DIFFUSION-DRIVEN BLOWUP OF NONNEGATIVE SOLUTIONS TO REACTION-DIFFUSION-ODE SYSTEMS

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ABSTRACT. In this paper we provide an example of a class of two reaction-diffusion-ODE equations with homogeneous Neumann boundary conditions, in which Turing-type instability not only destabilizes constant steady states but also induces blow-up of nonnegative spatially heterogeneous solutions. Solutions of this problem preserve nonnegativity and uniform boundedness of the total mass. Moreover, for the corresponding system with two non-zero diffusion coefficients, all nonnegative solutions are global in time. We prove that a removal of diffusion in one of the equations leads to a finite-time blow-up of some nonnegative spatially heterogeneous solutions.

Keywords: reaction-diffusion equations; Turing instability; blow-up of solutions.

1. Introduction

One of the major issues in study of reaction-diffusion equations describing pattern formation in biological or chemical systems is understanding of the mechanisms of pattern selection, i.e., of generation of stable patterns. Classical models of the pattern formation are based on diffusion-driven instability (DDI) of constant stationary solutions, which leads to emergence of stable patterns around this state. Such close-to-equilibrium patterns are regular and spatially periodic stationary solutions and their shape depend on a scaling coefficient related to the ratio between diffusion parameters. They are called Turing patterns after the seminal paper of Alan Turing [32].

Interestingly, a variety of possible patterns increases when some diffusion coefficient vanish, i.e., considering reaction-diffusion equations coupled to ordinary differential equations (ODEs). Such models arise, for example, when studying a coupling of diffusive processes with processes which are localized in space, such as growth processes [16, 17, 18, 24] or intracellular signaling [8, 11, 13, 33]. Their dynamics appear to be very different from that of classical reaction-diffusion models.

To understand the role of non-diffusive components in a pattern formation process, we focus on systems involving a single reaction-diffusion equation coupled to an ODE. It is an interesting case, since a scalar reaction-diffusion equation (in a bounded, convex domain and the Neumann boundary conditions) cannot exhibit stable spatially heterogeneous patterns [1]. Coupling it to an ODE fulfilling an autocatalysis condition at the equilibrium leads to DDI. However, in such a case, all regular Turing patterns are unstable, because
the same mechanism which destabilizes constant solutions, destabilizes also all continuous spatially heterogeneous stationary solutions, [15, 14]. This instability result holds also for discontinuous patterns in case of a specific class of nonlinearities, see also [15, 14]. Simulations of different models of this type indicate a formation of dynamical, multimodal, and apparently irregular and unbounded structures, the shape of which depends strongly on initial conditions [7, 17, 18, 24].

In this work, we attempt to make a next step towards understanding properties of solutions of reaction-diffusion-ODE systems. We focus on a specific example exhibiting diffusion-driven instability. We consider the following system of equations

\begin{align}
    u_t &= d \Delta u - au + u^p f(v), \quad \text{for } x \in \Omega, \ t > 0, \\
    v_t &= D \Delta v - bv - u^p f(v) + \kappa \quad \text{for } x \in \Omega, \ t > 0,
\end{align}

in a bounded domain $\Omega \subset \mathbb{R}^n$ with a sufficiently regular boundary $\partial \Omega$. In equations (1.1)-(1.2), an arbitrary function $f = f(v)$ satisfies

$$\tag{1.3} f \in C^1([0, \infty)), \quad f(v) > 0 \quad \text{for } v > 0, \quad \text{and } f(0) = 0.$$  

Moreover, we fix the constant parameters in (1.1)-(1.2) such that

$$\tag{1.4} d \geq 0, \quad D > 0, \quad p > 1, \quad a, b \in (0, \infty), \quad \kappa \in [0, \infty).$$

We supplement system (1.1)-(1.2) with the homogeneous Neumann boundary conditions

$$\tag{1.5} \frac{\partial u}{\partial n} = 0 \quad \text{(if } d > 0) \quad \text{and} \quad \frac{\partial v}{\partial n} = 0 \quad \text{for } x \in \partial \Omega, \ t > 0,$$

and with bounded, nonnegative, and continuous initial data

$$\tag{1.6} u(x, 0) = u_0(x), \quad v(x, 0) = v_0(x) \quad \text{for } x \in \Omega.$$  

As already mentioned above, if the diffusion in equation (1.1) is equal to zero, all regular stationary solutions to such reaction-diffusion-ODE problems are unstable, see [14] for the results in the case of more general equations. In this work, we show that dynamics of solutions to the initial-boundary value problem (1.1)-(1.6) may change drastically when $d > 0$ in equation (1.1) is replaced by $d = 0$. More precisely, the following scenario is valid.

- For non-degenerate diffusion coefficients $d > 0$ and $D > 0$, all nonnegative solutions to problem (1.1)-(1.6) are global-in-time. This result has been proved by other authors and, for the reader convenience, we discuss it in Section 2, see Remark 2.4.
- If $d = 0$ and $D > 0$ (i.e., we consider an ordinary differential equations coupled with a reaction-diffusion equation), there are solutions to problem (1.1)-(1.6) which blow-up in a finite time and at one point only. This is the main result of this work, proved in Theorem 3.1, below.

