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GLOBAL SOLUTIONS TO CHEMOTAXIS-HAPTOTAXIS TUMOR INVASION SYSTEM WITH TISSUE RE-ESTABLISHMENT

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Abstract. In this paper, we consider the chemotaxis-haptotaxis model of tumor invasion with the proliferation and tissue re-establishment term in dimensions one and two. We show the global in time existence of a unique classical solution for the the model in two dimensional spatial domain without any restrictions on the coefficients.

1. Introduction

In this paper, we are interested in the mathematical analysis on the system of partial differential equations modelling such tumor cell invasion, especially, the model suggested by Chaplain-Lolas[5].

There are many mathematical models describing tumor invasion in different mechanisms of various stages of the invasion([1, 2, 3, 4, 5, 7, 9] and see references therein). In most of the models, they adopted haptotaxis as the direct movement of tumor cells. But recently, Chaplain-Lolas [4, 5] suggested a model presenting the behavior of tumor cells by both haptotaxis and chemotaxis movements. There are a few results in mathematical analysis for this Chaplain-Lolas model[5]. Tao-Wang[13] proved the global-in-time existence of a classical solution to the system of the model in [5] neglecting tissue re-establishment in one dimensionsional spatial domains and in two and three dimensional domains under the assumption that the ratio $\frac{\chi}{\mu_1}$ in (1.1) is sufficiently small. Tao[11] showed the global-in-time existence for the model in two

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dimensional spatial domain without that assumption. For the haptotaxis only model, Walker-Webb[15] proved the unique global existence of classical solution to the system of a model not considering chemotaxis. Szymańska, Morales-Rodrigo, Lachowicz and Chaplain[10] also proved the unique global existence of a classical solution for a non-local system of haptotaxis model.

We note that the above mentioned analytical results are mainly focused on the tumor invasion model neglecting tissue re-establishment. As far as we know, the first analytical result for the tumor invasion model considering extracellular matrix(ECM) tissue re-establishment is [12]. In [12], Tao proved the global-in-time existence of a classical solution to a haptotaxis only model in [3] of two dimensions for $\mu_1 \geq \mu_2\lambda_2\xi$, where μ_1, μ_2, λ_2 and ξ are nonnegative constants in the system (1.1)–(1.3). Also boundedness of solutions in two and three dimensions is proved in [12] for the haptotaxis model. As indicated in [12], the models of tumor invasion with ECM tissue re-establishment are difficult to be analyzed for the regularity because of the strong coupling between ECM tissue density and tumor cell density. Very recently, Fan and Zhao[6] obtained global-in-time existence of smooth solution in three dimensions with the same assumption as [12] for the two dimensions.

The followings are the chemotaxis-haptotaxis model of tumor invasion suggested by Chaplain-Lolas[5] ;

(1.1)
$$\frac{\partial c}{\partial t} = \underbrace{\Delta c}_{dispersion} - \underbrace{\chi\nabla\cdot(c\nabla u)}_{chemotaxis} - \underbrace{\xi\nabla\cdot(c\nabla v)}_{haptotaxis} + \underbrace{\mu_1 c(1-c-\lambda_1 v)}_{proliferation}, \quad \text{in } \Omega_T,$$

(1.2)
$$\frac{\partial v}{\partial t} = -\underbrace{uv}_{degradation} + \underbrace{\mu_2 v(1-v-\lambda_2 c)}_{re-establishment}, \quad \text{in } \Omega_T,$$

(1.3)
$$\frac{\partial u}{\partial t} = \underbrace{\Delta u}_{dispersion} + \underbrace{c}_{production} - \underbrace{u}_{decay}, \quad \text{in } \Omega_T,$$

where Ω is a smooth bounded domain in $\mathbb{R}^2$, $\Omega_T := \Omega \times (0,T)$ for any $0 < T \leq \infty$, and the coefficients χ, ξ, μ_1, μ_2, λ_1 and λ_2 are nonnegative constants. Here, they denote the tumor cell density by c, the ECM protein density (in normal tissue) by v, and the urokinase Plasminogen Activator (uPA- a matrix(ECM) degrading enzyme). Also χ and ξ are the chemotactic and haptotactic coefficients, respectively, μ_1 the tumor cell proliferation rate, μ_2 the ECM re-establishment rate, and λ_1 and λ_2 the competition rates for space by the presence of ECM and by the presence of tumor cells. We impose boundary condition and initial data

$$\frac{\partial c}{\partial \nu} - \xi c \frac{\partial v}{\partial \nu} = 0 \text{ and } \frac{\partial u}{\partial \nu} = 0, \ \ (c(x,0),\, u(x,0),\, v(x,0)) = (c_0(x),\, u_0(x),\, v_0(x)).$$

Considering only the case χ, ξ, μ_1, μ_2, $\lambda_1 > 0$, we obtain the following results.

