

Received September 14, 2021, accepted September 15, 2021, date of publication September 20, 2021, date of current version September 29, 2021.

Digital Object Identifier 10.1109/ACCESS.2021.3113988

NNs-Based Adaptive Control for Genetic Regulatory Networks With Sensor Faults

BING LÜ¹ AND QIKUN SHEN^{1,2}

¹College of Bioscience and Biotechnology, Yangzhou University, Yangzhou 225009, China

²College of Information Engineering, Yangzhou University, Yangzhou 225127, China

Corresponding author: Qikun Shen (qkshen@yzu.edu.cn)

This work was supported in part by the National Natural Science Foundation of China under Grant 61873229 and Grant 61473250.

ABSTRACT This article considers an adaptive control problem of genetic regulatory networks, where unknown sensor faults are considered. By using the function approximation capability of neural networks, a neural-networks-based gene circuit control method is designed, where the unknown sensor faults are compensated. Comparing with the existing results where regulatory functions meet known SUM logic, the regulatory functions considered in this article are unknown and do not satisfy SUM logic. Furthermore, the fault negative influence on neural network function approximation, which is caused by state sensor faults, has been compensated. In sense of Lyapunov stability theory, the closed-loop system is asymptotically bounded and all the signals in the system converge to an adjustable neighborhood of the origin. Finally, some simulation results are given to show the effectiveness of the design method.

INDEX TERMS Genetic regulatory networks, gene circuit control, adaptive control.

I. INTRODUCTION

Gene regulatory networks (GRNs) have become a hot research issue in recent years. From the research about GRNs, the researchers can understand the relationship and influence among genes in a cell, further understand the cell manner and find ways to control cell behavior. For the research, the first task is to model for gene regulation networks (GRNs) [1], [2]. *Modeling for GRNs* is to construct a mathematical model for GRNs, which can reflect the relationship and influence among the genes in a cell. Based on the model, further research can be made. For example, stability analysis can be made for GRNs [3], [4]. Further, by using the model, gene circuit control also can be designed for the GRNs to obtain suitable function, which is called *gene circuit control design* [5]–[7]. In addition, to obtain the values of model parameters in the GRNs model, various filter design methods also are proposed for GRNs, which is within the scope of *GRNs identification* [8], [9]. However, in most of the existing results, an assumption should be satisfied, namely, for a gene, each transcription factor acts additively to regulate it, and each regulatory function is assumed to sum over all its inputs. The assumption is called *SUM regulatory logic* assumption in literature [1]–[12], [23]. In fact, in a cell,

GRNs are very complex, and the gene regulatory among the genes also is complex, which implies that the so-called SUM regulatory logic does not always hold. The purpose of *SUM regulatory logic* maybe to decrease the complexity and to easily understand the GRNs. That is to say, in some cases, gene regulatory does not satisfy the SUM logic and is nonlinear regulatory [17], where the regulatory function is a nonlinear function about the states of the other genes in a cell. Note that, in our previous results [17], stability control design was not considered. Obviously, the control design in the above literatures [1]–[12] do not suitable for the GRNs without *SUM regulatory logic*. Therefore, how to control for GRNs without *SUM regulatory logic* is necessary and more interesting, which is the first motivation of this work.

Sensors including state and output sensors may become faulty in the practical applications [17]–[20]. Due to the sensor faults, the precise values of the GRNs' states cannot be obtained and further cannot be used in *gene circuit control design*, and only the values polluted by the faults can be applied in the control design. Note that, the values polluted by the faults will affect not only control accuracy but also control performance. Thus, to increase control accuracy and performance of the GRNs with sensor faults, the faults should be compensated, and fault-tolerant control (FTC) design should be proposed. Up to now, to our best knowledge, however, sensor faults were not considered in most of the results about

The associate editor coordinating the review of this manuscript and approving it for publication was Jinquan Xu.

GRNs in literature. In fact, for control designing of dynamics systems including GRNs, state sensor fault compensation and FTC still is a challenging and open problem, which also motivates us for this work.

Neural networks (NNs) including radius basic function neural networks (RBFNNs) [15]–[17], can approximate any unknown smooth function on a compact set. For example, for an unknown continuous function $f(x)$ with state vector x , RBFNNs are used to approximated it. The input layer contains x , and the final output of the NNs, i.e., $\hat{f}(x, 1)$, also is dependent on state vector x . From NNs approximation theory, we know, on a compact set, $f(x) - \hat{f}(x, 1)$ is bounded and $\hat{f}(x, 1)$ can be seen an approximation of $f(x)$. Note that, it is via sensors that the signal x_a can be obtained by the designer and used in control designing. That is to say, only x_a , not x , can be using in RBFNNs, which implies that the NNs final output is $\hat{f}(x_a, 1)$. Obviously, in the fault-free case, $x = x_a$ and $\hat{f}(x_a, 1) = \hat{f}(x, 1)$. However, in the faulty case, things have changed a lot, where $\hat{f}(x_a, 1) \neq \hat{f}(x, 1)$ because of $x \neq x_a$. It implies that the state sensor faults affect the final output, further affect the approximation accuracy of the NNs. Hence, state sensor faults should be compensated when NNs are used to approximate an unknown smooth function. However, how to compensate for the sensor faults in NNs function approximation is necessary and important, which is a motivation of this work.

In this paper, we consider the gene circuit control design problem of GRNs without *SUM regulatory logic*, and propose a fault-tolerant gene circuit control method against state sensor faults. Comparing with the existing results in literature, the following contributions are emphasizing.

- (i) Unlike the previous results [1]–[6] where gene regulatory logic is SUM logic, the regulatory logic considered in this paper is not only unknown but also nonlinear;
- (ii) Different from [7]–[12] where the gene regulatory functions are known, the gene regulatory functions considered in this paper are unknown and will be approximated by NNs;
- (iii) The previous results about GRNs such as [1]–[12] where state sensor faults are not considered, the faults are considered and compensated to reduce their negative influence on NNs' function approximation.

The rest of this paper is organized as follows. In Section II, the preliminaries and problem formulation are presented. Main results are proposed In Section III. Section IV gives some simulations. Finally, Section V draws the conclusions.

II. MODEL FORMULATION AND PRELIMINARIES

In this section, the GRNs considered in this paper can have the following form,

$$\begin{cases} \dot{x}_{i,m}(t) = -a_i x_{i,m}(t) + g_i(x_p(t)) + u_{i,m} \\ \dot{x}_{i,p}(t) = -c_i x_{i,p}(t) + d_i x_{i,m}(t) + u_{i,p}, \end{cases} \quad (1)$$

where $x_{i,p}(t) \in R$ and $x_{i,m}(t) \in R$ respectively concentrations of protein and *m*RNA of the *i*th gene; $c_i > 0$ and $a_i > 0$

are degradation rates of protein and *m*RNA, respectively; $u_{i,m} \in R$ and $u_{i,p} \in R$ are the control input signals; d_i denotes translation rate, and $g_i(\cdot)$ is the feedback regulation of the protein on the transcription of the *i*th gene, which is a smooth function. Notice that, the function $g_i(\cdot)$ is unknown.

In this paper, for (1), an equilibrium point is assumed to be $(x_{i,m}^*, x_{i,p}^*)$. Define $z_{i,m} = x_{i,m}(t) - x_{i,m}^*$ and $z_{i,p} = x_{i,p} - z_{i,p}^*$. Then, it follows from (1) that

$$\begin{cases} \dot{z}_{i,m}(t) = -a_i z_{i,m}(t) + f_i + u_{i,m} + a_i x_{i,m}^* \\ \dot{z}_{i,p}(t) = -c_i z_{i,p}(t) + d_i z_{i,m}(t) + u_{i,p} + c_i x_{i,p}^*, \end{cases} \quad (2)$$

where $f_i = g_i(x_{1,p}(t), x_{2,p}(t), \dots, x_{n,p}(t)) - g_i(x_{1,p}^*(t), x_{2,p}^*(t), \dots, x_{n,p}^*(t))$.

