Global classical solutions to a doubly haptotactic cross-diffusion system modeling oncolytic virotherapy

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Abstract

This work studies a haptotaxis system proposed as a model for oncolytic virotherapy, accounting for interaction between uninfected cancer cells, infected cancer cells, extracellular matrix (ECM) and oncolytic virus. In addition to random movement, both uninfected and infected tumor cells migrate haptotactically toward higher ECM densities; moreover, besides degrading the non-diffusible ECM upon contact the two cancer cell populations are subject to an infection-induced transition mechanism driven by virus particles which are released by infected cancer cells, an which assault the uninfected part of the tumor.

The main results assert global classical solvability in an associated initial-boundary value problem posed in one- or two-dimensional domains with any given suitably regular initial data. This is achieved by discovering a quasi-Lyapunov functional structure that allows to appropriately cope with the presence of nonlinear zero-order interaction terms which apparently form the most significant additional mathematical challenge of the considered system in comparison to previously studied haptotaxis models.

Key words: haptotaxis; global smooth solutions; quasi-Lyapunov functional; $L \log L$ estimates
MSC (2010): 35A01, 35K57, 35Q92, 92C17

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1 Introduction

Oncolytic virus particles are often genetically-engineered reproducible virions that selectively bind to receptors on the surface of cancer cells, but not to the surface of normal healthy cells ([7]), and accordingly the term *oncolytic virotherapy* refers to the injection of replication-competent viruses into tumors. These then infect the latter, replicate inside them, and eventually cause their death. As infected cells die, the virus particles inside them are released and then proceed to infect adjacent cancer cells, thereby eventually leading to a reduced overall degrading impact on the surrounding healthy tissue and, in particular, the extracellular matrix (ECM).

However, not only virus clearance due to immune cells and circulating antibodies, but also physical barriers like ECM deposits or interstitial fluid pressure might restrict the efficacy of this therapy. To facilitate the understanding of such limitation mechanisms, the authors in [1] recently proposed a class of mathematical models to describe the spatio-temporal evolution in coupled ensembles of this type, concentrating on the population densities $u = u(x,t)$, $w = w(x,t)$ and $z = z(x,t)$ of uninfected and infected tumor cells, and of virions, respectively, as well as on the ECM-density $v = v(x,t)$. The underlying modeling hypotheses are that in addition to random motion, cancer cells can direct their movement toward regions of higher ECM densities, and that uninfected cells, apart from possibly proliferating logistically, are converted into an infected state upon contact with virus particles, whereas infected cells die owing to lysis. It is also assumed that the static ECM can be degraded by both types of cancer cells, possibly remodeled according to a logistic law. Finally accounting for release of free virus particles through infected cells, and including random diffusion and possible spontaneous decay in the virus population, following [1] we henceforth consider the PDE-ODE system given by

$$\begin{cases} u_t = D_u\Delta u - \xi_u\nabla\cdot(u\nabla v) + \mu_u u(1-u) - \rho_u uz, & x\in\Omega,\ t>0,\\ v_t = -(\alpha_u u + \alpha_w w)v + \mu_v v(1-v), & x\in\Omega,\ t>0,\\ w_t = D_w\Delta w - \xi_w\nabla\cdot(w\nabla v) - \delta_w w + \rho_w uz, & x\in\Omega,\ t>0,\\ z_t = D_z\Delta z - \delta_z z - \rho_z uz + \beta w, & x\in\Omega,\ t>0,\\ (D_u\nabla u - \xi_u u\nabla v)\cdot\nu = (D_w\nabla w - \xi_w w\nabla v)\cdot\nu = \frac{\partial z}{\partial\nu} = 0, & x\in\partial\Omega,\ t>0,\\ u(x,0)=u_0(x),\quad v(x,0)=v_0(x),\quad w(x,0)=w_0(x),\quad z(x,0)=z_0(x), & x\in\Omega, \end{cases} \tag{1.1}$$

in a bounded domain $\Omega \subset \mathbb{R}^n$ with smooth boundary, where $D_u, D_w, D_z, \xi_u, \alpha_u$ and α_w are positive parameters and $\xi_w, \mu_u, \mu_v, \rho_u, \rho_w, \rho_z, \beta, \delta_w$ and δ_z are nonnegative constants.

We note that besides possibly including two simultaneous haptotaxis processes, as its apparently most characteristic ingredient the model (1.1) contains the zero-order nonlinearity uz; indeed, this essentially superlinear production term seems to constitute a substantial difference between (1.1) and most haptotaxis ([9], [13], [24], [22]) and chemotaxis-haptotaxis systems ([16], [12], [10], [17], [20], [3], [8], [23], [11], [6], [18]) studied in the mathematical literature, and accordingly significant challenges arise even at the level of fundamental issues from basic solvability theory.

Main results. In order to appropriately address these, and to thereby establish a result on global existence in the framework of classical solutions, we shall subsequently concentrate on low-dimensional settings by assuming that $n \le 2$, and resort to convenient choices of initial data by requiring that

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

Our main results then indeed reveal global classical solvability, without any further restriction e.g. on the size of (u_0, v_0, w_0, z_0) in any of its components, and – by including the case $\mu_u = 0$ – actually without requiring the presence of a genuine quadratic degradation term in the first equation from (1.1):

Theorem 1.1 *Let $n \le 2$ and $\Omega \subset \mathbb{R}^n$ be a bounded domain with smooth boundary, and suppose that*

$$D_u, D_w, D_z, \xi_u, \alpha_u \text{ and } \alpha_w \text{ are positive,}$$

and that

$$\xi_w, \mu_u, \mu_v, \rho_u, \rho_w, \rho_z, \beta, \delta_w \text{ and } \delta_z \text{ are nonnegative,}$$

where

$$\rho_u + \rho_z > 0 \qquad \text{if} \qquad \rho_w > 0. \tag{1.3}$$

Then for any choice of u_0, v_0, w_0 and z_0 fulfilling (1.2), one can find $(u, v, w, z) \in (C^{2,1}(\overline{\Omega} \times [0,\infty)))^4$ such that u, w and z are positive and v is nonnegative in $\overline{\Omega} \times (0,\infty)$, and that (u, v, w, z) solves (1.1) in the classical sense.

Main ideas. A first and fundamental step in our a priori estimation procedure, applied to local-in-time solutions existing according to standard approaches, will consist in the observation that an adequate handling of both cross-diffusive interactions in (1.1) can be achieved by appropriately combining logarithmic entropies of the attracted quantities with a Dirichlet integral involving the square root of the haptoattractant. With regard to this basic strategy remaining quite in line with precedent studies on various types of systems containing haptotaxis ([16], [12], [24], [22]), in Section 4 we shall track the time evolution of

$$\begin{aligned} \mathcal{F}(t) \quad := \quad & A \int_\Omega \Big\{ u(\cdot,t) \ln u(\cdot,t) - u(\cdot,t) \Big\} + 2 \int_\Omega |\nabla \sqrt{v(\cdot,t)}|^2 \\ & + B \int_\Omega \Big\{ w(\cdot,t) \ln w(\cdot,t) - w(\cdot,t) \Big\} + \frac{1}{2} \int_\Omega z^2(\cdot,t), \qquad t > 0, \end{aligned}$$

with suitable $A > 0$ and $B > 0$ (see Lemma 4.5 below), where it will turn out that thanks to an interpolation-based argument, through a correspondingly dissipated quantity due to virus diffusion the last summand herein can be used to appropriately cope with the superlinear contribution induced by the presence of the crucial nonlinear production term $\rho_w uz$ in (1.1). Accordingly implying $L \log L$ estimates for both u and w (Lemma 4.6) will thereafter form a cornerstone for the derivation of higher regularity properties, and hence for the global extension of the solutions under consideration, in Section 5 and Section 6.

2 Local existence and extensibility

Following an idea widely used in related literature ([4], [5], [19] and [14]), let us set

$$\chi_u := \frac{\xi_u}{D_u} \qquad \text{and} \qquad \chi_w := \frac{\xi_w}{D_w},$$

and substitute

$$a = ue^{-\chi_u v} \qquad \text{as well as} \qquad b = we^{-\chi_w v}. \tag{2.1}$$

Then, namely, (1.1) is transformed to the equivalent system

$$\begin{cases} a_t = D_u e^{-\chi_u v}\nabla\cdot(e^{\chi_u v}\nabla a) + f(a,v,b,z), & x\in\Omega,\ t>0,\\ v_t = -(\alpha_u a e^{\chi_u v} + \alpha_w b e^{\chi_w v})v + \mu_v v(1-v), & x\in\Omega,\ t>0,\\ b_t = D_w e^{-\chi_w v}\nabla\cdot(e^{\chi_w v}\nabla b) + g(a,v,b,z), & x\in\Omega,\ t>0,\\ z_t = D_z\Delta z - \delta_z z - \rho_z a e^{\chi_u v} z + \beta b e^{\chi_w v}, & x\in\Omega,\ t>0,\\ \frac{\partial a}{\partial\nu} = \frac{\partial b}{\partial\nu} = \frac{\partial z}{\partial\nu} = 0, & x\in\partial\Omega,\ t>0,\\ a(x,0) = u_0(x)e^{-\chi_u v_0(x)},\ v(x,0) = v_0(x),\ b(x,0) = w_0(x)e^{\chi_w v_0(x)},\ z(x,0) = z_0(x), & x\in\Omega. \end{cases} \tag{2.2}$$

where for arbitrary nonnegative numbers a, v, b and z we have set

$$f(a,v,b,z) := \mu_u a(1-ae^{\chi_u v}) - \rho_u az + \chi_u a(\alpha_u a e^{\chi_u v} + \alpha_w b e^{\chi_w v})\cdot v - \chi_u\mu_v av(1-v) \tag{2.3}$$

and

$$g(a,v,b,z) := -\delta_w b + \rho_w aze^{(\chi_u-\chi_w)v} + \chi_w b(\alpha_u a e^{\chi_u v} + \alpha_w b e^{\chi_w v})\cdot v - \chi_w\mu_v bv(1-v). \tag{2.4}$$

In fact, in this framework a local theory can be developed by adapting quite well-established approaches in a straightforward manner.