Theorem 1.1. *Let $\Omega \subset \mathbb{R}^2$ and $\|(c_0, u_0, v_0)\|_{C^2} < \infty$. If $\lambda_2 \geq 0$, then there exists a unique global-in-time solution $(c,\, u,\, v) \in C^{2+\sigma, 1+\frac{\sigma}{2}}_{x,t}(\Omega_\infty)$ to the system* (1.1)–(1.3).

We will prove above Theorem in the following sections by obtaining some delicate a priori estimates in section 2 and using parabolic estimates in section 3.

2. A priori estimates

Throughout this section, we obtain some a priori estimates for solutions in $C^{2+\sigma,1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ on $[0,T]$.

For $\lambda_2 \geq 0$ and $\Omega \subset \mathbb{R}^2$, we have the following result by maximum principle.

Lemma 2.1. *If $(c,u,v) \in C^{2+\sigma,1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ is a solution to the system* (1.1)–(1.3), *then $c \geq 0$, $u \geq 0$ and $0 \leq v \leq 1$.*

For $\lambda_2 \geq 0$ and $\Omega \subset \mathbb{R}^2$, we have L^1 norm estimates for c.

Lemma 2.2. *If $(c,u,v) \in C^{2+\sigma,1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ is a solution to the system* (1.1)–(1.3), *we have*

(2.1)
$$\sup_{t\in[0,T]} \int_\Omega c(x,t)dx + \mu_1 \int_0^T \int_\Omega c^2 dxds \leq \left(\int_\Omega c_0(x)dx \right) (Te^{\mu_1 T} + 1).$$

Proof. If we integrate (1.1) over Ω, then we obtain

$$\frac{d}{dt} \int_\Omega c(x,t)dx + \mu_1 \int_\Omega c^2(x,t)dx + \mu_1\lambda_1 \int_\Omega v(x,t)c(x,t)dx = \mu_1 \int_\Omega c(x,t)dx.$$

Using Gronwall's inequality, we have (2.1). $\square$

For the further a priori estimates, we use the following equations which are equivalent to (1.1)–(1.3) by the transform $c = ae^{\xi v}$.

$$(2.2)\qquad \begin{cases} \dfrac{\partial u}{\partial t} - \Delta u + u = e^{\xi v} a, \\ \dfrac{\partial v}{\partial t} = -uv + \mu_2 v(1 - v - \lambda_2 a e^{\xi v}), \\ \dfrac{\partial a}{\partial t} - e^{-\xi v}\nabla \cdot (e^{\xi v}\nabla a) + e^{-\xi v}\nabla \cdot (\chi e^{\xi v} a \nabla u) \\ = \xi auv + \mu_1 a(1 - ae^{\xi v} - \lambda_1 v) - \mu_2 \xi av(1 - v - \lambda_2 e^{\xi v} a), \\ (a(x,0), u(x,0), v(x,0)) = (a_0(x), u_0(x), v_0(x)), \\ \dfrac{\partial a}{\partial \nu} = \dfrac{\partial u}{\partial \nu} = 0. \end{cases}$$

The advantage of the system (2.2) is that the boundary condition $\frac{\partial c}{\partial \nu} - \xi c \frac{\partial v}{\partial \nu} = 0$ is transformed into the condition $\frac{\partial a}{\partial \nu} = 0$. It is easy to check that if $(c,\, u,\, v) \in C^{2+\sigma, 1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ is a solution to the system (1.1)–(1.3), then $(a,\, u,\, v) \in C^{2+\sigma, 1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ is a solution to the system (2.2). We also note that $a(x,t) \le c(x,t) \le a(x,t)e^{\xi}$ because $0 \le v \le 1$. This makes it possible to replace $\|a\|_{L^2}$ and $\|\nabla a\|_{L^2}$ by $\|ae^{\frac{\xi v}{2}}\|_{L^2}$ and $\||\nabla a|\, e^{\frac{\xi v}{2}}\|_{L^2}$, respectively, and vice versa.

