Adv Syst Sci Appl 2022; **03**:1–17
Published online at https://ijassa.ipu.ru.

Stability and Bifurcation of a Delay Cancer Model in the Polluted Environment

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Abstract: It is well known that the spread of cancer or tumor growth increases in polluted environments. In this paper, the dynamic behavior of the cancer model in the polluted environment is studied taking into consideration the delay in clearance of the environment from their contamination. The set of differential equations that simulates this epidemic model is formulated. The existence, uniqueness, and the bound of the solution are discussed. The local and global stability conditions of disease-free and endemic equilibrium points are investigated. The occurrence of the Hopf bifurcation around the endemic equilibrium point is proved. The stability and direction of the periodic dynamics are studied. Finally, the paper is ended with a numerical simulation in order to validate the analytical results.

Keywords: Cancer, Environment Pollution, Time Delay, Stability, The Hopf Bifurcation.

1. INTRODUCTION

Cancer is an abnormal growth of cells that tend to proliferate in an uncontrolled way and in some cases to spread. In fact, cancer or tumor growth can be considered as not one disease but it is a group of more than one hundred different and distinctive diseases. Cancer can involve any tissue of the body and have many different forms in all body areas [2].

According to the World Health Organization, the cancer is one of the global diseases that affect the human as much as 18 million new cases annually, and more than half of the mortalities in 2018, and the numbers are expected to nearly double in 2040. Although there is many advanced experimental in developing interventional therapies for cancer such as immunotherapy, virotherapy, targeted drug therapies, and chemotherapy, in addition to the surgical resection, treatment options are still limited and the disease is considered fatal [5]. Therefore, we can consider the mathematical models as one of the ways for studying this disease. For a brief review of mathematical models describing tumor-immune dynamics see Tsygvintsev et al. [12]. Lestari et al [6] proposed a mathematical model of the spread of cancer with chemotherapy and then studied their dynamical behavior. Weerasinghe et al [14] discussed some models of plasticity, tumor progression, and metastasis using three broadly conceived mathematical modeling techniques: discrete, continuum, and hybrid, each with advantages and disadvantages. Simmons et al. [9] presented a brief overview of breast cancer, focusing on its heterogeneity, and then explained the role of mathematical modeling and simulation in teasing apart the underlying biophysical processes. In [8], Pillis and Radunskaya proposed and investigated the immune response to tumor invasion. Trisilowati et al. [11] proposed and analyzed the optimal control model of dendritic cell treatment of growing

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tumors. Moreover, Wilson and Levy [15] formulated a model to investigate the effect of immunotherapy on tumor growth. Recently, Abernathy et al [16], studied the long-term dynamics of a system of nonlinear differential equations that describes the role of virotherapy on tumors and the impact of immune response specific to fighting cancer. Al-Tuwairqi et al [1] presented a realistic mathematical model that describes the interaction between the innate immune system and uninfected tumor cells. This is based on the fact that both tumor and virus-infected cells are recognized by natural killer cells that are part of the innate immune system

On the other hand, there have been several papers proposed to show the effect of the time delay of some epidemic disease models as seen in Zuo et al. [17], which studied the impact of the media and delay on the spread of an epidemic. In [3], Cooke et al. proposed an epidemic model with two delays. Wang and Wu [13], investigated an SEIR model with delay. Recently, Naji and Majeed [7] studied the effect of delay on a stage structure prey-predator model.

In this article, it is assumed that cancer start outbreak due to environmental pollution, and then the effect of delay in cleaning up this environment on the dynamic behavior of the proposed system is discussed. So that, the next section deals with the formulation of the model and presents its main properties. In section 3, the stability analysis of the disease-free equilibrium point and endemic equilibrium point is discussed and the possibility of occurrence of the Hopf bifurcation is also studied. Section 4, discusses the stability and direction of the periodic dynamics that resulting from the Hopf bifurcation as the delay starting increases. Numerical simulations are used in section 5 to further understand the dynamics of the model. Finally, the paper is ended with a discussion section as given in section 6.

2. THE MATHEMATICAL FORMULATION OF CANCER MODEL

It is well known that one of the main reasons for the spread of cancer is the polluted environment. Hence, in case of existence of such disease in a population of size $N(t)$ at time t, then the population is divided into two compartments, namely susceptible compartment, which is denoted to their population's size at time t by $S(t)$ and cancer compartment, which contains all the individuals that infected by cancer and denoted to their population's size at time t by $C(t)$, such that $N(t) = S(t) + C(t)$. Moreover, it is assumed that the pollution level at time t in the environment is given by $E(t)$. On the other hand, since the delay in clearance of the environment from their contamination has a vital effect on the spread of cancer. Therefore, the effect of delay, with the amount of delay given by $\tau > 0$, is considered in the formulation of the model. Accordingly, the dynamics of the spread of cancer within such an environment can be represented in the following block diagram.

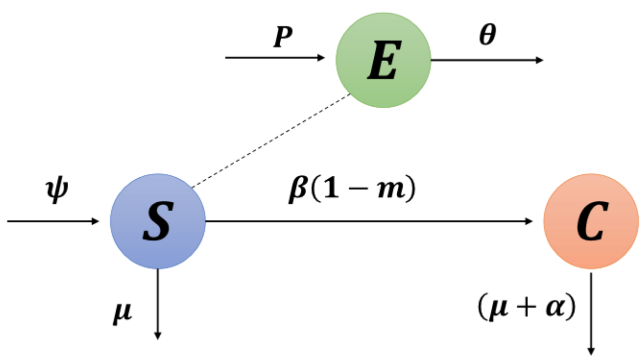

Fig. 2.1. The block diagram of Cancer model.

And the corresponding dynamic model has been formulated by the following system of nonlinear delay differential equations

$$\left.\begin{array}{l} \frac{dS}{dt} = \psi - \beta\left(1-m\right)S\left(t\right)E\left(t\right) - \mu S\left(t\right) \\ \frac{dC}{dt} = \beta\left(1-m\right)S\left(t\right)E\left(t\right) - \left(\mu+\alpha\right)C\left(t\right) \\ \frac{dE}{dt} = P - \theta E\left(t-\tau\right) \end{array}\right\}, \tag{2.1}$$

where $S\left(r\right) = S\left(0\right) > 0,\ C\left(r\right) = C(0) \geq 0$ and $E\left(r\right) = E\left(0\right) \geq 0$ for $r \in [-\tau, 0)$. It is assumed that all parameters in system (2.1) have the following description: $\psi > 0$ is the natural birth of susceptible; $\mu > 0$ represents the death rate of all populations; $\beta > 0$ represents the contact rate of the susceptible with the contaminated environment. However, the constant m represents the body resistance rate due to chromosomal fixed against environment effect such that $0 \leq m \leq 1$. While $P \geq 0$ is the pollution rate in the environment and $\theta > 0$ is the clearance rate in the environment.

Note that, all the interaction functions on the right-hand side of the system (2.1) are continuous and have continuous partial derivatives and hence the system has a unique solution in $\mathbb{R}^3_+$. Furthermore, the boundedness of the solution is shown in the following theorem.

Theorem 2.1:
All the solutions of system (2.1) with initial conditions belong to $\mathbb{R}^3_+$, are bounded.

