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ORIGINAL PAPER

Hopf bifurcation and multiple limit cycles in bio-chemical reaction of the morphogenesis process

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Abstract Morphogenetic process is an interesting but very hard bio-chemical problem. In this paper, we consider a bio-chemical model in temporal morphogenesis which is a generalization of the model studied by Gierer–Meinhardt. By using the theory of ordinary differential equations, it is shown that the model undergoes a Hopf bifurcation if the parameters in the model satisfy the following relationship: $\lambda = 2/(\rho_2 + x^*) - 1$. It is also proved that the close orbit created by the Hopf bifurcation is stable. The conditions that guarantee the system has three closely nested limit cycles are also obtained in the paper.

Keywords Hopf bifurcation · Temporal morphogenesis · Bio-chemical reaction · Limit cycles

1 Introduction

It is known that morphogenetic process is one of the most interesting problems in modern bi-chemistry. Much work has been devoted to this topic for the past decades [1–6], among which the first bio-chemical model of temporal organization in morphogenetic process was proposed by Gierer–Meinhardt [1]. If a is the activator concentration, and h, the inhibitor concentration, the model takes the form:

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$$\frac{\mathrm{d}a}{\mathrm{d}t} = \rho\rho_0 + c\rho\frac{a^2}{h} - \mu a,$$
$$\frac{\mathrm{d}h}{\mathrm{d}t} = c'\rho a^2 - \nu h, \tag{1}$$

where $\rho\rho_0$ is the source concentration for the activator and ρ the one for the inhibitor; μ and ν the degradation coefficients of a and h, respectively. The parameters c and c' are connected with the activator and inhibitor production. The system can be understood in this way: two molecules of activator are necessary to activate and one to inhibit the source.

System (1) was studied numerically in [1,7] and analytically in [2]. The possible existence of state self-sustained oscillations of the model was investigated [1], and then proved in [2] by using the Hopf bifurcation. However, conditions for the uniqueness of limit cycle of (1) have never been reported. Recently, Huang, et al. modified system (1) as follows [4,5]:

$$\frac{\mathrm{d}a}{\mathrm{d}t} = \rho\rho_0 + c\rho\frac{a^2}{h} - \mu a$$
$$\frac{\mathrm{d}h}{\mathrm{d}t} = \rho\left(c_1 a + c_2 a^2\right) - \nu h. \tag{2}$$

It is easy to see that term $c'a^2$ in the second equation of (1) is replaced by $c_1 a + c_2 a^2$ in system (2). This is because that, in the complicated morphogenetic bio-chemical process, the rate of change of the inhibition concentration is also proportional to the concentration of the activator, not just the square of it.

As is well known, the concept of limit cycles in a differential equation model is related to the periodic oscillation between the concentrations of the activator and inhibitor of the temporal organization in morphogenetic processes. Thus, any results regarding the limit cycles of the mathematical model are useful in understanding and analyzing the morphogenetic processes. In this paper, by using qualitative analysis, a Hopf bifurcation at $\lambda = 2/(\rho_2 + x^*) - 1$ is proved, and we also investigate stability property of the close orbits created by the bifurcation.

After the paper of May [8], the existence of one and only one limit cycle in a bi-chemical system became a primary problem in bio-mathematics. As a bichemist, a family of three closely nested limit cycles (the outer ones stable, the one in the middle unstable) is equally important. This is because a three closely nested limit cycles is better in describing bi-chemical reality. Our last theorem in the paper is for the conditions that guarantee the system has at least three closely nested limit cycles. Our results cover the main theorems in [1–3,7] as special cases $c_1 = 0$, $c_2 = c'$.