Let

$$\begin{aligned} x_m^* &= [x_{1,m}^*, x_{2,m}^*, \dots, x_{n,m}^*]^T, \\ x_p^* &= [x_{1,p}^*, x_{2,p}^*, \dots, x_{n,p}^*]^T, \\ z_m &= [z_{1,m}, z_{2,m}, \dots, z_{n,m}]^T \end{aligned}$$

and

$$\begin{aligned} z_p &= [z_{1,p}, z_{2,p}, \dots, z_{n,p}]^T, \\ u_m &= [u_{1,m}, u_{2,m}, \dots, u_{n,m}]^T, \\ u_p &= [u_{1,p}, u_{2,p}, \dots, u_{n,p}]^T, \end{aligned}$$

then (2) can be rewritten in the following compact form:

$$\begin{cases} \dot{z}_m = -Az_m + f + u_m + Ax_m^* \\ \dot{z}_p = -Cz_p + Dz_m + u_p + Cx_p^*, \end{cases} \quad (3)$$

where $A = \text{diag}\{a_1, \dots, a_n\}$, $C = \text{diag}\{c_1, \dots, c_n\}$, $D = \text{diag}\{d_1, \dots, d_n\}$, $f = [f_1, \dots, f_n]^T$, $x_m^* = [x_{1,m}^*, \dots, x_{n,m}^*]^T$, $x_p^* = [x_{1,p}^*, \dots, x_{n,p}^*]^T$.

The main task in this paper is to design external control input signals for the GRNs such that it is stable.

Note that, for convenience, $\bullet(t)$ is abbreviated to \bullet here and in the following.

From Lyapunov stability theory, we know, if f is known and the states of each gene in the cell can be precisely measured without sensor faults or measurement noises, then u_m and u_p can be designed as follows:

$$\begin{cases} u_m = K_m z_m - f - Ax_m^* \\ u_p = K_p z_p - Dz_m - Cx_p^* \end{cases} \quad (4)$$

where matrices $K_m \in R^{n \times n}$ and $K_p \in R^{n \times n}$ will be designed later.

Define the following Lyapunov function

$$V_1 = \frac{1}{2}(z_m^T z_m + z_p^T z_p).$$

Differentiating V_1 with respect to time t , it yields

$$\begin{aligned} \dot{V}_1 &= z_m^T \dot{z}_m + z_p^T \dot{z}_p \\ &= z_m^T (-Az_m + f + u_m + Ax_m^*) \\ &\quad + z_p^T [-Cz_p + Dz_m + u_p + Cx_p^*]. \end{aligned}$$

Substituting (4) into \dot{V}_1 , we have

$$\begin{aligned} \dot{V}_1 &= z_m^T(-Az_m + K_m z_m) + z_p^T(-Cz_p + K_p z_p) \\ &= z_m^T(-A + K_m)z_m + z_p^T(-C + K_p)z_p. \end{aligned} \quad (5)$$

Obviously, if K_m and K_p are designed such that

$$-A + K_m < 0 \quad \text{and} \quad -C + K_p < 0,$$

then, we have $\dot{V}_1 < 0$, which implies that (3) is stable. This means that the control objective in this paper is achieved.

However, we investigate a **special case** in this paper. In the case, not only $f(\cdot)$ is unknown, but also the states of each gene cannot be precisely measurable because of measurement noises or sensor faults. That is, the actual values of $x_{i,m}$ and $x_{i,p}$ cannot be obtained, which implies that $z_{i,m}$ and $x_{i,p}$ also cannot be obtained. Obviously, all of $f(\cdot)$, $x_{i,m}$, $x_{i,p}$, $z_{i,m}$ and $x_{i,p}$ cannot be used in the control design, which means that the above control input (4) is not reasonable and cannot be applied in the practical applications.

In the paper, sensor fault can be described as

$$x_{a,i,m} = x_{i,m} + b_{i,m}, \quad x_{a,i,p} = x_{i,p} + b_{i,p} \quad (6)$$

where $x_{a,i,m}$ and $x_{a,i,p}$ are actual observed values, $b_{i,m}$ and $b_{i,p}$ denote sensor faults, which are unknown but bounded.

Hence, **the main task in this paper** is, considering uncertainty $f(\cdot)$ and sensor faults, to design an adaptive control laws u_m and u_p such the GRNs are stable. In the control scheme, the fault negative effect on the control performance will be overcome by adaptive technique. In addition, neural networks will be used to approximate the unknown continuous functions, which will introduced in the following.

On the other hand, neural networks (NNs) can approximate any continuous function on a compact set. In this paper, radius basic function neural networks will be used to approximate the unknown functions f_i ($i = 1, 2, \dots, n$) in the following form,

$$f_i(z_p) = W_i^{*T} \xi_i(\bar{z}_p) + \varepsilon_i(\bar{z}_p)$$

where $\bar{z}_p = [z_p^T, 1]^T$, $\xi_i(\bar{z}_p) = [\xi_{i,1}(\bar{z}_p), \dots, \xi_{i,N_W}(\bar{z}_p)]^T$, $\xi_{i,j}(\bar{z}_p) = \exp(-\frac{\sum_{l=1}^{v_i} (z_{l,p}(t) - q_{j,l})^2}{(c_j)^2})$, N_W is the number of the RBFNNs, v_i is the dimension of \bar{z}_p , $c_{i,j} > 0$ is the width of the receptive field, and $q_{j,l} \in R$ ($j = 1, 2, \dots, N_W$) is the Gaussian function's center, $W_i^* \in R^{N_W}$ is the ideal weight vector defined as

$$\begin{aligned} W_i^* &= \arg \min_{W \in \Omega_W} [\sup_{z \in \Omega_p} |W_i^T \xi_i(\bar{z}_p) - f_i|], \\ \Omega_W &= \{W_i \mid \|W_i\| \leq w_{i,m}\}, \end{aligned}$$

with a constant $w_{i,m} > 0$, Ω_p denotes a large enough compact set, ε_i denotes the optimal approximation error.

From the results on NNs' approximation [15], [16], we know, both of W_i^* and $\varepsilon_i(\bar{z}_p)$ are bounded.

Note that, because of sensor faults, $z_{i,p}$ cannot be obtained, and only $z_{a,i,p}$ is obtained and used in the control design.

Let the symbol $\bar{z}_{a,p}$

$$\bar{z}_{a,p} = (z_{a,1,p}, z_{a,2,p}, \dots, z_{a,n,p})^T$$

Then, we have

$$\begin{aligned} f_i &= W_i^{*T} \xi_i(\bar{z}_p) + \varepsilon_i(\bar{z}_p) \\ &= W_i^{*T} \xi_i(\bar{z}_{a,p}) + W_i^{*T} [\xi_i(\bar{z}_p) - \xi_i(\bar{z}_{a,p})] + \varepsilon_i(\bar{z}_p) \\ &= W_i^{*T} \xi_i(\bar{z}_{a,p}) + e_{f,i}, \end{aligned} \quad (7)$$

where $e_{f,i} = W_i^{*T} [\xi_i(\bar{z}_p) - \xi_i(\bar{z}_{a,p})] + \varepsilon_i(\bar{z}_p)$.

It is well known that, W_i^* and $\varepsilon_i(\bar{z}_p)$ are bounded. And from the definition of $\xi_{i,j}(\cdot)$, we further know $|\xi_{i,j}(\cdot)| < 1$, which means that the norm of ξ_i also is bounded. Thus, $e_{f,i}$ also is bounded. That is to say, $|e_{f,i}| \leq M_{f,i}$, where $M_{f,i} > 0 \in R$ is an unknown constant.

Note that, unknown functions can be tackled via adaptive manner in other simpler ways [21], [22].

Now, in order to design control inputs, the following assumptions are introduced.

Assumption 1: There exists an unknown constant $M_{f,i} > 0 \in R$ such that $|e_{f,i}| \leq M_{f,i}$ over a compact set, for $i = 1, 2, \dots, n$.

Assumption 2: The sensor faults are bounded, and there exist two unknown constants $\bar{b}_{i,m}$ and $\bar{b}_{i,p}$ such that $|b_{i,m}| \leq \bar{b}_{i,m}$ and $|b_{i,p}| \leq \bar{b}_{i,p}$.

III. MAIN RESULTS

In this section, we will derive control inputs for the GRNs (1) from the Lyapunov stability point of view. In addition, using adaptive technique, the adaptive laws of sensor fault upper boundaries also are respectively derived. Finally, a theorem is given to summarize the main results in this paper.

