OSCILLATIONS OF CHAOTIC TYPE IN SYMMETRIC GENE NETWORKS OF SMALL DIMENSION

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SUMMARY

Motivation: Study of functioning laws of regulatory circuits of gene networks is one of the actual problems of mathematical biology.

Results: A mathematical model of a symmetric genetic construction consisting of three gene elements is considered. We show that the model can have aperiodic functioning regimes of chaotic type in spite of complete symmetry of the system with respect to permutation of variables.

Availability: Available on request.

INTRODUCTION

One of the actual problems of modern systemic biology is study of functioning laws of regulatory circuits of gene networks. In particular, we have the significant problem of research of relationships between structures of regulatory connections and kinds of mechanisms and dynamic characteristics of behavior of gene networks. In the framework of the problem it is important to study dynamic behavior of gene networks consisting of a small number (at most three) of identical genetic elements. Such gene networks can be simulated by systems of the form

\[ \frac{dx_i}{dt} = f(z, \tau) x_i, \quad i = 1, n. \]

Here \( z \) are logical parameters equaled to 0, 1, \( f \) is a function describing the mechanism of expression regulation of the genetic element, \( \tau \) is a delay characterizing matrix processes in biological systems. Presence of matrix processes is one of the important factors of gene networks because, together with the mechanism of genetic regulation of gene expression, it can be the cause of cyclic and more complicated (chaotic) types of dynamic behavior of genetic systems consisting only of one genetic element (Mackey, Glass, 1977). Therefore, in the general case, elimination of the delay from the system (1) bring into simplification of dynamics of their behavior. However, if \( n \) is odd and greater than 1 a complicated behavior can be obtained in the absence of the delay.
In this paper we propose a mathematical model of a symmetric molecular genetics system consisting of three identical genetic elements \((n = 3)\). The model can be represented by the autonomous system of equations

\[
\frac{dx_1}{dt} = P^{(m)}(u_1) - x_1, \quad \frac{dx_2}{dt} = P^{(m)}(u_2) - x_2, \quad \frac{dx_3}{dt} = P^{(m)}(u_3) - x_3, \quad m = 1, 2, ..., (2)
\]

where

\[
\begin{align*}
\alpha & = x_2 + x_3, \\
\beta & = x_3 + x_1, \\
\gamma & = x_1 + x_2,
\end{align*}
\]

\[
P^{(m)}(z) = \alpha \frac{P^{(m-1)}(z)}{1 + [P^{(m-1)}(z)]^2}, \quad m = 2, 3, ..., \quad P^{(1)}(z) = \frac{\alpha z}{1 + z^2}.
\]

We study behavior of limit solutions of the system with respect to the parameter \(\alpha\), meaning it limiting decisions the difference scheme used at integration of system (2). We propose a method to indicate domains of \(\alpha\) where the system has complicated aperiodic behavior.

**METHODS**

We study behavior of the model (2) with respect to the parameter \(\alpha\) by the method of evolutionary diagrams (Akhrumeeva et al., 1988). In the present paper two types of diagrams are proposed. Diagram of the first type (D1) displays properties of solutions of the autonomous system (2) with respect to discrete slowly varying values of the parameter \(\alpha\). For each \(\alpha\) graphs of the components \(x_1(t), x_2(t), x_3(t)\) are projected on the straight line \(\alpha = \text{const}\) of the \((\alpha, \gamma)\)-plane from values of \(t\) under which the graphs give limit solutions. Diagram of the second type (D2) plays the role of a filter that “filters out” limits solutions such as stable stationary solutions and limit cycles and keeps only oscillations of complicated structures. To achieve this purpose, on the straight line \(\alpha = \text{const}\) we project mappings of solutions onto the Poincare plane. Another variant of the filter (D3) uses the distance between solutions of (2) with undisturbed and slightly disturbed initial data.

**RESULTS**

Using the method of constructing D3, we define all partially symmetric and nonsymmetric stationary solutions and analogous limit cycles for the system (2). Then, using the package STEP (Fadeev et al., 1998), the obtained stationary solutions are taken as initial solutions for the parameter continuation method in order to study the dependence on the parameter \(\alpha\) and the stability. Using the methods of constructing D2 and D3, for \(m = 3, m = 4\) and different values of \(\gamma\), we indicate domains of \(\alpha\) where self-oscillations of complicated structure arise. An example of the filter (D3, \(m = 3, \gamma = 4\)) is represented in Fig. 1. The cross-hatched domain shows that there are oscillations of complicated structure for the corresponding values of \(\alpha\).
Figure 1. Evolutionary D3 \((m=3, \gamma=4)\) shows that there are oscillations of complicated structure for \(\alpha \geq 5.8\).

The aperiodic attractor of a chaotic type for \(\alpha = 8.5\) is represented in Fig. 2.

Figure 2. An aperiodic attractor of the system (2) for \(m=3, \alpha = 8.5, \gamma=4\).

DISCUSSION

Study of appearance conditions of chaos in deterministic systems is one of the fundamental problems of modern science. In the present paper we propose a mathematical model describing genetic systems consisting of three genetic elements. The model is a system of three ordinary differential equations. Unlike known autonomous systems with chaotic regimes of evolution, that system consists of completely identical (in form and parameters) equations and is symmetric with respect to permutation of variables. As a
function describing the regulatory mechanism we use the function proposed by Mackey and Glass in 1977 to simulate physiological processes. This function is ideal for description of genetic processes; in particular, processes of expression effectiveness regulation of genetic elements. The regulatory mechanism described by the function has the following characteristics: a small concentration of regulator gives expression activation, a large concentration – degradation. This mechanism is not exotic for living systems. For example, regulation of bacteriophage lambda promoter Prm efficacy has the same type (Ptashne et al., 1980). Therefore our model shows that construction of symmetric genetic makes from natural elements with behavior of chaotic types is fundamentally important. Note that, looking for necessary behavior, instead of using the very function we take its superposition of three order ($m = 3$), which complicates essentially the genetic mechanism because of its sensitivity to variations of concentrations of regulators. The result obtained in our paper poses the problem of study of relationships between symmetry and chaos in living (in particular, genetic) systems. We raise also the question about the role of chaos in functioning and evolution of living systems.

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