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Research Article

Stability Analysis of Delayed Genetic Regulatory Networks via a Relaxed Double Integral Inequality

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Time delay arising in a genetic regulatory network may cause the instability. This paper is concerned with the stability analysis of genetic regulatory networks with interval time-varying delays. Firstly, a relaxed double integral inequality, named as Wirtinger-type double integral inequality (WTDII), is established to estimate the double integral term appearing in the derivative of Lyapunov-Krasovskii functional with a triple integral term. And it is proved theoretically that the proposed WTDII is tighter than the widely used Jensen-based double inequality and the recently developed Wiringter-based double inequality. Then, by applying the WTDII to the stability analysis of a delayed genetic regulatory network, together with the usage of useful information of regulatory functions, several delay-range- and delay-rate-dependent (or delay-rate-independent) criteria are derived in terms of linear matrix inequalities. Finally, an example is carried out to verify the effectiveness of the proposed method and also to show the advantages of the established stability criteria through the comparison with some literature.

1. Introduction

In the past few years, genetic regulatory networks (GRNs), which describe the interactions of many molecules (DNA, RNA, proteins, etc.), have been becoming a new research area of biological and biomedical sciences [1–4]. Mathematical modelling based on the extracted functional information from the time-series data provides a useful tool for studying gene regulation processes in living organisms [5, 6], and a large variety of formalisms have been proposed to model and simulate GRNs, such as directed graphs, Boolean networks, and nonlinear differential equations [7]. Among them, the nonlinear differential equation model can provide more detailed understanding and insights into the nonlinear dynamical behavior exhibited by GRNs [8].

Since mRNAs and proteins in the GRNs may be synthesized at different locations, an important issue in modelling GRNs is that the slow processes of transcription, translation, and translocation result in sizable delays [9–11]. Time delays arising in the GRNs may lead to wrong prediction of dynamic behaviors [12, 13], which may lead to very serious consequences. The stability is essential for designing or controlling genetic regulatory networks [14]; it is of a great significance to study the influence of delays on the stability of the GRNs.

Up to now, a huge number of results on the stability of the delayed GRNs have been reported in the literature (see, e.g., [15–58]). The sufficient and necessary local stability criteria were firstly given for the GRNs with constant delay in [15, 16]. However, local stability is not enough for understanding nonlinear GRNs; the globally asymptotical stability of GRNs with SUM regulatory functions has been widely investigated [17–22]. Meanwhile, by taking into account the unavoidable uncertainties caused by modelling errors and parameter fluctuations, many scholars paid attentions to the robust stability analysis of the delayed GRNs [23–36]. Moreover, both the intrinsic noise derived from the random births and deaths of individual molecules and the extrinsic noise due to environment fluctuations make the gene regulation process an intrinsically noisy process [59]. Thus, many researches aimed at the robust stability analysis of the GRNs in consideration of those noises [37–46]. Also, some results have considered both the uncertainties and the noises [47–52]. In addition, based on the definition of convergence rate index, the exponential stability problem was also studied in [53–57].

On the other hand, no matter what type of stability problems is concerned, the analysis methods for finding stability criteria have always been an important topic. To the best of the authors' knowledge, there are mainly two methods that have been used for the delayed GRNs. The first type of method is the M-matrix-based method. For example, the delay- and rate-independent stability criteria were proposed in [20], the delay-independent but rate-dependent criteria were established in [23, 44], and the delay- and rate-dependent criteria were developed in [21, 22]. The stability of the GRNs through those M-matrix-based criteria is judged by verifying whether or not a matrix is a nonsingular M-matrix. Although the computational complexity is low, those criteria are just available for slow-varying delay case [20–23, 44]. However, the time delays encountered in GRNs may be fast-varying or random changing. The M-matrix-based method is inapplicable for those cases. The second type of method is based on the framework of Lyapunov-Krasovskii functional (LKF) and linear matrix inequality (LMI). The LKF-based method can be used to handle all time delays mentioned before and it is available for not only stability analysis but also many other problems, like controller synthesis, state estimation, filter design, passivity analysis, and so on [13, 59–70]. Meanwhile, the LMI-based criteria can be easily checked through MATLAB/LMI toolbox for determining the system stability. Therefore, most existing researches for the GRNs are based on this type of method [17–19, 25–43, 45–56].

The problem of stability analysis by using the LKF and the LMI is that the criterion obtained has more or less conservatism. It is well-known that the criterion with less conservatism means that it can derive an admissible maximum upper bound such that the understudied GRNs maintains global asymptotical stability. It is predictable that the form of the LKF candidate is tightly related to the conservatism of the obtained criteria. Thus, the key point of the stability analysis based on such framework is to find an LKF satisfying some requirements for ensuring the globally asymptotical stability of the GRNs.

In most researches, the used LKFs were constructed by introducing delay-based single and/or double integral terms into the typical nonintegral quadratic form of Lyapunov function for delay-free systems [17, 18, 28–33, 35–42, 46–50, 53–55]. Based on a predictable fact that the conservatism-reducing of criteria can be achieved by constructing more general LKF, two types of more general LKFs have been developed to reduce the conservatism. The first one is the delay-partition-based LKFs, which is constructed by dividing the delay interval into several small subintervals and then replacing the original integral terms with multiple new integral terms based on delay subintervals. This type of LKF has been used to investigate the robust stability of various GRNs [25, 26, 51], the exponential stability of switch GRNs [56], and the stochastic stability of jumping GRNs [27, 43, 45]. The other is the augmented LKF constructed by using various state vectors (current and delayed and/or integrated state vectors, etc.) to augment the quadratic terms of original LKFs, and it has been used to derive the improved stability criteria of the GRNs [19, 34, 52].

Beside the above-mentioned two types of improved LKFs, a new LKF including triple integral terms firstly developed in [71] is proved to be very useful to reduce the conservatism. However, only a few researches of the GRNs have applied such type of LKF. The LKF with triple integral terms was used to discuss the asymptotical stability of the GRNs [19, 34]. The following form of double integral term will be introduced into the derivative of the LKF with a triple integral term:

$$-\int_a^b \int_s^b y^T(u) Zy(u)\,du\,ds, \quad Z > 0. \tag{1}$$

As mentioned in [72], the effective estimation of the above term is strongly linked to the conservatism of the criteria. To the best of the authors' knowledge, for the researches referring to the triple integral term in the LKFs, most literature directly applied the Jensen-based double integral inequality (JBDII) (see (17) for details) to achieve the estimation task [34]. Although an improved integral inequality was developed in [19], it is also derived based on Jensen inequality. Very recently, a Wirtinger-based double integral inequality (WBDII) was developed to general linear time-delay system and it was proved to be less conservative than the JBDII [72]. However, such inequality has not been used to discuss the GRNs. Furthermore, the gap between term (1) and its estimated value obtained by the WBDII still leads to conservatism. Therefore, it can be expected that the results may be further improved if a new estimation method that brings tighter gap is applied for term (1). This is the motivation of the paper.

This paper further investigates the delay-dependent stability of the GRNs by developing a more effective inequality to estimate the double integral term (1). The contributions of the paper are summarized as follows:

(1) A relaxed double integral inequality, that is, Wiringter-type double integral inequality (WTDII), is established to estimate the double integral term. Compared with the widely used JBDII and the recently developed WTDII, the presented WTDII is theoretically proved to be the tightest.

(2) Two less conservative stability criteria of the GRNs are derived. For the GRNs with time-varying delays satisfying different conditions, two stability criteria are, respectively, established by applying the proposed WTDII to estimate the double integral terms appearing in the derivative of the LKFs.

The rest of the paper is organized as follows. Problem statements and preliminaries are presented in Section 2. In Section 3, the development and the comparison of the WTDII approach are discussed in detail. Two stability criteria of the GRN with time-varying delay are derived through the WTDII in Section 4. An example is given to show the validity

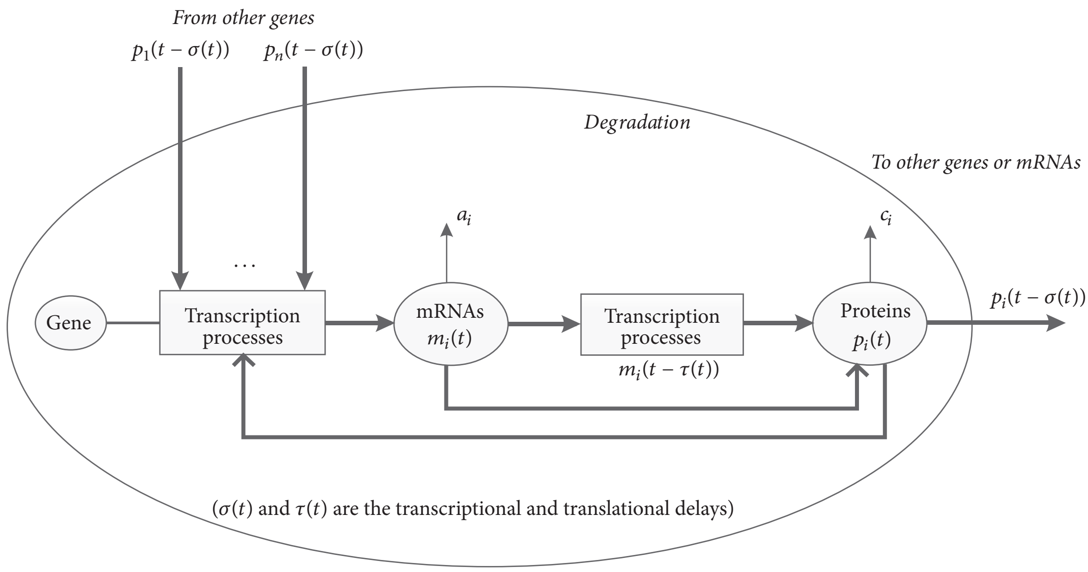

FIGURE 1: GRNs with time-varying feedback regulation delays and translational delays.

of the obtained results in Section 5. Finally, in Section 6, the conclusions are drawn.

In the Notations, the list of notations and abbreviations used throughout this paper is shown.

2. Problem Formulation and Preliminary

This section describes the problem to be investigated and gives some necessary preliminaries.

2.1. Problem Formulation. The following nonlinear differential equations have been used recently to describe the GRNs with time-varying feedback regulation delays and translational delays [28]:

$$\begin{aligned}\dot{m}_i(t) &= -a_i m_i(t) \\ &\quad + b_i\left(p_1(t-\sigma(t)), p_2(t-\sigma(t)), \ldots, p_n(t-\sigma(t))\right), \\ \dot{p}_i(t) &= -c_i p_i(t) + d_i m_i(t-\tau(t))\end{aligned} \quad (2)$$

as shown in Figure 1, where $m_i(t)$ and $p_i(t)$ are the concentrations of the ith mRNA and protein, respectively. $a_i > 0$ and $c_i > 0$ are the positive real numbers that represent the degradation rate of the ith mRNA and protein, respectively. $d_i > 0$ is the positive real number that represents the translating rate from mRNA i to protein i. b_i is the regulatory function of the ith gene. $\sigma(t)$ and $\tau(t)$ are the transcriptional and translational delays, respectively.

Since each transcription factor acts additively to regulate the gene, it is usual to assume that the regulatory function b_i satisfies the following SUM logic [37]:

$$b_i\left(p_1(t), p_2(t), \ldots, p_n(t)\right) = \sum_{j=1}^{n} b_{ij} p_j(t) \quad (3)$$

and b_{ij} is a monotonic function of the Hill form; that is,

$$b_{ij} = \begin{cases} \dfrac{\alpha_{ij}}{1+\left(x/\beta_j\right)^{H_j}}, & \text{if transcription factor } j \text{ represses gene } i \\ \dfrac{\alpha_{ij}\left(x/\beta_j\right)^{H_j}}{1+\left(x/\beta_j\right)^{H_j}}, & \text{if transcription factor } j \text{ activates gene } i, \end{cases} \quad (4)$$

where α_{ij} is bounded constant that denotes the dimensionless transcriptional rate of transcription factor j to gene i, β_j is a positive scalar, and H_j is the Hill coefficient that represents the degree of cooperativity.

The transcriptional and translational delays, $\sigma(t)$ and $\tau(t)$, are assumed to satisfy the following two different conditions.

