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Stability and bifurcation of fractional tumor-immune model with time delay

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Abstract The present study aims are to analyze a delay tumor-immune fractional-order system to describe the rivalry among the immune system and tumor cells. Given that the dynamics of this system depend on the time delay parameter, we examine the impact of time delay on this system to attain better compatibility with actuality. For this purpose, we analytically evaluated the stability of the system's equilibrium points. It is shown that Hopf bifurcation occurs in the fractional system when the delay parameter passes a certain value. Finally, by using numerical simulations, the analytical results were compared to the numerical results to acquire several dynamical behaviors of this system.

Keywords. Fractional differential equations, Time delay, Hopf bifurcation.

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1. Introduction

To date, cancer remains as one of the leading causes of fatality in the world; however, there is no complete information on its formation and elimination mechanism. When invasive species such as bacteria, viruses, or tumor cells reveal in the body, the immune system endeavors to detect and exterminate these species. Therefore modeling the interaction among the immune system and tumor cells, as one of the most important biological mathematical models, has been highly considered by many researchers [4, 5, 10, 11, 13, 15, 17]. The Kuznetsov-Taylor's model presented in [15], which explains the reaction of effective cells (ECs) to the growth of tumor cells (TCs), is different from other models because it considers the influence of TCs by ECs and simultaneously disables ECs. The dimensionless form of Kuznetsov and Taylor model,

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which studied in [11, 22], expressed as follows:

$$\begin{cases} \dfrac{dx}{dt} = \sigma + \omega xy - \delta x, \\ \\ \dfrac{dy}{dt} = \alpha y \left(1 - \beta y\right) - xy, \end{cases} \tag{1.1}$$

where x and y are population densities of effective cells and tumor cells, respectively. Moreover σ, δ, α and β are positive parameters and ω is a real number which describe in [23].

Due to the effect of memory in fractional derivative modeling, the fractional systems are more suitable for investigating the dynamics of biological models, compared to the integer-order systems. When a biological system is equipped with fractional derivative, the influence of memory is considered to the system because this kind of derivative is non-local. Memory and heredity are intrinsic properties of most biological systems, therefore fractional-order differential equations are mainly adapted with actual phenomena. Thus, studies related to the fractional order models have been widely noticed because of hereditary characteristics, memory, degrees of freedom and other benefits of these models. For this reason, there is been a growing trend in the application of fractional order dynamical systems in various scientific and engineering fields such as biology, physics, and chemistry [1, 2, 3, 6, 7, 12, 14, 18, 19, 20, 21].

This research seeks to study the fractional state of the system (1.1). By substituting Caputo fractional derivative with the integer-order derivative in system (1.1) and considering $\tau > 0$ as time delay parameter, we get the following delayed fractional system:

$$\begin{cases} D_*^n x(t) = \sigma + \omega x\left(t - \tau\right) y\left(t - \tau\right) - \delta x, \\ \\ D_*^n y(t) = \alpha y\left(1 - \beta y\right) - xy, \end{cases} \tag{1.2}$$

where $0 < n < 1$. For $n = 1$, system (1.2) studied in [11, 23, 24].
The purpose of this research is to evaluate the stability and complicated dynamics of system (1.2), with the numerical and analytical methods.

The residuum of the paper is structeded as follows: in section 2, the fundamentals of fractional calculus will be provided. Section 3, studies the stability of the system's equilibrium points and obtain conditions required for the existence of Hopf bifurcation. The numerical explorations in this study will be presented in Section 4. Finally, Section 5 summarizes the results obtained in the process.

2. Preliminaries

Definition 2.1. For $n \in \mathbb{R}_+$, the Riemann-Liouville fractional integral on $L_1[a, b]$ recalls as

$$J_a^n f(x) := \frac{1}{\Gamma(n)} \int_a^x (x-t)^{n-1} f(t) dt \ , x \in [a, b],$$

in which $\Gamma(.)$ is the Eulers gamma function.

Definition 2.2. For $n \in \mathbb{R}_+$ and $m = \lceil n \rceil$, the fractional Caputo derivative recalls as

$$D^n_{*a} f(x) := J_a^{m-n} f^{(m)}(x) = \frac{1}{\Gamma(m-n)} \int_a^x (x-t)^{m-n-1} f^{(m)}(t) dt,$$

which exists for almost everywhere $x \in [a, b]$.

Definition 2.3. Consider the following fractional differential system:

$$D^n_{*a} x(t) = f\left(x\left(t\right)\right), \ 0 < n < 1, \tag{2.1}$$

with initial condition $x(0) = x_0$ where $x\left(t\right) \in \mathbb{R}^n$, and $f : [0, \infty) \times \mathbb{R}^n \to \mathbb{R}^n$. Assume that $f\left(c\right) = 0$, thus c is defined as an equilibrium point of system (2.1). Let $Df\left(c\right)$ is the linearized matrix at the equilibrium point c. Then c is a hyperbolic equilibrium point if conditions $\lambda\left(Df\left(c\right)\right) \neq 0$ and $\left|\arg\left(\lambda\left(Df\left(c\right)\right)\right)\right| \neq \frac{n\pi}{2}$ satisfied for all eigenvalues λ of $Df\left(c\right)$.

Theorem 2.4. [8]
Consider the m-dimensional fractional order system:

$$D^n_{*a} x(t) = Ax\left(t\right), \ 0 < n < 1,$$

where A is an arbitrary fixed $m \times m$ matrix.
(a) *The solution $x\left(t\right) = 0$ of the above system is asymptotically stable, if and only if $|\arg(\lambda_j)| > \frac{n\pi}{2}$ satisfied for each eigenvalue $\lambda_j, (j = 1, 2, \ldots, m)$ of A .*
(b) *The solution $x\left(t\right) = 0$ of the above system is stable, if and only if $|\arg(\lambda_j)| \geq \frac{n\pi}{2}$ satisfied for all eigenvalues of A and all eigenvalues with $|\arg(\lambda_j)| = \frac{n\pi}{2}$ have the identical geometric and algebraic multiplicity.*

We memorialize the fractional version of the Hartman-Grobman Theorem as follows:

Theorem 2.5. [16] *Let the origin O is a hyperbolic equilibrium point of (2.1), then in the vicinity of O, the vector field $f\left(x\right)$ and its linearization vector field $Df\left(0\right)x$ are topologically equivalent.*

We attend that the condition hyperboic equilibrium is required in Theorem 2.5.

