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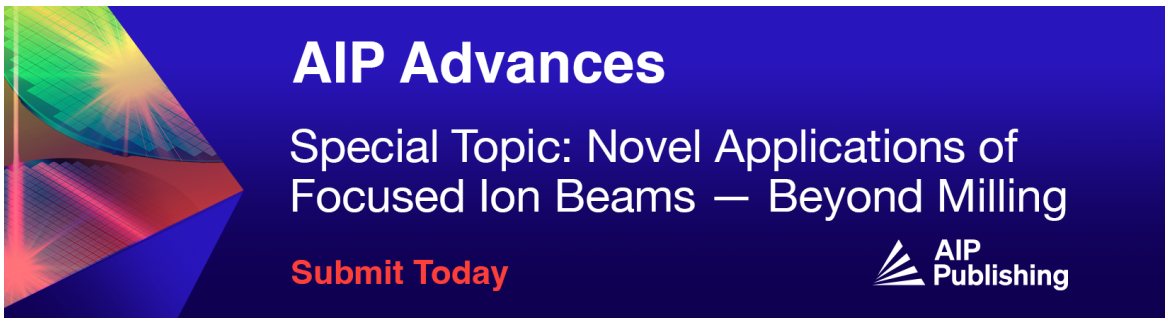

Dynamical analysis of a class of SEIR models through delayed strategies

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ABSTRACT

In recent decades, the mathematical modeling of infectious diseases, real-world problems, non-linear dynamical complex systems, etc., has increased significantly. According to World Health Organization, tobacco use is the cause of about 22% of cancer deaths. Another 10% are due to obesity, poor diet, lack of physical activity, and excessive drinking of alcohol. Approximately 5%–10% of cancers are due to inherited genetic defects. The objective is to investigate the impact of time delays in implementing control measures on the epidemic dynamics. The classification of cell population has four compartments: susceptible cells (x), cancer-infected cells (y), virus-free cells (v), and immune cells (z). Our focus is to find the equilibria of the problem and their stability. The stability of the solutions is of two types: locally asymptotic and globally asymptotic. The Routh–Hurwitz criterion, Volterra-type Lyapunov function, and LaSalle's invariance principle are used to verify the stability of solutions. The graphical behavior depicts the stable solutions to a real-world problem and supports the stability analysis of the problem. The findings contribute to the understanding of epidemic dynamics and provide valuable information for designing and implementing effective intervention strategies in public health systems.

I. INTRODUCTION

Cancer is a deadly disease that is becoming more common around the world nowadays. According to the 2020 World Health Organization report, there were ~0.019×10^9 new cases of cancer and the death rate was ~55%. The word cancer is given by the Greek physician Hippocrates (460–370 BC). Cancer is a group of different diseases, which bring about the distortion of cells and can attack other parts of the body. It develops due to the excessive growth of infected cells, named tumors in biological terms. Tumors are of two types: benign and malignant. Benign tumors are local to the organ/region where they develop, and malignant tumors attack other parts of the body, which is called metastasis. Every form of cancer has six stages. In the initial stage, one cannot trace a person's cancer because no symptom appears. Later on, cancer appears as an ulcer or as a mucous membrane in the affected organ. A person with lung cancer may find it hard to swallow things due to lung ulcers. Some individuals may face problems such as weight loss, exhaustion, distortion, skin damage, and feeling of weakness. Generally, cancer is caused by variations in the environment. In addition, in few cases, it is inherited by the patient from his parents. Some chemicals may cause cancer as well. For instance, the radiations of radioactive elements, ultraviolet rays, and carcinogens may increase the chances of falling susceptible to the disease. Ionizing radiation has high

