HOPF BIFURCATION IN HIGHER DIMENSIONAL DIFFERENTIAL SYSTEMS VIA THE AVERAGING METHOD

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Dedicated to the memory of Professor Ye Yanqian

Abstract. 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 $l \in \{0, 1, \ldots, 2^{n-3}\}$. As far as we know 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. For proving this result we use the averaging theory of first order. Additionally in dimension 4 we characterize the shape and the kind of stability of the bifurcated limit cycles. Moreover we apply our results first to the fourth order differential equation, and second to a simplified Marchuk model which describes the 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 the averaging theory of first order. We assume that these systems have a singularity at the origin, whose linear part has eigenvalues $\varepsilon a \pm bi$ and εc_k for $k = 3, \ldots, n$, where ε is a small parameter. Such systems can be written into the form

$$\begin{aligned} \dot{x} &= \varepsilon a x - b y + \sum_{i_1+\ldots+i_n=2} a_{i_1\ldots i_n} x^{i_1} y^{i_2} z_3^{i_3} \ldots z_n^{i_n} + \mathcal{A}, \\ \dot{y} &= b x + \varepsilon a y + \sum_{i_1+\ldots+i_n=2} b_{i_1\ldots i_n} x^{i_1} y^{i_2} z_3^{i_3} \ldots z_n^{i_n} + \mathcal{B}, \\ \dot{z}_k &= \varepsilon c_k z + \sum_{i_1+\ldots+i_n=2} c^{(k)}_{i_1\ldots i_n} x^{i_1} y^{i_2} z_3^{i_3} \ldots z_n^{i_n} + \mathcal{C}_k, \quad k = 3, \ldots, n \end{aligned} \tag{1}$$

where $a_{i_1\ldots i_n}$, $b_{i_1\ldots i_n}$, $c^{(k)}_{i_1\ldots i_n}$, a, b and c_k are real parameters, $ab \neq 0$, and $\mathcal{A}$, $\mathcal{B}$ and $\mathcal{C}_k$ are the Lagrange expression 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 averaging method of first order.

Theorem 1. *There exist $\mathcal{C}^3$ systems* (1) *for which $l \in \{0, 1, \ldots, 2^{n-3}\}$ limit cycles bifurcate from the origin at $\varepsilon = 0$, i.e. for ε 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 it follows immediately the next result.

Corollary 2. *There exist quadratic polynomial differential systems* (1) (*i.e. with $\mathcal{A} = \mathcal{B} = \mathcal{C}_k = 0$*) *for which $l \in \{0, 1, \ldots, 2^{n-3}\}$ limit cycles bifurcate from the origin at $\varepsilon = 0$, i.e. for ε 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 the limit cycles and the averaging theory has a long history (see for instance [2, 6, 8, 13, 14, 15, 16]), 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 [4] 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 system (1) into the form

$$
\begin{aligned}
\dot{x} &= \varepsilon a x - b y + \sum_{i+j+k+l=2} a_{ijkl} x^i y^j z^k w^l + \mathcal{A},\\
\dot{y} &= b x + \varepsilon a y + \sum_{i+j+k+l=2} b_{ijkl} x^i y^j z^k w^l + \mathcal{B},\\
\dot{z} &= \varepsilon c z + \sum_{i+j+k+l=2} c_{ijkl} x^i y^j z^k w^l + \mathcal{C},\\
\dot{w} &= \varepsilon d w + \sum_{i+j+k+l=2} d_{ijkl} x^i y^j z^k w^l + \mathcal{D},
\end{aligned} \tag{2}
$$

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 expression 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

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

where

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

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

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

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 system (2) either has no Hopf bifurcation or the averaging theory of first order that we are using cannot decide if there is a Hopf bifurcation.

