A chemotaxis-haptotaxis model: the roles of nonlinear diffusion and logistic source

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Abstract

This paper deals with a chemotaxis-haptotaxis model of cancer invasion of tissue (extracellular matrix, ECM). The model consists of a parabolic chemotaxis-haptotaxis PDE describing the evolution of cancer cell density, a parabolic PDE governing the evolution of matrix degrading enzyme concentration, and an ordinary differential equation reflecting the degradation of ECM. Following a recent approach proposed by Szymańska et al. (*Math. Mod. Meth. Appl. Sci. 19, 2009*), we assume that the migration of cancer cells through ECM is more like movement in a porous medium. Accordingly, we consider the self-diffusion coefficient $D(u)$ of cancer cells to be a nonlinear function generalizing the prototype $D(u) = (u+1)^{m-1}$ for some $m \geq 1$. Under the assumption that either $n \leq 8$ and $m > (2n^2 + 4n - 4)/(n^2 + 4n)$, or $n \geq 9$ and $m > (2n^2 + 3n + 2 - \sqrt{8n(n+1)})/(n^2 + 2n)$ (where n denotes the space dimension), and in presence of logistic dampening of cancer cell densities, the global existence of a unique classical solution to the model is proved by developing some L^p-estimate techniques that appear to be new in the context of chemotaxis-haptotaxis systems.

Key words: chemotaxis, haptotaxis, nonlinear diffusion, logistic source, cancer invasion model, global existence
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1 Introduction

Cancer invasion consists of several important steps involving different biological mechanisms, and a variety of mathematical models has been developed for various aspects of cancer invasion (see [2, 6, 7, 14], for instance). Gatenby and Gawlinski ([15]) proposed a reaction-diffusion population competition model to study how the tumor invades the surrounding normal tissue, the so-called extracellular matrix (ECM). They suggested that tumor cells create an acidic environment toxic to normal tissue, and that high acidity leads to the death of the normal tissue, which provides space for tumor cells to proliferate and invade into the surrounding tissue. Perumpanani and Byrne ([34]) experimentally found that ECM heterogeneity affects invasion. They established a model under the assumptions that ECM is degraded by proteases; in addition to random diffusion, the migration of tumor cells is biased towards a gradient of the non-diffusible ECM, which is referred to as *haptotaxis*; the protease production is proportional to the product of the tumor cell density and the collagen gel concentration. Chaplain and Anderson ([5]) also proposed a haptotaxis model of cancer invasion which is slightly different from the model in [34]. They assume that ECM is degraded by matrix degrading enzymes (MDEs) produced by cancer cells; in addition to random diffusion, the movement of tumor cells is directed by haptotaxis. Chaplain and Lolas ([7]) further suggested that, in addition to random diffusion and haptotactic movement, the migration of cancer cells is biased towards a gradient of the diffusible MDEs, a process known as *chemotaxis*. Besides, the proliferation of tumor cells and the remodeling of ECM are incorporated in the model of Chaplain and Lolas. Recently, Gerisch and Chaplain ([16]) proposed a non-local model which accounts for the important role of cell-cell adhesion in the tumor invasion process. Very recently, Chaplain et al. ([6]) adopted the approach in [16] and derived a PDE model of cancer invasion with two non-local integral terms for both cell-cell and cell-matrix adhesion. We mention that Szymańska *et al.* ([37]) developed another non-local model which studies the role of non-local kinetic terms modeling competition for space and degradation, and that Lachowicz ([25, 26]) constructed some microscopic models for tumor invasion and established some connections of his microscopic model in [26] to the macroscopic model in [5].

From a mathematical point of view, most of the frequently discussed models of cancer invasion belong to one of the categories of haptotaxis-only models (such as those in [5, 34]), chemotaxis-haptotaxis models (see [7], for instance), and non-local PDE models ([6, 16, 37]. Walker and Webb ([45]) examined the global existence of a unique solution to the haptotaxis-only models in [5]; Marciniak-Czochra and Ptashnyk ([30]) proved the uniform boundedness of solutions to the haptotaxis-only model from [5]. Liţcanu and Morales-Rodrigo ([29]) studied the asymptotic behavior of solutions to the haptotaxis-only model in [34] by refining their previous techniques developed in [28]. Tao and Wang ([41]) and Tao ([39]) studied the global existence of solutions to the chemotaxis-haptotaxis model from [7] for large logistic growth rate of cells in dimension 3 and for any positive logistic growth rate in dimension 2, respectively; Tao and Wang ([40]) also proved the global existence and boundedness of solutions to a simplified version of the chemotaxis-haptotaxis model proposed in [7]. Szymańska et al. ([37]) and Chaplain et al. ([6]) examined the

global existence of solutions to their respective non-local models. Here we should note that the question of global existence for the chemotaxis-haptotaxis model suggested in [7] remains open for small positive logistic growth rate of cells in dimension 3. As far as we know, there are only few results on the asymptotic behavior of solutions to the chemotaxis-haptotaxis model in [7].

Except for that in [15], all models mentioned above considered the cancer cell random motility, denoted by D, to be a constant, which leads to linear isotropic diffusion. As emphasized in the discussion section in [37], however, from a physical point of view migration of the cancer cells through the ECM should rather be regarded like movement in a porous medium, and so we are led to considering the cell motility D a *nonlinear* function of the cancer cell density, $D \equiv D(u)$, where we have in mind the specific choice $D(u) = D_0(u + \varepsilon_0)^{m-1}, m \geq 1, \varepsilon_0 > 0, D_0 > 0$. Here the assumption that ε_0 be positive excludes the degeneracy of the cell diffusion, reflecting that cancer cells at small densities will still undergo diffusion. This paper will focus on studying the relationship between the exponent m and the global existence of solutions to an accordingly modified variant of the Chaplain-Lolas chemotaxis-haptotaxis model of cancer invasion ([7]) with porous medium-type diffusion of cells.

To be more precise, following [7] we consider a coupled system of differential equations for the three unknown functions representing the cancer cell density $u = u(x,t)$, the MDE concentration $v = v(x,t)$ and the ECM density $w = w(x,t)$, where the evolution of the cell density is governed by

$$u_t = \overbrace{\nabla \cdot (D(u)\nabla u)}^{\text{porous medium diffusion}} - \overbrace{\chi \nabla \cdot (u\nabla v)}^{\text{chemotaxis}} - \overbrace{\xi \nabla \cdot (u\nabla w)}^{\text{haptotaxis}} + \overbrace{uf(u,w)}^{\text{proliferation}} . \qquad (1.1)$$

Here, $D(u)$ describes the density-dependent motility of cancer cells through the ECM, χ and ξ measure the chemotactic and haptotactic sensitivities, respectively, and $f(u,w)$ denotes the proliferation rate of the cells, which will be assumed to be of logistic type (cf. (1.6) below).

The MDE concentration is supposed to be influenced by diffusion, degradation, and production by cancer cells. Hence, the equation for the MDE concentration reads ([7])

$$v_t = \overbrace{D_v \Delta v}^{\text{diffusion}} + \overbrace{\alpha u}^{\text{production}} - \overbrace{\beta v}^{\text{decay}} , \qquad (1.2)$$

with positive constants D_v, α and β.

Recalling that the ECM can be regarded as static in the sense that it does not diffuse, we may assume that its evolution is governed only by degradation through MDEs upon contact. Following [5, 34, 41, 45], we neglect any remodeling of the ECM and thus obtain the equation

$$w_t = - \overbrace{\eta v w}^{\text{degradation}} , \qquad (1.3)$$

for the ECM, with some positive degradation rate η.