Let us recall V_1 and its time derivative \dot{V}_1 ,

$$\begin{aligned} V_1 &= \frac{1}{2}(z_m^T z_m + z_p^T z_p), \\ \dot{V}_1 &= z_m^T(-Az_m + f + u_m + Ax_m^*) \\ &\quad + z_p^T[-Cz_p + Dz_m + u_p + Cx_p^*]. \end{aligned}$$

Since $f_i(\cdot)$ is unknown, RBFNNs are used to approximate it. Since the actual values of the states cannot be obtained because of sensor faults, as doing in (7), $f_i(\cdot)$ can be approximated by NNs as follows:

$$f_i(z_p) = W_i^{*T} \xi_i(\bar{z}_{a,p}) + e_{f,i}.$$

Hence, unknown function vector $f(z_p)$ can be described as follows:

$$\begin{aligned} f(z_p) &= [f_1(z_p), f_2(z_p), \dots, f_n(z_p)]^T \\ &= [W_1^{*T} \xi_1(\bar{z}_{a,p}), W_2^{*T} \xi_2(\bar{z}_{a,p}), \dots, W_n^{*T} \xi_n(\bar{z}_{a,p})]^T \\ &\quad + [e_{f,1}(\bar{z}_{a,p}), e_{f,2}(\bar{z}_{a,p}), \dots, e_{f,n}(\bar{z}_{a,p})]^T \\ &= W^{*T} \xi(\bar{z}_{a,p}) + e(\bar{z}_{a,p}) \end{aligned} \quad (8)$$

where

$$\begin{aligned} W^T &= \text{diag}\{W_1^{*T}, W_2^{*T}, \dots, W_n^{*T}\} \\ \xi(\cdot) &= [\xi_1^T(\cdot), \xi_2^T(\cdot), \dots, \xi_n^T(\cdot)]^T \\ e(\bar{z}_{a,p}) &= [e_{f,1}(\bar{z}_{a,p}), e_{f,2}(\bar{z}_{a,p}), \dots, e_{f,n}(\bar{z}_{a,p})]^T \end{aligned}$$

Substituting (8) into \dot{V}_1 , we have

$$\dot{V}_1 = z_m^T[-Az_m + W^*T\xi(\cdot) + e(\cdot) + u_m] + z_p^T[-Cz_p + Dz_m + u_p] \quad (9)$$

Define control input u_m as follows:

$$u_m = K_m(z_{a,m} - \hat{b}_m) - \hat{W}^T\xi(\cdot) - \text{sgn}(z_{a,m})\hat{M}_f - Ax_m^* \quad (10)$$

where

$$\begin{aligned} \text{sgn}(z_{a,m}) &= \text{diag}\{\text{sgn}(z_{a,1,p}), \text{sgn}(z_{a,2,p}), \dots, \text{sgn}(z_{a,n,p})\} \\ \hat{M}_f &= [\hat{M}_{f,1}, \hat{M}_{f,2}, \dots, \hat{M}_{f,n}]^T \\ \hat{b}_m &= [\hat{b}_{1,m}, \dots, \hat{b}_{n,m}]^T \\ K_m &= \text{diag}\{k_{1,m}, \dots, k_{n,m}\} \end{aligned}$$

with design parameter $k_{i,m} < 0$ is a design parameter, $\hat{b}_{1,m}$ and $\hat{M}_{f,i}$ respectively the estimations of $b_{i,m}$ and $M_{f,i}$, $i = 1, 2, \dots, n$.

Now, substituting u_m into the first term of (9), it yields

$$\begin{aligned} &z_m^T[-Az_m + W^*T\xi(\cdot) + e(\cdot) + u_m + Ax_m^*] \\ &= -z_m^TAz_m + z_m^TW^*T\xi(\cdot) + z_m^Te(\cdot) + z_m^Tu_m \\ &\leq -z_m^TAz_m + z_m^TW^*T\xi(\cdot) + |z_m|^TM_f + z_m^Tu_m \\ &\leq -z_m^TAz_m + z_m^TW^*T\xi(\cdot) + |z_{a,m}|^TM_f + b_m^TM_f + z_m^Tu_m \\ &= -z_m^TAz_m + z_m^TW^*T\xi(\cdot) + |z_{a,m}|^TM_f + b_m^TM_f \\ &\quad + z_m^T[K_m(z_{a,m} - \hat{b}_m) - \hat{W}^T\xi(\cdot) - \text{sgn}(z_{a,m})\hat{M}_f] \quad (11) \end{aligned}$$

where $|z_{a,m}| = [|z_{a,1,m}|, \dots, |z_{a,n,m}|]$, $\tilde{W} = W^* - \hat{W}$ and $\tilde{M}_f = M_f - \hat{M}_f$, $e = [e_{f,1}, e_{f,2}, \dots, e_{f,n}]^T$ with $e_{f,i} = W_i^*T[\xi_i(\cdot) - \xi_i(\tilde{z}_p)] + \varepsilon_i(\tilde{z}_{a,p})$. where $\text{sgn}(z_{a,m}) = \text{diag}\{\text{sgn}(z_{a,1,m}), \dots, \text{sgn}(z_{a,n,m})\}$, $|e| = [|e_{1,f}|, \dots, |e_{n,f}|]^T$, $\tilde{M}_f = M_f^* - \hat{W}_f$, the property $\hat{M}_{i,f} > 0$ is used, which is ensured by the adaptive laws ().

In the following, we will analyze the terms in (11), respectively.

Since

$$\begin{aligned} z_{a,i,m} &= z_{i,m} - b_{i,m}, \\ z_{a,m} &= [z_{a,1,m}, \dots, z_{a,n,m}]^T, \quad b = [b_{1,m}, \dots, b_{n,m}]^T, \end{aligned}$$

we have

$$z_{a,m} = z_m - b_m,$$

Further, we have

$$\begin{aligned} &z_m^T(-Az_m + K_mz_{a,m} - K_m\hat{b}_m) \\ &= z_m^T(-Az_m + K_mz_m + K_mb_m - K_m\hat{b}_m) \\ &= -z_m^T(A - K_m)z_m + z_m^TK_m\tilde{b}_m \\ &= -z_m^T(A - K_m)z_m + (z_{a,m}^T - b_m^T)K_m\tilde{b}_m \\ &= -z_m^T(A - K_m)z_m + z_{a,m}^TK_m\tilde{b}_m - b_m^TK_m\tilde{b}_m \quad (12) \end{aligned}$$

From Young's Inequality, we have

$$\begin{aligned} &z_m^T(-Az_m + K_mz_{a,m} - K_m\hat{b}_m) \\ &= -z_m^T(A - K_m)z_m + z_{a,m}^TK_m\tilde{b}_m - b_m^TK_m\tilde{b}_m \end{aligned}$$

$$\begin{aligned} &\leq -z_m^T(A - K_m)z_m + z_{a,m}^TK_m\tilde{b}_m \\ &\quad + \frac{\eta_1}{2}\tilde{b}_m^TK_m^TK_m\tilde{b}_m + \frac{1}{2\eta_1}b_m^Tb_m \quad (13) \end{aligned}$$

where $\eta_1 > 0$ is a design parameter, and $\tilde{b}_m = b_m - \hat{b}_m$.

Though simple calculation and from Young's Inequality, we have

$$\begin{aligned} &z_m^T(W^*T\xi - \hat{W}^T\xi) = z_m^T\tilde{W}\xi \\ &= (z_{a,m}^T - b_m^T)\tilde{W}\xi \\ &= z_{a,m}^T\tilde{W}\xi - b_m^T\tilde{W}\xi \\ &\leq z_{a,m}^T\tilde{W}\xi + \frac{\eta_2}{2}\xi^T\tilde{W}^T\tilde{W}\xi + \frac{1}{2\eta_2}b_m^Tb_m \\ &\leq z_{a,m}^T\tilde{W}\xi + \frac{\eta_2}{2}\tilde{W}^T\xi^T\xi\tilde{W} + \frac{1}{2\eta_2}b_m^Tb_m \quad (14) \end{aligned}$$

where $\eta_2 > 0$ is a design parameter, and $\tilde{W} = W^* - \hat{W}$.