Lemma 2.1 *If $n \le 2$, D_u, D_w and D_z are positive and $\xi_u, \xi_w, \mu_u, \mu_v, \rho_u, \rho_w, \rho_z, \alpha_u, \alpha_w, \beta, \delta_w$ and δ_z are nonnegative, and if (1.2) holds, then there exist $T_{max} \in (0,\infty]$ and a unique quadruple $(a,v,b,z) \in (C^{2,1}(\overline{\Omega}\times[0,T_{max})))^4$ which solves (2.2) in the classical sense in $\Omega\times(0,T_{max})$, and which is such that*

$$\text{if } T_{max}<\infty, \quad \text{then} \quad \limsup_{t\nearrow T_{max}} \Big\{\|a(\cdot,t)\|_{L^\infty(\Omega)} + \|\nabla v(\cdot,t)\|_{L^4(\Omega)} + \|b(\cdot,t)\|_{L^\infty(\Omega)} + \|z(\cdot,t)\|_{L^\infty(\Omega)}\Big\} = \infty. \tag{2.5}$$

Moreover, a, b and z are positive in $\overline{\Omega}\times(0,T_{max})$, and $\sqrt{v} \in C^1(\overline{\Omega}\times[0,T_{max}))$ with

$$\partial_t\nabla\sqrt{v} = -\frac{\alpha_u u + \alpha_w w}{2}\nabla\sqrt{v} - \frac{1}{2}\sqrt{v}(\alpha_u\nabla u + \alpha_w\nabla w) + \frac{\mu_v}{2}(1-v)\nabla\sqrt{v} - \frac{\mu_v}{2}\sqrt{v}\nabla v \qquad \text{in } \Omega\times(0,T_{max}), \tag{2.6}$$

where u and w are as defined through (2.1).

Proof. The statements on local existence and extensibility can be proved by slightly adapting the arguments detailed in [16, Lemma 2.1 and Lemma 2.2], whereas (2.6) follows from a straightforward computation using the second equation from (2.2). $\square$

From now on, without further mentioning we will suppose that the requirements of Theorem 1.1 are met, and that $T_{max} \in (0,\infty]$ and (a,v,b,z) are as in Lemma 2.1, noting that then (u,v,w,z), with u and z as given by (2.1), forms a classical solution of (1.1) in $\Omega\times(0,T_{max})$.

3 Bounds for (u, v, w, z) in $L^1 \times L^\infty \times L^1 \times L^1$

The following basic bounds for u and v will be frequently used later on.

Lemma 3.1 *We have*

$$\int_\Omega u(\cdot,t) \le \max\left\{ \int_\Omega u_0 \, , \, |\Omega| \right\} \qquad \textit{for all } t \in (0, T_{max}) \tag{3.1}$$

and

$$v(x,t) \le K_v := \max\left\{ \|v_0\|_{L^\infty(\Omega)} \, , \, 1 \right\} \qquad \textit{for all } x \in \Omega \textit{ and } t \in (0, T_{max}). \tag{3.2}$$

Proof. We simply integrate the first equation in (1.1) and use the Cauchy-Schwarz inequality, which namely warrants that $(\int_\Omega u)^2 \le |\Omega| \int_\Omega u^2$ for all $t \in (0, T_{max})$, to see that

$$\frac{d}{dt} \int_\Omega u = \mu_u \int_\Omega u - \mu_u \int_\Omega u^2 - \rho_u \int_\Omega uz \le \mu_u \int_\Omega u - \frac{\mu_u}{|\Omega|} \cdot \left\{ \int_\Omega u \right\}^2 \qquad \text{for all } t \in (0, T_{max}),$$

from which in both cases $\mu_u = 0$ and $\mu_u > 0$ it follows by a comparison argument that (3.1) holds. Since $v_t \le \mu_v v(1-v)$ in $\Omega \times (0, T_{max})$ by (1.1), a comparison similarly shows that

$$v(x,t) \le \max\left\{ v_0(x) \, , \, 1 \right\} \qquad \text{for all } x \in \Omega \text{ and } t \in (0, T_{max}),$$

which clearly results in (3.2). □

Relying on (3.1), we can derive bounds for w and z in L^1 whenever $T_{max} < \infty$.

Lemma 3.2 *If $T_{max} < \infty$, then there exists $C > 0$ such that*

$$\int_\Omega w(\cdot,t) \le C \qquad \textit{for all } t \in (0, T_{max}) \tag{3.3}$$

and

$$\int_\Omega z(\cdot,t) \le C \qquad \textit{for all } t \in (0, T_{max}). \tag{3.4}$$

Proof. According to (1.1),

$$\frac{d}{dt} \int_\Omega u \le \mu_u \int_\Omega u - \rho_u \int_\Omega uz \qquad \text{for all } t \in (0, T_{max}) \tag{3.5}$$

and

$$\frac{d}{dt} \int_\Omega w \le \rho_w \int_\Omega uz \qquad \text{for all } t \in (0, T_{max}) \tag{3.6}$$

as well as

$$\frac{d}{dt} \int_\Omega z \le -\rho_z \int_\Omega uz + \beta \int_\Omega w \qquad \text{for all } t \in (0, T_{max}). \tag{3.7}$$

Thus, if $\rho_w = 0$, then trivially $\int_\Omega w \le \int_\Omega w_0$ for all $t \in (0, T_{max})$ and hence, by integration of (3.7),

$$\int_\Omega z \le \int_\Omega z_0 + \beta \cdot \left\{ \int_\Omega w_0 \right\} \cdot t \le \int_\Omega z_0 + \beta \cdot \left\{ \int_\Omega w_0 \right\} \cdot T_{max} \qquad \text{for all } t \in (0, T_{max}).$$

Otherwise, combining (3.5)-(3.7) shows that

$$
\begin{aligned}
\frac{d}{dt}\Big\{ \int_\Omega u + \frac{\rho_u+\rho_z}{\rho_w}\int_\Omega w + \int_\Omega z\Big\}
&\le \Big\{\mu_u\int_\Omega u - \rho_u\int_\Omega uz\Big\} + (\rho_u+\rho_z)\int_\Omega uz + \Big\{-\rho_z\int_\Omega uz + \beta\int_\Omega w\Big\} \\
&= \mu_u\int_\Omega u + \beta\int_\Omega w \\
&\le c_1\cdot\Big\{\int_\Omega u + \frac{\rho_u+\rho_z}{\rho_w}\int_\Omega w + \int_\Omega z\Big\} \qquad \text{for all } t\in(0,T_{max})
\end{aligned}
$$

with $c_1 := \max\Big\{\frac{\beta\rho_w}{\rho_u+\rho_z}\, ,\, \mu_u\Big\}$, because then $\rho_u+\rho_z>0$ due to (1.3). Thus, by integration,

$$
\int_\Omega u + \frac{\rho_u+\rho_z}{\rho_w}\int_\Omega w + \int_\Omega z \le \Big\{\int_\Omega u_0 + \frac{\rho_u+\rho_z}{\rho_w}\int_\Omega w_0 + \int_\Omega z_0\Big\}\cdot e^{c_1 t} \qquad \text{for all } t\in(0,T_{max}),
$$

from which (3.3) and (3.4) result also in this case. □

4 Analysis of a quasi-Lyapunov functional for (1.1)

In view of (2.5), in order to extend the local solution constructed in Lemma 2.1 so as to exist for all positive times, we are led to establishing a priori bounds for u and w in L^∞ whenever $T_{max}<\infty$. As an initial but crucial step, we shall firstly derive estimates for u and w in $L\log L$, which turn out to be consequences of a quasi-energy structure associated with (1.1).

4.1 Construction of a functional at most exponentially growing along trajectories

The first step of our construction simply consists in testing the first equation from (1.1) against $\ln u$.

