On Robust Stability of Stochastic Genetic Regulatory Networks With Time Delays: A Delay Fractioning Approach

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***Abstract*—Robust stability serves as an important regulation mechanism in system biology and synthetic biology. In this paper, the robust stability analysis problem is investigated for a class of nonlinear delayed genetic regulatory networks with parameter uncertainties and stochastic perturbations. The nonlinear function describing the feedback regulation satisfies the sector condition, the time delays exist in both translation and feedback regulation processes, and the state-dependent Brownian motions are introduced to reflect the inherent intrinsic and extrinsic noise perturbations. The purpose of the addressed stability analysis problem is to establish some easy-to-verify conditions under which the dynamics of the true concentrations of the messenger ribonucleic acid (mRNA) and protein is asymptotically stable irrespective of the norm-bounded modeling errors. By utilizing a new Lyapunov functional based on the idea of "delay fractioning", we employ the linear matrix inequality (LMI) technique to derive delay-dependent sufficient conditions ensuring the robust stability of the gene regulatory networks. Note that the obtained results are formulated in terms of LMIs that can easily be solved using standard software packages. Simulation examples are exploited to illustrate the effectiveness of the proposed design procedures.**

***Index Terms*—Genetic regulatory networks (GRNs), linear matrix inequality (LMI), Lyapunov–Krasovskii functional, robust stability, stochastic perturbation, time delays, uncertain system.**

I. Introduction

The past few years have witnessed the significant progress in the research area of gene engineering and other biological sciences. The mechanisms that have evolved to regulate the gene expression are known as genetic regulatory networks (GRNs). With the study of GRNs, scientists would be able to explain the interactions between genes and protein that form complex biological systems. It is of great importance to investigate and understand the gene regulatory process and the dynamic behaviors of the GRNs in living organisms [1], [2], [4], [7], [27].

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The modeling of GRNs is largely dependent on powerful tools of mathematics theory. In general, the GRNs can be described by two types of models, i.e., the discrete model (such as Boolean networks) and the continuous model (such as the differential equation model) [1], [7], [8], [21], [32]. Recently, among all the proposed GRN models, the differential equation models have received an increasing amount of research attention since the variables in gene dynamics are usually the concentrations of gene products (i.e., messenger ribonucleic acids (mRNAs) and proteins), which possess continuous values of the genetic regulatory systems (see [2], [3], [13], [14], [20], [27], [28], and the references therein). Our present research further examines the continuous GRN models with both time delays and norm-bounded parameter uncertainties.

It is well known that the existence of time delays is ubiquitous in biological, physical, chemical, and electrical dynamical systems [9]. In biological systems, particularly GRNs, time delays are unavoidable primarily due to the finite speed in the slow process of transcription, translation, and translocation. It has been shown in [13] and [14] that the time delays in GRNs may play an important role in the predictions of the dynamics of the mRNA and protein concentrations. Moreover, given the facts that GRNs are modeled from real-world gene expression time-series data, and that there are certain limitations with the current experimental techniques, it has now been well recognized that the modeling errors and parameter fluctuations are inevitable, which may cause poor performance or even instability of real genetic networks [2], [4], [10]. It should be pointed out that the system parameters identified from experimental data may form an unknown but bounded time-varying function (see [20] and [30]). When investigating the dynamical behaviors of GRNs, the parameter uncertainties (also called variations or fluctuations) should also be taken into account, and therefore, the stability robustness issue for GRNs emerges as a research topic of great importance.

On the other hand, the modeling of GRNs should be conducted in a way to interpret vast amounts of experimental data and the extracted functional information from observation data. Given the fact that biology networks or genetic networks are always subject to random fluctuations [1], [4], [18], [22],

[23], it is vitally important to consider the random effects including both the intrinsic and extrinsic noise perturbations [1], [14], [27], [29]. Both the modeling error and the stochastic disturbances could cause instability [29] of the networks and make it difficult to know the true dynamics of the network state. Therefore, an interesting problem of biological significance is to investigate the robust stochastic stability in the presence of time delays, parameter uncertainties, and stochastic disturbances for the addressed GRNs, which give rise to another motivation for the present research.

Although the robust stability of GRNs has stirred some initial research interests [2], [4], [20], one of the main issues aroused here is how to reduce the possible conservatism induced by the introduction of the Lyapunov functional when dealing with time delays, which leaves much room for further research by using the latest analysis techniques. Recently, the so-called "delay fractioning" approach, which is arguably the up-to-date delay-dependence analysis method, has independently been originated from [12] and [19] and further developed in [16], [17], [26], [33], and [35], and shown to lead to much less conservative results than most existing literature. It is, therefore, the main purpose of this paper to adopt the delay-fractioning approach for achieving a less conservative delay-dependence condition to guarantee the robust stability of the addressed GRNs.

