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Robust stability of interactional genetic regulatory networks with reaction-diffusion terms

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Abstract

We have analyzed the stability of interactional genetic regulatory networks with reaction-diffusion terms under Dirichlet boundary conditions in this article. Corresponding to interaction between unstable genetic regulatory networks and stable genetic regulatory networks, the model is given, and a stability criterion is proposed through construction of appropriate Lyapunov-Krasovskii functions and linear matrix inequalities (LMI). By means of a numerical simulation, we have proved the effectiveness and correctness of the theorem, and we analyzed the factors that influence the stability for interactional genetic regulatory networks.

Keywords: interactional genetic regulatory networks; Dirichlet boundary; reaction-diffusion; linear matrix inequalities

1 Introduction

Since 2002, the Alon research group has proposed the network module [1–3], network modules with several nodes become a hot research topic. Modeling and dynamic analysis of these genetic regulatory networks (GRNs), which are considered as important submodule of complex biology network, because a GRN can clarify the mechanism of biological network. At present, the models of genetic regulatory network include directed graphs [4–6], the Boolean model [7–11], the Bayesian model [12–16] and the differential equations model [17–27]. In these models, the differential equations model has obvious advantages, for example, the differential equations model is more accurate than the Boolean model in describing GRNs, and it has less computational complexity than the Bayesian model. The differential equations model is an open model, because a great deal about dynamic systems can be directly applied to this model, which has attracted a large number of other field experts to join the relevant research, and reaped rich fruits. A real biological network contains tens of thousands of nodes, while the simulations of these studies are based on a few nodes as the research object, the theoretical basis of its simplification is that the number of molecules involved in the chemical reaction is usually very low at a given moment.

Although there are many outstanding achievements in the study of differential equations as a model of the GRN, there are still some problems that needed further research.

On the one hand, the spatial diffusion phenomenon exists widely in the fields of physics, chemistry, biology, and so on, but most of the current studies on GRNs in terms of the spatial homogeneity of concentrations are for cell components. This proposition can lead to missing a lot of space information, but there are only five articles [19, 20, 23, 26, 27] about the study of GRNs with reaction-diffusion terms, and the five articles have only discussed the influence of reaction-diffusion terms on the time-delay conservatism,but they did not explore the essence of reaction-diffusion terms.

On the other hand, corresponding to the different biological signals, the change of the expression of a protein will affect the expression of gene, which makes the network achieve stability ultimately. Lest life activity is only the result of a local GRN, it also has extensive connections with the surrounding GRN, and the dynamical properties of these GRNs also directly affect the survival of the living body. For example, a virus cannot survive independently, and its replication and transmission must be completed by the synthesis system, the replication system and the protein transport system of the host cell. A large number of studies showed that, after the host is infected by the virus, when the virus is active, enzymes and mRNA concentrations for viral replication will be unstable; when the virus is repressed or dormant, the virus replication related enzymes and mRNA concentrations will tend to stability [28–31]. In recent years, it was found that there is a wide and complex relation between the virus and the host at the molecular level based on the proteins atlas of interaction between viral and host [32–35].

In this article we have proposed a model of interactional genetic regulatory networks (GRNs), and we analyzed the stability of interactional GRNs, the theoretical support for the above method is given from the aspect of dynamics. By numerical simulation, three significant conclusions are obtained.

2 Problem formulation

Two different nonlinear delayed GRNs are described by equations (1) and (2), respectively:

$$\begin{cases} \frac{\mathrm{d}u_{1i}(t)}{\mathrm{d}t} = -a_{1i}u_{1i}(t) + \sum_{j=1}^{n} \omega_{ij} f_j(v_{1j}(t-\sigma(t))), \\ \frac{\mathrm{d}v_{1i}(t)}{\mathrm{d}t} = -c_{1i}v_{1i}(t) + b_{1i}u_{1i}(t-\tau(t)), \quad i = 1, 2, \ldots, n_1, \end{cases} \tag{1}$$

$$\begin{cases} \frac{\mathrm{d}u_{2p}(t)}{\mathrm{d}t} = -a_{2p}u_{2p}(t) + \sum_{q=1}^{n} \varpi_{pq} g_q(v_{2q}(t-\sigma'(t))), \\ \frac{\mathrm{d}v_{2p}(t)}{\mathrm{d}t} = -c_{2p}v_{2p}(t) + b_{2p}u_{2p}(t-\tau'(t)), \quad p = 1, 2, \ldots, n_2, \end{cases} \tag{2}$$

where GRN (1) is stable, and GRN (2) is unstable, $u_{1i}(t), v_{1i}(t) \in R^{n_1}$ and $u_{2p}(t), v_{2p}(t) \in R^{n_2}$ are the concentrations of mRNA and protein of the ith and the pth nodes at the time t respectively; the parameters a_{1i} and a_{2p} are the degradation rates of the mRNA, c_{1i} and c_{2p} are the degradation rates of the protein, b_{1i} and b_{2p} are the translation rate; $f_i(x)$ and $g_p(y)$ are the Hill form regulatory functions, which represent the feedback regulation of the protein on the transcription, their forms are described by equation (3)

$$\begin{cases} f_j(x) = \frac{(\frac{x}{m_j})^{H_j}}{1+(\frac{x}{m_j})^{H_j}}, \\ g_q(y) = \frac{(\frac{y}{n_q})^{H_q}}{1+(\frac{y}{n_q})^{H_q}}, \end{cases} \tag{3}$$

where H_j and H_q are the Hill coefficients, m_j and n_q are positive constants, $\tau(t)$, $\tau'(t)$, $\sigma(t)$ and $\sigma'(t)$ are time-varying delays satisfying

$$\begin{cases} 0 \le \tau_1 \le \tau(\mathrm{t}) \le \tau_2, \quad 0 \le \sigma_1 \le \sigma(\mathrm{t}) \le \sigma_2, \\ \lambda_1 \le \dot{\tau} \le \lambda_2, \qquad \lambda_3 \le \dot{\sigma} \le \lambda_4, \\ 0 \le \tau_1' \le \tau'(\mathrm{t}) \le \tau_2', \qquad 0 \le \sigma_1' \le \sigma'(t) \le \sigma_2', \\ \eta_1 \le \dot{\tau}' \le \eta_2, \qquad \eta_3 \le \dot{\sigma}' \le \eta_4, \end{cases} \tag{4}$$

where $W_1 = (\omega_{ij}) \in R^{n_1 \times n_1}$ and $W_2 = (\varpi_{pq}) \in R^{n_2 \times n_2}$ are described as equations (5) and (6), α_{ij} and β_{pq} are the dimensionless transcriptional rates of transcriptional factor j to gene i and transcriptional factor q to gene p respectively.

$$\omega_{ij} = \begin{cases} \alpha_{ij} & \text{if transcription factor } j \text{ is an activator of gene } i, \\ 0 & \text{if there is no link from node } j \text{ to } i, \\ -\alpha_{ij} & \text{if transcription factor } j \text{ is a repressor of gene } i, \end{cases} \tag{5}$$

$$\varpi_{pq} = \begin{cases} \beta_{pq} & \text{if transcription factor } q \text{ is an activator of gene } p, \\ 0 & \text{if there is no link from node } q \text{ to } p, \\ -\beta_{pq} & \text{if transcription factor } q \text{ is a repressor of gene } p. \end{cases} \tag{6}$$

Considering the diffusion term, equations (1) and (2) can be rewrite as

$$\begin{cases} \frac{\partial u_{1i}(t,l)}{\partial t} = \sum_{k=1}^{L} \frac{\partial}{\partial l_k}(D_{ik} \frac{\partial u_{1i}(t,l)}{\partial l_k}) - a_{1i}u_{1i}(t,l) + \sum_{j=1}^{n} \omega_{ij} f_j(v_{1j}(t-\sigma(t),l)), \\ \frac{\partial v_{1i}(t,l)}{\partial t} = \sum_{k=1}^{L} \frac{\partial}{\partial l_k}(D_{ik}^* \frac{\partial v_{1i}(t,l)}{\partial l_k}) - c_{1i}p_{1i}(t) + b_{1i}u_{1i}(t-\tau(t)), \quad i = 1,2,\ldots,n_1 \end{cases} \tag{7}$$

$$\begin{cases} \frac{\partial u_{2p}(t,l)}{\partial t} = \sum_{k=1}^{L} \frac{\partial}{\partial l_k}(d_{pk} \frac{\partial u_{2p}(t,l)}{\partial l_k}) - a_{2p}u_{2p}(t,l) + \sum_{q=1}^{n} \varpi_{pq} g_q(v_{1q}(t-\sigma'(t),l)), \\ \frac{\partial v_{2p}(t,l)}{\partial t} = \sum_{k=1}^{L} \frac{\partial}{\partial l_k}(d_{pk}^* \frac{\partial v_{2p}(t,l)}{\partial l_k}) - c_{2p}v_{2p}(t,l) + b_{2p}u_{2p}(t-\tau'(t),l), \\ \quad p = 1,2,\ldots,n_2 \end{cases} \tag{8}$$

where $l = (l_1, l_2, \ldots, l_L)^{\mathrm{T}} \in \Sigma \subset R^c$, $\Sigma = \{l||l_k| \le L_k\}$, L_k is constant, $k = 1,2,\ldots L$, $D_{ik} = D_{ik}(t,l) > 0$, $D_{ik}^* = D_{ik}^*(t,l) > 0$, denote the transmission diffusion operator along the ith gene of mRNA and protein, respectively, $d_{pk} = d_{pk}(t,l) > 0$, $d_{pk}^* = d_{pk}^*(t,l) > 0$, denote the transmission diffusion operator along the pth gene of mRNA and protein, respectively.

