

ANALYSIS OF A FREE BOUNDARY PROBLEM FOR TUMOR
GROWTH WITH GIBBS-THOMSON RELATION
AND TIME DELAYS

SHIHE XU* AND MENG BAI

School of Mathematics and Statistics, Zhaoqing University
Zhaoqing, Guangdong 526061, China

FANGWEI ZHANG

College of Transport and Communications, Shanghai Maritime University
Shanghai 201306, China

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ABSTRACT. In this paper we study a free boundary problem for tumor growth with Gibbs-Thomson relation and time delays. It is assumed that the process of proliferation is delayed compared with apoptosis. The delay represents the time taken for cells to undergo mitosis. By employing stability theory for functional differential equations, comparison principle and some meticulous mathematical analysis, we mainly study the asymptotic behavior of the solution, and prove that in the case c (the ratio of the diffusion time scale to the tumor doubling time scale) is sufficiently small, the volume of the tumor cannot expand unlimitedly. It will either disappear or evolve to one of two dormant states as $t \rightarrow \infty$. The results show that dynamical behavior of solutions of the model are similar to that of solutions for corresponding nonretarded problems under some conditions.

1. Introduction. The process of tumor growth is a complex process. To describe the process, in recent years, an increasing number of mathematical models in forms of free boundary problems of partial differential equations have been proposed and studied, cf.[3, 4, 5, 6, 15, 16, 19, 21]. The process of tumor growth has several different stages, starting from the very early stage of solid tumor without necrotic core inside (see,e.g., [4, 8, 9, 10, 14]) to the process of necrotic core formation(see,e.g.,[2, 5, 7, 12]). Experiments suggest that changes in the proliferation rate can trigger changes in apoptotic cell loss and that these changes do not occur instantaneously: they are mediated by growth factors expressed by the tumor cells (see[2]). Following this idea, the study of time delayed mathematical model for tumor growth has drawn attentions of some other researchers(see,e.g.,[10, 11, 13, 22] and references cited therein).

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* Corresponding author: Shihe Xu.

In this paper we study the following problem:

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

$$\frac{\partial \sigma}{\partial r}(0, t) = 0, \quad \sigma(R(t), t) = G(t), \quad 0 < r < R(t), \quad t > 0, \quad (2)$$

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

$$\sigma(r, t) = \psi(r, t), \quad 0 < r < R(t), \quad -\tau \leq t \leq 0, \quad (4)$$

$$R(t) = \varphi(t), \quad -\tau \leq t \leq 0 \quad (5)$$

where $\lambda, \mu, \bar{\sigma}, \tilde{\sigma}, c$ and τ are positive constants. λ is the nutrient consumption rate; $\tilde{\sigma}$ is a threshold value of nutrient concentration for apoptosis; μ is the proliferation rate of tumor cells; r is the radial variable; the variable $\sigma(r, t)$ represents the nutrient concentration at radius r and time t ; the variable $R(t)$ represents the radius of the tumor at time t ; τ is the time delay in cell proliferation, i.e., τ is the length of the period that a tumor cell undergoes a full process of mitosis. $G(t)$ is a given function representing the external nutrient supply. φ and ψ are given nonnegative functions. The two terms on the right hand side of (3) are explained as follows: The first term is the total volume increase in a unit time interval induced by cell proliferation; $\mu\sigma$ is the cell proliferation rate in unit volume. The second term is total volume shrinkage in a unit time interval caused by cell apoptosis, or cell death due to aging. c represents the time scale of diffusion of nutrient and inhibitor compare to the time scale of the tumor doubling within the tumor and $c \ll 1$ (i.e., the time scale of the tumor doubling is more larger compared to the time scale of diffusion of nutrient and inhibitor within the tumor).

The model we studied in this paper is established by modifying the model studied in Wu [19] by considering the time delay effect as that in Byrne [3], i.e., introducing time delay in proliferation to the model studied in [19], we have the model (1)-(5). In Wu[19], under some assumptions, the author studied the model (1)-(5) without time delay (i.e., $\tau = 0$). In this paper, as [19], let

$$G(t) = \bar{\sigma}(1 - \gamma/R(t))H(R(t)), \quad (6)$$

where $H(\cdot)$ is a smooth function such that $H(r) = 0$ for $r \leq \gamma$, $H(r) = 1$ for $r \geq 2\gamma$ and $0 \leq H'(r) \leq 2/\gamma$ for $r \geq 0$. $G(t)$ is induced by Gibbs-Thomson relation, please see [18, 19, 20] for details.

Many other special cases where $\tau = 0$ have been studied. For example, $G(t)$ is assumed to be constant $\bar{\sigma}$ in Byrne and Chaplain [4], Friedman and Reitich [14], Cui[9] and $G(t)$ is assumed to be a periodic function in Xu[21].

Motivated by [8, 10, 14, 11], by employing stability theory for functional differential equations, comparison principle and some meticulous mathematical analysis, we mainly study the asymptotic behavior of the solution, and prove that in the case c (the ratio of the diffusion time scale to the tumor doubling time scale) is sufficiently small, the volume of the tumor cannot expand unlimitedly. It will either disappear or evolve to one of two dormant states as $t \rightarrow \infty$.

In this paper, we will study the model (1)-(5) under following assumptions:

(A₁) $\varphi \in C[-\tau, 0]$, $\varphi(t) > 0$ for $-\tau \leq t \leq 0$.

(A₂) $\psi \in C([0, \infty) \times [-\tau, 0])$, and $\psi(r, t) = G(t)$ for $r \geq R(t)$; $0 \leq \psi(r, t) \leq G(t)$ for $r \leq R(t)$.

(A₃) $\psi(r, 0) = \psi_0(r) \in C^2[0, R(0)]$, $0 \leq \psi_0(r) \leq \bar{\sigma}$, $\sigma'(0) = 0$ and $\sigma_0(0) = G(0)$.

The paper is organized as follows: In Section 2 the existence and uniqueness of a local and global solution to problem (1)-(5) is proved. Section 3 is devoted to the quasi-stationary case $c = 0$. In section 4, we discuss the asymptotic behavior of the solutions to problem (1)-(5). In the last section, we give a conclusion.

2. Global existence and uniqueness.

Lemma 2.1. *The function $p(x) = \frac{x \coth x - 1}{x^2}$ has the following properties:*

- (1) $p'(x) < 0$ for all $x > 0$, and $\lim_{x \rightarrow 0^+} p(x) = \frac{1}{3}$, $\lim_{x \rightarrow \infty} p(x) = 0$.
- (2) $x^3 p(x)$ is strictly monotone increasing for $x > 0$.

Proof. The proof of (1) can be found in [14] and the proof of (2) can be found in [10]. \square

From Lemma 2.1(1), we see that $\lim_{x \rightarrow 0^+} p(x) = 1/3$. Define $p(0) = 1/3$, then p is continuous on \mathbb{R} . In this paper, we define $p(0) = 1/3$.

Lemma 2.2. *If $(\sigma(r, t), R(t))$ is a solution to problem (1)-(5), then*

- (i) $0 \leq \sigma(r, t) \leq \bar{\sigma}$, for $0 \leq r \leq R(t)$, $t \geq 0$.
- (ii) $R(0) \exp(-\frac{\mu \tilde{\sigma} t}{3}) \leq R(t) \leq a \exp(\frac{bt}{3})$, for $t \geq 0$, where $a = \sqrt[3]{1 + \mu \bar{\sigma} \tau} |\varphi|$, $|\varphi| = \max_{-\tau \leq t \leq 0} \varphi(t)$, $b = \mu(\bar{\sigma} + \tilde{\sigma})$.
- (iii) For any $t > 0$, $-\frac{1}{3} \mu \tilde{\sigma} \leq \frac{R'(t)}{R(t)} \leq \frac{1}{3} \mu M$, where $M = \bar{\sigma} \exp(\mu \tilde{\sigma} \tau)$.
- (iv) For any $t > 0$, $R(0) \exp(-\frac{\mu \tilde{\sigma} t}{3}) \leq R(t) \leq R(0) \exp(\frac{\mu M t}{3})$.