Let us emphasize some consequences of these results.
Remark 1.1 (Diffusion-induced blow-up of nonnegative solutions). Nonnegative solutions to the following initial value problem for the system of ordinary differential equations:

\begin{align}
\frac{d}{dt} \bar{u} &= -a \bar{u} + \bar{u}^p f(\bar{v}), \\
\frac{d}{dt} \bar{v} &= -b \bar{v} - \bar{u}^p f(\bar{v}) + \kappa,
\end{align}

are global-in-time and bounded on \([0, \infty)\), see Remark 2.1 below. On the other hand, by Theorem 3.1 below, there are nonconstant initial conditions such that the corresponding solution to the reaction-diffusion-ODE problem (1.1)-(1.6) with \(d = 0\) and \(D > 0\) blows up at one point and in a finite time. This is a large class of examples, where the appearance of a diffusion in one equation leads to a blow-up of nonnegative solutions. First example of one reaction-diffusion equation coupled with one ODE, where some solutions blow up due to a diffusion, appeared in 1990 in the paper by Morgan [21]. Another reaction-diffusion-ODE system was given by Guedda and Kirane [5]. These examples are discussed in detail in the survey paper [2] as well as in the monograph [29, Ch. 33.2]. Here, let us also mention that a one point blow-up result, analogous to that one in Theorem 3.1 but for another reaction-diffusion-ODE system (with “activator-inhibitor” nonlinearities) has been recently obtained by us in [10].

Remark 1.2. It is much more difficult to provide a blow up of solutions in a system of reaction-diffusion equations with nonzero diffusion coefficients in both equations, rather than in only one (as in Remark 1.1), especially in the case of systems with a good “mass behavior” as discussed in Remark 2.3. First such an example was discovered by Mizoguchi et al. [20], where the term “diffusion-induced blow-up” was introduced. Another system of reaction-diffusion equations with such a property, supplemented with non-homogeneous Dirichlet conditions, was proposed by Pierre and Schmitt [26, 27]. We refer the reader to the survey paper [2] and to the monograph [29, Ch. 33.2] for more such examples and for additional comments.

At the end of this introduction, we would like to emphasize that the model (1.1)-(1.6) can be found in literature in context of several applications. Let us mention a few of them. For \(p = 2\), \(f(v) = v\), and suitably chosen coefficients, we obtain either the, so-called, Brussellator appearing in the modeling of chemical morphogenetic processes (see e.g. [32, 23]), the Gray-Scott model (also known as a model of glycolysis, see [3, 4]) or the Schnackenberg model (see [31] and [22, Ch. 3.4]). Recent mathematical results, as well as several other references on reaction-diffusion equations with such nonlinearities and with \(d > 0\) and \(D > 0\), may be found in, e.g., the monographs [22, 29, 30] and in the papers [25, 34, 35]. Let us close this introduction by a remark that we assume in this work that \(a > 0\) and \(b > 0\) for simplicity of the exposition, however, our blowup results can be easily modified to the case of arbitrary \(a \in \mathbb{R}\) and \(b \in \mathbb{R}\).
2. Global-in-time solutions for reaction-diffusion system

Results gathered in this section has been proved already by other authors and we recall them for the completeness of the exposition.

First, we recall that problem (1.1)-(1.6) supplemented with nonnegative initial data $u_0, v_0 \in L^\infty(\Omega)$ has a unique, nonnegative local-in-time solution $(u(x, t), v(x, t))$. Here, it suffices to rewrite it in the usual integral (Duhamel) form

\[
\begin{align*}
\frac{du}{dt} &= e^{t(d\Delta - aI)}u_0 + \int_0^t e^{(t-s)(d\Delta - aI)} \left( u^p f(v) \right) (s) \, ds, \\
\frac{dv}{dt} &= e^{t(D\Delta - bI)}v_0 - \int_0^t e^{(t-s)(D\Delta - bI)} \left( u^p f(v) \right) (s) \, ds + \int_0^t e^{(t-s)(D\Delta - bI)} \kappa \, ds,
\end{align*}
\]

where \( \left\{ e^{t(d\Delta - aI)} \right\}_{t \geq 0} \) is the semigroup of linear operators on \( L^q(\Omega) \) generated by \( d\Delta - aI \) with the Neumann boundary conditions. Since the nonlinearities in equations (1.1)-(1.2) are locally Lipschitz continuous, the existence of a local-in-time unique solution to (2.1)-(2.2) is a consequence of the Banach contraction principle, see e.g. either [30, Thm. 1, p. 111] or [9]. Such a solution is sufficiently regular for \( t \in (0, T_{\text{max}}) \), where \( T_{\text{max}} > 0 \) is the maximal time of its existence, and satisfies problem (1.1)-(1.6) in the classical sense. Moreover, this local-in-time solution \( (u(x, t), v(x, t)) \) is nonnegative, either by a maximum principle for parabolic equations if \( d > 0 \) or for reaction-diffusion-ODE systems if \( d = 0 \), see e.g. [15, Lemma 3.4] for similar considerations.

In the following, we review results on the existence of global-in-time nonnegative solutions to problem (1.1)-(1.6) with the both \( d > 0 \) and \( D > 0 \). We begin with the corresponding system of ODEs.

**Remark 2.1.** It is a routine reasoning to show that \( x \)-independent nonnegative solutions \( (\bar{u}, \bar{v}) \) of problem (1.1)-(1.6) are global-in-time and uniformly bounded. Indeed, such a solution \( u = \bar{u}(t) \) and \( v = \bar{v}(t) \) solves the Cauchy problem for the system of ODEs (1.7)-(1.8). From equations (1.7), we deduce the differential inequality

\[
\frac{d}{dt}(\bar{u} + \bar{v}) \leq - \min\{a, b\} (\bar{u} + \bar{v}) + \kappa
\]

which, after integration, implies that the sum \( \bar{u}(t) + \bar{v}(t) \) is bounded on the half-line \( [0, \infty) \). Hence, since both functions are nonnegative, we obtain \( \sup_{t \geq 0} \bar{u}(t) < \infty \) and \( \sup_{t \geq 0} \bar{v}(t) < \infty. \)