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

Theorem 3. *For a $\mathcal{C}^3$ system (2) with $G_1 \neq 0$ the following statements hold.*

(a)(a.1) *For $F_1 \neq 0$ and $A \neq 0$, if $B^2 - 4AC > 0$ and $(4AE - DB + D\sqrt{B^2 - 4AC})F_1 > 0$ (resp. $(4AE - DB - D\sqrt{B^2 - 4AC})F_1 > 0$), system (2) has a limit cycle $\Gamma_{1\varepsilon}$ (resp. $\Gamma_{2\varepsilon}$) tending to a singular point as $\varepsilon \searrow 0$. Moreover for suitable choice of the parameters system (2) can have the two limit cycles $\Gamma_{1\varepsilon}$ and $\Gamma_{2\varepsilon}$. In these last case both limit cycles tend to different singular points when $\varepsilon \searrow 0$.*

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

(a.3) For $F_1 = 0$, $F_2 \neq 0$ and $N_2 \neq 0$, if $\Delta > 0$ and $(\Gamma - (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta})G_1 > 0$ (resp. $(\Gamma + (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta})G_1 > 0$), system (2) has a limit cycle $\Gamma_{3\varepsilon}$ (resp. $\Gamma_{4\varepsilon}$) tending to the origin as $\varepsilon \searrow 0$. Moreover for suitable choice of the parameters system (2) can have the two limit cycles $\Gamma_{3\varepsilon}$ and $\Gamma_{4\varepsilon}$. In these last case both limit cycles tend to different singular points when $\varepsilon \searrow 0$.

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

(b) For $\varepsilon > 0$ sufficiently small the limit cycle $\Gamma_{1\varepsilon}$, $\Gamma_{2\varepsilon}$, $\overline{\Gamma}_{1\varepsilon}$, $\Gamma_{3\varepsilon}$, $\Gamma_{4\varepsilon}$ or $\overline{\Gamma}_{3\varepsilon}$ of statement (a) is given respectively by the graph

$$\begin{aligned}
r(\theta) &= \varepsilon\sqrt{\left(4AE - DB + D\sqrt{B^2 - 4AC}\right)/(F_1A^2)} + O(\varepsilon^2),\\
z(\theta) &= \varepsilon\left(B - \sqrt{B^2 - 4AC}\right)/(2A) + O(\varepsilon^2),\\
w(\theta) &= -\varepsilon\left(4aA + F_2(B - \sqrt{B^2 - 4AC})\right)/(2AF_1) + O(\varepsilon^2);
\end{aligned}$$

$$\begin{aligned}
r(\theta) &= \varepsilon\sqrt{\left(4AE - DB - D\sqrt{B^2 - 4AC}\right)/(F_1A^2)} + O(\varepsilon^2),\\
z(\theta) &= \varepsilon\left(B + \sqrt{B^2 - 4AC}\right)/(2A) + O(\varepsilon^2),\\
w(\theta) &= -\varepsilon\left(4aA + F_2(B + \sqrt{B^2 - 4AC})\right)/(2AF_1) + O(\varepsilon^2);
\end{aligned}$$

$$\begin{aligned}
r(\theta) &= \varepsilon\sqrt{\Phi/(G_1B^2F_1^2)} + O(\varepsilon^2),\\
z(\theta) &= \varepsilon C/B + O(\varepsilon^2),\\
w(\theta) &= -\varepsilon\,(2aB + CF_2))\,/(BF_1) + O(\varepsilon^2);
\end{aligned}$$

$$\begin{aligned}
r(\theta) &= \varepsilon\sqrt{\left(\Gamma - (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta}\right)/(G_1F_2^2N_2^2)} + O(\varepsilon^2),\\
z(\theta) &= -\varepsilon 2a/F_2 + O(\varepsilon^2),\\
w(\theta) &= -\varepsilon\left(\Lambda + \sqrt{\Delta}\right)/(2N_2F_2) + O(\varepsilon^2);
\end{aligned}$$

$$\begin{aligned}
r(\theta) &= \varepsilon\sqrt{\left(\Gamma + (2ac_{0011}N_2 + c_{0002}\Lambda)\sqrt{\Delta}\right)/(G_1F_2^2N_2^2)} + O(\varepsilon^2),\\
z(\theta) &= -\varepsilon 2a/F_2 + O(\varepsilon^2),\\
w(\theta) &= -\varepsilon\left(\Lambda - \sqrt{\Delta}\right)/(2N_2F_2) + O(\varepsilon^2);
\end{aligned}$$

or

$$\begin{aligned}
r(\theta) &= \varepsilon\sqrt{\Psi/(G_1F_2^2\Lambda^2)} + O(\varepsilon^2),\\
z(\theta) &= -\varepsilon 2a/F_2 + O(\varepsilon^2),\\
w(\theta) &= -\varepsilon 2aF/\Lambda + O(\varepsilon^2),
\end{aligned}$$

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

(c) *For the results of this section we need that system* (2) *be at least* $\mathcal{C}^4$.

