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Global Existence of Classical Solutions to a Cancer Invasion Model

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ABSTRACT

This paper deals with a chemotaxis-haptotaxis model of cancer invasion of tissue. The model consists of three reaction-diffusion-taxis partial differential equations describing interactions between cancer cells, matrix degrading enzymes, and the host tissue. The equation for cell density includes two bounded nonlinear density-dependent chemotactic and haptotactic sensitivity functions. In the absence of logistic damping, we prove the global existence of a unique classical solution to this model by some delicate a priori estimate techniques.

Keywords: Cancer Invasion Model; Chemotaxis; Haptotaxis; Global Existence

1. Introduction

Cancer invasion is associated with the degradation of the extra cellular matrix (ECM), which is degraded by matrix degrading enzymes (MDEs) secreted by tumor cells. The degradation creates spatial gradients which direct the migration of invasive cells either via chemotaxis (cellular locomotion directed in response to a concentration gradient of the diffusible MDE) or via haptotaxis (cellular locomotion directed in response to a concentration gradient of adhesive molecules along the ECM). Chaplain and Lolas [1] proposed a PDE model of cancer invasion of tissue, which considers the competition between the following several biological mechanisms: random diffusion, chemotaxis, haptotaxis and logistic growth.

Actually, cancer invasion is a very complex process which involves many various biological mechanisms. In fact, a variety of mathematical models have been developed for various aspects of cancer invasion, and various attempts to give more biologically relevant models have been made by different people (see [2], for instance). Gatenby and Gawlinski [3] useda reaction-diffusion population competition model to study how the tumor invades the surrounding normal tissue or ECM. They suggested that tumor cells createan acidic environment that is toxic to normal tissue, and the high acidity gives rise to the death of the normal tissue, which provides space for tumor cells to proliferate and invade into the surrounding tissue. In contrast to the acid-invasion mechanism, Perumpanani and Byrne [4] found that the ECM heterogeneity affects suchinvasion. They proposed a model under the assumptions that the ECM is degraded by proteases. The proliferation of tumor cells and the remodeling of the ECM are taken into account in the Chaplain and Lolas model. Recently, Gerisch and Chaplain [5] developed a novel non-local model which incorporates cell-cell adhesion and cell matrix adhesion, playing important roles in the tumor invasion process.

Very recently, Szymańka *et al*. [6] proposed a non-local model which focuses on the role of non-local kinetic terms modeling competition for space and degradation; Szymańka *et al*. [7] also discussed the influence of heat shock proteins on cancer invasion of tissue. The analytical results on various models of cancer invasion are mathematically interesting. Walker and Webb [8] proved the global existence solutions to the Chaplain and Anderson's model [9]. Walker [10] also established the global existence of solutions to an age and spatially-structured haptotaxis model, which can be regarded as an extension of the Chaplain and Anderson's model [9]. Marciniak-Czochra and Ptashnyk recently [11] proved the uniform boundedness of solutions to the haptotaxis model [9]. Szymańka *et al*. [6] proved the global existence of solutions to their non-local model.

Very recently, by refining their previous techniques developed in [12]. Litcanu and Morales-Rodrigo [13] studied the asymptotic behavior of solutions to Perumpanani and Byrne's model [4]. Paper [13], to our knowledge, is the first attempt to analytically discuss the asymptotic behavior of solutions for cancer invasion models. We should note that the cancer invasion models in [4-7,9,14]

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are haptotaxis only models. However, Chaplain and Lolas' model [1] is a parabolic-ODE-parabolic-chemotaxis-haptotaxis system. The global existence and uniqueness of classical solutions to this model has been proved for $\mu \geq 0$ (where μ is the growth rate of cancer cells) in one space dimension (see [15]), for $\mu > 0$ in two space dimensions (see [16]) and for large μ in three space dimensions (see [15]).We should note that the global existence is still open for small $\mu > 0$ in three space dimensions for the parabolic-ODE-parabolic chemotaxis-haptotaxis system and the parabolic-ODE-elliptic chemotaxis-haptotaxis system.

Recently, in addition to global existence and uniqueness, the uniform-in-time boundedness of solutions to a simplified parabolic-ODE-elliptic-chemotaxis-haptotaxis system has been proved for $\mu > 0$ in two space dimensions and for large μ in three space dimensions (see [17]).

This paper tries to analytically study a mathematical model of cancer invasion with $\mu = 0$. When $\mu = 0$, the solution Chaplain and Lolas' model can blow up in finite time (see Section 6, [15]). However, it is obvious that the blow-up of cancer cell density in finite time is biologically irrelevant. Hence, we need to deal with the following problem: how to reasonably modify the Chaplain and Lolas' model [1] to obtain the global existence, which is the cancer of the present paper.