**Remark 2.2.** A behavior of solutions the system of ODEs from (1.7) depends essentially on its parameters and, in the particular case of \( p = 2 \) and \( f(v) = v \), it has been studied in several recent works, because it appears in applications (see the discussion at the end of Introduction). For \( a > 0 \) and \( b > 0 \), this particular system has the trivial stationary nonnegative solution \( (\bar{u}, \bar{v}) = (0, \kappa/b) \) which is an asymptotically stable solution. If, moreover, \( \kappa^2 > 4a^2b \), we have two other nontrivial nonnegative stationary solutions which
satisfy the following system of equations
\[ \ddot{u} = \frac{a}{\dot{v}} \quad \text{and} \quad -b\dot{v} - \frac{a^2}{\dot{v}} + \kappa = 0. \]

Every such a constant nontrivial and stable solution of ODEs is an unstable solution of the reaction-diffusion-ODE problem (1.1)-(1.5), which means that it has a DDI property due to the autocatalysis \( f_u(\bar{u}, \bar{v}) = -a + 2\bar{a}\bar{v} = a > 0 \). We have prove the latter property in the recent works [15] and [14], where such instability phenomena have been studied for a model of early carcinogenesis and for a general model of reaction-diffusion-ODEs, respectively.

**Remark 2.3 (Control of mass).** A completely analogous reasoning as that one in Remark 2.1 shows that total mass \( \int_\Omega (u(x, t) + v(x, t)) \, dx \) of each nonnegative solution to the reaction-diffusion problem (1.1)-(1.6) with \( d \geq 0 \) and \( D \geq 0 \) does not blow up, and stays uniformly bounded in \( t > 0 \). Indeed, it suffices to sum up equations (1.1)-(1.2), integrate over \( \Omega \), and use the boundary condition to obtain the following counterpart of inequality (2.3)
\[
\frac{d}{dt} \int_\Omega (u(x, t) + v(x, t)) \, dx = -\int_\Omega (au(x, t) + bv(x, t)) \, dx + \int_\Omega \kappa \, dx \\
\leq -\min\{a, b\} \int_\Omega (u(x, t) + v(x, t)) \, dx + \kappa|\Omega|.
\]

Thus, the functions \( u(\cdot, t) \) and \( v(\cdot, t) \) stay bounded in \( L^1(\Omega) \) uniformly in time. In the next section, we show that this a priori estimate is not sufficient to prevent the blow-up of solutions in a finite time in the case of \( d = 0 \) and \( D > 0 \) in problem (1.1)-(1.6).

**Remark 2.4 (Global-in-time solutions).** Let \( f \in C^1([0, \infty)) \) be an arbitrary function satisfying conditions (1.3). Assume that \( d > 0 \) and \( D > 0 \) and other parameters satisfy conditions (1.4). Then, for all nonnegative and continuous initial conditions \( u_0, v_0 \in L^\infty(\Omega) \), a unique nonnegative solution of system (1.1)-(1.6) exists for all \( t \in (0, \infty) \). This result was proved by Masuda [19] and generalized by Hollis et al. [9] as well as by Haraux and Youkana [6] (see also the surveys [28] and [25, Thm. 3.1]).

Let us briefly sketch the proof of the global-in-time existence of solutions for the reader convenience and for the completeness of exposition. To show that a local-in-time solution to integral equations (2.1)-(2.2) can be continued globally in time it suffices to show a priori estimates
\[
\sup_{t \in [0, T_{\text{max}})} \|u(t)\|_\infty < \infty \quad \text{and} \quad \sup_{t \in [0, T_{\text{max}})} \|v(t)\|_\infty < \infty \quad \text{if} \quad T_{\text{max}} < \infty.
\]

First, we notice that, since \( u^0 f(v) \geq 0 \) for nonnegative \( u \) and \( v \), the function \( v(x, t) \) satisfies the inequalities
\[
0 \leq v(x, t) \leq \max\left\{ \|v_0\|_\infty, \frac{\kappa}{b} \right\} \quad \text{for all} \quad (x, t) \in \Omega \times [0, T_{\text{max}}),
\]
due to the comparison principle applied to the parabolic equation (1.2). Thus, the second inequality in (2.4) is an immediate consequence of estimate (2.5).
To find an analogous estimate for \( u(x,t) \), we observe that by equation (1.1)-(1.2), we have

\[
    u_t - d \Delta u + au = -v_t + D \Delta v - bv + \kappa.
\]

Thus, using the Duhamel principle, we obtain

\[
    u(t) = e^{t(d \Delta - aI)} u_0 + \int_0^t e^{(t-s)(d \Delta - aI)} v(s) \, ds + \int_0^t e^{(t-s)(d \Delta - aI)} \kappa \, ds.
\]

Since \( u_0 \in L^\infty(\Omega) \) and \( v \in L^\infty(\Omega \times [0,T_{max}]) \), by a standard \( L^p \)-regularity property of linear parabolic equations with the Neumann boundary conditions (see e.g. [12, Ch. III, §10]), we obtain that \( u \in L^q(\Omega \times [0,T_{max}]) \) for each \( q \in (1,\infty) \). Using this property in equation (2.1) and a well-known regularizing effect for linear parabolic equations ([12]), we complete the proof of a priori estimate \( \sup_{t \in [0,T_{max})} \| u(t) \|_\infty < \infty \). We refer the reader to [28, 25] for more details.

Remark 2.5. If \( \kappa = 0 \) in equation (1.2), applying e.g. [9, Theorem 2] we obtain that nonnegative solutions to problem (1.1)-(1.6) with non-degenerate diffusions \( d > 0 \) and \( D > 0 \) are not only global-in-time (as stated in Remark 2.4) but also uniformly bounded on \( \Omega \times [0,\infty) \). We do not know if this additional assumption on \( \kappa \) is necessary to show a uniform bound for solutions to this problem.

