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On attractors in dynamical systems modeling genetic networks

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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.

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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

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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 $F(X) = (f_1(X), \ldots, f_n(X))$ 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 component-wise. 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.*

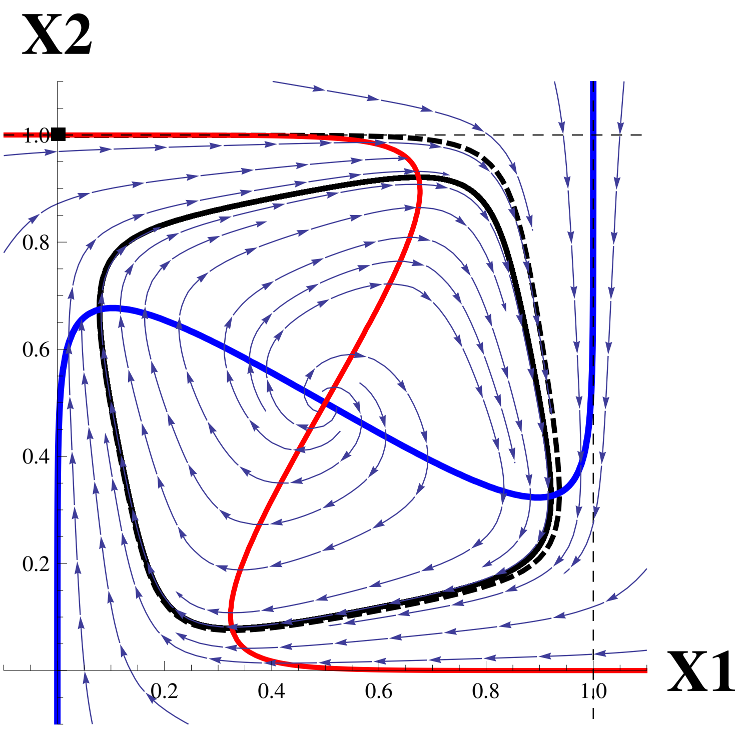

Figure 1: The limit cycle in system (10), $W = \{\{2.7, 3\}, \{-3, 2.7\}\}$, $\mu_1 = \mu_2 = 4$, $\theta_1 = 2.85, \theta_2 = -0.15$.

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

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu_1(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 - \theta_1)}} - x_1, \\ x_2' = \dfrac{1}{1 + e^{-\mu_2(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 - \theta_2)}} - x_2, \\ x_3' = \dfrac{1}{1 + e^{-\mu_3(w_{31}x_1 + w_{32}x_2 + w_{33}x_3 - \theta_3)}} - x_3, \end{cases} \tag{28}$$

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.

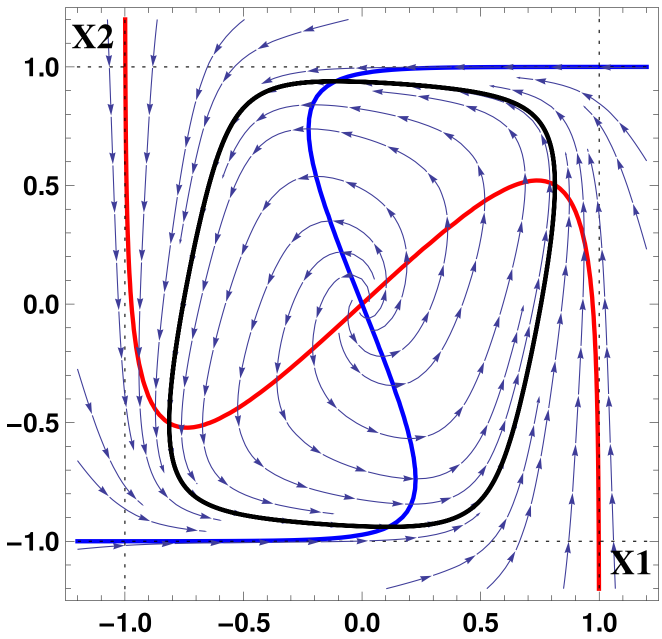

Figure 2: The limit cycle in system (21), $W = \{\{2.2, -1.3\}, \{3, 2.2\}\}$.