Lemma 4.1 *The obtained solution of (1.1) satisfies*

$$
\frac{d}{dt}\int_\Omega (u\ln u - u) + D_u\int_\Omega \frac{|\nabla u|^2}{u} \le \xi_u\int_\Omega \nabla u\cdot\nabla v + \frac{\mu_u|\Omega|}{2e} + \frac{\rho_u}{e}\int_\Omega z \qquad \textit{for all } t\in(0,T_{max}). \tag{4.1}
$$

Proof. We integrate by parts in the first equation from (1.1) to compute

$$
\begin{aligned}
\frac{d}{dt}\int_\Omega (u\ln u - u) &= \int_\Omega u_t\ln u \\
&= -D_u\int_\Omega \frac{|\nabla u|^2}{u} + \xi_u\int_\Omega \nabla u\cdot\nabla v + \mu_u\int_\Omega u(1-u)\ln u - \rho_u\int_\Omega u\ln u\cdot z
\end{aligned} \tag{4.2}
$$

for all $t\in(0,T_{max})$. Here we use that $s\ln s\ge -\frac{1}{e}$ for all $s>0$ to see that

$$
-\rho_u\int_\Omega u\ln u\cdot z \le \frac{\rho_u}{e}\int_\Omega z \qquad \text{for all } t\in(0,T_{max}),
$$

and rely on the fact that $s^2 \ln s \ge -\frac{1}{2e}$ for all $s > 0$ in estimating

$$\begin{aligned} \mu_u \int_\Omega u(1-u)\ln u &\le \mu_u \int_{\{u<1\}} u(-u)\ln u \\ &\le -\mu_u \int_{\{u<1\}} u^2 \ln u \\ &\le \frac{\mu_u |\Omega|}{2e} \qquad \text{for all } t \in (0, T_{max}). \end{aligned}$$

Therefore, (4.2) implies (4.1). □

A suitable neutralization of the first summand on the right-hand side of (4.1) can be achieved by making use of the dissipative term in the second equation from (1.1), in the context of the following lemma.

Lemma 4.2 *We have*

$$\begin{aligned} 2\frac{d}{dt}\int_\Omega |\nabla\sqrt{v}|^2 + \frac{\alpha_w}{2}\int_{\{v>0\}} \frac{w}{v}|\nabla v|^2 &\le -\alpha_u \int_\Omega \nabla u\cdot\nabla v - \alpha_w \int_\Omega \nabla v \cdot \nabla w \\ &\quad + 2\mu_v \int_\Omega |\nabla\sqrt{v}|^2 \qquad \textit{for all } t \in (0, T_{max}). \end{aligned} \tag{4.3}$$

Proof. On the basis of (2.6), for $t \in (0, T_{max})$ we derive the identity

$$\begin{aligned} 2\frac{d}{dt}\int_\Omega |\nabla\sqrt{v}|^2 &= 4\int_\Omega \nabla\sqrt{v}\cdot\partial_t\nabla\sqrt{v} \\ &= 4\int_\Omega \nabla\sqrt{v}\cdot\Big\{-\frac{\alpha_u u + \alpha_w w}{2}\nabla\sqrt{v} - \frac{1}{2}\sqrt{v}(\alpha_u\nabla u + \alpha_w \nabla w) \\ &\qquad + \frac{\mu_v}{2}(1-v)\nabla\sqrt{v} - \frac{\mu_v}{2}\sqrt{v}\nabla v\Big\} \\ &= -2\alpha_u \int_\Omega u|\nabla\sqrt{v}|^2 - 2\alpha_w\int_\Omega w|\nabla\sqrt{v}|^2 \\ &\quad -2\alpha_u\int_\Omega \sqrt{v}\nabla\sqrt{v}\cdot\nabla u - 2\alpha_w \int_\Omega \sqrt{v}\nabla\sqrt{v}\cdot\nabla w \\ &\quad +2\mu_v\int_\Omega |\nabla\sqrt{v}|^2 - 2\mu_v\int_\Omega v|\nabla\sqrt{v}|^2 - 2\mu_v\int_\Omega \sqrt{v}\nabla\sqrt{v}\cdot\nabla v. \end{aligned} \tag{4.4}$$

Here since $2\sqrt{v}\nabla\sqrt{v} = \nabla v$ in $\Omega \times (0, T_{max})$, we have

$$-2\alpha_u \int_\Omega \sqrt{v}\nabla\sqrt{v}\cdot\nabla u = -\alpha_u\int_\Omega \nabla u\cdot\nabla v \quad \text{and} \quad -2\alpha_w\int_\Omega \sqrt{v}\nabla\sqrt{v}\cdot\nabla w = -\alpha_w\int_\Omega \nabla v\cdot\nabla w$$

as well as

$$-2\mu_v\int_\Omega \sqrt{v}\nabla\sqrt{v}\cdot\nabla v = -\mu_v\int_\Omega |\nabla v|^2 \le 0$$

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

$$-2\alpha_u \int_\Omega u|\nabla\sqrt{v}|^2 \le 0 \quad \text{and} \quad -2\mu_v \int_\Omega v|\nabla\sqrt{v}|^2 \le 0 \qquad \text{for all } t \in (0, T_{max}).$$

Accordingly, (4.3) is a consequence of (4.4) and the fact that

$$2\alpha_w \int_\Omega w|\nabla\sqrt{v}|^2 \ge 2\alpha_w \int_{\{v>0\}} w|\nabla\sqrt{v}|^2 = \frac{\alpha_w}{2} \int_{\{v>0\}} \frac{w}{v}|\nabla v|^2$$

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

Now in the case when ξ_w is positive, the haptotaxis term in the third equation from (1.1) can be coped with in a flavor quite similar to the above; the nonlinear production term therein, however, requires different handling.

Lemma 4.3 *The inequality*

$$\frac{d}{dt}\int_\Omega (w\ln w - w) + D_w \int_\Omega \frac{|\nabla w|^2}{w} \le \xi_w \int_\Omega \nabla v \cdot \nabla w + \frac{\delta_w|\Omega|}{e} + \frac{4\rho_w}{e}\|u\|_{L^2(\Omega)}\|z\|_{L^4(\Omega)}\|w\|_{L^1(\Omega)}^{\frac{1}{4}} \quad (4.5)$$

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

Proof. We use the third equation in (1.1) to see that for all $t \in (0, T_{max})$,

$$\begin{aligned}
\frac{d}{dt}\int_\Omega (w\ln w - w) &= \int_\Omega w_t \ln w \\
&= \int_\Omega \ln w \cdot \Big\{ D_w \Delta w - \xi_w \nabla\cdot(w\nabla v) - \delta_w w + \rho_w uz \Big\} \\
&= -D_w \int_\Omega \frac{|\nabla w|^2}{w} + \xi_w \int_\Omega \nabla v\cdot\nabla w - \delta_w \int_\Omega w\ln w + \rho_w \int_\Omega uz\ln w, \quad (4.6)
\end{aligned}$$

where again since $s\ln s \ge -\frac{1}{e}$ for all $s > 0$,

$$-\delta_w \int_\Omega w\ln w \le \frac{\delta_w|\Omega|}{e} \qquad \text{for all } t \in (0, T_{max}). \quad (4.7)$$

Apart from that, we use that $\varphi(s) := s^{-\frac{1}{4}}\ln s$, $s > 0$, satisfies $\varphi'(s) = s^{-\frac{5}{4}} \cdot (1 - \frac{1}{4}\ln s) = 0$ if and only if $s = e^4$, so that $\varphi(s) \le \varphi(e^4) = \frac{4}{e}$ for all $s > 0$ and hence

$$\ln^4 s \le \Big(\frac{4}{e}\Big)^4 s \qquad \text{for all } s > 1.$$

Therefore, namely, by means of the Hölder inequality the rightmost summand in (4.6) can be estimated according to

$$\begin{aligned}
\rho_w \int_\Omega uz\ln w &\le \rho_w \int_{\{w>1\}} uz\ln w \\
&\le \rho_w \|u\|_{L^2(\Omega)}\|z\|_{L^4(\Omega)} \cdot \Big\{ \int_{\{w>1\}} \ln^4 w \Big\}^{\frac{1}{4}} \\
&\le \frac{4\rho_w}{e}\|u\|_{L^2(\Omega)}\|z\|_{L^4(\Omega)} \cdot \Big\{ \int_\Omega w \Big\}^{\frac{1}{4}} \qquad \text{for all } t \in (0, T_{max}),
\end{aligned}$$

which together with (4.7) we insert into (4.6) to arrive at (4.5). $\Box$

Whereas the expressions $\|w\|_{L^1(\Omega)}$ and $\|u\|_{L^2(\Omega)}$ appearing in (4.5) will turn out to be conveniently digestible through (3.3) and the dissipation rate in (4.1), the factor $\|z\|_{L^4(\Omega)}$ will be estimated by means of an interpolation argument relying on the following basic property.

Lemma 4.4 *We have*

$$\frac{1}{2}\frac{d}{dt}\int_\Omega z^2 + D_z\int_\Omega |\nabla z|^2 \le \beta\|w\|_{L^2(\Omega)}\|z\|_{L^2(\Omega)} \qquad \textit{for all } t\in(0,T_{max}). \tag{4.8}$$

Proof. We test the fourth equation in (1.1) by z to obtain that indeed

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\int_\Omega z^2 + D_z\int_\Omega |\nabla z|^2 &= -\delta_z\int_\Omega z^2 - \rho_z\int_\Omega uz^2 + \beta\int_\Omega wz \\ &\le \beta\int_\Omega wz \\ &\le \beta\|w\|_{L^2(\Omega)}\|z\|_{L^2(\Omega)} \qquad \text{for all } t\in(0,T_{max})\end{aligned}$$

by the Cauchy-Schwarz inequality. $\Box$

We are now ready to construct a quasi-Lyapunov functional by taking suitable linear combinations of the inequalities provided by Lemmata 4.1-4.4.