3. Blowup in a finite time for reaction-diffusion-ODE system

Our main goal in this work is to show that the result on the global-in-time existence of solutions to problem (1.1)-(1.6) recalled in Remark 2.4 is no longer true if \( d = 0 \). Thus, in the following, we consider the initial-boundary value problem for the reaction-diffusion-ODE system of the form

\[
    \begin{align*}
    u_t &= -au + w^p f(v), & & x \in \overline{\Omega}, \quad t \in [0,T_{max}), \\
    v_t &= \Delta v - bv - w^p f(v) + \kappa, & & x \in \Omega, \quad t \in [0,T_{max}), \\
    \frac{\partial v}{\partial n} &= 0, & & \text{on} \quad \partial \Omega \times [0,T_{max}), \\
    u(x,0) &= u_0(x), \quad v(x,0) = v_0(x) & & x \in \Omega, \quad t \in [0,T_{max}).
    \end{align*}
\]

Here, without loss of generality, we assume that \( 0 \in \Omega \), where \( \Omega \subset \mathbb{R}^n \) is an arbitrary bounded domain with a smooth boundary, and we rescale system (3.1)-(3.3) in such a way that the diffusion coefficient in equation (3.2) is equal to one.

In the following theorem, we prove that if \( u_0 \) is concentrated around an arbitrary point \( x_0 \in \Omega \) (we choose \( x_0 = 0 \), for simplicity) and if \( v_0(x) = \bar{v}_0 \) is a constant function, then the corresponding solution to problem (3.1)-(3.4) blows up in a finite time.

**Theorem 3.1.** Assume that \( f \in C^1([0,\infty)) \) satisfies \( \inf_{v \geq R} f(v) > 0 \) for each \( R > 0 \). Let \( p > 1 \) and \( a, b, \kappa \in (0,\infty) \) be arbitrary. There exist numbers \( \alpha \in (0,1), \varepsilon > 0, \) and \( R_0 > 0 \)
(depending on parameters of problem (3.1)-(3.4) and determined in the proof) such that if initial conditions \( u_0, v_0 \in C(\Omega) \) satisfy

\[
(3.5) \quad 0 < u_0(x) < \left( u_0(0)^{1-p} + 2\varepsilon^{-(p-1)}|x|^\alpha \right)^{-\frac{1}{p-1}} \quad \text{for all} \quad x \in \Omega
\]

\[
(3.6) \quad u_0(0) \geq \left( \frac{a}{(1-e^{(1-p)a})F_0} \right)^{\frac{1}{p-1}}, \quad \text{where} \quad F_0 = \inf_{v \geq R_0} f(v),
\]

\[
(3.7) \quad v_0(x) \equiv \bar{v}_0 > R_0 > 0 \quad \text{for all} \quad x \in \Omega,
\]

then the corresponding solution to problem (3.1)-(3.4) blows up at certain time \( T_{\text{max}} \leq 1 \). Moreover, the following uniform estimates are valid

\[
(3.8) \quad 0 < u(x,t) < \varepsilon|x|^{\frac{\alpha}{p-1}} \quad \text{and} \quad v(x,t) \geq R_0 \quad \text{for all} \quad (x,t) \in \Omega \times [0,T_{\text{max}}).
\]

Remark 3.2. It follows from assumption (3.5) that

\[
0 < u_0(x) < 2^{-\frac{1}{p-1}}\varepsilon|x|^{\frac{\alpha}{p-1}} \quad \text{for all} \quad x \in \Omega,
\]

for small \( \varepsilon > 0 \). On the other hand, assumption (3.6) requires \( u_0(0) \) to be sufficiently large. Both assumptions mean that the function \( u_0 \) has to be concentrated in a neighborhood of \( x = 0 \). □

Remark 3.3. Notice that both inequalities in (3.8) give us pointwise estimates of \( u(x,t) \) and \( v(x,t) \) up to a blow-up time \( T_{\text{max}} \). □

Remark 3.4. The classical solution \( u = u(x,t) \) in Theorem 3.1 becomes infinite at \( x = 0 \) as \( t \to T_{\text{max}} \) and is uniformly bounded for other points in \( \Omega \). It would be interesting to know whether it is possible to extend this solution (in a weak sense) beyond \( T_{\text{max}} \). □

The proof of Theorem 3.1 is preceded by a sequence of lemmas. We begin by preliminary properties of solutions on an maximal interval \([0,T_{\text{max}})\) of their existence. We skip the proof of the following lemma because such properties of the solutions have been already discussed in Section 2, see inequality (2.5).

**Lemma 3.5.** For all nonnegative \( u_0, v_0 \in C(\Omega) \), problem (3.1)-(3.4) has a unique non-negative solution on the maximal interval \([0,T_{\text{max}})\). Moreover,

\[
(3.9) \quad 0 \leq v(x,t) \leq \max \left\{ \|v_0\|_\infty, \frac{\kappa}{b} \right\} \quad \text{for all} \quad (x,t) \in \Omega \times [0,T_{\text{max}}).
\]

If \( T_{\text{max}} < \infty \), then \( \sup_{t \in [0,T_{\text{max}})} \|u(\cdot,t)\|_\infty = \infty \).

Now, we show that a constant lower bound for \( v(x,t) \) leads to the blow-up of \( u(x,t) \) in a finite time \( T_{\text{max}} \leq 1 \).

**Lemma 3.6.** Let \( u(x,t) \) be a solution of equation (3.1) and suppose that there exists a constant \( R_0 > 0 \) such that

\[
(3.10) \quad v(x,t) > R_0 \quad \text{for all} \quad (x,t) \in \Omega \times [0,T_{\text{max}}).
\]
If the initial condition satisfies
\begin{equation}
 u_0(0) \geq \left( \frac{a}{1 - e^{(p-1)a}F_0} \right)^{\frac{1}{p-1}}, \quad \text{where} \quad F_0 = \inf_{v \geq R_0} f(v),
\end{equation}
then $T_{\max} \leq 1$.

