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NETWORKS DESCRIBING DYNAMICAL SYSTEMS

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ABSTRACT. We consider systems of ordinary differential equations that arise in the theory of gene regulatory networks. These systems can be of arbitrary size but of definite structure that depends on the choice of regulatory matrices. Attractors play the decisive role in behaviour of elements of such systems. We study the structure of simple attractors that consist of a number of critical points for several choices of regulatory matrices.

1. Introduction

The problem of self-regulation in large systems is very actual. For instance, in telecommunication systems, where changes are rapid and unpredictable, one can construct an optimal virtual network topology (VNT) by establishing a set of lightpaths between nodes. To treat changing in time (fluctuating) traffic on a VNT, adaptive VNT control methods, which reconfigure VNTs according to traffic conditions on VNTs, should be invented. To develope such methods, one way is to observe "attractor selection" in biological systems that "adapt to unknown changes in their surrounding environments and recover their conditions." We consider an attractor selection that models the behaviour of gene regulatory and metabolic reaction networks in a cell. Biological explanation of processes and terms can be found in [1]–[4]. A comprehensive list of the related literature and overview of methods and types of models can be found in the reviews [5]–[7]. The attractor selection idea and discussions in [8] and [9] have influenced and motivated the choice of problems in this paper.

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It was mentioned in the literature that "nonlinear ordinary differential equations are probably the most-widespread formalism for modeling genetic regulatory networks" [5]. It is pointed out that an obvious drawback of this approach is the complexity of analysis of these models due to essentially nonlinear character of regular functions and large size of systems. Various approximations of linear and quasi-linear character are not sufficient to understand the mechanism of interactions between elements of networks. As a compromise, piece-wise linear (PWL) models were proposed and studied by the authors in [10] and other publications. On the other hand, there are examples of direct study of problems of this kind [11]. This paper is a definite contribution to the study of low dimension (up to order five) systems arising in models of gene regulatory networks.

2. Objectives of research

The dynamics of the expression level of the protein on the ith gene, x_i, is described by the differential system [2], [8]

$$\frac{dx_i}{dt} = f\Big(\sum w_{ij}x_j - \theta\Big)v_g - x_i v_g - \eta. \tag{1}$$

The x_i variables represent the deterministic behavior of gene i. The deterministic and stochastic behaviors are controlled by growth rate v_g, which represents the conditions of the metabolic reaction network. Regulations of protein expression levels on gene i by other genes are indicated by regulatory matrix w_{ij}, the elements of which take values from the interval $[-1, 1]$. Parameter η represents stochastic behavior. Parameter θ is a regulatory parameter which can be adjusted. The function f is S-shaped sigmoidal function depending on a parameter μ that controls steepness of the graph of f.

We consider the simplified system ($\eta = 0$)

$$\begin{cases} \dfrac{dx_1}{dt} = \dfrac{1}{1+e^{-\mu_1(w_{11}x_1+w_{12}x_2+\cdots+w_{1n}x_n-\theta_1)}}v_1 - x_1v_1, \\ \dfrac{dx_2}{dt} = \dfrac{1}{1+e^{-\mu_2(w_{21}x_1+w_{22}x_2+\cdots+w_{2n}x_n-\theta_2)}}v_2 - x_2v_2, \\ \dots \\ \frac{dx_n}{dt} = \frac{1}{1+e^{-\mu_n(w_{n1}x_1+w_{n2}x_2+\cdots+w_{nn}x_n-\theta_n)}}v_n - x_nv_n, \end{cases} \tag{2}$$

neglecting stochastic behaviour.

Parameters μ_i are the gain parameters of the sigmoidal functions.

Our goal is to clarify the structure of an attractive set for several choices of regulatory matrices W. It means that we should study the nonlinear system of differential equations, make conclusions on the number and location of critical points and reveal the character of critical points. On every stage of this problem we face nontrivial tasks to deal with.

