ANALYSIS OF A FREE BOUNDARY PROBLEM FOR AVASCULAR TUMOR GROWTH WITH A PERIODIC SUPPLY OF NUTRIENTS

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Abstract. In this paper we study a free boundary problem for the growth of avascular tumors. The establishment of the model is based on the diffusion of nutrient and mass conservation for the two processes proliferation and apoptosis (cell death due to aging). It is assumed the supply of external nutrients is periodic. We mainly study the long time behavior of the solution, and prove that in the case $c$ is sufficiently small, the volume of the tumor cannot expand unlimitedly. It will either disappear or evolve to a positive periodic state.

1. Introduction. Over the last forty years, a variety of partial differential equation models for tumor growth or therapy have been developed, cf. [1, 4–7, 13, 14, 20–25] and references therein. Most of those models are based on the reaction diffusion equations and mass conservation law. Analysis of such free boundary problems has drawn great interest, and many interesting results have been established, cf. [2, 3, 8–12, 16–19, 26–32] and references therein.

The model we study in this paper is as follows:

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

\[
\frac{\partial \sigma}{\partial r}(0, t) = 0, \quad \sigma(R(t), t) = \phi(t), \quad 0 < r < R(t), \quad t > 0, \tag{2}
\]

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

\[
R(0) = R_0, \tag{4}
\]

\[
\sigma(r, 0) = \sigma_0(r), \quad 0 \leq r \leq R_0. \tag{5}
\]

where $\sigma(r, t)$ represents nutrient concentration at radius $r$ and time $t$; $R(t)$ denote the external radius of tumor at time $t$; the term $\Gamma \sigma$ in (1) is the consumption rate of nutrient in a unit volume; $\phi(t)$ denotes the external concentration of nutrients, which is assumed to be a periodic function of a period $\omega$. The two terms on the
righthand side of (3) are explained as follows: The first term is the total volume increase in a unit time interval induced by cell proliferation, the proliferation rate is $s\sigma$; The second term is the total volume decrease in a unit time interval caused by natural death, and the natural death rate is $\tilde{s}\sigma$, here $\tilde{s}$ is a constant, $s$ is a scaling constant. $c = T_{\text{diffusion}}/T_{\text{growth}}$ is a positive constant which represents the ratio of the nutrient diffusion time scale to the tumor growth (e.g., tumor doubling) time scale, for details see (cf [16,19]). From [5,10] we know that $T_{\text{diffusion}} \approx 1\text{min}$ and $T_{\text{growth}} \approx 1\text{day}$, so that $c \ll 1$. $\sigma$ satisfies the compatibility condition $\sigma_0(R_0) = \phi(0)$.

The model presented in this paper is similar to the model of Friedman and Reitich [19], but with one modification. The modification is as follows: In [19], the external concentration of nutrients is assumed to be a constant, so that instead of that Eq. (2) employed here. In this paper, as can be seen from (2), we assume that the external concentration of nutrients is a periodic function of a period $\omega$. The idea of considering the periodic supply of external nutrients is motivated by [15]. In [15], through experiments, the authors observed that after an initial exponential growth phase leading to tumor expansion, growth saturation is observed even in the presence of a periodically applied nutrient supply. In this paper, we mainly discuss how the periodic supply of external nutrients influence the growth of avascular tumor growth. The results show the periodic supply of external nutrients have some influence on tumor growth. The main influence of the periodic supply of external nutrients on tumor growth is as follows: If $c$ is sufficiently small and $\phi_* > \tilde{\sigma}$, we prove that the volume of the tumor will evolve to a positive periodic state. If the external concentration of nutrients is assumed to be a constant $\bar{\sigma}(\tilde{\sigma})$ and $c$ is sufficiently small, Friedman and Reitich [19] have proved that the volume of the tumor will evolve to a positive steady state.

In the following of the paper, we assume that $\phi$ is a continuous differentiable function and always denote

$$\bar{\phi} = \frac{1}{\omega} \int_{0}^{\omega} \phi(t) dt, \quad \phi^* = \max_{0 \leq t \leq \omega} \phi(t), \quad \phi_* = \min_{0 \leq t \leq \omega} \phi(t)$$

and assume $\phi_* > 0$, then $\phi_* \leq \phi(t) \leq \phi^*$ for all $t \geq 0$ and $\phi_* \leq \bar{\phi} \leq \phi^*$ follows. Moreover, since $\phi$ is a continuous differentiable function of a period $\omega$, there exists a constant $K$ such that $|\phi(t)| < K$ for all $t \geq 0$.

