Critical mass for infinite-time blow-up in a haptotaxis system with nonlinear zero-order interaction

Youshan Tao*

School of Mathematical Sciences, Shanghai Jiao Tong University, Shanghai 200240, P.R. China

Michael Winkler[#] Institut für Mathematik, Universität Paderborn, 33098 Paderborn, Germany

Abstract

We consider the haptotaxis system

 $\left\{ \begin{array}{rcl} u_t &=& \Delta u - \nabla \cdot (u \nabla v), \\ v_t &=& -(u+w)v, \\ w_t &=& D_w \Delta w - w + uz, \\ z_t &=& D_z \Delta z - z - uz + \beta w, \end{array} \right.$

which arises as a simplified version of a recently proposed model for oncolytic virotherapy. When posed under no-flux boundary conditions in a smoothly bounded domain $\Omega \subset \mathbb{R}^2$, with positive parameters D_w , D_z and β , and along with initial conditions involving suitably regular data, this system is known to admit global classical solutions.

It is shown that with respect to infinite-time blow-up, this system exhibits a critical mass phenomenon related to the quantity $m_c := \frac{1}{(\beta-1)_+}$: In fact, it is seen that each solution fulfilling $\frac{1}{|\Omega|} \int_{\Omega} u(\cdot, 0) > m_c$ must be unbounded, and this is complemented by a boundedness result which inter alia asserts that for any choice of $m < m_c$ one can find a nontrivial set of solutions, particularly containing spatially heterogeneous solutions, each of which is bounded though satisfying $\frac{1}{|\Omega|} \int_{\Omega} u(\cdot, 0) = m$.

Key words: haptotaxis; infinite-time blow-up; critical mass MSC (2010): 35B44, 35K57, 35Q92, 92C17

taoys@sjtu.edu.cn

 $^{^{\#}}$ michael.winkler@math.uni-paderborn.de

1 Introduction

In a bounded domain $\Omega \subset \mathbb{R}^2$ and with positive parameters β, D_w and D_z , we consider the evolution system

$$\begin{cases}
 u_t = \Delta u - \nabla \cdot (u \nabla v), & x \in \Omega, \ t > 0, \\
 v_t = -(u+w)v, & x \in \Omega, \ t > 0, \\
 w_t = D_w \Delta w - w + uz, & x \in \Omega, \ t > 0, \\
 z_t = D_z \Delta z - z - uz + \beta w, & x \in \Omega, \ t > 0,
 \end{cases}$$
(1.1)

that can be viewed as a simplified version of a recently proposed model for a certain medical treatment of tumor diseases, also known as oncolytic virotherapy, in the course of which cancerous tissue is subject to virus particles selectively assaulting tumor cells. Indeed, as unknown quantities considering the population densities u, w and z of uninfected and infected cancer cells and of virions, and the distribution v of the so-called extracellular matrix (ECM) that represents yet uninvaded healthy tissue, the authors in [1] introduce more comprehensive systems of the form

$$\begin{cases}
 u_t = D_u \Delta u - \xi_u \nabla \cdot (u \nabla v) + \mu_u u(1-u) - \rho_u uz, & x \in \Omega, t > 0, \\
 v_t = -(\alpha_u u + \alpha_w w)v + \mu_v v(1-v), & x \in \Omega, t > 0, \\
 w_t = D_w \Delta w - \xi_w \nabla \cdot (w \nabla v) - \delta_w w + \rho_w uz, & x \in \Omega, t > 0, \\
 z_t = D_z \Delta z - \delta_z z - \rho_z uz + \beta w, & x \in \Omega, t > 0,
 \end{cases}$$
(1.2)

to describe the spatio-temporal evolution during such processes. Particularly, in this approach it is assumed that uninfected tumor cells, besides undergoing directed motion toward increasing levels of the non-diffusible ECM, proliferate according to a logistic law and are diminished in number through irreversible conversion into an infected state, and that the population of infected tumor cells performs similar migration, is augmented due to infection, and is degraded according to spontaneous death promoted by exhaustion due to virus production which in turn increases the number of virions. Apart from that, (1.2) accounts for virus decrease caused by natural death and by binding to uninfected tumor cells, for degradation of the ECM upon contact with tumor cells, and for a logistic-type remodeling of the ECM in the sense of spontaneous renewal of healthy tissue.

Models of this flavor not only go beyond classical reaction-diffusion-based descriptions by containing cross-diffusive contributions, but moreover also differ from related chemotaxis systems in that whenever $\xi_u > 0$, the associated tactic migration is directed by a non-diffusible cue. Inter alia due to their apparent relevance in several biological contexts ([3], [9], [5]), such *haptotaxis* mechanisms have been the objective of considerable efforts in the analytical literature ([24], [6], [4], [11], [12], [29], [28], [26], [27]), partially even in yet more intricate settings involving further processes such as additional chemotactic interaction ([19], [15], [13], [18], [20], [25], [2], [10], [14], [17], [16], [21]). Apparently reflecting an increased mathematical complexity going along with the introduction of such types of cross-diffusion, however, most studies in this field mainly focus on basic issues from elementary solution theory, hence concentrating on statements on global solvability in appropriate frameworks ([24], [17], [19], [15], [29], [26], [22]), and already the derivation of global boundedness features seems to pose challenges that so far could successfully be coped with only in a comparatively small number of cases ([18], [14], [2]); qualitative information beyond this, e.g. in the style of results on large time asymptotics, is apparently yet limited to very few and quite simple settings, and especially effects related to unboundedness properties seem widely unaddressed ([20], [11] [13], [27], [8]).

Main results. The purpose of this study is to rigorously detect a phenomenon related to the spontaneous emergence of large densities in (1.1), even up to the identification of critical parameter ranges therefor. This will potentially capture a mathematical feature also inherent to the more complex system (1.2) within appropriate constellations, because (1.2) can essentially be reduced to a normalized version of (1.1) upon neglecting haptotactic cross-diffusion of infected tumor cells and renewal of ECM, and upon considering the diffusive and haptotactic migration processes in (1.2) as the predominant mechanisms relevant to the evolution of uninfected tumor cells; whereas the former two simplification steps have already explicitly been discussed in the modeling literature ([1], [3]), the latter reduction seems to provide a reasonable approximation at least in the presence of abundantly many uninfected cells, and during a suitably short initial stage during which the correspondingly large number of uninfected cells has not undergone significant changes due to the zero-order mechanisms in the first equation from (1.2).

Specifically, we shall consider (1.1) in a bounded domain $\Omega \subset \mathbb{R}^2$ with smooth boundary, along with the boundary conditions

$$(\nabla u - u\nabla v) \cdot \nu = \frac{\partial w}{\partial \nu} = \frac{\partial z}{\partial \nu} = 0, \qquad x \in \partial\Omega, \ t > 0,$$
(1.3)

and the requirement that

$$u(x,0) = u_0(x), \quad v(x,0) = v_0(x), \quad w(x,0) = w_0(x), \quad z(x,0) = z_0(x), \qquad x \in \Omega,$$
(1.4)

where our hypotheses concerning the initial data will be that

$$u_0, v_0$$
 and w_0 are nonnegative functions from $C^{2+\vartheta}(\overline{\Omega})$ for some $\vartheta > 0$,
with $u_0 \neq 0, w_0 \neq 0, z_0 \neq 0, \sqrt{v_0} \in W^{1,2}(\Omega)$ and $\frac{\partial u_0}{\partial \nu} = \frac{\partial v_0}{\partial \nu} = \frac{\partial z_0}{\partial \nu} = 0$ on $\partial\Omega$. (1.5)

In this framework, namely, a recent result from [22] becomes applicable so as to assert global existence of a unique classical solution $(u, v, w, z) \in (C^{2,1}(\overline{\Omega} \times [0, \infty)))^4$ such that u, w and z are positive and vis nonnegative in $\overline{\Omega} \times (0, \infty)$ (see also Lemma 2.1 below); in particular, this rules out any occurrence of explosions within finite time.

