Asymptotic stability of spatial homogeneity in a haptotaxis model for oncolytic virotherapy

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Abstract

This work considers a model for oncolytic virotherapy, as given by the reaction-diffusion-taxis system

$$\begin{cases} u_t = \Delta u - \nabla \cdot (u\nabla v) - \rho uz, \\ v_t = -(u+w)v, \\ w_t = D_w \Delta w - w + uz, \\ z_t = D_z \Delta z - z - uz + \beta w, \end{cases}$$

in a smoothly bounded domain $\Omega \subset \mathbb{R}^2$, with parameters $D_w > 0, D_z > 0, \beta > 0$ and $\rho \geq 0$.

Previous analysis has asserted that for all reasonably regular initial data, an associated no-flux type initial-boundary value problem admits a global classical solution, and that this solution is bounded if $\beta < 1$, whereas whenever $\beta > 1$ and $\frac{1}{|\Omega|}\int_\Omega u(\cdot,0) > \frac{1}{\beta-1}$, infinite-time blow-up occurs at least in the particular case when $\rho = 0$.

In order to provide an appropriate complement to this, the present work reveals that for any $\rho \geq 0$ and arbitrary $\beta > 0$, at each prescribed level $\gamma \in (0, \frac{1}{(\beta-1)_+})$ one can identify an L^∞-neighborhood of the homogeneous distribution $(u,v,w,z) \equiv (\gamma,0,0,0)$ within which all initial data lead to globally bounded solutions that stabilize toward the constant equilibrium $(u_\infty,0,0,0)$ with some $u_\infty > 0$.

Key words: haptotaxis; boundedness; stability; cooperative parabolic system
MSC (2020): 35B40 (primary); 35B33, 35K57, 35Q92, 92C17 (secondary)

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1 Introduction

Oncolytic virus particles are engineered for killing cancer cells, but they are little harmful to healthy cells. The virions selectively adhere to the surface of cancer cells, then enter tumor cells via endocytosis, enlarge their quantity through replication, and eventually cause the death of tumor cells. Upon lysis of a tumor cell, a lot of new viruses are released, and they continue to infect adjacent tumor cells; the above process will be repeated until all tumor cells are eradicated. Accordingly, the visionary objective in this field is that due to the considerable replication competence of viruses, appropriately arranged treatments might provide efficient alternatives to conventional chemothapy, with all its limitations linked to drug transport ([24], [10]), and viral therapy has indeed already been used in several clinical trails ([3], [6], [14], [21]).

Nevertheless, oncolytic efficacy of this novel therapy is also limited, not only by virus clearance due to various immune responses ([1]), but also by physical barriers such as interstitial fluid pressure and extracellular matrix (ECM) deposit ([35], [38]). In order to figure out the role of the ECM in the spatio-temporal dynamics of virus spread within a macro tissue including cancer cells and evaluate general effectiveness of oncolytic virotherapy, the authors in [2] introduced a reaction-diffusion-taxis model that addresses the interaction between both uninfected and infected cancer cells, as well as ECM and oncolytic virus particles.

By neglecting any possible growth of uninfected tumor cells and ECM, in this study we consider a simplified version of an originally more comprehensive model proposed in [2], and will hence subsequently be concerned with the initial-boundary value problem

$$\begin{cases} u_t = \Delta u - \nabla\cdot(u\nabla v) - \rho uz, & x\in\Omega,\ t>0,\\ v_t = -(u+w)v, & x\in\Omega,\ t>0,\\ w_t = D_w\Delta w - w + uz, & x\in\Omega,\ t>0,\\ z_t = D_z\Delta z - z - uz + \beta w, & x\in\Omega,\ t>0,\\ (\nabla u - u\nabla v)\cdot\nu = \frac{\partial w}{\partial\nu} = \frac{\partial z}{\partial\nu} = 0, & x\in\partial\Omega,\ t>0,\\ u(x,0)=u_0(x),\quad v(x,0)=v_0(x),\quad w(x,0)=w_0(x),\quad z(x,0)=z_0(x), & x\in\Omega, \end{cases} \tag{1.1}$$

in a smoothly bounded domain $\Omega\subset\mathbb{R}^2$, with $\beta>0, D_w>0, D_z>0$ and $\rho\geq 0$, and with the unknown variables u,w,z and v denoting the population densities of uninfected cancer cells, infected cancer cells, virus particles and ECM, respectively. Here as a crucial assumption from [2] that marks a substantial difference between (1.1) and related more classical reaction-diffusion models for virus dynamics ([11], [19]), we emphasize the hypothesis that uninfected cancer cells can bias their motion upward ECM gradients due to attraction by some macromolecules trapped in ECM; due to the fact that the ECM does not move, the resulting cross-diffusive migration is toward a non-diffusible quantity and hence of haptotaxis type.

It is quite precisely this latter circumstance that brings about considerable challenges for the mathematical analysis of (1.1), especially when focusing on questions related to qualitative solution behavior. Indeed, previous studies concerned with related haptotaxis systems have mainly concentrated on establishing mere solution theories ([36], [26], [27], [22], [39], [23]), with the only few exceptions available in the literature addressing rather specific settings ([28], [17], [4]), [29], [13] [15], [37], [9]). After all, the crucial first equation in (1.1) accounts for an essentially superlinear dampening mechanism at least when ρ is positive, and some precedents have indeed revealed some significantly stabilizing effects of either precisely identical ([20], [34]) or related superlinear zero-order degradation terms in contexts of haptotaxis systems ([36], [27], [15], [22], [17]); in fact, it has recently been shown that if an additional logistic-type influence in the style of an extra summand $\mu u(1-u)$ in the first equation from (1.1), then solutions remain bounded and, if moreover $\beta < 1$, even approach the constant state $(1, 0, 0, 0)$ in the large time limit ([5]). In the absence of such further mechanisms, the identification of possible relaxing effects potentially induced by the accordingly remaining and somewhat weaker dampening term $-\rho uz$ seems much less obvious, especially in view of the coupling to the reaction-diffusion subsystem for w and z, which at least in the case $\beta > 1$ may itself apparently exhibit some strong tendency toward destibilization when forced by some appropriate u ([31]).

Correspondingly, beyond a basic result on global smooth solvability in widely arbitrary parameter settings and for all suitably regular initial data ([30]), the knowledge so far available for (1.1) seems restricted to findings either addressing qualitative features less subtle than precise convergence properties, e.g. in the style of pointwise lower bounds or even unboundedness phenomena, or concentrating on parameter constellations in which said (w, z)-subsystem remains subcritical in an appropriate sense. Specifically, in [33] it was seen that when $\rho = 1$, the size of β relative to the value $\beta = 1$ appears to be decisive with regard to the question whether or not solutions may persistently remain above arbitrarily large levels in their cancer cell population component u throughout evolution, and that hence for appropriate efficiency of virotherapy it might be advisable to assert virus reproduction rates fulfilling $\beta > 1$. A yet more drastic phenomenon indicating criticality of $\beta = 1$ has been revealed in the borderline case $\rho = 0$, in which, namely, solutions to (1.1) must be unbounded whenever $\beta > 1$ and $\frac{1}{|\Omega|}\int_\Omega u_0 > \frac{1}{\beta-1}$, whereas in the semitrivial case when $v_0 \equiv 0$, assuming that either $\beta \le 1$, or $\frac{1}{|\Omega|}\int_\Omega u_0 < \frac{1}{\beta-1}$, leads to globally bounded solutions ([31]). In extension of the latter, it has recently been found that also for general $\rho \ge 0$ and arbitrary v_0, the corresponding solution of (1.1) remains bounded when $\beta < 1$ ([32]). Apart from this, some slightly more comprehensive variants of (1.1) have been considered in [12] and [25], where in accordance with one of the models proposed in [2] the inclusion of two further haptotaxis mechanisms, both of infected tumor cells and virions, has been studied with respect to aspects of classical solvability and boundedness in the presence of certain suitably strong further zero-order degradation ([12]), and of global smooth solvability in spatially one-dimensional settings ([25]).