Since the analysis in this paper will not specifically depend on the positive rate constants

except m, χ, ξ, and μ in (1.1)-(1.3), for notational simplicity we may and will assume throughout that $D_v = \alpha = \beta = \eta = 1$. Thus, closing the system by convenient boundary conditions we shall subsequently consider the problem

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

in a bounded domain $\Omega \subset \mathbb{R}^n$, $n \geq 1$, with smooth boundary, where ∂_ν denotes differentiation with respect to the outward normal on $\partial\Omega$. The functions u_0, v_0 and w_0 are assumed to be nonnegative and to satisfy some smoothness assumptions to be specified below, and for simplicity we shall require throughout that

$$
\partial_\nu w_0 = 0 \qquad \text{for all } x \in \partial\Omega,
\tag{1.5}
$$

which, for instance, will clearly be satisfied if the initial ECM distribution w_0 has compact support in Ω. The diffusivity D and the source term f are supposed to generalize the prototypes

$$
D(u) = (u+1)^{m-1} \qquad \text{and} \qquad f(u,w) = \mu(1-u-w), \qquad u \geq 0, \ w \geq 0.
\tag{1.6}
$$

More precisely, we shall require that

$$
D \in C^2([0,\infty)) \qquad \text{and} \qquad f \in C^1([0,\infty) \times [0,\infty)),
\tag{1.7}
$$

that

$$
D(0) > 0,
\tag{1.8}
$$

and that there exist $m \geq 1, \delta > 0, \kappa > 0$ and $\mu > 0$ such that

$$
D(u) \geq \delta u^{m-1} \qquad \text{for all } u \geq 0
\tag{1.9}
$$

and

$$
f(u,w) \leq \kappa - \mu u \qquad \text{for all } u \geq 0 \text{ and } w \geq 0.
\tag{1.10}
$$

Under these assumptions, the main results of this paper can be stated as follows.

Theorem 1.1 *Let $\chi > 0$ and $\xi \geq 0$, and suppose that D and f satisfy (1.7), (1.8) and (1.10) with some positive constants κ and μ. Moreover, assume that D satisfies (1.9) with some $m \geq 1$ fulfilling*

$$
m > \begin{cases}
\frac{2n^2+4n-4}{n(n+4)} & \text{if } n \leq 8, \\
\frac{2n^2+3n+2-\sqrt{8n(n+1)}}{n(n+2)} & \text{if } n \geq 9,
\end{cases}
\tag{1.11}
$$

and some $\delta > 0$. Then for any triple $(u_0, v_0, w_0) \in W^{1,\infty}(\Omega) \times W^{1,\infty}(\Omega) \times W^{2,\infty}(\Omega)$ of nonnegative functions fulfilling (1.5), the problem (1.4) has at least one nonnegative classical solution which is global in time.

Unfortunately we have to leave open here the question whether the global solutions of (1.4) constructed above are bounded. Although Theorem 1.1 rules out blow-up in finite time, we suspect that uniform-in-time boundedness cannot be expected in this case, because the absence of diffusion in the third equation in (1.4) entails that ∇w should have a memory of ∇v over a historical time interval $[0, t]$ (see (2.9)).

The three-component chemotaxis-haptotaxis model (1.4) can be regarded as an extension of the celebrated two-component chemotaxis model proposed in 1970 by Keller and Segel [22]. This Keller-Segel model has greatly been extended and studied in the last three decades, and one striking feature of Keller-Segel type models is the possibility of admitting unbounded solutions under various sets of assumptions on model ingredients such as self-diffusivities, cross-diffusivities, the space dimension, or also the total mass of cells (see [17, 31, 21, 3, 8, 12, 48, 36, 35], for instance). A 'chemotactic collapse' of this type is frequently interpreted as predicting a spatial aggregation of cells which indeed occurs in some biologically relevant phenomena such as the aggregation of certain types of bacteria ([18, 22]). However, a number of different biological processes occurs after an initial aggregation mechanism ([18, 19, 22]). From such considerations, it seems necessary to develop some chemotaxis models which mathematically exclude blow-up. Some recent studies show that nonlinear chemotactic sensitivity functions ([4, 8, 19, 20, 50]), nonlinear (self-)diffusion ([9, 23, 24, 38]), or also logistic dampening ([33, 47, 44, 39, 43, 46]) may prevent blow-up of solutions.

The second goal of the present paper is to investigate in how far the interplay between effects of the latter two types can rule out finite-time blow-up. To this end, we observe that setting $\xi = 0$ in (1.4) leads to a discoupled system one part of which is the two-component parabolic-parabolic chemotaxis system with porous medium-type diffusion given by

$$
\begin{cases}
u_t = \nabla \cdot (D(u)\nabla u) - \chi \nabla \cdot (u\nabla v) + ug(u), & x \in \Omega, \ t > 0, \\
v_t = \Delta v - v + u, & x \in \Omega, \ t > 0, \\
\partial_\nu u = \partial_\nu v = 0, & x \in \partial\Omega, \ t > 0, \\
u(x, 0) = u_0(x), \quad v(x, 0) = v_0(x), & x \in \Omega,
\end{cases}
\tag{1.12}
$$

where in accordance with our assumptions on f, $g := f(\cdot, 0)$ belongs to $C^1([0, \infty)$ and satisfies

$$
g(u) \leq \kappa - \mu u \qquad \text{for all } u \geq 0
\tag{1.13}
$$

with some $\kappa > 0$ and $\mu > 0$.

It is known that in the linear diffusion case $D \equiv 1$, all solutions of (1.12) are global in time and bounded when either $n \geq 3$ and $\mu > 0$ is sufficiently large ([47]), or $n = 2$ and $\mu > 0$ is arbitrary ([33]). Similar conclusions apply to a simplified variant of (1.12) obtained on replacing the second PDE by the elliptic equation $0 = \Delta v - v + u$ ([44]). By weakening the solution concept, it is possible to construct certain global-in-time generalized solutions under the relaxed requirement that merely $g(u) \leq \kappa - u^\alpha$ holds for all $u \geq 0$ and some $\kappa > 0$ and $\alpha > \frac{n-1}{n}$ ([46]). In the recent work [32], such a generalized logistic growth term has been considered along with $D \equiv 1$ and the second equation in (1.12) replaced with

$v_t = \delta v - v + u^\beta$ with some $\beta \le 1$.

Under the assumption $g(u) \equiv 0$, Sugiyama [38] considered (1.12), inter alia, in the entire space $\Omega = \mathbb{R}^n$, $n \ge 1$, and proved global existence of (weak) solutions whenever $m \ge 2$, provided that the initial data satisfy some mild smoothness and decay hypotheses. The corresponding problem (1.12) in bounded domains $\Omega \subset \mathbb{R}^n$, $n \ge 2$ with $g \equiv 0$ was taken up by Kowalczyk and Szymańska in [24], where it was shown that in this case the weaker condition $m > 3 - \frac{4}{n}$ is already sufficient to ensure global existence of solutions for all sufficiently smooth initial data. We should point out that the two works [38, 24] at the same time provide uniform-in-time boundedness of solutions in (1.12), and that in this respect the condition $m > 2 - \frac{2}{n}$ found in the recent work [42] is optimal, because in [49] it has been shown that if $D(u) = (u+1)^{2-\frac{2}{n}-\varepsilon}$ for some $\varepsilon > 0$, $g \equiv 0$ and Ω is a ball, then (1.12) possesses some unbounded solutions.

In respect of global solvability for the chemotaxis-growth system (1.12), taking $\xi = 0$ in Theorem 1.1 we immediately obtain the following.

Corollary 1.2 *Let $\chi > 0$, and let $D \in C^2([0, \infty))$ satisfy (1.8) and (1.9) with some $\delta > 0$ and $m \ge 1$ such that (1.11) holds. Moreover, assume that $g \in C^1([0, \infty))$ fulfills (1.13) with positive constants κ and μ. Then for all nonnegative $u_0 \in W^{1,\infty}(\Omega)$ and $v_0 \in W^{1,\infty}(\Omega)$, the problem (1.12) has at least one global classical solution (u, v) for which both u and v are nonnegative in $\Omega \times (0, \infty)$.*

Observe that in the physically relevant space dimension $n = 3$, Theorem 1.1 and Corollary 1.2 assert global existence in both (1.4) and (1.12) whenever

$$m > \frac{26}{21}.$$

Let us finally mention that at the cost of some additional technical expense, all of our results can be carried over also the degenerate borderline case

$$D(u) = u^{m-1}, \qquad u \ge 0, \tag{1.14}$$

with $m > 1$ satisfying (1.11), in which the self-diffusion term in the first equation in (1.4) is precisely of porous medium-type. Indeed, since in all our estimates to be given in Section 3 below the dependence on D is only measured through m and δ in (1.9), performing the standard approximation of $D(u) = u^{m-1}$ by $D_\varepsilon(u) = (u + \varepsilon)^{m-1}$ we can derive uniform estimates for the corresponding approximate solutions $(u_\varepsilon, v_\varepsilon, w_\varepsilon)$ in $L^\infty(\Omega \times (0, T))$ for each fixed $T > 0$. These can be used to derive compactness properties which allow for taking $\varepsilon \to 0$ and end up with a nonnegative triple (u, v, w) which solves (1.4) in the natural weak sense. In order to keep the presentation as transparent as possible, we refrain from giving details on this here, but rather refer to [24, 38] for a similar reasoning.

