Stability of piecewise-linear models of genetic regulatory networks*

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This paper investigates the stability of the equilibria of the piecewise-linear models of genetic regulatory networks on the intersection of the thresholds of all variables. It first studies circling trajectories and derives some stability conditions by quantitative analysis in the state transition graph. Then it proposes a common Lyapunov function for convergence analysis of the piecewise-linear models and gives a simple sign condition. All the obtained conditions are only related to the constant terms on the right-hand side of the differential equation after bringing the equilibrium to zero.

Keywords: genetic regulatory networks, piecewise-linear model, Lyapunov function

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1. Introduction

In recent years there has been a growing interest in the study of the analysis and control of genetic regulatory networks.[1−25] This is partly due to recent advances in the experimental techniques used in genomics such as cDNA microarrays, oligonucleotidechips and the mass spectrometric identification of gel-separated proteins. Currently, it is impossible to build a model that generates the exact behaviour of the genetic regulatory networks owing to no or incomplete understanding of the biochemical reaction mechanisms underlying the interactions and the general absence of quantitative information on kinetic parameters and molecular concentrations. It is of significance to find an effective model which captures the main properties of the genetic regulatory networks and is convenient for numerical analysis. One of the most interesting approach to this problem is to use the piecewise-linear (PL) models originally proposed by Glass *et al.*[14] Numerous studies have been conducted to investigate the equilibria of this model, which lie on the threshold hyperplanes. For example, Gouzé *et al.*[18] introduced the Filippov solution to the PL models of genetic regulatory networks on threshold hyperplanes. Subsequently, de Jong *et al.*[8] presented a method for the qualitative simulation of genetic regulatory networks based on PL models. Founded on the works of Refs. [18] and [8], Casey *et al.*[5] put the problem of stability in this class of PL systems into the framework of differential inclusions and Filippov solutions, and proved several results on the stability of singular equilibria based on properties of the state transition graph. In the meantime, many studies have been made on periodic trajectories or limit cycles. However, the obtained results mainly focus on a special case where all degradation rates are assumed to be equal[10,12,19] and few results are established to tackle the general case where the degradation rates are different. To our knowledge, there are only two works (by Snoussi *et al.*[22] and Farcot *et al.*[11]) which do not require the uniform degradation assumption.

In this paper, we follow the work of Refs. [5], [8], and [18] and investigate the equilibria stability of the PL models of genetic regulatory networks with different degradation rates. The equilibrium considered in this paper is an isolated point lying on the intersection of the thresholds of all variables and there may be transition cycles around the equilibrium, which is different from Refs. [5] and [8] where the focal point is the stability of an equilibrium set contained in a switching domain and the given stability condition is that every contiguous regulatory domain should have a transition entering the switching domain. We first study

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the case where there exist transition cycles around the equilibrium in the state transition graph. In many situations, the transition cycles correspond to circling trajectories. It is almost impossible to analyse the stability of the equilibrium point in the existence of transition cycles by the state-transition-graph-based approach used in Refs. [5] and [8] which took no account of the detailed solution of the system. The approach adopted is to first perform a model transformation by bringing the equilibrium to zero and then including the quantitative analysis in the state transition graph. The derived conditions are only related to the constant terms on the right-hand side of the obtained system. In Ref. [11], the case where there are transition cycles around the equilibrium was also studied, but it is required that there is a compression function, which is hard to find and may not exist in some cases, to guarantee the convergence of the equilibrium of the system. Without considering the state transition graph, we study the stability of the equilibrium from a different angle by introducing a common Lyapunov function. As commonly known, it is not an easy task to construct a common Lyapunov function for switching systems, especially when the subsystems have different equilibrium points. Based on the introduced common Lyapunov function, we obtain a simple condition consisting of a sign sum of the constant terms on the right-hand side of the differential equation. Compared with the approach based on the state transition graph, the proposed Lyapunov approach needs no information about the solution of the system but only the dynamics of the system in each regulatory domain and might be employed to deal with the time-delay case for genetic regulatory networks.

The following notations will be used throughout this paper. The $\mathbb{R}^n_{\geq 0}$ denotes the set of all n-dimensional real column vectors whose entries are positive; $\mathbb{Z}^+$ denotes the set of the positive integers; A^{T} represents the transpose of the vector or matrix A; $\|\cdot\|_2$ refers to the 2-norm for vectors or matrices.

2. Models

The genetic regulatory network under consideration consists of n genes. Suppose that the protein concentration of the product of the i-th gene ($i \in \mathscr{I}$) has the dynamics (proposed originally by Ref. [14]) as follows:

$$\dot{x}_i = g_i(\boldsymbol{x}) - \gamma_i x_i, \quad x_i(0) = x_{0i}, \tag{1}$$

where $\mathscr{I} = \{1, 2, \ldots, n\}$ is an index set, $\boldsymbol{x} = (x_1, \ldots, x_n)^{\mathrm{T}}$, $g_i(\boldsymbol{x})$ denotes the expression rate which depends on the concentrations $\boldsymbol{x}$ of proteins in the cell and $\gamma_i x_i$ is the degradation rate. A primary feature of the genetic regulatory networks is the presence of threshold-like relationships between the system variables, i.e., below (or above) a certain value, a variable x_i has little or no effect on another variable x_j, whereas above (or below) this value the effect of x_i on x_j increases rapidly to a constant value. In this paper, these threshold-like relationships are described by step functions. The function $g_i : \mathbb{R}^n_{\geq 0} \to \mathbb{R}_{\geq 0}$ is defined as

$$g_i(\boldsymbol{x}) = \sum_{l \in \mathscr{I}} \kappa_{il} b_{il}(\boldsymbol{x}), \tag{2}$$

where $\kappa_{il} > 0$ is a rate parameter and $b_{il} : \mathbb{R}^n_{\geq 0} \to \{0, 1\}$ is a regulation function. The function $b_{il}(\boldsymbol{x})$ describes the conditions under which the protein encoded by the i-th gene is synthesized at a rate κ_{il} and is expressed as combinations of step functions $s^+, s^- : \mathbb{R}^2_{\geq 0} \to \{0, 1\}$:

$$s^+(x_j, \theta_j) = \begin{cases} 1, & x_j > \theta_j, \\ 0, & x_j < \theta_j, \end{cases} \quad \text{and} \quad s^-(x_j, \theta_j) = 1 - s^+(x_j, \theta_j). \tag{3}$$

Here, θ_j is called the threshold for the protein concentration x_j. It should be noted that at each threshold $x_j = \theta_j$, the step functions are not defined and hence neither are the regulation functions.

