Taxis-driven formation of singular hotspots in a May-Nowak type model for virus infection

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Abstract

A three-component reaction-diffusion system is considered which originates from an extension of the classical May-Nowak model for viral infections to situations in which spatially heterogeneous dynamics need to be accounted for. In accordance with recent developments in the modeling literature, a particular focus is on possible effects of taxis-type movement of uninfected toward infected cells, where in contrast to setting addressed by standard Keller-Segel type systems, the evolution of the considered attractant is influenced by an inherently *nonlinear* production mechanism.

Despite the accordingly increased mathematical challenges going along with an apparent lack of favorable structural properties that have facilitated accessibility of such classical Keller-Segel models to various techniques from parabolic blow-up analysis, the present study attempts to develop an approach capable of detecting taxis-driven aggregation phenomena in complex models of this form. In the framework of radially symmetric solutions to associated Neumann-type initial boundary value problems, through an analysis of a corresponding mass accumulation function a result on the occurrence of finite-time blow-up in two- or three-dimensional balls is derived. This rigorously confirms the potential of the considered model to describe the spontaneous emergence of locally high densities, as known from experimental observations in contexts of virus hotspot formation phenomena.

Key words: blow-up; virus dynamics; chemotaxis

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1 Introduction

Virus is commonly thought to propagate through susceptible cells via a circulatory process. Viruses attach, enter, and then infect target cells; the infected cells can release new virus particles due to replication of virus, and these new viruses further infect other uninfected cells.

Various spatially homogeneous models for the dynamics of a virus were proposed (cf. [37], [25], [26] and [27], for example). Both empirical data and mathematical analysis for such ODE models generally indicate two types of asymptotic behaviors, one of which being determined by some persistence of virus, while the other reflecting an eventual extinction of the virus population. The dependence of the decision between these options on certain key mechanisms can be carved out in a particularly clear manner already in the context of the simple May-Nowak model for the numbers u, v and w of uninfected cells, infected cells, and virions, as given by

$$\begin{cases} u_t = -d_1 u - \beta uw + r, \\ v_t = -d_2 v + \beta uw, \\ w_t = -d_3 w + kv, \end{cases} \tag{1.1}$$

where indeed the size of the so-called basic reporoduction number $R_0 := \frac{\beta kr}{d_1 d_2 d_3}$ relative to the critical value 1 is known to be accordingly determinant (see, e.g., [6], [26], [18], [30]).

An adequate description of virus dynamics in frameworks of phenomena involving spatial heterogeneity, however, evidently requires the use of more sophisticated models which appropriately account for respectively relevant migration mechanisms. Indeed, the ambition to understand the spatio-temporal dynamics of viral infections in general, and particularly of striking experimental observations such as the detection of certain virus infection hotspots ([12]), has stimulated efforts both on the experimental and on the modeling side: The relevance of a diffusion process of target cells has been experimentally found both *in vitro* and *in vivo* ([21], [13]), and some parabolic models for virus dynamics, essentially of classical reaction-diffusion type in the sense of augmenting ODE systems of the form in (1.1) by linear diffusion terms, were proposed and studied (cf. [17] and [31], for instance).

A chemotaxis model for virus infection. Apart from that, however, when virus (e.g. HIV) attacks the immune systems, target T cells have been found to be directed by the high concentration of cytokines from inflammations at spots of infection ([20], [13]), and an appropriate inclusion of such directed movement mechanisms apparently requires a passage toward a model class substantially more prone to instabilities: In fact, the authors in [32] suggest to accomplish this by means of the chemotaxis-type extension of (1.1) given by

$$\begin{cases} u_t = D_u \Delta u - \chi \nabla \cdot (u \nabla v) - \kappa_1 u - \kappa_2 uw + \lambda, \\ \tau_1 v_t = D_v \Delta v - \alpha v + \kappa_3 uw, \\ \tau_2 w_t = D_w \Delta w - \kappa_4 w + \kappa_5 v, \end{cases} \tag{1.2}$$

where D_u, D_v and D_w denote the respective diffusion coefficients of the functions $u = u(x,t), v = v(x,t)$ and $w = w(x,t)$, χ represents the strength of the cross-diffusive interaction, and $\tau_1 \geq 0$ and $\tau_2 \geq 0$ are parameters related to the speed at which v and w equilibrate. In the above model, it is assumed that healthy cells are produced at a rate λ and become infected at a rate κ_2, that infected cells are produced at the rate κ_3, that new viruses are produced by infected cells at a rate κ_5, and that all three populations undergo spontaneous death at rates κ_1, α and κ_4, respectively.

Numerical experiments now indicate that the introduction of the taxis term in (1.2) indeed goes along with a considerable trend toward support of spatial heterogeneity. Already in one-dimensional settings in which (1.2) is known to admit global bounded smooth solutions for arbitrarily large initial data ([43]), simulations reveal Turing-type instabilities for suitably large χ ([32]); beyond this, numerical evidence suggest that when posed in two-dimensional domains, besides facilitating effects of the latter flavor the system (1.2) may even enforce the spontaneous emergence of singularities ([32], [2]). Such mathematically extreme expressions of structure formation have meanwhile been understood to a considerable extent in frameworks of simpler taxis systems from the context of Keller-Segel models ([16], [22], [40]), but even the mere detection of blow-up phenomena so far has, in virtually all successful cases reported in the literature, relied on quite fragile structural properties of cross-diffusive interaction which most commonly disappear upon extending and complexifying the respective model.

Accordingly, for the three-component system (1.2) and some close relatives, knowledge assured by rigorous analysis seem yet limited to findings on global solvability in various particular settings. For instance, variants of (1.2) involving suitably strong regularizations of either the infection term $\kappa_3 uw$ ([36], [3], [9]), or the tactic contribution $-\chi\nabla\cdot(u\nabla v)$ ([15], [43]), have been found to possess global bounded solutions for widely arbitrary initial data; for (1.2) in its original form, however, results on global existence and boundedness are restricted to spatially one-dimensional settings ([43]), or to situations in which $|\chi|$ is appropriately small, possibly in dependence on the initial data ([2]). To the best of our knowledge, however, the literature by now does not provide any rigorous result on the occurrence of explosions in two- or higher-dimensional versions of (1.2).

Main results. A key obstacle to be adequately coped with by any expedient strategy toward addressing this latter issue seems to be linked to the circumstance that in sharp contrast to classical Keller-Segel type systems, the tactically directing signal in (1.2) is produced in a nonlinear manner, as becoming manifest in the contribution $+\kappa_3 uw$ to the second equation therein. Indeed, the occurrence of the additional factor w apparently rules out any persistence of the gradient-like structure that is known to go along with Keller-Segel type chemotactic interaction involving linear signal production ([23]), and that has formed an indispensable basis for blow-up detections in parabolic versions thereof ([19], [40]).

In order to nevertheless develop an approach capable of discovering singularity formation in (1.2), we recall from biological data that the migration speed is significantly increased upon infection: Indeed, the experiments reported in [44] that infected cells secrete some effector interacting with host proteins that regulate motility of cells, and thus this effector actually promotes motility of infected cells and accelerates the spread of infection; another experimental finding indicates that the translocated receptor in infected cells recruits other signalling proteins into a large protein complex leading to cell motility and invasive growth ([1]). In line with this and classical precedents concerned with corresponding parabolic-elliptic model limits in Keller-Segel systems ([16], [28]), we shall henceforth consider (1.2) in the borderline case $\tau_1 = 0$ that relates to a quasi-steady-state approximation of the equation describing the evolution of infected cells. In order to suitably carve out those properties of the zero-order terms in (1.2) that are genuinely required for our analysis, we shall subsequently be concerned with the generalization of the corresponding parabolic-elliptic-parabolic version of (1.2) given by

$$\begin{cases} u_t = D_u\Delta u - \chi\nabla\cdot(u\nabla v) + f(u,v,w), & x\in\Omega,\ t>0,\\ 0 = D_v\Delta v - \alpha v + ug(u,w), & x\in\Omega,\ t>0,\\ w_t = D_w\Delta w + h(u,v,w), & x\in\Omega,\ t>0,\\ \frac{\partial u}{\partial\nu} = \frac{\partial v}{\partial\nu} = \frac{\partial w}{\partial\nu} = 0, & x\in\partial\Omega,\ t>0,\\ u(x,0)=u_0(x), \quad w(x,0)=w_0(x), & x\in\Omega, \end{cases} \tag{1.3}$$

in a ball $\Omega = B_R(0) \subset \mathbb{R}^n$ with $n \in \{2,3\}$ and $R>0$. Here, D_u, D_v, D_w, α and χ are given positive constants, and throughout this paper the parameter functions f, g and h are assumed to satisfy the regularity assumptions

$$f \in C^1([0,\infty)^3), \quad g \in C^1([0,\infty)^2) \quad \text{and} \quad h \in C^1([0,\infty)^3) \tag{1.4}$$

as well as the two-sided estimates

$$f(u,v,w) \ge -uf_0(w) \quad \text{for all } (u,v,w)\in[0,\infty)^3 \qquad \text{with some nondecreasing } f_0 : [0,\infty)\to[0,\infty) \tag{1.5}$$

and

$$f(u,v,w) \le \lambda \quad \text{for all } (u,v,w)\in[0,\infty)^3 \qquad \text{with some } \lambda>0 \tag{1.6}$$

and

$$g(u,w) \ge g_0(w) \quad \text{for all } (u,w)\in[0,\infty)^2 \qquad \begin{array}{l}\text{with some nondecreasing } g_0 : [0,\infty)\to\mathbb{R}\\ \text{fulfilling } g_0>0 \text{ on } (0,\infty)\end{array} \tag{1.7}$$

as well as

$$g(u,w) \le g_1(w) \quad \text{for all } (u,w)\in[0,\infty)^2 \qquad \text{with some nondecreasing } g_1 : [0,\infty)\to[0,\infty) \tag{1.8}$$

and

$$h(u,v,w) \ge -h_0(w) \quad \text{for all } (u,v,w)\in[0,\infty)^3 \qquad \begin{array}{l}\text{with some nondecreasing } h_0 : [0,\infty)\to[0,\infty)\\ \text{such that } h_0(0)=0\end{array} \tag{1.9}$$

and

$$h(u,v,w) \le \beta\cdot(v+1) \quad \text{for all } (u,v,w)\in[0,\infty)^3 \qquad \text{with some } \beta>0. \tag{1.10}$$

