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Local existence and uniqueness of solutions to approximate systems of 1D tumor invasion model

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ABSTRACT

In the present paper, we propose a modified tumor invasion model which was originally proposed in Chaplain and Anderson (2003) [1]. And we show the local existence and uniqueness of solutions to approximate systems of the 1D modified tumor invasion model. Especially, we introduce a new function and show that our system is equivalent to the nonlinear second-order PDE, which should be reformulated by the new function. Roughly speaking, our system can be rewritten into only one second-order PDE and this fact is quite essential to show the local existence of solutions to the approximate systems.

1. Introduction

In [1] Chaplain and Anderson proposed the following PDEs-ODE system (S) := {(1.1)–(1.4)} to model a tumor invasion phenomenon:

$$n_t = \nabla \cdot (\kappa_n(f, m)\nabla n) - \nabla \cdot (n\chi(f)\nabla f) + F_1(n, f, m), \tag{1.1}$$

$$f_t = -F_2(f, m), \tag{1.2}$$

$$m_t = \kappa_m \Delta m + g(n, m) - h(n, m, f) - k(m, w), \tag{1.3}$$

$$w_t = \kappa_w \Delta w + l(m, f) - k(m, w) - \varepsilon_w w, \tag{1.4}$$

where the unknown functions n, f, m and w represent the concentrations of the tumor cells, the ECM (extracellular matrix), the active MDEs (matrix degrading enzymes) and the endogenous inhibitors, respectively.

The first equation (1.1) describes the kinetics of the tumor cells. In this equation, its flux is given by $-\kappa_n(f, m)\nabla n + n\chi(f)\nabla f$. The former $-\kappa_n(f, m)\nabla n$ represents the random motility of the tumor cells. And a non-negative function $\kappa_n(f, m)$ of f and m represents a chemokinetic response to the ECM and the active MDEs. Roughly speaking, the larger the concentration of the ECM or the active MDEs, the higher the random motility of the tumor cells. The latter $n\chi(f)\nabla f$ describes the haptotactic flux and $\hat{\chi}(f)$ is the haptotactic sensitivity of the tumor cells to the ECM, where $\hat{\chi}$ is the primitive of χ. Moreover, a non-negative function F_1 describes the proliferation of the tumor cells.

The second equation (1.2) describes the kinetics of the ECM. Actually, the ECM is degraded by the biochemical reaction between the ECM and the active MDEs. And its degradation process is described by ODE because this phenomenon is modelled in the meso-scale. By a non-negative function $F_2(f, m)$, we describe the decay rate of the ECM as the result of the biochemical reaction between the ECM and the active MDEs.

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The third equation (1.3) describes the kinetics of the active MDEs. A positive constant κ_m describes the diffusion coefficient of the active MDEs. A positive function $g(n, m)$ describes the production of the active MDEs by the tumor cells and themselves. And positive functions $h(n, m, f)$ and $k(m, w)$ describe the natural decay of the active MDEs, which depends upon the concentrations of the tumor cells and the ECM, and the neutralisation of the active MDEs by the biochemical reaction between the active MDEs and the endogenous inhibitors, respectively.

The fourth equation (1.4) describes the kinetics of the endogenous inhibitors. Positive constants κ_w, ε_w and a positive function $l(m, f)$ describe the diffusion coefficient of the endogenous inhibitors, the natural decay rate and the production by the ECM as a response to the active MDEs of the endogenous inhibitors, respectively.

Now, we propose a modified system of (S). For this, we suppose that the following conditions are satisfied:

(1) There does not exist any endogenous inhibitors. Hence, we do not consider (1.4).
(2) The degradation of the ECM occurs when they contact with the tumor cells and therefore we omit the equation for the active MDEs. Roughly speaking, the tumor cells have an influence on the degradation of the ECM directly and we almost identify the concentration of the tumor cells with that of the active MDEs. So, we do not have to consider (1.3). As a result, we drop out the variable m of the function F_1 in (1.1) and replace that of F_2 in (1.2) by n, namely, $F_1(n, f, m)$ and $F_2(f, m)$ are replaced by $F_1(n, f)$ and $F_2(f, n)$, respectively.
(3) The coefficient of the random motility is given by a function of space and time, not of the concentrations of the ECM and the active MDEs like $\kappa_n(f, m)$ in (1.1). The reason why it is a function of space and time will be explained below. Throughout this paper we denote it by $p = p(x, t)$ instead of $\kappa_n(f, m)$.
(4) The proliferation F_1 of the tumor cells in (1.1) is given by a function of space, time and the concentrations of the tumor cells as well as the ECM. The reason why it depends upon space and time will be also explained below. Moreover, we take the apoptosis of the tumor cells into consideration. So, the nonlinear function in (1.1), denoted by F, is expressed by the difference between non-negative functions F_1 (a proliferation of the tumor cells) and F_a (an apoptosis of the tumor cells), i.e., $F = F_1 - F_a$. As a result, we do not have to assume the non-negativeness of F throughout this paper.
(5) The haptotactic coefficient χ depends upon the concentration of the ECM. In [2], the following functions are reported as the typical examples of χ:

$$\chi(r) = -\frac{\chi_0}{r^2}, \quad \forall r \in (0, +\infty)$$

and

$$\chi(r) = -\frac{\chi_0 K}{(r+K)^3}, \quad \forall r \in [0, +\infty),$$

which are called the logarithmic law and the receptor law, respectively, where χ_0 and K are given positive constants.
(6) The decay of the ECM is directly proportional to the product of the concentrations of the tumor cells and the ECM. We denote by δ its proportion constant, which is positive. Here, you note that the condition (2) above is satisfied.

Under the above setting, we derive the following haptotaxis-degenerate system (P) $:=$ {(1.5), (1.6)} as a modified tumor invasion model of (S):

$$n_t = \nabla \cdot (p(x, t)\nabla n) - \nabla \cdot (n\chi(f)\nabla f) + F(x, t, n, f), \tag{1.5}$$

$$f_t = -\delta n f. \tag{1.6}$$

In below, we explain why a coefficient $p = p(x, t)$ of the random motility of the tumor cells and a function $F = F(x, t, n, f)$ depend upon space and time.

At first, we consider a function F. Recently, it is pointed out that heat shock proteins have influences on the apoptosis of the tumor cells and their dynamics are controlled by a stress of temperature, for example, in [3–6]. In order to take such influences of heat shock proteins into consideration, we assume that a nonlinear function F is a function of space, time and the concentrations of the tumor cells as well as the ECM. But we suppose that the tumor cells and the ECM do not have any influences on the dynamics of heat shock proteins.

Next, we consider a coefficient p. In (S), it is a function of the concentrations of the ECM and the active MDEs. In the process to derive (P), we identify the dynamics of the concentration of the tumor cells with that of the active MDEs. Hence, it must be a function of the concentrations of the tumor cells and the ECM. But, in (P) we suppose that it depends upon distributions of heat shock proteins. So, we give a coefficient of the random motility of the tumor cells by a function of space and time.

Throughout this paper, we impose the following mathematical assumptions to the prescribed data p, χ, F, n_0 and f_0. In below, let T be any positive and finite time and $\Omega := (-L, L)$ for some positive and finite constant L, which contains all tumor cells.

(A1) p is a non-negative and bounded function on $\overline{Q}_T := [-L, L] \times [0, T]$, that is, there exists a positive constant c_1 such that

$$0 \le p(x, t) \le c_1, \quad \text{a.a. } (x, t) \in \overline{Q}_T.$$