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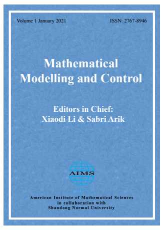

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Research article

Lebesgue sampling control of gene regulatory networks with stochastic disturbance: a Boolean network approach

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Abstract: The dynamic behavior and regulatory mechanisms of gene regulatory networks (GRNs) have attracted considerable attention in systems biology, as they play a crucial role in elucidating the principles of gene regulation, cellular evolution, and the pathogenesis of complex diseases. GRNs are widely modeled as Boolean networks (BNs) due to their intuitive logic, descriptive simplicity, and computational efficiency. In this paper, a robust set stabilization Lebesgue sampling control method was studied. First, a criterion was proposed to verify the robust set stabilization of BNs, and an algorithm was developed to design the sampled data state feedback controls (SDSFCs) within a given Lebesgue sampling region. Second, an improved sampling region was designed using the truth matrix method to reduce control update frequency while maintaining stability. Finally, the effectiveness of the proposed method was validated through a reduced model of the *lac* operon in *Escherichia coli*.

Keywords: gene regulatory networks; Lebesgue sampling; robust set stabilization; stochastic disturbances; semi-tensor product

1. Introduction

Gene regulatory networks (GRNs) are complex biological systems that determine the function of the cell through interactions among molecular regulators such as DNA, RNAs, proteins, and transcription factors [1]. These networks orchestrate gene expression programs in response to both internal signals and external environmental cues, thereby playing a fundamental role in various biological processes including cell differentiation, development, and disease progression. Understanding the dynamic behavior and regulatory mechanism from the system level is essential for uncovering the principles of cellular decision-making and for advancing therapeutic strategies in areas such as cancer, genetic disorders, and regenerative medicine [2–4].

To effectively analyze the structure and dynamics of GRNs, various mathematical models have been developed [5–8]. Among them, Boolean networks (BNs) [9] have emerged as a simple but powerful framework to describe the binary gene expression. In BNs, each node represents a gene, which is quantified as a binary variable indicating whether the gene is active (“1”) or inactive (“0”). Each edge denotes a regulatory interaction between genes and reflects the influence of one gene on another, which is captured through logical functions. To model gene intervention therapy technology, Boolean control networks (BCNs) [10] have been proposed by incorporating the binary control input into BNs. The application of control theory to Boolean models is particularly appealing to the medical community, as it offers great potential for guiding effective drug interventions and targeted manipulations, especially in the context of cancer [11–13].

Due to the intrinsic nonlinear and discrete nature of BNs, traditional analytical approaches are not readily applicable.

To address this issue, the semi-tensor product (STP) of matrices [14] has been introduced as a powerful tool that enables the logical expressions of the system into standard matrix forms. Based on this, classical control theory methods can be directly applied to analyze and control logical dynamic systems. Up to now, a multitude of fundamental and important results on BNs and BCNs have been studied via the STP method, such as stability and stabilization [15–17], controllability and observability [18–20], output tracking [21–24], and so on.

It is well known that the performance of practical GRNs may be affected by ubiquitous internal or external uncertainties [25–28]. For instance, intrinsic noise arises from the probabilistic nature of transcription and translation processes [29], while extrinsic noise results from environmental fluctuations such as temperature and pH variations [30]. These stochastic disturbances can drive the system toward instability [31, 32], as observed in cancer, which is widely regarded as a failure of the organism to cope with uncertainties such as genetic mutations [33]. Therefore, it is of great importance to design an appropriate control scheme under which the disturbed system can be robustly stabilized to a desired singleton state or a state set, which may correspond to a healthy gene expression pattern or a biologically meaningful steady-state attraction domain [34–37]. In recent years, a number of fundamental results on robust stabilization and robust set stabilization problems have been established [38–42]. However, current research on robust stabilization or set stabilization primarily focuses on deterministic disturbances, while stochastic disturbances have not been thoroughly studied.

Note that Lebesgue sampling control is a non-periodic control strategy [43], where the control input is updated only when the system state exhibits a significant deviation from a predefined condition. Compared with traditional time-driven sampling control [44], which updates the control input at fixed time intervals, Lebesgue sampling reduces computational and communication burdens by avoiding unnecessary updates when the system remains close to the desired trajectory. Using this control technique, the asynchronous stabilization problem of BCNs under a given Lebesgue sampling region was investigated in [45]. In addition, [46] studied the robust stabilization problem for BCNs under Lebesgue sampling. However, these existing works focus exclusively on stabilization to a singleton state, while the problem of robust set stabilization under Lebesgue sampling remains unaddressed.

The Lebesgue sampling control for set stabilization of BCNs with stochastic disturbances is studied for the first time in this paper. The main contributions are summarized as follows.

- For a given Lebesgue sampling region, a necessary and sufficient condition is presented to detect the robust set stabilization of the BCNs under SDSFCs. When the target set is reduced to a singleton, the proposed results naturally degenerate into the classical stabilization case. Moreover, the realization of set stabilization requires the computation of a robust control invariant set (RCIS), which is generally more complex than identifying a fixed point.
- For a given Lebesgue sampling signal, an improved Lebesgue sampling region is constructed via the truth matrix method. Compared with existing results, the proposed region is strictly larger under the same sampling signal, thus allowing less frequent controller updates. Furthermore, the truth matrix approach facilitates the direct identification of admissible controls for each state from its nonzero columns, which improves the efficiency and implementability of the control strategy.

The remainder of this paper is organized as follows. Section 2 presents the necessary preliminary concepts and notations. In Section 3, the robust set stabilization problem of BCNs with stochastic disturbance under SDSFCs is studied. Then, an example is presented in Section 4. In Section 5, a brief conclusion is provided.

2. Preliminaries

There are some necessary preliminaries in this section.

Notations:

- $\mathbb{Z}_+$ means the set of all positive integers.
- $\mathbb{R}_{c\times d}$ is the set of $c \times d$ real matrices.
- $\mathcal{D} := \{0, 1\}$, $\mathcal{D}^n := \underbrace{\mathcal{D} \times \mathcal{D} \times \cdots \times \mathcal{D}}_{n}$.

- $\mathrm{Col}_j(M)$ is the j-th column of matrix M.
- Δ_α represents $\left\{\delta_\alpha^j \mid j = 1,\ 2,\ \cdots,\ \alpha\right\}$, where $\delta_\alpha^j = \mathrm{Col}_j(I_\alpha)$.
- $M_{c\times d}$ is called a logical matrix, if $M = [\delta_c^{i_1}\ \delta_c^{i_2} \cdots \delta_c^{i_d}]$ and we briefly denote M by $M = \delta_c[i_1\ i_2 \cdots i_d]$. The set of $c \times d$ logical matrices is denoted by $\mathcal{L}_{c\times d}$.
- $\mathbf{0}_c := [\underbrace{0, 0, \cdots, 0}_{c}]^\top$, $\mathbf{1}_c := [\underbrace{1, 1, \cdots, 1}_{c}]^\top$.
- $o = lcm(o_1, o_2, \cdots, o_m)$ is the least common multiple of the positive integers $o_1, o_2, \cdots, o_m$.
- $\otimes$ is the Kronecker product.
- $A, B \subseteq \Delta_n$, $A\backslash B := \{x \in A | x \notin A \cap B\}$.
- $+_{\mathcal{B}}$: for any $a, b \in \mathcal{D}$, $a +_{\mathcal{B}} b = a \vee b$.

