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Research Article

Robust Invariant Set Analysis of Boolean Networks

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In this paper, the robust invariant set (RIS) of Boolean (control) networks with disturbances is investigated. First, for a given fixed point, consider a special set called immediate neighborhoods of the fixed point; then a discrete derivative of Boolean functions at the fixed point is used to analyze the robust invariance, based on which a sufficient condition is obtained. Second, for more general sets, the robust output control invariant set (ROCIS) of Boolean control networks (BCNs) is investigated by semitensor product (STP) of matrices. Then, under a given output feedback controller, we obtain a necessary and sufficient condition to check whether a given set is robust control invariant set (RCIS). Furthermore, output feedback controllers are designed to make a set to be a RCIS. Finally, the proposed methods are illustrated by a reduced model of the lac operon in *E. coli*.

1. Introduction

In 1969, Kauffman [1] firstly used Boolean networks (BNs), which are a kind of logical networks to study genetic regulatory networks. Then, BNs have attracted extensive attention and have become abstract modeling schemes in other different fields such as neural networks [2] and immune response [3]. In BNs, each gene expression has two states as "1" and "0" to represent "on" and "off," respectively. Moreover, interactions between the states of each gene depend on Boolean functions, which are composed of logical operators such as disjunction and conjunction and so on. The state evolution for each gene is updated by a Boolean function about the states of current neighborhoods.

When control inputs are added into BNs, then BNs can be called BCNs. Similarly, control inputs take two values: "0" implies that the application of that intervention is ceased at that time point, and "1" means that some interventions are applied in BNs. A new matrix product called semitensor product (STP) of matrices was proposed to investigate BNs and BCNs [4]. Based on this, a BN (or BCN) can be converted into the corresponding algebraic form by calculating its unique transition matrix. Therefore, many fundamental and interesting problems have been investigated for BNs and BCNs, such as the controllability [5, 6], stabilization [7–15], observability [16–19], disturbance decoupling problem [20] synchronization [21], function perturbations [22], optimal control [23–26], normalization problem [27], and others. The STP has also been widely applied in games [28, 29] and asynchronous sequential machines [30, 31]. In detail, [28] investigated the evolutionarily stable strategy of finite evolutionary networked games by STP and then designed event-triggered controllers such that systems could converge globally. In [29], the stochastic set stabilization of random evolutionary Boolean games was further investigated, and a constructive algorithm was proposed to calculate stochastic reachable sets. On the other hand, [30] and [31] investigated the reachability and skeleton matrix by STP, respectively.

Usually, some external disturbance inputs always exist in systems. For example, cancer can be defined as failures in the healthy mechanisms of biological systems, and it has been classified as a kind of genetic uncertainties consisting of mutations [32]. Therefore, designing controllers is of great importance such that the set of desirable cellular states of BCNs with disturbance inputs is robust. In other words, if the trajectories of BCNs with some initial states reach a given set, which is called robust control invariant set (RCIS) [33], then those trajectories will never leave the set no matter what disturbances are. The RCIS has attracted many scholars' attention and obtained many results [34–37]. In [33], Li et al. used STP to study the RCIS of BCNs and presented an effective procedure to design state feedback controllers. However, due to the limitation of measurement conditions and the impact of immeasurable variables, measured output information rather than state information is always used to analyze and control systems [38]. Therefore, we will design output feedback controllers such that the trajectories of BCNs starting from some initial states in a given set will never leave the given set, which is called robust output control invariant set (ROCIS). On the other hand, Robert analyzed the local convergence of BNs by the discrete derivative of Boolean functions at a fixed point [39], which is a novel approach to investigate BNs. Motivated by this, we use the discrete derivative method to investigate the RIS, which makes the computational complexity reduced compared with STP. To the best of our knowledge, there is no result concerning the ROCIS of BCNs. The contributions of this paper are listed as follows:

(i) The discrete derivative is used to analyze the robust invariance.

(ii) A necessary and sufficient condition is derived to check whether a given set is ROCIS under a given output feedback controller.

(iii) Output feedback controllers are designed to make a given set be a ROCIS.

The rest of this paper is organized as follows. Section 2 reviews some notations and preliminary results, which will be used in the latter. Section 3 presents the main results. Section 4 ends the paper with a brief conclusion.

2. Preliminaries

In this section, we give some necessary properties of the STP and list some useful notations.

(i) Let $[a,b]$ be the set $\{a, a+1, \ldots, b\}$ for integers $b > a$.

(ii) Denote by matrix $M_{m\times n}$ the set of $m \times n$ real matrices.

(iii) Set $\Delta_n := \{\delta_n^k : 1 \le k \le n\}$, where δ_n^k is the k-th column of identity matrix I_n.

(iv) Let $\mathrm{Col}_i(B)$ stand for the i-th column of the matrix B.