The initial conditions are given by

$$\begin{cases} u_{1i}(s,l) = \psi_{1i}(s,l), \quad s \in (-\infty,0], i = 1,2,\ldots,n_1 \\ v_{1i}(s,l) = \psi_{1i}^*(s,l), \quad s \in (-\infty,0], i = 1,2,\ldots,n_1 \end{cases} \tag{9}$$

$$\begin{cases} u_{2p}(s,l) = \psi_{2p}(s,l), \quad s \in (-\infty,0], p = 1,2,\ldots,n_2 \\ v_{2p}(s,l) = \psi_{2p}^*(s,l), \quad s \in (-\infty,0], p = 1,2,\ldots,n_2 \end{cases} \tag{10}$$

Here $\psi_{1i}(s,l)$, $\psi_{1i}^*(s,l)$, $\psi_{2p}(s,l)$ and $\psi_{2p}^*(s,l)$ are bounded and continuous on $(-\infty,0] \times \Sigma$.

Dirichlet boundary condition is considered:

$$\begin{cases} u_{1i}(t,l)=0, & l\in\partial\Sigma, t\in[-\kappa,+\infty), \\ v_{1i}(t,l)=0, & l\in\partial\Sigma, t\in[-\kappa,+\infty), \end{cases} \tag{11}$$

$$\begin{cases} u_{2p}(t,l)=0, & l\in\partial\Sigma, t\in[-\kappa,+\infty), \\ v_{2p}(t,l)=0, & l\in\partial\Sigma, t\in[-\kappa,+\infty). \end{cases} \tag{12}$$

The system (7) and system (8) can be rewritten in vector-matrix form:

$$\begin{cases} \frac{\partial u_1(t,l)}{\partial t}=\sum_{k=1}^{l}\frac{\partial}{\partial l_k}(D_k\frac{\partial u_1(t,l)}{\partial x_k})-A_1u_1(t,l)+W_1F(v_1(t-\sigma(t),l)), \\ \frac{\partial v_1(t,l)}{\partial t}=\sum_{k=1}^{l}\frac{\partial}{\partial l_k}(D_k^*\frac{\partial v_1(t,l)}{\partial l_k})-C_1v_1(t,l)+B_1u_1(t-\tau(t),l), \quad i=1,2,\ldots,n_1 \end{cases} \tag{13}$$

$$\begin{cases} \frac{\partial u_2(t,l)}{\partial t}=\sum_{k=1}^{l}\frac{\partial}{\partial l_k}(d_k\frac{\partial u_2(t,l)}{\partial x_k})-A_2u_2(t,l)+W_2G(v_2(t-\sigma'(t),l)), \\ \frac{\partial v_2(t,l)}{\partial t}=\sum_{k=1}^{l}\frac{\partial}{\partial l_k}(d_k^*\frac{\partial v_2(t,l)}{\partial l_k})-C_2v_2(t)+B_2u_2(t-\tau'(t),l), \quad p=1,2,\ldots,n_2 \end{cases} \tag{14}$$

$$\begin{aligned}
&A_1=\operatorname{diag}(a_{11},a_{12},\ldots,a_{1n_1}),\\
&B_1=\operatorname{diag}(b_{11},b_{12},\ldots,b_{1n_1}),\\
&C_1=\operatorname{diag}(c_{11},c_{12},\ldots,c_{1n_1}),\\
&A_2=\operatorname{diag}(a_{21},a_{22},\ldots,a_{2n_2}),\\
&B_2=\operatorname{diag}(b_{21},b_{22},\ldots,b_{2n_2}),\\
&C_2=\operatorname{diag}(c_{21},c_{22},\ldots,c_{2n_2}),\\
&D_k=\operatorname{diag}(D_{1k},D_{2k},\ldots,D_{n_1k}),\\
&D_k^*=\operatorname{diag}\bigl(D_{1k}^*,D_{2k}^*,\ldots,D_{n_1k}^*\bigr),\\
&d_k=\operatorname{diag}(d_{1k},d_{2k},\ldots,d_{n_2k}),\\
&d_k^*=\operatorname{diag}\bigl(d_{1k}^*,d_{2k}^*,\ldots,d_{n_2k}^*\bigr),\\
&u_1(t,l)=\bigl(u_{11}(t,l),u_{12}(t,l),\ldots,u_{1n_1}(t,l)\bigr)^{\mathrm{T}},\\
&v_1(t,l)=\bigl(v_{11}(t,l),v_{12}(t,l),\ldots,v_{1n_1}(t,l)\bigr)^{\mathrm{T}},\\
&u_2(t,l)=\bigl(u_{21}(t,l),u_{22}(t,l),\ldots,u_{2n_2}(t,l)\bigr)^{\mathrm{T}},\\
&v_2(t,l)=\bigl(v_{21}(t,l),v_{22}(t,l),\ldots,v_{2n_2}(t,l)\bigr)^{\mathrm{T}},\\
&F(v_{1j}\bigl(t-\sigma(t),l\bigr)=\bigl(f_1(v_{11}\bigl(t-\sigma(t),l\bigr),f_2(v_{12}\bigl(t-\sigma(t),l\bigr),\ldots,f_n\bigl(v_{1n_1}\bigl(t-\sigma(t),l\bigr)\bigr)^{\mathrm{T}},\\
&G(v_{2q}\bigl(t-\sigma'(t),l\bigr)=\bigl(g_1(v_{21}\bigl(t-\sigma'(t),l\bigr),g_2(v_{22}\bigl(t-\sigma'(t),l\bigr),\ldots,g_n\bigl(v_{2n_2}\bigl(t-\sigma'(t),l\bigr)\bigr)^{\mathrm{T}}.
\end{aligned}$$

$f_i(\cdot)$ and $g_p(\cdot)$ satisfy inequality (15) and inequality (16), respectively, because $f_i(\cdot)$ and $g_p(\cdot)$ are monotonically increase functions with saturation

$$0\le\frac{f_i(x_i)}{x_i}\le\varsigma_i, \quad \forall x_i\neq 0, i=1,2,\ldots,n_1 \tag{15}$$

$$0\le\frac{g_p(y_p)}{y_p}\le\chi_p, \quad \forall y_p\neq 0, p=1,2,\ldots,n_2 \tag{16}$$

i.e.

$$f^{\mathrm{T}}(x)\big(f(x) - K_1 x\big) \leq 0, \tag{17}$$

$$g^{\mathrm{T}}(y)\big(g(y) - K_2 y\big) \leq 0, \tag{18}$$

where $K_1 = \operatorname{diag}(\varsigma_1, \varsigma_2, \ldots, \varsigma_{n_1}) > 0$, $K_2 = \operatorname{diag}(\chi_1, \chi_2, \ldots,, \chi_{n_2})^{\mathrm{T}} > 0$, $x = [x_1, x_2, \ldots, x_{n_1}]^{\mathrm{T}}$ and $y = [y_1, y_2, \ldots, y_{n_2}]^{\mathrm{T}}$.

Lemma 1 *Let $f(v)$ be a real-valued function defined on $[a,b] \subset R$, with $f(a) = f(b) = 0$. If $f(v) \in C^1[a,b]$, then*

$$\int_a^b f^2(v)\,\mathrm{d}v \leq \frac{(b-a)^2}{\pi^2} \int_a^b \big[f'(v)\big]^2\,\mathrm{d}v. \tag{19}$$

Lemma 2 *If Σ is a bounded C^1 open set in R^n and $\eta, \varphi \in C^2(\overline{\Sigma})$, then*

$$\int_\Sigma \eta \Delta\varphi\,\mathrm{d}x = \int_\Sigma \eta\Delta\varphi\,\mathrm{d}x + \int_{\partial\Sigma} \left(\eta \frac{\partial\varphi}{\partial\overline{n}} - \varphi\frac{\partial\eta}{\partial\overline{n}}\right)\mathrm{d}S, \tag{20}$$

where $\frac{\partial\eta}{\partial\overline{n}}$ and $\frac{\partial\varphi}{\partial\overline{n}}$ are the directional derivatives of η and φ in the direction of the outward pointing normal $\overline{n}$ to the surface element $\mathrm{d}S$, *respectively. $\sum_{k=1}^{l} \frac{\partial}{\partial x_k}(D_k \frac{\partial}{\partial x_k})$ can be regarded as a Laplacian operator which is formally self-adjoint and a differential*; *in Lemma* 2 *we have an inner product for a function with Dirichlet boundary.*

Lemma 3 ([20]) *From the Green formula, under Dirichlet boundary conditions, and by using Lemma* 1 *and Lemma* 2, *we can obtain*

$$2\int_\Sigma \mu^{\mathrm{T}} \sum_{k=1}^{l} \frac{\partial}{\partial x_k}\left(\frac{\partial\mu}{\partial x_k}\right)\mathrm{d}x \leq -\frac{\pi^2}{2}\int_\Sigma \mu^{\mathrm{T}}\mu\,\mathrm{d}x. \tag{21}$$

Lemma 4 *Let $M > 0 \in R^{n\times n}$, a positive scalar $\vartheta > 0$, vector function $x : [0,\vartheta] \to R^n$ such that the integrations concerned are well defined, and they exist*:

$$\left(\int_0^\vartheta x(s)\,\mathrm{d}s\right)^{\mathrm{T}} M\left(\int_0^\vartheta x(s)\,\mathrm{d}s\right) \leq \vartheta\left(\int_0^\vartheta x(s)Mx(s)\,\mathrm{d}s\right). \tag{22}$$

Lemma 5 *For vectors $X, Y \in R^n$ are any positive definite matrix, and any scalar ε, there exists the following inequality*:

$$2X^TY \leq \varepsilon X^TX + \varepsilon^{-1}Y^TY. \tag{23}$$

Lemma 6 *For any vectors $X, Y \in R^n$, and any scalar $\varepsilon > 0$ are positive, there exists the following inequality*:

$$2X^THY \leq \varepsilon X^THX + \varepsilon^{-1}Y^THY. \tag{24}$$

3 Model of interactional GRNs

According to GRN (13) and (14), W_1 or W_2 express the interaction of genes in single GRN, we assumed that interaction of the different GRNs is like a single GRN. We have constructed a bidirectional coupling model for the type of interactional GRNs as equations (25) and (26), and we investigate a stability criterion under Dirichlet boundary condition.

