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Research article

Analysis of a free boundary problem for vascularized tumor growth with time delays and almost periodic nutrient supply

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Abstract: In this research, we have proposed and investigated a time-delayed free boundary problem concerning tumor growth in the presence of almost periodic nutrient supply with angiogenesis. This study primarily focused on examining the impact of almost periodic nutrient supply, angiogenesis, and time delay on tumor growth dynamics. We analyzed the existence, uniqueness, and exponential stability of almost periodic solutions. Furthermore, we established conditions for the disappearance of almost periodic oscillations in tumors. The existence and uniqueness of almost periodic solutions were proven, while sufficient conditions for the exponential stability of the unique solution were established. Finally, computer simulations were employed to illustrate our results.

Keywords: tumor growth; angiogenesis; almost periodic solution; existence and uniqueness; stability
Mathematics Subject Classification: 34K13, 35Q92

1. Introduction

Delay differential equations (DDEs), or functional differential equations, arise in models representing biological phenomena when considering the time-delays occurring in these phenomena. Mathematical modeling using such DDEs is widely applied for analysis and predictions in various areas of life sciences, including population dynamics, epidemiology, immunology, tumor growth, physiology, and neural networks. The memory or time-delays in these models are associated with the duration of hidden processes such as life cycle stages, the time between cell infection and new virus production, the infection period, the time between cell division and new cell production, and the immune period [3, 6, 10, 15, 17, 18, 20, 23–25]. Reference [17] covers important topics related to DDEs including numerical methods, stability analysis, inverse problems, parameter estimation, sensitivity analysis, optimal control, and time-delayed biological systems. In this paper, we investigate a free boundary problem for vascularized tumor growth with time delays and almost periodic nutrient supply. The mathematical model describing the tumor growth process considers cell division and death along with external almost periodic nutrient supply. Compared to the apoptosis process of tumor cells, the proliferation process exhibits a time delay. In the model, two unknown functions $\sigma(r,t)$ and $R(t)$ represent nutrient concentration and tumor radius, respectively. The mathematical model is given by:

$$c\frac{\partial \sigma}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial \sigma}{\partial r}\right) - \Gamma\sigma, \quad 0 < r < R(t), \quad t > 0, \tag{1.1}$$

$$\frac{\partial \sigma}{\partial r} + \alpha\left(\sigma - \psi(t)\right) = 0, \quad r = R(t), \quad t > 0, \tag{1.2}$$

$$\frac{d}{dt}\left(\frac{4\pi R^3(t)}{3}\right) = 4\pi\left(\int_0^{R(t-\tau)} s\sigma(r, t-\tau)r^2 dr - \int_0^{R(t)} s\tilde{\sigma} r^2 dr\right), \quad t > 0, \tag{1.3}$$

where $\Gamma\sigma$ represents the consumption rate of nutrients, and α is a constant denoting the density of blood vessels. The external concentration of nutrients is denoted by $\psi(t)$, while τ represents the time delay. Equation (1.3) originates from the law of conservation of mass. The term $4\pi\int_0^{R(t-\tau)} s\sigma(r,t-\tau)r^2 dr$ corresponds to the volume increase induced by cell proliferation, where $s\sigma$ denotes the proliferation rate. On the other hand, $4\pi\int_0^{R(t)} s\tilde{\sigma}r^2 dr$ accounts for the volume decrease caused by natural death, assuming a natural death rate of $s\tilde{\sigma}$. Additionally, we consider that $c = T_d/T_g \approx \frac{1minute}{1day} \ll 1$, which represents the ratio between the nutrient diffusion timescale and tumor growth timescale (see [10, 11] for further details). In this study, we will discuss the aforementioned model with respect to its initial condition given in Eq (1.4):

$$R(t) = \varphi(t), \quad -\tau \le t \le 0. \tag{1.4}$$

The proposed model is based on the framework presented in [12] with two modifications. First, we consider the provision of external nutrients as an almost periodic function, which is a more realistic assumption compared to the constant nutrient supply assumed in [12]. Second, we incorporate the impact of time delay in tumor cell proliferation, as observed in [3]. It is important to analyze the stability of tumor growth models with time-delay terms, and several methods such as Lyapunov exponents, the comparison principle, and stability theorems have been proposed by scholars (see for instance [6, 10, 14, 18, 22]). In particular, reference [6] investigates a special case where $\alpha = \infty$ and ψ is a positive constant using functional differential equations theory to establish existence, uniqueness, and asymptotic stability of steady-state solutions. Furthermore, researchers have also studied bifurcation phenomena in mathematical models for tumor growth with time-delay terms (e.g., [15, 16, 24, 26]), which are crucial for understanding tumor development mechanisms and predicting future trends. By considering almost periodic functions instead of exact periodicity due to their robustness under perturbations, our model provides a more realistic representation of actual tumor growth dynamics. This paper focuses on investigating the impact of almost periodic nutrient supply along with angiogenesis and time delay.

Several studies have investigated mathematical models for tumor growth in angiogenesis, including those by Friedman and Lam [12], Ye et al. [25], and Zhou et al. [26]. However, these studies assumed a constant provision of external nutrients. In this paper, we consider the external concentration of nutrients as a bounded almost periodic function and also incorporate time delays in tumor cell division.

While our previous work [25] also considered angiogenesis and time delays, it assumed a constant concentration of external nutrients. While we have previously proven the asymptotic stability of constant steady-state solutions [25], this paper investigates the case where the provision of external nutrients is almost periodic and establishes the existence, uniqueness, and stability of almost periodic solutions using a different methodology.

Noticing that $c \ll 1$, this paper focuses on the limiting case where $c = 0$. By employing spatial scale transformation, we can assume $\Gamma = 1$. Consequently, Eq (1.1) simplifies to the following form:

$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial\sigma}{\partial r}\right) = \sigma, \quad 0 < r < R(t), \quad t > 0. \tag{1.5}$$

Using the solution of (1.5), (1.2) is given by

$$\sigma(r,t) = \frac{\alpha}{\alpha + Rp(R)}\frac{l(r)}{l(R)}\psi(t), \tag{1.6}$$

where

$$p(x) = \frac{x\coth x - 1}{x^2}, \quad l(x) = \frac{\sinh x}{x}.$$

Substituting (1.6) into (1.3), we obtian

$$R'(t) = sR(t)\left[\frac{\alpha\psi(t-\tau)}{\alpha + R(t-\tau)p(R(t-\tau))}\frac{R^3(t-\tau)p(R(t-\tau))}{R^3(t)} - \frac{\tilde{\sigma}}{3}\right], \tag{1.7}$$

where $p(x) = \dfrac{x\coth x - 1}{x^2}$. Denoting $x = R^3$, after rescaling coefficients of $\psi(t), \tilde{\sigma}$ as follows

$$\hat{\psi} = s\psi \ , \ \hat{\tilde{\sigma}} = s\tilde{\sigma},$$

and dropping the hat notation, Eq (1.7) takes the form

$$x'(t) = 3\alpha\psi(t-\tau)F(x(t-\tau)) - \tilde{\sigma}x(t), \tag{1.8}$$

where

$$F(x) = \frac{xp(\sqrt[3]{x})}{\alpha + \sqrt[3]{x}p(\sqrt[3]{x})}.$$

Accordingly,

$$x_0(t) = \varphi^3(t), \quad -\tau \le t \le 0. \tag{1.9}$$

The remaining part of the paper is arranged as follows. In Section 2, some preliminaries are given. In Section 3, we prove the existence and uniqueness of the almost periodic solution to Eq (1.8). Section 4 is devoted to the stability of the unique positive almost periodic solution. In the last section, computer simulations and conclusions are given.

2. Preliminaries

Let

$$q(x) = xp(x) = \frac{x\coth x - 1}{x}, \quad k(x) = x^3 p(x), \quad g(x) = \frac{p(x)}{\alpha + q(x)}, \quad G(x) = x^3 g(x)$$

and

$$D(x) = \frac{p(x)}{p(\theta x)}, \quad S(x) = \frac{\theta p(\theta x)(\alpha + xp(x))}{p(x)(\alpha + \theta x p(\theta x))} = \frac{\alpha + q(x)}{\alpha D(x)/\theta + q(x)},$$

where α and θ are positive constants.