In some cases (for some choices of regulatory matrices) we can make comprehensive analysis but in some other cases we can treat only typical examples.

3. Uniform interrelations in a network

Interrelation of elements in a network is described by the so-called regulatory matrix W that contains entries with values in the interval $[-1, 1]$. If the element w_{ij} is positive this means that jth gene influences gene i positively by activation it through expression of protein. The rate of influence can be measured by the value of w_{ij}. Similarly, the negative entry means negative influence, namely, inhibition of a gene by other one. Let us consider several cases.

First, we study system (2) under the conditions that all $w_{ij} \geq 0$ or all $w_{ij} \leq 0$. So, either we have cross activation (all entries w_{ij} are non-negative) or we have cross-inhibition (all entries w_{ij} are non-positive).

3.1. Linearized system

Suppose we have found a number of critical points for system (2). In order to detect their character, one should follow the standard scheme and consider the linearized system

$$\begin{cases} u_1' = -v_1 u_1 + g_1(w_{11}u_1 + w_{12}u_2 + \cdots + w_{1n}u_n), \\ u_2' = -v_2 u_2 + g_2(w_{21}u_1 + w_{22}u_2 + \cdots + w_{2n}u_n), \\ \cdots \\ u_n' = -v_n u_n + g_n(w_{n1}u_1 + w_{n2}u_2 - \cdots + w_{nn}u_n), \end{cases} \tag{3}$$

where

$$g_i = v_i \mu_i \frac{e^{-\mu_i(w_{i1}x_1 + \cdots + w_{in}x_n - \theta_i)}}{[1 + e^{-\mu_i(w_{i1}x_1 + \cdots + w_{in}x_n - \theta_i)}]^2}, \tag{4}$$

$i = 1, 2, \ldots, n$, $(x_1, \ldots, x_n)$ is a critical point. Notice that all g_i are positive.

The coefficient matrix A of the system (3) is

$$A = \begin{pmatrix} -v_1 + w_{11}g_1 & w_{12}g_1 & \ldots & w_{1n}g_1 \\ w_{21}g_2 & -v_2 + w_{22}g_2 & \ldots & w_{2n}g_2 \\ \cdots & & & \\ w_{n1}g_n & w_{n2}g_n & \ldots & -v_n + w_{nn}g_n \end{pmatrix}. \tag{5}$$

3.2. The case $n = 2$

Let $n = 2$. The system (2) takes the form

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu_1(w_{11}x_1 + w_{12}x_2 - \theta_1)}} v_1 - v_1 x_1, \\ x_2' = \dfrac{1}{1 + e^{-\mu_2(w_{21}x_1 + w_{22}x_2 - \theta_2)}} v_2 - v_2 x_2. \end{cases} \tag{6}$$

The regulatory matrix is

$$W = \begin{pmatrix} w_{11} & w_{12} \\ w_{21} & w_{22} \end{pmatrix}, \tag{7}$$

where all entries are either non-negative or non-positive. The characteristic polynomial for this case is

$$\begin{aligned} \det|A - \lambda I| = \lambda^2 &+ \lambda(v_1 + v_2 - g_1 w_{11} - g_2 w_{22}) \\ &+ (v_1 v_2 - g_1 v_2 w_{11} - g_2 v_1 w_{22} \\ &+ g_1 g_2 w_{12} w_{21} - g_1 g_2 w_{11} w_{22}) = 0, \end{aligned} \tag{8}$$

where A is the coefficient matrix for the linearized system. Suppose that elements w_{12} and w_{21} of W are not zeros. The discriminant

$$D = (v_1 - v_2 - g_1 w_{11} + g_2 w_{22})^2 + 4 g_1 g_2 w_{12} w_{21} \tag{9}$$

of the quadratic equation (8) is then positive. The characteristic roots are

$$\begin{aligned} \lambda_1 &= \tfrac{1}{2}(-v_1 - v_2 + g_1 w_{11} + g_2 w_{22} - \sqrt{D}), \\ \lambda_2 &= \tfrac{1}{2}(-v_1 - v_2 + g_1 w_{11} + g_2 w_{22} + \sqrt{D}). \end{aligned} \tag{10}$$

The character of critical points depends on signs of λ_1 and λ_2.