2 The model

Performing the transform: $a = \frac{\nu c}{\mu c_2}x$, $h = \frac{\nu c^2}{\mu^2 c_2}y$, $\mathrm{d}t = \frac{y}{\mu}\mathrm{d}\tau$, and letting $\rho_1 = \frac{\rho_0 c_2}{\nu c}$, $\rho_2 = \frac{\mu c_1}{\nu c}$, $\lambda = \frac{\nu}{\mu}$, system (2) becomes

$$\frac{\mathrm{d}x}{\mathrm{d}\tau} = \rho\left(\rho_1 y + x^2\right) - xy$$
$$\frac{\mathrm{d}y}{\mathrm{d}\tau} = \rho\lambda\left(\rho_2 xy + x^2 y\right) - \lambda y^2. \tag{3}$$

The above change of time variables: $\mathrm{d}t = (y/\mu)\mathrm{d}\tau$ is similar to the one in Poincaré transformation ($\mathrm{d}\tau = \mathrm{d}t/z^m$, where z is also a state variable). It follows that system (3) is topologically equivalent to system (2) if $y \neq 0$, and any qualitative result for system (3) is also valid for system (2).

Due to the bi-chemical background, we just need to study system (3) in $\Omega^+ = \{(x, y)\,|x > 0, y > 0\}$. In the following discussion, we still use t instead of τ as our time variable.

A simple calculation tells that (3) has only one positive equilibrium point $A(x^*, y^*)$ in Ω^+, where

$$x^* = \frac{1 + \rho\rho_1 - \rho_2 + \sqrt{(1 + \rho\rho_1 - \rho_2)^2 + 4\rho\rho_1\rho_2}}{2}$$
$$y^* = \rho\rho_2 x^* + \rho x^{*2},$$

which is the nonzero solution of the system:

$$\rho\left(\rho_1 y + x^2\right) - xy = 0$$
$$\rho\left(\rho_2 x + x^2\right) - y = 0. \tag{4}$$

In order to discuss the Hopf bifurcation and the stability of the close orbits due to the bifurcation, we need to recall the following results for the existence and uniqueness of limit cycles in system (3) (see [5]):

Lemma 1 *All the solutions of system (3) are bounded in Ω^+ for $t > 0$.*

Lemma 2 *For $\lambda \geq 1$, there is no limit cycle in Ω^+.*

Lemma 3 *The necessary and sufficient condition for there is one and only one limit cycle in system (3) in Ω^+ is $\lambda < 2/(\rho_2 + x^*) - 1$.*

Denote

$$R = 2/(\rho_2 + x^*) - 1, \quad \mu = \lambda - R = \lambda - 2/(\rho_2 + x^*) + 1. \tag{5}$$

Lemma 4 *(i) if $\rho_2 + x^* > 2$, or if $\rho_2 + x^* < 2$ and $\lambda > 2/(\rho_2 + x^*) - 1$, then $A(x^*, y^*)$ is a stable node or focus of system (3);*
(ii) if $\lambda < 2/(\rho_2 + x^*) - 1$, then $A(x^*, y^*)$ is an unstable node or focus. We assume $\rho_2 + x^* < 2/(1 + \lambda)$ in the following discussion.

Theorem 1 *If $\mu = 0$, or $\lambda = 2/(\rho_2 + x^*) - 1$, then the equilibrium $A(x^*, y^*)$ of system (3) is a first order central focus, and it is stable if $1 < \rho_2 + x^* < 2$, and unstable if $\rho_2 + x^* < 1$.*

Proof By the transformation: $x = u + x^*$, $y = v + y^*$, system (3) is now

$$\begin{aligned}\frac{\mathrm{d}u}{\mathrm{d}t} &= (2\rho x^* - y^*)u + (\rho\rho_1 - x^*)v + \rho u^2 - uv\lambda,\\ \frac{\mathrm{d}v}{\mathrm{d}t} &= (\rho\rho_2\lambda y^* + 2\rho\lambda x^* y^*)u - \lambda y^* v\\ &\quad + (\rho\rho_2\lambda + 2\rho\lambda x^*)uv + \rho\lambda y^* u^2 - \lambda v^2 + \rho\lambda u^2 v.\end{aligned}$$

