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Algebraic Stability Criteria of Reaction Diffusion Genetic Regulatory Networks With Discrete and Distributed Delays

YINPING XIE [1], LING XIAO [2], LEIMIN WANG [3], (Member, IEEE), AND GAOHUA WANG [1,2]
[1]Department of Psychiatry, Renmin Hospital of Wuhan University, Wuhan 430074, China
[2]Institute of Neuropsychiatry, Renmin Hospital, Wuhan University, Wuhan 430074, China
[3]School of Automation, China University of Geosciences, Wuhan 430074, China

Corresponding author: Gaohua Wang (wgh6402@163.com)

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ABSTRACT This paper addresses the stability problem of genetic regulatory networks by involving the spatial diffusion of concentration, discrete and infinite distributed delays. By using the theories of partial differential equation and Lyapunov stability, the global exponential stability criteria in algebraic form are derived for reaction diffusion genetic regulatory networks (RDGRNs) with discrete and distributed delays. The derived stability conditions are simple and can be directly calculated by using the parameters of the networks. Moreover, the theoretical results are universal and can be applied to deal with the stability problem of RDGRNs with or without distributed delays. Eventually, the validity and feasibility of the results are illustrated by numerical simulations.

INDEX TERMS Global exponential stability, reaction diffusion, genetic regulatory networks, infinite distributed delays.

I. INTRODUCTION

DNA, RNA, proteins, and other small molecules, together with their regulatory relationships, form an extremely complex network known as the genetic regulatory network (GRN) [1]–[4]. The study of GRN can not only deepen people's understanding of biological growth and development process at the molecular level, but also is expected to play a great role in the diagnosis and treatment of complex diseases [5]–[8]. In the process of gene expression and regulation, due to the dynamic changes in the concentration of RNA and protein, the differential equation model which can provide a relatively accurate description has attracted more attention [9]. Recently, as one of the basic issue of the dynamic performance, the stability problem of GRNs in forms of differential equation has been extensively investigated [10]–[16].

In an actual genetic regulatory network, there are huge differences in various biochemical reaction rates, which leads to the existence of time delays that cannot be ignored [17]. The interplay of time delays may result in instability or oscillation in GRNs. Thus, it is of great significance to consider time delays in constructing the models of GRNs. In [18], the authors adopted a reduced-order method to discuss the stability of GRNs with discrete time delays. In [19], the stability and bifurcation problem was addressed for GRNs with time delays. Then, the time-varying delays were taken into account for switched GRNs in [20]. Wang *et al.* [21] presented a delay fractioning approach to handle the time-varying delays existed in GRNs. Moreover, the H_∞ control and robust control problems were fully discussed for GRNs with time delays in [22]–[24].

Besides, as the special case of time delays, the distributed delays are inevitable in the case that each macromolecule takes different length of time to activate in composite position under the massively parallel network architecture [25]–[29]. Thus, it is of great importance to consider distributed delays in dynamics of GRNs. Considering the discrete and distributed delays, authors in [30]–[35] studied the stability for delayed GRNs. Further, the global asymptotic and exponential stability of GRNs with discrete and infinite distributed delays was analyzed in [36], [37]. When the infinite distributed delays are involved, the global exponential stability problem of GRNs with mixed time delays is a difficult task, which deserves further investigation.

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In general, it is assumed in the aforementioned papers that the combined GRN is spatially homogeneous, that is, the concentration of cellular components is consistent in any region. Nevertheless, this assumption has certain limitations. For example, diffusion phenomena should be considered when regulatory proteins or metabolites move from one layer to another [38]–[40]. Therefore, we should consider the variation of both mRNA and protein with time and space, i.e., the new model of partial differential equation for GRNs with reaction diffusion [41], [42]. In the past decade, the stability analysis of reaction diffusion GRNs (RDGRNs) with time delays has been investigated and several matrix-based criteria have been derived by using the partial differential equation theory [43]–[51]. In [43]–[48], the stability, passivity, state estimation were analyzed for RDGRNs with constant discrete delays and time-varying discrete delays. Further, the asymptotic stability was extended to finite-time stability of RDGRNs with time-varying delays [49]–[51]. However, to the best of authors' knowledge, few results have been published for the stability of RDGRNs with time-varying delays, let alone the stability of RDGRNs with infinite distributed delays.

Inspired by the above discussions, this paper makes an attempt to handle the exponential stability problem for RDGRNs with discrete and distributed delays. The main advantages are as below.

1) The discrete delays, infinite distributed delays and reaction diffusion are all considered in constructing the general and accurate model of GRNs, which makes the model more generalized compared to GRNs with distributed delays in [30]–[37], and RDGRNs without distributed delays in [43]–[51].

2) The algebraic criteria obtained are simple and can be conveniently calculated by using the system parameters. Moreover, the theoretical results can be extended to other partial differential systems with or without distributed delays.

Then, the structure of this paper is presented. The GRNs, RDGRNs and problem formulation are presented in Section II. The stability results of RDGRNs with infinite distributed delays are given in Section III. Then, two examples and their simulations are shown in Section IV. The conclusion is offered in Section V.

II. PRELIMINARIES

In this paper, $\mathscr{R}$, $\mathscr{R}_+$ and $\mathscr{R}^m$ denote the set of real numbers, nonnegative real numbers and the m-dimensional Euclidean space. $m^\flat = \{1, 2, \ldots, m\}$ for a constant m. For a given constant Q, $\Theta = \{(\tau_1, \tau_2, \ldots, \tau_Q)^T \,||\tau_q| < \nu_q, q \in Q^\flat\}$ is a bounded compact set with smooth boundary $\partial\Theta$ and measure $\text{mes}\Theta > 0$.

Consider the following GRNs model with discrete delays [4]

$$\begin{cases} \dot{\bar{x}}_s(t) = -a_s\bar{x}_s(t) + \sum_{k=1}^{m} c_{sk}\bar{h}_k(\bar{y}_k(t-\lambda_1)) + U_s \\ \dot{\bar{y}}_s(t) = -b_s\bar{y}_s(t) + d_s\bar{x}_s(t-\lambda_2) \end{cases} \tag{1}$$

where $s, k \in m^\flat$. $\bar{x}_s(t)$ and $\bar{y}_s(t)$ are the concentrations of mRNA and protein of the sth node. a_s, b_s, d_s are the rate constants, $c_{sk} = \breve{c}_{sk}$ if k activates gene s, or $c_{sk} = -\breve{c}_{sk}$ if k represses gene s, or $c_{sk} = 0$ if there is no link between genes k and s. $U_s = \sum_{k\in S_s} \breve{c}_{sk}$ where S_s is the set involving all the repressors of gene s. λ_1, λ_2 are the delays. $\bar{h}_k(\bar{y})$ is the regulatory function of the protein on the transcription.

