DAUGAVPILS UNIVERSITY
Department of Environment and Technologies

Diana Ogorelova

DYNAMIC MODELS OF BIOLOGICAL NETWORKS

Doctoral Thesis
(thematically coherent set of scientific publications)
for obtaining the doctoral degree (Ph. D.) in Natural sciences
(Mathematics branch, Differential equations sub-branch)

Scientific supervisor
Professor, Dr.habil.math. Felix Sadyrbaev

Daugavpils, 2024

CONTENTS

GENERAL INFORMATION ON THE WORK

Ph.D. THESIS “Dynamic models of biological networks” was developed in Daugavpils University Department of Environment and Technologies during 2015 - 2024.

This work has been supported by the 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”.

Doctoral study programme: Mathematics, the sub-branch of “Differential equations”.

Author of the work: Diana Ogorelova.

Scientific supervisor: Professor, Dr.habil.math. Felix Sadyrbaev, Daugavpils University; Institute of Mathematics and Informatics of the University of Latvia.

The Reference list contains 65 items.

Keywords: differential equations, mathematical modeling, gene regulatory networks, neuronal networks, phase space, attractors, bifurcations.

The doctoral thesis is a set of scientific publications written and published during the years 2015 - 2024. All papers are published in scientific journals or in article books of some conferences. The set of publications contains 14 ([29]-[33], [35]-[41], [43], [54]) scientific articles, seven ([35], [36], [38], [40], [41], [43], [54]) were published in the journals indexed in SCOPUS and one of them ([39]) has been published in the Axioms MDPI (indexed in WoS, Q2) journal.

The promotional work is devoted to the study of systems of ordinary differential equations that arise in the theory of complex networks. The gene regulatory networks (GRN networks) and artificial neural networks (ANN networks) are networks of this type.

The ***object*** of the promotional work is a certain class of systems of ordinary differential equations (ODE). These systems have a special quasi-linear structure and contain both linear and nonlinear parts. The nonlinear part is represented by sigmoidal functions. The Gompertz function is selected of them.

Aims of research: The aim of the work is to study one class of systems of ordinary differential equations that arise in the theory of gene networks and artificial neural networks. These systems consist of nonlinear and linear parts. The nonlinear part is represented by sigmoidal functions, of which the Gompertz function and the hyperbolic tangent function are used in the work. Special attention is paid to the study of the properties of attractors, the analysis of the evolution of systems, and the prediction of the behavior of solutions.

The research tasks:

- define a system of ODE modeling GRN and using the Gompertz function as a nonlinearity;
- obtain formulas for the study of the critical points of GRN type systems;
- compare the results for GRN systems using Gompertz function with similar systems using other sigmoidal functions;
- transfer the results obtained for GRN systems to systems arising in ANN theory and containing the hyperbolic tangents function as a nonlinearity;
- compare the results obtained for GRN systems with the results obtained for ANN systems;
- compare the results of periodic attractors in GRN and ANN systems, as well as construct relevant examples;
- prove the existence of periodic attractors for GRN and ANN systems focusing on similarity of both systems;
- prove the existence of periodic attractors for GRN and ANN systems of order two, three and higher;

- detected sensitive dependence of solutions to ANN systems by calculating Lyapunov exponents;
- provide some observations and remarks on the problem of controllability and management of GRN and ANN systems.

Methods used in the study:

- linearization and local analysis of critical points;
- constructing periodic attractors by using Andronov–Hopf bifurcation from stable focus;
- constructing systems of higher dimensions by using low-dimensional blocks and then coupling systems by adding new elements;
- geometrical analysis of phase plane and phase spaces considering the nullclines;
- analyzing phase spaces and vector fields associated with GRN and ANN systems with respect to invariant sets;
- detecting of sensitive dependence of solutions to GRN and ANN systems by calculating Lyapunov exponents;
- extensive use of computational experiments in studying GRN and ANN systems.

The results were communicated at several conferences of different levels, including 11 International Scientific Conferences:

1. 82 st International Scientific Conference of the University of Latvia with the report "Remarks on mathematical modeling of gene and neuronal networks" (Riga, February 23, 2024);
2. International Conference of Numerical Analysis and Applied Mathematics 2023 (ICNAAM 2023) with the report "On control over system arising in the theory of neuronal networks" (Crete, Greece, September 11-17, 2023);
3. 26 th International Conference on Mathematical Modelling and Analysis with the report "Comparative analysis of models of genetic and neuronal networks" (Jurmala, May 30 - June 2, 2023);

4. 65 st International Scientific Conference of Daugavpils University with the report “On linearization on some system arising in the theory of neural networks, in the neighborhood of a critical point ” (Daugavpils, April 20, 2023);

5. 81 st International Scientific Conference of the University of Latvia with the report “On computation of parameters in Artificial Neural Networks mathematical models” (Riga, February 24, 2023);

6. 61 st International Conference on Vibroengineering with the report “On a three-dimensional neural network model” (Udaipur, India, December 12-13, 2022);

7. International Liberty Interdisciplinary Studies Conference with the report “Mathematical modeling of three-dimensional genetic regulatory networks using different sigmoidal functions” (Manhattan, New York, January 16-17, 2022);

8. 1 st International Symposium on Recent Advances in Fundamental and Applied Sciences (ISFAS-2021) with the report “Mathematical modelling of GRN using different sigmoidal functions” (Erzurum, Turkey, September 10-12, 2021);

9. 79 th Scientific Conference of the University of Latvia with the report “Andronov - Hopf bifurcation in 2D systems” (Riga, February 26, 2021);

10. 78 th Scientific Conference of the University of Latvia with the report “Gompertz function in the model of gene regulation network” (Riga, February 28, 2020);

11. 77 th Scientific Conference of the University of Latvia with the report “Z-shaped isoclines in GRN differential system” (Riga, February 18, 2019);

12. 76 th Scientific Conference of the University of Latvia with the report “Gompertz sigmoidal function in the 2-component network model” (Riga, February 23, 2018);

13. 60 th International Scientific Conference of Daugavpils University with the report “Critical points for sigmoidal function” (Daugavpils, April 27, 2018);

14. 12 th Latvian Mathematical Conference with the report “Critical points for sigmoidal function” (Ventspils, April 13- 14, 2018);

15. 11 th Latvian Mathematical Conference with the report “Solvability conditions of the resonant problem” (Daugavpils, April 14, 2016);

16. 57 th International Scientific Conference of Daugavpils University with the report “Dirichlet boundary value problem for one system of differential equations” (Daugavpils, April 12, 2015);

17. 56 th International Scientific Conference of Daugavpils University with the report “The Dirichlet boundary value problem for a system of two second-order differential equations” (Daugavpils, April 8, 2014).

1 INTRODUCTION

In this work, we consider problems arising in mathematical modeling of networks. We focus on modeling gene regulatory networks and artificial neuronal networks. Networks of this type are everywhere. They consist generally of elements which are usually called nodes and links between nodes. The nature of networks may be different. Networks are present in nature, human society, literally everywhere. They can be enormously large, like networks of astronomical objects, stars, planets, and galaxies. At the same time, they can be very small and even unrecognizable and not seen by unarmed eyes, for example, the gene networks in a living organism. To understand the structure and principles of functioning of networks in nature, scientists should collect huge files of the results of observations. These data are to be collected, systematized, analyzed, and classified. Sometimes and even usually this is a very hard task. To make this task easier, the mathematical modeling can be used. As usually, the mathematical models are objects existing in the virtual realm of mathematics. These objects should be created, step-by-step verifying their adequacy according to the researched phenomena. Experiments should be done in a model. The analysis is of a mathematical nature, and the mathematical tools, standard or created exactly for a particular object of the study, are to be used to analyze the model. The results are recorded, systematized, and classified. Hypotheses are formulated in order to understand better the object of the study. Hypotheses are to be verified, and either to be confirmed or disproved.

Simple networks, like groups of humans, small populations, a number of static objects can be investigated using the mathematical apparatus of the graph theory. Graphs consist of vertices, edges between vertices, and characteristics of both vertices and edges. Sometimes graphs can be visualized and analyzed straightforwardly. For networks of large size, this can be a complicated task. As an example, one might think of transportation networks, networks of industrial objects, and so on.

The structure and properties of networks may change over time, and these are the more interesting networks. Based on the analysis of the past of a network, and knowing its main principles of functioning, one may think about predicting of future states of networks. Depending on the nature of a network, this may be the most important challenge.

To illustrate this, let us speak about genetic networks. The existence of genetic networks was not known before the great finding in the field of genetics and biology in general. Now it is known, that genetic networks are present in any cell of any living organism. It can be imagined as a collection of nodes, which are to be called genes, which communicate with each other. How do they do this? They are sending messages in the form of proteins. These messages are accepted by other genes, and the whole network elaborates common reactions. For instance, a genetic network is responsible for the reaction of an organism to diseases. They govern the most important processes in the growing animal or human. Their activity is decisive in morphogenesis, the process of formation of the internal organs. Due to the investigation of geneticists, biologists, and zoologists, the spots on a leopard, and strips on tigers and zebras appear as the result of programming in genomics, and the formation of these properties takes place under the control of gene networks.

Another example of a network is a collection (huge) of neurons in a human's brain. Neurons accept electrical signals from other elements of a network and produce their own signals, which are transferred further. The collective reaction, quick or not, depending on a situation, helps a human to perform its usual functions, like work, communicating with society, and solving creative and algorithmically defined problems. It was amazing that a human can easily recognize images, which is a difficult task for robots and controllable devices. This type of network belongs to biological neural networks. There are still many problems that can be solved by humans better than a computer or other automaton can do. Attempts to copy the work of a human brain have led to artificial neural networks (ANN briefly). ANN is a collection of units, which are called artificial neurons. These units are connected. They can transmit an accepted signal to other units. An artificial neuron receives signals and transmits them after being processed to other neurons connected to it.

The dynamics of both types of networks, GRN (gene regulatory networks) and ANN can be modeled by ordinary differential equations. Each element of a network is denoted by x_i. The physical meaning of x_i is, of course, different for GRN and ANN. Mathematics as a fundamental science that knows many examples of physical, mechanical, chemical, etc. processes, which are quite different in nature, but described by similar mathematical models. This is the case for GRN and ANN. Both have a finite, but probably very large number of elements, which we will denote by x_i. Each x_i can be measured (mostly imaginary) by a number, which is denoted also x_i, but it is dependent on time, $x_i(t)$. So an investigator deals with a number of functions, which are dependent on each other. The collection of $x_i(t)$, $i = 1, 2, \dots$, forms the phase space, which mathematically is Euclidian. The relations between elements x_i should be described. One, very rough, way to do this, is to define the so called regulatory matrix, which is denoted usually W. It is $n \times n$ matrix, where n is the number of elements in a network. The element w_{ij} is a number, that characterizes the influence of an element x_j on the element x_i. The convention is, that positive elements of the matrix W mean activation, negativity means repression (also called inhibition), and zero value of w_{ij} means no relation. Once these preparations are made, the system of differential equations can be produced, which describes the dynamics of a network, since functions $x_i(t)$ change in time following the rules, defined by a system of ordinary differential equations (ODE briefly). The great feature of studying the relative system of ODE is that one might use the mathematical apparatus for the study of such systems and to make predictions on the behavior of solutions $x_i(t)$, which are considered now as solutions in a system of ODE. The mentioned systems were defined earlier for GRN networks, and for ANN networks. When we look at those systems, we observe certain similarities. That means that these systems can be studied simultaneously, and results obtained for GRN systems can be used for the study of ANN systems, and vice versa.

This is the main thrust of the presented work.

DESCRIPTION OF THE SET OF SCIENTIFIC PUBLICATIONS

Here we provide a brief description of the articles in the set of articles forming this thesis.

In the article "***Ogorelova D. Gompertz function in the model of gene regulation network. Proceedings LU MII, vol 18 (2018), 23–32***" 2D-model of gene regulation network is considered where the sigmoidal function is the Gompertz function. The description of attractors is obtained depending on parameters.

The article "***Ogorelova D. Description of critical points in equations arising in applications. Sigmoidal functions in network theories. Proceedings LU MII, vol 19 (2019), 50–56***" contains a description of a three-dimensional GRN type system, where nonlinearity may be any sigmoidal function. Then the author focuses on the case of Gompertz nonlinearity. Formulas for the linearization of the system are derived. Formulas are applied to analyze two examples.

The article "***Ogorelova D., Sadyrbaev F., Sengileyev V. Control in Inhibitory Genetic Regulatory Network Models Contemporary Mathematics (Singapore), 2020, 1(5), pp. 393-400***" studies the system of two first order ordinary differential equations arising in the gene regulatory networks theory. The structure of attractors for this system is described for three important behavioral cases: activation, inhibition, and mixed activation-inhibition. The geometrical approach combined with the vector field analysis allows for treating the problem in full generality. A number of propositions are stated and the proof is geometrical, avoiding complex analytics. Although not all the possible cases are considered, instructions are given on how to handle specific situations.

The article "***D. A. Ogorelova, F. Zh. Sadyrbaev. Gompertz function in the model of gene regulatory networks. Itogi Nauki i Tekhniki. Seriya "Sovremennaya Matematika i ee Prilozheniya. Tematicheskie Obzory", 2021, Vol. 195, pp. 88–96***" examines a network model (including gene regulatory networks), which consists of a system of two ordinary differential equations. This system contains several parameters and depends on the regulatory matrix, which describes interactions in this two-component network. We consider attracting sets of the system, which vary depending on the parameters and elements of the regulatory matrix. Our considerations are of a geometric nature, which allows us to identify and classify possible interactions in the network. The system of differential equations contains a sigmoidal function, which makes it possible to take into account the peculiarities of the networks response to external influences. The Gompertz function was chosen as the sigmoidal function, which allows us to compare the results with similar results for models of two-component networks based on the logistic sigmoidal function.

The article "***Ogorelova D., Sadyrbaev F. On a three-dimensional neural network model. Vibroengineering Procedia. 2022, vol. 47, pp. 69-73***" studies the dynamics of a model of neural networks. It is shown that the dynamical model of a three-dimensional neural network can have several attractors. These attractors can be in the form of stable equilibria and stable limit cycles. In particular, the model in a question can have two three-dimensional limit cycles.

In the article "***Ogorelova D. On a system of ordinary differential equations, arising in applications. Proceedings LU MII, vol 22 (2022), 5–12***", the two-dimensional system of ANN type is considered. The nonlinearity in the system is the hyperbolic tangent function. The coefficients at x_1 and x_2 which are interpreted as signals of two neurons for matrix A, which play the same role, as the regulatory matrix W in GRN theory. Several cases of interaction of two neurons are considered. The graphical analysis of nullclines is made and the characteristics of critical points are obtained. The article is well illustrated.

In the article "***Ogorelova D., Sadyrbaev F. Periodic attractors in GRN and ANN networks. IEEE Xplore, 2023, 4***" who provides the conditions for the existence of a periodic solution in two-dimensional systems of ordinary differential equations, which arise in the theory of genetic and artificial neural networks. The proof is based on Poincare-Andronov-Hopf bifurcation. Multidimensional attractors can be constructed using the two-dimensional ones. Illustrations and examples are provided.

The paper "***Samuilik I., Sadyrbaev F., Ogorelova D. Comparative Analysis of Models of Gene and Neural Networks. Contemporary Mathematics (Singapore), 2023, 4(2), pp. 217–229***" describes in the language of mathematics, the method of cognition of the surrounding world in which the description of the object is carried out the name is mathematical modeling. The study of the model is carried out using certain mathematical methods. The systems of the ordinary differential equations modeling artificial neuronal networks and the systems modeling the gene regulatory networks are considered. One system consists of a sigmoidal function which depends on linear combinations of the arguments minus the linear part. Other system consists of a sigmoidal function which depends on the hyperbolic tangent function. The linear combinations and hyperbolic tangent functions of the arguments are described by one regulatory matrix. For the three-dimensional cases, two types of matrices are considered and the behavior of the solutions of the system is analyzed. The attracting sets are constructed for several cases. Illustrative examples are provided.

The article "***Ogorelova, D., Sadyrbaev, F., Samuilik, I. On Targeted Control over Trajectories of Dynamical Systems Arising in Models of Complex Networks. Mathematics, 2023, 11(9), 2206***" considers the question of targeted control over trajectories of systems of differential equations encountered in the theory of genetic and neural networks. Examples are given of transferring trajectories corresponding to network states from the basin of attraction of one attractor to the basin of attraction of the target attractor. This article considers a system of ordinary differential equations that arises in the theory of gene networks. Each trajectory describes the current and future states of the network. The question of the possibility of reorienting a given trajectory from the initial state to the assigned attractor is considered. This implies only partial control of the network. The difficulty lies in the selection of parameters, the change of which leads to the goal. Similar problems arise when modeling the response of the bodies gene networks to serious diseases (e.g., leukemia). Solving such problems is the first step in the process of applying mathematical methods in medicine and pharmacology.

In the article "***Ogorelova D., Sadyrbaev F., Samuilik I. On attractors in dynamical systems modeling genetic networks. Advances in the Theory of Nonlinear Analysis and its Applications, 2023, 7(2), pp. 486-498***" is studied a dynamical system that arises in the theory of genetic networks. Attracting sets of a special kind is the focus of the study. These attractors appear as combinations of attractors of lower dimensions, which are stable limit cycles. The properties of attractors are studied. Visualizations and examples are provided.

The paper "***Ogorelova D. Mathematical modeling of gene and neuronal networks by ordinary differential equations. Proceedings LU MII, vol 23 (2023), 33–45***" contains an analysis of three-dimensional systems of ODE, arising in GRN networks theory and in ANN theory. The first system uses the logistic function $f(z) = \frac{1}{1+\exp^{-\mu z}}$ as a nonlinearity, and the second system uses the hyperbolic tangent function. The formulas for linearization around critical points are calculated analytically. The inhibition-activation case was analyzed. The Andronov-Hopf bifurcation is explained. The article is well illustrated.

The paper "***Ogorelova D., Sadyrbaev F. Remarks on mathematical modeling of gene and neuronal networks by ordinary differential equations. Axioms MDPI, 2024, 13(1), pp. 61***" considers the mathematical apparatus that uses dynamical systems that are fruitfully used in the theory of gene networks. The same is true for the theory of neural networks. In both cases, the purpose of the simulation is to study the properties of phase space, as well as the types and properties of attractors. The paper compares both models, notes their similarities, and considers a number of illustrative examples. A local analysis is carried out in the vicinity of critical points and the necessary formulas are derived.

The article "***Ogorelova D., Sadyrbaev F. Comparative Analysis of Models of Genetic and Neuronal Networks. Mathematical Modelling and Analysis, 2024, 29(2), pp. 277–287***" provides the comparative analysis of systems of ordinary differential equations, modeling gene regulatory networks and neuronal networks. Asymptotical behavior of solutions and types of attractors are of the study. Emphasis is made on the chaotic behavior of solutions.

In the article "***Ogorelova D., Sadyrbaev F. On control over the system arising in the theory of neuronal networks. International Conference of Numerical Analysis and Applied Mathematics 2023 (ICNAAM 2023). (in print)***" a multiparameter system of ordinary differential equations, arising in the theory of neuronal networks, is considered. The structure of this system presupposes the presence of attractors. The problem of control and management of this system by changing parameters is considered. The conditions are given for the transition of the trajectory from the basin of attraction of one attractor to another attractor. Examples and illustrations are provided.

2 CONCLUSIONS

The work is devoted to the study of systems of ordinary differential equations arising in mathematical models of GRN and ANN.
The main results of the Doctoral thesis are:

- analysis of the phase plane for two dimensional GRN system with the Gompertz nonlinearities, counting critical points and their characteristics;
- formulas for linearization and analysis of critical points in GRN and ANN systems;
- examples of periodic attractors in GRN and ANN systems;
- basic properties of ANN systems with hyperbolic tangent nonlinearities;
- comparison of GRN and ANN systems;
- local analysis of critical points of GRN and ANN systems for dimensions two and three;
- graphical images of nullclines for many relevant to the study cases;
- sensitive dependence of solutions to GRN and ANN systems by calculating Lyapunov exponents;
- control of two dimensional inhibitory GRN systems;
- control by changing parameters over systems with hyperbolic tangent nonlinearities.

References

[1] O. I. Abiodun et al. Comprehensive Review of Artificial Neural Network Applications to Pattern Recognition. IEEE Access, vol. 7, pp. 158820-158846, 2019, doi: 10.1109/ACCESS.2019.2945545.

[2] V. Acary, H. de Jong, B. Brogliato. Numerical simulation of piecewise-linear models of gene regulatory networks using complementarity system. Physica D: Nonlinear Phenomena Volume 269, 15 February 2014, Pages 103-119.

[3] Y. Ahmadian, K.D. Miller. What is the dynamical regime of cerebral cortex? Neuron, 109(21), 2021, 3373-3391.

[4] F.M. Alakwaa. Modeling of Gene Regulatory Networks: A Literature Review. *Journal of Computational Systems Biology* , 1 (2014), issue 1, 1-8.

[5] L. Alzubaidi, J. Zhang, A.J. Humaidi et al. Review of deep learning: concepts, CNN architectures, challenges, applications, future directions. J Big Data 8, 53 (2021). https://doi.org/10.1186/s40537-021-00444-8

[6] D.K. Arrowsmith and C.M. Place. Dynamical Systems. Differential equations, maps and haotic behavior. Chapman and Hall/CRC, London (1992).

[7] S. Atslega, D. Finaskins, F. Sadyrbaev. On a Planar Dynamical System Arising in the Network Control Theory, Mathematical Modelling and Analysis, 21 (2016), N 3, 385 - 398.

[8] E. Brokan and F. Sadyrbaev, Attraction in n-dimensional differential systems from network regulation theory, Mathematical Methods in the Applied Sciences 41, 2018, Issue 17, 7498-7509 https://doi.org/10.1002/mma.5086

[9] E. Brokan and F. Zh. Sadyrbaev. On attractors in gene regulatory systems, AIP Conference Proceedings 1809, 020010 (2017): Proc. of the 6th International Advances In Applied Physics And Materials Science Congress & Exhibition (APMAS 2016), 1-3 June 2016, Istanbul, Turkey,; doi: 10.1063/1.4975425

[10] E. Brokan, F. Sadyrbaev. On a differential system arising in the network control theory, Nonlinear Analysis: Modelling and Control, 21(5):687 701, 2016 doi:10.15388/NA.2016.5.8.

[11] E. Brokan, F. Zh. Sadyrbaev. On controllability of nonlinear dynamical network. AIP Conf Proc, 2116 (1), 040005 (2019) doi.org/10.1063/1.5114026

[12] F. Chapeau-Blondeau and G. Chauvet. Stable, Oscillatory, and Chaotic Regimes in the Dynamics of Small Neural Networks with Delay. Neural Networks, Vol. 5, pp. 735–743, 1992.

[13] S.P. Cornelius, W.L. Kath, A.E. Motter. Realistic control of network dynamic. Nature Communications, Volume 4, Article number: 1942 (2013), 1–9.

[14] A. Das, A.B. Roy, Pritha Das. Chaos in a three dimensional neural network. Applied Mathematical Modelling 24 (2000), 511-522.

[15] R. Edwards and L. Ironi. Periodic solutions of gene networks with steep sigmoidal regulatory functions. Physica D, 282 (2014), 1 - 15. https://doi.org/10.1016/j.physd.2014.04.013

[16] K. Funahashi, K. and Y. Nakamura. Approximation of dynamical systems by continuous time recurrent neural networks, Neural Networks 6, 1993, pp. 801-806.

[17] C. Furusawa, K. Kaneko. A generic mechanism for adaptive growth rate regulation. PLoS Comput Biol, 4(2008), 1, e3. 00350042. https://doi.org/10.1371/journal.pcbi.0040003. [Google Scholar]

[18] S. Haykin. Neural networks. A comprehensive foundation. Prentice Hall, 2nd edition, reprint from 1999.

[19] G. van der Heijden. Hopf bifurcation. www.ucl.ac.uk/ ucesgvd/hopf.pdf

[20] J.J. Hopfield. Neural network and physical system with emergent collactive computational abilities. Proc. Nat. Acad. Sci., USA 79(1982), 2554-2558.

[21] H.D. Jong. Modeling and Simulation of Genetic Regulatory Systems: A Literature Review, J. Comput Biol. 2002;9(1):67-103, DOI: 10.1089/10665270252833208

[22] Y. Koizumi et al. Adaptive Virtual Network Topology Control Based on Attractor Selection. Journal of Lightwave Technology (ISSN : 0733-8724), Vol.28 (06/2010), Issue 11, pp. 1720 - 1731 DOI:10.1109/JLT.2010.2048412

[23] Y. Koizumi, T. Miyamura, S. Arakawa, E. Oki, K. Shiomoto, and M. Murata, Application of attractor selection to adaptive virtual network topology control, in Proceedings of BIONETICS, pp. 1 - 8, Nov. 2008.

[24] Y. Koizumi, T. Miyamura, S. Arakawa, E. Oki, K. Shiomoto, and M. Murata, Robust virtual network topology control based on attractor selection, in Proceedings of ONDM, pp. 123 128, Feb. 2009.

[25] O. Kozlovska, I. Samuilik. Quasi-periodic solutions for a three-dimensional system in gene regulatory network. WSEAS Trans.on Systems, Vol. 22, 2023, 727–733.

[26] N. Kraynyukova, T. Tchumatchenko. Stabilized supralinear network can give rise to bistable, oscillatory, and persistent activity. Proceedings of the National Academy of Sciences, 115(13), 2018, 3464-3469.

[27] Y. Minami, Y. Koizumi, S. Arakawa, T. Miyamuray, K. Shiomotoy and M. Murata, "Benefits of Virtual Network Topology Control based on Attractor Selection in WDM Networks," International Journal on Advances in Internet Technology, vol 4 no 1 & 2, 2011.

[28] K. Nishida, "Fast and Accurate Virtual Network Reconfiguration using Two-Pathway Bayesian Attractor Model: Design and Evaluation," Master Thesis, Osaka Univ., 2021.

[29] Ogorelova D. Description of critical points in equations arising in applications. Proceedings LU MII, vol 19 (2019), 50–56.

[30] Ogorelova D. Gompertz function in the model of gene regulation network. Proceedings LU MII, vol 18 (2018), 23–32.

[31] Ogorelova D. Mathematical modelling of gene and neuronal networks by ordinary differential equations. Proceedings LU MII, vol 23 (2023), 33–45.

[32] Ogorelova D. On a system of ordinary differential equations, arising in applications. Proceedings LU MII, vol 22 (2022), 5–12.

[33] D. A. Ogorelova, F. Zh. Sadyrbaev. Gompertz function in the model of gene regulatory networks. Itogi Nauki i Tekhniki. Seriya "Sovremennaya Matematika i ee Prilozheniya. Tematicheskie Obzory", 2021, Vol. 195, pp. 88–96.

[34] Ogorelova D., Sadyrbaev F. Comparative Analysis of Models of Genetic and Neuronal Networks. Abstracts of MMA2023, May 30 - June 2, 2023, Jurmala, Latvia. 2023. pp.41.

[35] Ogorelova D., Sadyrbaev F. Comparative Analysis of Models of Genetic and Neuronal Networks. Mathematical Modelling and Analysis, 2024, 29(2), pp. 277–287.

[36] Ogorelova D., Sadyrbaev F. On a three-dimensional neural network model Vibroengineering Procedia. 2022, vol. 47, pp. 6973.

[37] Ogorelova D., Sadyrbaev F. On control over system arising in the theory of neuronal networks. International Conference of Numerical Analysis and Applied Mathematics 2023 (ICNAAM 2023), (in print).

[38] Ogorelova D., Sadyrbaev F. Periodic attractors in GRN and ANN networks. IEEE Xplore, 2023, pp. 4.

[39] Ogorelova D., Sadyrbaev F. Remarks on mathematical modeling of gene and neuronal networks by ordinary differential equations. Axioms MDPI, 2024, 13(1), 61.

[40] Ogorelova D., Sadyrbaev F., Samuilik I. On attractors in dynamical systems modeling genetic networks. Advances in the Theory of Nonlinear Analysis and its Applications, 2023, 7(2), pp. 486-498.

[41] Ogorelova D., Sadyrbaev F., Samuilik I. On Targeted Control over Trajectories of Dynamical Systems Arising in Models of Complex Networks. Mathematics, 2023, 11(9), 2206.

[42] Ogorelova D., Sadyrbaev F., Samuilik I., Sengileyev V. Sigmoidal functions in network theories. Proceedings LU MII, vol 17 (2017), 52–71.

[43] Ogorelova D., Sadyrbaev F., Sengileyev V. Control in Inhibitory Genetic Regulatory Network Models. Contemporary Mathematics (Singapore), 2020, 1(5), pp. 393-400.

[44] Ogorelova D., Sengileyev V. Comparison of Two Mathematical Models for Genetic Networks. 1st international symposium on recent advances in fundamental and applied sciences (ISFAS-2021) abstract and full text congress book, 2021, pp. 161.

[45] T. Ohba, S. Arakawa, and M. Murata, "Bayesian-based virtual network reconfiguration for dynamic optical networks," IEEE/OSA Journal of

Optical Communications and Networking, vol. 10, pp. 440-450, Apr. 2018.

[46] A. Panagiotis, "Activation Functions: Sigmoid vs Tanh," Baeldung. 2024.

[47] F. Sadyrbaev, I. Samuilik. V. Sengileyev. On Modelling of Genetic Regulatory Networks. WSEAS Trans. Electronics, vol. 12, 2021, 73-80.

[48] Sadyrbaev F., Ogorelova D., Samuilik I. A Nullclines Approach to the Study of 2D Artificial Network. Contemporary Mathematics (Singapore), 2019, 1(1), pp. 1-11.

[49] F. Sadyrbaev. Planar differential systems arising in network regulation theory. *Advanced Mathematical Models & Applications*, Vol.4, No.1, 2019, pp.70-78

[50] F. Sadyrbaev, S. Atslega, E. Brokan. (2020) Dynamical Models of Interrelation in a Class of Artificial Networks. In: Pinelas S., Graef J.R., Hilger S., Kloeden P., Schinas C. (eds) Differential and Difference Equations with Applications. ICDDEA 2019. Springer Proceedings in Mathematics & Statistics, vol 333. Springer, Cham.

[51] F. Sadyrbaev, V. Sengileyev, A. Silvans. On Coexistence of Inhibition and Activation in Genetic Regulatory Networks. 19 Intern. Confer. Numer. Analys and Appl. Mathematics, Rhodes, Greece, 20-26 September 2021, To appear in AIP Conference Proceedings.

[52] I. Samuilik, F. Sadyrbaev. On a dynamical model of genetic networks. WSEAS Trans. Bus. Econ, 2023, 20, pp. 104112.

[53] I. Samuilik, F. Sadyrbaev. On trajectories of a system modeling evolution of genetic networks. Math Biosci Eng, 2023, 20(2), 2232–2242.

[54] Samuilik I., Sadyrbaev F., Ogorelova D. Comparative Analysis of Models of Gene and Neural Networks. Contemporary Mathematics (Singapore), 2023, 4(2), pp. 217-229.

[55] Samuilik I., Sadyrbaev F., Ogorelova D. Mathematical modeling of three-dimensional genetic regulatory networks using logistic and Gompertz functions. WSEAS Transactions on Systems and Control, 2022, 17, pp. 101-107.

[56] I. Samuilik, F. Sadyrbaev, V. Sengileyev. Examples of periodic biological oscillators: transition to a six-dimensional system, WSEAS Trans. Computer Research, vol. 10, 2022, 50-54.

[57] Samuilik I., Ogorelova D. Mathematical Modelling of GRN Using Different Sigmoidal Functions. 1st international symposium on recent advances in fundamental and applied sciences (ISFAS-2021) abstract and full text congress book, 2021, pp. 491.

[58] T. Schlitt. Approaches to Modeling Gene Regulatory Networks: A Gentle Introduction. In: Silico Systems Biology. Methods in Molecular Biology (Methods and Protocols), Humana Press, vol. 1021 (2013),13–35,doi:10.1007/978-1-62703-450-0

[59] S. Sharma. Activation Functions in Neural Networks. Towards Data Science, 2017.

[60] J.C. Sprott. Elegant Chaos. World Scientific, Singapore, 2010.

[61] V. Vemuri. Artificial Neural Networks in Control Applications. Advances in Computers, Vol. 36, 1993, pp. 203–254.

[62] J. Vohradský. Neural network model of gene expression. The FASEB Journal, Vol. 15, March 2001, 846–854.

[63] Le-Zhi Wang, Ri-Qi Su, Zi-Gang Huang, Xiao Wang, Wen-Xu Wang, Celso Grebogi and Ying-Cheng Lai. A geometrical approach to control and controllability of nonlinear dynamical networks. Nature Communications, Volume 7, Article number: 11323 (2016), DOI: 10.1038/ncomms11323

[64] H. R. Wilson, J. D. Cowan. Excitatory and inhibitory interactions in localized populations of model neurons. Biophys J., vol 12 (1), 1972, pp. 1-24.

[65] K. Yamazaki, Vo-Ho Viet-Khoa, B. Darshan and Ngan Le. Spiking Neural Networks and Their Applications: A Review. Brain Sci. 2022, 12(7), 63; https://doi.org/10.3390/brainsci12070863

ORIGINAL PAPERS

Gompertz function in the model of gene regulation network

Diana Ogorelova

Summary.
2D-model of gene regulation network is considered where the sigmoidal function is the Gompertz function. The description of attractors is obtained depending on parameters.

MSC: 34C10, 34D45, 92C42

1 Introduction

In the theory of gene regulatory networks differential systems are of the type

$$x_i' = f(\sum w_{ij}x_j) - x_i. \tag{1}$$

This system describes interrelation between elements (genes) of a gene network. We omit the mechanism of this interrelation and focus on the mathematical aspect. The function $f(z)$ in this model is a continuous bounded monotonically increasing function (that is called *sigmoidal regulatory function*). Matrix W consists of entries describing the relation between nodes of the networks. There are various functions f possessing the desired properties. For instance, the function $f(z) = \frac{1}{1+e^{-\mu z}}$ meets the requirements. The argument z is substituted by $z = \Sigma w_{ij}x_j - \theta$ and it represents the input on a gene with threshold θ for increasing x_i. The function $f(z)$ is a sigmoidal (monotone and bounded) function and 2×2 matrix W consists of entries that take values from the set $\{-1, 0, 1\}$. Systems of this kind appear in gene regulatory theory. The structure of attracting sets is studied.

2 The Formulation of the Problem

Two-component gene regulatory networks are described by the differential system

$$\begin{cases} x_1' = f(x_2) - x_1, \\ x_2' = f(x_1) - x_2. \end{cases} \tag{2}$$

where $f(x)$ is a sigmoidal function.

Definition 1. *A function is called sigmoidal if the following is satisfied.*

1. *$f(x)$ monotonically increases from* 0 *to* 1, $x \in \mathrm{R}$*;*
2. *It has exactly one inflection point.*

Consider the Gompertz function $f(z) = e^{-e^{-\mu z}}$. This function is sigmoidal in the sense of Definition 1.

The system in extended form is

$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(x_2-\theta)}} - x_1, \\ \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(x_1-\theta)}} - x_2, \end{cases} \tag{3}$$

where μ and θ are positive parameters. Our goal is to study the phase portrait and the attracting sets of this system.

Gompertz function is sigmoidal function. The grapf of f and graphs of f' and f'' are depicted in Fig. 2.1 for the values of parameters $\mu = 6.5$ and $\theta = 0.3$. It is convex in some neighborhood of zero and then it is concave. It is bounded by 1 and it is monotonically increasing.

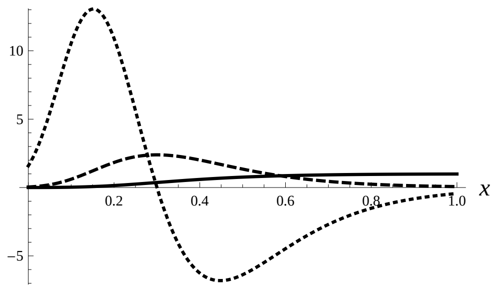


Fig. 2.1. Solid - $f(x)$, dashed - $f'(x)$, dotted - $f''(x)$

3 System for critical points

It is supposed that $f(z)$ is dependent also on a parameter μ that regulates steepness of the graph of f. We wish to state general properties of the system (3).

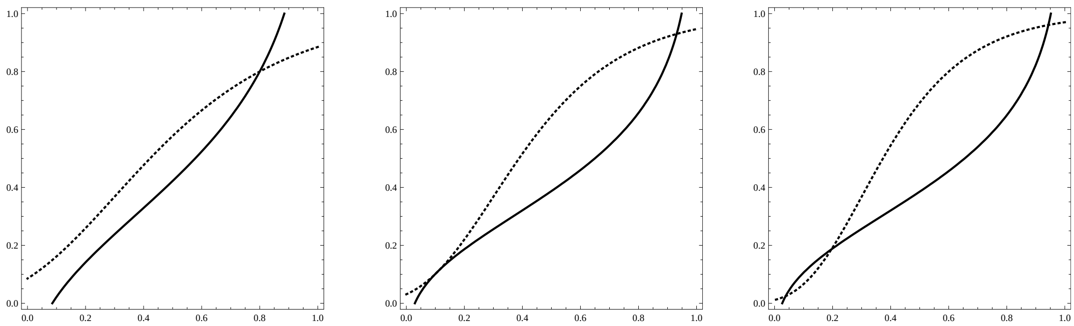
Critical points of this system are solutions of

$$\begin{cases} 0 = e^{-e^{-\mu(x_2-\theta)}} - x_1, \\ 0 = e^{-e^{-\mu(x_1-\theta)}} - x_2. \end{cases} \tag{4}$$

Lemma 1. *Any critical point is of the form (x, x). Therefore, the coordinate x of a critical point is defined from*

$$x = f(x). \tag{5}$$

The graphs of $y = f(x)$ and $y = f^{-1}(x)$ are depicted in Fig. 3.1.



a) $\theta = 0.3$, $\mu = 0.3$, 1 critical point

b) $\theta = 0.3$, $\mu \approx 4.15$, 2 critical point

c) $\theta = 0.3$, $\mu = 5$, 3 critical point

Fig. 3.1.

For $\mu < e$ we have the relation in Fig. 3.1.(a). For $\mu > e$ we have the relation in Fig. 3.1.(c).

It is evident that for some values of parameters there is exactly one critical point and for some values of μ and θ there are three points. As an intermediate state we have Fir. 3.1.(b) with exactly two critical points. Our goal is to clarify which values of parameters correspond to 1, 2 or 3 critical points.

3.1 Linearized system

The linearized system around a possible critical point (x_1, x_2) is

$$\begin{cases} u' = -u + \mu e^{-e^{-\mu(x_2-\theta)}-\mu(x_2-\theta)} \cdot v, \\ v' = \mu e^{-e^{-\mu(x_1-\theta)}-\mu(x_1-\theta)} \cdot u - v. \end{cases} \tag{6}$$

Since $x_1 = x_2$ the system looks

$$\begin{cases} u' = -u + \mu e^{-e^{-\mu(x-\theta)} - \mu(x-\theta)} \cdot v, \\ \\ v' = \mu e^{-e^{-\mu(x-\theta)} - \mu(x-\theta)} \cdot u - v. \end{cases} \tag{7}$$

Therefore, by (4) and Lemma 1, the coordinate x of any critical point (x, x) satisfies

$$x = e^{-e^{-\mu(x-\theta)}},$$

$$-\ln(x) = e^{-\mu(x-\theta)}.$$

Let consider $a = \mu e^{-e^{-\mu(x-\Theta)} - \mu(x-\Theta)} = \mu x(-\ln(x))$, then

$$\begin{cases} u' = -u + a \cdot v, \\ \\ v' = a \cdot u - v. \end{cases} \tag{8}$$

We get from $x = e^{-e^{-\mu(x-\theta)}}$ by logarithmation $\ln(-\ln(x)) = -\mu(x - \theta)$. For θ and $x \in (0, 1)$ we get the formula (9)

$$\theta = x + \frac{1}{\mu} \ln(-\ln(x)). \tag{9}$$

The relation (9) is visualized in Fig. 3.2

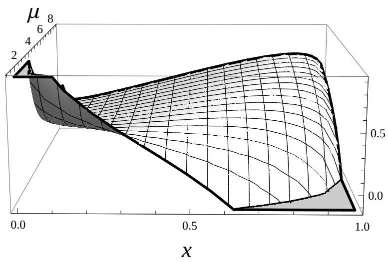
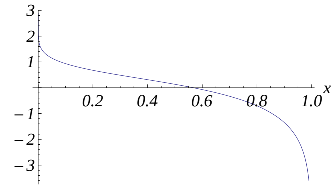


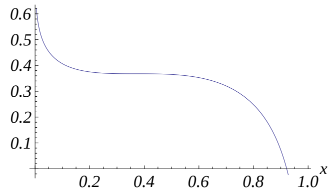
Fig. 3.2. The dependence of θ (for critical point (x, x)) of μ

Fig. 3.3 shows that for some μ and θ there are respectively one, two or three critical points.

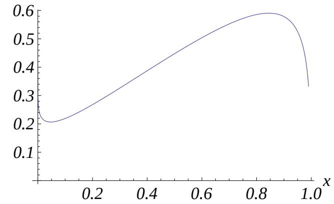
For different μ dependence θ of x is visualized below.



a)The dependence of θ of x for $\mu = 1$



b)The dependence of θ of x for $\mu = e$



c)The dependence of θ of x for $\mu = 7$

Fig. 3.3.

Look at the second and the third of pictures in Fig. 3.3. There is an interval where $\theta(x)$ is increasing. Let us make analysis of this.

One has that

$$\theta'(x) = 1 + \frac{1}{\mu}\frac{1}{x\ln x} \tag{10}$$

and $\theta'(x) = 0$ if

$$\frac{1}{x\ln x} = -\mu. \tag{11}$$

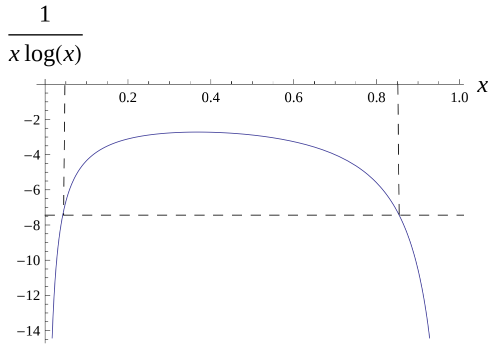


Fig. 3.4. The graph of $\frac{1}{x\ln x}$

The function $\theta'(x) > 0$ if $\frac{1}{x\ln x} > -\mu$. Denote solutions of the equation (11) $x_1(\mu)$ and $x_2(\mu)$ respectively. Horizontal dashed line in Fig. 3.4 is for $-\mu$ and two vertical dashed lines are for $x_1(\mu)$ and $x_2(\mu)$.

Consider

$$\theta_1(\mu) = x_1(\mu) + \frac{1}{\mu}\ln(-\ln(x_1(\mu)))$$

and

$$\theta_2(\mu) = x_2(\mu) + \frac{1}{\mu}\ln(-\ln(x_2(\mu))).$$

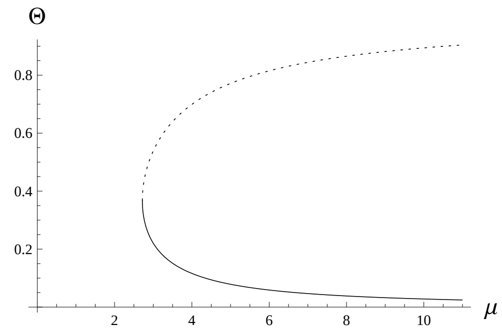


Fig. 3.5. The graphs of $\theta_1(\mu)$ and $\theta_2(\mu)$ together.

The region Ω between $\theta_1(\mu)$ (lower branch) and $\theta_2(\mu)$ (upper branch) corresponds to three critical points of the system, that is, for $(\mu, \theta) \in \Omega$ there are exactly three critical points.

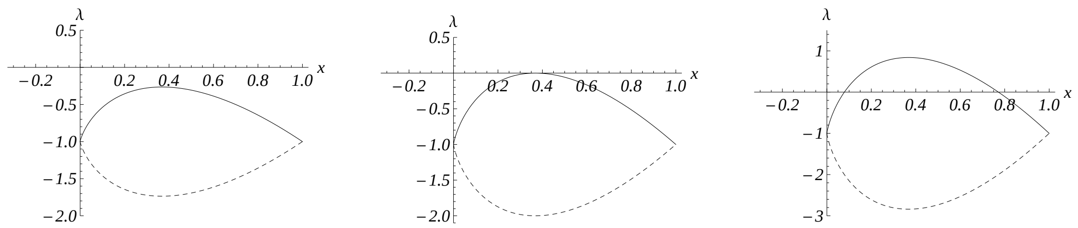
The characteristic equation for the linearized system (7) is

$$\det(A - \lambda I) = \begin{vmatrix} -1-\lambda & a \\ a & -1-\lambda \end{vmatrix} = \begin{vmatrix} -1-\lambda & \mu x(-\ln(x)) \\ \mu x(-\ln(x)) & -1-\lambda \end{vmatrix} = \tag{12}$$

$$= (-1-\lambda)^2 - \mu^2 x^2 (-\ln(x))^2 = 0$$

or $\lambda = -1 \pm a$. Therefore $\lambda_1 = -1 - a$ is always negative and $\lambda_2 = -1 + a$. There are three possibilities for critical points:

1. $\lambda_2 < 0$ then (x, x) is stable node;
2. $\lambda_2 = 0$ then (x, x) is stable degenerate point;
3. $\lambda_2 > 0$ then (x, x) is saddle point.



a) $\mu = 2$ b) $\mu = e$ c) $\mu = 5$

Fig. 3.6. Roots of characteristic equation (12), solid line is $\lambda_2 = -1 + \mu x(-\ln(x))$, dashed line is $\lambda_1 = -1 - \mu x(-\ln(x))$, for a) $\mu \in (0, e)$, b) $\mu = e$ and c) $\mu \in (e, +\infty)$

The dependence of λ -s of x and $x = e^{-e^{-\mu(x-\theta)}}$ of θ (for μ given) is depicted in Fig. 3.6.

We observed that attractors for system (2) are either stable nodes or degenerate points with $\lambda_1 < 0, \lambda_2 = 0$.

Proposition 1. The system (2) cannot have critical points of type focus.

Proof. It follows from (12), that $\lambda = -1 \pm \mu x(-\ln(x))$ and λ cannot be complex number. $\square$

Theorem 2. *There are four cases for system* (2)*:*

1. *There is exactly one critical point of the type stable node.*
2. *There is a unique critical point with* $\lambda_1 < 0, \lambda_2 = 0$*. It is degenerate stable critical point.*
3. *There are exactly two critical points, one of them is stable node, another one is degenerate stable critical point.*
4. *There are exactly three critical points. Side critical points are stable nodes, middle point is a saddle.*

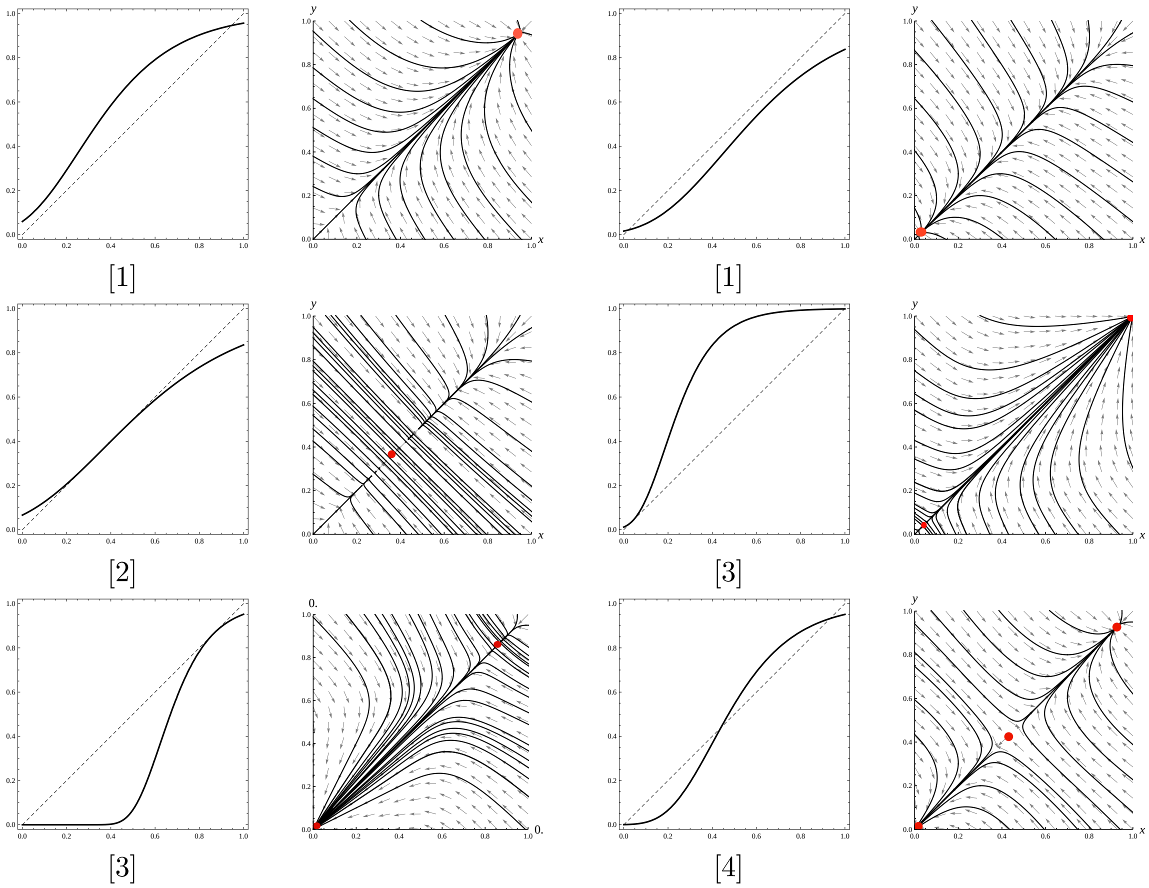


Fig. 3.7. Visualization of Theorem 1

Example 1. *Let consider* $\mu = 3$ *and* $\theta = 0.3$. *There are respectively one critical point* $(0.8, 0.8)$. *The phase portrait of system* (3) *for one critical point is*

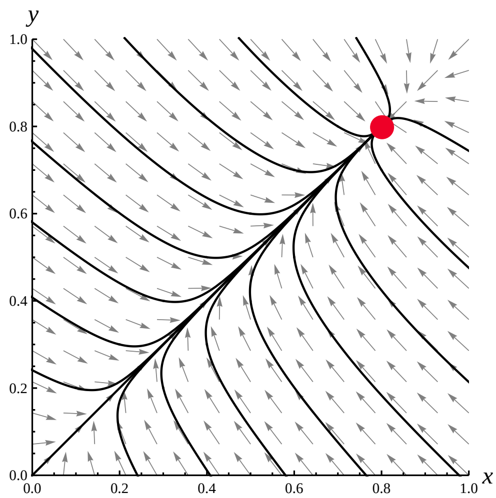


Fig. 3.8. Critical point is a stable node $(\lambda_1 < 0, \lambda_2 < 0)$

Example 2. *Let consider* $\mu = 4.15$ *and* $\theta = 0.3$. *There are respectively two critical points* $(0.93, 0.93)$ *and* $(0.11, 0.11)$. *The phase portrait of system* (3) *for two critical points is*

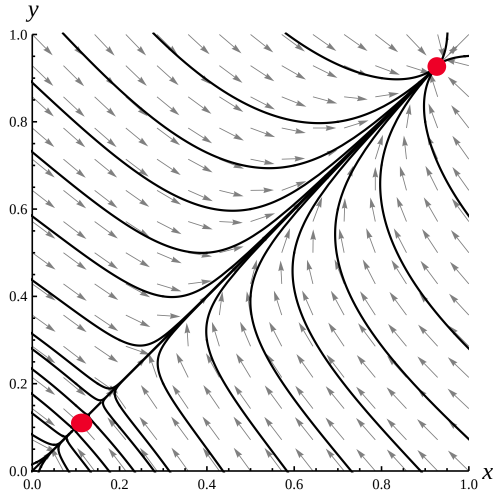


Fig. 3.9. First point is degenerate stable critical point, another one is stable node

Example 3. *Let consider* $\mu = 5$ *and* $\theta = 0.3$. *There are respectively three critical points* $(0.02, 0.02)$, $(0.21, 0.21)$, $(0.96, 0.96)$. *The phase portrait of system* (3) *for three critical points is*

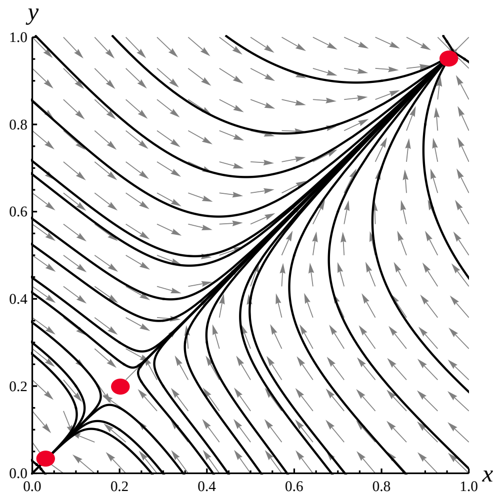


Fig. 3.10. Side critical points are stable nodes, middle point is a saddle

4 Summing up the results

We have defined the region Ω in (μ, θ)-plane with the properties:

- if $(\mu, \theta) \in \Omega$ then there are exactly three critical points with the properties - two side critical points are stable nodes, middle (central) point is a saddle;
- if $(\mu, \theta) \in \partial\Omega$ then there are exactly two critical points with the properties - the first critical point is stable node, the second is degenerate point $(\lambda_1 < 0, \lambda_2 = 0)$;
- if $(\mu, \theta) \in Q \setminus \overline{\Omega}$ then there is exactly one critical point with the properties - it is a stable node;
- the common point of lower and upper branches of $\partial\Omega$ corresponds to a unique critical point with $\lambda_1 < 0, \lambda_2 = 0$, depictedin Fig. 3.7 [2].