We shall moreover concentrate on radial solutions by supposing that

$$\begin{cases} u_0 \in C^0(\overline{\Omega}) \text{ is radially symmetric and nonnegative, and that}\\ w_0 \in C^0(\overline{\Omega}) \text{ is radially symmetric and positive in } \overline{\Omega}, \end{cases} \tag{1.11}$$

and we remark that by appropriate modification of the reasoning in [2], it is possible to show that within this setup, for suitably small values of $|\chi|$ a global and bounded solution can be found. In stark contrast to this, the main result of the present study now asserts that when $\chi>0$ is appropriately large, then indeed some such initial data can be found which evolve into certain infinite densities within finite time, hence reflecting hotspot formation, as observed in [12], in the sharp sense of singularity formation.

Theorem 1.1 *Let $\Omega = B_R(0) \subset \mathbb{R}^n$ with $n \in \{2,3\}$ and some $R > 0$, and suppose that $D_u > 0, D_v > 0, D_w > 0$ and $\alpha > 0$, and that f, g and h satisfy (1.4) as well as (1.5)-(1.10). Then given any radially symmetric and positive $w_0 \in C^0(\overline{\Omega})$, for each $m > 0$ one can find $r_\star = r_\star(m, w_0) \in (0, R)$ and $\chi_\star = \chi_\star(m, w_0) > 0$ such that whenever $\chi > \chi_\star$ and $u_0 \in C^0(\overline{\Omega})$ is a radially symmetric and nonnegative function fulfilling*

$$\int_\Omega u_0 \le m \tag{1.12}$$

and

$$\int_{B_{r_\star}(0)} u_0 \ge \frac{m}{2}, \tag{1.13}$$

the problem (1.3) possesses a classical solution which blows up in finite time; more precisely: There exist $T \in (0, \infty)$ and uniquely determined nonnegative functions

$$\begin{cases} u \in C^0(\overline{\Omega} \times [0,T)) \cap C^{2,1}(\overline{\Omega} \times (0,T)), \\ v \in C^{2,0}(\overline{\Omega} \times (0,T)) \qquad \textit{and} \\ w \in C^0(\overline{\Omega} \times [0,T)) \cap C^{2,1}(\overline{\Omega} \times (0,T)) \end{cases} \tag{1.14}$$

such that (u, v, w) solves (1.3) in the classical sense in $\Omega \times (0, T)$, but that

$$\limsup_{t \nearrow T} \Big\{ \|u(\cdot,t)\|_{L^\infty(\Omega)} + \|w(\cdot,t)\|_{L^\infty(\Omega)} \Big\} = \infty. \tag{1.15}$$

The statement in (1.15) can be sharpened under the further assumption that the function in (1.8) satisfies

$$g_1(w) \le \delta \cdot (w+1) \quad \text{for all } w \ge 0 \qquad \text{with some } \delta > 0. \tag{1.16}$$

Proposition 1.2 *If, apart from the hypotheses of Theorem 1.1, the condition (1.16) is satisfied, then in the situation of Theorem 1.1, instead of (1.15) the stronger conclusion*

$$\limsup_{t \nearrow T} \|u(\cdot,t)\|_{L^\infty(\Omega)} = \infty \tag{1.17}$$

holds.

Especially in view of the question which of the three population densities genuinely undergo explosions near blow-up times, beyond the basic statements in (1.15) and (1.17) the derivation of more detailed information about possible blow-up mechansisms forms an important topic for future research which, however, goes beyond the scope of the present study.

Challenges and main ideas. When compared to well-understood situations of blow-up proofs for radial solutions to parabolic-elliptic Keller-Segel systems ([16], [5], [22]), the present setting exposes its increased complexity through the circumstance that the scalar parabolic equation satisfied by the mass accumulation function, as defined by

$$z(s,t) := \frac{1}{n|B_1(0)|} \int_{B_{\sqrt[n]{s}}(0)} u(x,t)dx, \qquad s \in [0, R^n], \ t \ge 0,$$

contains certain spatially nonlocal ingredients, particularly in the corresponding taxis-induced contribution (Lemma 4.1). In order to appropriately control these, and especially to suitably bound the potentially destabilizing nonlinear action from below, in Section 3 we shall remain in the framework of the original variables and derive some preliminary estimates for (u, v, w), including a pointwise lower estimate for w, at least within some adequately small time intervals (Lemma 3.5). In Lemma 4.2, these preparations will be seen to imply a one-sided parabolic inequality for z that exclusively contains local ingredients, which thereafter will be further developed into a superlinearly forced autonomous ODI, again valid during suitably short time intervals, for the function given by

$$y(t) := \int_0^{s_0} (s_0 - s) z(s,t) ds, \qquad t > 0,$$

with the localization parameter $s_0 \in (0, R^n)$ still at our disposal (Lemma 4.4). A key step, quite immediately implying both Theorem 1.1 and Proposition 1.2, will then be accomplished in Lemma 4.5 which reveals that for suitably large values of the tactic sensitivity χ and sufficiently small s_0, the driving source in this ODI does not only compel a collapse of y, but that this singularity must indeed be formed prior to the end of said short time interval.

2 Local existence

To begin with, let us adapt approaches well-established in the context of parabolic-elliptic chemotaxis models (cf., e.g., [33] and [8]) to derive the following basic result on local existence and extensibility.

Lemma 2.1 *Let D_u, D_v, D_w and α be positive constants and $\chi \in \mathbb{R}$, and suppose that (1.4) and (1.5)-(1.10) as well as (1.11) hold. Then there exist $T_{max} \in (0, \infty]$ and uniquely determined nonnegative functions*

$$\begin{cases} u \in C^0(\overline{\Omega} \times [0, T_{max})) \cap C^{2,1}(\overline{\Omega} \times (0, T_{max})), \\ v \in C^{2,0}(\overline{\Omega} \times (0, T_{max})) \qquad \textit{and} \\ w \in C^0(\overline{\Omega} \times [0, T_{max})) \cap C^{2,1}(\overline{\Omega} \times (0, T_{max})), \end{cases} \tag{2.1}$$

such that $u(\cdot,t), v(\cdot,t)$ and $w(\cdot,t)$ are radially symmetric for all $t \in (0, T_{max})$, that (u, v, w) solves (1.3) in the classical sense in $\Omega \times (0, T_{max})$, and that

$$\textit{if } T_{max} < \infty, \textit{ then} \quad \limsup_{t \nearrow T_{max}} \Big\{ \|u(\cdot,t)\|_{L^\infty(\Omega)} + \|w(\cdot,t)\|_{L^\infty(\Omega)} \Big\} = \infty. \tag{2.2}$$

Proof. To construct a classical solution satisfying (2.1), we fix any $p > n$, which allows us to pick $\theta \in (\frac{n}{2p}, \frac{1}{2})$. Then the realization of $A := -\Delta$ under homogeneous Neumann boundary conditions in $L^p(\Omega)$ has the property that the domain of the definition of the fractional power $(A+1)^\theta$ satisfies $D((A+1)^\theta) \hookrightarrow L^\infty(\Omega)$ ([14]), and that thus there exists $c_1 > 0$ such that

$$\|\varphi\|_{L^\infty(\Omega)} \le c_1 \|(A+1)^\theta \varphi\|_{L^p(\Omega)} \qquad \text{for all } \varphi \in D(A). \tag{2.3}$$

Next, by continuity of the embedding $W^{2,p}(\Omega) \hookrightarrow W^{1,\infty}(\Omega)$ we may draw on elliptic regularity theory ([11]) to pick $c_2 > 0$ satisfying

$$\|\varphi\|_{W^{1,\infty}(\Omega)} \le c_2 \| - D_v \Delta\varphi + \alpha\varphi\|_{L^p(\Omega)} \qquad \text{for all } \varphi \in W^{2,p}(\Omega) \text{ such that } \frac{\partial\varphi}{\partial\nu} = 0 \text{ on } \partial\Omega. \tag{2.4}$$

Moreover, relying on standard smoothing estimates for the Neumann heat semigroup $(e^{tD_u\Delta})_{t\ge0}$ on Ω we can $c_3>0$ such that for all $t>0$, the operator $(A+1)^\theta e^{tD_u\Delta}\nabla\cdot$ can continuously be extended to all of $L^p(\Omega;\mathbb{R}^n)$, with

$$\|(A+1)^\theta e^{tD_u\Delta}\nabla\cdot\varphi\|_{L^p(\Omega)} \le c_3 t^{-\frac12-\theta}\|\varphi\|_{L^p(\Omega)} \qquad \text{for all } \varphi\in L^p(\Omega;\mathbb{R}^n) \tag{2.5}$$

