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Sufficient and necessary conditions for global stability of genetic regulator networks with time delays

Guopeng ZHOU[1,2], Jinhua HUANG[3*], Fengxia TIAN[2] & Xiaoxin LIAO[2,4]

[1]*School of Electrical and Electronic Engineering, Huazhong University of Science and Technology, Wuhan* 430074*, China;*
[2]*Institute of Engineering and Technology, Hubei University of Science and Technology, Xianning* 437100*, China;*
[3]*Department of Electric and Electronic Engineering, Wuhan Institute of Shipbuilding Technology, Wuhan* 430050*, China;*
[4]*College of Automation, Huazhong University of Science and Technology, Wuhan* 430074*, China*

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Abstract This paper is concerned with the global stability of the nonlinear model for genetic regulator networks (GRNs) with time delays. Four new sufficient and necessary conditions for global asymptotic stability and global exponential stability of the equilibrium point of GRNs are derived. Specifically, using comparing theorem and Dini derivation method, three weak sufficient conditions for global stability of GRNs with constant time delays are proposed. Finally, a general GRN model is used to illustrate the effectiveness of the proposed theoretical results. Compared with the previous results, some sufficient and necessary conditions for Lyapunov stability of GRNs are proposed, which are not seen before.

Keywords genetic regulator networks, time delay, global asymptotic stable, global exponential stable, comparing theorem, Dini derivative

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1 Introduction

Genetic regulator networks (GRNs) are biochemically dynamic systems which describe complicated interactions among two main species of gene products: mRNAs and proteins in the interactive transcription and translation processes. Due to their importance in system biology, GRNs explain the interactions between genes and proteins to form a complex system which performs complicated biological functions [1,2]. Also, GRNs may lead to engineering developments such as biotechnological design principles of synthetic GRNs [3,4] and new integrated circuits like neurochips learnt from biological neural networks. Several computational models for GRNs have been applied to investigate the behaviors of GRNs: Boolean models [5,6], Bayesian network models [7,8], Petri net models [9,10], and the differential equation models [2,11–13].

It should be mentioned that the differential equation models are largely used as the fundamental models for GRNs. As a dynamic system, the stability of GRNs is naturally of great importance, and it has attracted more attentions [12–23]. Chen et al. studied local stability and the bifurcation of GRNs

* Corresponding author (email: angela0412@126.com)

in [12]. Chesi et al. [13,14] studied robust stability of uncertain GRNs with SUM logic. Li et al. [16,17] studied stability of GRNs with time delay using LMI methods. Ren et al. [18,19] studied global and robust stability for a class of GRNs with time-variant delays and parameter uncertainties. Li et al. [20,21] studied monostability or multistability with different regulatory functions. Luo et al. [23] proposed some results of unconditional global exponential stability in sense of Lagrange for GRNs with time-variant delays and SUM logic. Some studies were about stability in sense of Lyapunov [16,18], while some others were about stability in sense of Lagrange [23,24].

Since GRNs are actually Lurie systems, which are linear systems plus nonlinear feedback terms, and sufficient and necessary conditions for absolute stability of Lurie systems are proposed (see references in [25,26]), people naturally raise the question whether the sufficient and necessary conditions for the stability of GRNs exist, unlike the existing literature of sufficient conditions. By analysis, we have found that GRNs with SUM logic are just with the excellent properties which Lurie systems have. Therefore, we can take advantage of the core idea of references [25,26], and aim to study the GRNs with SUM logic.

Generally, a cellular system is characterized with significant time delays [12–15]. In particular, for the transcription, translation, and translocation processes of GRNs, many researchers studied stability with time delays, that is, [16–19]. Nevertheless, they are mostly sufficient conditions, and the linear matrix inequalities (LMIs) are mainly used. It is well known that for the LMI solver, even any small dimensional matrix will meet a higher dimensional LMIs, and the results are conservative because of the strong conditions. So far, it is difficult to find the sufficient and necessary conditions of Lyapunov stability of GRNs. Referring to the previous results of sufficient and necessary conditions for stability [25–27], the main purpose of this paper is to study some sufficient and necessary conditions for global asymptotic stability and global exponential stability of the time-variant delay GRNs, respectively. Some novel ideas and methods will be investigated.

The rest of this paper is organized as follows. In Section 2, the GRNs considered in this paper are described, and some definitions and main problems are given. In Section 3, some sufficient and necessary conditions of global asymptotic stability and global exponential stability are proposed. Section 4 considers the GRNs with constant time delays, and some sufficient conditions of global stability are presented. In Section 5, one general example is given to demonstrate the effectiveness of the theoretical results obtained in the previous sections. Section 6 describes the conclusion.

2 Preliminaries

In this paper, we consider the GRNs with time delays consisting of n mRNAs and n proteins, which are described by the following equations [16,23]:

$$\begin{aligned} \frac{\mathrm{d}m_i}{\mathrm{d}t} &= -a_i m_i(t) + b_i(p_1(t-\tau_1(t)), \ldots, p_n(t-\tau_n(t))), \\ \frac{\mathrm{d}p_i}{\mathrm{d}t} &= -c_i p_i(t) + d_i m_i(t-\sigma_i(t)), \quad i = 1, 2, \ldots, n, \end{aligned} \tag{1}$$

where $m_i(t),\ p_i(t) \in \mathbb{R}$ are the concentrations of mRNA and protein of the ith node at time t, respectively. a_i, c_i are positive constants, which represent the degradation rates of the mRNA and the protein, respectively. $d_i > 0$ denotes the translation rate of the ith gene. b_i is a regulatory function of the ith gene; it is generally a nonlinear function of variables $p_1(t), p_2(t), \ldots, p_n(t)$ and has a form of monotonicity with each variable. $\tau_i(t), \sigma_i(t)$ are time delays, which are assumed satisfying $\tau_i(t) \in [0, \tau],\ \sigma_i(t) \in [0, \sigma]$ with $\tau, \sigma > 0$ positive constants, and let $\kappa = \max\{\tau, \sigma\}$.

The regulation function b_i plays an important role in the dynamics. Generally, the form of b_i may be very complicated; it depends on all biochemical reactions involved in this regulation. In this paper, the regulation function is described as $b_i(p_1(t), p_2(t), \ldots, p_n(t)) = \sum_{j=1}^{n} b_{ij}(p_j(t))$, which is called SUM logic [16,18]. That is, each transcriptional factor acts additively to regulate the ith gene or node. In many natural GRNs, this SUM logic exists [28]. b_{ij} is a monotonic function of Hill form [16]. If transcription factor j is an activator of gene i, then

$$b_{ij}(p_j(t)) = \alpha_{ij}\frac{(p_j(t)/\beta_j)^{H_j}}{1+(p_j(t)/\beta_j)^{H_j}}. \tag{2}$$

If transcription factor j is a repressor of gene i, then

$$b_{ij}(p_j(t)) = \alpha_{ij}\left(1-\frac{(p_j(t)/\beta_j)^{H_j}}{1+(p_j(t)/\beta_j)^{H_j}}\right), \tag{3}$$

where β_j is a positive constant, H_j is the Hill coefficient representing the degree of cooperativity, and $\alpha_{ij} > 0$ is a bounded constant representing the dimensionless transcription rate of the transcription factor j to the ith gene.

