STABILIZATION IN A CHEMOTAXIS MODEL FOR VIRUS INFECTION

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Abstract. This paper presents a qualitative analysis of a model describing the time and space dynamics of a virus which migrates driven by chemotaxis. The initial-boundary value problem related to applications of the model to a real biological dynamics is studied in detail. The main result consists in the proof of global existence and asymptotic stability.

1. Introduction. A minimal virus model to describe the dynamics of the number densities of a virus particles, interacting with infected and uninfected cells, was proposed by Wei et al. [38], see also [23, 25, 27]. This model rapidly attracted both applied mathematicians and biologists who devoted a great deal of attention to the mathematical problems generated by the ability of the model to depict emerging behaviors of interest in biology. Examples of further development and applications are given by [5, 12, 13].

Various modifications have been proposed in the literature with the aim of going beyond the the simple description delivered by population dynamics without internal variables. Therefore, various technical modifications have been proposed, for instance, by introducing models with internal structure [7, 37], stochastic interactions [11] and delay terms deemed to account also for the heterogeneity of individual entities of large biological systems [9], chapter 2. The books [9, 28] refer this specific model to the existing literature in population dynamics, while the book by Nowak shows how evolutionary game theory can be used to model interactions and virus dynamics [23].

An interesting development consists in introducing a space structure and study the virus dynamics coupled with a diffusion process. Therefore the overall dynamics can be modeled by a system of PDEs, while the qualitative analysis can be focused not only on the well-posedness of the initial-boundary value problem, but also on the study of pattern formation somehow related to the stability properties of the original dynamical system described by ODEs. The selection of the diffusion process

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can take advantage of recent studies specifically focused on biological tissues [35], which have subsequently motivated analytic studies reviewed in the survey [6].

This paper develops the aforementioned concepts focusing on the qualitative analysis of the initial-boundary value model, where space dynamics is a diffusion process induced by chemotaxis. This idea is founded on a biological interpretation on the dynamics of viruses which diffuse following the stimuli of chemoattractants, as an example they are attracted by concentration gradient [14, 22] of cytokines from inflammation at sites of infection. Chemotaxis can be modeled by the celebrated Keller-Segel model [18, 19], as well as by suitable modifications that can be obtained either by heuristic developments of the original model at the macroscopic scale [15, 33, 34], or by micro-macro derivation by asymptotic methods from the underlying description at the microscopic scale [3, 26]. A detailed study of modeling of interactions at the microscopic scale can lead to models with nonlinear degenerate diffusion terms [3] whose qualitative analysis has been studied in [4]. A possible development of the contents of our paper might consider new models that include this specific feature.

In more detail, the contents of this paper is proposed through three more sections. Section 2 consists of three parts, where the first one rapidly presents the ODE model and some known results on the initial value problem; the second part motivates the introduction of the diffusion dynamics and presents the related initial-boundary value problem which is object of the qualitative analysis; finally, the third part reports the main results of the qualitative analysis, namely global existence and asymptotic stability. The contents of remaining sections are devoted to proofs. In more detail, Section 3 shows how global existence can be proved, while Section 4 is devoted to stability analysis. The results concerning the qualitative analysis are related to the so called basic reproduction number [21], see Chapter 5 in [9].

2. Mathematical models and results. This section first presents the mathematical models which are object of the qualitative analysis and subsequently reports the main results achieved in this paper, while their proof is given in the next sections. In more detail, Subsection 2.1 rapidly introduces the minimal virus model mentioned in Section 1 and some stability results known in the literature, while the Subsection 2.2 motivates the interest in introducing diffusion dynamics and presents the specific mathematical model and related initial-boundary value problem studied in our paper. Finally, Subsection 2.3 reports the main results which have been achieved, namely global existence and asymptotic stability.

2.1. Basic virus dynamics model. Let us start from a model of virus dynamics which is considered the prototype of this type of biological competition:

\[
\begin{align*}
\frac{du}{dt} &= h - \beta uw - d_1 u, \quad t > 0, \\
\frac{dv}{dt} &= \beta uw - d_2 v, \quad t > 0, \\
\frac{dw}{dt} &= kv - d_3 w, \quad t > 0,
\end{align*}
\] (2.1)

where \( u, v \) and \( w \) correspond, respectively, to the population, namely the number, of healthy uninfected cells, of infected cells, and of viruses. This model reflects the following dynamics:
1. Healthy cells are constantly produced by the body at a rate \( h \), die at a rate \( d_1 u \) proportional to the current population, and become infected at a rate \( \beta uw \) proportional to their interaction with the virus population \( w \);

2. Infected cells are produced at the rate \( \beta uw \) and die at rate \( d_2 v \);

3. New virus is produced at a rate \( kv \) proportional to the number of infected cells, and die at a rate \( d_3 w \).

This model has been studied by several authors, for instance [5, 7, 17, 24, 25, 27, 38], who have studied the qualitative behavior of the solutions to the initial value problem enlightening a broad variety of asymptotic behaviors, related to the parameters of the model, which appear to be consistent with empirical data. An important role is acted by the so called basic reproduction number introduced by [21]

\[
R_0 := \beta \frac{hk}{d_1 d_2 d_3}. \tag{2.2}
\]