Lemma 2.1. *(1)* $p'(x) < 0$ *for* $x > 0$, $\lim_{x\to 0+} p(x) = 1/3$, $\lim_{x\to\infty} p(x) = 0$.

(2) $q'(x) > 0$ *for* $x \geq 0$. $\lim_{x\to 0} q(x) = 0$, $\lim_{x\to\infty} q(x) = 1$, *and* $q'(0) = 1/3$.

(3) $k'(x) > 0$ *and* $k''(x) > 0$ *for* $x > 0$.

(4) $\left(x^3 g(x)\right)' > 0$ *and* $\left(x^3 g(x)\right)'' > 0$ *for* $x > 0$.

(5) For any $\theta \in (0,1)$, $D'(x) < 0$ *for* $x > 0$ *and* $\lim_{x\to 0+} D(x) = 1, \lim_{x\to\infty} D(x) = \theta$.

(6) $S'(x) > 0$ *for* $x > 0$. *Moreover, for any* $\theta \in (0,1)$, $\lim_{x\to 0+} S(x) = \theta, \lim_{x\to\infty} S(x) = 1$.

(7) $F''(x) < 0$ *for* $x > 0$.

Proof. For the proof of (1) and (2), please see Lemmas 2.1 and 2.2 in [12]. For the proof of (3), please see [6]. Now, we prove (4)–(7).

(3) The fact that $k'(x) = (x^3 p(x))' > 0$ for $x > 0$ can be found in [6]. Next, we aim to prove that $k''(x) > 0$ for $x > 0$. Since

$$(x^3 p(x))' = 2x\coth x - \frac{x^2}{\sinh^2 x} - 1,$$

it follows that, by noticing $\cosh^2 x - \sinh^2 x = 1$,

$$\begin{aligned}(x^3 p(x))'' &= \frac{2\cosh x \sinh^2 x + 2x^2 \cosh x - 4x\sinh x}{\sinh^3 x} \\ &= \frac{2\sinh x(\cosh x \sinh x - x) + 2x(x\cosh x - \sinh x)}{\sinh^3 x} > 0.\end{aligned}$$

This result is derived from the facts:

$$\cosh x \sinh x - x > 0, \quad x\cosh x - \sinh x > 0,$$

for $x > 0$.

(4) From [23], noticing $k'(x) > 0$, it is known that:

$$\begin{aligned}(x^3 g(x))' &= \left(\frac{k(x)}{\alpha + q(x)}\right)' \\ &= \frac{k'(x)\alpha + k'(x)q(x) - q'(x)k(x)}{(\alpha + q(x))^2} \\ &= \frac{\alpha k'(x)}{(\alpha + q(x))^2} + \left(\frac{k(x)}{q(x)}\right)' \left(\frac{q(x)}{\alpha + q(x)}\right)^2 \\ &= \frac{\alpha k'(x)}{(\alpha + q(x))^2} + 2x\left(\frac{q(x)}{\alpha + q(x)}\right)^2 > 0.\end{aligned}$$

Then,

$$\begin{aligned}(x^3g(x))'' &= \left(\frac{k(x)}{\alpha+q(x)}\right)'' \\ &= \left(\frac{\alpha k'(x)}{(\alpha+q(x))^2}\right)' + \left(2x\frac{q^2(x)}{(\alpha+q(x))^2}\right)' \\ &= \alpha\frac{k''(x)(\alpha+q(x)) - 2q'(x)k'(x)}{(\alpha+q(x))^3} + \frac{2q(x)(q(x)+2xq'(x))}{(\alpha+q(x))^3}.\end{aligned}$$

By utilizing equation

$$q(x) + 2xq'(x) = xp(x) + 2x(p(x) + xp'(x)) = xp(x) + 2xq'(x) > 0, \tag{2.1}$$

for $x > 0$, we can deduce that $(x^3g(x))'' > 0$ for $x > 0$.

(5) For $0 < \theta < 1$, from [21], we know that $D'(x) = \left(\frac{p(x)}{p(\theta x)}\right)' < 0$ for any $x > 0$. From [5], we know that $\frac{p'(x)}{p'(\theta x)}$ is strictly monotone increasing if $0 < \theta < 1$, and

$$\lim_{x\to 0+}\frac{p'(x)}{p'(\theta x)} = \frac{1}{\theta},\quad \lim_{x\to\infty}\frac{p'(x)}{p'(\theta x)} = \theta^2.$$

Noting (1), it follows that

$$\lim_{x\to 0+}\frac{p(x)}{p(\theta x)} = 1,\quad \lim_{x\to\infty}\frac{p(x)}{p(\theta x)} = \lim_{x\to\infty}\frac{p'(x)}{\theta p'(\theta x)} = \theta.$$

Thus, $\lim_{x\to 0+} D(x) = 1$ and $\lim_{x\to\infty} D(x) = \theta$ follows.

(6) For $0 < \theta < 1$, from [21], we know that $D'(x) = \left(\frac{p(x)}{p(\theta x)}\right)' > 0$ for any $x > 0$. By direct computation, one can get

$$\begin{aligned}S'(x) &= \left(\frac{\alpha+q(x)}{\alpha D(x)/\theta + q(x)}\right)' \\ &= \frac{\alpha q'(x)(D(x)/\theta - 1) - \alpha D'(x)(\alpha+q(x))/\theta}{(\alpha D(x)/\theta + q(x))^2} \\ &> 0,\end{aligned}$$

where the facts $D(x) > \theta$, $q'(x) > 0$, and $D'(x) < 0$ have been used. For $\theta \in (0, 1)$, the facts that $\lim_{x\to 0+} S(x) = \theta, \lim_{x\to\infty} S(x) = 1$ follow from (5).

(7) Direct computation yields

$$F''(x) = \frac{1}{9y^2}\left[4g'(y) + yg''(y)\right]\big|_{y=\sqrt[3]{x}},$$

and

$$4g'(y) + yg''(y) = \frac{J(y)}{(\alpha+q(x))^3},$$

where

$$J(y) = \alpha^2[4p'(y) + yp''(y)] + \alpha[-4p^2(y) + y^2p''(y)p(y) - 2y^2(p'(y))^2] + V(y),$$

and

$$V(y) = -4p^2q - 2yp(y)q(y)p'(y) + 2yp^2q'(y).$$

From [20], we know that $4p'(y) + yp''(y) < 0$. Since

$$-4p^2(y) + y^2p''(y)p(y) - 2y^2(p'(y))^2 = yp(yp'' + 2p') - 2p(yp' + p) - 2(p^2 + y^2(p')^2) < 0$$

and

$$\begin{aligned} V(y) &= -4p^2q + 2yp(q'p - p'q) \\ &= -4p^2q + 2yp^3 \\ &= p^2(-4q + 2yp) \\ &= -2yp^3 < 0, \end{aligned}$$

it follows that $J(y) < 0$ for $y > 0$. Thus $4g'(y) + yg''(y) < 0$, then $F''(x) < 0$ follows. This completes the proof.

To discuss the existence and uniqueness of almost periodic solutions, let's recall some basic introductions about the symbols and results of almost periodic functions (see [2, 4, 9, 13, 19] for more details).

Definition 2.2. (see [4, 9]) *A function $g \in C(\mathbb{R})$ is called almost periodic if for all $\varepsilon > 0$, there exists $l(\varepsilon) > 0$ such that any interval I of length $l(\varepsilon)$ contains a number A with the property that*

$$\sup_{t \in R} |g(t + A) - g(t)| < \varepsilon.$$

The space of all the almost periodic functions is denoted by $C_{AP}(\mathbb{R})$.

Recall that $AP(X)$ is a Banach space with the sup norm.

Definition 2.3. (see [9]) *Let $M(\cdot)$ be an $n \times n$ continuous matrix defined on $\mathbb{R}$. The linear system*

$$Y'(t) = M(t)Y(t), \tag{2.2}$$

is said to admit an exponential dichotomy on R if there exists positive constants k, ω and a projection P such that

$$\|Y(t)PY^{-1}(-s)\| \leq ke^{-\omega(t-s)}, \quad t \geq s,$$

$$\|Y(t)(I - P)Y^{-1}(-s)\| \leq ke^{-\omega(s-t)}, \quad t \leq s,$$

for a fundamental solution matrix $Y(t)$ of (2.2).