With regard to the possibility of infinite-time blow-up, however, our subsequent analysis will discover a genuine critical mass phenomenon in the following sense.

Firstly, whenever the virus replication rate satisfies $\beta > 1$, for all initial distributions which with respect to the total mass in their first component exceed a certain value, the corresponding solution must become unbounded in the large time limit. Here and below, for $\varphi \in L^1(\Omega)$ we abbreviate $\overline{\varphi} := \frac{1}{|\Omega|} \int_{\Omega} \varphi$.

Theorem 1.1 Let $\Omega \subset \mathbb{R}^2$ be a bounded domain with smooth boundary, let $\beta > 1$, and suppose that u_0, v_0, w_0 and z_0 satisfy (1.5) with

$$\overline{u}_0 > \frac{1}{\beta - 1}.\tag{1.6}$$

Then the global classical solution $(u, v, w, z) \in (C^{2,1}(\overline{\Omega} \times [0, \infty)))^4$ of (1.1), (1.3), (1.4) from Lemma 2.1 below satisfies

$$\lim_{t \to \infty} \sup_{t \to \infty} \left\{ \|u(\cdot, t)\|_{L^{\infty}(\Omega)} + \|w(\cdot, t)\|_{L^{\infty}(\Omega)} + \|z(\cdot, t)\|_{L^{\infty}(\Omega)} \right\} = \infty.$$
(1.7)

Secondly, the mass level appearing in (1.6) indeed is critical with regard to the unboundedness feature encountered above, as indicated by the next result which inter alia also justifies the restriction on β made in Theorem 1.1.

Proposition 1.2 Let $\Omega \subset \mathbb{R}^2$ be a bounded domain with smooth boundary, and assume that $\beta > 0$ and that u_0, v_0, w_0 and z_0 satisfy (1.5) with $v_0 \equiv 0$ and

$$\overline{u}_0 < \frac{1}{(\beta - 1)_+}.\tag{1.8}$$

Then the global classical solution $(u, v, w, z) \in (C^{2,1}(\overline{\Omega} \times [0, \infty)))^4$ of (1.1), (1.3), (1.4) has the property that

$$\sup_{t>0} \left\{ \|u(\cdot,t)\|_{L^{\infty}(\Omega)} + \|v(\cdot,t)\|_{L^{\infty}(\Omega)} + \|w(\cdot,t)\|_{L^{\infty}(\Omega)} + \|z(\cdot,t)\|_{L^{\infty}(\Omega)} \right\} < \infty,$$

and moreover we have

$$w(\cdot,t) \to 0 \quad and \quad z(\cdot,t) \to 0 \quad in \ L^{\infty}(\Omega) \qquad as \ t \to \infty.$$

An interesting topic left open here concerns the question how far the explicit condition (1.8) remains sufficient to ensure boundedness also in contexts involving nontrivial haptoattractant components v. While this indeed seems to be true in the case $\beta < 1$, widely unconditionally in not depending on substantial further assumptions on the initial data ([23]), we suspect that the dynamics might be significantly richer in the more delicate situation in which $\beta \geq 1$; deeper analysis in this regard goes beyond the scope of the present work, however.

Ideas. We shall prove Theorem 1.1 via a contradiction argument, supposing that (1.7) was false. Such accordingly bounded solutions, namely, will be seen to necessarily satisfy $u(\cdot,t) \to \overline{u}_0$ and $v(\cdot,t) \to 0$ in $L^1(\Omega)$ as $t \to \infty$ (Lemma 3.6 and Lemma 3.7). For initial data fulfilling (1.6), this will enable us to choose b > 0 such that with some $t_0 > 0$ and C > 0 we have

$$\frac{d}{dt} \left\{ \int_{\Omega} \ln w + b \int_{\Omega} \ln z \right\} \ge C \qquad \text{for all } t > t_0, \tag{1.9}$$

which is incompatible with said boundedness assumption.

The complementing result from Proposition 1.2 will independently be derived in Section 5 by means of an argument based on the comparison principle for a suitably designed two-component cooperative parabolic system.

2 Preliminaries

Let us first recall from [22] the following basic result on unique global smooth solvability.

Lemma 2.1 Let $\Omega \subset \mathbb{R}^2$ be a bounded domain with smooth boundary, let $\beta > 0$, and suppose that (u_0, v_0, w_0, z_0) satisfies (1.5). Then the problem (1.1), (1.3), (1.4) 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 $\overline{\Omega} \times (0, \infty)$. Moreover,

$$\int_{\Omega} u(\cdot, t) = \int_{\Omega} u_0 \qquad \text{for all } t > 0, \tag{2.1}$$

and for any choice of $t_0 \ge 0$ we have

$$\|v(\cdot,t)\|_{L^{\infty}(\Omega)} \le \|v(\cdot,t_0)\|_{L^{\infty}(\Omega)} \qquad for \ all \ t > t_0.$$

$$(2.2)$$

Following a variable substitution extensively used in studying of haptotaxis systems ([6], [7], [24] and [17]), we set

$$a := ue^{-v} \tag{2.3}$$

and then we see that the crucial first sub-problem of (1.1), (1.3), (1.4) transforms to

$$\begin{cases} a_t = e^{-v} \nabla \cdot (e^v \nabla a) + a(ae^v + w)v, & x \in \Omega, \ t > 0, \\ \frac{\partial a}{\partial \nu} = 0, & x \in \partial\Omega, \ t > 0, \\ a(x,0) = u_0(x)e^{-v_0(x)}, & x \in \Omega. \end{cases}$$
(2.4)

3 Decay properties of $u - \overline{u}_0$ and v for arbitrary bounded solutions

In order to prepare our contradiction-based strategy toward a verification of Theorem 1.1, in this section we shall make sure that actually regardless of the size of $\beta > 0$, each global classical solution (u, v, w, z) must satisfy $(u(\cdot, t), v(\cdot, t)) \rightarrow (\overline{u}_0, 0)$ in $(L^1(\Omega))^2$. To avoid extensive notation, unless otherwise stated we shall assume throughout this section that (u_0, v_0, w_0, z_0) complies with (1.5), and that (u, v, w, z) is the global classical solution to (1.1), (1.3), (1.4) addressed in Lemma 2.1.