Let $\boldsymbol{g}(\boldsymbol{x}) = (g_1(\boldsymbol{x}), \ldots, g_n(\boldsymbol{x}))^{\mathrm{T}}$ and $\gamma = \mathrm{diag}\{\gamma_1, \ldots, \gamma_n\}$. Rewriting the system (1) in a matrix form, we have

$$\dot{\boldsymbol{x}} = \boldsymbol{g}(\boldsymbol{x}) - \gamma \boldsymbol{x}. \tag{4}$$

Definition 1 (Filippov solution)[26] Let $\boldsymbol{x}(t)$ be an absolutely continuous function. We say that $\boldsymbol{x}(t)$ is a Filippov solution of the system (4) on $[t_0, t_f]$ if,

for almost all $t \in [t_0, t_f]$,

$$\dot{\boldsymbol{x}}(t) \in \boldsymbol{H}(\boldsymbol{x}) = \overline{co}(\{\boldsymbol{g}(\boldsymbol{x}) - \gamma \boldsymbol{x} | \boldsymbol{x} \in D' \in R(D)\}), \quad (5)$$

where $\overline{co}$ denotes convex closure.

Throughout this paper, the solution of the system (4) will be discussed on the basis of Definition 1.

In the following, we will introduce some concepts and definitions about the phase space and the state transition graph (referring to Refs. [5] and [8].

2.1. Domains in phase space

Consider an n-dimensional phase space $\Omega = \Omega_1 \times \Omega_2 \times \ldots \times \Omega_n$, where $\Omega_i = \{x_i \in \mathbb{R}_{\geq 0} | 0 \leq x_i \leq m_i > \max_{\boldsymbol{x} \in \Omega}(g_i(\boldsymbol{x})/\gamma_i)\}$ for some positive parameter m_i. For the threshold θ_i of x_i, it is assumed that $\theta_i < m_i$. Define the sets $e_{i1} = \{x_i \in \Omega_i | 0 \leq x_i < \theta_i\}$, $e_{i2} = \{x_i \in \Omega_i | x_i = \theta_i\}$, and $e_{i3} = \{x_i \in \Omega_i | \theta_i < x_i \leq m_i\}$. For a region $D = d_1 \times \ldots \times d_n \subset \Omega$, if $d_i \in \{e_{i1}, e_{i2}, e_{i3}\}$ for any $i \in \mathscr{I}$, then the region D is called a domain. Furthermore, if $d_i \in \{e_{i1}, e_{i3}\}$ for any $i \in \mathscr{I}$, then the region D is called a regulatory domain. It is clear that in a regulatory domain none of the variables are equal to their corresponding threshold. Moreover, if D is a domain and there is at least one integer $i \in \mathscr{I}$ such that $d_i = e_{i2}$, then the region D is said to be a switching domain and the i-th variable x_i is a switching variable of D. For convenience of discussion, the set of the indexes of all switching variables of the domain D is denoted as V_D and the sets of regulatory and switching domains are denoted as $\mathscr{D}_r$ and $\mathscr{D}_s$, respectively.

For each domain D, define the sets $A(D) = \{D' \in \mathscr{D}_s | D' \subseteq \partial D\}$ and $R(D) = \{D' \in \mathscr{D}_r | D \subseteq \partial D'\}$. The set $A(D)$ consists of the switching domains lying on the boundary of D, whereas the set $R(D)$ consists of regulatory domains whose boundary contains the domain D. Two domains, D and D', are said to be contiguous if $D \in A(D')$ or $D' \in A(D)$. For clarity of the following discussion, we define that if $D \in \mathscr{D}_r$, then $R(D) = \{D\}$; if $D \in \mathscr{D}_s$, $D \notin A(D)$.

2.2. State transition graph

Let $D, D' \in \mathscr{D}$ be two contiguous domains. We say that there exists a transition from D to D' if one of the following two properties holds.

(i) If $D' \in A(D)$, then there exist $\boldsymbol{x}_0 \in D$ and a Filippov solution $\boldsymbol{x}_t(\boldsymbol{x}_0)$ defined on a finite time interval $[0, \tau]$ such that $\boldsymbol{x}_t(\boldsymbol{x}_0) \in D$ for all $t \in [0, \tau)$, and $\boldsymbol{x}_\tau(\boldsymbol{x}_0) \in D'$.

(ii) If $D \in A(D')$, then there exist $\boldsymbol{x}_0 \in D$ and a Filippov solution $\boldsymbol{x}_t(\boldsymbol{x}_0)$ defined on a finite time interval $[0, \tau]$ such that $\boldsymbol{x}_0(\boldsymbol{x}_0) = \boldsymbol{x}_0 \in D$, and $\boldsymbol{x}_t(\boldsymbol{x}_0) \in D'$ for all $t \in (0, \tau]$.

Clearly, a transition between two different domains is accomplished in finite time.

A state transition graph is a directed graph whose vertices are the domains of the system and whose edges are the transitions between these domains. A transition path of length $(h-1)$-th is a non-empty sequence of domains $\langle D_1, D_2, \ldots, D_h \rangle$ such that, for every i, $1 \leq i < h$, there exists a transition from D_i to D_{i+1}. A transition cycle is a transition path that begins and ends with the same domain, but otherwise all the domains are different.

Consider a transition path $\langle D_1, D_2, D_3 \rangle$, where $D_2 \in \mathscr{D}_s$. The switching domain D_2 is called a transparent wall with respect to D_1 and D_3 if when the solution of Eq. (4) enters D_2 from D_1, it immediately leaves D_2 for D_3 without any residence. Clearly, the residence time in D_2 is zero when the solutions of Eq. (4) go through D_1, D_2, D_3.

3. Equilibria and stability

The PL system (4) has two kinds of equilibrium points: one kind lies inside the regulatory domains and the another kind locates on the threshold hyperplanes (Ref. [21]). The former is easily handled and known to be asymptotically stable. The latter consists of the possible homeostatic points of the regulatory system and is as important as the former but causes a difficulty for the PL formalism due to discontinuities at the thresholds. Many results have been obtained on these points, e.g.,. Refs. [5], [8], [18], [21], and [22]. Moreover, considering the circling trajectories, we usually assume that the degradation rates are equal and few results have been established to tackle the general case where the degradation rates are different. To our knowledge, there are only two works (by Snoussi *et al.*[22] and Farcot *et al.*[11]) that do not require the uniform degradation assumption. Our objective is to follow the works of Refs. [5], [8], and [11] and give some conditions for the asymptotical stability of the equilibrium point on the interconnection of the thresholds of all variables with different degradation rates.

Define $\theta = (\theta_1, \theta_2, \ldots, \theta_n)^{\mathrm{T}}$. To prove that θ is an asymptotical equilibrium point, we need make a

model transformation. Let $\xi_i = x_i - \theta_i$ and $\boldsymbol{\xi} = (\xi_1, \xi_2, \ldots, \xi_n)^{\mathrm{T}}$. Then system (4) can be rewritten as

$$\dot{\boldsymbol{\xi}} = \boldsymbol{k}(\sigma) - \gamma\xi, \quad \boldsymbol{\xi}(t_0) = \boldsymbol{\xi}_0, \tag{6}$$

where $\boldsymbol{k}(\sigma) = [k_1(\sigma), k_2(\sigma), \ldots, k_n(\sigma)]^{\mathrm{T}} = \boldsymbol{g}(\theta + \xi) - \gamma\theta$, $\sigma(t) \in \{1, 2, \ldots, N\}$ denotes the domain index at time t and N denotes the number of all possible domains. Here, it should be noted that the switching threshold of each variable of $\boldsymbol{\xi}(t)$ becomes zero.