(cf. [39, Lemma 1.3], for instance). We now set $R_0 := \|u_0\|_{L^\infty(\Omega)} + \|w_0\|_{L^\infty(\Omega)} + 1$, and for $T\in(0,1)$ to be specified below we introduce the closed subset

$$S := \Big\{ (u,w)\in X \ \Big|\ \|u(\cdot,t)\|_{L^\infty(\Omega)} \le R_0 \quad \text{and} \quad \|w(\cdot,t)\|_{L^\infty(\Omega)} \le R_0 \quad \text{for all } t\in(0,T) \Big\}$$

of the Banach space

$$X := C^0(\bar\Omega\times[0,T]) \times C^0(\bar\Omega\times[0,T]).$$

Given $(\bar u,\bar w)\in S$, we then define $F(\bar u,\bar w)\equiv(u,w)$ by first letting $v:(0,T)\to W^{2,p}(\Omega)$ solve

$$\begin{cases} -D_v\Delta v + \alpha v = \bar u_+ g(\bar u_+,\bar w_+), & x\in\Omega,\ t\in(0,T), \\ \frac{\partial v}{\partial\nu} = 0, & x\in\partial\Omega,\ t\in(0,T), \end{cases} \tag{2.6}$$

in the standard sense of strong solutions ([11]), and by thereafter introducing

$$\begin{aligned} u(\cdot,t) := e^{tD_u\Delta}u_0 \quad &- \quad \chi\int_0^t e^{(t-s)D_u\Delta}\nabla\cdot(\bar u\nabla v)(\cdot,s)ds \\ &+ \quad \int_0^t e^{(t-s)D_u\Delta} f(\bar u_+,v,\bar w_+)(\cdot,s)ds, \qquad t\in(0,T), \end{aligned} \tag{2.7}$$

as well as

$$w(\cdot,t) := e^{tD_w\Delta}w_0 + \int_0^t e^{(t-s)D_w\Delta} h(\bar u_+,v,\bar w_+)(\cdot,s)ds, \qquad t\in(0,T), \tag{2.8}$$

where $\xi_+ := \max\{\xi,0\}$ for $\xi\in\mathbb{R}$, and where to verify well-definedness of u and w we note that a standard reasoning based on the continuity of $\bar u$ and $\bar w$ guarantees that v belongs to $C^0([0,T];W^{2,p}(\Omega))$, and that $v\ge0$ due to a straightforward comparison-type argument.

To show that F maps S into itself whenever T is suitably small, we first observe that thanks to (1.7), (1.8) and the inclusion $(\bar u,\bar w)\in S$,

$$0 \le \bar u_+ g(\bar u_+,\bar w_+) \le \bar u_+ g_1(\bar w_+) \le R_0 g_1(R_0), \tag{2.9}$$

which together with (2.6) and elliptic regularity theory as well as (2.4) ensures that

$$\|v(\cdot,t)\|_{W^{1,\infty}(\Omega)} \le c_4 := c_2\cdot R_0 g_1(R_0)\cdot|\Omega|^{\frac1p} \qquad \text{for all } t\in(0,T). \tag{2.10}$$

Moreover, in view of (2.7) we have

$$\begin{aligned} \|u(\cdot,t)\|_{L^\infty(\Omega)} \quad &\le \quad \|e^{tD_u\Delta}u_0\|_{L^\infty(\Omega)} + \chi\int_0^t \|e^{(t-s)D_u\Delta}\nabla\cdot(\bar u\nabla v)(\cdot,s)\|_{L^\infty(\Omega)}ds \\ &\qquad + \int_0^t \|e^{(t-s)D_u\Delta} f(\bar u_+,v,\bar w_+)(\cdot,s)\|_{L^\infty(\Omega)}ds \\ &:= \quad I_1(t)+I_2(t)+I_3(t) \end{aligned} \tag{2.11}$$

for all $t \in (0,T)$, where the parabolic maximum principle readily shows that

$$I_1(t) \le \|u_0\|_{L^\infty(\Omega)} \qquad \text{for all } t \in (0,T). \tag{2.12}$$

Apart from that, according to (2.3), (2.5), the inclusion $(\bar{u},\bar{w}) \in S$ and (2.10), we find that

$$\begin{aligned}
I_2(t) &\le c_1c_3\chi \int_0^t (t-s)^{-\frac12-\theta} \|(\bar{u}\nabla v)(\cdot,s)\|_{L^p(\Omega)} ds \\
&\le c_1c_3\chi \int_0^t (t-s)^{-\frac12-\theta} \|\bar{u}(\cdot,s)\|_{L^\infty(\Omega)} \cdot \|\nabla v(\cdot,s)\|_{L^\infty(\Omega)} \cdot |\Omega|^{\frac1p} ds \\
&\le c_1c_3\chi \cdot R_0 \cdot c_4 \cdot |\Omega|^{\frac1p} \int_0^t (t-s)^{-\frac12-\theta} ds \\
&\le \frac{c_1c_3c_4\chi R_0|\Omega|^{\frac1p}}{\frac12-\theta} \cdot T^{\frac12-\theta} \qquad \text{for all } t \in (0,T),
\end{aligned} \tag{2.13}$$

and due to (1.5), (1.6) and the maximum principle, again since $(\bar{u},\bar{w}) \in S$ we see that

$$\begin{aligned}
I_3(t) &\le \int_0^t \|f(\bar{u}_+, v, \bar{w}_+)(\cdot,s)\|_{L^\infty(\Omega)} ds \\
&\le \int_0^t \max\{\lambda,\ \|(\bar{u}_+ f_0(\bar{w}_+))(\cdot,s)\|_{L^\infty(\Omega)}\} ds \\
&\le \max\{\lambda,\ R_0 f_0(R_0)\} \cdot T \qquad \text{for all } t \in (0,T).
\end{aligned}$$

Combining this with (2.12)-(2.13), from (2.11 we obtain that

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} \le \|u_0\|_{L^\infty(\Omega)} + \frac{c_1c_3c_4\chi R_0|\Omega|^{\frac1p}}{\frac12-\theta} \cdot T^{\frac12-\theta} + \max\{\lambda,\ R_0 f_0(R_0)\} \cdot T \qquad \text{for all } t \in (0,T), \tag{2.14}$$

and using (1.9), (1.10) and (2.10) we similarly find that

$$\|w(\cdot,t)\|_{L^\infty(\Omega)} \le \|w_0\|_{L^\infty(\Omega)} + \max\{\beta(c_4+1),\ h_0(R_0)\} \cdot T \qquad \text{for all } t \in (0,T). \tag{2.15}$$

Therefore, if we take $T_1 = T_1(R_0) \in (0,1)$ sufficiently small such that

$$\frac{c_1c_3c_4\chi R_0|\Omega|^{\frac1p}}{\frac12-\theta} \cdot T_1^{\frac12-\theta} + \max\{\lambda,\ R_0 f_0(R_0)\} \cdot T_1 + \max\{\beta(c_4+1),\ h_0(R_0)\} \cdot T_1 < 1,$$

then from (2.14), (2.15) and the definition of R_0 we infer that whenever $T \in (0,T_1)$,

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} \le R_0 \quad \text{and} \quad \|w(\cdot,t)\|_{L^\infty(\Omega)} \le R_0 \qquad \text{for all } t \in (0,T),$$

and that hence, indeed, F maps S into itself for any such T. Likewise, a straighforward modification of the above reasoning finally yields $T = T(R_0) \in (0,T_1)$ with the property that, in fact, F even acts as a contraction on S and hence possesses a fixed point $(u,w) \in S$.

A standard argument now reveals that with v as accordingly determined through (2.6), $u \in L^\infty(\Omega \times$

$(0,T)) \cap L^2((0,T);W^{1,2}(\Omega))$ and $w \in L^\infty(\Omega \times (0,T)) \cap L^2((0,T);W^{1,2}(\Omega))$ solve the two initial-boundary value problems in

$$\begin{cases} u_t = D_u\Delta u - \chi\nabla\cdot(u\nabla v) + f(u_+,v,w_+), & x\in\Omega,\ t\in(0,T),\\ w_t = D_w\Delta w + h(u_+,v,w_+), & x\in\Omega,\ t\in(0,T),\\ \frac{\partial u}{\partial\nu} = \frac{\partial w}{\partial\nu} = 0, & x\in\partial\Omega,\ t\in(0,T),\\ u(x,0)=u_0(x), \quad w(x,0)=w_0(x), & x\in\Omega. \end{cases} \tag{2.16}$$

in the natural weak sense specified, e.g., in [29]. In view of boundedness of $u\nabla v$ and f in $L^\infty(\Omega)$, a standard result on Hölder regularity in quasi-linear parabolic equations [29, Theorem 1.3, Remark 1.4] therefore becomes applicable so as to yield $\gamma \in (0,1)$ such that $u \in C^{\gamma,\frac{\gamma}{2}}(\overline{\Omega}\times[0,T])$, whereupon a straightforward bootstrap procedure reveals that actually u and w belong to $C^0(\overline{\Omega}\times[0,T]) \cap C^{2,1}(\overline{\Omega}\times(0,T))$, that v lies in $C^{2,0}(\overline{\Omega}\times(0,T))$, and that (u,v,w) solves (2.16) and (2.6) in the classical sense in $\Omega\times(0,T)$. In particular, this enables us to twice invoke the parabolic maximum principle to conclude that besides v, also w and u are both nonnegative in $\Omega\times(0,T)$, and that hence (u,v,w) in fact forms a classical solution of (1.3) in $\Omega\times(0,T)$. The extensibility of this solution, up to some $T_{max}\in(0,\infty]$ fulfilling (2.2), follows from the exclusive dependence of T on (u_0,w_0) through its norm in $L^\infty(\Omega)\times L^\infty(\Omega)$, combined with the fact that thanks to the elliptic comparison principle and (1.8), v remains bounded as long as u and w are bounded.

