Mathematical Modelling and Analysis
Volume 29, Issue 2, 277–287, 2024
https://doi.org/10.3846/mma.2024.19714

Comparative Analysis of Models of Genetic and Neuronal Networks

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Received August 21, 2023; accepted March 8, 2024

Abstract. The comparative analysis of systems of ordinary differential equations, modeling gene regulatory networks and neuronal networks, is provided. In focus of the study are asymptotical behavior of solutions, types of attractors. Emphasis is made on the chaotic behavior of solutions.

Keywords: dynamical systems, gene regulatory network, artificial neural network, periodic solution, Lyapunov exponents.

AMS Subject Classification: 34A34; 34D45; 92B20; 92C42.

1 Introduction

There are two important fields of application for ordinary differential equations, namely, gene networks and neuronal networks. The evolution of these networks can be modeled by systems of ODE. These systems have much similarity but are not identical. The main goal of this article is to compare both systems. We consider first two-dimensional ones and then define four-dimensional systems. We are interested in attractors of both types systems.

Attractors of these systems are subsets of the phase space that attract the trajectories of the system. The simplest attractors are stable critical points (in other words, equilibrium states). More complex attractors are stable periodic solutions - limit cycles. In addition to those indicated, chaotic attractors are encountered more and more often, as real objects are studied. These attractors

are attracting more and more attention and are a popular object of study both for specialists in the natural sciences and for mathematicians, economists, and sociologists.

In this article, the authors focus on two somewhat similar, and in some ways significantly different objects, namely, genes and neural networks. The former are present in the cells of living organisms and participate in the processes of vital activity, response to the influence of the external environment and in the processes of formation of the organism. We will use the abbreviation GRN for gene networks. Second, neural networks are present in the brain of humans and higher animals and control the functions of living organisms. This management is extremely effective and is still the subject of study. It is natural to want to reproduce the processes taking place in the brain with their efficiency and apply them for management and control in various fields. At the moment, the solution of this problem is far from complete.

In attempts to study both gene networks and neural networks, mathematical methods have been used. From the point of view of mathematics, both types of these networks are a set of some elements, the nature of which is not so important, and the connections between them. The question is how these links can be described and whether non-trivial conclusions can be drawn from mathematical models that will help solve the problems of understanding the principles of network functioning and applying the knowledge gained in practical activities.

Let's focus on gene networks. They can be thought of as some kind of network nodes that interact with other nodes by sending messages (proteins) that tell other nodes to increase or decrease their activity. As a result, the state of the network changes as needed, and a collective reaction of the network to what is happening is developed. There are many unanswered questions here. In a simplified scheme, the main question is how the state of the system changes and what this will lead to. Among the mathematical models of gene networks, there are very simplified ones that use two answers to describe each element, yes or no, one or zero. And such models are useful and lead to the solution of some practical problems. Let us mention the tasks of automatic, without human intervention, solving the problems of managing telecommunication networks. Techniques and methods for the optimal allocation of resources in a given situation in telecommunication networks are described in the works [9]. The main idea of this methodology is to reproduce schemes and principles of gene network control in telecommunication networks. How successfully this task is solved can be judged by the publications [10]. Models based on the representation of gene networks as objects of graph theory, a well-developed area of discrete mathematics, are very useful.

It seems to be the most effective modeling of gene networks using systems of ordinary differential equations, where each equation describes a separate element of the network. These systems are quasi-linear, that is, they consist of linear and non-linear parts. In the linear part, a description of the network assumes that there is no communication between the elements. The nonlinear part contains information about the interaction of elements obtained on the basis of experimental data. These nonlinearities are limited, which corresponds

to the real nature of the interaction. The description of the interaction between the elements is contained in a special matrix built into the non-linear part of the system. This matrix is usually called a regulatory matrix and is denoted W. The corresponding system in the case of two, three, and four elements is given in the following sections. The solutions of the ODE system are vector functions that depend on time. At each given moment, the state of the simulated network is associated with the solution vector of the ODE system. By solving this system (numerically or analytically), one can obtain important information about the future states of the system, and, consequently, the network. That is why the study of attracting sets (attractors) in the system of ODEs is an important task.