Proof. For a fixed $v(x,t)$ with $(x,t) \in \Omega \times [0,T_{\max})$, we solve equation (3.1) with respect to $u(x,t)$ to obtain the following formula for all $(x,t) \in \Omega \times [0,T_{\max})$:
\begin{equation}
 u(x,t) = \frac{e^{-at}}{\left( \frac{1}{u_0(x)^{p-1}} - (p-1) \int_0^t f(v(x,s))e^{(1-p)as} \, ds \right)^{\frac{1}{p-1}}}. \tag{3.12}
\end{equation}
Thus, for $F_0 = \inf_{v \geq R_0} f(v)$, equation (3.12) leads to the following lower bound
\begin{equation}
 u(x,t) \geq \frac{e^{-at}}{\left( \frac{1}{u_0(x)^{p-1}} - (1 - e^{(1-p)at})a^{-1}F_0 \right)^{\frac{1}{p-1}}}. \tag{3.13}
\end{equation}
The proof of this lemma is complete because the right-hand side of inequality (3.13) for $x = 0$ blows up at some $t \leq 1$ under assumption (3.11). \hfill \Box

Next, we prove that a lower bound of $v(x,t)$, required in Lemma 3.6, is a consequence of a certain \textit{a priori} estimate imposed on $u(x,t)$.

\textbf{Lemma 3.7.} Assume that $v(x,t)$ is a solution of the reaction-diffusion equation (3.2) with an arbitrary function $u(x,t)$ and with a constant initial condition satisfying $v_0(x) \equiv \bar{v}_0 > 0$. Suppose that there are numbers $\varepsilon > 0$ and
\begin{equation}
 \alpha \in \left( 0, \frac{2(p-1)}{p} \right) \quad \text{if} \quad n \geq 2 \quad \text{and} \quad \alpha \in \left( 0, \frac{p-1}{p} \right) \quad \text{if} \quad n = 1
\end{equation}
such that
\begin{equation}
 0 < u(x,t) < \varepsilon |x|^{-\frac{\alpha}{p-1}} \quad \text{for all} \quad (x,t) \in \Omega \times [0,T_{\max}). \tag{3.14}
\end{equation}
Then, there is an explicit number $C_0 > 0$ independent of $\varepsilon$ (see equation (3.23) below) such that for all $\varepsilon > 0$ we have
\begin{equation}
 v(x,t) \geq \min \left\{ \bar{v}_0, \frac{\kappa}{b} \right\} - \varepsilon^p C_0 \quad \text{for all} \quad (x,t) \in \Omega \times [0,T_{\max}). \tag{3.15}
\end{equation}

Proof. We rewrite equation (3.2) in the usual integral form (cf. (2.2))
\begin{equation}
 v(t) = e^{t(\Delta - bt)} \bar{v}_0 + \int_0^t e^{(t-s)(\Delta - bt)} \kappa \, ds - \int_0^t e^{(t-s)(\Delta - bt)} \left( u^p f(v) \right) (s) \, ds. \tag{3.16}
\end{equation}
Here, the function given by first two terms on the right-hand side satisfies
\begin{equation}
 z(t) = e^{t(\Delta - bt)} \bar{v}_0 + \int_0^t e^{(t-s)(\Delta - b)} \kappa \, ds = e^{-bt} \bar{v}_0 + \frac{\kappa}{b} \left( 1 - e^{-bt} \right)
\end{equation}
because this is an $x$-independent solution of the problem
\begin{equation}
 z_t = \Delta z - bz + \kappa, \quad z(x,0) = \bar{v}_0 \tag{3.17}
\end{equation}
with the homogeneous Neumann boundary conditions. Thus
\begin{equation}
(3.20) \quad z(t) \geq \min \left\{ \bar{v}_0, \frac{K}{\beta} \right\} \quad \text{for all } t \in [0, T_{\text{max}}).
\end{equation}

Next, we recall the following well-known estimate
\begin{equation}
(3.21) \quad \|e^{t(\Delta-bI)}w_0\|_\infty \leq C_q \left( 1 + t^{-\frac{n}{2q}} \right) \|w_0\|_q \quad \text{for all } t > 0,
\end{equation}
which is satisfied for each \( w_0 \in L^q(\Omega) \), each \( q \in [1, \infty] \), and with a constant \( C_q = C(q, n, \Omega) \) independent of \( w_0 \) and of \( t \), see e.g. [30, p. 25].

Now, we compute the \( L^\infty \)–norm of equation (3.17). Using the lower bound (3.20), inequalities (3.21) and (3.9), as well as the a priori assumption on \( u \) in (3.15), we obtain the estimate
\begin{equation}
(3.22) \quad v(x, t) \geq z(t) - \int_0^t \|e^{(t-s)(\Delta-bI)}(u^p f(v))(s)\|_\infty \, ds \\
\geq \min \left\{ \bar{v}_0, \frac{K}{\beta} \right\} - \varepsilon^p C_q \left( \sup_{0 \leq v \leq R_1} f(v) \right) \int_0^t \left( 1 + (t-s)^{-\frac{n}{2q}} \right) \| \frac{\alpha p}{p-1} \|_q \, ds,
\end{equation}
where the constant \( R_1 \) is defined in (3.9). Here, we choose \( q > n/2 \) to have \( n/(2q) < 1 \), which leads to the equality
\begin{equation}
\int_0^t \left( 1 + (t-s)^{-\frac{n}{2q}} \right) ds = t + \left( 1 - \frac{n}{2q} \right)^{-1} t^{1-\frac{n}{2q}}.
\end{equation}

Moreover, we assure that \( q < n(p-1)/(\alpha p) \) or, equivalently, that \( \alpha p/(p-1) < n \) to have \( |x|^\frac{\alpha p}{p-1} \in L^q(\Omega) \). Such a choice of \( q \in [1, \infty) \) is always possible because \( \max\{1, n/2\} < n(p-1)/(\alpha p) \) under our assumptions on \( \alpha \) in (3.14).