From the definition of $\xi_{i,j}$ in Section II, we known, $|\xi_{i,j}| \leq 1, j = 1, \dots, N_W, i = 1, \dots, n$, then we have

$$\xi^T\xi \leq nN_W,$$

where $N_W > 0$ is the node number of NNs. Thus, (14) can be developed as

$$\begin{aligned} &z_m^T(W^*T\xi - \hat{W}^T\xi) = z_m^T\tilde{W}\xi \\ &\leq z_{a,m}^T\tilde{W}\xi + \frac{\eta_2}{2}\tilde{W}^T\xi^T\xi\tilde{W} + \frac{1}{2\eta_2}b_m^Tb_m \\ &\leq z_{a,m}^T\tilde{W}\xi + \frac{\eta_2nN_W}{2}\tilde{W}^T\tilde{W} + \frac{1}{2\eta_2}b_m^Tb_m \quad (15) \end{aligned}$$

By similar analysis, we have

$$\begin{aligned} &|z_{a,m}|^TM_f + b_m^TM_f - z_m^T\text{sgn}(z_{a,m})\hat{M}_f \\ &= z_{a,m}^T\text{sgn}(z_{a,m})M_f - z_{a,m}^T\text{sgn}(z_{a,m})\hat{M}_f + b_m^TM_f \\ &= z_{a,m}^T\text{sgn}(z_{a,m})\tilde{M}_f + b_m^TM_f + b_m^T\hat{M}_f \quad (16) \end{aligned}$$

Since

$$b_m^TM_f \leq \frac{\eta_3}{2}b_m^Tb_m + \frac{1}{2\eta_3}M_f^TM_f \quad (17)$$

we have

$$\begin{aligned} &b_m^T\hat{M}_f = b_m^T(M_f - \tilde{M}_f) = b_m^TM_f - b_m^T\tilde{M}_f \\ &\leq \frac{\eta_4}{2}b_m^Tb_m + \frac{1}{2\eta_4}M_f^TM_f \\ &\quad + \frac{\eta_5}{2}b_m^Tb_m + \frac{1}{2\eta_5}\tilde{M}_f^T\tilde{M}_f \quad (18) \end{aligned}$$

where $\eta_3 > 0, \eta_4 > 0$ and $\eta_5 > 0$ respectively design parameters.

Substituting (17) and (18) into (16), we have

$$\begin{aligned} &|z_{a,m}|^TM_f + b_m^TM_f - z_m^T\text{sgn}(z_{a,m})\hat{M}_f \\ &\leq z_{a,m}^T\text{sgn}(z_{a,m})\tilde{M}_f \\ &\quad + \frac{\eta_3 + \eta_4 + \eta_6}{2}b_m^Tb_m + (\frac{1}{2\eta_3} + \frac{1}{2\eta_4})M_f^TM_f \\ &\quad + \frac{1}{2\eta_5}\tilde{M}_f^T\tilde{M}_f \quad (19) \end{aligned}$$

Substituting (13), (15) and (19) into (11), we have

$$\begin{aligned} & z_m^T[-Az_m + W^{*T}\xi(\cdot) + e(\cdot) + u_m + Ax_m^*] \\ & \leq -z_m^T(A - K_m)z_m + z_{a,m}^TK_m\tilde{b}_m \\ & \quad + \frac{\eta_1}{2}\tilde{b}_m^TK_m^TK_m\tilde{b}_m + \frac{1}{2\eta_1}b_m^Tb_m \\ & \quad + z_{a,m}^T\tilde{W}\xi + \frac{\eta_2nN_W}{2}\tilde{W}^T\tilde{W} + \frac{1}{2\eta_2}b_m^Tb_m \\ & \quad + z_{a,m}^T\text{sgn}(z_{a,m})\tilde{M}_f + \frac{\eta_3 + \eta_4 + \eta_6}{2}b_m^Tb_m \\ & \quad + \left(\frac{1}{2\eta_3} + \frac{1}{2\eta_4}\right)M_f^TM_f + \frac{1}{2\eta_5}\tilde{M}_f^T\tilde{M}_f \end{aligned} \quad (20)$$

Re-ranging (20), it yields

$$\begin{aligned} & z_m^T[-Az_m + W^{*T}\xi(\cdot) + e(\cdot) + u_m + Ax_m^*] \\ & \leq -z_m^T(A - K_m)z_m \\ & \quad + z_{a,m}^T(K_m\tilde{b}_m + \tilde{W}\xi + \text{sgn}(z_{a,m})\tilde{M}_f) \\ & \quad \times \frac{\eta_1}{2}\tilde{b}_m^TK_m^TK_m\tilde{b}_m + \frac{\eta_2nN_W}{2}\tilde{W}^T\tilde{W} + \frac{1}{2\eta_5}\tilde{M}_f^T\tilde{M}_f \\ & \quad + \eta_{bm}b_m^Tb_m + \eta_{mM_f}M_f^TM_f \end{aligned} \quad (21)$$

where

$$\eta_{bm} = \frac{1}{2\eta_1} + \frac{1}{2\eta_2} + \frac{\eta_3 + \eta_4 + \eta_6}{2} \quad (22)$$

and

$$\eta_{mM_f} = \left(\frac{1}{2\eta_3} + \frac{1}{2\eta_4}\right). \quad (23)$$

Define u_p as follows:

$$u_p = K_p(z_{a,p} - \hat{b}_p) - D(z_{a,m} - \hat{b}_m) - Cx_p^*. \quad (24)$$

where $\hat{b}_p = [\hat{b}_{1,p}, \hat{b}_{2,p}, \dots, \hat{b}_{n,p}]^T$, which is an estimate of b_p , $b_p = [b_{1,p}, b_{2,p}, \dots, b_{n,p}]^T$, $\hat{b}_{i,p}$ is an estimate of $b_{i,p}$, $K_p = \text{diag}\{k_{1,p}, k_{2,p}, \dots, k_{n,p}\}$, $k_{i,p} < 0$ ($i = 1, \dots, n$) is a design parameter.

Now, let us consider the term $z_p^T(-Cz_p + Dz_m + u_p - Cx_p^*)$ in (9). Substituting (24) into it, we have

$$\begin{aligned} & z_p^T[-Cz_p + Dz_m + u_p - Cx_p^*] \\ & = -z_p^TCz_p + z_p^TDz_m \\ & \quad + z_p^TK_pz_{a,p} - z_p^TK_p\hat{b}_p - z_p^TDz_{a,m} + z_p^TD\hat{b}_m \\ & = -z_p^TCz_p + z_p^TDz_m + z_p^TK_pz_p + z_p^TK_p\tilde{b}_p \\ & \quad - z_p^TK_p\hat{b}_p - z_p^TDz_m + z_p^TD\tilde{b}_m - z_p^TD\hat{b}_m \\ & = -z_p^T(C - K_p)z_p + z_p^TK_p\tilde{b}_p + z_p^TD\tilde{b}_m \end{aligned} \quad (25)$$

where $\tilde{b}_m = b_m - \hat{b}_m$ and $\tilde{b}_p = b_p - \hat{b}_p$.

Note that,

$$\begin{aligned} z_p^TK_p\tilde{b}_p & = z_{a,p}^TK_p\tilde{b}_p - b_p^TK_p\tilde{b}_p \\ & \leq z_{a,p}^TK_p\tilde{b}_p + \frac{1}{2\gamma_1}\tilde{b}_p^TK_pK_p^T\tilde{b}_p + \frac{\gamma_1}{2}b_p^Tb_p \end{aligned} \quad (26)$$

where $\gamma_1 > 0$ is a design parameter, and

$$\begin{aligned} z_p^TD\tilde{b}_m & = z_{a,p}^TD\tilde{b}_m - b_m^TD\tilde{b}_m \\ & \leq z_{a,p}^TD\tilde{b}_m + \frac{1}{2\gamma_2}\tilde{b}_m^TDD^T\tilde{b}_m + \frac{\gamma_2}{2}b_m^Tb_m \end{aligned} \quad (27)$$

where $\gamma_2 > 0$ is a design parameter.