Since v_1 and v_2 are positive, one has that for $w_{11} \le 0$ and $w_{22} \le 0$ the first eigenvalue λ_1 is negative. The second eigenvalue λ_2 can be negative, zero or positive. Therefore, the following proposition is true.

Proposition 3.1. *In the case $w_{11} \le 0$ and $w_{22} \le 0$ any critical point of the system* (6) *is either stable node or a degenerate point (with $\lambda_1 < 0$ and $\lambda_2 = 0$) or a saddle point.*

Since D in (9) is positive both roots of the characteristic equation (8) are real and the following is true.

Proposition 3.2. *No critical points of the type focus are possible for system* (6).

Critical points of focus type can appear only if $w_{12} < 0 < w_{21}$ or $w_{12} > 0 > w_{21}$ and the inequality (11) holds

$$(v_1 - v_2 - g_1 w_{11} + g_2 w_{22})^2 + 4 g_1 g_2 w_{12} w_{21} < 0. \tag{11}$$

Proposition 3.3. *The necessary condition for the focus in system* (6) *is that* w_{12} *and* w_{21} *are of opposite signs.*

This condition does not fulfill under our assumptions about w_{ij} in this section.

4. Inhibition-activation

We consider the case of the regulatory matrix

$$W = \begin{pmatrix} 0 & -1 & -1 & \cdots & -1 \\ 1 & 0 & -1 & \cdots & -1 \\ \ldots \\ 1 & 1 & \cdots & 0 & -1 \\ 1 & 1 & \cdots & 1 & 0 \end{pmatrix} \tag{12}$$

and $\mu_1 = \mu_2 = \cdots = \mu_n$, $\theta_1 = \theta_2 = \cdots = \theta_n$, $v_i = 1$.

System (2) takes the form

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu(-x_2 - x_3 + \cdots - x_{n-1} - x_n - \theta)}} - x_1, \\ x_2' = \dfrac{1}{1 + e^{-\mu(x_1 - x_3 + \cdots - x_{n-1} - x_n - \theta)}} - x_2, \\ \ldots \\ x_{n-1}' = \dfrac{1}{1 + e^{-\mu(x_1 + x_2 + \cdots + x_{n-2} - x_n - \theta)}} - x_{n-1}, \\ x_n' = \dfrac{1}{1 + e^{-\mu(x_1 + x_2 + \cdots + x_{n-2} + x_{n-1} - \theta)}} - x_n. \end{cases} \tag{13}$$

4.1. Critical points

Critical points of system (13) are to be determined from

$$\begin{cases} x_1 = \dfrac{1}{1 + e^{-\mu(-x_2 - x_3 - \cdots - x_{n-1} - x_n - \theta)}}, \\ x_2 = \dfrac{1}{1 + e^{-\mu(x_1 - x_3 - \cdots - x_{n-1} - x_n - \theta)}}, \\ \ldots \\ x_{n-1} = \dfrac{1}{1 + e^{-\mu(x_1 + x_2 + \cdots + x_{n-2} - x_{n-1} - \theta)}}, \\ x_n = \dfrac{1}{1 + e^{-\mu(x_1 + x_2 + \cdots + x_{n-2} + x_{n-1} - \theta)}}. \end{cases} \tag{14}$$

Since the right-hand sides in (14) are positive but less than unity, all critical points locate in the n-dimensional unit cube $(0;1) \times (0;1) \times (0;1) \cdots \times (0;1)$.