Case 1. $\tau(t)$ and $\sigma(t)$ satisfy

$$\begin{gathered} 0 \le \tau_1 \le \tau(t) \le \tau_2, \\ 0 \le \sigma_1 \le \sigma(t) \le \sigma_2, \\ \dot{\tau}(t) \le \tau_d, \\ \dot{\sigma}(t) \le \sigma_d. \end{gathered} \quad (5)$$

Case 2. $\tau(t)$ and $\sigma(t)$ satisfy

$$\begin{gathered} 0 \le \tau_1 \le \tau(t) \le \tau_2, \\ 0 \le \sigma_1 \le \sigma(t) \le \sigma_2. \end{gathered} \quad (6)$$

Clearly, based on (3), GRN (2) can be rewritten as [19]

$$\begin{aligned}\dot{m}_i(t) &= -a_i m_i(t) + \sum_{j=1}^{n} w_{ij} g_j\left(p_j(t-\sigma(t))\right) + l_i, \\ \dot{p}_i(t) &= -c_i p_i(t) + d_i m_i(t-\tau(t)),\end{aligned} \quad (7)$$

where $l_i = \sum_{j\in\mathscr{V}_i} \alpha_{ij}$ with $\mathscr{V}_i$ being the set of all the transcription factors j which are repressors of gene i; $w_{ij} = \alpha_{ij}$ if transcription factor j activates gene i, $w_{ij} = 0$ if there is no connection between j and i, and $w_{ij} = -\alpha_{ij}$ if transcription factor j represses gene i; and $g_j(x) = (x/\beta_j)^{H_j}/(1 + (x/\beta_j)^{H_j})$, $x \geq 0$ is a monotonically increasing function satisfying

$$\rho \leq \frac{g_j(s_1) - g_j(s_2)}{s_1 - s_2} \leq \rho_i \tag{8}$$

with $\rho = \min_{s\geq 0} \dot{g}_j(s) = 0$ and

$$\rho_i = \max_{s\geq 0} \dot{g}_j(s) = \frac{\left(H_j - 1\right)^{(H_j-1)/H_j}\left(H_j + 1\right)^{(H_j+1)/H_j}}{4\beta_j H_j}. \tag{9}$$

GRN (7) can be expressed as the following vector-matrix form:

$$\begin{aligned} \dot{m}(t) &= -Am(t) + Wg\left(p\left(t - \sigma(t)\right)\right) + l, \\ \dot{p}(t) &= -Cp(t) + Dm(t - \tau(t)), \end{aligned} \tag{10}$$

where $m(t) = [m_1(t), m_2(t), \ldots, m_n(t)]^T$, $p(t) = [p_1(t), p_2(t), \ldots, p_n(t)]^T$, $A = \operatorname{diag}\{a_1, a_2, \ldots, a_n\} > 0$, $C = \operatorname{diag}\{c_1, c_2, \ldots, c_n\} > 0$, $D = \operatorname{diag}\{d_1, d_2, \ldots, d_n\} > 0$, $g(p(t)) = [g_1(p_1(t)), g_2(p_2(t)), \ldots, g_n(p_n(t))]^T$, $W = [w_{ij}]_{n\times n}$, and $l = [l_1, l_2, \ldots, l_n]$.

Let (m^*, p^*) be the equilibrium point (steady state) of (10); that is, $-Am^* + Wg(p^*) + l = 0$ and $-Cp^* + Dm^* = 0$. Using the transformations $x(t) = m(t) - m^*$ and $y(t) = p(t) - p^*$, one can shift the equilibrium point (m^*, p^*) to the origin and rewrite (10) as the following GRN:

$$\begin{aligned} \dot{x}(t) &= -Ax(t) + Wf\left(y\left(t - \sigma(t)\right)\right), \\ \dot{y}(t) &= -Cy(t) + Dx(t - \tau(t)), \end{aligned} \tag{11}$$

where $f(s) = [f_1(s), f_2(s), \ldots, f_n(s)]^T$ and $f_i(y(t)) = g_i(y(t) + p^*) - g_i(p^*)$ with $f_i(0) = 0$. Then,

$$\frac{f_i(s_1) - f_i(s_2)}{s_1 - s_2} = \frac{g_i(s_1 + p^*) - g_i(s_2 + p^*)}{s_1 + p^* - (s_2 + p^*)}. \tag{12}$$

Thus, it follows from (8) and $f_i(0) = 0$ that

$$0 \leq \frac{f_i(s_1) - f_i(s_2)}{s_1 - s_2} \leq \rho_i, \quad s_1 \neq s_2, \tag{13}$$

$$0 \leq \frac{f_i(s)}{s} \leq \rho_i, \quad s \neq 0. \tag{14}$$

This paper aims to analyze the asymptotical stability of GRN (2) and to determine the delay bounds, named as maximal admissible delay bounds (MADBs), under which the GRN is asymptotically stable. In order to achieve this aim, this paper will develop a new double integral inequality (i.e., WTDII) for estimating the double integral term (1) so as to derive some less conservative stability criteria.

2.2. Preliminaries. Several lemmas used to obtain the main results are given as follows.

For the estimation of single integral term, the most popular technique is Wirtinger-based inequality, shown as Lemma 1.

Lemma 1 (Wirtinger-based inequality [73]). *For symmetric positive-definite matrix $R \in \mathscr{R}^{n\times n}$, scalars $a < b$, and vector $\omega : [a,b] \mapsto \mathscr{R}^n$ such that the integration concerned is well defined, the following inequality holds:*

$$\int_a^b \omega^T(s) R\omega(s)\, ds \geq \frac{1}{b-a}\begin{bmatrix}\chi_a \\ \chi_b\end{bmatrix}^T \begin{bmatrix} R & 0 \\ 0 & 3R\end{bmatrix}\begin{bmatrix}\chi_a \\ \chi_b\end{bmatrix}, \tag{15}$$

where $\chi_a = \int_a^b \omega(s)ds$ and $\chi_b = \chi_a - (2/(b-a))\int_a^b\int_a^s \omega(u)du\,ds = -\chi_a + (2/(b-a))\int_a^b\int_s^b \omega(u)du\,ds$.

The auxiliary function-based integral inequality, which encompasses the Wirtinger-based inequality, has been developed in recent years.

Lemma 2 (auxiliary function-based integral inequality [74]). *For symmetric positive-definite matrix $R \in \mathscr{R}^{n\times n}$, scalars $a < b$, and vector $\omega : [a,b] \mapsto \mathscr{R}^n$ such that the integration concerned is well defined, the following inequality holds*

$$\begin{aligned} (b-a)\int_a^b \dot{\omega}^T(s) R\dot{\omega}(s)\, ds \\ \geq \chi_1^T R\chi_1 + 3\chi_2^T R\chi_2 + 5\chi_3^T R\chi_3, \end{aligned} \tag{16}$$

where $\chi_1 = \omega(b) - \omega(a)$, $\chi_2 = \omega(b) + \omega(a) - (2/(b-a))\int_a^b \omega(s)ds$, and $\chi_3 = \omega(b) - \omega(a) + (6/(b-a))\int_a^b \omega(s)ds - (12/(b-a)^2)\int_a^b\int_s^b \omega(u)du\,ds$.

For the estimation of double integral term, the JBDII is widely applied in [71], and, with its improvement, the WBDII was developed in [72] very recently, respectively shown as Lemmas 3 and 4.

Lemma 3 (Jensen-based double integral inequality (JBDII) [71]). *For symmetric positive-definite matrix $Z \in \mathscr{R}^{n\times n}$, scalars $a < b$, and vector $\nu : [a,b] \mapsto \mathscr{R}^n$ such that the integration concerned is well defined, the following inequality holds:*

$$\frac{(b-a)^2}{2}\int_a^b\int_s^b \nu^T(u) Z\nu(u)\, du\, ds \geq \chi_4^T Z\chi_4, \tag{17}$$

where $\chi_4 = \int_a^b\int_s^b \nu(u)du\,ds$.

Lemma 4 (Wirtinger-based double integral inequality (WBDII) [72]). *For symmetric positive-definite matrix $Z \in \mathscr{R}^{n\times n}$, scalars $a < b$, and vector $\nu : [a,b] \mapsto \mathscr{R}^n$ such* *that the integration concerned is well defined, the following inequality holds:*

$$\frac{(b-a)^2}{2}\int_a^b\int_s^b \nu^T(u) Z\nu(u)\,du\,ds \geq \chi_4^T Z\chi_4 + 2\chi_5^T Z\chi_5, \tag{18}$$

where $\chi_5 = -\chi_4 + (3/(b-a))\int_a^b\int_s^b\int_\theta^b \nu(u)du\,d\theta\,ds$ *with* χ_4 *given in Lemma 3.*

For time-varying delay, when using the integral inequality, the reciprocally convex lemma is needed, and its simple form can be reformulated as Lemma 5.

Lemma 5 (reciprocally convex combination lemma [75]). *For any vectors* β_1 *and* β_2*, symmetric matrix R, any matrix S, and real scalar* $0 \leq \alpha \leq 1$ *satisfying* $\left[\begin{smallmatrix} R & S \\ * & R\end{smallmatrix}\right] \geq 0$*, the following inequality holds:*

$$\frac{1}{\alpha}\beta_1^T R\beta_1 + \frac{1}{1-\alpha}\beta_2^T R\beta_2 \geq \begin{bmatrix}\beta_1\\ \beta_2\end{bmatrix}^T \begin{bmatrix} R & S\\ * & R\end{bmatrix}\begin{bmatrix}\beta_1\\ \beta_2\end{bmatrix}. \tag{19}$$

3. A Relaxed Double Integral Inequality and Its Advantages

This section develops a new integral inequality, that is, the WTDII, to estimate the double integral terms existing. The comparison of the WTDII and the existing double integral inequalities is also given.

Based on the technique of integral in parts, the following WTDII is given.

Lemma 6. *For symmetric positive-definite matrix* $Z \in \mathscr{R}^{n\times n}$*, scalars* $a < b$*, and vector* $\nu : [a,b] \mapsto \mathscr{R}^n$ *such that the integration concerned is well defined, the following inequality holds:*

$$\frac{(b-a)^2}{2}\int_a^b\int_s^b \nu^T(u) Z\nu(u)\,du\,ds \geq \chi_4^T Z\chi_4 + 8\chi_5^T Z\chi_5, \tag{20}$$

where χ_4 *and* χ_5 *are defined in Lemmas 3 and 4.*

Proof. For a function $\lambda(u) = k_1 + k_2 u$, the calculation through integration by parts leads to

$$\int_a^b\int_s^b \lambda(u)\nu(u)\,du\,ds = \lambda(a)\int_a^b\int_s^b \nu(u)\,du\,ds + 2k_2\int_a^b\int_s^b\int_\theta^b x(u)\,du\,d\theta\,ds. \tag{21}$$

By setting $\lambda(a) = -1$, $2k_2 = 3/(b-a)$, that is, $\lambda(u) = (-a-2b)/2(b-a) + (3/2(b-a))u$, the above equality is rewritten as

$$\int_a^b\int_s^b \lambda(u)\nu(u)\,du\,ds = \chi_5. \tag{22}$$

Then the following equality is obtained for any vector χ_0 and any matrix M:

$$\int_a^b\int_s^b \lambda(u)\chi_0^T M\nu(u)\,du\,ds = \chi_0^T M\chi_5. \tag{23}$$

Similarly, the following equalities are derived:

$$\begin{aligned}
&\int_a^b\int_s^b \chi_0^T L\nu(u)\,du\,ds = \chi_0^T L\chi_4,\\
&\int_a^b\int_s^b \chi_0^T LR^{-1}L^T\chi_0 du\,ds = \frac{(b-a)^2}{2}\chi_0^T LR^{-1}L^T\chi_0,\\
&\int_a^b\int_s^b \chi_0^T LR^{-1}M^T\lambda(u)\chi_0 du\,ds = 0,\\
&\int_a^b\int_s^b \lambda^2(u)\chi_0^T MR^{-1}M^T\chi_0 du\,ds\\
&\quad = \frac{(b-a)^2}{16}\chi_0^T MR^{-1}M^T\chi_0.
\end{aligned} \tag{24}$$

Therefore, using the above five equalities and the Schur complement derives the following equality:

$$\begin{aligned}
&\int_a^b\int_s^b \begin{bmatrix}\chi_0\\ \lambda(u)\chi_0\\ \nu(u)\end{bmatrix}^T \cdot \begin{bmatrix} LZ^{-1}L^T & LZ^{-1}M^T & L\\ * & MZ^{-1}M^T & M\\ * & * & Z\end{bmatrix}\begin{bmatrix}\chi_0\\ \lambda(u)\chi_0\\ \nu(u)\end{bmatrix} du\,ds\\
&= \int_a^b\int_s^b \nu^T(u) R\nu(u)\,du\,ds + \mathrm{Sym}\left\{\chi_0^T L\chi_4 + \chi_0^T M\chi_5\right\} + \frac{(b-a)^2}{2}\\
&\quad\cdot \chi_0^T\left(\frac{8LZ^{-1}L^T + MZ^{-1}M^T}{8}\right)\chi_0 \geq 0.
\end{aligned} \tag{25}$$

By letting $\chi_0^T = [\chi_4^T, \chi_5^T]$, $L = -(2/(b-a)^2)[Z, 0]^T$, and $M = -(16/(b-a)^2)[0, Z]$, that is, $\chi_0^T L = -(2/(b-a)^2)\chi_4^T Z$ and $\chi_0^T M = -(16/(b-a)^2)\chi_5^T Z$, then (25) leads to

$$\int_a^b\int_s^b \nu^T(u) Z\nu(u)\,du\,ds \geq \frac{2}{(b-a)^2}\left(\chi_4^T Z\chi_4 + 8\chi_5^T Z\chi_5\right). \tag{26}$$

Thus (20) holds. This completes the proof. □

Remark 7. Based on the comparison of the proposed WTDII (20) with the widely used JBDII (17) and the recently developed WBDII (18), it can be found that WTDII (20) provides the tightest estimation value of the double integral term (1).