Based on the model (1), in this paper, we consider the combined effect of spatial diffusion and infinite distributed delays. Then, it follows from system (1) that

$$\begin{cases} \frac{\partial \bar{x}_s(\tau,t)}{\partial t} = \sum_{q=1}^{Q} \frac{\partial}{\partial \tau_q}\left(\alpha_{sq}\frac{\partial \bar{x}_s(\tau,t)}{\partial \tau_q}\right) - a_s\bar{x}_s(\tau,t) \\ \qquad + \sum_{k=1}^{m} c_{sk}\bar{h}_k(\bar{y}_k(\tau,t-\lambda_1)) + U_s \\ \qquad + \sum_{k=1}^{m} f_{sk}\int_{-\infty}^{t} K(t-\sigma)\bar{h}_k(\bar{y}_k(\tau,\sigma))\mathrm{d}\sigma \\ \frac{\partial \bar{y}_s(\tau,t)}{\partial t} = \sum_{q=1}^{Q} \frac{\partial}{\partial \tau_q}\left(\beta_{sq}\frac{\partial \bar{y}_s(\tau,t)}{\partial \tau_q}\right) - b_s\bar{y}_s(\tau,t) \\ \qquad + d_s\bar{x}_s(\tau,t-\lambda_2) \\ \qquad + g_s\int_{-\infty}^{t} K(t-\sigma)\bar{x}_s(\tau,\sigma)\mathrm{d}\sigma \end{cases} \tag{2}$$

where $\bar{x}_s(\tau, t)$ and $\bar{y}_s(\tau, t)$ are the concentrations of mRNA and protein of the sth node at space τ and time t, and $\tau = (\tau_1, \tau_2, \ldots, \tau_Q)^T \in \Theta \subset \mathscr{R}^Q$. $\alpha_{sq} \geq 0, \beta_{sq} \geq 0$ are the transmission diffusion parameters. $g_s > 0$ and f_{sk} is similarly defined as c_{sk} in system (1). The delay kernel function $K(t) \in \mathscr{R}_+$ is continuous.

Remark 1: System (2) is generalized in light of the fact that it involves the spatial diffusion of concentration and the distributed delays of gene interaction. Moreover, the case of model with infinite distributed delays is also considered, which makes the model more general to better reflect the reaction of the gene networks.

For the regulatory functions and the distributed delays of system (2), we give the following hypotheses.

H1: For $k \in m^\flat$, there exist constant $l_k > 0$ such that

$$0 \leq \frac{\bar{h}_k(y) - \bar{h}_k(x)}{y - x} \leq l_k, \tag{3}$$

for all $x, y \in \mathscr{R}, x \neq y$.

H2: There exists positive constant ρ such that

$$\int_0^{+\infty} K(\sigma)\mathrm{d}\sigma = 1, \quad \int_0^{+\infty} \mathbf{e}^{\rho\sigma}K(\sigma)\mathrm{d}\sigma < \infty. \tag{4}$$

Assume that $x^*(\tau) = (x_1^*(\tau), x_2^*(\tau), \ldots, x_m^*(\tau))^T$ and $y^*(\tau) = (y_1^*(\tau), y_2^*(\tau), \ldots, y_m^*(\tau))^T$ are the equilibrium points of system (2). Then we obtain

$$\begin{cases} \frac{\partial x_s(\tau,t)}{\partial t} = \sum_{q=1}^{Q} \frac{\partial}{\partial \tau_q}\left(\alpha_{sq}\frac{\partial x_s(\tau,t)}{\partial \tau_q}\right) - a_s x_s(\tau,t) \\ \quad + \sum_{k=1}^{m} c_{sk} h_k(y_k(\tau, t-\lambda_1)) \\ \quad + \sum_{k=1}^{m} f_{sk}\int_{-\infty}^{t} K(t-\sigma)h_k(y_k(\tau,\sigma))\mathrm{d}\sigma \\ \frac{\partial y_s(\tau,t)}{\partial t} = \sum_{q=1}^{Q} \frac{\partial}{\partial \tau_q}\left(\beta_{sq}\frac{\partial y_s(\tau,t)}{\partial \tau_q}\right) - b_s y_s(\tau,t) \\ \quad + d_s x_s(\tau, t-\lambda_2) \\ \quad + g_s\int_{-\infty}^{t} K(t-\sigma)x_s(\tau,\sigma)\mathrm{d}\sigma \end{cases} \tag{5}$$

where $x_s(\tau,t) = \bar{x}_s(\tau,t) - x_s^*(\tau)$, $y_s(\tau,t) = \bar{y}_s(\tau,t) - y_s^*(\tau)$ and $h_k(y_k(\tau,\cdot)) = \bar{h}_k(\bar{y}_k(\tau,\cdot)) - \bar{h}_k(y_k^*(\tau))$. The the stability problem of equilibrium points of system (2) is changed into the stability problem of origin of system (5).

The boundary conditions of system (5) are $x_s(\tau,t) = 0$ and $y_s(\tau,t) = 0$ for $(\tau,t) \in \partial\Theta \times (-\infty,+\infty)$. The initial conditions of system (5) are $x_s(\tau,t) = \chi_s(\tau,\sigma)$ and $y_s(\tau,t) = \phi_s(\tau,\sigma)$ for $(\tau,\sigma) \in \Theta \times (-\infty, 0]$.

Define

$$\|z(\tau,t)\| = (\int_{\Theta}\sum_{s=1}^{m}|z_s(\tau,t)|^{\mathbb{p}}\mathrm{d}\tau)^{1/\mathbb{p}}, \tag{6}$$

$$\|z(\tau,\sigma)\| = (\int_{\Theta}\sup_{-\infty<\sigma\le 0}\sum_{s=1}^{m}|z_s(\tau,\sigma)|^{\mathbb{p}}\mathrm{d}\tau)^{1/\mathbb{p}} \tag{7}$$

where $\mathbb{p} \ge 2$, $z(\tau,t) = (z_1(\tau,t), z_2(\tau,t), \ldots, z_m(\tau,t))^T$, $z(\tau,\sigma) = (z_1(\tau,\sigma), z_2(\tau,\sigma), \ldots, z_m(\tau,\sigma))^T \in \mathscr{C}$, with $\mathscr{C} = \mathscr{C}(\Theta \times (-\infty,0], \mathscr{R}^m)$ denotes the Banach space of continuous functions.