Throughout this paper, C denotes a generic constant (its value may change from line to line) and ϵ a sufficiently small positive constant.

LEMMA 2.3. *Let $(a,\, u,\, v) \in C^{2+\sigma, 1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ be a solution to the system (2.2) and $\Omega \subset \mathbb{R}^2$. We have*

$$(2.3)\qquad \sup_{0\le t\le T} \|u(t)\|^2_{L^2} + 2\int_0^T \|\nabla u\|^2_{L^2} + \|u\|^2_{L^2} dt \le \|u_0\|^2_{L^2} + C\int_0^T \|a\|^2_{L^2} dt,$$

and

$$(2.4)\qquad \sup_{0\le t\le T} \|\nabla u(t)\|^2_{L^2} + \int_0^T \|\Delta u\|^2_{L^2} + \|\nabla u\|^2_{L^2} dt \le \|\nabla u_0\|^2_{L^2} + C\int_0^T \|a\|^2_{L^2} dt.$$

Proof. Taking scalar product the first equation of (2.2) with u, using $e^{\xi v} \le C$ and integrating over $[0,T]$, we have (2.3). Also taking scalar product the first equation of (2.2) with $-\Delta u$ and using

$$\left| \int_\Omega e^{\xi v} a \Delta u dx \right| \le C\|a\|^2_{L^2} + \frac{1}{2}\|\Delta u\|^2_{L^2},$$

we have (2.4) by integrating over $[0,T]$. $\square$

By (2.1), we obtain $c \in L^2(\Omega_T)$, hence $a \in L^2(\Omega_T)$ if $a_0 \in L^1(\Omega)$. By (2.3) and (2.4), we have

$u \in L^\infty(0,T;L^2(\Omega)) \cap L^\infty(0,T;H^1(\Omega))$ and $\nabla u,\, \Delta u \in L^2(\Omega_T)$ if $u_0 \in H^1(\Omega)$.

The following a priori estimates show that the regularity of ∇v and Δv is intimately related with the regularity of ∇a and Δa, respectively.

LEMMA 2.4. *Let* $(a,\, u,\, v) \in C^{2+\sigma,1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ *be a solution to the system* (2.2) *and* $\Omega \subset \mathbb{R}^2$. *We have*

(2.5)
$$\sup_{t\in(0,T]} \|\nabla v\|_{L^p} \le \left(\|\nabla v_0\|_{L^p} + C\int_0^T \|\nabla u\|_{L^p} + \|\nabla a\|_{L^p} dt\right)\exp(CT),$$

and

$$\sup_{t\in(0,T]} \|\Delta v\|_{L^p} \le \left(\|\Delta v_0\|_{L^p} + \int_0^T \|\Delta u\|_{L^p} + \|\Delta a\|_{L^p} dt\right)$$

$$\times \exp\left(C\int_0^T (\|\nabla u\|_{L^{2p}} + \|\nabla v\|_{L^{2p}} + \|\nabla a\|_{L^{2p}} + 1)dt\right) \tag{2.6}$$

for $1 < p < \infty$.

Proof. We have the following a priori estimate from the equation for v in (2.2) ;

$$\frac{1}{p}\frac{d}{dt}\|\nabla v\|^p_{L^p} + \int_\Omega u|\nabla v|^p dx + 2\mu_2\int_\Omega v|\nabla v|^p dx + \lambda_2\mu_2\int_\Omega (1+\xi v)ae^{\xi v}|\nabla v|^p dx$$
$$\le \|\nabla u\|_{L^p}\|\nabla v\|^{p-1}_{L^p} + \mu_2\|\nabla v\|^p_{L^p} + \mu_2\lambda_2 e^{\xi}\|\nabla a\|_{L^p}\|\nabla v\|^{p-1}_{L^p}.$$

By Gronwall's inequality, (2.5) follows directly.
For the estimate (2.6), we take Δ operator on the both sides of the equation for v :

$$\begin{aligned}
&\partial_t\Delta v + u\Delta v + 2v\Delta v + \mu_2\lambda_2(1+\xi v)\Delta v a e^{\xi v}\\
&= -2\nabla u\cdot\nabla v - \Delta u v + \mu_2\Delta v - 2\mu_2|\nabla v|^2 - 2\mu_2\lambda_2\xi|\nabla v|^2 a e^{\xi v}\\
&\quad - \mu_2\lambda_2\nabla a\cdot\nabla v(1+\xi v)e^{\xi v} - \mu_2\lambda_2\Delta a v e^{\xi v}.
\end{aligned}$$

