac{-B_0 + \sqrt{B^2 + 4A_0C_0}}{2A_0}$ will give the length of the delay for which stability is preserved.

3.3 Preservation of stability and Hopf-bifurcations

Let $\tau \ne 0$ and substituting $\lambda = \mu + iv$ in (4) and separating the real and imaginary parts then we obtain

$$\mu^2 - v^2 + + P_1\mu + P_2 + e^{-\mu\tau}(Q_1\mu + Q_2)\cos v\tau + e^{-\mu\tau}Q_1 v \sin v\tau = 0 \quad (14)$$

$$2\mu v + + P_1 v - e^{-\mu\tau}(Q_1\mu + Q_2)\sin v\tau + e^{-\mu\tau}Q_1 v \cos v\tau = 0 \quad (15)$$

If $\mu = 0 \text{ and } v \ne 0$ and at the values of τ we have to discuss the change stability in E^* and also taking λ is function of τ then from the equations (14) and (15)

$$v^4 + (P_1^2 - 2P_2 - Q_1^2)v^2 + (P_2^2 - Q_2^2) = 0 \quad (16)$$

To establish the Hopf bifurcation at $\tau = \overline{\tau}$, we have to show that $\frac{d\mu}{d\tau} \neq 0$. For this differentiating (14) and (15) with respect to τ and $\tau = \overline{\tau}, \mu = 0 \text{ and } v = \overline{v}$ we get

$$\begin{aligned} L\frac{d\mu}{d\tau} + M\frac{dv}{d\tau} &= U \\ -M\frac{d\mu}{d\tau} + L\frac{dv}{d\tau} &= V \end{aligned} \tag{17}$$

where

$L = P_1 - Q_2\tau\cos v\tau + Q_1\cos v\tau - Q_1 v\tau\sin v\tau$; $M = -2v - Q_2\tau\sin v\tau + Q_1\sin v\tau + Q_1 v\tau\cos v\tau$;
$U = Q_2 v\sin v\tau - Q_1 v^2\cos v\tau$; $V = Q_2 v\cos v\tau + Q_1 v^2\sin v\tau$;

Soling (17) we get

$\frac{d\mu}{d\tau}(\overline{\tau}) = \frac{LU - MV}{L^2 + M^2}$ and the sign of $\frac{d\mu}{d\tau}(\overline{\tau})$ is same as $LU - MV$.

$$LU - MV = \left(P_1Q_2v + 2Q_1v^3\right)\sin v\tau + \left(2Q_2v^2 - P_1Q_1v^2\right)\cos v\tau - Q_1^2v^2$$

$$= v\left[2v\left(Q_1v\sin v\tau + Q_2\cos v\tau\right) - P_1\left(Q_1v\cos v\tau - Q_2\sin v\tau\right) - Q_1^2v^2\right]$$

Let $\phi(h) = h^2 + A_1h + A_2$

Clearly $\phi(h)$ is the L.H.S. of (16) with $v^2 = h$ and $\phi(v^2) = 0$ then v is the first positive root of (16) and $\frac{d\mu}{d\tau} > 0$ at $\tau = \overline{\tau}$ and stability cannot take the place these values of τ and

$\frac{d\mu}{d\tau}(\overline{\tau}) = \frac{v^2}{L^2 + M^2}\frac{d\varphi}{dh}(v^2)$ where $\overline{\tau} = \frac{1}{\overline{v}}\arctan\frac{Q_1\overline{v}^3 - (P_2Q_1 + P_1Q_2)\overline{v}}{\overline{v}^2(Q_2 - P_1Q_1) - P_2Q_2} + \frac{n\pi}{\overline{v}}, n = 0,1,2,3...$

By Hopf bifurcation theorem we can state that if $M_1 > 0, \text{and } M_2 < 0$, then there exist $\overline{\tau} > 0$ such that E^* possesses a supercritical type Hopf-bifucrcation as τ increases and passes through $\overline{\tau}$.

4 Stochastic Stability Analysis

In this section we presented the environmental disturbances on the system (1) by white noise theory. These results are discussed at positive equilibrium point. To discuss the stability of the stochastic system, we consider the linearized model with the perturbations $x_1 \text{ and } x_2$. By using mean-square fluctuations we characterized the stochastic stability of the system. The stochastic perturbed system with delay is given by

$$\frac{dx(t)}{dt} = \left[rx\left(1 - \frac{x+y}{k}\right) - dx - \beta xy\right]dt + q_1\xi_1(t) \tag{18}$$

$$\frac{dy(t)}{dt}=\left[\beta x(t-\tau)y(t-\tau)+sy\left(1-\frac{x+y}{k}\right)-\alpha y\right]dt+q_2\xi_2(t)$$

Linearising above system with the perturbations $x_1(t)\,and\,x_2(t)$ i.e., $x=x_1+x^*, y=x_2+y^*$ then

