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OCCURRENCE VS. ABSENCE OF TAXIS-DRIVEN INSTABILITIES IN A MAY-NOWAK MODEL FOR VIRUS INFECTION

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Abstract. This work focuses on an extension to the May-Nowak model for virus dynamics, additionally accounting for diffusion in all components and chemotactically directed motion of healthy cells in response to density gradients in the population of infected cells. The first part of the paper presents a number of simulations with the aim of investigating how far the model can depict interesting patterns. A rigorous analysis of the initial-boundary value problem is presented in a second part, where a statement on global classical solvability for arbitrarily large initial data is derived under an appropriate smallness assumption on the chemotactic coefficient. Two additional results on asymptotic stabilisation indicate that the so-called basic reproduction number retains its crucial influence on the large time behaviour of solutions, as is well-known from results on the May-Nowak system.

Key words. virus infection, chemotaxis, pattern formation, global existence, asymptotics.

AMS subject classifications. 35B40, 35K57, 35Q92, 92C17.

1. Introduction. We present a study of a chemotaxis-based model for virus dynamics. This first section describes the model and the aims of the work. More precisely, we consider three interacting components $u = u(x,t)$, $v = v(x,t)$ and $w = w(x,t)$, respectively corresponding to the densities of healthy uninfected immune cells, infected immune cells and virus particles at position x and time t.

First, let us consider a classic prototype ordinary differential equation model for virus dynamics, formulated within a general population dynamics framework. Specifically, we consider the May-Nowak model [3],

$$\begin{cases} u_t = -d_1 u - \beta u w + r, & t > 0, \\ v_t = -d_2 v + \beta u w, & t > 0, \\ w_t = -d_3 w + k v, & t > 0, \end{cases} \tag{1.1}$$

where the variables $u = u(t)$, $v = v(t)$ and $w = w(t)$ depend on time only. The underlying modelling assumptions are that: (i) healthy cells are constantly produced by the body at rate r, die at rate $d_1 u$ and become infected on contact with virus, at rate $\beta u w$; (ii) infected cells are subsequently produced at rate $\beta u w$ and die at rate $d_2 v$; (iii) new virus particles are produced at rate kv and die at rate $d_3 w$.

This model has been quite comprehensively understood via a thorough qualitative analysis of corresponding initial value problems (for instance cf. [3], [16], [17]). A key quantity is the so named *basic reproduction number*

$$R_0 := \frac{\beta k r}{d_1 d_2 d_3}$$

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see [12], dictating the two essential forms of asymptotic behaviour related to the model. Beyond an always existing infection-free equilibrium $Q_0 := (\frac{r}{d_1}, 0, 0)$, for $R_0 > 1$ the system possesses an additional coexistence equilibrium reflecting virus persistence, namely the triple $Q^* := (u^*, v^*, w^*)$ with positive components

$$u^* := \frac{r}{d_1}\frac{1}{R_0}, \qquad v^* := \frac{d_1 d_3}{\beta k}(R_0 - 1) \qquad \text{and} \qquad w^* := \frac{d_1}{\beta}(R_0 - 1).$$

R_0 determines the role of these equilibria for the dynamics in (1.1), in that if $R_0 > 1$ then the coexistence state $Q^\star$ is globally asymptotically stable in the octant of solutions positive in all their components, whereas if $R_0 \le 1$ then the infection-free equilibrium Q_0 enjoys this property.

While the model has justifiably endured, it undoubtedly simplifies the underlying dynamics of viral infections; in particular, it disregards spatial effects by tacitly assuming virus dynamics to be essentially homogeneous in space. In practice, each of the above variables typically undergoes spatial movement, either undirected (random) or directed, and such considerations have stimulated further modelling developments ([11],[15],[22]). Chemotaxis has been hypothesised as a key immune cell guidance mechanism for more than a century, and the last few decades have shed significant light on the chemokines that guide cells to the sites of inflammation [13]. Chemotaxis can be incorporated into models via the celebrated Keller-Segel system ([10]): this framework has a well known capacity to facilitate spatial pattern formation and, appropriately modified, has been applied to explain aggregation phenomena in numerous systems ([18]), including immune dynamics. Significant analytical interest was sparked by the demonstration of spontaneous aggregate formation in the extreme sense of finite-time blow-up for some solutions to classical Keller-Segel systems and proliferation-driven relatives thereof ([7], [24]).

As a first step towards a comprehensive understanding of the dynamical interaction between the kinetics from (1.1) on the one hand and diffusive/chemotactic movement contributions on the other, we follow the modelling approach of [22] by assuming simple but reasonable structures for the migration mechanisms. In particular, we subsequently focus on the partially normalized cross-diffusive variant of (1.1) contained in the following parabolic initial-boundary value problem:

$$\begin{cases} u_t = D_u \Delta u - \chi \nabla \cdot (u \nabla v) - u - uw + r(x,t), & x \in \Omega,\ t > 0, \\ v_t = D_v \Delta v - v + uw, & x \in \Omega,\ t > 0, \\ w_t = D_w \Delta w - w + v, & x \in \Omega,\ t > 0, \\ \frac{\partial u}{\partial \nu} = \frac{\partial v}{\partial \nu} = \frac{\partial w}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0, \\ u(x,0) = u_0(x), \quad v(x,0) = v_0(x), \quad w(x,0) = w_0(x), & x \in \Omega, \end{cases} \tag{1.2}$$

where D_u, D_v and D_w denote the respective diffusion coefficients, henceforth considered fixed and positive, and where χ represents strength and direction of the cross-diffusive interaction. Noteworthy is that an explicit equation for a chemical chemokine is excluded, with the density distribution of infected cells providing a proxy for its distribution; such simplifications are commonly employed in Keller-Segel based models for immune dynamics, e.g. see ([18]). Here we note that, in comparison to (1.1), the parameters β, k, d_1, d_2 and d_3 have all been set to 1, which can partially be achieved by suitable rescaling ([20]), but is mainly motivated by the goal of keeping the presentation as simple as possible; indeed, all results obtained below remain qualitatively unchanged if these five parameters are allowed to attain more general positive values.

The three diffusion rates D_u, D_v and D_w are kept arbitrary in order to stress that our analysis places no requirement for any special relationship between any of these, as might be necessary for, e.g. Turing-type instabilities.

As for the reproduction function and the initial data in (1.2), we shall assume that

$$r \in C^1(\overline{\Omega} \times [0,\infty)) \cap L^\infty(\Omega \times (0,\infty)) \qquad \text{is nonnegative,} \tag{1.3}$$

and that with some $q > n$,

$$\begin{cases} u_0 \in C^0(\overline{\Omega}), & u_0 \geq 0 \text{ in } \Omega, \\ v_0 \in W^{1,q}(\Omega), & v_0 \geq 0 \text{ in } \Omega, \\ w_0 \in C^0(\overline{\Omega}), & w_0 \geq 0 \text{ in } \Omega. \end{cases} \tag{1.4}$$

Addressing this specific framework, Section 2 presents a suite of simulations, aiming for a heuristic understanding of the possible patterns when the model is applied to real flow conditions. The output motivates a rigorous analysis, to be performed in Section 3, in which firstly global existence is proved for arbitrary initial data but small chemotactic sensitivity and, secondly, two results on qualitative behaviour are derived which rigorously confirm that the basic reproduction number retains a crucial influence on the large time asymptotics of solutions.

2. Numerical studies. We obtain an overview of the potential dynamical properties of equations (1.2) through simulations for a variety of (r, χ) combinations and initial conditions. Note that here we restrict to constant r and two dimensions, specifically: (i) a square domain of side length $2l$, $\Omega_S = [-l, l] \times [-l, l]$; or (ii) a circular region of radius l, $\Omega_C = \{\mathbf{x} : |\mathbf{x}| < l\}$.

Virus-free and, for $r > 1$, coexistence steady states exist at $(r, 0, 0)$ and $(1, r-1, r-1)$ respectively. In the absence of spatial terms, the virus-free state becomes unstable for $r > 1$ and the coexistence one is stable. Under the addition of spatial terms, a standard Turing-type linear analysis (e.g. [22]) can be performed. Briefly, for $r > 1$ and χ sufficiently large, the coexistence steady state is unstable to heterogeneous perturbations, implying a chemotactic-driven instability (CDI) that forms a precursor to spatial patterning. The delimitation of the (r, χ) parameter space according to these basic stability properties is shown in Figure 2.1 (a).

In our subsequent simulations we consider two general sets of initial conditions. Firstly, we consider (IC1) randomised perturbations of the steady states. Specifically, for $r > 1$ we set $(u_0(x), v_0(x), w_0(x)) = (1, (r-1)(1+\rho_1(x)), (r-1)(1+\rho_2(x)))$, where $\rho_{1,2}(x)$ are random variables uniformly distributed on $(-0.01, 0.01)$, while for $r <= 1$ we set $(u_0(x), v_0(x), w_0(x)) = (r, \rho_1(x), \rho_2(x))$, where $\rho_{1,2}(x)$ are uniformly distributed in $(0, 0.01)$. Secondly, we consider (IC2) localised introductions of virus/infected cells at the origin: $(u_0(x), v_0(x), w_0(x)) = (1, \alpha e^{-|x|^2}, \alpha e^{-|x|^2})$. The form (IC1) tests the linear stability criteria above. (IC2) represents a "biological" initial condition, in which virus/infected cells are introduced into a virus-free population in a spatially-localised manner. The parameter α offers a measure for the size of this perturbation.

