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Stratifications and foliations in phase portraits of gene network models

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Abstract. Periodic processes of gene network functioning are described with good precision by periodic trajectories (limit cycles) of multidimensional systems of kinetic-type differential equations. In the literature, such systems are often called dynamical, they are composed according to schemes of positive and negative feedback between components of these networks. The variables in these equations describe concentrations of these components as functions of time. In the preparation of numerical experiments with such mathematical models, it is useful to start with studies of qualitative behavior of ensembles of trajectories of the corresponding dynamical systems, in particular, to estimate the highest likelihood domain of the initial data, to solve inverse problems of parameter identification, to list the equilibrium points and their characteristics, to localize cycles in the phase portraits, to construct stratification of the phase portraits to subdomains with different qualities of trajectory behavior, etc. Such an *à priori* geometric analysis of the dynamical systems is quite analogous to the basic section "Investigation of functions and plot of their graphs" of Calculus, where the methods of qualitative studies of shapes of curves determined by equations are exposed. In the present paper, we construct ensembles of trajectories in phase portraits of some dynamical systems. These ensembles are 2-dimensional surfaces invariant with respect to shifts along the trajectories. This is analogous to classical construction in analytic mechanics, i.e. the level surfaces of motion integrals (energy, kinetic moment, etc.). Such surfaces compose foliations in phase portraits of dynamical systems of Hamiltonian mechanics. In contrast with this classical mechanical case, the foliations considered in this paper have singularities: all their leaves have a non-empty intersection, they contain limit cycles on their boundaries. Description of the phase portraits of these systems at the level of their stratifications, and that of ensembles of trajectories allows one to construct more realistic gene network models on the basis of methods of statistical physics and the theory of stochastic differential equations.

Key words: oscillations; positive and negative feedbacks; gene network models; phase portraits; invariant domains and surfaces; invariant foliations; Poincaré map; Grobman–Hartman theorem; Frobenius–Perron theorem.

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Стратификации и слоения в фазовых портретах моделей генных сетей

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Аннотация. Периодические процессы функционирования широкого класса генных сетей с хорошей точностью описываются предельными циклами многомерных систем дифференциальных уравнений кинетического типа. Такие системы, часто называемые в литературе динамическими, составляются по схемам положительных и отрицательных связей между компонентами моделируемых сетей. Искомые функции в уравнениях описывают зависимость от времени концентраций этих компонент. При планировании вычислительных экспериментов с подобными математическими моделями полезно предварительно описать качественное поведение ансамблей траекторий соответствующих динамических систем, в частности оценить области максимального правдоподобия начальных данных, исследовать обратные задачи идентификации параметров, особые точки этих систем, локализовать в фазовых портретах положение циклов, в том числе предельных, стратифицировать фазовые портреты на подобласти с качественно различным поведением траекторий и т. п. Такой априорный геометрический анализ рассматриваемых моделей генных сетей полностью аналогичен хрестоматийному разделу начальных курсов математики «Исследование функций и построение графиков», в котором описываются методы наглядного представления поведения кривых, определяемых уравнениями. В настоящей статье в фазовых портретах динамических систем, моделирующих функционирование кольцевых генных сетей, конструируются двумерные поверхности, инвариантные относительно сдвигов вдоль траекторий, – ансамбли траекторий. Просматривается естественная аналогия с классической конструкцией аналитической механики – с поверхностями уровня интегралов движения (энергия, импульс и др.). Такие поверхности образуют слоения в фазовых портретах динамических систем гамильтоновой механики. В отличие от задач механики, для рассматриваемых нами моделей генных сетей слоения, образуемые инвариантными поверхностями, имеют особенности, все их слои содержат на своих границах предельные циклы. Описание фазовых портретов динамических систем в терминах их стратификаций и ансамблей их траекторий позволит строить более реалистичные модели генных сетей с использованием аппарата статистической физики и теории стохастических дифференциальных уравнений.

Ключевые слова: осцилляции; положительные и отрицательные связи; модели генных сетей; фазовые портреты; инвариантные области и поверхности; инвариантные слоения; отображение Пуанкаре; теорема Гробмана–Хартмана; теорема Фробениуса–Перрона.

Introduction

At present time, investigation of questions of existence of periodic trajectories (cycles) in phase portraits of systems of non-linear differential equations simulating functioning of various natural processes is carried out in most fields of applied mathematics. Detection of such cycles, their localization in the phase portraits, description of their characteristics, such as stability, (non)uniqueness, etc. have a long history (Poincaré, 1892). These problems have generated a whole range of research directions in pure mathematics: qualitative theory of differential equations, theory of dynamics systems, etc., which in turn have a great impact on corresponding applied disciplines. At their junction, the famous 16-th Hilbert's problem, and the "center-focus" problem, related to seemingly just a pictorial case of two differential equations with two unknown functions of one variable (time) have appeared.