This paper extends Chaplain and Lolas' model to a parabolic-parabolic-parabolic chemotaxis-haptotaxis system, and we study the global existence and boundedness of solutions to this model. This paper organized as follows: Section 2 describes the model. Section 3 proves the local existence and uniqueness of solutions. Section 4 establishes some a priori estimates and proves the global existence.

2. Mathematical Model

The mathematical model of cancer invasion is involved in the following three physical variables: cancer cell density $c(x,t)$, ECM density $v(x,t)$ and MDE concentration $u(x,t)$.

The equations describing the dynamics of each variable read as follows:

$$\frac{\partial c}{\partial t} = \underbrace{D_c \Delta c}_{\text{random motion}} - \underbrace{\nabla \cdot (\chi V_1(c) \nabla u)}_{\text{randommotion}} - \underbrace{\nabla . (\xi V_2(c) \nabla v)}_{\text{haptotaxis}}, \tag{1}$$

$$\frac{\partial v}{\partial t} = \underbrace{D_v \Delta v}_{\text{random motion}} - \underbrace{F(u) v}_{\text{proteolysis}} \tag{2}$$

$$\frac{\partial u}{\partial t} = \underbrace{D_u \Delta u}_{\text{diffusion}} + \underbrace{\alpha c}_{\text{production}} - \underbrace{\beta u}_{\text{decay}}, \tag{3}$$

where $D_c, D_v, D_u, \chi, \xi, \alpha$ and β are assumed to be positive constants and $V_1(c)$ and $V_2(c)$ are the density-dependent chemotactic and haptotactic sensitivity functions, respectively.

In Equation (1), the migration of cancer cells is assumed to be governed by random motion, chemotaxis and haptotaxis. In Equation (2) is assumed that ECM has random motion and its degradation by MDEs upon contact; for simplicity, we assume that no remodeling of the ECM takes place, as done in [15,18]. Since random motion ECM is so small hence we assume that D_v is small positive constant. In Equation (3), the MDE concentration is assumed to be influenced by diffusion, production and decay; specifically, MDE is produced by cancer cells, diffuses throughout ECM, and undergoes decay through simple degradation. We shall consider the system (1)-(3) in a bounded domain Ω in $\mathbb{R}^d$ $(\text{d} = 2 \text{ or } 3)$.

For any $0 < T < \infty$ we set

$$\Omega_T = \Omega \times \{0 < t < T\},$$

$$\partial\Omega_T = \partial\Omega \times \{0 < t < T\}.$$

To close the system of equations, we need to impose boundary and initial conditions.

Boundary conditions:

The boundary conditions are represented by the following equalities:

$$\frac{\partial c}{\partial n} = \frac{\partial u}{\partial n} = \frac{\partial v}{\partial n} = 0 \text{ on } \partial\Omega_T, \tag{4}$$

where *n* is the our ward normal vector to $\partial\Omega$.

Initial conditions: We prescribe the initial data

$$c(x,0) = c_0(x), v(x,0) = v_0(x), \\ u(x,0) = u_0(x), x \in \Omega \tag{5}$$

Throughout this paper we will assume that

$$V_i(c) \in C^1([0,+\infty)), V_i(c) \geq 0, V_i(0) = 0, \tag{6}$$

$$V_i'(c) \text{ is Lipschitz continuous}, \tag{7}$$

where $i = 1, 2$ and

$$F(u) \in C^1([0,+\infty)) \text{ and } F(u) \geq 0. \tag{8}$$

In Chaplain and Lolas' original model [1], it is assumed that $V_1(c) = \chi c, V_2(c) = \xi c$ and $F(u) = \gamma u$ (where χ, ξ and γ are some positive constants). For this choice of $V_1(c), V_2(c)$ and $F(u)$, although the assumptions (6)-(8) are satisfied but we would like to slightly modify the choice of $V_1(c), V_2(c)$ and $F(u)$ such that the modified model has a unique global solution. To this end, in addition to the assumptions (6)-(8), we will assume that

