Journal of Mathematical Chemistry 17 (1995) 55–67

Complete set of Hopf bifurcation in an autocatalytic ring network

F.M.C. Vieira [a,c] and P.M. Bisch [b,c]

[a] *Departamento de Física, Universidade Federal de Viçosa, 36570-000 Viçosa, Brazil*
[b] *Instituto de Biofísica "Carlos Chagas Filho", Universidade Federal do Rio de Janeiro, CCS - Bloco G, 22941-900 Rio de Janeiro, Brazil*
[c] *Centro Brasileiro de Pesquisas Físicas, Rua Xavier Sigaud 150, 22290 Rio de Janeiro, Brazil*

Received 14 July 1994; revised 18 October 1994

We investigate the Hopf bifurcation for a five species chemical ring network with an autocatalytic reaction. We show that the bifurcation hypersurface in the rate constants space is the boundary of a simply connected set. We use a numerical method to calculate this hypersurface.

1. Introduction

Nonlinear ordinary differential equations (ODE) may show interesting behavior like limit cycles (also known as self-oscillations) and chaos [1]. The implications of this kind of behavior for chemical and biological systems have already been discussed [2].

In particular, self-oscillatory biological systems are important as they may play the role of biological clocks [2]. Self-oscillations also seem to be important in cellular signaling process [3–5].

Mathematically, limit cycles often appear as solutions of ODEs through the so-called Hopf bifurcation [1].

In this paper we calculate the complete set of Hopf bifurcation for a particular ODE system for the whole space of parameters. It is shown that the system presents Hopf bifurcation in the boundaries of a simply connected set in the parameters space.

The ODE system we have studied arises in the context of active transport in biomembranes [6,7]. It is the dynamic equation of a chemical ring reaction network. Indeed, this chemical network is an extreme current of a larger network. Extreme currents are a major feature of stoichiometric network analysis developed by Clarke to study complex reaction networks [8]. This method is based on the decomposition of complex reaction networks to simpler ones (the extreme currents) which can be more readily analyzed. If one extreme current leads to instability then the whole system may become unstable by an appropriate choice of parameters.

The present reaction network seems to be important because it is the fundamental extreme network behind many different networks arising in active transport models [6,7]. The complete characterization of its Hopf bifurcation set is then worthwhile.

This paper is essentially analytical and we have employed computer algebra programs extensively. The final calculation of the Hopf bifurcation set has been done through numerical continuation methods [9,10].

2. The equations

In this paper we will show that it is possible to determine the complete set of Hopf bifurcation from a special chemical network. This chemical network is composed of five species and five reactions, namely,

$$\mathrm{A}' \xrightarrow{a} \mathrm{B}' ,$$

$$\mathrm{B}' \xrightarrow{b'} \mathrm{C}' ,$$

$$\mathrm{C}' \xrightarrow{c'} \mathrm{D}' ,$$

$$\mathrm{D}' \xrightarrow{d'} \mathrm{E}' ,$$

$$\mathrm{A}' + \mathrm{E}' \xrightarrow{e''} 2\mathrm{A}' ,$$

where A′, B′, C′, D′, and E′ are the chemical species and the symbols over the arrows denote the rate constant of each reaction.

The system of differential equations associated with this network is

$$\dot{A}' = -a \cdot A' + e'' \cdot A' \cdot E' ,$$

$$\dot{B}' = a \cdot A' - b' \cdot B' ,$$

$$\dot{C}' = b' \cdot B' - c' \cdot C' ,$$

$$\dot{D}' = c' \cdot C' - d' \cdot D' ,$$

$$\dot{E}' = d' \cdot D' - e'' \cdot A' \cdot E' ,$$

where A', B', C', D', and E' are the concentrations of the respective species. Here, the dot means derivative with respect to t'.

The different species represent different states of a single kind of protein whose total concentration is constant, that is $T' = A' + B' + C' + D' + E'$.

We can rescale the system setting $b = b'/a$, $c = c'/a$, $d = d'/a$, $e' = e''/a$ and $t = t'/a$. This transformation is, of course, simply a scale change, not affecting the main features of the system.

The system becomes

$$\dot{A}' = -A' + e' \cdot A' \cdot E' ,$$

$$\dot{B}' = A' - b \cdot B' ,$$

$$\dot{C}' = b \cdot B' - c \cdot C' ,$$

$$\dot{D}' = c \cdot C' - d \cdot D' ,$$

$$\dot{E}' = d \cdot D' - e' \cdot A' \cdot E' ;$$

now, the dot means derivative with respect to t.