Here, in the present paper, we study systems of kinetic equations of higher dimensions, considered as functioning of circular gene networks models:

$$\frac{dx_j}{dt} = f_j(x_{j-1}) - k_j x_j. \qquad (1)$$

It is assumed here and below that $j = 1, 2, \ldots, n$; $n \geq 3$, and that $j-1 = n$, if $j = 1$. In all these equations, non-negative functions $x_j(t)$ denote concentrations of species in the gene networks, and positive coefficients k_j characterize the rates of their degradations (Likhoshvai et al., 2020).

Consider the system (1) in the vector form $\frac{dX}{dt} = F(X)$, where the vector-function $X(t)$ is defined by its coordinate functions $x_j(t)$. The divergence of this vector-field $F(X)$ is constant and negative:

$$\operatorname{div} F(X) \equiv -k_1 - k_2 - \ldots - k_n < 0.$$

It is well-known (Arnold, 1989) that in this case, n-dimensional volume of any finite domain in the phase portrait decreases exponentially during the shifts of its points along trajectories of the system (1) as t grows. This does not mean that each such domain collapses to a point. For the dynamical systems considered here, these limit sets are two-dimensional invariant surfaces in their n-dimensional phase portraits.

We call the dynamical system (1) block-linear if for all j each function f_j which describes the rate of synthesis of the j-th component of the gene network is a step-function (threshold function)

$$f_j(y) \equiv L_j(y) = k_j a_j, \text{ if } 0 \leq y \leq 1;\ L_j(y) \equiv 0, \text{ if } y > 1;$$
$$\text{or } f_j(y) \equiv \Gamma_j(y) \equiv 0, \text{ if } 0 \leq y \leq 1;\ \Gamma_j(y) \equiv k_j a_j, \text{ if } y > 1.$$

Here, a_j are some positive constants. Decreasing functions L_j describe negative feedbacks in the gene network and increasing functions Γ_j correspond to positive feedbacks.

For one particular case $k_j = 1$ for all j, investigation of cycles of similar block-linear systems was realized in (Glass, Pasternack, 1978; Akinshin et al., 2013; Ayupova, Golubyatnikov, 2014; Golubyatnikov, Gradov, 2021). Under the same assumptions, questions of existence of cycles in smooth analogues of these systems were studied in (Elowitz, Leibler, 2000; Glyzin et al., 2016; Kolesov et al., 2016) in the cases when these systems are symmetric with respect to cyclic permutations of pairs of the variables x_j.

In recent publications (Golubyatnikov, Ivanov, 2018; Golubyatnikov, Minushkina, 2019, 2020; Likhoshvai et al., 2020; Ivanov, 2022), existence, uniqueness, and stability of the cycles of block-linear dynamical systems of some different dimensions with arbitrary positive coefficients k_j were proved with the help of stratification of phase portraits to subdomains according to behavior of trajectories. It was shown there that these phase portraits contain cycles if and only if $a_j > 1$ for all j and that the parallelepiped $Q^n = [0, a_1] \times [0, a_2] \times \ldots \times [0, a_n]$ in the positive octant of the space $\mathbb{R}^n$ is a positively invariant domain of the dynamical system (1). This means that trajectories of all points of the domain Q^n do not leave it and that all cycles of the system (1) are contained in the interior of Q^n. We consider below the dynamical systems of the type (1) in the case $a_j > 1$ for all j only. Physical interpretation of this condition means that the maximal rate of synthesis of any component of the gene network exceeds that of its degradation.

We decompose the domain Q^n by the planes $x_j = 1$ to 2^n smaller parallelepipeds, which we call blocks and enumerate by binary multi-indices: $\{\varepsilon_1 \varepsilon_2 \ldots \varepsilon_n\} = I_1(\varepsilon_1) \times I_2(\varepsilon_2) \times \ldots \times I_n(\varepsilon_n)$.