For the simplicity, denote $m = (\rho\rho_2\lambda y^* + 2\rho\lambda x^* y^*)$, $n = -\lambda y^*$, then we have

$$m = -\rho t(\rho_2 + 2x^*), \quad q + n^2 = \rho^2\lambda x^{*2}(\rho_2 + 2x^*).$$

Now we make another transformation:

$$u = \frac{\lambda y^*}{\rho\lambda y^*(\rho_2 + 2x^*)}X - \frac{\sqrt{q}}{\rho\lambda y^*(\rho_2 + 2x^*)}Y, \quad v = X, \quad \mathrm{d}\tau = \sqrt{q}\mathrm{d}t,$$

that is

$$\begin{aligned}X &= v,\\ Y &= -\frac{\rho\lambda y^*(\rho_2 + 2x^*)}{\sqrt{q}}u + \frac{\lambda y^*}{\sqrt{q}}v.\end{aligned}$$

Rewrite $\mathrm{d}\tau$ as $\mathrm{d}t$, system (3) is now equivalent to

$$\begin{aligned}\frac{\mathrm{d}X}{\mathrm{d}t} &= -Y + A_1X^2 + A_2Y^2 + A_3XY + A_4X^3 + A_5X^2Y + A_6XY^2,\\ \frac{\mathrm{d}Y}{\mathrm{d}t} &= X + B_1X^2 + B_2Y^2 + B_3XY + B_4X^3 + B_5X^2Y + B_6XY^2,\end{aligned} \tag{6}$$

where

$$\begin{aligned}A_1 &= -\frac{\rho n^3}{m^2\sqrt{q}}, \quad A_2 = -\frac{\rho n\sqrt{q}}{m^2}, \quad A_3 = -\left(\frac{2\rho n^2}{m^2} + \frac{1}{y^*}\right),\\ A_4 &= \frac{\rho\lambda n^2}{m^2\sqrt{q}}, \quad A_5 = \frac{2\rho n\lambda}{m^2}, \quad A_6 = \frac{\rho\lambda\sqrt{q}}{m^2},\\ B_1 &= \frac{\rho n^4 - \rho n^2 m - m^2 n}{m^2 q}, \quad B_2 = \frac{\rho n^2}{m^2} - \frac{\rho}{m},\\ B_3 &= \frac{1}{\sqrt{q}}\left(\frac{2\rho n^3}{m^2} + \frac{n}{y^*} - \frac{2\rho n + m}{m}\right),\\ B_4 &= -\frac{\rho\lambda n^3}{m^2\sqrt{q}}, \quad B_5 = -\frac{2\rho n^2\lambda}{m^2}, \quad B_6 = -\frac{\rho n\lambda}{m^2}.\end{aligned}$$

Using the following formal series:

$$F(X,Y) = X^2 + Y^2 + \sum_{i=3}^{\infty} F_i(X,Y), \tag{7}$$

where $F_i(X,Y)$ is the ith homogenous polynomial of X and Y whose coefficients will be determined late. Let the 3rd order homogenous polynomials in $\frac{\mathrm{d}F}{\mathrm{d}t}\big|_{(6)}$ be zero, we solve the system of equations:

$$\begin{aligned}
&2A_1X^3 + 2A_2XY^2 + 2A_3X^2Y - Y\frac{\partial F_3}{\partial X}\\
&+ X\frac{\partial F_3}{\partial Y} + 2B_1X^2Y + 2B_2Y^3 + 2B_3XY^2 = 0,\\
&-Y\frac{\partial F_3}{\partial X} + X\frac{\partial F_3}{\partial Y} = -2A_1X^3 - 2B_2Y^3 - (2A_2+2B_3)XY^2 - (2A_3+2B_1)X^2Y.
\end{aligned}$$