Moreover, since

$$\begin{aligned}&-x_2 - x_3 - \cdots - x_{n-1} - x_n < x_1 - x_3 - \cdots - x_{n-1} - x_n \\ &\quad < x_1 + x_2 - x_4 - \cdots - x_{n-1} - x_n < \cdots < x_1 + x_2 + \cdots + x_{n-2} + x_{n-1}\end{aligned}$$

it follows from (14) that $0 < x_1 < x_2 < \cdots < x_n < 1$.

Lemma 4.1. *For $n = 2$, the system (14) has a unique positive solution.*

P r o o f. For 2D system only. Indeed, the system (14) is

$$\begin{cases} x_1 = \dfrac{1}{1 + e^{-\mu(-x_2 - \theta)}}, \\ x_2 = \dfrac{1}{1 + e^{-\mu(x_1 - \theta)}}. \end{cases} \tag{15}$$

The function $x_1 = \frac{1}{1+e^{-\mu(-x_2-\theta)}}$ is decreasing in the interval $[0, 1]$. On the other hand, the second equation in (15) can be rewritten as

$$x_1 = \theta - \frac{1}{\mu} \log\left(\frac{1}{x_2} - 1\right). \tag{16}$$

This function monotonically increases from $-\infty$ to $+\infty$ in the interval $(0, 1)$. The graphs of both functions intersect only once. □

The above assertion seemingly is valid for n-dimensional case also. All calculations being made confirm this.

4.2. Location of a critical point

Suppose $(x_1, x_2, \ldots, x_n)$ is a critical point for the system (13), where $0 < x_1 < x_2 < \cdots < x_n < 1$. Then, due to (14), for any pair of consecutive x_i and x_{i+1} one has

$$\begin{cases} x_i &= \frac{1}{1+e^{-\mu(-x_{i+1}+X-\theta)}}, \\ x_{i+1} &= \frac{1}{1+e^{-\mu(\ x_i+X-\theta)}}, \end{cases} \tag{17}$$

where X means the remaining variables the same in both lines,

$$X = \sum_{k=1}^{i-1} x_k - \sum_{m=i+2}^{n} x_m. \tag{18}$$

It follows from (17) that

$$\begin{cases} e^{-\mu(-x_{i+1}+X-\theta)} &= \frac{1}{x_i} - 1, \\ e^{-\mu(\ x_i+X-\theta)} &= \frac{1}{x_{i+1}} - 1. \end{cases} \tag{19}$$

$$\begin{cases} \mu(x_{i+1} + X + \theta) &= \ln\left(\frac{1}{x_i} - 1\right), \\ \mu(-x_i + X + \theta) &= \ln\left(\frac{1}{x_{i+1}} - 1\right). \end{cases} \tag{20}$$

Eliminating X and θ from (20) one gets that

$$\mu = \frac{1}{x_{i+1} + x_i}\left[\ln\left(\frac{1}{x_i} - 1\right) - \ln\left(\frac{1}{x_{i+1}} - 1\right)\right]. \tag{21}$$

Therefore, there is a recurrent relation between coordinates of a critical point.

Proposition 4.1. *For any critical point* $(x_1, x_2, \ldots, x_n)$ *of the system* (13) *the following is true:*

$$\frac{1}{x_{i+1} + x_i}\left[\ln\left(\frac{1}{x_i} - 1\right) - \ln\left(\frac{1}{x_{i+1}} - 1\right)\right] = \frac{1}{x_i + x_{i-1}}\left[\ln\left(\frac{1}{x_{i-1}} - 1\right) - \ln\left(\frac{1}{x_i} - 1\right)\right], \qquad i = 2, \ldots, n-1. \tag{22}$$

