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Global attractivity of equilibrium in Gierer–Meinhardt system with activator production saturation and gene expression time delays[☆]

Shanshan Chen[a], Junping Shi[b,*]

[a] Department of Mathematics, Harbin Institute of Technology, Weihai, Shandong, 264209, PR China

[b] Department of Mathematics, College of William and Mary, Williamsburg, VA, 23187-8795, USA

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ABSTRACT

In this work we investigate a diffusive Gierer–Meinhardt system with gene expression time delays in the production of activators and inhibitors, and also a saturation in the activator production, which was proposed by Seirin Lee et al. (2010) [10]. We rigorously consider the basic kinetic dynamics of the Gierer–Meinhardt system with saturation. By using an upper and lower solution method, we show that when the saturation effect is strong, the unique constant steady state solution is globally attractive despite the time delays. This result limits the parameter space for which spatiotemporal pattern formation is possible.

1. Introduction

Since the pioneering work of Turing [1], Reaction–Diffusion systems have been used to demonstrate morphogenetic pattern formation [2–7]. During the process of cell division and differentiation, gene expressions control the establishment of stable patterns of differentiated cell types. Recent experimental studies have shown that timing of the pattern-forming events may have important implications in the development of the patterns [8,9,4,5,10,11]. In particular, there exists a considerable delay between the start of protein signal transduction (ligand–receptor binding) and the result (a gene production) via gene expression regulations [10].

In 1972, Gierer and Meinhardt [12] proposed a nonlinear reaction–diffusion model to describe the interaction dynamics of two chemical substances: (see [12, Eq. (12)])

$$\begin{cases} \dfrac{\partial a}{\partial t} = \rho_0 \ell_a + c\ell_a \dfrac{a^p}{h^q} - \nu_a a + D_a \dfrac{\partial^2 a}{\partial x^2}, \\ \dfrac{\partial h}{\partial t} = c'\ell_h \dfrac{a^r}{h^s} - \nu_h h + D_h \dfrac{\partial^2 h}{\partial x^2}, \end{cases} \tag{1.1}$$

where $a(x,t)$ and $h(x,t)$ are the concentrations of the activator and the inhibitor respectively; the reactions of activators and inhibitors are assumed to be power functions of a and h, and at the same time both substances are removed at a linear rate; the activator a and the inhibitor h diffuse in the environment with diffusion constant D_a and D_h respectively, and it is assumed that h diffuses faster than a; finally a constant source term for a initiates the whole reaction. Here ℓ_a, ρ_0, ℓ_h, c, ν_a, c', ν_h are all positive constant parameters, and the exponents p, q, r, s are all nonnegative. One of particular examples of exponents

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* Corresponding author. Tel.: +1 757 221 2030.
E-mail addresses: shij@math.wm.edu, jxshix@wm.edu (J. Shi).

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they considered was $q = 1, s = 0$, and $p = r = 2$. That is, two molecules of activator are necessary to activate, and one molecule of inhibitor is needed for inhibit; and the activators activate both substances and the inhibitors only inhibit the activator source.

On the other hand, by assuming a saturation of activator production for the case $q = 1, s = 0$, and $p = r = 2$ in (1.1), Gierer and Meinhardt [12] also considered (see [12, Eq. (16)])

$$\begin{cases} \dfrac{\partial a}{\partial t} = \rho_0 \ell_a + c\ell_a \dfrac{a^2}{(1+\kappa a^2)h} - \nu_a a + D_a \dfrac{\partial^2 a}{\partial x^2}, \\ \dfrac{\partial h}{\partial t} = c' \ell_h a^2 - \nu_h h + D_h \dfrac{\partial^2 h}{\partial x^2}. \end{cases} \tag{1.2}$$

For system (1.2), the activator concentration is limited to a maximum value so that the activated area forms an approximately constant proportion of the total structure size. Numerical simulation of concentration patterns were obtained in [12] as well as [13,14] for one and two-dimensional spatial domains.

Since then, the Gierer–Meinhardt system has been regarded as one of the prototype reaction–diffusion models of spatiotemporal pattern formation [15,16], and extensive research has been done for a more general Gierer–Meinhardt system in the form of (with $\kappa = 0$ or $\kappa > 0$)

$$\begin{cases} \dfrac{\partial u}{\partial t} = \epsilon^2 \Delta u - u + \rho_a \dfrac{u^p}{(1+\kappa u^p)v^q} + \sigma_a, & x \in \Omega,\ t > 0, \\ \tau \dfrac{\partial v}{\partial t} = D\Delta v - v + \rho_h \dfrac{u^r}{v^s} + \sigma_h, & x \in \Omega,\ t > 0, \\ \dfrac{\partial u(x,t)}{\partial \nu} = \dfrac{\partial v(x,t)}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0, \\ u(x,0) = u_0(x) > 0, \qquad v(x,0) = v_0(x) > 0, & x \in \Omega. \end{cases} \tag{1.3}$$

Here, Ω is a bounded smooth region in $\mathbb{R}^n$, $n \geq 1$ and the Laplace operator $\Delta w(x,t) = \sum_{i=1}^{n} \frac{\partial^2 w(x,t)}{\partial x_i^2}$ for $w = u, v$ shows the diffusion effect; $\frac{\partial w(x,t)}{\partial \nu}$ is the outer normal derivative of $w = u, v$, and a no-flux boundary condition is imposed; the coefficients ϵ, τ and D are positive constants, whereas κ is a nonnegative constant; the basic production terms $\sigma_a = \sigma_a(x)$, $\sigma_h = \sigma_h(x)$ are nonnegative, and the interaction coefficients $\rho_a = \rho_a(x)$, $\rho_h = \rho_h(x)$ are positive over $\overline{\Omega}$. Up to now, there are many research results on the nonhomogeneous steady state solutions (such as multi-peak steady state solutions, etc.) of the Gierer–Meinhardt system (1.1), (see Refs. [17–25]) and the Gierer–Meinhardt system with saturation (1.2), (see Refs. [26–29]), and the *a priori* estimates, global existence and asymptotic behavior of the solution [30–35].

In this paper we assume that σ_a, ρ_a and ρ_h are positive constants, the basic production term $\sigma_h(x) \equiv 0$, and the saturation parameter κ is a positive constant. Then system (1.3) becomes:

$$\begin{cases} \dfrac{\partial u}{\partial t} = \epsilon^2 \Delta u - u + \rho_a \dfrac{u^p}{(1+\kappa u^p)v^q} + \sigma_a, & x \in \Omega,\ t > 0, \\ \tau \dfrac{\partial v}{\partial t} = D\Delta v - v + \rho_h \dfrac{u^r}{v^s}, & x \in \Omega,\ t > 0, \\ \dfrac{\partial u(x,t)}{\partial \nu} = \dfrac{\partial v(x,t)}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0, \\ u(x,0) = u_0(x) > 0, \qquad v(x,0) = v_0(x) > 0, & x \in \Omega \end{cases} \tag{1.4}$$

where $\rho_a, \kappa, \sigma_a, \rho_h, \epsilon, \tau$ and D are positive constants. We show that when the saturation constant κ is large then the unique constant steady state solution is globally attractive, hence no spatiotemporal pattern is possible. In [28] assuming $p = r = 2, s = 0$ and $q = 1$, Morimoto showed that system (1.4) admits a radially symmetric steady state solution when κ is small, and the global stability proved here implies that (1.4) cannot have such radially symmetric steady state solution when κ is large.

In recent studies Gaffney and Monk [8] and Seirin Lee et al. [10] (see also [36,37]) considered the effect of gene expression time delays on morphogenesis and pattern formation. The time delays in the feedback can be caused by the signal transduction, gene transcription and mRNA translation in the process of gene expression [10]. Here we consider the Gierer–Meinhardt system with gene expression time delays and saturation of activator induced activator production as proposed in [10] (model I with saturation of activator induced activator production in [10]):

$$\begin{cases} \dfrac{\partial u}{\partial t} = D_1 \dfrac{\partial^2 u}{\partial x^2} + k_1 - k_2 u(x,t) + k_3 \dfrac{u^2(x,t-\gamma)}{(1+\kappa u^2(x,t-\gamma))v(x,t-\gamma)}, \\ \dfrac{\partial v}{\partial t} = D_2 \dfrac{\partial^2 v}{\partial x^2} + k_4 u^2(x,t-\gamma) - k_5 v(x,t), \end{cases} \tag{1.5}$$

where u, v are the concentrations of the activator and the inhibitor respectively; k_i $(1 \le i \le 5)$ are positive and indicate the production rate, the decay rates and the rate of gene product interaction of morphogens, $\kappa \ge 0$ represents the effect of the saturation, and $\gamma \ge 0$ is the gene expression time delay in the morphogen induced protein production.

Indeed we consider a generalized nonlocal Gierer–Meinhardt system with gene expression time delays:

$$\begin{cases} \dfrac{\partial u}{\partial t} = \epsilon^2 \Delta u - u + \rho_a \displaystyle\int_\Omega k_1(x,y) \frac{u^p(y,t-\gamma)}{(1+\kappa u^p(y,t-\gamma))v^q(y,t-\gamma)} dy + \sigma_a, & x \in \Omega,\ t > 0, \\ \tau \dfrac{\partial v}{\partial t} = D\Delta v - v + \rho_h \displaystyle\int_\Omega k_2(x,y) u^r(y,t-\gamma) dy & x \in \Omega,\ t > 0, \\ \dfrac{\partial u(x,t)}{\partial \nu} = \dfrac{\partial v(x,t)}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0, \\ u(x,t) = u_0(x,t) > 0, \qquad v(x,t) = v_0(x,t) > 0, & x \in \Omega,\ t \in [-\gamma, 0], \end{cases} \tag{1.6}$$

following the general version in Suzuki and Takagi [34]. And the dispersal kernel functions $k_i(x,y)$, $(i = 1, 2)$, satisfy the following property (see, for example [38,39]):

(K) Either $k_i(x,y) = \delta(x-y)$ (Dirac Delta function), or $k_i(x,y)$ is a continuous and nonnegative function such that $\int_\Omega k_i(x,y)dy = 1$ for any $x \in \Omega$ and the linear operator

$$L_i(\phi)(x) := \int_\Omega k_i(x,y)\phi(y)dy$$

is strictly positive on $C(\overline{\Omega}, \mathbb{R})$ in the sense that

$$L_i(C(\overline{\Omega}, \mathbb{R}_+) \setminus \{0\}) \subset C(\overline{\Omega}, \mathbb{R}_+) \setminus \{0\}.$$

The generalization of (1.5) to a nonlocal model as in (1.6) is motivated by recent work in [40,41,38,42], as the effects of diffusion and time delays are not independent of each other, and the individuals have not been at the same point in space at previous time. Hence a spatial averaging of the population in the past time should be added to take account of that effect in the models, and a detailed review on that topic can be found in Gourley, So and Wu [42]. Such formulation for the models in a bounded domain first appeared in Gourley and So [38], and see also [40,41,43,39]. In Section 4, we will also comment on the validity of assumption (K).

Note that when $k_i(x,y) = \delta(x-y)$, $(i = 1, 2)$, system (1.6) reduces to the following time-delayed reaction–diffusion system (as in [10]):

$$\begin{cases} \dfrac{\partial u}{\partial t} = \epsilon^2 \Delta u - u + \rho_a \dfrac{u^p(x,t-\gamma)}{(1+\kappa u^p(x,t-\gamma))v^q(x,t-\gamma)} + \sigma_a, & x \in \Omega,\ t > 0, \\ \tau \dfrac{\partial v}{\partial t} = D\Delta v - v + \rho_h u^r(x,t-\gamma) & x \in \Omega,\ t > 0, \\ \dfrac{\partial u(x,t)}{\partial \nu} = \dfrac{\partial v(x,t)}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0, \\ u(x,t) = u_0(x,t) > 0, \qquad v(x,t) = v_0(x,t) > 0, & x \in \Omega,\ t \in [-\gamma, 0]. \end{cases} \tag{1.7}$$

Again our main result is that the unique constant steady state solution is globally asymptotically stable when the saturation constant κ is large, but the result for the delayed system (1.6) is that the exponent s in system (1.4) is 0 in (1.6). While this shows the restriction of the mathematical method of proving the global stability, it may suggest that the additional feedback of v^s term in (1.4) could enrich the dynamics. We use a upper–lower solution method for the proof of global stability, which was developed by Pao [44–47], and see also related work in [48,49]. We remark that the global stability of constant equilibrium in a scalar delayed reaction–diffusion equation have also been proved by using dynamical system approach [50,51], Lyapunov method [52,53], and fluctuation method [43,39].

