



Global existence of a two-dimensional chemotaxis–haptotaxis model with remodeling of non-diffusible attractant

Peter Y.H. Pang^a, Yifu Wang^{b,*}

^a Department of Mathematics, National University of Singapore, 10 Lower Kent Ridge Road, 119076, Republic of Singapore

^b School of Mathematics and Statistics, Beijing Institute of Technology, Beijing 100081, People's Republic of China

Received 3 September 2016; revised 22 November 2016

Available online 22 March 2017

Abstract

This paper deals with the cancer invasion model

$$\begin{cases} u_t = \Delta u - \chi \nabla \cdot (u \nabla v) - \xi \nabla \cdot (u \nabla w) + \mu u(1 - u - w), & x \in \Omega, \, t > 0, \\ v_t = \Delta v - v + u, & x \in \Omega, \, t > 0, \\ w_t = -vw + \eta w(1 - w - u), & x \in \Omega, \, t > 0 \end{cases}$$

in a bounded smooth domain $\Omega \subset \mathbb{R}^2$ with zero-flux boundary conditions, where χ, ξ, μ and η are positive parameters. Compared to previous mathematical studies, the novelty here lies in: first, our treatment of the full parabolic chemotaxis–haptotaxis system; and second, allowing for positive values of η , reflecting processes with self-remodeling of the extracellular matrix. Under appropriate regularity assumptions on the initial data (u_0, v_0, w_0) , by using adapted L^p -estimate techniques, we prove the global existence and uniqueness of classical solutions when μ is sufficiently large, i.e., in the high cell proliferation rate regime. © 2017 Elsevier Inc. All rights reserved.

MSC: 35B45; 35K55; 35Q92; 92C17

Keywords: Chemotaxis; Haptotaxis; Cancer invasion; Tissue remodeling; Logistic proliferation

* Corresponding author.

E-mail address: wangyifu@bit.edu.cn (Y. Wang).

1. Introduction

Cell migration plays an important role in a wide variety of physiological and pathophysiological processes, including embryo development, skin wound healing, cancer invasion and metastasis (see [18] for an overview). *Chemotaxis* is the oriented movement of cells along concentration gradients of chemicals produced by the cells themselves or in their environment, and is a significant mechanism of directional migration of cells. A classical mathematical model for chemotaxis was proposed by Keller and Segel [16] to describe aggregation processes in the slime mould dictyostelium discoideum directed by the chemical cyclic adenosine monophosphate (cAMP). During the past four decades, a number of variations and extensions of the Keller–Segel model have been proposed and extensively studied; see Hillen and Painter [12,24] for a wide variety of examples. *Haptotaxis* is another important mechanism of cell migration. It is the oriented movement of cells along a gradient of cellular adhesion, which is often facilitated by chemoattractants or enzymes bound in the extracellular matrix (ECM).

Recently, there have been increasing biological and mathematical interests in mathematical models of cancer invasion ([2,4,5,10,22,25,29,36]). It has been biologically demonstrated that cancer invasion is associated with the degradation of the extracellular matrix (ECM) by matrix degrading enzymes (MDE) such as the urokinase-type plasminogen activator (uPA) secreted by tumor cells. The classical Keller–Segel model has been extended by Chaplain and Lolas [4,5] to describe processes of cancer invasion, where, in addition to random diffusion, cancer cells migrate both following the gradient of the diffusible MDE by chemotaxis, and following the gradient of the non-diffusible ECM through detecting the ECM material vitronectin (VN) by haptotaxis. Following the model proposed in [4,5], we consider the chemotaxis–haptotaxis system

$$\begin{cases} u_t = \Delta u - \chi \nabla \cdot (u \nabla v) - \xi \nabla \cdot (u \nabla w) + \mu u(1 - u - w), & x \in \Omega, t > 0, \\ v_t = \Delta v - v + u, & x \in \Omega, t > 0, \\ w_t = -vw + \eta w(1 - w - u), & x \in \Omega, t > 0, \\ \frac{\partial u}{\partial \nu} - \chi u \frac{\partial v}{\partial \nu} - \xi u \frac{\partial w}{\partial \nu} = \frac{\partial v}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, \\ u(x, 0) = u_0(x), v(x, 0) = v_0(x), w(x, 0) = w_0(x), & x \in \Omega \end{cases} \quad (1.1)$$

in a bounded domain $\Omega \subset \mathbb{R}^n$ ($n = 2$) with smooth boundary $\partial\Omega$, where u, v and w represent the cancer cell density, MDE concentration and ECM density, respectively; χ and ξ measure the chemotactic and haptotactic sensitivities, respectively; μ is the proliferation rate of the cells, η denotes the remodeling rate of the ECM; and $\partial/\partial\nu$ denotes the outward normal derivative on $\partial\Omega$. As for the initial data (u_0, v_0, w_0) , we assume throughout this paper that for some $\vartheta \in (0, 1)$

$$\begin{cases} u_0(x) \geq 0, v_0(x) \geq 0, w_0(x) \geq 0, \\ u_0 \in C^{2+\vartheta}(\bar{\Omega}), v_0 \in C^{2+\vartheta}(\bar{\Omega}), w_0 \in C^{2+\vartheta}(\bar{\Omega}), \\ \frac{\partial u_0}{\partial \nu} = \frac{\partial v_0}{\partial \nu} = \frac{\partial w_0}{\partial \nu} = 0 \text{ on } \partial\Omega. \end{cases} \quad (1.2)$$

When $w \equiv 0$, (1.1) is reduced to the Keller–Segel system with logistic source

$$\begin{cases} u_t = \Delta u - \chi \nabla \cdot (u \nabla v) + \mu u(1 - u), & x \in \Omega, t > 0, \\ v_t = \Delta v + u - v, & x \in \Omega, t > 0, \\ \frac{\partial u}{\partial \nu} = \frac{\partial v}{\partial \nu} = 0, & x \in \partial \Omega, t > 0, \\ u(x, 0) = u_0(x), v(x, 0) = v_0(x), & x \in \Omega. \end{cases} \quad (1.3)$$

This chemotaxis-only system has been widely studied by many authors during the past four decades, where a main issue of the investigation was whether the solutions are bounded or blow up (see e.g. [6–8,11,15,23,24,37–40]). It is known that an arbitrarily small $\mu > 0$ can guarantee the boundedness of solutions when $n = 2$ [23], while for $n > 2$ solutions may blow up in finite time [11,40], and any given threshold can be surpassed by the solutions to the parabolic–elliptic analogues of (1.3) with a small diffusion coefficient for u and $\mu \in (0, 1)$. On the other hand, for $n > 2$, an appropriately large μ (as compared to the chemotactic coefficient χ) can exclude unbounded solutions [39,41], and the nontrivial constant equilibrium is a global attractor [41]. It is also known that the nonlinear self-diffusion of cells may prevent blow-up of solutions [8,15,37].

When $\chi = 0$, (1.1) becomes the haptotaxis-only system

$$\begin{cases} u_t = \Delta u - \xi \nabla \cdot (u \nabla w) + u(1 - u - w), & x \in \Omega, t > 0, \\ v_t = \Delta v + u - v, & x \in \Omega, t > 0, \\ w_t = -vw + \eta w(1 - w - u), & x \in \Omega, t > 0, \\ \frac{\partial u}{\partial \nu} = \frac{\partial v}{\partial \nu} = \frac{\partial w}{\partial \nu} = 0, & x \in \partial \Omega, t > 0, \\ u(x, 0) = u_0(x), v(x, 0) = v_0(x), w(x, 0) = w_0(x), & x \in \Omega. \end{cases} \quad (1.4)$$

Global existence and asymptotic behavior of solutions to (1.4) have been investigated in [20,21,36] and [27] for the case $\eta = 0$ and $\eta \neq 0$, respectively.

With regard to the chemotaxis–haptotaxis system, it is noted that, as the diffusion rate of MDE is much greater than that of cancer cells in many realistic situations, the second equation in (1.1) may be replaced by $0 = \Delta v - v + u$, resulting in the so-called simplified chemotaxis–haptotaxis system, which is a parabolic–elliptic-ode system. For this simplified system without the self-modeling of ECM, boundedness and stability results have been established [30,33,34]; uniform-in-time boundedness has also been proved for any $\mu > 0$ in two dimensions and for large μ in three dimensions [30], and for $\mu > \frac{(n-2)_+}{n} \chi$ in higher dimensions [33].

The full parabolic chemotaxis–haptotaxis system, however, is much more mathematically challenging. We note that, while the global existence of classical solutions to the full chemotaxis–haptotaxis model has been proved for any $\mu > 0$ in two dimensions [26] and for large μ in three dimensions [29], the global existence for the full chemotaxis–haptotaxis model remains open for small μ in three dimensions even when the remodeling of ECM is absent. We also note that it is only very recent that progress on the global boundedness of solutions have been made [3,19,28,31,42].

We further note that, with some exceptions such as [27], the mathematical study of cancer invasion models has so far largely focused on cases where the remodeling of the ECM is absent. While simulations have suggested that the effect of ECM remodeling is probably not significant when the remodeling rate η is not too large, this has not been rigorously established ([13]). In

recent paper, Tao and Winkler [35] investigated a situation where, concurrent with degradation by MDE upon contact, ECM is able to remodel back to a healthy level in a logistic manner in the absence of cancer cells and compete for space with cancer cells. Under this situation, they proved global existence for the two-dimensional simplified chemotaxis–haptotaxis system

$$\begin{cases} u_t = \Delta u - \chi \nabla \cdot (u \nabla v) - \xi \nabla \cdot (u \nabla w) + \mu u(1 - u - w), & x \in \Omega, t > 0, \\ 0 = \Delta v - v + u, & x \in \Omega, t > 0, \\ w_t = -vw + \eta w(1 - w - u), & x \in \Omega, t > 0, \\ \frac{\partial u}{\partial \nu} - \chi u \frac{\partial v}{\partial \nu} - \xi u \frac{\partial w}{\partial \nu} = \frac{\partial v}{\partial \nu} = 0, & x \in \partial \Omega, t > 0, \\ u(x, 0) = u_0(x), w(x, 0) = w_0(x), & x \in \Omega. \end{cases} \quad (1.5)$$

The main technical difficulty in their proof stems from the effects of the strong coupling in (1.5) on the spatial regularity of u, v and w when $\eta > 0$. When $\eta = 0$, one can establish a one-sided pointwise estimate which connects Δw to v , and thus may easily estimate the chemotaxis-related integral term $\int_{\Omega} u^{p-1} \nabla u \cdot \nabla v dx$ by directly multiplying the parabolic equation for cancer cell density by u^p and using the elliptic equation for the MDE concentration (see [33,34] for instance). However, for the model (1.5) with $\eta > 0$, one needs to estimate the chemotaxis-related integral term $\int_{\Omega} a^p |\nabla v|^2 dx$ with $a = ue^{\xi w}$ (see equation (3.28) in [35]), which proves to be much more technically demanding. Indeed, the authors of [35] derived an a priori estimate for $\|\nabla v(\cdot, t)\|_{L^2(\Omega)}$ by using an energy-like inequality and an elliptic estimate, and then estimate $\int_{\Omega} a^p |\nabla v|^2 dx$ by applying a variant of the Gagliardo–Nirenberg inequality involving an $L \log^r L$ -type norm.