Proof. (i) By the maximum principle, we immediately have $0 \leq \sigma(r, t) \leq \bar{\sigma}$, for $0 \leq r \leq R(t)$, $t \geq 0$.

(ii) From (3), one can get

$$-\frac{\mu \tilde{\sigma} R(t)}{3} \leq \frac{dR(t)}{dt} \leq \frac{\mu}{3R^2(t)} [\bar{\sigma} R^3(t - \tau) - \tilde{\sigma} R^3(t)], t > 0, \quad (7)$$

which implies that $R(t) \geq R(0) \exp(-\frac{\mu \tilde{\sigma} t}{3})$ and

$$\frac{d\eta(t)}{dt} \leq \mu[\bar{\sigma} \eta(t - \tau) - \tilde{\sigma} \eta(t)],$$

where $\eta = R^3$. By Lemma 3.1 in [10] and Theorem 3.1 in Chapter 1 [17], we have

$$\eta(t) \leq a^3 \exp(bt)$$

for $t \geq 0$, where $a = \sqrt[3]{1 + \mu \bar{\sigma} \tau} |\varphi|$, $|\varphi| = \max_{-\tau \leq t \leq 0} \varphi(t)$, $b = \mu(\bar{\sigma} + \tilde{\sigma})$. Then $R(t) \leq a \exp(\frac{bt}{3})$ follows.

(iii) By the left-hand side of the inequality (7), we have $(R \exp(\frac{\mu \tilde{\sigma} t}{3}))' \geq 0$. It follows that

$$\left(\frac{R(t - \tau)}{R(t)} \right)^3 \leq \exp(\mu \tilde{\sigma} \tau). \quad (8)$$

From the right-hand side of the inequality (7), we know

$$\frac{R'}{R} \leq \frac{1}{3} \mu \bar{\sigma} \left(\frac{R(t - \tau)}{R(t)} \right)^3 \leq \frac{1}{3} \mu M, \quad (9)$$

where $M = \bar{\sigma} \exp(\mu \tilde{\sigma} \tau)$.

(iv) It can be easily got from (iii). \square

Theorem 2.3. *Assume that the conditions (A_1) , (A_2) and (A_3) are satisfied, then problem (1)-(5) has a unique solution $(\sigma(r, t), R(t))$ for all $t \geq -\tau$.*

Proof. For arbitrary $T > 0$, we introduce a metric space (M_T, d) as follows: The set M_T consists of vector functions $(\sigma(r, t), R(t))$ satisfying

(I) $R \in C[-\tau, T] \cap C^1[0, T]$, $R(t) = \varphi(t)$ for $-\tau \leq t \leq 0$, and for $0 < t \leq T$,

$$-\frac{1}{3}\mu\tilde{\sigma} \leq \frac{R'(t)}{R(t)} \leq \frac{1}{3}\mu M.$$

(II) $\sigma \in C([0, \infty) \times [-\tau, T])$, and

$$0 \leq \sigma(r, t) \leq \bar{\sigma}, \quad 0 \leq r \leq R(t), \quad 0 < t \leq T,$$

$$\sigma(R(t), t) = G(t), \quad 0 < t \leq T,$$

$$\sigma(r, t) = \psi(r, t), \quad -\tau \leq t \leq 0.$$

The metric d is defined by

$$d((\sigma_1, R_1), (\sigma_2, R_2))$$

$$= \max_{r \geq 0, -\tau \leq t \leq T} |\sigma_1(r, t) - \sigma_2(r, t)| + \max_{-\tau \leq t \leq T} |R_1(t) - R_2(t)|.$$

It is clear that (M_T, d) is a complete metric space.

Define a mapping $F : (\sigma, R) \rightarrow (\hat{\sigma}, \hat{R})$ in the following way.

$$c \frac{\partial \hat{\sigma}}{\partial t} = \frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial \hat{\sigma}}{\partial r} \right) - \lambda \sigma, \quad 0 < r < R(t), \quad t > 0, \quad (10)$$

$$\frac{\partial \hat{\sigma}}{\partial r}(0, t) = 0, \quad \hat{\sigma}(\hat{R}(t), t) = G(t), \quad 0 < r < R(t), \quad t > 0, \quad (11)$$

$$\frac{d\hat{R}}{dt} = \frac{\mu \hat{R}(t)}{R^3(t)} \left(\int_0^{R(t-\tau)} \mu \sigma(r, t-\tau) r^2 dr - \int_0^{R(t)} \mu \tilde{\sigma} r^2 dr \right), \quad t > 0, \quad (12)$$

$$\hat{\sigma}(r, t) = \psi(r, t), \quad 0 < r < R(t), \quad -\tau \leq t \leq 0, \quad (13)$$

$$\hat{R}(t) = \varphi(t), \quad -\tau \leq t \leq 0. \quad (14)$$

Define $\sigma(r, t) = G(t)$ for $r \geq R(t)$. Using similar arguments [9], we can prove F is a contraction for $T > 0$ is small. Therefore, Banach fixed point theorem implies the local existence and uniqueness of a solution to the problem (1)-(5). By a continuation theorem, to prove global existence and uniqueness, we only need to prove that the local solution can not blow up or tend to zero in a finite time interval. This can be got from Lemma 2.2(ii). \square

3. The quasi-stationary case $c = 0$. In this section, we study the the quasi-stationary case $c = 0$. To reduce the number of coefficients, by a resealing arguments, we always set $\lambda = \mu = \bar{\sigma} = 1$ as [19].

The solution of (1)-(2) is

$$\sigma(r, t) = \left(1 - \frac{\gamma}{R(t)}\right) \frac{R(t) \sinh r}{r \sinh R(t)} H(R(t)). \quad (15)$$

Substituting (15) into (3), we have

$$\frac{dR}{dt} = \frac{1}{R^2} \left[R_\tau^3 p(R_\tau) \left(1 - \frac{\gamma}{R_\tau}\right) H(R_\tau) - \frac{\tilde{\sigma}}{3} R^3 \right], \quad (16)$$

where $R_\tau = R(t - \tau)$, $p(x) = \frac{x \coth x - 1}{x^2}$. Thus, for the quasi-stationary case, we only need to study Eq.(16) with initial condition (5).

Denote

$$f(x, y) = \frac{1}{x^2} \left[y^3 p(y) \left(1 - \frac{\gamma}{y}\right) H(y) - \frac{\tilde{\sigma}}{3} x^3 \right] \quad (17)$$

and

$$K(x) = 3p(x) \left(1 - \frac{\gamma}{x}\right) H(x). \quad (18)$$

The function (18) has properties as follows, please see [18] or [19]:

- (1) $K(x) = 0$ for $0 < x \leq \gamma$; $K(x) > 0$ for $x > \gamma$ and $\lim_{x \rightarrow \infty} K(x) = 0$.
- (2) $K(x)$ has a unique extremum point $r_\# \in [2\gamma, 2\gamma + 2]$ such that $K'(x) > 0$ for $\gamma < x < r_\#$, $K'(x) = 0$ for $x = r_\#$, $K'(x) < 0$ for $x > r_\#$ and $0 < \theta_* := K(r_\#) = \max_{x>0} K(x) < 1$.

