

Article

Two Nested Limit Cycles in Two-Species Reactions

Ilona Nagy ^{1,*}, Valery G. Romanovski ^{2,3,4} and János Tóth ^{1,5}

¹ Department of Mathematical Analysis, Budapest University of Technology and Economics, Egry J. u. 1., H-1111 Budapest, Hungary; jtoth@math.bme.hu

² Center for Applied Mathematics and Theoretical Physics, SI-2000 Maribor, Slovenia; valerij.romanovskij@um.si

³ Faculty of Electrical Engineering and Computer Science, University of Maribor, SI-2000 Maribor, Slovenia

⁴ Faculty of Natural Science and Mathematics, University of Maribor, SI-2000 Maribor, Slovenia

⁵ Laboratory for Chemical Kinetics, Eötvös Loránd University, Pázmány P. sétány 1/A, H-1117 Budapest, Hungary

* Correspondence: nagy@math.bme.hu; Tel.: +36-1463-5141

† These authors contributed equally to this work.

Received: 24 August 2020; Accepted: 22 September 2020; Published: 25 September 2020



Abstract: We search for limit cycles in the dynamical model of two-species chemical reactions that contain seven reaction rate coefficients as parameters and at least one third-order reaction step, that is, the induced kinetic differential equation of the reaction is a planar cubic differential system. Symbolic calculations were carried out using the Mathematica computer algebra system, and it was also used for the numerical verifications to show the following facts: the kinetic differential equations of these reactions each have two limit cycles surrounding the stationary point of focus type in the positive quadrant. In the case of Model 1, the outer limit cycle is stable and the inner one is unstable, which appears in a supercritical Hopf bifurcation. Moreover, the oscillations in a neighborhood of the outer limit cycle are slow-fast oscillations. In the case of Model 2, the outer limit cycle is unstable and the inner one is stable. With another set of parameters, the outer limit cycle can be made stable and the inner one unstable.

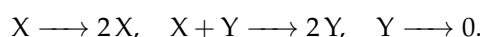
Keywords: limit cycles; two-species reactions; third-order reaction step; Hopf bifurcation

MSC: 34C07; 34D99; 34C25; 80A30

1. Introduction

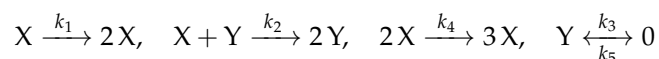
This paper is a part of a series of works [1–5] on the existence or absence of limit cycles in two- and three-species chemical reactions endowed with mass action kinetics. A very recent paper [6] by Valenzuela et al. is similar to ours, but they use the normal form theory, which is computationally not very efficient. (A few of our papers on models with non mass action—rational—kinetics are [7,8].)

Let us review the history of the topics shortly. Although similar models were known even in the XIXth century [9], the first model with some chemical relevance and showing oscillatory behavior was the Lotka–Volterra reaction [10–12].



Frank-Kamenetsky [13] used it to describe the oxidation of hydrocarbons, or—in [14]—as a model of cold flames. The induced kinetic differential equation of this reaction shows **conservative oscillations**: its stationary point is a center around which a family of periodic trajectories—parametrized by the initial conditions—appears. People interested in applications were

looking for a natural model with (stable) limit cycles, because this corresponds to the experimental observation that the trajectories tend to a periodic one on the long run. According to the general view, the first reaction (called Brusselator) with an induced kinetic differential equation having a limit cycle was constructed by Prigogine and Lefever in [15]. However, Frank-Kamenetsky and Salnikov in an extremely well-written early paper [16] constructed the reaction.



with the induced kinetic differential equation

$$\dot{x} = k_1x - k_2xy + k_4x^2 \quad \dot{y} = k_2xy - k_3y + k_5$$

having a limit cycle and only containing second-order terms (second-order reaction steps).

In the sixties and seventies of the twentieth century, the oscillatory Belousov–Zhabotinsky reaction was the topic of active (mainly experimental) research [17,18]. Ding-Hsü [19] was the first to use explicitly Hopf’s theorem to prove the existence of a limit cycle in the induced kinetic differential equation of a reaction, namely that of the Oregonator, leading to a three-variable differential equation with a second degree right hand side. It is worth citing him to show how happy he was to find this tool for this purpose: “thereby to publicize Hopf’s theorem. This theorem is not as well known and available as it should be”.

As to the more theoretical investigations, one should mention the Póta–Hanusse–Tyson–Light theorem, actually proven by Póta [20] stating that two-species bimolecular systems cannot have limit cycles (see an alternative proof in [21]). Schnakenberg [22] and following him Császár et al. [23] constructed classes of reactions which showed limit cycles—numerically.

A possible classification of problems in reaction kinetics (but also in other fields of applied sciences) might be this [24] [Ch. 11]. Models are formulated and their properties are investigated by the methods of the qualitative theory, or by numerical and other methods: this approach is the **direct approach**. A more interesting direction for the chemist (biologist, etc.) is the **inverse approach**: given some measurements of qualitative properties of a phenomenon, we look for models with this behavior. A special case of this is parameter estimation, when the model structure is known and it is only the numerical values of the model parameters we are looking for. All the research mentioned up to this point solved **direct problems**: given a reaction or its kinetic differential equation, some properties of it are found. (Note that whereas the route from reactions to differential equations is straightforward [24,25], it is far from being true in the opposite direction, see, e.g., [26].) Our present paper also belongs to this category. However, Escher [27,28] formulated and solved a series of **inverse problems**: given a dynamic behavior (e.g., existence of a limit cycle) he constructed reactions to show the given phenomenon.

In this paper, we present two reactions among two species and not higher than third-order reaction steps, then show that both models can have two limit cycles with appropriate values of the parameters (reaction rate coefficients by meaning). Although we present illustrating figures coming from numerical calculations, we emphasize that our proofs are rigorous and use no approximations. The novelty of our treatment is that we use focus quantities to find limit cycles symbolically in a kinetic differential equation. Although the framework of our work is simple, the computations are cumbersome both for the human and the computer, and also needs ingenuity.

The structure of our paper is as follows. Section 2 describes a method to find limit cycles. Next, in Section 3 we discuss our Model 1 in detail. For Model 2, the same investigations will be carried out in less detail in Section 4. Figures illustrate the rigorous results throughout. Finally, we mention that our *Mathematica* notebooks are available online [29] and also as a supplementary material.

2. A Method to Find Limit Cycles

Here—following [30]—we summarize briefly how we can find two limit cycles in the planar differential system $\dot{u} = P \circ (u, v)$, $\dot{v} = Q \circ (u, v)$, where P and Q are functions (here: polynomials) dependent on some parameters, by a local investigation of a singular point.

1. As a first step, the singular point (u_0, v_0) of the system is shifted into the origin using the substitution $x = u - u_0$, $y = v - v_0$, so in the new coordinates the system is written as

$$\dot{x} = \tilde{P} \circ (x, y), \quad \dot{y} = \tilde{Q} \circ (x, y). \tag{1}$$

Let us denote the Jacobian matrix of this system at the origin by J and let λ_1 and λ_2 be the eigenvalues. Next, the parameters are chosen in such a way that $\text{trace}(J) = 0$.

2. Then we look for a polynomial $\Phi(x, y) = \sum_{k+s=2}^6 \phi_{ks} x^k y^s$ such that

$$\frac{\partial \Phi}{\partial x} \dot{x} + \frac{\partial \Phi}{\partial y} \dot{y} = g_1(x^2 + y^2)^2 + g_2(x^2 + y^2)^3 + h.o.t \tag{2}$$

and the quadratic part of $\Phi(x, y)$,

$$\Phi_0(x, y) = \phi_{20}x^2 + \phi_{11}xy + \phi_{02}y^2$$

is a positive definite quadratic form. The coefficients g_1 and g_2 in (2) depend on parameters of system (1) and are called **focus (or Lyapunov) quantities**.