In this paper, we are concerned with the robust stability analysis problem for a class of uncertain GRNs with and without noise perturbations, where the time delays exist in both the translation process and the feedback regulation process, and the nonlinear function describing the feedback regulation is assumed to satisfy the sector condition. By utilizing a novel Lyapunov–Krasovskii functional and the linear matrix inequality (LMI) technique, sufficient delay-dependent conditions ensuring the robust stability of the gene regulatory model are established. The obtained results are formulated in the form of LMIs that are easily solvable by using standard software packages. Simulation examples with three component genetic networks are used to illustrate the effectiveness of the developed theoretical results.

Notations: The notations used throughout this paper are fairly standard. $\mathfrak{R}^n$ and $\mathfrak{R}^{n\times m}$ denote the n-dimensional Euclidean space and the set of $n\times m$ real matrices, respectively, and $|\cdot|$ is the Euclidean norm on $\mathfrak{R}^n$. $P>0$ means that matrix P is real, symmetric, and positive definite. I and 0 denote the identity matrix and the zero matrix with compatible dimensions, respectively, $\mathrm{diag}\{\cdots\}$ stands for a block-diagonal matrix, and $\mathrm{col}\{\cdots\}$ denotes a matrix column with blocks given by the matrices in $\{\cdots\}$. The superscript "T" stands for matrix transposition, and the asterisk "$*$" in a matrix is used to represent the term that is induced by symmetry. The Kronecker product of matrices $Q\in\mathbb{R}^{m\times n}$ and $R\in\mathbb{R}^{p\times q}$ is a matrix in $\mathbb{R}^{mp\times nq}$ and denoted as $Q\otimes R$. Moreover, let $(\Omega,\mathcal{F},\{\mathcal{F}_t\}_{t\ge 0},\mathcal{P})$ be a complete probability space with a filtration $\{\mathcal{F}_t\}_{t\ge 0}$ satisfying the usual conditions (i.e., the filtration contains all $\mathcal{P}$-null sets and is right continuous). Denote by $L^p_{\mathcal{F}_0}([-h,0];\mathfrak{R}^n)$ the family of all $\mathcal{F}_0$-measurable $\mathcal{C}([-h,0];\mathfrak{R}^n)$-valued random variables $\xi=\{\xi(\theta):-h\le\theta\le 0\}$ such that $\sup_{-h\le\theta\le 0}\mathbb{E}\{|\xi(\theta)|^p\}<\infty$, where $\mathbb{E}\{\cdot\}$ stands for the mathematical expectation operator with respect to the given probability measure $\mathcal{P}$. Matrix dimensions, if they are not explicitly stated, are assumed to be compatible for algebraic operations.

II. Model Description and Preliminaries

In this paper, we consider a GRN with time delays existing in both the translation process and the feedback regulation process, which can be described by the following differential equations:

$$\Sigma:\begin{cases}\frac{dm_i(t)}{dt}=-a_im_i(t)+\sum\limits_{j=1}^{n}b_{ij}f_j\left(p_j(t-\sigma)\right)+\eta_i\\ \frac{dp_i(t)}{dt}=-c_ip_i(t)+d_im_i(t-\tau)\end{cases}\tag{1}$$

where $i=1,2,\ldots,n$, $m_i(t)$, $p_i(t)\in\mathfrak{R}$ denote, respectively, the concentrations of mRNA and protein of the ith gene at time t, a_i and c_i are the degradation rates of mRNA and protein of the ith gene, respectively, d_i represents the translation rate, $f_j(p_j(s))$ denotes the feedback regulation of the protein on the transcription, which is generally a nonlinear function with monotonicity and satisfies certain conditions given later, the two positive scalars τ and σ denote, respectively, the translation time delay and the feedback regulation delay, η_i is the base transcriptional rate of the repressor of gene i, and the matrix $B=(b_{ij})\in\mathfrak{R}^{n\times n}$ is defined as

$$b_{ij}:\begin{cases}>0, & \text{if transcription factor } j \text{ is an activator of gene } i\\ =0, & \text{if there is no link from gene } i \text{ to gene } j\\ <0, & \text{if transcription factor } j \text{ is a repressor of gene } i\end{cases}.\tag{2}$$