Definition 2.1. *([14]) The STP of $C \in \mathbb{R}_{q\times w}$ and $D \in \mathbb{R}_{s\times r}$ is defined as $C \ltimes D = (C \otimes I_{\frac{a}{w}})(D \otimes I_{\frac{a}{s}})$, where $a = lcm(w, s)$.*

Remark 2.1. *The STP is a generalization of the ordinary matrix product, thus we can omit the symbol "$\ltimes$" without confusion.*

The fundamental properties of the STP are as follows.

Lemma 2.1. *([14]) $X \in \mathbb{R}_k$ and $Y \in \mathbb{R}_p$ are two column vectors. Then,*

$$W_{[k,p]}XY = YX,$$

where $W_{[k,p]} := [I_p \otimes \delta_k^1, I_p \otimes \delta_k^2, \cdots, I_p \otimes \delta_k^k]$ is the swap matrix.

Define a bijection $\rho : \mathcal{D} \to \Delta_2$ by $\rho(1) = \delta_2^1$ and $\rho(0) = \delta_2^2$. Each Boolean variable X_i is mapped into their vector form $x_i = \rho(X_i)$. Then any nonlinear logical function can be written in an algebraic form.

Lemma 2.2. *([14]) Assume $f : \mathcal{D}^n \to \mathcal{D}$ is a logical function. There exists a unique matrix $L_f \in \mathcal{L}_{2\times 2^n}$ such that f can be converted into the following form:*

$$\rho(f(X_1, X_2, \cdots, X_n)) = L_f \ltimes_{i=1}^n x_i,$$

where $x_i \in \Delta_2$ is the vector form of X_i, $i \in \{1, 2, \cdots, n\}$, and L_f is the structure matrix of function f.

3. Main results

3.1. Problem formulation

A BCN with n states, m control inputs, and q disturbances is described as follows:

$$X(t+1) = f(\Xi(t), U(t), X(t)), \tag{3.1}$$

where $X(t) = (X_1(t), X_2(t), \cdots, X_n(t)) \in \mathcal{D}^n$, $U(t) = (U_1(t), U_2(t), \cdots, U_m(t)) \in \mathcal{D}^m$, and $\Xi(t) = (\Xi_1(t), \Xi_2(t), \cdots, \Xi_q(t)) \in \mathcal{D}^q$ denote the state variable, control inputs, and exogenous disturbance inputs at time t. $f : \mathcal{D}^{m+n+q} \to \mathcal{D}$ is a logical function. The q components of the disturbance inputs are mutually independent and satisfy

$$\mathbb{P}\{\Xi_i(t) = 1\} = \mathrm{a}_i,\ \ \mathbb{P}\{\Xi_i(t) = 0\} = 1 - \mathrm{a}_i.$$

We are given nonempty Lebesgue sampling region $\Lambda_\tau \subseteq \mathcal{D}^n$, where $\tau \in \mathbb{Z}_+$ is the Lebesgue sampling signal. If $X(t) \in \Lambda_\tau$, the SDSFC of system (3.1) in the next τ steps is

$$U(t) = h(X(t_k)), \tag{3.2}$$

where $t \in [t_k, t_k + \tau)$, t_k is the k-th sampled instant, and h is a logical function. When $X(t) \notin \Lambda_\tau$, the SDSFC of system (3.1) is

$$U(t) = g(X(t)), \tag{3.3}$$

where g is a logical function.

Next, we give the definition of robust set stabilization with stochastic disturbances for system (3.1).

Definition 3.1. *Ω^* is a nonempty set. System (3.1) is said to be robustly globally stabilizable to Ω^* for a given Lebesgue sampling region Λ_τ, if for each $X_0 \in \mathcal{D}^n$, there exist a positive integer T and an SDSFC such that*

$$\mathbb{P}\{X(t) \in \Omega^*\} = 1$$

holds for $t \geq T$ and $\Xi(t) \in \mathcal{D}^q$.

The set stabilization problem based on the logical form is complicated, so we consider converting the original system into an algebraic form.

Denote the vector form of $X_i(t)$ by $x_i(t)$, and then there is a one-to-one correspondence between $X(t) = (X_1(t), X_2(t), \cdots, X_n(t)) \in \mathcal{D}^n$ and $x(t) = \ltimes_{i=1}^n x_i(t) \in \Delta_{2^n}$. Similarly, we denote the vector forms of $U_i(t)$ and $\Xi_i(t)$ by $u_i(t)$ and $\xi_i(t)$, respectively, $U(t)$ can be expressed in vector form as $u(t) = \ltimes_{i=1}^m u_i(t)$ and $\Xi(t)$ can be expressed as $\xi(t) = \ltimes_{i=1}^{q}\xi_i(t)$. Particularly, Lebesgue sampling region Λ_τ can be converted to set Λ'_τ, where all the elements are expressed in their vector form. Via the STP, system (3.1) is converted to

$$x(t+1) = Fu(t)x(t)\xi(t), \tag{3.4}$$

where $F \in \mathcal{L}_{2^n\times 2^{n+m+q}}$. The SDSFC $u(t)$ is represented as

$$u(t) = \begin{cases} Hx(t_k), & \text{if } x(t_k) \in \Lambda'_\tau \text{ and } t \in [t_k, t_k+\tau), \\ Gx(t), & \text{if } x(t) \notin \Lambda'_\tau, \end{cases} \tag{3.5}$$

where $H \in \mathcal{L}_{2^m\times 2^n}$ and $G \in \mathcal{L}_{2^m\times 2^n}$ are called the state feedback gain matrices of (3.2) and (3.3), respectively.

When $x(t_k) \in \Lambda'_\tau$, the control (3.5) will keep constant within τ steps, and then we can obtain

$$\begin{aligned} x(t_k+\tau) &= Fu(t_k+\tau-1)x(t_k+\tau-1)\xi(t_k+\tau-1) \\ &= Fu(t_k+\tau-1)Fu(t_k+\tau-2)x(t_k+\tau-2) \\ &\quad \ltimes \xi(t_k+\tau-2)\xi(t_k+\tau-1) \\ &= \cdots\cdots \\ &= Fu(t_k+\tau-1)Fu(t_k+\tau-2)\cdots Fu(t_k)x(t_k) \\ &\quad \ltimes \xi(t_k)\cdots\xi(t_k+\tau-1). \end{aligned}$$

Due to fact that the control fact that the control is consistent in $[t_k, t_k+\tau)$, we can get

$$x(t_k+\tau) = (Fu(t_k))^\tau x(t_k)\widetilde{\xi}(t_k), \tag{3.6}$$

where $\widetilde{\xi}(t_k) = \ltimes_{j=t}^{t+\tau-1}\xi(j)$. For convenience, system (3.6) can be converted into

$$\begin{aligned} x(t_k+\tau) &= (Fu(t_k))^\tau x(t_k)\widetilde{\xi}(t_k) \\ &= (Fu(t_k))^\tau W_{[2^{q\tau},2^n]}\widetilde{\xi}(t_k)x(t_k), \end{aligned} \tag{3.7}$$

and we can aggregate the τ steps into one step.

