

On cycles in 6D circular gene networks models

Minushkina L.S.*

Novosibirsk State University, Novosibirsk, Russia

* l.minushkina@g.nsu.ru

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Motivation and Aim: In this paper we study a six-component gene network model with positive and negative feedback. The aim is to find the conditions of existence of a cycle and construct an invariant surface for trajectories of a dynamical system.

Methods and Algorithms: We consider a non-linear dynamical system

$$\frac{dx_i}{dt} = L_i(y_{i-1}) - \Gamma_i(x_i), \frac{dy_i}{dt} = G_i(x_i) - \gamma_i(y_i) \quad (1)$$

where positive variables x_i, y_i denote the concentrations of components of gene network, L_i are smooth monotonically decreasing functions and Γ_i, G_i, γ_i are smooth monotonically increasing functions. Hereinafter $i = 1, 2, 3, i - 1 := 3, i = 1$.

A symmetric six-dimensional model of synthetic molecular repressilator was suggested in [1] with linear degradation rate Γ_i, γ_i and synthesis rate L_i, G_i . A similar smooth non-symmetric dynamical system was studied in [2] with smooth L_i and linear Γ_i, γ_i, G_i . In paper [3] the sufficient conditions of existence of a cycle were stated for an analogous six-dimensional system with discontinuous right-hand sides where negative and positive feedback are expressed by decreasing and increasing step functions and degradation rate is linear.

In this paper, we consider only such cases when for all i inequalities

$$\sup \Gamma_i \geq L_i(0), \quad \sup \gamma_i \geq \sup G_i$$

hold so the values of $\Gamma_i^{-1}(L_i(0))$ and $\gamma_i^{-1}(\sup G_i)$ are defined.

The trajectories of system (1) entering the domain

$$Q = \prod_{i=1}^3 [0, \Gamma_i^{-1}(L_i(0))] \times [0, \gamma_i^{-1}(\sup G_i)] \quad (2)$$

do not leave it as time grows. The domain Q contains a unique equilibrium point S_0 of system (1) and the coordinates of S_0 are determined from the equation

$$y_3 = \gamma_3^{-1}(G_3(\Gamma_3^{-1}(L_3(\gamma_2^{-1}(G_2(\Gamma_2^{-1}(L_2(\gamma_1^{-1}(G_1(\Gamma_1^{-1}(L_1(y_3)))))))))))$$

Let us divide the invariant parallelepiped Q into 64 smaller parallelepipeds (blocks) by drawing the hyperplanes through the point S_0 and enumerate them by the binary multiindices as in [5]. In this paper, we study the trajectories of system (1) passing through the blocks according to the following diagram

$$\begin{aligned} & \dots \rightarrow \{110011\} \rightarrow \{010011\} \rightarrow \{000011\} \rightarrow \{001011\} \rightarrow \{001111\} \rightarrow \{001101\} \rightarrow \\ & \rightarrow \{001100\} \rightarrow \{101100\} \rightarrow \{111100\} \rightarrow \{110100\} \rightarrow \{110000\} \rightarrow \{110010\} \rightarrow \dots \end{aligned} \quad (3)$$

Results: A characteristic polynomial of the linearization matrix in a small neighborhood of S_0 has a form

$$P(\lambda) = (\lambda + p_1)(\lambda + p_2)(\lambda + p_3)(\lambda + q_1)(\lambda + q_2)(\lambda + q_3) + k_1 k_2 k_3 l_1 l_2 l_3,$$

where $p_i = \Gamma'_i, q_i = \gamma'_i, l_i = -L'_i, k_i = G'_i$.

For sufficiently large k_i, l_i compared to p_i, q_i the equilibrium point S_0 is hyperbolic and conditions of the Hartman–Grobman theorem are met so the characteristic polynomial has at least a pair of complex conjugate roots λ_1, λ_2 with positive real part.

Theorem. If the characteristic polynomial of linearization matrix of dynamical system (1) has at least two complex conjugate roots with positive real parts and does not have imaginary roots, then system (1) has a cycle $\mathcal{C}$ passing through the blocks of diagram (2).

According to the Hartman–Grobman theorem, there exist neighborhoods U_1, U_2, V_1, V_2 of hyperbolic equilibrium point S_0 and a homeomorphism $h: U_1 \cup U_2 \rightarrow V_1 \cup V_2$ such that $\Phi = h^{-1} \circ D\Phi \circ h$ on U_1 . The plane Π_1^2 spanned by vectors $Re Z$ and $Im Z$ where Z is a complex eigenvector corresponding to λ_1 is contained in the union of the blocks of diagram (2). Let us draw a segment in a small neighborhood of S_0 and after a certain number of iterations of the linear part $D\Phi$ of the Poincaré map Φ we obtain a nested segment sequence bounded by the fixed point U of $D\Phi$. With continuous change of coordinates h a given sequence goes into a nested arc sequence bounded by the arc joining S_0 and $h^{-1}(U)$. The trajectories of all points lying on this arc form a two-dimensional invariant surface of system (1) bounded by a cycle $\mathcal{C}$.

Conclusion: Thus, the sufficient conditions for the existence of a cycle in the invariant domain have been proven for circular gene network model with nonlinear degradation. It has been also shown that the cycle limits a two-dimensional invariant surface containing the trajectories of considered dynamical system. The results generalize the results obtained in [2, 3].

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