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NONLINEAR STABILITY OF A HETEROGENEOUS STATE IN A PDE-ODE MODEL FOR ACID-MEDIATED TUMOR INVASION

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Abstract. This work studies a general reaction-diffusion model for acid-mediated tumor invasion, where tumor cells produce excess acid that primarily kills healthy cells, and thereby invade the microenvironment. The acid diffuses and could be cleared by vasculature, and the healthy and tumor cells are viewed as two species following logistic growth with mutual competition. A key feature of this model is the density-limited diffusion for tumor cells, reflecting that a healthy tissue will spatially constrain a tumor unless shrunk. Under appropriate assumptions on model parameters and on initial data, it is shown that the unique heterogeneous state is *nonlinearly* stable, which implies a long-term coexistence of the healthy and tumor cells in certain parameter space. Our theoretical result suggests that acidity may play a significant role in heterogeneous tumor progression.

1. Introduction.

Why does a cancer tumor possess the ability to invade its microenvironment? An alternative explanation is the so-called acid-mediated invasion hypothesis that tumor cells produce an excess of acid, which could kill the surrounding healthy cells, and thereby achieve a selective advantage over neighboring healthy cells (see [5]). Gatenby and Gawlinski [4] initially proposed a reaction-diffusion model incorporated the acid-mediated invasion hypothesis. In their model, tumor and healthy cells are viewed as two species that mutually restrain in the sense that the former limits the latter by producing excess acid, whereas the latter curb the diffusion of the former by its density. Taking more biologically realistic information into account, McGillen et al. [9] recently extended the Gatenby-Gawlinski model to a general reaction-diffusion model. First, they added the terms symbolizing the Lotka-Volterra-type mutual competition between healthy and tumor cells for resource needed for survival. In addition, since some biological experiments observe that tumor cells may not exhibit complete acid resistance (see [2, 11]), they also add

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a term for acid-mediated tumor cell death. Let u represent the density of healthy cells, v the density of tumor cells, and w the concentration of extracellular lactic acid in excess of normal tissue acid concentrations. Then the McGillen-Gaffney-Martin-Maini model reads

$$\begin{cases} u_t = u(1-u-a_2 v) - d_1 uw, & x \in \Omega,\ t>0, \\ v_t - D\nabla\cdot((1-u)\nabla v) = r_2 v(1-v-a_1 u) - d_2 vw, & x \in \Omega,\ t>0, \\ w_t - \Delta w = c(v-w), & x \in \Omega,\ t>0, \\ \frac{\partial v}{\partial \nu} = \frac{\partial w}{\partial \nu} = 0, & x \in \partial\Omega,\ t>0, \\ u(x,0)=u_0(x), \quad v(x,0)=v_0(x), \quad w(x,0)=w_0(x), & x\in\Omega, \end{cases} \tag{1.1}$$

in a bounded domain $\Omega \subset \mathbb{R}^n$, $n \geq 1$, with smooth boundary, where $\frac{\partial}{\partial \nu}$ denotes differentiation with respect to outward normal on $\partial\Omega$, and the non-dimensional parameters $a_1 > 0, a_2 > 0, d_1 \geq 0, d_2 \geq 0, r_2 > 0, D > 0$ and $c > 0$ are constants. Here we mention that tumor capacity for acid resistance is reflected by $d_2 \leq d_1$, and the readers may refer to [9] for more detailed biological explanations on other parameters or terms appearing in (1.1). We also note that, in the limiting case when $a_1 = a_2 = d_2 = 0$, (1.1) reproduces the original Gatenby-Gawlinski model [4].

Fasano et al. [3] studied the Gatenby-Gawlinski model and showed rich properties of various traveling waves. Very recently, McGillen et al. [9] performed numerical exploration and an asymptotic traveling wave analysis of the generalized model (1.1). They constructed an *asymptotic approximation traveling wave solution* to (1.1) and characterized the invasive behaviors of tumor cells. The studies in [3, 9] suggest that acidity may play a significant role in tumor progression ([6]).

Depending on parameter regimes, the system (1.1) exhibits four equilibrium points: a trivial state $(u,v,w) = (0,0,0)$, a health state $(u,v,w) = (1,0,0)$, a heterogeneous state $(u,v,w) = (u^*,v^*,w^*)$ with $u^* \neq 0$, $v^* \neq 0$ and $w^* \neq 0$, and a homogeneous tumor state $(u,v,w) = (0, \frac{1}{1+d_2/r_2}, \frac{1}{1+d_2/r_2})$. In [9], the authors have discussed the *linear* stability of the above four stationary points. However, the *nonlinear* stability of the above four stationary states is very challenging. In particular, this work is interested in the nonlinear stability of the heterogeneous state, which may imply a long-term coexistence of the healthy and tumor cells in certain parameter space. For this purpose, we further assume that the model parameters fulfill

$$a_1 < 1, \tag{1.2}$$

$$1 - a_1 a_2 - a_1 d_1 > \frac{d_2}{r_2} \qquad \text{and} \tag{1.3}$$

$$d_1 < 1 + \frac{d_2}{r_2} - a_2. \tag{1.4}$$

Simple computation yields that the unique positive constant steady state of system (1.1) is given by

$$u^* = 1 - \frac{(1-a_1)(a_2+d_1)}{1+\frac{d_2}{r_2} - a_1 a_2 - a_1 d_1} \quad \text{and} \quad v^* = w^* = \frac{1-a_1}{1+\frac{d_2}{r_2} - a_1 a_2 - a_1 d_1}. \tag{1.5}$$

Under the assumptions (1.2)-(1.4), it is readily checked that this steady state fulfills

$$0 < u^* < 1 \qquad \text{and} \qquad 0 < v^* < 1. \tag{1.6}$$

As to the initial data, we assume throughout that u_0, v_0 and w_0 satisfy

$$\begin{cases} u_0 \in W^{2,\infty}(\Omega), \quad 0 < u_0 < 1 \quad \text{in } \bar{\Omega}, \\ v_0 \in W^{2,\infty}(\Omega), \quad v_0 > 0 \quad \text{in } \bar{\Omega}, \\ w_0 \in W^{2,\infty}(\Omega), \quad w_0 \geq 0 \quad \text{in } \bar{\Omega}. \end{cases} \tag{1.7}$$

Under these assumptions, our main result reads as follows.

Theorem 1.1. *Let $a_1 > 0, a_2 > 0, d_1 \geq 0, d_2 \geq 0, r_2 > 0, D > 0$ and $c > 0$ satisfy (1.2)-(1.4). Then for any triple $(u_0, v_0, w_0) \in W^{2,\infty}(\Omega) \times W^{2,\infty}(\Omega) \times W^{2,\infty}(\Omega)$ of nonnegative function fulfilling (1.7), the problem (1.1) possesses a unique nonnegative classical solution which is global in time. Moreover, this global solution enjoys the property*

$$\|u(\cdot,t) - u^*\|_{L^\infty(\Omega)} + \|v(\cdot,t) - v^*\|_{L^\infty(\Omega)} + \|w(\cdot,t) - w^*\|_{L^\infty(\Omega)} \to 0 \ \textit{exponentially},$$

as $t \to +\infty$.