Main result. According to the above, except for the case when $v \equiv 0$ and hence any tactic migration actually is absent, in the case $\beta > 1$ the dynamical features of (1.1) seem widely unexplored in any planar domain; in fact, the existing literature apparently even leaves open the question whether at all some nontrivial bounded solutions can be found in the presence of such supercritical virus production rates. The purpose of the present study is to develop a method capable of asserting that this can indeed be achieved for a considerably large set of initial data which are located in some neighborhood of certain spatially homogeneous distributions. To make this more precise, importing the precise framework underlying the basic theory from [30] we shall henceforth assume that $\Omega \subset \mathbb{R}^2$ is a bounded domain with smooth boundary, and that

$$\begin{cases} u_0, v_0, w_0 \text{ and } z_0 \text{ are nonnegative functions from } \bigcup_{\vartheta\in(0,1)} C^{2+\vartheta}(\overline{\Omega}), \\ \text{with } u_0 \not\equiv 0,\ w_0 \not\equiv 0,\ z_0 \not\equiv 0,\ \sqrt{v_0} \in W^{1,2}(\Omega) \text{ and } \frac{\partial u_0}{\partial\nu} = \frac{\partial v_0}{\partial\nu} = \frac{\partial w_0}{\partial\nu} = \frac{\partial z_0}{\partial\nu} = 0 \text{ on } \partial\Omega, \end{cases} \tag{1.2}$$

recalling that then (1.1) admits a unique global classical solution (cf. also Lemma 2.1 below).

Our main result now makes sure that whenever the corresponding initial deviation from certain constant values is suitably small, these solutions will remain globally bounded, and even approach some constant profiles asymptotically; in fact, we shall see that a statement of this flavor can also be established in the borderline case $\rho = 0$ in which no zero-order degrading influence acts on the resepctive first solution components, and that in this latter case the associated domain of attraction even contains arbitrarily large w_0 and z_0. As our method actually applies to any choice of $\beta > 0$, the following formulation includes the range $\beta < 1$ in which, in fact, a slightly more comprehensive result has already been achieved in [32]:

Theorem 1.1 *Let $\Omega \subset \mathbb{R}^2$ be a bounded domain with smooth boundary, and let $\beta > 0$ and $\gamma \in (0, \frac{1}{(\beta-1)_+})$. Then for each $M > 0$ one can find $\varepsilon = \varepsilon(\beta, \gamma, M) > 0$ with the property that whenever $\rho \ge 0$ and u_0, v_0, w_0 and z_0 are such that (1.2) holds and that*

$$\|u_0 - \gamma\|_{L^\infty(\Omega)} < \varepsilon \tag{1.3}$$

and

$$\|v_0\|_{L^\infty(\Omega)} < \varepsilon \tag{1.4}$$

as well as

$$\|w_0\|_{L^\infty(\Omega)} < \min\Big\{\frac{\varepsilon}{\rho}\, ,\, M\Big\}, \tag{1.5}$$

and

$$\|z_0\|_{L^\infty(\Omega)} < \min\Big\{\frac{\varepsilon}{\rho}\, ,\, M\Big\}, \tag{1.6}$$

there exists $u_\infty > 0$ such that solution of (1.1) satisfies

$$u(\cdot, t) \to u_\infty \qquad \text{in } L^\infty(\Omega) \tag{1.7}$$

and

$$v(\cdot, t) \to 0 \qquad \text{in } L^\infty(\Omega) \tag{1.8}$$

as well as

$$w(\cdot, t) \to 0 \qquad \text{in } L^\infty(\Omega) \tag{1.9}$$

and

$$z(\cdot, t) \to 0 \qquad \text{in } L^\infty(\Omega) \tag{1.10}$$

as $t \to \infty$. Moreover, in the particular case when $\rho = 0$ we have $u_\infty = \overline{u}_0$, so that for any $\gamma \in (0, \frac{1}{(\beta-1)_+})$ the corresponding steady state solution $(\gamma, 0, 0, 0)$ of (1.1) is asymptotically stable with respect to the norm in $(L^\infty(\Omega))^4$ in the above sense.

Organization of the paper. Our strategy will be based on the design of a self-map type reasoning, which presupposes a certain assumption on smallness and decay of z within an appropriate time interval, finally seen to actually be all of $[0, \infty)$ (Definition 3.1), in order to derive appropriate boundedness and stabilization features of the solution as a whole, which especially are consistent with said hypothesis. Mainly due to fairly straightforward implications on pointwise lower bounds for u and uniform decay of v (Lemma 4.1), the core of our analysis will reveal that throughout the interval within which our assumption holds, w and z, along with a transformed version of u, form a subsolution to a cooperative parabolic system (Corollary 4.2). Closing the loop of arguments will thus become possible through a derivation of upper estimates for u, w and, particularly, for z by means of an associated comparison principle (Lemma 4.4). On the basis of further temporally uniform regularity properties thereby implied, as seen through an appropriately organized bootstrap procedure, thanks to a known conditional statement on stabilization in the first solution component with respect to the norm in $L^2(\Omega)$ (Lemma 2.2) the outcome of this key step will be found to entail the claimed main result in Section 5.

2 Preliminaries. Global existence and a conditional stabilization result for u

Let us first recall that the conclusion of [30] asserts global smooth solvability:

Lemma 2.1 *Let $\Omega \subset \mathbb{R}^2$ be a bounded domain with smooth boundary, let $\beta > 0$ and $\rho \geq 0$, and suppose that (u_0, v_0, w_0, z_0) satisfies (1.2). Then the problem (1.1) possesses a uniquely determined classical solution $(u, v, w, z) \in (C^{2,1}(\overline{\Omega} \times [0, \infty)))^4$ for which v is nonnegative, and for which u, w and z are positive in $\overline{\Omega} \times (0, \infty)$.*

Following well-established basic strategy to conveniently reformulate the haptotactic interaction in (1.1), as widely used in related literature ([7], [8], [36], [27]), let us set

$$a := ue^{-v} \tag{2.1}$$

to see on the basis of (1.1) that

$$\begin{cases} a_t = e^{-v}\nabla \cdot (e^v \nabla a) + a(ae^v + w)v - \rho a z, & x \in \Omega, \ t > 0, \\ \frac{\partial a}{\partial \nu} = 0, & x \in \partial\Omega, \ t > 0, \\ a(x, 0) = a_0(x) := u_0(x)e^{-v_0(x)}, & x \in \Omega. \end{cases} \tag{2.2}$$

In order to complete our small list of tokens imported from the literature, let us already here recall from [32] that appropriate assumptions on boundedness of (a, w, z) and decay of v and z are sufficient to ensure stabilization of a in $L^2(\Omega)$. This will be referred to in Section 5 below.

Lemma 2.2 *Let $\beta > 0$, $\gamma > 0$ and $\rho \geq 0$, and suppose that for some initial data filfilling (1.2), the corresponding solution of (1.1) is such that*

$$\sup_{t>0} \Big\{ \|a(\cdot, t)\|_{L^\infty(\Omega)} + \|w(\cdot, t)\|_{L^\infty(\Omega)} + \|z(\cdot, t)\|_{L^\infty(\Omega)} \Big\} < \infty, \tag{2.3}$$

that

$$v(\cdot, t) \to 0 \quad \text{in } L^\infty(\Omega) \qquad \text{as } t \to \infty, \tag{2.4}$$

and that moreover

$$\int_0^\infty \int_\Omega z < \infty. \tag{2.5}$$

Then there exists $u_\infty > 0$ with the property that

$$\|u(\cdot, t) - u_\infty\|_{L^2(\Omega)} \to 0 \qquad \text{as } t \to \infty.$$

Proof. This can be seen by means of a verbatim copy of the reasoning from [32, Lemma 6.5, Lemma 6.6 and Lemma 6.7]. □

3 Some pointwise estimates for u and v

Next intending to set the frame for the announced self-map type argument, we first formulate an observation which, although being quite elementary, contains the origin of our restriction on γ in Theorem 1.1.

Lemma 3.1 *Let $\beta > 0$ and $\gamma \in (0, \frac{1}{(\beta-1)_+})$. Then there exist $K_1(\beta,\gamma) > 0$ and $\delta = \delta(\beta,\gamma) \in (0,1)$ such that*

$$\frac{\gamma}{1-\delta} < K_1(\beta,\gamma) < \frac{\gamma+1-\delta}{\beta}. \tag{3.1}$$

Proof. As our hypothesis $\gamma < \frac{1}{(\beta-1)_+}$ warrants that $\gamma < \frac{\gamma+1}{\beta}$, the number

$$K_1(\beta,\gamma) := \frac{1}{2}\Big(\gamma + \frac{\gamma+1}{\beta}\Big)$$

satisfies $\gamma < K_1(\beta,\gamma) < \frac{\gamma+1}{\beta}$. Therefore, the claim follows by means of an argument based on continuous dependence. $\square$

We can thereby unambiguously formulate the core assumption underlying our subsequent analysis:

Definition 3.1 *Given $\beta > 0$ and $\gamma \in (0, \frac{1}{(\beta-1)_+})$, we let*

$$K_2(\beta,\gamma) := \max\Big\{1\,,\,\frac{1}{K_1(\beta,\gamma)}\Big\} \ge 1,$$

where $K_1(\beta,\gamma) > 0$ and $\delta(\beta,\gamma) \in (0,1)$ are as provided by Lemma 3.1.