$$V_1(c) \text{ and } V_2(c) \text{ are bounded for any } c \geq 0, \tag{9}$$

$$F(u) \text{ is bounded for any } u \geq 0. \tag{10}$$

For example, we may take $V_1(c)=\frac{\chi c}{1+\epsilon_1 c}$, $V_2(c)=\frac{\xi c}{1+\epsilon_2 c}$ and $F(u)=\frac{\delta u}{1+\epsilon_3 u}$ (ϵ_1,ϵ_2 and ϵ_3 are small positive constants). Clearly $V_1(c)\to\chi c$ as $\epsilon_1\to 0, V_2(c)\to\xi c$ as $\epsilon_2\to 0$ and $F(u)\to\delta u$ as $\epsilon_3\to 0$. For this choiceof $V_1(c), V_2(c)$, and $F(u)$, the assumptions (6)-(10) are satisfied. Another choice of $V_1(c)$ and $V_2(c)$ satisfying (9) is that $V_1(c)\equiv 0$ and $V_2(c)\equiv 0$ for $c\ge c_m$, which has a clear biologically relevant interpretation: the cancer cells stop to accumulate at a given point of the tumor tissue after their density attains a maximal density c_m. A similar assumption for a prey taxis sensitivity function was made in [19].

In next section we will prove the local existence and uniqueness of a solution for the system (1)-(5) by a fixed point argument.

3. Local Existence and Uniqueness

Throughout this paper we assume that

$$\begin{aligned} &c_0(x)\ge 0, v_0(x)\ge 0, u_0(x)\ge 0,\\ &\partial\Omega\in C^{2+\sigma}, 0<\sigma<1,\\ &c_0(x), v_0(x), u_0(x)\in C^{\sigma+2}(\bar{\Omega}),\\ &\frac{\partial c_0(x)}{\partial n}=\frac{\partial v_0(x)}{\partial n}=\frac{\partial u_0(x)}{\partial n}=0 \text{ on } \partial\Omega. \end{aligned} \tag{11}$$

For brevity we set

$$U=(c,v,u) \tag{12}$$

For notations' convenience, in what follows we denote various constants which are independent of T by A_0, whereas we denote various constants which depend on T by A .The constants A_0 and A may be different from line to line.

In the following, under the assumptions (6)-(8) and (11), we shall prove that the system (1)-(5) has a unique local (in time) smooth solution.

Theorem 3.1. Under the assumptions (6)-(8), there existsa unique solution $U\in C^{2+\sigma,1+\sigma/2}(\Omega_T)$ of the system (1)-(5) for some small $T>0$ which depends on $\|U(.,0)\|_{C^{2+\sigma}(\Omega)}$.

Proof. We shall prove the local existence by a fixed point argument. We introduce the Banach space X of the vector function U (defined in (12)) with norm

$$\|U\|=\|U\|_{C^{1+\sigma,\sigma/2}(\Omega_T)}\ (0<T<1)$$

and a subset

$$X_M=\{U\in X:\|U\|\le M\},$$

where

$$\begin{aligned} M:&=\|c_0(x)\|_{C^{2+\sigma}(\Omega)}+\|v_0(x)\|_{C^{2+\sigma}(\Omega)}\\ &+\|u_0\|_{C^{2+\sigma}(\Omega)}+1\\ &=\|U(.,0)\|_{C^{2+\sigma}(\Omega)}+1 \end{aligned}$$

Given any $U\in X_M$, we define a corresponding. Function $\bar{U}=FU$ by $\bar{U}=(\bar{c},\bar{v},\bar{u})$, where $\bar{U}$ satisfies the equations

$$\frac{\partial\bar{v}}{\partial t}-D_v\Delta\bar{v}+F(u)\bar{v}=0 \text{ in } \Omega_T, \tag{13}$$

$$\frac{\partial\bar{v}}{\partial n}=0 \text{ on } \partial\Omega_T, \tag{14}$$

$$\bar{v}(x,0)=v_0(x) \text{ in } \Omega, \tag{15}$$

$$\frac{\partial\bar{u}}{\partial t}-D_u\Delta\bar{u}+\beta\bar{u}=\alpha c \text{ in } \Omega_T, \tag{16}$$

$$\frac{\partial\bar{u}}{\partial n}=0 \text{ on } \partial\Omega_T, \tag{17}$$

$$\bar{u}(x,0)=u_0(x) \text{ in } \Omega, \tag{18}$$

$$\frac{\partial\bar{c}}{\partial t}-D_c\Delta\bar{c}=h_1(c,\bar{u},\bar{v}) \text{ in } \Omega_T, \tag{19}$$

$$\frac{\partial\bar{c}}{\partial n}=0 \text{ on } \partial\Omega_T, \tag{20}$$

$$\bar{c}(x,0)=c_0(x) \text{ in } \Omega, \tag{21}$$

where

$$\begin{aligned} h_1(c,\bar{u},\bar{v})&=-\nabla\cdot(\chi V_1(c)\nabla\bar{u})\\ &\quad-\nabla\cdot(\xi V_2(c)\nabla\bar{v})\\ &=-\chi V_1(c)\Delta\bar{u}-\xi V_2(c)\Delta\bar{v}\\ &\quad-(\chi V_1'(c)\nabla\bar{u}+\xi V_2'(c)\nabla\bar{v})\cdot\nabla c \end{aligned} \tag{22}$$

