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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

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

Here Φ_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 $\frac{\partial \Phi_i}{\partial x_i}(x_{i-1}, x_i) \leqslant \delta_i < 0$. The system (1) and each of its odd-dimensional analogues has a unique stationary point M_*.

Lemma. *Topological index of the stationary point M_* 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 Φ_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, Π is a positively invariant domain of (1). The best values of ε_i and A_i satisfy the system

$$\Phi_i(A_{i-1}, \varepsilon_i) = 0, \; \Phi_i(\varepsilon_{i-1}, A_i) = 0.$$

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

$$Q_{abc} = \{ \boldsymbol{x} \in \Pi \mid x \gtrless_a x_*, \, y \gtrless_b y_*, \, z \gtrless_c z_* \},$$

$a, b, c \in \{0, 1\}$, the symbol $\gtrless_0$ denotes $\leqslant$, and $\gtrless_1$ denotes $\geqslant$. One can verify that the parallelepipeds Q_{000} and Q_{111} can be excluded from the invariant domain. The union of remaining 6 parallelepipeds $\widetilde{\Pi} \subset \Pi$ is again a positively invariant domain of the system (1). Denote their common faces as follows: $F_{001} = Q_{001} \cap Q_{011}$, $F_{011} = Q_{011} \cap Q_{010}$, $F_{010} = Q_{010} \cap Q_{110}$ etc. The shifts along the trajectories of the system (1) define a sequence of smooth mappings

$$\ldots \to F_{001} \to F_{011} \to F_{010} \to F_{110} \to F_{100} \to F_{101} \to F_{001} \to \ldots \tag{2}$$

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

The characteristic equation of linearization of (1) near the point M_* has one negative eigenvalue $\lambda_1 < 0$ corresponding to an eigenvector e_1 with positive coordinates. Let λ_2, λ_3 be its other eigenvalues. If $\mathrm{Re}\,\lambda_2$, $\mathrm{Re}\,\lambda_3 < 0$, then the point M_* is stable and attracts all trajectories of the system (1). The previous lemma implies that the signs of $\mathrm{Re}\,\lambda_2$, $\mathrm{Re}\,\lambda_3$ coincide.

Let $\mathrm{Re}\,\lambda_2$, $\mathrm{Re}\,\lambda_3 > 0$. In this case the stationary point M_* is unstable. Since the vectors $\pm e_1$ are directed from M_* into Q_{000} or Q_{111}, the invariant domain of our system can be reduced to $(\widetilde{\Pi} \setminus U)$ where U is some neighborhood of the point M_*. Consider the intersection $F' = (\widetilde{\Pi} \setminus U) \cap F_{001}$ and composition φ_6 of 6 consecutive shifts $\varphi_6 : F_{001} \to F_{001}$ in (2) which maps the compact contractible set F' into itself $\varphi_6 : F' \to F'$. 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 $\varphi_6(M_0) = M_0$. So, trajectory of this point is a closed cycle, and we have proved

Theorem 1. *If* $\operatorname{Re}\lambda_2$, $\operatorname{Re}\lambda_3 > 0$, *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 $\widetilde{\Pi}$ can be reduced to the union of 6 trihedral prisms $P_{abc} \subset Q_{abc}$, $1 \leqslant a + b + c \leqslant 2$ 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 $\operatorname{Re}\lambda_2$ and $\operatorname{Re}\lambda_3$ 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 to 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 $\operatorname{Re}\lambda_2$, $\operatorname{Re}\lambda_3$, 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 ν_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 ν_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* Φ_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.*

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