Recall that the stationary solution which is denoted by $(\sigma_s(r), R_s)$ for $R_s > 0$ satisfies the following two equations.

$$\sigma_s(r) = \left(1 - \frac{\gamma}{R_s}\right) \frac{R_s \sinh r}{r \sinh R_s} H(R_s), \quad (19)$$

$$F(R_s, R_s) = \frac{1}{3} [K(R_s) - \tilde{\sigma}] R_s = 0. \quad (20)$$

From [18, 19], we know that there exists a positive constant $\theta_* = K(r_\#) = \max_{x>0} K(x)$ such that the following assertions hold:

- (P1) If $\tilde{\sigma} > \theta_*$, then Eq. $F(x, x) = 0$ has no positive solution.
- (P2) If $\tilde{\sigma} = \theta_*$, then Eq. $F(x, x) = 0$ has a unique positive solution R_s .
- (P3) If $0 < \tilde{\sigma} < \theta_*$, then Eq. $F(x, x) = 0$ has two positive solutions R_{s1} and R_{s2} satisfying $R_{s1} < R_{s2}$ with $F'(R_{s1}, R_{s1}) > 0$ and $F'(R_{s2}, R_{s2}) < 0$, where $F'(x, x)$ represents the derivative of F with respect to x .

Then we can get

Theorem 3.1. (i) If $\tilde{\sigma} > \theta_*$, problem (1)-(5) has no positive stationary solution.

(ii) If $\tilde{\sigma} = \theta_*$, problem (1)-(5) has a unique positive stationary solution $(\sigma_s(r), R_s)$.

(iii) If $0 < \tilde{\sigma} < \theta_*$, problem (1)-(5) has two positive stationary solutions $(\sigma_{s1}(r), R_{s1})$ and $(\sigma_{s2}(r), R_{s2})$ satisfying $R_{s1} < R_{s2}$.

Lemma 3.2. Consider the initial value problem of a delay differential equation

$$\dot{x}(t) = f(x(t), x(t - \tau)), \quad t > 0, \quad (21)$$

$$x(t) = x^0(t), \quad -\tau \leq t \leq 0. \quad (22)$$

Assume that the function f is defined and continuously differentiable in $R_+ \times R_+$ and strictly monotone increasing in the second variable, we have following results:

(1) If x_s be a positive solution of equation $f(x, x) = 0$ such that $f(x, x) > 0$ for x less than but near x_s , $f(x, x) < 0$ for x greater than but near x_s . Let (c, d) be the (maximal) interval containing only the root x_s of equation $f(x, x) = 0$. If $x(t)$ be the solution of the problem of (21), (22), assume that $x^0(t) \in C[-\tau, 0]$, and $c < x^0(t) < d$ for $-\tau \leq t \leq 0$. Then $\lim_{t \rightarrow \infty} x(t) = x_s$.

(2) If $f(x, x) < 0$ for all $x > 0$, then $\lim_{t \rightarrow \infty} x(t) = 0$.

(3) If x_s be a positive solution of equation $f(x, x) = 0$ such that $f(x, x) < 0$ for $0 < x < x_s$ and $f(0, 0) = 0$. If $x(t)$ be the solution of the problem of (21), (22), assume that $x^0(t) \in C[-\tau, 0]$ and $0 \leq x^0(t) < x_s$ for $-\tau \leq t \leq 0$, then $\lim_{t \rightarrow \infty} x(t) = 0$.

(4) If x_s be a positive solution of equation $f(x, x) = 0$ such that $f(x, x) < 0$ for $x > x_s$. If $x(t)$ be the solution of the problem of (21), (22), assume that $x^0(t) \in C[-\tau, 0]$ and $x^0(t) > x_s$ for $-\tau \leq t \leq 0$, then $\lim_{t \rightarrow \infty} x(t) = x_s$.

Proof. For the proof of (1) and (2), please see Lemma 3.4 in [10]. Next, following the idea of [10], we prove (3). First we claim that if $x^0(t) < x_s$ for $-\tau \leq t \leq 0$, then $x(t) < x_s$ for all $t > 0$. If not, there exists a point t_0 such that

$$x(t_0) = x_s, \quad x'(t_0) > 0, \quad x(t) < x_s \text{ for } t < t_0. \quad (23)$$

On the other hand,

$$x'(t_0) = f(x(t_0), x(t_0 - \tau)) < f(x_s, x_s) = 0,$$

which is in contradiction with (23). Thus the claim is true.

In the following, we prove: If $0 \leq x^0(t) < x_s$ for $-\tau \leq t \leq 0$, then $\lim_{t \rightarrow \infty} x(t) = 0$. Consider the following initial problem:

$$\dot{x}(t) = f(x(t), x(t - \tau)), \quad t > 0, \quad (24)$$

$$x(t) = C < x_s, \quad -\tau \leq t \leq 0. \quad (25)$$

By the assumption we see that $f(x, x) < 0$ for $x \neq x_s$. Thus $x'(0+) = f(C, C) < 0$. It follows that there exists a small $\delta > 0$ such that $x'(t) < 0$ for $0 < t < \delta$. We claim that for any $t > 0$, if $x'(t) \geq 0$ then $x(t) < x(t - \tau)$. Indeed, since $x(t) < x_s$, we have $f(x(t), x(t)) < 0$. Thus if $x(t - \tau) \leq x(t)$, then

$$x'(t) = f(x(t), x(t - \tau)) \leq f(x(t), x(t)) < 0,$$

which contradicts the condition $x'(t) \geq 0$. Hence the assertion holds. It follows immediately that

$$x(t) < C < x_s$$

for all $t > 0$. The above assertion ensures that if $[t_1, t_2]$ is an interval in which $x(t)$ is monotone nondecreasing then $t_2 - t_1 < \tau$. Thus only two cases are possible: either (i) there exists a t_0 such that $x(t)$ is monotone nonincreasing for $t \geq t_0$, or (ii) for any $t_0 > 0$, $x(t)$ is oscillating in (t_0, ∞) . In the first case one can easily deduce that $\lim_{t \rightarrow \infty} x(t) = 0$ holds. In what follows we consider the second case. We only need to prove that

$$\limsup_{t \rightarrow \infty} x(t) = 0. \quad (26)$$

Denote $x^* = \limsup_{t \rightarrow \infty} x(t)$. Clearly, we can find a monotone increasing sequence of numbers $\{t_n\}$ such that $t_n \rightarrow \infty$, $x(t_n) \rightarrow x^*$, and every t_n is a local maximum

point of the function $x = x(t)$. Since $x'(t_n) = 0$, we have $x(t_n) < x(t_n - \tau)$ ($n = 1, 2, \dots$), which implies that

$$x^* = \limsup_{t \rightarrow \infty} x(t) \geq \limsup_{n \rightarrow \infty} x(t_n - \tau) \geq \liminf_{n \rightarrow \infty} x(t_n - \tau) \geq \lim_{n \rightarrow \infty} x(t_n) = x^*.$$

Therefore, $\lim_{n \rightarrow \infty} x(t_n - \tau) = x^*$. Since

$$0 = x'(t_n) = f(x(t_n), x(t_n - \tau)), n = 1, 2, \dots \quad (27)$$

Letting $n \rightarrow \infty$, we can get $f(x^*, x^*) = 0$. Since $x(t) < C < x_s$, we have $x^* = 0$. Thus (26) is proved.