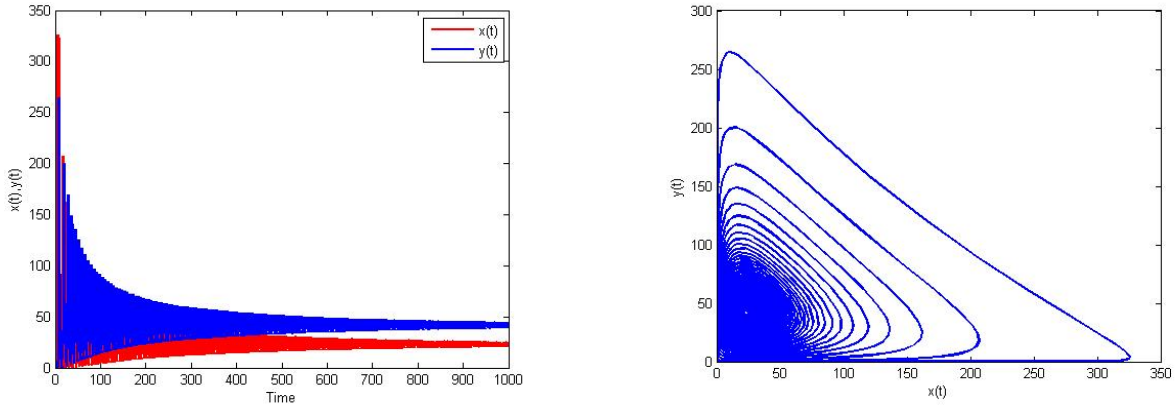

Fig. 2 The trajectories and phase graphs of system (1) with the parameter values as $r=2; k=400; d=0.211; \beta=0.035; s=0.01; \alpha=0.814;$ and $\tau=0.09$ is stable.

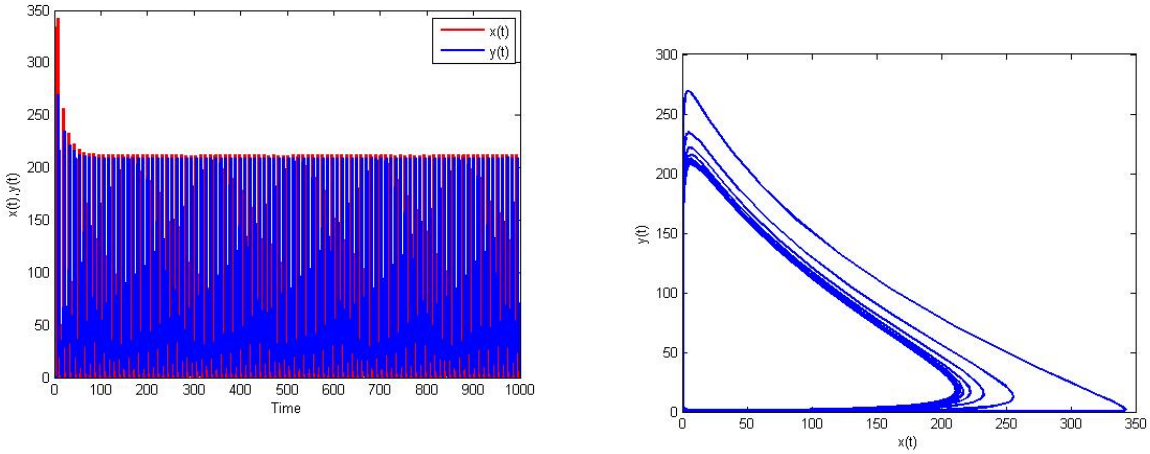

Fig. 3 The trajectories and phase graphs of system (1) with the parameter values as $r=2; k=400; d=0.211; \beta=0.035; s=0.01; \alpha=0.814;$ and $\tau=0.2$ is unstable and a periodic orbit bifurcate from E^*

$$\frac{dx_1(t)}{dt}=\frac{-2rx^*x_1}{k}-\frac{-rx^*x_2}{k}-\beta x^*x_2+q_1\xi_1(t) \tag{19}$$

$$\frac{dx_2(t)}{dt}=\beta x_1(t-\tau)-\frac{sy^*x_1}{k}-\frac{2sy^*x_2}{k}+q_2\xi_2(t)$$

Applying Fourier transforms both sides and we obtain,

$$q_1\xi_1(t)=\left(i\omega+\frac{2rx^*}{k}\right)x_1(\omega)+\left(\frac{rx^*}{k}+\beta x^*\right)x_2(\omega)$$

$$q_2\xi_2(t)=\left(\frac{sy^*}{k}-\beta e^{-i\omega\tau}\right)x_1(\omega)+\left(i\omega+\frac{2sy^*}{k}\right)x_2(\omega)$$