Then, system (1) can be rewritten as

$$\begin{aligned}\frac{\mathrm{d}m_i}{\mathrm{d}t} &= -a_i m_i(t) + \sum_{j=1}^{n} w_{ij} g_j(p_j(t-\tau_j(t))) + I_i,\\ \frac{\mathrm{d}p_i}{\mathrm{d}t} &= -c_i p_i(t) + d_i m_i(t-\sigma_i(t)),\quad i=1,2,\ldots,n,\end{aligned} \tag{4}$$

where $g_j(x) = (x/\beta_j)^{H_j}/(1+(x/\beta_j)^{H_j})$ is a monotonically increasing function with saturation, $W = (w_{ij}) \in \mathbb{R}^{n\times n}$ is a coupling matrix of the GRNs, which is defined as follows: if there is no link from node j to node i, $w_{ij}=0$; if transcription factor j is an activator of gene i, $w_{ij}=\alpha_{ij}$; if transcription factor j is a repressor of gene i, $w_{ij}=-\alpha_{ij}$. I_i is defined as a basal rate $I_i=\sum_{j\in V_i}\alpha_{ij}$, in which V_i is the set of repressors of gene i. $g_j(x)$ is a sigmoid-type function if $H_j>1$, then, $xg_j(x)>0$ when $x\neq 0$.

Let $C_{[-\kappa,0]}$ be the Banach space of continuous functions $\phi:[-\kappa,0]\to\mathbb{R}^n, \psi:[-\kappa,0]\to\mathbb{R}^n$ with the norm $\|\phi\|=\sup_{s\in[-\kappa,0]}\|\phi(s)\|$ and $\|\psi\|=\sup_{s\in[-\kappa,0]}\|\psi(s)\|$.

Let $m=[m_1,m_2,\ldots,m_n]^{\mathrm{T}}$, $p=[p_1,p_2,\ldots,p_n]^{\mathrm{T}}$. By the well-known Brouwer fixed point theorem [29], there exists one equilibrium point (m^*,p^*) for system (4) such that

$$-a_i m_i^* + \sum_{j=1}^{n} w_{ij} g_j(p_j^*) + I_i = 0,\quad -c_i p_i^* + d_i m_i^* \ = 0,\quad i=1,2,\ldots,n. \tag{5}$$

Now, we shift the equilibrium point (m^*,p^*) to the origin by letting $\tilde{m}=m-m^*$, $\tilde{p}=p-p^*$. Then, system (4) becomes

$$\begin{aligned}\frac{\mathrm{d}\tilde{m}_i}{\mathrm{d}t} &= -a_i\tilde{m}_i(t) + \sum_{j=1}^{n} w_{ij}(g_j(p_j(t-\tau_j(t))) - g_j(p_j^*)),\\ \frac{\mathrm{d}\tilde{p}_i}{\mathrm{d}t} &= -c_i\tilde{p}_i(t) + d_i\tilde{m}_i(t-\sigma_i(t)),\quad i=1,2,\ldots,n.\end{aligned} \tag{6}$$

Since $g_j(x)$ is a monotonically increasing function with saturation and differentiable, it satisfies

$$0 \leqslant \frac{\mathrm{d}g_j(x)}{\mathrm{d}x} \leqslant k_j,\quad i=1,2,\ldots,n, \tag{7}$$

where k_j is a positive constant. Let $\ell_{ij}=\sup|w_{ij}\dot{g}_j(\cdot)|$. Let $\tilde{m}(t,t_0,\phi,\psi)$, $\tilde{p}(t,t_0,\phi,\psi)$ be the solutions of system (6) with initials $\phi,\ \psi\in C_{[-\kappa,0]}$. We propose the following definitions.

Definition 1. The zero solution of system (6) (i.e., the corresponding equilibrium point (m^*,p^*) of system (4)) is globally asymptotically stable if $\forall\epsilon>0$, $\exists\delta>0$, for $\phi,\psi\in C_{[-\kappa,0]}$ and $\|(\phi,\psi)\|<\delta$, such that

$$\|(\tilde{m}(t,t_0,\phi,\psi),\tilde{p}(t,t_0,\phi,\psi))\| < \epsilon, \tag{8}$$

and for any $\phi,\psi\in C_{[-\kappa,0]}$

$$\lim_{t\to+\infty}\|(\tilde{m}(t,t_0,\phi,\psi),\tilde{p}(t,t_0,\phi,\psi))\| = 0, \tag{9}$$

where (8) implies that (m^*,p^*) is stable in sense of Lyapunov, and (9) implies that (m^*,p^*) is globally attractive.

Definition 2. The zero solution of system (6) (i.e., the corresponding equilibrium point (m^*, p^*) of system (4)) is globally asymptotically stable on partial variable $\tilde{m}$ or $\tilde{p}$ if $\forall\epsilon > 0$, $\exists\delta > 0$, for $\phi, \psi \in C_{[-\kappa,0]}$ and $\|(\phi, \psi)\| < \delta$, such that

$$\|\tilde{m}(t, t_0, \phi, \psi)\| < \epsilon, \tag{10}$$

or

$$\|\tilde{p}(t, t_0, \phi, \psi)\| < \epsilon. \tag{11}$$

And for any $\phi, \psi \in C_{[-\kappa,0]}$, it holds that

$$\lim_{t\to+\infty} \|\tilde{m}(t, t_0, \phi, \psi)\| = 0, \tag{12}$$

or

$$\lim_{t\to+\infty} \|\tilde{p}(t, t_0, \phi, \psi)\| = 0. \tag{13}$$

Definition 3. The zero solution of system (6) (i.e., the corresponding equilibrium point (m^*, p^*) of system (4)) is globally exponentially stable if $\forall\phi, \psi \in C_{[-\kappa,0]}$, it holds that

$$\|(\tilde{m}(t, t_0, \phi, \psi), \tilde{p}(t, t_0, \phi, \psi))\| < M(\phi, \psi)\mathrm{e}^{-\lambda(t-t_0)}, \tag{14}$$

where $M(\phi, \psi) > 0,\ \lambda > 0$ are constants.

Definition 4. The zero solution of system (6) (i.e., the corresponding equilibrium point (m^*, p^*) of system (4)) is globally exponentially stable on partial variable $\tilde{m}$ or $\tilde{p}$ if $\forall\phi,\ \psi \in C_{[-\kappa,0]}$, it holds that

$$\|\tilde{m}(t, t_0, \phi, \psi)\| < M(\phi, \psi)\mathrm{e}^{-\lambda(t-t_0)}, \tag{15}$$

or

$$\|\tilde{p}(t, t_0, \phi, \psi)\| < M(\phi, \psi)\mathrm{e}^{-\lambda(t-t_0)}, \tag{16}$$

where $M(\phi, \psi) > 0,\ \lambda > 0$ are constants.

3 Sufficient and necessary conditions for global stability of GRNs with time-varying delays

In this section, we will propose some sufficient and necessary conditions for global asymptotic stability and global exponential stability of the zero solution of system (6).

Theorem 1. The sufficient and necessary condition for global asymptotic stability of the zero solution of system (6) (i.e., the corresponding equilibrium point (m^*, p^*) of system (4)) is that the zero solution of system (6) is globally asymptotically stable on partial variable $\tilde{m}(t, t_0, \phi, \psi)$ or $\tilde{p}(t, t_0, \phi, \psi)$.

Proof. Necessity. Since the zero solution of system (6) on all variables is globally asymptotically stable, the zero solution of system (6) on any partial variables is globally asymptotically stable. Then, the necessity obviously holds.

Sufficiency. The proof consists of two cases.