(v) Matrix $L = [\delta_m^{i_1}, \delta_m^{i_2}, \ldots, \delta_m^{i_n}]$ is called a logical matrix, and simply denote it by $L = \delta_m[i_1, i_2, \ldots, i_n]$.

(vi) Let $\mathbf{1}_{2^k}$ denote the row vector of length 2^k with all entries being 1.

Definition 1 ([4]). For any given two matrices $A \in M_{m\times n}$ and $B \in M_{p\times q}$, the STP of A and B is defined as

$$A \ltimes B = \left(A \otimes I_{l/n}\right)\left(B \otimes I_{l/p}\right), \tag{1}$$

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

Proposition 2 ([4]). *Let $X \in \mathscr{R}^m$ be a column and N be any matrix. Then*

$$X \ltimes N = \left(I_m \otimes N\right) \ltimes X. \tag{2}$$

Definition 3 ([40]). Let $M \in \mathscr{M}_{p\times m}, N \in \mathscr{M}_{q\times m}$. Then, the Khatri-Rao product is defined as

$$\begin{aligned} M * N &= \left[\mathrm{Col}_1(M) \ltimes \mathrm{Col}_1(N) \cdots \mathrm{Col}_m(M) \ltimes \mathrm{Col}_m(N)\right] \\ &\in \mathscr{M}_{pq\times m}. \end{aligned} \tag{3}$$

The notation $\overline{\nabla}$ represents that when the two values denoted by A and B taking from $\mathscr{D}$ are the same, then $A\overline{\nabla}B = 0$. Otherwise, the result equals 1.

A logical domain, denoted by $\mathscr{D}$ is defined as $\mathscr{D} = \{0, 1\}$, and $\mathscr{D}^n = \underbrace{\mathscr{D} \times \cdots \times \mathscr{D}}_{n}$. If identifying $0 \sim \delta_2^2$ and $1 \sim \delta_2^1$, then $\Delta_2 \sim \mathscr{D}$, and $\Delta_{2^n} \sim \mathscr{D}^n$, where "$\sim$" represents two different forms of the same object. If $X \in \mathscr{D}^n$, then we say X is in a scalar form. If $X \in \Delta_{2^n}$, we say X is in a vector form. In the sequel, to distinguish the scalar form and the vector form of a variable, we use the notation X for a variable in $\mathscr{D}^n$, while we use the notation x for its vector variable in Δ_2. In short, $X \in \mathscr{D}$, but $x \in \Delta_2$.

The following lemma is important for the algebraic expressions of logical functions.

Lemma 4 ([4]). *Consider a logical function $f(X_1, X_2, \ldots, X_n) : \mathscr{D}^n \longrightarrow \mathscr{D}$. There exists a unique matrix $M_f \in \mathscr{L}_{2\times 2^n}$, called the structure matrix of f, such that*

$$f\left(X_1, X_2, \ldots, X_n\right) = M_f \ltimes \ltimes_{i=1}^n x_i, \tag{4}$$

where $\ltimes_{i=1}^n x_i = x_1 \ltimes x_2 \cdots \ltimes x_n \in \Delta_{2^n}$.

For example, the structure matrix of logical function $\vee$ is $\delta_2[1, 1, 1, 2]$. And the structure matrix of logical function $\wedge$ is $\delta_2[1, 2, 2, 2]$.

Definition 5. Assume that there are n-dimensional row vectors $X^1 = (X_{11}, X_{12}, \ldots, X_{1n})$ and $X^2 = (X_{21}, X_{22}, \ldots, X_{2n})$, $X_{ij} \in \mathscr{D}, i \in [1, 2], j \in [1, n]$, respectively. The distance vector denoted by $d(X^1, X^2)$ between X^1 and X^2 is defined; that is, $d(X^1, X^2) = ((X_{11}\overline{\nabla}X_{21}), (X_{12}\overline{\nabla}X_{22}), \ldots, (X_{1n}\overline{\nabla}X_{2n}))^T$.

Assume that $X = (X_1, X_2, \ldots, X_n)^T \in \mathscr{D}^n$, and then define a bijection $\mathscr{J} : \mathscr{D}^n \longrightarrow \Delta_{2^n}$ [4], where

$$\mathscr{J}(X) = \ltimes_{s=1}^n \delta_2^{2-X_s} = \delta_{2^n}^k \tag{5}$$

with $k = (1-X_1)2^{n-1} + (1-X_2)2^{n-2} + \cdots + (1-X_{n-1})2 + (2-X_n)$. Furthermore, we can also define $\mathscr{J}^{-1} : \Delta_{2^n} \longrightarrow \mathscr{D}^n$, where

$$\mathscr{J}^{-1}\left(\delta_{2^n}^k\right) = \left(X_1, X_2, \ldots, X_n\right)^T \tag{6}$$

with $X_1 = 2 - \lceil k/2^{n-1} \rceil$ and $X_i = 2 - \lceil (k - (\sum_{j=1}^{i}(1 - X_j)2^{n-j}))/2^{n-i} \rceil$, $i \in [2, n]$.