4.3. Linearized system

To get the character of possible critical points, consider the linearized system

$$\begin{cases} u_1' = -u_1 - \dfrac{\mu e^{-\mu(-x_2 - x_3 - \cdots - x_n - \theta)}}{[1 + e^{-\mu(-x_2 - x_3 - \cdots - x_n - \theta)}]^2}(u_2 + u_3 + \cdots + u_n), \\ u_2' = -u_2 - \dfrac{\mu e^{-\mu(x_1 - x_3 - \cdots - x_n - \theta)}}{[1 + e^{-\mu(x_1 - x_3 - \cdots - x_n - \theta)}]^2}(-u_1 + u_3 + \cdots + u_n), \\ \cdots \\ u_n' = -u_n - \dfrac{\mu e^{-\mu(x_1 + x_2 - \cdots + x_{n-1} - \theta)}}{[1 + e^{-\mu(x_1 + x_2 - \cdots + x_{n-1} - \theta)}]^2}(-u_1 - u_3 - \cdots - u_{n-1}). \end{cases} \tag{23}$$

We can simplify (23) by introducing

$$k_1 = \frac{e^{-\mu(-x_2 - x_3 - \cdots - x_n - \theta)}}{[1 + e^{-\mu(-x_2 - x_3 - \cdots - x_n - \theta)}]^2}, \tag{24}$$

$$k_2 = \frac{e^{-\mu(x_1 - x_3 - \cdots - x_n - \theta)}}{[1 + e^{-\mu(x_1 - x_3 - \cdots - x_n - \theta)}]^2}, \tag{25}$$

$$\cdots$$

$$k_n = \frac{e^{-\mu(x_1 + x_2 - \cdots + x_{n-1} - \theta)}}{[1 + e^{-\mu(x_1 + x_2 - \cdots + x_{n-1} - \theta)}]^2}. \tag{26}$$

This notation is valid onward till the end of the paper. Values of k_i are always positive and less than unity.

The linearized system can by written as

$$\begin{cases} u_1' = -u_1 - \mu k_1(u_2 + u_3 + \cdots + u_n), \\ u_2' = -u_2 - \mu k_2(-u_1 + u_3 + \cdots + u_n), \\ \cdots \\ u_n' = -u_n - \mu k_n(-u_1 - u_2 - \cdots - u_{n-1}). \end{cases} \tag{27}$$

The coefficient matrix A of the system (27) is

$$A = \begin{pmatrix} -1 & -\mu k_1 & -\mu k_1 & \cdots & -\mu k_1 \\ \mu k_2 & -1 & -\mu k_2 & \cdots & -\mu k_2 \\ \cdots \\ \mu k_n & \mu k_n & \cdots & -\mu k_n & -1 \end{pmatrix} \tag{28}$$

and the equation for the characteristic values is

$$\det(A - \lambda I) = \begin{vmatrix} -1-\lambda & -\mu k_1 & -\mu k_1 & \cdots & -\mu k_1 \\ \mu k_2 & -1-\lambda & -\mu k_2 & \cdots & -\mu k_2 \\ \cdots \\ \mu k_n & \mu k_n & \cdots & -\mu k_n & -1-\lambda \end{vmatrix} = 0. \tag{29}$$

4.4. Low-dimensional cases

4.4.1. Two-dimensional system

Consider the case

$$W = \begin{pmatrix} 0 & -1 \\ 1 & 0 \end{pmatrix}. \tag{30}$$

The system (2) then is

$$\begin{cases} x_1' = \dfrac{1}{1 + e^{-\mu(-x_2 - \theta)}} - x_1, \\ x_2' = \dfrac{1}{1 + e^{-\mu(\ \ x_1 - \theta)}} - x_2. \end{cases} \tag{31}$$

The linearized system can by written as

$$\begin{cases} u_1' = -u_1 - \mu k_1 u_2, \\ u_2' = \quad \mu k_2 u_1 - u_2 \end{cases} \tag{32}$$

with the coefficient matrix

$$A = \begin{pmatrix} -1 & -\mu k_1 \\ \mu k_2 & -1 \end{pmatrix}. \tag{33}$$

The roots of the characteristic equation

$$\det|A - \lambda I| = \lambda^2 + 2\lambda + \mu^2 k_1 k_2 + 1 = 0 \tag{34}$$

are

$$\begin{cases} \lambda_1 = -1 - \mu\sqrt{k_1 k_2}\, i, \\ \lambda_2 = -1 + \mu\sqrt{k_1 k_2}\, i, \end{cases} \tag{35}$$

where $i = \sqrt{-1}$. It appears that only one type of critical point is possible for the 2D system. Since $\lambda_{1,2}$ are complex numbers, the type of a critical point is stable focus [12].