This analytical result implies the coexistence of the healthy and tumor cells whenever the parameter conditions (1.2)-(1.4) are satisfied, and it also demonstrates that the generalized model (1.1) is amenable to rigorous nonlinear analysis in addition to approximate traveling wave analysis. Let us further examine our parameter assumptions (1.2)-(1.4). Since the healthy state $(u, v, w) = (1, 0, 0)$ is linearly stable if $a_1 > 1$ ([9]), it is unlikely that the heterogeneous state $(u, v, w) = (u^*, v^*, w^*)$ is nonlinearly stable if $a_1 > 1$. We also note that the heterogeneous state does not exist if $a_1 = 1$. Therefore, the assumption (1.2) is really necessary for the stability of the heterogeneous state. We next turn to the assumption (1.4). One observation is that the heterogeneous state is linearly unstable if $d_1 > 1 + \frac{d_2}{r_2} - a_2$ ([9]), and the other simple fact is that the heterogeneous state will disappear according to the first formula in (1.5) if $d_1 = 1 + \frac{d_2}{r_2} - a_2$. The above two considerations yield that the assumption (1.4) is also necessary for the stability of the heterogeneous state. Indeed, when the assumptions (1.2) and (1.4) hold, the previous numerical simulation found heterogeneous invasion ([9, Fig. 3a]). From this perspective, Theorem 1.1 analytically confirms some key numerical exploration performed in [9].

However, from biological point of view, the main contribution of this work may lie in finding the parameter condition (1.3), which along with (1.2) and (1.4) warrants the nonlinear stability of the heterogeneous state by Theorem 1.1. To better understand the assumption (1.3), we first see that in the limiting case when $d_2 = 0$, (1.3) is an immediate consequence of (1.4) thanks to $0 < a_1 < 1$. By continuity, when $d_2 > 0$ sufficiently small and other parameters are fixed, (1.3) still results from (1.4). Hence, when $d_2 > 0$, the assumption (1.3) essentially says that d_2 should be small compared with d_1 and r_2. Importantly, this corresponds to the *acid resistance hypothesis* that is central to the model (1.1), and moreover, it actually plays a significant role in the proof of a key Lemma (see Lemma 3.3 below).

The system (1.1) can also be viewed as a generalization of a classical mutual-competition system ([8]). However, a novel feature of the model (1.1) is the density-limited tumor diffusion term in the second equation, which might give rise to the *degeneracy* of the parabolic equation. One main task of our analysis is to exclude this possibility of degeneracy. Namely, under the assumptions (1.2)-(1.4) on model parameters and the assumption (1.7) on initial data, we aim at proving that there exists a positive constant $\lambda < 1$ such that

$$u(x,t) \leq \lambda \qquad \text{for all } x \in \Omega \text{ and } t > 0,$$

which entails that the diffusion coefficient $1-u \geq 1-\lambda > 0$. To achieve this, we apply the rectangle method idea to the system where the sub and super solutions that we construct are homogeneous in space (see for instance [10] and reference therein). In Section 3 we analyze the existence of solutions of the auxiliary system of ODEs used to obtain the sub and super-solutions. Moreover, as a crucial preparation for demonstrating the nonlinear stability of the heterogeneous state, we show that the super-solution approximates the sub-solution as time goes to infinity, where the assumption (1.3) plays an important role as aforementioned (see the proof of Lemma 3.3 below). In Section 4 we employ a comparison argument (cf. e.g. [10]) to connect the solution of the PDE system (1.1) to the sub and super-solutions, and thereby complete the proof of Theorem 1.1. As a starting point of our rigorous mathematical analysis, we begin with establishing the local existence in Sections 2.

2. **Local existence and an extensibility criterion.** We shall use a straightforward fixed point argument to prove the local existence of solutions to the system (1.1), as well as an extensibility criterion.

Lemma 2.1. *Let $a_1 > 0, a_2 > 0, d_1 \geq 0, d_2 \geq 0, r_2 > 0, D > 0$ and $c > 0$, and let (1.7) hold. Then there exist $T_{max} \in (0, \infty]$ and a unique triple*

$$(u, v, w) \in C^{1,1}(\bar{\Omega} \times [0, T_{max})) \times \big(C^0(\bar{\Omega} \times [0, T_{max})) \cap C^{2,1}(\bar{\Omega} \times (0, T_{max}))\big)^2$$

solving (1.1) classically in $\Omega \times (0, T_{max})$. These functions have the properties

$$0 < u < 1 \qquad in\ \Omega \times (0, T_{max}), \tag{2.1}$$

$$0 < v \leq \max\{1, \|v_0\|_{L^\infty(\Omega)}\} \qquad in\ \Omega \times (0, T_{max}), \tag{2.2}$$

$$0 < w \leq \max\{1, \|v_0\|_{L^\infty(\Omega)}, \|w_0\|_{L^\infty(\Omega)}\} \qquad in\ \Omega \times (0, T_{max}), \tag{2.3}$$

and, moreover, we have the following dichotomy:

$$either\ T_{max} = \infty, \qquad or \qquad \limsup_{t \nearrow T_{max}} \|u(\cdot, t)\|_{L^\infty(\Omega)} = 1. \tag{2.4}$$

Proof. We let $R_0 := \frac{1}{2}(\|u_0\|_{L^\infty(\Omega)} + 1)$, and we have $R_0 < 1$ thanks to the assumption on u_0 in (1.7). We denote $|\Omega| := \mathrm{diam}\Omega$. Since $W^{2,\infty}(\Omega) \hookrightarrow C^{1+\alpha}(\bar{\Omega})$ for any $0 < \alpha < 1$, we can define

$$R := 2(\|u_0\|_{C^{\frac{4}{3}}(\bar{\Omega})} + \|w_0\|_{C^{\frac{1}{3}}(\bar{\Omega})} + 1).$$

For $0 < T \leq 1$, we then let

$$X := C^{\frac{4}{3}, \frac{1}{6}}(\bar{\Omega} \times [0, T]) \times C^{\frac{1}{3}, \frac{1}{6}}(\bar{\Omega} \times [0, T])$$

with norm $\|(\tilde{u}, \tilde{w})\|_X := \|\tilde{u}\|_{C^{\frac{4}{3}, \frac{1}{6}}(\bar{\Omega} \times [0,T])} + \|\tilde{w}\|_{C^{\frac{1}{3}, \frac{1}{6}}(\bar{\Omega} \times [0,T])}$. We consider the closed set

$$S = \Big\{(\tilde{u}, \tilde{w}) \in X \,\Big|\, \|(\tilde{u}, \tilde{w})\|_X \leq R \text{ with } 0 \leq \tilde{u} \leq R_0 \text{ and } \tilde{w} \geq 0 \text{ in } \bar{\Omega} \times [0, T]\Big\}.$$

