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Regularity of solutions to a free boundary problem modeling tumor growth by Stokes equation

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ABSTRACT

In this paper we investigate regularity of solutions to a free boundary problem modeling tumor growth in fluid-like tissues. The model equations include a quasi-stationary diffusion equation for the nutrient concentration, and a Stokes equation with a source representing the proliferation density of the tumor cells, subject to a boundary condition with stress tensor effected by surface tension. This problem is a fully nonlinear problem involving nonlocal terms. Based on the employment of the functional analytic method and the theory of maximal regularity, we prove that the free boundary of this problem is real analytic in temporal and spatial variables for initial data of less regularity.

1. Introduction

Mathematical models and analysis of solid tumor growth, which consider the tumor tissue as a density of proliferating cells, have been developed and studied in many literatures, cf. [1,4–9,11,20,23–25] and the references cited therein. Most of the models assume that the tumor tissue has the structure of a porous medium for which Darcy's law applies (see, e.g. [5–9,23,24]). However, there exist tumors for which the tissue is more naturally modeled as a fluid. For example, in early stages of breast cancer the tumor is confined to the duct of a mammary gland, which consists of epithelial cells, a meshwork of proteins and extracellular fluid. In modeling, this leads to the employment of the Stokes equation rather than the Darcy's law to model the tumor growth [15–19].

The purpose of this paper is to study regularity of solutions to such tumor growth models by Stokes equation:

$$\Delta\sigma = f(\sigma) \quad \text{in } \Omega(t),\ t>0, \tag{1.1}$$

$$\nabla\cdot\mathbf{v} = g(\sigma) \quad \text{in } \Omega(t),\ t>0, \tag{1.2}$$

$$-\nu\Delta\mathbf{v} + \nabla p - \frac{\nu}{3}\nabla(\nabla\cdot\mathbf{v}) = 0 \quad \text{in } \Omega(t),\ t>0, \tag{1.3}$$

$$\sigma = \bar{\sigma} \quad \text{on } \Gamma(t),\ t>0, \tag{1.4}$$

$$\mathbf{T}(\mathbf{v},p)\hat{\mathbf{n}} = -\gamma\kappa\hat{\mathbf{n}} \quad \text{on } \Gamma(t),\ t>0, \tag{1.5}$$

$$V_{\hat{\mathbf{n}}} = \mathbf{v}\cdot\hat{\mathbf{n}} \quad \text{on } \Gamma(t),\ t>0, \tag{1.6}$$

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$$\int_{\Omega(t)} \mathbf{v}\,dx = 0, \quad t > 0, \tag{1.7}$$

$$\int_{\Omega(t)} \mathbf{v} \times x\,dx = 0, \quad t > 0. \tag{1.8}$$

Here $\sigma = \sigma(t,x)$, $\mathbf{v} = \mathbf{v}(t,x) = (v_1(t,x), v_2(t,x), v_3(t,x))$ and $p = p(t,x)$ are unknown functions defined on the time–space manifold $\bigcup_{t\geqslant 0}(\{t\} \times \Omega(t))$, where $\Omega(t)$ is an a priori unknown time-dependent domain in $\mathbb{R}^3$ whose boundary, which we denote by $\Gamma(t)$, is moving and has to be determined together with σ, $\mathbf{v}$ and p. In this model, Δ represents the Laplacian in the x-variable, $\hat{\mathbf{n}}$, κ and $V_{\hat{\mathbf{n}}}$ denote the outward unit normal field, the mean curvature and the normal velocity, respectively, of the free boundary $\Gamma(t)$, and ν, $\bar{\sigma}$ and γ are positive constants. The sign of κ is fixed on by the convention that $\kappa \geqslant 0$ at points where $\Gamma(t)$ is convex with respect to $\Omega(t)$. $\mathbf{T}(\mathbf{v}, p)$ denotes the stress tensor, i.e.,

$$\mathbf{T}(\mathbf{v}, p) = \nu\big[\nabla \otimes \mathbf{v} + (\nabla \otimes \mathbf{v})^T\big] - \left(p + \frac{2\nu}{3}\nabla \cdot \mathbf{v}\right)\mathbf{I},$$

where $\mathbf{I}$ represents the unit tensor. Later on we shall assume without loss of generality that the viscosity coefficient $\nu = 1$, since the general case can be easily reduced into this special case by rescaling (cf. [21]). f and g are general real analytic functions defined on $[0, +\infty)$ with f monotone increasing. It should be mentioned that since our interest lies in the analyticity of solutions in time and space variables, the assumptions on f and g are formulated in the analytic class. Typical examples of f and g are linear functions like

$$f(\sigma) = \lambda_1\sigma, \qquad g(\sigma) = \lambda_2(\sigma - \hat{\sigma}),$$

where λ_1, λ_2 and $\hat{\sigma}$ are positive constants, or of logistic type (cf. [5,19,25]). This problem is imposed with the initial condition

$$\Gamma(0) = \Gamma_0, \tag{1.9}$$

where Γ_0 is a given smooth closed hypersurface in $\mathbb{R}^3$ and encloses a bounded domain Ω_0 such that $\Omega(0) = \Omega_0$.