2.1. Aggregation vs. collapse. Our first simulations test the linear stability properties. Representations are plotted in Figure 2.1 for parameter combinations expected to (i) give rise to CDI, and (ii) give rise to spatially uniform solutions. Numerical simulations confirm these properties. In the situation where CDI occurs, highly concentrated aggregates form and simulations ultimately "fail" (solutions non-computable to a desired tolerance, representing "numerical blow-up") beyond some critical time. In the following we use "finite-time blow-up" and "numerical blow-up" synonymously, although we note that a formal proof of the former is outside our present aims.

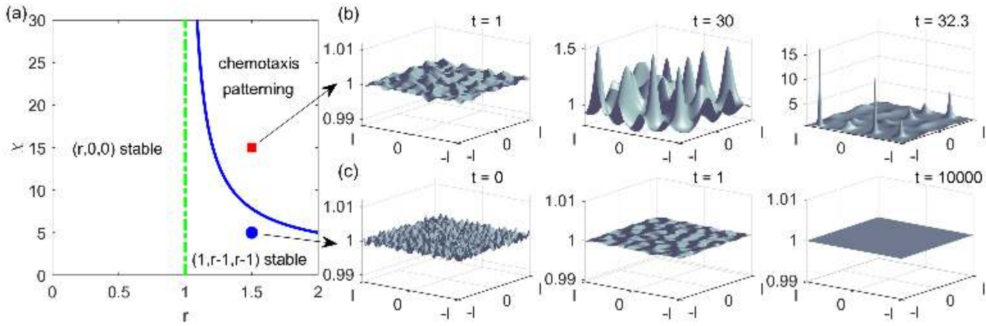

FIG. 2.1. *(a) Division of (r, χ) parameter space according to linear stability properties: (left of dashed green line) $(r, 0, 0)$ is linearly stable to homogeneous and inhomogeneous perturbations of the steady state; (below blue solid line/right of green line) $(1, r-1, r-1)$ is stable to homogeneous and inhomogeneous perturbations of the steady state; (above solid blue line) $(1, r-1, r-1)$ is driven unstable by inhomogeneous perturbations of the steady state (CDI). (b-c) u-solutions of (1.2) under (IC1) for the two parameter sets indicated in (a). Here we consider the square domain (Ω_S with $l = 10$). Vertical axis plots $u(x, t)$ as a function of x, with separate panels showing the solution at successive time points.*

2.2. Parameter space evaluation. The above simulations (and further investigations, not shown) suggest two general model outcomes: ***collapse***, where spatial inhomogeneities disappear and solutions converge to one of the two uniform steady state solutions (according to r); ***blow-up***, in which solutions diverge from the uniform solution, populations aggregate and concentrate before finite time blow-up.

We investigate this more formally by deriving a *critical chemotactic sensitivity* curve, $\chi^*(r)$, where the switch from collapse to blow-up is observed. To calculate $\chi^*(r)$, for each discrete value of $r \in (0, 2]$ we numerically solve with initial guess $\chi = \chi_0$ until either blow-up occurs or solutions have converged to a steady state distribution. Once evaluated, χ is either increased or decreased and we repeat until we determine $\chi^*(r) = (\chi_b(r) + \chi_s(r))/2$ such that $|(\chi_b(r) - \chi_g(r))/\chi_b(r)| < 0.001$.

In the above, $\chi_b(r)$ and $\chi_g(r)$ are respectively the lowest found value of χ for which blow-up occurs and the largest found value for which solutions converge to a steady state, for the given initial conditions and r value. Due to the cost of accurate 2D solutions, we restrict to (IC2) and a circular domain Ω_C, allowing us to exploit radial symmetry and reduce to a 1D radial line.

Figure 2.2(a) plots $\chi^*(r)$ using $\alpha = 0.01$ in (IC2), i.e. a smallish introduction of virus/infection into the healthy population. For comparison, we also include a plot of the critical χ required for CDI. First, our numerical results surprisingly suggest that blow-up occurs for $r < 1$, given sufficiently large χ. This is somewhat unexpected, given the general status of $r = 1$ as the arbitrator of whether an infection persists or dies out. Figure 2.2(a) shows the extension of the $\chi^*(r)$ curve into the range $r < 1$; for $r > 1$ it follows closely along that for CDI. Simulations that employ (χ, r) combinations where $r < 1$ and χ is taken just above the curve $\chi^*(r)$ show the accumulation of cells at the site of virus introduction and eventual blow-up, see Figure 2.2 (b) and Figure 2.2 (f,g) for time-evolution of the maximum density. Summarising, chemotaxis-induced aggregation allow for virus persistence, in the form of blow-up, even for $r < 1$. We remark that similar observations are observed for smaller α, albeit under larger χ as well as for (IC1).

Second, our numerical solutions indicate (for 2D geometries) a straight partitioning of parameter space into blow-up or collapse: no simulations yielded non-uniform aggregates that exist globally in time. To illustrate this, we consider solutions for select (r, χ) corresponding to points lying marginally above/below the critical $\chi^*(r)$ curve: specifically, for each $\chi^*(r)$ we consider the points $(r, \chi^*(r) \pm \epsilon)$, where ϵ is chosen to generate a point within 0.1% of the critical $\chi^*(r)$. Figures 2.2(b-e) plot solutions for $r = 0.75$ and $r = 1.25$: just above the χ^* curve, e.g. Figure 2.2 (b-c), concentrations form and blow-up occurs; just below the $\chi^*(r)$ curve, Figure 2.2 (d-e), aggregations eventually disperse and solutions converge to a uniform steady state. This dichotomy between blow-up and collapse is further highlighted in Figures 2.2(f-i), where the time evolution of the maximum density of u (i.e. $\max\{u(x,t) : x \in \Omega_C\}$) is plotted for simulations using parameter sets just above and below the curve $\chi^*(r)$.

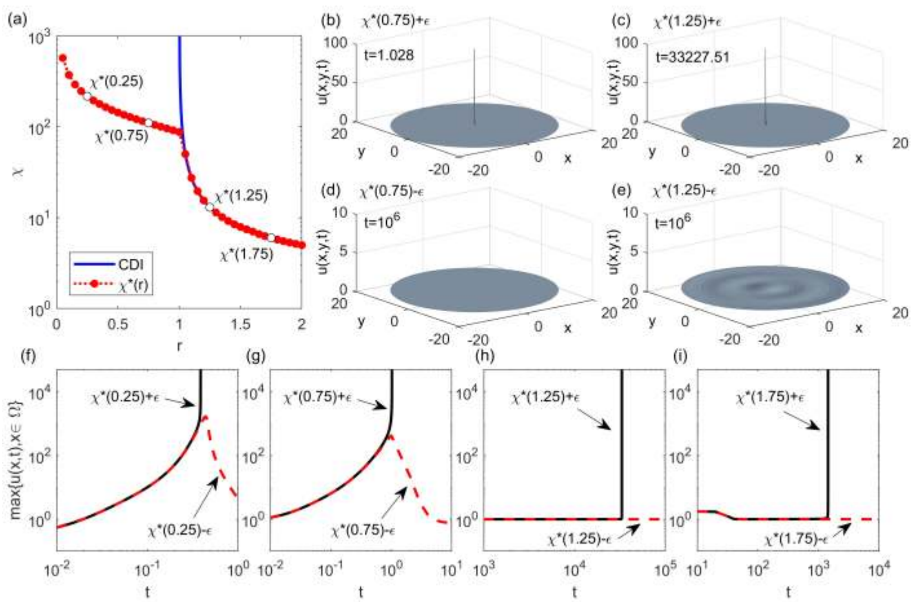

FIG. 2.2. *(a) Critical $\chi^*(r)$ for (IC2) with $\alpha = 0.01$. We also include the region where CDI is predicted for comparison. (b-e) Simulations showing the eventual distribution of $u(x,t)$ for distinct (r,χ): (b) $(0.75, \chi^*(0.75) + \epsilon)$; (c) $(1.25, \chi^*(1.25) + \epsilon)$; (d) $(0.75, \chi^*(0.75) - \epsilon)$; (e) $(1.25, \chi^*(1.25) - \epsilon)$. In each case we plot $u(x,t)$ either just before numerical blow-up occurs or at a time when the solution has converged to a homogeneous steady state. (f-i) Time evolution showing how the maximum density of $u(x,t)$ changes, for parameter combinations $(r,\chi) =$: (f) $(0.25, \chi^*(0.25) \pm \epsilon)$, (g) $(0.75, \chi^*(0.75) \pm \epsilon)$, (h) $(1.25, \chi^*(1.25) \pm \epsilon)$, (i) $(1.75, \chi^*(1.75) \pm \epsilon)$. For all simulations we solve equations (1.2) using Ω_C for $l = 20$ and (IC2) with $\alpha = 0.01$.*

2.3. Dependence on the initial data. Finally, we explore how the size of the initial data impacts on the critical chemotactic sensitivity. Specifically, we now determine $\chi^*(r, \alpha)$ for a range of α (recall that α represents the size of virus/disease introduction in (IC2)). Plots of $\chi^*(r, \alpha)$ are shown for $\alpha = 0.1, 1.0$ and 10.0 in Figure 2.3 (a). Increasing α lowers the critical chemotactic sensitivity necessary for aggregation/blow-up. However, for all (r, α) combinations we can find a strictly positive χ under which solutions exist globally in time and converge to the uniform steady state. To test this more robustly, we consider a fixed r (arbitrarily set at $r = 0.5$) and determine $\chi^*(r, \alpha)$ for a broad range of α (8 orders of magnitude), Figure 2.3 (b). For small α, χ^* is approximately inversely proportional to the size of α. For large α, however, the curve flattens. Even for very large α (e.g. $\alpha = 10^4$) we observe globally existing solutions (Figure 2.3 (c)), given sufficiently small χ.