Theorem 2.6. *(Final Value Theorem). Suppose that $\mathcal{L}\{f(t)\}$ has no singularities in the closed right half-plane $\{s \in \mathbb{C} : Re(s) \geq 0\}$, except for possibly a simple pole at the origin. Then we have the following equality:*

$$\lim_{t \to +\infty} f(t) = \lim_{s \to 0^+} s\mathcal{L}\{f(t)\}.$$

3. Stability and hopf bifurcation in the fractional system

Consider system (1.2) and suppose that $\omega > 0$. By regarding the following equatings

$$D^n_* x(t) = 0, \ D^n_* y(t) = 0,$$

obviously, that system (1.2) possess at most two non-negative equilibria. This poins are detected as follows:

(A): For $\alpha\delta < \sigma$, system (1.2) has only one positive equilibrium point $E_0 = \left(\frac{\sigma}{\delta}, 0\right)$.

(B): For $\alpha\delta > \sigma$, in addition of E_0, there exists a new equilibrium point $E_1 = (x_1, y_1)$ where

$$x_1 = \frac{-\alpha\left(\beta\delta - \omega\right) + \sqrt{\Delta}}{2\omega}, \ y_1 = \frac{\alpha\left(\beta\delta + \omega\right) - \sqrt{\Delta}}{2\alpha\beta\omega},$$

in which

$$\Delta = \alpha^2\left(\beta\delta - \omega\right)^2 + 4\alpha\beta\sigma\omega.$$

At first, we set $\tau = 0$ and demonstrate the stability properties of equilibrium points of system (1.2) in the following Theorems:

Theorem 3.1. *Assume $\tau = 0$, then E_0 is locally asymptotically stable if $\alpha\delta < \sigma$, otherwise it is a saddle point.*

Proof. For $\tau = 0$, the jacobian matrix of system (1.2) evaluated at E_0 is given by

$$J|_{E_0} = \begin{pmatrix} -\delta & \frac{\omega\sigma}{\delta} \\ 0 & \alpha - \frac{\sigma}{\delta} \end{pmatrix},$$

the eigenvalues of $J|_{E_0}$ are $\lambda_1 = -\delta < 0$ and $\lambda_2 = \alpha - \frac{\sigma}{\delta}$. If $\alpha\delta < \sigma$ then both eigenvalues λ_1 and λ_2 are negative real numbers which satisfied $|\arg(\lambda_{1,2})| = \pi > \frac{n\pi}{2}$, so E_0 is locally asymptotically stable. While for $\alpha\delta > \sigma$ then $|\arg(\lambda_2)| = 0 < \frac{n\pi}{2}$, which complet the proof. □

Before we check the stability of E_1, let us taking

$$G_1 = \omega y_1 + \alpha - \left(\delta + 2\alpha\beta y_1 + x_1\right),$$

$$G_2 = \omega\alpha y_1 + 2\alpha\beta\delta y_1 + \delta x_1 - \left(2\alpha\beta\omega y_1^2 + \delta\alpha\right).$$

Theorem 3.2. *Suppose $\tau = 0$, if $G_2 > 0$, then E_1 is locally asymptotically stable if one of the following mutually exclusive statements hold:*

(i) $G_1 < 0$ *and* $G_1^2 - 4G_2 \geq 0$.

$$\textbf{(ii)} \quad G_1^2 - 4G_2 < 0 \quad \textit{and} \quad \sqrt{\left|G_1^2 - 4G_2\right|} > \tan\left(\frac{n\pi}{2}\right) G_1 \tag{3.1}$$

Proof. For $\tau = 0$, the jacobian matrix of system (1.2) calculated at E_1 derived as

$$J|_{E_1} = \begin{pmatrix} \omega y_1 - \delta & \omega x_1 \\ -y_1 & \alpha - 2\alpha\beta y_1 - x_1 \end{pmatrix}.$$

Let $\lambda_j, \ j = 1, 2$ be the eigenvalues corresponding to the $J|_{E_1}$ then we achieve:

$$tr\left(J|_{E_1}\right) = \lambda_1 + \lambda_2 = \omega y_1 + \alpha - (\delta + 2\alpha\beta y_1 + x_1) = G_1,$$

$$\det\left(J|_{E_1}\right) = \lambda_1\lambda_2 = \omega\alpha y_1 + 2\alpha\beta\delta y_1 + \delta x_1 - \left(2\alpha\beta\omega y_1^2 + \delta\alpha\right) = G_2,$$

and the characteristic equation computed at E_1 is

$$\lambda^2 - G_1\lambda + G_2 = 0,$$

therefore

$$\lambda_j = \frac{G_1 \pm \sqrt{G_1^2 - 4G_2}}{2}, \ j = 1, 2,$$

(**i**) If $G_1^2 - 4G_2 \geq 0$, then λ_1 and λ_2 are real. Since $G_2 > 0$, if $G_1 < 0$, then λ_1 and λ_2 are real and negative. Thus $|\arg(\lambda_{1,2})| = \pi > \frac{n\pi}{2}$, which proves the stability of E_1.