This system has two steady states:

$$(\text{ss1}') \quad A'_0 = B'_0 = C'_0 = D'_0 = 0 , \quad E'_0 = T' ,$$

$$(\text{ss2}') \quad \begin{cases} E'_0 = 1/e' , \\ A'_0 = (T' - E'_0)/(1 + (1/b' + 1/c' + 1/d')) , \\ B'_0 = A'_0/b , \\ C'_0 = A'_0/c , \\ D'_0 = A'_0/d . \end{cases}$$

The steady state ss2′ will be physically meaningful if and only if $T' > 1/e'$. This condition will be taken implicitly.

The stability of the steady states is given by the eigenvalues of the Jacobian matrix **J** of the ODE evaluated at the steady states [1].

It is easy to show that **J** evaluated at ss1′ will always have at least one eigenvalue with a positive real part. Therefore, this steady state will always be unstable. Of course, it cannot generate a Hopf bifurcation. The calculation of the Jacobian **J** evaluated at ss2′ shows that systems with the same values for b, c, d, and e'. A'_o will have the same stability pattern. It induces the following transformation, which is also a simple scale change:

$$A = A'/A'_0 , \quad B = B'/A'_0 , \quad C = C'/A'_0 , \quad D = D'/A'_0 ,$$

$$E = E'/A'_0 , \quad T = T'/A'_0 , \quad e = e' \cdot A'_0 .$$

Now we have the adimensional system with which we will work:

$$\dot{A} = -A + e \cdot A \cdot E,$$
$$\dot{B} = A - b \cdot B,$$
$$\dot{C} = b \cdot B - c \cdot C,$$
$$\dot{D} = c \cdot C - d \cdot D,$$
$$\dot{E} = d \cdot D - e \cdot A \cdot E, \tag{1}$$

with the conservation condition $T = 1 + 1/b + 1/c + 1/d + 1/e$.

For this system the physically meaningful steady state is

$$\text{(ss2)} \quad \begin{cases} A_0 = 1, \\ B_0 = 1/b, \\ C_0 = 1/c, \\ D_0 = 1/d, \\ E_0 = 1/e. \end{cases}$$

The Jacobian **J** at ss2 is

$$\begin{bmatrix} 0 & 0 & 0 & 0 & e \\ 1 & -b & 0 & 0 & 0 \\ 0 & b & -c & 0 & 0 \\ 0 & 0 & c & -d & 0 \\ -1 & 0 & 0 & d & -e \end{bmatrix}.$$

The characteristic polynomial associated with **J** ($\mathrm{Det}[\mathbf{J} - \mathbf{x} \cdot \mathbf{I}] = 0$, where **I** is the 5×5 identity matrix) is

$$\mathbf{x}^5 + \mathbf{x}^4(b + c + d + e) + \mathbf{x}^3(bc + bd + cd + e + be + ce + de)$$
$$+ \mathbf{x}^2(bcd + be + ce + bce + de + bde + cde) + \mathbf{x}(bce + bde + cde + bcde) = 0.$$

This polynomial has one trivial root due to total concentration conservation. It simply means that the system has its dynamics restricted to a hyperplane in the species concentration space.

Thus, the stability of the dynamical system will be given by the signs from the real parts of the solutions of

$$\mathbf{x}^4 + a_1 \cdot \mathbf{x}^3 + a_2 \cdot \mathbf{x}^2 + a_3 \cdot \mathbf{x} + a_4 = 0, \tag{2}$$

where

$$a_1 = b + c + d + e,$$

$$a_2 = bc + bd + cd + e + be + ce + de,$$

$$a_3 = bcd + be + ce + bce + de + bde + cde\,,$$

$$a_4 = bce + bde + cde + bcde\,.$$

Let us apply the Routh–Hurwitz criterion to study the stability of the steady state [8].

Let R_3 and R_2 be the two Routh–Hurwitz determinants of eq. (2):

$$R_3 = \begin{vmatrix} a_1 & a_3 & 0 \\ 1 & a_2 & a_4 \\ 0 & a_1 & a_3 \end{vmatrix}$$

and

$$R_2 = \begin{vmatrix} a_1 & a_3 \\ 1 & a_2 \end{vmatrix}.$$

Since the parameters a_1, a_2, a_3 and $a_4 > 0$ and $R_2 > 0\ \forall\ b,\ c,\ d,\ e > 0$, ss2 will be unstable if and only if $R_3 < 0$. At this point it is important to say that for a similar network with only four species the physically meaningful steady state is always asymptotically stable [8]. In that sense the present system seems to be the simplest system in its class to show non trivial behavior.

