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QUALITATIVE ANALYSIS OF A MODEL FOR CO-CULTURE OF BACTERIA AND AMOEBAE

Laura Fumanelli

Center for Information Technology
Bruno Kessler Foundation
via Sommarive 18, I-38123 Trento Povo, Italy

Pierre Magal

Institut de Mathématiques de Bordeaux, UMR CNRS 5251 - Case 36
Université Victor Segalen Bordeaux 2
3ter place de la Victoire 33076 Bordeaux Cedex, France

Dongmei Xiao and Xiao Yu

Department of Mathematics
Shanghai Jiao Tong University
Shanghai 200240, China

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Abstract. In this article we analyze a mathematical model presented in [11]. The model consists of two scalar ordinary differential equations, which describe the interaction between bacteria and amoebae. We first give the sufficient conditions for the uniform persistence of the model, then we prove that the model can undergo Hopf bifurcation and Bogdanov-Takens bifurcation for some parameter values, respectively.

1. **Introduction.** Mathematical modeling of bacterial growth has recently attracted increasing attention, also in connection with the problem of nosocomial infections, and different models of growth at the bacterial level have been investigated, in order to understand specific mechanisms of pathogenesis and improve the efficacy of drugs and antibiotics in controlling human infections [17, 8] (and references therein). We also refer to [9] (and reference therein) for more information on models for bacteria populations.

The ability of an organism to cause an infection in a human or animal host is given by its virulence, whose factors can be determined from a genetic point of view [14]. To this end, mammalian hosts are generally used as model hosts for studies on pathogenic bacteria, because their mechanisms of infection are thought to be similar

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to those occurring in humans. However, non-mammalian organisms have also been recently used, such as the nematode *C. elegans*, the insect *D. melanogaster* [15], and the social amoeba *D. discoideum* [5, 10].

In this context, a recent study [11] has been developed on virulence of different strains of the opportunistic human pathogen *Pseudomonas aeruginosa*, by performing co-culture experiments with *Dictyostelium discoideum*. The interaction is characterized by the capability of bacteria of attacking amoebae that, in turn, feed upon bacteria, so that a cross action between the two populations is observed.

Based on these experiments, in [11] a mathematical model has also been developed to describe the interaction between the two populations and to derive the evolution of the system with respect to a few relevant parameters. The model is not a typical predator-prey one, because bacteria are both victims (amoebae feed upon them) and predators (they are pathogenic and thus able to kill amoeba cells). The specific features of the model are:

- in the absence of interactions between both populations, bacteria follow logistic growth, while amoebae decay exponentially;
- amoebae feed on bacteria through a mass-action mechanism, and grow proportionally to the uptake of bacteria;
- bacteria attack and kill amoeba cells through a Holling-type mechanism.

The above peculiarities are included in the following mathematical model, in dimensionless form (see [11] for details):

$$\begin{cases} \dot{u}(t) = \underbrace{u(t)\left(1-u(t)\right)}_{\text{logistic growth of bacteria}} - \underbrace{u(t)v(t)}_{\text{predation of bacteria by amoebae}} \\ \dot{v}(t) = \underbrace{\delta u(t)v(t)}_{\text{predation yield}} - \underbrace{\mu v(t)}_{\text{mortality of amoebae}} - \underbrace{\gamma\frac{u(t)v(t)}{1+Tv(t)}}_{\text{infection of amoebae by bacteria}} \end{cases}, \tag{1}$$

where $u(t)$ is the number of bacteria at time t, and $v(t)$ is the number of amoebae at time t, $\delta > 0$ is the growth rate of amoebae, $\mu > 0$ is the natural mortality rate of amoebae, $\gamma > 0$ is the rate at which bacteria kill amoebae and $T > 0$ is the handling time of amoebae by bacteria.

In [11], existence and stability of positive steady states have been studied under two particular assumptions arising from the experimental framework: namely, it is supposed that $\mu \ll 1$ because the timescale of interactions is small compared with the lifetime of amoebae, and $T \ll 1$ to account for the fast killing of amoebae by bacteria.

In the present work, instead, the dynamics of the same model is explored for the general case: existence and stability of steady states is analyzed in detail, uniform persistence is shown, and a bifurcation analysis is performed. In particular in this article we prove that model undergoes Bogdanov-Takens bifurcation.
The plan of the paper is the following. In section 2 conditions for the existence of nonnegative equilibria are provided. In section 3 we perform a local analysis of equilibria. Section 4 is devoted to Hopf bifurcation. In section 5 we show that Bogdanov-Takens bifurcation occurs.

2. **Preliminary.** We can rewrite model (1) more comfortably as follows:

$$\begin{cases} \dot{u} = u(1-u-v), \\ \dot{v} = v\left(-\mu + \delta u - \dfrac{\gamma u}{1+Tv}\right), \end{cases} \tag{2}$$

We can see that the u-axis and v-axis are invariant under the flow of system (2). Thus $[0,+\infty)\times[0,+\infty)$ is positively invariant (i.e. forward invariant) for (2). In this section, we first describe the equilibria of system (2). Then we will turn to its dissipativity property, and the uniform persistence for system (2).

Equilibria: We first observe that $(1,0)$ and $(0,0)$ are equilibria for all permissible values of parameters. So we just seek conditions for the existence of positive equilibria in $(0,+\infty)\times(0,+\infty)$, which is equivalent to looking for the positive solutions of the following equations

$$\begin{aligned} 1-u-v &= 0, \\ -\mu + \delta u - \frac{\gamma u}{1+Tv} &= 0. \end{aligned} \tag{3}$$

It is clear that equations (3) have no positive solutions if either $\frac{\mu}{\delta}\geq 1$ or u is in the interval $(0,\frac{\mu}{\delta})\cup[1,+\infty)$ or if v is in the interval $[1,+\infty)$. From now on, we shall consider (3) only in the case where $\frac{\mu}{\delta}<u<1$ and $0<v<1$. Thus, (3) is equivalent to

$$v = 1-u,\ u = \frac{\mu}{\delta} + \frac{\gamma u}{\delta(1+T)-\delta T u}.$$

Set

$$f(u) := \frac{\mu}{\delta} + \frac{\gamma u}{\delta(1+T)-\delta T u},\ g(u) := \frac{\gamma u}{\delta(1+T)-\delta T u},\ u\in\left[0, \frac{(1+T)}{T}\right).$$

Then f, g are convex and increasing functions. Moreover

$$f'(u) = g'(u) = \frac{\gamma(1+T)}{\delta((1+T)-Tu)^2}\geq 0,\ f''(u) = g''(u) = \frac{2\gamma(1+T)T}{\delta((1+T)-Tu)^3}\geq 0.$$

It is readily checked that if f has a positive fixed point $u\in(0,1)$, then $\frac{\mu}{\delta}<u<1$, so we just need to discuss conditions for the existence of the fixed point $u\in(0,1)$. The equation $f(u)=u$ is equivalent to the second order equation

$$\delta T u^2 - (\delta(1+T)-\gamma+\mu T)u + \mu(T+1) = 0,$$

having

$$\Delta := (\delta(1+T)-\gamma+\mu T)^2 - 4\delta(T+1)\mu T.$$

Then

$$\begin{aligned} \Delta &= (\delta(1+T)+\mu T)^2 - 2\gamma(\delta(1+T)+\mu T) + \gamma^2 - 4\delta(T+1)\mu T \\ &= (\delta(1+T)-\mu T)^2 - 2\gamma(\delta(1+T)-\mu T) + \gamma^2 - 2\gamma\mu T \end{aligned}$$

so we also have

$$\Delta = (\delta(1+T)-\gamma-\mu T)^2 - 2\mu T\gamma.$$

Set

$$\overline{u}_{\pm} = \frac{(\delta(1+T)-\gamma+\mu T)\pm\sqrt{\Delta}}{2\delta T},$$

and

$$\overline{v}_{\pm} = 1-\overline{u}_{\pm}.$$

whenever $\Delta \geq 0$.

We have

$$f(0) = \frac{\mu}{\delta} < 1, \; f'(0) = \frac{\gamma}{\delta(T+1)},$$
$$f(1) = \frac{\mu+\gamma}{\delta}, \; f'(1) = \frac{\gamma(T+1)}{\delta}, \; g(1) = \frac{\gamma}{\delta}.$$

By using the fact that f is a convex and increasing function, together with the fact that $f = \frac{\mu}{\delta} + g$, we obtain the following result.