Moreover, if $\rho \ge 0$ and $\varepsilon > 0$, and if (u_0, v_0, w_0, z_0) are such that (1.2) and (1.3) and (1.4) as well as

$$\rho \|w_0\|_{L^\infty(\Omega)} < \varepsilon, \tag{3.2}$$

and

$$\rho \|z_0\|_{L^\infty(\Omega)} < \varepsilon, \tag{3.3}$$

then we define

$$S(\beta,\gamma,\varepsilon) := \Big\{ T > 0 \ \Big| \ \rho\|z(\cdot,t)\|_{L^\infty(\Omega)} < 2K_2(\beta,\gamma)\varepsilon e^{-\delta(\beta,\gamma)t} \ \textit{for all}\ t \in (0,T) \Big\} \tag{3.4}$$

and

$$T(\beta,\gamma,\varepsilon) := \sup S(\beta,\gamma,\varepsilon) \in (0,\infty]. \tag{3.5}$$

A first and rather basic conclusion from the hypothesis included in (3.4) can be obtained by a simple comparison argument.

Lemma 3.2 *Let $\beta > 0$, $\gamma \in (0, \frac{1}{(\beta-1)_+})$ and $\rho \ge 0$, and assume that (1.2) as well as (1.3), (1.4), (3.2) and (3.3) hold with some $\varepsilon > 0$. Then*

$$u(x,t) \ge \Big\{ \min_{y\in\overline{\Omega}} a_0(y) \Big\} \cdot e^{-\frac{2K_2\varepsilon}{\delta}} \qquad \textit{for all } x \in \Omega \textit{ and } t \in (0,T), \tag{3.6}$$

where $K_2 = K_2(\beta,\gamma) > 0$, $T = T(\beta,\gamma,\varepsilon) \in (0,\infty]$ and $\delta = \delta(\beta,\gamma) \in (0,1)$ are as in Definition 3.1 and Lemma 3.1, respectively.

PROOF. According to (2.2) and our definition of S,

$$\begin{aligned} a_t &\ge e^{-v}\nabla\cdot(e^v\nabla a) - \rho a z \\ &\ge e^{-v}\nabla\cdot(e^v\nabla a) - 2K_2\varepsilon e^{-\delta t} a \qquad \text{in } \Omega\times(0,T), \end{aligned} \tag{3.7}$$

and to derive a lower bound for a from this, we let $c_1 := \min_{y\in\overline{\Omega}} a_0(y)$ and $\underline{a}(x,t) := \psi(t)$, $(x,t)\in \overline{\Omega}\times[0,\infty)$, where

$$\psi(t) := c_1 e^{-\frac{2K_2\varepsilon}{\delta}(1-e^{-\delta t})}, \qquad t\ge 0.$$

As thus $\psi'(t) = -2K_2\varepsilon e^{-\delta t}\psi(t)$ for $t>0$ and $\psi(0)=c_1$, it follows that

$$\underline{a}_t - e^{-v}\nabla\cdot(e^v\nabla\underline{a}) + 2K_2\varepsilon e^{-\delta t}\underline{a} = \psi'(t) + 2K_2\varepsilon e^{-\delta t}\psi(t) = 0 \qquad \text{in } \Omega\times(0,T),$$

and that $\underline{a}(x,0) = c_1 \le a_0(x)$ for all $x\in\Omega$, so that by means of the comparison principle we obtain that $\underline{a}\le a$ in $\Omega\times(0,T)$. Since $\psi(t)\ge c_1 e^{-\frac{2K_2\varepsilon}{\delta}}$ for all $t\ge 0$, this entails (3.6). $\square$

The following implication of the latter for the behavior of v is quite obvious.

Lemma 3.3 *If $\beta>0$, $\gamma\in(0,\frac{1}{(\beta-1)_+})$ and $\rho\ge 0$, and if (1.2) as well as (1.3), (1.4), (3.2) and (3.3) hold with some $\varepsilon>0$, then*

$$v(x,t) \le \|v_0\|_{L^\infty(\Omega)}\cdot\exp\Big\{-\Big\{\min_{y\in\overline{\Omega}} a_0(y)\Big\}\cdot e^{-\frac{2K_2\varepsilon}{\delta}}\cdot t\Big\} \qquad \textit{for all } x\in\Omega \textit{ and } t\in(0,T), \tag{3.8}$$

where again $K_2 = K_2(\beta,\gamma)>0$, $T=T(\beta,\gamma,\varepsilon)\in(0,\infty]$ and $\delta=\delta(\beta,\gamma)\in(0,1)$ are as in Definition 3.1 and Lemma 3.1.

PROOF. In view of the nonnegativity of v and w, (1.1) together with (3.6) implies that $v_t = -(u+w)v \le -c_1 v$ in $\Omega\times(0,T)$, where $c_1 := \{\min_{y\in\overline{\Omega}} a_0(y)\}\cdot e^{-\frac{2K_2\varepsilon}{\delta}}$. Hence,

$$v(x,t)\le v_0(x)e^{-c_1 t} \le \|v_0\|_{L^\infty(\Omega)} e^{-c_1 t} \qquad \text{for all } x\in\Omega \text{ and } t\in(0,T),$$

which establishes (3.8), as claimed. $\square$

4 Boundedness of u and decay of (w,z)

This section contains the core of our analysis by deriving and adequately exploiting the cooperative parabolic system (4.6) in order to establish suitable upper bounds for u as well as for w and z. As a first step toward this, we refine the pointwise estimates from Lemma 3.2 and Lemma 3.3 by now imposing an appropriate smallness assumption on the parameter ε in our hypotheses (1.3), (1.4), (3.2) and (3.3).

Lemma 4.1 *Let $\beta>0$ and $\gamma\in(0,\frac{1}{(\beta-1)_+})$. Then there exists $\varepsilon_\star(\beta,\gamma)>0$ such that if $\rho\ge 0$, and if (1.2), (1.3) and (1.4) as well as (3.2) and (3.3) hold with some $\varepsilon\in(0,\varepsilon_\star(\beta,\gamma))$, then*

$$u(x,t)\ge \gamma - \Big(\frac{2K_2}{\delta}\gamma+\gamma+2\Big)\cdot\varepsilon \qquad \textit{for all } x\in\Omega \textit{ and } t\in(0,T) \tag{4.1}$$

and

$$v(x,t) \le \varepsilon e^{-\frac{\gamma}{2}t} \qquad \textit{for all } x \in \Omega \textit{ and } t \in (0,T). \tag{4.2}$$

Here, as before, $K_2 = K_2(\beta,\gamma) > 0$, $T = T(\beta,\gamma,\varepsilon) \in (0,\infty]$ *and* $\delta = \delta(\beta,\gamma) \in (0,1)$ *are taken from Definition 3.1 and Lemma 3.1.*

PROOF. By l'Hospital's rule, abbreviating $c_1 := \frac{2K_2}{\delta} + 1$, we see that

$$\lim_{\varepsilon \searrow 0} \frac{(c_1\gamma + 2 - e^{-c_1\varepsilon}) \cdot \varepsilon}{1 - e^{-c_1\varepsilon}} = \lim_{\varepsilon \searrow 0} \frac{c_1\gamma + 2 - e^{-c_1\varepsilon} + c_1\varepsilon e^{-c_1\varepsilon}}{c_1 e^{-c_1\varepsilon}} = \gamma + \frac{1}{c_1} > \gamma,$$

so that it is possible to pick $\varepsilon_1 = \varepsilon_1(\beta,\gamma) > 0$ in such a way that

$$(c_1\gamma + 2 - e^{-c_1\varepsilon}) \cdot \varepsilon \ge \gamma \cdot (1 - e^{-c_1\varepsilon}) \qquad \text{for all } \varepsilon \in (0,\varepsilon_1)$$

and hence

$$(\gamma - \varepsilon)e^{-c_1\varepsilon} \ge \gamma - (c_1\gamma + 2) \cdot \varepsilon \qquad \text{for all } \varepsilon \in (0,\varepsilon_1). \tag{4.3}$$