It has been shown that the necessary and sufficient conditions for the Hopf bifurcation may be written in terms of Routh–Hurwitz determinants [11,12].

Let $\mathbf{P} = \mathbf{P}(b, c, d, e) = R_3$ [appendix 1, eq. (a)]. In the case of system 1 the necessary and sufficient conditions for Hopf bifurcation reduce to

$$\mathbf{P} = 0\,,$$

$$\partial\mathbf{P}/\partial b \neq 0 \quad \text{or} \quad \partial\mathbf{P}/\partial c \neq 0 \quad \text{or} \quad \partial\mathbf{P}/\partial d \neq 0 \quad \text{or} \quad \partial\mathbf{P}/\partial e \neq 0\,.$$

The condition on partial derivatives is the transversality condition. From Thom's transversality theorem [1,17] it is known that this condition will be generically fulfilled. Therefore, our main goal is to study the condition $\mathbf{P} = 0$.

Let

$$\mathcal{P} = \{(b, d, d, e)\,; b, c, d, e \in \mathbf{R}_+\}\,,$$

$$\mathcal{N} = \{b, c, d, e) \in \mathcal{P}; \mathbf{P}(b, c, d, e) < 0\}\,,$$

$$\mathcal{Z} = \partial\mathcal{N}\,.$$

In the following section we will prove that $\mathcal{N}$ is a simply connected set. Then, in the next section, we use continuation methods [9,10] to calculate $\mathcal{Z}$. We also give simple reasoning to show that the points of $\mathcal{Z}$ not representing a Hopf bifurcation point belong, at most, to a zero measure set. That gives a complete description of the Hopf bifurcation set for eq. (1).

3. The set $\mathcal{N}$

One may easily verify that **P** is invariant under any permutation among b, c and d. First we study the (b, c)-quadrant, i.e., we consider d and e given and we study the restriction of $\mathcal{N}$ to the first quadrant $(b>0,\ c>0)$ of the (b, c)-plane. Indeed, by invariance under permutation, the conclusions are valid for (b, d) and (c, d)-quadrants.

(i) The (b-c)-quadrant

Take $c = r \cdot b$. For fixed values of r we may study the sign variation of **P** along a ray coming from origin in the (b, c)-quadrant. **P** becomes

$$\mathbf{P} = \alpha \cdot b^5 + \beta \cdot b^4 + \gamma \cdot b^3 + \delta \cdot b^2 + \epsilon \cdot b + \zeta\,,$$

where $\alpha, \beta, \gamma, \delta, \epsilon$ and ζ are functions of d, e, r [appendix 1, eq. (b)].

In this case α, β, ϵ and $\zeta > 0\ \forall\, d, e, r > 0$. Since only γ and δ may be negative, applying Descartes' sign rule [13] one may prove that **P** will have at most two zeros for $b > 0$. So, **P** will be negative at most for a unique line segment along rays in the first (b, c)-quadrant (see fig. 1).

Take $c = h/b$. For fixed values of h we may study the sign variation along hyperbolas in the first (b, c)-quadrant. Multiplying **P** by b^3 (it will have no influence on **P** sign since $b > 0$) we have

$$b^3 \cdot \mathbf{P} = \alpha \cdot b^6 + \beta \cdot b^5 + \gamma \cdot b^4 + \delta \cdot b^3 + \epsilon \cdot b^2 + \zeta \cdot b + \eta\,,$$

where $\alpha, \beta, \gamma, \delta, \epsilon, \zeta$ and η are functions of d, e, r [appendix 1, eq. (c)].

In this case $\alpha, \beta, \zeta, \eta > 0\ \forall\, d, e, h > 0$.

Once again applying Descartes' sign rule, since only γ, δ and ϵ may be negative one proves that **P** will be negative at most for two disjoint regions in a hyperbola in the first (b, c)-quadrant.