For $(\tilde{u}, \tilde{w}) \in S$, we let $\Psi((\tilde{u}, \tilde{w})) := (u, w)$ denote the solution of the two decoupled systems

$$\begin{cases} w_t - \Delta w = c(v - w) & x \in \Omega,\ t > 0, \\ \frac{\partial w}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0, \\ w(x, 0) = w_0(x), & x \in \Omega \end{cases} \tag{2.5}$$

and

$$\begin{cases} u_t = u(1-u-a_2 v) - d_1 u\tilde{w}, & x\in\Omega,\, t>0,\\ u(x,0)=u_0(x), & x\in\Omega, \end{cases} \tag{2.6}$$

where v is an intermediate variable that connects $(\tilde{u},\tilde{w})$ to (u,w), and it is the solution of

$$\begin{cases} v_t - D\nabla\cdot((1-\tilde{u})\nabla v) = r_2 v(1-v-a_1\tilde{u}-d_2\tilde{w}), & x\in\Omega,\, t>0,\\ \frac{\partial v}{\partial \nu}=0, & x\in\partial\Omega,\, t>0,\\ v(x,0)=v_0(x), & x\in\Omega. \end{cases} \tag{2.7}$$

We claim that if T is sufficiently small, then the mapping Ψ acts as a contraction from S into itself. To see this, we let $(\tilde{u},\tilde{w})\in S$ and we note that the local existence of a uniquely determined nonnegative classical solution to (2.7) in $\Omega\times[0,T_1]$ with some $T_1\le T$ follows from [1, Theorems 14.4 and 14.6]. Thanks to $\tilde{u}\ge 0, \tilde{w}\ge 0, 1-\tilde{u}\ge 1-R_0>0$ and $v_0>0$, the parabolic comparison principle yields

$$0<v\le \max\{1,\ \|v_0\|_{L^\infty(\Omega)}\} \qquad \text{in } \Omega\times(0,T_1). \tag{2.8}$$

This in conjunction with the extensibility criterion in [1, Theorem 15.5] further asserts $T_1=T$. Moreover, using (2.8) and noting $(\tilde{u},\tilde{w})\in S$ and $v_0\in W^{2,\infty}(\Omega)$, from standard parabolic L^p theory we obtain

$$\|v\|_{W_p^{2,1}(\Omega\times[0,T])}\le C_1 \tag{2.9}$$

for any $p>1$, with some $C_1>0$ which, as all constants $C_2, C_3, \ldots$ appearing below, is allowed to depend on $R_0, R, \|v_0\|_{W^{2,\infty}(\Omega)}, \|w_0\|_{W^{2,\infty}(\Omega)}$, and $\|u_0\|_{W^{2,\infty}(\Omega)}$ only. Picking any $p>2n$ and using the Sobolev embedding, we find

$$\|v\|_{C^{\frac{3}{2},\frac{1}{4}}(\bar{\Omega}\times[0,T])}\le C_2. \tag{2.10}$$

Similarly, since v satisfies (2.8) and (2.10), the *linear* parabolic problem (2.5) has a unique classical solution w in $\Omega\times[0,T]$ and w enjoys the properties

$$0<w\le \max\{\|v\|_{L^\infty(\Omega\times[0,T])},\ \|w_0\|_{L^\infty(\Omega)}\} \qquad \text{in } \Omega\times(0,T) \tag{2.11}$$

and

$$\|w\|_{C^{\frac{3}{2},\frac{1}{4}}(\bar{\Omega}\times[0,T])}\le C_3. \tag{2.12}$$

We next turn to the Bernoulli-type ODE problem (2.6) which is clearly explicitly solvable in $\Omega\times[0,T]$. Since $0<u_0<1$, two straightforward ODE comparison arguments yield

$$0<u\le \max\{1,\ \|u_0\|_{L^\infty(\Omega)}\}=1 \qquad \text{in } \Omega\times[0,T]. \tag{2.13}$$

In order to improve the bound of u from the upper, we derive further estimate on u. Knowing v and w are both uniformly Hölder continuous with respect to x with exponent $\frac{1}{2}$, in view of (2.6), $w_0\in W^{2,\infty}(\Omega)\hookrightarrow C^{\frac{1}{2}}(\bar{\Omega})$ and the boundedness of u we obtain $C_4>0$ such that

$$\|u(\cdot,t)\|_{C^{\frac{1}{2}}(\bar{\Omega})}\le C_4 \quad \text{and} \quad \|u_t(\cdot,t)\|_{C^{\frac{1}{2}}(\bar{\Omega})}\le C_4 \qquad \text{for all } t\in[0,T]. \tag{2.14}$$

Similarly, on differentiating the first equation in (2.6) with respect to x, using (2.10), (2.12), $w_0\in W^{2,\infty}(\Omega)\hookrightarrow C^{\frac{3}{2}}(\bar{\Omega})$ and arguing in a straightforward manner (cf. [12, (2.53)-(2.58) for details]), we obtain some $C_5>0$ such that

$$\|\nabla u(\cdot,t)\|_{C^{\frac{1}{2}}(\bar{\Omega})}\le C_5 \quad \text{and} \quad \|(\nabla u)_t(\cdot,t)\|_{C^{\frac{1}{2}}(\bar{\Omega})}\le C_5 \qquad \text{for all } t\in[0,T]. \tag{2.15}$$

This along with (2.14) yields some $C_6 > 0$ such that

$$\|u\|_{C^{\frac{3}{2},\frac{3}{2}}(\bar\Omega\times[0,T])} \le C_6. \tag{2.16}$$

This entails that

$$\begin{aligned}\|u\|_{L^\infty(\bar\Omega\times[0,T])} &\le \|u_0\|_{L^\infty(\bar\Omega)} + \|u-u_0\|_{L^\infty(\bar\Omega\times[0,T])}\\ &\le \|u_0\|_{L^\infty(\bar\Omega)} + T^{\frac{1}{2}}\,\|u\|_{C^{0,\frac{1}{2}}(\bar\Omega\times[0,T])}\\ &\le \|u_0\|_{L^\infty(\bar\Omega)} + T^{\frac{1}{2}}C_6 \end{aligned}\tag{2.17}$$

and that

$$\begin{aligned}&\|u\|_{C^{\frac{4}{3},\frac{1}{6}}(\bar\Omega\times[0,T])}\\ &\le \|u\|_{C^{1,0}(\bar\Omega\times[0,T])} + \|u\|_{C^{\frac{4}{3},0}(\bar\Omega\times[0,T])} + \|u\|_{C^{1,\frac{1}{6}}(\bar\Omega\times[0,T])}\\ &\le 2\|u_0\|_{C^{\frac{4}{3}}(\bar\Omega)} + \|u-u_0\|_{C^{1,0}(\bar\Omega\times[0,T])} + \|u-u_0\|_{C^{\frac{4}{3},0}(\bar\Omega\times[0,T])} + \|u\|_{C^{1,\frac{1}{6}}(\bar\Omega\times[0,T])}\\ &\le 2\|u_0\|_{C^{\frac{4}{3}}(\bar\Omega)} + T\|u\|_{C^{1,1}(\bar\Omega\times[0,T])} + T\|u_t\|_{C^{\frac{4}{3},0}(\bar\Omega\times[0,T])} + T^{\frac{1}{2}-\frac{1}{6}}\|u\|_{C^{1,\frac{1}{2}}(\bar\Omega\times[0,T])}\\ &\le 2\|u_0\|_{C^{\frac{4}{3}}(\bar\Omega)} + T\|u\|_{C^{1,1}(\bar\Omega\times[0,T])} + T\Big(1+|\Omega|^{\frac{1}{2}-\frac{1}{3}}\Big)\|u_t\|_{C^{\frac{3}{2},0}(\bar\Omega\times[0,T])}\\ &+T^{\frac{1}{3}}\|u\|_{C^{1,\frac{1}{2}}(\bar\Omega\times[0,T])}\\ &\le 2\|u_0\|_{C^{\frac{4}{3}}(\bar\Omega)} + 3T^{\frac{1}{3}}\Big(1+|\Omega|^{\frac{1}{6}}\Big)C_6\end{aligned}$$

thanks to $T \le 1$. Similarly, we have

$$\|w\|_{C^{\frac{1}{3},\frac{1}{6}}(\bar\Omega\times[0,T])} \le 2\|w_0\|_{C^{\frac{1}{3}}(\bar\Omega)} + 3T^{\frac{1}{12}}\Big(1+|\Omega|^{\frac{1}{6}}\Big)C_3. \tag{2.18}$$