Our analysis here shows that a strong saturation effect plays a role of stabilizing the constant steady state even when the delays exist. That is, when κ is sufficiently large, the constant steady state is globally stable and no complex spatiotemporal patterns appear despite gene expression delays. This shows that in the delayed Gierer–Meinhardt system with saturation, the degree of saturation is the most important parameter for the dynamics, while the time-delay is a secondary parameter which can be the determining factor in the small saturation case. This is one step to rigorously analyze the dynamical behavior of this prototype biological pattern formation system. Another step is to analyze the bifurcation of the system using the time-delay as bifurcation parameter when κ is small, which has been reported in [10]. The instability of the constant equilibrium for a small κ but a large delay has been rigorously proved in our other work [54]. Hence the present work complements the one in [54,10].

The rest of this paper is organized as follows. In Section 2, we present some preliminaries: in Section 2.1, the basic dynamics of the kinetic model is presented; and in Section 2.2, we recall the comparison method of the reaction–diffusion systems with delay effect. In Section 3, we prove the global stability of the unique constant steady state solution with respect to the reaction–diffusion system without the delay effect (1.4). In Section 4, we prove the global stability of the unique constant steady state solution with respect to the reaction–diffusion system with gene expression time delays (1.6) for any delay $\gamma > 0$. Section 5 contains some concluding remarks. Throughout the paper, $(a, b) > 0$ means $a > 0$ and $b > 0$ for $(a, b) \in \mathbb{R}^2$.

2. Preliminaries

2.1. Analysis of the kinetic system

In this subsection, we analyze the following kinetic system corresponding to system (1.4):

$$\begin{cases} \dfrac{du}{dt} = -u + \rho_a \dfrac{u^p}{(1+\kappa u^p)v^q} + \sigma_a, & t > 0, \\ \tau \dfrac{dv}{dt} = -v + \rho_h \dfrac{u^r}{v^s}, & t > 0, \\ u(0) = u_0 > 0, \quad v(0) = v_0 > 0. \end{cases} \tag{2.1}$$

In this subsection, we always assume that $\rho_a, \rho_h, \sigma_a, \tau, p, q, r > 0$, and $s, \kappa \geq 0$.

Lemma 2.1. *Suppose that the parameters $\rho_a, \rho_h, \sigma_a, \tau, p, q, r > 0$, and $s, \kappa \geq 0$. If*

$$\frac{p-1}{r} < \frac{q}{s+1}, \tag{2.2}$$

then system (2.1) has a unique positive constant equilibrium (u_*, v_*), where $v_* = (\rho_h u_*^r)^{\frac{1}{s+1}}$.

Proof. If (u, v) is an equilibrium of system (2.1), then (u, v) satisfies

$$-u + \rho_a \frac{u^p}{(1+\kappa u^p)v^q} + \sigma_a = 0, \qquad -v + \rho_h \frac{u^r}{v^s} = 0,$$

which implies u satisfies

$$1 + \kappa u^p = \rho_a \rho_h^{-\frac{q}{s+1}} \frac{u^{p-\frac{qr}{s+1}}}{u - \sigma_a}. \tag{2.3}$$

Define

$$I_1(u) := \rho_a \rho_h^{-\frac{q}{s+1}} \frac{u^{p-\frac{qr}{s+1}}}{u - \sigma_a},$$

and it can be easily verified that $I_1(u)$ is a strictly decreasing function for $u > \sigma_a$ if (2.2) is satisfied. Moreover $\lim_{u\to\sigma_a^+} I_1(u) = \infty$, $\lim_{u\to\infty} I_1(u) = 0$ if (2.2) is satisfied. On the other hand, the function $I_2(u) := 1 + \kappa u^p$ satisfies $I_2(0) = 1$ and it is increasing on $(0, \infty)$. Hence if (2.2) is satisfied, then the system has a unique positive constant equilibrium (u_*, v_*), where u_* is the unique positive root of (2.3), and $v_* = (\rho_h u_*^r)^{\frac{1}{s+1}}$. □

From the proof of Lemma 2.1, we define $\beta > \sigma_a$ to be the unique point such that $I_1(\beta) = 1$. That is, β is the unique point satisfying

$$\rho_a^{-1} \rho_h^{\frac{q}{s+1}} (\beta - \sigma_a) = \beta^{p-\frac{qr}{s+1}}. \tag{2.4}$$

For fixed parameters $\rho_a, \sigma_a, \rho_h, p, q, r, s$, we regard u_* as a function of κ and $u_*(0) = \beta$. Then one can show that $u_*(\kappa)$ is strictly decreasing in κ. Indeed by differentiating $1 + \kappa u_*^p(\kappa) = I_1(u_*(\kappa))$, and using that $I_1'(u) < 0$ for $u > \sigma_a$, we see that $u_*'(\kappa) < 0$. Since $1 + \kappa u_*^p(\kappa) = I_1(u_*(\kappa))$, we have $I_1(u_*(\kappa)) \to \infty$ as $\kappa \to \infty$. Hence $\lim_{\kappa\to\infty} u_*(\kappa) = \sigma_a$ and $\lim_{\kappa\to 0^+} u_*(\kappa) = \beta$.

We can now arrive at the following result about the local stability of the equilibrium (u_*, v_*).

Theorem 2.2. *Suppose that the parameters $\rho_a, \rho_h, \sigma_a, \tau, p, q, r > 0$, $s, \kappa \geq 0$, β is defined as in Eq. (2.4), and $p/r \leq q/(s+1)$.*

1. *If*

$$\frac{\beta - \sigma_a}{\beta} < \frac{1}{p}\left(1 + \frac{s+1}{\tau}\right), \tag{2.5}$$

then (u_*, v_*) is locally asymptotically stable for any $\kappa \geq 0$.

2. *If*

$$\frac{\beta-\sigma_a}{\beta} \geq \frac{1}{p}\left(1+\frac{s+1}{\tau}\right), \tag{2.6}$$

then there exists $\overline{\kappa} \geq 0$ such that

(i) *if $\kappa > \overline{\kappa}$, then (u_*, v_*) is locally asymptotically stable;*
(ii) *if $\kappa < \overline{\kappa}$, then (u_*, v_*) is unstable;*
(iii) *system (2.1) undergoes a Hopf bifurcation when $\kappa = \overline{\kappa}$ at the positive equilibrium (u_*, v_*), and (2.1) possesses at least one periodic orbit for any $\kappa < \overline{\kappa}$;*
(iv) *if $\frac{\beta-\sigma_a}{\beta} = \frac{1}{p}\left(1+\frac{s+1}{\tau}\right)$, then $\overline{\kappa} = 0$.*

Proof. Since the Jacobian matrix at the positive equilibrium (u_*, v_*) is

$$\begin{pmatrix} -1+\rho_a \dfrac{pu_*^{p-1}}{(1+\kappa u_*^p)^2 v_*^q} & -q\rho_a \dfrac{u_*^p}{1+\kappa u_*^p} v_*^{-q-1} \\ \dfrac{r\rho_h}{\tau}\dfrac{u_*^{r-1}}{v_*^s} & -\dfrac{s+1}{\tau} \end{pmatrix},$$

using Eq. (2.3) and $v_* = (\rho_h u_*^r)^{\frac{1}{s+1}}$, we can calculate the determent of Jacobian matrix to be

$$D(u_*) = \frac{1}{\tau}\left[s+1+\rho_a \rho_h^{-\frac{q}{s+1}} \frac{u_*^{p-1-\frac{qr}{s+1}}}{1+\kappa u_*^p}\left(-\frac{p(s+1)}{1+\kappa u_*^p}+qr\right)\right],$$

and the trace of Jacobian matrix is

$$T(u_*) = -\left(1+\frac{s+1}{\tau}\right)+\rho_a^{-1}\rho_h^{\frac{q}{s+1}} p u_*^{-p-1+\frac{qr}{s+1}}(u_*-\sigma_a)^2.$$

Since $p/r \leq q/(s+1)$, we see that for any $\sigma_a < u_* \leq \beta$, $D(u_*) > 0$ and $T'(u) > 0$ for $u > \sigma_a$. If (2.5) is satisfied, then $T(\beta) < 0$. Hence for any $\sigma_a < u_* < \beta$, $T(u_*) < 0$, which implies that (u_*, v_*) is locally asymptotically stable for any $\kappa \geq 0$ if (2.5) is satisfied.

On the other hand, if (2.6) is satisfied, by using $T'(u) > 0$ and $T(\sigma_a) < 0$, then we see that there exists a unique $\overline{u}_*$ such that $T(u_*) > 0$ for $u_* > \overline{u}_*$, $T(u_*) < 0$ for $u_* < \overline{u}_*$, and $T(\overline{u}_*) = 0$. Since $u_*(\kappa)$ is strictly decreasing in κ, there exists $\overline{\kappa} \geq 0$ such that when $\kappa > \overline{\kappa}$, then (u_*, v_*) is locally asymptotically stable; when $\kappa < \overline{\kappa}$, then (u_*, v_*) is unstable, and

$$\left.\frac{dT(u(\kappa))}{d\kappa}\right|_{\kappa=\overline{\kappa}} = \left.\frac{dT(u)}{du}\right|_{u=u(\kappa)} \cdot \left.\frac{du(\kappa)}{d\kappa}\right|_{\kappa=\overline{\kappa}} < 0.$$

System (2.1) undergoes a Hopf bifurcation at the positive equilibrium (u_*, v_*) for $\kappa = \overline{\kappa}$, and from Poincáre–Bendixson theory, system (2.1) possesses a periodic orbit when $\kappa < \overline{\kappa}$. It is easy to verify that if $\frac{\beta-\sigma_a}{\beta} = \frac{1}{p}\left(1+\frac{s+1}{\tau}\right)$, then $\overline{\kappa} = 0$. □

Remark 2.3. We notice that β is a numerical value which depends on all other parameters except κ and τ, and in general β cannot be explicitly solved. Also the condition $p/r \leq q/(s+1)$ in Theorem 2.2 is more restrictive than $(p-1)/r < q/(s+1)$ in Lemma 2.1. But for the special case $p = r = 2$, $s = 0$ and $q = 1$ as in (1.2), one can directly calculate $\beta = \sigma_a + \rho_a\rho_h^{-1}$ and $\frac{\beta-\sigma_a}{\beta_a} = \frac{\rho_a\rho_h^{-1}}{\sigma_a+\rho_a\rho_h^{-1}}$ in Theorem 2.2. We choose $\sigma_a = 0.5$, $\rho_a = 1$, $\rho_h = 1$, and $\tau = 4$, then in this case we have that $\overline{\kappa} \approx 0.0234$ (see Fig. 1).

We also remark that here we have only given some elementary analysis of the kinetic model, and a more detailed study of the dynamics of (2.1) is still missing. For the non-saturation case $\kappa = 0$, the kinetic model (2.1) was recently considered in [55].

2.2. Comparison methods for delayed reaction–diffusion systems [47]

In this subsection, we recall some known results on the upper–lower solution methods for reaction–diffusion systems with delays and Neumann boundary condition proposed by Pao [45,47]. This method can also be applied to reaction–diffusion system without delays, as in Pao [44].