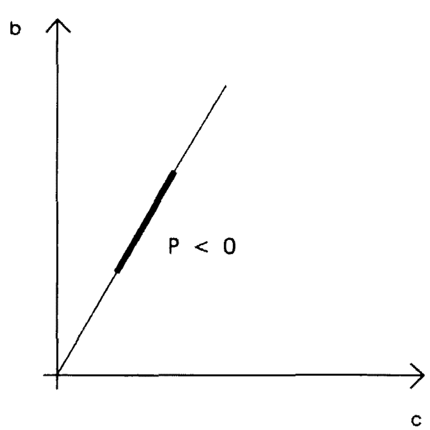

Fig. 1. Sign behavior of **P** along a ray in the positive (*b*-*c*)-quadrant.

As $\mathbf{P}$ is invariant under permutation between b and c, if $\mathbf{P}(b_0, c_0) < 0$ then we have $\mathbf{P}(b_0, c_0) = \mathbf{P}(c_0, b_0) < 0$.

In the next paragraph we show that $\mathbf{P}(\sqrt{b_0 \cdot c_0}, \sqrt{b_0 \cdot c_0}) \leqslant \mathbf{P}(b_0, c_0)$.

The function $\mathbf{P}$ may be written as

$$\mathbf{P} = \sum a_{ij} b^i c^j ,$$

where $a_{ij} = a_{ij}(e, d)$ and $a_{ij} = a_{ji}$. We will show that $\mathbf{P}(b_0, c_0) - \mathbf{P}(\sqrt{b_0 \cdot c_0}, \sqrt{b_0 \cdot c_0}) \geqslant 0$.

$$\begin{aligned}\mathbf{P}(b_0, c_0) - \mathbf{P}(\sqrt{b_0 \cdot c_0}, \sqrt{b_0 \cdot c_0}) &= \sum (a_{ij}/2)(b_0^i c_0^j + b_0^j c_0^i - 2(b_0 c_0)^{(i+j)/2}) \\ &= \sum (a_{ij}/2)(b_0 c_0)^j (b_0^{i-j} + c_0^{i-j} - 2(b_0 c_0)^{(i-j)/2}) \\ &= \sum (a_{ij}/2)(b_0 c_0)^j (b_0^{(i-j)/2} - c_0^{(i-j)/2})^2 ,\end{aligned}$$

so

$$\mathbf{P}(b_0, c_0) \geqslant \mathbf{P}(\sqrt{b_0 c_0}, \sqrt{b_0 c_0}) .$$

Under the coordinate change $c = h/b$, the points $(\sqrt{b_0 \cdot c_0}, \sqrt{b_0 \cdot c_0})$ and (b_0, c_0) belong to the same hyperbola. But we cannot have three disjoint negative regions of P on this hyperbola in the (b, c)-quadrant (see fig. 2). Therefore, this negative region will be unique and it will necessarily cross the (b, c)-quadrant bissetrix.

The bissetrix is a special ray (the one for which $r = 1$). Along this ray there may be at most one line segment for which $\mathbf{P} < 0$.

So, we have proven that in the (b, c), (b, d), (c, d)-quadrants we will have at most one simply connected set for which $\mathbf{P} < 0$.

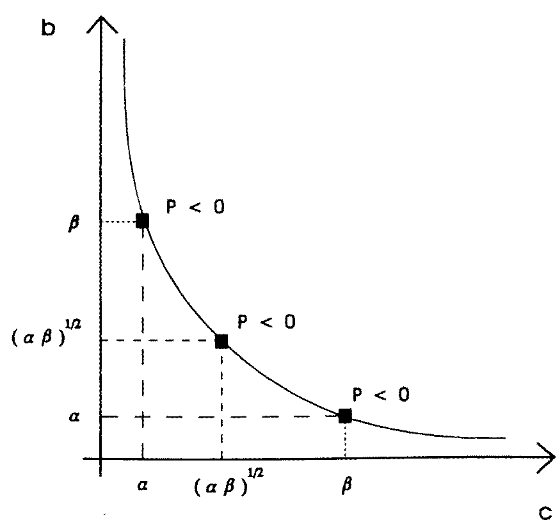

Fig. 2. Sign behavior of $\mathbf{P}$ along hyperbolas in the positive (b-c)-quadrant. α and β are any different positive real numbers.

