

On attracting sets in artificial networks: cross activation

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Abstract. Mathematical models of artificial networks can be formulated in terms of dynamical systems describing the behaviour of a network over time. The interrelation between nodes (elements) of a network is encoded in the regulatory matrix. We consider a system of ordinary differential equations that describes in particular also genomic regulatory networks (GRN) and contains a sigmoidal function. The results are presented on attractors of such systems for a particular case of cross activation. The regulatory matrix is then of particular form consisting of unit entries everywhere except the main diagonal. We show that such a system can have not more than three critical points. At least $n-1$ eigenvalues corresponding to any of the critical points are negative. An example for a particular choice of sigmoidal function is considered.

1 Introduction

Artificial neural networks can be used successfully to model dynamics of gene expression in a living cell [1]. Investigation of mathematical models for gene regulatory networks (GRNs) had become a challenging problem for mathematicians and biologists. The mathematical models based on differential equations can help to understand the organization within cells and their dynamics. Such models can be found in [1], [2], [3]. GRN therefore are networks of interacting over time elements. This interaction is organized so that the living organism is able to adapt to changes in the outside environment. Genes produce proteins that regulate other genes. A particular gene regulates a number of other genes and they, in turn, regulate the activity of many genes downstream. On the other hand, a particular gene is influenced and regulated by many genes upstream. [4]. All together they form a genomic regulatory network of elements turning each other on and off. There are attempts in the literature to transfer principles of self-organization in GRN to networks of different nature. For instance, in telecommunication systems, where changes are rapid and unpredictable, one can construct an optimal virtual network topology (VNT) [2], [3] by establishing a set of lightpaths between nodes. To treat changing in time (fluctuating) traffic on a VNT, adaptive VNT control methods should be invented, which reconfigure VNTs according to traffic conditions on VNTs. To develop such methods, one way is to observe attractor selection in biological systems (GRN in particular) that adapt to unknown changes in their surrounding environments and recover their conditions. The mathematical models for GRN [5-7] and telecommunication networks [2], [3] have similar features. In this article we consider the dynamical system model that appears in [1], [2], [3]. Our goal is to describe attractors for the dynamical system in a

particular case. The system of differential equations contains the so called regulatory matrix W that is used to roughly describe the relations between elements of a modelled network. In order to deal with possibly simple objects it is proposed that entries of regulatory matrix W can be of only three kinds: -1 ; 0 and $+1$, that corresponds respectively to inhibition, no relation and activation. Properties of dynamical systems modelling the network strongly depend on the structure of matrix W . The study of related differential systems which are 1) nonlinear, 2) depend on parameters and 3) may be of arbitrary size, is a highly nontrivial task. Even in the simplest cases the analysis of such systems provide nontrivial results. For instance, in the work [8] the simplified system (for a network of two elements) of the form

$$\begin{cases} x_1' = \frac{1}{1 + e^{-\mu(x_2 - \theta)}} - x_1, \\ x_2' = \frac{1}{1 + e^{-\mu(x_1 - \theta)}} - x_2 \end{cases} \quad (1)$$

was considered. It was proved that this system can have up to three critical points depending on the values of parameters μ and θ . The characteristics of critical points were given. Later [9] it was shown that n -dimensional system with regulatory matrix

$$W = \begin{pmatrix} 0 & 1 & \vdots & 1 \\ 1 & 0 & \vdots & 1 \\ \dots & \dots & \dots & \dots \\ 1 & 1 & \vdots & 0 \end{pmatrix} \quad (2)$$

also can have up to three critical points of the form (x, \dots, x) (lying on the bisectrix) of definite type. This case was called "cross activation". The types of critical

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points and their dependence on two parameters were revealed. In what follows we try to accomplish the same task for systems that contain arbitrary sigmoidal function in their description. By sigmoidal function $f(z)$ we call a monotonically increasing to the unity continuous function that is positive at $z=0$ and has exactly one point of inflexion (that separates convexity from concavity). The function $f(z)=(1+\exp(-\mu z))^{-1}$ used in system (1) is of this kind but there are many other sigmoidal functions. Sigmoidal functions have typical S-shaped form. There is usually a parameter μ that regulates how steep is the graph of S-shaped function.