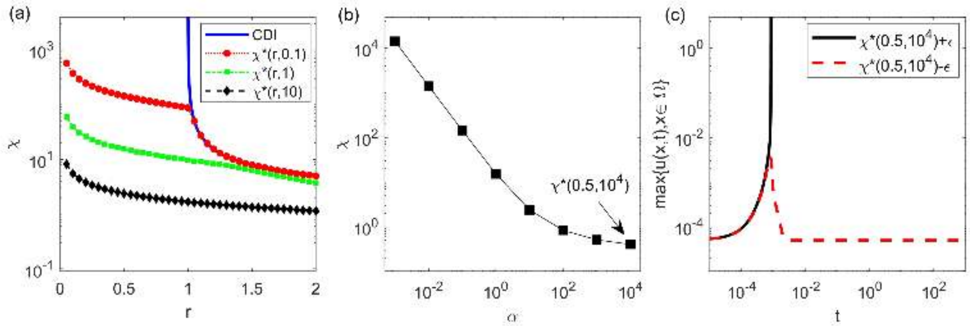

FIG. 2.3. *(a) Critical χ^* according to the size of the initial perturbation, where we plot $\chi^*(r, \alpha)$ for $\alpha = 0.1, 1, 10$. (b) Plot of $\chi^*(r, \alpha)$ as a function of α, using $r = 0.5$. (c). Time evolution of* $\max\{u(x,t) : x \in \Omega_C\}$ *for choices of χ that lie marginally above and below the point marked in (b). Other details as in Figure 2.2.*

3. Rigorous analysis. This section addresses the initial-boundary value problem presented in Section 1 by means of rigorous analysis, firstly focusing on basic questions related to global existence theory, and thereafter investigating aspects related to large time behaviour.

3.1. Main results. We underline that, in stark contrast to the classical Keller-Segel model with linear production of signal, the chemoattractant production rate in (1.2) is a product of u and w, hence growing in an essentially superlinear manner with respect to the unknown (u, v, w), of which seemingly no component enjoys any evident *a priori* bound with respect to the norm in $L^\infty(\Omega)$. At a naive level, compared to the Keller-Segel system, this may be suspected as increasing the destabilizing potential in the sense of enhancing the tendency towards blow-up of solutions; a rigorous verification thereof, however, goes far beyond the scope of the present work. In any event, it seems obvious that such nonlinear signal production mechanisms give rise to substantial further challenges for the development of any theory on global existence of solutions. In particular, it is most likely to be expected that results on unconditional global existence of classical solutions, involving chemotactic sensitivities χ and initial data of arbitrary size, are not available. In line with this, the few precedents concerned with existence theories for May-Nowak-chemotaxis systems in the analytical literature seem to exclusively address modified models that account for certain saturation effects acting to *a priori* reduce the potential strength of driving nonlinearities ([2], [9], [25], [5]).
In fact, for any choice of initial data compatible with (1.4), it is possible to identify a smallness condition on $|\chi|$ that ensures global existence of a classical solution, as contained in the first of our main results in this part:

THEOREM 3.1. *Let $n \geq 1$ and $\Omega \subset \mathbb{R}^n$ be a bounded domain with smooth boundary, let $D_u > 0, D_v > 0$ and $D_w > 0$, and suppose that r satisfies (1.3). Then for all*

u_0, v_0 and w_0 fulfilling (1.4) with some $q > n$, there exist $\chi_0 > 0$ and $L > 0$ with the property that whenever $\chi \in \mathbb{R}$ is such that

$$|\chi| \le \chi_0, \tag{3.1}$$

the problem (1.2) possesses a globally defined classical solution which is uniquely determined by the inclusions

$$\begin{cases} u \in C^0(\overline{\Omega} \times [0,\infty)) \cap C^{2,1}(\overline{\Omega} \times (0,\infty)), \\ v \in C^0([0,\infty); W^{1,q}(\Omega)) \cap C^{2,1}(\overline{\Omega} \times (0,\infty)), \\ w \in C^0(\overline{\Omega} \times [0,\infty)) \cap C^{2,1}(\overline{\Omega} \times (0,\infty)), \end{cases} \tag{3.2}$$

and which is such that $u \ge 0, v \ge 0$ and $w \ge 0$ in $\Omega \times (0,\infty)$ as well as

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} + \|v(\cdot,t)\|_{W^{1,q}(\Omega)} + \|w(\cdot,t)\|_{L^\infty(\Omega)} \le L \qquad \textit{for all } t > 0. \tag{3.3}$$

We emphasise that inter alia by being valid without restriction on the size of the initial data, Theorem 3.1 apparently goes somewhat beyond typical statements on global existence of small-data solutions in parabolic problems driven by nonlinearities that are of essentially superlinear nature not only at large, but also at small values of the unknown, and thus remain conveniently controllable along small trajectories. Indeed, unlike in typical examples for results of this form that address either chemotaxis systems ([4]) or more general semilinear parabolic problems ([21]), or also the Navier-Stokes system ([6]), the requirements of Theorem 3.1 are mild enough as to allow for arbitrary sizes for the nonlinearity uw in the second equation from (1.2), at least initially.

Next, addressing the large time behaviour of these solutions in situations of spatially and temporally constant rates of cell production, we note that in the particular context of (1.2) with $r \equiv const. = R$, the basic reproduction number precisely equals R. In fact, the following two statements indicate that this number retains its criticality with respect to the dynamical support of either the infection-free equilibrium $(R, 0, 0)$ or the coexistence state $(u^\star, v^\star, w^\star)$, in a certain weakened sense.

Firstly, if R is subcritical then for any given initial data and thereafter fixed and suitably small values of $|\chi|$, the infected cell and virus particle populations will both become extinct asymptotically, and the healthy cells become homogeneously distributed over the entire domain at a positive level:

THEOREM 3.2. *Suppose that $D_u > 0, D_v > 0$ and $D_w > 0$, that $r \equiv R$ with some $R > 0$ such that $R < 1$, and that (1.4) holds with some $q > n$. Then there exists $\chi_1 > 0$ such that if $\chi \in [-\chi_1, \chi_1]$, then (1.2) admits a unique nonnegative global classical solution (u, v, w) fulfilling (3.2) which satisfies*

$$u(\cdot,t) \to R, \;\; v(\cdot,t) \to 0 \;\; \textit{and} \;\; w(\cdot,t) \to 0 \;\; \textit{in } L^\infty(\Omega) \;\; \textit{as} \quad t \to \infty. \tag{3.4}$$

If, conversely, R exceeds the basic reproduction number then in quite the same flavour as above, under small values of $|\chi|$ solutions reflect spatially homogeneous coexistence:

THEOREM 3.3. *Assume that $D_u > 0, D_v > 0$ and $D_w > 0$, that $r \equiv R$ with some $R > 1$, and that with some $q > n$, u_0, v_0 and w_0 satisfy (1.4) and are such that either $v_0 \not\equiv 0$ or $w_0 \not\equiv 0$. Then there exists $\chi_2 > 0$ with the property that if $\chi \in [-\chi_2, \chi_2]$, then (1.2) possesses a unique nonnegative global classical solution (u, v, w) fulfilling (3.2) as well as*

$$u(\cdot,t) \to 1, \;\; v(\cdot,t) \to R-1 \;\; \textit{and} \;\; w(\cdot,t) \to R-1 \;\; \textit{in } L^\infty(\Omega) \;\; \textit{as} \;\; t \to \infty. \tag{3.5}$$

Summarising, our results rigorously confirm that for small choices of $|\chi|$ but arbitrarily large initial data, the nonlinearities do not substantially destabilize the system (1.2), and that for possibly yet smaller $|\chi|$ the solution behaviour does not even essentially differ from that in (1.1) at least on large time scales.

3.2. Proofs: Global existence.

3.2.1. Local existence and L^1 bounds. To begin, let us formulate the following basic statement on local existence and extensibility of solutions. A proof can be achieved by means of a standard contraction mapping argument, as presented e.g. in [8] in a closely related setting, so that we may omit details here.

LEMMA 3.4. *Suppose that (1.3) and (1.4) hold with some $q > n$, and let D_u, D_v and D_w be positive and $\chi \in \mathbb{R}$. Then there exist $T_{max} \in (0, \infty]$ and a uniquely determined triple of nonnegative functions*

$$\begin{cases} u \in C^0(\overline{\Omega} \times [0, T_{max})) \cap C^{2,1}(\overline{\Omega} \times (0, T_{max})), \\ v \in C^0([0, T_{max}); W^{1,q}(\Omega)) \cap C^{2,1}(\overline{\Omega} \times (0, T_{max})) \qquad \textit{and} \\ w \in C^0(\overline{\Omega} \times [0, T_{max})) \cap C^{2,1}(\overline{\Omega} \times (0, T_{max})), \end{cases}$$

such that (u, v, w) solves (1.2) classically in $\Omega \times (0, T_{max})$, and such that

$$\textit{if } T_{max} < \infty, \textit{ then } \quad \limsup_{t \nearrow T_{max}} \Big\{ \|u(\cdot, t)\|_{L^\infty(\Omega)} + \|v(\cdot, t)\|_{W^{1,q}(\Omega)} + \|w(\cdot, t)\|_{L^\infty(\Omega)} \Big\} = \infty. \tag{3.6}$$

The following L^1 bounds for these solutions are essentially immediate but of great importance.