References

[1] V. Acary, H. de Jong, B. Brogliato. Numerical simulation of piecewise-linear models of gene regulatory networks using complementarity system. Physica D: Nonlinear Phenomena Volume 269, 15 February 2014, Pages 103-119.

[2] D.K. Arrowsmith and C.M. Place. Dynamical Systems. Differential equations, maps and haotic behavior. Chapman and Hall/CRC, London (1992).

[3] S. Atslega, D. Finaskins, F. Sadyrbaev. On a Planar Dynamical System Arising in the Network Control Theory, Mathematical Modelling and Analysis, 21 (2016), N 3, 385 - 398.

[4] E. Brokan and F. Zh. Sadyrbaev. On attractors in gene regulatory systems, AIP Conference Proceedings 1809, 020010 (2017): Proc. of the 6th International Advances In Applied Physics And Materials Science Congress & Exhibition (APMAS 2016), 1-3 June 2016, Istanbul, Turkey,; doi: 10.1063/1.4975425

[5] Y. Koizumi, T. Miyamura, S. Arakawa, E. Oki, K. Shiomoto, and M. Murata, "Robust virtual network topology control based on attractor selection," in Proceedings of ONDM, pp. 123 – 128, Feb. 2009.

[6] Y. Koizumi et al. Adaptive Virtual Network Topology Control Based on Attractor Selection. Journal of Lightwave Technology (ISSN : 0733-8724), Vol.28 (06/2010), Issue 11, pp. 1720 - 1731 DOI:10.1109/JLT.2010.2048412

[7] Y. Koizumi, T. Miyamura, S. Arakawa, E. Oki, K. Shiomoto, and M. Murata, "Application of attractor selection to adaptive virtual network topology control," in Proceedings of BIONETICS, pp. 1 -– 8, Nov. 2008.

D. Ogorelova. Gomperca funkcija gēnu regulēšanas sistēmas modelī.
Anotācija. Tiek apskatīts gēnu regulēšanas sistēmas 2-dimensiju modelis, kurā par sigmoidālu funkciju kalpo Gomperca funkcija. Sistēmas atraktori tiek apskatīti atkarībā no iebūvētiem parametriem.

Д. Огорелова. Функция Гомперца в модели генной регулятивной сети.
Аннотация. В статье рассматривается 2-мерная модель генной регулятивной сети, в которой сигмоидальной функцией является функция Гомперца. Получено описание аттракторов системы в зависимости от параметров.

Daugavpils University
Daugavpils, Vienibas str. 13
diana.ogorelova@daugvt.lv

Received 13.12.2018

Description of critical points for some system arising in applications

Diana Ogorelova

Summary. 3D-model of gene regulation network is considered where the sigmoidal function is the Gompertz function. The description of attractors is obtained depending on parameters.

MSC: 34C10, 34D45, 92C42

1 Introduction

Various models of different type networks can be described by dynamical system

$$\begin{cases} x' = f_1(x, y, z, \mu_1, \theta_1, w_{11}, w_{12}, w_{13}) - \gamma_1 x, \\ y' = f_2(x, y, z, \mu_2, \theta_2, w_{21}, w_{22}, w_{23}) - \gamma_2 y, \\ z' = f_3(x, y, z, \mu_3, \theta_3, w_{31}, w_{32}, w_{33}) - \gamma_3 z, \end{cases} \tag{1}$$

where f_i are sigmoidal functions. This system reflects the interrelation between nodes of a network. Nodes are denoted x_i. In majority of papers on the subject the logistic sigmoidal function $f(z) = \frac{1}{1+e^{-\mu z}}$ was used. As a sigmoidal function we have chosen the Gompertz function

$$f(z) = e^{-e^{-\mu z}},$$

where μ is a parameter.

Systems of the form (1) are believed to model telecommunication ([7], [8], [9]) and genetic regulatory networks ([1]). The review articles [2], [6], [10] can be used by interested reader to explore the topic.

2 Preliminary result

Three-component gene regulatory networks are described by the differential system (1) where f is a sigmoidal function and

$$\begin{cases} f_1 = \exp(-\exp[-\mu_1(w_{11}x + w_{12}y + w_{13}z - \theta_1)]), \\ f_2 = \exp(-\exp[-\mu_2(w_{21}x + w_{22}y + w_{23}z - \theta_2)]), \\ f_3 = \exp(-\exp[-\mu_3(w_{31}x + w_{32}y + w_{33}z - \theta_3)]). \end{cases} \tag{2}$$

We assume that μ_1, μ_2 and μ_3 are positive, as well as γ_1, γ_2 and γ_3.

First consider the nullclines of the system (1) which are given by

$$\begin{cases} \gamma_1 x = \exp(-\exp[-\mu_1(w_{11}x + w_{12}y + w_{13}z - \theta_1)]), \\ \gamma_2 y = \exp(-\exp[-\mu_2(w_{21}x + w_{22}y + w_{23}z - \theta_2)]), \\ \gamma_3 z = \exp(-\exp[-\mu_3(w_{31}x + w_{32}y + w_{33}z - \theta_3)]). \end{cases} \tag{3}$$

It is supposed that Gompertz function is dependent also on a parameter μ that regulates steepness of the graph of f. We wish to state general properties of the system (3).

Critical points of this system are solutions of

$$\begin{cases} 0 = \exp(-\exp[-\mu_1(w_{11}x + w_{12}y + w_{13}z - \theta_1)]) - \gamma_1 x, \\ 0 = \exp(-\exp[-\mu_2(w_{21}x + w_{22}y + w_{23}z - \theta_2)]) - \gamma_2 y, \\ 0 = \exp(-\exp[-\mu_3(w_{31}x + w_{32}y + w_{33}z - \theta_3)]) - \gamma_3 z. \end{cases} \tag{4}$$

In order to detect the type of the critical point consider the linearized system

$$\begin{cases} u' = (-\gamma_1 + g_1\mu_1 w_{11})u + g_1\mu_1 w_{12} v + g_1\mu_1 w_{13} w, \\ v' = g_2\mu_2 w_{21} u + (-\gamma_2 + g_2\mu_2 w_{22})v + g_2\mu_2 w_{23} w, \\ w' = g_3\mu_3 w_{31} u + g_3\mu_3 w_{32} v + (-\gamma_3 + g_3\mu_3 w_{33})w, \end{cases} \tag{5}$$

where

$$\begin{cases} g_1 = \exp(-\exp[-\mu_1(w_{11}x + w_{12}y + w_{13}z - \theta_1)] - \mu_1(w_{11}x + w_{12}y + w_{13}z - \theta_1), \\ g_2 = \exp(-\exp[-\mu_2(w_{21}x + w_{22}y + w_{23}z - \theta_2)] - \mu_2(w_{21}x + w_{22}y + w_{23}z - \theta_2), \\ g_3 = \exp(-\exp[-\mu_1(w_{31}x + w_{32}y + w_{33}z - \theta_3)] - \mu_3(w_{31}x + w_{32}y + w_{33}z - \theta_3) \end{cases} \tag{6}$$

and x, y, z are coordinates of a critical point. The characteristic equation for the linearized system (5) is

$$\det(A - \lambda I) = \begin{vmatrix} (-\gamma_1 + g_1\mu_1 w_{11}) - \lambda & g_1\mu_1 w_{12} & g_1\mu_1 w_{13} \\ g_2\mu_2 w_{21} & (-\gamma_2 + g_2\mu_2 w_{22}) - \lambda & g_2\mu_2 w_{23} \\ g_3\mu_3 w_{31} & g_3\mu_3 w_{32} & (-\gamma_3 + g_3\mu_3 w_{33}) - \lambda \end{vmatrix} = \tag{7}$$
$$= -\lambda^3 + D\lambda^2 + E\lambda + F = 0$$

where

$$D = -\gamma_1 - \gamma_2 - \gamma_3 + g_1\mu_1 w_{11} + g_2\mu_2 w_{22} + g_3\mu_3 w_{33}, \tag{8}$$

$$E = -\gamma_1\gamma_2 - \gamma_1\gamma_3 - \gamma_2\gamma_3 + \gamma_1 g_2\mu_2 w_{22} + \gamma_1 g_3\mu_3 w_{33} \\ + \gamma_2 g_1\mu_1 w_{11} + \gamma_2 g_3\mu_3 w_{33} + \gamma_3 g_1\mu_1 w_{11} + \gamma_3 g_2\mu_2 w_{22} - \\ - g_1\mu_1 w_{11} g_2\mu_2 w_{22} - g_1\mu_1 w_{11} g_3\mu_3 w_{33} - g_2\mu_2 w_{22} g_3\mu_3 w_{33} + \\ + g_1\mu_1 w_{12} g_2\mu_2 w_{21} + g_1\mu_1 w_{13} g_3\mu_3 w_{31} + g_2\mu_2 w_{23} g_3\mu_3 w_{32}, \tag{9}$$

$$F = -\gamma_1\gamma_2\gamma_3 + \gamma_1\gamma_3 g_2\mu_2 w_{22} + \gamma_1\gamma_2 g_3\mu_3 w_{33} + \gamma_2\gamma_3 g_1\mu_1 w_{11} - \\ - \gamma_1 g_2\mu_2 w_{22} g_3\mu_3 w_{33} + \gamma_1 g_2\mu_2 w_{23} g_3\mu_3 w_{32} - \gamma_2 g_1\mu_1 w_{11} g_3\mu_3 w_{33} + \\ + \gamma_2 g_1\mu_1 w_{13} g_3\mu_3 w_{31} - \gamma_3 g_1\mu_1 w_{11} g_2\mu_2 w_{22} + \gamma_3 g_1\mu_1 w_{12} g_2\mu_2 w_{21} + \\ + g_1\mu_1 w_{11} g_2\mu_2 w_{22} g_3\mu_3 w_{33} - g_1\mu_1 w_{11} g_2\mu_2 w_{23} g_3\mu_3 w_{32} + \\ + g_1\mu_1 w_{13} g_2\mu_2 w_{21} g_3\mu_3 w_{32} - g_1\mu_1 w_{12} g_2\mu_2 w_{21} g_3\mu_3 w_{33} + \\ + g_1\mu_1 w_{12} g_2\mu_2 w_{23} g_3\mu_3 w_{31} - g_1\mu_1 w_{13} g_2\mu_2 w_{22} g_3\mu_3 w_{31}. \tag{10}$$

We consider the three possibilities for critical points:

1. $\lambda_{1,2,3} < 0$ then (x, y, z) is stable node;
2. $\lambda_1 < 0$, $\lambda_2 > 0$, $\lambda_3 \in R$ then (x, y, z) is saddle point;
3. $\lambda_1 \in R$, $\lambda_{2,3} = \alpha \pm i\beta$ then (x, y, z) is focus:
   - $\lambda_1 < 0$ and $\alpha < 0$ then (x, y, z) is stable focus;
   - $\lambda_1 \in R$ and $\alpha > 0$ then (x, y, z) is unstable focus.

2.1 A particular case

We are interested also in a particular case where $w_{ii} = 0, i = 1, 2, 3$. Then formulas (8), (9), (10) take the form

$$D_* = -\gamma_1 - \gamma_2 - \gamma_3, \tag{11}$$

$$E_* = -\gamma_1\gamma_2 - \gamma_1\gamma_3 - \gamma_2\gamma_3 + g_1\mu_1 w_{12} g_2\mu_2 w_{21} + g_1\mu_1 w_{13} g_3\mu_3 w_{31} + g_2\mu_2 w_{23} g_3\mu_3 w_{32}, \tag{12}$$

$$F_* = -\gamma_1\gamma_2\gamma_3 + \gamma_1 g_2\mu_2 w_{23} g_3\mu_3 w_{32} + \gamma_2 g_1\mu_1 w_{13} g_3\mu_3 w_{31} + \gamma_3 g_1\mu_1 w_{12} g_2\mu_2 w_{21} + \\ + g_1\mu_1 w_{13} g_2\mu_2 w_{21} g_3\mu_3 w_{32} + g_1\mu_1 w_{12} g_2\mu_2 w_{23} g_3\mu_3 w_{31}. \tag{13}$$

2.2 Reminder on cubic equations

Consider the cubic equation

$$\lambda^3 - E\lambda - F = 0. \tag{14}$$

Any general cubic equation (with the quadratic term) can be reduced to the above form. The Cardano formula for the roots of (14) has the form:

$$\lambda = \sqrt[3]{\frac{F}{2} + \sqrt{\frac{(-F)^2}{4} + \frac{(-E)^3}{27}}} + \sqrt[3]{\frac{F}{2} - \sqrt{\frac{(-F)^2}{4} + \frac{(-E)^3}{27}}}. \tag{15}$$

In this formula one must choose, for each of the three values of the cube root

$$\alpha = \sqrt[3]{\frac{F}{2} + \sqrt{\frac{(-F)^2}{4} + \frac{(-E)^3}{27}}}, \tag{16}$$

that value of the cube root

$$\beta = \sqrt[3]{\frac{F}{2} - \sqrt{\frac{(-F)^2}{4} + \frac{(-E)^3}{27}}}, \tag{17}$$

for which the relation $\alpha\beta = \frac{E}{3}$ holds (such a value of β always exists). In the Cardano formula, E and F are arbitrary complex numbers. In the case of real coefficients E and F, the property of the roots being real or imaginary depends on the sign of the discriminant of the equation,

$$\mathbf{D} = -27(-F)^2 - 4(-E)^3 = -108\left(\frac{(-F)^2}{4} + \frac{(-E)^3}{27}\right). \tag{18}$$

When $\mathbf{D} > 0$ all three roots are real and distinct. However, according to Cardano's formula, the roots are expressed in terms of cube roots of imaginary quantities. Although in this case both the coefficients and the roots are real, the roots cannot be expressed in terms of the coefficients by means of radicals of real numbers; for this reason, the above case is called irreducible.

When $\mathbf{D} = 0$, all roots are real; when E and F are both non-zero, there is one double and one single root; and when E and F are both zero, there is one triple root.

When $\mathbf{D} < 0$, all three roots are distinct, one of them being a real number and the other two — conjugate complex numbers.

3 Examples

Consider a number of examples illustrating (and confirming) our analysis.

1-st Example. Set the parameters to

$$\mu_1 = 7, \mu_2 = 7, \mu_3 = 13, \theta_1 = 0.5, \theta_2 = 0.3, \theta_3 = 0.7, \gamma_1 = 0.62, \gamma_2 = 0.42, \gamma_3 = 0.1,$$
$$w_{11} = 0, w_{12} = 1, w_{13} = -1, w_{21} = 1, w_{22} = 0, w_{23} = -1, w_{31} = 1, w_{32} = 0.1, w_{33} = 0.$$

The system of ODE then takes the form

$$\begin{cases} x' = \exp(-\exp[-7(y-z-0.5)]) - 0.62x, \\ y' = \exp(-\exp[-7(x-z-0.3)]) - 0.42y, \\ z' = \exp(-\exp[-13(x+0.1y-0.7)]) - 0.1z. \end{cases} \tag{19}$$

In order to detect the type of the first critical point consider the linearized system

$$\begin{cases} u' = -0.62u + 1.11983 \cdot 10^{-12}v - 1.11983 \cdot 10^{-12}w, \\ v' = 0.01624u - 0.42v - 0.01624w, \\ w' = 1.77831 \cdot 10^{-3881}u + 1.77831 \cdot 10^{-3882}v - 0.1w. \end{cases} \tag{20}$$

The characteristic equation for the linearized system (20) is

$$-\lambda^3 - 1.14\lambda^2 - 0.3644\lambda - 0.02604 = 0$$

The first critical point is $(7.7448 \cdot 10^{-15}; 0.000676438; 0)$: Values of λ for this critical point is

$$\begin{cases} \lambda_1 = -0.62, \\ \lambda_2 = -0.42, \\ \lambda_3 = -0.1. \end{cases} \tag{21}$$

In this example the 3D system of the (1) has one critical point (stable node in 2D-subspace and a attraction in the remaining).

In order to detect the type of the second critical point consider the linearized system

$$\begin{cases} u' = -0.62u + 2.55801v - 2.55801w, \\ v' = 2.53905u - 0.42v - 2.53905w, \\ w' = 1.19739u + 0.119739v - 0.1w. \end{cases} \tag{22}$$

The characteristic equation for the linearized system (22) is

$$-\lambda^3 - 1.14\lambda^2 + 2.76355\lambda - 9.4061 = 0$$

The second critical point is $(0.526218; 0.733372; 0.249572)$: Values of λ for this critical point is

$$\begin{cases} \lambda_1 = -3.05369, \\ \lambda_2 = 0.956843 - 1.47129i, \\ \lambda_3 = 0.956843 + 1.47129i. \end{cases} \tag{23}$$

In this example the 3D system of the (1) has another critical point (unstable focus).

2-nd Example. Set the parameters to Consider a number of examples illustrating (and confirming) our analysis. For parameters

$$\mu_1 = 0.3, \mu_2 = 3, \mu_3 = 0.8, \theta_1 = 0.3, \theta_2 = 0.01, \theta_3 = 1, \gamma_1 = 1, \gamma_2 = 1, \gamma_3 = 1,$$
$$w_{11} = 0, w_{12} = -5, w_{13} = 0, w_{21} = 10, w_{22} = 0, w_{23} = 0, w_{31} = -3, w_{32} = 0, w_{33} = 0.$$

The system of ODE then takes the form

$$\begin{cases} x' = \exp(-\exp[-0.3(-5y - 0.5)]) - x, \\ y' = \exp(-\exp[-3(10x - 0.01)]) - y, \\ z' = \exp(-\exp[-0.8(-3x - 1)]) - z. \end{cases} \tag{24}$$

In order to detect the type of the critical point consider the linearized system

$$\begin{cases} u' = -u - 0.189317v, \\ v' = 6.98811u - v, \\ w' = -0.509481u - w. \end{cases} \tag{25}$$

The characteristic equation for the linearized system (25) is

$$-\lambda^3 - 3\lambda^2 - 4.32297\lambda - 2.32297 = 0$$

The critical point is $(0.0388611; 0.725311; 0.0868913)$: Values of λ for this critical point is

$$\begin{cases} \lambda_1 = -1, \\ \lambda_2 = -1 - 1.1502i, \\ \lambda_3 = -1 + 1.1502i. \end{cases} \tag{26}$$

In this example the 3D system of the (1) has one critical point (stable focus).

References

[1] V. Acary, H. de Jong, B. Brogliato. Numerical simulation of piecewise-linear models of gene regulatory networks using complementarity system. Physica D: Nonlinear Phenomena Volume 269, 15 February 2014, Pages 103-119.

[2] F. M. Alakwaa, Modeling of Gene Regulatory Networks: A Literature Review, *Journal of Computational Systems Biology*, **1**(1):67-103, 2002.

[3] D.K. Arrowsmith and C.M. Place. Dynamical Systems. Differential equations, maps and haotic behavior. Chapman and Hall/CRC, London (1992).

[4] S. Atslega, D. Finaskins, F. Sadyrbaev. On a Planar Dynamical System Arising in the Network Control Theory, Mathematical Modelling and Analysis, 21 (2016), N 3, 385 - 398.

[5] E. Brokan and F. Zh. Sadyrbaev. On attractors in gene regulatory systems, AIP Conference Proceedings 1809, 020010 (2017): Proc. of the 6th International Advances In Applied Physics And Materials Science Congress & Exhibition (APMAS 2016), 1-3 June 2016, Istanbul, Turkey,; doi: 10.1063/1.4975425

[6] H. D. Jong, Modeling and Simulation of Genetic Regulatory Systems: A Literature Review. *Journal of computational biology*, **9**, 67 – 103 (2002).

[7] Y. Koizumi, T. Miyamura, S. Arakawa, E. Oki, K. Shiomoto, and M. Murata, "Robust virtual network topology control based on attractor selection," in Proceedings of ONDM, pp. 123 – 128, Feb. 2009.

[8] Y. Koizumi et al. Adaptive Virtual Network Topology Control Based on Attractor Selection. Journal of Lightwave Technology (ISSN : 0733-8724), Vol.28 (06/2010), Issue 11, pp. 1720 - 1731 DOI:10.1109/JLT.2010.2048412

[9] Y. Koizumi, T. Miyamura, S. Arakawa, E. Oki, K. Shiomoto, and M. Murata, "Application of attractor selection to adaptive virtual network topology control," in Proceedings of BIONETICS, pp. 1 -– 8, Nov. 2008.

[10] N. Vijesh, S. K. Chakrabarti, J. Sreekumar, Modeling of gene regulatory networks: A review, *J. Biomedical Science and Engineering*, **6**:223-231, 2013.

D. Ogorelova. Gomperca funkcija gēnu regulēšanas sistēmas modelī.
Anotācija. Tiek apskatīts gēnu regulēšanas sistēmas 3-dimensiju modelis, kurā par sigmoidālu funkciju kalpo Gomperca funkcija.

Д. Огорелова. Функция Гомперца в модели генной регулятивной сети.
Аннотация. В статье рассматривается 3-мерная модель генной регулятивной сети, в которой сигмоидальной функцией является функция Гомперца.

Daugavpils University
Daugavpils, Vienibas str. 13
diana.ogorelova@daugvt.lv

Received 10.12.2019.

UNIVERSAL WISER
PUBLISHER

Control in Inhibitory Genetic Regulatory Network Models

D. Ogorelova[1], F. Sadyrbaev[1,2*], V. Sengileyev[1]
[1]Faculty of Natural Sciences and Mathematics, Daugavpils University, Daugavpils, Latvia
[2]Institute of Mathematics and Computer Science, University of Latvia, Riga, Latvia
Email: felix@latnet.lv

Abstract: The system of two the first order ordinary differential equations arising in the gene regulatory networks theory is studied. The structure of attractors for this system is described for three important behavioral cases: activation, inhibition, mixed activation-inhibition. The geometrical approach combined with the vector field analysis allows treating the problem in full generality. A number of propositions are stated and the proof is geometrical, avoiding complex analytic. Although not all the possible cases are considered, the instructions are given what to do in any particular situation.
Keywords: gene regulatory networks, control, attractors

1. Introduction

Theory of genetic regulatory networks (GRN in short) is in the center of biomathematics. There are several ways of modelling GRN, for instance, boolean algebras, graph theory and more, [1-3]. Modelling in terms of dynamical systems allows to follow evolution of GRN. The system we wish to study, appears in multiple contexts[4-6] in vectorial form

$$x_i' = f(\sum w_{ij}x_j - \theta_i) - x_i. \qquad (1)$$

This system describes interrelation between elements (genes) of a gene network. We omit the mechanism of this interrelation (one can consult [3-5]) and focus on the mathematical aspect. The function $f(z)$ in this model is a continuous bounded monotonically increasing function (that is called *sigmoidal regulatory function*). Matrix $W = (w_{ij})$ consists of entries describing the relation between nodes of the networks. There are various functions f possessing the desired properties. For instance, the function $f(z) = \frac{1}{1+e^{-uz}}$ meets the requirements. The argument z is substituted by $z = \Sigma w_{ij}x_j - \theta$ and it represents the input on a gene with threshold θ for increasing x_i. The function $f(z)$ is a sigmoidal (monotone and bounded) function and 2×2 matrix W_{ij} consists of entries that take values from the set $\{-1, 0, 1\}$. The decisive role in the evolution of a GRN play attracting sets. The structure of attracting sets of system (1) is studied. The ability of controlling the network by change of adjustable parameters is in a focus. Let us recall the citation from [5]: “For a given set of parameters, the multiple attractors (for example, stable steady states) and the corresponding basins are fixed. In the absence of stochasticity, for a given initial condition, the system will approach one of the attractors. Each attractor has specific biological significance, which can be regarded as either desired or undesired, depending on the particular function of interest. Suppose, without any control, the system is in an undesired attractor or is in its basin of attraction. The question is how to steer the system from the undesired state to a desired state.” The purpose of our article is to show and explain in geometrical and analytical terms, how to do this for system (2).

2. Problem

Two-component gene regulatory networks, where the stochasticity terms are neglected, are described[7] by the differential system

DOI: https://doi.org/10.37256/cm.152020538

$$\begin{cases} \frac{dx_1}{dt} = f(-\mu_1(w_{11}x_1 + w_{12}x_2 - \theta_1)) - x_1, \\ \frac{dx_2}{dt} = f(-\mu_2(w_{21}x_1 + w_{22}x_2 - \theta_2)) - x_2, \end{cases} \tag{2}$$

where f is a sigmoidal function.

Definition 1. A function is called sigmoidal if the following is satisfied.

1. $f(x)$ monotonically increases from 0 to 1, $x \in R$;
2. It has exactly one inflection point.

Two typical examples of sigmoidal functions more often used in modelling GRN, are the Gompertz function $f(z) = e^{-\mu(z-\theta)}$ and the logistic function $f(z) = 1/(1 + e^{-\mu(z-\theta)})$. The argument z can be complicated. The 2D system, where f is the Gompertz function, is

$$\begin{cases} \frac{dx_1}{dt} = e^{-e^{-\mu_1(w_{11}x_1 + w_{12}x_2 - \theta_1)}} - x_1, \\ \frac{dx_2}{dt} = e^{-e^{-\mu_2(w_{21}x_1 + w_{22}x_2 - \theta_2)}} - x_2. \end{cases} \tag{3}$$

GRN model in this form was studied in [8-9]. Since we wish to consider systems with any sigmoidal function, we will use the form (2).

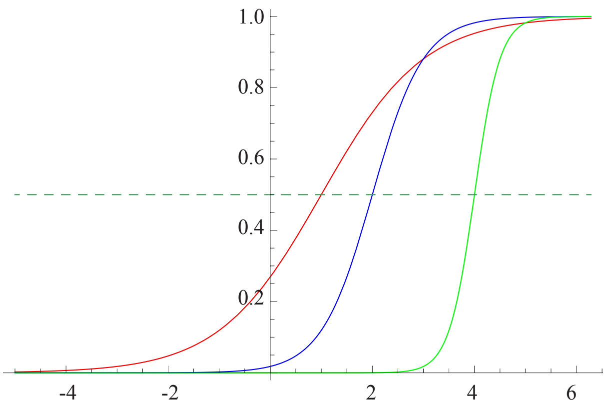


Figure 1. Red: $\mu = \theta = 1$, Blue: $\mu = \theta = 2$, Green: $\mu = \theta = 4$, f is Gompertz function

Since we focus on the inhibition case, we assume that w_{12} and w_{21} are negative. The diagonal elements w_{11} and w_{22} are set to zero, unless otherwise stated.

Problem: Describe possible attracting sets for the inhibition case.

3. Facts

Let us list the main facts about 2D-system (2).

1. The left sides of (2) are zeros on the nullclines[10] which are given as

$$\begin{cases} x_1 = f(-\mu_1(w_{11}x_1 + w_{12}x_2 - \theta_1)), \\ x_2 = f(-\mu_2(w_{21}x_1 + w_{22}x_2 - \theta_2)). \end{cases} \tag{4}$$

2. Equilibria (critical points) of system (2) are solutions of the system (4).

3. For w_{11} and w_{21} negative, and $w_{11} = w_{22} = 0$ there are at most three equilibria; the minimal number of equilibria is one. This follows from the S-shape of both nullclines. If w_{11} and/or w_{22} are not zero, then the nullclines may be Z-shaped and the number of critical points can be up to nine.

4. The vector field $(P(x_1, x_2), Q(x_1, x_2))$,

$$P(x_1, x_2) := f(-\mu_1(w_{11}x_1 + w_{12}x_2 - \theta_1)) - x_1,$$

$$Q(x_1, x_2) := f(-\mu_2(w_{21}x_1 + w_{22}x_2 - \theta_2)) - x_2,$$

is directed inward on the border of the rectangle $D = \{0 \le x_1 \le 1, 0 \le x_2 \le 1\}$ and, therefore, all trajectories of system (2), which start at the border ∂D, enter the region D, and no trajectory escapes. In other words, the region D is invariant under the trajectories of system (2).

5. The nullclines (4) can intersect only in the interior of D. Therefore all equilibria are in the interior of D.

6. If w_{12} and w_{21} are non-zero, and $w_{11} = w_{22} = 0$, and the nullclines (4) intersect transversally, then two cases are possible:

a) there is one equilibrium and it is attractive;

b) there are three equilibria and two of them are stable nodes and one is a saddle point.

7. If nullclines (4) are tangent at some point, then this point is degenerate critical point with one characteristic number $\lambda = 0$.

8. No periodic solutions (closed trajectories) exist in system (2) for w_{12} and w_{21} negative, and $w_{11} = w_{22} = 0$.

9. In the case 6a (one stable equilibrium) any trajectory that starts in D, tends to this equilibrium. The vector field ($P(x_1, x_2)$, $Q(x_1, x_2)$) is directed then to a unique critical point.

10. In the case 6b (two stable equilibria and a saddle point) there are subsets $D_1 \subset D$ and $D_2 \subset D$ such that if the trajectory starts in D_1, it goes to the first stable equilibrium, if the trajectory starts in D_2, it goes to the second stable equilibrium.

Some of these facts were known and some were proved in [8-9, 11-14]. Similar technique was used in the works [15-17].

4. Basins of attraction

Let us look at the below pictures Figure 2a to Figure 2c. The first one (Figure 2a) shows two nullclines of the system and three critical points. The middle point is a saddle, both side points are stable equilibria. This can be confirmed by the vector field analysis and the exploration of the respective linearized system. We omit these steps. Each of these equilibria has a basin of attraction, denoted by D_1 and D_2. Basins of attractions are separated by separatrixes of the saddle point. Any trajectory starting at any time moment at a point in D_1, will tend eventually to an upper stable equilibrium. Similarly, any trajectory starting at a point in D_2, will tend to a lower stable equilibrium.

Consider now the problem. Imagine a trajectory started at a point in D_1. Then its future is predefined, it will go to an upper equilibrium. By some reason (which will be explained later) we need the trajectory to go to a lower equilibrium. We are able to adjust some parameters in system (2), say, θ_1 and/or θ_2.

Tuning the first nullcline can be done by changing the parameter θ_1. The result is seen in Figure 2d and Figure 2e. The initial state is seen in Figure 2a. There are two attractors at the side critical points. By changing θ_1 from 0.02 to −1.5 we eliminate the upper attractor, while the second (lower) attractor remains. The trajectory continues, as time increases, to the unique attractor. So by a single operation the trajectory can be redirected to the lower equilibrium.

By changing θ_1 from 0.02 to 0.35 the opposite result can be achieved. The lower attractor is eliminated and the upper one remains. So trajectories that were tending to the lower attractor are redirected to the upper one.

5. Normal and undesired states of GRN

In the work [5] an example of realistic GRN was discussed. The GRN considered corresponds to a kind of cancer, where cancerous states are identified with “undesired” attractors. If the current system states, that is, the vector $x(t)$ is in the basin of attraction of “undesired” attractor, the system (which corresponds to a living organism) will tend to an “undesired” attractor with the negative consequences. The problem is, using adjustable parameters, to redirect the vector $x(t)$ from “undesired” attractor to a normal one. Mathematically (in a model) this can be (sometimes) done by skillfully tuning the system. This is what we did in the preceding section to the two-dimensional system. In the system being considered in [5] the dimensionality of the considered system is not too large (60 nodes, of which three nodes only were attractive). It was mentioned in [5], that also reverse process is available, that is, driving a system into opposite direction. This is another aspect of the problem. We have shown, considering our simple 2D system, that, operating by parameters θ, we can control the system.

In real situations, management and pertirbation of these parameters should be left to biologists and medics.

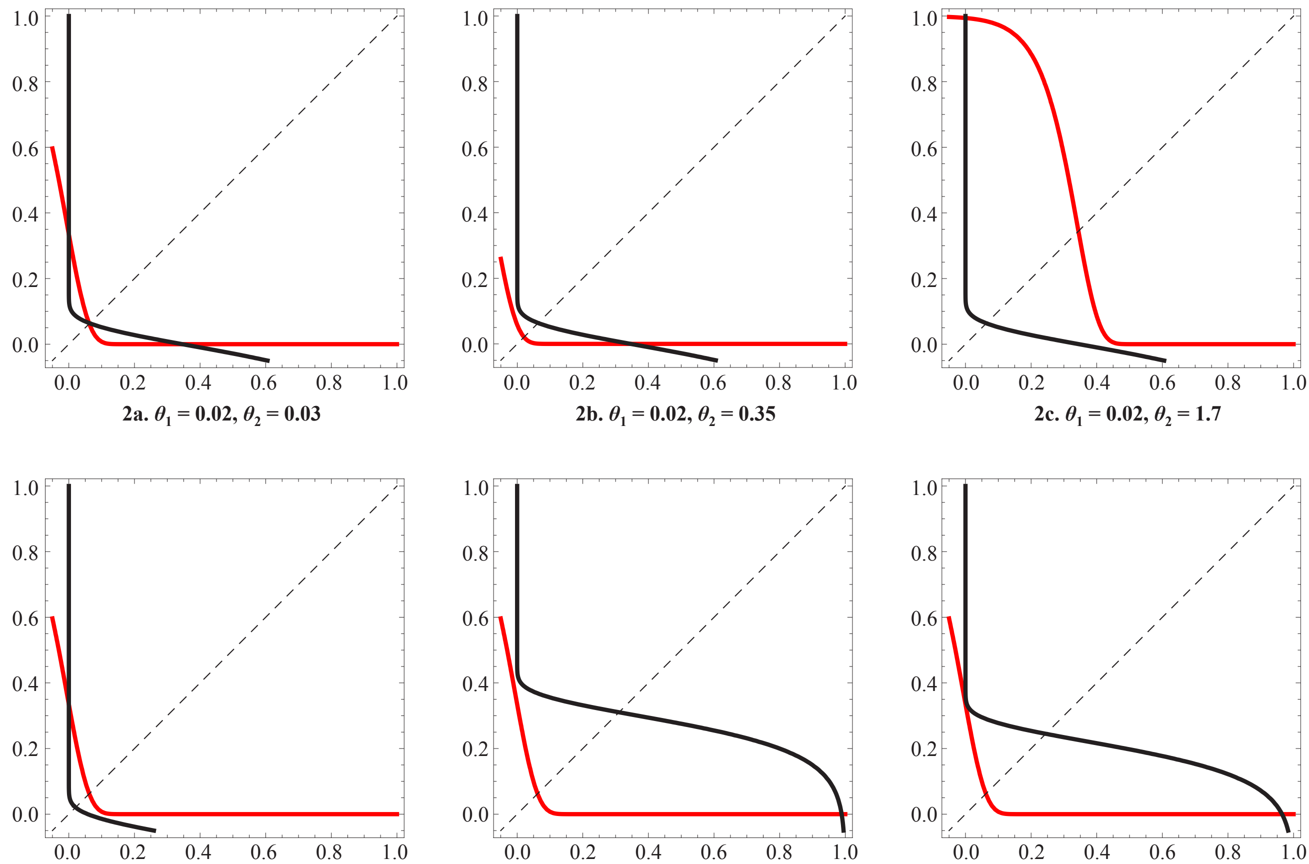
We believe, that in a similar manner systems of higher dimensions can be controlled.

6. Examples

In the below examples $\mu_1 = \mu_2 = 3.0$. The sigmoidal function is the Gompertz one, (3). The numerical data for illustrations are chosen arbitrarily to show the desired behavior of solutions.

Set $\theta_1 = 0.02$ and change θ_2. Initially $\theta_2 = 0.03$ and the nullclines are depicted in Figure 2a. Increasing θ_2 eliminates the upper stable equilibrium and redirects all the trajectories to the lower equilibrium as shown in Figure 2a. Increasing θ_2 eliminates the upper stable equilibrium and redirects all the trajectories to the lower equilibrium as shown in Figure 2b. If the upper attractor is idendified with the normal system state, and trajectories should be redirected to the upper equilibrium, the parameter θ_2 needs to decrease. This is shown in Figure 2c.

The same results can be obtained by changing the second adjustable parameter, θ_1. The needed operations are explained and illustrated by Figure 2d and Figure 2e.



2a. $\theta_1 = 0.02$, $\theta_2 = 0.03$ **2b. $\theta_1 = 0.02$, $\theta_2 = 0.35$** **2c. $\theta_1 = 0.02$, $\theta_2 = 1.7$**

2d. $\theta_1 = 0.35$, $\theta_2 = 0.03$ **2e. $\theta_1 = 1.5$, $\theta_2 = 0.03$** **2f. $\theta_1 = 1.11$, $\theta_2 = 0.03$**

Figure 2. Nullclines for system (3)

It is to be noted, that passage from the initial state (Figure 2a) to other states with a unique equilibrium is through the intermediate "touch" state, when two isoclines are touching each other. There are an "upper" touch and a "lower" touch, leading to a single equilibrium. The "upper" touch is shown in Figure 2f.

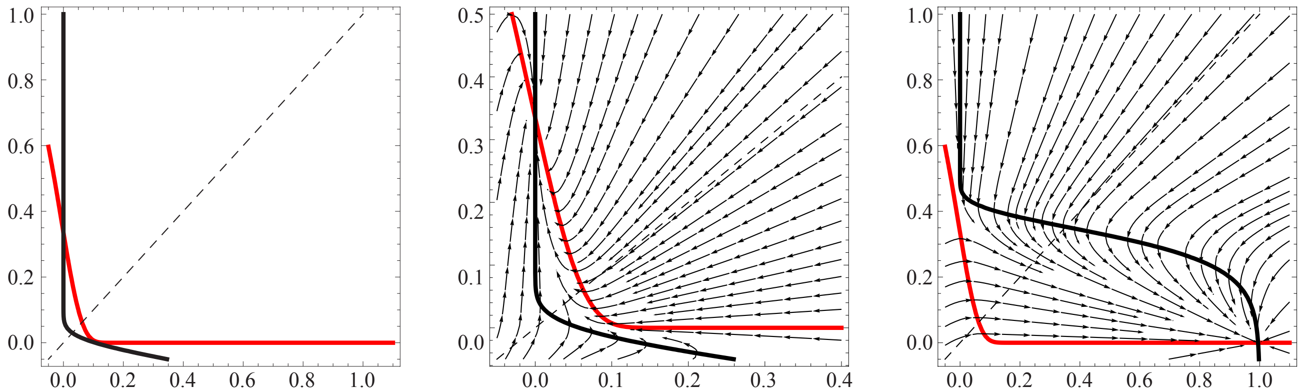
7. Analytics

Consider the inhibition case, where the modelling system is

$$\begin{cases} \dfrac{dx_1}{dt} = f(\mu_1(\alpha x_2 - \theta_1)) - x_1, \\ \dfrac{dx_2}{dt} = f(\mu_2(\beta x_1 - \theta_2)) - x_2, \end{cases} \tag{5}$$

α and β are negative, $f(z)$ is a sigmoidal function. Suppose that nullclines are located as shown in Figure 2a. The parameters μ_1, μ_2, θ_1, θ_2, α, β are fixed. There are three cross-points, respectively p_1, p_2, p_3 (from upper left to lower right). Two side points, p_1 and p_3, are stable nodes and the middle point p_2 is a saddle.

Our goal is to control this system, redirecting trajectories to a desired (normal) stable node. For this, we will change θ_1. Let p_3 be a normal attracting state. Let θ_{1upper} be the value, corresponding to the upper touch point. In the example in Section 6 $\theta_{1upper} = -1.11$ (Figure 2f) and the current value $\theta_1 = 0.02$. Let θ_{1lower} be the value of θ_1, corresponding to the lower touch point (Figure 3a). The current value of θ_1, by our assumption, is between θ_{1upper} and θ_{1lower}. For θ_1 values greater than θ_{1lower} the upper attractor remains and all the trajectories tend to it (Figure 3b). For θ_1 values less than θ_{1upper} the upper attractor remains and all the trajectories tend to it (Figure 3c).



3a. $\theta_1 = 0.27$, $\theta_2 = 0.03$ **3b. $\theta_1 = 0.35$, $\theta_2 = 0.03$** **3c. $\theta_1 = -1.75$, $\theta_2 = 0.03$**

Figure 3. Moving the first nullcline (red)

The nullclines are defined by

$$\begin{cases} x_1 = f(\mu_1(\alpha x_2 - \theta_1)), \\ x_2 = f(\mu_2(\beta x_1 - \theta_2)), \end{cases} \tag{6}$$

It follows that

$$\frac{dx_1}{dx_2} = \frac{\partial}{\partial x_2} f(\mu_1(\alpha x_2 - \theta_1)),$$

$$\frac{dx_2}{dx_1} = \frac{\partial}{\partial x_1} f(\mu_2(\beta x_1 - \theta_2)).$$

At a point, where two nullclines are touching, the relation

$$1 = \frac{\partial}{\partial x_2} f(\mu_1(\alpha x_2 - \theta_1)) \frac{\partial}{\partial x_1} f(\mu_2(\beta x_1 - \theta_2)) \tag{7}$$

must be satisfied.

For given f, μ_1, μ_2, α, β, θ_2, the values of θ_{1upper} and θ_{1lower} can be found solving the system (6), (7).

Remark. The system can be managed also changing the parameter θ_2 instead of θ_1. For the touching points of nullclines then the values θ_{2left} and θ_{2right} should be used.

8. Symmetric case

Consider the particular case

$$\begin{cases} \frac{dx_1}{dt} = f(\mu(-x_2-\theta)) - x_1 = \frac{1}{1+e^{-\mu(-x_2-\theta)}} - x_1, \\ \frac{dx_2}{dt} = f(\mu(-x_1-\theta)) - x_2 = \frac{1}{1+e^{-\mu(-x_1-\theta)}} - x_2, \end{cases} \tag{8}$$

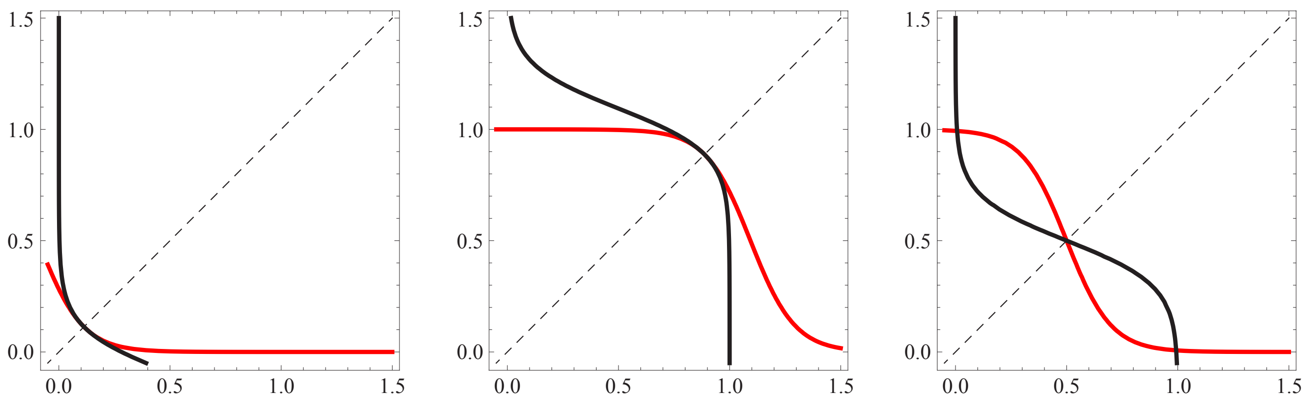
where f is a logistic function and $\mu_1 = \mu_2$ and $\theta_1 = \theta_2$. This corresponds to both elements of GRN acting symmetrically. Mathematically this case can be entirely analyzed.

The system

$$\begin{cases} 1 = \frac{\partial}{\partial x_2} f(\mu(-x_2-\theta)) \frac{\partial}{\partial x_1} f(\mu(-x_1-\theta)) \\ x_1 = f(\mu(-x_2-\theta)), \\ x_2 = f(\mu(-x_1-\theta)) \end{cases} \tag{9}$$

defines the touching points of nullclines.

For instance, set $\mu = 10$ and let θ be free. Due to symmetry in system (8), a unique equilibrium always exists on the bisectrix and both touch points are also on the bisecrtrix (Figure 4a and Figure 4b). For the intermediate value $\theta = -0.5$ the nullclines are depicted in Figure 4c.



4a. θ = 0.093642 **4b. θ = −1.093642** **4c. θ = −0.5**

Figure 4. Nullclines for system (8)

The coordinate x of a unique critical point of the form (x, x) satisfies the relation $x = f(\mu(-x-\theta))$. Then

$$\theta = -x + \frac{1}{\mu}\log\left(\frac{1}{x} - 1\right). \tag{10}$$

The characteristic numbers $\lambda_{1,2} = -1 \pm \mu x(1-x)$ can be obtained by linearizing system (8) around the equilibrium (x, x). Elementary analysis of $\lambda_2 = -1 + \mu x(1-x)$ shows that λ_2 can be positive only for $x \in (x_1, x_2)$, where

$$x_1(\mu) := \frac{1}{2} - \frac{\sqrt{\mu^2 - 4\mu}}{2\mu}, \; x_2(\mu) := \frac{1}{2} + \frac{\sqrt{\mu^2 - 4\mu}}{2\mu}. \tag{11}$$

We can obtain, following the arguments in [14] and using (10) and (11), the figure depicted in Figure 5.

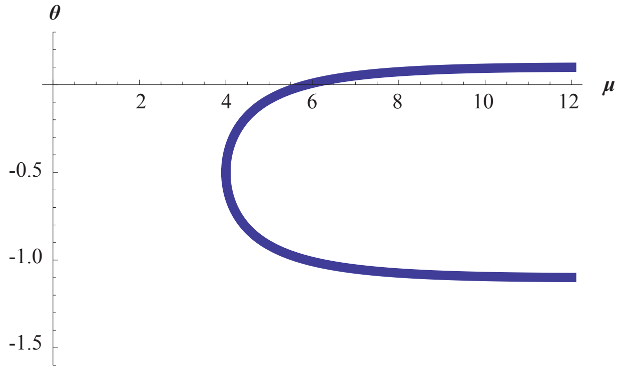


Figure 5. The bifurcation curve $\theta(\mu)$

This figure is defined by two branches

$$\theta_1(\mu) := -x_1(\mu) + \frac{1}{\mu}\log(\frac{1}{x_1(\mu)} - 1),$$

$$\theta_2(\mu) := -x_2(\mu) + \frac{1}{\mu}\log(\frac{1}{x_2(\mu)} - 1), \tag{12}$$

where x_1 and x_2 are defined in (11).

9. Conclusions

Typical behavior of solutions in an inhibition models of GRN is described. The possibility of managing and controlling of 2D inhibition GRN systems is emphasized and analyzed in terms of the phase plane. It is shown how to eliminate unwanted attractors and redirect the trajectories of the system in the right direction by changing the adjustable parameters θ. The proposed method is easy to implement, geometrically check, and allows for an accurate mathematical description. This approach is a perspective for studying and managing multi-dimensional systems.

References

[1] H. D. Jong. Modeling and Simulation of Genetic Regulatory Systems: A Literature Review. *J. Comput Biol.* 2002; 9(1): 67-103. Available from: doi:10.1089/10665270252833208.

[2] T. Schlitt. Approaches to Modeling Gene Regulatory Networks: A Gentle Introduction. *In Silico Systems Biology*. Humana Press; 2013. p.13-35. Available from: doi:10.1007/978-1-62703-450-0.

[3] A. Spirov, D. Holloway. Using evolutionary computations to understand the design and evolution of gene and cell regulatory networks. *Methods.* 2013; 62(1): 39-55. Available from: doi:10.1016/j.ymeth.2013.05.013.

[4] Y. Wang. Review of Wagner's Artificial Gene Regulatory Networks Model and its Applications for Understanding Complex Biological Systems. *COJ Rob Artificial Intel.* Crimson Publishers; 2019. Available from: https://crimsonpublishers.com/cojra/pdf/COJRA.000501.pdf.

[5] Le-Zhi Wang, Ri-Qi Su, Zi-Gang Huang, Xiao Wang, Wen-Xu Wang, Celso Grebogi, Ying-Cheng Lai. A geometrical approach to control and controllability of nonlinear dynamical networks. *Nature Communications.* 2016; 7: 11323. Available from: doi:10.1038/ncomms11323.

[6] Yuki Koizumi, Takashi Miyamura, Shin'ichi Arakawa, Eiji Oki, Kohei Shiomoto, Masayuki Murata. Adaptive Virtual Network Topology Control Based on Attractor Selection. *J. Lightwave Technol.* 2010; 28(11): 1720-1731. Available from: doi:10.1109/JLT.2010.2048412.

[7] C. Furusawa, K. Kaneko. A generic mechanism for adaptive growth rate regulation. *PLoS Comput Biol*. 2008; 4(1): e3. Available from: doi:10.1371/journal.pcbi.0040003.

[8] D. Ogorelova. Gompertz function in the model of gene regulatory network. *Proceedings of IMCS of University of*

Latvia. 2018; 18: 23-32.
[9] F. Sadyrbaev, D. Ogorelova, I. Samuilik. A nullclines approach to the study of 2D artificial network. *Contemporary Mathematics*. 2019; 1(1): 1-11. Available from: https://doi.org/10.37256/cm.11201976.1-11.
[10] D. K. Arrowsmith, C. M. Place. *Dynamical Systems: Differential equations, maps and haotic behavior, subsection 1.4.2*. London: Chapman and Hall/CRC; 1992. Available from: https://doi.org/10.1201/9781315141541.
[11] S. Atslega, D. Finaskins, F. Sadyrbaev. On a Planar Dynamical System Arising in the Network Control Theory. *Math. Modelling and Analysis.* 2016; 21(3): 385-398.
[12] E. Brokan, F. Zh. Sadyrbaev. On attractors in gene regulatory systems. *AIP Conference Proceedings*. 2017. Turkey: Istanbul; Available from: https://doi.org/10.1063/1.4975425.
[13] F. Sadyrbaev. Planar differential systems arising in network regulation theory. *Advanced Mathematical Models & Applications.* 2019; 4: 70-78.
[14] V. Sengileyev. On decreasing sigmoidal function: inhibition. *Proceedings of IMCS of University of Latvia*. 2018; 18: 43-53.
[15] M. Marin, R. Agarwal, L. Codarcea. A mathematical model for three-phase-lag dipolar thermoelastic bodies. *J Inequal Appl.* 2017; 109. Available from: https://doi.org/10.1186/s13660-017-1380-5.
[16] I. A. Abbas, M. Marin. Analytical solution of thermoelastic interaction in a half-space by pulsed laser heating. *Physica E-Low-Dimensional Systems & Nanostructures*. 2017; 87: 254-260. Available from: https://doi.org/10.1016/j.physe.2016.10.048.
[17] M. M. Bhatti, A. Riaz, R. Ellahi, M. Marin. Study of heat and mass transfer in the Eyring-Powell model of fluid propagating peristaltically through a rectangular compliant channel. *Heat Transf Res*. 2019; 50(16): 1539-1560. Available from: doi:10.1615/HeatTransRes.2019025622.

D. A. Ogorelova, F. Zh. Sadyrbaev, Gompertz function in the model of gene regulatory networks, *Itogi Nauki i Tekhniki. Ser. Sovrem. Mat. Pril. Temat. Obz.*, 2021, Volume 195, 88–96

DOI: 10.36535/0233-6723-2021-195-88-96

ИТОГИ НАУКИ И ТЕХНИКИ.
Современная математика и ее приложения.
Тематические обзоры.
Том 195 (2021). С. 88–96
DOI: 10.36535/0233-6723-2021-195-88-96

УДК 517.9

ФУНКЦИЯ ГОМПЕРЦА В МОДЕЛИ ГЕННЫХ РЕГУЛЯТОРНЫХ СЕТЕЙ

© 2021 г. **Д. А. ОГОРЕЛОВА, Ф. Ж. САДЫРБАЕВ**

Аннотация. Исследуется сетевая модель (включающих генные регуляторные сети), состоящая из системы двух обыкновенных дифференциальных уравнений. Данная система содержит ряд параметров и зависит от регуляторной матрицы, описывающей взаимодействия в данной двухкомпонентной сети. Рассматривается вопрос о притягивающих множествах данной системы, которые меняются в зависимости от параметров и элементов регуляторной матрицы. Рассмотрение носит в основном геометрический характер, что позволяет выявить и классифицировать возможные взаимодействия в сети. В системе дифференциальных уравнений присутствует сигмоидальная функция, позволяющая учесть особенности ответной реакции сети на внешние воздействия. В качестве сигмоидальной функции выбрана функция Гомперца, что позволяет сравнить результаты с аналогичными результатами для моделей двухкомпонентных сетей, в которых используется логистическая сигмоидальная функция.