Definition 1: The origin of system (5) is said to be globally exponentially stable, if given initial conditions $\chi, \phi \in \mathscr{C}$, there exist $\upsilon > 0$ and $\varrho \ge 1$ such that

$$\|x(\tau,t)\|^{\mathbb{p}} + \|y(\tau,t)\|^{\mathbb{p}} \le \varrho(\|\chi\|^{\mathbb{p}} + \|\phi\|^{\mathbb{p}})\mathbf{e}^{-\upsilon t}. \tag{8}$$

Lemma 1 [38]: Give a compact set $\Theta = \{\tau = (\tau_1, \tau_2, \ldots, \tau_Q)^T \,||\tau_q| < \nu_q, q \in Q^\flat\}$ and function $h(\tau) \in \mathscr{C}^1(\Theta)$ with $h(\tau)|_{\partial\Theta} = 0$, then for $\mathbb{p} \ge 2$, $q \in Q^\flat$

$$\int_{\Theta}|h(\tau)|^{\mathbb{p}}\mathrm{d}\tau \le \frac{\mathbb{p}^2\nu_q^2}{4}\int_{\Theta}|h(\tau)|^{\mathbb{p}-2}|\frac{\partial h}{\partial \tau_q}|^2\mathrm{d}\tau. \tag{9}$$

III. MAIN RESULTS

This section presents the global exponential stability results for RDGRNs with discrete and distributed delays.

Theorem 1: Assume that H1 and H2 hold, then system (2) is globally exponentially stable if the following two inequalities hold

$$-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\alpha_{sq}}{\mathbb{p}\nu_q^2} - \mathbb{p}a_s + |d_s| + |g_s| + \sum_{k=1}^{m}(\mathbb{p}-1)(|c_{sk}|l_k + |f_{sk}|l_k) < 0, \tag{10}$$

$$-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\beta_{sq}}{\mathbb{p}\nu_q^2} - \mathbb{p}b_s + \sum_{k=1}^{m}(|c_{ks}|l_s + |f_{ks}|l_s) + (\mathbb{p}-1)(|d_s| + |g_s|) < 0. \tag{11}$$

Proof: Consider the functions

$$W_s(\xi_s) = \xi_s - \sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\alpha_{sq}}{\mathbb{p}\nu_q^2} - \mathbb{p}a_s + |d_s|\mathbf{e}^{\xi_s\lambda_2} + |g_s|\int_0^{+\infty}\mathbf{e}^{\xi_s\sigma}K(\sigma)\mathrm{d}\sigma + \sum_{k=1}^{m}(\mathbb{p}-1)(|c_{sk}|l_k + |f_{sk}|l_k), \tag{12}$$

$$M_s(\zeta_s) = \zeta_s - \sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\beta_{sq}}{\mathbb{p}\nu_q^2} - \mathbb{p}b_s + \sum_{k=1}^{m}\left(|c_{ks}|l_s\mathbf{e}^{\zeta_s\lambda_1} + |f_{ks}|l_s\int_0^{+\infty}\mathbf{e}^{\zeta_s\sigma}K(\sigma)\mathrm{d}\sigma + (\mathbb{p}-1)(|d_s| + |g_s|)\right). \tag{13}$$

Then, it is obvious from H2 and the conditions (10) and (11) that

$$W_s(0) < 0, \quad M_s(0) < 0. \tag{14}$$

Since functions $W_s(\xi_s)$ and $M_s(\zeta_s)$ are continuous with respect to ξ_s and ζ_s, respectively, there exist $\tilde{\xi}_s$ and $\tilde{\zeta}_s$ such that $W_s(\tilde{\xi}_s) \le 0$, $M_s(\tilde{\zeta}_s) \le 0$ and $W_s(\xi_s) < 0$, $M_s(\zeta_s) < 0$ for $\xi_s \in [0, \tilde{\xi}_s)$, $\zeta_s \in [0, \tilde{\zeta}_s)$. Take $\delta = \min_{s\in m^\flat}\{\tilde{\xi}_s, \tilde{\zeta}_s\}$, then for all $s \in m^\flat$

$$W_s(\delta) = \delta - \sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\alpha_{sq}}{\mathbb{p}\nu_q^2} - \mathbb{p}a_s + |d_s|\mathbf{e}^{\delta\lambda_2} + |g_s|\int_0^{+\infty}\mathbf{e}^{\delta\sigma}K(\sigma)\mathrm{d}\sigma + \sum_{k=1}^{m}(\mathbb{p}-1)(|c_{sk}|l_k + |f_{sk}|l_k) \le 0, \tag{15}$$

$$M_s(\delta) = \delta - \sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\beta_{sq}}{\mathbb{p}\nu_q^2} - \mathbb{p}b_s + \sum_{k=1}^{m}\left(|c_{ks}|l_s\mathbf{e}^{\delta\lambda_1} + |f_{ks}|l_s\int_0^{+\infty}\mathbf{e}^{\delta\sigma}K(\sigma)\mathrm{d}\sigma\right) + (\mathbb{p}-1)(|d_s| + |g_s|) \le 0. \tag{16}$$

Construct the Lyapunov-Krasovskii functional

$$V(t) = \int_{\Theta}\sum_{s=1}^{m}\Big[F_s(t) + G_s(t) + \sum_{k=1}^{m}\Big(|c_{sk}|l_k\int_{t-\lambda_1}^{t}\mathbf{e}^{\delta\lambda_1}G_k(\sigma)\mathrm{d}\sigma + |f_{sk}|l_k\int_{-\infty}^{0}\int_{t+\theta}^{t}\mathbf{e}^{-\delta\theta}K(-\theta)G_k(\sigma)\mathrm{d}\sigma\mathrm{d}\theta\Big)$$

$$+|d_s|\int_{t-\lambda_2}^{t}\mathbf{e}^{\delta\lambda_2}F_s(\sigma)\mathrm{d}\sigma$$
$$+|g_s|\int_{-\infty}^{0}\int_{t+\theta}^{t}\mathbf{e}^{-\delta\theta}K(-\theta)F_s(\sigma)\mathrm{d}\sigma\mathrm{d}\theta\Big]\mathrm{d}\tau \tag{17}$$

where $F_s(t)=\mathbf{e}^{\delta t}|x_s(\tau,t)|^{\mathbb{p}}$, $G_s(t)=\mathbf{e}^{\delta t}|y_s(\tau,t)|^{\mathbb{p}}$.