2 Local existence

We shall use a straightforward fixed point argument to prove local existence of solutions to the system (1.4), as well as a standard extensibility criterion. Since both v and w enter the first PDE in (1.4) through their derivatives, even up to order two, we cannot expect such a criterion to involve zero-order norms, such as $\|\cdot\|_{L^\infty(\Omega)}$, of these compenents. It turns out here, however, that as in the case of pure chemotaxis systems (cf. [20], for instance) no second-order derivatives of v need to be controlled in order to extend a solution, and that the same is true for w.

Lemma 2.1 *Let $\chi > 0, \xi \geq 0$, let D and f satisfy (1.7) and (1.8), and suppose that $u_0 \in W^{1,\infty}(\Omega)$, $v_0 \in W^{1,\infty}(\Omega)$ and $w_0 \in W^{2,\infty}(\Omega)$ are nonnegative and such that (1.5) holds. Then there exist $T_{max} \in (0, \infty]$ and a triple (u, v, w) of functions from $C^0(\bar\Omega \times [0, T_{max})) \cap C^{2,1}(\Omega \times (0, T_{max}))$ solving (1.4) classically in $\Omega \times (0, T_{max})$. These functions satisfy the inequalities*

$$u \geq 0, \qquad v \geq 0 \qquad and \qquad 0 \leq w \leq \|w_0\|_{L^\infty(\Omega)} \qquad in \ \Omega \times (0, T_{max}), \qquad (2.1)$$

and moreover we have the following dichotomy:

$$Either \ T_{max} = \infty, \qquad or \ \limsup_{t \nearrow T_{max}} \Big(\|u(t)\|_{L^\infty(\Omega)} + \|v(t)\|_{W^{1,\infty}(\Omega)} + \|w(t)\|_{W^{1,\infty}(\Omega)} \Big) = \infty.$$
$$(2.2)$$

PROOF.   With $T > 0$ small to be fixed below, in the space $X := L^\infty(\Omega \times (0, T))$ we consider the closed bounded convex subset

$$S := \Big\{ \overline{u} \in X \ \Big| \ 0 \leq \overline{u} \leq M + 1 \text{ a.e. in } \Omega \times (0, T) \Big\}$$

with $M := \|u_0\|_{L^\infty(\Omega)}$. For $\overline{u} \in S$, we let $F\overline{u} \equiv u$ denote the solution of

$$\begin{cases} u_t = \nabla \cdot (\hat{D}(\overline{u})\nabla u) - \chi \nabla \cdot (u \nabla v) - \xi \nabla \cdot (u \nabla w) + u\hat{f}(u, w), & x \in \Omega, \ t > 0, \\ \partial_\nu u = 0, & x \in \partial\Omega, \ t > 0, \\ u(x, 0) = u_0(x), & x \in \Omega, \end{cases} \qquad (2.3)$$

where

$$\hat{D}(z) := \begin{cases} D(0) & \text{if } z < 0, \\ D(z) & \text{if } 0 \leq z \leq M + 1, \\ D(M + 1) & \text{if } z > M + 1, \end{cases} \qquad (2.4)$$

and

$$\hat{f}(z, w) := \begin{cases} f(0, w) & \text{if } z < 0, \\ f(z, w) & \text{if } 0 \leq z \leq M + 1, \\ f(M + 1, w) & \text{if } z > M + 1, \end{cases} \qquad (2.5)$$

and where v and w are the solutions of

$$\begin{cases} v_t = \Delta v - v + \hat{u}(x, t), & x \in \Omega, \ t > 0, \\ \partial_\nu v(x, t) = 0, & x \in \partial\Omega, \ t > 0, \\ v(x, 0) = v_0(x), & x \in \Omega, \end{cases} \qquad (2.6)$$

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and

$$\begin{cases} w_t = -vw, & x \in \Omega, \ t > 0, \\ w(x,0) = w_0(x), & x \in \Omega, \end{cases} \tag{2.7}$$

with

$$\hat{u}(x,t) := \begin{cases} \overline{u}(x,t) & \text{if } x \in \Omega \text{ and } t \in (0,T), \\ 0 & \text{if } x \in \Omega \text{ and } t \geq T. \end{cases} \tag{2.8}$$

Standard parabolic theory states that this decoupled system has globally defined weak solution triple u, v, w, and if we pick any $q > \frac{n+2}{2}$, then thanks to linear parabolic regularity results ([10]) we know that the a priori estimate

$$\|\nabla v\|_{L^q(\Omega \times (0,1))} \leq c_1$$

holds with some $c_1 > 0$ which, as all constants $c_2, c_3, \dots$ appearing below, is allowed to depend on $M = \|u_0\|_{L^\infty(\Omega)}, \|v_0\|_{W^{1,\infty}(\Omega)}$ and $\|w_0\|_{W^{1,\infty}(\Omega)}$ only. Since (2.7) is explicitly solved according to

$$w(x,t) = w_0(x) \cdot e^{\int_0^t v(x,s)ds}, \qquad x \in \Omega, \ t > 0, \tag{2.9}$$

from this we also gain that

$$\|\nabla w\|_{L^q(\Omega \times (0,1))} \leq c_2$$

is valid with some $c_2 > 0$. Therefore the PDE in (2.3) can be rewritten in the form

$$u_t = \nabla \cdot \left(\hat{D}(\overline{u})\nabla u + g(x,t)u \right) + \hat{f}(u), \qquad x \in \Omega, \ t > 0,$$

where $\|g\|_{L^q(\Omega \times (0,1))} \leq c_3$ for some $c_3 > 0$. Consequently, parabolic theory first provides a constant $c_4 > 0$ such that $\|u\|_{L^\infty(\Omega \times (0,1))} \leq c_4$, and then yields $c_5 > 0$ satisfying $\|u\|_{C^{\alpha,\frac{\alpha}{2}}(\overline{\Omega} \times [0,1])} \leq c_5$. (In fact, these statements are implicitly proved in [27, Theorem V.2.1] and in [27, Theorem V.1.1], respectively, but stated there only for the case of Dirichlet rather than Neumann boundary conditions.) In particular, this implies that $\|u(t)\|_{L^\infty(\Omega)} \leq \|u_0\|_{L^\infty(\Omega)} + c_5 t^{\frac{\alpha}{2}}$ for all $t \in (0,1)$, and hence proves that $\|u\|_{L^\infty(\Omega \times (0,T))} \leq M + 1$ if $T \in (0,1)$ was chosen small enough such that $c_5 T^{\frac{\alpha}{2}} \leq 1$. We conclude that for such T, F maps S into itself, and since a straightforward reasoning shows that F is continuous and $\overline{F(S)}$ is compact in X, the Schauder fixed point theorem ensures the existence of a fixed point $u \in S$ of F. Recalling (2.4), (2.5) and (2.8) and once again invoking parabolic regularity theory, we easily see that u, along with the corresponding solutions v and w of (2.6) and (2.7), indeed solves (1.4) classically in $\Omega \times (0,T)$. The property (2.2) now results upon a standard extendibility argument, because our above choice of T only depends on the norm of the initial data in $L^\infty(\Omega) \times W^{1,\infty}(\Omega) \times W^{1,\infty}(\Omega)$. Moreover, (2.1) is an immediate consequence of the parabolic comparison principle and the formula (2.9). $\qquad \square$

3 Proof of the main results

Throughout the sequel we let (u, v, w) denote the maximally extended classical solution of (1.4) obtained in Lemma 2.1. Our approach towards proving its global existence is based on a contradictory argument: Assuming that (u, v, w) be *not* global in time, from (2.2) we would know that either u or v must be unbounded in $\Omega \times (0, T_{max})$. In a series of steps we shall show that this does not occur.

3.1 Interpolation inequalities

The following lemma will be used in a testing procedure in Lemma 3.5 to estimate integrals involving high powers of the first component u in terms of a corresponding integral stemming from a diffusive term in (1.4), provided that u is a priori known to be bounded in some space $L^\infty((0, T_{max}); L^p(\Omega))$. The proof combines the inequalities of Young and Gagliardo-Nirenberg in a straightforward way.