Proof
Let $\left(S\left(t\right), C\left(t\right), E\left(t\right)\right)$ be any solution of system (2.1) with initial conditions belongs to $\mathbb{R}^3_+$. Hence, by adding the first two equations in system (2.1) to each other we get:

$$\frac{dS}{dt} + \frac{dC}{dt} = \psi - \mu N - \alpha C.$$

Therefore, it is obtained that:

$$\frac{dN}{dt} + \mu N \leq \psi.$$

Then, solving the above inequality by using the Gronwall lemma we obtain for $t \to \infty$ that:

$$N \leq \frac{\psi}{\mu}.$$

Similarly, from the 3^{rd} equation in the system (2.1) we have:

$$\frac{dE}{dt} = P - \theta E.$$

This implies that:

$$\frac{dE}{dt} + \theta E = P.$$

Hence for $t \to \infty$, we have $E(t) \leq \frac{P}{\theta}$. This completes the proof. □

Now, since the variable C in the second equation of system (2.1) dose not appear in the other two equations, then the following system, say system (2.3), can be solved independently. Then by substituting the obtained solution, say (S_v, E_v) in second equation of system (2.1), we obtain the following solution:

$$C(t)=\frac{\beta(1-m)S_vE_v}{\mu+\alpha}, \tag{2.2}$$

where (S_v, E_v) is a solution of the system:

$$\left.\begin{aligned}\frac{dS}{dt}&=\psi-\beta(1-m)S(t)E(t)-\mu S(t)\\ \frac{dE}{dt}&=P-\theta E(t-\tau)\end{aligned}\right\}. \tag{2.3}$$

3. ANALYSIS OF SYSTEM 2.3

In this section, the existence and their stability analysis are carried out. It is easy to verify that system (2.3) has two equilibrium points and can be described as follows:

1. The first point is called the disease-free equilibrium point *DFEP*, which is denoted by $e_0=(S_0,0)$, where:

$$S_0=\frac{\psi}{\mu}. \tag{3.4}$$

   Clearly, e_0 exists provided that:

$$P=0. \tag{3.5}$$

2. The other point is called the endemic equilibrium point *EEP* and that denoted by $e_1=(S_1,E_1)$, where:

$$\left.\begin{aligned}S_1&=\frac{\psi\theta}{\beta(1-m)P+\mu\theta}\\ E_1&=\frac{P}{\theta}\end{aligned}\right\}. \tag{3.6}$$

Obviously, e_1 exists uniquely in the interior of the positive quadrant of the $SE-$plane provided that:

$$P>0. \tag{3.7}$$

Now, to analyze the stability of the above equilibrium points the general Jacobian matrix for the system (2.3) at any point, say (S,E), can be written as:

$$J(S,E)=\begin{bmatrix}-[\beta(1-m)E+\mu] & -\beta(1-m)S\\ 0 & -\theta e^{-\lambda\tau}\end{bmatrix}. \tag{3.8}$$

Accordingly, the Jacobian matrix of system (2.3) at the *DFEP* that given in Eq. (3.4), becomes:

$$J(e_0)=\begin{bmatrix}-\mu & -\beta(1-m)S_0\\ 0 & -\theta e^{-\lambda\tau}\end{bmatrix}. \tag{3.9}$$

Then, the characteristic equation of the matrix (3.9) can be written as:

$$\lambda^2+\mu\lambda+(\theta\lambda+\mu\theta)e^{-\lambda\tau}=0. \tag{3.10}$$

Obviously, when $\tau=0$, Eq. (3.10) becomes:

$$\lambda^2 + (\mu + \theta)\lambda + \mu\theta = 0. \tag{3.11}$$

Clearly, the eigenvalues in such a case can be written as:

$$\lambda_1^{[\tau=0]} = -\mu, \lambda_2^{[\tau=0]} = -\theta.$$

Hence, e_0 is always locally asymptotically stable for $\tau = 0$.

Furthermore, by using the function $h(S, E) = \left(\frac{1}{SE}\right)$ as the Dulac function, which is a continuously differentiable unction in a simply connected $\Omega \subset \mathbb{R}_+^2$ such that $\partial(hf(S, E)/\partial S + \partial(hg(S, E)/\partial E$ dose not change the sign in Ω and vanishes at most on a set of measure zero then the system (2.3) not have periodic orbits in Ω. Therefore, it is easy to verify that system (2.3) with $\tau = 0$ has no periodic dynamics and hence e_0 is always globally asymptotically stable. On the other hand, since the *DFEP* exists under the condition (3.5), hence system (2.3) can be reduce to a single equation due to the fact $\acute{E} < 0$. Therefore, the system (2.3) has no periodic dynamics when $\tau > 0$ and $P = 0$, and hence e_0 is always globally absolutely stable [10] for all $\tau \geq 0$.

Now the stability of the *EEP* of system 2.3 that given by (3.6), is investigated using the linearization technique. Accordingly, the Jacobian matrix that given in (3.8) of system (2.3) at the *EEP* can be written as:

$$J(e_1) = \begin{bmatrix} -\left[\beta(1-m)E_1 + \mu\right] & -\beta(1-m)S_1 \\ 0 & -\theta e^{-\lambda\tau} \end{bmatrix}. \tag{3.12}$$

Hence, the characteristic equation of $J(e_1)$ can be written:

$$\lambda^2 + B_1\lambda + (B_2\lambda + B_3)e^{-\lambda\tau} = 0, \tag{3.13}$$

where $B_1 = \beta(1-m)E_1 + \mu$, $B_2 = \theta$, and $B_3 = \theta\left[\beta(1-m)E_1 + \mu\right]$.

So for $\tau = 0$, then Eq. (3.13) becomes:

$$\lambda^2 + (B_1 + B_2)\lambda + B_3 = 0. \tag{3.14}$$

It easy to see that the roots of the above equation have negative real parts. Consequently, whenever the *EEP* exists, it is always locally asymptotically stable (LAS). Indeed, it is globally asymptotically stable as mentioned above with the help of the Dulac criterion.

Now, for $\tau > 0$, assume that Eq. (3.13) has a pair of purely imaginary roots, say $\lambda = \pm i\omega$ with $\omega > 0$, cross the imaginary axis. Hence, by substituting $\lambda = i\omega$ in Eq. (3.13) we get:

$$-\omega^2 + iB_1\omega + (iB_2\omega + B_3)(\cos\omega\tau - isin\,\omega\tau) = 0.$$

Therefore, by separating the real and imaginary parts we obtain:

$$\left.\begin{array}{r} B_1\omega = B_3\sin\omega\tau - B_2\omega\cos\omega\tau \\ -\omega^2 = -B_2\omega\sin\omega\tau - B_3\cos\omega\tau \end{array}\right\}. \tag{3.15}$$

Clearly, squaring the equations in Eq. (3.15) and adding to each other gives that:

$$\omega^4 + \left(B_1^2 - B_2^2\right)\omega^2 - B_3^2 = 0, \tag{3.16}$$

set $K = \omega^2$, then Eq. (3.14) becomes:

$$K^2 + \left(B_1^2 - B_2^2\right)K - B_3^2 = 0. \tag{3.17}$$

Clearly, by using Descartes' rule of signs, Eq. (3.17) has a unique positive root, namely $K = \omega_0^2$. Hence, ω_0 is a positive root of Eq. (3.16) too. Therefore, there is at least a pair of purely imaginary roots $\pm i\omega_0$ satisfying Eq.(3.13).

Substituting ω_0 in Eq. (3.15) and then solving the resulting equation with respect to τ we get that:

$$\tau_j = \frac{1}{\omega_0} sin^{-1} \frac{\omega_0 \left(B_1 B_3 + B_2 {\omega_0}^2\right)}{\left({B_2}^2 {\omega_0}^2 + {B_3}^2\right)} + \frac{2j\pi}{\omega_0}; \;\; j = 0, 1, 2, \cdots \tag{3.18}$$

Now, define that $\tau_0 = \min_{j \geq 0} \tau_j$, then $\lambda(\tau) = \gamma(\tau) + i\omega(\tau)$ be a root of Eq. 3.13, such that $\gamma(\tau_0) = 0$ and $\omega(\tau_0) = \omega_0$. Then we have the following theorem.

Theorem 3.1:
Assume that condition (3.7) holds. Then the EEP is conditionally stable.

