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## HOPF BIFURCATION IN HIGHER DIMENSIONAL DIFFERENTIAL SYSTEMS VIA THE AVERAGING METHOD

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*Dedicated to the memory of Professor Ye Yanqian*

We study the Hopf bifurcation of  $\mathcal{C}^3$  differential systems in  $\mathbb{R}^n$  showing that  $l$  limit cycles can bifurcate from one singularity with eigenvalues  $\pm bi$  and  $n - 2$  zeros with  $l \in \{0, 1, \dots, 2^{n-3}\}$ . As far as we know this is the first time that it is proved that the number of limit cycles that can bifurcate in a Hopf bifurcation increases exponentially with the dimension of the space. To prove this result, we use first-order averaging theory. Further, in dimension 4 we characterize the shape and the kind of stability of the bifurcated limit cycles. We apply our results to certain fourth-order differential equations and then to a simplified Marchuk model that describes immune response.

### 1. Introduction and statement of the main results

In this work we study the Hopf bifurcation of  $\mathcal{C}^3$  differential systems in  $\mathbb{R}^n$  with  $n \geq 3$  by using first-order averaging theory. We assume that these systems have a singularity at the origin, whose linear part has eigenvalues  $\varepsilon a \pm bi$  and  $\varepsilon c_k$  for  $k = 3, \dots, n$ , where  $\varepsilon$  is a small parameter. Such systems can be written in the form

$$\begin{aligned}
 \dot{x} &= \varepsilon ax - by + \sum_{i_1+\dots+i_n=2} a_{i_1\dots i_n} x^{i_1} y^{i_2} z_3^{i_3} \dots z_n^{i_n} + \mathcal{A}, \\
 \dot{y} &= bx + \varepsilon ay + \sum_{i_1+\dots+i_n=2} b_{i_1\dots i_n} x^{i_1} y^{i_2} z_3^{i_3} \dots z_n^{i_n} + \mathcal{B}, \\
 \dot{z}_k &= \varepsilon c_k z_k + \sum_{i_1+\dots+i_n=2} c_{i_1\dots i_n}^{(k)} x^{i_1} y^{i_2} z_3^{i_3} \dots z_n^{i_n} + \mathcal{C}_k, \quad k = 3, \dots, n,
 \end{aligned}
 \tag{1}$$

where  $a_{i_1\dots i_n}, b_{i_1\dots i_n}, c_{i_1\dots i_n}^{(k)}, a, b$  and  $c_k$  are real parameters,  $ab \neq 0$ , and  $\mathcal{A}, \mathcal{B}$  and  $\mathcal{C}_k$  are the Lagrange expressions of the error function of third order in the expansion of the functions of the system in Taylor series.

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Our first result is on the number of limit cycles which can bifurcate from the origin by using the first-order averaging method.

**Theorem 1.** *There exist  $\mathcal{C}^3$  systems (1) for which  $l \in \{0, 1, \dots, 2^{n-3}\}$  limit cycles bifurcate from the origin at  $\varepsilon = 0$ , that is, for  $\varepsilon$  sufficiently small the system has exactly  $l$  limit cycles in a neighborhood of the origin and these limit cycles tend to the origin when  $\varepsilon \searrow 0$ .*

Theorem 1 is proved in Section 3. From the proof of Theorem 1 the next result follows immediately.

**Corollary 2.** *There exist quadratic polynomial differential systems (1) (that is, with  $\mathcal{A} = \mathcal{B} = \mathcal{C}_k = 0$ ) for which  $l \in \{0, 1, \dots, 2^{n-3}\}$  limit cycles bifurcate from the origin at  $\varepsilon = 0$ , that is, for  $\varepsilon$  sufficiently small the system has exactly  $l$  limit cycles in a neighborhood of the origin and these limit cycles tend to the origin when  $\varepsilon \searrow 0$ .*

The study of limit cycles and averaging theory has a long history; see for instance [Marsden and McCracken 1976; Sanders and Verhulst 1985; Ye et al. 1986; Zhang et al. 1992; Verhulst 1991; Li 2003; Buică and Llibre 2004]. But as far as we know our result is the first one showing that the number of bifurcated limit cycles in a Hopf bifurcation can grow exponentially with the dimension of the system.

For lower dimensional systems we have more precise results than the ones stated in Theorem 1. See [Llibre et al. 2007] for a proof of Theorem 1 in dimension 3 restricted to quadratic polynomial differential systems, and for sufficient conditions for the existence or not of one limit cycle and its kind of stability. In dimension 4 we write the system (1) as

$$\begin{aligned}
 \dot{x} &= \varepsilon ax - by + \sum_{i+j+k+l=2} a_{ijkl} x^i y^j z^k w^l + \mathcal{A}, \\
 \dot{y} &= bx + \varepsilon ay + \sum_{i+j+k+l=2} b_{ijkl} x^i y^j z^k w^l + \mathcal{B}, \\
 \dot{z} &= \varepsilon cz + \sum_{i+j+k+l=2} c_{ijkl} x^i y^j z^k w^l + \mathcal{C}, \\
 \dot{w} &= \varepsilon dw + \sum_{i+j+k+l=2} d_{ijkl} x^i y^j z^k w^l + \mathcal{D},
 \end{aligned}
 \tag{2}$$

where  $a_{ijkl}, b_{ijkl}, c_{ijkl}, d_{ijkl}, a, b, c$  and  $d$  are real parameters,  $ab \neq 0$ , and  $\mathcal{A}, \mathcal{B}, \mathcal{C}$  and  $\mathcal{D}$  are the Lagrange expressions of the error function of third order in the expansion of the functions of the system in Taylor series. Without loss we assume that  $b > 0$ . Set

$$\begin{aligned}
 A &= KG_1 - LG_2, \\
 B &= 2a(N_2F_1 - 2N_3F_2) + cF_1^2G_2 + dF_1F_2G_1, \\
 C &= 2a(2aN_3 - dF_1G_1), \\
 D &= 2a(M_1F_1^2 + 2M_2F_1F_2 + M_3F_2^2) + cKF_1 + dLF_2, \\
 (3) \quad E &= -a(2aM_2F_1 + 2aM_3F_2 + dL), \\
 \Lambda &= dF_2G_1 - 2aN_2, \quad F = cF_2G_2 + 2aN_1, \quad \Delta = \Lambda^2 - 8aN_3F, \\
 \Gamma &= -8a^2c_{0002}N_3^2 + 4acF_2N_3^2 - 2ac_{0011}N_3\Lambda - c_{0002}(\Lambda^2 + \Delta)/2, \\
 \Phi &= 2c_{0011}CF_1(2aB + CF_2) - 2cBCF_1^2 - 2c_{0020}C^2F_1^2 - 2c_{0002}(2aB + CF_2)^2, \\
 \Psi &= 4a((cF_2 - 2ac_{0020})\Lambda^2 + 2ac_{0011}F_2\Lambda F - 2ac_{0002}F_2^2F^2),
 \end{aligned}$$

where

$$\begin{aligned}
 F_1 &= a_{1001} + b_{0101}, \quad F_2 = a_{1010} + b_{0110}, \quad G_1 = c_{0200} + c_{2000}, \quad G_2 = d_{0200} + d_{2000}, \\
 K &= d_{0020}F_1^2 - d_{0011}F_1F_2 + d_{0002}F_2^2, \quad L = c_{0020}F_1^2 - c_{0011}F_1F_2 + c_{0002}F_2^2, \\
 M_1 &= c_{0020}d_{0011} - c_{0011}d_{0020}, \quad M_2 = c_{0002}d_{0020} - c_{0020}d_{0002}, \\
 M_3 &= c_{0011}d_{0002} - c_{0002}d_{0011}, \\
 N_1 &= d_{0020}G_1 - c_{0020}G_2, \quad N_2 = d_{0011}G_1 - c_{0011}G_2, \quad N_3 = d_{0002}G_1 - c_{0002}G_2.
 \end{aligned}$$

Using these quantities we will be able to control the number of bifurcated limit cycles in the Hopf bifurcation of the system (2) and their kind of stability. Our basic assumptions are

$$F_1^2 + F_2^2 \neq 0, \quad G_1^2 + G_2^2 \neq 0.$$

Because if  $F_1^2 + F_2^2 = 0$  from the proof of our next theorem we can see that system (2) cannot present a Hopf bifurcation, and if  $G_1^2 + G_2^2 = 0$  then the system (2) either has no Hopf bifurcation or first-order averaging theory that we are using cannot decide if there is a Hopf bifurcation.

Our results on the Hopf bifurcation of the system (2) are the following.