2 General information

We consider systems of the form

$$\frac{dx_i}{dt} = f(\sum W_{ij}x_j - \theta) - x_i, \quad (3)$$

where f is a sigmoidal function, W is a regulatory matrix defined by (2) and θ is a parameter. Our goal is to describe attractors for such a system. In extended form the system (3) looks as

$$\begin{cases} x'_1 = f(x_2 + x_3 + \dots + x_n - \theta) - x_1, \\ \dots \dots \dots \\ x'_n = f(x_1 + x_2 + \dots + x_{n-1} - \theta) - x_n, \end{cases} \quad (4)$$

where θ is a positive parameter. To find the critical points one has to consider the system

$$\begin{cases} x_1 = f(x_2 + x_3 + \dots + x_n - \theta), \\ x_2 = f(x_1 + x_3 + \dots + x_n - \theta), \\ \dots \dots \dots \\ x_n = f(x_1 + x_2 + \dots + x_{n-1} - \theta). \end{cases} \quad (5)$$

Due to monotonicity of $f(z)$ the following is true.

Lemma 1. All critical points (x_1, \dots, x_n) lie on the diagonal of a unit n -dimensional cube, that is, $x_1=x_2=\dots=x_n$.

Proof. Divide the second line in (5) by the first line. Suppose that $x_2 > x_1$. One gets

$$1 < \frac{x_2}{x_1} = \frac{f(x_1 + x_3 + \dots + x_n - \theta)}{f(x_2 + x_3 + \dots + x_n - \theta)} < 1.$$

The contradiction is obtained. Similarly the case $x_2 < x_1$ can be considered. Therefore $x_2 = x_1$. Considering the second and the third lines one can prove that $x_2 = x_3$. And so on. \square

In view of the above lemma to find the critical points one has to solve the scalar equation

$$x = f((n-1)x - \theta). \quad (6)$$

We thus have arrived at the statement.

Theorem 1. System (4) can have no more than three critical points.

The proof follows from the fact that the straight line $y=x$ cannot intersect S-shaped graph more than three times.

After detecting the critical points further analysis can be made in order to describe the attractors of the system.

We show the analysis of some particular case. The case of the logistic function $f(z)=(1+\exp(-\mu z))^{-1}$ will be considered.

3 SYSTEM: GENE REGULATION

The system

$$\begin{cases} x'_1 = \frac{1}{1 + e^{-\mu(x_2+x_3+\dots+x_n-\theta)}} - x_1, \\ \dots \dots \dots \\ x'_n = \frac{1}{1 + e^{-\mu(x_1+x_2+\dots+x_{n-1}-\theta)}} - x_n, \end{cases} \quad (7)$$

appears in the gene regulation theory [1], [5]. The parameters μ and θ are positive. In view of the results of the previous section all critical points are of the form (x, \dots, x) (n times), where x is to be determined from the relation

$$\theta = \frac{1}{\mu} \log\left(\frac{1}{x} - 1\right) + (n-1)x \quad (8)$$

Analyzing this relation one obtains two branches

$$x_{1,2} = \frac{1}{2} \pm \sqrt{\frac{1}{4} - \frac{1}{(n-1)\mu}}$$

Putting these branches into (7) two branches $\theta_1(\mu)$ and $\theta_2(\mu)$ can be defined that bound the region Ω in the (μ, θ) plane.

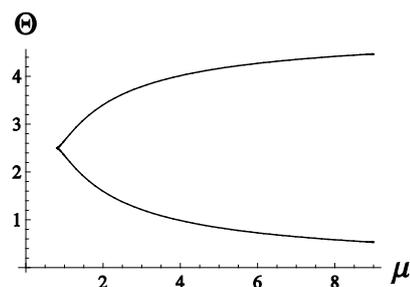


Fig. 1. Region Ω (bounded by two branches) for $n=6$.