We first consider the linear parabolic (13)-(15). By (8), (11) and the parabolic Schauder theory (for example, see [20]) there exists a unique solution $\bar{v}$, and

$$\|\bar{v}\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)}\le A_0\|\bar{v}(x,0)\|_{C^{2+\sigma}(\Omega)}\le A_0 M \tag{23}$$

Similarly, from $U\in X_M$, (11) and the parabolic Schauder theory, problem (16)-(18) has a unique solution $\bar{u}$ satisfying

$$\begin{aligned} \|\bar{u}\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)}&\le A_0\left(\|\bar{u}(x,0)\|_{C^{2+\sigma}(\Omega)}+\|\alpha c\|_{C^{\sigma,\sigma/2}(\Omega_T)}\right)\\ &\le A_0 M \end{aligned} \tag{24}$$

We now turn to the linear parabolic problem (19)-(21). Using $U\in X_M$, (23) and (24) and noting $V_1'(c)$ and

$V_2'(c)$ are Lipschitz continuous, we have

$$\|h_1\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A_0 M, \tag{25}$$

Hence, by Schauder theory as before, the problem (19)-(21) admits a unique solution $\bar{c}$ satisfying

$$\|\bar{c}\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A_0\left(\|\bar{c}(x,0)\|_{C^{2+\sigma}(\Omega)} + \|h_1\|_{C^{\sigma,\sigma/2}(\Omega_T)}\right) \le A_0 M \tag{26}$$

We conclude from (23), (24) and (26) that

$$\|\bar{U}\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A_0 M. \tag{27}$$

By direct calculations, we obtain

$$\|\bar{U}(x,t) - \bar{U}(x,0)\|_{C^{1+\sigma,\sigma/2}(\Omega_T)} \le A_0 \eta(T) \|\bar{U}\|_{C^{1+\sigma,\sigma/2}(\Omega_T)}$$

where $\eta(T) \to 0$ if $T \to 0$. If we further take T sufficiently small, then by (27)

$$\begin{aligned}
\|\bar{U}(x,t)\|_{C^{1+\sigma,\sigma/2}(\Omega_T)} &\le \|\bar{U}(x,0)\|_{C^{1+\sigma}(\Omega)} + \|\bar{U}(x,t) - \bar{U}(x,0)\|_{C^{1+\sigma,\sigma/2}(\Omega_T)} \\
&\le \|\bar{U}(x,0)\|_{C^{1+\sigma}(\Omega)} + A_0\eta(T)\|\bar{U}\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \\
&\le \|\bar{U}(x,0)\|_{C^{1+\sigma}(\Omega)} + A_0\eta(T) M \\
&\le \|\bar{U}(x,0)\|_{C^{1+\sigma}(\Omega)} + 1 \\
&\le M.
\end{aligned}$$

Hence, $\bar{U} \in X_M$, *i.e.* F maps X_M into itself. We next show that F is a contraction mapping. Take U_1, U_2 in X_M, and set $\bar{U}_1 = FU_1$ and $\bar{U}_2 = FU_2$. setting

$$\delta = \|U_1 - U_2\|$$

We derive from (13) that

$$\delta = \|U_1 - U_2\| \frac{\partial(\bar{v}_1 - \bar{v}_2)}{\partial t} - D_v \Delta(\bar{v}_1 - \bar{v}_2) + F(u_1)(\bar{v}_1 - \bar{v}_2) = \bar{v}_2\left(F(u_2) - F(u_1)\right),$$

where

$$\|\bar{v}_2(F(u_2) - F(u_1))\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A_0\|U_1 - U_2\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A_0\delta.$$

Hence, since $(\bar{v}_1 - \bar{v}_2)\big|_{t=0} = 0,$ Schauder theory yields

$$\|\bar{v}_1 - \bar{v}_2\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A_0\delta. \tag{28}$$

Similarly, we derive from (16) and $(\bar{u}_1 - \bar{u}_2)\big|_{t=0} = 0,$ that

$$\begin{aligned}
\|\bar{u}_1 - \bar{u}_2\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} &\le A_0\|c_1 - c_2\|_{C^{\sigma,\sigma/2}(\Omega_T)} \\
&\le A_0\|U_1 - U_2\|_{C^{\sigma,\sigma/2}(\Omega_T)} \\
&\le A_0\delta
\end{aligned} \tag{29}$$