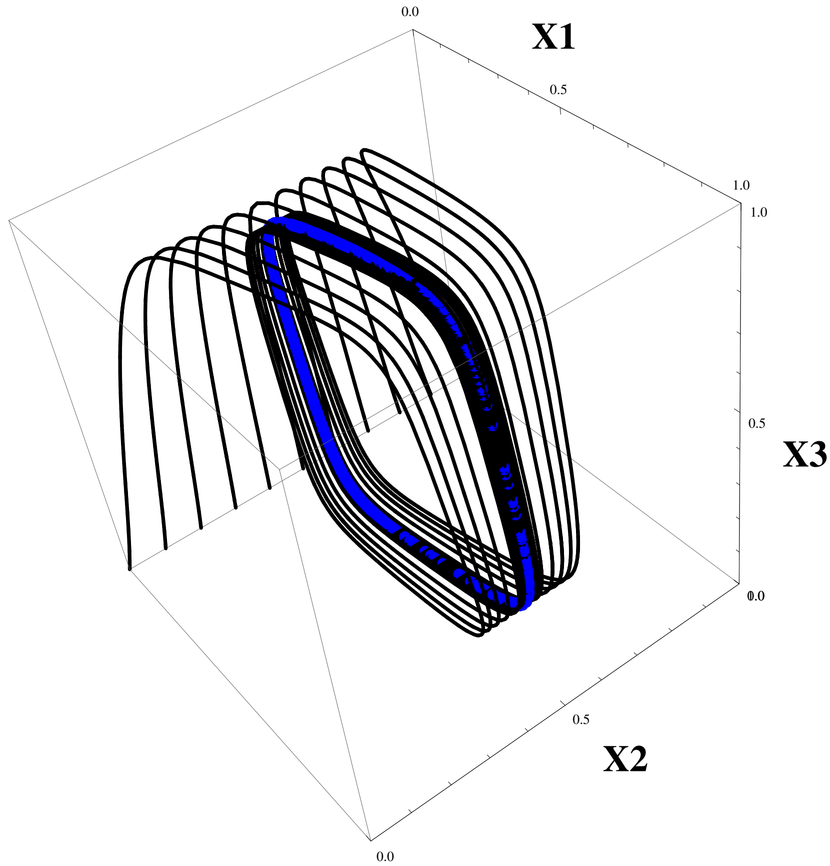

Figure 3: Limit cycle in system (28) with the matrix (29) and several trajectories, $\mu_1 = \mu_3 = 4$, $\mu_2 = 3$, $\theta_1 = 2.85$, $\theta_2 = 0.5$, $\theta_3 = -0.15$.

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.

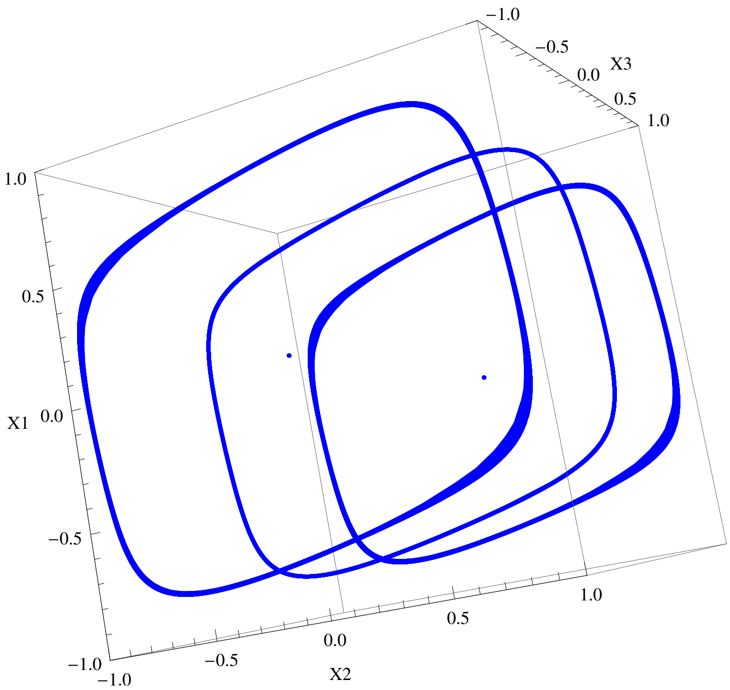

Figure 4: The limit cycles in system (30), $W = \{\{2.2, -1.3, 0\}, \{3, 2.2, 0\}, \{0, 0, 2.2\}\}$.

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

$$\begin{cases} \dfrac{dx_1}{dt} = \dfrac{1}{1 + e^{-\mu_1(w_{11}x_1 + w_{12}x_2 + w_{13}x_3 + w_{14}x_4 - \theta_1)}} - x_1, \\ \dfrac{dx_2}{dt} = \dfrac{1}{1 + e^{-\mu_2(w_{21}x_1 + w_{22}x_2 + w_{23}x_3 + w_{24}x_4 - \theta_2)}} - x_2, \\ \dfrac{dx_3}{dt} = \dfrac{1}{1 + e^{-\mu_3(w_{31}x_1 + w_{32}x_3 + w_{33}x_3 + w_{34}x_4 - \theta_3)}} - x_3, \\ \dfrac{dx_4}{dt} = \dfrac{1}{1 + e^{-\mu_4(w_{41}x_1 + w_{42}x_2 + w_{43}x_3 + w_{44}x_4 - \theta_4)}} - x_4 \end{cases} \tag{35}$$

