Mathematical Biosciences and Engineering

http://www.aimspress.com/journal/mbe

MBE, 21(2): 2344–2365.
DOI: 10.3934/mbe.2024103
Received: 16 November 2023
Revised: 08 January 2024
Accepted: 09 January 2024
Published: 15 January 2024

Research article

Linear stability for a free boundary problem modeling the growth of tumor cord with time delay

Haihua Zhou[1], **Yaxin Liu**[2], **Zejia Wang**[2] **and Huijuan Song**[2,*]

[1] School of Mathematics and Statistics, Hengyang Normal University, Hengyang 421010, China
[2] School of Mathematics and Statistics, Jiangxi Normal University, Nanchang 330022, China

* **Correspondence:** Email: songhj@jxnu.edu.cn; Tel: +8615070416026.

Abstract: This paper was concerned with a free boundary problem modeling the growth of tumor cord with a time delay in cell proliferation, in which the cell location was incorporated, the domain was bounded in $\mathbb{R}^2$, and its boundary included two disjoint closed curves, one fixed and the other moving and a priori unknown. A parameter μ represents the aggressiveness of the tumor. We proved that there exists a unique radially symmetric stationary solution for sufficiently small time delay, and this stationary solution is linearly stable under the nonradially symmetric perturbations for any $\mu > 0$. Moreover, adding the time delay in the model leads to a larger stationary tumor. If the tumor aggressiveness parameter is bigger, the time delay has a greater effect on the size of the stationary tumor, but it has no effect on the stability of the stationary solution.

Keywords: free boundary problem; tumor cord; time delay; stability; stationary solution

1. Introduction

Over the past few decades, considerable attention has been paid to the rigorous analysis of mathematical models describing tumor growth and great progress has been achieved. Most work in this direction focuses on the sphere-shaped or nearly sphere-shaped tumor models; see [1–9] and the references therein. Observing that the work concerning models for tumors having different geometric configurations from spheroids is less frequent, in this paper we are interested in the situation of tumor cord–a kind of tumor that grows cylindrically around the central blood vessel and receives nutrient materials (such as glucose and oxygen) from the blood vessel [10]. The model only describes the evolution of the tumor cord section perpendicular to the length direction of the blood vessel due to the cord's uniformity in that direction. Assume that the radius of the blood vessel is r_0 and denote by J and $\Gamma(t)$ the section of the blood vessel wall and the section of the exterior surface of the tumor cord, respectively, then $J = \left\{x \in \mathbb{R}^2; |x| = r_0\right\}$. We also denote by $\Omega(t)$ the region of the section of the tumor cord, so that $\Omega(t)$ is an annular-like bounded domain in $\mathbb{R}^2$ and $\partial\Omega(t) = J \cup \Gamma(t)$. The mathematical formulation of the tumor model under study is as follows:

$$c\sigma_t(x,t) - \Delta\sigma(x,t) + \sigma(x,t) = 0, \qquad x \in \Omega(t),\ t > 0, \tag{1.1}$$

$$-\Delta p(x,t) = \mu[\sigma(\xi(t-\tau; x,t), t-\tau) - \tilde{\sigma}], \qquad x \in \Omega(t),\ t > 0, \tag{1.2}$$

$$\begin{cases} \dfrac{\mathrm{d}\xi}{\mathrm{d}s} = -\nabla p(\xi, s), & t-\tau \le s \le t, \\ \xi = x, & s = t, \end{cases} \tag{1.3}$$

$$\sigma(x,t) = \bar{\sigma}, \quad \partial_{\vec{n}} p(x,t) = 0, \qquad x \in J,\ t > 0, \tag{1.4}$$

$$\partial_{\vec{\nu}}\sigma(x,t) = 0, \quad p(x,t) = \gamma\kappa(x,t), \qquad x \in \Gamma(t),\ t > 0, \tag{1.5}$$

$$V(x,t) = -\partial_{\vec{\nu}} p(x,t), \qquad x \in \Gamma(t),\ t > 0, \tag{1.6}$$

$$\Gamma(t) = \Gamma_0, \qquad -\tau \le t \le 0, \tag{1.7}$$

$$\sigma(x,t) = \sigma_0(x), \qquad x \in \Omega_0,\ -\tau \le t \le 0, \tag{1.8}$$

$$p(x,t) = p_0(x), \qquad x \in \Omega_0,\ -\tau \le t \le 0. \tag{1.9}$$

Here, σ and p denote the nutrient concentration and pressure within the tumor, respectively, which are to be determined together with $\Omega(t)$, and $c = T_{\text{diffusion}}/T_{\text{growth}}$ is the ratio of the nutrient diffusion time scale to the tumor growth (e.g., tumor doubling) time scale; thus, it is very small and can sometimes be set to be 0 (quasi-steady state approximation). Assume that the time delay τ is reflected between the time at which a cell commences mitosis and the time at which the daughter cells are produced and $\xi(s; x,t)$ represents the cell location at time s as cells are moving with the velocity field $\vec{V}$, then the function $\xi(s; x,t)$ satisfies

$$\begin{cases} \dfrac{\mathrm{d}\xi}{\mathrm{d}s} = \vec{V}(\xi, s), & t-\tau \le s \le t, \\ \xi|_{s=t} = x. \end{cases} \tag{1.10}$$

In other words, ξ tracks the path of the cell currently located at x. (1.3) is further derived from (1.10) under the assumption of a porous medium structure for the tumor, where Darcy's law $\vec{V} = -\nabla p$ holds true. Because of the presence of time delay, the tumor grows at a rate that is related to the nutrient concentration when it starts mitosis and a combination of the conservation of mass and Darcy's law yields (1.2), in which μ represents the growth intensity of the tumor and $\tilde{\sigma}$ is the nutrient concentration threshold required for tumor cell growth. Additionally, $\bar{\sigma}$ is the nutrient concentration in the blood vessel, $\bar{\sigma} > \tilde{\sigma}$, V, κ and $\vec{\nu}$ denote the normal velocity, the mean curvature and the unit outward normal field of the outer boundary $\Gamma(t)$, respectively, $\vec{n}$ denotes the unit outward normal field of the fixed inner boundary J, and γ is the outer surface tension coefficient. Thus, the boundary condition $\sigma = \bar{\sigma}$ on J indicates that the tumor receives constant nutrient supply from the blood vessel, $\partial_{\vec{\nu}}\sigma = 0$ on $\Gamma(t)$ implies that the nutrient cannot pass through $\Gamma(t)$, $\partial_{\vec{n}} p = 0$ on J means that tumor cells cannot pass through the blood vessel wall, $p = \gamma\kappa$ on $\Gamma(t)$ is due to the cell-to-cell adhesiveness, and $V = -\partial_{\vec{\nu}} p$ on $\Gamma(t)$ is the well-known Stefan condition representing that the normal velocity of the tumor cord outer boundary $\Gamma(t)$ is the same with that of tumor cells adjacent to $\Gamma(t)$. Finally, $\sigma_0(x)$, $p_0(x)$, Γ_0 are given initial data and $\Omega(t) = \Omega_0$ for $-\tau \le t \le 0$.

Before going to our interest, we prefer to recall some relevant works. Models for the growth of the strictly cylindrical tumor cord were studied in [11–13]. For the model (1.1)–(1.9) without the time delay, if $c = 0$, Zhou and Cui [14] showed that the unique radially symmetric stationary solution exists and is asymptotically stable for any sufficiently small perturbations. Meanwhile, if $c > 0$, Wu et al. [15] proved that the stationary solution is locally asymptotically stable provided that c is small enough. On the other hand, Zhao and Hu [16] considered the multicell spheroids with time delays. For the case $c = 0$, they analyzed the linear stability of the radially symmetric stationary solution as well as the impact of the time delay.

Motivated by the works [14–16], here we aim to discuss the linear stability of stationary solutions to the problem (1.1)–(1.9) with the quasi-steady-state assumption, i.e., $c = 0$, and investigate the effect of time delay on tumor growth. Our first main result is given below.

Theorem 1.1. *For small time delay τ, the problem* (1.1)–(1.9) *admits a unique radially symmetric stationary solution.*

Next, in order to deal with the linear stability of the radially symmetric stationary solution, denoted by $(\sigma_*, p_*, \Omega_*)$, where $\Omega_* = \{x \in \mathbb{R}^2 : r_0 < r = |x| < R_*\}$, we assume that the initial conditions are perturbed as follows:

$$\begin{aligned} \Omega(t) &= \{x \in \mathbb{R}^2 : r_0 < r < R_* + \varepsilon\rho_0(\theta)\}, && -\tau \le t \le 0, \\ \sigma(r,\theta,t) &= \sigma_*(r) + \varepsilon w_0(r,\theta), \quad p(r,\theta,t) = p_*(r) + \varepsilon q_0(r,\theta), && -\tau \le t \le 0. \end{aligned}$$

The linearized problem of (1.1)–(1.9) at $(\sigma_*, p_*, \Omega_*)$ is then obtained by substituting

$$\Omega(t): \ r_0 < r < R_* + \varepsilon\rho(\theta,t) + O(\varepsilon^2), \tag{1.11}$$

$$\sigma(r,\theta,t) = \sigma_*(r) + \varepsilon w(r,\theta,t) + O(\varepsilon^2), \tag{1.12}$$

$$p(r,\theta,t) = p_*(r) + \varepsilon q(r,\theta,t) + O(\varepsilon^2) \tag{1.13}$$

into (1.1)–(1.9) and collecting the ε-order terms. Now, we can state the second main result of this paper.

Theorem 1.2. *For small time delay τ, the radially symmetric stationary solution $(\sigma_*, p_*, \Omega_*)$ of* (1.1)–(1.9) *with $c = 0$ is linearly stable, i.e.,*

$$\max_{0\le\theta\le2\pi} |\rho(\theta,t)| \le Ce^{-\delta t}, \quad t > 0 \tag{1.14}$$

for some positive constants C and δ.

Remark 1.1. *Compared with results of the problem modeling the growth of tumor cord without time delays in [14], the introduction of the time delay does not affect the stability of the radially symmetric stationary solution even under non-radial perturbations. However, as we shall see in Subsection 3.3, the numerical result shows that adding time delay would result in a larger stationary tumor. Moreover, the stronger the growth intensity of the tumor is, the greater the influence of time delay on the size of the stationary tumor is.*

Remark 1.2. *Compared with results of the nearly sphere-shaped tumor model with time delays in [16], which state that the radially symmetric stationary solution is linearly stable for small μ in the sense that* $\lim_{t\to\infty} \max_{0\le\theta\le2\pi} |\rho(\theta,t) - (a_1\cos\theta + b_1\sin\theta)| = 0$ *for some constants a_1 and b_1, the radially symmetric stationary solution of tumor cord with the time delay is linearly stable for any $\mu > 0$ in the normal sense.*

This paper is organized as follows. In Section 2, we give the proof of Theorem 1.1 by first transforming the free boundary problem into an equivalent problem with fixed boundary and then applying the contraction mapping principle combined with L^p estimates to this fixed boundary problem. In Section 3, we prove Theorem 1.2 and Remark 1.1 by first introducing the linearization of (1.1)–(1.9) at the radially symmetric stationary solution $(\sigma_*, p_*, \Omega_*)$, and then making a delicate analysis of the expansion in the time delay τ provided that τ is sufficiently small. A brief conclusion in Section 4 completes the paper.