3. Keeping $\text{trace}(J) = 0$ and Φ_0 positive definite we look for values of parameters of system (1) to set the values of g_1 and g_2 in the following way.
 - (a) First, if $g_1 = 0$ and $g_2 < 0$ then, since Φ is a positive definite Lyapunov function, the origin is a stable focus.
 - (b) If we now take a small perturbation, so that g_1 becomes positive (while g_2 remains negative), then an unstable focus arises at the origin and a stable limit cycle appears around the singular point.
4. Finally, the parameters are perturbed in such a way that $\text{trace}(J) \neq 0$ and $\text{Re}(\lambda_{1,2}) < 0$. In this case, the origin becomes stable, and if the perturbation is sufficiently small, then the outer stable limit cycle is preserved (but can be shifted) and an unstable limit cycle appears between the origin and the outer stable limit cycle as a result of a supercritical Hopf bifurcation. Since we cannot say in advance what perturbations are “sufficiently small”, the existence of two limit cycles in a specific perturbed system should be also verified numerically.

Similarly, if in step 3a we look for parameters such that $g_1 = 0$ and $g_2 > 0$ at the beginning and achieve that $\text{Re}(\lambda_{1,2}) > 0$, $g_1 < 0$, $g_2 > 0$ in the end, then the outer limit cycle will be unstable and the inner one will be stable.

3. Model 1

We investigate the induced kinetic differential equation of the reaction in Figure 1.

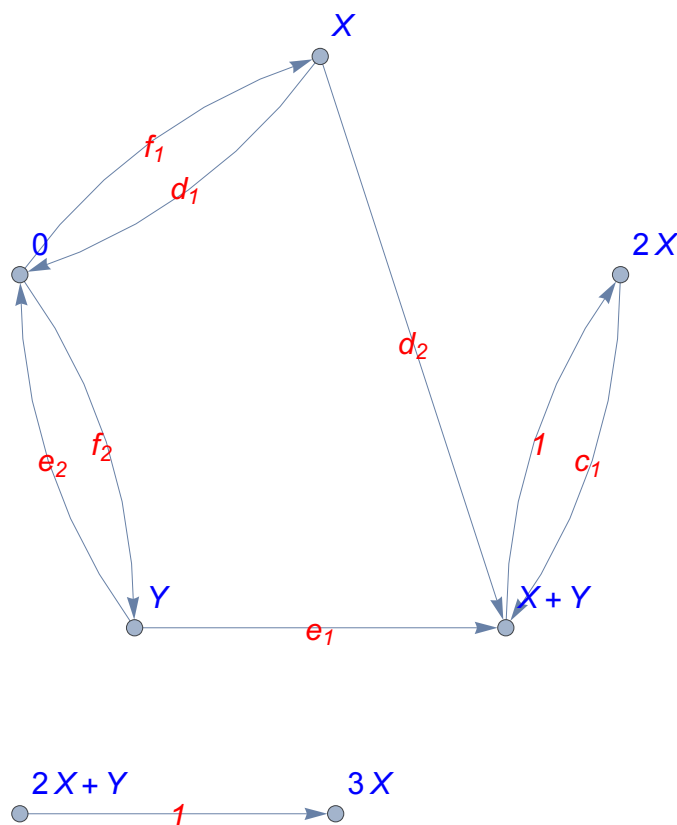


Figure 1. The reaction inducing the system (3).

Assuming mass action type kinetics, i.e., the dynamical system:

$$\begin{aligned} \dot{x} &= x^2y + xy - c_1x^2 - d_1x + e_1y + f_1, \\ \dot{y} &= -x^2y - xy + c_1x^2 + d_2x - e_2y + f_2. \end{aligned} \tag{3}$$

where $x(t) \geq 0$ and $y(t) \geq 0$ denote the concentrations of two chemical species and $c_1, d_1, d_2, e_1, e_2, f_1, f_2$ are the reaction rate coefficients, all supposed to be positive. The meaning of reaction rate coefficients can be found in standard textbooks on chemical kinetics or in [24]. The reader who is not an insider will understand the signs if (s)he glances a look at Figure 1.

3.1. Symbolic Preparations

Let us denote the singular point of system (3) in the first quadrant by $A(x_0, y_0)$. To simplify the calculations, we consider the case when $x_0 = 1$. Solving the system $\dot{x} = 0, \dot{y} = 0$ for d_1 and y_0 , we get that

$$d_1 = \frac{d_2(2 + e_1) + c_1(e_1 - e_2) + (2 + e_2)f_1 + (2 + e_1)f_2}{2 + e_2}, \tag{4}$$

$$y_0 = \frac{c_1 + d_2 + f_2}{2 + e_2}. \tag{5}$$

Let us emphasize again that the assumption $x_0 = 1$ implies that the reaction rate coefficients are not independent, (4) should hold among them.

Now, shifting the singular point $A(x_0, y_0)$ into the origin with the transformation $x_1 = x - x_0, y_1 = y - y_0$, we get that the transformed system is

$$\begin{aligned} \dot{x}_1 &= -\frac{1}{2+e_2}(c_1x_1 - d_2x_1 + c_1e_1x_1 + d_2e_1x_1 + c_1e_2x_1 + 2f_1x_1 \\ &\quad + e_2f_1x_1 - f_2x_1 + e_1f_2x_1 + c_1x_1^2 - d_2x_1^2 + c_1e_2x_1^2 - f_2x_1^2 - 4y_1 \\ &\quad - 2e_1y_1 - 2e_2y_1 - e_1e_2y_1 - 6x_1y_1 - 3e_2x_1y_1 - 2x_1^2y_1 - e_2x_1^2y_1), \\ \dot{y}_1 &= -\frac{1}{2+e_2}(-c_1x_1 + d_2x_1 - 2c_1e_2x_1 - d_2e_2x_1 + 3f_2x_1 - c_1x_1^2 \\ &\quad + d_2x_1^2 - c_1e_2x_1^2 + f_2x_1^2 + 4y_1 + 4e_2y_1 + e_2^2y_1 + 6x_1y_1 + 3e_2x_1y_1 \\ &\quad + 2x_1^2y_1 + e_2x_1^2y_1). \end{aligned} \tag{6}$$

Let J denote the Jacobian matrix of system (6) at the origin. The necessary condition for a Hopf bifurcation at the origin (and also at the point $A(x_0, y_0)$) is that the matrix J has pure imaginary eigenvalues (and the necessary condition for this is that the trace of J is zero).

Calculating the trace of J , we get that

$$\text{trace}(J) = -\frac{4 + c_1 - d_2 + c_1e_1 + d_2e_1 + 4e_2 + c_1e_2 + e_2^2 + 2f_1 + e_2f_1 - f_2 + e_1f_2}{2 + e_2} \tag{7}$$

Solving $\text{trace}(J) = 0$ for c_1 gives

$$c_1 = \frac{d_2 - d_2e_1 - (2 + e_2)(2 + e_2 + f_1) + f_2 - e_1f_2}{1 + e_1 + e_2}. \tag{8}$$

In this case, the eigenvalues of J are of the form $\lambda_{1,2} = \pm i\sqrt{\beta}$, where

$$\begin{aligned} \beta &= \frac{1}{1 + e_1 + e_2}(-2e_1 + 2d_2e_1 + d_2e_1^2 + 2e_2 - 2d_2e_2 + e_1e_2 - d_2e_1e_2 - e_2^2 + e_1e_2^2 - e_2^3 \\ &\quad + 2f_1 + e_1f_1 + 4e_2f_1 + 2e_1e_2f_1 + 2f_2 + 5e_1f_2 + 2e_1^2f_2). \end{aligned} \tag{9}$$

