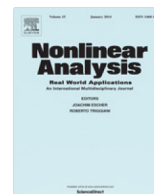




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Bifurcation for a free-boundary tumor model with angiogenesis

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ABSTRACT

We consider a free boundary tumor model with vasculature which supply nutrients to the tumor, so that $\frac{\partial \sigma}{\partial n} + \beta(\sigma - \bar{\sigma}) = 0$ holds on the boundary, where a positive constant β is the rate of nutrient supply to the tumor and $\bar{\sigma}$ is the nutrient concentration outside the tumor. The tumor cells proliferate at a rate μ . We show that for each $\mu_2, \mu_4, \mu_6, \mu_8, \dots$, symmetry-breaking stationary solutions bifurcate from the radially symmetric stationary solutions.

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1. Introduction

Over the last few decades, an increasing number of mathematical models describing solid tumor growth have been studied and developed; these models are classified into discrete cell-based models and continuum models. At the tissue level, continuum models provide a very good approximation. These models incorporate a system of partial differential equations, where variables such as cell density (or volume fractions), nutrient (i.e., oxygen and glucose), etc. are tracked. Modeling, mathematical analysis, numerical simulations were carried out in numerous papers, such as [1–45] and the references cited there. Lowengrub et al. [46] provided a systematic survey of tumor model studies.

Angiogenesis is an important physiological process through which new blood vessels form from pre-existing vessels. It is an essential process in wound healing. However, in a live tissue, angiogenesis is a process that tumor cells secrete cytokines that stimulate the vascular system to grow toward the tumor. That is to say,

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the tumor possesses its own vasculature, then nutrient that is essential to the survival of the tumor may be supplied via the capillary network. The tumor core is nonnecrotic and no chemical inhibitor is present. Analysis of this model can lead to a better understanding of the growing mechanism of the tumor and may also assist in the treatment of cancer.

We denote the concentration of nutrients by σ , distributed uniformly throughout the tumor, then σ satisfies a reaction–diffusion equation

$$\frac{\partial \sigma}{\partial t} = D\Delta\sigma + \Gamma(\sigma_B - \sigma) - \lambda\sigma \quad \text{in } \Omega(t), \tag{1.1}$$

where $\Omega(t)$ is the tumor domain at time t with a moving boundary $\partial\Omega(t)$, D represents diffusion coefficient, $\Gamma(\sigma_B - \sigma)$ denotes the nutrient supplied by the vasculature with Γ being the transfer rate of nutrient in blood tissue and σ_B being the concentration of nutrients in the vasculature, and $\lambda\sigma$ describes the consumption of the nutrient by cells accompanied with λ being the rate of consumption. This model was proposed in [6] to describe the evolution of tumor growth.

By appropriate change of variables and non-dimensional scales (cf. [28], see also [6,10]), (1.1) can be rewritten as

$$c\frac{\partial \sigma}{\partial t} = \Delta\sigma - \sigma \quad \text{in } \Omega(t), \tag{1.2}$$

where c is a small parameter. The tumor tissue with angiogenesis receives nutrients through its own vasculature, so it is natural to assume that σ satisfies the boundary condition (see [28]):

$$\frac{\partial \sigma}{\partial \mathbf{n}} + \beta(t)(\sigma - \bar{\sigma}) = 0 \quad \text{on } \partial\Omega(t), \tag{1.3}$$

where \mathbf{n} is the outward normal, $\beta(t)$ is a positive-valued function which may vary in time and $\bar{\sigma}$ is the nutrient concentration outside the tumor. Angiogenesis results in an increase in $\beta(t)$; on the other hand, if the tumor is treated with anti-angiogenic drugs, $\beta(t)$ will decrease and the starved tumor will shrink.

The pressure p stems from the transport of cells which proliferate or die. As in [10,31], we shall make the assumption that the tumor tissue behaves like a porous medium. Let \mathbf{V} be the velocity field of the tumor cell movement, then $\mathbf{V} = -\nabla p$ by Darcy’s law. Combining with the conservation of mass, $\text{div}\mathbf{V} = \mu(\sigma - \tilde{\sigma})$, we get

$$-\Delta p = \mu(\sigma - \tilde{\sigma}) \quad \text{in } \Omega(t), \tag{1.4}$$

where μ is a parameter expressing the “intensity” of the expansion by mitosis and $\tilde{\sigma}$ is a threshold concentration. As in [4,8], the cell-to-cell adhesiveness leads to the boundary condition:

$$p = \kappa \quad \text{on } \partial\Omega(t), \tag{1.5}$$

where κ is the mean curvature. Furthermore, assuming the continuity of the velocity field up to the boundary of the domain, we derive

$$\mathbf{V}_{\mathbf{n}} = \mathbf{V} \cdot \mathbf{n} = -\nabla p \cdot \mathbf{n} = -\frac{\partial p}{\partial \mathbf{n}} \quad \text{on } \partial\Omega(t), \tag{1.6}$$

where $\mathbf{V}_{\mathbf{n}}$ is the velocity of the free boundary in the direction \mathbf{n} .

In this paper, we assume that

$$\beta(t) \equiv \beta \tag{1.7}$$

is a positive constant.

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