Case 1. At the outset, assume that the zero solution of (6) on partial variable $\tilde{m}(t, t_0, \phi, \psi)$ is globally asymptotically stable, that is, $\forall\tilde{\epsilon} > 0$, $\exists\delta(\tilde{\epsilon}) > 0$, when $0 < \delta(\tilde{\epsilon}) < \min\{\frac{\epsilon}{2}, \tilde{\epsilon}\}$, it holds that

$$|\tilde{m}_i(t, t_0, \phi, \psi)| < \tilde{\epsilon}, \quad |\tilde{m}_i(t - \sigma_i(t), t_0, \phi, \psi)| < \delta(\tilde{\epsilon}) < \tilde{\epsilon}. \tag{17}$$

Consider the second equation of system (6), we have

$$\tilde{p}_i(t, t_0, \phi, \psi) = \mathrm{e}^{-c_i(t-t_0)}\tilde{p}_i(t_0, t_0, \phi, \psi) + \int_{t_0}^{t} \mathrm{e}^{-c_i(t-s)} d_i\tilde{m}_i(s - \sigma_i(s), t_0, \phi, \psi)\mathrm{d}s.$$

Then, $\forall\epsilon > 0$ and $\epsilon > \max_{1\leqslant i\leqslant n}\{\frac{2d_i\tilde{\epsilon}}{c_i}\}$, one has

$$|\tilde{p}_i(t, t_0, \phi, \psi)| \leqslant \mathrm{e}^{-c_i(t-t_0)}|\tilde{p}_i(t_0, t_0, \phi, \psi)| + \int_{t_0}^{t} \mathrm{e}^{-c_i(t-s)} d_i|\tilde{m}_i(s - \sigma_i(s), t_0, \phi, \psi)|\mathrm{d}s$$

$$\leqslant \delta + \mathrm{e}^{-c_i t}\int_{t_0}^{t}\mathrm{e}^{c_i s}d_i\tilde{\epsilon}\mathrm{d}s \leqslant \delta + \frac{d_i\tilde{\epsilon}}{c_i}\left(1-\mathrm{e}^{-c_i(t-t_0)}\right)$$
$$\leqslant \delta + \frac{d_i\tilde{\epsilon}}{c_i} \leqslant \frac{\epsilon}{2}+\frac{\epsilon}{2}=\epsilon, \quad i=1,2,\ldots,n. \tag{18}$$

Then, the zero solution of system (6) (i.e., the equilibrium point (m^*, p^*) of system (4)) is stable in sense of Lypunov on partial variable $\tilde{p}$.

Since $\tilde{m}$ is globally asymptotically stable, one has

$$\lim_{t\to+\infty}\tilde{m}(t,t_0,\phi,\psi)=\lim_{t\to+\infty}[\tilde{m}_1(t,t_0,\phi,\psi),\ldots,\tilde{m}_n(t,t_0,\phi,\psi)]^{\mathrm{T}}=0.$$

Using L'Hospital's Rule [30], it yields

$$\begin{aligned}\lim_{t\to+\infty}\tilde{p}_i(t,t_0,\phi,\psi) &= \lim_{t\to+\infty}\mathrm{e}^{-c_i(t-t_0)}\tilde{p}_i(t_0,t_0,\phi,\psi)+\lim_{t\to+\infty}\mathrm{e}^{-c_i t}\int_{t_0}^{t}\mathrm{e}^{c_i s}d_i\tilde{m}_i(s-\sigma_i(s),t_0,\phi,\psi)\mathrm{d}s\\ &= 0+\lim_{t\to+\infty}\frac{\mathrm{e}^{c_i t}d_i\tilde{m}_i(t-\sigma_i(t),t_0,\phi,\psi)}{c_i\mathrm{e}^{c_i t}}\\ &= \frac{d_i}{c_i}\lim_{t\to+\infty}\tilde{m}_i(t-\sigma_i(t),t_0,\phi,\psi)=0.\end{aligned} \tag{19}$$

Then, the zero solution of system (6) on partial variable $\tilde{p}$ is globally attractive. And thus, global asymptotic stability of the zero solution of system (6) on partial variable $\tilde{m}$ implies global asymptotic stability of the zero solution of system (6) on partial variable $\tilde{p}$. Consequently, the zero solution of system (6) is globally asymptotically stable on all variables.

Case 2. It is assumed that the zero solution of (6) on partial variable $\tilde{p}(t,t_0,\phi,\psi)$ is globally asymptotically stable. Then, $\forall\epsilon>0$ and $\forall\tilde{\epsilon}>0$ such that the inequality $\sum_{j=1}^{n}\frac{\ell_{ij}\tilde{\epsilon}}{a_i}\leqslant\frac{\epsilon}{2}$ holds, $\exists\delta>0$, when $0<\delta<\min\{\frac{\epsilon}{2},\tilde{\epsilon}\}$ and $\|(\phi,\psi)\|<\delta$, such that

$$|\tilde{p}_j(t,t_0,\phi,\psi)|<\tilde{\epsilon},\quad |\tilde{p}_j(t-\tau_j(t),t_0,\phi,\psi)|<\delta<\tilde{\epsilon}. \tag{20}$$

Then, it yields

$$|\tilde{p}_j(t-\tau_j(t),t_0,\phi,\psi)|\leqslant\max\{|\tilde{p}_j(t-\tau_j(t),t_0,\phi,\psi)|,\quad|\tilde{p}_j(t,t_0,\phi,\psi)|\}<\tilde{\epsilon}.$$

Consider the first equation of system (6) and use mean valued theorem [30], one has

$$\begin{aligned}|\tilde{m}_i(t,t_0,\phi,\psi)| &\leqslant \mathrm{e}^{-a_i(t-t_0)}|\tilde{m}_i(t_0,t_0,\phi,\psi)|+\int_{t_0}^{t}\mathrm{e}^{-a_i(t-s)}\sum_{j=1}^{n}|w_{ij}(g_j(p_j(t-\tau_j(t)))-g_j(p_j^*))|\mathrm{d}s\\ &\leqslant \delta+\mathrm{e}^{-a_i t}\int_{t_0}^{t}\mathrm{e}^{a_i s}\sum_{j=1}^{n}|w_{ij}\dot{g}_j(\xi)\|\tilde{p}_j(s-\tau_j(s))|\mathrm{d}s\\ &\leqslant \delta+\mathrm{e}^{-a_i t}\int_{t_0}^{t}\mathrm{e}^{a_i s}\sum_{j=1}^{n}\ell_{ij}\tilde{\epsilon}\mathrm{d}s\leqslant\frac{\epsilon}{2}+\frac{\sum_{j=1}^{n}\ell_{ij}\tilde{\epsilon}}{a_i}\left(1-\mathrm{e}^{-a_i(t-t_0)}\right)\\ &\leqslant \frac{\epsilon}{2}+\frac{\epsilon}{2}=\epsilon,\quad i=1,2,\ldots,n.\end{aligned} \tag{21}$$

Thus, the zero solution of system (6) is stable in sense of Lypunov on partial variable $\tilde{m}(t)$.