It follows that

$$\begin{aligned}
F_3(X,Y) = &-2A_1X^2Y + 2B_2XY^2 - \frac{2}{3}(2A_3 + A_2 + B_3)Y^3\\
&+ \frac{2}{3}(A_3 + B_1 + 2B_2)X^3.
\end{aligned}$$

Substitute $F_3(X,Y)$ into (6), and then let the 4th order homogenous polynomials in $\frac{\mathrm{d}F}{\mathrm{d}t}\big|_{(6)}$ be zero, and solve the equation

$$\begin{aligned}
-Y\frac{\partial F_4}{\partial X} + X\frac{\partial F_4}{\partial Y} = &-2A_4X^4 - (2A_5+2B_4)X^3Y - (2A_6+2B_5)X^2Y^2 - 2B_6XY^3\\
&-(B_1X^2+B_2Y^2+B_1XY)\frac{\partial F_3}{\partial Y} - (A_1X^2 + A_2Y^2 + A_3XY)\frac{\partial F_3}{\partial X}\\
= &\ \omega_1X^4 + \omega_2X^3Y + \omega_3X^2Y^2 + \omega_4XY^3 + \omega_5Y^4,
\end{aligned}$$

where,

$$\begin{aligned}
\omega_1 &= -2(A_4 + A_1A_3 + 2A_1B_2),\\
\omega_2 &= -2A_5 - 2B_4 - 4B_1B_2 + 2A_1B_3 + 4A_2 - 2A_3^2 - 2A_3B_1 - 4A_3B_2,\\
\omega_3 &= 4A_1B_1 + 2B_1B_3 - 2A_6 - 2B_5 - 4B_2B_3 - 2A_2A_3 - 4A_2B_2 + 4A_1A_3,\\
\omega_4 &= 4A_1B_3 + 2A_2B_3 + 2B_3^2 - 2B_6 - 4B_2^2 + 4A_1A_2 - 2A_3B_2,\\
\omega_5 &= 4A_1B_2 + 2B_2B_3.
\end{aligned}$$

Use the polar coordinates: $X = r\cos\theta$, $Y = r\sin\theta$, then

$$\frac{\mathrm{d}F_4(\cos\theta,\sin\theta)}{\mathrm{d}\theta} = H_4(\cos\theta,\sin\theta)$$
$$= \omega_1\cos^4\theta + \omega_2\cos^3\theta\sin\theta + \omega_3\cos^2\theta\sin^2\theta + \omega_4\cos\theta\sin^3\theta.$$

Let C_4 be defined as $-\frac{1}{2\pi}\int_0^{2\pi} H_4(\cos\theta,\sin\theta)$, then

$$\begin{aligned}
C_4 &= -\frac{1}{8}(3\omega_1 + 3\omega_5 + \omega_3)\\
&= -\frac{1}{4q}(-3A_4\sqrt{q} - A_6\sqrt{q} - B_5\sqrt{q} - A_1A_3 + B_2B_3 + 2A_1B_1 + B_1B_3\\
&\quad - A_2A_3 - 2A_2B_2)\\
&= -\frac{1}{4m^2q\sqrt{q}}(-\rho\lambda n^2mq - 4\rho^2n^3q - \rho n^2mq + \rho\lambda m^2q + 2\rho^2nmq\\
&\quad + \rho m^2q - \rho mn^4 - \rho\lambda n^4m - 2\rho^2n^5 + \rho\lambda n^2m^2 + 2\rho^2n^3m + 3\rho n^2m^2\\
&\quad + \lambda nm^3 + nm^3 - 2\rho^2nq^2)\\
&= -\frac{1}{4nq\sqrt{q}(\rho_2+2x^*)}\Big[\lambda n^2(n^2+q) + n^2(n^2+q) + \rho\lambda n(\rho_2+2x^*)(n^2+q)\\
&\quad - 2\rho n(n^2+q) + \rho n(\rho_2+2x^*)(n^2+q) + 2\rho n^3(\rho_2+2x^*)\\
&\quad - \rho\lambda n^3(\rho_2+2x^*)^2 - \rho n^3(\rho_2+2x^*)^2 - 2\rho^4\lambda^2x^{*4}(\rho_2+2x^*)\Big]\\
&= -\frac{\rho^4\lambda^2x^{*4}(\rho_2+2x^*)}{2\lambda y^*q\sqrt{q}}(\rho_2 + x^* - 1).
\end{aligned}$$

