S(e)MR ISSN 1813-3304

СИБИРСКИЕ ЭЛЕКТРОННЫЕ МАТЕМАТИЧЕСКИЕ ИЗВЕСТИЯ

Siberian Electronic Mathematical Reports

http://semr.math.nsc.ru

Том 18, №1, стр. 464–473 (2021) УДК 514.745.82

DOI 10.33048/semi.2021.18.032 MSC 37N25

ON UNIQUENESS AND STABILITY OF A CYCLE IN ONE GENE NETWORK

V.P. GOLUBYATNIKOV, L.S.MINUSHKINA

Abstract. We describe necessary and suffcient conditions for uniqueness and stability of a cycle in an invariant domain of phase portrait of one Glass-Pasternack type block-linear dynamical system that simulates functioning of one natural gene network. Existence of such a cycle, geometry and combinatorics of phase portraits of similar systems were studied in our previous publications.

Keywords: circular gene network, fixed points, cycles, piecewise linear dynamical systems, phase portraits, invariant domains, Poincaré map.

1. Introduction

We study one dynamic system which describes biochemical processes of synthesis and degradation in circular gene networks where the velocity of synthesis of each substance depends on concentration of the previous one as follows:

$$\frac{dx_1}{dt} = L(y_4) - k_1x_1; \quad \frac{dy_2}{dt} = \Gamma_2(x_1) - k_2y_2; \quad \frac{dy_3}{dt} = \Gamma_3(y_2) - k_3y_3; \quad \frac{dy_4}{dt} = \Gamma_4(y_3) - k_4y_4, \tag{1}$$

see [1–4], where various cases of similar systems were considered. In our studies here, monotonically decreasing step function L, and monotonically increasing functions Γ_j are defined by the following relations

$$L(z) = \begin{cases} a_1k_1, & 0 \leqslant z \leqslant 1; \\ 0, & z > 1; \end{cases} \qquad \Gamma_j(z) = \begin{cases} 0, & 0 \leqslant z \leqslant 1; \\ b_jl_j, & z > 1; \end{cases} \qquad j = 2, 3, 4; \tag{2}$$

Golubyatnikov, V.P., Minushkina, L.S., On uniqueness and stability of a cycle in one gene network model.

Partially supported by SB RAS (0314-2019-0011).

Received January, 28, 2021, published April, 27, 2021.

they describe negative feedback and, respectively, positive feedbacks in the gene network. As it was shown in [5,6], cycles in the phase portrait of the system (1) and its analogues do exist if and only if

$$a_1 > 1, \qquad b_j > 1, \tag{3}$$

and we assume in the sequel, that these conditions are satisfied.

Biological interpretations of analogous dynamical systems of different dimensions are described in [7–10], see also references therein. It should be emphasized here that most of publications on piecewise-linear modelling of circular gene networks were devoted to one very particular case $k_j = 1$ for all $j = 1, 2, \dots d$ in the equations of d-dimensional dynamical systems of the type (1), see for example [1,11,12], where the questions of existence of cycles in phase portraits of some similar dynamical systems were studied. Under these conditions, trajectories of the dynamical systems are piecewise linear as well, and this simplifies analysis of the phase portraits of gene networks models. Same assumptions $k_j = 1$ were done in some publications on smooth gene networks models, see [13,14].

The negative coefficients $(-k_j)$ in these dynamical systems describe the rates of degradations of biological components in the gene networks, so it is quite artificial to assume that for different components, these coefficients coincide. Now, starting from our recent publications [5,6], we consider the general case of arbitrary positive k_j's.

Block-linear dynamical systems similar to (1) are studied intensively from different viewpoints in various domains related to the Qualitative Theory of Differential Equations and its applications since [15,16] and till now, see for example [17–19].

2. State Transition Diagram

As it was shown in [6,20], trajectories of all points of parallelepiped

$$\mathcal{Q}^4 = [0, a_1] \times [0, b_2] \times [0, b_3] \times [0, b_4]$$

do not leave it as t grows, i.e., $\mathcal{Q}^4$ is a positively invariant domain in the phase portrait of the dynamical system (1). Due to (3), the point $E = (1, 1, 1, 1)$ of discontinuity of all step functions in the equations of (1) is contained in the interior of $\mathcal{Q}^4$. Following [1,20], let us draw four hyperplanes $x_1 = 1$, $y_j = 1$ parallel to coordinate planes so that we obtain $2^4 = 16$ smaller parallelepipeds, intersecting in the point E, which we call blocks from now.

Definition 1. *The valence $V(B)$ of a block $B \subset \mathcal{Q}^4$ is a number of its 3-dimensional faces such that trajectories of their points come out of B to its adjacent blocks.*

This decomposition of the invariant domain $\mathcal{Q}^4$ consists of eight one-valent blocks, and eight three-valent blocks. We are focused here on study of behaviour of trajectories of the system (1) in the domain $W_1 \subset \mathcal{Q}^4$ composed by the one-valent blocks.