All of the above applies to a large extent to neural networks. Artificially built on the model of real neural networks, networks are called artificial neural networks and are denoted by ANN.

ANNs can also be modeled by ODE systems according to the previously described scheme, and both ODE systems are similar. We are going to look at both types of ODE systems, draw parallels and note the differences. Particular attention is paid to attractors in systems of both types. Previously the comparison was made between three-dimensional systems, modeling GRN and ANN [16]. In this paper we consider first two-dimensional systems of both kinds, and then we construct four-dimensional GRN and ANN systems, comparing their characteristics, such as the ability to have periodic attractors, Lyapunov exponents etc.

The gene system (2.1) have appeared first in [19] (see also [12]). It was used in [4,7] and in more recent papers [1,2,3,11,13,14,15]. Periodic solutions were in a focus in [5,20]. For neuronal systems consult [6,8]. Chaos in differential equations have been studied in [17].

2 GRN and ANN in general

The general system, which is used to model GRN of n elements, is

$$\begin{cases} x_1' = f_1(w_{11}x_1 + \ldots + w_{1n}x_n - \theta_1) - v_1x_1, \\ x_2' = f_2(w_{21}x_1 + \ldots + w_{2n}x_n - \theta_2) - v_2x_2, \\ \ldots \quad \ldots \quad \ldots, \\ x_n' = f_n(w_{n1}x_1 + \ldots + w_{nn}x_n - \theta_n) - v_nx_n, \end{cases} \tag{2.1}$$

where $f_i(z)$ are sigmoidal functions, which are monotonically increasing from zero to unity and have a single inflection point. They are chosen to be smooth. In the sequel we use the Gompertz function $f(z) = e^{-e^{-\mu z}}$. The parameter μ characterizes the incline of the graph in vicinity of the inflection point. If μ tends to positive infinity, the graph of the function tends to be piece-wise linear with almost vertical middle segment and two infinite segments almost zero and almost unity. The parameters v_i are for the natural decay of solutions (exponentially tending to zero) in the absence of a nonlinear part. The matrix $W = w_{ij}$ is for the description of interaction of the elements x_i. The positive w_{ij} means activation of x_i by x_j. Similarly, the negative value of w_{ij} means inhibition (repression) and zero value of w_{ij} means no interaction. The system

(2.1) is used as a (simple) model of interaction of genes in a living organism. The parameters μ are for the individual characterstics of genes, the parameters θ are for the thresholds, upon reaching which the gene begins to respond.

The general system, which is used to model ANN of n elements, is

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh\left(w_{11}x_1 + w_{12}x_2 + \ldots + w_{1n}x_n\right) - b_1x_1, \\ \dfrac{dx_2}{dt} = \tanh\left(w_{21}x_1 + w_{22}x_2 + \ldots + w_{2n}x_n\right) - b_2x_2, \\ \ldots \quad \ldots \quad \ldots, \\ \dfrac{dx_n}{dt} = \tanh\left(w_{n1}x_1 + w_{n2}x_2 + \ldots + w_{nn}x_n\right) - b_nx_n. \end{cases} \tag{2.2}$$

The hyperbolic tangent function $\tanh(z)$ is sigmoidal, but its range of values is $(-1, 1)$. This system is understood as a set of neurons (identified as x_i), where each element absorbs signals from other ones, and elaborate its own single output. More details on systems (2.1) can be found in [4] and [8]. On application of the system (3.1) in multi-dimensional setting for medica purposes the reference [18] should be consulted.