Proof
It is well known that the equilibrium point e_1 is conditionally stable if it is asymptotically stable for $\tau \in [0, \tau_0)$. Moreover, as shown above, the equilibrium point e_1 is globally asymptotically stable for $\tau = 0$ and the transcendental characteristic equation given by Eq. (3.13) has at least a pair of purely imaginary roots $\pm i\omega_0$ at $\tau = \tau_0$.

Consequently, if we assume that $\lambda(\tau) = \gamma(\tau) + i\omega(\tau)$ is an eigenvalue of Eq. (3.13) with $\gamma(\tau_0) = 0$ and $\omega(\tau_0) = \omega_0 > 0$, where τ_0 is given by Eq. (3.18) then the proof follows if we can show that the following transversality condition hold.

$$\left[\frac{d(Re\lambda(\tau))}{d\tau}\right]_{\tau=\tau_0} \neq 0. \tag{3.19}$$

By deriving Eq. (3.13) with respect to τ we obtain that:

$$\left[2\lambda + B_1 + B_2 e^{-\lambda\tau} - \tau(B_2\lambda + B_3)e^{-\lambda\tau}\right] \frac{d\lambda}{d\tau} = \lambda(B_2\lambda + B_3)e^{-\lambda\tau}. \tag{3.20}$$

Therefore, we obtain that:

$$\left[\frac{d\lambda}{d\tau}\right]^{-1} = \frac{(2\lambda + B_1)}{-\lambda(\lambda^2 + B_1\lambda)} + \frac{B_2}{\lambda(B_2\lambda + B_3)} - \frac{\tau}{\lambda}. \tag{3.21}$$

Since $\lambda = i\omega_0$ at $\tau = \tau_0$, then Eq. (3.21) can be rewritten as:

$$\left[\frac{d\lambda}{d\tau}\right]^{-1}_{\tau=\tau_0} = \frac{2i\omega_0 + B_1}{B_1{\omega_0}^2 + i{\omega_0}^3} + \frac{B_2}{-B_2{\omega_0}^2 + i\omega_0 B_3} - \frac{\tau_0}{i\omega_0}.$$

Now since

$$sgn\left[\frac{d(Re\lambda)}{d\tau}\right]_{\tau=\tau_0} = sgn\left[Re\left(\frac{d\lambda}{d\tau}\right)^{-1}\right]_{\lambda=i\omega_0}. \tag{3.22}$$

Accordingly, from the fact:

$$Re\left[\frac{2i\omega_0 + B_1}{B_1{\omega_0}^2 + i{\omega_0}^3}\right] = \frac{2{\omega_0}^2 + {B_1}^2}{{\omega_0}^2({B_1}^2 + {\omega_0}^2)},$$

$$Re\left[\frac{B_2}{i\omega_0 B_3 - B_2{\omega_0}^2}\right] = \frac{-{B_2}^2}{{B_2}^2\,{\omega_0}^2 + {B_3}^2},$$

$$Re\left[\frac{\tau_0}{i\omega_0}\right] = 0.$$

Hence, we obtain that:

$$\left[Re\left(\frac{d\lambda}{d\tau}\right)\right]^{-1}_{\tau=\tau_0} = \frac{2{\omega_0}^2 + {B_1}^2}{{\omega_0}^2({B_1}^2 + {\omega_0}^2)} - \frac{{B_2}^2}{{B_2}^2\,{\omega_0}^2 + {B_3}^2} > 0.$$

Therefore, $\frac{d(Re\lambda(\tau))}{d\tau}$ at $\tau = \tau_0$ is not equal zero and does not change sign. Clearly, the obtained result shows that the eigenvalue of characteristic equation Eq. (3.13) crosses the imaginary axis from left to right as τ passes through τ_0. Hence system (2.3) losses its stability and undergoes the Hopf bifurcation at $\tau = \tau_0$. Thus the proof is complete. □

4. STABILITY AND DIRECTION OF THE HOPF BIFURCATION

In the previous section, we have shown that system (2.3) undergoes the Hopf bifurcation near the *EEP* at $\tau = \tau_j$. In this section, however, the direction of the Hopf bifurcation and their stability at $\tau = \tau_0$ is investigated. The normal form theory and center manifold theorem are used in this investigation, see [4].

Let $x_1 = S - S_1$, $x_2 = E - E_1$, $\overline{x}_i(t) = x_i(\tau t)$ and $\tau = \tau_0 + u$, then we drop the bars for simplification of notations. Therefore system (2.3) is transformed into functional differential equations in $C = C\left([-1, 0], R^2\right)$ as:

$$\dot{x}\,(t) = L_u\,(x_t) + H\,(u, x_t)\,, \tag{4.23}$$

where $x\,(t) = (x_1, x_2)^T \in \mathbb{R}^2$, $L_u : C \to \mathbb{R}^2$ and $H{:}\mathbb{R}\times C \to \mathbb{R}^2$ are given as:

$$\left.\begin{aligned} L_u\,(\Gamma) = (\tau_0 + u)\begin{bmatrix} -\left[\beta\,(1-m)\,E_1 + \mu\right] & -\beta(1-m)S_1 \\ 0 & 0 \end{bmatrix}\begin{bmatrix} \Gamma_1(0) \\ \Gamma_2(0) \end{bmatrix} \\ +\,(\tau_0 + u)\begin{bmatrix} 0 & 0 \\ 0 & -\theta \end{bmatrix}\begin{bmatrix} \Gamma_1(-1) \\ \Gamma_2(-1) \end{bmatrix} \end{aligned}\right\}, \tag{4.24}$$

and

$$H\,(u, \Gamma) = (\tau_0 + u)\begin{bmatrix} -\beta(1-m)\Gamma_1(0)\Gamma_2(0) \\ 0 \end{bmatrix}, \tag{4.25}$$

here $\Gamma(v) = (\Gamma_1(v), \Gamma_2(v))^T \in C$. Now, by the Riesz representation theorem, there exists a function of bounded variation, say $\eta(v, u)$ for $v \in [-1, 0]$, such that:

$$L_u\Gamma = \int_{-1}^{0} d\eta\,(v, u)\,\Gamma\,(v), \Gamma \in C. \tag{4.26}$$

Here we can choose:

$$\left.\begin{aligned} \eta\,(v, u) = (\tau_0 + u)\begin{bmatrix} -\left[\beta\,(1-m)\,E_1 + \mu\right] & -\beta(1-m)S_1 \\ 0 & 0 \end{bmatrix}\delta\,(v) \\ -\,(\tau_0 + u)\begin{bmatrix} 0 & 0 \\ 0 & -\theta \end{bmatrix}\delta\,(v+1) \end{aligned}\right\}, \tag{4.27}$$

where $\delta(v)$ is the Dirac function, which define as follows, then Eq. (4.26) is satisfied.

$$\delta(v) = \begin{cases} 1 & v = 0. \\ 0 & v \neq 0. \end{cases} \tag{4.28}$$

For $\Gamma \in C^1([-1,0], R^2)$, define:

$$A(u)\Gamma(v) = \begin{cases} \frac{d\Gamma(v)}{dv} & -1 \leq v < 0. \\ \int_{-1}^{0} d\eta(\varsigma, u)\Gamma(\varsigma) & v = 0. \end{cases} \tag{4.29}$$

And

$$R(u)\Gamma(v) = \begin{cases} 0 & -1 \leq v < 0. \\ H(u, \Gamma) & v = 0. \end{cases} \tag{4.30}$$

Hence, system (4.23) can be transformed into an operator differential equation of the form:

$$\acute{x}_t = A(u)x_t + R(u)x_t, \tag{4.31}$$

where $x_t = x(t+v)$, $v \in [-1, 0]$.