energy to increase the chances of gene mutation. It includes radiation caused by gamma rays, x rays, and radon. Non-ionizing radiation does not have enough energy to cause cancer. Rock and soil produce radon gas. When uranium and thorium are broken down, they produce radium. The chances of lung cancer are higher in those living in the areas of radon gas. Radiation with high energy, such as gamma rays and x rays, can easily produce gene mutation and result in the production of tumors in the exposed body. Explosions in nuclear power plants and atomic bombs are the major sources of these types of radiation. However, radiation is also used in cancer treatment, called radiotherapy. Radiotherapies are of two types: external and internal therapy. Radiation therapy can help in destroying the affected DNA. This helps to stop cell division, so tumor size shrinks. This technique takes from weeks to a month to operate. Radiation therapy also has some side effects, such as killing of nearby healthy cells. This technique is also costly. The patient needs to take a special diet that contains more proteins and calories to maintain physical health. Carcinogens are chemicals that can cause cancer in humans. Carcinogens are of three types: chemical, physical, and oncogenic carcinogens, which can be found naturally and are mainly found in tobacco. Carcinogenic foods include processed meat, alcohol, soft drinks, fruits, vegetables, eggs, and tomatoes. Some examples of carcinogenic materials are benzene, vinyl chloride, nickel, and asbestos. Malinzi *et al.* proposed a prospect in which they describe the application of mathematical modeling in the treatment of cancer.[1] Salim *et al.* proposed a dynamic model of prostate cancer using vaccination delay.[2] Valle *et al.* presented a mathematical model to explain and check the correctness of chemoimmunotherapy for cancer treatment.[3] Alqudah presented a numerical analysis of the mathematical model of cancer cells with chemotherapy.[4] Nave *et al.* proposed a prospectus of the dynamical model to treat breast cancer.[5] Jarrett *et al.* proposed a mathematical model of breast cancer constrained by magnetic resonance data.[6] Jin studied the global and local convergence of a dynamic cancer model.[7] Ji *et al.* proposed a mathematical model to explain the role of medication in the treatment of prostate cancer and the development of metastatic bone disease.[8] Nakanishi and Hirata proposed a mathematical model for scheduling hormone therapy to treat prostate cancer.[9] Solís-Pérez *et al.* proposed a fractional mathematical model of breast cancer.[10] Lai and Friedman proposed a mathematical model to check the validity of two drugs in treating cancer.[11] Sigal *et al.* presented a mathematical model of cancer cells with target immunotherapy.[12] Medina reviewed the metabolic behavior of cancer disease using mathematical modeling.[13] Jordão and Tavares described the role of mathematical modeling in curing cancer.[14] The computation efficiency of numerical methods in the mathematical modeling of influenza with vaccination strategies and that of gonorrhea diseases is studied in Refs. 15 and 16. Bratus *et al.* studied a dynamic model of cancer by maximizing the time delay.[17] Magi *et al.* proposed a dynamic model to explain the current situation and spread of cancer.[18] The research of Xu *et al.* is based on a delayed mathematical model for cancer treatment and the growth of cancer cells in the presence of continuous medication.[19] Barbarossa *et al.* proposed a delayed mathematical model of cancer with immune response.[20] Yang *et al.* studied a construction project's delay analysis selection model.[21] Ajayi and Chinda studied the impact of construction delay-controlling parameters on project schedules.[22] Cui and Xu analyzed mathematical models for the growth of tumors with time delays in cell proliferation.[23] Villasana and Radunskaya presented a delay differential equation model for tumor growth.[24] In the field of epidemiology, mathematical modeling has a key role. In addition, an important type of mathematical modeling is delay modeling, which is very useful in dealing with real-life problems, especially epidemic diseases. Cancer is a dreadful disease. In addition, it is a major issue and causes deaths on a large scale, as mentioned above. So, delay modeling is an important factor in dealing with this horrible disease. In Sec. II, the cancer delay model is presented along with its equilibrium points. Section III presents the analysis of the model that contains equilibria, positivity and boundedness, reproduction number of the model, and sensitivity analysis of the reproduction number to each of its parameters. In Secs. IV and V, the local stability and global stability are discussed. In Sec. VII, the conclusion and results are presented.

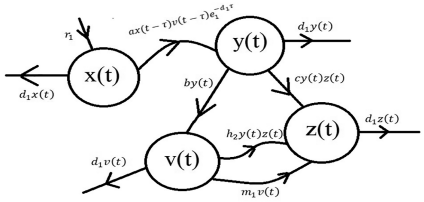

FIG. 1. Flow chart of the delayed cancer disease model.

II. MODEL FORMULATION

For simplicity, it is assumed that $N(t)$ represents the total population of the cell, which is further divided into four compartments: uninfected cells, infected cells, virus-free cells, and immune cells. Their numbers at a given time t are represented by $x(t)$, $y(t)$, $v(t)$, and $z(t)$, respectively. The dynamics of cell population is shown in Fig. 1.

The system of delay differential equations from the presented flow chart is given by

$$\frac{dx}{dt} = r_1 - ax(t-\tau)v(t-\tau)e_1^{-d_1\tau} - d_1x(t), \quad t \geq 0\ \tau \leq t, \tag{1}$$

$$\frac{dy}{dt} = ax(t-\tau)v(t-\tau)e_1^{-d_1\tau} - cy(t)z(t) - d_1y(t) - by(t), \quad t \geq 0\ \tau \leq t, \tag{2}$$

$$\frac{dv}{dt} = by(t) - h_2y(t)z(t) - d_1v(t) - m_1v(t), \quad t \geq 0, \tag{3}$$

$$\frac{dz}{dt} = cy(t)z(t) + h_2y(t)z(t) - d_1z(t) + m_1v(t), \quad t \geq 0, \tag{4}$$

$$x = x_0 \geq 0, \quad y = y_0 \geq 0, \quad v = v_0 \geq 0, \quad z = z_0 \geq 0.$$

III. ANALYSIS OF MODEL

The cancer trivial equilibrium point (CTE—C_0), cancer-free cell equilibrium point ($CFCE$—C_1), and cancer existing cell equilibrium point ($CECE$—C_2) are as follows:

$$C_0 = (x^0, y^0, v^0, z^0) = (0,0,0,0),$$
$$C_1 = (x^1, y^1, v^1, z^1) = \left(\frac{r_1}{d_1}, 0, 0, 0\right), \quad \text{and} \quad C_2 = (x^*, y^*, v^*, z^*),$$

where

$$x^* = \frac{r_1}{av^* e_1^{-d_1\tau} + d_1}, \quad y^* = \frac{ar_1 v^* e_1^{-d_1\tau}}{\left(av^* e_1^{-d_1\tau} + d_1\right)(cz^* + d_1 + b)} = \beta,$$
$$v^* = \frac{h_2\beta z^* - b\beta}{d_1 + m_1}, \quad z^* = \frac{-m_1 y}{c\beta + h_2\beta - d_1}.$$

A. Model properties

Theorem 1. For given $t \geq 0, \tau \leq t$, and initial conditions, the system preserves the positivity of the solution at the system of Eqs. (1)–(4).

Proof. It is clear from the system of Eqs. (1)–(4) that

$$\left.\frac{dx}{dt}\right|_{x=0} = r_1 \geq 0, \quad \left.\frac{dy}{dt}\right|_{y=0} = axve_1^{-d_1\tau} \geq 0,$$
$$\left.\frac{dv}{dt}\right|_{v=0} = by - h_2yz \geq 0, \quad \left.\frac{dz}{dt}\right|_{z=0} = m_1 v \geq 0,$$

which shows that the positivity is reserved in the system.