$$\begin{cases} \frac{\mathrm{d}u_1(t,l)}{\mathrm{d}t} = \sum_{k=1}^{l} \frac{\partial}{\partial l_k}(D_k \frac{\partial u_1(t,l)}{\partial x_k}) - A_1 u_1(t,l) + W_1 F(v_1(t-\sigma(t),l)) \\ \qquad + W_1^* G(v_2(t-\sigma'(t),l)), \\ \frac{\mathrm{d}v_1(t,l)}{\mathrm{d}t} = \sum_{k=1}^{l} \frac{\partial}{\partial l_k}(D_k^* \frac{\partial v_1(t,l)}{\partial l_k}) - C_1 v_1(t,l) + B_1 u_1(t-\tau(t),l), \quad i = 1,2,\ldots,n_1 \end{cases} \tag{25}$$

$$\begin{cases} \frac{\mathrm{d}u_2(t,l)}{\mathrm{d}t} = \sum_{k=1}^{l} \frac{\partial}{\partial l_k}(d_k \frac{\partial u_2(t,l)}{\partial x_k}) - A_2 u_2(t,l) \\ \qquad + W_2 G(v_2(t-\sigma'(t),l)) + W_2^* F(v_1(t-\sigma(t),l)), \\ \frac{\mathrm{d}v_2(t,l)}{\mathrm{d}t} = \sum_{k=1}^{l} \frac{\partial}{\partial l_k}(d_k^* \frac{\partial v_2(t,l)}{\partial l_k}) - C_2 v_2(t,l) + b_{2p} u_2(t-\tau'(t),l), \quad p = 1,2,\ldots,n_2 \end{cases} \tag{26}$$

where $W_1^* = (\omega_{iq}) \in R^{n_1 \times n_2}$, $W_2^* = (\varpi_{pj}^*) \in R^{n_2 \times n_1}$ are described by equations (27) and (28), α_{iq}^* and β_{pj}^* are the dimensionless transcriptional rates of transcriptional factor q of GRN (26) to gene i of GRN (25) and transcriptional factor j of GRN (25) to gene p of GRN (26), respectively.

$$\omega_{iq} = \begin{cases} \alpha_{iq}^* & \text{if transcription factor } q \text{ is an activator of gene } i, \\ 0 & \text{if there is no link from node } q \text{ to } i, \\ -\alpha_{iq}^* & \text{if transcription factor } q \text{ is a repressor of gene } i, \end{cases} \tag{27}$$

$$\varpi_{pj}^* = \begin{cases} \beta_{pj}^* & \text{if transcription factor } j \text{ is an activator of gene } p, \\ 0 & \text{if there is no link from node } q \text{ to } p, \\ -\beta_{pj}^* & \text{if transcription factor } j \text{ is a repressor of gene } p. \end{cases} \tag{28}$$

Theorem *For given scalars* τ_2, σ_2, τ_2', σ_2', λ_1, λ_2, η_1 *and* η_2 *satisfying equation* (4), *GRN* (25) *and GRN* (26) *under a Dirichlet boundary condition are robust stable if there exist matrices* $P_i^{\mathrm{T}} = P_i > 0$ *and* $\Lambda_i^{\mathrm{T}} = \Lambda_i > 0$ $(i = 1,\ldots,4)$; $R_i^{\mathrm{T}} = R_i > 0$ $(i = 1,\ldots 12)$; $Q_i^{\mathrm{T}} = Q_i > 0$ $(i = 1,\ldots,6)$, *such that the following linear matrices inequalities* (*LMIs*) *hold*:

$$\Pi_1 = -P_1 A_1 - \frac{\pi^2}{2} P_1 D_L + R_1 + \sigma_2^2 Q_1,$$

$$\Pi_2 = -R_1 + R_2,$$

$$\Pi_3 = (\lambda_2 - 1)R_2 + (1 - \lambda_1)R_3 + B_1^{\mathrm{T}} P_2 B_1,$$

$$\Pi_4 = -2\Lambda_2 + K\Lambda_2 K + (\lambda_4 - 1)Q_3,$$

$$\Pi_5 = -2P_3 A_2 - \frac{\pi^2}{2} P_3 d_L + \varepsilon P_3 W_2 + R_7 + \sigma_2'^2 Q_4,$$

$$\Pi_6 = -R_7 + R_8,$$

$$\Pi_7 = (\eta_2 - 1)R_8 + (1 - \eta_1)R_9 + B_2^{\mathrm{T}} P_4 B_2,$$

$$\Pi_8 = (\eta_4 - 1)Q_6 - 2\Lambda_4 + K\Lambda_4 K + \frac{P_3 W_2}{\varepsilon},$$

$$\Omega_1 = -P_2 C_1 - \frac{\pi^2}{2} P_2 D_L^* + P_2 + R_4 + \tau_2^2 Q_2,$$

$$\Omega_2 = -R_4 + R_5,$$

$$\Omega_3 = (\lambda_4 - 1)R_5 + (1 - \lambda_3)R_6 + K_1 \Lambda_2 K_1, \ \Omega_4 = Q_3 - 2\Lambda_1,$$

$$\Omega_5 = -2P_4 C_2 - \frac{\pi^2}{2} P_4 d_L^* + P_4 + R_{10} + \tau_2'^2 Q_5,$$

$$\Omega_6 = -R_{10} + R_{11},$$

$$\Omega_7 = (\eta_4 - 1)R_{11} + (1 - \eta_3)R_{12} + K_2 \Lambda_4 K_2,$$

$$\Omega_8 = Q_6 - 2\Lambda_3,$$

$$\Xi_1 = \begin{bmatrix} \Pi_1 & 0 & 0 & 0 & 0 & P_1 W_1 & 0 & 0 & 0 & 0 & 0 & P_1 W_1^* \\ * & \Pi_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & -R_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & \Pi_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & -Q_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & \Pi_4 & W_2^* P_3 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & * & \Pi_5 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & * & * & \Pi_6 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & * & * & * & -R_9 & 0 & 0 & 0 \\ * & * & * & * & * & * & * & * & * & \Pi_7 & 0 & 0 \\ * & * & * & * & * & * & * & * & * & * & -Q_4 & 0 \\ * & * & * & * & * & * & * & * & * & * & * & \Pi_8 \end{bmatrix}$$
$$< 0, \tag{29}$$

$$\Xi_2 = \begin{bmatrix} \Omega_1 & 0 & 0 & 0 & 0 & K_1 \Lambda_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & \Omega_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & -R_6 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & \Omega_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & -Q_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & \Omega_4 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & * & \Omega_5 & 0 & 0 & 0 & 0 & K_2 \Lambda_3 \\ * & * & * & * & * & * & * & \Omega_6 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & * & * & * & -R_{12} & 0 & 0 & 0 \\ * & * & * & * & * & * & * & * & * & \Omega_7 & 0 & 0 \\ * & * & * & * & * & * & * & * & * & * & -Q_5 & 0 \\ * & * & * & * & * & * & * & * & * & * & * & \Omega_8 \end{bmatrix}$$
$$< 0. \tag{30}$$

Proof Define a Lyapunov-Krasovskii functional candidate for GRN (13) as

$$V(t,l) = \sum_{i=1}^{8} V_i(t,l) \tag{31}$$

where

$$V_1(t,l) = \int_\Sigma u_1^T(t,l)P_1u_1(t,l)\,\mathrm{d}l + \int_\Sigma v_1^T(t,l)P_2v_1(t,l)\,\mathrm{d}l, \tag{32}$$

$$\begin{aligned} V_2(t,l) = {} & \int_\Sigma \int_{t-\tau_1}^{t} u_1^T(s,l)R_1u_1(s,l)\,\mathrm{d}s\,\mathrm{d}l + \int_\Sigma \int_{t-\tau(t)}^{t-\tau_1} u_1^T(s,l)R_2u_1(s,l)\,\mathrm{d}s\,\mathrm{d}l \\ & + \int_\Sigma \int_{t-\tau_2}^{t-\tau(t)} u_1^T(s,l)R_3u_1(s,l)\,\mathrm{d}s\,\mathrm{d}l \\ & + \int_\Sigma \int_{t-\sigma_1}^{t} v_1^T(s,l)R_4v_1(s,l)\,\mathrm{d}s\,\mathrm{d}l + \int_\Sigma \int_{t-\sigma(t)}^{t-\sigma_1} v_1^T(s,l)R_5v_1(s,l)\,\mathrm{d}s\,\mathrm{d}l \\ & + \int_\Sigma \int_{t-\sigma_2}^{t-\sigma(t)} v_1^T(s,l)R_6v_1(s,l)\,\mathrm{d}s\,\mathrm{d}l, \end{aligned} \tag{33}$$

$$\begin{aligned} V_3(t,l) = {} & \tau \int_\Sigma \int_{-\tau(t)}^{0} \int_{t+s}^{t} u_1^T(s,l)Q_1u_1(s,l)\,\mathrm{d}\theta\,\mathrm{d}s\,\mathrm{d}l \\ & + \sigma \int_\Sigma \int_{-\sigma(t)}^{0} \int_{t+s}^{t} v_1^T(s,l)Q_2v_1(s,l)\,\mathrm{d}\theta\,\mathrm{d}s\,\mathrm{d}l, \end{aligned} \tag{34}$$

$$V_4(t,m,p) = \int_\Sigma \int_{t-\sigma(t)}^{t} F^T\big(v_1(s,l)\big)Q_3F\big(v_1(s,l)\big)\,\mathrm{d}s\,\mathrm{d}l, \tag{35}$$

$$V_5(t,l) = \int_\Sigma u_2^T(t,l)P_3u_1(t,l)\,\mathrm{d}l + \int_\Sigma v_2^T(t,l)P_4v_2(t,l)\,\mathrm{d}l, \tag{36}$$