Next, taking Δv as a test function to obtain the following ;

$$\begin{aligned}
&\frac{1}{p}\frac{d}{dt}\|\Delta v\|^p_{L^p} \le C\|\nabla u\|_{L^{2p}}\|\nabla v\|_{L^{2p}}\|\Delta v\|^{p-1}_{L^p} + C\|\Delta u\|_{L^p}\|\Delta v\|^{p-1}_{L^p}\\
&+C\|\nabla v\|^2_{L^{2p}}(1+\|a\|_{L^\infty})\|\Delta v\|^{p-1}_{L^p}\\
&+C\|\nabla v\|_{L^{2p}}\|\nabla a\|_{L^{2p}}\|\Delta v\|^{p-1}_{L^p} + C\|\Delta a\|_{L^p}\|\Delta v\|^{p-1}_{L^p} + C\|\Delta v\|^p_{L^p}.
\end{aligned}$$

Then applying Gronwall's inequality to the above, we obtain (2.6). This completes the proof. □

By using the transformed equation of a instead of the equation of c, we can obtain L^2 a priori estimates because the $W^{1,p}$ estimates of v is not necessary. The following is a key estimate to prove existence of a regular solution without restrictions on the coefficients. We have $\|a\|_{L^2}^4$ in the right hand side and it can be estimated by using Gronwall's inequality and the fact that $a \in L^2(\Omega_T)$ by (2.1).

LEMMA 2.5. *Let $\lambda_2 \geq 0$ and $(a, u, v) \in C_{x,t}^{2+\sigma,1+\frac{\sigma}{2}}(\Omega_T)$ be a solution to the system* (2.2) *on $\Omega \subset \mathbb{R}^2$. Then we have*

$$a \in L^\infty(0, T; L^2(\Omega)) \cap L^2(0, T; \dot{H}^1(\Omega)), \text{ and } \nabla u \in L^\infty(0, T; L^4(\Omega)),$$

and furthermore,

$$\|a\|_{L^\infty(0,T;L^2(\Omega))} + \|\nabla a\|_{L^2(0,T;L^2(\Omega))} + \|\nabla u\|_{L^\infty(0,T;L^4(\Omega))} \leq C(\|a_0\|_{L^2(\Omega)}, \|\nabla u_0\|_{L^4(\Omega)}, T).$$

Proof. We note that

$$\frac{\partial a}{\partial t} \cdot a e^{\xi v} = \frac{1}{2}\frac{\partial}{\partial t}\left(a^2 e^{\xi v}\right) - \frac{\xi \mu_2}{2} a^2 e^{\xi v} v + \frac{\xi}{2} a^2 e^{\xi v}\left(uv + \mu_2 v^2 + \mu_2 \lambda_2 a v e^{\xi v}\right).$$

Multiplying equation of a in (2.2) by $ae^{\xi v}$ and integrating over Ω, we have

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\int_\Omega a^2 e^{\xi v} dx + \int_\Omega |\nabla a|^2 e^{\xi v} dx + \frac{\xi}{2}\int_\Omega a^2 e^{\xi v} uv dx \\
&\quad + \mu_1 \int_\Omega a^3 e^{2\xi v} dx + (\mu_1 \lambda_1 + \mu_2 \xi_2)\int_\Omega v a^2 e^{\xi v} dx \\
&= \chi \int_\Omega (\nabla a \cdot \nabla u) a e^{\xi v} dx + \xi \int_\Omega a^2 u v e^{\xi v} dx + \mu_1 \int_\Omega a^2 e^{\xi v} dx \\
&\quad + \frac{\mu_2 \xi}{2}\int_\Omega a^2 v^2 e^{\xi v} dx + \frac{\mu_2 \lambda_2 \xi}{2}\int_\Omega v a^3 e^{2\xi v} dx \\
&\quad + \frac{\mu_2 \xi}{2}\int_\Omega a^2 v e^{\xi v} dx := I_1 + I_2 + I_3 + I_4 + I_5 + I_6.
\end{aligned}$$