Lemma 2.4. (see [9]) *If the linear system (2.2) admits an exponential dichotomy with a projection P, then the almost periodic system*

$$Y'(t) = M(t)Y(t) + g(t),$$

has a unique almost periodic solution $Y(t)$ given by

$$Y(t) = \int_{-\infty}^{t} Y(t)PY^{-1}(s)g(s)ds - \int_{t}^{+\infty} Y(t)(I - P)Y^{-1}(s)g(s)ds.$$

Theorem 2.5. (see [7–9]) *Suppose that P is a normal and solid cone of a real Banach space X. Let P^0 be the interior of P. Suppose further that the operator A from P^0 to P^0 is a nondecreasing operator. Assume that there exists a function $\phi : (0,1) \times P^0 \to (0,+\infty)$ such that for any $\vartheta \in (0,1)$ and $x \in P^0$, then the following holds*

(1) $\phi(\vartheta, x) > \vartheta$.

(2) $\phi(\vartheta, \cdot)$ is nondecreasing in P^0.

(3) $A(\vartheta x) \geq \phi(\vartheta, x)A(x)$.

Assume further that there exists $z \in P^0$ such that $A(z) \geq z$. Then A has a unique fixed point x^* in P^0. Moreover, for any initial $x_0 \in P^0$, the iterative sequence defined by

$$x_n = A(x_{n-1}), \quad n \in N, \tag{2.3}$$

satisfies

$$\|x_n - x^*\| \to 0 \ \ (n \to \infty). \tag{2.4}$$

3. The existence and uniqueness of the almost periodic solution

Rewrite the problems (1.8) and (1.9) in the following form:

$$x(t) = x_0(0)e^{-\tilde{\sigma}t} + 3\alpha \int_0^t \psi(s-\tau)e^{-\tilde{\sigma}(t-s)}F(x(s-\tau))ds.$$

Then, by the method of steps, the problems (1.8) and (1.9) have a unique solution $x(t)$ which exists for all $t \geq 0$. From Lemma 2.1, it follows that $F(x) \geq 0$ for all $x \geq 0$. Then, by Theorem 1.1 in [1], it is easy to get get that the solution to problems (1.8) and (1.9) is nonnegative.

For the remainder of the paper, we always assume that $\psi(t)$ is a positive almost periodic function and denote

$$\psi^* = \sup_{t\in\mathbb{R}} \psi(t), \quad \psi_* = \inf_{t\in\mathbb{R}} \psi(t).$$

By Definition 2.3 and Lemma 2.4, it is not hard to get:

Lemma 3.1. *There exists a nonnegative almost periodic solution to Eq (1.8) given by*

$$x(t) = 3\alpha \int_{-\infty}^t \psi(s-\tau)F(x(s-\tau))e^{-\tilde{\sigma}(t-s)}ds, \quad t \in R. \tag{3.1}$$

Actually, Eq (1.8) is equivalent to (3.1) in the sense of nonnegative almost periodic solutions, i.e., every nonnegative almost periodic solution of Eq (1.8) is also a nonnegative almost periodic solution of (3.1), and vice versa.

Theorem 3.2. *(1) If $\psi_* > \tilde{\sigma}$, there exists one unique positive almost periodic solution x^* to Eq (1.8). Moreover, for any initial value function $x_0 \in C_{AP}(\mathbb{R})$ with positive infimum, the iterative sequence*

$$x_k(t) = 3\alpha \int_{-\infty}^t \psi(s-\tau)f(x_{k-1}(s-\tau))e^{-\tilde{\sigma}(t-s)}ds, \quad k = 1,2,3... \tag{3.2}$$

satisfies

$$\|x_k - x^*\| \to 0, \quad k \to \infty. \tag{3.3}$$

(2) If $\psi^* < \tilde{\sigma}$, then Eq (1.8) has exactly one unique almost periodic solution which equals zero. Moreover, for any nonnegative initial value function $x_0 \in C_{AP}(\mathbb{R})$, the iterative sequence

$$x_k(t) = 3\alpha \int_{-\infty}^{t} \psi(s-\tau)F(x_{k-1}(s-\tau))e^{-\tilde{\sigma}(t-s)}ds, \quad k = 1, 2, 3... \tag{3.4}$$

satisfies

$$\|x_k\| \to 0, \quad k \to \infty. \tag{3.5}$$

Proof. (1). Let

$$P = \{x \in C_{AP}(\mathbb{R}) : x(t) \geq 0, t \in \mathbb{R}\}.$$

Then, P is a normal and solid cone in $C_{AP}(\mathbb{R})$ and its interior

$$P^0 = \{x \in C_{AP}(\mathbb{R}) : \exists \varepsilon > 0, such \;\; that \;\; x(t) > \varepsilon, t \in \mathbb{R}\}.$$

Define an operator A on P^0 in the following way:

$$A(x)(t) = 3\alpha \int_{-\infty}^{t} \psi(s-\tau)F(x(s-\tau))e^{-\tilde{\sigma}(t-s)}ds. \tag{3.6}$$

The fact

$$F'(x) = \frac{1}{y^2}G'(y)|_{y=\sqrt[3]{x}} > 0, \tag{3.7}$$

implies that F is monotone increasing for $x > 0$. It follows that A is a nondecreasing operator.

Next, let us prove that A is from P^0 to P^0. Since

$$\lim_{x\to 0} g(\sqrt[3]{x}) = \lim_{x\to 0} \frac{p(\sqrt[3]{x})}{\alpha + q(\sqrt[3]{x})} = \frac{1}{3\alpha},$$

and $\psi_* > \tilde{\sigma}$, noticing g is decreasing (see Lemma 2.1), there exists $\epsilon > 0$ such that

$$g(\sqrt[3]{\epsilon}) = \frac{p(\sqrt[3]{\epsilon})}{\alpha + q(\sqrt[3]{\epsilon})} > \frac{\tilde{\sigma}}{3\alpha\psi_*},$$

which implies

$$3\alpha g(\sqrt[3]{\epsilon})\frac{\psi_*}{\tilde{\sigma}} > 1.$$

If $x_0 \in P^0$, there exists $\epsilon_0 > 0$ such that $x_0(t) \geq \epsilon_0$ for all $t \in R$. It follows that

$$\begin{aligned} A(x_0)(t) &\geq 3\alpha \int_{-\infty}^{t} \psi_* F(\epsilon_0)e^{-\tilde{\sigma}(t-s)}ds \\ &= 3\alpha \frac{\psi_*}{\tilde{\sigma}} \epsilon_0 g(\epsilon_0) \end{aligned}$$

$$
\begin{aligned}
&> 3\alpha\frac{\psi_*}{\tilde{\sigma}}\epsilon_0 g(\sqrt[3]{\epsilon_0})\\
&> \epsilon_0,
\end{aligned}
$$

for all $t \in R$, which means that $A(x_0) \in P^0$. And for $\epsilon_2 \in (0, \epsilon_1)$, we obtain

$$
\begin{aligned}
A(\epsilon_2)(t) &\geq 3\alpha \int_{-\infty}^{t} \psi_* F(\epsilon_2) e^{-\tilde{\sigma}(t-s)} ds\\
&= 3\frac{\psi_*}{\tilde{\sigma}}\epsilon_2 g(\sqrt[3]{\epsilon_2})\\
&> 3\frac{\psi_*}{\tilde{\sigma}}\epsilon_2 g(\sqrt[3]{\epsilon_1})\\
&> \epsilon_2.
\end{aligned}
$$