More specifically, compared with the widely used JBDII (17), the extra positive term $8\chi_5^T Z\chi_5$ reduces the gap between the original double integral term (1) and its estimated value; and, compared with the recently developed WBDII (18), the extra positive term $6\chi_5^T Z\chi_5$ reduces the estimation gap. As mentioned in [72–74], it is helpful to reduce the conservatism by reducing such estimation gap. Therefore, the proposed WTDII (20) will lead to less conservative criteria than the ones derived by JBDII (17) [19] or WBDII (18).

By setting $\nu(u) = \dot{\omega}(u)$, the following lemma can be directly obtained from Lemma 6.

Lemma 8. *For symmetric positive-definite matrix $Z \in \mathscr{R}^{n\times n}$, scalars $a < b$, and vector $\dot{\omega} : [a, b] \mapsto \mathscr{R}^n$ such that the integration concerned is well defined, the following inequality holds:*

$$\int_a^b \int_s^b \dot{\omega}^T(u) Z\dot{\omega}(u)\,du\,ds \geq 2\theta_1^T Z\theta_1 + 16\theta_2^T Z\theta_2, \tag{27}$$

where $\theta_1 = (1/(b-a))\chi_4|_{\nu(u)=\dot{\omega}(u)} = \omega(b) - \int_a^b(\omega(s)/(b-a))ds$ *and* $\theta_2 = (1/(b-a))\chi_5|_{\nu(u)=\dot{\omega}(u)} = -(1/2)\omega(b) - \int_a^b(\omega(s)/(b-a))ds + 3\int_a^b\int_s^b(\omega(u)/(b-a)^2)du\,ds$.

4. Delay-Dependent Stability Analysis of GRN

This section derives delay-dependent stability criteria of GRN (2) by constructing the LKF with triple integral terms and applying the proposed WTDII (20) to estimate the double integral terms appearing in its derivative.

The following notations are introduced at first for simplifying the representation of subsequent parts:

$$\begin{aligned}
\tau_{1\tau}(t) &= \tau(t) - \tau_1,\\
\tau_{2\tau}(t) &= \tau_2 - \tau(t),\\
\sigma_{1\sigma}(t) &= \sigma(t) - \sigma_1,\\
\sigma_{2\sigma}(t) &= \sigma_2 - \sigma(t),\\
x_{\tau_1}(t) &= x(t-\tau_1),\\
y_{\sigma_1}(t) &= y(t-\sigma_1),\\
x_{\tau}(t) &= x(t-\tau(t)),\\
y_{\sigma}(t) &= y(t-\sigma(t)),\\
x_{\tau_2}(t) &= x(t-\tau_2),\\
y_{\sigma_2}(t) &= y(t-\sigma_2),\\
v_1(t) &= \int_{t-\tau_1}^{t} \frac{x(s)}{\tau_1} ds,\\
v_4(t) &= \int_{t-\tau_1}^{t}\int_s^t \frac{x(u)}{\tau_1^2} du\,ds,\\
v_2(t) &= \int_{t-\tau(t)}^{t-\tau_1} \frac{x(s)}{\tau_{1\tau}(t)} ds,\\
v_5(t) &= \int_{t-\tau(t)}^{t-\tau_1}\int_s^{t-\tau_1} \frac{x(u)}{\tau_{1\tau}^2(t)} du\,ds,\\
v_3(t) &= \int_{t-\tau_2}^{t-\tau(t)} \frac{x(s)}{\tau_{2\tau}(t)} ds,\\
v_6(t) &= \int_{t-\tau_2}^{t-\tau(t)}\int_s^{t-\tau(t)} \frac{x(u)}{\tau_{2\tau}^2(t)} du\,ds,\\
v_7(t) &= \int_{t-\sigma_1}^{t} \frac{x(s)}{\sigma_1} ds,\\
v_{10}(t) &= \int_{t-\sigma_1}^{t}\int_s^t \frac{x(u)}{\sigma_1^2} du\,ds,\\
v_8(t) &= \int_{t-\sigma(t)}^{t-\sigma_1} \frac{x(s)}{\sigma_{1\sigma}(t)} ds,\\
v_{11}(t) &= \int_{t-\sigma(t)}^{t-\sigma_1}\int_s^{t-\sigma_1} \frac{x(u)}{\sigma_{1\sigma}^2(t)} du\,ds,\\
v_9(t) &= \int_{t-\sigma_2}^{t-\sigma(t)} \frac{x(s)}{\sigma_{2\sigma}(t)} ds,\\
v_{12}(t) &= \int_{t-\sigma_2}^{t-\sigma(t)}\int_s^{t-\sigma(t)} \frac{x(u)}{\sigma_{2\sigma}^2(t)} du\,ds,
\end{aligned}$$

$$\begin{aligned}
\zeta(t) = \big[&x^T(t), x^T(t-\tau_1), x^T(t-\tau(t)), x^T(t-\tau_2),\\
&v_1^T(t), v_2^T(t), \ldots, v_6^T(t), y^T(t), y^T(t-\sigma_1),\\
&y^T(t-\sigma(t)), y^T(t-\sigma_2), v_7^T(t), v_8^T(t), \ldots, v_{12}^T(t),\\
&f^T(y(t)), f^T(y(t-\sigma_1)), f^T(y(t-\sigma(t))),\\
&f^T(y(t-\sigma_2))\big]^T,
\end{aligned} \tag{28}$$

$$\begin{aligned}
e_x &= [-A, 0_{n\times 21n}, W, 0_{n\times n}],\\
e_y &= [0_{n\times 2n}, D, 0_{n\times 7n}, -C, 0_{n\times 13n}],\\
e_0 &= [0_{n\times 24n}],\\
e_i &= [0_{n\times(i-1)n}, I_{n\times n}, 0_{n\times(24-i)n}], \quad i = 1, 2, \ldots, 24,\\
\Sigma &= \operatorname{diag}\{\rho_1, \rho_2, \ldots, \rho_n\}.
\end{aligned} \tag{29}$$

4.1. Stability of GRN (2) with Delay Satisfying (5). For GRN (2) with a delay satisfying (5), the following stability criterion is derived by using the proposed WTDII (27), together with Lemmas 1, 2, and 5, to estimate the derivative of the LKF.

Theorem 9. *For given scalars τ_i, σ_i, $i = 1, 2$, τ_d, and σ_d, GRN (2) with the time delay satisfying (5) and regulatory function satisfying (3) is asymptotically stable, if there exist symmetric matrices $P > 0$, $Q_i > 0$, $R_j > 0$, $Z_k > 0$, $i = 1, 2, \ldots, 6$, $j = 1, 2, \ldots, 5$, and $k = 1, 2, \ldots, 4$; diagonal matrices $\Lambda_1 > 0$, $\Lambda_2 > 0$, $H_j > 0$, $j = 1, 2, \ldots, 4$, $U_{lk} >$*

0, $l = 1, 2, \ldots, 4$, *and* $k = l+1, \ldots, 4$; *and any matrices* S_i, $i = 1, 2$, *such that the following LMIs hold:*

$$\begin{bmatrix} \widetilde{R}_{2i+1} & S_i \\ * & \widetilde{R}_{2i+1} \end{bmatrix} > 0, \quad i = 1, 2, \tag{30}$$

$$\Psi_1 = \Xi_{\tau(t)}\big|_{\tau(t)=\tau_1} + \sum_{i=1}^{8} \Xi_i \leq 0, \tag{31}$$

$$\Psi_2 = \Xi_{\tau(t)}\big|_{\tau(t)=\tau_2} + \sum_{i=1}^{8} \Xi_i \leq 0, \tag{32}$$

where $\tau_{12} = \tau_2 - \tau_1$, $\sigma_{12} = \sigma_2 - \sigma_1$, *and*

$$\begin{aligned} \Xi_{\tau(t)} = &-\tau_{1\tau}(t)\left[e_6^T R_2 e_6 + 3(2e_9 - e_6)^T R_2 (2e_9 - e_6)\right] \\ &- \tau_{2\tau}(t)\left[e_7^T R_2 e_7 + 3(2e_{10} - e_7)^T R_2 (2e_{10} - e_7)\right], \end{aligned} \tag{33}$$

$$\Xi_1 = \Xi_{11} + \Xi_{11}^T, \tag{34}$$

$$\begin{aligned} \Xi_{11} = &\begin{bmatrix} e_1 \\ e_{11} \end{bmatrix}^T P \begin{bmatrix} e_x \\ e_y \end{bmatrix} + \left[(\Sigma e_{11} - e_{21})^T \Lambda_1 + e_{21}^T \Lambda_2\right] \\ &\cdot e_y, \end{aligned} \tag{35}$$

$$\begin{aligned} \Xi_2 = &e_1^T Q_1 e_1 - e_2^T (Q_1 - Q_2 - Q_3) e_2 - e_4^T Q_2 e_4 - (1 \\ &- \tau_d) e_3^T Q_3 e_3, \end{aligned} \tag{36}$$

$$\Xi_3 = \Xi_{31} + \Xi_{32} + \Xi_{33}, \tag{37}$$

$$\Xi_{31} = e_x^T \left(\tau_1^2 R_1 + \tau_{12}^2 R_3\right) e_x + \tau_{12} e_1^T R_2 e_1, \tag{38}$$

$$\Xi_{32} = E_1^T \widetilde{R}_1 E_1, \quad \widetilde{R}_1 = \operatorname{diag}\{R_1, 3R_1, 5R_1\}, \tag{39}$$

$$\begin{aligned} \Xi_{33} = &\begin{bmatrix} E_2 \\ E_3 \end{bmatrix}^T \begin{bmatrix} \widetilde{R}_3 & S_1 \\ * & \widetilde{R}_3 \end{bmatrix} \begin{bmatrix} E_2 \\ E_3 \end{bmatrix}, \\ &\widetilde{R}_3 = \operatorname{diag}\{R_3, 3R_3, 5R_3\}, \end{aligned} \tag{40}$$

$$\Xi_4 = \Xi_{41} + \Xi_{42} + \Xi_{43}, \tag{41}$$

$$\Xi_{41} = e_x^T \left(\frac{\tau_1^2}{2} Z_1 + \frac{\tau_2^2 - \tau_1^2}{2} Z_2 - \tau_1 \tau_{12} Z_2\right) e_x, \tag{42}$$

$$\begin{aligned} \Xi_{42} = &-2[e_1 - e_5]^T Z_1 [e_1 - e_5] - 16\left[3e_8 - \frac{e_1}{2}\right. \\ &\left.- e_5\right]^T Z_1 \left[3e_8 - \frac{e_1}{2} - e_5\right], \end{aligned} \tag{43}$$

$$\begin{aligned} \Xi_{43} = &-2[e_2 - e_6]^T Z_2 [e_2 - e_6] - 16\left[3e_9 - \frac{e_2}{2}\right. \\ &\left.- e_6\right]^T Z_2 \left[3e_9 - \frac{e_2}{2} - e_6\right] - 2[e_3 - e_7]^T Z_2 [e_3 \\ &- e_7] - 16\left[3e_{10} - \frac{e_3}{2} - e_7\right]^T Z_2 \left[3e_{10} - \frac{e_3}{2} - e_7\right], \end{aligned} \tag{44}$$