For example, assume that $X = (1, 0, 0, 1) \in \mathscr{D}^4$; then, by (5), one has that $\mathscr{J}(X) = \delta_{16}^7$.

3. Main Results

We consider the following system with n disturbance inputs:

$$\begin{aligned} X_1(t+1) &= f_1(\xi_1(t), X_1(t), \ldots, X_n(t)), \\ &\vdots \\ X_n(t+1) &= f_n(\xi_n(t), X_1(t), \ldots, X_n(t)), \end{aligned} \tag{7}$$

where $X_i \in \mathscr{D}$ and $\xi_i \in \mathscr{D}, i \in [1, n]$. $f_i : \mathscr{D}^{n+1} \longrightarrow \mathscr{D}, i \in [1, n]$ is a logical function.

For each f_i, there exists a unique structure matrix $M_{f_i}, i \in [1, n]$, by Lemma 4. Let $x(t) = \ltimes_{i=1}^{n} x_i(t) \in \Delta_{2^n}$ and $\xi(t) = \ltimes_{i=1}^{n} \xi_i(t) \in \Delta_{2^n}$, then system (7) can be converted into the following forms:

$$\begin{aligned} x_1(t+1) &= M_{f_1} \ltimes \xi_1(t) \ltimes x(t) = M_{f_1} \ltimes (\mathbf{I}_2 \otimes \mathbf{1}_{2^{n-1}}) \\ &\quad \ltimes \xi(t) \ltimes x(t) \\ &:= \overline{M}_{f_1} \ltimes \xi(t) \ltimes x(t), \\ &\vdots \\ x_n(t+1) &= M_{f_n} \ltimes \xi_n(t) \ltimes x(t) = M_{f_n} \ltimes \mathbf{1}_{2^{n-1}} \ltimes \xi(t) \\ &\quad \ltimes x(t) \\ &:= \overline{M}_{f_n} \ltimes \xi(t) \ltimes x(t), \end{aligned} \tag{8}$$

where $\overline{M}_{f_i} = M_{f_i} \ltimes (\mathbf{I}_{2^i} \otimes \mathbf{1}_{2^{n-i}}), i \in [1, n-1]$ and $\overline{M}_{f_n} = M_{f_n} \ltimes \mathbf{1}_{2^{n-1}}$. Multiplying all the equations in (8) together, we get

$$x(t+1) = L \ltimes \xi(t) \ltimes x(t), \tag{9}$$

where $L = \overline{M}_{f_1} * \overline{M}_{f_2} * \cdots * \overline{M}_{f_n} \in \mathscr{L}_{2^n \times 2^{2n}}$ with $*$ is the Khatri-Rao product [40]. Split L into 2^n equal blocks denoted by $L_i \in \mathscr{L}_{2^n \times 2^n}, i \in [1, 2^n]$, and then one has

$$\begin{aligned} x(t+1) &= L \ltimes \xi(t) \ltimes x(t), \\ &= [L_1 \ \ L_2 \cdots L_{2^n}] \ltimes \xi(t) \ltimes x(t). \end{aligned} \tag{10}$$

Given a state denoted by $X \in \mathscr{D}^n$, we denote the immediate neighborhoods of X by $\mathscr{I}(X)$ [39]; that is,

$$\mathscr{I}(X) = \left\{X' : d\left(X', X\right) = e_i, \ i \in [1, n]\right\}, \tag{11}$$

where $e_i, i \in [1, n]$ represents the i-th column of identify matrix $\mathbf{I}_n$. For example, assume that $X = (1, 0, 1) \in \mathscr{D}^3$, and then, based on the above definition, one has that $\mathscr{I}(X) = \{(0, 0, 1), (1, 1, 1), (1, 0, 0)\}$. Assume that $\mathscr{I}(X) = \{X^1, X^2, \ldots, X^n\}$, where $d(X^i, X) = e_i, i \in [1, n]$. Let $\mathscr{I}'(X) = \mathscr{I}(X) \cup \{X\}$.

Definition 6. Assume that two n-dimensional Boolean row vectors $X^1 = (X_{11}, X_{12}, \ldots, X_{1n})$ and $X^2 = (X_{21}, X_{22}, \ldots, X_{2n})$. We say that $X^1 \leq X^2$ if, for any $i \in [1, n]$, $X_{1i} \leq X_{2i}$.

For example, there are two vectors as $X^1 = (1, 0, 1, 1)$ and $X^2 = (1, 0, 1, 0)$. We have $X_{11} = X_{21} = 1, X_{12} = X_{22} = 0, X_{13} = X_{23} = 1$, and $X_{14} = 1 \geq X_{24} = 0$, and then $X^1 \geq X^2$.