It is easy to get that

$$F(\vartheta x) = \zeta(\vartheta, x)F(x),$$

for all $0 < \vartheta < 1$ and $x \in (0, +\infty)$, where $\zeta(\vartheta, x) = \sqrt{\vartheta}S(y)|_{\theta=\sqrt{\vartheta}, y=\sqrt{x}}$. Let

$$\phi(\vartheta, x) = \zeta(\vartheta, \inf_{t\in R} x(t)), \quad x \in P^0.$$

By Lemma 2.1 (6), one can get that $\zeta(\vartheta, .)$ is strictly monotone increasing in $(0, +\infty)$ and $\lim_{x\to 0}\zeta(\vartheta, x) = \vartheta$, which implies $\zeta(\vartheta, x) > \vartheta$ for $\vartheta \in (0, 1)$ and $x \in (0, +\infty)$. Therefore,

$$\phi(\vartheta, x) > \vartheta, \quad \vartheta \in (0, 1), \quad x \in P^0.$$

Also, by the fact that $\zeta(\vartheta, \cdot)$ is strictly monotone increasing in $(0, +\infty)$, one can get that $\phi(\vartheta, \cdot)$ is nondecreasing in P^0. It follows that

$$
\begin{aligned}
A(\vartheta x)(t) &= 3\alpha \int_{-\infty}^{t} \psi(s-\tau)F(\vartheta x(s-\tau))e^{-\tilde{\sigma}(t-s)} ds\\
&= 3\alpha \int_{-\infty}^{t} \psi(s-\tau)x(s-\tau)g(\sqrt[3]{x(s-\tau)})\zeta(\vartheta, x(t-\tau))e^{-\tilde{\sigma}(t-s)} ds\\
&\geq 3\alpha \int_{-\infty}^{t} \psi(s-\tau)x(s-\tau)g(\sqrt[3]{x(s-\tau)})\phi(\vartheta, x)e^{-\tilde{\sigma}(t-s)} ds\\
&\geq 3\alpha\phi(\vartheta, x) \int_{-\infty}^{t} \psi(s-\tau)x(s-\tau)g(\sqrt[3]{x(s-\tau)})e^{-\tilde{\sigma}(t-s)} ds\\
&= \phi(\vartheta, x)A(x)(t).
\end{aligned}
$$

By Theorem 2.5 (see (2.3) and (2.4)), Eq (3.1) has exactly one positive almost periodic solution $x^* \in P^0$. Then, by Lemma 2.4, x^* is just the unique almost periodic solution with a positive infimum to Eq (1.8). Moreover, (3.2) and (3.3) follow from (2.3) and (2.4).

(2). By Lemma 3.1, Eq (1.8) has a nonnegative almost periodic solution

$$x(t) = 3\alpha \int_{-\infty}^{t} \psi(s-\tau)F(x(s-\tau))e^{-\tilde{\sigma}(t-s)} ds, \quad t \in R. \tag{3.8}$$

Define operator $A : C_{AP}(R) \to C_{AP}(R)$ as follows:

$$A(x)(t) = 3\alpha \int_{-\infty}^{t} \psi(s-\tau)F(x(s-\tau))e^{-\tilde{\sigma}(t-s)}ds. \tag{3.9}$$

Next, we show that A is a contraction operator. For any $x, y \in C_{AP}(R)$,

$$\begin{aligned}
||A(x)(t) - A(y)(t)|| &= 3\alpha|| \int_{-\infty}^{t} \psi(s-\tau)[F(x(s-\tau)) - F(y(s-\tau))]e^{-\tilde{\sigma}(t-s)}ds|| \\
&\leq 3\alpha \int_{-\infty}^{t} \psi^*|F'(\xi(t))|e^{-\tilde{\sigma}(t-s)}ds||x-y||,
\end{aligned}$$

where $\xi(t)$ lies between $x(t)$ and $y(t)$. For any $x > 0$, since

$$F'(x) = \frac{1}{3y^2}G'(y)|_{y=\sqrt[3]{x}} > 0,$$

and $g'(\sqrt[3]{x}) < 0$, it follows that $|F'(x)| \leq g(\sqrt[3]{x}) \leq 1/3$. Then,

$$|A(x)(t) - A(y)(t)| \leq \frac{\psi^*}{\tilde{\sigma}}||x-y||,$$

which implies that A is a contraction operator since $\psi^* < \tilde{\sigma}$. Therefore, Eq (1.8) has exactly one nonnegative almost periodic solution $x(t)$. If we define $p(0) = 1/3$, then p is continuous on $\mathbb{R}$. Therefore, zero is also an almost periodic solution of Eq (1.8). By the uniqueness, we have $x(t) \equiv 0$. Since

$$\begin{aligned}
||x_k(t)|| &= 3\alpha \left\| \int_{-\infty}^{t} \psi(s-\tau)f(x_{k-1}(s-\tau))e^{-\tilde{\sigma}(t-s)}ds \right\| \\
&\leq \frac{\psi^*}{\tilde{\sigma}}||x_{k-1}|| \\
&\leq \left(\frac{\psi^*}{\tilde{\sigma}}\right)^2 ||x_{k-2}|| \\
&\leq \cdots \\
&\leq \left(\frac{\psi^*}{\tilde{\sigma}}\right)^k ||x_0||,
\end{aligned}$$

and $\frac{\psi^*}{\tilde{\sigma}} < 1$, we can get $||x_k|| \to 0, \ \ k \to \infty$. This completes the proof of Theorem 3.2.

Remark. Theorem 3.2 (2) implies that if $\psi^* < \tilde{\sigma}$, Eq (1.8) has no positive almost periodic solution.

4. Exponential stability of the unique positive almost periodic solution

Lemma 4.1. Assume that the function $F(x, y)$ is defined on $\mathbb{R}_+ \times \mathbb{R}_+$ and continuously differentiable. Suppose $\frac{\partial F}{\partial y} > 0$ for $(x, y) \in \mathbb{R}_+ \times \mathbb{R}_+$. For any $T > 0$, if $z_1, z_2 \in C[-\tau, T) \cap C^1(0, T)$ satisfy the following inequalities:

$$z_1{}'(t) \geq F(z_1(t), z_1(t-\tau)) \ \text{ for } \ t > 0, \tag{4.1}$$

$$z_2{}'(t) \le F(z_2(t), z_2(t-\tau)) \ \text{ for } \ t > 0, \tag{4.2}$$

$$z_1(t) \ge z_2(t) \ \text{ for } \ -\tau \le t \le 0, \tag{4.3}$$

then, $z_1(t) \ge z_2(t)$ for $t \ge -\tau$.
Proof. Please see Lemma 3.1 in [6].
Lemma 4.2. *Consider the following problem*

$$x'(t) = F(x(t), x(t-\tau)) \ \text{ for } \ t > 0, \tag{4.4}$$

$$x(t) = x_0(t) \ \text{ for } \ -\tau \le t \le 0. \tag{4.5}$$

Assume that the function F is defined on $\mathbb{R}_+ \times \mathbb{R}_+$ and continuously differentiable. Suppose $\frac{\partial F}{\partial y} > 0$ for $(x, y) \in \mathbb{R}_+ \times \mathbb{R}_+$. Let x_s be a positive solution of equation $F(x, x) = 0$ such that

$$(x - x_s)F(x, x) < 0 \ \text{ for } \ x \ne x_s.$$

If $x(t)$ is the solution of the problem of (4.4), (4.5), and $x_0(t) \in C[-\tau, 0]$ for $-\tau \le t \le 0$, then,

$$\lim_{t\to\infty} x(t) = x_s.$$

Proof. Please see Lemma 3.4 in [6].