In [2], the authors have studied the limiting case where $c = 0$. By using a comparison method, the authors discussed the dynamical behavior of solutions to the model. In [2], Necessary and sufficient conditions for the global stability of tumor free equilibrium are given; the conditions under which there exists a unique periodic solution to the model are determined and they also show that the unique periodic solution is a global attractor of all other positive solutions. In the limiting case where $c = 0$ Eq.(1), (2) can be solved exactly, and the exact expression of the evolution equation for $R$ can be obtained. This is clearly not the case for present model and the method used in [2] can not be used to present model. Using Banach fixed point theorem, a comparison method and some mathematical techniques, we mainly prove the existence and uniqueness of the global solution to the problem and asymptotic behavior of the solutions to the problem. The results show that in the case $c$ is sufficiently small and $\phi_* > \tilde{\sigma}$, the volume of the tumor cannot expand unlimitedly and it will tend to a positive periodic state. We also show that in the
case $c$ is sufficiently small and $\bar{\sigma} < \sigma$, the volume of the tumor also cannot expand unlimittedly and it will disappear as $t \to \infty$.

The paper is arranged as follows: In Section 2 we prove the existence and uniqueness of the global solution to the system (1)-(5). Section 3 is devoted to the long time behavior of the solutions to the system (1)-(5).

2. Global existence and uniqueness. We shall prove a global existence and uniqueness theorem for the problem (1)-(5) under the following assumption:

(H) $\sigma(r,0) = \sigma_0(r)$ is twice weakly differentiable on $[0,R(0)]$ [i.e., $\sigma_0(r) \in C^1[0,R_0]$ and $\sigma_0''(r)$ is Lipschitz continuous], weak derivative $\sigma_0'' \in L^\infty[0,R_0]$ and $\sigma_0'(0) = 0$, $\sigma_0(R_0) = \phi(0)$.

**Lemma 2.1.** If $c < \frac{\Gamma \phi_*}{K}$, assume $\sigma(r,t), R(t)$ is a solution to problem (1)-(5), then the following prior estimates hold:

(i) $0 \leq \sigma(r,t) \leq \phi(t)$, $0 \leq r \leq R(t)$, $t \geq 0$,

(ii) $M_1 \leq \frac{\dot{R}(t)}{R(t)} \leq M_2$ for $t \geq 0$, where $M_1 = -\frac{s\bar{\sigma}}{3}$, $M_2 = \frac{s\bar{\sigma} - s\bar{\sigma}}{3}$,

(iii) $R_0 e^{M_1 t} \leq R(t) \leq R_0 e^{M_2 t}$ for $t \geq 0$.

**Proof.** If $c < \frac{\Gamma \phi_*}{K}$, clearly, $\bar{\sigma} = 0$ and $\bar{\sigma} = \phi(t)$ are respectively lower and upper solutions of the system (1), (2) and (5). We have $0 \leq \sigma(r,t) \leq \phi(t)$, $0 \leq r \leq R(t)$, $t \geq 0$. Then

\[
-\frac{1}{R^2(t)} \int_0^{R(t)} s\bar{\sigma}^r dr \leq \frac{dR(t)}{dR} \leq \frac{s}{3R^2(t)} [\phi(t)R^3(t) - \bar{\sigma}R^3(t)], t > 0,
\]

which implies that $R(t) \geq R_0 e^{-\bar{\sigma}t} = R_0 e^{M_1 t}$ and $R(t) \leq R_0 e^{(\bar{\sigma} + \bar{\sigma})t} = R_0 e^{M_2 t}$, then (ii) and (iii) follows. \hfill $\Box$

**Theorem 2.2.** Assume that the condition (H) is satisfied and $c$ is sufficient small ($c < \frac{\Gamma \phi_*}{K}$). Then the system (1)-(5) has a unique solution $\sigma(r,t), R(t)$ for all $t \geq 0$.

**Proof.** For arbitrary $T > 0$, we introduce a metric space $(S_T, d)$ as follows: The set $S_T$ consists of vector functions $(\sigma(r,t), R(t))$, where $\sigma(r,t)$ is defined on $[0,\infty) \times [0,T]$, $R(t)$ is defined on $[0,T]$, and they satisfy the following conditions:

(I) $R \in C([0,T]) \cap C^1[0,T]$, $R(0) = R_0$, and

\[
R_0 e^{M_1 t} \leq R(t) \leq R_0 e^{M_2 t}, for 0 < t \leq T.
\]  

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

\[
\sigma(r,t) \leq \phi(t), for 0 \leq r \leq R(t), 0 < t \leq T,
\]

\[
\sigma(r,t) = \phi(t), for r \geq R(t), 0 < t \leq T,
\]

\[
\sigma(r,0) = \sigma_0(r), for 0 < r \leq R_0.
\]