Furthermore, observing that

$$\lim_{\varepsilon \searrow 0} (\gamma - \varepsilon)e^{-c_1\varepsilon} = \gamma > \frac{\gamma}{2} \qquad \text{as } \varepsilon \searrow 0,$$

we can fix $\varepsilon_2 = \varepsilon_2(\beta,\gamma) > 0$ fulfilling

$$(\gamma - \varepsilon)e^{-c_1\varepsilon} \ge \frac{\gamma}{2} \qquad \text{for all } \varepsilon \in (0,\varepsilon_2). \tag{4.4}$$

Therefore, if we let

$$\varepsilon_\star \equiv \varepsilon_\star(\beta,\gamma) := \min\Big\{\gamma, \varepsilon_1(\beta,\gamma)\,,\, \varepsilon_2(\beta,\gamma)\Big\}$$

and assume (1.2), (1.3), (1.4), (3.2) and (3.3) with some $\varepsilon \in (0,\varepsilon_\star)$, then since

$$a_0(x) = u_0(x)e^{-v_0(x)} \ge (\gamma - \varepsilon)e^{-\varepsilon} \qquad \text{for all } x \in \Omega \tag{4.5}$$

by (1.3), (1.4) and (2.1), and since thus

$$u(x,t) \ge (\gamma - \varepsilon)e^{-\varepsilon}e^{-\frac{2K_2\varepsilon}{\delta}} = (\gamma - \varepsilon)e^{-c_1\varepsilon} \qquad \text{for all } x \in \Omega \text{ and } t \in (0,T)$$

by Lemma 3.2 and the fact that $\varepsilon_\star \le \gamma$, using the restriction $\varepsilon_\star \le \varepsilon_1$ we firstly obtain (4.1) as a consequence of (4.3). Apart from that, the inequality $\varepsilon_\star \le \varepsilon_2$ in conjunction with Lemma 3.3 and (1.4) ensures that (4.5), secondly, guarantees that

$$\begin{aligned} v(x,t) &\le \varepsilon \exp\Big\{ - (\gamma - \varepsilon)e^{-\varepsilon} \cdot e^{-\frac{2K_2\varepsilon}{\delta}} \cdot t\Big\} \\ &= \varepsilon \exp\Big\{ - (\gamma - \varepsilon)e^{-c_1\varepsilon} \cdot t\Big\} \\ &\le \varepsilon e^{-\frac{\gamma}{2}t} \qquad \text{for all } x \in \Omega \text{ and } t \in (0,T) \end{aligned}$$

thanks to (4.4). □

For such choices of ε this directly entails that, indeed, the triple (a,w,z) forms a subsolution of a cooperative reaction-diffusion system.

Corollary 4.2 *Let $\beta > 0$ and $\gamma \in (0, \frac{1}{(\beta-1)_+})$, and let $\varepsilon_\star(\beta,\gamma) > 0$ be as in Lemma 4.1. Then whenever $\rho \ge 0$ and (1.2), (1.3) and (1.4) as well as (3.2) and (3.3) hold with some $\varepsilon \in (0, \varepsilon_\star(\beta,\gamma))$, the solution of (1.1) satisfies*

$$\begin{cases} a_t \le e^{-v}\nabla\cdot(e^v\nabla a) + \varepsilon e^{\varepsilon} e^{-\frac{\gamma}{2}t}a^2 + \varepsilon e^{-\frac{\gamma}{2}t}aw, & x\in\Omega,\ t>0, \\ w_t \le D_w\Delta w - w + e^{\varepsilon}az, & x\in\Omega,\ t>0, \\ z_t \le D_z\Delta z - \Big\{\gamma + 1 - \Big(\frac{2K_2}{\delta}\gamma + \gamma + 2\Big)\cdot\varepsilon\Big\}\cdot z + \beta w, & x\in\Omega,\ t\in(0,T), \end{cases} \tag{4.6}$$

where once more $K_2 = K_2(\beta,\gamma) > 0$, $T = T(\beta,\gamma,\varepsilon) \in (0,\infty]$ and $\delta = \delta(\beta,\gamma) \in (0,1)$ are given by Definition 3.1 and Lemma 3.1.

Proof. In (2.2), we only need to use (2.1), (4.1) and (4.2) to see that thanks to the fact that $e^v \le e^\varepsilon$ in $\Omega\times(0,T)$ by the latter, we have

$$a(ae^v + w)v \le a(ae^\varepsilon + w)\cdot\varepsilon e^{-\frac{\gamma}{2}t}$$

and

$$-w + uz = -w + ae^v z \le -w + e^\varepsilon az$$

as well as

$$-z - uz + \beta w \le -z - \Big\{\gamma - \Big(\frac{2K_2}{\delta}\gamma + \gamma + 2\Big)\cdot\varepsilon\Big\}\cdot z + \beta w$$

in $\Omega\times(0,T)$. □

Our construction of an appropriate supersolution to (4.6) will, in its crucial first component, involve a spatially homogeneous time-dependent function taken from the family of solutions to quadratically forced Bernoulli-type ODE problems addressed in the following lemma (cf. (4.24) below).

Lemma 4.3 *Let $\gamma > 0$ and $A > 0$. Then there exists $\varepsilon_{\star\star} = \varepsilon_{\star\star}(\gamma, A) > 0$ such that if $\varepsilon \in (0, \varepsilon_{\star\star})$, then the initial value problem*

$$\begin{cases} \varphi'(t) = \varepsilon e^\varepsilon e^{-\frac{\gamma}{2}t}\varphi^2(t) + A\varepsilon e^{-\frac{\gamma}{2}t}\varphi(t), & t>0, \\ \varphi(0) = \gamma + \varepsilon, \end{cases} \tag{4.7}$$

possesses a globally defined solution $\varphi \in C^1([0,\infty))$ fulfilling

$$\varphi(t) \le \gamma + (16\gamma + 72A + 1)\cdot\varepsilon \qquad \textit{for all } t > 0. \tag{4.8}$$

Proof. Given $\gamma > 0$ and $A > 0$, we abbreviate $c_1 := 16\gamma + 72A + 1$ and let

$$\varepsilon_{\star\star} = \varepsilon_{\star\star}(\gamma, A) := \min\Big\{\ln 2\,,\ \frac{\gamma}{c_1}\,,\ \frac{\gamma\ln 2}{2A}\Big\}. \tag{4.9}$$

Then assuming that $\varepsilon \in (0,\varepsilon_{\star\star})$ and letting $\varphi \in C^1([0,T_\varepsilon))$ denote tha corresponding solution of (4.7), extended up to its maximal existence time $T_\varepsilon \in (0,\infty]$, by explicitly solving (4.7) we see that

$$\frac{1}{\varphi(t)} = \frac{1}{\gamma+\varepsilon} \cdot \exp\Big\{ -A\varepsilon \int_0^t e^{-\frac{\gamma}{2}s} ds \Big\} - \varepsilon e^\varepsilon \int_0^t \exp\Big\{ -A\varepsilon \int_s^t e^{-\frac{\gamma}{2}\sigma} d\sigma \Big\} \cdot e^{-\frac{\gamma}{2}s} ds \qquad \text{for all } t \in (0,T_\varepsilon). \tag{4.10}$$

Here since

$$\int_0^t e^{-\frac{\gamma}{2}s} ds \le \frac{2}{\gamma} \qquad \text{for all } t>0, \tag{4.11}$$

we obtain that

$$\frac{1}{\gamma+\varepsilon} \cdot \exp\Big\{ -A\varepsilon \int_0^t e^{-\frac{\gamma}{2}s} ds \Big\} \ge \frac{1}{\gamma+\varepsilon} \cdot e^{-\frac{2A\varepsilon}{\gamma}} \qquad \text{for all } t>0,$$

whereas simply estimating

$$\int_s^t e^{-\frac{\gamma}{2}\sigma} d\sigma \ge 0 \qquad \text{for all } s \ge 0 \text{ and } t \ge s,$$

noting that $e^\varepsilon \le 2$ by (4.9) we find that again due to (4.11),

$$\begin{aligned} \varepsilon e^\varepsilon \int_0^t \exp\Big\{ -A\varepsilon \int_s^t e^{-\frac{\gamma}{2}\sigma} d\sigma \Big\} \cdot e^{-\frac{\gamma}{2}s} ds &\le 2\varepsilon \int_0^t e^{-\frac{\gamma}{2}s} ds \\ &\le \frac{4\varepsilon}{\gamma} \qquad \text{for all } t>0. \end{aligned}$$