$$\begin{aligned} \Xi_5 = &\begin{bmatrix} e_{11} \\ e_{21} \end{bmatrix}^T Q_4 \begin{bmatrix} e_{11} \\ e_{21} \end{bmatrix} + \begin{bmatrix} e_{12} \\ e_{22} \end{bmatrix}^T (Q_5 + Q_6 - Q_4) \\ &\cdot \begin{bmatrix} e_{12} \\ e_{22} \end{bmatrix} - \begin{bmatrix} e_{14} \\ e_{24} \end{bmatrix}^T Q_5 \begin{bmatrix} e_{14} \\ e_{24} \end{bmatrix} - (1 - \sigma_d) \begin{bmatrix} e_{13} \\ e_{23} \end{bmatrix}^T \\ &\cdot Q_6 \begin{bmatrix} e_{13} \\ e_{23} \end{bmatrix}, \end{aligned} \tag{45}$$

$$\Xi_6 = \Xi_{61} + \Xi_{62} + \Xi_{63}, \tag{46}$$

$$\Xi_{61} = e_y^T \left(\sigma_1^2 R_4 + \sigma_{12}^2 R_5\right) e_y, \tag{47}$$

$$\Xi_{62} = E_4^T \widetilde{R}_4 E_4, \quad \widetilde{R}_4 = \operatorname{diag}\{R_4, 3R_4, 5R_4\}, \tag{48}$$

$$\begin{aligned} \Xi_{63} = &\begin{bmatrix} E_5 \\ E_6 \end{bmatrix}^T \begin{bmatrix} \widetilde{R}_5 & S_2 \\ * & \widetilde{R}_5 \end{bmatrix} \begin{bmatrix} E_5 \\ E_6 \end{bmatrix}, \\ &\widetilde{R}_5 = \operatorname{diag}\{R_5, 3R_5, 5R_5\}, \end{aligned} \tag{49}$$

$$\Xi_7 = \Xi_{71} + \Xi_{72} + \Xi_{73}, \tag{50}$$

$$\Xi_{71} = e_y^T \left(\frac{\sigma_1^2}{2} Z_3 + \frac{\sigma_2^2 - \sigma_1^2}{2} Z_4 - \sigma_1 \sigma_{12} Z_4\right) e_y, \tag{51}$$

$$\begin{aligned} \Xi_{72} = &-2[e_{11} - e_{15}]^T Z_3 [e_{11} - e_{15}] - 16\left[3e_{18} - \frac{e_{11}}{2}\right. \\ &\left.- e_{15}\right]^T Z_3 \left[3e_{18} - \frac{e_{11}}{2} - e_{15}\right], \end{aligned} \tag{52}$$

$$\begin{aligned} \Xi_{73} = &-2[e_{12} - e_{16}]^T Z_4 [e_{12} - e_{16}] - 16\left[3e_{19} - \frac{e_{12}}{2}\right. \\ &\left.- e_{16}\right]^T Z_4 \left[3e_{19} - \frac{e_{12}}{2} - e_{16}\right] - 2[e_{13} - e_{17}]^T \\ &\cdot Z_4 [e_{13} - e_{17}] - 16\left[3e_{20} - \frac{e_{13}}{2} - e_{17}\right]^T \\ &\cdot Z_4 \left[3e_{20} - \frac{e_{13}}{2} - e_{17}\right], \end{aligned} \tag{53}$$

$$\Xi_8 = \Xi_{81} + \Xi_{81}^T, \tag{54}$$

$$\begin{aligned} \Xi_{81} = &\sum_{i=1}^{4} \left[(\Sigma e_{1i} - e_{2i})^T H_i e_{2i}\right] \\ &+ \sum_{i=1}^{4} \sum_{j=i+1}^{4} \left[\Sigma(e_{1i} - e_{1j}) - (e_{2i} - e_{2j})\right]^T \\ &\cdot U_{ij} (e_{2i} - e_{2j}), \end{aligned} \tag{55}$$

$$E_1 = \begin{bmatrix} e_1 - e_2 \\ e_1 + e_2 - 2e_5 \\ e_1 - e_2 + 6e_5 - 12e_8 \end{bmatrix}, \tag{56}$$

$$E_2 = \begin{bmatrix} e_2 - e_3 \\ e_2 + e_3 - 2e_6 \\ e_2 - e_3 + 6e_6 - 12e_9 \end{bmatrix}, \quad (57)$$

$$E_3 = \begin{bmatrix} e_3 - e_4 \\ e_3 + e_4 - 2e_7 \\ e_3 - e_4 + 6e_7 - 12e_{10} \end{bmatrix}, \quad (58)$$

$$E_4 = \begin{bmatrix} e_{11} - e_{12} \\ e_{11} + e_{12} - 2e_{15} \\ e_{11} - e_{12} + 6e_{15} - 12e_{18} \end{bmatrix}, \quad (59)$$

$$E_5 = \begin{bmatrix} e_{12} - e_{13} \\ e_{12} + e_{13} - 2e_{16} \\ e_{12} - e_{13} + 6e_{16} - 12e_{19} \end{bmatrix}, \quad (60)$$

$$E_6 = \begin{bmatrix} e_{13} - e_{14} \\ e_{13} + e_{14} - 2e_{17} \\ e_{13} - e_{14} + 6e_{17} - 12e_{20} \end{bmatrix}. \quad (61)$$

Proof. Construct the following LKF candidate:

$$V(t) = \sum_{i=1}^{7} V_i(t), \quad (62)$$

where

$$\begin{aligned}
V_1(t) &= \begin{bmatrix} x(t) \\ y(t) \end{bmatrix}^T P \begin{bmatrix} x(t) \\ y(t) \end{bmatrix} + \sum_{i=1}^{n} \int_0^{y_i} [\lambda_{1i}(\rho_i s - f_i(s)) \\
&\quad + \lambda_{2i} f_i(s)]\, ds, \\
V_2(t) &= \int_{t-\tau_1}^{t} x^T(s) Q_1 x(s)\, ds + \int_{t-\tau_2}^{t-\tau_1} x^T(s) \\
&\quad \cdot Q_2 x(s)\, ds + \int_{t-\tau(t)}^{t-\tau_1} x^T(s) Q_3 x(s)\, ds, \\
V_3(t) &= \tau_1 \int_{-\tau_1}^{0} \int_{t+\theta}^{t} \dot{x}^T(s) R_1 \dot{x}(s)\, ds\, d\theta \\
&\quad + \int_{-\tau_2}^{-\tau_1} \int_{t+\theta}^{t} [x^T(s) R_2 x(s) \\
&\quad + \tau_{12} \dot{x}^T(s) R_3 \dot{x}(s)]\, ds\, d\theta, \\
V_4(t) &= \int_{-\tau_1}^{0} \int_{\theta}^{0} \int_{t+s}^{t} \dot{x}^T(u) Z_1 \dot{x}(u)\, du\, ds\, d\theta \\
&\quad + \int_{-\tau_2}^{-\tau_1} \int_{\theta}^{-\tau_1} \int_{t+s}^{t} \dot{x}^T(u) Z_2 \dot{x}(u)\, du\, ds\, d\theta, \\
V_5(t) &= \int_{t-\sigma_1}^{t} \begin{bmatrix} y(s) \\ f(y(s)) \end{bmatrix}^T Q_4 \begin{bmatrix} y(s) \\ f(y(s)) \end{bmatrix} ds \\
&\quad + \int_{t-\sigma_2}^{t-\sigma_1} \begin{bmatrix} y(s) \\ f(y(s)) \end{bmatrix}^T Q_5 \begin{bmatrix} y(s) \\ f(y(s)) \end{bmatrix} ds \\
&\quad + \int_{t-\sigma(t)}^{t-\sigma_1} \begin{bmatrix} y(s) \\ f(y(s)) \end{bmatrix}^T Q_6 \begin{bmatrix} y(s) \\ f(y(s)) \end{bmatrix} ds, \\
V_6(t) &= \sigma_1 \int_{-\sigma_1}^{0} \int_{t+\theta}^{t} \dot{y}^T(s) R_4 \dot{y}(s)\, ds\, d\theta \\
&\quad + \sigma_{12} \int_{-\sigma_2}^{-\sigma_1} \int_{t+\theta}^{t} \dot{y}^T(s) R_5 \dot{y}(s)\, ds\, d\theta, \\
V_7(t) &= \int_{-\sigma_1}^{0} \int_{\theta}^{0} \int_{t+s}^{t} \dot{y}^T(u) Z_3 \dot{y}(u)\, du\, ds\, d\theta \\
&\quad + \int_{-\sigma_2}^{-\sigma_1} \int_{\theta}^{-\sigma_1} \int_{t+s}^{t} \dot{y}^T(u) Z_4 \dot{y}(u)\, du\, ds\, d\theta
\end{aligned} \quad (63)$$

and $P > 0$, $Q_i > 0$, $R_j > 0$, $Z_k > 0$, $i = 1, 2, \ldots, 6$, $j = 1, 2, \ldots, 5$, and $k = 1, 2, \ldots, 4$ are the symmetric positive-definite matrices and $\Lambda_i = \operatorname{diag}\{\lambda_{i1}, \lambda_{i2}, \ldots, \lambda_{in}\} > 0$, $i = 1, 2$, are the symmetric positive-definite diagonal matrices.

Calculating the derivative of the LKF along the solutions of GRN (11) yields

$$\dot{V}(t) = \sum_{i=1}^{7} \dot{V}_i(t), \quad (64)$$

where

$$\begin{aligned}
\dot{V}_1(t) &= 2 \begin{bmatrix} x(t) \\ y(t) \end{bmatrix}^T P \begin{bmatrix} \dot{x}(t) \\ \dot{y}(t) \end{bmatrix} \\
&\quad + 2\left\{[\Sigma y(t) - f(y(t))]^T \Lambda_1 + f^T(y(t)) \Lambda_2\right\} \\
&\quad \cdot \dot{y}(t) = \zeta^T(t) \left(\Xi_{11} + \Xi_{11}^T\right) \zeta(t), \\
\dot{V}_2(t) &= x^T(t) Q_1 x(t) + x_{\tau_1}^T(t) \left(Q_2 + Q_3 - Q_1\right) x_{\tau_1}(t) \\
&\quad - x_{\tau_2}^T(t) Q_2 x_{\tau_2}(t) - (1 - \dot{\tau}(t)) x_{\tau}^T(t) Q_3 x_{\tau}(t) \\
&\le x^T(t) Q_1 x(t) + x_{\tau_1}^T(t) \left(Q_2 + Q_3 - Q_1\right) x_{\tau_1}(t) \\
&\quad - x_{\tau_2}^T(t) Q_2 x_{\tau_2}(t) - \left(1 - \tau_d\right) x_{\tau}^T(t) Q_3 x_{\tau}(t) \\
&= \zeta^T(t) \Xi_2 \zeta(t), \\
\dot{V}_3(t) &= \dot{x}^T(t) \left(\tau_1^2 R_1 + \tau_{12}^2 R_3\right) \dot{x}(t) + \tau_{12} x^T(t) R_2 x(t) \\
&\quad - \tau_1 \int_{t-\tau_1}^{t} \dot{x}^T(s) R_1 \dot{x}(s)\, ds \\
&\quad - \int_{t-\tau_2}^{t-\tau_1} \left(x^T(s) R_2 x(s) + \tau_{12} \dot{x}^T(s) R_3 \dot{x}(s)\right) ds,
\end{aligned}$$

$$\dot{V}_4(t) = \dot{x}^T(t)\left(\frac{\tau_1^2}{2}Z_1 + \frac{\tau_2^2-\tau_1^2}{2}Z_2 - \tau_1\tau_{12}Z_2\right)\dot{x}(t)$$
$$- \int_{t-\tau_1}^{t}\int_{s}^{t}\dot{x}^T(u)Z_1\dot{x}(u)\,du\,ds$$
$$- \int_{t-\tau_2}^{t-\tau_1}\int_{s}^{t-\tau_1}\dot{x}^T(u)Z_2\dot{x}(u)\,du\,ds,$$