Let us enumerate all blocks by binary multi-indices $\{\varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_4\}$, where $\varepsilon_i = 1$ if $x_i > 1$, and $\varepsilon_i = 0$ otherwise. It is convenient to represent W_1 as a subdomain of 4-dimensional Boolean cube where the blocks correspond to vertices, and transitions from block to block play role of edges. We call such representation State Transition Diagram. The following proposition is well-known in the cases of dynamical systems of the type (1), see [11,12].

Proposition 1. *For any pair B_1, B_2 of adjacent blocks, trajectories of all points of their common 3-dimensional face $F = B_1 \cap B_2$ pass only in one direction: either from B_1 to B_2 or from B_2 to B_1.*

Construction of the State Transition Diagram (4) composed by the one-valent blocks follows the Algorithm described in [21]. Each transition here is defined uniquely since each blocks in W_1 is one-valent. Hence, trajectories of all points of W_1 pass from one block to another according to the following diagram

$$\begin{array}{ccccc}
\{1111\} & \xrightarrow{F_0=\{x_1=1\}} & \{0111\} & \xrightarrow{F_1=\{y_2=1\}} & \{0011\} \\
{\scriptstyle F_7=\{y_4=1\}}\uparrow & & & & \downarrow{\scriptstyle F_2=\{y_3=1\}} \\
\{1110\} & & & & \{0001\} \\
{\scriptstyle F_6=\{y_3=1\}}\uparrow & & & & \downarrow{\scriptstyle F_3=\{y_4=1\}} \\
\{1100\} & \xleftarrow{F_5=\{y_2=1\}} & \{1000\} & \xleftarrow{F_4=\{x_1=1\}} & \{0000\}
\end{array} \qquad (4)$$

It is worthy to note that similar Diagrams in different forms were studied for various dynamical systems of "biochemical kinetics", both, in smooth and piecewise linear cases, see [1, 3, 22], and especially [23], where one of the main objects of studies was called the "Integer-Valued Lyapunov Function" which is very similar to the valence of a vertex of an oriented graph.

3. Poincaré map

In order to simplify notations and calculations, let us introduce new coordinate system

$$\tilde{x}_1 = x_1 - 1; \quad \tilde{y}_j = y_j - 1,\ j = 2, 3, 4$$

such that the point $E = (1, 1, 1, 1)$ becomes the new origin O. For convenience we omit tilde from now keeping in mind new variables. The system (1) has a linear form in each block from the diagram (4). Let us fix an interior point $X^{(0)} \in F_0 = \{1111\} \cap \{0111\}$ with coordinates

$$x_1^{(0)} = 0; \quad y_2^{(0)} > 0; \quad y_3^{(0)} > 0; \quad y_4^{(0)} > 0.$$

Here $F_0 = [0, b_2 - 1] \times [0, b_3 - 1] \times [0, b_4 - 1]$. According to the Proposition 1, trajectory of any such point $X^{(0)} \in F_0$ enters the block $\{0111\}$, where the system (1) has a form

$$\begin{cases} \dot{x}_1 = -k_1(x_1 + 1); \\ \dot{y}_2 = -l_2(y_2 + 1); \\ \dot{y}_3 = l_3 b_3 - l_3(y_3 + 1); \\ \dot{y}_4 = l_4 b_4 - l_4(y_4 + 1). \end{cases}$$

Trajectories of the system in this block are described as follows:

$$x_1(t) = (x_1^{(0)} + 1)e^{-k_1 t} - 1; \quad y_2(t) = (y_2^{(0)} + 1)e^{-l_2 t} - 1;$$

$$y_3(t) = (b_3 - 1) + (y_3^{(0)} - (b_3 - 1))e^{-l_3 t}; \quad y_4(t) = (b_4 - 1) + (y_4^{(0)} - (b_4 - 1))e^{-l_4 t}.$$

Solution to the Cauchy problem for this system with the initial data $X^{(0)}$ gives us coordinates of the point $X^{(1)}$ where this trajectory intersects the next face $F_1 = \{0111\} \cap \{0011\}$, see (4):

$$x_1^{(1)} = (1 + y_2^{(0)})^{-\frac{k_1}{l_2}} - 1; \quad y_2^{(1)} = 0;$$

$$y_3^{(1)} = (b_3 - 1) + \frac{y_3^{(0)} - (b_3 - 1)}{(1 + y_2^{(0)})^{\frac{l_3}{l_2}}}; \quad y_4^{(1)} = (b_4 - 1) + \frac{y_4^{(0)} - (b_4 - 1)}{(1 + y_2^{(0)})^{\frac{l_4}{l_2}}}.$$

These formulae describe the first shift of the initial point along the trajectory $f_0 : F_0 \to F_1$. Remaining transitions in the diagram (4) can be represented in a similar way. Composition of eight such shifts $\Psi = f_7 \circ f_6 \circ f_5 \circ f_4 \circ f_3 \circ f_2 \circ f_1 \circ f_0 : F_0 \to F_0$ is called Poincaré map (of the cycle which we are going to find). It maps any point of the face F_0 to an interior point of F_0.