The eigenvalues will be purely imaginary if $\beta > 0$. Then system (6) with the substitution for c_1 in (8) (and using the variables x and y instead of x_1 and y_1) will be the following:

$$\begin{aligned} \dot{x} &= \frac{1}{1 + e_1 + e_2}(2x + 2e_1x + 3e_2x + e_1e_2x + e_2^2x + 2x^2 + d_2e_1x^2 \\ &\quad + 3e_2x^2 + e_2^2x^2 + f_1x^2 + e_2f_1x^2 + e_1f_2x^2 + 2y + 3e_1y + e_1^2y \\ &\quad + 2e_2y + e_1e_2y + 3xy + 3e_1xy + 3e_2xy + x^2y + e_1x^2y + e_2x^2y), \\ \dot{y} &= -\frac{1}{1 + e_1 + e_2}(2x + d_2e_1x + 5e_2x - d_2e_2x + 2e_2^2x + f_1x + 2e_2f_1x \\ &\quad + f_2x + 2e_1f_2x + 2x^2 + d_2e_1x^2 + 3e_2x^2 + e_2^2x^2 + f_1x^2 + e_2f_1x^2 \\ &\quad + e_1f_2x^2 + 2y + 2e_1y + 3e_2y + e_1e_2y + e_2^2y + 3xy + 3e_1xy + 3e_2xy + x^2y + e_1x^2y + e_2x^2y). \end{aligned} \tag{10}$$

Now, in order to apply the procedure described in the previous section, we look for a polynomial

$$\Phi(x, y) = \sum_{k+s=2}^6 \phi_{ks}x^ky^s \tag{11}$$

such that

$$\frac{\partial \Phi}{\partial x} \dot{x} + \frac{\partial \Phi}{\partial y} \dot{y} = g_1(x^2 + y^2)^2 + g_2(x^2 + y^2)^3 + h.o.t. \tag{12}$$

Calculating the quadratic part of (11) we get that

$$\Phi_2 = \frac{1}{2}\phi_{11} \left(\frac{(d_2(e_1 - e_2) + (1 + 2e_2)(2 + e_2 + f_1) + f_2 + 2e_1f_2)}{(2 + e_2)(1 + e_1 + e_2)}x^2 + 2xy + \frac{2 + e_1}{2 + e_2}y^2 \right),$$

where ϕ_{11} can be chosen arbitrarily, so we set $\phi_{11} = 1$. Now, let

$$A := \begin{pmatrix} \frac{d_2(e_1 - e_2) + (1 + 2e_2)(2 + e_2 + f_1) + f_2 + 2e_1f_2}{2(2 + e_2)(1 + e_1 + e_2)} & \frac{1}{2} \\ \frac{1}{2} & \frac{2 + e_1}{2(2 + e_2)} \end{pmatrix}$$

The determinants of the upper-left main minors of A are

$$A_{11} = \frac{d_2(e_1 - e_2) + (1 + 2e_2)(2 + e_2 + f_1) + f_2 + 2e_1f_2}{(1 + e_1 - e_2)(2(2 + e_2)(1 + e_1 + e_2))},$$

$$\det(A) = -((2e_1 - 2d_2e_1 - d_2e_1^2 - 2e_2 + 2d_2e_2 - e_1e_2 + d_2e_1e_2 + e_2^2 - e_1e_2^2 + e_2^3 - 2f_1 - e_1f_1 - 4e_2f_1 - 2e_1e_2f_1 - 2f_2 - 5e_1f_2 - 2e_1^2f_2)/(4(2 + e_2)^2(1 + e_1 + e_2))). \tag{13}$$

At this point, the positive definiteness of A together with the previous conditions cannot be decided, so in order to simplify the further calculations, we fix the values of two more reaction rate coefficients f_1 and f_2 as

$$f_1 = 1, f_2 = 2 \tag{14}$$

and proceed with calculating g_1 . This gives

$$g_1 = (-36 - 105e_1 - 30d_2e_1 - 120e_1^2 - 50d_2e_1^2 - 6d_2^2e_1^2 - 56e_1^3 - 28d_2e_1^3 - 7d_2^2e_1^3 - 6e_1^4 - 6d_2e_1^4 - 2d_2^2e_1^4 - 75e_2 + 12d_2e_2 - 159e_1e_2 - 8d_2e_1e_2 + 6d_2^2e_1e_2 - 113e_1^2e_2 - 9d_2e_1^2e_2 + 7d_2^2e_1^2e_2 - 18e_1^3e_2 - d_2e_1^3e_2 + 2d_2^2e_1^3e_2 - 36e_2^2 + 13d_2e_2^2 - 65e_1e_2^2 + 18d_2e_1e_2^2 - 30e_1^2e_2^2 - 6e_1^3e_2^2 - 4d_2e_1^3e_2^2 + 9e_2^3 + d_2e_2^3 - 6e_1e_2^3 + 7d_2e_1e_2^3 - e_1^2e_2^3 + 4d_2e_1^2e_2^3 + 6e_2^4 + 7e_1e_2^4 - 2e_1^2e_2^4 + 2e_1e_2^5)/((2 + e_2)(123 + 234e_1 + 34d_2e_1 + 137e_1^2 + 30d_2e_1^2 + 3d_2^2e_1^2 + 26e_1^3 + 2d_2e_1^3 + 3e_1^4 + 330e_2 - 34d_2e_2 + 348e_1e_2 + 16d_2e_1e_2 - 6d_2^2e_1e_2 + 68e_1^2e_2 + 6e_1^3e_2 + 307e_2^2 - 46d_2e_2^2 + 3d_2^2e_2^2 + 126e_1e_2^2 + 10d_2e_1e_2^2 + 11e_1^2e_2^2 + 116e_2^3 - 12d_2e_2^3 + 12e_1e_2^3 + 16e_2^4)). \tag{15}$$

We calculated the value of g_2 in (12) as a function of d_2, e_1, e_2 , however, the expression is very complicated, it is contained in [29]. To simplify it, again we fix the values of two further reaction rate coefficients, e_1 and d_2 as

$$e_1 = 1/2, d_2 = 20, \tag{16}$$

then the formula for g_2 is

$$\begin{aligned}
 g_2 = & - \left((2(-126512084933352295 + 478399692835658985e_2 \right. \\
 & - 762458375238510816e_2^2 + 730329622432012315e_2^3 \\
 & - 466875108129002500e_2^4 + 180057388265535584e_2^5 \\
 & - 42412278548678749e_2^6 + 7565318705371668e_2^7 - 1899913140260206e_2^8 \\
 & + 200501244715092e_2^9 + 44607817747872e_2^{10} + 18408318367872e_2^{11} \\
 & + 8352995841088e_2^{12} + 1190085589888e_2^{13} + 348608893184e_2^{14} \\
 & + 33760183296e_2^{15} + 6787676672e_2^{16} + 473953280e_2^{17} + 64299008e_2^{18} \\
 & + 2555904e_2^{19} + 196608e_2^{20}) / (3(2 + e_2)(83 - 42e_2 + 8e_2^2)(-73 + 85e_2 \\
 & (+e_2^2 + 2e_2^3))^2(109 - 25e_2 + 32e_2^2 + 4e_2^3)(17163 - 19172e_2 + 12044e_2^2 \\
 & \left. - 1888e_2^3 + 256e_2^4)(23933 - 29628e_2 + 23764e_2^2 - 2976e_2^3 + 512e_2^4)) \right). \tag{17}
 \end{aligned}$$

Using the requirement that negative cross-effect cannot be present in a kinetic differential equation [24] [Theorem 6.27] and conditions (4), (5), (8), (9), (13)–(17) and the Reduce command of Mathematica [31], the numerical solution of the semi-algebraic system

$$g_1 = 0 \wedge g_2 < 0 \wedge A_{11} > 0 \wedge \det(A) > 0 \wedge y_0 > 0 \wedge \beta > 0 \wedge c_1 > 0 \wedge d_1 > 0 \wedge e_2 > 0$$

for e_2 is

$$e_2 \approx -0.771291. \tag{18}$$

Similarly, we found that $g_2 > 0$ is not possible for g_2 defined by (17). For the value of e_2 in (18), the numerical value of g_2 is

$$g_2 \approx -0.0278896$$

and also the condition $\text{trace}(J) = 0$ holds. From $A_{11} > 0$ and $\det(A) > 0$ it follows that Φ_2 is a positive definite quadratic form, so the function $\Phi(x, y)$ defined in (11) is a positive definite Lyapunov function in a sufficiently small neighbourhood of the origin. This together with conditions $g_1 = 0$ and $g_2 < 0$ means that its Lie derivative given in (12) is negative definite, so the origin is a stable focus.