In more detail, it can be rapidly shown that the system always possesses the infection-free equilibrium \( Q_0 := (h/d_1, 0, 0) := (u_*, 0, 0) \), while whenever \( R_0 > 1 \), the system has a coexistence equilibrium \( Q^* := (u^*, v^*, w^*) \), where

\[
\begin{align*}
  u^* &= \frac{h}{d_1 R_0}, & v^* &= \frac{d_1 d_3}{\beta k} (R_0 - 1), & w^* &= \frac{d_1}{\beta} (R_0 - 1). \tag{2.3}
\end{align*}
\]

In addition, the following holds true (cf. [21] for instance):

i) If \( R_0 > 1 \), then \( Q^* \) is globally stable;

ii) If \( R_0 \leq 1 \), then \( Q_0 \) is globally stable.

It is plain that, in spite of its popularity, this model contains various simplifications of the real underlying dynamics of viral infections. In particular, the specific features of structured population models that include delay terms and internal variables are not considered. In addition, the model is derived at the scale of population dynamics, where pattern formation is not accounted for. Therefore some modeling development is needed to depict this important feature by which a virus can diffuse in tissues. Indeed, the formation of space patterns can be studied by taking advantage of the immediate ability of this simple model to lead equilibrium configurations and their stability properties. Some specific models are proposed in the next subsection looking ahead to a qualitative analysis of mathematical problems.

2.2. Chemotaxis models for virus dynamics. Space patterns related to virus dynamics can be studied by models, where diffusion is induced by chemotaxis phenomena, see Chapter 5 of [28] and the two surveys [33, 34]. In fact, target cells are attracted by the concentration gradient of cytokines from inflammations at sites of infection see [14, 22] and more in detail [30], where the following chemotaxis model was proposed:

\[
\begin{align*}
  u_t &= D_u \Delta u - \chi \nabla \cdot (u \nabla v) + h - \beta uw - d_1 u, & x \in \Omega, t > 0, \\
  v_t &= D_v \Delta v + \beta uw - d_2 v, & x \in \Omega, t > 0, \\
  w_t &= D_w \Delta w + kv - d_3 w, & x \in \Omega, t > 0, \\
  \frac{\partial u}{\partial \nu} &= \frac{\partial v}{\partial \nu} = \frac{\partial w}{\partial \nu} = 0, & x \in \partial \Omega, t > 0, \\
  u(x, 0) &= u_0(x), & v(x, 0) &= v_0(x), & w(x, 0) &= w_0(x), & x \in \Omega,
\end{align*}
\tag{2.4}
\]
where, in addition to a linear diffusion term, a chemotaxis term is inserted in the first equation to account for the aforementioned gradient’s attraction. The authors after having written the model by dimensionless variables develop a linear stability analysis and subsequently an interesting numerical analysis which illuminates some specific features of pattern formation such as the onset of hot spots. This is an important feature considering that their localization can contribute to detect early HIV infections.

In addition, numerical work in [30] shows that the model exhibits a blow up of solutions in finite time for sufficiently large $\chi$. Therefore a specific assumption has been proposed in [30] to control this distinct feature. In more detail, the authors assume that the term $\chi$ decay with $u$. An alternative to this assumption can be inspired by the Beddington-DeAngelis model [2, 8] on the functional response $\beta uv$ which grows with $u$ and $w$, but saturates for large values of this variables. More precisely, the following assumption has been proposed in [36]:

$$\beta uv \rightarrow \frac{\beta uv}{1 + au + bw},$$

while the interested reader is referred to [15] for further heuristic regularized models and to [3] for derivation of macroscopic models from the underlying description at the scale of cells. Additional phenomenological studies [20] on the biological phenomena under consideration suggest to introduce a space structure on the terms $h, \beta$ and $k$, namely $h \rightarrow h(x), \beta \rightarrow \beta(x)$ and $h \rightarrow h(x)$; as well as a nonlinear cross diffusion in the diffusion term $D_w$, namely $D_w \rightarrow D_w(v)$, which corresponds to repulsion dynamics of superinfecting virions by infected cells [10, 36].