Now, we defined the adjoint operator A^* of A, where $\psi \in C^1\left([-1,0], (R^2)^*\right)$, by:

$$A^*(0)\psi(s) = \begin{cases} -\frac{d\psi(s)}{ds} & 0 < s \leq 1, \\ \int_{-1}^{0} d\eta^T(\varsigma, 0)\psi(-\varsigma) & s = 0, \end{cases} \tag{4.32}$$

with a bilinear inner product form:

$$\langle \psi(s), \Gamma(v) \rangle = \overline{\psi}(0)\Gamma(0) - \int_{v=-1}^{0} \int_{\xi=0}^{v} \overline{\psi}^T(\xi - v)\, d\eta(v)\, \Gamma(\xi)\, d\xi, \tag{4.33}$$

where, $\eta(v) = \eta(v, 0)$. Clearly, $A(0)$ and $A^*(0)$ are adjoint operators. Now since $\pm i\tau_0\omega_0$ are the eigenvalues of $A(0)$ as we show in the previous section then they are also eigenvalues of $A^*(0)$. Furthermore, we need to find the eigenvector q of A corresponding to $i\tau_0\omega_0$ and the eigenvector q^* of A^* corresponding to $-i\tau_0\omega_0$ so that they satisfying the normalization conditions $\langle q^*, q \rangle = 1$ and $\langle q^*, \overline{q} \rangle = 0$, as determined in the following theorem.

Theorem 4.1:
The eigenvectors of $A(0)$ and A^* corresponding to $i\tau_0\omega_0$ and $-i\tau_0\omega_0$ are given by $q(v) = (1, r_1)^T e^{iv\tau_0\omega_0}$ and $q^*(s) = D(1, r_2)^T e^{is\tau_0\omega_0}$ respectively, where:

$$r_1 = -\frac{[i\omega_0 + \beta(1-m)E_1 + \mu]}{\beta(1-m)S_1},$$

$$r_2 = \frac{\beta(1-m)S_1}{i\omega_0 - \theta e^{i\omega_0\tau_0}},$$

$$\overline{D} = \left[1 + r_1\overline{r_2} - \tau_0\theta r_1\overline{r_2}e^{-i\omega_0\tau_0}\right]^{-1}.$$

Proof
Since $q(v) = (1, r_1)^T e^{iv\tau_0\omega_0}$, is the eigenvector of $A(0)$ corresponding to $i\tau_0\omega_0$, then:

$$A(0)q(v) = i\tau_0\omega_0\, q(v).$$

So, we obtain:

$$A\left(0\right)q\left(0\right)e^{iv\tau_0\omega_0} = i\tau_0\omega_0\, q\left(0\right)e^{iv\tau_0\omega_0}.$$

Now according to the definition of $A\left(0\right)$, we get

$$\tau_0\begin{pmatrix} i\omega_0+\beta\left(1-m\right)E_1+\mu & \beta\left(1-m\right)S_1 \\ 0 & i\omega_0+\theta e^{-i\omega_0\tau_0}\end{pmatrix}\begin{pmatrix}1\\ r_1\end{pmatrix}=\begin{pmatrix}0\\ 0\end{pmatrix}.$$

Consequently, we obtain that:

$$r_1=-\frac{\left[i\omega_0+\beta\left(1-m\right)E_1+\mu\right]}{\beta\left(1-m\right)S_1}.$$

Similarly, since $q^*\left(s\right)=D(1,r_2)^Te^{is\tau_0\omega_0}$ is the eigenvector of A^* corresponding to $-i\tau_0\omega_0$, hence:

$$A^*q^*\left(s\right)=-i\tau_0\omega_0q^*\left(s\right).$$

From the definition of A^* we obtain:

$$\tau_0\begin{pmatrix} i\omega_0-\left[\beta\left(1-m\right)E_1+\mu\right] & 0 \\ -\beta\left(1-m\right)S_1 & i\omega_0-\theta e^{-i\omega_0\tau_0}\end{pmatrix}\begin{pmatrix}1\\ r_2\end{pmatrix}=\begin{pmatrix}0\\ 0\end{pmatrix}.$$

Such that:

$$r_2=\frac{\beta\left(1-m\right)S_1}{i\omega_0-\theta e^{i\omega_0\tau_0}}.$$

To guarantee that $\langle\, q^*\left(s\right),q\left(v\right)\,\rangle=1$, then the parameter D should be determined, so by using Eq. (4.33), we get that:

$$\begin{aligned}\langle q^*\left(s\right),q(v)\rangle &= \overline{D}\left(1,\overline{r_2}\right)\begin{pmatrix}1\\ r_1\end{pmatrix}\\ &-\textstyle\int_{v=-1}^{0}\int_{\xi=0}^{v}\overline{D}\left(1,\overline{r_2}\right)e^{-i(\xi-v)\omega_0\tau_0}d\eta\left(v\right)\begin{pmatrix}1\\ r_1\end{pmatrix}e^{i\xi\omega_0\tau_0}d\xi\\ &=\overline{D}\left\{1+r_1\overline{r_2}-\textstyle\int_{-1}^{0}\left(1,\overline{r_2}\right)ve^{iv\omega_0\tau_0}d\eta\left(v\right)\begin{pmatrix}1\\ r_1\end{pmatrix}\right\}\\ &=\overline{D}\left\{1+r_1\overline{r_2}+\left[\tau_0\left(1,\overline{r_2}\right)\begin{pmatrix}0\\ -\theta r_1\end{pmatrix}\right]e^{-i\omega_0\tau_0}\right\}\\ &=\overline{D}\left\{1+r_1\overline{r_2}-\tau_0\theta r_1\overline{r_2}e^{-i\omega_0\tau_0}\right\}.\end{aligned}$$

Thus we can choose D so that:

$$\overline{D}=\left[1+r_1\overline{r_2}-\tau_0\theta r_1\overline{r_2}e^{-i\omega_0\tau_0}\right]^{-1}.$$

In addition, it can be easily verify that $\langle q^*,\overline{q}\rangle=0$ by applying the adjoint property $\langle\varphi,A\Gamma\rangle=\langle A^*\varphi,\Gamma\rangle$, as follows:

$$\begin{aligned} i\tau_0\omega_0\langle q^*,\overline{q}\rangle &= \langle -i\tau_0\omega_0q^*,\overline{q}\rangle=\langle A^*q^*,\overline{q}\rangle=\langle q^*,A\overline{q}\rangle\\ &=\langle q^*,i\tau_0\omega_0\overline{q}\rangle=-i\tau_0\omega_0\langle q^*,\overline{q}\rangle\end{aligned}.$$

Then, we have $\langle q^*,\overline{q}\rangle=0$.

In the following, the technique given by Hassard et al. [4] to compute the coordinates describing center manifold C_0 at $u=0$ is used.

Define

$$\left.\begin{array}{l} z\left(t\right)=\left\langle q^{*},x_t\right\rangle \\ w\left(t,v\right)=x_t\left(v\right)-z\left(t\right)q\left(v\right)-\overline{z}\left(t\right)\ \overline{q}\left(v\right)=x_t\left(v\right)-2Re\left\{z\left(t\right)q\left(v\right)\right\} \end{array}\right\}, \quad (4.34)$$

where $x_t\left(v\right)=x(t+v)$ be the solution of Eq. (4.24). Also, on the center manifold C_0, we have:

$$w\left(t,v\right)=\ w\left(z\left(t\right),\overline{z}\left(t\right),v\right), \quad (4.35)$$

here $w\left(z\left(t\right),\overline{z}\left(t\right),v\right)=w_{20}\left(v\right)\frac{z^2}{2}+w_{11}\left(v\right)z\overline{z}+w_{02}\left(v\right)\frac{\overline{z^2}}{2}+\ldots$, such that, $z(t)$ and $\overline{z}(t)$ are local coordinates of center manifold C_0 in the direction of q^* and $\overline{q^*}$, respectively. Clearly, we know that $x_t\in C_0$ of Eq. (4.31), since $u=0$, we know that $\langle\varphi,A\Gamma\rangle=\langle A^*\varphi,\Gamma\rangle$, for $\langle\Gamma,\varphi\rangle\in D(A)\times D(A)$, then:

$$\acute{z}(t)=\langle q^*,x'(t)\rangle=\langle q^*,A(0)x_t+R(0)x_t\rangle \qquad =\langle q^*,A\left(0\right)x_t\rangle+\langle q^*,R\left(0\right)x_t\rangle=\langle A$$

