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Stability Analysis of Boolean Networks with Partial Information

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***Abstract*— This paper addresses the stability (the existence and uniqueness of an point attractor) of Boolean networks under the assumption that partial information is available. By considering that a Boolean network is described by the *network structure* (connection rule among the nodes) and the *Boolean function* (transition rule of the state), we propose a new stability notion, called the *structural stability*, where the Boolean function is assumed to be unknown. For the structural stability, we present a necessary and sufficient condition, which is a simple condition characterized by the graph topology representing the network structure. Several examples are given to demonstrate our result.**

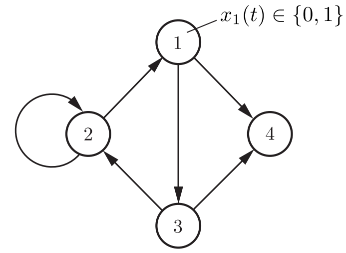

Fig. 1. Example of Boolean network.

I. Introduction

Boolean networks are networked systems composed of dynamical nodes with binary state, as illustrated in Fig. 1. The nodes are connected to other nodes and the state transitions are described by Boolean functions. Since Boolean networks are simple and thus considered as a promising model of genetic networks, the analysis and control have attracted wide interest during the last decade.

So far, a number of results have been obtained for Boolean networks, such as identification [7], [8], stability analysis (attractor analysis) [1]–[3], controllability and observability analysis [4]–[6], and control [5], [9]–[11]. Some other results have also been summarized in [12], [13]. One of the features of the existing results on analysis and control is that problems are addressed with the full information of a Boolean network. In other words, they cannot be applied unless the system is perfectly identified. On the other hand, the perfect identification is often difficult because the number of experimental data for the identification exponentially grows with the number of nodes or with the maximum in-degree [7]. In fact, as easily imagined, the identification almost corresponds to constructing the truth table of a logic circuit. Therefore, analysis and control techniques with partial information would be useful in many cases.

This paper thus addresses the stability (the existence and uniqueness of an point attractor) of Boolean networks under the assumption that partial information is available. First, we propose a new stability notion, called the *structural stability*, for Boolean networks. By considering that a Boolean network is described by the *network structure*, i.e., the connection rule among the nodes, and the *Boolean function*, i.e., the transition rule of the state, it is introduced as a stability notion under the assumption that the network structure is known but the Boolean function is unknown. Such a stability concept is useful especially in analyzing gene regulatory networks, because a number of network structures have been identified so far (see, e.g., KEGG database [14]), while relatively few transition rules are identified. Next, a necessary and sufficient condition for the structural stability is presented. This condition is characterized by the topology of the graph representing the network structure, which allows us to understand and check the structural stability.

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Notation: For the Boolean variables $x \in \{0,1\}$ and $y \in \{0,1\}$, the logical OR and the logical AND are denoted by $x \vee y$ and $x \wedge y$, respectively. We use $\bar{x}$ to express the negation of the Boolean variable x. The Boolean function $f : \{0,1\}^n \to \{0,1\}$ is said to be *dependent on* x_i if there exists a tuple $(x_1, x_2, \ldots, x_{i-1}, x_{i+1}, \ldots, x_n) \in \{0,1\}^{n-1}$ such that $f(x_1, x_2, \ldots, x_{i-1}, x_i, x_{i+1} \ldots, x_n) \neq f(x_1, x_2, \ldots, x_{i-1}, \bar{x}_i, x_{i+1}, \ldots, x_n)$ where $\bar{x}_i$ is the negation of x_i as defined above. For example, $x_1 \wedge x_2$ is dependent on x_1 and also it is dependent on x_2, while $(x_1 \wedge x_2) \vee ((\bar{x}_1 \wedge x_2) \vee x_3)$ is not dependent on x_1 because of $(x_1 \wedge x_2) \vee ((\bar{x}_1 \wedge x_2) \vee x_3) = x_2 \vee x_3$. If f is dependent on $x_1, x_2, \ldots, x_n$, then f is said to be *minimally represented*. For the finite set $\mathbf{S}$, we denote by $|\mathbf{S}|$ its cardinality. The directed graph G is called *acyclic* if G has no directed cycles. Finally, for the Boolean variables $x_1, x_2, \ldots, x_n$ and the set $\mathbf{I} := \{i_1, i_2, \ldots, i_m\} \subset \{1, 2, \ldots, n\}$, let $[x_i]_{i \in \mathbf{I}} := [x_{i_1} \ x_{i_2} \ \cdots \ x_{i_m}]^\top$. For instance, $[x_i]_{i \in \mathbf{I}} = [x_2 \ \ x_4 \ \ x_6]^\top$ for $\mathbf{I} := \{2, 4, 6\}$.