It follows

$$\begin{aligned}
D^+V(t) &= \int_\Theta\sum_{s=1}^{m}\Big\{\mathbf{e}^{\delta t}\Big[\frac{\mathbb{p}}{2}|x_s(\tau,t)|^{\mathbb{p}-2}\frac{\partial x_s^2(\tau,t)}{\partial t}+\delta|x_s(\tau,t)|^{\mathbb{p}}\\
&\quad+\frac{\mathbb{p}}{2}|y_s(\tau,t)|^{\mathbb{p}-2}\frac{\partial y_s^2(\tau,t)}{\partial t}+\delta|y_s(\tau,t)|^{\mathbb{p}}\Big]\\
&\quad+\sum_{k=1}^{m}\Big[\mathbf{e}^{\delta\lambda_1}|c_{sk}|l_k(G_k(t)-G_k(t-\lambda_1))\\
&\quad+|f_{sk}|l_k\Big(\int_{-\infty}^{0}\mathbf{e}^{-\delta\theta}K(-\theta)G_k(t)\mathrm{d}\theta\\
&\quad-\int_{-\infty}^{0}\mathbf{e}^{-\delta\theta}K(-\theta)G_k(t+\theta)\mathrm{d}\theta\Big)\Big]\\
&\quad+|d_s|\mathbf{e}^{\delta\lambda_2}(F_s(t)-F_s(t-\lambda_2))\\
&\quad+|g_s|\Big(\int_{-\infty}^{0}\mathbf{e}^{-\delta\theta}K(-\theta)F_s(t)\mathrm{d}\theta\\
&\quad-\int_{-\infty}^{0}\mathbf{e}^{-\delta\theta}K(-\theta)F_s(t+\theta)\mathrm{d}\theta\Big)\Big\}\mathrm{d}\tau\\
&\le \int_\Theta\sum_{s=1}^{m}\mathbf{e}^{\delta t}\Big\{\mathbb{p}|x_s(\tau,t)|^{\mathbb{p}-2}x_s(\tau,t)\\
&\quad\times\sum_{q=1}^{Q}\frac{\partial}{\partial\tau_q}\Big(\alpha_{sq}\frac{\partial x_s(\tau,t)}{\partial\tau_q}\Big)-\mathbb{p}a_s|x_s(\tau,t)|^{\mathbb{p}}\\
&\quad+\sum_{k=1}^{m}\mathbb{p}|x_s(\tau,t)|^{\mathbb{p}-1}\Big(|c_{sk}||h_k(y_k(\tau,t-\lambda_1))|\\
&\quad+|f_{sk}|\int_{-\infty}^{t}K(t-\sigma)|h_k(y_k(\tau,\sigma))|\mathrm{d}\sigma\Big)\\
&\quad+\mathbb{p}|y_s(\tau,t)|^{\mathbb{p}-2}y_s(\tau,t)\sum_{q=1}^{Q}\frac{\partial}{\partial\tau_q}\Big(\beta_{sq}\frac{\partial y_s(\tau,t)}{\partial\tau_q}\Big)\\
&\quad-\mathbb{p}b_s|y_s(\tau,t)|^{\mathbb{p}}+\mathbb{p}|y_s(\tau,t)|^{\mathbb{p}-1}\Big(|d_s||x_s(\tau,t-\lambda_2)|\\
&\quad+|g_s|\int_{-\infty}^{t}K(t-\sigma)|x_s(\tau,\sigma)|\mathrm{d}\sigma\Big)\\
&\quad+\delta(|x_s(\tau,t)|^{\mathbb{p}}+|y_s(\tau,t)|^{\mathbb{p}})\\
&\quad+\sum_{k=1}^{m}\Big[|c_{sk}|l_k(\mathbf{e}^{\delta\lambda_1}|y_k(\tau,t)|^{\mathbb{p}}-|y_k(\tau,t-\lambda_1)|^{\mathbb{p}})\\
&\quad+|f_{sk}|l_k\Big(\int_{-\infty}^{0}\mathbf{e}^{-\delta\theta}K(-\theta)|y_k(\tau,t)|^{\mathbb{p}}\mathrm{d}\theta\\
&\quad-\int_{-\infty}^{0}K(-\theta)|y_k(\tau,t+\theta)|^{\mathbb{p}}\mathrm{d}\theta\Big)\Big]\\
&\quad+|d_s|(\mathbf{e}^{\delta\lambda_2}|x_s(\tau,t)|^{\mathbb{p}}-|x_s(\tau,t-\lambda_2)|^{\mathbb{p}})\\
&\quad+|g_s|\Big(\int_{-\infty}^{0}\mathbf{e}^{-\delta\theta}K(-\theta)|x_s(\tau,t)|^{\mathbb{p}}\mathrm{d}\theta\\
&\quad-\int_{-\infty}^{0}K(-\theta)|x_s(\tau,t+\theta)|^{\mathbb{p}}\mathrm{d}\theta\Big)\Big\}\mathrm{d}\tau.
\end{aligned}\tag{18}$$

Recall the classical Young's inequality $yx\le 1/\varpi_1\, y^{\varpi_1}+1/\varpi_2\, x^{\varpi_2}$ for $y>0, x>0$ with constants $\varpi_1>0, \varpi_2>0$ satisfying $1/\varpi_1+1/\varpi_2=1$, it follows from H1 and H2 that

$$\begin{aligned}
&\sum_{k=1}^{m}\mathbb{p}|c_{sk}||x_s(\tau,t)|^{\mathbb{p}-1}|h_k(y_k(\tau,t-\lambda_1))|\\
&\quad\le\sum_{k=1}^{m}|c_{sk}|l_k((\mathbb{p}-1)|x_s(\tau,t)|^{\mathbb{p}}+|y_k(\tau,t-\lambda_1)|^{\mathbb{p}}),
\end{aligned}\tag{19}$$

$$\begin{aligned}
&\mathbb{p}|d_s||y_s(\tau,t)|^{\mathbb{p}-1}|x_s(\tau,t-\lambda_2))|\\
&\quad\le|d_s|((\mathbb{p}-1)|y_s(\tau,t)|^{\mathbb{p}}+|x_s(\tau,t-\lambda_2)|^{\mathbb{p}}),
\end{aligned}\tag{20}$$

$$\begin{aligned}
&\sum_{k=1}^{m}\mathbb{p}|f_{sk}||x_s(\tau,t)|^{\mathbb{p}-1}\int_{-\infty}^{t}K(t-\sigma)|h_k(y_k(\tau,\sigma))|\mathrm{d}\sigma\\
&\quad\le\sum_{k=1}^{m}|f_{sk}|l_k((\mathbb{p}-1)|x_s(\tau,t)|^{\mathbb{p}}\\
&\qquad+\int_{-\infty}^{t}K(t-\sigma)|y_k(\tau,\sigma)|^{\mathbb{p}}\mathrm{d}\sigma),
\end{aligned}\tag{21}$$

$$\begin{aligned}
&\mathbb{p}|g_s||y_s(\tau,t)|^{\mathbb{p}-1}\int_{-\infty}^{t}K(t-\sigma)|x_s(\tau,\sigma))|\mathrm{d}\sigma\\
&\quad\le|g_s|((\mathbb{p}-1)|y_s(\tau,t)|^{\mathbb{p}}\\
&\qquad+\int_{-\infty}^{t}K(t-\sigma)|x_s(\tau,\sigma)|^{\mathbb{p}}\mathrm{d}\sigma).
\end{aligned}\tag{22}$$