Quite similar transition formulae for some other block-linear dynamical systems of the type (1) were derived in [5, 24, 25].

4. Positive Jacobian matrix

Just for simplicity of notations, we reduce the proof of existence and uniqueness of a cycle in the domain W_1 to that of existence and uniqueness of a non-zero fixed point of the "normalized" Poincaré map

$$\Phi = (\varphi_1, \varphi_2, \varphi_3) : K^3(u_1, u_2, u_3) \to K^3(u_1, u_2, u_3)$$

of the unit 3D cube $K^3 = [0, 1]^3$ into itself. Here $\Phi = \mathcal{L}^{-1} \circ \Psi \circ \mathcal{L}$, and $\mathcal{L} : K^3 \to F_0 \subset W_1$ is linear diffeomorphism

$$\mathcal{L}(u_1, u_2, u_3) = (0, (b_1 - 1)u_1, (b_2 - 1)u_2, (b_3 - 1)u_3).$$

Note that by definition, $\varphi_j(0, 0, 0) = 0$, and for all remaining points $(u_1, u_2, u_3) \in K^3$, the following inequalities hold: $0 < \varphi_j(u_1, u_2, u_3) < 1$, $j = 1, 2, 3$.

As in [24], simple calculations imply the following

Proposition 2. *a) The first derivatives of all functions φ_j are positive, and all their second derivatives are negative;*

b) The map Φ is injective, and its Jacobian $\det J(\Phi)$ *is strictly positive at any point of K^3;*

c) $\left.\dfrac{d\varphi_1(u_1, 0, 0)}{du_1}\right|_{u_1=0} > 1.$

Lemma 1. *There exists an unique point $u_1^0 \in (0, 1)$ such that $\varphi_1(u_1^0, 0, 0) = u_1^0$.*

Actually, this fact is shown in [24], all arguments here follow the scheme of proofs of the Lemmas 2, 3, 4 below: The function $\Delta_0(u_1) := \varphi_1(u_1, 0, 0) - u_1$ vanishes at $u_1 = 0$, $\Delta_0(1) < 0$, and $\left.\dfrac{d\Delta_0}{du_1}\right|_{u_1=0} > 0$, see the Figure 1.

1. Let us fix any non-zero point $(u_2, u_3) \in [0, 1] \times [0, 1]$, and consider analogous function $\Delta_1(u_1, u_2, u_3) = \varphi_1(u_1, u_2, u_3) - u_1$. Clearly, for all non-zero (u_2, u_3) the following inequalities hold: $\Delta_1(0, u_2, u_3) > 0$ and $\Delta_1(1, u_2, u_3) < 0$. Hence, at some point $u_1 = \psi_1(u_2, u_3)$ the function $\Delta_1(\psi_1(u_2, u_3), u_2, u_3)$ vanishes, see the Figure 2. The simple case $u_2 = u_3 = 0$ is explained in the Lemma 1.

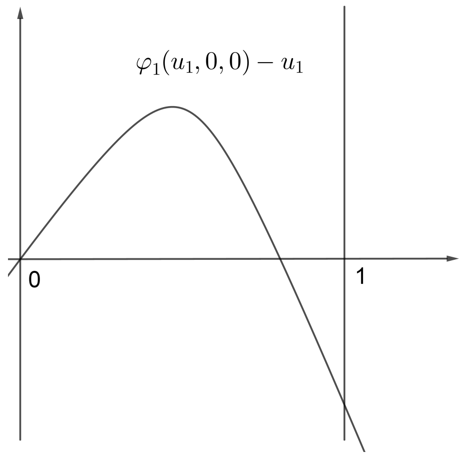

FIGURE 1. Graph of the function $\varphi_1(u_1, 0, 0) - u_1$

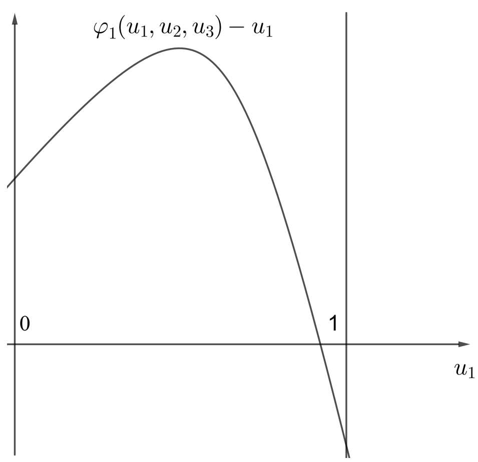

FIGURE 2. Graph of $\Delta_1(u_1, u_2, u_3)$ for fixed (u_2, u_3)