Lemma 4.2. *Critical points of the system* (31)*, if any, are of the type stable focus.*

4.4.2. Three-dimensional system

Let the regulatory matrix be

$$W = \begin{pmatrix} 0 & -1 & -1 \\ 1 & 0 & -1 \\ 1 & 1 & 0 \end{pmatrix}. \tag{36}$$

The linearized system now is

$$\begin{cases} u_1' = -u_1 - \mu k_1 u_2 - \mu k_1 u_3, \\ u_2' = \mu k_2 u_1 - u_2 - \mu k_2 u_3, \\ u_3' = \mu k_3 u_1 + \mu k_3 u_2 - u_3 \end{cases} \tag{37}$$

with the coefficient matrix

$$A = \begin{pmatrix} -1 & -\mu k_1 & -\mu k_1 \\ \mu k_2 & -1 & -\mu k_2 \\ \mu k_3 & \mu k_3 & -1 \end{pmatrix}. \tag{38}$$

The characteristic equation

$$\det|A - \lambda I| = -\lambda^3 - 3\lambda^2 - \mu^2(k_1 k_2 + k_1 k_3 + k_2 k_3)(\lambda + 1) - 3\lambda - 1 = 0 \tag{39}$$

has the roots

$$\begin{cases} \lambda_1 = -1, \\ \lambda_2 = -1 - \mu\sqrt{k_1 k_2 + k_1 k_3 + k_2 k_3}\, i, \\ \lambda_3 = -1 + \mu\sqrt{k_1 k_2 + k_1 k_3 + k_2 k_3}\, i. \end{cases} \tag{40}$$

Lemma 4.3. *Any critical point of the 3D system* (13) *with the regulatory matrix* (36) *is a sink ([13, p.102]): there is 2D-subspace with a stable focus and attraction in the remaining dimension.*

Consider the example illustrating (and confirming) our analysis.

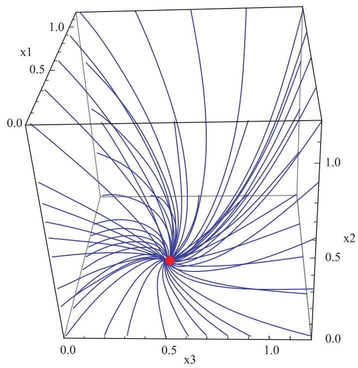

FIGURE 1. The phase portrait for 3D system (13), $\mu = 1$, $\Theta = 0.5$.

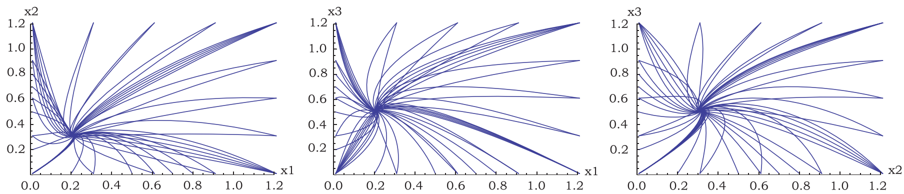

FIGURE 2. Projections of the phase space for 3D system (13) on the 2D coordinate planes.

For parameters $\mu = 1$ and $\theta = 0.5$, the critical point is (0.211336, 0.311244, 0.505645). The values of λ for this critical point are

$$\begin{cases} \lambda_1 = -1, \\ \lambda_2 = -1 - 0.36191\, i, \\ \lambda_3 = -1 + 0.36191\, i. \end{cases} \tag{41}$$

In this example, the 3D system (13) has one critical point (stable focus in 2D-subspace and attraction in the third dimension).