Theorem 2.1. *Assume first that $f(0) < 1$ and $f'(0) < 1$. Then the following assertions hold:*

(a) If $\Delta > 0$ we have the following alternatives:
- *(i) If $f(1) < 1$ there is one positive equilibrium $E_0(u_0, v_0) := (\overline{u}_-, \overline{v}_-)$;*
- *(ii) If $f(1) = 1$ and $f'(1) > 1$ there is one positive equilibrium $E_0(u_0, v_0) := (\overline{u}_-, \overline{v}_-)$;*
- *(iii) If $f(1) > 1$ and $f'(1) > 1$, there are two positive equilibria $E_1(u_1, v_1) := (\overline{u}_+, \overline{v}_+)$ and $E_2(u_2, v_2) := (\overline{u}_-, \overline{v}_-)$;*
- *(iv) If either $f(1) > 1$ or $f'(1) \leq 1$, there is no positive equilibrium.*

(b) If $\Delta = 0$ then
- *(i) If $f'(1) > 1$, there is one positive equilibrium $E_0(u_0, v_0) = (\overline{u}_-, \overline{v}_-) = (\overline{u}_+, \overline{v}_+)$;*
- *(ii) If $f'(1) \leq 1$, there is no positive equilibrium.*

(c) If $\Delta < 0$, then there is no equilibrium.

Furthermore, if either $f'(0) \geq 1$ or $f(0) \geq 1$, then there is no positive equilibrium.

We summarize Theorem 2.1 in Figure 1 and Figure 2.

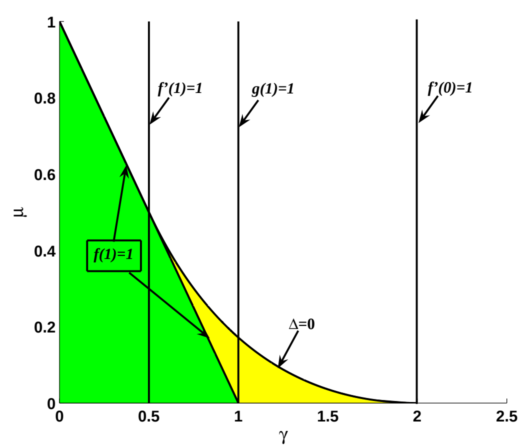

Figure 1: *Number of equilibria in the $(\mu, \gamma)-$plane of parameters. In this figure $T = 1$ and $\delta = 1$. In the green region, the system has one interior equilibrium. In the yellow region, the system has two interior equilibria. In the white region, the system has no interior equilibrium.*

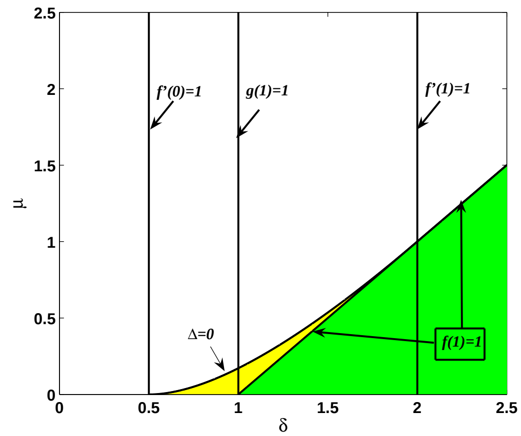

Figure 2: *Number of equilibria in the $(\mu, \delta)-$plane of parameters. In this figure $T = 1$ and $\gamma = 1$. In the green region, the system has one interior equilibrium. In the yellow region, the system has two interior equilibria. In the white region, the system has no interior equilibrium.*

Dissipativity and uniform persistence: We first observe that the subregions

$$\partial D_0 := \left\{(u, v) \in [0, +\infty)^2 : u = 0\right\}$$

and

$$\partial D_1 := \left\{(u, v) \in [0, +\infty)^2 : v = 0\right\}$$

are positively (forward) invariant by the flow. Set

$$D_1 := \{(u, v) : u \in [0, 1]\,, \text{ and } v \geq 0\}\,.$$

Since

$$\dot{u} \leq u(1 - u)$$

we deduce that

$$u(t) \leq \max\left(1, u(0)\right) =: \kappa_0, \forall t \geq 0$$

and

$$\limsup_{t \to +\infty} u(t) \leq 1.$$

Moreover, we have

$$\begin{aligned} \dot{u} &= u(1 - u - v), \\ \dot{v} &\leq v\left(-\mu + u\right), \end{aligned}$$

thus

$$\begin{aligned} (\delta u + v)' &\leq \delta u(\kappa_0 - u) - \mu v \leq \delta \kappa_0(\kappa_0 - u) - \mu v \leq \delta \kappa_0^2 - \delta \kappa_0 u - \mu v \\ &\leq \delta \kappa_0^2 - \min\left(\kappa_0, \mu\right)\left(\delta u + v\right). \end{aligned}$$

So we obtain

$$(\delta u + v)' \leq \delta \kappa_0^2 - \min\left(\kappa_0, \mu\right)\left(\delta u + v\right).$$

Set

$$D_2 := \left\{ (u,v) \in [0,+\infty)^2 : (\delta u + v) \leq \frac{\delta}{\min(1,\mu)} \right\}.$$

In the following proposition, we use the terminology and the results of Hale [12], and we derive the existence of a global attractor for system (2).

Proposition 2.2. *System (2) is point dissipative, and every solution of (2) is attracted by the bounded domain $D_1 \cap D_2$, that is to say that*

$$\limsup_{t\to+\infty} u(t) \leq 1, \text{ and } \limsup_{t\to+\infty} (\delta u(t) + v(t)) \leq \frac{\delta}{\min(1,\mu)}.$$

Moreover $D = D_1 \cap D_2$ is a positively invariant subregion by the semiflow, and system (2) has a global attractor in D.

Uniform persistence: It is clear that ∂D_0 and ∂D_1 are positively invariant. Set

$$M_0 = (0,+\infty) \times (0,+\infty),$$

and

$$\partial M_0 = \mathbb{R}_+^2 \setminus (0,+\infty) \times (0,+\infty) = \partial D_0 \cup \partial D_1.$$

Now, by combining Proposition 2.2 with some local analysis around $(0,0)$ and $(1,0)$, and by applying the result of Hale and Waltman [13], one derives

Proposition 2.3. *System (2) is uniformly persistent with respect to the pair (∂M_0, M_0) if*

$$\delta > \gamma + \mu \ (\Leftrightarrow f(1) < 1).$$

That is, there exists $\varepsilon > 0$, such that for $(u(0), v(0)) \in M_0$, then

$$\liminf_{t\to+\infty} u(t) > \varepsilon \text{ and } \liminf_{t\to+\infty} v(t) > \varepsilon.$$

Furthermore , if $\delta < \gamma + \mu$ ($\Leftrightarrow f(1) > 1$), then $(1,0)$ is locally exponentially stable.

Remark 2.4. *As a consequence of Theorem 2.1, if there exist two equilibria in $(0,\infty)^2$, we must have $\delta < \gamma + \mu$. In this case, by Proposition 2.3, we deduce that the equilibrium on the boundary $(1,0)$ must be locally exponentially stable.*

3. **Local dynamics of nonnegative equilibria.** In this section, we discuss local dynamics of system (2). First, we calculate the jacobian matrix at the equilibrium (u,v), which is

$$J(u,v) := \begin{pmatrix} 1-2u-v & -u \\ \delta v - \gamma \dfrac{v}{1+Tv} & \delta u - \mu - \gamma \frac{u}{(1+Tv)^2} \end{pmatrix}.$$

Obviously, $J(0,0) = \begin{pmatrix} 1 & 0 \\ 0 & -\mu \end{pmatrix}$, so $O(0,0)$ is a hyperbolic saddle for all permissible choices of parameters.

Note that $J(1,0) = \begin{pmatrix} -1 & -1 \\ 0 & -(\mu+\gamma-\delta) \end{pmatrix}$. Therefore, we have the following lemma.

Lemma 3.1. *(i) Equilibrium $E(1,0)$ is a stable node if $\mu+\gamma-\delta > 0$;*

(ii) equilibrium $E(1,0)$ is a saddle-node if $\mu+\gamma-\delta = 0$ and $\gamma T + \gamma - \delta \neq 0$; equilibrium $E(1,0)$ is a stable degenerate node if $\mu+\gamma-\delta = 0$ and $\gamma T+\gamma-\delta = 0$;

(iii) equilibrium $E(1,0)$ is a saddle if $\mu+\gamma-\delta<0$.

Proof. Conclusions (i) and (iii) are clear. We only prove conclusion (ii).