For the full chemotaxis–haptotaxis model (1.1), we take a slightly different approach. Instead of the integral $\int_{\Omega} a^p |\nabla v|^2 dx$, we make use of $L^q - L^p$ estimates for the heat semigroup to estimate the chemotaxis-related term $\int_0^t \int_{\Omega} e^{-(p+1)(t-s)} a^p |\nabla v|^2 dx ds$ (see (3.8) below). This approach allows us to establish a uniform bound for $\|a(\cdot, t)\|_{C(\Omega)}$ with respect to time $t \in (0, \infty)$. In comparison, [35] showed that $\|a(\cdot, t)\|_{C(\Omega)}$ was locally bounded in $(0, \infty)$ (see Lemma 3.12 of [35]).

The main result of the present paper, which establishes the global existence of smooth solutions to the full chemotaxis–haptotaxis model (1.1) with the remodeling of the ECM, is as follows:

Theorem 1.1. *Let $\chi > 0$, $\xi > 0$, $\eta > 0$. Then there exists a positive constant $\mu^*(\chi^2, \xi)$ such that for $\mu > \xi \eta \max\{\|w_0\|_{L^\infty(\Omega)}, 1\} + \mu^*(\chi^2, \xi)$, the problem (1.1) admits a unique global solution $(u, v, w) \in (C^{2,1}(\bar{\Omega} \times [0, \infty)))^3$, where $\|u(\cdot, t)\|_{L^\infty(\Omega)}$ is uniformly bounded for $t \in (0, \infty)$.*

This structure of the paper is as follows. In Section 2, we recall some preliminary results, prove the local well-posedness of (1.1) and also provide a convenient criterion for extensibility of local solutions. In Section 3, we adapt some L^p -estimate techniques to raise the a priori estimates of solutions from $L^1(\Omega)$ to $L^k(\Omega)$, $k > 2$, and then use the Alikakos–Moser iteration (see e.g. [1] and Lemma A.1 of [32]) to establish Theorem 1.1.

2. Local existence and extensibility criterion

We first recall the following Gagliardo–Nirenberg interpolation inequality [9]:

Let $\Omega \subset \mathbb{R}^n$ be a bounded domain with smooth boundary, let l, k be any integers satisfying $0 \leq l < k$, and let $1 \leq q, r \leq \infty$, and $p \in \mathbb{R}^+$, $\frac{l}{k} \leq \theta \leq 1$ such that

$$\frac{1}{p} - \frac{l}{n} = \theta \left(\frac{1}{q} - \frac{k}{n} \right) + (1 - \theta) \frac{1}{r}. \quad (2.1)$$

Then for any $u \in W^{k,q}(\Omega) \cap L^r(\Omega)$, there exist two positive constants c_1 and c_2 depending only on Ω, q, k, r and n such that the following inequality holds:

$$\|D^l u\|_{L^p(\Omega)} \leq c_1 \|D^k u\|_{L^q(\Omega)}^\theta \|u\|_{L^r(\Omega)}^{1-\theta} + c_2 \|u\|_{L^r(\Omega)}; \quad (2.2)$$

with the following exception: If $1 < q < \infty$ and $k - l - \frac{n}{q}$ is a non-negative integer, then (2.2) holds for θ satisfying $\frac{l}{k} \leq \theta < 1, r > 1$ (see also [30]).

We also recall some fundamental estimates for solutions to the following inhomogeneous linear heat equation problem:

$$\begin{cases} v_t = \Delta v - v + u, & x \in \Omega, \ t > 0, \\ \frac{\partial v}{\partial \nu} = 0, & x \in \partial\Omega, \ t > 0, \\ v(x, 0) = v_0(x), & x \in \Omega. \end{cases} \quad (2.3)$$

These estimates can be derived from standard regularity arguments involving the variation-of-constants formula for v and $L^q - L^p$ estimates for the heat semigroup (see [14, Lemma 4.1] for instance).

Lemma 2.1 ([15, Lemma 2.1], [43, Lemma 2.2]). *Let $T > 0$, $1 \leq p \leq \infty$, $v_0 \in L^p(\Omega)$ and $u \in L^1(0, T; L^p(\Omega))$. Then (2.3) has a unique solution $v \in C([0, T]; L^p(\Omega))$ given by*

$$v(t) = e^{-t} e^{t\Delta} v_0 + \int_0^t e^{-(t-s)} e^{(t-s)\Delta} u(s) ds, \quad t \in [0, T],$$

where $e^{t\Delta}$ is the semigroup generated by the Neumann Laplacian. In addition, let $1 \leq r \leq \infty$, $1 \leq q \leq p < \frac{nq}{n-q}$, $v_0 \in W^{1,p}(\Omega) \cap W^{2,r}(\Omega)$ and $u \in L^\infty(0, T; L^q(\Omega)) \cap L^r(0, T; L^r(\Omega))$. Then for every $t \in (0, T)$,

$$\|v(t)\|_{L^p(\Omega)} \leq \|v_0\|_{L^p(\Omega)} + c_3 \|u\|_{L^\infty((0,T); L^q(\Omega))}, \quad (2.4)$$

$$\|\nabla v(t)\|_{L^p(\Omega)} \leq \|\nabla v_0\|_{L^p(\Omega)} + c_3 \|u\|_{L^\infty((0,T); L^q(\Omega))}, \quad (2.5)$$

$$\int_0^t \int_\Omega e^{rs} |\Delta v(x, s)|^r dx ds \leq c_3 \int_0^t \int_\Omega e^{rs} |u(x, s)|^r dx ds + c_3 \|v_0\|_{W^{2,r}(\Omega)}, \quad (2.6)$$

where c_3 is a positive constant depending on p, q, r and n .

For the convenience in some parts of our subsequent analysis, we introduce the variable transformation [29,30,35]

$$a = ue^{-\xi w},$$

upon which (1.1) takes the form

$$\begin{cases} a_t = e^{-\xi w} \nabla \cdot (e^{\xi w} \nabla a) - e^{-\xi w} \nabla \cdot (\chi e^{\xi w} a \nabla v) + \xi a v w \\ \quad + a(\mu - \xi \eta w)(1 - e^{\xi w} a - w), \quad x \in \Omega, \quad t > 0, \\ v_t = \Delta v - v + e^{\xi w} a, \quad x \in \Omega, \quad t > 0, \\ w_t = -v w + \eta w(1 - w - e^{\xi w} a), \quad x \in \Omega, \quad t > 0, \\ \frac{\partial a}{\partial \nu} = \frac{\partial v}{\partial \nu} = \frac{\partial w}{\partial \nu} = 0, \quad x \in \partial \Omega, \quad t > 0, \\ a(x, 0) = a_0(x) = u_0(x) e^{-\xi w_0(x)}, \quad v_0(x, 0) = v_0(x), \quad w(x, 0) = w_0(x), \quad x \in \Omega. \end{cases} \quad (2.7)$$

It is observed that (1.1) and (2.7) are equivalent within the concept of classical solutions.

Next, we present a result concerning the local existence of classical solutions to (2.7), along with a convenient extensibility criterion, which is proved by means of a fixed point argument inspired by [34,35]. We remark that the extensibility criterion in (2.9) below involves $\|\nabla w(\cdot, t)\|_{L^5(\Omega)}$. As this term is time-dependent, we are not able to establish the global boundedness of solutions to (1.1). We note that a similar problem was faced in [35] (see Lemma 2.2 and (3.48) in [35] for instance, where they used $\|\nabla w(\cdot, t)\|_{L^4(\Omega)}$), which also prevented the establishment of global boundedness.

Lemma 2.2. *Let $\chi > 0$, $\xi > 0$ and $\mu > 0$, and assume that u_0 , v_0 and w_0 satisfy (1.2) with some $\vartheta \in (0, 1)$. Then the problem (2.7) admits a unique classical solution*

$$\begin{cases} a \in C^0(\bar{\Omega} \times [0, T_{\max})) \cap C^{2,1}(\bar{\Omega} \times (0, T_{\max})) \\ v \in C^0(\bar{\Omega} \times [0, T_{\max})) \cap C^{2,1}(\bar{\Omega} \times (0, T_{\max})) \\ w \in C^{2,1}(\bar{\Omega} \times [0, T_{\max})) \end{cases} \quad (2.8)$$

with $a \geq 0$, $v \geq 0$ and $0 \leq w \leq \max\{1, \|w_0\|_{L^\infty(\Omega)}\}$, where T_{\max} denotes the maximal existence time. In addition, if $T_{\max} < +\infty$, then

$$\|a(\cdot, t)\|_{L^\infty(\Omega)} + \|\nabla w(\cdot, t)\|_{L^5(\Omega)} \rightarrow \infty \quad \text{as } t \nearrow T_{\max}. \quad (2.9)$$

Proof. We shall prove the local existence by a fixed point argument. We introduce the Banach space X of functions (a, w) with norm

$$\|(a, w)\|_X = \|a\|_{C^{1,0}(\bar{Q} \times [0, T])} + \|w\|_{C(0, T; W^{1,5}(\Omega))} \quad (0 < T < 1)$$

and a closed subset S given by

$$S = \left\{ (a, w) \in X : w \geq 0, a(x, 0) = a_0(x), w(x, 0) = w_0(x), \frac{\partial a}{\partial \nu} = 0, \|(a, w)\|_X \leq M \right\}$$

with $M = 2\|a_0\|_{C^1(\bar{\Omega})} + 4\|w_0\|_{W^{1,5}(\Omega)} + 2$.