When $x(t_k) \notin \Lambda'_\tau$, the control is updated over time. After substituting SDSFC (3.5) into system (3.4), then for the given Lebesgue sampling region, we can get a new system:

$$x(t+1) = \begin{cases} (Fu(t))^\tau W_{[2^{q\tau},2^n]}\widetilde{\xi}(t)x(t), & x(t) \in \Lambda'_\tau, \\ Fu(t)W_{[2^q,2^n]}\xi(t)x(t), & x(t) \notin \Lambda'_\tau. \end{cases}$$

Taking the mathematical expectation on disturbance variables, we get

$$x(t+1) = \begin{cases} (Fu(t))^\tau W_{[2^{q\tau},2^n]}\tilde{\gamma}x(t), & x(t) \in \Lambda'_\tau, \\ Fu(t)W_{[2^q,2^n]}\gamma x(t), & x(t) \notin \Lambda'_\tau, \end{cases} \tag{3.8}$$

where $\tilde{\gamma} = (\ltimes_{i=1}^{q}[\mathrm{w}_i, 1-\mathrm{w}_i]^\top)^\tau$ and $\gamma = \ltimes_{i=1}^{q}[\mathrm{w}_i, 1-\mathrm{w}_i]^\top$.

We can study the set stabilization problem of system (3.4) via system (3.8).

3.2. Set stabilization and control design of the BCNs for a given Lebesgue sampling region

In this subsection, we consider whether there exist SDSFCs such that system (3.8) can achieve robust set stabilization to $\mathbf{\Omega} \subseteq \Delta_{2^n}$ for a given Lebesgue sampling region Λ'_τ. If system (3.8) can converge to the set $\mathbf{\Omega}$, then it must converge to its control invariant set. The RCIS and largest robust control invariant set (LRCIS) with a given Lebesgue sampling region Λ'_τ are defined as follows.

Definition 3.2. *$\mathbf{\Omega_S} \subseteq \Delta_{2^n}$ is a nonempty set. Giving a Lebesgue sampled region Λ'_τ, $\mathbf{\Omega_S}$ is called an RCIS of BCN (3.4) with a probability of one, if there exists an SDSFC (3.5) such that*

$$\mathbb{P}\{x(t+1) \in \mathbf{\Omega_S} | x(t) \in \mathbf{\Omega_S}\} = 1.$$

The union of all RCISs of $\mathbf{\Omega_S}$ is still an RCIS of $\mathbf{\Omega_S}$. It is said to be the LRCIS of $\mathbf{\Omega_S}$, denoted by $\mathbf{\Omega_S^*}$.

If $\mathbf{\Omega} \cap \Lambda'_\tau = \emptyset$, the method to compute the RCISs of $\mathbf{\Omega_S}$ for a given Lebesgue sampling region Λ'_τ is the same as the method in reference [39]. So in this paper, we have the following assumption.

Assumption 3.1. $\mathbf{\Omega} \cap \Lambda'_\tau \neq \emptyset$.

Denote $W_{[2^{q\tau},2^n]}\tilde{\gamma} := W_1$, $W_{[2^q,2^n]}\gamma := W_2$ and define

$$\mathbf{S(j)} = \begin{cases} 1, \text{ if } \delta_{2^n}^j \in \Lambda'_\tau, \\ 0, \text{ otherwise.} \end{cases}$$

Then we calculate $\mathbf{\Omega_S^*}$ by constructing truth matrices. We construct matrix $T_{\mathbf{\Omega|\Omega}}$, where

$$[T_{\mathbf{\Omega|\Omega}}]_{p,j} = \begin{cases} 1, & \text{if } \prod_{t=1}^{\tau}\sum_{\delta_{2^n}^i\in\mathbf{\Omega}}\mathrm{Row}_i(\mathbf{S(j)}(F\delta_{2^m}^p)^t \\ & W_1\delta_{2^n}^j) + \sum_{\delta_{2^n}^i\in\mathbf{\Omega}}\mathrm{Row}_i((1-\mathbf{S(j)}) \\ & F\delta_{2^m}^p W_2\delta_{2^n}^j) = 1, \ \forall\delta_{2^n}^j \in \mathbf{\Omega}, \\ 0, & \text{otherwise.} \end{cases}$$

Denote $\mathbf{\Omega_1} = \{\delta_{2^n}^j | \mathrm{Col}_j(T_{\mathbf{\Omega|\Omega}}) \neq \mathbf{0}_{2^n}\}$, and then it is clear that $\mathbf{\Omega_1} \subseteq \mathbf{\Omega}$. If $\mathbf{S(j)} = 0$, then $\sum_{\delta_{2^n}^i\in\mathbf{\Omega}}\mathrm{Row}_i(F\delta_{2^m}^p W_2\delta_{2^n}^j) = 1$, which implies that state $\delta_{2^n}^j \in \mathbf{\Omega_1}$ can reach $\mathbf{\Omega}$ in one step under control $\delta_{2^m}^p$ with a probability of one. If $\mathbf{S(j)} = 1$, then

$$\prod_{t=1}^{\tau}\sum_{\delta_{2^n}^i\in\mathbf{\Omega}}\text{Row}_i\left(\mathbf{S(j)}(F\delta_{2^m}^p)^t W_1\delta_{2^n}^j\right)=1,$$

which shows that state $\delta_{2^n}^j \in \mathbf{\Omega}_1$ can reach $\mathbf{\Omega}$ at each step $t \in [1,\tau]$ under control $\delta_{2^m}^p$ with a a probability of of 1.

In system (3.7), we aggregate the τ steps into one step, so we also regard τ steps as one-step here. Thus $\mathbf{\Omega_1}$ is the one-step reachable set of $\mathbf{\Omega}$ with a probability of one. If $\mathbf{\Omega_1}=\emptyset$, then $\mathbf{\Omega}_{\boldsymbol{S}}^*=\emptyset$. If $\mathbf{\Omega_1}=\mathbf{\Omega}$, then $\mathbf{\Omega}_{\boldsymbol{S}}^*=\mathbf{\Omega}$, otherwise, $\mathbf{\Omega}$ is not an RCIS.