Here, each index ε_j equals 0 or 1, and $I_j(0) = [0, 1]$, $I_j(1) = (1, a_j]$. Let E be the common point of all these blocks (all its coordinates equal one). In each of these blocks, the equations of the system (1) take the simplest linear form

$$\frac{dx_j}{dt} = k_j(x_j - a_j(1 - \varepsilon_{j-1})),$$

and solution to the Cauchy problem for this system has a simple representation

$$x_j(t) = a_j(1 - \varepsilon_{j-1}) + (x_j(0) - a_j(1 - \varepsilon_{j-1}))\exp(-k_j t). \quad (2)$$

In the present paper, for some low dimensional block-linear dynamical systems considered as models of gene networks functioning, we study the behavior of ensembles of their trajectories and show the existence of families of two-dimensional surfaces that are invariant with respect to shifts along trajectories of these systems and contain their cycles. This makes the qualitative analysis of trajectory behavior and interpretation of numerical experiments with these models much simpler.

Three-dimensional dynamical system

In the papers (Golubyatnikov et al., 2018; Golubyatnikov, Ivanov, 2018), we considered a 3D block-linear dynamic system:

$$\frac{dx_1}{dt} = L_1(x_3) - k_1x_1;\ \frac{dx_2}{dt} = L_2(x_1) - k_2x_2;\ \frac{dx_3}{dt} = L_3(x_2) - k_3x_3. \quad (3)$$

Trajectories of all points of the block $\{001\}$ pass through six blocks of decomposition of the domain Q^3 from block to block according to arrows of the following diagram only:

$$\ldots\to\{001\}\to\{011\}\to\{010\}\to$$
$$\{110\}\to\{100\}\to\{101\}\to\{001\}\ldots \quad (4)$$

Denote by W_1^3 a union of blocks listed in the diagram, this is a positive invariant domain of the system (3), its interior is homeomorphic to torus. Note that trajectories of points of two blocks, $\{000\}$ and $\{111\}$, eventually leave them in the invariant domain W_1^3 and further stay there. Thus, cycles of the system (3) do not intersect these two blocks (Golubyatnikov et al., 2018). Stratification of phase portrait of the system (3) consists of two parts: the domain W_1^3 and the union of two blocks, $\{000\}$, $\{111\}$.

Consider a two-dimensional face $F_0 = \{001\} \cap \{011\}$ which separates the blocks $\{001\}$ and $\{011\}$ as well as other faces F_m which separate incident blocks of the diagram (4):

$$F_1 = \{011\} \cap \{010\},\ F_2 = \{010\} \cap \{110\},$$
$$F_3 = \{110\} \cap \{100\}, \ldots\ F_5 = \{101\} \cap \{001\}.$$

After transition along all six arrows of this diagram, trajectories of all points of the face F_0 return to it, each trajectory with its own time. Composition $\Psi: F_0 \to F_0$ of all these six shifts from face F_m to face F_{m+1}, $m = 0, 1, 2, 3, 4$, and $F_5 \to F_0$ is called the Poincaré map.

On the face F_0, let us introduce a coordinate system $(w_1; w_2)$ with the origin at the point $E_3 = (1; 1; 1)$ such that coordinates w_1, w_2 of all points of this face are non-negative: $w_1 = 1 - x_2$; $w_2 = x_3 - 1$. Let the Poincaré map be written by equation

$$\Psi(w_1; w_2) = (\psi_1(w_1; w_2);\ \psi_2(w_1; w_2)).$$

The main technical result of the papers (Golubyatnikov et al., 2018; Golubyatnikov, Ivanov, 2018) is the following

Lemma 1: a) *the Poincaré map is monotonic: if for points* $A(v_1; v_2)$ *and* $B(w_1; w_2)$ *relations* $v_1 < w_1$ *and* $v_2 < w_2$, *are satisfied then* $\psi_1(v_1; v_2) < \psi_1(w_1; w_2)$ *and* $\psi_2(v_1; v_2) < \psi_2(w_1; w_2)$. *For this partial order relation, we use a notation:* $A \prec B$, $\Psi(A) \prec \Psi(B)$;

b) *if* w_1 *and* w_2 *are sufficiently small then* $w_1 < \psi_1(w_1; w_2)$ *and* $w_2 < \psi_2(w_1; w_2)$, *i. e.*, $B \prec \Psi(B)$;

c) *at each point of the face* F_0, *the first derivatives of the coordinate functions* ψ_1 *and* ψ_2 *are strictly positive and their second derivatives are strictly negative.*

This implies that the Poincaré map $\Psi: F_0 \to F_0$ has two fixed points exactly; one of them is the point E_3 which lies at the boundary of F_0 and the other one, denoted by P_*, is contained in the interior of the face F_0 (Golubyatnikov, Ivanov, 2018). Trajectory of the point P_* returns to this point after transition through the blocks of the diagram (4) and, therefore, it is a cycle. Since the map Ψ has just one nontrivial fixed point P_*, the system (3) does not have any other cycles.