From (15), we can see that g_1 is a polynomial in d_2, e_1, e_2 and $d_2 = 20, e_1 = 1/2$ and e_2 defined by (18) is a simple root of the equation $g_1 = 0$. Thus, we can choose a small perturbation of any of the parameters d_2, e_1, e_2 such that g_1 becomes negative. Hence, after such a perturbation a stable limit cycle bifurcates from the origin.

Now, from (7) and (8) it is obvious that we can take an arbitrarily small perturbation of any of the parameters d_2, e_i, f_i ($i = 1, 2$) such that an unstable limit cycle appears from the origin in a supercritical Hopf bifurcation. Thus, the resulting perturbed system has two limit cycles.

Remark 1. We mention that we have performed some computational experiments changing the parameters f_1, f_2, d_2, e_1, e_2 trying to find values of the parameters for which $\text{trace}(J) = 0, g_1 = 0, g_2 > 0$, but we failed to find such values.

3.2. Numerical Results for Model 1

In this section we present the numerical study confirming the existence of two limit cycles in system (3) and illustrate the results with figures created with the Wolfram Language.

3.2.1. The Appearance of the First Limit Cycle

For the values of the parameters defined by (4), (8), (14), (16) and (18) we first perturb the parameter e_2 such that g_1 becomes positive. If

$$e_2 = \frac{78}{100}$$

then we get that

$$g_1 \approx 0.015511 > 0, \quad g_2 \approx -0.666999 < 0, \quad \text{trace}(J) = 0.$$

It means that the origin becomes unstable and a stable limit cycle appears around the singular point.

In this case, the parameter settings for system (3) are the following: $c_1 = \frac{1229}{5700} \approx 0.215614$, $d_1 = \frac{59173}{2850} \approx 20.7625$, $d_2 = 20$, $e_1 = \frac{1}{2}$, $e_2 = \frac{78}{100}$, $f_1 = 1$, $f_2 = 2$. The singular point of the system in the first quadrant is $A(x_0, y_0) = (1, 7.99123)$ and the eigenvalues of the Jacobian matrix are $\lambda_{1,2} \approx \pm 1.06195i$.

The trajectories can be seen in Figures 2 and 3, where the initial point $(x_0, y_0 + d)$ is denoted in red and $A(x_0, y_0)$ is denoted in orange. Picture (a) shows the behavior of the trajectories in the phase plain, and pictures (b) and (c) show the solutions as a function of time. Where the shape of the trajectories makes it possible, we also denoted the direction of the trajectories with an arrow.

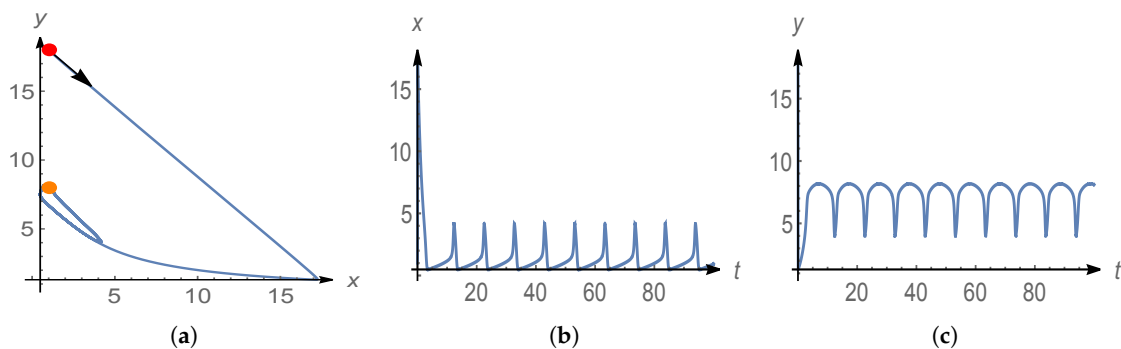


Figure 2. Model 1 with one stable limit cycle. The trajectory is going inward, approaching the limit cycle. The distance of the initial point from the singular point is $d = 10$.

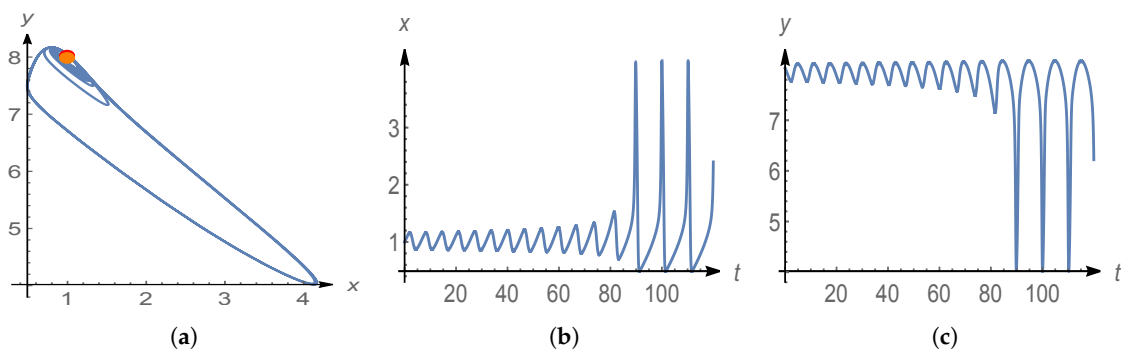


Figure 3. Model 1 with one stable limit cycle. The trajectory is going outward approaching the limit cycle. The distance of the initial point from the singular point is $d = 0.038$.

3.2.2. The Appearance of the Second Limit Cycle

Next, we perturb the parameter c_1 such that $\text{trace}(J)$ becomes negative. If $c_1 = \frac{22}{100}$, then we get that

$$g_1 \approx 0.015511 > 0, \quad g_2 \approx -0.666999 < 0, \quad \text{trace}(J) \approx -0.00359712 < 0.$$

Since the trace of J is now negative, it means that the eigenvalues of J have negative real parts. It means that the origin becomes stable and an unstable limit cycle appears between the origin and the outer stable limit cycle as a result of a supercritical Hopf bifurcation. The perturbation for c_1 must be sufficiently small to ensure that when the inner limit cycle appears, the outer one is still preserved.

In this case, the parameter settings for system (3) are the following: $c_1 = \frac{22}{100}$, $d_1 = \frac{72148}{3475} \approx 20.762$, $d_2 = 20$, $e_1 = \frac{1}{2}$, $e_2 = \frac{78}{100}$, $f_1 = 1$, $f_2 = 2$. The singular point of the system in the first quadrant is $A(x_0, y_0) = (1, 7.99281)$ and the eigenvalues of the Jacobian matrix are $\lambda_{12} \approx -0.00179856 \pm 1.0619i$.