By Eq (1.7), we can get

$$3\alpha\psi_* F(x(t-\tau)) - \tilde{\sigma}x(t) \le x'(t) \le 3\alpha\psi^* F(x(t-\tau)) - \tilde{\sigma}x(t).$$

Consider the following two initial value problems

$$z'(t) = 3\alpha\psi_* F(z(t-\tau)) - \tilde{\sigma}z(t), \tag{4.6}$$
$$z_0(t) = \varphi(t), \ \ -\tau \le t \le 0, \tag{4.7}$$

and

$$y'(t) = 3\alpha\psi^* F(y(t-\tau)) - \tilde{\sigma}y(t), \tag{4.8}$$
$$y_0(t) = \varphi(t), \ \ -\tau \le t \le 0. \tag{4.9}$$

Define

$$F_1(x, y) = 3\alpha\psi_* F(y) - \tilde{\sigma}x, \ \ F_2(x, y) = 3\alpha\psi^* F(y) - \tilde{\sigma}x.$$

From (3.7), we know that F_1 and F_2 are monotone increasing in y. Since $\psi_* > \tilde{\sigma}$, by Lemma 2.1, one can get

$$0 < \frac{\alpha p(x)}{\alpha + q(x)} = \frac{\alpha G(x)}{x^3} = \alpha g(x) < 1/3,$$

for all $x > 0$. Then, when $\psi_* > \tilde{\sigma}$ (i.e., $0 < \frac{\tilde{\sigma}}{3\psi^*} < \frac{\tilde{\sigma}}{3\psi_*} < \frac{1}{3}$), it follows that the equations

$$F_1(x, x) = 3\alpha x\psi_*[g(\sqrt[3]{x}) - \frac{\tilde{\sigma}}{3\psi_*}] = 0$$

and

$$F_2(x,x) = 3\alpha x\psi^*[g(\sqrt[3]{x}) - \frac{\tilde{\sigma}}{3\psi^*}] = 0,$$

have a unique positive constant solution x_1 and x_2, respectively, and $x_1 < x_2$, where the fact that $g'(x) < 0$ for $x > 0$ is used.

Lemma 4.3. *If $\psi_* > \tilde{\sigma}$, then the following assertion holds:*

$$x_1 = \lim_{t\to\infty} z(t) \le \underline{x} = \liminf_{t\to\infty} x(t) \le \limsup_{t\to\infty} x(t) = \bar{x} \le \lim_{t\to\infty} y(t) = x_2.$$

Moreover, there exists $T > 0$ such that

$$x(t) > x_1/2 > 0, \tag{4.10}$$

for $t > T$.

Proof. Since $g'(x) < 0$, we have $(x - x_1)F(x,x) < 0$ for $x \neq x_1$. By Lemma 4.2, for any nonnegative initial value function $x_0(t)$, one can get

$$\lim_{t\to\infty} z(t) = x_1, \tag{4.11}$$

where $x(t)$ is the solution of (4.6) and (4.7). Similarly, it is easy to get that for any nonnegative initial value function $x_0(t)$, one can get

$$\lim_{t\to\infty} y(t) = x_2, \tag{4.12}$$

where $y(t)$ is the solution of (4.8) and (4.9). Using Lemmas 4.1 and 4.2, one can get

$$x_1 = \lim_{t\to\infty} z(t) \le \underline{x} = \liminf_{t\to\infty} x(t) \le \limsup_{t\to\infty} x(t) = \bar{x} \le \lim_{t\to\infty} y(t) = x_2.$$

Thus, (4.10) follows. This completes the proof.

The solution to Eq (1.8) is related to α. Denote $x(t) = x(t,\alpha)$. Assume $\alpha_1 \le \alpha_2$. Consider the following two problems

$$y_1'(t) = 3\alpha_1\psi(t)F(y_1(t-\tau)) - \tilde{\sigma}y_1(t), \tag{4.13}$$

$$y_1(t) = \varphi(t), \quad -\tau \le t \le 0 \tag{4.14}$$

and

$$y_2'(t) = 3\alpha_2\psi(t)F(y_2(t-\tau)) - \tilde{\sigma}y_2(t), \tag{4.15}$$

$$y_2(t) = \varphi(t), \quad -\tau \le t \le 0. \tag{4.16}$$

By Lemma 4.1, it is easy to get that $x(t,\alpha_1) \le x(t,\alpha_2)$. Then,

Lemma 4.4. *The solution to Eq (1.8) is monotone increasing in α.*

Theorem 4.5. *(I) If $\psi_* > \tilde{\sigma}$ and $\tilde{\sigma} - \psi^*(\frac{\tilde{\sigma}}{\psi_*} + 3A_0) > 0$ hold, where $A_0 = 1/3\sqrt[3]{x_1}g'(\sqrt[3]{x_1})$, then there exists $\tau_0 > 0$ such that for all $\tau \in (0,\tau_0)$, the unique almost periodic positive solution to Eq (1.8) is exponentially stable.*

(II) If $\psi^* < \tilde{\sigma}$, then there exists $\tau_1 > 0$ such that for all $\tau \in (0,\tau_1)$, every solution to Eq (1.8) exponentially asymptotically tends to 0.

Remark. By selecting appropriate parameters, the condition $\tilde{\sigma}-\psi^{*}(\frac{\tilde{\sigma}}{\psi_{*}}+3A_0)>0$ in Theorem 4.5 (I) can be satisfied. Actually, let

$$l(y)=\tilde{\sigma}\left(\frac{1}{y}-\frac{1}{\psi^{*}}\right)+\frac{3A_0}{\psi^{*}}.$$

Then, $l'(y)<0$ and $\lim_{y\to 0+}l(y)=+\infty$. By Lemmas 2.1 (1) and (3), g is decreasing, thus $A_0<0$. Then $l(\psi^{*})=\frac{3A_0}{\psi^{*}}<0$. Thus, there exists a positive constant l_0 such that $l(y)<0$ for $l_0<y<\psi^{*}$. Since

$$\tilde{\sigma}-\psi^{*}(\frac{\tilde{\sigma}}{\psi_{*}}+3A_0)>0\Leftrightarrow\tilde{\sigma}\left(\frac{1}{\psi_{*}}-\frac{1}{\psi^{*}}\right)+\frac{3A_0}{\psi^{*}}<0,$$

the conditions in Theorem 4.5 (I) will be satisfied if we choose the almost function $\psi(t)$ satisfying $\psi_{*}\in(l_0,\psi^{*})$ and $\tilde{\sigma}$ satisfying $\tilde{\sigma}<\psi_{*}$.

Proof. (I) Since $\tilde{\sigma}-\psi^{*}(\frac{\tilde{\sigma}}{\psi_{*}}+3A_0)>0$, due to the sign preserving property of continuous functions, there exists $\eta>0$ which is small enough such that

$$\tilde{\sigma}-\psi^{*}\left(\frac{\tilde{\sigma}}{\psi_{*}}+3(A_0+\eta)\right)>0.$$

Let

$$\vartheta(\tau)=\tilde{\sigma}-\psi^{*}\left(\frac{\tilde{\sigma}}{\psi_{*}}+3(A_0+\eta)\right)e^{\tilde{\sigma}\tau},$$

where $A_0=\frac{1}{3}\sqrt[3]{x_1}g'(\sqrt[3]{x_1})<0$. Then

$$\vartheta(0)=\tilde{\sigma}-\psi^{*}\left(\frac{\tilde{\sigma}}{\psi_{*}}+3(A_0+\eta)\right)>0,\tag{4.17}$$

which implies that there exists a constant $\tau_0>0$ such that

$$\theta(\tau)>\frac{\theta(0)}{2}>0,$$

for all $\tau\in(0,\tau_0)$.

Let $x(t)$ be an arbitrary solution of (1.8) and $x^{*}(t)$ is the unique almost periodic solution of (1.8). Then,

$$x(t)=x_0e^{-\tilde{\sigma}t}+3\alpha\int_0^t e^{-\tilde{\sigma}(t-s)}\psi(s-\tau)F(x(s-\tau))ds,$$

and

$$x(t)=x_0e^{-\tilde{\sigma}t}+3\alpha\int_0^t e^{-\tilde{\sigma}(t-s)}\psi(s-\tau)F(x^{*}(s-\tau))ds,$$

for all $t\geq 0$. Then we can get

$$x(t)-x^{*}(t)=(x_0(0)-x_0^{*}(0))e^{-\tilde{\sigma}t}+3\alpha\int_0^t e^{-\tilde{\sigma}(t-s)}\psi(s-\tau)\left(F(x(s-\tau))-F(x^{*}(s-\tau))\right)ds.$$

It follows that

$$|x(t)-x^*(t)| \le (x_0(0)-x_0^*(0))e^{-\tilde{\sigma}t} + 3\alpha\int_0^t e^{-\tilde{\sigma}(t-s)}\psi(s-\tau)|F(x(s-\tau))-F(x^*(s-\tau))|ds.$$

