CLOSED TRAJECTORIES IN THE GENE NETWORKS

Golubyatnikov V.P.*, Makarov E.V.2

1 Institute of Mathematics SB RAS, Novosibirsk, Russia; 2 Siberian Department of International Institute for Nonlinear Science RAS, Novosibirsk, Russia

* Corresponding author: e-mail: glbtn@math.nsc.ru

Keywords: dynamic systems, Hopf theorem, fixed point theorem, mathematical model

Summary

Motivation: Multistability is an important property of gene network functioning. Estimating of the possible numbers of limit cycles and stationary points of dynamical systems is a fundamental problem of theoretical and applied mathematics.

Results: We prove the existence of limit cycles for some classes of the gene networks models.

Availability: http://www.bionet.nsc.ru/integration

Introduction

Detection of closed trajectories in any particular dynamic system is in general a very difficult mathematical problem, even in the low-dimensional cases. Some its particular cases are related to the classical Hilbert’s 16-th problem and to the Poincare’s Center-Focus problem. Here, we consider special dynamic systems as models of the gene networks. We study their periodic trajectories and stationary points. The existence of these regimes is very important from the viewpoint of the gene networks design meeting the needs of biotechnology, biocomputing and gene therapy, see (Elowitz, Leibner, 2000; Gardner et al., 2000; Golubyatnikov et al., 2003).

Model

For the models of the gene networks introduced in (Likhoshvai et al., 2001), we consider here corresponding 3-dimensional dynamic systems.

\[
\frac{dx_i}{dt} = \frac{\alpha}{1 + x_{i-1}^\gamma} - x_i; \quad \alpha > 0; \quad i = 1, 2, 3. \tag{1}
\]

\[
\frac{dx_i}{dt} = \frac{\alpha}{1 + x_{i-1}^\gamma + x_{i+2}^\mu} - x_i; \quad \alpha > 0; \quad i = 1, 2, 3. \tag{2}
\]

\[
\frac{dx_i}{dt} = \frac{\alpha}{1 + x_{i-1}^\gamma \cdot x_{i+2}^\mu} - x_i; \quad \alpha > 0; \quad i = 1, 2, 3. \tag{3}
\]

We assume that \( \gamma > \mu > 1; \ i-1=3, \ i-2=2 \) for \( i=1 \), and \( i-2=3 \) for \( i=2 \). Each dynamic system (1), (2), (3) is symmetric with respect to cyclic permutation of the variables \( x_3 \rightarrow x_1 \rightarrow x_2 \rightarrow x_3 \). We shall occasionally use notations \( x_1 = x, \ x_2 = y, \ x_3 = z \).

Linearizations of these systems near their stationary points are described by the matrix

\[
A = \begin{pmatrix}
-1 & -p & -q \\
-q & -1 & -p \\
-p & -q & -1
\end{pmatrix}
\] (4)
One of its eigenvalues \( \lambda_1 = -1 - p - q \) corresponds to the vector \((1,1,1)\). For \( p \neq q \), the other eigenvalues \( \lambda_2, \lambda_3 \) of \( A \) are complicated and \( 2 \Re \lambda_{2,3} = p + q - 2. \) All the trajectories of the systems (1), (2), (3) eventually enter the cube \( Q = [0, \alpha] \times [0, \alpha] \times [0, \alpha] \subset \mathbb{R}^3 \) and do not leave it. The diagonal \( \Delta = \{ x = y = z \} \) contains exactly one stationary point \( M^{(i)} \) of each of these system. Here the index \( j \) corresponds to their equation numbers (1), (2) or (3).

Results and Discussions

1. The behavior of the trajectories of the system (1) is much more simple than in (2) and (3). Let \( r(X) \) be the vector, which joins any non-diagonal point \( X \) with its projection onto \( \Delta \) and let \( v(X) = \frac{dt}{dX} r(X) \). The vector product \([r(X), v(X)]\) is parallel to \( \Delta \). For any non-diagonal point \( X \), the coordinates of \([r(X), v(X)]\) are strictly negative. Thus, we obtain

**Theorem 1.** All the trajectories of the system (1) outside the diagonal \( \Delta \) turn around \( \Delta \) with a positive angular velocity.

It follows from this theorem that outside the diagonal \( \Delta \), the dynamical system (1) has no stationary point. Its linearization in a small neighborhood of its stationary point \( M^{(i)} \in \Delta \) is described by (4) with \( q = \gamma (x^{(i)}_0)^{\gamma + 1} \alpha^{-1}, p = 0. \)

For \( \alpha(\gamma - 2) < \gamma x^{(i)}_0 \), the real parts of \( \lambda_{2,3} \) are negative, in this case the stationary point \( M^{(i)} \) is the unique attraction of all the trajectories of (1). If \( \alpha(\gamma - 2) > \gamma x^{(i)}_0 \), then \( M^{(i)} \) is not stable. The angular velocities of the trajectories of the system (1) outside of small neighborhood \( U(\Delta) \) of \( \Delta \) are bounded away the zero. For a positive value \( t_0 \), each point in \( D = Q \setminus U(\Delta) \) makes at least one complete turn around \( \Delta \) during \( t_0 \). Let \( t_1 = D \cap H_1 \{ x_i > x_2 = x_3 \} \) \( t_2 = D \cap H_2 \{ x_2 > x_i = x_3 \} \) and \( t_3 = D \cap H_3 \{ x_3 > x_i = x_2 \} \). According to theorem 1, the trajectory of each point \( M \in T_1 \) arrives to \( T_1 \) at a moment \( t_1(M) < t_0 \). Let \( \tau_1 : T_3 \to T_1 \) be the shift in the points of \( T_3 \) along the trajectories.