2. Radially symmetric stationary solutions

In this section, we study radially symmetric stationary solutions $(\sigma_*, p_*, \Omega_*)$ to the system (1.1)–(1.9), which satisfy

$$-\Delta_r\sigma_*(r) + \sigma_*(r) = 0, \quad \sigma_*(r_0) = \bar{\sigma}, \quad \sigma_*'(R_*) = 0, \qquad r_0 < r < R_*, \tag{2.1}$$

$$-\Delta_r p_*(r) = \mu[\sigma_*(\xi(-\tau; r, 0)) - \tilde{\sigma}], \quad p_*'(r_0) = 0, \quad p_*(R_*) = \frac{\gamma}{R_*}, \qquad r_0 < r < R_*, \tag{2.2}$$

$$\begin{cases} \frac{d\xi}{ds}(s; r, 0) = -\frac{\partial p_*}{\partial r}(\xi(s; r, 0)), & -\tau \le s \le 0, \\ \xi(s; r, 0) = r, & s = 0, \end{cases} \tag{2.3}$$

$$\int_{r_0}^{R_*} [\sigma_*(\xi(-\tau; r, 0)) - \tilde{\sigma}] r dr = 0, \tag{2.4}$$

where Δ_r is the radial part of the Laplacian in $\mathbb{R}^2$.

Before proceeding further, let us recall that the modified Bessel functions $K_n(r)$ and $I_n(r)$, standard solutions of the equation

$$r^2 y'' + r y' - (r^2 + n^2) y = 0, \quad r > 0, \tag{2.5}$$

have the following properties:

$$I_{n+1}(r) = I_{n-1}(r) - \frac{2n}{r} I_n(r), \quad K_{n+1}(r) = K_{n-1}(r) + \frac{2n}{r} K_n(r), \qquad n \ge 1, \tag{2.6}$$

$$I_n'(r) = \frac{1}{2}[I_{n-1}(r) + I_{n+1}(r)], \quad K_n'(r) = -\frac{1}{2}[K_{n-1}(r) + K_{n+1}(r)], \qquad n \ge 1, \tag{2.7}$$

$$I_n'(r) = I_{n-1}(r) - \frac{n}{r} I_n(r), \quad K_n'(r) = -K_{n-1}(r) - \frac{n}{r} K_n(r), \qquad n \ge 1, \tag{2.8}$$

$$I_n'(r) = \frac{n}{r} I_n(r) + I_{n+1}(r), \quad K_n'(r) = \frac{n}{r} K_n(r) - K_{n+1}(r), \qquad n \ge 0, \tag{2.9}$$

$$I_n(r) K_{n+1}(r) + I_{n+1}(r) K_n(r) = \frac{1}{r}, \qquad n \ge 0 \tag{2.10}$$

and

$$I_n'(r) > 0, \qquad K_n'(r) < 0.$$

Proof of Theorem 1.1 In view of (2.5), the solution of (2.1) is clearly given by

$$\sigma_*(r) = \bar{\sigma} \frac{I_0(r)K_1(R_*) + I_1(R_*)K_0(r)}{I_0(r_0)K_1(R_*) + I_1(R_*)K_0(r_0)}. \tag{2.11}$$

Introducing the notations:

$$\hat{r} = \frac{r - r_0}{R_* - r_0}, \qquad \hat{\sigma}(\hat{r}) = \sigma_*(r), \qquad \hat{p}(\hat{r}) = (R_* - r_0)p_*(r), \qquad \hat{\xi}(s, \hat{r}, 0) = \frac{\xi(s, r, 0) - r_0}{R_* - r_0},$$

(2.1)–(2.4) reduces to the following system after dropping the "ˆ" in the above variables:

$$\frac{\partial^2\sigma}{\partial r^2} + \frac{R_* - r_0}{r(R_* - r_0) + r_0}\frac{\partial\sigma}{\partial r} = (R_* - r_0)^2\sigma, \quad \sigma(0) = \bar{\sigma}, \quad \sigma'(1) = 0, \tag{2.12}$$

$$\begin{cases} \frac{\partial^2 p}{\partial r^2} + \frac{R_*-r_0}{r(R_*-r_0)+r_0}\frac{\partial p}{\partial r} = -\mu(R_* - r_0)^3 \\ \qquad \left[\sigma\left(r + \frac{1}{(R_*-r_0)^3}\int_{-\tau}^{0}\frac{\partial p}{\partial r}((R_* - r_0)\xi(s; r, 0) + r_0)ds\right) - \tilde{\sigma}\right], \\ p'(0) = 0, \qquad p(1) = \frac{\gamma(R_*-r_0)}{R_*}, \end{cases} \tag{2.13}$$

$$\begin{cases} \frac{d\xi}{ds}(s; r, 0) = -\frac{1}{(R_*-r_0)^3}\frac{\partial p}{\partial r}((R_* - r_0)\xi(s; r, 0) + r_0), & -\tau \le s \le 0, \\ \xi(s; r, 0) = r, & s = 0, \end{cases} \tag{2.14}$$

$$\int_0^1 [r(R_* - r_0) + r_0]\Big[\sigma\Big(r + \frac{1}{(R_* - r_0)^3} \int_{-\tau}^{0}\frac{\partial p}{\partial r}((R_* - r_0)\xi(s; r, 0) + r_0)ds\Big) - \tilde{\sigma}\Big]dr = 0. \tag{2.15}$$

It is clear that (2.12) can be solved explicitly. For convenience, we extend the solution of (2.12) outside [0,1]:

$$\sigma(r; R_*) = \begin{cases} \bar{\sigma}\frac{I_0(r(R_* - r_0) + r_0)K_1(R_*) + I_1(R_*)K_0(r(R_* - r_0) + r_0)}{I_0(r_0)K_1(R_*) + I_1(R_*)K_0(r_0)}, & 0 \le r \le 1, \\ \bar{\sigma}\frac{I_0(R_*)K_1(R_*) + I_1(R_*)K_0(R_*)}{I_0(r_0)K_1(R_*) + I_1(R_*)K_0(r_0)}, & 1 < r \le 2. \end{cases} \tag{2.16}$$

Assume that $R_{\min}$ and $R_{\max}$ are positive constants to be determined later and $r_0 < R_{\min} < R_{\max}$. For any $R_* \in [R_{\min}, R_{\max}]$, we will prove that p is also uniquely determined by applying the contraction mapping principle.

Noticing that 0 is a lower solution of (2.14), but there is no assurance that $\xi(s; r, 0) \le 1$ for $-\tau \le s \le 0$, we suppose $\xi(s; r, 0) \in [0, 2]$ and take

$$X = \left\{p \in W^{2,\infty}[0, 2]; \|p\|_{W^{2,\infty}[0,2]} \le M\right\},$$

where $M > 0$ is to be determined. For each $p \in X$, we first solve for ξ from (2.14) and substitute it into (2.13), then the following system

$$\begin{cases} \frac{\partial^2 \bar{p}}{\partial r^2} + \frac{R_*-r_0}{r(R_*-r_0)+r_0}\frac{\partial \bar{p}}{\partial r} = -\mu(R_* - r_0)^3 \\ \qquad \left[\sigma\left(r + \frac{1}{(R_*-r_0)^3}\int_{-\tau}^{0}\frac{\partial p}{\partial r}((R_* - r_0)\xi(s; r, 0) + r_0)ds\right) - \tilde{\sigma}\right], \\ \bar{p}(1) = \frac{\gamma(R_*-r_0)}{R_*}, \quad \frac{\partial \bar{p}}{\partial r}(0) = 0 \end{cases} \tag{2.17}$$

allows a unique solution $\bar{p} \in W^{2,\infty}[0, 1]$. Applying the strong maximum principle combined with the Hopf lemma to (2.1) shows that $\sigma(r; R_*) \le \bar{\sigma}$. Thus, integrating (2.17), we obtain

$$\left\|\frac{1}{r(R_* - r_0) + r_0}\frac{\partial \bar{p}}{\partial r}\right\|_{L^\infty[0,1]} \le \frac{\mu}{2}(R_{\max} - r_0)^2(\bar{\sigma} + \widetilde{\sigma}), \tag{2.18}$$

$$\|\bar{p}\|_{L^\infty[0,1]} \leq \frac{\gamma(R_{\max}-r_0)}{R_{\min}} + \frac{\mu}{4}R_{\max}^2(R_{\max}-r_0)(\bar{\sigma}+\widetilde{\sigma}), \tag{2.19}$$

$$\left\|\frac{\partial^2\bar{p}}{\partial r^2}\right\|_{L^\infty[0,1]} \leq \frac{3\mu}{2}(R_{\max}-r_0)^3(\bar{\sigma}+\widetilde{\sigma}). \tag{2.20}$$

Define the mapping

$$\mathcal{L}p(r) = \begin{cases} \bar{p}(r), & 0 \leq r \leq 1, \\ \bar{p}(1) + \bar{p}'(1)(r-1), & 1 < r \leq 2, \end{cases} \quad p \in X,$$

then $\|\mathcal{L}p\| \in W^{2,\infty}[0,2]$ and $\|\mathcal{L}p\|_{W^{2,\infty}[0,2]} \leq 2\|\bar{p}\|_{W^{2,\infty}[0,1]}$. Combining (2.18)–(2.20), we find

$$\begin{aligned}\|\mathcal{L}p\|_{W^{2,\infty}[0,2]} \leq & 2\Big\{\frac{\mu}{2}(R_{\max}-r_0)^2(\bar{\sigma}+\widetilde{\sigma}) + \frac{3\mu}{2}(R_{\max}-r_0)^3(\bar{\sigma}+\widetilde{\sigma}) \\ & + \frac{\gamma(R_{\max}-r_0)}{R_{\min}} + \frac{\mu}{4}R_{\max}^2(R_{\max}-r_0)(\bar{\sigma}+\widetilde{\sigma})\Big\} \triangleq M_1. \end{aligned} \tag{2.21}$$

If we choose $M \geq M_1$, then $\mathcal{L}p \in X$ by (2.21) and $\mathcal{L}$ maps X to itself.

We now show that $\mathcal{L}$ is a contraction. Given $p^{(1)}, p^{(2)} \in X$, one can first get $\xi^{(1)}, \xi^{(2)}$ from the following two systems:

$$\begin{cases} \frac{d\xi^{(1)}}{ds}(s;r,0) = -\frac{1}{(R_*-r_0)^3}\frac{\partial p^{(1)}}{\partial r}\Big((R_*-r_0)\xi^{(1)}(s;r,0)+r_0\Big), & -\tau \leq s \leq 0, \\ \xi^{(1)}(s;r,0) = r, & s = 0, \end{cases} \tag{2.22}$$

$$\begin{cases} \frac{d\xi^{(2)}}{ds}(s;r,0) = -\frac{1}{(R_*-r_0)^3}\frac{\partial p^{(2)}}{\partial r}\Big((R_*-r_0)\xi^{(2)}(s;r,0)+r_0\Big), & -\tau \leq s \leq 0, \\ \xi^{(2)}(s;r,0) = r, & s = 0. \end{cases} \tag{2.23}$$