Given any $(a, w) \in S$, we define a corresponding function $(\bar{a}, \bar{w}) \equiv F(a, w)$ where (\bar{a}, \bar{w}) , along with v , satisfies the three decoupled problems

$$\begin{cases} v_t = \Delta v - v + e^{\xi w} a, & (x, t) \in Q_T = \Omega \times (0, T), \\ \frac{\partial v}{\partial \nu} = 0, & x \in \partial\Omega, \ 0 < t < T, \\ v(x, 0) = v_0(x), & x \in \Omega; \end{cases} \quad (2.10)$$

$$\begin{cases} \bar{w}_t = -v\bar{w} + \eta\bar{w}(1 - w - e^{\xi w} a), & (x, t) \in Q_T, \\ \bar{w}(x, 0) = w_0(x), & x \in \Omega; \end{cases} \quad (2.11)$$

and

$$\begin{cases} \bar{a}_t - \Delta \bar{a} + f(x, t) \cdot \nabla \bar{a} + g(x, t) \bar{a} = \xi a v w - \chi a \Delta v, & (x, t) \in Q_T, \\ \frac{\partial \bar{a}}{\partial \nu} = 0, & x \in \partial\Omega, \ 0 < t < T, \\ \bar{a}(x, 0) = a_0(x), & x \in \Omega, \end{cases} \quad (2.12)$$

where

$$\begin{aligned} f(x, t) &= \chi \nabla v - \xi \nabla w, \\ g(x, t) &= \chi \xi \nabla v \cdot \nabla w + (\xi \eta w - \mu)(1 - e^{\xi w} a - w). \end{aligned}$$

As $(a, w) \in S$, by the parabolic L^p -theory (see [17, Theorem 2.1] for instance), (2.10) admits a unique solution v satisfying

$$\|v\|_{W^{2,1}_{C^{\frac{6}{5}, \frac{3}{5}}}(Q_T)} \leq C_1(M), \quad (2.13)$$

where $C_1(M)$, as all the numbers $C_2(M), C_3(M), \dots$, appearing below, is a constant that depends on M but not on T . By the Sobolev embedding $W^{2,1}_p(Q_T) \hookrightarrow C^{1+\lambda, \frac{1+\lambda}{2}}(\overline{Q_T})$ ($p > 4, \lambda = 1 - \frac{4}{p}$) [17, Lemma II.3.3], it follows from (2.13) that

$$\|v\|_{C^{\frac{6}{5}, \frac{3}{5}}(\overline{Q_T})} \leq C_2(M). \quad (2.14)$$

Next we turn to the linear ODE problem (2.11), which can be rewritten as

$$\bar{w}_t = h_1(x, s)\bar{w}, \quad \bar{w}(x, 0) = w_0(x) \quad (2.15)$$

where $h_1(x, t) = -v + \eta(1 - w - e^{\xi w} a)$. It is clear that (2.15) admits a unique solution

$$\bar{w}(x, t) = w_0(x) e^{\int_0^t h_1(x, s) ds} \geq 0 \quad (2.16)$$

and thus

$$\nabla \bar{w}(x, t) = \nabla w_0(x) e^{\int_0^t h_1(x, s) ds} + w_0(x) e^{\int_0^t h_1(x, s) ds} \int_0^t \nabla h_1(x, s) ds. \quad (2.17)$$

Noting that $W^{1,5}(\Omega) \hookrightarrow C(\bar{\Omega})$, $\|h_1\|_{C(\bar{Q}_T)} \leq C_3(M)$ and $\|\nabla h_1(\cdot, t)\|_{L^5(\Omega)} = \|-\nabla v - \eta \nabla w - \xi \eta e^{\xi w} a \nabla w - \eta e^{\xi w} \nabla a\|_{L^5(\Omega)} \leq C_4(M)$, we get

$$\begin{aligned} \|\bar{w}(\cdot, t)\|_{L^5(\Omega)} &\leq \|w_0\|_{L^5(\Omega)} e^{C_3(M)T}, \\ \|\nabla \bar{w}(\cdot, t)\|_{L^5(\Omega)} &\leq \|\nabla w_0\|_{L^5(\Omega)} e^{C_3(M)T} + \|w_0\|_{L^\infty(\Omega)} e^{C_3(M)T} C_4(M)T \end{aligned}$$

and thus

$$\begin{aligned} \|\bar{w}(\cdot, t)\|_{W^{1,5}(\Omega)} &\leq \|w_0\|_{W^{1,5}(\Omega)} e^{C_3(M)T} + \|w_0\|_{L^\infty(\Omega)} e^{C_3(M)T} C_4(M)T \\ &\leq 2\|w_0\|_{W^{1,5}(\Omega)} + 1 \\ &\leq \frac{M}{2} \end{aligned} \quad (2.18)$$

provided that T is sufficiently small such that $C_3(M)T \leq \ln 2$ and $2\|w_0\|_{L^\infty(\Omega)} C_4(M)T \leq 1$.

We are now in the position to consider the parabolic problem (2.12). From (2.14) and $(a, w) \in S$, we have

$$\|f(\cdot, t)\|_{L^5(\Omega)} \leq C_5(M), \quad \|g(\cdot, t)\|_{L^5(\Omega)} \leq C_5(M), \quad \|\xi a v w - \chi a \Delta v\|_{L^5(Q_T)} \leq C_5(M).$$

By the parabolic L^p -theory, we get

$$\|\bar{a}\|_{W^{2,1}_5(Q_T)} \leq C_6(M), \quad (2.19)$$

which in conjunction with a Sobolev embedding inequality in the two-dimensional setting [17, Lemma II.3.3] implies

$$\|\bar{a}\|_{C^{\frac{6}{5}, \frac{3}{5}}(\bar{Q}_T)} \leq C_7(M). \quad (2.20)$$

This yields

$$\begin{aligned} \|\bar{a}\|_{C^{1,0}(\bar{Q}_T)} &\leq \|\bar{a} - a_0\|_{C^{1,0}(\bar{Q}_T)} + \|a_0\|_{C^1(\bar{\Omega})} \\ &\leq T^{\frac{3}{5}} \|\bar{a}\|_{C^{1, \frac{3}{5}}(\bar{Q}_T)} + \|a_0\|_{C^1(\bar{\Omega})} \\ &\leq T^{\frac{3}{5}} C_7(M) + \|a_0\|_{C^1(\bar{\Omega})} \\ &\leq \frac{M}{2} \end{aligned} \quad (2.21)$$

provided that $T \in (0, 1)$ is sufficiently small such that $T^{\frac{3}{5}} C_7(M) \leq 1$. Hence, from (2.16), (2.18) and (2.21), it follows that $(\bar{a}, \bar{w}) \in S$ provided that T is sufficiently small. This establishes that F maps S into itself.

We next show that F is contractive on S . To this end, take $(a_1, w_1), (a_2, w_2) \in S$ and set $(\bar{a}_1, \bar{w}_1) \equiv F(a_1, w_1)$, $(\bar{a}_2, \bar{w}_2) \equiv F(a_2, w_2)$.

From (2.10), it follows that

$$\begin{cases} (v_1 - v_2)_t = \Delta(v_1 - v_2) - (v_1 - v_2) + e^{\xi w_1} a_1 - e^{\xi w_2} a_2, & (x, t) \in Q_T = \Omega \times (0, T), \\ \frac{\partial}{\partial \nu}(v_1 - v_2) = 0, & x \in \partial\Omega, 0 < t < T, \\ (v_1 - v_2)(x, 0) = 0, & x \in \Omega, \end{cases}$$

where

$$\begin{aligned} \|e^{\xi w_1} a_1 - e^{\xi w_2} a_2\|_{L^\infty(Q_T)} &\leq \|e^{\xi w_1} (a_1 - a_2)\|_{L^\infty(Q_T)} + \|(e^{\xi w_1} - e^{\xi w_2}) a_2\|_{L^\infty(Q_T)} \\ &\leq e^{\xi M} \|a_1 - a_2\|_{L^\infty(Q_T)} + \|e^{\xi w_1} - e^{\xi w_2}\|_{L^\infty(Q_T)} \|a_2\|_{L^\infty(Q_T)} \\ &\leq e^{\xi M} \|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + M e^{\xi M} \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))} \\ &\leq C_8(M) (\|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}) \end{aligned}$$

due to $W^{1,5}(\Omega) \hookrightarrow C(\overline{\Omega})$. For $T \in (0, 1)$, the parabolic L^p -theory yields

$$\|v_1 - v_2\|_{W^{2,1}_5(Q_T)} \leq C_9(M) (\|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}) \quad (2.22)$$

and

$$\|v_1 - v_2\|_{C^{1,0}(\overline{Q_T})} \leq C_9(M) (\|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}).$$

The Sobolev embedding theorem, along with Lemma A in the Appendix, then gives

$$\|\overline{w}_1 - \overline{w}_2\|_{C(0,T;W^{1,5}(\Omega))} \leq T C_{10}(M) (\|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}). \quad (2.23)$$

We now consider the equation for $\overline{a}_1 - \overline{a}_2$. From (2.12), we derive that

$$\begin{cases} (\overline{a}_1 - \overline{a}_2)_t - \Delta(\overline{a}_1 - \overline{a}_2) + \tilde{f}(x, t) \cdot \nabla(\overline{a}_1 - \overline{a}_2) + h_4(\overline{a}_1 - \overline{a}_2) = h_5, & (x, t) \in Q_T, \\ \frac{\partial}{\partial \nu}(\overline{a}_1 - \overline{a}_2) = 0, & x \in \partial\Omega, 0 < t < T, \\ (\overline{a}_1 - \overline{a}_2)(x, 0) = 0, & x \in \Omega \end{cases} \quad (2.24)$$

where

$$\begin{aligned} \tilde{f} &= \chi \nabla v_1 - \xi \nabla w_1, \\ h_4 &= \chi \xi \nabla v_1 \cdot \nabla w_1 + (\xi \eta w_1 - \mu)(1 - e^{\xi w_1} a_1 - w_1), \\ h_5 &= (\chi \nabla v_2 - \chi \nabla v_1 + \xi \nabla w_1 - \xi \nabla w_2) \cdot \nabla \overline{a}_2 + [\chi \xi \nabla v_2 \cdot \nabla w_2 - \chi \xi \nabla v_1 \cdot \nabla w_1 \\ &\quad + (\xi \eta w_2 - \mu)(1 - e^{\xi w_2} a_2 - w_2) - (\xi \eta w_1 - \mu)(1 - e^{\xi w_1} a_1 - w_1)] \overline{a}_2 \\ &\quad + \xi(a_1 v_1 w_1 - a_2 v_2 w_2) + \chi(a_2 \Delta v_2 - a_1 \Delta v_1). \end{aligned}$$

As $(a_j, w_j) \in S$ ($j = 1, 2$), by (2.14), (2.20), (2.22) and (2.23), we get

$$\begin{aligned}\|\tilde{f}\|_{C(0,T;L^5(\Omega))} &\leq C_{11}(M), \\ \|h_4\|_{C(0,T;L^5(\Omega))} &\leq C_{11}(M), \\ \|h_5\|_{L^5(Q_T)} &\leq C_{12}(M)(\|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}).\end{aligned}$$

Hence, again, as $0 < T < 1$, by the parabolic L^p -theory, we get

$$\|\bar{a}_1 - \bar{a}_2\|_{W^{2,1}_{5^*}(Q_T)} \leq C_{13}(M)(\|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}), \quad (2.25)$$

which together with the Sobolev embedding inequality, implies that

$$\|\bar{a}_1 - \bar{a}_2\|_{C^{\frac{6}{5}, \frac{3}{5}}(Q_T)} \leq C_{14}(M)(\|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}). \quad (2.26)$$

Noting that $\bar{a}_1(x, 0) - \bar{a}_2(x, 0) = 0$ and proceeding as in the proof of (2.21), we arrive at

$$\begin{aligned}\|\bar{a}_1 - \bar{a}_2\|_{C^{1,0}(Q_T)} &= \|(\bar{a}_1 - \bar{a}_2)(x, t) - \bar{a}_1(x, 0) - \bar{a}_2(x, 0)\|_{C^{1,0}(Q_T)} \\ &\leq T^{\frac{3}{5}} \|\bar{a}_1 - \bar{a}_2\|_{C^{1, \frac{3}{5}}(Q_T)} \\ &\leq T^{\frac{3}{5}} C_{14}(M)(\|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}).\end{aligned} \quad (2.27)$$

From (2.27) and (2.23), we see that F is contractive on S if T is sufficiently small such that $TC_{10}(M) + T^{\frac{3}{5}}C_{14}(M) < \frac{1}{2}$. Thus, by the contraction mapping theorem, F possesses a unique fixed point $(a, w) \in S$, which via (2.10) induces a solution triple (a, v, w) of (2.7). Furthermore, by the parabolic maximum principle and the ODE comparison argument, one can see that $a, v > 0$ and $w > 0$, respectively.