(**ii**) From $G_1^2 - 4G_2 < 0$, it is evident that λ_1 and λ_2 are conjugate complex and we acquire:

$$\lambda_j = \frac{G_1 \pm i\sqrt{\left|G_1^2 - 4G_2\right|}}{2}, \ j = 1, 2. \tag{3.2}$$

$$|\lambda_1 - \overline{\lambda_1}| = \sqrt{\left|G_1^2 - 4G_2\right|}. \tag{3.3}$$

Making use of (3.1) and (3.3), we conclude that

$$\left|\lambda_1 - \overline{\lambda_1}\right| > \tan\left(\frac{n\pi}{2}\right)\left(\lambda_1 + \overline{\lambda_1}\right) \Longrightarrow \left|Im\left(\lambda_1\right)\right| > \tan\left(\frac{n\pi}{2}\right)\left(Re\lambda_1\right). \tag{3.4}$$

This ensures that $|\arg(\lambda_{1,2})| > \frac{n\pi}{2}$. Thus statement (**ii**) follows. □

Now, we suppose that $\tau > 0$ and attain sufficient conditions for stability the delay fractional order system (1.2):

Linearizing system (1.2) at equlibrium point $\overset{*}{E} = \left(\overset{*}{x}, \overset{*}{y}\right)$ takes the form:

$$\begin{cases} D_*^n x(t) = -\delta x + \omega\overset{*}{y}x\,(t-\tau) + \omega\overset{*}{x}y\,(t-\tau), \\ \\ D_*^n y(t) = -\overset{*}{y}x + \left(\alpha - 2\alpha\beta\overset{*}{y} - \overset{*}{x}\right)y, \end{cases} \tag{3.5}$$

to investigate the stability of the equlibrium point of system (3.5), we provide the following Theorem:

Theorem 3.3. *The equlibrium point* $\overset{*}{E} = \left(\overset{*}{x}, \overset{*}{y}\right)$ *is asymptotically stable if all roots of the characteristic equation det* $(\Delta(s)) = 0$ *have negative real part, in which*

$$\Delta(s) = \begin{pmatrix} s^n + \delta - \omega\overset{*}{y}e^{-s\tau} & -\omega\overset{*}{x}e^{-s\tau} \\ \\ \overset{*}{y} & s^n - \left(\alpha - 2\alpha\beta\overset{*}{y} - \overset{*}{x}\right) \end{pmatrix}.$$

Proof. Assume that $X(s)$ and $Y(s)$ are the Laplace transform of $x(t)$ and $y(t)$, respectively. Utilizing Laplace transform on both sides of system (3.5), yields:

$$\begin{cases} \left(s^n + \delta - \omega \overset{*}{y} e^{-s\tau}\right) X(s) - \omega \overset{*}{x} e^{-s\tau} Y(s) = x(0) + A + B, \\ \overset{*}{y} X(s) + \left(s^n - \left(\alpha - 2\alpha\beta \overset{*}{y} - \overset{*}{x}\right)\right) Y(s) = y(0), \end{cases}$$

in which

$$A = -\omega \overset{*}{y} \int_{-\tau}^{0} e^{-s\tau} x(t) dt, \;\; B = -\omega \overset{*}{x} \int_{-\tau}^{0} e^{-s\tau} y(t) dt.$$

Thus

$$\begin{pmatrix} s^n + \delta - \omega \overset{*}{y} e^{-s\tau} & -\omega \overset{*}{x} e^{-s\tau} \\ \overset{*}{y} & s^n - \left(\alpha - 2\alpha\beta \overset{*}{y} - \overset{*}{x}\right) \end{pmatrix} \begin{pmatrix} X(s) \\ Y(s) \end{pmatrix} = \begin{pmatrix} x(0) + A + B \\ y(0) \end{pmatrix}. \tag{3.6}$$

Multiplying s on both sides of (3.6) implies

$$\Delta(s) \begin{pmatrix} sX(s) \\ sY(s) \end{pmatrix} = \begin{pmatrix} s\left(x(0) + A + B\right) \\ sy(0) \end{pmatrix}. \tag{3.7}$$

If all roots of the characteristic equation $\det\left(\Delta\left(s\right)\right) = 0$ situate in open left half complex plane, (i.e., $Re(s) < 0$), then for all roots that $Re(s) \geq 0$, we have $\det\left(\Delta\left(s\right)\right) \neq 0$. Since $s \to 0^+$, then $s\left(x(0) + A + B\right) \to 0$ and $sy(0) \to 0$. Therefore equation (3.7) has a unique solution $(sX(s), sY(s))$ when $s \to 0^+$, and

$$\lim_{s \to 0^+} sX(s) = 0, \;\; \lim_{s \to 0^+} sY(s) = 0.$$

From the hypothesis of all roots of the characteristic equation and Theorem 2.6, we get

$$\lim_{t \to +\infty} x(t) = 0, \;\; \lim_{t \to +\infty} y(t) = 0.$$

Thus we proved the stability of the equlibrium point of system (3.5). □

Let us now turn to determine the stability of the equilibrium points by employing Theorem 3.3.

Theorem 3.4.
(i) *If $\alpha\delta < \sigma$, then E_0 is locally asymptotically stable for all $\tau > 0$.*

(ii) *If $\alpha\delta > \sigma$, then E_0 is unstable for all $\tau > 0$.*

Proof. The linearized system (1.2) at E_0 is attained as:

$$\begin{cases} D_*^n x(t) = \omega \dfrac{\sigma}{\delta} y(t-\tau) - \delta x, \\ D_*^n y(t) = \left(\alpha - \dfrac{\sigma}{\delta}\right) y. \end{cases}$$

We compute $\Delta(s)$ as

$$\Delta(s) = \begin{pmatrix} s^n + \delta & -\omega \dfrac{\sigma}{\delta} e^{-s\tau} \\ 0 & s^n - (\alpha - \dfrac{\sigma}{\delta}) \end{pmatrix},$$

with the characteristic equation

$$\det\left(\Delta\left(s\right)\right) = \left(s^n + \delta\right)\left(s^n - \left(\alpha - \frac{\sigma}{\delta}\right)\right) = 0. \tag{3.8}$$

(**i**) If $\alpha\delta < \sigma$, we have

$$\lambda_1 = s_1^n = -\delta < 0,$$
$$\lambda_2 = s_2^n = \alpha - \frac{\sigma}{\delta} < 0,$$

therefore

$$\left|\arg\left(\lambda_i\right)\right| = \pi > \frac{n\pi}{2} \Longrightarrow \left|\arg\left(\lambda_i\right)^{\frac{1}{n}}\right| > \frac{\pi}{2},$$
$$\Longrightarrow \left|\arg\left(s_i\right)\right| > \frac{\pi}{2}.$$

Thus all roots of equation (3.8) have negative real parts and according to Theorem 3.3, E_0 is locally asymptotically stable for all $\tau > 0$.