Since $\tilde{p}$ is globally asymptotically stable, it holds that

$$\lim_{t\to+\infty}\tilde{p}(t,t_0,\phi,\psi)=\lim_{t\to+\infty}[\tilde{p}_1(t,t_0,\phi,\psi),\ldots,\tilde{p}_n(t,t_0,\phi,\psi)]^{\mathrm{T}}=0.$$

Using L'Hospital's Rule [30], one has

$$\lim_{t\to+\infty}\tilde{m}_i(t,t_0,\phi,\psi)=\lim_{t\to+\infty}\mathrm{e}^{-a_i(t-t_0)}\tilde{m}_i(t_0,t_0,\phi,\psi)+\lim_{t\to+\infty}\mathrm{e}^{-a_i t}\int_{t_0}^{t}\mathrm{e}^{a_i s}\sum_{j=1}^{n}w_{ij}\dot{g}_j(\xi)\tilde{p}_j(s-\tau_j(s))\mathrm{d}s$$

$$
\begin{aligned}
&= 0 + \lim_{t\to+\infty} \frac{\mathrm{e}^{a_i t}\sum_{j=1}^{n} w_{ij}\dot{g}_j(\xi)\tilde{p}_j(t-\tau_j(t))}{a_i \mathrm{e}^{a_i t}} \\
&= 0 + \lim_{t\to+\infty} \frac{1}{a_i}\sum_{j=1}^{n} w_{ij}\dot{g}_j(\xi)\tilde{p}_j(t-\tau_j(t)) = 0.
\end{aligned} \tag{22}
$$

Then, the zero solution of system (6) is globally attractive. And thus, the zero solution of system (6) (i.e., the equilibrium point (m^*, p^*) of system (4)) is globally asymptotically stable on partial variable $\tilde{m}$.

Consequently, the zero solution of system (6) is globally asymptotically stable on all variables $\tilde{m}$ and $\tilde{p}$. The proof is complete.

Remark 1. This theorem proposes the sufficient and necessary condition for global asymptotic stability of the zero solution of system (6); it only needs the zero solution of system (6) be globally asymptotically stable on partial variable $\tilde{m}$ or $\tilde{p}$. The famous L'Hospital's Rule and mean value theorem are used to solve this problem.

Theorem 2. The sufficient and necessary condition for global exponential stability of the zero solution of system (6) (i.e., the corresponding equilibrium point (m^*, p^*) of system (4)) is that the zero solution of (6) is globally exponentially stable on partial variable $\tilde{m}$ or $\tilde{p}$.

Proof. Necessity. Since the zero solution of system (6) is globally exponentially stable, there exist two positive constants $K(\phi,\psi) > 0$ and $\lambda > 0$, such that

$$
\begin{aligned}
&\|\tilde{m}(t,t_0,\phi,\psi)\| \leqslant \|(\tilde{m}(t,t_0,\phi,\psi),\tilde{p}(t,t_0,\phi,\psi))\| \leqslant K(\phi,\psi)\mathrm{e}^{-\lambda(t-t_0)}, \\
&\|\tilde{p}(t,t_0,\phi,\psi)\| \leqslant \|(\tilde{m}(t,t_0,\phi,\psi),\tilde{p}(t,t_0,\phi,\psi))\| \leqslant K(\phi,\psi)\mathrm{e}^{-\lambda(t-t_0)}.
\end{aligned} \tag{23}
$$

Accordingly, the necessity is obvious.

Sufficiency. The proof consists of two cases.

Case 1. At the outset, assume that the zero solution of (6) on partial variable $\tilde{m}(t,t_0,\phi,\psi)$ is globally exponentially stable, that is,

$$
|\tilde{m}_i(t,t_0,\phi,\psi)| < K_1(\phi,\psi)\mathrm{e}^{-\lambda_1(t-t_0)}, \quad i=1,2,\ldots,n, \tag{24}
$$

where $K_1(\phi,\psi) > 0,\ \lambda_1 > 0$ are constants. It is easy to obtain that

$$
\begin{aligned}
|\tilde{m}_i(t-\sigma_i(t),t_0,\phi,\psi)| &< K_1(\phi,\psi)\mathrm{e}^{-\lambda_1(t-\sigma_i(t)-t_0)} = K_1(\phi,\psi)\mathrm{e}^{\lambda_1\sigma_i(t)}\mathrm{e}^{-\lambda_1(t-t_0)} \\
&\leqslant K_1(\phi,\psi)\mathrm{e}^{\lambda_1\kappa}\mathrm{e}^{-\lambda_1(t-t_0)} = \tilde{K}_1(\phi,\psi)\mathrm{e}^{-\lambda_1(t-t_0)}, \quad i=1,2,\ldots,n,
\end{aligned}
$$

where $\tilde{K}_1(\phi,\psi) = K_1(\phi,\psi)\mathrm{e}^{\lambda_1\kappa}$.

Consider the second equation of system (6), one has

$$
\begin{aligned}
|\tilde{p}_i(t,t_0,\phi,\psi)| &\leqslant \mathrm{e}^{-c_i(t-t_0)}|\tilde{p}_i(t_0,t_0,\phi,\psi)| + d_i\int_{t_0}^{t}\mathrm{e}^{-c_i(t-s)}\tilde{K}_1(\phi,\psi)\mathrm{e}^{-\lambda_1(s-t_0)}\mathrm{d}s \\
&= \mathrm{e}^{-c_i(t-t_0)}|\tilde{p}_i(t_0,t_0,\phi,\psi)| + d_i\tilde{K}_1(\phi,\psi)\mathrm{e}^{-(c_i-\lambda_1)t}\mathrm{e}^{-\lambda_1(t-t_0)}\int_{t_0}^{t}\mathrm{e}^{(c_i-\lambda_1)s}\mathrm{d}s \\
&= \mathrm{e}^{-c_i(t-t_0)}|\tilde{p}_i(t_0,t_0,\phi,\psi)| + \frac{d_i\tilde{K}_1(\phi,\psi)}{c_i-\lambda_1}\big(1-\mathrm{e}^{-(c_i-\lambda_1)(t-t_0)}\big)\mathrm{e}^{-\lambda_1(t-t_0)}.
\end{aligned}
$$

Without loss of generality, assuming that $c_i > \lambda_1$, $i=1,2,\ldots,n$, it holds that

$$
|\tilde{p}_i(t,t_0,\phi,\psi)| \leqslant \left(|\tilde{p}_i(t_0,t_0,\phi,\psi)| + \frac{d_i\tilde{K}_1(\phi,\psi)}{c_i-\lambda_1}\right)\mathrm{e}^{-\lambda_1(t-t_0)} \leqslant H_1(\phi,\psi)\mathrm{e}^{-\lambda_1(t-t_0)}, \tag{25}
$$

where $H_1(\phi,\psi) = \max_{1\leqslant i\leqslant n}\left\{|\tilde{p}_i(t_0,t_0,\phi,\psi)| + \frac{d_i\tilde{K}_1(\phi,\psi)}{c_i-\lambda_1}\right\}$. Then, the zero solution of system (6) is globally exponentially stable on partial variable $\tilde{p}$. Thus, the zero solution of system (6) on all variables $\tilde{p}$, $\tilde{m}$ is globally exponentially stable.