$$\begin{aligned} V_6(t,l) = {} & \int_\Sigma \int_{t-\tau_1'}^{t} u_2^T(s,l)R_7u_2(s,l)\,\mathrm{d}s\,\mathrm{d}l + \int_\Sigma \int_{t-\tau'(t)}^{t-\tau_1'} u_2^T(s,l)R_8u_2(s,l)\,\mathrm{d}s\,\mathrm{d}l \\ & + \int_\Sigma \int_{t-\tau_2'}^{t-\tau'(t)} u_2^T(s,l)R_9u_2(s,l)\,\mathrm{d}s\,\mathrm{d}l \\ & + \int_\Sigma \int_{t-\sigma_1'}^{t} v_2^T(s,l)R_{10}v_2(s,l)\,\mathrm{d}s\,\mathrm{d}l + \int_\Sigma \int_{t-\sigma'(t)}^{t-\sigma_1'} v_2^T(s,l)R_{11}v_2(s,l)\,\mathrm{d}s\,\mathrm{d}l \\ & + \int_\Sigma \int_{t-\sigma_2'}^{t-\sigma'} v_2^T(s,l)R_{12}v_2(s,l)\,\mathrm{d}s\,\mathrm{d}l \end{aligned} \tag{37}$$

$$\begin{aligned} V_7(t,l) = {} & \tau' \int_\Sigma \int_{-\tau'(t)}^{0} \int_{t+s}^{t} u_2^T(s,l)Q_4u_2(s,l)\,\mathrm{d}\theta\,\mathrm{d}s\,\mathrm{d}l \\ & + \sigma' \int_\Sigma \int_{-\sigma'(t)}^{0} \int_{t+s}^{t} v_2^T(s,l)Q_5v_2(s,l)\,\mathrm{d}\theta\,\mathrm{d}s\,\mathrm{d}l, \end{aligned} \tag{38}$$

$$V_8(t,l) = \int_\Sigma \int_{t-\sigma'(t)}^{t} G^{\mathrm{T}}\big(v_2(s,l)\big)Q_6G\big(v_2(s,l)\big)\,\mathrm{d}s\,\mathrm{d}l, \tag{39}$$

then, computing the derivatives of $V_i(t,m,p)$ ($i = 1,2,3$), we can get

$$\begin{aligned} \frac{\partial V_1(t,l)}{\partial t} & = 2\int_\Sigma u_1^{\mathrm{T}}(t,l)P_1\frac{\partial u_1(t,l)}{\partial t}\,\mathrm{d}l + 2\int_\Sigma v_1^{\mathrm{T}}(t,l)P_2\frac{\partial v_1(t,l)}{\partial t}\,\mathrm{d}l \\ & = 2\int_\Sigma u_1^{\mathrm{T}}(t,l)P_1\Bigg[\sum_{k=1}^{l}\frac{\partial}{\partial l_k}\bigg(D_k\frac{\partial u_1(t,l)}{\partial l_k}\bigg) - A_1u_1(t,l)W_1F\big(v_1\big(t-\sigma(t),l\big)\big) \end{aligned}$$

$$
\begin{aligned}
&+ W_1^{*} G\bigl(v_2\bigl(t-\sigma'(t),l\bigr)\bigr)\Biggr] \\
&+ 2\int_{\Sigma} v_1^{\mathrm{T}}(t,l) P_2 \Biggl[\sum_{k=1}^{l} \frac{\partial}{\partial l_k}\biggl(D_k^{*}\frac{\partial u_1(t,l)}{\partial l_k}\biggr) \\
&- C_1 v_1(t,l) + B_1 u_1\bigl(t-\tau(t),l\bigr)\Biggr],
\end{aligned}
\tag{40}
$$

$$
\begin{aligned}
\frac{\partial V_2(t,l)}{\partial t} ={}& \int_{\Sigma} u_1^{\mathrm{T}}(t,l) R_1 u_1(t,l)\,\mathrm{d}l - \int_{\Sigma} \bigl(u_1^{\mathrm{T}}(t-\tau_1,l) R_1 u_1(t-\tau_1,l)\,\mathrm{d}l\bigr) \\
&+ \int_{\Sigma} u_1^{\mathrm{T}}(t-\tau_1,l) R_2 u_1(t-\tau_1,l)\,\mathrm{d}l \\
&- \bigl(1-\dot{\tau}(t)\bigr)\int_{\Sigma} u_1^{\mathrm{T}}\bigl(t-\tau(t),l\bigr) R_2 u_1\bigl(t-\tau(t),l\bigr)\,\mathrm{d}l \\
&+ \bigl(1-\dot{\tau}(t)\bigr)\int_{\Sigma} u_1^{\mathrm{T}}\bigl(t-\tau(t),l\bigr) R_3 u_1\bigl(t-\tau(t),l\bigr)\,\mathrm{d}l \\
&- \int_{\Sigma} u_1^{\mathrm{T}}(t-\tau_2,l) R_3 u_1(t-\tau_2,l)\,\mathrm{d}l \\
&+ \int_{\Sigma} v_1^{\mathrm{T}}(t,l) R_4 v_1(t,l)\,\mathrm{d}l - \int_{\Sigma} v_1^{\mathrm{T}}(t-\sigma_1,l) R_4 v_1(t-\sigma_1,l)\,\mathrm{d}l \\
&+ \int_{\Sigma} v_1^{\mathrm{T}}(t-\sigma_1,l) R_5 v_1(t-\sigma_1,l)\,\mathrm{d}l \\
&- \bigl(1-\dot{\sigma}(t)\bigr)\int_{\Sigma} v_1^{\mathrm{T}}\bigl(t-\sigma(t),l\bigr) R_5 v_1\bigl(t-\sigma(t),l\bigr)\,\mathrm{d}l \\
&+ \bigl(1-\dot{\sigma}(t)\bigr)\int_{\Sigma} v_1^{\mathrm{T}}\bigl(t-\sigma(t),l\bigr) R_6 v_1\bigl(t-\sigma(t),l\bigr)\,\mathrm{d}l \\
&- \int_{\Sigma} v_1^{\mathrm{T}}(t-\sigma_2,l) R_6 v_1(t-\sigma_2,l)\,\mathrm{d}l \\
\leq{}& \int_{\Sigma} u_1^{\mathrm{T}}(t,l) R_1 u_1(t,l)\,\mathrm{d}l - \int_{\Sigma} u_1^{\mathrm{T}}(t-\tau_1,l) R_1 u_1(t-\tau_1,l)\,\mathrm{d}l \\
&+ \int_{\Sigma} u_1^{\mathrm{T}}(t-\tau_1,l) R_2 u_1(t-\tau_1,l)\,\mathrm{d}l \\
&- (1-\lambda_2)\int_{\Sigma} u_1^{\mathrm{T}}\bigl(t-\tau(t),l\bigr) R_2 u_1\bigl(t-\tau(t),l\bigr)\,\mathrm{d}l \\
&+ (1-\lambda_1)\int_{\Sigma} u_1^{\mathrm{T}}\bigl(t-\tau(t),l\bigr) R_3 u_1\bigl(t-\tau(t),l\bigr)\,\mathrm{d}l \\
&- \int_{\Sigma} u_1^{\mathrm{T}}(t-\tau_2,l) R_3 u_1(t-\tau_2,l)\,\mathrm{d}l \\
&+ \int_{\Sigma} v_1^{\mathrm{T}}(t,l) R_4 v_1(t,l)\,\mathrm{d}l - \int_{\Sigma} v_1^{\mathrm{T}}(t-\sigma_1,l) R_4 v_1(t-\sigma_1,l)\,\mathrm{d}l \\
&+ \int_{\Sigma} v_1^{\mathrm{T}}(t-\sigma_1,l) R_5 v_1(t-\sigma_1,l)\,\mathrm{d}l \\
&- (1-\lambda_4)\int_{\Sigma} v_1^{\mathrm{T}}\bigl(t-\sigma(t),l\bigr) R_5 v_1\bigl(t-\sigma(t),l\bigr)\,\mathrm{d}l \\
&+ (1-\lambda_3)\int_{\Sigma} v_1^{\mathrm{T}}\bigl(t-\sigma(t),l\bigr) R_6 v_1\bigl(t-\sigma(t),l\bigr)\,\mathrm{d}l
\end{aligned}
$$