Integrating (2.22) and (2.23) with regard to s over the interval $[-\tau, 0]$ and making a subtraction yield

$$\begin{aligned}\left|\xi^{(1)}-\xi^{(2)}\right| \leq & \frac{\tau}{(R_*-r_0)^3}\max_{\substack{-\tau\leq s\leq 0\\ 0\leq r\leq 1}}\Bigg[\left|\frac{\partial p^{(1)}}{\partial r}((R_*-r_0)\xi^{(1)}+r_0) - \frac{\partial p^{(2)}}{\partial r}((R_*-r_0)\xi^{(1)}+r_0)\right| \\ & + \left|\frac{\partial p^{(2)}}{\partial r}((R_*-r_0)\xi^{(1)}+r_0) - \frac{\partial p^{(2)}}{\partial r}((R_*-r_0)\xi^{(2)}+r_0)\right|\Bigg] \\ \leq & \frac{\tau}{(R_*-r_0)^3}\left\|p^{(1)}-p^{(2)}\right\|_{W^{2,\infty}[0,2]} + \frac{\tau M}{(R_*-r_0)^2}\max_{\substack{-\tau\leq s\leq 0\\ 0\leq r\leq 1}}\left|\xi^{(1)}-\xi^{(2)}\right| \end{aligned}$$

for all $-\tau \leq s \leq 0$ and $0 \leq r \leq 1$. Consequently,

$$\max_{\substack{-\tau\leq s\leq 0\\ 0\leq r\leq 1}}\left|\xi^{(1)}-\xi^{(2)}\right| \leq \frac{\tau}{(R_*-r_0)^3 - \tau M(R_*-r_0)}\left\|p^{(1)}-p^{(2)}\right\|_{W^{2,\infty}[0,2]}. \tag{2.24}$$

Next, we substitute $\xi^{(1)}, \xi^{(2)}$ into (2.17) and solve for $\bar{p}^{(1)}$ and $\bar{p}^{(2)}$, respectively, then it follows from (2.17) that $\left(\bar{p}^{(1)}-\bar{p}^{(2)}\right)(1) = 0$, $\frac{\partial}{\partial r}\left(\bar{p}^{(1)}-\bar{p}^{(2)}\right)(0) = 0$ and

$$-\frac{\partial^2}{\partial r^2}(\bar{p}^{(1)}-\bar{p}^{(2)}) - \frac{R_*-r_0}{r(R_*-r_0)+r_0}\frac{\partial}{\partial r}(\bar{p}^{(1)}-\bar{p}^{(2)})$$

$$
\begin{aligned}
=&\mu(R_*-r_0)^3\Big[\sigma\Big(r+\frac{1}{(R_*-r_0)^3}\int_{-\tau}^0\frac{\partial p^{(1)}}{\partial r}((R_*-r_0)\xi^{(1)}(s;r,0)+r_0)ds\Big)\\
&\qquad-\sigma\Big(r+\frac{1}{(R_*-r_0)^3}\int_{-\tau}^0\frac{\partial p^{(2)}}{\partial r}((R_*-r_0)\xi^{(2)}(s;r,0)+r_0)ds\Big)\Big].
\end{aligned}
$$

Using (2.24), we derive

$$
\begin{aligned}
&\left\|\frac{1}{r(R_*-r_0)+r_0}\frac{\partial}{\partial r}\left(\bar{p}^{(1)}-\bar{p}^{(2)}\right)\right\|_{L^\infty[0,1]}\\
\le&\frac{\mu}{2}(R_*-r_0)^2\Big\|\sigma\Big(r+\frac{1}{(R_*-r_0)^3}\int_{-\tau}^0\frac{\partial p^{(1)}}{\partial r}((R_*-r_0)\xi^{(1)}+r_0)ds\Big)\\
&\qquad-\sigma\Big(r+\frac{1}{(R_*-r_0)^3}\int_{-\tau}^0\frac{\partial p^{(2)}}{\partial r}((R_*-r_0)\xi^{(2)}+r_0)ds\Big)\Big\|_{L^\infty[0,1]}\\
\le&\frac{\mu}{2(R_*-r_0)}\left\|\frac{\partial\sigma}{\partial r}\right\|_{L^\infty[0,2]}\int_{-\tau}^0\Big(\frac{\partial p^{(1)}}{\partial r}((R_*-r_0)\xi^{(1)}+r_0)-\frac{\partial p^{(2)}}{\partial r}((R_*-r_0)\xi^{(2)}+r_0)\Big)ds\\
\le&\frac{\mu\tau}{2(R_*-r_0)}\left\|\frac{\partial\sigma}{\partial r}\right\|_{L^\infty[0,2]}\Big(\left\|p^{(1)}-p^{(2)}\right\|_{W^{2,\infty}[0,2]}+(R_*-r_0)\left\|p^{(2)}\right\|_{W^{2,\infty}[0,2]}\max_{\substack{-\tau\le s\le 0\\0\le r\le 1}}\left|\xi^{(1)}-\xi^{(2)}\right|\Big)\\
\le&M_2\tau\left\|p^{(1)}-p^{(2)}\right\|_{W^{2,\infty}[0,2]}
\end{aligned}
$$

and similarly,

$$
\begin{aligned}
\left\|\bar{p}^{(1)}-\bar{p}^{(2)}\right\|_{L^\infty[0,1]}&\le M_3\tau\left\|p^{(1)}-p^{(2)}\right\|_{W^{2,\infty}[0,2]},\\
\left\|\tfrac{\partial^2}{\partial r^2}\left(\bar{p}^{(1)}-\bar{p}^{(2)}\right)\right\|_{L^\infty[0,1]}&\le M_4\tau\left\|p^{(1)}-p^{(2)}\right\|_{W^{2,\infty}[0,2]},
\end{aligned}
$$

where

$$
\begin{aligned}
M_2&=\frac{\mu\bar{\sigma}R_{\max}}{2r_0}\frac{(R_{\max}-r_0)^3}{(R_{\min}-r_0)^2-M\tau},\\
M_3&=\frac{\mu\bar{\sigma}R_{\max}^3}{4r_0}\frac{(R_{\max}-r_0)^2}{(R_{\min}-r_0)^2-M\tau},\\
M_4&=\frac{3\mu\bar{\sigma}R_{\max}}{2r_0}\frac{(R_{\max}-r_0)^4}{(R_{\min}-r_0)^2-M\tau}.
\end{aligned}
$$

Here, we employed the fact that

$$
\left\|\frac{\partial\sigma}{\partial r}\right\|_{L^\infty[0,2]}=\left\|\frac{\partial\sigma}{\partial r}\right\|_{L^\infty[0,1]}\le\frac{\bar{\sigma}R_{\max}}{r_0}(R_{\max}-r_0)^2
$$

by (2.1) and $\sigma\le\bar{\sigma}$. Let $M_5=M_2+M_3+M_4$, then M_5 is independent of τ and

$$
\left\|\bar{p}^{(1)}-\bar{p}^{(2)}\right\|_{W^{2,\infty}[0,1]}\le M_5\tau\left\|p^{(1)}-p^{(2)}\right\|_{W^{2,\infty}[0,2]},
$$

which together with $\mathcal{L}p^{(1)}(1)=\mathcal{L}p^{(2)}(1)=\frac{\gamma(R_*-r_0)}{R_*}$ and $(\mathcal{L}p^{(1)})'(0)=(\mathcal{L}p^{(2)})'(0)=0$ implies that

$$
\left\|\mathcal{L}p^{(1)}-\mathcal{L}p^{(2)}\right\|_{W^{2,\infty}[0,2]}\le 2M_5\tau\left\|p^{(1)}-p^{(2)}\right\|_{W^{2,\infty}[0,2]}.
$$

Hence, if τ is sufficiently small such that $2M_5\tau < 1$, then we derive a contracting mapping $\mathcal{L}$. The existence and uniqueness of p are therefore obtained.

It suffices to prove that there exists a unique $R_* \in [R_{\min}, R_{\max}]$ satisfying (2.15). Substituting (2.16) into (2.15), we find that it is equivalent to solving the following equation for R:

$$G(R,\tau) = \int_0^1 \frac{r(R-r_0)+r_0}{R+r_0}\Big[\sigma_*\Big(r + \frac{1}{(R-r_0)^3} \int_{-\tau}^0 \frac{\partial p_*}{\partial r}((R-r_0)\xi(s;r,0)+r_0)ds\Big) - \tilde{\sigma}\Big]dr = 0.$$

Clearly,

$$\begin{aligned} G(R,0) &= \int_0^1 \Big(\sigma_*(r;R) - \tilde{\sigma}\Big)\frac{r(R-r_0)+r_0}{R+r_0}dr \\ &= \int_0^1 \sigma_*(r;R)\frac{r(R-r_0)+r_0}{R+r_0}dr - \frac{\tilde{\sigma}}{2}. \end{aligned}$$

Using Lemma 3.1 and Theorem 3.2 in [14] and the condition $\bar{\sigma} > \tilde{\sigma}$, we know that

$$\lim_{R\to r_0} G(R,0) = \frac{\bar{\sigma}-\tilde{\sigma}}{2} > 0, \quad \lim_{R\to\infty} G(R,0) = -\frac{\tilde{\sigma}}{2} < 0, \quad \frac{\partial G(R,0)}{\partial R} < 0,$$

which implies that the equation $G(R,0) = 0$ has a unique solution, denoted by R_S, and

$$G\Big(\frac{1}{2}(R_S + r_0), 0\Big) > 0, \quad G\Big(\frac{3}{2}R_S, 0\Big) < 0.$$

Since

$$\frac{\partial G(R,\tau)}{\partial R} = \frac{\partial G(R,0)}{\partial R} + \frac{\partial^2 G(R,\eta)}{\partial R \partial \tau}\tau + O(\tau^2), \qquad 0 \le \eta \le \tau$$

when τ is sufficiently small, $\frac{\partial G(R,\tau)}{\partial R}$ and $\frac{\partial G(R,0)}{\partial R}$ have the same sign. Thus, $G(R,\tau)$ is monotone decreasing in R. Using the fact that $G(R,\tau)$ is continuous in τ, we further have

$$G\Big(\frac{1}{2}(R_S + r_0), \tau\Big) > 0, \quad G\Big(\frac{3}{2}R_S, \tau\Big) < 0.$$

Hence, when τ is sufficiently small, the equation $G(R,\tau) = 0$ has a unique solution R_*. Taking $R_{\min} = \frac{1}{2}(R_S + r_0)$ and $R_{\max} = \frac{3}{2}R_S$, we complete the proof of the theorem.

3. Linear stability

This section is devoted to the linear stability of the radially symmetric stationary solution $(\sigma_*, p_*, \Omega_*)$ of the problem (1.1)–(1.9) and the effect of time delay on the stability and the size of the stationary tumor. Let $(\sigma, p, \Omega(t))$, given by (1.11)–(1.13), be solutions to (1.1)–(1.9), and denote by $\vec{e}_r$, $\vec{e}_\theta$ the unit normal vectors in r, θ directions, respectively. Written in the rectangular coordinates in $\mathbb{R}^2$,

$$\vec{e}_r = (\cos\theta, \sin\theta)^T, \quad \vec{e}_\theta = (-\sin\theta, \cos\theta)^T.$$

Using the notation $\xi_1(s;r,\theta,t)$, $\xi_2(s;r,\theta,t)$ for the polar radius and angle of $\xi(s;r,\theta,t)$, respectively, we have

$$\xi(s;r,\theta,t) = \xi_1(s;r,\theta,t)\vec{e}_r(\xi) = \xi_1(s;r,\theta,t)(\cos\xi_2(s;r,\theta,t), \sin\xi_2(s;r,\theta,t))^T.$$

Expand ξ_1, ξ_2 in ε as

$$\begin{cases} \xi_1 = \xi_{10} + \varepsilon\xi_{11} + O(\varepsilon^2), \\ \xi_2 = \xi_{20} + \varepsilon\xi_{21} + O(\varepsilon^2), \end{cases} \tag{3.1}$$

then we derive from (1.3) and (1.13) that

$$\begin{cases} \frac{\mathrm{d}\xi_{10}}{\mathrm{d}s} = -\frac{\partial p_*}{\partial r}(\xi_{10}), \quad t-\tau \le s \le t, \\ \xi_{10}\big|_{s=t} = r; \end{cases} \tag{3.2}$$

$$\begin{cases} \frac{\mathrm{d}\xi_{11}}{\mathrm{d}s} = -\frac{\partial^2 p_*}{\partial r^2}(\xi_{10})\xi_{11} - \frac{\partial q}{\partial r}(\xi_{10}, \xi_{20}, s), \quad t-\tau \le s \le t, \\ \xi_{11}\big|_{s=t} = 0; \end{cases} \tag{3.3}$$

$$\begin{cases} \frac{\mathrm{d}\xi_{20}}{\mathrm{d}s} = 0, \quad t-\tau \le s \le t, \\ \xi_{20}\big|_{s=t} = \theta; \end{cases} \tag{3.4}$$

$$\begin{cases} \frac{\mathrm{d}\xi_{21}}{\mathrm{d}s} = -\frac{1}{\xi_{10}^2}\frac{\partial q}{\partial \theta}(\xi_{10}, \xi_{20}, s), \quad t-\tau \le s \le t, \\ \xi_{21}\big|_{s=t} = 0. \end{cases} \tag{3.5}$$

It is evident that $\xi_{20} \equiv \theta$. Noticing that the equation for ξ_{10} is the same as that for ξ_* in the radially symmetric case, ξ_{10} is independent of θ.