It remains to observe that uniqueness of solutions within the class of nonnegative functions fulfilling (2.1) can be verified by means of a fairly standard testing procedure, as detailed for related problems e.g. in [35] and in [38], and that therefore $(u(\cdot,t),v(\cdot,t),w(\cdot,t))$ must inherit radial symmetry from u_0 and w_0. □

Without further explicit mentioning, throughout the sequel we shall refer to the above solution whenever $\chi>0$ and $u(u_0,w_0)$ satisfies (1.11).

3 A lower bound for w and an L^p estimate for v for small times

In order to create an appropriate framework for our qualitative analysis, let us introduce the conditions

$$\int_\Omega u_0 \le m \tag{3.1}$$

as well as

$$w_0(x) \ge \ell \qquad \text{for all } x\in\Omega \tag{3.2}$$

and

$$w_0(x) \le L \qquad \text{for all } x\in\Omega, \tag{3.3}$$

with positive parameters m,ℓ and L to be commented on in more detail below.

In this setting, we can readily derive a statement on mass control within short time intervals in the following quantitative manner.

Lemma 3.1 *Let $m > 0$. Then if $\chi \in \mathbb{R}$, and if u_0 and w_0 satisfy (1.11) as well as (3.1), it follows that*

$$\int_\Omega u(\cdot,t) \le 2m \qquad \text{for all } t \in \Big(0\,,\, \min\Big\{\frac{m}{\lambda|\Omega|}\,,\, T_{max}\Big\}\Big). \tag{3.4}$$

Proof. According to (1.6), an integration of the first equation in (1.3) shows that

$$\frac{d}{dt}\int_\Omega u = \int_\Omega f(u,v,w) \le \lambda|\Omega| \qquad \text{for all } t \in (0,T_{max})$$

and hence

$$\int_\Omega u(\cdot,t) \le \int_\Omega u_0 + \lambda|\Omega|t \qquad \text{for all } t \in (0,T_{max}),$$

which due to (3.1) immediately results in (3.4). □

As a preparation for our subsequent selections of parameters, let us recall two standard results from elliptic and parabolic regularity theory.

Lemma 3.2 *Let $p \ge 1$ be such that $p < \frac{n}{n-2}$. Then there exists $K_1(p) > 0$ such that*

$$\|\varphi\|_{L^p(\Omega)} \le K_1(p)\|-D_v\Delta v + \alpha v\|_{L^1(\Omega)} \qquad \text{for all } \varphi \in C^2(\overline{\Omega}) \text{ fulfilling } \tfrac{\partial\varphi}{\partial\nu} = 0 \text{ on } \partial\Omega. \tag{3.5}$$

Proof. This is a classical result from the regularity theory of elliptic boundary value problems with inhomogeneities in L^1 spaces ([7]). □

Lemma 3.3 *Let $p \ge 1$. Then there exists $K_2(p) > 0$ such that*

$$\|e^{D_w t\Delta}\varphi\|_{L^\infty(\Omega)} \le K_2(p)t^{-\frac{n}{2p}}\|\varphi\|_{L^p(\Omega)} \qquad \text{for all } \varphi \in C^0(\overline{\Omega}) \text{ and any } t \in (0,1), \tag{3.6}$$

where $(e^{t\Delta})_{t\ge 0}$ denotes the Neumann heat semigroup over Ω.

Proof. The claimed inequality describes a well-known smoothing property of the heat semigroup (see e.g. [39]). □

In combining the latter two properties to derive an upper bound for w and an L^p bound for v, again for suitably small times, we will make essential use of our overall assumption that $n \le 3$:

Lemma 3.4 *Let $m > 0, L > 0$ and $p \in (\frac{n}{2}, \frac{n}{n-2})$. Then there exist $t_\star = t_\star(m,L,p) > 0$ and $M = M(m,L,p) > 0$ with the property that whenever $\chi \in \mathbb{R}$ and u_0 and w_0 are such that (1.11) as well as (3.1) and (3.3) hold, we have*

$$\|w(\cdot,t)\|_{L^\infty(\Omega)} \le 2L \qquad \text{for all } t \in \Big(0, \min\{t_\star, T_{max}\}\Big) \tag{3.7}$$

and

$$\|v(\cdot,t)\|_{L^p(\Omega)} \le M \qquad \text{for all } t \in \Big(0, \min\{t_\star, T_{max}\}\Big). \tag{3.8}$$

Proof. Given $m>0, L>0$ and $p\in(\frac{n}{2},\frac{n}{n-2})$, we let

$$t_\star \equiv t_\star(m,L,p) := \left\{ \frac{m}{\lambda|\Omega|}\ ,\ 1\ ,\ \left\{ \frac{(1-\frac{n}{2p})L}{2\beta K_2(p)\cdot\Big(2K_1(p)g_1(2L)m+|\Omega|^{\frac{1}{p}}\Big)} \right\}^{\frac{1}{1-\frac{n}{2p}}} \right\}, \tag{3.9}$$

where $K_1(p)$ and $K_2(p)$ denote the constants provided by Lemma 3.2 and Lemma 3.3, respectively. Then supposing that $\chi\in\mathbb{R}$ and that u_0 and w_0 satisfy (1.11), (3.1) and (3.3), we see from the latter that

$$T := \sup\left\{ \widetilde{T}\in\Big(0,\min\{t_\star,T_{max}\}\Big)\ \Bigg|\ \|w(\cdot,t)\|_{L^\infty(\Omega)}<2L \qquad \text{for all } t\in[0,\widetilde{T}) \right\} \tag{3.10}$$

is well-defined and positive, and we claim that actually $T=\min\{t_\star,T_{max}\}$.

To see this, assuming on the contrary that $T<\min\{t_\star,T_{max}\}$, we would firstly obtain that due to Lemma 2.1, w is continuous at $t=T$ and hence

$$\|w(\cdot,T)\|_{L^\infty(\Omega)}=2L. \tag{3.11}$$

On the other hand, the second equation in (1.3) together with (1.8) and our definition of T implies that

$$\begin{aligned} -D_v\Delta v+\alpha v &= ug(u,w) \\ &\le ug_1(w) \\ &\le g_1(2L)u \qquad \text{in } \Omega\times(0,T), \end{aligned}$$

whereas Lemma 3.1 asserts that

$$\int_\Omega u(\cdot,t)\le 2m \qquad \text{for all } t\in(0,T)$$

due to (3.1) and the first restriction on $t_\star$ contained in (3.9). Accordingly, since $p<\frac{n}{n-2}$ we may invoke Lemma 3.2 to infer that

$$\begin{aligned} \|v(\cdot,t)\|_{L^p(\Omega)} &\le K_1(p)g_1(2L)\|u(\cdot,t)\|_{L^1(\Omega)} \\ &\le 2K_1(p)g_1(2L)m \qquad \text{for all } t\in(0,T). \end{aligned} \tag{3.12}$$

Next, by means of a variation-of-constants formula associated with the third equation in (1.3) we can rely on the ordering property of $(e^{D_w t\Delta})_{t\ge0}$ and on (3.3) and (1.10) in estimating

$$\begin{aligned} w(\cdot,t) &= e^{D_w t\Delta}w_0+\int_0^t e^{D_w(t-s)\Delta}h\Big(u(\cdot,s),v(\cdot,s),w(\cdot,s)\Big)ds \\ &\le \|w_0\|_{L^\infty(\Omega)}+\int_0^t e^{D_w(t-s)\Delta}\Big\{\beta\cdot\Big(v(\cdot,s)+1\Big)\Big\}ds \\ &\le L+\beta\int_0^t \Big\|e^{D_w(t-s)\Delta}\Big(v(\cdot,s)+1\Big)\Big\|_{L^\infty(\Omega)}ds \qquad \text{for all } t\in(0,T_{max}), \end{aligned} \tag{3.13}$$

where thanks to (3.12) and Lemma 3.3, the latter being applicable due to the condition $t_\star \le 1$ asserted by (3.9), for all $t \in [0,T]$ we have

$$\begin{aligned}
\beta \int_0^t \Big\| e^{D_w(t-s)\Delta}\Big(v(\cdot,s)+1\Big)\Big\|_{L^\infty(\Omega)} ds &\le \beta K_2(p) \int_0^t (t-s)^{-\frac{n}{2p}} \|v(\cdot,s)+1\|_{L^p(\Omega)} ds \\
&\le \beta K_2(p) \int_0^t (t-s)^{-\frac{n}{2p}} \Big\{ \|v(\cdot,s)\|_{L^p(\Omega)} + |\Omega|^{\frac{1}{p}} \Big\} ds \\
&\le \beta K_2(p) \cdot \Big\{ 2K_1(p) g_1(2L) m + |\Omega|^{\frac{1}{p}} \Big\} \cdot \int_0^t (t-s)^{-\frac{n}{2p}} ds \\
&= \beta K_2(p) \cdot \Big\{ 2K_1(p) g_1(2L) m + |\Omega|^{\frac{1}{p}} \Big\} \cdot \frac{t^{1-\frac{n}{2p}}}{1-\frac{n}{2p}},
\end{aligned}$$

because $p > \frac{n}{2}$. In light of the third restriction on $t_\star$ entailed by (3.9), from (3.13) and the nonnegativity of w we thus obtain that

$$\begin{aligned}
\|w(\cdot,t)\|_{L^\infty(\Omega)} &\le L + \beta K_2(p) \cdot \Big\{ 2K_1(p) g_1(2L) m + |\Omega|^{\frac{1}{p}} \Big\} \cdot \frac{t_\star^{1-\frac{n}{2p}}}{1-\frac{n}{2p}} \\
&\le L + \frac{L}{2} \qquad \text{for all } t \in [0,T],
\end{aligned}$$

which contradicts (3.11) and thereby verifies that indeed $T = \min\{t_\star, T_{max}\}$. By (3.10), this directly shows (3.7), whereas (3.8) results from (3.12) if we let $M \equiv M(m,L,p) := 2K_1(p) g_1(2L) m$. □