(**ii**) If $\alpha\delta > \sigma$, we get

$$\lambda_1 = s_1^n = -\delta < 0,$$
$$\lambda_2 = s_2^n = \alpha - \frac{\sigma}{\delta} > 0,$$

therefore

$$\left|\arg\left(\lambda_1\right)\right| = \pi > \frac{n\pi}{2} \Longrightarrow \left|\arg\left(\lambda_1\right)^{\frac{1}{n}}\right| > \frac{\pi}{2} \Longrightarrow \left|\arg\left(s_1\right)\right| > \frac{\pi}{2},$$
$$\left|\arg\left(\lambda_2\right)\right| = 0 < \frac{n\pi}{2} \Longrightarrow \left|\arg\left(\lambda_2\right)^{\frac{1}{n}}\right| < \frac{\pi}{2} \Longrightarrow \left|\arg\left(s_2\right)\right| < \frac{\pi}{2}.$$

Thus equation (3.8) has a root with positive real part, which proves (**ii**). □

Now, we discuss the stability of equilibrium point E_1 and by regarding time delay as the bifurcation parameter gain conditions for occurrence of Hopf bifurcation.

Linearizing system (1.2) refers to the equilibrium point $E_1 = (x_1, y_1)$ yields the following linear system

$$\begin{cases} D_*^n x(t) = -\delta x + \omega y_1 x(t-\tau) + \omega x_1 y(t-\tau), \\ D_*^n y(t) = -y_1 x + (\alpha - 2\alpha\beta y_1 - x_1)\, y. \end{cases}$$

According to Theorem 3.3, $\Delta(s)$ is equal to

$$\Delta(s) = \begin{pmatrix} s^n + \delta - \omega y_1 e^{-s\tau} & -\omega x_1 e^{-s\tau} \\ y_1 & s^n - \alpha + 2\alpha\beta y_1 + x_1 \end{pmatrix}, \tag{3.9}$$

by setting

$$a = \delta + \alpha\beta y_1,\ b = -\omega y_1,\ c = \omega\alpha y_1 (1 - 2\beta y_1),\ d = \alpha\beta y_1\delta,$$

the associated characteristic equation of (3.9) is

$$\det(\Delta(s)) = s^{2n} + as^n + (bs^n + c)\, e^{-s\tau} + d = 0. \tag{3.10}$$

Let $s = i\xi = \xi\left(\cos\left(\frac{\pi}{2}\right) + i\sin\left(\frac{\pi}{2}\right)\right)$ is a root of eqution (3.10). By replacing s into (3.10) and separating the real and imaginary parts we obtain following equations:

$$\begin{aligned} &\xi^{2n}\cos(n\pi) + a\xi^n\cos\left(\frac{n\pi}{2}\right) + b\xi^n\cos\left(\frac{n\pi}{2}\right)\cos(\xi\tau) + b\xi^n\sin\left(\frac{n\pi}{2}\right)\sin(\xi\tau) \\ &\qquad + c\cos(\xi\tau) + d = 0, \\ &\xi^{2n}\sin(n\pi) + a\xi^n\sin\left(\frac{n\pi}{2}\right) + b\xi^n\sin\left(\frac{n\pi}{2}\right)\cos(\xi\tau) - b\xi^n\cos\left(\frac{n\pi}{2}\right)\sin(\xi\tau) \\ &\qquad - c\sin(\xi\tau) = 0. \end{aligned} \tag{3.11}$$

By taking

$$\varphi_1 = \xi^{2n}\cos(n\pi) + a\xi^n\cos\left(\frac{n\pi}{2}\right) + d,$$

$$\varphi_2 = \xi^{2n}\sin(n\pi) + a\xi^n\sin\left(\frac{n\pi}{2}\right),$$

$$\varphi_3 = b\xi^n\cos\left(\frac{n\pi}{2}\right) + c,$$

$$\varphi_4 = b\xi^n\sin\left(\frac{n\pi}{2}\right),$$

equations (3.11) can equivalently be written as

$$\begin{cases} \varphi_1 + \varphi_3\cos(\xi\tau) + \varphi_4\sin(\xi\tau) = 0, \\ \varphi_2 + \varphi_4\cos(\xi\tau) - \varphi_3\sin(\xi\tau) = 0. \end{cases} \tag{3.12}$$

From (3.12) we derive:

$$\cos(\xi\tau) = -\frac{\varphi_1\varphi_3 + \varphi_2\varphi_4}{\varphi_3^2 + \varphi_4^2}, \tag{3.13}$$

$$\sin(\xi\tau) = \frac{\varphi_2\varphi_3 - \varphi_1\varphi_4}{\varphi_3^2 + \varphi_4^2}. \tag{3.14}$$

As we know $\cos^2(\xi\tau) + \sin^2(\xi\tau) = 1$, then by using (3.13) and (3.14), we get

$$\varphi_3^2 + \varphi_4^2 = \varphi_1^2 + \varphi_2^2. \tag{3.15}$$

Thus by substituting the values of $\varphi_1, \varphi_2, \varphi_3, \varphi_4$ in (3.15) and simplification we get:

$$h(\xi) = \xi^{4n} + B_3\xi^{3n} + B_2\xi^{2n} + B_1\xi^n + B_0 = 0, \tag{3.16}$$

in which

$$B_0 = d^2 - c^2,$$

$$B_1 = 2ad\cos\left(\frac{n\pi}{2}\right) - 2cb\cos\left(\frac{n\pi}{2}\right),$$

$$B_2 = 2d\cos(n\pi) + a^2 - b^2,$$

$$B_3 = 2a\cos\left(\frac{n\pi}{2}\right).$$

Now we express the following Theorem:

Theorem 3.5.
(**i**) *If* $B_i > 0,\ i = 0,1,2,3$, *then equation* (3.10) *has no root with zero real part for all* $\tau \geq 0$.
(**ii**) *If* $B_i > 0,\ i = 1,2,3$ *and* $B_0 < 0$, *then equation* (3.10) *has a pair of purely imaginary roots* $\pm i\xi_0$ *when*

$$\tau_j = \frac{1}{\xi_0}\arccos\left(-\frac{\varphi_1\varphi_3 + \varphi_2\varphi_4}{\varphi_3^2 + \varphi_4^2}\right) + \frac{2j\pi}{\xi_0},\ j = 0,1,2,\ldots \tag{3.17}$$

where ξ_0 *is a unique positive zero of equation* (3.16).