Substituting (1.11)–(1.13) and (3.1)–(3.5) into (1.1), (1.2), (1.4)–(1.6), using the mean-curvature formula in the 2-dimensional case for the curve $r = \rho(\theta)$:

$$\kappa = \frac{\rho^2 + 2\rho_\theta^2 - \rho\cdot\rho_{\theta\theta}}{(\rho^2 + (\rho_\theta)^2)^{3/2}}$$

and collecting the ε-order terms, we obtain the linearized system in $B_{R_*} \times \{t > 0\}$:

$$\Delta\omega(r,\theta,t) = \omega(r,\theta,t), \quad \omega(r_0,\theta,t) = 0, \quad \frac{\partial\omega}{\partial r}(R_*,\theta,t) + \sigma_*(R_*)\rho(\theta,t) = 0, \tag{3.6}$$

$$\begin{cases} \Delta q(r,\theta,t) = -\mu\frac{\partial\sigma_*}{\partial r}(\xi_{10}(t-\tau;r,t))\xi_{11}(t-\tau;r,\theta,t) - \mu w(\xi_{10}(t-\tau;r,t),\theta,t-\tau), \\ \frac{\partial q}{\partial r}(r_0,\theta,t) = 0, \quad q(R_*,\theta,t) + \frac{\gamma}{R_*^2}\Big(\rho(\theta,t) + \frac{\partial^2\rho}{\partial\theta^2}(\theta,t)\Big) = 0, \end{cases} \tag{3.7}$$

$$\frac{\partial\rho(\theta,t)}{\partial t} = -\frac{\partial q}{\partial r}(R_*,\theta,t) - \frac{\partial^2 p_*}{\partial r^2}(R_*,\theta,t)\rho(\theta,t). \tag{3.8}$$

Due to the presence of the time delay, the linearization problem (3.6)–(3.8) cannot be solved explicitly. Assume that ω, q, ρ and ξ_{11} have the following Fourier expansions:

$$\begin{cases} \omega(r,\theta,t) = A_0(r,t) + \sum_{n=1}^\infty[A_n(r,t)\cos n\theta + B_n(r,t)\sin n\theta], \\ q(r,\theta,t) = E_0(r,t) + \sum_{n=1}^\infty[E_n(r,t)\cos n\theta + F_n(r,t)\sin n\theta], \\ \rho(\theta,t) = a_0(t) + \sum_{n=1}^\infty[a_n(t)\cos n\theta + b_n(t)\sin n\theta], \\ \xi_{11}(s;r,\theta,t) = e_0(s;r,t) + \sum_{n=1}^\infty[e_n(s;r,t)\cos n\theta + f_n(s;r,t)\sin n\theta]. \end{cases} \tag{3.9}$$

Substituting (3.9) into (3.6)–(3.8) yields the following system in $B_{R_*} \times \{t > 0\}$:

$$\begin{cases} \frac{\partial^2 A_n}{\partial r^2}(r,t) + \frac{1}{r}\frac{\partial A_n}{\partial r}(r,t) - \frac{n^2}{r^2}A_n(r,t) = A_n(r,t), \\ A_n(r_0,t) = 0, \quad \frac{\partial A_n}{\partial r}(R_*,t) + \sigma_*(R_*)a_n(t) = 0, \end{cases} \tag{3.10}$$

$$\begin{cases} \frac{\partial^2 B_n}{\partial r^2}(r,t) + \frac{1}{r}\frac{\partial B_n}{\partial r}(r,t) - \frac{n^2}{r^2}B_n(r,t) = B_n(r,t), \\ B_n(r_0,t) = 0, \quad \frac{\partial B_n}{\partial r}(R_*,t) + \sigma_*(R_*)b_n(t) = 0, \end{cases} \tag{3.11}$$

$$\begin{cases} \frac{\partial^2 E_n}{\partial r^2}(r,t) + \frac{1}{r}\frac{\partial E_n}{\partial r}(r,t) - \frac{n^2}{r^2}E_n(r,t) \\ \qquad = -\mu\frac{\partial \sigma_*}{\partial r}(\xi_{10}(t-\tau;r,t))e_n(t-\tau;r,t) - \mu A_n(\xi_{10}(t-\tau;r,t),t-\tau), \\ \frac{\partial E_n}{\partial r}(r_0,t) = 0, \quad E_n(R_*,t) + \frac{\gamma(1-n^2)}{R_*^2}a_n(t) = 0, \end{cases} \tag{3.12}$$

$$\begin{cases} \frac{\partial^2 F_n}{\partial r^2}(r,t) + \frac{1}{r}\frac{\partial F_n}{\partial r}(r,t) - \frac{n^2}{r^2}F_n(r,t) \\ \qquad = -\mu\frac{\partial \sigma_*}{\partial r}(\xi_{10}(t-\tau;r,t))f_n(t-\tau;r,t) - \mu B_n(\xi_{10}(t-\tau;r,t),t-\tau), \\ \frac{\partial F_n}{\partial r}(r_0,t) = 0, \quad F_n(R_*,t) + \frac{\gamma(1-n^2)}{R_*^2}b_n(t) = 0, \end{cases} \tag{3.13}$$

$$\begin{cases} \frac{\partial e_n}{\partial s}(s;r,t) = -\frac{\partial^2 p_*}{\partial r^2}(\xi_{10})e_n(s;r,t) - \frac{\partial E_n}{\partial r}(\xi_{10},s), \quad t-\tau \le s \le t, \\ e_n \mid_{s=t} = 0, \end{cases} \tag{3.14}$$

$$\begin{cases} \frac{\partial f_n}{\partial s}(s;r,t) = -\frac{\partial^2 p_*}{\partial r^2}(\xi_{10})f_n(s;r,t) - \frac{\partial F_n}{\partial r}(\xi_{10},s), \quad t-\tau \le s \le t, \\ f_n \mid_{s=t} = 0, \end{cases} \tag{3.15}$$

$$\frac{\mathrm{d}a_n(t)}{\mathrm{d}t} = -\frac{\partial^2 p_*}{\partial r^2}(R_*)a_n(t) - \frac{\partial E_n}{\partial r}(R_*,t), \tag{3.16}$$

$$\frac{\mathrm{d}b_n(t)}{\mathrm{d}t} = -\frac{\partial^2 p_*}{\partial r^2}(R_*)b_n(t) - \frac{\partial F_n}{\partial r}(R_*,t). \tag{3.17}$$

Since it is impossible to solve the systems (2.1)–(2.4) and (3.10)–(3.17) explicitly and the time delay τ is actually very small, in what follows, we analyze the expansion in τ for (2.1)–(2.4) and (3.10)–(3.17).

3.1. Expansion in τ

Let

$$\begin{aligned} R_* &= R_*^0 + \tau R_*^1 + O(\tau^2), \\ \sigma_* &= \sigma_*^0 + \tau\sigma_*^1 + O(\tau^2), \\ p_* &= p_*^0 + \tau p_*^1 + O(\tau^2), \\ A_n &= A_n^0 + \tau A_n^1 + O(\tau^2), \\ B_n &= B_n^0 + \tau B_n^1 + O(\tau^2), \\ E_n &= E_n^0 + \tau E_n^1 + O(\tau^2), \\ F_n &= F_n^0 + \tau F_n^1 + O(\tau^2), \\ a_n &= a_n^0 + \tau a_n^1 + O(\tau^2), \\ b_n &= b_n^0 + \tau b_n^1 + O(\tau^2). \end{aligned}$$

Substitute these expansions into (2.1)–(2.4) and (3.10)–(3.17). Since $a_n(t)$ and $b_n(t)$ have the same asymptotic behavior at ∞, we will only make an analysis of $a_n(t)$. For this, we discuss the expansions of R_*, σ_*, p_*, A_n, E_n and a_n. Since the equations for the expansions of σ_*, p_*, A_n, E_n and a_n are the same as those in [16], here we only compute the expansions of the boundary conditions of σ_*, p_*, A_n and E_n.

- *Expansions of the boundary conditions of* σ_**:*
  It follows from (2.10) and (2.11) that

$$\begin{aligned}\sigma_*(r) =&\bar{\sigma}\frac{K_1(R_*)I_0(r)+I_1(R_*)K_0(r)}{I_0(r_0)K_1(R_*)+I_1(R_*)K_0(r_0)}\\ =&\bar{\sigma}\frac{K_1(R_*^0)I_0(r)+I_1(R_*^0)K_0(r)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}+\tau\frac{\bar{\sigma}R_*^1}{R_*^0}\frac{I_0(r_0)K_0(r)-K_0(r_0)I_0(r)}{[I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)]^2}+O(\tau^2),\end{aligned}$$

  which implies

$$\sigma_*^0(r) = \bar{\sigma}\frac{K_1(R_*^0)I_0(r)+I_1(R_*^0)K_0(r)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}, \tag{3.18}$$

$$\sigma_*^1(r) = \frac{\bar{\sigma}R_*^1}{R_*^0}\frac{I_0(r_0)K_0(r)-K_0(r_0)I_0(r)}{[I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)]^2}. \tag{3.19}$$

  By the boundary conditions in (2.1), we find

$$\begin{aligned}&\sigma_*^0(r_0)+\tau\sigma_*^1(r_0)+O(\tau^2)=\bar{\sigma},\\ &\frac{\partial\sigma_*^0}{\partial r}(R_*^0)+\tau\frac{\partial^2\sigma_*^0}{\partial r^2}(R_*^0)R_*^1+\tau\frac{\partial\sigma_*^1}{\partial r}(R_*^0)+O(\tau^2)=0.\end{aligned}$$

- *Expansions of the boundary conditions of* p_**:*
  One obtains from the boundary conditions in (2.2) that

$$\begin{aligned}&\frac{\partial p_*^0}{\partial r}(r_0)+\tau\frac{\partial p_*^1}{\partial r}(r_0)+O(\tau^2)=0,\\ &p_*^0(R_*^0)+\tau\frac{\partial p_*^0}{\partial r}(R_*^0)R_*^1+\tau p_*^1(R_*^0)+O(\tau^2)=\frac{\gamma}{R_*^0}-\tau\frac{\gamma R_*^1}{(R_*^0)^2}+O(\tau^2).\end{aligned}$$