Lemma 4.5 *Let*

$$A := \frac{\alpha_u}{\xi_u} \tag{4.9}$$

and, with $K_v > 0$ taken from Lemma 3.1,

$$B := \begin{cases} \frac{\alpha_w}{\xi_w} & \textit{if } \xi_w > 0, \\ \frac{\alpha_w K_v}{D_w} & \textit{if } \xi_w = 0, \end{cases} \tag{4.10}$$

and define

$$\begin{aligned}\mathcal{F}(t) \;:=\; & A\int_\Omega \Big\{u(\cdot,t)\ln u(\cdot,t) - u(\cdot,t)\Big\} + 2\int_\Omega |\nabla\sqrt{v(\cdot,t)}|^2 \\ & + B\int_\Omega \Big\{w(\cdot,t)\ln w(\cdot,t) - w(\cdot,t)\Big\} + \frac{1}{2}\int_\Omega z^2(\cdot,t), \qquad t\in[0,T_{max}).\end{aligned} \tag{4.11}$$

Then if $T_{max} < \infty$, there exists $C > 0$ such that

$$\mathcal{F}'(t) \le \mu_v\mathcal{F}(t) + C \qquad \textit{for all } t\in(0,T_{max}). \tag{4.12}$$

Proof. Regardless of whether or not ξ_w is positive, combining Lemma 4.1 and Lemma 4.2 with Lemma 4.3 and Lemma 4.4 shows that due to our choice of A,

$$\mathcal{F}'(t) \le A\cdot\Big\{ -D_u\int_\Omega \frac{|\nabla u|^2}{u} + \xi_u\int_\Omega \nabla u\cdot\nabla v + \frac{\mu_u|\Omega|}{2e} + \frac{\rho_u}{e}\int_\Omega z\Big\}$$

$$
\begin{aligned}
&+\Big\{-\frac{\alpha_w}{2}\int_{\{v>0\}}\frac{w}{v}|\nabla v|^2-\alpha_u\int_\Omega\nabla u\cdot\nabla v-\alpha_w\int_\Omega\nabla v\cdot\nabla w+2\mu_v\int_\Omega|\nabla\sqrt{v}|^2\Big\}\\
&+B\cdot\Big\{-D_w\int_\Omega\frac{|\nabla w|^2}{w}+\xi_w\int_\Omega\nabla v\cdot\nabla w+\frac{\delta_w|\Omega|}{e}+\frac{4\rho_w}{e}\|u\|_{L^2(\Omega)}\|z\|_{L^4(\Omega)}\|w\|^{\frac14}_{L^1(\Omega)}\Big\}\\
&+\Big\{-D_z\int_\Omega|\nabla z|^2+\beta\|w\|_{L^2(\Omega)}\|z\|_{L^2(\Omega)}\Big\}\\
= &-AD_u\int_\Omega\frac{|\nabla u|^2}{u}-BD_w\int_\Omega\frac{|\nabla w|^2}{w}-D_z\int_\Omega|\nabla z|^2\\
&-\frac{\alpha_w}{2}\int_{\{v>0\}}\frac{w}{v}|\nabla v|^2-(\alpha_w-B\xi_w)\int_\Omega\nabla v\cdot\nabla w+2\mu_v\int_\Omega|\nabla\sqrt{v}|^2\\
&+\frac{A\rho_u}{e}\int_\Omega z+\frac{4B\rho_w}{e}\|u\|_{L^2(\Omega)}\|z\|_{L^4(\Omega)}\|w\|^{\frac14}_{L^1(\Omega)}+\beta\|w\|_{L^2(\Omega)}\|z\|_{L^2(\Omega)}\\
&+c_1\qquad\text{for all } t\in(0,T_{max}),
\end{aligned}
\tag{4.13}
$$

where $c_1 := \frac{A\mu_u|\Omega|}{2e}+\frac{B\delta_w|\Omega|}{e}$. Here in the case when $\xi_w>0$ and hence $\alpha_w-B\xi_w=0$ by (4.10), we trivially have

$$
-\frac{\alpha_w}{2}\int_{\{v>0\}}\frac{w}{v}|\nabla v|^2-(\alpha_w-B\xi_w)\int_\Omega\nabla v\cdot\nabla w=-\frac{\alpha_w}{2}\int_{\{v>0\}}\frac{w}{v}|\nabla v|^2\le 0\qquad\text{for all } t\in(0,T_{max}),
\tag{4.14}
$$

whereas otherwise we may use that $\nabla v=0$ in $\{v=0\}$ to see that due to Young's inequality, (3.2) and (4.10),

$$
\begin{aligned}
-\frac{\alpha_w}{2}\int_{\{v>0\}}\frac{w}{v}|\nabla v|^2-(\alpha_w-B\xi_w)\int_\Omega\nabla v\cdot\nabla w &= -\frac{\alpha_w}{2}\int_{\{v>0\}}\frac{w}{v}|\nabla v|^2-\alpha_w\int_\Omega\nabla v\cdot\nabla w\\
&\le \frac{\alpha_w}{2}\int_{\{v>0\}}\frac{v}{w}|\nabla w|^2\\
&\le \frac{\alpha_w K_v}{2}\int_\Omega\frac{|\nabla w|^2}{w}\\
&\le \frac{BD_w}{2}\int_\Omega\frac{|\nabla w|^2}{w}\qquad\text{for all } t\in(0,T_{max}).
\end{aligned}
\tag{4.15}
$$

To next estimate the zeor-order expressions on the right of (4.13), we first note that according to our assumption that T_{max} be finite, Lemma 3.1 and Lemma 3.2 provide positive constants c_2, c_3 and c_4 such that

$$
\int_\Omega u(\cdot,t)\le c_2,\quad \int_\Omega w(\cdot,t)\le c_3\quad\text{and}\quad\int_\Omega z(\cdot,t)\le c_4\qquad\text{for all } t\in(0,T_{max}),
\tag{4.16}
$$

whereas employing the one- and two-dimensional Gagliardo-Nirenberg inequalities and a Poincaré inequality readily yield $c_5>0$, $c_6>0$ and $c_7>0$ fulfilling

$$
\|\varphi\|^4_{L^4(\Omega)}\le c_5\|\nabla\varphi\|^2_{L^2(\Omega)}\|\varphi\|^2_{L^2(\Omega)}+c_5\|\varphi\|^4_{L^2(\Omega)}\qquad\text{for all }\varphi\in W^{1,2}(\Omega)
\tag{4.17}
$$

as well as

$$\frac{c_2 c_3^{\frac{1}{2}} c_5 B^2 \rho_w^2}{e^2 A D_u} \|\varphi\|_{L^4(\Omega)}^2 \le \frac{D_z}{2} \|\nabla\varphi\|_{L^2(\Omega)}^2 + c_6 \|\varphi\|_{L^1(\Omega)}^2 \qquad \text{for all } \varphi \in W^{1,2}(\Omega) \tag{4.18}$$

and

$$\frac{c_3 c_5 \beta^2}{8 B D_w} \|\varphi\|_{L^2(\Omega)}^2 \le \frac{D_z}{2} \|\nabla\varphi\|_{L^2(\Omega)}^2 + c_7 \|\varphi\|_{L^1(\Omega)}^2 \qquad \text{for all } \varphi \in W^{1,2}(\Omega). \tag{4.19}$$

Therefore, namely, in (4.13) we can firstly use (4.16) to estimate

$$\frac{A\rho_u}{e} \int_\Omega z \le \frac{A\rho_u c_4}{e} \qquad \text{for all } t \in (0, T_{max}) \tag{4.20}$$

and then combine (4.16) with Young's inequality, (4.17) and (4.18) to see that

$$\begin{aligned}
&\frac{4B\rho_w}{e} \|u\|_{L^2(\Omega)} \|z\|_{L^4(\Omega)} \|w\|_{l^1(\Omega)}^{\frac{1}{4}} \\
&\quad \le \frac{4Bc_3^{\frac{1}{4}}\rho_w}{e} \|u\|_{L^2(\Omega)} \|z\|_{L^4(\Omega)} \\
&\quad \le \frac{4AD_u}{c_2 c_5} \|u\|_{L^2(\Omega)}^2 + \frac{c_2 c_3^{\frac{1}{2}} c_5 B^2 \rho_w^2}{e^2 A D_u} \|z\|_{L^4(\Omega)}^2 \\
&\quad = \frac{4AD_u}{c_2 c_5} \|\sqrt{u}\|_{L^4(\Omega)}^4 + \frac{c_2 c_3^{\frac{1}{2}} c_5 B^2 \rho_w^2}{e^2 A D_u} \|z\|_{L^4(\Omega)}^2 \\
&\quad \le \frac{4AD_u}{c_2} \|\nabla\sqrt{u}\|_{L^2(\Omega)}^2 \|\sqrt{u}\|_{L^2(\Omega)}^2 + \frac{4AD_u}{c_2} \|\sqrt{u}\|_{L^2(\Omega)}^4 + \frac{D_z}{2} \|\nabla z\|_{L^2(\Omega)}^2 + c_6 \|z\|_{L^1(\Omega)}^2 \\
&\quad \le \frac{AD_u}{c_2} \cdot \left\{ \int_\Omega \frac{|\nabla u|^2}{u} \right\} \cdot \int_\Omega u + \frac{4AD_u}{c_2} \cdot \left\{ \int_\Omega u \right\}^2 + \frac{D_z}{2} \int_\Omega |\nabla z|^2 + c_6 \cdot \left\{ \int_\Omega z \right\}^2 \\
&\quad \le AD_u \int_\Omega \frac{|\nabla u|^2}{u} + \frac{D_z}{2} \int_\Omega |\nabla z|^2 + 4c_2 A D_u + c_4^2 c_6 \qquad \text{for all } t \in (0, T_{max}).
\end{aligned} \tag{4.21}$$

