ON NONLINEAR DYNAMICAL SYSTEMS
AS MODELS OF THE GENE NETWORKS

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The main aim of our work is to give mathematical explanation of numerical experiments with limit cycles oscillations in gene networks models, see [1-3]. These experiments are performed in collaboration of Sobolev Institute of Mathematics and Institute of Cytology and Genetics of SB RAS. We consider here the following dynamical systems as models of the gene networks with negative feedbacks

\[ \dot{x} = \Phi_1(z, x), \quad \dot{y} = \Phi_2(x, y), \quad \dot{z} = \Phi_3(y, z). \quad (1) \]

Here \( \Phi_i \) are sufficiently smooth and monotonically decreasing with respect to both their arguments so, that \( x, y, z \in [0, \infty) \). We assume that \( \Phi_i(x_i-1, 0) > 0 \) and \( \partial \Phi_i/\partial x_i(x_i-1, x_i) \leq \delta_i < 0 \). The system (1) and each of its odd-dimensional analogues has a unique stationary point \( M_\ast \).

**Lemma.** Topological index of the stationary point \( M_\ast \) in odd-dimensional dynamical system of the type (1) equals \(-1\).

Let \( \alpha_i = \Phi_i(0, 0) \) be the maximal value of the function \( \Phi_i \). For large values of \( t \) all trajectories of the system (1) enter some parallelepiped \( \Pi = [\varepsilon_1, A_1] \times [\varepsilon_2, A_2] \times [\varepsilon_3, A_3] \). Here, one can take for the beginning \( \varepsilon_i = 0 \) and \( A_i = \alpha_i/\delta_i \). Hence, \( \Pi \) is a positively invariant domain of (1). The best values of \( \varepsilon_i \) and \( A_i \) satisfy the system

\[ \Phi_i(A_{i-1}, \varepsilon_i) = 0, \quad \Phi_i(\varepsilon_{i-1}, A_i) = 0. \]

Consider the planes parallel to the coordinate ones and containing the point \( M_\ast = (x_\ast, y_\ast, z_\ast) \). They compose the subdivision \( \Pi = \bigcup Q_{abc} \), where

\[ Q_{abc} = \{ x \in \Pi \mid x \geq_a x_\ast, y \geq_b y_\ast, z \geq_c z_\ast \}, \]

\( a, b, c \in \{0, 1\} \), the symbol \( \geq_0 \) denotes \( \leq \), and \( \geq_1 \) denotes \( \geq \). One can verify that the parallelepipeds \( Q_{000} \) and \( Q_{111} \) can be excluded from the invariant domain. The union of remaining 6 parallelepipeds \( \Pi \subset \Pi \) is again a positively invariant domain of the system (1). Denote their common faces as follows: \( F_{001} = Q_{001} \cap Q_{011}, \quad F_{011} = Q_{011} \cap Q_{010}, \quad F_{010} = Q_{010} \cap Q_{110} \) etc. The shifts along the trajectories of the system (1) define a sequence of smooth mappings

\[ \ldots \rightarrow F_{001} \rightarrow F_{011} \rightarrow F_{010} \rightarrow F_{110} \rightarrow F_{100} \rightarrow F_{101} \rightarrow F_{001} \rightarrow \ldots \]

(2)

Similar diagram was constructed in [4] for quite different class of dynamical systems.

The characteristic equation of linearization of (1) near the point \( M_\ast \) has one negative eigenvalue \( \lambda_1 < 0 \) corresponding to an eigenvector \( e_1 \) with positive coordinates. Let \( \lambda_2, \lambda_3 \) be its other eigenvalues. If \( \Re \lambda_2, \Re \lambda_3 < 0 \), then the point \( M_\ast \) is stable and attracts all trajectories of the system (1). The previous lemma implies that the signs of \( \Re \lambda_2, \Re \lambda_3 \) coincide.

Let \( \Re \lambda_2, \Re \lambda_3 > 0 \). In this case the stationary point \( M_\ast \) is unstable. Since the vectors \( \pm e_1 \) are directed from \( M_\ast \) into \( Q_{000} \) or \( Q_{111} \), the invariant domain of our system can be reduced to \( (\Pi \setminus U) \) where \( U \) is some neighborhood of the point \( M_\ast \). Consider the intersection \( F' = (\Pi \setminus U) \cap F_{001} \) and composition \( \varphi_6 \) of 6 consecutive shifts \( \varphi_6 : F_{001} \rightarrow F_{001} \) in (2) which maps the compact contractible set \( F' \) into itself \( \varphi_6 : F' \rightarrow F' \). According to the well-known torus
principle. Brouwer’s fixed point theorem implies existence of at least one point \( M_0 \in F' \) such that \( \varphi_0(M_0) = M_0 \). So, trajectory of this point is a closed cycle, and we have proved

**Theorem 1.** If \( \Re \lambda_2, \Re \lambda_3 > 0 \), then the dynamical system (1) has at least one periodic trajectory in the invariant domain.

If \( \Phi_i(u, w) = f_i(u) - w \), then this invariant domain \( \tilde{\Pi} \) can be reduced to the union of 6 trihedral prisms \( P_{abc} \subset Q_{abc} \), \( 1 \leq a + b + c \leq 2 \) spanned on the intersections listed in (2). Each of these prisms \( P_{abc} \) is obtained by excising from \( Q_{abc} \) along one of its diagonal planes, see [2]. Further reductions of this invariant domain can be realized as well. Note that in this case \( \Re \lambda_2 \) and \( \Re \lambda_3 \) are complex conjugate.

Brouwer’s fixed point theorem does not guarantee uniqueness and stability of this cycle. Numerical experiments show that the trajectories of the systems of the type (1) do not approach the cycles monotonically, so, their stability can not be proved with the help of elementary estimates. In some particular cases, for small positive values of \( \Re \lambda_2, \Re \lambda_3 \), uniqueness and stability of this cycle in a small neighborhood of \( M_* \) can be obtained by methods of Andronov – Hopf bifurcation theory. An explicit formula for the first Lyapunov parameter \( \nu_1 \) was obtained in [3] in the case of symmetric systems (1) with

\[
\Phi_1(z, x) = f(z) - x; \quad \Phi_2(x, y) = f(x) - y; \quad \Phi_3(y, z) = f(y) - z. \tag{3}
\]

There, a domain of parameters corresponding to \( \nu_1 < 0 \) was described, and this inequality implies stability the bifurcation cycle, see also [1]. In the case of asymmetric dynamical system of a general type the explicit analytic expression for \( \nu_1 \) is too cumbersome, but it can be easily used in analysis of the numerical experiments.

Similar results on existence of periodic trajectories and their bifurcations can be obtained for other odd-dimensional asymmetric dynamical systems of the type (1). The even-dimensional dynamical systems of this type have usually several stationary points, so their analysis is much more difficult.

Using extended Poincaré-Benedixon theorem estimates of the norm of the transfer matrix and the amenable stability approach elaborated by R.A.Smith ([5], see also [6]), we obtain

**Theorem 2.** If the functions \( \Phi_i \) have the form (3) and satisfy the conditions of the theorem 1, and \( -3/2 < f'(x) < -1/2 \) for all points in the invariant domain, then the system (1) has at least one periodic trajectory which is orbitally stable in the invariant domain.

The work was supported by the leading scientific schools grant 8526.2006.1 and the interdisciplinary grant 46 of SB RAS. The authors are indebted to E. P. Volokitin for discussions.

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