$(c.1)$ *For $F_1 > 0$ and $A \neq 0$, the limit cycle $\Gamma_{1\varepsilon}$ (resp. $\Gamma_{2\varepsilon}$) has at least one–dimensional stable (resp. unstable) manifold, and consequently the limit cycle is not a global repeller (resp. 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 $\overline{\Gamma}_{1\varepsilon}$ has at least one–dimensional stable (resp. unstable) manifold provided that $B > 0$ (resp. $B < 0$). 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 $\Gamma_{3\varepsilon}$ (resp. $\Gamma_{4\varepsilon}$) has at least one–dimensional stable (resp. 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 $\overline{\Gamma}_{3\varepsilon}$ has at least one–dimensional stable (resp. unstable) manifold provided that $\Delta > 0$ (resp. $\Delta < 0$).*

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 system (2). So the Hopf bifurcation depends only on these 18 parameters.

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

Other studies on the Hopf bifurcation using the averaging theory in a different way than ours have been made by Chow and Mallet–Paret [8]. 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 [1].

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

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

where p, q, k, l are real parameters satisfying $p = -(2a + c + d)\varepsilon$, $q = b^2 + (a^2 + 2ac + 2ad + cd)\varepsilon^2$, $k = -\varepsilon\left(b^2c + b^2d + (a^2c + a^2d + 2acd)\varepsilon^2\right)$, $l = cd\varepsilon^2\left(b^2 + a^2\varepsilon\right)$, and f is a $\mathcal{C}^3$ function with f and its first order partial derivatives vanishing at the origin of 4-dimensional space. We have the following results.

Theorem 4. *For $0 < \varepsilon \ll 1$ 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*

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

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

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

where the b_i's 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 equation (4).

The second application is on the simplified system of immune response without influence of damaged organ and time delay

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

given in [7] by Marchuk.

Theorem 5. *There is an open set in the parameter spaces for which 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. 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 [2]. 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. We remind here that continuity of some finite dimensional function is a sufficient condition for the existence of its Brouwer degree (see [11] for precise definitions).

Theorem 6. *We consider the following differential system*

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

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

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

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* $z \in \overline{V} \setminus \{b\}$ *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 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 $\zeta : D \times (-\varepsilon_f, \varepsilon_f) \to \mathbb{R}^n$ defined by

$$\zeta(z,\varepsilon) = \int_0^T \left[\varepsilon f(t, x(t,z,\varepsilon)) + \varepsilon^2 R(t, x(t,z,\varepsilon), \varepsilon)\right] dt. \tag{8}$$

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 ζ *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* ε^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 ζ 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 $f^0 : D \to \mathbb{R}^n$ be a 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 (i.e. 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 $z \in \overline{V} \setminus \{b\}$. Then $d_B(f^0, V, b) \in \{-1, 1\}$.*

The following theorem is proved in [3], it provides the asymptotic stability of the limit cycles obtained by the averaging theory only with the 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 ε sufficiently small if all the eigenvalues of the Jacobian matrix of f^0 at b have negative (resp. positive) real part, then the limit cycle $\varphi(\cdot,\varepsilon)$ is asymptotically stable (resp. 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 [14] or in [5].