Consider two vector-valued function $\mathbf{f}, \mathbf{g} : \mathcal{O} \times \mathcal{O}^* \to \mathbb{R}^2$, where $\mathcal{O}$ and $\mathcal{O}^*$ are subsets of $\mathbb{R}^2$ and

$$\mathbf{f}(\mathbf{u}, \mathbf{w}) = (f_1(\mathbf{u}, \mathbf{w}), f_2(\mathbf{u}, \mathbf{w})), \quad (\mathbf{u}, \mathbf{w}) \in \mathcal{O} \times \mathcal{O}^*,$$
$$\mathbf{g}(\mathbf{l}, \mathbf{m}) = (g_1(\mathbf{l}, \mathbf{m}), g_2(\mathbf{l}, \mathbf{m})), \quad (\mathbf{l}, \mathbf{m}) \in \mathcal{O} \times \mathcal{O}^*.$$

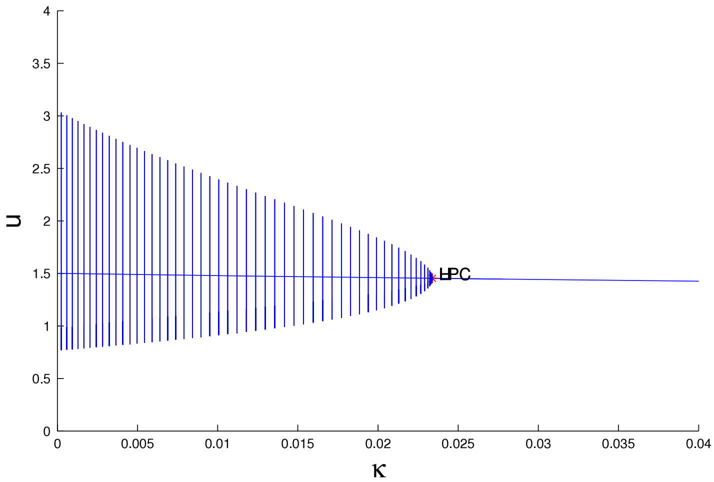

Fig. 1. Hopf bifurcation diagram with parameter κ. Here $p = r = 2$, $s = 0$, $q = 1$, $\sigma_a = 0.5$, $\rho_a = 1$, $\rho_h = 1$. The horizontal axis is κ, the vertical axis is u, and the vertical lines represent the u-range of the periodic orbits. Here a family of limit cycles bifurcate from the Hopf point $\overline{\kappa} \approx 0.0234$ and the direction of the Hopf bifurcation is backward and supercritical. The diagram is plotted using `Matcont`.

By writing the vector $\mathbf{u}$, $\mathbf{w}$, $\mathbf{l}$ and $\mathbf{m}$ in the split form

$$\mathbf{u} \equiv (u_i, [\mathbf{u}]_{a_i}, [\mathbf{u}]_{b_i}), \qquad \mathbf{w} \equiv ([\mathbf{w}]_{e_i}, [\mathbf{w}]_{d_i}), \qquad \mathbf{l} \equiv ([\mathbf{l}]_{\alpha_i}, [\mathbf{l}]_{\beta_i}), \qquad \mathbf{m} \equiv ([\mathbf{m}]_{\gamma_i}, [\mathbf{m}]_{\delta_i})$$

where $[\mathbf{v}]_\sigma$ denotes a vector with σ number of components of $\mathbf{v}$ for $\mathbf{v} = \mathbf{u}, \mathbf{w}, \mathbf{l}$ or $\mathbf{m}$, the function $\mathbf{f}(\mathbf{u}, \mathbf{w})$ is said to be quasimonotone in $\mathcal{O} \times \mathcal{O}^*$ if for any $i = 1, 2$, there exist nonnegative integers a_i, b_i, e_i and d_i satisfying the relations

$$a_i + b_i = 1, \qquad e_i + d_i = 2 \tag{2.7}$$

such that the function

$$f_i(\mathbf{u}, \mathbf{w}) \equiv f_i(u_i, [\mathbf{u}]_{a_i}, [\mathbf{u}]_{b_i}, [\mathbf{w}]_{e_i}, [\mathbf{w}]_{d_i})$$

is nondecreasing in each component of $[\mathbf{u}]_{a_i}$ and $[\mathbf{w}]_{e_i}$, and is nonincreasing in each component of $[\mathbf{u}]_{b_i}$ and $[\mathbf{w}]_{d_i}$. Similarly, the function $\mathbf{g}(\mathbf{l}, \mathbf{m})$ is said to be quasimonotone in $\mathcal{O} \times \mathcal{O}^*$ if for any $i = 1, 2$, there exist nonnegative integers α_i, β_i, γ_i and δ_i satisfying the relations

$$\alpha_i + \beta_i = 2, \qquad \gamma_i + \delta_i = 2 \tag{2.8}$$

such that the function

$$g_i(\mathbf{l}, \mathbf{m}) \equiv g_i([\mathbf{l}]_{\alpha_i}, [\mathbf{l}]_{\beta_i}, [\mathbf{m}]_{\gamma_i}, [\mathbf{m}]_{\delta_i})$$

is nondecreasing in each component of $[\mathbf{l}]_{\alpha_i}$ and $[\mathbf{m}]_{\gamma_i}$, and is nonincreasing in each component of $[\mathbf{l}]_{\beta_i}$ and $[\mathbf{m}]_{\delta_i}$.

We consider the following general reaction–diffusion system with delay and nonlocal effect:

$$\begin{cases} \dfrac{\partial u_1}{\partial t} = D_1 \Delta u_1 + f_1(u_1(x,t), u_2(x,t), u_1(x,t-\gamma), u_2(x,t-\gamma)) \\ \qquad + \displaystyle\int_\Omega k_1(x,y) g_1(u_1(y,t), u_2(y,t), u_1(y,t-\gamma), u_2(y,t-\gamma)) dy, & x \in \Omega,\ t > 0, \\ \dfrac{\partial u_2}{\partial t} = D_2 \Delta u_2 + f_2(u_1(x,t), u_2(x,t), u_1(x,t-\gamma), u_2(x,t-\gamma)) \\ \qquad + \displaystyle\int_\Omega k_2(x,y) g_2(u_1(y,t), u_2(y,t), u_1(y,t-\gamma), u_2(y,t-\gamma)) dy, & x \in \Omega,\ t > 0, \\ \dfrac{\partial u_1(x,t)}{\partial \nu} = \dfrac{\partial u_2(x,t)}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0, \\ u_1(x,t) = \phi_1(x,t) \ge 0, \qquad u_2(x,t) = \phi_2(x,t) \ge 0, & x \in \Omega,\ t \in [-\gamma, 0], \end{cases} \tag{2.9}$$

where the kernel functions $k_1(x, y)$ and $k_2(x, y)$ satisfy the second assumption in (K). If k_i is the Delta function in (1.6), then we can simply assume $k_i \equiv 0$ in (2.9). Suppose that there exist two vectors $\underline{\mathbf{c}}$ and $\overline{\mathbf{c}}$ in $\mathbb{R}^2$ such that $\underline{\mathbf{c}} \le \overline{\mathbf{c}}$ and for $i = 1, 2$,

$$\begin{aligned} & f_i(\overline{c}_i, [\overline{\mathbf{c}}]_{a_i}, [\underline{\mathbf{c}}]_{b_i}, [\overline{\mathbf{c}}]_{e_i}, [\underline{\mathbf{c}}]_{d_i}) + g_i([\overline{\mathbf{c}}]_{\alpha_i}, [\underline{\mathbf{c}}]_{\beta_i}, [\overline{\mathbf{c}}]_{\gamma_i}, [\underline{\mathbf{c}}]_{\delta_i}) \le 0, \\ & f_i(\underline{c}_i, [\underline{\mathbf{c}}]_{a_i}, [\overline{\mathbf{c}}]_{b_i}, [\underline{\mathbf{c}}]_{e_i}, [\overline{\mathbf{c}}]_{d_i}) + g_i([\underline{\mathbf{c}}]_{\alpha_i}, [\overline{\mathbf{c}}]_{\beta_i}, [\underline{\mathbf{c}}]_{\gamma_i}, [\overline{\mathbf{c}}]_{\delta_i}) \ge 0; \end{aligned} \tag{2.10}$$

$\mathbf{f}(\mathbf{u},\mathbf{w})$ and $\mathbf{g}(\mathbf{l},\mathbf{m})$ are quasimonotone in a subset $\langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle \times \langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle$ where $\langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle = \{\mathbf{c}\in\mathbb{R}^2 : \underline{\mathbf{c}} \le \mathbf{c} \le \overline{\mathbf{c}}\}$, and for each $i = 1, 2$, $f_i(\mathbf{u},\mathbf{w})$ and $g_i(\mathbf{l},\mathbf{m})$ satisfy the Lipschitz condition

$$\begin{aligned} &\left|f_i(\mathbf{u},\mathbf{w}) - f_i(\mathbf{u}',\mathbf{w}')\right| \le K_i(\left|\mathbf{u}-\mathbf{u}'\right| + \left|\mathbf{w}-\mathbf{w}'\right|),\\ &\left|g_i(\mathbf{l},\mathbf{m}) - g_i(\mathbf{l}',\mathbf{m}')\right| \le K_i(\left|\mathbf{l}-\mathbf{l}'\right| + \left|\mathbf{m}-\mathbf{m}'\right|) \end{aligned} \tag{2.11}$$

for $(\mathbf{u},\mathbf{w})$, $(\mathbf{u}',\mathbf{w}')$, $(\mathbf{l},\mathbf{m})$ and $(\mathbf{l}',\mathbf{m}')$ in $\langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle \times \langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle$ and some $K_i > 0$. Following [47] we define two sequences of constant vectors $\{\overline{\mathbf{c}}^m\} = \{(\overline{c}_1^m, \overline{c}_2^m)\}$, $\{\underline{\mathbf{c}}^m\} = \{(\underline{c}_1^m, \underline{c}_2^m)\}$, from the recursion relations

$$\begin{aligned} \overline{c}_i^m &= \overline{c}_i^{m-1} + \frac{1}{K_i} f_i(\overline{c}_i^{m-1}, [\overline{\mathbf{c}}^{m-1}]_{a_i}, [\underline{\mathbf{c}}^{m-1}]_{b_i}, [\overline{\mathbf{c}}^{m-1}]_{e_i}, [\underline{\mathbf{c}}^{m-1}]_{d_i}),\\ &\quad + \frac{1}{K_i} g_i([\overline{\mathbf{c}}^{m-1}]_{\alpha_i}, [\underline{\mathbf{c}}^{m-1}]_{\beta_i}, [\overline{\mathbf{c}}^{m-1}]_{\gamma_i}, [\underline{\mathbf{c}}^{m-1}]_{\delta_i}),\\ \underline{c}_i^m &= \underline{c}_i^{m-1} + \frac{1}{K_i} f_i(\underline{c}_i^{m-1}, [\underline{\mathbf{c}}^{m-1}]_{a_i}, [\overline{\mathbf{c}}^{m-1}]_{b_i}, [\underline{\mathbf{c}}^{m-1}]_{e_i}, [\overline{\mathbf{c}}^{m-1}]_{d_i}),\\ &\quad + \frac{1}{K_i} g_i([\underline{\mathbf{c}}^{m-1}]_{\alpha_i}, [\overline{\mathbf{c}}^{m-1}]_{\beta_i}, [\underline{\mathbf{c}}^{m-1}]_{\gamma_i}, [\overline{\mathbf{c}}^{m-1}]_{\delta_i}), \end{aligned} \tag{2.12}$$

for $m = 1, 2, \ldots,\ i = 1, 2$ and $\overline{\mathbf{c}}^0 = \overline{\mathbf{c}}$, $\underline{\mathbf{c}}^0 = \underline{\mathbf{c}}$. From [47, Lemma 2.1] and [45], the sequences $\{\overline{\mathbf{c}}^m\}$ and $\{\underline{\mathbf{c}}^m\}$ satisfy the monotonicity property

$$\underline{\mathbf{c}} \le \underline{\mathbf{c}}^m \le \underline{\mathbf{c}}^{m+1} \le \overline{\mathbf{c}}^{m+1} \le \overline{\mathbf{c}}^m \le \overline{\mathbf{c}}, \quad m = 1, 2, \ldots. \tag{2.13}$$