$$\dot{V}_5(t) = \begin{bmatrix} y(t) \\ f(y(t)) \end{bmatrix}^T Q_4 \begin{bmatrix} y(t) \\ f(y(t)) \end{bmatrix}$$
$$+ \begin{bmatrix} y_{\sigma_1}(t) \\ f(y(t-\sigma_1)) \end{bmatrix}^T (Q_5 + Q_6 - Q_4)$$
$$\cdot \begin{bmatrix} y_{\sigma_1}(t) \\ f(y(t-\sigma_1)) \end{bmatrix} - \begin{bmatrix} y_{\sigma_2}(t) \\ f(y(t-\sigma_2)) \end{bmatrix}^T$$
$$\cdot Q_5 \begin{bmatrix} y_{\sigma_2}(t) \\ f(y(t-\sigma_2)) \end{bmatrix} - (1-\dot{\sigma}(t))$$
$$\cdot \begin{bmatrix} y_{\sigma}(t) \\ f(y(t-\sigma(t))) \end{bmatrix}^T Q_6 \begin{bmatrix} y_{\sigma}(t) \\ f(y(t-\sigma(t))) \end{bmatrix}$$
$$\leq \zeta^T(t)\,\Xi_5\zeta(t),$$

$$\dot{V}_6(t) = \dot{y}^T(t)\left(\sigma_1^2R_4 + \sigma_{12}^2R_5\right)\dot{y}(t)$$
$$- \sigma_1\int_{t-\sigma_1}^{t}\dot{y}^T(s)R_4\dot{y}(s)\,ds$$
$$- \sigma_{12}\int_{t-\sigma_2}^{t-\sigma_1}\dot{y}^T(s)R_5\dot{y}(s)\,ds,$$

$$\dot{V}_7(t) = \dot{y}^T(t)\left(\frac{\sigma_1^2}{2}Z_3 + \frac{\sigma_2^2-\sigma_1^2}{2}Z_4 - \sigma_1\sigma_{12}Z_4\right)\dot{y}(t)$$
$$- \int_{t-\sigma_1}^{t}\int_{s}^{t}\dot{y}^T(u)Z_3\dot{y}(u)\,du\,ds$$
$$- \int_{t-\sigma_2}^{t-\sigma_1}\int_{s}^{t-\sigma_1}\dot{y}^T(u)Z_4\dot{y}(u)\,du\,ds, \tag{65}$$

where Ξ_{11}, Ξ_2, and Ξ_5 are defined in (35), (36), and (45), respectively.

Using Lemma 2 to estimate the R_1-dependent single integral terms in $\dot{V}_3(t)$ yields

$$\begin{aligned} -\tau_1\int_{t-\tau_1}^{t}\dot{x}^T(s)R_1\dot{x}(s)\,ds &\leq -\eta_1^T(t)\widetilde{R}_1\eta_1(t) \\ &= \zeta^T(t)\,\Xi_{32}\zeta(t), \end{aligned} \tag{66}$$

where $\widetilde{R}_1$ and Ξ_{32} are defined in (39) and

$$\eta_1(t) = \begin{bmatrix} x(t) - x_{\tau_1}(t) \\ x(t) + x_{\tau_1}(t) - 2v_1(t) \\ x(t) - x_{\tau_1}(t) + 6v_1(t) - 12v_4(t) \end{bmatrix}. \tag{67}$$

Using Lemma 1 to estimate the R_2-dependent single integral terms in $\dot{V}_3(t)$ yields

$$\begin{aligned} &-\int_{t-\tau_2}^{t-\tau_1}x^T(s)Rx(s)\,ds = -\int_{t-\tau(t)}^{t-\tau_1}x^T(s)Rx(s)\,ds \\ &\quad - \int_{t-\tau_2}^{t-\tau(t)}x^T(s)Rx(s)\,ds \leq -\tau_{1\tau}(t) \\ &\quad \cdot \left[v_2^T(t)R_2v_2(t)\right. \\ &\quad \left. + 3\left(2v_5(t) - v_2(t)\right)^T R_2\left(2v_5(t) - v_2(t)\right)\right] \\ &\quad - \tau_{2\tau}(t)\left[v_3^T(t)R_2v_3(t)\right. \\ &\quad \left. + 3\left(2v_6(t) - v_3(t)\right)^T R_2\left(2v_6(t) - v_3(t)\right)\right] \\ &\quad = \zeta^T(t)\,\Xi_{\tau(t)}\zeta(t), \end{aligned} \tag{68}$$

where $\Xi_{\tau(t)}$ is defined in (33).

Using Lemmas 2 and 5, together with (30), to estimate the R_3-dependent single integral terms in $\dot{V}_3(t)$ yields

$$\begin{aligned} &-\tau_{12}\int_{t-\tau_2}^{t-\tau_1}\dot{x}^T(s)R_3\dot{x}(s)\,ds \\ &\quad = -\tau_{12}\int_{t-\tau(t)}^{t-\tau_1}\dot{x}^T(s)R_3\dot{x}(s)\,ds \\ &\qquad - \tau_{12}\int_{t-\tau_2}^{t-\tau(t)}\dot{x}^T(s)R_3\dot{x}(s)\,ds \\ &\quad \leq -\frac{\tau_{12}}{\tau(t)-\tau_1}\left\{\eta_2^T(t)\widetilde{R}_3\eta_2(t)\right\} \\ &\qquad - \frac{\tau_{12}}{\tau_2-\tau(t)}\left\{\eta_3^T(t)\widetilde{R}_3\eta_3(t)\right\} \\ &\quad \leq -\begin{bmatrix} \eta_2(t) \\ \eta_3(t) \end{bmatrix}^T \begin{bmatrix} \widetilde{R}_3 & S_1 \\ * & \widetilde{R}_3 \end{bmatrix} \begin{bmatrix} \eta_2(t) \\ \eta_3(t) \end{bmatrix} = \zeta^T(t)\,\Xi_{33}\zeta(t), \end{aligned} \tag{69}$$

where $\widetilde{R}_3$ and Ξ_{33} are defined in (40) and

$$\begin{aligned} \eta_2(t) &= \begin{bmatrix} x_{\tau_1}(t) - x_{\tau}(t) \\ x_{\tau_1}(t) + x_{\tau}(t) - 2v_2(t) \\ x_{\tau_1}(t) - x_{\tau}(t) + 6v_2(t) - 12v_5(t) \end{bmatrix}, \\ \eta_3(t) &= \begin{bmatrix} x_{\tau}(t) - x_{\tau_2}(t) \\ x_{\tau}(t) + x_{\tau_2}(t) - 2v_3(t) \\ x_{\tau}(t) - x_{\tau_2}(t) + 6v_3(t) - 12v_6(t) \end{bmatrix}. \end{aligned} \tag{70}$$

Using Lemma 8 to estimate the Z_1-dependent double integral terms in $\dot{V}_4(t)$ yields

$$\begin{aligned}
&-\int_{t-\tau_1}^{t}\int_{s}^{t}\dot{x}^T(u)Z_1\dot{x}(u)\,du\,ds \le -2\left[x(t)-v_1(t)\right]^T \\
&\cdot Z_1\left[x(t)-v_1(t)\right]+16\left[3v_4(t)-\frac{x(t)}{2}-v_1(t)\right]^T \\
&\cdot Z_1\left[3v_4(t)-\frac{x(t)}{2}-v_1(t)\right]=\zeta^T(t)\,\Xi_{42}\zeta(t),
\end{aligned} \quad (71)$$

where Ξ_{42} is defined in (43).

Using Lemma 8 to estimate the Z_2-dependent double integral terms in $\dot{V}_4(t)$ yields

$$\begin{aligned}
&-\int_{t-\tau_2}^{t-\tau_1}\int_{s}^{t-\tau_1}\dot{x}^T(u)Z_2\dot{x}(u)\,du\,ds \\
&=-\int_{t-\tau(t)}^{t-\tau_1}\int_{s}^{t-\tau_1}\dot{x}^T(u)Z_2\dot{x}(u)\,du\,ds \\
&-\int_{t-\tau_2}^{t-\tau(t)}\int_{s}^{t-\tau_1}\dot{x}^T(u)Z_2\dot{x}(u)\,du\,ds \\
&\le-\int_{t-\tau(t)}^{t-\tau_1}\int_{s}^{t-\tau_1}\dot{x}^T(u)Z_2\dot{x}(u)\,du\,ds \\
&-\int_{t-\tau_2}^{t-\tau(t)}\int_{s}^{t-\tau(t)}\dot{x}^T(u)Z_2\dot{x}(u)\,du\,ds \\
&\le-2\left[x_{\tau_1}(t)-v_2(t)\right]^T Z_2\left[x_{\tau_1}(t)-v_2(t)\right] \\
&-16\left[3v_5(t)-\frac{x_{\tau_1}(t)}{2}-v_2(t)\right]^T \\
&\cdot Z_2\left[3v_5(t)-\frac{x_{\tau_1}(t)}{2}-v_2(t)\right] \\
&-2\left[x_\tau(t)-v_3(t)\right]^T Z_2\left[x_\tau(t)-v_3(t)\right] \\
&-16\left[3v_6(t)-\frac{x_\tau(t)}{2}-v_3(t)\right]^T \\
&\cdot Z_2\left[3v_6(t)-\frac{x_\tau(t)}{2}-v_3(t)\right]=\zeta^T(t)\,\Xi_{43}\zeta(t),
\end{aligned} \quad (72)$$

where Ξ_{43} is defined in (44).

Similarly, using Lemmas 2, 5, and 8 to estimate the single and double integral terms in $\dot{V}_6(t)$ and $\dot{V}_7(t)$ yields

$$\begin{aligned}
&-\sigma_1\int_{t-\sigma_1}^{t}\dot{x}^T(s)R_4\dot{x}(s)\,ds\le\zeta^T(t)\,\Xi_{62}\zeta(t), \\
&-\sigma_{12}\int_{t-\sigma_2}^{t-\sigma_1}\dot{x}^T(s)R_5\dot{x}(s)\,ds\le\zeta^T(t)\,\Xi_{63}\zeta(t), \\
&-\int_{t-\sigma_1}^{t}\int_{s}^{t}\dot{x}^T(u)Z_3\dot{x}(u)\,du\,ds\le\zeta^T(t)\,\Xi_{72}\zeta(t), \\
&-\int_{t-\sigma_2}^{t-\sigma_1}\int_{s}^{t-\sigma_1}\dot{x}^T(u)Z_4\dot{x}(u)\,du\,ds\le\zeta^T(t)\,\Xi_{73}\zeta(t),
\end{aligned} \quad (73)$$

where Ξ_{62}, Ξ_{63}, Ξ_{72}, and Ξ_{73} are defined in (48)–(53).

Taking into account the assumption of the activation function, (13) and (14), the following inequalities hold [76, 77]:

$$\begin{aligned}
&h_i(s)=2\left[\Sigma y(s)-f(y(s))\right]^T H_i f(y(s))\ge 0, \\
&u_{ij}(s_1,s_2)=2\left[\Sigma(y(s_1)-y(s_2))\right. \\
&\quad\left.-(f(y(s_1))-f(y(s_2)))\right]^T U_{ij}\times(f(y(s_1)) \\
&\quad-f(y(s_2)))\ge 0,
\end{aligned} \quad (74)$$

where H_i, $i=1,2,\ldots,4$, and U_{ij}, $i=1,2,\ldots,4$, $j=i+1,\ldots,4$, are the symmetric diagonal matrices. Thus, the following inequality holds:

$$\begin{aligned}
H(t)+U(t)&=h_1(t)+h_2(t-\sigma_1)+h_3(t-\sigma(t)) \\
&\quad+h_4(t-\sigma_2)+u_{12}(t,t-\sigma_1) \\
&\quad+u_{13}(t,t-\sigma(t))+u_{14}(t,t-\sigma_2) \\
&\quad+u_{23}(t-\sigma_1,t-\sigma(t)) \\
&\quad+u_{24}(t-\sigma_1,t-\sigma_2) \\
&\quad+u_{34}(t-\sigma(t),t-\sigma_2) \\
&=\zeta^T(t)\,\Xi_8\zeta(t)\ge 0,
\end{aligned} \quad (75)$$

where Ξ_8 is defined in (54).

Finally, combining (64), (65), (66), (68), (69), (71), (72), (73), and (75) yields

$$\dot{V}(t)\le\zeta^T(t)\left[\Xi_{\tau(t)}+\sum_{i=1}^{8}\Xi_i\right]\zeta(t), \quad (76)$$

where the related notations are defined in (31).