We further detect whether $\mathbf{\Omega_1}$ is an RCIS. Construct $T_{\mathbf{\Omega_1}|\mathbf{\Omega_1}}$ as

$$[T_{\mathbf{\Omega_1}|\mathbf{\Omega_1}}]_{p,j}=\begin{cases}1,\ \text{if}\ \prod_{t=1}^{\tau}\sum_{\delta_{2^n}^i\in\mathbf{\Omega_1}}\text{Row}_i\mathbf{S(j)}(F\delta_{2^m}^p)^t\\ W_1\delta_{2^n}^j+\sum_{\delta_{2^n}^i\in\mathbf{\Omega_1}}\text{Row}_i(1-\mathbf{S(j)})F\delta_{2^m}^p\\ W_2\delta_{2^n}^j=1,\ \forall\delta_{2^n}^j\in\mathbf{\Omega_1},\\ 0,\ \text{otherwise}.\end{cases}$$

Denote $\mathbf{\Omega_2}=\{\delta_{2^n}^j|\text{Col}_j(T_{\mathbf{\Omega_1}|\mathbf{\Omega_1}})\neq\mathbf{0}_{2^n}\}$, and it is clear that $\mathbf{\Omega_2}\subseteq\mathbf{\Omega_1}$. The discussion of $\mathbf{\Omega_2}$ is similar to $\mathbf{\Omega_1}$. By recursive calculations, we can obtain a positive integer $\mathbf{d}\in\{1,2,\cdots,|\mathbf{\Omega}|\}$ such that $\mathbf{\Omega_d}=\mathbf{\Omega_{d-1}}$, and then we get that $\mathbf{\Omega}_{\boldsymbol{S}}^*=\mathbf{\Omega_{d-1}}$. On this basis, an algorithm (Algorithm 1) is proposed to calculate the LRCIS $\mathbf{\Omega}_{\boldsymbol{S}}^*$.

Algorithm 1 The calculation of LRCIS $\mathbf{\Omega}_{\boldsymbol{S}}^*$.

Require: $F,\mathbf{\Omega}$
Ensure: $\mathbf{\Omega}_{\boldsymbol{S}}^*$

```
1: Initialize Ω_0 = Ω, d = 1;
2: while d ≤ |Ω| do
3:     Construct T_{Ω_{d-1}|Ω_{d-1}};
4:     Compute Ω_d;
5:     if Ω_d = ∅ then
6:         Ω*_S = ∅, stop;
7:     else if Ω_d = Ω_{d-1} then
8:         Ω*_S = Ω_d
9:     end if
10:    d := d + 1
11: end while
```

Above all, we know that $\mathbf{\Omega}_i\subseteq\mathbf{\Omega}_{i-1}$, $i\in[1,\mathbf{d}]$. If $\delta_{2^n}^j\in\mathbf{\Omega}_i$, there is at least one control $\delta_{2^m}^p$ which can drive $\delta_{2^n}^j$ to $\mathbf{\Omega}_{i-1}$. If $\delta_{2^n}^j\in\mathbf{\Omega}_{\boldsymbol{S}}^*\cap\Lambda_\tau'$, then $\delta_{2^m}^{h_j}=\delta_{2^m}^p$. If $\delta_{2^n}^j\in\mathbf{\Omega}_{\boldsymbol{S}}^*\backslash(\mathbf{\Omega}_{\boldsymbol{S}}^*\cap\Lambda_\tau')$, then $\delta_{2^m}^{g_j}=\delta_{2^m}^p$. Therefore, we can get the corresponding state feedback gain matrices satisfying

$$\begin{cases}H_{|\mathbf{\Omega}_{\boldsymbol{S}}^*\cap\Lambda_\tau'}\leq(T_{\mathbf{\Omega_d}|\mathbf{\Omega_d}})_{|\mathbf{\Omega}_{\boldsymbol{S}}^*\cap\Lambda_\tau'},\\ G_{|\mathbf{\Omega}_{\boldsymbol{S}}^*\backslash(\mathbf{\Omega}_{\boldsymbol{S}}^*\cap\Lambda_\tau')}\leq(T_{\mathbf{\Omega_d}|\mathbf{\Omega_d}})_{|\mathbf{\Omega}_{\boldsymbol{S}}^*\backslash(\mathbf{\Omega}_{\boldsymbol{S}}^*\cap\Lambda_\tau')},\end{cases}$$

which can keep the robust control invariance of $\mathbf{\Omega}_{\boldsymbol{S}}^*$.

If $\mathbf{\Omega}_{\boldsymbol{S}}^*=\emptyset$, then system (3.1) cannot achieve robust set stabilization for the given Lebesgue sampling region Λ_τ'. If $\mathbf{\Omega}_{\boldsymbol{S}}^*\neq\emptyset$, we use the truth matrix method to determine whether the system can reach $\mathbf{\Omega}_{\boldsymbol{S}}^*$ under SDSFC (3.5).

Denote $R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)=\mathbf{\Omega}_{\boldsymbol{S}}^*$ and $\Theta_1=\Delta_{2^n}\backslash R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)$. Construct $T_{R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)|\Theta_1}$ as

$$[T_{R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)|\Theta_1}]_{p,j}=\begin{cases}1, & \text{if}\ \sum_{\delta_{2^n}^i\in R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)}\text{Row}_i((\mathbf{S(j)}\\ & (F\delta_{2^m}^p)^\tau W_1+(1-\mathbf{S(j)})F\delta_{2^m}^p\\ & W_2)\delta_{2^n}^j)=1,\forall\delta_{2^n}^j\in\Theta_1,\\ 0, & \text{otherwise}.\end{cases}$$

Calculate $R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*):=\{\delta_{2^n}^j|\text{Col}_j(T_{R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)|\Theta_1})\neq\mathbf{0}_{2^n}\}$, and then for any $\delta_{2^n}^j\in R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)$, $R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)$ is one-step reachable from $\delta_{2^n}^j$ under control $\delta_{2^m}^p$.

If $R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)\bigcup R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)=\Delta_{2^n}$, system (3.1) can achieve robust set stabilization, otherwise, we will check whether $R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)=\emptyset$.

If $R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)=\emptyset$, then system (3.1) cannot achieve robust set stabilization. Otherwise, denote $\Theta_2=\Delta_{2^n}\backslash(R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)\bigcup R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*))$, and construct $T_{R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)|\Theta_2}$, where

$$[T_{R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)|\Theta_2}]_{p,j}=\begin{cases}1, & \text{if}\ \sum_{\delta_{2^n}^i\in R_0(\mathbf{\Omega}_{\boldsymbol{S}}^*)\bigcup R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)}\text{Row}_i(\\ & (\mathbf{S(j)}(F\delta_{2^m}^p)^\tau W_1+(1-\mathbf{S(j)})\\ & F\delta_{2^m}^p W_2)\delta_{2^n}^j)=1,\forall\delta_{2^n}^j\in\Theta_2,\\ 0, & \text{otherwise}.\end{cases}$$

Calculate $R_2(\mathbf{\Omega}_{\boldsymbol{S}}^*):=\{\delta_{2^n}^j|\text{Col}_j(T_{R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)|\Theta_2})\neq\mathbf{0}_{2^n}\}$. The discussion of $R_2(\mathbf{\Omega}_{\boldsymbol{S}}^*)$ is similar to $R_1(\mathbf{\Omega}_{\boldsymbol{S}}^*)$. By recursive calculations, there exists a positive integer $\widehat{k}$ such that either

$$\bigcup_{k=0}^{\widehat{k}}R_k(\mathbf{\Omega}_{\boldsymbol{S}}^*)=\Delta_{2^n}$$

or

$$R_{\widehat{k}}(\mathbf{\Omega}_{\boldsymbol{S}}^*)=\emptyset.$$

If $\bigcup_{k=0}^{\widehat{k}} R_k(\mathbf{\Omega}_{\mathcal{S}}^*) = \Delta_{2^n}$, we know that each $R_i(\mathbf{\Omega}_{\mathcal{S}}^*)$, $i \in [1, \widehat{k}]$, has at least one state, and for any $i, j \in [1, \widehat{k}]$, $i \neq j$, $R_i(\mathbf{\Omega}_{\mathcal{S}}^*) \cap R_j(\mathbf{\Omega}_{\mathcal{S}}^*) = \emptyset$. If $R_k(\mathbf{\Omega}_{\mathcal{S}}^*) = \emptyset$, then $R_{k+1}(\mathbf{\Omega}_{\mathcal{S}}^*) = \emptyset$, so there are at most $2^n - |\mathbf{\Omega}_{\mathcal{S}}^*|$ nonempty sets.

