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Brief paper

On algorithms for state feedback stabilization of Boolean control networks☆

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ABSTRACT

This paper deals with the algorithms for state feedback stabilization of Boolean control networks (BCNs). By resorting to the semi-tensor product (STP) technique, the labelled digraph that can be used to completely characterize the dynamics of BCNs is derived, which leads to an equivalent graphical description for the stabilization of BCNs. What is more interesting is the fact that the existence of a state feedback control law stabilizing the BCN to some given equilibrium point can be characterized in terms of its spanning in-tree. Consequently, two in-tree search algorithms, namely, the breadth-first search and the depth-first search, are proposed to design the state feedback stabilizing law when global stabilization is feasible. Besides, some basic properties about the tree-search algorithms are addressed. A biological example is employed to illustrate the applicability and usefulness of the developed algorithms.

1. Introduction

A major objective of genetic regulatory network (GRN) modelling concerns developing computational approaches for identification and discovery of potential targets for therapeutic intervention in diseases such as cancer. Based on the large-scale microarray data retrieved from biological experiments, many mathematical models including the Boolean model, the Bayesian network model and the differential equation model have been proposed and utilized to reconstruct the GRNs aiming at deciphering the underlying gene regulatory mechanisms. Recently, many experimental results have confirmed that the highly simplified Boolean networks (BNs), originally introduced by Kauffman (1969), are capable of predicting the dynamical sequence of protein activation patterns of GRNs. A practical example is the cell cycle control network of yeast (Davidich & Bornholdt, 2008). The modality of BNs has established a natural framework for providing detailed understanding and insights of the dynamic behaviour exhibited by large genetic networks.

In a Boolean model, only two states (i.e., ON and OFF) are used to represent the expression level of each gene, and the state of a gene is determined by a pre-assigned logic function concerning about the states of other related genes. Moreover, it has been recognized that many biological systems have exogenous perturbations that can be described as 'control' (Fauré & Thieffry, 2009), which should be taken into account in the BNs in order to have more appropriate models. Therefore, the concept of Boolean control networks (BCNs) has been formally put forward by adding binary inputs to the BNs (Akutsu, Hayashida, Ching, & Ng, 2007). For instance, the binary input may represent whether a certain medicine is administered or not when modelling the progression of a disease. And the BCNs with inputs have been widely utilized to analyse and design the therapeutic intervention strategies. The central focus here is to design efficient and computational control sequence steering the whole network from an undesirable location (implying a diseased state) to a desirable one (corresponding to a healthy state). It is worth pointing out that if the established BCN is controllable, then the control sequence can be designed by means of a time invariant state feedback law (Fornasini & Valcher, 2013). This characteristic of the BCNs partly motivates the present research.

With the advent of semi-tensor product (STP) technique (Cheng, Qi, & Li, 2011), which reduces a BN (BCN) to a positive linear (bilinear switched) system whose input and state variables are canonical vectors, a considerable amount of research attention has been inspired. Consequently, several analysis and control problems, which include but are not limited to, controllability and observability (Cheng & Qi, 2009; Laschov & Margaliot, 2012; Li & Wang, 2015; Li, Xie, & Wang, 2016; Zhang & Zhang, 2016, 2013), stability and stabilization (Cheng, Qi, Li, & Liu, 2011),

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optimal control (Fornasini & Valcher, 2014; Laschov & Margaliot, 2011), system decomposition (Zou & Zhu, 2014), and network synchronization (Chen, Liang, Huang, & Cao, 2017; Li, 2014), have been extensively investigated in recent years. These results make significant contributions for gaining deep insights into the dynamics of genetic networks and uncovering the complex relationships between genes within the genome.

Many recent findings have provided experimental evidence for the spontaneous emergence of ordered collective behaviour of gene activity (Huang, 1999), which is an important property of real GRNs. And, the BCNs that can be stabilized to the equilibrium points also exhibit this behaviour. In the context of a cellular signal transduction network, there is abundant justification in the assertion that these equilibrium points correspond to different functional states, such as death or unregulated growth (Huang & Ingber, 2000; Saadatpour, Wang, Liao, Liu, Loughran, Albert, & Albert, 2011; Zhang, Ma, & Liu, 2016). Moreover, the consideration of state feedback stabilization issue for complex GRNs modelled by BCNs may pave the way towards the development of systematic approaches for effective therapeutic intervention of diseases. As such, determining the equilibrium points of a BCN and constructing their stabilizing controllers are of fundamental and practical importance. Recent studies on feedback stabilization of BCNs are fruitful, and many important theoretical results have been reported in the literature. To mention just a few, some analysis criteria for the existence of a stabilizing state feedback controller have been obtained in Fornasini and Valcher (2013), it has also been shown that if a BCN is stabilizable to the equilibrium point, then the stabilization can be achieved by means of a time invariant state feedback control law. In the remarkable paper (Li, Yang, & Chu, 2013), a general control design approach has been proposed when stabilization is feasible via the state feedback scheme. Later, the investigation has been extended to the probabilistic BCNs (Li, Yang, & Chu, 2014). Inspired by Li et al. (2013), the stabilizing output feedback problem has been addressed in Li and Wang (2013), where an algebraic characterization of a logical matrix has been presented which describes the stabilizing time invariant output feedback control law. In the interesting paper (Bof, Fornasini, & Valcher, 2015), some constructive algorithms have been given to test the existence of a stabilizing output feedback law. Pinning controllability and trajectory controllability analysis of BNs have been carried out in Lu, Zhong, Huang, and Cao (2016) and Lu, Zhong, Ho, Tang, and Cao (2016), respectively. Very recently, in Li (2016), pinning control design has been further discussed for the stabilization of BCNs.

