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Stationary solutions of a free boundary problem modeling the growth of tumors with Gibbs–Thomson relation

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Abstract

In this paper we study a free boundary problem modeling tumor growth. The model consists of two elliptic equations describing nutrient diffusion and pressure distribution within tumors, respectively, and a first-order partial differential equation governing the free boundary, on which a Gibbs–Thomson relation is taken into account. We first show that the problem may have none, one or two radial stationary solutions depending on model parameters. Then by bifurcation analysis we show that there exist infinite many branches of non-radial stationary solutions bifurcating from given radial stationary solution. The result implies that cell-to-cell adhesiveness is the key parameter which plays a crucial role on tumor invasion.

MSC: 35B32; 35Q92; 35R35

Keywords: Free boundary problem; Tumor growth; Stationary solution; Bifurcation

1. Introduction

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

$$\Delta\sigma = \lambda\sigma \qquad \text{in } \Omega, \tag{1.1}$$

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$$\Delta p = -\mu(\sigma - \tilde{\sigma}) \qquad \text{in } \Omega, \tag{1.2}$$

$$\sigma = \bar{\sigma}(1 - \gamma\kappa) \qquad \text{on } \partial\Omega, \tag{1.3}$$

$$p = \bar{p} \qquad \text{on } \partial\Omega, \tag{1.4}$$

$$\partial_n p = 0 \qquad \text{on } \partial\Omega, \tag{1.5}$$

where $\sigma = \sigma(x)$ and $p = p(x)$ denote concentration of nutrient and internal pressure within tumor's region $\Omega \subset \mathbb{R}^3$, respectively. σ, p and Ω are unknown and have to be determined together. κ is the mean curvature and ∂_n is the outward normal derivative on free boundary $\partial\Omega$, respectively. $\lambda, \bar{\sigma}, \bar{p}, \tilde{\sigma}, \gamma, \mu$ are positive dimensionless constants, where λ is the nutrient consumption rate, $\bar{\sigma}$ and $\bar{p}$ represent constant external nutrient concentration and pressure, $\tilde{\sigma}$ is the threshold value of nutrient concentration at which tumor cell's birth and death meet the balance, γ is cell-to-cell adhesiveness, and μ is the proliferation rate of tumor cells.

The above problem is a stationary version of mathematical model for the growth of solid tumors established by Byrne and Chaplain [3]. The motion of cells within a solid tumor is regarded as an incompressible fluid flow in a porous medium. Equation (1.1) describes the diffusion and consumption of nutrient within tumor region; Equation (1.2) is formulated by mass conservation law div $\mathbf{v} = \mu(\sigma - \tilde{\sigma})$ and Darcy's law $\mathbf{v} = -\nabla p$, where $\mathbf{v}$ is the velocity of tumor cells; Equation (1.3) is due to a Gibbs–Thomson relation, which means the gap (experimentally observed) of nutrient concentration across tumor boundary is proportional to the local mean curvature (cf. [3,19]); Equation (1.4) means the pressure on tumor boundary is constant; The evolution of free boundary is governed by $V_n = -\partial_n p$ where V_n is the velocity of boundary in the direction of outward normal, so equation (1.5) means the solid tumor is in a dormant state.

Neglecting the gap of nutrient concentration across boundary, another natural physical boundary condition can be imposed as follows (cf. [11,18]):

$$\sigma = \bar{\sigma}, \qquad p = \gamma\kappa \qquad \text{on } \partial\Omega, \tag{1.6}$$

and by considering evolutionary condition of free boundary:

$$V_n = -\partial_n p \qquad \text{on } \partial\Omega, \tag{1.7}$$

we get a Hele-Shaw type tumor model (1.1)–(1.2), (1.6)–(1.7). In recent decades, mathematical analysis of this kind of tumor models has attracted a lot of attention and many illuminative results have been obtained. Friedman and Reitich [15] first proved that the Hele-Shaw type tumor model (1.1)–(1.2), (1.6)–(1.7) has a unique radial stationary solution for $0 < \tilde{\sigma}/\bar{\sigma} < 1$, and it is globally asymptotically stable under radially symmetric perturbations. By employing a power series method they also proved that in two-dimensional case there exist infinite many branches of symmetry-breaking stationary solutions bifurcating from the radial one in [16]. Fontelos and Friedman [10] generalized this result into three-dimensional case. Later, Borisovich and Friedman [1], Cui and Escher [7] simplified the proof by reformulating the problem as a bifurcation problem and using classical Crandall–Rabinowitz bifurcation theorem. Motivated by bifurcation result, Friedman and Hu [12], Cui and Escher [8] studied asymptotic stability of the radial stationary solution under non-radial perturbations. For extended studies of Hele-Shaw type tumor models, we refer readers to [6,11,14] and references therein.