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Asymptotic behavior of solutions of a free-boundary tumor model with angiogenesis

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A R T I C L E I N F O

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A B S T R A C T

This paper is concerned with a free boundary problem modeling the growth of solid tumor spheroid with angiogenesis. The model comprises a coupled system of two elliptic equations describing the distribution of nutrient concentration σ and inner pressure p within the tumor tissue. Angiogenesis results in a new boundary condition $\partial_{\mathrm{n}}\sigma + \beta(\sigma - \overline{\sigma}) = 0$ instead of the widely studied condition $\sigma = \overline{\sigma}$ over the moving boundary, where β is a positive constant. We first prove that this problem admits a unique radial stationary solution, and this solution is globally asymptotically stable under radial perturbations. Then we establish local well-posedness of the problem and study asymptotic stability of the radial stationary solution under non-radial perturbations. A positive threshold value γ_* is obtained such that the radial stationary solution is asymptotically stable for $\gamma > \gamma_*$ and unstable for $0 < \gamma < \gamma_*$.

1. Introduction

In this paper we consider the following free boundary problem modeling tumor growth:

$$\begin{cases} \triangle\sigma = \sigma, & \text{in } \Omega(t) \times (0,\infty), \\ \partial_{\mathrm{n}}\sigma + \beta(\sigma - \overline{\sigma}) = 0, & \text{on } \partial\Omega(t) \times (0,\infty), \\ \triangle p = -g(\sigma), & \text{in } \Omega(t) \times (0,\infty), \\ p = \gamma\kappa, & \text{on } \partial\Omega(t) \times (0,\infty), \\ V_{\mathrm{n}} = -\partial_{\mathrm{n}} p, & \text{on } \partial\Omega(t) \times (0,\infty), \\ \Omega(0) = \Omega_0. \end{cases} \tag{1.1}$$

Here $\sigma = \sigma(x,t)$ and $p = p(x,t)$ are unknown functions describing the nutrient concentration and the internal pressure within the tumor tissue, $\Omega(t) \subseteq \mathbb{R}^3$ is an unknown domain with a free boundary $\partial\Omega(t)$ moving as time t, Ω_0 is the given initial domain with its sufficiently smooth boundary $\partial\Omega_0$ at time $t = 0$, β is a positive constant describing the ability of tumor cells to absorb the nutrient from outward of the tumor via its own vasculature, $\overline{\sigma}$ denotes the constant nutrient concentration outside the tumor, γ is another positive

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constant which stands for the surface tension coefficient, n is the outward unit normal field of $\partial\Omega(t)$, ∂_{n} is the normal boundary derivative in the direction n, κ is the mean curvature of $\partial\Omega(t)$ whose sign is positive when $\Omega(t)$ is a ball, and V_{n} denotes the normal velocity of the boundary points in the direction n. We further assume that g is a given nonlinear function satisfying the following condition (A):

$(A1)$ $g \in C^{\infty}[0,\infty)$;

$(A2)$ $g'(\sigma) > 0$ for all $\sigma \in [0,\infty)$; $g(\widetilde{\sigma}) = 0\,\text{for some}\,\widetilde{\sigma} > 0$;

$(A3)$ $\widetilde{\sigma} < \overline{\sigma}$.

In the past few decades, several mathematical models describing the growth of tumor tissue in many kinds of mechanism have been proposed and taken into consideration. Researchers carried out numerous methods such as rigorous analysis and numerical simulations to study these models [1–11]. The above model (1.1) is usually called *tumor model with angiogenesis* (see [10]). Angiogenesis plays a significant role when tumor cells secrete cytokines that stimulate the vascular system to grow toward the tumor, and tumor tissue with angiogenesis has its own vasculature which acts as a transmitting path for receiving nutrient, so it is natural to assume that

$$\partial_{\mathrm{n}}\sigma + \beta(t)(\sigma - \overline{\sigma}) = 0, \qquad \text{on}\,\partial\Omega(t) \times (0,\infty).$$

As is mentioned in [10], angiogenesis is a process resulting in an increase in the positive-valued function $\beta(t)$. On the other hand, $\beta(t)$ will be decreasing and become very small when the tumor tissue is treated with anti-angiogenic drugs, hence the tumor will starve to death and shrink in this case. However, throughout this paper we only consider the special case that $\beta(t)$ identically equals to a positive constant β independent of t. The above system (1.1) with the boundary condition $\sigma = \overline{\sigma}$ was widely studied by Friedman and Reitich [12], Friedman and Hu [13,14], Cui [15], Cui and Escher [5,6], and so on. The reason why we focus our work on the third boundary condition is that in biological sense the barrier effect of tumor surface contributes to the decrease of nutrient diffusing through its surface into the center, and we know nothing about the precise amount caused by this reduction, so the results obtained in the existing literatures are incapable of explaining the new model. The smaller the constant β is, the stronger the barrier effect of the tumor surface will be, and $\beta = \infty$ coincides with the first boundary condition $\sigma = \overline{\sigma}$, so the new model with the third boundary condition is much more realistic and results will cover those on the first boundary condition. Moreover, if the boundary is nonlinear with Gibbs–Thomson relation, Wu [16], Wu and Zhou [17] investigated different radial stationary solutions and studied the asymptotic behavior of each radial stationary solution.

To state our main results in this paper we need some notation preparation. We first consider the radial stationary solution of problem (1.1), denoted by $(\sigma_s(r), p_s(r), \Omega_s)$, where the radius of ball Ω_s is R_s. In this case, we see that in Ω_s, the Laplacian operator $\triangle = \triangle_r = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial}{\partial r}\right)$, then $\triangle\sigma = \sigma_s''(r) + \frac{2}{r}\sigma_s'(r)$ and $\triangle p = p_s''(r) + \frac{2}{r}p_s'(r)$. Since $\sigma_s(r), p_s(r)$ are spherically symmetric, we have additional conditions

$$\sigma_s'(0) = 0, \quad p_s'(0) = 0.$$

On $\partial\Omega_s$, the normal derivatives of σ and p in the radial direction n are $\partial_{\mathrm{n}}\sigma = \sigma_s'(R)$ and $\partial_{\mathrm{n}}p = p_s'(R)$. We have in particular $\kappa \equiv \frac{1}{R_s}$ for a sphere of radius R_s, and $V_{\mathrm{n}} \equiv 0$ when considering the stationary solutions in this case.

A triple $(\sigma_s(r), p_s(r), \Omega_s)$ with $\Omega_s = \{0 \leqslant r < R_s\}$ is called a *radial stationary solution* of problem (1.1) if it satisfies the following system of equations:

$$\begin{cases} \sigma_s''(r) + \dfrac{2}{r}\sigma_s'(r) = \sigma_s(r), & 0 < r < R_s, \\ \sigma_s'(0) = 0, \quad \sigma_s'(R_s) + \beta(\sigma_s(R_s) - \overline{\sigma}) = 0, & \\ p_s''(r) + \dfrac{2}{r}p_s'(r) = -g(\sigma_s(r)), & 0 < r < R_s, \\ p_s'(0) = 0, \quad p_s(R_s) = \gamma R_s^{-1}, & \\ p_s'(R_s) = 0. & \end{cases} \tag{1.2}$$