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On robust control invariance of Boolean control networks☆

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ABSTRACT

This paper investigates the robust control invariance of Boolean control networks (BCNs) via the semi-tensor product of matrices. Firstly, based on an algebraic state space representation of BCNs, two necessary and sufficient conditions are presented to check whether or not a given set is a robust control invariant set under a given state feedback controller. Secondly, by defining a series of suitable sets, all possible state feedback gain matrices under which a given set is a robust control invariant set are characterized. An illustrative example is presented to demonstrate the obtained new results.

1. Introduction

As an effective model for the study of genetic regulatory networks (GRNs), Boolean networks have attracted a lot of attentions from scholars and many excellent results have been established over the past few decades (Akutsu, Hayashida, Ching, & Ng, 2007; Chaves, 2009; Kauffman, 1969; Pal, Datta, Bittner, & Dougherty, 2006; Zhao, Kim, & Filippone, 2013). In a Boolean network, each gene is represented by a node with two possible states, i.e. "0" and "1", where the "1" represents the state "on" corresponding to a gene that is being transcribed and the "0" the state "off" corresponding to a gene that is not being transcribed. A directed edge from one node to another represents the interaction between genes, the mutual regulation of which is described by a Boolean function.

For the purpose of manipulating Boolean networks, binary control inputs and outputs are added to the network dynamics, which yields Boolean control networks (BCNs). The control of Boolean networks is one of the most important issues in systems biology because it is crucial to the treatment of some diseases like cancer (Srihari, Raman, Leong, & Ragan, 2014). Recently, an algebraic state space representation (ASSR) has been proposed for the analysis and control of Boolean networks based on the semi-tensor product of matrices (Cheng, Qi, & Li, 2011). Using the ASSR, many control problems of Boolean networks were solved, which include the controllability (Chen & Sun, 2014; Cheng & Qi, 2009; Li & Sun, 2011; Liu, Chen, Lu, & Wu, 2015; Zhang & Zhang, 2013), the stabilization (Li, Yang, & Chu, 2013), the optimal control (Chen, Li, & Sun, 2015; Fornasini & Valcher, 2014; Laschov & Margaliot, 2011) and the disturbance decoupling (Cheng, 2011; Yang, Li, & Chu, 2013). For other applications of the ASSR, please refer to Cheng and Qi (2010), Lu, Zhong, Li, Ho, and Cao (2015), Suo and Sun (2015), Xu and Hong (2013), and Zou and Zhu (2014).

It is noted that when modeling a genetic regulatory network (GRN), disturbance inputs may need to be considered (Chen & Wang, 2006; Cheng, 2011; Yang et al., 2013). The disturbances of GRNs are mainly produced by biological uncertainties, experimental noises and interacting latent variables. These disturbance inputs may prohibit the effectiveness of control strategies in keeping the cellular states of the GRN in a desirable set. Thus, it is necessary for us to design a suitable control strategy under which the set of desirable cellular states of the GRN is robust to the disturbance inputs, that is, if the GRN's trajectory reaches the set of desirable cellular states, it will stay there forever regardless of the disturbance inputs. The corresponding set is called robust control invariant set. In the last two decades, the problem of robust control invariant sets has been well studied for both linear systems (Rakovic, Kerrigan, Mayne, & Kouramas, 2007; Tarraf & Bauso, 2014) and nonlinear systems (Blanchini, 1999) due to its wide applications in robust

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control synthesis and analysis, robust time-optimal control and robust predictive control methods. As a suitable model of GRNs, the study of robust control invariant sets is also important for BCNs. However, to our best knowledge, there is no result available on robust control invariance for BCNs. It should be pointed out that although Parise, Valcher, and Lygeros (2014) investigated the robust control invariance for the differential equation model of GRNs, one cannot apply the method proposed in Parise et al. (2014) to study the robust control invariance of a BCN because of its discrete and logical nature. Therefore, we should develop new methods for the robust control invariance of BCNs.

In this paper, using the ASSR, we investigate the robust control invariance of BCNs. We present two necessary and sufficient conditions to check whether or not a given set is a robust control invariant set under a given state feedback control. In addition, we propose an effective procedure to characterize all possible state feedback gain matrices under which a given set is a robust control invariant set. Finally, we apply the obtained new results to the regulation of the lac operon in the *Escherichia coli*.

The rest of this paper is organized as follows. Section 2 presents some preliminary results on the semi-tensor product of matrices. Section 3 gives the problem formulation. Section 4 investigates the robust control invariance of BCNs and presents the main results of this paper. Section 5 gives an illustrative example to support our new results, which is followed by a brief conclusion in Section 6.

Notation. $\mathbb{R}$ denotes the set of real numbers. $\mathcal{D} := \{1, 0\}$, and $\mathcal{D}^n := \underbrace{\mathcal{D} \times \cdots \times \mathcal{D}}_{n}$. $\Delta_n := \{\delta_n^k : k = 1, \ldots, n\}$, where δ_n^k denotes the kth column of the identity matrix I_n. For compactness, $\Delta := \Delta_2$. An $n \times m$ matrix M is called a logical matrix, if $M = [\delta_n^{i_1}\ \delta_n^{i_2} \cdots \delta_n^{i_m}]$, which is briefly expressed as $M = \delta_n[i_1\ i_2 \cdots i_m]$. Denote the set of $n \times m$ logical matrices by $\mathcal{L}_{n\times m}$. Given a real matrix $A \in \mathbb{R}^{m\times n}$, $Col_i(A)$ denotes the ith column of A, and $(A)_{i,j}$ denotes the (i, j)th element of A.