Case 2. Assume that the zero solution of system (6) on partial variable $\tilde{p}(t,t_0,\phi,\psi)$ is globally exponentially stable. Then, there exist two positive constants $K_2(\phi,\psi)>0$ and $\lambda_2>0$, such that

$$|\tilde{p}_i(t,t_0,\phi,\psi)| \leqslant K_2(\phi,\psi)\mathrm{e}^{-\lambda_2(t-t_0)}, \quad i=1,2,\ldots,n. \tag{26}$$

Consider the first equation of system (6), one has

$$\begin{aligned}|\tilde{m}_i(t,t_0,\phi,\psi)| &\leqslant \mathrm{e}^{-a_i(t-t_0)}|\tilde{m}_i(t_0,t_0,\phi,\psi)| + \mathrm{e}^{-a_i t}\int_{t_0}^{t}\mathrm{e}^{a_i s}\sum_{j=1}^{n}|w_{ij}\dot{g}_j(\xi)||\tilde{p}_j(s-\tau_j(s))|\mathrm{d}s\\ &\leqslant \mathrm{e}^{-a_i(t-t_0)}|\tilde{m}_i(t_0,t_0,\phi,\psi)| + \mathrm{e}^{-a_i t}\int_{t_0}^{t}\mathrm{e}^{a_i s}\sum_{j=1}^{n}\ell_{ij}K_2(\phi,\psi)\mathrm{e}^{-\lambda_2(s-\tau_j(s)-t_0)}\mathrm{d}s\\ &\leqslant \mathrm{e}^{-a_i(t-t_0)}|\tilde{m}_i(t_0,t_0,\phi,\psi)| + \mathrm{e}^{-a_i t}\int_{t_0}^{t}\mathrm{e}^{a_i s}\sum_{j=1}^{n}\ell_{ij}K_2(\phi,\psi)\mathrm{e}^{\lambda_2\kappa}\mathrm{e}^{-\lambda_2(s-t_0)}\mathrm{d}s\\ &= \mathrm{e}^{-a_i(t-t_0)}|\tilde{m}_i(t_0,t_0,\phi,\psi)| + \mathrm{e}^{-\lambda_2(t-t_0)}\mathrm{e}^{-(a_i-\lambda_2)t}\sum_{j=1}^{n}\ell_{ij}\tilde{K}_2(\phi,\psi)\int_{t_0}^{t}\mathrm{e}^{(a_i-\lambda_2)s}\mathrm{d}s\\ &= \mathrm{e}^{-a_i(t-t_0)}|\tilde{m}_i(t_0,t_0,\phi,\psi)| + \frac{\sum_{j=1}^{n}\ell_{ij}\tilde{K}_2(\phi,\psi)}{a_i-\lambda_2}\left(1-\mathrm{e}^{-(a_i-\lambda_2)(t-t_0)}\right)\mathrm{e}^{-\lambda_2(t-t_0)},\end{aligned}$$

where $\tilde{K}_2(\phi,\psi)=K_2(\phi,\psi)\mathrm{e}^{\lambda_2\kappa}$. Without loss of generality, assuming that $a_i>\lambda_2$, $i=1,2,\ldots,n$, it holds that

$$|\tilde{m}_i(t,t_0,\phi,\psi)| \leqslant H_2(\phi,\psi)\mathrm{e}^{-\lambda_2(t-t_0)}, \tag{27}$$

where $H_2(\phi,\psi)=\max_{1\leqslant i\leqslant n}\{|\tilde{m}_i(t_0,t_0,\phi,\psi)|+\frac{\sum_{j=1}^{n}\ell_{ij}\tilde{K}_2(\phi,\psi)}{a_i-\lambda_2}\}>0$.

Then, the zero solution of system (6) (i.e., the equilibrium point (m^*,p^*) of system (4)) is globally exponentially stable on partial variable $\tilde{m}$. And thus, the zero solution of system (6) on all variables $\tilde{m}$, $\tilde{p}$ is globally exponentially stable. The proof is complete.

Theorem 3. The sufficient and necessary condition for global asymptotic stability of the zero solution of system (6) (i.e., the corresponding equilibrium point (m^*,p^*) of system (4)) is that

(I) $\tilde{m}_1,\tilde{m}_2,\ldots,\tilde{m}_{[\frac{n}{2}]+1},\tilde{p}_{[\frac{n}{2}]+2},\ldots,\tilde{p}_n$ are globally asymptotically stable

or

(II) $\tilde{p}_1,\tilde{p}_2,\ldots,\tilde{p}_{[\frac{n}{2}]+1},\tilde{m}_{[\frac{n}{2}]+2},\ldots,\tilde{m}_n$ are globally asymptotically stable,

where $[\frac{n}{2}]$ is the maximal integral number which is not larger than $\frac{n}{2}$.

Proof. Necessity. The necessity is obvious.

Sufficiency. The proof consists of two cases.

Case 1. Assume condition (I) holds. Then, for $i=1,2,\ldots,[\frac{n}{2}]+1$, $\forall\tilde{\epsilon}>0$, $\exists\delta(\tilde{\epsilon})>0$, when $0<\delta(\tilde{\epsilon})<\min\{\frac{\epsilon}{2},\tilde{\epsilon}\}$, it holds that

$$|\tilde{m}_i(t,t_0,\phi,\psi)|<\tilde{\epsilon}, \quad |\tilde{m}_i(t-\sigma_i(t),t_0,\phi,\psi)|<\delta(\tilde{\epsilon})<\tilde{\epsilon}, \tag{28}$$

and for any ϕ, $\psi\in C_{[\kappa,0]}$, it holds that

$$\lim_{t\to+\infty}\tilde{m}_i(t,t_0,\phi,\psi)=0. \tag{29}$$

Solving the differential equation about variable $\tilde{p}_i$, $i=1,2,\ldots,[\frac{n}{2}]+1$, of system (6), one has

$$\tilde{p}_i(t,t_0,\phi,\psi)=\mathrm{e}^{-c_i(t-t_0)}\tilde{p}_i(t_0,t_0,\phi,\psi)+\int_{t_0}^{t}\mathrm{e}^{-c_i(t-s)}d_i\tilde{m}_i(s-\sigma_i(s),t_0,\phi,\psi)\mathrm{d}s.$$

Then, $\forall\epsilon>\max_{1\leqslant i\leqslant[\frac{n}{2}]+1}\{\frac{2d_i\tilde{\epsilon}}{c_i}\}$, we have

$$|\tilde{p}_i(t,t_0,\phi,\psi)| \leqslant \mathrm{e}^{-c_i(t-t_0)}|\tilde{p}_i(t_0,t_0,\phi,\psi)|+\int_{t_0}^{t}\mathrm{e}^{-c_i(t-s)}d_i|\tilde{m}_i(s-\sigma_i(s),t_0,\phi,\psi)|\mathrm{d}s$$

$$\leqslant \delta + \mathrm{e}^{-c_i t}\int_{t_0}^{t} \mathrm{e}^{c_i s} d_i \tilde{\epsilon} \mathrm{d}s \leqslant \delta + \frac{d_i\tilde{\epsilon}}{c_i}\left(1-\mathrm{e}^{-c_i(t-t_0)}\right)$$
$$\leqslant \delta + \frac{d_i\tilde{\epsilon}}{c_i} \leqslant \frac{\epsilon}{2}+\frac{\epsilon}{2} = \epsilon, \quad i=1,2,\ldots,\left[\frac{n}{2}\right]+1.$$

Then, the zero solution of system (6) on variable $\tilde{p}_i,\ i=1,2,\ldots,[\frac{n}{2}]+1$ is stable in sense of Lypunov. Accordingly, the zero solution of system (6) on variable $\tilde{p}_i,\ i=1,2,\ldots,n$ is stable in sense of Lypunov.

Using L'Hospital's Rule [30], one has

$$\begin{aligned}\lim_{t\to+\infty}\tilde{p}_i(t,t_0,\phi,\psi) &= \lim_{t\to+\infty}\mathrm{e}^{-c_i(t-t_0)}\tilde{p}_i(t_0,t_0,\phi,\psi) + \lim_{t\to+\infty}\mathrm{e}^{-c_i t}\int_{t_0}^{t}\mathrm{e}^{c_i s} d_i\tilde{m}_i(s-\sigma_i(s),t_0,\phi,\psi)\mathrm{d}s \\ &= 0 + \lim_{t\to+\infty}\frac{\mathrm{e}^{c_i t} d_i\tilde{m}_i(t-\sigma_i(t),t_0,\phi,\psi)}{c_i\mathrm{e}^{c_i t}} = \frac{d_i}{c_i}\lim_{t\to+\infty}\tilde{m}_i(t-\sigma_i(t),t_0,\phi,\psi) \\ &= 0, \quad i=1,2,\ldots,\left[\frac{n}{2}\right]+1. \end{aligned} \tag{30}$$

Then, the zero solution of system (6) is globally asymptotically stable on partial variable $\tilde{p}$. Referring to Theorem 1, the zero solution of system (6) is globally asymptotically stable on all variables $\tilde{m}$ and $\tilde{p}$.

