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Brief paper

Further results on feedback stabilization control design of Boolean control networks[☆]

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ABSTRACT

This paper investigates designing all possible feedback stabilizers for Boolean control networks (BCNs). Some new results on the feedback stabilization control design of BCNs are presented. The main tool used in the paper is the semi-tensor product of matrices. First, the complete family of reachable sets is defined for BCNs. Then it is shown that all the complete families of reachable sets determine all possible state feedback stabilizers. Second, using all the complete families of reachable sets, all possible state feedback stabilizers are obtained. Third, a necessary and sufficient condition is obtained for the existence of output feedback stabilizers. Based on this condition, all possible output feedback stabilizers are designed for BCNs. Finally, the obtained new results are applied to the regulation of the lactose operon in *Escherichia coli*.

1. Introduction

In systems biology, Boolean network is a proper model to describe gene regulatory networks. This model was firstly introduced by Kauffman (1969), and then it was extensively studied by many biologists, physicists, and system scientists (Akutsu, Hayashida, Ching, & Ng, 2007; Ay, Xu, & Kahveci, 2009; Veliz-cuba & Stigler, 2011; Zhao, Kim, & Filippone, 2013). Boolean network is a kind of finite dynamical systems, where the state of each gene can be quantized by a Boolean value: active (1) or inactive (0). Consequently, the state of each gene can be determined by a Boolean difference equation depending on the activation of its neighbors.

It was shown in Ideker, Galitski, and Hood (2001) that "Gene regulatory networks are defined by trans and cis logic. ... Both of these types of regulatory networks have input and output". By adding suitable inputs and outputs to Boolean networks, one can conveniently manipulate Boolean networks and develop (optimal) control strategies, which can enable medical scientists to dispense medicines for the treatment of some diseases. Boolean networks with inputs and outputs are called Boolean control networks (BCNs). A major goal of systems biology is to develop new mathematical tools for the control of BCNs (Akutsu et al., 2007).

Recently, an algebraic state space representation (ASSR) has been proposed for the analysis and control of Boolean networks via the semi-tensor product of matrices (Cheng, Qi, & Li, 2011; Cheng, Qi, & Zhao, 2012). Using this framework, the dynamics of a Boolean (control) network can be converted into a linear (bilinear) discrete-time system. Consequently, the classic control methods can be applied to analyze Boolean (control) networks. In the last decade, the ASSR has attracted a great attention from biologists and system scientists, and there have been lots of excellent results on the control of Boolean networks. These results include controllability and observability (Fornasini & Valcher, 2013a; Laschov & Margaliot, 2012; Li & Sun, 2011; Liu, Chen, Lu, & Wu, 2015; Zhao, Cheng, & Qi, 2010), stability and stabilization (Bof, Fornasini, & Valcher, 2015; Cheng, Qi, Li, & Liu, 2011; Fornasini & Valcher, 2013b; Guo, Wang, Gui, & Yang, 2015; Li & Wang, 2013; Li, Yang, & Chu, 2013; Li & Yu, 2016), synchronization (Lu, Zhong, Li, Ho, & Cao, 2015; Zhong, Lu, Liu, & Cao, 2014), optimal control (Chen, Li, & Sun, 2015; Laschov & Margaliot, 2011), and solutions for other control problems (Feng, Yao, & Cui, 2013; Li, Wang, & Xie, 2015; Li, Xie, & Wang, 2016; Lu, Li, Liu, & Li, 2017; Xu & Hong, 2013; Yang, Li, & Chu, 2013; Zhang, Zhang, & Xie, 2015; Zou & Zhu, 2014).