Thus

$$\left.\begin{array}{l} \acute{z}\left(t\right)=i\omega_0\tau_0z\left(t\right)+\overline{q^*}^T(0)H(0,w\left(t,0\right)+2Re\left\{z\left(t\right)q(0)\right\}) \\ \quad=i\omega_0\tau_0z\left(t\right)+\overline{q^*}^T\left(0\right)H_0\left(z,\overline{z}\right) \end{array}\right\}, \quad (4.36)$$

here $H_0\left(z,\overline{z}\right)=H(0,\ z,\overline{z})$, Now rewrite Eq. (4.36) as:

$$\acute{z}\left(t\right)=i\omega_0\tau_0z\left(t\right)+g\left(z,\overline{z}\right), \quad (4.37)$$

where

$$g\left(z,\overline{z}\right)=\frac{1}{2}g_{20}z^2+g_{11}z\overline{z}+\frac{1}{2}g_{02}\overline{z}^2+\frac{1}{2}g_{21}z^2\overline{z}+\ldots$$

So according to the Eq. (4.34) with the Eq. (4.31), we obtain:

$$\begin{array}{c} \acute{w}\left(t,v\right)=x'_t\left(v\right)-\acute{z}\left(t\right)q\left(v\right)-\acute{\overline{z}}\left(t\right)\ \overline{q}\left(v\right) \\ \left.\begin{array}{l} =A(0)x_t+R(0)\,x_t-i\omega_0\tau_0z(t)q(v)-\overline{q^*}^T(0)H_0(z,\overline{z})q(v) \\ \quad+i\omega_0\tau_0\overline{z}\left(t\right)\overline{q}\left(v\right)-q^{*T}\left(0\right)\overline{H}_0\left(z,\overline{z}\right)\overline{q}\left(v\right) \end{array}\right\} \\ \left.\begin{array}{l} =A(0)x_t+R(0)x_t-A(0)z(t)q\left(v\right)-A(0)\overline{z}(t)\overline{q}\left(v\right) \\ \quad-2Re\left\{\overline{q^*}^T(0)H_0(z,\overline{z})q(v)\right\} \end{array}\right\} \\ =A(0)w(t,v)+R(0)x_t-2Re\left\{\overline{q^*}^T(0)H_0(z,\overline{z})q(v)\right\}. \end{array}$$

Therefore, it is obtain that:

$$\acute{w}\left(t,v\right)=\left\{\begin{array}{ll} A\left(0\right)w\left(t,v\right)-2Re\left\{\overline{q^*}^T\left(0\right)H_0\left(z,\overline{z}\right)q\left(v\right)\right\} & \text{for } v\in[-1,0). \\ A\left(0\right)w\left(t,0\right)+H_0\left(z,\overline{z}\right)-2Re\left\{\overline{q^*}^T\left(0\right)H_0\left(z,\overline{z}\right)q\left(0\right)\right\} & \text{for } v=0. \end{array}\right. \quad (4.38)$$

Accordingly, we can rewrite Eq. (4.38) for $v\in[-1,0)$ as follows:

$$\acute{w}\left(t,v\right)=Aw\left(t,v\right)+G\left(z,\overline{z},v\right), \quad (4.39)$$

where

$$G(z,\overline{z},v)=G_{20}(v)\frac{z^2}{2}+G_{11}z\overline{z}+G_{02}\frac{\overline{z}^2}{2}+\dots$$

So, differentiate the two sides of (4.35), gives that:

$$\acute{w}=w_z\acute{z}+w_{\overline{z}}\acute{\overline{z}}. \tag{4.40}$$

Then, using the Eqs. (4.35), (4.36) and (4.39) give that:

$$\begin{array}{c}(A-2i\tau_0\omega_0)\,w_{20}(v)=-G_{20}(v)\,,\\ Aw_{11}(v)=-G_{11}(v)\,,\\ (A+2i\tau_0\omega_0)\,w_{02}(v)=-G_{02}(v)\,.\end{array} \tag{4.41}$$

According to Eqs. (4.36) and (4.37), we have that:

$$g(z,\overline{z})=\overline{q^*}^T(0)\,H_0(z,\overline{z})=\frac{1}{2}g_{20}z^2+g_{11}z\overline{z}+\frac{1}{2}g_{02}\overline{z}^2+\frac{1}{2}g_{21}z^2\overline{z}+\dots, \tag{4.42}$$

where $\overline{q^*}^T(0)=\overline{D}(1,\overline{r}_2)$.

Also from Eq. (4.34), it gets that:

$$x(t+v)=(x_1(t+v)\,,x_2(t+v))^T=zq(v)+\overline{zq}(v)+w(t,v)\,,$$

here $q(v)=(1,r_1)^Te^{iv\tau_0\omega_0}$.

Hence by Eq. (4.35), it is obtained that:

$$\begin{aligned}x_1(t+0)&=z+\overline{z}\ +w^{(1)}(t,0)\\ &=z+\overline{z}+w_{20}^{(1)}(0)\tfrac{z^2}{2}+w_{11}^{(1)}(0)\,z\overline{z}+w_{02}^{(1)}(0)\tfrac{\overline{z}^2}{2}+\dots,\\ x_2(t+0)&=zr_1+\overline{zr}_1+w^{(2)}(t,0)\\ &=zr_1+\overline{zr}_1+w_{20}^{(2)}(0)\tfrac{z^2}{2}+w_{11}^{(2)}(0)\,z\overline{z}+w_{02}^{(2)}(0)\tfrac{\overline{z}^2}{2}+\dots,\\ x_1(t-1)&=ze^{-i\tau_0\omega_0}\ +\overline{z}e^{i\tau_0\omega_0}\ +w^{(1)}(t,-1)\\ &=ze^{-i\tau_0\omega_0}\ +\overline{z}e^{i\tau_0\omega_0}\ +w_{20}^{(1)}(-1)\tfrac{z^2}{2}\\ &\quad+w_{11}^{(1)}(-1)\,z\overline{z}+w_{02}^{(1)}(-1)\tfrac{\overline{z}^2}{2}+\dots,\\ x_2(t-1)&=zr_1e^{-i\tau_0\omega_0}\ +\overline{zr}_1e^{i\tau_0\omega_0}\ +w^2(t,-1)\\ &=zr_1e^{-i\tau_0\omega_0}\ +\overline{zr}_1e^{i\tau_0\omega_0}\ +w_{20}^{(2)}(-1)\tfrac{z^2}{2}\\ &\quad+w_{11}^{(2)}(-1)\,z\overline{z}+w_{02}^{(2)}(-1)\tfrac{\overline{z}^2}{2}+\dots.\end{aligned} \tag{4.43}$$

Now, substituting Eq. (4.25), when $u=0$ and $\Gamma(v)\equiv x(t+v)$ in Eq. (4.42), gives that:

$$g(z,\overline{z})=\overline{D}\tau_0(1,\overline{r_2})\begin{pmatrix}-\beta(1-m)\,x_1(t+0)\,x_2(t+0)\\ 0\end{pmatrix}.$$

Therefore, the following is obtained:

$$\left.\begin{aligned}g(z,\overline{z})=&-\overline{D}\tau_0\beta(1-m)\big[\,r_1z^2+(r_1+\overline{r}_1)\,z\overline{z}+\overline{r}_1\overline{z}^2\\ &+\Big(2w_{11}^{(2)}(0)+w_{20}^{(2)}(0)+2r_1w_{11}^{(1)}(0)+\overline{r}_1w_{20}^{(1)}(0)\Big)\tfrac{z^2\overline{z}}{2}\\ &+\Big(2w_{11}^{(2)}(0)+w_{20}^{(2)}(0)+2\overline{r}_1w_{11}^{(1)}(0)+r_1w_{02}^{(1)}(0)\Big)\tfrac{z\,\overline{z}^2}{2}+\cdots\big]\end{aligned}\right\}. \tag{4.44}$$