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 ε 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

$$x = r\cos\theta, \quad y = r\sin\theta, \quad z_i = z_i, \quad i = 3, \dots, n, \tag{9}$$

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

$$
\begin{aligned}
\dot r &= \varepsilon a r + \sum_{i_1+\ldots+i_n=2} (a_{i_1\ldots i_n}\cos\theta + b_{i_1\ldots i_n}\sin\theta)\times \\
&\qquad (r\cos\theta)^{i_1}(r\sin\theta)^{i_2} z_3^{i_3}\ldots z_n^{i_n} + O(3),\\
\dot\theta &= \frac{1}{r}\Bigg(br + \sum_{i_1+\ldots+i_n=2} (b_{i_1\ldots i_n}\cos\theta - a_{i_1\ldots i_n}\sin\theta)\times \\
&\qquad (r\cos\theta)^{i_1}(r\sin\theta)^{i_2} z_3^{i_3}\ldots z_n^{i_n} + O(3)\Bigg),\\
\dot z_k &= \varepsilon c_k z_k + \sum_{i_1+\ldots+i_n=2} c^{(k)}_{i_1\ldots i_n}(r\cos\theta)^{i_1}(r\sin\theta)^{i_2} z_3^{i_3}\ldots z_n^{i_n} + O(3),
\end{aligned}
\tag{10}
$$

for $k = 3,\ldots,n$, where $O(3) = O_3(r, z_3,\ldots,z_n)$.

As usual $\mathbb{Z}_+$ denotes the set of all non–negative 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 $(r, z_3,\ldots,z_n) = (0,0,\ldots,0)$ we have $\dot\theta\neq 0$. Then choosing θ as the new independent variable system (10) in a neighborhood of $(r, z_3,\ldots,z_n) = (0,0,\ldots,0)$ becomes

(11)

$$
\begin{aligned}
\frac{dr}{d\theta} &= \frac{r\left(\varepsilon a r + \sum\limits_{i_1+\ldots+i_n=2}(a_{i_1\ldots i_n}\cos\theta + b_{i_1\ldots i_n}\sin\theta)(r\cos\theta)^{i_1}(r\sin\theta)^{i_2}z_3^{i_3}\ldots z_n^{i_n} + O(3)\right)}{br + \sum\limits_{i_1+\ldots+i_n=2}(b_{i_1\ldots i_n}\cos\theta - a_{i_1\ldots i_n}\sin\theta)(r\cos\theta)^{i_1}(r\sin\theta)^{i_2}z_3^{i_3}\ldots z_n^{i_n} + O(3)},\\
\frac{dz_k}{d\theta} &= \frac{r\left(\varepsilon c_k z_k + \sum\limits_{i_1+\ldots+i_n=2} c^{(k)}_{i_1\ldots i_n}(r\cos\theta)^{i_1}(r\sin\theta)^{i_2}z_3^{i_3}\ldots z_n^{i_n} + O(3)\right)}{br + \sum\limits_{i_1+\ldots+i_n=2}(b_{i_1\ldots i_n}\cos\theta - a_{i_1\ldots i_n}\sin\theta)(r\cos\theta)^{i_1}(r\sin\theta)^{i_2}z_3^{i_3}\ldots z_n^{i_n} + O(3)},
\end{aligned}
$$

for $k = 3,\ldots,n$. We note that this system is 2π periodic in the variable θ.

For applying the averaging theory of Section 2 and proving Theorem 1 we rescale the variables

$$
(r, z_3,\ldots,z_n) = (\rho\varepsilon, \eta_3\varepsilon,\ldots,\eta_n\varepsilon). \tag{12}
$$

Then system (11) becomes

(13)

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

where

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

We note that system (13) has the form of (6) in the averaging theorem with $x = (\rho, \eta_3, \ldots, \eta_n)$, $t = \theta$, $f(\theta, \rho, \eta_3, \ldots, \eta_n) = (f_1(\theta, \rho, \eta_3, \ldots, \eta_n), f_3(\theta, \rho, \eta_3, \ldots, \eta_n), \ldots, f_n(\theta, \rho, \eta_3, \ldots, \eta_n))$ and $T = 2\pi$. The averaged system of (13) is

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

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

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

with

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

After some calculations we have that

$$\begin{aligned} f_1^0 &= \frac{1}{2b}\rho\left(2a + \sum_{j=3}^{n}(a_{10e_j} + b_{01e_j})\eta_j\right), \\ f_k^0 &= \frac{1}{2b}\left(2c_k\eta_k + \left(c_{20\mathbf{0}_{n-2}}^{(k)} + c_{02\mathbf{0}_{n-2}}^{(k)}\right)\rho^2 + 2\sum_{3\le i\le j\le n} c_{00e_{ij}}^{(k)}\eta_i\eta_j\right), \end{aligned}$$

for $k = 3, \ldots, n$, where $e_j \in \mathbb{Z}_+^{n-2}$ is the unit vector with the jth entry equal to 1, and $e_{ij} \in \mathbb{Z}_+^{n-2}$ has the sum of the ith and jth entries equal to 2 and the other equal to 0.