Lemma 3.1 *Let $m \geq 1$. Assume that $T_{max} < \infty$, and that there exist $p \geq 1$ and $c > 0$ such that*

$$\int_\Omega u^p(t) \leq c \qquad \text{for all } t \in (0, T_{max}). \tag{3.1}$$

Then for each $\gamma \geq 1$ and any number $q \geq 1$ fulfilling

$$q \leq \frac{2p}{n} + m + \gamma - 1 \tag{3.2}$$

and

$$(n - 2)q \leq n(m + \gamma - 1), \tag{3.3}$$

one can pick $C > 0$ such that

$$\int_\Omega u^q(t) \leq C \cdot \left(\int_\Omega u^{m+\gamma-3}(t) |\nabla u(t)|^2 + 1 \right) \qquad \text{for all } t \in (0, T_{max}).$$

PROOF.   We may assume $q > p$. By (3.3), we have $\frac{2q}{m+\gamma-1} \leq \frac{2n}{(n-2)_+}$ and hence know that $W_2^1(\Omega)$ is continuously embedded into $L^{\frac{2q}{m+\gamma-1}}(\Omega)$. We can therefore apply the Gagliardo-Nirenberg inequality ([13]) to find $c_1 > 0$ such that

$$
\begin{aligned}
\int_\Omega u^q(t) &= \left\| u^{\frac{m+\gamma-1}{2}}(t) \right\|_{L^{\frac{2q}{m+\gamma-1}}(\Omega)}^{\frac{2q}{m+\gamma-1}} \\
&\leq c_1 \left\| \nabla u^{\frac{m+\gamma-1}{2}}(t) \right\|_{L^2(\Omega)}^{\frac{2q}{m+\gamma-1} \cdot a} \cdot \left\| u^{\frac{m+\gamma-1}{2}}(t) \right\|_{L^{\frac{2p}{m+\gamma-1}}(\Omega)}^{\frac{2q}{m+\gamma-1} \cdot (1-a)} \\
&\quad + c_1 \left\| u^{\frac{m+\gamma-1}{2}}(t) \right\|_{L^{\frac{2p}{m+\gamma-1}}(\Omega)}^{\frac{2q}{m+\gamma-1}} \qquad \text{for all } t \in (0, T_{max})
\end{aligned}
\tag{3.4}
$$

is valid with $a \in (0, 1]$ determined by

$$-\frac{n(m + \gamma - 1)}{2q} = \left(1 - \frac{n}{2} \right) a - \frac{n(m + \gamma - 1)}{2p}(1 - a),$$

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that is, with

$$a = \frac{\frac{n(m+\gamma-1)}{2} \cdot \left(\frac{1}{p} - \frac{1}{q}\right)}{1 - \frac{n}{2} + \frac{n(m+\gamma-1)}{2p}}.$$

Thus, from (3.4) and (3.1) we obtain

$$\int_\Omega u^q(t) \leq c_1 \cdot \|\nabla u^{\frac{m+\gamma-1}{2}}(t)\|_{L^2(\Omega)}^{\frac{2q}{m+\gamma-1} \cdot a} \cdot c^{\frac{q}{p}(1-a)} + c_1 \cdot c^{\frac{q}{p}} \qquad \text{for all } t \in (0, T_{max}). \qquad (3.5)$$

Since

$$\left(1 - \frac{n}{2} + \frac{n(m+\gamma-1)}{2p}\right) \cdot \frac{q}{m+\gamma-1} \cdot a \;=\; \frac{nq}{2p} - \frac{n}{2}$$

$$\leq\; \frac{n}{2} \cdot \left(\frac{2}{n} + \frac{m+\gamma-1}{p}\right) - \frac{n}{2}$$

$$=\; 1 - \frac{n}{2} + \frac{n(m+\gamma-1)}{2p}$$

due to (3.2), it follows that

$$b := \frac{2q}{m+\gamma-1} \cdot a \leq 2.$$

Therefore (3.5) easily yields

$$\int_\Omega u^q(t) \leq c_2 \|\nabla u^{\frac{m+\gamma-1}{2}}(t)\|_{L^2(\Omega)}^2 + c_2 \qquad \text{for all } t \in (0, T_{max})$$

with some $c_2 > 0$, where we have used Young's inequality with exponents $\frac{2}{b}$ and $\frac{2}{2-b}$ if $b < 2$. Now the identity

$$\|\nabla u^{\frac{m+\gamma-1}{2}}(t)\|_{L^2(\Omega)}^2 = \left(\frac{m+\gamma-1}{2}\right)^2 \int_\Omega u^{m+\gamma-3}(t)|\nabla u(t)|^2, \qquad t \in (0, T_{max}),$$

completes the proof. $\qquad\qquad\square$

The next lemma recalls a standard interpolation inequality frequently employed in the study of nonlinear parabolic equations (see [11], for instance), and indicates how it can be used to derive estimates for the third solution component w.

Lemma 3.2 *Suppose that $T_{max} < \infty$, and that for some $p \geq 2$ we have*

$$\|v(t)\|_{L^\infty((0,T_{max});W^{1,2}(\Omega))} \leq c \quad \text{for all } t \in (0, T_{max}) \qquad \text{and} \qquad \|v\|_{L^p((0,T_{max});W^{2,p}(\Omega))} \leq c \tag{3.6}$$

with a positive constant c. Then there exists $C > 0$ such that

$$\int_0^{T_{max}} \int_\Omega |\nabla v|^{\frac{(n+2)p}{n}} \leq C \tag{3.7}$$

and

$$\int_\Omega |\nabla w(t)|^{\frac{(n+2)p}{n}} \leq C \qquad \text{for all } t \in (0, T_{max}). \tag{3.8}$$

PROOF.   The estimate in (3.7) follows upon a standard embedding argument involving the Gagliardo-Nirenberg inequality: Indeed, using (3.6) we see that

$$\int_0^T \|\nabla v(t)\|_{L^{\frac{(n+2)p}{n}}(\Omega)}^{\frac{(n+2)p}{n}} dt \leq c_1 \int_0^T \|v(t)\|_{W^{2,p}(\Omega)}^p \cdot \|v(t)\|_{W^{1,2}(\Omega)}^{\frac{2p}{n}} dt \leq c_2$$

with certain constants $c_1 > 0$ and $c_2 > 0$.

In order to derive the claimed bound for ∇w, we note that the ODE $w_t = -vw$ can be solved to yield the explicit representation

$$w(x,t) = w_0(x) \cdot e^{-\int_0^t v(x,s)ds}, \qquad x \in \Omega, \ t \in (0, T_{max}).$$

Therefore,

$$\nabla w(x,t) = e^{-\int_0^t v(x,s)ds} \cdot \left\{ \nabla w_0(x) - w_0(x) \cdot \int_0^t \nabla v(x,s)ds \right\} \qquad \text{for all } x \in \Omega \text{ and } t \in (0, T_{max}).$$

Now using (3.7), this easily proves (3.8) upon an integration over $x \in \Omega$.   □

3.2   Elementary preparations for a bootstrap argument

The following lemma provides some elementary material that will be essential to our bootstrap procedure. It essentially makes use of our overall assumption that m satisfy (1.11).

Lemma 3.3 *Suppose that $m \geq 1$ satisfies (1.11), and let*

$$\varphi_1(x) := \frac{(m-1) \cdot \left[(n+2)x + 2\right] + \frac{(n+2)x(x+1)}{n} - 2x}{n}, \qquad x \in \mathbb{R}.$$

Moreover, set

$$x_0 := \begin{cases} 1 & \text{if } n \leq 3, \\ \dfrac{n^2 - n - 2}{n+2} & \text{if } n \geq 4, \end{cases}$$

and

$$\varphi_2(x) := \begin{cases} \dfrac{(m-1) \cdot \left[(n^2 + n - 2)x + n - 2\right]}{n^2 - n - 2 - (n+2)x} & \text{if } x \in [1, x_0), \\ +\infty & \text{if } x \geq x_0, \end{cases} \qquad (3.9)$$

and finally let

$$\phi(x) := \min\{\varphi_1(x), \varphi_2(x)\}, \qquad x \geq 1. \qquad (3.10)$$

