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Global boundedness in a three-dimensional chemotaxis–haptotaxis model

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ABSTRACT

This paper studies the chemotaxis–haptotaxis model of cancer invasion

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

in a bounded smooth domain $\Omega \subset \mathbb{R}^3$ with zero-flux boundary conditions, where the parameters χ, ξ and μ are positive. It is shown that the corresponding initial–boundary problem possesses a unique classical solution which is global in time and bounded under the explicit condition $\mu \geq \left(\frac{11}{2} + \xi^2\|w_0\|^2_{L^\infty(\Omega)}\right)\chi^2 + \frac{37}{2} + 4\xi^2\|w_0\|^2_{L^\infty(\Omega)}$ and suitable regularity assumptions on the initial data (u_0, v_0, w_0).

1. Introduction

Cancer invasion is associated with the degradation of the extracellular matrix (ECM), which is degraded by matrix degrading enzymes (MDEs) such as the urokinase-type plasminogen activator (uPA) secreted by cancer cells. The degradation provides space for cancer cells to proliferate and invade into the surrounding tissue. In addition to random diffusion, the migration of cancer cells is biased towards a gradient of the diffusible MDEs by chemotaxis which as a significant mechanism of directional migration of cells is the movement of cells in response to concentration gradients of a chemical signal emitted by the cells themselves in many biological process, and towards a gradient of the nondiffusible ECM through detecting the ECM material vitronectin VN adhered therein by haptotaxis (see [1]). In addition, the cancer cells undergo birth and death in a logistic manner, competing for space with the ECM. The MDE is assumed to be produced by cancer cells, and to diffuse and decay, whereas the ECM is assumed to be degraded up contact with MDE. The combination of these two cell migration mechanisms forms the core of the modeling approach pursued by Chaplain and Lolas to describe cancer cell invasion into surrounding healthy tissue. Except for the model [2], a variety of mathematical models describing the different stages of cancer invasion and metastasis have been developed before (see [1–10]). According to the model proposed in [2], we shall consider the system

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

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where the variables u, v, w denote the cancer cell density, the MDE concentration and the ECM density, respectively. $\Omega \subset \mathbb{R}^n$ $(n \geq 1)$ is the physical domain which is assumed to be an open bounded connected subset with smooth boundary, denoted by $\partial\Omega$, and $\partial/\partial\nu$ denotes the derivative with respect to the outer normal of $\partial\Omega$. The parameters χ, ξ, μ are positive constants and $\tau \in \{0, 1\}$. Throughout the paper, we assume that with some $\theta \in (0, 1)$, the initial data (u_0, v_0, w_0) satisfy

$$\begin{cases} u_0 \in C^0(\overline{\Omega}) \text{ with } u_0 \geq 0 \text{ in } \Omega, \text{ and } u_0 \not\equiv 0, \\ v_0 \in W^{1,\infty}(\Omega) \text{ with } v_0 \geq 0 \text{ in } \Omega, \\ w_0 \in C^{2+\theta}(\overline{\Omega}) \text{ with } w_0 > 0 \text{ in } \overline{\Omega}, \text{ and } \frac{\partial w_0}{\partial \nu} = 0 \text{ on } \partial\Omega. \end{cases} \tag{1.2}$$

Due to the condition $\frac{\partial w_0}{\partial \nu} = 0$ it is already ensured that $\frac{\partial w}{\partial \nu} = 0$ on $\partial\Omega$ and for $t > 0$, so that $\frac{\partial u}{\partial \nu} = \frac{\partial w}{\partial \nu} = 0$ on $\partial\Omega$.

The first three equations of (1.1) with $w = 0$ form the following Keller–Segel chemotaxis system [11]

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

which was used in mathematical biology to model the aggregation phase in the slime mold of Dictyostelium discoideum in response to the chemical cyclic adenosine monophosphate (cAMP). The main issue of the investigation in the mathematical analysis of system (1.3) is whether the solutions of the models are bounded or blow-up (see [12–34]). For example, if all effect of the logistic source are ignored by letting $\mu \equiv 0$, a striking feature of system (1.3) is that some of its solutions blow up in finite time for $n \geq 2$ (see [13,15,18,21,30,31,34]). For instance, Tello and Winkler [26] proved that if $\tau = 0$ and $\mu > \frac{(n-2)_+}{n}\chi$, the system admits a unique global classical which is bounded for any regular initial data. Moreover, for the case $\tau = 1$, it is known that bounded solutions exist in one and two space dimensions for any $\mu > 0$ [23] and that the same result holds for $\mu > \mu_0$ with some $\mu_0(\chi) > 0$ in higher dimensions [29] but $\mu_0(\chi)$ is unexplicit. Recently, it is worth mentioning that if the term $\mu u(1-u)$ was replaced by the term $u - \mu u^r$ in (1.3), where $\mu > 0$ and $r \geq 2$, Lin et al. [19] identified an explicit condition on the parameters χ, μ and r to ensure global existence and boundedness and investigated the solutions of (1.3) stabilize towards a constant equilibrium for $n = 2,3$. Anyhow, the logistic source in (1.3) has a certain blow-up preventing effect on chemotaxis models.

When $\chi = 0$, (1.1) is reduced to the haptotaxis-only system

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

The mathematical literature on it is comparatively thin due to the lack of appropriate regularization of the solution component w which reflects a nonlocal memory-type feature of the haptotactic transport term in (1.4). As for the global existence and the large time behavior of solution to model (1.4), we refer to [10,35–41].

In realistic situations, the diffusion rate of MDE is much greater than that of cancer cells. If one may follow an approach of quasi-steady-state approximation for the second equation in (1.1) and the ability of ECM to spontaneously renew is included, the Chaplain–Lolas model (1.1) becomes

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

which has been widely investigated by many authors (see [42–45]). For example, for system (1.5) without tissue remodeling (i.e. $\eta = 0$), Tao and Wang [42] proved that model (1.5) possesses a unique global bounded classical solution for any $\mu > 0$ for $n = 2$, and for large $\mu > 0$ in $n = 3$. Tao and Winkler [45] investigated the global existence and boundedness under an explicit condition on μ and proved the solution of (1.5) approaches to the steady state $(1, 1, 0)$. In [44], the authors extended the results of [45], which shows that the haptotaxis term does not affect the boundedness of solution and that accordingly the chemotaxis process essentially dominates the whole system. Particularly, Tao and Winkler [43] obtained the existence and uniqueness of a global classical solution to (1.5) with $\eta > 0$ by constructing energy-like inequality for $n = 2$. Moreover, compared to the chemotaxis–haptotaxis system (1.5), a natural question is whether similar results hold for the fully parabolic–parabolic-ODE chemotaxis–haptotaxis system (1.1). For instance, some authors give a partially positive answer in this direction. In [46], Tao established the global boundedness of solutions for any $\chi > 0$, $\xi > 0$ and $\mu > 0$ in the two-dimensional setting. Moreover, Cao [47] also dealt with the global boundedness in $n = 3$ for sufficiently large $\frac{\mu}{\chi}$. Unfortunately, the hypothesis on the parameters is not explicit. Recently, Wang and Ke [41] extend the results of [48] to higher dimensions on convex domain. More results about Cauchy problem are obtained (see [38,49–55]).

Motivated by the arguments in [54,56–62], we investigate the global dynamical properties of the fully parabolic–parabolic-ODE system (1.1) with $\tau = 1$ under some explicit conditions in three dimensional bounded domain. As compared

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to the chemotaxis-only system (1.3), the chemotaxis–haptotaxis system (1.1) is much less understood due to the lack of appropriate regularization of the solution component w which reflects a nonlocal memory-type feature of the haptotactic transport term. We can state the main result as follows:

Theorem 1.1. *Let $\tau = 1$ in (1.1), $\Omega \subset \mathbb{R}^3$ be an arbitrary smooth bounded domain. Suppose that the positive parameters χ, ξ and μ satisfy*

$$\mu \geq \Big(\frac{11}{2} + \xi^2\|w_0\|^2_{L^\infty(\Omega)}\Big)\chi^2 + \frac{37}{2} + 4\xi^2\|w_0\|^2_{L^\infty(\Omega)}. \tag{1.6}$$

Then for any (u_0, v_0, w_0) fulfilling (1.2), problem (1.1) possesses a unique global classical solution (u, v, w) which is bounded in the sense that

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} + \|v(\cdot,t)\|_{W^{1,\infty}(\Omega)} + \|w(\cdot,t)\|_{L^\infty(\Omega)} \leq C \tag{1.7}$$

with constant $C > 0$ that is independent of t.