In the same paper, for the fixed points E_3 and P_* of the Poincaré map, Jacobian matrices $J_2(E_3)$ and $J_2(P_*)$ were calculated and it was shown that the eigenvalues $\lambda_1(P_*)$, $\lambda_2(P_*)$ of the matrix $J_2(P_*)$ are different, positive and do not exceed one, which means exponential stability of the cycle of the system (3). We denote this cycle discovered in (Golubyatnikov, Ivanov, 2018) by $\mathbb{C}_3$. Lemma 1 also implies that both these Jacobian matrices are positive, so it is possible to use the Frobenius–Perron theorem (Gantmacher, 1959) in our studies.

Note that the determinant of Jacobian matrix $J_2(E_3)$ is equal to one and for its eigenvalues $\lambda_1(E_3)$, $\lambda_2(E_3)$, relations $\lambda_1(E_3) > 1 > \lambda_2(E_3) > 0$ are true. So, for the map Ψ, hypothesis of Grobman–Hartman theorem (Hartman, 1964) is fulfilled. This implies that in a sufficiently small neighborhood $U(E_3) \subset F_0$ of the point E_3, the Poincaré map is linearized by some continuous (in general terms, non-smooth) change of variables $(w_1; w_2) \Rightarrow (u_1; u_2)$. In such a coordinate system, $\Psi(u_1; u_2) = (\lambda_1(E_3) \cdot u_1;\ \lambda_2(E_3) \cdot u_2)$.

For sufficiently small $\varepsilon > 0$, we denote by $T_\varepsilon^2 \subset U(E_3)$ a triangle $0 \le u_1 + u_2 < \varepsilon$ with one vertex at the point E_3 and let $\widehat{F_0}$ be a truncated face $F_0 \backslash T_\varepsilon^2$.

Choose two segments $[0, \alpha_1]$ and $[0, \alpha_0] \subset [0, \alpha_1]$ in this neighborhood so that $\alpha_1 = \lambda_1(E_3) \cdot \alpha_0$. Let N_1 and N_0, respectively, be the right endpoints of these segments, then $\Psi([0, \alpha_0]) = [0, \alpha_1]$ and $\Psi(N_0) = N_1$; in the original coordinate system $(w_1; w_2)$, the segments $[0, \alpha_0]$ and $[0, \alpha_1]$ are represented by arcs $D_0 \subset D_1$ with a common endpoint E_3. Consider action of iterations of the Poincaré map to these arcs:

$$\Psi(D_0) = D_1 \subset D_2 \coloneqq \Psi(D_1) \subset D_3 \coloneqq \Psi(D_2) \subset D_4 \ldots$$

The union D_* of infinite sequence of mutually embedded arcs D_k is a continuous monotonic arc connecting the points E_3 and P_*; after transition along arrows of the diagram (4), trajectories of points of D_* return to this arc: the semi-interval $D_1 \backslash D_0$ passes to semi-interval $D_2 \backslash D_1$ which passes in turn to $D_3 \backslash D_2$, etc. Thus, trajectories of points of the arc D_* generate an invariant (non-smooth) surface Σ^2 bounded by the cycle $\mathbb{C}_3$

in the invariant domain $W_1^3 \subset Q^3$. By the construction, this surface contains the point E_3.

Starting such constructions of small segments $[N_0, N_1]$ in a neighborhood $U(E_3)$ with points N_0 which do not lie on the axis E_3u_1 and considering the images of these segments under iterations of the Poincaré map Ψ, we obtain a family of continuous monotonic arcs which leave the neighborhood $U(E_3)$ and do not contain the point E_3. For each pair of points $N_0, N_1 \subset U(E_3)\backslash E_3u_1$ such that $\Psi(N_0) = N_1$, the sequence $N_k = \Psi(N_{k-1})$ tends monotonically to the fixed point P_* of the Poincaré map Ψ (Golubyatnikov et al., 2018). Here, each segment $[N_0, N_1]$ generates, as above, a monotonic arc $D_*(N_0)$ being invariant with respect to the Poincaré map. Trajectories of points of such an arc, in their turn, form an invariant 2D surface $\Sigma^2(N_0)$ which intersects the surface Σ^2 by the cycle $\mathbb{C}_3$ exactly.