(4) The proof is similar to that of (3), we omit it here. This completes the proof. \square

Theorem 3.3. *In quasi-stationary case $c = 0$, the nonnegative solution of (16) exists for $t \geq -\tau$ with nonnegative initial value φ and the dynamics of solutions to this equation is as follows:*

(I) *If $\tilde{\sigma} > \theta_*$, for any nonnegative initial value φ , $\lim_{t \rightarrow \infty} R(t) = 0$.*

(II) *If $\tilde{\sigma} = \theta_*$, then in the case $\max_{-\tau \leq t \leq 0} \varphi(t) < R_s$, we have $\lim_{t \rightarrow \infty} R(t) = 0$ and in the case $\min_{-\tau \leq t \leq 0} \varphi(t) > R_s$, we have $\lim_{t \rightarrow \infty} R(t) = R_s$.*

(III) *If $0 < \tilde{\sigma} < \theta_*$, then in the case $\max_{-\tau \leq t \leq 0} \varphi(t) < R_{s1}$, we have $\lim_{t \rightarrow \infty} R(t) = 0$ and in the case $\min_{-\tau \leq t \leq 0} \varphi(t) > R_{s1}$, we have $\lim_{t \rightarrow \infty} R(t) = R_{s2}$.*

Proof. Let $\eta = R^3$, then (16) takes the form as follows

$$\frac{d\eta}{dt} = 3\eta_\tau p(\sqrt[3]{\eta_\tau}) \left(1 - \frac{\gamma}{\sqrt[3]{\eta_\tau}}\right) H(\sqrt[3]{\eta_\tau}) - \tilde{\sigma}\eta \quad (28)$$

and the initial condition $\eta(t) = \varphi^3(t)$ for $-\tau \leq t \leq 0$, where $\eta_\tau = \eta(t - \tau)$. It is obvious that every solution to equation (28) exists for all $t > 0$, because we may rewrite this equation in the following functional form:

$$\eta(t) = \eta(0) \exp(-\tilde{\sigma}t) + 3 \exp(-\tilde{\sigma}t) \int_0^t \exp(\tilde{\sigma}\xi) \eta_\tau p(\sqrt[3]{\eta_\tau}) \left(1 - \frac{\gamma}{\sqrt[3]{\eta_\tau}}\right) H(\sqrt[3]{\eta_\tau}) d\xi \quad (29)$$

and solve it using the step method (see, e.g., [17]) on intervals $[n\tau, (n+1)\tau]$, $n \in \mathbb{N}$. Therefore, the solution of (16) exists for $t \geq -\tau$.

Now, for any nonnegative initial value φ , we prove that every solution to equation (16) is nonnegative. Actually, since $\eta = R^3$, we only need to prove every solution to equation (28) is nonnegative for any nonnegative initial value φ . Let

$$G(s) = 3sp(\sqrt[3]{s}) \left(1 - \frac{\gamma}{\sqrt[3]{s}}\right) H(\sqrt[3]{s}).$$

By Lemma 2.1, noticing the properties of function H , it is easy to get $G(s) > 0$ for $s > 0$. By Lemma 1.1 in [1], one can get that the solution to equation (28) is nonnegative for any nonnegative initial value φ .

In the following, we will study the dynamics of solutions to equation (16). By direct computation, we have

$$\frac{\partial f}{\partial y} = \frac{1}{x^2} \left[\gamma y p(y) H(y) + H'(y) y^3 p(y) \left(1 - \frac{\gamma}{y}\right) + (y^3 p(y))' \left(1 - \frac{\gamma}{y}\right) H(y) \right].$$

By Lemma 2.1 (1),(2) and the properties of function H , we can get $\frac{\partial f}{\partial y} > 0$. Thus f is strictly monotone increasing in the second variable. By the properties of

$K(x)$ and noticing the fact

$$f(x, x) = \frac{1}{3}[K(x) - \tilde{\sigma}]x, \quad (30)$$

it immediately follows that

(S1) If $\tilde{\sigma} > \theta_*$, then $f(x, x) < 0$ for all $x > 0$.

(S2) If $\tilde{\sigma} = \theta_*$, then $f(x, x) < 0$ for all $x \neq R_s$.

(S3) If $0 < \tilde{\sigma} < \theta_*$, then $f(x, x) < 0$ for all $x < R_{s1}$, $f(x, x) > 0$ for all $R_{s1} < x < R_{s2}$ and $f(x, x) < 0$ for all $x > R_{s2}$.

By (S1) and Lemma 3.2(2), we can get: If $\tilde{\sigma} > \theta_*$, for any nonnegative initial value φ , $\lim_{t \rightarrow \infty} R(t) = 0$.

By (S2) and Lemma 3.2(3) and Lemma 3.2 (4), we can get: If $\tilde{\sigma} = \theta_*$, then in the case $\max_{-\tau \leq t \leq 0} \varphi(t) < R_s$, we have $\lim_{t \rightarrow \infty} R(t) = 0$ and in the case $\min_{-\tau \leq t \leq 0} \varphi(t) > R_s$, we have $\lim_{t \rightarrow \infty} R(t) = R_s$.

By (S3) and Lemma 3.2(1) and Lemma 3.2 (3), we can get: If $0 < \tilde{\sigma} < \theta_*$, then in the case $\max_{-\tau \leq t \leq 0} \varphi(t) < R_{s1}$, we have $\lim_{t \rightarrow \infty} R(t) = 0$ and in the case $\min_{-\tau \leq t \leq 0} \varphi(t) > R_{s1}$, we have $\lim_{t \rightarrow \infty} R(t) = R_{s2}$. This completes the proof. \square

4. Stability of stationary solutions. In this section, we study stability of stationary solutions to (1)-(5).

Lemma 4.1. *Let $(\sigma(r, t), R(t))$ be the solution to (1)-(5). If $\tilde{\sigma} > \bar{\sigma}$, then for any $c > 0$ and the initial function φ , there holds*

$$\lim_{t \rightarrow \infty} R(t) = 0. \quad (31)$$

Proof. By Lemma 2.2 (i) and (3), one can get

$$-\frac{\tilde{\sigma}R(t)}{3} \leq \frac{dR(t)}{dt} \leq \frac{1}{3R^2(t)} [\bar{\sigma}R^3(t - \tau) - \tilde{\sigma}R^3(t)], t > 0, \quad (32)$$

which implies that $R(t) \geq R(0) \exp(-\frac{\tilde{\sigma}t}{3})$ and

$$\frac{d\eta(t)}{dt} \leq \bar{\sigma}\eta(t - \tau) - \tilde{\sigma}\eta(t),$$

where $\eta = R^3$. Consider the initial problem

$$\frac{d\omega(t)}{dt} = \bar{\sigma}\omega(t - \tau) - \tilde{\sigma}\omega(t), t > 0; \omega(t) = \varphi^3(t), -\tau \leq t \leq 0.$$

Since $\tilde{\sigma} > \bar{\sigma}$, then by a well-known result of retarded differential equations (see [17]), we have

$$\lim_{t \rightarrow \infty} \omega(t) = 0.$$

By Lemma 3.1 in [10], we can get $\eta(t) \leq \omega(t)$. Thus, $\lim_{t \rightarrow \infty} \eta(t) = 0$. Then $\lim_{t \rightarrow \infty} R(t) = 0$ follows. This completes the proof. \square

Lemma 4.2. [19] *Let $(\sigma(r, t), R(t))$ be the solution to (1)-(5) and $(v(r, t), R(t))$ be the solution to the quasi-stationary case of (1)-(5), where*

$$v(r, t) = \left(1 - \frac{\gamma}{R(t)}\right) \frac{R(t) \sinh r}{r \sinh R(t)} H(R(t)).$$

For some $T > 0$ and $\varepsilon > 0$

$$|R'(t)| \leq L \leq L_0, \varepsilon \leq R(t) \leq \frac{1}{\varepsilon}. \quad (33)$$

Assume further that for $0 \leq r \leq R_0$,

$$|\sigma(r, 0) - v(r, 0)| \leq M \leq M_0. \quad (34)$$

Then, there exists a positive constant C independent of c, T, L, M and R_0 but depend of ε and γ such that

$$|\sigma(r, t) - v(r, t)| \leq C(Lc + Me^{-\frac{t}{c}}) \quad (35)$$

for arbitrary $0 \leq r \leq R(t), 0 \leq t \leq T$.