Likewise, Young's inequality and (4.17) along with (4.19) show that

$$\begin{aligned}
&\beta \|w\|_{L^2(\Omega)} \|z\|_{L^2(\Omega)} \\
&\quad \le \frac{2BD_w}{c_3 c_5} \|w\|_{L^2(\Omega)}^2 + \frac{c_3 c_5 \beta^2}{8BD_w} \|z\|_{L^2(\Omega)}^2 \\
&\quad \le \frac{2BD_w}{c_3} \|\nabla\sqrt{w}\|_{L^2(\Omega)}^2 \|\sqrt{w}\|_{L^2(\Omega)}^2 + \frac{2BD_w}{c_3} \|\sqrt{w}\|_{L^2(\Omega)}^2 + \frac{D_z}{2} \|\nabla z\|_{L^2(\Omega)}^2 + c_7 \|z\|_{L^1(\Omega)}^2 \\
&\quad = \frac{BD_w}{2c_3} \cdot \left\{ \int_\Omega \frac{|\nabla w|^2}{w} \right\} \cdot \int_\Omega w + \frac{2BD_w}{c_3} \cdot \left\{ \int_\Omega w \right\}^2 + \frac{D_z}{2} \int_\Omega |\nabla z|^2 + c_7 \cdot \left\{ \int_\Omega z \right\}^2 \\
&\quad \le \frac{BD_w}{2} \int_\Omega \frac{|\nabla w|^2}{w} + \frac{D_z}{2} \int_\Omega |\nabla z|^2 + 2c_3 B D_w + c_4^2 c_7 \qquad \text{for all } t \in (0, T_{max}),
\end{aligned}$$

which together with (4.14), (4.15), (4.20) and (4.21) reveals that (4.13) implies the inequality

$$\mathcal{F}'(t) \le 2\mu_v \int_\Omega |\nabla\sqrt{v}|^2 + c_8 \qquad \text{for all } t \in (0, T_{max}) \tag{4.22}$$

with $c_8 := c_1 + \frac{A\rho_u c_4}{e} + 4c_2 A D_u + c_4^2 c_6 + 2c_3 B D_w + c_4^2 c_7$. Here we rewrite

$$2\int_\Omega |\nabla\sqrt{v}|^2 = \mathcal{F}(t) - A\int_\Omega (u\ln u - u) - B\int_\Omega (w\ln w - w) - \frac{1}{2}\int_\Omega z^2 \qquad \text{for } t\in(0,T_{max}),$$

and note that

$$-s\ln s + s \le s\cdot(1-\ln s)_+ \le e \qquad \text{for all } s>0,$$

so that

$$2\mu_v\int_\Omega |\nabla\sqrt{v}|^2 \le \mu_v\mathcal{F}(t) + (A+B)e\mu_v \qquad \text{for all } t\in(0,T_{max}).$$

Therefore, (4.22) implies (4.12) if we let $C := c_8 + (A+B)e\mu_v$. $\Box$

4.2 Consequences. Bounds for a and b in $L\log L$

As a consequence of (4.12), we first improve our knowledge on regularity of the quantities a and b from (2.1) as follows:

Lemma 4.6 *If $T_{max}<\infty$, then there exists $C>0$ such that*

$$\int_\Omega a(\cdot,t)|\ln a(\cdot,t)| \le C \qquad \textit{for all } t\in(0,T_{max}) \tag{4.23}$$

and

$$\int_\Omega b(\cdot,t)|\ln b(\cdot,t)| \le C \qquad \textit{for all } t\in(0,T_{max}) \tag{4.24}$$

PROOF. Due to the hypothesis that $T_{max}<\infty$, an integration of (4.12) provides $c_1>0$ such that the function $\mathcal{F}$ defined in (4.11) has the property that

$$\mathcal{F}(t)\le c_1 \qquad \text{for all } t\in(0,T_{max}). \tag{4.25}$$

Now by (2.1), the pointwise inequality $a\ln a \ge -\frac{1}{e}$ in $\Omega\times(0,T_{max})$, and (3.2),

$$\begin{aligned}
\int_\Omega a|\ln a| &= \int_\Omega ue^{-\chi_u v}|\ln a| \\
&\le \int_\Omega u|\ln a| \\
&= \int_\Omega u\ln a - 2\int_{\{a<1\}} u\ln a \\
&= \int_\Omega u\ln(ue^{-\chi_u v}) - 2\int_{\{a<1\}} e^{\chi_u v} a\ln a \\
&= \int_\Omega u\ln u - \chi_u\int_\Omega uv - 2\int_{\{a<1\}} e^{\chi_u v} a\ln a \\
&\le \int_\Omega u\ln u + 2e^{\chi_u K_v - 1}|\Omega| \qquad \text{for all } t\in(0,T_{max})
\end{aligned}$$

and, similarly,

$$\int_\Omega b|\ln b| \le \int_\Omega w\ln w + 2e^{\chi_w K_v - 1}|\Omega| \qquad \text{for all } t\in(0,T_{max}),$$

so that according to (4.11),

$$\begin{aligned}
\mathcal{F}(t) &\ge A\cdot\Big\{\int_\Omega u\ln u - \int_\Omega u\Big\} + B\cdot\Big\{\int_\Omega w\ln w - \int_\Omega w\Big\} \\
&\ge A\cdot\Big\{\int_\Omega a|\ln a| - 2e^{\chi_u K_v - 1}|\Omega| - \int_\Omega u\Big\} + B\cdot\Big\{\int_\Omega b|\ln b| - 2e^{\chi_w K_v - 1}|\Omega| - \int_\Omega w\Big\}
\end{aligned}$$

for all $t\in(0,T_{max})$. In view of (3.1) and (3.3), both (4.23) and (4.24) thus result from (4.25). $\square$

5 L^∞ estimates for a, b and z

In order to next improve the above information so as to provide, inter alia, L^p bounds for a and b in any L^p space with finite $p>1$ in Lemma 5.3, let us note the following elementary properties of the zero-order nonlinearities in (2.2).

Lemma 5.1 *There exists $C>0$ such that the functions f and g introduced in (2.3) and (2.4) satisfy*

$$\Big|f(a(x,t),v(x,t),b(x,t),z(x,t))\Big| \le C\cdot\Big(a^2(x,t)+b^2(x,t)+z^2(x,t)+1\Big) \qquad \textit{for all } x\in\Omega \textit{ and } t\in(0,T_{max}) \tag{5.1}$$

as well as

$$\Big|g(a(x,t),v(x,t),b(x,t),z(x,t))\Big| \le C\cdot\Big(a^2(x,t)+b^2(x,t)+z^2(x,t)+1\Big) \qquad \textit{for all } x\in\Omega \textit{ and } t\in(0,T_{max}). \tag{5.2}$$

Proof. We combine the definition of f with (3.2) and Young's inequality to obtain that throughout $\Omega\times(0,T_{max})$,

$$\begin{aligned}
|f(a,v,b,z)| &\le \mu_u a + \mu_u e^{\chi_u K_v} a^2 + \rho_u a z \\
&\quad + \chi_u\alpha_u K_v e^{\chi_u K_v} a^2 + \chi_u \alpha_u K_v e^{\chi_w K_v} ab \\
&\quad + \chi_u\mu_v K_v a + \chi_u\mu_v K_v^2 a \\
&\le \frac12\mu_u(a^2+1) + \mu_u e^{\chi_u K_v}a^2 + \frac12\rho_u(a^2+z^2) \\
&\quad + \chi_u\alpha_u K_v e^{\chi_u K_v} a^2 + \frac12\chi_u\alpha_u K_v e^{\chi_w K_v}(a^2+b^2) \\
&\quad + \frac12\chi_u\mu_v K_v(a^2+1) + \frac12\chi_u\mu_v K_v^2(a^2+1).
\end{aligned}$$

This establishes (5.1), and (5.2) can be derived quite similarly. $\square$

The following second preparation for Lemma 5.3 is a special case of the statement from [16, Lemma A.5], which in turn can be regarded as a variant of a Gagliardo-Nirenberg inequality originally derived in [2].