Although the state feedback stabilization for BCNs has stirred some initial research interests (Fornasini & Valcher, 2013; Li et al., 2013), one of the main issues aroused here is, from the computational point of view, how to design a systematic procedure (or algorithm), which can be resorted to stabilize the BCNs both applicably and efficiently, and this leaves enormous room for further discussion/investigation by using the search algorithms developed in graph theory. The so called tree-search plays a vital vole when determining a shortest path tree, which is strongly related to stabilization for BCNs. It is, therefore, the main purpose of this paper to adapt the tree-search approach for designing efficient algorithms that provide state feedback matrices guaranteeing the global stabilization of BCNs. In this paper, we are concerned with the problem of designing globally stabilizing state feedback controllers for BCNs. Based on the algebraic representation of logical dynamics in terms of the STP technique, the labelled digraph which can be used to characterize the dynamics of BCNs is obtained. Consequently, two search algorithms, namely, breadth-first search and depth-first search, are proposed to construct the stabilizing feedback control law when global stabilization via state feedback is feasible.

The remaining part of the paper is organized as follows. Section 2 formulates the problem addressed, and some notations and preliminaries on the STP of matrices are also introduced. Section 3 presents the main results and algorithms of this paper. In Section 4, a biological example is given, and a brief conclusion is drawn in Section 5.

2. Problem formulation and preliminaries

Given $k, n \in \mathbb{N}$ with $k \le n$, denote the set $\{k, k+1, \ldots, n\}$ by $[k, n]$. Δ_k is used to represent the set of all k-dimensional canonical vectors $\{\delta_k^i | i = 1, 2, \ldots, k\}$, where δ_k^i is the ith canonical vector of size k. A matrix $B \in \mathbb{R}^{m\times n}$ is called a logical matrix if the columns set of B, denoted by $\mathrm{Col}(B)$, satisfies $\mathrm{Col}(B) \subset \Delta_m$. Let $\mathrm{Row}_i(B)$ be the ith row of matrix B. The set of all $m \times n$ logical matrices is represented by $\mathcal{L}_{m\times n}$. For $B = [\delta_m^{i_1}\ \delta_m^{i_2}\ \cdots\ \delta_m^{i_n}] \in \mathcal{L}_{m\times n}$, denote it by $B = \delta_m[i_1, i_2, \ldots, i_n]$ for simplicity.

Definition 1 (*Cheng, Qi, & Li, 2011*)**.** The STP of two matrices $B \in \mathbb{R}^{m\times n}$ and $C \in \mathbb{R}^{p\times q}$ is defined as

$$B \ltimes C = (B \otimes I_{\alpha/n})(C \otimes I_{\alpha/p}),$$

where $\alpha = \mathrm{lcm}(n, p)$ is the least common multiple of n and p, and '$\otimes$' is the tensor (or Kronecker) product.

Obviously, there is a bijective correspondence between the Boolean variable set $\mathcal{D} := \{1, 0\}$ and the canonical vector set Δ_2. With some abuse of notation, the Boolean variable $\varrho \in \mathcal{D}$ is always identified with the vector $\boldsymbol{\varrho} = \delta_2^{2-\varrho} \in \Delta_2$, which is usually expressed as $\varrho \sim \boldsymbol{\varrho}$ if no confusion arises. It should be noted that such correspondence can be extended naturally to the bijection between $\mathcal{D}^n$ and Δ_{2^n} via the STP. The following lemma is fundamental for the matrix expression of logical functions.

Lemma 2 (*Cheng, Qi, & Li, 2011*)**.** *Let $f(x_1, x_2, \ldots, x_n) : \mathcal{D}^n \to \mathcal{D}$ be a logical function. Then, there exists a unique matrix $M_f \in \mathcal{L}_{2\times 2^n}$, called the structure matrix of f, such that $f(x_1, x_2, \ldots, x_n) = M_f \ltimes_{i=1}^n x_i$, $x_i \in \Delta_2$.*

A BCN with n nodes and m binary inputs is described by the following equations:

$$x_i(t+1) = f_i(X(t), U(t)), \quad i = 1, 2, \ldots, n \tag{1a}$$

where $X(t) = (x_1(t), x_2(t), \ldots, x_n(t)) \in \mathcal{D}^n$ and $U(t) = (u_1(t), u_2(t), \ldots, u_m(t)) \in \mathcal{D}^m$ denote, respectively, the n-dimensional state variable and the m-dimensional input variable at time t, and $f_i : \mathcal{D}^{m+n} \to \mathcal{D}$ $(i = 1, 2, \ldots, n)$ are the Boolean functions. First of all, the global stabilizability of BCN (1a) is defined as follows.

Definition 3 (*Li et al., 2013*)**.** For a given state $X_e \in \mathcal{D}^n$, the BCN (1a) is said to be globally stabilizable to X_e if for every $X(0) \in \mathcal{D}^n$, there exist $U(t)$ for $t \in \mathbb{N}$ and $\tau \in \mathbb{N}$ such that $X(t) = X_e$ for every $t \ge \tau$.

The objective of this paper is to effectively design a *computational* state feedback controller

$$u_j(t) = h_j(X(t)), \quad j = 1, 2, \ldots, m \tag{1b}$$

where $h_j(\cdot)$ is a logical function from $\mathcal{D}^n$ to $\mathcal{D}$, such that the overall closed-loop system (1) is globally stabilizable to the given state $X_e \in \mathcal{D}^n$.

Next, to facilitate the analysis, the above problem is reformulated by resorting to the algebraic representation of the logical functions. In terms of the STP technique, $X(t)$ and $U(t)$ can be represented as canonical vectors in Δ_N with $N := 2^n$ and Δ_M with $M := 2^m$, respectively. From Lemma 2 and the property of