Therefore, if LMIs (31) and (32) hold, then the following holds for a sufficiently small scalar $\epsilon>0$ based on convex combination method [78, 79]:

$$\dot{V}(t)\le-\epsilon\left(\|x(t)\|^2+\|y(t)\|^2\right) \quad (77)$$

which shows the asymptotical stability of GRN (2) with time delay satisfying (5). This completes the proof. □

4.2. Stability of GRN (11) with Delay Satisfying (6). For some cases, the change rates of the time-varying delays are unmeasurable, that is, time delay satisfying (6). For this case, the following stability criterion can be derived by using the proposed WTDII (27), together with Lemmas 1, 2, 5, and 8, to estimate the derivative of the LKF.

Theorem 10. *For given scalars τ_i and σ_i, $i=1,2$, GRN (2) with the time delay satisfying (6) and regulatory function satisfying (3) is asymptotically stable, if there exist symmetric matrices $P>0$, $Q_i>0$, $R_j>0$, $Z_k>0$, $i=1,2,4,5$, $j=1,2,\ldots,5$, and $k=1,2,\ldots,4$; diagonal matrices $\Lambda_1>0$, $\Lambda_2>0$, $H_j>$*

0, $j = 1,2,3,4$, $U_{lk} > 0$, $l = 1,2,\ldots,4$, *and* $k = l+1,\ldots,4$; *and any matrices* S_i, $i = 1,2$, *such that the following LMIs hold:*

$$\begin{bmatrix} \widetilde{R}_{2i+1} & S_i \\ * & \widetilde{R}_{2i+1} \end{bmatrix} > 0, \quad i = 1,2,$$

$$\begin{aligned} \Psi_3 &= \Xi_{\tau(t)}\big|_{\tau(t)=\tau_1} + \sum_{i=1,3,4,6,7} \Xi_i + \overline{\Xi}_2 + \overline{\Xi}_5 \\ &\le 0, \\ \Psi_4 &= \Xi_{\tau(t)}\big|_{\tau(t)=\tau_2} \sum_{i=1,3,4,6,7} \Xi_i + \overline{\Xi}_2 + \overline{\Xi}_5 \\ &\le 0, \end{aligned} \tag{78}$$

where Ξ_i, $i = 1,3,4,6,7$, *are defined in Theorem 9 and*

$$\begin{aligned} \overline{\Xi}_2 &= e_1^T Q_1 e_1 - e_2^T (Q_1 - Q_2) e_2 - e_4^T Q_2 e_4, \\ \overline{\Xi}_5 &= \begin{bmatrix} e_{11} \\ e_{21} \end{bmatrix}^T Q_4 \begin{bmatrix} e_{11} \\ e_{21} \end{bmatrix} + \begin{bmatrix} e_{12} \\ e_{22} \end{bmatrix}^T (Q_5 - Q_4) \begin{bmatrix} e_{12} \\ e_{22} \end{bmatrix} \\ &\quad - \begin{bmatrix} e_{14} \\ e_{24} \end{bmatrix}^T Q_5 \begin{bmatrix} e_{14} \\ e_{24} \end{bmatrix}. \end{aligned} \tag{79}$$

Proof. The above stability criterion can be obtained by setting $Q_3 = 0$ and $Q_6 = 0$ in Theorem 9. □

4.3. Some Remarks. This part gives some remarks for the above criteria.

Remark 11. During the proof of the above two stability criteria, the double integral terms arising in the derivative of the LKFs are estimated by using the proposed WTDII, that is, Lemma 8. As discussed in Section 3, the WTDII is tighter than the widely used JBDII (17), which was used for the GRN [19, 34], and the recently developed WBDII (18), which has not been used for the GRN. Thus, the proposed criteria are less conservative than the ones reported in [19, 34].

Remark 12. Compared with the literature, more information of regulatory function has been used during the proof of criteria. Specifically, in the literature, only (14) is used during the estimation of the derivative of the LKF, while, in this paper, extra information of regulatory function (13) is also used for estimating task. It has been proved in [77] that such additional information is helpful to reduce the conservatism.

Remark 13. The conditions given in Theorems 9 and 10 are in the form of LMI. Such LMI conditions can be easily checked by using MATLAB/LMI toolbox [80]. One can refer to [81–83] for more details.

Remark 14. Although this paper has just investigated the asymptotical stability, the proposed method can be extended to the robust stability analysis by taking into account the parameter uncertainties and/or noises of the GRNs. Moreover, the proposed method can also be extended to other problems discussed in Section 2, like controller synthesis, state estimation, filter design, passivity analysis, and so on [13, 59–70].

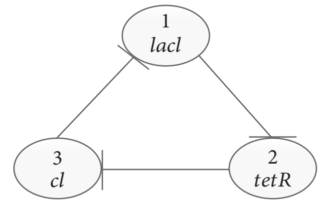

Figure 2: The repressilator network.

5. Illustrative Example

In this section, an example will be presented to illustrate the effectiveness of our results. As mentioned in Section 2, the important aim of the stability analysis of delayed GRNs is to determine the MADBs. And the stability criterion that provides bigger MADBs is less conservative than the one that gives smaller ones. Therefore, the advantages of the proposed criteria are demonstrated via the comparison of the MADBs calculated by various criteria. Moreover, the index of the number of variables (NoV) is applied to show the complexity of criteria.

Example 1. For the GRN model which is theoretically predicted and experimentally investigated in *Escherichia coli* in [4], the genetic network is composed of three repressilators *(lacl*, *tetR*, and *cl)* which form a cyclic negative feedback loop, each repressor protein inhibits the transcription of its downstream repressor gene, as shown in Figure 2, the protein of *lacl* represses the gene transcription of *tetR*, and the protein of *tetR* inhibits the gene transcription of *cl* simultaneously, and, finally, the transcription of *lacl* is inhibited by *cl*, which completes the cycle.

The kinetics of the genetic network are modelled as the GRN (2) with the following parameters [19]:

$$\begin{aligned} A &= \operatorname{diag}\{3,3,3\}, \\ C &= \operatorname{diag}\{2.5,2.5,2.5\}, \\ W &= \begin{bmatrix} 0 & 0 & -2.5 \\ -2.5 & 0 & 0 \\ 0 & -2.5 & 0 \end{bmatrix}, \\ D &= \begin{bmatrix} 0.8 \\ 0.8 \\ 0.8 \end{bmatrix}, \\ b_i(x) &= \frac{x^2}{1+x^2}, \quad i = 1,2,\ldots,n. \end{aligned} \tag{80}$$

It follows from (9) and (29) that

$$\Sigma = \operatorname{diag}\left\{\frac{3\sqrt{3}}{8}, \frac{3\sqrt{3}}{8}, \frac{3\sqrt{3}}{8}\right\}. \tag{81}$$

Table 1: The MADBs of τ_2 for various τ_1 and the NoVs of various criteria.

Criteria	NoVs	τ_1		
		0.1	0.5	1
[29, 31, 34]	—	<5.5	<5.9	<6.4
[19]	$40.5n^2 + 16.5n$	5.5	5.91	6.41
Theorem 9	$32n^2 + 22n$	9.2681	9.6682	10.1681

Table 2: The MADBs of τ_2 for various τ_1 and the NoVs of various criteria.

Criteria	NoVs	τ_1		
		0	1	2
[19]	$38n^2 + 15n$	2.3101	3.3101	4.3102
[19]	$29.5n^2 + 20.5n$	4.1647	5.1647	6.1646

(1) Calculation Results. The first study case is that the changing rates of the time-varying delays are measurable; that is, delays satisfy (5). Assume that $\sigma_1 = 0.1$, $\sigma_2 = 0.3$, $\sigma_d = 0.7$, and $\tau_d = 1.5$ [19], and the MADBs of τ_2 with respect to various τ_1 obtained by the proposed criteria are given in Table 1, where the MADBs reported in the literature are also listed for comparison.

The second study case is that the changing rates of the time-varying delays are nonmeasurable; that is, delays satisfy (6). Assume that $\sigma_1 = 1$ and $\sigma_2 = 2$, and the MADBs of τ_2 with respect to various τ_1 obtained by the proposed criteria, together with the ones provided by the least literature [19], are given in Table 2.

Moreover, the NoVs of criteria reported in the least literature [19] and that of criteria established in this paper are also given in tables to compare the computation complexity.

From the results in the tables, it can be easily found that the proposed stability criteria can provide the larger MADBs for two cases compared to those given in the existing literature. It shows that the proposed criteria are indeed less conservative than the ones reported in the literature. On the other hand, it is found that the NoV of the proposed criteria (Theorem 9) is smaller than the one reported in [19], $(40.5n^2 + 16.5n) - (32n^2 + 22n) = 8.5n^2 - 5.5n > 0$ and $(38n^2 + 15n) - (29.5n^2 + 20.5n) = 8.5n^2 - 5.5n > 0$ for any n. Both of those observations show the advantages of the proposed criterion.

(2) Simulation Verification. From the given parameters, the equilibrium points of the GRN can be obtained as

$$m^* = [0.7840, 0.7840, 0.7840],$$
$$p^* = [0.2509, 0.2509, 0.2509]. \tag{82}$$

Simulation studies for the following two types of time-varying delays are carried out.

Case 1. The initial conditions $m(t) = [0.70, 0.85, 0.80]^T$, $t \in [-10.1681, 0]$, and $p(t) = [0.15, 0.20, 0.30]^T$, $t \in [-0.3, 0]$, and the following delays satisfy $\sigma_1 = 0.1$, $\sigma_2 = 0.3$, $\sigma_d = 0.7$, $\tau_1 = 1$, $\tau_2 = 10.1681$, and $\tau_d = 1.5$:

$$\tau(t) = 9.1681 \sin^2(0.1636t) + 1,$$
$$\sigma(t) = 0.2 \sin^2(3.5t) + 0.1. \tag{83}$$

Case 2. The initial conditions $m(t) = [0.70, 0.85, 0.80]^T$, $t \in [-6.1746, 0]$, and $p(t) = [0.15, 0.20, 0.30]^T$, $t \in [-2, 0]$, and the random delays satisfy $\sigma_1 = 1$, $\sigma_2 = 2$, $\tau_1 = 2$, $\tau_2 = 6.1746$.

Based on Tables 1 and 2, the GRN with the above delays, respectively, is stable. The trajectories of the concentrations of mRNA and protein are shown in Figures 3 and 4. The results show that they are stable at their equilibrium points.

6. Conclusions

This paper has investigated the stability of the GRN with time-varying delays, and its contributions have been revealed from two aspects. The novel WTDII has been developed for the estimation of the double integral terms, and it has been also proved to be tighter than the widely used JBDII and the recently developed WBDII for the same task. Then, with benefit from the WTDII, two LMI-based stability criteria with less conservatism have been derived for checking the stability of the GRN with time delays. Finally, the advantages of the proposed inequality and the established criteria have been verified through an example.

Notations

$\|\cdot\|$:	The Euclidean vector norm
$\mathscr{R}^{n\times m}$:	The set of all $n \times m$ real matrices
N^T (N^{-1}):	The transpose (inverse) of the matrix N
$P > 0$:	P is a real positive-definite matrix
diag$\{\cdots\}$:	A block-diagonal matrix
I (0):	The identity (zero) matrix
Sym$\{X\}$:	$X + X^T$
$\begin{bmatrix} X & Y \\ * & Z \end{bmatrix}$:	$\begin{bmatrix} X & Y \\ Y^T & Z \end{bmatrix}$

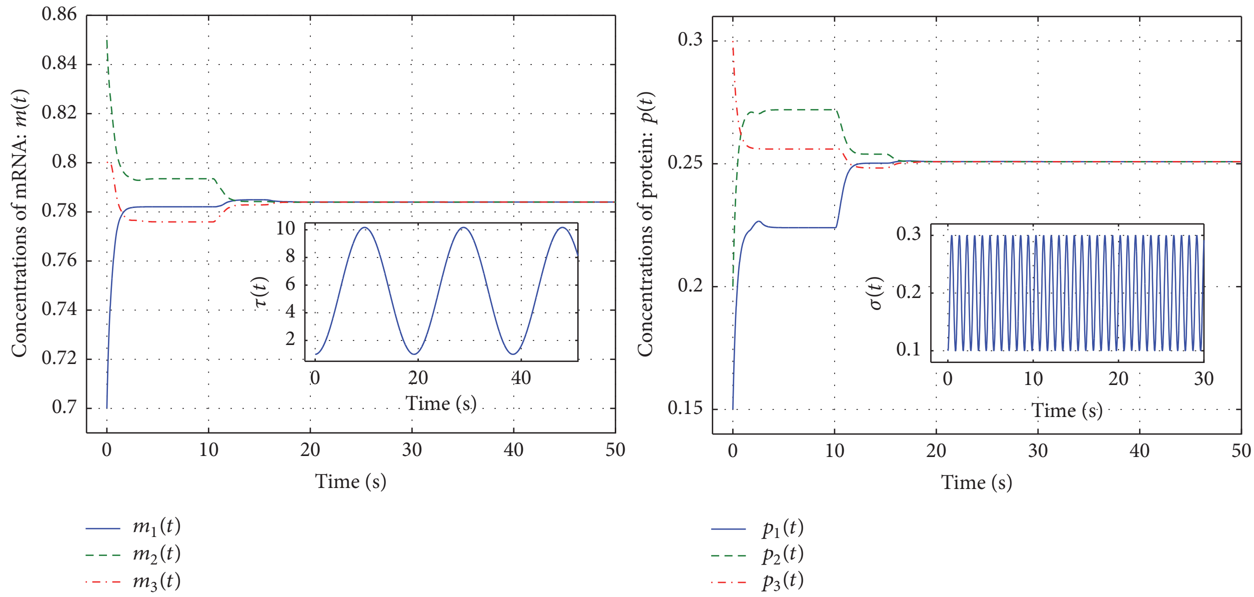

Figure 3: The trajectories of concentrations of mRNA and protein for Case 1.