The metric $d$ is defined by

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

It is clear that $(S_T, d)$ is a complete metric space.
We define a mapping $F : (\sigma(r,t), R(t)) \to (\bar{\sigma}(r,t), \bar{R}(t))$ in the following way:

$$c \frac{\partial \bar{\sigma}}{\partial t} = \Delta_r \bar{\sigma}(r,t) - \Gamma \sigma(r,t), \ 0 < r < \bar{R}(t), \ t > 0,$$

(8)

$$\frac{\partial \bar{\sigma}}{\partial r}(0,t) = 0, \ \bar{\sigma}(\bar{R}(t), t) = \phi(t), \ t > 0,$$

(9)

$$\frac{d\bar{R}(t)}{dt} = \frac{s \bar{R}(t)}{R^3(t)} \left[ \int_0^{R(t)} \sigma(r,t) r^2 dr - \int_0^{R(t)} \tilde{\sigma}r^2 dr \right], \ t > 0,$$

(10)

$$R(0) = R_0,$$

(11)

$$\sigma(r,0) = \sigma_0(r), 0 \leq r \geq R_0.$$

(12)

And define $\tilde{\sigma}(r,t) = \phi(t)$, for $r > \tilde{R}(t), 0 \leq t \leq T$. Using similar arguments as that in [10, 11], 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). Using Lemma 2.1, we can get the global existence and uniqueness of the solution.

3. Long time behavior of the solutions to (1)-(5). In this section, we study asymptotic behavior of the solutions to (1)-(5). First we consider the case $\tilde{\phi} < \tilde{\sigma}$.

**Theorem 3.1.** If $\tilde{\phi} < \tilde{\sigma}$, then for any $0 < c < \frac{\Gamma \phi_*}{R}$ and the initial value $R_0 > 0$, there holds

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

**Proof.** By Lemma 2.1 (i) and the Eq.(3), we have

$$- \frac{s}{R^2(t)} \int_0^{R(t)} \tilde{\sigma} r^2 dr \leq \frac{dR(t)}{dt} \leq \frac{s}{3R^2(t)} [\phi(t)R^3(t) - \tilde{\sigma} R^3(t)], \ t > 0.$$  

(13)

From the left inequality above we can get

$$R(t) \geq R_0 e^{-\frac{\phi_* t}{s}}.$$

By the right inequality of (13), we have for $\xi \in [0, \omega]$

$$R(\xi + n\omega) \leq R(\xi) e^{\left(\frac{\phi_* - \tilde{\sigma}}{s} - \frac{n\omega}{s}\right) \xi} \to 0, \ n \to \infty.$$

(14)

Next, we consider the case $\tilde{\phi} > \tilde{\sigma}$. Consider the corresponding quasi-stationary version of the problem (1)-(5)

$$\Delta_r v(r,t) = \Gamma v, \ 0 < r < R(t), \ t > 0,$$

(14)

$$\frac{\partial v}{\partial r}(0,t) = 0, \ v(R(t), t) = \phi(t), \ t > 0,$$

(15)

$$\frac{4\pi R^3(t)}{3} \frac{dv}{dt} = 4\pi \int_0^{R(t)} sv(r,t) r^2 dr - 4\pi \int_0^{R(t)} s\tilde{\sigma} r^2 dr, \ t > 0.$$  

(16)

The solution to (14),(15) is

$$v(r,t) = \frac{\phi(t)R(t)}{\sinh \sqrt{\Gamma} r} \frac{\sinh \sqrt{\Gamma} r}{r}.$$  

(17)
Substituting (17) to (16), we have
\[\frac{dR}{dt} = sR(t) \left[ \phi(t)p(\sqrt{tR(t)}) - \frac{\delta}{3} \right]\]  
(18)
where \( p(x) = \frac{x \coth x - 1}{x^2} \).

**Lemma 3.2.** Let \( \phi(t) \) be a positive periodic function of period \( \omega \). Assume that \( \phi_* > \sigma \) holds. Then

(I) there exists a unique \( \omega \)-periodic positive solution \( \bar{R}(t) \) to Eq. (18).