II. Problem Formulation

A. System Description

Consider the following Boolean network

$$\begin{cases} x_1(t+1) &= f_1([x_j(t)]_{j \in \mathbf{N}_1}), \\ x_2(t+1) &= f_2([x_j(t)]_{j \in \mathbf{N}_2}), \\ &\vdots \\ x_n(t+1) &= f_n([x_j(t)]_{j \in \mathbf{N}_n}) \end{cases} \tag{1}$$

where $x_i(t) \in \{0,1\}$ is the state of node i, $\mathbf{N}_i \subseteq \{1,2,\ldots,n\}$ is the index set of the *neighbors* of node i, i.e., the nodes connected to node i, and $f_i : \{0,1\}^{|\mathbf{N}_i|} \to \{0,1\}$ is a Boolean function. It is assumed here that f_i $(i = 1,2,\ldots,n)$ are minimally represented.

An example of a Boolean network is given by

$$\begin{cases} x_1(t+1) = \bar{x}_2(t), \\ x_2(t+1) = \bar{x}_2(t) \wedge x_3(t), \\ x_3(t+1) = x_1(t), \\ x_4(t+1) = x_1(t) \vee \bar{x}_3(t). \end{cases} \tag{2}$$

In this system, the index sets of the neighbors are $\mathbf{N}_1 = \{2\}$, $\mathbf{N}_2 = \{2,3\}$, $\mathbf{N}_3 = \{1\}$, and $\mathbf{N}_4 = \{1,3\}$, and the system evolves as, for instance, $(1,0,0,1) \to (1,0,1,1) \to (1,1,1,1) \to (0,0,1,1) \to (1,1,0,0) \to (0,0,1,1) \to (1,1,0,0) \to \cdots$ for the initial state $(x_1(0), x_2(0), x_3(0), x_4(0)) = (0,0,0,0)$.

For simplicity of notation, this system is denoted by $\Sigma(G,F)$ where G is the directed graph representing the network structure, i.e., with the node set $\{1,2,\ldots,n\}$ and the edge set $\{(j,i) \in \{1,2,\ldots,n\} \times \{1,2,\ldots,n\} \,|\, j \in \mathbf{N}_i\}$, and F is the set of the functions $f_1, f_2, \ldots, f_n$. For example, if the network structure is given by Fig. 1, then the node set and the edge set of G are given by $\{1,2,3,4\}$ and $\{(1,3),(1,4),(2,1),(2,2),(3,2),(3,4)\}$, respectively.

B. Definition of Structural Stability

For the Boolean network $\Sigma(G,F)$, let us introduce the notion of *structural stability*.

Since $\Sigma(G,F)$ has the only 2^n state values, the state x reaches a previously visited state in a finite time. Thus the state eventually fall into a cycle. That is, by letting $x(t)$ be the collection of $x_i(t)$ $(i = 1,2,\ldots,n)$, there exist a finite time $t \in \{0,1,\ldots\}$ and a vector sequence $(a_1, a_2, \ldots, a_p) \in \{0,1\}^{np}$ such that $x(t+1) = a_1$, $x(t+2) = a_2$, …, $x(t+p) = a_p$, $x(t+p+1) = a_1$, $x(t+p+2) = a_2$, …. The sequence $(a_1, a_2, \ldots, a_p)$ is called the *attractor* and p is called the *length*. In particular, the attractor of length 1 is called the *point attractor*. For example, $((0,0,1,1),(1,1,0,0))$ is an attractor of length 2 of the Boolean network in (2).

Next, we introduce an equivalence relation to Boolean networks. Consider the Boolean network $\Sigma(G,F^*)$, which is different from $\Sigma(G,F)$ in terms of the Boolean function. The system $\Sigma(G,F^*)$ is said to be *structurally-equivalent* to $\Sigma(G,F)$. In other words, if a Boolean network is structurally-equivalent to a Boolean network, they have the same network structure but different Boolean functions.

The *stability* and the *structural stability* are defined as follows.

Definition 1: (i) The Boolean network $\Sigma(G,F)$ is said to be *stable* if there exists a unique point attractor for $\Sigma(G,F)$.
(ii) The Boolean network $\Sigma(G,F)$ is said to be *structurally-stable* if all the structurally-equivalent Boolean networks to $\Sigma(G,F)$ are stable. ∎

The main purpose of this paper is to clarify the condition on the network structure G under which $\Sigma(G,F)$ is structurally-stable.

III. Structural Stability Condition

For the stability problem, we obtain the following result.

Theorem 1: The Boolean network $\Sigma(G,F)$ is structurally-stable if and only if the graph G is acyclic.

Proof: This is proven by the following two facts:
(i) If the graph G is acyclic, $\Sigma(G,F^*)$ is stable for any Boolean function F^*.
(ii) If the graph G is not acyclic, there exists a Boolean function F^* such that $\Sigma(G,F^*)$ has at least two attractors.

Fact (i) is a direct consequence of the discrete fixed point theorem (see, e.g., [15]).