Case 2. On the other hand, suppose condition (II) holds. It is easy to obtain that the zero solution on variables $\tilde{m}_1,\tilde{m}_2,\ldots,\tilde{m}_{[\frac{n}{2}]+1}$ is globally asymptotically stable. Thus, the zero solution of system (6) on variables $\tilde{m}_1,\tilde{m}_2,\ldots,\tilde{m}_n$ is globally asymptotically stable. Referring to Theorem 1, the zero solution of system (6) on all variables is globally asymptotically stable. The proof is complete.

Theorem 4. The sufficient and necessary condition for global exponential stability of the zero solution of system (6) is

(I) $\tilde{m}_1,\tilde{m}_2,\ldots,\tilde{m}_{[\frac{n}{2}]+1},\tilde{p}_{[\frac{n}{2}]+2},\ldots,\tilde{p}_n$ are globally exponentially stable

or

(II) $\tilde{p}_1,\tilde{p}_2,\ldots,\tilde{p}_{[\frac{n}{2}]+1},\tilde{m}_{[\frac{n}{2}]+2},\ldots,\tilde{m}_n$ are globally exponentially stable.

Proof. Necessity. The necessity is obvious.

Sufficiency. The proof can follow Theorems 2 and 3. It is omitted here.

4 Sufficient conditions for global stability of GRNs with constant time delays

Consider the general GRNs with constant time delays as follows:

$$\begin{aligned}\frac{\mathrm{d}m_i}{\mathrm{d}t} &= -a_i m_i(t) + \sum_{j=1}^{n} w_{ij} g_j(p_j(t-\tau_j)) + I_i, \\ \frac{\mathrm{d}p_i}{\mathrm{d}t} &= -c_i p_i(t) + d_i m_i(t-\sigma_i), \quad i=1,2,\ldots,n,\end{aligned} \tag{31}$$

where $\tau_j,\ \sigma_i,\ i,\ j=1,2,\ldots,n$, are positive constants.

Assuming that (m^*,p^*) is the equilibrium point of system (31), let $\tilde{m}=m-m^*$, $\tilde{p}=p-p^*$. It is easy to obtain that

$$\begin{aligned}\frac{\mathrm{d}\tilde{m}_i}{\mathrm{d}t} &= -a_i\tilde{m}_i(t) + \sum_{j=1}^{n} w_{ij}(g_j(p_j(t-\tau_j)) - g_j(p_j^*)), \\ \frac{\mathrm{d}\tilde{p}_i}{\mathrm{d}t} &= -c_i\tilde{p}_i(t) + d_i\tilde{m}_i(t-\sigma_i), \quad i=1,2,\ldots,n.\end{aligned} \tag{32}$$

Local linearization is used to study the local asymptotic stability of system (32) in [12], and a sufficient condition for local asymptotic stability is obtained. We will use comparing theorem [31] and the conception of unconditional stability [24,26] to study the problems of global asymptotic stability and global exponential stability.

Let's take the Dini derivation of $|\tilde{m}_i|,\ |\tilde{p}_i|$ along system (32) as follows:

$$D^+|\tilde{m}_i| \leqslant -a_i|\tilde{m}_i(t)| + \sum_{j=1}^{n}\ell_{ij}|\tilde{p}_j(t-\tau_j)|, \quad D^+|\tilde{p}_i| \leqslant -c_i|\tilde{p}_i(t)| + d_i|\tilde{m}_i(t-\sigma_i)|, \quad i=1,2,\ldots,n. \tag{33}$$

Consider the comparing equation of (33):

$$\begin{aligned} \frac{\mathrm{d}\tilde{M}_i}{\mathrm{d}t} &= -a_i\tilde{M}_i + \sum_{j=1}^{n}\ell_{ij}\tilde{P}_j(t-\tau_j), \\ \frac{\mathrm{d}\tilde{P}_i}{\mathrm{d}t} &= -c_i\tilde{P}_i + d_i\tilde{M}_i(t-\sigma_i), \quad i=1,2,\ldots,n, \end{aligned} \tag{34}$$

one can obtain the following result.

Theorem 5. The zero solution of system (32) is globally exponentially stable if $\forall \tau_j > 0,\ \sigma_i > 0,\ \forall w \in (-\infty, +\infty)$, and the following conditions hold.

(I) The matrix $\begin{pmatrix} \mathrm{diag}(-a_i)_{n\times n} & (\ell_{ij})_{n\times n} \\ \mathrm{diag}(d_i)_{n\times n} & \mathrm{diag}(-c_i)_{n\times n} \end{pmatrix}$ is Hurwitz.

(II) $\begin{vmatrix} \mathrm{diag}(-a_i)_{n\times n} - E_{n\times n}\mathrm{e}^{-iw} & (\ell_{ij})_{n\times n}\mathrm{e}^{-iw\tau_j} \\ \mathrm{diag}(d_i)_{n\times n}\mathrm{e}^{-iw\sigma_i} & \mathrm{diag}(-c_i)_{n\times n}\mathrm{e}^{-iw\tau_j} \end{vmatrix} \neq 0.$

Proof. Referring to [31], conditions (I) and (II) are the sufficient and necessary condition of global exponential stability for comparing system (34), that is, there exist two constants $K(\phi,\psi) > 0$ and $\lambda > 0$, such that $\|(\tilde{M},\tilde{P})\| \leqslant K(\phi,\psi)\mathrm{e}^{-\lambda(t-t_0)}$.

Using comparing theorem [31], one has

$$|\tilde{m}_i(t,t_0,\phi,\psi)| \leqslant |\tilde{M}_i(t,t_0,\phi,\psi)|, \quad |\tilde{p}_i(t,t_0,\phi,\psi)| \leqslant |\tilde{P}_i(t,t_0,\phi,\psi)|.$$

Then, it holds that

$$\|(\tilde{m}(t,t_0,\phi,\psi),\tilde{p}(t,t_0,\phi,\psi))\| \leqslant \|(\tilde{M}(t,t_0,\phi,\psi),\tilde{P}(t,t_0,\phi,\psi))\| \leqslant K(\phi,\psi)\mathrm{e}^{-\lambda(t-t_0)}.$$

Consequently, the result holds.

Theorem 6. If there exist constants $\xi_i,\ \eta_i > 0,\ i=1,2,\ldots,n$, which satisfy

(I) $\xi_i a_i > \eta_i d_i,\ \eta_i c_i \geqslant \sum_{j=1}^{n}\xi_j\ell_{ji}$,

or

(II) $\xi_i a_i \geqslant \eta_i d_i,\ \eta_i c_i > \sum_{j=1}^{n}\xi_j\ell_{ji}$.

Then, the zero solution of system (32) is globally asymptotically stable.