Let now $u := u(x,t), v := v(x,t)$ and $w := w(x,t)$ denote the densities of uninfected cells, infected cells and virus, at location $x$ and time $t$, respectively. To slightly reduce the complexity of the model in [36], we assume that the infected cells are unable to recover into healthy state and that a possible absorption effect [1] of virus is neglected. Then, a simplified version of the mathematical model in [36] for virus infection dynamics reads as follows:

\[
\begin{align*}
  u_t &= D_u \Delta u - \chi \nabla \cdot (u \nabla v) + h(x) - \beta(x) \frac{uw}{1 + au + bw} - d_1 u, \quad x \in \Omega, \ t > 0, \\
  v_t &= D_v \Delta v + \beta(x) \frac{uw}{1 + au + bw} - d_2 v, \quad x \in \Omega, \ t > 0, \\
  w_t &= \nabla \cdot (D_w(v) \nabla w) + k(x)v - d_3 w, \quad x \in \Omega, \ t > 0, \\
  \frac{\partial u}{\partial \nu} = \frac{\partial v}{\partial \nu} = \frac{\partial w}{\partial \nu} = 0, \quad x \in \partial \Omega, \ t > 0, \\
  u(x,0) &= u_0(x), \quad v(x,0) = v_0(x), \quad w(x,0) = w_0(x), \quad x \in \Omega,
\end{align*}
\]  

(2.5)

where $\Omega \subset \mathbb{R}^n, n \geq 1$, is a bounded domain with smooth boundary, $D_u, D_v, \chi, d_1, d_2, d_3$ and $a$ are positive constants, $b$ is a nonnegative parameter, and $h(x), k(x)$ and $\beta(x)$ are given positive functions. Throughout this paper we shall assume that

$$h(x), k(x), \beta(x) \in C^\alpha(\Omega) \quad \text{with some } \alpha \in (0,1) \quad (2.6)$$

and

$$D_w(v) = D_0 + g(v), \quad (2.7)$$
where $D_0$ stands for random diffusion rate of free virions and $g \in C^2(\mathbb{R}^+, \mathbb{R}^+)$ fulfilling $g(0) = 0$ is a prescribed increasing function of $v$, addressing the repulsion of super-infecting virions by infected cells.

2.3. Main results. The global existence for a corresponding reaction-diffusion model without any chemotaxis effect was obtained in [36, Theorem 2.1]. However, as far as we know, the global existence for the virus-chemotaxis model (2.5) has not been addressed yet. So our first goal of this work is to identify the global well-posedness of the initial-boundary value problem (2.5). More precisely, we have:

**Theorem 2.1.** Let $\Omega \subset \mathbb{R}^n$, $n \geq 1$, be a bounded domain with smooth boundary, and suppose that the parameters $D_u, D_v, \chi, d_1, d_2, d_3$ and $a$ are positive, the parameter $b$ is nonnegative, the parameter functions $h(x), k(x)$ and $\beta(x)$ are positive and satisfy (2.6) and the prescribed function $D_w(\cdot)$ complies with the assumption (2.7). Then for all nonnegative initial data $(u_0, v_0, w_0)$ from $C^0(\bar{\Omega}) \times W^{1,\infty}(\bar{\Omega}) \times W^{1,\infty}(\bar{\Omega})$, the problem (2.5) possesses a global classical solution

$$(u, v, w) \in \left( C^0(\bar{\Omega} \times [0, \infty)) \cap C^{2,1}(\Omega \times (0, \infty)) \right)^3,$$

such that $u$, $v$ and $w$ are nonnegative in $\bar{\Omega} \times (0, \infty)$, and such that $(u, v, w)$ is bounded in the sense that

$$\|u(\cdot, t)\|_{L^\infty(\Omega)} + \|v(\cdot, t)\|_{L^\infty(\Omega)} + \|w(\cdot, t)\|_{L^\infty(\Omega)} \leq C$$

for all $t > 0$ (2.8) with some $C > 0$.

A crucial step in the proof of Theorem 2.1 is to establish the coupled $L^p$ estimates for $v$ and $w$ (see Lemma 3.3 and Lemma 3.4 below). When the parameter functions $h(x), k(x)$ and $\beta(x)$ are spatially homogeneous, the model (2.5) takes the following simplified version

$$
\begin{align*}
&\begin{cases}
  u_t = D_u \Delta u - \chi \nabla \cdot (u \nabla v) + h - \beta \frac{u w}{1 + a u + b w} - d_1 u, & x \in \Omega, t > 0,
  \\
v_t = D_v \Delta v + \beta \frac{u w}{1 + a u + b w} - d_2 v, & x \in \Omega, t > 0,
  \\
w_t = \nabla \cdot (D_w(v) \nabla w) + k v - d_3 w, & x \in \Omega, t > 0,
  \\
\frac{\partial u}{\partial \nu} = \frac{\partial v}{\partial \nu} = \frac{\partial w}{\partial \nu} = 0, & x \in \partial \Omega, t > 0,
  \\
u(x, 0) = u_0(x), & x \in \Omega,
\end{cases}
\end{align*}
$$

where $h, k$ and $\beta$ are positive constants. Obviously, this simplified model always has an infection-free steady state $E_0 := (\frac{a}{b}, 0, 0) := (u_*, 0, 0)$. Only the local linear stability of $E_0$ was discussed in [36]. Under suitable parameter conditions, the present work further asserts the global asymptotic stability of this infection-free steady state when $R_0 < 1$. More precisely:

**Theorem 2.2.** Let $\Omega \subset \mathbb{R}^n$, $n \geq 1$, be a bounded domain with smooth boundary, and assume that the prescribed function $D_w(\cdot)$ fulfills the assumption (2.7), that the parameters $D_u, D_v, \chi, d_1, d_2, d_3, a, h, k$ and $\beta$ are positive, and that $b$ is nonnegative. If

$$R_0 \leq 1 \quad (2.10)$$

and

\[ \beta \frac{k}{ad_2d_3} < 1. \quad (2.11) \]

Then for arbitrary nonnegative initial data \((u_0, v_0, w_0)\) from \(C^0(\bar{\Omega}) \times W^{1,\infty}(\Omega) \times W^{1,\infty}(\Omega)\), the solution \((u, v, w)\) of (2.9) satisfies

\[ \|u(\cdot, t) - u_*\|_{L^\infty(\Omega)} + \|v(\cdot, t)\|_{L^\infty(\Omega)} + \|w(\cdot, t)\|_{L^\infty(\Omega)} \to 0 \quad \text{as} \quad t \to \infty. \quad (2.12) \]

The stability condition in Theorem 2.2 is independent of the chemotactic coefficient \(\chi\) and the parameter \(b\), but it strongly depends on the parameter \(a\). We observe that the condition (2.11) holds whenever \(a = 0\) and \(c\) is suitably large. Moreover, it seems that the condition (2.11) is necessary for the validity of (2.12). To figure this out, when

\[ R_0 > 1 + \frac{ah}{d_1}, \quad \text{and} \quad \frac{\beta k}{ad_2d_3} > 1, \]

the system (2.9) with \(b = 0\) has a coexistence equilibrium \(E_* = (u_*, v_*, w_*)\), where

\[ u_* = \frac{h}{d_1R_0 - ah}, \quad v_* = \frac{d_1d_3(R_0 - 1 - \frac{ah}{d_1})}{\beta k - ad_2d_3}, \quad \text{and} \quad w_* = \frac{d_1k(R_0 - 1 - \frac{ah}{d_1})}{\beta k - ad_2d_3}. \]

Complex patterns might occur around \((u_*, v_*, w_*)\) for small \(a\) and \(\chi > 0\); see [30] for the numerical verifications for the case when \(a = 0\) and \(\chi > 0\).

Our derivation of the stabilization result in Theorem 2.2 will be based on investigating the corresponding Lyapunov functionals

\[ \int_{\Omega} \left( u - u_* - u_* \ln \frac{u}{u_*} \right) + \int_{\Omega} v + \gamma \int_{\Omega} w + \eta \int_{\Omega} v^2 + \tau \int_{\Omega} w^2 \]

for suitably chosen \(\gamma > 0, \eta > 0\) and \(\tau > 0\).

3. Global existence for (2.5). Proof of Theorem 2.1. As a consequence of the assumption (2.6) we can find some constant \(L > 0\) such that

\[ 0 < h(x) \leq L, \quad 0 < k(x) \leq L \quad \text{and} \quad 0 < \beta(x) \leq L \quad \text{for all} \quad x \in \bar{\Omega}. \quad (3.13) \]

We begin with the local existence, which can be proven by a straightforward fixed-point argument (cf. [31], for instance).

**Lemma 3.1.** Let \(\Omega \subset \mathbb{R}^n, n \geq 1\), be a bounded domain with smooth boundary, suppose that the parameters \(D_u, D_v, \chi, d_1, d_2, d_3, a\) are positive, the parameter \(b\) is nonnegative, the parameter functions \(h(x), k(x)\) and \(\beta(x)\) are positive and satisfy (2.6) and the prescribed function \(D_w(\cdot)\) complies with the assumption (2.7), and assume that \(u_0, v_0\) and \(w_0\) are nonnegative functions from \(C^0(\bar{\Omega}), W^{1,\infty}(\Omega)\) and \(W^{1,\infty}(\Omega)\), respectively. Then there exist \(T_{\max} \in (0, \infty]\) and a classical solution \((u, v, w)\) of (2.5) in \(\Omega \times (0, T_{\max})\), satisfying

\[ (u, v, w) \in \left( C^0(\bar{\Omega} \times [0, T_{\max}]) \cap C^{2,1}(\bar{\Omega} \times (0, T_{\max})) \right)^3, \]

such that \(u, v\) and \(w\) are nonnegative in \(\Omega \times (0, T_{\max})\), and such that

either \(T_{\max} = \infty\), or \(\lim_{t \to T_{\max}} \sup_{\Omega} \|u(\cdot, t)\|_{L^\infty(\Omega)} = \infty. \quad (3.14)\]