Based on the Lemma 1 in [38] and the Green formula in [52], it yields

$$\begin{aligned}
&\int_\Theta\mathbb{p}|x_s(\tau,t)|^{\mathbb{p}-2}x_s(\tau,t)\sum_{q=1}^{Q}\frac{\partial}{\partial\tau_q}\Big(\alpha_{sq}\frac{\partial x_s(\tau,t)}{\partial\tau_q}\Big)\mathrm{d}\tau\\
&\quad=-\mathbb{p}(\mathbb{p}-1)\int_\Theta|x_s(\tau,t)|^{\mathbb{p}-2}\sum_{q=1}^{Q}\alpha_{sq}\Big(\frac{\partial|x_s(\tau,t)|}{\partial\tau_q}\Big)^2\mathrm{d}\tau\\
&\quad\le-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\alpha_{sq}}{\mathbb{p}\nu_q^2}\int_\Theta|x_s(\tau,t)|^{\mathbb{p}}\mathrm{d}\tau,
\end{aligned}\tag{23}$$

$$\begin{aligned}
&\int_\Theta\mathbb{p}|y_s(\tau,t)|^{\mathbb{p}-2}y_s(\tau,t)\sum_{q=1}^{Q}\frac{\partial}{\partial\tau_q}\Big(\beta_{sq}\frac{\partial y_s(\tau,t)}{\partial\tau_q}\Big)\mathrm{d}\tau\\
&\quad=-\mathbb{p}(\mathbb{p}-1)\int_\Theta|y_s(\tau,t)|^{\mathbb{p}-2}\sum_{q=1}^{Q}\beta_{sq}\Big(\frac{\partial|y_s(\tau,t)|}{\partial\tau_q}\Big)^2\mathrm{d}\tau\\
&\quad\le-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\beta_{sq}}{\mathbb{p}\nu_q^2}\int_\Theta|y_s(\tau,t)|^{\mathbb{p}}\mathrm{d}\tau.
\end{aligned}\tag{24}$$

Thus, it follows from (18)-(24) that

$$D^+V(t)\le\int_\Theta\sum_{s=1}^{m}\mathbf{e}^{\delta t}\Big\{\Big(-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\alpha_{sq}}{\mathbb{p}\nu_q^2}+\delta-\mathbb{p}a_s$$

$$
\begin{aligned}
&+\sum_{k=1}^{m}(\mathbb{p}-1)(|c_{sk}|l_k+|f_{sk}|l_k)\Big)|x_s(\tau,t)|^{\mathbb{P}}\\
&+\Big(-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\beta_{sq}}{\mathbb{p}\nu_q^2}+\delta-\mathbb{p}b_s\\
&+(\mathbb{p}-1)(|d_s|+|g_s|)\Big)|y_s(\tau,t)|^{\mathbb{P}}\\
&+\sum_{k=1}^{m}|f_{sk}|l_k\int_{-\infty}^{t}K(t-\sigma)|y_k(\tau,\sigma)|^{\mathbb{P}}\mathrm{d}\sigma\\
&+|g_s|\int_{-\infty}^{t}K(t-\sigma)|x_s(\tau,\sigma)|^{\mathbb{P}}\mathrm{d}\sigma\\
&+\sum_{k=1}^{m}\Big[|c_{sk}|l_k\mathbf{e}^{\delta\lambda_1}|y_k(\tau,t)|^{\mathbb{P}}\\
&+|f_{sk}|l_k\Big(\int_{-\infty}^{0}\mathbf{e}^{-\delta\theta}K(-\theta)|y_k(\tau,t)|^{\mathbb{P}}\mathrm{d}\theta\\
&-\int_{-\infty}^{0}K(-\theta)|y_k(\tau,t+\theta)|^{\mathbb{P}}\mathrm{d}\theta\Big)\Big]\\
&+|d_s|\mathbf{e}^{\delta\lambda_2}|x_s(\tau,t)|^{\mathbb{P}}\\
&+|g_s|\Big(\int_{-\infty}^{0}\mathbf{e}^{-\delta\theta}K(-\theta)|x_s(\tau,t)|^{\mathbb{P}}\mathrm{d}\theta\\
&-\int_{-\infty}^{0}K(-\theta)|x_s(\tau,t+\theta)|^{\mathbb{P}}\mathrm{d}\theta\Big)\Big\}\mathrm{d}\tau\\
\le&\int_{\Theta}\sum_{s=1}^{m}\mathbf{e}^{\delta t}\Big\{\Big(-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\alpha_{sq}}{\mathbb{p}\nu_q^2}+\delta-\mathbb{p}a_s\\
&+|d_s|\mathbf{e}^{\delta\lambda_2}+|g_s|\int_{0}^{+\infty}\mathbf{e}^{\delta\sigma}K(\sigma)\mathrm{d}\sigma\\
&+\sum_{k=1}^{m}(\mathbb{p}-1)(|c_{sk}|l_k+|f_{sk}|l_k)\Big)|x_s(\tau,t)|^{\mathbb{P}}\\
&+\Big[-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\beta_{sq}}{\mathbb{p}\nu_q^2}+\delta-\mathbb{p}b_s\\
&+\sum_{k=1}^{m}\Big(|c_{ks}|l_s\mathbf{e}^{\delta\lambda_1}+|f_{ks}|l_s\int_{0}^{+\infty}\mathbf{e}^{\delta\sigma}K(\sigma)\mathrm{d}\sigma\Big)\\
&+(\mathbb{p}-1)(|d_s|+|g_s|)\Big]|y_s(\tau,t)|^{\mathbb{P}}\Big\}\mathrm{d}\tau\le 0. \qquad (25)
\end{aligned}
$$