Lemma 4.3. Let $(\sigma(r, t), R(t))$ be the solution to (1)-(5). Denote $|\varphi| = \max_{-\tau \leq t \leq 0} \varphi(t)$. (1) If there exist two positive constants K and δ such that one of the following two conditions

- either $\max\{|\varphi|e^{\frac{M\tau}{3}}, R_{s2}\} + \delta \leq K$;
- or $|\varphi|e^{\frac{M\tau}{3}} + \delta \leq K < R_{s1}$

holds. Then there exists a positive constant c_0 independent of c such that for arbitrary $t \geq 0$ and $c \in (0, c_0]$,

$$R(t) \leq K. \quad (36)$$

(2) If there exists a positive constant δ such that $\varphi(t) \geq (R_{s1} + \delta) \exp(\frac{\tilde{\sigma}\tau}{3})$ for $-\tau \leq t \leq 0$. Then there exists a positive constant c_0 independent of c such that for arbitrary $t \geq 0$ and $c \in (0, c_0]$,

$$R(t) \geq R_{s1} + \delta > R_{s1}. \quad (37)$$

Proof. (1) Let $\max\{|\varphi|e^{\frac{M\tau}{3}}, R_{s2}\} + \delta \leq K$ holds. By Lemma 2.2 (iv), noticing that $\mu = 1$, we have

$$R(0) \exp(-\frac{\tilde{\sigma}\tau}{3}) \leq R(t) \leq R(0) \exp(\frac{M\tau}{3}) \leq |\varphi| \exp(\frac{M\tau}{3}) + \delta$$

for $0 \leq t \leq \tau$. Thus, for $0 \leq t \leq \tau$, $R(t) \leq K$. Assume (36) is not valid for some t , then there exists $T > \tau$ such that

$$R(t) \leq K$$

for $0 \leq t < T$ and $R(T) = K$. Then $R'(T) \geq 0$. By Lemma 2.2(iii), for $0 \leq t < T$, we can get $|R'(t)| \leq L_0$, where L_0 is a positive constant independent of c and T . Obviously, $|\sigma(r, 0) - v(r, 0)| \leq G(0) \leq \bar{\sigma}$. By Lemma 4.2, we have

$$|\sigma(r, t) - v(r, t)| \leq C(Lc + e^{-\frac{t}{c}}) \quad (38)$$

for $0 \leq r \leq R(t), 0 \leq t < T$ and $0 < c \leq c_0$. Therefore, for $t > \tau$,

$$\begin{aligned} R'(t) &= \frac{1}{R^2(t)} \left[\int_0^{R(t-\tau)} \sigma(r, t-\tau) r^2 dr - \int_0^{R(t)} \tilde{\sigma} r^2 dr \right] \\ &\leq \frac{1}{R^2(t)} \left[\int_0^{R(t-\tau)} v(r, t-\tau) r^2 dr + \frac{C(Lc + e^{-\frac{t-\tau}{c}}) R^3(t-\tau)}{3} \right] - \frac{\tilde{\sigma} R(t)}{3} \\ &= \frac{1}{3} R(t) \left[3p(R(t-\tau)) \frac{R^3(t-\tau)}{R^3(t)} \left(1 - \frac{\gamma}{R(t-\tau)} \right) H(R(t-\tau)) - \tilde{\sigma} \right. \\ &\quad \left. + C(Lc + e^{-\frac{t-\tau}{c}}) \frac{R^3(t-\tau)}{R^3(t)} \right] \\ &\leq \frac{1}{3} R(t) \left[3p(R(t-\tau)) \frac{R^3(t-\tau)}{R^3(t)} - \tilde{\sigma} + C(Lc + e^{-\frac{t-\tau}{c}}) \frac{R^3(t-\tau)}{R^3(t)} \right]. \end{aligned}$$

It follows that

$$\begin{aligned} R'(T) &\leq \frac{1}{3}R(T) \left[3p(R(T-\tau)) \frac{R^3(T-\tau)}{R^3(T)} - \tilde{\sigma} + C(Lc + e^{-\frac{T-\tau}{c}}) \frac{R^3(T-\tau)}{R^3(T)} \right] \\ &< \frac{1}{3}R(T) \left[3p(R(T)) - \tilde{\sigma} + C(Lc + e^{-\frac{T-\tau}{c}}) \right], \end{aligned}$$

where we have used the fact that $x^3p(x)$ is monotone increasing (see Lemma 2.1 (2)). Since

$$3p(R(T)) - \tilde{\sigma} = 3p(K) - \tilde{\sigma} < 3p(R_{s_2}) - \tilde{\sigma} = 0,$$

then there exists $c_0 > 0$ sufficiently small such that $R'(T) < 0$ when $c \in (0, c_0]$. It is a contraction to $R'(T) \geq 0$. Therefore, the assertion $R(t) \leq K$ holds.

Let $|\varphi|e^{\frac{M\tau}{3}} + \delta \leq K < R_{s1}$. By Lemma 2.2 (iv), noticing that $\mu = 1$, we have

$$R(0) \exp\left(-\frac{\tilde{\sigma}\tau}{3}\right) \leq R(t) \leq R(0) \exp\left(\frac{M\tau}{3}\right)$$

for $0 \leq t \leq \tau$. Thus, for $0 \leq t \leq \tau$, $R(t) \leq K$. Assume (36) is not valid for some t , then there exists $T > \tau$ such that

$$R(t) \leq K$$

for $0 \leq t < T$ and $R(T) = K$. Then $R'(T) \geq 0$. By Lemma 2.2 (iii), for $0 \leq t < T$, we can get $|R'(t)| \leq L_0$, where L_0 is a positive constant independent of c and T . Obviously, $|\sigma(r, 0) - v(r, 0)| \leq G(0) \leq \bar{\sigma}$. By Lemma 4.2, we have

$$|\sigma(r, t) - v(r, t)| \leq C(Lc + e^{-\frac{t}{c}}) \quad (39)$$

for $0 \leq r \leq R(t)$, $0 \leq t < T$ and $0 < c \leq c_0$. Therefore, for $t > \tau$,

$$\begin{aligned} R'(t) &= \frac{1}{R^2(t)} \left[\int_0^{R(t-\tau)} \sigma(r, t-\tau) r^2 dr - \int_0^{R(t)} \tilde{\sigma} r^2 dr \right] \\ &\leq \frac{1}{R^2(t)} \left[\int_0^{R(t-\tau)} v(r, t-\tau) r^2 dr + \frac{C(Lc + e^{-\frac{t-\tau}{c}}) R^3(t-\tau)}{3} \right] - \frac{\tilde{\sigma} R(t)}{3} \\ &= \frac{1}{3} R(t) \left[3p(R(t-\tau)) \frac{R^3(t-\tau)}{R^3(t)} \left(1 - \frac{\gamma}{R(t-\tau)} \right) H(R(t-\tau)) - \tilde{\sigma} \right. \\ &\quad \left. + C(Lc + e^{-\frac{t-\tau}{c}}) \frac{R^3(t-\tau)}{R^3(t)} \right]. \end{aligned}$$

It follows that

$$\begin{aligned} R'(T) &\leq \frac{1}{3} R(T) \left[3p(R(T-\tau)) \frac{R^3(T-\tau)}{R^3(T)} \left(1 - \frac{\gamma}{R(T-\tau)} \right) H(R(T-\tau)) - \tilde{\sigma} \right. \\ &\quad \left. + C(Lc + e^{-\frac{T-\tau}{c}}) \frac{R^3(T-\tau)}{R^3(T)} \right] \\ &\leq \frac{1}{3} R(T) \left[3p(R(T)) \left(1 - \frac{\gamma}{R(T)} \right) H(R(T)) - \tilde{\sigma} + C(Lc + e^{-\frac{T-\tau}{c}}) \right], \end{aligned}$$

where we have used the fact that $3p(x)(1 - \frac{\gamma}{x})H(x)$ is monotone increasing for $0 < x \leq R_{s1}$ (see Section 3). Since

$$3p(R(T)) \left(1 - \frac{\gamma}{R(T)} \right) H(R(T)) - \tilde{\sigma} < 3p(R_{s1}) \left(1 - \frac{\gamma}{R_{s1}} \right) H(R_{s1}) - \tilde{\sigma} = 0,$$

then there exists $c_0 > 0$ sufficiently small such that $R'(T) < 0$ when $c \in (0, c_0]$. It is a contraction to $R'(T) \geq 0$. Therefore, the assertion $R(t) \leq K$ holds.