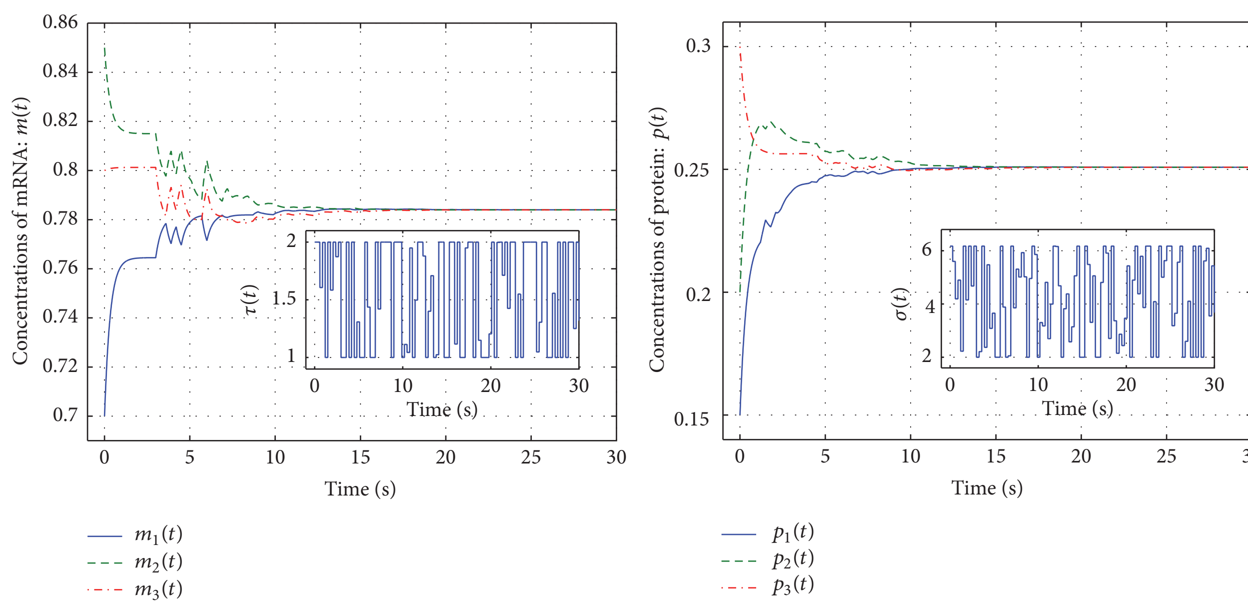

Figure 4: The trajectories of concentrations of mRNA and protein for Case 2.

GRNs:	Genetic regulatory networks
LKF:	Lyapunov-Krasovskii function
LMI:	Linear matrix inequality
JBDII:	Jensen-based double integral inequality
WBDII:	Wirtinger-based double integral inequality
WTDII:	Wiringter-type double integral inequality
MADB:	Maximal admissible delay bounds
NoV:	The number of variables.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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References

[1] Z. Wang, X. Liu, Y. Liu, J. Liang, and V. Vinciotti, "An extended Kalman filtering approach to modeling nonlinear dynamic gene

regulatory networks via short gene expression time series," *IEEE Transactions on Computational Biology and Bioinformatics*, vol. 6, no. 3, pp. 410–419, 2009.

[2] S. Mitra, R. Das, and Y. Hayashi, "Genetic networks and soft computing," *IEEE Transactions on Computational Biology and Bioinformatics*, vol. 8, no. 1, pp. 94–107, 2011.

[3] N. Noman and H. Iba, "Inferring gene regulatory networks using differential evolution with local search heuristics," *IEEE Transactions on Computational Biology and Bioinformatics*, vol. 4, no. 4, pp. 634–647, 2007.

[4] M. B. Elowitz and S. Leibier, "A synthetic oscillatory network of transcriptional regulators," *Nature*, vol. 403, no. 6767, pp. 335–338, 2000.

[5] P. Smolen, D. A. Baxter, and J. H. Byrne, "Mathematical modeling of gene networks," *Neuron*, vol. 26, no. 3, pp. 567–580, 2000.

[6] Z. Wang, F. Yang, D. W. C. Ho, S. Swift, A. Tucker, and X. Liu, "Stochastic dynamic modeling of short gene expression time-series data," *IEEE Transactions on NanoBioscience*, vol. 7, no. 1, pp. 44–55, 2008.

[7] T. Schlitt and A. Brazma, "Current approaches to gene regulatory network modelling," *BMC Bioinformatics*, vol. 8, no. 6, article no. S9, 2007.

[8] L. Qian, H. Wang, and E. R. Dougherty, "Inference of noisy nonlinear differential equation models for gene regulatory networks using genetic programming and Kalman filtering," *IEEE Transactions on Signal Processing*, vol. 56, no. 7, part 2, pp. 3327–3339, 2008.

[9] H. Hirata, S. Yoshiura, T. Ohtsuka et al., "Oscillatory expression of the BHLH factor Hes1 regulated by a negative feedback loop," *Science*, vol. 298, no. 5594, pp. 840–843, 2002.

[10] P. Smolen, D. A. Baxter, and J. H. Byrne, "A reduced model clarifies the role of feedback loops and time delays in the Drosophila circadian oscillator," *Biophysical Journal*, vol. 83, no. 5, pp. 2349–2359, 2002.

[11] I. Hoteit, N. Kharma, and L. Varin, "Computational simulation of a gene regulatory network implementing an extendable synchronous single-input delay flip-flop," *BioSystems*, vol. 109, no. 1, pp. 57–71, 2012.

[12] D. Bratsun, D. Volfson, L. S. Tsimring, and J. Hasty, "Delay-induced stochastic oscillations in gene regulation," *Proceedings of the National Acadamy of Sciences of the United States of America*, vol. 102, no. 41, pp. 14593–14598, 2005.

[13] X. Wan, L. Xu, H. Fang, and G. Ling, "Robust non-fragile H∞ state estimation for discrete-time genetic regulatory networks with Markov jump delays and uncertain transition probabilities," *Neurocomputing*, vol. 154, pp. 162–173, 2015.

[14] A. Becskel and L. Serrano, "Engineering stability in gene networks by autoregulation," *Nature*, vol. 405, no. 6786, pp. 590–593, 2000.

[15] L. Chen and K. Aihara, "Stability of genetic regulatory networks with time delay," *IEEE Transactions on Circuits and Systems I: Fundamental Theory and Applications*, vol. 49, no. 5, pp. 602–608, 2002.

[16] F.-X. Wu, "Stability and bifurcation of ring-structured genetic regulatory networks with time delays," *IEEE Transactions on Circuits and Systems I: Regular Papers*, vol. 59, no. 6, pp. 1312–1320, 2012.

[17] F. Ren and J. Cao, "Asymptotic and robust stability of genetic regulatory networks with time-varying delays," *Neurocomputing*, vol. 71, no. 4–6, pp. 834–842, 2008.

[18] W. Zhang, J.-A. Fang, and Y. Tang, "New robust stability analysis for genetic regulatory networks with random discrete delays and distributed delays," *Neurocomputing*, vol. 74, no. 14-15, pp. 2344–2360, 2011.

[19] X. Zhang, L. Wu, and S. Cui, "An improved integral inequality to stability analysis of genetic regulatory networks with interval time-varying delays," *IEEE Transactions on Computational Biology and Bioinformatics*, vol. 12, no. 2, pp. 398–409, 2015.

[20] F.-X. Wu, "Delay-independent stability of genetic regulatory networks," *IEEE Transactions on Neural Networks and Learning Systems*, vol. 22, no. 11, pp. 1685–1693, 2011.

[21] X. Zhang, A. Yu, and G. Zhang, "M-matrix-based delay-range-dependent global asymptotical stability criterion for genetic regulatory networks with time-varying delays," *Neurocomputing*, vol. 113, pp. 8–15, 2013.

[22] X. Zhang, L. Wu, and J. Zou, "Globally asymptotic stability analysis for genetic gegulatory networks with mixed delays: An M-matrix-based approach," *IEEE/ACM Transactions on Computational Biology and Bioinformatics*, pp. 10–1109, 2015.

[23] F. Wu, "Global and robust stability analysis of genetic regulatory networks with time-varying delays and parameter uncertainties," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 5, no. 4, pp. 391–398, 2011.

[24] Y. Wang, Z. Wang, and J. Liang, "On robust stability of stochastic genetic regulatory networks with time delays: A delay fractioning approach," *IEEE Transactions on Systems, Man, and Cybernetics, Part B: Cybernetics*, vol. 40, no. 3, pp. 729–740, 2010.

[25] Q. Zhu, L. Jiang, W. Yao, C.-K. Zhang, and C. Luo, "Robust Load Frequency Control with Dynamic Demand Response for Deregulated Power Systems Considering Communication Delays," *Electric Power Components and Systems*, vol. 45, no. 1, pp. 75–87, 2017.

[26] P. Balasubramaniam and R. Sathy, "Robust asymptotic stability of fuzzy Markovian jumping genetic regulatory networks with time-varying delays by delay decomposition approach," *Communications in Nonlinear Science and Numerical Simulation*, vol. 16, no. 2, pp. 928–939, 2011.

[27] P. Balasubramaniam, R. Sathy, and R. Rakkiyappan, "A delay decomposition approach to fuzzy Markovian jumping genetic regulatory networks with time-varying delays," *Fuzzy Sets and Systems*, vol. 164, no. 1, pp. 82–100, 2011.

[28] Z. Wang, H. Gao, J. Cao, and X. Liu, "On delayed genetic regulatory networks with polytopic uncertainties: Robust stability analysis," *IEEE Transactions on NanoBioscience*, vol. 7, no. 2, article no. 8, pp. 154–163, 2008.

[29] H. Wu, X. Liao, W. Feng, S. Guo, and W. Zhang, "Robust stability for uncertain genetic regulatory networks with interval time-varying delays," *Information Sciences*, vol. 180, no. 18, pp. 3532–3545, 2010.

[30] J. H. Koo, D. H. Ji, S. C. Won, and J. H. Park, "An improved robust delay-dependent stability criterion for genetic regulatory networks with interval time delays," *Communications in Nonlinear Science and Numerical Simulation*, vol. 17, no. 8, pp. 3399–3405, 2012.

[31] W. Wang and S. Zhong, "Delay-dependent stability criteria for genetic regulatory networks with time-varying delays and nonlinear disturbance," *Communications in Nonlinear Science and Numerical Simulation*, vol. 17, no. 9, pp. 3597–3611, 2012.

[32] L.-P. Tian, J. Wang, and F.-X. Wu, "Robust and global delay-dependent stability for genetic regulatory networks with parameter uncertainties," *IEEE Transactions on NanoBioscience*, vol. 11, no. 3, pp. 251–258, 2012.

[33] J. Liu and D. Yue, "Asymptotic and robust stability of T-S fuzzy genetic regulatory networks with time-varying delays," *International Journal of Robust and Nonlinear Control*, vol. 22, no. 8, pp. 827–840, 2012.