So comparing the coefficients in Eq. (4.44) with those in Eq. (4.42) gives that:

$$\begin{aligned} g_{20} &= -2\overline{D}\tau_0\beta\left(1-m\right)r_1, \\ g_{11} &= -\overline{D}\tau_0\beta\left(1-m\right)\left(r_1+\overline{r}_1\right), \\ g_{02} &= -2\overline{D}\tau_0\beta\left(1-m\right)\overline{r}_1, \\ g_{21} &= -\overline{D}\tau_0\beta\left(1-m\right)\left(2w_{11}^{(2)}\left(0\right)+w_{20}^{(2)}\left(0\right)+2r_1w_{11}^{(1)}\left(0\right)+\overline{r}_1w_{20}^{(1)}\left(0\right)\right). \end{aligned} \tag{4.45}$$

Since Eq. (4.45) contains w_{11} and w_{20}, hence it needs to compute them.
Now, from Eqs. 4.38 and (4.39), for $v \in [-1, 0)$, we have:

$$G\left(z,\overline{z},v\right) = -\overline{q}^{*T}\left(0\right)H_0\left(z,\overline{z}\right)q\left(v\right) - q^{*T}\left(0\right)H_0\left(z,\overline{z}\right)\overline{q}\left(v\right).$$

Then by using Eqs. (4.36) and (4.37), it obtains that:

$$G\left(z,\overline{z},v\right) = -g\left(z,\overline{z}\right)q\left(v\right) - \overline{g}\left(z,\overline{z}\right)\overline{q}\left(v\right). \tag{4.46}$$

By comparing coefficients in both sides gives:

$$\begin{aligned} G_{20}\left(v\right) &= -g_{20}q\left(v\right) - \overline{g}_{02}\overline{q}\left(v\right), \\ G_{11}\left(v\right) &= -g_{11}q\left(v\right) - \overline{g}_{11}\overline{q}\left(v\right), \end{aligned} \tag{4.47}$$

Now, substituting Eqs. (4.47) into Eqs. (4.41) respectively gives that:

$$\begin{aligned} w'_{20}\left(v\right) &= 2i\tau_0\omega_0w_{20}\left(v\right) + g_{20}q\left(v\right) + \overline{g}_{02}\overline{q}\left(v\right), \\ w'_{11}\left(v\right) &= g_{11}q\left(v\right) + \overline{g}_{11}\overline{q}\left(v\right). \end{aligned} \tag{4.48}$$

Now by solving Eqs. (4.48), it is easy to verify that the solutions are written respectively as:

$$\begin{aligned} w_{20}\left(v\right) &= -\tfrac{g_{20}q(0)}{i\tau_0\omega_0}e^{i\tau_0\omega_0v} - \tfrac{\overline{g}_{02}\overline{q}(0)}{3i\tau_0\omega_0}e^{-i\tau_0\omega_0v} + K_1e^{2i\tau_0\omega_0v}, \\ w_{11}\left(v\right) &= \tfrac{g_{11}q(0)}{i\tau_0\omega_0}e^{i\tau_0\omega_0v} - \tfrac{\overline{g}_{11}\overline{q}(0)}{i\tau_0\omega_0}e^{-i\tau_0\omega_0v} + K_2. \end{aligned} \tag{4.49}$$

where $K_1 = \left(K_1^{(1)}, K_1^2\right)$ and $K_2 = \left(K_2^{(1)}, K_2^2\right)$ are constants vectors to be determined in the following.

From the definition of A when $v = 0$, and Eqs. (4.41), it is obtained that:

$$\int_{-1}^{0} d\eta\left(v\right)w_{20}\left(v\right) = 2i\tau_0\omega_0w_{20}\left(0\right) - G_{20}(0). \tag{4.50}$$

$$\int_{-1}^{0} d\eta\left(v\right)w_{11}\left(v\right) = -G_{11}(0). \tag{4.51}$$

Also from Eqs. (4.38) and (4.39), it is easy to verify that:

$$G_{20}\left(0\right) = -g_{20}q\left(0\right) - \overline{g}_{02}\overline{q}\left(0\right) + 2\tau_0\begin{bmatrix} r_1\beta\left(1-m\right) \\ 0 \end{bmatrix}. \tag{4.52}$$

$$G_{11}\left(0\right) = -g_{11}q\left(0\right) - \overline{g}_{11}\overline{q}\left(0\right) + 2\tau_0\begin{bmatrix} \beta\left(1-m\right)\left(r_1+\overline{r}_1\right) \\ 0 \end{bmatrix}. \tag{4.53}$$

Therefore by substituting Eqs. (4.49) and (4.52) into Eq. (4.50), and then using the results:

$$\begin{gathered}\left(i\tau_0\omega_0 I - \int_{-1}^{0} e^{i\tau_0\omega_0 v} d\eta\left(v\right)\right) q\left(0\right) = 0,\\ \left(-i\tau_0\omega_0 I - \int_{-1}^{0} e^{-i\tau_0\omega_0 v} d\eta\left(v\right)\right) \overline{q}\left(0\right) = 0.\end{gathered} \tag{4.54}$$

It is obtained that:

$$\left(2i\tau_0\omega_0\, I - \int_{-1}^{0} e^{2i\tau_0\omega_0 v} d\eta\left(v\right)\right) K_1 = 2\tau_0 \begin{bmatrix} r_1\beta(1-m) \\ 0 \end{bmatrix}. \tag{4.55}$$

Similarly, by substituting Eqs. (4.49) and (4.53) into Eq. (4.51), and then using Eqs. (4.54), it is obtained that:

$$K_2 \int_{-1}^{0} d\eta\left(v\right) = -2\tau_0 \begin{bmatrix} \beta\left(1-m\right)\left(r_1+\overline{r}_1\right) \\ 0 \end{bmatrix}. \tag{4.56}$$

Now, using Eq. (4.28) with $u=0$ into Eqs. (4.55) and (4.56), gives that:

$$\begin{bmatrix} 2i\omega_0 + \beta\left(1-m\right)E_1 + \mu & \beta\left(1-m\right)S_1 \\ 0 & 2i\omega_0 + \theta e^{-2i\omega_0\tau_0} \end{bmatrix} K_1 = 2 \begin{bmatrix} r_1\beta(1-m) \\ 0 \end{bmatrix}. \tag{4.57}$$

$$\begin{bmatrix} -\beta\left(1-m\right)E_1 - \mu & -\beta\left(1-m\right)S_1 \\ 0 & -\theta \end{bmatrix} K_2 = -2 \begin{bmatrix} \beta\left(1-m\right)\left(r_1+\overline{r}_1\right) \\ 0 \end{bmatrix}. \tag{4.58}$$

Accordingly, solving the linear systems given by Eqs. (4.57) and (4.58), gives that:

$$\begin{gathered}K_1^{(1)} = \frac{2r_1\beta(1-m)[2i\omega_0+\theta e^{-2i\omega_0\tau_0}]}{[2i\omega_0+\beta(1-m)E_1+\mu][2i\omega_0+\theta e^{-2i\omega_0\tau_0}]},\\ K_1^{(2)} = 0.\end{gathered} \tag{4.59}$$

And

$$\begin{gathered}K_2^{(1)} = \frac{2\beta(1-m)(r_1+\overline{r}_1)}{[\beta(1-m)E_1+\mu]},\\ K_2^{(2)} = 0.\end{gathered} \tag{4.60}$$

Consequently, all the values of $g_{ij};\ i=0,1,2;\ j=0,1,2$ given in Eqs. (4.45) can be determined by the parameters and delay. Thus, it can calculate the following quantities:

$$\begin{gathered}C_1\left(0\right) = \frac{i}{2\tau_0\omega_0}\left(g_{20}g_{11} - 2|g_{11}|^2 - \frac{|g_{02}|^2}{3}\right) + \frac{g_{21}}{2},\\ \mu_2 = \frac{-Re\{C_1(0)\}}{Re\{\lambda'(\tau_0)\}},\\ \beta_2 = 2Re\left\{C_1(0)\right\},\\ T_2 = -\frac{Im\ \{C_1(0)\}+\mu_2 Im\ \{\lambda'(\tau_0)\}}{\tau_0\omega_0}.\end{gathered} \tag{4.61}$$

□

These quantities are used to determine the direction of the Hopf bifurcation and stability of bifurcated periodic solutions of system (2.3) at the critical value τ_0 as shown in the following theorem.