We next turn to the equation for $\bar{c}_1 - \bar{c}_2$:

$$\frac{\partial(\bar{c}_1 - \bar{c}_2)}{\partial t} - D_c\Delta(\bar{c}_1 - \bar{c}_2) = h_2 \tag{30}$$

where

$$\begin{aligned}
h_2 = &-\chi V_1(c_1)\Delta(\bar{u}_1 - \bar{u}_2) - \chi\Delta\bar{u}_2\left(V_1(c_1) - V_1(c_2)\right) \\
&- \xi V_2(c_1)\Delta(\bar{v}_1 - \bar{v}_2) - \xi\Delta\bar{v}_2\left(V_2(c_1) - V_2(c_2)\right) \\
&- \chi V_1'(c_1)\nabla c_1 \cdot \nabla(\bar{u}_1 - \bar{u}_2) - \chi V_1'(c_1)\nabla\bar{u}_2 \cdot \nabla(c_1 - c_2) \\
&- \chi\left(V_1'(c_1) - V_1'(c_2)\right)\nabla\bar{u}_2 \cdot \nabla c_2 \\
&- \xi V_2'(c_1)\nabla c_1 \cdot \nabla(\bar{v}_1 - \bar{v}_2) - \xi V_2'(c_1)\nabla\bar{v}_2 \cdot \nabla(c_1 - c_2) \\
&- \xi\left(V_2'(c_1) - V_2'(c_2)\right)\nabla\bar{v}_2 \cdot \nabla c_2
\end{aligned}$$

Noting $V_1'(c)$ and $V_2'(c)$ are Lipschitz continuous and using (6), (7), (27), (28) and (29), we have

$$\|h_2\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A_0\delta.$$

By Schauder theory, since $(\bar{c}_1 - \bar{c}_2)\big|_{t=0} = 0,$

$$\|\bar{c}_1 - \bar{c}_2\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A_0\|h_2\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A_0\delta. \tag{31}$$

Combining this with (28) and (29), we get

$$\|\bar{U}_1 - \bar{U}_2\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A_0\delta.$$

Nothing $(\bar{U}_1 - \bar{U}_2)(x,0) \equiv 0$ and proceeding as before, we have

$$\begin{aligned}
\|\bar{U}_1 - \bar{U}_2\|_{C^{1+\sigma,\sigma/2}(\Omega_T)} &\le A_0\eta(T)\|\bar{U}_1 - \bar{U}_2\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \\
&\le A_0\eta(T)\delta = A_0\eta(T)\|U_1 - U_2\|_{C^{1+\sigma,\sigma/2}(\Omega_T)}
\end{aligned} \tag{32}$$

Taking T small such that $A_0\eta(T) < \frac{1}{2}$ we conclude from (32) that F is a contraction in X_M. By the contraction mapping theorem F has a unique fixed point U in X_M which is the unique solution of (1)-(5).

4. A Priori Estimates and Global Existence

To continue the local solution established in the above section to all $t > 0$ we need to establish some a priori estimates. Throughout this section, in addition to the assumptions (6)-(8) and (11) we assume that the assumptions (9) and (10) hold.

Noting $V_1(0) = V_2(0) = 0,\ c_0(x) \ge 0,\ v_0(x) \ge 0$ and $u_0(x) \ge 0,$ and using the maximum principle, we easily prove the following lemma.

Lemma 4.1. Assume that $U = (c,v,u) \in C^{2,1}(\Omega_T)$ is a solution to (1)-(5), then

$$c \geq 0,\ v \geq 0,\ u \geq 0. \tag{33}$$

Lemma 4.2. Assume that $U = (c, v, u) \in C^{2,1}(\Omega_T)$ is a solution to (1)-(5) then for $p > 2$, we have