Hence there exist limits $\tilde{\mathbf{c}}$ and $\check{\mathbf{c}}$ such that $\lim_{m\to\infty} \overline{\mathbf{c}}^m = \tilde{\mathbf{c}}$ and $\lim_{m\to\infty} \underline{\mathbf{c}}^m = \check{\mathbf{c}}$. From [47, Theorem 2.2], [47, Corollary 2.1] and [45], the asymptotical dynamics of the reaction–diffusion system with delays (2.9) can be obtained as follows:

Theorem 2.4 (*[47]*). *Suppose there exist $\underline{\mathbf{c}} \le \overline{\mathbf{c}}$ satisfying (2.10), $\mathbf{f}(\mathbf{u},\mathbf{w})$ and $\mathbf{g}(\mathbf{l},\mathbf{m})$ are quasimonotone and satisfy (2.11) in $\langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle \times \langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle$. Then for any initial condition $\phi = (\phi_1, \phi_2)$ in $\langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle$, the solution $\mathbf{u}(x,t) = (u_1(x,t), u_2(x,t))$ of system (2.9) satisfies the relation*

$$\underline{\mathbf{c}} \le \mathbf{u}(x,t) \le \overline{\mathbf{c}}, \quad t \in (0,\infty),\ x \in \overline{\Omega}. \tag{2.14}$$

If, in addition, $\check{\mathbf{c}} = \tilde{\mathbf{c}} = \mathbf{c}^*$, then $\mathbf{c}^*$ is the unique steady state solution of system (2.9) in $\langle \underline{\mathbf{c}}, \overline{\mathbf{c}}\rangle$ and

$$\lim_{t\to\infty} \mathbf{u}(x,t) = \mathbf{c}^*, \quad \text{uniformly for } x \in \overline{\Omega}. \tag{2.15}$$

Corollary 2.5 (*[47]*). *Let the conditions in Theorem 2.4 hold, and let*

$$\mathbf{u}(x,t) = (u_1(x,t), u_2(x,t))$$

be the solution of system (2.9) of an arbitrary initial function ϕ. If there exists $t^* > 0$ such that

$$\underline{\mathbf{c}} \le \mathbf{u}(x,t) \le \overline{\mathbf{c}}, \quad \text{for } t^* - \tau \le t \le t^*,\ x \in \overline{\Omega},$$

then $\mathbf{u}(x,t)$ satisfies (2.14) for all $t > t^*$. Moreover if $\check{\mathbf{c}} = \tilde{\mathbf{c}}$, then (2.15) holds.

Remark 2.6. For reaction–diffusion systems without delays, $\mathbf{f}(\mathbf{u},\mathbf{w}) = \mathbf{f}(\mathbf{u})$. And since $\mathbf{f}$ is independent of $\mathbf{w}$, then the choice of e_i and d_i does not affect the equation. The general theory of upper–lower solutions of such systems have been considered in pp. 424–431 of [44], for example.

Remark 2.7. 1. For system (1.4) without delays, $\mathbf{g}(\mathbf{l},\mathbf{m}) = \mathbf{0}$, and $\mathbf{f}(\mathbf{u}) = (f_1(\mathbf{u}), f_2(\mathbf{u}))$, where

$$\begin{aligned} f_1(\mathbf{u}) &= -u + \rho_a \frac{u^p}{(1+\kappa u^p)v^q} + \sigma_a,\\ f_2(\mathbf{u}) &= \frac{1}{\tau}\left(-v + \rho_h \frac{u^r}{v^s}\right), \end{aligned}$$

and $\mathbf{u} = (u, v)$. Here $a_1 = 0, b_1 = 1, a_2 = 1, b_2 = 0$, $[\mathbf{u}]_{b_1} = v$ and $[\mathbf{u}]_{a_2} = u$. In this case, the nonlinearity (f_1, f_2) is called mixed quasimonotone as one of a_i and one of b_i are not zero. Hence the coupled upper solution $(\overline{c}_1, \overline{c}_2)$ and lower solution $(\underline{c}_1, \underline{c}_2)$ of system (1.4) satisfy

$$\begin{aligned} &0 \ge \sigma_a - \overline{c}_1 + \rho_a \frac{\overline{c}_1^p}{(1+\kappa \overline{c}_1^p)\underline{c}_2^q}, \qquad 0 \ge \rho_h \frac{\overline{c}_1^r}{\underline{c}_2^s} - \overline{c}_2,\\ &0 \le \sigma_a - \underline{c}_1 + \rho_a \frac{\underline{c}_1^p}{(1+\kappa \underline{c}_1^p)\overline{c}_2^q}, \qquad 0 \le \rho_h \frac{\underline{c}_1^r}{\overline{c}_2^s} - \underline{c}_2. \end{aligned} \tag{2.16}$$

2. For system (1.7) with local delays, $\mathbf{g}(\mathbf{l},\mathbf{m})=\mathbf{0}$, $\mathbf{f}(\mathbf{u},\mathbf{w})=(f_1(\mathbf{u},\mathbf{w}),f_2(\mathbf{u},\mathbf{w}))$ are defined as

$$f_1(\mathbf{u},\mathbf{w})=-u+\rho_a\frac{w^p}{(1+\kappa w^p)z^q}+\sigma_a,$$
$$f_2(\mathbf{u},\mathbf{w})=\frac{1}{\tau}\left(-v+\rho_h w^r\right),$$

where $\mathbf{u}=(u,v)$, $\mathbf{w}=(w,z)$. Here

$$a_1=0,\quad b_1=1,\quad e_1=1,\quad d_1=1,$$
$$a_2=1,\quad b_2=0,\quad e_2=2,\quad d_2=0,$$

and

$$[\mathbf{u}]_{b_1}=v,\quad [\mathbf{w}]_{e_1}=w,\quad [\mathbf{w}]_{d_1}=z,$$
$$[\mathbf{u}]_{a_2}=u,\quad [\mathbf{w}]_{e_2}=(w,z).$$

Hence the pair of numbers $(\bar{c}_1,\bar{c}_2)$ and $(\underline{c}_1,\underline{c}_2)$ defined in (2.16) are still upper- and lower-solutions of (1.7). We notice that here variables u and z are both missing in f_2, hence (a_2,b_2) can also be $(0,1)$, and (e_2,d_2) can also be $(1,1)$. This does not affect the choice of upper- and lower-solutions.

3. For system (1.6) with nonlocal delays, $\mathbf{f}(\mathbf{u})=(f_1(\mathbf{u}),f_2(\mathbf{u}))$ and $\mathbf{g}(\mathbf{m})=(g_1(\mathbf{m}),g_2(\mathbf{m}))$ are defined as

$$f_1(\mathbf{u})=-u+\sigma_a,\qquad f_2(\mathbf{u})=-\frac{1}{\tau}v,$$
$$g_1(\mathbf{m})=\rho_a\frac{w^p}{(1+\kappa w^p)z^q},\qquad g_2(\mathbf{m})=\frac{1}{\tau}\left(\rho_h w^r\right),$$

where $\mathbf{u}=(u,v)$, $\mathbf{m}=(w,z)$. Here

$$\gamma_1=1,\quad \delta_1=1,\quad \text{and}\quad \gamma_2=2,\quad \delta_2=0,$$

and

$$[\mathbf{m}]_{\gamma_1}=w,\quad [\mathbf{w}]_{\delta_1}=z,\quad \text{and}\quad [\mathbf{w}]_{e_2}=(w,z).$$

Hence the pair of numbers $(\bar{c}_1,\bar{c}_2)$ and $(\underline{c}_1,\underline{c}_2)$ defined in (2.16) are still upper- and lower-solutions of (1.6). Here we remark that a_i,b_i,c_i,d_i,α_i and β_i for $i=1,2$ can be any nonnegative integers satisfying Eqs. (2.7) and (2.8).

3. Global attractivity for system without delay and nonlocal effect

In this section we analyze system (1.4) which is without the delay effect. For more precise asymptotic behavior of the solutions, we recall the following well-known result, and for the convenience of readers, we also sketch a proof.

Lemma 3.1. *Assume that $h:(0,\infty)\to\mathbb{R}$ is a smooth function so that $h(w)(w-w_0)<0$ for any $w>0$ and $w\neq w_0$, $h(w_0)=0$. Consider the initial–boundary value problem*

$$\begin{cases}\tau\dfrac{\partial w}{\partial t}=D\Delta w+h(w), & x\in\Omega,\ t>t_0,\\ \dfrac{\partial w(x,t)}{\partial\nu}=0, & x\in\partial\Omega,\ t>t_0,\\ w(x,t_0)>0, & x\in\Omega\end{cases}\tag{3.1}$$

where $\tau,D>0$, $t_0\in\mathbb{R}$, then $w(x,t)$ exists for all $t>t_0$, $w(x,t)\to w_0$ uniformly for $x\in\overline{\Omega}$ as $t\to\infty$.

Proof. Let $M=\max\{\max_{x\in\overline{\Omega}}w(x,t_0),w_0\}$ and $m=\min\{\min_{x\in\overline{\Omega}}w(x,t_0),w_0\}$. Then it is easy to see that $u_M(t)\ge w(x,t)\ge u_m(t)$, where $u_M(t)$ and $u_m(t)$ are the solutions of $\tau u'=h(u)$ with initial conditions $u_M(t_0)=M$ and $u_m(t_0)=m$ respectively. Then the convergence of $w(x,t)$ follows from the convergence of $u_M(t)$ and $u_m(t)$. □

First we prove that any solution of system (1.4) is attracted by an invariant rectangular region.