$$
\begin{aligned}
&- \int_{\Sigma} v_1^{\mathrm{T}}(t-\sigma_2,l) R_6 v_1(t-\sigma_2,l)\,\mathrm{d}l, \qquad (41) \\
\frac{\partial V_3(t,l)}{\partial t} &= \tau^2(t) \int_{\Sigma} u_1^{\mathrm{T}}(t,l) Q_1 u_1(t,l)\,\mathrm{d}l - \tau(t) \int_{\Sigma} \int_{t-\tau(t)}^{t} u_1^{\mathrm{T}}(s,l) Q_1 u_1(s,l)\,\mathrm{d}s\,\mathrm{d}l \\
&\quad + \sigma^2(t) \int_{\Sigma} v_1^{\mathrm{T}}(t,l) Q_2 v_1(t,l)\,\mathrm{d}l - \sigma(t) \int_{\Sigma} \int_{t-\sigma(t)}^{t} v_1^{\mathrm{T}}(s,l) Q_2 v_1(s,l)\,\mathrm{d}s\,\mathrm{d}l \\
&\le \tau_2^2 \int_{\Sigma} u_1^{\mathrm{T}}(t,l) Q_1 u_1(t,l)\,\mathrm{d}l - \int_{\Sigma} \left[\int_{t-\tau(t)}^{t} u_1(s,l)\,\mathrm{d}s \right]^{\mathrm{T}} Q_1 \left[\int_{t-\tau(t)}^{t} u_1(s,l)\,\mathrm{d}s \right] \mathrm{d}l \\
&\quad + \sigma_2^2 \int_{\Sigma} v_1^{\mathrm{T}}(t,l) Q_2 v_1(t,l)\,\mathrm{d}l \\
&\quad - \int_{\Sigma} \left[\int_{t-\sigma(t)}^{t} v_1(s,l)\,\mathrm{d}s \right]^{\mathrm{T}} Q_2 \left[\int_{t-\sigma(t)}^{t} v_1(s,l)\,\mathrm{d}s \right] \mathrm{d}l, \qquad (42) \\
\frac{\partial V_4(t,l)}{\partial t} &= \int_{\Sigma} F^{\mathrm{T}}\big(v_1(t,l)\big) Q_3 F\big(v_1(t,l)\big)\,\mathrm{d}l \\
&\quad - \big(1-\dot{\sigma}(t)\big) \int_{\Sigma} F^{\mathrm{T}}\big(v_1\big(t-\sigma(t),l\big)\big) Q_3 F\big(v_1\big(t-\sigma(t),l\big)\big)\,\mathrm{d}l \\
&\le \int_{\Sigma} F^{\mathrm{T}}\big(v_1(t,l)\big) Q_3 F\big(v_1(t,l)\big)\,\mathrm{d}l \\
&\quad + (\lambda_2 - 1) \int_{\Sigma} F^{\mathrm{T}}\big(v_1\big(t-\tau(t),l\big)\big) Q_3 F\big(v_1\big(t-\tau(t),l\big)\big)\,\mathrm{d}l, \qquad (43) \\
\frac{\partial V_5(t,l)}{\partial t} &= 2 \int_{\Sigma} u_2^{\mathrm{T}}(t,l) P_3 \frac{\partial u_2(t,l)}{\partial t}\,\mathrm{d}l + 2 \int_{\Sigma} v_2^{\mathrm{T}}(t,l) P_4 \frac{\partial v_2(t,l)}{\partial t}\,\mathrm{d}l \\
&= 2 \int_{\Sigma} u_2^{\mathrm{T}}(t,l) P_3 \Bigg[\sum_{k=1}^{l} \frac{\partial}{\partial l_k} \left(D_k \frac{\partial u_2(t,l)}{\partial l_k} \right) - A_2 u_2(t,l) \\
&\quad + W_2 G\big(v_2\big(t-\sigma'(t),l\big)\big) + W_2^* F\big(v_1\big(t-\sigma(t),l\big)\big) \Bigg] \\
&\quad + 2 \int_{\Sigma} v_2^{\mathrm{T}}(t,l) P_4 \Bigg[\sum_{k=1}^{l} \frac{\partial}{\partial l_k} \left(D_k^* \frac{\partial u_2(t,l)}{\partial l_k} \right) \\
&\quad - C_2 v_2(t,l) + B_2 u_2\big(t-\tau'(t),l\big) \Bigg], \qquad (44) \\
\frac{\partial V_6(t,l)}{\partial t} &= \int_{\Sigma} u_2^{\mathrm{T}}(t,l) R_7 u_2(t,l)\,\mathrm{d}l - \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau_1',l\big) R_7 u_2\big(t-\tau_1',l\big)\,\mathrm{d}l \\
&\quad + \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau_1',l\big) R_8 u_2\big(t-\tau_1',l\big)\,\mathrm{d}l \\
&\quad - \big(1-\dot{\tau}'(t)\big) \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau'(t),l\big) R_8 u_2\big(t-\tau'(t),l\big)\,\mathrm{d}l \\
&\quad + \big(1-\dot{\tau}'(t)\big) \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau'(t),l\big) R_9 u_2\big(t-\tau'(t),l\big)\,\mathrm{d}l \\
&\quad - \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau_2',l\big) R_9 u_2\big(t-\tau_2',l\big)\,\mathrm{d}l \\
&\quad + \int_{\Sigma} v_2^{\mathrm{T}}(t,l) R_{10} v_2(t,l)\,\mathrm{d}l
\end{aligned}
$$

$$
\begin{aligned}
&- \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau_2',l\big)R_9 u_2\big(t-\tau_2',l\big)\,\mathrm{d}l \\
&+ \int_{\Sigma} v_2^{\mathrm{T}}(t,l)R_{10} v_2(t,l)\,\mathrm{d}l \\
&- \int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma_1',l\big)R_{10} v_2\big(t-\sigma_1',l\big)\,\mathrm{d}l + \int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma_1',l\big)R_{11} v_2\big(t-\sigma_1',l\big)\,\mathrm{d}l \\
&- \big(1-\dot{\sigma}'(t)\big)\int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma'(t),l\big)R_{11} v_2\big(t-\sigma'(t),l\big)\,\mathrm{d}l \\
&+ \big(1-\dot{\sigma}'(t)\big)\int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma'(t),l\big)R_{12} v_2\big(t-\sigma'(t),l\big)\,\mathrm{d}l \\
&- \int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma_2',l\big)R_{12} v_2\big(t-\sigma_2',l\big)\,\mathrm{d}l \\
\le{}& \int_{\Sigma} u_2^{\mathrm{T}}(t,l)R_7 u_2(t,l)\,\mathrm{d}l - \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau_1',l\big)R_7 u_2\big(t-\tau_1',l\big)\,\mathrm{d}l \\
&+ \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau_1',l\big)R_8 u_2\big(t-\tau_1',l\big)\,\mathrm{d}l \\
&- (1-\eta_2)\int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau'(t),l\big)R_8 u_2\big(t-\tau'(t),l\big)\,\mathrm{d}l \\
&+ (1-\eta_1)\int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau'(t),l\big)R_9 u_2\big(t-\tau'(t),l\big)\,\mathrm{d}l \\
&- \int_{\Sigma} u_2^{\mathrm{T}}\big(t-\tau_2',l\big)R_9 u_2\big(t-\tau_2',l\big)\,\mathrm{d}l + \int_{\Sigma} v_2^{\mathrm{T}}(t,l)R_{10} v_2(t,l)\,\mathrm{d}l \\
&- \int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma_1',l\big)R_{10} v_2\big(t-\sigma_1',l\big)\,\mathrm{d}l + \int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma_1',l\big)R_{11} v_2\big(t-\sigma_1',l\big)\,\mathrm{d}l \\
&- (1-\eta_4)\int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma'(t),l\big)R_{11} v_2\big(t-\sigma'(t),l\big)\,\mathrm{d}l \\
&+ (1-\eta_3)\int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma'(t),l\big)R_{12} v_2\big(t-\sigma'(t),l\big)\,\mathrm{d}l \\
&- \int_{\Sigma} v_2^{\mathrm{T}}\big(t-\sigma_2',l\big)R_{12} v_2\big(t-\sigma_2',l\big)\,\mathrm{d}l,
\end{aligned} \tag{45}
$$

$$
\begin{aligned}
\frac{\partial V_7(t,l)}{\partial t} ={}& \tau'^2(t)\int_{\Sigma} u_2^{\mathrm{T}}(t,l)Q_4 u_2(t,l)\,\mathrm{d}l - \tau'(t)\int_{\Sigma}\int_{t-\tau'}^{t} u_2^{\mathrm{T}}(s,l)Q_4 u_2(s,l)\,\mathrm{d}s\,\mathrm{d}l \\
&+ \sigma'^2(t)\int_{\Sigma} v_2^{\mathrm{T}}(t,l)Q_5 v_2(t,l)\,\mathrm{d}l - \sigma'(t)\int_{\Sigma}\int_{t-\sigma'}^{t} v_2^{\mathrm{T}}(s,l)Q_5 v_2(s,l)\,\mathrm{d}s\,\mathrm{d}l \\
\le{}& \tau_2'^2\int_{\Sigma} u_2^{\mathrm{T}}(t,l)Q_4 u_2(t,l)\,\mathrm{d}l - \int_{\Sigma}\left[\int_{t-\tau'}^{t} u_2(s,l)\,\mathrm{d}s\right]^{\mathrm{T}} Q_4\left[\int_{t-\tau'}^{t} u_2(s,l)\,\mathrm{d}s\right]\mathrm{d}l \\
&+ \sigma_2'^2\int_{\Sigma} v_2^{\mathrm{T}}(t,l)Q_5 v_2(t,l)\,\mathrm{d}l \\
&- \int_{\Sigma}\left[\int_{t-\sigma'}^{t} v_2(s,l)\,\mathrm{d}s\right]^{\mathrm{T}} Q_5\left[\int_{t-\sigma'}^{t} v_2(s,l)\,\mathrm{d}s\right]\mathrm{d}l,
\end{aligned} \tag{46}
$$

$$
\begin{aligned}
\frac{\partial V_8(t,l)}{\partial t} ={}& \int_{\Sigma} G^{\mathrm{T}}\big(v_2(t,l)\big)Q_6 F\big(v_2(t,l)\big)\,\mathrm{d}l \\
&- \big(1-\dot{\sigma}'\big)\int_{\Sigma} G^{\mathrm{T}}\big(v_2\big(t-\sigma',l\big)\big)Q_6 G\big(v_2\big(t-\sigma',l\big)\big)\,\mathrm{d}l
\end{aligned}
$$

$$\begin{aligned}
&\leq \int_{\Sigma} G^{\mathrm{T}}\big(v_2(t,l)\big)Q_6 G\big(v_2(t,l)\big)\,\mathrm{d}l \\
&\quad + (\eta_2 - 1)\int_{\Sigma} G^{\mathrm{T}}\big(v_2(t-\sigma,l)\big)Q_6 G\big(v_2\big(t-\sigma',l\big)\big)\,\mathrm{d}l.
\end{aligned} \tag{47}$$