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

Using Theorem 6 for studying the limit cycles of system (13) we only need to compute the non–degenerate singularities of system (14). Since the transformation from the cartesian coordinates $(r, z_3, \ldots, z_n)$ to the cylindrical ones $(\rho, \eta_3, \ldots, \eta_n)$ 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

$$\begin{aligned} &2a + \sum_{j=3}^{n}(a_{10e_j} + b_{01e_j})\eta_j = 0, \\ &2c_k\eta_k + \left(c_{20\mathbf{0}_{n-2}}^{(k)} + c_{02\mathbf{0}_{n-2}}^{(k)}\right)\rho^2 + 2\sum_{3\le i\le j\le n} c_{00e_{ij}}^{(k)}\eta_i\eta_j = 0, \quad k = 3, \ldots, n. \end{aligned} \tag{15}$$

Since the coefficients of system (15) are independent and arbitrary. In order to simplify the notation we write system (15) as

$$a+\sum_{j=3}^{n} a_j\eta_j = 0, \quad c_0^{(k)}\rho^2+c_k\eta_k+\sum_{3\le i\le j\le n} c_{ij}^{(k)}\eta_i\eta_j = 0, \quad k=3,\dots,n, \tag{16}$$

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:

$$a + a_3\eta_3 = 0, \tag{17}$$

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

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

with all the coefficients non–zero. Equations (19) can be treated as quadratic algebraic equations in η_k. Substituting the unique solution η_{30} of η_3 in (17) into (19) with $k=4$, then this last equation has exactly two different solutions η_{41} and η_{42} for η_4 choosing conveniently c_4. Introducing the two solutions (η_{30}, η_{4i}), $i=1,2$, into (19) with $k=5$ and choosing conveniently the values of the coefficients of equation (19) with $k=5$ and $(\eta_3,\eta_4)=(\eta_{30},\eta_{4i})$ we get two different solutions η_{5i1} and η_{5i2} of η_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 equation (18) has a positive solution ρ 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 the Bezout Theorem, see for instance [12]), 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 $k \in \{0, 1, \ldots, 2^{n-3}\}$ 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

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

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

$$
\dot{y} = \varepsilon f^0(y), \qquad y = (\rho, \xi, \eta), \tag{21}
$$

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

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

As we have explained in the proof of Theorem 1, we consider the singularities with $\rho > 0$ of the averaged system (21). By some tedious calculations we obtain that for $F_1 \neq 0$ and $A \neq 0$ the singularities with $\rho > 0$ of (21) are $S_1 = (\rho_1, \xi_1, \eta_1)$ with

$$
\rho_1 = \sqrt{\frac{4AE - DB + D\sqrt{B^2 - 4AC}}{F_1 A^2}}, \quad \xi_1 = \frac{B - \sqrt{B^2 - 4AC}}{2A},
$$
$$
\eta_1 = -\frac{4aA + F_2(B - \sqrt{B^2 - 4AC})}{2AF_1},
$$

if $B^2-4AC>0$ and $(4AE-DB+D\sqrt{B^2-4AC})F_1>0$; or $S_2=(\rho_2,\xi_2,\eta_2)$ with

$$\rho_2=\sqrt{\frac{4AE-DB-D\sqrt{B^2-4AC}}{F_1A^2}},\ \ \xi_2=\frac{B+\sqrt{B^2-4AC}}{2A},$$
$$\eta_2=-\frac{4aA+F_2(B+\sqrt{B^2-4AC})}{2AF_1},$$

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

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 ε sufficiently small system (20) has two limit cycles that we denoted by $\Gamma_{i\varepsilon}$, $i=1,2$, and $\Gamma_{i\varepsilon}\to S_i$, $i=1,2$, 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

$$\overline{S}_1=(\overline{\rho}_1,\overline{\xi}_1,\overline{\eta}_1)=\left(\sqrt{\frac{\Phi}{G_1B^2F_1^2}},\frac{C}{B},-\frac{2aB+CF_2}{BF_1}\right).$$

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

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

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

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

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

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

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

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

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) and consequently the whole proof of statement (a).