The following mass properties immediately results from simple integrations of equations in (2.5) with respect to \(x \in \Omega\).
Lemma 3.2. The solution of (2.5) satisfies
\[ \int_{\Omega} u(\cdot, t) \leq m := \max \left\{ \int_{\Omega} u_0 + \int_{\Omega} v_0, \frac{L|\Omega|}{\min\{d_1, d_2\}} \right\} \text{ for all } t \in (0, T_{\text{max}}) \] (3.15)

and
\[ \int_{\Omega} v(\cdot, t) \leq m := \max \left\{ \int_{\Omega} u_0 + \int_{\Omega} v_0, \frac{L|\Omega|}{\min\{d_1, d_2\}} \right\} \text{ for all } t \in (0, T_{\text{max}}) \] (3.16)
as well as
\[ \int_{\Omega} w(\cdot, t) \leq M := \max \left\{ \int_{\Omega} w_0, \frac{L m d_3}{d_1} \right\} \text{ for all } t \in (0, T_{\text{max}}). \] (3.17)

Proof. Adding the second equation to the first one in (2.5) and integrating the resulting equation we obtain
\[ \frac{d}{dt} \left\{ \int_{\Omega} u + \int_{\Omega} v \right\} = \int_{\Omega} h(x) - d_1 \int_{\Omega} u - d_2 \int_{\Omega} v \leq L \cdot |\Omega| - \min\{d_1, d_2\} \cdot \left\{ \int_{\Omega} u + \int_{\Omega} v \right\} \text{ for all } t \in (0, T_{\text{max}}). \]

Upon an ODE comparison, this entails (3.15) and (3.16). Integrating the third equation in (2.5) and invoking (3.16), we prove (3.17).

The following energy-type inequalities can be regarded as a corner stone for establishing a priori \( L^p \) estimates.

Lemma 3.3. Let \( p \geq 2 \). Then for all \( t \in (0, T_{\text{max}}) \), we have
\[ \frac{d}{dt} \int_{\Omega} v^p + d_2 p \int_{\Omega} v^p + \frac{4(p-1)D_v}{p} \int_{\Omega} |\nabla v|^2 \leq \frac{pL}{a} \int_{\Omega} v^{p-1} w \] (3.18)

and
\[ \frac{d}{dt} \int_{\Omega} w^p + d_3 p \int_{\Omega} w^p + \frac{4(p-1)D_0}{p} \int_{\Omega} |\nabla w|^2 \leq pL \int_{\Omega} w^{p-1} v. \] (3.19)

Proof. We multiply the second equation in (2.5) by \( v^{p-1} \) and integrate by parts to find on using (3.13) that
\[ \frac{1}{p} \frac{d}{dt} \int_{\Omega} v^p = -(p-1)D_v \int_{\Omega} v^{p-2} |\nabla v|^2 + \int_{\Omega} \beta(x) \cdot \frac{1}{a} \cdot \frac{a u}{1 + au + bw} \cdot v^{p-1} w - d_2 \int_{\Omega} v^p \leq -4 \frac{(p-1)D_v}{p^2} \int_{\Omega} |\nabla v|^2 + \frac{L}{a} \int_{\Omega} v^{p-1} w - d_2 \int_{\Omega} v^p \]

for all \( t \in (0, T_{\text{max}}) \), this implies (3.18), whereas (3.19) can be proven similarly.

By a coupled estimate argument together with an Ehrling-type lemma we obtain the following.

Lemma 3.4. Let \( p \geq 2 \). Then there exists \( C := C(p) > 0 \) such that
\[ \int_{\Omega} v^p(\cdot, t) \leq C \text{ for all } t \in (0, T_{\text{max}}) \] (3.20)

and
\[ \int_{\Omega} w^p(\cdot, t) \leq C \text{ for all } t \in (0, T_{\text{max}}). \] (3.21)
Proof. Adding (3.19) to (3.18) yields
\[
\frac{d}{dt}\left\{ \int_{\Omega} v^p + \int_{\Omega} w^p \right\} + c_1\left\{ \int_{\Omega} v^p + \int_{\Omega} w^p \right\} + \frac{4(p-1)D_v}{p} \int_{\Omega} |\nabla v^\frac{p}{2}|^2 + \frac{4(p-1)D_0}{p} \int_{\Omega} |\nabla w^\frac{p}{2}|^2 \\
\leq \frac{pL}{a} \int_{\Omega} v^{p-1}w + pL \int_{\Omega} w^{p-1}v
\] (3.22)
for all \( t \in (0, T_{\text{max}}) \), where \( c_1 := \min\{d_2, d_3\} \cdot p \). Here the Young inequality entails
\[
\frac{pL}{a} \int_{\Omega} v^{p-1}w + pL \int_{\Omega} w^{p-1}v \leq c_2 \int_{\Omega} v^p + c_2 \int_{\Omega} w^p
\] for all \( t \in (0, T_{\text{max}}) \) (3.23) with \( c_2 := pL(1 + \frac{1}{a}) \), and we use an Ehrling-type lemma along with (3.16) to find \( c_3 > 0 \) such that
\[
c_2 \int_{\Omega} v^p \leq c_5 \left\| \nabla v \right\|_{L^2(\Omega)}^2 + c_3 m^p \quad \text{for all} \quad t \in (0, T_{\text{max}}). \] (3.24)
Similarly, we can obtain some \( c_4 > 0 \) satisfying
\[
c_2 \int_{\Omega} w^p \leq \frac{4(p-1)D_0}{p} \int_{\Omega} |\nabla w^\frac{p}{2}|^2 + c_4 M^p \quad \text{for all} \quad t \in (0, T_{\text{max}}). \] (3.25)
Collecting (3.22)-(3.25) we see that the function
\[
y(t) := \int_{\Omega} v^p(\cdot,t) + \int_{\Omega} w^p(\cdot,t), \quad t \in (0, T_{\text{max}}),
\]
satisfies the differential inequality
\[
y'(t) + c_1 y(t) \leq c_5 \quad \text{for all} \quad t \in (0, T_{\text{max}})
\]
with \( c_5 := c_3 m^p + c_4 M^p \). Upon an ODE comparison, this yields (3.20) and (3.21) with
\[
C := \max\left\{ \int_{\Omega} u^p_0 + \int_{\Omega} w^p_0, \frac{c_5}{c_1} \right\}.
\]
This immediately leads to the boundedness property of \( \nabla v \) in \( L^\infty(\Omega) \).