If we now take $T \in (0,1)$ sufficiently small that

$$T \le \min\left\{\left(\frac{1-\|u_0\|_{L^\infty(\Omega)}}{2C_6}\right)^2, \left(\frac{1}{3\Big(1+|\Omega|^{\frac{1}{6}}\Big)C_6}\right)^3, \left(\frac{1}{3\Big(1+|\Omega|^{\frac{1}{6}}\Big)C_3}\right)^{12}\right\}$$

then we derive that

$$\|u\|_{L^\infty(\bar\Omega\times[0,T])} \le R_0 \qquad \text{and} \qquad \|(u,w)\|_X \le R.$$

This shows that $(u,w) \in S$ and thus that Ψ maps S into itself.

By a straightforward adaption of the above reasoning it can been obtained that if T is further diminished then Ψ is contractive on S. Therefore, by the contraction mapping principle, Ψ possesses a unique fixed point in S which generates a solution (u,v,w) of (1.1) in $\Omega\times T$. Invoking standard parabolic regularity theory [7], we see that (u,v,w) solves (1.1) in the classical sense.

Moreover (u,v,w) can be extended to some $T_{max} \in (0,\infty]$ by standard argument. Since the above choice of T depends on $\|u_0\|_{L^\infty(\bar\Omega)}$, $\|u_0\|_{C^{\frac{4}{3}}(\bar\Omega)}$, $\|w_0\|_{C^{\frac{1}{3}}(\bar\Omega)}$ and $|\Omega|$ only, a standard extensibility argument guarantees that (u,v,w) can be extended up to some maximal $T_{max} \in (0,\infty]$. Indeed, if $T_{max} < \infty$ and $\limsup_{t\nearrow T_{max}} \|u(\cdot,t)\|_{L^\infty(\Omega)} < 1$, then for any sufficiently small $\eta > 0$ we have

$$\|u(\cdot,T_{max}-\eta)\|_{L^\infty(\Omega)} \le \lambda < 1, \quad \|u(\cdot,T_{max}-\eta)\|_{C^{\frac{4}{3}}(\bar\Omega)} \le C_7$$

and

$$\|w(\cdot,T_{max}-\eta)\|_{C^{\frac{1}{3}}(\bar\Omega)} \le C_7$$

with λ and C_7 being independent of η and T_{max}, where the latter two estimates are derived as proceeding in the proof of (2.12) and (2.16). Thus if we take $T_{max}-\eta$ as a new initial time, then we can extend (u,v,w) to some $T_2 := (T_{max}-\eta)+$

$T_0(\lambda, C_7, |\Omega|) > T_{max}$ whenever η is sufficiently small, which contradicts the definition of T_{max}. This proves (2.4). □

To prove the solution of (1.1) exists on $\Omega \times (0, \infty)$, by (2.4) we need to establish the a priori estimate

$$\|u(\cdot, t)\|_{L^\infty(\Omega)} \leq \lambda \qquad \text{for all } t > 0$$

with some $0 < \lambda < 1$. This will be one of the objectives of next two sections.

3. Auxiliary problem: A system of ODEs.

In order to obtain sub and super solutions with homogeneous space distribution to the system (1.1), we consider the following system of ODEs

$$\begin{cases} \overline{u}' = \overline{u}\left[1 - \overline{u} - a_2\underline{v} - d_1\underline{w}\right], & t > 0, \\ \underline{u}' = \underline{u}\left[1 - \underline{u} - a_2\overline{v} - d_1\overline{w}\right], & t > 0, \\ \overline{v}' = \overline{v}\left[r_2 - r_2\overline{v} - r_2 a_1\underline{u} - d_2\underline{w}\right], & t > 0, \\ \underline{v}' = \underline{v}\left[r_2 - r_2\underline{v} - r_2 a_1\overline{u} - d_2\overline{w}\right], & t > 0, \\ \overline{w}' = c(\overline{v} - \overline{w}), & t > 0, \\ \underline{w}' = c(\underline{v} - \underline{w}), & t > 0, \end{cases} \tag{3.1}$$

with initial data

$$\overline{u}(0) = \overline{u}_0, \quad \underline{u}(0) = \underline{u}_0, \quad \overline{v}(0) = \overline{v}_0, \quad \underline{v}(0) = \underline{v}_0, \quad \overline{w}(0) = \overline{w}_0, \quad \underline{w}(0) = \underline{w}_0. \tag{3.2}$$

From now on, we fix

$$\begin{array}{ll} \overline{u}_0 := \max\{\max_{\bar\Omega} u_0, u^*\}, & \underline{u}_0 := \min\{\min_{\bar\Omega} u_0, u^*\}, \\ \overline{v}_0 := \max\{\max_{\bar\Omega} v_0, v^*\}, & \underline{v}_0 := \min\{\min_{\bar\Omega} v_0, v^*\}, \\ \overline{w}_0 := \max\{\max_{\bar\Omega} w_0, w^*\}, & \underline{w}_0 := \min\{\min_{\bar\Omega} w_0, w^*\}. \end{array} \tag{3.3}$$

From (1.6) and (1.7) we infer that $(\overline{u}_0, \underline{u}_0, \overline{v}_0, \underline{v}_0, \overline{w}_0, \underline{w}_0)$ fulfills

$$0 < \underline{u}_0 \leq u^* \leq \overline{u}_0 < 1, \quad 0 < \underline{v}_0 \leq v^* \leq \overline{v}_0 < \infty, \quad 0 \leq \underline{w}_0 \leq w^* \leq \overline{w}_0 < \infty, \tag{3.4}$$

which will be used later on (see the proofs of Lemmata 3.1-3.3 and 4.1 below).

We first study the global existence of (3.1) in the following lemma.

Lemma 3.1. *The problem (3.1)-(3.2) admits a unique global solution carrying the property*

$$\begin{array}{ll} 0 < \overline{u} \leq 1, & 0 < \underline{u} \leq 1, \\ 0 < \overline{v} \leq \max\{1, \overline{v}_0\}, & 0 < \underline{v} \leq 1, \\ 0 < \overline{w} \leq \max\{1, \overline{v}_0, \overline{w}_0\}, & 0 < \underline{w} \leq 1 \end{array} \tag{3.5}$$

for all $t > 0$.