- *Expansion of* (2.4)*:*
  In view of (4.31) in [16], there holds

$$\begin{aligned}0 =& \int_{r_0}^{R_*}[\sigma_*(\xi(-\tau;r,0))-\widetilde{\sigma}]rdr\\ =& \int_{r_0}^{R_*}[\sigma_*^0(r)-\widetilde{\sigma}]rdr+\tau\int_{r_0}^{R_*^0}\left(\frac{\partial\sigma_*^0}{\partial r}(r)\frac{\partial p_*^0}{\partial r}(r)+\sigma_*^1(r)\right)rdr+O(\tau^2).\end{aligned} \tag{3.20}$$

  Using (3.18), we compute

$$\begin{aligned}\int_{r_0}^{R_*}[\sigma_*^0(r)-\widetilde{\sigma}]rdr =& \int_{r_0}^{R_*}\left(\bar{\sigma}\frac{K_1(R_*^0)I_0(r)+I_1(R_*^0)K_0(r)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}-\widetilde{\sigma}\right)rdr\\ =&\bar{\sigma}r_0\frac{I_1(R_*^0)K_1(r_0)-I_1(r_0)K_1(R_*^0)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}+\frac{\widetilde{\sigma}}{2}[r_0^2-(R_*^0)^2]\end{aligned}$$

$$+\tau R_*^1\left(\frac{\bar{\sigma}}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}-\tilde{\sigma}R_*^0\right)+O(\tau^2). \tag{3.21}$$

A combination of (3.20) and (3.21) gives

$$\tau\Big[\frac{\bar{\sigma}R_*^1}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}-\tilde{\sigma}R_*^0R_*^1+\int_{r_0}^{R_*^0}\left(\frac{\partial\sigma_*^0}{\partial r}(r)\frac{\partial p_*^0}{\partial r}(r)+\sigma_*^1(r)\right)rdr\Big]$$
$$+\bar{\sigma}r_0\frac{I_1(R_*^0)K_1(r_0)-I_1(r_0)K_1(R_*^0)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}+\frac{\widetilde{\sigma}}{2}[r_0^2-(R_*^0)^2]+O(\tau^2)=0. \tag{3.22}$$

- *Expansions of the boundary conditions of A_n:*
  We derive from the boundary conditions in (3.10) that

$$A_n^0(r_0,t)+\tau A_n^1(r_0,t)+O(\tau^2)=0,$$
$$0=\frac{\partial A_n^0}{\partial r}(R_*^0+\tau R_*^1,t)+\tau\frac{\partial A_n^1}{\partial r}(R_*^0,t)+[\sigma_*^0(R_*^0+\tau R_*^1)+\tau\sigma_*^1(R_*^0)][a_n^0(t)+\tau a_n^1(t)]+O(\tau^2)$$
$$=\frac{\partial A_n^0}{\partial r}(R_*^0,t)+\sigma_*^0(R_*^0)a_n^0(t)+\tau\Big(\frac{\partial^2 A_n^0}{\partial r^2}(R_*^0,t)R_*^1+\frac{\partial A_n^1}{\partial r}(R_*^0,t)+\frac{\partial\sigma_*^0}{\partial r}(R_*^0,t)R_*^1a_n^0(t)$$
$$+\sigma_*^0(R_*^0)a_n^1(t)+\sigma_*^1(R_*^0)a_n^0(t)\Big)+O(\tau^2).$$

- *Expansions of the boundary conditions of E_n:*
  Substituting the expansion of E_n into the boundary conditions in (3.12) yields

$$\frac{\partial E_n^0}{\partial r}(r_0,t)+\tau\frac{\partial E_n^1}{\partial r}(r_0,t)+O(\tau^2)=0,$$
$$0=E_n^0(R_*^0+\tau R_*^1,t)+\tau E_n^1(R_*^0,t)+\gamma\frac{1-n^2}{(R_*^0+\tau R_*^1)^2}[a_n^0(t)+\tau a_n^1(t)]+O(\tau^2)$$
$$=E_n^0(R_*^0,t)+\gamma\frac{1-n^2}{(R_*^0)^2}a_n^0(t)+\tau\Big(\frac{\partial E_n^0}{\partial r}(R_*^0,t)R_*^1+E_n^1(R_*^0,t)$$
$$-2\gamma\frac{1-n^2}{(R_*^0)^3}R_*^1a_n^0(t)+\gamma\frac{1-n^2}{(R_*^0)^2}a_n^1(t)\Big)+O(\tau^2).$$

3.2. Zeroth-order terms in τ

Collecting all zeroth-order terms in τ leads to the following system for $r_0<r<R_*^0$:

$$-\frac{\partial^2\sigma_*^0}{\partial r^2}-\frac{1}{r}\frac{\partial\sigma_*^0}{\partial r}=-\sigma_*^0,\qquad \sigma_*^0(r_0)=\bar{\sigma},\qquad \frac{\partial\sigma_*^0}{\partial r}(R_*^0)=0, \tag{3.23}$$
$$-\frac{\partial^2 p_*^0}{\partial r^2}-\frac{1}{r}\frac{\partial p_*^0}{\partial r}=\mu(\sigma_*^0-\tilde{\sigma}),\quad \frac{\partial p_*^0}{\partial r}(r_0)=0,\quad p_*^0(R_*^0)=\frac{\gamma}{R_*^0}, \tag{3.24}$$
$$\bar{\sigma}r_0\frac{I_1(R_*^0)K_1(r_0)-I_1(r_0)K_1(R_*^0)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}+\frac{\widetilde{\sigma}}{2}[r_0^2-(R_*^0)^2]=0, \tag{3.25}$$
$$\begin{cases}-\frac{\partial^2 A_n^0}{\partial r^2}-\frac{1}{r}\frac{\partial A_n^0}{\partial r}+\left(\frac{n^2}{r^2}+1\right)A_n^0=0,\\ A_n^0(r_0,t)=0,\quad \frac{\partial A_n^0}{\partial r}(R_*^0,t)+\sigma_*^0(R_*^0)a_n^0(t)=0,\end{cases} \tag{3.26}$$

$$\begin{cases} -\frac{\partial^2 B_n^0}{\partial r^2} - \frac{1}{r}\frac{\partial B_n^0}{\partial r} + \left(\frac{n^2}{r^2}+1\right)B_n^0 = 0, \\ B_n^0(r_0,t) = 0, \quad \frac{\partial B_n^0}{\partial r}(R_*^0,t) + \sigma_*^0(R_*^0)b_n^0(t) = 0, \end{cases} \tag{3.27}$$

$$\begin{cases} -\frac{\partial^2 E_n^0}{\partial r^2} - \frac{1}{r}\frac{\partial E_n^0}{\partial r} + \frac{n^2}{r^2}E_n^0 = \mu A_n^0, \\ \frac{\partial E_n^0}{\partial r}(r_0,t) = 0, \quad E_n^0(R_*^0,t) = \gamma\frac{n^2-1}{(R_*^0)^2}a_n^0(t), \end{cases} \tag{3.28}$$

$$\begin{cases} -\frac{\partial^2 F_n^0}{\partial r^2} - \frac{1}{r}\frac{\partial F_n^0}{\partial r} + \frac{n^2}{r^2}F_n^0 = \mu B_n^0, \\ \frac{\partial F_n^0}{\partial r}(r_0,t) = 0, \quad F_n^0(R_*^0,t) = \gamma\frac{n^2-1}{(R_*^0)^2}b_n^0(t), \end{cases} \tag{3.29}$$

$$\frac{\mathrm{d}a_n^0(t)}{\mathrm{d}t} = -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0)a_n^0(t) - \frac{\partial E_n^0}{\partial r}(R_*^0,t), \tag{3.30}$$

$$\frac{\mathrm{d}b_n^0(t)}{\mathrm{d}t} = -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0)b_n^0(t) - \frac{\partial F_n^0}{\partial r}(R_*^0,t). \tag{3.31}$$

A direct calculation gives

$$\begin{aligned} \frac{\partial p_*^0}{\partial r}(r) = {} & \frac{\mu\bar{\sigma}}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}\Big\{K_1(R_*^0)\left(\frac{r_0}{r}I_1(r_0)-I_1(r)\right) \\ & + I_1(R_*^0)\left(K_1(r)-\frac{r_0}{r}K_1(r_0)\right)\Big\} + \frac{\mu\tilde{\sigma}r}{2} - \frac{\mu\tilde{\sigma}r_0^2}{2r}, \end{aligned} \tag{3.32}$$

$$\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0) = \frac{\mu\bar{\sigma}}{R_*^0[(R_*^0)^2-r_0^2]}\frac{2r_0R_*^0[I_1(R_*^0)K_1(r_0)-I_1(r_0)K_1(R_*^0)] - (R_*^0)^2 + r_0^2}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}, \tag{3.33}$$

$$A_n^0(r,t) = \frac{\bar{\sigma}a_n^0(t)h_n(r_0,R_*^0)}{R_*^0}\frac{K_n(r_0)I_n(r)-I_n(r_0)K_n(r)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}, \tag{3.34}$$

$$\frac{\partial A_n^0}{\partial r}(r,t) = \frac{-\bar{\sigma}a_n^0(t)h_n(r_0,R_*^0)}{R_*^0[I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)]}\frac{1}{h_n(r_0,r)}, \tag{3.35}$$

$$\frac{\partial^2 A_n^0}{\partial r^2}(R_*^0,t) = \frac{-\bar{\sigma}a_n^0(t)h_n(r_0,R_*^0)g_n(r_0,R_*^0)}{R_*^0[I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)]}, \tag{3.36}$$

where

$$h_n(r_0,x) = \frac{1}{I_n(r_0)\left(\frac{n}{x}K_n(x)-K_{n+1}(x)\right) - K_n(r_0)\left(\frac{n}{x}I_n(x)+I_{n+1}(x)\right)}, \tag{3.37}$$

$$\begin{aligned} g_n(r_0,x) = {} & I_n(r_0)\left[\left(1+\frac{n(n-1)}{x^2}\right)K_n(x) + \frac{1}{x}K_{n+1}(x)\right] \\ & - K_n(r_0)\left[\left(1+\frac{n(n-1)}{x^2}\right)I_n(x) - \frac{1}{x}I_{n+1}(x)\right]. \end{aligned}$$

Let $\eta_n^0 = E_n^0 + \mu A_n^0$, then we find from (3.26) and (3.28) that η_n^0 satisfies

$$-\frac{\partial^2 \eta_n^0}{\partial r^2} - \frac{1}{r}\frac{\partial \eta_n^0}{\partial r} + \frac{n^2}{r^2}\eta_n^0 = 0,$$

whose solution is

$$\eta_n^0(r,t) = C_1(t)r^n + C_2(t)r^{-n}$$

and thus,

$$E_n^0(r,t) = \eta_n^0(r,t) - \mu A_n^0(r,t) = C_1(t)r^n + C_2(t)r^{-n} - \mu A_n^0(r,t), \tag{3.38}$$

where $C_1(t)$ and $C_2(t)$ are to be determined by the boundary conditions in (3.28). By (2.10), (3.34), (3.35) and (3.37), we get

$$\begin{aligned} C_1(t) =& \frac{\mu\bar{\sigma}a_n^0(t)h_n(r_0,R_*^0)}{nR_*^0[(R_*^0)^{2n}+r_0^{2n}]}\frac{n(R_*^0)^n[I_n(R_*^0)K_n(r_0)-I_n(r_0)K_n(R_*^0)]+r_0^n}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)} \\ &+\frac{(n^2-1)\gamma a_n^0(t)}{(R_*^0)^{2n}+r_0^{2n}}(R_*^0)^{n-2}, \end{aligned} \tag{3.39}$$

$$\begin{aligned} C_2(t) =& \frac{\mu\bar{\sigma}a_n^0(t)h_n(r_0,R_*^0)r_0^n(R_*^0)^n}{nR_*^0[(R_*^0)^{2n}+r_0^{2n}]}\frac{nr_0^n[I_n(R_*^0)K_n(r_0)-I_n(r_0)K_n(R_*^0)]-(R_*^0)^n}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)} \\ &+\frac{(n^2-1)\gamma a_n^0(t)}{(R_*^0)^{2n}+r_0^{2n}}r_0^{2n}(R_*^0)^{n-2}. \end{aligned} \tag{3.40}$$

