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Analysis of a free boundary problem modeling the growth of multicell spheroids with angiogenesis ☆

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Abstract

In this paper we study a free boundary problem modeling the growth of vascularized tumors. The model is a modification to the Byrne–Chaplain tumor model that has been intensively studied during the past two decades. The modification is made by replacing the Dirichlet boundary value condition with the Robin condition, which causes some new difficulties in making rigorous analysis of the model, particularly on existence and uniqueness of a radial stationary solution. In this paper we successfully solve this problem. We prove that this free boundary problem has a unique radial stationary solution which is asymptotically stable for large surface tension coefficient, whereas unstable for small surface tension coefficient. Tools used in this analysis are the geometric theory of abstract parabolic differential equations in Banach spaces and spectral analysis of the linearized operator.

MSC: 35R35; 35B35; 35B40

Keywords: Free boundary problem; Tumor growth; Well-posedness; Stationary solution; Asymptotic stability

1. Introduction

It has been recognized for over eighty years that under a constant circumstance, an evolutionary tumor (or a multicell spheroid in a different phrase) will finally evolve into a stationary or

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dormant state [1]. During 1970's, Greenspan proposed the first mathematical model in the form of free boundary problem of reaction diffusion equations to explain this phenomenon [22,23]. His model was very well improved by Byrne and Chaplain during 1990's [3,4]. Since then many different tumor models have been established by different groups of researchers, cf. the reviewing articles [2,16] and references cited therein. Rigorous mathematical analysis of those tumor models has attracted much attention over the past two decades, and many interesting results have been obtained, cf. [5–13,17,18,20,21,25–30] and references cited therein.

In this paper we study the following free boundary problem modeling the growth of vascularized tumors:

$$\begin{cases} \Delta\sigma = f(\sigma), & x \in \Omega(t),\ t > 0, \\ -\Delta p = g(\sigma), & x \in \Omega(t),\ t > 0, \\ \partial_{\mathbf{n}}\sigma = \beta(\bar{\sigma} - \sigma), & x \in \partial\Omega(t),\ t > 0, \\ p = \gamma\kappa, & x \in \partial\Omega(t),\ t > 0, \\ V_{\mathbf{n}} = -\partial_{\mathbf{n}} p, & x \in \partial\Omega(t),\ t > 0, \\ \Omega(0) = \Omega_0. \end{cases} \tag{1.1}$$

Here $\Omega(t)$ is the domain in $\mathbb{R}^n$ occupied by the tumor at time t, $\sigma = \sigma(x,t)$ and $p = p(x,t)$ are the nutrient concentration in the tumor region and the pressure between tumor cells, respectively, $\partial_{\mathbf{n}}$ represents the derivative in the direction of the outward normal $\mathbf{n}$ of the tumor surface $\partial\Omega(t)$, $\bar{\sigma}$ is a positive constant reflecting the constant concentration of nutrient in the host tissue of the tumor, κ is the mean curvature of the tumor surface $\partial\Omega(t)$ whose sign is designated by the convention that for the sphere it is positive, V_{n} is the normal velocity of the tumor surface movement, β is a positive constant reflecting the ability that the tumor attracts blood vessel from its host tissue, γ is another positive constant reflecting the surface tension of the tumor surface and is usually referred to as *surface tension coefficient*, f and g are given functions with $f(\sigma)$ being the (normalized) consumption rate of nutrient by tumor cells when its concentration is at level σ and $g(\sigma)$ the (normalized) proliferation rate of tumor cells when the nutrient concentration is at level σ, and Ω_0 is the domain that the tumor initially occupies. Naturally, from physical viewpoint we have $n = 3$; but for mathematical interest we consider the general case $n \geqslant 2$.

The above model, in the case that f and g are linear functions

$$f(\sigma) = \lambda\sigma \quad \text{and} \quad g(\sigma) = \mu(\sigma - \tilde{\sigma}), \tag{1.2}$$

was proposed by Friedman and Lam in [19] as an essential modification to the corresponding model of Byrne and Chaplain mentioned above. The modification is made by considering nutrient supply mechanism of the tumor in a different viewpoint from that of Byrne and Chaplain. Indeed, in the model of Byrne and Chaplain [3,4], tumor surface is obstacle-free to nutrient diffusion, so that instead of the Robin boundary condition in the third line of (1.1) (referred to as $(1.1)_3$ in what follows), in their model the Dirichlet boundary condition

$$\sigma = \bar{\sigma}, \quad x \in \partial\Omega(t),\ t > 0 \tag{1.3}$$

is imposed, which means that nutrient in the host tissue diffuses into the tumor from its surface without any obstruction, and the effect of vascularization of the tumor is reflected in the structure of the function f: Roughly speaking, the denser the capillary vessel of the tumor is, the larger the

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