Consider the state transition graph of the system (6). Transitions between contiguous domains often form transition cycles. It is easy to see that the solution of system (6) along the transitions which do not belong to any transition cycle will ultimately either reach a transition cycle or enter a domain and not go away after finite transitions. So we can judge whether the solution converges to the equilibrium point by analysing the transition cycles or the domain that the solution eventually reaches. In many situations, the transition cycles correspond to circling trajectories. It is almost impossible to analyse the stability of the equilibrium point, around which there exist transition cycles, just based on the state transition graph. In Theorem 1, we will focus on the case of circling trajectories by including quantitative analysis in the state transition graph and give conditions for the stability of the system in $\Omega \in \mathbb{R}^n$. Moreover, without considering the state transition graph, we will study the stability of the equilibrium point from a different angle by introducing a Lyapunov function in Theorem 2.

Before presenting Theorem 1, we need to make some more preparation. Denote $\lfloor \boldsymbol{B} \rfloor_{i_1,i_2}^{j_1,j_2}$ as the matrix obtained by deleting all the rows whose indices belong to $V_{D_{i_1}} \cup V_{D_{i_2}}$ and all the columns whose indices belong to $V_{D_{j_1}} \cup V_{D_{j_2}}$ from the matrix $\boldsymbol{B}$ denote $\lfloor g \rfloor_{i_1,i_2}$ as the vector obtained by deleting all the entries whose indices belong to $V_{D_{i_1}} \cup V_{D_{i_2}}$ from the column vector g, where V_{D_k} is the index set of all switching variables of the domain D_k. From matrix theory, it is easy to see that $\|\boldsymbol{A}y\|_2 \leq \|\boldsymbol{A}\|_2 \|y\|_2$.

Lemma 1 Consider a transition path $\langle D_1, D_2, D_3 \rangle$, where D_2 is a switching domain. The following statements hold.

(a) If the domain D_2 is a transparent wall with respect to the domains D_1 and D_3, then $V_{D_3} \subset V_{D_2}$.

(b) If the domain D_2 is not a transparent wall with respect to the domains D_1 and D_3, then $V_{D_2} \subset V_{D_3}$.

Proof a) Since D_2 is a transparent wall with respect to the domains D_1 and D_3, the resident time in D_2 is zero. Also, $\xi_i \neq 0$ and $\dot{\xi}_i$ is finite for any $i \in (\mathscr{I} - V_{D_2})$. Thus, ξ_i cannot become zero for any $i \in (\mathscr{I} - V_{D_2})$ when trajectories go through the domain D_2. This implies that $V_{D_3} \subset V_{D_2}$.

b) It is clear that $\xi_i = 0$ for any $i \in V_{D_2}$. Then $\dot{\xi}_i$ is constant in D_2 from system (6). If $\dot{\xi}_i \neq 0$, then the resident time for the system (6) in D_2 is zero. This means that the domain D_2 is a transparent wall with respect to the domains D_1 and D_3, which is a contradiction. So $\dot{\xi}_i = 0$ for any $i \in V_{D_2}$. Therefore, $\xi_i = 0$ for any $i \in V_{D_2}$ at the switching time from D_2 to D_3 (when trajectories leave the domain D_2 and enter the domain D_3). That is, there is a point in D_3 such that $\dot{\xi}_i = 0$ for any $i \in V_{D_2}$. According to the definition of the domain, $\xi_i = 0$ for any $i \in V_{D_2}$ in D_3. This implies $V_{D_2} \subset V_{D_3}$. □

Let $\Omega \subset \mathbb{R}^n$. We first study the simplest case in the presence of a transition cycle with different degradation rates. Consider the domains, $D_1, D_2, \ldots, D_{2\mu}$, where $\mu > 0$ is an integer, $D_{2i-1} \in R(\{\theta\})$ and $D_{2i} \in A(\{\theta\})$. Suppose that all transitions form a transition cycle in the sequence of $\langle D_1, D_2, \ldots, D_{2\mu}, D_1 \rangle$. We have the following lemma.

Lemma 2 Let $\mathscr{B}(0) \in \Omega$ be a sufficiently small ball around the origin. If

$$F = \|\lfloor \boldsymbol{\Phi}(1) \rfloor_{2,1}^{1,2\mu}\| \|\lfloor \boldsymbol{\Phi}(2\mu) \rfloor_{2\mu,1}^{2\mu,2\mu-1}\| \times \prod_{i=2}^{2\mu-1} \|\lfloor \boldsymbol{\Phi}(i) \rfloor_{i,i+1}^{i,i-1}\| < \rho < 1 \tag{7}$$

for some positive constant $0 < \rho < 1$, then the solution of the system (6) with initial condition $\boldsymbol{\xi}_0 \in \bigcup_{i=1}^{2\mu} (D_i \bigcap \mathscr{B}(0))$ converges to the origin as $t \to +\infty$, where $\boldsymbol{\Phi}(i) = I - \frac{1}{k_{q_i}(i)} \boldsymbol{k}(i) \boldsymbol{e}_{q_i}^{\mathrm{T}}$, $q_i \in V_{D_i} \cup V_{D_{i+1}} - V_{D_i} \cap V_{D_{i+1}}$, and $\boldsymbol{e}_{q_i} \in \mathbb{R}^n$ stands for the column vector in which only the q_i-th entry is 1 and all the other entries are 0.

Proof Under the assumption, the solution of the system (6) starting in a regulatory domain D_i $(i = 1, 3, \ldots, 2l-1)$ will reach the switching domain D_{i+1} in finite time. Then we need only to analyse the solutions starting in the switching domains. Without loss of generality, take $\boldsymbol{\xi}_0(t_0) = \boldsymbol{\xi}_0 \in D_{2l} \cap \mathscr{B}(\theta)$. Denote t_i as the switching times for $i \in Z^+$ and ξ_{p_j} as the switching variable of the switching domain D_{2j}, $\{p_j\} = V_{D_{2j}}$, for $j = 1, 2, \ldots, \mu$. It is easy to see that $\xi(t) \in D_1$ for $t \in (t_0, t_1)$ and ξ_{p_1} is the switching variable at time t_1. Evidently, $\xi_{p_1}(t_0) \neq 0$, $\xi_{p_1}(t_1) = 0$

and $k_{p_1}(1) \neq 0$. (If $k_{p_1}(1) = 0$, it would take infinite time for the solution to reach the switching domain D_2.) It follows from Eq. (5) that

$$t_1 - t_0 = \frac{1}{\gamma_{p_1}} \ln \frac{k_{p_1}(1) - \xi_{p_1}(t_0)\gamma_{p_1}}{k_{p_1}(1)}.$$