It is easy to see that $\rho_2 + x^* - 1 \neq 0$, otherwise $y^* = \rho x^*(\rho_2 + x^*) = \rho x^*$, which implies that $x^* = 0$. Therefore, $C_4 \neq 0$, and the equilibrium $A(x^*, y^*)$ is a first-order central focus. If $1 < \rho_2 + x^* < 2$, then $C_4 < 0$ and $A(x^*, y^*)$ is stable; it is unstable if $\rho_2 + x^* < 1$. The proof of Theorem 1 is complete. □

Before we go to next theorem, we introduce the following Lemma [9].

Lemma 5 *Consider the system*

$$\frac{\mathrm{d}x}{\mathrm{d}t} = X(x, y, \mu), \quad \frac{\mathrm{d}y}{\mathrm{d}t} = Y(x, y, \mu), \tag{8}$$

where, $(x, y) \in U \subseteq R^2$, *the parameter* $\mu \in J \subseteq R$, X *and* Y *are analytic functions of* x, y, μ. *If for* $\mu = 0$, $(0, 0)$ *is a stable (or unstable) central focus of system* (8), *and if for* $\mu > 0$, *it is a unstable (or stable) focus, then for sufficiently small* $\mu > 0$, *there exists at least one stable (or unstable) limit cycle around* $(0, 0)$; *furthermore, when* $\mu \to 0$, *the limit cycle approaches to* $(0, 0)$. *If the above condition* $\mu > 0$ *is changed to* $\mu < 0 \quad (0 < |\mu| << 1)$, *the conclusion is also true.*

For system (3), choose μ in (5) as a bifurcation parameter.

Theorem 2 *System* (3) *undergoes a Hopf bifurcation at* $\mu = 0$*, or at* $\lambda = 2/(\rho_2 + x^*) - 1$*. The periodic solution created by the bifurcation is stable if* $1 < \rho_2 + x^* < 2$ *and unstable if* $\rho_2 + x^* < 1$.

Proof In the case of $1 < \rho_2 + x^* < 2$, by Theorem 1, at $\mu = 0$, $A(x^*, y^*)$ is a stable first order central focus. By Lemma 4(ii), for $\mu < 0$, $A(x^*, y^*)$ is unstable focus, then Lemma 5 implies that for $0 < |\mu| << 1$, there exists a stable limit cycle surrounding the equilibrium point A. For the case when $\rho_2 + x^* < 1$, Theorem 1 implies that at $\mu = 0$, $A(x^*, y^*)$ is a unstable first order central focus, and Lemma 4(i) indicates, for $\mu > 0$, $A(x^*, y^*)$ is stable focus, then Lemma 5 implies that for $0 < \mu << 1$, there exists an unstable limit cycle surrounding A. Theorem 2 is proved.