2. Preliminaries

In this section, we recall some preliminary results on the semi-tensor product of matrices, which will be used later.

Definition 1 (Cheng et al., 2011)**.** The semi-tensor product of two matrices $A \in \mathbb{R}^{m\times n}$ and $B \in \mathbb{R}^{p\times q}$ is defined as

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

where $\alpha = lcm(n, p)$ is the least common multiple of n and p, and $\otimes$ is the Kronecker product.

Remark 1. When $n = p$, the semi-tensor product of matrices becomes the conventional matrix product. Thus, it is a generalization of the conventional matrix product. We can simply call it "product" and omit the symbol "$\ltimes$" if no confusion arises.

Proposition 1 (Cheng et al., 2011)**.** *Let $X \in \mathbb{R}^{p\times 1}$ be a column vector and $A \in \mathbb{R}^{m\times n}$. Then*

$$X \ltimes A = (I_p \otimes A) \ltimes X. \tag{2}$$

Using the semi-tensor product of matrices, one can convert a Boolean function into an algebraic form. Identifying $1 \sim \delta_2^1$ and $0 \sim \delta_2^2$, then $\Delta \sim \mathcal{D}$, where "$\sim$" denotes two different forms of the same object. In the sequel, we mostly use δ_2^1 and δ_2^2 to express Boolean variables and call them the vector form of Boolean variables. We have the following result.

Lemma 1 (Cheng et al., 2011)**.** *Let $f(x_1, x_2, \ldots, x_s) : \mathcal{D}^s \mapsto \mathcal{D}$ be a Boolean function. Then, there exists a unique matrix $M_f \in \mathcal{L}_{2\times 2^s}$, called the structural matrix of f, such that*

$$f(x_1, x_2, \ldots, x_s) = M_f \ltimes_{i=1}^s x_i, \quad x_i \in \Delta, \tag{3}$$

where $\ltimes_{i=1}^s x_i = x_1 \ltimes \cdots \ltimes x_s$.

For example, the structural matrices for Negation ($\neg$), Conjunction ($\wedge$) and Disjunction ($\vee$) are $M_n = \delta_2[2\ 1]$, $M_c = \delta_2[1\ 2\ 2\ 2]$ and $M_d = \delta_2[1\ 1\ 1\ 2]$, respectively.

3. Problem formulation

Consider the following Boolean control network:

$$\begin{cases} x_1(t+1) = f_1(X(t), U(t), \Xi(t)), \\ x_2(t+1) = f_2(X(t), U(t), \Xi(t)), \\ \vdots \\ x_n(t+1) = f_n(X(t), U(t), \Xi(t)), \end{cases} \tag{4}$$

where $X(t) = (x_1(t), x_2(t), \ldots, x_n(t)) \in \mathcal{D}^n$, $U(t) = (u_1(t), \ldots, u_m(t)) \in \mathcal{D}^m$ and $\Xi(t) = (\xi_1(t), \ldots, \xi_q(t)) \in \mathcal{D}^q$ are states, control inputs and disturbance inputs, respectively, and $f_i : \mathcal{D}^{m+n+q} \mapsto \mathcal{D}$, $i = 1, \ldots, n$ are Boolean functions.

Now, we give the definition of a robust control invariant set of BCNs.

Definition 2 (*Robust Control Invariant Set*)**.** Consider the system (4). A nonempty set $S \subseteq \mathcal{D}^n$ is said to be a robust control invariant set, if there exists a state feedback control in the form of

$$\begin{cases} u_1(t) = \varphi_1(x_1(t), x_2(t), \ldots, x_n(t)), \\ \vdots \\ u_m(t) = \varphi_m(x_1(t), x_2(t), \ldots, x_n(t)), \end{cases} \tag{5}$$

where $\varphi_i : \mathcal{D}^n \mapsto \mathcal{D}$, $i = 1, \ldots, m$ are Boolean functions, such that for the closed-loop system consisting of (4) and (5), $X(t) \in S$ implies $X(t+1) \in S$, $\forall\ \Xi(t) \in \mathcal{D}^q$.

In the following, we convert (4) and (5) into equivalent algebraic forms via the semi-tensor product of matrices.

Using the vector form of Boolean variables and setting $x(t) = \ltimes_{i=1}^n x_i(t)$, $u(t) = \ltimes_{i=1}^m u_i(t)$ and $\xi(t) = \ltimes_{i=1}^q \xi_i(t)$, by Lemma 1, one can convert (4) and (5) into

$$x(t+1) = L\xi(t)u(t)x(t), \tag{6}$$

and

$$u(t) = Kx(t), \tag{7}$$

respectively, where $L \in \mathcal{L}_{2^n\times 2^{m+n+q}}$ is called the state transition matrix of (6), and $K \in \mathcal{L}_{2^m\times 2^n}$ the state feedback gain matrix. Moreover, the nonempty set S can be converted to a subset of Δ_{2^n}.

Given a nonempty set $S = \left\{\delta_{2^n}^{i_1}, \ldots, \delta_{2^n}^{i_p}\right\} \subseteq \Delta_{2^n}$ with $1 \le i_1 < \cdots < i_p \le 2^n$, we study the following two problems.

Problem 1: For a given state feedback gain matrix $K \in \mathcal{L}_{2^m\times 2^n}$, check whether or not S is a robust control invariant set of the system (4) under the control $u(t) = Kx(t)$.

Problem 2: Find all possible state feedback gain matrices under which S is a robust control invariant set of the system (4).