Thus, for the constant
\begin{equation}
(3.23) \quad C_0 = C_q \left( \sup_{0 \leq v \leq R_1} f(v) \right) \| \frac{\alpha p}{p-1} \|_q \left( T_{\text{max}} + \left( 1 - \frac{n}{2q} \right)^{-1} T_{\text{max}}^{1-\frac{n}{2q}} \right),
\end{equation}
inequality (3.22) implies the lower bound (3.16). \( \square \)

Now, let us recall a classical result on the Hölder continuity of solutions to the inhomogeneous heat equation.

**Lemma 3.8.** Let \( f \in L^\infty([0, T], L^q(\Omega)) \) with some \( q > \frac{n}{2} \) and \( T > 0 \). Denote
\begin{equation}
(3.24) \quad w(x, t) = \int_0^t e^{(t-\tau)(\Delta-bI)} f(x, \tau) \, d\tau,
\end{equation}
where \( \{e^{t(\Delta-bI)}\}_{t \geq 0} \) is the semigroup of linear operators on \( L^q(\Omega) \) generated by \( \Delta-bI \) with the homogeneous Neumann boundary conditions. There exist numbers \( \beta \in (0, 1) \) and \( C = C > 0 \) depending on \( \sup_{0 \leq t \leq T} \| f(\cdot, t) \|_q \) such that
\begin{equation}
(3.24) \quad |w(x, t) - w(y, t)| \leq C |x-y|^{\beta} \quad \text{for all } x, y \in \Omega \quad \text{and} \quad t \in [0, T].
\end{equation}
Proof. Note that the function \( w(x,t) \) is the solution of the problem
\[
w_t = D \Delta w - bw + f, \quad w(x,0) = 0
\]
supplemented with the Neumann boundary conditions. Hence, estimate (3.24) is a classical and well-known result on the H"older continuity of solutions to linear parabolic equations, see e.g. [12, Ch. III, §10].

We apply Lemma 3.8 to show the H"older continuity of \( v(x,t) \).

**Lemma 3.9.** Let \( v(x,t) \) be a nonnegative solution of the problem
\[
(3.25) \quad v_t = \Delta v - bv - u^p f(v) + \kappa \quad \text{for} \ x \in \Omega, \ t \in [0,T_{\text{max}}) \\
(3.26) \quad \frac{\partial v}{\partial n} = 0 \quad \text{on} \ \partial \Omega \times [0,T_{\text{max}}), \\
(3.27) \quad v(x,0) = \bar{v}_0 \quad \text{for} \ x \in \Omega, \ t \in [0,T_{\text{max}}),
\]
where \( \bar{v}_0 > 0 \) is a positive constant and \( u(x,t) \) is a nonnegative function. There exists a constant \( \alpha \in (0,1) \) satisfying also (3.14), such that if the a priori estimate (3.15) for \( u(x,t) \) holds true with some \( \varepsilon > 0 \), then
\[
|v(x,t) - v(y,t)| \leq \varepsilon \beta C |x-y|^\alpha \quad \text{for all} \ (x,t) \in \Omega \times [0,T_{\text{max}}),
\]
where the constant \( C > 0 \) is independent of \( \varepsilon \).

Proof. As in the proof of Lemma 3.7, we use the following integral equation
\[
v(x,t) = e^{-bt} \bar{v}_0 + \frac{\kappa}{b} \left( 1 - e^{-bt} \right) - \int_0^t e^{(\Delta-b)(t-s)} \left( u^p f(v) \right)(s) \, ds.
\]
Suppose that \( u(x,t) \) satisfies the a priori estimate (3.15) with a certain number \( \alpha \in (0,1) \) satisfying relations (3.14). Since \( f(v) \in L^\infty(\Omega \times [0,T_{\text{max}})) \) by (3.9) and since
\[
|u^p(x,t)| \leq \varepsilon \beta C \beta |x|^{-\beta(p-1)}
\]
by assumption (3.15), we obtain
\[
u^p f(v) \in L^\infty([0,T_{\text{max}}), L^q(\Omega)) \quad \text{for some} \ q > n/2,
\]
see the proof of Lemma 3.7. Thus, by Lemma 3.8, there exist constants \( C > 0 \) and \( \beta \in (0,1) \), independent of \( \varepsilon \) such that \( |v(x,t) - v(y,t)| \leq \varepsilon \beta C |x-y|^\beta \) for all \( x,y \in \Omega \) and \( t \in [0,T_{\text{max}}) \). Without loss of generality, we can assume that \( \beta \) satisfies the conditions in (3.14) (we can always take it smaller).

The proof is completed, if \( \beta \geq \alpha \). On the other hand, if \( \beta < \alpha \), we suppose the a priori estimate \( 0 \leq u(x,t) < \varepsilon |x|^{-\beta(p-1)} \) for all \( x \in \Omega \) and \( t \in [0,T_{\text{max}}) \). Thus, there exists a constant \( C = C(\alpha, \beta, p, \Omega) > 0 \) such that
\[
0 \leq u(x,t) < \varepsilon |x|^{-\frac{\beta}{p-1}} = \varepsilon |x|^{-\frac{\alpha}{\beta(p-1)}} \leq C \varepsilon |x|^{-\frac{\alpha}{\beta}}.
\]
Hence, repeating the reasoning in the preceding paragraph of this proof, we obtain again the estimate \( |v(x,t) - v(y,t)| \leq \varepsilon \beta C |x-y|^\beta \) for all \( x,y \in \Omega \) and \( t \in [0,T_{\text{max}}) \).
Proof of Theorem 3.1. By Lemmas 3.6 and 3.7, it suffices to show the a priori estimate

\[
0 < u(x, t) < \varepsilon |x|^{-\frac{\alpha}{p-1}} \quad \text{for all} \quad (x, t) \in \Omega \times [0, T_{\max})
\]

with \(T_{\max} \leq 1\), under the assumption that \(\varepsilon > 0\) is sufficiently small.