For the multiple limit cycles, we denote (x_p, y_p) as the coordinates of P and recall the annular region $CDEFHC$ in [5], where C is the point defined as $C(\rho\rho_1, \rho^2\rho_1\rho_2 + \rho^3\rho_1^2)$, and $D = D(1 + \rho\rho_1, y_C)$ the intersection of the lines $y = y_C$ and $x = 1+\rho\rho_1$. It follows that D is on the right of the line $x = x^*$ because

$$x^* = \frac{1 + \rho\rho_1 - \rho_2 + \sqrt{(1 + \rho\rho_1 - \rho_2)^2 + 4\rho\rho_1\rho_2}}{2} \leq 1 + \rho\rho_1.$$

Consider the auxiliary system:

$$\begin{aligned} \frac{\mathrm{d}x}{\mathrm{d}t} &= \rho x^2 - y, \\ \frac{\mathrm{d}y}{\mathrm{d}t} &= \lambda y(\rho x^2 - y). \end{aligned} \tag{9}$$

For $y < \rho x^2$, the trajectory of system (9) passing through point D is the curve DE: $y = c_0 e^{\lambda x}$, where, $c_0 = y_C e^{-\lambda(1+\rho\rho_1)}$. Since this curve goes to $+\infty$ exponentially as x increases, and the isocline $y = \rho x^2/(x - \rho\rho_1)$ has a linear asymptote $y = \rho x + 2\rho^2\rho_1$, then the curve DE must intersect with $y = \rho x^2/(x - \rho\rho_1)$, say, at point $E(x_E, y_E)$. Assume the line $x = x_E$ intersects with $y = \rho x^2 + \rho\rho_2 x$ at $F(x_F, y_F)$, and the line $y = y_F$ with $x = \rho\rho_1$ at H. It is proved that the region bounded by the boundaries of $CDEFHC$ is a Poincaré-Bendixson annular region and all limit cycles around the equilibrium $A(x^*, y^*)$ are inside the region [5].

Consider the following auxiliary system

$$\begin{aligned} \frac{\mathrm{d}x}{\mathrm{d}t} &= x\,(F_i(x) - y) \\ \frac{\mathrm{d}y}{\mathrm{d}t} &= y(\lambda\rho(\rho_2 x + x^2) - \lambda y), \\ & \quad x(0) > 0, \quad y(0) > 0, \quad i = 1, 2. \end{aligned} \tag{10.i}$$

The functions $F_1(x) = \rho x^2/(x - \rho\rho_1)$, and F_2 will be determined later.

Suppose (x_e, y_e) is the equilibrium point of (10.i). In other words,

$$x_e = \frac{1}{2}\left(1+\rho\rho_1-\rho_2+\sqrt{(1+\rho\rho_1-\rho_2)^2+4\rho\rho_1\rho_2}\right),$$
$$y_e = F_1(x_e) = F_2(x_e).$$

Let $P_0 = (x_0, y_0)$, with $\rho\rho_1 < x_0 < x_e$, $0 < y_0 < y_e$, be a point on the parabola $y = \rho x^2 + \rho\rho_2 x$, Γ_i be the orbit of system (10.i) starting at P_0. Suppose that A_i, Q_i, B_i are the first points (in time spent) of intersecting with the curves: $y = \rho x^2+\rho\rho_2 x$, $x > x_e$, $y = y_e$, $\rho\rho_1 < x < x_e$, and $y = \rho x^2 + \rho\rho_2 x$, $x < x_e$, respectively. Let J be the intersection of $y = y_e$ and $y = \rho x^2/(x-\rho\rho_1)$ with $\rho\rho_1 < x_J < 2\rho\rho_1 \le x_e$. □

Then, we have the following Lemma 6.

Lemma 6 *Suppose*

$$\begin{aligned} F_1(x) &\le F_2(x) \quad \textit{for } x \in [\rho\rho_1, x_e], \\ F_1(x) &\ge F_2(x) \quad \textit{for } x \in [x_e, x_E], \end{aligned} \tag{11}$$

with strict inequality for some $x \in [0, x_e]$ *and* $[x_e, x_E]$*, respectively. Then*

$$(i)\ y_{A_1} > y_{A_2}, \quad (ii)\ y_{B_1} < y_{B_2}, \quad (iii)\ x_{Q_1} < x_{Q_2},$$
$$(iv)\ y_{B_i} \le F_i(x_{Q_i}) \ \ \textit{for } \rho\rho_1 < x < x_e, \quad i = 1, 2.$$