(II) for any other positive solutions \( R(t) \) to Eq. (18), the following assertion holds:
\[
\lim_{t \to \infty} |R(t) - \bar{R}(t)| = 0.
\]  
(19)

**Proof.** Since the proof have been given in [2], we only sketch out it as follows for reader’s convenience. Consider the following two equations
\[
f_1(x) := 3\sigma_* f(x) - \sigma x = [3\sigma_* p(\sqrt{x}) - \sigma]x = 0,
\]
\[
f_2(x) := 3\sigma^* f(x) - \sigma x = [3\sigma^* p(\sqrt{x}) - \sigma]x = 0.
\]

For (I), firstly, they proved that above two equations have a unique positive constant solutions \( x_1 \) and \( x_2 \) respectively. Moreover, they also proved that if \( x_0 \in [x_1, x_2] \), then \( x(t) \in [x_1, x_2] \) for all \( t \geq 0 \). Next, denote \( x(t) = x(t, 0, x_0) \), and define a mapping \( F : [x_1, x_2] \to [x_1, x_2] \) as follows: for each \( x_0 \in [x_1, x_2] \), \( F(x_0) = \bar{x}_0 \). By using the fixed point theorem, they proved (I).

For (II), they used the method of reduction to absurdity. Assume that \( x(t) > \bar{x}(t) \)(the proof when \( x(t) < \bar{x}(t) \) is similar). Set
\[
x(t) = \bar{x}(t)e^{y(t)}.
\]
By direct computation, one can get
\[
y'(t) + 3\phi(t)[f(\bar{x})e^y - f(\bar{x}e^y)] = 0.
\]
First, prove \( \lim_{t \to \infty} y(t) \) exists, then prove \( \lim_{t \to \infty} y(t) = 0 \). Thus,
\[
\lim_{t \to \infty} |x(t) - \bar{x}(t)| = \lim_{t \to \infty} \bar{x}(t)[e^{y(t)} - 1] = 0
\]
follows. This completes the proof of (II). \( \square \)

**Lemma 3.3.** Let \( (\sigma(r, t), R(t)) \) be the solution to (1)-(5). Assume that the condition \((H)\) is satisfied and for some \( 0 < T \leq \infty \) and \( \varepsilon > 0 \)
\[
|\dot{R}(t)| \leq L \leq L_0, \ |\phi(t)| \leq K \leq K_0, \ \varepsilon \leq R(t) \leq \frac{1}{\varepsilon}.
\]  
(20)
Assume further that \( 0 \leq r \leq R_0 \),
\[
|\sigma(r, 0) - v(r, 0)| \leq M \leq M_0.
\]  
(21)
Then there exist positive constants \( c_0 \) and \( C \) independent of \( c, T, L, M, K \) and \( R_0 \) but depend of \( \varepsilon, L_0, M_0, K_0 \) such that
\[
|\sigma(r, t) - v(r, t)| \leq CL(c + e^{\frac{Lt}{\varepsilon}})
\]  
(22)
for arbitrary \( 0 \leq r \leq R(t), 0 \leq t < T \) and \( 0 < c \leq c_0 \).
Proof. By direct computation, we have
\[
\frac{\partial v}{\partial t} = \phi(t) \frac{\dot{R}(t) \sinh \sqrt{\Gamma} r}{r \sinh \sqrt{\Gamma} R(t)} + \phi(t) \frac{\dot{R}(t) \cosh \sqrt{\Gamma} R(t) \sinh \sqrt{\Gamma} r}{(r \sinh \sqrt{\Gamma} R(t))^2} + \phi(t) \frac{R(t) \sinh \sqrt{\Gamma} r}{r \sinh \sqrt{\Gamma} R(t)}.
\]

Hypothesis (20) implies that
\[|\frac{\partial v}{\partial t}| \leq C L,
\]
for \(0 < r < R(t), t \geq 0\), where \(C\) depends only on \(\phi^*, \Gamma\) and \(\varepsilon\). Since the function \(q(r) := \frac{R(t) \sinh \sqrt{\Gamma} r}{r \sinh \sqrt{\Gamma} R(t)}\) is monotone increasing for \(r > 0\) and \(q(R) = 1\), one can get \(q(r) \leq 1\) for \(0 \leq r \leq R(t)\). Let \(\sigma_\pm(r, t) = v \pm \frac{(C_L + K) \varepsilon}{t} \pm M e^{-\frac{t}{2}}\). Then
\[
c \frac{\partial \sigma_+}{\partial t} - \Delta r \sigma_+ + \Gamma \sigma_+ \geq -C L c + C L c = 0,
\]
where \(\Delta r = \frac{\partial^2}{\partial r^2} + \frac{1}{r} \frac{\partial}{\partial r} + \frac{\partial^2}{\partial \theta^2} \leq 0\).

