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Brief paper

On Boolean control networks with maximal topological entropy[☆]

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ABSTRACT

Boolean control networks (BCNs) are discrete-time dynamical systems with Boolean state-variables and inputs that are interconnected via Boolean functions. BCNs are recently attracting considerable interest as computational models for genetic and cellular networks with exogenous inputs.

The topological entropy of a BCN with m inputs is a nonnegative real number in the interval $[0, m \log 2]$. Roughly speaking, a larger topological entropy means that asymptotically the control is "more powerful". We derive a necessary and sufficient condition for a BCN to have the maximal possible topological entropy. Our condition is stated in the framework of Cheng's algebraic state-space representation of BCNs. This means that verifying this condition incurs an exponential time-complexity. We also show that the problem of determining whether a BCN with n state variables and $m = n$ inputs has a maximum topological entropy is NP-hard, suggesting that this problem cannot be solved in general using a polynomial-time algorithm.

1. Introduction

Boolean networks (BNs) are useful modeling tools for dynamical systems whose state-variables can attain two possible values. Examples range from artificial neural networks with ON/OFF type neurons (see, e.g. Hassoun, 1995), to models for the emergence of social consensus between simple agents that can either agree or disagree with a certain opinion (see, e.g. Green, Leishman, & Sadedin, 2007).

There is a growing interest in modeling biological systems using BNs and, in particular, genetic regulation networks, where each gene can be either expressed (ON) or not expressed (OFF) (Chaos et al., 2006; Kauffman, Peterson, Samuelsson, & Troein, 2003; Li, Long, Lu, Ouyang, & Tang, 2004). Although being highly abstract, BNs seem to capture the real behavior of gene-regulatory processes well (Bornholdt, 2008; Hopfensitz et al., 2012).

Kauffman (1969) has studied the order and stability of large, randomly constructed nets of such binary genes. He also related the behavior of these random nets to various cellular control processes, including cell differentiation, by associating every possible cell type with a stable attractor of the BN. This work has stimulated the analysis of large-scale BNs using tools from the theory of complex systems and statistical physics (see, e.g. Albert & Barabasi, 2000; Aldana, 2003; Drossel, Mihaljev, & Greil, 2005; Kauffman, 1993).

BNs have also been used to model various cellular processes including the complex cellular signaling network controlling stomatal closure in plants (Li, Assmann, & Albert, 2006), the molecular pathway between two neurotransmitter systems, the dopamine and glutamate receptors (Gupta, Bisht, Kukreti, Jain, & Brahmachari, 2007), carcinogenesis, and the effects of therapeutic intervention (Szallasi & Liang, 1998).

BNs with (Boolean) inputs are referred to as Boolean control networks (BCNs). BCNs have been used to model biological systems with exogenous inputs. For example, Faure, Naldi, Chaouiya, and Thieffry (2006) (see also Faure & Thieffry, 2009) have developed a BCN model for the core network regulating the mammalian cell cycle. Here the nine state-variables represent the activity/inactivity of nine different proteins: Rb, E2F, CycE, CycA, p27, Cdc20, Cdh1, UbcH10, and CycB, and the single Boolean input represents the activity/inactivity of CycD in the cell.

Cheng, Qi, and Li (2011) have developed an *algebraic state-space representation* (ASSR) of BCNs (and, in particular, of BNs). This representation has proved useful for studying control-theoretic questions, as they reduce a BCN to a positive linear switched system whose input, state and output variables are canonical vectors. Topics that have been analyzed using the ASSR include optimal control

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(Laschov & Margaliot, 2011, 2013; Zhao, Li, & Cheng, 2011), controllability and observability (Cheng & Qi, 2009; Fornasini & Valcher, 2013; Laschov & Margaliot, 2012; Li & Sun, 2011), identification (Cheng & Zhao, 2011), disturbance decoupling (Cheng, 2011), and more.

The ASSR of a BN with n state-variables and m inputs includes a $2^n \times 2^{n+m}$ matrix. Thus, any algorithm based on the ASSR has an exponential time complexity. A natural question is whether better algorithms exist. Zhao (2005) has shown that determining whether a BN has a fixed point is NP-complete. Akutsu, Hayashida, Ching, and Ng (2007) have shown that several control problems for BCNs are NP-hard. Laschov, Margaliot, and Even (2013) have shown that the observability problem for BCNs is also NP-hard. Thus, unless $P = NP$, these analysis problems for BCNs cannot be solved in polynomial time.

Hochma, Margaliot, Fornasini, and Valcher (2013) noted the connection between BCNs and *symbolic dynamics* (SD). The main object of study in SD is *shift spaces* (Lind & Marcus, 1995). The set of all possible trajectories of a BCN is a shift space, so many results and analysis tools from SD are immediately applicable to BCNs. In particular, Hochma et al. (2013) noted that an important notion from SD called topological entropy can be defined for BCNs, and computed using the Perron root of a certain non-negative matrix that appears in the ASSR of a BCN. The topological entropy of a BCN with n state-variables and m inputs (we always assume that $m \le n$) is a number in the range $[0, m\log 2]$ that indicates how "rich" the control is.

In this paper, we derive a necessary and sufficient condition for a BCN to have a maximal topological entropy. This condition is stated in terms of the ASSR. We also show that for a BCN with n state variables and $m = n$ inputs the problem of determining whether the BCN has maximal topological entropy is NP-hard. This implies that unless $P = NP$, there does not exist an algorithm with polynomial time complexity that solves this problem.

The remainder of this note is organized as follows. Section 2 reviews BNs, BCNs, and some definitions and tools from SD. Section 3 includes our main results. Section 4 concludes and describes some possible directions for further research.