Based on (17) and (25), we can get

$$
\begin{aligned}
&\int_{\Theta}\sum_{s=1}^{m}\mathbf{e}^{\delta t}(|x_s(\tau,t)|^{\mathbb{P}}+|y_s(\tau,t)|^{\mathbb{P}})\mathrm{d}\tau\\
&\le\int_{\Theta}\sum_{s=1}^{m}\Big(|x_s(\tau,0)|^{\mathbb{P}}+|y_s(\tau,0)|^{\mathbb{P}}\\
&+\sum_{k=1}^{m}|c_{ks}|l_s\int_{-\lambda_1}^{0}\mathbf{e}^{\delta(\lambda_1+\sigma)}|y_s(\tau,\sigma)|^{\mathbb{P}}\mathrm{d}\sigma\\
&+\sum_{k=1}^{m}|f_{ks}|l_s\times\int_{-\infty}^{0}\int_{\theta}^{0}\mathbf{e}^{\delta(\sigma-\theta)}K(-\theta)|y_s(\tau,\sigma)|^{\mathbb{P}}\mathrm{d}\sigma\mathrm{d}\theta\\
&+|d_s|\int_{-\lambda_2}^{0}\mathbf{e}^{\delta(\lambda_2+\sigma)}|x_s(\tau,\sigma)|^{\mathbb{P}}\mathrm{d}\sigma\\
&+|g_s|\int_{-\infty}^{0}\int_{\theta}^{0}\mathbf{e}^{\delta(\sigma-\theta)}K(-\theta)|x_s(\tau,\sigma)|^{\mathbb{P}}\mathrm{d}\sigma\mathrm{d}\theta\Big)\mathrm{d}\tau\\
&\le\tilde{\delta}\int_{\Theta}\sup_{-\infty<\sigma\le 0}\sum_{s=1}^{m}(|\chi_s(\tau,\sigma)|^{\mathbb{P}}+|\phi_s(\tau,\sigma)|^{\mathbb{P}})\mathrm{d}\tau \qquad (26)
\end{aligned}
$$

where $\tilde{\delta}=\max_s\{1+|d_s|\lambda_2\mathbf{e}^{\delta\lambda_2}+|g_s|\int_0^{+\infty}\mathbf{e}^{\delta\sigma}K(\sigma)\mathrm{d}\sigma, 1+\sum_{k=1}^{m}(|c_{ks}|l_s\lambda_1\mathbf{e}^{\delta\lambda_1}+|f_{ks}|l_s\int_0^{+\infty}\mathbf{e}^{\delta\sigma}K(\sigma)\mathrm{d}\sigma)\}$.

Thus,

$$
\|x(\tau,t)\|^{\mathbb{P}}+\|y(\tau,t)\|^{\mathbb{P}}\le\tilde{\delta}(\|\chi\|^{\mathbb{P}}+\|\phi\|^{\mathbb{P}})\mathbf{e}^{-\delta t}. \qquad (27)
$$

In light of Definition 1, the origin of system (5) is globally exponentially stable, which implies that the equilibrium points of system (2) is globally exponentially stable. The proof is completed. ■

Without the distributed delays, system (5) is changed into the following RDGRNs with discrete delays

$$
\begin{cases}
\dfrac{\partial x_s(\tau,t)}{\partial t}=\displaystyle\sum_{q=1}^{Q}\frac{\partial}{\partial\tau_q}\Big(\alpha_{sq}\frac{\partial x_s(\tau,t)}{\partial\tau_q}\Big)-a_sx_s(\tau,t)\\
\qquad+\displaystyle\sum_{k=1}^{m}c_{sk}h_k(y_k(\tau,t-\lambda_1))\\
\dfrac{\partial y_s(\tau,t)}{\partial t}=\displaystyle\sum_{q=1}^{Q}\frac{\partial}{\partial\tau_q}\Big(\beta_{sq}\frac{\partial y_s(\tau,t)}{\partial\tau_q}\Big)-b_sy_s(\tau,t)\\
\qquad+d_sx_s(\tau,t-\lambda_2).
\end{cases}
\qquad (28)
$$

Then we can get the following Corollary 1. In addition, we can get Corollary 2 for system (1).

Corollary 1: Assume H1 holds, then system (28) is globally exponentially stable if the following two inequalities hold

$$
-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\alpha_{sq}}{\mathbb{p}\nu_q^2}-\mathbb{p}a_s+|d_s|+\sum_{k=1}^{m}(\mathbb{p}-1)|c_{sk}|l_k<0, \qquad (29)
$$

$$
-\sum_{q=1}^{Q}\frac{4(\mathbb{p}-1)\beta_{sq}}{\mathbb{p}\nu_q^2}-\mathbb{p}b_s+\sum_{k=1}^{m}|c_{ks}|l_s+(\mathbb{p}-1)|d_s|<0. \qquad (30)
$$

Corollary 2: Assume H1 holds, then system (1) is globally exponentially stable if the following two inequalities hold

$$
-\mathbb{p}a_s+|d_s|+\sum_{k=1}^{m}(\mathbb{p}-1)|c_{sk}|l_k<0, \qquad (31)
$$

$$
-\mathbb{p}b_s+\sum_{k=1}^{m}|c_{ks}|l_s+(\mathbb{p}-1)|d_s|<0. \qquad (32)
$$

Remark 2: The model of RDGRNs with discrete and distributed delays is general compared with the models in [30]–[37], [43]–[51]. The models in [30]–[37] are restricted to be delayed ordinary differential equations.

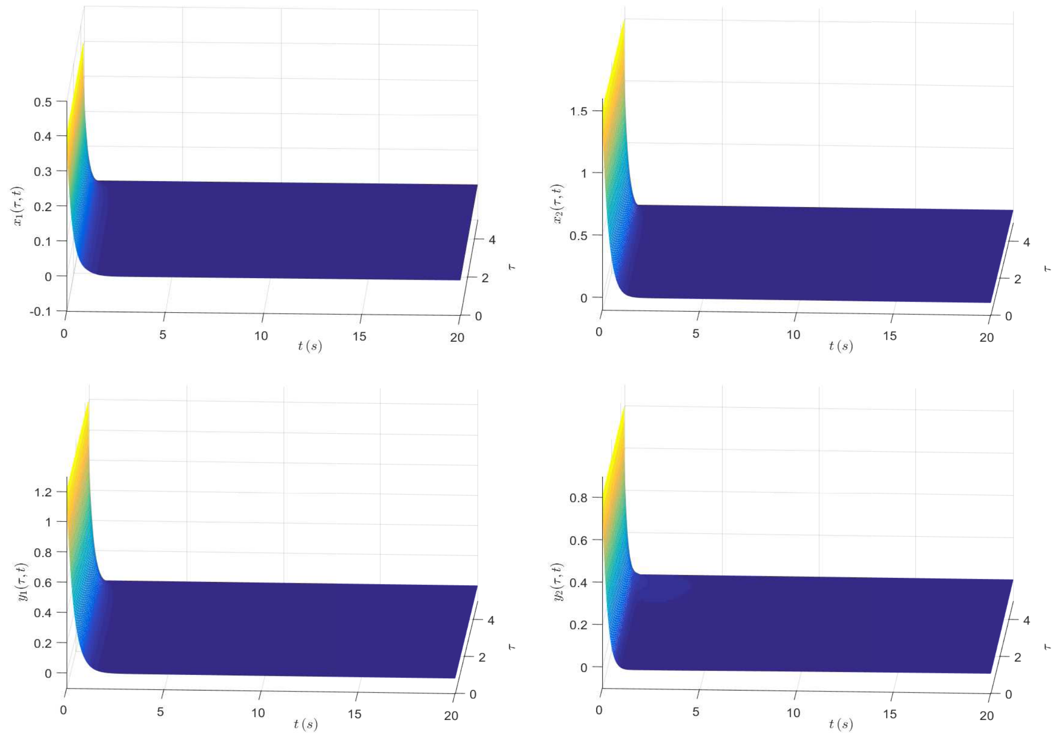

FIGURE 1. The state trajectories of $x_1(\tau, t), x_2(\tau, t)$ and $y_1(\tau, t), y_2(\tau, t)$ in Example 1.