(2) Let $\varphi(t) \geq (R_{s1} + \delta) \exp(\frac{\tilde{\sigma}t}{3})$ for $-\tau \leq t \leq 0$. By Lemma 2.2(iv), noticing that $\mu = 1$, we have

$$R_{s1} + \delta \leq R(0) \exp(-\frac{\tilde{\sigma}\tau}{3}) \leq R(t) \leq R(0) \exp(\frac{M\tau}{3})$$

for $0 \leq t \leq \tau$. Thus, for $0 \leq t \leq \tau$, $R(t) > R_{s1} + \delta$. Assume (37) is not valid for some t , then there exists $T > \tau$ such that

$$R(t) > R_{s1} + \delta.$$

for $0 \leq t < T$ and $R(T) = R_{s1} + \delta$. If $R(T) = R_{s1} + \delta$, then $R'(T) \leq 0$. By Lemma 2.2 (iii), for $0 \leq t < T$, we can get $|R'(t)| \leq L_0$, where L_0 is a positive constant independent of c and T . Obviously, $|\sigma(r, 0) - v(r, 0)| \leq G(0) \leq \tilde{\sigma}$. By Lemma 4.2, we have

$$|\sigma(r, t) - v(r, t)| \leq C(Lc + e^{-\frac{t}{c}}) \quad (40)$$

for $0 \leq r \leq R(t)$, $0 \leq t < T$ and $0 < c \leq c_0$. Therefore, for $t > \tau$,

$$\begin{aligned} R'(t) &= \frac{1}{R^2(t)} \left[\int_0^{R(t-\tau)} \sigma(r, t-\tau) r^2 dr - \int_0^{R(t)} \tilde{\sigma} r^2 dr \right] \\ &\geq \frac{1}{R^2(t)} \left[\int_0^{R(t-\tau)} v(r, t-\tau) r^2 dr - \frac{C(Lc + e^{-\frac{t-\tau}{c}}) R^3(t-\tau)}{3} \right] - \frac{\tilde{\sigma} R(t)}{3} \\ &= \frac{1}{3} R(t) \left[3p(R(t-\tau)) \frac{R^3(t-\tau)}{R^3(t)} \left(1 - \frac{\gamma}{R(t-\tau)} \right) H(R(t-\tau)) - \tilde{\sigma} \right. \\ &\quad \left. - C(Lc + e^{-\frac{t-\tau}{c}}) \frac{R^3(t-\tau)}{R^3(t)} \right]. \end{aligned}$$

It follows that

$$\begin{aligned} R'(T) &\geq \frac{1}{3} R(T) \left[3p(R(T-\tau)) \frac{R^3(T-\tau)}{R^3(T)} \left(1 - \frac{\gamma}{R(T-\tau)} \right) H(R(T-\tau)) - \tilde{\sigma} \right. \\ &\quad \left. - C(Lc + e^{-\frac{T-\tau}{c}}) \frac{R^3(T-\tau)}{R^3(T)} \right] \\ &\geq \frac{1}{3} R(T) \left[3p(R_{s1} + \delta) \frac{(R_{s1} + \delta)^3}{R_{s1}^3} \left(1 - \frac{\gamma}{(R_{s1} + \delta)^3} \right) H(R_{s1} + \delta) - \tilde{\sigma} \right. \\ &\quad \left. - C(Lc + e^{-\frac{T-\tau}{c}}) \right] \\ &\geq \frac{1}{3} R(T) \left[3p(R_{s1} + \delta) \left(1 - \frac{\gamma}{(R_{s1} + \delta)^3} \right) H(R_{s1} + \delta) - \tilde{\sigma} - C(Lc + e^{-\frac{T-\tau}{c}}) \right], \end{aligned}$$

where we have used the fact that $3x^3p(x)(1 - \frac{\gamma}{x})H(x)$ is monotone increasing (see Section 3). By the fact that $3p(x)(1 - \frac{\gamma}{x})H(x) > 0$ for $R_{s1} < x < R_{s2}$ (see Section 3), for $0 < \delta < R_{s2} - R_{s1}$, we have

$$3p(R_{s1} + \delta) \left(1 - \frac{\gamma}{(R_{s1} + \delta)^3} \right) H(R_{s1} + \delta) - \tilde{\sigma} > 0.$$

Then there exists $c_0 > 0$ sufficiently small such that $R'(T) > 0$ when $c \in (0, c_0]$. It is a contraction to $R'(T) \leq 0$. Therefore, the assertion $R(t) > R_{s1} + \delta$ holds. This completes the proof. \square

Remark 1. Lemma 4.3 in [19] is the special case of Lemma 4.3 (1) above where $\tau = 0$.

Lemma 4.4. Let $(\sigma(r, t), R(t))$ be the solution to (1)-(5). Let $\delta > 0$ satisfies $0 < \delta < \min\{R_{s2} - R_{s1}, 1/R_{s2}\}$ and $(R_{s1} + \delta) \exp(-\frac{\tilde{\sigma}\tau}{3}) \leq \varphi(t) < 1/\delta$, $-\tau \leq t \leq 0$. For a given $\alpha_0 > 0$, there exist constant C, θ, T_0 and c_0 independent of c such that the following assertions hold: If $0 < c \leq c_0$, for any $\alpha \in (0, \alpha_0]$, if the inequalities

$$|R(t) - R_{s2}| \leq \alpha, \quad |\sigma(r, t) - \sigma_{s2}(r)| \leq \alpha \quad (41)$$

hold for all $0 \leq r \leq R(t)$, $t \geq -\tau$ and $|R'(t)| \leq \alpha$ holds for all $0 \leq r \leq R(t)$, $t \geq 0$. Then also the inequalities

$$|R(t) - R_{s2}| \leq C\alpha(c + e^{-\theta t}), \quad |R'(t)| \leq C\alpha(c + e^{-\theta t}), \quad |\sigma(r, t) - \sigma_{s2}(r)| \leq C\alpha(c + e^{-\theta t}) \quad (42)$$

hold for all $0 \leq r \leq R(t)$, $t \geq T_0 + \tau$.

Proof. Since $\delta > 0$ satisfies $0 < \delta < \min\{R_{s2} - R_{s1}, 1/R_{s2}\}$ and $(R_{s1} + \delta) \exp(-\frac{\tilde{\sigma}\tau}{3}) \leq \varphi(t) < 1/\delta$, $-\tau \leq t \leq 0$, noticing $1/\delta > R_{s2}$, by Lemma 4.3, one can get $R_{s1} + \delta \leq R(t) < 1/\delta$ for $t \geq 0$. Let

$$G(x, y) = \frac{f(x, y)}{x},$$

where $f(x, y) = \frac{1}{x^2} \left[y^3 p(y) \left(1 - \frac{\gamma}{y} \right) H(y) - \frac{\tilde{\sigma}}{3} x^3 \right]$ is defined by (17). Since

$$\frac{1}{R^2(t)} \left[\int_0^{R(t-\tau)} v(r, t-\tau) r^2 dr - \int_0^{R(t)} \tilde{\sigma} r^2 dr \right] = R(t)G(R(t), R(t-\tau)), \quad (43)$$

we can get

$$\begin{aligned} |R'(t) - R(t)G(R(t), R(t-\tau))| &= \left| \frac{1}{R^2(t)} \int_0^{R(t-\tau)} [\sigma(r, t-\tau) - v(r, t-\tau)] r^2 dr \right| \\ &\leq \frac{1}{3} R(t) C\alpha \left(c + e^{-\frac{t-\tau}{c}} \right) \frac{R^3(t-\tau)}{R^3} \\ &= \frac{1}{3\delta^3 R_{s1}^3} R(t) C\alpha \left(c + e^{-\frac{t-\tau}{c}} \right) \\ &=: C_2 \alpha R(t) \left(c + e^{-\frac{t-\tau}{c}} \right) \end{aligned}$$