Definition 7. Consider system (7), and assume that X is one of the fixed points for any disturbance. If, for any $X^i \in \mathscr{I}(X)$ and disturbance input $\xi(t) \in \mathscr{D}^n$, $X^i(t+1) \in \mathscr{I}'(X)$, then $\mathscr{I}'(X)$ is said to be a RIS.

Definition 8 ([39]). Consider system (7) with disturbance inputs. For any given state $X \in \mathscr{D}^n$ and when $\xi_i(t) \equiv 1$(*or* $\xi_i(t) \equiv 0$), the discrete derivative of Boolean functions at state X, denoted by $D^{\xi^1}(X)$(*or* $D^{\xi^0}(X)$), is an $n \times n$ Boolean matrix with its elements given as follows:

$$\left(D^{\xi^1}(X)\right)_{i,j} = \begin{cases} 1, & \text{if } f_i(1, X) \neq f_i\left(1, X^j\right), \\ 0, & \text{otherwise,} \end{cases} \tag{12}$$

or

$$\left(D^{\xi^0}(X)\right)_{i,j} = \begin{cases} 1, & \text{if } f_i(0, X) \neq f_i\left(0, X^j\right), \\ 0, & \text{otherwise.} \end{cases} \tag{13}$$

Based on Definition 8, we further define another $n \times n$ Boolean matrix; that is,

$$(D(X))_{i,j} = \left(D^{\xi^1}(X)\right)_{i,j} \vee \left(D^{\xi^0}(X)\right)_{i,j}. \tag{14}$$

It can be learned from the construction of $D(X)$ that for any $X^i \in \mathscr{I}(X), i \in [1, n]$, and $\xi(t) = \delta_{2^n}^{j_t} \in \Delta_{2^n}$, we get

$$\begin{aligned} &d\left(\mathscr{J}^{-1}\left(L_{j_t}\mathscr{J}\left(X^i\right)\right), \mathscr{J}^{-1}\left(L_{j_t}\mathscr{J}(X)\right)\right) \\ &\quad \leq D(X) \ltimes d\left(X^i, X\right). \end{aligned} \tag{15}$$

Theorem 9. *Consider system (7) with the fixed point X for any disturbance. If D(X) has at most one 1 in each column, then $\mathscr{I}'(X)$ is a RIS.*

Proof. If each column of $D(X)$ can only be zero vector or a basis vector, then it can be learned from (15) that the state can be guaranteed in the set $\mathscr{I}'(X)$ beginning from any initial state $X^i \in \mathscr{I}(X), i \in [1, n]$, in every step, which completes the proof. □

Example 10. Consider a BN with the fixed point X being (1, 1) for any disturbance:

$$\begin{aligned} X_1(t+1) &= X_1(t) \vee \xi_1(t), \\ X_2(t+1) &= X_1(t) \vee X_2(t) \vee \xi_2(t). \end{aligned} \tag{16}$$

One has $\mathscr{I}((1, 1)) = \{(0, 1), (1, 0)\}$ and $\mathscr{I}'((1, 1)) = \{(0, 1), (1, 0), (1, 1)\}$. Let $\xi_1 = \xi_2 = 1$ and $\xi_1 = \xi_2 = 0$, respectively, and we can get

$$D^{\xi^1}((1, 1)) = \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \tag{17}$$

and

$$D^{\xi^0}((1,1)) = \begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix}. \quad (18)$$

Therefore,

$$D((1,1)) = \begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix}. \quad (19)$$

Since $\mathrm{Col}_1(D((1,1))) = (1,0)^T$ and $\mathrm{Col}_2(D((1,1))) = (0,0)^T$, then Theorem 9 holds. Therefore, $\mathcal{I}'((1,1))$ is a RIS.

Remark 11. It is learned from Theorem 9 that matrix $D(X)$ with dimension $n \times n$ (not $2^n \times 2^n$) can be constructed, based on which the RIS is analyzed. Therefore, compared with the results obtained by STP in [35], the computational complexity is reduced from $\mathcal{O}(2^n)$ to $\mathcal{O}(n^2)$. Unfortunately, the method of discrete derivative can only be used to analyze some special systems in the form of (7). In the sequel, we will further analyze more general sets and design output feedback controllers such that the set is robust for any disturbance inputs.

In the following, consider a BCN with n nodes, p outputs, q disturbance inputs, and m inputs as

$$\begin{aligned} X_1(t+1) &= f_1\big(\xi_1(t),\ldots,\xi_q(t),U_1(t),\ldots,U_m(t),\\ &\quad X_1(t),\ldots,X_n(t)\big),\\ &\ \ \vdots\\ X_n(t+1) &= f_n\big(\xi_1(t),\ldots,\xi_q(t),U_1(t),\ldots,U_m(t),\\ &\quad X_1(t),\ldots,X_n(t)\big),\\ Y_1(t) &= h_1\left(X_1(t),\ldots,X_n(t)\right),\\ &\ \ \vdots\\ Y_p(t) &= h_p\left(X_1(t),\ldots,X_n(t)\right), \end{aligned} \quad (20)$$

where $f_i : \mathcal{D}^{q+m+n} \longrightarrow \mathcal{D}$ and $h_\alpha : \mathcal{D}^n \longrightarrow \mathcal{D}$ are logical functions, $i \in [1,n]$, $\alpha \in [1,p]$.