Therefore, (4.10) entails that

$$\begin{aligned} e^{\frac{2A\varepsilon}{\gamma}} \cdot \Big\{ \frac{\gamma+c_1\varepsilon}{\varphi(t)} - 1 \Big\} &\ge e^{\frac{2A\varepsilon}{\gamma}} \cdot \Big\{ (\gamma+c_1\varepsilon) \cdot \Big\{ \frac{1}{\gamma+\varepsilon} \cdot e^{-\frac{2A\varepsilon}{\gamma}} - \frac{4\varepsilon}{\gamma} \Big\} - 1 \Big\} \\ &= \frac{\gamma+c_1\varepsilon}{\gamma+\varepsilon} - e^{\frac{2A\varepsilon}{\gamma}} \cdot \Big\{ 1 + \frac{4(\gamma+c_1\varepsilon)}{\gamma} \cdot \varepsilon \Big\} \qquad \text{for all } t \in (0,T_\varepsilon), \end{aligned} \tag{4.12}$$

where since $\varepsilon \le \gamma$ by (4.9),

$$\frac{\gamma+c_1\varepsilon}{\gamma+\varepsilon} = 1 + \frac{c_1-1}{\gamma+\varepsilon} \cdot \varepsilon \ge 1 + \frac{c_1-1}{2\gamma} \cdot \varepsilon, \tag{4.13}$$

because $c_1>1$. Furthermore, relying on the fact that $e^s \le 1+2s$ for all $s \in [0,\ln 2]$ we can make use of the rightmost restriction contained in (4.9) to see that since clearly $c_1\varepsilon \le \gamma$ and $\varepsilon \le 1$ by (4.9),

$$\begin{aligned} e^{\frac{2A\varepsilon}{\gamma}} \cdot \Big\{ 1 + \frac{4(\gamma+c_1\varepsilon)}{\gamma} \cdot \varepsilon \Big\} &\le \Big(1 + \frac{4A\varepsilon}{\gamma} \Big) \cdot (1+8\varepsilon) \\ &= 1 + \Big(\frac{4A}{\gamma} + 8 \Big) \cdot \varepsilon + \frac{32A\varepsilon}{\gamma} \cdot \varepsilon \\ &\le 1 + \Big(\frac{36A}{\gamma} + 8 \Big) \cdot \varepsilon. \end{aligned}$$

As thus, by (4.13),

$$\frac{\gamma+c_1\varepsilon}{\gamma+\varepsilon} - e^{\frac{2A\varepsilon}{\gamma}} \cdot \Big\{1+\frac{4(\gamma+c_1\varepsilon)}{\gamma}\cdot\varepsilon\Big\} \ge \Big\{\frac{c_1-1}{2\gamma} - \Big(\frac{36A}{\gamma}+8\Big)\Big\}\cdot\varepsilon = 0$$

according to our choice of c_1, from (4.12) we infer that indeed $\varphi(t) \le \gamma + c_1\varepsilon$ for all $t \in (0, T_\varepsilon)$, which implies that in fact we must have $T_\varepsilon = \infty$, and that (4.8) holds. □

Based on the latter, we can now quite easily find spatially constant supersolutions to (4.6) with properties favorable for our purposes, and thereby accomplish the main step in our reasoning.

Lemma 4.4 *Let $\beta > 0$, $\gamma \in (0, \frac{1}{(\beta-1)_+})$ and $M > 0$. Then there exist $\varepsilon_{\star\star\star} = \varepsilon_{\star\star\star}(\beta,\gamma,M) > 0$ and $C = C(\beta,\gamma,M) > 0$ with the property that if $\rho \ge 0$ and (1.2) as well as (1.3)-(1.6) hold with some $\varepsilon \in (0, \varepsilon_{\star\star\star})$, we have*

$$u(x,t) \le C \qquad \textit{for all } x\in\Omega \textit{ and } t\in(0,T) \tag{4.14}$$

and

$$w(x,t) \le K_1K_2 \cdot \min\Big\{\frac{\varepsilon}{\rho}\,,\, M\Big\}\cdot e^{-\delta t} \qquad \textit{for all } x\in\Omega \textit{ and } t\in(0,T) \tag{4.15}$$

as well as

$$z(x,t) \le K_2 \cdot \min\Big\{\frac{\varepsilon}{\rho}\,,\, M\Big\}\cdot e^{-\delta t} \qquad \textit{for all } x\in\Omega \textit{ and } t\in(0,T), \tag{4.16}$$

with $K_i = K_i(\beta,\gamma) > 0$, $i \in \{1,2\}$, $T = T(\beta,\gamma,\varepsilon) \in (0,\infty]$ and $\delta = \delta(\beta,\gamma) \in (0,1)$ taken from Definition 3.1 and Lemma 3.1.

Proof. As Lemma 3.1 warrants that $\frac{\gamma}{1-\delta} < K_1 < \frac{\gamma+1-\delta}{\beta}$, given $M > 0$ we can fix $\varepsilon_1 = \varepsilon_1(\beta,\gamma,M) \in (0,1)$ such that

$$\frac{(\gamma+c_1\varepsilon_1)e^{\varepsilon_1}}{1-\delta} \le K_1 \le \frac{\gamma+1-c_2\varepsilon_1-\delta}{\beta}, \tag{4.17}$$

where we have set

$$c_1 \equiv c_1(\beta,\gamma,M) := 16\gamma + 72K_1K_2M + 1 \qquad \text{and} \qquad c_2 \equiv c_2(\beta,\gamma) := \frac{2K_2(\beta,\gamma)}{\delta(\beta,\gamma)}\cdot\gamma + \gamma + 2. \tag{4.18}$$

Then letting

$$\varepsilon_{\star\star\star} \equiv \varepsilon_{\star\star\star}(\beta,\gamma,M) := \min\Big\{\varepsilon_1(\beta,\gamma,M)\,,\,\varepsilon_\star(\beta,\gamma)\,,\,\varepsilon_{\star\star}(\gamma,K_1K_2M)\Big\} \tag{4.19}$$

with $\varepsilon_\star(\cdot,\cdot) > 0$ and $\varepsilon_{\star\star}(\cdot,\cdot)$ taken from Lemma 4.1 and Lemma 4.3, we henceforth assume that $\rho \ge 0$, and that (1.2) and (1.3)-(1.6) are satisfied with some $\varepsilon \in (0, \varepsilon_{\star\star\star})$. We then abbreviate

$$B := \max\Big\{\|z_0\|_{L^\infty(\Omega)}\,,\,\frac{1}{K_1}\cdot\|w_0\|_{L^\infty(\Omega)}\Big\} \tag{4.20}$$

as well as

$$A := K_1B, \tag{4.21}$$

and first note that then due to (1.5), (1.6) and our definition of K_2,

$$B < K_2M \qquad \text{and} \qquad A < K_1K_2M \tag{4.22}$$

as well as

$$B < \frac{K_2\varepsilon}{\rho} \qquad \text{and} \qquad A < \frac{K_1K_2\varepsilon}{\rho}. \tag{4.23}$$