(ii) The (b-c-d)-orthant

Let $\mathbf{P}(b, c, d) < 0$ for a given e, with $b > c > d$. By invariance under permutation, $\mathbf{P}$ will have the same value, at least, at the points (b, c, d), (b, d, c), (c, b, d), (c, d, b), (d, b, c), (d, c, b). Moreover, there are paths linking these points through (b, c), (b, d), (c, d)-quadrants on which $\mathbf{P}$ has negative value, namely,

(b, c, d) to (c, b, d) through a (b, c)-quadrant,

(c, b, d) to (d, b, c) through a (b, d)-quadrant,

(d, b, c) to (d, c, b) through a (c, d)-quadrant,

(d, c, b) to (c, d, b) through a (b, c)-quadrant,

(c, d, b) to (b, d, c) through a (b, d)-quadrant,

(b, d, c) to (b, c, d) through a (c, d)-quadrant.

Let $\mathcal{N}_{bcd}$ be the set $\mathcal{N}$ restricted to the (b, c, d)-orthant. The set $\mathcal{N}_{bcd}$ will be a 3D solid around the $(b = c = d)$-line.

Indeed, the set $\mathcal{N}_{bcd}$ must intersect the $(b = c = d)$-line. Suppose that $\mathcal{N}_{bcd}$ does not intersect the $(b = c = d)$-line. Then there is a cylinder around this line which also does not intersect the set $\mathcal{N}_{bcd}$ ($\mathcal{N}_{bcd}$ is obviously an open set). If we take a (b, c)-quadrant which intersect this cylinder the set $\mathcal{N}$ restricted to this quadrant cannot be simply connected. As the set $\mathcal{N}$ restricted to a (b, c), (b, d), (c, d)-quadrant must be a simply connected set, the set $\mathcal{N}_{bcd}$ will intersect the $(b = c = d)$-line.

Now take $c = b$ and $d = b$. $\mathbf{P}$ is of the form

$$\mathbf{P} = \alpha \cdot b^6 + \beta \cdot b^5 + \gamma \cdot b^4 + \delta \cdot b^3 + \epsilon \cdot b^2 + \zeta \cdot b + \eta,$$

where $\alpha, \beta, \gamma, \delta, \epsilon, \zeta$ and η are functions of e [appendix 1, eq. (d)].

We have α, β, δ, ϵ, ζ, $\eta > 0 \ \forall \ e > 0$. By Descartes' sign rule $\mathbf{P}$ will be negative only for a single interval in the $b > 0$ set. We can conclude that the set $\mathcal{N}_{bcd}$ is simply connected.

(iii) The axis "e"

A set X is simply connected if and only if every closed curve in X is contractible to a point of X [15,16].

We have already shown that for a fixed value of e the set $\mathcal{N}$ restricted to the (b-c-d)-orthant is simply connected. The contractions referred above could be done through appropriate quadrants.

So for each value of e a closed curve in $\mathcal{N}$ can be contracted to a point. So, these closed curves become lines, and the set $\mathcal{N}$ will not be simply connected if and only if these lines are not connected, i.e., if there are at least two disjoint subsets of the set $E = \{e; e > 0\}$ for which $\mathcal{N}_{bcd}$ is not the null set.

As $\mathcal{N}_{bcd}$ always intersect the ($b = c = d$)-line, it is sufficient to see whether there are two disjoint subsets of E for which the intersection of $\mathcal{N}_{bcd}$ and the ($b = c = d$)-line is not the null set.

Let $b = c = d = l$. We will study the set $\mathcal{N}$ restricted to the (l, e)-quadrant.

The polynomial $\mathbf{P}$ becomes

$$\mathbf{P} = 8l^6 + 25l^5e + 24l^4e^2 - 3l^4e + 8l^3e^3 + 10l^3e^2 + 9l^2e^3 + 3le^3 .$$

If $l = e = 0$ then $\mathbf{P} = 0$. We may apply the well known Newton's polygon method to study branches of solution of the equation $\mathbf{P} = 0$ near the origin [14]. The Newton polygon associated with equation 2 is shown in fig. 3. The point (4,1) is the only one which corresponds to a negative coefficient in eq. (3). As it is a vertex at the bottom of the Newton polygon it may lead to branches of solutions of $\mathbf{P} = 0$ at the origin.

There are two branches $e = l^{3/2}$ and $e = \frac{8}{3}l^2$. Close to the origin, they are the boundary of a region in which $\mathbf{P}$ is negative (we will refer to this region as N) (fig. 4).

We will see now that the intersection of $\mathcal{N}$ with the (l, e)-quadrant is simply connected. This is the last step required to prove that $\mathcal{N}$ itself is a simply connected set.