Methods used in the paper: An energy-type estimate as a source of a priori estimates Motivated by the arguments of the chemotaxis-only model [19], we will develop the coupled functional $y_1(t) := \kappa_1\int_\Omega u^2(\cdot,t) + \frac{5}{2}\int_\Omega |\nabla v(\cdot,t)|^4 + \frac{1}{2}\int_\Omega |\Delta v(\cdot,t)|^2 + \int_\Omega |\nabla v(\cdot,t)|^2 + \int_\Omega u(\cdot,t)|\nabla v(\cdot,t)|^2$ for all $t \in (0,T)$, where κ_1 is defined below. Moreover, the key step in our proof of the global boundedness is to deal with the difficulty term $\int_\Omega u(\cdot,t)\nabla w(\cdot,t)\cdot\nabla|\nabla v(\cdot,t)|^2$ which stems from the lack of appropriate regularization of the solution component w, reflecting a nonlocal memory-type feature of the haptotactic transport term in (1.1) (see Lemma 3.3). This will enable us to estimate both $\int_\Omega |\nabla v(\cdot,t)|^4$ and $\int_\Omega |\Delta v(\cdot,t)|^2$ which is very important in the analysis of global boundedness (see Lemma 3.8).

This paper is organized as follows. In Section 2, we recall some preliminary results. In Section 3, we develop the coupled function $y_1(t) := \kappa_1\int_\Omega u^2(\cdot,t) + \frac{5}{2}\int_\Omega |\nabla v(\cdot,t)|^4 + \frac{1}{2}\int_\Omega |\Delta v(\cdot,t)|^2 + \int_\Omega |\nabla v(\cdot,t)|^2 + \int_\Omega u(\cdot,t)|\nabla v(\cdot,t)|^2$ for all $t \in (0,T)$ to estimate $\int_\Omega |\nabla v(\cdot,t)|^4$ and $\int_\Omega |\Delta v(\cdot,t)|^2$.

Throughout this paper, we use symbols C, c_i, C_i (i=0,1,2...) as some generic positive constants. Moreover, for simplicity, the integral $\int_\Omega u(x)dx$ is written as $\int_\Omega u(x)$.

2. Local existence of classical solutions

We first recall the local solvability of (1.1) which is based on well-established methods involving the Schauder fixed point theorem and the standard regularity theory of parabolic equations.

Lemma 2.1. *Let $\chi > 0$, $\xi > 0$ and $\mu > 0$. Then for any initial data (u_0, v_0, w_0) fulfilling (1.2), the problem (1.1) admits a unique classical solution*

$$\begin{aligned} &u \in C^0(\overline{\Omega}\times[0,T_{\max}))\cap C^{2,1}(\overline{\Omega}\times(0,T_{\max})),\\ &v \in C^0(\overline{\Omega}\times[0,T_{\max}))\cap C^{2,1}(\overline{\Omega}\times(0,T_{\max}))\cap L^\infty_{loc}([0,T_{\max};W^{1,q}))(q>3),\\ &w \in C^{2,1}(\overline{\Omega}\times[0,T_{\max})) \end{aligned} \tag{2.1}$$

with

$$u \geq 0,\quad v \geq 0 \ \text{ and } \ 0 \leq w \leq \|w_0\|_{L^\infty(\Omega)} \ \text{ for all } \ (x,t) \in \Omega\times(0,T_{\max}),$$

where $T_{\max}$ denotes the maximal existence time. Moreover, if $T_{\max} < \infty$, then

$$\limsup_{t\nearrow T_{\max}}(\|u(\cdot,t)\|_{L^\infty(\Omega)} + \|v(\cdot,t)\|_{W^{1,\infty}(\Omega)} + \|w(\cdot,t)\|_{W^{1,\infty}(\Omega)}) = \infty$$

and the solution of (1.1) gained above satisfies

(i) $\|u(\cdot,t)\|_{L^1(\Omega)} \leq m := \max\Big\{\|u_0\|_{L^1(\Omega)}, |\Omega|\Big\}$ *for all* $t \in (0,T_{\max})$;

(ii) $\|v(\cdot,t)\|_{L^1(\Omega)} \leq \max\Big\{\|v_0\|_{L^1(\Omega)}, m\Big\}$ *for all* $t \in (0,T_{\max})$;

(iii) $\|\nabla v(\cdot,t)\|^2_{L^2(\Omega)} \leq \frac{(\mu+4)m}{4\mu} + \|\nabla v_0\|^2_{L^2(\Omega)}$ *for all* $t \in (0,T_{\max})$;

(iv) $\|v(\cdot,t)\|_{L^{\frac{2n}{n-2}}(\Omega)} \leq c_1\Big(\frac{(\mu+4)m}{4\mu} + \|\nabla v_0\|^2_{L^2(\Omega)}\Big)^{\frac{1}{2}} + c_2\max\Big\{\|v_0\|_{L^1(\Omega)}, m\Big\}$ *for all* $t \in (0,T_{\max})$.

Proof. The claims concerning local-in-time existence of the classical solution to problem (1.1) follow from well-known parabolic regularity theory and fixed point argument. For details, we refer the reader to [45].

(ii) **Uniqueness**. Proceeding as in [26,29], we shall obtain the uniqueness of local solution. Assume that both (u_1, v_1, w_1) and (u_2, v_2, w_2) solve (1.1) in the classical sense in $\Omega\times(0,T)$, we fix $T_0 \in (0,T)$ and let U, V and W be defined by

$$U := u_1 - u_2,\ V := v_1 - v_2 \text{ and } W := w_1 - w_2$$

and, hence,

$$U(x,0)=0,\ \ V(x,0)=0 \text{ and } W(x,0)=0.$$

From (2.1), we know that there exist positive constants c_j $(j=1,2,3,4)$ such that

$$\|u_i\|_{W^{1,\infty}(\Omega\times(0,T))}\le c_1 \text{ for } i=1,2, \tag{2.2}$$

$$\|v_i\|_{L^\infty(\Omega\times(0,T))}\le c_2 \text{ for } i=1,2 \tag{2.3}$$

and

$$\|\nabla v_i\|_{L^\infty(\Omega\times(0,T))}\le c_3 \text{ for } i=1,2 \tag{2.4}$$

as well as

$$\|\nabla w_i\|_{L^\infty(\Omega\times(0,T))}\le c_4 \text{ for } i=1,2. \tag{2.5}$$

Moreover, we operate the first equation of system (1.1) to obtain

$$\begin{aligned} U_t &= \Delta U-\chi\nabla\cdot(u_1\nabla V)-\chi\nabla\cdot(U\nabla v_2)-\xi\nabla\cdot(u_1\nabla W)-\xi\nabla\cdot(U\nabla w_2)\\ &\quad+\mu(1-u_1-u_2)U-\mu w_1U-\mu u_2W \end{aligned} \tag{2.6}$$

and

$$V_t=\Delta V+U-V \tag{2.7}$$

as well as

$$W_t=-v_1W-w_2V. \tag{2.8}$$

Now multiplying (2.6) by U and integrating it over Ω by parts, we obtain

$$\begin{aligned} \frac{1}{2}\frac{d}{dt}\int_\Omega U^2+\int_\Omega|\nabla U|^2 &= \chi\int_\Omega u_1\nabla U\cdot\nabla V+\chi\int_\Omega U\nabla v_2\cdot\nabla U\\ &\quad+\xi\int_\Omega u_1\nabla W\cdot\nabla U+\xi\int_\Omega U\nabla w_2\cdot\nabla U\\ &\quad-\mu\int_\Omega w_1U^2-\mu\int_\Omega u_2WU+\mu\int_\Omega(1-u_1-u_2)U^2 \end{aligned} \tag{2.9}$$

for all $t\in(0,T)$. Next we use the Hölder's inequality, Young's inequality, (2.2) and (2.4) to conclude that

$$\begin{aligned} \chi\int_\Omega u_1\nabla U\cdot\nabla V &\le |\chi|c_1\int_\Omega|\nabla U||\nabla V|\\ &\le \frac{1}{8}\|\nabla U\|^2_{L^2(\Omega)}+2\chi^2c_1^2\|\nabla V\|^2_{L^2(\Omega)} \end{aligned} \tag{2.10}$$