Substituting (26) and (27) into (25), we have

$$\begin{aligned} & z_p^T[-Cz_p + Dz_m + u_p] \\ & = -z_p^T(C - K_p)z_p + z_p^TK_p\tilde{b}_p + z_p^TD\tilde{b}_m \\ & \leq -z_p^T(C - K_p)z_p + z_{a,p}^TK_p\tilde{b}_p + z_{a,p}^TD\tilde{b}_m \\ & \quad + \frac{1}{2\gamma_1}\tilde{b}_p^TK_pK_p^T\tilde{b}_p + \frac{\gamma_1}{2}b_p^Tb_p \\ & \quad + \frac{1}{2\gamma_2}\tilde{b}_m^TDD^T\tilde{b}_m + \frac{\gamma_2}{2}b_m^Tb_m \end{aligned} \quad (28)$$

Further, substituting (21) and (28) into (9), we have

$$\begin{aligned} \dot{V}_1 & \leq -z_m^T(A - K_m)z_m \\ & \quad + z_{a,m}^T(K_m\tilde{b}_m + \tilde{W}\xi + \text{sgn}(z_{a,m})\tilde{M}_f) \\ & \quad \times \frac{\eta_1}{2}\tilde{b}_m^TK_m^TK_m\tilde{b}_m + \frac{\eta_2nN_W}{2}\tilde{W}^T\tilde{W} \\ & \quad + \frac{1}{2\eta_5}\tilde{M}_f^T\tilde{M}_f + \eta_{bm}b_m^Tb_m + \eta_{mM_f}M_f^TM_f \\ & \quad - z_p^T(C - K_p)z_p + z_{a,p}^TK_p\tilde{b}_p + z_{a,p}^TD\tilde{b}_m \\ & \quad + \frac{1}{2\gamma_1}\tilde{b}_p^TK_pK_p^T\tilde{b}_p + \frac{\gamma_1}{2}b_p^Tb_p \\ & \quad + \frac{1}{2\gamma_2}\tilde{b}_m^TDD^T\tilde{b}_m + \frac{\gamma_2}{2}b_m^Tb_m \end{aligned} \quad (29)$$

Re-ranging (29), we have

$$\begin{aligned} \dot{V}_1 & \leq -z_m^T(A - K_m)z_m - z_p^T(C - K_p)z_p \\ & \quad + z_{a,m}^T(K_m\tilde{b}_m + \tilde{W}\xi + \text{sgn}(z_{a,m})\tilde{M}_f) \\ & \quad + z_{a,p}^T(K_p\tilde{b}_p + D\tilde{b}_m) \\ & \quad + \tilde{b}_m^T\left(\frac{\eta_1}{2}K_m^TK_m + \frac{1}{2\gamma_2}DD^T\right)\tilde{b}_m + \frac{1}{2\eta_5}\tilde{M}_f^T\tilde{M}_f \\ & \quad + \frac{1}{2\gamma_1}\tilde{b}_p^TK_pK_p^T\tilde{b}_p + \frac{\eta_2nN_W}{2}\tilde{W}^T\tilde{W} \\ & \quad + (\eta_{bm} + \frac{\gamma_2}{2})b_m^Tb_m + \eta_{mM_f}M_f^TM_f + \frac{\gamma_1}{2}b_p^Tb_p \end{aligned} \quad (30)$$

Define Lyapunov function

$$\begin{aligned} V_2 & = V_1 + \frac{1}{2\beta_W}\tilde{W}^T\tilde{W} + \frac{1}{2\beta_M}\tilde{M}_f^T\tilde{M}_f \\ & \quad + \frac{1}{2\beta_m}\tilde{b}_m^T\tilde{b}_m + \frac{1}{2\beta_p}\tilde{b}_p^T\tilde{b}_p \end{aligned} \quad (31)$$

where $\beta_W > 0$, $\beta_M > 0$, $\beta_m > 0$ and $\beta_p > 0$ are design parameters, respectively.

Differentiating V_2 with respect to time t , we have

$$\begin{aligned} \dot{V}_2 & = \dot{V}_1 - \frac{1}{\beta_W}\tilde{W}^T\dot{\tilde{W}} - \frac{1}{\beta_M}\tilde{M}_f^T\dot{\tilde{M}}_f \\ & \quad - \frac{1}{\beta_m}\tilde{b}_m^T\dot{\tilde{b}}_m - \frac{1}{\beta_p}\tilde{b}_p^T\dot{\tilde{b}}_p \end{aligned} \quad (32)$$

Substituting (30) into (32), we have

$$\begin{aligned} \dot{V}_2 \leq & -z_m^T(A - K_m)z_m - z_p^T(C - K_p)z_p \\ & + \tilde{b}_m^T[(K_m z_{a,m} + Dz_{a,p})^T - \frac{1}{\beta_m} \dot{\hat{b}}_m] \\ & + \tilde{W}^T(\xi z_{a,m} - \frac{1}{\beta_W} \dot{\hat{W}}) \\ & + \tilde{M}_f^T(\text{sgn}(z_{a,m})z_{a,m} - \frac{1}{\beta_M} \dot{\hat{M}}_f) \\ & + \tilde{b}_p(K_p z_{a,p}^T - \frac{1}{\beta_p} \dot{\hat{b}}_p) \\ & + \tilde{b}_m^T(\frac{\eta_1}{2} K_m^T K_m + \frac{1}{2\gamma_2} DD^T) \tilde{b}_m + \frac{1}{2\eta_5} \tilde{M}_f^T \tilde{M}_f \\ & + \frac{1}{2\gamma_1} \tilde{b}_p^T K_p K_p^T \tilde{b}_p + \frac{\eta_2 n N_W}{2} \tilde{W}^T \tilde{W} \\ & + (\eta_{bm} + \frac{\gamma_2}{2}) b_m^T b_m + \eta_{mMf} M_f^T M_f + \frac{\gamma_1}{2} b_p^T b_p \end{aligned} \quad (33)$$

Define the following adaptive laws as follows:

$$\dot{\hat{b}}_m = \beta_m(K_m z_{a,m} + Dz_{a,p})^T - \kappa_m \hat{b}_m \quad (34)$$

$$\dot{\hat{W}} = \beta_W \xi z_{a,m} - \kappa_W \hat{W} \quad (35)$$

$$\dot{\hat{M}}_f = \beta_M \text{sgn}(z_{a,m})z_{a,m} - \kappa_M \hat{M}_f \quad (36)$$

$$\dot{\hat{b}}_p = \beta_p K_p z_{a,p}^T - \kappa_p \hat{b}_p \quad (37)$$

where $\kappa_m > 0$, $\kappa_W > 0$, $\kappa_M > 0$ and $\kappa_p > 0$ are design parameters, respectively.

Substituting the adaptive laws (34)-(37) into (33), it yields

$$\begin{aligned} \dot{V}_2 \leq & -z_m^T(A - K_m)z_m - z_p^T(C - K_p)z_p \\ & + \frac{\kappa_m}{\beta_m} \tilde{b}_m^T \hat{b}_m + \frac{\kappa_W}{\beta_W} \tilde{W}^T \hat{W} + \frac{\kappa_M}{\beta_M} \tilde{M}_f^T \hat{M}_f + \frac{\kappa_p}{\beta_p} \tilde{b}_p^T \hat{b}_p \\ & + \tilde{b}_m^T(\frac{\eta_1}{2} K_m^T K_m + \frac{1}{2\gamma_2} DD^T) \tilde{b}_m + \frac{1}{2\eta_5} \tilde{M}_f^T \tilde{M}_f \\ & + \frac{1}{2\gamma_1} \tilde{b}_p^T K_p K_p^T \tilde{b}_p + \frac{\eta_2 n N_W}{2} \tilde{W}^T \tilde{W} \\ & + (\eta_{bm} + \frac{\gamma_2}{2}) b_m^T b_m + \eta_{mMf} M_f^T M_f + \frac{\gamma_1}{2} b_p^T b_p \end{aligned} \quad (38)$$

From Young's inequality, we have

$$\frac{\kappa_W}{\beta_W} \tilde{W}^T \hat{W} \leq -\frac{\kappa_W}{2\beta_W} \tilde{W}^T \tilde{W} + \frac{\kappa_W}{2\beta_W} W^{*T} W^*. \quad (39)$$

By the similar analysis, we also have

$$\frac{\kappa_M}{\beta_M} \tilde{M}_f^T \hat{M}_f \leq -\frac{\kappa_M}{2\beta_M} \tilde{M}_f^T \tilde{M}_f + \frac{\kappa_M}{2\beta_M} M_f^T M_f^T, \quad (40)$$

$$\frac{\kappa_m}{\beta_m} \tilde{b}_m^T \hat{b}_m \leq -\frac{\kappa_m}{\beta_m} \tilde{b}_m^T \tilde{b}_m + \frac{\kappa_m}{\beta_m} b_m^T b_m, \quad (41)$$

$$\frac{\kappa_p}{\beta_p} \tilde{b}_p^T \hat{b}_p \leq -\frac{\kappa_p}{\beta_p} \tilde{b}_p^T \tilde{b}_p + \frac{\kappa_p}{\beta_p} b_p^T b_p. \quad (42)$$