**Theorem 3.** Consider a  $\mathcal{C}^3$  system (2) with  $G_1 \neq 0$ .

(a.1) Suppose  $F_1 \neq 0$ ,  $A \neq 0$ , and  $B^2 - 4AC > 0$ . If

$$4AE - DB + D\sqrt{B^2 - 4AC}F_1 > 0 \quad \text{or} \quad 4AE - DB - D\sqrt{B^2 - 4AC}F_1 > 0,$$

the system has a limit cycle tending to a singular point as  $\varepsilon \searrow 0$ . We denote this limit cycle by  $\Gamma_{1\varepsilon}$  in the first case and by  $\Gamma_{2\varepsilon}$  in the second. When both inequalities are satisfied, distinct limit cycles  $\Gamma_{1\varepsilon}$  and  $\Gamma_{2\varepsilon}$  exist, tending to different singular points as  $\varepsilon \searrow 0$ .

(a.2) Suppose  $F_1 \neq 0$ ,  $A = 0$ ,  $B \neq 0$  and  $\Phi G_1 > 0$ . Then the system has a limit cycle  $\bar{\Gamma}_{1\varepsilon}$  tending to the origin as  $\varepsilon \searrow 0$ .

(a.3) Suppose  $F_1 = 0$ ,  $F_2 \neq 0$ ,  $N_2 \neq 0$ , and  $\Delta > 0$ . If

$$(\Gamma - (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta})G_1 > 0$$

or

$$(\Gamma + (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta})G_1 > 0$$

the system has a limit cycle tending to a singular point as  $\varepsilon \searrow 0$ . We denote this limit cycle by  $\Gamma_{3\varepsilon}$  in the first case and by  $\Gamma_{4\varepsilon}$  in the second. When both inequalities are satisfied, distinct limit cycles  $\Gamma_{3\varepsilon}$  and  $\Gamma_{4\varepsilon}$  exist, tending to different singular points as  $\varepsilon \searrow 0$ .

(a.4) For  $F_1 = 0$ ,  $F_2 \neq 0$  and  $N_2 = 0$ , if  $\Lambda \neq 0$  and  $\Psi G_1 > 0$ , the system (2) has a limit cycle  $\bar{\Gamma}_{3\varepsilon}$  tending to the origin as  $\varepsilon \searrow 0$ .

(b) For  $\varepsilon > 0$  sufficiently small the limit cycles from statements (a.1)–(a.4) are given by the graphs

$$\Gamma_{1\varepsilon} \begin{cases} r(\theta) = \varepsilon \sqrt{(4AE - DB + D\sqrt{B^2 - 4AC})/(F_1 A^2) + O(\varepsilon^2)}, \\ z(\theta) = \varepsilon (B - \sqrt{B^2 - 4AC})/(2A) + O(\varepsilon^2), \\ w(\theta) = -\varepsilon (4aA + F_2(B - \sqrt{B^2 - 4AC}))/(2AF_1) + O(\varepsilon^2); \end{cases}$$

$$\Gamma_{2\varepsilon} \begin{cases} r(\theta) = \varepsilon \sqrt{(4AE - DB - D\sqrt{B^2 - 4AC})/(F_1 A^2) + O(\varepsilon^2)}, \\ z(\theta) = \varepsilon (B + \sqrt{B^2 - 4AC})/(2A) + O(\varepsilon^2), \\ w(\theta) = -\varepsilon (4aA + F_2(B + \sqrt{B^2 - 4AC}))/(2AF_1) + O(\varepsilon^2); \end{cases}$$

$$\bar{\Gamma}_{1\varepsilon} \begin{cases} r(\theta) = \varepsilon \sqrt{\Phi/(G_1 B^2 F_1^2) + O(\varepsilon^2)}, \\ z(\theta) = \varepsilon C/B + O(\varepsilon^2), \\ w(\theta) = -\varepsilon (2aB + CF_2)/(BF_1) + O(\varepsilon^2); \end{cases}$$

$$\Gamma_{3\varepsilon} \begin{cases} r(\theta) = \varepsilon \sqrt{(\Gamma - (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta})/(G_1 F_2^2 N_2^2) + O(\varepsilon^2)}, \\ z(\theta) = -\varepsilon 2a/F_2 + O(\varepsilon^2), \\ w(\theta) = -\varepsilon (\Lambda + \sqrt{\Delta})/(2N_2 F_2) + O(\varepsilon^2); \end{cases}$$

$$\Gamma_{4\varepsilon} \begin{cases} r(\theta) = \varepsilon \sqrt{(\Gamma + (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta})/(G_1 F_2^2 N_2^2) + O(\varepsilon^2)}, \\ z(\theta) = -\varepsilon 2a/F_2 + O(\varepsilon^2), \\ w(\theta) = -\varepsilon (\Lambda - \sqrt{\Delta})/(2N_2 F_2) + O(\varepsilon^2); \end{cases}$$

$$\bar{\Gamma}_{3\varepsilon} \begin{cases} r(\theta) = \varepsilon \sqrt{\Psi/(G_1 F_2^2 \Lambda^2) + O(\varepsilon^2)}, \\ z(\theta) = -\varepsilon 2a/F_2 + O(\varepsilon^2), \\ w(\theta) = -\varepsilon 2aF/\Lambda + O(\varepsilon^2), \end{cases}$$

where  $\theta \in \mathbb{S}^1$  and the coordinates  $(r, z, w)$  and  $\theta$  are defined at the beginning of Section 4.

For the remaining statements we need the system (2) to be at least  $\mathcal{C}^4$ .

- (c.1) For  $F_1 > 0$  and  $A \neq 0$ , the limit cycle  $\Gamma_{1\epsilon}$  (respectively  $\Gamma_{2\epsilon}$ ) has at least one-dimensional stable (respectively unstable) manifold, and consequently the limit cycle is not a global repeller (respectively attractor). For  $F_1 < 0$  and  $A \neq 0$  the one-dimensional invariant manifold of the limit cycle has converse stability than for  $F_1 > 0$ .
- (c.2) For  $F_1 > 0$ ,  $A = 0$  and  $B \neq 0$ , the limit cycle  $\bar{\Gamma}_{1\epsilon}$  has at least one-dimensional stable (respectively unstable) manifold provided that  $B > 0$  (respectively  $B < 0$ ). For  $F_1 < 0$  the one-dimensional invariant manifold of the limit cycle has a different stability than for  $F_1 > 0$ .
- (c.3) For  $F_1 = 0$ ,  $F_2 > 0$  and  $N_2 \neq 0$  the limit cycle  $\Gamma_{3\epsilon}$  (respectively  $\Gamma_{4\epsilon}$ ) has at least one-dimensional stable (respectively unstable) manifold. For  $F_1 = 0$ ,  $F_2 < 0$  and  $N_2 \neq 0$ , the one-dimensional invariant manifold of the limit cycles has a different stability than for  $F_2 > 0$ .
- (c.4) For  $F_1 = 0$ ,  $F_2 \neq 0$ ,  $N_2 = 0$  and  $\Lambda \neq 0$ , the limit cycle  $\bar{\Gamma}_{3\epsilon}$  has at least one-dimensional stable (respectively unstable) manifold provided that  $\Delta > 0$  (respectively  $\Delta < 0$ ).

Theorem 3 will be proved in Section 4.

We note that the quantities defined in (3) depend only on the following 18 parameters:  $a, b, c, d, a_{1010}, a_{1001}, b_{0110}, b_{0101}, c_{2000}, c_{0200}, c_{0020}, c_{0011}, c_{0002}, d_{2000}, d_{0200}, d_{0020}, d_{0011}, d_{0002}$  of the 44 parameters of the system (2). So the Hopf bifurcation depends only on these 18 parameters.

We remark that in (a.2) we need  $B \neq 0$ , and in (a.4) we need  $\Lambda \neq 0$ . Otherwise, as it follows from the proof of Theorem 3, first-order averaging theory cannot decide on the existence of a Hopf bifurcation.

Other studies on the Hopf bifurcation using averaging theory in a different way than ours have been made by Chow and Mallet-Paret [Marsden and McCracken 1976, Section 4.C]. Their results are more general than the present ones, but ours are more precise and provide also the stability of the bifurcated Hopf limit cycles. A related generalized Hopf bifurcation can be found in [Aguirre and Seibert 1999].