By assumption (3.5) (see Remark 3.2), we have \(0 < u_0(x) < \varepsilon |x|^{-\frac{\alpha}{p-1}}\) for all \(x \in \Omega\), hence, by a continuity argument, inequality (3.28) is satisfied on a certain initial time interval. Suppose that there exists \(T_1 \in (0, 1)\) such that the solution of problem (3.1)-(3.4) exists on the interval \([0, T_1]\) and satisfies

\[
\sup_{x \in \Omega} |x|^{-\frac{\alpha}{p-1}} u(x, t) < \varepsilon \quad \text{for all} \quad t < T_1,
\]

\[
\sup_{x \in \Omega} |x|^{-\frac{\alpha}{p-1}} u(x, t) = \varepsilon \quad \text{for} \quad t = T_1.
\]

From now on, we are going to use the explicit formula for \(u(x, t)\) in (3.12) and the Hölder regularity of \(v(x, t)\) from Lemma 3.8. First, we estimate the denominator of the fraction in (3.12) using assumption (3.5) as follows

\[
\frac{1}{u_0(x)^{p-1}} - (p-1) \int_0^t f(v(x, s)) e^{(1-p)as} \, ds
\]

\[
\geq 2\varepsilon^{p-1} |x|^{\alpha} + \frac{1}{u_0(0)^{p-1}} - (p-1) \int_0^t f(v(0, s)) e^{(1-p)as} \, ds
\]

\[
+ (p-1) \int_0^t (f(v(0, s)) - f(v(x, s))) e^{(1-p)as} \, ds.
\]

By the definition of \(T_{\max}\) and formula (3.12), we immediately obtain

\[
\frac{1}{u_0(0)^{p-1}} - (p-1) \int_0^t f(v(0, s)) e^{(1-p)as} \, ds > 0 \quad \text{for all} \quad t \in [0, T_{\max}).
\]

Next, we use our hypothesis (3.29) and (3.30) together with the Hölder continuity of \(v(x, t)\) established in Lemma 3.9 to find constants \(C > 0\) and \(\alpha \in (0, 1)\) (satisfying also (3.14)), the both independent of \(\varepsilon \geq 0\), such that

\[
|f(v(0, s)) - f(v(x, s))| \leq C\varepsilon^p |x|^{\alpha} \quad \text{for all} \quad t \in [0, T_1].
\]

Hence, since \(T_1 \leq T_{\max} \leq 1\), we obtain the following bound for the last term on the right-hand side of (3.31):

\[
(p-1) \int_0^t |f(v(0, s)) - f(v(x, s))| e^{(1-p)as} \, ds \leq \varepsilon^p Ca^{-1} |x|^{\alpha}
\]

for all \((x, t) \in \Omega \times [0, T_1]\). Consequently, applying inequalities (3.32) and (3.33) in (3.31) we obtain the lower bound for the denominator in (3.12)

\[
\frac{1}{u_0(x)^{p-1}} - (p-1) \int_0^t f(v(x, s)) e^{(1-p)as} \, ds \geq 2\varepsilon^{-(p-1)} - \varepsilon^p Ca^{-1} |x|^{\alpha}
\]
for all \((x, t) \in \Omega \times [0, T_1]\). Finally, we choose \(\varepsilon > 0\) so small that 
\[
2\varepsilon^{-(p-1)} - \varepsilon^p Ca^{-1} > \varepsilon^{-(p-1)}
\]
and we substitute estimate (3.34) in equation (3.12) to obtain
\[
0 < u(x, t) \leq \frac{e^{-at}}{\left(2\varepsilon^{-(p-1)} - \varepsilon^p Ca^{-1}\right)|x|^\alpha} \leq \frac{\varepsilon}{|x|^\frac{\alpha}{p-1}} \quad \text{for all} \quad (x, t) \in \Omega \times [0, T_1].
\]
This inequality for \(t = T_1\) contradicts our hypothesis (3.30).

Thus, estimate (3.28) holds true on the whole interval \([0, T_{\text{max}}]\). Then, by Lemma 3.7, the function \(v(x, t)\) is bounded from below by a constant \(R_0 = \min \left\{ \bar{v}_0, \frac{\varepsilon}{p} \right\} - \varepsilon^p C_0\) which is positive provided \(\varepsilon > 0\) is sufficiently small. Finally, Lemma 3.6 implies that \(u(x, t)\) blows up at \(x = 0\) and at certain \(T_{\text{max}} \leq 1\), if \(u_0(0)\) satisfies inequality (3.6). \(\square\)

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References

[1] R. Casten, C. Holland, Instability results for reaction-diffusion equations with Neumann boundary conditions, J. Differential Equations, 27 (1978), pp. 266–273.

[2] M. Fila and K. Ninomiya, “Reaction-diffusion” systems: blow-up of solutions that arises or vanishes under diffusion, Russian Math. Surveys, 60 (2005), pp. 1217–1235.

[3] P. Gray and S. Scott, Sustained oscillations and other exotic patterns of behavior in isothermal reactions, J. Phys. Chemistry, 89 (1985), pp. 22–32.

[4] Chemical Waves and Instabilities, Clarendon, Oxford, 1990.

[5] M. Guetta and M. Kirane, Diffusion terms in systems of reaction diffusion equations can lead to blow up, J. Math. Anal. Appl., 218 (1998), pp. 325–327.

[6] A. Haraux and A. Youkana, On a result of K. Masuda concerning reaction-diffusion equations, Tôhoku. Math. J., 40 (1988), pp. 159–163.