According to Lemma 3, we have

$$2\int_{\Sigma} u_1^{\mathrm{T}}(t,l)P_1 \sum_{k=1}^{l} \frac{\partial}{\partial l_k}\left(D_k \frac{\partial u_1(t,l)}{\partial l_k}\right)\mathrm{d}l \leq -\frac{\pi^2}{2}\int_{\Sigma} u_1^{\mathrm{T}}(t,l)P_1 D_L u_1(t,l)\,\mathrm{d}l, \tag{48}$$

$$2\sum_{k=1}^{l}\int_{\Sigma} v_1^{\mathrm{T}}(t,l)P_2 \frac{\partial}{\partial l_k}\left(D_k^* \frac{\partial v_1(t,l)}{\partial l_k}\right)\mathrm{d}l \leq -\frac{\pi^2}{2}\int_{\Sigma} v_1^{\mathrm{T}}(t,l)P_2 D_L^* v_1(t,l)\,\mathrm{d}l, \tag{49}$$

$$2\int_{\Sigma} u_2^{\mathrm{T}}(t,l)P_3 \sum_{k=1}^{l} \frac{\partial}{\partial l_k}\left(d_k \frac{\partial u_2(t,l)}{\partial l_k}\right)\mathrm{d}l \leq -\frac{\pi^2}{2}\int_{\Sigma} u_2^{\mathrm{T}}(t,l)P_3 d_L u_2(t,l)\,\mathrm{d}l, \tag{50}$$

$$2\sum_{k=1}^{l}\int_{\Sigma} v_2^{\mathrm{T}}(t,l)P_4 \frac{\partial}{\partial l_k}\left(d_k^* \frac{\partial v_2(t,l)}{\partial l_k}\right)\mathrm{d}l \leq -\frac{\pi^2}{2}\int_{\Sigma} v_2^{\mathrm{T}}(t,l)P_4 d_L^* v_2(t,l)\,\mathrm{d}l, \tag{51}$$

where

$$\begin{aligned}
&\left(u_1^{\mathrm{T}}(t,l)P_1 D_k \frac{\partial u_1(t,l)}{\partial l_k}\right)_{k=1}^{L} = \left(u_1^{\mathrm{T}}(t,l)P_1 D_1 \frac{\partial u_1^{\mathrm{T}}(t,l)}{\partial l_1}, \ldots, u_1^{\mathrm{T}}(t,l)P_1 D_L \frac{\partial u_1^{\mathrm{T}}(t,l)}{\partial l_L}\right), \\
&\left(v_1^{\mathrm{T}}(t,l)P_2 D_k^* \frac{\partial v_1(t,l)}{\partial l_k}\right)_{k=1}^{L} = \left(v_1^{\mathrm{T}}(t,l)P_2 D_k^* \frac{\partial v_1(t,l)}{\partial l_1}, \ldots, v_1^{\mathrm{T}}(t,l)P_2 D_L^* \frac{\partial v_1(t,l)}{\partial l_L}\right), \\
&\left(u_2^{\mathrm{T}}(t,l)P_3 d_k \frac{\partial u_2(t,l)}{\partial l_k}\right)_{k=1}^{L} = \left(u_2^{\mathrm{T}}(t,l)P_3 d_1 \frac{\partial u_2^{\mathrm{T}}(t,l)}{\partial l_1}, \ldots, u_2^{\mathrm{T}}(t,l)P_3 d_L \frac{\partial u_2^{\mathrm{T}}(t,l)}{\partial l_L}\right), \\
&\left(v_2^{\mathrm{T}}(t,l)P_4 d_k^* \frac{\partial v_2(t,l)}{\partial l_k}\right)_{k=1}^{L} = \left(v_2^{\mathrm{T}}(t,l)P_4 d_k^* \frac{\partial v_2(t,l)}{\partial l_1}, \ldots, v_2^{\mathrm{T}}(t,l)P_4 d_L^* \frac{\partial v_2(t,l)}{\partial l_L}\right).
\end{aligned}$$

Considering inequalities (17) and (18), for diagonal matrices $\Lambda_1 > 0$, $\Lambda_2 > 0$, $\Lambda_3 > 0$ and $\Lambda_4 > 0$, the following inequalities hold:

$$2F^{\mathrm{T}}\big(v_1(t,l)\big)\Lambda_1 F\big(v_1(t,l)\big) - 2v_1^{\mathrm{T}}(t,l)K_1\Lambda_1 F\big(v_1(t,l)\big) \leq 0, \tag{52}$$

$$\begin{aligned}
&2F^{\mathrm{T}}\big(v_1\big(t-\sigma(t),l\big)\big)\Lambda_2 F\big(v_1\big(t-\sigma(t),l\big)\big) \\
&\quad - 2v_1^{\mathrm{T}}\big(t-\sigma(t),l\big)K_1\Lambda_2 F\big(v_1\big(t-\sigma(t),l\big)\big) \leq 0,
\end{aligned} \tag{53}$$

$$2G^{\mathrm{T}}\big(v_2(t,l)\big)\Lambda_3 G\big(v_2(t,l)\big) - 2v_2^{\mathrm{T}}(t,l)K_2\Lambda_3 G\big(v_2(t,l)\big) \leq 0, \tag{54}$$

$$\begin{aligned}
&2G^{\mathrm{T}}\big(v_2\big(t-\sigma'(t),l\big)\big)\Lambda_4 G\big(v_2\big(t-\sigma'(t),l\big)\big) \\
&\quad - 2v_2^{\mathrm{T}}\big(t-\sigma'(t),l\big)K_2\Lambda_4 G\big(v_2\big(t-\sigma'(t),l\big)\big) \leq 0.
\end{aligned} \tag{55}$$

According to Lemma 5, we have inequalities as follows:

$$\begin{aligned}
&2v_1^{\mathrm{T}}\big(t-\sigma(t),l\big)K_1\Lambda_2 F\big(v_1\big(t-\sigma(t),l\big)\big) \\
&\quad \leq v_1^{\mathrm{T}}\big(t-\sigma(t),l\big)K_1\Lambda_2 K_1 v_1\big(t-\sigma(t),l\big) \\
&\qquad + F^{\mathrm{T}}\big(v_1\big(t-\sigma(t),l\big)\big)\Lambda_2 F\big(v_1\big(t-\sigma(t),l\big)\big),
\end{aligned} \tag{56}$$

$$\begin{aligned}&2v_2^{\mathrm{T}}\bigl(t-\sigma'(t),l\bigr)K_2\Lambda_4 G\bigl(v_2\bigl(t-\sigma'(t),l\bigr)\bigr)\\&\quad\le v_2^{\mathrm{T}}\bigl(t-\sigma'(t),l\bigr)K_2\Lambda_4K_2v_2\bigl(t-\sigma'(t),l\bigr)\\&\qquad+G^{\mathrm{T}}\bigl(v_2\bigl(t-\sigma'(t),l\bigr)\bigr)\Lambda_4G\bigl(v_2\bigl(t-\sigma'(t),l\bigr)\bigr),\end{aligned}\tag{57}$$

$$\begin{aligned}&2v_1^{\mathrm{T}}(t,l)P_2B_1u_1\bigl(t-\tau(t),l\bigr)\\&\quad\le v_1^{\mathrm{T}}(t,l)P_2v_1(t,l)+u_1\bigl(t-\tau(t),l\bigr)B_1^{\mathrm{T}}P_2B_1u_1\bigl(t-\tau(t),l\bigr),\end{aligned}\tag{58}$$

$$\begin{aligned}&2v_2^{\mathrm{T}}(t,l)P_4B_2u_2\bigl(t-\tau'(t),l\bigr)\\&\quad\le v_2^{\mathrm{T}}(t,l)P_4v_2(t,l)+u_2\bigl(t-\tau'(t),l\bigr)B_2^{\mathrm{T}}P_4B_2u_2\bigl(t-\tau'(t),l\bigr).\end{aligned}\tag{59}$$

According to Lemma 6, for a positive scalar ε, there exist

$$\begin{aligned}&2u_2(t,l)\mathrm{P}_3W_2G\bigl(v_2\bigl(t-\sigma'(t),l\bigr)\bigr)\\&\quad\le \varepsilon u_2^{\mathrm{T}}(t,l)\mathrm{P}_3W_2u_2(t,l)+\frac{1}{\varepsilon}G^{\mathrm{T}}\bigl(v_2\bigl(t-\sigma'(t),l\bigr)\bigr)\mathrm{P}_3W_2G\bigl(v_2\bigl(t-\sigma'(t),l\bigr)\bigr).\end{aligned}\tag{60}$$

Taking equations (40)-(47) into consideration, derivatives of $V(t,m,p)$ $(i=1,2,3)$ can be formed as follows:

$$\frac{\partial V(t,l)}{\partial t}=\sum_{i=1}^{8}\frac{\partial V_i(t,l)}{\partial t}.\tag{61}$$

Taking inequalities (48)-(60) into consideration, equation (61) is rewritten as

$$\begin{aligned}\frac{\partial V(t,l)}{\partial t}&=\sum_{i=1}^{8}\frac{\partial V_i(t,l)}{\partial t}\\&\le\int_{\Sigma}\bigl[\xi_1^{\mathrm{T}}(t,l)\Xi_1\xi_1(t,l)+\xi_2^{\mathrm{T}}(t,l)\Xi_2\xi_2(t,l)\bigr]\,dl<0,\end{aligned}\tag{62}$$

for $\zeta(t,x)\neq 0$, where

$$\begin{aligned}\xi_1={}&\biggl[u_1^T(t,l),u_1^T(t-\tau_1,l),u_1^T(t-\tau_2,l),u_1^T(t-\tau,l),\biggl[\int_{t-\tau}^{t}u_1(s,l)\,ds\biggr]^{\mathrm{T}},\\&F^{\mathrm{T}}\bigl(v_1\bigl(t-\sigma(t),l\bigr)\bigr),u_2^T(t,l),u_2^T\bigl(t-\tau_1',l\bigr),u_1^T\bigl(t-\tau_2',l\bigr),u_2^T\bigl(t-\tau',l\bigr),\\&\biggl[\int_{t-\tau'}^{t}u_2(s,l)\,ds\biggr]^{\mathrm{T}},G^{\mathrm{T}}\bigl(v_2\bigl(t-\sigma'(t),l\bigr)\bigr)\biggr]^{\mathrm{T}},\\\xi_2={}&\biggl[v_1^T(t,l),v_1^T(t-\sigma_1,l),v_1^T(t-\sigma_2,l),v_1^T(t-\sigma,l),\biggl[\int_{t-\sigma}^{t}v_1(s,l)\,ds\biggr]^{\mathrm{T}},F^{\mathrm{T}}\bigl(v_1(t,l)\bigr),\\&v_2^T(t,l),v_2^T\bigl(t-\sigma_1',l\bigr),v_1^T\bigl(t-\sigma_2',l\bigr),v_2^T\bigl(t-\sigma',l\bigr),\\&\biggl[\int_{t-\sigma'}^{t}v_2(s,l)\,ds\biggr]^{\mathrm{T}},G^{\mathrm{T}}\bigl(v_2(t,l)\bigr)\biggr]^{\mathrm{T}}.\end{aligned}$$