Lemma 2. *There exists a unique point* $u_1 = \psi_1(u_2, u_3)$ *in the interval* $(0, 1)$ *such that*

$$\Delta_1(\psi_1(u_2, u_3), u_2, u_3) = 0, \qquad \textit{or} \qquad \varphi_1(\psi_1(u_2, u_3), u_2, u_3) = \psi_1(u_2, u_3). \quad (5)$$

Existence of such a point is shown above. It follows from the Proposition 2 that the second derivative of $\Delta_1(u_1, u_2, u_3)$ with respect to u_1 is strictly negative (recall that u_2, u_3 are fixed). Thus its first derivative at the point $u_1 = \psi_1(u_2, u_3)$ should be strictly negative as well, and one has at the point $P_1 = (\psi_1(u_2, u_3), u_2, u_3)$

$$\frac{\partial \Delta_1}{\partial u_1} < 0, \qquad \text{or} \qquad \frac{\partial \varphi_1}{\partial u_1} < 1. \quad (6)$$

Hence, it follows from (6) that the function $u_1 = \psi_1(u_2, u_3)$ is determined uniquely and is smooth.

Let us calculate derivatives of (5) with respect to u_2 and to u_3 at the point P_1:

$$\frac{\partial\varphi_1}{\partial u_1}\frac{\partial\psi_1}{\partial u_2}+\frac{\partial\varphi_1}{\partial u_2}=\frac{\partial\psi_1}{\partial u_2};\qquad \frac{\partial\varphi_1}{\partial u_1}\frac{\partial\psi_1}{\partial u_3}+\frac{\partial\varphi_1}{\partial u_3}=\frac{\partial\psi_1}{\partial u_3};\quad \text{or}$$

$$\frac{\partial\psi_1}{\partial u_2}\left(1-\frac{\partial\varphi_1}{\partial u_1}\right)=\frac{\partial\varphi_1}{\partial u_2},\qquad \frac{\partial\psi_1}{\partial u_3}\left(1-\frac{\partial\varphi_1}{\partial u_1}\right)=\frac{\partial\varphi_1}{\partial u_3}. \tag{7}$$

Positivity of the matrix $J(\Phi)$ and inequalities (6) imply that at the point P_1 one has

$$\frac{\partial\psi_1}{\partial u_2}>0,\qquad \frac{\partial\psi_1}{\partial u_3}>0. \tag{8}$$

In a similar way, one can verify that the second derivatives of $\psi_1(u_2,u_3)$ at the point P_1 are negative as well.

2. Given $(u_2,u_3)\in[0,1]\times[0,1]$, consider the function

$$\Delta_2(u_2,u_3)=\varphi_2(\psi_1(u_2,u_3),u_2,u_3)-u_2.$$

As in the Lemma 2, $\Delta_2(0,u_3)>0$ and $\Delta_2(1,u_3)<0$ for all $u_3\in[0,1]$, so at some point $u_2=\psi_2(u_3)$ one has $\Delta_2(u_2,u_3)=0$.

For a fixed u_3, graph of the function $\Delta_2(u_2,u_3)$ is convex, cf. the Figure 2. The proof of this fact follows from direct calculations:

$$\frac{\partial}{\partial u_2}\left(\varphi_2(\psi_1(u_2,u_3),u_2,u_3)-u_2\right)=\frac{\partial\varphi_2}{\partial u_1}\frac{\partial\psi_1}{\partial u_2}+\frac{\partial\varphi_2}{\partial u_2}-1.$$

$$\frac{\partial}{\partial u_3}\left(\varphi_2(\psi_1(u_2,u_3),u_2,u_3)-u_2\right)=\frac{\partial\varphi_2}{\partial u_1}\frac{\partial\psi_1}{\partial u_3}+\frac{\partial\varphi_2}{\partial u_3}>0.$$

It was indicated above that the second derivatives of φ_j and ψ_1 are negative, thus inequalities (8) imply that the second derivatives of the compositions are negative as well:

$$\frac{\partial^2}{\partial u_2^2}\left(\varphi_2(\psi_1(u_2,u_3),u_2,u_3)-u_2\right)=\frac{\partial^2\varphi_2}{\partial u_1^2}\left(\frac{\partial\psi_1}{\partial u_2}\right)^2+\frac{\partial\varphi_2}{\partial u_1}\frac{\partial^2\psi_1}{\partial u_2^2}+\frac{\partial^2\varphi_2}{\partial u_2^2}<0. \tag{9}$$

In a similar way, one can verify inequalities $\dfrac{\partial^2}{\partial u_3^2}\left(\varphi_2(\psi_1(u_2,u_3),u_2,u_3)-u_2\right)<0$, and $\dfrac{\partial^2}{\partial u_2\partial u_3}\left(\varphi_2(\psi_1(u_2,u_3),u_2,u_3)-u_2\right)<0$.