4.4.3. Four-dimensional system

Consider the regulatory matrix

$$W = \begin{pmatrix} 0 & -1 & -1 & -1 \\ 1 & 0 & -1 & -1 \\ 1 & 1 & 0 & -1 \\ 1 & 1 & 1 & 0 \end{pmatrix}. \tag{42}$$

The linearized system is

$$\begin{cases} u_1' = -u_1 - \mu k_1 u_2 - \mu k_1 u_3 - \mu k_1 u_4, \\ u_2' = \mu k_2 u_1 - u_2 - \mu k_2 u_3 - \mu k_2 u_4, \\ u_3' = \mu k_3 u_1 + \mu k_3 u_2 - u_3 - \mu k_3 u_4, \\ u_4' = \mu k_4 u_1 + \mu k_4 u_2 + \mu k_4 u_3 - u_4 \end{cases} \tag{43}$$

with the coefficient matrix

$$A = \begin{pmatrix} -1-\lambda & -\mu k_1 & -\mu k_1 & -\mu k_1 \\ \mu k_2 & -1-\lambda & -\mu k_2 & -\mu k_2 \\ \mu k_3 & \mu k_3 & -1-\lambda & -\mu k_3 \\ \mu k_4 & \mu k_4 & -\mu k_4 & -1-\lambda \end{pmatrix}. \tag{44}$$

The characteristic equation is

$$\begin{aligned} \det|A - \lambda I| = \lambda^4 + 4\lambda^3 \\ + \mu^2(k_1k_2 + k_1k_3 + k_1k_4 + k_2k_3 + k_2k_4 + k_3k_4)\lambda^2 + 6\lambda^2 \\ + 2\mu^2(k_1k_2 + k_1k_3 + k_1k_4 + k_2k_3 + k_2k_4 + k_3k_4)\lambda + 4\lambda \\ + \mu^2(k_1k_2 + k_1k_3 + k_1k_4 + k_2k_3 + k_2k_4 + k_3k_4) + 1 = 0. \end{aligned} \tag{45}$$

Let

$$S_{k1} = k_1k_2 + k_1k_3 + k_1k_4 + k_2k_3 + k_2k_4 + k_3k_4, \tag{46}$$

then the above equation can be written in a simplified form

$$\begin{aligned} \det|A - \lambda I| = \lambda^4 + 4\lambda^3 + \mu^2(S_{k1})\lambda^2 + 6\lambda^2 \\ + 2\mu^2(S_{k1})\lambda + 4\lambda + \mu^2(S_{k1}) + 1 + k_1k_2k_3k_4\mu^4 = 0. \end{aligned} \tag{47}$$

After rearrangement of terms we get

$$(\lambda + 1)^4 + \mu^2(S_{k1})(\lambda + 1)^2 + k_1k_2k_3k_4\mu^4 = 0. \tag{48}$$

Denote

$$G_{4d} = \sqrt{S_{k1}^2 - 4k_1k_2k_3k_4} \tag{49}$$

and notice that $S_{k1}^2 - 4k_1k_2k_3k_4 > 0$. The roots of the characteristic equation (48) are then

$$\begin{cases} \lambda_1 = -1 - \dfrac{\mu}{\sqrt{2}}\sqrt{S_{k1} + G_{4d}}\, i, \\ \lambda_2 = -1 + \dfrac{\mu}{\sqrt{2}}\sqrt{S_{k1} + G_{4d}}\, i, \\ \lambda_3 = -1 - \dfrac{\mu}{\sqrt{2}}\sqrt{S_{k1} - G_{4d}}\, i, \\ \lambda_4 = -1 + \dfrac{\mu}{\sqrt{2}}\sqrt{S_{k1} - G_{4d}}\, i. \end{cases} \tag{50}$$