The trajectories can be seen in Figures 4–7, where the initial point $(x_0, y_0 + d)$ is denoted in red and $A(x_0, y_0)$ is denoted in orange. Picture (a) shows the behavior of the trajectories in the phase plain, and pictures (b) and (c) show the solutions as a function of time.

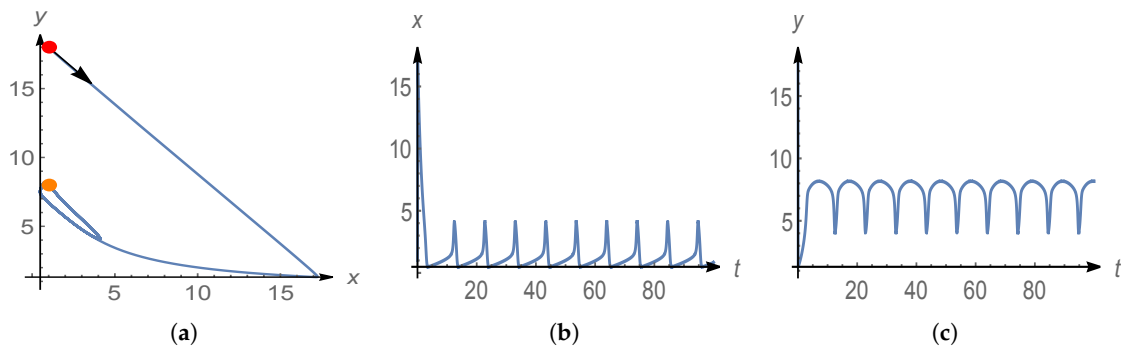


Figure 4. Model 1 with a stable outer and an unstable inner limit cycle. The trajectory is going inward, approaching the large limit cycle as t tends to $+\infty$. The distance of the initial point from the singular point is $d = 10$.

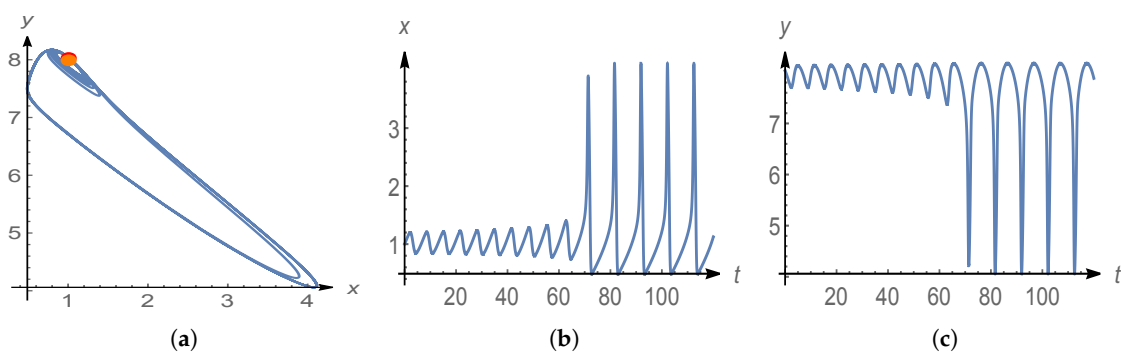


Figure 5. Model 1 with a stable outer and an unstable inner limit cycle. The trajectory is going outward, approaching the large limit cycle as t tends to $+\infty$ and the small limit cycle as t tends to $-\infty$. The distance of the initial point from the singular point is $d = 0.042$.

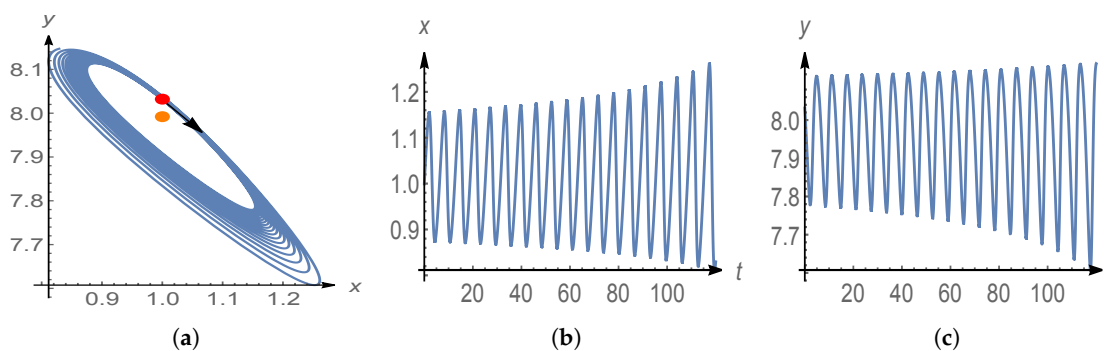


Figure 6. Model 1 with a stable outer and an unstable inner limit cycle. The trajectory is going outward, approaching the large limit cycle as t tends to $+\infty$ and the small limit cycle as t tends to $-\infty$. The distance of the initial point from the singular point is $d = 0.038$.

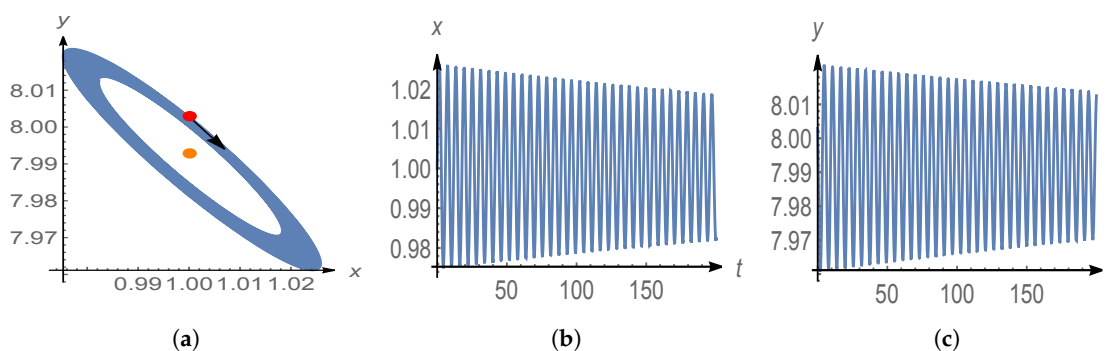


Figure 7. Model 1 with a stable outer and an unstable inner limit cycle. The trajectory is going inward, approaching the singular point as t tends to $+\infty$ and the small limit cycle as t tends to $-\infty$. The distance of the initial point from the singular point is $d = 0.01$.

4. Model 2

We investigate the following dynamical system:

$$\begin{aligned} \dot{x} &= x^2y - xy - c_1x^2 - d_1x + e_1y + f_1, \\ \dot{y} &= -x^2y + xy + c_1x^2 + d_2x - e_2y + f_2. \end{aligned} \tag{19}$$

where $x(t) \geq 0$ and $y(t) \geq 0$ denote the concentrations of two chemical species and

$$c_1, d_1, d_2, e_1, e_2, f_1, f_2 \geq 0. \tag{20}$$

are the reaction rate coefficients. Actually, the system is the induced kinetic differential equation of the reaction in Figure 8 assuming mass action type kinetics.