When suitably utilized in the course of a comparison argument, the upper bound for w provided by (3.7) can be seen to actually imply a pointwise lower estimate for the same solution component:

Lemma 3.5 *Let $m > 0, \ell > 0$ and $L > 0$. Then there exists $t_{\star\star} = t_{\star\star}(m,\ell,L) > 0$ such that if $\chi \in \mathbb{R}$ and (1.11), (3.1), (3.2) as well as (3.3) hold, then*

$$w(x,t) \ge \frac{\ell}{2} \qquad \textit{for all } x \in \Omega \textit{ and any } t \in \Big(0, \min\{t_{\star\star}, T_{max}\}\Big). \tag{3.14}$$

Proof. Picking an arbitrary $p \in (\frac{n}{2}, \frac{n}{n-2})$, with $t_\star(m,L,p) > 0$ as given by Lemma 3.4 we define

$$t_{\star\star} \equiv t_{\star\star}(m,\ell,L) := \min\Big\{ t_\star(m,L,p)\, , \, \frac{\ell}{2h_0(2L)} \Big\}. \tag{3.15}$$

Then assuming $\chi \in \mathbb{R}$ to be given and u_0 and w_0 to satisfy (1.11), (3.1), (3.2) and (3.3), from Lemma 3.4 we know that since $t_{\star\star} \le t_\star(m,L,p)$ we have

$$w(x,t) \le 2L \qquad \text{for all } x \in \Omega \text{ and } t \in \Big(0, \min\{t_{\star\star}, T_{max}\}\Big).$$

Therefore, due to (1.9) the third equation in (1.3) implies that

$$\begin{aligned}
w_t &= D_w \Delta w + h(u,v,w) \\
&\ge D_w \Delta w - h_0(w) \\
&\ge D_w \Delta w - h_0(2L) \qquad \text{in } \Omega \times \Big(0, \min\{t_{\star\star}, T_{max}\}\Big)
\end{aligned}$$

and that hence, in view of a simple comparison argument and (3.2),

$$\begin{aligned} w(x,t) &\geq \inf_{y\in\Omega} w_0(y) - h_0(2L)\cdot t \\ &\geq \ell - h_0(2L)\cdot t \qquad \text{for all } x\in\Omega \text{ and } t\in\Big(0,\min\{t_{\star\star},T_{max}\}\Big). \end{aligned}$$

As $h_0(2L)\cdot t_{\star\star} \leq \frac{\ell}{2}$ by (3.15), this already establishes (3.14). □

4 Unbounded radial solutions. Proof of Theorem 1.1

Our goal in this section consists in deriving a suitable parabolic differential inequality for the mass accumulation function $z:\ [0,R^n]\times[0,T_{max})\to[0,\infty)$ defined by

$$z(s,t) := \frac{1}{n|B_1(0)|}\int_{B_{\sqrt[n]{s}}(0)} u(x,t)dx, \qquad s\in[0,R^n],\ t\in[0,T_{max}), \tag{4.1}$$

where our particular ambition will be to make sure that the respective constants appearing therein will depend on the initial data only through the parameters in (3.1), (3.2) and (3.3), thus particularly being essentially independent of how far u_0 may reflect concentration of mass near the origin. We note that basing blow-up arguments on functions of the form (4.1) has a long history in the analysis of chemotaxis systems ([16], [5], [22]), also accounting for more involved cell migration mechanisms or also additional cell proliferation ([8], [4], [10]); due to an apparently lacking robustness with regard to the introduction of further complexity, corresponding blow-up proofs for a system involving additional components seem restricted to quite exceptional situations ([34]).

In the present context, this cumulated density can readily be verified to satisfy a scalar parabolic equation which, besides including a diffusion degeneracy of dimension-dependent strength, in its potentially destabilizing taxis-related part contains a nonlocal nonlinearity:

Lemma 4.1 *Suppose that $\chi\in\mathbb{R}$ and that (1.11) holds, and let z be as defined in (4.1). Then*

$$\begin{aligned} z_t &= n^2 D_u s^{2-\frac{2}{n}} z_{ss} + \frac{\chi}{D_v|B_1(0)|}\cdot z_s\cdot\int_{B_{s^{1/n}}(0)} u(\cdot,t)g\Big(u(\cdot,t),w(\cdot,t)\Big) \\ &\quad -\frac{\alpha\chi}{D_v|B_1(0)|}\cdot z_s\cdot\int_{B_{s^{1/n}}(0)} v(\cdot,t) + \frac{1}{n|B_1(0)|}\int_{B_{s^{1/n}}(0)} f\Big(u(\cdot,t),v(\cdot,t),w(\cdot,t)\Big) \end{aligned} \tag{4.2}$$

in $(0,R^n)\times(0,T_{max})$.

Proof. Using the standard notation in radial variables, $(u,v,w)=(u,v,w)(r,t)$ for $r=|x|\in[0,R]$ and $t\in[0,T_{max})$, we differentiate

$$z(s,t) = \int_0^{s^{\frac{1}{n}}} \rho^{n-1}u(\rho,t)d\rho, \qquad s\in[0,\mathbb{R}^n],\ t\in[0,T_{max}),$$

to see that

$$z_s(s,t) = \frac{1}{n}u(r,t) \quad \text{and} \quad z_{ss}(s,t) = \frac{1}{n^2}s^{\frac{1}{n}-1}u_r(r,t), \qquad s=r^n\in(0,R^n),\ t\in(0,T_{max}),$$

and that thus, by (1.3),

$$\begin{aligned}
z_t(s,t) &= \int_0^{s^{\frac{1}{n}}} \rho^{n-1} u_t(\rho,t)d\rho \\
&= \int_0^{s^{\frac{1}{n}}} \rho^{n-1} \cdot \Big\{ D_u \rho^{1-n}(\rho^{n-1}u_r)_r - \chi\rho^{1-n}(\rho^{n-1}uv_r)_r + f(u,v,w)\Big\} d\rho \\
&= D_u \cdot s^{1-\frac{1}{n}} u_r - \chi s^{1-\frac{1}{n}} uv_r + \int_0^{s^{\frac{1}{n}}} \rho^{n-1} f(u,v,w)d\rho \\
&= D_u \cdot n^2 s^{2-\frac{2}{n}} z_{ss} - n\chi s^{1-\frac{1}{n}} z_s v_r + \int_0^{s^{\frac{1}{n}}} \rho^{n-1} f(u,v,w)d\rho
\end{aligned}$$

for all $s \in (0,R^n)$ and $t \in (0,T_{max})$. As the second equation in (1.3) shows that $D_v(r^{n-1}v_r)_r = \alpha r^{n-1}v - r^{n-1}ug(u,w)$ for all $r \in (0,R)$ and $t \in (0,T_{max})$ and hence

$$s^{1-\frac{1}{n}} v_r = r^{n-1}v_r = \frac{\alpha}{D_v}\int_0^{s^{\frac{1}{n}}} \rho^{n-1} v d\rho - \frac{1}{D_v}\int_0^{s^{\frac{1}{n}}} \rho^{n-1} ug(u,w)d\rho, \qquad s = r^n \in (0,R^n),\ t \in (0,T_{max}),$$

this readily implies (4.2). $\Box$

An observation of crucial importance for our subsequent reasoning now reveals that thanks to our preparations from Section 3, and especially of Lemma 3.5, the nonlocal contributions to (4.2) can be estimated in terms of exclusively local expressions that will turn out as quite conveniently manageable; in particular, the cross-diffusive remnant entering the accordingly obtained parabolic inequality for z attains the Burgers-type functional form familiar from classical Keller-Segel analysis ([16], [5]) whenever the chemotactic sensitivity parameter χ is positive. We emphasize, however, that again the following statement addresses small time intervals only, the length of which once more depending on the parameters in (3.1), (3.2) and (3.3):

Lemma 4.2 *Let $m > 0, \ell > 0$ and $L > 0$, and suppose that $\varepsilon > 0$. Then there exist positive constants $t_{\star\star\star} = t_{\star\star\star}(m,\ell,L,\varepsilon)$, $\gamma_1 = \gamma_1(\ell)$, $\gamma_2 = \gamma_2(m,L,\varepsilon)$ and $\gamma_3 = \gamma_3(L)$ such that if $\chi > 0$ and if (3.1), (3.2) and (3.3) hold, then the function z introduced in (4.1) satisfies*

$$z_t \ge n^2 D_u s^{2-\frac{2}{n}} z_{ss} + \gamma_1 \chi z z_s - \gamma_2 \chi s^{\frac{2}{n}-\varepsilon} z_s - \gamma_3 z \qquad in\ (0,R^n) \times \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big). \tag{4.3}$$