for all $t\in(0,T_0)$ and

$$\begin{aligned} \chi\int_\Omega U\nabla v_2\cdot\nabla U &\le |\chi|c_3\int_\Omega|U||\nabla U|\\ &\le \frac{1}{8}\|\nabla U\|^2_{L^2(\Omega)}+2\chi^2c_3^2\|U\|^2_{L^2(\Omega)} \end{aligned}$$

for all $t\in(0,T_0)$ as well as

$$\begin{aligned} -\mu\int_\Omega u_2WU &\le |\mu|c_1\int_\Omega|W||U|\\ &\le \frac{1}{4}\|W\|^2_{L^2(\Omega)}+\mu^2c_1^2\|U\|^2_{L^2(\Omega)} \end{aligned}$$

for all $t\in(0,T_0)$. In view of the boundedness of u_1 and u_2 in $\Omega\times(0,T_0)$, we arrive at

$$\mu\int_\Omega(1-u_1-u_2)U^2\le\mu(1+\|u_1\|_{L^\infty}+\|u_2\|_{L^\infty})\|U\|^2_{L^2(\Omega)}\le\mu(1+2c_1)\|U\|^2_{L^2(\Omega)}$$

for all $t \in (0, T_0)$. In view of (2.2) and (2.5), we can apply the Young inequality to obtain that

$$\begin{aligned}\xi \int_\Omega u_1 \nabla W \cdot \nabla U &\leq |\xi| c_1 \int_\Omega |\nabla W||\nabla U| \\ &\leq 2\xi^2 c_1^2 \|\nabla W\|^2_{L^2(\Omega)} + \frac{1}{8}\|\nabla U\|^2_{L^2(\Omega)}\end{aligned}$$

for all $t \in (0, T_0)$ and

$$\begin{aligned}\xi \int_\Omega U \nabla w_2 \cdot \nabla U &\leq |\xi| c_4 \int_\Omega |U||\nabla U| \\ &\leq 2\xi^2 c_4^2 \|U\|^2_{L^2(\Omega)} + \frac{1}{8}\|\nabla U\|^2_{L^2(\Omega)}\end{aligned} \tag{2.11}$$

for all $t \in (0, T_0)$. Substituting (2.10)–(2.11) into (2.9), we can obtain

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\int_\Omega U^2 + \frac{1}{2}\int_\Omega |\nabla U|^2 &\leq \left(\mu(1 + 2c_1 + \mu c_1^2) + 2\xi^2 c_4^2 + 2\chi^2 c_2^2\right)\int_\Omega U^2 \\ &\quad + 2\xi^2 c_1^2 \int_\Omega |\nabla W|^2 + 2\chi^2 c_1^2 \int_\Omega |\nabla V|^2 + \frac{1}{4}\int_\Omega |W|^2\end{aligned} \tag{2.12}$$

for all $t \in (0, T_0)$. Testing (2.7) against V_t and (2.8) against W, respectively, we can obtain

$$\frac{1}{2}\frac{d}{dt}\Big(\int_\Omega |V|^2 + \int_\Omega |\nabla V|^2\Big) + \int_\Omega V_t^2 \leq \frac{1}{2}\int_\Omega V_t^2 + \frac{1}{2}\int_\Omega |U|^2 \tag{2.13}$$

for all $t \in (0, T_0)$ and

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\int_\Omega |W|^2 &= -\int_\Omega v_1|W|^2 - \int_\Omega w_2 W V \leq \int_\Omega |w_2\|V\|W| \\ &\leq c_5^2 \int_\Omega |V|^2 + \frac{1}{4}\int_\Omega |W|^2\end{aligned} \tag{2.14}$$

for all $t \in (0, T_0)$ due to the fact $v_1 > 0$ as well as

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\int_\Omega |\nabla W|^2 &= -\int_\Omega W \nabla W \cdot \nabla v_1 - \int_\Omega v_1 |\nabla W|^2 \\ &\quad - \int_\Omega V \nabla W \cdot \nabla w_2 - \int_\Omega w_2 \nabla W \cdot \nabla V\end{aligned} \tag{2.15}$$

for all $t \in (0, T_0)$. Since $|\nabla v_1|$, v_1, ∇w_2 and w_2 are bounded on $\Omega \times [0, T]$, we can apply Young's inequality to obtain that

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\int_\Omega |\nabla W|^2 &\leq c_3 \int_\Omega ||W|\nabla W| + c_2 \int_\Omega |\nabla W|^2 \\ &\quad + c_4 \int_\Omega |V||\nabla W| + c_5 \int_\Omega |\nabla W||\nabla V| \\ &\leq \frac{c_3}{2}\int_\Omega |W|^2 + \Big(\frac{c_3}{2} + c_2 + \frac{c_4}{2} + \frac{c_5}{2}\Big)\int_\Omega |\nabla W|^2 \\ &\quad + \frac{c_4}{2}\int_\Omega |V|^2 + \frac{c_5}{2}\int_\Omega |\nabla V|^2\end{aligned} \tag{2.16}$$

for all $t \in (0, T_0)$ where $c_5 := \|w_0\|_{L^\infty(\Omega)}$. Therefore, from (2.12)–(2.14) and (2.16) we can obtain the inequality

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\left\{\int_\Omega U^2 + \int_\Omega V^2 + \int_\Omega |\nabla V|^2 + \int_\Omega W^2 + \int_\Omega |\nabla W|^2\right\} \\
&\le \left(\mu(1+2c_1+\mu c_1^2) + 2\xi^2 c_4^2 + 2\chi^2 c_2^2 + \frac{1}{2}\right)\int_\Omega U^2 + \left(c_5^2 + \frac{c_4}{2}\right)\int_\Omega |V|^2 \\
&\quad + \left(\frac{c_3}{2} + c_2 + \frac{c_4}{2} + \frac{c_5}{2} + 2\xi^2 c_1^2\right)\int_\Omega |\nabla W|^2 + \left(\frac{c_3}{2} + \frac{1}{2}\right)\int_\Omega W^2 \\
&\quad + \left(2\chi^2 c_1^2 + \frac{c_5}{2}\right)\int_\Omega |\nabla V|^2 \\
&\le c_6\left\{\int_\Omega U^2 + \int_\Omega V^2 + \int_\Omega |\nabla V|^2 + \int_\Omega W^2 + \int_\Omega |\nabla W|^2\right\} \quad \text{for all } t \in (0, T_0),
\end{aligned} \tag{2.17}$$

where $c_6 := \max\left\{\mu(1+2c_1+\mu c_1^2) + 2\xi^2 c_4^2 + 2\chi^2 c_2^2 + \frac{1}{2}, c_5^2 + \frac{c_4}{2}, \frac{c_3}{2} + c_2 + \frac{c_4}{2} + \frac{c_5}{2} + 2\xi^2 c_1^2, \frac{c_3}{2} + \frac{1}{2}, 2\chi^2 c_1^2 + \frac{c_5}{2}\right\}$. By (2.17) and Gronwall's lemma we have $U \equiv 0$, $V \equiv 0$ and $W \equiv 0$ in $\Omega \times (0, T_0)$ and hence $u_1 = u_2$, $v_1 = v_2$ and $w_1 = w_2$ in $\Omega \times (0, T)$ due to $T_0 \in (0, T)$ is arbitrary which implies the uniqueness of solutions.

Moreover, noticing that L^1-norm of the component solutions u and v of (1.1) are bounded by integrating the first equation over Ω, we can obtain (i)–(iv) in quite a similar way to Lemma 3.1 in [41]. □

Since the third equation in (1.1) is an ODE, w can be expressed explicitly in terms of v. This results in the representation formulate as follows:

Lemma 2.2 (See [47]). *Let (u, v, w) be a classical solution of (1.1) in $\Omega \times (0, T)$, and assume that (1.2) holds. Then*

$$w(x, t) = w_0(x)e^{-\int_0^t v(x,s)ds} \tag{2.18}$$

and

$$\nabla w(x, t) = \nabla w_0(x)e^{-\int_0^t v(x,s)ds} - w_0(x)e^{-\int_0^t v(x,s)ds}\int_0^t \nabla v(x, s)ds \tag{2.19}$$

as well as

$$\begin{aligned}
\Delta w(x, t) \ge\ & \Delta w_0(x)e^{-\int_0^t v(x,s)ds} - 2e^{-\int_0^t v(x,s)ds}\nabla w_0(x)\cdot\int_0^t \nabla v(x, s)ds \\
& - \frac{1}{e}w_0(x) - w_0(x)v(x, t)e^{-\int_0^t v(x,s)ds}
\end{aligned} \tag{2.20}$$

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

The following lemma on a upper bound for $\int_\Omega |\nabla w(\cdot, t)|^2$ is important for our arguments.