According to the above reasoning, one can see that the maximal existence time T_{\max} of solution (a, v, w) satisfies

$$\text{either } T_{\max} = \infty \text{ or } \|a(\cdot, t)\|_{C^1(\overline{\Omega})} + \|\nabla w(\cdot, t)\|_{L^5(\Omega)} \rightarrow \infty \text{ as } t \nearrow T_{\max}. \quad (2.28)$$

However, this extensibility criterion can be weakened by (2.9) of Lemma 2.2. Indeed, suppose that $T_{\max} < \infty$, but $\|a(\cdot, t)\|_{L^\infty(\Omega)} + \|\nabla w(\cdot, t)\|_{L^5(\Omega)} \leq C_1$ for some $C_1 > 0$ and all $t \in (0, T_{\max})$. Then by the reasoning in the proof of Lemma 2.2 in [35], using the parabolic L^p -theory and the Sobolev embedding theorem in the two-dimensional setting, one can show that $\|a\|_{W^{2,1}_5(Q_{T_{\max}})} \leq C_2$ and hence $\|a(\cdot, t)\|_{C^1(\overline{\Omega})} + \|\nabla w(\cdot, t)\|_{L^5(\Omega)} \leq C_3$ for $t \in (0, T_{\max})$, which contradicts the extensibility criterion (2.28) and thereby establishes that $T_{\max} = \infty$.

By the standard bootstrapping arguments involving parabolic Schauder estimates [17] and the condition (1.2), one can conclude that (a, v, w) enjoys the regularity properties in (2.8) (see [27] for details).

3. Proof of the main result

According to Lemma 2.2, we need to establish a priori estimates for $\|a(\cdot, t)\|_{C(\Omega)}$ and $\|w(\cdot, t)\|_{W^{1,5}(\Omega)}$ in order to establish the global existence of solutions to (1.1). Here, one essential analytic difficulty stems from the fact that the chemotaxis and haptotaxis terms in the first equation in (1.1) require different L^p -estimate techniques, since ECM density satisfies an ODE

whereas MDE concentration satisfies a parabolic PDE. This paper adapts L^p -estimate techniques to raise the a priori estimates from $L^1(\Omega)$ to $L^k(\Omega)$, $k > 2$.

Before proving the main result, we shall introduce some notations. For simplicity, the variable of integration in an integral will be omitted without ambiguity, e.g., the integral $\int_{\Omega} f(x)dx$ is written as $\int_{\Omega} f(x)$. In what follows, c_i ($i = 4, 5, \dots$) denotes constants that are independent of t . In addition, we may assume that $w_0(x) \leq 1$ without loss of generality.

According to the local existence results of Section 2, $(u(\cdot, s), v(\cdot, s), w(\cdot, s)) \in (C^2(\bar{\Omega}))^3$ for any $s \in (0, T_{\max})$. Hence without loss of generality, we can assume that there exists a constant $C > 0$ such that

$$\|u_0\|_{C^2(\bar{\Omega})} + \|v_0\|_{C^2(\bar{\Omega})} + \|w_0\|_{C^2(\bar{\Omega})} \leq C. \quad (3.1)$$

The following properties of solutions of (1.1) are well known:

Lemma 3.1. *Let (u, v, w) be a solution of (1.1). Then:*

- (i) $\|u(\cdot, t)\|_{L^1(\Omega)} \leq \max\{|\Omega|, \|u_0\|_{L^1(\Omega)}\}$ for all $t \in (0, T_{\max})$,
- (ii) $\|v(\cdot, t)\|_{L^1(\Omega)} \leq \max\{|\Omega|, \|u_0\|_{L^1(\Omega)}, \|v_0\|_{L^1(\Omega)}\}$ for all $t \in (0, T_{\max})$,
- (iii) $\|\nabla v(\cdot, t)\|_{L^2(\Omega)}^2 \leq (1 + \frac{2}{\mu}) \max\{|\Omega|, \|u_0\|_{L^1(\Omega)}\} + \|\nabla v_0\|_{L^2(\Omega)}^2$ for all $t \in (0, T_{\max})$.

Proof. (i) Integrating the first equation in (1.1) with respect to $x \in \Omega$, we have

$$\frac{d}{dt} \int_{\Omega} u(x, t) \leq \mu \int_{\Omega} u(x, t) - \mu \int_{\Omega} u^2(x, t), \quad (3.2)$$

since $w \geq 0$ by Lemma 2.2. Moreover, by the Cauchy–Schwarz inequality, we get

$$\frac{d}{dt} \int_{\Omega} u(x, t) + \mu \int_{\Omega} u(x, t) \leq \mu |\Omega|,$$

which implies that $\|u(\cdot, t)\|_{L^1(\Omega)} \leq \max\{|\Omega|, \|u_0\|_{L^1(\Omega)}\}$.

(ii) Integrating the second equation in (1.1) with respect to $x \in \Omega$ yields

$$\frac{d}{dt} \int_{\Omega} v(x, t) + \int_{\Omega} v(x, t) \leq \int_{\Omega} u(x, t) \leq \sup_{t \geq 0} \int_{\Omega} u(x, t).$$

So (ii) follows from the non-negativity of v and (i).

(iii) Multiplying the second equation in (1.1) by $-\Delta v$ and integrating over Ω , we find

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\Omega} |\nabla v(x, t)|^2 + \int_{\Omega} |\Delta v(x, t)|^2 + \int_{\Omega} |\nabla v(x, t)|^2 \\ &= - \int_{\Omega} u \Delta v \leq \int_{\Omega} |\Delta v(x, t)|^2 + \frac{1}{4} \int_{\Omega} u^2(x, t) \end{aligned}$$

and thus

$$\frac{d}{dt} \int_{\Omega} |\nabla v(x, t)|^2 + \int_{\Omega} |\nabla v(x, t)|^2 \leq \frac{1}{2} \int_{\Omega} u^2(x, t).$$

Combining this with (3.2), we obtain

$$\frac{d}{dt} \int_{\Omega} (u(x, t) + \mu |\nabla v(x, t)|^2) + \int_{\Omega} (u(x, t) + \mu |\nabla v(x, t)|^2) \leq (\mu + 1) \int_{\Omega} u(x, t).$$

This, together with the Gronwall lemma and the estimate (i), yields

$$\int_{\Omega} u(x, t) + \int_{\Omega} \mu |\nabla v(x, t)|^2 \leq (\mu + 2) \max\{|\Omega|, \|u_0\|_{L^1(\Omega)}\} + \mu \|\nabla v_0\|_{L^2(\Omega)}^2$$

and hence (iii) holds.

Lemma 3.2. *Let (a, v, w) be a solution of (2.7). Then there exists a positive constant $\mu^*(\chi^2, \xi)$ such that if $\mu > \xi\eta + \mu^*(\chi^2, \xi)$, then*

$$\|a(\cdot, t)\|_{L^k(\Omega)} \leq C \quad (3.3)$$

is valid for all $t \in (0, T_{\max})$ for some $k > 2$ and $C > 0$.

Proof. By (2.7) and integration by parts, we obtain

$$\begin{aligned} \frac{d}{dt} \int_{\Omega} e^{\xi w} a^p &= \xi \int_{\Omega} e^{\xi w} a^p (-vw + \eta w(1 - w - e^{\xi w} a)) + p \int_{\Omega} a^{p-1} \nabla \cdot (e^{\xi w} \nabla a) \\ &\quad - p\chi \int_{\Omega} a^{p-1} \nabla \cdot (e^{\xi w} a \nabla v) + p\xi \int_{\Omega} e^{\xi w} a^p vw \\ &\quad + p \int_{\Omega} e^{\xi w} a^p (\mu - \xi\eta w)(1 - e^{\xi w} a - w) \\ &\leq -p(p-1) \int_{\Omega} e^{\xi w} a^{p-2} |\nabla a|^2 + p(p-1)\chi \int_{\Omega} e^{\xi w} a^{p-1} \nabla a \cdot \nabla v \\ &\quad + (p-1)\xi \int_{\Omega} e^{\xi w} a^p vw - p \int_{\Omega} e^{2\xi w} a^{p+1} (\mu - \xi\eta w) \\ &\quad + \int_{\Omega} e^{\xi w} a^p (p\mu(1-w) - \xi\eta w(p-1)(1-w)) \\ &\leq -\frac{p(p-1)}{2} \int_{\Omega} e^{\xi w} a^{p-2} |\nabla a|^2 + \frac{p(p-1)}{2} \chi^2 \int_{\Omega} e^{\xi w} a^p |\nabla v|^2 \\ &\quad + p\mu \int_{\Omega} e^{\xi w} a^p - p(\mu - \xi\eta) \int_{\Omega} e^{2\xi w} a^{p+1} + (p-1)\xi \int_{\Omega} e^{\xi w} a^p v. \end{aligned} \quad (3.4)$$