□

4 Numerical simulation

Consider the reaction-diffusion-delayed GRN (25), (26) with the following parameters:

$$k=1,\qquad L=100,\qquad \gamma=1,\qquad \gamma'=0.3,\qquad K_1=K_2=0.65I,$$

$$A_1 = \operatorname{diag}(3,3,3,3,3), \qquad B_1 = \operatorname{diag}(0.8,0.8,0.8,0.8,0.8),$$

$$C_1 = \operatorname{diag}(2.5,2.5,2.5,2.5,2.5),$$

$$D_1 = \operatorname{diag}(0.1,0.1,0.1,0.1,0.1), \qquad D_1^* = \operatorname{diag}(0.2,0.2,0.2,0.2,0.2),$$

$$W_1 = \begin{bmatrix} 0 & 0 & 1 & 1 & -1 \\ -1 & 1 & 0 & 0 & 0 \\ 0 & -1 & 0 & 1 & 0 \\ 0 & -1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 \end{bmatrix}, \qquad W_1^* = \begin{bmatrix} \gamma & 0 & 0 \\ \gamma & 0 & 0 \\ 0 & 0 & -\gamma \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},$$

$$A_2 = \operatorname{diag}(0.1,0.1,0.1), \qquad B_2 = \operatorname{diag}(1.8,1.8,1.8), \qquad C_2 = \operatorname{diag}(2.3,2.3,2.3),$$

$$d_1 = \operatorname{diag}(0.1,0.1,0.1), \qquad d_1^* = \operatorname{diag}(0.2,0.2,0.2),$$

$$W_2 = \begin{bmatrix} 2.4 & -2.4 & 0 \\ 2.4 & -2.4 & 0 \\ 2.4 & 0 & -2.4 \end{bmatrix}, \qquad W_2^* = \begin{bmatrix} -\gamma' & -\gamma' & 0 & 0 & 0 \\ 0 & 0 & \gamma' & \gamma' & 0 \\ 0 & \gamma' & 0 & 0 & -\gamma' \end{bmatrix}.$$

$$\tau = 1.5 + 0.5\sin(t), \qquad \sigma = 2.2 + 0.8\sin(t),$$

$$\tau' = 3.6 + 0.4\sin(t), \qquad \sigma' = 2.9 + 0.6\sin(t),$$

where

$$f_i(x) = \frac{x^2}{1+x^2}, \qquad g_i(y) = \frac{y^2}{1+y^2} \quad (i = 1,2,\ldots,n).$$

By using the Toolbox YALMIP in MATLAB to solve the LMI (29) and (30) we can obtain feasible solutions, the processes of asymptotic stability of mRNA concentration and protein concentration under Dirichlet boundary conditions are shown by Figures 1-8. It is obvious that the proposed theory is feasible. The topological structure of interactional GRNs is shown by Figure 9.

We set up the rules to measure the stabilizing time of interactional GRNs as follows:

$$\begin{aligned} \gamma(t) = \int_\Sigma \bigl(& w_i \bigl|u_{1i}(t,l) - u_{1i}(t-\delta,l)\bigr| + w_i' \bigl|v_{1i}(t,l) v_{1i}(t-\delta,l)\bigr| + w_p \bigl|u_{2p}(t,l) - u_{2p}(t-\delta,l)\bigr| \\ & + w_p' \bigl|v_{2p}(t,l) - v_{2p}(t-\delta,l)\bigr| \bigr)\,\mathrm{d}l, \end{aligned} \tag{63}$$

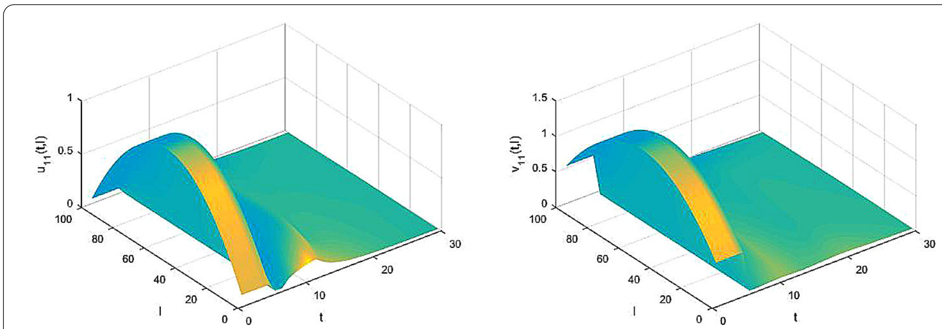

Figure 1 The trajectory of $u_{11}(t,l)$ and $v_{11}(t,l)$.

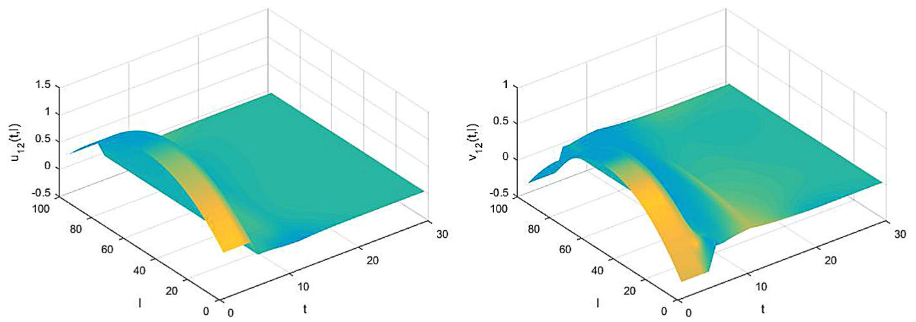

Figure 2 The trajectory of $u_{12}(t,l)$ and $v_{12}(t,l)$.

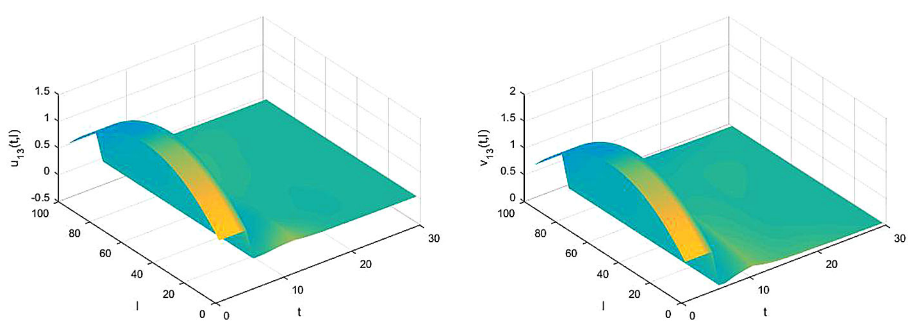

Figure 3 The trajectory of $u_{13}(t,l)$ and $v_{13}(t,l)$.

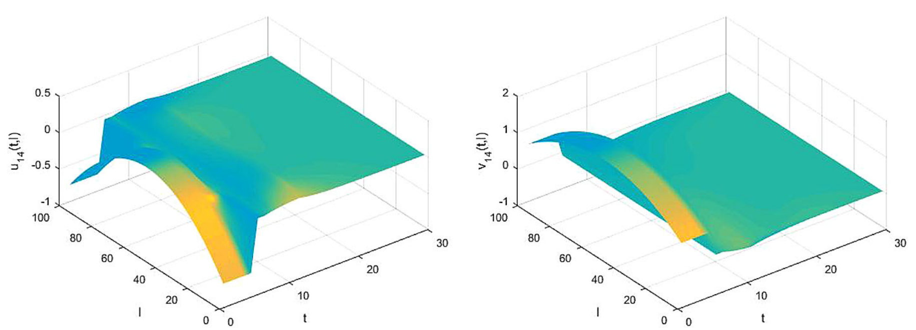

Figure 4 The trajectory of $u_{14}(t,l)$ and $v_{14}(t,l)$.

$$\begin{cases} \Theta(t) = 1, & \gamma(t) > \delta_0, \\ \Theta(t) = 2, & \gamma(t) \leq \delta_0, \end{cases} \tag{64}$$

where $w_i > 0$, $w_i' > 0$ ($i = 1, \dots, n_1$); $w_p > 0$, $w_p' > 0$ ($p = 1, \dots, n_2$) are weights of u_{1i}, v_{1i}, u_{2p} and v_{2p}, respectively, δ_0 is a positive small quantity, $\Theta(t)$ is a quantity for stability identification. When $\Theta(t) = 2$, it indicates interactional GRNs are stable; when $\Theta(t) = 1$, it indicates interactional GRNs are unstable.