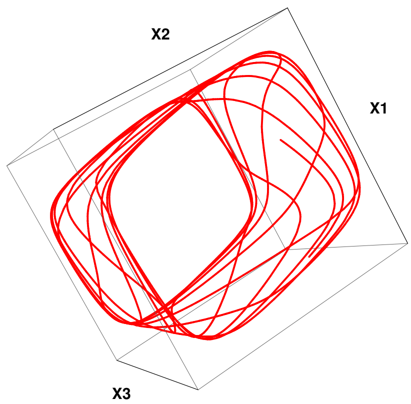

Figure 5: Projection onto the subspace (x_1, x_2, x_3)

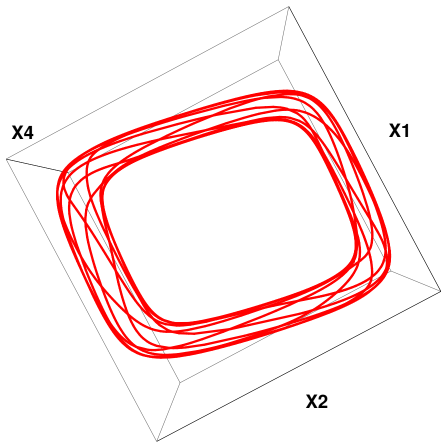

Figure 6: Projection onto the subspace (x_1, x_2, x_4)

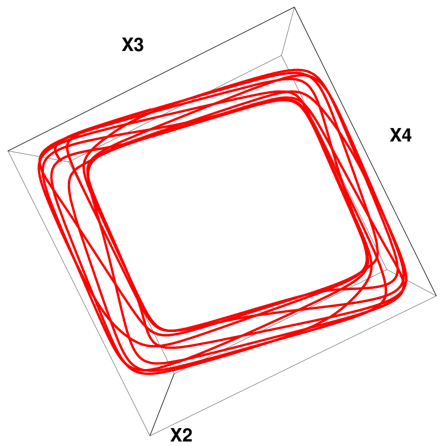

Figure 7: Projection onto the subspace (x_2, x_3, x_4)

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.

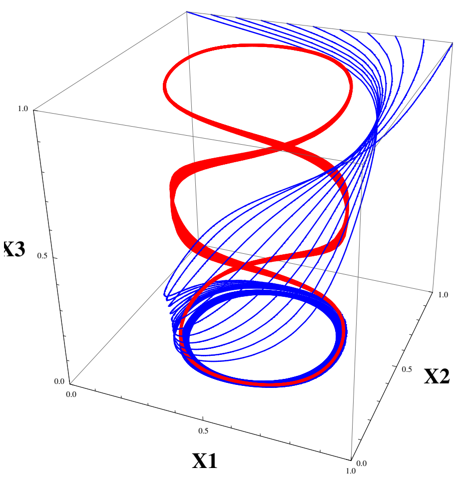

Figure 8: (x_1, x_2, x_3)-projections of the 4D attractor (red) and eleven trajectories (blue)

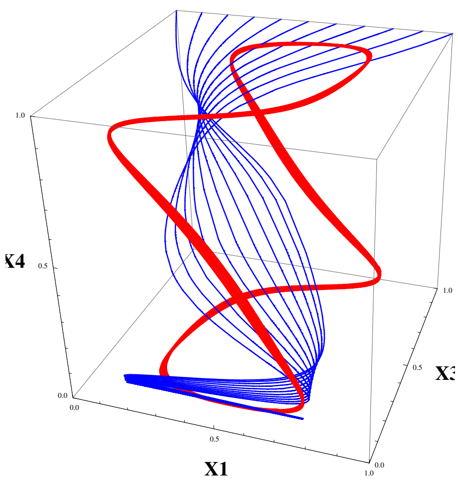

Figure 9: (x_1, x_3, x_4)-projections of the 4D attractor (red) and several trajectories (blue)

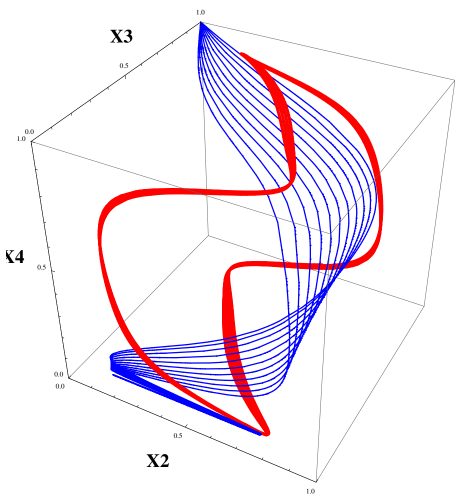

Figure 10: (x_2, x_3, x_4)-projections of the 4D attractor (red) and several trajectories (blue)

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).

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