In order to construct a corresponding supersolution triple $(\widehat{a}, \widehat{w}, \widehat{z})$, based on the above choices we let

$$\widehat{a}(x,t) := \varphi(t), \qquad x \in \overline{\Omega},\ t \geq 0, \tag{4.24}$$

as well as

$$\widehat{w}(x,t) := Ae^{-\delta t}, \qquad x \in \overline{\Omega},\ t \geq 0,$$

and

$$\widehat{z}(x,t) := Be^{-\delta t}, \qquad x \in \overline{\Omega},\ t \geq 0,$$

where in accordance with Lemma 4.3, $\varphi \in C^1([0,\infty))$ denotes the solution of (4.7). Then thanks to the latter,

$$\begin{aligned} &\widehat{a}_t - e^{-v}\nabla\cdot(e^v\nabla\widehat{a}) - \varepsilon e^{\varepsilon}e^{-\frac{\gamma}{2}t}\widehat{a}^2 - \varepsilon e^{-\frac{\gamma}{2}t}\widehat{a}\widehat{w} \\ &\quad= \varphi'(t) - \varepsilon e^{\varepsilon}e^{-\frac{\gamma}{2}t}\varphi^2(t) - A\varepsilon e^{-\frac{\gamma}{2}t}e^{-\delta t}\varphi(t) \\ &\quad\geq \varphi'(t) - \varepsilon e^{\varepsilon}e^{-\frac{\gamma}{2}t}\varphi^2(t) - A\varepsilon e^{-\frac{\gamma}{2}t}\varphi(t) \\ &\quad= 0 \qquad \text{in } \Omega\times(0,T), \end{aligned} \tag{4.25}$$

while the upper estimate in (4.8) along with the second inequality in (4.22) and our definition of c_1 guarantees that

$$\begin{aligned} \widehat{w}_t - D_w\Delta\widehat{w} + \widehat{w} - e^{\varepsilon}\widehat{a}\widehat{z} &= -\delta Ae^{-\delta t} + Ae^{-\delta t} - e^{\varepsilon}Be^{-\delta t}\varphi \\ &\geq -\delta Ae^{-\delta t} + Ae^{-\delta t} - (\gamma + c_1\varepsilon)e^{\varepsilon}Be^{-\delta t} \\ &= \Big\{(1-\delta)A - (\gamma+c_1\varepsilon)e^{\varepsilon}B\Big\}\cdot e^{-\delta t} \\ &\geq 0 \qquad \text{in } \Omega\times(0,\infty), \end{aligned} \tag{4.26}$$

because by (4.21) and the left inequality in (4.17),

$$\begin{aligned} (1-\delta)A - (\gamma+c_2\varepsilon)e^{\varepsilon}B &= \Big\{(1-\delta)c_1 - (\gamma+c_2\varepsilon)e^{\varepsilon}\Big\}\cdot B \\ &\geq \Big\{(1-\delta)c_1 - (\gamma+c_2\varepsilon_1)e^{\varepsilon_1}\Big\}\cdot B \\ &\geq 0. \end{aligned}$$

Likewise,

$$\begin{aligned} &\widehat{z}_t - D_z\Delta\widehat{z} + \Big\{\gamma + 1 - \Big(\frac{2K_2}{\delta}\gamma + \gamma + 2\Big)\cdot\varepsilon\Big\}\cdot\widehat{z} - \beta\widehat{w} \\ &\quad= -\delta Be^{-\delta t} + (\gamma+1-c_2\varepsilon)\cdot Be^{-\delta t} - \beta Ae^{-\delta t} \\ &\quad= (\gamma+1-c_2\varepsilon-\delta-K_1\beta)Be^{-\delta t} \\ &\quad\geq 0 \qquad \text{in } \Omega\times(0,\infty), \end{aligned} \tag{4.27}$$

for

$$\gamma+1-c_2\varepsilon-\delta-K_1\beta \ge \gamma+1-c_2\varepsilon_1-\delta-K_1\beta \ge 0$$

due to the right inequality in (4.17). Since, apart from that,

$$a_0(x)=u_0(x)e^{-v_0(x)} \le u_0(x) \le \gamma+\varepsilon=\varphi(0)=\widehat{a}(x,0) \qquad \text{for all } x\in\Omega$$

by (1.3), and since (4.20) and (4.21) guarantee that

$$w_0(x) \le \|w_0\|_{L^\infty(\Omega)} \le K_1B=A=\widehat{w}(x,0) \qquad \text{for all } x\in\Omega$$

and

$$z_0(x) \le \|z_0\|_{L^\infty(\Omega)} \le B=\widehat{z}(x,0) \qquad \text{for all } x\in\Omega,$$

we may make use of the fact that the parabolic system in (4.6) is cooperative to conclude from a corresponding comparison principle that

$$a\le\widehat{a}, \quad w\le\widehat{w} \quad \text{and} \quad z\le\widehat{z} \qquad \text{in } \Omega\times(0,\infty).$$

By definition of $\widehat{w}$ and $\widehat{z}$, in view of (4.22) and (4.23) the two latter inequalities directly yield (4.15) and (4.16), while (4.14) is a consequence of the bounds for φ and v asserted by Lemma 4.3 and Lemma 4.1. $\Box$

Through (4.16), the latter especially enables us to close the loop implictly opened in Definition 3.1.

Corollary 4.5 *Let $\beta>0$, $\gamma\in(0,\frac{1}{(\beta-1)_+})$, $\rho\ge0$ and $M>0$, and suppose that (1.2) and (1.3)-(1.6) hold with some $\varepsilon\in(0,\varepsilon_{\star\star\star})$, where $\varepsilon_{\star\star\star}=\varepsilon_{\star\star\star}(\beta,\gamma,M)>0$ is as given by Lemma 4.4. Then in Definition 3.1 we have $T(\beta,\gamma,\varepsilon)=\infty$.*

Proof. Since (4.16) particularly entails that

$$\rho\|z(\cdot,t)\|_{L^\infty(\Omega)} \le K_2(\beta,\gamma)\varepsilon e^{-\delta(\beta,\gamma)t} \qquad \text{for all } t\in(0,T(\beta,\gamma,\varepsilon)),$$

assuming that $T(\beta,\gamma,\varepsilon)$ be finite would readily lead to a contradiction to the defintion of $S(\beta,\gamma,\varepsilon)$ and the continuity of z. $\Box$

5 A global Hölder bound for u. Proof of Theorem 1.1

In view of Lemma 4.4 and Corollary 4.5, it remains to be shown that the L^2 stabilization process in the first solution component, as thus clearly asserted by Lemma 2.2, in fact can be turned into the uniform convergence statement in (1.7). This will be achieved on the basis on the following boundedness property of the haptotactic gradient in (1.1), as resulting from a series of testing procedures applied to the first three equations therein.

Lemma 5.1 *Let $\beta>0$, $\gamma\in(0,\frac{1}{(\beta-1)_+})$, $\rho\ge0$ and $M>0$, and assume (1.2) and (1.3)-(1.6) with some $\varepsilon\in(0,\varepsilon_{\star\star\star})$, and with $\varepsilon_{\star\star\star}=\varepsilon_{\star\star\star}(\beta,\gamma,M)>0$ taken from Lemma 4.4. Then there exists $C>0$ such that*

$$\int_\Omega |\nabla v(\cdot,t)|^4 \le C \qquad \textit{for all } t>0. \tag{5.1}$$

PROOF. Relying on Lemma 4.4, let us pick $c_1 > 0, c_2 > 0$ and $c_3 > 0$ such that

$$u(x,t) \le c_1, \quad w(x,t) \le c_2 \quad \text{and} \quad z(x,t) \le c_3 \qquad \text{for all } x \in \Omega \text{ and } t > 0, \tag{5.2}$$

which due to (2.1) and Lemma 3.3 particularly means that

$$f = f(x,t) := a(ae^v + w)v, \qquad x \in \Omega\, t > 0,$$

satisfies

$$|f(x,t)| \le c_5 := c_1 \cdot (c_1 + c_2) \cdot c_4 \qquad \text{for all } x \in \Omega \text{ and } t > 0$$

with $c_4 := \|v_0\|_{L^\infty(\Omega)}$. Therefore, testing the identity

$$a_t = \Delta a + \nabla v \cdot \nabla a + f(x,t), \qquad x \in \Omega,\ t > 0,$$

as contained in (2.2), by $-\Delta a$ and using Young's inequality shows that

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\int_\Omega |\nabla a|^2 + \int_\Omega |\Delta a|^2 &= -\int_\Omega (\nabla v \cdot \nabla a)\Delta a - \int_\Omega f\Delta a \\
&\le \frac{1}{2}\int_\Omega |\Delta a|^2 + \int_\Omega |\nabla v \cdot \nabla a|^2 + \int_\Omega f^2 \\
&\le \frac{1}{2}\int_\Omega |\Delta a|^2 + \int_\Omega |\nabla v|^2 |\nabla a|^2 + c_5^2|\Omega| \qquad \text{for all } t > 0.
\end{aligned} \tag{5.3}$$

Here we combine a Gagliardo-Nirenberg type interpolation with standard elliptic regularity theory to find $c_6 > 0$ fulfilling

$$\|\nabla\varphi\|_{L^4(\Omega)}^4 \le c_6 \|\Delta\varphi\|_{L^2(\Omega)}^2 \|\varphi\|_{L^\infty(\Omega)}^2 \qquad \text{for all } \varphi \in W^{2,2}(\Omega) \text{ such that } \tfrac{\partial\varphi}{\partial\nu} = 0 \text{ on } \partial\Omega, \tag{5.4}$$

which, again thanks to (5.2) and (2.1), firstly implies that

$$\frac{1}{2}\int_\Omega |\Delta a|^2 \ge \frac{1}{2c_1^2 c_6}\int_\Omega |\nabla a|^4 \qquad \text{for all } t > 0.$$