Using (3.35) and (3.38)–(3.40), we further derive

$$\begin{aligned} \frac{\partial E_n^0}{\partial r}(r,t) =& \frac{\mu\bar{\sigma}a_n^0(t)h_n(r_0,R_*^0)}{R_*^0[I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)]}\Big\{r_0^n\frac{r^{n-1}+(R_*^0)^{2n}r^{-n-1}}{(R_*^0)^{2n}+r_0^{2n}} \\ &+n(R_*^0)^n\frac{r^{n-1}-r_0^{2n}r^{-n-1}}{(R_*^0)^{2n}+r_0^{2n}}[I_n(R_*^0)K_n(r_0)-I_n(r_0)K_n(R_*^0)] \\ &+\frac{1}{h_n(r_0,r)}\Big\}+n(n^2-1)\gamma a_n^0(t)(R_*^0)^{n-2}\frac{r^{n-1}-r_0^{2n}r^{-n-1}}{(R_*^0)^{2n}+r_0^{2n}}. \end{aligned} \tag{3.41}$$

Substituting (3.33) and (3.41) into (3.30) yields

$$\frac{\mathrm{d}a_n^0(t)}{\mathrm{d}t} = U_n(r_0,R_*^0)a_n^0(t), \tag{3.42}$$

whose solution is explicitly given by

$$a_n^0(t) = a_n^0(0)\exp\{U_n(r_0,R_*^0)t\}. \tag{3.43}$$

Here,

$$\begin{aligned} U_n(r_0,R_*^0) =& \frac{\mu\bar{\sigma}h_n(r_0,R_*^0)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}\Big[\frac{2r_0(I_1(r_0)K_1(R_*^0)-I_1(R_*^0)K_1(r_0))}{h_n(r_0,R_*^0)[(R_*^0)^2-r_0^2]} \\ &+\frac{n}{(R_*^0)^2}\frac{(R_*^0)^{2n}-r_0^{2n}}{(R_*^0)^{2n}+r_0^{2n}}(I_n(r_0)K_n(R_*^0)-I_n(R_*^0)K_n(r_0))-\frac{2r_0^n(R_*^0)^{n-2}}{(R_*^0)^{2n}+r_0^{2n}}\Big] \\ &-\frac{\gamma n(n^2-1)}{(R_*^0)^3}\frac{(R_*^0)^{2n}-r_0^{2n}}{(R_*^0)^{2n}+r_0^{2n}}. \end{aligned} \tag{3.44}$$

It was proven in Lemma 4.4 of [14] that $U_n(r_0,R_*^0) < 0$ for any $n \geq 0$. Thus, we have the following:

Lemma 3.1. *For any $n \geq 0$, there exists $\delta > 0$ such that $|a_0^n(t)| \leq |a_0^n(0)|e^{-\delta t}$ for all $t > 0$.*

Lemma 3.1 shows that $a_n^0(t)$ decays to 0 exponentially at $+\infty$; hence, when $\tau = 0$, the radially symmetric stationary solution is asymptotically stable for all $\mu > 0$.

3.3. Sign of R^1_*

Recalling that $R_* = R^0_* + \tau R^1_* + O(\tau^2)$, in order to see the effect of the time delay τ on the size of the stationary tumor, in this subsection we discuss the sign of R^1_* by a theoretical analysis combined with numerical simulations.

We obtain from (3.22) that

$$\frac{\bar{\sigma} R^1_*}{I_0(r_0)K_1(R^0_*) + I_1(R^0_*)K_0(r_0)} - \tilde{\sigma} R^0_* R^1_* + \int_{r_0}^{R^0_*} \left(\frac{\partial \sigma^0_*}{\partial r}(r) \frac{\partial p^0_*}{\partial r}(r) + \sigma^1_*(r) \right) r dr = 0, \tag{3.45}$$

then by using (2.6)–(2.10), (3.18), (3.19), (3.25) and (3.32), one can solve (3.45) to obtain

$$R^1_* = -\frac{\mu \bar{\sigma}}{2R^0_*} \frac{T(r_0, R^0_*)}{S(r_0, R^0_*)}, \tag{3.46}$$

where

$$T(r_0, R^0_*) = 1 - r_0^2 [I_0(r_0)K_1(R^0_*) + I_1(R^0_*)K_0(r_0)]^2 + r_0^2 \frac{(R^0_*)^2 - r_0^2 - 4}{(R^0_*)^2 - r_0^2} [I_1(R^0_*)K_1(r_0) - I_1(r_0)K_1(R^0_*)]^2,$$

$$S(r_0, R^0_*) = \frac{2r_0}{(R^0_*)^2 - r_0^2} [I_1(r_0)K_1(R^0_*) - I_1(R^0_*)K_1(r_0)][I_0(r_0)K_1(R^0_*) + I_1(R^0_*)K_0(r_0)] + \frac{1}{(R^0_*)^2}.$$

Since

$$U_0(r_0, R^0_*) = \frac{\mu \bar{\sigma}}{[I_0(r_0)K_1(R^0_*) + I_1(R^0_*)K_0(r_0)]^2} S(r_0, R^0_*)$$

by (3.44), we know $S(r_0, R^0_*) < 0$. Additionally, we numerically compute the function $T(r_0, R^0_*)$ and find it is positive (see Figure 1). Hence, it follows from (3.46) that $R^1_* > 0$ and R^1_* is monotone increasing in μ.

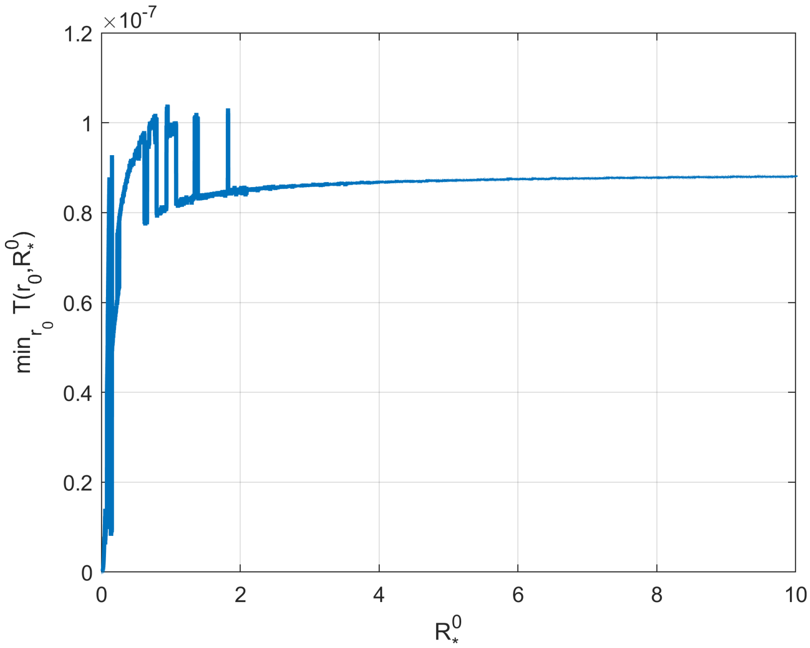

Figure 1. The graph of $\min_{0.0001 \le r_0 < R^0_*} T(r_0, R^0_*)$ with $R^0_* \in [0.0001, 10]$.

Remark 3.1. *The discussion above indicates that the presence of the time delay leads to a larger stationary tumor. Furthermore, the bigger the tumor aggressive parameter μ is, the greater the effect of time delay on the size of the stationary tumor is.*

3.4. First-order terms in τ

Now, we tackle the system consisting of all the first-order terms in τ for $r_0 < r < R_*^0$:

$$-\frac{\partial^2\sigma_*^1}{\partial r^2} - \frac{1}{r}\frac{\partial\sigma_*^1}{\partial r} = -\sigma_*^1, \quad \sigma_*^1(r_0) = 0, \quad \frac{\partial\sigma_*^1}{\partial r}(R_*^0) + \frac{\partial^2\sigma_*^0}{\partial r^2}(R_*^0)R_*^1 = 0, \tag{3.47}$$

$$\begin{cases} -\frac{\partial^2 p_*^1}{\partial r^2} - \frac{1}{r}\frac{\partial p_*^1}{\partial r} = \mu\frac{\partial\sigma_*^0}{\partial r}\frac{\partial p_*^0}{\partial r} + \mu\sigma_*^1, \\ \frac{\partial p_*^1}{\partial r}(r_0) = 0, \quad p_*^1(R_*^0) = -\frac{\gamma R_*^1}{(R_*^0)^2} - \frac{\partial p_*^0}{\partial r}(R_*^0)R_*^1, \end{cases} \tag{3.48}$$

$$\frac{\bar\sigma R_*^1}{I_0(r_0)K_1(R_*^0) + I_1(R_*^0)K_0(r_0)} - \tilde\sigma R_*^0 R_*^1 + \int_{r_0}^{R_*^0}\left(\frac{\partial\sigma_*^0}{\partial r}(r)\frac{\partial p_*^0}{\partial r}(r) + \sigma_*^1(r)\right)rdr = 0, \tag{3.49}$$

$$\begin{cases} -\frac{\partial^2 A_n^1}{\partial r^2} - \frac{1}{r}\frac{\partial A_n^1}{\partial r} + \left(\frac{n^2}{r^2} + 1\right)A_n^1 = 0, \\ A_n^1(r_0, t) = 0, \quad \frac{\partial^2 A_n^0}{\partial r^2}(R_*^0, t)R_*^1 + \frac{\partial A_n^1}{\partial r}(R_*^0, t) + \sigma_*^0(R_*^0)a_n^1(t) + \sigma_*^1(R_*^0)a_n^0(t) = 0, \end{cases} \tag{3.50}$$

$$\begin{cases} -\frac{\partial^2 B_n^1}{\partial r^2} - \frac{1}{r}\frac{\partial B_n^1}{\partial r} + \left(\frac{n^2}{r^2} + 1\right)B_n^1 = 0, \\ B_n^1(r_0, t) = 0, \quad \frac{\partial^2 B_n^0}{\partial r^2}(R_*^0, t)R_*^1 + \frac{\partial B_n^1}{\partial r}(R_*^0, t) + \sigma_*^0(R_*^0)b_n^1(t) + \sigma_*^1(R_*^0)b_n^0(t) = 0, \end{cases} \tag{3.51}$$

$$\begin{cases} -\frac{\partial^2 E_n^1}{\partial r^2} - \frac{1}{r}\frac{\partial E_n^1}{\partial r} + \frac{n^2}{r^2}E_n^1 = \mu\frac{\partial\sigma_*^0}{\partial r}\frac{\partial E_n^0}{\partial r} + \mu\frac{\partial A_n^0}{\partial r}\frac{\partial p_*^0}{\partial r} - \mu\frac{\partial A_n^0}{\partial t} + \mu A_n^1, \\ \frac{\partial E_n^1}{\partial r}(r_0, t) = 0, \ E_n^1(R_*^0, t) = \gamma\frac{n^2-1}{(R_*^0)^2}a_n^1(t) - \frac{\partial E_n^0}{\partial r}(R_*^0, t)R_*^1 - 2\gamma\frac{n^2-1}{(R_*^0)^3}R_*^1 a_n^0(t), \end{cases} \tag{3.52}$$