Then, the definition of a ROCIS of BCNs is presented as follows.

Definition 12. Consider system (20). A nonempty set $S \subseteq \mathcal{D}^n$ is said to be a ROCIS, if there exists an output feedback control as

$$\begin{aligned} U_1(t) &= g_1\big(Y_1(t),\ldots,Y_p(t)\big),\\ &\ \ \vdots\\ U_m(t) &= g_m\big(Y_1(t),\ldots,Y_p(t)\big), \end{aligned} \quad (21)$$

where $g_\beta : \mathcal{D}^p \longrightarrow \mathcal{D}$, $\beta \in [1,m]$ are Boolean functions such that, for the closed-loop system consisting of (20) and (21), $X(t) \in S$ implies $X(t+1) \in S$.

It can be learned from Lemma 4 that we can find unique structure matrices M_{f_i}, M_{h_α}, and M_{g_β} for logical functions f_i, h_α, and g_β in (20) and (21), respectively, $i \in [1,n]$, $\alpha \in [1,p]$, $\beta \in [1,m]$. Then the equivalent forms of (20) and (21) are

$$\begin{aligned} x_1(t+1) &= M_{f_1} \ltimes \xi(t) \ltimes u(t) \ltimes x(t),\\ &\ \ \vdots\\ x_n(t+1) &= M_{f_n} \ltimes \xi(t) \ltimes u(t) \ltimes x(t),\\ y_1(t+1) &= M_{h_1} \ltimes x(t),\\ &\ \ \vdots\\ y_p(t+1) &= M_{h_p} \ltimes x(t), \end{aligned} \quad (22)$$

and

$$\begin{aligned} u_1(t) &= M_{g_1} \ltimes y(t),\\ &\ \ \vdots\\ u_m(t) &= M_{g_m} \ltimes y(t), \end{aligned} \quad (23)$$

respectively, where $x(t) = \ltimes_{i=1}^n x_i(t)$, $y(t) = \ltimes_{i=1}^p y_i(t)$, $\xi(t) = \ltimes_{i=1}^q \xi_i(t)$, and $u(t) = \ltimes_{i=1}^m u_i(t)$.

Multiply the equations in (22), and (23), respectively; then (20) and (21) can be converted into the following forms:

$$\begin{aligned} x(t+1) &= L \ltimes \xi(t) \ltimes u(t) \ltimes x(t),\\ y(t) &= K \ltimes x(t), \end{aligned} \quad (24)$$

and

$$u(t) = G \ltimes y(t), \quad (25)$$

respectively, and $L = M_{f_1} * \cdots * M_{f_r} \in \mathcal{L}_{2^r \times 2^n}$, $K = M_{h_1} * \cdots * M_{h_r} \in \mathcal{L}_{2^p \times 2^n}$, and $G = M_{g_1} * \cdots * M_{g_m} \in \mathcal{L}_{2^m \times 2^p}$.

Assume that a given nonempty set $S = \{\delta_{2^n}^{i_1}, \delta_{2^n}^{i_2}, \ldots, \delta_{2^n}^{i_r}\}$ with $1 \le i_1 < i_2 < i_r \le 2^n$, and we analyze the following two problems:

(i) Problem 1: For a given output feedback matrix $G \in \mathcal{L}_{2^m \times 2^p}$, analyze whether the set S is a ROCIS of system (20) under control system $u(t) = Gy(t)$.

(ii) Problem 2: Design output feedback controllers such that S is a ROCIS of system (20).

Plug (25) into (24), then one has that

$$\begin{aligned} x(t+1) &= L \ltimes \xi(t) \ltimes G \ltimes y(t) \ltimes x(t)\\ &= L \ltimes \xi(t) \ltimes G \ltimes K \ltimes x(t) \ltimes x(t)\\ &= L \ltimes \xi(t) \ltimes G \ltimes K \ltimes \Phi_n \ltimes x(t)\\ &= L \ltimes \left(I_{2^q} \otimes \left(G \ltimes K \ltimes \Phi_n\right)\right) \ltimes \xi(t) \ltimes x(t),\\ &:= \widetilde{L} \ltimes \xi(t) \ltimes x(t), \end{aligned} \quad (26)$$

where $\widetilde{L} = L(I_{2^q} \otimes GK\Phi_N)$, and $\Phi_n = \mathrm{Diag}\{\delta_{2^n}^1, \delta_{2^n}^2, \ldots, \delta_{2^n}^{2^n}\} \in \mathscr{L}_{2^{2n}\times 2^n}$ is the power-reducing matrix satisfying $x(t) \ltimes x(t) = \Phi_n x(t)$.