Lemma 5.2 *Let $p > 1$ and $\varepsilon > 0$. Then there exists $K(p,\varepsilon) > 0$ such that for each nonnegative $\varphi \in W^{1,2}(\Omega)$,*

$$\|\varphi\|_{L^{\frac{2(p+1)}{p}}(\Omega)}^{\frac{2(p+1)}{p}} \le \varepsilon \|\nabla\varphi\|_{L^2(\Omega)}^2 \cdot \int_\Omega \varphi^{\frac{2}{p}} |\ln\varphi| + K(p,\varepsilon) \cdot \Big\{ \|\varphi\|_{L^{\frac{2}{p}}(\Omega)}^{\frac{2(p+1)}{p}} + 1 \Big\}. \tag{5.3}$$

We can now proceed to turn the outcome of Lemma 4.6 into the following by means of some quite straightforward L^p testing procedures, combined with appropriate interpolation relying on Lemma 5.2.

Lemma 5.3 *Suppose that $T_{max} < \infty$. Then for all $p \ge 2$ there exists $C(p) > 0$ such that*

$$\int_\Omega a^p(\cdot,t) \le C(p) \qquad \textit{for all } t \in (0,T_{max}) \tag{5.4}$$

and

$$\int_\Omega b^p(\cdot,t) \le C(p) \qquad \textit{for all } t \in (0,T_{max}) \tag{5.5}$$

as well as

$$\int_\Omega z^{p+1}(\cdot,t) \le C(p) \qquad \textit{for all } t \in (0,T_{max}). \tag{5.6}$$

PROOF. Fixing $c_1 > 0$ such that in accordance with Lemma 5.1 we have

$$f(a,v,b,z) \le c_1 a^2 + c_1 b^2 + c_1 z^2 + c_1 \qquad \text{in } \Omega \times (0,T_{max}),$$

we begin by testing the first equation in (2.2) against $e^{\chi_u v} a^{p-1}$, which due to Young's inequality, (3.2) and the fact that $v_t \le \mu_v v$, namely, results in the inequality

$$\begin{aligned}
\frac{d}{dt}\int_\Omega e^{\chi_u v} a^p &= p\int_\Omega e^{\chi_u v} a^{p-1} \cdot \Big\{ D_u e^{-\chi_u v} \nabla \cdot (e^{\chi_u v}\nabla a) + f(a,v,b,z) \Big\} + \chi_u \int_\Omega e^{\chi_u v} a^p v_t \\
&= -p(p-1)D_u \int_\Omega e^{\chi_u v} a^{p-2} |\nabla a|^2 + p\int_\Omega e^{\chi_u v} a^{p-1} f(a,v,b,z) + \chi_u \int_\Omega e^{\chi_u v} a^p v_t \\
&\le -p(p-1)D_u \int_\Omega e^{\chi_u v} a^{p-2} |\nabla a|^2 \\
&\quad + pc_1 e^{\chi_u K_v} \cdot \Big\{ \int_\Omega a^{p+1} + \int_\Omega a^{p-1} b^2 + \int_\Omega a^{p-1} z^2 + \int_\Omega a^{p-1} \Big\} \\
&\quad + \chi_u \mu_v K_v e^{\chi_u K_v} \int_\Omega a^p \\
&\le -p(p-1)D_u \int_\Omega e^{\chi_u v} a^{p-2} |\nabla a|^2 \\
&\quad + pc_1 e^{\chi_u K_v} \cdot \Big\{ 4\int_\Omega a^{p+1} + \int_\Omega b^{p+1} + \int_\Omega z^{p+1} + |\Omega| \Big\} \\
&\quad + \chi_u \mu_v K_v e^{\chi_u K_v} \cdot \Big\{ \int_\Omega a^{p+1} + |\Omega| \Big\} \qquad \text{for all } t \in (0,T_{max}),
\end{aligned}$$

so that

$$\frac{d}{dt}\int_\Omega e^{\chi_u v}a^p + c_2\int_\Omega |\nabla a^{\frac{p}{2}}|^2 \le c_3\int_\Omega a^{p+1} + c_3\int_\Omega b^{p+1} + c_3\int_\Omega z^{p+1} + c_3 \qquad \text{for all } t\in(0,T_{max}) \quad (5.7)$$

with $c_2 := \frac{4(p-1)D_u}{p}$ and $c_3 := \Big\{4pc_1 e^{\chi_u K_v} + \chi_u\mu_v K_v e^{\chi_u K_v}\Big\}\cdot\max\{1\,,\,|\Omega|\}$. Similarly, based on the third equation in (2.2) and the pointwise estimate for $g(a,v,b,z)$ from Lemma 5.1 we infer the existence of $c_4>0$ and $c_5>0$ such that

$$\frac{d}{dt}\int_\Omega e^{\chi_w v}b^p + c_4\int_\Omega |\nabla b^{\frac{p}{2}}|^2 \le c_5\int_\Omega a^{p+1} + c_5\int_\Omega b^{p+1} + c_5\int_\Omega z^{p+1} + c_5 \qquad \text{for all } t\in(0,T_{max}). \quad (5.8)$$

We finally multiply the fourth equation in (2.2) by z^p to see upon integrating by parts that again by Young's inequality and (3.2),

$$\begin{aligned}
\frac{1}{p+1}\frac{d}{dt}\int_\Omega z^{p+1} &= -pD_z\int_\Omega z^{p-1}|\nabla z|^2 - \delta_z\int_\Omega z^{p+1} - \rho_z\int_\Omega a e^{\chi_u v}z^{p+1} + \beta\int_\Omega b e^{\chi_w v}z^p \\
&\le \beta e^{\chi_w K_v}\int_\Omega b z^p \\
&\le \beta e^{\chi_w K_v}\int_\Omega b^{p+1} + \beta e^{\chi_w K_v}\int_\Omega z^{p+1} \qquad \text{for all } t\in(0,T_{max}),
\end{aligned}$$

and that thus

$$\frac{d}{dt}\int_\Omega z^{p+1} \le c_6\int_\Omega b^{p+1} + c_6\int_\Omega z^{p+1} \qquad \text{for all } t\in(0,T_{max}) \quad (5.9)$$

with $c_6 := (p+1)\beta e^{\chi_w K_v}$.

In summary, (5.7), (5.8) and (5.9) show that for all $t\in(0,T_{max})$,

$$\begin{aligned}
&\frac{d}{dt}\Big\{\int_\Omega e^{\chi_u v}a^p + \int_\Omega e^{\chi_w v}b^p + \int_\Omega z^{p+1}\Big\} + c_2\int_\Omega|\nabla a^{\frac{p}{2}}|^2 + c_4\int_\Omega|\nabla b^{\frac{p}{2}}|^2 \\
&\quad\le (c_3+c_5)\int_\Omega a^{p+1} + (c_3+c_5+c_6)\int_\Omega b^{p+1} + (c_3+c_5+c_6)\int_\Omega z^{p+1} + c_3 + c_5, \qquad (5.10)
\end{aligned}$$

where in order to appropriately estimate the first two summands on the right we rely on the fact that according to Lemma 4.6, there exists $c_7>0$ fulfilling

$$\int_\Omega a|\ln a| \le c_7 \quad\text{and}\quad \int_\Omega b|\ln b| \le c_7 \qquad \text{for all } t\in(0,T_{max}).$$

After two applications of Lemma 5.2, namely, these inequalities, combined with the observation that (3.1) and Lemma 3.2 provide $c_8>0$ such that

$$\int_\Omega a \le \int_\Omega u \le c_8 \quad\text{and}\quad \int_\Omega b \le \int_\Omega w \le c_8 \qquad \text{for all } t\in(0,T_{max}),$$

reveal that with $K(\cdot,\cdot)$ as provided by Lemma 5.2 we have

$$
\begin{aligned}
(c_3+c_5)\int_\Omega a^{p+1} &= (c_3+c_5)\|a^{\frac{p}{2}}\|_{L^{\frac{2(p+1)}{p}}(\Omega)}^{\frac{2(p+1)}{p}} \\
&\le \frac{2c_2}{pc_7}\|\nabla a^{\frac{p}{2}}\|_{L^2(\Omega)}^2 \int_\Omega a|\ln a^{\frac{p}{2}}| + K\Big(p, \frac{2c_2}{p(c_3+c_5)c_7}\Big)\cdot\Big\{\|a^{\frac{p}{2}}\|_{L^{\frac{2}{p}}(\Omega)}^{\frac{2(p+1)}{p}} + 1\Big\} \\
&= \frac{c_2}{c_7}\cdot\Big\{\int_\Omega |\nabla a^{\frac{p}{2}}|^2\Big\}\cdot\int_\Omega a|\ln a| + K\Big(p, \frac{2c_2}{p(c_3+c_5)c_7}\Big)\cdot\Big\{\Big\{\int_\Omega a\Big\}^{p+1}+1\Big\} \\
&\le c_2\int_\Omega |\nabla a^{\frac{p}{2}}|^2 + K\Big(p, \frac{2c_2}{p(c_3+c_5)c_7}\Big)\cdot(c_8^{p+1}+1) \qquad \text{for all } t\in(0,T_{max}),
\end{aligned}
$$

and that similarly

$$
(c_3+c_5+c_6)\int_\Omega b^{p+1} \le c_4\int_\Omega |\nabla b^{\frac{p}{2}}|^2 + K\Big(p, \frac{2c_4}{p(c_3+c_5+c_6)c_7}\Big)\cdot(c_8^{p+1}+1) \qquad \text{for all } t\in(0,T_{max}).
$$