3.1. Linearization

To detect types of critical points use the standard linearization procedure. The linearized at a critical point (x, \dots, x) system is

$$\begin{cases} u_1' = -u_1 + \mu(1-x)xu_2 + \dots + \mu(1-x)xu_n, \\ u_2' = -u_2 + \mu(1-x)xu_1 + \dots + \mu(1-x)xu_n, \\ \dots \dots \dots \dots \dots \\ u_n' = -u_n + \mu(1-x)xu_1 + \dots + \mu(1-x)xu_{n-1}. \end{cases}$$

The characteristic values for the above linear system are to be determined from the equation

$$\begin{pmatrix} -1-\lambda & \mu x(1-x) & \vdots & \mu x(1-x) \\ \mu x(1-x) & -1-\lambda & \vdots & \mu x(1-x) \\ \dots & \dots & \dots & \dots \\ \mu x(1-x) & \mu x(1-x) & \vdots & -1-\lambda \end{pmatrix} = 0$$

This equation, due to its specific structure, can be solved and the roots are

$$\lambda_1 = \dots = \lambda_{n-1} = -\mu x(1-x) - 1, \\ \lambda_n = (n-1)\mu x(1-x) - 1$$

Since for any possible critical point the first $n-1$ characteristic values λ_i are negative (recall that $x \in (0,1)$), the n -dimensional neighbourhood of any critical point contains $(n-1)$ -dimensional attracting subspace. As to the remaining characteristic value λ_n (that determines the behaviour along the remaining 1-dimensional subspace), it may be negative, zero or positive. Let us detect the sign of λ_n .

Lemma 2. If (μ, Θ) is in $ext \Omega$, then the characteristic number λ_n is negative for a respective unique critical point;
 if (μ, Θ) belongs to $\partial\Omega$, λ_n is negative for the first critical point and λ_n is zero for the second one, corresponding to an extremum of $\Theta(x)$;
 if (μ, Θ) is in $int \Omega$, λ_n is positive for one (in the middle) critical point and negative for two other (side) critical points; λ_n is zero also for a unique critical point corresponding to the vertex of Ω .

Theorem 2. An attracting set for system (7) consists of at most three critical points. The number of critical points and their character depend on the choice of parameters (η, θ) . The following is true:

- 1) If $(\mu, \Theta) \in ext \Omega$, the attracting set consists of one critical point (attraction in all dimensions);
- 2) If $(\mu, \Theta) \in \partial\Omega$, the attracting set consists of two critical points, one attracting in all dimensions (all characteristic numbers are negative) and the second one attracting in $(n-1)$ -dimensions and degenerate (the respective λ is zero) in the remaining dimension; the same (the respective λ is zero) is the character of the critical point corresponding to the vertex of region Ω ;

3) if $(\mu, \Theta) \in int \Omega$, there are three critical points; the middle point is attracting in $(n-1)$ -dimensions and repelling in the remaining dimension (the respective λ is positive); the two side critical points are attracting in all dimensions.

3.2. Conclusion

Systems of the form (4) arise in mathematical models of artificial networks including GRN networks. In the case of cross activation (the regulatory matrix consists of unit entries except the main diagonal) all critical points are on the bisectrix of a unit n -dimensional cube. The maximal number of critical points is three. At least $n-1$ eigenvalues (roots of the characteristic equations) for any critical point are negative. The cases of two and one critical points are possible.

References

1. J. Vohradský, FASEB J. **15**(3/2001), 846-54.
2. Y. Koizumi et al., Journal of Lightwave Technology, **8** (06/2010), Issue 11, 1720 – 1731. (8)
3. Y. Koizumi, T. Miyamura, S. Arakawa, E. Oki, K. Shiimoto, and M. Murata, in Proceedings of BIONETICS, Nov. 2008, 1– 8.
4. A. Wuensche, Pac Symp Biocomput. 1998:89-102.
5. F. M. Alakwaa, Journal of Computational Systems Biology, **1**(1/2002), 67-103.
6. A. Crombach, P. Hogeweg, PLoS Comput Biol **4**(7), 2008: e1000112. doi:10.1371/journal.pcbi.1000112
7. A. Tušek and Ž. Kurtanjek, Ch. 5 in “Applied Biological Engineering - Principles and Practice” Ed. by Ganesh R. Naik, ISBN 978-953-51-0412-4, 674 pages, Publisher: InTech, DOI: 10.5772/2101
8. S. Atslega, D. Finaskins and F. Sadyrbaev, Mathematical Modelling and Analysis, **21** (3/2016), 385-398 DOI:10.3846/13926292.2016.1172131
9. E. Brokan and F. Sadyrbaev, Attracting Sets in Gene Regulatory Systems. In : *Proceedings SMMS 2015*, November 22-23, 2015, Chiang Mai, Thailand, pp. 135-138. DEStech Publication, Inc., Lancaster, U.S.A.