Lemma 2.3. *Assume that (u, v, w) is a classical solution of (1.1). Then we have*

$$\int_\Omega |\nabla w(\cdot, t)|^2 \le 2\int_\Omega |\nabla w_0|^2 + \frac{|\Omega|}{2e}\|w_0\|^2_{L^\infty(\Omega)} + \|w_0\|^2_{L^\infty(\Omega)}\cdot\int_\Omega v(\cdot, t)$$

for all $t \in (0, T_{\max})$.

Proof. The proof of this lemma is completely similar to Lemma 4.3 in [41], so we omit it here. □

The following lemma provides an estimate for $-\Delta w$ in the corresponding interior part. The main ideas we use come from [46] .

Lemma 2.4. *Let (u, v, w) solve (1.1) in $\Omega \times (0, T)$ with some (u_0, v_0, w_0) satisfying (1.2). Then*

$$-\Delta w(x, t) \le ||w_0||_{L^\infty(\Omega)}\cdot v(x, t) + \kappa_0 \quad \text{for all } x \in \Omega \text{ and } t \in (0, T),$$

where

$$\kappa_0 := ||\Delta w_0||_{L^\infty(\Omega)} + 4||\nabla\sqrt{w_0}||^2_{L^\infty(\Omega)} + \frac{||w_0||_{L^\infty(\Omega)}}{e}.$$

To build a bound for $\|u(\cdot, t)\|_{L^p(\Omega)}$ for all large p, we need the following Gagliardo–Nirenberg inequality.

Lemma 2.5 (*Gagliardo–Nirenberg Inequality*)**.** *Let $r \in (0, \alpha)$ and $\psi \in W^{1,2}(\Omega) \cap L^r(\Omega)$. Then there exists a constant $C_{GN} > 0$ such that*

$$\|\psi\|_{L^\alpha(\Omega)} \le C_{GN}\left(\|\nabla\psi\|_{L^2(\Omega)}^{\lambda^*}\|\psi\|_{L^r(\Omega)}^{1-\lambda^*} + \|\psi\|_{L^r(\Omega)}\right) \tag{2.21}$$

holds with $\lambda^* \in (0, 1)$ satisfying

$$\lambda^* = \frac{\frac{n}{r} - \frac{n}{\alpha}}{1 - \frac{n}{2} + \frac{n}{r}}.$$

3. Global boundedness

In this section, we will obtain the boundedness of the solutions to (1.1) under an explicit condition on the parameters χ, ξ and μ. The main step is to establish a uniform bound of $u(x, t)$ in (1.1) with respect to the norm in $L^p(\Omega)$ for certain $p \in (1, \infty)$. To achieve this, we firstly need to obtain some estimates for $\int_\Omega u^2(x, t)$, $\int_\Omega |\nabla v(x, t)|^4$, $\int_\Omega u(x, t)|\nabla v(x, t)|^2$ and $\int_\Omega |\Delta v(x, t)|^2$. Moreover, since ECM density satisfies an ordinary differential equation (ODE), we must overcome the essential analytic difficulty which stems from the fact that the chemotaxis and haptotaxis terms in the first equation of (1.1) require the different L^p-estimate techniques.

Lemma 3.1. *Let $T \in (0, T_{\max})$, $\chi > 0$, $\xi > 0$ and $\mu > 0$, and assume (1.2) holds. Then the solution of (1.1) satisfies*

$$\frac{d}{dt}\int_\Omega u^2 + \int_\Omega |\nabla u|^2 \le \chi^2\int_\Omega u^2|\nabla v|^2 - \mu\int_\Omega u^3 + C_4 \tag{3.1}$$

for all $t \in (0, T)$ where C_4 is defined below.

Proof. We multiply the first equation in (1.1) by u and integrate over Ω to obtain, for all $t \in (0, T)$,

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\int_\Omega u^2 &= \int_\Omega u\Big(\Delta u - \chi\nabla\cdot(u\nabla v) - \xi\nabla\cdot(u\nabla w) + \mu u(1 - u - w)\Big)\\
&= -\int_\Omega |\nabla u|^2 + \chi\int_\Omega u\nabla u\cdot\nabla v + \xi\int_\Omega u\nabla u\cdot\nabla w + \mu\int_\Omega u^2(1 - u - w)\\
&\le -\int_\Omega |\nabla u|^2 + \chi\int_\Omega u\nabla u\cdot\nabla v - \frac{\xi}{2}\int_\Omega u^2\Delta w + \mu\int_\Omega u^2(1 - u)
\end{aligned} \tag{3.2}$$

according to the nonnegativity of w. By Young's inequality, we derive that

$$\chi\int_\Omega u\nabla u\cdot\nabla v \le \frac{1}{2}\int_\Omega |\nabla u|^2 + \frac{\chi^2}{2}\int_\Omega u^2|\nabla v|^2 \tag{3.3}$$

for all $t \in (0, T)$. To deal with the third and last terms on the right side of the inequality (3.2), we apply Lemma 2.4 and Young's inequality to obtain that for all $t \in (0, T)$

$$\begin{aligned}
-\frac{\xi}{2}\int_\Omega u^2\Delta w &\le \frac{\xi}{2}\|w_0\|_{L^\infty(\Omega)}\int_\Omega u^2 v + \frac{\xi\kappa_0}{2}\int_\Omega u^2\\
&\le \frac{\mu}{4}\int_\Omega u^3 + \frac{8}{27\mu^2}\left(\xi\|w_0\|_{L^\infty(\Omega)}\right)^3\int_\Omega v^3 + \frac{\xi\kappa_0}{2}\int_\Omega u^2.
\end{aligned} \tag{3.4}$$

Furthermore, Young's inequality applied again to the third term on the right-hand side of (3.4) yields that for all $t \in (0, T)$

$$\left(\frac{\xi\kappa_0}{2} + \mu\right)\int_\Omega u^2 \le \frac{\mu}{4}\int_\Omega u^3 + C_1 \text{ for all } t \in (0, T), \tag{3.5}$$

where $C_1 := \frac{64}{27\mu^2}\left(\frac{\xi\kappa_0}{2} + \mu\right)^3|\Omega| > 0$. Now we turn to estimating the second integral on the right side of (3.4). In fact, according to the Gagliardo–Nirenberg inequality, we can use Lemma 2.1 to obtain that there exist some constants $C_i > 0$ $(i = 2, 3)$ fulfilling

$$\begin{aligned}
\|v\|_{L^3(\Omega)}^3 &\le (C_2\|\nabla v\|_{L^2(\Omega)}^{\frac{4}{5}}\|v\|_{L^1(\Omega)}^{\frac{1}{5}} + C_2\|v\|_{L^1(\Omega)})^3\\
&\le C_3.
\end{aligned} \tag{3.6}$$

This, combined with (3.3)–(3.5) readily yields that

$$\frac{1}{2}\frac{d}{dt}\int_\Omega u^2 \le -\frac{1}{2}\int_\Omega |\nabla u|^2 + \frac{\chi^2}{2}\int_\Omega u^2|\nabla v|^2 - \frac{\mu}{2}\int_\Omega u^3 + C_4$$

for all $t \in (0, T)$ with $C_4 := \frac{64}{27\mu^2}\left(\frac{\xi\kappa_0}{2} + \mu\right)^3|\Omega| + \frac{8}{27\mu^2}\left(\xi\|w_0\|_{L^\infty(\Omega)}\right)^3 C_3$. Then we can obtain the desired result. □

Lemma 3.2. *Let (u, v, w) solve (1.1) with $n = 3$. Then the inequality*

$$\frac{d}{dt}\int_\Omega |\nabla v|^4 + 4\int_\Omega |\nabla v|^4 + \int_\Omega \left|\nabla|\nabla v|^2\right|^2 \le 7\int_\Omega u^2|\nabla v|^2 + 2\int_{\partial\Omega} |\nabla v|^2 \frac{\partial|\nabla v|^2}{\partial\nu} \tag{3.7}$$

holds for all $t \in (0, T)$, where $T \in (0, T_{\max})$.