Theorem 4.2:
The direction of the Hopf bifurcation is determined by the sign of μ_2 at the critical value τ_0, so that

1. *The the Hopf bifurcation is supercritical if $\mu_2 > 0$ and the Hopf bifurcation is subcritical if $\mu_2 < 0$.*
2. *The stability of bifurcated periodic solutions is determined by β_2 so that the periodic solutions are stable if $\beta_2 < 0$ and unstable if $\beta_2 > 0$.*
3. *The period of bifurcated periodic solutions is determined by β_2 so that the period increases if $T_2 > 0$ and decreases if $T_2 < 0$.*

5. NUMERICAL SIMULATION

In this section, the obtained results are illustrated using numerical simulation. The following set of hypothetical parameters set is adopted throughout this section.

$$\begin{array}{l} \psi = 0.87, \ \ \beta = 0.010, \quad m = 0.05, \quad \mu = 0.015, \\ P = 0, \ \alpha = 0.3, \theta = 0.2, \ \tau = 7.7 < \ \ \tau_0 \cong 7.85. \end{array} \tag{5.62}$$

All the obtained trajectories of the system (2.1) are drawn using the MATLAB of version 8. Starting from different sets of initial data, system (2.1) is solved numerically using the parameters set given in Eq. (5.62) and then the obtained trajectories are drawn in Fig. (5.2).

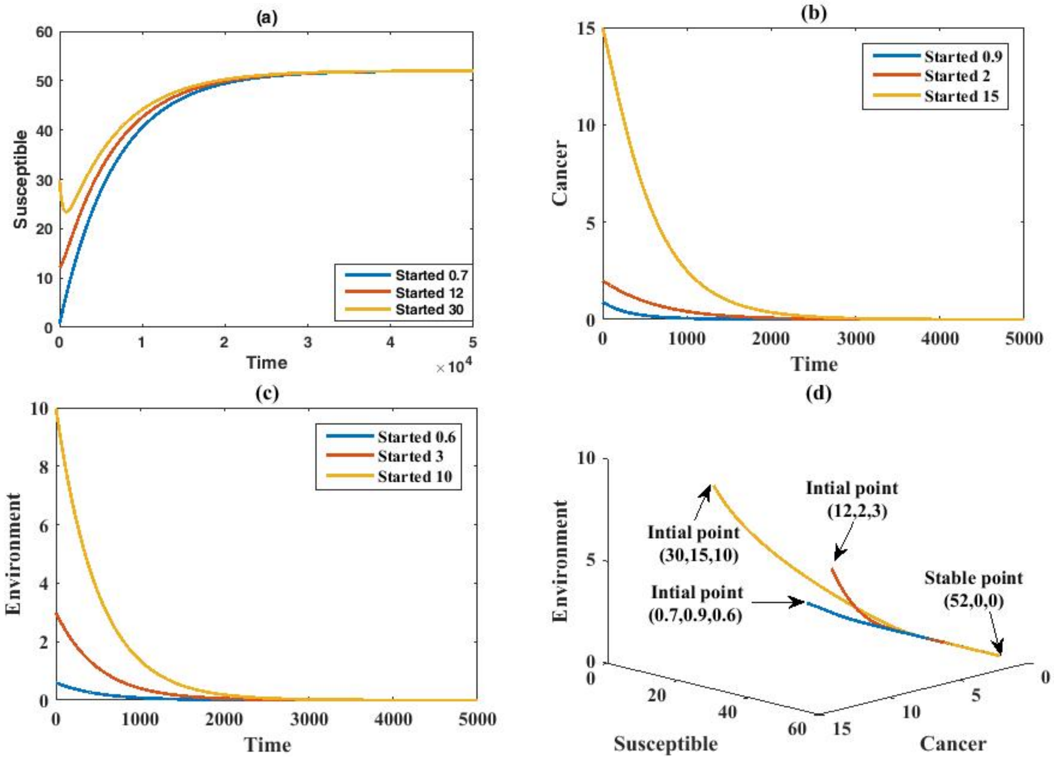

Fig. 5.2. : The trajectories of the system (2.1) using data given by Eq. (5.62) approach to *DFEP*. (a) Trajectories of Susceptible. (b) Trajectories of Cancer. (c) Trajectories of Environment. (d) 3D phase plot for globally asymptotically stable *DFEP*.

Clearly, Fig. (5.2) illustrates that system (2.1) has a globally asymptotically stable *DFEP* for that data (5.62). However, for the same data given by Eq. (5.62) with $P = 0.6$, it is observed that, although that system (2.1) is solved with different sets of initial points, it has a globally asymptotically stable *EEP* given by $E_1 = (17.9, 1.6, 3)$ as shown in Fig. (5.3) below.

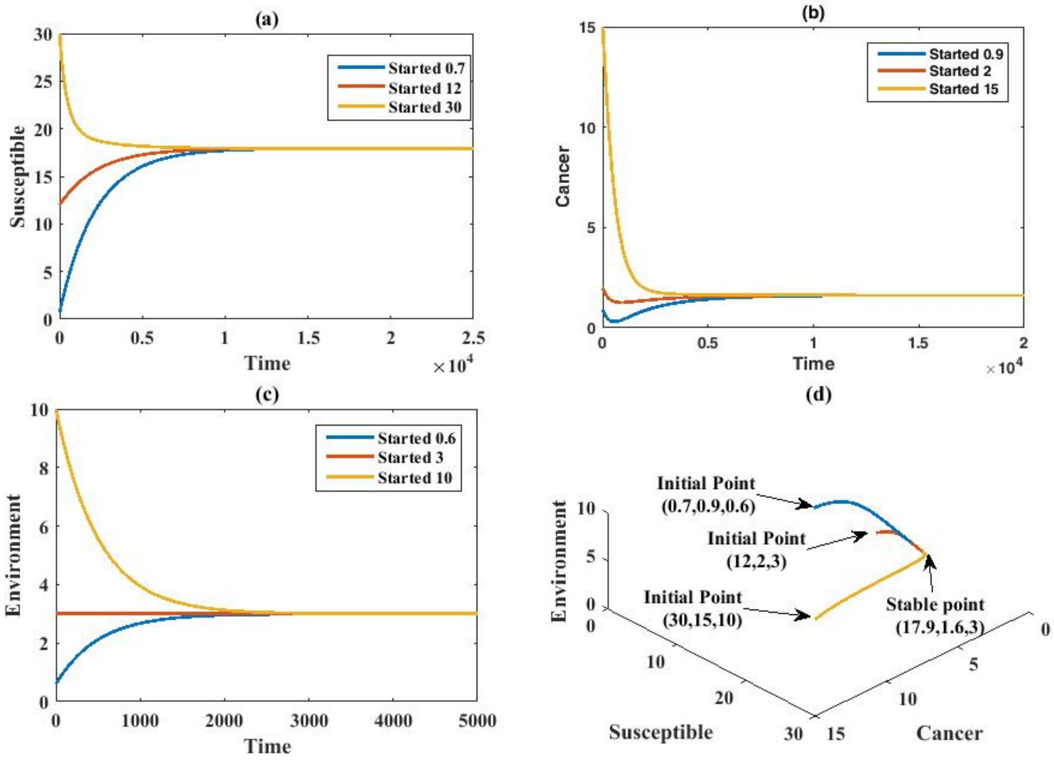

Fig. 5.3. : The trajectories of the system (2.1) using data given by Eq. (5.62) with $P = 0.6$ approach to *EEP*. (a) Trajectories of Susceptible. (b) Trajectories of Cancer. (c) Trajectories of Environment. (d) 3D phase plot for globally asymptotically stable *EEP*.