Both systems have an invariant set in the phase space. The first system has an invariant set $\{0 < x_i < 1/v_i,\ i = 1, 2, \ldots, n\}$. The vector field, generated by (2.1), is directed inward on faces of the invariant set, which can be checked by direct inspection, taking into account the range of values for the sigmoidal functions f_i, which is $(0, 1)$, and positivity of the coefficients v_i. Similarly, the second system (2.2) has an invariant set $\{-1/b_i < x_i < 1/b_i,\ i = 1, 2, \ldots, n\}$.

This is the reason why both systems always have critical points. Moreover, both systems have attractors, which locate in the invariant sets.

3 2D genetic system

Genetic networks can be modeled by systems of ordinary differential equations. Consider the two-dimensional system with the Gompertz function

$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(w_{11}x_1 + w_{12}x_2 - \theta_1)}} - b_1x_1, \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(w_{21}x_1 + w_{22}x_2 - \theta_2)}} - b_2x_2, \end{cases} \tag{3.1}$$

where μ, θ_i and b_i are parameters.

Proposition 1. *There exists at least one critical point. All critical points* (x, y) *are in* $(0, \frac{1}{b_1}) \times (0, \frac{1}{b_2})$.

Proof. The nullclines of the system (3.1) are given by the relations

$$\begin{cases} b_1x_1 = e^{-e^{-\mu(w_{11}x_1 + w_{12}x_2 - \theta_1)}}, \\ b_2x_2 = e^{-e^{-\mu(w_{21}x_1 + w_{22}x_2 - \theta_2)}}. \end{cases} \tag{3.2}$$

The critical points are solutions of the system (3.2). The first nullcline stretches in the strip $0 < x_1 < 1/b_1$, since the range of values of the functions on the right

sides in (3.2) is $(0, 1)$, and the coefficients b_i are positive. Similarly, the second nullcline extends from $-\infty$ to $+\infty$ in the 'orthogonal' strip $0 < x_2 < 1/b_2$. Both strips meet in the rectangle $0 < x_1 < 1/b_1,\ 0 < x_2 < 1/b_2$ and intersect there. □

The number of critical points is finite, and cannot exceed the number nine (for the two-dimensional case). This (nine points) can happen when both nullclines have a Z-shaped form, one Z is normal, and the second Z is rotated at the angle ninety grades.

We will construct an example of a two-dimensional system of the form (3.1), which defines rotating vector field. Let the coefficient matrix in (3.1) be

$$W = \begin{pmatrix} 1 & 2 \\ -2 & 1 \end{pmatrix}, \tag{3.3}$$

and $\mu = 4$, $b_1 = b_2 = 1$, $\theta_1 = 1.2, \theta_2 = -0.5$. There is one critical point and a limit cycle exists.

It is depicted in Figure 1 together with the nullclines and the vector field.

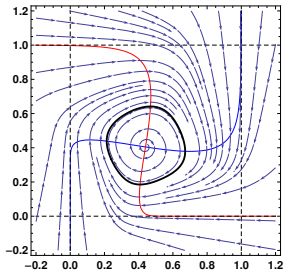

Figure 1. The closed trajectory of the system (3.1) with the regulatory matrix (3.3), $b_1 = b_2 = 1$, $\mu = 4$, $\theta_1 = 1.2, \theta_2 = -0.5$.

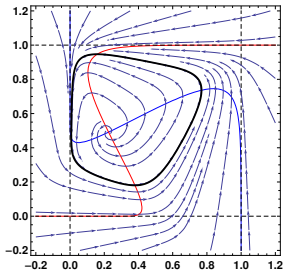

Figure 2. The attractors in system (3.1), with matrix (3.4), $b_1 = b_2 = 1$, $\mu = 4$, $\theta_1 = -0.5, \theta_2 = 1.2$.

Now we construct the second two-dimensional system. Let the coefficient matrix in (3.1) be

$$W = \begin{pmatrix} 1.7 & -2 \\ 2 & 1.7 \end{pmatrix}, \tag{3.4}$$

and $\mu = 4$, $b_1 = b_2 = 1$, $\theta_1 = -0.5, \theta_2 = 1.2$. There is one critical point and limit cycle exists.