Substituting (39)-(42) into (38), we further have

$$\begin{aligned} \dot{V}_2 \leq & -z_m^T(A - K_m)z_m - z_p^T(C - K_p)z_p \\ & - (\frac{\kappa_W}{2\beta_W} - \frac{\eta_2 n N_W}{2}) \tilde{W}^T \tilde{W} \end{aligned}$$

$$\begin{aligned} & - (\frac{\kappa_M}{2\beta_M} - \frac{1}{2\eta_5}) \tilde{M}_f^T \tilde{M}_f \\ & - \tilde{b}_m^T (\frac{\kappa_m}{\beta_m} I - \frac{\eta_1}{2} K_m^T K_m + \frac{1}{2\gamma_2} DD^T) \tilde{b}_m \\ & - (\frac{\kappa_p}{\beta_p} - \frac{1}{2\gamma_1}) \tilde{b}_p^T \tilde{b}_p \\ & + \frac{\kappa_W}{2\beta_W} W^{*T} W^* \\ & + (\frac{\kappa_M}{2\beta_M} + \eta_{mMf}) M_f^T \\ & + (\frac{\kappa_m}{\beta_m} + \eta_{bm} + \frac{\gamma_2}{2}) b_m^T b_m \\ & + (\frac{\kappa_p}{\beta_p} + \frac{\gamma_1}{2}) b_p^T b_p \end{aligned} \quad (43)$$

By the design parameters are chosen suitably, we can obtain

$$\begin{aligned} \lambda_W &= \frac{\kappa_W}{2\beta_W} - \frac{\eta_2 n N_W}{2} < 0 \\ \lambda_M &= \frac{\kappa_M}{2\beta_M} - \frac{1}{2\eta_5} < 0 \\ \Lambda_m &= \frac{\kappa_m}{\beta_m} I - \frac{\eta_1}{2} K_m^T K_m + \frac{1}{2\gamma_2} DD^T < 0 \\ \lambda_p &= \frac{\kappa_p}{\beta_p} - \frac{1}{2\gamma_1} < 0 \end{aligned} \quad (44)$$

Then, (43) can be re-written as

$$\begin{aligned} \dot{V}_2 \leq & -z_m^T(A - K_m)z_m - z_p^T(C - K_p)z_p \\ & - \lambda_W \tilde{W}^T \tilde{W} - \lambda_M \tilde{M}_f^T \tilde{M}_f \\ & - \tilde{b}_m^T \Lambda_m \tilde{b}_m - \lambda_p \tilde{b}_p^T \tilde{b}_p + \mu \leq -\lambda V_2 + \mu \end{aligned} \quad (45)$$

where

$$\begin{aligned} \lambda &= \min\{\lambda_W, \lambda_M, \lambda_p, \lambda_m, \frac{1}{\beta_W}, \frac{1}{\beta_M}, \frac{1}{\beta_m}, \frac{1}{\beta_p}\} \\ \lambda_m &= \min\{\sigma_{\min}(A - K_m), \sigma_{\min}(C - K_p), \sigma_{\min}(\Lambda_m)\} \\ \mu &= \frac{\kappa_W}{2\beta_W} W^{*T} W^* + (\frac{\kappa_M}{2\beta_M} + \eta_{mMf}) M_f^T \\ & + (\frac{\kappa_m}{\beta_m} + \eta_{bm} + \frac{\gamma_2}{2}) b_m^T b_m + (\frac{\kappa_p}{\beta_p} + \frac{\gamma_1}{2}) b_p^T b_p \end{aligned} \quad (46)$$

and the symbol $\sigma_{\min}(\bullet)$ denotes the minimum eigenvalue of matrix \bullet .

From (45) and the definition of V_2 , it can be seen that, if $V_2 \geq \frac{\mu}{\lambda}$, then $\dot{V}_2 < 0$. Thus, all the signals in the closed-loop system are uniformly bounded, namely,

$$\begin{aligned} \|z_m\| &\leq \sqrt{\frac{2\mu}{\lambda}}, \quad \|z_p\| \leq \sqrt{\frac{2\mu}{\lambda}}, \quad \|\tilde{M}_f\| \leq \sqrt{\frac{2\beta_M \mu}{\lambda}}, \\ \|\tilde{W}\| &\leq \sqrt{\frac{2\beta_W \mu}{\lambda}}, \quad \|\tilde{b}_m\| \leq \sqrt{\frac{2\beta_m \mu}{\lambda}}, \quad \|\tilde{b}_p\| \leq \sqrt{\frac{2\beta_p \mu}{\lambda}}. \end{aligned} \quad (47)$$

which implies that all closed-loop signals converge to an invariant compact set Ω defined as

$$\Omega = \left\{ \begin{pmatrix} z_m, \\ z_p, \\ \tilde{M}_f, \\ \tilde{W}, \\ \tilde{b}_m, \\ \tilde{b}_p \end{pmatrix} \left| \begin{pmatrix} \|z_m\| \leq \sqrt{\frac{2\mu}{\lambda}}, \|z_p\| \leq \sqrt{\frac{2\mu}{\lambda}}, \\ \|W\| \leq \sqrt{\frac{2\beta_W\mu}{\lambda}}, \|\tilde{M}_f\| \leq \sqrt{\frac{2\beta_M\mu}{\lambda}}, \\ \|\tilde{b}_p\| \leq \sqrt{\frac{2\beta_p\mu}{\lambda}}, \|\tilde{b}_m\| \leq \sqrt{\frac{2\beta_p\mu}{\lambda}} \end{pmatrix} \right. \right\}.$$

Now, let us propose the following theorem to summarize the analysis.

Theorem 1: Consider the GRNs (1) with Assumptions 1 and 2. If control inputs (10), (24) and adaptive laws (34)-(37) are adopted, then, (3) is asymptotically stable, all the signals in the closed-loop system are bounded and converge to an adjustable compact set Ω .

Proof: From the above analysis, it is easy to obtain the result. the detailed proof is omitted here. ■

IV. SIMULATION RESULTS

In this section, let us consider the following GRNs, which contains three genes,

$$\begin{cases} \dot{x}_{1,m}(t) = -3.4x_{1,m} + f_1(x_{1,m}(t), x_{2,m}(t), x_{3,m}(t)) \\ \dot{x}_{1,p}(t) = 0.9x_{1,p} + 0.3x_{1,m}(t) \\ \dot{x}_{2,m}(t) = -3.6x_{2,m} + f_2(x_{1,m}(t), x_{2,m}(t), x_{3,m}(t)) \\ \dot{x}_{2,p}(t) = 0.8x_{2,p} + 0.2x_{2,m}(t) \\ \dot{x}_{3,m}(t) = -3x_{3,m} + f_3(x_{1,m}(t), x_{2,m}(t), x_{3,m}(t)) \\ \dot{x}_{3,p}(t) = 0.7x_{3,p} + 0.35x_{3,m}(t) \end{cases}$$

where unknown gene regulatory functions have the following forms

$$\begin{aligned} f_1(\cdot) &= -0.125 \frac{x_{3,p}^2(t)}{1 + x_{3,p}^2(t)}, \\ f_2(\cdot) &= -0.126 x_{1,p}(t)x_{3,p}(t), \\ f_3(\cdot) &= -0.127 \frac{x_{1,p}^2(t)}{1 + x_{1,p}^2(t)}. \end{aligned}$$

As doing in (2), the above GRNs can be re-written as

$$\begin{cases} \dot{x}_m(t) = -Ax_m(t) + f \\ \dot{x}_p(t) = -Cx_p(t) + Dx_m(t), \end{cases}$$

where $x_m = [x_{1,m}, x_{2,m}, x_{3,m}]^T$, $x_p = [x_{1,p}, x_{2,p}, x_{3,p}]^T$, $f = [f_1, f_2, f_3]^T$,

$$A = \begin{bmatrix} 3.4 & 0 & 0 \\ 0 & 3.6 & 0 \\ 0 & 0 & 3 \end{bmatrix}, \quad C = \begin{bmatrix} 0.9 & 0 & 0 \\ 0 & 0.8 & 0 \\ 0 & 0 & 0.7 \end{bmatrix}$$

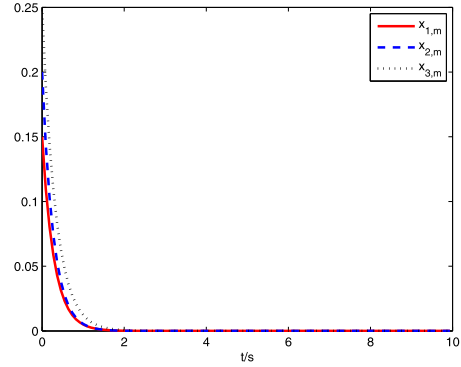


FIGURE 1. The states x_m .