We now consider some applications of our Theorem 3. The first one is on the existence of periodic solutions of the fourth order differential equation

$$(4) \quad \frac{d^4x}{dt^4} + p \frac{d^3x}{dt^3} + q \frac{d^2x}{dt^2} + k \frac{dx}{dt} + lx = f\left(x, \frac{dx}{dt}, \frac{d^2x}{dt^2}, \frac{d^3x}{dt^3}\right),$$

where  $p, q, k, l$  are real parameters satisfying

$$\begin{aligned} p &= -(2a+c+d)\varepsilon, & q &= b^2+(a^2+2ac+2ad+cd)\varepsilon^2, \\ k &= -\varepsilon(b^2c+b^2d+(a^2c+a^2d+2acd)\varepsilon^2), & l &= cd\varepsilon^2(b^2+a^2\varepsilon), \end{aligned}$$

and  $f$  is a  $\mathbb{C}^3$  function whose first-order partial derivatives vanish at the origin of 4-dimensional space.

**Theorem 4.** *For  $0 < \varepsilon \ll 1$ , the system (4) has an isolated periodic solution in a neighborhood of the trivial solution  $x = 0$  if one of the following conditions holds:*

(i)  $b_4 \neq 0, cb_4 + db_3 \neq 0$  and

$$\Phi^* = a(b_1 + b_5) (cd(cb_4 + db_3) - 2ab_4^2(c^2b_{10} + cdb_9 + d^2b_8)) > 0;$$

(ii)  $b_4 = 0, b_3 \neq 0, d \neq 0$  and

$$\Psi^* = a(b_1 + b_5) (cd^2b_3 - 2a(c^2b_3^2b_{10} - cdb_3b_9 - d^2b_8)) > 0,$$

where the  $b_i$  are defined in Section 5.

In Section 5 we will prove Theorem 4 and we will present a more detailed statement on the existence and shape of the periodic solution of (4).

The second application is to a system defined by Marchuk [1980] as a simplified model of an immune system, with no influence from damaged organs but with time delay:

$$(5) \quad \begin{aligned} \frac{dX}{dt} &= (\beta - \gamma Z)X, & \frac{dY}{dt} &= \alpha XZ - \mu_1(Y - \delta), \\ \frac{dZ}{dt} &= \rho Y - (\mu_2 + \eta\gamma X)Z, & \frac{dW}{dt} &= \sigma X - \mu_3 W, \end{aligned}$$

**Theorem 5.** *There is an open set in parameter space for which the system (5) has at least one limit cycle.*

A more detailed statement and a proof of Theorem 5 will be given in Section 6, where we will present the conditions for the existence and stability of limit cycles coming from a Hopf bifurcation.

## 2. The first-order averaging method for periodic orbits

The aim of this section is to present the first-order averaging method as it was obtained in [Buică and Llibre 2004]. Differentiability of the vector field is not needed. The specific conditions for the existence of a simple isolated zero of the averaged function are given in terms of the Brouwer degree. In fact the Brouwer degree theory is the key point in the proof of this theorem.

**Theorem 6.** Consider the following differential system

$$(6) \quad \dot{x}(t) = \varepsilon f(t, x) + \varepsilon^2 R(t, x, \varepsilon),$$

where  $f : \mathbb{R} \times D \rightarrow \mathbb{R}^n$ ,  $R : \mathbb{R} \times D \times (-\varepsilon_f, \varepsilon_f) \rightarrow \mathbb{R}^n$  are continuous functions,  $T$ -periodic in the first variable, and  $D$  is an open subset of  $\mathbb{R}^n$ . Define  $f^0 : D \rightarrow \mathbb{R}^n$  as

$$(7) \quad f^0(z) = \frac{1}{T} \int_0^T f(s, z) ds,$$

and assume that

- (i)  $f$  and  $R$  are locally Lipschitz with respect to  $x$ ;
- (ii) for  $b \in D$  with  $f^0(b) = 0$ , there exists a neighborhood  $V$  of  $b$  such that  $f^0(z) \neq 0$  for all  $z \in \bar{V} \setminus \{b\}$  and  $d_B(f^0, V, b) \neq 0$ , (where  $d_B(f^0, V, b)$  denotes the Brouwer degree of  $f^0$  in the neighborhood  $V$  of  $b$ ).

Then, for  $|\varepsilon| > 0$  sufficiently small, there exists an isolated  $T$ -periodic solution  $\varphi(\cdot, \varepsilon)$  of the system (6) such that  $\varphi(b, 0) = b$ .

Here we will need some facts from the proof of Theorem 6. Hypothesis (i) assures the existence and uniqueness of the solution of each initial value problem on the interval  $[0, T]$ . Hence, for each  $z \in D$ , it is possible to denote by  $x(\cdot, z, \varepsilon)$  the solution of (6) with the initial value  $x(0, z, \varepsilon) = z$ . We consider also the function  $\zeta : D \times (-\varepsilon_f, \varepsilon_f) \rightarrow \mathbb{R}^n$  defined by

$$(8) \quad \zeta(z, \varepsilon) = \int_0^T (\varepsilon f(t, x(t, z, \varepsilon)) + \varepsilon^2 R(t, x(t, z, \varepsilon), \varepsilon)) dt.$$

From the proof of Theorem 6 we extract the following facts.

**Remark 7.** Under the assumptions of Theorem 6 for every  $z \in D$  the following relation holds:

$$x(T, z, \varepsilon) - x(0, z, \varepsilon) = \zeta(z, \varepsilon).$$

Moreover the function  $\zeta$  can be written in the form

$$\zeta(z, \varepsilon) = \varepsilon f^0(z) + O(\varepsilon^2),$$

where  $f^0$  is given by (7) and the symbol  $O(\varepsilon^2)$  denotes a bounded function on every compact subset of  $D \times (-\varepsilon_f, \varepsilon_f)$  multiplied by  $\varepsilon^2$ . Moreover, for  $|\varepsilon|$  sufficiently small,  $z = \varphi(0, \varepsilon)$  is an isolated zero of  $\zeta(\cdot, \varepsilon)$ .

Note that from Remark 7 it follows that a zero  $z$  of the function  $\zeta(z, \varepsilon)$  provides initial conditions for a periodic orbit of the system of period  $T$ . Consequently the zeros of  $f^0(z)$  when  $f^0(z)$  is not identically zero also provides periodic orbits of period  $T$ .

For a given system there is the possibility that the function  $\zeta$  is not globally differentiable, but the function  $f^0$  is. In fact, only differentiability in some neighborhood of a fixed isolated zero of  $f^0$  could be enough. When this is the case, one can use the following remark in order to verify the hypothesis (ii) of Theorem 6.

**Remark 8.** Let  $f^0 : D \rightarrow \mathbb{R}^n$  be a  $\mathcal{C}^1$  function with  $f^0(b) = 0$ , where  $D$  is an open subset of  $\mathbb{R}^n$  and  $b \in D$ . Whenever  $b$  is a simple zero of  $f^0$  (that is, the Jacobian of  $f^0$  at  $b$  is not zero), then there exists a neighborhood  $V$  of  $b$  such that  $f^0(z) \neq 0$  for all  $z \in \bar{V} \setminus \{b\}$ . Then  $d_B(f^0, V, b) \in \{-1, 1\}$ .

The following theorem of [Buică et al. 2007] provides the asymptotic stability of the limit cycles obtained by averaging theory only with the  $\mathcal{C}^1$  differentiability of  $f$  and a Lipschitz assumption on  $R$ .

**Theorem 9.** *If the function  $f$  of (6) is  $\mathcal{C}^1$  and the function  $R$  is Lipschitz in a neighborhood of the limit cycle  $\varphi(\cdot, \varepsilon)$  given in Theorem 6 by the simple zero  $b$  of  $f^0$ , then for  $\varepsilon$  sufficiently small if all the eigenvalues of the Jacobian matrix of  $f^0$  at  $b$  have negative (respectively positive) real part, then the limit cycle  $\varphi(\cdot, \varepsilon)$  is asymptotically stable (respectively unstable).*

Of course if the function  $f$  of (6) is  $\mathcal{C}^2$  and the function  $R$  is  $\mathcal{C}^1$  then we have better information on the kind of stability of the limit cycle  $\varphi(\cdot, \varepsilon)$  given in Theorem 6. A proof of this result can be found in [Verhulst 1991] or in [Guckenheimer and Holmes 1990].