Split $\widetilde{L}$ into 2^q equal blocks as

$$\widetilde{L} = \left[\widetilde{L}_1 \ \ \widetilde{L}_2 \ \ \cdots \ \ \widetilde{L}_{2^q}\right], \tag{27}$$

where $\widetilde{L}_\mu \in \mathscr{L}_{2^n\times 2^{n+m}}$, $\mu \in [1, 2^q]$, and then it follows from (26) that

$$x(t+1) = \left[\widetilde{L}_1 \ \ \widetilde{L}_2 \ \ \cdots \ \ \widetilde{L}_{2^q}\right] \ltimes \xi(t) \ltimes x(t). \tag{28}$$

Therefore, based on Definition 12, we have the following result.

Theorem 13. *For a given set $S = \{\delta_{2^n}^{i_1}, \ldots, \delta_{2^n}^{i_r}\}$ and an output feedback gain matrix G, set S is a ROCIS of system (20) under the output feedback control $u(t) = G \ltimes y(t)$ if and only if, for any $\mu \in [1, 2^q]$, $x(t) \in S$, and then $\widetilde{L}_\mu \ltimes x(t) \in S$.*

Proof. It is easy to see that the sufficiency holds, and we only need to prove the necessity. Consider (28); since $S = \{\delta_{2^n}^{i_1}, \ldots, \delta_{2^n}^{i_r}\}$ is a ROCIS of system (20) under the output feedback control $u(t) = Gy(t)$, then, for any $\xi(t) = \delta_{2^q}^{\mu}$, $\mu \in [1, 2^q]$, and any $x(t) \in S$, one has

$$\begin{aligned} x(t+1) &= \left[\widetilde{L}_1 \ \ \widetilde{L}_2 \ \ \cdots \ \ \widetilde{L}_{2^q}\right] \ltimes \delta_{2^q}^{\mu} \ltimes x(t) \\ &= \widetilde{L}_\mu \ltimes x(t) \in S. \end{aligned} \tag{29}$$

From the arbitrariness of $\xi(t)$ and $x(t)$, the conclusion holds. □

Remark 14. As mentioned above that set $\mathscr{D}^n$ is equivalent to Δ_{2^n}. Based on STP, the algebraic expression of system (20) can be obtained. Therefore, it will be better to write set $\mathscr{S}$ in vector form in Theorem 13 compared with Definition 12.

In the following, we discuss Problem 2, and then controller (25) will be designed. Suppose that $K = \delta_{2^p}[k_1 \ \ k_2 \cdots k_{2^n}] \in \mathscr{L}_{2^p\times 2^n}$ and $G = \delta_{2^m}[b_1 \ \ b_2 \cdots b_{2^p}] \in \mathscr{L}_{2^m\times 2^p}$, which will be designed. On one hand, for system (26) with $u(t) = Gy(t)$, $\xi(t) = \delta_{2^q}^{\mu}$, and $x(t) = \delta_{2^n}^{i_v} \in S, \mu \in [1, 2^q], v \in [1, r]$, one has that

$$\begin{aligned} x(t+1) &= L \ltimes \xi(t) \ltimes G \ltimes K \ltimes x(t) \ltimes x(t) \\ &= L \ltimes \delta_{2^q}^{\mu} \ltimes G \ltimes K \ltimes \delta_{2^n}^{i_v} \ltimes \delta_{2^n}^{i_v} \\ &= L_\mu \ltimes \delta_{2^m} \ltimes \left[b_{k_1} \ \ b_{k_2} \cdots b_{k_{2^n}}\right] \ltimes \delta_{2^n}^{i_v} \ltimes \delta_{2^n}^{i_v} \\ &= L_\mu \ltimes \delta_{2^m}^{b_{k_{i_v}}} \ltimes \delta_{2^n}^{i_v} \\ &= \mathrm{Col}_{(b_{k_{i_v}}-1)2^n+i_v}\left(L_\mu\right). \end{aligned} \tag{30}$$

On the other hand, we define the following sets:

$$S' = \left\{i_j : \delta_{2^n}^{i_j} \in S\right\}. \tag{31}$$

Obviously, $S' = \{i_1, i_2, \ldots, i_r\}$. For each $k_{i_v} \in [1, 2^p]$, $v \in [1, r]$,

$$\vartheta\left(k_{i_v}\right) = \left\{\lambda : \mathrm{Col}_\lambda(K) = \delta_{2^p}^{k_{i_v}}, \lambda \in \left[1, 2^n\right]\right\}, \tag{32}$$

and then denote

$$\varphi\left(k_{i_v}\right) = \vartheta\left(k_{i_v}\right) \cap S'. \tag{33}$$