***Ключевые слова*:** генная регулятивная сеть, фазовый портрет, качественный анализ, численный анализ.

GOMPERTZ FUNCTION IN THE MODEL OF GENE REGULATORY NETWORKS

© 2021 **D. A. OGORELOVA, F. Zh. SADYRBAEV**

Abstract. We examine a network model (including gene regulatory networks), which consists of a system of two ordinary differential equations. This system contains several parameters and depends on the regulatory matrix, which describes interactions in this two-component network. We consider attracting sets of the system, which vary depending on the parameters and elements of the regulatory matrix. Our considerations are of geometric nature, which allows us to identify and classify possible interactions in the network. The system of differential equations contains a sigmoidal function, which makes it possible to take into account peculiarities of the network's response to external influences. The Gompertz function was chosen as the sigmoidal function, which allows us to compare the results with similar results for models of two-component networks based on the logistic sigmoidal function.

***Keywords and phrases*:** gene regulatory network, phase portrait, qualitative analysis, numerical analysis.

***AMS Subject Classification*:** 34Cxx

1. Постановка задачи. Двухэлементная генная регуляторная сеть (ГРС) описывается дифференциальной системой

$$\begin{cases} x_1' = f(w_{11}x_1 + w_{12}x_2 - \theta_1) - x_1, \\ x_2' = f(w_{21}x_1 + w_{22}x_2 - \theta_2) - x_2, \end{cases} \tag{1}$$

где $f(x)$ — сигмоидальная функция. Функция $f(x)$ называется *сигмоидальной*, если она монотонно строго возрастает от нуля до единицы при возрастании аргумента x от $-\infty$ до $+\infty$ и имеет ровно одну точку перегиба. Примером сигмоидальной функции является логистическая функция $f(z) = (1+e^{-\mu z})^{-1}$. Эта функция использовалась в математических моделях сетей в [3,4,6]. Другим примером сигмоидальной функции является функция Гомперца (Gompertz) $f(z) = e^{-e^{-\mu z}}$, которую мы используем в данной статье. График этой функции приведен на рис. 1.

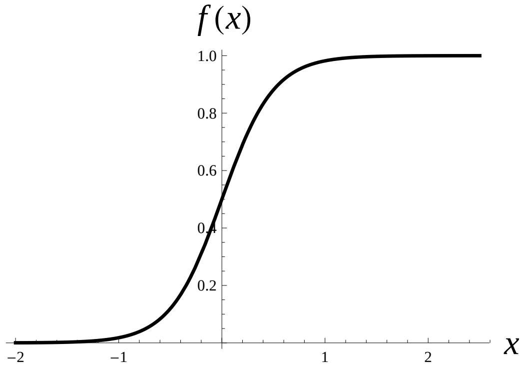


Рис. 1. Функция Гомперца.

Система, которую мы рассматриваем в данной статье, имеет вид

$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(w_{11}x_1+w_{12}x_2-\theta_1)}} - x_1, \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(w_{21}x_1+w_{22}x_2-\theta_2)}} - x_2, \end{cases} \tag{2}$$

где $\mu > 0$ и θ — параметры. Наша цель — классифицировать возможные случаи и описать аттракторы данной системы.

2. Взаимодействие. Типы взаимодействия в сети описываются регуляторной матрицей

$$W = \begin{pmatrix} w_{11} & w_{12} \\ w_{21} & w_{22} \end{pmatrix}.$$

Элементы матрицы могут принимать различные значения. Известны четыре основных типа взаимодействия. В описании этих типов участвуют изоклины нуля системы (2), которые описываются далее.

A: Активация: регуляторная матрица имеет структуру

$$W = \begin{pmatrix} * & + \\ + & * \end{pmatrix},$$

где w_{12} и w_{21} положительны, а элементы w_{11} и w_{22} могут принимать любые значения (это отмечается звездочками). Запись $\{\{+,+\}\{+,+\}\}$, например, означает матрицу W со всеми положительными элементами.

B: Ингибиция: регуляторная матрица имеет вид

$$W = \begin{pmatrix} * & - \\ - & * \end{pmatrix},$$

где элементы w_{12} и w_{21} отрицательны, а элементы w_{11} и w_{22} могут принимать произвольные значения.

C: Активация-ингибиция: регуляторная матрица имеет вид

$$W = \begin{pmatrix} * & + \\ - & * \end{pmatrix},$$

где элемент w_{12} положителен, элемент w_{21} отрицателен, а элементы w_{11} и w_{22} могут принимать любые значения.

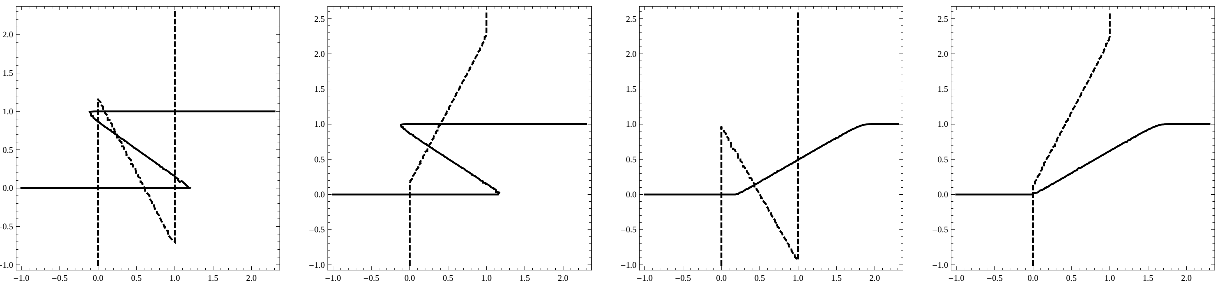


Рис. 2. Визуализация всех случаев активации:
(a) $\{\{+,+\}\{+,+\}\}$; (b) $\{\{-,+\}\{+,+\}\}$; (c) $\{\{+,+\}\{+,-\}\}$; (d) $\{\{-,+\}\{+,-\}\}$.

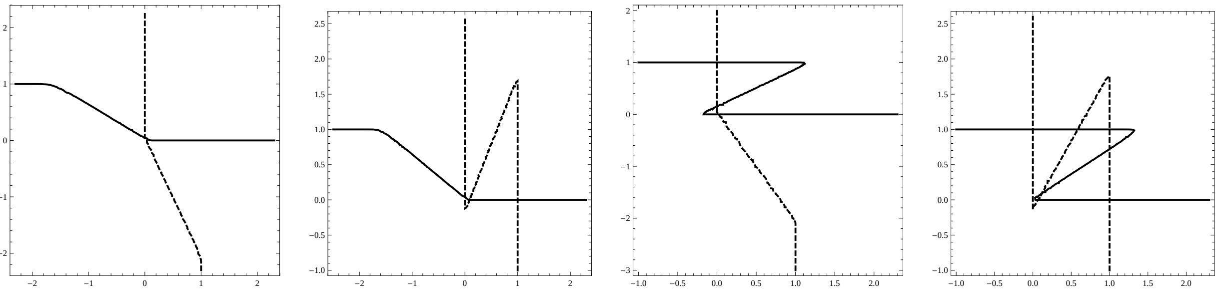


Рис. 3. Визуализация всех случаев ингибиции:
(a) $\{\{-,-\}\{-,-\}\}$; (b) $\{\{+,-\}\{-,-\}\}$; (c) $\{\{-,-\}\{-,+\}\}$; (d) $\{\{+,-\}\{-,+\}\}$.

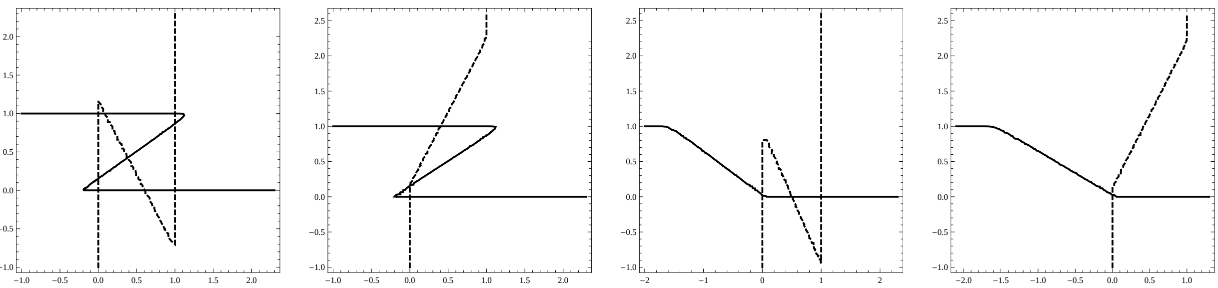


Рис. 4. Визуализация всех случаев типа активация-ингибиция:
(a) $\{\{+,+\}\{-,+\}\}$; (b) $\{\{-,+\}\{-,+\}\}$; (c) $\{\{+,+\}\{-,-\}\}$; (d) $\{\{-,+\}\{-,-\}\}$.

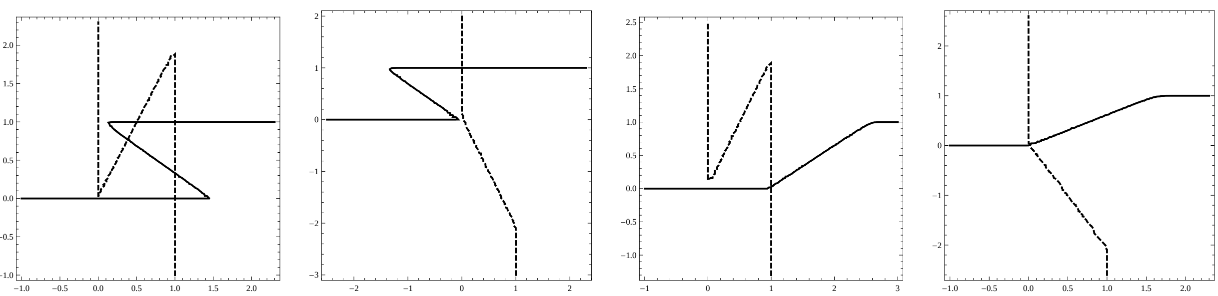


Рис. 5. Визуализация всех случаев типа ингибиция-активация:
(a) $\{\{+,-\}\{+,+\}\}$; (b) $\{\{-,-\}\{+,+\}\}$; (c) $\{\{+,-\}\{+,-\}\}$; (d) $\{\{-,-\}\{+,-\}\}$.

D: Ингибиция-активация: регуляторная матрица имеет вид

$$W = \begin{pmatrix} * & - \\ + & * \end{pmatrix},$$

где элемент w_{12} отрицателен, элемент w_{21} положителен, а элементы w_{11} и w_{22} могут принимать любые значения.

При наличии ненулевых элементов на главной диагонали матрицы W изоклины нуля могут принимать Z-образную форму. Параметр μ влияет на остроту углов в фигуре Z. Параметр θ регулирует сдвиг графика сигмоидальной функции, а соотношение величин элементов w_{ij} влияет на наклон сегментов графика (Z-образной фигуры).

Предложение 1. *Все критические точки системы* (2) *находятся в единичном квадрате* $(0,1) \times (0,1)$ *и множество критических точек непусто.*

Справедливость утверждения вытекает из вида изоклин и свойств сигмоидальной функции.

Предложение 2. *Критические точки, являющиеся точками касания изоклин нуля, вырождены, т.е. одно из характеристических чисел* λ *равно нулю.*

Это предложение может быть доказано (см. [9]) рассмотрением соответствующей линеаризованной системы и соответствующего характеристического уравнения. Отметим, что изоклины нуля в силу определяющих их уравнений гладкие и не имеют сингулярностей, несмотря на Z-образную форму.

Далее рассматриваются все типичные случаи расположения критических точек, приводятся характеристики критических точек. Мы также рассматриваем численные примеры и соответствующие фазовые портреты.

2.1. Случай A: Активация. Рассмотрим случай максимального числа критических точек (положений равновесия). Пусть дана регуляторная матрица

$$W = \begin{pmatrix} 10 & 5 \\ 2 & 3 \end{pmatrix}.$$

Система (2) принимает вид

$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(10x_1+5x_2-\theta_1)}} - x_1, \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(2x_1+3x_2-\theta_2)}} - x_2. \end{cases} \tag{3}$$

Функции в правой части зависят от параметра μ, который регулирует остроту углов в графиках изоклин нуля. Критические точки находятся из системы

$$\begin{cases} x_1 = e^{-e^{-\mu(10x_1+5x_2-\theta_1)}}, \\ x_2 = e^{-e^{-\mu(2x_1+3x_2-\theta_2)}}. \end{cases} \tag{4}$$

Для выбранных значений параметров изоклины нуля изображены на рис. 6(a).

При анализе критических точек получены следующие результаты:

(i) тип критической точки $(0;0)$ с меткой 1 — устойчивый узел при характеристических числах $(\lambda_1 = -1, \lambda_2 = -1)$;
(ii) тип критической точки $(0{,}6;0)$ с меткой 2 — седло при $(\lambda_1 = -1,\ \lambda_2 = 59{,}96)$;
(iii) тип критической точки $(1;0)$ с меткой 3 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -1)$;
(iv) тип критической точки $(1;0{,}16)$ с меткой 4 — седло при $(\lambda_1 = -1,\ \lambda_2 = 16{,}41)$;
(v) тип критической точки $(0{,}26;0{,}67)$ с меткой 5 — неустойчивый узел при $(\lambda_1 = 75{,}3,\ \lambda_2 = 8{,}8)$;
(vi) тип критической точки $(0;0{,}87)$ с меткой 6 — седло при $(\lambda_1 = -1,\ \lambda_2 = 6{,}5)$;
(vii) тип критической точки $(0;0{,}99)$ с меткой 7 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -0{,}99)$;
(viii) тип критической точки $(0{,}1;0{,}99)$ с меткой 8 — седло при $(\lambda_1 = -0{,}99,\ \lambda_2 = 43{,}9)$;
(ix) тип критической точки $(1;1)$ с меткой 9 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -0{,}9)$.

Фазовый портрет с векторным полем на рис. 6(b) подтверждает результаты анализа.

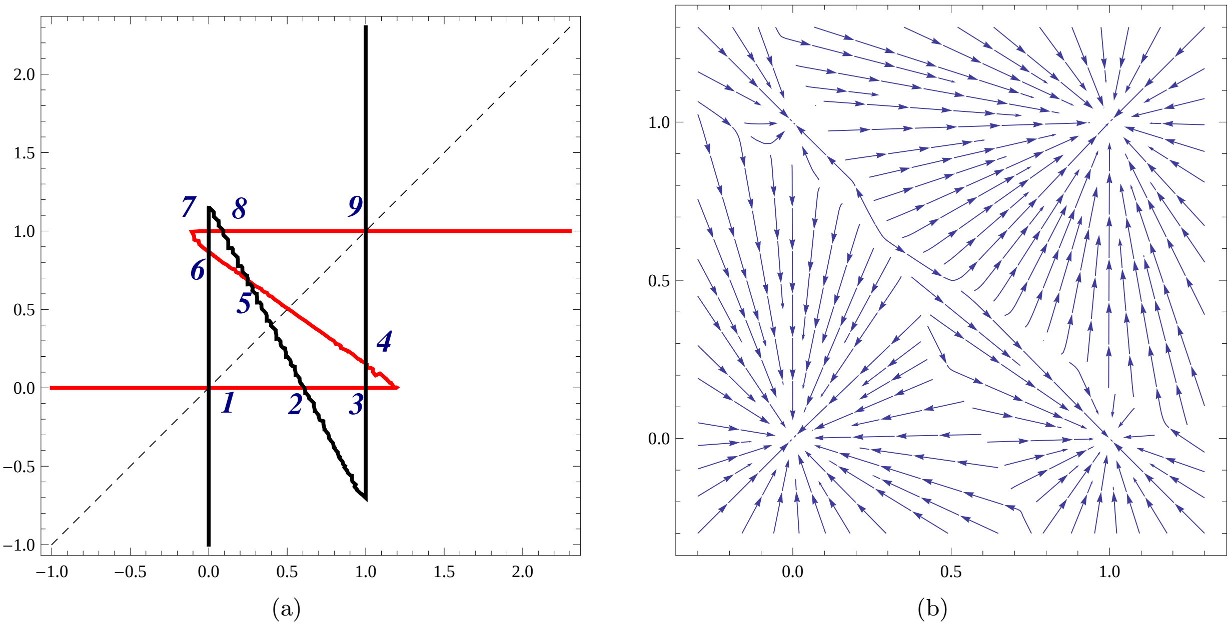


Рис. 6. Изоклины нуля (a) и фазовый портрет (b) системы (3) с девятью критическими точками. Значения параметров $\mu = 20$, $\theta_1 = 6$, $\theta_2 = 2{,}5$, $w_{11} = 10$, $w_{12} = 5$, $w_{21} = 2$, $w_{22} = 3$.

2.2. Случай B: Ингибиция. Снова рассмотрим пример ингибиторного поведения, при котором число критических точек в системе максимально. Структура регуляторной матрицы

$$W = \begin{pmatrix} + & - \\ - & + \end{pmatrix}.$$

Для выбранной регуляторной матрицы

$$W = \begin{pmatrix} 10 & -5 \\ -2 & 3 \end{pmatrix}$$

система принимает вид

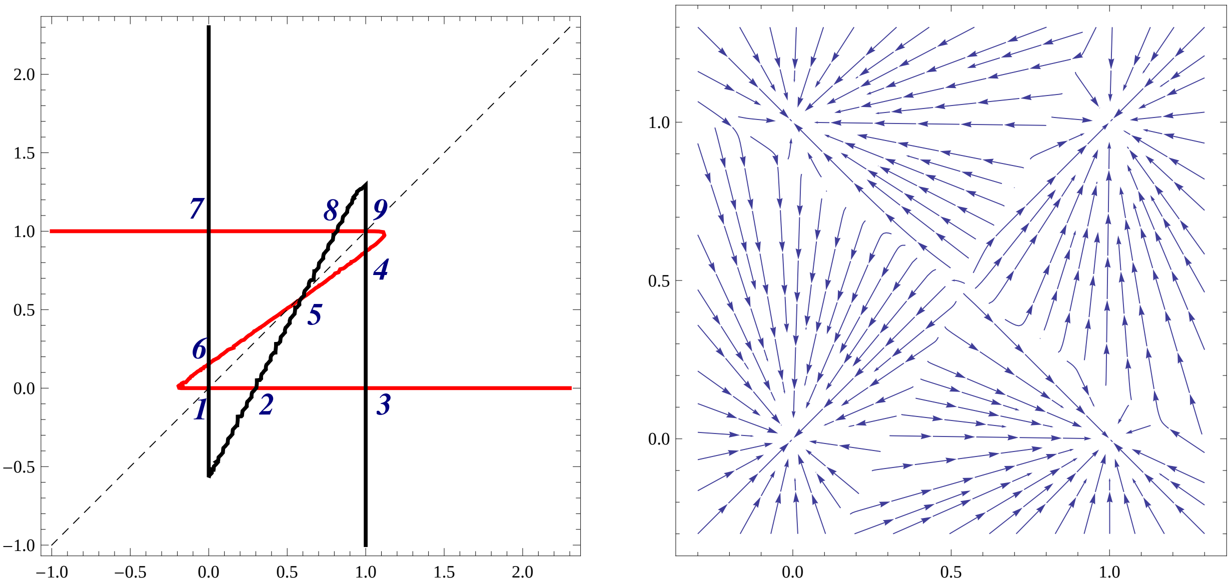
$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(10x_1 - 5x_2 - \theta_1)}} - x_1, \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(-2x_1 + 3x_2 - \theta_2)}} - x_2. \end{cases} \tag{5}$$

Критические точки находятся из системы уравнений

$$\begin{cases} x_1 = e^{-e^{-\mu(10x_1 - 5x_2 - \theta_1)}}, \\ x_2 = e^{-e^{-\mu(-2x_1 + 3x_2 - \theta_2)}}. \end{cases} \tag{6}$$

Изоклины нуля при конкретных выбранных значениях параметров изображены на рис. 7(a). Фазовый портрет с векторным полем, приведенный на рис. 7(b), подтверждает результаты анализа критических точек:

(i) тип критической точки $(0; 0)$ с меткой 1 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -1)$;
(ii) тип критической точки $(0{,}3; 0)$ с меткой 2 — седло при $(\lambda_1 = -1,\ \lambda_2 = 71{,}2)$;
(iii) тип критической точки $(1; 0)$ с меткой 3 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -1)$;
(iv) тип критической точки $(1; 0{,}87)$ с меткой 4 — седло при $(\lambda_1 = -1,\ \lambda_2 = 6{,}5)$;
(v) тип критической точки $(0{,}59; 0{,}57)$ с меткой 5 — неустойчивый узел при $(\lambda_1 = 10{,}4,\ \lambda_2 = 69{,}4)$;
(vi) тип критической точки $(0; 0{,}16)$ с меткой 6 — седло при $(\lambda_1 = -1,\ \lambda_2 = 16{,}4)$;
(vii) тип критической точки $(0; 0{,}1)$ с меткой 7 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -1)$;
(viii) тип критической точки $(0{,}81; 1)$ с меткой 8 — седло при $(\lambda_1 = -0{,}99,\ \lambda_2 = 33{,}5)$;



(a) (b)

Рис. 7. Изоклины нуля (a) и фазовый портрет (b) системы (5) с девятью критическими точками. Значения параметров $\mu = 20$, $\theta_1 = 3$, $\theta_2 = 0{,}5$, $w_{11} = 10$, $w_{12} = -5$, $w_{21} = -2$, $w_{22} = 3$.

(ix) тип критической точки $(1; 0{,}99)$ с меткой 9 — устойчивый узел при ($\lambda_1 = -1$, $\lambda_2 = -0{,}99$).

2.3. Случай C: Активация-Ингибиция. Рассмотрим случай максимально возможного числа критических точек для регуляторной матрицы со структурой

$$W = \begin{pmatrix} + & + \\ - & + \end{pmatrix}.$$

При конкретной регуляторной матрице

$$W = \begin{pmatrix} 10 & 5 \\ -2 & 3 \end{pmatrix}$$

система дифференциальных уравнений принимает вид

$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(10x_1+5x_2-\theta_1)}} - x_1, \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(-2x_1+3x_2-\theta_2)}} - x_2. \end{cases} \tag{7}$$

Критические точки суть решения системы

$$\begin{cases} x_1 = e^{-e^{-\mu(10x_1+5x_2-\theta_1)}}, \\ x_2 = e^{-e^{-\mu(-2x_1+3x_2-\theta_2)}}. \end{cases} \tag{8}$$

Изоклины нуля при выбранных значениях параметров изображены на рис. 8(a), а фазовый портрет и векторное поле — на рис. 8(b). Результаты анализа критических точек:

(i) тип критической точки $(0; 0)$ с меткой 1 — устойчивый узел при ($\lambda_1 = -1$, $\lambda_2 = -1$);
(ii) тип критической точки $(0{,}6; 0)$ с меткой 2 — седло при ($\lambda_1 = -1$, $\lambda_2 = 59{,}96$);
(iii) тип критической точки $(1; 0)$ с меткой 3 — устойчивый узел при ($\lambda_1 = -1$, $\lambda_2 = -1$);
(iv) тип критической точки $(1; 0{,}87)$ с меткой 4 — седло при ($\lambda_1 = -1$, $\lambda_2 = 6{,}5$);
(v) тип критической точки $(0{,}39; 0{,}43)$ с меткой 5 — неустойчивый узел при ($\lambda_1 = 35{,}1$, $\lambda_2 = 58{,}2$);
(vi) тип критической точки $(0; 0{,}16)$ с меткой 6 — седло при ($\lambda_1 = -1$, $\lambda_2 = 16{,}4$);
(vii) тип критической точки $(0; 1)$ с меткой 7 — устойчивый узел при ($\lambda_1 = -1$, $\lambda_2 = -1$);

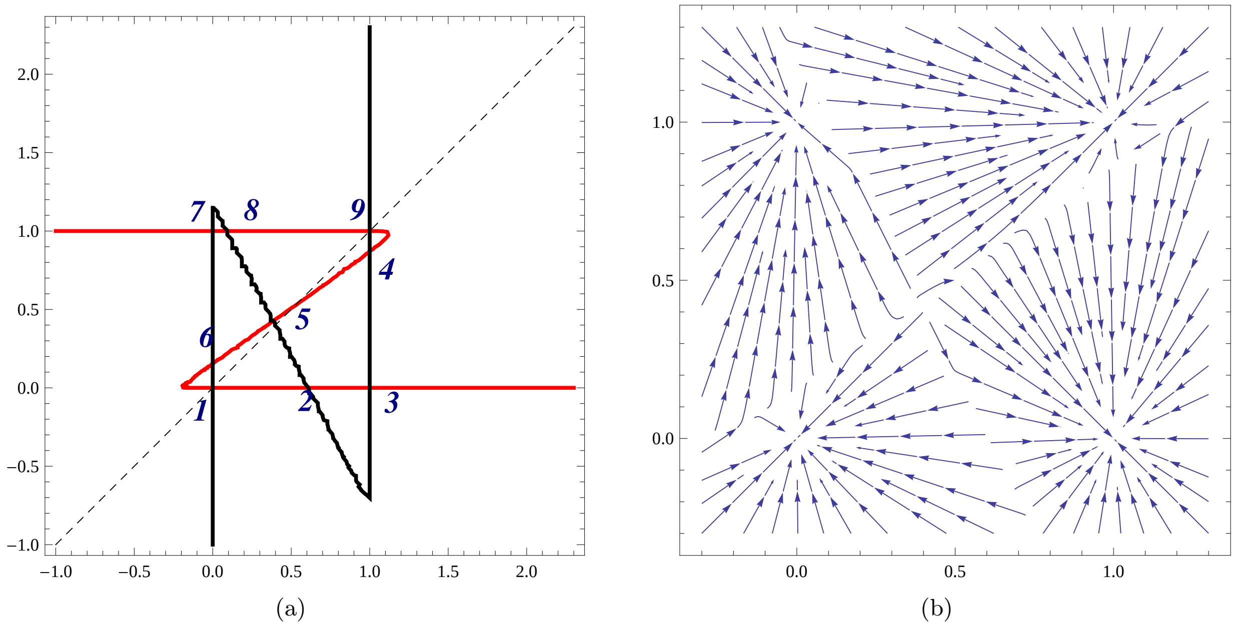


Рис. 8. Изоклины нуля (a) и фазовый портрет (b) системы (7) с девятью критическими точками. Значения параметров $\mu = 20$, $\theta_1 = 6$, $\theta_2 = 0{,}5$, $w_{11} = 10$, $w_{12} = 5$, $w_{21} = -2$, $w_{22} = 3$.

(viii) тип критической точки $(0{,}1; 1)$ с меткой 8 — седло при $(\lambda_1 = -1,\ \lambda_2 = 43{,}9)$;
(ix) тип критической точки $(1; 0{,}99)$ с меткой 9 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -0{,}99)$.

2.4. Случай D: Ингибиция-активация. Снова рассмотрим случай максимального числа критических точек для варианта «ингибиция-активация», которому соответствует регуляторная матрица структуры

$$W = \begin{pmatrix} + & - \\ + & + \end{pmatrix}.$$

При выбранных элементах регуляторной матрицы

$$W = \begin{pmatrix} 10 & -5 \\ 2 & 3 \end{pmatrix}$$

система дифференциальных уравнений принимает вид

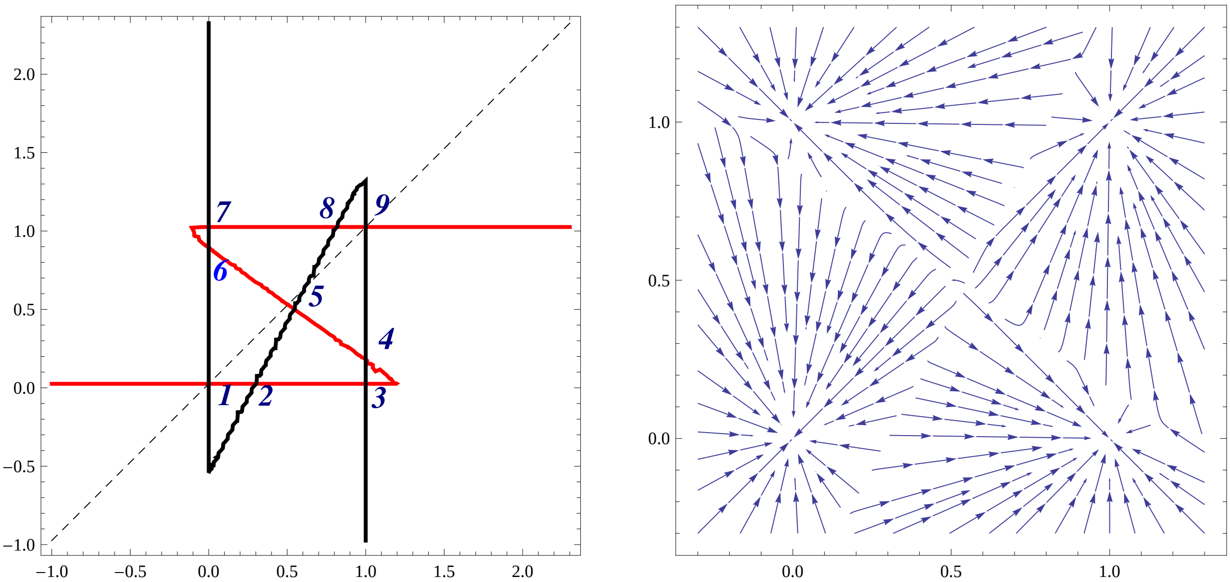
$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(10x_1 - 5x_2 - \theta_1)}} - x_1, \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(2x_1 + 3x_2 - \theta_2)}} - x_2. \end{cases} \tag{9}$$

Критические точки находятся из системы

$$\begin{cases} x_1 = e^{-e^{-\mu(10x_1 - 5x_2 - \theta_1)}}, \\ x_2 = e^{-e^{-\mu(2x_1 + 3x_2 - \theta_2)}}, \end{cases} \tag{10}$$

определяющей изоклины нуля. Изоклины изображены на рис. 9(a), а фазовый портрет с векторным полем — на рис. 9(b). Результаты анализа критических точек:

(i) тип критической точки $(0; 0)$ с меткой 1 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -1)$;
(ii) тип критической точки $(0{,}3; 0)$ с меткой 2 — седло при $(\lambda_1 = -1,\ \lambda_2 = 71{,}2)$;
(iii) тип критической точки $(1; 0)$ с меткой 3 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -1)$;
(iv) тип критической точки $(1; 0{,}16)$ с меткой 4 — седло при $(\lambda_1 = -1,\ \lambda_2 = 16{,}4)$;
(v) тип критической точки $(0{,}54; 0{,}48)$ с меткой 5 — неустойчивый узел $(\lambda_1 = 36{,}2,\ \lambda_2 = 49{,}4)$;.



(a) (b)

Рис. 9. Изоклины нуля (a) и фазовый портрет (b) системы (9) с девятью критическими точками. Значения параметров $\mu = 20$, $\theta_1 = 3$, $\theta_2 = 2{,}5$, $w_{11} = 10$, $w_{12} = -5$, $w_{21} = 2$, $w_{22} = 3$.

(vi) тип критической точки $(0; 0{,}86)$ с меткой 6 — седло при $(\lambda_1 = -1,\ \lambda_2 = 6{,}5)$;
(vii) тип критической точки $(0; 0{,}99)$ с меткой 7 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -0{,}9)$;
(viii) тип критической точки $(0{,}8; 1)$ с меткой 8 — седло при $(\lambda_1 = -1,\ \lambda_2 = 33{,}5)$;
(ix) тип критической точки $(1; 1)$ с меткой 9 — устойчивый узел при $(\lambda_1 = -1,\ \lambda_2 = -0{,}9)$.

3. Заключение. Для систем вида (1), моделирующих двухэлементные генные сети, имеют место следующие факты:

(1) всегда существует положение равновесия;
(2) максимальное число положений равновесия (критических точек), за исключением вырожденных случаев, равно девяти;
(3) структура множества критических точек при их максимальном количестве одна и та же для всех рассмотренных случаев: четыре устойчивых узла, четыре седла и неустойчивый узел в центре;
(4) возможно любое число критических точек от одной до девяти;
(5) аттракторы системы могут состоять из одной или нескольких критических точек;
(6) возможна классификация типичных поведений системы по положениям изоклин нуля;
(7) детальное исследование критических точек с вычислением характеристических значений можно заменить геометрическим анализом взаимного расположения изоклин нуля;
(8) функция Гомперца применима при качественном и количественном исследовании моделей генных сетей;
(9) возможно управление (контроль) системой путем изменения регулируемых параметров;
(10) возможно построение системы (модели) с нужными свойствами путем задания соответствующих изоклин нуля и затем синтеза нужной системы.

СПИСОК ЛИТЕРАТУРЫ

1. *Демиденко Г. В., Колчанов Н. А., Лихошвай В. А., Матушкин Ю. Г., Фадеев С. И.* Математическое моделирование регулярных контуров генных сетей// Ж. вычисл. мат. мат. физ. — 2004. — *44*, № 12. — С. 2276—2295.

2. *Acary V., de Jong H., Brogliato B.* Numerical simulation of piecewise-linear models of gene regulatory networks using complementarity system// Phys. D: Nonlin. Phenom. — 2014. — *269.* — P. 103–119.
3. *Atslega S., Finaskins D., Sadyrbaev F.* On a planar dynamical system arising in the network control theory// Math. Model. Anal. — 2016. — *21*, № 3. — P. 385–398.
4. *Brokan E., Sadyrbaev F. Zh.* On attractors in gene regulatory systems// AIP Conf. Proc. — 2017. — *1809.* — 020010.
5. *Koizumi Y. et al.* Robust virtual network topology control based on attractor selection// Opt. Network Design Model. — 2009. — P. 123—128.
6. *Koizumi Y. et al.* Adaptive virtual network topology control based on attractor selection// J. Lightwave Technol. — 2010. — *28*, № 11. — P. 1720–1731.
7. *Koizumi Y. et al.* Application of attractor selection to adaptive virtual network topology control// Bionetics — 2008. — *11.* — P. 1-–8.
8. *Sadyrbaev F.* Planar differential systems arising in network regulation theory// Adv. Math. Models Appl. — 2019. — *4*, № 1. — P. 70–78.
9. *Sadyrbaev F., Ogorelova D., Samuilik I.* A nullclines approach to the study of 2D artificial network// Contemp. Math. — 2019. — *1*, № 1. — P. 1–11.

Огорелова Диана Айваровна
Даугавпилсский университет, Даугавпилс, Латвия
E-mail: `dian4ik1601@inbox.lv`

Садырбаев Феликс Жармухамедович
Даугавпилсский университет, Даугавпилс, Латвия;
Институт математики и информатики Латвийского университета, Рига, Латвия
E-mail: `felix@latnet.lv`

On a three-dimensional neural network model

Diana Ogorelova[1], Felix Sadyrbaev[2]
[1]Department of Natural Sciences and Mathematics, Daugavpils University, Daugavpils, Latvia
[2]Institute of Mathematics and Computer Science, University of Latvia, Riga, Latvia
[1]Corresponding author
E-mail: [1]*diana.ogorelova@du.lv*, [2]*felix@latnet.lv*

Received 14 November 2022; received in revised form 1 December 2022; accepted 6 December 2022
DOI https://doi.org/10.21595/vp.2022.23059

Check for updates

61st International Conference on Vibroengineering in Udaipur, India, December 12-13, 2022

Abstract. The dynamics of a model of neural networks is studied. It is shown that the dynamical model of a three-dimensional neural network can have several attractors. These attractors can be in the form of stable equilibria and stable limit cycles. In particular, the model in question can have two three-dimensional limit cycles.

Keywords: neural networks, mathematical modeling, attractors.

1. Introduction

The theory of neural networks appeared as an attempt to understand the structure and principles of the functioning of the human brain. Now it is rich in results and practically significant field of research in natural sciences. Artificial neural networks (ANN) can be understood as computing systems inspired by biological neural networks. Their mathematical models can be formulated in terms of systems of quasi-linear differential equations of the form Eq. (1). Each dependent variable x_i is associated with a neuron. It accepts signals from other neurons (this is called input) and elaborates its own signal (it is called output) which is sent to a network. The nonlinearity is called the response function, or activation function. Usually, a sigmoidal function like $f(z) = 1/(1 + \exp(-z))$ or $\tanh(z)$ is used. Recent attempts to introduce other response functions may be found in [6]-[9]. The system:

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh(a_{11}x_1 + \cdots + a_{1n}x_n) - b_1x_1, \\ \dfrac{dx_2}{dt} = \tanh(a_{21}x_1 + \cdots + a_{2n}x_n) - b_2x_2, \\ \cdots \\ \dfrac{dx_n}{dt} = \tanh(a_{n1}x_1 + \cdots + a_{nn}x_n) - b_nx_n. \end{cases} \tag{1}$$

Appears in neurodynamics [1], [2]. It is of general nature, and for appropriate choice of parameters a_i and b_j it may have rich dynamics. Moreover, for sufficiently large n it can approximate (on a finite interval) any dynamical system [3]. The dynamics of solutions is a valuable object of investigation. Especially future states of a modeled neural networks are important to know. For this, the analysis of the phase space is needed. Future states are heavily dependent on attractors of the system, [4], [5]. In this note we will show that the three-dimensional system of the form Eq. (1) can have stable equilibria in the form of stable focuses. For the appropriate choice of parameters, it can have limit cycles attracting other solutions.

2. Two-dimensional system

Consider the system:

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh(a_{11}x_1 + a_{12}x_2) - b_1x_1, \\ \dfrac{dx_2}{dt} = \tanh(a_{21}x_1 + a_{22}x_2) - b_2x_2. \end{cases} \tag{2}$$

Proposition 1. System Eq. (2) can have stable critical points of the type stable focus.

Proof by construction the example. Set $a_{11} = k$, $a_{12} = 1.5$, $a_{21} = -1.5$, $a_{22} = k$, $k = 0.2$, $b_1 = b_2 = 1$, see Fig. 1.

Proposition 2. System Eq. (2) can have a limit cycle.

Proof by constructing the example. Set $a_{11} = k$, $a_{12} = 1.5$, $a_{21} = -1.5$, $a_{22} = k$, $k = 1.2$, $b_1 = b_2 = 1$, see Fig. 2.

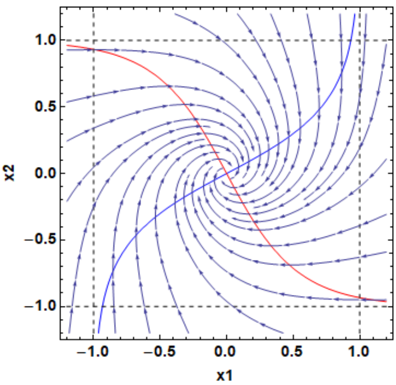


Fig. 1. Stable focus as in Proposition 1

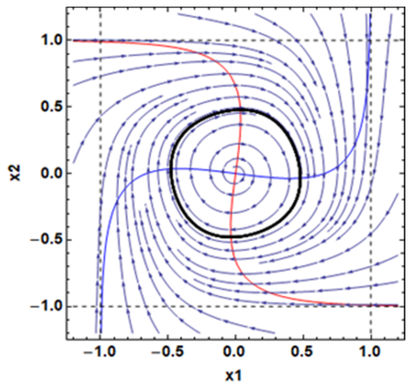


Fig. 2. Limit cycle as in Proposition 2

3. Three-dimensional system

Consider the three-dimensional system of the form Eq. (1):

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3) - b_1x_1, \\ \dfrac{dx_2}{dt} = \tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3) - b_2x_2, \\ \dfrac{dx_3}{dt} = \tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3) - b_3x_3. \end{cases} \tag{3}$$

Proposition 3. System Eq. (3) can have three limit cycles.

Proof by construction the example. Let the coefficient matrix in Eq. (3) be:

$$A = \begin{pmatrix} 1.2 & 1.5 & 0 \\ -1.5 & 1.2 & 0 \\ 0 & 0 & 1.2 \end{pmatrix}, \quad b_1 = b_2 = b_3 = 1,$$

and see Fig. 4.

The nullclines for the system Eq. (3) are given by the relations:

$$\begin{cases} 0 = \tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3) - b_1x_1, \\ 0 = \tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3) - b_2x_2, \\ 0 = \tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3) - b_3x_3. \end{cases} \tag{4}$$

There are three periodic solutions. The respective trajectories are located in three planes (blue ones in Fig. 3). The critical points inside the limit cycles have the following characteristic numbers: $\lambda_1 = -0.32$, $\lambda_{2,3} = 0.2 \pm 1.5i$ for the critical points at (0; 0; ±0.65857). The central critical point (0;0;0) has $\lambda_1 = 0.2$, $\lambda_{2,3} = 0.2 \pm 1.5i$. Trajectories go away from the central critical point.

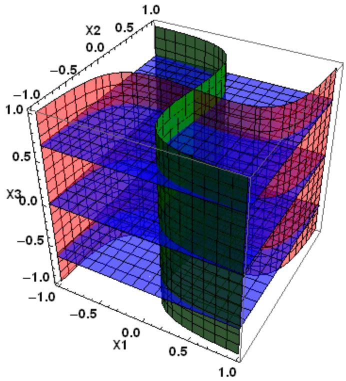


Fig. 3. Nullclines of the system Eq. (3), matrix A

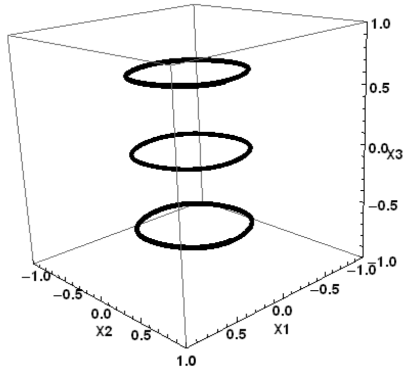


Fig. 4. Three periodic trajectories of the system Eq. (3)

4. Perturbation of three-dimensional system

Let the coefficients of the system Eq. (3) be perturbed as:

$$A_1 = \begin{pmatrix} 1.2 & 1.5 & 0.1 \\ -1.5 & 1.2 & -0.1 \\ -0.2 & -0.2 & 1.2 \end{pmatrix}. \quad (5)$$

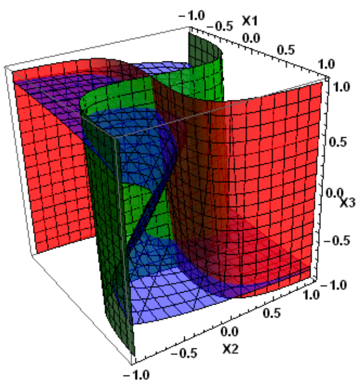


Fig. 5. Nullclines of the system Eq. (3) with the coefficient matrix A_1

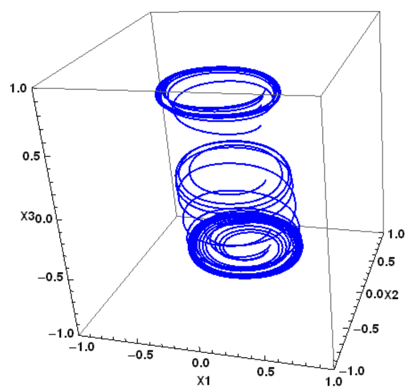


Fig. 6. Two periodic attractors of the system Eq. (3), coefficient matrix A_1, and converging some other trajectories. The middle limit cycles are destroyed

There are still three critical points at (–0.051; –0.039;0.68723), (0; 0; 0), (0.051; 0.039; –0.68723). Their characteristic numbers are: $\lambda_1 = -0.3543$, $\lambda_{2,3} = 0.19 \pm 1.4946i$ for the first and the third critical points, and $\lambda_1 = 0.2266$, $\lambda_{2,3} = 0.1866 \pm 1.5i$ for the central point.

Let the coefficients of the system Eq. (3) be perturbed as:

$$A_2 = \begin{pmatrix} 1.2 & 1.5 & 1.3 \\ -1.5 & 1.2 & -0.1 \\ -0.4 & -0.1 & 1.2 \end{pmatrix}. \quad (6)$$

There are still three critical points at (0.0527; 0.6533; –0.76188), (0;0;0), (–0.0527; –0.6533; 0.76188). Their characteristic numbers are: $\lambda_1 = -0.4434$, $\lambda_{2,3} = 0.089 \pm 1.1882i$ for the first and the third critical points, and $\lambda_1 = 0.2921$, $\lambda_{2,3} = 0.1539 \pm 1.6632$™ for the central point.

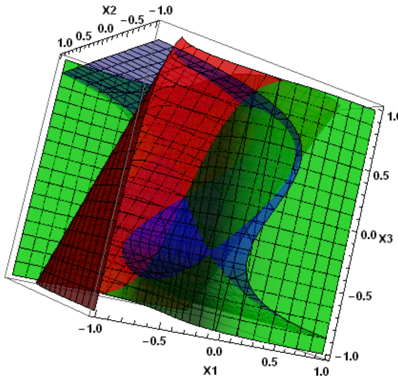


Fig. 7. Nullclines of the system Eq. (3) with the coefficient matrix A_2

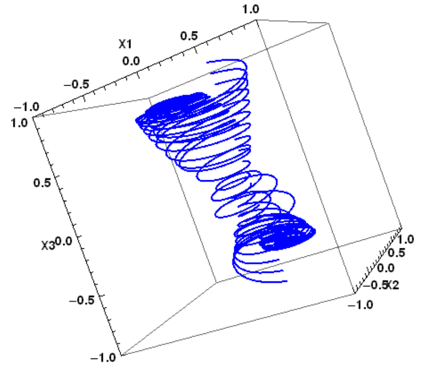


Fig. 8. Two periodic attractors of the system Eq. (3), coefficient matrix A_2, and converging trajectories

5. Conclusions

Dynamical systems, arising in neurodynamic, can have periodic attractors in the form of the limit cycles. Periodic attractors in two-dimensional systems appear as the result of Andronov-Hopf bifurcation, where the bifurcating parameter is the value at the main diagonal of the coefficients matrix A. Three-dimensional systems can have two attractors in the form of limit cycles. Small perturbation of the coefficient matrix A can destroy limit cycles lying in a non-stable manifold (that is, in the middle plane in the example above). It seems that two side attractors (which were in stable manifolds) are preserved under the perturbations saving the types of the corresponding critical points. For practical purposes, special attention should be paid to perturbations that preserve the structure of the nullclines and, as a consequence, characteristics of equilibria (critical points).

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".

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] S. Haykin, *Neural Networks. A Comprehensive Foundation*. Prentice Hall, 1998.

[2] J. C. Sprott, *Elegant Chaos*. Singapore: World Scientic, 2010.

[3] K.-I. Funahashi and Y. Nakamura, "Approximation of dynamical systems by continuous time recurrent neural networks," *Neural Networks*, Vol. 6, No. 6, pp. 801–806, Jan. 1993, https://doi.org/10.1016/s0893-6080(05)80125-x

[4] D. Ogorelova, F. Sadyrbaev, and V. Sengileyev, “Control in inhibitory genetic regulatory network models,” *Contemporary Mathematics*, Vol. 1, Oct. 2020, https://doi.org/10.37256/cm.152020538

[5] I. Samuilik and F. Sadyrbaev, “Modelling three dimensional gene regulatory networks,” *WSEAS Transactions on Systems and Control*, Vol. 16, pp. 755–763, 2021.

[6] A. Afzal, J. K. Bhutto, A. Alrobaian, A. Razak Kaladgi, and S. A. Khan, “Modelling and computational experiment to obtain optimized neural network for battery thermal management data,” *Energies*, Vol. 14, No. 21, p. 7370, Nov. 2021, https://doi.org/10.3390/en14217370

[7] S.-L. Shen, N. Zhang, A. Zhou, and Z.-Y. Yin, “Enhancement of neural networks with an alternative activation function tanhLU,” *Expert Systems with Applications*, Vol. 199, p. 117181, Aug. 2022, https://doi.org/10.1016/j.eswa.2022.117181

[8] E. Trentin, “Networks with trainable amplitude of activation functions,” *Neural Networks*, Vol. 14, No. 4-5, pp. 471–493, May 2001, https://doi.org/10.1016/s0893-6080(01)00028-4

[9] H. Zhu, H. Zeng, J. Liu, and X. Zhang, “Logish: A new nonlinear nonmonotonic activation function for convolutional neural network,” *Neurocomputing*, Vol. 458, pp. 490–499, Oct. 2021, https://doi.org/10.1016/j.neucom.2021.06.067

On a system of ordinary differential equations, arising in applications

Diana Ogorelova

Summary. 3D-model of artificial neural network is considered where the sigmoidal function is the hyperbolic tangent. The description of attractors is obtained depending on parameters.

MSC: 34C10, 34D45, 92C42

1 Introduction

The theory of neural networks is an actively investigated field [1]. It studied relations between neurons in a human brain. Neurons are imagined as elements of a neural network, communicating with each other by means of electric signals. In the book [2] a system of ordinary differential equations is proposed as a model of neural network. This system has much similarity to systems, which model gene regularity networks (GRN in short).

The two-dimensional GRN system can be written as

$$\begin{cases} x' = f_1(x, y, \mu_1, \theta_1, w_{11}, w_{12}) - \gamma_1 x, \\ y' = f_2(x, y, \mu_2, \theta_2, w_{21}, w_{22}) - \gamma_2 y, \end{cases} \tag{1}$$

where f_i are sigmoidal functions, increasing from zero to unity as the argument goes from $-\infty$ to $+\infty$. The function $f(z) = \frac{1}{1+e^{-\mu z}}$ is an example. Another example is the Gompertz function $f(z) = e^{-e^{-\mu z}}$. There are many other sigmoidal functions.

In the study of neural networks the system

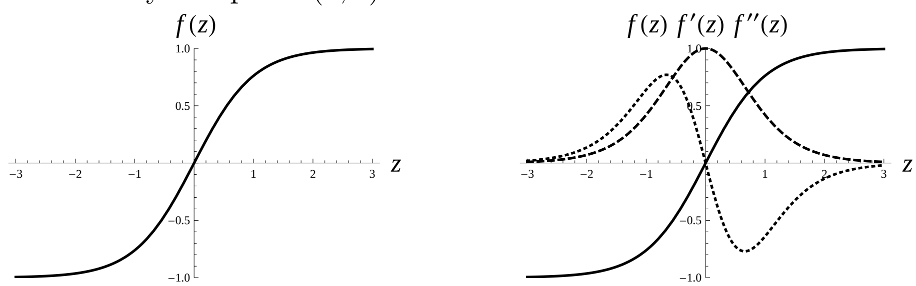
$$x_i' = \tanh(\sum_{j=1}^{n} a_{ij} x_j - \theta_i) - b_i x_i$$

is used [2, §6.10]. Here n is the number of neurons in a network. Our intent in this note is to describe some properties of a 2D neuronal system.

2 Hyperbolic tangent function

Consider the function $\tanh z = \dfrac{e^z - e^{-z}}{e^z + e^{-z}}$.

Function $\tanh z$ is a sigmoidal function, that is, each $\tanh z$ is monotonically increasing from minus unity to unity as the argument z goes from $-\infty$ to $+\infty$ and, moreover, the graph of $\tanh z$ has only one point $(0;0)$ of inflexion.



a) Sigmoidal function $f(z) = tanhz$

b) Solid - $f(x)$, dashed - $f'(x)$, dotted - $f''(x)$

Fig. 2.1.

Consider the Hyperbolic tangent function in the form $f(z) = \tanh(\mu z - \theta)$, where μ and θ are positive parameters.

If the parameter $\mu \to +\infty$, then graph of sigmoidal functions takes the piece-wise linear form. If the parameter $\mu \to 0$, then the graph of the sigmoid function is smoothed out. The parameter θ is responsible for the shift of the graph of sigmoidal function. If $\theta \to +\infty$, then the graph shifts to the right. If $\theta \to -\infty$, then the graph shifts to the left.

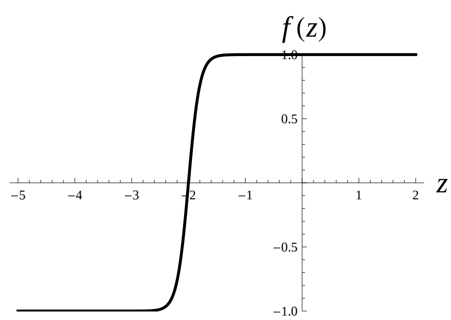


Fig. 2.2.Hyperbolic tangent function at the form $f(z) = \tanh(\mu z - \theta)$, where $\mu = 5$ and $\theta = -2$.

Our goal is to study the phase portrait and the attracting sets of this function.

3 2D neuronal system

Consider the system

$$\begin{cases} x' = \tanh(w_{11}x + w_{12}y) - b_1 x, \\ y' = \tanh(w_{21}x + w_{22}y) - b_2 y, \end{cases} \tag{2}$$

where w_{ij}, b_i are parameters.