The matrix form of above system is given by

$$\overline{\xi}(\omega)=M(\omega)X(\omega) \tag{20}$$

and denoting the elements of $M(\omega)$ are $m_{11},m_{12},m_{21}\,\&\,m_{22}$ (row wise) then

$M(\omega)=\begin{bmatrix} m_{11} & m_{12} \\ m_{21} & m_{22} \end{bmatrix}$ where

$$\overline{\xi}(\omega)=\begin{bmatrix} q_1\xi_1(t) \\ q_2\xi_2(t) \end{bmatrix};\quad X(\omega)=\begin{bmatrix} x_1(\omega) \\ x_2(\omega) \end{bmatrix};\quad m_{11}=i\omega+\frac{2rx^*}{k};m_{12}=\frac{rx^*}{k}+\beta x^*;$$

$$m_{21}=\frac{sy^*}{k}-\beta e^{-i\omega\tau};m_{22}=i\omega+\frac{2sy^*}{k}.$$

Here $M(\omega)$ is non-singular matrix then inverse of this matrix exist, therefore from (20)

$$X(\omega)=M^{-1}(\omega)\overline{\xi}(\omega)=N(\omega)\overline{\xi}(\omega) \tag{21}$$

Where $N(\omega)=\begin{bmatrix} n_{11} & n_{12} \\ n_{21} & n_{22} \end{bmatrix}=M^{-1}(\omega)=\begin{bmatrix} \dfrac{m_{22}(\omega)}{|M(\omega)|} & -\dfrac{m_{12}(\omega)}{|M(\omega)|} \\ -\dfrac{m_{21}(\omega)}{|M(\omega)|} & \dfrac{m_{11}(\omega)}{|M(\omega)|} \end{bmatrix}$

Now from the spectral density, we define

$$S_g(\omega)d\omega=\lim_{T\to\infty}\frac{\overline{|\overline{g}(\omega)|^2}}{T}$$

Where $g(t)$ a random function with is mean zero and $S_g(\omega)$ represents the variance of the elements of $g(t)$ within the interval $[\omega,\omega+d\omega]$.

The inverse transform of $S_g(\omega)$ is the auto covariance function is given by

$$C_g(\tau')=\frac{1}{2\pi}\int_{-\infty}^{\infty}S_g(\omega)e^{i\omega\tau'}d\omega$$

and the variance function $g(t)$ is given by

$$\sigma^2{}_g = C_g(0) = \frac{1}{2\pi}\int_{-\infty}^{\infty} S_g d\omega$$

From (21), the mean value of the population is $\overline{x}_i = \sum_{j=1}^{2} n_{ij}\xi_j(\omega)$ where $b_{ij}, i, j = 1,2$

Therefore, $S_{x_i} = \sum_{j=1}^{2} q_j \left|n_{ij}(\omega)\right|^2$, $(i = 1,2)$

The fluctuations of $x_i (i = 1,2)$ are given by

$$\sigma^2{}_{x_i} = \frac{1}{2\pi}\int_{-\infty}^{\infty} S_{x_i} d\omega = \frac{1}{2\pi}\sum_{j=1}^{2}\int_{-\infty}^{\infty} q_j \left|n_{ij}(\omega)\right|^2 d\omega$$

Therefore, from above variances and from system (18), we can find

$$\sigma_{x_1}^2 = \frac{1}{2\pi}\left[q_1 \int_{-\infty}^{\infty} \left|\frac{m_{22}(\omega)}{|M(\omega)|}\right|^2 d\omega + q_2 \int_{-\infty}^{\infty} \left|\frac{-m_{12}(\omega)}{|M(\omega)|}\right|^2 d\omega \right]$$

$$\sigma_{x_2}^2 = \frac{1}{2\pi}\left[q_1 \int_{-\infty}^{\infty} \left|\frac{-m_{21}(\omega)}{|M(\omega)|}\right|^2 d\omega + q_2 \int_{-\infty}^{\infty} \left|\frac{m_{11}(\omega)}{|M(\omega)|}\right|^2 d\omega \right]$$

Where $|M(\omega)| = M_1(\omega) + iM_2(\omega)$ and

$$M_1(\omega) = -\left(\omega^2 - \frac{3rsx^* y^*}{k^2} + \frac{s\beta x^* y^*}{k} - \frac{r\beta x^*}{k}\cos\omega\tau - \beta^2 x^* \cos\omega\tau \right)$$

$$M_2(\omega) = -\left(-\frac{2sy^*\omega}{k} - \frac{2rx^*\omega}{k} + \frac{r\beta x^*}{k}\sin\omega\tau + \beta^2 x^* \sin\omega\tau \right)$$

