Example of Chaotic Behavior in Systems of Ordinary Differential Equations Arising in Modeling of Gene Regulatory Networks

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Abstract

The three-dimensional system of ordinary differential equations arising in mathematical models of genetic networks is considered. The systems under consideration first appeared in the study of neural networks. They were later applied by several authors to the treatment of genetic regulatory networks and telecommunication networks. In this article, we will focus on genetic networks. The proposed equation models the evolution of the genetic regulatory network. The system has attractors in the phase space that strongly influence the behavior of the trajectories and other important properties of the network. Attractors are built in systems with dimensions greater than three. These attractors are not solutions themselves, but they attract periodic solutions of the system. A system of equations can exhibit chaotic behavior that is not easy to detect. An information is provided about possible attracting sets in the phase space. The role of attracting sets is discussed. An example of the system possessing the attractor of chaotic nature is constructed.

Keywords [1]

Dynamical systems, gene regulatory networks, attractors, sensitive dependence on the initial data, chaotic behavior

1. Introduction

In this note, we consider systems of ordinary differential equations of the form

$$\begin{cases} x'_1 = \dfrac{1}{1 + e^{-\mu_1(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 - \theta_1)}} - v_1 x_1, \\ x'_2 = \dfrac{1}{1 + e^{-\mu_2(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 - \theta_2)}} - v_2 x_2, \\ x'_3 = \dfrac{1}{1 + e^{-\mu_3(w_{31}x_1 + w_{32}x_2 + w_{31}x_3 - \theta_3)}} - v_3 x_3. \end{cases} \tag{1}$$

This system appears in multiple contexts. Generally it can be interpreted as the model of three interacting elements [1]. These elements can be of different nature. Their status at the time moment t is described by the state vector $X(t)= (x_1(t),x_2(t),x_3(t))$. Future states of a network strongly depend on the attracting sets in the phase space (x_1,x_2,x_3). The attracting sets must exist, as we will see later. The system (1) is quasi-linear.

The nonlinearity is represented by the sigmoidal function $f(z) = \frac{1}{1+e^{-\mu z}}$, which is continuous, bounded, and monotonically increasing from zero to unity. In the absence of the nonlinear terms, the system (1) is linear and solutions exponentially degrade to zero, since the coefficients v_i are supposed to be positive. The slopes μ_i of the exponential functions are positive, θ_i are adjustable parameters interpreted as thresholds. The interrelations between elements of a network is described by the constant matrix

Dynamical System Modeling and Stability Investigation (DSMSI-2023), December 19-21, 2023, Kyiv, Ukraine
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$$W = \begin{pmatrix} w_{11} & w_{12} & w_{13} \\ w_{21} & w_{22} & w_{23} \\ w_{31} & w_{32} & w_{33} \end{pmatrix}. \tag{2}$$

The entries can be of arbitrary sign. Zero entry w_{ij} corresponds to no-relation between the elements x_i and x_j, the positivity (resp.: the negativity) of w_{ij} is associated with activation (resp.: inhibition) of the element x_j by the element x_i. The self-activation and self-inhibition are allowed. Under these conditions the dynamics of solutions of the system (1) can be rich. Our purpose here is briefly review possible behavior of solutions. Before to go, we mention that the system (1) was used in models of neuronal populations [2-4], in the theory of telecommunication networks [5]. The practical applications in bio-medicine were indicated in [6-8].

2. Properties of system (1)

In the study of system (1) very efficient is the geometrical approach, based on the analyzing of the nullclines. The nullclines are subsets of the phase space, where the trajectories change their direction. The nullclines are defined by the system of equations

$$\begin{cases} v_1 x_1 = \frac{1}{1 + e^{-\mu_1(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 - \theta_1)}}, \\ v_2 x_2 = \frac{1}{1 + e^{-\mu_2(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 - \theta_2)}}, \\ v_3 x_3 = \frac{1}{1 + e^{-\mu_3(w_{31}x_1 + w_{32}x_2 + w_{31}x_3 - \theta_3)}}. \end{cases} \tag{3}$$

The common points of the nullclines are the critical points (equilibria). The local analysis of the system (1) around the critical points is standard and can be made by linearization of system (1) at critical points and defining their types.

The system (1) has the following properties:

1. There exists an invariant set $Q_3 = \{0 < x_i < 1/v_i, \quad i = 1, 2, 3\}$;
2. All critical points are in Q_3;
3. There exists at least one critical point;
4. The system (1) can have multiple critical points, but their number is limited;
5. The system (1) can have stable critical points, which are the simplest attractors;
6. The system (1) can have stable critical points, which are the simplest attractors;
7. The system (1) can have an attractor in the form of a stable periodic solution (limit cycle).