Based on the above analysis, we provide a theorem to detect whether system (3.4) can achieve robust set stabilization under stochastic disturbances for given Lebesgue sampling region Λ'_τ.

Theorem 3.1. *System (3.4) can achieve robust set stabilization with stochastic disturbances for given Lebesgue sampling region Λ'_τ under SDSFC (3.5), if and only if there is an integer $\widehat{k} \in \{1, 2, \cdots, 2^n - |\mathbf{\Omega}_{\mathcal{S}}^*|\}$, such that*

$$\bigcup_{k=0}^{\widehat{k}} R_k(\mathbf{\Omega}_{\mathcal{S}}^*) = \Delta_{2^n}. \tag{3.9}$$

Proof. (Necessity) Assume $\bigcup_{k=0}^{\widehat{k}} R_k(\mathbf{\Omega}_{\mathcal{S}}^*) \neq \Delta_{2^n}$, and then there exists $x'(t) \in \Delta_{2^n} \backslash (\bigcup_{k=0}^{2^n - |\mathbf{\Omega}_{\mathcal{S}}^*|} R_k(\mathbf{\Omega}_{\mathcal{S}}^*))$ such that no control can drive it to $\mathbf{\Omega}_{\mathcal{S}}^*$. It means that system (3.4) cannot achieve globally robust set stabilization with stochastic disturbances for given Lebesgue sampled region Λ'_τ under SDSFC (3.5), which is a contradicting issue. Therefore, the necessity is demonstrated.

(Sufficiency) Assume (3.9) holds. According to the computation of the robust reachable sets, all states in $R_1(\mathbf{\Omega}_{\mathcal{S}}^*)$ can reach $\mathbf{\Omega}_{\mathcal{S}}^*$ in one step. All states in $R_2(\mathbf{\Omega}_{\mathcal{S}}^*)$ can reach $R_1(\mathbf{\Omega}_{\mathcal{S}}^*)$ in one step, and then $R_2(\mathbf{\Omega}_{\mathcal{S}}^*)$ can reach $\mathbf{\Omega}_{\mathcal{S}}^*$ in two steps. After an iterative calculation, we know that all states in Δ_{2^n} can reach $\mathbf{\Omega}_{\mathcal{S}}^*$. Therefore, system (3.4) can achieve robust set stabilization with stochastic disturbances for given Lebesgue sampling region Λ'_τ under SDSFC (3.5). □

When Theorem 3.1 holds, Algorithm 2 is given to design the controller as follows.

Algorithm 2 Design of the SDSFC (3.5).

Require: $F, \mathbf{\Omega}_{\mathcal{S}}^*, T_{\mathbf{\Omega}_{\mathcal{S}}^* | \mathbf{\Omega}_{\mathcal{S}}^*}$
Ensure: H, G
Initialize $R_0(\mathbf{\Omega}_{\mathcal{S}}^*) = \mathbf{\Omega}_{\mathcal{S}}^*$, $k = 1$;
while $k \leq 2^n - |\mathbf{\Omega}_{\mathcal{S}}^*|$ **do**
  Compute $\Theta_k = \Delta_{2^n} \backslash \bigcup_{t=0}^{k-1} R_t(\mathbf{\Omega}_{\mathcal{S}}^*)$;
  Construct $T_{R_{k-1}(\mathbf{\Omega}_{\mathcal{S}}^*) | \Theta_k}$;
  Calculate $R_k(\mathbf{\Omega}_{\mathcal{S}}^*)$;
  if $\bigcup_{i=0}^{k} R_i(\mathbf{\Omega}_{\mathcal{S}}^*) = \Delta_{2^n}$ **then**
    Denote $\widehat{k} := k$
    Construct $(H)_{|\Lambda'_\tau} \leq (\widetilde{T})_{|\Lambda'_\tau}$ and $(G)_{|\Delta_{2^n} \backslash \Lambda'_\tau} \leq (\widetilde{T})_{|\Delta_{2^n} \backslash \Lambda'_\tau}$, stop;
  else if $R_k(\mathbf{\Omega}_{\mathcal{S}}^*) = \emptyset$ **then**
    Denote $\widehat{k} := k$
    Construct $\widetilde{T}$;
    Construct

$$\begin{cases} \mathrm{Col}_j(H)_{|\Lambda'_\tau} \leq (\widetilde{T})_{|\Lambda'_\tau}, \\ \mathrm{Col}_j(H)_{|\Delta_{2^n} \backslash \Lambda'_\tau} \leq (\mathbf{1}_{2^n})_{|\Delta_{2^n} \backslash \Lambda'_\tau}, \\ \mathrm{Col}_j(G)_{|\Delta_{2^n} \backslash \Lambda'_\tau} \leq (\widetilde{T})_{|\Delta_{2^n} \backslash \Lambda'_\tau}, \\ \mathrm{Col}_j(G)_{|\Lambda'_\tau} \leq (\widetilde{T})_{|\Lambda'_\tau}. \end{cases} \tag{3.10}$$

  end if
  $k := k + 1$
end while

3.3. *Designing the Lebesgue sampling region for the given Lebesgue sampling signal*

When robust set stabilization cannot be achieved for a given Lebesgue sampling region, it is necessary to design a suitable sampling region. Besides, if the system can achieve robust set stabilization under a state feedback control, in order to save the control costs, we can consider designing a Lebesgue sampling region to improve the original state feedback control. So in this part, we aim to investigate how to design a new Lebesgue sampling for a given Lebesgue sampling signal τ, which mainly focuses on the construction of a Lebesgue sampling region and the control design.

It is easy to see that the LRCIS contained in $\mathbf{\Omega}$ for a given Lebesgue sampling region must be a subset of the LRCIS contained in $\mathbf{\Omega}$ under a state feedback control. Then we have the following lemma.

Lemma 3.1. *If system (3.4) can achieve robust set stabilization to $\mathbf{\Omega}$ for a given Lebesgue sampling region*

Λ'_τ *under an SDSFC, then it must achieve robust set stabilization to* $\mathbf{\Omega}$ *under a state feedback control.*

Proof. Assume that the LRCISs contained in $\mathbf{\Omega}$ for a given Lebesgue sampling region and under a state feedback control are $\hat{\mathbf{\Omega}}$ and $\widehat{\mathbf{\Omega}}^*_S$, respectively. Obviously, $\hat{\mathbf{\Omega}} \subseteq \widehat{\mathbf{\Omega}}^*_S$. The states in system (3.4) under Lebesgue sampling controls can be divided into two parts, $x \in \Lambda'_\tau$ and $x \notin \Lambda'_\tau$.