Theorem 2. The solution $(x, y, v, z\varepsilon R_+^4)$ of the system of Eqs. (1)–(4) is bounded.

Proof. Let us suppose the population function as follows:

$$N(t) = x(t) + y(t) + v(t) + z(t),$$

$$\frac{dN}{dt} = r_1 - d_1 N,$$

$$\frac{dN}{dt} \leq r_1 - d_1 N.$$

Using Gronwall's inequality gives the following results:

$$N(t) \leq N(0)e_1^{-d_1 t} + \frac{r_1}{d_1}, \quad t \geq 0, \qquad \limsup_{t\to\infty} N(t) \leq \frac{r_1}{d_1}.$$

B. Reproduction number

The reproduction number of the delayed cancer model using the next-generation matrix method is determined as follows:

Assume that
$$\begin{bmatrix} y' \\ v' \\ z' \end{bmatrix} = \begin{bmatrix} 0 & \frac{ar_1 e_1^{-d_1\tau}}{d_1} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} y \\ v \\ z \end{bmatrix} - \begin{bmatrix} d_1 + b & 0 & 0 \\ -b & d_1 + m_1 & 0 \\ 0 & -m_1 & d_1 \end{bmatrix} \begin{bmatrix} y \\ v \\ z \end{bmatrix}.$$

Let $A = \begin{bmatrix} 0 & \frac{ar_1 e_1^{-d_1\tau}}{d_1} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$ and $B = \begin{bmatrix} d_1 + b & 0 & 0 \\ -b & d_1 + m_1 & 0 \\ 0 & -m_1 & d_1 \end{bmatrix}$,

where A and B are the transmission and transition matrices, respectively. Now, we have to find AB^{-1},

$$AB^{-1} = \begin{bmatrix} \frac{abr_1 e_1^{-d_1\tau}}{d_1(d_1+b)(d_1+m_1)} & \frac{ar_1 e_1^{-d_1\tau}}{d_1(d_1+m_1)} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

Now, the most significant eigenvalue of AB^{-1} is the reproduction number denoted by R_0 and is given by

$$R_0 = \frac{abr_1 e_1^{-d_1\tau}}{d_1(d_1+b)(d_1+m_1)}.$$

C. Sensitivity of parameters

The sensitivity of parameters in epidemic models refers to how changes in specific model parameters affect the overall behavior and outcomes of the model. Sensitivity analysis helps researchers understand the impact of parameter values on the model's predictions. By systematically varying parameter values, one can assess how sensitive the model's results are to changes in each parameter. This analysis provides insights into which parameters have the most significant influence on the model's outcomes, helping identify critical factors that drive the spread and control of an epidemic. To determine such parameters, consider the following calculations:

$$C_a = \frac{\frac{\partial R_0}{R_0}}{\frac{\partial a}{a}} = \frac{a}{R_0} \times \frac{r_1 b e_1^{-d_1\tau}}{d_1(d_1+b)(d_1+m_1)}$$
$$= \frac{1}{R_0} \times \frac{ar_1 b e_1^{-d_1\tau}}{d_1(d_1+b)(d_1+m_1)} = \frac{1}{R_0} \times R_0 = 1 > 0.$$

By repeating this process on other parameters, the following results are found:

$$C_{r_1} = 1 > 0, \qquad C_b = \frac{d_1}{d_1 + b} > 0, \qquad C_{m_1} = -\frac{m_1}{d_1 + m_1} < 0,$$

$$C_{d_1} = -\frac{\left[\tau d_1(d_1+b)(d_1+m_1) + \left(2m_1 d_1 + 3d_1^2 + bm_1 + 2d_1 b\right)\right]}{\left[(d_1+b)(d_1+m_1)\right]} < 0.$$

From the above analysis, it is found that some of the parameters have positive sensitivity indices, such as a, r_1, and b, and some of the parameters have negative sensitivity indices, such as m_1 and d_1. It means that a, r_1, and b have a direct relation with R_0 and m_1 and d_1 have an inverse relation with the reproduction number.

IV. LOCAL STABILITY

Theorem 3. If $R_0 < 1$, then cancer-free cell equilibrium point, $C_1 = (x^1, y^1, v^1, z^1) = \left(\frac{r_1}{d_1}, 0, 0, 0\right)$, is asymptotically stable locally. Otherwise, C_1 is unstable.

Proof. At $C_1 = (x^1, y^1, v^1, z^1) = \left(\frac{r_1}{d_1}, 0, 0, 0\right)$, the system of Eqs. (1)–(4) becomes

$$J_c\left(\frac{r_1}{d_1},0,0,0\right)=\begin{bmatrix} -d_1 & 0 & -a\left(\frac{r_1}{d_1}\right)e_1^{-d_1\tau} & 0 \\ 0 & -d_1-b & a\left(\frac{r_1}{d_1}\right)e_1^{-d_1\tau} & 0 \\ 0 & b & -d_1-m_1 & 0 \\ 0 & 0 & m_1 & -d_1 \end{bmatrix}.$$

By evaluating $\left|J_c|_{c_1}-\lambda I\right|=0$, we have found the following negative eigenvalues $-d_1-\lambda=0$, which gives $\lambda=-d_1<0$ and the polynomial $\lambda^2+a_0\lambda+a_1=0$.

Here, $a_0=2d_1+b$ and $a_1=d_1^2+m_1d_1+bm_1+bd_1-ba\left(\frac{r_1}{d_1}\right)e_1^{-d_1\tau}$.

Since $a_0,a_1>0$ if $R_0<1$, the cancer-free cell equilibrium point is locally asymptotically stable.