By (15) and (20), we have
\[
\frac{\partial \sigma_+}{\partial r}(0, t) = 0, \sigma_+(R(t), t) > \phi(t), \text{ for } t > 0, \sigma_+(r, 0) \geq \sigma_0(r) \text{ for } 0 \leq r \leq R(0).
\]

Then by comparison principle we obtain
\[\sigma_+(r, t) \geq \sigma(r, t) \text{ for } 0 \leq r \leq R(t), 0 \leq t < T.\]

Similarly arguments can prove that
\[\sigma_-(r, t) \leq \sigma(r, t) \text{ for } 0 \leq r \leq R(t), 0 \leq t < T.\]

Hence (22) holds. This completes the proof. \(\square\)

Lemma 3.4. Let \(p(x) = \frac{x \coth x - 1}{x^2}\). Then the following assertions hold:

(1) \(p'(x) < 0\) for all \(x > 0\), and \(\lim_{x \to 0^+} p(x) = \frac{1}{3}\), \(\lim_{x \to \infty} p(x) = 0\).

(2) \(\frac{xp''(x)}{p'(x)}\) is strictly decreasing for any \(x > 0\), and \(-2 < \frac{xp''(x)}{p'(x)} < 1\).

(3) \(x^3p(x)\) is strictly monotone increasing for \(x > 0\).

(4) \(\lim_{x \to 0^+} xp'(x) = 0\).

Proof. The proof of (1) can be found in [19] and the proof of (3),(4) can be found in [12]. Next we prove (2), from Lemma 3.3 [10] we know that
\[
\frac{xp''(x)}{p'(x)} = \frac{2(sin^3 x - x^3 \cosh x)}{(x^2 + x \cosh x \sinh x - 2 \sinh^2 x \sinh - 2),
\]
and \(\frac{xp''(x)}{p'(x)}\) is strictly monotone decreasing for all \(x > 0\). By simple computation, it follows that
\[
\lim_{x \to \infty} \frac{xp''(x)}{p'(x)} = -2.
\]

From [28] we know that \(\lim_{x \to 0} \frac{xp''(x)}{p'(x)} = 1\), then we have \(-2 < \frac{xp''(x)}{p'(x)} < 1\). This completes the proof. \(\square\)
**Lemma 3.5.** Let \((\sigma(r, t), R(t))\) is the solution to (1)-(5). Assume that the condition (H) is satisfied. If \(\phi_0 > \bar{\sigma}\), assume for some \(\varepsilon > 0, \varepsilon \leq R_0 \leq \frac{1}{\varepsilon}\), then there exists a positive constant \(c_0\) independent of \(c\), such that

\[
\frac{1}{2} \min(R(t), \varepsilon) < R(t) < 2 \max(R(t), \frac{1}{\varepsilon})
\]

(23)

for arbitrary \(t \geq 0\) and \(0 < c \leq c_0\), where \(\bar{R}(t)\) is as that in Lemma 3.2.

**Proof.** Assume that (23) is not valid for some \(t\). It follows that there exists \(T > 0\) such that for \(0 \leq t < T\),

\[
\frac{1}{2} \min(\bar{R}(t), \varepsilon) < R(t) < 2 \max(\bar{R}(t), \frac{1}{\varepsilon})
\]

and either \(R(T) = 2 \max(\bar{R}(T), \frac{1}{\varepsilon})\) or \(R(T) = \frac{1}{2} \min(\bar{R}(T), \varepsilon)\).

If \(R(T) = 2 \max(\bar{R}(T), \frac{1}{\varepsilon})\), by the fact that \(\frac{1}{2} \min(\bar{R}(t), \varepsilon) < R(t) < 2 \max(\bar{R}(t), \frac{1}{\varepsilon})\) for \(0 \leq t < T\), and \(R(T) = 2 \max(\bar{R}(T), \frac{1}{\varepsilon})\), we have that

\[
\lim_{t \to T^-} \frac{R(t) - R(T)}{t - T} = R'(T) \geq 0.
\]

(24)

By (13) and the fact that for \(0 \leq t < T, \frac{1}{2} \min(\bar{R}(T), \varepsilon) < R(t) < 2 \max(\bar{R}(T), \frac{1}{\varepsilon})\), we have \(|R'(t)| \leq L_0, L_0\) is a positive constant independent of \(c\) and \(T\). Obviously \(|\sigma(r, 0) - v(r, 0)| \leq \phi^*\). By Lemma 3.3, it follows

\[
|\sigma(r, t) - v(r, t)| \leq C(e^{\frac{\varepsilon - \varepsilon_0}{\varepsilon}})
\]