Next, (ii) is proven. Without loss of generality, we assume that $(1,2,\ldots,r)$ is a cycle of the graph G $(r \le n)$. Then consider the Boolean network $\Sigma(G,F^*)$ given by

$$\begin{cases} x_1(t+1) = \bigwedge_{j \in \mathbf{N}_1} x_j(t), \\ x_2(t+1) = \bigwedge_{j \in \mathbf{N}_2} x_j(t), \\ \qquad \vdots \\ x_n(t+1) = \bigwedge_{j \in \mathbf{N}_n} x_j(t) \end{cases} \tag{3}$$

where we assume that $\bigwedge_{j \in \mathbf{N}_i} x_j(t) = 1$ if $\mathbf{N}_i = \emptyset$. This system is structurally-equivalent to $\Sigma(G,F)$.

For the system $\Sigma(G,F^*)$, the state value $(1,1,\ldots,1)$ is an attractor because $x_i(t) = 1$ $(i = 1,2,\ldots,n)$ imply $x_i(t+1) = \bigwedge_{j \in \mathbf{N}_i} x_j(t) = 1$ $(i = 1,2,\ldots,n)$ and so $x_i(\infty) = 1$ $(i = 1,2,\ldots,n)$ hold.

Another attractor is in the form of

$$((0,0,\ldots,\underset{\substack{\uparrow \\ r\text{-th}}}{0},*,*,\ldots,*),(0,0,\ldots,0,*,*,\ldots,*),\ldots) \tag{4}$$

where $*$ stands for some unspecified value. In fact, (3) can be rewritten as

$$\begin{cases} x_1(t+1) = x_r(t) \wedge \left(\bigwedge_{j \in \mathbf{N}_1 \setminus \{r\}} x_j(t)\right), \\ x_2(t+1) = x_1(t) \wedge \left(\bigwedge_{j \in \mathbf{N}_2 \setminus \{1\}} x_j(t)\right), \\ \qquad \vdots \\ x_r(t+1) = x_{r-1}(t) \wedge \left(\bigwedge_{j \in \mathbf{N}_r \setminus \{r-1\}} x_j(t)\right), \\ x_{r+1}(t+1) = \bigwedge_{j \in \mathbf{N}_{r+1}} x_j(t), \\ x_{r+2}(t+1) = \bigwedge_{j \in \mathbf{N}_{r+2}} x_j(t), \\ \qquad \vdots \\ x_n(t+1) = \bigwedge_{j \in \mathbf{N}_n} x_j(t) \end{cases} \tag{5}$$

because $(1,2,\ldots,r)$ is a cycle. So if $x_i(t) = 0$ $(i = 1,2,\ldots,r)$, then $x_i(t+1) = 0$ $(i = 1,2,\ldots,r)$, which means $x_i(\infty) = 0$ $(i = 1,2,\ldots,r)$.

In this way, (ii) is proven. ∎

This theorem characterizes the structural-stability by the topology of the network structure G.

IV. Examples

The Boolean network in (2) is not structurally-stable from Theorem 1. In fact, its network structure G is given by Fig. 1 and is cyclic (e.g., $(1, 3, 2, 2, \ldots, 2)$ is a cycle).

On the other hand, the Boolean network

$$\Sigma_1 : \begin{cases} x_1(t+1) \;=\; x_5(t), \\ x_2(t+1) \;=\; \bar{x}_1(t), \\ x_3(t+1) \;=\; x_2(t) \vee x_5(t), \\ x_4(t+1) \;=\; \bar{x}_1(t) \wedge x_2(t), \\ x_5(t+1) \;=\; 1 \end{cases} \tag{6}$$

is structurally-stable, because the network structure G is illustrated as Fig. 2 and is acyclic.

Finally,

$$\Sigma_2 : \begin{cases} x_1(t+1) \;=\; x_5(t), \\ x_2(t+1) \;=\; \bar{x}_1(t), \\ x_3(t+1) \;=\; x_2(t), \\ x_4(t+1) \;=\; \bar{x}_1(t) \wedge (x_2(t) \vee \bar{x}_4(t)), \\ x_5(t+1) \;=\; \bar{x}_3(t) \end{cases} \tag{7}$$

is not structurally-stable. In fact, the network structure G is given by Fig. 3 and is cyclic.

Finally, it should be noted that Theorem 1 is useful not only for the stability test but also for the synthesis of Boolean networks. For instance, the first and final Boolean networks could be changed into a structurally-stable network by removing two edges so as to be acyclic. Moreover, if one wants to construct an oscillator based on the second Boolean networks, then it turns out from the theorem that, at least, some edges have to be added to the system so as to be cyclic.

V. Conclusion

A stability problem has been considered for Boolean networks. First, we have proposed a structural stability notion for a case where partial system information is available. We have derived a necessary and sufficient condition, which clarifies that the system is structurally stable if and only if the network structure is acyclic. Finally, some examples are given to show the effectiveness of the condition and the application to design problems.

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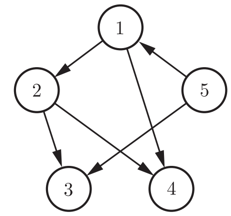

Fig. 2. Network structure G of Σ_1.

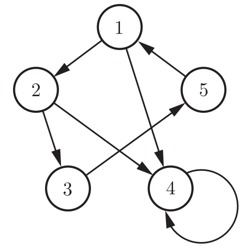

Fig. 3. Network structure G of Σ_2.

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