Then for any $j \in \mathscr{I}$,

$$\begin{aligned}
\xi_j(t_1) &= \frac{k_j(1)}{\gamma_j} + \mathrm{e}^{-\gamma_j(t_1-t_0)}\left(\xi_j(t_0) - \frac{k_j(1)}{\gamma_j}\right) \\
&= \frac{k_j(1)}{\gamma_j} + \left(1 - \frac{\xi_{p_1}(t_0)\gamma_{p_1}}{k_{p_1}(1)}\right)^{-\gamma_j/\gamma_{p_1}} \\
&\quad \times \left(\xi_j(t_0) - \frac{k_j(1)}{\gamma_j}\right) \\
&= \frac{k_j(1)}{\gamma_j} + \left[1 + \left(-\frac{\gamma_j}{\gamma_{p_1}}\right) \times \left(-\frac{\xi_{p_1}(t_0)\gamma_{p_1}}{k_{p_1}(1)}\right)\right] \\
&\quad \times (\xi_j(t_0) - \frac{k_j(1)}{\gamma_j}) + o(\xi_{p_1}^2(t_0)) \\
&= \frac{k_j(1)}{\gamma_j} + \xi_j(t_0) + \frac{\xi_{p_1}(t_0)\xi_j(t_0)\gamma_j}{k_{p_1}(1)} \\
&\quad - \frac{k_j(1)}{\gamma_j} - \frac{\xi_{p_1}(t_0)k_j(1)}{k_{p_1}(1)} + o(\xi_{p_1}^2(t_0)) \\
&= \xi_j(t_0) + \frac{\xi_{p_1}(t_0)\xi_j(t_0)\gamma_j}{k_{p_1}(1)} \\
&\quad - \frac{\xi_{p_1}(t_0)k_{j1}}{k_{p_1}(1)} + o(\xi_{p_1}^2(t_0)). \qquad (8)
\end{aligned}$$

Rewriting Eq. (8) in matrix form, we have

$$\begin{aligned}
\boldsymbol{\xi}(t_1) &= (I - \frac{1}{k_{p_1}(1)}\boldsymbol{k}(1)\boldsymbol{e}_{p_1}^{\mathrm{T}} + \frac{1}{k_{p_1}(1)}\gamma\boldsymbol{\xi}(t_0)\boldsymbol{e}_{p_1}^{\mathrm{T}} \\
&\quad + o(\mathbf{1}_n\boldsymbol{\xi}^{\mathrm{T}}(t_0)\boldsymbol{e}_{p_1}\boldsymbol{e}_{p_1}^{\mathrm{T}}))\xi(t_0) \\
&\triangleq \boldsymbol{A}(t_1)\boldsymbol{\xi}(t_0),
\end{aligned}$$

where $\mathbf{1}_n = [1, 1, \ldots, 1]^{\mathrm{T}} \in \mathbb{R}^n$. Note that $\xi_{p_1}(t_1) = 0$ and $\xi_{p_l}(t_0) = 0$. Then we have

$$\lfloor \boldsymbol{\xi}(t_1) \rfloor_1 = \lfloor \boldsymbol{A}(t_1) \rfloor_1^{\mu} \lfloor \boldsymbol{\xi}(t_0) \rfloor_{\mu} = \lfloor \boldsymbol{A}(t_1) \rfloor_{1,2}^{1,2\mu} \lfloor \boldsymbol{\xi}(t_0) \rfloor_{\mu}.$$

Thus,

$$\|\boldsymbol{\xi}(t_1)\|_2 \leq \|\lfloor \boldsymbol{A}(t_1) \rfloor_{1,2}^{1,2\mu}\| \|\boldsymbol{\xi}(t_0)\|_2.$$

Similarly, it can be obtained that

$$\|\xi(t_j)\|_2 \leq \|\lfloor \boldsymbol{A}(t_j) \rfloor_{2j-1,2j}^{2j-1,2j-2}\| \|\xi(t_{j-1})\|_2, (2 \leq j \leq \mu),$$

where

$$\begin{aligned}
\boldsymbol{A}(t_j) &= I - \frac{1}{k_{p_j}(2j-1)}\boldsymbol{k}(2j-1)\boldsymbol{e}_{p_j}^{\mathrm{T}} \\
&\quad + \frac{1}{k_{p_j}(2j-1)}\gamma\xi(t_{j-1})\boldsymbol{e}_{p_j}^{\mathrm{T}} \\
&\quad + o(\mathbf{1}_n\xi^{\mathrm{T}}(t_{j-1})\boldsymbol{e}_{p_j}\boldsymbol{e}_{p_j}^{\mathrm{T}}).
\end{aligned}$$

On the other hand, it is easy to see that $V_{D_{2\mu}} \cup V_{D_1} - V_{D_{2\mu}} \cap V_{D_1} = V_{D_{2\mu}} \cup V_{D_1} = V_{D_{2\mu}} \cup V_{D_{2\mu-1}} = V_{D_{2\mu}}$ and $V_{D_i} \cup V_{D_{i+1}} - V_{D_i} \cap V_{D_{i+1}} = V_{D_i} \cup V_{D_{i+1}} = V_{D_i} \cup V_{D_{i-1}} = V_{D_i}$ for $i = 2, 4, \ldots, 2\mu - 2$. Thus, $\|\lfloor \boldsymbol{\Phi}(i) \rfloor_{V_{D_i} \cup V_{D_{i+1}}}^{V_{D_i} \cup V_{D_{i-1}}}\| = \|\lfloor \boldsymbol{\Phi}(2\mu) \rfloor_{V_{D_{2\mu}} \cup V_{D_1}}^{V_{D_{2\mu}} \cup V_{D_{2\mu-1}}}\| = 1$ ($i = 2, 4, \ldots, 2\mu - 2$). Also, since $\boldsymbol{\xi}_0 \in \mathscr{B}(\theta)$ is sufficiently small, $\boldsymbol{\xi}(t_i)$ for $1 \leq i \leq \mu$ are also sufficiently small. Then, the condition (7) implies that

$$\|\lfloor \boldsymbol{A}(t_1) \rfloor_{1,2}^{1,2\mu}\| \prod_{j=2}^{\mu} \|\lfloor \boldsymbol{A}(t_j) \rfloor_{2j-1,2j}^{2j-1,2j-2}\| < \rho < 1.$$

Thus, $\|\boldsymbol{\xi}(t_\mu)\|_2 < \rho\|\boldsymbol{\xi}(t_0)\|_2$. By induction, we easily see that when the solution of the system (6) returns to the domain $D_{2\mu}$ for the m-th time, $\|\boldsymbol{\xi}(t_{i\mu})\|_2 < \rho^m\|\boldsymbol{\xi}(t_0)\|_2$ for any $m \in \mathbb{Z}^+$. Similarly, it can be proved that when the solution of the system (6) returns to the domain D_{2j} for the m-th time, $\|\boldsymbol{\xi}(t_{i\mu+j})\|_2 \leq \rho^i\|\boldsymbol{\xi}(t_j)\|_2$ for any $m \in \mathbb{Z}^+$ and $j = 1, 2, \ldots, \mu - 1$. It follows that $\lim\limits_{i \to +\infty} \boldsymbol{\xi}(t_i) = 0$. Consequently, $\lim\limits_{t \to +\infty} \boldsymbol{\xi}(t) = 0$. (For linear systems, the system gains are finite in finite time.) □

Remark 1 It should be noted that in Lemma 2, we do not assume that each variable ξ_i activates the production of the next variable ξ_{i+1}, which is different from Ref. [11].