At some \( t_1(M) + t_2(M) < t_0 \), the point \( M \) arrives at \( T_2 \). Let \( \tau_2 : T_1 \to T_2, \tau_3 : T_2 \to T_3 \) be analogous shifts. Later, at the moment \( t_1(M) + t_2(M) + t_3(M) < t_0 \), the point \( M \) returns to \( T_3 \) for the first time. Let \( \psi_1 : T_1 \to T_1, \psi_2 : T_2 \to T_1, \psi_3 : T_3 \to T_2 \) be the rotations of compact contractible sets \( T_j \) around \( \Delta \) by the angle \( 120^\circ \).

Consider now the composition \( \psi_1 \circ \tau_1 : T_3 \to T_3 \) of continuous mappings \( \tau_1 \) and \( \psi_1 \). The fixed point theorem implies that there is a point \( \tilde{M}_0(x_0, x_0, z_0) \) such that \( \psi_1 \circ \tau_1(M_0) = \tilde{M}_0 \), or, equivalently, the shift \( \tau_1(M_0) \) of this point is obtained by rotation of \( M_0 \) around the diagonal \( \Delta \).

Since the system (1) is symmetric with respect to \( x_i \to x_j \), the composition \( \psi_2 \circ \tau_2 : T_1 \to T_1 \) maps the point \( \tau_1(M_0) \) to itself, hence, the shift \( \tau_2 \circ \tau_1(M_0) = (x_0, z_0, x_0) \) coincides with the rotation \( \psi_2 \circ \psi_1^{-1} \) of \( M_0 \). Finally, \( \psi_3 \circ \tau_3 : T_2 \to T_2 \) maps the point \( \tau_2 \circ \tau_1(M_0) \) into itself.
hence, \( \tau \sigma_2 \sigma_1(M_0) \) coincides with the result of the complete turn \( \varphi_2^{-1} \sigma_2^{-1} \sigma_1^{-1}(M_0) \), and we obtain

**Theorem 2.** For \( \Re \lambda_{2,3} > 0 \), the dynamic system (1) has at least one periodic trajectory symmetric with respect to the permutation of the variables.

It should be reminded that the fixed point theorem does not ensure the uniqueness and stability of this periodic trajectory.

2. Some results on the uniqueness and stability of such a cycle can be obtained from the Hopf bifurcation theorem, see (Marsden, McCracken, 1976).

In contrast with the dynamic system (1), the behavior of trajectories of the systems (2) and (3) is much more complicated. Trajectory of the system (3) in Figure 1 does not have a constant direction of rotation around \( \Delta \). Here \( \alpha = 3.237, \gamma = 1.725, \mu = 1.434 \).

![Fig. 1. Limit cycle of the system (3).](image)

The systems (2) and (3) can have three stable stationary points in the neighborhoods of the non-diagonal vertices of the cube \( Q \) and three unstable stationary points outside \( \Delta \).

Linearization of the system (2) in small neighborhoods of its stationary point \( M_{2}^{(2)} \) is described by the matrix (4) with \( p = \mu \cdot (x_{2}^{(2)})^{\mu+1} \alpha^{-1} \), \( q = \gamma \cdot (x_{2}^{(2)})^{\gamma+1} \alpha^{-1} \). Similar expressions can be derived for the system (3). For each of our systems, if \( \Re \lambda_{2,3} = 0 \) at \( \gamma = \gamma_0 \), then \( \frac{d}{d\gamma}(\Re \lambda_{2,3}) > 0 \) at \( \gamma = \gamma_0 \). The Hopf bifurcation theorem implies that for \( \gamma > \gamma_0 \) sufficiently near \( \gamma_0 \), some small neighborhood of the point \( M_{2}^{(i)} \), \( i = 1,2,3 \), contains a periodic cycle of the system (1), (2) or (3). Figure 2 shows the convergence of two trajectories of the system (2) to the limit cycle from outside and inside. Here \( \alpha = 5.908, \gamma = 2.981, \mu = 2.0 \). Similar phenomena were observed in the system (3). If \( \alpha>2 \) and \( \gamma+\mu>4 \), this system does not have the Hopf bifurcation. Some of our constructions can be accomplished in \( R^n, n>3 \).
Acknowledgements

The work was supported by the leading scientific schools grant N 311.2003.1 of the President of the Russian Federation, by the grant No. 03-01-00328 of the RFBR and by the interdisciplinary grant No 119 of SB RAS. The authors are indebted to J.P. Francoise and Y.N. Yomdin, and especially to V.A. Likhoshvai and K.V. Storozhuk for helpful discussions.

References


Fig. 2. The Hopf bifurcation in the system (2).