The property 1 can be proved by direct inspection of the vector field, defined by system (1), on the boundary of Q_3. It should be noted that the linear parts in (3) dominate over the nonlinear parts in the right hand sides of system (3). Then attractors in that system must exist [16]. –The property 2 is clear, since the nullclines can intersect only in Q_3. The property 3 can be proved by application of the Bohl-Brower fixed point theorem to the system (1) and the set Q_3. The property 4 follows from the analysis of the system (3) and the properties of the sigmoidal function $f(z) = \frac{1}{1+e^{-\mu z}}$. The properties 5 to 7 can be proved by constructing the examples. All the above mentioned can be found in the references [9-11], [17-19] and references therein.

There are multiple examples for the three-dimensional systems of ordinary differential equations to have chaotic attractors. A plenty of examples can be found in the book [20]. The great majority of these examples are for systems with polynomial nonlinearities. In contrast, the examples of chaotic attractors for systems of the form (1) are few. We can refer only two results in [13] and [21].

3. Cases

It is an easy matter to obtain the two-dimensional system of the form

$$\begin{cases} x'_1 = \frac{1}{1 + e^{-\mu_1(w_{11}x_1 + w_{12}x_2 - \theta_1)}} - v_1 x_1, \\ x'_2 = \frac{1}{1 + e^{-\mu_2(w_{21}x_1 + w_{22}x_2 - \theta_2)}} - v_2 x_2, \end{cases}$$

which has one, two or more stable critical points. The number of critical points cannot exceed the number nine, for the two-dimensional systems.

The rotating vector field can be constructed by choosing the regulatory matrices of the structure

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

Where k>0, a b < 0. By changing k, the limit cycles can be obtained as in [9-11, 17-19]. The two-dimensional limit cycles can be raised to the three dimensional case by a simple trick. Let the three dimensional matrix W be of the form

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

where r and is such that the equation

$$0 = \frac{1}{1 + e^{-\mu_3(rx_3 - \theta_3)}} - v_3 x_3$$

has three roots. Then the third nullcline for the three-dimensional system consists of three parallel planes, in each of them there exists the two-dimensional limit cycle, which was built earlier.

Using similar constructions, the periodic attracting sets can be obtained in systems of the form (2) with higher dimensionalities.

4. Example

Consider system (1) with the following set (*) of parameters:

μ_1=4.29, μ_2 =4.7; μ_3=3.5; v_1=0.135, v_2=0.1, v_3=0.25; θ_1=0.64; θ_2=0.5; θ_3=0.4;

w_{11}= 0; w_{12}=–0.01; w_{13}=1.26;

w_{21}=–0.98; w_{22}=0.021; w_{23}=5.25;

w_{31}= 0; w_{32}=–1; w_{33}=2.

Let the trajectory start at $x_1(0)$=0; $x_2(0)$=0; $x_3(0)$=0.2.

The phase portrait is depicted below.

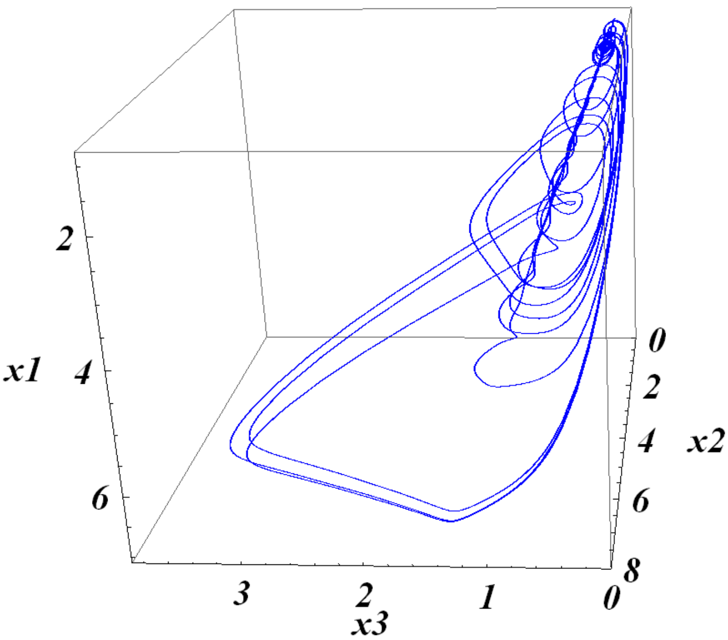

Figure 1: Chaotic behavior in system (1) with the parameters (*).

The time series (x_1(t), x_2(t), x_3(t)) are depicted in Figure 2.