Then

$$\phi(x) > x \qquad \text{for all } x \in [1, +\infty). \qquad (3.11)$$

PROOF.   We define

$$\psi_1(x) := \frac{n^2}{n+2} \cdot (\varphi_1(x) - x), \qquad x \in \mathbb{R},$$

and claim that thanks to (1.11) we have

$$\psi_1(x) > 0 \qquad \text{for all } x \geq 1. \tag{3.12}$$

To verify this, we rewrite ψ_1 according to

$$\psi_1(x) = x^2 + \left[(m-2)n + 1\right] \cdot x + \frac{2(m-1)n}{n+2}, \qquad x \in \mathbb{R},$$

and compute

$$
\begin{aligned}
\psi_1(1) &= 1 + (m-2)n + 1 + \frac{2(m-1)n}{n+2} \\
&= (m-1) \cdot \frac{n^2 + 4n}{n+2} + 2 - n. \tag{3.13}
\end{aligned}
$$

Now if $n \leq 8$ then (1.11) says that

$$m - 1 > \frac{n^2 - 4}{n^2 + 4n}, \tag{3.14}$$

and hence we obtain from (3.13) that

$$\psi_1(1) > \frac{n^2 - 4}{n+2} + 2 - n = 0.$$

Since moreover

$$\psi_1'(x) = 2x + (m-2)n + 1, \qquad x \in \mathbb{R},$$

and accordingly

$$
\begin{aligned}
\psi_1'(1) &= 2 + (m-2)n + 1 \\
&> \frac{n^2 - 4}{n+4} + 3 - n \\
&= \frac{8 - n}{n+4}
\end{aligned}
$$

by (3.14), we conclude from the convexity of ψ_1 that (3.12) holds whenever $n \leq 8$. In the case $n \geq 9$, (1.11) tells us that

$$m - 1 > \frac{n^2 + n + 2 - \sqrt{8n(n+1)}}{n^2 + 2n}. \tag{3.15}$$

Here we note that

$$\frac{n-3}{n} > \frac{n^2-4}{n^2+4n} \quad \text{and} \quad \frac{n-3}{n} > \frac{n^2+n+2-\sqrt{8n(n+1)}}{n^2+2n} \qquad \text{for } n \geq 9,$$

from which we obtain

$$\psi_1(1) = \frac{n^2+4n}{n+2}\left[(m-1) - \frac{n^2-4}{n^2+4n}\right] > 0 \quad \text{and} \quad \psi_1'(1) = n\left[(m-1) - \frac{n-3}{n}\right] \geq 0$$

in the case $m-1 \geq \frac{n-3}{n}$, and hence immediately arrive at (3.12) by the convexity of ψ_1 in this case. We thus only need to consider those m for which both (3.15) and $m-1 < \frac{n-3}{n}$ hold. Observing that ψ_1 attains its minimum over $\mathbb{R}$ at $x_m := \frac{(2-m)n-1}{2}$, and computing

$$\begin{aligned}
\psi_1(x_m) &= -\frac{1}{4}\cdot\left[(1-m)n+n-1\right]^2 + \frac{2(m-1)n}{n+2} \\
&= \frac{n^2}{4}\cdot\left\{\frac{8n(n+1)}{n^2(n+2)^2} - \left[m-1-\frac{n^2+n+2}{n(n+2)}\right]^2\right\},
\end{aligned}$$

we easily see that for such m we have $\psi_1(x) > 0$ for all $x \in \mathbb{R}$.

Having thereby asserted (3.12), as a consequence we note that

$$\varphi_1(x) > x \qquad \text{for all } x \geq 1. \tag{3.16}$$

As to φ_2, we consider the case $n \geq 4$ only and, proceeding similarly, let

$$\psi_2(x) := (m-1)\left[(n^2+n-2)x+n-2\right] - x\cdot\left[n^2-n-2-(n+2)x\right], \qquad x \geq 1,$$

so that

$$\psi_2'(x) = 2(n+2)x + m(n^2+n-2) - 2n^2 + 4, \qquad x \geq 1.$$

Now by straightforward estimates using $\sqrt{8n(n+1)} < \sqrt{8}(n+1)$ when $n \geq 9$, it can easily be checked that (1.11) implies

$$m > \frac{2n^2-8}{n^2+2n-4} \qquad \text{and} \qquad m > \frac{2n^2-2n-8}{n^2+n-2}.$$

We thus have

$$\psi_2(1) = m(n^2+2n-4) - 2n^2 + 8 > 0$$

and

$$\psi_2'(1) = m(n^2+n-2) - 2n^2 + 2n + 8 > 0.$$

By convexity of ψ_2, we conclude that ψ_2 is positive on $[1,\infty)$. This yields

$$\varphi_2(x) > x \qquad \text{for all } x \geq 1,$$

and thus, in conjunction with (3.16), proves that ϕ, as defined through (3.10), satisfies (3.11). $\qquad\square$

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3.3 Iterative improvement of bounds in $L^\gamma(\Omega)$

As a first step towards proving boundedness of our solution, let us collect some basic estimates for u and v in comparatively large function spaces.

Lemma 3.4 *Suppose that $T_{max} < \infty$. Then there exists $C > 0$ such that*

$$\|u\|_{L^\infty((0,T_{max});L^1(\Omega))} \le C, \tag{3.17}$$

$$\|u\|_{L^2((0,T_{max});L^2(\Omega))} \le C, \tag{3.18}$$

$$\|v\|_{L^\infty((0,T_{max});W^{1,2}(\Omega))} \le C \qquad and \tag{3.19}$$

$$\|v\|_{L^2((0,T_{max});W^{2,2}(\Omega))} \le C. \tag{3.20}$$

PROOF.   Integrating the first equation in (1.4) in view of (1.10) yields

$$\frac{d}{dt} \int_\Omega u = \int_\Omega u f(u,w) \le \kappa \int_\Omega u - \mu \int_\Omega u^2 \le \frac{\kappa^2}{2\mu}|\Omega| - \frac{\mu}{2} \int_\Omega u^2 \qquad \text{for all } t \in (0, T_{max}),$$

which on another integration with respect to t immediately gives (3.17) and (3.18). Next, testing the second equation in (1.4) by $-\Delta v$ and using Young's inequality we obtain

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

for all $t \in (0, T_{max})$. Integrated in time, in view of (3.18) this shows that

$$\int_\Omega |\nabla v(t)|^2 \le c_1 \quad \text{for all } t \in (0, T_{max}) \qquad \text{and} \qquad \int_0^{T_{max}} \int_\Omega |\Delta v|^2 \le c_1 \tag{3.21}$$

holds with some $c_1 > 0$. Since moreover

$$\frac{d}{dt} \int_\Omega v = -\int_\Omega v + \int_\Omega u \qquad \text{for all } t \in (0, T_{max})$$

by simple integration of the second equation in (1.4), recalling (3.17) we see that v is bounded in $L^\infty((0, T_{max}); L^1(\Omega))$ Therefore (3.21) immediately entails (3.19) and (3.20) thanks to the equivalence of $\|\cdot\|_{W_2^2(\Omega)}$ to $\|\Delta(\cdot)\|_{L^2(\Omega)} + \|\nabla(\cdot)\|_{L^2(\Omega)} + \|\cdot\|_{L^1(\Omega)}$ for functions satisfying homogeneous Neumann boundary conditions ([13]). $\square$

The following lemma can be used to improve our knowledge on integrability of u, provided that m satisfies (1.11). Its repeated application will form the core of our regularity proof.

Lemma 3.5 *Let $m \ge 1$ be such that (1.11) holds, and let ϕ denote the function introduced in Lemma 3.3. Suppose that $T_{max} < \infty$, and there exist $\beta \ge 1$ and $c > 0$ such that*

$$\int_\Omega u^\beta(t) \le c \qquad for\ all\ t \in (0, T_{max}) \tag{3.22}$$

and

$$\int_0^{T_{max}} \int_\Omega u^{\beta+1} \le c. \tag{3.23}$$

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Then for all $\gamma \in [1, \infty)$ satisfying $\gamma \leq \phi(\beta)$ there exists $C > 0$ such that

$$\int_\Omega u^\gamma(t) \leq C \qquad \text{for all } t \in (0, T_{max}) \tag{3.24}$$

and

$$\int_0^{T_{max}} \int_\Omega u^{\gamma+1} \leq C. \tag{3.25}$$

PROOF.   Multiplying the first equation in (1.4) by $u^{\gamma-1}$ and integrating in space we obtain

$$\frac{1}{\gamma}\frac{d}{dt}\int_\Omega u^\gamma + (\gamma-1)\int_\Omega D(u)u^{\gamma-2}|\nabla u|^2 = (\gamma-1)\chi\int_\Omega u^{\gamma-1}\nabla u \cdot \nabla v$$
$$+(\gamma-1)\xi\int_\Omega u^{\gamma-1}\nabla u \cdot \nabla w$$
$$+\int_\Omega u^\gamma f(u,w) \tag{3.26}$$