Therefore, through two applications of Young's inequality we infer from (5.4) that

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\int_\Omega |\nabla a|^2 + \frac{1}{2c_1^2 c_6}\int_\Omega |\nabla a|^4 + \int_\Omega |\nabla a|^2 &\le \int_\Omega |\nabla v|^2|\nabla a|^2 + c_5^2|\Omega| + \int_\Omega |\nabla a|^2 \\
&\le \frac{1}{8c_1^2 c_6}\int_\Omega |\nabla a|^4 + 2c_1^2 c_6 \int_\Omega |\nabla v|^4 + c_5^2|\Omega| \\
&\quad + \frac{1}{8c_1^2 c_6}\int_\Omega |\nabla a|^4 + 2c_1^2 c_6|\Omega| \qquad \text{for all } t > 0
\end{aligned}$$

and hence

$$\frac{d}{dt}\int_\Omega |\nabla a|^2 + c_7\int_\Omega |\nabla a|^4 + 2\int_\Omega |\nabla a|^2 \le c_8 \int_\Omega |\nabla v|^4 + c_8 \qquad \text{for all } t > 0 \tag{5.5}$$

with $c_7 := \frac{1}{2c_1^2 c_6}$ and $c_8 := \max\{4c_1^2 c_6\,,\,2c_5^2|\Omega| + 4c_1^2 c_6|\Omega|\}$.

In order to appropriately compensate the first summand on the right of (5.5), we next use the second equation in (2.2) to see that

$$\begin{aligned}
\frac{1}{4}\frac{d}{dt}\int_\Omega |\nabla v|^4 &= -\int_\Omega |\nabla v|^2 \nabla v\cdot\nabla(ave^v + vw) \\
&= -\int_\Omega a(v+1)e^v|\nabla v|^4 - \int_\Omega ve^v|\nabla v|^2\nabla v\cdot\nabla a \\
&\quad -\int_\Omega w|\nabla v|^4 - \int_\Omega v|\nabla v|^2\nabla v\cdot\nabla w \qquad \text{for all } t>0, \qquad (5.6)
\end{aligned}$$

where the second last summand is nonpositive, where we moreover recall the uniform positivity statement for $u = ae^v$ from Lemma 3.2 to pick $c_9 \in (0,4]$ fulfilling

$$\int_\Omega a(v+1)e^v|\nabla v|^4 \ge \int_\Omega ae^v|\nabla v|^4 \ge c_9\int_\Omega |\nabla v|^4 \qquad \text{for all } t>1, \qquad (5.7)$$

and where by Lemma 3.3 and Young's inequality,

$$\begin{aligned}
-\int_\Omega v|\nabla v|^2\nabla v\cdot\nabla w &\le c_4\int_\Omega |\nabla v|^3|\nabla w| \\
&= \int_\Omega \Big\{\frac{c_9}{2}|\nabla v|^4\Big\}^{\frac{3}{4}}\cdot\Big\{\Big(\frac{2}{c_9}\Big)^{\frac{3}{4}}c_4|\nabla w|\Big\} \\
&\le \frac{c_9}{2}\int_\Omega |\nabla v|^4 + \frac{8c_4^4}{c_9^3}\int_\Omega |\nabla w|^4 \qquad \text{for all } t>0. \qquad (5.8)
\end{aligned}$$

Now in estimating the second summand on the right-hand side of (5.6) we proceed slightly more carefully in order to retain a potentially small factor: Indeed, given any $t_0 \ge 0$ we may combine our definition of c_4 with Lemma 3.3 to obtain that, again by Young's inequality,

$$\begin{aligned}
-\int_\Omega ve^v|\nabla v|^2\nabla v\cdot\nabla a &\le \|v(\cdot,t_0)\|_{L^\infty(\Omega)}e^{c_4}\int_\Omega |\nabla v|^3|\nabla a| \\
&= \int_\Omega \Big\{\frac{c_9}{4}|\nabla v|^4\Big\}^{\frac{3}{4}}\cdot\Big\{\Big(\frac{4}{c_9}\Big)^{\frac{3}{4}}e^{c_4}\|v(\cdot,t_0)\|_{L^\infty(\Omega)}|\nabla a|\Big\} \\
&\le \frac{c_9}{4}\int_\Omega |\nabla v|^4 + \frac{64e^{4c_4}}{c_9^3}\|v(\cdot,t_0)\|_{L^\infty(\Omega)}^4\int_\Omega |\nabla a|^4 \qquad \text{for all } t>t_0. \quad (5.9)
\end{aligned}$$

If we write $c_{10} := \max\Big\{\frac{32c_4^4}{c_9^3}\,,\,\frac{256e^{4c_4}}{c_9^3}\Big\}$, from (5.6)-(5.9) we thus infer that whenever $t_0 \ge 1$,

$$\frac{d}{dt}\int_\Omega |\nabla v|^4 + c_9\int_\Omega |\nabla v|^4 \le c_{10}\|v(\cdot,t_0)\|_{L^\infty(\Omega)}^4\int_\Omega |\nabla a|^4 + c_{10}\int_\Omega |\nabla w|^4 \qquad \text{for all } t>t_0. \qquad (5.10)$$

We finally multiply the third equation in (1.1) by $-\Delta w$ and use Young's inequality and (5.2) in a straightforward manner to derive the inequality

$$\frac{1}{2}\frac{d}{dt}\int_\Omega |\nabla w|^2 + D_w\int_\Omega |\Delta w|^2 + \int_\Omega |\nabla w|^2 = -\int_\Omega uz\Delta w$$

$$\leq \frac{D_w}{2}\int_\Omega |\Delta w|^2 + \frac{2}{D_w}\int_\Omega u^2 z^2$$
$$\leq \frac{D_w}{2}\int_\Omega |\Delta w|^2 + \frac{2c_1^2c_3^2|\Omega|}{D_w} \qquad \text{for all } t>0,$$

where a second application of (5.4) in conjunction with (5.2) shows that

$$\frac{D_w}{2}\int_\Omega |\Delta w|^2 \geq \frac{D_w}{2c_2^2c_6}\int_\Omega |\nabla w|^4 \qquad \text{for all } t>0,$$

so that, in fact,

$$\frac{d}{dt}\int_\Omega |\nabla w|^2 + c_{11}\int_\Omega |\nabla w|^4 + 2\int_\Omega |\nabla w|^2 \leq c_{12} \qquad \text{for all } t>0 \tag{5.11}$$

with $c_{11} := \frac{D_w}{c_2^2c_6}$ and $c_{12} := \frac{4c_1^2c_3^2|\Omega|}{D_w}$.

Now in order to suitably combine (5.5), (5.10) and (5.11), we abbreviate

$$b_1 := \frac{2c_8}{c_9} \qquad \text{and} \qquad b_2 := \frac{c_{10}b_1}{c_{11}},$$

and rely on the decay property of v asserted by Lemma 3.3 to fix $t_0 \geq 1$ large enough such that

$$c_{10}b_1\|v(\cdot,t_0)\|^4_{L^\infty(\Omega)} \leq c_7.$$

Then (5.5), (5.10) and (5.11) imply that

$$y(t) := \int_\Omega |\nabla a(\cdot,t)|^2 + b_1\int_\Omega |\nabla v(\cdot,t)|^4 + b_2\int_\Omega |\nabla w(\cdot,t)|^2, \qquad t\geq t_0,$$