Theorem 3.2. *Suppose that the parameters $\rho_a,\rho_h,\sigma_a,\tau,p,q,r,\kappa,\epsilon,D>0$, $s\ge 0$. Choose a constant ϵ_0 so that*

$$0<\epsilon_0<\min\left\{\frac{\sigma_a}{2},\rho_h^{\frac{1}{s+1}}\left(\frac{\sigma_a}{2}\right)^{\frac{r}{s+1}}\right\},$$

and define

$$\underline{c}_1=\sigma_a-\epsilon_0,\qquad \underline{c}_2=(\rho_h\underline{c}_1^r)^{1/(s+1)}-\epsilon_0,$$
$$\bar{c}_1=\sigma_a+\rho_a\frac{1}{\kappa\underline{c}_2^q}+\epsilon_0,\qquad \bar{c}_2=(\rho_h\bar{c}_1^r)^{1/(s+1)}+\epsilon_0.$$

Then this chosen $(\underline{c}_1, \underline{c}_2)$ *and* $(\overline{c}_1, \overline{c}_2)$ *satisfy*

$$0 < \underline{c}_1 < \sigma_a < \sigma_a + \rho_a \frac{1}{\kappa \underline{c}_2^q} < \overline{c}_1, \qquad 0 < \underline{c}_2 < (\rho_h \underline{c}_1^r)^{1/(s+1)} < (\rho_h \overline{c}_1^r)^{1/(s+1)} < \overline{c}_2, \tag{3.2}$$

and for any initial value $\phi = (u_0(x), v_0(x))$, *where* $u_0(x) > 0$, $v_0(x) > 0$ *for all* $x \in \overline{\Omega}$, *system (1.4) has a unique global solution* $(u(x,t), v(x,t))$, *and there exists* $t_0(\phi)$ *such that* $(u(x,t), v(x,t))$ *satisfies*

$$(\underline{c}_1, \underline{c}_2) \le (u(x,t), v(x,t)) \le (\overline{c}_1, \overline{c}_2),$$

for any $t > t_0(\phi)$. *In particular,*

$$\liminf_{t\to\infty} u(x,t) \ge \sigma_a, \qquad \liminf_{t\to\infty} v(x,t) \ge (\rho_h \sigma_a^r)^{1/(s+1)},$$
$$\limsup_{t\to\infty} u(x,t) \le \sigma_a + \rho_a \frac{1}{\kappa (\rho_h \sigma_a^r)^{q/(s+1)}}, \quad \text{and}$$
$$\limsup_{t\to\infty} v(x,t) \le \left(\rho_h \left(\sigma_a + \rho_a \frac{1}{\kappa (\rho_h \sigma_a^r)^{q/(s+1)}}\right)^r\right)^{1/(s+1)}.$$

Proof. Since $u(x,t)$ satisfies

$$\frac{\partial u}{\partial t} = \epsilon^2 \Delta u + \sigma_a - u + \rho_a \frac{u^p}{(1+\kappa u^p) v^q} \ge \epsilon^2 \Delta u + \sigma_a - u,$$

and the Neumann boundary condition, and the solution of $u_t = \epsilon^2 \Delta u + \sigma_a - u$ with same initial condition converges to σ_a from Lemma 3.1, from the comparison principle of parabolic equations, for the initial value ϕ there exists $t_1(\phi) > 0$ such that for any $t > t_1(\phi)$, $u(x,t) \ge \underline{c}_1 = \sigma_a - \epsilon_0 > 0$. And consequently $v(x,t)$ satisfies

$$\tau \frac{\partial v}{\partial t} = D\Delta v - v + \rho_h \frac{u^r}{v^s} \ge D\Delta v - v + \frac{\rho_h \underline{c}_1^r}{v^s}$$

for $t > t_1(\phi)$. Again we apply Lemma 3.1 to the equation

$$\tau \frac{\partial v}{\partial t} = D\Delta v - v + \frac{\rho_h \underline{c}_1^r}{v^s}, \tag{3.3}$$

and any positive solution of (3.3) converges to the steady state $(\rho_h \underline{c}_1^r)^{1/(s+1)}$. Since $\epsilon_0 < \min\left\{\frac{\sigma_a}{2}, \rho_h^{\frac{1}{s+1}} \left(\frac{\sigma_a}{2}\right)^{\frac{r}{s+1}}\right\}$, we see that $\underline{c}_2 = (\rho_h \underline{c}_1^r)^{1/(s+1)} - \epsilon_0 > 0$. Hence there exists $t_2(\phi) \ge t_1(\phi)$ such that for any $t > t_2(\phi)$, $v(x,t) \ge \underline{c}_2$. And consequently for $t > t_2(\phi)$,

$$\frac{\partial u}{\partial t} = \epsilon^2 \Delta u + \sigma_a - u + \rho_a \frac{u^p}{(1+\kappa u^p) v^q} \le \epsilon^2 \Delta u + \sigma_a - u + \frac{\rho_a}{\kappa \underline{c}_2^q}.$$

Similar to the last two steps, any positive solution of

$$\frac{\partial u}{\partial t} = \epsilon^2 \Delta u + \sigma_a - u + \frac{\rho_a}{\kappa \underline{c}_2^q}$$

converges to the steady state $\sigma_a + \frac{\rho_a}{\kappa \underline{c}_2^q}$. Hence there exists $t_3(\phi) \ge t_2(\phi)$ such that for any $t > t_3(\phi)$, $u(x,t) \le \overline{c}_1 = \sigma_a + \rho_a \frac{1}{\kappa \underline{c}_2^q} + \epsilon_0$, and correspondingly

$$\tau \frac{\partial v}{\partial t} = D\Delta v - v + \rho_h \frac{u^r}{v^s} \le D\Delta v - v + \frac{\rho_h \overline{c}_1^r}{v^s}$$

for $t > t_3(\phi)$. Finally observe that the steady state solution of

$$\tau\frac{\partial v}{\partial t} = D\Delta v - v + \frac{\rho_h \overline{c}_1^r}{v^s}$$

is $(\rho_h \overline{c}_1^r)^{1/(s+1)}$. Hence there exists $t_0(\phi) > t_3(\phi)$ such that for any $t > t_0(\phi)$, $v(x,t) \le \overline{c}_2 = (\rho_h\overline{c}_1^r)^{1/(s+1)} + \epsilon_0$. □

Remark 3.3. Define $X^+ = \{\phi \in C(\overline{\Omega}, \mathbb{R}^2) : \phi > (0,0)^T\}$, and then from Theorem 3.2, there exists a semiflow $\Phi(t) = U(\cdot, t) : X^+ \to X^+$ induced by system (1.4), where $U(x,t)$ is the solution of system (1.4). Using the comparison principle of parabolic equations, we can obtain that for any initial value $\phi = (u_0(x), v_0(x))$ satisfying $(\underline{c}_1, \underline{c}_2) \le \phi \le (\overline{c}_1, \overline{c}_2)$, the corresponding solution $(u(x,t), v(x,t))$ satisfies $(\underline{c}_1, \underline{c}_2) \le (u(x,t), v(x,t)) \le (\overline{c}_1, \overline{c}_2)$. Then define

$$M := \{\phi \in C(\overline{\Omega}) : (\underline{c}_1, \underline{c}_2) \le \phi \le (\overline{c}_1, \overline{c}_2)\}, \tag{3.4}$$

and M is positively invariant and is attracting. Then from [56, Theorem 3.4.8], $\Phi(t) = U(\cdot,t) : X^+ \to X^+$ has a global compact attractor.

Next we want to give some results of the global compact attractor of the semiflow $\Phi(t)$. Using the upper and lower solution method [44,46,47], we can obtain when the saturation effect is strong, system (1.4) has a unique positive constant steady state (u_*, v_*) which is the global attractor of semiflow $\Phi(t) = U(\cdot, t) : X^+ \to X^+$.

Theorem 3.4. *Suppose that the parameters $\rho_a, \rho_h, \sigma_a, \tau, p, q, r, \kappa, \epsilon, D > 0$, and $s \ge 0$. Then there exists κ_0 depending only on σ_a, ρ_a and ρ_h such that for any $\kappa > \kappa_0$, system (1.4) has a unique positive constant steady state solution (u_*, v_*), which is the global attractor of the semiflow $\Phi(t) = U(\cdot,t) : X^+ \to X^+$. That is, for any initial value $\phi = (u_0(x), v_0(x))$, where $u_0(x) > 0$, $v_0(x) > 0$, the corresponding solution $(u(x,t), v(x,t))$ of system (1.4) converges uniformly to (u_*, v_*) as $t \to \infty$.*

Proof. From Theorem 3.2, we know that $\overline{c}_1, \underline{c}_1, \overline{c}_2$ and $\underline{c}_2$ satisfy (3.2). From (3.2), we obtain that

$$\begin{aligned} &0 \ge \sigma_a - \overline{c}_1 + \rho_a\frac{\overline{c}_1^p}{(1+\kappa\overline{c}_1^p)\underline{c}_2^q}, \qquad 0 \ge \rho_h\frac{\overline{c}_1^r}{\overline{c}_2^s} - \overline{c}_2,\\ &0 \le \sigma_a - \underline{c}_1 + \rho_a\frac{\underline{c}_1^p}{(1+\kappa\underline{c}_1^p)\overline{c}_2^q}, \qquad 0 \le \rho_h\frac{\underline{c}_1^r}{\underline{c}_2^s} - \underline{c}_2. \end{aligned} \tag{3.5}$$

Then $(\overline{c}_1, \overline{c}_2)$ and $(\underline{c}_1, \underline{c}_2)$ is a pair of coupled upper and lower solution of system (1.4). It is clear that there exists $K > 0$ such that for any $(\underline{c}_1, \underline{c}_2) \le (u_1, v_1), (u_2, v_2) \le (\overline{c}_1, \overline{c}_2)$,

$$\begin{aligned} &\left| -u_1 + \rho_a\frac{u_1^p}{(1+\kappa u_1^p)v_1^q} + u_2 - \rho_a\frac{u_2^p}{(1+\kappa u_2^p)v_2^q}\right| \le K(|u_1-u_2| + |v_1-v_2|),\\ &\tau^{-1}\left|\rho_h\frac{u_1^r}{v_1^s} - v_1 - \rho_h\frac{u_2^r}{v_2^s} + v_2\right| \le K(|u_1-u_2|+|v_1-v_2|). \end{aligned}$$

We define two iteration sequences $(\overline{c}_1^m, \overline{c}_2^m)$ and $(\underline{c}_1^m, \underline{c}_2^m)$ as follows: for $m \ge 1$,

$$\begin{aligned} \overline{c}_1^m &= \overline{c}_1^{m-1} + \frac{1}{K}\left(\sigma_a - \overline{c}_1^{m-1} + \rho_a\frac{(\overline{c}_1^{m-1})^p}{(1+\kappa(\overline{c}_1^{m-1})^p)(\underline{c}_2^{m-1})^q}\right),\\ \overline{c}_2^m &= \overline{c}_2^{m-1} + \frac{1}{K}\left(\rho_h\frac{(\overline{c}_1^{m-1})^r}{(\overline{c}_2^{m-1})^s} - \overline{c}_2^{m-1}\right),\\ \underline{c}_1^m &= \underline{c}_1^{m-1} + \frac{1}{K}\left(\sigma_a - \underline{c}_1^{m-1} + \rho_a\frac{(\underline{c}_1^{m-1})^p}{(1+\kappa(\underline{c}_1^{m-1})^p)(\overline{c}_2^{m-1})^q}\right),\\ \underline{c}_2^m &= \underline{c}_2^{m-1} + \frac{1}{K}\left(\rho_h\frac{(\underline{c}_1^{m-1})^r}{(\underline{c}_2^{m-1})^s} - \underline{c}_2^{m-1}\right), \end{aligned}$$

where $(\overline{c}_1^0, \overline{c}_2^0) = (\overline{c}_1, \overline{c}_2)$ and $(\underline{c}_1^0, \underline{c}_2^0) = (\underline{c}_1, \underline{c}_2)$. Then for $m \ge 1$, $(\underline{c}_1, \underline{c}_2) \le (\underline{c}_1^m, \underline{c}_2^m) \le (\underline{c}_1^{m+1}, \underline{c}_2^{m+1}) \le (\overline{c}_1^{m+1}, \overline{c}_2^{m+1}) \le (\overline{c}_1^m, \overline{c}_2^m) \le (\overline{c}_1, \overline{c}_2)$, and there exist $(\tilde{c}_1, \tilde{c}_2)$ and $(\check{c}_1, \check{c}_2)$ such that $(\overline{c}_1, \overline{c}_2) \ge (\tilde{c}_1, \tilde{c}_2) \ge (\check{c}_1, \check{c}_2) \ge (\underline{c}_1, \underline{c}_2)$ which satisfy $\lim_{m\to\infty}\overline{c}_1^m = \tilde{c}_1$, $\lim_{m\to\infty}\overline{c}_2^m = \tilde{c}_2$, $\lim_{m\to\infty}\underline{c}_1^m = \check{c}_1$, $\lim_{m\to\infty}\underline{c}_2^m = \check{c}_2$ and

$$\begin{aligned} &0 = \sigma_a - \tilde{c}_1 + \rho_a\frac{\tilde{c}_1^p}{(1+\kappa\tilde{c}_1^p)\check{c}_2^q}, \qquad 0 = \rho_h\frac{\tilde{c}_1^r}{\tilde{c}_2^s} - \tilde{c}_2,\\ &0 = \sigma_a - \check{c}_1 + \rho_a\frac{\check{c}_1^p}{(1+\kappa\check{c}_1^p)\tilde{c}_2^q}, \qquad 0 = \rho_h\frac{\check{c}_1^r}{\check{c}_2^s} - \check{c}_2. \end{aligned} \tag{3.6}$$