Proof Let the vector $\overline{V_i}$ be defined as

$$\overline{V_i} = \left(x(F_i(x)-y),\, y(\rho\lambda(\rho_2 x + x^2) - \lambda y),\, 0\right), \quad i = 1, 2. \tag{12}$$

Consider the cross product of $\overline{V_1}$ and $\overline{V_2}$,

$$\overline{V_1} \times \overline{V_2} = \left(0, 0, \lambda x y(\rho\rho_2 x + \rho x^2 - y)(F_1(x) - F_2(x))\right). \tag{13}$$

Since (11),

$$\lambda x y(\rho\rho_2 x + \rho x^2 - y)(F_1(x) - F_2(x)) \ge 0, \quad \text{for } \rho\rho_1 < x \le x_E.$$

Hence, the flow of (10.1) is always directed outside with respect to the one of (10.2). Therefore, (i)–(iii) hold. Suppose Γ_i intersects with the isocline $y - F_i(x) = 0 \ \ (\rho\rho_1 \le x \le x_e)$ at S_i. Then, since

$$\frac{dy}{dt} < 0 \quad \text{for } \rho\rho_1 < x < x_e,\, y > \rho x^2 + \rho\rho_2 x,$$
$$\frac{dx}{dt} < 0 \quad \text{for } \rho\rho_1 < x < x_e,\, F_i(x) - y < 0, \quad i = 1, 2,$$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = 0 \quad \text{for } F_i(x) - y = 0, \quad i = 1, 2,$$
$$\frac{\mathrm{d}x}{\mathrm{d}t} > 0 \quad \text{for } \rho\rho_1 < x < x_e, F_i(x) - y > 0, \quad i = 1, 2,$$

we have

$$x_{S_i} \leq x_{Q_i} \quad \text{and} \quad y_{B_1} \leq y_{Q_1} = F_i(x_{Q_i}), \quad i = 1, 2.$$

Thus (*iv*) is also valid and the proof of Lemma 6 is completed.

Now following the argument of the existence of limit cycles in [10,11], there exists $\delta > 0$ such that

$$y_0 - y_{B_1}(y_0) < 0 \quad \text{for all } y_0 \in (0, \delta).$$

Here B_1 is the intersection of the orbit $\Gamma_1(x_e, y_0)$ and the parabola $y = \rho x^2 + \rho\rho_2 x$, $\rho\rho_1 < x < x_e$. It follows that $y_{B_1}(y_0)$, the y coordinate of B_1, is a continuous function of y_0.

Fix δ, any orbit starting at the point $(x_0, y_0) = \left(\frac{-\rho\rho_2+\sqrt{\rho^2\rho_2^2+4\rho y_0}}{2\rho}, y_0\right)$ with $y_0 \in (\delta/2, y_e)$ will be remained in the region: $\{(x, y)\,|\,y > 0, \rho\rho_2 < x < x_E\}$. Moreover, by the boundedness of solutions with the initial vales $x(0) = x_0 = \frac{-\rho\rho_2+\sqrt{\rho^2\rho_2^2+4\rho y_0}}{2\rho}$, $y(0) = y_0 \in (\delta/2, y_e)$ (see [10,11]), we can assume, if a limit cycle of system (3) exists, it must be inside a circle. Suppose it is inside the circle

$$(x - x_e)^2 + (y - y_e)^2 = r_0^2, \quad r_0 \in (0, y_e). \tag{14}$$

Define $F_2(x)$ as

$$F_2(x) = \begin{cases} F(x) & \rho\rho_1 < x \leq x_J, \\ y_e & x_J \leq x \leq x_E. \end{cases} \tag{15}$$

Clearly, $F_2(x)$ is continuous and satisfies Lipschitz's condition.