It is depicted in Figure 2 together with the nullclines and the vector field.

The vector field, defined by the system (3.1), is directed inward on the border of the box. The rotation of the vector field is counter-clock wise.

4 Example for 4D GRN-system

Consider the system

$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(w_{11}x_1+w_{12}x_2+w_{13}x_3+w_{14}x_4-\theta_1)}} - b_1x_1, \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(w_{21}x_1+w_{22}x_2+w_{23}x_3+w_{24}x_4-\theta_2)}} - b_2x_2, \\ \dfrac{dx_3}{dt} = e^{-e^{-\mu(w_{31}x_1+w_{32}x_2+w_{33}x_3+w_{34}x_4-\theta_3)}} - b_3x_3, \\ \dfrac{dx_4}{dt} = e^{-e^{-\mu(w_{41}x_1+w_{42}x_2+w_{43}x_3+w_{44}x_4-\theta_4)}} - b_4x_4 \end{cases} \tag{4.1}$$

with the parameters $b_1 = b_2 = b_3 = b_4 = 1, \mu = 4$, $\theta_1 = \theta_4 = 1.2, \theta_2 = \theta_3 = -0.5$ and regulatory matrix

$$W = \begin{pmatrix} 1 & 2 & 0 & 0 \\ -2 & 1 & 0 & 0 \\ 0 & 0 & 1.7 & -2 \\ 0 & 0 & 2 & 1.7 \end{pmatrix}.$$

It consists of two independent 2D systems. The first 2D system has the stable periodic solution with the period $T_1 \approx 3.19$. The second one has the periodic solution with the period $T_2 \approx 7.68$. Therefore the period attractor exists for the 4D system (4.1). This system has been studied numerically (Wolfram Mathematica), provided a description of the phase space and images of 3D projections.

The oscillatory solutions are shown in Figure 3 and the attractor is shown in Figure 4.

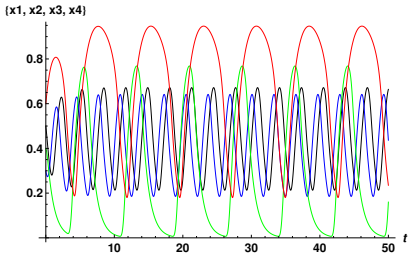

Figure 3. Solution (x_1, x_2, x_3, x_4) of system (4.1).

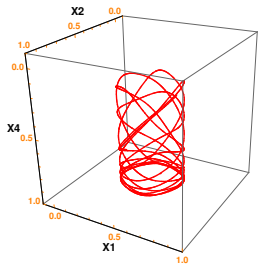

Figure 4. The projection of the attractor on 3D (x_1, x_2, x_4)-subspace of the system (4.1).

5 2D neuronal system

Consider the system, arising in the theory of neuronal networks. The hyperbolic tangent sigmoid function is used in the model.

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh\left(w_{11}x_1 + w_{12}x_2\right) - b_1x_1, \\ \dfrac{dx_2}{dt} = \tanh\left(w_{21}x_1 + w_{22}x_2\right) - b_2x_2, \end{cases} \tag{5.1}$$

where b_i are parameters.

Proposition 2. *There exists at least one critical point. All critical points* (x, y) *are in* $(-\frac{1}{b_1}, \frac{1}{b_1}) \times (-\frac{1}{b_2}, \frac{1}{b_2})$.

Let the coefficient matrix in (5.1) be

$$W = \begin{pmatrix} 2 & 2 \\ -2 & 2 \end{pmatrix}, \tag{5.2}$$

and $b_1 = b_2 = 1$. There is one critical point and limit cycle exists.

It is depicted in Figure 5 together with the nullclines and the vector field.