When $\mu+\gamma-\delta=0$, then $E(1,0)$ has one zero eigenvalue. So $E(1,0)$ is degenerate. To determine the topological classification of the equilibrium, we first move $E(1,0)$ to the origin and expand system (2) in a power series around the origin. Let $x_1=u-1$, $x_2=v$. Then system (2) can be transformed into

$$\begin{cases} \dot{x_1} = -x_1 - x_2 - x_1^2 - x_1x_2, \\ \dot{x_2} = (\delta-\gamma)x_1x_2 + (\gamma T+\gamma-\delta)x_2^2 + \gamma T x_1 x_2^2 - \gamma T^2 x_2^3 + R(x_1,x_2,\lambda), \end{cases} \tag{4}$$

where $\lambda=(\delta,\mu,\gamma,T)$, and $R(x_1,x_2,\lambda)$ is a power series in (x_1,x_2) at least of the fourth order. Making the affine transformation

$$y_1 = x_1 + x_2,\ y_2 = x_2$$

and time reversal, system (4) is transformed into

$$\begin{cases} \dot{y_1} = \psi_1(y_1,y_2,\lambda), \\ \dot{y_2} = \psi_2(y_1,y_2,\lambda), \end{cases} \tag{5}$$

where $\lambda=(\delta,\mu,\gamma,T)$ and

$$\psi_1(y_1,y_2,\lambda) = y_1 + y_1^2 - (\delta-\gamma+1)y_1y_2 - (\gamma T+\gamma-\delta)y_2^2 + P_1(y_1,y_2,\lambda),$$
$$\psi_2(y_1,y_2,\lambda) = (\gamma-\delta)y_1y_2 - (\gamma T+\gamma-\delta)y_2^2 - \gamma T y_1 y_2^2 + \gamma T(T+1)y_2^3 + P_2(y_1,y_2,\lambda)$$

where $P_1(y_1,y_2,\lambda)$ is a power series in (y_1,y_2) at least of the third order, $P_2(y_1,y_2,\lambda)$ is a power series in (y_1,y_2) at least of the fourth order.

According to the implicit function theorem, we can get that there exists a smooth function $y_1=\phi(y_2,\lambda)$ in a small neighborhood of the origin such that $\psi_1(\phi(y_2,\lambda),y_2,\lambda)\equiv 0$ in this small neighborhood of the origin, where $\phi(y_2,\lambda) = (\gamma T+\gamma-\delta)y_2^2 + O(y_2^3)$.

Plugging $y_1=\phi(y_2,\lambda)$ into $\psi_2(y_1,y_2,\lambda)$, we have

$$\psi_2(y_1,y_2,\lambda) = -(\gamma T+\gamma-\delta)y_2^2 + \gamma T(T+1)y_2^3 - (\delta-\gamma)(\gamma T+\gamma-\delta)y_2^3 + O(y_2^4).$$

From Theorem 7.1 in Chapter 2 of [19], we obtain that equilibrium $(0,0)$ of system (5) is a saddle-node if $\gamma T+\gamma-\delta\neq 0$, while it is an unstable degenerate node if $\gamma T+\gamma-\delta=0$. This implies that statement (ii) is true since the time in (4) is reversed with respect to (5). □

Let us consider positive equilibria $E_i(u_i,v_i)$, $i=0,1,2$, and use the notation of Theorem 2.1. By some computations, we get

$$J(u_i,v_i) = \begin{pmatrix} -u_i & -u_i \\ \mu\dfrac{v_i}{u_i} & \gamma\dfrac{Tu_iv_i}{(1+Tv_i)^2} \end{pmatrix} \tag{6}$$

The characteristic equation of $J(u_i,v_i)$ is

$$\lambda^2 + u_i\left(1-\frac{\gamma T v_i}{(1+Tv_i)^2}\right)\lambda + v_i\left(\mu - \frac{\gamma T u_i^2}{(1+Tv_i)^2}\right) = 0. \tag{7}$$

Note that (u_i,v_i) is a positive solution of (3). From Theorem 2.1 and the property of the roots of the characteristic equation (7), we have

Lemma 3.2. *Equilibrium $E_1(u_1,v_1)$ is a hyperbolic saddle, $E_2(u_2,v_2)$ is not degenerate and it is not a saddle (i.e. $det(J(u_2,v_2))>0$), where $0<u_2<u_1<1$. Equilibrium $E_0(u_0,v_0)$ has the following topological classification:*

(i) $E_0(u_0, v_0)$ *is not degenerate if condition (a)-(i) holds. Furthermore under the conditions in (a)-(ii) (i.e.* $f(1) = 1$, $f'(1) > 1$*), there are three cases for* $E_0(u_0, v_0)$*. More precisely,* $E_0(u_0, v_0)$ *is a locally asymptotically stable node or focus if either* $T + 1 \geq \delta$ *or*

$$\begin{cases} T+1<\delta, \\ \gamma<\frac{\delta^2}{(T+1)(\delta-T-1)}; \end{cases}$$

$E_0(u_0, v_0)$ *is an unstable node or focus if*

$$\begin{cases} T+1<\delta, \\ \gamma>\frac{\delta^2}{(T+1)(\delta-T-1)}; \end{cases}$$

$E_0(u_0, v_0)$ *is a weak focus or center if*

$$\begin{cases} T+1<\delta, \\ \gamma=\frac{\delta^2}{(T+1)(\delta-T-1)}. \end{cases}$$

(ii) $E_0(u_0, v_0)$ *is degenerate if condition (b)-(i) holds. More precisely,* $E_0(u_0, v_0)$ *is a cusp if*

$$\begin{cases} \mu=\dfrac{\delta}{T}\left(\sqrt{T+1}-\sqrt{\dfrac{\gamma}{\delta}}\right)^2, \\ \gamma=\left(\sqrt{\dfrac{T+1}{\delta}}+\sqrt{\dfrac{\delta}{T+1}}\right)^2, \\ \delta>\dfrac{T+1}{T}; \end{cases}$$

$E_0(u_0, v_0)$ *is a saddle-node if*

$$\begin{cases} \mu=\dfrac{\delta}{T}\left(\sqrt{T+1}-\sqrt{\dfrac{\gamma}{\delta}}\right)^2, \\ \gamma\neq\left(\sqrt{\dfrac{T+1}{\delta}}+\sqrt{\dfrac{\delta}{T+1}}\right)^2, \\ \dfrac{\delta}{T+1}<\gamma<\delta(T+1). \end{cases}$$

From Theorem 2.1 and Lemma 3.2, we have

Theorem 3.3. *(1) If system (2) has only two equilibria* $O(0, 0)$ *and* $E(1, 0)$*, then* $E(1, 0)$ *is a global attractor which attracts all orbits in the interior of the first quadrant if one of the following conditions holds:*
(a) $\mu - \gamma + \delta > 0$*;*
(b) $\mu - \gamma + \delta = 0$ *and* $\gamma T + \gamma - \delta = 0$*;*

(2) If system (2) has three equilibria $O(0, 0)$*,* $E_0(u_0, v_0)$ *and* $E(1, 0)$*, then system (2) will undergo some bifurcations around* $E_0(u_0, v_0)$*, such as saddle-node bifurcation, Hopf bifurcation and Bogdanov-Takens bifurcation for some parameters.*

(3) If system (2) has four equilibria $O(0, 0)$*,* $E_1(u_1, v_1)$*,* $E_2(u_2, v_2)$ *and* $E(1, 0)$*, then* $O(0, 0)$ *and* $E_1(u_1, v_1)$ *are hyperbolic,* $E(1, 0)$ *is a stable node and* $E_2(u_2, v_2)$ *will undergo Hopf bifurcation for some parameters.*

4. **Hopf bifurcation of system (2).** In this section, we will assume that one of conditions (a)-(i), (a)-(ii) or (a)-(iii) of Theorem 2.1 is satisfied. We will consider γ as a bifurcation parameter of the system, and we will provide some conditions to derive Hopf bifurcation around $(\overline{u}_-, \overline{v}_-)$ with respect to γ. We recall that $\overline{u}_- \in (\mu/\delta, 1)$ and $\overline{v}_- = 1 - \overline{u}_-$ satisfy the second equation in (3), that is

$$\begin{aligned} & -\mu + \delta\overline{u}_- - \frac{\gamma\overline{u}_-}{1+T\overline{v}_-} = 0 \\ \Leftrightarrow\ & \frac{\mu}{\overline{u}_-} = \delta - \frac{\gamma}{1+T\overline{v}_-} \\ \Leftrightarrow\ & \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-} = \frac{1}{(1+T\overline{v}_-)}. \end{aligned}$$