Because of the continuity of F', for any $\eta > 0$, there exists $\delta > 0$ such that when $|z(t)-x_1| < \delta$, there holds

$$|F'(z(t)) - F'(x_1)| < \eta. \tag{4.18}$$

Since $\lim_{t\to\infty} z(t) = x_2$, for the above δ, there exists $T > \tau > 0$ such that when $t > T-\tau$, there holds

$$|z(t)-x_1| < \delta.$$

Thus, there exists $T > 0$ such that when $t > T-\tau$, (4.18) holds. It follows that for $t > T-\tau$, there holds

$$F'(z(t)) \le F'(x_1) + \eta. \tag{4.19}$$

Let $u(t) = |x(t)-x^*(t)|e^{\tilde{\sigma}t}$. We can get for $t > T$,

$$u(t) \le \tilde{M} + 3\alpha\int_T^t e^{\tilde{\sigma}s}\psi(s-\tau)|F'(\xi)|.|x(s-\tau)-x^*(s-\tau)|ds,$$

where $\xi = \vartheta x(t-\tau) + (1-\vartheta)x^*(t-\tau)$, $\vartheta \in (0,1)$, and

$$\tilde{M} = |x_0(0)-x_0^*(0)| + 3\alpha\int_0^T e^{\tilde{\sigma}s}\psi(s-\tau)|F'(\xi)|.|x(s-\tau)-x^*(s-\tau)|ds.$$

By the fact that

$$|F'(\xi)| = g(\sqrt[3]{\xi}) + 1/3\sqrt[3]{\xi}g'(\sqrt[3]{\xi}) < g(\sqrt[3]{\xi}) < 1/3,$$

we have

$$\begin{aligned}\tilde{M} &= |x_0(0)-x_0^*(0)| + 3\alpha\int_0^T e^{\tilde{\sigma}s}\psi(s-\tau)|F'(\xi)|.|x(s-\tau)-x^*(s-\tau)|ds\\ &\le |x_0(0)-x_0^*(0)| + \alpha\int_0^T e^{\tilde{\sigma}s}\psi(s-\tau).|x(s-\tau)-x^*(s-\tau)|ds =: M.\end{aligned}$$

It follows that

$$u(t) \le M + 3\alpha\int_T^t e^{\tilde{\sigma}s}\psi(s-\tau)|F'(\xi)|.|x(s-\tau)-x^*(s-\tau)|ds,$$

for $t > T$. Notice that $z(t)$ is a solution of (4.6) and (4.7), then by Lemma 4.1, one can get

$$\xi = \vartheta x(t-\tau) + (1-\vartheta)x^*(t-\tau) \ge z(t-\tau).$$

Since $F''(x) < 0$ for all $x > 0$, then there exists $T > 0$ such that for $t > T$,

$$\begin{aligned}u(t) &\le M + 3\alpha\int_T^t e^{\tilde{\sigma}s}\psi(s-\tau)|F'(\xi)|.|x(s-\tau)-x^*(s-\tau)|ds\\ &\le M + 3\alpha\int_T^t e^{\tilde{\sigma}s}\psi(s-\tau)F'(z(s-\tau)).|x(s-\tau)-x^*(s-\tau)|ds\end{aligned}$$

$$
\begin{aligned}
&\le M + 3\alpha \int_T^t e^{\tilde{\sigma}s}\psi(s-\tau)(F'(x_1)+\eta)|x(s-\tau)-x^*(s-\tau)|ds \\
&\le M + 3\alpha \int_T^t e^{\tilde{\sigma}s}\psi^*\left(\frac{\tilde{\sigma}}{3\alpha\psi_*}+A_0+\eta\right)u(s-\tau)ds \\
&\le M + 3\alpha \int_0^t e^{\tilde{\sigma}\tau}\psi^*\left(\frac{\tilde{\sigma}}{3\alpha\psi_*}+A_0+\eta\right)u(s)ds \\
&\le M + 3\alpha \int_{-\tau}^{t-\tau} e^{\tilde{\sigma}\tau}\psi^*\left(\frac{\tilde{\sigma}}{3\alpha\psi_*}+A_0+\eta\right)u(s)ds \\
&= M + 3\alpha \int_{-\tau}^{0} e^{\tilde{\sigma}\tau}\psi^*\left(\frac{\tilde{\sigma}}{3\alpha\psi_*}+A_0+\eta\right)u(s)ds + 3\alpha \int_{0}^{t-\tau} e^{\tilde{\sigma}\tau}\psi^*\left(\frac{\tilde{\sigma}}{3\alpha\psi_*}+A_0+\eta\right)u(s)ds \\
&\le M_1 + \alpha \int_0^t e^{\tilde{\sigma}\tau}\psi^*\left(\frac{\tilde{\sigma}}{\alpha\psi_*}+3(A_0+\eta)\right)u(s)ds \\
&= M_1 + \int_0^t e^{\tilde{\sigma}\tau}\left(\frac{\psi^*\tilde{\sigma}}{\psi_*}+3\alpha\psi^*(A_0+\eta)\right)u(s)ds,
\end{aligned}
$$

where

$$
M = |x_0(0)-x_0^*(0)| + \alpha \int_0^T e^{\tilde{\sigma}s}\psi(s-\tau)|x(s-\tau)-x^*(s-\tau)|ds,
$$

and $M_1 = M + 3\alpha \int_{-\tau}^0 e^{\tilde{\sigma}\tau}\psi^*(\frac{\tilde{\sigma}}{3\alpha\psi^*}+A_0+\eta)u(s)ds$ and Lemma 2.1 has been used. By the Gronwall inequality, one can get

$$
u(t) \le M_1 e^{\kappa t},
$$

where $\kappa = e^{\tilde{\sigma}\tau}\psi^*(\frac{\tilde{\sigma}}{\psi_*}+3(A_0+\eta))$. It follows that

$$
|x(t)-x^*(t)| \le M_1 e^{(\kappa-\tilde{\sigma})t} = M_1 e^{-(\tilde{\sigma}-\kappa)t} \le M_1 e^{-\gamma t},
$$

where

$$
\gamma = \tilde{\sigma} - \psi^*\left(\frac{\tilde{\sigma}}{\psi_*}+3(A_0+\eta)\right)e^{\tilde{\sigma}\tau} > 0,
$$

for $\tau \in (0,\tau_0)$ and η is sufficiently small, which means $x^*(t)$ is exponentially stable. The proof of Theorem 4.5 (I) is complete.

(II) Let

$$
L(\tau) = \tilde{\sigma} - \psi^* e^{\tilde{\sigma}\tau}.
$$

Then $L(0) = \tilde{\sigma} - \psi^* > 0$, thus there exists $\tau_1 > 0$ such that $L(\tau) > 0$ for any $\tau \in (0,\tau_1)$. Let $v(t) = |x(t)|e^{\tilde{\sigma}t}$. We can get

$$
\begin{aligned}
v(t) &\le C + 3\int_0^t e^{\tilde{\sigma}s}\psi(s-\tau)|x(s-\tau)|g(\sqrt[3]{x(s-\tau)})|ds \\
&\le C + \int_0^t e^{\tilde{\sigma}s}\psi^*|x(s-\tau)|ds \\
&\le C + \int_{-\tau}^{t-\tau} e^{\tilde{\sigma}\tau}\psi^* v(s)ds
\end{aligned}
$$

$$= C + \int_{-\tau}^{0} e^{\tilde{\sigma}\tau}\psi^* v(s)ds + \int_{0}^{t-\tau} e^{\tilde{\sigma}\tau}\psi^* v(s)ds$$
$$\leq C_1 + \int_{0}^{t} e^{\tilde{\sigma}\tau}\psi^* v(s)ds,$$

where $C = x_0(0), C_1 = C + \int_{-\tau}^{0} e^{\tilde{\sigma}\tau}\psi^* v(s)ds$. By the Gronwall inequality, one can get

$$u(t) \leq C_1 e^{\kappa t}.$$

It follows that

$$|x(t)| \leq C_1 e^{(\kappa-\tilde{\sigma})t} = C_1 e^{-(\tilde{\sigma}-\kappa)t} \leq C_1 e^{-(\tilde{\sigma}-\psi^* e^{\tilde{\sigma}\tau})t},$$

for $\tau \in (0, \tau_1)$, which means $x^*(t)$ is exponentially stable since $\tilde{\sigma} - \psi^* e^{\tilde{\sigma}\tau} > 0$. This completes the proof.