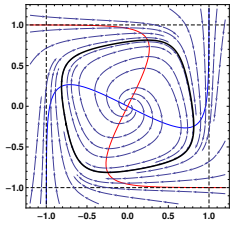

Figure 5. The attractors in system (5.1), with matrix (5.2), $b_1 = b_2 = 1$.

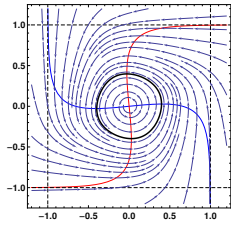

Figure 6. The attractors in system (5.1), with matrix (5.3), $b_1 = b_2 = 1$.

Let the coefficient matrix in (5.1) be

$$W = \begin{pmatrix} 1.2 & -2 \\ 2 & 1.2 \end{pmatrix}, \tag{5.3}$$

and $b_1 = b_2 = 1$. There is one critical point and limit cycle exists. It is depicted in Figure 6 together with the nullclines and the vector field. The vector field, defined by the system (5.1), is directed inward on the border of the box.

6 Example for 4D ANN-system

Consider the system

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh\left(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 + w_{14}x_4\right) - b_1x_1, \\ \dfrac{dx_2}{dt} = \tanh\left(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 + w_{24}x_4\right) - b_2x_2, \\ \dfrac{dx_3}{dt} = \tanh\left(w_{31}x_1 + w_{32}x_2 + w_{33}x_3 + w_{34}x_4\right) - b_3x_3, \\ \dfrac{dx_4}{dt} = \tanh\left(w_{41}x_1 + w_{42}x_2 + w_{43}x_3 + w_{44}x_4\right) - b_4x_4 \end{cases} \tag{6.1}$$

with the parameters $b_1 = b_2 = b_3 = b_4 = 1$ and regulatory matrix

$$W = \begin{pmatrix} 2 & 2 & 0 & 0 \\ -2 & 2 & 0 & 0 \\ 0 & 0 & 1.2 & -2 \\ 0 & 0 & 2 & 1.2 \end{pmatrix}.$$

It also consists of two independent 2D systems. The first 2D system has the stable periodic solution with the period $T_1 \approx 6.85$. The second one has the periodic solution with the period $T_2 \approx 3.76$. Therefore the period attractor exists for the 4D system (6.1). The oscillatory solutions are shown in Figure 7.

The attractor is shown in Figure 8.

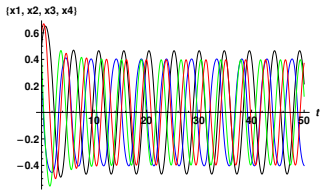

Figure 7. Solution (x_1, x_2, x_3, x_4) of system (6.1).

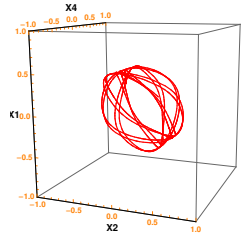

Figure 8. The projection of the attractor on 3D subspace on (x_1, x_2, x_4) of system (6.1).

7 Conclusions

Both GRN and ANN systems have similar behavior. The results, obtained for gene networks, can in many cases be transferred to neuronal systems, and vice versa. Depending on the matrix W, the genetic system can have attractors such as stable equilibria, limit cycles, and, for higher dimensions, also chaotic attractors. The critical points and nullclines can be shifted and moved by manipulating of the parameters θ. One critical point always can be placed into the center of the invariant set by the appropriate choice of θ.

The ANN system is comparatively easier to study since it has not parameters μ and θ. It also can have attractors in the form of stable equilibria and limit cycles. Higher order samples of neuronal systems can be constructed by composing several two dimensional systems with known behavior into larger ones. In this way systems of any dimension can be constructed possessing attractors. The chaotic behavior of solutions can be observed for 4D systems and higher, as shown in the Appendix.

Acknowledgements

ESF Project No.8.2.2.0/20/I/003 Strengthening of Professional Competence of Daugavpils University Academic Personnel of Strategic Specialization Branches 3rd Call.