Then the matrix $J(\overline{u}_-, \overline{v}_-)$ becomes

$$\begin{aligned} J(\overline{u}_-, \overline{v}_-) &= \begin{pmatrix} -\overline{u}_- & -\overline{u}_- \\ \mu\dfrac{\overline{v}_-}{\overline{u}_-} & \gamma\dfrac{T\overline{u}_-\overline{v}_-}{(1+T\overline{v}_-)^2} \end{pmatrix} \\ &= \begin{pmatrix} -\overline{u}_- & -\overline{u}_- \\ \overline{v}_-\left(\delta - \gamma\dfrac{1}{1+T\overline{v}_-}\right) & -\mu + \overline{u}_-\left(\delta - \gamma\frac{1}{(1+T\overline{v}_-)^2}\right) \end{pmatrix} \\ &= \begin{pmatrix} -\overline{u}_- & -\overline{u}_- \\ \overline{v}_-\frac{\mu}{\overline{u}_-} & -\mu + \overline{u}_-\left(\delta - \gamma\left(\frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right)^2\right) \end{pmatrix} \\ &= \begin{pmatrix} -\overline{u}_- & -\overline{u}_- \\ \frac{\mu(1-\overline{u}_-)}{\overline{u}_-} & -\mu + \delta\overline{u}_- - \frac{(\delta\overline{u}_- - \mu)^2}{\gamma\overline{u}_-} \end{pmatrix}, \end{aligned}$$

so we obtain

$$J(\overline{u}_-, \overline{v}_-) = \begin{pmatrix} -\overline{u}_- & -\overline{u}_- \\ \frac{\mu(1-\overline{u}_-)}{\overline{u}_-} & (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right] \end{pmatrix}.$$

Now we study the existence of purely imaginary roots for $J(\overline{u}_-, \overline{v}_-)$. So we look for the value of $\overline{u}_-$ such that $J(\overline{u}_-, \overline{v}_-)$ has a purely imaginary eigenvalue $i\omega$ with $\omega > 0$. This is equivalent to

$$\begin{aligned} & J(\overline{u}_-, \overline{v}_-)\begin{pmatrix} x \\ y \end{pmatrix} = i\omega\begin{pmatrix} x \\ y \end{pmatrix} \\ \Leftrightarrow & \begin{cases} -\overline{u}_-(x+y) = i\omega x \\ \frac{\mu(1-\overline{u}_-)}{\overline{u}_-}x + (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right]y = i\omega y \end{cases} \\ \Leftrightarrow & \begin{cases} y = \left(-1 - \frac{i\omega}{\overline{u}_-}\right)x \\ \frac{\mu(1-\overline{u}_-)}{\overline{u}_-}x + (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right]y = i\omega y \end{cases} \\ \Leftrightarrow & \begin{cases} y = \left(-1 - \frac{i\omega}{\overline{u}_-}\right)x \\ \frac{\mu(1-\overline{u}_-)}{\overline{u}_-} + (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right]\left(-1 - \frac{i\omega}{\overline{u}_-}\right) = i\omega\left(-1 - \frac{i\omega}{\overline{u}_-}\right) \end{cases} \end{aligned}$$

so we obtain

$$\frac{\mu\,(1-\overline{u}_-)}{\overline{u}_-} + (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right]\left(-1 - \frac{i\omega}{\overline{u}_-}\right) = i\omega\left(-1 - \frac{i\omega}{\overline{u}_-}\right).$$

By identifying the real and the imaginary parts, we obtain the system

$$\begin{cases} \frac{\mu(1-\overline{u}_-)}{\overline{u}_-} - (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right] = \frac{\omega^2}{\overline{u}_-} \\ (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right]\frac{\omega}{\overline{u}_-} = \omega \end{cases}$$

$$\Leftrightarrow \begin{cases} \overline{u}_- = (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right] \\ \frac{\omega^2}{\overline{u}_-} = \frac{\mu(1-\overline{u}_-)}{\overline{u}_-} - \overline{u}_- \end{cases}$$

$$\Leftrightarrow \begin{cases} \overline{u}_- = (\delta\overline{u}_- - \mu)\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right] \\ \omega^2 = \mu - \mu\overline{u}_- - \overline{u}_-^2 \end{cases}$$

$$\Leftrightarrow \begin{cases} 1 = \gamma\frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\left[1 - \frac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-}\right] \\ \omega^2 = \mu - \mu\overline{u}_- - \overline{u}_-^2 \end{cases};$$

but $\dfrac{(\delta\overline{u}_- - \mu)}{\gamma\overline{u}_-} = \dfrac{1}{(1+T\overline{v}_-)}$, thus this is also equivalent to

$$\begin{cases} 1 = \gamma\frac{1}{(1+T\overline{v}_-)}\left[1 - \frac{1}{(1+T\overline{v}_-)}\right] \\ \omega = \mu - \mu\overline{u}_- - \overline{u}_-^2 \end{cases}$$

$$\Leftrightarrow \begin{cases} (1+T\overline{v}_-)^2 = \gamma\left[(1+T\overline{v}_-) - 1\right] \\ \omega = \mu - \mu\overline{u}_- - \overline{u}_-^2 \end{cases}$$

$$\Leftrightarrow \begin{cases} (1+T\overline{v}_-)^2 - \gamma(1+T\overline{v}_-) + \gamma = 0 \\ \omega = \mu + \frac{\mu^2}{4} - \left(\overline{u}_- + \frac{\mu}{2}\right)^2. \end{cases}$$

Therefore we have

$$\omega = \mu - \mu\overline{u}_- - \overline{u}_-^2 > 0 \text{ and } \overline{u}_- > 0 \Leftrightarrow \overline{u}_- \leq \sqrt{\mu + \frac{\mu^2}{4}} - \frac{\mu}{2}.$$

Set

$$\chi^*(\gamma) := \frac{\gamma - \sqrt{\gamma(\gamma-4)}}{2} > 1 \ \forall\ \gamma > 4. \tag{8}$$

which is the smallest solution of $x^2 - \gamma x + \gamma = 0$ whenever $\gamma > 4$. We have

$$\chi^*(\gamma) > 2 \text{ for } \forall\ \gamma > 4.$$

Thus we must have $\gamma > 4$, and

$$(1+T\overline{v}_-) = \chi^*(\gamma) \Leftrightarrow T\overline{u}_- = (1+T) - \chi^*(\gamma).$$

If $\gamma \geq (\mu+\delta)(1+T)$, the above inequality is always satisfied. If instead $\gamma < (\mu+\delta)(1+T)$, then we need to impose the condition

$$\overline{u}_- < \frac{\mu(2+T)}{(\mu+\delta)(1+T) - \gamma}.$$

So we finally obtain

$$\begin{cases} \overline{u}_- = T^{-1}\left[(1+T) - \chi^*(\gamma)\right] =: u_0^* \\ 0 < \overline{u}_- < \sqrt{\mu + \frac{\mu^2}{4}} - \frac{\mu}{2}. \end{cases} \tag{9}$$

Lemma 4.1. *Let one of conditions (a)-(i), (a)-(ii) or (a)-(iii) of Theorem 2.1 be satisfied, and assume that $\gamma > 4$. Then the spectrum of $J(u_-, v_-)$ consists of a pair of purely imaginary eigenvalues $\{-i\omega, i\omega\}$ if and only if*

$$\mu = T^{-1}\left[(1+T) - \chi^*(\gamma)\right]\left[\delta - \frac{\gamma}{\chi^*(\gamma)}\right], \tag{10}$$

whenever

$$\frac{\gamma}{\chi^*(\gamma)} < (\delta + \mu), \tag{11}$$

$$(1+T) - T\left[\sqrt{\mu + \frac{\mu^2}{4}} - \frac{\mu}{2}\right] < \chi^*(\gamma) < (1+T). \tag{12}$$

Proof. It remains to find some conditions to verify $u_- = u_0^*$. But $\overline{u}_-$ is the unique positive solution of

$$u = \frac{\mu}{\delta} + \frac{\gamma u}{\delta[1+T-Tu]}$$

and $(1+T-Tu_0^*) = \chi^*(\gamma)$, so it is sufficient to verify

$$\begin{array}{l} \delta u_0^* = \mu + \frac{\gamma u_0^*}{\chi^*(\gamma)} \Leftrightarrow u_0^* = \frac{\mu}{\left[\delta - \frac{\gamma}{\chi^*(\gamma)}\right]} \\ \Leftrightarrow T^{-1}[(1+T) - \chi^*(\gamma)] = \frac{\mu}{\left[\delta - \frac{\gamma}{\chi^*(\gamma)}\right]}. \end{array}$$