Hölder's inequality, interpolation inequality and Young's inequality gives us that

$$\begin{aligned}
|I_1| &= \chi \left|\int_\Omega (\nabla a \cdot \nabla u) a e^{\xi v} dx\right| \leq C\|\nabla u\|_{L^4}\|\nabla a\|_{L^2}\|a\|_{L^4} \\
&\leq C\|\nabla u\|_{L^4}\|a\|_{L^2}^{\frac{1}{2}}\|\nabla a\|_{L^2}^{\frac{3}{2}} \leq C\|\nabla u\|_{L^4}^4\|a e^{\frac{\xi v}{2}}\|_{L^2}^2 + \epsilon\|e^{\frac{\xi v}{2}}\nabla a\|_{L^2}^2.
\end{aligned}$$

For the other terms, we have

$$|I_2| \le C\|u\|_{L^3}\|a\|_{L^3}^2 \le C\|u\|_{L^2}^{\frac{2}{3}}\|\nabla u\|_{L^2}^{\frac{1}{3}}\|a\|_{L^2}^{\frac{4}{3}}\|\nabla a\|_{L^2}^{\frac{2}{3}}$$
$$\le C\|u\|_{L^2}\|\nabla u\|_{L^2}^{\frac{1}{2}}\|a\|_{L^2}^2 + \epsilon\||\nabla a|e^{\frac{\xi v}{2}}\|_{L^2}^2,$$

and

$$|I_3|,\ |I_4|,\ |I_6| \le C\int_\Omega a^2 e^{\xi v}dx.$$

I_5 can be estimated as follows :

$$|I_5| \le C\|a\|_{L^3}^3 \le C\|a\|_{L^2}^2\|\nabla a\|_{L^2} \le C\|a\|_{L^2}^4 + \epsilon\||\nabla a|e^{\frac{\xi v}{2}}\|_{L^2}^2.$$

Combining all the above estimates, we have

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega a^2 e^{\xi v}dx + \int_\Omega |\nabla a|^2 e^{\xi v}dx \\
&\quad + \mu_1\int_\Omega a^3 e^{2\xi v}dx + (\mu_1\lambda_1 + \mu_2\xi)\int_\Omega va^2e^{\xi v}dx \\
&\le C\|\nabla u\|_{L^4}^4\|ae^{\frac{\xi v}{2}}\|_{L^2}^2 + C\|u\|_{L^2}\|\nabla u\|_{L^2}^{\frac{1}{2}}\|a\|_{L^2}^2 \\
&\quad + C\int_\Omega a^2e^{\xi v}dx + C\|ae^{\frac{\xi v}{2}}\|_{L^2}^2\|a\|_{L^2}^2.
\end{aligned} \tag{2.7}$$

Taking ∇ operator on the equation of u in (2.2), multiplying $|\nabla u|^2\nabla u$, and integrating over Ω, we obtain

$$\begin{aligned}
&\frac{1}{4}\frac{d}{dt}\|\nabla u\|_{L^4}^4 + \frac{3}{4}\|\nabla|\nabla u|^2\|_{L^2}^2 + \|\nabla u\|_{L^4}^4 \\
&\le \|a\|_{L^4}\|\nabla|\nabla u|^2\|_{L^2}\|\nabla u\|_{L^4} \\
&\le C\|a\|_{L^2}\|\nabla a\|_{L^2}\|\nabla u\|_{L^4}^2 + \epsilon\|\nabla|\nabla u|^2\|_{L^2}^2 \\
&\le \epsilon\|\nabla|\nabla u|^2\|_{L^2}^2 + \epsilon\||\nabla a|e^{\frac{\xi v}{2}}\|_{L^2}^2 + C\|a\|_{L^2}^2\|\nabla u\|_{L^4}^4.
\end{aligned} \tag{2.8}$$

Now choosing ϵ to be sufficiently small positive constant and adding (2.7) and (2.8) to obtain

$$\begin{aligned}
&\frac{d}{dt}\left(\int_\Omega a^2e^{\xi v}dx + \int_\Omega |\nabla u|^4dx\right) + \int_\Omega |\nabla a|^2e^{\xi v}dx \\
&\quad + \int_\Omega |\nabla|\nabla u|^2|^2dx + \mu_1\int_\Omega a^3e^{2\xi v}dx + \int_\Omega |\nabla u|^4dx \\
&\le C\|u\|_{L^2}\|\nabla u\|_{L^2}^{\frac{1}{2}}\|ae^{\frac{\xi v}{2}}\|_{L^2}^2 + C(\|a\|_{L^2}^2 + 1)(\|\nabla u\|_{L^4}^4 + \|ae^{\frac{\xi v}{2}}\|_{L^2}^2),
\end{aligned}$$

