Chaos, Solitons & Fractals 44 (2011) 218–225

Contents lists available at ScienceDirect

Chaos, Solitons & Fractals

Nonlinear Science, and Nonequilibrium and Complex Phenomena

journal homepage: www.elsevier.com/locate/chaos

Letter

Existence of traveling wavefronts for Sherratt's avascular tumor model

Huiyan Zhu [a,1], Chunhua Ou [b,*,2]

[a] School of Mathematics and Physics, University of South China, Hengyang, 421001 Hunan, PR China
[b] Department of Mathematics and Statistics, Memorial University of Newfoundland, Canada A1C 5S7

ARTICLE INFO

Article history:
Received 9 September 2010
Accepted 27 January 2011
Available online 5 March 2011

ABSTRACT

In this paper, we revisit Sherratt's avascular tumor growth system modeled in terms of the continuum densities of proliferating, quiescent and necrotic cells, together with the consideration of the generic nutrient supply from underlying tissue and cell movement of contact inhibition. By adopting a perturbation method combined with the Banach fixed point theorem, we theoretically justify the existence of the traveling wavefronts for this model.

1. Introduction

Tumor development typically contains three distinct stages, i.e., avascular, vascular and metastasis, each of which has specific problems that need to be solved by different researchers. For instance, for the growth of a solid tumor, at first a normal cell develops into a tumor one due to gene mutations triggered by environmental and hereditary effects. After abnormal division, such a cell becomes a mass of cells called non-metastatic solid tumor. With sufficient nutrients supplied by the body, this solid tumor continues to grow beyond a certain threshold and then forms its own spiral vessel tissue, through which, some of the tumor cells can escape from the primary location via the circulatory system (metastasis). As such, this process (angiogenesis) can generate the secondary tumor elsewhere in the body and causes the patients to die or reduces permanently their quality of life.

Due to some characteristics of avascular tumor growth, such as the undetectable size of the cell masses or long-term dormant state, it is difficult to conduct experimental researches in vivo. As such, mathematical modeling has become a promising research method for analysis of avascular tumor growth in past decades. The earliest work related to this was done by Thomlinson and Gray [13]. Among previous modeling, the ODE model of Mueller-Klieser [7] is a good study for the avascular tumor growth. In this paper, the author predicted the variation in the concentration of oxygen and other nutrient through a spheroid, and determined the diffusion coefficients by experimental data.

In 1972, Greenspan [5] developed a PDE model. Taking into account spatial structure, he separated the proliferating, quiescent and necrotic cell into three different compartments. Lately, this approach has been extended by Byrne [1] and Friedman and Reitich [4]. By using a weakly nonlinear analysis, Byrne extended previous results to show the interaction of the amplitudes of the asymmetric modes. Friedman and Reitich discussed a model of tumor which grows or shrinks due to proliferation of cells that depends on nutrient concentration modeled by a diffusion equation. After assuming that the tumor is spherically symmetric and its boundary is an unknown function of time t, they gave detailed analytical studies of solutions of the model.

Because separation of proliferating, quiescent and necrotic cell into different compartments led to the problem to determine the location of the interfaces between the compartments, in 1997 and 1999, Ward and King [14,15] constructed a nonlinear PDE model describing the spatial structure of avascular tumor growth that does not assume distinct cell layers, and instead proposed a continuum of cells in two states, living or dead cell populations together with quiescent cells ignored for simplicity. Numerical

* Corresponding author.
E-mail addresses: zhuhuiyan@126.com (H. Zhu), ou@mun.ca (C. Ou).

[1] This work was supported by the Natural Science Foundation of China (11071060) and the project of Hunan Provincial Science & Technology Department (2010GK3013).
[2] This work was supported by NSERC grant of Canada and the IRIF grant of the province of Newfoundland and Labrador.

0960-0779/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.chaos.2011.01.011

solutions of the model showed that after a period of time, the variables settle to a constant profile propagating at a fixed speed, and the growth ultimately either tends to a steady-state (growth saturation) or becomes linear. Both the travelling wave and steady-state limits of the model are derived and studied.

In 2001, Sherratt and Chaplain [11] introduced a new mathematical model for avascular-tumor growth. They modeled it in terms of continuum densities of proliferating, quiescent and necrotic cell, with a generic nutrient supply from underlying tissue, which arise in the two-dimensional condition of a tumor growth within an epithelium. Based on the cell movement of contact inhibition of migration (see [12]), they considered the following reaction–diffusion model:

$$\begin{cases} \frac{\partial p}{\partial t} = \frac{\partial}{\partial x}\left[\frac{p}{p+q}\frac{\partial}{\partial x}(p+q)\right] + g(c)p(1-p-q-n) - f(c)p, \\ \frac{\partial q}{\partial t} = \frac{\partial}{\partial x}\left[\frac{q}{p+q}\frac{\partial}{\partial x}(p+q)\right] + f(c)p - h(c)q, \\ \frac{\partial n}{\partial t} = h(c)q, \\ \frac{\partial c}{\partial t} = D_c\frac{\partial}{\partial x}\left(\frac{\partial}{\partial x}c\right) + k_1c_0[1-\alpha(p+q+n)] - k_1c - k_2pc. \end{cases} \tag{1.1}$$