Proof. We observe that the system is autonomous; namely, the right hand side parts of the equations are independent of t, and polynomials. Since such polynomials are of order 1 and 2, by Picard- Lindelöf theorem we have the existence and uniqueness of solutions

$$\overline{u}, \underline{u}, \overline{v}, \underline{v}, \overline{w}, \underline{w} \in C^\infty(0, T^*_{max})$$

for some $T^*_{max} > 0$ satisfying

$$\lim_{t \to T^*_{\max}} \left(|\underline{u}| + |\overline{u}| + |\underline{v}| + |\overline{v}| + |\underline{w}| + |\overline{w}| + T^*_{max} \right) = \infty. \tag{3.6}$$

Alternatively, the above existence and uniqueness of solutions to the system (3.1)-(3.2) can be proved by a straightforward fixed point argument similar to that proceeded in Section 2.

From the continuity of function $\underline{u}$ and the fact that $\underline{u}_0 > 0$, we see that if there exists $t_0 > 0$ such that $\underline{u}(t_0) < 0$, then there exists $t_1 < t_0$ such that $u(t_1) = 0$. In such case, the backward solution $\underline{u} = 0$ in $(0, t_1)$, which contradicts the fact that $\underline{u}_0 > 0$. In the same way we prove that $\overline{u}$, $\underline{v}$ and $\overline{v}$ are positive functions. Integrating the equation for $\underline{w}$ and $\overline{w}$ we have

$$\overline{w} = \overline{w}_0 e^{-ct} + \int_0^t c e^{-c(t-s)} \overline{v}(s) ds \qquad \text{and} \tag{3.7}$$

$$\underline{w} = \underline{w}_0 e^{-ct} + \int_0^t c e^{-c(t-s)} \underline{v}(s). \tag{3.8}$$

Since $\overline{w}_0 > 0$, $\underline{w}_0 \geq 0$, $\overline{v} > 0$ and $\underline{v} > 0$ we obtain

$$0 < \underline{w}, \quad 0 < \overline{w}, \qquad t \in (0, T^*_{max}).$$

Since $\underline{v} > 0$ and $\underline{w} > 0$, we get the inequality

$$\underline{u}_t \leq \underline{u}(1 - \underline{u})$$

and upon ODE comparison it results in

$$\underline{u} \leq \max\{1, \underline{u}_0\} = 1$$

due to (3.4). In the same way we obtain

$$\overline{u} \leq \max\{1, \overline{u}_0\} = 1, \qquad \underline{v} \leq \max\{1, \underline{v}_0\} \qquad \text{and} \qquad \overline{v} \leq \max\{1, \overline{v}_0\},$$

where we have used (3.4) once more. By (3.7) and (3.8) and the boundedness of $\underline{v}$ and $\overline{v}$ we have that, by a straightforward computation

$$\overline{w} \leq \max \left\{ \overline{w}_0, \sup_{t \in (0, T^*_{max})} \{\overline{v}(t)\} \right\} = \max\{1, \overline{v}_0, \overline{w}_0\} \qquad \text{and}$$

$$\underline{w} \leq \max \left\{ \underline{w}_0, \sup_{t \in (0, T^*_{max})} \{\underline{v}(t)\} \right\} = \max\{1, \underline{v}_0, \underline{w}_0\} = 1$$

thanks to $\underline{v}_0 \leq v^* < 1$ and $\underline{w}_0 \leq w^* < 1$ by (3.4) and (1.6), which proves, by (3.6) that thereby $T^*_{\max} = \infty$ and proves the lemma. □

We need to further compare the sizes of $\overline{u}$, $\overline{v}$, $\overline{w}$ with those of $\underline{u}$, $\underline{v}$, $\underline{w}$, respectively.

Lemma 3.2. *The solution of problem (3.1)-(3.2) enjoys the property*

$$\underline{u} \leq u^* \leq \overline{u}, \qquad \underline{v} \leq v^* \leq \overline{v} \qquad \textit{and} \qquad \underline{w} \leq w^* \leq \overline{w} \tag{3.9}$$

for all $t > 0$.

Proof. For any function $g = g(t) : t \in (0, \infty) \longmapsto (-\infty, +\infty)$, we define

$$g_+ := \max\{g, 0\} \qquad \text{and} \qquad g_- := \min\{g, 0\}.$$

Then we have

$$g_+ \geq 0, \;\; g_- \leq 0, \;\; g \equiv g_+ + g_-, \;\; g_+ \cdot g_- \equiv 0, \;\; g \cdot g_+ = g_+^2 \;\text{ and }\; g \cdot g_- = g_-^2. \tag{3.10}$$

In order to prove $u^* \le \overline{u}$, we only need to prove $(u^* - \overline{u})_+ = 0$. Let u^*, v^* and w^* defined in (1.5) then, we find

$$\overline{u}' = \overline{u}\Big[(u^* - \overline{u}) + a_2(v^* - \underline{v}) + d_1(w^* - \underline{w})\Big],$$

where we have used the fact that $1 = u^* + a_2 v^* + d_1 w^*$. We multiply the above equation by $-(u^* - \overline{u})_+$ to obtain

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}(u^* - \overline{u})_+^2 &= \overline{u}[-(u^* - \overline{u})_+^2 + a_2(u^* - \overline{u})_+(\underline{v} - v^*) + d_1(u^* - \overline{u})_+(\underline{w} - w^*)] \\ &\le \overline{u}[-(u^* - \overline{u})_+^2 + a_2(u^* - \overline{u})_+(\underline{v} - v^*)_+ + d_1(u^* - \overline{u})_+(\underline{w} - w^*)_+]\end{aligned}$$

thanks to $a_2 > 0$, $d_1 > 0$ and (3.10). Using Young's inequality in conjunction with Lemma 3.1, we see that

$$\frac{d}{dt}(u^* - \overline{u})_+^2 \le k_0[(\underline{v} - v^*)_+^2 + (\underline{w} - w^*)_+^2], \tag{3.11}$$

where $k_0 := \max\{a_2^2, d_1^2\}$. In the same way we have

$$\frac{d}{dt}(\underline{u} - u^*)_+^2 \le k_0[(v^* - \overline{v})_+^2 + (w^* - \overline{w})_+^2], \tag{3.12}$$

$$\frac{d}{dt}(v^* - \overline{v})_+^2 \le k_1[(\underline{u} - u^*)_+^2 + (\underline{w} - w^*)_+^2] \quad \text{and} \tag{3.13}$$

$$\frac{d}{dt}(\underline{v} - v^*)_+^2 \le k_1[(u^* - \overline{u})_+^2 + (w^* - \overline{w})_+^2] \tag{3.14}$$

with $k_1 := r_2 \max\{1, \overline{v}_0\} \cdot \max\{a_1^2, d_2^2\}$, where we have used Lemma 3.1 and the fact that $\underline{u}_0 < \overline{u}_0 < 1$ and $\underline{v}_0 < \overline{v}_0$ thanks to (3.4). We consider now the equation for $\overline{w}$ to find

$$\overline{w}' = c(\overline{v} - \overline{w}) = c(\overline{v} - v^*) + c(w^* - \overline{w}).$$

As before, we multiply this by $-(w^* - \overline{w})_+$ to obtain

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}(w^* - \overline{w})_+^2 &= c(v^* - \overline{v})(w^* - \overline{w})_+ - c(w^* - \overline{w})_+^2 \\ &\le c(v^* - \overline{v})_+(w^* - \overline{w})_+ - c(w^* - \overline{w})_+^2,\end{aligned}$$

which implies, by Young′ inequality,

$$\frac{d}{dt}(w^* - \overline{w})_+^2 \le \frac{c}{4}(v^* - \overline{v})_+^2. \tag{3.15}$$