Remark 2 When the system (6) is considered in a sufficiently small ball around the origin, the term $-\gamma\xi$ is very small in comparison with the nonzero constant term $\boldsymbol{k}(\sigma)$ and the nonzero term $\boldsymbol{k}(\sigma)$ plays a main role in determining the solution trajectories. So, as shown in the proof of Lemma 2, the dynamic variation of the system (6) in each domain D_i can be described by $\boldsymbol{\Phi}(i)$ and the solution gain in each domain D_i can be approximately measured by $\|\lfloor \boldsymbol{\Phi}(i) \rfloor_{i,i+1}^{i,i-1}\|$ in view of the fact that the switching variables remain zero in D_i.

In the following, we will consider the stability of the system (6) when there exist multiple transition cycles under the following two assumptions.

Assumption 1 There are altogether l transition cycles, denoted by $c_1, c_2, \ldots, c_l$. The path sequence of each cycle c_j ($j = 1, 2, \ldots, l$) as $\{D_{1j}, D_{2j}, \ldots, D_{\mu_j j}, D_{1j}\}$, where μ_j is the number of domains in the transition cycle c_j. Each domain D_{ij} ($i = 1, 2, \ldots, \mu_j, j = 1, 2, \ldots, l$) is assumed to have m_{ij} switching variables, denoted by $\{\xi_{p_{ij}^1}, \xi_{p_{ij}^2}, \ldots, \xi_{p_{ij}^{m_{ij}}}\}$.

Assumption 2 Denote $\mathscr{D}_{tc} = \{D_{kj} \mid j = 1, \ldots, l, k = 1, \ldots, \mu_j\}$. There are no transitions from

any domain $D_i \in (\mathscr{D}_s \cup \mathscr{D}_r - \mathscr{D}_{tc})$ to any domain $D_k \in \mathscr{D}_{tc}$.

Assumption 3 The solution trajectories starting in a domain $D_i \in (\mathscr{D}_s \cup \mathscr{D}_r - \mathscr{D}_{tc})$ finally converge to the domain $\{\theta\}$.

Figure 1 shows an example of a 3-dimensional phase space and figure 2 shows an example of a state transition graph in the phase space as shown in Fig. 1. It is easy to see that the assumptions 1 and 2 are satisfied and there are totally four transition circles: $\langle D_1, D_2, D_3, D_6, D_9, D_8, D_7, D_4, D_1\rangle$, $\langle D_7, D_4, D_1, D_{10}, D_{11}, D_{12}, D_{15}, D_{18}, D_{17}, D_{16}, D_7\rangle$, $\langle D_{10}, D_{11}, D_{12}, D_{15}, D_{18}, D_{17}, D_{16}, D_{13}, D_{10}\rangle$, and $\langle D_{19}, D_{20}, D_{21}, D_{24}, D_{27}, D_{26}, D_{25}, D_{22}, D_{19}\rangle$. Since transitions describe the tendency of the solutions of the system and different solutions may go through the same domains, then the transition cycles are allowed to be connected and share common domains.

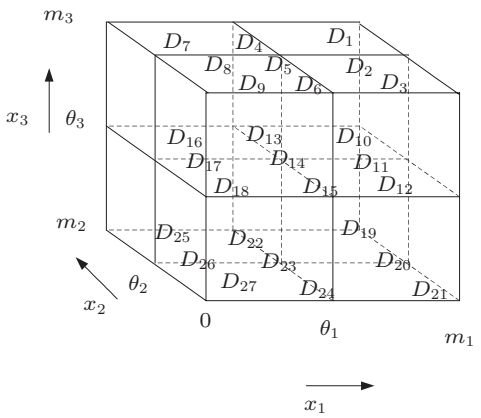


Fig. 1. One example of a 3-dimensional phase space.

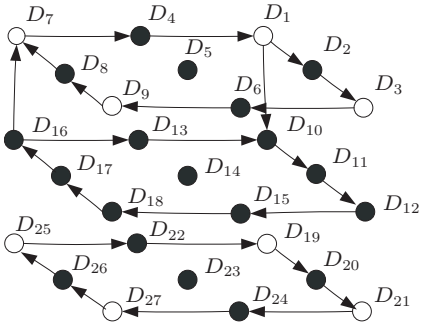


Fig. 2. One example of a state transition graph in the phase space as shown in Fig. 1.

Theorem 1 Under the assumptions 1, 2, and 3, if

$$F_j = \|\lfloor \boldsymbol{\Phi}_j(1)\rfloor_{1j,2j}^{1j,\mu_j j}\| \|\lfloor \boldsymbol{\Phi}_j(\mu_j)\rfloor_{\mu_j j,1j}^{\mu_j j,(\mu_j-1)j}\| \times \prod_{i=2}^{\mu_j-1} \|\lfloor \boldsymbol{\Phi}_j(i)\rfloor_{ij,(i+1)j}^{ij,(i-1)j}\| < \rho < 1, \quad (9)$$

for $j = 1, 2, \ldots, l$, then the system (6) is locally asymptotically stable, where $0 < \rho < 1$ is a scalar,

$$\boldsymbol{\Phi}_j(i) = I - \frac{1}{k_{q_{ij}}(ij)} \boldsymbol{k}(ij) \boldsymbol{e}_{q_{ij}}^{\mathrm{T}},$$

$q_{ij} \in V_{D_{(i+1)j}} \cup V_{D_{ij}} - V_{D_{(i+1)j}} \cap V_{D_{ij}}$ and $\boldsymbol{e}_{q_{ij}} \in \mathbb{R}^n$ stands for the column vector in which only the q_{ij}-th entry is 1 and all the other entries are 0.

Proof Since what we considered is the local stability of the system (6), we can study the solution of the system (6) in a sufficiently small ball $\mathscr{B}(0)$ around the origin by calculating the system gain along each transition cycle and then following the lines of the proof of Lemma 2 this theorem can be proved. However, four points should be emphasized.

1) If D_{ij} is a transparent wall, by Lemma 1, $V_{D_{ij}} \cup V_{D_{(i+1)j}} = V_{D_{ij}}$. Hence, $q_{ij} \in V_{D_{ij}}$. Then by simple calculations, it is easy to see that $\|\lfloor \boldsymbol{\Phi}_j(i)\rfloor_{ij,(i+1)j}^{ij,(i-1)j}\| = 1$.