Therefore, (5.10) implies that writing

$$
c_9 := \max\Big\{c_3+c_5+c_6\,,\ K\Big(p, \frac{2c_2}{p(c_3+c_5)c_7}\Big)\cdot(c_8^{p+1}+1)\,,\ K\Big(p, \frac{2c_4}{p(c_3+c_5+c_6)c_7}\Big)\cdot(c_8^{p+1}+1)\Big\},
$$

for

$$
y(t) := \int_\Omega e^{\chi_u v(\cdot,t)} a^p(\cdot,t) + \int_\Omega e^{\chi_w v(\cdot,t)} b^p(\cdot,t) + \int_\Omega z^{p+1}(\cdot,t), \qquad t\in[0,T_{max}),
$$

we have

$$
y'(t) \le c_9\int_\Omega z^{p+1} + c_9 \le c_9 y(t) + c_9 \qquad \text{for all } t\in(0,T_{max})
$$

and hence

$$
\begin{aligned}
y(t) &\le y(0)e^{c_9 t} + c_9\int_0^t e^{c_9(t-s)}ds \\
&= y(0)e^{c_9 t} + e^{c_9 t} - 1 \\
&\le (y(0)+1)e^{c_9 T_{max}} \qquad \text{for all } t\in(0,T_{max}),
\end{aligned}
$$

which entails (5.4), (5.5) and (5.6). $\square$

Along with parabolic smoothing properties, the latter yields a bound for z in L^∞.

Lemma 5.4 *If $T_{max}<\infty$, then there exists $C>0$ such that*

$$
\|z(\cdot,t)\|_{L^\infty(\Omega)} \le C \qquad \text{for all } t\in(0,T_{max}). \tag{5.11}
$$

PROOF. According to known smoothing properties of the Neumann heat semigroup $(e^{\sigma\Delta})_{\sigma\geq 0}$ on Ω ([21]), we fix $c_1 > 0$ such that

$$\|e^{tD_z\Delta}\varphi\|_{L^\infty(\Omega)} \leq c_1(1+t^{-\kappa})\|\varphi\|_{L^2(\Omega)} \qquad \text{for each } \varphi \in C^0(\overline{\Omega}) \text{ and any } t > 0, \tag{5.12}$$

where $\kappa := \frac{n}{4} < 1$. We next invoke Lemma 5.3 along with (3.2) to see that since we are assuming that T_{max} be finite, there must exist $c_2 > 0$ fulfilling

$$\|w(\cdot,t)\|_{L^2(\Omega)} \leq c_2 \qquad \text{for all } t \in (0,T_{max}). \tag{5.13}$$

As

$$\begin{aligned} z(\cdot,t) &= e^{t(D_z\Delta-\delta_z)}z_0 - \rho_z\int_0^t e^{(t-s)(D_z\Delta z-\delta_z)}\{u(\cdot,s)z(\cdot,s)\}ds + \beta\int_0^t e^{(t-s)(D_z\Delta z-\delta_z)}w(\cdot,s)ds \\ &\leq e^{-\delta_z t}\|z_0\|_{L^\infty(\Omega)} + \beta\int_0^t e^{(t-s)(D_z\Delta z-\delta_z)}w(\cdot,s)ds \quad \text{in } \Omega \qquad \text{for all } t\in(0,T_{max}) \end{aligned}$$

by (1.1) and the comparison principle, due to the nonnegativity of z we may combine (5.12) with (5.13) to infer that

$$\begin{aligned} \|z(\cdot,t)\|_{L^\infty(\Omega)} &\leq e^{-\delta_z t}\|z_0\|_{L^\infty(\Omega)} + c_1\beta\int_0^t \Big(1+(t-s)^{-\kappa}\Big)e^{-\delta_z(t-s)}\|w(\cdot,s)\|_{L^2(\Omega)}ds \\ &\leq \|z_0\|_{L^\infty(\Omega)} + c_1c_2\beta\int_0^t\Big(1+(t-s)^{-\kappa}\Big)ds \\ &= \|z_0\|_{L^\infty(\Omega)} + c_1c_2\beta\cdot\Big(t+\frac{t^{1-\kappa}}{1-\kappa}\Big) \\ &\leq \|z_0\|_{L^\infty(\Omega)} + c_1c_2\beta\cdot\Big(T_{max}+\frac{T_{max}^{1-\kappa}}{1-\kappa}\Big) \qquad \text{for all } t\in(0,T_{max}), \end{aligned}$$

and conclude as intended. $\square$

Based on a Moser-type iteration method, we finally achieve L^∞ bounds also for a and b.

Lemma 5.5 *Assume that $T_{max} < \infty$. Then one can find $C > 0$ fulfilling*

$$\|a(\cdot,t)\|_{L^\infty(\Omega)} \leq C \qquad \textit{for all } t\in(0,T_{max}) \tag{5.14}$$

as well as

$$\|b(\cdot,t)\|_{L^\infty(\Omega)} \leq C \qquad \textit{for all } t\in(0,T_{max}) \tag{5.15}$$

PROOF. As a consequence of Lemma 5.3, Lemma 5.1 and our hypothesis that T_{max} be finite, for each $p > 1$ we obtain $c_1(p) > 0$ and $c_2(p) > 0$ such that

$$\|a(\cdot,t)\|_{L^p(\Omega)} \leq c_1(p) \quad \text{and} \quad \Big\|f(a(\cdot,t),v(\cdot,t),b(\cdot,t),z(\cdot,t))\Big\|_{L^p(\Omega)} \leq c_2(p) \qquad \text{for all } t\in(0,T_{max}).$$

Therefore, (5.14) can be derived by means of a Moser-type iteration argument on the basis of the first equation in (2.2) in quite a standard manner. For details in a closely related setting, we may refer to

[16] or [15].

Likewise, (5.15) results from the observation that given $p > 1$, from Lemma 5.3 and Lemma 5.1 we gain $c_3(p) > 0$ and $c_4(p) > 0$ satisfying

$$\|b(\cdot,t)\|_{L^p(\Omega)} \le c_3(p) \qquad \text{and} \qquad \Big\| g(a(\cdot,t), v(\cdot,t), b(\cdot,t), z(\cdot,t)) \Big\|_{L^p(\Omega)} \le c_4(p)$$

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

□

6 Controlling ∇v in L^4. Proof of Theorem 1.1

In light of (2.5) and the outcomes of Lemma 5.4 and Lemma 5.5, our overall goal will be accomplished once we can establish a bound for ∇v with respect to the norm in $L^4(\Omega)$. In the following lemma, this will be achieved through an appropriate combination of three further testing processes, essentially on the L^∞ estimates for a, b and z just asserted.

Lemma 6.1 *If $T_{max} < \infty$, then with some $C > 0$ we have*

$$\int_\Omega |\nabla v(\cdot,t)|^4 \le C \qquad \textit{for all } t \in (0, T_{max}). \tag{6.1}$$

Proof. Let us first combine the Gagliardo-Nirenberg inequality with standard elliptic regularity theory to fix $c_1 > 0$ such that

$$\|\nabla \varphi\|_{L^4(\Omega)}^2 \le c_1 \|\Delta \varphi\|_{L^2(\Omega)} \|\varphi\|_{L^\infty(\Omega)} \qquad \text{for all } \varphi \in C^2(\overline{\Omega}) \text{ fulfilling } \tfrac{\partial \varphi}{\partial \nu} = 0 \text{ on } \partial\Omega, \tag{6.2}$$

an employ Lemma 5.5 to see that according to (2.3), (2.4) and the assumed finiteness of T_{max}, there exist positive constants c_2, c_3, c_4 and c_5 such that

$$\|a(\cdot,t)\|_{L^\infty(\Omega)} \le c_2 \qquad \text{for all } t \in (0, T_{max}) \tag{6.3}$$

and

$$\|b(\cdot,t)\|_{L^\infty(\Omega)} \le c_3 \qquad \text{for all } t \in (0, T_{max}) \tag{6.4}$$

as well as

$$\int_\Omega f^2(a(\cdot,t), v(\cdot,t), b(\cdot,t), z(\cdot,t)) \le c_4 \qquad \text{for all } t \in (0, T_{max}) \tag{6.5}$$

and

$$\int_\Omega g^2(a(\cdot,t), v(\cdot,t), b(\cdot,t), z(\cdot,t)) \le c_5 \qquad \text{for all } t \in (0, T_{max}). \tag{6.6}$$