As stated in [11], $p(x,t)$,$q(x,t)$ and $n(x,t)$ represent the proliferating, quiescent and necrotic cell densities, respectively. $c(x,t)$ is the concentration of the generic nutrient. The product of the fraction $p/(p+q)$ and the overall flux $-\nabla(p+q)$ indicates the flux for population p, with the flux of quiescent cells given similarly, both unaffected by necrotic cells. $g(c)$ denotes the proliferating cell division rate. The proliferating cell becomes quiescent at a rate $f(c)(<g(c))$, and the quiescent cell turns into necrotic at a rate $h(c)$. c_0 is the nutrient concentration in the absence of a tumor cell population; D_c, k_1 and k_2 are constant; the parameter $\alpha \in (0,1]$ (see [11,12] for details). To simply the model, in [11] Sherratt and Chaplain assumed that the nutrient kinetics are always at a quasi-steady state, that is, the density of the nutrient is given by

$$c = \frac{c_0[1-\alpha(p+q+n)]}{1+\frac{p}{\gamma}},$$

where the constant $\gamma = \frac{k_1}{k_2}$. As such, system (1.1) reduces to

$$\begin{cases} \frac{\partial p}{\partial t} = \frac{\partial}{\partial x}\left[\frac{p}{p+q}\frac{\partial}{\partial x}(p+q)\right] + g(c)p(1-p-q-n) - f(c)p, \\ \frac{\partial q}{\partial t} = \frac{\partial}{\partial x}\left[\frac{q}{p+q}\frac{\partial}{\partial x}(p+q)\right] + f(c)p - h(c)q, \\ \frac{\partial n}{\partial t} = h(c)q, \\ c = \frac{c_0[1-\alpha(p+q+n)]}{1+\frac{p}{\gamma}}. \end{cases} \tag{1.2}$$

The existence of traveling waves of (1.2) was formally (not rigorously) analyzed in [11]. By the standard stability analysis near the equilibrium (0,0,0), they showed that the wave speed a must satisfy

$$a \geqslant 2\sqrt{g(c_0)-f(c_0)}.$$

When the wave speed is large, a formal analysis of waves, by neglecting the highest derivatives in the travelling wave equations corresponding to system (1.2), was provided. Numerical simulation was carried out there to confirm their analysis. Biologically, here the wave patterns (p,q,n), connecting the two steady states $(0,0,s_0)$ and $(0,0,0)$ with a moving speed c, indicates the advancing pulses of proliferating and quiescent cells with a gradually growing necrotic behind. These phenomena can be numerically observed by the choice of some appropriate initial data [11].

Although recently there are considerable new contributions in the modeling of avascular tumor growth (see e.g., [10,6] and references therein), the goal of this paper is only concerned with the mathematical understanding of the wavefronts for the model in [11]. We will theoretically prove the existence of traveling wave solution for (1.1) with large wave speeds by using a fixed point theorem. We should mention that the method here is developed from the past references Faria et al. [3], Ou and Wu [8,9] and Zhu et al. [16], but there are significant differences:

- The diffusion term in [3,8,9] is linear, but now in our case the contact inhibition gives the non-linear diffusion $\frac{\partial}{\partial x}\left[\frac{p}{p+q}\frac{\partial}{\partial x}(p+q)\right]$.
- In the past results, all of them require that the reduced system at the equilibria is hyperbolic in the sense that characteristic equation of its linearized system has no solution λ with the real part of λ equal to zero. However, in our case, for the linearized system of (2.4) near the equilibria $(0,0,0)$ or $(0,0,s_0)$, there always exists one eigenvalue equal to zero; see Remark 2.1.

In the rest of this paper, we first prove the existence of traveling waves for some special cases by the fixed point theorem, and in Section 3, we will discuss how to extend our method to study the traveling wave solution for general system (1.2).

2. Traveling wave solutions with large wave speed

In this section, we want to prove rigorously the existence of traveling waves to (1.2). To simplify our analysis, we first assume that the cell division rate $g(c) = 1$. Moreover, since the fourth equation in (1.2) gives a complicated relation

$$c = \frac{c_0[1-\alpha(p+q+n)]}{1+\frac{p}{\gamma}},$$

we may assume that γ is sufficiently large so that $p/\gamma \approx 0$ and thus we have a simple equality

$$c = c_0[1-\alpha(p+q+n)].$$

In fact, as we can see from Fig. 3 in [11], the parameter γ is equal to 10 and the density of p is less than 0.4, and the quotient $p/\gamma \leqslant 0.04$. This type of simplification greatly facilitates our analysis and we have the following system