Types of interaction are described by the so called regulatory matrix $W = (w_{ij})$. The regulatory matrix elements can take any reasonable values

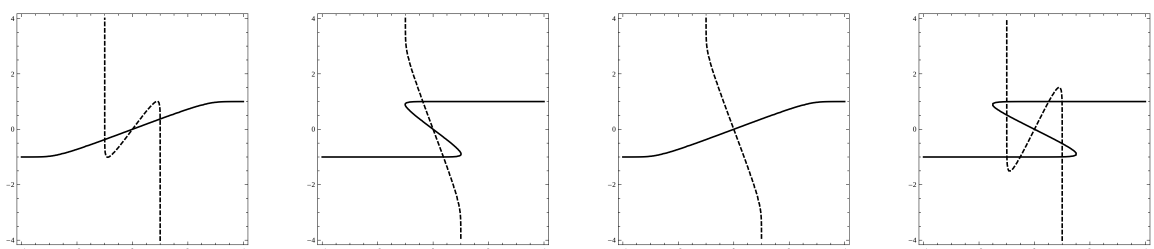
$$W = \begin{pmatrix} w_{11} & w_{12} \\ w_{21} & w_{22} \end{pmatrix}.$$

The elements of regulatory matrix w_{ij} responsible for the nullclines shapes. There exist four cases for type of interaction.

Case 1: Activation The regulatory matrix for this case in the form

$$W = \begin{pmatrix} * & + \\ + & * \end{pmatrix},$$

where elements w_{11} and w_{22} can take any reasonable values, but elements w_{12} and w_{21} are positive.



[1] $w_{11} = 6, w_{12} = 3, w_{21} = 3, w_{22} = 6, b_1 = b_2 = 1$

[2] $w_{11} = -6, w_{12} = 3, w_{21} = 3, w_{22} = -6, b_1 = b_2 = 1$

[3] $w_{11} = -6, w_{12} = 3, w_{21} = 3, w_{22} = 6, b_1 = b_2 = 1$

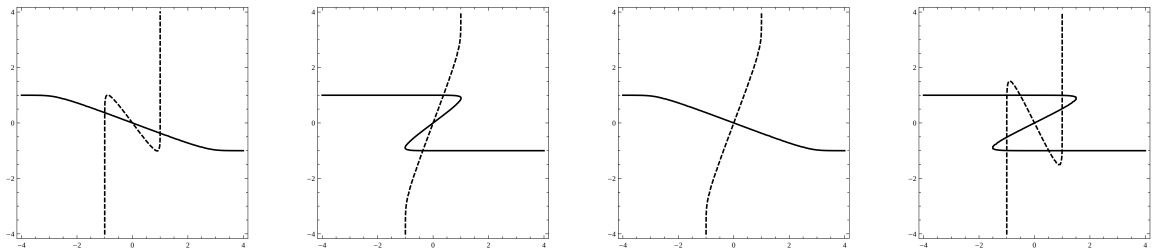
[4] $w_{11} = 6, w_{12} = 2, w_{21} = 2, w_{22} = -6, b_1 = b_2 = 1$

Fig. 3.1. Visualization of all cases

Case 2: Inhibition. The regulatory matrix for this case in the form

$$W = \begin{pmatrix} * & - \\ - & * \end{pmatrix},$$

where elements w_{11} and w_{22} can take any reasonable values, but elements w_{12} and w_{21} are negative.



[5]$w_{11} = 6, w_{12} = -3, w_{21} = -3, w_{22} = 6, b_1 = b_2 = 1$

[6]$w_{11} = -6, w_{12} = -3, w_{21} = -3, w_{22} = -6, b_1 = b_2 = 1$

[7] $w_{11} = -6, w_{12} = -3, w_{21} = -3, w_{22} = 6, b_1 = b_2 = 1$

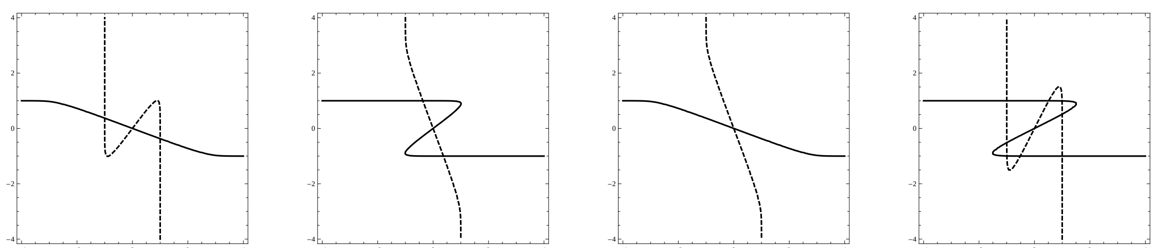
[8] $w_{11} = 6, w_{12} = -2, w_{21} = -2, w_{22} = -6, b_1 = b_2 = 1$

Fig. 3.2. Visualization of all cases

Case 3: Activation - Inhibition. The regulatory matrix for this case in the form

$$W = \begin{pmatrix} * & + \\ - & * \end{pmatrix},$$

where elements w_{11} and w_{22} can take any reasonable values element, but w_{12} is positive and element w_{21} is negative.



[9] $w_{11} = 6, w_{12} = 3, w_{21} = -3, w_{22} = 6, b_1 = b_2 = 1$

[10] $w_{11} = -6, w_{12} = 3, w_{21} = -3, w_{22} = -6, b_1 = b_2 = 1$

[11] $w_{11} = -6, w_{12} = 3, w_{21} = -3, w_{22} = 6, b_1 = b_2 = 1$

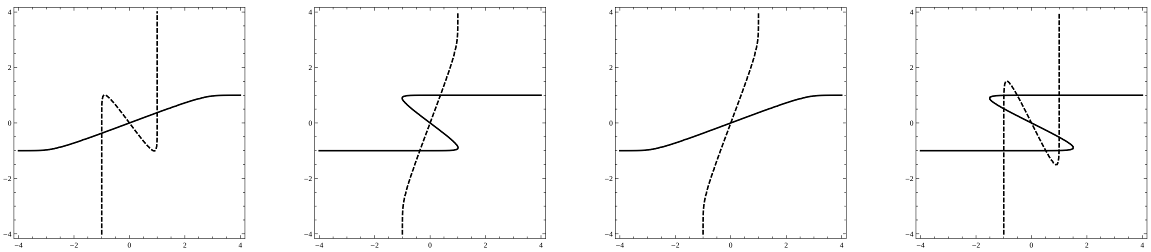
[12] $w_{11} = 6, w_{12} = 2, w_{21} = -2, w_{22} = -6, b_1 = b_2 = 1$

Fig. 3.3. Visualization of all cases

Case 4: Inhibition - Activation. The regulatory matrix for this case in the form

$$W = \begin{pmatrix} * & - \\ + & * \end{pmatrix},$$

where elements w_{11} and w_{22} can take any reasonable values but element w_{12} is negative and element w_{21} is positive.



[13] $w_{11} = 6, w_{12} = -3, w_{21} = 3, w_{22} = 6, b_1 = b_2 = 1$

[14]$w_{11} = -6, w_{12} = -3, w_{21} = 3, w_{22} = -6, b_1 = b_2 = 1$

[15]$w_{11} = -6, w_{12} = -3, w_{21} = 3, w_{22} = 6, b_1 = b_2 = 1$

[16]$w_{11} = 6, w_{12} = -2, w_{21} = 2, w_{22} = -6, b_1 = b_2 = 1$

Fig. 3.4. Visualization of all cases

Corollary. *There exists at least one critical point and the maximal number of critical points is nine.*

Proposition 1. All critical points (x, y) are in $(-1, 1) \times (-1, 1)$.

The vector field, defined by the system (2), is directed inward on the border of the box

$$Q_2 = \{(x, y) : |x| < \frac{1}{b_1}, |y| < \frac{1}{b_2}\}.$$

No trajectory can escape the box.

4 Critical points

The system in extended form is

$$\begin{cases} x' = \tanh[\mu_1(w_{11}x + w_{12}y - \theta_1)] - b_1 x, \\ y' = \tanh[\mu_2(w_{21}x + w_{22}y - \theta_2)] - b_2 y, \end{cases} \tag{3}$$

where μ_i and b_i are positive parameters.The coefficient matrix is

$$W = \begin{pmatrix} w_{11} & w_{12} \\ w_{21} & w_{22} \end{pmatrix}.$$

The nullclines are given by the equations

$$\begin{cases} x = \dfrac{1}{b_1} \tanh[\mu_1(w_{11}x + w_{12}y - \theta_1)], \\ y = \dfrac{1}{b_2} \tanh[\mu_2(w_{21}x + w_{22}y - \theta_2)]. \end{cases} \tag{4}$$

There exists at least one critical point. For analysis of critical points we need the linearized system (3).

For analysis of critical points we need the linearized system. It is

$$\begin{cases} u' = (-b_1 + f_{1x}) \cdot u + f_{1y} \cdot v, \\ v' = f_{2x} \cdot u + (-b_2 + f_{2y}) \cdot v, \end{cases} \tag{5}$$

where

$$\begin{cases} f_1 = \tanh[\mu_1(w_{11}x + w_{12}y - \theta_1)], \\ f_2 = \tanh[\mu_2(w_{21}x + w_{22}y - \theta_2)]. \end{cases} \tag{6}$$

$$A = \begin{vmatrix} -b_1 + f_{1x} & f_{1y} \\ f_{2x} & -b_2 + f_{2y} \end{vmatrix} \tag{7}$$

$$A - \lambda I = \begin{vmatrix} -b_1 + f_{1x} - \lambda & f_{1y} \\ f_{2x} & -b_2 + f_{2y} - \lambda \end{vmatrix} \tag{8}$$

and the characteristic equation is

$$det|A - \lambda I| = (-b_1 + f_{1x} - \lambda)(-b_2 + f_{2y} - \lambda) - (f_{1y})(f_{2x}) = b_1 b_2 - b_1 f_{2y} + b_1\lambda - \\ b_2 f_{1x} + f_{1x} f_{2y} - f_{1x}\lambda + b_2\lambda - f_{2y}\lambda + \lambda^2 - f_{1y} f_{2x} = \lambda^2 + (b_1 - f_{1x} + b_2 - f_{2y})\lambda + \\ +(b_1 b_2 - b_1 f_{2y} - b_2 f_{1x} + f_{1x} f_{2y} - f_{1y} f_{2x}) = 0. \tag{9}$$

To simplify we can write the characteristic equation as

$$\lambda^2 + B\lambda + C = 0, \tag{10}$$

$$B = b_1 - f_{1x} + b_2 - f_{2y}, \tag{11}$$

$$C = b_1 b_2 - b_1 f_{2y} - b_2 f_{1x} + f_{1x} f_{2y} - f_{1y} f_{2x}. \tag{12}$$

Example 1. Let consider the regulatory matrix in the form

$$W = \begin{pmatrix} 3 & 3 \\ -3 & 2 \end{pmatrix},$$

$b_1 = b_2 = \mu_1 = \mu_2 = 1, \theta_1 = \theta_2 = 0.1$. There are respectively one critical point $(-0.018; 0.045)$. The phase portrait of system (3) for one critical point is

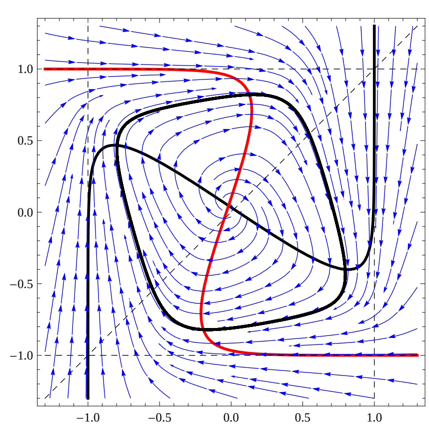


Fig. 4.1. Limit cycle. Critical point is a unstable focus
$(\lambda_1 = 1.49744 - 2.95413i, \lambda_2 = 1.49744 + 2.95413i)$

Example 2. Let consider the regulatory matrix of the form

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

$b_1 = b_2 = \mu_1 = \mu_2 = 1, \theta_1 = \theta_2 = 0.1$. There are respectively three critical points $(-0.995; -0.968), (0.1; 0.05), (0.993; 0.951)$. The phase portrait of system (3) for three critical points is

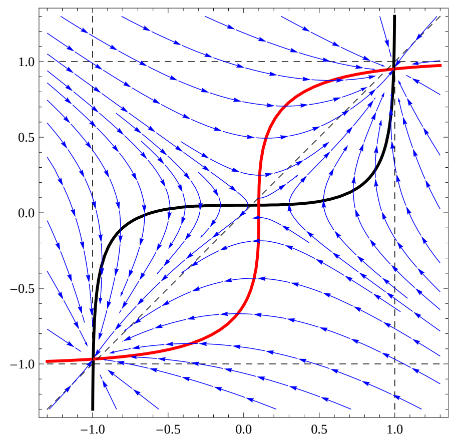


Fig. 4.2. Side critical points are stable nodes, middle point is a saddle

Example 3. Let consider the regulatory matrix of the form

$$W = \begin{pmatrix} 3 & 1 \\ 1 & 3 \end{pmatrix},$$

$b_1 = b_2 = \mu_1 = \mu_2 = 1, \theta_1 = \theta_2 = 0.1$. There are respectively nine critical points. The phase portrait of system (3) for nine critical points is

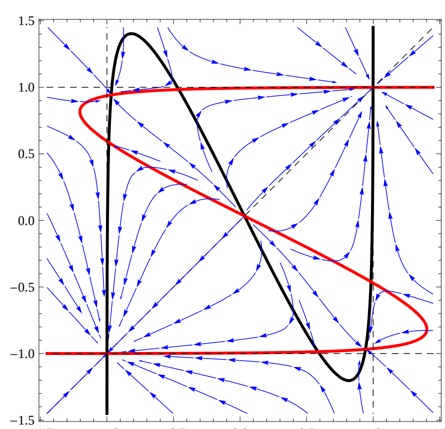


Fig. 4.3. Four side critical points are stable nodes, four critical points are saddle and middle point is unstable node

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".

References

[1] S. Haykin. Neural Networks. Prentice Hall, 2nd ed. - Russian translation, 2006. London (1992).

[2] J.C. Sprott. Elegant Chaos. World Scientific, Singapore, 2010. 3, 385 - 398.

[3] C. Furusawa and K. Kaneko. A generic mechanism for adaptive growth rate regulation. *PLoSComputational Biology*, 4:e3, 2008.

[4] H. D. Jong. Modeling and Simulation of Genetic Regulatory Systems: A Literature Review. J. Computational Biology, 9(1), 2002,67-103. doi: 10.1089/10665270252833208

[5] V.W. Noonburg, Differential Equations: From Calculus to Dynamical Systems, Providence, Rhode Island: MAA Press, 2019, 2nd edition.

[6] H. R. Wilson , J. D. Cowan (1972) Excitatory and inhibitory interactions in localized populations of model neurons, Biophys J., Jan;12(1):1-24

D. Ogorelova. Par parasto diferenciālvienādojumu sistēmu, sastopamu lietojumos.
Anotācija. Tiek apskatīts mākslīga neironu tikla sistēmas 3-dimensiju modelis, kurā par sigmoidālu funkciju kalpo hiperboliskais tangenss.

Д. Огорелова. О системе обыкновенных дифференциальных уравнений, возникающей в приложениях.
Аннотация. В статье рассматривается 3-мерная модель искусственной нейронной сети, в которой сигмоидальной функцией является гиперболический тангенс.

Daugavpils University
Daugavpils, Vienibas str. 13
diana.ogorelova@du.lv

Received 14.11.2022.

Periodic attractors in GRN and ANN networks

1st Ogorelova Diana
Department of Mathematics and Natural Sciences
Daugavpils University
Daugavpils, Latvia
Diana.Ogorelova@du.lv

2nd Sadyrbaev Felix
Institute of Mathematics and Computer Science
University of Latvia
Riga, Latvia
0000-0001-5074-804X

***Abstract*—We provide the conditions for the existence of a periodic solution in two-dimensional systems of ordinary differential equations, which arise in the theory of genetic and artificial neural networks. The proof is based on Poincare-Andronov-Hopf bifurcation. Multidimensional attractors can be constructed using the two-dimensional ones. Illustrations and examples are provided.**

***Index Terms*—Mathematical modelling, genetic regulatory networks, differential equations, attractors.**

I. Introduction

Large networks are in the focus of investigation in late decades due to their applicability in practical studies. Genetic regulatory networks (GRN) have applications in medicine [7] and are studied extensively by methods of mathematical modeling. The relative information can be found in [1], [2], [3], [6], [5], [15], [17], [13]. Of particular interest are the evolution of GRN and predicting future states. For this, modeling using dynamic systems is efficient. We consider models of GRN networks using quasi-linear ordinary differential equations of the form (1). The nonlinearity is represented by a sigmoidal function. We use logistic function. Some other sigmoidal functions, Hill's function [7], Gompertz function [15], etc., also can be used. The special attention is paid to attractors, since they form future states of a network. In this paper, we deal with periodic attractors. Systems of ordinary differential equations that model GRN are similar to those that are used to model artificial neuronal networks (ANN) ([4], [14], [12]), [11]. So we treat them together, and try to compare both.

We consider the two-dimensional systems of the form

$$\begin{cases} x_1' = \frac{1}{1+e^{-\mu_1(kx_1+ax_2-\theta_1)}} - x_1, \\ x_2' = \frac{1}{1+e^{-\mu_2(bx_1+kx_2-\theta_2)}} - x_2. \end{cases} \tag{1}$$

and

$$\begin{cases} x_1' = \tanh(kx_1+ax_2) - x_1, \\ x_2' = \tanh(bx_1+kx_2) - x_2. \end{cases} \tag{2}$$

The system (1) first appeared in the work [18] (see also [10]) as the model of two-dimensional neuronal networks. Systems of the form (2) were discussed in [16, Ch. 6].

Both systems can suffer the Poincare-Andronov-Hopf (in short: Hopf bifurcation) bifurcation with respect to the parameter k.

We suggest that
(A1): $a \cdot b < 0$;
(A2): k is positive.

Under these conditions the vector field is whirling (clockwise for $a > 0$, $b < 0$ and counter-clockwise for $a < 0$, $b > 0$). The nullclines are given by

$$\begin{cases} 0 = \tanh(kx_1+ax_2) - x_1, \\ 0 = \tanh(bx_1+kx_2) - x_2. \end{cases} \tag{3}$$

The critical points are solutions of (3). It is possible that there is a single critical point P.

Suppose that a and b have been chosen. It is known that by certain choice of the parameters θ a critical point can be placed at the origin $(0,0)$ for ANN system and at the point $(0.5, 0.5)$ for GRN system [9]. Let θ be chosen appropriately for any choice of k, a, b and P is put at the central position. Suppose that P is a single critical point. It can be shown by standard linearization analysis that for k small P is stable focus and the real part of the characteristic numbers is negative. It serves as an attractor for system (2). The point P is characterized by the characteristic numbers $\lambda_{1,2} = \alpha(k) + \beta(k)i$, where $i = \sqrt{-1}$.

For some larger k the real part $\alpha(k)$ passes through zero and stays positive. A periodic solution appears. This is called usually the Hopf bifurcation. It can be observed any time, when experimenting with systems (1) and (2) and choosing the parameter k appropriately.

Our aim is to prove this precisely (using some existing proof for general planar systems). Then we show how now precisely justified periodic solutions (limit cycles) can be used to construct periodic attractors for systems of even dimensionality.

II. GRN-system

Consider the system (1) under the conditions (A1) and (A2). The vector field rotates then in the unit square $Q_2 = \{0 < x_1 < 1, 0 < x_2 < 1\}$ clock-wise, if $a > 0$ (respectively $b < 0$), or counter-clock-wise, if $a < 0$.) The nullclines

$$\begin{cases} x_1 = \frac{1}{1+e^{-\mu_1(kx_1+ax_2-\theta_1)}}, \\ x_2 = \frac{1}{1+e^{-\mu_2(bx_1+kx_2-\theta_2)}}. \end{cases} \tag{4}$$

intersect at the point $(0.5, 0.5)$, if $\theta_1 = 0.5(k+a)$, $\theta_2 = 0.5(b+k)$. This can be checked immediately. This trick was used also in a more general situation in the paper [9]. This does not exclude the possibility of the existence of more critical points. All of them must locate in Q_2. If the nullclines (4) intersect only ones, a single critical point (it then is at $(0.5, 0.5)$) has characteristic values (this is the result of standard linearization analysis)

$$\lambda_{1,2} = -1 + k \pm \sqrt{|a\,b|}i, \quad i = \sqrt{-1} \tag{5}$$

for the special choice of $\mu_1 = \mu_2 = 4$. This critical point is a stable focus for small k and an unstable one for larger k.

Since the rotating vector field is repelling in a neighborhood of the unstable focus but is directed inward on the borders of Q_2, the existence of a periodic solution is expected. In multiple examples for various choices of the parameters a, b, k (satisfying the conditions (A1) and (A2)) the periodic solutions were constructed computationally.

Consider the result formulated in [8].

For the system

$$\begin{cases} x' = f_\mu(x, y), \\ y' = g_\mu(x, y), \end{cases} \tag{6}$$

depending on the parameter μ, the following is true.

Proposition 2.1: Let (x_0, y_0) be the critical point of (6) and $\lambda(\mu) = \alpha(\mu) \pm i\beta(\mu)$.

Suppose that for certain $\mu = \mu_0$ the following conditions are satisfied:

1. $\alpha(\mu_0) = 0, \quad \beta(\mu_0) = \omega \neq 0$;

2. $d\alpha(\mu)/d\mu \neq 0|_{\mu=\mu_0} =$ d;

3. a $\neq 0$, where a$=1/16(f_{xxx} + f_{xyy} + g_{xxy} + g_{yyy}) + 1/16\omega(f_{xy}(f_{xx} + f_{yy}) - g_{xy}(g_{xx} + g_{yy}) - f_{xx}g_{xx} + f_{yy}g_{yy})$ with $f_{xy} = \partial^2 f_\mu/(\partial x \partial y)(x_0, y_0)$ at $\mu = \mu_0$, etc.

Then a unique curve of periodic solutions bifurcates from the fixed point into the region $\mu > \mu_0$ if a·d < 0.

Let us check the system (1) for these conditions. The bifurcation parameter is k. The real part of λ is $\alpha(k) = -1+k$. The imaginary part is $\beta(k) = \sqrt{|a\,b|}$. So the condition 1 and 2 in Proposition 2.1 are satisfied. The condition 3 is tricky. Using Wolfram Mathematica for analytical calculation of the expression in the condition 3, [8], we arrive to the following assertion.

Proposition 2.2: The expression (denoted a) in the condition 3 of [8] for the system (1), where $\theta_1 = 0.5(k + a)$, $\theta_2 = 0.5(b + k)$, is

$$\mathsf{a} = k((-0.0625a^2 - 0.0625k^2)\mu_1^3 + (-0.0625b^2 - 0.0625k^2)\mu_2^3). \tag{7}$$

So for $k > 0$ the condition 3 in Proposition 2.1 is fulfilled.

III. Example for GRN-system

In this section we provide examples of periodic attractors for four-dimensional and five dimensional systems.

All GRN-systems are of the form

$$\begin{cases} x_1' = \frac{1}{1+e^{-\mu_1(w_{11}x_1+w_{12}x_2+\ldots+w_{1n}x_n-\theta_1)}} - x_1, \\ x_2' = \frac{1}{1+e^{-\mu_2(w_{21}x_1+w_{22}x_2+\ldots+w_{2n}x_n-\theta_2)}} - x_2, \\ \ldots \\ x_n' = \frac{1}{1+e^{-\mu_n(w_{n1}x_1+w_{n2}x_2+\ldots+w_{nn}x_n-\theta_n)}} - x_n, \end{cases} \tag{8}$$

Example. Consider system (8) for $n = 4$.

$$\begin{cases} x_1' = \frac{1}{1+e^{-4(2x_1+3x_2-2.5)}} - x_1, \\ x_2' = \frac{1}{1+e^{-4(-3x_1+2x_2+0.5)}} - x_2, \\ x_3' = \frac{1}{1+e^{-4(2x_3+3x_4-2.5)}} - x_3, \\ x_4' = \frac{1}{1+e^{-4(-3x_3+2x_4+0.5)}} - x_4. \end{cases} \tag{9}$$

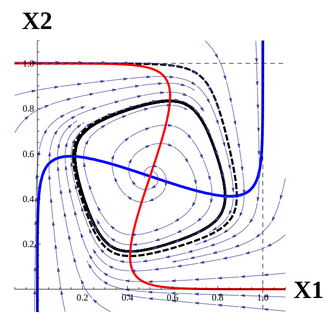


Fig. 1. The limit cycle in the 2D system corresponding to the first and the second equations in (9), with the nullclines (blue and red), the vector field and a solution, tending to the limit cycle (dashed).

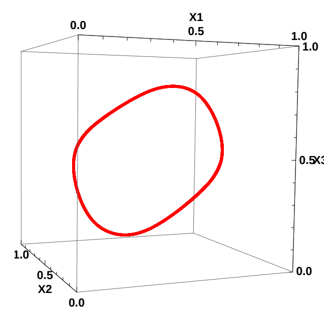


Fig. 2. The projection of the attractor in the system (9) onto (x_1, x_2, x_3)-space.

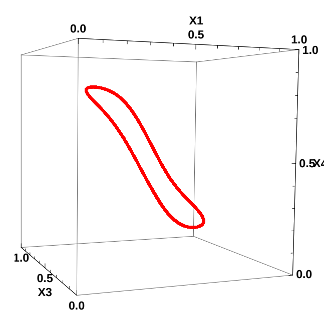


Fig. 3. The projection of the attractor in the system (9) onto (x_1, x_3, x_4)-space.

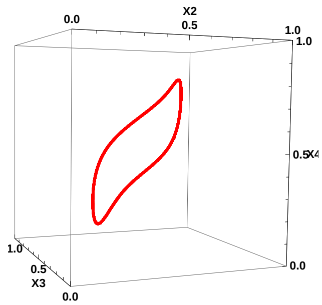


Fig. 4. The projection of the attractor in the system (9) onto (x_2, x_3, x_4)-space.

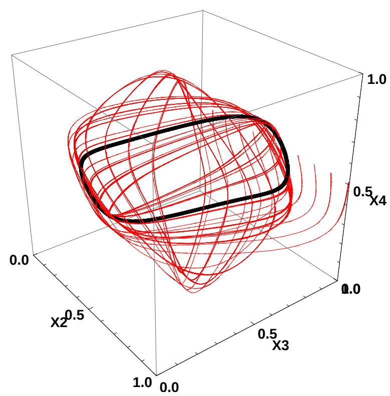


Fig. 5. Ten solutions of the system (9) (red), and the attractor (black). The projection onto (x_2, x_3, x_4)-space.

IV. ANN-SYSTEM

The hyperbolic tangent sigmoid function represents the hidden layer of sigmoid neurons followed by an output layer of positive linear neurons.

Consider a system (2). The vector field rotates in the square $G_2 = \{-1 < x_1 < 1, -1 < x_2 < 1\}$. The nullclines

$$\begin{cases} x_1 = \tanh(kx_1 + ax_2), \\ x_2 = \tanh(bx_1 + kx_2) \end{cases} \tag{10}$$

intersect at the point $(0, 0)$. If the nullclines (10) have a single cross-point (it is then at $(0, 0)$) and if we analyze the linearized system for nullclines (10), the characteristic values for the critical point are the same (5) as for GRN-system. This critical point is a stable focus, if $k < 1$ and an unstable one for $k > 1$. we can show that the conditions in Proposition 2.1 are fulfilled.

Proposition 4.1: The expression (denoted a) in the condition 3 of [8] for the system (2), is

$$\mathsf{a} = 1/16(-2a^2k - 2b^2k - 4k^3). \tag{11}$$

Calculations were made in Wolfram Mathematica analytically. Of course, the expression above is negative for $k > 0$. So Proposition 2.1 holds and the existence of periodic solutions in ANN-system (2) is confirmed also theoretically.

V. EXAMPLE FOR ANN-SYSTEM

Consider the four-dimensional system, where we provide examples of periodic attractors.

All ANN-systems for four-dimensional system are of the form

$$\begin{cases} x_1' = \tanh(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 + w_{14}x_4) - x_1, \\ x_2' = \tanh(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 + w_{24}x_4 - x_2, \\ x_3' = \tanh(w_{31}x_1 + w_{32}x_2 + w_{33}x_3 + w_{34}x_4 - x_3, \\ x_4' = \tanh(w_{41}x_1 + w_{42}x_2 + w_{43}x_3 + w_{44}x_4 - x_4. \end{cases} \tag{12}$$

Consider system (12) where $\theta_i = 0$ and regulatory matrix is

$$W = \begin{pmatrix} k & a & 0 & 0 \\ b & k & 0 & 0 \\ 0 & 0 & k & a \\ 0 & 0 & b & k \end{pmatrix}.$$

Example 1.

$$\begin{cases} x_1' = \tanh(2x_1 - x_2) - x_1, \\ x_2' = \tanh(3x_1 + 2x_2) - x_2, \\ x_3' = \tanh(2x_3 - x_4) - x_3, \\ x_4' = \tanh(3x_3 + 2x_4) - x_4. \end{cases} \tag{13}$$

This system is studied numerically (Wolfram Mathematica), providing description of the phase space and images of 2D and 3D projections.

The oscillatory solutions as shown in Figure 6 and Figure 7.

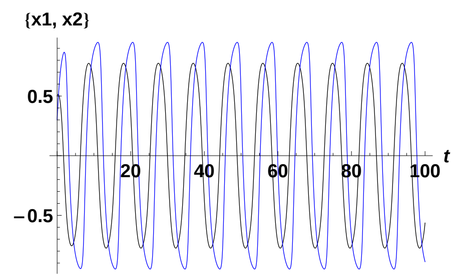


Fig. 6. Solutions $(x_1(t), x_2(t))$ of the system (13).

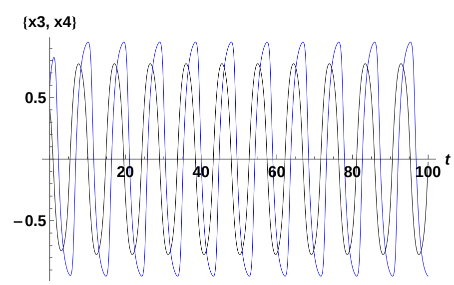


Fig. 7. Solutions $(x_3(t), x_4(t))$ of the system (13).

The attractor as shown in Figure 8 and Figure 9.

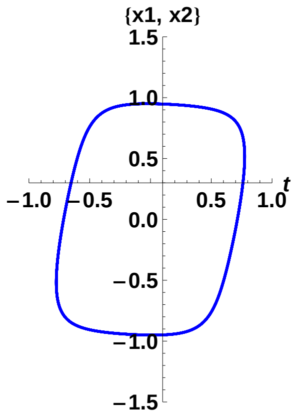


Fig. 8. The projection of the attractor of system (13) onto 2D (x_1, x_2)-subspace.

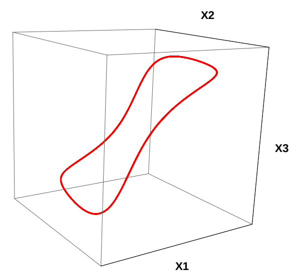


Fig. 9. The projection of the attractor of system (13) onto 3D (x_1, x_2, x_3)-subspace.

VI. Conclusions

Both GRN and ANN systems are similar. The question about possible attractors is in focus for both systems. The periodic attractors can exist in systems of both types, To be sure, one may first investigate the two-dimensional systems, construct periodic solutions, and then compose systems of higher dimensions, where the matrices of parameters are block-matrices with 2D blocks. Attractors emerge in new phase space. It is not difficult to construct 2D systems with periodic solutions, which are represented by closed trajectories. As to the precise mathematical proof of their existence, it is to be mentioned, that periodic solutions in known examples emerge as the result of Andronov-Hopf bifurcation. We consider systems with the matrices of special structure, depending on the parameter k. In this system the vector field, generated by differential equations, is rotating. For k small a single critical point (this is the requirement) is a stable focus. Under increasing of k the real part of the characteristic numbers passes through zero, the critical point changes its type to unstable focus and the limit cycle emerges. We have shown that for our two systems under mild conditions the hypotheses of a theorem, ensuring the existence of a branch (with respect to k) of periodic solutions, are fulfilled.

Then, based on the proven existence of periodic solutions, the examples of 2D attractors in the form of limit cycles, are constructed. These examples are used to construct systems of dimension four.

Acknowledgment

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".

References

[1] S. Atslega, D. Finaskins, F. Sadyrbaev. On a Planar Dynamical System Arising in the Network Control Theory, Mathematical Modelling and Analysis, **21 (2016)**, N 3, 385 - 398.
[2] E. Brokan and F. Zh. Sadyrbaev. On attractors in gene regulatory systems, AIP Conference Proceedings 1809, 020010 (2017): Proc. of the 6th International Advances In Applied Physics And Materials Science Congress & Exhibition (APMAS 2016), 1-3 June 2016, Istanbul, Turkey,; doi: 10.1063/1.4975425
[3] E. Brokan and F. Sadyrbaev, Attraction in n-dimensional differential systems from network regulation theory, em Mathematical Methods in the Applied Sciences 41, 2018, Issue 17, 7498-7509 https://doi.org/10.1002/mma.5086
[4] A. Das, A.B. Roy, Pritha Das. Chaos in a three dimensional neural network. Applied Mathematical Modelling 24 (2000) 511-522.
[5] R. Edwards and L. Ironi. Periodic solutions of gene networks with steep sigmoidal regulatory functions. Physica D, 282 (2014), 1 - 15. https://doi.org/10.1016/j.physd.2014.04.013
[6] C. Furusawa and K. Kaneko. A generic mechanism for adaptive growth rate regulation, PLoS Computational Biology, vol. 4, p. e3, Jan. 2008.
[7] Le-Zhi Wang, Celso Grebogi et al., A geometrical approach to control and controllability of nonlinear dynamical networks. Nature Communications, Volume 7, Article number: 11323 (2016), DOI: 10.1038/ncomms11323
[8] G. van der Heijden. Hopf bifurcation. www.ucl.ac.uk/~ucesgvd/hopf.pdf
[9] O. Kozlovska, F. Sadyrbaev. Models of genetic networks with given properties. WSEAS Transactions on Computer Research, 2022, 10, pp. 43-49.
[10] Noonburg V.W. Differential Equations: From Calculus to Dynamical Systems, Providence, Rhode Island: MAA Press, 2019, 2nd edition.
[11] D. Ogorelova, F. Sadyrbaev. On a three-dimensional neural network model. Vibroengineering Procedia, 2022, 47, pp. 6973.
[12] F. Sadyrbaev, D. Ogorelova, I. Samuilik. A nullclines approach to the study of 2D artificial network. Contemporary mathematics, 2019, Nov. 4, 1(1), 1-11.
[13] F. Sadyrbaev, I. Samuilik, V. Sengileyev. On modelling of genetic regulatory networks. WSEAS Transactions on Electronics, 2021, 12, pp. 73-80.
[14] I. Samuilik, F. Sadyrbaev. On a dynamical model of genetic networks WSEAS Transactions on Business and Economics, 2023, 20, pp. 104112.
[15] I. Samuilik, F. Sadyrbaev, D. Ogorelova. Mathematical modeling of three-dimensional genetic regulatory networks using logistic and Gompertz functions. WSEAS Transactions on Systems and Control, 2022, 17, pp. 101107.
[16] J.C. Sprott. Elegant chaos.Algebraically simple chaotic flows. World scientific, 2010.
[17] N. Vijesh, S. K. Chakrabarti, J. Sreekumar, "Modeling of gene regulatory networks: A review," J. Biomedical Science and Engineering, **6**:223-231, 2013.
[18] Wilson HR, Cowan JD. Excitatory and inhibitory interactions in localized populations of model neurons. Biophys J., vol 12 (1), 1972, pp. 1-24.

Contemporary Mathematics
http://ojs.wiserpub.com/index.php/CM/

Research Article

Comparative Analysis of Models of Gene and Neural Networks

Inna Samuilik[1*], **Felix Sadyrbaev**[2], **Diana Ogorelova**[2]

[1]Department of Engineering Mathematics, Riga Technical University, Riga, Latvia
[2]Department of Natural Sciences and Mathematics, Daugavpils University, Daugavpils, Latvia
Email: Inna.Samuilika@rtu.lv

Received: 31 January 2023; **Revised:** 29 March 2023; **Accepted:** 3 April 2023

Abstract: In the language of mathematics, the method of cognition of the surrounding world in which the description of the object is carried out the name is mathematical modeling. The study of the model is carried out using certain mathematical methods. The systems of the ordinary differential equations modeling artificial neuronal networks and the systems modeling the gene regulatory networks are considered. The one system consists of a sigmoidal function which depends on linear combinations of the arguments minus the linear part. The other system consists of a sigmoidal function which depends on the hyperbolic tangent function. The linear combinations and hyperbolic tangent functions of the arguments are described by one regulatory matrix. For the three-dimensional cases, two types of matrices are considered and the behavior of the solutions of the system is analyzed. The attracting sets are constructed for several cases. Illustrative examples are provided. The list of references consists of 19 items.

***Keywords*:** gene regulatory network, artificial neural network, chaotic solution, periodic solution, Lyapunov exponents

MSC: 34A34, 34D45, 92B20, 92D15

1. Introduction

Complex regulatory networks are being explored in many areas of science, including biochemistry, biology [1-2], ecology, and engineering. Gene regulatory network (GRN in short) is a complex dynamical system that is present in living organisms and which is constantly changing their states responding to fluctuations in their environment [3]. For a complete description of gene networks, it is necessary to analyze the processes occurring in them at the level of the whole organism. In this case, it is possible to describe gene networks, some parts of which are distributed over various large compartments of their organism, such as organs and tissues. In many cases, it is possible to determine the direction of processes within a specific fragment of the gene network. The main approaches to the description of gene networks and modeling their dynamics are a logical description; a description of the gene network using a system of nonlinear differential equations [3]; stochastic gene network models; graph theory [1], Boolean modeling [1]. Nonlinear ordinary differential equations are the most-widespread formalism for modeling genetic regulatory networks [4-7].

An artificial neural network (ANN in short) is a mathematical model created in the likeness of biological neural networks [8]. Similar to a natural analog, an artificial neural network consists of neurons and synapses [9]. Neural networks are used to solve many problems: recognition and generation of images (face identification in video

DOI: https://doi.org/10.37256/cm.4220232404

surveillance systems); speech and language (language for chat-bots and service robots); weather prediction; medical diagnosis [9-10]; business fields [11-12]; traffic monitoring systems [13].

In our paper, we use nonlinear ordinary differential equations to model the GRN and ANN. Our goal is to describe the behavior of the systems and to compare the results of GRN and ANN. In our previous papers on GRN networks multiple results on attractors and their properties were obtained. By comparison with models of neuronal networks we wish to show that similar results can be presented for neuronal networks. Our consideration is geometrical. The main intent is to use the 2D and 3D projections on different subspaces, to construct the graphs of systems solutions. Visualizations are provided. The dynamics of Lyapunov exponents are shown. Calculations and visualizations are performed using Wolfram Mathematics.

2. Gene regulatory network

Consider the three-dimensional system

$$\begin{cases} x_1' = \dfrac{1}{1+e^{-\mu_1(w_{11}x_1+w_{12}x_2+w_{13}x_3-\theta_1)}} - v_1x_1, \\ x_2' = \dfrac{1}{1+e^{-\mu_2(w_{21}x_1+w_{22}x_2+w_{23}x_3-\theta_2)}} - v_2x_2, \\ x_3' = \dfrac{1}{1+e^{-\mu_3(w_{31}x_1+w_{32}x_2+w_{33}x_3-\theta_3)}} - v_3x_3. \end{cases} \tag{1}$$

In the context of GRN theory, this system describes the three-element network. The link between any two elements x_i and x_j is associated with the element w_{ij} of the regulatory matrix

$$W = \begin{pmatrix} w_{11} & w_{12} & w_{13} \\ w_{21} & w_{22} & w_{23} \\ w_{31} & w_{32} & w_{33} \end{pmatrix}.$$

Positivity of w_{ij} means the activation of x_i by x_j, negativity means inhibition, and zero value is for no relation. System (1) was studied, in particular, in the paper [14].

$$\begin{cases} v_1x_1 = \dfrac{1}{1+e^{-\mu_1(w_{11}x_1+w_{12}x_2+w_{13}x_3-\theta_1)}}, \\ v_2x_2 = \dfrac{1}{1+e^{-\mu_2(w_{21}x_1+w_{22}x_2+w_{23}x_3-\theta_2)}}, \\ v_3x_3 = \dfrac{1}{1+e^{-\mu_3(w_{31}x_1+w_{32}x_2+w_{33}x_3-\theta_3)}}. \end{cases} \tag{2}$$

All critical points are located in the open parallelepiped

$$\left\{(x_1, x_2, x_3) : 0 < x_1 < \frac{1}{v_1},\ 0 < x_2 < \frac{1}{v_2},\ 0 < x_3 < \frac{1}{v_3}\right\} \tag{3}$$

2.1 *An example of the system (1) with a periodic solution*

Let the coefficient matrix in (1) be

$$W = \begin{pmatrix} 2.5 & -1.5 & 0 \\ 4 & 2.5 & 0 \\ 0 & 0 & 1.2 \end{pmatrix} \tag{4}$$

and $v_1 = v_2 = v_3 = 1$; $\mu_1 = 2.3$; $\mu_2 = 1.9$; $\mu_3 = 1$; $\theta_1 = 0.5$; $\theta_2 = 2.5$; $\theta_3 = 1$.

There is one critical point (0.320154; 0.418536; 0.36235). The characteristic numbers are λ_1 = -0.72 and $\lambda_{2,3}$ = 0.2 ± 1.18i. The type of critical point is an unstable saddle-focus. The nullclines of the system (1) and the stable periodic solution are depicted in Figure 1 and Figure 2. The graphs of $x_i(t)$, i = 1, 2, 3 of the system (1) with the regulatory matrix (4) are depicted in Figure 3.

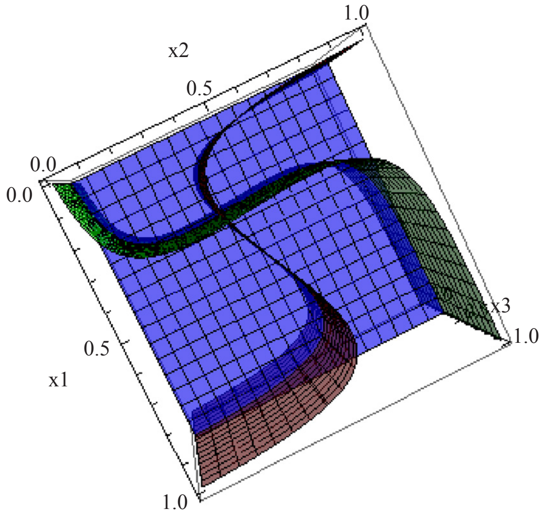


Figure 1. The nullclines of the system (1) with the regulatory matrix (4).

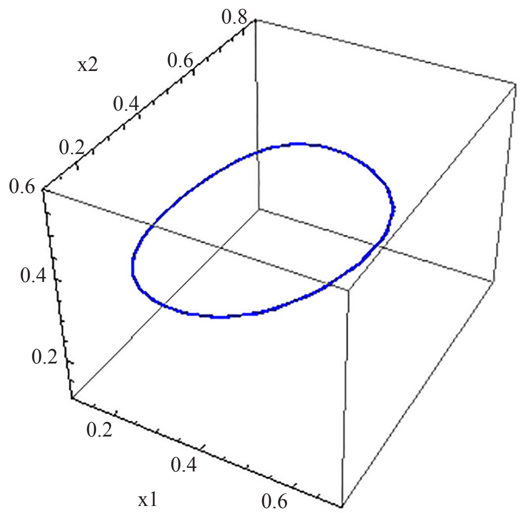


Figure 2. The periodic solution of the system (1) with the regulatory matrix (4).

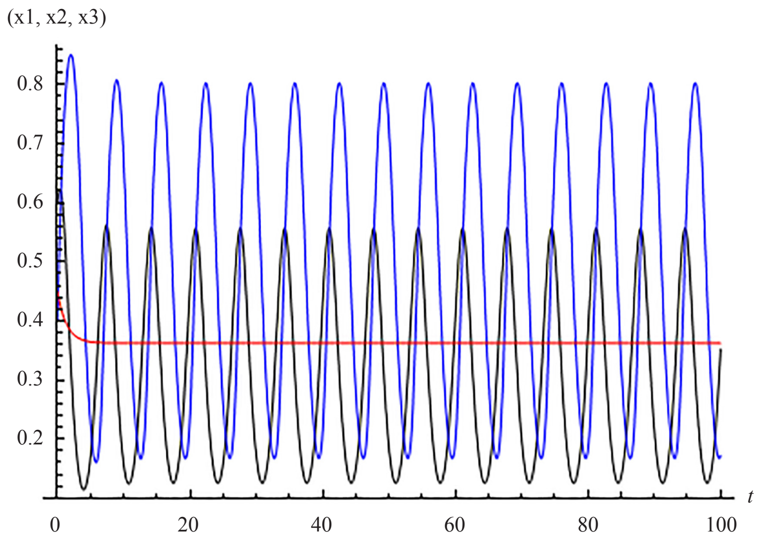


Figure 3. The graphs of $x_i(t)$, $i = 1, 2, 3$ of the system (1) with the regulatory matrix (4).

Similar systems are considered in paper [14].

The dynamics of Lyapunov exponents ($LE_1 = 0$, $LE_2 = -0.3166$; $LE_3 = -0.7227$) are shown in Figure 4. The following set of LEs characterizes the stable limit cycle.

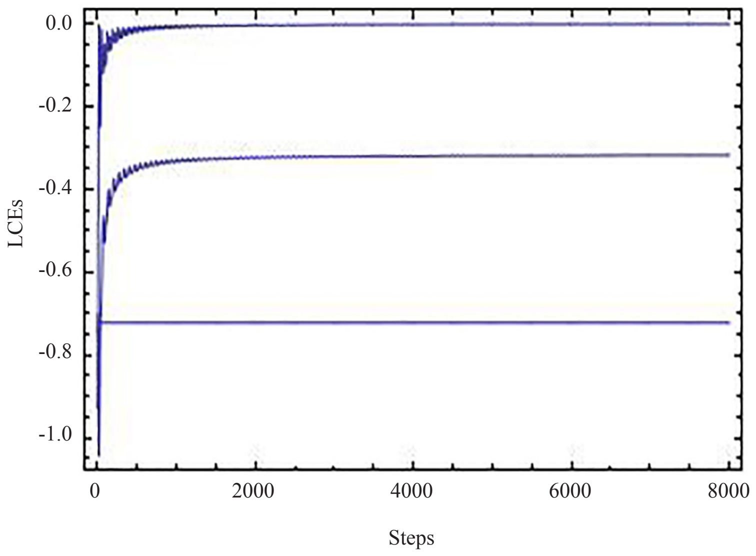


Figure 4. The dynamics of Lyapunov exponents.

The sum of Lyapunov exponents of the system (1) with the regulatory matrix (4) is negative that is why it is a dissipative system.

2.2 *An example of the system (2) with a chaotic solution*

Under chaos in ancient Greek mythology understood the pre-life confusion. Greek “chaos” is the infinite first everyday mass, which subsequently gave rise to all the existing. Physicists call this science-"nonlinear dynamics", mathematicians-"chaos theory", all the rest-"nonlinear science".

Chaos is a multifaceted phenomenon that is not easily classified or identified. There is no universally accepted definition for chaos, but the following characteristics are nearly always displayed by the solutions of chaotic systems [15].

There are several characteristics that identify the behavior of chaotic systems [16]. Usually to identify a chaotic system scientists use the method of Lyapunov exponents [16]. A 3D dynamical system is chaotic if it has one positive Lyapunov exponent (LE in short) [17]. Also, a system is said to be dissipative if the sum of all Lyapunov exponents of the system (1) is negative [18].

Consider the system (1), where $v_1 = 0.65$, $v_2 = 0.42$, $v_3 = 0.1$, $\mu_1 = \mu_2 = 7$, $\mu_3 = 13$, $\theta_1 = 0.5$, $\theta_2 = 0.3$, $\theta_3 = 0.7$.

The regulatory matrix of the system (1) is

$$W = \begin{pmatrix} 0 & 1 & -5.63 \\ 1 & 0 & 0.133 \\ 1 & 0.02 & 0.03 \end{pmatrix} \tag{5}$$

The initial conditions are

$$x_1(1) = 0.2; x_2(1) = 1.3; x_3(1) = 0.4. \tag{6}$$

There is one critical point. The characteristic equation for critical point (0.370688; 1.59227; 0.223125) is $-\lambda^3 + A\lambda^2 + B\lambda + C = 0$, where $A = -1.16149$; $B = -0.428566$; $C = -0.689604$. Solving the equation, we have $\lambda_1 = -1.257$; $\lambda_{2,3} = 0.0477516 \pm 0.739143i$. The type of critical point is an unstable saddle-focus. The nullclines of the system (1) with the regulatory matrix (4) and the chaotic attractor of the system (1) with the regulatory matrix (4) are depicted in Figure 5 and Figure 6. The graphs of $x_i(t)$, $i = 1, 2, 3$ of the system (1) with the regulatory matrix (4) are shown in Figure 7.

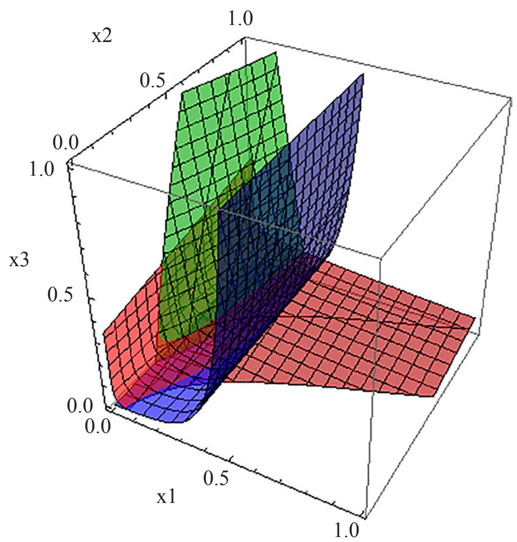


Figure 5. The nullclines of the system (1) with the regulatory matrix (4).

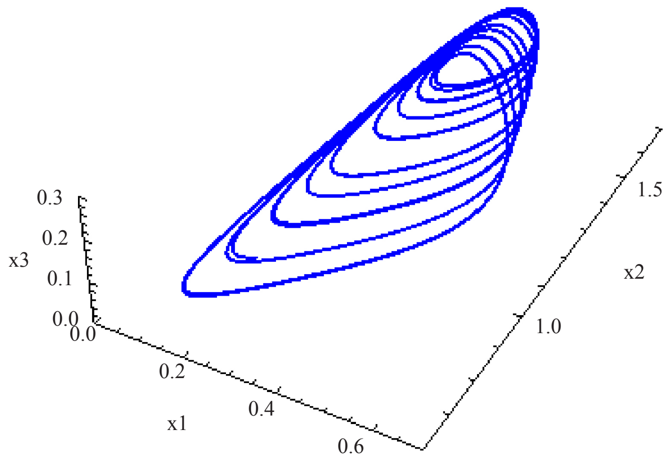


Figure 6. The chaotic attractor of the system (1) with the regulatory matrix (4).

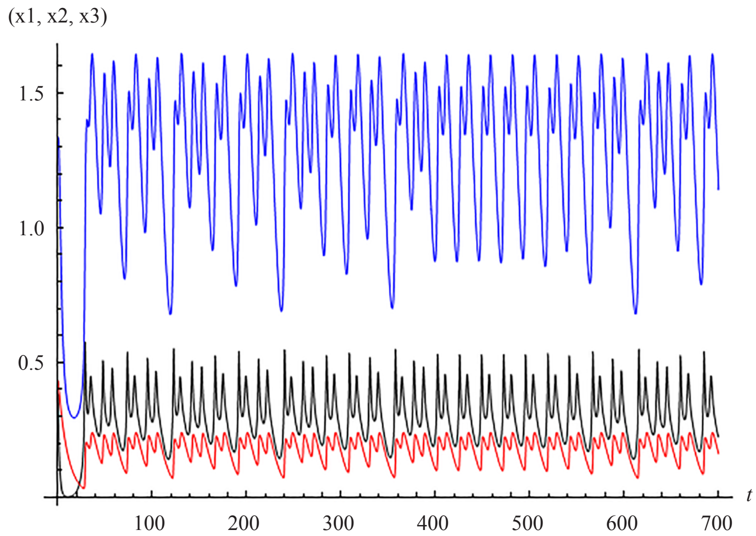


Figure 7. The graphs of $x_i(t)$, i = 1, 2, 3 of the system (1) with the regulatory matrix (4).

Similar systems were considered in papers [14], [19] and [20].

The dynamics of Lyapunov exponents ($LE_1 = 0.03$, $LE_2 = 0$; $LE_3 = -1.16$) are shown in Figure 8.

At the end of the 70s of the last century, the Kaplan-Yorke formula was proposed to estimate the fractal size-in terms of Lyapunov exponents [12].

Let calculate the Kaplan-Yorke dimension using the formula

$$D_{KY} = j + \frac{1}{|L_{j+1}|} \sum_{j=1}^{j} L_j$$

with j representing the index such that

$$\sum_{j=1}^{j} L_j > 0, \ \sum_{j=1}^{j+1} L_j < 0$$

Such formula is considered in papers [12, 21].

Kaplan-Yorke dimension for the system (1) with the regulatory matrix (5) is D_{KY} = 2.03. The sum of Lyapunov exponents of the system (1) with the regulatory matrix (5) is negative that is why it is a dissipative system. The dynamics of Lyapunov exponents are shown in Figure 8.