In the same way we obtain

$$\frac{d}{dt}(\underline{w} - w^*)_+^2 \le \frac{c}{4}(\underline{v} - v^*)_+^2. \tag{3.16}$$

We add (3.11) -(3.16) to have

$$\begin{aligned}&\frac{d}{dt}\left[(u^* - \overline{u})_+^2 + (\underline{u} - u^*)_+^2 + (v^* - \overline{v})_+^2 + (\underline{v} - v^*)_+^2 + (w^* - \overline{w})_+^2 + (\underline{w} - w^*)_+^2\right] \\ &\le k_2\left[(u^* - \overline{u})_+^2 + (\underline{u} - u^*)_+^2 + (v^* - \overline{v})_+^2 + (\underline{v} - v^*)_+^2 + (w^* - \overline{w})_+^2 + (\underline{w} - w^*)_+^2\right]\end{aligned}$$

with $k_2 := \max\{k_0 + \frac{c}{4},\ k_0 + k_1\}$. Applying Gronwall's Lemma and using

$$(u^* - \overline{u}_0)_+ = (\underline{u}_0 - u^*)_+ = (v^* - \overline{v}_0)_+ = (\underline{v}_0 - v^*)_+ = (w^* - \overline{w}_0)_+ = (\underline{w}_0 - w^*)_+ = 0$$

thanks to (3.4) we prove that

$$(u^* - \overline{u})_+^2 = (\underline{u} - u^*)_+^2 = (v^* - \overline{v})_+^2 = (\underline{v} - v^*)_+^2 = (w^* - \overline{w})_+^2 = (\underline{w} - w^*)_+^2 = 0,$$

which ends the proof. □

We next assert that $(\overline{u},\overline{v},\overline{w})$ actually approximate $(\underline{u},\underline{v},\underline{w})$ as time goes to infinity.

Lemma 3.3. *The solution of problem (3.1)-(3.2) fulfills*

$$|\overline{u}-\underline{u}|+|\overline{v}-\underline{v}|+|\overline{w}-\underline{w}|\longrightarrow 0 \quad \textit{exponentially}, \qquad \textit{as } t\to\infty.$$

Proof. We first introduce the numbers

$$\begin{aligned}
\epsilon &:= \frac{1}{2}\Big(\frac{1}{a_1r_2}-\frac{d_1+a_2}{r_2-d_2}\Big),\\
A_1 &:= \frac{1}{a_1r_2}-\epsilon = \frac{1}{2}\Big(\frac{1}{a_1r_2}+\frac{d_1+a_2}{r_2-d_2}\Big) \qquad \text{and}\\
A_2 &:= \frac{1}{2}\Big((r_2+d_2)A_1-a_2+d_1\Big).
\end{aligned}$$

Here we note that the assumption (1.3) yields $\epsilon>0$ and guarantees $A_1>0$ thanks to the fact that $r_2-d_2>0$ is an immediate consequence of the assumption (1.3), whereas $A_2>0$ is due to the fact that

$$\begin{aligned}
A_2 &> \frac{1}{2}\Big((r_2+d_2)\cdot\frac{d_1+a_2}{r_2-d_2}-a_2+d_1\Big)\\
&> \frac{1}{2}\Big(d_1+a_2-a_2+d_1\Big)\\
&= d_1.
\end{aligned}$$

Moreover, by the assumption (1.3) we see that ϵ, A_1 and A_2 satisfy

$$1-A_1r_2a_1>0, \qquad i.e. \quad A_1<\frac{1}{r_2a_1}, \tag{3.17}$$

$$A_1r_2-a_2-A_2>0, \qquad i.e. \quad A_2<A_1r_2-a_2 \qquad \text{and} \tag{3.18}$$

$$A_2-d_1-A_1d_2>0, \qquad i.e. \quad A_2>d_1+A_1d_2, \tag{3.19}$$

because

$$\begin{aligned}
A_1r_2-a_2-A_2 &= \frac{1}{2}(r_2-d_2)\cdot\Big(A_1-\frac{d_1+a_2}{r_2-d_2}\Big)\\
&= \frac{1}{2}(r_2-d_2)\cdot\Big(\frac{1}{r_2a_1}-\frac{d_1+a_2}{r_2-d_2}-\epsilon\Big)\\
&= \frac{1}{4}(r_2-d_2)\cdot\Big(\frac{1}{r_2a_1}-\frac{d_1+a_2}{r_2-d_2}\Big)>0
\end{aligned}$$

and

$$\begin{aligned}
A_2-d_1-A_1d_2 &= \frac{1}{2}(r_2-d_2)\cdot\Big(A_1-\frac{d_1+a_2}{r_2-d_2}\Big)\\
&= A_1r_2-a_2-A_2>0.
\end{aligned}$$

We now go back to (3.1). Since $\overline{u}>0$, $\underline{u}>0$, $\overline{v}>0$ and $\underline{v}>0$ by Lemma 3.1, the system (3.1) becomes

$$\begin{cases} \frac{\overline{u}'}{\overline{u}} = \Big[1 - \overline{u} - a_2 \underline{v} - d_1 \underline{w}\Big], & t > 0, \\ \frac{\underline{u}'}{\underline{u}} = \Big[1 - \underline{u} - a_2 \overline{v} - d_1 \overline{w}\Big], & t > 0, \\ \frac{\overline{v}'}{\overline{v}} = \Big[r_2 - r_2 \overline{v} - r_2 a_1 \underline{u} - d_2 \underline{w}\Big], & t > 0, \\ \frac{\underline{v}'}{\underline{v}} = \Big[r_2 - r_2 \underline{v} - r_2 a_1 \overline{u} - d_2 \overline{w}\Big], & t > 0, \\ \overline{w}' = c(\overline{v} - \overline{w}), & t > 0, \\ \underline{w}' = c(\underline{v} - \underline{w}), & t > 0, \end{cases} \tag{3.20}$$

which yields the system

$$\begin{cases} \frac{d}{dt} \ln \frac{\overline{u}}{\underline{u}} = -(\overline{u} - \underline{u}) + a_2(\overline{v} - \underline{v}) + d_1(\overline{w} - \underline{w}), & t > 0, \\ \frac{d}{dt} \ln \frac{\overline{v}}{\underline{v}} = -r_2(\overline{v} - \underline{v}) + r_2 a_1(\overline{u} - \underline{u}) + d_2(\overline{w} - \underline{w}) & t > 0, \\ \frac{d}{dt}(\overline{w} - \underline{w}) = -c(\overline{w} - \underline{w}) + c(\overline{v} - \underline{v}), & t > 0. \end{cases} \tag{3.21}$$

Multiplying the second equation by A_1 and the third equation by A_2/c and adding the resulting equations to the first equation, we arrive at

$$\begin{aligned} \frac{d}{dt}\left[\ln \frac{\overline{u}}{\underline{u}} + A_1 \ln \frac{\overline{v}}{\underline{v}} + \frac{A_2}{c}(\overline{w} - \underline{w})\right] &= -(1 - A_1 r_2 a_1)(\overline{u} - \underline{u}) \\ -(A_1 r_2 - a_2 - A_2)(\overline{v} - \underline{v}) &- (A_2 - d_1 - A_1 d_2)(\overline{w} - \underline{w}). \end{aligned} \tag{3.22}$$