$$\|c\|_{L^p(\Omega_T)} \leq A, \tag{34}$$

$$\|v\|_{W_p^{2,1}(\Omega_T)} \leq A_0, \tag{35}$$

$$\|u\|_{W_p^{2,1}(\Omega_T)} \leq A. \tag{36}$$

Proof. For $p > 2$, we derive from

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega c^p \mathrm{d}x &= p\int_\Omega c^{p-1}c_t \mathrm{d}x = -p(p-1)D_c\int_\Omega c^{p-2}|\nabla c|^2 \mathrm{d}x \\ &+ \chi p(p-1)\int_\Omega c^{p-2}V_1(c)\nabla c\cdot\nabla u \mathrm{d}x \\ &+ \xi p(p-1)\int_\Omega c^{p-2}V_2(c)\nabla c\cdot\nabla v \mathrm{d}x \\ &\leq \frac{-4(p-1)D_c}{p}\int_\Omega \left|\nabla c^{2/2}\right|^2 \mathrm{d}x \\ &+ A_0\chi p(p-1)\int_\Omega c^{p-2}\nabla c\cdot\nabla u \mathrm{d}x \\ &+ \xi p(p-1)\int_\Omega c^{p-2}V_2(c)\nabla c\cdot\nabla v \mathrm{d}x.\end{aligned} \tag{37}$$

We now consider the integral $\int_\Omega c^{p-2}\nabla c\cdot v\nabla u \mathrm{d}x$. By Equation (3) and the parabolic L^p estimate [20] we have

$$\begin{aligned}\|u\|_{W_p^{2,1}(\Omega_T)} &\leq A_0\left(\|u_0\|_{W_p^2(\Omega)} + \|\alpha c\|_{L^p(\Omega_T)}\right) \\ &\leq A_0 + A_0\|c\|_{L^p(\Omega_T)},\end{aligned} \tag{38}$$

In particular,

$$\|u\|_{L^p(\Omega_T)} + \|u_t\|_{L^p(\Omega_T)} \leq A_0 + A_0\|c\|_{L^p(\Omega_T)} \tag{39}$$

Multiplying Equation (3) by c^{p-1} and integrating in Ω_t, we obtain

$$\begin{aligned}(p-1)D_u\int_0^t\int_\Omega c^{p-2}\nabla c\cdot\nabla u \mathrm{d}x\mathrm{d}t &= \alpha\int_0^t\int_\Omega c^p \mathrm{d}x\mathrm{d}t \\ &- \beta\int_0^t\int_\Omega c^{p-1}u \mathrm{d}x\mathrm{d}t - \int_0^t\int_\Omega c^{p-1}u_t \mathrm{d}x\mathrm{d}t\end{aligned}$$

And there for, by Young's inequality and estimate (39), we have

$$\begin{aligned}&(p-1)D_u\int_0^t\int_\Omega c^{p-2}\nabla c\cdot\nabla u \mathrm{d}x\mathrm{d}t \leq A_0(p)\int_0^t\int_\Omega c^p \mathrm{d}x\mathrm{d}t \\ &+\int_0^t\int_\Omega |u|^p \mathrm{d}x\mathrm{d}t + \int_0^t\int_\Omega |u_t|^p \mathrm{d}x\mathrm{d}t \leq A_0(p)\int_0^t\int_\Omega c^p \mathrm{d}x\mathrm{d}t + A_0.\end{aligned} \tag{40}$$

Also, by Equation (2) and the parabolic L^p estimate we have

$$\|v\|_{W_p^{2,1}(\Omega_T)} \leq A_0\|v_0\|_{W_p^2(\Omega)} \leq A_0 \tag{41}$$

In particular,

$$\|\nabla v\|_{L^p(\Omega_T)} \leq A_0. \tag{42}$$

By (9), Young's inequality and estimate (42)

$$\begin{aligned}&\int_0^t\int_\Omega c^{p-2}V_2(c)\nabla c\cdot\nabla v \mathrm{d}x\mathrm{d}t \leq A_0\int_0^t\int_\Omega c^{p-2}|\nabla c||\nabla v| \mathrm{d}x\mathrm{d}t \\ &\leq \epsilon\int_0^t\int_\Omega c^{p-2}|\nabla c|^2 \mathrm{d}x\mathrm{d}t + A_0(\epsilon)\int_0^t\int_\Omega c^{p-2}|\nabla v|^2 \mathrm{d}x\mathrm{d}t \\ &\leq \frac{4\epsilon}{p^2}\int_0^t\int_\Omega \left|\nabla c^{p/2}\right|^2 \mathrm{d}x\mathrm{d}t + A_0(p,\epsilon)\int_0^t\int_\Omega c^p \mathrm{d}x\mathrm{d}t \\ &+ \int_0^t\int_\Omega |\nabla v|^p \mathrm{d}x\mathrm{d}t \leq \frac{4\epsilon}{p^2}\int_0^t\int_\Omega \left|\nabla c^{p/2}\right|^2 \mathrm{d}x\mathrm{d}t \\ &+ A_0(p,\epsilon)\int_0^t\int_\Omega c^p \mathrm{d}x\mathrm{d}t + A_0\end{aligned} \tag{43}$$