Some first information about such solutions can be gained through a standard testing procedure:

Lemma 3.1 Let $\beta > 0$. Then

$$\int_{\Omega} e^{v(\cdot,t)} a^2(\cdot,t) + 2 \int_0^t \int_{\Omega} e^v |\nabla a|^2 \le \int_{\Omega} u_0^2 + \|u\|_{L^{\infty}(\Omega \times (0,t))}^2 \cdot \int_{\Omega} v_0 \quad \text{for all } t > 0.$$
(3.1)

PROOF. On the basis of (2.4) and (2.3), we compute

$$\frac{d}{dt} \int_{\Omega} e^{v} a^{2} = 2 \int_{\Omega} e^{v} a \cdot \left\{ e^{-v} \nabla \cdot (e^{v} \nabla a) - av_{t} \right\} + \int_{\Omega} e^{v} a^{2} v_{t}$$

$$= -2 \int_{\Omega} e^{v} |\nabla a|^{2} - \int_{\Omega} e^{v} a^{2} v_{t}$$

$$= -2 \int_{\Omega} e^{v} |\nabla a|^{2} - \int_{\Omega} u^{2} e^{-v} v_{t} \quad \text{for all } t > 0,$$
(3.2)

where given $t_0 > 0$ we may use the nonpositivity of v_t in estimating

$$-\int_{\Omega} u^2 e^{-v} v_t = \int_{\Omega} u^2 e^{-v} |v_t|$$

$$\leq ||u||^2_{L^{\infty}(\Omega \times (0,t_0))} \int_{\Omega} |v_t|$$

$$= -||u||^2_{L^{\infty}(\Omega \times (0,t_0))} \int_{\Omega} v_t \quad \text{for all } t \in (0,t_0).$$

For any such t_0 , integrating (3.2) over $t \in (0, t_0)$ thus shows that

$$\begin{split} \int_{\Omega} e^{v(\cdot,t_0)} a^2(\cdot,t_0) + 2 \int_0^{t_0} \int_{\Omega} e^{v} |\nabla a|^2 &\leq \int_{\Omega} e^{v_0} a^2(\cdot,0) - \|u\|_{L^{\infty}(\Omega \times (0,t_0))}^2 \cdot \left\{ \int_{\Omega} v(\cdot,t_0) - \int_{\Omega} v_0 \right\} \\ &\leq \int_{\Omega} e^{v_0} a^2(\cdot,0) + \|u\|_{L^{\infty}(\Omega \times (0,t_0))}^2 \cdot \int_{\Omega} v_0 \\ &= \int_{\Omega} u_0^2 e^{-v_0} + \|u\|_{L^{\infty}(\Omega \times (0,t_0))}^2 \cdot \int_{\Omega} v_0 \end{split}$$

and hence establishes the claim due to the inequality $e^{-v_0} \leq 1$.

Now assuming the first solution component to be bounded, from the above we immediately obtain the following basic stabilization feature of a:

Corollary 3.2 Let $\beta > 0$, and suppose that

$$\sup_{t>0} \left\{ \|u(\cdot,t)\|_{L^{\infty}(\Omega)} + \|w(\cdot,t)\|_{L^{\infty}(\Omega)} + \|z(\cdot,t)\|_{L^{\infty}(\Omega)} \right\} < \infty.$$
(3.3)

Then

$$\int_0^\infty \int_\Omega |\nabla a|^2 < \infty \tag{3.4}$$

and

$$\int_0^\infty \|a(\cdot,t) - \overline{a(\cdot,t)}\|_{L^2(\Omega)}^2 dt < \infty.$$
(3.5)

PROOF. According to the hypotheses (3.3), we can find $c_1 > 0$ such that

 $u(x,t) \leq c_1$ for all $x \in \Omega$ and t > 0.

By nonnegativity of v, (3.1) therefore particularly implies that

$$2\int_0^t \int_\Omega |\nabla a|^2 \le 2\int_0^t \int_\Omega e^v |\nabla a|^2 \le \int_\Omega u_0^2 + c_1^2 \int_\Omega v_0 \qquad \text{for all } t > 0,$$

and that thus (3.4) holds. The property in (3.5) thereupon becomes a direct consequence of a Poincaré inequality.

In order to improve this yet quite weak decay information, we next intend to augment the above by suitable further regularity properties in the course of a second testing procedure applied to (2.4), an immediate outcome of which is the following.

Lemma 3.3 Let $\beta > 0$. Then

$$\int_{0}^{t} \int_{\Omega} e^{v} a_{t}^{2} + \int_{\Omega} e^{v(\cdot,t)} |\nabla a(\cdot,t)|^{2} \\
\leq \int_{\Omega} e^{v_{0}} |\nabla (u_{0}e^{-v_{0}})|^{2} + \frac{1}{2} ||u||_{L^{\infty}(\Omega \times (0,t))}^{2} \cdot \left\{ ||u||_{L^{\infty}(\Omega \times (0,t))} + ||w||_{L^{\infty}(\Omega \times (0,t))} \right\} \cdot \int_{\Omega} v_{0}^{2} \quad (3.6)$$

for all t > 0.

PROOF. On multiplying the first equation in (2.4) by $e^{v}a_{t}$ and integrating by parts, we see that

$$\int_{\Omega} e^{v} a_{t}^{2} = \int_{\Omega} a_{t} \nabla \cdot (e^{v} \nabla a) - \int_{\Omega} e^{v} a a_{t} v_{t}$$
$$= -\int_{\Omega} e^{v} \nabla a \cdot \nabla a_{t} - \int_{\Omega} e^{v} a a_{t} v_{t} \quad \text{for all } t > 0, \qquad (3.7)$$

where by nonpositivity of v_t ,

$$-\int_{\Omega} e^{v} \nabla a \cdot \nabla a_{t} = -\frac{1}{2} \int_{\Omega} e^{v} \partial_{t} |\nabla a|^{2}$$

$$= -\frac{1}{2} \frac{d}{dt} \int_{\Omega} e^{v} |\nabla a|^{2} + \frac{1}{2} \int_{\Omega} e^{v} |\nabla a|^{2} v_{t}$$

$$\leq -\frac{1}{2} \frac{d}{dt} \int_{\Omega} e^{v} |\nabla a|^{2} \quad \text{for all } t > 0.$$
(3.8)

Moreover, relying on Young's inequality and once again on the identity $v_t = -(u+w)v$ we obtain that for each $t_0 > 0$ and any $t \in (0, t_0)$,

$$\begin{split} -\int_{\Omega} e^{v} a a_{t} v_{t} &\leq \frac{1}{2} \int_{\Omega} e^{v} a_{t}^{2} + \frac{1}{2} \int_{\Omega} e^{v} a^{2} v_{t}^{2} \\ &= \frac{1}{2} \int_{\Omega} e^{v} a_{t}^{2} + \frac{1}{4} \int_{\Omega} u^{2} e^{-v} (u+w) |\partial_{t} v^{2}| \\ &\leq \frac{1}{2} \int_{\Omega} e^{v} a_{t}^{2} - \frac{1}{4} \|u\|_{L^{\infty}(\Omega \times (0,t_{0}))}^{2} \cdot \left\{ \|u\|_{L^{\infty}(\Omega \times (0,t_{0}))} + \|w\|_{L^{\infty}(\Omega \times (0,t_{0}))} \right\} \cdot \frac{d}{dt} \int_{\Omega} v^{2}. \end{split}$$

Together with (3.8) inserted into (3.7), after a time integration this shows that

$$\begin{split} \frac{1}{2} \int_{0}^{t_{0}} \int_{\Omega} e^{v} a_{t}^{2} + \frac{1}{2} \int_{\Omega} e^{v(\cdot,t_{0})} |\nabla a(\cdot,t_{0})|^{2} \\ & \leq \quad \frac{1}{2} \int_{\Omega} e^{v_{0}} |\nabla a(\cdot,0)|^{2} \\ & \quad -\frac{1}{4} \|u\|_{L^{\infty}(\Omega \times (0,t_{0}))}^{2} \cdot \left\{ \|u\|_{L^{\infty}(\Omega \times (0,t_{0}))} + \|w\|_{L^{\infty}(\Omega \times (0,t_{0}))} \right\} \cdot \left\{ \int_{\Omega} v^{2}(\cdot,t_{0}) - \int_{\Omega} v_{0}^{2} \right\} \end{split}$$

for all $t_0 > 0$. Rewriting $\nabla a(\cdot, 0) = \nabla (u_0 e^{-v_0})$ according to (2.3), since $\int_{\Omega} v^2(\cdot, t_0) \ge 0$ for all $t_0 > 0$ we immediately obtain (3.6) from this.