Proof. Invoking that $\nabla v \cdot \nabla \Delta v = \frac{1}{2}\Delta|\nabla v|^2 - |D^2 v|^2$ and using the second equation in (1.1) and several integration by parts, we find that

$$\begin{aligned}
\frac{1}{4}\frac{d}{dt}\int_\Omega |\nabla v|^4 &= \int_\Omega |\nabla v|^2 \nabla v \cdot \nabla\Big(\Delta v - v + u\Big) \\
&= \frac{1}{2}\int_\Omega |\nabla v|^2 \Delta|\nabla v|^2 - \int_\Omega |\nabla v|^2|D^2 v|^2 - \int_\Omega |\nabla v|^4 \\
&\quad - \int_\Omega u\nabla\cdot\left(|\nabla v|^2\nabla v\right) \\
&= -\frac{1}{2}\int_\Omega \left|\nabla|\nabla v|^2\right|^2 + \frac{1}{2}\int_{\partial\Omega} |\nabla v|^2\frac{\partial|\nabla v|^2}{\partial\nu} - \int_\Omega |\nabla v|^2|D^2 v|^2 \\
&\quad - \int_\Omega |\nabla v|^4 - \int_\Omega u|\nabla v|^2\Delta v - \int_\Omega u\nabla v\cdot\nabla|\nabla v|^2
\end{aligned} \tag{3.8}$$

for all $t \in (0, T)$. Therefore, along with the pointwise inequality $|\Delta v| \le \sqrt{3}|D^2 v|$, using Young's inequality leads to, for all $t \in (0, T)$,

$$\begin{aligned}
-\int_\Omega u|\nabla v|^2\Delta v &\le \sqrt{3}\int_\Omega u|\nabla v|^2|D^2 v| \\
&\le \int_\Omega |\nabla v|^2|D^2 v|^2 + \frac{3}{4}\int_\Omega u^2|\nabla v|^2
\end{aligned}$$

for all $t \in (0, T)$. In order to further estimate the last integral term on the right side of (3.8), we use Young's inequality again to obtain

$$-\int_\Omega u\nabla v\cdot\nabla|\nabla v|^2 \le \frac{1}{4}\int_\Omega \left|\nabla|\nabla v|^2\right|^2 + \int_\Omega u^2|\nabla v|^2$$

for all $t \in (0, T)$. Inserting these inequalities into (3.8) we discover that (3.7) holds. □

Since the haptotaxis term $\nabla w(\cdot, t)$ might become unbounded in $L^\infty(\Omega)$, we must deal with the difficulty term $\int_\Omega u(\cdot, t)\nabla w(\cdot, t)\cdot\nabla|\nabla v(\cdot, t)|^2$.

Lemma 3.3. *Let (u, v, w) be the solution of (1.1) with nonnegative initial data (u_0, v_0, w_0) satisfying (1.2). For any $\chi > 0$, $\xi > 0$ and $\mu > 0$, then*

$$\begin{aligned}
\frac{d}{dt}\int_\Omega u|\nabla v|^2 &\le \Big(\frac{5}{2} + \xi^2\|w_0\|^2_{L^\infty(\Omega)}\Big)\int_\Omega |\nabla u|^2 + \frac{3}{2}\int_\Omega \left|\nabla|\nabla v|^2\right|^2 + \frac{1}{2}\int_\Omega |\nabla v_t|^2 \\
&\quad + \left(\chi^2 + 1 + 4\xi^2\|w_0\|^2_{L^\infty(\Omega)} - \mu\right)\int_\Omega u^2|\nabla v|^2 - 2\xi\int_\Omega uw|D^2 v|^2 \\
&\quad + (\mu - 2)\int_\Omega u|\nabla v|^2 + \int_{\partial\Omega} u\frac{\partial|\nabla v|^2}{\partial\nu} + \xi\int_{\partial\Omega} uw\frac{\partial|\nabla v|^2}{\partial\nu} \\
&\quad - 2\int_\Omega u|D^2 v|^2
\end{aligned} \tag{3.9}$$

holds for all $t \in (0, T)$, where $T \in (0, T_{\max})$.

Proof. From the nonnegativity of w, (1.1) and the pointwise identity $\nabla v\cdot\nabla\Delta v=\frac{1}{2}\Delta|\nabla v|^2-|D^2v|^2$, an integration by parts gives

$$\begin{aligned}\frac{d}{dt}\int_\Omega u|\nabla v|^2 &= \int_\Omega\Big(\Delta u-\chi\nabla\cdot(u\nabla v)-\xi\nabla\cdot(u\nabla w)+\mu u(1-u-w)\Big)|\nabla v|^2\\
&\quad+2\int_\Omega u\nabla v\cdot\nabla\big(\Delta v-v+u\big)\\
&\le -\int_\Omega\nabla u\cdot\nabla|\nabla v|^2+\chi\int_\Omega u\nabla v\cdot\nabla|\nabla v|^2+\xi\int_\Omega u\nabla w\cdot\nabla|\nabla v|^2\\
&\quad+\mu\int_\Omega u(1-u)|\nabla v|^2+2\int_\Omega u\nabla v\cdot\nabla\Delta v-2\int_\Omega u|\nabla v|^2\\
&\quad+2\int_\Omega u\nabla u\cdot\nabla v\\
&= -2\int_\Omega\nabla u\cdot\nabla|\nabla v|^2+\chi\int_\Omega u\nabla v\cdot\nabla|\nabla v|^2+2\int_\Omega u\nabla u\cdot\nabla v\\
&\quad-\xi\int_\Omega w\nabla u\cdot\nabla|\nabla v|^2-\xi\int_\Omega uw\Delta|\nabla v|^2+\big(\mu-2\big)\int_\Omega u|\nabla v|^2\\
&\quad+\int_{\partial\Omega}u\frac{\partial|\nabla v|^2}{\partial\nu}-2\int_\Omega u|D^2v|^2-\mu\int_\Omega u^2|\nabla v|^2\\
&\quad+\xi\int_{\partial\Omega}uw\frac{\partial|\nabla v|^2}{\partial\nu}\end{aligned}\tag{3.10}$$

for all $t\in(0,T)$. Now by straightforward estimates and using the pointwise identity $\nabla v\cdot\nabla\Delta v=\frac{1}{2}\Delta|\nabla v|^2-|D^2v|^2$ again, it yields that

$$\begin{aligned}\frac{d}{dt}\int_\Omega u|\nabla v|^2 &\le -2\int_\Omega\nabla u\cdot\nabla|\nabla v|^2+\chi\int_\Omega u\nabla v\cdot\nabla|\nabla v|^2+2\int_\Omega u\nabla u\cdot\nabla v\\
&\quad-\xi\int_\Omega w\nabla u\cdot\nabla|\nabla v|^2-2\xi\int_\Omega uw\nabla v\cdot\nabla\Delta v-2\xi\int_\Omega uw|D^2v|^2\\
&\quad+\big(\mu-2\big)\int_\Omega u|\nabla v|^2+\int_{\partial\Omega}u\frac{\partial|\nabla v|^2}{\partial\nu}-2\int_\Omega u|D^2v|^2\\
&\quad-\mu\int_\Omega u^2|\nabla v|^2+\xi\int_{\partial\Omega}uw\frac{\partial|\nabla v|^2}{\partial\nu}\end{aligned}\tag{3.11}$$

for all $t\in(0,T)$ and using the fact $v_t=\Delta v-v+u$ and the nonnegativity of u and w we find that

$$\begin{aligned}-2\xi\int_\Omega uw\nabla v\cdot\nabla\Delta v &= -2\xi\int_\Omega uw\nabla v\cdot\nabla(v_t+v-u)\\
&\le -2\xi\int_\Omega uw\nabla v\cdot\nabla v_t+2\xi\int_\Omega uw\nabla u\cdot\nabla v\\
&\le 4\xi^2\int_\Omega u^2w^2|\nabla v|^2+\frac{1}{2}\int_\Omega|\nabla v_t|^2+\frac{1}{2}\int_\Omega|\nabla u|^2\\
&\le 4\xi^2\big|\big|w_0\big|\big|^2_{L^\infty(\Omega)}\int_\Omega u^2|\nabla v|^2+\frac{1}{2}\int_\Omega|\nabla v_t|^2+\frac{1}{2}\int_\Omega|\nabla u|^2\end{aligned}$$

for all $t\in(0,T)$. Then we use Young's inequality again to obtain that

$$-2\int_\Omega\nabla u\cdot\nabla|\nabla v|^2\le\int_\Omega|\nabla u|^2+\int_\Omega\big|\nabla|\nabla v|^2\big|^2$$

for all $t\in(0,T)$. Similarly, we can estimate the second and third terms on the right-hand side of (3.11) according to

$$\chi\int_\Omega u\nabla v\cdot\nabla|\nabla v|^2\le\chi^2\int_\Omega u^2|\nabla v|^2+\frac{1}{4}\int_\Omega\big|\nabla|\nabla v|^2\big|^2$$

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

$$2\int_\Omega u\nabla u\cdot\nabla v \le \int_\Omega |\nabla u|^2 + \int_\Omega u^2|\nabla v|^2$$

for all $t \in (0,T)$. Furthermore, we may recall Lemma 2.2 and make use of Young's inequality again to find that

$$-\xi\int_\Omega w\nabla u\cdot\nabla|\nabla v|^2 \le \xi^2\|w_0\|^2_{L^\infty(\Omega)}\int_\Omega|\nabla u|^2 + \frac{1}{4}\int_\Omega\left|\nabla|\nabla v|^2\right|^2$$

for all $t \in (0,T)$. Hence, (3.9) results from above inequalities immediately. □

To absorb the third term on the right-hand side of the inequality (3.9), we next state the following lemma.