$$\begin{cases} -\frac{\partial^2 F_n^1}{\partial r^2} - \frac{1}{r}\frac{\partial F_n^1}{\partial r} + \frac{n^2}{r^2}F_n^1 = \mu\frac{\partial\sigma_*^0}{\partial r}\frac{\partial F_n^0}{\partial r} + \mu\frac{\partial B_n^0}{\partial r}\frac{\partial p_*^0}{\partial r} - \mu\frac{\partial B_n^0}{\partial t} + \mu B_n^1, \\ \frac{\partial F_n^1}{\partial r}(r_0, t) = 0, \ F_n^1(R_*^0, t) = \gamma\frac{n^2-1}{(R_*^0)^2}b_n^1(t) - \frac{\partial F_n^0}{\partial r}(R_*^0, t)R_*^1 - 2\gamma\frac{n^2-1}{(R_*^0)^3}R_*^1 b_n^0(t), \end{cases} \tag{3.53}$$

$$\begin{aligned} \frac{\mathrm{d}a_n^1(t)}{\mathrm{d}t} &= -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0)a_n^1(t) - \frac{\partial^3 p_*^0}{\partial r^3}(R_*^0)R_*^1 a_n^0(t) \\ &\quad - \frac{\partial^2 p_*^1}{\partial r^2}(R_*^0)a_n^0(t) - \frac{\partial^2 E_n^0}{\partial r^2}(R_*^0, t)R_*^1 - \frac{\partial E_n^1}{\partial r}(R_*^0, t), \end{aligned} \tag{3.54}$$

$$\begin{aligned} \frac{\mathrm{d}b_n^1(t)}{\mathrm{d}t} &= -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0)b_n^1(t) - \frac{\partial^3 p_*^0}{\partial r^3}(R_*^0)R_*^1 b_n^0(t) \\ &\quad - \frac{\partial^2 p_*^1}{\partial r^2}(R_*^0)b_n^0(t) - \frac{\partial^2 F_n^0}{\partial r^2}(R_*^0, t)R_*^1 - \frac{\partial F_n^1}{\partial r}(R_*^0, t). \end{aligned} \tag{3.55}$$

To obtain the asymptotic behavior of $a_n^1(t)$ as ∞, by (3.54) and the boundedness of the modified Bessel functions $I_n(r)$ and $K_n(r)$ on $[r_0, R_*^0]$, it suffices to analyze $\frac{\partial E_n^1}{\partial r}(R_*^0, t)$. For this purpose, in view of (3.52), we first compute $A_n^1(r, t)$. Solving (3.50) yields

$$A_n^1(r, t) = \frac{\bar\sigma h_n(r_0, R_*^0)}{R_*^0}\frac{I_n(r_0)K_n(r) - K_n(r_0)I_n(r)}{I_0(r_0)K_1(R_*^0) + I_1(R_*^0)K_0(r_0)}V_n(r_0, R_*^0, R_*^1, a_n^0(t), a_n^1(t)) \tag{3.56}$$

with

$$V_n(r_0, R_*^0, R_*^1, a_n^0(t), a_n^1(t)) = a_n^0(t)R_*^1 h_n(r_0, R_*^0)g_n(r_0, R_*^0) - a_n^1(t)$$

$$+ a_n^0(t)R_*^1\frac{I_0(R_*^0)K_0(r_0)-I_0(r_0)K_0(R_*^0)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)},$$

where we have employed (2.8)–(2.10), (3.19), (3.36) and (3.37). Furthermore,

$$\frac{\partial A_n^1}{\partial r}(r,t)=\frac{\bar{\sigma}h_n(r_0,R_*^0)V_n(r_0,R_*^0,R_*^1,a_n^0(t),a_n^1(t))}{R_*^0[I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)]}\frac{1}{h_n(r_0,r)}. \tag{3.57}$$

Next, being similar to the computation of E_n^0, we set $\eta_n^1 = E_n^1 + \mu A_n^1$, then we derive from (3.50), (3.52) and (3.56) that

$$\begin{cases} -\frac{\partial^2\eta_n^1}{\partial r^2}-\frac{1}{r}\frac{\partial\eta_n^1}{\partial r}+\frac{n^2}{r^2}\eta_n^1=\mu\frac{\partial\sigma_*^0}{\partial r}\frac{\partial E_n^0}{\partial r}+\mu\frac{\partial A_n^0}{\partial r}\frac{\partial p_*^0}{\partial r}-\mu\frac{\partial A_n^0}{\partial t}, \\ \frac{\partial\eta_n^1}{\partial r}(r_0,t)=\mu\frac{\partial A_n^1}{\partial r}(r_0,t), \quad \eta_n^1(R_*^0,t)=E_n^1(R_*^0,t)+\mu A_n^1(R_*^0,t). \end{cases} \tag{3.58}$$

For brevity, we introduce the differential operator $L_n = -\partial_{rr}-\frac{1}{r}\partial_r+\frac{n^2}{r^2}$ and write $\eta_n^1 = u_n^{(1)}+u_n^{(2)}+u_n^{(3)}+u_n^{(4)}$, where $u_n^{(1)}$, $u_n^{(2)}$, $u_n^{(3)}$ and $u_n^{(4)}$ solve the following problems, respectively:

$$\begin{cases} L_n u_n^{(1)} = \mu\frac{\partial\sigma_*^0}{\partial r}\frac{\partial E_n^0}{\partial r}, \\ \frac{\partial u_n^{(1)}}{\partial r}(r_0,t)=0, \quad u_n^{(1)}(R_*^0,t)=0; \end{cases} \tag{3.59}$$

$$\begin{cases} L_n u_n^{(2)} = \mu\frac{\partial A_n^0}{\partial r}\frac{\partial p_*^0}{\partial r}, \\ \frac{\partial u_n^{(2)}}{\partial r}(r_0,t)=0, \quad u_n^{(2)}(R_*^0,t)=0; \end{cases} \tag{3.60}$$

$$\begin{cases} L_n u_n^{(3)} = -\mu\frac{\partial A_n^0}{\partial t}, \\ \frac{\partial u_n^{(3)}}{\partial r}(r_0,t)=0, \quad u_n^{(3)}(R_*^0,t)=0; \end{cases} \tag{3.61}$$

$$\begin{cases} L_n u_n^{(4)} = 0, \\ \frac{\partial u_n^{(4)}}{\partial r}(r_0,t)=\mu\frac{\partial A_n^1}{\partial r}(r_0,t), \quad u_n^{(4)}(R_*^0,t)=E_n^1(R_*^0,t)+\mu A_n^1(R_*^0,t). \end{cases} \tag{3.62}$$

Let us first estimate $u_n^{(1)}$. By (3.18), (3.41) and (3.59), we have

$$\begin{aligned} L_n u_n^{(1)} =& \mu\bar{\sigma}a_n^0(t)\frac{K_1(R_*^0)I_1(r)-I_1(R_*^0)K_1(r)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}\Big\{n(n^2-1)\gamma(R_*^0)^{n-2}\frac{r^{n-1}-r_0^{2n}r^{-n-1}}{(R_*^0)^{2n}+r_0^{2n}} \\ &+\frac{\mu\bar{\sigma}h_n(r_0,R_*^0)}{R_*^0[I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)]}\Big[\frac{1}{h_n(r_0,r)}+r_0^n\frac{r^{n-1}+(R_*^0)^{2n}r^{-n-1}}{(R_*^0)^{2n}+r_0^{2n}} \\ &+n(R_*^0)^n\frac{r^{n-1}-r_0^{2n}r^{-n-1}}{(R_*^0)^{2n}+r_0^{2n}}(I_n(R_*^0)K_n(r_0)-I_n(r_0)K_n(R_*^0))\Big]\Big\}. \end{aligned} \tag{3.63}$$

Based on the properties of the modified Bessel functions $I_n(r)$ and $K_n(r)$, the righthand side of (3.63) is less than $Q(n)a_n^0(t)$ when $r_0 \le r < R_*^0$. Here, $Q(n)$ denotes a polynomial function of n. Similar estimates can be established for $u_n^{(2)}$ and $u_n^{(3)}$ by (3.60) and (3.61).

Lemma 3.2. *Consider the elliptic problem*

$$-\Delta\omega(x,t)+\frac{n^2}{|x|^2}\omega(x,t)=b(x,t), \qquad x\in\Omega_R, \tag{3.64}$$

$$\partial_{\vec{n}}\omega\Big|_{|x|=r_0} = 0, \quad \omega\Big|_{|x|=R} = 0, \tag{3.65}$$

where $\Omega_R = \{x \in \mathbb{R}^2 : r_0 < |x| < R\}$. *If* $b(x,t) = b(|x|,t)$ *and* $b(\cdot,t) \in L^2(\Omega_R)$, *then the problem* (3.64) *and* (3.65) *admits a unique solution* ω *in* $H^2(\Omega_R)$ *with estimates*

$$\|\omega(\cdot,t)\|_{H^2(\Omega_R)} \le C\Big(\int_{r_0}^R |b(r,t)|^2 r dr\Big)^{1/2}; \tag{3.66}$$

$$\Big\|\partial_{\vec{\nu}}\omega(\cdot,t)\Big\|_{L^\infty(\partial B_R)} \le C\Big(\int_{r_0}^R |b(r,t)|^2 r dr\Big)^{1/2}, \tag{3.67}$$

where the constant C *in* (3.66) *and* (3.67) *is independent of* n.

The lemma can be proven by combining the proofs of [16, Lemma 4.6] and [17, Lemma 3.2]. The details are omitted here.

Lemma 3.2 ensures the existence and uniqueness of $u_n^{(k)}$ in $H^2(\Omega_*)$ for $k = 1,2,3$. Furthermore, there holds

$$\left|\frac{\partial u_n^{(1)}}{\partial r}(R_*^0,t)\right| + \left|\frac{\partial u_n^{(2)}}{\partial r}(R_*^0,t)\right| + \left|\frac{\partial u_n^{(3)}}{\partial r}(R_*^0,t)\right| \le Ce^{-\delta t}. \tag{3.68}$$

Obviously, the solution $u_n^{(4)}$ to the problem (3.62) has the form:

$$u_n^{(4)}(r,t) = C_5(t)r^n + C_6(t)r^{-n}, \tag{3.69}$$

where $C_5(t)$ and $C_6(t)$ are determined by the boundary conditions in (3.62). Using (2.10), (3.41), (3.56), (3.57) and the boundary conditions in (3.52), we get

$$\begin{aligned} C_5(t) =&\frac{a_n^1(t)}{(R_*^0)^{2n} + r_0^{2n}}\Big\{\frac{\mu\bar{\sigma}h_n(r_0,R_*^0)}{R_*^0[I_0(r_0)K_1(R_*^0) + I_1(R_*^0)K_0(r_0)]}\Big[\frac{r_0^n}{n} + (R_*^0)^n(K_n(r_0)I_n(R_*^0) \\ &- I_n(r_0)K_n(R_*^0))\Big] + \gamma(n^2-1)(R_*^0)^{n-2}\Big\} + H_1(r_0,R_*^0,R_*^1)a_n^0(t), \end{aligned} \tag{3.70}$$

$$\begin{aligned} C_6(t) =&\frac{a_n^1(t)r_0^n(R_*^0)^n}{(R_*^0)^{2n} + r_0^{2n}}\Big\{\frac{\mu\bar{\sigma}h_n(r_0,R_*^0)}{R_*^0[I_0(r_0)K_1(R_*^0) + I_1(R_*^0)K_0(r_0)]}\Big[-\frac{(R_*^0)^n}{n} + r_0^n(K_n(r_0)I_n(R_*^0) \\ &- I_n(r_0)K_n(R_*^0))\Big] + \frac{\gamma(n^2-1)r_0^n}{(R_*^0)^2}\Big\} + H_2(r_0,R_*^0,R_*^1)a_n^0(t), \end{aligned} \tag{3.71}$$

where H_1, H_2 are functions of r_0, R_*^0 and R_*^1.