Theorem 4. The cancer existing cell equilibrium (CECE) point, $C_2=\left(x^*,y^*,v^*,z^*\right)$, is stable in local sense, if $R_0>1$.

Proof. The Jacobian matrix of the system of Eqs. (1)–(4) at the cancer existing cell equilibrium point is as follows:

$$J\left(x^*,y^*,v^*,z^*\right)=\begin{bmatrix} -av^*e_1^{-d_1\tau}-d_1 & 0 & -ax^*e_1^{-d_1\tau} & 0 \\ av^*e_1^{-d_1\tau} & -cz^*-d_1-b & ax^*e_1^{-d_1\tau} & -cy^* \\ 0 & b-h_2z^* & -d_1-m_1 & -h_2y^* \\ 0 & cz^*+h_2z^* & m_1 & cy^*+h_2y^*-d_1 \end{bmatrix}.$$

For eigenvalues, put $|J-\lambda I|=0$,

$$\begin{vmatrix} -av^*e_1^{-d_1\tau}-d_1-\lambda & 0 & -ax^*e_1^{-d_1\tau} & 0 \\ av^*e_1^{-d_1\tau} & -cz^*-d_1-b-\lambda & ax^*e_1^{-d_1\tau} & -cy^* \\ 0 & b-h_2z^* & -d_1-m_1-\lambda & -h_2y^* \\ 0 & cz^*+h_2z^* & m_1 & cy^*+h_2y^*-d_1-\lambda \end{vmatrix}=0.$$

On evaluating the above determinant, we have the following polynomial:

$$\begin{aligned}\lambda^4+(A+d_1+F-I-B)\lambda^3+(AF-AB-AI-d_1F-DF+BI-FI-CF-DH)\lambda^2\\ -(ABI-ABF-AFI-ACE-ADH+d_1BI-d_1BF-d_1FI-d_1I-d_1CE-d_1DH+BFI\\ +m_1G+CEI-CGH-CEm_1-DHF+ACE)\lambda+(ABFI+AGm_1+ACEI-ACGH\\ -ADEm_1-ADHF+BFTd_1+Gd_1m_1+d_1CEI-CGHd_1-DEm_1d_1-DHFd_1-ACEI+ACHG)=0.\end{aligned}$$

Here,

$$m_0=1,\qquad m_1=A+d_1+F-I-B,$$

$$m_2=AF-AB-AI-d_1F-DF+BI-FI-CF-DH,$$

$$\begin{aligned}m_3=ABI-ABF-AFI-ACE-ADH+d_1BI-d_1BF\\ -d_1FI-d_1I-d_1CE-d_1DH+BFI+m_1G+CEI\\ -CGH-CEm_1-DHF+ACE,\end{aligned}$$

$$\begin{aligned}m_4=ABFI+AGm_1+ACEI-ACGH-ADEm_1-ADHF\\ +BFTd_1+Gd_1m_1+d_1CEI-CGHd_1-DEm_1d_1\\ -DHFd_1-ACEI+ACHG,\end{aligned}$$

where

$$A=ave_1^{-d_1\tau},\quad B=-d_1-b-cy,\quad C=axe_1^{-d_1\tau},$$
$$D=-cy,\quad E=b-h_2z^*,\quad F=d_1+m_1$$
$$G=-h_2y,\quad H=cz+h_2z,\quad I=cy-d_1+h_2y.$$

$m_0,m_1>0$, $m_1m_2-m_0m_3>0$, $(m_1m_2-m_0m_3)(m_3)-{m_1}^2m_4>0$, and $m_4>0$ if $R_O>1$.

Hence, the cancer existing equilibrium of the given system of Eqs. (1)–(4) is stable in local sense.

V. GLOBAL STABILITY

Theorem 5. The cancer-free equilibrium point $C_1=(x_1,y_1,v_1,z_1)=(\frac{r_1}{d_1},0,0,0)$ is stable in global sense, if $R_0<1$.

TABLE I. Values of the parameters.

Parameters	Descriptions	Values (per day)/Source[25]
r_1	The growth rate of cells	0.5 (assumed)
a	The rate of infection of cells	5.1 (fitted)
d_1	The rate of mortality of cells	0.5 (assumed)
c	The rate of transport capacity of cells	3.048 (CFCE) 5.048 (CECE)
b	The releasing rate of new particles with burst size	0.22–0.89 (fitted)
h_1	The rate of immunity of cells	0.36–0.66 (fitted)
m_1	The immunity's rate of stimulation of infected cells	0.6–0.9 (fitted)
τ	The delay parameter	≥0

Proof. Consider the Lyapunov function $G : \chi \to \mathrm{R}$ defined as follows:

$$G = \left(x - x_1 - x_1 \log \frac{x}{x_1}\right) + y + v + z \quad \forall (x, y, v, z) \varepsilon \chi,$$

$$\frac{dG}{dt} = \left(1 - \frac{x_1}{x}\right)\frac{dx}{dt} + \frac{dy}{dt} + \frac{dv}{dt} + \frac{dz}{dt},$$

$$\begin{aligned}\frac{dG}{dt} = &\left(\frac{x - x_1}{x}\right)(r_1 - axve_1^{-d_1\tau} - d_1 x)\\ &+ (axve_1^{-d_1\tau} - cyz - d_1 y - by)\\ &+ (by - h_2 yz - d_1 v - m_1 v) + (cyz + h_2 yz - d_1 z + m_1 v),\end{aligned}$$