If system (3.4) can achieve robust set stabilization to $\mathbf{\Omega}$ for a given Lebesgue sampling region Λ'_τ under an SDSFC, then we determine whether there exists a state feedback control $u(t) = Kx(t)$ such that system (3.4) can achieve robust set stabilization to $\mathbf{\Omega}$. For any state $x(0) \in R_1(\hat{\mathbf{\Omega}})$, we discuss it in two cases.

Case 1: $x(0) = \delta^i_{2^n} \notin \Lambda'_\tau$. In this case, there is a control $u(0) = G\delta^i_{2^n} = \mathrm{Col}_i(G)$, such that $x(0)$ can robustly reach $\hat{\mathbf{\Omega}}$ with a probability of one. Thus, for $x(0) = \delta^i_{2^n}$, we can design the control as $u = K\delta^i_{2^n} = \mathrm{Col}_i(K) = \mathrm{Col}_i(G)$.

Case 2: $x(0) = \delta^i_{2^n} \in \Lambda'_\tau$. For the state $\delta^i_{2^n} \in \Lambda'_\tau$, there exists a control $u(0) = H\delta^i_{2^n} = \mathrm{Col}_i(H)$, such that $x(0)$ can robustly reach $\hat{\mathbf{\Omega}}$ at the τ-th step. The evolutionary trajectories of $x(0)$ can be shown in Figure 1, where Γ_j, $j \in [1, \tau-1]$, represents the state sets that $x(0)$ can robustly reach at the t-th step under the control $u(0)$ with a probability of one.

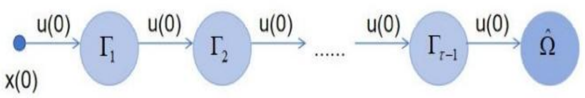

Figure 1. Evolutionary trajectories of $x(0)$ under control u.

We obtain that $x(0)$ and all the states in Γ_j, $j \in [1, \tau - 1]$, can robustly reach $\hat{\mathbf{\Omega}}$ under control $u(0) = \mathrm{Col}_i(H)$. Therefore, we can design the corresponding control for all these states as $u = K\delta^i_{2^n} = \mathrm{Col}_i(K) = \mathrm{Col}_i(H)$.

For $x(0) \in R_2(\hat{\mathbf{\Omega}})$, we first check whether the state belongs to Γ_j, $j \in [1, \tau-1]$. For $x(0) = \delta^i_{2^n} \in \Gamma_j$, $j \in [1, \tau-1]$, the corresponding control has been designed. If $x(0) \notin \Gamma_j$, $j \in [1, \tau-1]$, we also discuss it in two cases, and the control design method is similar to $x(0) \in R_1(\hat{\mathbf{\Omega}})$.

Case 1: $x(0) = \delta^i_{2^n} \notin \Lambda'_\tau$. If $x(0) \notin \Lambda'_\tau$, the corresponding control can be designed as $u = K\delta^i_{2^n} = \mathrm{Col}_i(K) = \mathrm{Col}_i(G)$ such that $x(0)$ can robustly reach $R_1(\hat{\mathbf{\Omega}}) \cup \hat{\mathbf{\Omega}}$.

Case 2: $x(0) = \delta^i_{2^n} \in \Lambda'_\tau$. If $x(0) \in \Lambda'_\tau$, the control can be designed as $u = \mathrm{Col}_i(K) = \mathrm{Col}_i(H)$, and then $x(0)$ can robustly reach $R_1(\hat{\mathbf{\Omega}}) \cup \hat{\mathbf{\Omega}}$ with a probability of one.

Similarly, for $x(0) = \delta^i_{2^n} \in R_{t^*}(\hat{\mathbf{\Omega}})$, $t^* \in [3, 2^n]$, we can also design the corresponding control $u = \mathrm{Col}_i(K)$ such that the evolutionary trajectories of $x(0)$ evolve to $\widehat{\mathbf{\Omega}}^*_S$ with a probability of one. Thus, system (3.4) can achieve robust set stabilization to $\widehat{\mathbf{\Omega}}^*_S$ under state feedback control $u(t) = Kx(t)$. □

If system (3.4) cannot achieve robust set stabilization to $\mathbf{\Omega}$ under a state feedback control, then it cannot achieve robust set stabilization to $\mathbf{\Omega}$ for any given Lebesgue sampling region, and we need not further study the stabilization problem of the system. Naturally, we have the following assumption.

Assumption 3.2. *System (3.4) can achieve robust set stabilization under a state feedback control.*

For the sake of distinction, we do not regard the τ steps as one step in the following. We denote the new Lebesgue sampling region as Λ^*_τ, and let

$$\Lambda^0_\tau = \{\delta^j_{2^n} \in \widehat{\mathbf{\Omega}}^*_S | \prod_{t=1}^{\tau} \sum_{\delta^i_{2^n} \in \widehat{\mathbf{\Omega}}^*_S} \mathrm{Row}_i((F\delta^p_{2^m})^t W_1 \delta^j_{2^n}) = 1\}, \tag{3.11}$$

where $\prod_{t=1}^{\tau} \sum_{\delta^i_{2^n} \in \widehat{\mathbf{\Omega}}^*_S} \mathrm{Row}_i((F\delta^p_{2^m})^t W_1 \delta^j_{2^n}) = 1$ means that state $\delta^j_{2^n}$ in Λ^0_τ can remain $\widehat{\mathbf{\Omega}}^*_S$ within τ steps under control $H\delta^j_{2^n} = \delta^p_{2^m}$, that is, the evolutionary trajectories of $\delta^j_{2^n}$ can remain in the $\widehat{\mathbf{\Omega}}^*_S$ under control $\delta^p_{2^m}$. We can put all states in Λ^0_τ into the new Lebesgue sampling region Λ^*_τ.

Next we continue to determine the other states in Λ^*_τ. Denote $\Upsilon_0 = \widehat{\mathbf{\Omega}}^*_S = R^\tau_0(\Upsilon_0)$, and we can design Lebesgue-type robust reachable sets $R^\tau_k(\Upsilon_0)$ as

$$R^\tau_k(\Upsilon_0) = \{\delta^j_{2^n} | \sum_{\delta^i_{2^n} \in \bigcup_{l=0}^{k-1} R^\tau_l(\Upsilon_0)} \mathrm{Row}_i((F\delta^{p_j}_{2^m})^\tau W_1 \delta^j_{2^n}) = 1\} \setminus \bigcup_{l=0}^{k-1} R^\tau_l(\Upsilon_0). \tag{3.12}$$

For any $\delta^j_{2^n} \in R^\tau_k(\Upsilon_0)$, there exists a control $\delta^{p_j}_{2^m}$ such that it can reach $\bigcup_{l=0}^{k_1-1} R^\tau_l(\Upsilon_0)$ at the τ-th step. If $R^\tau_{k_1}(\Upsilon_0) = \emptyset$, then let $\Psi_1 = \bigcup_{l=1}^{k_1-1} R^\tau_l(\Upsilon_0)$. If $\Upsilon_0 \cup \Psi_1 = \Delta_{2^n}$, it shows that all states can reach $\widehat{\mathbf{\Omega}}^*_S$. Then the new Lebesgue sampling region can be represented as $\Lambda^*_\tau := \Lambda^0_\tau \cup \Psi_1$.