Now, since

$$E_n^1(r,t) = \eta_n^1 - \mu A_n^1 = u_n^{(1)} + u_n^{(2)} + u_n^{(3)} + u_n^{(4)} - \mu A_n^1,$$

we derive

$$\frac{\partial E_n^1}{\partial r}(R_*^0,t) = \frac{\partial u_n^{(1)}}{\partial r}(R_*^0,t) + \frac{\partial u_n^{(2)}}{\partial r}(R_*^0,t) + \frac{\partial u_n^{(3)}}{\partial r}(R_*^0,t) + \frac{\partial u_n^{(4)}}{\partial r}(R_*^0,t) - \mu\frac{\partial A_n^1}{\partial r}(R_*^0,t). \tag{3.72}$$

By (3.33), (3.57) and (3.69)–(3.72), we obtain from (3.54) that

$$\frac{\mathrm{d}a_n^1(t)}{\mathrm{d}t} = -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0)a_n^1(t) - \frac{\partial^3 p_*^0}{\partial r^3}(R_*^0)R_*^1 a_n^0(t) - \frac{\partial^2 p_*^1}{\partial r^2}(R_*^0)a_n^0(t) - \frac{\partial^2 E_n^0}{\partial r^2}(R_*^0,t)R_*^1 - \frac{\partial E_n^1}{\partial r}(R_*^0,t)$$

$$
\begin{aligned}
=&a_n^1(t)\Big\{\frac{\mu\bar{\sigma}h_n(r_0,R_*^0)}{I_0(r_0)K_1(R_*^0)+I_1(R_*^0)K_0(r_0)}\Big[\frac{n}{(R_*^0)^2}\frac{(R_*^0)^{2n}-r_0^{2n}}{(R_*^0)^{2n}+r_0^{2n}}(I_n(r_0)K_n(R_*^0)-I_n(R_*^0)K_n(r_0))\\
&\quad+\frac{2r_0(I_1(r_0)K_1(R_*^0)-I_1(R_*^0)K_1(r_0))}{(R_*^0)^2-r_0^2}\frac{1}{h_n(r_0,R_*^0)}-\frac{2r_0^n(R_*^0)^{n-2}}{(R_*^0)^{2n}+r_0^{2n}}\Big]\\
&\quad-\frac{\gamma n(n^2-1)}{(R_*^0)^3}\frac{(R_*^0)^{2n}-r_0^{2n}}{(R_*^0)^{2n}+r_0^{2n}}\Big\}+\tilde{H}(n,r_0,R_*^0,R_*^1)a_n^0(t)\\
&-\frac{\partial u_n^{(1)}}{\partial r}(R_*^0,t)-\frac{\partial u_n^{(2)}}{\partial r}(R_*^0,t)-\frac{\partial u_n^{(3)}}{\partial r}(R_*^0,t)\\
=&a_n^1(t)U_n(r_0,R_*^0)-\frac{\partial u_n^{(1)}}{\partial r}(R_*^0,t)-\frac{\partial u_n^{(2)}}{\partial r}(R_*^0,t)-\frac{\partial u_n^{(3)}}{\partial r}(R_*^0,t)+\tilde{H}(n,r_0,R_*^0,R_*^1)a_n^0(t),
\end{aligned}
$$

where $\tilde{H}$ is a known function of n, r_0, R_*^0, R_*^1 and satisfies

$$
|\tilde{H}(n,r_0,R_*^0,R_*^1)|\le C. \tag{3.73}
$$

Thus, using Lemma 3.1, (3.68) and (3.73) gives

$$
\begin{aligned}
&\left|\frac{\mathrm{d}a_n^1(t)}{\mathrm{d}t}-a_n^1(t)U_n(r_0,R_*^0)\right|\\
\le&|\tilde{H}(n,r_0,R_*^0,R_*^1)a_n^0(t)|+\left|\frac{\partial u_n^{(1)}}{\partial r}(R_*^0,t)\right|+\left|\frac{\partial u_n^{(2)}}{\partial r}(R_*^0,t)\right|+\left|\frac{\partial u_n^{(3)}}{\partial r}(R_*^0,t)\right|\\
\le&Ce^{-\delta t}.
\end{aligned}\tag{3.74}
$$

In addition, for $n \ge 0$, Lemma 3.1 implies

$$
-U_n(r_0,R_*^0)>\delta>0.
$$

Therefore, applying [16, Lemma 4.7] to (3.74) yields

$$
|a_n^1(t)|\le Ce^{-\delta t},\qquad t>0, \tag{3.75}
$$

i.e., $a_n^1(t)$ decays exponentially as $t\to\infty$. Noticing that $b_n(t)$ and $a_n(t)$ have the same asymptotic behavior, we also have

$$
|b_n^0(t)|+|b_n^1(t)|\le Ce^{-\delta t},\qquad t>0. \tag{3.76}
$$

Proof of Theorem 1.2 The desired result (1.14) follows from Lemma 3.1, (3.75) and (3.76). The proof is complete.

Remark 3.2. *The results on tumor cord without time delays in [14] show that the radially symmetric stationary solution is asymptotically stable under nonradially symmetric perturbations. Here, our Theorem 1.2 says that such asymptotic stability does not be affected by small time delay.*

4. Conclusions

In this paper, we have investigated the effects of a time delay in cell proliferation on the growth of tumor cords, where the domain is a bounded subset in $\mathbb{R}^2$ and its boundary consists of two disjoint closed curves, one fixed and the other moving and a priori unknown. The existence, uniqueness and linear stability of the radially symmetric stationary solution were studied.

Here are some interesting findings. 1) Adding the time delay would not change the stability of the radially symmetric stationary solution when compared with the same system without delay [14], but adding the time delay would result in a larger stationary tumor. The bigger the tumor growth intensity μ is, the greater impact that time delay has on the size of the stationary tumor. 2) By the result of [16], we know that for tumor spheroids with the same time delay, there exists a threshold $\mu_* > 0$ for the tumor aggressiveness constant μ such that only for $\mu < \mu_*$, the radially symmetric stationary solution is linearly stable under non-radial perturbations. For tumor cords, however, from Theorem 1.2 we saw that the radially symmetric stationary solution is always linearly stable, regardless of the value of μ. It showed that there is an essential difference between tumor cords and tumor spheroids with the same time delay.

We think that the linear stability analysis for the full system without quasi-steady state simplification, i.e., $c > 0$, may be very challenging, which we expect to solve in future work.

Use of AI tools declaration

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

Acknowledgments

The authors would like to thank the reviewers for their valuable suggestions. This work was partly supported by the National Natural Science Foundation of China (No. 12161045 and No. 12261047), Jiangxi Provincial Natural Science Foundation (No. 20224BCD41001 and No. 20232BAB201010), the Science and Technology Planning Project from Educational Commission of Jiangxi Province, China (No. GJJ2200319), the Scientific Research Project of Hunan Provincial Education Department, China (No. 22B0725, No. 23B0670 and No. 23C0234), and the Research Initiation Project of Hengyang Normal University, China (No. 2022QD01).

Conflict of interest

The authors declare there is no conflict of interest.

References

1. B. Bazaliy, A. Friedman, A free boundary problem for an elliptic parabolic system: application to a model of tumor growth, *Commun. Partial Differ. Equations*, **28** (2003), 517–560. https://doi.org/10.1081/PDE-120020486

2. B. Bazaliy, A. Friedman, Global existence and asymptotic stability for an elliptic-parabolic free boundary problem: An application to a model of tumor growth, *Indiana Univ. Math. J.*, **52** (2003), 1265–1304.

3. S. Cui, Analysis of a mathematical model for the growth of tumors under the action of external inhibitors, *J. Math. Biol.*, **44** (2002), 395–426. https://doi.org/10.1007/s002850100130

4. S. Cui, Analysis of a free boundary problem modeling tumor growth, *Acta Math. Sin. (Engl. Ser.)*, **21** (2005), 1071–1082. https://doi.org/10.1007/s10114-004-0483-3

5. S. Cui, Well-posedness of a multidimensional free boundary problem modelling the growth of nonnecrotic tumors, *J. Funct. Anal.*, **245** (2007), 1–18. https://doi.org/10.1016/j.jfa.2006.12.020

6. S. Cui, J. Escher, Asymptotic behavior of solutions of a multidimensional moving boundary problem modeling tumor growth, *Commun. Partial Differ. Equations*, **33** (2008), 636–655. https://doi.org/10.1080/03605300701743848

7. S. Cui, S. Xu, Analysis of mathematical models for the growth of tumors with time delays in cell proliferation, *J. Math. Anal. Appl.*, **336** (2007), 523–541. https://doi.org/10.1016/j.jmaa.2007.02.047

8. S. Xu, Analysis of tumor growth under direct effect of inhibitors with time delays in proliferation, *Nonlinear Anal. Real World Appl.*, **11** (2010), 401–406. https://doi.org/10.1016/j.nonrwa.2008.11.002

9. S. Xu, Q. Zhou, M. Bai, Qualitative analysis of a time-delayed free boundary problem for the tumor growth under the action of external inhibitors, *Math. Methods Appl. Sci.*, **38** (2015), 4187–4198. https://doi.org/10.1002/mma.3357

10. J. V. Moore, P. S. Hasleton, C. H. Buckley, Tumour cords in 52 human bronchial and cervical squamous cell carcinomas: Inferences for their cellular kinetics and radiobiology, *Br. J. Cancer*, **51** (1985), 407–413. https://doi.org/10.1038/bjc.1985.55

11. J. Dyson, R. Villella-Bressan, G. Webb, The steady state of a maturity structured tumor cord cell population, *Discrete Contin. Dyn. Syst. Ser. B*, **4** (2004), 115–134. https://doi.org/10.3934/dcdsb.2004.4.115

12. J. Dyson, R. Villella-Bressan, G. Webb, The evolution of a tumor cord cell population, *Commun. Pure Appl. Anal.*, **3** (2004), 331–352. https://doi.org/10.3934/cpaa.2004.3.331

13. G. F. Webb, The steady state of a tumor cord cell population, *J. Evol. Equations*, **2** (2002), 425–438. https://doi.org/10.1007/PL00012598

14. F. Zhou, S. Cui, Well-posedness and stability of a multidimensional moving boundary problem modeling the growth of tumor cord, *Discrete Contin. Dyn. Syst.*, **21** (2008), 929–943. https://doi.org/10.3934/dcds.2008.21.929

15. J. Wu, F. Zhou, S. Cui, Analysis of an elliptic-parabolic free boundary problem modelling the growth of non-necrotic tumor cord, *J. Math. Anal. Appl.*, **352** (2009), 184–205. https://doi.org/10.1016/j.jmaa.2008.06.028

16. X. Zhao, B. Hu, The impact of time delay in a tumor model, *Nonlinear Anal. Real World Appl.*, **51** (2020), 1–29. https://doi.org/10.1016/j.nonrwa.2019.103015

17. A. Friedman, B. Hu, Bifurcation from stability to instability for a free boundary problem arising in a tumor model, *Arch. Ration. Mech. Anal.*, **180** (2006), 293–330. https://doi.org/10.1007/s00205-005-0408-z