Integrating with respect to t on both sides (37), noting (11) and using estimates (40) and (43) and taking ϵ sufficiently small, we obtain

$$\begin{aligned}\int_\Omega c^p \mathrm{d}x &\leq \frac{4(p-1)}{p}(\xi\epsilon - D_c)\int_0^t\int_\Omega \left|\nabla c^{p/2}\right|^2 \mathrm{d}x\mathrm{d}s \\ &+ A_0(p,\epsilon)\int_0^t\int_\Omega c^p + A_0(p) \\ &\leq A_0(p)\int_0^t\int_\Omega c^p \mathrm{d}x\mathrm{d}t + A_0(p).\end{aligned}$$

Gronwall's lemma yields

$$\int_0^T\int_\Omega c^p \mathrm{d}x\mathrm{d}t \leq A(p). \tag{44}$$

Now, by (39) and (44) we have

$$\|u\|_{W_p^{2,1}(\Omega_T)} \leq A(p). \tag{45}$$

This completes the proof of lemma 4.2.

In the following result we obtaina better bound of c, a L^∞—bound. Let $p > 1$ and define $B := -D_c\Delta + I$, with domain $D(B) = \left\{c \in W_p^2(\Omega): \frac{\partial c}{\partial n} = 0 \text{ on } \partial\Omega\right\}$ For each $\theta \geq 0$, define the sectorial operator B^θ (see [21]) and $X_\theta := D(B^\theta)$ with the norm $\|c\|_{X_\theta} = \|B^\theta c\|_{L^p}$.

Lemma 4.3. Let $2\theta < 1$, then for $t \in [t_0, T)$ where $t_0 > 0$, we have

$$\|c(t)\|_{X_\theta} \leq A. \tag{46}$$

Proof. We have that

$$\begin{aligned}c(t) &= e^{-tB}c_0 \\ &+ \int_0^t e^{-(t-s)B}\left[-\nabla\cdot(\chi V_1(c)\nabla u) - \nabla\cdot(\xi V_2(c)\nabla v) + c\right]\mathrm{d}s\end{aligned}$$

and so

$$\|c(t)\|_{X_\theta} \le \| \|e^{-tB}c_0\|_{X_\theta}$$
$$+\int_0^t \left\|e^{-(t-s)B}\left[-\nabla\cdot\left(\chi V_1(c)\nabla u\right)-\nabla\cdot\left(\xi V_2(c)\nabla v\right)+c\right]\right\|_{X_\theta}\mathrm{d}s \tag{47}$$

By [21] (Theorem 1.4.3) and (11)

$$\left\|e^{-tB}c_0\right\|_{X_\theta} \le A_0 t^{-\theta}e^{-\varrho t}\|c_0\|_{L^p(\Omega)} \le A_0 t^{-\theta}e^{-\varrho t} \tag{48}$$

and, by (34),

$$\begin{aligned}\left\|e^{-(t-s)B}c\right\|_{X_\theta} &\le A_0(t-s)^{-\theta}e^{-\varrho(t-s)}\|c\|_{L^p(\Omega)}\\ &\le A(t-s)^{-\theta}e^{-\varrho(t-s)},\end{aligned} \tag{49}$$

where $Q\in(0,1)$. Moreover, by [22] (Lemma 2.1), (9), (35) and (36), we obtain

$$\begin{aligned}&\left\|e^{-(t-s)B}\left[-\nabla\cdot\left(\chi V_1(c)\nabla u\right)-\nabla\cdot\left(\xi V_2(c)\nabla v\right)\right]\right\|_{X_\theta}\\ &\le A_0\left\|e^{(t-s)\Delta}\left[-\nabla\cdot\left(\chi V_1(c)\nabla u\right)-\nabla\cdot\left(\xi V_2(c)\nabla v\right)\right]\right\|_{X_\theta}\\ &\le A_0(\epsilon)(t-s)^{-\theta-\frac{1}{2}-\epsilon}e^{-\varrho(t-s)}\left\|\chi V_1(c)\nabla u+\xi V_2(c)\nabla v\right\|_{L^p(\Omega)}\\ &\le A(\epsilon)(t-s)^{-\theta-\frac{1}{2}-\epsilon}e^{-\varrho(t-s)},\end{aligned} \tag{50}$$

where $\epsilon>0$ such that $-\theta-\frac{1}{2}-\epsilon>-1$.