Proof. (**i**) From $B_i > 0,\ i = 0,1,2,3$, we achieve

$$h(0) = B_0 > 0,$$

and

$$h'(\xi) = 4n\xi^{4n-1} + 3nB_3\xi^{3n-1} + 2nB_2\xi^{2n-1} + nB_1\xi^{n-1} > 0,$$

so equation (3.16) doesn't have any real root. Thus equation (3.10) has no purely imaginary root, which proves (**i**).

(**ii**) We know $h(0) = B_0 < 0$, and we conclude that

$$\lim_{\xi\to+\infty} h(\xi) = +\infty,$$

so, equation (3.16) has at least one positive real root. Furthermore

$$h'(\xi) > 0,$$

i.e., $h(\xi)$ is strictly increasing which leads that equation (3.16) has only one positive real root such as ξ_0. So (ξ_0, τ_j) is a root of (3.12), where τ_j as given in equation (3.17). Clearly $\pm i\xi_0$ is a pair of purely imaginary roots of (3.10) when $\tau = \tau_j,\ j = 0, 1, 2, ...$. This completes the proof. □

To obtain the conditions for Hopf bifurcation, the following hypothesis is required:

(H) $\dfrac{\eta_3\eta_1 + \eta_4\eta_2}{\eta_1^2 + \eta_2^2} \neq 0,$

where

$$\begin{aligned}
\eta_1 &= 2n\xi^{2n-1}\cos\left(\frac{(2n-1)\pi}{2}\right) + na\xi^{n-1}\cos\left(\frac{(n-1)\pi}{2}\right)\\
&\quad + bn\xi^{n-1}\cos\left(\frac{(n-1)\pi}{2} - \xi\tau\right) - \tau b\xi^{n}\cos\left(\frac{n\pi}{2} - \xi\tau\right) - \tau c\cos(\xi\tau),\\
\eta_2 &= 2n\xi^{2n-1}\sin\left(\frac{(2n-1)\pi}{2}\right) + na\xi^{n-1}\sin\left(\frac{(n-1)\pi}{2}\right)\\
&\quad + bn\xi^{n-1}\sin\left(\frac{(n-1)\pi}{2} - \xi\tau\right) - \tau b\xi^{n}\sin\left(\frac{n\pi}{2} - \xi\tau\right) + \tau c\sin(\xi\tau),\\
\eta_3 &= b\xi^{n+1}\cos\left(\frac{(n+1)\pi}{2} - \xi\tau\right) + c\xi\sin(\xi\tau),\\
\eta_4 &= b\xi^{n+1}\sin\left(\frac{(n+1)\pi}{2} - \xi\tau\right) + c\xi\cos(\xi\tau),
\end{aligned}$$

and we indicate the following Theorem:

Theorem 3.6. *Let $s(\tau) = \mu(\tau) + i\xi(\tau)$ is a root of equation (3.10) near $\tau = \tau_j$ verifying $\mu(\tau_j) = 0,\ \xi(\tau_j) = \xi_0$, then*

$$Re\left(\frac{ds}{d\tau}\right)\Big|_{(\tau=\tau_0,\xi=\xi_0)} \neq 0.$$

Proof. Taking the derivative of the characteristic equation (3.10) with respect to τ, gives:

$$\frac{ds}{d\tau} = \frac{\left(bs^{n+1} + cs\right)e^{-s\tau}}{2ns^{2n-1} + nas^{n-1} + e^{-s\tau}\left(bns^{n-1} - \tau bs^{n} - \tau c\right)}, \tag{3.18}$$

By substituting $s = i\xi = \xi e^{\frac{i\pi}{2}}$ into (3.18) and separating the real and imaginary parts, we have

$$\frac{ds}{d\tau} = \frac{\eta_3 + i\eta_4}{\eta_1 + i\eta_2} = \frac{\eta_3\eta_1 + \eta_4\eta_2}{\eta_1^2 + \eta_2^2} + \frac{\eta_4\eta_1 - \eta_3\eta_2}{\eta_1^2 + \eta_2^2}i,$$

then we deduce that

$$Re\left(\frac{ds}{d\tau}\right) = \frac{\eta_3\eta_1 + \eta_4\eta_2}{\eta_1^2 + \eta_2^2}.$$

Obviously, due to hypothesis (**H**) the transversality condition is satisfied. This completes the proof. □

Theorem 3.7. *Under the assumptions $a+b>0$ and $c+d>0$, the following results hold:*

(**i**) *If $B_i>0,\ i=0,1,2,3$, then the equilibrium point $E_1=(x_1,y_1)$ is locally asymptotically stable for all $\tau\geq 0$.*

(**ii**) *If $B_0<0,\ B_i>0,\ i=1,2,3$, then the equilibrium E_1 is locally asymptotically stable for all $0\leq\tau<\tau_0$.*

(**iii**) *If all conditions as given in* (**ii**) *hold, then for $\tau>\tau_0$ the equilibrium E_1 is unstable and system(1.2) undergoes Hopf bifurcation at E_1 when $\tau=\tau_j,\ j=0,1,2,3,\ldots$.*

Proof. (**i**) For $\tau=0,\ s^n=\lambda$ the characteristic equation (3.10) turn into

$$\lambda^2+(a+b)\,\lambda+(c+d)=0, \tag{3.19}$$

under conditions $a+b>0,\ c+d>0$ all roots of equation (3.19) have negative real parts. Hence all roots of equation (3.10) have negative real parts for $\tau=0$. Conclusion (**i**) of Theorem 3.5 denotes that for all $\tau\geq 0$, equation (3.10) doesn't have any root with zero real part. Thus, all roots of equation (3.10) have negative real parts for all $\tau\geq 0$ and E_1 is locally asymptotically stable for all $\tau\geq 0$.