In a similar way, one can construct invariant surfaces which do not intersect the neighborhood $U(E_3)$ in the domain W_1^3. Let $U(P_*) \subset \widehat{F_0}$ be a neighborhood of the nontrivial fixed point P_*, where the map Ψ can be linearized. We save the notations $(u_1; u_2)$ for these linearized coordinates. For sufficiently small $\varepsilon > 0$, the Poincaré map transforms the ellipsis $S_1^1 \subset U(P_*)$ with equation $\lambda_1(P_*)u_1^2 + \lambda_2(P_*)u_2^2 = \varepsilon^2$ to the circle S_0^1 with the equation $u_1^2 + u_2^2 = \varepsilon^2$. Let $I_1(M_0)$ be a segment which joins the point $M_1 \in S_1^1$ with its image $M_0 = \Psi(M_1) \in S_0^1$. All such segments are contained in $U(P_*)$ in the ring between S_0^1 and S_1^1. Each of these segments generates a sequence of continuous arcs $D_k(M_0)$, they are invariant with respect to the Poincaré map, and $\Psi(D_k(M_0)) = D_{k-1}(M_0)$. For each of these arcs, trajectories of its points generate in W_1^3 an invariant surface bounded by the cycle $\mathbb{C}_3$.

Theorem 1. *There exists two-dimensional invariant foliation in the invariant domain W_1^3 of the dynamical system* (3); *its leaves fill W_1^3 and contain the cycle $\mathbb{C}_3$ on their boundaries. One of these leaves contains the point E_3.*

Four-dimensional dynamical system

Recently, in the papers (Ayupova, Golubyatnikov, 2019; Golubyatnikov, Minushkina, 2021), we considered a four-dimensional block-linear system

$$\frac{dx_1}{dt} = L_1(x_4) - k_1x_1; \ \frac{dx_r}{dt} = \Gamma_r(x_{r-1}) - k_rx_r; \ r = 2, 3, 4. \qquad (5)$$

In particular case, when $k_j = 1$ for all j, questions of existence, uniqueness, and stability of cycles of such systems were studied in (Glass, Pasternack, 1978). Smooth analogues of similar systems were considered in (Hastings et al., 1977; Mallet-Paret, Smith, 1990).

An invariant domain Q^4 of the system (5) is decomposed by hyperplanes $x_j = 1$ to 16 blocks $\{\varepsilon_1\varepsilon_2\varepsilon_3\varepsilon_4\}$. Blocks of this decomposition listed in the following diagram form an invariant subdomain W_1^4 in the phase portrait of (5)

$$\ldots \to \{1111\} \to \{0111\} \to \{0011\} \to \{0001\} \to$$
$$\{0000\} \to \{1000\} \to \{1100\} \to \{1110\} \to \{1111\} \to \ldots \quad (6)$$

The arrows of this diagram show the only possible direction of trajectory transition from one block to another. The subdomain W_1^4 is one of two parts of stratification of the phase portrait of the system (5). For each block not listed here, trajectories of its points can pass to three adjacent blocks, two of them are contained in W_1^4, and one is in $Q^4\backslash W_1^4$ (this is the second part of the stratification mentioned above). Algorithms of construction of such diagrams for the systems of arbitrary dimensions, both smooth and blocks-linear, are described in (Kazantsev, 2015; Kirillova, Minushkina, 2019).

As in previous sections, let us denote by $\mathcal{F}_0$ an intersection of two adjacent blocks $\{1111\} \cap \{0111\}$ in the diagram (6). After eight steps according to its arrows under shifts along trajectories, all points of this three-dimensional face return to $\mathcal{F}_0$. Let $\Psi_4: \mathcal{F}_0 \to \mathcal{F}_0$ be a corresponding Poincaré map, $T_\varepsilon^3 \subset U(E_4)$ be a pyramid $0 \le u_1 + u_2 + u_3 < \varepsilon$ with the vertex at the point $E_4 = (1; 1; 1; 1)$, and $\widehat{\mathcal{F}}_0$ be a truncated face $\mathcal{F}_0 \backslash T_\varepsilon^3$.

In the paper (Golubyatnikov, Minushkina, 2021), it was shown that all statements of Lemma 1 are true for the map Ψ_4, thus, this map has two fixed points exactly: E_4 and the point Π_* which is contained in the interior of the face $\mathcal{F}_0$. This means that the invariant domain W_1^4 of the system (5) contains one cycle exactly, let us denote it by $\mathbb{C}_4$. The following results were also established there.