LEMMA 3.5. *If (1.3) and (1.4) hold with some $q > n$, and if $D_u > 0$, $D_v > 0$, $D_w > 0$ and $\chi \in \mathbb{R}$, then*

$$\int_\Omega u(\cdot, t) + \int_\Omega v(\cdot, t) \le m_{uv} := \max\Big\{ \int_\Omega u_0 + \int_\Omega v_0 \,,\, |\Omega| \cdot \|r\|_{L^\infty(\Omega \times (0,\infty))} \Big\}, \tag{3.7}$$

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

$$\int_\Omega w(\cdot, t) \le m_w := \max\Big\{ \int_\Omega w_0 \,,\, m_{uv} \Big\} \qquad \textit{for all } t \in (0, T_{max}). \tag{3.8}$$

Proof. Adding the first two equations in (1.2), integrating over Ω and invoking an ODE comparison we readily obtain (3.7), whereupon (3.8) can be proved similarly. □

3.2.2. Preparing a loop of arguments. Let us now examine the extent to which supposedly present L^∞ bounds for u and w influence the regularity of all three components in (1.2), where a particular emphasis will be on the independence of χ of respectively obtained features.

Firstly, and already very importantly, combining the L^1 bound for v from Lemma 3.5 with a straightforward argument relying on well-known smoothing properties of the heat semigroup enables us to derive the following estimate for ∇v, which on its right-hand side depends on the assumed bound for w in a sublinear manner.

LEMMA 3.6. *Suppose that (1.3) and (1.4) hold with some $q > n$, and let $D_u > 0, D_v > 0$ and $D_w > 0$. Then there exists $K_1 > 0$ with the following property: If for* *some $\chi \in \mathbb{R}$, $M > 0$ and $N > 0$ there exists $T \in (0, T_{max})$ such that the solution of (1.2) satisfies for all $t \in (0,T)$ the following inequalities:*

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} \le M \quad \textit{for all} \quad t \in (0,T) \tag{3.9}$$

and

$$\|w(\cdot,t)\|_{L^\infty(\Omega)} \le N \quad \textit{for all} \quad t \in (0,T), \tag{3.10}$$

then

$$\|\nabla v(\cdot,t)\|_{L^q(\Omega)} \le K_1 \cdot (MN^\theta + 1) \quad \textit{for all } t \in (0,T), \quad \textit{with } \theta := \frac{q-1}{q} \in (0,1). \tag{3.11}$$

Proof. According to known smoothing properties of the Neumann heat semigroup $(e^{\sigma\Delta})_{\sigma \ge 0}$ ([23]), we can fix $c_1 > 0$ and $c_2 > 0$ such that for all $\sigma > 0$ we have $\|\nabla e^{\sigma D_v \Delta}\varphi\|_{L^q(\Omega)} \le c_1 \|\varphi\|_{W^{1,q}(\Omega)}$ for all $\varphi \in W^{1,q}(\Omega)$ and $\|\nabla e^{\sigma D_v \Delta}\varphi\|_{L^q(\Omega)} \le c_2(1+\sigma^{-\frac{1}{2}})\|\varphi\|_{L^q(\Omega)}$ for all $\varphi \in L^q(\Omega)$, and use this together with a variation-of-constants representation of v to estimate

$$\begin{aligned}
\|\nabla v(\cdot,t)\|_{L^q(\Omega)} &= \left\| \nabla e^{tD_v(\Delta-1)}v_0 + \int_0^t \nabla e^{(t-s)D_v(\Delta-1)}[u(\cdot,s)w(\cdot,s)]ds \right\|_{L^q(\Omega)} \\
&\le c_1 e^{-D_v t}\|v_0\|_{W^{1,q}(\Omega)} + c_2 \int_0^t \left(1 + (t-s)^{-\frac{1}{2}}\right) e^{-D_v(t-s)} \|u(\cdot,s)w(\cdot,s)\|_{L^q(\Omega)} ds
\end{aligned} \tag{3.12}$$

for all $t \in (0,T)$. Herein by the Hölder inequality,

$$\begin{aligned}
\|u(\cdot,s)w(\cdot,s)\|_{L^q(\Omega)} &\le \|u(\cdot,s)\|_{L^\infty(\Omega)}\|w(\cdot,s)\|_{L^q(\Omega)} \\
&\le \|u(\cdot,s)\|_{L^\infty(\Omega)}\|w(\cdot,s)\|_{L^\infty(\Omega)}^\theta \|w(\cdot,s)\|_{L^1(\Omega)}^{1-\theta} \quad \text{for all } s \in (0,T),
\end{aligned}$$

whence combining our hypotheses (3.9) and (3.10) with (3.8) shows that

$$\|u(\cdot,s)w(\cdot,s)\|_{L^q(\Omega)} \le MN^\theta m_w^{1-\theta} \qquad \text{for all } s \in (0,T).$$

Therefore, (3.12) implies that

$$\begin{aligned}
\|\nabla v(\cdot,t)\|_{L^q(\Omega)} &\le c_1 e^{-D_v t}\|v_0\|_{W^{1,q}(\Omega)} + c_2 m_w^{1-\theta} MN^\theta \int_0^t \left(1 + (t-s)^{-\frac{1}{2}}\right) e^{-D_v(t-s)} ds \\
&\le c_1 \|v_0\|_{W^{1,q}(\Omega)} + c_2 c_3 m_w^{1-\theta} MN^\theta \qquad \text{for all } t \in (0,T)
\end{aligned}$$

with $c_3 := \int_0^\infty (1+\sigma^{-\frac{1}{2}})e^{-D_v\sigma}d\sigma$, so that (3.11) follows if we let

$$K_1 := \max\{c_1\|v_0\|_{W^{1,q}(\Omega)}, c_2 c_3 m_w^{1-\theta}\},$$

for instance. □

Again with thanks to parabolic smoothing, the above estimate can be quite directly transformed into a corresponding pointwise upper inequality for w.

LEMMA 3.7. *Assume that (1.3) and (1.4) are satisfied with some $q > n$, and let $D_u > 0, D_v > 0$ and $D_w > 0$. Then one can find $K_2 > 0$ such that if $\chi \in \mathbb{R}, M > 0$*

and $N > 0$ are such that (3.9) and (3.10) hold for the solution of (1.2) with some $T \in (0, T_{max})$, then

$$\|w(\cdot,t)\|_{L^\infty(\Omega)} \le K_2 \cdot (MN^\theta + 1) \qquad \textit{for all } t \in (0,T), \tag{3.13}$$

where $\theta \in (0,1)$ is as in Lemma 3.6.

Proof. As our assumption $q > n$ warrants that $W^{1,q}(\Omega) \hookrightarrow L^\infty(\Omega)$, we can find $c_1 > 0$ such that

$$\|\varphi\|_{L^\infty(\Omega)} \le c_1 \|\nabla\varphi\|_{l^q(\Omega)} + c_1 \|\varphi\|_{L^1(\Omega)} \qquad \text{for all } \varphi \in W^{1,q}(\Omega),$$

and that thus Lemma 3.6 in conjunction with (3.7) warrants that

$$\|v(\cdot,t)\|_{L^\infty(\Omega)} \le c_1 K_1 \cdot (MN^\theta + 1) + c_1 m_{uv} \qquad \text{for all } t \in (0,T). \tag{3.14}$$

Now since $\overline{w}(x,t) := \max\Big\{ \|w_0\|_{L^\infty(\Omega)},\, c_1 K_1 \cdot (MN^\theta + 1) + c_1 m_{uv} \Big\}$, $\quad (x,t) \in \overline{\Omega} \times [0,T)$, satisfies $\overline{w}(x,0) \ge \|w_0\|_{L^\infty(\Omega)} \ge w(x,0)$ for all $x \in \Omega$ as well as

$$\overline{w}_t - D_w \Delta \overline{w} + \overline{w} - v = \overline{w} - v \ge c_1 K_1 \cdot (MN^\theta + 1) + c_1 m_{uv} - v \ge 0$$
$$\text{for all } x \in \Omega \text{ and } t \in (0,T)$$

by (3.14), from a comparison principle we directly conclude that $w \le \overline{w}$ in $\Omega \times (0,T)$, which readily entails (3.13) with $K_2 := \max\{\|w_0\|_{L^\infty(\Omega)}, c_1 m_{uv}, c_1 K_1\}$. $\square$

Finally, arguing in a similar manner we can establish a corresponding L^∞ bound for u which now in its essential part contains $|\chi|$ as a factor.

LEMMA 3.8. *If (1.3) and (1.4) hold with some $q > n$, and if $D_u > 0, D_v > 0$ and $D_w > 0$, then there exists $K_3 > 0$ with the property that whenever $\chi \in \mathbb{R}, M > 0$ and $N \ge 1$ are such that the solution of (1.2) satisfies (3.9) and (3.10) for some $T \in (0, T_{max})$, we have*

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} \le K_3 \cdot \Big\{ (M^2 N^\theta + 1)|\chi| + 1 \Big\} \qquad \textit{for all } t \in (0,T) \tag{3.15}$$

with $\theta \in (0,1)$ taken from Lemma 3.6.