Corollary 3.5. There exists \( C > 0 \) such that the solution of (2.5) satisfies
\[
\|\nabla v(\cdot, t)\|_{L^\infty(\Omega)} \leq C \quad \text{for all} \quad t \in (0, T_{\text{max}}). \] (3.26)

Proof. We rewrite the second equation in the form
\[
v_t - D_v \Delta v + d_2 v = f(x,t), \quad x \in \Omega, \ t \in (0, T_{\text{max}}),
\]
where
\[
f(x,t) := \beta \frac{uw}{1 + au + bw}.
\]
Since Lemma 3.4 along with (3.13) guarantees that
\[
|f| = \left| \beta(x) \cdot \frac{1}{a} \cdot \frac{au}{1 + au + bw} \cdot w \right| \leq \frac{L}{a} w \in L^p(\Omega)
\]
for any \( p > n \) and all \( t \in (0, T_{\text{max}}), \)
an application of Lemma 4.1 in [16] yields (3.26).

We are now in a position to prove Theorem 2.1.

Proof of Theorem 2.1. An application of a Moser-type iteration (cf. [32, Lemma A.1]) along with Lemma 3.4 and Corollary 3.5 entails the existence of \(c_1 > 0\) satisfying
\[
\|u(\cdot, t)\|_{L^\infty(\Omega)} \leq c_1 \quad \text{for all } t \in (0, T_{\max}).
\]
Thanks to the extensibility criterion (3.14) in Lemma 3.1, this ensures that \((u, v, w)\) is global in time.

4. Global asymptotic stability in (2.9). Proof of Theorem 2.2. Under the assumptions in Theorem 2.2, from Theorem 2.1 we infer that the problem (2.9) admits a unique global smooth solution that is nonnegative and bounded. Hence, there exists some constant \(A > 0\) such that the solution of (2.9) satisfies
\[
0 \leq u \leq A, \quad 0 \leq v \leq A \quad \text{and} \quad 0 \leq w \leq A \quad \text{for all } x \in \bar{\Omega} \, \text{and any } t > 0.
\]
As a preparation for constructing suitable functionals for our purpose, we have the following.

Lemma 4.1. Let \(u_* := \frac{h}{d_1}\). Then the solution of (2.9) satisfies
\[
\frac{d}{dt} \int_\Omega \left( u - u_* - u_* \ln \frac{u}{u_*} \right) \leq -\frac{\chi^2}{4D_u} u_* \int_\Omega |\nabla v|^2 - \frac{d_1}{A} \int_\Omega (u - u_*)^2 - \beta \int_\Omega \frac{uw}{1 + au + bw} + \beta u_* \int_\Omega w
\]
for all \(t > 0\).

Proof. Since \(u\) is positive in \(\bar{\Omega} \times (0, \infty)\) by the maximum principle and the assumption that \(h > 0\), we may test the first equation in (2.9) by \(1 - u_* \ln \frac{u}{u_*}\) to obtain using integration by parts that
\[
\frac{d}{dt} \int_\Omega \left( u - u_* - u_* \ln \frac{u}{u_*} \right) = -D_u u_* \int_\Omega |\nabla u|^2 + \chi u_* \int_\Omega \frac{\nabla u}{u} \cdot \nabla v - d_1 \int_\Omega \frac{(u - u_*)^2}{u}
\]
\[-\beta \int_\Omega (u - u_*) \cdot \frac{w}{1 + au + bw}
\]
for all \(t > 0\). As by Young’s inequality along with (4.27) we can estimate
\[
|\chi u_* \int_\Omega \frac{\nabla u}{u} \cdot \nabla v| \leq D_u u_* \int_\Omega |\nabla u|^2 + \frac{\chi^2}{4D_u} u_* \int_\Omega |\nabla v|^2 \quad \text{for all } t > 0
\]
and
\[
-\beta \int_\Omega (u - u_*) \cdot \frac{w}{1 + au + bw} = -\beta \int_\Omega \frac{uw}{1 + au + bw} + \beta u_* \int_\Omega \frac{w}{1 + au + bw}
\]
\[\leq -\beta \int_\Omega \frac{uw}{1 + au + bw} + \beta u_* \int_\Omega w \quad \text{for all } t > 0
\]
as well as
\[
-d_1 \int_\Omega \frac{(u - u_*)^2}{u} \leq -\frac{d_1}{A} \int_\Omega (u - u_*)^2 \quad \text{for all } t > 0,
\]
this implies (4.28).
The following basic observations are readily checked.