Lemma 3. *For any $u_3\in(0,1]$, the interval $(0,1)$ contains a unique point $u_2=\psi_2(u_3)$ such that*

$$\Delta_2(\psi_1(\psi_2(u_3),u_3),\psi_2(u_3),u_3)=0,$$

$$\textit{or}\qquad \varphi_2(\psi_1(\psi_2(u_3),u_3),\psi_2(u_3),u_3)=\psi_2(u_3). \tag{10}$$

Existence of such a point is shown above. Let $\psi_2':=\dfrac{\partial\psi_2}{\partial u_3}$. It follows from the inequalities (9) that at the point $u_2=\psi_2(u_3)$ the first derivative of $\Delta_2(u_2,u_3)$ with respect to u_2 is strictly negative:

$$\frac{\partial}{\partial u_2}\left[\varphi_2(\psi_1(u_2,u_3),u_2,u_3)-u_2\right]=\frac{\partial\varphi_2}{\partial u_1}\frac{\partial\psi_1}{\partial u_2}+\frac{\partial\varphi_2}{\partial u_2}-1<0. \tag{11}$$

Hence, the equation (10) defines the smooth function $u_2=\psi_2(u_3)$ uniquely.

At the same time, calculation of $\dfrac{d\Delta_2(\psi_2(u_3),u_3)}{du_3}$ gives us

$$\frac{\partial\varphi_2}{\partial u_1}\frac{\partial\psi_1}{\partial u_2}\psi_2' + \frac{\partial\varphi_2}{\partial u_1}\frac{\partial\psi_1}{\partial u_3} + \frac{\partial\varphi_2}{\partial u_2}\psi_2' + \frac{\partial\varphi_2}{\partial u_3} = \psi_2',$$

$$\text{or} \quad \psi_2'\left(1 - \frac{\partial\varphi_2}{\partial u_1}\frac{\partial\psi_1}{\partial u_2} - \frac{\partial\varphi_2}{\partial u_2}\right) = \frac{\partial\varphi_2}{\partial u_1}\frac{\partial\psi_1}{\partial u_3} + \frac{\partial\varphi_2}{\partial u_3}.$$

Right-hand side of the last equality is positive, so (11) implies that $\psi_2' > 0$.

3. Consider now similar function $\Delta_3(u_3) = \varphi_3(\psi_1(\psi_2(u_3),u_3),\psi_2(u_3),u_3) - u_3$, here $u_3 \in [0,1]$.

Lemma 4. *Second derivative of* $\Delta_3(u_3)$ *is negative.*

We have

$$\frac{\partial\Delta_3}{\partial u_3} = \frac{\partial\varphi_3}{\partial u_1}\frac{\partial\psi_1}{\partial u_2}\psi_2' + \frac{\partial\varphi_3}{\partial u_2}\psi_2' + \frac{\partial\varphi_3}{\partial u_3} - 1. \tag{12}$$

$$\frac{\partial^2\Delta_3}{\partial u_3^2} = \frac{\partial^2\varphi_3}{\partial u_1^2}\left(\frac{\partial\psi_1}{\partial u_2}\psi_2'\right)^2 + \frac{\partial\varphi_3}{\partial u_1}\left(\frac{\partial^2\psi_1}{\partial u_2^2}\right)(\psi_2')^2 + \frac{\partial\varphi_3}{\partial u_1}\frac{\partial\psi_1}{\partial u_2}\psi_2'' + \ldots + \frac{\partial^2\varphi_3}{\partial u_3^2} < 0.$$

Each summand here contains exactly one negative factor, all the remaining factors are positive. As in the previous Lemmas, and on the Figure 1, we have $\Delta_3(1) < 0$ and $\Delta_3(0) > 0$, hence there exists a unique point $u_3^0 \in (0,1)$ such that $\Delta_3(u_3^0) = \varphi_3(\psi_1(\psi_2(u_3^0),u_3^0),\psi_2(u_3^0),u_3^0) - u_3^0 = 0$, or

$$\varphi_3(\psi_1(\psi_2(u_3^0),u_3^0),\psi_2(u_3^0),u_3^0) = u_3^0. \tag{13}$$

Moreover, at this point $u_3^0 \in (0,1)$ one has $\dfrac{d\Delta_3}{du_3} < 0$, and $\psi_2' > 0$. Hence,

$$\psi_2'\left(\frac{\partial\varphi_3}{\partial u_1}\frac{\partial\psi_1}{\partial u_2} + \frac{\partial\varphi_3}{\partial u_2}\right) < 1 - \frac{\partial\varphi_3}{\partial u_1}\frac{\partial\psi_1}{\partial u_3} - \frac{\partial\varphi_3}{\partial u_3}, \quad \text{thus} \quad \frac{\partial\varphi_3}{\partial u_3} < 1. \tag{14}$$