Proof. Using that $\frac{p-1}{p} \to \frac{2}{n}$ as $p \nearrow \frac{n}{n-2}$, given $\varepsilon > 0$ we can fix $p = p(\varepsilon) \in (\frac{n}{2}, \frac{n}{n-2})$ such that

$$\frac{p-1}{p} \ge \frac{2}{n} - \varepsilon, \tag{4.4}$$

and for $m > 0, \ell > 0$ and $L > 0$ we thereafter let

$$t_{\star\star\star} \equiv t_{\star\star\star}(m,\ell,L,\varepsilon) := \min\Big\{ t_\star(m,L,p(\varepsilon)),\, t_{\star\star}(m,\ell,L) \Big\} \tag{4.5}$$

with $t_\star(\cdot,\cdot,\cdot)$ and $t_{\star\star}(\cdot,\cdot,\cdot)$ as determined by Lemma 3.4 and Lemma 3.5, respectively. Then taking any $\chi > 0$ and (u_0, w_0) fulfilling (1.11), (3.1), (3.2) and (3.3), from Lemma 3.5 and the second restriction in (4.5) we know that $w \geq \frac{\ell}{2}$ in $\Omega \times (0, \min\{t_{\star\star\star}, T_{max}\})$, so that by (1.7),

$$g(u,w) \geq g_0(w) \geq g_0\Big(\frac{\ell}{2}\Big) \qquad \text{in } \Omega \times \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big).$$

Since evidently z_s is nonnegative, the second summand on the right of (4.2) can therefore be estimated according to

$$\begin{aligned} \frac{\chi}{D_v|B_1(0)|} \cdot z_s \cdot \int_{B_{s^{1/n}}(0)} ug(u,w) &\geq \frac{g_0(\frac{\ell}{2})\chi}{D_v|B_1(0)|} \cdot z_s \cdot \int_{B_{s^{1/n}}(0)} u \\ &= \frac{ng_0(\frac{\ell}{2})}{D_v} \cdot \chi z z_s \qquad \text{in } (0,R^n) \times \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big). \end{aligned} \tag{4.6}$$

Next, using that (4.5) warrants that also $t_{\star\star\star} \leq t_\star(m, L, p(\varepsilon))$, we may invoke Lemma 3.4 to see that thanks to the Hölder inequality and (4.4),

$$\begin{aligned} \int_{B_{s^{1/n}}(0)} v &\leq \Big\{\int_\Omega v^p\Big\}^{\frac{1}{p}} \cdot \Big|B_{s^{\frac{1}{n}}}(0)\Big|^{\frac{p-1}{p}} \\ &\leq M(m,L,p) \cdot \Big|B_{s^{\frac{1}{n}}}(0)\Big|^{\frac{p-1}{p}} \\ &= M(m,L,p) \cdot |B_1(0)|^{\frac{p-1}{p}} \cdot s^{\frac{p-1}{p}} \\ &\leq M(m,L,p) \cdot |B_1(0)|^{\frac{p-1}{p}} \cdot (R^n)^{\frac{p-1}{p}-(\frac{2}{n}-\varepsilon)} \cdot s^{\frac{2}{n}-\varepsilon} \end{aligned}$$

for all $s \in (0, R^n)$ and $t \in (0, \min\{t_{\star\star\star}, T_{max}\})$, so that in (4.2) we have

$$\frac{\alpha\chi}{D_v|B_1(0)|} \cdot z_s \cdot \int_{B_{s^{1/n}}(0)} v \leq \frac{\alpha M(m,L,p)(R^n)^{\frac{p-1}{p}-(\frac{2}{n}-\varepsilon)}}{D_v|B_1(0)|^{\frac{1}{p}}} \cdot \chi s^{\frac{2}{n}-\varepsilon} z_s \qquad \text{in } (0,R^n) \times \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big). \tag{4.7}$$

Finally, as Lemma 3.4 ensures that $w \leq 2L$ in $\Omega \times (0, \min\{t_{\star\star\star}, T_{max}\})$ and hence

$$f(u,v,w) \geq -uf_0(w) \geq -f_0(2L)u \qquad \text{in } \Omega \times \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big)$$

by (1.5), the rightmost summand in (4.2) can be controlled from below according to

$$\frac{1}{n|B_1(0)|} \int_{B_{s^{1/n}}(0)} f(u,v,w) \geq -\frac{f_0(2L)}{n|B_1(0)|} \int_{B_{s^{1/n}}(0)} u = -f_0(2L)z \quad \text{in } (0,R^n) \times \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big).$$

Together with (4.6) and (4.7), this entails (4.3) upon evident choices of γ_1, γ_2 and γ_3. $\square$

By modifying previous methods concerned with blow-up detections in simpler Keller-Segel systems ([5], [42], [41]), the testing procedure in the next argument focuses on the behavior of z near the origin. As a consequence, this turns (4.3) into an ODI that describes the evolution of a correspondingly obtained functional as follows.

Lemma 4.3 *Suppose that $m > 0, \ell > 0, L > 0$ and $\varepsilon \in (0, \frac{2}{n}]$, and let $t_{\star\star\star} = t_{\star\star\star}(m, \ell, L, \varepsilon) > 0$ as well as $\gamma_1 = \gamma_1(\ell) > 0, \gamma_2 = \gamma_2(m, L, \varepsilon) > 0$ and $\gamma_3 = \gamma_3(L) > 0$ be as given by Lemma 4.2. Then whenever $\chi > 0$ and (1.11), (3.1), (3.2) and (3.3) are satisfied, the function z defined in (4.1) has the property that for any choice of $s_0 \in (0, R^n)$,*

$$\begin{aligned}\frac{d}{dt}\int_0^{s_0}(s_0 - s)z(s,t)ds \ &\geq \ -2n(n-1)D_u\int_0^{s_0} s^{1-\frac{1}{n}}z(s,t)ds + \frac{\gamma_1\chi}{2}\int_0^{s_0} z^2(s,t)ds \\ &\quad -\gamma_2\chi\int_0^{s_0} s^{\frac{2}{n}-\varepsilon}z(s,t)ds \\ &\quad -\gamma_3\int_0^{s_0}(s_0 - s)z(s,t)ds \qquad \textit{for all } t \in \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big). \qquad (4.8)\end{aligned}$$

PROOF. Given $s_0 \in (0, R^n)$, we multiply (4.3) by $s_0 - s$ and integrate over $(0, s_0)$ to see that for all $t \in (0, \min\{t_{\star\star\star}, T_{max}\})$,

$$\begin{aligned}\frac{d}{dt}\int_0^{s_0}(s_0 - s)z \ &\geq \ n^2 D_u\int_0^{s_0}(s_0 - s)s^{2-\frac{2}{n}}z_{ss} + \gamma_1\chi\int_0^{s_0}(s_0 - s)zz_s \\ &\quad -\gamma_2\chi\int_0^{s_0}(s_0 - s)s^{\frac{2}{n}-\varepsilon}z_s - \gamma_3\int_0^{s_0}(s_0 - s)z. \qquad (4.9)\end{aligned}$$

Here we integrate by parts several times to find that since $z_s \geq 0$ in $(0, R^n) \times (0, T_{max})$ and $z(0,t) = 0$ for all $t \in (0, T_{max})$,

$$\begin{aligned}n^2 D_u\int_0^{s_0}(s_0 - s)s^{2-\frac{2}{n}}z_{ss} \ &= \ n^2 D_u\int_0^{s_0} s^{2-\frac{2}{n}}z_s - \Big(2 - \frac{2}{n}\Big)n^2 D_u\int_0^{s_0}(s_0 - s)s^{1-\frac{2}{n}}z_s \\ &\quad +n^2 D_u(s_0 - s)s^{2-\frac{2}{n}}z_s\Big|_{s=0}^{s=s_0} \\ &\geq \ -\Big(2 - \frac{2}{n}\Big)n^2 D_u\int_0^{s_0}(s_0 - s)s^{1-\frac{2}{n}}z_s \\ &= \ -\Big(2 - \frac{2}{n}\Big)n^2 D_u\int_0^{s_0} s^{1-\frac{1}{n}}z + \Big(1 - \frac{2}{n}\Big)\Big(2 - \frac{2}{n}\Big)n^2 D_u\int_0^{s_0}(s_0 - s)s^{-\frac{2}{n}}z \\ &\quad -\Big(2 - \frac{2}{n}\Big)n^2 D_u(s_0 - s)s^{1-\frac{2}{n}}z\Big|_{s=0}^{s=s_0} \\ &\geq \ -\Big(2 - \frac{2}{n}\Big)n^2 D_u\int_0^{s_0} s^{1-\frac{1}{n}}z \qquad \text{for all } t \in \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big)\end{aligned}$$