Furthermore, by the Young inequality, we obtain

$$\begin{aligned}
& \frac{d}{dt} \int_{\Omega} e^{\xi w} a^p + \frac{p(p-1)}{2} \int_{\Omega} e^{\xi w} a^{p-2} |\nabla a|^2 + (p+1) \int_{\Omega} e^{\xi w} a^p + p(\mu - \xi \eta) \int_{\Omega} e^{2\xi w} a^{p+1} \\
& \leq \frac{p(p-1)}{2} \chi^2 \int_{\Omega} e^{\xi w} a^p |\nabla v|^2 + (p\mu + p+1) \int_{\Omega} e^{\xi w} a^p + (p-1)\xi \int_{\Omega} e^{\xi w} a^p v \\
& \leq \frac{p(p-1)}{2} \chi^2 \int_{\Omega} e^{\xi w} a^p |\nabla v|^2 + 2\varepsilon_1 \int_{\Omega} e^{2\xi w} a^{p+1} + \varepsilon_1^{-p} (p-1)^{p+1} \xi^{p+1} \int_{\Omega} v^{p+1} \\
& \quad + \varepsilon_1^{-p} (p\mu + p+1)^{p+1} |\Omega|, \tag{3.5}
\end{aligned}$$

and thus

$$\begin{aligned}
& \frac{d}{dt} \int_{\Omega} e^{\xi w} a^p + (p+1) \int_{\Omega} e^{\xi w} a^p + (p(\mu - \xi \eta) - 2\varepsilon_1) \int_{\Omega} e^{2\xi w} a^{p+1} \\
& \leq \frac{p(p-1)}{2} \chi^2 \int_{\Omega} e^{\xi w} a^p |\nabla v|^2 + \varepsilon_1^{-p} (p-1)^{p+1} \xi^{p+1} \int_{\Omega} v^{p+1} + \varepsilon_1^{-p} (p\mu + p+1)^{p+1} |\Omega|. \tag{3.6}
\end{aligned}$$

Now we shall obtain an estimate for $\|a(\cdot, t)\|_{L^k(\Omega)}$ for some $k > 2$. Applying the variation-of-constants formula to (3.6), we have

$$\begin{aligned}
& \int_{\Omega} e^{\xi w} a^p(\cdot, t) + (p(\mu - \xi \eta) - 2\varepsilon_1) \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{2\xi w} a^{p+1}(\cdot, s) ds \\
& \leq \int_{\Omega} u_0^p + \frac{p(p-1)}{2} \chi^2 \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{\xi w} a^p(\cdot, s) |\nabla v(\cdot, s)|^2 ds \\
& \quad + \varepsilon_1^{-p} (p-1)^{p+1} \xi^{p+1} \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} v^{p+1}(\cdot, s) ds + \varepsilon_1^{-p} (p\mu + p+1)^{p+1} |\Omega|. \tag{3.7}
\end{aligned}$$

In order to estimate the second term on the right hand side of (3.7), we use the Young inequality to get

$$\begin{aligned}
& \frac{p(p-1)}{2} \chi^2 \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{\xi w} a^p(\cdot, s) |\nabla v(\cdot, s)|^2 ds \\
& \leq \varepsilon_2 \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{2\xi w} a^{p+1}(\cdot, s) ds + \varepsilon_2^{-p} C(p, \chi) \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} |\nabla v(\cdot, s)|^{2(p+1)} ds \\
& \tag{3.8}
\end{aligned}$$

where $C(p, \chi) = (\frac{p(p-1)\chi^2}{2})^{p+1}$.

From Lemma 3.1(ii) and (iii), it follows that if $\mu \geq 1$, $\|\nabla v(\cdot, s)\|_{L^2(\Omega)} \leq c_4$ with $c_4 = (3 \max\{|\Omega|, \|u_0\|_{L^1(\Omega)}\} + \|\nabla v_0\|_{L^2(\Omega)}^2)^{\frac{1}{2}}$, and thereby $\|v\|_{L^p(\Omega)} \leq C(p)$ for all $p \geq 1$. On the other hand, by the elliptic L^p -estimate, $\|v\|_{W^{2,p}(\Omega)} \leq C_p(\|\Delta v\|_{L^p(\Omega)} + \|v\|_{L^p(\Omega)})$ for any $v \in W^{2,p}(\Omega)$ with $\frac{\partial v}{\partial \nu} = 0$. Hence by the Gagliardo–Nirenberg inequality, we have

$$\begin{aligned} & \|\nabla v(\cdot, s)\|_{L^{2(p+1)}(\Omega)}^{2(p+1)} \\ & \leq \|v(\cdot, s)\|_{W^{2,p+1}(\Omega)}^{p+1} \|\nabla v(\cdot, s)\|_{L^2(\Omega)}^{p+1} \\ & \leq 2^{p+1} C_{p+1}^{p+1} (\|\Delta v(\cdot, s)\|_{L^{p+1}(\Omega)}^{p+1} + \|v(\cdot, s)\|_{L^{p+1}(\Omega)}^{p+1}) \|\nabla v(\cdot, s)\|_{L^2(\Omega)}^{p+1} \\ & \leq 2^{p+1} C_{p+1}^{p+1} \|\Delta v(\cdot, s)\|_{L^{p+1}(\Omega)}^{p+1} + c_5. \end{aligned} \quad (3.9)$$

Therefore applying (2.6) of Lemma 2.1 with $r = p + 1$, we obtain

$$\begin{aligned} & \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} |\nabla v(\cdot, s)|^{2(p+1)} ds \\ & \leq 2^{p+1} C_{p+1}^{p+1} \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} |\Delta v(\cdot, s)|^{p+1} ds + c_5 |\Omega| \\ & \leq 2^{p+1} C_{p+1}^{p+1} (c_3 \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} u^{p+1}(\cdot, s) ds + c_3 \|v_0\|_{W^{2,p+1}(\Omega)} + c_5 |\Omega|) \\ & \leq 2^{p+1} C_{p+1}^{p+1} e^{\xi(p-1)} c_3 \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{2\xi w} a^{p+1}(\cdot, s) ds + c_6. \end{aligned} \quad (3.10)$$

Now we turn to estimating the third integral on the right hand side of (3.7). In fact, according to the Gagliardo–Nirenberg inequality,

$$\|v\|_{L^{p+1}(\Omega)}^{p+1} \leq (c_1 \|\nabla v\|_{L^2(\Omega)}^{\frac{p}{p+1}} \|v\|_{L^1(\Omega)}^{\frac{1}{p+1}} + c_2 \|v\|_{L^1(\Omega)})^{p+1},$$

and thus by Lemma 3.1, we have

$$\begin{aligned} & \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} v^{p+1}(\cdot, s) ds \\ & \leq \int_0^t e^{-(p+1)(t-s)} (c_1 \|\nabla v(\cdot, s)\|_{L^2(\Omega)}^{\frac{p}{p+1}} \|v(\cdot, s)\|_{L^1(\Omega)}^{\frac{1}{p+1}} + c_2 \|v(\cdot, s)\|_{L^1(\Omega)})^{p+1} ds \\ & \leq c_7. \end{aligned} \quad (3.11)$$

Collecting (3.7), (3.8), (3.10) and (3.11), we obtain

$$\begin{aligned}
& \int_{\Omega} e^{\xi w} a^p(\cdot, t) + (p(\mu - \xi \eta) - 2\varepsilon_1) \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{2\xi w} a^{p+1}(\cdot, s) ds \\
& \leq \int_{\Omega} u_0^p + \varepsilon_2 \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{2\xi w} a^{p+1}(\cdot, s) ds + \varepsilon_1^{-p} (p\mu + p + 1)^{p+1} |\Omega| \\
& \quad + \varepsilon_2^{-p} C(p, \chi) c_3 2^{p+1} C_{p+1}^{p+1} e^{\xi(p-1)} \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{2\xi w} a^{p+1}(\cdot, s) ds + \\
& \quad + \varepsilon_2^{-p} C(p, \chi) c_6 + \varepsilon_1^{-p} (p-1)^{p+1} \xi^{p+1} c_7
\end{aligned}$$

and

$$\begin{aligned}
& \int_{\Omega} e^{\xi w} a^p(\cdot, t) + (p(\mu - \xi \eta) - \varepsilon_2 - \varepsilon_2^{-p} C(p, \chi) c_3 2^{p+1} C_{p+1}^{p+1} e^{\xi(p-1)} - 2\varepsilon_1) \\
& \quad \cdot \int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{2\xi w} a^{p+1}(\cdot, s) ds \\
& \leq \int_{\Omega} u_0^p + \varepsilon_1^{-p} (p\mu + p + 1)^{p+1} |\Omega| + \varepsilon_2^{-p} C(p, \chi) c_6 + \varepsilon_1^{-p} (p-1)^{p+1} \xi^{p+1} c_7.
\end{aligned} \tag{3.12}$$

What remains now is to show that

$$\|a(\cdot, t)\|_{L^k(\Omega)} \leq C \tag{3.13}$$

for all $t \in (0, T_{\max})$ for some $k > 2$. To this end, we write

$$f(x) := x + x^{-p} C(p, \chi) c_3 2^{p+1} C_{p+1}^{p+1} e^{\xi(p-1)}$$

for $x > 0$ and let $x_*(p) > 0$ be the minimum point of $f(x)$. Further, write $g(p) = p(\mu - \xi \eta) - x_*(p) - x_*^{-p}(p) C(p, \chi) c_3 2^{p+1} C_{p+1}^{p+1} e^{\xi(p-1)}$. Then one can easily verify that $g(2) > 1$ provided $\mu > \xi \eta + \mu^*(\chi^2, \xi)$, where $\mu^*(\chi^2, \xi) = 1 + \frac{1}{2}(x_*(2) + 8x_*^{-2}(2)\chi^6 c_3 C_3^3 e^{\xi})$. At this point, we note that $g(p)$ is continuous with respect to $p \in (0, +\infty)$. Thus, by the continuity of g , we conclude that for some $p > 2$ close enough to 2 (and by taking $\varepsilon_1 = \frac{1}{4}$), the coefficient of $\int_0^t \int_{\Omega} e^{-(p+1)(t-s)} e^{2\xi w} a^{p+1}(\cdot, s) ds$ in (3.12) is positive, and thereby

$$\int_{\Omega} e^{\xi w} a^p(\cdot, t) \leq \int_{\Omega} u_0^p + \varepsilon_1^{-p} (p\mu + p + 1)^{p+1} |\Omega| + \varepsilon_2^{-p} C(p, \chi) c_6 + \varepsilon_1^{-p} (p-1)^{p+1} \xi^{p+1} c_7,$$

which together with $0 \leq w(x, t) \leq \max\{1, \|w_0\|_{L^\infty(\Omega)}\}$ immediately implies that the inequality (3.13) is valid. This completes the proof of Lemma 3.2.