Proof. Once more relying on a well known regularization feature of the Neumann heat semigroup ([23]), we fix $c_1 > 0$ with the property that whenever $\varphi \in C^1(\overline{\Omega})$ is such that $\varphi \cdot \nu = 0$ we have

$$\|e^{\sigma D_u \Delta} \nabla \cdot \varphi\|_{L^\infty(\Omega)} \le c_1 (1 + \sigma^{-\frac{1}{2} - \frac{n}{2q}}) \|\varphi\|_{L^q(\Omega)} \qquad \text{for all } \sigma > 0.$$

Three times using that moreover $e^{-\sigma D_u \Delta} \varphi \le \max_{x \in \overline{\Omega}} \varphi(x)$ in Ω for all $\sigma > 0$ and each $\varphi \in C^0(\overline{\Omega})$ due to the maximum principle, by means of a Duhamel formula associated with the first equation in (1.2) we see that

$$
\begin{aligned}
u(\cdot,t) &= e^{tD_u(\Delta-1)}u_0 - \chi\int_0^t e^{(t-s)D_u(\Delta-1)}\nabla\cdot\Big(u(\cdot,s)\nabla v(\cdot,s)\Big)ds \\
&\qquad - \int_0^t e^{(t-s)D_u(\Delta-1)}[u(\cdot,s)w(\cdot,s)]ds + \int_0^t e^{(t-s)D_u(\Delta-1)}r(\cdot,s)ds \\
&\le e^{-D_ut}\|u_0\|_{L^\infty(\Omega)} + |\chi|\int_0^t e^{-D_u(t-s)}\Big\|e^{(t-s)D_u\Delta}\nabla\cdot\Big(u(\cdot,s)\nabla v(\cdot,s)\Big)\Big\|_{L^\infty(\Omega)}ds \\
&\qquad + \int_0^t e^{-D_u(t-s)}\|r(\cdot,s)\|_{L^\infty(\Omega)}ds \\
&\le e^{-D_ut}\|u_0\|_{L^\infty(\Omega)} + c_1|\chi|\int_0^t\Big(1+(t-s)^{-\frac12-\frac{n}{2q}}\Big)e^{-D_u(t-s)}\Big\|u(\cdot,s)\nabla v(\cdot,s)\Big\|_{L^q(\Omega)}ds \\
&\qquad + \|r\|_{L^\infty(\Omega\times(0,\infty))}\int_0^t e^{-D_u(t-s)}ds \quad \text{in } \Omega \quad \text{for all } t\in(0,T).
\end{aligned}
\tag{3.16}
$$

Here, thanks to (3.9) and (3.11),

$$
\begin{aligned}
\Big\|u(\cdot,s)\nabla v(\cdot,s)\Big\|_{L^q(\Omega)} &\le \|u(\cdot,s)\|_{L^\infty(\Omega)}\|\nabla v(\cdot,s)\|_{L^q(\Omega)} \\
&\le M\cdot K_1(MN^\theta+1) \le 2K_1M^2N^\theta + \frac{K_1}{4} \quad \text{for all } s\in(0,T),
\end{aligned}
$$

because $M \le M^2 + \frac14 \le M^2N^\theta + \frac14$ due to Young's inequality and our assumption that $N \ge 1$. In consequence, (3.16) thus shows that

$$
\|u(\cdot,t)\|_{L^\infty(\Omega)} \le e^{-D_ut}\|u_0\|_{L^\infty(\Omega)} + c_1c_2|\chi|\cdot\Big(2K_1M^2N^\theta + \frac{K_1}{4}\Big) + \frac{1}{D_u}\|r\|_{L^\infty(\Omega\times(0,\infty))}
$$

for all $t\in(0,T)$, with $c_2 := \int_0^\infty(1+\sigma^{-\frac12-\frac{n}{2q}})e^{-D_u\sigma}d\sigma$ being finite according to the hypothesis that $q>n$. Abbreviating $K_3 := \max\{\|u_0\|_{L^\infty(\Omega)} + \frac{1}{D_u}\|r\|_{L^\infty(\Omega\times(0,\infty))}, 2c_1c_2K_1\}$, we thereby readily arrive at (3.15). □

3.2.3. Closing the loop. Proof of Theorem 3.1. Now, using the fact that the constant θ in (3.13) is smaller than 1 and that the right-hand side can be conveniently controlled as long as $|\chi|$ is small, by first choosing the numbers M and N suitably large and then $\chi_0>0$ appropriately small, we close the above circle of arguments and thereby establish our main result on global solvability in (1.2).

PROOF of Theorem 3.1. With $K_2>0, K_3>0$ and $\theta\in(0,1)$ taken from Lemma 3.7, Lemma 3.8 and Lemma 3.6, respectively, we first choose $M>0$ such that

$$
M > \|u_0\|_{L^\infty(\Omega)} \quad \text{and} \tag{3.17}
$$

$$
M \ge 4K_3. \tag{3.18}
$$

We thereafter fix $N\ge1$ large enough satisfying

$$
N > \|w_0\|_{L^\infty(\Omega)}, \tag{3.19}
$$

$$
N \ge (4K_2M)^{\frac{1}{1-\theta}} \quad \text{and} \tag{3.20}
$$

$$N \geq 4K_2, \tag{3.21}$$

and finally let

$$\chi_0 := \frac{M}{4K_3 \cdot (M^2 N^\theta + 1)}. \tag{3.22}$$

Then given $\chi \in [-\chi_0, \chi_0]$, we let (u, v, w) denote the corresponding maximally extended solution of (1.2) in $\Omega \times (0, T_{max})$, $T_{max} \in (0, \infty]$, and define

$$S := \left\{ T_0 \in (0, T_{max}) \,\middle|\, \|u(\cdot,t)\|_{L^\infty(\Omega)} \leq M \text{ and } \|w(\cdot,t)\|_{L^\infty(\Omega)} \leq N \text{ for all} t \in (0, T_0) \right\}.$$

Here we note that by continuity of u and w, (3.17) and (3.19) ensure that indeed S is not empty and thus $T := \sup S$ a well-defined element of $(0, \infty]$.

Moreover, an application of Lemma 3.8 shows that thanks to (3.22) and (3.18),

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} \leq K_3 \cdot (M^2 N^\theta + 1)|\chi| + K_3 \leq \frac{M}{4} + \frac{M}{4} = \frac{M}{2} \quad \text{for all } t \in (0, T),$$

whereas combining (3.20) with (3.21), from Lemma 3.7 we obtain that

$$\|w(\cdot,t)\|_{L^\infty(\Omega)} \leq K_2 \cdot M N^\theta + K_2 \leq K_2 \cdot \frac{N^{1-\theta}}{4K_2} \cdot N^\theta + \frac{N}{4} = \frac{N}{2} \quad \text{for all } t \in (0, T).$$

Again by continuity of u and w, it is therefore clear that actually $T = T_{max}$ and that hence, in particular,

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} \leq M \quad \text{and} \quad \|w(\cdot,t)\|_{L^\infty(\Omega)} \leq N \qquad \text{for all } t \in (0, T_{max}). \tag{3.23}$$

As a consequence thereof, Lemma 3.6 implies that

$$\|\nabla v(\cdot,t)\|_{L^q(\Omega)} \leq K_1 \cdot (M N^\theta + 1) \qquad \text{for all } t \in (0, T_{max}), \tag{3.24}$$

so that in view of (3.7) and Lemma 3.4 we conclude that we must have $T_{max} = \infty$, and that thus (3.3) results from (3.23) and (3.24) with some appropriately large $L > 0$. $\square$

3.3. Proofs: Stabilization.

3.3.1. Some general observations. Next, in order to verify Theorem 3.2 and Theorem 3.3 we shall from now on assume that

$$r \equiv R = const. \quad \text{in } \Omega \times (0, \infty),$$

and prepare our detection of suitable gradient structures inherent to (1.2), to be substantiated in Lemma 3.13 and Lemma 3.14 below, by some quite straightforward observations. The first of these actually merely recall what has been used in the derivation of Lemma 3.5 already.

LEMMA 3.9. *Suppose that $D_u > 0, D_v > 0, D_w > 0, \chi \in \mathbb{R}$ and $r \equiv R > 0$, and that $(u, v, w) \in (C^{2,1}(\overline{\Omega} \times (0, \infty)))^3$ is a global classical solution of the boundary value problem in (1.2). Then*

$$\frac{d}{dt} \int_\Omega u = -\int_\Omega u - \int_\Omega uw + R|\Omega| \qquad \textit{and} \tag{3.25}$$

$$\frac{d}{dt}\int_\Omega v = -\int_\Omega v + \int_\Omega uw \qquad \textit{as well as} \tag{3.26}$$

$$\frac{d}{dt}\int_\Omega w = -\int_\Omega w + \int_\Omega v \tag{3.27}$$

for all $t > 0$.

Proof. All three identities can immediately be obtained upon integrating the respective equation from (1.2) over Ω. □

Furthermore, the evolution of corresponding logarithmic integrals can be described by the following inequalities.