Consider the system (10.*i*) and the orbit: $\Gamma_i(x_0, y_0)$ starting at (x_0, y_0), $i = 1, 2$. We are in a position to prove the theorem of the existence of multiple limit cycles. □

Theorem 3 *In addition to* (11)*, if system* (3) *satisfies*

(i) $\rho_2 + x^* < 2/(1 + \lambda)$,

(ii) *there exists* $\bar{y} \in (0, y_e - r_0)$ *such that* $\bar{y} > F(x_{Q_2}(\bar{y}))$,

where $Q_2(= S_2$*, in such defined* $F_2)$ *is the intersection of* $\Gamma_2(x_e, \bar{y})$ *and the line segment* $y = y_e$, $\rho\rho_1 < x < x_e$*, then system* (3) *has at least three nested limit cycles around* (x_e, y_e).

Proof Define the function $\rho(y_0)$ as

$$\rho(y_0) = y_0 - y_{B_1}(y_0), \tag{16}$$

where B_1 is the intersection of $\Gamma_1(x_0, y_0)$ and the parabola $y = \rho x^2 + \rho\rho_2 x$, for $\rho\rho_1 < x < x_e$. Since (x_e, y_e) is unstable, if $y_0 < y_e$ and y_0 is sufficiently close to y_e,

$$\rho(y_0) > 0. \tag{17}$$

By Lemma 3, system (3) has at least one limit cycle around (x_e, y_e). Thus, we can find a $y_1 \in (y_e - r_0, y_e)$ such that

$$\rho(y_1) = 0. \tag{18}$$

The stability of the above limit cycle implies that there exists $\delta_1 > 0$ such that

$$\rho(y_0) < 0 \quad \text{for } y_0 \in (y_1 - \delta_1, y_1). \tag{19}$$

Now, by Lemma 6 and (*ii*),

$$\begin{aligned} y_{B_1}(\bar{y}) &\le F_1\left(x_{S_1}(\bar{y})\right) \\ &< \bar{y}. \end{aligned}$$

Thus

$$\rho(\bar{y}) > 0. \tag{20}$$

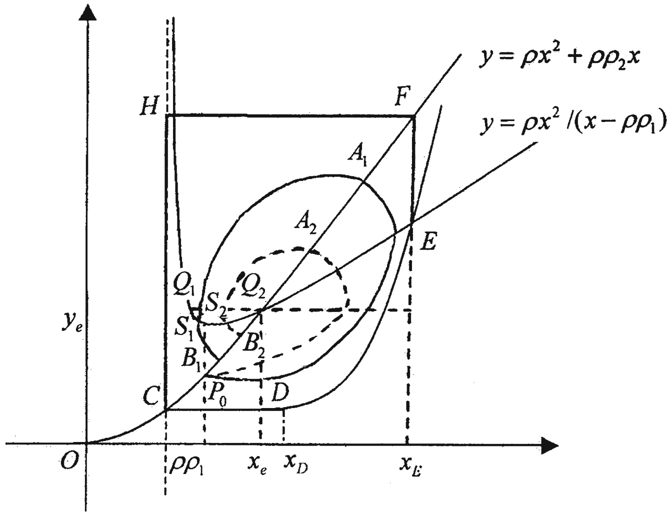

Fig. 1 The flow of (10.1) is always directed outside with respect to the flow of (10.2)

Since $\rho(y_0)$ is continuous with respect to y_0, there exist

$$y_2 \in (\bar{y}, y_1) \quad \text{and} \quad y_3 \in (0, \bar{y}),$$

such that

$$\rho(y_2) = \rho(y_3) = \rho(y_1) = 0.$$

Clearly each orbit starting at $\left(\left(-\rho\rho_2 + \sqrt{\rho^2\rho_2^2 + 4\rho y_i}\right)/(2\rho), y_i\right)$, $i = 1, 2, 3$ is a limit cycle of system (3). We thus complete the proof of Theorem 3. (Fig. 1). $\square$

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