So, we have proved that Φ maps the point $U_0 = (\psi_1(\psi_2(u_3^0),u_3^0),\psi_2(u_3^0),u_3^0)$ to itself:

$\varphi_1(\psi_1(\psi_2(u_3^0),u_3^0),\psi_2(u_3^0),u_3^0) = \psi_1(\psi_2(u_3^0),u_3^0)$, see (5),
$\varphi_2(\psi_1(\psi_2(u_3^0),u_3^0),\psi_2(u_3^0),u_3^0) = \psi_2(u_3^0)$, see (10),
$\varphi_3(\psi_1(\psi_2(u_3^0),u_3^0),\psi_2(u_3^0),u_3^0) = u_3^0$, see (13).

This implies uniqueness of a fixed point of the Poincaré map $\Psi : F_0 \to F_0$ in the interior of the face F_0. Hence, we have shown uniqueness of a cycle in the union W_1 of the one-valent blocks in the phase portrait of the dynamical system (1):

Theorem 1. *The one-valent domain* W_1 *in the phase portrait of the system* (1) *contains exactly one cycle* $\mathcal{C}$ *that passes from block to block according to the arrows of the diagram* (4)*; this cycle contains the unique fixed point* $P_0 = \mathcal{L}^{-1}U_0$ *of the Poincaré map* $\Psi : F_0 \to F_0$.

On should note that outside of such one-valent domains W_1 the phase portraits of some higher-dimensional analogues of the dynamical system (1) can contain other cycles, or invariant surfaces, see [6,11,20].

5. Stability of the cycle $\mathcal{C}$

Following [24], we study now the Jacobian matrix J_Φ of the Poincaré map Φ at its fixed point U_0. Let tr_Φ be its trace. All elements $a_{ij} = \dfrac{\partial \varphi_i}{\partial u_j}$ of J_Φ are strictly positive, and $\det J_\Phi > 0$, see the Proposition 1. As in was shown in the previous section, $a_{jj} < 1$ for $j = 1, 2, 3$. Hence, $\dfrac{\mathrm{tr}_\Phi}{3} < 1$.

Note that the origin $O \in K^3$ is a trivial fixed point of Φ, diagonal elements of the Jacobian matrix J_0 at this point satisfy the opposite inequalities $\left.\dfrac{\partial \varphi_j}{\partial u_j}\right|_O > 1$, see the Figure 1 and [24].

Theorem 2. *The cycle $\mathcal{C}$ is stable.*

Proof. First, we shall show that moduli of all eigenvalues of the matrix J_Φ are less than some positive $\lambda_1 < 1$. The charactristic polynomial of J_Φ has the form

$$P(\lambda) = -\lambda^3 + \lambda^2 \cdot \mathrm{tr}_\Phi - \lambda \cdot I_2 + \det J_\Phi,$$

where I_2 is "the second invariant" of the matrix J_Φ. Thus, $P(0) > 0$, and $\dfrac{d^2 P}{d\lambda^2} < 0$ for all $\lambda > \dfrac{\mathrm{tr}_\Phi}{3}$.

Let $\psi'_{1i} = \dfrac{\partial \psi_1}{\partial u_i}$, $i = 2, 3$, and $\psi'_2 = \dfrac{\partial \psi_2}{\partial u_3}$. It follows from the Lemma 2 that

$$\psi'_{12} \cdot (1 - a_{11}) = a_{12}, \qquad \psi'_{13} \cdot (1 - a_{11}) = a_{13}, \qquad 0 < a_{11} < 1. \tag{15}$$

Similarly, the Lemma 3 implies that

$$a_{21}\psi'_{12}\psi'_2 + a_{21}\psi'_{13} + a_{22}\psi'_2 + a_{23} = \psi'_2, \qquad a_{21}\psi'_{1,2} + a_{22} < 1, \tag{16}$$

and the following inequality actually coincides with (13)

$$a_{31}\psi'_{13} + \psi'_2\,(a_{31}\psi'_{12} + a_{32}) < 1 - a_{33}.$$

Hence, the relations (14), (15), (16) imply that

$$\frac{a_{21}a_{13}}{1 - a_{11}} + a_{23} = \psi'_2 \cdot \left(1 - a_{22} - \frac{a_{21}a_{12}}{1 - a_{11}}\right);$$

$$a_{21}a_{12} < (1 - a_{22})(1 - a_{11}); \tag{17}$$

and

$$\left(\frac{a_{31}a_{12}}{1 - a_{11}} + a_{32}\right)\psi'_2 < 1 - a_{33} - \frac{a_{31}a_{13}}{1 - a_{11}}.$$

Thus,

$$\psi'_2 = \frac{a_{23}(1 - a_{11}) + a_{21}a_{13}}{(1 - a_{22})(1 - a_{11}) - a_{21}a_{12}} < \frac{(1 - a_{11})(1 - a_{33}) - a_{13}a_{31}}{a_{32}(1 - a_{11}) + a_{31}a_{12}}.$$

Direct calculations show that this is equivalent to the inequality $P(1) < 0$.