For any integer $v \in [1, r]$, define

$$\begin{aligned} \Gamma_{i_v} = \Big\{ & b_{k_{i_v}} \in \left[1, 2^m\right] : \mathrm{Col}_{(b_{k_{i_v}}-1)2^n+i_v}\left(L_\mu\right) \\ & \in S, \text{for any } \mu \in \left[1, 2^q\right]\Big\}. \end{aligned} \tag{34}$$

For each $\varphi(k_{i_v})$, we construct a set, denoted by $\mathscr{W}(k_{i_v})$, as

$$\mathscr{W}\left(k_{i_v}\right) = \begin{cases} \bigcap_{\lambda\in\varphi(k_{i_v})} \Gamma_\lambda, & \varphi\left(k_{i_v}\right) \neq \emptyset, \\ \left[1, 2^m\right], & \varphi\left(k_{i_v}\right) = \emptyset. \end{cases} \tag{35}$$

Then, the result about the existence of output feedback controllers can be obtained.

Theorem 15. *$S = \{\delta_{2^n}^{i_1}, \ldots, \delta_{2^n}^{i_r}\}$ is a ROCIS of system (20) by an output feedback control, if and only if, for any $k_{i_v} \in [1, 2^p]$, $v \in [1, r]$,*

$$\mathscr{W}\left(k_{i_v}\right) \neq \emptyset. \tag{36}$$

Moreover, if (36) holds, then output feedback matrices under which S is a ROCIS are constructed as

$$G = \delta_{2^m}\left[b_1 \ \ b_2 \cdots b_{2^p}\right] \tag{37}$$

with

$$b_\iota \in \begin{cases} \mathscr{W}\left(k_{i_v}\right), & \textit{if } \iota = k_{i_v}, v \in [1, r], \\ \left[1, 2^m\right], & \textit{otherwise}. \end{cases} \tag{38}$$

Proof. (Sufficiency): Suppose that (36) holds. We construct controller (37). Then, for $K = \delta_{2^p}[k_1 \ \ k_2 \cdots k_{2^n}]$, one has

$$GK = \delta_{2^m}\left[b_{k_1} \ \ b_{k_2} \cdots b_{k_{2^n}}\right]. \tag{39}$$

Moreover, for any $\xi(t) = \delta_{2^q}^{\mu}$, $\mu \in [1, 2^q]$, and $x(t) = \delta_{2^n}^{i_v} \in S$, $v \in [1, r]$, we have that $b_{k_{i_v}} \in \mathscr{W}(k_{i_v}) \subseteq \Gamma_{i_v}$, and then it can be learned from (34) that $x(t+1) = \mathrm{Col}_{(b_{k_{i_v}}-1)2^n+i_v}(L_\mu) \in S$, for all $\mu \in [1, 2^q]$. Therefore, S is a ROCIS of system (20).

(Necessity): Suppose that S is a ROCIS of system (20) with control $u(t) = Gy(t)$, and then, for any $\xi(t) = \delta_{2^q}^{\mu}$, $\mu \in [1, 2^q]$, one can obtain that $x(t) = \delta_{2^n}^{i_v} \in S$, $v \in [1, r]$, which means that (36) holds.

In fact, if (36) does not hold, then there exists an integer $v_1 \in [1, r]$ such that $\mathscr{W}(k_{i_{v_1}}) = \emptyset$. In this case, it can be learned from (35) that $\varphi(k_{i_{v_1}}) \neq \emptyset$ and $\bigcap_{\lambda\in\varphi(k_{i_{v_1}})} \Gamma_\lambda = \emptyset$. Assume that $\varphi(k_{i_{v_1}}) = \{j_1, j_2, \ldots, j_\epsilon\}$, i.e., $k_{j_1} = k_{j_2} = \cdots = k_{j_\epsilon} = k_{i_{v_1}}$, then we have $b_{k_{j_1}} = b_{k_{j_2}} = \cdots = b_{k_{j_\epsilon}} = b_{k_{i_{v_1}}}$. Since S is a ROCIS of system (20) with control $u(t) = G \ltimes y(t)$, then $b_{k_{i_{v_1}}} \in \bigcap_{\lambda\in\varphi(k_{i_{v_1}})} \Gamma_\lambda$, which is a contradiction to $\bigcap_{\lambda\in\varphi(k_{i_{v_1}})} \Gamma_\lambda = \emptyset$. As a result, for any $v \in [1, r]$, $\mathscr{W}(k_{i_v}) \neq \emptyset$. □