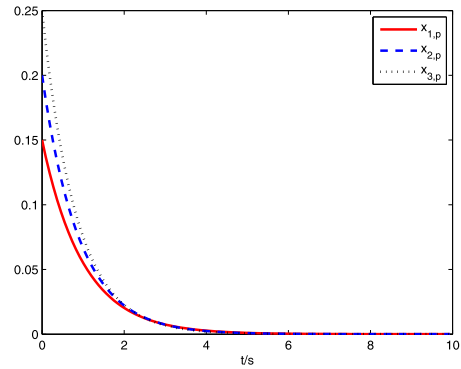


FIGURE 2. The states x_p .

$$D = \begin{bmatrix} 0.3 & 0 & 0 \\ 0 & 0.2 & 0 \\ 0 & 0 & 0.35 \end{bmatrix}.$$

Adding control inputs $u_x \in R^n$ and $u_y \in R^n$ to the above equation, then we have

$$\begin{cases} \dot{x}_m(t) = -Ax_m(t) + f + u_m \\ \dot{x}_p(t) = -Cx_p(t) + Dx_m(t) + u_p, \end{cases}$$

where $u_m = [u_{1,m}, u_{2,m}, u_{3,m}]^T$ and $u_p = [u_{1,p}, u_{2,p}, u_{3,p}]^T$.

In this paper, sensor faults are set as follows: $b_{1,m} = 0.1 \sin(x_{1,m})$, $b_{2,m} = 0.1 \sin(x_{2,m})$, $b_{3,m} = 0.1 \sin(x_{3,m})$, $b_{1,p} = 0.1 \cos(x_{1,p})$, $b_{2,p} = 0.1 \cos(x_{2,p})$, $b_{3,p} = 0.1 \cos(x_{3,p})$.

The initial states are set as: $x_m(0) = [0.15, 0.20, 0.25]^T$, $x_p(0) = [0.15, 0.20, 0.25]^T$. Weight vector $\hat{W}_i \in R^{10}$, $i = 1, 2, 3$ are taken randomly in interval (0, 1]. The design parameters are set as follows: $\beta_l = 10$, $l = W, M, m, p$, $\eta_d = 0.1$, $d = 1, 2, 3, 4, 5$, $\kappa_m = \kappa_W = \kappa_M = \kappa_p = 0.15$. In this simulation, it is assumed that equilibrium point is the origin. In this simulation, the sample time is 0.08s.

Simulation results are given in Fig.1-4. Figures 1 and 2. clearly show that $x_{1,m}$, $x_{2,m}$, $x_{3,m}$, $x_{1,p}$, $x_{2,p}$ and $x_{3,p}$ can asymptotically converge to the adjustable neighborhood of the origin. Figures 1 and 2 further show that, by using the fault-tolerant control inputs (10) and (24) with the adaptive laws (34)-(37), the GRNs are asymptotical stable and the

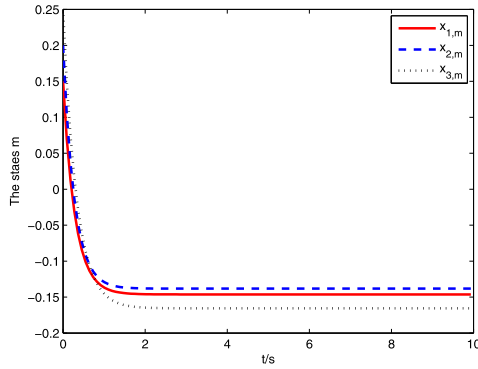


FIGURE 3. The states x_m .

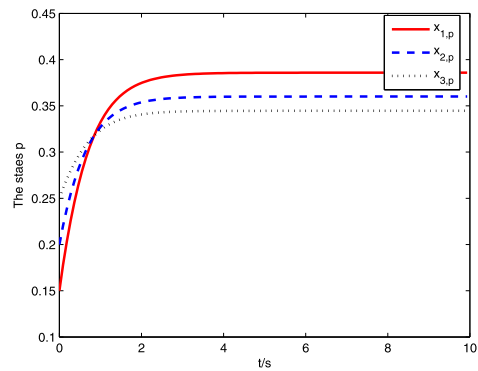


FIGURE 4. The states x_p .

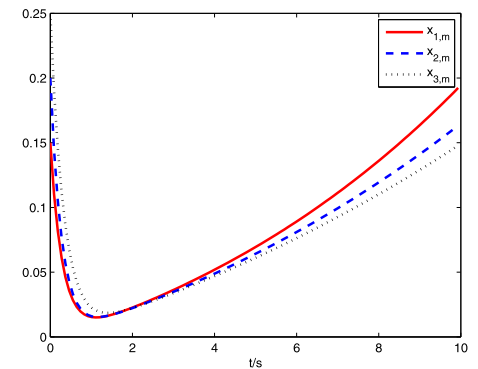


FIGURE 5. The states x_m .

states of the GRNs asymptotically converge to the adjustable neighborhood of the origin.

However, if the faults are not considered and compensated in control design, namely, there are no fault compensation terms in (10) and (24), the situation will change greatly. From Figures 3 and 4, we find, the states of the GRNs do not asymptotically converge to the adjustable neighborhood of the origin, which means that the control objective defined in Section II is not obtained.

In order to further show the effectiveness of the control design in this paper, according to the previous works [17], [28]–[30], another control design is applied. The simulation results can be given in Figures 5 and 6. From Figures 5 and 6, we find, if the faults exist in sensors and fault have not been compensated in control design, the states are

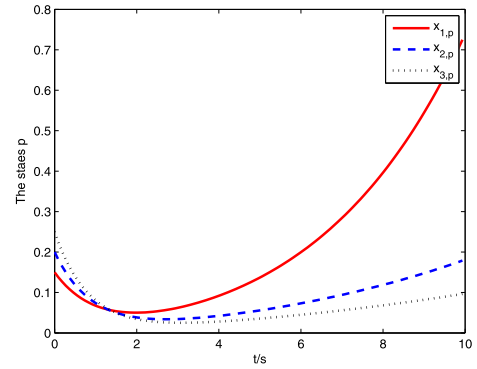


FIGURE 6. The states x_p .

divergent, and the trajectories of the states cannot converge to the origin. From the above simulation results, the presented control strategy in this paper works very effectively.

V. CONCLUSION

In this paper, the gene circuit control design is studied for the GRNs with nonlinear gene regulatory logic, which are subject to sensor faults. Based on neural networks, a control method is presented. In the method, the unknown gene regulatory functions are approximated by neural networks, and the unknown sensor faults are compensated. Simulation results show that the proposed method is effective.