**Theorem 10.** *If the function  $f$  of (6) is  $\mathcal{C}^2$  and the function  $R$  is  $\mathcal{C}^1$  in a neighborhood of a simple zero  $b$  of  $f^0$ , then for  $\varepsilon$  sufficiently small the stability or instability of the limit cycle  $\varphi(\cdot, \varepsilon)$  given in Theorem 6 is given by the stability or instability of the singularity  $b$  of the averaged system  $\dot{z} = \varepsilon f^0(z)$ . In fact the singularity  $b$  has the stability behavior of the Poincaré map associated to the limit cycle  $\varphi(\cdot, \varepsilon)$ .*

### 3. Proof of Theorem 1

Doing the cylindrical change of coordinates

$$(9) \quad x = r \cos \theta, \quad y = r \sin \theta, \quad z_i = z_i, \quad i = 3, \dots, n,$$

in the region  $r > 0$ , the system (1) becomes

$$(10) \quad \begin{aligned} \dot{r} &= \varepsilon ar + \sum (a_{i_1 \dots i_n} \cos \theta + b_{i_1 \dots i_n} \sin \theta) (r \cos \theta)^{i_1} (r \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} + O(3), \\ \dot{\theta} &= \frac{1}{r} (br + \sum (b_{i_1 \dots i_n} \cos \theta - a_{i_1 \dots i_n} \sin \theta) (r \cos \theta)^{i_1} (r \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} + O(3)), \\ \dot{z}_k &= \varepsilon c_k z_k + \sum c_{i_1 \dots i_n}^{(k)} (r \cos \theta)^{i_1} (r \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} + O(3), \quad k = 3, \dots, n, \end{aligned}$$

where  $O(3) = O_3(r, z_3, \dots, z_n)$  and the sums range over  $i_1 + \dots + i_n = 2$ .

As usual  $\mathbb{Z}_+$  denotes the set of all nonnegative integers. Taking  $a_{00e_{ij}} = b_{00e_{ij}} = 0$  where  $e_{ij} \in \mathbb{Z}_+^{n-2}$  has the sum of the entries equal to 2, it is easy to show that in a suitable small neighborhood of  $(r, z_3, \dots, z_n) = (0, 0, \dots, 0)$  we have  $\dot{\theta} \neq 0$ . Then choosing  $\theta$  as the new independent variable, the system (10) becomes, in a neighborhood of  $(r, z_3, \dots, z_n) = (0, 0, \dots, 0)$ ,

$$(11) \quad \begin{aligned} \frac{dr}{d\theta} &= \frac{r(\varepsilon ar + \sum (a_{i_1 \dots i_n} \cos \theta + b_{i_1 \dots i_n} \sin \theta)(r \cos \theta)^{i_1} (r \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} + O(3))}{br + \sum (b_{i_1 \dots i_n} \cos \theta - a_{i_1 \dots i_n} \sin \theta)(r \cos \theta)^{i_1} (r \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} + O(3)}, \\ \frac{dz_k}{d\theta} &= \frac{r(\varepsilon c_k z_k + \sum c_{i_1 \dots i_n}^{(k)} (r \cos \theta)^{i_1} (r \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} + O(3))}{br + \sum (b_{i_1 \dots i_n} \cos \theta - a_{i_1 \dots i_n} \sin \theta)(r \cos \theta)^{i_1} (r \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} + O(3)}, \end{aligned}$$

$k = 3, \dots, n,$

where the sums range over  $i_1 + \dots + i_n = 2$ . Note that this system is periodic of period  $2\pi$  in  $\theta$ .

To apply the averaging theory of Section 2 in the proof of Theorem 1 we rescale the variables, setting

$$(12) \quad (r, z_3, \dots, z_n) = (\rho\varepsilon, \eta_3\varepsilon, \dots, \eta_n\varepsilon).$$

The system (11) becomes

$$(13) \quad \begin{aligned} \frac{d\rho}{d\theta} &= \varepsilon f_1(\theta, \rho, \eta_3, \dots, \eta_n) + \varepsilon^2 g_1(\theta, \rho, \eta_3, \dots, \eta_n, \varepsilon), \\ \frac{d\eta_k}{d\theta} &= \varepsilon f_k(\theta, \rho, \eta_3, \dots, \eta_n) + \varepsilon^2 g_k(\theta, \rho, \eta_3, \dots, \eta_n, \varepsilon), \quad k = 3, \dots, n, \end{aligned}$$

where

$$\begin{aligned} f_1 &= \frac{1}{b} \left( a\rho + \sum_{i_1 + \dots + i_n = 2} (a_{i_1 \dots i_n} \cos \theta + b_{i_1 \dots i_n} \sin \theta)(\rho \cos \theta)^{i_1} (\rho \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} \right), \\ f_k &= \frac{1}{b} \left( c\eta_k + \sum_{i_1 + \dots + i_n = 2} c_{i_1 \dots i_n}^{(k)} (\rho \cos \theta)^{i_1} (\rho \sin \theta)^{i_2} z_3^{i_3} \dots z_n^{i_n} \right). \end{aligned}$$

The system (13) has the form (6) in the averaging theorem with  $x = (\rho, \eta_3, \dots, \eta_n)$ ,  $t = \theta$ ,  $T = 2\pi$ , and

$$\begin{aligned} f(\theta, \rho, \eta_3, \dots, \eta_n) &= (f_1(\theta, \rho, \eta_3, \dots, \eta_n), f_3(\theta, \rho, \eta_3, \dots, \eta_n), \dots, f_n(\theta, \rho, \eta_3, \dots, \eta_n)) \end{aligned}$$

The averaged system of (13) is

$$(14) \quad \dot{y} = \varepsilon f^0(y), \quad y = (\rho, \eta_3, \dots, \eta_n) \in \Omega,$$

where  $\Omega$  is a suitable neighborhood of the origin  $(\rho, \eta_3, \dots, \eta_n) = (0, 0, \dots, 0)$ , and

$$f^0(y) = (f_1^0(y), f_3^0(y), \dots, f_n^0(y)),$$

with

$$f_i^0(y) = \frac{1}{2\pi} \int_0^{2\pi} f_i(\theta, \rho, \eta_3, \dots, \eta_n) d\theta, \quad i = 1, 3, \dots, n.$$

After some calculations we obtain

$$f_1^0 = \frac{1}{2b} \rho \left( 2a + \sum_{j=3}^n (a_{10e_j} + b_{01e_j}) \eta_j \right),$$

$$f_k^0 = \frac{1}{2b} \left( 2c_k \eta_k + (c_{200n-2}^{(k)} + c_{020n-2}^{(k)}) \rho^2 + 2 \sum_{3 \leq i < j \leq n} c_{00e_{ij}}^{(k)} \eta_i \eta_j \right), \quad k = 3, \dots, n,$$

where  $e_j \in \mathbb{Z}_+^{n-2}$  is the unit vector with the  $j$ -th entry equal to 1, and  $e_{ij} \in \mathbb{Z}_+^{n-2}$  has the sum of the  $i$ -th and  $j$ -th entries equal to 2 and the other equal to 0.

Now we shall apply Theorem 6 for obtaining limit cycles of the system (13). After the rescaling (12), these limits will become infinitesimal limit cycles for the system (11), which will tend to origin when  $\varepsilon \searrow 0$ , consequently they will be bifurcated limit cycles of the Hopf bifurcation of the system (11) at the origin.

Using Theorem 6 for studying the limit cycles of the system (13) we only need to compute the nondegenerate singularities of the system (14). Since the transformation from the cartesian coordinates  $(r, z_3, \dots, z_n)$  to the cylindrical ones  $(\rho, \eta_3, \dots, \eta_n)$  is not a diffeomorphism at  $\rho = 0$ , we deal with the zeros having the coordinate  $\rho > 0$  of the averaged function  $f^0$ . So we need to compute the roots of the algebraic equations

$$(15) \quad \begin{aligned} 2a + \sum_{j=3}^n (a_{10e_j} + b_{01e_j}) \eta_j &= 0, \\ 2c_k \eta_k + (c_{200n-2}^{(k)} + c_{020n-2}^{(k)}) \rho^2 + 2 \sum_{3 \leq i < j \leq n} c_{00e_{ij}}^{(k)} \eta_i \eta_j &= 0, \quad k = 3, \dots, n. \end{aligned}$$

Since the coefficients of this system are independent and arbitrary, we can simplify the notation by writing the system as

$$(16) \quad \begin{aligned} a + \sum_{j=3}^n a_j \eta_j &= 0, \\ c_0^{(k)} \rho^2 + c_k \eta_k + \sum_{3 \leq i < j \leq n} c_{ij}^{(k)} \eta_i \eta_j &= 0, \quad k = 3, \dots, n, \end{aligned}$$

where  $a_j, c_0^{(k)}, c_k$  and  $c_{ij}^{(k)}$  are arbitrary constants.