for all $t \in (0, T_{max})$. Since by (1.10) and Young's inequality,

$$\int_\Omega u^\gamma f(u,w) \leq \kappa\int_\Omega u^\gamma - \mu\int_\Omega u^{\gamma+1}$$
$$\leq -\frac{\mu}{2}\int_\Omega u^{\gamma+1} + c_1 \qquad \text{for all } t \in (0, T_{max})$$

holds with some $c_1 > 0$, in view of (1.9) we obtain the estimate

$$\frac{1}{\gamma}\frac{d}{dt}\int_\Omega u^\gamma + (\gamma-1)\delta\int_\Omega u^{m+\gamma-3}|\nabla u|^2 + \frac{\mu}{2}\int_\Omega u^{\gamma+1} \leq (\gamma-1)\chi\int_\Omega u^{\gamma-1}\nabla u \cdot \nabla v$$
$$+(\gamma-1)\xi\int_\Omega u^{\gamma-1}\nabla u \cdot \nabla w + c_1 \tag{3.27}$$

for all $t \in (0, T_{max})$. Here, again by Young's inequality,

$$(\gamma-1)\chi\int_\Omega u^{\gamma-1}\nabla u \cdot \nabla v \leq \frac{(\gamma-1)\delta}{4}\int_\Omega u^{m+\gamma-3}|\nabla u|^2 + c_2\int_\Omega u^{-m+\gamma+1}|\nabla v|^2 \tag{3.28}$$

and

$$(\gamma-1)\lambda\int_\Omega u^{\gamma-1}\nabla u \cdot \nabla w \leq \frac{(\gamma-1)\delta}{4}\int_\Omega u^{m+\gamma-3}|\nabla u|^2 + c_2\int_\Omega u^{-m+\gamma+1}|\nabla w|^2 \tag{3.29}$$

hold with a certain $c_2 > 0$ for all $t \in (0, T_{max})$. In order to further estimate the respective second terms on the right hand sides of (3.28) and (3.29) in an effective manner, let us first note that according to parabolic regularity theory in Sobolev spaces ([10]), our assumption (3.23) ensures that v is bounded in $L^{\beta+1}((0, T_{max}); W^{2,\beta+1}(\Omega))$. Therefore an application of Lemma 3.2 shows that

$$\int_0^{T_{max}} \int_\Omega |\nabla v|^{\frac{(n+2)(\beta+1)}{n}} \leq c_3 \tag{3.30}$$

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and

$$\int_\Omega |\nabla w(t)|^{\frac{(n+2)(\beta+1)}{n}} \le c_3 \quad \text{for all } t \in (0, T_{max}) \tag{3.31}$$

are valid with some $c_3 > 0$. Accordingly, let us estimate the integrals in question by invoking Young's inequality with the conjugate exponents $\frac{(n+2)(\beta+1)}{(n+2)(\beta+1)-2n}$ and $\frac{(n+2)(\beta+1)}{2n}$, observing that the latter is greater than one since $\beta \ge 1$. We thereby see that for arbitrary $\varepsilon > 0$,

$$c_2\left(\int_\Omega u^{-m+\gamma+1}|\nabla v|^2 + \int_\Omega u^{-m+\gamma+1}|\nabla w|^2\right) \le \varepsilon \int_\Omega u^{(-m+\gamma+1)\cdot\frac{(n+2)(\beta+1)}{(n+2)(\beta+1)-2n}}$$
$$+c_4\varepsilon^{-\theta}\cdot\left(\int_\Omega |\nabla v|^{\frac{(n+2)(\beta+1)}{n}} + \int_\Omega |\nabla w|^{\frac{(n+2)(\beta+1)}{n}}\right) \tag{3.32}$$

holds for all $t \in (0, T_{max})$ and some $c_4 > 0$ with $\theta := \frac{(n+2)(\beta+1)-2n}{2n}$.

We next claim that our restriction $\gamma \le \phi(\beta)$ ensures that

$$q := (-m+\gamma+1)\cdot\frac{(n+2)(\beta+1)}{(n+2)(\beta+1)-2n}$$

satisfies both

$$q \le \frac{2\beta}{n} + m + \gamma - 1 \tag{3.33}$$

and

$$(n-2)q \le n(m+\gamma-1). \tag{3.34}$$

Indeed, (3.33) is equivalent to saying that $I_1(\gamma) \le 0$, where

$$\begin{aligned}
I_1(x) &:= (-m+x+1)(n+2)(\beta+1) - \left(\frac{2\beta}{n}+m+x-1\right)\cdot\left[(n+2)(\beta+1)-2n\right] \\
&= 2nx - \left\{2(m-1)\left[(n+2)\beta+2\right] + \frac{2(n+2)\beta(\beta+1)}{n} - 4\beta\right\}, \qquad x \ge 1.
\end{aligned}$$

Here, noting that $I_1(x)$ is increasing in $x \ge 1$, according to the definitions of ϕ and φ_1 in Lemma 3.3, we see that

$$I_1(\gamma) \le I_1(\phi(\beta)) \le I_1(\varphi_1(\beta)) = 0. \tag{3.35}$$

This yields (3.33).

As to (3.34), we note that we evidently may restrict ourselves to the case $n \ge 2$, in which we need to show that $I_2(\gamma) \le 0$, where

$$\begin{aligned}
I_2(x) &:= (n-2)(-m+x+1)(n+2)(\beta+1) - n(m+x-1)\left[(n+2)(\beta+1)-2n\right] \\
&= 2\left\{n^2-n-2-(n+2)\beta\right\}\cdot x - 2(m-1)\left\{(n^2+n-2)\beta+n-2\right\}, \qquad x \ge 1.
\end{aligned}$$

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Now if $J_2 := n^2 - n - 2 - (n+2)\beta$ is positive, we have $\beta < \frac{n^2-n-2}{n+2}$ and thus necessarily $n \geq 4$, because $\beta \geq 1$. Recalling the notation from Lemma 3.3, in this case we thus know that $\beta < x_0$ and hence

$$
\begin{aligned}
I_2(x) &= 2J_2 \cdot \left(x - \varphi_2(\beta) \right) \\
&\leq 2J_2 \cdot \left(\phi(\beta) - \varphi_2(\beta) \right) \\
&\leq 0 \qquad \text{for all } x \in [1, \phi(\beta)],
\end{aligned}
$$

because $\phi \leq \varphi_2$. In particular, this means that

$$ I_2(\gamma) \leq 0 \qquad \text{if } J_2 > 0. \tag{3.36} $$

On the other hand, if $J_2 \leq 0$ then

$$ I_2(x) \leq -2(m-1)\left\{ (n^2+n-2)\beta + n - 2 \right\} \qquad \text{for all } x \geq 1, $$

which in view of our assumptions $m \geq 1$ and $\beta \geq 1$ can be combined so as to yield

$$
\begin{aligned}
I_2(x) &\leq -2(m-1)\left\{ n^2 + 2(n-2) \right\} \\
&\leq 0 \qquad \text{for all } x \geq 1,
\end{aligned}
$$

because we presently only consider $n \geq 2$. Together with (3.36) this proves that $I_2(\gamma) \leq 0$.

Having thereby established (3.33) and (3.34), using (3.22) we may apply Lemma 3.1 with $p := \beta$ to obtain

$$ \int_\Omega u^{(-m+\gamma+1) \cdot \frac{(n+2)(\beta+1)}{(n+2)(\beta+1)-2n}} \leq c_5 \int_\Omega u^{m+\gamma-3}|\nabla u|^2 + c_6 \qquad \text{for all } t \in (0, T_{max}) $$

with appropriately large $c_5 > 0$ and $c_6 > 0$. Upon fixing $\varepsilon := \frac{(\gamma-1)\delta}{4c_5}$ now, from (3.32) we consequently derive

$$
\begin{aligned}
c_2 &\left(\int_\Omega u^{-m+\gamma+1}|\nabla v|^2 + \int_\Omega u^{-m+\gamma+1}|\nabla w|^2 \right) \\
&\leq \frac{(\gamma-1)\delta}{4} \int_\Omega u^{m+\gamma-3}|\nabla u|^2 + \frac{(\gamma-1)\delta c_6}{4c_5} \\
&\quad + c_6 \cdot \left(\frac{4c_5}{(\gamma-1)\delta} \right)^\theta \cdot \left(\int_\Omega |\nabla v|^{\frac{(n+2)(\beta+1)}{n}} + \int_\Omega |\nabla w|^{\frac{(n+2)(\beta+1)}{n}} \right)
\end{aligned} \tag{3.37}
$$

for all $t \in (0, T_{max})$. All in all, collecting (3.27), (3.28), (3.29), (3.30), (3.31) and (3.37) we conclude that

$$ \frac{1}{\gamma}\frac{d}{dt}\int_\Omega u^\gamma + \frac{(\gamma-1)\delta}{4}\int_\Omega u^{m+\gamma-3}|\nabla u|^2 + \frac{\mu}{2}\int_\Omega u^{\gamma+1} \leq c_7 \qquad \text{for all } t \in (0, T_{max}) $$

is valid with some $c_7 > 0$, which after integration readily yields (3.24) and (3.25) on choosing C appropriately large. $\qquad \square$

Now a bootstrap procedure leads to the following statement on boundedness of u in $L^\infty((0, T_{max}); L^\gamma(\Omega))$ for any fixed $\gamma < \infty$, provided that $T_{max} < \infty$.