For proving statement (b) of Theorem 3 we observe that the limit cycles $\Gamma_{i\varepsilon}$ for $i = 1, 2$ can be written into 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

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

and

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

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

Doing 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 $\overline{\Gamma}_{1\varepsilon}$, $\Gamma_{3\varepsilon}$ and $\Gamma_{4\varepsilon}$ and $\overline{\Gamma}_{3\varepsilon}$. Hence statement (b) of Theorem 3 is proved.

By Theorem 10 and the determinants (22) (resp. (23),(24) and (25)) of the Jacobian matrix of (21) at S_1 and S_2 (resp. $\overline{S}_3$, S_3 and S_4, and $\overline{S}_3$), it follows easily the proof of statement (c) of Theorem 3.

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

5. Application 1: 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

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

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

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

We assume

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

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

$$\dot{x}_1 = x_2,\ \dot{x}_2 = x_3,\ \dot{x}_3 = x_4,\ \dot{x}_4 = -lx_1 - kx_2 - qx_3 - px_4 + f(x_1, x_2, x_3, x_4). \tag{27}$$

Taking the change of variables

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

with

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

system (27) becomes

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

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

Write

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

We note that 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 system (29) the relevant quantities in (3) become

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

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

Corollary 11. *For $0 < \varepsilon \ll 1$ the following statements hold*

(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*

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

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

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

(b) *The periodic solution has the asymptotic expression*

$$x = \frac{-2ad}{(c-d)(cb_4+db_5)(b^2+(a-c)^2\varepsilon^2)} + \frac{2ab_4(cb_4+db_3)(b_1+b_5)+cb_3}{(c-d)(b^2+(a-d)^2\varepsilon^2)} + O(\varepsilon),$$

if the condition (i) holds, or

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

if the condition (ii) holds.

(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 ε sufficiently small. Because $b_4 = -1/(6\varepsilon)+O(1)$, $cb_4+db_3=-1/(6\varepsilon)+O(\varepsilon)$, and $\Phi^*=45/324+O(\varepsilon^2)$. So it has an isolated periodic solution in a neighborhood of $x=0$.
Example 2: The system

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

satisfies condition (ii) of Corollary 11 for μ and ε sufficiently small. Because $b_4 = 0$, $b_3 = -4+O(\varepsilon)$ (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 2: The Marchuk simplified system of immune response

The system

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

was given in [7] by Marchuk for describing a simplified system of immune response with no influence of damaged organ, where $\overline{C}$ is a constant level of plasma cells in a healthy organism, and the biological meaning of the coordinates and coefficients are given in [7, 10]. For practical meaning we assume that all the coefficients do not vanish. In [7, 9] the authors studied the stability of the equilibrium states.

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

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

The first one has the 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 system (5) in a neighborhood of the singularity Q. We denote its coordinates by (x^*, y^*, z^*, w^*).

In order that system (5) at Q has the form (2), we choose the parameters as

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

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 system (2), which can be chosen arbitrarily but with $ab \neq 0$. We remark that the choice of μ_3 follows from the fact that $-\mu_3$ is an eigenvalue of Q. We take the translation of coordinates