(**ii**) By substituting $\tau=0$ and $s^n=\lambda$ in the characteristic equation (3.10), we get to equation (3.19). By applying the Routh-Hurwitz criterion, all roots of equation (3.19) have negative real parts if and only if $a+b>0$ and $c+d>0$, i.e.,

$$\left|\arg(\lambda_i)\right|>\frac{n\pi}{2}\Longrightarrow\left|\arg(\lambda_i^{\frac{1}{n}})\right|>\frac{\pi}{2}\Longrightarrow\left|\arg(s_i)\right|>\frac{\pi}{2},\ i=1,2.$$

Therefore all roots of equation (3.10) have negative real parts for $\tau=0$. From the conclusion (**ii**) of Theorem 3.5, the definition of τ_0 suggests that all roots of equation (3.10) have negative real parts for $\tau\in[0,\tau_0)$, so equilibrium E_1 is locally asymptotically stable for all $0\leq\tau<\tau_0$.

(**iii**) Theorem 3.6, reveals that equation (3.10) has at least a pair of roots with positive real parts when $\tau>\tau_0$. Also implies that the condition of crossing the imaginary axis occurs. Thus under the given assumptions the Hopf bifurcation occurs at $\tau=\tau_j$, $j=0,1,2,3,\ldots$. □

4. Numerical results

In this section, we carry out numerical simulations to elucidate the effects of time delay and confirm theoretical results. For numerical simulation, we apply the fractional Adams-Bashforth-Moulton method [9]. It is shown that for the following system

$$\begin{cases} D_{*0}^{n}x(t)=f(t,x(t)),\\ x(0)=x_0. \end{cases} \tag{4.1}$$

The fractional variant of the one-step Adams-Moulton method is given by:

$$x_{i+1} = \sum_{j=0}^{\lceil n\rceil-1} \frac{t_{i+1}^j}{j!} x_0^{(j)} + \frac{h^n}{\Gamma(n+2)} \sum_{j=0}^{i} a_{j,i+1} f(t_j, x_j) + \frac{h^n}{\Gamma(n+2)} f(t_{i+1}, x_{i+1}^P),$$

in which

$$a_{j,i+1} = \begin{cases} i^{n+1} - (i-n)(i+1)^n, \ j=0 \\ (i-j+2)^{n+1} + (i-j)^{n+1} - 2(i-j+1)^{n+1}, \ 1 \leq j \leq i, \end{cases}$$

and x_{i+1}^P is determined by the one-step Adams-Bashforth method, i.e.,

$$x_{i+1}^P = \sum_{j=0}^{\lceil n\rceil-1} \frac{t_{i+1}^j}{j!} x_0^{(j)} + \frac{1}{\Gamma(n)} \sum_{j=0}^{i} b_{j,i+1} f(t_j, x_j),$$

where

$$b_{j,i+1} = \frac{h^n}{n}\big((i+1-j)^n - (i-j)^n\big).$$

In Figures 1 and 2, numerical simulations are shown for $\tau = 0$.
In Figure 1, the phase portrait of system (1.2) plotted for the parameter values of$\alpha = 1.636$, $\beta = 0.002$, $\sigma = 0.7$, $\delta = 0.3747$, $\omega = 0.04$, $n = 0.97$ and different initial values x_0 and y_0. In this case we obtain $\alpha\delta = 0.6130 < \sigma = 0.7$. Thus according to the Theorem 3.1, $E_0 = (1.8682, 0)$ is locally asymptotically stable.
In Figure 2, numerical simulations are performed for the parameter values of $\alpha = 1.636, \beta = 0.002, \sigma = 0.1181$, $\delta = 0.3747$, $\omega = 0.04$ and $n = 0.97$. In this case we obtain $G_1 = -0.0979 < 0$, $G_2 = 0.4875 > 0$, therefore

$$G_1^2 - 4G_2 = -1.9403 < 0, \ \sqrt{\left|G_1^2 - 4G_2\right|} = 1.3930 > \tan\left(\frac{n\pi}{2}\right) G_1 = -2.0770.$$

Thus, according to the conclusion (ii) of Theorem 3.2, $E_1 = (1.6113, 7.5352)$ is locally asymptotically stable.

Now, we fix the parameter values and initial values as

$$\alpha = 1.636, \ \beta = 0.002, \ \sigma = 0.1181, \ \delta = 0.3747, \ \omega = 0.04, x_0 = 1.5, \ y_0 = 7.5. \tag{4.2}$$

and varying the fractional order n and the delay parameter τ.
By varing the fractional order in the range $0.5 \leq n \leq 1$, we can calculate the corresponding ξ_0 and τ_0 which are written in Table 1. Table 1 and Figure 3 illustrate that the onset of Hopf bifurcation befalls as the fractional order increases.

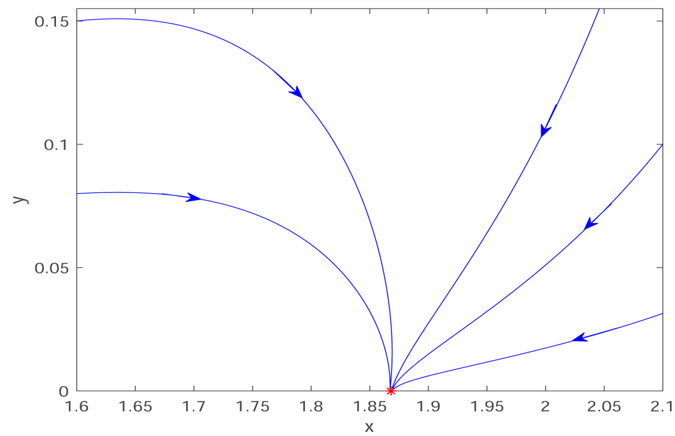
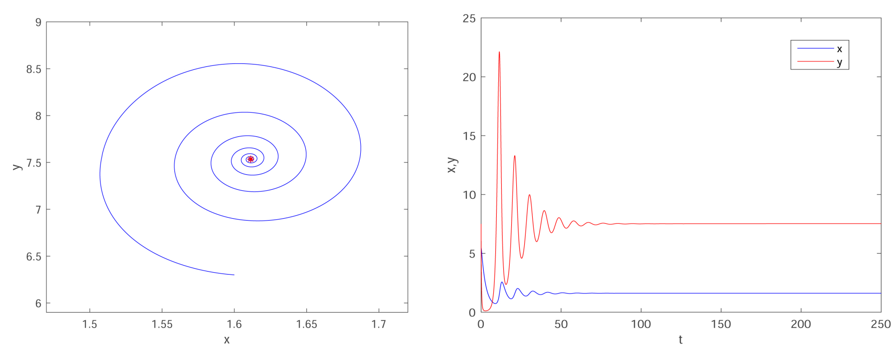


FIGURE 1. Phase portrait of system (1.2) for $\alpha = 1.636$, $\beta = 0.002$, $\sigma = 0.7$, $\delta = 0.3747$, $\omega = 0.04$ and $n = 0.97$. for $\tau = 0$, $E_0 = (1.8682, 0)$ is locally asymptotically stable.