Lemma 4.4. *Any critical point of the 4D system* (13) *is a sink: there are two 2D-subspaces with a stable focus.*

4.4.4. Five-dimensional system

Consider the 5D differential system with the regulatory matrix

$$W = \begin{pmatrix} 0 & -1 & -1 & -1 & -1 \\ 1 & 0 & -1 & -1 & -1 \\ 1 & 1 & 0 & -1 & -1 \\ 1 & 1 & 1 & 0 & -1 \\ 1 & 1 & 1 & 1 & 0 \end{pmatrix}. \tag{51}$$

Introduce the notation

$$S_{g1} = k_1k_2 + k_1k_3 + k_1k_4 + k_1k_5 + k_2k_3 + k_2k_4 + k_2k_5 + k_3k_4 + k_3k_5 + k_4k_5 \tag{52}$$

and

$$S_{g2} = k_1k_2k_3k_4 + k_1k_2k_3k_5 + k_1k_2k_4k_5 + k_1k_3k_4k_5 + k_2k_3k_4k_5. \tag{53}$$

The characteristic equation is now

$$\det|A - \lambda I| = \lambda^5 + 5\lambda^4 + \mu^2(S_{g1})\lambda^3 + 10\lambda^3 + 3\mu^2(S_{g1})\lambda^2 + 10\lambda^2 + \mu^4(S_{g2})\lambda + 3\mu^2(S_{g1})\lambda + 5\lambda + \mu^4(S_{g2}) + \mu^2(S_{g1}) + 1 = 0. \tag{54}$$

After rearrangement of terms one obtains

$$(\lambda+1)^5 + \mu^2(S_{g1})(\lambda+1)^3 + \mu^4(S_{g2})(\lambda+1) = (\lambda+1)\big[(\lambda+1)^4 + \mu^2(S_{g1})(\lambda+1)^2 + \mu^4(S_{g2})\big] = 0. \tag{55}$$

Denote

$$G_{5d} = \sqrt{S_{g1}^2 - 4S_{g2}} \tag{56}$$

and notice that

$$S_{g1}^2 - 4S_{g2} = (k_1k_2 - k_2k_4)^2 + (k_1k_3 - k_2k_5)^2 + (k_1k_5 - k_2k_4)^2 + (k_1k_4 - k_3k_5)^2 + (k_2k_3 - k_4k_5)^2 > 0.$$

The characteristic values for the linearized system are then

$$\begin{cases} \lambda_1 = -1, \\ \lambda_1 = -1 - \dfrac{\mu}{\sqrt{2}}\sqrt{S_{g1} + G_{5d}}\, i, \\ \lambda_2 = -1 + \dfrac{\mu}{\sqrt{2}}\sqrt{S_{g1} + G_{5d}}\, i, \\ \lambda_3 = -1 - \dfrac{\mu}{\sqrt{2}}\sqrt{S_{g1} - G_{5d}}\, i, \\ \lambda_4 = -1 + \dfrac{\mu}{\sqrt{2}}\sqrt{S_{g1} - G_{5d}}\, i. \end{cases} \tag{57}$$

Lemma 4.5. *Any critical point of the 5D system is a sink: there are two 2D--subspaces with a stable focus and attraction in the remaining dimension.*

5. Conclusions

The structure of attractors for two-dimensional systems with uniform (non--negative or non-positive elements) regulatory matrices is simple and they (attractors) cannot contain any critical points of the type focus.

In low-dimension inhibition-activation systems, only one critical point was detected. For n-dimensional systems with n even, the characteristic equation for a single critical point has pairs of conjugate complex eigenvalues λ and the real parts of all eigenvalues are equal to -1. Therefore, a critical point is the stable focus in all 2D-subspaces.

For n odd, all λ-s except one are pairs of complex values with real parts equal to -1. The remaining λ is -1. A critical point is the stable focus in all 2D-subspaces and attracted in the remaining dimension.

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