and

$$\begin{aligned}\gamma_1\chi\int_0^{s_0}(s_0 - s)zz_s \ &= \ \frac{\gamma_1\chi}{2}\int_0^{s_0}(s_0 - s)(z^2)_s \\ &= \ \frac{\gamma_1\chi}{2}\int_0^{s_0} z^2 + \frac{\gamma_1\chi}{2}(s_0 - s)z^2\Big|_{s=0}^{s=s_0} \\ &= \ \frac{\gamma_1\chi}{2}\int_0^{s_0} z^2 \qquad \text{for all } t \in \Big(0, \min\{t_{\star\star\star}, T_{max}\}\Big)\end{aligned}$$

as well as

$$
\begin{aligned}
-\gamma_2\chi\int_0^{s_0}(s_0-s)s^{\frac{2}{n}-\varepsilon}z_s &= -\gamma_2\chi\int_0^{s_0}s^{\frac{2}{n}-\varepsilon}z+\Big(\frac{2}{n}-\varepsilon\Big)\gamma_2\chi\int_0^{s_0}(s_0-s)s^{-\frac{n-2}{n}-\varepsilon}z \\
&\quad -\gamma_2\chi(s_0-s)s^{\frac{2}{n}-\varepsilon}z\Big|_{s=0}^{s=s_0} \\
&\ge -\gamma_2\chi\int_0^{s_0}s^{\frac{2}{n}-\varepsilon}z \qquad \text{for all } t\in\Big(0,\min\{t_{\star\star\star},T_{max}\}\Big),
\end{aligned}
$$

because $\varepsilon\le\frac{2}{n}$. Therefore, (4.9) implies (4.8). $\square$

Suitable interpolation next turns the latter into a quadratically forced autonomous ODI for the functional under consideration, again restricted to small time intervals, and yet containing coefficients that depend on the parameters in (3.1), (3.2) and (3.3):

Lemma 4.4 *Let $m>0,\ell>0$, $L>0$ and $\varepsilon\in(0,\frac{2}{n}]$. Then there exist positive constants $\Gamma_1=\Gamma_1(\ell),\Gamma_2=\Gamma_2(L),\Gamma_3=\Gamma_3(\ell)$ and $\Gamma_4=\Gamma_4(m,\ell,L,\varepsilon)$ such that for any choice of $\chi>0$ and (u_0,w_0) fulfilling (1.11), (3.1), (3.2) and (3.3), with z as in (4.1) we have*

$$
\begin{aligned}
\frac{d}{dt}\int_0^{s_0}(s_0-s)z(s,t)ds &\ge \Gamma_1\cdot\frac{\chi}{s_0^3}\cdot\Big\{\int_0^{s_0}(s_0-s)z(s,t)ds\Big\}^2 \\
&\quad -\Gamma_2\cdot\int_0^{s_0}(s_0-s)z(s,t)ds-\Gamma_3\cdot\frac{s_0^{3-\frac{2}{n}}}{\chi}-\Gamma_4\cdot\chi\cdot s_0^{\frac{n+4}{n}-2\varepsilon} \qquad (4.10)
\end{aligned}
$$

for all $t\in(0,\min\{t_{\star\star\star},T_{max}\})$ and any $s_0\in(0,R^n)$, where $t_{\star\star\star}=t_{\star\star\star}(m,\ell,L,\varepsilon)>0$ is as given by Lemma 4.2.

Proof. With $\gamma_1=\gamma_1(\ell)>0,\gamma_2=\gamma_2(m,L,\varepsilon)>0$ and $\gamma_3=\gamma_3(L)>0$ as introduced in Lemma 4.2, on the right-hand side of (4.8) we use Young's inequality to estimate

$$
\begin{aligned}
2n(n-1)D_u\int_0^{s_0}s^{1-\frac{1}{n}}z &\le \frac{\gamma_1\chi}{8}\int_0^{s_0}z^2+\frac{[2n(n-1)D_u]^2}{4\cdot\frac{\gamma_1\chi}{8}}\int_0^{s_0}s^{2-\frac{2}{n}}ds \\
&= \frac{\gamma_1\chi}{8}\int_0^{s_0}z^2+\frac{8n^2(n-1)^2D_u^2}{\gamma_1\chi}\cdot\frac{s_0^{3-\frac{2}{n}}}{3-\frac{2}{n}} \qquad (4.11)
\end{aligned}
$$

and

$$
\begin{aligned}
\gamma_2\chi\int_0^{s_0}s^{\frac{2}{n}-\varepsilon}z &\le \frac{\gamma_1\chi}{8}\int_0^{s_0}z^2+\frac{(\gamma_2\chi)^2}{4\cdot\frac{\gamma_1\chi}{8}}\int_0^{s_0}s^{\frac{4}{n}-2\varepsilon}ds \\
&= \frac{\gamma_1\chi}{8}\int_0^{s_0}z^2+\frac{2\gamma_2^2\chi}{\gamma_1}\cdot\frac{s_0^{\frac{n+4}{n}-2\varepsilon}}{\frac{n+4}{n}-2\varepsilon} \qquad (4.12)
\end{aligned}
$$

for all $t\in(0,\min\{t_{\star\star\star},T_{max}\})$. As furthermore the Cauchy-Schwarz inequality ensures that

$$
\int_0^{s_0}(s_0-s)z\le s_0\cdot\int_0^{s_0}z\le s_0^{\frac{3}{2}}\cdot\Big\{\int_0^{s_0}z^2\Big\}^{\frac{1}{2}} \qquad \text{for all } t\in\Big(0,\min\{t_{\star\star\star},T_{max}\}\Big)
$$

and hence

$$\frac{\gamma_1\chi}{4}\int_0^{s_0} z^2 \ge \frac{\gamma_1\chi}{4s_0^3}\cdot\left\{\int_0^{s_0}(s_0-s)z\right\}^2 \qquad \text{for all } t\in\Big(0,\min\{t_{\star\star\star},T_{max}\}\Big),$$

on combining this with (4.11), (4.12) and (4.8) we readily derive (4.10) with $\Gamma_1(\ell) := \frac{\gamma_1}{4}, \Gamma_2(L) := \gamma_3, \Gamma_3(\ell) := \frac{8n^2(n-1)^2D_u^2}{\gamma_1\cdot(3-\frac{2}{n})}$ and $\Gamma_4(m,\ell,L,\varepsilon) := \frac{2\gamma_2^2}{\gamma_1\cdot(\frac{n+4}{n}-2\varepsilon)}$. □

Now a task of central importance consists in making sure that for suitably large chemotactic sensitivities χ, and for appropriately small localization parameters s_0, a condition on initial mass concentration in the flavor of that from Theorem 1.1 ensures that the driving nonlinearity on the right-hand side of (4.10) indeed enforces blow-up, and that, first and foremost, this collapse occurs within the considered time interval. An accordingly careful parameter selection forms the technical core of the following key step toward our proof of Theorem 1.1.

Lemma 4.5 *Let $m>0, \ell>0$ and $L>0$. Then there exist $r_0 = r_0(m,\ell,L)\in(0,R)$ and $\chi_0 = \chi_0(m,\ell,L)>0$ with the following property: If $\chi>\chi_0$ and if u_0 and w_0 satisfy (1.11), (3.1), (3.2) and (3.3) as well as*

$$\int_{B_{r_0}(0)} u_0 \ge \frac{m}{2}, \tag{4.13}$$

then $T_{max}<\infty$.

PROOF. We fix any $\varepsilon\in(0,\frac{2}{n})$, and given $m>0,\ell>0$ and $L>0$ we let $\Gamma_1=\Gamma_1(\ell)>0$, $\Gamma_2=\Gamma_2(L)>0$, $\Gamma_3=\Gamma_3(\ell)>0$, $\Gamma_4=\Gamma_4(m,\ell,L,\varepsilon)>0$ and $t_{\star\star\star}=t_{\star\star\star}(m,\ell,L,\varepsilon)>0$ be as thereupon provided by Lemma 4.4 and Lemma 4.2, respectively. Since $\varepsilon<\frac{2}{n}$, we can then pick $s_0=s_0(m,\ell,L)\in(0,R^n)$ small enough such that

$$s_0^{\frac{2}{n}-\varepsilon} \le \frac{m\sqrt{\Gamma_1}}{32\sqrt{6}n|B_1(0)|\sqrt{\Gamma_4}} \tag{4.14}$$

and thereafter choose $\chi_0=\chi_0(m,\ell,L)>0$ large fulfilling

$$\chi_0 \ge \frac{192n|B_1(0)|\Gamma_2 s_0}{m\Gamma_1} \tag{4.15}$$

and

$$\chi_0 \ge \frac{32\sqrt{6}n|B_1(0)|\sqrt{\Gamma_3}s_0^{1-\frac{1}{n}}}{m\sqrt{\Gamma_1}} \tag{4.16}$$

as well as

$$\chi_0 \ge \frac{64n|B_1(0)|s_0}{m\Gamma_1 t_{\star\star\star}}. \tag{4.17}$$

We now suppose that $\chi>\chi_0$ and that (u_0,w_0) satisfies (1.11), (3.1), (3.2), (3.3) and (4.13) with

$$r_0 := \left(\frac{s_0}{2}\right)^{\frac{1}{n}}, \tag{4.18}$$

and claim that then necessarily $T_{max}\le t_{\star\star\star}$.