(a) (b)

FIGURE 2. Phase portrait of system (1.2) for $\alpha = 1.636$, $\beta = 0.002$, $\sigma = 0.1181$, $\delta = 0.3747$, $\omega = 0.04$ and $n = 0.97$. for $\tau = 0$, $E_1 = (1.6113, 7.5352)$ is locally asymptotically stable.

In Figure 4 and 5, numerical simulations are shown for $n = 0.97$. In this case $B_0 = -0.2286 < 0$, $B_1 = 0.0139 > 0$, $B_2 = 0.0502 > 0$, $B_3 = 0.0376 > 0$. By Theorem 3.5, equation (3.10) has a pair of purely imaginary roots given by $\pm 0.6492i$. Therefore we can get $\tau_0 = 0.3669$ and

$$Re\left(\frac{ds}{d\tau}\right)\Big|_{(\tau_0=0.3669,\xi=0.6492)} = 0.1882 \neq 0.$$

TABLE 1. The effects of n on ξ_0 and τ_0 for system (1.2).

Fractional order n	Critical frequency ξ_0	Bifurcation point τ_0
0.5	0.2277	7.3999
0.55	0.2734	5.6160
0.6	0.3196	4.3335
0.65	0.3659	3.3711
0.7	0.4119	2.6234
0.75	0.4576	2.0257
0.8	0.5027	1.5362
0.85	0.5470	1.1269
0.9	0.5903	0.7783
0.95	0.6326	0.4768
0.97	0.6492	0.3669
1	0.6736	0.2119

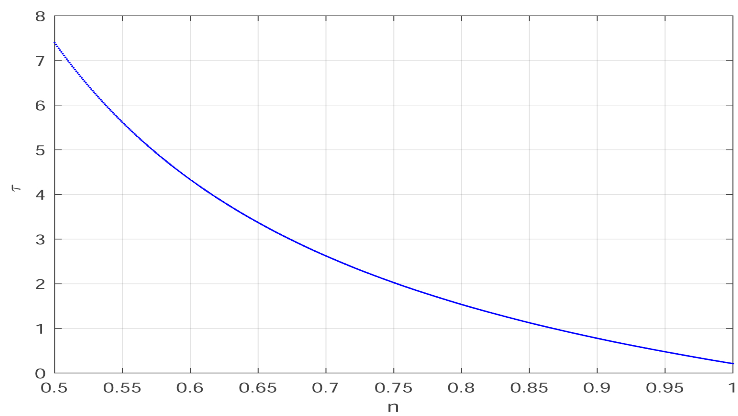


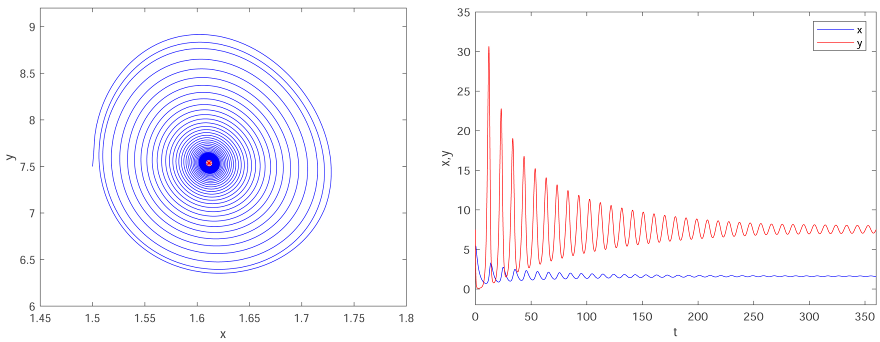
FIGURE 3. The influence of n depending on τ for system (1.2).

In addition $a + b = 0.098 > 0$ and $c + d = 0.4874 > 0$, so according to Theorem 3.7 system (1.2) undergoes a Hopf bifurcation at $E_1 = (1.6113, 7.5352)$ when $\tau_0 = 0.3669$.

In Figure 4, for $\tau = 0.3 < \tau_0 = 0.3669$, $E_1 = (1.6113, 7.5352)$ is locally asymptotically stable. In Figure 5, by increasing τ to $\tau = 0.4 > \tau_0 = 0.3669$, the equilibrium $E_1 = (1.6113, 7.5352)$ losses its stability and a limit cycle appears around E_1 (see Figure 5).

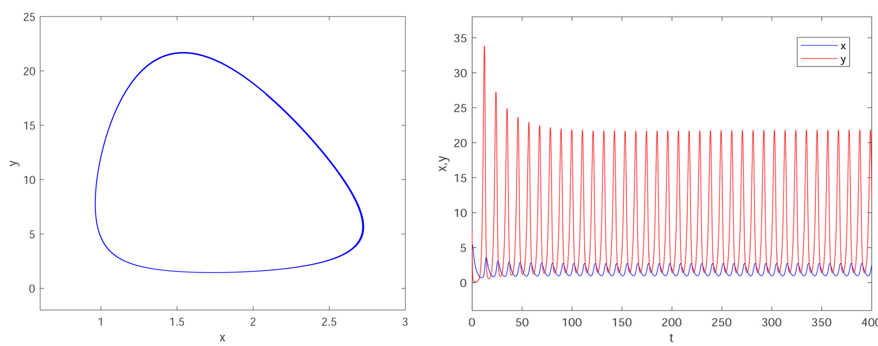
For $n = 0.95$, we conclude $B_0 = -0.2286 < 0$, $B_1 = 0.0232 > 0$, $B_2 = 0.0504 > 0$, $B_3 = 0.0627 > 0$. By Theorem 3.5, equation (3.10) has a pair of purely imaginary roots given by $\pm 0.6326i$. Therefore we can get $\tau_0 = 0.4768$ and

$$Re\left(\frac{ds}{d\tau}\right)\Big|_{(\tau_0=0.4768,\xi=0.6326)} = 0.1755 \neq 0.$$



(a) (b)

FIGURE 4. Phase portrait of system (1.2) for $\alpha = 1.636$, $\beta = 0.002$, $\sigma = 0.1181$, $\delta = 0.3747$, $\omega = 0.04$ and $n = 0.97$. for $\tau = 0.3 < \tau_0 = 0.3669$, $E_1 = (1.6113, 7.5352)$ is locally asymptotically stable.