This along with (3.17)-(3.19) entails

$$\frac{d}{dt}\left[\ln \frac{\overline{u}}{\underline{u}} + A_1 \ln \frac{\overline{v}}{\underline{v}} + \frac{A_2}{c}(\overline{w} - \underline{w})\right] \le -C_1[(\overline{u} - \underline{u}) + (\overline{v} - \underline{v}) + (\overline{w} - \underline{w})] \tag{3.23}$$

with $C_1 := \min\{1 - A_1 r_2 a_1,\ 1 - A_1 r_2 a_1,\ A_2 - d_1 - A_1 d_2\} > 0$. From this and Lemma 3.2 we obtain

$$\frac{d}{dt}\left[\ln \frac{\overline{u}}{\underline{u}} + A_1 \ln \frac{\overline{v}}{\underline{v}} + \frac{A_2}{c}(\overline{w} - \underline{w})\right] \le 0$$

and thus we have

$$\left[\ln \frac{\overline{u}}{\underline{u}} + A_1 \ln \frac{\overline{v}}{\underline{v}} + \frac{A_2}{c}(\overline{w} - \underline{w})\right] \le \left[\ln \frac{\overline{u}_0}{\underline{u}_0} + A_1 \ln \frac{\overline{v}_0}{\underline{v}_0} + \frac{A_2}{c}(\overline{w}_0 - \underline{w}_0)\right] < \infty. \tag{3.24}$$

We introduce the constant k defined by

$$k := \left[\ln \frac{\overline{u}_0}{\underline{u}_0} + A_1 \ln \frac{\overline{v}_0}{\underline{v}_0} + \frac{A_2}{c}(\overline{w}_0 - \underline{w}_0)\right].$$

This implies

$$\ln \frac{\overline{u}}{\underline{u}} < k \qquad \text{and} \qquad A_1 \ln \frac{\overline{v}}{\underline{v}} < k$$

and give us, thanks to Lemma 3.2

$$\ln \frac{u^*}{\underline{u}} < k \qquad \text{and} \qquad A_1 \ln \frac{v^*}{\underline{v}} < k$$

and therefore

$$\underline{u} > \epsilon_0 > 0 \qquad \text{and} \qquad \underline{v} > \delta_0 > 0, \tag{3.25}$$

where $\epsilon_0 := u^* e^{-k}$ and $\delta_0 := v^* e^{-k/A_1}$.

On the other hand, invoking the basic inequality $\ln\frac{b}{a} \le \frac{1}{a}(b-a)$ for any $b > a > 0$ thanks to the Mean Value Theorem, from (3.23) and (3.25) we infer that

$$\frac{d}{dt}\left[\ln\frac{\overline{u}}{\underline{u}} + A_1\ln\frac{\overline{v}}{\underline{v}} + \frac{A_2}{c}(\overline{w}-\underline{w})\right] \le -C_2\left[\ln\frac{\overline{u}}{\underline{u}} + A_1\ln\frac{\overline{v}}{\underline{v}} + \frac{A_2}{c}(\overline{w}-\underline{w})\right]$$

with $C_2 := C_1\cdot\min\{\epsilon_0, \frac{\delta_0}{A_1}, \frac{c}{A_2}\} > 0$. Applying Gronwall's Lemma we get

$$\ln\frac{\overline{u}}{\underline{u}} + A_1\ln\frac{\overline{v}}{\underline{v}} + \frac{A_2}{c}(\overline{w}-\underline{w}) \le k_0 e^{-C_2 t}.$$

Using the basic inequality $\frac{1}{b}(b-a) \le \ln\frac{b}{a}$ for any $b > a > 0$ thanks to the Mean Value Theorem once again and noticing Lemmata 3.1 and 3.2, we obtain

$$|\overline{u}-\underline{u}| + \frac{A_1}{\max\{1,\overline{v}_0\}}\cdot|\overline{v}-\underline{v}| + \frac{A_2}{c}\cdot|\overline{w}-\underline{w}| \le k_0 e^{-C_2 t},$$

which ends the proof. □

From (3.25) we have that $\underline{u}$ and $\underline{v}$ has a positive bound from the below. In the following we shall refine the upper bound of $\overline{u}$, which plays a crucial role in the proof of the global existence (see Section 4 below).

Lemma 3.4. *The solution of problem (3.1)-(3.2) satisfies*

$$\overline{u} \le \max\Big\{1 - a_2\delta_0, \overline{u}_0\Big\}, \tag{3.26}$$

where $\delta_0 > 0$ is defined in (3.25).

Proof. $\overline{u}$ satisfies

$$\overline{u}_t = \overline{u}(1 - \overline{u} - a_2\underline{v} - d_1\underline{w}).$$

Since $\underline{v} > \delta_0$ and $\underline{w} > 0$ we find

$$\overline{u}_t \le \overline{u}(1 - \overline{u} - a_2\delta_0)$$

Upon an ODE comparison, this proves (3.26). □

4. Comparison argument. The proof of Theorem 1.1.

We shall prove $(\overline{u}, \overline{v}, \overline{w})$ and $(\underline{u}, \underline{v}, \underline{w})$ are actually the sup and sub-solutions of the PDE system (1.1).

Lemma 4.1. *Let (u, v, w) be the classical solution to (1.1) with initial data fulfilling (1.7), and let $(\overline{u}, \underline{u}, \overline{v}, \underline{v}, \overline{w}, \underline{w})$ be the solution to (3.1)-(3.2) with initial data taken as in (3.3). Then we have*

$$\begin{aligned} &\underline{u} \le u \le \overline{u}, && x\in\Omega,\ t\in(0,T_{max}),\\ &\underline{v} \le v \le \overline{v}, && x\in\Omega,\ t\in(0,T_{max}) \quad \textit{and}\\ &\underline{w} \le w \le \overline{w}, && x\in\Omega,\ t\in(0,T_{max}). \end{aligned}$$

Proof. We introduce the unknowns variables $\overline{U}$, $\underline{U}$, $\overline{V}$, $\underline{V}$, $\overline{W}$ and $\underline{W}$ defined by

$$\overline{U}(x,t) := \overline{u}(t) - u(x,t), \qquad \underline{U}(x,t) := u(x,t) - \underline{u}(t), \tag{4.1}$$

$$\overline{V}(x,t) := \overline{v}(t) - v(x,t), \qquad \underline{V}(x,t) := v(x,t) - \underline{v}(t) \tag{4.2}$$

and

$$\overline{W}(x,t) := \overline{w}(t) - w(x,t), \qquad \underline{W}(x,t) := w(x,t) - \underline{w}(t). \tag{4.3}$$

We operate equations (3.1) and (1.1) to obtain

$$\overline{U}_t = \overline{U}(1 - \overline{u} - a_2\underline{v} - d_1\underline{w}) + u(-\overline{U} + a_2\underline{V} + d_1\underline{W}).$$

In order to prove $u \leq \overline{u}$, we only need to prove $\overline{U}_- = 0$. For this purpose, we multiply the previous equation by $\overline{U}_-$ to obtain