Proof. Consider the radially unbounded Lyapunov function as follows:

$$V = \sum_{i=1}^{n}\xi_i|\tilde{m}_i(t)| + \sum_{i=1}^{n}\eta_i|\tilde{p}_i(t)| + \sum_{i=1}^{n}\eta_i\int_{t-\sigma_i}^{t}d_i|\tilde{m}_i(s)|\mathrm{d}s + \sum_{i=1}^{n}\xi_i\sum_{j=1}^{n}\int_{t-\tau_j}^{t}\ell_{ij}|p_j(s)|\mathrm{d}s. \tag{35}$$

Taking upper right hand Dini derivation along system (32), it yields

$$\begin{aligned} D^+V|_{(32)} \leqslant\ & \sum_{i=1}^{n}\xi_i\Big(-a_i|\tilde{m}_i(t)| + \sum_{j=1}^{n}\ell_{ij}|\tilde{p}_j(t-\tau_j)|\Big) + \sum_{i=1}^{n}\eta_i(-c_i|\tilde{p}_i(t)| + d_i|\tilde{m}_i(t-\sigma_i)|) + \sum_{i=1}^{n}\eta_i d_i|\tilde{m}_i(t)| \\ & - \sum_{i=1}^{n}\eta_i d_i|\tilde{m}_i(t-\sigma_i)| + \sum_{i=1}^{n}\xi_i\sum_{j=1}^{n}\ell_{ij}|\tilde{p}_j(t)| - \sum_{i=1}^{n}\xi_i\sum_{j=1}^{n}\ell_{ij}|\tilde{p}_j(t-\tau_j)| \\ =\ & \sum_{i=1}^{n}(-\xi_i a_i + \eta_i d_i)|\tilde{m}_i(t)| + \sum_{i=1}^{n}\Big(-\eta_i c_i + \sum_{j=1}^{n}\xi_j\ell_{ji}\Big)|\tilde{p}_i(t)|. \end{aligned}$$

When condition (I) holds, one has

$$D^+V|_{(32)} \leqslant \sum_{i=1}^{n}(-\xi_i a_i + \eta_i d_i)|\tilde{m}_i(t)| < 0, \quad \text{if } \tilde{m}(t) \neq 0.$$

Using LaSalle invariant theorem [24], the zero solution of system (32) on partial variable $\tilde{m}$ is globally asymptotically stable. Then, in the light of Theorem 2, the zero solution of system (32) on all variables $\tilde{m}$ and $\tilde{p}$ is globally asymptotically stable.

When condition (II) holds, one has

$$D^+V|_{(32)} \leqslant \sum_{i=1}^{n}\Big(-\eta_i c_i + \sum_{j=1}^{n}\xi_j \ell_{ji}\Big)|\tilde{p}_i(t)| < 0, \quad \text{if } \tilde{p}(t) \neq 0.$$

Then, the zero solution of system (32) on partial variable $\tilde{p}$ is globally asymptotically stable. And thus, the zero solution of system (32) on all variables $\tilde{m}$ and $\tilde{p}$ is globally asymptotically stable.

Consequently, the zero solution of system (32) is globally asymptotically stable if any condition of (I) or (II) holds.

Corollary 1. If there exist positive constants $\xi_i,\ \eta_i > 0,\ i = 1, 2, \ldots, n$, it holds that

$$\xi_i a_i > \eta_i d_i, \quad \eta_i c_i > \sum_{j=1}^{n}\xi_j \ell_{ji}.$$

Then, the zero solution of system (32) is globally exponentially stable.

Proof. Consider the same Lyapunov function of (35) and take the upper right-hand Dini derivative, we have

$$D^+V|_{(32)} \leqslant \sum_{i=1}^{n}(-\xi_i a_i + \eta_i d_i)|\tilde{m}_i(t)| + \sum_{i=1}^{n}\Big(-\eta_i c_i + \sum_{j=1}^{n}\xi_j \ell_{ji}\Big)|\tilde{p}_i(t)| \leqslant -K\|(\tilde{m}, \tilde{p})\|, \tag{36}$$

where $K > 0$ is a constant. Then, the zero solution of system (32) is globally exponentially stable.

Theorem 7. The zero solution of system (32) is globally exponentially stable if the following matrix is a M-matrix:

$$A = \begin{pmatrix} \mathrm{diag}(a_i)_{n\times n} & (-\ell_{ij})_{n\times n} \\ \mathrm{diag}(-d_i)_{n\times n} & \mathrm{diag}(c_i)_{n\times n} \end{pmatrix}. \tag{37}$$

Proof. Since A is a M-matrix, A^{T} is a M-matrix. Furthermore, there exists a positive constant vector $\zeta = [\xi_1, \xi_2, \ldots, \xi_n, \eta_1, \eta_2, \ldots, \eta_n]^{\mathrm{T}} > 0$, such that $A^{\mathrm{T}}\zeta > 0$ [24]. Then, it holds that

$$-\xi_i a_i + \eta_i d_i < 0, \quad -\eta_i c_i + \sum_{j=1}^{n}\xi_j \ell_{ji} < 0.$$

Then, referring to Corollary 1, the result is obtained.

5 Illustrative example

For the purpose of illustrating the effectiveness of our theoretical results in the previous sections, we present a famous GRNs composed of three nodes with time-varying delays and constant time delays, respectively.

The genetic repressilatory network has been theoretically predicted and experimentally verified in [3] and [4]. It consists of three repressor protein concentrations p_i and their mRNA concentrations m_i (where i is lacl, tetR, cl). The dynamic model is described by

$$\dot{m}_i(t) = -m_i(t) + \frac{\alpha}{1 + p_j^h(t-\tau_j)}, \quad \dot{p}_i(t) = -c_i p_i(t) + d_i m_i(t-\sigma_i). \tag{38}$$

where $m_i \in \mathbb{R},\ p_i \in \mathbb{R}$. $i =$ lacl, tetR, cl and $j =$ cl, lacl, tetR. If lacl $= 1$, tetR $= 2$, cl $= 3$, then, (i, j) has the following three pairs of values to be selected: $(1, 2),\ (2, 3),\ (3, 1)$. $h > 0$ is a Hill coefficient, $c_i > 0$ denotes the protein decay rate, and d_i represents the translation rate of ith gene.

For convenience of our discussion, we introduce some parameters and time-varying delays into system (38) and rewrite them as follows:

$$\dot{m}_i(t) = -a_i m_i(t) + \sum_{j=1}^{n} w_{ij}\frac{p_j^{h_j}(t-\tau_j(t))}{1 + p_j^{h_j}(t-\tau_j(t))} + I_i, \quad \dot{p}_i(t) = -c_i p_i(t) + d_i m_i(t-\sigma_i(t)), \tag{39}$$

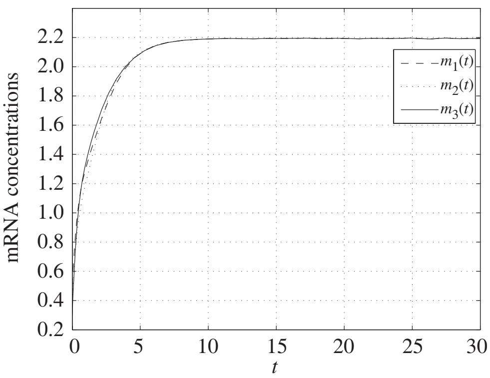

Figure 1 The trajectory of the mRNA concentrations of (39) with $a_1 = a_2 = a_3 = 2$.

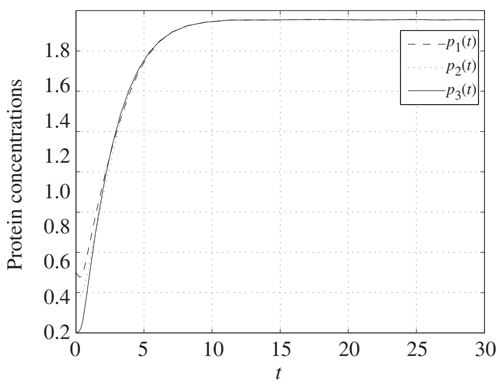

Figure 2 The trajectory of the protein concentrations of (39) with $a_1 = a_2 = a_3 = 2$.

