J. Math. Anal. Appl. 450 (2017) 532–543

Contents lists available at ScienceDirect

Journal of Mathematical Analysis and Applications

www.elsevier.com/locate/jmaa

Analysis of a mathematical model for tumor growth with Gibbs–Thomson relation

Junde Wu

Department of Mathematics, Soochow University, Suzhou, Jiangsu 215006, PR China

ARTICLE INFO

Article history:
Received 28 October 2016
Available online 24 January 2017
Submitted by Y. Du

Keywords:
Free boundary problem
Tumor growth
Global existence
Asymptotic behavior

ABSTRACT

In this paper we study a mathematical model for the growth of nonnecrotic solid tumor. The tumor is assumed to be radially symmetric and its radius $R(t)$ is an unknown function of time t as tumor growth, and the model is in the form of a free boundary problem. The feature of the model is that a Gibbs–Thomson relation is taken into account, which results an interesting phenomenon that there exist two stationary solutions (depending on the model parameters). The global existence and uniqueness of solution are established. By denoting c the ratio of the diffusion time scale to the tumor doubling time scale, we prove that for sufficiently small $c > 0$, the stationary solution with the larger radius is asymptotically stable, and the other smaller one is unstable.

1. Introduction

In the last several decades, great attention has been attracted to mathematical models of tumor growth for their own both biological and mathematical interests, cf. [7,11–13] and references therein. Mathematical analysis of these models can help us understanding the mechanism of tumor growth and accessing tumor treatment strategy. On the other hand, a lot of mathematical challenges arise in tumor models, and many interesting and illuminative results have been established, cf. [3–10,15,16,18] and references therein.

In this paper we study a tumor model in the form of a free boundary problem. Since solid tumors grow with spheroid-shaped, tumor region is assumed to be a spheroid with radius $R(t)$ at time $t > 0$, the proliferation of tumor cells is assumed to be dependent only on located concentration of nutrient $\sigma(r, t)$, which is diffusing within tumor region, and tumor growth is governed by the mass conservation law. The model considered here is given as follows:

$$c\frac{\partial \sigma}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\Big(r^2\frac{\partial \sigma}{\partial r}\Big) - \lambda\sigma \qquad \text{for } r < R(t), \quad t > 0, \tag{1.1}$$

E-mail address: wujund@suda.edu.cn.

http://dx.doi.org/10.1016/j.jmaa.2017.01.051

$$\frac{\partial \sigma}{\partial r}(0,t) = 0, \qquad \sigma(R(t),t) = G(t) \qquad \text{for } \ t > 0, \tag{1.2}$$

$$\frac{dR}{dt} = \frac{1}{R^2} \int_0^R \mu(\sigma - \tilde{\sigma}) r^2 dr \qquad \text{for } \ t > 0, \tag{1.3}$$

$$\sigma(r,0) = \sigma_0(r) \qquad \text{for } \ 0 \le r \le R_0, \tag{1.4}$$

$$R(0) = R_0, \tag{1.5}$$

where c, λ, $\tilde{\sigma}$, μ are positive dimensionless constants, among which c is the ratio of the nutrient diffusion time scale ($\sim$ minutes) to the tumor doubling time scale ($\sim$ days), and $c \ll 1$; λ is the nutrient consumption rate; $\tilde{\sigma}$ is a threshold value of nutrient concentration for apoptosis; μ is the proliferation rate of tumor cells; $G(t)$ is a given function representing the external nutrient supply; $\sigma_0(r)$ and R_0 are the given initial data.

In Byrne and Chaplain [1], the external nutrient concentration is assumed to be constant $\bar{\sigma}$, i.e., $G(t) = \bar{\sigma}$. In this case, Friedman and Reitich [10] proved that the tumor model (1.1)–(1.5) has a unique radially symmetric stationary solution for $0 < \tilde{\sigma} < \bar{\sigma}$, and it is asymptotically stable for sufficiently small c. Later, Cui [3] extended the result to the inhibitor-presence case and Cui [4] further investigated the above model with general nutrient consumption function and cell proliferation function. Recently, Xu [17] considered the case that $G(t)$ is given by a periodic function, global well-posedness and some asymptotic behavior of solutions were derived.

One disadvantage of above assumptions on $G(t)$ is that the nutrient is continuous across the tumor boundary, but the flux of nutrient is not. By contrast, Byrne and Chaplain [2] assumed that energy is expended in maintaining the tumor's compactness by cell-to-cell adhesion on tumor boundary and the nutrient acts as a source of energy, so the nutrient concentration on the tumor boundary is less than the external supply $\bar{\sigma}$, and the difference satisfies a Gibbs–Thomson relation, i.e., the difference of nutrient concentration across the tumor boundary $r = R(t)$ is proportional to the mean curvature which is given by $1/R(t)$. More precisely, Byrne and Chaplain [2] assumed that $G(t) = \bar{\sigma}(1 - \gamma/R(t))$, where γ is a positive constant representing the cell-to-cell adhesiveness. In quasi-stationary case $c = 0$ and replacing $\lambda\sigma$ by λ of equation (1.1), Byrne and Chaplain [2] studied existence and uniqueness of solution and the linear stability of stationary solutions, numerical verification was also performed.

Roose, Chapman and Maini [13] pointed out that the tumor model (1.1)–(1.5) with $G(t) = \bar{\sigma}(1 - \gamma/R(t))$, which is induced by Gibbs–Thomson relation, has a number of interesting points. Though it seems speculative, it may be possible to check its veracity in experiment. It is significant to analyze how the Gibbs–Thomson relation affects the growth of tumors, which can be also tested in experiments and clinical laboratory. Note that for any positive constant γ, if $R(t) < \gamma$, then $G(t) = \bar{\sigma}(1 - \gamma/R(t)) < 0$. It is unreasonable since the nutrient concentration must be always nonnegative. For this reason, we introduce a simple modification and let

$$G(t) = \bar{\sigma}(1 - \gamma/R(t))H(R(t)), \tag{1.6}$$

where $H(\cdot)$ is a smooth function such that $H(r) = 0$ for $r \le \gamma$, $H(r) = 1$ for $r \ge 2\gamma$, and $0 \le H'(r) \le 1/\gamma$. In this paper, we shall make a rigorous analysis of problem (1.1)–(1.5) with $G(t)$ given by (1.6), and study the effect of Gibbs–Thomson relation.

In Section 2, we shall prove the global existence and uniqueness of solution, based on a priori estimate and fixed point method. In Section 3, we study the quasi-stationary case $c = 0$. We shall prove that there may exist two, or a unique, or none radially symmetric stationary solutions depending on model parameters. It is interesting that there may exist two radially symmetric stationary solutions, which is different from the uniqueness of stationary solution for constant $G(t) = \bar{\sigma}$ in [10] and periodic function $G(t)$ in [17]. By