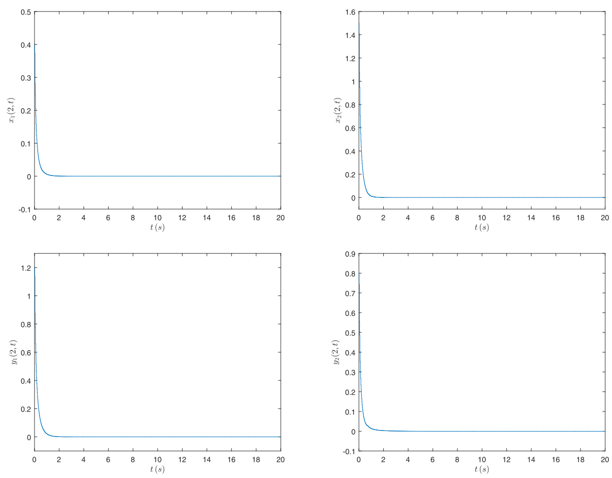

FIGURE 2. Choose $\tau = 2$, the state trajectories of $x_1(2, t), x_2(2, t)$ and $y_1(2, t), y_2(2, t)$ in Example 1.

Since the model in this paper can be viewed as a special case of delayed partial differential equations in light of effect of the reaction diffusion, it shows superiority in the case of nonuniform space. Moreover, although the models in [43]–[51] consider the diffusion effect, they do not consider the distributed delays.

Remark 3: Our results show the advantages compared to the ones in [35] where the stability of GRNs with distributed delays was studied, and the one in [42], [48] where the state estimation of RDGRNs were studied, respectively. On the one hand, the constant distributed delays are required to be bounded and the reaction diffusion is not considered in [35]. In addition, the distributed delays are not considered in [42], [48]. On the other hand, The algebraic criteria in this paper is easy to be checked and calculated compared to the ones in [42], [48] where large numbers of matrices need to be concluded.

Remark 4: The delay-independent results in Theorem 1 can be further improved. On the one hand, we can adopt the new lemmas as well as new inequalities in [53], [54] to reduce the conservativeness and obtain the delay-dependent results. On the other hand, the constant discrete delays can be extended to the time-varying case after simple modification of the Lyapunov-Krasovskii functional in proof of Theorem 1.

Remark 5: Based on the algebraic conditions of Theorem 1, Corollaries 1 and 2 show the extended $\mathbb{p}$-norm based results of GRNs without distributed delays, which implies that the earlier results are further complemented. Moreover, the results in this paper can be easily extended to deal with other delayed partial differential systems with or without distributed delays.

IV. NUMERICAL SIMULATIONS

Two examples are provided to show the effectiveness of results obtained in previous section.

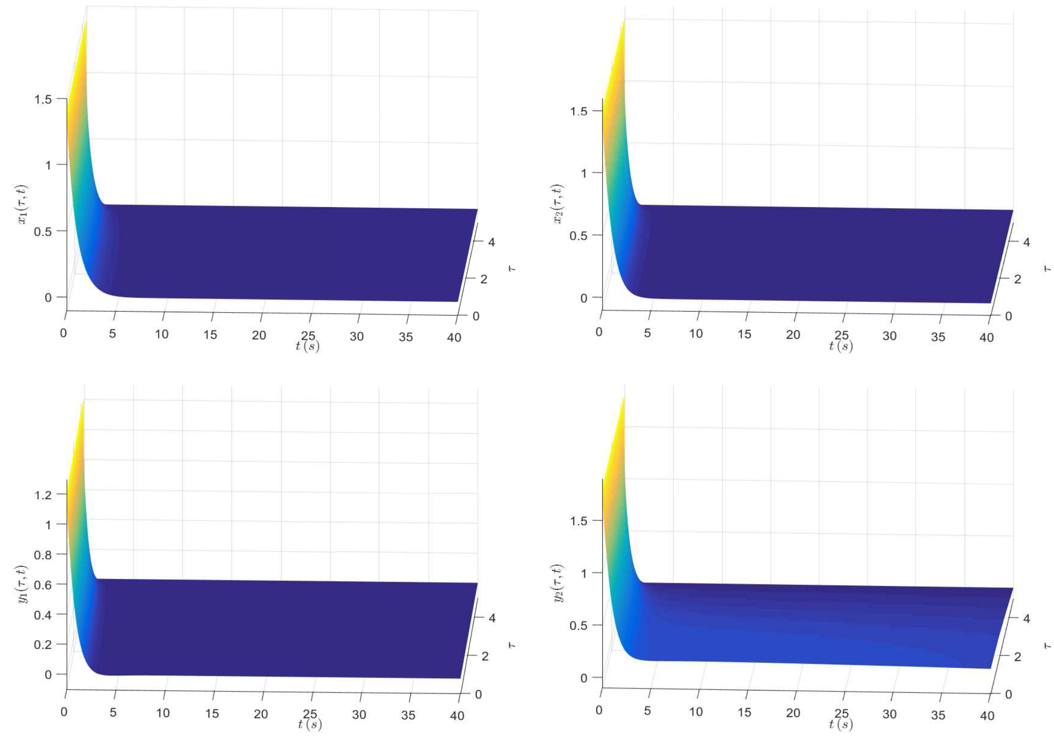

FIGURE 3. The state trajectories of $x_1(\tau,t), x_2(\tau,t)$ and $y_1(\tau,t), y_2(\tau,t)$ in Example 2.