Since the map Φ has a unique fixed point U_0 in the interior of K^3, one shall find exactly this point if in the Lemma 3 the variable u_3 would be expressed as a function of u_2, or in Lemma 2 u_2 would be represented as $u_2 = u_2(u_1, u_3)$ etc. So, the proofs of the inequalities (18) are similar to that of (17).

$$a_{31}a_{13} < (1 - a_{33})(1 - a_{11}); \qquad a_{23}a_{32} < (1 - a_{22})(1 - a_{33}). \tag{18}$$

The sum of the inequalities (17) and (18) has the form

$$3 - 2\mathrm{tr}_\Phi + I_2 > 0 \quad \text{or} \quad \left.\frac{dP}{d\lambda}\right|_{\lambda=1} < 0. \tag{19}$$

Since $P(0) > 0$ and $P(1) < 0$, the inequality (19), and convexity of the graph of $P(\lambda)$ near $\lambda = 1$ imply that the interval $(0, 1)$ contains at least one eigenvalue of the matrix J_Φ, and none of these eigenvalues exceeds $\lambda = 1$.

Proposition 3. *Characteristic polynom $P(\lambda)$ does not have multiple roots.*

Proof of this proposition follows from some simple manipulations with quadratic equation $P'(\lambda) = -3\lambda^2 + 2tr_\Phi\lambda - I_2 = 0$.

If the interval $(0, 1)$ contains only one positive eigenvalue $\lambda_1 < 1$ of J_Φ, then the Frobenius-Perron theorem, see [26], implies that moduli of the remaining two eigenvalues of this matrix do not exceed λ_1.

If this interval contains all three eigenvalues of J_Φ, then $I_2 > 0$. Due to the Proposition 3, the matrix J_Φ can be diagonalized in both cases, and the moduli of all diagonal elements here do not exceed some positive $\lambda_1 < 1$.

As it was shown in [5, 6, 25], for dynamical systems of the type (1), trajectory of each point of the face $F_0 \subset W_1$ is attracted to trajectory of one of fixed points of the Poincaré map Ψ. According to the Theorem 1, this fixed point P_0 is unique, so trajectories of all points of the invariant domain W_1 are attracted by the cycle $\mathcal{C}$. Moreover, for any point of the domain W_1, its trajectory tends to the cycle $\mathcal{C}$ exponentially after some finite iteration of Ψ, cf. [24].

Hence, the cycle $\mathcal{C}$ is stable, and Theorem 2 is proved.

The authors are indebted to I.I.Matveeva, V.V.Ivanov, S.A.Kantor, and unknown referee for helpful discussions and critical comments.

The work was partially supported by by the Program of fundamental scientific researches of the SB RAS N I.1.5., project N 0314-2019-0011.

References

[1] L. Glass, J.S. Pasternack, *Stable oscillations in mathematcal models of biological control systems*, J. Math. Bio., **6** (1978), 207–223. Zbl 0391.92001

[2] N.B. Ayupova, V.P. Golubyatnikov, *On two classes of nonlinear dynamical systems: the four-dimensional case*, Sib. Math. J., **56**:2 (2015), 231–236. Zbl 1357.37043

[3] S. Hastings, J. Tyson, D. Webster, *Existence of periodic solutions for negative feedback cellular control systems*, J. Differ. Equations, **25** (1977), 39–64. Zbl 0361.34038

[4] T. Gedeon, *Cyclic feedback systems*, Mem. AMS., **134**, MEMO/0637, (1998). Zbl 0991.34051

[5] V.P. Golubyatnikov, V.V. Ivanov, L.S. Minushkina, *On existence of a cycle in one asymmetric gene network model*, Sib. Zh. Chist. Prikl. Mat., **18**:3 (2018), 27–35. Zbl 1438.37055

[6] V.P. Golubyatnikov, L.S. Minushkina, *Monotonicity of the Poincaré mapping in some models of circular gene networks*, J. Appl. Ind. Math., **13**:3 (2019), 472–479. Zbl 1438.37057

[7] T. Gedeon, M. Pernarowski, A. Wilander, *Cyclic feedback systems with quorum sensing coupling*, Bull. Math. Biol., **78**:6 (2016), 1291–1317. Zbl 1348.92021

[8] S. Yuan, D. Wu, G. Lan, H. Wang, *Noise-induced transitions in a nonsmooth producer-grazer model with stoichiometric constraints*, Bull. Math. Biol., **82**:5 (2020), Paper No. 55. Zbl 1443.92195

[9] T.A. Bukharina, A.A. Akinshin, V.P. Golubyatnikov, D.P. Furman, *Numerical models of the central regulatory circuit of the morphogenesis system of Drosophila*, J. Appl. Ind. Math., **14**:2 (2020), 249–255.