for $t \geq \tau$. By the fact that

$$e^{-\frac{t-\tau}{c}} \leq e^{-\frac{\tau}{c}} \leq \frac{c}{\tau}$$

for $t \geq 2\tau$, thus it follows that for $t \geq 2\tau$

$$|R'(t) - R(t)G(R(t), R(t-\tau))| \leq C_3 \alpha c R(t). \quad (44)$$

where C_3 is a positive constant independent of α and c . Here and hereafter, for easy of notation we use the same notation to denote various different positive constants independent of α and c . Consider the initial value problem

$$\frac{dR^\pm}{dt} = R^\pm(t)[G(R^\pm(t), R^\pm(t-\tau)) \pm C\alpha c], \quad t \geq 0, \quad (45)$$

$$R(t) = \varphi(t), \quad -\tau \leq t \leq 0. \quad (46)$$

By (P3), it is easy to get that there exists $c_0 > 0$ such that for $c \in (0, c_0]$, the Eqs. $G(x, x) \pm C\alpha c = 0$ has two positive solutions R_{s1}^\pm and R_{s2}^\pm respectively, and satisfy

$$R_{s1}^+ < R_{s1} < R_{s1}^- < R_{s1} + \delta/2 < R_{s2}^- < R_{s2} < R_{s2}^+.$$

By similar proof as that of Theorem 3.3, it is not hard to get that the nonnegative solution of (45) exists for $t \geq -\tau$ with nonnegative initial value (46) and

$$\lim_{t \rightarrow \infty} R^\pm(t) = R_{s2}^\pm. \quad (47)$$

By the fact that $p(x)$ is monotone decreasing for all $x > 0$, we can get

$$|R_{s2}^\pm - R_{s2}| \leq C\alpha c. \quad (48)$$

Since $\frac{\partial f}{\partial y} > 0$ and $G(x, y) = f(x, y)/x$, we can get $\frac{\partial G}{\partial y} > 0$, thus $G(x, y) \pm C\alpha c$ is monotone increasing in y . By comparison principle (cf. [10] Lemma 3.1), we have

$$R^-(t) \leq R(t) \leq R^+(t) \quad (49)$$

for $t \geq 0$. By linearizing Eqs.(45) at the stationary point R_{s2}^+ and R_{s2}^- respectively, one can get

$$\frac{dR^+}{dt} = -A_1 R^+(t) + B_1 R^+(t - \tau), \quad (50)$$

$$\frac{dR^-}{dt} = -A_2 R^-(t) + B_2 R^-(t - \tau), \quad (51)$$

where

$$A_1 = A_2 = 3Q(R_{s2}^+), \quad B_1 = B_2 = 3Q(R_{s2}^+) + R_{s2}^+ Q'(R_{s2}^+),$$

and

$$Q(x) = \frac{x \coth x - 1}{x^2} (1 - \frac{\gamma}{x}) H(x) = p(x) (1 - \frac{\gamma}{x}) H(x).$$

From [19] we know that $Q'(R_{s2}^\pm) < 0$, $Q(R_{s2}^\pm) > 0$. Since

$$3Q(R_{s2}^\pm) + Q'(R_{s2}^\pm) R_{s2}^\pm = x^{-2} (x^3 Q(x))' |_{x=R_{s2}^\pm} = \frac{\partial f}{\partial y} |_{x=y=R_{s2}^\pm} > 0,$$

it follows that

$$A_1 > B_1 > 0, \quad A_2 > B_2 > 0$$

for $c \in (0, c_0]$ and $\alpha \in (0, \alpha_0]$. This implies that all complex roots of the characteristic equations of Eqs.(50) and (51) are located in the left half plane. Therefore, noticing (47), there exist positive constants M, θ_0 and T_0 such that for $t > T_0$,

$$|R^\pm(t) - R_{s2}^\pm| \leq M e^{-\theta_1 t} |\varphi| - R_{s2}^\pm|. \quad (52)$$

Then we can get that for any $t \geq T_0$,

$$\begin{aligned} |R(t) - R_{s2}| &\leq \max |R^\pm(t) - R_{s2}| \\ &\leq \max |R^\pm(t) - R_{s2}^\pm| + \max |R_{s2}^\pm - R_{s2}| \\ &\leq M e^{-\theta_1 t} \max |\varphi| - R_{s2}^\pm| + C\alpha c \\ &\leq M e^{-\theta_1 t} (|\varphi| - R_{s2}^\pm| + \max |R_{s2} - R_{s2}^\pm|) + C\alpha c \\ &\leq C\alpha (c + e^{-\theta_1 t}). \end{aligned}$$

By the mean value theorem and the fact that

$$v_{s2}(r) = \sigma_{s2}(r) = \left(1 - \frac{\gamma}{R_{s2}}\right) \frac{R_{s2} \sinh r}{r \sinh R_{s2}} H(R_{s2}),$$

we have

$$|v(r, t) - \sigma_{s2}(r)| \leq |v(r, t) - v_{s2}(r)| \leq C |R(t) - R_{s2}| \leq C\alpha \quad (53)$$

for $0 \leq r \leq R(t)$. It follows that

$$|\sigma(r, t) - v(r, t)| \leq |\sigma(r, t) - \sigma_{s2}(r)| + |v(r, t) - v_{s2}(r)| \leq C\alpha. \quad (54)$$

In particular, $|\sigma(r, 0) - v(r, 0)| \leq C\alpha$ for $0 \leq r \leq R(0)$. Since $|R'(t)| \leq \alpha$ for all $t \geq 0$, by Lemma 4.2 there exists a positive constant c_0 independent of c and α such that

$$|\sigma(r, t) - v(r, t)| \leq C\alpha(c + e^{-\frac{t}{c_0}}) \quad (55)$$

for $0 \leq r \leq R(t)$, $t \geq 0$, $0 < \alpha \leq \alpha_0$ and $0 < c \leq c_0$.

Denote

$$h(t) = \frac{1}{R^3(t)} \left[\int_0^{R(t-\tau)} \mu\sigma(r, t-\tau)r^2 dr - \int_0^{R(t)} \mu\tilde{\sigma}r^2 dr \right].$$

Since $R_{s1} + \delta \leq R(t) < 1/\delta$ for $t \geq 0$, we have

$$\begin{aligned} |R(t)(h(t) - G(R(t), R(t-\tau)))| &= \left| \frac{1}{R^2(t)} \left[\int_0^{R(t-\tau)} [\sigma(r, t-\tau) - v(r, t-\tau)]r^2 dr \right] \right| \\ &\leq \frac{1}{3}R(t)C\alpha(c + e^{-\frac{t-\tau}{c}}) \left(\frac{R^3(t-\tau)}{R^3(t)} \right) \\ &\leq C\alpha(c + e^{-\frac{t-\tau}{c_0}}) \\ &\leq C\alpha(c + e^{-\frac{t}{c_0}}) \end{aligned}$$

for $t \geq 2\tau$. By the mean value theorem and the fact $R_{s1} + \delta \leq R(t) < 1/\delta$ for $t \geq 0$, we can get

$$\begin{aligned} |G(R(t), R(t-\tau))| &= |G(R(t), R(t-\tau)) - G(R_{s2}, R_{s2})| \\ &= |p(R(t-\tau)) \left(\frac{R^3(t-\tau)}{R^3(t)} \right) - p(R(t-\tau)) \left(\frac{R_{s2}^3}{R_{s2}^3} \right)| \\ &\leq C(|R(t) - R_{s2}| + |R(t-\tau) - R_{s2}|) \\ &\leq C\alpha(c + e^{-\theta_1 t}) \end{aligned}$$

for $t \geq T_0 + \tau$. Then $|R'(t)| \leq C\alpha(c + e^{-\theta_1 t})$ follows from $R'(t) = R(t)h(t)$. Let $\theta = \min\{\theta_1, -\frac{1}{c_0}\}$. Then $|\sigma(r, t) - \sigma_{s2}(r)| \leq C\alpha(c + e^{-\theta t})$ follows from (53), (55) and

$$|\sigma(r, t) - \sigma_{s2}(r)| \leq |\sigma(r, t) - v(r, t)| + |v(r, t) - \sigma_{s2}(r)|.$$

The proof of Lemma 4.4 is completed. \square

Theorem 4.5. *Let $(\sigma(r, t), R(t))$ be the solution to (1)-(5). Assume $0 < \tilde{\sigma} < \theta_*$.*

(1) *Suppose for some small $\varepsilon > 0$, $0 < |\varphi|e^{\frac{M\tau}{3}} \leq R_{s1} - \varepsilon$ holds. Then there exists a positive constant c_0 independent of c such that*

$$\lim_{t \rightarrow \infty} R(t) = 0$$

for $0 < c \leq c_0$.