Example 1: Consider the RDGRNs with discrete and distributed delays.

$$\begin{cases} \dfrac{\partial x_s(\tau,t)}{\partial t} = \alpha_s \dfrac{\partial^2 x_s(\tau,t)}{\partial \tau^2} - a_s x_s(\tau,t) \\ \qquad + \sum_{k=1}^{2} c_{sk} h_k(y_k(\tau, t-\lambda_1)) \\ \qquad + \sum_{k=1}^{2} f_{sk} \int_{-\infty}^{t} K(t-\sigma) h_k(y_k(\tau,\sigma)) \mathrm{d}\sigma \\ \dfrac{\partial y_s(\tau,t)}{\partial t} = \beta_s \dfrac{\partial^2 y_s(\tau,t)}{\partial \tau^2} - b_s y_s(\tau,t) \\ \qquad + d_s x_s(\tau, t-\lambda_2) \\ \qquad + g_s \int_{-\infty}^{t} K(t-\sigma) x_s(\tau,\sigma) \mathrm{d}\sigma \end{cases} \tag{33}$$

where $s = 1,2, \tau \in \Theta = [0,5], \alpha_1 = \alpha_2 = \beta_1 = \beta_2 = 0.08, a_1 = a_2 = b_1 = b_2 = 3, c_{11} = 0.1, c_{12} = -0.1, c_{21} = -0.1, c_{22} = 0, f_{11} = -0.2, f_{12} = -0.1, f_{21} = 0.1, f_{22} = 0, d_1 = d_2 = 0.1, g_1 = g_2 = 1$, the delays $\lambda_1 = \lambda_2 = 1, K(\sigma) = \mathbf{e}^{-\sigma}$, and functions $h_1(y) = h_2(y) = y^2/(1+y^2)$.

It is easy to check that the conditions of Theorem 1 are fulfilled based on the chosen parameters in system (33). Then the globally exponentially stability of system (33) is ensured according to the results of Theorem 1. The time and space evolutions of $x_1(\tau,t), x_2(\tau,t)$ and $y_1(\tau,t), y_2(\tau,t)$ are shown in Fig. 1. Choose $\tau = 2$, Fig. 2 illustrates the state trajectories of $x_1(2,t), x_2(2,t)$ and $y_1(2,t), y_2(2,t)$. From Figs. 1 and 2, we come to the conclusion that the origin of system (33) is exponentially stable.

Example 2: Based on system (33), if the effect of distributed delays are missed, then we get the RDGRNs with discrete delays as follows.

$$\begin{cases} \dfrac{\partial x_s(\tau,t)}{\partial t} = \alpha_s \dfrac{\partial^2 x_s(\tau,t)}{\partial \tau^2} - a_s x_s(\tau,t) \\ \qquad + \sum_{k=1}^{2} c_{sk} h_k(y_k(\tau, t-\lambda_1)) \\ \dfrac{\partial y_s(\tau,t)}{\partial t} = \beta_s \dfrac{\partial^2 y_s(\tau,t)}{\partial \tau^2} - b_s y_s(\tau,t) \\ \qquad + d_s x_s(\tau, t-\lambda_2) \end{cases} \tag{34}$$

where $s = 1,2, \tau \in \Theta = [0,5], \alpha_1 = \alpha_2 = \beta_1 = \beta_2 = 0.09, a_1 = a_2 = b_1 = b_2 = 1, c_{11} = -0.1, c_{12} = 0.1, c_{21} = 0.2, c_{22} = -0.2, d_1 = d_2 = -0.1$, the delays $\lambda_1 = \lambda_2 = 1$, and functions $h_1(y) = h_2(y) = y^2/(1+y^2)$.

It is easy to check that the conditions of Corollary 1 are fulfilled based on the chosen parameters in system (34). Then the globally exponentially stability of system (34) is ensured according to the results of Corollary 1. The time and space evolutions of $x_1(\tau,t), x_2(\tau,t)$ and $y_1(\tau,t), y_2(\tau,t)$ are shown in Fig. 3. Choose $\tau = 1$, Fig. 4 illustrates the state trajectories of $x_1(1,t), x_2(1,t)$ and $y_1(1,t), y_2(1,t)$. From Figs. 3 and 4, we come to the conclusion that the origin of system (34) is exponentially stable.

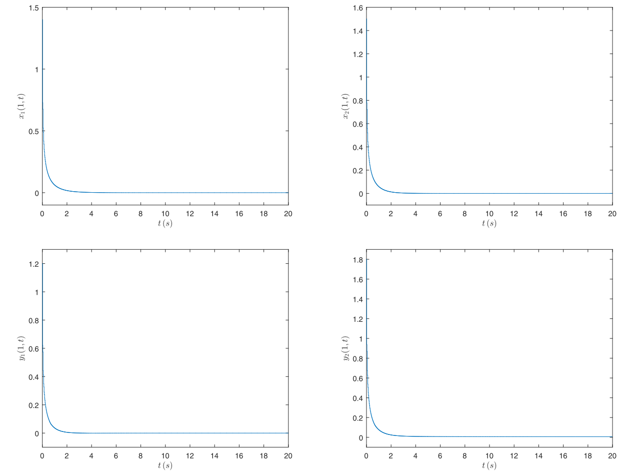

FIGURE 4. Choose $\tau = 1$, the state trajectories of $x_1(1,t), x_2(1,t)$ and $y_1(1,t), y_2(1,t)$ in Example 2.

V. CONCLUSION

This paper has considered the infinite distributed delays and reaction diffusion in constructing the model of the genetic regulatory networks. By employing the Lyapunov stability and partial differential system theories, the easily verified algebraic criteria have been derived for the RDGRNs with discrete and infinite distributed delays. What are noteworthy are that the criteria can be simply calculated by using the parameters of the RDGRNs, and the obtained results are available for other partial differential systems with or without distributed delays. Finally, two RDGRNs with or without distributed delays and their numerical simulations have been presented to confirm the efficacy of the theoretical results. Since the time-varying delays, noise and disturbance are inevitable on the basis of the complex environment of biological reaction process, future studies may focus on the stability problem of RDGRNs with time-varying delays and stochastic disturbances.

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YINPING XIE received the B.S. degree in bioengineering from Northwest Agriculture and Forestry University, Shaanxi, China, in 2011, and the M.S. degree in cell biology from the Wuhan University, Wuhan, China, in 2013, where she is currently pursuing the Ph.D. degree. Her research interests include genetic networks and bioinformatics.

LING XIAO received the B.S., M.S., and Ph.D. degrees from Wuhan University, Wuhan, China, in 1999, 2002, and 2013, respectively, all in clinical medicine. She is currently a Doctor with the Department of Psychiatry, Renmin Hospital of Wuhan University, Wuhan. Her research interests include genetic networks and bioinformatics.

LEIMIN WANG (Member, IEEE) received the Ph.D. degree in control science and engineering from the Huazhong University of Science and Technology, Wuhan, China, in 2016. He is currently an Associate Professor with the School of Automation, China University of Geosciences, Wuhan. His current research interests include dynamics of memristive systems, neural networks, and genetic regulatory networks.

GAOHUA WANG received the B.S., M.S., and Ph.D. degrees from Wuhan University, Wuhan, China, in 1985, 1991, and 2003, respectively, all in clinical medicine. He is currently a Professor with the Institute of Neuropsychiatry, Wuhan. His research interest includes diagnosis and treatment of depression.