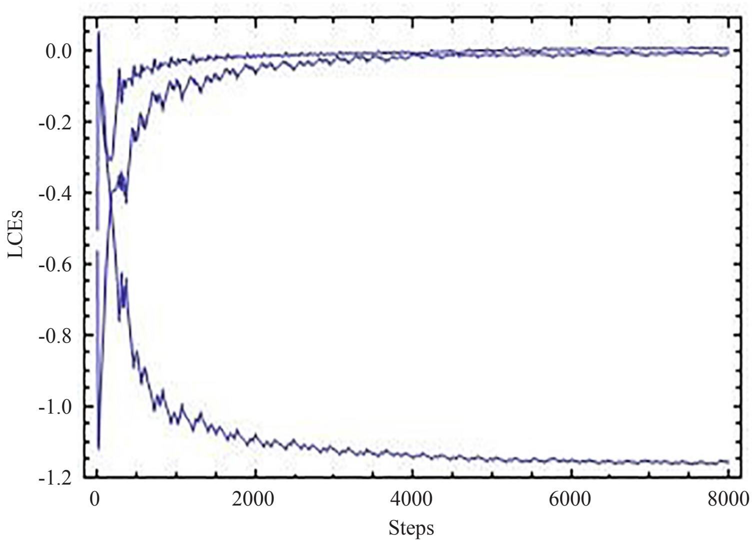


Figure 8. The dynamics of Lyapunov exponents.

3. Artificial neural network

Consider the three-dimensional system

$$\begin{cases} x_1' = \tanh(w_{11}x_1 + w_{12}x_2 + w_{13}x_3) - b_1x_1, \\ x_2' = \tanh(w_{21}x_1 + w_{22}x_2 + w_{23}x_3) - b_2x_2, \\ x_3' = \tanh(w_{31}x_1 + w_{32}x_2 + w_{33}x_3) - b_3x_3. \end{cases} \tag{7}$$

The system (7) is considered in papers [22, 23].

The nullclines are given as

$$\begin{cases} b_1x_1 = \tanh(w_{11}x_1 + w_{12}x_2 + w_{13}x_3), \\ b_2x_2 = \tanh(w_{21}x_1 + w_{22}x_2 + w_{23}x_3), \\ b_3x_3 = \tanh(w_{31}x_1 + w_{32}x_2 + w_{33}x_3). \end{cases} \tag{8}$$

All critical points are located in the open parallelepiped

$$\left\{(x_1, x_2, x_3) : -\frac{1}{b_1} < x_1 < \frac{1}{b_1}, \ -\frac{1}{b_2} < x_2 < \frac{1}{b_2}, \ -\frac{1}{b_3} < x_3 < \frac{1}{b_3}\right\}. \tag{9}$$

3.1 *Examples of the system (7) with regulatory matrices (4) and (5)*

Consider the coefficient matrix (4) and $b_1 = b_2 = b_3 = 1$.

There are three critical points. First critical point is (0; 0; 0). The characteristic numbers are $\lambda_1 = 0.2$ and $\lambda_{2,3} = 1.5 \pm 2.45i$. The type of critical point is an unstable focus-node. Second critical point is (0; 0; 0.66). The characteristic numbers are $\lambda_1 = -0.32$ and $\lambda_{2,3} = 1.5 \pm 2.45i$. The type of critical point is an unstable saddle-focus. Third critical point is (0; 0; -0.66). The characteristic numbers are $\lambda_1 = -0.32$ and $\lambda_{2,3} = 1.5 \pm 2.45i$. The type of critical point is an unstable saddle-focus. The nullclines of the system (7) with the regulatory matrix (4) and three periodic solutions of the system (7) with the regulatory matrix (4) are shown in Figure 9 and Figure 10. The graphs of $x_i(t)$, $i = 1, 2, 3$ of the system (7) with the regulatory matrix (4) are depicted in Figure 11.

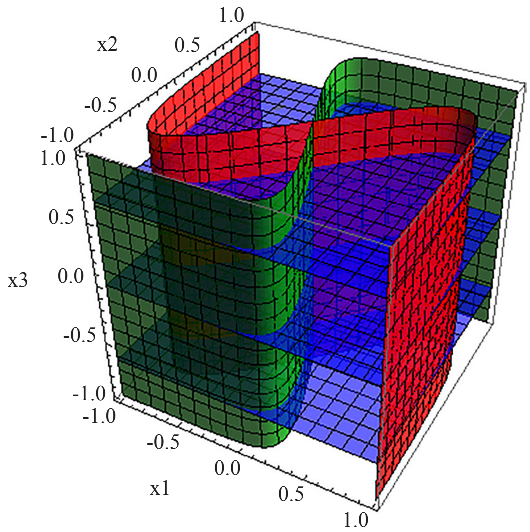


Figure 9. The nullclines of the system (7) with the regulatory matrix (4).

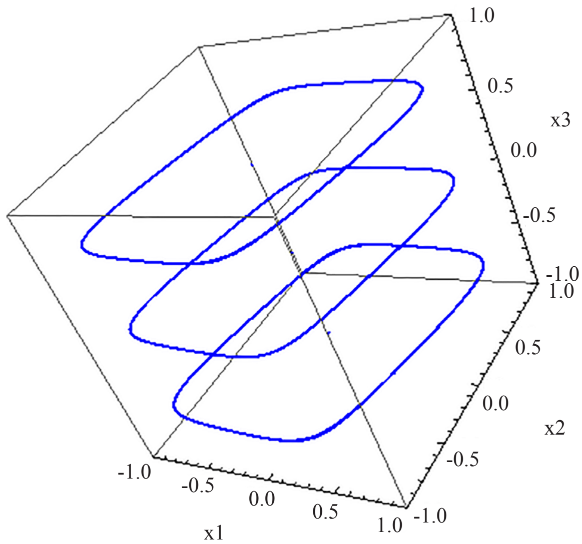


Figure 10. Three periodic solutions of the system (7) with the regulatory matrix (4).

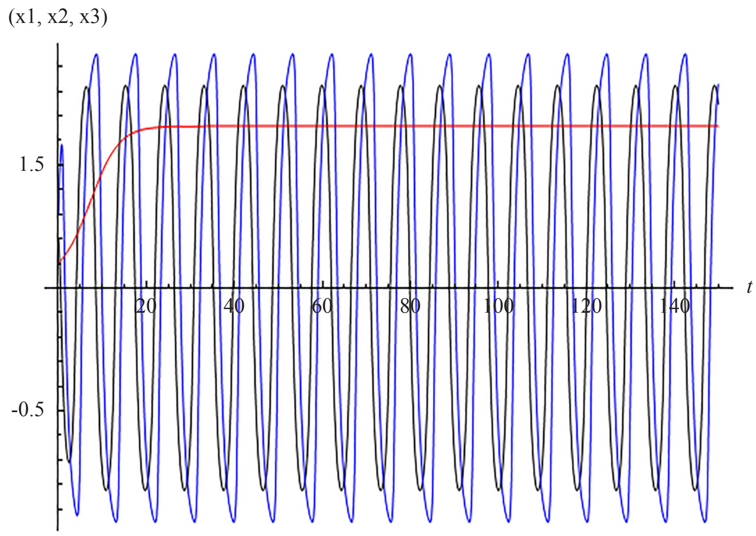


Figure 11. The graphs of $x_i(t)$, i = 1, 2, 3 of the system (7) with the regulatory matrix (4).

Similar systems are considered in paper [22].

The dynamics of Lyapunov exponents (LE_1 = 0, LE_2 = -0.32; LE_3 = -0.78) are shown in Figure 12. The following set of LEs characterizes the stable limit cycle.

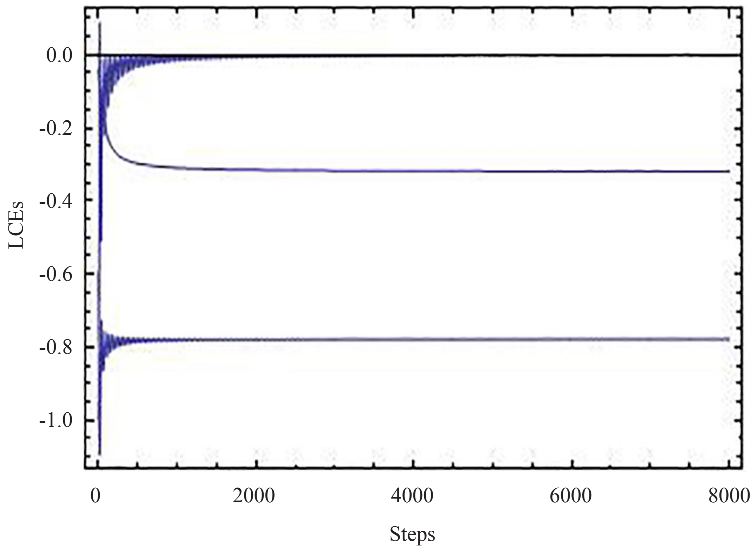


Figure 12. The dynamics of Lyapunov exponents.

The sum of Lyapunov exponents of the system (1) with the regulatory matrix (5) is negative that is why it is a dissipative system.

Consider the coefficient matrix (5) and b_1 = 0.65, b_2 = 0.42, b_3 = 0.1. The coefficients of regulatory matrix and parameters are the same. The initial conditions are (6). There is no chaotic solution. The nullclines of the system (7) with the regulatory matrix (5) and the solution of the system (7) with the regulatory matrix (5) and the initial conditions (6) are shown in Figure 13 and Figure 14. The graphs of $x_i(t)$, i = 1, 2, 3 of the system (7) with the regulatory matrix (5) are depicted in Figure 15.

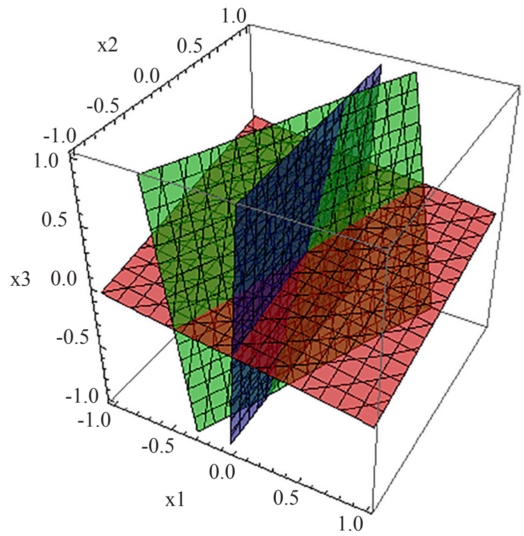


Figure 13. The nullclines of the system (7) with the regulatory matrix (5).

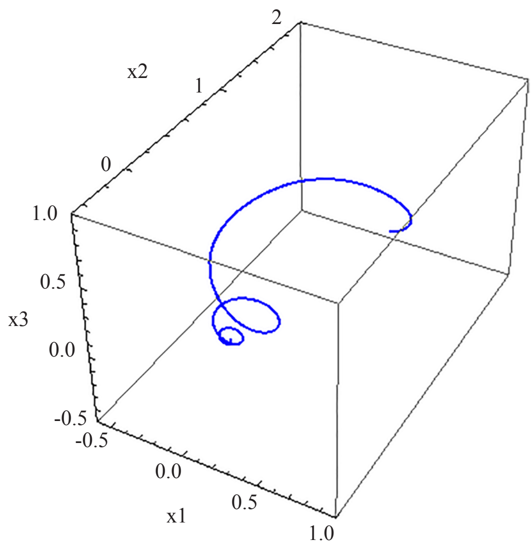


Figure 14. The solution of the system (7) with the regulatory matrix (5) and the initial conditions (6).

The dynamics of Lyapunov exponents (LE_1 = -0.32, LE_2 = -0.33; LE_3 = -0.49) are shown in Figure 16. The following set of LEs characterizes the stable fixed point.

The sum of Lyapunov exponents of the system (1) with the regulatory matrix (5) is negative that is why it is a dissipative system.

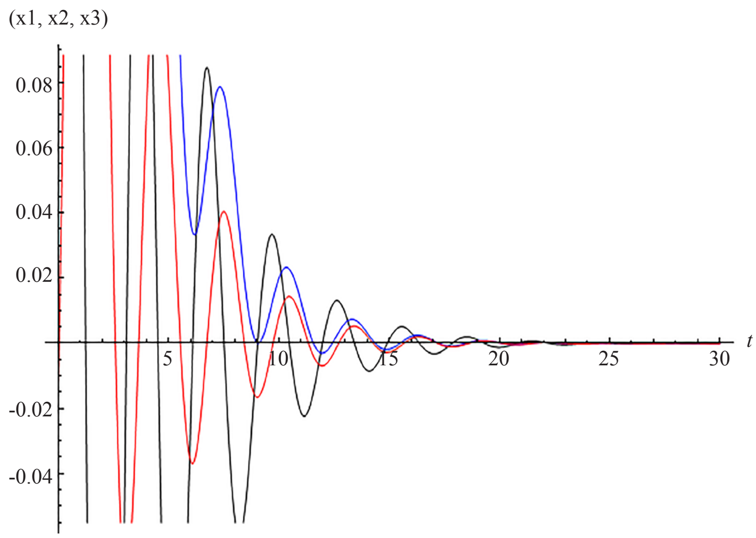


Figure 15. The graphs of $x_i(t)$, $i = 1, 2, 3$ of the system (7) with the regulatory matrix (5).

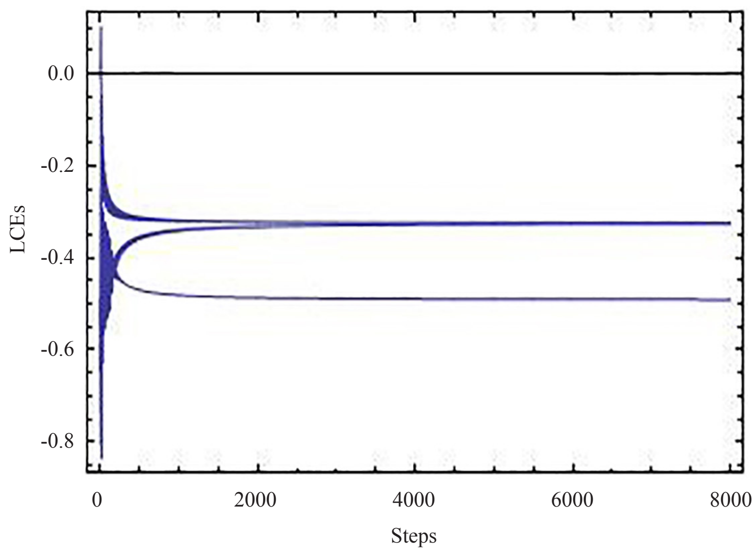


Figure 16. The dynamics of Lyapunov exponents.

4. Conclusion

The article deals with models of three-dimensional genetic and neural networks with a certain set of parameters and two different regulatory matrices. In a genetic system with a matrix (4), the existence of a periodic solution is shown. For a neural system with the same matrix, the existence of three periodic solutions is shown. In a genetic system with a matrix (5), a solution with chaotic behavior is indicated. This is evidenced by the Lyapunov curves, the three-dimensional graphics of the solution and the graphs of the three components of the solution. At the same time, in a neural system with the same regulatory matrix, this solution does not detect chaotic behavior. This observation is in line with statement [23, section 6.10.1] that the minimum dimension of systems of the form (7) in which chaos is possible is four.

Conflict of interest

The authors declare no competing financial interest.

References

[1] Assieh S, Réka A. Boolean modeling of biological regulatory networks: A methodology tutorial. *Methods*. 2013; 62(1): 3-12. Available from: https://doi.org/10.1016/j.ymeth.2012.10.012.

[2] Spirov A, Holloway D. Using evolutionary computations to understand the design and evolution of gene and cell regulatory networks. *Methods*. 2013; 62(1): 3955. Available from: https://doi.org/10.1016/j.ymeth.2013.05.013.

[3] Sadyrbaev F, Ogorelova D, Samuilik I. A nullclines approach to the study of 2D artificial network. *Contemporary Mathematics.* 2019; 1(1): 1-11. Available from: https://doi.org/10.37256/cm.11201976.1-11.

[4] Alakwaa F. Modeling of gene regulatory networks: A literature review. *Journal of Computational Systems Biology*. 2014; 1(1): 102. Available from: https://doi.org/10.15744/2455-7625.1.102.

[5] Samuilik I, Sadyrbaev F. Genetic engineering-construction of a network of arbitrary dimension with periodic attractor. *Vibroengineering PROCEDIA*. 2022; 46: 67-72. Available from: https://doi.org/10.21595/vp.2022.22992.

[6] Kozlovska O, Sadyrbaev F. Models of genetic networks with given properties. *WSEAS Transactions on Computer Research*. 2022; 10: 43-49. Available from: https://doi.org/10.37394/232018.2022.10.6.

[7] Sadyrbaev F. Modelling the evolution of complex networks arising in applications. *Human-Assisted Intelligent Computing: Modelling, simulations and applications*. IOP Publishing, Bristol, United Kingdom; 2022. Available from: https://iopscience.iop.org.

[8] Samuilik I, Sadyrbaev F. On a dynamical model of genetic networks. *WSEAS Transactions on Business and Economics*. 2023; 20: 104-112. Available from: https://doi.org/10.37394/23207.2023.20.11.

[9] Zigunovs M. The Alzheimer's disease impact on artificial neural networks*. Environment. Technologies. Resources. Proceedings of the International Scientific and Practical Conference*. 2021; 2: 205-209. Available from: https://doi.org/10.17770/etr2021vol2.6632.

[10] Amato F, López A, Peña-Méndez EM, Vaňhara P, Hampl A, Havel J. Artificial neural networks in medical diagnosis. *Journal of Applied Biomedicine*. 2013; 11(2): 47-58. Available from: https://doi.org/10.2478/v10136-012-0031-x.

[11] Li EY. Artificial neural networks and their business applications. *Information & Management*. 1994; 27(5): 303-313. Available from: https://doi.org/10.1016/0378-7206(94)90024-8.

[12] Samuilik I. On a six-dimensional artificial neural network model. *WSEAS Transactions on Systems and Control*. 2023; 18: 58-64. Available from: https://doi.org/10.37394/23203.2022.18.6.

[13] Canepa E, Claudel C. A dual model/artificial neural network framework for privacy analysis in traffic monitoring systems. *Transportation Research Part C: Emerging Technologies*. 2019; 105: 126-144. Available from: https://doi.org/10.1016/j.trc.2019.05.031.

[14] Samuilik I, Sadyrbaev F. On trajectories of a system modeling evolution of genetic networks. *Mathematical Biosciences and Engineering*. 2023; 20(2): 2232-2242. Available from: https://doi.org/10.3934/mbe.2023104.

[15] Lynch S. *Dynamical systems with applications using mathematica*. Publisher: Birkhauser; 2017. Available from: https://doi.org/10.1007/978-0-8176-4586-1.

[16] Sukono, Yuningsih SH, Rusyaman E, Vaidyanathan S, Sambas A. Investigation of chaos behavior and integral sliding mode control on financial risk model. *AIMS Mathematics*. 2022; 7(10): 18377-18392. Available from: https://doi.org/10.3934/math.20221012.

[17] Gritli H, Khraief N, Belghith S. Further investigation of the period-three route to chaos in the passive compass-gait biped model. In: Vaidyanathan AAS. (ed.) *Handbook of Research on Advanced Intelligent Control Engineering and Automation*. Publisher: IGI Global. Hershey, PA: Engineering Science; 2015. p.279-300. Available from: https://doi.org/10.4018/978-1-4666-7248-2.ch010.

[18] Sayed WS, Radwan AG, Fahmy HAH. Chaos and bifurcation in controllable jerk-based self-excited attractors. *Nonlinear Dynamical Systems with Self-Excited and Hidden Attractors*. Springer; 2018. p.45-70. Available from: https://doi.org/10.1007/978-3-319-71243-7_2.

[19] Das A, Roy AB, Das P. Chaos in a three dimensional general model of neural network. *International Journal of Bifurcation and Chaos*. 2002; 12: 2271-2281.

[20] Das A, Roy AB, Das P. Chaos in a three dimensional general model of neural network. *International Journal of*

Bifurcation and Chaos. 2002; 12(10): 2271-2281. Available from: https://doi.org/10.1142/S0218127402005820.
[21] Samuilik I. Lyapunov exponents and kaplan-yorke dimension for five-dimensional system. *WSEAS Transactions on Systems*. 2022; 21: 268-275. Available from: https://doi.org/10.37394/23202.2022.21.29.
[22] Ogorelova D, Sadyrbaev F. On a three-dimensional neural network model. *Vibroengineering PROCEDIA*. 2022; 47: 69-73. Available from: https://doi.org/10.21595/vp.2022.23059.
[23] Sprott JC. *Elegant chaos: Algebraically simple chaotic flows*. Singapore: World Scientific Publishing; 2010.

mathematics

MDPI

Article

On Targeted Control over Trajectories of Dynamical Systems Arising in Models of Complex Networks

Diana Ogorelova [1], Felix Sadyrbaev [2] and Inna Samuilik [3,*]

[1] Department of Natural Sciences and Mathematics, Daugavpils University, LV-5401 Daugavpils, Latvia
[2] Institute of Mathematics and Computer Science, University of Latvia, LV-1459 Riga, Latvia
[3] Department of Engineering Mathematics, Riga Technical University, LV-1048 Riga, Latvia
* Correspondence: inna.samuilika@rtu.lv

Abstract: The question of targeted control over trajectories of systems of differential equations encountered in the theory of genetic and neural networks is considered. Examples are given of transferring trajectories corresponding to network states from the basin of attraction of one attractor to the basin of attraction of the target attractor. This article considers a system of ordinary differential equations that arises in the theory of gene networks. Each trajectory describes the current and future states of the network. The question of the possibility of reorienting a given trajectory from the initial state to the assigned attractor is considered. This implies an only partial control of the network. The difficulty lies in the selection of parameters, the change of which leads to the goal. Similar problems arise when modeling the response of the body's gene networks to serious diseases (e.g., leukemia). Solving such problems is the first step in the process of applying mathematical methods in medicine and pharmacology.

Keywords: network control; attracting sets; dynamical system; phase portrait; gene regulatory networks; artificial neural systems

MSC: 34B15; 34B23; 34C60; 34D45

check for updates

Citation: Ogorelova, D.; Sadyrbaev, F.; Samuilik, I. On Targeted Control over Trajectories of Dynamical Systems Arising in Models of Complex Networks. *Mathematics* **2023**, *11*, 2206. https://doi.org/10.3390/math11092206

Academic Editor: Xinsong Yang

Received: 15 February 2023
Revised: 1 May 2023
Accepted: 5 May 2023
Published: 8 May 2023

1. Introduction

Let us start with the following citation: "Complex systems are networks made of a number of components that interact with each other, typically in a nonlinear fashion. Complex systems may arise and evolve through self-organization, such that they are neither completely regular nor completely random, permitting the development of emergent behavior at macroscopic scales. Complex systems science is a rapidly growing scientific research area that fills the huge gap between the two traditional views that consider systems made of either completely independent or completely coupled components... These properties can be found in many real-world systems, e.g., gene regulatory networks within a cell, physiological systems of an organism, brains and other neural systems" [1].

We proceed with considering gene regulatory networks (GRNs in short). Living cells in an organism form complicated systems that can be studied using mathematical methods as well. The aim of these studies is to understand the complexity of these systems and the structure of their interrelations. Every element of such systems can influence others activating or inhibiting them. The gene regulatory system (GRN) is defined as a network of genes and their activating–inhibiting connections. Different mathematical models were used to analyze networks [2]. Models using differential equations are especially effective since they treat networks as dynamical objects and involve the concept of an attractor. Differential equations allow for describing oscillatory behavior, stationary solutions, and cyclical patterns. Nonlinear ordinary differential equations are widespread mathematical tools for studying the regulatory interactions between genes. The time-dependent variables

$x(t)$ represent the concentration of gene products mRNAs or proteins. These variables are positive-valued.

It was noticed by biologists that cells of living organisms are adaptable to changes in an environment even if these changes are very rapid. It was proposed to use attractor selection as the principal mechanism of adaptation to unknown changes in biological systems [3].

The main idea of attractor selection is that the system is driven by deterministic and stochastic components. Attractors are a part of the solution space. Conditions of such system are controlled by a simple feedback. When conditions of a system are suitable (close to one of the attractors), it is driven almost only by deterministic behavior, and stochastic influence is very limited. When conditions of the systems are poor, the system is driven mostly by stochastic behavior. In this case, the system randomly fluctuates in search for a new attractor. When it is found, deterministic behavior again dominates over stochastic [4].

On the other hand, the system can be controlled by changing the adjustable parameters (if any). Then, stochastic behavior can be neglected (this is our assumption) and only the deterministic model can be studied. If we use the attractor selection mechanism for network resource management, at first we should define a regulatory matrix $W = \{w_{ij}\}$, which shows relationships between node pairs, that is, how each node pair affects each other including itself. As it was proposed by some authors ([5], for instance), three types of influence exist, namely activation, inhibition, and no relation, corresponding to positive, negative values of w_{ij} in the interval $[-1, 1]$, or zero. We do not restrict the range of values for the entries w_{ij}.

Some authors consider GRNs in the conditions of serious disease [6–8]. The mathematical model consists of a system of ordinary differential equations, which possess some remarkable properties. This system depends on multiple parameters, some of which are adjustable. The properties of this system imply the existence of attractors. These attractors can also be multiple. The above-mentioned authors associate the disease with special states of GRNs. It is claimed that the trajectory, which reflects the current system state, will tend to a "wrong" attractor. This can be improved by reasonably selected control means. Mathematically, these means are imagined as the changing of the adjustable parameters so that the trajectory changes its direction and goes to an attractor corresponding to a normal state.

In this article, we consider models of GRN, consisting of ordinary differential equations. We elaborate the scheme of control and managing trajectories in a GRN network. The aim is to redirect a trajectory from an initial point to a targeted attractor. Examples for two-dimensional systems are provided.

The problem of treating complex networks, and modeling them using mathematical means and notions, is very important due to the existence of networks in nature and technology. In our reference list, we have collected some sources, which are useful for first addressing the problem. In [9], the main objectives for the study on the border of biology and mathematics were discussed. As one of the main problems, the understanding of "the structure and the dynamics of the complex intercellular web of interactions that contribute to the structure and function of a living cell" was manifested. In [10], configurations of networks are discussed, focusing on links and nodes overlapping and considering mostly physical networks. In [11], the notion of "sensors" is introduced. It is noted that, in most cases, not all parameters can be treated explicitly, and principles of management of networks should be invented making use of only a group of available parameters. A notion of an observable system is invented. An important problem of estimating the internal state of a system from experimentally available data is discussed. In [12], the controllability of complex networks is discussed. It starts with the declaration that "the ultimate proof of our understanding of natural… systems is reflected in our ability to control them". Let us mention several remarks. It is noted that "a framework to control complex self-organized systems is lacking". It is known that genetic networks in a model are driven by systems with sparse regulatory matrices W. The authors of [12] have considered this point. They conclude that "sparse inhomogeneous networks, which emerge in many real complex systems, are the most difficult to control". In many sources, the controllability of a system is explained as "a dynamical system is controllable if, with a suitable choice of inputs, it can be driven from any initial state to any desired final state in a finite time". In our article, the goal is moderate. We wish to indicate means that will help to redirect a trajectory from an initial position in the phase space to a desired attractor, which is usually a stable equilibrium. The book [13] in Part II provides a great amount of information on the topic of Control of Nonlinear Systems. Several models of Control Design are proposed. Available methods of Nonlinear Control Design are discussed, as well as Robust and Adaptive controls, mathematical tools for control, and much more.

When considering genetic systems, the knowledge of the structure of phase space and the influence of parameters on the phase space structure increase the effectiveness of mathematical modeling significantly. We suggest that the geometrical approach, based on the study of isoclines and their locations, is rather natural and may lead to deeply penetrating into the essence of the problems' results. We try to illustrate this point by our treatment of a two-dimensional case. The results for higher dimensional systems need more facts and examples. In the reference list, however, one can find articles, concerning genetic systems of orders three, four, six [8,14,15], and even general ones, for arbitrary n [16,17].

We also consider systems of ordinary differential equations, which appear in the neurodynamics theory (we call them ANN systems, from Artificial Neural Networks). These systems naturally research in parallel to GRN systems, since both types of systems have many similarities. There are, however, essential differences, such as lacking parameters and the broader region of action in ANN differential equations, which have a similar structure and exhibit similar behavior. The parameters and their meaning are different, however. Therefore, the treatment of ANN model needs special attention. It is to be mentioned that neural networks are typically not associated directly with differential equations, but with difference equations or maps.

We focus on problems of control and management of GRN and ANN systems.

In order to become familiar with the topic, the resources [9–13,16–22] are useful.

2. GRN System

The dynamical system of the form

$$x_i' = f(\sum w_{ij}x_j - \theta_i)v_g - x_i v_g - \eta \tag{1}$$

is used to model genetic regulatory networks [2,5] and telecommunications networks [4] as well. This system first appeared in [23]. The function $f(z)$ is a sigmoid function, that is, monotonically increasing from 0 to 1 as z changes from $-\infty$ to $+\infty$, having only one point of inflexion, like the function $\dfrac{1}{1+e^{-\mu z}}$, v_g is a parameter that controls deterministic behavior and η is stochastic term. We neglect the stochastic term in (1), so $\eta = 0$. Neglecting the stochastic term and assuming $v_g = 1$, $\theta_i = \theta$ for all i, we can write the dynamical system in extended form

$$\begin{cases} x_1' = f(w_{11}x_1 + \ldots + w_{1n}x_n - \theta) - x_1, \\ x_2' = f(w_{21}x_1 + \ldots + w_{2n}x_n - \theta) - x_2, \\ \ldots \quad \ldots \quad \ldots, \\ x_n' = f(w_{n1}x_1 + \ldots + w_{nn}x_n - \theta) - x_n, \end{cases} \tag{2}$$

where w_{ij} are entries of the regulatory matrix W.

The equilibrium states can be detected from the system

$$\begin{cases} x_1 = f(x_2 + x_3 + \ldots + x_n - \theta), \\ x_2 = f(x_1 + x_3 + \ldots + x_n - \theta), \\ \ldots \quad \ldots \quad \ldots, \\ x_n = f(x_1 + x_2 + \ldots + x_{n-1} - \theta). \end{cases} \tag{3}$$

The current state of the system is described by the vector $x(t)$. Attractors of systems of the form (2) were studied in [16,17].

General properties of systems (2) were studied and the results can be found in the related literature [2,5,21].

Of the most importance to our analysis of these systems are two facts.

The unity cube $Q_n = \{0 < x_i < 1,\ i = 1, \ldots, n\}$ is an invariant domain for systems of the form (2). The vector field on the border of Q_n is directed inside. This can be understood by the inspection of the vector field on the faces of Q_n. The difference $f_i(\ldots) - x_i$ is either positive or negative, depending on the choice of a face of Q_n.

The second remarkable fact about systems of the form (2) is that their nullclines, defined by (3), can intersect only within Q_n. They do, and at least one equilibrium exists. The total number of equilibria depends on the dimensionality and parameters of a system, but it is finite.

3. Description of the State Space for System (2)

To be specific, consider the case example

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu\,(w_{11}x_1 + w_{12}x_2 + \ldots + w_{1n}x_n - \theta)}} - x_1, \\ x_2' = \dfrac{1}{1 + e^{-\mu\,(w_{21}x_1 + w_{22}x_2 + \ldots + w_{2n}x_n - \theta)}} - x_2, \\ \ldots \\ x_n' = \dfrac{1}{1 + e^{-\mu\,(w_{n1}x_1 + w_{n2}x_2 + \ldots + w_{nn}x_n - \theta)}} - x_n, \end{cases} \tag{4}$$

which corresponds to the particular choice of $f(z) = \frac{1}{1+e^{-\mu z}}$. The system state is described by the vector $X(t) = (x_1(t), \ldots, x_n(t))$. Equilibria of the system are to be found from the system

$$\begin{cases} x_1 = \dfrac{1}{1 + e^{-\mu\,(w_{11}x_1 + w_{12}x_2 + \ldots + w_{1n}x_n - \theta)}}, \\ x_2 = \dfrac{1}{1 + e^{-\mu\,(w_{21}x_1 + w_{22}x_2 + \ldots + w_{2n}x_n - \theta)}}, \\ \ldots \\ x_n = \dfrac{1}{1 + e^{-\mu\,(w_{n1}x_1 + w_{n2}x_2 + \ldots + w_{nn}x_n - \theta)}}. \end{cases} \tag{5}$$

Multiple critical points of different nature can occur, depending on the choice of parameters μ and θ and elements of the regulatory matrix W. Even for $n = 2$ and simple W, the number of isolated critical points can be up to nine.

3.1. Attractors

We will denote the attractors of the system (4) A_i. Each attractor has its basin of attraction, denoted B_i. Each B_i is a subset of the phase space $(x_1, \ldots, x_n)$. If the current system state $X(t)$ is in B_i, then the system state vector $X(t)$ will tend to B_i. Attractors different of the equilibrium points are also available. Periodic attractors can be constructed easily. Examples of periodic attractors for 2D, 3D, and 4D GRN systems can be found in [14], as well as the discussion and related references. Periodic solutions in GRN systems with steep sigmoid functions were studied in [24]. Chaotic attractors can appear in GRN systems, but examples are rare.

Attractors can also be distinguished by the property to be "undesired" and "normal". In real substances, this may correspond to the disease state of an organism and, respectively, to the healthy state [7]. Therefore, the problem of driving the system from the undesired state (that is, in the basin of attraction of some equilibrium) to a normal state arises. This is the problem of the controllability type that is generally difficult to solve. We propose the schemes of how to drive the system to a normal state. We will also show how these schemes work in a particular situation. This particularity is due to the specific regulatory matrix W, which corresponds to the case of the cross-activation network. The respective regulatory matrix is of the form

$$W = \begin{pmatrix} 0 & 1 & \dots & 1 \\ 1 & 0 & \dots & 1 \\ \dots & \dots & \dots & \dots \\ 1 & 1 & \dots & 0 \end{pmatrix}. \tag{6}$$

The system (4) then takes the form

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu\,(x_2 + \ldots + x_n - \theta)}} - x_1, \\ x_2' = \dfrac{1}{1 + e^{-\mu\,(x_1 + x_3 + \ldots + x_n - \theta)}} - x_2, \\ \dots \\ x_n' = \dfrac{1}{1 + e^{-\mu\,(x_1 + x_2 + \ldots + x_{n-1} - \theta)}} - x_n. \end{cases} \tag{7}$$

3.2. Influence of Parameters on the Structure of the Phase Plane of 2D GRN Systems

The general system of ordinary differential equations which is often used to model genetic networks, in case of the two dimensions (two-element network) is

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu_1\,(w_{11}x_1 + w_{12}x_2 - \theta_1)}} - v_1 x_1, \\ x_2' = \dfrac{1}{1 + e^{-\mu_2\,(w_{21}x_1 + w_{22}x_2 - \theta_2)}} - v_2 x_2. \end{cases} \tag{8}$$

It is a quasi-linear system, where the nonlinearity is represented by the logistic function $f(z) = 1/(1 + e^{-\mu z})$. Parameters μ and v are positive. Let us describe the influence of parameters on the phase plane, and especially on the mutual location of isoclines. Isoclines are curves, where x_1' or x_2' are constant. Especially useful are nullclines, which are given by the relations

$$\begin{cases} 0 = \dfrac{1}{1 + e^{-\mu\,(w_{11}x_1 + w_{12}x_2 - \theta_1)}} - v_1 x_1, \\ 0 = \dfrac{1}{1 + e^{-\mu\,(w_{21}x_1 + w_{22}x_2 - \theta_2)}} - v_2 x_2. \end{cases} \tag{9}$$

Critical points (alternatively, equilibria) are solutions of the system of two equations (9).

Let us list the properties of the system (8). Some of these properties are evident. Proofs of other properties are scattered over the related literature, mentioned above.

1. There is an invariant set $Q_2 = \{0 < x_i < 1/v_i,\ i = 1,2\}$ with the following properties:
   - 1a The vector field defined by the system (8) is directed inward on the border of Q_2;
   - 1b The nullclines (9) can intersect only in Q_2;
   - 1c The nullclines intersect at least once. The total number of intersections is finite. For the 2D case, the maximal number of critical points is nine. For this, both nullclines have to be Z-shaped;
2. By changing θ_i, the nullclines can be shifted; by changing θ_1, the first nullcline can be shifted in the vertical direction; by changing θ_2, the second nullcline is moved horizontally, preserving shape;
3. By changing μ_i, the shapes of the nullclines can be changed; for sufficiently large values of μ_i, the three segments of a sigmoid curve, representing a nullcline, become almost straight. In this case, the system (8) is almost piece-wise linear; for the study of the case of piece-wise linear system consult [24];
4. By changing v_i, the parallelepiped Q_2 can be made stretched or compressed; for $v_1 = v_2 = 1$ Q_2, it is a unit square;

5. Signs of elements of the regulatory matrix

$$W = \begin{pmatrix} w_{11} & w_{12} \\ w_{21} & w_{22} \end{pmatrix}. \quad (10)$$

are of great importance. The typical cases are

5a Activation: $w_{11} \geq 0, w_{22} \geq 0, w_{21} > 0, w_{12} > 0$;
5b Inhibition: $w_{11} \leq 0, w_{22} \leq 0$,
5c Mixed: $w_{11} \geq 0, w_{22} \geq 0, w_{21}w_{12} < 0$;

More on the classification of systems by properties of the regulatory matrices can be found in [19,25].

Remark 1. *The system (8) with the matrix*

$$W = \begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}, \quad (11)$$

where $a > 0$, $b > 0$ can have one, two, or three critical points. This depends on other parameters. The case $\mu_1 = mu_2 = \mu$, $\theta_1 = \theta_2 = theta$ was studied, and the region Ω was defined in the (μ, θ)-plane, which decomposes the plane with respect to the number of critical points.

Remark 2. *The system (8) with the matrix*

$$W = \begin{pmatrix} k & -a \\ -a & k \end{pmatrix}, \quad (12)$$

where $a > 0$, $k > 0$ can have one stable critical point; then, (under k increasing) a stable periodic trajectory, and then multiple critical points, of which some are attractive.

Remark 3. *The conditions for the system (8) to have a single critical point were obtained in [26]. If this point is non-attractive (a saddle, or a repelling one), then the system has a limit cycle (through Andronov–Hopf bifurcation).*

3.3. Inhibition Case in 2D GRN Systems

Consider the two-dimensional (2D abbreviated) system of ODE of the form (2)

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu\,(w_{11}x_1 + w_{12}x_2 - \theta_1)}} - x_1, \\ x_2' = \dfrac{1}{1 + e^{-\mu\,(w_{21}x_1 + w_{22}x_2 - \theta_2)}} - x_2. \end{cases} \quad (13)$$

Look at Figures 1–3. Calculations are performed and pictures are created using Wolfram Mathematica tools, see Appendix A. Let the regularity matrix in (13) be

$$W = \begin{pmatrix} 0 & -1 \\ -1 & 0 \end{pmatrix}. \quad (14)$$

This corresponds to the inhibition case. The nullclines (red and black) intersect three times. The green circle in Figure 1 corresponds to the current state of the 2D system. Due to the vector field, the current state is in the basin of attraction of the lower critical point, which is a stable node.

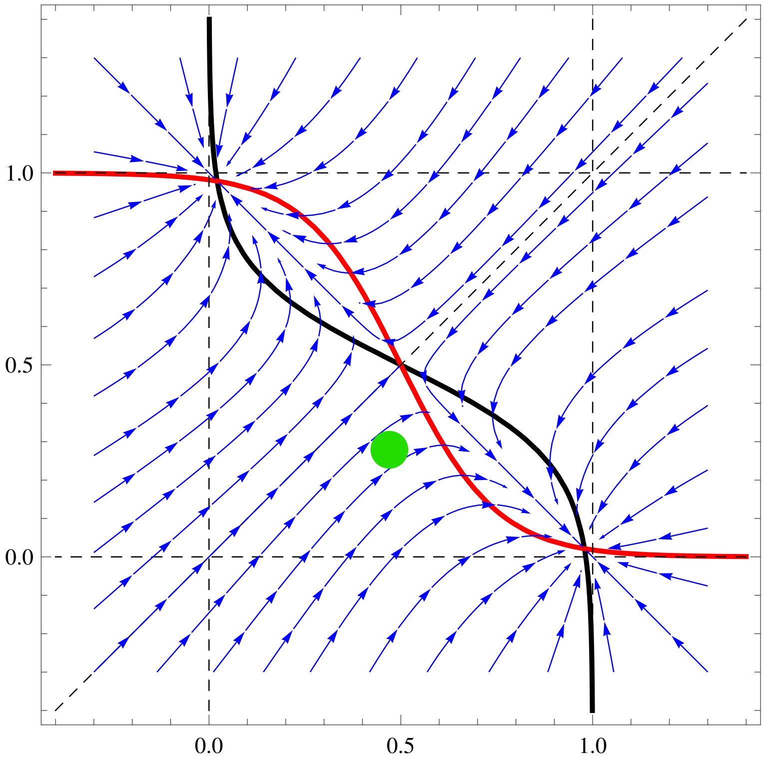


Figure 1. The phase plane for system (13) with the matrix (14), $\mu_1 = \mu_2 = 8$, $\theta_1 = -0.5$, $\theta_2 = -0.5$.

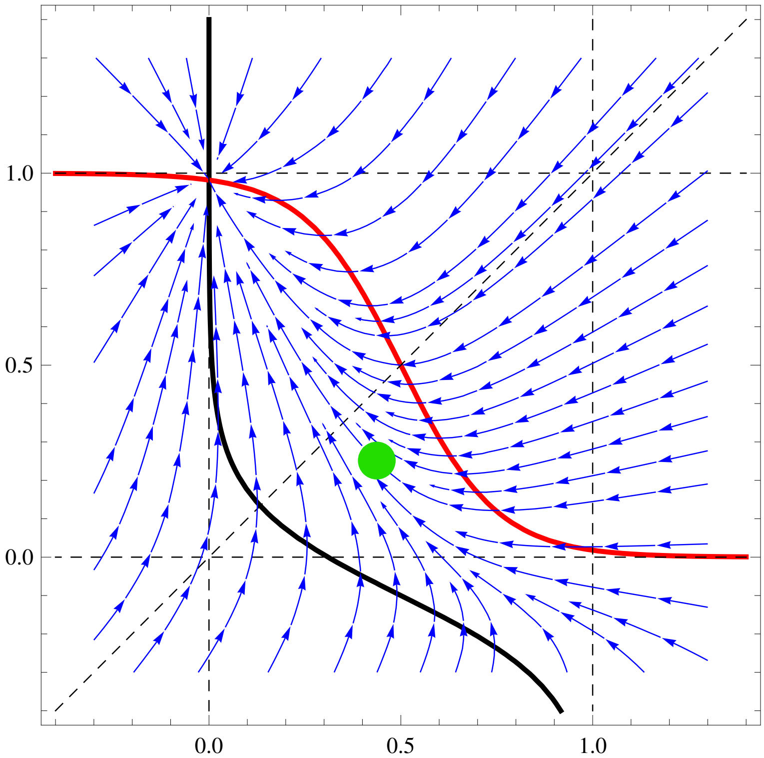


Figure 2. The phase plane for system (13) with the matrix (14), $\mu_1 = \mu_2 = 8$, $\theta_1 = 0.1$, $\theta_2 = -0.5$.

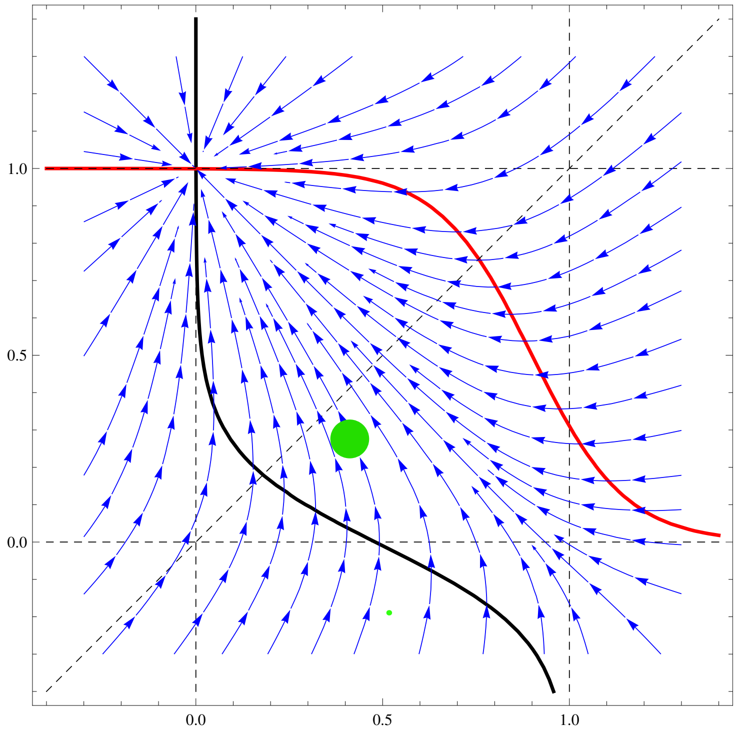


Figure 3. The phase plane for system (13) with the matrix (14), $\mu_1 = \mu_2 = 8$, $\theta_1 = 0.01$, $\theta_2 = -0.9$.

3.4. Controllability by Changing θ

The goal is to redirect the current trajectory, emanating from the green spot, to the upper right critical point, which is conventionally the "normal" one. This can be achieved by manipulating the adjustable parameter θ. Change θ_1 from its current value -0.5 to the value 0.1. This corresponds to the shift of the first nullcline (black one) down. As the result, only one, the upper left, critical point remains, and their type is not changed. It is a stable node. The effect of this action is seen in Figure 2. The flow of the vector field will lead the green spot to the left upper, now unique, critical point, which is identified as "normal" attractor. The goal is achieved, and the system will go to the right state.

3.5. Controllability by Changing Both θ

It is clear that changing both parameters θ in (13) will lead to the shifting of both nullclines. The second nullcline (red one) can move in a horizontal direction. The change of the parameters θ_1 and θ_2 from their current values to the values 0.01 and -0.9, respectively, will lead to the configuration depicted in Figure 3. The selected trajectory will go to the desired attractive critical point at the upper-left corner.

Proposition 1. *In the case of inhibition (the regulatory matrix is (14)), any of the side critical points can be made a unique global attractor by appropriate choices of the parameters θ.*

4. Driving the System from One State to Another One—ANN Case

Systems of the form

$$\begin{cases} x_1' = \tanh(a_{11}x_1 + a_{12}x_2 + \ldots + a_{1n}x_n) - x_1, \\ x_2' = \tanh(a_{21}x_1 + a_{22}x_2 + \ldots + a_{2n}x_n) - x_2, \\ \ldots \\ x_n' = \tanh(a_{n1}x_1 + a_{n2}x_2 + \ldots + a_{nn}x_n) - x_n \end{cases} \tag{15}$$

arise in the theory of artificial neural networks ([27], Chapter 6). The hyperbolic tangent function $\tanh z$ is a sigmoid function, but its range of values is $(-1, 1)$. The invariant domain for the system (15) is the open cube $G_n = \{-1 < x_i < 1,\ i = 1, 2, \ldots, n\}$. The nullclines are defined by the equations

$$\begin{cases} 0 = \tanh(a_{11}x_1 + a_{12}x_2 + \ldots + a_{1n}x_n) - x_1, \\ 0 = \tanh(a_{21}x_1 + a_{22}x_2 + \ldots + a_{2n}x_n) - x_2, \\ \ldots \\ 0 = \tanh(a_{n1}x_1 + a_{n2}x_2 + \ldots + a_{nn}x_n) - x_n \end{cases} \tag{16}$$

The cross-points of the nullclines are critical points (equilibria). At least one critical point exists in G_n for the n-dimensional system (15). There is much similarity between GRN systems and ANN systems.

Consider the two-dimensional version of (15)

$$\begin{cases} x_1' = \tanh(a_{11}x_1 + a_{12}x_2) - x_1, \\ x_2' = \tanh(a_{21}x_1 + a_{22}x_2) - x_2 \end{cases} \tag{17}$$

The nullclines of the system (17) are defined by the equations

$$\begin{cases} 0 = \tanh(a_{11}x_1 + a_{12}x_2) - x_1, \\ 0 = \tanh(a_{21}x_1 + a_{22}x_2) - x_2 \end{cases} \tag{18}$$

Our goal is to establish the control over the ANN system. This system has less parameters than the GRN system. The only possibility for the system (17) to be controlled changing the parameters is to change the entries of the matrix

$$A = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}. \tag{19}$$

We will show that this is possible.

Look at Figures 4 and 5. Let the regularity matrix in (13) be

$$A = \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix}. \tag{20}$$

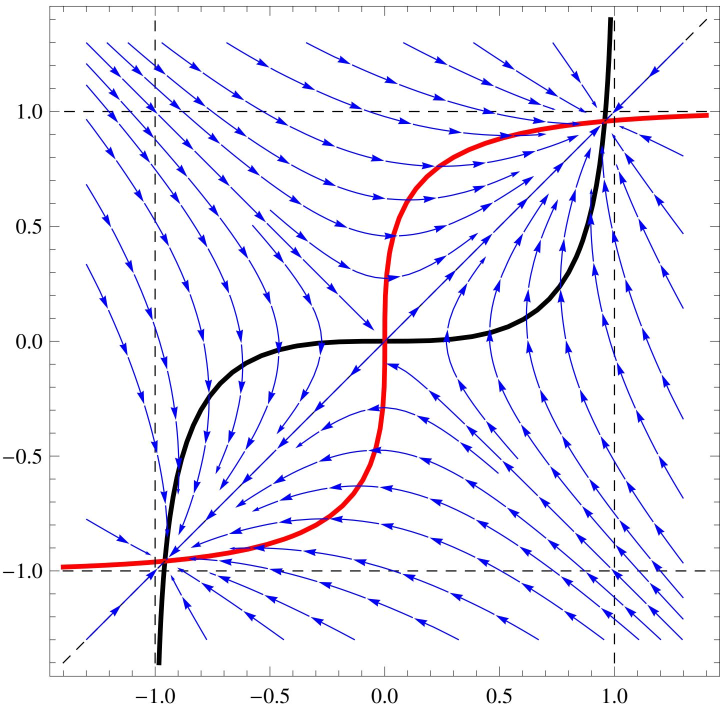


Figure 4. The phase plane for the system (17) with the matrix (20).

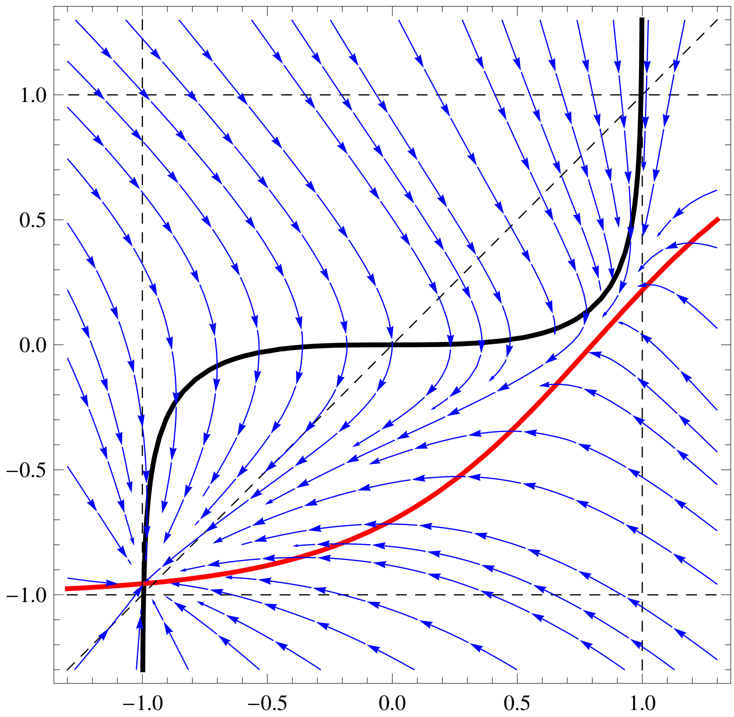


Figure 5. The phase plane for the system (17) with the matrix (21).

The nullclines (red and black) intersect three times, as seen in Figure 4. Suppose that the trajectory, corresponding to the current system state, tends to the upper-right critical point. It is a stable node.

Controllability by Changing an Element of A

The goal is to redirect the current trajectory to the lower-left critical point, which is also attractive. For this, we can only change some entries of the matrix A. Let the new matrix be

$$A = \begin{pmatrix} 1 & 2 \\ 1 & 0.1 \end{pmatrix}. \tag{21}$$

Figure 5 shows a new configuration of nullclines. There is a unique critical point of the type stable node. The trajectory will go to the desired attractor. The goal is achieved.