(2) *Suppose for some small $\varepsilon > 0$, $(R_{s1} + \varepsilon)\exp(\frac{\tilde{\sigma}\tau}{3}) \leq \varphi(t) \leq \frac{1}{\varepsilon}$ holds for $-\tau \leq t \leq 0$. Then there exists a positive constant c_0 independent of c such that*

$$\lim_{t \rightarrow \infty} R(t) = R_{s2}$$

for $0 < c \leq c_0$.

Assume $\theta_* < \tilde{\sigma} < 1$, then the following assertion holds.

(3) For any initial value φ satisfying (A₁), there exists a positive constant c_0 such that for $0 < c < c_0$, there holds

$$\lim_{t \rightarrow \infty} R(t) = 0.$$

Proof. (1) Choose $\varepsilon > 0$ sufficiently small such that $K = R_{s1}e^{\frac{M\tau}{3}} - \varepsilon/2 > 0$ and let $\delta = \varepsilon/2$. Then $|\varphi|e^{\frac{M\tau}{3}} + \delta \leq K < R_{s1}$. By Lemma 4.3, we know that there exists $c_1 > 0$ such that for $c \in (0, c_1]$, there holds $R(t) \leq K$ for $t \geq 0$. From the proof of Lemma 4.3, we know that

$$R'(t) \leq \frac{1}{3}R(t) \left[3p(R_\tau) \frac{R_\tau^3}{R^3(t)} \left(1 - \frac{\gamma}{R_\tau} \right) H(R_\tau) - \tilde{\sigma} + C(Lc + e^{-\frac{t-\tau}{c}}) \frac{R_\tau^3}{R^3(t)} \right],$$

where $R_\tau = R(t - \tau)$. Consider the following initial value problem

$$\rho'(t) = \frac{1}{3}\rho(t) \left[3p(\rho_\tau) \frac{\rho_\tau^3}{\rho^3(t)} \left(1 - \frac{\gamma}{\rho_\tau} \right) H(\rho_\tau) - \tilde{\sigma} + C(Lc + e^{-\frac{t-\tau}{c}}) \frac{\rho_\tau^3}{\rho^3(t)} \right], \quad t \geq 2\tau, \quad (56)$$

$$\rho(t) = R(t), \quad \tau \leq t \leq 2\tau, \quad (57)$$

where $\rho_\tau = \rho(t - \tau)$. Let

$$L(x, y) = \frac{1}{3}x \left[3p(y) \frac{y^3}{x^3} \left(1 - \frac{\gamma}{y} \right) H(y) - \tilde{\sigma} + C(Lc + e^{-\frac{t-\tau}{c}}) \frac{y^3}{x^3} \right].$$

Then $L(x, x) = \frac{1}{3}x \left[K(x) - \tilde{\sigma} + C(Lc + e^{-\frac{t-\tau}{c}}) \right]$. Obviously, from (S3) in Section 3 we know $K(x) - \tilde{\sigma} < 0$ for $x < R_{s1}$ and $L(0, 0) = 0$. By the fact that

$$e^{-\frac{t-\tau}{c}} \leq e^{-\frac{\tau}{c}} \leq \frac{c}{\tau}$$

for $t \geq 2\tau$. Then there exists $c_2 > 0$ such that $L(x, x) < 0$ for $x < R_{s1}$ and $0 < c \leq c_2$. Form Lemma 2.1 (2), we know that $y^3p(y)$ is monotone increasing in y , it follows that $\frac{\partial L}{\partial y} > 0$. By Lemma 3.2(3), we have $\lim_{t \rightarrow \infty} \rho(t) = 0$. Set $c_0 = \min\{c_1, c_2\}$. By Lemma 3.1 in [10], we can get $R(t) \leq \rho(t)$ for $0 < c < c_0$. Thus, $\lim_{t \rightarrow \infty} R(t) = 0$.

(2) Choose $\varepsilon > 0$ sufficiently small. Let $K = \max\{R_{s2}, \frac{1}{\varepsilon}\} + \varepsilon$ and $\delta = \min\{\varepsilon, R_{s2} - R_{s1}, \frac{1}{R_{s2}}\}$. Then $\max\{|\varphi|, R_{s2}\} + \delta \leq K$. Since $(R_{s1} + \varepsilon) \exp(\frac{\tilde{\sigma}\tau}{3}) \leq \varphi \leq \frac{1}{\varepsilon}$, by Lemma 4.3, one can get $R_{s1} \leq R(t) \leq K$ for all $t \geq 0$. It follows that

$$|R(t) - R_{s2}| \leq K + R_{s2} =: \alpha_1. \quad \text{From (32), we get that } |R'(t)| \leq \frac{\bar{\sigma}K^3}{3R_{s1}^2} + \frac{\tilde{\sigma}K}{3} =: \alpha_2.$$

Since $0 \leq \bar{\sigma} \leq \bar{\sigma} = 1$ (see Lemma 2.2 (i)), one can get $|\sigma(r, t) - \sigma_{s2}(r)| \leq 2$. We see that the conditions of Lemma 4.4 hold for $\alpha = \alpha_0 =: \max\{\alpha_1, \alpha_2, 2\}$. Let C and θ be as in (42), take c_0 smaller and T_0 larger such that $C\alpha_0(c + e^{-\theta T_0}) < 1/2$. Then by successively applying Lemma 4.4 over the time interval $[nT_0 + \tau, +\infty)$ as that in [8, 14], one can get the desired assertion.

(3) The proof is similar to that of (1), if $\theta_* < \tilde{\sigma} < 1$, we just need to notice that $L(x, x) < 0$ for all $x > 0$ (see (S1) in Section 3), and then by Lemma 3.2(2), the assertion $\lim_{t \rightarrow \infty} R(t) = 0$ follows. The proof of Theorem 4.5 is completed. \square

5. Conclusion. In this paper we study a free boundary problem for tumor growth with Gibbs-Thomson relation and time delays. It is assumed that the process of proliferation is delayed compared with apoptosis. The delay represents the time taken for cells to undergo mitosis. We mainly study the asymptotic behavior of the solution, and prove that in the case c (the ratio of the diffusion time scale to the tumor doubling time scale) is sufficiently small, the volume of the tumor cannot expand unlimitedly. It will either disappear or evolve to a dormant state as $t \rightarrow \infty$. The results show that dynamical behavior of solutions of the model are similar to that of solutions for corresponding nonretarded problems. More precisely, the stability of solutions to quasi-stationary case, please compare Theorem 3.1 in [19]. For the stability of solutions to (1)-(5), please see Theorem 4.5 in [19]. We hope that the analysis methods and the results would be useful to analysis of other similar retarded differential equations.

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E-mail address: shihe56789@163.com

E-mail address: 124204602@qq.com

E-mail address: fangweizhang@aliyun.com