By $0 \leq w(x, t) \leq \max\{1, \|w_0\|_{L^\infty(\Omega)}\}$, Lemma 3.2 and Lemma 2.1, we immediately have

Lemma 3.3. *Under the same assumptions as in Theorem 1.1, there exists $C > 0$ independent of T_{\max} such that the solution (u, v, w) of (1.1) satisfies*

$$\|v(\cdot, t)\|_{W^{1,\infty}(\Omega)} \leq C \quad \text{for all } t \in (0, T_{\max}). \quad (3.14)$$

Now we turn to estimating $\|u(\cdot, t)\|_{L^\infty(\Omega)}$ for $t \in (0, T_{\max})$. First, we note that while $\|\nabla v(\cdot, t)\|_{L^\infty(\Omega)}$ is bounded by (3.14), $\|\nabla w(\cdot, t)\|_{L^\infty(\Omega)}$ may be unbounded. Therefore, Lemma A.1 in [32] cannot be directly applied to the first equation in (1.1) to get the boundedness of $\|u(\cdot, t)\|_{L^\infty(\Omega)}$ via Moser–Alikakos iteration.

Lemma 3.4. *Under the assumptions of Theorem 1.1, there exists $C > 0$ independent of T_{\max} such that the solution (u, v, w) of (1.1) satisfies*

$$\|u(\cdot, t)\|_{L^\infty(\Omega)} \leq C \quad \text{for all } t \in (0, T_{\max}). \quad (3.15)$$

Proof. Applying the Young inequality, one obtains from (2.7) that for any $p > 2$

$$\begin{aligned} & \frac{d}{dt} \int_{\Omega} e^{\xi w} a^p + \frac{p(p-1)}{2} \int_{\Omega} e^{\xi w} a^{p-2} |\nabla a|^2 + \int_{\Omega} e^{\xi w} a^p \\ & \leq p(p-1) \chi \int_{\Omega} e^{\xi w} a^{p-1} \nabla a \cdot \nabla v + p(\xi \eta - \mu) \int_{\Omega} e^{2\xi w} a^{p+1} \\ & \quad + (p-1) \xi \int_{\Omega} e^{\xi w} a^p v w + (p\mu + 1) \int_{\Omega} e^{\xi w} a^p \\ & \leq \frac{p(p-1)}{4} \int_{\Omega} e^{\xi w} a^{p-2} |\nabla a|^2 + p(p-1) \chi^2 \sup_{0 \leq t < T_{\max}} \|\nabla v(\cdot, t)\|_{L^\infty(\Omega)} \int_{\Omega} e^{\xi w} a^p \\ & \quad + pc_8 \left(\sup_{0 \leq t < T_{\max}} \|v(\cdot, t)\|_{L^\infty(\Omega)} + 1 \right) \int_{\Omega} e^{\xi w} a^p + p(\xi \eta - \mu) \int_{\Omega} e^{2\xi w} a^{p+1}. \end{aligned} \quad (3.16)$$

Combining this with Lemma 3.3, we obtain

$$\begin{aligned} & \frac{d}{dt} \int_{\Omega} e^{\xi w} a^p + c_9 \int_{\Omega} |\nabla a^{\frac{p}{2}}|^2 + \int_{\Omega} e^{\xi w} a^p \\ & \leq c_{10} p^2 \int_{\Omega} a^p. \end{aligned} \quad (3.17)$$

By the Gagliardo–Nirenberg inequality (see (2.2)),

$$\begin{aligned} c_{10} p^2 \int_{\Omega} a^p &= c_{10} p^2 \|a^{\frac{p}{2}}\|_{L^2(\Omega)}^2 \\ &\leq c_{11} p^2 \|\nabla a^{\frac{p}{2}}\|_{L^2(\Omega)} \cdot \|a^{\frac{p}{2}}\|_{L^1(\Omega)} + c_{11} p^2 \|a^{\frac{p}{2}}\|_{L^1(\Omega)}^2. \end{aligned}$$

Therefore, an application of the Young inequality yields

$$c_{10}p^2 \int_{\Omega} a^p \leq c_9 \int_{\Omega} |\nabla a^{\frac{p}{2}}|^2 + c_{11}p^2 \|a^{\frac{p}{2}}\|_{L^1(\Omega)}^2 + c_{12}p^4 \|a^{\frac{p}{2}}\|_{L^1(\Omega)}^2. \quad (3.18)$$

Inserting (3.18) into (3.17), we get

$$\begin{aligned} \frac{d}{dt} \int_{\Omega} e^{\xi w} a^p + \int_{\Omega} e^{\xi w} a^p &\leq c_{11}p^2 \|a^{\frac{p}{2}}\|_{L^1(\Omega)}^2 + c_{12}p^4 \|a^{\frac{p}{2}}\|_{L^1(\Omega)}^2 \\ &\leq c_{13}p^4 (\max\{1, \|a^{\frac{p}{2}}\|_{L^1(\Omega)}\})^2. \end{aligned} \quad (3.19)$$

Letting $p_k = 2^k$ and

$$M_k = \max\{1, \sup_{t \in (0, T_{\max})} \int_{\Omega} a^{p_k}(\cdot, t)\}$$

for $k = 1, 2, \dots$, we obtain from (3.19) that

$$\begin{aligned} \frac{d}{dt} \int_{\Omega} e^{\xi w} a^{p_k} + \int_{\Omega} e^{\xi w} a^{p_k} &\leq c_{13}p_k^4 (\max\{1, \|a^{\frac{p_k}{2}}\|_{L^1(\Omega)}\})^2 \\ &= c_{13}p_k^4 M_{k-1}^2, \end{aligned}$$

which, upon a comparison argument, yields

$$M_k \leq \max\{b^k M_{k-1}^2, e^{\xi} |\Omega| \cdot \|a_0\|_{L^\infty(\Omega)}^{p_k}\} \quad (3.20)$$

where the constant $b > 1$ is independent of k .

Now, if $b^k M_{k-1}^2 \leq e^{\xi} |\Omega| \cdot \|a_0\|_{L^\infty(\Omega)}^{p_k}$ for infinitely many $k \geq 1$, we get (3.15) with $C = e^{\xi} \|u_0\|_{L^\infty(\Omega)}$. Conversely, if $b^k M_{k-1}^2 > e^{\xi} |\Omega| \cdot \|a_0\|_{L^\infty(\Omega)}^{p_k}$ for all sufficiently large k , then

$$M_k \leq b^k M_{k-1}^2 \quad (3.21)$$

for all sufficiently large k , and thus (3.21) is still valid for all $k \geq 1$ upon enlarging b if necessary. Hence $\ln M_k \leq k \ln b + 2 \ln M_{k-1}$ for all $k \geq 1$. By a straightforward induction, we get

$$\ln M_k \leq (k+2) \ln b + 2^k (\ln M_0 + 2 \ln b)$$

and thus

$$M_k \leq b^{k+2+2^{k+1}} M_0^{2^k}. \quad (3.22)$$

From (3.22) and Lemma 3.1, it follows that (3.15) is valid with

$$C = e^{\xi} b^2 \max\{1 + |\Omega|, \|u_0\|_{L^1(\Omega)}\}.$$

According to Lemma 2.2, it remains for us to establish a priori estimates for $\|\nabla w(\cdot, t)\|_{L^5(\Omega)}$. The following lemma bridges $\|\nabla w(\cdot, t)\|_{L^q(\Omega)}^q$ and $\int_0^t \|\nabla a(\cdot, s)\|_{L^q(\Omega)}^q ds$.

Lemma 3.5. Let (a, v, w) be a classical solution of (2.7) in Q_T . Then, under the assumptions of Theorem 1.1, for all $t \in (0, T)$ and $q \geq 2$,

$$\|\nabla w(\cdot, t)\|_{L^q(\Omega)}^q \leq c_{14} e^{c_{14}t} (\|\nabla w_0\|_{L^q(\Omega)}^q + 1 + \int_0^t \|\nabla a(\cdot, s)\|_{L^q(\Omega)}^q ds), \quad (3.23)$$

where the constant $c_{14} > 0$ is independent of T .

Proof. By Lemmas 3.3 and 3.4, we have $\|a(\cdot, t)\|_{L^\infty(\Omega)} \leq C$ and $\|v(\cdot, t)\|_{W^{1,\infty}(\Omega)} \leq C$ for all $0 < t < T$, where $C > 0$ is independent of T . Hence proceeding as in the proof of Lemma 4.2 in [27] or Lemma 2.3 in [35], we can prove (3.23). In fact, by the third equation of (2.7) and direct calculations, we have

$$\nabla w_t = h_6 \nabla w - (w \nabla v + \eta w e^{\xi w} \nabla a)$$

where

$$h_6 = -v + \eta(1 - w - e^{\xi w} a) \leq \eta.$$

Applying the method of constant variation, we have

$$\nabla w(x, t) = \nabla w_0(x) e^{\int_0^t h_6(x,s) ds} - \int_0^t (w \nabla v + \eta w e^{\xi w} \nabla a)(x, \tau) e^{\int_\tau^t h_6(x,s) ds} d\tau,$$

and thus

$$\|\nabla w(\cdot, t)\|_{L^q(\Omega)}^q \leq 2^q e^{q\eta t} \|\nabla w_0\|_{L^q(\Omega)}^q + 2^q e^{q\eta t} \int_\Omega \left(\int_0^t |w \nabla v + \eta w e^{\xi w} \nabla a|(x, \tau) d\tau \right)^q dx.$$

Together with (3.14), this implies (3.23) for some large constant $c_{14} > 0$ independent of T .

Lemma 3.6. Let (a, v, w) be a classical solution of (2.7) in Q_T . Then, under the assumptions of Theorem 1.1, there exists $C(T) > 0$ such that

$$\int_0^t \|\Delta a(\cdot, s)\|_{L^2(\Omega)}^2 ds + \|\nabla a(\cdot, t)\|_{L^2(\Omega)}^2 \leq C(T) \quad (3.24)$$

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

Proof. The first equation in (2.7) can be rewritten as

$$a_t - \Delta a + (\chi \nabla v - \xi \nabla w) \cdot \nabla a = \tilde{h}(x, t), \quad (x, t) \in Q_T, \quad (3.25)$$

where

$$\tilde{h}(x, t) = \xi a v w - \chi a \Delta v - \chi \xi a \nabla v \cdot \nabla w + a(\mu - \xi \eta w)(1 - e^{\xi w} a - w).$$

Multiplying (3.25) by $-\Delta a$, and using Lemmas 3.3 and 3.4, we have

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \int_{\Omega} |\nabla a|^2 + \int_{\Omega} |\Delta a|^2 &= \int_{\Omega} (\chi \nabla v \cdot \nabla a - \xi \nabla w \cdot \nabla a) \Delta a - \int_{\Omega} \tilde{h} \Delta a \\ &\leq \frac{1}{2} \int_{\Omega} |\Delta a|^2 + 2\xi^2 \int_{\Omega} |\nabla w \cdot \nabla a|^2 + 2\chi^2 \int_{\Omega} |\nabla v \cdot \nabla a|^2 \\ &\quad + c_{15} \int_{\Omega} |\nabla v \cdot \nabla w|^2 + c_{15} \int_{\Omega} |\Delta v|^2 + c_{15} \\ &\leq \frac{1}{2} \int_{\Omega} |\Delta a|^2 + 2\xi^2 \int_{\Omega} |\nabla w \cdot \nabla a|^2 + c_{16} \int_{\Omega} |\nabla a|^2 + \\ &\quad + c_{16} \int_{\Omega} |\nabla w|^2 + c_{15} \int_{\Omega} |\Delta v|^2 + c_{16}. \end{aligned} \quad (3.26)$$