Consider a more complicated case. Let the coefficients of the system (17) be the entries of the matrix

$$A = \begin{pmatrix} 3 & 1 \\ 3 & 6 \end{pmatrix}. \tag{22}$$

The nullclines and the vector field are depicted in Figure 6. There are nine critical points, of which four are attractive. The green spots stand for the initial states of the system (17). The trajectories starting from these points will go to the stable critical points at the upper-left and lower-right locations. Let them be conventionally "undesired" ones. The goal is to redirect them to the attractive critical points at the upper-right and lower-left positions. This can be achieved by manipulating the elements of the matrix A. Let the element "6" in (22) be changed to the value "4". The new matrix is

$$A = \begin{pmatrix} 3 & 1 \\ 3 & 4 \end{pmatrix}. \tag{23}$$

The new configuration of nullclines is depicted in Figure 7. The green spots are (approximately) on the border of the basins of attraction of the desired critical points. When released, the trajectories will go to the new attractors at the upper-right and/or lower-left locations, depending on where they are exactly, in the basin of attraction of the upper attractor, or in the basin of attraction of the opposite one. The goal is achieved.

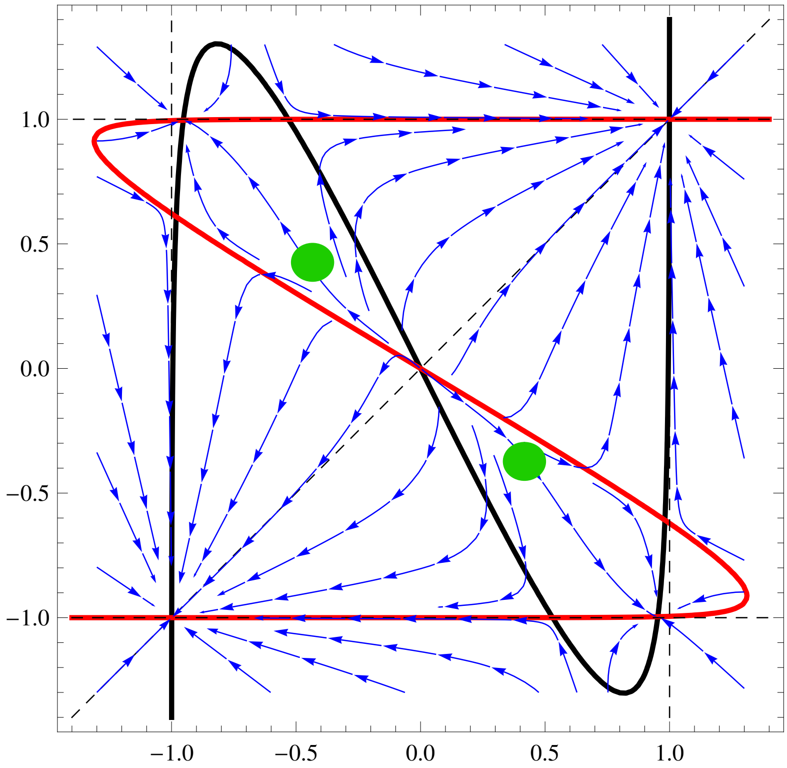


Figure 6. The phase plane for the system (17) with the matrix (22), where the green circles denote the initial states.

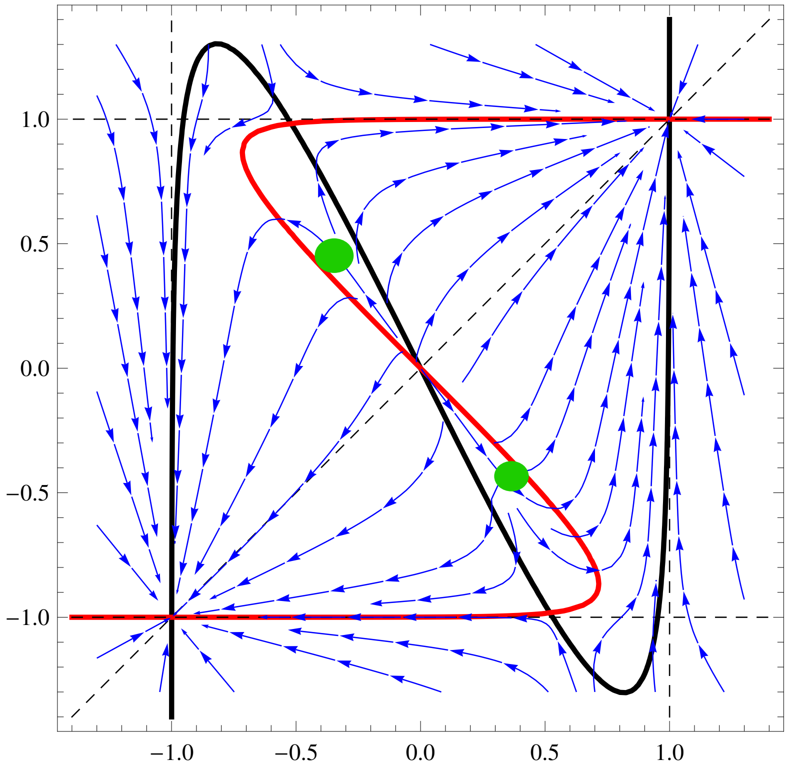


Figure 7. The phase plane for the system (17) with the matrix (23), where the green circles denote the initial states.

Proposition 2. *The trajectories of the system (17) can be redirected from a given attractive critical point to another one by changing the elements of the matrix A.*

5. Conclusions

Control over GRN systems and ANN systems is possible if by control we mean changing the properties of a system in the desired direction. In particular, it can be implemented by manipulating the nullclines. This is easier for GRN systems since they have more parameters. The most promising and geometrically understandable is changing the θ parameters. In ANN systems, the nullclines can be manipulated by the elements of the matrix A. Knowledge of the basins of attraction is a prerequisite for the implementation of control. The bistable GRN system of differential equations modeling the activation case or inhibition case can be driven from one attractor to another using several techniques. First, elements of the regulatory matrix W can be changed appropriately. Second, the parameter θ can control this process.

The following quote outlines possible further research in this direction. "Because of the conceptual similarities between engineering and biological regulatory mechanisms, . . . these tools are now being used to analyze biochemical and genetic networks" [28] (p. 1).

Author Contributions: Software, graphics and Section 4, D.O.; Writing—review & editing, F.S.; Project administration, I.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by 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" grant number 8.2.2.0/20/I/003.

Data Availability Statement: No data from public repositories were used. The Wolfram Mathematica fragment in Appendix A allows to check the data obtained and repeat calculations.

Acknowledgments: 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. The authors also would like to thank anonymous referees for their constructive suggestions.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

The models are validated experimentally using Wolfram Mathematica programming. The code for computing and visualization of examples follows.

```
a11=1;a12=1;a21=1;a22=1;b1=1;b2=1; f1[x_,y_]:=Tanh[a11 x+a12 y]-b1
x; f2[x_,y_]:=Tanh[a21 x+a22 y]-b2 y;
ContourPlot[{f1[x,y]==0,f2[x,y]==0,x==y, x==1, x==-1, y==1,
y==-1},{x,-1.4,1.4},{y,-1.4,1.4},ContourStyle->
{{Thick,Black},{Thick,Red},Dashed, Dashed, Dashed, Dashed,
Dashed},AxesLabel-> {Style[x,15],Style[y,15]}]

a11=1;a12=1;a21=5;a22=-5;b1=1;b2=1;
ContourPlot[{f1[x,y]==0,f2[x,y]==0,x==y, x==1, x==-1, y==1,
y==-1},{x,-1.4,1.4},{y,-1.4,1.4},ContourStyle->
{{Thick,Black},{Thick,Red},Dashed, Dashed, Dashed, Dashed,
Dashed},AxesLabel-> {Style[x,15],Style[y,15]}]

Clear[x,y];
a11=1;a12=2;a21=1;a22=0.1;b1=1;b2=1;\[CapitalTheta]1=0.1;
\[CapitalTheta]2=0.8;
\[Mu]1=1; \[Mu]2=1; f1[x_,y_]:=Tanh[\[Mu]1 (a11 x+a12
y-\[CapitalTheta]1)]-b1 x; f2[x_,y_]:=Tanh[\[Mu]2 (a21 x+a22
y-\[CapitalTheta]2)]-b2 y;
```

```
nc2=ContourPlot[{f1[x,y]==0,f2[x,y]==0,x==y,x==1, x==-1, y==1,
y==-1},{x,-1.3,1.3},{y,-1.3,1.3},ContourStyle->
{{Thick,Black},{Thick,Red},Dashed,Dashed,Dashed,Dashed,Dashed},
AxesLabel->{Style[x,15],Style[y,15]}]

a11=3;a12=1;a21=3;a22=6;b1=1;b2=1; f1[x_,y_]:=Tanh[a11 x+a12 y]-b1
x; f2[x_,y_]:=Tanh[a21 x+a22 y]-b2 y;
nc1=ContourPlot[{f1[x,y]==0,f2[x,y]==0,x==y, x==1, x==-1, y==1,
y==-1},{x,-1.4,1.4},{y,-1.4,1.4},ContourStyle->
{{Thick,Black},{Thick,Red},Dashed, Dashed, Dashed, Dashed,
Dashed},AxesLabel-> {Style[x,15],Style[y,15]}]

sp1=StreamPlot[{ f1[x,y], f2[x,y]}, {x, -1.3, 1.3}, {y, -1.3, 1.3},
Axes -> True, Frame->True, AxesLabel -> {Style["x",Black, FontSize->
16],Style["y",Black,Italic,FontSize-> 16]}, StreamPoints ->40,
StreamStyle-> {Blue}]

Show[nc1, sp1]

a11=3;a12=1;a21=3;a22=4;b1=1;b2=1; f1[x_,y_]:=Tanh[a11 x+a12 y]-b1
x; f2[x_,y_]:=Tanh[a21 x+a22 y]-b2 y;
nc2=ContourPlot[{f1[x,y]==0,f2[x,y]==0,x==y, x==1, x==-1, y==1,
y==-1},{x,-1.4,1.4},{y,-1.4,1.4},ContourStyle->
{{Thick,Black},{Thick,Red},Dashed, Dashed, Dashed, Dashed,
Dashed},AxesLabel-> {Style[x,15],Style[y,15]}]

sp2=StreamPlot[{ f1[x,y], f2[x,y]}, {x, -1.3, 1.3}, {y, -1.3, 1.3},
Axes -> True, Frame->True, AxesLabel -> {Style["x",Black, FontSize->
16],Style["y",Black,Italic,FontSize-> 16]}, StreamPoints ->40,
StreamStyle-> {Blue}]

Show[nc2, sp2]
```

References

1. Sayama, H. Introduction to the Modeling and Analysis of Complex Systems. Milne Open Textbooks. 14. 2015. Available online: https://knightscholar.geneseo.edu/oer-ost/14 (accessed on 14 February 2023).
2. De Jong, H. Modeling and Simulation of Genetic Regulatory Systems: A Literature Review. *J. Comput. Biol.* **2002**, *9*, 67–103. [CrossRef] [PubMed]
3. Brokan, E.; Sadyrbaev, F.Z. On controllability of nonlinear dynamical network. *AIP Conf. Proc.* **2019**, *2116*, 040005. [CrossRef]
4. Koizumi, Y.; Miyamura, T.; Arakawa, S.I.; Oki, E.; Shiomoto, K.; Murata, M. Adaptive Virtual Network Topology Control Based on Attractor Selection. *J. Light. Technol.* **2010**, *28*, 1720–1731. [CrossRef]
5. Furusawa, C.; Kaneko, K. A generic mechanism for adaptive growth rate regulation. *PLoS Comput. Biol.* **2008**, *4*, e3. [CrossRef]
6. Cornelius, S.P.; Kath, W.L.; Motter, A.E. Realistic control of network dynamic. *Nat. Commun.* **2013**, *4*, 1942. [CrossRef]
7. Wang, L.-Z.; Su, R.-Q.; Huang, Z.-G.; Wang, X.; Wang, W.-X.; Grebogi, C.; Lai, Y.-C. A geometrical approach to control and controllability of nonlinear dynamical networks. *Nat. Commun.* **2016**, *7*, 11323. [CrossRef]
8. Samuilik, I.; Sadyrbaev, F. On trajectories of a system modeling evolution of genetic networks. *Math. Eng.* **2023**, *20*, 2232–2242. [CrossRef]
9. Barabási, A.-L.; Oltvai, Z.N. Network biology: Understanding the cell's functional organization. *Nat. Rev. Genet.* **2004**, *5*, 101–113. [CrossRef]
10. Dehmamy, N.; Milanlouei, S.; Barabási, A.-L. A structural transition in physical networks. *Nature* **2018**, *563*, 676–680. [CrossRef]
11. Liu, Y.-Y.; Slotine, J.-J.; Barabási, A.-L. Observability of complex systems. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 2460–2465. [CrossRef]
12. Liu, Y.-Y.; Slotine, J.-J.; Barabási, A.-L. Controllability of complex networks. *Nature* **2011**, *473*, 167–173. [CrossRef] [PubMed]
13. Slotine, J.J.; Li, W. *Applied Nonlinear Control*; Prentice Hall: Hoboken, NJ, USA, 1991.
14. Sadyrbaev, F.; Samuilik, I.; Sengileyev, V. On modelling of genetic regulatory networks. *WSEAS Trans. Electron.* **2021**, *12*, 72–80. [CrossRef]

15. Samuilik, I.; Sadyrbaev, F. On a dynamical model of genetic networks. *WSEAS Trans. Bus. Econ.* **2023**, *20*, 104–112. [CrossRef]
16. Brokan, E.; Sadyrbaev, F.Z. On Attractors in Gene Regulatory Systems. *AIP Conf. Proc.* **2017**, *1809*, 020010. [CrossRef]
17. Brokan, E.; Sadyrbaev, F. Attraction in n-dimensional differential systems from network regulation theory. *Math. Methods Appl. Sci.* **2018**, *41*, 7498–7509. [CrossRef]
18. Brokan, E.; Sadyrbaev, F. On a differential system arising in the network control theory. *Nonlinear Anal. Model. Control* **2016**, *21*, 5. [CrossRef]
19. Ogorelova, D.; Sadyrbaev, F.; Sengileyev, V. Control in inhibitory genetic regulatory networks. *Contemp. Math.* **2020**, *1*, 393–400. [CrossRef]
20. Vinayagama, A.; Gibsonb, T.E.; Lee, H.-J.; Yilmazeld, B.; Roeseld, C.; Hua, Y.; Kwona, Y.; Sharma, A.; Liu, Y.-Y.; Perrimona, N.; et al. Controllability Analysis of the Directed Human Protein Interaction Network Identifies Disease Genes and Drug Targets. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 4976–4981. [CrossRef]
21. Vohradský, J. Neural network model of gene expression. *FASEB J.* **2001**, *15*, 846–854. [CrossRef]
22. Wuensche, A. Genomic regulation modeled as a network with basins of attraction. *Proc. Pac. Symp. Biocomput.* **1998**, *3*, 89–102.
23. Wilson, H.R.; Cowan, J.D. Excitatory and inhibitory interactions in localized populations of model neurons. *Biophys. J.* **1972**, *12*, 1–24. [CrossRef] [PubMed]
24. Edwards, R.; Ironi, L. Periodic solutions of gene networks with steep sigmoidal regulatory functions. *Physic D* **2014**, *282*, 1–15. [CrossRef]
25. Sadyrbaev, F. Planar differential systems arising in network regulation theory. *Adv. Math. Model. Appl.* **2019**, *4*, 70–78.
26. Kozlovska, O.; Sadyrbaev, F. Models of genetic networks with given properties. *WSEAS Trans. Comp. Res.* **2022**, *10*, 43–49. [CrossRef]
27. Sprott, J.C. *Elegant Chaos: Algebraically Simple Chaotic Flow*; World Scientific: Singapore, 2010.
28. Iglesias, P.A.; Ingalls, B.P. (Eds.) *Control Theory and Systems Biology*; MIT Press: Cambridge, MA, USA; London, UK, 2010.

Advances in the Theory of Nonlinear Analysis and its Applications 7 (2023) No. 2, 486–498.
https://doi.org/10.31197/atnaa.232379
Available online at www.atnaa.org
Research Article

Advances in the Theory of Nonlinear Analysis and its Applications
ISSN: 2587-2648
Peer-Reviewed Scientific Journal

On attractors in dynamical systems modeling genetic networks

Diana Ogorelova[a], Felix Sadyrbaev[b], Inna Samuilik[c]

[a]*Faculty of Natural and Health Sciences, Daugavpils University, Daugavpils, Latvia.*
[b]*Institute of Mathematics and Computer Science, University of Latvia, Riga, Latvia.*
[c]*Department of Engineering Mathematics,Riga Technical University, Riga, Latvia.*

Abstract

A dynamical system that arises in the theory of genetic networks, is studied. Attracting sets of a special kind is the focus of the study. These attractors appear as combinations of attractors of lower dimensions, which are stable limit cycles. The properties of attractors are studied. Visualizations and examples are provided.

Keywords: Genetic networks Attractors Phase space Dynamical system Neural networks.
2010 MSC: 34C60, 34D45, 92B20.

1. Introduction

The theory of genetic regulatory networks (GRN in short) is at the core of modern biology. A lot of information was collected and stored performing the experimental work. The data stored need registration, classification, and usage for creating theories, managing, and employing them for practical purposes. As a result of data collection and arrangement, the mathematical models are elaborated, which can be studied independently. Their correspondence to real phenomena can be checked and the respective corrections can be made. Fortunately, we have some dynamic mathematical models, that were probated and used, when formulating aims and hypotheses. Let us mention the works [1], [14], [11], where real genetic networks were considered concerning the treatment of leukemia. This disease was considered as an abnormality in

Email addresses: diana.ogorelova@du.lv (Diana Ogorelova), felix@latnet.lv (Felix Sadyrbaev), Inna.Samuilika@rtu.lv (Inna Samuilik)

Received January 12, 2023; Accepted: June 08, 2023; Online: June 18, 2023.

the functioning of a genetic subsystem, which was described mathematically as a 60-dimensional system of ordinary differential equations. This system has, possibly, rich dynamics, and several attractors, in the form of stable equilibria, exist. The disease was interpreted as tending the current state of a genetic subsystem to a "wrong" attractor. The recommendation for (mathematical) treatment of that was to change the adjustable parameters to redirect the "wrong" trajectory to a normal attractor. This interpretation requires studying in detail the structure of a genetic network and the reactions of the system to changes in parameters. Since the problem of the mathematical treatment of so large system is not easy, we wish concentrate on possible types of attractors, which can cause some periodic processes in GRN subsystems.

2. Periodic solution

For the second order ordinary differential equations (ODE) periodic solutions generate closed trajectories in the phase plane. Any closed trajectory cannot intersect itself if an equation is autonomous. If another second order equation is taken, which also has a periodic solution, generating its trajectory, both equations can be combined into the fourth order system. If equations of harmonic oscillations are taken, namely,

$$x'' + \omega_1^2 x = 0, \quad y'' + \omega_2^2 y = 0, \tag{1}$$

and the ratio $\frac{\omega_1}{\omega_2}$ is the rational number, in a four-dimensional phase space complicated constructions can emerge. Three the second order equations can be considered thus obtaining 6D-bodies, and so on.

If a general the first order system of ODE is considered, and if it can be decomposed into independent subsystems, which have periodic solutions, the same phenomenon can be observed. If the resulting n-dimensional constructions are obtained, and the system of ODE describes some notable processes, the natural question arises: what is the meaning of these structures, do they bear some important information about phenomena they are modeling, and how this information can be used to create more constructions, not necessarily periodic, and what is their meaning.

The situation, just described, can occur, when considering the systems of ODE, written in vectorial form

$$X' = F(X) - X, \tag{2}$$

where $F(X) = (f_1(X), \dots, f_n(X))$ with any f_i being a sigmoidal function. Sigmoidal functions $f_i(z)$ are monotonically increasing from zero to unity on the entire z-axis and have a single inflection point. One such function is $f(z) = 1/(1+\exp(-\mu(z-\theta)))$, where $\mu > 0$ and θ are parameters. The above system then looks as

$$\begin{cases} \dfrac{dx_1}{dt} = \dfrac{1}{1+e^{-\mu_1(w_{11}x_1+w_{12}x_2+\ldots+w_{1n}x_n-\theta_1)}} - x_1, \\ \dfrac{dx_2}{dt} = \dfrac{1}{1+e^{-\mu_2(w_{21}x_1+w_{22}x_2+\ldots+w_{2n}x_n-\theta_2)}} - x_2, \\ \ldots \\ \dfrac{dx_n}{dt} = \dfrac{1}{1+e^{-\mu_n(w_{n1}x_1+w_{n2}x_2+\ldots+w_{nn}x_n-\theta_n)}} - x_n. \end{cases} \tag{3}$$

This system was used to model gene regulatory networks in a number of papers ([3], [5]), [8], [9]. Different sigmoidal functions can be used also, for instance, the Hill's function [14], the Gompertz function [12], which supposedly model the behavior, organization and evolution of genetic networks. This system was used first in [15] (see also [6]) to model a population of neurons.

3. System

We consider system (3). It has remarkable properties.

Proposition 3.1. *The vector field, defined by the system (3), is directed inward the unit cube Q_n on the border ∂Q_n.*

Proof. Consider the unit cube $Q_n = \{x \in R^n : 0 \leq x \leq 1\}$, where the inequalities are understood componentwise. The opposite faces of Q_n along the x_1-direction are defined by $\{x_1 = 0\} \bigcap Q_n$ and $\{x_1 = 1\} \bigcap Q_n$. The component $x_1' = \frac{1}{1+e^{-\mu_1(w_{11}x_1+w_{12}x_2+\ldots+w_{1n}x_n-\theta_1)}} - x_1$ of the vector X' is positive at the hyperplane $x_1' = 0$, due to positivity of the sigmoidal function f_1. On the opposite face $x_1 = 1$, the value of $x_1' = f_1 - x_1$ is negative, due to the value range $(0, 1)$ of the sigmoidal function. A similar check can be made in the directions of all axes x_i, $i = 2, \ldots, n$. □

Proposition 3.2. *The system has a critical point inside the domain Q_n.*

Proof. Critical points (also called *equilibria*) of the system (3) can be defined as solutions of the system

$$\begin{cases} 0 = \dfrac{1}{1 + e^{-\mu_1(w_{11}x_1+w_{12}x_2+\ldots+w_{1n}x_n-\theta_1)}} - x_1, \\ 0 = \dfrac{1}{1 + e^{-\mu_2(w_{21}x_1+w_{22}x_2+\ldots+w_{2n}x_n-\theta_2)}} - x_2, \\ \ldots \\ 0 = \dfrac{1}{1 + e^{-\mu_n(w_{n1}x_1+w_{n2}x_2+\ldots+w_{nn}x_n-\theta_n)}} - x_n. \end{cases} \tag{4}$$

In vectorial form

$$0 = F(X) - X, \text{ or } X = F(X). \tag{5}$$

The mapping $M : X \to F(X)$ satisfies the conditions of the Bohl-Brower fixed point theorem with respect to the domain Q_n, therefore a solution of the system (5) in Q_n exists. □

Remark 3.3. *Notice, that a critical point need not be unique. In what follows, we will construct examples with multiple critical points.*

Proposition 3.4. *The necessary and sufficient condition for the system (3) to have a periodic solution, is: the boundary value problem (2),*

$$X(a) = X(b) \tag{6}$$

has a solution for some pair $a < b$.

Proof. Necessity. If a periodic solution $X(t)$ with the minimal period T exists, then $X(0) = X(T)$ and the boundary value problem (2), $X(0) = X(T)$ has a solution.

Sufficiency. Suppose, the BVP (2), (6) has a solution $X(t)$. Then the correspondent trajectory in the phase space R^n is closed. By autonomity of the system, the function $X(t - (b - a))$ is also a solution. Its trajectory at $t = b$ is at the same start point $X(a)$ and goes the same way, as the first trajectory, due to the uniqueness of a solution of the respective Cauchy problem. Hence $X(t)$ is the periodic solution. □

Remark 3.5. *In the above proof $(b - a)$ need not to be the minimal period, and the periodic solution may be constant (then the trajectory is a point in the phase space).*

Proposition 3.6. *The system has an attractor in Q_n.*

Proof. This follows from the 'trapping property' of the set Q_n. It is 'positively invariant' ([7, Definition 2, page 99]), that is, all trajectories starting at Q_n stay there for future times. Then there exists ([7]) an attractor, which is an invariant compact set, attracting trajectories from some neighborhood U. □

Remark 3.7. *Simple example of attractors are stable critical points and limit cycles.*

4. Attractors

In this section we construct periodic attractors for two and three dimensional systems. Then we show how these attractors can be used to construct the ones for higher dimensional systems. This approach can be used without any restrictions on the dimensionality of a network. Afterward zero spaces can be filled with non-zero elements thus obtaining more and more complicated structures.

4.1. Attractors for 2D systems

Consider the two-dimensional system

$$\begin{cases} x_1' = \dfrac{1}{1+e^{-\mu_1(w_{11}x_1+w_{12}x_2-\theta_1)}} - x_1, \\ x_2' = \dfrac{1}{1+e^{-\mu_2(w_{21}x_1+w_{22}x_2-\theta_2)}} - x_2, \end{cases} \tag{7}$$

where μ_1 and μ_2 are positive. It can be studied using the nullclines approach. Let us show how. Let the regulatory matrix be of the form

$$W = \begin{pmatrix} k & a \\ b & k \end{pmatrix}, \tag{8}$$

and $k > 0$.

Proposition 4.1. *Suppose*

$$\theta_1 = 0.5(k+a), \quad \theta_2 = 0.5(b+k). \tag{9}$$

Then the system

$$\begin{cases} x_1' = \dfrac{1}{1+e^{-\mu_1(kx_1+ax_2-\theta_1)}} - x_1, \\ x_2' = \dfrac{1}{1+e^{-\mu_2(bx_1+kx_2-\theta_2)}} - x_2 \end{cases} \tag{10}$$

has the critical point at $(0.5, 0.5)$.

Proof. The equalities

$$\begin{cases} 0 = \dfrac{1}{1+e^{-\mu_1(k0.5+a0.5-\theta_1)}} - 0.5, \\ 0 = \dfrac{1}{1+e^{-\mu_2(b0.5+k0.5-\theta_2)}} - 05 \end{cases} \tag{11}$$

hold due to the specific values of θ_1 and θ_2. □

Let us detect the type of the critical point $(0.5, 0.5)$. For this, linearize the system at this point. One gets

$$\begin{cases} u_1' &= -u_1 + \mu_1 k g_1 u_1 &+ \mu_1 a g_1 u_2, \\ u_2' &= -u_2 + \mu_2 b g_2 u_1 &+ \mu_2 k g_2 u_2. \end{cases} \tag{12}$$

where

$$g_1 = \frac{e^{-\mu_1(k0.5+a0.5-\theta_1)}}{[1+e^{-\mu_1(b0.5+k0.5-\theta_1)}]^2} = 1/4,$$

$$g_2 = \frac{e^{-\mu_2(k0.5+a0.5-\theta_2)}}{[1+e^{-\mu_2(b0.5+k0.5-\theta_2)}]^2} = 1/4.$$

The linear system (12) takes the form

$$\begin{cases} u_1' &= -u_1 + 0.25(\mu_1 k u_1 &+ \mu_1 a u_2), \\ u_2' &= -u_2 + 0.25(\mu_2 b u_1 &+ \mu_2 k u_2). \end{cases} \tag{13}$$

The coefficient matrix for (13) is

$$A = \begin{pmatrix} \frac{1}{4}\mu_1 k - 1 & \frac{1}{4}\mu_1 a \\ \frac{1}{4}\mu_2 b & \frac{1}{4}\mu_2 k - 1 \end{pmatrix}. \tag{14}$$

The characteristic equation $\det(A - \lambda E) = 0$ (E is the unit matrix) takes the form

$$\begin{aligned} \det(A-\lambda E) &= (\tfrac{1}{4}\mu_1 k - (1+\lambda))(\tfrac{1}{4}\mu_2 k - (1+\lambda)) - \tfrac{1}{16}\mu_1\mu_2 ab \\ &= (1+\lambda)^2 - (\tfrac{1}{4}k(\mu_1+\mu_2)(1+\lambda) + \tfrac{1}{16}\mu_1\mu_2(k^2-ab) = 0. \end{aligned} \tag{15}$$

The roots of the equation (15) are

$$\lambda = -1 + \frac{1}{8}k(\mu_1 + \mu_2) \pm \sqrt{\frac{1}{64}k^2(\mu_1 - \mu_2)^2 + \frac{1}{16}\mu_1\mu_2\, a\, b}. \tag{16}$$

From this we obtain several useful assertions. Denote $P = (0.5, 0.5)$.

Proposition 4.2. *The necessary condition for the point P to be a focus is $a\,b < 0$.*

Proposition 4.3. *The sufficient conditions for the point P to be a focus are:*

$$\begin{aligned} \tfrac{1}{4}k^2(\mu_1 - \mu_2)^2 + \mu_1\mu_2\, a\, b < 0, \\ -1 + \tfrac{1}{8}k(\mu_1 + \mu_2) \neq 0. \end{aligned} \tag{17}$$

Proposition 4.4. *The sufficient condition for the point P to be a stable focus is*

$$k < 4 \min\Big\{\frac{2}{\mu_1 + \mu_2},\ \frac{-\mu_1\mu_2\, a\, b}{|\mu_1 - \mu_2|}\Big\}. \tag{18}$$

Proof. It can be verified that then the discriminant in (16) is negative and the real parts of λ-s in (16) are also negative. □

Proposition 4.5. *The sufficient condition for the point P to be an unstable focus is*

$$\frac{8}{\mu_1 + \mu_2} < k < \frac{-4\mu_1\mu_2\, a\, b}{|\mu_1 - \mu_2|}. \tag{19}$$

Proof. The right sides in (18) and (19) are supposed to be $+\infty$, if $\mu_1 = \mu_2$. The discriminant in (16) is negative due to the second part of (19). The first inequality in (19) ensures that the real parts of λ-s in (16) are positive. □

Remark 4.6. *For $\mu_1 = \mu_2 = 4$ the condition (19) reduces to $1 < k$.*

Theorem 4.7. *Suppose the system is of the form (10), where $k > 0$, $a\,b < 0$ and θ_1, θ_2 are as in (9). Suppose also that the point P is a single critical point of the type unstable focus.*

Then there exists the limit cycle in Q_2.

Proof. Consider the nullclines of the system (10). They intersect at the point P only. Generally, they look (for matrices as in (8)) as shown in Figure 1. Our intent is to consider trajectories that start at one of the nullclines and define the return map, which will be shown to have a fixed point. The vector field is clock-wise rotating in a neighborhod of P, since it is a focus. By continuity, it is whirling in the whole Q_2. The nullclines divide the region Q_2 into four sectors. In each of them, the vector field is rotating clock-wise with the angular speed separated from zero, if outside of some vicinity of P. No trajectory escapes Q_2. This is a consequence of Proposition 3.1. Consider one of the nullclines. Let it be, for definiteness, the one going in the horizontal direction, $x_2 = \frac{1}{1+e^{-\mu_2(bx_1+kx_2-\theta_2)}}$ (the red one in Figure 1). Denote N_1 its fragment inside Q_2. The point P belongs to N_1. Trajectories, that start at N_1 close enough to P, cross N_1 after one rotation. This cross-point is further from P, since the type of P is an unstable focus. Move along N_1 towards the upper left cross point, denoted S, with the segment $B = \{(0, x_2) : 0 < x_2 < 1\}$ (it is the left border of Q_2). Such a point is unique since the vector field cannot be tangent to the border of Q_2 by Proposition 3.1. (The point S is marked by the small black square in Figure 1). Any trajectory starting at N_1 rotates, governed by the vector field in Q_2, and returns back to N_1 in a finite time (because there is no critical point other than P). Look at point S. Since it is the end point of N_1, the trajectory starting at S, returns to N_1 at some interior point of N_1. Due to the continuity of the return map, there exists a point on N_1, which is a fixed point of the return map. It corresponds to a closed trajectory. □

It was observed, that system suffers Andronov-Hopf bifurcation if $w_{11} = w_{22} = k$, $w_{12}w_{21} < 0$. For $k > 0$ small the system has a unique critical point of the type stable focus. It is a single attractor. If k increases, the real parts of characteristic numbers $\lambda_{1,2}$ of a single critical point pass through zero and the type of a critical point becomes unstable focus. The stable limit cycle emerges and now it is a single attractor of the system. This transformation was described in the articles [13], [10].

Remark 4.8. *There are conditions in [4] for the system*

$$\begin{aligned} x' &= f_\mu(x, y), \\ y' &= g_\mu(x, y) \end{aligned} \tag{20}$$

with a single critical point (x_0, y_0) *at* $\mu = \mu_0$ *to suffer the Hopf bifurcation. Let* $\lambda(\mu_0)$ *be the characteristic value of* (x_0, y_0). *These conditions are: 1) for some* μ_0 *(do not mix with* μ *in our systems) the real part of* $\lambda(\mu_0)$ *is zero; 2) the imaginary part of* $\lambda(\mu)$ *is monotonically increasing in* μ; *3) the expression* $a{=}1/16(f_{xxx} + f_{xyy} + g_{xxy} + g_{yyy}) + 1/16\omega(f_{xy}(f_{xx} + f_{yy}) - g_{xy}(g_{xx} + g_{yy}) - f_{xx}g_{xx} + f_{yy}g_{yy})$ *computed at* (x_0, y_0, μ_0) *is negative (*ω *stands for the imaginary part of* λ*).*

All three conditions fulfill for our system (10) and for the critical point $(0.5, 0.5)$, *which is supposed to be a focus. The last expression, computed analytically in Wolfram Mathematica, is* $\mathtt{a}{=}k((-0.0625a^2 - 0.0625k^2)\mu_1^3 + (-0.0625b^2 - 0.0625k^2)\mu_2^3)$, *which is negative for* μ_1, μ_2 *positive.*

Example 4.9. *Consider system (10), where,* $\mu_1 = \mu_2 = 4$, $\Theta_1 = 0.5(w_{11} + w_{12})$, $\Theta_2 = 0.5(w_{21} + w_{22})$, $w_{11} = w_{22} = 2.7$, $w_{12} = -w_{21} = 3$. *Since the conditions of Theorem 4.7 are fulfilled, limit cycle exists. It is depicted in Figure 1 together with the nullclines and the vector field.*

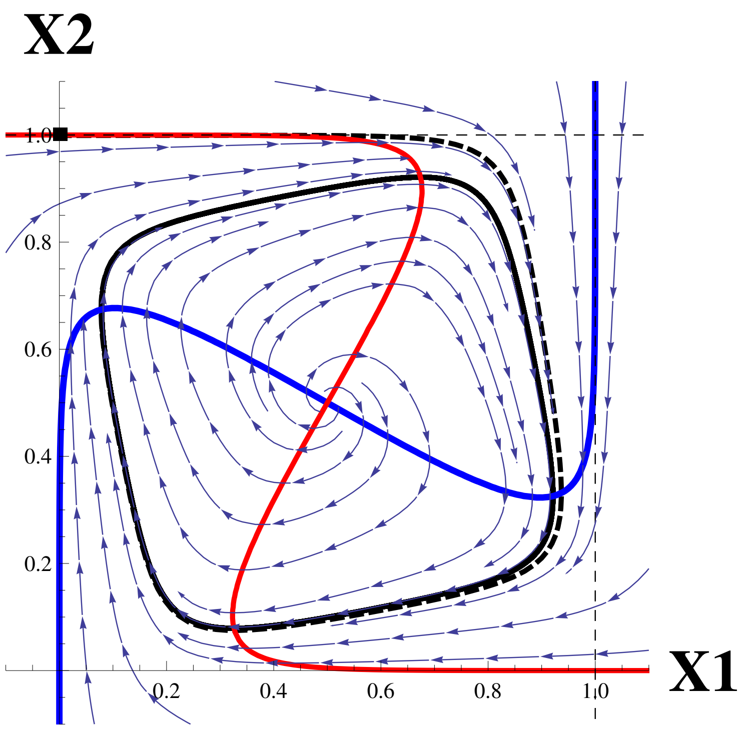


Figure 1: The limit cycle in system (10), $W = \{\{2.7, 3\}, \{-3, 2.7\}\}$, $\mu_1 = \mu_2 = 4$, $\theta_1 = 2.85, \theta_2 = -0.15$.

4.2. Attractors for 2D neuronal systems

Consider the system

$$\begin{cases} x_1' = \tanh(w_{11}x_1 + w_{12}x_2) - x_1, \\ x_2' = \tanh(w_{21}x_1 + w_{22}x_2) - x_2, \end{cases} \tag{21}$$

where w_{ij} are parameters. Let the regulatory matrix be of the form

$$W = \begin{pmatrix} k & a \\ b & k \end{pmatrix}, \tag{22}$$

and $a \cdot b < 0$, $k > 0$.

Then the system

$$\begin{cases} x_1' = \tanh(kx_1 + ax_2) - x_1, \\ x_2' = \tanh(bx_1 + kx_2) - x_2 \end{cases} \tag{23}$$

has the critical point at $(0, 0)$.

The nullclines are given by the equations

$$\begin{cases} x_1 = \tanh(kx_1 + ax_2), \\ x_2 = \tanh(bx_1 + kx_2). \end{cases} \tag{24}$$

There exists at least one critical point. For analysis of critical points, we need the linearized system (24) for any equilibrium of the form (x_1^*, x_2^*). It is

$$\begin{cases} u_1' & = -u_1 + kg_1u_1 & +ag_1u_2, \\ u_2' & = -u_2 + bg_2u_1 & +kg_2u_2, \end{cases} \tag{25}$$

where

$$g_1 = \mathrm{sech}\,(\mathrm{kx}_1^* + \mathrm{ax}_2^*)^2,$$
$$g_2 = \mathrm{sech}\,(\mathrm{bx}_1^* + \mathrm{kx}_2^*)^2.$$

The characteristic equation $\det(A - \lambda E) = 0$ takes the form

$$\begin{aligned} \det(A - \lambda E) &= (kg_1 - (1 + \lambda))(kg_2 - (1 + \lambda)) - a\,b\,g_1g_2 = \\ &= \lambda^2 + (2 - k(g_1 + g_2))\lambda + (g_1g_2(k^2 - ab) - k(g_1 + g_2) + 1) = 0. \end{aligned} \tag{26}$$

The roots of the equation (26) are

$$\lambda = -1 + \frac{1}{2}k(g_1 + g_2) \pm \sqrt{\frac{1}{4}k^2(g_1 - g_2)^2 + g_1g_2\,a\,b}. \tag{27}$$

Example 4.10. *Consider system (21), where* $w_{11} = w_{22} = 2.2$, $w_{12} = -1.3, w_{21} = 3$. *There exists the limit cycle. It is depicted in Figure 2 together with the nullclines and the vector field.*

4.3. Attractors for 3D systems

Immense now the above obtained limit cycle (Figure 1) into the 3D space. For this, consider the 3D system

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu_1(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 - \theta_1)}} - x_1, \\[2ex] x_2' = \dfrac{1}{1 + e^{-\mu_2(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 - \theta_2)}} - x_2, \\[2ex] x_3' = \dfrac{1}{1 + e^{-\mu_3(w_{31}x_1 + w_{32}x_2 + w_{33}x_3 - \theta_3)}} - x_3, \end{cases} \tag{28}$$

where the regulatory matrix is

$$W = \begin{pmatrix} 2.7 & 0 & 3 \\ 0 & 1 & 0 \\ -3 & 0 & 2.7 \end{pmatrix}, \tag{29}$$

$\mu_1 = \mu_3 = 4$, $\mu_2 = 3$, $\theta_1 = 2.38$, $\theta_2 = 0.5$, $\theta_3 = -0.15$. The x_2-nullcline is a plane, which corresponds to a unique root of the equation $\frac{1}{1+e^{-\mu_2(x_2-\theta_2)}} = x_2$. The vector field is orthogonal to x_2-nullcline and directed towards it. The 2D periodic trajectory from Figure 1 appears as a periodic 3D trajectory, which can be seen in Figure 3. This trajectory serves as a global attractor in Q_2.

The resulting 3D limit cycle is depicted in Figure 3.

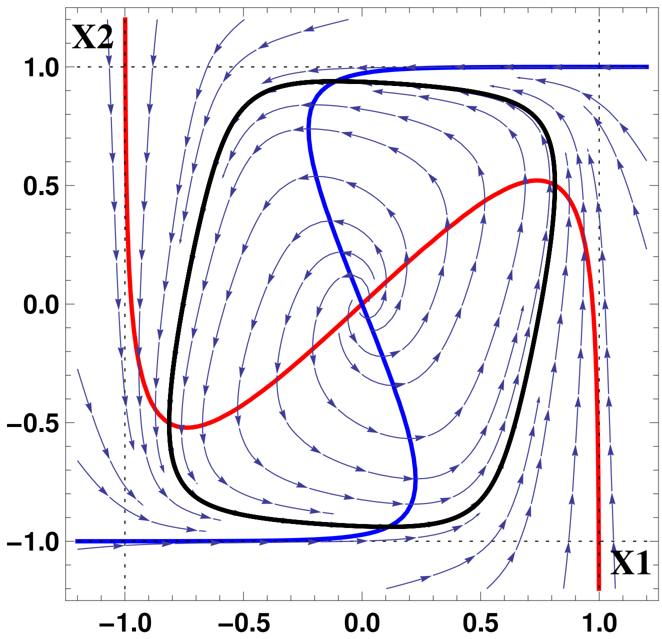


Figure 2: The limit cycle in system (21), $W = \{\{2.2, -1.3\}, \{3, 2.2\}\}$.

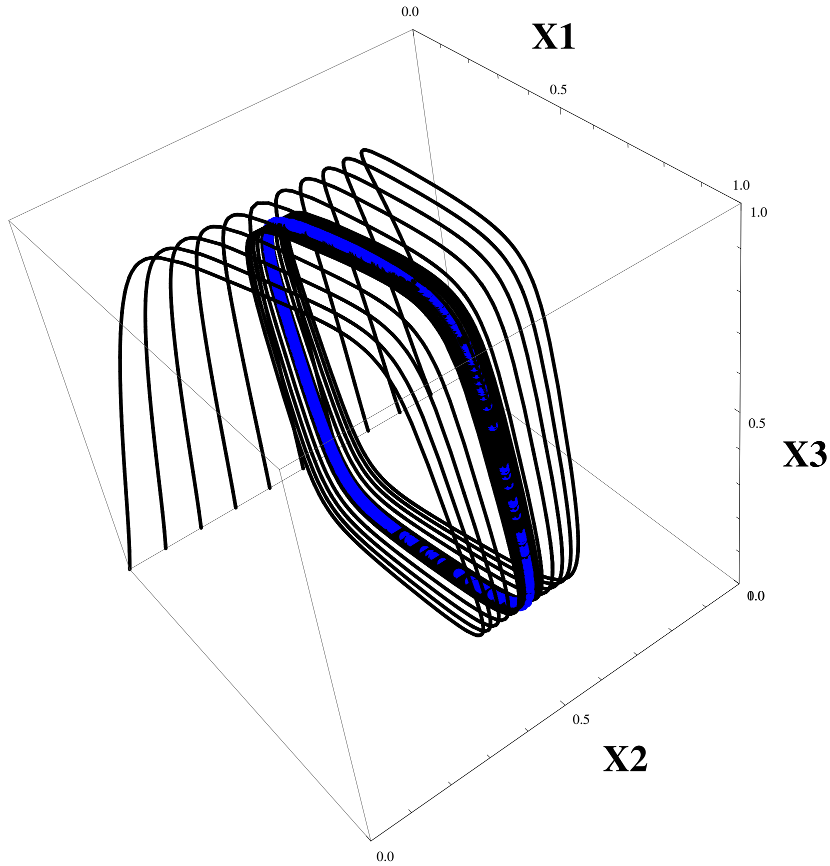


Figure 3: Limit cycle in system (28) with the matrix (29) and several trajectories, $\mu_1 = \mu_3 = 4$, $\mu_2 = 3$, $\theta_1 = 2.85$, $\theta_2 = 0.5$, $\theta_3 = -0.15$.

4.4. Attractors for 3D neuronal systems

Immense the above obtained limit cycle (Figure 2) into the 3D space. For this, consider the 3D system

$$\begin{cases} x_1' = \tanh(w_{11}x_1 + w_{12}x_2 + w_{13}x_3) - x_1, \\ x_2' = \tanh(w_{21}x_1 + w_{22}x_2 + w_{23}x_3) - x_2, \\ x_3' = \tanh(w_{31}x_1 + w_{32}x_2 + w_{33}x_3) - x_3, \end{cases} \tag{30}$$

where the regulatory matrix is

$$W = \begin{pmatrix} 2.2 & -1.3 & 0 \\ 3 & 2.2 & 0 \\ 0 & 0 & 2.2 \end{pmatrix}. \tag{31}$$

The 2D periodic trajectory from Figure 2 appears as a periodic 3D trajectory, which can be seen in Figure 4.

The resulting 3D limit cycles are depicted in Figure 4.

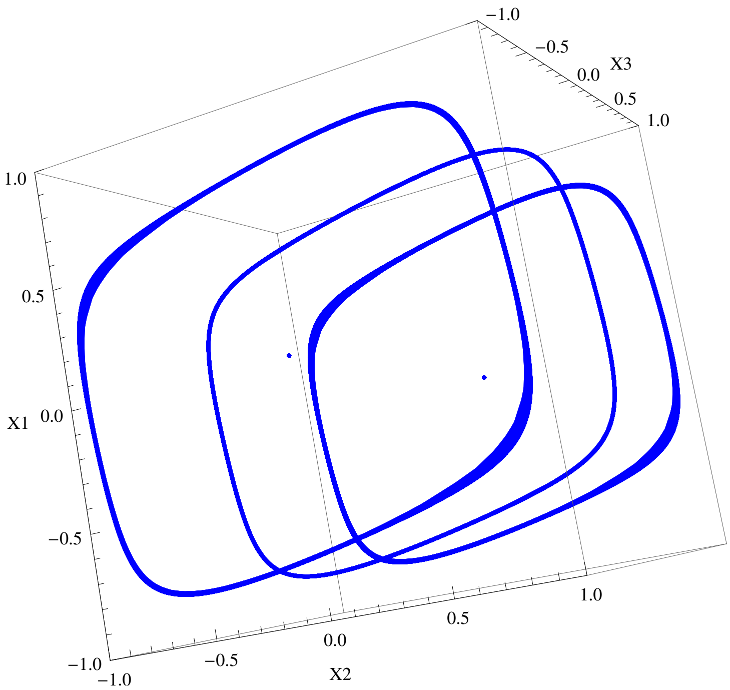


Figure 4: The limit cycles in system (30), $W = \{\{2.2, -1.3, 0\}, \{3, 2.2, 0\}, \{0, 0, 2.2\}\}$.

4.5. Attractors for higher order systems

Consider system (3) for $n = 5$. Let the regulatory matrix be

$$W = \begin{pmatrix} 2.7 & 3 & 0 & 0 & 0 \\ -3 & 2.7 & 0 & 0 & 0 \\ 0 & 0 & 2.7 & 0 & 3 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & -3 & 0 & 2.7 \end{pmatrix}, \tag{32}$$

and $\mu_1 = \mu_2 = \mu_3 = \mu_5 = 4$, $\mu_4 = 3$, $\theta_1 = \theta_3 = 2.85$, $\theta_2 = \theta_5 = -0.15$, $\theta_4 = 0.5$.

It consists of two independent systems of order 2 and 3. Each of these systems has a limit cycle. The resulting system of order five has an attractor, which is obtained by combination of two previously constructed limit cycles of orders 2 and 3, respectively. Let us call such an attractor *periodic attractor*.

We claim that the following is true.

Theorem 4.11. *For any dimension n the system (3) can have a periodic attractor.*

Proof. Case $n = 2$. The limit cycle exists under certain conditions, Theorem 4.7.

Case $n = 3$. The 2D limit cycle, which exists under certain conditions, can be immersed in the three dimensional space using the special construction described in the previous subsection. It becomes the 3D limit cycle attracting trajectories in Q_2. Other type 3D limit cycles can be found as well [2].

Case $n = 4$. Take two 2D systems, each possessing a limit cycle. Construct 4D regulatory matrix with two 2D blocks on the main diagonal. Let T_1 be the period of the first limit cycle, and T_2 similarly. Then, if $iT_1 = jT_2$, where i and j are arbitrary positive integers, these two limit cycles generate a periodic attractor for $4D$ system, composed of two 2D systems.

Case $n = 5$. Combine 2D system with 3D one, assuming that both have limit cycles of periods T_1 and T_2. If positive integers i and j exist such that $iT_1 = jT_2$, then a periodic attractor can be constructed for 5D system.

Case $n = 6$. Two combinations are possible, as $6 = 2 + 2 + 2$, and then the periods T_i should relate as $iT_1 = jT_2 = mT_3$, where i, j, m are positive integers. Trivially, $i = j = m = 1$, $T_1 = T_2 = T_3$.

And so on.

An alternative reasoning could be the following. It is possible to have a 2D system with the limit cycle of period τ_1 and a 3D system with the period τ_2 such that $2\tau_1 = \tau_2$. If n is even, compose big system of $n/2$ two-dimensional ones, where all periods are τ_1. If n is odd and $n \geq 5$, compose big system of $(n-3)/2$ two-dimensional ones and one three-dimensional system with the period τ_2. □

4.6. Attractors for 4D neuronal systems

Consider the 4D system

$$\begin{cases} x_1' = \tanh(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 + w_{14}x_4) - x_1, \\ x_2' = \tanh(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 + w_{24}x_4) - x_2, \\ x_3' = \tanh(w_{31}x_1 + w_{32}x_2 + w_{33}x_3 + w_{34}x_4) - x_3, \\ x_4' = \tanh(w_{41}x_1 + w_{42}x_2 + w_{43}x_3 + w_{44}x_4) - x_4, \end{cases} \tag{33}$$

where the regulatory matrix is

$$W = \begin{pmatrix} 2.2 & -1.3 & 0 & 0 \\ 3 & 2.2 & 0 & 0 \\ 0 & 0 & 4 & -5 \\ 0 & 0 & 3 & 4 \end{pmatrix}. \tag{34}$$

It consists of two independent 2D systems, and each have the limit cycle as a 2D attractor. The system (33) has therefore a 4D period attractor. 3D projections of trajectories tending to this 4D period attractor are depicted in Figures 5 to 7.

The result of Theorem 4.11 is valid also for n-dimensional systems of the form (33), since there are examples of 2D and 3D neuronal systems, which have periodic attractors.

5. Example

Consider the system

$$\begin{cases} \dfrac{dx_1}{dt} = \dfrac{1}{1 + e^{-\mu_1(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 + w_{14}x_4 - \theta_1)}} - x_1, \\ \dfrac{dx_2}{dt} = \dfrac{1}{1 + e^{-\mu_2(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 + w_{24}x_4 - \theta_2)}} - x_2, \\ \dfrac{dx_3}{dt} = \dfrac{1}{1 + e^{-\mu_3(w_{31}x_1 + w_{32}x_3 + w_{33}x_3 + w_{34}x_4 - \theta_3)}} - x_3, \\ \dfrac{dx_4}{dt} = \dfrac{1}{1 + e^{-\mu_4(w_{41}x_1 + w_{42}x_2 + w_{43}x_3 + w_{44}x_4 - \theta_4)}} - x_4 \end{cases} \tag{35}$$

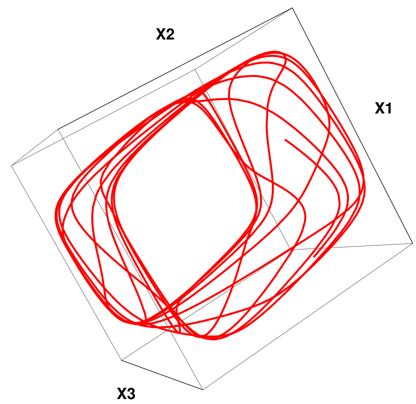


Figure 5: Projection onto the subspace (x_1, x_2, x_3)

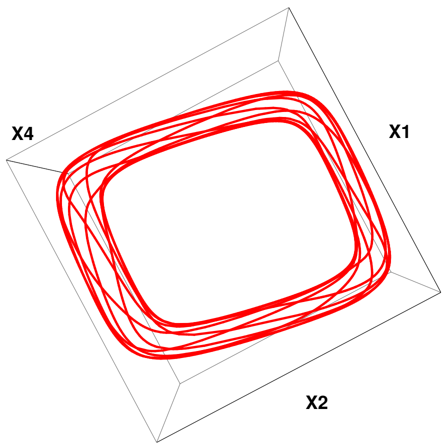


Figure 6: Projection onto the subspace (x_1, x_2, x_4)

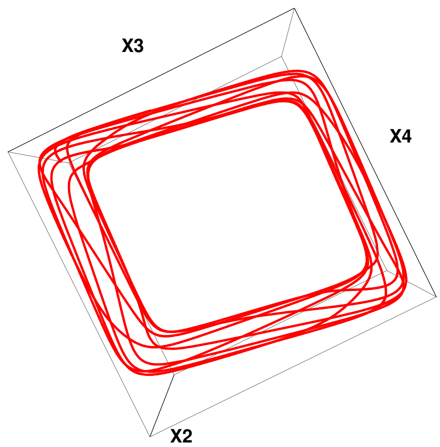


Figure 7: Projection onto the subspace (x_2, x_3, x_4)

with the regulatory matrix

$$W = \begin{pmatrix} 1.2 & 1 & 0 & 0 \\ -1 & 1.2 & 0 & 0 \\ 0 & 0 & 2.257 & 1 \\ 0 & 0 & -1 & 2.257 \end{pmatrix}, \tag{36}$$

the parameters $\mu_1 = \mu_2 = \mu_3 = \mu_4 = 4$, $\theta_1 = 1.1$, $\theta_2 = 0.1$, $\theta_3 = 1.6285$, $\theta_4 = 0.6285$. It is uncoupled. The first 2D system has the stable periodic solution with the period $\tau_1 \approx 7.28$. The second one has the periodic solution with the period $\tau_2 \approx 22.74$. So τ_2 is very close to $3\tau_1$. By small perturbation of the elements 1.2 in the matrix (36) these periods can be made such that the relation $3\tau_1 = \tau_2$ holds exactly. Therefore the period attractor exists for the 4D system (35).