2) If D_{ij} is not a transparent wall, by Lemma 1, $V_{D_{(i+1)j}} \cup V_{D_{ij}} = V_{D_{(i+1)j}}$ and $V_{D_{(i+1)j}} \cap V_{D_{ij}} = V_{D_{ij}}$. Thus, $V_{D_{(i+1)j}} \cup V_{D_{ij}} - V_{D_{(i+1)j}} \cap V_{D_{ij}}$ is the set of the variables which vanish to zero when the solution goes from the domain D_i to the domain D_{i+1}.

3) Consider the solution of the system (6) traveling along the path $\langle D_{(i-1)j}, D_{ij}, D_{(i+1)j}\rangle$. Note that in each domain, the switching variables are kept zero. Thus, ξ_k is zero for any $k \in V_{D_{ij}} \cup V_{D_{(i-1)j}}$ at the switching time from $D_{(i-1)j}$ to D_{ij} whereas ξ_k is zero for any $k \in V_{D_{ij}} \cup V_{D_{(i+1)j}}$ at the switching time from D_{ij} to $D_{(i+1)j}$. So, we use the matrix $\lfloor \boldsymbol{\Phi}_j(i)\rfloor_{ij,(i+1)j}^{ij,(i-1)j}$ to calculate the system gains.

4) The solution trajectories starting in a domain $D_i \in \mathscr{D}_{tc}$ either finally converge to a domain $D_j \in \mathscr{D}_s \cup \mathscr{D}_r - \mathscr{D}_{tc}$ or remain in the domains belonging to $\mathscr{D}_{tc}$. Then from the assumption 3 and following the lines of the proof of Lemma 2, this theorem can be proved. □

Remark 3 The condition (9) is only related to the constant terms of the right-hand side of the system in each domain and the switching variables of every two contiguous domains in each transition cycle. We can check the condition (9) in three steps: i) perform a model transformation as that in system (6); ii) find out all possible transition cycles in the state transition graph and the switching variables of each domain in each transition cycle and then check whether assumptions 2 and 3 are satisfied; iii) check whether the condition (9) is satisfied.

In Ref. [5], Casey *et al.* investigated the stability of an equilibrium set contained in a switching domain. They showed that the equilibrium set is asymptotically stable if every contiguous regulatory domain D_σ has a transition entering the switching domain. In particular, if the equilibrium set is a single point and lies on the intersection of the thresholds of all variables, the equilibrium set is asymptotically stable. In this case, it is easy to see that $\mathrm{sgn}(\xi_j)k_j(\sigma) < 0$ for any $j \in \mathscr{I}$ in each regulatory domain D_σ, where

$$\mathrm{sgn}(\xi_j) = \begin{cases} 1, & \xi_j > 0, \\ 0, & \xi_j = 0, \\ -1, & \xi_j < 0. \end{cases} \tag{10}$$

Motivated by this, we will use the Lyapunov approach to analyse the system (6). Though numerous results have been obtained with the Lyapunov approach for switching systems,[27] few can be applied directly to the system (6) due to the fact that all subsystems of system (6) do not have a common equilibrium point and the specific solution cannot be obtained in each regulatory domain.

Theorem 2 Let $\Omega \subset \mathbb{R}^n$. If $\sum\limits_{j=1}^{n} \mathrm{sgn}(\xi_j)k_j(\sigma) \leq 0$ in each regulatory domain $D_\sigma \in R(\{\theta\})$, then the system (6) is asymptotically stable. Further, if $\sum\limits_{j=1}^{n} \mathrm{sgn}(\xi_j)k_j(\sigma) < 0$ for each $D_\sigma \in R(\{\theta\})$, the solution of the system (6) will approach θ in finite time.

Proof Define a Lyapunov function for the system (6) as follows:

$$V(t) = \sum_{j=1}^{n} |\xi_j(t)|.$$

Let $\varphi(\sigma) = [\varphi_1(\sigma), \varphi_2(\sigma), \ldots, \varphi_n(\sigma)]^{\mathrm{T}}$ be an arbitrary vector in a domain D_σ. Calculating $\dot{V}(t)$, we have

$$\begin{aligned} \dot{V}(t) \in & \sum_{j=1}^{n} \overline{co}(\{\mathrm{sgn}(\varphi_j(\sigma))(k_j(\sigma) \\ & - \gamma_j\xi_j(t)) \mid \varphi(\sigma) \in D_\sigma, D_\sigma \in R(D)\}) \\ \leq & \max_{\sigma} \Bigg\{ \sum_{j=1}^{n} [\mathrm{sgn}(\varphi_j(\sigma))k_j(\sigma) \\ & - \gamma_j \mathrm{sgn}(\xi_j(t))\xi_j(t)] \mid \varphi(\sigma) \in D_\sigma, D_\sigma \in R(D) \Bigg\} \\ = & \eta - \sum_{j=1}^{n} \gamma_{\min} \mathrm{sgn}(\xi_j(t))\xi_j(t) \\ \leq & - \sum_{j=1}^{n} \gamma_{\min} \mathrm{sgn}(\xi_j(t))\xi_j(t) \\ = & -\gamma_{\min} V(t), \end{aligned} \tag{11}$$

where

$$\eta = \max_{D_\sigma \in R(\{\theta\})} \left\{ \sum_{j=1}^{n} \mathrm{sgn}(\varphi_j(\sigma))k_j(\sigma) \right\} \leq 0$$

and $\gamma_{\min} = \min\limits_{j}\{\gamma_j\} > 0$. It follows that $\dot{V}(t)/V(t) < -\gamma_{\min}$. Thus, $V(t) \leq V(0)\, \mathrm{e}^{-\gamma_{\min} t}$. This means that $\boldsymbol{\xi}(t)$ vanishes exponentially fast with a speed of $\gamma_{\min}$ as $t \to +\infty$. Moreover, if $\sum\limits_{j=1}^{n} \mathrm{sgn}(\xi_j)k_j(\sigma) < 0$ for each regulatory domain D_σ, then it follows from formula (11) that $\dot{V}(t) \leq \eta < 0$. Consequently, $\xi(t)$ will approach θ in finite time. □

Remark 4 It should be noted that all the analysis in Theorem 2 is based on the differential inclusion and nonsmooth analysis, which allows the Lyapunov function to be nonsmooth.

Remark 5 Generally, the Lyapunov function is adopted in the quadratic form, but invalid here due to the special structure of the system (6). Moreover, it should be pointed out that the common Lyapunov function adopted in Theorem 2 does not require that each subsystem should be asymptotically stable, different from the generally used Lyapunov functions where all subsystems should be asymptotically stable.

Remark 6 The condition given in Theorem 2 is much simpler than that given in Theorem 1 and it is only related to the constant terms of the right-hand side of the system in each regulatory domain. Also, it needs no information about the transition information and can be applied to the cases not covered by Refs. [5] and [8]. Moreover, since the approach is based on Lyapunov functions, the results obtained in Theorem 2 might be extended to the time-delay case. Nevertheless, the use of Lyapunov functions may neglect the information of the relationship between two contiguous domains, which makes the results obtained somewhat conservative.