LEMMA 3.10. *Let* $D_u > 0, D_v > 0, D_w > 0, \chi \in \mathbb{R}$ *and* $r \equiv R > 0$, *and let* $(u, v, w) \in (C^{2,1}(\overline{\Omega} \times (0, \infty)))^3$ *be a nonnegative global classical solution of the boundary value problem in (1.2). i) If* $u > 0$ *in* $\overline{\Omega} \times (0, \infty)$, *then*

$$\frac{d}{dt}\int_\Omega \ln u \ge -\frac{\chi^2}{4D_u}\int_\Omega |\nabla v|^2 - |\Omega| - \int_\Omega w + R\int_\Omega \frac{1}{u} \qquad \textit{for all } t > 0. \tag{3.28}$$

ii) If v *is positive and bounded in* $\overline{\Omega} \times (0, \infty)$, *then*

$$\frac{d}{dt}\int_\Omega \ln v \ge \frac{D_v}{\|v\|^2_{L^\infty(\Omega\times(0,\infty))}}\int_\Omega |\nabla v|^2 - |\Omega| + \int_\Omega \frac{uw}{v} \qquad \textit{for all } t > 0. \tag{3.29}$$

iii) Under the assumption that $w > 0$ *in* $\overline{\Omega} \times (0, \infty)$, *we have*

$$\frac{d}{dt}\int_\Omega \ln w \ge -|\Omega| + \int_\Omega \frac{v}{w} \qquad \textit{for all } t > 0. \tag{3.30}$$

Proof. i) By positivity of u, we may test the first equation in (1.2) by $\frac{1}{u}$ to obtain

$$\frac{d}{dt}\int_\Omega \ln u = D_u\int_\Omega \frac{|\nabla u|^2}{u^2} - \chi\int_\Omega \frac{1}{u}\nabla u\cdot\nabla v - |\Omega| - \int_\Omega w + R\int_\Omega \frac{1}{u} \qquad \text{for all } t > 0.$$

Since

$$-\chi\int_\Omega \frac{1}{u}\nabla u\cdot\nabla v \le D_u\int_\Omega \frac{|\nabla u|^2}{u^2} + \frac{\chi^2}{4D_u}\int_\Omega |\nabla v|^2 \qquad \text{for all } t > 0$$

by Young's inequality, this entails (3.28).

ii) Likewise, using the second equation in (1.2) we compute

$$\frac{d}{dt}\int_\Omega \ln v = D_v\int_\Omega \frac{|\nabla v|^2}{v^2} - |\Omega| + \int_\Omega \frac{uw}{v} \qquad \text{for all } t > 0$$

and estimate

$$D_v\int_\Omega \frac{|\nabla v|^2}{v^2} \ge \frac{D_v}{\|v\|^2_{L^\infty(\Omega\times(0,\infty))}}\int_\Omega |\nabla v|^2 \qquad \text{for all } t > 0$$

to achieve (3.29).

iii) Finally, from the third equation we similarly derive the identity

$$\frac{d}{dt}\int_\Omega \ln w = D_w \int_\Omega \frac{|\nabla w|^2}{w^2} - |\Omega| + \int_\Omega \frac{v}{w} \qquad \text{for all } t>0,$$

which directly implies (3.30). □

Finally, the last contribution to the energy functional used in Lemma 3.13 has the following property.

LEMMA 3.11. *Assume that $D_u>0, D_v>0, D_w>0, \chi\in\mathbb{R}$ and $r\equiv R>0$, and that $(u,v,w)\in (C^{2,1}(\overline{\Omega}\times(0,\infty)))^3$ is a nonnegative global classical solution of the boundary value problem in (1.2) for which v is bounded. Then*

$$\frac{1}{2}\frac{d}{dt}\int_\Omega v^2 \le -D_v\int_\Omega |\nabla v|^2 + \|v\|_{L^\infty(\Omega\times(0,\infty))}\cdot \int_\Omega uw \qquad \textit{for all } t>0. \tag{3.31}$$

Proof. In view of the nonnegativity of both u and w, this readily results on testing the second equation in (1.2) by v. □

Now, as an independent further ingredient for our convergence arguments in both cases $R<1$ and $R>1$, let us recall standard parabolic regularity theory to obtain the following temporally uniform higher order bounds, valid in fact for arbitrary global bounded solutions.

LEMMA 3.12. *Let $D_u>0, D_v>0$ and $D_w>0$, and suppose that $r\equiv R>0$ and that $(u,v,w)\in (C^{2,1}(\overline{\Omega}\times(0,\infty)))^3$ is a global bounded classical solution of the boundary value problem in (1.2) for some $\chi\in\mathbb{R}$. Then there exist $\theta\in(0,1)$ and $C>0$ such that for all $t>1$ one has*

$$\|u\|_{C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[t,t+1])} + \|v\|_{C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[t,t+1])} + \|w\|_{C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[t,t+1])} \le C. \tag{3.32}$$

Proof. Using that (u,v,w) is bounded, applying parabolic gradient Hölder regularity theory ([14]) to the second and the third equation in (1.2) we obtain $\theta_1\in(0,1)$ and $c_1>0$ such that

$$\|v\|_{C^{1+\theta_1,\frac{1+\theta_1}{2}}(\overline{\Omega}\times[t,t+1])} + \|w\|_{C^{1+\theta_1,\frac{1+\theta_1}{2}}(\overline{\Omega}\times[t,t+1])} \le c_1 \quad \text{for all } t>1.$$

Thereafter, we may invoke parabolic Hölder estimates ([19]) to conclude on the basis of the first equation in (1.2) that there exist $\theta_2\in(0,1)$ and $c_2>0$ fulfilling $\|u\|_{C^{\theta_2,\frac{\theta_2}{2}}(\overline{\Omega}\times[t,t+1])} \le c_2$ for all $t>1$. According to standard parabolic Schauder estimates ([14]), when applied to the second and third equations from (1.2) this firstly entails that with some $\theta_3\in(0,1)$ and $c_3>0$ we have

$$\|v\|_{C^{2+\theta_3,1+\frac{\theta_3}{2}}(\overline{\Omega}\times[t,t+1])} + \|w\|_{C^{2+\theta_3,1+\frac{\theta_3}{2}}(\overline{\Omega}\times[t,t+1])} \le c_3 \qquad \text{for all } t>1,$$

and that, as a consequence thereof and of the first equation in (1.2), we can find $\theta_4\in(0,1)$ and $c_4>0$ such that finally also $\|u\|_{C^{2+\theta_4,1+\frac{\theta_4}{2}}(\overline{\Omega}\times[t,t+1])} \le c_4$ for all $t>1$, as claimed. □

3.3.2. The case $R<1$. Proof of Theorem 3.2. Now in the case $R<1$, by suitable combination of Lemma 3.9, Lemma 3.11 and Lemma 3.10 it is possible to construct a genuine Lyapunov functional for (1.2) whenever $|\chi|$ and v are appropriately small.

LEMMA 3.13. *Assume that $D_u>0, D_v>0, D_w>0$ and $r\equiv R$ with $R\in(0,1)$, and let $L_v>0$. Then there exist $\chi_1^\star=\chi_1^\star(R,L_v)>0$, $a>0, b>0, d>0$ and $\delta>0$ with the property that if for some $\chi\in[-\chi_1^\star,\chi_1^\star]$ we are given a nonnegative global bounded classical solution $(u,v,w)\in(C^{2,1}(\overline{\Omega}\times(0,\infty)))^3$ of the boundary value problem in (1.2) such that u is positive in $\overline{\Omega}\times(0,\infty)$ and that*

$$\|v(\cdot,t)\|_{L^\infty(\Omega)}\le L_v \quad \textit{for all } t>0, \tag{3.33}$$

then

$$\mathcal{F}_1(t):=\int_\Omega\Big\{u(\cdot,t)-R-R\ln\frac{u(\cdot,t)}{R}\Big\}+a\int_\Omega v(\cdot,t)+b\int_\Omega w(\cdot,t)+\frac{d}{2}\int_\Omega v^2(\cdot,t), \qquad t>0, \tag{3.34}$$

satisfies

$$\frac{d}{dt}\mathcal{F}_1(t)\le-\int_\Omega\frac{(u(\cdot,t)-R)^2}{u(\cdot,t)}-\delta\int_\Omega v(\cdot,t)-\delta\int_\Omega w(\cdot,t) \quad \textit{for all } t>0. \tag{3.35}$$

Proof. Using that $R<1$, we can fix $a\in(0,1)$ such that $a>R$ and thereafter choose $b\in(R,a)$. Then

$$d:=\frac{1-a}{L_v} \tag{3.36}$$

and hence also

$$\chi_1^\star:=\sqrt{\frac{4D_uD_vd}{R}} \tag{3.37}$$

are positive, and to verify the claimed conclusion upon these selections, we assume that $\chi\in\mathbb{R}$ is such that $|\chi|\le\chi_1^\star$, and that (u,v,w) is a nonnegative global bounded classical solution of the boundary value problem in (1.2) such that $u>0$ in $\overline{\Omega}\times(0,\infty)$. Then, due to the latter positivity assumption, we may combine Lemma 3.9 and Lemma 3.11 with Lemma 3.10 to see that, thanks to (3.33),

$$\begin{aligned}\frac{d}{dt}\mathcal{F}_1(t)\le&-\int_\Omega u-\int_\Omega uw+R|\Omega|+\frac{R\chi^2}{4D_u}\int_\Omega|\nabla v|^2+R|\Omega|+R\int_\Omega w-R^2\int_\Omega\frac{1}{u}\\&-a\int_\Omega v+a\int_\Omega uw-b\int_\Omega w+b\int_\Omega v-dD_v\int_\Omega|\nabla v|^2+dL_v\int_\Omega uw\\=&\Big(\frac{R\chi^2}{4D_u}-dD_v\Big)\int_\Omega|\nabla v|^2-\int_\Omega u+2R|\Omega|-R^2\int_\Omega\frac{1}{u}\\&+(b-a)\int_\Omega v+(R-b)\int_\Omega w+(dL_v+a-1)\int_\Omega uw \quad \text{for all } t>0.\end{aligned}\tag{3.38}$$