Compared to Model 1, here the signs of the terms xy are changed. After repeating the steps (4)–(13) with this new system, we get that

$$d_1 = \frac{c_1(e_1 - e_2) + e_2f_1 + e_1(d_2 + f_2)}{e_2} \tag{21}$$

$$c_1 = \frac{d_2 - d_2e_1 - e_2(e_2 + f_1) + f_2 - e_1f_2}{-1 + e_1 + e_2}. \tag{22}$$

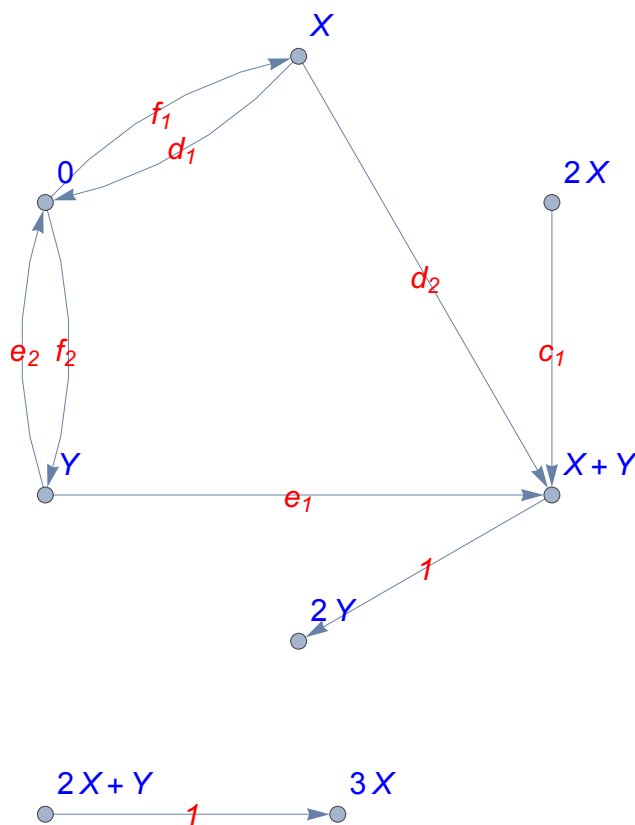


Figure 8. The reaction inducing the system (19).

Setting the values f_1 and f_2 as

$$f_1 = \frac{1}{2}, f_2 = \frac{1}{10} \tag{23}$$

and proceeding with the calculations, we obtain that both g_1 and g_2 are functions of d_2, e_1, e_2 . Investigating the possible values of e_1 and d_2 numerically, we find that when for example $d_2 = 1/100$ and $0.128 < e_1 < 0.213$ then $g_1 = 0, g_2 > 0$ is possible; and when $d_2 = 1/100$ and $0.264 < e_1 < 0.5$ or $0.213 < e_1 < 0.228$ then $g_1 = 0, g_2 < 0$ is possible.

Here, we want to achieve that the outer limit cycle is unstable (that is, $g_2 > 0$), so we choose these parameters as

$$d_2 = \frac{1}{100}, e_1 = \frac{18}{100}. \tag{24}$$

With this, we find that $g_1 = 0, g_2 < 0$ and $g_1 = g_2 = 0$ cannot be the case and $g_1 = 0, g_2 > 0$ is only possible when

$$e_2 \approx 0.29582 \tag{25}$$

where e_2 is a root of a fifth-degree polynomial. With the parameter settings (21)–(25) we get that the system has three singular points in the first quadrant: $A(1, 1.30837)$, $B(0.809127, 2.04744)$ and $C(0.457223, 3.41004)$ and

$$g_1 \approx 0 \quad g_2 \approx 0.0276312 > 0 \quad \text{trace}(J) \approx 0$$

where J denotes the Jacobian matrix at A . In this case the point A is an unstable focus.

As a next step, keeping $c_1, d_1, d_2, e_1, f_1, f_2$ the same as in (21)–(24), we perturb e_2 as

$$e_2 = \frac{278}{1000} \tag{26}$$

and obtain that the system has three singular points in the first quadrant: $A(1, 1.23247)$, $B(0.7895, 2.26181)$ and $C(0.414968, 4.09327)$ and

$$\begin{aligned} g_1 &\approx -0.0090896 < 0 \\ g_2 &\approx 0.0400065 > 0 \\ \text{trace}(J) &\approx 0 \end{aligned}$$

where J denotes the Jacobian matrix at A . In this case, the point A becomes stable and an unstable limit cycle appears around A .

Finally, perturbing c_1 as

$$c_1 = \frac{233}{1000} \tag{27}$$

we get that the system has three singular points in the first quadrant: $A(1, 1.23381)$, $B(0.789796, 2.26142)$ and $C(0.414926, 4.09403)$ and

$$g_1 \approx -0.0090896 < 0 \quad g_2 \approx 0.0400065 > 0 \quad \text{trace}(J) \approx 0.000726619 > 0$$

where J denotes the Jacobian matrix at A . In this case, the point A becomes unstable and a stable limit cycle appears between A and the outer unstable limit cycle. We have to check numerically that the perturbations are small enough, that is, the outer cycle is preserved when the inner cycle appears. This is shown in Figures 9–11.

To sum up the final step, the parameter settings are $c_1 = \frac{233}{1000}$, $d_1 = \frac{67983}{139000} \approx 0.489086$, $d_2 = \frac{1}{100}$, $e_1 = \frac{18}{100}$, $e_2 = \frac{278}{1000}$, $f_1 = \frac{1}{2}$, $f_2 = \frac{1}{10}$. The system has three singular points in the first quadrant: $A(1, 1.23381)$ (unstable focus, orange), $B(0.789796, 2.26142)$ (saddle, green), $C(0.414926, 4.09403)$ (real sink, blue). The initial point is denoted by red and the distance of the initial point from the singular point by d .

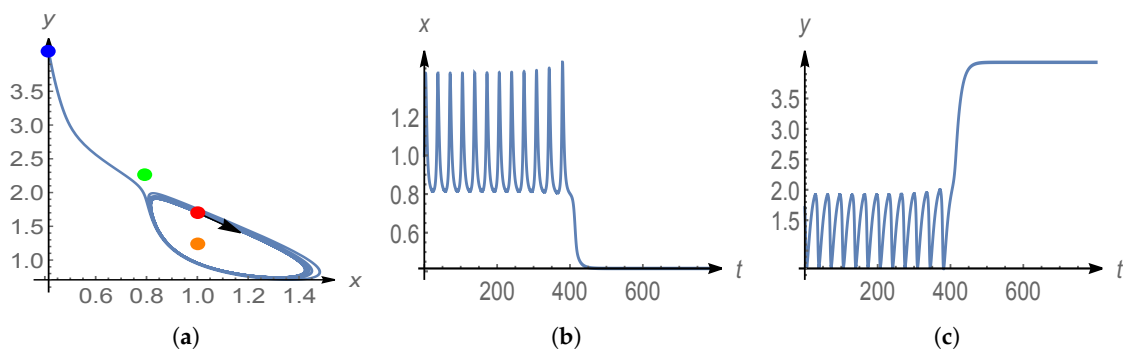


Figure 9. Model 2 with an unstable outer and a stable inner limit cycle. The trajectory is going outward, approaching the point C as $t \rightarrow \infty$ and the outer limit cycle as $t \rightarrow -\infty$ ($d = 0.47$).

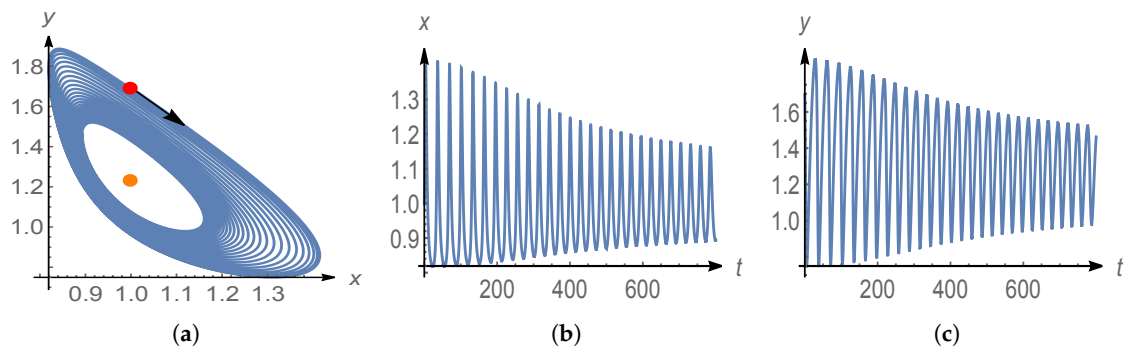


Figure 10. Model 2 with an unstable outer and a stable inner limit cycle. The trajectory is going inward, approaching the inner limit cycle as $t \rightarrow \infty$ and the outer limit cycle as $t \rightarrow -\infty$ ($d = 0.46$).