[7] S. Härtling and A. Marciniak-Czochra, Spike patterns in a reaction-diffusion ODE model with Turing instability, Math. Methods Appl. Sci., 37 (2014), pp. 1377–1391.

[8] S. Hock, Y.-K. Ng, J. Hasenauer, D. Wittmann, D. Lutter, D. Trumbach, W. Wurst, N. Prakash, and F. Theis, Sharpening of expression domains induced by transcription and microRNA regulation within a spatio-temporal model of mid-hindbrain boundary formation, BMC Systems Biology, 7 (2013), p. 48.

[9] S. L. Hollis, R. H. Martin, and M. Pierre, Global existence and boundedness in reaction-diffusion systems, SIAM J. Math. Anal., 18 (1987), pp. 744–761.

[10] G. Karch, K. Suzuki, and J. Zienkiewicz, Finite-time blow-up in general activator-inhibitor system, preprint, (2014).

[11] V. Klika, R. E. Baker, D. Headon, and E. A. Gaffney, The influence of receptor-mediated interactions on reaction-diffusion mechanisms of cellular self-organisation, Bull. Math. Biol., 74 (2012), pp. 935–957.
[12] O. A. Ladyzenskaja, V. A. Solonnikov, and N. N. Ural’ceva, Linear and quasilinear equations of parabolic type, Translated from the Russian by S. Smith. Translations of Mathematical Monographs, Vol. 23, American Mathematical Society, Providence, R.I., 1968.

[13] A. Marciniak-Czochra, Receptor-based models with diffusion-driven instability for pattern formation in hydra, J. Biol. Sys., 11 (2003), pp. 293–324.

[14] A. Marciniak-Czochra, G. Karch, and K. Suzuki, Unstable patterns in autocatalytic reaction-diffusion-ODE systems, arXiv:1301.2002 [math.AP], (2013).

[15] ______, Unstable patterns in reaction-diffusion model of early carcinogenesis, J. Math. Pures Appl. (9), 99 (2013), pp. 509–543.

[16] A. Marciniak-Czochra and M. Kimmel, Dynamics of growth and signaling along linear and surface structures in very early tumors, Comput. Math. Methods Med., 7 (2006), pp. 189–213.

[17] ______, Modelling of early lung cancer progression: influence of growth factor production and cooperation between partially transformed cells, Math. Models Methods Appl. Sci., 17 (2007), pp. 1693–1719.

[18] ______, Reaction-diffusion model of early carcinogenesis: the effects of influx of mutated cells, Math. Model. Nat. Phenom., 3 (2008), pp. 90–114.

[19] K. Masuda, On the global existence and asymptotic behavior of solutions of reaction-diffusion equations, Hokkaido Mathematical Journal, 12 (1983), pp. 360–370.

[20] N. Mizoguchi, H. Ninomiya, and E. Yanagida, Diffusion-induced blowup in a nonlinear parabolic system, J. Dynamics and Differential Equations, 10 (1998), pp. 619–638.

[21] J. Morgan, On a question of blow-up for semilinear parabolic systems, Differential Integral Equations, 3 (1990), pp. 973–978.

[22] J. D. Murray, Mathematical biology. II, vol. 18 of Interdisciplinary Applied Mathematics, Springer-Verlag, New York, third ed., 2003. Spatial models and biomedical applications.

[23] G. Nicolis and I. Prigogine, Self-organization in nonequilibrium systems. From dissipative structures to order through fluctuations, Wiley-Interscience [John Wiley & Sons], New York-London-Sydney, 1977.

[24] K. Pham, A. Chauviere, H. Hatzikirou, X. Li, H. M. Byrne, V. Cristini, and J. Lowengrub, Density-dependent quiescence in glioma invasion: instability in a simple reaction-diffusion model for the migration/proliferation dichotomy, J. Biol. Dyn., 6 (2012), pp. 54–71.

[25] M. Pierre, Global existence in reaction-diffusion systems with control of mass: a survey, Milan J. Math., 78 (2010), pp. 417–455.

[26] M. Pierre and D. Schmitt, Blowup in reaction-diffusion systems with dissipation of mass, SIAM J. Math. Anal., 28 (1997), pp. 259–269.

[27] M. Pierre and D. Schmitt, Blowup in reaction-diffusion systems with dissipation of mass, SIAM Rev. 42 (2000), pp. 93–106.

[28] J. Prüss, Maximal regularity for evolution equations in $L^p$-spaces., Conf. Semin. Mat. Univ. Bari 285 (2002), pp. 1–39.

[29] P. Quittner and P. Souplet, Superlinear parabolic problems, Birkhäuser Advanced Texts: Basler Lehrbücher. [Birkhäuser Advanced Texts: Basel Textbooks], Birkhäuser Verlag, Basel, 2007. Blow-up, global existence and steady states.

[30] F. Rotte, Global solutions of reaction-diffusion systems, vol. 1072 of Lecture Notes in Mathematics, Springer-Verlag, Berlin, 1984.

[31] J. Schnackenberg, Simple chemical reaction systems with limit cycle behaviour, J. Theor. Biol., 81 (1979), pp. 389–400.

[32] A. M. Turing, The chemical basis of morphogenesis, Philos. Trans. R. Soc. London Ser. B, 237 (1952), pp. 37–72.
[33] D. Umulis, M. Serpe, M. B. O'Connor, and H. G. Othmer, Robust, bistable patterning of the dorsal surface of the Drosophila embryo, J. Biol. Sys., 103 (2006), pp. 11613–11618.

[34] Y. You, Global attractor of the Gray-Scott equations, Commun. Pure Appl. Anal., 7 (2008), pp. 947–970.

[35] Y. You and S. Zhou, Global dissipative dynamics of the extended Brusselator system, Nonlinear Anal. Real World Appl., 13 (2012), pp. 2767–2789.

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