□

Remark 4.2. *In the special case* $f(1) = \frac{\mu+\gamma}{\delta} = 1$, *we obtain a unique point in the* (γ, μ)*-plane of parameters*

$$\delta_0 = (T+1)^2, \ \gamma_0 = \frac{(T+1)^2}{T}, \ \textit{and } \mu_0 = \frac{(T+1)^2(T-1)}{T},$$

all the conditions of Lemma 4.1 are satisfied for $T > 1$. *Indeed, in this case we have*

$$\chi^*(\gamma_0) = \frac{T+1}{T}.$$

Condition (11) is satisfied as long as $\gamma_0 > 4$ *is equivalent to* $T > 1$, *and*

$$\begin{array}{l} \mu = T^{-1}[(1+T) - \chi^*(\gamma)]\left[\delta - \frac{\gamma}{\chi^*(\gamma)}\right] \\ \Leftrightarrow \mu = \frac{(T+1)(T-1)}{T^2}\left[\delta - \frac{\gamma T}{T+1}\right] \\ \Leftrightarrow T^2\mu = \delta\left(T^2 - 1\right) - T(T-1)\gamma. \end{array}$$

Now, since $\delta = \mu + \gamma$, *we obtain*

$$\mu = \gamma[T-1],$$

thus (10) is satisfied. Moreover for $T > 1$, *we clearly have*

$$\chi^*(\gamma) < (1+T),$$

and

$$\overline{u}_- = \frac{(1+T) - \chi^*(\gamma)}{T} = \frac{T^2-1}{T^2} = \frac{\mu}{T(T+1)}.$$

Moreover one deduces that

$$\omega = \mu - \mu\overline{u}_- - \overline{u}_-^2 > 0, \ \textit{for } T > 1.$$

Transversality condition: To prove the occurrence of Hopf bifurcation it remains to prove the transversality condition. Now we consider γ as a parameter, and for each γ, we consider $\overline{u}_-(\gamma)$ the unique solution in $(0,1)$ of

$$\delta T\overline{u}_-(\gamma)^2 - (\delta(1+T) - \gamma + \mu T)\overline{u}_-(\gamma) + \mu(T+1) = 0.$$

By deriving this expression, we obtain

$$\begin{aligned}&\overline{u}_-(\gamma)'\left[2\delta T\overline{u}_-(\gamma)-(\delta(1+T)-\gamma+\mu T)\right]+\overline{u}_-(\gamma)=0\\ &\Leftrightarrow \overline{u}_-(\gamma)'\left[\delta T\overline{u}_-(\gamma)^2+\left[\delta T\overline{u}_-(\gamma)^2-(\delta(1+T)-\gamma+\mu T)\overline{u}_-(\gamma)^2\right]\right]+\overline{u}_-(\gamma)^2=0\\ &\Leftrightarrow \overline{u}_-(\gamma)'\left[\delta T\overline{u}_-(\gamma)^2-\mu(T+1)\right]+\overline{u}_-(\gamma)^2=0\end{aligned}$$

thus if $\delta T\overline{u}_-(\gamma)^2\neq\mu(T+1)$, then

$$\frac{d\overline{u}_-}{d\gamma}=\frac{\overline{u}_-{}^2}{[\mu(T+1)-\delta T\overline{u}_-(\gamma)^2]}. \tag{13}$$

Moreover

$$\begin{aligned}&\delta T\overline{u}_-(\gamma)^2\neq\mu(T+1)\\ &\Leftrightarrow -(\delta(1+T)-\gamma+\mu T)\overline{u}_-(\gamma)\neq 0\\ &\Leftrightarrow -(\delta(1+T)-\gamma+\mu T)\neq 0.\end{aligned} \tag{14}$$

Now

$$Trace\,(J(\overline{u}_-(\gamma),\overline{v}_-(\gamma)))=-\overline{u}_-(\gamma)+(\delta\overline{u}_-(\gamma)-\mu)\left[1-\frac{(\delta\overline{u}_-(\gamma)-\mu)}{\gamma\overline{u}_-(\gamma)}\right]$$

and since $\frac{(\delta\overline{u}_--\mu)}{\gamma\overline{u}_-}=\frac{1}{(1+T\overline{v}_-)}$ with $\overline{v}_-(\gamma)=1-\overline{u}_-(\gamma)$, we have

$$Trace\,(J(\overline{u}_-(\gamma),\overline{v}_-(\gamma)))=-\overline{u}_-+\tfrac{\gamma\overline{u}_-}{(1+T\overline{v}_-)}\left[1-\tfrac{1}{(1+T\overline{v}_-)}\right]$$

thus

$$Trace\,(J(\overline{u}_-(\gamma),\overline{v}_-(\gamma)))=\overline{u}_-\left[-1+\left[\frac{\gamma T\overline{v}_-}{(1+T\overline{v}_-)^2}\right]\right].$$

The main result of this section is the following theorem.

Theorem 4.3. *Let* $(\mu_0,\gamma_0,\delta_0,T_0)\in(0,+\infty)^4$, *with* $\gamma_0>4$. *Assume that one of conditions (a)-(i), (a)-(ii) or (a)-(iii) of Theorem 2.1 is satisfied, and conditions (10)-(12) hold for* $(\mu_0,\gamma_0,\delta_0,T_0)$. *Then there exists* $\gamma=\gamma_0$ *such that*

$$-\chi^*(\gamma_0)^3+\gamma_0T_0(1+T_0)(\chi^*(\gamma_0)-1)\neq 0, \tag{15}$$

$$\gamma_0\neq\delta_0(1+T_0)+\mu_0T_0. \tag{16}$$

System (2) undergoes Hopf bifurcation around $E_0(\overline{u}_-,\overline{v}_-)$, *when* γ *passes through* γ_0.

Proof. We first note that (16) implies $\overline{u}_-(\gamma_0)'\neq 0$. Moreover, we have $\overline{u}_-(\gamma)'=-\overline{v}_-(\gamma)'$, thus

$$\begin{aligned}\tfrac{dTrace(J(\overline{u}_-(\gamma),\overline{v}_-(\gamma)))}{d\gamma}&=\overline{u}_-'\left[-1+\left[\tfrac{\gamma T\overline{v}_-}{(1+T\overline{v}_-)^2}\right]\right]\\ &\quad+\gamma T\overline{u}_-\left[\left[\tfrac{(1+T\overline{v}_-)^2-2T\overline{v}_-(1+T\overline{v}_-)}{(1+T\overline{v}_-)^4}\right]\overline{v}_-'\right]\\ &=\overline{u}_-'\left\{\tfrac{-(1+T\overline{v}_-)^3+\gamma T[-1+2\overline{v}_-+T\overline{v}_-]}{(1+T\overline{v}_-)^3}\right\},\end{aligned}$$

but by assumption

$$\overline{v}_-=1-u_0^*=1-T^{-1}\left[(1+T)-\chi^*(\gamma_0)\right],$$

so

$$T\overline{v}_-=\left[\chi^*(\gamma_0)-1\right].$$

Thus

$$\begin{aligned}T\left[-1+2\overline{v}_-+T\overline{v}_-\right]&=T\left(\left[\chi^*(\gamma_0)-2\right]+2\left[1-T^{-1}\left[(1+T)-\chi^*(\gamma_0)\right]\right]\right)\\ &=T\left(\chi^*(\gamma_0)-T^{-1}\left[(1+T)-\chi^*(\gamma_0)\right]\right)\\ &=(1+T)(\chi^*(\gamma_0)-1)\end{aligned}$$

and

$$(1 + T\overline{v}_-) = \chi^*(\gamma_0),$$

so finally

$$\frac{dTrace\left(J(\overline{u}_-(\gamma), \overline{v}_-(\gamma))\right)}{d\gamma} = \frac{\overline{u}'_-}{(1 + T\overline{v}_-)^3}\left\{-\chi^*(\gamma_0)^3 + \gamma T(1+T)(\chi^*(\gamma_0) - 1)\right\},$$

and the result follows. □

To be more precise about the Hopf bifurcation occurring in this problem, we draw a bifurcation diagram in Figure 3, and some numerical simulations are presented in Figure 4.