Denote by  $\mathcal{C}$  the set of algebraic systems of form (16). We claim that there is a system belonging to  $\mathcal{C}$  which has exactly  $2^{n-3}$  simple roots. The claim can be verified by the example

$$(17) \quad a + a_3 \eta_3 = 0,$$

$$(18) \quad c_0^{(3)} \rho^2 + c_3 \eta_3 + \sum_{3 \leq i \leq j \leq n} c_{ij}^{(3)} \eta_i \eta_j = 0,$$

$$(19) \quad c_k \eta_k + \sum_{3 \leq i \leq j \leq k} c_{ij}^{(k)} \eta_i \eta_j = 0, \quad k = 4, \dots, n,$$

with all the coefficients nonzero. Equations (19) can be treated as quadratic algebraic equations in  $\eta_k$ . Substituting the unique solution  $\eta_{30}$  of  $\eta_3$  in (17) into (19) with  $k = 4$ , then this last equation has exactly two different solutions  $\eta_{41}$  and  $\eta_{42}$  for  $\eta_4$  choosing conveniently  $c_4$ . Introducing the two solutions  $(\eta_{30}, \eta_{4i}), i = 1, 2$ , into (19) with  $k = 5$  and choosing conveniently the values of the coefficients of (19) with  $k = 5$  and  $(\eta_3, \eta_4) = (\eta_{30}, \eta_{4i})$  we get two different solutions  $\eta_{5i1}$  and  $\eta_{5i2}$  of  $\eta_5$  for each  $i$ . Moreover playing with the coefficients of the equations, the four solutions  $(\eta_{30}, \eta_{4i}, \eta_{5ij})$  for  $i, j = 1, 2$ , are distinct. By induction we can prove that for suitable choice of the coefficients equations (17) and (19) have  $2^{n-3}$  different roots  $(\eta_3, \dots, \eta_n)$ . Since  $\eta_3 = \eta_{30}$  is fixed, for any given  $c_{ij}^{(3)}$  there exist values of  $c_3$  and  $c_0^{(3)}$  such that (18) has a positive solution  $\rho$  for each of the  $2^{n-3}$  solutions  $(\eta_3, \dots, \eta_n)$  of (17) and (19). Since the  $2^{n-3}$  solutions are different, and the number of the solutions of (17)–(19) is the maximum that the equations can have by Bézout’s Theorem, it follows that every solution is simple, and consequently the determinant of the Jacobian of the system evaluated at it is not zero. This proves the claim.

Using the same arguments which allow us to prove the claim, we also can prove that we can choose the coefficients of the previous system in order that it has  $0, 1, \dots, 2^{n-3} - 1$  simple real solutions.

Taking the averaged system (14) with  $f^0$  having the convenient coefficients as in (17)–(19), the averaged system (14) has exactly  $k \in \{0, 1, \dots, 2^{n-3}\}$  singularities with the components  $\rho > 0$ . Moreover the determinants of the Jacobian matrix  $\partial f^0 / \partial y$  at these singularities do not vanish, because all the singularities are simple. By Theorem 6 and Section 2 we get that there are systems of form (1) which have  $k \in \{0, 1, \dots, 2^{n-3}\}$  limit cycles. This proves Theorem 1.

### 4. Proof of Theorem 3

Following the proof of Theorem 1 after the change of variables  $x = r \cos \theta, y = r \sin \theta, z = z$  and  $w = w$ , and the rescaling  $(r, z, w) = (\rho \varepsilon, \xi \varepsilon, \eta \varepsilon)$  we get from

(2) that

$$(20) \quad \begin{aligned} \frac{d\rho}{d\theta} &= \varepsilon A_1(\theta, \rho, \zeta, \eta) + \varepsilon^2 B_1(\theta, \rho, \zeta, \eta, \varepsilon), \\ \frac{d\zeta}{d\theta} &= \varepsilon A_2(\theta, \rho, \zeta, \eta) + \varepsilon^2 B_2(\theta, \rho, \zeta, \eta, \varepsilon), \\ \frac{d\rho}{d\theta} &= \varepsilon A_3(\theta, \rho, \zeta, \eta) + \varepsilon^2 B_3(\theta, \rho, \zeta, \eta, \varepsilon), \end{aligned}$$

where the  $A_i$  can be got from the proof of Theorem 1. We do not present them here. The averaged system associated to (20) is

$$(21) \quad \dot{y} = \varepsilon f^0(y), \quad y = (\rho, \zeta, \eta),$$

where  $f^0(y) = (f_1^0(y), f_2^0(y), f_3^0(y))$  with

$$\begin{aligned} f_1^0 &= \frac{1}{2b}\rho(2a + (a_{1010} + b_{0110})\zeta + (a_{1001} + b_{0101})\eta), \\ f_2^0 &= \frac{1}{2b}(2c\zeta + (c_{0200} + c_{2000})\rho^2 + 2(c_{0020}\zeta^2 + c_{0011}\zeta\eta + c_{0002}\eta^2)), \\ f_3^0 &= \frac{1}{2b}(2d\eta + (d_{0200} + d_{2000})\rho^2 + 2(d_{0020}\zeta^2 + d_{0011}\zeta\eta + d_{0002}\eta^2)). \end{aligned}$$

As explained in the proof of Theorem 1, we consider the singularities with  $\rho > 0$  of the averaged system (21). Some tedious calculations show that for  $F_1 \neq 0$  and  $A \neq 0$  the singularities with  $\rho > 0$  of (21) are  $S_1 = (\rho_1, \zeta_1, \eta_1)$  with

$$\begin{aligned} \rho_1 &= \sqrt{\frac{4AE - DB + D\sqrt{B^2 - 4AC}}{F_1 A^2}}, \quad \zeta_1 = \frac{B - \sqrt{B^2 - 4AC}}{2A}, \\ \eta_1 &= -\frac{4aA + F_2(B - \sqrt{B^2 - 4AC})}{2AF_1}, \end{aligned}$$

if  $B^2 - 4AC > 0$  and  $(4AE - DB + D\sqrt{B^2 - 4AC})F_1 > 0$ ; or  $S_2 = (\rho_2, \zeta_2, \eta_2)$  with

$$\begin{aligned} \rho_2 &= \sqrt{\frac{4AE - DB - D\sqrt{B^2 - 4AC}}{F_1 A^2}}, \quad \zeta_2 = \frac{B + \sqrt{B^2 - 4AC}}{2A}, \\ \eta_2 &= -\frac{4aA + F_2(B + \sqrt{B^2 - 4AC})}{2AF_1}, \end{aligned}$$

if  $B^2 - 4AC > 0$  and  $(4AE - DB - D\sqrt{B^2 - 4AC})F_1 > 0$ .

We treat  $A, B, C, D, E$  as polynomials in  $F_i$  and  $G_i$  for  $i = 1, 2$ . Then  $AE$  has the terms with degree 4, but  $DB$  and  $D\sqrt{B^2 - 4AC}$  has the terms with the lowest degree 5. So by choosing the values of  $F_1, F_2, G_1$  and  $G_2$  suitably small, that is, the values of  $a_{1001}, a_{1010}, b_{0110}, b_{0101}, c_{0200}, c_{2000}, d_{0200}, d_{2000}$ , and the

convenient choice of the other parameters we can prove that  $S_1$  and  $S_2$  can appear simultaneously.

From other tedious calculations we get that

$$(22) \quad \det \left( \frac{\partial f^0}{\partial y} \right) \Big|_{S_1} = -\rho_1^2 \frac{\sqrt{B^2 - 4AC}}{2b^3 F_1} \quad \text{and} \quad \det \left( \frac{\partial f^0}{\partial y} \right) \Big|_{S_2} = \rho_2^2 \frac{\sqrt{B^2 - 4AC}}{2b^3 F_1}.$$

Hence it follows from the assumptions of statement (a.1) of Theorem 3 and the previous discussions that  $S_1$  and  $S_2$  can appear simultaneously and are different, and that the determinants of the Jacobian matrix of (21) at  $S_1$  and  $S_2$  are both different from zero. By Section 2 we obtain that for  $\varepsilon$  sufficiently small the system (20) has two limit cycles that we denoted by  $\Gamma_{i\varepsilon}$ ,  $i = 1, 2$ , and  $\Gamma_{i\varepsilon} \rightarrow S_i$ ,  $i = 1, 2$ , as  $\varepsilon \searrow 0$ . Hence statement (a.1) of Theorem 3 is proved.