Here from (3.37) we know that $\frac{R\chi^2}{4D_u}-dD_v\le0$, and (3.36) warrants that $dL_v+a-1=0$, whereas our choices of a and b ensure that $b-a<0$ and $R-b<0$. As furthermore

$$-\int_\Omega u+2R|\Omega|-R^2\int_\Omega\frac{1}{u}=-\int_\Omega\frac{(u-R)^2}{u} \qquad \text{for all } t>0,$$

from (3.38) we readily obtain (3.35) if we let $\delta := \min\{a-b, b-R\}$, for instance. □

Now, since a bound of the form (3.33) has been asserted by Theorem 3.1 for all χ with a fixed interval around the origin, the above lemma together with the regularity properties in Lemma 3.12 readily entail convergence in the claimed flavour whenever $|\chi|$ is small enough:

PROOF of Theorem 3.2. According to Theorem 3.1, there exist $\chi_0 > 0$ and $c_1 > 0$ such that for any choice of $\chi \in [-\chi_0, \chi_0]$, the problem (1.2) possesses a unique global classical solution (u,v,w) such that (3.2) holds, and such that moreover

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} \le c_1 \qquad \text{for all } t>0 \tag{3.39}$$

as well as

$$\|v(\cdot,t)\|_{L^\infty(\Omega)} \le c_1 \qquad \text{for all } t>0. \tag{3.40}$$

Now, writing $\chi_1 := \min\{\chi_0\,,\,\chi_1^\star\}$ with $\chi_1^\star = \chi_1^\star(R,c_1) > 0$ as given by Lemma 3.13, we henceforth assume that $\chi \in [-\chi_1, \chi_1]$ and note that the inequality $\chi_1 \le \chi_0$ warrants that the above statements on existence and boundedness hold. Moreover, due to the nonnegativity of $u(\cdot,\tau)$ in Ω and the positivity of R, from the strong maximum principle applied to the first equation in (1.2) it follows that $u>0$ in $\overline{\Omega}\times(\tau,\infty)$ for arbitrary $\tau>0$. As thus u indeed is positive throughout $\overline{\Omega}\times(0,\infty)$, relying on the restriction $\chi_1 \le \chi_1^\star$ we may apply Lemma 3.13 to see that with $\mathcal{F}_1$ taken from (3.34) and some $c_2>0$ we have

$$\frac{d}{dt}\mathcal{F}_1(t) + \int_\Omega \frac{(u-R)^2}{u} + c_2\int_\Omega v + c_2\int_\Omega w \le 0 \qquad \text{for all } t>0. \tag{3.41}$$

Since clearly $\mathcal{F}_1$ is nonnegative due to the fact that $\xi - R - R\ln\frac{\xi}{R} \ge 0$ for all $\xi>0$, and since $\mathcal{F}_1(1)$ is finite by positivity of $u(\cdot,1)$ in $\overline{\Omega}$, integrating (3.41) shows that

$$\int_1^\infty\int_\Omega \frac{(u-R)^2}{u} + c_2\int_1^\infty\int_\Omega v + c_2\int_1^\infty\int_\Omega w < \infty,$$

which due to (3.39) implies that

$$\int_1^\infty\int_\Omega (u-R)^2 < \infty, \quad \int_1^\infty\int_\Omega v < \infty \quad \text{and} \quad \int_1^\infty\int_\Omega w < \infty. \tag{3.42}$$

As $u-R, v$ and w are all uniformly continuous in $\Omega\times(1,\infty)$ due to Lemma 3.12, by means of an elementary argument it follows from (3.42) that indeed all three statements in (3.4) must hold. □

3.3.3. The case $R>1$. Proof of Theorem 3.3. In the case $R>1$, in view of the expected nontrivial behaviour in the second and third solution components, our construction of a Lyapunov functional is slightly more involved; yet, appropriately absorbing ill-signed contributions by dissipation-induced quantities becomes possible when $|\chi|$ and v are sufficiently small:

LEMMA 3.14. *Assume that $D_u>0, D_v>0$ and $D_w>0$ and that $r\equiv R>1$, and let $L_v>0$. Then there exists $\chi_2^\star = \chi_2^\star(R,L_v)>0$ such that whenever $\chi\in[-\chi_2^\star,\chi_2^\star]$ and $(u,v,w)\in(C^{2,1}(\overline{\Omega}\times(0,\infty)))^3$ is a global classical solution of the boundary value problem in (1.2) such that u,v and w are positive in $\overline{\Omega}\times(0,\infty)$ with*

$$\|v(\cdot,t)\|_{L^\infty(\Omega)} \le L_v \qquad \textit{for all } t>0, \tag{3.43}$$

for

$$\mathcal{F}_2(t) := \int_\Omega \Big\{u(\cdot,t) - 1 - \ln u(\cdot,t)\Big\} + \int_\Omega \Big\{v(\cdot,t) - (R-1) - (R-1)\ln\frac{v(\cdot,t)}{R-1}\Big\} + \int_\Omega \Big\{w(\cdot,t) - (R-1) - (R-1)\ln\frac{w(\cdot,t)}{R-1}\Big\}, \quad t>0, \tag{3.44}$$

we have

$$\frac{d}{dt}\mathcal{F}_2(t) \le -\int_\Omega \frac{(u-1)^2}{u} - \frac{(R-1)D_v}{2L_v^2}\int_\Omega |\nabla v|^2 \qquad \textit{for all } t>0. \tag{3.45}$$

Proof. Given $R>1$ and $L_v>0$, we let

$$\chi_2^\star := \sqrt{\frac{2(R-1)D_uD_v}{L_v^2}} \tag{3.46}$$

and suppose that $\chi\in\mathbb{R}$ such that $|\chi|\le\chi_2^\star$, and that $(u,v,w)\in(C^{2,1}(\overline{\Omega}\times(0,\infty)))^3$ is a global classical solution of the boundary value problem in (1.2) fulfilling $u>0, v>0$ and $w>0$ in $\overline{\Omega}\times(0,\infty)$ as well as (3.43). Then, besides Lemma 3.9, we may invoke Lemma 3.10 to see that

$$\begin{aligned}
\frac{d}{dt}\mathcal{F}_2(t) \le & -\int_\Omega u - \int_\Omega uw + R|\Omega| + \frac{\chi^2}{4D_u}\int_\Omega |\nabla v|^2 + |\Omega| + \int_\Omega w - R\int_\Omega \frac{1}{u}\\
& -\int_\Omega v + \int_\Omega uw - \frac{(R-1)D_v}{L_v^2}\int_\Omega |\nabla v|^2 + (R-1)|\Omega| - (R-1)\int_\Omega \frac{uw}{v}\\
& -\int_\Omega w + \int_\Omega v + (R-1)|\Omega| - (R-1)\int_\Omega \frac{v}{w}\\
= & \Big(\frac{\chi^2}{4D_u} - \frac{(R-1)D_v}{L_v^2}\Big)\int_\Omega |\nabla v|^2 - \int_\Omega u + (3R-1)|\Omega| - R\int_\Omega \frac{1}{u}\\
& -(R-1)\int_\Omega \frac{uw}{v} - (R-1)\int_\Omega \frac{v}{w} \quad \text{for all } t>0,
\end{aligned} \tag{3.47}$$

where according to (3.46) we have $\frac{\chi^2}{4D_u} - \frac{(R-1)D_v}{L_v^2} \le -\frac{(R-1)D_v}{2L_v^2}$. Rewriting

$$-\int_\Omega u = -\int_\Omega \frac{(u-1)^2}{u} - 2|\Omega| + \int_\Omega \frac{1}{u} \qquad \text{for } t>0,$$

from (3.47) we thus obtain that for all $t>0$,

$$\begin{aligned}
\frac{d}{dt}\mathcal{F}_2(t) \le & -\int_\Omega \frac{(u-1)^2}{u} - \frac{(R-1)D_v}{2L_v^2}\int_\Omega |\nabla v|^2\\
& +(3R-3)|\Omega| - (R-1)\int_\Omega \frac{1}{u} - (R-1)\int_\Omega \frac{uw}{v} - (R-1)\int_\Omega \frac{v}{w}\\
= & -\int_\Omega \frac{(u-1)^2}{u} - \frac{(R-1)D_v}{2L_v^2}\int_\Omega |\nabla v|^2 + (R-1)\int_\Omega \Big\{3 - \frac{1}{u} - \frac{uw}{v} - \frac{v}{w}\Big\}.
\end{aligned} \tag{3.48}$$

Now since the arithmetic mean-geometric mean inequality warrants that herein

$$\frac{1}{u} + \frac{uw}{v} + \frac{v}{w} \ge 3\sqrt[3]{\frac{1}{u}\cdot\frac{uw}{v}\cdot\frac{v}{w}} = 3 \qquad \text{in } \Omega\times(0,\infty),$$

the estimate (3.45) is a consequence of (3.48). □

By a reasoning in similar spirit to that followed in the proof of Theorem 3.2, enriched by an additional argument needed to deal with some lacking direct implication of finiteness of the total dissipation on convergence in the second and third component, we finally arrive at our main result on qualitative behaviour in the case $R > 1$.