Lemma 3.4. *Let (u,v,w) be the solution of (1.1). Then we have*

$$\frac{d}{dt}\int_\Omega|\Delta v|^2 + \int_\Omega|\nabla v_t|^2 \le 2\int_\Omega|\nabla v|^2 + 2\int_\Omega|\nabla u|^2 \tag{3.12}$$

for all $t \in (0,T)$, where $T \in (0,T_{\max})$.

Proof. We test both sides of $v_t = \Delta v - v + u$ by $-\Delta v_t$ and integrate over $x \in \Omega$ to find that

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\int_\Omega|\Delta v|^2 + \int_\Omega|\nabla v_t|^2 &= -\int_\Omega\nabla v\cdot\nabla v_t + \int_\Omega\nabla u\cdot\nabla v_t\\ &\le \int_\Omega|\nabla v|^2 + \int_\Omega|\nabla u|^2 + \frac{1}{2}\int_\Omega|\nabla v_t|^2\end{aligned}$$

for all $t \in (0,T)$. We can obtain (3.12) by an elementary computation. □

With the help of the following lemma, we can deal with Lemma 3.4 better.

Lemma 3.5. *Let (u,v,w) be the solution of (1.1). Then we have*

$$\frac{d}{dt}\int_\Omega|\nabla v|^2 + \int_\Omega|\Delta v|^2 + 2\int_\Omega|\nabla v|^2 \le \int_\Omega u^2 \tag{3.13}$$

for all $t \in (0,T)$, where $T \in (0,T_{\max})$.

Proof. We multiply the second equation in (1.1) by $-\Delta v$ and integrate by parts to see, using Young's inequality, that

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\int_\Omega|\nabla v|^2 &= -\int_\Omega|\Delta v|^2 - \int_\Omega|\nabla v|^2 + \int_\Omega\nabla u\cdot\nabla v\\ &= -\int_\Omega|\Delta v|^2 - \int_\Omega|\nabla v|^2 - \int_\Omega u\Delta v\\ &\le -\frac{1}{2}\int_\Omega|\Delta v|^2 - \int_\Omega|\nabla v|^2 + \frac{1}{2}\int_\Omega u^2\end{aligned}$$

for all $t \in (0,T)$, as claimed. □

Lemma 3.6. *Let $n = 3$, $T \in (0,T_{\max})$, $\chi > 0$, $\xi > 0$ and $\mu > 0$, and assume (1.2) holds, then the solution of (1.1) satisfies*

$$\begin{aligned}&\frac{d}{dt}\left(\kappa_1\int_\Omega u^2 + \frac{5}{2}\int_\Omega|\nabla v|^4 + \frac{1}{2}\int_\Omega|\Delta v|^2 + \int_\Omega|\nabla v|^2 + \int_\Omega u|\nabla v|^2\right)\\ &\quad+\int_\Omega|\nabla u|^2 + 10\int_\Omega|\nabla v|^4 + \int_\Omega\left|\nabla|\nabla v|^2\right|^2 + \int_\Omega|\Delta v|^2\\ &\quad+\int_\Omega|\nabla v|^2 + \int_\Omega u|\nabla v|^2 + \kappa_1\mu\int_\Omega u^3\\ &\le \kappa_2\int_\Omega u^2|\nabla v|^2 + \int_\Omega u^2 - 2\xi\int_\Omega uw\left|D^2v\right|^2 + 5\int_{\partial\Omega}|\nabla v|^2\frac{\partial|\nabla v|^2}{\partial\nu}\\ &\quad+(\mu-1)\int_\Omega u|\nabla v|^2 + \int_{\partial\Omega}u\frac{\partial|\nabla v|^2}{\partial\nu} + \xi\int_{\partial\Omega}uw\frac{\partial|\nabla v|^2}{\partial\nu} - 2\int_\Omega u\left|D^2v\right|^2 + C_5\end{aligned} \tag{3.14}$$

for all $t \in (0,T)$, where $\kappa_1 := \frac{9}{2} + \xi^2\|w_0\|^2_{L^\infty(\Omega)}$, $\kappa_2 := \left(\frac{11}{2} + \xi^2\|w_0\|^2_{L^\infty(\Omega)}\right)\chi^2 + \frac{37}{2} + 4\xi^2\|w_0\|^2_{L^\infty(\Omega)} - \mu$ and $C_5 := \kappa_1 C_4$ independent of t.

Proof. We can cancel some integral terms via an appropriate linear combination of the inequalities gained in (3.1), (3.7), (3.9), (3.12) and (3.13), then we can easily derive (3.14). □

Lemma 3.7. *Let $n = 3$, $T \in (0, T_{\max})$, $\chi > 0$, $\xi > 0$ and $\mu > 0$. Assume that the initial data (u_0, v_0, w_0) satisfies (1.2) and the positive parameters χ, ξ and μ fulfill (1.6). Then there exists $C > 0$ such that the solution of (1.1) satisfies*

$$\int_\Omega u^2 + \int_\Omega v^2 + \int_\Omega |\nabla v|^4 + \int_\Omega |\Delta v|^2 \le C \quad \text{for all} \quad t \in (0, T). \tag{3.15}$$

Proof. Writing

$$y_1(t) := \kappa_1 \int_\Omega u^2 + \frac{5}{2}\int_\Omega |\nabla v|^4 + \frac{1}{2}\int_\Omega |\Delta v|^2 + \int_\Omega |\nabla v|^2 + \int_\Omega u|\nabla v|^2 \quad \text{for all} \quad t \in (0, T) \tag{3.16}$$

and invoking Lemma 3.6, we see that $y_1(t)$ satisfies

$$y_1'(t) + y_1(t) + h(t) \le z(t) \quad \text{for all} \quad t \in (0, T) \tag{3.17}$$

where

$$h(t) := \int_\Omega |\nabla u|^2 + \frac{15}{2}\int_\Omega |\nabla v|^4 + \int_\Omega \left|\nabla|\nabla v|^2\right|^2 + \frac{1}{2}\int_\Omega |\Delta v|^2 + \kappa_1\mu \int_\Omega u^3 \tag{3.18}$$

