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Function perturbation of mix-valued logical networks with impacts on limit sets

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ABSTRACT

In this paper, function perturbation of mix-valued logical networks is first proposed and investigated via semi-tensor product (STP) of matrices. Motivated by the concept of one-bit perturbation in Boolean networks, the definition of general perturbation in mix-valued logical networks is presented and the algebraic expression of the perturbed networks is given by STP. The impacts of function perturbation on fixed points and limit cycles are discussed by analyzing the changes of transition matrix in algebraic form. In addition to identifying one perturbation in mix-valued logical networks, a new way to identify multi-perturbation is given. This new method can be used in producing or removing fixed points and thus exerting effects on limit cycles. All of the theoretical results also hold for Boolean and k-valued logical networks. Finally, the results of perturbation identification are applied to the WNT5A gene network, which shows broad prospects of application.

1. Introduction

In 1969, Kauffman presented “the behavior of large nets of randomly interconnected binary (on-off) ‘genes’” by utilizing Boolean networks for the first time [1]. Since then, Boolean networks came into widespread use in plenty of areas. A Boolean network is a set of interacting nodes where each node takes value from {0,1}. Gene states can be quantized to two levels: True or False [2]. And the states of genes affect one another by the following logical rules. Thus, Boolean networks became a powerful tool in describing and analyzing gene networks as they can describe important characteristics of genes and their interactions. In the meantime, Boolean networks have been widely applied in neural networks, economic networks and many other fields. For instance, their potential as learning systems was investigated and exploited by employing metaheuristic methods [3]. The authors in [4] studied the stabilization and controllability issues of the hybrid switching and impulsive higher order Boolean networks. Their properties have also been studied sufficiently, such as topological structure and dynamic characteristics [5,6]. The attractors (fixed points and cycles) of a Boolean network play an important role in representing features of living organisms. For example, in cells' interactions, attractors of Boolean networks indicate the cell types [7] and some attractors can form a limit cycle. Hence, finding attractors is of significance and has been well studied [8–10]. However, the lack of useful tool for logical process leads to the difficulty in analyzing Boolean networks.

In recent years, with the emergence of a new matrix product, called semi-tensor product (STP) proposed in [11], many complex problems which hindered the theoretical and practical development of Boolean networks have been solved. STP is a generalization of the conventional matrix product, which can compute the product of arbitrary matrices without considering whether the dimensions of two multiplied matrices match with each other. Moreover, STP has advantages over conventional matrix product since it remains all the major properties of conventional matrix product and satisfies certain pseudo-commutative properties [2].

STP approach has been successfully applied to Boolean networks. Cheng et al. [12] defined Boolean control networks and investigated their structures and realization problems. In [13], the controllability and observability of Boolean control networks were studied and the identification problem was solved. Besides, partial stability of Boolean networks and stabilization of Boolean control networks were investigated in [14]. Recently, the authors in [15] presented and discussed l_1-gain and model reduction problems of Boolean control networks, which is also based on STP. Furthermore, the general singular Boolean networks were proposed and discussed in [16].

As we mentioned above, Boolean network is significant and becomes a hot and fruitful topic in biology networks. But it has limitations in describing more precise systems such as neural networks. Therefore, k-valued networks [17,18] and mix-valued networks [19]

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come forth, which are natural generalizations of Boolean networks. For example, in [19], the definition, calculation as well as the main properties of mix-valued logic are systematically proposed.

Robustness is an important property in Boolean networks, k-valued networks and mix-valued networks. Perturbation of the states in biology networks is a crucial aspect of robustness. Fixed points and limit cycles are the main characteristics of steady-state properties so it is necessary to analyze the effects on fixed points and limit cycles when discussing perturbations. In Boolean networks, perturbation of the states has been well studied by plenty of methods, such as statistical method [20] and analytical method [21]. However, these methods did not give a certain algebraic formulation to solve perturbation problems. Recently, Meng and Feng [22] have applied STP to investigate the changes of fixed points and limit cycles under perturbations of Boolean networks, which is the first to give a clear algebraic formulation of perturbations of the states. Also, in [22], a method of identifying one-bit perturbation was presented and applied to a D. melanogaster segmentation polarity gene network.

To the best of our knowledge, there are few literatures about the perturbations in mix-valued logical networks. Motivated by [22], in this paper, we use the powerful tool STP to study function perturbation problems in mix-valued logical networks. The advantage of using semi-tensor product is that it gives us algebraic formulations to depict the changes of fixed points and cycles. So the robustness can be easily solved by just calculating the transition matrix of the mix-valued logical networks. Besides, mix-valued logical networks render us more precise descriptions on diverse systems than Boolean networks since in mix-valued logical networks, each node can be perturbed to several possible values, not only 0 and 1.

In our paper, the definition and the algebraic form of general perturbation in mix-valued logical networks are first presented. We have obtained results about the changes of fixed points and cycles under perturbations in mix-valued logical networks and given equivalent conditions in the form of algebraic equalities. Through those results, we can see how fixed points and cycles changed with the influence of perturbation. Compared to the existing literatures [20,21], the results in our paper are easy to understand and much simpler to be used in addressing perturbation problems due to clear algebraic formulations. Moreover, all the results in this paper have a wide range of applications since they also hold for Boolean networks and k-valued logical networks. Identification problem is considered in this paper as two aspects: identifying single general perturbation and identifying multi-perturbation in mix-valued logical networks, which can be used to change limit set of a network, such as producing new attractors or removing existing attractors. Finally, the methods of identifying perturbations are applied in a WNT5A gene network. The results obtained in this paper can be degenerated to Boolean networks case, which are coincident with results in [22].