When $\gamma' \in \{0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0\}$, $\gamma = 0.4$, $w_i = w_i' = w_p = w_p' = 1/16$, $\delta_0 = 0.1$, the evolutions of $\Theta(t)$ with γ' are shown by Figure 10, it is found that the increase of coupling strength γ' will lengthen the stabilizing time of interactional GRNs. Further-

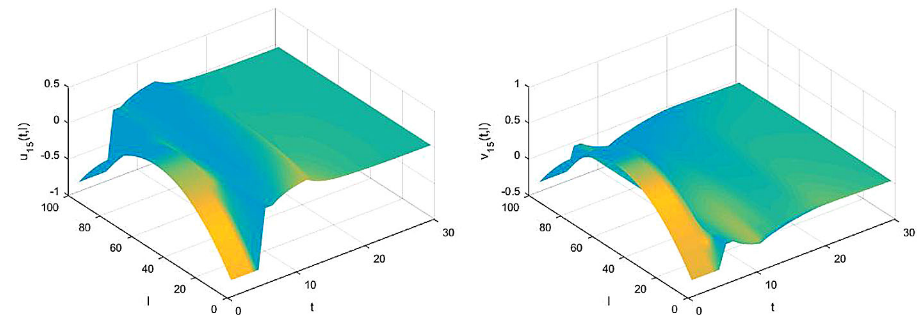

Figure 5 **The trajectory of $u_{15}(t,l)$ and $v_{15}(t,l)$.**

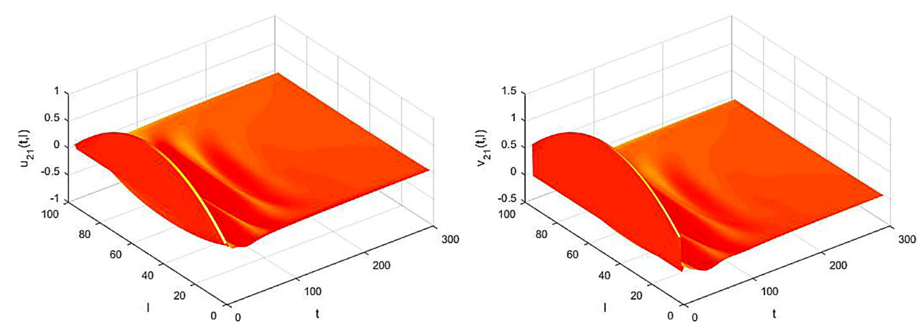

Figure 6 **The trajectory of $u_{21}(t,l)$ and $v_{21}(t,l)$.**

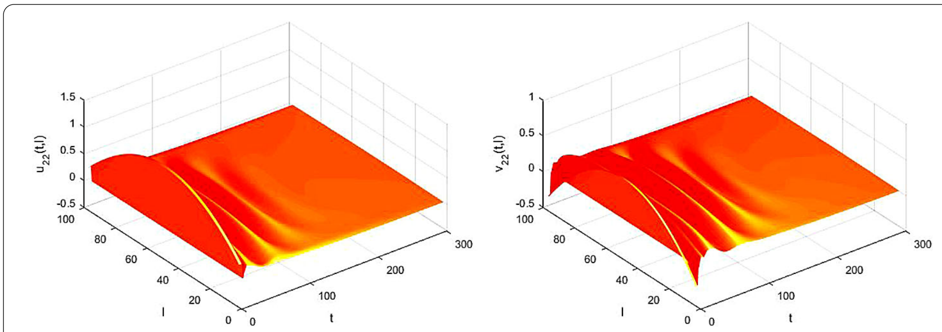

Figure 7 **The trajectory of $u_{22}(t,l)$ and $v_{22}(t,l)$.**

more, we can find that the iterative number of solution of LMIs and the time of reaching a steady state have the same change with different γ' as shown in Figure 11, therefore we utilize the iterative number to characterize the time of reaching steady state, because of the independence of the initial condition and the step size for the iterative number. When $\gamma \in \{0, 0, 2, 0.4, 0.6, 0.8, 1.0\}$, the performance of number of iterations with γ' and γ is shown in Figure 12, where the color represents the time of reaching a steady state.

5 Discussion

Further numerical simulations show that:

(I) Interactional GRNs without reaction-diffusion terms cannot reach a steady state, because of the defection of information from reaction-diffusion terms. In other

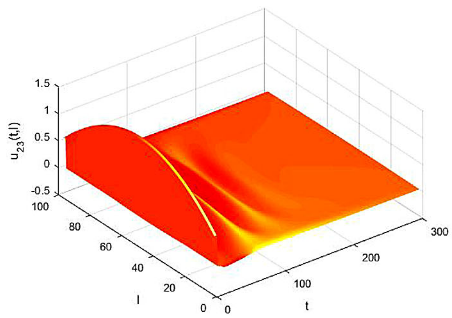

Figure 8 **The trajectory of $u_{23}(t,l)$ and $v_{23}(t,l)$.**

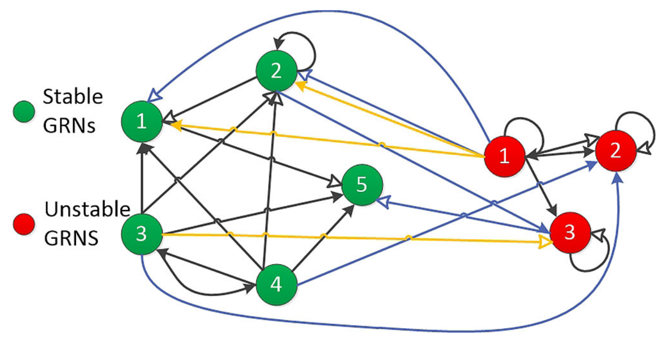

Figure 9 **The topological structure of interactional GRNs.**

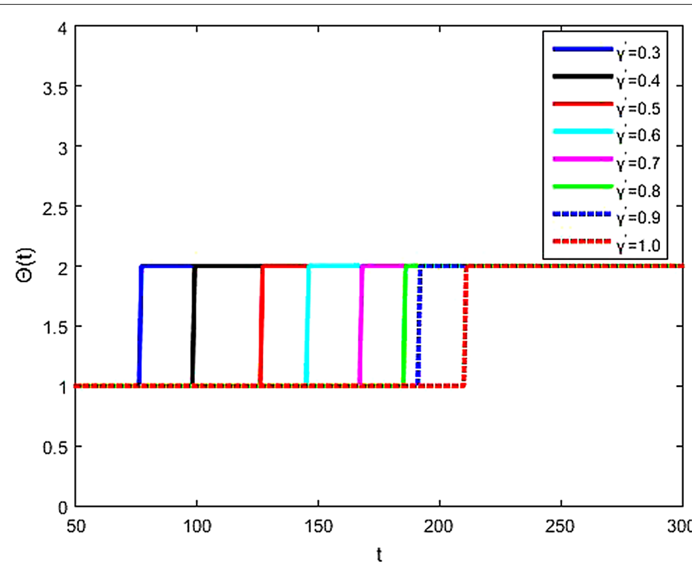

Figure 10 **The evolution of $\Theta(t)$ with γ'.**

words, reaction-diffusion terms are important and indispensable for interactional GRNs.

(II) γ and γ' have an absolute effect on the time of reaching steady state as shown in Figure 12, the increase of coupling strength γ' and γ will collectively lengthen the stabilizing time of interactional GRNs.

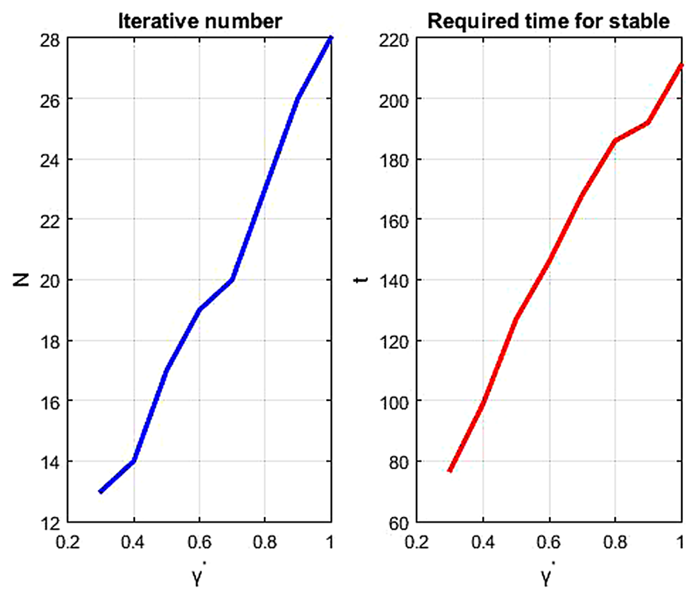

Figure 11 Iterative number and required time for stable with different γ' ($\gamma = 0.0.4$).

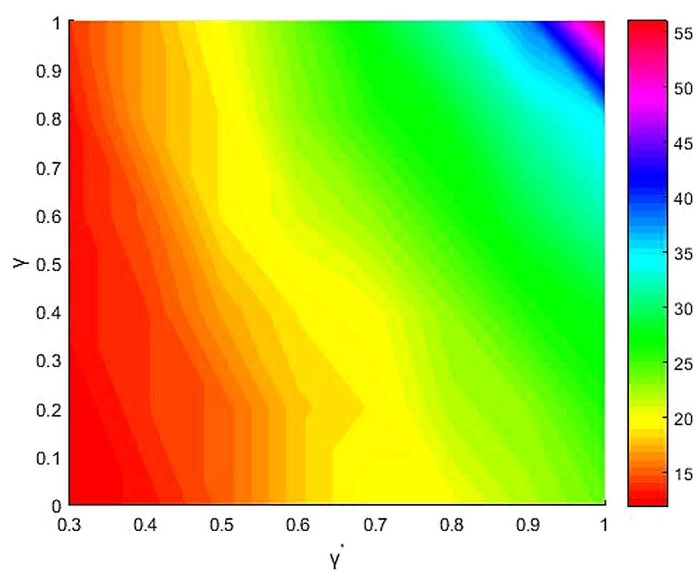

Figure 12 Performance of number of iterations with γ' and γ.

(III) The matrices W_2 and W_2^* qualitatively affect the stability of the interactional GRNs, in other words, the topological structure of the unstable GRNs and W_2^* are very important for the stability of the interactional GRNs. The out-degree and in-degree of stable GRNs as well as the coupling term of W_1^* can change at will, but the out-degree and in-degree of unstable GRNs and the coupling term of W_2^* cannot change freely.

6 Conclusion

In this paper, we have constructed a model for interactional GRNs with reaction-diffusion terms under a Dirichlet boundary condition, and we analyzed the robust stability of interactional GRNs. Through constructing appropriate Lyapunov-Krasovskii functions and linear matrix inequalities (LMIs), we have given stability criteria corresponding to interactional GRNs. By numerical simulations, we found three important conclusions: interactional GRNs without reaction-diffusion terms cannot reach a steady state, because of the defection of information from reaction-diffusion terms, in other words, reaction-diffusion terms are important and indispensable for interactional GRNs; due to the smaller coupling strength γ' (in a certain range) and γ, interactional GRNs tend to become stable more quickly; the topological structures of the unstable GRNs and coupling term of W_2^* determine the stability of interactional GRNs.

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Competing interests
The authors declare that they have no competing interests.

Authors' contributions
All authors have made equal contributions to the writing of this paper. All authors have read and approved the final version of the manuscript.

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