To verify this, assuming on the contrary that $T_{max} > t_{\star\star\star}$ we would obtain from Lemma 4.4 that with z taken from (4.1),

$$y(t) := \int_0^{s_0} (s_0 - s) z(s,t) ds, \qquad t \in [0, T_{max}),$$

was well-defined on $[0, t_{\star\star\star}]$ with

$$y'(t) \geq \frac{\Gamma_1 \chi}{s_0^3} y^2(t) - \Gamma_2 y(t) - \frac{\Gamma_3 s_0^{3-\frac{2}{n}}}{\chi} - \Gamma_4 \chi s_0^{\frac{n+4}{n} - 2\varepsilon} \qquad \text{for all } t \in (0, t_{\star\star\star}). \tag{4.19}$$

Furthermore, (4.18) and (4.13) warrant that

$$z(s,0) \geq z\Big(\frac{s_0}{2}, 0\Big) = \frac{1}{n|B_1(0)|} \int_{B_{r_0}(0)} u_0 \geq \frac{m}{2n|B_1(0)|} \qquad \text{for all } s \in \Big(\frac{s_0}{2}, R^n\Big),$$

so that

$$\begin{aligned} y(0) &\geq \int_{\frac{s_0}{2}}^{s_0} (s_0 - s) z(s,0) ds \\ &\geq \frac{m}{2n|B_1(0)|} \int_{\frac{s_0}{2}}^{s_0} (s_0 - s) ds \\ &= \frac{m s_0^2}{16 n |B_1(0)|}. \end{aligned} \tag{4.20}$$

Therefore,

$$S := \left\{ \widetilde{T} \in (0, t_{\star\star\star}) \;\middle|\; y(t) > \frac{m s_0^2}{32 n |B_1(0)|} \text{ for all } t \in [0, \widetilde{T}) \right\}$$

is not empty and hence $T := \sup S$ is well-defined with $T \in (0, t_{\star\star\star}]$, and our first goal is to make sure that

$$y'(t) \geq \frac{\Gamma_1 \chi}{2 s_0^3} \cdot y^2(t) \qquad \text{for all } t \in (0, T). \tag{4.21}$$

To see this on the basis of (4.19), we first combine the definition of S with (4.15) to obtain

$$\begin{aligned} \frac{\Gamma_2 y(t)}{\frac{1}{6} \cdot \frac{\Gamma_1 \chi}{s_0^3} \cdot y^2(t)} &= \frac{6 \Gamma_2 s_0^3}{\Gamma_1 \chi y(t)} \\ &< \frac{192 n |B_1(0)| \Gamma_2 s_0}{m \Gamma_1 \chi_0} \\ &\leq 1 \qquad \text{for all } t \in (0, T) \end{aligned}$$

and hence

$$\Gamma_2 y(t) \leq \frac{1}{6} \cdot \frac{\Gamma_1 \chi}{s_0^3} \cdot y^2(t) \qquad \text{for all } t \in (0, T). \tag{4.22}$$

Similarly, (4.16) ensures that

$$\begin{aligned}
\frac{\frac{\Gamma_3 s_0^{3-\frac{2}{n}}}{\chi}}{\frac{1}{6}\cdot\frac{\Gamma_1\chi}{s_0^3}\cdot y^2(t)} &= \frac{6\Gamma_3 s_0^{6-\frac{2}{n}}}{\Gamma_1\chi^2 y^2(t)} \\
&< \frac{6144 n^2 |B_1(0)|^2 \Gamma_3 s_0^{2-\frac{2}{n}}}{m^2\Gamma_1\chi_0^2} \\
&\le 1 \qquad \text{for all } t\in(0,T),
\end{aligned}$$

whereas

$$\begin{aligned}
\frac{\Gamma_4\chi s_0^{\frac{n+4}{n}-2\varepsilon}}{\frac{1}{6}\cdot\frac{\Gamma_1\chi}{s_0^3}\cdot y^2(t)} &= \frac{6\Gamma_4 s_0^{\frac{4n+4}{n}-2\varepsilon}}{\Gamma_1 y^2(t)} \\
&< \frac{6144 n^2 |B_1(0)|^2 \Gamma_4 s_0^{\frac{4}{n}-2\varepsilon}}{m^2\Gamma_1} \\
&\le 1 \qquad \text{for all } t\in(0,T)
\end{aligned}$$

due to (4.14). As thus also

$$\frac{\Gamma_3 s_0^{3-\frac{2}{n}}}{\chi} \le \frac{1}{6}\cdot\frac{\Gamma_1\chi}{s_0^3}\cdot y^2(t) \qquad \text{for all } t\in(0,T)$$

and

$$\Gamma_4\chi s_0^{\frac{n+4}{n}-2\varepsilon} \le \frac{1}{6}\cdot\frac{\Gamma_1\chi}{s_0^3}\cdot y^2(t) \qquad \text{for all } t\in(0,T),$$

in view of (4.22) we infer from (4.19) that indeed (4.21) is valid.

Now since (4.21) in particular entails that y is increasing on $[0,T]$, from this we firstly obtain that in fact $T = t_{\star\star\star}$, and that therefore, secondly, we may integrate (4.21) over $t\in(0,t_{\star\star\star})$ to see that

$$\frac{\Gamma_1\chi}{2s_0^3}\cdot t_{\star\star\star} \le \frac{1}{y(0)} - \frac{1}{y(t_{\star\star\star})} \le \frac{1}{y(0)},$$

which in conjunction with (4.20) and (4.17) leads to the absurd conclusion that

$$\begin{aligned}
t_{\star\star\star} &\le \frac{2s_0^3}{\Gamma_1\chi}\cdot\frac{16n|B_1(0)|}{ms_0^2} \\
&= \frac{32n|B_1(0)|s_0}{m\Gamma_1\chi} \\
&\le \frac{t_{\star\star\star}}{2}
\end{aligned}$$

and thereby shows that actually we must indeed have had $T_{max} \le t_{\star\star\star}$. □

The proof of our main result on singularity formation in the original problem (1.3) hence in essence reduces to a mere reformulation of the above:

PROOF of Theorem 1.1. For fixed positive radial $w_0 \in C^0(\overline{\Omega})$ and $m > 0$, we let $\ell := \inf_{x\in\Omega} w_0(x)$ and $L := \sup_{x\in\Omega} w_0(x)$ and take $r_\star \equiv r_\star(m, w_0) := r_0(m, \ell, L) \in (0, R)$ as well as $\chi_\star \equiv \chi_\star(m, w_0) := \chi_0(m, \ell, L) > 0$ as obtained in Lemma 4.5. Then the latter together with Lemma 2.1 immediately establishes the claim. $\square$

Two fairly straightforward applications of maximum principles finally facilitate the claimed conclusion on unboundedness of the first solution component whenever (1.16) holds:

PROOF of Proposition 1.2. If (1.17) was false, then there would exist $c_1 > 0$ such that

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} \le c_1 \qquad \text{for all } t \in (0, T_{max}), \tag{4.23}$$

whence according to the second equation in (1.3), (1.8) and (1.16) we would have

$$\begin{aligned} -D_v\Delta v + \alpha v &= ug(u,w) \\ &\le ug_1(w) \\ &\le \delta u(w+1) \\ &\le \delta c_1(w+1) \qquad \text{in } \Omega \times (0,T). \end{aligned}$$

As a consequence of the maximum principle, this would entail that

$$\alpha\|v(\cdot,t)\|_{L^\infty(\Omega)} \le \delta c_1 \cdot \Big\{ \|w(\cdot,t)\|_{L^\infty(\Omega)} + 1 \Big\} \qquad \text{for all } t \in (0,T) \tag{4.24}$$

and that thus, by the third equation in (1.3) and (1.10),

$$\begin{aligned} w_t &= D_w\Delta w + h(u,v,w) \\ &\le D_w\Delta w + \beta\cdot(v+1) \\ &\le D_w\Delta w + \frac{\beta\delta c_1}{\alpha}\|w(\cdot,t)\|_{L^\infty(\Omega)} + \frac{\beta\delta c_1}{\alpha} + \beta \qquad \text{for all } x \in \Omega \text{ and } t \in (0,T). \end{aligned}$$

By means of a parabolic comparison argument, from this we could conclude that

$$\begin{aligned} \|w(\cdot,t)\|_{L^\infty(\Omega)} &\le \|w_0\|_{L^\infty(\Omega)} + \int_0^t \Big\{ \frac{\beta\delta c_1}{\alpha}\|w(\cdot,s)\|_{L^\infty(\Omega)} + \frac{\beta\delta c_1}{\alpha} + \beta \Big\} ds \\ &\le \|w_0\|_{L^\infty(\Omega)} + \Big(\frac{\beta\delta c_1}{\alpha} + \beta\Big)\cdot T + \frac{\beta\delta c_1}{\alpha}\int_0^t \|w(\cdot,s)\|_{L^\infty(\Omega)} ds \qquad \text{for all } t \in (0,T), \end{aligned}$$

which due to the Grönwall lemma would entail that

$$\|w(\cdot,t)\|_{L^\infty(\Omega)} \le \Big\{ \|w_0\|_{L^\infty(\Omega)} + \Big(\frac{\beta\delta c_1}{\alpha} + \beta\Big)\cdot T \Big\} \cdot e^{\frac{\beta\delta c_1}{\alpha}\cdot T} \qquad \text{for all } t \in (0,T).$$

Together with (4.23) and (4.24), this would mean that

$$\limsup_{t\nearrow T} \Big\{ \|u(\cdot,t)\|_{L^\infty(\Omega)} + \|v(\cdot,t)\|_{L^\infty(\Omega)} + \|w(\cdot,t)\|_{L^\infty(\Omega)} \Big\} < \infty$$

and thereby contradict (1.15), so that actually the hypothesis (4.23) must have been false. $\square$

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