$$\frac{dG}{dt} = (x - x_1)\left(\frac{r_1}{\mathrm{x}} - ave_1^{-d_1\tau} - d_1\right) + axve_1^{-d_1\tau} - d_1 y - d_1 v - d_1 z,$$

$$\begin{aligned}\frac{dG}{dt} = &(x - x_1)\left(\frac{r_1}{\mathrm{x}} - ave_1^{-d_1\tau} - \frac{r_1}{x_1} + ave_1^{-d_1\tau}\right)\\ &- d_1\left(v - \frac{axve_1^{-d_1\tau}}{\mathrm{d_1}}\right) - d_1(y + z),\end{aligned}$$

$$\frac{dG}{dt} = (x - x_1)\left(\frac{r_1}{x} - \frac{r_1}{x_1}\right) - d_1\left(v - \frac{axve_1^{-d_1\tau}}{\mathrm{d_1}}\right) - d_1(y + z),$$

$$\frac{dG}{dt} = (x - x_1)\left(\frac{r_1 x_1 - r_1 x}{x x_1}\right) - d_1\left(v - \frac{axve_1^{-d_1\tau}}{\mathrm{d_1}}\right) - d_1(y + z),$$

$$\frac{dG}{dt} = \left(\frac{-r_1(x - x_1)^2}{x x_1}\right) - d_1 v\left(1 - \frac{axe_1^{-d_1\tau}}{\mathrm{d_1}}\right) - d_1(y + z).$$

$\frac{dG}{dt} < 0$ if $R_0 < 1$, and $\frac{dG}{dt} = 0$ if $x = x_1, y = 0, v = 0,$ and $z = 0$. Therefore, by LaSalle's Invariance Principle (LIP), C_0 is stable in global sense.

Theorem 6. cancer existing cell equilibrium point (CECE—C^*), $C^* = (x^*, y^*, v^*, z^*)$, is stable in global sense, if $R_0 > 1$.

Proof. Consider a Lyapunov function $G : \chi \to \mathbb{R}$ defined as

$$\begin{aligned}G = &\left(x - x^* - x^* \log \frac{x}{x^*}\right) + \left(y - y^* - y^* \log \frac{y}{y^*}\right)\\ &+ \left(v - v^* - v^* \log \frac{v}{v^*}\right) + \left(z - z^* - z^* \log \frac{z}{z^*}\right),\end{aligned}$$

$$\begin{aligned}\frac{dG}{dt} = &\frac{d}{dx}\left(x - x^* - x^* \log \frac{x}{x^*}\right)\frac{dx}{dt} + \frac{d}{dy}\left(y - y^* - y^* \log \frac{y}{y^*}\right)\frac{dy}{dt}\\ &+ \frac{d}{dv}\left(v - v^* - v^* \log \frac{v}{v^*}\right)\frac{dv}{dt} + \frac{d}{dz}\left(z - z^* - z^* \log \frac{z}{z^*}\right)\frac{dz}{dt},\end{aligned}$$

$$\begin{aligned}\frac{dG}{dt} = &\left(\frac{x - x^*}{x}\right)(r_1 - axve_1^{-d_1\tau} - d_1 x)\\ &+ \left(\frac{y - y^*}{y}\right)(axve_1^{-d_1\tau} - cyz - d_1 y - by)\\ &+ \left(\frac{v - v^*}{v}\right)(by - h_2 yz - d_1 v - m_1 v)\\ &+ \left(\frac{z - z^*}{z}\right)(cyz + h_2 yz - d_1 z + m_1 v),\end{aligned}$$

$$\begin{aligned}\frac{dG}{dt} = &\left(x - x^*\right)\left(\frac{r_1}{\mathrm{x}} - ave_1^{-d_1\tau} - d_1\right)\\ &+ (y - y^*)\left(\frac{axve_1^{-d_1\tau}}{\mathrm{y}} - cz - d_1 - b\right)\\ &+ (v - v^*)\left(\frac{by}{v} - \frac{h_2 yz}{v} - d_1 - m_1\right)\\ &+ (z - z^*)\left(cy + h_2 y - d_1 + \frac{m_1 v}{z}\right),\end{aligned}$$