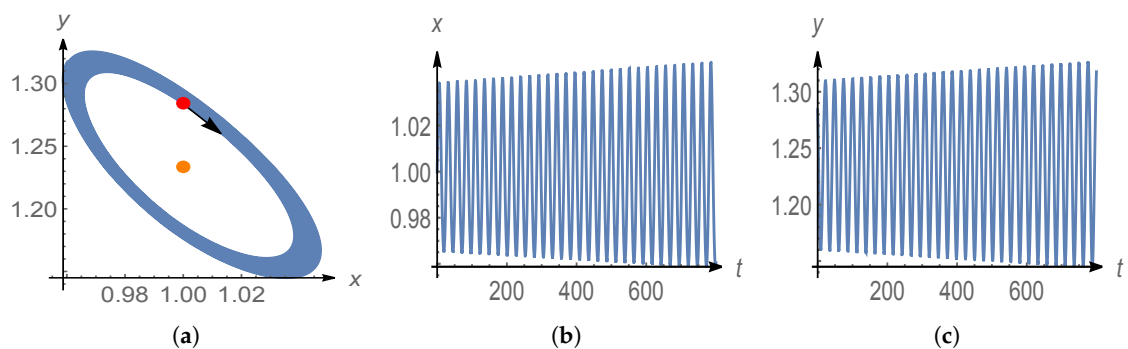


Figure 11. Model 2 with an unstable outer and a stable inner limit cycle. The trajectory is going outward, approaching the inner limit cycle as $t \rightarrow \infty$ and the point A as $t \rightarrow -\infty$ ($d = 0.05$).

Finally, we would like to remark that in Model 2 it is also possible that the outer limit cycle is stable and inner one is unstable. To achieve this, we repeated the procedure described above with the following parameter settings: $c_1 = \frac{79}{100}$, $d_1 = \frac{26331}{21100} \approx 1.24791$, $d_2 = \frac{4}{10}$, $e_1 = \frac{3}{10}$, $e_2 = \frac{633}{1000}$, $f_1 = 1$, $f_2 = 1$. We obtained that the system has one singular point in the first quadrant: $A(x_0, y_0) = (1, 3.45972)$ and

$$g_1 \approx 0.00642203 > 0 \quad g_2 \approx -0.301207 < 0 \quad \text{trace}(J) \approx -0.00119905 < 0$$

where J denotes the Jacobian matrix at A which is a stable focus. The trajectories can be seen in Figures 12–14, where the initial point $(x_0, y_0 + d)$ is denoted in red and $A(x_0, y_0)$ is denoted in orange.

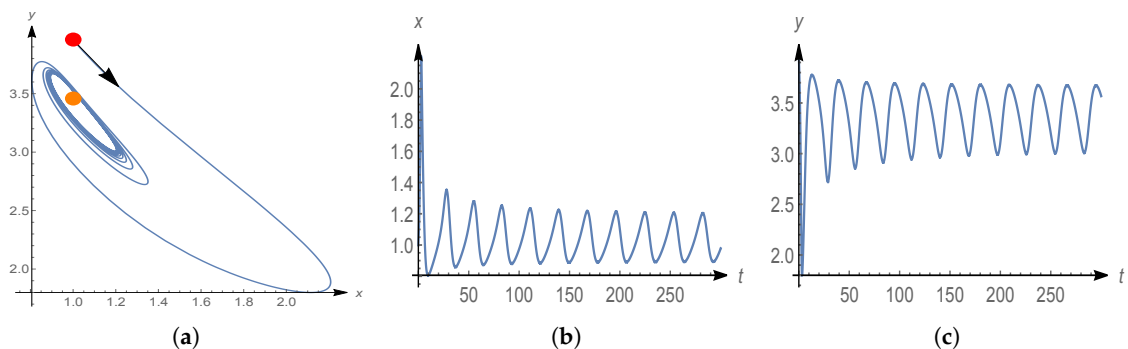


Figure 12. Model 2 with a stable outer and an unstable inner limit cycle. The trajectory is going inward, approaching the large limit cycle as $t \rightarrow \infty$ ($d = 0.5$).

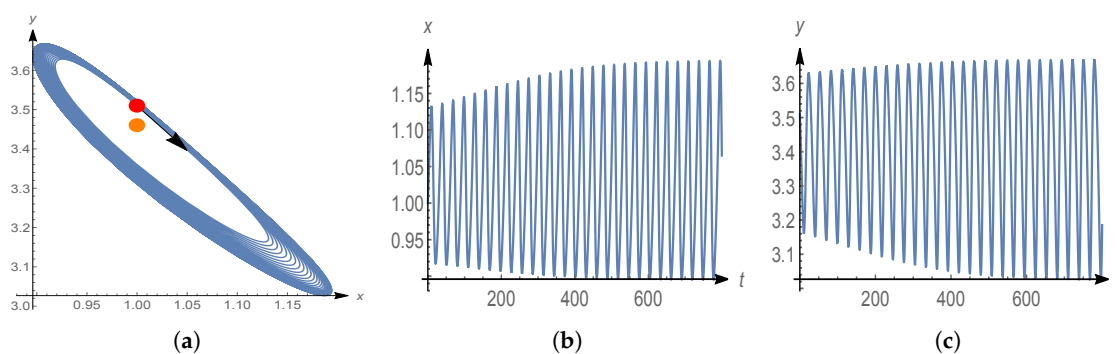


Figure 13. Model 2 with a stable outer and an unstable inner limit cycle. The trajectory is going outward, approaching the outer limit cycle as $t \rightarrow \infty$ and the inner limit cycle as $t \rightarrow -\infty$ ($d = 0.05$).

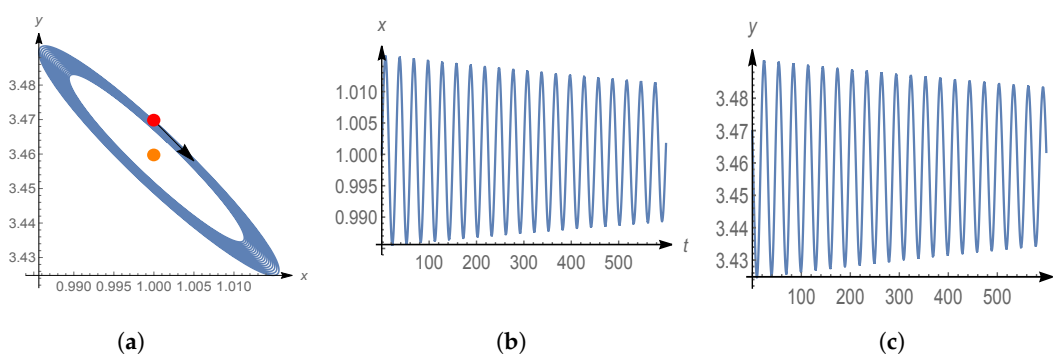


Figure 14. Model 2 with a stable outer and an unstable inner limit cycle. The trajectory is going inward, approaching the point A as $t \rightarrow \infty$ and the small limit cycle as $t \rightarrow -\infty$ ($d = 0.01$).