Now, to show the effect of varying the body resistance rate (m) due to chromosomal fixed against environment effect on the system behavior, the system is solved numerically for different values, say $m = 0.1,\ 0.7$ respectively, keeping other parameters fixed as given in Eq. (5.62) with $P = 0.6$, and then the solution of system (2.1) is drawn in Figs. (5.4a) and (5.4b).

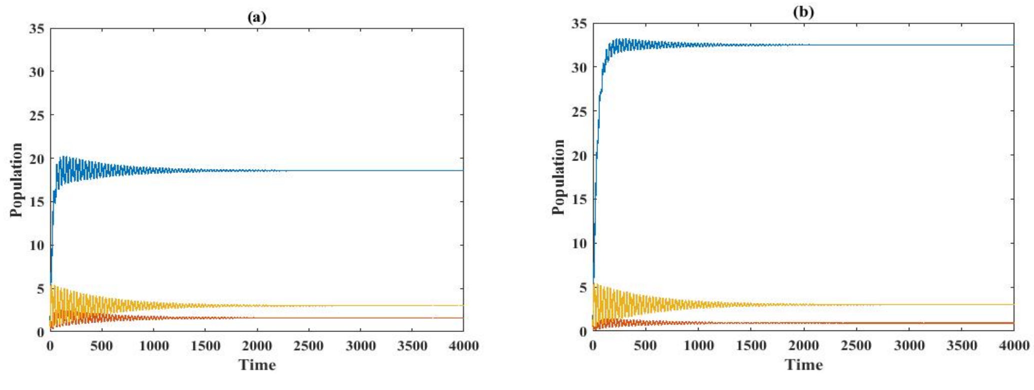

Fig. 5.4. : Time series of the trajectory of the system (2.1) using data given by Eq. (5.62) with $P = 0.6$ and different values of m. (a) Trajectory approaches to *EEP* given by $e_1 = (18, 1.5, 3)$ when $m = 0.1$. (b) Trajectory approaches to *EEP* given by $e_1 = (32, 0.92, 3)$ when $m = 0.7$.

Clearly, in Fig. (5.4) as m increases, the trajectory of the system (2.1) still approaches asymptotically to the *EEP* point. In fact, it is observed that as m increases the number of individuals with cancer decreases, and the number of susceptible increases without any effect of environment.

Now, the dynamical behavior of the system (2.1) near the *EEP* point under the effect of increasing the time delay is investigated. The system (2.1) is solved numerically for the set of parameter values given by Eq. (5.62) with $P = 0.6$ and $\tau = 7.86$ then the trajectory of the system (2.1) is drawn in Figs. (5.5a-5.5e).

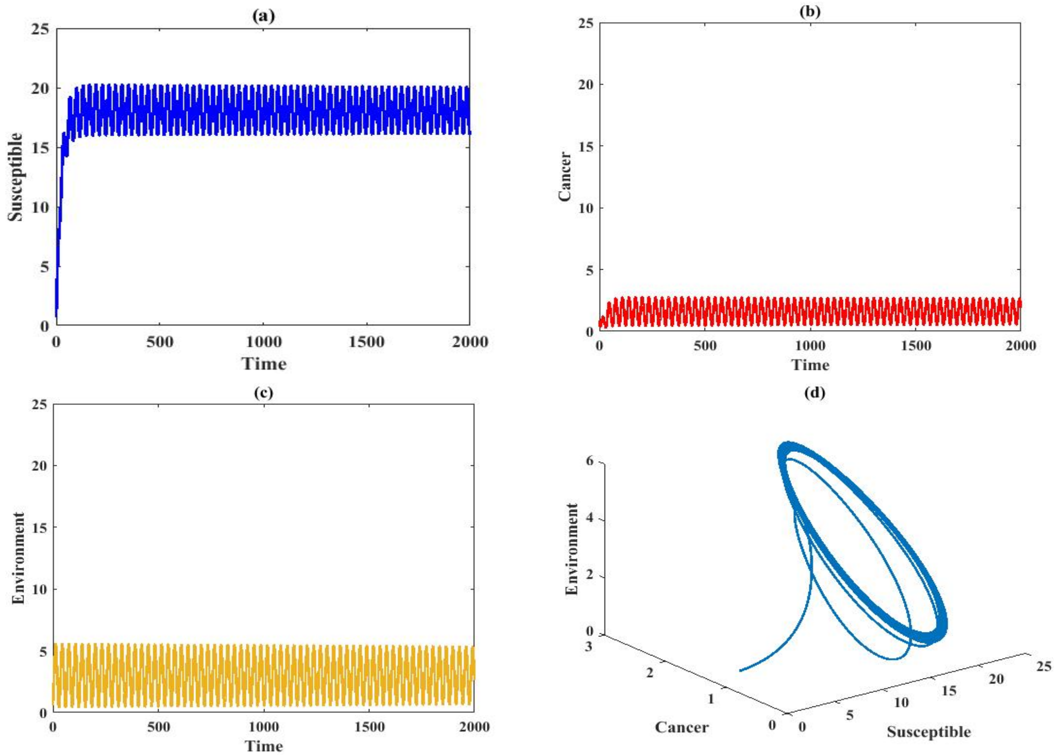

Fig. 5.5. : The existence of periodic solution near *EEP* of the system (2.1) for data given by equation (5.62) with $p = 0.6$ *and* $\tau = 7.86$. (a) Trajectories of Susceptible. (b) Trajectories of Cancer. (c) Trajectories of Environment. (d) 3D periodic solution.

6. CONCLUSION

In this paper, a mathematical model that describes the spread of cancer in a polluted environment incorporating delay in cleaning up the environment from the contaminated has been proposed and studied. The properties of the solution are discussed. It is observed that the proposed model has two equilibrium points namely *DFEP* and *EEP*. The stability analysis of the model shows that the *DFEP* is globally asymptotically stable for all $\tau \geq 0$. While the *EEP* is conditionally stable so that it's globally asymptotically stable for all $\tau \in [0,\ \tau_0)$ and there is the Hopf bifurcation at τ_0.

However, it is an unstable point for $\tau > \tau_0$ and periodic dynamics occurred. The stability and direction of the periodic dynamics are also investigated analytically by finding the normal form using the center manifold theory as well as numerically. It is observed that for the hypothetical set of data given by Eq. (5.62) with $p = 0.6$ the *EEP* is still globally asymptotically stable for $0 \leq$ ô $< \tau_0 \cong 7.853$. While the Hopf bifurcation occurs and periodic solutions bifurcate near the *EEP* point as τ passes through the above critical value τ_0. On the other hand, all the quantities, which are given in Eqs. (4.61), are determined for the periodic dynamics drawn in Fig. 5.5 as $C_1(0) = 7.360 - 77.426i$, $\beta_2 = 14.72 > 0$, $\mu_2 = -0.294 < 0$ and $T_2 = 51.873 > 0$. Therefore, according to theorem (4.2), the periodic resulting from the Hopf bifurcation is subcritical, unstable, and the size of the period increases.

ACKNOWLEDGEMENTS

The authors are thankful to the referees for their valuable suggestions.

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