(25)

for arbitrary \(0 \leq r \leq R(t), 0 \leq t < T\) and \(0 < c \leq c_0\). Then we have for \(t > 0\)

\[
R'(t) = \frac{1}{R^2(t)} \left[ \int_0^{R(t)} \sigma(r, t)r^2dr - \int_0^{R(t)} s\sigma r^2dr \right]
\]

\[
\leq \frac{1}{R^2(t)} \left[ \int_0^{R(t)} sv(r, t)r^2dr + \frac{8}{3} C(e^{\frac{\varepsilon - \varepsilon_0}{\varepsilon}})R^3(t) \right] - \frac{3}{\varepsilon} s\bar{\sigma} R(t)
\]

\[
= \frac{1}{3} R(t)[3s\phi(t)p(\sqrt{\Gamma} R(t)) - s\bar{\sigma} + C(e^{\frac{\varepsilon - \varepsilon_0}{\varepsilon}})]
\]

It follows that for \(T > 0\)

\[
R'(T) \leq \frac{1}{3} R(T)[3s\phi(T)p(\sqrt{\Gamma} R(T)) - s\bar{\sigma} + C(e^{\frac{\varepsilon - \varepsilon_0}{\varepsilon}})].
\]

From Lemma 3.4 (1) we known function \(p(x)\) is monotone decreasing for any \(x > 0\), noticing \(R(T) > \frac{1}{\varepsilon}\), we have \(3s\phi(T)p(\sqrt{\Gamma} R(T)) - s\bar{\sigma} < 3s\phi(T)p(\frac{\sqrt{T}}{\varepsilon}) - s\bar{\sigma} < 0\) by choosing \(\varepsilon\) sufficiently small, then if \(c_0\) is sufficiently small and \(0 < c \leq c_0\) it follows that \(R'(T) < 0\) which contracts to the fact \(R'(T) \geq 0\).

If \(R(T) = \frac{1}{2} \min(\bar{R}(T), \varepsilon)\), similar arguments can prove the desired assertion. This completes the proof.

**Lemma 3.6.** Let \(\bar{v}(r, t) = \frac{\phi(t)\bar{R}(t)}{\sinh \sqrt{\Gamma} \bar{R}(t)} \frac{\sinh \sqrt{\Gamma} r}{r}\). Assume that the condition (H) and \(\phi_* > \bar{\sigma}\) are satisfied. Let \((\sigma(r, t), R(t))\) be a solution of the problem (1)-(5).
Assume further that for some $\varepsilon > 0$ and all $t \geq 0$,
\[ \varepsilon \leq R(t) \leq \frac{1}{\varepsilon}. \] (26)

Then there exist positive constants $c_0, T_0$ and $C$ independent of $c$ such that the following assertions holds: If $0 < c \leq c_0$, for any $\alpha \in (0, \alpha_0]$, if the inequalities
\[ |R(t) - \bar{R}(t)| \leq \alpha, \quad |R'(t)| \leq \alpha, \quad |\sigma(r, t) - \bar{v}(r, t)| \leq \alpha \] (27)
hold for all $0 \leq r \leq R(t), t \geq 0$, then also the inequalities
\[ |R(t) - \bar{R}(t)| \leq C\alpha c + d(t), \quad |\sigma(r, t) - \bar{v}(r, t)| \leq C\alpha + d(t) \] (28)
hold for all $0 \leq r \leq R(t), t \geq T_0$, where $\lim_{t \to \infty} d(t) = 0$.

Proof. Let $\bar{v}(r, t) = \frac{\phi(t)\bar{R}(t)}{\sinh \sqrt{T_R(t)}}$. By the mean value theorem and the inequality (26), we have
\[ |v(r, t) - \bar{v}(r, t)| \leq C|R(t) - \bar{R}(t)| \leq C\alpha \] (29)
for all $0 \leq r \leq R(t), t \geq 0$. Here and hereafter we use the same notation $C$ to denote various different costive constants independent of $c$ and $\alpha$. It follows that
\[ |\sigma(r, t) - v(r, t)| \leq |\sigma(r, t) - \bar{v}(r, t)| + |v(r, t) - \bar{v}(r, t)| \leq C\alpha \]
for all $0 \leq r \leq R(t), t \geq 0$. In particular,
\[ |\sigma_0(r) - v(r, 0)| \leq C\alpha, \quad 0 \leq r \leq R_0. \]
Since $|R'(t)| \leq \alpha$ for all $t \geq 0$, by Lemma 3.3, there exists positive constants $c_0$ such that
\[ |\sigma(r, t) - v(r, t)| \leq C\alpha (c + e^{-\frac{\Gamma t}{3}}) \] (30)
for arbitrary $0 \leq r \leq R(t), t \geq 0$ and $0 < c \leq c_0$.