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Appendix

If we change a little bit the regulatory matrix, the behavior of solutions tends to be chaotic. We provide the matrix W, solutions with given initial data, the projection of an attractor and Lyapunov curves. For both gene system (4.1) and neuronal system (6.1). Consider first the system (4.1), where the regulatory matrix is

$$W = \begin{pmatrix} 1 & 2 & 0 & -0.6 \\ -2 & 1 & 0 & 0 \\ 0 & 0 & 1.7 & -2 \\ 0.5 & 0 & 2 & 1.7 \end{pmatrix}. \tag{7.1}$$

Let us recall that the elements added to the matrix, have the following meaning. The added element at the upper right corner describes inhibition of the first element x_1 by the last one x_4. Conversely, the element at the lower left corner is for the activation of the element x_4 by the first one x_1. Without these elements the system has a periodic attractor. So adding inhibition and activation appropriately brings the disbalance in the system, and this leads to chaotic behavior.

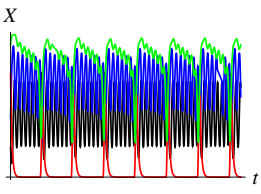

Figure 9. Solutions for system(4.1) with perturbed regulatory matrix (7.1) and $\theta_1 = \theta_4 = 1.2, \theta_2 = \theta_3 = -0.5, \mu = 4$.

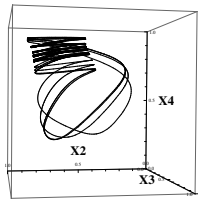

Figure 10. The projection of the attractor on 3D subspace on (x_2, x_3, x_4) of system (4.1) with perturbed regulatory matrix (7.1).

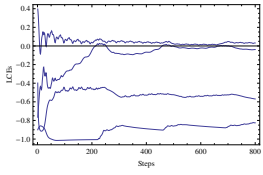

Figure 11. The dynamics of Lyapunov exponents for system(4.1) with perturbed regulatory matrix (7.1) and $\theta_1 = \theta_4 = 1.2, \theta_2 = \theta_3 = -0.5$, $\mu = 4$.

Some solutions are depicted in Figure 9. The respective trajectory tends to an attractor. The 3D projection of this trajectory is shown in Figure 10.

The Lyapunov curves are constructed with the aim to detect the sensitive dependence of solutions to the initial data. The Lyapunov curves for our example are depicted in Figure 11.

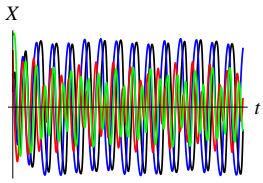

Figure 12. Solutions for system (6.1) with perturbed regulatory matrix (7.2).

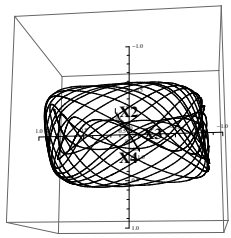

Figure 13. The projection of the attractor on 3D subspace on (x_2, x_3, x_4) of system (6.1) with perturbed regulatory matrix (7.2).

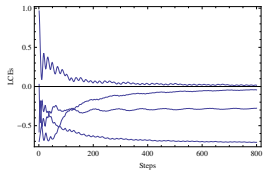

Figure 14. The dynamics of Lyapunov exponents for system (6.1) with perturbed regulatory matrix (7.2).

Following the same scheme, consider the neuronal system (6.1) with the matrix (7.2)

$$W = \begin{pmatrix} 2 & 2 & 0 & -0.6 \\ -2 & 2 & 0 & 0 \\ 0 & 0 & 1.2 & -2 \\ 0.4 & 0 & 2 & 1.2 \end{pmatrix}. \tag{7.2}$$

Some solutions are depicted in Figure 12.

The trajectory tends to an attractor, formed by two two-dimensional limit cycles. The 3D projection of this trajectory is shown in Figure 13. The Lyapunov curves in Figure 14 provide indications to the chaotic behavior of solutions.