Among the above control problems of BCNs, the stabilization is one of the most important issues. The solvability of stabilization problem can not only help medical scientists design therapeutic interventions that steer a particular gene regulatory network to a desirable/healthy state, but also reveal how the structure and organization of the system contribute to the system stability. Recently, the stabilization of BCNs has been studied using the ASSR (Bof et al., 2015; Cheng, Qi, Li, & Liu, 2011; Fornasini & Valcher, 2013b; Li & Wang, 2013; Li et al., 2013; Li & Yu, 2016). Cheng, Qi, Li, & Liu

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(2011) firstly presented some necessary and sufficient conditions for the open-loop stabilization and state feedback stabilization of BCNs. Fornasini and Valcher (2013b) and Li et al. (2013) proposed a novel procedure to design state feedback stabilizers[1] for BCNs by constructing a series of reachable sets. Bof et al. (2015) and Li and Wang (2013) established some effective algorithms to design output feedback stabilizers of BCNs. However, as was pointed out in Bof et al. (2015), Li et al. (2013), Fornasini and Valcher (2016) and Li and Wang (2013), one cannot obtain all possible feedback stabilizers for BCNs by using the above results. Particularly, Fornasini and Valcher (2016) pointed out that "a complete solution for output feedback stabilization of BCNs is still missing and represents a challenging open problem". On the other hand, when treating some diseases like cancer, the optimal control policies are necessary in the sense of minimum treatment cycle and minimum cost (Vahedi, Faryabi, Chamberland, Datta, & Dougherty, 2009). If one can design all possible feedback stabilizers for the disease treatment, the optimal control policies will be founded. Hence, designing all possible feedback stabilizers for BCNs is a meaningful topic in both theoretical developments and practical applications. Therefore, it deserves further investigation.

In this paper, using the ASSR, we investigate designing all possible feedback stabilizers for BCNs, and present some new results on the feedback stabilization control design of BCNs. The main contributions of this paper are as follows.

- The complete family of reachable sets is firstly obtained for BCNs. It is also shown that all the complete families of reachable sets can determine all possible state feedback stabilizers.
- Based on all the complete family of reachable sets, one can easily obtain all possible state feedback stabilizers for BCNs. Hence, we solve the challenging problem proposed in Bof et al. (2015), Li et al. (2013) and Li and Wang (2013).
- Using the results on the design of all possible state feedback stabilizers and the method proposed in Li and Wang (2013), we show how to design all possible output feedback stabilizers for BCNs, which was an open problem proposed in Fornasini and Valcher (2016).

The rest of this paper is organized as follows. Section 2 formulates the problem studied in the paper. In Section 3, we investigate how to design all possible feedback stabilizers for BCNs. The main results of this paper are also presented. An illustrative example is given in Section 4. Section 5 is a conclusion.

Notations: $\mathbb{R}$, $\mathbb{N}$ and $\mathbb{Z}_+$ denote the sets of real numbers, natural numbers and positive integers, respectively. $\mathcal{D} := \{1, 0\}$, and $\mathcal{D}^n := \underbrace{\mathcal{D} \times \cdots \times \mathcal{D}}_{n}$. $\Delta_n := \{\delta_n^k \mid k = 1, \ldots, n\}$, where δ_n^k denotes the kth column of the identity matrix I_n. Δ_2 is briefly denoted by Δ. An $n \times t$ matrix M is called a logical matrix, if $M = [\delta_n^{i_1}\ \delta_n^{i_2}\ \cdots\ \delta_n^{i_t}]$. We express M briefly as $M = \delta_n[i_1\ i_2\ \cdots\ i_t]$. Denote the set of $n \times t$ logical matrices by $\mathcal{L}_{n\times t}$. $Col_i(A)$ denotes the ith column of the matrix A.

2. Problem formulation

Consider the following Boolean control network:

$$\begin{cases} x_i(t+1) = f_i(X(t), U(t)),\ i = 1, 2, \ldots, n, \\ y_j(t) = h_j(X(t)),\ j = 1, \ldots, p, \end{cases} \tag{1}$$

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 $Y(t) = (y_1(t), \ldots, y_p(t)) \in \mathcal{D}^p$ are states, control inputs and outputs of the system (1), respectively, and $f_i : \mathcal{D}^{m+n} \mapsto \mathcal{D}, i = 1, \ldots, n$ and $h_j : \mathcal{D}^n \mapsto \mathcal{D}, j = 1, \ldots, p$ are logical functions. Given an initial state $X_0 \in \mathcal{D}^n$ and a control sequence $U : \mathbb{N} \mapsto \mathcal{D}^m$, denote the state trajectory of the system (1) by $X(t; X_0, U)$.