3D projections of trajectories tending to this 4D period attractor are depicted in Figures 8 to 10.

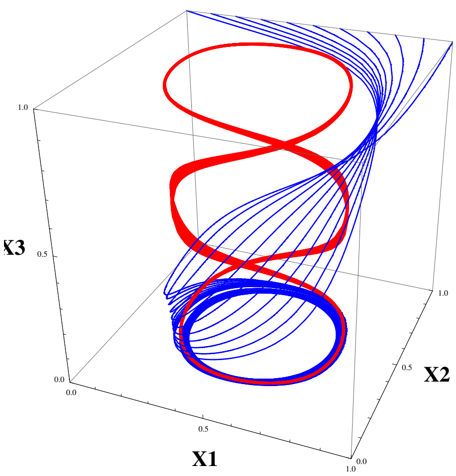


Figure 8: (x_1, x_2, x_3)-projections of the 4D attractor (red) and eleven trajectories (blue)

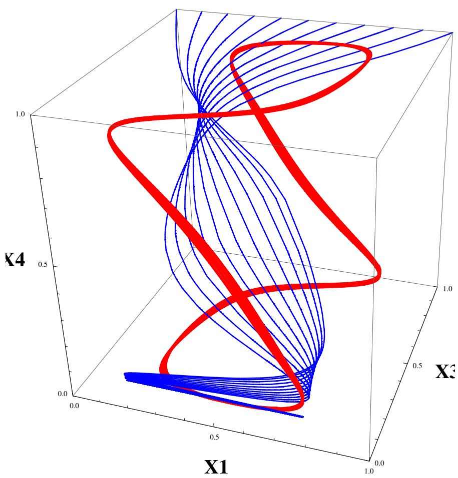


Figure 9: (x_1, x_3, x_4)-projections of the 4D attractor (red) and several trajectories (blue)

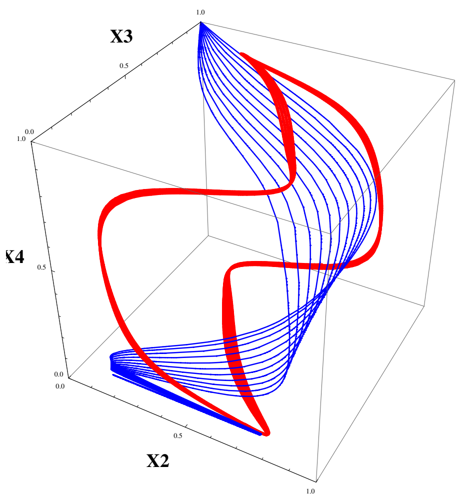


Figure 10: (x_2, x_3, x_4)-projections of the 4D attractor (red) and several trajectories (blue)

6. Conclusion

Closed figures can be obtained as attractors for systems of the form (3). They can be constructed for any dimension. For higher dimensions (greater than five) they can be constructed in multiple ways. Therefore, a periodic attractor of an arbitrary order can be obtained by combining periodic attractors of lower dimensionalities. If it is accepted, that systems (3) describe genetic networks adequately, GRN of any size allows for periodic processes. The same is true for arbitrary dimensional systems of the form (33).

7. 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".

References

[1] S.P. Cornelius, W.L. Kath, A.E. Motter. Realistic control of network dynamic. Nature Communications, Volume 4, Article number: 1942 (2013), 1–9.

[2] R. Edwards and L. Ironi. Periodic solutions of gene networks with steep sigmoidal regulatory functions. Physica D, 282 (2014), 1 - 15. https://doi.org/10.1016/j.physd.2014.04.013

[3] C. Furusawa, K. Kaneko. A generic mechanism for adaptive growth rate regulation. PLoS Comput Biol 4(1), 2008: e3. doi:10.1371/journal.pcbi.0040003

[4] G. van der Heijden. Hopf bifurcation. www.ucl.ac.uk/~ucesgvd/hopf.pdf

[5] H.D. Jong. Modeling and Simulation of Genetic Regulatory Systems: A Literature Review, J. Comput Biol. 2002;9(1):67-103, DOI: 10.1089/10665270252833208

[6] V.W. Noonburg Differential Equations: From Calculus to Dynamical Systems, Providence, Rhode Island: MAA Press, 2019, 2nd edition.

[7] L. Perko. Differential Equations and Dynamical Systems, 3rd Edition.

[8] F. Sadyrbaev, S. Atslega, E. Brokan. (2020) Dynamical Models of Interrelation in a Class of Artificial Networks. In: Pinelas S., Graef J.R., Hilger S., Kloeden P., Schinas C. (eds) Differential and Difference Equations with Applications. ICDDEA 2019. Springer Proceedings in Mathematics & Statistics, vol 333. Springer, Cham.

[9] F. Sadyrbaev, V. Sengileyev, A. Silvans. On Coexistence of Inhibition and Activation in Genetic Regulatory Networks. 19 Intern. Confer. Numer. Analys and Appl. Mathematics, Rhodes, Greece, 20-26 September 2021, To appear in AIP Conference Proceedings.

[10] F. Sadyrbaev, I. Samuilik. V. Sengileyev. On Modelling of Genetic Regulatory Networks. WSEAS Trans. Electronics, vol. 12, 2021, 73-80.

[11] I. Samuilik, F. Sadyrbaev. Mathematical Modelling of Leukemia Treatment. WSEAS Trans. of Computers, vol. 20, 2021, 274-281.

[12] I. Samuilik, F. Sadyrbaev, D. Ogorelova. Mathematical modeling of three-dimensional genetic regulatory networks using logistic and Gompertz functions, WSEAS Trans. on Systems and Control, vol. 17, 2022, 101-107.

[13] I. Samuilik, F. Sadyrbaev, V. Sengileyev. Examples of periodic biological oscillators: transition to a six-dimensional system, WSEAS Trans. Computer Research, vol. 10, 2022, 50-54.

[14] Le-Zhi Wang, Ri-Qi Su, Zi-Gang Huang, Xiao Wang, Wen-Xu Wang, Grebogi Celso and Ying-Cheng Lai: A geometrical approach to control and controllability of nonlinear dynamical networks. Nature Communications, Volume 7, Article number: 11323 (2016), DOI: 10.1038/ncomms11323

[15] H.R. Wilson, J.D. Cowan. Excitatory and inhibitory interactions in localized populations of model neurons. Biophys J., vol 12 (1), 1972, pp. 1-24.

Mathematical modelling of gene and neuronal networks by ordinary differential equations

Diana Ogorelova

Summary. The system of ordinary differential equations that models a type of artificial networks is considered. The system consists of a sigmoidal function which depends on linear combinations of the arguments minus the linear part. The linear combinations of the arguments are described by the regulatory matrix W. For the three-dimensional cases several types of matrices W are considered and behavior of solutions of the system is analyzed.

MSC: 34C60, 34D45, 92B20

1 Introduction

In this article, we study Neural Networks, called also Artificial Neural Networks (ANN), and their mathematical models, using ordinary differential equations. The motivation for the study of ANN went from the attempts to understand the principles and organization of the human brain. Understanding came that human brains work differently from digital computers. Its effectiveness comes from high complexity, nonlinear mode of regulation, and parallelism of actions. The elements of the human brain were called *neurons*. These elements perform calculations still faster than the fastest digital computers. The human brain is able to perceive information about the environment in the form of images, and, moreover, it can process the received information needed for interaction with the environment.

At birth, the human brain has a ready structure for learning, which in familiar terms is understood as experience. So the neural network is designed to model the way in which the human brain solves usual problems and performs a particular task. A particular interest in ANN stems from the fact that an important group of neural networks performs needed to solve a problem computations through the process of learning. So, following [2], generally, ANN can be imagined as a parallel distributed processor, consisting of simple processing units, which is able to gain experiential knowledge and make it available for use.

Artificial Neural Networks (ANNs) consist of a number of elements which are connected. “Each neuron has a sigmoid transfer function, and a continuous positive and bounded output activity that evolves according to weighted sums of the activities in the networks. Neural networks with arbitrary connections are often called recurrent networks” [11]. No conditions are imposed to restrict synaptic values. There are two types of recurrent neural networks: discrete time recurrent neural networks and continuous time ones. The dynamics of the continuous time recurrent neural network with n units, can be described by the system of ordinary differential equations (ODE)([4])

$$x_i' = -b_i x_i + f_i(\Sigma a_{ij} x_j) + I_i(t), \tag{1}$$

where x_i is the internal state of the i-th unit, b_i is the time constant for the i-th unit, a_{ij} are connection weights, $I_i(t)$ is the input to the i-th unit, and $f_i(\Sigma a_{ij} x_j)$ is the response function of the i-th unit. Usually f is taken as a sigmoidal function. There are particular response functions that are non-negative. For instance, functions $f_i(z) = (1 + \exp(\mu_i(z - \theta_i))^{-1}$ were used in [1]. More general cases can be modeled by the system using the function $f_i(z) = \tanh(a_i z - \theta_i)$, which takes values in the open interval $(-1, 1)$. If the recurrent neural networks without input are considered, the system

$$x_i' = f_i(\Sigma(a_{ij} x_j - \theta_i)) - b_i x_i \tag{2}$$

can be considered.

The mathematical model using ordinary differential equations, is

$$\begin{cases} \dfrac{dx_1}{dt} = 2\dfrac{1}{1 + e^{(a_{11}x_1 + a_{12}x_2 + a_{13}x_n - \theta_1)}} - 1 - b_1 x_1, \\[2ex] \dfrac{dx_2}{dt} = 2\dfrac{1}{1 + e^{(a_{21}x_1 + a_{22}x_2 + aw_{23}x_n - \theta_2)}} - 1 - b_2 x_2, \\[2ex] \dfrac{dx_3}{dt} = 2\dfrac{1}{1 + e^{(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3)}} - 1 - b_3 x_3, \end{cases} \tag{3}$$

The same system can be written as ([3])

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3 - \theta_1) - b_1 x_1, \\[2ex] \dfrac{dx_2}{dt} = \tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3 - \theta_2) - b_2 x_2, \\[2ex] \dfrac{dx_3}{dt} = \tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3) - b_3 x_3, \end{cases} \tag{4}$$

The elements of this 3D network are called neurons. The connections between them are synapses (or nerves). There is an algorithm that describes how the impulses are propagated through the network. In the above model this algorithm is encoded by the matrix

$$W = \begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix}. \tag{5}$$

Each neuron accepts signals from others and produces a single output. The extent to which the input of neuron i is driven by the output of neuron j is characterized by its output and synaptic weight a_{ij}. The dynamic evolution leads to attractors of the system (4) and it was experimentally observed in neural systems. In theoretical modeling the emphasis is put on the attractors of a system. We wish to study them for the system (4).

Similar systems arise in the theory of genetic regulatory networks. The difference is that the nonlinearity is represented by a positive valued sigmoidal functions. One of such systems is

$$\begin{cases} \dfrac{dx_1}{dt} = \dfrac{1}{1+e^{-\mu_1(a_{11}x_1+a_{12}x_2+a_{13}x_n-\theta_1)}} - b_1x_1, \\ \dfrac{dx_2}{dt} = \dfrac{1}{1+e^{-\mu_2(a_{21}x_1+a_{22}x_2+a_{23}x_n-\theta_2)}} - b_2x_2, \\ \dfrac{dx_3}{dt} = \dfrac{1}{1+e^{-\mu_3(a_{31}x_1+a_{32}x_2+a_{33}x_3-\theta_3)}} - b_3x_3. \end{cases} \tag{6}$$

Systems of the form (6) were studied before by many authors. The interested reader may consult the works ([5], [6], [7], [9], [10], [13], [14]). Similar systems appear in the theory of telecommunication networks ([8]).

In this article we study the different dynamic regimes for the system (4) which can be observed under various conditions. In particular, we first speak about critical points in the system (4) and evaluate the number of them. Then we focus on periodic regimes, study their attractiveness for other trajectories. This can be done, under some restrictions, for systems of relatively high dimensionality. Also the evidences of chaotic behavior are presented.

2 Preliminary results

2.1 Invariant set

Consider 3D system (4).

Proposition 2.1. System (4) has an invariant set $Q_3 = \{\frac{-1}{b_1} < x_1 < \frac{1}{b_1}, \frac{-1}{b_2} < x_2 < \frac{1}{b_2}, \frac{-1}{b_3} < x_3 < \frac{1}{b_3}\}$.

Proof. By inspection of the vector field generated by the system (4) on the opposite faces of the three-dimensional cube Q_3. Notice, that the value range for the function tanh z is $(-1, 1)$. $\square$

2.2 Nullclines

The nullclines for the system are defined by the relations

$$\begin{cases} x_1 = \dfrac{1}{b_1}\tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3 - \theta_1), \\ x_2 = \dfrac{1}{b_2}\tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3 - \theta_2), \\ x_3 = \dfrac{1}{b_3}\tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3). \end{cases} \quad (7)$$

Example 2.2.
Consider the system with the matrix

$$W = \begin{pmatrix} 1 & 2.5 & 0 \\ -2.5 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} \quad (8)$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = \theta_2 = 0.03, \theta_3 = 0.3$.

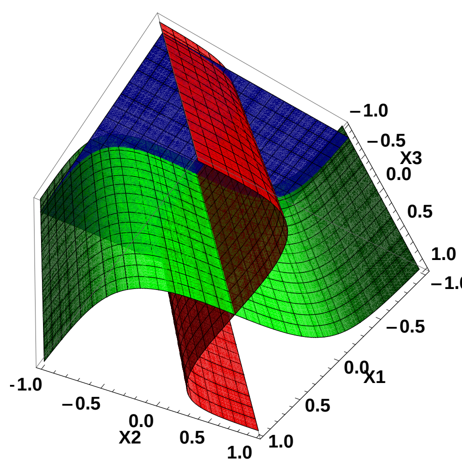


Fig. 2.1.Nullclines for system (4) (x_1 - red, x_2 - green, x_3 - blue).

2.3 Critical points

The critical points for the system (4) are the cross points of the nullclines. They can be found from the system

$$\begin{cases} x_1 - \dfrac{1}{b_1}\tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3 - \theta_1) = 0, \\ \\ x_2 - \dfrac{1}{b_2}\tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3 - \theta_2) = 0, \\ \\ x_3 - \dfrac{1}{b_3}\tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3) = 0. \end{cases} \tag{9}$$

Proposition 2.2.
All critical points are in the invariant set.

The nullclines are located in the sets $\{\frac{-1}{b_1} < x_1 < \frac{1}{b_1}, \frac{-1}{b_2} < x_2 < \frac{1}{b_2}, \frac{-1}{b_3} < x_3 < \frac{1}{b_3}\}$ rspectively and these sets intersect by the invariant set Q_3 only.$\square$

Proposition 2.3.
At least one critical point exists.

The invariant set Q_3 may be considered as a topological ball. Since the vector field on the border is directed inward, Q_3 is mapped into itself continuously. Then there exists a fixed point of the mapping Q_3 to Q_3, defined by the system (7). $\square$

Remark. The number of critical points may be greater, up to 27, but finite.

Remark. Both assertions 2.3 and 2.3 are valid for the n-dimensional case also.

Example 2.3.
Consider the system (4) with the matrix

$$W = \begin{pmatrix} 1 & 2 & 0 \\ -2 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} \tag{10}$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = 0.8, \theta_2 = 0.3, \theta_3 = 0.2$. There is one critical point $(-0.162; 0.399; -0.731)$.

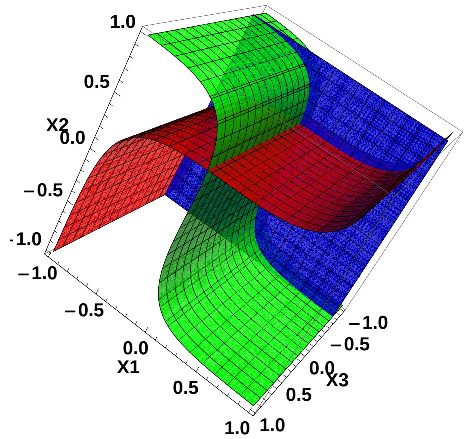


Fig. 2.2.Nullclines for system (4) (x_1 - red, x_2 - green, x_3 - blue).

Example 2.4.
Consider example of multiple critical points and the system (4) with the matrix

$$W = \begin{pmatrix} 1.5 & 2 & 0 \\ -2 & 1.5 & 0 \\ 0 & 0 & 1.5 \end{pmatrix} \tag{11}$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = 0.7, \theta_2 = 0.3, \theta_3 = 0.01$.

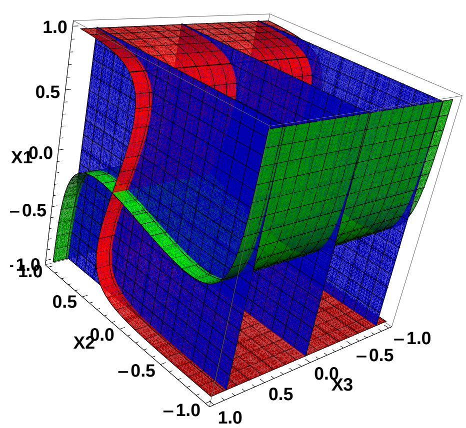


Fig. 2.3.Nullclines for system (4) (x_1 - red, x_2 - green, x_3 - blue).

There are three critical points $(-0.067;\ 0.367;\ 0.854)$, $(-0.067;\ 0.367;\ 0.020)$ and $(-0.067;\ 0.367;\ -0.863)$.

2.4 Linearization at a critical point

The linearized system for any critical point (x_1^*, x_2^*, x_3^*) is

$$\begin{cases} u_1' = -b_1u_1 + a_{11}g_1u_1 + a_{12}g_1u_2 + a_{13}g_1u_3, \\ u_2' = -b_2u_2 + a_{21}g_2u_1 + a_{22}g_2u_2 + a_{23}g_2u_3, \\ u_3' = -b_3u_3 + a_{31}g_3u_1 + a_{32}g_3u_2 + a_{33}g_3u_3, \end{cases} \tag{12}$$

where

$$g_1 = \frac{4e^{-2(a_{11}x_1^*+a_{12}x_2^*+a_{13}x_3^*-\theta_1)}}{[1+e^{-2(a_{11}x_1^*+a_{12}x_2^*+a_{13}x_3^*-\theta_1)}]^2}, \tag{13}$$

$$g_2 = \frac{4e^{-2(a_{21}x_1^*+a_{22}x_2^*+a_{23}x_3^*-\theta_2)}}{[1+e^{-2(a_{21}x_1^*+a_{22}x_2^*+a_{23}x_3^*-\theta_2)}]^2}, \tag{14}$$

$$g_3 = \frac{4e^{-2(a_{31}x_1^*+a_{32}x_2^*+a_{33}x_3^*-\theta_3)}}{[1+e^{-2(a_{31}x_1^*+a_{32}x_2^*+a_{33}x_3^*-\theta_3)}]^2}. \tag{15}$$

One has

$$A - \lambda I = \begin{vmatrix} a_{11}g_1 - b_1 - \lambda & a_{12}g_1 & a_{13}g_1 \\ a_{21}g_2 & a_{22}g_2 - b_2 - \lambda & a_{23}g_2 \\ a_{31}g_3 & a_{32}g_3 & a_{33}g_3 - b_3 - \lambda \end{vmatrix} \tag{16}$$

and the characteristic equation for $b_1 = b_2 = b_3 = 1$ is

$$\begin{aligned} &\det|A - \lambda I| = -\Lambda^3 + (a_{11}g_1 + a_{22}g_2 + a_{33}g_3)\Lambda^2 + \\ &+[g_1g_2(a_{12}a_{21} - a_{11}a_{22}) + g_1g_3(a_{13}a_{31} - a_{11}a_{33}) + \\ &+g_2g_3(a_{23}a_{32} - a_{22}a_{33})]\Lambda + \\ &+g_1g_2g_3(a_{11}a_{22}a_{33} + a_{12}a_{23}a_{31} + a_{13}a_{21}a_{32} - \\ &-a_{11}a_{23}a_{32} - a_{12}a_{21}a_{33} - a_{13}a_{22}a_{31}) = 0, \end{aligned} \tag{17}$$

where $\Lambda = \lambda + 1$.

3 Inhibition-activation

Consider the system

$$\begin{cases} x_1' = \tanh(a_{12}x_2 + a_{13}x_3 - \theta_1) - x_1, \\ x_2' = \tanh(a_{21}x_1 + a_{23}x_3 - \theta_2) - x_2, \\ x_3' = \tanh(a_{31}x_1 + a_{32}x_2 - \theta_3) - x_3. \end{cases} \tag{18}$$

where a_{12}, a_{13}, a_{23} are negative, a_{21}, a_{31}, a_{32} are positive.
We consider the specific case

$$W = \begin{pmatrix} 0 & -1 & -1 \\ 1 & 0 & -1 \\ 1 & 1 & 0 \end{pmatrix} \tag{19}$$

$\theta_1 = \theta_2 = \theta_3 = \theta$. The system then has a single critical point. Introduce where

$$g_1 = \frac{4e^{-2(-x_2-x_3-\theta)}}{[1+e^{-2(-x_2-x_3-\theta)}]^2}, \tag{20}$$

$$g_2 = \frac{4e^{-2(x_1-x_3-\theta)}}{[1+e^{-2(x_1-x_3-\theta)}]^2}, \tag{21}$$

$$g_3 = \frac{4e^{-2(x_1+x_2-\theta)}}{[1+e^{-2(x_1+x_2-\theta)}]^2}. \tag{22}$$

Values of g_i are in the range $(0, 1)$. The linearized system now is

$$\begin{cases} u_1' = -u_1 - g_1 u_2 - g_1 u_3, \\ u_2' = -u_2 + g_2 u_1 - g_2 u_3, \\ u_3' = -u_3 + g_3 u_1 + g_3 u_2, \end{cases} \tag{23}$$

The characteristic equation can be obtained from

$$A - \lambda I = \begin{vmatrix} -1-\lambda & -g_1 & -g_1 \\ g_2 & -1-\lambda & -g_2 \\ g_3 & g_3 & -1-\lambda \end{vmatrix} \tag{24}$$

and

$$\begin{aligned} &\det|A - \lambda I| = -\lambda^3 - 3\lambda^2 + (g_1g_2 + g_1g_3 + g_2g_3 - 3)\lambda \\ &+(g_1g_2 + g_1g_3 + g_2g_3 - 1) = 0. \end{aligned} \tag{25}$$

The characteristic numbers are

$$\begin{cases} \lambda_1 = -1, \\ \lambda_2 = -1 - \sqrt{g_1g_2 + g_1g_3 + g_2g_3}\, i, \\ \lambda_3 = -1 + \sqrt{g_1g_2 + g_1g_3 + g_2g_3}\, i. \end{cases} \tag{26}$$

Proposition 3.1. A critical point of the system (18) under the above conditions is 3D-focus, that is, the following is true: there is 2D-subspace with a stable focus and attraction in the remaining dimension.

4 Systems with stable periodic solutions. Andronov - Hopf type bifurcations.

4.1 2D case

We first study the second order system

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh(kx_1 + bx_2 - \theta_1) - b_1x_1, \\[2ex] \dfrac{dx_2}{dt} = \tanh(ax_1 + kx_2 - \theta_2) - v_2x_2, \end{cases} \tag{27}$$

where $b = -a = 2$, and $k > 0$ is the parameter.

Choose k small enough, so that a unique critical point be a stable focus. Then increase k until the stable focus turns to unstable one. Then the limit cycle emerges, surrounding the critical point. This is called Andronov - Hopf bifurcation for 2D systems.

Example 4.1.
Consider the system (27) with the matrix

$$W = \begin{pmatrix} k & 2 \\ -2 & k \end{pmatrix} \tag{28}$$

and $k = 0.7, b_1 = b_2 = 1, \theta_1 = 0.2, \theta_2 = 0.4.$

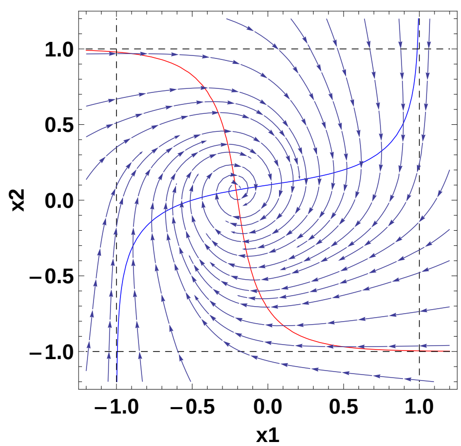


Fig. 4.1.Nullclines and vector feld for system (27) (x_1 - blue, x_2 - red).

There is one critical point the stable focus.
If choose k the stable focus turns to unstable one. Then the limit cycle emerges, surrounding the critical point.

Example 4.2.
Consider the system (27) with the matrix

$$W = \begin{pmatrix} k & 2 \\ -2 & k \end{pmatrix} \tag{29}$$

and $k = 1.2, b_1 = b_2 = 1, \theta_1 = 0.2, \theta_2 = 0.4.$

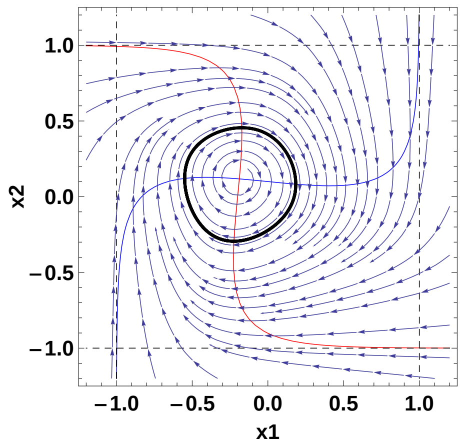


Fig. 4.2.The limit cycle in system (27) (x_1 - blue, x_2 - red).

4.2 3D case

Consider now the 3D system with the matrix

$$W = \begin{pmatrix} k & 0 & b \\ 0 & a_{22} & 0 \\ a & 0 & k \end{pmatrix} \tag{30}$$

where a, b, k are as in 2D system (27). The second nullcline is defined by the relation

$$x_2 = \frac{1}{b_2} \tanh(a_{22}x_2 - \theta_2). \tag{31}$$

Choose the parameters so that the equation (31) has three roots. Then the second nullcline is a union of three parallel planes.

Example 4.3.

Consider picture of nullclines. There are three periodic solutions in system (31) with the matrix

$$W = \begin{pmatrix} 1.5 & 0 & 2 \\ 0 & 2.7 & 0 \\ -2 & 0 & 1.5 \end{pmatrix} \tag{32}$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = 0.2, \theta_2 = 0, \theta_3 = 0.3.$

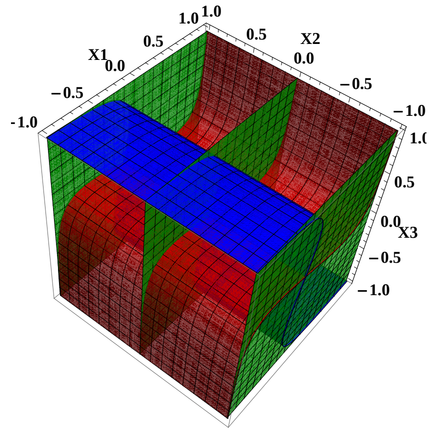


Fig. 4.3.The nullclines of the system (31) with the regulatory matrix (32).

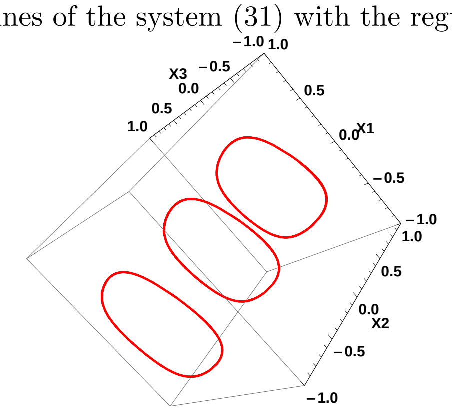


Fig. 4.4.Three periodic solutions of the system (31) with the regulatory matrix (32).

5 Conclusions

The behavior of solutions of systems of the form (3) strongly depends on the structure of weight matrix W. Any system (3) has at least one critical point in the region $D = (\frac{-1}{b_1}, \frac{1}{b_1}) \times (\frac{-1}{b_2}, \frac{1}{b_2}) \times (\frac{-1}{b_3}, \frac{1}{b_3})$. No trajectory of the system (3) can escape this region. Multiple critical points are possible. Stable nodes, stable and unstable 3D-focuses and saddle points can occur. Systems with a triangular matrix W cannot have focuses. Inhibition-activation systems of Section 3 have a critical point that is a focus. The coefficient conditions are possible for a critical point to be a focus. No attracting critical points may exist in D. The trajectories tend then to a pattern of regular form. No chaotic behavior was observed yet.

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".

References

[1] A. Das, A.B. Roy, Pritha Das. Chaos in a three dimensional neural network. Applied Mathematical Modelling 24 (2000) 511-522.

[2] S. Haykin. Neural networks. A comprehensive foundation. Prentice Hall, 2nd edition, reprint from 1999.

[3] J.C. Sprott. Elegant Chaos. World Scienti-c, Singapore, 2010.

[4] K. Funahashi, K. and Y. Nakamura, Y. (1993). Approximation of dynamical systems by continuous time recurrent neural networks, Neural Networks 6, pp. 801-806, 1993.

[5] T. Schlitt. Approaches to Modeling Gene Regulatory Networks: A Gentle Introduction. In: Silico Systems Biology. Methods in Molecular Biology (Methods and Protocols), Humana Press, vol. 1021 (2013),13–35,doi:10.1007/978-1-62703-450-0

[6] Wilson HR, Cowan JD. Excitatory and inhibitory interactions in localized populations of model neurons. Biophys J., vol 12 (1), 1972, pp. 1-24.

[7] Furusawa C, Kaneko K (2008), A generic mechanism for adaptive growth rate regulation. PLoS Comput Biol 4, 1, e3. 0035–0042. https://doi.org/10.1371/journal.pcbi.0040003. [Google Scholar]

[8] Koizumi Y. et al. Adaptive Virtual Network Topology Control Based on Attractor Selection. Journal of Lightwave Technology. 2010; 28 (11): 1720-1731. DOI: 10.1109/JLT.2010.2048412

[9] E. Brokan and F. Zh. Sadyrbaev. On attractors in gene regulatory systems, AIP Conference Proceedings 1809, 020010 (2017): Proc. of the 6th International Advances In Applied Physics And Materials Science Congress & Exhibition (APMAS 2016), 1-3 June 2016, Istanbul, Turkey,; doi: 10.1063/1.4975425

[10] E. Brokan and F. Sadyrbaev, Attraction in n-dimensional differential systems from network regulation theory, em Mathematical Methods in the Applied Sciences 41, 2018, Issue 17, 7498-7509 https://doi.org/10.1002/mma.5086

[11] F. Chapeau-Blondeau and G. Chauvet. Stable, Oscillatory, and Chaotic Regimes in the Dynamics of Small Neural Networks with Delay. Neural Networks, Vol. 5, pp. 735–743, 1992.

[12] F. Sadyrbaev, D. Ogorelova, I. Samuilik. A nullclines approach to the study of 2D artificial network. Contemporary mathematics, 2019.

[13] H. D. Jong. Modeling and Simulation of Genetic Regulatory Systems: A Literature Review, J. Comput Biol. 2002;9(1):67-103, DOI: 10.1089/10665270252833208

[14] Le-Zhi Wang, Ri-Qi Su, Zi-Gang Huang, Xiao Wang, Wen-Xu Wang, Celso Grebogi and Ying-Cheng Lai, A geometrical approach to control and controllability of nonlinear dynamical networks. Nature Communications, Volume 7, Article number: 11323 (2016), DOI: 10.1038/ncomms11323

D. Ogorelova. Gēnu un neironu tīklu matemātiskā modelēšana ar parastiem diferenciālvienādojumiem.

Anotācija. Tiek aplūkota parasto diferenciālvienādojumu sistēma, kas modelē makslīgo tīklu veidu. Sistēma sastāv no sigmoidālas funkcijas, kas ir atkarīga no lineārām argumentu kombinācijām mīnus lineārā daļa. Argumentu lineārās kombinācijas ir aprakstītas ar regulējošo matricu W. Trīsdimensiju gadījumiem tiek aplūkoti vairāki matricu veidi W un analizēta sistēmas risinājumu uzvedī ba.

Д. Огорелова. Математическое моделирование генных и нейронных сетей обыкновенными дифференциальными уравнениями.

Аннотация. Рассмотрена система обыкновенных дифференциальных уравнений, моделирующая разновидность искусственных сетей. Система состоит из сигмоидальной функции, которая зависит от линейных комбинаций аргументов за вычетом линейной части. Линейные комбинации аргументов описываются регулирующей матрицей W. Для трехмерных случаев рассмотрено несколько типов матриц W и проанализировано поведение решений системы.

Daugavpils University
Daugavpils, Vienibas str. 13
diana.ogorelova@du.lv

Received 11.12.2023.

axioms

Article

Remarks on the Mathematical Modeling of Gene and Neuronal Networks by Ordinary Differential Equations

Diana Ogorelova [1,*] and Felix Sadyrbaev [1,2]

[1] Faculty of Natural Sciences and Mathematics, Daugavpils University, Vienibas Street 13, LV-5401 Daugavpils, Latvia; felix@latnet.lv
[2] Institute of Mathematics and Computer Science, University of Latvia, Rainis Boulevard 29, LV-1459 Riga, Latvia
* Correspondence: diana.ogorelova@du.lv

Abstract: In the theory of gene networks, the mathematical apparatus that uses dynamical systems is fruitfully used. The same is true for the theory of neural networks. In both cases, the purpose of the simulation is to study the properties of phase space, as well as the types and the properties of attractors. The paper compares both models, notes their similarities and considers a number of illustrative examples. A local analysis is carried out in the vicinity of critical points and the necessary formulas are derived.

Keywords: neuronal networks; dynamical systems; artificial networks; critical points; attractors

MSC: 34C60; 34D45; 92B20

check for updates

Citation: Ogorelova, D.; Sadyrbaev, F. Remarks on the Mathematical Modeling of Gene and Neuronal Networks by Ordinary Differential Equations. *Axioms* **2024**, *13*, 61. https://doi.org/10.3390/axioms13010061

Academic Editor: Ming-Feng Ge

Received: 6 November 2023
Revised: 7 January 2024
Accepted: 11 January 2024
Published: 19 January 2024

1. Introduction

In this article, we study Neural Networks, called also Artificial Neural Networks (ANN), and their mathematical models, using ordinary differential equations. The motivation for the study of ANNs came from attempts to understand the principles and organization of the human brain. Understanding came that human brains work differently from digital computers. Their effectiveness comes from high complexity, nonlinear modes of regulation, and parallelism of actions. The elements of the human brain were called neurons.

These elements still perform calculations faster than the fastest digital computers. The human brain is able to perceive information about the environment in the form of images and, moreover, it can process the received information needed for interaction with the environment.

At birth, the human brain has a ready structure for learning which, in familiar terms, is understood as experience. So, the neural network is designed to model the way in which the human brain solves usual problems and performs a particular task. A particular interest in ANN stems from the fact that an important group of neural networks is needed to solve a problem computations through the process of learning. So, following [1], an ANN can generally be imagined as a parallel distributed processor, consisting of separate units, which is able to analyze experimental data and prepare them for use.

Many natural processes involve networks of elements that affect each other following a general pattern of conditions and the updating rules for any elements. Both genomic networks and neuronal networks are of this kind. In mathematical models of networks of both types, the regulatory effect of one element to the outputs of other elements is defined by a weight matrix. Therefore, the models describing the evolution of these networks have a lot in common. But, there are also differences. This paper compares models using systems of ordinary differential equations. To distinguish between these systems, we use the designations GRN system and ANN system. At the same time, we realize that the term ANN system has too general a meaning. An ANN system in the established sense is understood as a network that operates according to certain rules and is focused on performing certain tasks. At the same time, the networks undergo training and thus improve their qualities. This article looks at neural networks from a different point of view. We are interested in the behavior of systems of both types for different forms of interaction of elements. The structure of both systems assumes the presence of attractors that determine future states. The description and comparison of possible attractors for the systems of both types is our result.

ANNs are made up of many interconnected elements. Weighted signals from different elements are received by a separate element and processed. A positive signal is understood as an excitatory connection, while negative one means an inhibitory connection. The received signals are linearly summed and modified by a nonlinear sigmoidal function which is called an activation one. The activation function controls the amplitude of an output. "Each neuron has a sigmoid transfer function, and a continuous positive and bounded output activity that evolves according to weighted sums of the activities in the networks. Neural networks with arbitrary connections are often called recurrent networks" [2]. The dynamics of the continuous time recurrent neural network with n units, can be described by the system of ordinary differential equations (ODE) ([3])

$$x_i' = -b_i x_i + f_i(\Sigma a_{ij} x_j) + I_i(t), \tag{1}$$

where x_i is the internal state of the i-th unit, b_i is the time constant for the i-th unit, a_{ij} are connection weights, $I_i(t)$ is the input to the i-th unit, and $f_i(\Sigma a_{ij} x_j)$ is the response function of the i-th unit. Usually, f is taken as a sigmoidal function. There are particular response functions that are non-negative. For instance, functions $f_i(z) = (1 + \exp(\mu_i(z - \theta_i))^{-1}$ were used in [4]. More general cases can be modeled by the system using the function $f_i(z) = \tanh(a_i z - \theta_i)$, which takes values in the open interval $(-1, 1)$. If the recurrent neural networks without input are considered, the system

$$x_i' = f_i(\Sigma(a_{ij} x_j - \theta_i)) - b_i x_i \tag{2}$$

can be considered.

Applications of Artificial Neural Networks are multiple. They can be used in different fields. These fields can be categorized as function approximations, including time series prediction and modeling; pattern and sequence recognition, novelty detection and sequential decision making; and data processing, including filtering and clustering. For applications in Machine Learning (ML), Deep Learning and related problems, consult the review article [5]. For neuroscience applications and their relation to ML, and machine learning using biologically realistic models of neurons to carry out the computation, consider the review [6]. The problems of pattern recognition by ANNs, including applications in manufacturing industries, were studied and analyzed in the review paper [7]. In the paper [8], the ANN approach is applied for the study of a genetic system.

In this article, we mainly study properties of the mathematical model of a three-dimensional ANN, but part of our results will refer to two-dimensional or, more generally, to n-dimensional networks. In particular, we provide information on the types of possible attractors, and their birth and evolution under changes in multiple parameters. The asymptotic properties of the system are important for prediction of future states. This, in turn, can provide instruments for control and management of the modeling network. We use analytical tools for the study of the phase space and its elements. A set of formulas is obtained for the local analysis near equilibria. The necessary data for the analysis were collected by conducting computational experiments and constructing several examples. A broader study involves examining the model and interpreting the findings for the actual process being modeled. Examples of this approach are the works [9,10].

Let us describe the structure of the paper. The Problem formulation section provides the necessary material for the study. The Preliminary results section describes some basic properties of the main systems of ordinary differential equations. It deals also with technical details concerning nullclines, critical points, local analysis by linearization, and some special cases. The next two sections concern some particular but important cases. The systems possessing critical points of the type focus, and systems exhibiting the inhibition-activation behavior, are treated. Both types of systems can have periodic solutions, and that means that cyclic processes can occur in the modeled network. The system of the special triangular structure is analyzed in Section 6. It is convenient for analysis and the main conclusions can be transferred to systems of arbitrary dimensions. The process of birth of stable periodic trajectories from stable critical points of the type focus is considered in Section 7. The mechanism of the Andronov–Hopf bifurcation is illustrated for two-dimensional and three-dimensional neuronal systems. As a by-product, an example of a 3D system that has three limit cycles is constructed. Some suggestions on the management of neuronal systems are provided in Section 7. The possibility of effectively changing the properties of the system, and therefore to partially controlling the network in question, is emphasized. The last section summarizes the results obtained so far, and outlines further studies in this direction.

2. Problem Formulation

The mathematical model using ordinary differential equations, is

$$\begin{cases} \dfrac{dx_1}{dt} = 2\dfrac{1}{1+e^{-2(a_{11}x_1+a_{12}x_2+a_{13}x_3-\theta_1)}} - 1 - b_1x_1, \\[2ex] \dfrac{dx_2}{dt} = 2\dfrac{1}{1+e^{-2(a_{21}x_1+a_{22}x_2+aw_{23}x_3-\theta_2)}} - 1 - b_2x_2, \\[2ex] \dfrac{dx_3}{dt} = 2\dfrac{1}{1+e^{-2(a_{31}x_1+a_{32}x_2+a_{33}x_3-\theta_3)}} - 1 - b_3x_3. \end{cases} \tag{3}$$

The same system can be written as ([11])

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3 - \theta_1) - b_1x_1, \\[2ex] \dfrac{dx_2}{dt} = \tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3 - \theta_2) - b_2x_2, \\[2ex] \dfrac{dx_3}{dt} = \tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3) - b_3x_3, \end{cases} \tag{4}$$

since

$$2\frac{1}{1+e^{-2z}} - 1 = \frac{1-e^{-2z}}{1+e^{-2z}} = -\frac{e^{-2z}-1}{e^{-2z}+1} = -\tanh(-z) = \tanh(z).$$

The elements of this 3D network are called neurons. The connections between them are synapses (or nerves). There is an algorithm that describes how the impulses are propagated through the network. In the above model, this algorithm is encoded by the matrix

$$W = \begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix}. \tag{5}$$

Each neuron accepts signals from others and produces a single output. The extent to which the input of neuron i is driven by the output of neuron j is characterized by its output and synaptic weight a_{ij}. The dynamic evolution leads to attractors of the system (4), and it was experimentally observed in neural systems. In theoretical modeling, the emphasis is put on the attractors of a system. We wish to study them for System (4).

Similar systems arise in the theory of genetic regulatory networks. The difference is that the nonlinearity is represented by a positive valued sigmoidal functions. One of such systems is

$$\begin{cases} \dfrac{dx_1}{dt} = \dfrac{1}{1+e^{-\mu_1(a_{11}x_1+a_{12}x_2+a_{13}x_3-\theta_1)}} - b_1x_1, \\ \dfrac{dx_2}{dt} = \dfrac{1}{1+e^{-\mu_2(a_{21}x_1+a_{22}x_2+a_{23}x_3-\theta_2)}} - b_2x_2, \\ \dfrac{dx_3}{dt} = \dfrac{1}{1+e^{-\mu_3(a_{31}x_1+a_{32}x_2+a_{33}x_3-\theta_3)}} - b_3x_3. \end{cases} \quad (6)$$

Notice that System (3), and therefore also System (4), can be obtained from System (6), where $\mu_i = 2$, $i = 1,2,3$, by two arithmetic operations, namely multiplication of the nonlinearity in (6) by 2 and subtracting 1. This changes the range of values in (3) to $(-1,1)$.

Systems of the form (6) were studied before by many authors. The interested reader may consult the works ([12–20]). Similar systems appear in the theory of telecommunication networks ([21]).

In this article, we study the different dynamic regimes for System (4) which can be observed under various conditions. In particular, we first speak about critical points in System (4) and evaluate the number of them. Then, we focus on periodic regimes, study their attractiveness for other trajectories. This can be performed, under some restrictions, for systems of relatively high dimensionality. Also, the evidences of chaotic behavior are presented.

3. Preliminary Results

This section contains the description of basic properties of systems under consideration, and provides information about nullclines, critical points, and their role in the study.

3.1. Invariant Set

Consider the 3D system (4).

Proposition 1. *System (4) has an invariant set* $Q_3 = \{-1/b_1 < x_1 < 1/b_1, -1/b_2 < x_2 < 1/b_2, -1/b_3 < x_3 < 1/b_3\}$.

Proof. By inspection of the vector field generated by System (4) on the opposite faces of the three-dimensional cube Q_3. Notice, that the value range for the function tanh z is $(-1,1)$. □

3.2. Nullclines

The nullclines for the system are defined by the relations

$$\begin{cases} x_1 = \dfrac{1}{b_1}\tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3 - \theta_1), \\ x_2 = \dfrac{1}{b_2}\tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3 - \theta_2), \\ x_3 = \dfrac{1}{b_3}\tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3). \end{cases} \quad (7)$$

Example 1. *Consider the system with the matrix*

$$W = \begin{pmatrix} 1.2 & 1.5 & 0 \\ -1.5 & 1.2 & 0 \\ 0 & 0 & 1.2 \end{pmatrix} \quad (8)$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = \theta_2 = 0.5, \theta_3 = 1$.

The three nullclines for system (4) with matrix (8) are depicted in Figure 1.

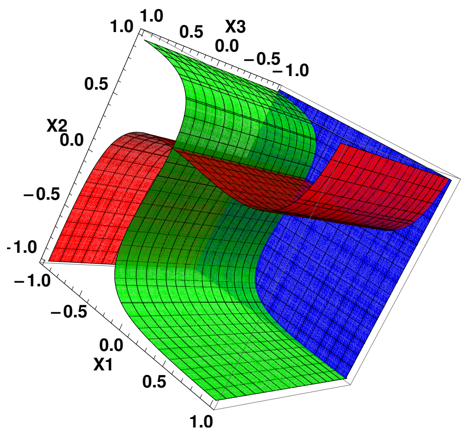


Figure 1. The nullclines for System (4) with Matrix (8) (x_1—red, x_2—green, x_3—blue).

3.3. Critical Points

The critical points, which are also called the equilibria, can be obtained from System (4). Geometrically, they are the cross points of the nullclines. The nullclines are defined by the relations

$$\begin{cases} x_1 - \dfrac{1}{b_1}\tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3 - \theta_1) = 0, \\ x_2 - \dfrac{1}{b_2}\tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3 - \theta_2) = 0, \\ x_3 - \dfrac{1}{b_3}\tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3) = 0. \end{cases} \tag{9}$$

Proposition 2. *All critical points are in the invariant set.*

The nullclines are located in the sets $\{-1/b_1 < x_1 < 1/b_1, -1/b_2 < x_2 < 1/b_2, -1/b_3 < x_3 < 1/b_3\}$, respectively, and these sets intersect by the invariant set Q_3 only.

Proposition 3. *At least one critical point exists.*

The invariant set Q_3 may be considered as a topological ball. Since the vector field on the border is directed inward, Q_3 is mapped into itself continuously. The continuous contraction mapping Q_3 to Q_3 has a fixed point. Any fixed point is a solution of the system (7).

Remark 1. *The number of critical points may be greater, up to 27, but finite.*

Remark 2. *Both assertions 2 and 3 are valid for the n-dimensional case also.*

Example 2. *Consider System (4) with the matrix*

$$W = \begin{pmatrix} 1.2 & 2 & 0 \\ -2 & 1.2 & 0 \\ 0 & 0 & 1.2 \end{pmatrix} \tag{10}$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = 0.7, \theta_2 = 0.3, \theta_3 = 0.25$. *There is one critical point* $(-0.122; 0.362; 0.640)$.

The three nullclines for system (4) with matrix (10) are depicted in Figure 2.

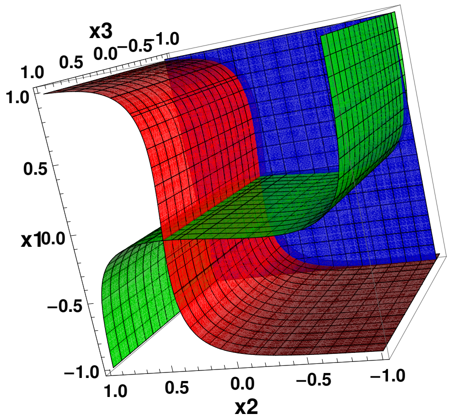


Figure 2. The nullclines for system (4) (x_1—red, x_2—green, x_3—blue) with Matrix (10).

Example 3. *Consider example of multiple critical points and the system (4) with the matrix*

$$W = \begin{pmatrix} 1.2 & 2 & 0 \\ -2 & 1.2 & 0 \\ 0 & 0 & 1.2 \end{pmatrix} \tag{11}$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = 0.7, \theta_2 = 0.3, \theta_3 = 0.01.$

The three nullclines for system (4) with matrix (11) are depicted in Figure 3.

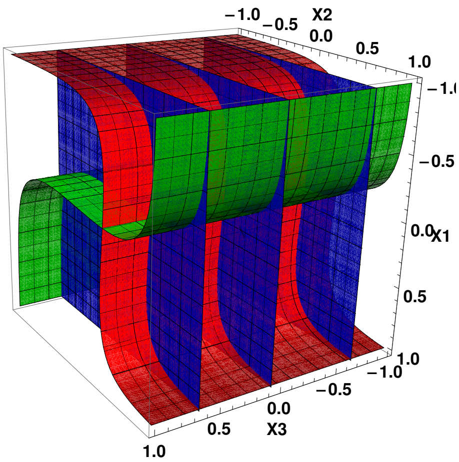


Figure 3. The nullclines for System (4) (x_1—red, x_2—green, x_3—blue) with Matrix (11).

There are three critical points $(-0.122;\, 0.362;\, 0.640)$, $(-0.122;\, 0.362;\, 0.050)$ and $(-0.122;\, 0.362;\, -0.675)$.

3.4. Linearization at a Critical Point

Let (x_1^*, x_2^*, x_3^*) be a critical point. The linearization around it is given by the system

$$\begin{cases} u_1' = -b_1u_1 + a_{11}g_1u_1 + a_{12}g_1u_2 + a_{13}g_1u_3, \\ u_2' = -b_2u_2 + a_{21}g_2u_1 + a_{22}g_2u_2 + a_{23}g_2u_3, \\ u_3' = -b_3u_3 + a_{31}g_3u_1 + a_{32}g_3u_2 + a_{33}g_3u_3, \end{cases} \tag{12}$$

where

$$g_1 = \frac{4e^{-2(a_{11}x_1^* + a_{12}x_2^* + a_{13}x_3^* - \theta_1)}}{[1 + e^{-2(a_{11}x_1^* + a_{12}x_2^* + a_{13}x_3^* - \theta_1)}]^2}, \tag{13}$$

$$g_2 = \frac{4e^{-2(a_{21}x_1^* + a_{22}x_2^* + a_{23}x_3^* - \theta_2)}}{[1 + e^{-2(a_{21}x_1^* + a_{22}x_2^* + a_{23}x_3^* - \theta_2)}]^2}, \tag{14}$$

$$g_3 = \frac{4e^{-2(a_{31}x_1^* + a_{32}x_2^* + a_{33}x_3^* - \theta_3)}}{[1 + e^{-2(a_{31}x_1^* + a_{32}x_2^* + a_{33}x_3^* - \theta_3)}]^2}. \tag{15}$$

One has

$$A - \lambda I = \begin{vmatrix} a_{11}g_1 - b_1 - \lambda & a_{12}g_1 & a_{13}g_1 \\ a_{21}g_2 & a_{22}g_2 - b_2 - \lambda & a_{23}g_2 \\ a_{31}g_3 & a_{32}g_3 & a_{33}g_3 - b_3 - \lambda \end{vmatrix} \tag{16}$$

and the characteristic equation for $b_1 = b_2 = b_3 = 1$ is

$$\begin{array}{l} \det|A - \lambda I| = -\Lambda^3 + (a_{11}g_1 + a_{22}g_2 + a_{33}g_3)\Lambda^2 \\ +[g_1g_2(a_{12}a_{21} - a_{11}a_{22}) + g_1g_3(a_{13}a_{31} - a_{11}a_{33}) \\ +g_2g_3(a_{23}a_{32} - a_{22}a_{33})]\Lambda \\ +g_1g_2g_3(a_{11}a_{22}a_{33} + a_{12}a_{23}a_{31} + a_{13}a_{21}a_{32} \\ -a_{11}a_{23}a_{32} - a_{12}a_{21}a_{33} - a_{13}a_{22}a_{31}) = 0, \end{array} \tag{17}$$

where $\Lambda = \lambda + 1$.