and apply the Gronwall inequality for the following inequality ;

$$
\begin{aligned}
&\sup_{t\in(0,T]}\left(\int_\Omega a^2e^{\xi v}dx+\int_\Omega|\nabla u|^4dx\right)\\
&\quad+\int_0^T\int_\Omega|\nabla a|^2e^{\xi v}dxdt+\int_0^T\int_\Omega|\nabla|\nabla u|^2|^2dxdt\\
&\quad+\int_0^T\int_\Omega a^3e^{2\xi v}dxdt+\int_0^T\int_\Omega|\nabla u|^4dxdt\\
&\le C\left(\|a_0\|_{L^2}^2+\|\nabla u_0\|_{L^4}^4\right)\exp\left(C\int_0^T\|u\|_{L^2}\|\nabla u\|_{L^2}^{\frac{1}{2}}+\|a\|_{L^2}^2+1dt\right).
\end{aligned}
$$

Using Lemmas 2.2 and 2.3, the right hand side of above is bounded by the initial data and T. This completes the proof. $\square$

For the higher order regularity, $\|a\|_{L^\infty(0,T;\dot H^1)}$ is estimated simultaneously with $\|\nabla v\|_{L^\infty(0,T;L^4)}$ in the next lemma(see also Lemma 4.2 in [12]).

LEMMA 2.6. *Let $\lambda_2\ge 0$ and $(a,\,u,\,v)\in C^{2+\sigma,1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ be a solution to the system (2.2) on $\Omega\subset\mathbb{R}^2$. Then we have*

$$a\in L^\infty(0,\,T;\dot H^1(\Omega))\cap L^2(0,\,T;\dot H^2(\Omega))\ \text{ and } \nabla v\in L^\infty(0,\,T;L^4(\Omega)),$$

and furthermore,

$$
\begin{aligned}
&\|a\|_{L^\infty(0,T;\dot H^1(\Omega))}+\|\Delta a\|_{L^2(0,T;L^2(\Omega))}+\|\nabla v\|_{L^\infty(0,T;L^4(\Omega))}\\
&\le C(\|a_0\|_{\dot H^1(\Omega)},\,\|\nabla v_0\|_{L^4},\,\|u_0\|_{\dot H^2(\Omega)},\,T).
\end{aligned}
$$

Proof. Taking ∇ operator on the second equation of (2.2), multiplying $|\nabla v|^2\nabla v$ and integrating over Ω, we have

(2.9)
$$
\begin{aligned}
&\frac{1}{4}\frac{d}{dt}\|\nabla v\|_{L^4}^4+\int_\Omega u|\nabla v|^4dx+\mu_2\lambda_2\int_\Omega ae^{\xi v}|\nabla v|^4dx+C\int_\Omega v|\nabla v|^4dx\\
&\le\int_\Omega|\nabla u||\nabla v|^3dx+\mu_2\lambda_2\int_\Omega|\nabla a||\nabla v|^3e^{\xi v}dx+\mu_2\int_\Omega|\nabla v|^4dx\\
&\le\|\nabla u\|_{L^4}\|\nabla v\|_{L^4}^3+C\|\nabla a\|_{L^4}\|\nabla v\|_{L^4}^3+C\|\nabla v\|_{L^4}^4\\
&\le C\|\nabla u\|_{L^4}^4+C(\|\nabla a\|_{L^2}^{\frac{2}{3}}+1)\|\nabla v\|_{L^4}^4+\epsilon\|\Delta a\|_{L^2}^2.
\end{aligned}
$$

Multiplying $-\Delta a$ to the equation of a in (2.2) and integrating over Ω, we obtain

(2.10)

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\|\nabla a\|_{L^2}^2 + \|\Delta a\|_{L^2}^2 \le -\xi\int_\Omega \nabla v\cdot\nabla a\Delta a dx + \chi\int_\Omega \nabla a\cdot\nabla u\Delta a dx\\
&+\chi\xi\int_\Omega a(\nabla v\cdot\nabla u)\Delta a dx - \xi\int_\Omega auv\Delta a dx + \mu_2\xi\int_\Omega av(1-v-\lambda_2 e^{\xi v}a)\Delta a dx\\
&+\chi\int_\Omega a\Delta u\Delta a dx - \mu_1\int_\Omega a(1-e^{\xi v}a-\lambda_1 v)\Delta a dx\\
&:= I_1+I_2+I_3+I_4+I_5+I_6+I_7.
\end{aligned}$$