Otherwise, we find which states can reach Ψ_1 in one step, which can be represented as

$$R_1(\Psi_1) = \{\delta_{2^n}^j | \sum_{\delta_{2^n}^i \in (\Psi_1 \bigcup \widehat{\Omega}_S^*)} \mathrm{Row}_i(F\delta_{2^m}^{p_j} W_1 \delta_{2^n}^j) = 1\}.$$

Let $\Upsilon_1 = R_1(\Psi_1) = R_0^\tau(\Upsilon_1)$ and we construct Lebesgue-type robust reachable sets $R_k^\tau(\Upsilon_1)$ as

$$R_k^\tau(\Upsilon_1) = \left\{\delta_{2^n}^j \middle| \sum_{\delta_{2^n}^i \in \bigcup_{h=0}^{k-1} R_h^\tau(\Upsilon_1)} \mathrm{Row}_i\left((F\delta_{2^m}^{p_j})^\tau W_1 \delta_{2^n}^j\right) = 1\right\} \setminus \bigcup_{h=0}^{k-1} R_h^\tau(\Upsilon_1) \cup \Psi_1.$$

If $R_{k_2}^\tau(\Upsilon_1) = \emptyset$, let $\Psi_2 = \bigcup_{l=1}^{k_2-1} R_l^\tau(\Upsilon_1)$. If $\Upsilon_0 \cup \Upsilon_1 \cup \Psi_1 \cup \Psi_2 = \Delta_{2^n}$, then $\Lambda_\tau^* := \Lambda_\tau^0 \cup \Psi_1 \cup \Psi_2$. Otherwise, we find which states can reach Ψ_2 in one step, where

$$R_1(\Psi_2) = \{\delta_{2^n}^j | \sum_{\delta_{2^n}^i \in \Psi_2} \mathrm{Row}_i(F\delta_{2^m}^{p_j} W_1 \delta_{2^n}^j) = 1\}.$$

Then we denote it by $\Upsilon_2 = R_1(\Psi_2)$. By recursive calculations, we obtain $\Psi_t = \bigcup_{l=1}^{k_t-1} R_l^\tau(\Upsilon_{t-1})$ and $\Upsilon_t = R_1(\Psi_t)$ until there exists an integer t^*, such that $R_1(\Psi_{t^*}) = \emptyset$ holds. Then the Lebesgue sampling region we designed can be represented as

$$\Lambda_\tau^* := \Lambda_\tau^0 \cup \Psi_1 \cup \Psi_2 \cup \cdots \cup \Psi_{t^*}.$$

Theorem 3.2. *If Assumption 3.2 holds, then system (3.4) can achieve robust set stabilization with stochastic disturbances for the new Lebesgue sampling region* Λ_τ^* *under SDSFC (3.5).*

Remark 3.1. *Through the above procedure, we get an improved Lebesgue sampling region* Λ_τ^**, and the improved SDSFCs with the new Lebesgue sampling region* Λ_τ^* *can be designed by Algorithm 2, which could reduce the control costs.*

Remark 3.2. *In our paper, we add states in* Λ_τ^**, as many as possible so that the improved Lebesgue sampling region is larger than that in the existing references for the same Lebesgue sampling signal. Thus, the frequency of controller updates can be reduced.*

Remark 3.3. *This study focuses on robust set stabilization of BCNs under Lebesgue sampling. While the proposed framework has demonstrated effectiveness under this non-periodic sampling scheme, it is worth noting that other non-periodic sampling strategies such as self-triggered [22] or event-triggered control [47] may also be applicable and offer complementary advantages. Extending the current approach to these alternative paradigms represents a promising direction for future research.*

4. An illustrative example

To demonstrate the effectiveness of the proposed method, we provide a classical GRN modeled as a BCN.

Example 1. Let us consider the BCN proposed in [48], which is a reduced Boolean model of the *lac* operon in *Escherichia coli*. This model highlights that *lac* mRNA and lactose constitute the core regulatory components of the *lac* operon. The model is defined by the following logical update rules:

$$\begin{cases} X_1(t+1) = \neg U_1(t) \wedge (X_2(t) \vee X_3(t)), \\ X_2(t+1) = \neg U_1(t) \wedge U_2(t) \wedge X_1(t), \\ X_3(t+1) = \neg U_1(t) \wedge (U_2(t) \vee (\Xi(t) \wedge X_1(t))), \end{cases} \tag{4.1}$$

where X_1 denotes *lac* mRNA, X_2 represents lactose at high concentrations, X_3 corresponds to lactose at medium concentrations, and U_1 and U_2 represent extracellular glucose and lactose, respectively. Ξ represents environmental noise, such as fluctuations in temperature or pH. The stochastic disturbance $\Xi(t)$ is modeled as a Bernoulli random variable with

$$\mathbb{P}\{\Xi(t) = 1\} = 0.8, \quad \mathbb{P}\{\Xi(t) = 0\} = 0.2,$$

indicating that the disturbance is active with a probability of 0.8 and inactive with a probability of 0.2.

Identify "$1 \sim \delta_2^1$" and "$0 \sim \delta_2^2$". Denote the vector forms of $X_i(t)$ by $x_i(t)$, $U_i(t)$ by $u_i(t)$, and $\Xi(t)$ by $\xi(t)$, respectively. Let $x(t) = \ltimes_{i=1}^3 x_i(t)$, $u(t) = \ltimes_{i=1}^2 u_i(t)$. Using the STP method, system (4.1) can be expressed in algebraic form as

$$x(t+1) = Fu(t)x(t)\xi(t), \tag{4.2}$$

where

$$F = \delta_8[8,8,8,8,8,8,8,8,8,8,8,8,8,8,8,8,\\ 8,8,8,8,8,8,8,8,8,8,8,8,8,8,8,8,\\ 1,1,1,5,3,3,3,7,1,1,1,5,3,3,3,7,\\ 3,3,3,7,4,4,4,8,4,4,4,8,4,4,4,8].$$

Assume the sampling interval is $\tau = 2$ and the Lebesgue sampling region is $\Lambda_2 = \{\delta_8^2, \delta_8^4, \delta_8^6, \delta_8^8\}$. Our goal is to determine whether the system can be robustly stabilized to the gene expression pattern encoded in the set $\mathbf{\Omega} = \{\delta_8^1, \delta_8^3, \delta_8^4, \delta_8^5\}$, which may correspond to functionally favorable or healthy regulatory states.

First, we can obtain $T_{\mathbf{\Omega}|\mathbf{\Omega}}$ by Algorithm 1 as

$$T_{\mathbf{\Omega}|\mathbf{\Omega}} = \begin{bmatrix} 0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0\\ 1&0&1&1&1&0&0&0\\ 1&0&1&0&1&0&0&0 \end{bmatrix}.$$

We have $\mathbf{\Omega_1} = \{\delta_8^1, \delta_8^3, \delta_8^4, \delta_8^5\} = \mathbf{\Omega}$, so the LRCIS $\mathbf{\Omega}_{\mathcal{S}}^* = \{\delta_8^1, \delta_8^3, \delta_8^4, \delta_8^5\}$.