Example 16. Let us consider a reduced model of the lac operon in *E. coli* [33, 41]:

$$\begin{aligned} X_1(t+1) &= \neg U_1(t) \wedge \left(X_2(t) \vee X_3(t)\right), \\ X_2(t+1) &= \neg U_1(t) \wedge U_2(t) \wedge X_1(t) \wedge \xi(t), \\ X_3(t+1) &= \neg U_1(t) \wedge \left(U_2(t) \vee \left(U_3(t) \wedge X_1(t)\right)\right), \end{aligned} \tag{40a}$$

where X_1, X_2, and X_3 are state variables denoting the lac mRNA, the lactose in high concentrations, and the lactose in medium concentrations, respectively; U_1, U_2, and U_3 are inputs variables representing the extracellular lactose, the high extracellular lactose, and the medium extracellular lactose, respectively; ξ is an external disturbance. The output equations are given by

$$\begin{aligned} Y_1(t) &= \neg X1(t) \wedge \left(X_2(t) \vee X_3(t)\right), \\ Y_2(t) &= \left(X_1(t) \wedge X_3(t)\right) \\ &\quad \vee \left(\neg X_1(t) \wedge X_2(t) \wedge X_3(t)\right), \\ Y_3(t) &= \neg X_1(t) \wedge X_3(t). \end{aligned} \tag{40b}$$

And the robust set $S = \{(X_1, X_2, X_3) : X_1 = 1, X_2 \vee X_3 = 1\}$.

Obviously, $S = \{\delta_8^1, \delta_8^2, \delta_8^3\}$, and then $S' = \{1, 2, 3\}$. Let $x(t) = x_1(t) \ltimes x_2(t) \ltimes x_3(t)$, $u(t) = u_1(t) \ltimes u_2(t) \ltimes u_3(t)$, and $y(t) = y_1(t) \ltimes y_2(t) \ltimes y_3(t)$, and then we have

$$\begin{aligned} x(t+1) &= L \ltimes \xi(t) \ltimes u(t) \ltimes x(t), \\ y(t) &= K \ltimes x(t), \end{aligned} \tag{41}$$

where

$$\begin{aligned} L = \delta_8 [\, & 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8 \\ & 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8 \\ & 1\ 1\ 1\ 5\ 3\ 3\ 3\ 7\ 1\ 1\ 1\ 5\ 3\ 3\ 3\ 7 \\ & 3\ 3\ 3\ 7\ 4\ 4\ 4\ 8\ 4\ 4\ 4\ 8\ 4\ 4\ 4\ 8 \\ & 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8 \\ & 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8\ 8 \\ & 3\ 3\ 3\ 7\ 3\ 3\ 3\ 7\ 3\ 3\ 3\ 7\ 3\ 3\ 3\ 7 \\ & 3\ 3\ 3\ 7\ 4\ 4\ 4\ 8\ 4\ 4\ 4\ 8\ 4\ 4\ 4\ 8 \,], \end{aligned} \tag{42}$$

and

$$K = \delta_8 [1\ 3\ 1\ 3\ 2\ 3\ 5\ 7]. \tag{43}$$

In this example, one can get $k_1 = k_3 = 1$, and $k_2 = 3$, and then we have $\vartheta(1) = \{1, 3\}$ and $\vartheta(3) = \{2, 4\}$. Therefore, $\varphi(1) = S' \cap \vartheta(1) = \{1, 3\}$, and $\varphi(3) = S' \cap \vartheta(3) = \{2\}$. From (34), we have $\Gamma_1 = \Gamma_2 = \Gamma_3 = \{5, 6, 7\}$, which means that $\mathscr{W}(1) = \{5, 6, 7\}$, and $\mathscr{W}(3) = \{5, 6, 7\}$. By Theorem 15, S is a ROCIS of system (40a) and (40b) with the disturbance ξ, and the output feedback gain matrices are

$$G = \delta_8 [b_1\ b_2\ \cdots\ b_8] \tag{44}$$

with $b_1 \in \mathscr{W}(1)$, $b_3 \in \mathscr{W}(3)$, and $b_i \in [1, 8]$, $i = 2, 4, 5, 6, 7, 8$. For example, let $b_1 = b_3 = 6$, $b_4 = b_5 = 5$, and $b_2 = b_6 = b_7 = b_8 = 1$, and then the corresponding output feedback control is

$$\begin{aligned} U_1(t) &= \left[X_1(t) \wedge \neg\left(X_2(t) \longrightarrow X_3(t)\right)\right] \\ &\quad \vee \left[\neg X_1(t) \wedge \neg\left(X_2(t) \vee X_3(t)\right)\right], \\ U_2(t) &= 1, \\ U_3(t) &= X_1(t) \wedge \neg X_3(t). \end{aligned} \tag{45}$$

4. Conclusion

In this paper, the RIS of BNs (BCNs) with disturbances was investigated. A special set called immediate neighborhood of a given fixed point was considered; then the discrete derivative of Boolean functions at the fixed point was used to analyze the robust invariance; based on this a sufficient condition was obtained. Furthermore, the ROCIS of BCNs was considered by STP. A necessary and sufficient condition was obtained to check whether a given set is RCIS under a given output feedback controller. Finally, for a given set, output feedback controllers were designed such that the set is RCIS.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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