4. Numerical examples

To illustrate Theorems 1 and 2, let us first consider a two-gene network with the following equations:

$$\begin{cases} \dot{x}_1 = \kappa_{11} s^+(x_2, \theta_2) s^-(x_1, \theta_1) \\ \qquad + \kappa_{12} s^+(x_2, \theta_2) s^+(x_1, \theta_1) - \gamma_1 x_1, \\ \dot{x}_2 = \kappa_{21} s^-(x_2, \theta_2) s^-(x_1, \theta_1) \\ \qquad + \kappa_{22} s^+(x_2, \theta_2) s^-(x_1, \theta_1) - \gamma_2 x_2, \end{cases} \tag{12}$$

in three cases:

Case 1 $\kappa_{11}=2$, $\kappa_{12}=3$, $\kappa_{21}=4$, $\kappa_{22}=2.5$, $\gamma_1=1$, $\gamma_2=2$, $\theta_1=\theta_2=1$;

Case 2 $\kappa_{11}=3, \kappa_{12}=2, \kappa_{21}=2, \kappa_{22}=3$, $\gamma_1=1$, $\gamma_2=1$, $\theta_1=\theta_2=1$;

Case 3 $\kappa_{11}=4, \kappa_{12}=3, \kappa_{21}=3, \kappa_{22}=2$ and $\gamma_1=2$, $\gamma_2=1$, $\theta_1=\theta_2=1$.

Let $\xi_1=x_1-1$ and $\xi_2=x_2-1$. The system (12) can be rewritten as

$$\begin{cases} \dot{\xi}_1 = \kappa_{11}s^+(\xi_2+1,\theta_2)s^-(\xi_1+1,\theta_1) \\ \qquad +\kappa_{12}s^+(\xi_2+1,\theta_2)s^+(\xi_1+1,\theta_1) \\ \qquad -\gamma_1-\gamma_1\xi_1, \\ \dot{\xi}_2 = \kappa_{21}s^-(\xi_2+1,\theta_2)s^-(\xi_1+1,\theta_1) \\ \qquad +\kappa_{22}s^+(\xi_2+1,\theta_2)s^-(\xi_1+1,\theta_1) \\ \qquad -\gamma_2-\gamma_2\xi_2. \end{cases} \tag{13}$$

By simple calculations, we have that the system (12) has the same transitions for all three cases as shown in Fig. 3. It is clear that the assumptions 1 and 2 are satisfied and there is only one transition circle c_1, whose path sequence is $\langle D_1,\ D_2,\ D_3,\ D_4,\ D_5,\ D_6,\ D_7,\ D_8,\ D_1\rangle$. Clearly, $\mu_1=8$. Moreover, in the domain D_9, the dynamics of the system (12) is $\dot{\xi}_1=\dot{\xi}_2=0$. Then it is easy to see that the solution trajectories starting in the domain D_9 remain in the domain D_9 all the time in the absence of disturbances. Thus, the assumption 3 is satisfied.

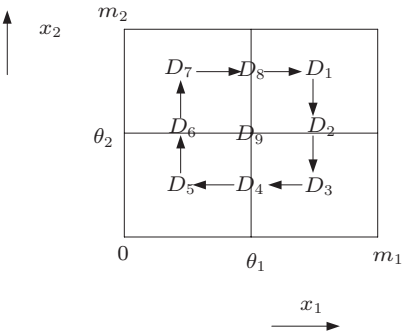


Fig. 3. State transition graph of the system (12).

Consider Case 1. Note that $D_{11}=D_1$, $D_{21}=D_2$, and $D_{81}=D_8$. Then, $V_{D_1}\cup V_{D_2}-V_{D_1}\cap V_{D_2}=\{2\}$, i.e., $q_{11}=2$. Then

$$\begin{aligned} \|\lfloor \boldsymbol{\Phi}_1(1)\rfloor_{11,21}^{11,81}\| &= \|\lfloor I-\frac{1}{k_2(1)}\boldsymbol{k}(1)\boldsymbol{e}_2^{\mathrm{T}}\rfloor_{1,2}^{1,8}\| \\ &= \|\lfloor T\rfloor_{1,2}^{1,8}\| = \|1\| = 1, \end{aligned}$$

where $T=\begin{bmatrix}1&1\\0&0\end{bmatrix}$. Similarly, it can be obtained that

$$\begin{aligned} \|\lfloor \boldsymbol{\Phi}_1(2)\rfloor_{21,31}^{21,11}\| &= \|\lfloor \boldsymbol{\Phi}_1(4)\rfloor_{41,51}^{41,31}\| = \|\lfloor \boldsymbol{\Phi}_1(6)\rfloor_{61,71}^{61,51}\| \\ &= \|\lfloor \boldsymbol{\Phi}_1(8)\rfloor_{81,11}^{81,71}\| = 1, \\ \|\lfloor \boldsymbol{\Phi}_1(3)\rfloor_{31,41}^{31,21}\| &= 2, \end{aligned}$$

and

$$\|\lfloor \boldsymbol{\Phi}_1(5)\rfloor_{51,61}^{51,41}\| = \|\lfloor \boldsymbol{\Phi}_1(7)\rfloor_{71,81}^{71,61}\| = 0.5.$$

Thus, $F_1=0.5$. Then applying Theorem 1, we can easily see that the system (12) is locally asymptotically stable at D_9 (i.e., $\{\theta\}$). It should be noted that $\sum_{j=1}^{n}\mathrm{sgn}(\xi_j)k_j(\sigma)>0$ in D_7 and thus Theorem 2 cannot be applied.

For Case 2, it can be obtained that $F_1=1$ and thus Theorem 1 cannot be applied. But note that $\sum_{j=1}^{n}\mathrm{sgn}(\xi_j)k_j(\sigma)=0$ in each regulatory domain. Then, applying Theorem 2, the system (12) is asymptotically stable at D_9.

For Case 3, it can also be obtained that $F_1=0.25$ and $\sum_{j=1}^{n}\mathrm{sgn}(\xi_j)k_j(\sigma)\le 0$ in each regulatory domain. Both conditions of Theorems 1 and 2 are satisfied and thus the system (12) is asymptotically stable at D_9.

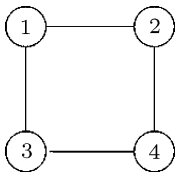


Fig. 4. State trajectories of the system (12) for Case 1.

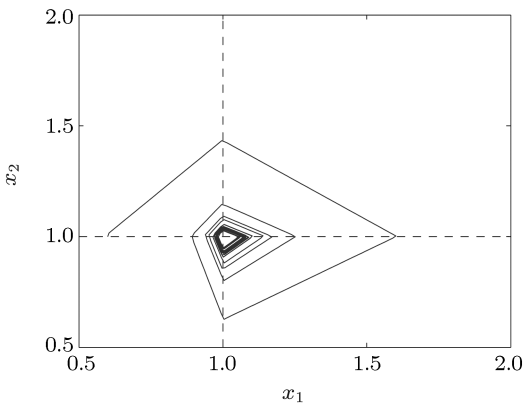


Fig. 5. State trajectories of the system (12) for Case 2.