From (3.6), we obtain that $\tilde{c}_1, \check{c}_1 > \sigma_a$, $\tilde{c}_1 \le \sigma_a + \frac{\rho}{\kappa(\sigma_a)^{\frac{rq}{s+1}}}$, where $\rho = \rho_a \rho_h^{-\frac{q}{s+1}}$, and consequently $\check{c}_1$ and $\tilde{c}_1$ satisfy

$$\check{c}_1 = \rho^{\frac{s+1}{rq}} \left(\frac{\tilde{c}_1^p}{(1+\kappa \tilde{c}_1^p)(\tilde{c}_1 - \sigma_a)} \right)^{\frac{s+1}{rq}}, \qquad \tilde{c}_1 = \rho^{\frac{s+1}{rq}} \left(\frac{\check{c}_1^p}{(1+\kappa \check{c}_1^p)(\check{c}_1 - \sigma_a)} \right)^{\frac{s+1}{rq}}. \tag{3.7}$$

Define $R(x) := \rho^{\frac{s+1}{rq}} \left(\frac{x^p}{(1+\kappa x^p)(x-\sigma_a)} \right)^{\frac{s+1}{rq}}$; we notice that

$$R'(x) = \rho^{\frac{s+1}{rq}} \frac{s+1}{rq} \frac{x^\mu(-\kappa x^{p+1} + (p-1)x - \sigma_a p)}{(1+\kappa x^p)^{\frac{s+1}{qr}+1} (x-\sigma_a)^{\frac{s+1}{qr}+1}}, \tag{3.8}$$

where $\mu = \frac{p(s+1)}{qr} - 1$. Define $\sigma_* = \sigma_a + \frac{\rho}{\kappa(\sigma_a)^{\frac{rq}{s+1}}}$. Hence if $\mu \ge 0$, $p > 1$, and $\kappa > \frac{(p-1)\rho}{(\sigma_a)^{\frac{rq}{s+1}+1}}$, then

$$\kappa \sigma_a^{p+1} - (p-1)\sigma_* + \sigma_a p \ge \kappa \sigma_a^{p+1} > 0,$$

and consequently,

$$-R'(x) \ge \rho^{\frac{s+1}{rq}} \frac{s+1}{rq} \frac{\sigma_a^\mu \left(\kappa \sigma_a^{p+1} - (p-1)\sigma_* + \sigma_a p\right)}{\left(1+\kappa \sigma_*^p\right)^{\frac{s+1}{qr}+1} (\sigma_* - \sigma_a)^{\frac{s+1}{qr}+1}} \tag{3.9}$$

for any $x \in (\sigma_a, \sigma_*]$, and if $\mu < 0$, $p > 1$, and $\kappa > \frac{(p-1)\rho}{(\sigma_a)^{\frac{rq}{s+1}+1}}$, then

$$-R'(x) \ge \rho^{\frac{s+1}{rq}} \frac{s+1}{rq} \frac{\sigma_*^\mu \left(\kappa \sigma_a^{p+1} - (p-1)\sigma_* + \sigma_a p\right)}{\left(1+\kappa \sigma_*^p\right)^{\frac{s+1}{qr}+1} (\sigma_* - \sigma_a)^{\frac{s+1}{qr}+1}} \tag{3.10}$$

for any $x \in (\sigma_a, \sigma_*]$. If $\mu \ge 0$, $p \le 1$, and $\kappa > \frac{(p-1)\rho}{(\sigma_a)^{\frac{rq}{s+1}+1}}$, then

$$-R'(x) \ge \rho^{\frac{s+1}{rq}} \frac{s+1}{rq} \frac{\sigma_a^\mu \left(\kappa \sigma_a^{p+1} + \sigma_a p\right)}{\left(1+\kappa \sigma_*^p\right)^{\frac{s+1}{qr}+1} (\sigma_* - \sigma_a)^{\frac{s+1}{qr}+1}} \tag{3.11}$$

for any $x \in (\sigma_a, \sigma_*]$, and if $\mu < 0$, $p \le 1$, and $\kappa > \frac{(p-1)\rho}{(\sigma_a)^{\frac{rq}{s+1}+1}}$, then

$$-R'(x) \ge \rho^{\frac{s+1}{rq}} \frac{s+1}{rq} \frac{\sigma_*^\mu \left(\kappa \sigma_a^{p+1} + \sigma_a p\right)}{\left(1+\kappa \sigma_*^p\right)^{\frac{s+1}{qr}+1} (\sigma_* - \sigma_a)^{\frac{s+1}{qr}+1}} \tag{3.12}$$

for any $x \in (\sigma_a, \sigma_*]$.

Let $H(\rho, \sigma_a, \kappa)$ be the right hand side of Eqs. (3.9) and (3.10) if $\mu \ge 0$ and $\mu < 0$, respectively for $p > 1$ and be the right hand side of Eqs. (3.11) and (3.12) if $\mu \ge 0$ and $\mu < 0$, respectively for $p \le 1$. Since for any fixed σ_a and ρ, $\lim_{\kappa \to \infty} H(\rho, \sigma_a, \kappa) = +\infty$, then there exists $\kappa_0(\sigma_a, \rho)$ such that $-R'(x) > 1$ for any $\kappa > \kappa_0$ and $x \in (\sigma_a, \sigma_*]$. Then from the intermediate-value theorem,

$$\check{c}_1 - \tilde{c}_1 = R(\tilde{c}_1) - R(\check{c}_1) = R'(\theta)(\tilde{c}_1 - \check{c}_1) \le \vartheta(\tilde{c}_1 - \check{c}_1)$$

for some $\theta \in (\check{c}_1, \tilde{c}_1)$, $\vartheta < -1$ and hence $\check{c}_1 = \tilde{c}_1$.

From Theorem 2.4 and Corollary 2.5, we obtain that there exists κ_0 depending only on σ_a, ρ_a and ρ_h such that for any $\kappa > \kappa_0$, system (1.4) has a unique positive constant steady state solution (u_*, v_*), which is the global attractor of the semiflow $\Phi(t) = U(t, \cdot) : X^+ \to X^+$. □

Remark 3.5. If $p > 1$ and $\kappa > \frac{(p-1)\rho}{(\sigma_a)^{\frac{rq}{s+1}+1}}$, then

$$\kappa \sigma_a^{p+1} - (p-1)\left(\sigma_a + \frac{\rho}{\kappa(\sigma_a)^{\frac{rq}{s+1}}}\right) + \sigma_a p \ge \kappa \sigma_a^{p+1}.$$

If $\kappa > \frac{\rho}{(\sigma_a)^{\frac{rq}{s+1}}}$, then

$$\left(1+\kappa\left(\sigma_a+\frac{\rho}{\kappa(\sigma_a)^{\frac{rq}{s+1}}}\right)^p\right)^{\frac{s+1}{qr}+1}\left(\frac{\rho}{\kappa(\sigma_a)^{\frac{rq}{s+1}}}\right)^{\frac{s+1}{qr}+1} \le \left(1+\frac{\rho}{(\sigma_a)^{\frac{qr}{s+1}}}(\sigma_a+1)^p\right)^{\frac{s+1}{qr}+1}.$$

So if $\mu = \frac{p(s+1)}{qr} - 1 \ge 0$, we can choose

$$\kappa_0 = \max\left\{\frac{(p-1)\rho}{(\sigma_a)^{\frac{rq}{s+1}+1}}, \frac{\rho}{(\sigma_a)^{\frac{rq}{s+1}}}, \frac{\left(1+\frac{\rho}{(\sigma_a)^{\frac{qr}{s+1}}}(\sigma_a+1)^p\right)^{\frac{s+1}{qr}+1}}{\rho^{\frac{s+1}{rq}}\frac{s+1}{rq}\sigma_a^{\mu+p+1}}\right\}$$

in Theorem 3.4. Similarly, we can choose κ_0 in the case of $\mu < 0$.

We consider a special case of $p = r = 2$, $s = 0$ and $q = 1$, and choose $\sigma_a = 0.5$, $\rho_a = 1$, $\rho_h = 1$, and $\tau = 4$. Then we can choose $\kappa_0 \approx 505.965$ in Theorem 3.4, and from Theorem 2.2 we can compute the Hopf bifurcation point is $\overline{\kappa} \approx 0.0234$. Hence there is a rather large gap between the regimes of global stability and oscillatory behavior.

Remark 3.6. Since $\lim_{\rho\to 0} H(\rho, \sigma_a, \kappa) = \lim_{\sigma\to\infty} H(\rho, \sigma_a, \kappa) = \infty$, using the same method as in Theorem 3.4, we can obtain that

1. there exists σ_H depending only on ρ and κ such that for any $\sigma_a > \sigma_H$, (u_*, v_*) is globally asymptotically stable;
2. there exists ρ_H depending only on κ and σ_a such that for any $\rho < \rho_H$, (u_*, v_*) is globally asymptotically stable.

4. Global attractivity for system with nonlocal gene expression time delays

In this section we analyze system (1.6) and assume the gene expression time delay $\gamma > 0$. Denote $X = C(\overline{\Omega}, \mathbb{R}^2)$, and define $A : \mathrm{Dom}(A) \subset X \to X$ by

$$A\phi = \left(\epsilon^2\Delta\phi_1 - \phi_1, \frac{D}{\tau}\Delta\phi_2 - \frac{1}{\tau}\phi_2\right)^T$$

for $\phi = (\phi_1, \phi_2)^T \in X$. It is well known that A generates an analytic, compact and strongly positive semigroup $T(t)$ on X [57]. Let $\mathcal{C} = C([-\gamma, 0], X)$, and define $F : \mathcal{C} \to X$ by

$$F(U)(x) = \begin{pmatrix} \sigma_a + \rho_a \displaystyle\int_\Omega k_1(x,y)\frac{u^p(y,-\gamma)}{(1+\kappa u^p(y,-\gamma))v^q(y,-\gamma)}dy \\ \displaystyle\frac{\rho_h}{\tau}\int_\Omega k_2(x,y)u^r(y,-\gamma)dy \end{pmatrix}, \tag{4.1}$$

where $U = (u, v)^T \in \mathcal{C}$ and each of $k_i(x, y)$ satisfies the assumption (K). Then we consider the following integral equation

$$\begin{cases} U(t) = T(t)\phi(0) + \displaystyle\int_0^t T(t-s)F(U_s)ds, & t > 0, \\ U_0 = \phi \in \mathcal{C}, \end{cases} \tag{4.2}$$

whose solution is called the mild solution of (1.6). Denote

$$\mathcal{C}^+ = \{\phi = (\phi_1, \phi_2)^T \in \mathcal{C} : \phi_1 > 0, \phi_2 > 0\}.$$

Theorem 4.1. *Suppose that the parameters $\rho_a, \rho_h, \sigma_a, \tau, p, q, r, \kappa, \epsilon, D, \gamma > 0, s \ge 0$. Then for any initial value $\phi \in \mathcal{C}^+$, Eq. (4.2) has a unique positive solution $U(\phi, t)$ exists on $[0, \infty)$, and $U(\phi, t)$ is a classical solution of system (1.6) when $t > \gamma$.*

Proof. For any initial values $\phi \in \mathcal{C}^+$, from [57, Theorem 4.3.1], we know that when $0 < t \le \gamma$, Eq. (4.2) has a unique solution $U(t) > 0$ satisfying

$$\begin{cases} U(t) = T(t)\phi(0) + \displaystyle\int_0^t T(t-s)F(U_s)ds, & t > 0, \\ U_0 = \phi \in \mathcal{C}^+. \end{cases}$$

Repeating the above procedure iteratively, we can obtain that the mild solution $U(t) > 0$ (solution of (4.2)) is unique and exists on $[0, \infty)$. Furthermore, from [57, Theorem 4.3.1], $U(t)$ is locally Hölder continuous on $(0, \infty)$. Then from [57, Corollary 4.3.3], we obtain that $U(t)$ is the classical solution of (1.6) when $t > \gamma$. □

Furthermore by using the same method in Section 3, we can easily arrive at the following result of asymptotic bounds of solutions.