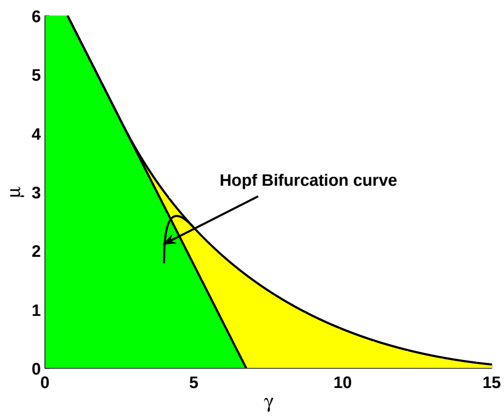

Figure 3: *The curve (10) with $T = 1.6$ and $\delta = 3(T+1)^2/(2T) = 6.7600$. Hopf bifurcation occurs when γ crosses this curve.*

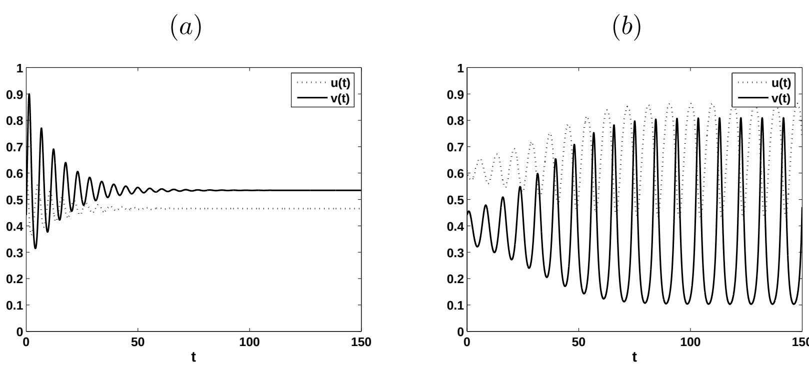

Figure 4: *Solution to system (2), with $T = 1.6$, $\delta = 7.56$, and $\mu = 2.835$. We fix $\gamma = 2.7250$ in figure (a), and $\gamma = 4.7250$ in figure (b). Due to the Hopf bifurcation, by increasing the value of the parameter γ, we pass from a stable regime to a regime with undamped oscillations.*

5. **Bogdanov-Takens bifurcation of system (2).** In this section, we consider the bifurcation of cusp as the parameters vary in a small neighborhood of $(\delta_0, \mu_0, \gamma_0, T_0)$, where

$$\begin{cases} \mu_0 = \left(\sqrt{\dfrac{T_0+1}{\delta_0 T_0}} - \sqrt{\dfrac{\delta_0 T_0}{T_0+1}}\right)^2, \\ \gamma_0 = \left(\sqrt{\dfrac{T_0+1}{\delta_0}} + \sqrt{\dfrac{\delta_0}{T_0+1}}\right)^2, \\ \delta_0 > \dfrac{T_0+1}{T_0}. \end{cases} \tag{17}$$

Under condition (17), system (2) has a unique positive equilibrium $(u^*, v^*) = \left(1 - \dfrac{T_0+1}{\delta_0 T_0}, \dfrac{T_0+1}{\delta_0 T_0}\right)$. Now we consider the system

$$\begin{cases} \dot{u}(t) = u(t) - u^2(t) - u(t)v(t), \\ \dot{v}(t) = \delta_0 u(t)v(t) - \mu_0 v(t) - \gamma_0 \dfrac{u(t)v(t)}{1+T_0 v(t)}. \end{cases} \tag{18}$$

First of all, we translate the positive equilibrium (u^*, v^*) to the origin and expand system (18) in a power series around the origin. Let $x = u - u^*$, $y = v - v^*$. Then system (18) can be written as

$$\begin{cases} \dot{x} = -u^* x - u^* y - x^2 - xy, \\ \dot{y} = u^* x + u^* y + \dfrac{1}{v^*} xy + \dfrac{u^*}{v^*(1+T_0 v^*)} y^2 + P(x,y), \end{cases} \tag{19}$$

where $P(x, y)$ is a smooth function in (x, y) at least of the third order. Next we derive the normal form of system (19) in the small neighborhood of the origin. Making the affine transformation

$$u = x, \;\; v = -u^* x - u^* y,$$

we can see that system (19) becomes

$$\begin{cases} \dot{u} = v + \dfrac{1}{u^*} uv, \\ \dot{v} = u^* \dfrac{T_0+1}{1+T_0 v^*} u^2 + \dfrac{T_0 u^* v^* - u^*}{v^*(1+T_0 v^*)} uv - \dfrac{1}{v^*(1+T_0 v^*)} v^2 + Q(u,v), \end{cases} \tag{20}$$

where $Q(u, v)$ is a smooth function in (u, v) at least of the third order.

Let

$$x = u + \left(-\frac{1}{2u^*} + \frac{1}{2v^*(1+T_0 v^*)}\right) u^2, \;\; y = v + \frac{1}{v^*(1+T_0 v^*)} uv.$$

Then system (20) is transformed into

$$\begin{cases} \dot{x} = y + R_1(x,y), \\ \dot{y} = d_1 x^2 + d_2 xy + R_2(x,y), \end{cases} \tag{21}$$

where $d_1 = u^* \dfrac{T_0+1}{1+T_0 v^*}$, $d_2 = \dfrac{T_0 u^* v^* - u^*}{v^*(1+T_0 v^*)}$, and R_1 and R_2 are smooth functions in (x, y) at least of the third order.

Note that

$$d_1 = u^* \frac{T_0+1}{1+T_0 v^*} > 0, \;\; d_2 = \frac{T_0 u^* v^* - u^*}{v^*(1+T_0 v^*)} = \frac{u^*(T_0+1-\delta_0)}{\delta_0 v^*(1+T_0 v^*)}.$$

From the normal form of a nilpotent singular point in [3],[6] and [7], we have

Theorem 5.1. *The positive equilibrium* (u^*, v^*) *of system* (18) *is a cusp of codimension* 2 *if* $\delta_0 \neq T_0 + 1$, *while it is a cusp of codimension at least* 3 *if* $\delta_0 = T_0 + 1$ *and* $T_0 < 1$.

If $T_0 + 1 - \delta_0 = 0$, then bifurcation of high codimension will occur. Computations of the normal form are complicated, and will be the subject of future work. In the following we always assume that $T_0 + 1 - \delta_0 \neq 0$. Now we study the normal form of system (2.1) in the small neighborhood of (u^*, v^*) if parameters (δ, μ, γ, T) vary in the small neighborhood of $(\delta_0, \mu_0, \gamma_0, T_0)$.

For convenience, we denote

$$(\delta_0, \mu_0, \gamma_0, T_0) = (a_1^0, a_2^0, a_3^0, a_4^0) = a^0,\ (\delta, \mu, \gamma, T) = (a_1, a_2, a_3, a_4) = a.$$

From (21), we know that system (2.1) in a small neighborhood of (u^*, v^*) can be rewritten as

$$\begin{cases} \dot{x} = y + w_1(x, y, a), \\ \dot{y} = d_1 x^2 + d_2 xy + w_2(x, y, a), \end{cases} \tag{22}$$

where $w_1, w_2 \in C^\infty(\mathbb{R}^2 \times \mathbb{R}^5, \mathbb{R})$, $w_1(x, y, a^0) = R_1(x, y)$, $w_2(x, y, a^0) = R_2(x, y)$.

Lemma 5.2. *Assume that* (x, y, a) *is in a small neighborhood of* $(0, 0, a^0)$. *If* $T_0 + 1 - \delta_0 \neq 0$, *then system (22) is* C^∞ *equivalent to*

$$\begin{cases} \dot{x} = y, \\ \dot{y} = \varphi_1(a) + \varphi_2(a)x + x^2 + \psi(a)y + \left[\dfrac{d_2}{\sqrt{d_1}} + \beta(a)\right] xy + R(x, y, a), \end{cases} \tag{23}$$

where φ_1, φ_2, ψ, *and* β *are smooth functions,* $\varphi_1(a^0) = \varphi_2(a^0) = \psi(a^0) = \beta(a^0) = 0$, R *is a* C^∞ *function in* (x, y) *at least of the third order.*

Proof. Consider the parameter-dependent nonsingular change of variables

$$x_1 = x, x_2 = y + w_1(x, y, a),$$

then system (22) can be written as

$$\begin{cases} \dot{x_1} = x_2, \\ \dot{x_2} = P_1(x_1, a) + x_2 P_2(x_1, a) + x_2^2 \Psi(x_1, x_2, a), \end{cases} \tag{24}$$

where $P_1, P_2, \Psi \in C^\infty$ and

$$P_1(0, a^0) = \frac{\partial P_1(0, a^0)}{\partial x_1} = 0, \frac{\partial^2 P_1(0, a^0)}{\partial x_1^2} = 2d_1 > 0$$
$$P_2(0, a^0) = 0, \frac{\partial P_2(0, a^0)}{\partial x_1} = d_2 \neq 0, \Psi(0, 0, a^0) = 0.$$