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Lemma 3.6 *Let $m \geq 1$ satisfy (1.11), and suppose that $T_{max} < \infty$. Then for all $\gamma \in [1, \infty)$ there exists $C > 0$ such that*

$$\int_\Omega u^\gamma(t) \leq C \qquad \text{for all } t \in (0, T_{max}). \tag{3.38}$$

PROOF.   We define a sequence $(\gamma_k)_{k \in \mathbb{N}} \subset [1, \infty)$ by setting $\gamma_0 := 1$ and

$$\gamma_{k+1} := \phi(\gamma_k) \qquad \text{for } k \geq 0, \tag{3.39}$$

where ϕ is given by (3.10). Then Lemma 3.3 implies that $\gamma_{k+1} = \phi(\gamma_k) > \gamma_k$ for all $k \in \mathbb{N}$, which entails that $\gamma_k \nearrow \gamma_\infty$ as $k \to \infty$ for some $\gamma_\infty \leq \infty$. We claim that

$$\gamma_\infty = \infty. \tag{3.40}$$

In fact, if γ_∞ was finite, then taking $k \to \infty$ in both sides of (3.39) and using the continuity of function ϕ would yield the conclusion $\gamma_\infty = \phi(\gamma_\infty)$. This contradiction to (3.11) establishes (3.40).

We now repeatedly apply Lemma 3.5 to $\beta := \gamma_k$ and $\gamma := \gamma_{k+1}$ for $k = 0, ..., k_0$. Here we observe that in accordance with (3.39), for the first step the requirements in (3.22) and (3.23) are asserted by (3.17) and (3.18), whereas for $k = 1, ..., k_0$ we use the respective outcome of the previous step to guarantee (3.22) and (3.23). We thereby see upon a straightforward induction that for all $k \in \{0, ..., k_0 + 1\}$ there exists $c_k > 0$ such that

$$\int_\Omega u^{\gamma_k}(t) \leq c_k \qquad \text{for all } t \in (0, T_{max}). \tag{3.41}$$

Since $\gamma_k \nearrow \infty$, (3.41) precisely asserts (3.38). $\qquad\square$

3.4 L^∞ estimates and proof of the main results

From Lemma 3.6 we can easily derive higher order estimates for v and w.

Lemma 3.7 *Let $m \geq 1$ satisfy (1.11), and assume that $T_{max} < \infty$. Then for all $p \in [1, \infty)$ there exists $C > 0$ such that*

$$\|v\|_{L^p((0,T_{max});W^{2,p}(\Omega))} \leq C \tag{3.42}$$

and

$$\|w\|_{L^p((0,T_{max});W^{2,p}(\Omega))} \leq C. \tag{3.43}$$

PROOF.   In view of Lemma 3.6, (3.42) is an immediate consequence of the parabolic smoothing action in the second PDE in (1.4) ([10]). Now assuming $p > 2$ without loss of generality, we apply Δ to both sides of the third equation in (1.4) and multiply the resulting identity by $|\Delta w|^{p-2}\Delta w$. After an integration we obtain

$$\begin{aligned}
\frac{1}{p}\frac{d}{dt}\int_\Omega |\Delta w|^p &= \int_\Omega |\Delta w|^{p-2}\Delta w \cdot (-v\Delta w - 2\nabla v \cdot \nabla w - w\Delta v) \\
&= -\int_\Omega v|\Delta w|^2 - 2\int_\Omega (\nabla v \cdot \nabla w)|\Delta w|^{p-2}\Delta w \\
&\quad - \int_\Omega w|\Delta w|^{p-2}\Delta w \Delta v \qquad \text{for all } t \in (0, T_{max}). \tag{3.44}
\end{aligned}$$

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Here, the first term on the right is non-positive, whereas by Young's inequality we have

$$-\int_\Omega w|\Delta w|^{p-2}\Delta w\Delta v \leq \int_\Omega |\Delta w|^p + c_1\int_\Omega |\Delta v|^p$$

and

$$-2\int_\Omega (\nabla v\cdot\nabla w)|\Delta w|^{p-2}\Delta w \leq \int_\Omega |\Delta w|^p + c_1\int_\Omega |\nabla v|^p|\nabla w|^p$$

for all $t \in (0, T_{max})$ and some $c_1 > 0$, where we have used that $0 \leq w \leq \|w_0\|_{L^\infty(\Omega)}$ in $\Omega \times (0, T_{max})$. Once more by Young's inequality we find

$$\int_\Omega |\nabla v|^p|\nabla w|^p \leq \frac{1}{2}\int_\Omega |\nabla v|^{2p} + \frac{1}{2}\int_\Omega |\nabla w|^{2p},$$

so that from (3.44) we altogether infer that

$$\frac{d}{dt}\int_\Omega |\Delta w|^p \leq 2p\int_\Omega |\Delta w|^p + c_2 a(t) \qquad \text{for all } t \in (0, T_{max}) \tag{3.45}$$

holds with some $c_2 > 0$ and

$$a(t) := \int_\Omega |\Delta v|^p + \int_\Omega |\nabla v|^{2p} + \int_\Omega |\nabla w|^{2p}, \qquad t \in (0, T_{max}).$$

Since (3.42) in conjunction with (3.19) and Lemma 3.2 states that $\int_0^{T_{max}} a(t)dt$ is finite, an integration of (3.45) finally establishes (3.43). $\qquad\square$

Now by a standard iteration procedure we immediately obtain boundedness of u in $\Omega \times (0, T_{max})$, provided that $T_{max} < \infty$.

Lemma 3.8 *Let $m \geq 1$ fulfill (1.11), and assume that $T_{max} < \infty$. Then there exists $c > 0$ such that*

$$\|u(t)\|_{L^\infty(\Omega)} \leq c \qquad \text{for all } t \in (0, T_{max})$$

and

$$\|v(t)\|_{W^{1,\infty}(\Omega)} + \|w(t)\|_{W^{1,\infty}(\Omega)} \leq c \qquad \text{for all } t \in \left(\frac{T_{max}}{2}, T_{max}\right).$$

PROOF.   The estimate for u easily follows from Lemma 3.6 and Lemma 3.7 upon an iteration procedure of Alikakos-Moser type (see [1]; cf. [42, Lemma 4.1] for a version appropriate for the present setting). The statement on v and w is again a direct consequence of parabolic regularity theory. $\qquad\square$

We are now in the position to prove our main results.

PROOF   (of Theorem 1.1 and Corollary 1.2).   Both assertions are immediate consequences of Lemma 3.8 and the extendibility criterion provided by Lemma 2.1. $\qquad\square$

References

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

[2] N. Bellomo, N. K. Li and P. K. Maini, *On the foundations of cancer modelling: selected topics, speculations, and perspectives*, Math. Mod. Meth. Appl. Sci. 18 (2008), 593-646.

[3] P. Biler, *Local and global solvability of some parabolic systems modelling chemotaxis*, Adv. Math. Sci. Appl. 8 (1998), 715-743.

[4] V. Calvez and J. A. Carrillo, *Volume effects in the Keller-Segel model: energy estimates preventing blow-up*, J. Math. Pures Appl. (9), 86 (2006), 155-175.

[5] M. A. J. Chaplain and A. R. A. Anderson, *Mathematical modelling of tissue invasion*, Cancer Modelling and Simulation (Ed. L. Preziosi), Chapman & Hall/CRT (2003), 267-297.