We now estimate $I_1,\cdots,I_7$ as follows ;

$$\begin{aligned}
|I_1| &\le C\|\nabla v\|_{L^4}\|\nabla a\|_{L^4}\|\Delta a\|_{L^2} \le C\|\nabla v\|_{L^4}\|\nabla a\|_{L^2}^{\frac{1}{2}}\|\Delta a\|_{L^2}^{\frac{3}{2}}\\
&\le \epsilon\|\Delta a\|_{L^2}^2 + C\|\nabla v\|_{L^4}^4\|\nabla a\|_{L^2}^2,\\
|I_2| &\le C\|\nabla a\|_{L^2}^2\|\nabla u\|_{L^4}^4 + \epsilon\|\Delta a\|_{L^2}^2,\\
|I_3| &\le C\|a\|_{L^\infty}\|\nabla u\|_{L^4}\|\nabla v\|_{L^4}\|\Delta a\|_{L^2} \le C\|a\|_{L^3}^{\frac{3}{5}}\|\nabla u\|_{L^4}\|\nabla v\|_{L^4}\|\Delta a\|_{L^2}^{\frac{7}{5}}\\
&\le C\|a\|_{L^3}^2\|\nabla u\|_{L^4}^{\frac{10}{3}}\|\nabla v\|_{L^4}^{\frac{10}{3}} + \epsilon\|\Delta a\|_{L^2}^2,\\
|I_4| &\le C\|a\|_{L^2}\|u\|_{L^\infty}\|\Delta a\|_{L^2} \le C\|a\|_{L^2}^2\|u\|_{L^\infty}^2 + \epsilon\|\Delta a\|_{L^2}^2,\\
|I_5|,\ |I_7| &\le C\|a\|_{L^4}^4 + C\|a\|_{L^2}^2 + \epsilon\|\Delta a\|_{L^2}^2\\
&\le C\|a\|_{L^2}^2\|\nabla a\|_{L^2}^2 + C\|a\|_{L^2}^2 + \epsilon\|\Delta a\|_{L^2}^2,\\
|I_6| &\le C\|a\|_{L^4}^2\|\Delta u\|_{L^4}^2 + \epsilon\|\Delta a\|_{L^2}^2 \le C\|a\|_{L^2}\|\nabla a\|_{L^2}\|\Delta u\|_{L^4}^2 + \epsilon\|\Delta a\|_{L^2}^2.
\end{aligned}$$

Adding (2.9) and (2.10) and absorbing ϵ terms to the left hand side, we obtain

$$\begin{aligned}
&\frac{d}{dt}(\|\nabla a\|_{L^2}^2 + \|\nabla v\|_{L^4}^4) + \|\Delta a\|_{L^2}^2\\
&\le C(\|\nabla a\|_{L^2}^2 + \|a\|_{L^2}^2\|\nabla u\|_{L^4}^4 + 1)\|\nabla v\|_{L^4}^4 + C(\|\nabla u\|_{L^4}^4)\|\nabla a\|_{L^2}^2\\
&\quad + C\|\nabla u\|_{L^4}^4 + C\|a\|_{L^2}^2(1+\|u\|_{L^\infty}^2).
\end{aligned}$$

By Gronwall's inequality, we have the desired estimates. □

Note that L^p estimate of ∇v $(2<p<\infty)$ can be obtained directly from Lemma 2.6. But L^∞-estimate of ∇v is not clear. Since the proof is just a calculation as previous lemmas, we present the following Lemma without proof.

Lemma 2.7. *Let* $\lambda_2 \geq 0$ *and* $(a,\, u,\, v) \in C^{2+\sigma, 1+\frac{\sigma}{2}}_{x,t}(\Omega_T)$ *be a solution to the system* (2.2) *on* $\Omega \subset \mathbb{R}^2$. *Then we have*

$$a \in L^\infty(0,\, T; \dot{H}^2(\Omega)) \cap L^2(0,\, T; \dot{H}^3(\Omega)) \text{ and } \quad \Delta v \in L^\infty(0, T; L^4(\Omega)),$$

and furthermore,

$$\begin{aligned}&\|a\|_{L^\infty(0,\,T;\dot{H}^1(\Omega))} + \|\Delta a\|_{L^2(0,\,T;L^2(\Omega))} + \|\Delta v\|_{L^\infty(0,T;L^4(\Omega))}\\ &\leq C(\|a_0\|_{H^2(\Omega)},\, \|\Delta v_0\|_{L^4},\, T).\end{aligned}$$

3. Proof of theorem

The local existence and uniqueness of classical solution to the system (2.2) can be shown by using the standard contraction mapping methods as [8] and [13]. See [8] and [11] for the details.