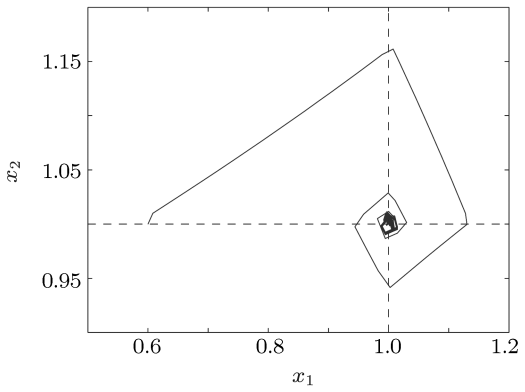


Fig. 6. State trajectories of the system (12) for Case 3.

Figures 4–6 show the state trajectories of the system (12) for Cases 1–3. It is clear that all state trajectories asymptotically converge to the switching domain D_9, which is consistent with Theorems 1 and 2.

From Cases 1–3, the approaches used in Theorems 1 and 2 have no absolute advantage over each other. They can be combined to analyse the stability of the PL models of genetic regulatory networks. To illustrate this, we present the following example.

Consider a three-gene network with the following equations:

$$\begin{cases} \dot{x}_1 = \kappa_{11}s^+(x_2,\theta_2)s^-(x_1,\theta_1) \\ \qquad + \kappa_{12}s^+(x_2,\theta_2)s^+(x_1,\theta_1) - \gamma_1 x_1, \\ \dot{x}_2 = \kappa_{21}s^-(x_2,\theta_2)s^-(x_1,\theta_1) \\ \qquad + \kappa_{22}s^+(x_2,\theta_2)s^-(x_1,\theta_1) - \gamma_2 x_2, \\ \dot{x}_3 = \kappa_{31} - \gamma_3 x_3, \end{cases} \tag{14}$$

where $\kappa_{11} = 2$, $\kappa_{12} = 3$, $\kappa_{21} = 4$, $\kappa_{22} = 2.5$, $\kappa_{31} = 3$, $\gamma_1 = 1$, $\gamma_2 = 2$, $\gamma_3 = 3$, and $\theta_1 = \theta_2 = \theta_3 = 1$.

Let $\xi_1 = x_1 - 1$, $\xi_2 = x_2 - 1$, and $\xi_3 = x_3 - 1$. The system (14) can be rewritten as

$$\begin{cases} \dot{\xi}_1 = \kappa_{11}s^+(\xi_2+1,\theta_2)s^-(\xi_1+1,\theta_1) \\ \qquad + \kappa_{12}s^+(\xi_2+1,\theta_2)s^+(\xi_1+1,\theta_1) \\ \qquad - \gamma_1 - \gamma_1\xi_1, \\ \dot{\xi}_2 = \kappa_{21}s^-(\xi_2+1,\theta_2)s^-(\xi_1+1,\theta_1) \\ \qquad + \kappa_{22}s^+(\xi_2+1,\theta_2)s^-(\xi_1+1,\theta_1) \\ \qquad - \gamma_2 - \gamma_2\xi_2, \\ \dot{\xi}_3 = \kappa_{31} - \gamma_3 - \gamma_3\xi_3 = -\gamma_3\xi_3. \end{cases} \tag{15}$$

By simple calculations, the system (14) has the transitions shown in Fig. 7.

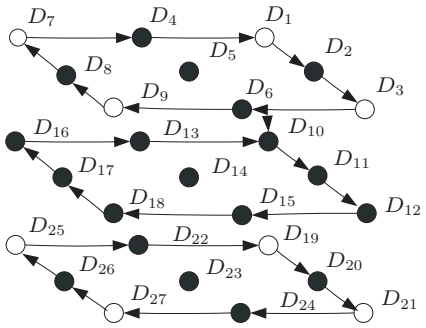


Fig. 7. The state transition graph for the system (14) with the phase space shown in Fig. 1.

It is clear that the assumptions 1 and 2 are satisfied and there are three transition circles in total c_1, c_2, c_3, whose path sequences are $\langle D_1, D_2, D_3, D_6, D_9, D_8, D_7, D_4, D_1\rangle$, $\langle D_{10}, D_{11}, D_{12}, D_{15}, D_{18}, D_{17}, D_{16}, D_{13}, D_{10}\rangle$, and $\langle D_{19}, D_{20}, D_{21}, D_{24}, D_{27}, D_{26}, D_{25}, D_{22}, D_{19}\rangle$, respectively. Moreover, in the domains D_5 and D_{13}, the system (15) can be written as

$$\begin{cases} \dot{\xi}_1 = 0, \\ \dot{\xi}_2 = 0, \\ \dot{\xi}_3 = -\gamma_3\xi_3. \end{cases}$$

Then it is easy to see that the solution trajectories starting in the domains D_5 and D_{23} finally converge to the domain D_{14} (i.e., $\{\theta\}$). Moreover, it is easy to see that there are no transitions from or to the domain D_{14}. Clearly, the assumption 3 is satisfied.

However, by simple calculations, we have $F_1 > 1, F_2 > 1, F_3 > 1$ and thus Theorem 1 can be directly applied. To analyse the stability of the system, we can combine Theorems 1 and 2. Consider the transition circle c_1 without considering the third variable ξ_3. As discussed in case 1) of the system (12), it is easy to see that

$$\lim_{t\to+\infty}\xi_1(t) = \lim_{t\to+\infty}\xi_2(t) = 0.$$

On the other hand, construct a Lyapunov function $V = |\xi_3|$. Calculating $\dot{V}$, we have $\dot{V} = -\gamma_3 V(t) \le 0$, which means that $\lim_{t\to+\infty}\xi_3(t) = 0$. Similar results can be obtained for the transition circles c_2 and c_3. That is, the system (14) is locally asymptotically stable.

Figure 8 shows the state trajectories of the system (14). It is clear that the state trajectories asymptotically converge to the switching domain D_{14}, which is

consistent with our theoretical analysis.

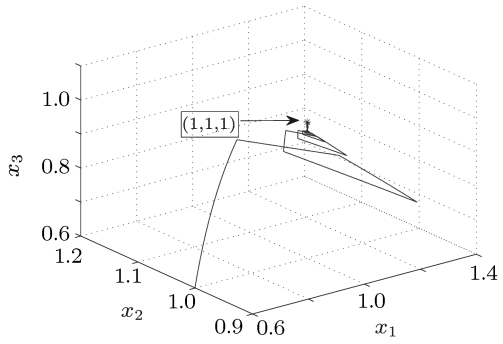


Fig. 8. State trajectories of the system (14).

5. Conclusions

This paper investigates the stability of the PL models of genetic regulatory networks. Sufficient conditions are presented on the stability of the equilibria lying on the intersection of the thresholds of all variables. All of the obtained conditions are only related to the constant terms on the right-hand side of the differential equation. It is worthwhile noting that future investigations could be directed towards considering the time-delay case, which is more general.

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