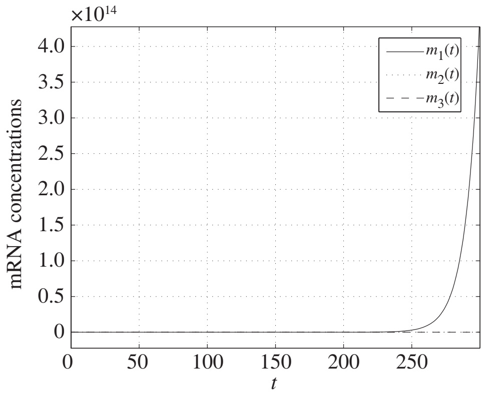

Figure 3 The trajectory of the mRNA $m(t)$ of (39) with $a_1 = -0.1,\ a_2 = a_3 = 2$.

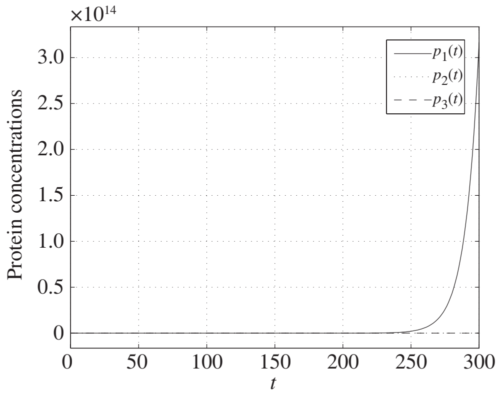

Figure 4 The trajectory of the protein $p(t)$ of (39) with $a_1 = -0.1,\ a_2 = a_3 = 2$.

where $a_i = 2,\ c_i = 1,\ d_i = 0.8,\ h_j = 2,\ \tau_j(t) = (|\sin(t)| + 1)/4,\ \sigma_i(t) = (|\cos(t)| + 1)/8$ and

$$W = \begin{bmatrix} 0 & 2.5 & 0 \\ 0 & 0 & 2.5 \\ 2.5 & 0 & 0 \end{bmatrix}, \quad I = \begin{bmatrix} 2.5 \\ 2.5 \\ 2.5 \end{bmatrix}.$$

The equilibrium point can be computed as (m^*, p^*), where $m_1^* = m_2^* = m_3^* = 2.1936,\ p_1^* = p_2^* = p_3^* = 1.7549$. For the initial states, $m_0 = [1, 0.8, 0.6]^{\mathrm{T}},\ p_0 = [0.5, 0.4, 0.2]^{\mathrm{T}},\ \phi_{s\in[-\kappa,0]} = m_0,\ \psi_{s\in[-\kappa,0]} = p_0$. The trajectories of mRNA and protein concentrations in system (39) with $a_1 = a_2 = a_3 = 2$ are plotted in Figure 1 and Figure 2, respectively. They indicate that this system is globally asymptotically stable on all variables $m(t)$ and $p(t)$. If we only change one parameter $a_1 = 2$ to $a_1 = -0.1$, we can obtain Figures 3 and 4. It is easy to see that $m_1(t)$ and $p_1(t)$ are unstable.

Now, we consider system (39) with constant time delay, and the system can be described as follows:

$$\dot{m}_i(t) = -a_i m_i(t) + \sum_{j=1}^{n} w_{ij} g_j(t - \tau_j) + I_i, \quad \dot{p}_i(t) = -c_i p_i(t) + d_i m_i(t - \sigma_i), \tag{40}$$

where $g_j(t - \tau_j) = p_j^{h_j}(t - \tau_j)/(1 + p_j^{h_j}(t - \tau_j))$. It is easy to see that $|\dot{g}_j(\cdot)| \leqslant 0.65$. Let the parameters $c_i,\ d_i,\ w_{ij},\ I_i$ be the same values presented previously, and $a_i = 2,\ i = 1, 2, 3$. Then, one has $\ell_{12} = |w_{12}\dot{g}_2(\cdot)| \leqslant 2.5 \times 0.65 = 1.625,\ \ell_{23} = |w_{23}\dot{g}_3(\cdot)| \leqslant 1.625,\ \ell_{31} = |w_{31}\dot{g}_1(\cdot)| \leqslant 1.625,\ \ell_{11} = \ell_{13} = \ell_{21} = \ell_{22} = \ell_{32} = \ell_{33} = 0$.

Let $\xi_1 = \xi_2 = \xi_3 = 0.5,\ \eta_1 = \eta_2 = \eta_3 = 1$, then

$$-\xi_1 a_1 + \eta_1 d_1 = -0.2 < 0,\ -\xi_2 a_2 + \eta_2 d_2 = -0.2 < 0,\ -\xi_3 a_3 + \eta_3 d_3 = -0.2 < 0,$$

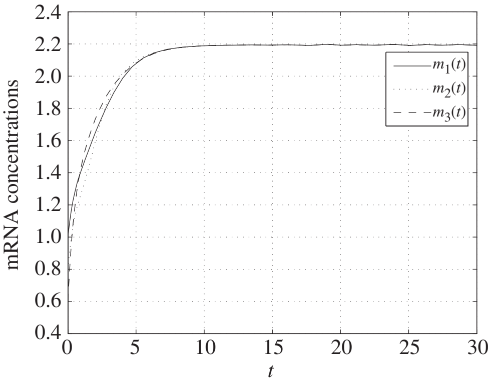

Figure 5 The trajectory of the mRNA concentrations of (40) with $a_1 = 2, a_2 = a_3 = 2$.

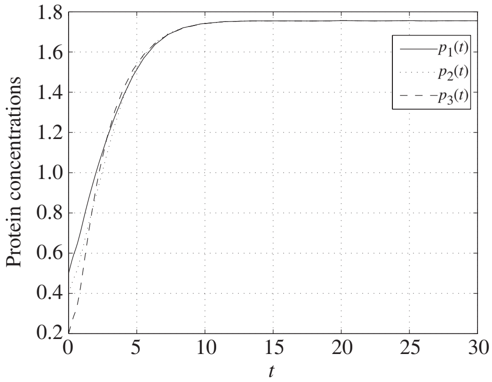

Figure 6 The trajectory of the protein concentrations of (40) with $a_1 = 2, a_2 = a_3 = 2$.

$$-\eta_1 c_1 + \sum_{j=1}^{3} \xi_j \ell_{j1} = -0.1875 < 0, \ -\eta_2 c_2 + \sum_{j=1}^{3} \xi_j \ell_{j2} = -0.1875 < 0, \ -\eta_3 c_3 + \sum_{j=1}^{3} \xi_j \ell_{j3} = -0.1875 < 0.$$

By Theorem 7, system (40) is globally exponentially stable. Figures 5 and 6 show trajectories of the mRNA and protein concentrations of system (40) with the same initial states as given previously.

6 Conclusion

In this paper, we studied global asymptotic stability and global exponential stability of GRNs with time-varying delays and constant time delays. Four sufficient and necessary conditions for global asymptotic stability and global exponential stability of GRNs with time-varying delays are proposed. Specially, three sufficient conditions for global asymptotic stability and global exponential stability of GRNs with constant time delays are presented. Then, a famous example is given to illustrate our proposed results such as global asymptotic stability, global exponential stability, and instability.

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Conflict of interest The authors declare that they have no conflict of interest.

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