5. Computer simulations

In this section, the results of computer simulations are presented. By using MATLAB R2016a, we present some examples of solutions of Eq (1.8) for different parameter values (see Figures 1–6). The model parameter values used in the simulations are given with the figures' captions.

Let $\psi(t) = 5 + \frac{1}{2}[\cos(t) + \sin(\sqrt{2}t)]$. Then $\psi^* = 6, \psi_* = 4$. Assume $\alpha = 1, \tau = 0.1$, and $\tilde{\sigma} = 1$. The solution to

$$g(\sqrt[3]{x}) = \frac{\tilde{\sigma}}{3\psi_*\alpha} = \frac{1}{6}$$

is $x \approx 10.16$. It follows that

$$A_0 = \frac{1}{3}\sqrt[3]{x}g'(\sqrt[3]{x}) \approx -0.339.$$
$$\gamma = \tilde{\sigma} - \psi^*(\frac{\tilde{\sigma}}{\alpha\psi_*} + 3A_0)e^{\tilde{\sigma}\tau} \approx 0.166 > 0.$$

The conditions of Theorem 4.5 (I) are satisfied.

Let $\psi(t) = 5 + \cos(t) + \sin(\sqrt{2}t)$. Then $\psi^* = 7, \psi_* = 3$. Assume $\alpha = 1, \tau = 1$, and $\tilde{\sigma} = 20$. Then

$$\tilde{\sigma} - \psi^* e^{\tilde{\sigma}\tau} = 20 - 7 * e > 0.$$

The conditions of Theorem 4.5 (II) are satisfied.

Let $\psi(t) = 5 + \cos(t) + \sin(\sqrt{2}t)$. Then $\psi^* = 7, \psi_* = 3$. Assume $\alpha = 1, \tau = 2$, and $\tilde{\sigma} = 1$. The solution to

$$g(\sqrt[3]{x}) = \frac{\tilde{\sigma}}{3\psi_*\alpha} = \frac{1}{9},$$

is $x \approx 56.0247$. It follows that

$$A_0 = \frac{1}{3}\sqrt[3]{x}g'(\sqrt[3]{x}) \approx -0.0297.$$
$$\gamma = \tilde{\sigma} - \psi^*(\frac{\tilde{\sigma}}{\alpha\psi_*} + 3A_0)e^{\tilde{\sigma}\tau} \approx -11.6326 < 0.$$

The conditions of Theorem 4.5 (I) are not satisfied. Assume $\alpha = 1, \tau = 2$, and $\tilde{\sigma} = 10$. Then

$$\tilde{\sigma} - \psi^* e^{\tilde{\sigma}\tau} = 10 - 7 * e^2 < 0.$$

So these parameter values do not meet the conditions of Theorem 4.5 (II).

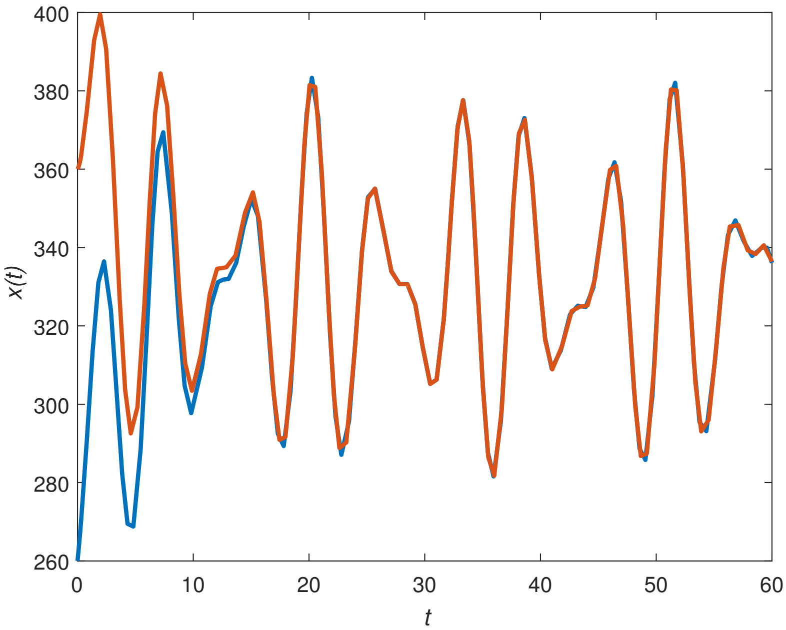

Figure 1. The corresponding curves of the solutions to Eq (1.8) for $\psi(t) = 5 + 1/2\cos(t) + 1/2\sin(\sqrt{2}t), \alpha = 1, \tilde{\sigma} = 1, \tau = 0.1$, and $x_0 = 260, 360$, respectively.

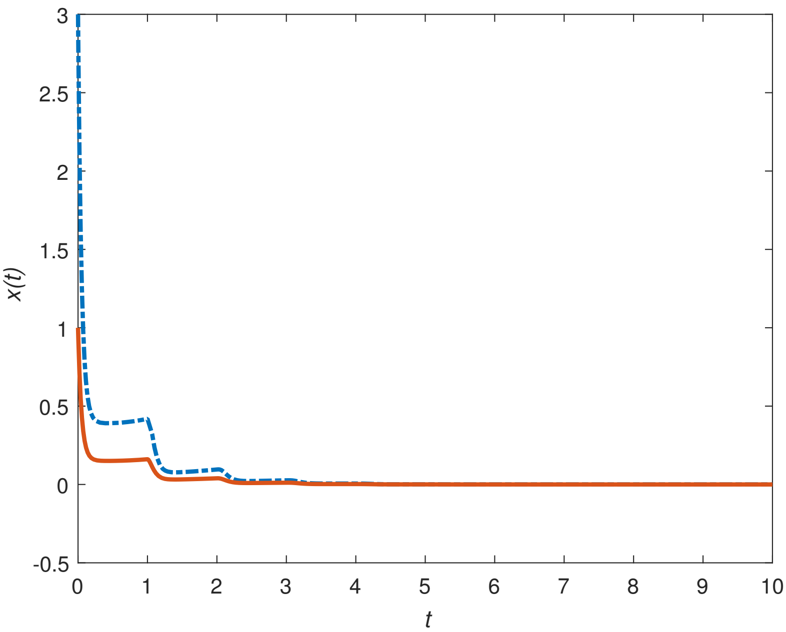

Figure 2. The corresponding curves of the solutions to Eq (1.8) for $\psi(t) = 5 + \cos(t) + \sin(\sqrt{2}t), \alpha = 1, \tilde{\sigma} = 20, \tau = 1$, and $x_0 = 3, 1$, respectively.

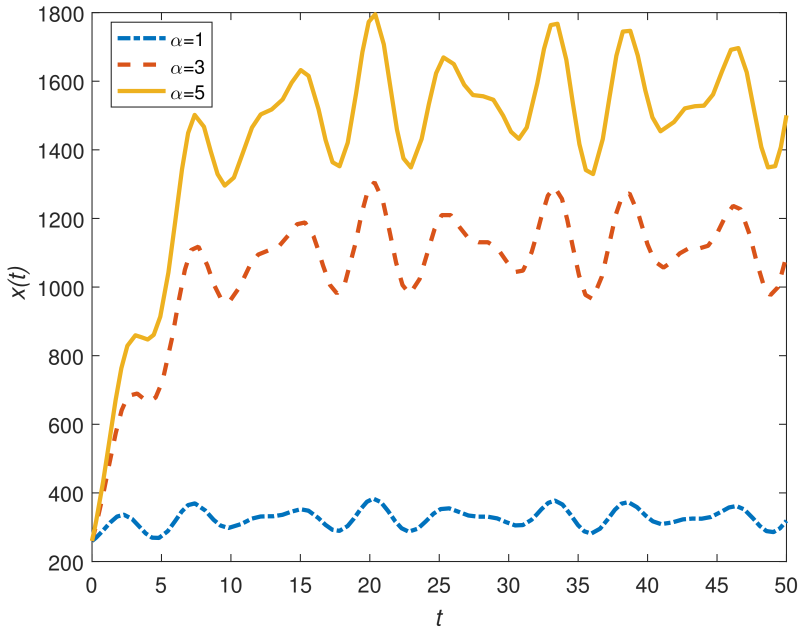

Figure 3. The corresponding curves of the solutions to Eq (1.8) for $\psi(t) = 5 + \frac{1}{2}[\cos(t) + \sin(\sqrt{2}t)]$, $\tilde{\sigma} = 1, \tau = 0.1$, $x_0 = 260$, and $\alpha = 1, 3, 5$, respectively.