Take a point (l_2, e_2) outside N. Take a point (l_1, e_1) inside N such that $l_1 < l_2$, $e_1 < e_2$. There are $k, n > 0$ such that $l_1 = k \cdot e_1^n$ $l_2 = k \cdot e_2^n$ ($n = \log(e_2/e_1)/\log(l_2/l_1)$). Now take two natural numbers o and m with the conditions $m < n < o$, $o - m = 1$. If we substitute $l = k \cdot e^o$ or $l = k \cdot e^m$ in $\mathbf{P}$ we will always have at most one negative

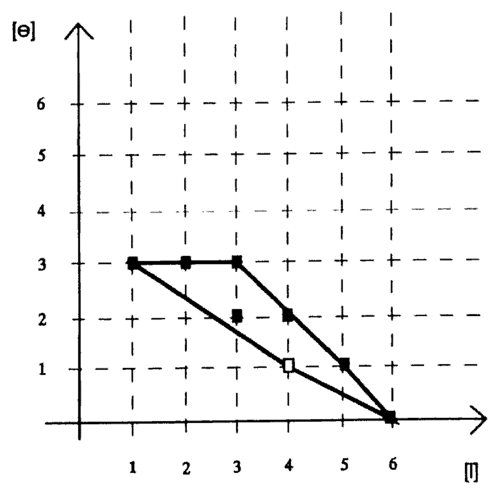

Fig. 3. Newton polygon associated with eq. (3). The black dots are associated with positive coefficients. The white dot is associated with the negative coefficient. The axis define the exponents of l and e, respectively, for each monomial.

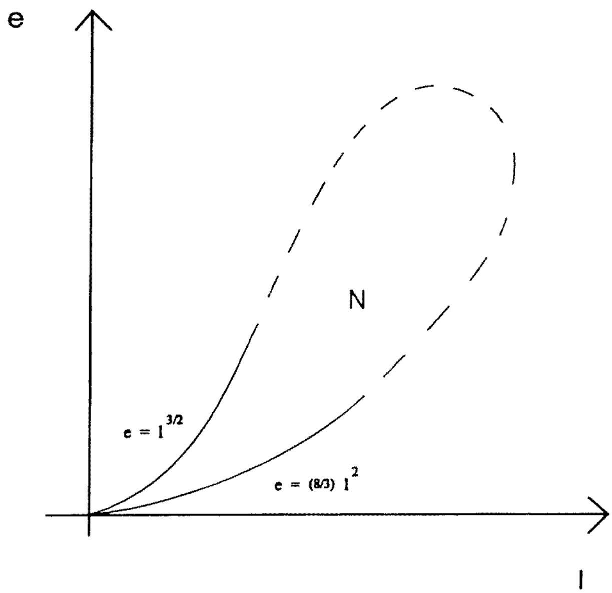

Fig. 4. Region N in the positive (e-l)-quadrant. The $\mathbf{P} = 0$ branches of solutions at the origin are indicated.

coefficient. Once more, by Descartes' sign rule it means that **P** will be negative at most for a single interval on the set $e > 0$.

If we take $l = k \cdot e^n$, **P** will have an intermediate value between the cases where $l = k \cdot e^o$, and $l = k \cdot e^m$. Therefore, if **P** is negative at the point (l_2, e_2), it cannot be outside N.

We conclude that the set $\mathcal{N}$ is simply connected.

4. The hypersurface $\mathcal{Z}$

As $\mathcal{N}$ is simply connected and limited then $\mathcal{Z}$ is a closed hypersurface.

The points of $\mathcal{Z}$ for which

$$\partial \mathbf{P}/\partial b = 0 \quad \text{and} \quad \partial \mathbf{P}/\partial c = 0 \quad \text{and} \quad \partial \mathbf{P}/\partial d = 0 \quad \text{and} \quad \partial \mathbf{P}/\partial e = 0$$

are those for which Hopf bifurcation does not occur.

Each one of these conditions defines a hypersurface in $\mathbf{R}^4$. These hypersurfaces are different analytical manifolds, so they will intersect at most in a zero measure set. To see that take f and g two different analytical functions from **R** to **R**. The function $f - g$ is also analytical. The function $h \equiv 0$ is the only one analytical function to be null for a set with non-zero measure. So, unless $f = g$ the function $f - g$ will be null only in a zero measure set. The same applies to analytical manifolds.

In other words, "almost every" point in the hypersurface $\mathcal{Z}$ is a Hopf bifurcation point for some one of the parameters b, c, d or e.