[34] W. Wang, S. Zhong, and F. Liu, "New delay-dependent stability criteria for uncertain genetic regulatory networks with time-varying delays," *Neurocomputing*, vol. 93, pp. 19–26, 2012.

[35] P.-L. Liu, "Robust stability analysis of genetic regulatory network with time delays," *ISA Transactions®*, vol. 52, no. 3, pp. 326–334, 2013.

[36] W. Wang, S. Zhong, S. Kiong Nguang, and F. Liu, "Novel delay-dependent stability criterion for uncertain genetic regulatory networks with interval time-varying delays," *Neurocomputing*, vol. 121, pp. 170–178, 2013.

[37] C. Li, L. Chen, and K. Aihara, "Stability of genetic networks with SUM regulatory logic: Lur'e system and LMI approach," *IEEE Transactions on Circuits and Systems I: Regular Papers*, vol. 53, no. 11, pp. 2451–2458, 2006.

[38] C. Li, L. Chen, and K. Aihara, "Stochastic stability of genetic networks with disturbance attenuation," *IEEE Transactions on Circuits and Systems II: Express Briefs*, vol. 54, no. 10, pp. 892–896, 2007.

[39] H. Wu, X. Liao, S. Guo, W. Feng, and Z. Wang, "Stochastic stability for uncertain genetic regulatory networks with interval time-varying delays," *Neurocomputing*, vol. 72, no. 13-15, pp. 3263–3276, 2009.

[40] Q. Zhou, S. Xu, B. Chen, H. Li, and Y. Chu, "Stability analysis of delayed genetic regulatory networks with stochastic disturbances," *Physics Letters A*, vol. 373, no. 41, pp. 3715–3723, 2009.

[41] Y. He, L.-Y. Fu, J. Zeng, and M. Wu, "Stability of genetic regulatory networks with interval time-varying delays and stochastic perturbation," *Asian Journal of Control*, vol. 13, no. 5, pp. 625–634, 2011.

[42] W. Zhang, J.-a. Fang, and Y. Tang, "Robust stability for genetic regulatory networks with linear fractional uncertainties," *Communications in Nonlinear Science and Numerical Simulation*, vol. 17, no. 4, pp. 1753–1765, 2012.

[43] W. Zhang, J.-a. Fang, and Y. Tang, "Stochastic stability of Markovian jumping genetic regulatory networks with mixed time delays," *Applied Mathematics and Computation*, vol. 217, no. 17, pp. 7210–7225, 2011.

[44] L.-P. Tian, Z.-K. Shi, L.-Z. Liu, and F.-X. Wu, "M-matrix-based stability conditions for genetic regulatory networks with time-varying delays and noise perturbations," *IET Systems Biology*, vol. 7, no. 5, pp. 214–222, 2013.

[45] Y. Zhu, Q. Zhang, Z. Wei, and L. Zhang, "Robust stability analysis of Markov jump standard genetic regulatory networks with mixed time delays and uncertainties," *Neurocomputing*, vol. 110, pp. 44–50, 2013.

[46] W. Wang, S. Zhong, F. Liu, and J. Cheng, "Robust delay-probability-distribution-dependent stability of uncertain stochastic genetic regulatory networks with random discrete delays and distributed delays," *International Journal of Robust and Nonlinear Control*, vol. 24, no. 16, pp. 2574–2596, 2014.

[47] Y. Sun, G. Feng, and J. Cao, "Stochastic stability of Markovian switching genetic regulatory networks," *Physics Letters A*, vol. 373, no. 18-19, pp. 1646–1652, 2009.

[48] R. Rakkiyappan and P. Balasubramaniam, "Delay-probability-distribution-dependent stability of uncertain stochastic genetic regulatory networks with mixed time-varying delays: an LMI approach," *Nonlinear Analysis: Hybrid Systems*, vol. 4, no. 3, pp. 600–607, 2010.

[49] Y. Sun, G. Feng, and J. Cao, "Robust stochastic stability analysis of genetic regulatory networks with disturbance attenuation," *Neurocomputing*, vol. 79, pp. 39–49, 2012.

[50] W. Wang and S. Zhong, "Stochastic stability analysis of uncertain genetic regulatory networks with mixed time-varying delays," *Neurocomputing*, vol. 82, no. 1, pp. 143–156, 2012.

[51] Y. Wang, A. Yu, and X. Zhang, "Robust stability of stochastic genetic regulatory networks with time-varying delays: A delay fractioning approach," *Neural Computing and Applications*, vol. 23, no. 5, pp. 1217–1227, 2013.

[52] W. Wang, S. K. Nguang, S. Zhong, and F. Liu, "Robust stability analysis of stochastic delayed genetic regulatory networks with polytopic uncertainties and linear fractional parametric uncertainties," *Communications in Nonlinear Science and Numerical Simulation*, vol. 19, no. 5, pp. 1569–1581, 2014.

[53] X. Lou, Q. Ye, and B. Cui, "Exponential stability of genetic regulatory networks with random delays," *Neurocomputing*, vol. 73, no. 4-6, pp. 759–769, 2010.

[54] Z. Wang, X. Liao, S. Guo, and H. Wu, "Mean square exponential stability of stochastic genetic regulatory networks with time-varying delays," *Information Sciences*, vol. 181, no. 4, pp. 792–811, 2011.

[55] W. Zhang, J.-a. Fang, and W. Cui, "Exponential stability of switched genetic regulatory networks with both stable and unstable subsystems," *Journal of The Franklin Institute*, vol. 350, no. 8, pp. 2322–2333, 2013.

[56] Y. Yao, J. Liang, and J. Cao, "Stability analysis for switched genetic regulatory networks: an average dwell time approach," *Journal of The Franklin Institute*, vol. 348, no. 10, pp. 2718–2733, 2011.

[57] W. Zhang, Y. Tang, X. Wu, and J.-A. Fang, "Stochastic stability of switched genetic regulatory networks with time-varying delays," *IEEE Transactions on NanoBioscience*, vol. 13, no. 3, pp. 336–342, 2014.

[58] Q. Zhou, X. Shao, H. Reza Karimi, and J. Zhu, "Stability of genetic regulatory networks with time-varying delay: delta operator method," *Neurocomputing*, vol. 149, pp. 490–495, 2015.

[59] Z. Wang, J. Lam, G. Wei, K. Fraser, and X. Liu, "Filtering for nonlinear genetic regulatory networks with stochastic disturbances," *Institute of Electrical and Electronics Engineers Transactions on Automatic Control*, vol. 53, no. 10, pp. 2448–2457, 2008.

[60] J. Liang, J. Lam, and Z. Wang, "State estimation for Markov-type genetic regulatory networks with delays and uncertain mode transition rates," *Physics Letters A*, vol. 373, no. 47, pp. 4328–4337, 2009.

[61] W. Yu, J. Lu, Z. D. Wang, J. Cao, and Q. Zhou, "Robust H∞ control and uniformly bounded control for genetic regulatory network with stochastic disturbance," *IET Control Theory & Applications*, vol. 4, no. 9, pp. 1687–1706, 2010.

[62] D. Zhang and L. Yu, "Passivity analysis for stochastic Markovian switching genetic regulatory networks with time-varying delays," *Communications in Nonlinear Science and Numerical Simulation*, vol. 16, no. 8, pp. 2985–2992, 2011.

[63] P. Li and J. Lam, "Disturbance analysis of nonlinear differential equation models of genetic SUM regulatory networks," *IEEE Transactions on Computational Biology and Bioinformatics*, vol. 8, no. 1, pp. 253–259, 2011.

[64] Y. He, J. Zeng, M. Wu, and C.-K. Zhang, "Robust stabilization and H∞ controllers design for stochastic genetic regulatory networks with time-varying delays and structured uncertainties," *Mathematical Biosciences*, vol. 236, no. 1, pp. 53–63, 2012.

[65] Y. Liu and H. Jiang, "Exponential stability of genetic regulatory networks with mixed delays by periodically intermittent control," *Neural Computing and Applications*, vol. 21, no. 6, pp. 1263–1269, 2012.

[66] L. Chen, Y. Zhou, and X. Zhang, "Guaranteed cost control for uncertain genetic regulatory networks with interval time-varying delays," *Neurocomputing*, vol. 131, pp. 105–112, 2014.

[67] C. Ma, Q. Zeng, L. Zhang, and Y. Zhu, "Passivity and passification for Markov jump genetic regulatory networks with time-varying delays," *Neurocomputing*, vol. 136, pp. 321–326, 2014.

[68] L. Lu, Z. Xing, and B. He, "Non-uniform sampled-data control for stochastic passivity and passification of Markov jump genetic regulatory networks with time-varying delays," *Neurocomputing*, vol. 171, pp. 434–443, 2016.

[69] L. Li and Y. Yang, "On sampled-data control for stabilization of genetic regulatory networks with leakage delays," *Neurocomputing*, vol. 149, pp. 1225–1231, 2015.

[70] R. Anbuvithya, K. Mathiyalagan, R. Sakthivel, and P. Prakash, "Sampled-data state estimation for genetic regulatory networks with time-varying delays," *Neurocomputing*, vol. 151, no. 2, pp. 737–744, 2015.

[71] J. Sun, G. P. Liu, J. Chen, and D. Rees, "Improved delay-range-dependent stability criteria for linear systems with time-varying delays," *Automatica*, vol. 46, no. 2, pp. 466–470, 2010.

[72] M. Park, O. Kwon, J. H. Park, S. Lee, and E. Cha, "Stability of time-delay systems via Wirtinger-based double integral inequality," *Automatica*, vol. 55, pp. 204–208, 2015.

[73] A. Seuret and F. Gouaisbaut, "Wirtinger-based integral inequality: Application to time-delay systems," *Automatica*, vol. 49, no. 9, pp. 2860–2866, 2013.

[74] P. Park, W. I. Lee, and S. Y. Lee, "Auxiliary function-based integral inequalities for quadratic functions and their applications to time-delay systems," *Journal of The Franklin Institute*, vol. 352, no. 4, pp. 1378–1396, 2015.

[75] P. Park, J. W. Ko, and C. Jeong, "Reciprocally convex approach to stability of systems with time-varying delays," *Automatica*, vol. 47, no. 1, pp. 235–238, 2011.

[76] C.-K. Zhang, Y. He, L. Jiang, Q. H. Wu, and M. Wu, "Delay-dependent stability criteria for generalized neural networks with two delay components," *IEEE Transactions on Neural Networks and Learning Systems*, vol. 25, no. 7, pp. 1263–1276, 2014.

[77] C.-K. Zhang, Y. He, L. Jiang, and M. Wu, "Stability analysis for delayed neural networks considering both conservativeness and complexity," *IEEE Transactions on Neural Networks and Learning Systems*, vol. 27, no. 7, pp. 1486–1501, 2016.

[78] C. Zhang, Y. He, L. Jiang, and M. Wu, "Notes on Stability of Time-Delay Systems: Bounding Inequalities and Augmented Lyapunov-Krasovskii Functionals," *IEEE Transactions on Automatic Control*, vol. 62, no. 10, pp. 5331–5336, 2017.

[79] C.-K. Zhang, Y. He, L. Jiang, M. Wu, and H.-B. Zeng, "Summation inequalities to bounded real lemmas of discrete-time systems with time-varying delay," *Institute of Electrical and Electronics Engineers Transactions on Automatic Control*, vol. 62, no. 5, pp. 2582–2588, 2017.

[80] G. Balas, R. Chiang, A. Packard, and M. Safonov, *Robust Control Toolbox Users Guide*, MathWorks, 2010.

[81] W. Yao, L. Jiang, Q. H. Wu, J. Y. Wen, and S. J. Cheng, "Delay-dependent stability analysis of the power system with a wide-area damping controller embedded," *IEEE Transactions on Power Systems*, vol. 26, no. 1, pp. 233–240, 2011.

[82] C.-K. Zhang, L. Jiang, Q. H. Wu, Y. He, and M. Wu, "Delay-dependent robust load frequency control for time delay power systems," *IEEE Transactions on Power Systems*, vol. 28, no. 3, pp. 2192–2201, 2013.

[83] C.-K. Zhang, L. Jiang, Q. H. Wu, Y. He, and M. Wu, "Further results on delay-dependent stability of multi-area load frequency control," *IEEE Transactions on Power Systems*, vol. 28, no. 4, pp. 4465–4474, 2013.