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

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. Then system (5) becomes

$$
\begin{aligned}
\frac{dx}{dt} &= \varepsilon a x - b y + v_1 G(x,y,z,w),\\
\frac{dy}{dt} &= b x + \varepsilon a y + v_2 G(x,y,z,w),\\
\frac{dz}{dt} &= \varepsilon c z + v_3 G(x,y,z,w),\\
\frac{dw}{dt} &= \varepsilon w + v_4 G(x,y,z,w),
\end{aligned}
\tag{32}
$$

where

$$
\begin{aligned}
v_1 &= \frac{1}{b\mathcal{N}}\left(b^2\left(\beta^2 - a\beta\varepsilon + c\varepsilon(a\varepsilon+\mu_1)\right)\right.\\
&\quad \left. +(\beta - a\varepsilon)(a\varepsilon+\mu_1)\left(a\varepsilon(\beta - c\varepsilon) + \beta(c\varepsilon+\mu_1)\right)\right),\\
v_2 &= \frac{1}{\mathcal{N}}\left(-\beta\left(b^2 + (\mu_1 + a\varepsilon)^2\right) + c\varepsilon\left(b^2 + (\beta - a\varepsilon)^2\right)\right),\\
v_3 &= \frac{1}{\mathcal{N}}(c\varepsilon - \beta)\left(b^2 - \beta\mu_1 + a\varepsilon(a\varepsilon - 2\beta)\right),\\
v_4 &= \frac{1}{\mathcal{N}}\left((c\varepsilon - \beta)\left(b^2 - 2a\beta\varepsilon + a^2\varepsilon^2\right) - d\beta\mu_1\varepsilon + \beta^2(\mu_1 + c\varepsilon - d\varepsilon)\right),
\end{aligned}
$$

and

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

with

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

We remark that 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 system (32) all the parameters in (3) different from Λ, Γ, Δ, F_2, G_1 and G_2 vanish. Moreover we have

$$\begin{aligned}
F_2 &= \frac{1}{\mathcal{N}_1}\Big(-\left(b^2+\mu_1^2\right)b^2\beta + \left(b^2c(b^2-\beta^2) - 2\beta\mu_1(ab^2+c\beta\mu_1)\right)\varepsilon \\
&\quad + \left((c^2-2a^2)b^2\beta - \mu_1(2b^2c^2 + 2c\beta^2(c+2a) + \beta\mu_1\ell)\right)\varepsilon^2 \\
&\quad + \left(b^2c(a^2+\ell) - c\beta^2(2a^2-\ell) - 2a\beta\mu_1(\ell-2c^2)\right)\varepsilon^3 \\
&\quad - \left(a\beta(a^3-5ac^2-2c^3) + 2a^2c^2\mu_1\right)\varepsilon^4 + a^2c\ell\varepsilon^5\Big), \\
G_1 &= \frac{a\varepsilon(c\varepsilon-\beta)(b^2-\beta\mu_1-2a\beta\varepsilon+a^2\varepsilon^2)}{\beta\delta\mu_1(c\varepsilon+\mu_1)(b^2+(a-c)^2\varepsilon^2)(\beta+\mu_1)^2(b^2+(a\varepsilon+\mu_1)^2)}, \\
\Lambda &= dF_2G_1, \quad \Delta = \Lambda^2, \\
\Psi G_1 &= -8a^2\Lambda^2\frac{ac\varepsilon^2(c\varepsilon-\beta)^2(b^2-2a\beta\varepsilon+a^2\varepsilon^2-\beta\mu_1)^2}{\beta^2\delta^2\mu_1^2(b^2+(a-c)^2\varepsilon^2)^3(\beta+\mu_1)^4(b^2+(a\varepsilon+\mu_1)^2)^2},
\end{aligned}$$

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

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

In short we have the next result.

Corollary 12. *For $0 < \varepsilon \ll 1$ if the parameters of 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* (*resp. stable*) *manifolds if $c > 0$ and $d > 0$* (*resp $c < 0$ and $d < 0$*), *or two dimensional unstable* (*resp. stable*) *and one dimensional stable* (*resp. unstable*) *manifolds if $c > 0$ and $d < 0$* (*resp. $c < 0$ and $d > 0$*).

Proof. The first statement follows from Theorem 3 and the expressions of F_2, G_1, Λ and ΨG_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

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

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

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

where $E_a = b^2a_5v_1 + b^2a_6v_2$, $E_b = -4aba_3v_3 + bca_5v_1 + bca_6v_2$ and $E_c = 4a^2a_3v_3 - 2aca_5v_1 - 2aca_6v_2$. Direct calculations show that

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

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

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