Again, the right-hand side herein can be appropriately controlled whenever our solution is assumed to be bounded, hence implying the following conclusion for any such solution: **Corollary 3.4** If $\beta > 0$ and (3.3) holds, then

$$\int_0^\infty \int_\Omega a_t^2 < \infty \tag{3.9}$$

and

$$\sup_{t>0} \int_{\Omega} |\nabla a(\cdot, t)|^2 < \infty.$$
(3.10)

PROOF. Assuming (3.3), we can fix $c_1 > 0$ and $c_2 > 0$ such that

$$u(x,t) \le c_1$$
 and $w(x,t) \le c_2$ for all $x \in \Omega$ and $t > 0$,

whence (3.6) entails that

$$\begin{split} \int_{0}^{t} \int_{\Omega} a_{t}^{2} + \int_{\Omega} |\nabla a(\cdot, t)|^{2} &\leq \int_{0}^{t} \int_{\Omega} e^{v} a_{t}^{2} + \int_{\Omega} e^{v(\cdot, t)} |\nabla a(\cdot, t)|^{2} \\ &\leq \int_{\Omega} e^{v_{0}} |\nabla (u_{0} e^{v_{0}})|^{2} + \frac{1}{2} c_{1}^{2} (c_{1} + c_{2}) \int_{\Omega} v_{0}^{2} \quad \text{for all } t > 0, \end{split}$$

and that thus both (3.9) and (3.10) are valid.

Now combining Corollary 3.2 with the compactness properties implicitly entailed by Corollary 3.4 yields the following stabilization feature of a whenever the solution is bounded.

Lemma 3.5 Let $\beta > 0$, and assume that (3.3) holds. Then

$$a(\cdot,t) - \overline{a(\cdot,t)} \to 0 \quad in \ L^2(\Omega) \qquad as \ t \to \infty.$$
 (3.11)

PROOF. If the claim was false, then we could find $(t_k)_{k\in\mathbb{N}} \subset (0,\infty)$ such that $t_k \to \infty$ as $k \to \infty$, and such that for $\psi(x,t) := a(x,t) - \overline{a(\cdot,t)}$, $(x,t \in \Omega \times (0,\infty))$, we have

$$\inf_{k\in\mathbb{N}} \|\psi(\cdot, t_k)\|_{L^2(\Omega)} > 0.$$

As our hypothesis on validity of (3.3) warrants applicability of Corollary 3.4, from the latter along with (2.1) we readily infer that $(\psi(\cdot, t))_{t>0}$ is bounded in $W^{1,2}(\Omega)$ and thus relatively compact in $L^2(\Omega)$, whence on passing to a subsequence if necessary we may assume that with some $0 \neq \psi_{\infty} \in L^2(\Omega)$,

$$\psi(\cdot, t_k) \to \psi_{\infty} \quad \text{in } L^2(\Omega) \qquad \text{as } k \to \infty.$$
 (3.12)

We now observe that as a second consequence of Corollary 3.4, $c_1 := \int_0^\infty \int_\Omega a_t^2$ is finite, so that since

$$\left|\partial_t \overline{a(\cdot,t)}\right|^2 = \frac{1}{|\Omega|^2} \left| \int_{\Omega} a_t \right|^2 \le \frac{1}{|\Omega|} \int_{\Omega} a_t^2 \quad \text{for all } t > 0$$

by the Cauchy-Schwarz inequality, it follows that

$$\int_{0}^{\infty} \int_{\Omega} \psi_{t}^{2} \leq 2 \int_{0}^{\infty} \int_{\Omega} \left\{ a_{t}^{2} + \left| \partial_{t} \overline{a(\cdot, t)} \right|^{2} \right\} \\
\leq 4 \int_{0}^{\infty} \int_{\Omega} a_{t}^{2} \\
\leq 4c_{1}.$$
(3.13)

Therefore, the mean value theorem together with the Cauchy-Schwarz inequality shows that

$$\begin{aligned} \|\psi(\cdot,t) - \psi(\cdot,t_k)\|_{L^2(\Omega)}^2 &= \int_{\Omega} \left| \int_{t_k}^t \psi_t(x,s) ds \right|^2 dx \\ &\leq \int_{\Omega} \left\{ \int_{t_k}^t \psi_t^2(x,s) ds \right\} \cdot (t-t_k) dx \\ &\leq (t-t_k) \int_{t_k}^{\infty} \int_{\Omega} \psi_t^2 \\ &\leq \int_{t_k}^{\infty} \int_{\Omega} \psi_t^2 \quad \text{ for all } t \in (t_k,t_k+1) \text{ and each } k \in \mathbb{N}, \end{aligned}$$

whence (3.13) ensures that

$$\int_{t_k}^{t_k+1} \|\psi(\cdot,t) - \psi(\cdot,t_k)\|_{L^2(\Omega)}^2 dt \to 0 \quad \text{as } k \to \infty$$

and that thus, by (3.12),

$$\int_{t_k}^{t_k+1} \|\psi(\cdot,t) - \psi_{\infty}\|_{L^2(\Omega)}^2 dt \leq 2 \int_{t_k}^{t_k+1} \|\psi(\cdot,t) - \psi(\cdot,t_k)\|_{L^2(\Omega)}^2 dt + 2\|\psi(\cdot,t_k) - \psi_{\infty}\|_{L^2(\Omega)}^2 d$$

Apart from this, from Corollary 3.2 we know that

$$\int_{t_k}^{t_k+1} \|\psi(\cdot, t)\|_{L^2(\Omega)}^2 dt \le \int_{t_k}^{\infty} \|\psi(\cdot, t)\|_{L^2(\Omega)}^2 dt \to 0 \qquad \text{as } k \to \infty$$

and that hence

$$\begin{split} \|\psi_{\infty}\|_{L^{2}(\Omega)}^{2} &= \int_{t_{k}}^{t_{k}+1} \left\| (\psi(\cdot,t) - \psi_{\infty}) - \psi(\cdot,t) \right\|_{L^{2}(\Omega)}^{2} dt \\ &\leq 2 \int_{t_{k}}^{t_{k}+1} \|\psi(\cdot,t) - \psi_{\infty}\|_{L^{2}(\Omega)}^{2} dt + 2 \int_{t_{k}}^{t_{k}+1} \|\psi(\cdot,t)\|_{L^{2}(\Omega)}^{2} dt \\ &\to 0 \quad \text{as } k \to \infty \end{split}$$

thanks to (3.14). This contradiction to the nontriviality of ψ_{∞} confirms that a sequence $(t_k)_{k \in \mathbb{N}}$ with the indicated properties in fact cannot exist, and that accordingly (3.11) must be satisfied.

Making strong use of the fact that the quantity \overline{a} entering (3.11) is bounded from below due to our overall assumption that $u_0 \neq 0$, thanks to the downward monotonicity of v we can already derive the announced decay property of v from Lemma 3.5.