[6] M. A. J. Chaplain, M. Lachowicz, Z. Szymańska and D. Wrzosek, *Mathematical modelling of cancer invasion: the importance of cell-cell adhension and cell-matrix adhension*, preprint.

[7] M. A. J. Chaplain and G. Lolas, *Mathematical modelling of cancer invasion of tissue: The role of the urokinase plasminogen activation system*, Math. Mod. Meth. Appl. Sci. 15 (2005), 1685-1734.

[8] T. Cieślak and P. Laurençot, *Finite time blow-up for radially symmetric solutions to a critical quasilinear Smoluchowski-Poisson system*, C. R. Acad. Sci. Paris, Ser. I 347 (2009), 237-242.

[9] T. Cieślak and M. Winkler, *Finite-time blow-up in a quasilinear system of chemotaxis*, Nonlinearity 21 (2008), 1057-1076.

[10] R. Denk, M. Hieber and J. Prüss, $\mathcal{R}$*-boundedness, fourier multipliers and problems of elliptic and parabolic type*, Mem. Amer. Math. Soc. 166 (2003), no. 788.

[11] E. DiBenedetto, *Degenerate Parabolic Equations*, Springer-Verlag, New York, 1993.

[12] K. Djie, M. Winkler, *Boundedness and finite-time collapse in a chemotaxis system with volume-filling effect*, Nonlinear Analysis TMA 72, 2 (2010), 1044-1064.

[13] A. Friedman, *Partial Differential Equations*, Holt, Rinehart & Winston, New York, 1969.

[14] A. Friedman and G. Lolas, *Analysis of a mathematical model of tumor lymphangiogenesis*, Math. Mod. Meth. Appl. Sci. 1 (2005), 95-107.

[15] R. A. Gatenby and E. T. Gawlinski, *A reaction-diffusion model of cancer invasion*, Cancer Res. 56 (1996), 5745-5753.

[16] A. Gerisch and M. A. J. Chaplain, *Mathematical modelling of cancer cell invasion of tissue: Local and non-local models and the effect of adhesion*, J. Theor. Biol. 250 (2008), 684-704.

[17] M. A. Herrero and J. L. L. Velázquez, *A blow-up mechanism for a chemotaxis model*, Ann. Sc. Norm. Super. Pisa Cl. Sci. (4), 24 (1997), 633-683.

[18] T. Hillen and K. J. Painter, *A user's guide to PDE models for chemotaxis*, J. Math. Biol. 58 (2009), 183-217.

[19] T. Hillen and K. J. Painter, *Global existence for a parabolic chemotaxis model with prevention of overcrowding*, Adv. Appl. Math. 26 (2001), 281-301.

[20] D. Horstmann and M. Winkler, *Boundedness vs. blow-up in a chemotaxis system*, J. Diff. Eqns. 215 (2005), 52-107.

[21] W. Jäger and S. Luckhaus, *On explosions of solutions to a system of partial differential equations modelling chemotaxis*, Trans. Amer. Math. Soc. 329 (1992), 819-824.

[22] E. F. Keller and L. A. Segel, *Initiation of slime mold aggregation viewed as an instaility*, J. Theor. Biol. 26 (1970), 399-415.

[23] R. Kowalczyk, *Preventing blow-up in a chemotaxis model*, J. Math. Anal. Appl. 305 (2005), 566-585.

[24] R. Kowalczyk and Z. Szymańska, *On the global existence of solutions to an aggregation model*, J. Math. Anal. Appl. 343 (2008), 379-398.

[25] M. Lachowicz, *Micro and meso scales of description corresponding to a model of tissue invasion by solid tumours*, Math. Mod. Meth. Appl. Sci. 15 (2005), 1667-1683.

[26] M. Lachowicz, *Towards microscopic and nonlocal models of tumour invasion of tissue*, Selected Topics in Cancer Modeling (Eds. N. Bellomo, M. Chaplain, E. De Angelis), Birkhauser, Boston (2008), 49-63.

[27] O. A. Ladyzenskaja, V. A. Solonnikov and N. N. Ural'ceva, *Linear and Quasi-Linear Equations of Parabolic Type,* Amer. Math. Soc. Transl., Vol. 23, Providence, RI, 1968.

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[28] G. Liţcanu and C. Morales-Rodrigo, *Global solutions and asymptotic behavior for a parabolic degenerate coupled system arising from biology*, Nonlinear Analysis 72 (2010), 77-98.

[29] G. Liţcanu and C. Morales-Rodrigo, *Asymptotic behaviour of global solutions to a model of cell invasion*, Math. Mod. Meth. Appl. Sci. 20 (2010), 1721-1758.

[30] A. Marciniak-Czochra and M. Ptashnyk, *Boundness of solutions of a haptotaxis model*, Math. Mod. Meth. Appl. Sci. 20 (2010), 449-476.

[31] T. Nagai, *Blowup of nonradial solutions to parabolic-elliptic systems modeling chemotaxis in two-dimensional domains*, J. Inequal. Appl. 6 (2001), 37-55.

[32] E. Nakaguchi, K. Osaki, *Global Existence of Solutions to a Parabolic-Parabolic System for Chemotaxis with Weak Degradation*, Nonlinear Anal. 74 (2011), 286-297.

[33] K. Osaki, T. Tsujikawa, A. Yagi and M. Mimura, *Exponential attractor for a chemotaxis-growth system of equations*, Nonlinear Anal. 51 (2002), 119-144.

[34] A. J. Perumpanani and H, M. Byrne, *Extracellular matrix concentration exerts selection pressure on invasive cells*, European Journal of cancer 8 (1999), 1274-1280.

[35] B. Perthame, *Transport Equations in Biology*, Birkhäuser-Basel Verlag, Switzerland, 2007.

[36] M. Rascle and C. Ziti, *finite time blow-up in some models of chemotaxis*, J. Math. Biol. 33 (1995), 388-414.

[37] Z. Szymańska, C. Morales-Rodrigo, M. Lachowicz and M. Chaplain, *Mathematical modelling of cancer invasion of tissue: The role and effect of nonlocal interactions*, Math. Mod. Meth. Appl. Sci. 19 (2009), 257-281.

[38] Y. Sugiyama, *Time global existence and asymptotic behavior of solutions to degenerate quasi-linear parabolic systems of chemotaxis*, Differential and Integral Equations 20 (2007), 133-180.

[39] Y. Tao, *Global existence of classical solutions to a combined chemotaxis-haptotaxis model with logistic source*, J. Math. Anal. Appl. 354 (2009), 60-69.

[40] Y. Tao and M. Wang, *A combined chemotaxis-haptotaxis system: The role of logistic source*, SIAM J. Math. Anal. 41 (2009), 1533-1558.

[41] Y. Tao and M. Wang, *Global solution for a chemotactic-haptotactic model of cancer invasion*, Nonlinearity 21 (2008), 2221-2238.

[42] Y. Tao and M. Winkler, *Boundedness in a quasilinear parabolic-parabolic Keller-Segel system with subcritical sensitivity*, preprint.

[43] J. I. Tello, *Mathematical analysis and stability of a chemotaxis model with logistic term*, Math. Methods Appl. Sci 27 (2004), 1865-1880.

[44] J. I. Tello and M. Winkler, *A chemotaxis system with logistic source*, Commun. Partial Differential Equations 32 (2007), 849-877.

[45] C. Walker and G. F. Webb, *Global existence of classical solutions for a haptotaxis model*, SIAM J. Math. Anal. 38 (2007), 1694-1713.

[46] M. Winkler, *Chemotaxis with logistic source: Very weak global solutions and their boundedness properties*, J. Math. Anal. Appl. 348 (2008), 708-729.

[47] M. Winkler, *Boundedness in the higher-dimensional parabolic-parabolic chemotaxis system with logistic source*, Commun. Partial Differential Equations 35 (2010), 1516-1537.

[48] M. Winkler, *Aggregation vs. global diffusive behavior in the higher-dimensional Keller-Segel model*, J. Differential Equations 248 (2010), 2889-2905.

[49] M. Winkler, *Does a 'volume-filling effect' always prevent chemotactic collapse?*, Math. Meth. Appl. Sci. 33 (2010), 12-24.

[50] D. Wrzosek, *Global attractor for a chemotaxis model with prevention of overcrowding*, Nonlinear Anal. TMA 59 (2004), 1293-1310.