(a) (b)

FIGURE 5. Phase portrait of system (1.2) for $\alpha = 1.636$, $\beta = 0.002$, $\sigma = 0.1181$, $\delta = 0.3747$, $\omega = 0.04$ and $n = 0.97$. For $\tau = 0.4 > \tau_0 = 0.3669$, $E_1 = (1.6113, 7.5352)$ is unstable and a limit cycle emerges around E_1.

In addition $a + b = 0.098 > 0$ and $c + d = 0.4874 > 0$, so according to Theorem 3.7 system (1.2) undergoes a Hopf bifurcation at $E_1 = (1.6113, 7.5352)$ when $\tau_0 = 0.4768$. Thus for $\tau = 0.15, 0.3 < \tau_0 = 0.4768$, the equilibrium $E_1 = (1.6113, 7.5352)$ is locally asymptotically stable which depicted in Figures 6 and 7. When $n = 1$, we can derive the values $\xi_0 = 0.6736$ and $\tau_0 = 0.2119$. Thus for $\tau = 0.15 < \tau_0 = 0.2119$, the equilibrium $E_1 = (1.6113, 7.5352)$ is locally asymptotically stable, see Figure 6. Also,

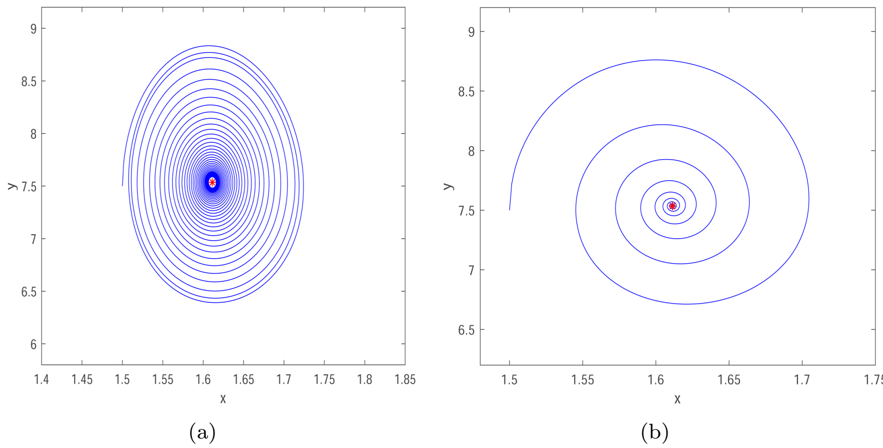


FIGURE 6. Phase portrait of system (1.2) for $\alpha = 1.636$, $\beta = 0.002$, $\sigma = 0.1181$, $\delta = 0.3747$, $\omega = 0.04$ and $\tau = 0.15$. $E_1 = (1.6113, 7.5352)$ is locally asymptotically stable. (a) for $n = 1$, (b) for $n = 0.95$.

in Figure 7, we observe that for $\tau = 0.3 > \tau_0 = 0.2119$, E_1 is unstable.

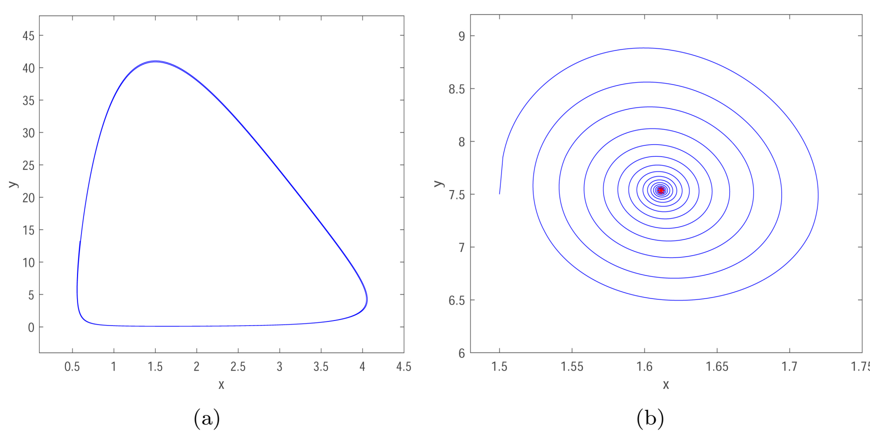


FIGURE 7. Phase portrait of system (1.2) for $\alpha = 1.636$, $\beta = 0.002$, $\sigma = 0.1181$, $\delta = 0.3747$, $\omega = 0.04$ and $\tau = 0.3$. (a) for $n = 1$, $E_1 = (1.6113, 7.5352)$ is unstable and system has a periodic solution, (b) for $n = 0.95$, E_1 is locally asymptotically stable.

In Figures 6 and 7, we compare system (1.2) in the fractional and classical cases. Our obtained results show that the fractional system is more stable than the classical case.

5. CONCLUTION

The present study introduced a tumor-immune fractional-order system along with the time delay parameter, in order to describe the interaction betwixt effective cells and tumor cells. In this paper, we investigated the stability of the system's equilibrium points under the impact of the delay and proved the occurrence of the Hopf bifurcation in this system, by selecting τ as the bifurcation parameter. Finally, we conducted numerical simulations for specified values of the parameters, in which the results were fully consistent with the obtained theoretical results. It was observed that the fractional-order and the time delay play an important role in the stability of the system. In addition, when the parameter τ becomes larger than the specified value, the system's equilibrium point loses its stability, resulting in creating more complex dynamical behaviors of the system, including limit cycle and oscillating behaviors.

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