Next, we design the SDSFC by Algorithm 2. Let $\Theta_1 = \Delta_8 \backslash \mathbf{\Omega}_{\mathcal{S}}^*$, and then $\Theta_1 = \{\delta_8^2, \delta_8^6, \delta_8^7, \delta_8^8\}$. We can construct truth matrix $T_{R_0(\mathbf{\Omega}_{\mathcal{S}}^*)|\Theta_1}$ as

$$T_{R_0(\mathbf{\Omega}_{\mathcal{S}}^*)|\Theta_1} = \begin{bmatrix} 0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0\\ 0&1&0&0&0&1&1&1\\ 0&1&0&0&0&0&1&0 \end{bmatrix},$$

so $R_1(\mathbf{\Omega}_{\mathcal{S}}^*) = \{\delta_8^2, \delta_8^6, \delta_8^7, \delta_8^8\}$. Based on the above discussion, we can get

$$R_0(\mathbf{\Omega}_{\mathcal{S}}^*) \bigcup R_1(\mathbf{\Omega}_{\mathcal{S}}^*) = \Delta_8,$$

and

$$\widetilde{T} = R_0(\mathbf{\Omega}_{\mathcal{S}}^*)|\Theta_1 +_{\mathcal{B}} T_{\mathbf{\Omega}_{\mathcal{S}}^*|\mathbf{\Omega}_{\mathcal{S}}^*} = \begin{bmatrix} 0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0\\ 1&1&1&1&1&1&1&1\\ 1&1&1&0&1&0&1&0 \end{bmatrix}.$$

According to (3.10) and $\widetilde{T}$, we can obtain one of the SDSFCs as

$$u(t) = \begin{cases} Hx(t_k), & \text{if } x(t_k) \in \Lambda_2 \text{ and } t \in [t_k, t_k+1), \\ Gx(t), & \text{otherwise,} \end{cases} \tag{4.3}$$

where

$$H = \delta_4[2,3,4,3,1,3,2,3]$$

and

$$G = \delta_4[4,1,3,3,4,1,4,2].$$

Through Theorem 3.1, system (4.2) can achieve robust set stabilization with stochastic disturbances for given Lebesgue sampling region Λ_2 under SDSFC (4.3). The state transformation graph of system (4.2) is shown in Figure 2.

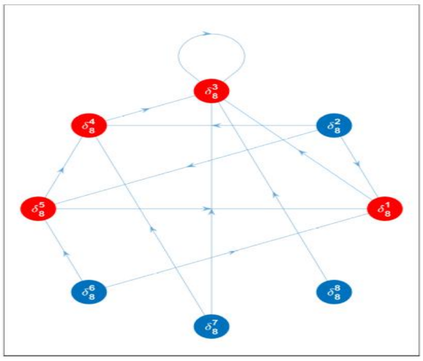

Figure 2. State transformation of system (4.2) under (4.3).

To further reduce the frequency of controller updates—a biologically desirable goal to minimize external interventions—we apply the proposed method to construct an improved sampling region.

First, let $\mathbf{S(j)} = 0$, and we have that the LRCIS contained in $\mathbf{\Omega}$ under state feedback controls is $\widehat{\mathbf{\Omega}}_{\mathcal{S}}^* = \{\delta_8^1, \delta_8^3, \delta_8^5\}$. Next we find which states can remain in $\widehat{\mathbf{\Omega}}_{\mathcal{S}}^*$ within τ steps under the same control according to (3.11), and we have

$$\Lambda_2^0 = \widehat{\mathbf{\Omega}}_{\mathcal{S}}^* = \{\delta_8^1, \delta_8^3, \delta_8^5\}.$$

Denote $\Upsilon_0 = \widehat{\mathbf{\Omega}}_{\mathcal{S}}^* = R_0^\tau(\Upsilon_0)$ and design Lebesgue-type robust reachable sets $R_k^\tau(\Upsilon_0)$ by (3.12), where $R_1^\tau(\Upsilon_0)$ can be obtained as follows:

$$R_1^\tau(\Upsilon_0) = \{\delta_8^2, \delta_8^4, \delta_8^6, \delta_8^7, \delta_8^8\}.$$

Obviously, $R_2^\tau(\Upsilon_0) = \emptyset$ and $\Upsilon_0 \cup R_1^\tau(\Upsilon_0) = \Delta_8$. Let $\Psi_1 = R_1^\tau(\Upsilon_0)$, and then the new Lebesgue sampling region can be derived as

$$\Lambda_2^* = \{\delta_8^1, \delta_8^2, \delta_8^3, \delta_8^4, \delta_8^5, \delta_8^6, \delta_8^7, \delta_8^8\}.$$

Similar to the above procedure, the improved SDSFCs under new Lebesgue sampling region Λ_2^* can be designed by Algorithm 2. Let $\Theta_1' = \Delta_8 \backslash \widehat{\mathbf{\Omega}}_{\mathcal{S}}^* = \{\delta_8^2, \delta_8^4, \delta_8^6, \delta_8^7, \delta_8^8\}$, and we have the truth matrix $\widetilde{T}$ as

$$\widetilde{T} = R_0(\widehat{\mathbf{\Omega}}_{\mathcal{S}}^*)|\Theta_1' +_{\mathcal{B}} T_{\widehat{\mathbf{\Omega}}_{\mathcal{S}}^*|\widehat{\mathbf{\Omega}}_{\mathcal{S}}^*}$$
$$= \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 1 & 1 & 1 & 1 & 1 & 1 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}.$$

Therefore, one of the improved SDSFCs is designed as

$$u'(t) = \begin{cases} H'x(t_k), & \text{if } x(t_k) \in \Lambda_2 \text{ and } t \in [t_k, t_k + 1), \\ G'x(t), & \text{otherwise,} \end{cases}$$

where

$$H' = \delta_4[4, 3, 3, 3, 3, 3, 3, 3]$$

and

$$G' = \delta_4[1, 1, 2, 3, 1, 2, 4, 2].$$

This improved control design significantly reduces the number of sampling-triggered updates, making it more suitable for potential implementation in gene regulation therapies where control interventions should be as infrequent and minimally invasive as possible.

5. Conclusions

In this study, we have explored, for the first time, the problem of robust set stabilization for BCNs with stochastic disturbances under Lebesgue sampling—a non-uniform control strategy particularly relevant to biological systems where interventions may be costly or limited. Our study established a formal algebraic framework for BCNs under stochastic perturbations and proposed a necessary and sufficient criterion for achieving robust set stabilization. An efficient algorithm based on the truth matrix method was developed to design stochastic disturbance SDSFCs within a given Lebesgue sampling region.

To further reduce the control frequency and potential intervention burden, an improved sampling region and corresponding SDSFCs were constructed, allowing for more flexible and cost—efficient regulation strategies. Although this sampling approach reduces the frequency of external interventions—a critical advantage for biomedical applications such as gene therapy—it may lead to longer convergence times. Future research will focus on optimizing the controller design to balance intervention efficiency with faster convergence, aiming to enable more practical and minimally invasive control strategies for stochastic gene regulatory networks and other biological systems. This framework holds promise for improving the design of therapeutic interventions in the context of noisy gene expression, such as in cancer or genetic disorders.

Use of Generative-AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

The authors declare that there are no conflicts of interest.

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