3.5. Regulatory Matrices With Zero Diagonal Elements

Set $a_{11} = a_{22} = a_{33} = 0$. The regulatory matrix is

$$W = \begin{pmatrix} 0 & a_{12} & a_{13} \\ a_{21} & 0 & a_{23} \\ a_{31} & a_{32} & 0 \end{pmatrix} \tag{18}$$

and the system of differential equations takes the form

$$\begin{cases} x_1' = \tanh(a_{12}x_2 + a_{13}x_3 - \theta_1) - x_1, \\ x_2' = \tanh(a_{21}x_1 + a_{23}x_3 - \theta_2) - x_2, \\ x_3' = \tanh(a_{31}x_1 + a_{32}x_2 - \theta_3) - x_3. \end{cases} \tag{19}$$

Let (x_1^*, x_2^*, x_3^*) be a critical point. The respective linearized system around it is

$$\begin{cases} u_1' = -u_1 + a_{12}g_1u_2 + a_{13}g_1u_3, \\ u_2' = -u_2 + a_{21}g_2u_1 + a_{23}g_2u_3, \\ u_3' = -u_3 + a_{31}g_3u_1 + a_{32}g_3u_2, \end{cases} \tag{20}$$

where g_1, g_2, g_3, given in (13) to (15), are computed assuming that the regulatory matrix is (18). The characteristic equation for $\Lambda = \lambda + 1$ takes the form

$$-\Lambda^3 + B\Lambda + C = 0, \tag{21}$$

where

$$B = g_1g_2(a_{12}a_{21}) + g_1g_3(a_{13}a_{31}) + g_2g_3(a_{23}a_{32}), \tag{22}$$

$$C = g_1g_2g_3(a_{12}a_{23}a_{31} + a_{13}a_{21}a_{32}). \tag{23}$$

Equation (21) has the form

$$y^3 + py + q = 0. \tag{24}$$

Recall the Cardano formulas for Equation (24). This equation has complex roots if

$$Q := \left(\frac{p}{3}\right)^3 + \left(\frac{q}{2}\right)^2 \tag{25}$$

is positive. The complex roots can be obtained as

$$y_{2,3} = -\frac{a+b}{2} \pm i(a-b)\frac{\sqrt{3}}{2}, \tag{26}$$

where

$$a = (-\frac{q}{2} + \sqrt{Q})^{\frac{1}{3}}, \quad b = (-\frac{q}{2} - \sqrt{Q})^{\frac{1}{3}}$$

are real cubic roots satisfying $a \cdot b = -\frac{p}{3}$. The real root of Equation (24) is $y_1 = a + b$.

Example 4. *Consider System (19) with the matrix*

$$W = \begin{pmatrix} 0 & 1.2 & 2 \\ -2 & 0 & 1.2 \\ 0.1 & 0.1 & 0 \end{pmatrix} \tag{27}$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = 0.3, \theta_2 = 0.3, \theta_3 = 0.01.$

The three nullclines for system (19) with matrix (53) are depicted in Figure 4.

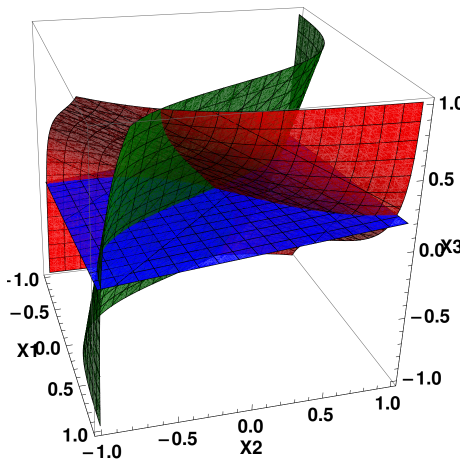


Figure 4. The nullclines for System (19) (x_1—red, x_2—green, x_3—blue) with Matrix (53).

There is a single critical point $(-0.496; 0.311; -0.308)$. The characteristic numbers obtained by the linearization process are $\lambda_1 = -1.125, \lambda_{2,3} = -0.937 \pm 1.178i$.

4. Focus Type Critical Points

Consider again Equation (21). In our notation,

$$Q := -\left(\frac{B}{3}\right)^3 + \left(\frac{C}{2}\right)^2. \tag{28}$$

Suppose that $Q > 0$. Let (x_1^*, x_2^*, x_3^*) be a critical point in question. The associated characteristic numbers λ are

$$\begin{aligned} \lambda_1 &= -1 + (a+b), \\ \lambda_{2,3} &= -1 - \frac{a+b}{2} \pm i(a-b)\frac{\sqrt{3}}{2}, \end{aligned} \tag{29}$$

where

$$a = \left(\frac{C}{2} + \sqrt{Q}\right)^{\frac{1}{3}}, \quad b = \left(\frac{C}{2} - \sqrt{Q}\right)^{\frac{1}{3}} \tag{30}$$

are the real values of cubic roots, and Q is given by (28). We will call such a critical point 3D-focus. It is unstable if the real part $-1 - \frac{a+b}{2}$ is positive. We arrive at the following assertion.

Proposition 4. *Let (x_1^*, x_2^*, x_3^*) be a critical point of the system (19). Suppose that*

$$\left(\frac{C}{2}\right)^2 > \left(\frac{B}{3}\right)^3. \tag{31}$$

Then, $Q > 0$ and this critical point is a 3D-focus.

Proof. Follows from (28) to (30). □

Corollary 1. *Suppose the condition $B < 0$ holds for a critical point. Then, this point is a 3D-focus.*

Proof. The relation (31) is fulfilled if $B < 0$. □

Proposition 5. *Suppose (x_1^*, x_2^*, x_3^*) is a critical point of type focus of the system (19). This point is an unstable focus if the condition $-1 - \frac{a+b}{2} > 0$ holds.*

Proof. Follows from (29), since then the real part of $\lambda_{2,3}$ in (29) is positive. □

Example 5. *Consider System (19) with the matrix*

$$W = \begin{pmatrix} 0 & 1.5 & 3 \\ -3 & 0 & 1.5 \\ 3 & 0.1 & 0 \end{pmatrix} \tag{32}$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = 0.6, \theta_2 = 0.3, \theta_3 = 0.1$.

The three nullclines for system (19) with matrix (32) are depicted in Figure 5.

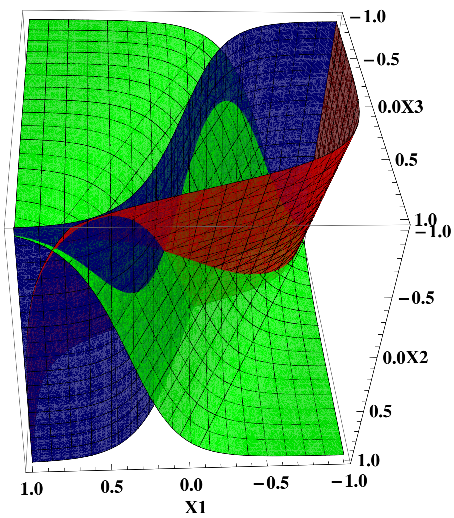


Figure 5. The nullclines for System (19) (x_1—red, x_2—green, x_3—blue).

The system has three critical points: p_1, p_2 and p_3 at $(0.790; -0.836; 0.975)$, $(0.176; -0.248; 0.384)$ and $(-0.982; 0.819; -0.995)$. The characteristic numbers λ are given in Table 1.

Table 1. The characteristic numbers λ.

-	λ_1	λ_2	λ_3
p_1	−0.9268	−1.0366 − 0.6101 i	−1.0366 + 0.6101 i
p_2	1.1972	−2.0986 − 0.8406 i	−2.0986 + 0.8406 i
p_3	−0.9821	−1.0090 − 0.2189 i	−1.0090 + 0.2189 i

5. Inhibition-Activation

Consider the system

$$\begin{cases} x_1' = \tanh(a_{12}x_2 + a_{13}x_3 - \theta_1) - x_1, \\ x_2' = \tanh(a_{21}x_1 + a_{23}x_3 - \theta_2) - x_2, \\ x_3' = \tanh(a_{31}x_1 + a_{32}x_2 - \theta_3) - x_3, \end{cases} \tag{33}$$

where a_{12}, a_{13}, a_{23} are negative, a_{21}, a_{31}, a_{32} are positive.

Let the regulatory matrix be

$$W = \begin{pmatrix} 0 & -1 & -1 \\ 1 & 0 & -1 \\ 1 & 1 & 0 \end{pmatrix}, \tag{34}$$

and $\theta_1 = \theta_2 = \theta_3 = \theta$. There is a single critical point. Introduce

$$g_1 = \frac{4e^{-2(-x_2-x_3-\theta)}}{[1+e^{-2(-x_2-x_3-\theta)}]^2}, \tag{35}$$

$$g_2 = \frac{4e^{-2(x_1-x_3-\theta)}}{[1+e^{-2(x_1-x_3-\theta)}]^2}, \tag{36}$$

$$g_3 = \frac{4e^{-2(x_1+x_2-\theta)}}{[1+e^{-2(x_1+x_2-\theta)}]^2}. \tag{37}$$

The range of values of g_i is the interval $(0, 1)$. The linearized system is

$$\begin{cases} u_1' = -u_1 - g_1u_2 - g_1u_3, \\ u_2' = -u_2 + g_2u_1 - g_2u_3, \\ u_3' = -u_3 + g_3u_1 + g_3u_2. \end{cases} \tag{38}$$

One can obtain the matrix

$$A - \lambda I = \begin{vmatrix} -1-\lambda & -g_1 & -g_1 \\ g_2 & -1-\lambda & -g_2 \\ g_3 & g_3 & -1-\lambda \end{vmatrix} \tag{39}$$

and the characteristic equation

$$\begin{aligned} \det|A - \lambda I| = -\lambda^3 - 3\lambda^2 + (g_1g_2 + g_1g_3 + g_2g_3 - 3)\lambda \\ +(g_1g_2 + g_1g_3 + g_2g_3 - 1) = 0. \end{aligned} \tag{40}$$

The roots of the characteristic equation are

$$\begin{cases} \lambda_1 = -1, \\ \lambda_2 = -1 - \sqrt{g_1g_2 + g_1g_3 + g_2g_3}\, i, \\ \lambda_3 = -1 + \sqrt{g_1g_2 + g_1g_3 + g_2g_3}\, i. \end{cases} \tag{41}$$

Summing up, we arrive at the following assertion.

Proposition 6. *A critical point of System (33) under the above conditions is 3D-focus; that is, the following is true: there is 2D-subspace with a stable focus and attraction in the remaining dimension.*

6. The Case of Triangular Regulatory Matrix

We consider the special case of the regulatory matrix being in triangular form,

$$W = \begin{pmatrix} a_{11} & a_{12} & \ldots & a_{1n} \\ 0 & a_{22} & \ldots & a_{2n} \\ \ldots & & & \\ 0 & 0 & \ldots & a_{nn} \end{pmatrix}. \tag{42}$$

Since the presentation for the general case differs little from the three-dimensional case, let us consider the n-dimensional variant. The system of differential equations takes the form

$$\begin{cases} x_1' = \tanh(a_{11}x_1 + a_{12}x_2 + \ldots + a_{1n}x_n - \theta_1) - x_1, \\ x_2' = \tanh(\qquad a_{22}x_2 + \ldots + a_{2n}x_n - \theta_2) - x_2, \\ \ldots \\ x_n' = \tanh(\qquad\qquad a_{nn}x_n - \theta_n) - x_n, \end{cases} \tag{43}$$

where $n > 1$. Suppose that the coefficients a_{ij} take values in the interval $(0;1]$.

6.1. Critical Points

The critical points of System (43) can be determined from

$$\begin{cases} x_1 = \tanh(a_{11}x_1 + a_{12}x_2 + \ldots + a_{1n}x_n - \theta_1), \\ x_2 = \tanh(\qquad a_{22}x_2 + \ldots + a_{2n}x_n - \theta_2), \\ \ldots \\ x_n = \tanh(\qquad\qquad a_{nn}x_n - \theta_n). \end{cases} \tag{44}$$

Since the right sides in (44) are less than unity in modulus, all critical points locate in $(-1;1) \times (-1;1) \times \ldots \times (-1;1)$. Due to sigmoidal character of the function $\tanh z$, the last equation in (44) may have one , two or three roots.

Proposition 7. *There are, at most, three values for x_n in System (44).*

Proposition 8. *At most, 3^n critical points are possible in System (43).*

Proof. The last equation in (44) may have, at most, three roots, due to the S-shape of the graph to a sigmoidal function on the right side. Consequently, the penultimate equation in (44) may have, at most, 3×3 roots x_{n-1}. In total, there are nine roots. Proceeding in this way, we obtain, at most, 3^n roots for the very first equation in (44), and therefore, at most 3^n critical points for System (43). Hence, the proof. □

6.2. Linearized System

The linearized system is

$$\begin{cases} u_1' = -u_1 + a_{11}g_1u_1 + a_{12}g_1u_2 + \ldots + a_{1n}g_1u_n, \\ u_2' = -u_2 + a_{22}g_2u_2 + \ldots + a_{2n}g_2u_n, \\ \ldots \\ u_n' = -u_n + a_{nn}g_nu_n, \end{cases} \tag{45}$$

where

$$g_1 = \frac{4e^{-2(a_{11}x_1 + a_{12}x_2 + \ldots + a_{1n}x_n - \theta_1)}}{[1 + e^{-2(a_{11}x_1 + a_{12}x_2 + \ldots + a_{1n}x_n - \theta_1)}]^2}, \tag{46}$$

$$g_2 = \frac{4e^{-2(a_{22}x_2+\ldots+a_{2n}x_n-\theta_2)}}{[1+e^{-2(a_{22}x_2+\ldots+a_{2n}x_n-\theta_2)}]^2}, \tag{47}$$

$$\ldots$$

$$g_n = \frac{4e^{-2(a_{nn}x_n-\theta_n)}}{[1+e^{-2(a_{nn}x_n-\theta_n)}]^2}. \tag{48}$$

The values of g_i are positive and not greater than unity. The characteristic values for a critical point are to be obtained from

$$A - \lambda I = \begin{vmatrix} a_{11}g_1 - 1 - \lambda & a_{12}g_1 & \ldots & a_{1n}g_1 \\ 0 & a_{22}g_2 - 1 - \lambda & \ldots & a_{2n}g_2 \\ \ldots & \ldots & \ldots & \ldots \\ 0 & 0 & \ldots & a_{nn}g_n - 1 - \lambda \end{vmatrix} \tag{49}$$

and

$$\begin{aligned} &\det|A - \lambda I| = (a_{11}g_1 - 1 - \lambda)(a_{22}g_2 - 1 - \lambda)\ldots \\ &\ldots(a_{nn}g_n - 1 - \lambda) = 0. \end{aligned} \tag{50}$$

Evidently,

$$\begin{cases} \lambda_1 = -1 + a_{11}g_1, \\ \lambda_2 = -1 + a_{22}g_2, \\ \ldots \\ \lambda_n = -1 + a_{nn}g_n. \end{cases} \tag{51}$$

Therefore, the characteristic values for any critical point are real, and the following assertion follows.

Proposition 9. *The triangular system (43) cannot have critical points of type focus.*

7. Systems with Stable Periodic Solutions: Andronov–Hopf Type Bifurcations

7.1. 2D Case

We first study the second-order system

$$\begin{cases} \dfrac{dx_1}{dt} = \tanh(kx_1 + bx_2 - \theta_1) - b_1x_1, \\[2ex] \dfrac{dx_2}{dt} = \tanh(ax_1 + kx_2 - \theta_2) - v_2x_2, \end{cases} \tag{52}$$

where $b = -a = 2$, and $k > 0$ is the parameter. Choose a k small enough that a unique critical point is a stable focus. Then, increase k until the stable focus turns to unstable one. Then, the limit cycle emerges, surrounding the critical point. This is called Andronov–Hopf bifurcation for 2D systems.

Example 6. *Consider System (52) with the matrix*

$$W = \begin{pmatrix} k & 2 \\ -2 & k \end{pmatrix} \tag{53}$$

and $k = 0.5$, $b_1 = b_2 = 1$, $\theta_1 = 0.1$, $\theta_2 = 0.3$.

The two nullclines and vector field for system (52) with matrix (53) are depicted in Figure 6.

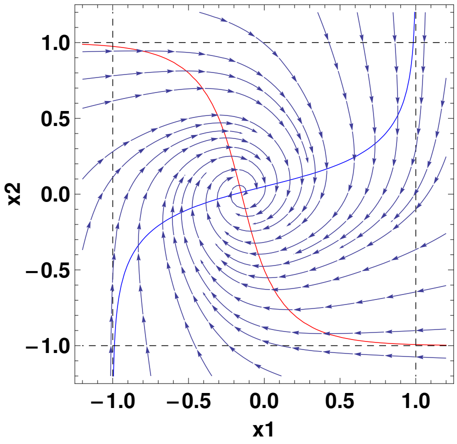


Figure 6. The nullclines and vector field for System (52) (x_1—blue, x_2—red) with Matrix (53).

There is one critical point: the stable focus. If the parameter k increases, the stable focus turns to an unstable one. Then, the limit cycle emerges, surrounding the critical point.

Example 7. *Consider System (52) with the matrix*

$$W = \begin{pmatrix} k & 2 \\ -2 & k \end{pmatrix} \tag{54}$$

and $k = 1.1, b_1 = b_2 = 1, \theta_1 = 0.1, \theta_2 = 0.3.$

The two nullclines, vector field and limit cycle for system (52) with matrix (54) are depicted in Figure 7.

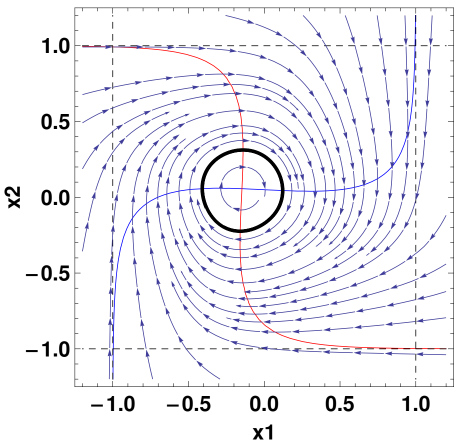


Figure 7. The limit cycle in System (52) (x_1—blue, x_2—red) with Matrix (54).

7.2. 3D Case

Consider now the 3D system with the matrix

$$W = \begin{pmatrix} k & 0 & b \\ 0 & a_{22} & 0 \\ a & 0 & k \end{pmatrix}, \tag{55}$$

where a, b, k are as in 2D system (52). The second nullcline is defined by the relation

$$x_2 = \frac{1}{b_2}\tanh(a_{22}x_2 - \theta_2). \tag{56}$$

Choose the parameters so that Equation (56) has three roots. Then, the second nullcline is a union of three parallel planes.

Example 8. *Consider picture of nullclines in Figure 8. There are three periodic solutions in System (56) with the matrix (57) are depicted in Figure 9.*

$$W = \begin{pmatrix} 1.5 & 0 & 2 \\ 0 & 2.5 & 0 \\ -2 & 0 & 1.5 \end{pmatrix} \tag{57}$$

and $b_1 = b_2 = b_3 = 1, \theta_1 = 0.1, \theta_2 = 0, \theta_3 = 0.2.$

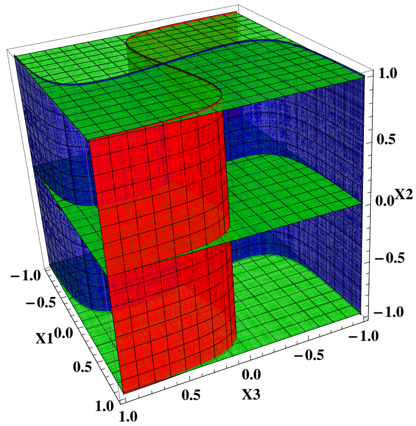


Figure 8. The nullclines of System (56) with the regulatory matrix (57).

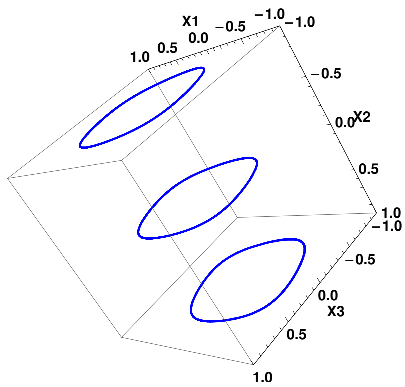


Figure 9. The three periodic solutions of System (56) with the regulatory matrix (57).

8. Control and Management of ANN

First, a citation from [22]: "Models of ANN are specified by three basic entities: models of the neurons themselves–that is, the node characteristics; models of synaptic interconnections and structures–that is, net topology and weights; and training or learning rules—that is, the method of adjusting the weights or the way the network interprets the information it receives".

In this section, we discuss the problem of changing the behavior of the trajectories of System (4). This may be interpreted as partial control over the system. The system has as parameters the coefficients a_{ij}, the values θ_i and b_i in the linear part. Properties of the system may be changed by varying any of mentioned.

We would like demonstrate how a system of the form (4) can be modified so that trajectories start to tend to some of indicated attractor. For this, consider the system (4), which has as attractors three limit cycles. This can be performed via three operations: (1) put the entries of the 2D regulatory matrix, which corresponds to 2D system with the limit cycle L, to the four corners of a 3D matrix A; (2) choose the middle element of the 3D matrix A so, that the equation $x_2 = \tanh(a_{22}x_2 - \theta_2)$ with respect to x_2 has exactly three roots

$r_1 < r_2 < r_3$; (3) set the four remaining values of a_{ij} to zero. Set also b_i to unity. After finishing these preparations, the second nullcline will be three parallel planes P_i, going through $x_2 = r_i$, $i = 1, 2, 3$. Each of these planes will contain the limit cycle. Two side limit cycles will attract trajectories from their neighborhoods. The middle limit cycle will attract only trajectories, lying in the plane P_2.

Now, let us solve the problem of control. Let the limit cycle at P_3 be conditionally "bad". The problem is to change the system so that all trajectories in Q_3 are attracted to the limit cycle which, at the beginning of the process, was in the plane P_1. Problems of this kind may arise often. In the paper [20], a similar problem was treated mathematically for genetic networks.

Solution: Change θ_2 so that the equation $x_2 = \tanh(a_{22}x_2 - \theta_2)$ has now the unique root near P_1. The second nullcline is now the plane, passing near r_1. This operation is possible, since the graph of $\tanh(a_{22}x_2 - \theta_2)$ is sigmoidal, and changing θ_2 means shifting the original plane P_1 in both directions. After that, only one attractor (limit cycle) remains. The problem is solved.

In neuronal systems, the θ parameters express the threshold of a response function f ([4]). In genetic networks, θ_i stands for the influence of external input on gene i, which modulates the gene's sensitivity of response ([23]). The technique of changing the θ parameters and thus shifting the nullclines was applied in the work [24] for building the partial control over model of genetic network.

9. Conclusions

Modeling of genetic and neural networks, using dynamical systems, is effective in both cases. The advantage of this approach, compared with other models, is the possibility of following the evolution of modeled networks. Both systems have invariant sets trapping the trajectories. As a consequence, the attracting sets exist. The structure and properties of attractors are important for the prediction of future states of networks. Both systems must have critical points. These points may be attractive (stable) or repelling. The limit cycles are possible in both cases. The attractors, exhibiting sensitivity to the initial data, are possible for three-dimensional GRN and ANN systems. Systems with specific structures can have predictable properties. For instance, the triangular systems cannot have critical points of the focus type. In contrast, the inhibition-activation systems typically have critical points of this type, and can suffer bifurcations of Andronov–Hopf type. Partial control and management are possible for GRN and ANN systems. In particular, some realistically large-sized GRN systems allow for control and management by changing the adjustable parameters. This problem is relevant to modern medicine.

Author Contributions: Writing—review & editing, D.O. and F.S. The authors contributed equally to the creation of this article. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: No data created in this article.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Haykin, S. Neural networks. In *A Comprehensive Foundation*, 2nd ed.; Prentice Hall: Hoboken, NJ, USA, 1999.
2. Chapeau-Blondeau, F.; Chauvet, G. Stable, Oscillatory, and Chaotic Regimes in the Dynamics of Small Neural Networks with Delay. *Neural Netw.* **1992**, *5*, 735–743.
3. Funahashi, K.; Nakamura, Y. Approximation of dynamical systems by continuous time recurrent neural networks. *Neural Netw.* **1993**, *6*, 801–806.
4. Das, A.; Roy, A.B.; Das, P. Chaos in a three dimensional neural network. *Appl. Math. Model.* **2000**, *24*, 511–522. [CrossRef]
5. Alzubaidi, L.; Zhang, J.; Humaidi, A.J.; et al. Review of deep learning: Concepts, CNN architectures, challenges, applications, future directions. *J. Big Data* **2021**, *8*, 53. [CrossRef] [PubMed]

6. Yamazaki, K.; Vo-Ho, V.K.; Darshan, B.; Le, N. Spiking Neural Networks and Their Applications: A Review. *Brain Sci.* **2022**, *12*, 63. [CrossRef]
7. Abiodun, O.I.; Jantan, A.; Omolara, A.E.; Dada, K.V.; Umar, A.M.; Linus, O.U.; Arshad, H.; Kazaure, A.A.; Gana, U.; Kiru, M.U. Comprehensive Review of Artificial Neural Network Applications to Pattern Recognition. *IEEE Access* **2019**, *7*, 158820–158846. [CrossRef]
8. Vohradský, J. Neural network model of gene expression. *Faseb J.* **2001**, *15*, 846–854. [CrossRef]
9. Kraynyukova, N.; Tchumatchenko, T. Stabilized supralinear network can give rise to bistable, oscillatory, and persistent activity. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, 3464–3469.
10. Ahmadian, Y.; Miller, K.D. What is the dynamical regime of cerebral cortex? *Neuron* **2021**, *109*, 3373–3391. [CrossRef]
11. Sprott, J.C. *Elegant Chaos*; World Scientific: Singapore, 2010.
12. Wilson, H.R.; Cowan, J.D. Excitatory and inhibitory interactions in localized populations of model neurons. *Biophys. J.* **1972**, *12*, 1–24.
13. Furusawa, C.; Kaneko, K. A generic mechanism for adaptive growth rate regulation. *PLoS Comput. Biol.* **2008**, *4*, e3. [CrossRef]
14. Alakwaa, F.M. Modeling of Gene Regulatory Networks: A Literature Review. *J. Comput. Syst. Biol.* **2014**, *1*, 1. [CrossRef]
15. Brokan, E.; Sadyrbaev, F. On a differential system arising in the network control theory. *Nonlinear Anal. Model. Control.* **2016**, *21*, 687–701. [CrossRef]
16. Schlitt, T. Approaches to Modeling Gene Regulatory Networks: A Gentle Introduction. In *Silico Systems Biology*; Methods in Molecular Biology (Methods and Protocols); Humana: Totowa, NJ, USA, 2013; Volume 1021, pp. 13–35. [CrossRef]
17. Jong, H.D. Modeling and Simulation of Genetic Regulatory Systems: A Literature Review. *J. Comput Biol.* **2002**, 9, 67–103. [CrossRef]
18. Ogorelova, D.; Sadyrbaev, F.; Sengileyev, V. Control in Inhibitory Genetic Regulatory Network Models. *Contemp. Math.* **2020**, *1*, 421–428. [CrossRef]
19. Sadyrbaev, F.; Ogorelova, D.; Samuilik, I. A nullclines approach to the study of 2D artificial network. *Contemp. Math.* **2019**, *1*, 1–11. [CrossRef]
20. Wang, L.Z.; Su, R.Q.; Huang, Z.G.; Wang, X.; Wang, W.X.; Grebogi, C.; Lai, Y.C. A geometrical approach to control and controllability of nonlinear dynamical networks. *Nat. Commun.* **2016**, *7*, 11323. [CrossRef]
21. Koizumi, Y.; Miyamura, T.; Arakawa, S.I.; Oki, E.; Shiomoto, K.; Murata, M. Adaptive Virtual Network Topology Control Based on Attractor Selection. *J. Light. Technol.* **2010**, *28*, 1720–1731. [CrossRef]
22. Vemuri, V. Artificial Neural Networks in Control Applications. *Adv. Comput.* **1993**, *36*, 203–254.
23. Kozlovska, O.; Samuilik, I. Quasi-periodic solutions for a three-dimensional system in gene regulatory network. *WSEAS Trans. Syst.* **2023**, *22*, 727–733. [CrossRef]
24. Ogorelova, D.; Sadyrbaev, F.; Samuilik, I. On Targeted Control over Trajectories on Dynamical Systems Arising in Models of Complex Networks. *Mathematics* **2023**, *11*, 2206. [CrossRef]

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

Diana Ogorelova[a] and Felix Sadyrbaev[b]

[a] *Daugavpils University*
Parades iela 1, LV-5401 Daugavpils, Latvia
[b] *Institute of Mathematics and Computer Science, University of Latvia*
Rainis boul. 29, LV-1459 Riga, Latvia
E-mail(*corresp.*): diana.ogorelova@du.lv
E-mail: felix@latnet.lv

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.

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. $\square$

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.

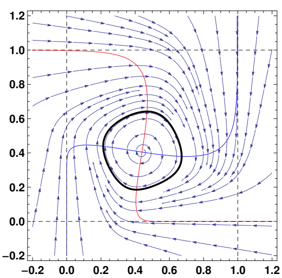


Figure 1. The closed trajectory of the system (3.1) with the regulatory matrix (3.3), $b_1 = b_2 = 1$, $\mu = 4$, $\theta_1 = 1.2, \theta_2 = -0.5$.

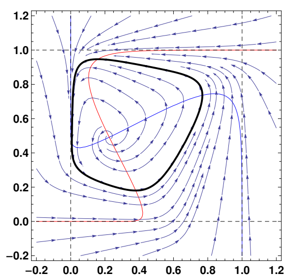


Figure 2. The attractors in system (3.1), with matrix (3.4), $b_1 = b_2 = 1$, $\mu = 4$, $\theta_1 = -0.5, \theta_2 = 1.2$.

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

$$\begin{cases} \dfrac{dx_1}{dt} = e^{-e^{-\mu(w_{11}x_1+w_{12}x_2+w_{13}x_3+w_{14}x_4-\theta_1)}} - b_1 x_1, \\ \dfrac{dx_2}{dt} = e^{-e^{-\mu(w_{21}x_1+w_{22}x_2+w_{23}x_3+w_{24}x_4-\theta_2)}} - b_2 x_2, \\ \dfrac{dx_3}{dt} = e^{-e^{-\mu(w_{31}x_1+w_{32}x_2+w_{33}x_3+w_{34}x_4-\theta_3)}} - b_3 x_3, \\ \dfrac{dx_4}{dt} = e^{-e^{-\mu(w_{41}x_1+w_{42}x_2+w_{43}x_3+w_{44}x_4-\theta_4)}} - b_4 x_4 \end{cases} \tag{4.1}$$

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.

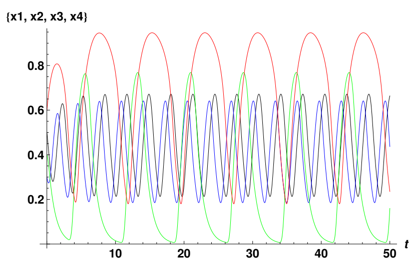


Figure 3. Solution (x_1, x_2, x_3, x_4) of system (4.1).

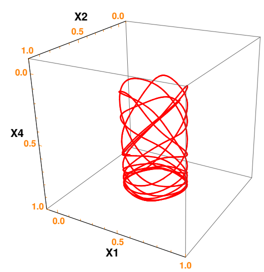


Figure 4. The projection of the attractor on 3D (x_1, x_2, x_4)-subspace of the system (4.1).

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.

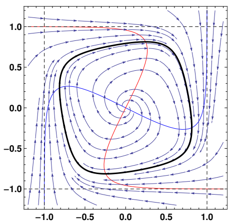


Figure 5. The attractors in system (5.1), with matrix (5.2), $b_1 = b_2 = 1$.

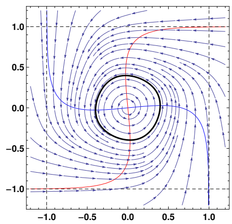


Figure 6. The attractors in system (5.1), with matrix (5.3), $b_1 = b_2 = 1$.

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.

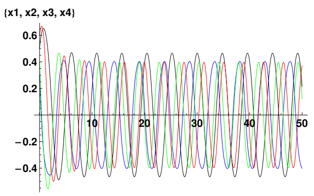


Figure 7. Solution (x_1, x_2, x_3, x_4) of system (6.1).

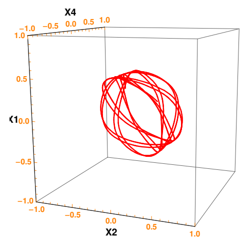


Figure 8. The projection of the attractor on 3D subspace on (x_1, x_2, x_4) of system (6.1).

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.

References

[1] S. Atslega, D. Finaskins and F. Sadyrbaev. On a planar dynamical system arising in the network control theory. *Mathematical Modelling and Analysis*, **21**(3):385–398, 2016. https://doi.org/10.3846/13926292.2016.1172131.

[2] E. Brokan and F. Sadyrbaev. On attractors in gene regulatory systems. *AIP Conference Proceedings*, **1809**:2–10, 2017. https://doi.org/10.1063/1.4975425.

[3] E. Brokan and F. Sadyrbaev. Attraction in n-dimensional differential systems from network regulation theory. *Mathematical Methods in the Applied Sciences*, **41**(17):7498–7509, 2018. https://doi.org/10.1002/mma.5086.

[4] A. Das, A.B. Roy and P. Das. Chaos in a three dimensional neural network. *Applied Mathematical Modelling*, **24**(7):511–522, 2000. https://doi.org/10.1016/S0307-904X(99)00046-3.

[5] R. Edwards and L. Ironi. Periodic solutions of gene networks with steep sigmoidal regulatory functions. *Physica D: Nonlinear Phenomena*, **282**:1–15, 2014. https://doi.org/10.1016/j.physd.2014.04.013.

[6] K. Funahashi and Y. Nakamura. Approximation of dynamical systems by continuous time recurrent neural networks. *Neural Networks*, **6**(6):801–806, 1993. https://doi.org/10.1016/S0893-6080(05)80125-X.

[7] C. Furusawa and K. Kaneko. A generic mechanism for adaptive growth rate regulation. *PLoS Computational Biology*, **1**(4):35–42, 2008. https://doi.org/10.1371/journal.pcbi.0040003.

[8] S. Haykin. *Neural networks. A comprehensive foundation.* Prentice Hall, Singapore, 1998.

[9] Y. Koizumi and et al. Adaptive virtual network topology control based on attractor selection. *Journal of Lightwave Technology*, **28**(11):1720–1731, 2010. https://ieeexplore.ieee.org/document/5452985

[10] Y. Koizumi, T. Miyamura, S. Arakawa, E. Oki, K. Shiomoto and M. Murata. Application of attractor selection to adaptive virtual network topology control. *Proceedings of BIONETICS*, pp. 1–8, 2008. https://doi.org/10.5555/1512504.1512516.

[11] O. Kozlovska and F. Sadyrbaev. Models of genetic networks with given properties. *WSEAS Transactions on Computer Research*, **10**:43–49, 2022. https://doi.org/10.37394/232018.2022.10.6.

[12] V.W. Noonburg. *Differential Equations: From Calculus to Dynamical Systems, 2nd edition.* Providence, Rhode Island: MAA Press, 2019.

[13] D. Ogorelova, F. Sadyrbaev and V. Sengileyev. Control in inhibitory genetic regulatory network models. *Contemporary Mathematics*, **1**(5):421–428, 2020. https://doi.org/10.37256/cm.152020538.

[14] F. Sadyrbaev, D. Ogorelova and I. Samuilik. A nullclines approach to the study of 2d artificial network. *Contemporary Mathematics*, **1**(1):1–11, 2019. https://doi.org/10.37256/cm.11201976.1-11.

[15] F. Sadyrbaev, I. Samuilik and V. Sengileyev. On modelling of genetic regulatory networks. *WSEAS Transactions in Electronics*, **12**:73–80, 2021. https://doi.org/10.37394/232017.2021.12.10.

[16] I. Samuilik, F. Sadyrbaev and D. Ogorelova. Comparative analysis of models of gene and neural networks. *Contemporary Mathematics*, **4**(2):217–22, 2023. https://doi.org/10.37256/cm.4220232404.

[17] J.C. Sprott. *Elegant Chaos.* World Scientific, Singapore, 2010.

[18] L.-Z. Wang, R.-Q. Su, Z.-G. Huang, X. Wang, W.-X. Wang, C. Grebogi and Y.-C. Lai. A geometrical approach to control and controllability of non-linear dynamical networks. *Nature Communications*, **7**(11323):1–11, 2016. https://doi.org/10.1038/ncomms11323.

[19] H.R. Wilson and J.D. Cowan. Excitatory and inhibitory interactions in localized populations of model neurons. *Biophys J.*, **12**(1):1–24, 1972. https://doi.org/10.1016/S0006-3495(72)86068-5.

[20] W. Ye, X. Huang, X. Huang, P. Li, Q. Xia and G. Hu. Self-sustained oscillations of complex genomic regulatory networks. *Physics Letters A*, **374**:2521–2526, 2010. https://doi.org/10.1016/j.physleta.2010.04.015.

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.

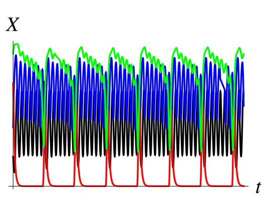


Figure 9. Solutions for system(4.1) with perturbed regulatory matrix (7.1) and $\theta_1 = \theta_4 = 1.2, \theta_2 = \theta_3 = -0.5, \mu = 4$.

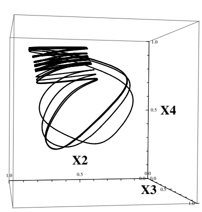


Figure 10. The projection of the attractor on 3D subspace on (x_2, x_3, x_4) of system (4.1) with perturbed regulatory matrix (7.1).

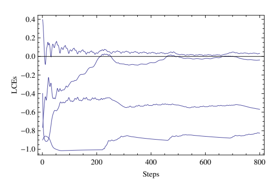


Figure 11. The dynamics of Lyapunov exponents for system(4.1) with perturbed regulatory matrix (7.1) and $\theta_1 = \theta_4 = 1.2, \theta_2 = \theta_3 = -0.5$, $\mu = 4$.

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.

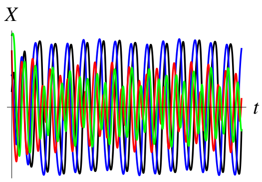


Figure 12. Solutions for system (6.1) with perturbed regulatory matrix (7.2).

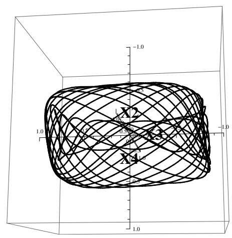


Figure 13. The projection of the attractor on 3D subspace on (x_2, x_3, x_4) of system (6.1) with perturbed regulatory matrix (7.2).

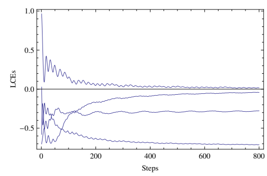


Figure 14. The dynamics of Lyapunov exponents for system (6.1) with perturbed regulatory matrix (7.2).

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.

On control over system arising in the theory of neuronal networks

Diana Ogorelova[1,b)] and Felix Sadyrbaev[2,a),c)]

[1] *Daugavpils University, Parades street 1, LV-5401, Daugavpils, Latvia.*
[2] *Institute of Mathematics and Computer Science, University of Latvia, Rainis boul. 29, LV-1429, Riga, Latvia.*

[a)] Corresponding author: felix@latnet.lv
[b)] diana.ogorelova@du.lv
[c)] URL: https://www.researchgate.net/profile/Felix-Sadyrbaev

Abstract. A multiparameter system of ordinary differential equations, arising in the theory of neuronal networks, is considered. The structure of this system presupposes the presence of attractors. The problem of control and management of this system by changing parameters is considered. The conditions are given for the transition of the trajectory from the basin of attraction of one attractor to another attractor. Examples and illustrations are provided.

INTRODUCTION

Artificial neural networks (ANN) have appeared as attempts to model the functioning of the human brain. The study of ANN became a very popular field of application of mathematical methods and has resulted in the creation of multiple efficient tools to deal with real-world practices. In some models [7], [5] the neurons are considered as simple input-output elements which can accept a cumulative signal from many other elements and produce their own response (which is transferred further). When looking for dynamics of this process, one can find in the literature two approaches using systems of ordinary differential equations. The first one is represented by systems of the form

$$\begin{cases} x_1' = \dfrac{1}{1+e^{-\mu_1 (w_{11}x_1+w_{12}x_2+\ldots+w_{1n}x_n-\theta_1)}} - v_1x_1, \\ x_2' = \dfrac{1}{1+e^{-\mu_2 (w_{21}x_1+w_{22}x_2+\ldots+w_{2n}x_n-\theta_2)}} - v_2x_2, \\ \ldots \\ x_n' = \dfrac{1}{1+e^{-\mu_n (w_{n1}x_1+w_{n2}x_2+\ldots+w_{nn}x_{nn}-\theta_n)}} - v_3x_n, \end{cases} \tag{1}$$

which appears in different contexts and for different dimensions in [20], [19], [3], [8], [9], [6], [4]. The three dimensional version, aiming to model simple neuronal network, was studied in [5]. Elements x_i in (1) are interpreted ([5]) as neurons, and the elements w_{ij} are the weights of “the synaptic connection from neuron i to neuron j”. The sigmoidal response function $f(z) = \frac{1}{1+e^{-\mu(z-\theta)}}$ makes the system nonlinear. The parameters θ_i and μ_i are respectively the threshold and the slope of a response function. We emphasize presence of the threshold parameter θ_i in each equation. The value of the response function is always positive since the range of the sigmoidal function is an open interval $(0, 1)$. The constant positive coefficients v_i are the degradation rates (without the nonlinearities solutions of system (1) exponentially tend to zero). Some authors allow v_i be dependent on the variables x_i.

On the other hand, another system

$$\begin{cases} x_1' = \tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3) - b_1x_1, \\ x_2' = \tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3) - b_2x_2, \\ x_3' = \tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3) - b_3x_3 \end{cases} \tag{2}$$

can be used to model neuronal network ([10], [18, Ch. 6.10]). The system (2) is a three-dimensional version. The advantage is that the response can be also negative now, since the range of values of the hyperbolic tangent function is $(-1, 1)$. The present model has as an output a set of trajectories which can tend to different attractors. In the next section some properties of system (3) are listed. An example is provided of a system which have three nontrivial attractors (closed trajectories). The ability to manage system (3) by changing parameters θ is demonstrated. The structure of the phase space changes, and a selected trajectory falls into the basin of attraction of the desired attractor. For the practical use of similar approaches, see [2], [1], [9], [12],[15], [13].

Control by changing nullclines

Consider the system (2). Let us modify it by introducing the threshold parameter.

$$\begin{cases} x_1' = \tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3 - \theta_1) - b_1x_1, \\ x_2' = \tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3 - \theta_2) - b_2x_2, \\ x_3' = \tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3) - b_3x_3. \end{cases} \tag{3}$$

Let for simplicity $b_i = 1$ for $i = 1, 2, 3$. For our purposes this is not restriction of generality.

We will need the nullclines, which are defined by the system

$$\begin{cases} x_1 = \tanh(a_{11}x_1 + a_{12}x_2 + a_{13}x_3 - \theta_1), \\ x_2 = \tanh(a_{21}x_1 + a_{22}x_2 + a_{23}x_3 - \theta_2), \\ x_3 = \tanh(a_{31}x_1 + a_{32}x_2 + a_{33}x_3 - \theta_3). \end{cases} \tag{4}$$

The critical points (which are called also the equilibria), are solutions of the system (4).

This system has the following properties:
1) It has an invariant set $Q_3 = \{-1 < x_i < 1,\ i = 1, 2, 3\}$;
2) It has at least one critical point;
3) It can have multiple critical points, but their number is limited;
4) It can have stable critical points, which are the simplest attractors;
5) It can have an attractor in the form of a stable periodic solution (limit cycle);
6)It can have an attractor in the form of a stable periodic solution (limit cycle);

These properties were confirmed by appropriate proofs and the construction of examples in the works [1] to [4], [11] to [17].

Assertion. We claim that the system (3) can be controlled by changing the parameters θ_i.

Geometric justification for this is the following. The three-dimensional system has three nullclines. The critical points are points of intersections of nullclines. The mutual location of nullclines define the existence of other attractors also, including stable closed trajectories, serving as attractors.

Example

Consider system (2) with coefficients a_{ij} as in the matrix below

$$A = \begin{pmatrix} 2.2 & -1.3 & 0 \\ 3 & 2.2 & 0 \\ 0 & 0 & 2.2 \end{pmatrix}, \tag{5}$$

and $b_i = 1$ for $i = 1, 2, 3$. The system takes the form

$$\begin{cases} x_1' = \tanh(2.2x_1 - 1.3x_2 - \theta_1) - x_1, \\ x_2' = \tanh(3x_1 + 2.2x_2 - \theta_2) - x_2, \\ x_3' = \tanh(2.2x_3 - \theta_3) - x_3, \end{cases} \tag{6}$$

where $\theta_i = 0$ for $i = 1, 2, 3$. The nullclines are given by

$$\begin{cases} x_1 = \tanh(2.2x_1 - 1.3x_2 - \theta_1), \\ x_2 = \tanh(3x_1 + 2.2x_2 - \theta_2), \\ x_3 = \tanh(2.2x_3 - \theta_3), \end{cases} \tag{7}$$

where $\theta_i = 0$ for $i = 1, 2, 3$. The two-dimensional system

$$\begin{cases} x_1 = \tanh(2.2x_1 - 1.3x_2), \\ x_2 = \tanh(3x_1 + 2.2x_2) \end{cases} \tag{8}$$

has the limit cycle which serves as an attractor. The third equation (with respect to x_3) in (7)

$$x_3 = \tanh(2.2x_3) \tag{9}$$

has exactly three roots, say $z_1 < z_2 < z_3$. The third nullcline is a union of three planes $x_3 = z_i$, $i = 1, 2, 3$, and in any plane the limit cycle (8) appears as a two-dimensional closed trajectory. Denote them C_1, C_2, C_3. The trajectories C_1 and C_3, corresponding to respectively z_1 and z_3, attract trajectories from their neighborhoods, but C_2 attracts the trajectories that locate only on the plane $x_3 = z_2$. The trajectories C_1 and C_3 (red and blue ones) are depicted in Figure 2(left) together with a couple of trajectories (red and blue) tending to them.

Suppose that the problem of control is to send all the trajectories starting in the unit cube Q_3, to C_3 (blue attractor). This is possible for system (7) if the parameters θ_i are chosen appropriately.

Solution. Do not change the coefficient matrix A and b_i, but set $\theta_1 = -0.01$, $\theta_2 = -0.01$, $\theta_3 = -0.9$. This affects all nullclines. The third nullcline is defined by the equation

$$x_3 = \tanh(2.2x_3) + 0.9. \tag{10}$$

Both equations (9) and (10) are visualized in Figure 1. Under the new choice of θ_3 the equation (10) has only one root. Consequently, only one attractor remains in Q_3 in the form of a closed trajectory. It is shown in Figure 2 on the right.

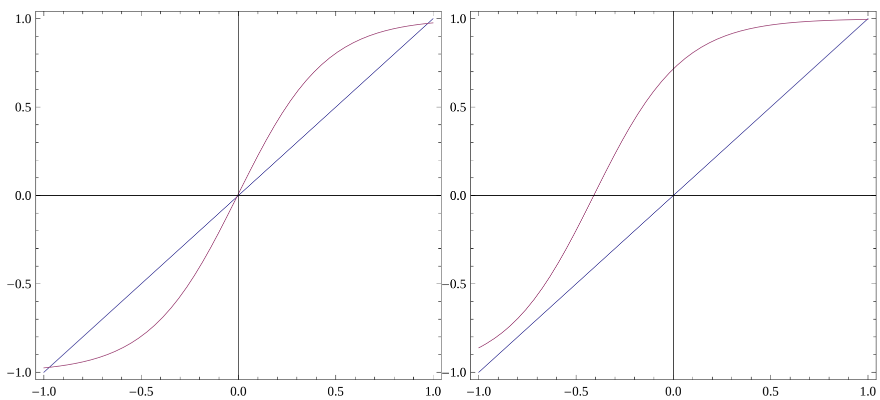


FIGURE 1. Visualization of equations (9) (left) and (10) (right).

Conclusion

There are at least two forms of dynamical mathematical models for neuronal networks. The first one uses the positive valued response function, depending also on the threshold parameter θ. The second one uses the response function with broader value range including negative values. Combining both forms makes it possible to obtain a (partially) controlled system. In this note, we have demonstrated a geometrically transparent control that allows us to reorient the trajectories to the chosen attractor.

REFERENCES

[1] E. Brokan, F. Zh. Sadyrbaev, On Attractors in Gene Regulatory Systems, in. *Proceedings of the APMAS 2016*, AIP Conf Proc, 1809, edited by A.Y. Oral et al., (020010), 2017. doi: 10.1063/1.4975425.

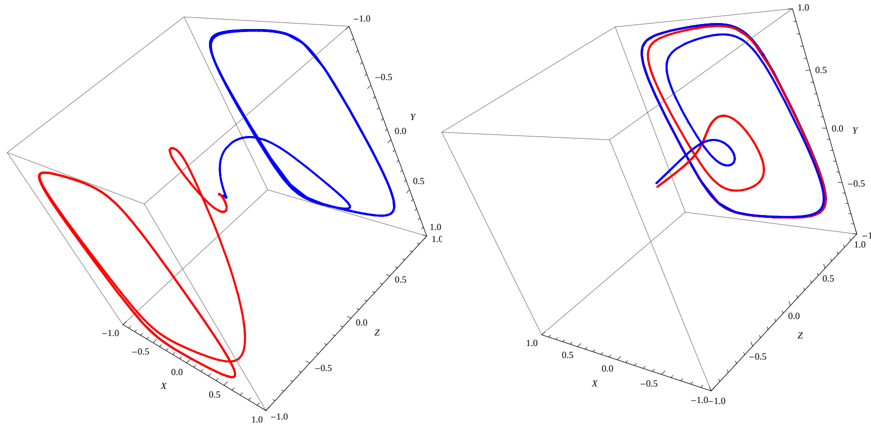


FIGURE 2. Attractors in system (6) with $\theta_i = 0$ for $i = 1, 2, 3$ (left) and new $\theta_1 = \theta_2 = -0.01$, $\theta_3 = -0.9$ (right).

[2] E. Brokan, F. Zh. Sadyrbaev. On controllability of nonlinear dynamical network. AIP Conf Proc, 2116 (1), 040005 (2019) doi.org/10.1063/1.5114026

[3] E. Brokan and F. Sadyrbaev. Attraction in n-dimensional differential systems from network regulation theory. Math. Methods Appl. Sci., 2018, Volume 41, Issue 17, 7498-7509 https://doi.org/10.1002/mma.5086

[4] E. Brokan, F. Sadyrbaev. On a differential system arising in the network control theory. Nonlinear Anal-Model, 2016 — Journal article DOI: 10.15388/NA.2016.5.8

[5] A. Das, A.B. Roy and Pritha Das. Chaos in a three dimensional neural network. Appl. Math. Model, 24(2000), 511-522.

[6] C. Furusawa and K. Kaneko, A generic mechanism for adaptive growth rate regulation. PLoSComput. Biol, 4:e3, 2008.

[7] J.J. Hopfield. Neural network and physical system with emergent collactive computational abilities. Proc. Nat. Acad. Sci., USA 79(1982), 2554-2558.

[8] Y. Koizumi et al. Adaptive Virtual Network Topology Control Based on Attractor Selection. JLT (ISSN :0733-8724), Vol.28 (06/2010), Issue 11, pp. 1720 - 1731 DOI:10.1109/JLT.2010.2048412

[9] Le-Zhi Wang, Ri-Qi Su, Zi-Gang Huang, Xiao Wang, Wen-Xu Wang, Celso Grebogi and Ying-Cheng Lai. A geometrical approach to control and controllability of nonlinear dynamical networks. Nat. Commun., Volume 7, Article number: 11323 (2016), DOI: 10.1038/ncomms11323

[10] S. Haykin. Neural Networks–A Comprehensive Foundation (2nd edn), Prentice Hall, Upper Saddle River, NJ.

[11] O. Kozlovska, F. Sadyrbaev. Models of genetic networks with given properties. WSEAS Trans. Comput, Vol. 10, 2022, 43-49.

[12] Marin Marin, M.I.A. Othman, S. Vlase, L. Codarcea-Munteanu. Thermoelasticity of Initially Stressed Bodies with Voids: A Domain of Influence. Symmetry, 2019, 11(4), 573.

[13] D. Ogorelova, F. Sadyrbaev, V. Sengileyev. Control in inhibitory genetic regulatory networks. Contemp. Math. Vol.1(2020), Iss.5, 393-400.

[14] D. Ogorelova, F. Sadyrbaev, I. Samuilik. On targeted control over trajectories of dynamical systems arising in models of complex networks. Mathematics 2023, 11(9), 2206.

[15] D. Ogorelova, F. Sadyrbaev, I. Samuilik. On attractors in dynamical systems modeling genetic networks. ATNAA, 7(2023), Issue 2, 486–498.

[16] I. Samuilik, F. Sadyrbaev. On trajectories of a system modeling evolution of genetic networks. Math Biosci Eng, 2023, 20(2), 2232–2242.

[17] I. Samuilik, F. Sadyrbaev. On a dynamical model of genetic networks. WSEAS Trans. Bus. Econ, 2023, 20, pp. 104112.

[18] J.C. Sprott. Elegant Chaos: Algebraically Simple Chaotic Flow. World Scientific, Singapore, 2010.

[19] J. Vohradský. Neural network model of gene expression. FASEB J., 15(3/2001), 846-854.

[20] H.R. Wilson, J.D. Cowan. Excitatory and inhibitory interactions in localized populations of model neurons. Biophys J., vol 12 (1), 1972, pp. 1-24.