The rest of this paper is organized as follows. Section 2 presents some notations and fundamental theories of STP which will be used later in this paper. In Section 3, we propose a new sort of perturbation of mix-valued logical networks and derive the main results of perturbation's effects on topological structure of networks. Section 4 establishes new methods of identifying one perturbation and multi-perturbation in mix-valued logical networks. Besides, we use the methods of perturbation identification to identify and alter attractors in a WNT5A gene network. Section 5 concludes the paper.

2. Notations and preliminaries

2.1. Notations

At first, we introduce some notations which will be used later in this paper.

- $\mathcal{R}^{m\times n}$: the set of $m \times n$ real matrices.
- δ_n^i: the i-th column of the identity matrix I_n.
- $\mathcal{D}_k:=\{\frac{k-i}{k-1} \mid i=1,2,\dots,k\}$. If $k=2$, $\mathcal{D}_2:=\{0,1\}$.
- $\Delta_n:=\{\delta_n^i \mid i=1,\dots,n\}$. Denote $\delta_n^i \sim \frac{n-i}{n-1}$ and we have $\Delta_n \sim \mathcal{D}_n$.
- $x \in \Delta_n$ means the logical variable x takes the value from Δ_n.
- A matrix $L \in \mathcal{R}^{n\times m}$ is called a logical matrix if the columns of L, denoted by $Col(L)$, are of the form of δ_n^i. That is, $Col(L) \subseteq \Delta_n$. And $Col_i(L)$ represents the i-th column of L. Denote by $\mathcal{L}_{n\times m}$ the set of $n \times m$ logical matrices.
- If $L \in \mathcal{L}_{n\times m}$, then it has the form $L=[\delta_n^{i_1}, \delta_n^{i_2},\dots,\delta_n^{i_m}]$. For notational compactness we write this as $L=\delta_n[i_1,i_2,\dots,i_m]$.
- Let $A=(a_{ij}) \in \mathcal{R}^{m\times n}, B \in \mathcal{R}^{p\times q}$. The Kronecker product of matrices A and B is defined as

$$A \otimes B := \begin{bmatrix} a_{11}B & a_{12}B & \cdots & a_{1n}B \\ a_{21}B & a_{22}B & \cdots & a_{2n}B \\ \vdots & \vdots & \ddots & \vdots \\ a_{m1}B & a_{m2}B & \cdots & a_{mn}B \end{bmatrix}.$$

2.2. Preliminaries

In this subsection, necessary preliminaries on STP which play an important role in this paper are introduced.

Definition 1. [23] Let $A \in \mathcal{R}^{m\times n}$ and $B \in \mathcal{R}^{p\times q}$. The STP of matrices A and B, denoted by $A \ltimes B$, is defined as

$$A \ltimes B = (A \otimes I_{l/n})(B \otimes I_{l/p}), \tag{1}$$

where $l = lcm\{n,p\}$ is the least common multiple of n and p.

Remark 1. We can see that STP of matrices is a generalization of the conventional matrix product. If $n=p$, STP of matrices becomes the conventional product. We omit the symbol $\ltimes$ later in this paper if it dose not lead to confusion.

Definition 2. [2] A swap matrix $W_{[m,n]}$ is an $mn \times mn$ matrix, defined as follows: label its columns by $(11,12,\dots,1n,\dots,m1,m2,\dots,mn)$, label its rows by $(11,21,\dots,m1,\dots,1n,2n,\dots,mn)$, and then the element at the position $[(I,J),(i,j)]$ is

$$w_{(I,J),(i,j)} = \delta_{i,j}^{I,J} = \begin{cases} 1, & I=i, J=j; \\ 0, & otherwise. \end{cases} \tag{2}$$

Lemma 2.1. *[2,17]*

1. *Let $X \in \mathcal{R}^m$ and $Y \in \mathcal{R}^n$ be two column vectors. Then*
$$W_{[m,n]}XY = YX. \tag{3}$$
2. *Given $A \in \mathcal{R}^{m\times n}$, let $Z \in \mathcal{R}^t$ be a column vector. Then*
$$ZA = (I_t \otimes A)Z. \tag{4}$$
3. *Let $X \in \mathcal{R}^n$, $Y \in \mathcal{R}^q$ be two column vectors and $A \in \mathcal{R}^{m\times n}, B \in \mathcal{R}^{p\times q}$ be two given matrices. Then*
$$(AX)\ltimes(BY) = (A \otimes B)(X \ltimes Y). \tag{5}$$
Furthermore, if $X=Y \in \mathcal{R}^n, n=q$, then (5) becomes
$$(AX)\ltimes(BX) = (A * B)X, \tag{6}$$
where $A * B = [Col_1(A) \otimes Col_1(B),\dots,Col_n(A) \otimes Col_n(B)]$ is the