2. Preliminaries

We begin by reviewing BCNs and their ASSRs. Let $\mathcal{S} := \{0, 1\}$. A BCN is a discrete-time logical dynamical system

$$\begin{aligned} X_1(k+1) &= f_1(X_1(k), \dots, X_n(k), U_1(k), \dots, U_m(k)),\\ &\vdots \\ X_n(k+1) &= f_n(X_1(k), \dots, X_n(k), U_1(k), \dots, U_m(k)), \end{aligned} \tag{1}$$

where $X_i, U_i \in \mathcal{S}$, and each f_i is a Boolean function, i.e. $f_i : \mathcal{S}^{n+m} \to \mathcal{S}$. It is useful to write this in vector form as

$$X(k+1) = f(X(k), U(k)). \tag{2}$$

A BN is a BCN without inputs, i.e.

$$X(k+1) = f(X(k)). \tag{3}$$

Cheng et al. (2011) have developed an algebraic state-space representation of BCNs using the semi-tensor product of matrices. This topic has been described in many publications, so we review it briefly.

Let $I_{k,k}$ denote the $k \times k$ identity matrix, and let $e_k^i \in \mathcal{S}^k$ denote the ith canonical vector of size k, i.e., the ith column of $I_{k,k}$. Let $\mathcal{L}^{k\times n} \subset \mathcal{S}^{k\times n}$ denote the set of $k \times n$ matrices whose columns are all canonical vectors.

Using the semi-tensor product (Cheng et al., 2011) of matrices, denoted by $\ltimes$, the state-vector $\begin{bmatrix} X_1(k) & \cdots & X_n(k) \end{bmatrix}'$ of a BCN is converted into a state-vector $x(k) \in \mathcal{L}^{2^n}$. Basically, $x(k)$ is the set of all the possible minterms of the $X_i(k)$s, so $x(k)$ is a canonical vector for all k. Similarly, the input vector $\begin{bmatrix} U_1(k) & \cdots & U_m(k) \end{bmatrix}'$ is converted into a vector $u(k) \in \mathcal{L}^{2^m}$. Since any Boolean function can be represented as a sum of minterms, the dynamics (1) can be represented in the bilinear form

$$x(k+1) = L \ltimes u(k) \ltimes x(k). \tag{4}$$

The matrix $L \in \mathcal{L}^{2^n \times 2^{n+m}}$ is called the *transition matrix* of the BCN.

Algorithms for converting a BCN from the form (2) to its ASSR (4), and vice versa, may be found in Cheng et al. (2011). Similarly, the BN (3) may be represented in the ASSR

$$x(k+1) = Lx(k), \tag{5}$$

where $x(k) \in \mathcal{L}^{2^n}$ and $L \in \mathcal{L}^{2^n \times 2^n}$.

The fact that a BN may be represented in a linear form using the vector of minterms has been known for a long time (see, e.g., Cull, 1971, 1975), but the ASSR provides an explicit algebraic form that is particularly suitable for control-theoretic analysis.

Given the ASSR (5) of a BN, we can associate with it a directed graph $G = G(V, E)$, where $V = \{e_{2^n}^1, \dots, e_{2^n}^{2^n}\}$, and there is a directed edge from vertex $e_{2^n}^j$ to vertex $e_{2^n}^i$ if and only if $[L]_{ij} = 1$. In other words, there is a directed edge from vertex $e_{2^n}^j$ to vertex $e_{2^n}^i$ if and only if $x(k) = e_{2^n}^j$ implies that $x(k+1) = e_{2^n}^i$.

We now briefly review some results from Hochma et al. (2013) derived by relating BCNs and symbolic dynamics (SD) (Lind & Marcus, 1995). SD has evolved from analyzing general dynamical systems by discretizing the state-space into finitely many pieces, each labeled by a different symbol. An orbit of the dynamical system is then transformed into a *symbolic orbit* composed of the sequence of symbols corresponding to the successive pieces visited by the orbit. The original evolution is transformed into a symbolic dynamics given by a shift operator σ. The main object of study in SD is *shift spaces*.

Given the BCN (2), define its *set of state-trajectories of length j* by

$$\begin{aligned} \mathcal{A}_S^j := \{&X(0)X(1)\cdots X(j-1) :\\ &X(k+1) = f(X(k), U(k)),\ U(k) \in \mathcal{S}^m,\ X(0) \in \mathcal{S}^n\}, \end{aligned}$$

i.e., the state trajectories of length j over all possible controls and initial conditions. Note that for a BN this becomes

$$\{X(0)\cdots X(j-1) : X(k+1) = f(X(k)),\ X(0) \in \mathcal{S}^n\}.$$

The *topological entropy* of a BCN is

$$h_S := \lim_{j\to\infty} \frac{1}{j} \log |\mathcal{A}_S^j|. \tag{6}$$

In other words, h_S is the asymptotic "growth rate" of the number of state-sequences of a given length. A higher h_S corresponds to a "richer" control in the sense that asymptotically more state-sequences can be produced.

Example 1. Consider the BCN:

$$\begin{aligned} X_1(k+1) &= U_1(k),\\ X_2(k+1) &= U_2(k),\\ &\vdots\\ X_m(k+1) &= U_m(k),\\ X_{m+1}(k+1) &= f_1(X_1(k), \dots, X_n(k)),\\ X_{m+2}(k+1) &= f_2(X_1(k), \dots, X_n(k)),\\ &\vdots\\ X_n(k+1) &= f_{n-m}(X_1(k), \dots, X_n(k)). \end{aligned} \tag{7}$$