This model, which considers only proliferating tumor cells, is a simplified version of the tumor growth model proposed by Franks et al. to mimic the early stages of the growth of ductal carcinoma in the breast [15–18] and concisely reformulated by Friedman [19]. In this model, $\Omega(t)$ stands for the domain occupied by the tumor at time t with the free boundary $\Gamma(t)$, Ω_0 denotes the domain initially occupied by the tumor so that $\Gamma_0 = \partial\Omega_0$ represents the initial shape of the tumor. σ represents the nutrient concentration and satisfies the quasi-stationary diffusion equation (1.1) with $f(\sigma)$ denoting the nutrient consumption rate, subject to the boundary condition (1.4) meaning that the tumor receives constant nutrient supply from the tumor surface. $\mathbf{v}$ represents the velocity of the fluid, $g(\sigma)$ stands for the tumor cell proliferation rate, and Eq. (1.2) follows from the law of conservation of mass. Note that the tumor tissue is treated as a fluid rather than a porous medium, so that the Stokes equation replaces Darcy's law to model the tumor growth and leads to Eq. (1.3), where p denotes the pressure inside the tumor. The tumor is assumed to be held together by the forces of cell-to-cell adhesion with constant intensity γ, so that Eq. (1.5) is employed. Eq. (1.6) reflects the kinematic condition on the boundary $\Gamma(t)$. Finally, since the system of Eqs. (1.2), (1.3) and (1.5) has six-dimensional kernel V_0 consisting of rigid motions $\mathbf{v}_0 = \mathbf{a} + \mathbf{b} \times x$, the scalar constrains (1.7) and (1.8) are added to this model (cf. [22]). For more details about this model we refer the readers to the literatures [15–22].

The problem (1.1)–(1.9), which is usually called the *quasi-stationary model*, has been well studied in the past a few years. More precisely, in [19] Friedman established local well-posedness of this model and obtained a unique radial stationary solution for the special case $f(\sigma) = \lambda_1\sigma$ and $g(\sigma) = \lambda_2(\sigma - \hat{\sigma})$. Shortly after in [22] Friedman and Hu proved that this model, also for the special case $f(\sigma) = \lambda_1\sigma$ and $g(\sigma) = \lambda_2(\sigma - \hat{\sigma})$, has a series of non-radial stationary solutions bifurcating from this radial stationary solution. Later on in [29] Wu and Cui proved that for a class of monotone increasing smooth functions f and g, the unique radial stationary solution of this model is asymptotically stable under non-radial perturbations, provided the surface tension coefficient γ is larger than a threshold value $\gamma_* > 0$, while for $0 < \gamma < \gamma_*$ this radial stationary solution is unstable.

If the quasi-stationary diffusion equation (1.1) is replaced by its non-stationary version

$$c\partial_t\sigma - \Delta\sigma = -f(\sigma),$$

where the positive constant $c > 0$ denotes the ratio between the nutrient diffusion time and the tumor-cell doubling time and is very small, then the resulting problem is called the *evolutionary model* of (1.1)–(1.9). In [21] Friedman and Hu proved that the radial stationary solution of the evolutionary model for the special case $f(\sigma) = \lambda_1\sigma$ and $g(\sigma) = \lambda_2(\sigma - \hat{\sigma})$ is linearly asymptotically stable for small (λ_2/γ), i.e., there exists a threshold value $(\lambda_2/\gamma)_*$ such that if we denote by $(\sigma_s, \mathbf{v}_s, p_s, \Gamma_s)$ this stationary solution, then in the case $(\lambda_2/\gamma) < (\lambda_2/\gamma)_*$ the trivial solution of the linearization at $(\sigma_s, \mathbf{v}_s, p_s, \Gamma_s)$ of the original problem is asymptotically stable, and in the case $(\lambda_2/\gamma) > (\lambda_2/\gamma)_*$ the radial stationary solution is unstable. More recently, in [30] Wu and Cui improved this linearly asymptotically stable result to be asymptotically