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

$$\begin{aligned} z(t) := {} & \kappa_2 \int_\Omega u^2|\nabla v|^2 + (\kappa_1 + 1)\int_\Omega u^2 - 2\xi \int_\Omega uw\left|D^2 v\right|^2 + 5\int_{\partial\Omega} |\nabla v|^2 \frac{\partial|\nabla v|^2}{\partial\nu} \\ & + (\mu - 1)\int_\Omega u|\nabla v|^2 + \int_{\partial\Omega} u\frac{\partial|\nabla v|^2}{\partial\nu} + \xi\int_{\partial\Omega} uw\frac{\partial|\nabla v|^2}{\partial\nu} \\ & - 2\int_\Omega u\left|D^2 v\right|^2 + C_5 \end{aligned} \tag{3.19}$$

for all $t \in (0, T)$. Now we will estimate the integrals on the right of (3.19) appropriately. By Young's inequality we can estimate

$$(\mu - 1)\int_\Omega u|\nabla v|^2 \le \frac{(\mu - 1)^2}{4}\int_\Omega u^2 + \int_\Omega |\nabla v|^4 \tag{3.20}$$

for all $t \in (0, T)$. Furthermore, we can utilize the boundary integral estimates in [63] to find a constant $c_1 > 0$ such that

$$\frac{\partial|\nabla v|^2}{\partial\nu} \le c_1|\nabla v|^2 \quad \text{on} \quad \partial\Omega \times (0, T),$$

this means that

$$\begin{aligned} & 5\int_{\partial\Omega} |\nabla v|^2\frac{\partial|\nabla v|^2}{\partial\nu} + \int_{\partial\Omega} u\frac{\partial|\nabla v|^2}{\partial\nu} + \xi\int_{\partial\Omega} uw\frac{\partial|\nabla v|^2}{\partial\nu} \\ & \le c_2\int_{\partial\Omega} u|\nabla v|^2 + c_2\int_{\partial\Omega} |\nabla v|^4 \end{aligned} \tag{3.21}$$

for all $t \in (0, T_{\max})$, where $c_2 := \max\left\{\left(1 + \xi\|w_0\|_{L^\infty(\Omega)}\right)c_1, 5c_1\right\}$. Apart from this, the boundary trace embedding $W^{r+\frac{1}{2},2}(\Omega) \hookrightarrow L^2(\partial\Omega)$ for $r > 0$ along with the embedding

$$W^{1,2}(\Omega) \hookrightarrow\hookrightarrow W^{\frac{1}{2},2}(\Omega) \hookrightarrow L^1(\Omega)$$

provides some $\eta > 0$ and $c_4(\eta) > 0$ fulfilling

$$\int_{\partial\Omega} \phi^2 \le \eta\int_\Omega |\nabla\phi|^2 + c_4(\eta)\left(\int_\Omega |\phi|\right)^2 \tag{3.22}$$

for any $\phi \in W^{1,2}(\Omega)$, inserting $\eta := \frac{1}{c_3}$ to (3.22) yields some constants $c_i > 0\,(i = 3, 4, 5)$ fulfilling

$$\begin{aligned}
&\int_{\partial\Omega} u\frac{\partial|\nabla v|^2}{\partial\nu} + 5\int_{\partial\Omega} |\nabla v|^2\frac{\partial|\nabla v|^2}{\partial\nu} + \xi\int_{\partial\Omega} uw\frac{\partial|\nabla v|^2}{\partial\nu}\\
&\le c_2\int_{\partial\Omega} u|\nabla v|^2 + c_2\int_{\partial\Omega}|\nabla v|^4 \le c_3\int_{\partial\Omega} u^2 + c_3\int_{\partial\Omega}|\nabla v|^4\\
&\le \int_\Omega |\nabla u|^2 + c_3c_4(\eta)\Big(\int_\Omega u\Big)^2 + \int_\Omega \big|\nabla|\nabla v|^2\big|^2 + c_3c_4(\eta)\Big(\int_\Omega |\nabla v|^2\Big)^2\\
&\le \int_\Omega |\nabla u|^2 + c_3c_4(\eta)\Big(\int_\Omega u\Big)^2 + \int_\Omega \big|\nabla|\nabla v|^2\big|^2 + c_5 \quad \text{for all} \quad t\in(0,T)
\end{aligned} \tag{3.23}$$

by Young's inequality and Lemma 2.1. Thereupon, (3.17)–(3.20) and (3.23) readily assert that

$$y_1'(t) + y_1(t) \le \Big(\frac{(\mu_1-1)^2}{2} + \kappa_1 + c_3c_4(\eta) + 1\Big)\int_\Omega u^2 - \kappa_1\mu\int_\Omega u^3 + c_6$$

for all $t \in (0, T)$, which proves (3.15) by once more using Young's inequality. □

Lemma 3.7 yields the following useful corollary which will be used in the proof of Lemma 3.8.

Corollary 3.1. *Let $n = 3$, $T \in (0, T_{\max})$, and assume that the initial data (u_0, v_0, w_0) satisfies (1.2) and the positive parameters χ, ξ and μ fulfill (1.6). Then there exists $C > 0$ independent of T such that the solution of (1.1) possesses the property*

$$\big|\big|v(\cdot,t)\big|\big|_{L^\infty(\Omega)} \le C \tag{3.24}$$

for all $t \in (0, T)$ and for any $4 \le q < \infty$ there exists $M_1(q) > 0$ such that the solution of (1.1) satisfies

$$\int_\Omega |\nabla v|^q \le M_1(q) \tag{3.25}$$

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

Proof. The estimates (3.24) and (3.25) immediately result from Lemma 2.1, the Sobolev embedding $W^{1,4}(\Omega) \hookrightarrow C^0(\overline{\Omega})$ and the standard parabolic regularity theory (see [17]). □

Lemma 3.8. *Let $n = 3$, $T \in (0, T_{\max})$, and assume $\chi > 0$, $\xi > 0$ and $\mu > 0$ satisfy (1.6), and suppose that the assumption (1.2) holds. Then for any $p > 2$ there exists $C = C(q) > 0$ independent of T such that the solution of (1.1) fulfills*

$$\|u(\cdot,t)\|_{L^p(\Omega)} \le C \ \text{ for all } \ t\in(0,T). \tag{3.26}$$

Proof. Multiplying the first equation in (1.1) by pu^{p-1} and integrating by parts, we find that

$$\begin{aligned}
\frac{1}{p}\frac{d}{dt}\int_\Omega u^p &= \int_\Omega u^{p-1}\Big(\Delta u - \chi\nabla\cdot(u\nabla v) - \xi\nabla\cdot(u\nabla w) + \mu u(1-u-w)\Big)\\
&\le -(p-1)\int_\Omega u^{p-2}|\nabla u|^2 + \chi(p-1)\int_\Omega u^{p-1}\nabla u\cdot\nabla v\\
&\quad - \frac{\xi(p-1)}{2p}\int_\Omega u^p\Delta w + \mu\int_\Omega u^p(1-u)\\
&\le -\frac{(p-1)}{2}\int_\Omega u^{p-2}|\nabla u|^2 + \frac{\chi^2(p-1)}{2}\int_\Omega u^p|\nabla v|^2 - \frac{\xi(p-1)}{2p}\int_\Omega u^p\Delta w\\
&\quad + \mu\int_\Omega u^p(1-u)\\
&\le -\frac{(p-1)}{2}\int_\Omega u^{p-2}|\nabla u|^2 + \frac{\chi^2(p-1)}{2}\int_\Omega u^p|\nabla v|^2\\
&\quad + \frac{\xi(p-1)}{2p}\big|\big|w_0\big|\big|_{L^\infty(\Omega)}\int_\Omega u^p v + \Big(\frac{\kappa_0\xi(p-1)}{2p} + \mu\Big)\int_\Omega u^p - \mu\int_\Omega u^{p+1}
\end{aligned} \tag{3.27}$$

for all $t \in (0, T)$. From Lemma 3.7, Hölder's inequality implies that there exists $C_4 > 0$ such that

$$\int_\Omega u^p|\nabla v|^2 \le \Big(\int_\Omega u^{2p}\Big)^{\frac12}\Big(\int_\Omega |\nabla v|^4\Big)^{\frac12} \le C_4\Big(\int_\Omega u^{2p}\Big)^{\frac12} \tag{3.28}$$

and

$$\int_\Omega u^p v \le \left(\int_\Omega u^{2p}\right)^{\frac{1}{2}} \left(\int_\Omega v^2\right)^{\frac{1}{2}} \le C_5\Big(\int_\Omega u^{2p}\Big)^{\frac{1}{2}}$$

for all $t \in (0, T)$. Moreover, an application of the Gagliardo–Nirenberg inequality (see Lemma 2.5) and the fact $(a+b)^r \le 2^r(a^r+b^r)$ for all $a, b \ge 0, r > 0$ provide some constants $C_6 > 0$ satisfying

$$\begin{aligned} C_6\left(\int_\Omega u^{2p}\right)^{\frac{1}{2}} &= C_6\|u^{\frac{p}{2}}\|^2_{L^4(\Omega)} \\ &\le C_6C_{GN}^2\left(\|\nabla u^{\frac{p}{2}}\|^{\lambda}_{L^2(\Omega)}\cdot\|u^{\frac{p}{2}}\|^{1-\lambda}_{L^{\frac{2}{p}}(\Omega)} + \|u^{\frac{p}{2}}\|_{L^{\frac{2}{p}}(\Omega)}\right)^2 \\ &\le 4C_6C_{GN}^2\left(\|\nabla u^{\frac{p}{2}}\|^{2\lambda}_{L^2(\Omega)} m^{p(1-\lambda)} + m^p\right) \end{aligned}$$