5. Discussion

We investigated two reaction networks, and have found two nested limit cycles in both of them. We did the calculations symbolically, as far as it did not become impossible. Recent methods in the qualitative theory of differential equations helped to do this.

Either with the development of computers or theory, we hope that larger parts of such investigations will be possible to be carried out symbolically, thus making possible the mapping of the whole parameter space. Furthermore, we hope to understand better the role of the common x^2y term.

Supplementary Materials: The *Mathematica* notebooks are available online at <http://www.mdpi.com/2227-7390/8/10/1658/s1>.

Author Contributions: I.N. did the formal analysis, V.G.R. provided the methodology, and J.T. did the writing—review and editing. All authors have read and agreed to the published version of the manuscript.

Funding: I.N. and J.T. acknowledge the support of the National Research, Development and Innovation Office (2018-2.1.11-TÉT-SI-2018-00007 and SNN 125739). V.G.R. was supported by the Slovenian Research Agency (program P1-0306, projects N1-0063 and BI-HU/19-20-002).

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References

1. Antonov, V.; Dolićanin, D.; Romanovski, V.G.; Tóth, J. Invariant planes and periodic oscillations in the May–Leonard asymmetric model. *MATCH Commun. Math. Comput. Chem.* **2016**, *76*, 455–474.
2. Arcet, B.; Dolićanin, D.; Đekić, D.D.; Maćešić, S.; Romanovski, V.G. Limit cycles in the model of hypothalamic-pituitary-adrenal axis activity. *MATCH Commun. Math. Comput. Chem.* **2020**, *83*, 331–343.
3. Ferćec, B.; Nagy, I.; Romanovski, V.G.; Szederkényi, G.; Tóth, J. Limit Cycles in a Two-Species Reaction. *J. Nonlinear Model. Anal.* **2019**, *1*, 283–300.
4. Li, Y.; Romanovski, V.G. Hopf Bifurcations in a Predator–Prey Model with an Omnivore. *Qual. Theory Dyn. Syst.* **2019**, *18*, 1201–1224. [[CrossRef](#)]
5. Pantea, C.; Romanovski, V.G. Qualitative studies of some biochemical models. *Vestn. St. Petersburg. Univ. Math.* **2020**, *53*, 214–222. [[CrossRef](#)]
6. Valenzuela, L.M.; Blé, G.; Falconi, M.; Guerrero, D. Hopf and Bautin bifurcations in a generalized Lengyel–Epstein system. *J. Math. Chem.* **2020**, *58*, 497–515. [[CrossRef](#)]
7. Drexler, D.A.; Nagy, I.; Romanovski, V.; Tóth, J.; Kovács, L. Qualitative analysis of a closed-loop model of tumor growth control. In Proceedings of the 2018 IEEE 18th International Symposium on Computational Intelligence and Informatics (CINTI), Budapest, Hungary, 21–22 November 2018; pp. 000329–000334.
8. Dukarić, M.; Errami, H.; Jerala, R.; Lebar, T.; Romanovski, V.G.; Tóth, J.; Weber, A. On three genetic repressilator topologies. *React. Kinet. Mech. Catal.* **2019**, *126*, 3–30. [[CrossRef](#)]
9. Verhulst, P.H. Notice sur la loi que la population poursuit dans son accroissement. *Corresp. Math. Phys.* **1838**, *10*, 113–121.
10. Lotka, A.J. Contribution to the Theory of Periodic Reaction. *J. Phys. Chem.* **1910**, *14*, 271–274. [[CrossRef](#)]
11. Lotka, A.J. Analytical Note on Certain Rhythmic Relations in Organic Systems. *Proc. Natl. Acad. Sci. USA* **1920**, *6*, 410–415. [[CrossRef](#)]
12. Volterra, V. Variazioni e fluttuazioni del numero d’individui in specie animali conviventi. *Mem. Acad. Lincei Roma* **1926**, *2*, 31–113.
13. Frank-Kamenetskii, D.A. Periodicheskie processy v kinetike oksislitelnykh reaktcii (The periodical processes in the kinetics of oxidation reaction). *Dokl. SSSR* **1939**, *25*, 67–69.
14. Frank-Kamenetskii, D.A. *Diffusion and Heat Transfer in Chemical Kinetics*; USSR Academy of Science Press: Moscow-Leningrad, Russia, 1947. (In Russian)
15. Prigogine, I.; Lefever, R. Symmetry breaking instabilities in dissipative systems. II. *J. Chem. Phys.* **1968**, *48*, 1695–1700. [[CrossRef](#)]
16. Frank-Kamenetsky, D.A.; Salnikov, I.E. On the possibility of auto-oscillation in homogeneous chemical systems with quadratic autocatalysis. *J. Phys. Chem.* **1943**, *17*, 79–86. (In Russian)
17. Edelson, D.; Noyes, R.M.; Field, R.J. Mechanistic details of the Belousov–Zhabotinsky oscillations. II. The organic reaction subset. *Int. J. Chem. Kinet.* **1979**, *11*, 155–164. [[CrossRef](#)]
18. Zhabotinsky, A.M. Periodic oxidizing reactions in the liquid phase. *Dokl. Akad. Nauk* **1964**, *157*, 392–395. (In Russian)
19. Hsü, I.D. Existence of periodic solutions for the Belousov–Zaikin–Zhabotinskiĭ reaction by a theorem of Hopf. *J. Differ. Equ.* **1976**, *20*, 399–403. [[CrossRef](#)]
20. Póta, G. Two-component bimolecular systems cannot have limit cycles: A complete proof. *J. Chem. Phys.* **1983**, *78*, 1621–1622. [[CrossRef](#)]
21. Schuman, B.; Tóth, J. No limit cycle in two species second order kinetics. *Bull. Sci. Math.* **2003**, *127*, 222–230. [[CrossRef](#)]
22. Schnakenberg, J. Simple chemical reaction systems with limit cycle behaviour. *J. Theor. Biol.* **1979**, *81*, 389–400. [[CrossRef](#)]
23. Császár, A.; Jicsinszky, L.; Turányi, T. Generation of model reactions leading to limit cycle behavior. *React. Kinet. Catal. Lett.* **1982**, *18*, 65–71. [[CrossRef](#)]
24. Tóth, J.; Nagy, A.L.; Papp, D. *Reaction Kinetics: Exercises, Programs and Theorems*; Springer Nature: Berlin/Heidelberg, Germany; New York, NY, USA, 2018.
25. Feinberg, M. *Foundations of Chemical Reaction Network Theory*; Springer: Berlin/Heidelberg, Germany, 2019.
26. Craciun, G.; Szederkényi, G.; Johnston, M.D.; Tonello, E.; Tóth, J.; Yu, P. Realizations of kinetic differential equations. *Math. Biosci. Eng.* **2020**, *17*, 862–892. [[CrossRef](#)] [[PubMed](#)]

27. Escher, C. Models of Chemical Reaction Systems with Exactly Evaluable Limit Cycle Oscillations and their Bifurcation Behaviour. *Berichte Bunsenges. Phys. Chem.* **1980**, *84*, 387–391. [[CrossRef](#)]
28. Escher, C. Bifurcation and coexistence of several limit cycles in models of open two-variable quadratic mass-action systems. *Chem. Phys.* **1981**, *63*, 337–348. [[CrossRef](#)]
29. Nagy, I. Calculations for Two Nested Limit Cycles in Two-Species Reactions with Wolfram Mathematica. Available online: http://math.bme.hu/~nagy/Mathematica_notebooks/index.html (accessed on 24 August 2020).
30. Dumortier, F.; Llibre, J.; Artés, J.C. *Qualitative Theory of Planar Differential Systems*; Springer: Berlin/Heidelberg, Germany, 2006.
31. WRI. Mathematica 11.3. Available online: <http://www.wolfram.com> (accessed on 8 March 2018).



© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).