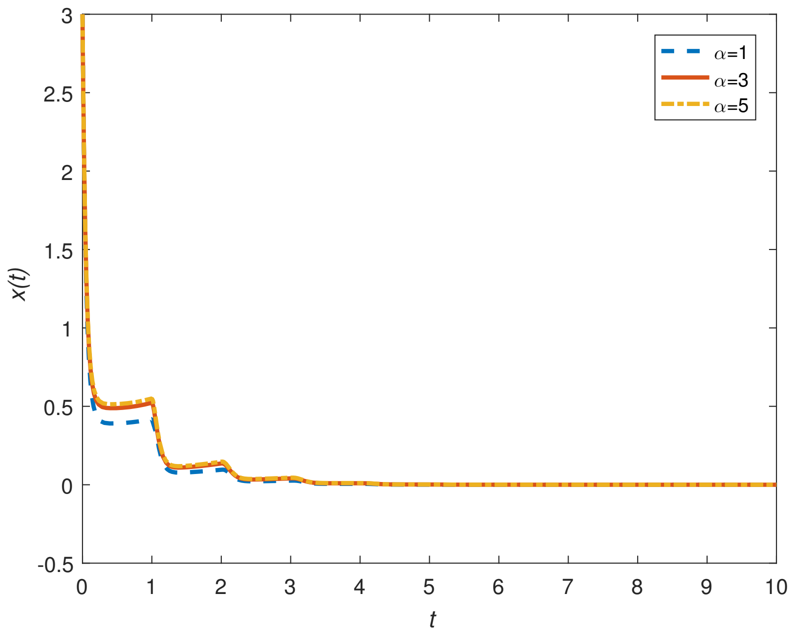

Figure 4. The corresponding curves of the solutions to Eq (1.8) for $\psi(t) = 5 + \cos(t) + \sin(\sqrt{2}t)$, $\tilde{\sigma} = 20, \tau = 1$, $x_0 = 3$, and $\alpha = 1, 3, 5$, respectively.

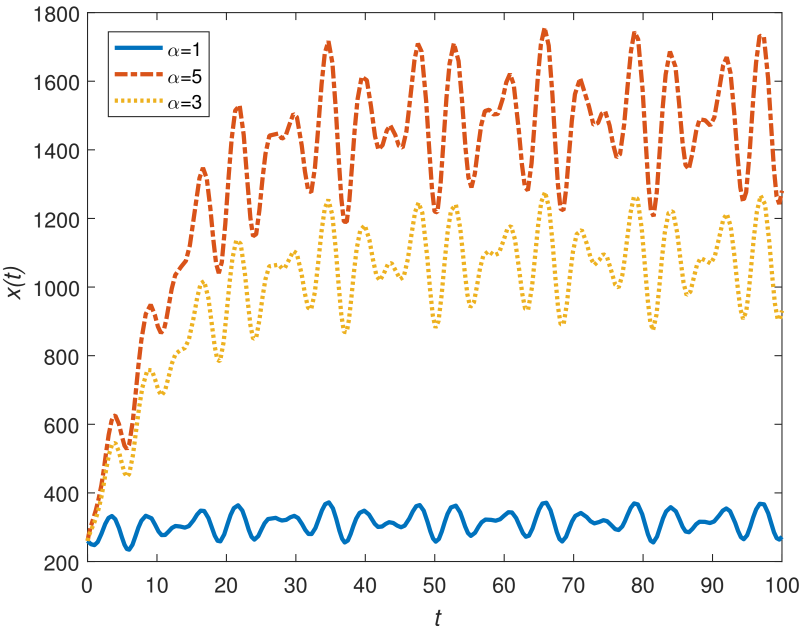

Figure 5. The corresponding curves of the solutions to Eq (1.8) for $\psi(t) = 5 + \cos(t) + \sin(\sqrt{2}t)$, $\tilde{\sigma} = 1, \tau = 2$, $x_0 = 260$, and $\alpha = 1, 3, 5$, respectively.

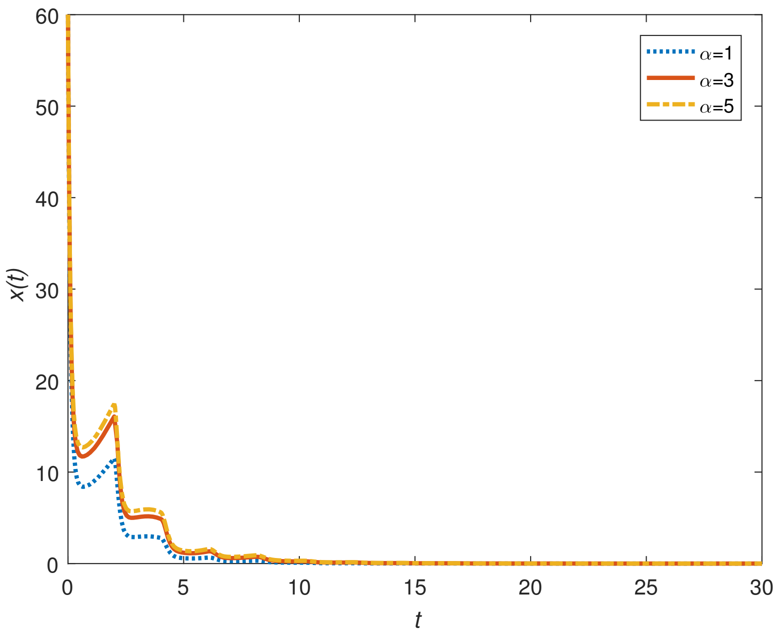

Figure 6. The corresponding curves of the solutions to Eq (1.8) for $\psi(t) = 5 + \cos(t) + \sin(\sqrt{2}t)$, $\tilde{\sigma} = 10, \tau = 2$, $x_0 = 60$, and $\alpha = 1, 3, 5$, respectively.

In Figure 1, the behavior of the solutions covered by Theorem 4.5 (I) is presented. Numerical simulation results indicate that, for certain parameter values satisfying Theorem 4.5 (I) and different constant initial values, the tumor will asymptotically tend towards an almost periodic solution. Figure 2 illustrates the behavior of the solutions covered by Theorem 4.5 (II). It is observed that, for specific parameter values and different constant initial values satisfying Theorem 4.5 (II), the tumor will disappear. In Figures 3 and 4, the behavior of the solutions is presented for varying α representing blood vessel density. Numerical simulation results demonstrate that when other parameters remain unchanged, the solution increases with increasing α without affecting its final trend of the solution.

Figures 5 and 6 indicate that even if the conditions of Theorem 4.5 are not met, the solution of the problem may exponentially asymptotically tend to the unique almost periodic solution or exponentially asymptotically tend to 0. This indicates that the conditions for exponential asymptotic stability in Theorem 4.5 are only sufficient conditions.

6. Conclusions

The focus of this study lied in investigating the impact of almost periodic nutrient supply, angiogenesis, and time delay on tumor growth. Our results demonstrated that an almost periodic nutrient supply led to a unique almost periodic solution for this problem (refer to Theorem 3.2). Furthermore, we established that this unique solution was exponentially asymptotically stable under certain parameter conditions, while the presence of time delay did not affect the final growth trend of the tumor (see Theorem 4.5). Additionally, when keeping other parameters constant, our findings indicated that the solution increased with an increase in α, which represents the intensity of angiogenesis; however, it should be noted that the magnitude of α did not affect the final trend of the solution (refer to Lemma 4.4 and Theorem 4.5).

Use of AI tools declaration

The authors declare that they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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