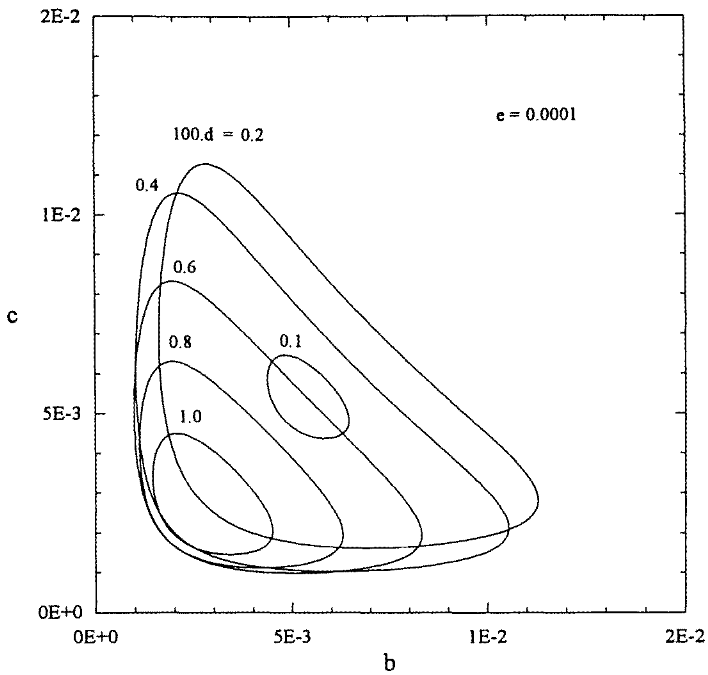

Fig. 5. Hypersurface Z through slices of constant values for d.

To construct this hypersurface we calculate slices through fixed values of d. We have employed established numerical continuation methods [9,10]. The hypersurface Z is shown in fig. 5.

5. Conclusion

In this paper we showed that it is possible to define completely the bifurcation set for a specific system. Of course, we do not claim that the line of investigation pursued here is the shortest one, but the mathematical tools we have employed are in the most part very elementary. The importance of this result is that the system studied here is the simplest one in its class to show non trivial behavior. A thorough comprehension of some basic systems may be of great help in the study of the more complex ones.

Appendix 1

Eq. (a):

$$\begin{aligned}\mathbf{P}(b,c,d,e) &= c^3d^2e + c^2d^3e + c^3e^2 + c^2de^2 + c^3de^2 + cd^2e^2 + 2c^2d^2e^2 \\ &+ d^3e^2 + cd^3e^2 + ce^3 + c^2e^3 + de^3 + 2cde^3 + c^2de^3 + d^2e^3 + cd^2e^3 \\ &+ b^3(c^2d + cd^2 + c^2e + 2cde + d^2e + e^2 + ce^2 + de^2) + b^2(c^3d + 2c^2d^2 \\ &+ cd^3 + c^3e - cde + 4c^2de + 4cd^2e + d^3e + ce^2 + 2c^2e^2 + de^2 + 4cde^2 \\ &+ 2d^2e^2 + e^3 + ce^3 + de^3) + b(c^3d^2c^2 + d^3 - c^2de + 2c^3de - cd^2e \\ &+ 4c^2d^2e + 2cd^3e + c^2e^2 + c^3e^2 + cde^2 + 4c^2de^2 + d^2e^2 + 4cd^2e^2 \\ &+ d^3e^2 + e^3 + 2ce^3 + c^2e^3 + 2de^3 + 2cde^3 + d^2e^3)\,.\end{aligned}$$

Eq. (b):

$$\begin{aligned}\mathbf{P}(\mathbf{b},d,e,r) &= \mathbf{b}^5(r^2d + r^3d + r^2e + r^3e) \\ &+ \mathbf{b}^4(rd^2 + 2r^2d^2 + r^3d^2 + 2rde + 4r^2de + 2r^3de + re^2 + 2r^2e^2 + r^3e^2) \\ &+ \mathbf{b}^3(rd^3 + r^2d^3 - rde - r^2de + d^2e + 4rd^2e + 4r^2d^2e + r^3d^2e + e^2 \\ &+ re^2 + r^2e^2 + r^3e^2 + de^2 + 4rde^2 + 4r^2de^2 + r^3de^2 + re^3 + r^2e^3) \\ &+ \mathbf{b}^2(-(rd^2e) + d^3e + 2rd^3e + r^2d^3e + de^2 + rde^2 + r^2de^2 \\ &+ 2d^2e^2 + 4rd^2e^2 + 2r^2d^2e^2 + e^3 + 2re^3 + r^2e^3 + de^3 + 2rde^3 + r^2de^3) \\ &+ \mathbf{b}(d^2e^2 + rd^2e^2 + d^3e^2 + rd^3e^2 + e^3 + re^3 + 2de^3 + 2rde^3 + d^2e^3 + rd^2e^3) \\ &+ d^3e^2 + de^3 + d^2e^3\,.\end{aligned}$$