If  $F_1 \neq 0$ ,  $A = 0$  and  $B \neq 0$ , the averaged system (21) has the unique singularity

$$\bar{S}_1 = (\bar{\rho}_1, \bar{\xi}_1, \bar{\eta}_1) = \left( \sqrt{\frac{\Phi}{G_1 B^2 F_1^2}}, \frac{C}{B}, -\frac{2aB + C F_2}{B F_1} \right).$$

Recall that we have assumed  $G_1 \neq 0$ . The determinant of the Jacobian matrix of (21) at  $\bar{S}_1$  is

$$(23) \quad \det \left( \frac{\partial f^0}{\partial y} \right) \Big|_{\bar{S}_1} = -\bar{\rho}_1^2 \frac{B}{2b^3 F_1}.$$

Therefore using Section 2 it follows statement (a.2) of Theorem 3.

If  $F_1 = 0$ ,  $F_2 \neq 0$  and  $N_2 \neq 0$ , the averaged system (21) has the singularities

$$S_3 = (\rho_3, \xi_3, \eta_3) = \left( \sqrt{\frac{\Gamma - (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta}}{G_1 F_2^2 N_2^2}}, -\frac{2a}{F_2}, -\frac{\Lambda + \sqrt{\Delta}}{2N_2 F_2} \right),$$

if  $(\Gamma - (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta})G_1 > 0$ ; and

$$S_4 = (\rho_4, \xi_4, \eta_4) = \left( \sqrt{\frac{\Gamma + (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta}}{G_1 F_2^2 N_2^2}}, -\frac{2a}{F_2}, -\frac{\Lambda - \sqrt{\Delta}}{2N_2 F_2} \right),$$

if  $(\Gamma + (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta})G_1 > 0$ . The determinants of the Jacobian matrix of (21) at  $S_3$  and  $S_4$  are respectively

$$(24) \quad \det \left( \frac{\partial f^0}{\partial y} \right) \Big|_{S_3} = -\rho_3^2 \frac{\sqrt{\Delta F_2^2}}{2b^3 F_2} \quad \text{and} \quad \det \left( \frac{\partial f^0}{\partial y} \right) \Big|_{S_4} = \rho_4^2 \frac{\sqrt{\Delta F_2^2}}{2b^3 F_2}.$$

Again from Section 2 it follows statement (a.3) of Theorem 3.

If  $F_1 = 0, F_2 \neq 0, N_2 = 0$  and  $\Lambda \neq 0$ , the averaged system (21) has the unique singularity

$$\bar{S}_3 := (\bar{\rho}_3, \bar{\xi}_3, \bar{\eta}_3) = \left( \sqrt{\frac{\Psi}{G_1 F_2^2 \Lambda^2}}, -\frac{2a}{F_2}, -\frac{2aF}{\Lambda} \right).$$

The determinant of the Jacobian matrix of (21) at  $\bar{S}_3$  is

$$(25) \quad \det \left( \frac{\partial f^0}{\partial y} \right) \Big|_{\bar{S}_3} = -\bar{\rho}_3^2 \frac{\Lambda}{2b^3}.$$

After a similar treating as those in the proof of the case  $S_1$  and  $S_2$ , we can finished the proof of statement (a.4).

For proving statement (b) of Theorem 3 we observe that the limit cycles  $\Gamma_{i\varepsilon}$  for  $i = 1, 2$  can be written in the form  $\{(r_i(\theta), z_i(\theta), w_i(\theta)); \theta \in \mathbb{S}^1\}$ , and that the singularities  $S_1$  and  $S_2$  in the coordinates  $(r, z, w)$  are respectively

$$\left( \varepsilon \sqrt{\frac{4AE - DB + D\sqrt{B^2 - 4AC}}{F_1 A^2}}, \varepsilon \frac{B - \sqrt{B^2 - 4AC}}{2A}, -\varepsilon \frac{4aA + F_2(B - \sqrt{B^2 - 4AC})}{2AF_1} \right),$$

$$\left( \varepsilon \sqrt{\frac{4AE - DB - D\sqrt{B^2 - 4AC}}{F_1 A^2}}, \varepsilon \frac{B + \sqrt{B^2 - 4AC}}{2A}, -\varepsilon \frac{4aA + F_2(B + \sqrt{B^2 - 4AC})}{2AF_1} \right).$$

Now the proof of statement (b) of Theorem 3 for the limit cycles  $\Gamma_{i\varepsilon}$  with  $i = 1, 2$  follows from Section 2.

In a similar way as for the limit cycles  $\Gamma_{1\varepsilon}$  and  $\Gamma_{2\varepsilon}$  we can get the conclusion for the other limit cycles  $\bar{\Gamma}_{1\varepsilon}, \Gamma_{3\varepsilon}$  and  $\Gamma_{4\varepsilon}$  and  $\bar{\Gamma}_{3\varepsilon}$ . Hence statement (b) of Theorem 3 is proved.

By Theorem 10 and the determinants (22) (respectively (23), (24) and (25)) of the Jacobian matrix of (21) at  $S_1$  and  $S_2$  (respectively  $\bar{S}_3, S_3$  and  $S_4$ , and  $\bar{S}_3$ ), the proof of statements (c.1)–(c.4) of Theorem 3 easily follows.

We remark that the characteristic equations of the system (21) at  $S_i, i = 1, 2, 3, 4$ , are extremely complicated in the expression. So we do not pursue further analysis on them to obtain more information on the dimensions of stable and unstable manifolds of the limit cycles  $\Gamma_{i\varepsilon}, i = 1, 2, 3, 4$ .

**5. Application to fourth-order differential equations**

Now we want to apply our Theorem 3 to study the existence of periodic solutions of higher order differential equations. We consider the following fourth order differential equation

$$(26) \quad \frac{d^4x}{dt^4} + p \frac{d^3x}{dt^3} + q \frac{d^2x}{dt^2} + k \frac{dx}{dt} + lx = f \left( x, \frac{dx}{dt}, \frac{d^2x}{dt^2}, \frac{d^3x}{dt^3} \right),$$

where  $p, q, k, l$  are real parameters, and  $f$  is a  $\mathcal{C}^3$  function with the expansion

$$\begin{aligned} f \left( x, \frac{dx}{dt}, \frac{d^2x}{dt^2}, \frac{d^3x}{dt^3} \right) &= a_1x^2 + a_2x \frac{dx}{dt} + a_3x \frac{d^2x}{dt^2} + a_4x \frac{d^3x}{dt^3} + a_5 \left( \frac{dx}{dt} \right)^2 \\ &+ a_6 \frac{dx}{dt} \frac{d^2x}{dt^2} + a_7 \frac{dx}{dt} \frac{d^3x}{dt^3} + a_8 \left( \frac{d^2x}{dt^2} \right)^2 \\ &+ a_9 \frac{d^2x}{dt^2} \frac{d^3x}{dt^3} + a_{10} \left( \frac{d^3x}{dt^3} \right)^2 + O(3). \end{aligned}$$

We assume

$$\begin{aligned} p &= -(2a+c+d)\varepsilon, & q &= b^2 + (a^2 + 2ac + 2ad + cd)\varepsilon^2, \\ k &= -\varepsilon(b^2c + b^2d + (a^2c + a^2d + 2acd)\varepsilon^2), & l &= cd\varepsilon^2(b^2 + a^2\varepsilon). \end{aligned}$$

Set  $x_1 = x, x_2 = \dot{x}_1, x_3 = \dot{x}_2, x_4 = \dot{x}_3$  and the dot denotes derivative with respect to the time  $t$ . Equation (26) can be written as the system

$$(27) \quad \begin{aligned} \dot{x}_1 &= x_2, & \dot{x}_2 &= x_3, & \dot{x}_3 &= x_4, \\ x_4 &= -lx_1 - kx_2 - qx_3 - px_4 + f(x_1, x_2, x_3, x_4). \end{aligned}$$

Applying the change of variables

$$(28) \quad (x, y, z, w)^T = M(x_1, x_2, x_3, x_4)^T,$$

with

$$M = \begin{pmatrix} -acd\varepsilon^3 & ac\varepsilon^2 + ad\varepsilon^2 + cd\varepsilon^2 & -a\varepsilon - c\varepsilon - d\varepsilon & 1 \\ bcd\varepsilon^2 & -bc\varepsilon - bd\varepsilon & b & 0 \\ -d\varepsilon(b^2 + a^2\varepsilon^2) & b^2 + a^2\varepsilon^2 + 2ad\varepsilon^2 & -2a\varepsilon - d\varepsilon & 1 \\ -c\varepsilon(b^2 + a^2\varepsilon^2) & b^2 + a^2\varepsilon^2 + 2ac\varepsilon^2 & -2a\varepsilon - c\varepsilon & 1 \end{pmatrix},$$

the system (27) becomes

$$(29) \quad \begin{aligned} \dot{x} &= \varepsilon ax - by + g(x, y, z, w), & \dot{y} &= bx + \varepsilon ay, \\ \dot{z} &= \varepsilon cz + g(x, y, z, w), & \dot{w} &= \varepsilon dw + g(x, y, z, w), \end{aligned}$$

where  $g(x, y, z, w) = f(M^{-1}(x, y, z, w)^T)$ .