By the fact that $t e^{-t} < 1 (\Leftrightarrow e^{-t} < \frac{1}{t})$ for $t > 0$, one can get that $e^{-\frac{\Gamma t}{3}} \leq \frac{c}{\Gamma t}$ for $t \geq T_0 > 1$. Since
\[ \frac{1}{\Gamma^2} \int_0^{R(t)} (sv - s\bar{v})r^2 dr = sR(t)|\phi(t)p(R(t)) - \frac{\bar{v}}{3}|, \] (31)
then there exists $T_0 > 1$, when $t > T_0$, there holds
\[ \left| \frac{dR}{dt} - sR(t)[\phi P(R(t)) - \frac{\bar{v}}{3}] \right| \leq \frac{1}{\Gamma^2 R(t)} \left[ s\alpha R(t)R^2(t) - \frac{\bar{v}}{3} \right] \leq \frac{sC\alpha (c + e^{-\frac{\Gamma t}{3}})R^3(t)}{\Gamma^2(t)} \]
\[ = \frac{1}{3} R(t)[s\alpha (c + e^{-\frac{\Gamma t}{3}})] \]
\[ \leq sC\alpha c R(t). \]

Consider initial value problems
\[ \frac{dR^\pm}{dt} = sR^\pm(t)[\phi(t)p(R^\pm(t)) - \frac{\bar{v}}{3} \pm C\alpha], \quad R^\pm(0) = R_0. \] (32)
Similar arguments as that in [2] Theorem 3.1, one can prove the following assertions: Let $\phi(t)$ be a positive periodic function of period $\omega$. Assume that $\phi_\ast > \bar{\sigma}$ holds. Then there exist positive constants $c_0$ independent of $c$ such that if $0 < c < c_0$

(I) there exists a unique $\omega$-periodic positive solution $\bar{R}(t)$ to Eq. (32).

(II) for any other positive solutions $\bar{R}_\pm(t)$ to (32) and (33), the following assertion holds:

$$
\lim_{t\to\infty} [R_\pm(t) - \bar{R}_\pm(t)] = 0.
$$

Consider the following initial problems

$$
\frac{dR}{dt} = sR(\{\phi^* p(R(t)) - \frac{\bar{\sigma}}{3} + C\alpha c],
$$

$$
R(0) = R_0.
$$

and

$$
\frac{dR}{dt} = sR(\{\phi^* p(R(t)) - \frac{\bar{\sigma}}{3} - C\alpha c],
$$

$$
R(0) = R_0.
$$

Denote the solution to (37), (38) by $R_1(t)$ and the solution to (35), (36) by $R_2(t)$. Since $\phi_\ast > \bar{\sigma}$, there exists positive constants $a_0$ and $c_0$ such that $\frac{\bar{\sigma} + C\alpha c}{3\phi_\ast} < \frac{1}{3}$ if $\alpha \in (0, a_0]$ and $c \in (0, c_0]$. By Lemma 3.4 (1), there exists unique positive constant solution to problems (37), (38) and (35), (36) which denoted by $R_{\phi_\ast}$ and $R_{\phi_\ast}^*$ respectively. One can easily prove

$$
\lim_{t\to\infty} R_1(t) = R_{\phi_\ast}^*, \lim_{t\to\infty} R_2(t) = R_{\phi_\ast}^*.
$$

By the comparison principle, one can get

$$
R_1(t) < R^-(t) \leq \bar{R}(t) \leq R^+(t) < R_2(t).
$$

By the fact that $p(x)$ is decreasing, one can get $|R_{\phi_\ast}^* - R_{\phi_\ast}^*| \leq C\alpha c$. For any $t \geq 0$,

$$
|R(t) - \bar{R}(t)| \\
\leq \max |R^+(t) - \bar{R}^+(t)| \\
\leq \max |R^+(t) - \bar{R}^+(t)| + \max |\bar{R}^+(t) - \bar{R}(t)| \\
\leq \max |R^+(t) - \bar{R}^+(t)| + |R_2(t) - R_1(t)| \\
\leq \max |R^+(t) - \bar{R}^+(t)| + |R_2(t) - R_1(t)| + |R_{\phi_\ast}^* - R_{\phi_\ast}^*| + |R_1(t) - R_{\phi_\ast}^*| \\
\leq d_1(t) + |R_{\phi_\ast}^* - R_{\phi_\ast}^*| \\
\leq d_1(t) + C\alpha c,
$$