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\overline{U}_-^2 &= \overline{U}_-^2(1-\overline{u}-a_2\underline{v}-d_1\underline{w}) - u\overline{U}_-^2 + a_2u\overline{U}_-\underline{V} + d_1u\overline{U}_-\underline{W} \\ &\leq \overline{U}_-^2 + a_2u\overline{U}_-\underline{V}_- + d_1u\overline{U}_-\underline{W}_-\end{aligned}$$

thanks to (3.10). This in conjunction with the Young inequality yields

$$\frac{1}{2}\frac{d}{dt}\overline{U}_-^2 \leq (1+u^2)\overline{U}_-^2 + \frac{a_2^2}{2}\underline{V}_-^2 + \frac{d_1^2}{2}\underline{W}_-^2$$

and after integration over Ω

$$\frac{1}{2}\frac{d}{dt}\int_\Omega \overline{U}_-^2 \leq \int_\Omega (1+u^2)\overline{U}_-^2 + \frac{a_2^2}{2}\int_\Omega \underline{V}_-^2 + \frac{d_1^2}{2}\int_\Omega \underline{W}_-^2. \tag{4.4}$$

In the same fashion we obtain

$$\frac{1}{2}\frac{d}{dt}\int_\Omega \underline{U}_-^2 \leq \int_\Omega (1+u^2)\underline{U}_-^2 + \frac{a_2^2}{2}\int_\Omega \overline{V}_-^2 + \frac{d_1^2}{2}\int_\Omega \overline{W}_-^2. \tag{4.5}$$

We now consider the equation for v

$$v_t - D\nabla\cdot\Big((1-u)\nabla v\Big) = r_2 v\Big(1 - v - a_1 u - \frac{d_2}{r_2}w\Big),$$

and combine with (3.1) to obtain

$$\overline{V}_t - D\nabla\cdot\Big((1-u)\nabla\overline{V}\Big) = r_2\left[\overline{V}\Big(1-\overline{v}-a_1\underline{u}-\frac{d_2}{r_2}\underline{w}\Big) + v\Big(-\overline{V}+a_1\underline{U}+\frac{d_2}{r_2}\underline{W}\Big)\right].$$

We multiply this by $\overline{V}_-$ and integrate over Ω, to obtain

$$\begin{aligned}&\frac{1}{2}\frac{d}{dt}\int_\Omega \overline{V}_-^2 + D\int_\Omega (1-u)|\nabla\overline{V}_-|^2 \\ &= r_2\int_\Omega \Big[\overline{V}_-^2(1-\overline{v}-a_1\underline{u}-\tfrac{d_2}{r_2}\underline{w}) - v\overline{V}_-^2 + a_1 v\underline{U}\overline{V}_- + \tfrac{d_2}{r_2}v\underline{W}\overline{V}_-\Big] \\ &\leq r_2\int_\Omega \Big[\overline{V}_-^2(1-\overline{v}-a_1\underline{u}-\tfrac{d_2}{r_2}\underline{w}) - v\overline{V}_-^2 + a_1 v\underline{U}_-\overline{V}_- + \tfrac{d_2}{r_2}v\underline{W}_-\overline{V}_-\Big]\end{aligned}$$

where we have used the fact that $a_1 v\underline{U}_+\overline{V}_- \leq 0$ and $\frac{d_2}{r_2}v\underline{W}_+\overline{V}_- \leq 0$. Thanks to Young's inequality and Lemma 3.1 we have

$$\frac{1}{2}\frac{d}{dt}\int_\Omega \overline{V}_-^2 + D\int_\Omega (1-u)|\nabla\overline{V}_-|^2 \leq r_2\int_\Omega \Big[(1+v^2)\overline{V}_-^2 + \frac{a_1^2}{2}\underline{U}_-^2 + \frac{d_2^2}{2r_2^2}\underline{W}_-^2\Big]. \tag{4.6}$$

In the same way we obtain

$$\frac{1}{2}\frac{d}{dt}\int_\Omega \underline{V}_-^2 + D\int_\Omega (1-u)|\nabla\underline{V}_-|^2 \leq r_2\int_\Omega \Big[(1+v^2)\underline{V}_-^2 + \frac{a_1^2}{2}\overline{U}_-^2 + \frac{d_2^2}{2r_2^2}\overline{W}_-^2\Big]. \tag{4.7}$$

In the same fashion we can obtain the equations for $\overline{W}$ and $\underline{W}$

$$\overline{W}_t - \Delta\overline{W} = c(\overline{V} - \overline{W})$$

and

$$\underline{W}_t - \Delta\underline{W} = c(\underline{V} - \underline{W}).$$

We multiplying those by $\overline{W}_-$ and $\underline{W}_-$ respectively and integrate by parts to get, thanks to Cauchy-Swartz inequality

$$\frac{1}{2}\frac{d}{dt}\int_\Omega \overline{W}_-^2 + \int_\Omega |\nabla\overline{W}_-|^2 \leq \frac{c}{2}\int_\Omega \Big(\overline{V}_-^2 + \overline{W}_-^2\Big) \tag{4.8}$$

and

$$\frac{1}{2}\frac{d}{dt}\int_\Omega \underline{W}_-^2 + \int_\Omega |\nabla \underline{W}_-|^2 \le \frac{c}{2}\int_\Omega \left(\underline{V}_-^2 + \underline{W}_-^2\right). \tag{4.9}$$

We define the function Y given by

$$Y(t) := \int_\Omega \left(\overline{U}_-^2 + \overline{V}_-^2 + \overline{W}_-^2 + \underline{U}_-^2 + \underline{V}_-^2 + \underline{W}_-^2\right),$$

and we add equations (4.4)-(4.9) to obtain

$$\frac{d}{dt}Y(t) \le kY(t) \tag{4.10}$$

with $k := \max\{4 + a_1^2,\ a_2^2 + c + 2r_2(1 + \max\{1, \|v_0\|_{L^\infty(\Omega)}\}),\ c + d_1 + \frac{d_2^2}{r_2^2}\}$, where we have used (2.1) and (2.2). On the other hand, (3.3) entails that

$$Y(0) = 0. \tag{4.11}$$

Since $Y(t) \ge 0$, from (4.10) and (4.11) we infer that

$$Y(t) \equiv 0, \qquad t \in [0, T_{max}),$$

which proves

$$\underline{u} \le u \le \overline{u}, \qquad \underline{v} \le v \le \overline{v} \qquad \text{and} \qquad \underline{w} \le w \le \overline{w}.$$

This ends the proof of the lemma. □

We are now in a position to prove Theorem 1.1.

Proof of Theorem 1.1. In view of (3.4) and Lemmata 3.1, 3.4 and 4.1, we obtain

$$0 < u < \lambda := \max\left\{1 - a_2\delta_0, \overline{u}_0\right\} < 1 \qquad \text{for all } x \in \Omega \text{ and } t \in (0, T_{max}).$$

Then the assertion of global existence is an immediate consequence of this and the extensibility criterion provided by lemma 2.1, whereas the asymptotic behavior of the solutions

$$\|u - u^*\|_{L^\infty(\Omega)} + \|u - w^*\|_{L^\infty(\Omega)} + \|u - w^*\|_{L^\infty(\Omega)} \to 0 \quad \text{exponentally,} \quad \text{as } t \to \infty$$

is a consequence of Lemma 3.3 and Lemma 4.1 □

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