**Lemma 4.2.** The solution of (2.9) satisfies

\[ \frac{d}{dt} \int_{\Omega} v = \beta \int_{\Omega} \frac{uw}{1 + au + bw} - d_2 \int_{\Omega} v \quad \text{for all } t > 0 \]  

and

\[ \frac{d}{dt} \int_{\Omega} w = k \int_{\Omega} v - d_3 \int_{\Omega} w \quad \text{for all } t > 0 \]  

and

\[ \frac{1}{2} \frac{d}{dt} \int_{\Omega} v^2 \leq -D_v \int_{\Omega} |\nabla v|^2 + \beta \int_{\Omega} \frac{uw}{1 + au + bw} - d_2 \int_{\Omega} v^2 \quad \text{for all } t > 0 \]  

as well as

\[ \frac{1}{2} \frac{d}{dt} \int_{\Omega} w^2 \leq k \int_{\Omega} v - d_3 \int_{\Omega} w^2 \quad \text{for all } t > 0. \]

**Proof.** From an integration of the second and the third equations in (2.9) we immediately obtain (4.29) and (4.30). We multiply the second equation in (2.9) by \( v \) to see using integration by parts that

\[ \frac{1}{2} \frac{d}{dt} \int_{\Omega} v^2 \leq -D_v \int_{\Omega} |\nabla v|^2 + \beta \int_{\Omega} \frac{uw}{1 + au + bw} - d_2 \int_{\Omega} v^2 \quad \text{for all } t > 0. \]

Since we can estimate

\[ \beta \int_{\Omega} \frac{uw}{1 + au + bw} \leq \beta \int_{\Omega} \frac{au}{1 + au + bw} \leq \beta \int_{\Omega} vw \quad \text{for all } t > 0, \]

this entails (4.31). Finally, (4.32) can be proven in quite a similar manner. □

With the above preparations we now can design an appropriate Lyapunov functional with desired properties.

**Lemma 4.3.** Let \( R_0 \leq 1 \), assume that (2.11) hold, and let

\[ F(t) := \int_{\Omega} \left(u - u_* - \frac{u}{u_*} \ln \frac{u}{u_*}\right) + \int_{\Omega} v + \xi \int_{\Omega} w + \chi^2 \frac{D_u D_v}{8D_u D_v} u_* \int_{\Omega} v^2 + \chi^2 \frac{D_u D_v}{8D_u D_v} u_* \frac{\beta}{ak} \int_{\Omega} w^2, t > 0 \]  

with some \( \gamma \in \left[ \frac{\beta u_*}{d_3}, \frac{d_2}{k} \right] \) and

\[ E(t) := \int_{\Omega} (u - u_*)^2 + \int_{\Omega} v^2 + \int_{\Omega} w^2, \quad t > 0. \]

Then we have

\[ F'(t) \leq -\delta E(t) \quad \text{for all } t > 0 \]  

with some \( \delta > 0 \).

**Proof.** In view of the assumption that \( R_0 \leq 1 \) we can fix \( \gamma > 0 \) satisfying

\[ \frac{\beta u_*}{d_3} \leq \gamma \leq \frac{d_2}{k} \]

and according to the hypothesis (2.11) we can also fix \( \varepsilon > 0 \) sufficiently small such that

\[ \frac{ad_2}{\beta} > \frac{1}{\frac{d_2}{k} - \varepsilon}. \]
We then collect the inequalities and the identities established in Lemma 4.1 and Lemma 4.2 to see that

