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Bifurcation for a free boundary problem modeling the growth of tumors with a drug induced nonlinear proliferation rate

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Abstract

In this paper, we study a free boundary model describing growth of tumors under action of drugs. To our knowledge, in theoretical discussion for free boundary problems, the proliferation rate in tumor models discussed in previous bifurcation results is a linear function of nutrients and inhibitors. Whereas in this paper we consider the net proliferation rate as a nonlinear function depending on both nutrients and drugs. First, the existence and the uniqueness of radially symmetric stationary solutions are obtained. Second, we prove that symmetry-breaking solutions bifurcate from the radially symmetric stationary solutions when the concentration of drug on the boundary of tumor is less than one in the rescaled model.

MSC: 35J60; 35R35; 35B32; 92C37; 35K55

Keywords: Free boundary; Bifurcation; Existence and uniqueness

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1. Introduction

Mathematical modeling of tumor growth has drawn an increasing attention from both medical scientists and mathematicians, to find out the constraint mechanism and quantitative relationship between nutrients (such as oxygen and glucose) and inhibitors (such as inhibitory materials developed from the immune system of the body, anti-cancer drugs and radiation administered by medical treatment). As solid tumors grow or shrink over time, it is natural to describe them by a PDE free boundary problem. Many theoretical and computational results have highlighted the inhibitor or nutrient delivery and uptake in live tumors in the past several decades (see [1–30] and the references cited therein). Most of the known results on bifurcation branch of tumor models were focused on the proliferation rate linearly depending on the nutrient and inhibitor. Until to 2007, the authors of the paper [6] dealt with the problem in the absence of inhibitors, in which the consumption of nutrient and the proliferation rate are general nonlinear functions. Because there are no explicit radially symmetric stationary solutions for the nonlinear problems, the power series method no longer applies. By reducing the bifurcation problem into the abstract form, they established the bifurcation result on the considered problem.

In 2014, Wu et al. [31] studied the effect of interstitial pressure on therapeutic agent transport in the tumor blood and lymphatic vascular systems and obtained some numerical simulation results. In this paper, inspired by [31] and [32], we propose a model fully considering the restraining effect of the drug and the nutrient during the tumor treatment. The transportation of nutrient and drug in the vasculature and the lymphatic drainage is introduced. We assume also that the proliferation rate λ_p depends nonlinearly on both the nutrient concentration $\tilde{\sigma}$ and the drug concentration $\tilde{D}$. To our best knowledge, only linear proliferation rate of both nutrient and inhibitor is discussed in theoretical bifurcation results in the literature.

The authors in [31] introduced the effect of drug to the net proliferation/death rate λ_p in the tumor's proliferating region Ω_p:

$$\lambda_p = \lambda_M \tilde{\sigma}(1 - \lambda_{effect}\tilde{D}) - \lambda_A, \tag{1.1}$$

where the cell mitosis/death rate is proportional to the amount of nutrient and the apoptosis may occur, λ_M is the mitosis rate, and λ_A is the apoptosis rate. Further, λ_{effect} is the rate of drug-induced cell death, which represents a simple pharmacodynamic model. When $\lambda_{effect}\tilde{D} \leq 1$, the net proliferation is reduced. When $\lambda_{effect}\tilde{D} > 1$, cell death is introduced, which will contribute to tumor shrinkage.

As usual, it is assumed that the cell velocity is proportional to the forces following Darcy's law, because cellular motion within the ECM is approximated here as an incompressible fluid flow in a porous medium. We model all solid phases moving with a single cellular velocity field:

$$\mathbf{v}_c = -\tilde{\mu}\nabla p_c + \chi_E \nabla E, \tag{1.2}$$

where p_c denotes the tumor hydrostatic pressure, $\tilde{\mu}$ is the cell-mobility modeling the net effects of cell-cell and cell-matrix adhesion, E is the ECM density and χ_E is the haptotaxis coefficient. We associate the growth and death of tumor cells with the rate of volume change by assuming that the tumor cell density is constant in the proliferating region:

$$\nabla \cdot \mathbf{v}_c = \lambda_p. \tag{1.3}$$

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