Inserting (48)-(50) into (47) and noting $\theta+\frac{1}{2}+\epsilon<1$ and $\theta<1$, we obtain

$$\begin{aligned}\|c(t)\|_{X_\theta} &\le A_0 t^{-\theta}e^{-\varrho t}\\ &+A(\epsilon)\int_0^t\left[(t-s)^{-\theta-\frac{1}{2}-\epsilon}e^{-\varrho(t-s)}+(t-s)^{-\theta}e^{-\varrho(t-s)}\right]\mathrm{d}s\\ &\le A(t_0)\end{aligned}$$

for all $t\in[t_0,T)(0<t_0<T)$.

This completes the proof of lemma 4.3. □

Lemma 4.4. We have that

$$\|c(t)\|_{L^\infty(\Omega)} \le A \text{ for all } t\in[0,T). \tag{51}$$

Proof. Let $P>d, 2\theta\in\left(\frac{d}{p},1\right)$. since $2\theta>\frac{d}{p}$ we have by [21] (Theorem 1.6.1) that

$$X_\theta \to c(\bar{\Omega})$$

Thanks to lemma 4.3 we have that

$$\|c(t)\|_{L^\infty(\Omega)} \le A(t_0) \text{ for } t>t_0>0.$$

Moreover, the local existence Theorem yields $\|c(t)\|_{L^\infty(\Omega)} \le A_0$ for $t<t_0$.

Therefore

$$\|c(t)\|_{L^\infty(\Omega)} \le A \text{ for all } t\in[0,T).$$

This completes the proof of Lemma 4.4. □

Lemma 4.5. We have that

$$\|c\|_{W_p^{2,1}(\Omega_T)} \le A \tag{52}$$

Proof. By the Sobolev embedding theorem (see [20], (Lemma 3.3, p. 80)), if we take p sufficiently large, then (35) and (36) yields

$$\|\nabla v\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A_{0,}\ \|\nabla u\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A, \tag{53}$$

and therefore

$$\|\nabla v\|_{L^\infty(\Omega_T)} \le A_{0,}\ \|\nabla u\|_{L^\infty(\Omega_T)} \le A, \tag{54}$$

By (7) and (51), we have

$$\left\|V_1'(c)\right\|_{L^\infty(\Omega)} \le A, \left\|V_2'(c)\right\|_{L^\infty(\Omega)} \le A. \tag{55}$$

Now, Equation (1) can be rewritten as

$$\begin{aligned}&\frac{\partial c}{\partial t}-D_C\Delta c+\left(\chi V_1'(c)\nabla u+\xi V_2'(c)\nabla v\right).\nabla c\\ &=-\chi V_1(c)\Delta u-\xi V_2(c)\Delta v\end{aligned}$$

where

$$\left\|\chi V_1'(c)\nabla u+\xi V_2'(c)\nabla v\right\|_{L^\infty(\Omega)} \le A \tag{56}$$

$$\left\|\chi V_1(c)\Delta u+\xi V_2(c)\Delta v\right\|_{L^p(\Omega_T)} \le A \tag{57}$$

By (9), (35), (36), (53) and (55). These, along with (11) and the parabolic L^p estimate, yield the estimate (52). □

Lemma 4.6. Assume that $U=(c,v,u)\in C^{2,1}(\Omega_T)$ is a solution to (1)-(5), then

$$\|U\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A. \tag{58}$$

Proof. By (52) and the Sobolev embedding theorem (taking p large),

$$\|c\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A. \tag{59}$$

Also, (35), (36) and the Sobolev embedding theorem (taking p large) yield

$$\|v\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A_0, \|u\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A. \tag{60}$$

Now, from (3), (11), (59) and the parabolic Schauder estimates we have

$$\|u\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A \tag{61}$$

Also, the parabolic Schauder estimates yield

$$\|v\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A_0. \tag{62}$$

Finally, we conclude from (61) and (62) that

$$\left\|\chi V_1'(c)\nabla u + \xi V_2'(c)\nabla v\right\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A$$

$$\left\|\chi V_1(c)\Delta u + \xi V_2(c)\Delta v\right\|_{C^{\sigma,\sigma/2}(\Omega_T)} \le A$$

Hence, by the parabolic Schauder estimates, we obtain

$$\|c\|_{C^{2+\sigma,1+\sigma/2}(\Omega_T)} \le A. \quad (63)$$

This completes the proof of Lemma 4.6. □

With a priori estimate (58), we can extend the local classical solution established in Theorem 3.1 to all $t > 0$, as done in [15]. Namely we have

Theorem 4.7. There exists a unique global solution $U \in C^{2+\sigma,1+\sigma/2}(\Omega_T)$ of the system (1)-(5) for any given $T > 0$.

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