\[
\mathcal{F}'(t) \leq \frac{\chi^2}{4D_u} u_* \int_{\Omega} |\nabla v|^2 - \frac{d_1}{A} \int_{\Omega} (u - u_*)^2 - \beta \int_{\Omega} \frac{uw}{1 + au + bw} + \beta u_* \int_{\Omega} w \\
+ \left\{ \beta \int_{\Omega} \frac{uw}{1 + au + bw} - d_2 \int_{\Omega} v \right\} \\
+ \gamma \cdot \left\{ k \int_{\Omega} v - d_3 \int_{\Omega} w \right\} \\
+ \frac{\chi^2}{4D_uD_v} u_* \cdot \left\{ -D_v \int_{\Omega} |\nabla v|^2 + \frac{\beta}{a} \int_{\Omega} vw - d_2 \int_{\Omega} v^2 \right\} \\
+ \frac{\chi^2}{4D_uD_v} u_* \cdot \frac{\beta}{a k} \cdot \left\{ k \int_{\Omega} vw - d_3 \int_{\Omega} w^2 \right\} \\
= -\frac{d_1}{A} \int_{\Omega} (u - u_*)^2 - (d_2 - \gamma k) \int_{\Omega} v - (\gamma d_3 - \beta u_*) \int_{\Omega} w \\
+ \frac{\chi^2}{4D_uD_v} u_* \cdot \frac{\beta}{a} \cdot \left\{ 2 \int_{\Omega} vw - \frac{ad_2}{\beta} \int_{\Omega} v^2 - \frac{d_3}{k} \int_{\Omega} w^2 \right\} \\
\leq -\frac{d_1}{A} \int_{\Omega} (u - u_*)^2 + \frac{\chi^2}{4D_uD_v} u_* \cdot \frac{\beta}{a} \cdot \left\{ 2 \int_{\Omega} vw - \frac{ad_2}{\beta} \int_{\Omega} v^2 - \frac{d_3}{k} \int_{\Omega} w^2 \right\}
\]

for all \( t > 0 \),

thanks to \( d_2 - \gamma k \geq 0 \) and \( \gamma d_3 - \beta u_* \geq 0 \) by (4.36). Here by Young’s inequality we can estimate

\[
\frac{\chi^2}{4D_uD_v} u_* \cdot \frac{\beta}{a} \cdot \left\{ 2 \int_{\Omega} vw - \frac{ad_2}{\beta} \int_{\Omega} v^2 - \frac{d_3}{k} \int_{\Omega} w^2 \right\} \\
\leq \frac{\chi^2}{4D_uD_v} u_* \cdot \frac{\beta}{a} \cdot \left\{ \left( \frac{d_3}{k} - \varepsilon \right) \int_{\Omega} w^2 + \frac{1}{\frac{ak}{\beta} - \varepsilon} \int_{\Omega} v^2 - \frac{ad_2}{\beta} \int_{\Omega} v^2 - \frac{d_3}{k} \int_{\Omega} w^2 \right\} \\
= \frac{\chi^2}{4D_uD_v} u_* \cdot \frac{\beta}{a} \cdot \left\{ - \left( \frac{ad_2}{\beta} - \frac{1}{\frac{ak}{\beta} - \varepsilon} \right) \int_{\Omega} v^2 - \varepsilon \int_{\Omega} w^2 \right\} \quad \text{for all } t > 0,
\]

this yields (4.35) with

\[
\delta := \min \left\{ \frac{d_1}{A}, \frac{\chi^2}{4D_uD_v} u_* \cdot \frac{\beta}{a} \cdot \left( \frac{ad_2}{\beta} - \frac{1}{\frac{ak}{\beta} - \varepsilon} \right), \frac{\chi^2}{4D_uD_v} u_* \cdot \frac{\beta}{a} \cdot \varepsilon \right\} > 0
\]

thanks to (4.37).

Relying on the dissipative property (4.35) of the functional \( \mathcal{F}(t) \), we can build the exponential stability of the solution.

**Lemma 4.4.** Suppose that \( R_0 \leq 1 \) and the assumptions (2.7) and (2.11) are valid. Then we have

\[
\|u(\cdot, t) - u_*\|_{L^\infty(\Omega)} + \|v(\cdot, t)\|_{L^\infty(\Omega)} + \|w(\cdot, t)\|_{L^\infty(\Omega)} \to 0 \quad \text{as } t \to \infty. \quad (4.38)
\]

**Proof.** Since \((u, v, w)\) is a global and bounded smooth solution of (2.9), the Hölder regularity estimates for bounded solutions of semilinear parabolic equations (see [29, Theorem 1.3], for instance) yield some \( \theta \in (0, 1) \) and \( c > 0 \) such that

\[
\|u\|_{C^{0, \frac{\theta}{2}}(\Omega \times [t, t+1])} \leq c \quad \text{for all } t > 1. \quad (4.39)
\]
On the other hand, from (4.35) we infer that
\[
\int_1^\infty \int_\Omega (u - u^\ast)^2 < \infty, \quad \int_1^\infty \int_\Omega v^2 < \infty \quad \text{and} \quad \int_1^\infty \int_\Omega w^2 < \infty.
\]
Using this weak convergence information along with the uniform continuity of \(u\) in \(\Omega \times (1, \infty)\) implied by (4.39) and reasoning by a contradiction argument (cf. [31], for instance), we obtain
\[
\|u(\cdot, t) - u^\ast\|_{L^\infty(\Omega)} \to 0 \quad \text{as} \quad t \to \infty,
\]
whereas the statement on the convergence of \(v\) and \(w\) can be proven in a quite similar manner.

We are now in a position to complete the proof of Theorem 2.2.

**Proof of Theorem 2.2.** The assertions immediately result from Lemma 4.4.

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