Lemma 3.6 Let $\beta > 0$, and assume (3.3). Then

$$v(\cdot, t) \to 0 \quad in \ L^1(\Omega) \qquad as \ t \to \infty.$$
 (3.15)

PROOF. Since v is nonnegative with $\frac{d}{dt} \int_{\Omega} v \leq 0$ for all t > 0 by (1.1) and (1.3), it is sufficient to make sure that

$$\liminf_{t \to \infty} \int_{\Omega} v(\cdot, t) = 0.$$
(3.16)

To achieve this, using that $u \ge a$ by (2.3) and that $w \ge 0$, according to (1.1) and (1.3) we estimate

$$\frac{d}{dt} \int_{\Omega} v = -\int_{\Omega} (u+w)v \le -\int_{\Omega} av \quad \text{for all } t > 0, \qquad (3.17)$$

where we note that

$$\begin{aligned} -\int_{\Omega} a(\cdot,t)v(\cdot,t) &= -\overline{a(\cdot,t)} \int_{\Omega} v(\cdot,t) - \int_{\Omega} \left(a(\cdot,t) - \overline{a(\cdot,t)} \right) v(\cdot,t) \\ &\leq -\overline{a(\cdot,t)} \int_{\Omega} v(\cdot,t) + \|a(\cdot,t) - \overline{a(\cdot,t)}\|_{L^{2}(\Omega)} \|v(\cdot,t)\|_{L^{2}(\Omega)} \quad \text{for all } t > 0 \end{aligned}$$

due to the Cauchy-Schwarz inequality. Since $v \leq c_1 := \|v_0\|_{L^{\infty}(\Omega)}$ in $\Omega \times (0, \infty)$ by (2.2), and since thus $\|v(\cdot, t)\|_{L^2(\Omega)} \leq c_1 |\Omega|^{\frac{1}{2}}$ for all t > 0 and

$$\overline{a(\cdot,t)} = \frac{1}{|\Omega|} \int_{\Omega} u(\cdot,t) e^{-v(\cdot,t)} \ge e^{-c_1} \cdot \frac{1}{|\Omega|} \int_{\Omega} u(\cdot,t) = c_2 := e^{-c_1} \overline{u}_0 \qquad \text{for all } t > 0$$

thanks to (2.1), this shows that

$$-\int_{\Omega} a(\cdot, t)v(\cdot, t) \leq -c_2 \int_{\Omega} v(\cdot, t) + f(t) \quad \text{for all } t > 0,$$

with $f(t) := c_1 |\Omega|^{\frac{1}{2}} \cdot ||a(\cdot,t) - \overline{a(\cdot,t)}||_{L^2(\Omega)}, t > 0$. Accordingly, from (3.17) we obtain that $y(t) := \int_{\Omega} v(\cdot,t), t \ge 0$, satisfies

$$y'(t) \le -c_2 y(t) + f(t)$$
 for all $t > 0$, (3.18)

which due to Lemma 3.5 indeed entails (3.16): Namely, assuming on the contrary that (3.16) be false, we could find $t_0 > 0$ and $c_3 > 0$ such that $y(t) \ge c_3$ for all $t > t_0$. On the other hand, from Lemma 3.5 we know that $f(t) \to 0$ as $t \to \infty$, and that thus there exists $t_1 > t_0$ fulfilling $f(t) \le \frac{1}{2}c_2c_3$ for all $t > t_1$. For such large t, (3.18) would thus entail that

$$y'(t) \le -c_2c_3 + \frac{1}{2}c_2c_3$$
 for all $t > t_1$,

and thereby clearly contradicts the nonnegativity of v on $\Omega \times (0, \infty)$. The proof is thus complete. \Box In view of the latter, the intended stabilization feature of u can now be obtained in quite a straightforward manner from Lemma 3.5, (2.3) and (2.2).

Lemma 3.7 Let $\beta > 0$, and suppose that (1.5) and (3.3) are satisfied. Then

$$u(\cdot, t) \to \overline{u}_0 \quad in \ L^1(\Omega) \qquad as \ t \to \infty.$$
 (3.19)

PROOF. Recalling that $u = e^{v}a$, for t > 0 we estimate

$$\int_{\Omega} |u(\cdot,t) - \overline{u}_{0}| = \int_{\Omega} \left| e^{v(\cdot,t)} a(\cdot,t) - \overline{u}_{0} \right| \\
= \int_{\Omega} \left| e^{v(\cdot,t)} \left(a(\cdot,t) - \overline{a(\cdot,t)} \right) + e^{v(\cdot,t)} \left(\overline{a(\cdot,t)} - \overline{u}_{0} \right) + (e^{v(\cdot,t)} - 1) \overline{u}_{0} \right| \\
\leq \int_{\Omega} e^{v(\cdot,t)} |a(\cdot,t) - \overline{a(\cdot,t)}| + \int_{\Omega} e^{v(\cdot,t)} |\overline{a(\cdot,t)} - \overline{u}_{0}| + \overline{u}_{0} \int_{\Omega} |e^{v(\cdot,t)} - 1|, \quad (3.20)$$

where according to the Cauchy-Schwarz inequality, (2.2) and Lemma 3.5,

$$\int_{\Omega} e^{v(\cdot,t)} |a(\cdot,t) - \overline{a(\cdot,t)}| \leq \left\{ \int_{\Omega} e^{2v(\cdot,t)} \right\}^{\frac{1}{2}} \cdot ||a(\cdot,t) - \overline{a(\cdot,t)}||_{L^{2}(\Omega)} \\
\leq e^{||v_{0}||_{L^{\infty}(\Omega)}} |\Omega|^{\frac{1}{2}} \cdot ||a(\cdot,t) - \overline{a(\cdot,t)}||_{L^{2}(\Omega)} \\
\rightarrow 0 \quad \text{as } t \rightarrow \infty.$$
(3.21)

Furthermore, we note that since $0 \le 1 - e^{-s} \le s$ for all $s \ge 0$ we can utilize Lemma 3.6 to see that, again by (2.2),

$$\begin{aligned} \overline{u}_0 \int_{\Omega} |e^{v(\cdot,t)} - 1| &= \overline{u}_0 \int_{\Omega} e^{v(\cdot,t)} \cdot |1 - e^{-v(\cdot,t)}| \\ &\leq \overline{u}_0 e^{\|v_0\|_{L^{\infty}(\Omega)}} \int_{\Omega} v(\cdot,t) \\ &\to 0 \quad \text{as } t \to \infty \end{aligned}$$
(3.22)

and that, similarly and additionally due to (2.1),

$$\int_{\Omega} e^{v(\cdot,t)} |\overline{a(\cdot,t)} - \overline{u}_{0}| = \left\{ \frac{1}{|\Omega|} \int_{\Omega} e^{v(\cdot,t)} \right\} \cdot \left| \int_{\Omega} u(\cdot,t) (e^{-v(\cdot,t)} - 1) \right| \\
\leq e^{\|v_{0}\|_{L^{\infty}(\Omega)}} \|u(\cdot,t)\|_{L^{\infty}(\Omega)} \int_{\Omega} |e^{-v(\cdot,t)} - 1| \\
\rightarrow 0 \quad \text{as } t \rightarrow \infty,$$
(3.23)

because we are yet assuming that u is bounded in $\Omega \times (0, \infty)$. In conclusion, combining (3.20) with (3.21)-(3.23) we arrive at (3.19).