By the Young inequality, we obtain that for any $\epsilon > 0$, there exists a constant $C(\epsilon) > 0$ such that

$$2\xi^2 \int_{\Omega} |\nabla w \cdot \nabla a|^2 + c_{16} \int_{\Omega} |\nabla a|^2 \leq \epsilon \int_{\Omega} |\nabla a|^4 + C(\epsilon) \int_{\Omega} |\nabla w|^4 + C(\epsilon),$$

which together with (3.26) yields

$$\begin{aligned} \frac{d}{dt} \int_{\Omega} |\nabla a|^2 + \int_{\Omega} |\Delta a|^2 \\ \leq \epsilon \int_{\Omega} |\nabla a|^4 + C(\epsilon) \int_{\Omega} |\nabla w|^4 + 2c_{15} \int_{\Omega} |\Delta v|^2 + C(\epsilon). \end{aligned} \quad (3.27)$$

Using the Gagliardo–Nirenberg inequality in conjunction with (3.15), we obtain

$$\begin{aligned} \|\nabla a(\cdot, t)\|_{L^4(\Omega)}^4 &\leq c_{17} \|\Delta a(\cdot, t)\|_{L^2(\Omega)}^2 \|a(\cdot, t)\|_{L^\infty(\Omega)}^2 + c_{17} \|a(\cdot, t)\|_{L^\infty(\Omega)}^4 \\ &\leq c_{18} \|\Delta a(\cdot, t)\|_{L^2(\Omega)}^2 + c_{18}. \end{aligned} \quad (3.28)$$

Inserting (3.28) into (3.27) and taking $\epsilon = \frac{1}{2c_{18}}$, we obtain

$$\frac{d}{dt} \int_{\Omega} |\nabla a|^2 + \frac{1}{2} \int_{\Omega} |\Delta a|^2 \leq c_{19} \int_{\Omega} |\nabla w|^4 + c_{19} \int_{\Omega} |\Delta v|^2 + c_{19}. \quad (3.29)$$

Applying Lemma 3.5 with $q = 4$ to (3.29) and using (3.28), we get

$$\begin{aligned}
& \frac{d}{dt} \int_{\Omega} |\nabla a|^2 + \frac{1}{2} \int_{\Omega} |\Delta a|^2 \\
& \leq c_{14}c_{19}e^{c_{14}t} (\|\nabla w_0\|_{L^4(\Omega)}^4 + 1 + \int_0^t \|\nabla a(\cdot, s)\|_{L^4(\Omega)}^4 ds) + c_{19} \int_{\Omega} |\Delta v|^2 + c_{19} \\
& \leq c_{14}c_{19}e^{c_{14}t} (\|\nabla w_0\|_{L^4(\Omega)}^4 + 1 + c_{18} \int_0^t \|\Delta a(\cdot, s)\|_{L^2(\Omega)}^2 ds + c_{14}c_{18}t) + c_{19} \int_{\Omega} |\Delta v|^2 + c_{19}.
\end{aligned}$$

Upon integration, we get

$$\begin{aligned}
& \|\nabla a(\cdot, t)\|_{L^2(\Omega)}^2 + \frac{1}{2} \int_0^t \|\Delta a(\cdot, s)\|_{L^2(\Omega)}^2 ds - \|\nabla a_0\|_{L^2(\Omega)}^2 \\
& \leq c_{14}c_{19}e^{c_{14}t} (t\|\nabla w_0\|_{L^4(\Omega)}^4 + t + c_{18}t \int_0^t \|\Delta a(\cdot, s)\|_{L^2(\Omega)}^2 ds + c_{18}t^2) \\
& \quad + c_{19} \int_0^t \|\Delta v(\cdot, s)\|_{L^2(\Omega)}^2 ds + c_{19}t
\end{aligned} \tag{3.30}$$

Taking $0 < t_1 < \min\{1, T\}$ such that $c_{14}c_{18}c_{19}e^{c_{14}t_1}t_1 \leq \frac{1}{4}$ and applying parabolic L^2 -theory to the second equation in (2.7), we conclude that for any $t \in (0, t_1]$,

$$\begin{aligned}
& \|\nabla a(\cdot, t)\|_{L^2(\Omega)}^2 + \frac{1}{4} \int_0^t \|\Delta a(\cdot, s)\|_{L^2(\Omega)}^2 ds \\
& \leq \|\nabla a_0\|_{L^2(\Omega)}^2 + c_{20}\|\nabla w_0\|_{L^4(\Omega)}^4 + c_{21}\|a\|_{L^2(\Omega \times (0, t_1))} + c_{22} \\
& \leq \|\nabla a_0\|_{L^2(\Omega)}^2 + c_{20}\|\nabla w_0\|_{L^4(\Omega)}^4 + c_{23}.
\end{aligned} \tag{3.31}$$

From (3.28), (3.31) and Lemma 3.5, it follows that

$$\|\nabla w(\cdot, t_1)\|_{L^4(\Omega)}^4 \leq C(\|\nabla a_0\|_{L^2(\Omega)}^2, \|\nabla w_0\|_{L^4(\Omega)}^4).$$

Now, we can repeat the above procedure by taking t_1 as the initial time, and thereby extend the estimate (3.31) to the time interval $[0, T]$ after finitely many steps.

We are now in the position to prove Theorem 1.1.

Proof of Theorem 1.1. Suppose on the contrary that $T_{\max} < \infty$. In view of Lemma 3.4, there exists $c_1 > 0$ such that $\|a(\cdot, t)\|_{L^\infty(\Omega)} \leq c_1$ for all $t \in (0, T_{\max})$. On the other hand, combining (3.28) with (3.24) yields

$$\int_0^t \|\nabla a(\cdot, s)\|_{L^4(\Omega)}^4 ds \leq c_2$$

for some constant $c_2 > 0$, which in conjunction with Lemma 3.5 proves that $\|\nabla w(\cdot, t)\|_{L^4(\Omega)} \leq c_3$ for all $t \in (0, T_{\max})$. Since $\|\chi \nabla v - \xi \nabla w\|_{L^\infty(0,t;L^4(\Omega))} \leq c_4$ and $\|\tilde{h}\|_{L^4(\Omega \times (0,t))} \leq c_4$ for some $c_4 > 0$ for all $t \in (0, T_{\max})$, applying the parabolic L^p -theory (see [17, Theorem 2.1]) to (3.25) yields

$$\|\nabla a\|_{L^5(\Omega \times (0,t))} \leq c_5 \|a\|_{W_4^{2,1}(\Omega \times (0,t))} \leq c_6$$

for some $c_5 > 0$ and $c_6 > 0$. Combining this with Lemma 3.5, we obtain some $c_7 > 0$ such that $\|\nabla w(\cdot, t)\|_{L^5(\Omega)} \leq c_7$ for all $t \in (0, T_{\max})$. This contradicts the extensibility criterion (2.9) in Lemma 2.2 and thereby proves that $T_{\max} = \infty$.

Acknowledgments

This work is partially supported by the NUS AcRF grant R-146-000-213-112 (PYHP), and by the NNSFC grant 11571363 and the Beijing Key Laboratory on MCAACI (YW). This work was completed while YW visited the National University of Singapore in 2016. The authors would like to express their thanks to the referee for insightful comments and constructive suggestions which led to significant improvements to the paper.

Appendix A

In this appendix section, we put together some estimates for solutions of the third equation in (2.11) that are used in the proof of Lemma 2.2.

Lemma A. Suppose that $0 < T < 1$, $v_j \in C^{\frac{6}{5}, \frac{3}{5}}(Q_T)$, $w_j \in C(0, T; W^{1,5}(\Omega))$ and $a_j \in C^{1,0}(\overline{Q_T})$ ($j = 1, 2$), and $\|a_j\|_{C^{1,0}(\overline{Q_T})} \leq M$, $\|w_j\|_{C(0,T;W^{1,5}(\Omega))} \leq M$ and $\|v_j\|_{C^{\frac{6}{5}, \frac{3}{5}}(Q_T)} \leq M$. Then the solutions \overline{w}_1 and \overline{w}_2 of the ordinary differential equations

$$\overline{w}_{jt} = -v_j \overline{w}_j + \eta \overline{w}_j (1 - w_j - e^{\xi w_j} a_j), \quad w_j(x, 0) = w_0(x) \geq 0, \quad j = 1, 2 \quad (\text{A.1})$$

satisfy

$$\begin{aligned} & \|\overline{w}_1 - \overline{w}_2\|_{C(0,T;W^{1,5}(\Omega))} \\ & \leq TC(M)(\|v_1 - v_2\|_{C^{1,0}(\overline{Q_T})} + \|a_1 - a_2\|_{C^{1,0}(\overline{Q_T})} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}), \end{aligned} \quad (\text{A.2})$$

where $C(M)$ is a constant depending only upon M .