[10] V.A. Likhoshvai, V.P. Golubyatnikov, T.M. Khlebodarova, *Limit cycles in models of circular gene networks regulated by negative feedbacks loops*, BMC Bioinformatics, **21** (2020), Article number: 255.

[11] Yu. A.Gaidov, V.P. Golubyatnikov, *On cycles and other geometric phenomena in phase portraits of some nonlinear dynamical systems*, in Rovenski, Vladimir (ed.) et al., *Geometry and its applications. Selected papers based on the presentations at the 2nd international workshop on geometry and symbolic computation, Haifa, Israel, May 15–18, 2013*, Springer Proceedings in Mathematics & Statistics, **72** (2014), 225–233. Zbl 1348.34063

[12] V.P. Golubyatnikov, A.E. Kalenykh, *Structure of phase portraits of nonlinear dynamical systems*, J. Math. Sci., New York, **215**:4 (2016), 475–483. Zbl 1349.34154

[13] A.Yu. Kolesov, N.Kh. Rozov, V.A. Sadovnichii, *Periodic solutions of traveling-wave type in circular gene networks*, Izv. Math. **80**:3 (2016), 523–548. Zbl 06629497

[14] A.A. Akinshin, V.P. Golubyatnikov, *Geometric characteristics of cycles in some symmetric dynamical systems*, Vestn. Novosib. Gos. Univ., Ser. Mat. Mekh. Inform., **12**:2 (2012), 3–12. Zbl 1289.37048

[15] A.A. Andronov, A.A. Vitt, S.E. Khaikin, *Theory of oscillations*, Pergamon Press, Oxford, 1966. Zbl 0188.56304

[16] L. Glass, *Combinatorial and topological methods in nonlinear chemical kinetics*, J. Chem. Phys., **63** (1975), 1325–1335.

[17] R. Wilds, L. Glass, *Contrasting methods for symbolic analysis of biological regulatory networks*, Phys Rev E Stat Nonlin Soft Matter Phys., **80** (2009), 062902.

[18] A. Berbache, *Two limit cycles for a class of discontinuous piecewise linear differential systems with two pieces*, Sib. Électron. Math. Izv., **17** (2020), 1488–1515. Zbl 1452.34001

[19] J. Llibre, D.D. Novaes, M.A. Teixeira, *Maximum number of limit cycles for certain piecewise linear dynamical systems*, Nonlinear Dyn., **82**:3 (2015), 1159–1175. Zbl 1348.34065

[20] N.B. Ayupova, V.P. Golubyatnikov, *Structure of the phase portrait of a piecewise-linear dynamical system*, Journal of Applied and Industrial Mathematics. **13**:4 (2019), 606–611.

[21] N.E. Kirillova, L.S. Minushkina, *On discretization of phase portraits of circular dynamical systems*, Izvestiya of Altai State University. Mathematics and Mechanics, **2019**:4(108) (2019), 82–85.

[22] Yu.A. Gaidov, V.P. Golubyatnikov, A.G. Kleshchev A.G., E.P. Volokitin, *Modeling of asymmetric gene networks functioning with different types of regulation*, Biophysics, **51** (2006), Article number 61.

[23] J. Mallet-Paret, H. Smith, *The Poincaré-Bendixson theorem for monotone cyclic feedback systems*, J. Dyn. Differ. Equations, **2**:4 (1990), 367–421. Zbl 0712.34060

[24] V.P. Golubyatnikov, V.V. Ivanov, *Uniqueness and stability of a cycle in 3-dimensional block-linear circular gene network models*, Sib. Zh. Chist. Prikl. Mat., **18**:4 (2018), 19–28. Zbl 1438.37054

[25] V.P. Golubyatnikov, V.V. Ivanov, *Cycles in the odd-dimensional models of circular gene networks*, J. Appl. Ind. Math., **12**:4 (2018), 648–657. Zbl 1438.37053

[26] F.R. Gantmacher, *The theory of matrices*, Chelsea Publishing Co., New York, 1959. MR0107649

Vladimir Petrovich Golubyatnikov
Sobolev Institute of Mathematics,
4, Koptyuga ave.,
Novosibirsk, 630090, Russia
Email address: `vladimir.golubyatnikov1@fulbrightmail.org`

Liliya Sergeevna Minushkina
Novosibirsk State University,
2, Pirogova str.,
Novosibirsk, 630090, Russia
Email address: `l.minushkina@g.nsu.ru`