Theorem 4.2. *Suppose that the parameters $\rho_a, \rho_h, \sigma_a, \tau, p, q, r, \kappa, \epsilon, D, \gamma > 0$. Choose a constant ϵ_0 so that*

$$0 < \epsilon_0 < \min\left\{\frac{\sigma_a}{2}, \rho_h\left(\frac{\sigma_a}{2}\right)^r\right\},$$

and define

$$\underline{c}_1 = \sigma_a - \epsilon_0, \qquad \underline{c}_2 = \rho_h \underline{c}_1^r - \epsilon_0,$$
$$\overline{c}_1 = \sigma_a + \rho_a \frac{1}{\kappa \underline{c}_2^q} + \epsilon_0, \qquad \overline{c}_2 = \rho_h \overline{c}_1^r + \epsilon_0.$$

Then this chosen $(\underline{c}_1, \underline{c}_2)$ and $(\overline{c}_1, \overline{c}_2)$ satisfy

$$0 < \underline{c}_1 < \sigma_a < \sigma_a + \rho_a \frac{1}{\kappa \underline{c}_2^q} < \overline{c}_1, \qquad 0 < \underline{c}_2 < \rho_h \underline{c}_1^r < \rho_h \overline{c}_1^r < \overline{c}_2, \tag{4.3}$$

and for any initial value $\phi = (u_0(x,t), v_0(x,t))$, where $u_0(x,t) > 0$, $v_0(x,t) > 0$ for all $(x,t) \in \overline{\Omega} \times [-\gamma, 0]$, there exists $t_0(\phi)$ such that the corresponding solution $(u(x,t), v(x,t))$ of system (1.6) satisfies

$$(\underline{c}_1, \underline{c}_2) \le (u(x,t), v(x,t)) \le (\overline{c}_1, \overline{c}_2),$$

for any $t > t_0(\phi)$. In particular,

$$\liminf_{t\to\infty} u(x,t) \ge \sigma_a, \qquad \liminf_{t\to\infty} v(x,t) \ge \rho_h \sigma_a^r,$$
$$\limsup_{t\to\infty} u(x,t) \le \sigma_a + \rho_a \frac{1}{\kappa(\rho_h \sigma_a^r)^q}, \quad \textit{and}$$
$$\limsup_{t\to\infty} v(x,t) \le \rho_h \left(\sigma_a + \rho_a \frac{1}{\kappa(\rho_h \sigma_a^r)^q}\right)^r.$$

Proof. From Theorem 4.1, we know that for any initial values $\phi = (u_0(x), v_0(x))$, $u_0(x) > 0$, $v_0(x) > 0$, the corresponding solution $(u(x,t), v(x,t))$ of system (1.6) exists and is positive for all $t > 0$.

Since $u(x,t)$ satisfies

$$\frac{\partial u}{\partial t} = \epsilon^2 \Delta u + \sigma_a - u + \rho_a \int_\Omega k_1(x,y) \frac{u^p(y, t-\gamma)}{(1+\kappa u^p(y,t-\gamma))v^q(y,t-\gamma)} dy$$
$$\ge \epsilon^2 \Delta u + \sigma_a - u,$$

and the Neumann boundary condition, and the solution of $u_t = \epsilon^2 \Delta u + \sigma_a - u$ with same initial condition converges to σ_a from Lemma 3.1, then from the comparison principle of parabolic equations, for the initial value ϕ there exists $t_1(\phi) > 0$ such that for any $t > t_1(\phi)$, $u(x,t) \ge \underline{c}_1 = \sigma_a - \epsilon_0 > 0$. And consequently $v(x,t)$ satisfies

$$\tau \frac{\partial v}{\partial t} = D\Delta v - v + \rho_h \int_\Omega k_2(x,y) u^r(y, t-\gamma) dy$$
$$\ge D\Delta v - v + \rho_h \underline{c}_1^r$$

for $t > t_1(\phi) + \gamma$. Again we apply Lemma 3.1 to the equation

$$\tau \frac{\partial v}{\partial t} = D\Delta v - v + \rho_h \underline{c}_1^r, \tag{4.4}$$

and any positive solution of (4.4) converges to the steady state $\rho_h \underline{c}_1^r$. Since $\epsilon_0 < \min\left\{\frac{\sigma_a}{2}, \rho_h\left(\frac{\sigma_a}{2}\right)^r\right\}$, then $\underline{c}_2 = \rho_h \underline{c}_1^r - \epsilon_0 > 0$. Hence there exists $t_2(\phi) \ge t_1(\phi) + \gamma$ such that for any $t > t_2(\phi)$, $v(x,t) \ge \underline{c}_2$. And consequently for $t > t_2(\phi) + \gamma$,

$$\frac{\partial u}{\partial t} = \epsilon^2 \Delta u + \sigma_a - u + \rho_a \int_\Omega k_1(x,y) \frac{u^p(y, t-\gamma)}{(1+\kappa u^p(y,t-\gamma))v^q(y,t-\gamma)} dy$$
$$\le \epsilon^2 \Delta u + \sigma_a - u + \frac{\rho_a}{\kappa \underline{c}_2^q}.$$

Similar to the last two steps, any positive solution of

$$\frac{\partial u}{\partial t} = \epsilon^2 \Delta u + \sigma_a - u + \frac{\rho_a}{\kappa \underline{c}_2^q}$$

converges to the steady state $\sigma_a + \frac{\rho_a}{\kappa \underline{c}_2^q}$. Hence there exists $t_3(\phi) \geq t_2(\phi) + \gamma$ such that for any $t > t_3(\phi)$, $u(x, t) \leq \overline{c}_1 = \sigma_a + \rho_a \frac{1}{\kappa \underline{c}_2^q} + \epsilon_0$, and correspondingly

$$\tau \frac{\partial v}{\partial t} = D\Delta v - v + \rho_h \int_\Omega k_2(x, y) u^r(y, t-\gamma) dy \leq D\Delta v - v + \rho_h \overline{c}_1^r$$

for $t > t_3(\phi) + \gamma$. Finally observe that the steady state solution of

$$\tau \frac{\partial v}{\partial t} = D\Delta v - v + \rho_h \overline{c}_1^r$$

is $\rho_h \overline{c}_1^r$. Hence there exists $t_0(\phi) > t_3(\phi) + \gamma$ such that for any $t > t_0(\phi)$, $v(x, t) \leq \overline{c}_2 = (\rho_h \overline{c}_1^r)^{1/(s+1)} + \epsilon_0$. □

Remark 4.3. From the proof of Theorem 4.2, if $s > 0$, then we cannot have the above result of asymptotic bounds of solutions with delays. So we only have the result of bound and global stability for the case of $s = 0$ in this section.

We can also arrive at the following result using the upper and lower solutions method [46,47] by using the similar argument as Theorem 3.4:

Theorem 4.4. *Suppose that the parameters $\rho_a, \rho_h, \sigma_a, \tau, p, q, r, \kappa, \epsilon, D, \gamma > 0$. Then there exists $\kappa_0 > 0$ depending only on σ_a, ρ_a and ρ_h such that for any $\kappa > \kappa_0$, there exists a unique positive constant steady state solution (u_*, v_*) of system (1.6) which is the global attractor of the semiflow $\Phi(t) = U_t(\cdot) : \mathcal{C}^+ \to \mathcal{C}^+$. That is, for any initial values $\phi \in \mathcal{C}^+$, the corresponding solution $(u(x, t), v(x, t))$ converges uniformly to (u_*, v_*) as $t \to \infty$.*

Remark 4.5. Similar to Remark 3.6,

1. there exists σ_H depending only on ρ and κ such that for any $\sigma_a > \sigma_H$, for any positive initial values, the corresponding solution $(u(x, t), v(x, t))$ converges uniformly to (u_*, v_*) as $t \to \infty$;
2. there exists ρ_H depending only on κ and σ_a such that for any $\rho < \rho_H$, for any positive initial values, the corresponding solution $(u(x, t), v(x, t))$ converges uniformly to (u_*, v_*) as $t \to \infty$.

Remark 4.6. The integral operator $L(\phi)(x) = \int_\Omega k(x, y)\phi(y)dy$ defined in (K) is of Fredholm type [58]. The positivity assumption on the linear operator L is easily satisfied if the kernel function $k(x, y) > 0$ for $x, y \in \overline{\Omega}$. The assumption that $\int_\Omega k(x, y)dy = 1$ is equivalent to that the constant function $\phi(x) = 1$ is the eigenfunction corresponding to the principal eigenvalue 1 of L. In many applications, it is also assumed that the kernel $k(x, y)$ is symmetric so that $k(x, y) = k(y, x)$ for $x, y \in \overline{\Omega}$. Under this additional assumption, it is known that $k(x, y)$ must be of form

$$k(x, y) = 1 + \sum_{i=2}^{\infty} \lambda_i \phi_i(x) \phi_i(y), \tag{4.5}$$

where $(\lambda_i, \phi_i(x))$ is the eigenpair of the Fredholm integral operator L satisfying

$$1 = \lambda_1 < |\lambda_2| \leq |\lambda_3| \leq \cdots, \quad \int_\Omega \phi_i^2(x) dx = 1,$$

see [59, p. 243] or [58, p. 63, Theorem 14]. A Fredholm integral operator L with kernel as in (4.5) is known as the Hilbert–Schmidt operator. In the case L is also positive, Mercer's Theorem ([59, p. 245] or [58, p. 90, Theorem 17]) implies that the convergence in (4.5) is uniform and absolute.

5. Conclusions

The role of time delay in a spatiotemporal pattern formation process has received attention in recent research [60,54,61,8,62,10,11]. It adds one more dimension to the already complex reaction–diffusion models which exhibit patterns such as nonhomogeneous steady states and spatiotemporal oscillation [54,10,11]. On the other hand, for certain parameter ranges, the system can achieve the global stability hence no nontrivial patterns exist despite the time delays [50,47]. In this paper, we consider the impact of the saturation rate κ on the dynamics of the Gierer–Meinhardt system with diffusion, gene expression delay and saturation of activator production. For small κ, time-periodic patterns can appear as result of Hopf bifurcation from the homogeneous steady state [54]; and for large κ, the system always stabilizes at the homogeneous steady state in the Gierer–Meinhardt system with saturation and gene expression delays (see Theorem 4.4). Indeed our approach of upper–lower solutions defines an attraction region in the phase space for all parameter ranges, and this attraction region shrinks to a single point for large κ. Identifying this attraction region will be helpful for further analysis of pattern formation dynamics.

For a reaction–diffusion system modeling spatial chemical reactions, it has been shown that the variation of certain system parameters can trigger the transition from a globally asymptotically stable equilibrium to multiple spatially nonhomogeneous steady states or spatially nonhomogeneous time-periodic orbits via a sequence of steady state or Hopf bifurcations [63–65]. Such transitions also occur for the Gierer–Meinhardt system with diffusion and saturation of activator production with κ as the bifurcation parameter, even without the gene expression delay [66]. On the other hand, it is well known that a larger delay usually destabilizes the homogeneous steady state, as shown in [67,49,64] for example, and for the Gierer–Meinhardt system with diffusion, delay and saturation of activator production (that is (1.7)), such an instability/bifurcation result was proved recently in [54]. Instability/bifurcation analysis for the nonlocal system (1.6) is not known yet, as the analytical form of the steady state is not known.