where $d_1(t) = \max |R^+(t) - \bar{R}^+(t)| + |R_2(t) - R_{\phi_\ast}^*| + |R_1(t) - R_{\phi_\ast}^*|$. By (34) and (39), we can get $\lim_{t\to\infty} d_1(t) = 0$. That in turn implies (by (29)) that

$$
|\nu(r, t) - \bar{\nu}(r, t)| \leq C\alpha c + d_2(t)
$$

for $0 \leq r \leq R(t)$ and $t \geq 0$, where $d_2(t) = C\alpha d_1(t)$. By (30), one can get

$$
|\sigma(r, t) - \bar{\sigma}(r, t)| \leq C\alpha c + d(t)
$$

for $0 \leq r \leq R(t)$ and $t \geq 0$, where $d(t) = d_2(t) + C\alpha c^{-\frac{r_0}{d(t)}}$. Then the desired assertions follows. □
Theorem 3.7. Assume that the condition \((H)\) is satisfied. Let \((\sigma(r,t), R(t))\) be a solution of the problem \((1)-(5)\). Suppose further that \(\phi_* > \sigma\). Then for sufficient small \(\varepsilon > 0\) there exist positive constants \(c_0\) and \(C\) independent of \(c\) such that if
\[
\varepsilon \leq R_0 \leq \frac{1}{\varepsilon} \quad \text{and} \quad 0 < c \leq c_0 \quad \text{hold},
\]
then
\[
\lim_{t \to \infty} |R(t) - \bar{R}(t)| = 0, \quad \lim_{t \to \infty} |\sigma(r,t) - \bar{v}(r,t)| = 0 \quad (40)
\]

Proof. By Lemma 3.5, it follows that there exists \(c_0 > 0\) such that if \(0 < c \leq c_0\)
\[
\frac{1}{2} \min (\bar{R}(t), \varepsilon) < R(t) < 2 \max (\bar{R}(t), \frac{1}{\varepsilon}), \quad t \geq 0,
\]
where \(\bar{R}(t)\) is the unique \(\omega\)-periodic positive solution to Eq.\((18)\) as before. So that without loss of generality we may assume that (26) holds for all \(t \geq 0\). Besides,
\[
|R(t) - \bar{R}(t)| \leq \frac{2}{\varepsilon} + 3\bar{R}(t) \leq \frac{2}{\varepsilon} + 3R^* =: \alpha_1, \quad \text{where} \quad R^* = \max_{0 \leq t \leq \omega} \bar{R}.
\]
By Lemma 2.1 (ii), we have
\[
|R'(t)| \leq 2 \max \{|M_1|, |M_2|\} \phi^* =: \alpha_2.
\]
Since clearly \(|\sigma(r,t) - \bar{v}(r,t)| \leq 2\phi(t) \leq 2\phi^*\) for all \(0 \leq r \leq R(t)\) and \(t \geq 0\).
Then (27) holds for \(0 < \alpha \leq \alpha_0 =: \max \{\alpha_1, \alpha_2, 2\phi^*\}\). By Lemma 3.6, for all \(0 \leq r \leq R(t), t \geq 0\),
\[
|R(t) - \bar{R}(t)| \leq C\alpha_0 c + d(t), \quad |\sigma(r,t) - \bar{v}(r,t)| \leq C\alpha_0 c + d(t).
\]
Choose \(T_0\) sufficient large and \(c_0\) sufficient small such that \(d(T_0) < \frac{\alpha_0}{4}\) and \(C\alpha_0 < \frac{1}{4}\).
Set \(\alpha = C\alpha_0 (c + d(T_0))\), then
\[
|R(t) - \bar{R}(t)| \leq \alpha \leq \frac{1}{2}\alpha_0, \quad |\sigma(r,t) - \bar{v}(r,t)| \leq \alpha \leq \frac{1}{2}\alpha_0.
\]
Then use \(R(T_0)\) as initial value, by Lemma 3.6 again, one can get
\[
|R(t) - \bar{R}(t)| \leq C\alpha c + d(t - T_0) \leq \alpha \leq \left(\frac{1}{2}\right)^2\alpha_0, \quad t \geq 2T_0,
\]
\[
|\sigma(r,t) - \bar{v}(r,t)| \leq C\alpha c + d(t - T_0) \leq \alpha \leq \left(\frac{1}{2}\right)^2\alpha_0, \quad t \geq 2T_0.
\]
By induction, one can get
\[
|R(t) - \bar{R}(t)| \leq \left(\frac{1}{2}\right)^k\alpha_0, \quad |\sigma(r,t) - \bar{v}(r,t)| \leq \left(\frac{1}{2}\right)^k\alpha_0, \quad t \geq kT_0.
\]
Therefore (40) holds. \(\square\)

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