holds for some constants $C_{GN} > 0$, with $\lambda \in (0, 1)$ provided by

$$\lambda = \frac{\frac{3p}{2} - \frac{3}{4}}{1 - \frac{3}{2} + \frac{3p}{2}}.$$

In view of Lemma 2.1, Young's inequality yields $C_7 > 0$ fulfilling

$$\begin{aligned} C_6\left(\int_\Omega u^{2p}\right)^{\frac{1}{2}} &\le 4C_6C_{GN}^2\left(\Big(\|\nabla u^{\frac{p}{2}}\|^2_{L^2(\Omega)} + 1\Big)m^{p(1-\lambda)} + m^p\right) \\ &\le \frac{2}{p}\int_\Omega |\nabla u^{\frac{p}{2}}|^2 + C_7, \end{aligned}$$

where $C_6 := C_4 + C_5$. Clearly Young's inequality yields that u^p can be controlled by u^{p+1}. Consequently, $y_2(t) := \int_\Omega u^p dx$ satisfies

$$y_2'(t) + y_2(t) \le C_8 \quad \text{for all} \quad t \in (0, T)$$

with some $C_8 > 0$. Upon an ODE comparison argument, we can obtain (3.26). □

Corollary 3.2. *Let $n = 3$, $T \in (0, T_{\max})$, and assume that the initial data (u_0, v_0, w_0) satisfies (1.2) and the positive parameters χ, ξ and μ fulfill (1.6). Then there exists $C > 0$ independent of T such that the solution of (1.1) possesses the property*

$$\big|\big|v(\cdot, t)\big|\big|_{W^{1,\infty}(\Omega)} \le C \tag{3.29}$$

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

Proof. According to Lemma 3.8 and the standard parabolic regularity theory (see [17]), (3.29) immediately follows. □

As compared to the analysis of the classical Keller–Segel model, we cannot directly apply the well-known Moser–Alikakos iteration [64] to the first equation in (1.1) to gain the boundedness of $u(\cdot, t)$ in $L^\infty(\Omega)$ since $\nabla w(\cdot, t)$ might become unbounded in $L^\infty(\Omega)$. Moreover, we can apply the methods in [47] and Lemma 2.1 to obtain the assertion of (1.1).

Lemma 3.9. *Let $n = 3$, $T \in (0, T_{\max})$, and assume that the initial data (u_0, v_0, w_0) satisfies (1.2) and the positive parameters χ, ξ and μ fulfill (1.6). Then there exists $C > 0$ independent of T such that the solution of (1.1) satisfies*

$$\|u(\cdot, t)\|_{L^\infty(\Omega)} \le C \quad \textit{for all} \quad t \in (0, T). \tag{3.30}$$

Proof. We multiply the first equation in (1.1) by pu^{p-1} and integrate over Ω to obtain that

$$\begin{aligned}
\frac{1}{p}\frac{d}{dt}\int_\Omega u^p &= \int_\Omega u^{p-1}\Big(\Delta u - \chi\nabla\cdot(u\nabla v) - \xi\nabla\cdot(u\nabla w) + \mu u(1-u-w)\Big)\\
&\le -\frac{(p-1)}{2}\int_\Omega u^{p-2}|\nabla u|^2 + \frac{\chi^2(p-1)}{2}\int_\Omega u^p|\nabla v|^2\\
&\quad - \frac{\xi(p-1)}{p}\int_\Omega u^p\Delta w + \mu\int_\Omega u^p - \mu\int_\Omega u^{p+1}\\
&\le -\frac{(p-1)}{2}\int_\Omega u^{p-2}|\nabla u|^2 + \frac{\chi^2(p-1)}{2}\int_\Omega u^p|\nabla v|^2\\
&\quad + \frac{\xi(p-1)}{p}\|w_0\|_{L^\infty(\Omega)}\int_\Omega u^p v + \frac{\xi(p-1)\kappa_0}{p}\int_\Omega u^p + \mu\int_\Omega u^p\\
&\quad - \mu\int_\Omega u^{p+1}
\end{aligned}$$

for any $p > 1$ and all $t \in (0,T)$. This, along with Corollary 3.2 and Lemma 2.5 leads to

$$\frac{d}{dt}\int_\Omega u^p + \int_\Omega u^p + \int_\Omega |\nabla u^{\frac{p}{2}}|^2 \le c_1p^2\int_\Omega u^p \tag{3.31}$$

for any $p \ge 2$ and all $t \in (0,T)$, where $c_1 > 0$. We can use the Gagliardo–Nirenberg inequality (see Lemma 2.5) to obtain that

$$\begin{aligned}
c_1p^2\int_\Omega u^p &= c_1p^2\|u^{\frac{p}{2}}\|^2_{L^2(\Omega)}\\
&\le c_2p^2\|\nabla u^{\frac{p}{2}}\|^{\frac{6}{5}}_{L^2(\Omega)}\cdot\|u^{\frac{p}{2}}\|^{\frac{4}{5}}_{L^1(\Omega)} + c_2p^2\|u^{\frac{p}{2}}\|^2_{L^1(\Omega)},
\end{aligned}\tag{3.32}$$

which combined with the Young inequality readily yields that

$$c_1p^2\int_\Omega u^p \le \int_\Omega |\nabla u^{\frac{p}{2}}|^2 + c_3p^2\|u^{\frac{p}{2}}\|^2_{L^1(\Omega)} + c_3p^5\|u^{\frac{p}{2}}\|^2_{L^1(\Omega)}. \tag{3.33}$$

We collect (3.31) and (3.33) to get

$$\begin{aligned}
\frac{d}{dt}\int_\Omega u^p + \int_\Omega u^p &\le c_4p^5\|u^{\frac{p}{2}}\|^2_{L^1(\Omega)}\\
&\le c_4p^5(\max\{1, \|u^{\frac{p}{2}}\|^2_{L^1(\Omega)}\})^2.
\end{aligned}\tag{3.34}$$

Now we let $p_i := 2^i$ and $M_i(T) := \max\{1, \sup_{t\in(0,T)}\int_\Omega u^{p_i}(\cdot,t)\}$ for $T \in (0, T_{\max})$ with $i = 1, 2, \ldots$, which combined with (3.34) implies that for any $t \in (0,T)$

$$\frac{d}{dt}\int_\Omega u^{p_i} + \int_\Omega u^{p_i} \le c_4p_i^5(\max\{1, \|u^{\frac{p_i}{2}}\|^2_{L^1(\Omega)}\})^2 \le c_4p_i^5M^2_{i-1}(T), \tag{3.35}$$

where all above positive constants c_i ($i = 1, 2, 3, 4$) are independent of T as well as of $p \ge 2$. Upon a comparison argument, we can find $b > 1$ independent of i such that

$$M_i(T) \le \max\{b^iM^2_{i-1}(T), |\Omega|\|u_0\|^{p_i}_{L^\infty(\Omega)}\}. \tag{3.36}$$

Next we will divide the proof into two cases.

Case 1. For infinitely many $i \ge 1$, if $b^iM^2_{i-1}(T) \le \|u_0\|^{p_i}_{L^\infty(\Omega)}$, then we derive that $\sup_{t\in(0,T)}\|u(\cdot,t)\|_{L^\infty(\Omega)} \le \|u_0\|_{L^\infty(\Omega)}$ in a quite similar way to Lemma 4.1 in [46].

Case 2. If $b^iM^2_{i-1}(T) > \|u_0\|^{p_i}_{L^\infty(\Omega)}$ for all sufficiently large i, then

$$M_i(T) \le b^iM^2_{i-1}(T) \tag{3.37}$$

for all $i \ge 1$ upon enlarging b if necessary. Then

$$\ln M_i(T) \le i\ln b + 2\ln M_{i-1}(T) \ \text{ for all } \ i \ge 1,$$

which implies that

$$\ln M_i(T) \le (i+2)\ln b + 2^i(\ln M_0 + 2\ln b)$$

and thus

$$M_i(T) \leq b^{i+2+2^{i+1}} M_0^{2^i}. \tag{3.38}$$

It follows from the above cases that (3.30) holds as $T \to T_{\max}$, where $C = b^2 \max\{1 + |\Omega|, \|u_0\|_{L^1(\Omega)}\}$. □

Proof of Theorem 1.1. The statement of global classical solvability and boundedness is a straightforward consequence of Lemmas 2.1 and 3.9 (see [41,46]). □

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