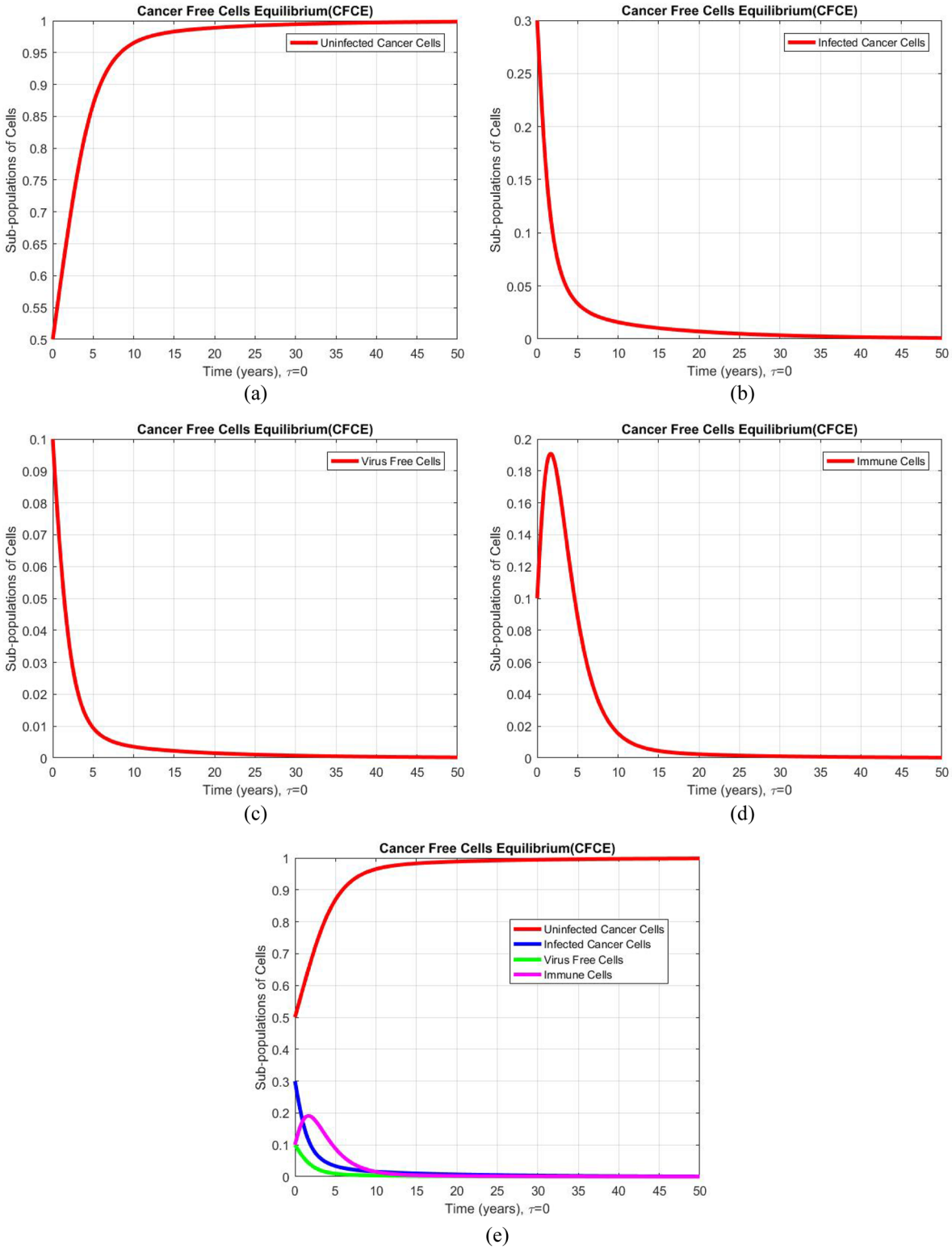

FIG. 2. (a) Behavior of uninfected cancer cells at CFCE. (b) Behavior of infected cancer cells at CFCE. (c) Behavior of virus-free cells at CFCE. (d) Behavior of uninfected immune cells at CFCE. (e) Combined graphical behavior of all sub-populations of cells at CFCE.