4 Blow-up of supercritical-mass solutions. Proof of Theorem 1.1

Guided by the stabilization result from Lemma 3.7, a natural strategy toward describing the large time behavior of w and z for a given bounded solution (u, v, w, z) seems to consist in making sure that in an appropriate sense, the action of u in the third and fourth equations from (1.1) can be compared to that of the constant \overline{u}_0 . Lemma 4.2 will reveal that an argument based on this naive idea can indeed be successfully performed upon suitably passing to the variables $\ln w$ and $\ln z$ and hence aiming at an inequality of the form in (1.9). Since u will enter the corresponding integration procedure only through the quantity $\int_{\Omega} \sqrt{u}$, the L^1 topology appearing in Lemma 3.7 in fact is sufficient to justify said approximation, as confirmed by the following auxiliary statement. **Lemma 4.1** Let $(\varphi_k)_{k \in \mathbb{N}} \subset L^1(\Omega; [0, \infty))$ be such that

 $\varphi_k \to \varphi_\infty \quad in \ L^1(\Omega) \qquad as \ k \to \infty$ (4.1)

with some $\varphi_{\infty} \in L^1(\Omega)$. Then

$$\int_{\Omega} \sqrt{\varphi_k} \to \int_{\Omega} \sqrt{\varphi_{\infty}} \qquad as \ k \to \infty.$$
(4.2)

PROOF. If this was false, then there would exist $c_1 > 0$ and a subsequence $(\varphi_{k_j})_{j \in \mathbb{N}}$ of $(\varphi_k)_{k \in \mathbb{N}}$ such that

$$\left| \int_{\Omega} \sqrt{\varphi_{k_j}} - \int_{\Omega} \sqrt{\varphi_{\infty}} \right| \ge c_1 \quad \text{for all } j \in \mathbb{N}.$$

$$(4.3)$$

According to (4.1) and a well-known result on a.e. pointwise approximation properties of L^1 -convergent sequences, with some further subsequence $(\varphi_{k_{j_i}})_{i \in \mathbb{N}}$ of $(\varphi_{k_j})_{j \in \mathbb{N}}$ we then moreover had $\varphi_{k_{j_i}} \to \varphi_{\infty}$ a.e. in Ω and hence also $\sqrt{\varphi_{k_{j_i}}} \to \sqrt{\varphi_{\infty}}$ a.e. in Ω as $i \to \infty$. Since $\sqrt{\varphi_{k_{j_i}}} \leq \frac{1}{2}\varphi_{k_{j_i}} + \frac{1}{2}$ in Ω by Young's inequality for all $i \in \mathbb{N}$, again in view of (4.1) we may invoke a dominated convergence theorem to see that along this subsequence,

$$\int_{\Omega} \sqrt{\varphi_{k_{j_i}}} \to \int_{\Omega} \sqrt{\varphi_{\infty}} \qquad \text{as } i \to \infty,$$

which contradicts (4.3) and thereby proves (4.2).

Indeed, we can thereby make Lemma 3.7 accessible to find b > 0 such that the functional in (1.9) enjoys the property announced there.

Lemma 4.2 Let $\beta > 1$ and (u_0, v_0, w_0, z_0) be such that (1.5) as well as (1.6) hold, and assume that the solution of (1.1), (1.3), (1.4) from Lemma 2.1 is such that (3.3) holds. Then there exist $b > 0, t_0 > 0$ and C > 0 such that

$$\frac{d}{dt} \left\{ \int_{\Omega} \ln w + b \int_{\Omega} \ln z \right\} \ge C \qquad \text{for all } t > t_0.$$

$$\tag{4.4}$$

PROOF. Since our assumptions on β and u_0 particularly ensure that $2\beta \overline{u}_0 - \overline{u}_0 > (\beta - 1)\overline{u}_0 > 1$, the number

$$b := \frac{2\beta \overline{u}_0 - \overline{u}_0 - 1}{(\overline{u}_0 + 1)^2}$$

is positive. Moreover,

$$\begin{split} \left\{1+b+b\overline{u}_{0}\right\}^{2} &-\left\{2\sqrt{b\beta}\cdot\sqrt{\overline{u}_{0}}\right\}^{2} = \left\{1+b^{2}+b^{2}\overline{u}_{0}^{2}+2b+2b\overline{u}_{0}+2b^{2}\overline{u}_{0}\right\}-4b\beta\overline{u}_{0}\\ &= \left(\overline{u}_{0}^{2}+2\overline{u}_{0}+1\right)\cdot b^{2}-\left(4\beta\overline{u}_{0}-2\overline{u}_{0}-2\right)\cdot b+1\\ &= \left(\overline{u}_{0}+1\right)^{2}\cdot\left\{b^{2}-2\cdot\frac{2\beta\overline{u}_{0}-\overline{u}_{0}-1}{(\overline{u}_{0}+1)^{2}}\cdot b+\frac{1}{(\overline{u}_{0}+1)^{2}}\right\}\\ &= \left(\overline{u}_{0}+1\right)^{2}\cdot\left\{-\frac{\left(2\beta\overline{u}_{0}-\overline{u}_{0}-1\right)^{2}}{(\overline{u}_{0}+1)^{4}}+\frac{1}{(\overline{u}_{0}+1)^{2}}\right\}\\ &= 1-\left(\frac{2\beta\overline{u}_{0}-\overline{u}_{0}-1}{\overline{u}_{0}+1}\right)^{2}\\ &< 0 \end{split}$$

due to the fact that

$$\frac{2\beta\overline{u}_0-\overline{u}_0-1}{\overline{u}_0+1}-1=\frac{2\beta\overline{u}_0-\overline{u}_0-1-\overline{u}_0-1}{\overline{u}_0+1}=2\cdot\frac{(\beta-1)\overline{u}_0-1}{\overline{u}_0+1}>0$$

by (1.6). Accordingly,

$$2\sqrt{b\beta} \cdot \sqrt{\overline{u}_0} > 1 + b + b\overline{u}_0,$$

so that we can pick $\delta>0$ small enough such that

$$c_1 := 2\sqrt{b\beta} \cdot (\sqrt{\overline{u}_0} - \delta) - (1 + b + b\overline{u}_0) > 0.$$

$$(4.5)$$

To conclude our selection process, we finally combine Lemma 3.7 with Lemma 4.1 to see that thanks to our assumption (3.3) we have

$$\int_{\Omega} \sqrt{u(\cdot, t)} \to \int_{\Omega} \sqrt{\overline{u}_0} = \sqrt{\overline{u}_0} \cdot |\Omega| \quad \text{as } t \to \infty,$$

whence, in particular, we can find $t_0 > 0$ fulfilling

$$\int_{\Omega} \sqrt{u(\cdot, t)} \ge (\sqrt{\overline{u_0}} - \delta) \cdot |\Omega| \quad \text{for all } t > t_0.$$
(4.6)