Lemma 2: a) *the Jacobi matrices $J_3(E_4)$ and $J_3(\Pi_*)$ and their determinants are positive*;
b) $\det J_3(E_4) = \lambda_1(E_4) \cdot \lambda_2(E_4) \cdot \lambda_3(E_4) = 1$;
c) *magnitudes of eigenvalues of the matrix $J_3(\Pi_*)$ are less than one.*

This implies the exponential stability of the cycle $\mathbb{C}_4$ and possibility of linearization of the Poincaré map Ψ_4 in some small neighborhood $U(\Pi_*)$ of its fixed point Π_*. According to the Frobenius–Perron theorem, one of the eigenvalues of the matrix $J_3(\Pi_*)$ is positive and greater than the magnitudes of the remaining eigenvalues. The same applies to the eigenvalues of the matrix $J_3(E_4)$. Let us enumerate the eigenvalues of Jacobi matrices in order of decreasing of their absolute values: $\lambda_1 > |\lambda_2| \ge |\lambda_3|$. Let $(u_1; u_2; u_3)$ be the coordinates where Ψ_4 is linear

$$\Phi(u_1; u_2; u_3) = (\lambda_1(\Pi_*) \cdot u_1; \lambda_2(\Pi_*) \cdot u_2; \lambda_3(\Pi_*) \cdot u_3).$$

As in the case of the system (3), for a sufficiently small $\varepsilon > 0$, the Poincaré map translates the ellipsoid S_1^2 with the equation $\lambda_1(\Pi_*)u_1^2 + |\lambda_2(\Pi_*)|u_2^2 + |\lambda_3(\Pi_*)|u_3^2 = \varepsilon^2$ to the sphere S_0^2 with the equation $u_1^2 + u_2^2 + u_3^2 = \varepsilon^2$.

Theorem 2. *If $a_j > 1$ for all $j = 1, 2, 3, 4$, and the Jacobi matrix $J_3(E_4)$ of the Poincaré map does not have eigenvalues with unit module then there exists an invariant foliation in the domain W_1^4; its leaves fill this invariant domain and contain the cycle $\mathbb{C}_4$. One of these leaves contains the point E_4.*

Dynamical systems of higher dimensions

In the papers (Gaidov, Golubyatnikov, 2014; Ayupova, Golubyatnikov, 2021), we considered a five-dimensional block linear dynamical system

$$\dot{x}_1 = L_1(x_5) - k_1x_1; \ \dot{x}_2 = L_2(x_1) - k_2x_2; \ \ldots \ \dot{x}_5 = L_5(x_4) - k_5x_5, \quad (7)$$

for which, as in previous sections, an invariant domain $Q^5 = [0, a_1] \times [0, a_2] \times \ldots \times [0, a_5]$ and its decomposition to blocks by the hyperplanes $x_j = 1$ were constructed. Ten blocks of this decomposition form a stratum $W_1^5 \subset Q^5$ which is invariant with respect to shifts along trajectories of the system (7) passing through the blocks according to arrows of a cyclic diagram, similar to (4) and (6):

$$\begin{gathered} \ldots\to\{10101\}\to\{00101\}\to\{01101\}\to\{01001\}\to \\ \{01011\}\to\{01010\}\to\{11010\}\to\{10010\}\to \\ \{10110\}\to\{10100\}\to\{10101\}\to\ldots \end{gathered}$$

Points of the four-dimensional face $F_0^4 = \{10101\}\cap\{00101\}$ under shifts along their trajectories after ten steps along the arrows of the diagram return to the face F_0^4.

For such a Poincaré map $\Psi_5{:}F_0^4\to F_0^4$, an analogue of Lemma 1 implies that the face F_0^4 contains two fixed points of this map exactly: the point $E_5 = (1;\ 1;\ 1;\ 1;\ 1)$ and a point Π_*^5 in the interior of this face. The domain W_1^5 contains one cycle exactly. Let us denote it by $\mathbb{C}_5$. This cycle is stable and passes through the point Π_*^5 (Ayupova, Golubyatnikov, 2021).

As in previous sections, an analogue of Lemma 2 holds: Jacobi matrices $J_4(E_5)$, $J_4(\Pi_*^5)$ and their determinants are positive, $\det J_4(E_5) = 1$.

The magnitudes of eigenvalues of the matrix $J_4(\Pi_*^5)$ do not exceed one. In the case when these Jacobi matrices do not have any eigenvalues modulo equal to 1, construction of the invariant surface $\Sigma^2 \subset W_1^5$ with the boundary $\mathbb{C}_5$ and an invariant foliation in the domain W_1^5 is carried out exactly in the same way as above.

In the paper (Golubyatnikov, Gradov, 2021), conditions under which a non-invariant stratum $Q^5\setminus(W_1^5\cup\{00000\}\cup\{11111\})$ of the phase portrait of the five-dimensional system (7) contains one more of its cycle were established.