Eq. (c):

$$\begin{aligned}\mathbf{b}^3\cdot\mathbf{P}(\mathbf{b},d,e,h) &= \mathbf{b}^6(d^2e + e^2 + de^2) \\ &+ \mathbf{b}^5(hd^2 + 2hde + d^3e + he^2 + de^2 + 2d^2e^2 + e^3 + de^3) \\ &+ \mathbf{b}^4(h^2d + hd^3 + h^2e - hde + 4hd^2e + he^2 + 4hde^2 + d^2e^2 \\ &+ d^3e^2 + e^3 + he^3 + 2de^3 + d^2e^3) \\ &+ \mathbf{b}^3(2h^2d^2 + 4h^2de - hd^2e + 2hd^3e + 2h^2e^2 + hde^2 + 4hd^2e^2 \\ &+ d^3e^2 + 2he^3 + de^3 + 2hde^3 + d^2e^3) \\ &+ \mathbf{b}^2(h^3d + h^2d^3 + h^3e - h^2de + 4h^2d^2e + h^2e^2 + 4h^2de^2 \\ &+ hd^2e^2 + hd^3e^2 + he^3 + h^2e^3 + 2hde^3 + hd^2e^3) \\ &+ \mathbf{b}(h^3d^2 + 2h^3de + h^2d^3e + h^3e^2 + h^2de^2 + 2h^2d^2e^2 + h^2e^3 \\ &+ h^2de^3) + h^3d^2e + h^3e^2 + h^3de^2\,.\end{aligned}$$

Eq. (d):

$$\mathbf{P} = 8b^6 + 24b^5e + 24b^4e^2 - 3b^4e + 8b^3e^3 + 10b^3e^2 + 9b^2e^3 + 3be^3\,.$$

References

[1] J. Guckenheimer and P. Holmes, *Nonlinear Oscillations, Dynamical Systems and Bifurcation of Vector Fields* (Springer, New York, 1983).
[2] G. Nicolis and I. Prigogine, *Self-Organization in Non-Equilibrium Systems* (Wiley, New York, 1977).
[3] O.H. Petersen and M. Wakui, J. Memb. Biol. 118 (1990) 93.
[4] J. Lechleiter, S. Girard, E. Peralta and D. Clapham, Science 252 (1991) 123.
[5] E.A. Mayer, A. Kodner, X.P. Sun, J. Wilkes, D. Scott and G. Sachs, J. Memb. Biol. 125 (1992) 107.
[6] F.M.C. Vieira and P.M. Bisch, Notas de Física (CBPF/RJ-16/92), Preprint (1993).
[7] F.M.C. Vieira and P.M. Bisch, Eur. Biophys. J. 23 (1994) 277.
[8] B.L. Clarke, Adv. Chem. Phys. 43 (1980) 1.
[9] M. Kubíček and M. Marek, *Computational Methods in Bifurcation Theory and Dissipative Structures* (Springer, New York, 1983).
[10] R. Seydel, *From Equilibrium to Chaos. Practical Bifurcation and Stability Analysis* (Elsevier, New York, 1988).
[11] J.H. Swart, Quaestiones Math. 13 (1990) 17.
[12] H. Farkas and P.L. Simon, J. Math. Chem. 9 (1992) 323.
[13] F. Cajori, *An Introduction to the Theory of Equations* (Dover, New York, 1969).
[14] M.M. Vainberg and V.A. Trenogin, *Theory of Branching of Solutions of Non-linear Equations* (Noordhoof, Leyden, 1974).
[15] S. Lipschutz, *General Topology* (McGraw-Hill, New York, 1965).
[16] W.S. Massey, *Algebraic Topology: An Introduction* (Harbrace College Mathematics Series, New York, 1967).
[17] V. Guillemin and A. Pollack, *Differential Topology* (Prentice-Hall, Englewood Cliffs, 1974).