Therefore, namely, when multiplying the identity $a_t = D_u \Delta a + \xi_u \nabla v \cdot \nabla a + f(a, v, b, z)$ by $-\Delta a$ and integrating by parts, due to Young's inequality, the Cauchy-Schwarz inequality, (6.2), (6.3) and (6.5) we can estimate

$$
\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\int_\Omega |\nabla a|^2 + D_u\int_\Omega |\Delta a|^2 \\
&\quad = -\xi_u\int_\Omega (\nabla v\cdot\nabla a)\Delta a - \int_\Omega f(a,v,b,z)\Delta a \\
&\quad \le \frac{D_u}{4}\int_\Omega |\Delta a|^2 + \frac{2\xi_u^2}{D_u}\int_\Omega |\nabla v\cdot\nabla a|^2 + \frac{2}{D_u}\int_\Omega f^2(a,v,b,z) \\
&\quad \le \frac{D_u}{4}\int_\Omega |\Delta a|^2 + \frac{2\xi_u^2}{D_u}\|\nabla v\|_{L^4(\Omega)}^2\|\nabla a\|_{L^4(\Omega)}^2 + \frac{2}{D_u}\int_\Omega f^2(a,v,b,z) \\
&\quad \le \frac{D_u}{4}\int_\Omega |\Delta a|^2 + \frac{2c_1\xi_u^2}{D_u}\|\nabla v\|_{L^4(\Omega)}^2\|\Delta a\|_{L^2(\Omega)}\|a\|_{L^\infty(\Omega)} + \frac{2}{D_u}\int_\Omega f^2(a,v,b,z) \\
&\quad \le \frac{D_u}{4}\int_\Omega |\Delta a|^2 + \frac{2c_1c_2\xi_u^2}{D_u}\|\nabla v\|_{L^4(\Omega)}^2\|\Delta a\|_{L^2(\Omega)} + \frac{2}{D_u}\int_\Omega f^2(a,v,b,z) \\
&\quad \le \frac{D_u}{2}\int_\Omega |\Delta a|^2 + \frac{4c_1^2c_2^2\xi_u^4}{D_u^3}\int_\Omega |\nabla v|^4 + \frac{2c_4}{D_u} \qquad \text{for all } t\in(0,T_{max}).
\end{aligned}
$$

Since, again by (6.2) and (6.3),

$$
\frac{D_u}{2}\int_\Omega |\Delta a|^2 \ge \frac{D_u}{2c_1^2c_2^2}\int_\Omega |\nabla a|^4 \qquad \text{for all } t\in(0,T_{max}),
$$

this implies that

$$
\frac{d}{dt}\int_\Omega |\nabla a|^2 + c_6\int_\Omega |\nabla a|^4 \le c_7\int_\Omega |\nabla v|^4 + c_7 \qquad \text{for all } t\in(0,T_{max}) \tag{6.7}
$$

with $c_6 := \frac{D_u}{c_1^2c_2^2}$ and $c_7 := \max\left\{\frac{8c_1^2c_2^2\xi_u^4}{D_u^3}\,,\ \frac{4c_4}{D_u}\right\}$, and in much the same manner, relying on (6.2), (6.4), (6.6) and the third equation in (2.2) we find $c_8 > 0$ and $c_9 > 0$ fulfilling

$$
\frac{d}{dt}\int_\Omega |\nabla b|^2 + c_8\int_\Omega |\nabla b|^4 \le c_9\int_\Omega |\nabla v|^4 + c_9 \qquad \text{for all } t\in(0,T_{max}). \tag{6.8}
$$

We next test the second equation from (2.2) against $|\nabla v|^2\nabla v$ to see by neglecting several nonpositive contributions and employing (3.2) and Young's inequality that

$$
\begin{aligned}
\frac{1}{4}\frac{d}{dt}\int_\Omega |\nabla v|^4 &= \int_\Omega |\nabla v|^2\nabla v\cdot\nabla\Big\{-\alpha_u a v e^{\chi_u v} - \alpha_w b v e^{\chi_w v} + \mu_v v - \mu_v v^2\Big\} \\
&= -\alpha_u\int_\Omega a(1+\chi_u v)e^{\chi_u v}|\nabla v|^4 - \alpha_w\int_\Omega b(1+\chi_w v)e^{\chi_w v}|\nabla v|^4 \\
&\quad -\alpha_u\int_\Omega v e^{\chi_u v}|\nabla v|^2\nabla v\cdot\nabla a - \alpha_w\int_\Omega v e^{\chi_w v}|\nabla v|^2\nabla v\cdot\nabla b \\
&\quad +\mu_v\int_\Omega |\nabla v|^4 - 2\mu_v\int_\Omega v|\nabla v|^4 \\
&\le \alpha_u K_v e^{\chi_u K_v}\int_\Omega |\nabla v|^3|\nabla a| + \alpha_w K_v e^{\chi_w K_v}\int_\Omega |\nabla v|^3|\nabla b| + \mu_v\int_\Omega |\nabla v|^4
\end{aligned}
$$

$$
\begin{aligned}
&\leq \frac{1}{4}\int_\Omega |\nabla a|^4 + \frac{3}{4}\cdot (\alpha_u K_v e^{\chi_u K_v})^{\frac{4}{3}} \int_\Omega |\nabla v|^4 \\
&\quad +\frac{1}{4}\int_\Omega |\nabla b|^4 + \frac{3}{4}\cdot (\alpha_w K_v e^{\chi_w K_v})^{\frac{4}{3}} \int_\Omega |\nabla v|^4 \\
&\quad +\mu_v \int_\Omega |\nabla v|^4 \qquad \text{for all } t\in(0,T_{max}),
\end{aligned}
$$

so that

$$
\frac{d}{dt}\int_\Omega |\nabla v|^4 \leq \int_\Omega |\nabla a|^4 + \int_\Omega |\nabla b|^4 + c_{10}\int_\Omega |\nabla v|^4 \qquad \text{for all } t\in(0,T_{max}) \tag{6.9}
$$

if we let $c_{10} := 3(\alpha_u K_v e^{\chi_u K_v})^{\frac{4}{3}} + 3(\alpha_w K_v e^{\chi_w K_v})^{\frac{4}{3}} + 4\mu_v$.

Now combining (6.7) and (6.8) with (6.9) shows that

$$
\begin{aligned}
&\frac{d}{dt}\Big\{\frac{1}{c_6}\int_\Omega |\nabla a|^2 + \frac{1}{c_8}\int_\Omega |\nabla b|^2 + \int_\Omega |\nabla v|^4\Big\} \\
&\qquad \leq \frac{1}{c_6}\cdot\Big\{-c_6\int_\Omega |\nabla a|^4 + c_7\int_\Omega |\nabla v|^4 + c_7\Big\} \\
&\qquad\quad +\frac{1}{c_8}\cdot\Big\{-c_8\int_\Omega |\nabla b|^4 + c_9\int_\Omega |\nabla v|^4 + c_9\Big\} \\
&\qquad\quad +\int_\Omega |\nabla a|^4 + \int_\Omega |\nabla b|^4 + c_{10}\int_\Omega |\nabla v|^4 \\
&\qquad = \Big(\frac{c_7}{c_6} + \frac{c_9}{c_8} + c_{10}\Big)\int_\Omega |\nabla v|^4 + \frac{c_7}{c_6} + \frac{c_9}{c_8} \\
&\qquad \leq \Big(\frac{c_7}{c_6} + \frac{c_9}{c_8} + c_{10}\Big)\cdot\Big\{\frac{1}{c_6}\int_\Omega |\nabla a|^2 + \frac{1}{c_8}\int_\Omega |\nabla b|^2 + \int_\Omega |\nabla v|^4\Big\} \\
&\qquad\quad +\frac{c_7}{c_6} + \frac{c_9}{c_8} \qquad \text{for all } t\in(0,T_{max}),
\end{aligned}
$$

which upon an integration implies that writing $c_{11} := \frac{c_7}{c_6} + \frac{c_9}{c_8} + c_{10}$, $c_{12} := \frac{c_7}{c_6} + \frac{c_9}{c_8}$ and $c_{13} := \frac{1}{c_6}\int_\Omega |\nabla a(\cdot,0)|^2 + \frac{1}{c_8}\int_\Omega |\nabla b(\cdot,0)|^2 + \int_\Omega |\nabla v_0|^4$ we have

$$
\begin{aligned}
\frac{1}{c_6}\int_\Omega |\nabla a|^2 + \frac{1}{c_8}\int_\Omega |\nabla b|^2 + \int_\Omega |\nabla v|^4 &\leq c_{13}e^{c_{11}t} + c_{12}\int_0^t e^{c_{11}(t-s)}ds \\
&= \Big(c_{13} + \frac{c_{12}}{c_{11}}\Big)\cdot e^{c_{11}t} - \frac{c_{12}}{c_{11}} \qquad \text{for all } t\in(0,T_{max}).
\end{aligned}
$$

Once more since $T_{max} < \infty$, this particularly entails (6.1). $\square$

Thereby our main result has essentially been proved already.

PROOF of Theorem 1.1. Thanks to the equivalence of (1.1) and (2.2) in the considered framework of classical solutions, we only need to combine the outcomes of Lemma 5.5, Lemma 5.4 and Lemma 6.1 with the statements on local existence and extensibility from Lemma 2.1. $\square$

Acknowledgement. Youshan Tao was supported by the *National Natural Science Foundation of China (No. 11861131003).* The second author 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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