Definition 1. For a given equilibrium $X_e = (x_1^e, x_2^e, \ldots, x_n^e) \in \mathcal{D}^n$, system (1) is said to be globally stabilizable to X_e, if there exist a positive integer τ and a control sequence $U : \mathbb{N} \mapsto \mathcal{D}^m$ such that $X(t; X_0, U) = X_e$ holds for $\forall X_0 \in \mathcal{D}^n$ and $\forall t \geq \tau$.

The objective of this paper is to design all possible state feedback stabilizers in the form of

$$\begin{cases} u_1(t) = k_1(x_1(t), x_2(t), \ldots, x_n(t)), \\ \vdots \\ u_m(t) = k_m(x_1(t), x_2(t), \ldots, x_n(t)), \end{cases} \tag{2}$$

where $k_i : \mathcal{D}^n \mapsto \mathcal{D}, i = 1, \ldots, m$ are logical functions, which makes system (1) globally stabilizable to a given equilibrium $X_e = (x_1^e, x_2^e, \ldots, x_n^e) \in \mathcal{D}^n$.

In the following, we convert the system (1) and the state feedback control (2) into equivalent algebraic forms, respectively. To this end, we recall some necessary preliminaries on the algebraic expression of logical functions via the semi-tensor product of matrices. For details, please see (Cheng, Qi, & Li, 2011, 2012).

Definition 2 (*Cheng, Qi, & Li, 2011*)**.** The semi-tensor product of two matrices $A \in \mathbb{R}^{m\times n}$ and $B \in \mathbb{R}^{p\times q}$ is

$$A \ltimes B = (A \otimes I_{\frac{\alpha}{n}})(B \otimes I_{\frac{\alpha}{p}}), \tag{3}$$

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

Let $\Delta \sim \mathcal{D}$, where $1 \sim \delta_2^1$, $0 \sim \delta_2^2$, and "$\sim$" denotes two different expressions of the same thing. Given a logical variable $x \in \mathcal{D}$, the vector form of $x = 1$ is $x = \delta_2^1$, and the vector form of $x = 0$ is $x = \delta_2^2$. Then, we have the following result on the algebraic expression of logical functions.

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

$$f(x_1, x_2, \ldots, x_s) = M_f \ltimes_{i=1}^s x_i, \quad x_i \in \Delta, \tag{4}$$

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

Remark 1.

1. The semi-tensor product of matrices is a generalization of the conventional matrix product. Thus, we omit the symbol "$\ltimes$" if no confusion arises.
2. The structural matrices of 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.

Using the vector form of logical variables and setting $x(t) = \ltimes_{i=1}^n x_i(t) \in \Delta_{2^n}$, $u(t) = \ltimes_{i=1}^m u_i(t) \in \Delta_{2^m}$ and $y(t) = \ltimes_{i=1}^p y_i(t) \in \Delta_{2^p}$, by Lemma 1, one can convert (1) and (2) into

$$\begin{cases} x(t+1) = L \ltimes u(t) \ltimes x(t), \\ y(t) = Hx(t), \end{cases} \tag{5}$$

and

$$u(t) = Kx(t), \tag{6}$$

respectively, where $L \in \mathcal{L}_{2^n\times 2^{m+n}}$ is the state transition matrix, $H \in \mathcal{L}_{2^p\times 2^n}$ is the output matrix, and $K \in \mathcal{L}_{2^m\times 2^n}$ is the state

[1] A state (output) feedback stabilizer is a state (output) feedback control which can stabilize the considered system to a given equilibrium.