References

[1] A.M. Turing, The chemical basis of morphogenesis, Philos. Trans. R. Soc. Lond. Ser. B 237 (1952) 37–72.
[2] A. Elragig, S. Townley, A new necessary condition for Turing instabilities, Math. Biosci. 239 (2012) 131–138.
[3] M. Liao, X. Tang, C. Xu, Stability and instability analysis for a ratio-dependent predator–prey system with diffusion effect, Nonlinear Anal. RWA 12 (2011) 1616–1626.
[4] L.G. Morelli, K. Uriu, S. Ares, A.C. Oates, Computational approaches to developmental patterning, Science 336 (2012) 187–191.
[5] S. Roth, Mathematics and biology: a Kantian view on the history of pattern formation theory, Dev. Genes Evol. 221 (2011) 255–279.
[6] C. Xu, J. Wei, Hopf bifurcation analysis in a one-dimensional Schnakenberg reaction–diffusion model, Nonlinear Anal. RWA 13 (2012) 1961–1977.
[7] J. Zhou, C. Mu, Positive solutions for a three-trophic food chain model with diffusion and Beddington–Deangelis functional response, Nonlinear Anal. RWA 12 (2011) 902–917.
[8] E.A. Gaffney, N.A.M. Monk, Gene expression time delays and Turing pattern formation systems, Bull. Math. Biol. 68 (2006) 99–130.
[9] L.S. Krezel, Vertebrate development: taming the nodal waves, Curr. Biol. 13 (2003) R7–R9.
[10] S. Seirin Lee, E.A. Gaffney, N.A.M. Monk, The influence of gene expression time delays on Gierer–Meinhardt pattern formation system, Bull. Math. Biol. 72 (2010) 2139–2160.
[11] S. Sen, P. Ghosh, S.S. Riaz, D.S. Ray, Time-delay-induced instabilities in reaction–diffusion systems, Phys. Rev. E 80 (2008) 046212.
[12] A. Gierer, H. Meinhardt, A theory of biological pattern formation, Kybernetik 12 (1972) 30–39.
[13] A. Gierer, H. Meinhardt, Applications of a theory of biological pattern formation based on lateral inhibition, J. Cell Sci. 15 (1974) 321–376.
[14] A. Gierer, Generation of biological patterns and form: some physical, mathematical and logical aspects, Prog. Biophys. Mol. Biol. 37 (1981) 1–47.
[15] L. Edelstein-Keshet, Mathematical Models in Biology, in: The Random House/Birkhäuser Mathematics Series, Random House, Inc., New York, 1988.
[16] J.D. Murray, Mathematical Biology, third ed., Springer-Verlag, Berlin, Heidelberg, 2002.
[17] D. Iron, M. Ward, J. Wei, The stability of spike solutions to the one-dimensional Gierer–Meinhardt model, Physica D 150 (2001) 25–62.
[18] T. Kolokolnikov, W. Sun, M.J. Ward, J. Wei, The stability of a stripe for the Gierer–Meinhardt model and the effect of saturation, SIAM J. Appl. Dyn. Syst. 5 (2006) 313–363.
[19] Y. Nec, M.J. Ward, Dynamics and stability of spike-type solutions to a one dimensional Gierer–Meinhardt model with sub-diffusion, Physica D 241 (2012) 947–963.
[20] I. Takagi, Stability of bifurcating solutions of the Gierer–Meinhardt systems, Tôhoku Math. J. (2) 31 (1979) 221–246.
[21] I. Takagi, Point-condensation for a reaction–diffusion system, J. Differential Equations 61 (1986) 208–249.
[22] J. Wei, M. Winter, On the two-dimensional Gierer–Meinhardt system with strong coupling, SIAM J. Math. Anal. 30 (1999) 1241–1263.
[23] J. Wei, M. Winter, Spikes for the two-dimensional Gierer–Meinhardt system: the weak coupling case, J. Nonlinear Sci. 11 (2001) 415–458.
[24] J. Wei, M. Winter, Spikes for the Gierer–Meinhardt system in two dimensions: the strong coupling case, J. Differential Equations 178 (2002) 478–518.
[25] J. Wei, M. Winter, Existence, classification and stability analysis of multiple-peaked solutions for the Gierer–Meinhardt system in $\mathbb{R}^1$, Methods Appl. Anal. 14 (2007) 119–163.
[26] K. Kurata, K. Morimoto, Construction and asymptotic behavior of multi-peak solutions to the Gierer–Meinhardt system with saturation, Commun. Pure Appl. Anal. 7 (2008) 1443–1482.
[27] K. Morimoto, Construction of multi-peak solutions to the Gierer–Meinhardt system with saturation and source term, Nonlinear Anal. TMA 71 (2009) 2532–2557.
[28] K. Morimoto, Point-condensation phenomena and saturation effect for the one-dimensional Gierer–Meinhardt system, Ann. Inst. H. Poincaré Anal. Non Linéaire 27 (2010) 973–995.
[29] J. Wei, M. Winter, On the Gierer–Meinhardt system with saturation, Commun. Contemp. Math. 6 (2004) 259–277.
[30] S. Abdelmalek, H. Louafi, A. Youkana, Existence of global solutions for a Gierer–Meinhardt system with three equations, Electron. J. Differential Equations 55 (2012) 1–8.
[31] H. Jiang, Global existence of solutions of an activator–inhibitor system, Discrete Contin. Dyn. Syst. A 14 (2006) 737–751.
[32] H. Jiang, W.-M. Ni, A priori estimates of stationary solutions of an activator–inhibitor system, Indiana Univ. Math. J. 56 (2007) 681–732.
[33] K. Suzuki, I. Takagi, On the role of the source terms in an activator–inhibitor system proposed by Gierer and Meinhardt, in: Asymptotic Analysis and Singularities, Elliptic and Parabolic PDEs and Related Problems, in: Adv. Stud. Pure Math., vol. 47-2, Math. Soc. Japan, Tokyo, 2007, pp. 749–766.
[34] K. Suzuki, I. Takagi, Collapse of patterns and effect of basic production terms in some reaction–diffusion systems, in: Current Advances in Nonlinear Analysis and Related Topics, in: GAKUTO Internat. Ser. Math. Sci. Appl., vol. 32, Gakko-Tosho, Tokyo, 2010, pp. 163–187.
[35] I. Takagi, A priori estimates for stationary solutions of an activator–inhibitor model due to Gierer and Meinhardt, Tôhoku Math. J. (2) 34 (1982) 113–132.
[36] S. Seirin Lee, E.A. Gaffney, Aberrant behaviours of reaction diffusion self-organisation models on growing domains in the presence of gene expression time delays, Bull. Math. Biol. 72 (2010) 2161–2179.
[37] S. Seirin Lee, E.A. Gaffney, R.E. Baker, The dynamics of Turing patterns for morphogen-regulated growing domains with cellular response delays, Bull. Math. Biol. 73 (2011) 2527–2551.
[38] S.A. Gourley, J.W.-H. So, Dynamics of a food-limited population model incorporating nonlocal delays on a finite domain, J. Math. Biol. 44 (2002) 49–78.
[39] X. Zhao, Global attractivity in a class of nonmonotone reaction–diffusion equations with time delay, Can. Appl. Math. Q. 17 (2009) 271–281.
[40] N.F. Britton, Spatial structures and periodic travelling waves in an integro-differential reaction–diffusion population model, SIAM J. Appl. Math. 50 (1990) 1663–1688.
[41] S.A. Gourley, N.F. Britton, A predator prey reaction diffusion system with nonlocal effects, J. Math. Biol. 34 (1996) 297–333.
[42] S.A. Gourley, J.W.-H. So, J.H. Wu, Nonlocality of reaction–diffusion equations induced by delay: biological modeling and nonlinear dynamics, J. Math. Sci. 124 (2004) 5119–5153.
[43] H.R. Thieme, X. Zhao, A non-local delayed and diffusive predator–prey model, Nonlinear Anal. RWA 2 (2001) 145–160.
[44] C.V. Pao, Nonlinear Parabolic and Elliptic Equations, Plenum Press, New York, 1992.
[45] C.V. Pao, Coupled nonlinear parabolic systems with time delays, J. Math. Anal. Appl. 196 (1995) 237–265.
[46] C.V. Pao, Dynamics of nonlinear parabolic systems with time delays, J. Math. Anal. Appl. 198 (1996) 751–779.
[47] C.V. Pao, Convergence of solutions of reaction–diffusion systems with time delays, Nonlinear Anal. 48 (2002) 349–362.
[48] S. Chen, J. Shi, Global stability in a diffusive Holling–Tanner predator–prey model, Appl. Math. Lett. 25 (2012) 614–618.

[49] S. Chen, J. Shi, J. Wei, Global stability and Hopf bifurcation in a delayed diffusive Leslie–Gower predator–prey system, Internat. J. Bifur. Chaos 22 (2012) 1250061.
[50] W.Z. Huang, Global dynamics for a reaction–diffusion equation with time delay, J. Differential Equations 143 (1998) 293–326.
[51] T.S. Yi, X.F. Zou, Global attractivity of the diffusive Nicholson blowflies equation with Neumann boundary condition: a non-monotone case, J. Differential Equations 245 (2008) 3376–3388.
[52] Y. Kuang, H.L. Smith, Global stability in diffusive delay Lotka–Volterra systems, Differential Integral Equations 4 (1991) 117–128.
[53] Y. Kuang, H.L. Smith, Convergence in Lotka–Volterra type diffusive delay systems without dominating instantaneous negative feedbacks, J. Aust. Math. Soc. Ser. B 34 (1993) 471–494.
[54] S. Chen, J. Shi, J. Wei, Time delay-induced instabilities and Hopf bifurcations in general reaction–diffusion systems, J. Nonlinear Sci. (2013). http://dx.doi.org/10.1007/s00332-012-9138-1 (in press).
[55] W.-M. Ni, K. Suzuki, I. Takagi, The dynamics of a kinetic activator–inhibitor system, J. Differential Equations 229 (2006) 426–465.
[56] J.K. Hale, Asymptotic Behavior of Dissipative System, American Mathematical Society, Providence, RI, 1988.
[57] A. Pazy, Semigroups of Linear Operators and Applications to Partial Differential Equations, Springer, New York, 1983.
[58] H. Hochstadt, Integral Equations, Wiley Interscience, New York, 1973.
[59] F. Riesz, B. Sz-Nagy, Functional Analysis, Ungar, New York, 1955.
[60] M. Bodnar, A. Bartlomiejczyk, Stability of delay induced oscillations in gene expression of Hes1 protein model, Nonlinear Anal. RWA 13 (2012) 2227–2239.
[61] S. Dutta, D.S. Ray, Effects of delay in a reaction–diffusion system under the influence of an electric field, Phys. Rev. E 77 (2008) 036202.
[62] P. Ghosh, Control of the Hopf–Turing transition by time-delayed global feedback in a reaction–diffusion system, Phys. Rev. E 84 (2011) 016222.
[63] J.Y. Jin, J.P. Shi, J.J. Wei, F.Q. Yi, Bifurcations of patterned solutions in diffusive Lengyel–Epstein system of CIMA chemical reaction, Rocky Mountain J. Math. (2013) (in press).
[64] F.Q. Yi, E.A. Gaffney, P.K. Maini, S. Seirin Lee, Turing instability and Hopf bifurcation in a delayed reaction–diffusion Schnakenberg system, Preprint, 2011.
[65] F.Q. Yi, J.J. Wei, J.P. Shi, Bifurcation and spatiotemporal patterns in a homogeneous diffusive predator–prey system, J. Differential Equations 246 (2009) 1944–1977.
[66] S. Chen, J. Shi, J. Wei, Bifurcation analysis of the Gierer–Meinhardt system with a saturation in the activator production (2012) (submitted for publication).
[67] S. Chen, J. Shi, J. Wei, The effect of delay on a diffusive predator–prey system with Holling Type-II predator functional response, Commun. Pure Appl. Anal. 12 (2013) 481–501.