Now going back to (1.1) and (1.3), we use the positivity of w and z in $\overline{\Omega} \times (0, \infty)$, as asserted by Lemma 2.1, to compute

$$\frac{d}{dt} \int_{\Omega} \ln w = \int_{\Omega} \frac{1}{w} \cdot \left\{ D_w \Delta w - w + uz \right\}$$
$$= D_w \int_{\Omega} \frac{|\nabla w|^2}{w^2} - |\Omega| + \int_{\Omega} \frac{uz}{w} \quad \text{for all } t > 0$$

and

$$\frac{d}{dt} \int_{\Omega} \ln z = \int_{\Omega} \frac{1}{z} \cdot \left\{ D_z \Delta z - z - uz + \beta w \right\}$$
$$= D_z \int_{\Omega} \frac{|\nabla z|^2}{z^2} - |\Omega| - \overline{u}_0 |\Omega| + \beta \int_{\Omega} \frac{w}{z} \quad \text{for all } t > 0$$

according to (2.1). On dropping two nonpositive summands, we thus infer that

$$\frac{d}{dt} \left\{ \int_{\Omega} \ln w + b \int_{\Omega} \ln z \right\} \geq -|\Omega| + \int_{\Omega} \frac{uz}{w} + b \cdot \left\{ -|\Omega| - \overline{u}_0 |\Omega| + \beta \int_{\Omega} \frac{w}{z} \right\} \\
= -(1 + b + b\overline{u}_0) \cdot |\Omega| + \int_{\Omega} \frac{uz}{w} + b\beta \int_{\Omega} \frac{w}{z} \quad \text{for all } t > 0, \quad (4.7)$$

where the validity of $A+B\geq 2\sqrt{AB}$ for all $A\geq 0$ and $B\geq 0$ entails that

$$\begin{split} \int_{\Omega} \frac{uz}{w} + b\beta \int_{\Omega} \frac{w}{z} &= \int_{\Omega} \left(\frac{uz}{w} + b\beta \frac{w}{z} \right) \\ &\geq \int_{\Omega} 2\sqrt{\frac{uz}{w} \cdot b\beta \frac{w}{z}} \\ &= 2\sqrt{b\beta} \int_{\Omega} \sqrt{u} \quad \text{ for all } t > 0. \end{split}$$

As a consequence of (4.6), from (4.7) we therefore obtain that

$$\frac{d}{dt} \left\{ \int_{\Omega} \ln w + b \int_{\Omega} \ln z \right\} \geq -(1 + b + b\overline{u}_0) \cdot |\Omega| + 2\sqrt{b\beta} \cdot (\sqrt{\overline{u}_0} - \delta) \cdot |\Omega|$$
$$= c_1 |\Omega| \quad \text{for all } t > t_0,$$

and that hence the claimed property results from the positivity feature of c_1 stated in (4.5). According to the positivity of both b and C in (4.4), our main result on unboundedness of arbitrary supercritical-mass solutions thereby becomes rather evident:

PROOF of Theorem 1.1. If (1.7) was not satisfied, then (3.3) would hold and hence, by Lemma 4.2, we could find b > 0, $t_0 > 0$ and $c_1 > 0$ such that

$$\frac{d}{dt} \left\{ \int_{\Omega} \ln w + b \int_{\Omega} \ln z \right\} \ge c_1 \quad \text{for all } t > t_0,$$

and that thus

$$\int_{\Omega} \ln w(\cdot, t) + b \int_{\Omega} \ln z(\cdot, t) \ge c_1 \cdot (t - t_0) + \int_{\Omega} \ln w(\cdot, t_0) + b \int_{\Omega} \ln z(\cdot, t_0) \quad \text{for all } t > t_0.$$

Since, again by Lemma 2.1, $w(\cdot, t_0)$ and $z(\cdot, t_0)$ are positive throughout $\overline{\Omega}$ and hence $\int_{\Omega} \ln w(\cdot, t_0) + b \int_{\Omega} \ln z(\cdot, t_0) > -\infty$, this is incompatible with the boundedness properties of w and z particularly contained in (3.3).

5 Boundedness in subcritical cases. Proof of Proposition 1.2

Let us finally complement Theorem 1.1 by means of a parabolic comparison argument, applicable to small-mass solutions with trivial second component, in the announced manner:

PROOF of Proposition 1.2. Using that $1 - (\beta - 1)\overline{u}_0$ is positive, we can fix $\delta \in (0, \overline{u}_0)$ such that

$$1 - (\beta - 1)\overline{u}_0 > (\beta + 1)\delta,$$

which ensures that

$$1 + \overline{u}_0 - \delta > \beta \overline{u}_0 + \beta \delta$$

and that thus, by a comparison argument, we can find $\eta \in (0, 1)$ suitably small fulfilling

$$(1-\eta)(1+\overline{u}_0-\delta-\eta) \ge \beta \cdot (\overline{u}_0+\delta).$$
(5.1)

Thereupon, relying on the fact that $v \equiv 0$ by (1.1), (1.4) and (1.3) and our assumption on v_0 , we observe that thus actually being a solution of $u_t = \Delta u$ under homogeneous Neumann boundary conditions, according to well-known asymptotic properties of the heat equation the component u satisfies $u(\cdot, t) \to \overline{u}_0$ in $L^{\infty}(\Omega)$ as $t \to \infty$, so that there exists $t_0 > 0$ such that

$$\overline{u}_0 - \delta \le u(x, t) \le \overline{u}_0 + \delta \quad \text{for all } x \in \Omega \text{ and } t > t_0.$$
(5.2)

Keeping this value of t_0 fixed, we firstly use the boundedness of $w(\cdot, t_0)$ and $z(\cdot, t_0)$ in defining the numbers

$$B := \max\left\{ \|z(\cdot, t_0)\|_{L^{\infty}(\Omega)}, \frac{\beta}{1 + \overline{u}_0 - \delta - \eta} \cdot \|w(\cdot, t_0)\|_{L^{\infty}(\Omega)} \right\} \quad \text{and} \quad A := \frac{1 + \overline{u}_0 - \delta - \eta}{\beta} B, \quad (5.3)$$

and introduce

$$\widehat{w}(x,t) := Ae^{-\eta(t-t_0)} \quad \text{and} \quad \widehat{z}(x,t) := Be^{-\eta(t-t_0)}, \qquad x \in \overline{\Omega}, \ t \ge t_0.$$
(5.4)

To see that then

 $w \le \widehat{w} \quad \text{and} \quad z \le \widehat{z} \qquad \text{in } \Omega \times (t_0, \infty),$ (5.5)

we note that by (1.1) and (5.2),

$$w_t = D_w \Delta w - w + uz$$

$$\leq D_w \Delta w - w + (\overline{u}_0 + \delta)z \quad \text{in } \Omega \times (t_0, \infty)$$
(5.6)

and

$$z_t = D_z \Delta z - z - uz + \beta w$$

$$\leq D_z \Delta z - (1 + \overline{u}_0 - \delta) z + \beta w \quad \text{in } \Omega \times (t_0, \infty), \qquad (5.7)$$

whereas by (5.4),

$$\begin{aligned} \widehat{w}_t - D_w \Delta \widehat{w} + \widehat{w} - (\overline{u}_0 + \delta) \widehat{z} &= -\eta A e^{-\eta (t - t_0)} + A e^{-\eta (t - t_0)} - (\overline{u}_0 + \delta) B e^{-\eta (t - t_0)} \\ &= \left\{ (1 - \eta) A - (\overline{u}_0 + \delta) B \right\} \cdot e^{-\eta (t - t_0)} \quad \text{in } \Omega \times (t_0, \infty) \end{aligned}$$

and

$$\begin{aligned} \widehat{z}_t - D_z \Delta \widehat{z} + (1 + \overline{u}_0 - \delta) \widehat{z} - \beta \widehat{w} &= -\eta B e^{-\eta(t - t_0)} + (1 + \overline{u}_0 - \delta) B e^{-\eta(t - t_0)} - \beta A e^{-\eta(t - t_0)} \\ &= \left\{ (1 + \overline{u}_0 - \delta - \eta) B - \beta A \right\} \cdot e^{-\eta(t - t_0)} \quad \text{in } \Omega \times (t_0, \infty). \end{aligned}$$