REFERENCES

- [1] S. Ben-Tabou and E. H. Davidson, “Modeling the dynamics of transcriptional gene regulatory networks for animal development,” *Develop. Biol.*, vol. 325, no. 2, pp. 317–328, Jan. 2009.
- [2] Z. Yu, H. Chen, J. You, J. Liu, H.-S. Wong, G. Han, and L. Li, “Adaptive fuzzy consensus clustering framework for clustering analysis of cancer data,” *IEEE/ACM Trans. Comput. Biol. Bioinf.*, vol. 12, no. 3, pp. 568–582, Jul./Aug. 2015.
- [3] L. Chen and K. Aihara, “Stability of genetic regulatory networks with time delay,” *IEEE Trans. Circuits Syst. I, Fundam. Theory Appl.*, vol. 49, no. 5, pp. 602–608, May 2014.
- [4] C. Li, L. Chen, and K. Aihara, “Stability of genetic networks with SUM regulatory logic: Lur’e system and LMI approach,” *IEEE Trans. Circuits Syst. I, Reg. Papers*, vol. 53, no. 11, pp. 2451–2458, Nov. 2006.
- [5] S. Zhan, J. F. Miller, and A. M. Tyrrell, “An evolutionary system using development and artificial genetic regulatory networks for electronic circuit design,” *Biosystems*, vol. 98, no. 3, pp. 176–192, Dec. 2009.
- [6] F. Menolascina, M. di Bernardo, and D. di Bernardo, “Analysis, design and implementation of a novel scheme for *in-vivo* control of synthetic gene regulatory networks,” *Automatica*, vol. 47, no. 6, pp. 1265–1270, Jun. 2011.
- [7] P. Rué and J. Garcia-Ojalvo, “Gene circuit designs for noisy excitable dynamics,” *Math. Biosci.*, vol. 231, no. 1, pp. 90–97, May 2011.
- [8] B.-S. Chen and W.-S. Wu, “Robust filtering circuit design for stochastic gene networks under intrinsic and extrinsic molecular noises,” *Math. Biosci.*, vol. 211, no. 2, pp. 342–355, Feb. 2008.
- [9] H. Jiao, M. Shi, Q. K. Shen, J. Zhu, and P. Shi, “Filter design with adaptation to time-delay parameters for genetic regulatory networks,” *IEEE/ACM Trans. Comput. Biol. Bioinf.*, vol. 15, no. 1, pp. 323–328, 2018.
- [10] L. Li and Y. Yang, “On sampled-data control for stabilization of genetic regulatory networks with leakage delays,” *Neurocomputing*, vol. 149, pp. 1225–1231, Feb. 2015.
- [11] W. Pan, Z. Wang, H. Gao, Y. Li, and M. Du, “On multistability of delayed genetic regulatory networks with multivariable regulation functions,” *Math. Biosci.*, vol. 228, no. 1, pp. 100–109, 2010.
- [12] H. Moradi and V. J. Majd, “Robust control of uncertain nonlinear switched genetic regulatory networks with time delays: A redesign approach,” *Math. Biosci.*, vol. 275, pp. 10–17, May 2016.

- [13] Y. Sun, G. Feng, and J. Cao, "A new approach to dynamic fuzzy modeling of genetic regulatory networks," *IEEE Trans. Nanobiosci.*, vol. 9, no. 4, pp. 263–272, Dec. 2010.
- [14] E. Klipp, R. Herwig, A. Kowald, C. Wierling, H. Lehrach, *Systems Biology in Practice: Concepts, Implementation and Application*. Hoboken, NJ, USA: Wiley, 2008.
- [15] Q. Shen, P. Shi, T. Zhang, and C.-C. Lim, "Novel neural control for a class of uncertain pure-feedback systems," *IEEE Trans. Neural Netw. Learn. Syst.*, vol. 25, no. 4, pp. 718–727, Apr. 2014.
- [16] Q. Shen, P. Shi, J. Zhu, S. Wang, and Y. Shi, "Neural networks based distributed adaptive control of nonlinear multi-agent systems," *IEEE Trans. Neural Netw. Learn. Syst.*, vol. 31, no. 3, pp. 1010–1021, Mar. 2020.
- [17] H. Jiao, L. Zhang, Q. Shen, J. Zhu, and P. Shi, "Robust gene circuit control design for time-delayed genetic regulatory networks without SUM regulatory logic," *IEEE/ACM Trans. Comput. Biol. Bioinf.*, vol. 15, no. 6, pp. 2086–2093, Nov. 2018.
- [18] Q. Shen, P. Shi, R. K. Agarwal, and Y. Shi, "Adaptive neural network-based filter design for nonlinear systems with multiple constraints," *IEEE Trans. Neural Netw. Learn. Syst.*, vol. 32, no. 7, pp. 3256–3261, Jul. 2021.
- [19] Q. Fu, Q. Shen, and Z. Jia, "Cooperative adaptive tracking control for unknown nonlinear multi-agent systems with signal transmission faults," *Circuits, Syst., Signal Process.*, vol. 39, no. 3, pp. 1335–1352, Mar. 2020.
- [20] Q. Shen, B. Jiang, and V. Cocquemot, "Fuzzy logic system-based adaptive fault-tolerant control for near-space vehicle attitude dynamics with actuator faults," *IEEE Trans. Fuzzy Syst.*, vol. 21, no. 2, pp. 289–300, Apr. 2013.
- [21] S. Roy, S. Baldi, and L. M. Fridman, "On adaptive sliding mode control without a priori bounded uncertainty," *Automatica*, vol. 111, Jan. 2020, Art. no. 108650, doi: [10.1016/j.automatica.2019.108650](https://doi.org/10.1016/j.automatica.2019.108650).
- [22] S. Roy, J. Lee, and S. Baldi, "A new adaptive-robust design for time delay control under state-dependent stability condition," *IEEE Trans. Control Syst. Technol.*, vol. 29, no. 1, pp. 420–427, Jan. 2021.
- [23] L. Wu, K. Liu, J. Lü, and H. Gu, "Finite-time adaptive stability of gene regulatory networks," *Neurocomputing*, vol. 338, pp. 222–232, Apr. 2019.
- [24] W. Qi, G. Zong, and F. Shun Su, "Fault detection for semi-Markov switching systems in the presence of positivity constraints," *IEEE Trans. Cybern.*, early access, Aug. 3, 2021, doi: [10.1109/TCYB.2021.3096948](https://doi.org/10.1109/TCYB.2021.3096948).
- [25] W. Qi, G. Zong, and W. X. Zheng, "Adaptive event-triggered SMC for stochastic switching systems with semi-Markov process and application to boost converter circuit model," *IEEE Trans. Circuits Syst. I, Reg. Papers*, vol. 68, no. 2, pp. 786–796, Feb. 2021.
- [26] W. Qi, Y. Hou, G. Zong, and C. K. Ahn, "Finite-time event-triggered control for semi-Markovian switching cyber-physical systems with FDI attacks and applications," *IEEE Trans. Circuits Syst. I, Reg. Papers*, vol. 68, no. 6, pp. 2665–2674, Jun. 2021.
- [27] Y. Jin, W. Qi, and G. Zong, "Finite-time synchronization of delayed semi-Markov neural networks with dynamic event-triggered scheme," *Int. J. Control. Autom. Syst.*, vol. 19, no. 6, pp. 2297–2308, Jun. 2021.
- [28] X. Zhang, Z. Zhang, Y. Wang, and C. Liu, "Guaranteed cost control of genetic regulatory networks with multiple time-varying discrete delays and multiple constant distributed delays," *IEEE Access*, vol. 8, pp. 80175–80182, 2020.
- [29] Y. Xie, L. Xiao, L. Wang, and G. Wang, "Algebraic stability criteria of reaction diffusion genetic regulatory networks with discrete and distributed delays," *IEEE Access*, vol. 9, pp. 16410–16418, 2021.
- [30] L. Zhang, X. Zhang, Y. Xue, and X. Zhang, "New method to global exponential stability analysis for switched genetic regulatory networks with mixed delays," *IEEE Trans. Nanobiosci.*, vol. 19, no. 2, pp. 308–314, Apr. 2020.



BING LÜ received the B.Sc. degree in agronomy, the M.Sc. degree in plant physiology, and the Ph.D. degree in crop genetics and breeding from Yangzhou University, Yangzhou, China, in 1996, 1999, and 2007, respectively. She is currently an Associate Professor with the College of Bio-science and Biotechnology, Yangzhou University. Her research interests include signal transduction, stress physiology, and growth and development physiology in plants.



QIKUN SHEN received the B.Sc. degree in computer science and applications from the Chinese University of Mining and Technology, Xuzhou, China, in 1996, the M.Sc. degree in computer science and applications from Yangzhou University, Yangzhou, China, in 2007, and the Ph.D. degree in control theory and control engineering from Nanjing University of Aeronautics and Astronautics, China, in 2015.

He is currently a Professor with the College of Information Engineering, Yangzhou University. His research interests include distributed control, consensus control, fault-tolerant control, adaptive control, fuzzy control, neural networks-based control, and intelligent control.

• • •