Similar constructions can be done for a block-linear analogue of the six-dimensional Elowitz–Leibler system (Elowitz, Leibler, 2000) studied in (Minushkina, 2021; Golubyatnikov, Minushkina, 2022)

$$\begin{gathered} \dot m_1 = L_1(p_3)-k_1m_1;\ \dot p_1 = \Gamma_1(m_1)-l_1p_1;\ \dot m_2 = L_2(p_1)-k_2m_2; \\ \dot p_2 = \Gamma_2(m_2)-l_2p_2;\ \dot m_3 = L_3(p_2)-k_3m_3;\ \dot p_3 = \Gamma_3(m_3)-l_3p_3. \quad (8) \end{gathered}$$

Here, the variables m_j and p_j and denote concentrations of three mRNAs and proteins TetR, LacI and λcl, corresponding to them (Elowitz, Leibler, 2000; Kolesov et al., 2016).

An invariant domain $Q^6 = \Pi_{j=1}^{3}[0,\ a_j]\times[0,\ b_j]$, where b_j are the maximum values of step functions Γ_j divided by the coefficients l_j, $j = 1, 2, 3$, is decomposed by six hyperplanes $m_j = 1$, $p_j = 1$, $j = 1, 2, 3$, to 64 blocks which form a stratification of Q^6 to three subdomains, W_1^6, W_3^6, and W_5^6, with different qualitative trajectory behavior.

The domain W_5^6 consists of 12 blocks, from which trajectories can transit to 5 adjacent blocks. In the symmetric case when $k_j = l_j = 1$, there are no cycles in this subdomain. However, W_5^6 contains a two-dimensional invariant surface consisting of piecewise linear trajectories attracting by the point $E_6 = (1;\ 1;\ 1;\ 1;\ 1;\ 1)$ in a spiral way.

In the domain W_1^6 formed by 12 blocks, from which trajectories can enter one adjacent block only, the Poincaré map contains a unique non-trivial fixed point Π_*^6, the trajectory of which is a stable limit cycle for all trajectories in this domain (Golubyatnikov, Minushkina, 2022).

In the domain W_3^6 which consists of 40 blocks, state transition diagram has a more complicated combinatorial structure. At present time, transitions of trajectories from one block to another in this subdomain have not been studied completely yet.

For smooth analogues of the dynamical system (8), the uniqueness of equilibrium point was established in (Ayupova et al., 2017). As in the case of block linear systems, hyperplanes passing through the equilibrium point and being parallel to coordinate ones decompose the invariant domain Q^6 to 64 blocks. If a linearization matrix of such smooth system in its equilibrium point has eigenvalues with positive and negative real parts and does not have any imaginary eigenvalues then the invariant domain W_1^6 contains a cycle $\mathbb{C}_6$ of this sytem (Ayupova et al., 2017). In the paper (Kirillova, 2020), conditions of existence of an invariant surface bounded by the cycle $\mathbb{C}_6$ in the domain W_1^6 were obtained.

Results of numerical experiments

The lefthand part of Figure shows 100 trajectories of the dynamical system (3). Each of these trajectories is contained in a corresponding leaf of the foliation in W_1^3 near the invariant surface Σ^2. The values of parameters of this system are: $k_1 = 0.4$; $k_2 = 0.3$; $k_3 = 0.6$; $a_1 = 1.3$; $a_2 = 1.4$; $a_3 = 1.7$. The initial data are chosen in a random way in a rectangular neighborhood of the point E_3. The righthand part of this Figure shows results of similar experiments with a smooth analogue of the system (3):

$$\frac{dx}{dt} = \frac{10}{1+z^3} - x;\ \frac{dy}{dt} = \frac{10}{1+x^3} - y;\ \frac{dz}{dt} = \frac{10}{1+y^3} - z.$$

Here, one can clearly see its invariant surface.