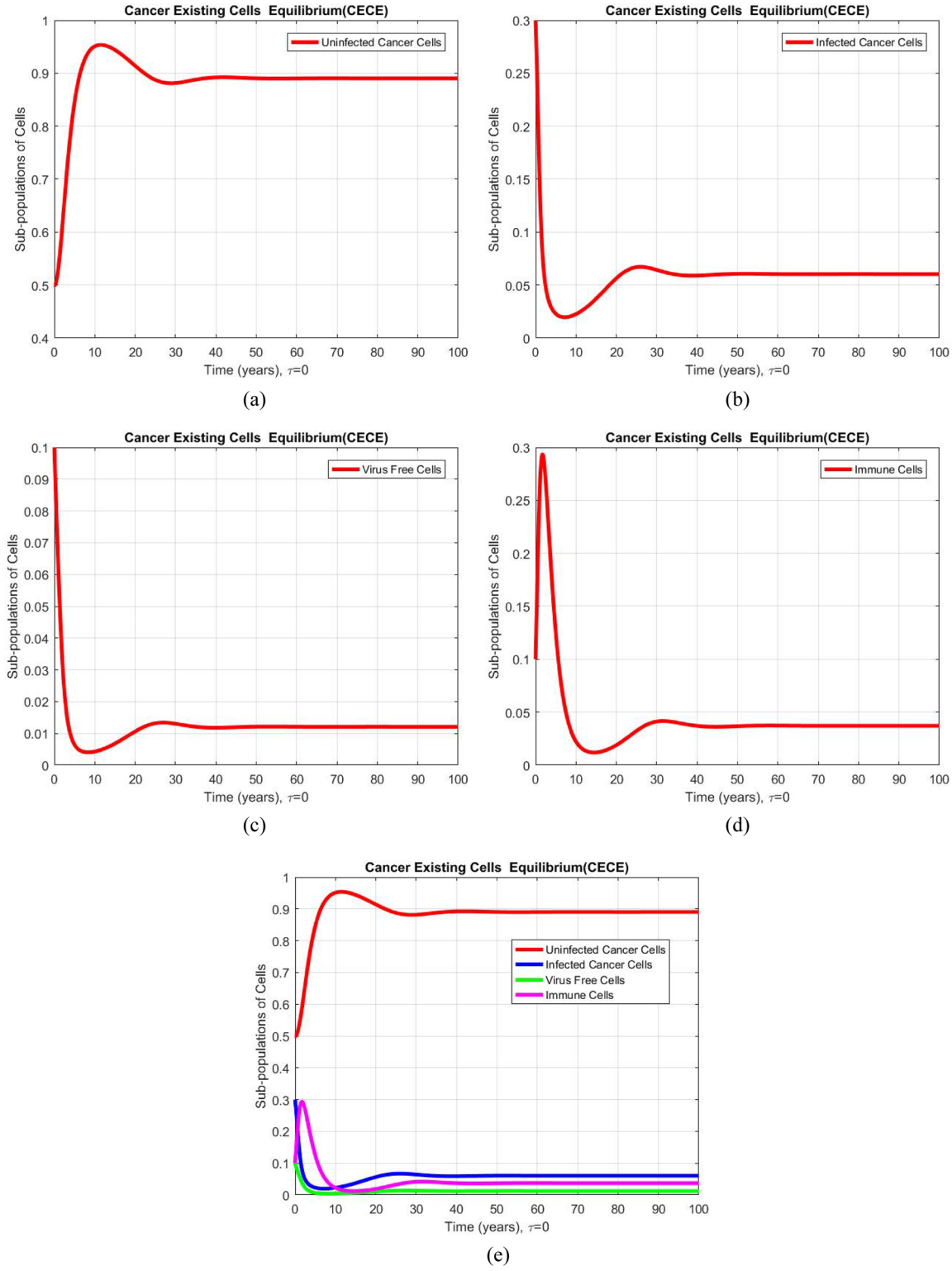

FIG. 3. (a) Behavior of uninfected cancer cells at CECE. (b) Behavior of infected cancer cells at CECE. (c) Behavior of virus-free cells at CECE. (d) Behavior of uninfected immune cells at CECE. (e) Combined graphical behavior of all sub-populations of cells at CECE.

$$\frac{dG}{dt} = (x - x^*)\left(\frac{r_1}{x} - ave_1^{-d_1\tau} - \frac{r_1}{x^*} + ave_1^{-d_1\tau}\right) + (y - y^*)\left(\frac{axve_1^{-d_1\tau}}{y} - cz - b + cz + b - \frac{axve_1^{-d_1\tau}}{y^*}\right) + (v - v^*)\left(\frac{by}{v} - \frac{h_2yz}{v} - m_1 + m_1 - \frac{by}{v^*} + \frac{h_2yz}{v^*}\right) + (z - z^*)\left(cy + h_2y + \frac{m_1v}{z} - cy - h_2y - \frac{m_1v}{z^*}\right),$$

$$\frac{dG}{dt} = \frac{-r_1(x - x^*)^2}{xx^*} - \frac{axve_1^{-d_1\tau}(y - y^*)^2}{yy^*} - \frac{by(v - v^*)^2}{vv^*} - \frac{h_2yz(v - v^*)^2}{vv^*} - \frac{m_1v(z - z^*)^2}{zz^*}.$$

$\frac{dG}{dt} \le 0$ for $R_0 < 1$, and also $\frac{dF}{dt} = 0$ only if $x = x^*, y = y^*, v = v^*$, and $z = z^*$. Hence, by LaSalle's Invariance Principle (LIP), C^* is stable in global sense.