Since the definition of A in (5.3) ensures that

$$(1 + \overline{u}_0 - \delta - \eta)B - \beta A = 0$$

and that

$$(1-\eta)A - (\overline{u}_0 + \delta)B = \frac{(1-\eta)(1+\overline{u}_0 - \delta - \eta)}{\beta}B - (\overline{u}_0 + \delta)B \ge 0$$

thanks to (5.1), it hence follows that

$$\widehat{w}_t \ge D_w \Delta \widehat{w} - \widehat{w} + (\overline{u}_0 + \delta)\widehat{z} \qquad \text{in } \Omega \times (t_0, \infty)$$
(5.8)

and

$$\widehat{z}_t = D_z \Delta \widehat{z} - \widehat{z} - (1 + \overline{u}_0 - \delta) \widehat{z} + \beta \widehat{w} \quad \text{in } \Omega \times (t_0, \infty).$$
(5.9)

As furthermore $\widehat{w}(x,t_0) = A = \frac{1+\overline{w}_0 - \delta - \eta}{\beta} B \geq \frac{1+\overline{w}_0 - \delta - \eta}{\beta} \cdot \frac{\beta}{1+\overline{w}_0 - \delta - \eta} \|w(\cdot,t_0)\|_{L^{\infty}(\Omega)} \geq w(x,t_0)$ and $\widehat{z}(x,t_0) = B \geq z(x,t_0)$ for all $x \in \Omega$ by (5.4) and (5.2), relying on an evident cooperativity property of the parabolic system addressed in (5.6)-(5.9) we conclude from an associated comparison principle that in fact (5.5) holds, which in turn readily implies the claimed statements.

Acknowledgement. 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).

References

- [1] ALZAHRANI, T., RALUCA EFTIMIE, R., DUMITRU TRUCU, D.: Multiscale modelling of cancer response to oncolytic viral therapy. Math. Biosci. **310**, 76-95 (2019)
- [2] CAO, X.: Boundedness in a three-dimensional chemotaxis-haptotaxis system.
 Z. Angew. Math. Phys. 67, 11 (2016)
- [3] CHAPLAIN, M.A.J., LOLAS, G.: Mathematical modelling of cancer cell invasion of tissue: the role of the urokinase plasminogen activation system. Math. Mod. Meth. Appl. Sci. 18, 1685-1734 (2005)
- [4] CORRIAS, L., PERTHAME, B., ZAAG, H.: A chemotaxis model motivated by angiogenesis. C. R. Math. Acad. Sci. Paris 336, 141-146 (2003)
- [5] ENGWER, C., HUNT, A., SURULESCU, C.: Effective equations for anisotropic glioma spread with proliferation: a multiscale approach and comparisons with previous settings. Math. Med. Biol. 33, 435-459 (2016)
- [6] FONTELOS, M.A., FRIEDMAN, A., HU, B.: Mathematical analysis of a model for the initiation of angiogenesis. SIAM J. Math. Anal. 33, 1330-1355 (2002)
- [7] FRIEDMAN, A., TELLO, J.I.: Stability of solutions of chemotaxis equations in reinforced random walks. J. Math. Anal. Appl. 272, 138-163 (2002)
- [8] HILLEN, T., PAINTER, K.J., WINKLER, M.: Convergence of a cancer invasion model to a logistic chemotaxis model. Math. Mod. Meth. Appl. Sci. 23, 165-198 (2013)
- [9] LEVINE, H.A., SLEEMAN, B.D., NILSEN-HAMILTON, M.: Mathematical modeling of the onset of capillary formation initiating angiogenesis. J. Math. Biol. 42, 195-238 (2001)
- [10] LI, Y., LANKEIT, J.: Boundedness in a chemotaxis-haptotaxis model with nonlinear diffusion. Nonlinearity 29, 1564-1595 (2016)
- [11] LIŢCANU, G., MORALES-RODRIGO, C.: Asymptotic behavior of global solutions to a model of cell invasion. Math. Models Methods Appl. Sci. 20, 1721-1758 (2010)

- [12] MARCINIAK-CZOCHRA, A., PTASHNYK, M.: Boundedness of solutions of a haptotaxis model. Math. Models Methods Appl. Sci. 20, 449-476 (2010)
- [13] MORALES-RODRIGO, C., TELLO, J.I.: Global existence and asymptotic behavior of a tumor angiogenesis model with chemotaxis and haptotaxis. Math. Models Methods Appl. Sci. 24, 427-464 (2014)
- [14] PANG, P.Y.H., WANG, Y.: Global boundedness of solutions to a chemotaxis-haptotaxis model with tissue remodeling. Math. Mod. Meth. Appl. Sci. 28, 2211-2235 (2018)
- [15] STINNER, C., SURULESCU, C., WINKLER, M.: Global weak solutions in a PDE-ODE system modeling multiscale cancer cell invasion. SIAM J. Math. Anal. 46, 1969-2007 (2014)
- [16] TAO, Y.: Global existence of classical solutions to a combined chemotaxis-haptotaxis model with logistic source. J. Math. Anal. Appl. 354, 60-69 (2009)
- [17] TAO, Y., WANG, M.: A combined chemotaxis-haptotaxis system: The role of logistic source. SIAM J. Math. Anal. 41, 1533-1558 (2009)
- [18] TAO, Y., WINKLER, M.: Dominance of chemotaxis in a chemotaxis-haptotaxis model. Nonlinearity 27 (6), 1225-1239 (2014)
- [19] TAO, Y., WINKLER, M.: Energy-type estimates and global solvability in a two-dimensional chemotaxis-haptotaxis model with remodeling of non-diffusible attractant. J. Differential Eq. 257, 784-815 (2014)
- [20] TAO, Y., WINKLER, M.: Large time behavior in a mutidimensional chemotaxis-haptotaxis model with slow signal diffusion. SIAM J. Math. Anal. 47, 4229-4250 (2015)
- [21] TAO, Y., WINKLER, M.: A chemotaxis-haptotaxis system with haptoattractant remodeling: boundedness enforced by mild saturation of signal production. Commun. Pure Appl. Anal. 18, 2047-2067 (2019)
- [22] TAO, Y., WINKLER, M.: Global classical solutions to a doubly haptotactic cross-diffusion system modeling oncolytic virotherapy. J. Differential Equations, DOI: 10.1016/j.jde.2019.10.046
- [23] TAO, Y., WINKLER, M.: A critical virus production rate for blow-up suppression in a haptotatxis model for oncolytic virotherapy. Preprint
- [24] WALKER, C., WEBB, G.F.: Global existence of classical solutions for a haptotaxis model. SIAM J. Math. Anal. 38, 1694-1713 (2007)
- [25] WANG, Y.: Boundedness in the higher-dimensional chemotaxis-haptotaxis model with nonlinear diffusion. J. Differential Equations 260, 1975-1989 (2016)
- [26] WINKLER, M., SURULESCU, C.: A global weak solutions to a strongly degenerate haptotaxis model. Commun. Math. Sci. 15, 1581-1616 (2017)
- [27] WINKLER, M.: Singular structure formation in a degenerate haptotaxis model involving myopic diffusion. J. Math. Pures Appl. 112, 118-169 (2018)

- [28] ZHIGUN, A., SURULESCU, C., HUNT, A.: A strongly degenerate diffusion-haptotaxis model of tumour invasion under the go-or-grow dichotomy hypothesis. Math. Methods Appl. Sci. 41, 2403-2428 (2018)
- [29] ZHIGUN, A., SURULESCU, C., UATAY, A.: Global existence for a degenerate haptotaxis model of cancer invasion. Z. Angew. Math. Phys. 67, Art. 146, 29 pp (2016)