satisfies

$$\begin{aligned}
y'(t) + \frac{c_9}{2}y(t) \ &\leq \ \Big\{-c_7\int_\Omega |\nabla a|^4 - 2\int_\Omega |\nabla a|^2 + c_8\int_\Omega |\nabla v|^4 + c_8\Big\} \\
&\quad + b_1\cdot\Big\{-c_9\int_\Omega |\nabla v|^4 + c_{10}\|v(\cdot,t_0)\|^4_{L^\infty(\Omega)}\int_\Omega |\nabla a|^4 + c_{10}\int_\Omega |\nabla w|^4\Big\} \\
&\quad + b_2\cdot\Big\{-c_{11}\int_\Omega |\nabla w|^4 - 2\int_\Omega |\nabla w|^2 + c_{12}\Big\} \\
&\quad + \frac{c_9}{2}\cdot\Big\{\int_\Omega |\nabla a|^2 + b_1\int_\Omega |\nabla v|^4 + b_2\int_\Omega |\nabla w|^2\Big\} \\
&= \ \Big\{-c_7 + c_{10}b_1\|v(\cdot,t_0)\|^4_{L^\infty(\Omega)}\Big\}\cdot\int_\Omega |\nabla a|^4 \\
&\quad + \Big\{c_8 - \frac{c_9}{2}b_1\Big\}\cdot\int_\Omega |\nabla v|^4 \\
&\quad + \{c_{10}b_1 - c_{11}b_2\}\cdot\int_\Omega |\nabla w|^4
\end{aligned}$$

$$
\begin{aligned}
&+\Big\{-2+\frac{c_9}{2}\Big\}\cdot\int_\Omega|\nabla a|^2 \\
&+\Big\{-2b_2+\frac{c_9}{2}b_2\Big\}\cdot\int_\Omega|\nabla w|^2 \\
&+c_8+c_{12}b_2 \\
\le\ & c_8+c_{12}b_2 \qquad \text{for all } t>t_0,
\end{aligned}
$$

because $c_9 \le 4$. As thus

$$
y(t) \le c_{13} := \max\Big\{y(t_0)\,,\ \frac{2(c_8+c_{12}b_2)}{c_9}\Big\} \qquad \text{for all } t \ge t_0
$$

by an ODE comparison argument, it particularly follows that

$$
\int_\Omega |\nabla v(\cdot,t)|^4 \le c_{14} := \max\Big\{\sup_{s\in(0,t_0)}\int_\Omega|\nabla v(\cdot,s)|^4,\ \frac{c_{13}}{b_1}\Big\} \qquad \text{for all } t>0,
$$

with finiteness of c_{14} guaranteed by Lemma 2.1. $\square$

Thanks to the fact that the integrability exponent in (5.1) exceeeds the considered spatial dimension, through standard parabolic regularity theory this implies a uniform Hölder bound for u:

Lemma 5.2 *Suppose that $\beta>0$, $\gamma\in(0,\frac{1}{(\beta-1)_+})$, $\rho\ge 0$ and $M>0$, and that (1.2) and (1.3)-(1.6) are valid with some $\varepsilon\in(0,\varepsilon_{\star\star\star})$, where $\varepsilon_{\star\star\star}=\varepsilon_{\star\star\star}(\beta,\gamma,M)>0$ is as given by Lemma 4.4. Then there exist $\theta\in(0,1)$ and $C>0$ such that*

$$
\|u\|_{C^{\theta,\frac{\theta}{2}}(\overline{\Omega}\times[t,t+1])} \le C \qquad \textit{for all } t>0.
$$

Proof. We rewrite the first equation in (1.1) according to $u_t=\Delta u-\nabla\cdot\psi_1(x,t)+\psi_2(x,t)$, $x\in\Omega,\ t>0$, where $\psi_1(x,t):=u(x,t)\nabla v(x,t)$ and $\psi_2(x,t):=-\rho u(x,t)z(x,t)$, $x\in\Omega,\ t>0$. Since (4.14) together with the outcome of Lemma 5.1 ensures that ψ_1 belongs to $L^p((0,\infty);L^q(\Omega;\mathbb{R}^2))$ with $p:=\infty$ and $q:=4$ satisfying $\frac{1}{p}+\frac{2}{q}=\frac{1}{2}<1$, and since ψ_2 in bounded by (4.14) and (4.16), this directly results from well-known theory on Hölder regularity of bounded solutions to scalar parabolic equations ([18]). $\square$

Straightforward interpolation between the latter and the basic convergence result from Lemma 2.2 finally yields uniform stabilization also in the first solution component:

Lemma 5.3 *Let $\beta>0$, $\gamma\in(0,\frac{1}{(\beta-1)_+})$, $\rho\ge 0$ and $M>0$, and suppose that (1.2) and (1.3)-(1.6) hold with some $\varepsilon\in(0,\varepsilon_{\star\star\star})$, where $\varepsilon_{\star\star\star}=\varepsilon_{\star\star\star}(\beta,\gamma,M)>0$ is taken from Lemma 4.4. Then there exists $u_\infty>0$ such that*

$$
u(\cdot,t)\to u_\infty \quad \textit{in } L^\infty(\Omega) \qquad \textit{as } t\to\infty. \tag{5.12}
$$

Proof. Since Lemma 4.4 together with Lemma 4.1 clearly ensures boundedness of (u,w,z) in $\Omega\times(0,\infty)$, finiteness of $\int_0^\infty\int_\Omega z$ as well as decay to zero of $\|v(\cdot,t)\|_{L^\infty(\Omega)}$ as $t\to\infty$, we may invoke Lemma 2.2 to find $u_\infty>0$ such that

$$
u(\cdot,t)\to u_\infty \quad \text{in } L^2(\Omega) \qquad \text{as } t\to\infty, \tag{5.13}
$$

and in line with Lemma 5.2, we can thereupon pick $\theta \in (0,1)$ and $c_1 > 0$ such that

$$\|u(\cdot,t) - u_\infty\|_{C^\theta(\overline{\Omega})} \le c_1 \qquad \text{for all } t > 0. \tag{5.14}$$

Given $\eta > 0$ we next use the compactness of the first among the continuous embeddings $C^\theta(\overline{\Omega}) \hookrightarrow L^\infty(\Omega) \hookrightarrow L^2(\Omega)$ to pick $c_2(\eta) > 0$ such that in accordance with an associated Ehrling lemma we have

$$\|\varphi\|_{L^\infty(\Omega)} \le \frac{\eta}{2c_1}\|\varphi\|_{C^\theta(\overline{\Omega})} + c_2(\eta)\|\varphi\|_{L^2(\Omega)} \qquad \text{for all } \varphi \in C^\theta(\overline{\Omega}), \tag{5.15}$$

and rely on (5.13) in verifying that for any such η we can find $t_0(\eta) > 0$ fulfilling

$$\|u(\cdot,t) - u_\infty\|_{L^2(\Omega)} \le \frac{\eta}{2c_2(\eta)} \qquad \text{for all } t > t_0(\eta).$$

Combining this with (5.15) and (5.14) shows that

$$\begin{aligned}
\|u(\cdot,t) - u_\infty\|_{L^\infty(\Omega)} &\le \frac{\eta}{2c_1}\|u(\cdot,t) - u_\infty\|_{C^\theta(\overline{\Omega})} + c_2(\eta)\|u(\cdot,t) - u_\infty\|_{L^2(\Omega)} \\
&\le \frac{\eta}{2c_1} \cdot c_1 + c_2(\eta) \cdot \frac{\varepsilon}{2c_2(\eta)} = \eta \qquad \text{for all } t > t_0(\eta)
\end{aligned}$$

and hence establishes (5.12), for $\eta > 0$ was arbitrary. □

Accomplishing our main results now reduces to merely extracting the respectively relevant pieces of information from the above statements:

Proof of Theorem 1.1. Applying Lemma 4.1 and Lemma 4.4 to any fixed $\varepsilon \in (0, \min\{\varepsilon_\star, \varepsilon_{\star\star\star}\})$, with $\varepsilon_\star = \varepsilon_\star(\beta,\gamma) > 0$ and $\varepsilon_{\star\star\star} = \varepsilon_{\star\star\star}(\beta,\gamma,M) > 0$ as introduced there, assuming (1.2), and (1.3)-(1.6) we immediately obtain (1.8) from Lemma 4.1 and (1.7) from Lemma 5.3, whereas (1.9) and (1.10) are direct consequences of Lemma 4.4 when combined with Corollary 4.5. In the borderline case when $\rho = 0$, finally, the identity $u_\infty = \overline{u}_0$ readily results from (1.8) and the evident fact that $\int_\Omega u(\cdot,t) = \int_\Omega u_0$ for all $t > 0$ by (1.1). □

Acknowledgement. The authors warmly thank the reviewer for several helpful comments. Youshan Tao was supported by the *National Natural Science Foundation of China (No. 11861131003).* Michael Winkler acknowledges support of the *Deutsche Forschungsgemeinschaft* in the context of the project *Emergence of structures and advantages in cross-diffusion systems* (No. 411007140, GZ: WI 3707/5-1).

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