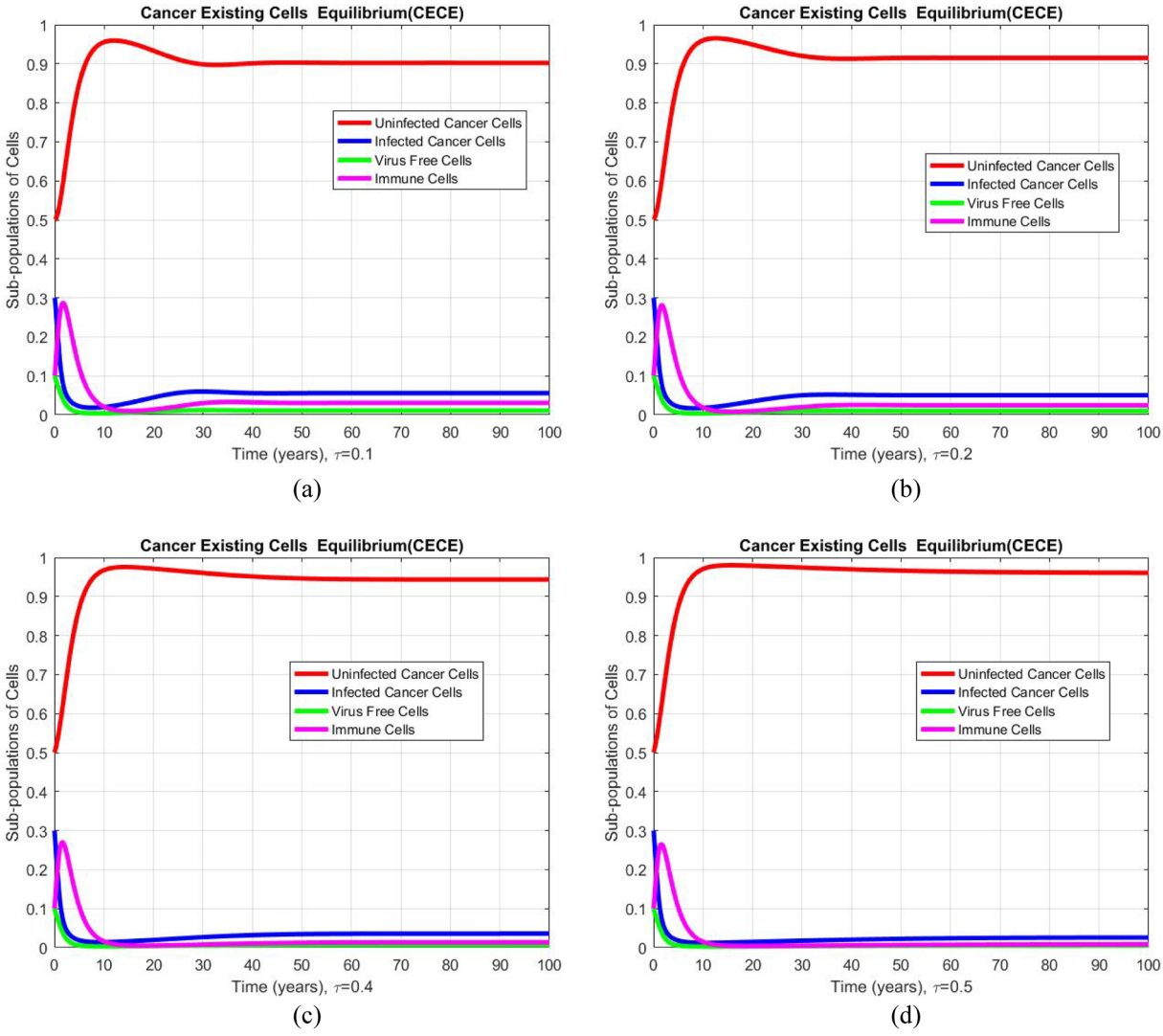

FIG. 4. (a) Combined graphical behavior of all sub-populations of cells at CECE when $\tau = 0.1$. (b) Combined graphical behavior of all sub-populations of cells at CECE when $\tau = 0.2$. (c) Combined graphical behavior of all sub-populations of cells at CECE when $\tau = 0.5$. (d) Combined graphical behavior of all sub-populations of cells at CECE when $\tau = 0.5$.

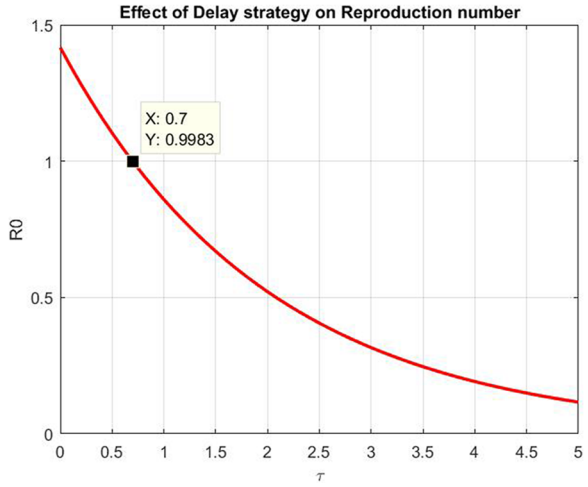

FIG. 5. Comparison of the reproduction number and the delay term.

VI. SIMULATIONS

In this section, the simulation results of the model are displayed with the use of the parameters whose values are shown in Table I.

VII. RESULTS AND CONCLUSION

Case 1: Without delay effect: The model's behavior for cancer-free equilibrium shown in Figs. 2(a)–2(e) converges. The model's behavior for cancer-existing compensation shown in Figs. 3(a)–3(e) converges. Case 2: With delay effect: Figs. 4(a)–4(d) show that the susceptibility of uninfected cells increases with delay tactics, and the infectivity decreases and even converges to zero. Figure 5 shows the comparison of the delay term with the reproduction number. Figure 6 displays the effect of the delay strategies on infected cells. In this article, we investigated a real-life application of the mathematical analysis of a delayed cancer model. The model is based on four sub-populations of cells: susceptible, infected, uninfected, and immune. The model analysis includes positivity, boundedness, equilibria, and threshold number with local and global stabilities. The sensitivity of the parameters is one of the outcomes of the model. Linearization of the model is developed by well-known results, such as the Jacobian and Routh–Hurwitz criteria. Furthermore, preventive measures could be supportive to control or eradicate cancer, such as a balanced diet, a healthy weight, and frequent physical activities. The researchers in this study employ mathematical techniques to investigate how the introduction of delays in implementing these strategies impacts the behavior and outcomes of the SEIR models. By incorporating uncertainties into the model, the study aims to capture the realistic dynamics and time-dependent nature of the spread of infectious diseases. The findings of this study contribute to the understanding of how delayed strategies can influence the dynamics of infectious diseases. The insights gained from this analysis can help inform public health policymakers and practitioners in designing more effective disease control and prevention systems, taking into account the time delays associated with the implementation of interventions.

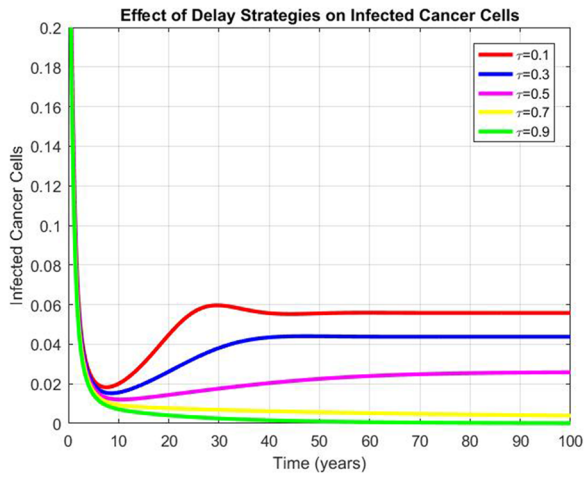

FIG. 6. Display of the effect of the delay term on an infective cell.

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AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflicts to disclose.

Author Contributions

Wafa F. Alfwzan: Funding acquisition (equal); Methodology (equal); Project administration (equal). **Dumitru Baleanu**: Funding acquisition (equal); Supervision (equal). **Ali Raza**: Conceptualization (equal); Data curation (equal); Writing – original draft (equal); Writing – review & editing (equal). **Muhammad Rafiq**: Project administration (equal); Resources (equal); Software (equal); Validation (equal); Visualization (equal). **Nauman Ahmed**: Investigation (equal); Software (equal); Visualization (equal).

DATA AVAILABILITY

The data that support the findings of this study are available within the article.

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