Applying the Malgrange Preparation theorem (see [4], p. 43) to the function $P_1(x_1, a)$, we have

$$P_1(x_1, a) = (\varphi_1(a) + \varphi_2(a)x_1 + x_1^2) B_1(x_1, a),$$

where $\varphi_1, \varphi_2, B_1 \in C^\infty$ and $B_1(0, a^0) = d_1$, $\varphi_i(a^0) = 0$, i=1,2. Therefore, system (24) becomes

$$\begin{cases} \dot{x_1} = x_2, \\ \dot{x_2} = \left[\varphi_1(a) + \varphi_2(a)x_1 + x_1^2 + \dfrac{x_2 P_2(x_1, a)}{B_1(x_1, a)} + \dfrac{x_2^2 \Psi(x_1, x_2, a)}{B_1(x_1, a)}\right] B_1(x_1, a), \end{cases} \tag{25}$$

Since $\Psi(0, a^0) = 0$ and $B_1(0, a^0) = d_1 > 0$, there exists a function $\psi(a)$ such that $\frac{P_2(0,a)}{\sqrt{B_1(0,a)}} = \psi(a)$. Set

$$x = x_1,\ y = \frac{x_2}{\sqrt{B_1(x_1, a)}},\ \tau = \int_0^t \sqrt{B_1(x_1(s), a)}ds.$$

Then system (25) becomes

$$\begin{cases} \dfrac{dx}{d\tau} = y, \\ \dfrac{dy}{d\tau} = \varphi_1(a) + \varphi_2(a)x + x^2 + \dfrac{yP_2(x, a)}{\sqrt{B_1(x, a)}} + y^2 G(x, y, a). \end{cases} \tag{26}$$

Expanding the function $\frac{P_2(x,a)}{\sqrt{B_1(x,a)}}$ in a power series of x around $x = 0$, we have

$$\frac{P_2(x, a)}{\sqrt{B_1(x, a)}} = \psi(a) + \left(\frac{d_2}{\sqrt{d_1}} + \beta(a)\right) x + F(x, a),$$

where β is a smooth function, $F(x, a)$ is a C^∞ function of (x, a), $\frac{\partial F(0,a)}{\partial x} = 0$ and $\beta(a^0) = 0$.

If we set

$$R(x, y, a) = yF(x, a) + y^2 G(x, y, a),$$

then system (26) is transformed into system (23). Thus, the result follows. □

We now choose δ and μ as the bifurcation parameters and fix $(\gamma, T) = (\gamma_0, T_0)$ to study if system (2.1) can undergo Bogdanov-Takens bifurcation in the small neighborhood of (u^*, v^*) as parameters δ and μ vary in the small neighborhood of (δ_0, μ_0).

Consider

$$\begin{cases} \dot{u}(t) = u(t) - u^2(t) - u(t)v(t), \\ \dot{v}(t) = (\delta_0 - \lambda_1)u(t)v(t) - (\mu_0 - \lambda_2)v(t) - \gamma_0 \dfrac{u(t)v(t)}{1 + T_0 v(t)}, \end{cases} \tag{27}$$

where δ_0, μ_0, γ_0 and T_0 satisfy condition (17) and $T_0 + 1 - \delta_0 \neq 0$, and $\lambda = (\lambda_1, \lambda_2)$ is a parameter vector in a small neighborhood of $(0, 0)$. Let

$$x = u - u^*, y = v - v^*$$

$$\begin{cases} \dot{x} = -u^*x - u^*y - x^2 - xy, \\ \dot{y} = v^*(-\lambda_1 u^* + \lambda_2) + (u^* - \lambda_1 v^*)x + (u^* + \lambda_2 - \lambda_1 u^*)y \\ \qquad + \left(\dfrac{1}{v^*} - \lambda_1\right) xy + \dfrac{u^*}{v^*(1 + T_0 v^*)} y^2 + P(x, y, \lambda), \end{cases} \tag{28}$$

where $P(x, y, \lambda)$ is a smooth function in (x, y) at least of the third order. Making the affine transformation

$$u = x, v = -u^*x - u^*y,$$

we see that system (28) becomes

$$\begin{cases} \dot{u} = v + \dfrac{1}{u^*}uv, \\ \dot{v} = u^*v^*(u^*\lambda_1 - \lambda_2) + [(u^*v^* - {u^*}^2)\lambda_1 + u^*\lambda_2]u + (-u^*\lambda_1 + \lambda_2)v \\ \qquad + \left(\dfrac{u^*(T_0+1)}{1+T_0v^*} - u^*\lambda_1\right)u^2 + \left(\dfrac{u^*(T_0+1-\delta_0)}{\delta_0 v^*(1+T_0v^*)} - \lambda_1\right)uv - \dfrac{1}{1+T_0v^*}v^2 \\ \qquad +Q(u,v,\lambda). \end{cases} \tag{29}$$

Let

$$\begin{aligned} &A(\lambda) = u^*v^*(u^*\lambda_1 - \lambda_2), \\ &B(\lambda) = (u^*v^* - {u^*}^2)\lambda_1 + u^*\lambda_2, \\ &C(\lambda) = -u^*\lambda_1 + \lambda_2,\ D(\lambda) = -u^*\lambda_1,\ E(\lambda) = -\lambda_1, \end{aligned}$$

where $\lambda = (\lambda_1, \lambda_2)$.

Following the process for the normal form of system (20), system (29) can be transformed into

$$\begin{cases} \dot{x} = y + R_1(x,y,\lambda), \\ \dot{y} = A(\lambda) + \left(B(\lambda) + \dfrac{A(\lambda)}{v^*(1+T_0v^*)}\right)x + C(\lambda)y \\ \qquad +(d_1 + c_1(\lambda))x^2 + (d_2 + E(\lambda))xy + R_2(x,y,\lambda), \end{cases} \tag{30}$$

where $d_1 = u^*\dfrac{T_0+1}{1+T_0v^*} > 0,\ d_2 = \dfrac{u^*(T_0+1-\delta_0)}{\delta_0 v^*(1+T_0v^*)} \neq 0$, $c_1(\lambda)$ is a smooth function of λ, R_1 and R_2 are smooth functions in (x,y) at least of the third order and the coefficients depend smoothly on λ_1 and λ_2.

By Lemma 5.2, system (30) can be changed into the following system

$$\begin{cases} \dot{x} = y, \\ \dot{y} = \dfrac{A(\lambda)}{d_1} + \phi_1(\lambda) + \left[\dfrac{B(\lambda) + \frac{A(\lambda)}{v^*(1+T_0v^*)}}{d_1} + \phi_2(\lambda)\right]x + \left[\dfrac{C(\lambda)}{\sqrt{d_1}} + \phi_3(\lambda)\right]y, \\ \qquad +x^2 + \left[\dfrac{d_2}{\sqrt{d_1}} + \phi_4(\lambda)\right]xy + R(x,y,\lambda), \end{cases} \tag{31}$$

where ϕ_1,ϕ_2 and ϕ_3 are smooth functions of λ at least of the second order, ϕ_4 is a smooth function of λ at least of the first order, R is a smooth function in (x,y) at least of the third order. Let

$$u = x - \frac{1}{2}\left[\frac{B(\lambda) + \frac{A(\lambda)}{v^*(1+T_0v^*)}}{d_1} + \phi_2(\lambda)\right], v = y.$$

Then system (31) becomes

$$\begin{cases} \dot{u} = v, \\ \dot{v} = \mu_1 + \mu_2 v + u^2 + \left(\dfrac{d_2}{\sqrt{d_1}} + \psi_4\right)uv + Q(u,v,\lambda), \end{cases} \tag{32}$$

where $Q(u,v,\lambda)$ is a smooth function in (u,v) at least of the third order,

$$\mu_1 = \frac{A(\lambda)}{d_1} + \psi_1(\lambda),\ \mu_2 = \frac{C(\lambda)}{\sqrt{d_1}} - \frac{d_2}{2d_1^{\frac{3}{2}}}\left[B(\lambda) + \frac{A(\lambda)}{v^*(1+T_0v^*)}\right] + \psi_2(\lambda), \tag{33}$$

and ψ_1,ψ_2 and ψ_4 have the same properties of ϕ_1,ϕ_2 and ϕ_4.