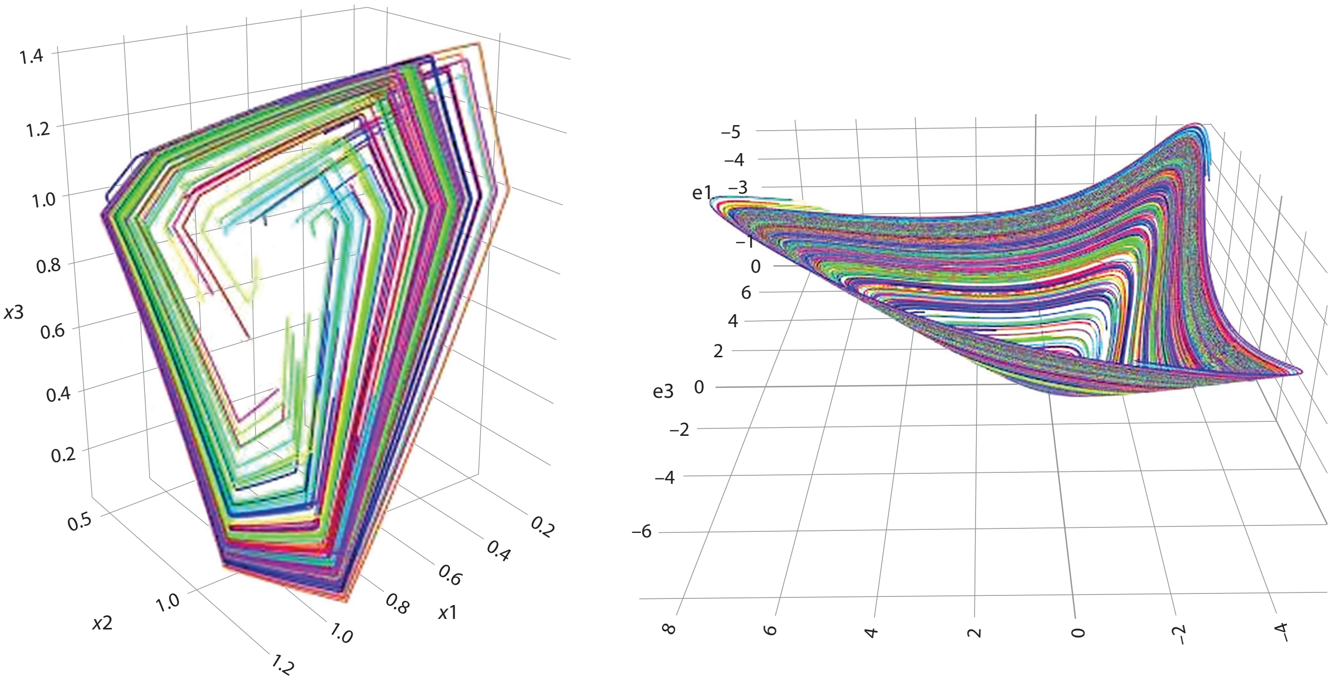
It was shown in (Golubyatnikov et al., 2018; Ayupova, Golubyatnikov, 2021; Golubyatnikov, Minushkina, 2021; Minushkina, 2021) that trajectories of block-linear dynamical systems (3), (5), (7), (8) are piecewise smooth, the discontinuities of their derivatives are located on the planes $x_j = 1$, this is clearly seen on the left part of Figure.

In order to perform numerical simulations of trajectories of (3), we have developed a software project using the R programming language (https://www.r-project.org/) and the Shiny package (https://shiny.rstudio.com/). The source code is available on GitHub: https://github.com/AndreyAkinshin/pwLLL.

The simulations are performed in the cloud; the results are described at https://aakinshin.net/posts/dscs2/. The library ggplot (https://ggplot2.tidyverse.org/) is used here, as well as the package deSolve (http://desolve.r-forge.r-project.org/) that contains integration routines previously used to simulate other systems of gene networks. The user interface allows one to specify all parameters of the system (3).

Conclusion

In this paper, we have described a construction of invariant foliations, i. e. the families of invariant two-dimensional surfaces in phase portraits of low-dimensional block-linear models of circular gene networks. It was shown that on each leaf of



Results of numerical experiments with trajectories of the 3D systems.

these foliations, trajectories of all its points are repelled by the boundary of the central part of the phase portrait and they are attracted by the limit cycle which describes an oscillating functioning of the corresponding gene network. Theorem 1 is illustrated by numerical experiments.

For the kinetic dynamical systems under consideration, the leaves of invariant foliations in the phase portraits play the role of level surfaces of collections of motion integrals studied in classical mechanics (Poincaré, 1892; Arnold, 1989). Reduction of dimensions of invariant subsets in the phase portraits allows us to give a digestible description of trajectories behavior and, in particular, simplifies considerably numerical experiments with such gene networks models (Likhoshvai et al., 2020). Construction of the foliations mentioned above and investigation of their geometric properties can be useful in studies of dynamical characteristics of more complicated models of gene networks functioning when a description of a big system is given on the basis of known results on its subsystems which have a simpler structure.

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