Proof of Theorem 3.3. Again relying on Theorem 3.1, we can fix $\chi_0 > 0$ and $c_1 > 0$ such that whenever $\chi \in [-\chi_0, \chi_0]$, (1.2) is uniquely solvable by a triple (u, v, w) of bounded functions satisfying (3.2) as well as

$$\|v(\cdot, t)\|_{L^\infty(\Omega)} \le c_2 \qquad \text{for all } t > 0. \tag{3.49}$$

We thereupon take $\chi_2^\star = \chi_2^\star(R, c_2) > 0$ as provided by Lemma 3.14, and our goal is to verify that the claimed conclusion holds if we let $\chi_2 := \min\{\chi_0\,,\,\chi_2^\star\}$. To see this, given $\chi \in \mathbb{R}$ such that $|\chi| \le \chi_2$ we firstly use that $\chi \le \chi_0$ to make sure that, on the basis of the above, indeed a unique global bounded classical solution with the mentioned properties, in particular fulfilling (3.49), exists. Again through the positivity of R and nonnegativity of u, the strong maximum principle shows that in fact u is positive throughout $\overline{\Omega} \times (0, \infty)$. By the same token we know that in the case $v_0 \not\equiv 0$, in view of the second equation in (1.2) we furthermore have $v > 0$ in $\overline{\Omega} \times (0, \infty)$, and hence also $w > 0$ in $\overline{\Omega} \times (0, \infty)$ due to the third equation therein. Likewise, when $w_0 \not\equiv 0$ we firstly conclude from the strong maximum principle that $w > 0$ in $\overline{\Omega} \times (0, \infty)$, and thereafter infer that v also has this positivity property.

Having thereby asserted the hypotheses of Lemma 3.14, we may use our restriction $\chi_2 \le \chi_2^\star$ to obtain from the latter that there exists $c_2 > 0$ such that the function $\mathcal{F}_2$ introduced in (3.44) satisfies

$$\frac{d}{dt}\mathcal{F}_2(t) + \int_\Omega \frac{(u-1)^2}{u} + c_2 \int_\Omega |\nabla v|^2 \le 0 \qquad \text{for all } t > 0.$$

As $\mathcal{F}_2$ is nonnegative and $\mathcal{F}_2(1)$ is finite due to the above positivity features of u, v and w, this entails that

$$\int_1^\infty \int_\Omega \frac{(u-1)^2}{u} + c_2 \int_1^\infty \int_\Omega |\nabla v|^2 < \infty$$

and that hence

$$\int_1^\infty \int_\Omega (u-1)^2 < \infty \qquad \text{and} \qquad \int_1^\infty \int_\Omega |\nabla v|^2 < \infty,$$

because u is bounded. With thanks once more to Lemma 3.12, these properties imply that

$$u(\cdot, t) - 1 \to 0 \quad \text{in } L^\infty(\Omega) \qquad \text{and} \qquad \nabla v(\cdot, t) \to 0 \quad \text{in } L^\infty(\Omega) \tag{3.50}$$

as $t \to \infty$, for $u - 1$ and ∇v are uniformly continuous in $\Omega \times (1, \infty)$ by (3.32).

Now in order to draw further conclusions for the asymptotics of v and w from this, intending to take full advantage of Lemma 3.12 we employ the latter to fix $\theta \in (0, 1)$ and $c_3 > 0$ such that

$$\|u-1\|_{C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[t,t+1])} + \|w\|_{C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[t,t+1])} \le c_3 \qquad \text{for all } t > 1. \tag{3.51}$$

To deduce from this that

$$u_t(\cdot,t)\to 0 \quad \text{and} \quad \Delta u(\cdot,t)\to 0 \quad \text{in } L^\infty(\Omega) \qquad \text{as } t\to\infty, \tag{3.52}$$

given $\varepsilon>0$ we use that due to the Arzelà-Ascoli theorem the first within the two continuous embeddings in $C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[0,1]) \hookrightarrow C^{2,1}(\overline{\Omega}\times[0,1]) \hookrightarrow L^\infty(\Omega\times(0,1))$ is compact to infer from an associated Ehrling-type lemma that there exists $c_4>0$ such that for all $\varphi\in C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[0,1])$ one has

$$\|\varphi\|_{C^{2,1}(\overline{\Omega}\times[0,1])} \le \frac{\varepsilon}{2c_3}\|\varphi\|_{C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[0,1])} + c_4\|\varphi\|_{L^\infty(\Omega\times(0,1))}.$$

As (3.50) warrants the existence of $t_0>1$ such that for $U^{(t)}(x,s):=u(x,t+s)$, $(x,s)\in\overline{\Omega}\times[0,1]$, $t>1$, we have $\|U^{(t)}-1\|_{L^\infty(\Omega\times(0,1))}<\frac{\varepsilon}{2c_4}$ for all $t>t_0$, in view of (3.51) this implies that

$$\begin{aligned}\|U^{(t)}-1\|_{C^{2,1}(\overline{\Omega}\times[0,1])} &\le \frac{\varepsilon}{2c_3}\|U^{(t)}-1\|_{C^{2+\theta,1+\frac{\theta}{2}}(\overline{\Omega}\times[0,1])} + c_4\|U^{(t)}-1\|_{L^\infty(\Omega\times(0,1))}\\ &< \frac{\varepsilon}{2c_3}\cdot c_3 + c_4\cdot\frac{\varepsilon}{2c_4} = \varepsilon \qquad \text{for all } t>t_0.\end{aligned}$$

In particular, for for all $t>t_0$, one has

$$\|u_t(\cdot,t)\|_{L^\infty(\Omega)} = \|\partial_s(U^{(t)}-1)(\cdot,0)\|_{L^\infty(\Omega)} \le \|U^{(t)}-1\|_{C^{2,1}(\overline{\Omega}\times[0,1])} < \varepsilon$$

and, similarly, for all $t>t_0$, one has

$$\|\Delta u(\cdot,t)\|_{L^\infty(\Omega)} = \|\Delta(U^{(t)}-1)(\cdot,0)\|_{L^\infty(\Omega)} \le \|U^{(t)}-1\|_{C^{2,1}(\overline{\Omega}\times[0,1])} < \varepsilon.$$

Having thereby verified (3.52), we proceed to show that

$$w(\cdot,t)\to R-1 \quad \text{in } L^\infty(\Omega) \qquad \text{as } t\to\infty. \tag{3.53}$$

Indeed, if this was false, then according to the equicontinuity property of w contained in (3.51) and again the Arzelà-Ascoli theorem we could pick $(t_k)_{k\in\mathbb{N}}\subset(1,\infty)$ such that $t_k\to\infty$ as $k\to\infty$ and

$$w(\cdot,t_k)\to w_\infty \quad \text{in } L^\infty(\Omega) \qquad \text{as } k\to\infty \tag{3.54}$$

with some $w_\infty\in C^0(\overline{\Omega})$ satisfying $w_\infty\not\equiv R-1$. By continuity of w_∞, we could then easily find $\varphi\in C_0^\infty(\Omega)$ such that

$$\int_\Omega w_\infty\varphi \ne (R-1)\int_\Omega\varphi, \tag{3.55}$$

and testing the first equation in (1.2) against φ would show that

$$\begin{aligned}\int_\Omega u_t(\cdot,t_k)\varphi &= D_u\int_\Omega \Delta u(\cdot,t_k)\varphi + \chi\int_\Omega u(\cdot,t_k)\nabla v(\cdot,t_k)\cdot\nabla\varphi\\ &\quad -\int_\Omega u(\cdot,t_k)\varphi - \int_\Omega u(\cdot,t_k)w(\cdot,t_k)\varphi + R\int_\Omega\varphi \qquad \text{for all } k\in\mathbb{N}.\end{aligned}$$

Here using (3.52), (3.50) and (3.54) allows for taking $k\to\infty$ to conclude that

$$0 = -\int_\Omega\varphi - \int_\Omega w_\infty\varphi + R\int_\Omega\varphi,$$

which contradicts (3.55) and hence establishes (3.53).

Finally, in much the same manner as in (3.52) we can now derive from (3.51) that as a consequence of (3.53) we have $w_t(\cdot,t) \to 0$ and $\Delta w(\cdot,t) \to 0$ in $L^\infty(\Omega)$ as $t \to \infty$. Therefore, in view of the third equation in (1.2) we obtain that, again due to (3.54), we have $v(\cdot,t) = w_t(\cdot,t) - \Delta w(\cdot,t) + w(\cdot,t) \to R-1$ in $L^\infty(\Omega)$ as $t \to \infty$, whereby the proof of (3.5) is completed. □

4. Conclusions. We have investigated an extension of a classical model for virus infection that accounts for spatial dynamics and, in particular, the directed movement of healthy cells towards inflammation following viral infection. The critical role played by the "basic reproduction number" for classical ODE models retains an important role with respect to predicting asymptotic behaviour, dichotomising parameter space into regions where solutions evolve to virus-persisting or virus-free states under positive (but sufficiently small) chemotactic responses. Yet, simulations appear a divergence in behaviour under larger chemotactic responses, where the addition of chemotaxis can allow virus to persist even when $R_0 < 1$.

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