Write

$$g(x, y, z, w) = b_1x^2 + b_2xy + b_3xz + b_4xw + b_5y^2 + b_6yz + b_7yw + b_8z^2 + b_9zw + b_{10}w^2 + O(3).$$

The coefficients of  $g$  are functions depending on the entries of the matrix  $M$  and on the coefficients of  $f$ , which we do not give here explicitly. Now for the system (29) the relevant quantities in (3) become

$$\begin{aligned} F_1 &= b_4, & F_2 &= b_3, & G_1 &= G_2 = b_1 + b_5, & M_i &= N_i = 0, & i &= 1, 2, 3, \\ A &= 0, & B &= (cb_4^2 + db_3b_4)(b_1 + b_5), & C &= -2adb_4(b_1 + b_5), \\ \Lambda &= db_3(b_1 + b_5), & F &= cb_3(b_1 + b_5), \\ \Phi &= 4ab_4^2(b_1 + b_5)^2 (cd(cb_4 + db_3) - 2ab_4^2(c^2b_{10} + cdb_9 + d^2b_8)), \\ \Psi &= 4ab_3^2(b_1 + b_5)^2 (cd^2b_3 - 2a(c^2b_3^2b_{10} - cdb_3b_9 + d^2b_8)). \end{aligned}$$

Since  $A = 0$  and  $N_2 = 0$ , applying Theorem 3 we get the next result.

**Corollary 11.** *Suppose  $0 < \varepsilon \ll 1$ .*

(a) *System (26) has an isolated periodic solution in a neighborhood of the trivial solution  $x = 0$  if one of the following conditions holds:*

(i)  *$b_4 \neq 0$ ,  $cb_4 + db_3 \neq 0$  and*

$$\Phi^* = a(b_1 + b_5)(cd(cb_4 + db_3) - 2ab_4^2(c^2b_{10} + cdb_9 + d^2b_8)) > 0;$$

(ii)  *$b_4 = 0$ ,  $b_3 \neq 0$ ,  $d \neq 0$  and*

$$\Psi^* = a(b_1 + b_5)(cd^2b_3 - 2a(c^2b_3^2b_{10} - cdb_3b_9 + d^2b_8)) > 0.$$

(b) *The periodic solution has, under condition (i), the asymptotic expression*

$$x = \frac{-2ad}{(c-d)(cb_4 + db_3)(b^2 + (a-c)^2\varepsilon^2)} + \frac{2ab_4(cb_4 + db_3)(b_1 + b_5) + cb_3}{(c-d)(b^2 + (a-d)^2\varepsilon^2)} + O(\varepsilon),$$

*and under condition (ii) the asymptotic expression*

$$x = \frac{-2a}{(c-d)b_3(b^2 + (a-c)^2\varepsilon^2)} + \frac{2ac}{(c-d)d(b^2 + (a-d)^2\varepsilon^2)} + O(\varepsilon).$$

(c) *The isolated periodic solution is a limit cycle.*

The proof of Corollary 11 follows from Theorem 3 and the change of coordinates (9) and (28). The following examples show that do there exist systems of form (26) satisfying the conditions of Corollary 11.

**Example 1.** The system

$$\frac{d^4x}{dt^4} - 5\varepsilon \frac{d^3x}{dt^3} + (1 + 9\varepsilon^2) \frac{d^2x}{dt^2} - \varepsilon(3 + 7\varepsilon^2) \frac{dx}{dt} + 2\varepsilon^2(1 + \varepsilon)x = x \frac{dx}{dt} + \frac{7}{6}x \frac{d^3x}{dt^3},$$

satisfies condition (i) of Corollary 11 for  $\varepsilon$  sufficiently small. Because the equality  $b_4 = -1/(6\varepsilon) + O(1)$  holds, we have that  $cb_4 + db_3 = -1/(6\varepsilon) + O(\varepsilon)$ , and  $\Phi^* = 45/324 + O(\varepsilon^2)$ . So it has an isolated periodic solution in a neighborhood of  $x = 0$ .

**Example 2.** The system

$$\begin{aligned} \frac{d^4x}{dt^4} - 2\varepsilon \frac{d^3x}{dt^3} + \frac{d^2x}{dt^2} + 2\varepsilon^3 \frac{dx}{dt} - (1 + \varepsilon)\varepsilon^2 x \\ = -x^2 + \mu x \frac{dx}{dt} - 2x \frac{d^2x}{dt^2} + \mu x \frac{d^3x}{dt^3} + 2 \left( \frac{dx}{dt} \right)^2 - \frac{dx}{dt} \frac{d^2x}{dt^2}, \end{aligned}$$

satisfies condition (ii) of Corollary 11 for  $\mu$  and  $\varepsilon$  sufficiently small. As  $b_4 = 0$ ,  $b_3 = -4 + O(\varepsilon)$  (or  $-4 + O(\varepsilon^2)$  if  $\mu = 0$ ),  $d = 1$  and  $\Psi^* = 69/(2\varepsilon^2) + O(1/\varepsilon)$  (or  $69/(2\varepsilon^2) + O(1)$  if  $\mu = 0$ ). So it has an isolated periodic solution in a neighborhood of  $x = 0$ .

### 6. Application to the Marchuk system of immune response

The system

$$(30) \quad \begin{aligned} \frac{dV}{dt} &= (\beta - \gamma F)V, & \frac{dC}{dt} &= \alpha V(t - \tau)F(t - \tau) - \mu_c(C - \bar{C}), \\ \frac{dF}{dt} &= \rho C - (\mu_f + \eta\gamma V)F, & \frac{dm}{dt} &= \sigma V - \mu_m m, \end{aligned}$$

was introduced by Marchuk [1980] as a simplified model of an immune system with no influence from damaged organs.  $\bar{C}$  is a constant level of plasma cells in a healthy organism, and the biological meaning of the coordinates and coefficients is given in [Marchuk 1980; Marzeniuk and Nakonechny 2003]. For practical meaning we assume that none of the coefficients vanish. In [Marchuk 1980; Martsenyuk 2004] the authors studied the stability of the equilibrium states.

We will apply our Theorem 3 to the system (30) without the time delay for studying the existence of the periodic solutions. Thus we consider system (5). It has two singularities

$$\begin{aligned} P &= \left( 0, \delta, \frac{\delta\rho}{\mu_2}, 0 \right), \\ Q &= \left( \frac{\mu_1(\beta\mu_2 - \delta\gamma\rho)}{\beta(\alpha\rho - \eta\gamma\mu_1)}, \frac{\alpha\beta\mu_2 - \delta\eta\gamma^2\mu_1}{\gamma(\alpha\rho - \eta\gamma\mu_1)}, \frac{\beta}{\gamma}, \frac{\mu_1\sigma(\beta\mu_2 - \delta\gamma\rho)}{\beta\mu_3(\alpha\rho - \eta\gamma\mu_1)} \right). \end{aligned}$$

The first has eigenvalues  $-\mu_1, -\mu_2, -\mu_3, \beta - \delta\gamma\rho/\mu_2$ . Theorem 3 cannot be applied to it. We consider the possible appearance of limit cycles of the system (5) in a neighborhood of the singularity  $Q$ . We denote its coordinates by  $(x^*, y^*, z^*, w^*)$ .