The variances of $x_i (i = 1,2)$ are given by

$$\sigma_{x_1}^2 = \frac{1}{2\pi}\left[q_1 \int_{-\infty}^{\infty} \frac{\left|m_{22}(\omega)\right|^2}{M_1^2(\omega) + M_2^2(\omega)} d\omega + q_2 \int_{-\infty}^{\infty} \frac{\left|m_{12}(\omega)\right|^2}{M_1^2(\omega) + M_2^2(\omega)} d\omega \right]$$

$$\sigma_{x_2}^2 = \frac{1}{2\pi}\left[q_1 \int_{-\infty}^{\infty} \frac{\left|m_{21}(\omega)\right|^2}{M_1^2(\omega) + M_2^2(\omega)} d\omega + q_2 \int_{-\infty}^{\infty} \frac{\left|m_{11}(\omega)\right|^2}{M_1^2(\omega) + M_2^2(\omega)} d\omega \right] \quad (22)$$

Where $|m_{11}|^2 = \omega^2 + \left(\frac{2rx^*}{k}\right)^2$; $|m_{12}|^2 = \left(\frac{rx^*}{k} + \beta x^*\right)^2$

$$|m_{21}|^2 = \left(\frac{sy^*}{k} - \beta\cos\omega\tau\right)^2 + (\beta\sin\omega\tau)^2; |m_{22}|^2 = \omega^2 + \left(\frac{2sy^*}{k}\right)^2$$

The results in (22) gives the variances of the system (18) populations x and y. Generally, to find these integrals it is very difficult. Therefore, by using numerical simulations we can explain these results easily. Taking different parameter values and for the some time lag we can calculate variance and this is small then the corresponding population is stable, otherwise unstable.

5 Conclusion and Discussions

In this paper we have formulated a delayed cancer model with infected cells and antiseptic tumor cells. Breast cancer risk assessments using statistical data based on epidemiologic data are valid; however, no single model includes family history, estrogen-dependent mechanisms, and abnormal breast disease. For this reason it is helpful to use different models in a specialized risk assessment clinic, but this requires a full understanding of the strengths and powers of a particular relationship.

From Fig. 2, we have a tendency to look at how quickly the positive balance of program (1) is stabilized as at home. Modeling within this state of affairs produces sustainable energy. With the same set of parameter values, we find that when the system is stable, it can be seen in Fig. 2 and when it is unstable Fig3 with constant stability. That means the system changes its behavior from stable to unstable when time delay crosses its critical value, which gives Hopf-bifurcation. From the biological point of view delay has influence in spread of virus in tumor cells. Conjointly one should bear in mind the pause to allow for the management of the germ cell growth. The existence of time-resolved solutions is consistent in cancer models. It means that the tumor level can get around a difficult and immediate purpose despite no other treatment. We have accomplished numerical simulation of the random model quickly so as to add the increasing white noise of the same amount of fluctuations present in the system and that we often look at the fluctuations in the amplitude of the sounds (Fig. 4).

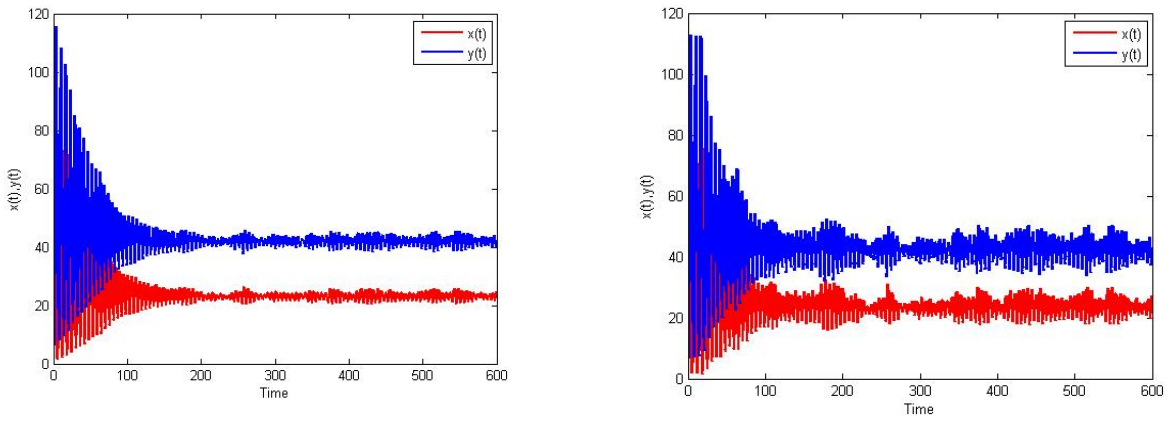

Fig. 4 The trajectories of system (18) with the parameter values as $r = 2; k = 400; d = 0.211; \beta = 0.035; s = 0.01; \alpha = 0.814;$ and $q_1 = 0.1, q_2 = 0.4$ (left figure) & $q_1 = 0.7, q_2 = 0.9$ (right figure)

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