Proposition 3.1. *There exists a unique solution* $(a,\, u,\, v) \in C^{2+\sigma, 1+\frac{\sigma}{2}}_{x,t}$ (Ω_T) *to the system* (2.2) *for sufficiently small* T *which depends on* $\|(a_0,\, u_0,\, v_0)\|_{C^{2+\sigma}_x(\Omega)}$.

We now consider the global existence of a solution to the system (2.2).

Proof of Theorem 1.1. Let us define the Sobolev space

$$W^{2,1}_q(\Omega_T) = \{w \in L^q(\Omega_T) \mid \|w\|_{W^{2,1}_q(\Omega_T)} < \infty\}$$

with the norm

$$\|w\|_{W^{2,1}_q(\Omega_T)} = \|w\|_{L^q(\Omega_T)} + \|\nabla w\|_{L^q(\Omega_T)} + \|\nabla^2 w\|_{L^q(\Omega_T)} + \|\partial_t w\|_{L^q(\Omega_T)}$$

for $q \geq 1$ and $T > 0$. Suppose that T^* is a finite maximal time validating the solution (a, u, v) in Proposition 3.1. For any $T \in (0,\, T^*]$, we have

$$\|\Delta u\|_{L^p(0,T;L^p(\Omega))} + \|\frac{\partial u}{\partial t}\|_{L^p(0,T;L^p(\Omega))} \leq C(\|u_0\|_{W^{2,p}(\Omega)} + \|c\|_{L^p(0,T;L^p(\Omega))}). \tag{3.1}$$

By using Lemma 2.6, the right hand side of (3.1) is bounded by a constant which depends on M ($\|u_0\|_{W^{2,p}(\Omega)}$ and $\|c_0\|_{H^1(\Omega)}$ are controlled by M). Then the Sobolev embedding for sufficiently large p gives us that

$$\|\nabla u\|_{C^{\sigma, \frac{\sigma}{2}}_{x,t}(\Omega_T)} \leq C(M).$$

To apply the parabolic L^p estimate for a, we rewrite the equation of a in the non-divergence form

$$\begin{aligned}(3.2)\qquad &\frac{\partial a}{\partial t} - \Delta a - (\xi\nabla v - \chi\nabla u)\cdot\nabla a + (\chi\xi\nabla u\cdot\nabla v + \chi\Delta u)a \\ &= \xi auv + \mu_1 a(1 - e^{\xi v}a - \lambda_1 v) - \mu_2\xi av(1 - v - \lambda_2 e^{\xi v}a).\end{aligned}$$

By the boundedness of $\|\nabla u\|_{C_{x,t}^{\sigma,\frac{\sigma}{2}}(\Omega_T)}$ and by Lemma 2.4 and Lemma 2.7, we obtain for any $p \geq 2$,

$$\|\xi\nabla v - \chi\nabla u\|_{L^\infty(\Omega_T)} \leq C(M), \quad \|\chi\xi\nabla u\cdot\nabla v + \chi\Delta u\|_{L^p(\Omega_T)} \leq C(M),$$

$$\|\xi auv + \mu_1 a(1 - e^{\xi v}a - \lambda_1 v) - \mu_2\xi av(1 - v - \lambda_2 e^{\xi v}a)\|_{L^p(\Omega_T)} \leq C(M).$$

Here, using the parabolic L^p estimates, we have

$$\|a\|_{W_p^{2,1}(\Omega_T)} \leq C(M).$$

For a sufficiently large p, we have the following from Sobolev's embedding

$$\|\nabla a\|_{C_{x,t}^{\sigma,\frac{\sigma}{2}}(\Omega_T)} \leq C(M), \quad \|\nabla v\|_{C_{x,t}^{\sigma,\frac{\sigma}{2}}(\Omega_T)} \leq C(M).$$

By Schauder estimates of parabolic equations, we finally have

$$\|(a,u,v)\|_{C_{x,t}^{2+\sigma,1+\frac{\sigma}{2}}(\Omega_T)} \leq C(M).$$

This contradicts to the assumption that T^* is a finite maximal time, and we conclude $T^* = \infty$. □

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