For the system (5) at  $Q$  to have the form (2), we choose the parameters as

$$(31) \quad \begin{aligned} \mu_3 &= -d\varepsilon, \\ \mu_2 &= \frac{b^2\beta - \beta^2\mu_1 - (2a\beta^2 + b^2c + \beta^2c)\varepsilon + m_2\beta\varepsilon^2 - a^2c\varepsilon^3}{\beta(\beta + \mu_1)}, \\ \eta &= \frac{\alpha(b^2\beta + \beta\mu_1^2 + m_1\varepsilon + m_2\beta\varepsilon^2 - a^2c\varepsilon^3)\rho}{\gamma\beta(c\varepsilon + \mu_1)(b^2 + a^2\varepsilon^2 + 2a\mu_1\varepsilon + \mu_1^2)}, \\ \rho &= \frac{\beta(b^2\mu_1 - \beta\mu_1^2 - m_1\varepsilon + m_2\mu_1\varepsilon^2 + a^2c\varepsilon^3)}{\delta\gamma\mu_1(\beta + \mu_1)}, \end{aligned}$$

where  $m_1 = (2a\beta\mu_1 + c\beta\mu_1 - b^2c)$ ,  $m_2 = (a^2 + 2ac)$ , and  $a, b, c$  and  $d$  are the coefficients of the linear part of the system (2), which can be chosen arbitrarily but with  $ab \neq 0$ . We remark that the choice of  $\mu_3$  follows from the fact that  $-\mu_3$  is an eigenvalue of  $Q$ . We take the coordinate translation

$$x_1 = X - x^*, \quad x_2 = Y - y^*, \quad x_3 = Z - z^*, \quad x_4 = W - w^*,$$

and an invertible linear change of coordinates  $(x, y, z, w)^T = M(x_1, x_2, x_3, x_4)^T$ , where  $T$  denotes the transpose of a matrix. The system (5) then becomes

$$(32) \quad \begin{aligned} \frac{dx}{dt} &= \varepsilon ax - by + v_1 G(x, y, z, w), & \frac{dy}{dt} &= bx + \varepsilon ay + v_2 G(x, y, z, w), \\ \frac{dz}{dt} &= \varepsilon cz + v_3 G(x, y, z, w), & \frac{dw}{dt} &= \varepsilon w + v_4 G(x, y, z, w), \end{aligned}$$

where, setting  $\mathcal{N} = \beta\delta\mu_1(c\varepsilon + \mu_1)(\beta + \mu_1)^2(b^2 + (a\varepsilon + \mu_1)^2)(b^2 + (a - c)^2\varepsilon^2)^2$ , we have defined

$$v_1 = \frac{1}{b\mathcal{N}}(b^2(\beta^2 - a\beta\varepsilon + c\varepsilon(a\varepsilon + \mu_1)) + (\beta - a\varepsilon)(a\varepsilon + \mu_1)(a\varepsilon(\beta - c\varepsilon) + \beta(c\varepsilon + \mu_1))),$$

$$v_2 = \frac{1}{\mathcal{N}}(-\beta(b^2 + (\mu_1 + a\varepsilon)^2) + c\varepsilon(b^2 + (\beta - a\varepsilon)^2)),$$

$$v_3 = \frac{1}{\mathcal{N}}(c\varepsilon - \beta)(b^2 - \beta\mu_1 + a\varepsilon(a\varepsilon - 2\beta)),$$

$$v_4 = \frac{1}{\mathcal{N}}((c\varepsilon - \beta)(b^2 - 2a\beta\varepsilon + a^2\varepsilon^2) - d\beta\mu_1\varepsilon + \beta^2(\mu_1 + c\varepsilon - d\varepsilon)),$$

$$G = b^2c\varepsilon x^2 + (b^2 + (a - c)a\varepsilon^2)(a - c)\varepsilon y^2 + c\varepsilon(c\varepsilon + \mu_1)^2 z^2 \\ - (b^3 + a^2b\varepsilon^2 - bc^2\varepsilon^3)xy - 2bc\varepsilon(c\varepsilon + \mu_1)xz + (b^2 + (a^2 - c^2)\varepsilon^2)(c\varepsilon + \mu_1)yz.$$

The expression of the matrix  $M = (a_{ij})$  is extremely long, we do not present it here. We got the matrix  $M$  with mathematica via the choices of  $m_{22} = 0$ , and  $m_{23} = m_{33} = m_{43} = \delta\gamma\mu_1(\beta + \mu_1)(c\varepsilon + \mu_1)(b^2 + (a\varepsilon + \mu_1)^2)$ .

For the system (32) all the parameters in (3) other than  $\Lambda, F, \Delta, F_2, G_1$  and  $G_2$  vanish. Moreover we have  $\Lambda = dF_2G_1, \Delta = \Lambda^2$ ,

$$\begin{aligned}
 F_2 &= \frac{1}{\mathcal{N}_1} \left( - (b^2 + \mu_1^2)b^2\beta + (b^2c(b^2 - \beta^2) - 2\beta\mu_1(ab^2 + c\beta\mu_1))\varepsilon \right. \\
 &\quad + ((c^2 - 2a^2)b^2\beta - \mu_1(2b^2c^2 + 2c\beta^2(c + 2a) + \beta\mu_1\ell))\varepsilon^2 \\
 &\quad + (b^2c(a^2 + \ell) - c\beta^2(2a^2 - \ell) - 2a\beta\mu_1(\ell - 2c^2))\varepsilon^3 \\
 &\quad \left. - (a\beta(a^3 - 5ac^2 - 2c^3) + 2a^2c^2\mu_1)\varepsilon^4 + a^2c\ell\varepsilon^5 \right), \\
 G_1 &= \frac{a\varepsilon(c\varepsilon - \beta)(b^2 - \beta\mu_1 - 2a\beta\varepsilon + a^2\varepsilon^2)}{\beta\delta\mu_1(c\varepsilon + \mu_1)(b^2 + (a - c)^2\varepsilon^2)(\beta + \mu_1)^2(b^2 + (a\varepsilon + \mu_1)^2)}, \\
 \Psi G_1 &= -8a^2\Lambda^2 \frac{ac\varepsilon^2(c\varepsilon - \beta)^2(b^2 - 2a\beta\varepsilon + a^2\varepsilon^2 - \beta\mu_1)^2}{\beta^2\delta^2\mu_1^2(b^2 + (a - c)^2\varepsilon^2)^3(\beta + \mu_1)^4(b^2 + (a\varepsilon + \mu_1)^2)^2},
 \end{aligned}$$

where  $\ell = a^2 - 2ac - c^2$  and

$$\mathcal{N}_1 = \beta\delta\mu_1(b^2 + (a - c)^2\varepsilon^2)^2(\beta + \mu_1)^2(b^2 + (a\varepsilon + \mu_1)^2).$$

**Corollary 12.** *For  $0 < \varepsilon \ll 1$ , if the parameters of the system (5) satisfy (31),  $b^2 - \beta\mu_1 \neq 0$  and  $ac < 0$ , then it has a limit cycle in a vicinity of the singularity  $Q$ . Moreover the limit cycle has three dimensional unstable (respectively stable) manifolds if  $c > 0$  and  $d > 0$  (respectively  $c < 0$  and  $d < 0$ ), or two dimensional unstable (respectively stable) and one dimensional stable (respectively unstable) manifolds if  $c > 0$  and  $d < 0$  (respectively  $c < 0$  and  $d > 0$ ).*

*Proof.* The first statement follows from Theorem 3 and the expressions of  $F_2, G_1, \Lambda$  and  $\Psi G_1$ .

For proving the second statement, we denote the six coefficients of the polynomial  $G$  by  $a_1, \dots, a_6$ . Then the averaged system (21) becomes

$$\begin{aligned}
 \frac{d\rho}{d\theta} &= \frac{1}{2b}\rho(2a + (v_1a_5 + v_2a_6)\xi), \\
 \frac{d\xi}{d\theta} &= \frac{1}{2b}(2c\xi + v_3(a_2 + a_1)\rho^2 + 2v_3a_3\xi^2), \\
 \frac{d\eta}{d\theta} &= \frac{1}{2b}(2d\eta + v_4(a_2 + a_1)\rho^2 + 2v_4a_3\xi^2).
 \end{aligned}
 \tag{33}$$

It has a unique singularity with  $\rho > 0$ , denoted by  $S$ . System (33) at  $S$  has the eigenvalues

$$\lambda_1 = \frac{d}{b}, \quad \lambda_{23} = \frac{E_b \pm \sqrt{E_b^2 - 4E_a E_c}}{2E_a},$$

where  $E_a = b^2 a_5 v_1 + b^2 a_6 v_2$ ,  $E_b = -4aba_3 v_3 + bca_5 v_1 + bca_6 v_2$  and  $E_c = 4a^2 a_3 v_3 - 2aca_5 v_1 - 2aca_6 v_2$ . Direct calculations show that

$$E_a E_c = \frac{-2ac}{b^2 \delta^2 \mu_1^2 (\beta + \mu_1)^2} + O(\epsilon), \quad E_a E_b = \frac{c}{b \delta^2 \mu_1^2 (\beta + \mu_1)^2} + O(\epsilon).$$

So the second statement of the corollary follows easily from the eigenvalues of  $S$  via Theorem 10. This proves the corollary.  $\square$

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