Proof. From (A.1), it follows that

$$(\overline{w}_1 - \overline{w}_2)_t = h_2(\overline{w}_1 - \overline{w}_2) + h_3, \quad \overline{w}_1(x, 0) - \overline{w}_2(x, 0) = 0 \quad (\text{A.3})$$

where $h_2 = -v_1 + \eta(1 - w_1 - e^{\xi w_1} a_1)$, $h_3 = (v_2 - v_1)\overline{w}_2 + \eta\overline{w}_2(w_2 - w_1 + e^{\xi w_2} a_2 - e^{\xi w_1} a_1)$. It is easy to see that

$$(\bar{w}_1 - \bar{w}_2)(x, t) = \int_0^t e^{\int_s^t h_2(x, \tau) d\tau} h_3(x, s) ds$$

and

$$(\nabla \bar{w}_1 - \nabla \bar{w}_2)(x, t) = \int_0^t e^{\int_s^t h_2(x, \tau) d\tau} \nabla h_3(x, s) ds + \int_0^t e^{\int_s^t h_2(x, \tau) d\tau} h_3(x, s) \int_s^t \nabla h_2(x, \tau) d\tau ds.$$

Since

$$\|h_2\|_{C(Q_T)} \leq C(M),$$

$$\|\nabla h_2\|_{C(0,T;L^5(\Omega))} = \|\nabla v_1 + \eta(\nabla w_1 - e^{\xi w_1} \nabla a_1 - e^{\xi w_1} a_1 \nabla w_1)\|_{C(0,T;L^5(\Omega))} \leq C(M),$$

$$\|h_3\|_{C(Q_T)} \leq C(M)(\|v_1 - v_2\|_{C(Q_T)} + \|a_1 - a_2\|_{C(Q_T)} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))})$$

and

$$\begin{aligned} & \|\nabla h_3\|_{C(0,T;L^5(\Omega))} \\ &= \|(\nabla v_2 - \nabla v_1)\bar{w}_2 + (v_2 - v_1)\nabla \bar{w}_2 + \eta\nabla \bar{w}_2(w_2 - w_1 + e^{\xi w_2} a_2 - e^{\xi w_1} a_1) + \\ & \quad + \eta\bar{w}_2((\nabla w_2 - \nabla w_1) + e^{\xi w_2}(\nabla a_2 - \nabla a_1) + e^{\xi w_2} a_2(\nabla w_2 - \nabla w_1) + \\ & \quad (e^{\xi w_2} - e^{\xi w_1})\nabla a_1 + (e^{\xi w_2} a_2 - e^{\xi w_1} a_1)\nabla w_1)\|_{C(0,T;L^5(\Omega))} \\ &\leq C(M)(\|v_1 - v_2\|_{C^{1,0}(Q_T)} + \|a_1 - a_2\|_{C^{1,0}(Q_T)} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}), \end{aligned}$$

we have

$$\begin{aligned} & \|\bar{w}_1(\cdot, t) - \bar{w}_2(\cdot, t)\|_{L^5(\Omega)} \\ &\leq \|\bar{w}_1 - \bar{w}_2\|_{C(Q_T)} |\Omega|^{\frac{1}{5}} \\ &\leq TC(M)(\|v_1 - v_2\|_{C(Q_T)} + \|a_1 - a_2\|_{C(Q_T)} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}) \end{aligned}$$

and

$$\begin{aligned} & \|\nabla \bar{w}_1(\cdot, t) - \nabla \bar{w}_2(\cdot, t)\|_{L^5(\Omega)} \\ &\leq e^{C(M)T} (\|h_3\|_{C(Q_T)} T + 1) \int_0^T \|\nabla h_3(\cdot, s)\|_{L^5(\Omega)} ds \\ &\leq TC(M)(\|v_1 - v_2\|_{C^{1,0}(Q_T)} + \|a_1 - a_2\|_{C^{1,0}(Q_T)} + \|w_1 - w_2\|_{C(0,T;W^{1,5}(\Omega))}). \end{aligned}$$

References

- [1] N.D. Alikakos, L^p bounds of solutions of reaction–diffusion equations, *Comm. Partial Differential Equations* 4 (1979) 827–868.

- [2] S. Azañeroian, M.L. Stracke, H. Krutzsch, E. Schiffmann, L.A. Liotta, Signal transduction for chemotaxis and haptotaxis by matrix molecules in tumor cells, *J. Cell Biol.* 110 (1990) 1427–1438.
- [3] X. Cao, Boundedness in a three-dimensional chemotaxis–haptotaxis model, *Z. Angew. Math. Phys.* 67 (2016) 11.
- [4] M.A.J. Chaplain, G. Lolas, Mathematical modelling of cancer invasion of tissue: the role of the urokinase plasminogen activation system, *Math. Models Methods Appl. Sci.* 15 (2005) 1685–1734.
- [5] M.A.J. Chaplain, G. Lolas, Mathematical modelling of tissue invasion: dynamic heterogeneity, *Netw. Heterog. Media* 1 (2006) 399–439.
- [6] T. Cieślak, Quasilinear nonuniformly parabolic system modelling chemotaxis, *J. Math. Anal. Appl.* 326 (2007) 1410–1426.
- [7] T. Cieślak, C. Stinner, Finite-time blowup and global-in-time unbounded solutions to a parabolic–parabolic quasilinear Keller–Segel system in higher dimensions, *J. Differential Equations* 252 (2012) 5832–5851.
- [8] T. Cieślak, M. Winkler, Finite-time blow-up in a quasilinear system of chemotaxis, *Nonlinearity* 21 (2008) 1057–1076.
- [9] A. Friedman, *Partial Differential Equations*, Holt–Rinehart–Winston, 1969.
- [10] A. Friedman, G. Lolas, Analysis of a mathematical model of tumor lymphangiogenesis, *Math. Models Methods Appl. Sci.* 15 (2005) 95–107.
- [11] M. Herrero, J. Velázquez, A blow-up mechanism for a chemotaxis model, *Ann. Sc. Norm. Super. Pisa Cl. Sci.* 24 (4) (1997) 633–683.
- [12] T. Hillen, K.J. Painter, A user’s guide to PDE models for chemotaxis, *J. Math. Biol.* 58 (2009) 183–217.
- [13] T. Hillen, K. Painter, M. Winkler, Convergence of a cancer invasion model to a logistic chemotaxis model, *Math. Models Methods Appl. Sci.* 23 (2013) 165–198.
- [14] D. Horstmann, M. Winkler, Boundedness vs. blow-up in a chemotaxis system, *J. Differential Equations* 215 (1) (2005) 52–107.
- [15] S. Ishida, K. Seki, T. Yokota, Boundedness in quasilinear Keller–Segel systems of parabolic–parabolic type on non-convex bounded domains, *J. Differential Equations* 256 (2014) 2993–3010.
- [16] E.F. Keller, L.A. Segel, Initiation of slime mold aggregation viewed as an instability, *J. Theoret. Biol.* 26 (1970) 399–415.
- [17] O.A. Ladyženskaja, V.A. Solonnikov, N.N. Uralceva, *Linear and Quasi-Linear Equations of Parabolic Type*, Amer. Math. Soc. Transl., vol. 23, AMS, Providence, RI, 1968.
- [18] D.A. Lauffenburger, A.F. Horwitz, Cell migration: a physically integrated molecular process, *Cell* 84 (1996) 359–369.
- [19] Y. Li, J. Lankeit, Boundedness in a chemotaxis–haptotaxis model with nonlinear diffusion, *Nonlinearity* 29 (2016) 1564–1595.
- [20] G. Lițanu, C. Morales-Rodrigo, Asymptotic behavior of global solutions to a model of cell invasion, *Math. Models Methods Appl. Sci.* 20 (2010) 1721–1758.
- [21] A. Marciniak-Czochra, M. Ptashnyk, Boundedness of solutions of a haptotaxis model, *Math. Models Methods Appl. Sci.* 20 (2010) 449–476.
- [22] C. Morales-Rodrigo, J. Tello, Global existence and asymptotic behavior of a tumor angiogenesis model with chemotaxis and haptotaxis, *Math. Models Methods Appl. Sci.* 24 (2014) 427–464.
- [23] K. Osaki, T. Tsujikawa, A. Yagi, M. Mimura, Exponential attractor for a chemotaxis–growth system of equations, *Nonlinear Anal.* 51 (2002) 119–144.
- [24] K.J. Painter, T. Hillen, Volume-filling and quorum-sensing in models for chemosensitive movement, *Can. Appl. Math. Q.* 10 (2002) 501–543.
- [25] Z. Szymańska, C. Morales-Rodrigo, M. Lachowicz, M. Chaplain, Mathematical modelling of cancer invasion of tissue: the role and effect of nonlocal interactions, *Math. Models Methods Appl. Sci.* 19 (2009) 257–281.
- [26] Y. Tao, Global existence of classical solutions to a combined chemotaxis–haptotaxis model with logistic source, *J. Math. Anal. Appl.* 354 (2009) 60–69.
- [27] Y. Tao, Global existence for a haptotaxis model of cancer invasion with tissue remodeling, *Nonlinear Anal. Real World Appl.* 12 (2011) 418–435.
- [28] Y. Tao, Boundedness in a two-dimensional chemotaxis–haptotaxis system, *arXiv:1407.7382*, 2014.
- [29] Y. Tao, M. Wang, Global solution for a chemotactic–haptotactic model of cancer invasion, *Nonlinearity* 21 (2008) 2221–2238.
- [30] Y. Tao, M. Wang, A combined chemotaxis–haptotaxis system: the role of logistic source, *SIAM J. Math. Anal.* 41 (2009) 1533–1558.
- [31] Y. Tao, M. Winkler, A chemotaxis–haptotaxis model: the roles of nonlinear diffusion and logistic source, *SIAM J. Math. Anal.* 43 (2011) 685–704.

- [32] Y. Tao, M. Winkler, Boundedness in a quasilinear parabolic–parabolic Keller–Segel system with subcritical sensitivity, *J. Differential Equations* 252 (2012) 692–715.
- [33] Y. Tao, M. Winkler, Dominance of chemotaxis in a chemotaxis–haptotaxis model, *Nonlinearity* 27 (2014) 1225–1239.
- [34] Y. Tao, M. Winkler, Boundedness and stabilization in a multi-dimensional chemotaxis–haptotaxis model, *Proc. Roy. Soc. Edinburgh Sect. A* 144 (2014) 1067–1084.
- [35] Y. Tao, M. Winkler, Energy-type estimates and global solvability in a two-dimensional chemotaxis–haptotaxis model with remodeling of non-diffusible attractant, *J. Differential Equations* 257 (2014) 784–815.
- [36] C. Walker, G.F. Webb, Global existence of classical solutions for a haptotaxis model, *SIAM J. Math. Anal.* 38 (2007) 1694–1713.
- [37] L. Wang, Y. Li, C. Mu, Boundedness in a parabolic–parabolic quasilinear chemotaxis system with logistic source, *Discrete Contin. Dyn. Syst. Ser. A* 34 (2014) 789–802.
- [38] M. Winkler, Chemotaxis with logistic source: very weak global solutions and their boundedness properties, *J. Math. Anal. Appl.* 348 (2008) 708–729.
- [39] M. Winkler, Boundedness in the higher-dimensional parabolic–parabolic chemotaxis system with logistic source, *Comm. Partial Differential Equations* 35 (2010) 1516–1537.
- [40] M. Winkler, Blow-up in a higher-dimensional chemotaxis system despite logistic growth restriction, *J. Math. Anal. Appl.* 384 (2011) 261–272.
- [41] M. Winkler, Global asymptotic stability of constant equilibria in a fully parabolic chemotaxis system with strong logistic dampening, *J. Differential Equations* 257 (2014) 1056–1077.
- [42] Y. Wang, Boundedness in the higher-dimensional chemotaxis–haptotaxis model with nonlinear diffusion, *J. Differential Equations* 260 (2016) 1975–1989.
- [43] C. Yang, X. Cao, Z. Jiang, S. Zheng, Boundedness in a quasilinear fully parabolic Keller–Segel system of higher dimension with logistic source, *J. Math. Anal. Appl.* 430 (2015) 585–591.