Note that

$$\det\begin{pmatrix} \frac{\partial\mu_1}{\partial\lambda_1} & \frac{\partial\mu_1}{\partial\lambda_2} \\ \frac{\partial\mu_2}{\partial\lambda_1} & \frac{\partial\mu_2}{\partial\lambda_2} \end{pmatrix}_{(0,0)} = -\frac{d_2}{2d_1^{\frac{5}{2}}}u^{*2}v^{*2} \neq 0.$$

Thus, the parameter transformation (33) is a homeomorphism in a small neighborhood of the origin, and μ_1 and μ_2 are independent parameters.

By theorems in [2], [3], [16] and [18], we know that system (32) undergoes the Bogdanov-Takens bifurcation when λ is in a small neighborhood of the origin. The local representations of the bifurcation curves are as follows:

(a) The saddle-node bifurcation curve is

$$SN = \{(\lambda_1, \lambda_2) : \mu_1(\lambda_1, \lambda_2) = 0\}$$

(b) The Hopf bifurcation curve is

$$H = \left\{(\lambda_1, \lambda_2) : \mu_2(\lambda_1, \lambda_2) = \frac{d_2}{\sqrt{d_1}}\sqrt{-\mu_1(\lambda_1, \lambda_2)}, \mu_1(\lambda_1, \lambda_2) < 0\right\}$$

(c) The homoclinic bifurcation curve is

$$HL = \left\{(\lambda_1, \lambda_2) : \mu_2(\lambda_1, \lambda_2) = \frac{5d_2}{7\sqrt{d_1}}\sqrt{-\mu_1(\lambda_1, \lambda_2)}, \mu_1(\lambda_1, \lambda_2) < 0\right\}.$$

According to the bifurcation curves and the sign of $d_1 d_2$, we now summarize the dynamics of system (27) in a small neighborhood of (u^*, v^*) as parameters (δ, μ) vary in a small neighborhood of (δ_0, μ_0) in the following theorem, where δ_0,μ_0,γ_0, and T_0 satisfy the conditions (17) and $T_0 + 1 - \delta_0 \neq 0$.

Theorem 5.3. *There exists a small neighborhood of (u^*, v^*) such that system (27) undergoes Bogdanov-Takens bifurcation as parameters (δ, μ) are in a small neighborhood of (δ_0, μ_0). More precisely,*

(i) system (27) has a unique positive equilibrium if parameters (δ, μ) are on the saddle-node bifurcation curve SN;

(ii) system (27) has two positive equilibria (one is a saddle and the other is a weak focus of order one) if parameters (δ, μ) are on the Hopf bifurcation curve H;

(iii) system (27) has two positive equilibria (one is a saddle and the other is a hyperbolic focus) and a homoclinic loop if parameters (δ, μ) are on the homoclinic bifurcation curve HL;

(iv) system (27) has two positive equilibria (one is a saddle and the other is a hyperbolic focus) and a limit cycle if parameters (δ, μ) are in the region between the Hopf bifurcation curve H and the homoclinic bifurcation curve HL. The limit cycle is stable if $\max\{T_0 + 1, \frac{T_0+1}{T_0}\} < \delta_0$, while it is unstable if $T_0 + 1 - \delta_0 > 0$ and $T_0 > 1$.

We give the numerical simulation of system (27) in two cases: I. $\max\{T_0 + 1, \frac{T_0+1}{T_0}\} < \delta_0$; II. $T_0 + 1 - \delta_0 > 0$ and $T_0 > 1$.

Case I. Taking $\delta_0 = 20, \mu_0 = 2.25, T_0 = 0.25$ and $\gamma = 18.0625$, then system (27) has a unique positive equilibrium $(0.75, 0.25)$ if $\lambda_1 = \lambda_2 = 0$. In the interior of the first quadrant there exists a unique orbit of system (27) which converges to this positive equilibrium, and all other orbits of system (27) converge to the boundary equilibrium $(1, 0)$.

When $\lambda_1 = -0.36$ and $\lambda_2 = -0.265$, system (27) has two positive equilibria and one stable limit cycle. Taking the initial condition $(u, v) = (0.73, 0.27)$, we can see that the solution of system (27) converges to a stable limit cycle as t tends to positive infinity.

Case II. Taking $\delta_0 = 5.5, \mu_0 = 3.2, T_0 = 10$ and $\gamma = 4.5$, then system (27) has a unique positive equilibrium $(0.8, 0.2)$ if $\lambda_1 = \lambda_2 = 0$. In the interior of the first quadrant there exists a unique orbit of system (27) which converges to this positive equilibrium, and all other orbits of system (27) converge to the boundary equilibrium $(1, 0)$.

When $\lambda_1 = -0.324$ and $\lambda_2 = -0.259$, system (27) has two positive equilibria and one unstable limit cycle. Taking the initial condition $(u, v) = (0.7995, 0.2005)$, we can see that the solution of system (27) converges to an unstable limit cycle as t tends to negative infinity.

To conclude this section, we explain further the Bogdanov-Takens bifurcation point in Figure 5, and some numerical simulations are presented in Figure 6.

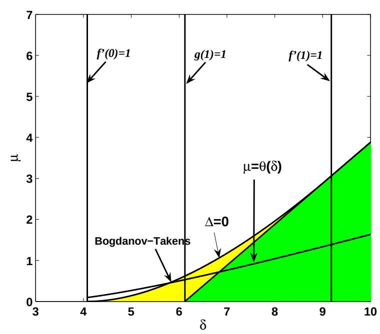

Figure 5: *The map* $\theta(\delta) := \left(\sqrt{\frac{T_0+1}{\delta T_0}} - \sqrt{\frac{\delta T_0}{T_0+1}}\right)^2$ *on the* $(\mu, \delta)-$ *plane. The intersection point between the curve* $\mu = \theta(\delta)$ *and the curve* $\Delta = 0$ *corresponds to the Bogdanov-Takens bifurcation point.*

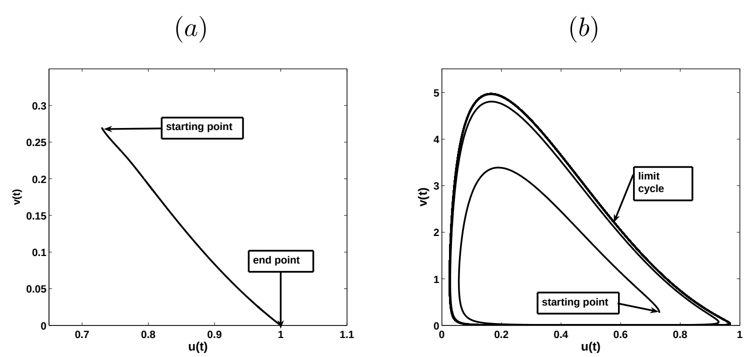

Figure 6: *Solution to system (2), with* $\gamma = 7.429$ *and* $T = 10$. *We fix* $\delta = 2.1$ *and* $\mu = 0.4329$ *in figure* (a), *and we fix* $\delta = 2.0567$ *and* $\mu = 0.04329$ *in figure* (b). *These sets of parameters are a "small" perturbation of the Bogdanov-Takens bifurcation point. We observe that we can pass from a stable unique equilibrium attracting all the orbits, to a heteroclinic orbit going from the interior equilibrium to the equilibrium* $(u, v) = (1, 0)$ *on the boundary.*

6. **Conclusion.** In this work we have shown that the dynamics of the proposed model is quite rich. In particular, dropping the assumptions considered in [11] (small natural mortality rate for amoebae and small handling time during the killing process by bacteria) leads to a great increase in the complexity of the dynamics: both Hopf and Bogdanov-Takens bifurcations may occur for proper choices of parameters. Specifically, for sufficiently large values of the virulence parameter γ, an increase in the natural mortality of amoebae μ gives chance of observing Hopf bifurcation and thus oscillations in the two populations. Moreover, fixing the parameters accounting for the killing of amoebae by bacteria (namely, γ and T), the system may undergo Bogdanov-Takens bifurcation for suitable values of the parameters related to growth, δ, and natural mortality of amoebae μ.

Our theoretical investigation suggests that, depending on the aggressiveness of the bacterial strain, on the growth and mortality rates of amoebae and on the initial number of cells, a quite complex biological system, in which both predator-prey and host-pathogen interactions occur, may show a large variety of behaviors. Unfortunately, the experimental framework does not allow an easy investigation of the (transient) behavior of the two populations; in fact, there are some practical limitations (for instance due to frequency and precision of observations) that may affect the measurement of possible oscillations in the number of cells. This makes the empirical validation of the results derived by the mathematical analysis of the model challenging.

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E-mail address: lfumanelli@fbk.eu
E-mail address: pierre.magal@u-bordeaux2.fr
E-mail address: xiaodm@sjtu.edu.cn
E-mail address: sjtuyuxiao@sjtu.edu.cn