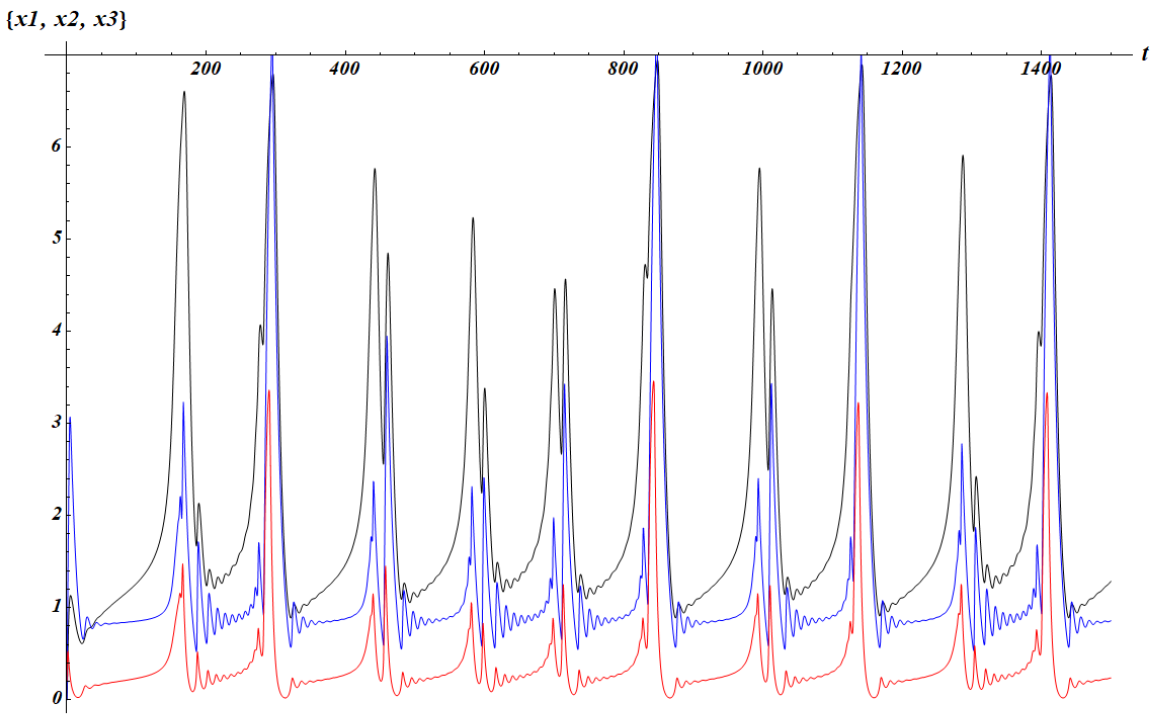

Figure 2: Solutions of the system (1) with the parameters (*).

The plot of Lyapunov curves indicates the sensitive dependence on the initial data. The Lyapunov numbers are (0.0119394, 0.000229502, –0.0430462), which fit the Table 1 (below) on page 28 in the book [20].

Table 1

Charscteristics of the attractors for a bounded three-dimensional flow

λ_1	λ_2	λ_3	**Attractor**	**Dimension**	**Dynamic**
-	-	-	Equilibrium point	0	Static
0	-	-	Limit cycle	1	Periodic
0	0	-	Attracting 2-torus	2	Quasiperiodic
0	0	0	Invariant	1 or 2	(Quasi) periodic
+	0	-	Strange	2 to 3	Chaotic

5. Conclusion

One more (of very few) chaotic attractor was found in the three-dimensional system (1), which is supposed to model the basic features of genetic networks. The trajectory in Figure 1 tends to a bounded attractor, which is neither a stable equilibrium nor a limit cycle. The sensitive dependence of solutions on the initial data is confirmed by the location of the respective Lyapunov curves [19-21]. The Lyapunov exponents are negative, almost zero, and positive. We guess that many of the strange attractors, listed in the book [22] (8) for polynomial systems, can be obtained also for systems of the form (1), where the dimensionality and the number of parameters should be increased.

6. References

[1] Abdalla Hassan Musa Hassan, Applications: Systems of Differential Equations and Dynamic Systems. International Journal of Mathematics and Physical Sciences Research ISSN 2348-5736 (Online) Vol. 5, Issue 2, pp. 108-113.

[2] André C. Marreiros, Stefan J. Kiebel, Karl J. Friston, A dynamic causal model study of neuronal population dynamics, NeuroImage, Volume 51, Issue 1, 2010, pp. 91-101

[3] Coombes, S. (2023). Next generation neural population models. Frontiers in Applied Mathematics and Statistics, 9, Article 112822. https://doi.org/10.3389/fams.2023.1128224

[4] Kiyoshi Kotani, Akihiko Akao, Hayato Chiba, Bifurcation of the neuronal population dynamics of the modified theta model: Transition to macroscopic gamma oscillation, Physica D: Nonlinear Phenomena, Volume 416, 2021, 132789. https://doi.org/10.1016/j.physd.2020.132789.

[5] S. H. Mnaathr, Design and Simulation Networking Operating Model for Virtual Network System (VNS), 2021 7th International Engineering Conference “Research & Innovation amid Global Pandemic IEC), Erbil, Iraq, 2021, pp. 26-31, doi: 10.1109/IEC52205.2021.9476099.

[6] Samuilik, Inna. Genetic engineering – construction of a network of four dimensions with a chaotic attractor. Vibroengineering PROCEDIA. 2022,44. 66-70. 10.21595/vp.2022.22829.

[7] Mavroudis, Panteleimon; Jusko, William. (2021). Mathematical modeling of mammalian circadian clocks affecting drug and disease responses. Journal of Pharmacokinetics and Pharmacodynamics. 48. 1-12. 10.1007/s10928-021-09746-z.

[8] Afzal, Asif; Bhutto, Dr; Alrobaian, Abdulrahman; Kaladgi, Abdul Razak; Khan, Sher. Modelling and Computational Experiment to Obtain Optimized Neural Network for Battery Thermal Management Data Energies. 2021, 14. 7370. 10.3390/en14217370.

[9] Samuilik, Inna. Mathematical Modeling of Four-dimensional Genetic Regulatory Networks Using a Logistic Function. WSEAS TRANSACTIONS ON COMPUTER RESEARCH. (2022). 10. 112-119. 10.37394/232018.2022.10.15.

[10] Muscoloni, Alessandro; Michieli, Umberto; Zhang, Yingtao; Cannistraci, Carlo. Adaptive Network Automata Modelling of Complex Networks. 2022, 10.20944/preprints202012.0808.v3.

[11] Cannistraci, Carlo. Modelling Self-Organization in Complex Networks Via a Brain-Inspired Network Automata Theory Improves Link Reliability in Protein Interactomes. Scientific Reports. 2018, 8. 10.1038/s41598-018-33576-8.

[12] Sayama, Hiroki et al. “Modeling complex systems with adaptive networks.”Comput. Math. Appl. 65 (2013): 1645-1664.A. Das, A.B. Roy, Pritha Das. Chaos in a three dimensional neural network. Applied Mathematical Modelling, 24(2000), 511-522.

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

[14] Le-Zhi Wang, C. Grebogi, et al. A geometrical approach to control and controllability of nonlinear dynamical networks, Nature Communications, Vol. 7, Article number:11323 (2016), DOI: 10.1038/ncomms11323

[15] L. Perko. Differential Equations and Dynamical Systems. Springer-Verlag New York, 2001.

[16] F. Sadyrbaev, I. Samuilik, V. Sengileyev. On Modelling of Genetic Regulatory Networks. WSEAS Transactions on Electronics,2021, Vol. 12, No. 1, 73.-80.lpp. ISSN 1109-9445. e-ISSN 2415-1513. doi:10.37394/232017.2021.12.10

[17] I. Samuilik, F. Sadyrbaev. Modelling Three Dimensional Gene Regulatory Networks. WSEAS Transactions on Systems and Control. 2021, Vol. 12, No. 1, 73.-80.lpp. ISSN 1109-9445. e-ISSN 2415-1513. doi:10.37394/232017.2021.12.10

[18] J. C. Sprott. Elegant Chaos Algebraically Simple Chaotic Flows. World Scientific Publishing Company, 2010, 302 pages. https://doi.org/10.1142/7183

[19] O. Kozlovska, F. Sadyrbaev. On attractors in systems of ordinary differential equations arising in models of genetic networks. Vibroengineering PROCEDIA. May 2023, Volume 49, 137-140.

[20] M. Sandri. Numerical calculation of Lyapunov exponents, The Mathematica Journal, 1996.

[21] Koçak, Hüseyin; Palmer, Ken. Lyapunov Exponents and Sensitive Dependence. Journal of Dynamics and Differential Equations. 2010, 22, pp. 381-398.

[22] Demir, Bünyamin; Kocak, Sahin. A note on positive Lyapunov exponent and sensitive dependence on initial conditions. Chaos Solitons and Fractals - CHAOS SOLITON FRACTAL., 2001, 12, pp. 2119-2121.

[23] Caligiuri, Annalisa; Eguiluz, Victor; Di Gaetano, Leonardo & Galla, Tobias & Lacasa, Lucas. (2023). Lyapunov Exponents for Temporal Networks. 10.48550/arXiv.2301.12966.

[24] Meyers RA. Encyclopedia of Physical Science and Technology. 3rd ed. Academic Press; 2002.