For simplicity, the GRN Σ can be rewritten in the following compact matrix form:

$$\Sigma':\begin{cases}\frac{dm(t)}{dt}=-Am(t)+Bf\left(p(t-\sigma)\right)+\eta\\ \frac{dp(t)}{dt}=-Cp(t)+Dm(t-\tau)\end{cases}\tag{3}$$

where $m(t)=\mathrm{col}\{m_1(t),m_2(t),\ldots,m_n(t)\}$, $p(t)=\mathrm{col}\{p_1(t),p_2(t),\ldots,p_n(t)\}$, $A=\mathrm{diag}\{a_1,a_2,\ldots,a_n\}$, $C=\mathrm{diag}\{c_1,c_2,\ldots,c_n\}$, $D=\mathrm{diag}\{d_1,d_2,\ldots,d_n\}$, $\eta=\mathrm{col}\{\eta_1,\eta_2,\ldots,\eta_n\}$, and $f(p(t-\sigma))=\mathrm{col}\{f_1(p_1(t-\sigma)),f_2(p_2(t-\sigma)),\ldots,f_n(p_n(t-\sigma))\}\in\mathfrak{R}^n$.

The initial condition of the GRN Σ' is given by

$$m(t)=\phi(t)\quad p(t)=\varphi(t)\quad -\varrho\le t\le 0\quad \varrho\triangleq\max\{\tau,\sigma\}$$

where $\phi(\cdot)$ and $\varphi(\cdot)$ are continuous functions.

Let $\mathrm{col}\{m^*,p^*\}\in\mathfrak{R}^{2n}$ be an equilibrium point of Σ', which is a solution of the following nonlinear equations:

$$\begin{cases}-Am+Bf(p)+\eta=0\\ -Cp+Dm=0\end{cases}.\tag{4}$$

In the following, let us shift the unknown equilibrium point $\mathrm{col}\{m^*,p^*\}$ to the origin by defining

$$x=m-m^*\quad y=p-p^*\tag{5}$$

then, the system (Σ') becomes

$$\Sigma'' : \begin{cases} \frac{dx(t)}{dt} = -Ax(t) + Bg\left(y(t-\sigma)\right) \\ \frac{dy(t)}{dt} = -Cy(t) + Dx(t-\tau) \end{cases} \tag{6}$$

where $g(y(t)) = \mathrm{col}\{g_1(y_1(t)), g_2(y_2(t)), \ldots, g_n(y_n(t))\}$, with the ith component being $g_i(y_i(t)) = f_i(y_i(t) + p_i^*) - f_i(p_i^*)$.

As discussed in Section I, the GRN model parameters identified from real-world time series are largely dependent on the selection of fixed points, and the relevant constants vary with the experiment data. Therefore, we further take the structure uncertainties into account and have the following more generalized model:

$$\Sigma''' : \begin{cases} \frac{dx(t)}{dt} = -\left(A + \Delta A(t)\right)x(t) + \left(B + \Delta B(t)\right)g(y(t-\sigma)) \\ \frac{dy(t)}{dt} = -\left(C + \Delta C(t)\right)y(t) + \left(D + \Delta D(t)\right)x(t-\tau) \end{cases}. \tag{7}$$

Here, $\Delta A(t)$, $\Delta B(t)$, $\Delta C(t)$, and $\Delta D(t)$ are unknown matrices with appropriate dimensions denoting the uncertain parameters, which satisfy the following admissible uncertainty condition:

$$\begin{bmatrix} \Delta A(t) & \Delta B(t) \\ \Delta C(t) & \Delta D(t) \end{bmatrix} = \begin{bmatrix} M_1 \\ M_2 \end{bmatrix} H(t)[N_1 \quad N_2] \tag{8}$$

where M_i and N_i $(i = 1, 2)$ are known real constant matrices, and $H(t)$ is a time-varying and unknown Lebesgue-measurable matrix-valued function subjected to the following condition:

$$H^T(t)H(t) \leq I \qquad \forall t > 0. \tag{9}$$

Remark 1: In practice, this kind of norm-bounded uncertainty described by (8) and (9) is frequently encountered in many engineering problems of robust analysis of uncertain dynamic systems (see, for instance, [30] and the references therein), which may result from the variation of operating points, aging of devices, identification errors, etc. Many practical systems possess parameter uncertainties that can be either exactly modeled or over bounded by (9).

For the sake of convenience, we denote the following hereafter:

$$\begin{aligned} A(t) &= A + \Delta A(t) \quad & B(t) &= B + \Delta B(t) \\ C(t) &= C + \Delta C(t) \quad & D(t) &= D + \Delta D(t). \end{aligned}$$

Assumption 1: The nonlinear function $f_i(\cdot)$ is continuous and bounded and satisfies the following inequality:

$$0 \leq \frac{f_j(u) - f_j(v)}{u - v} \leq \kappa_j, \quad j = 1, 2, \ldots, n \tag{10}$$

for all $u, v \in \mathfrak{R}$, $u \neq v$.

Remark 2: It follows from Assumption 1 that the nonlinear feedback regulation function $g_j(\cdot)$ in system Σ''' satisfies the sector-like condition, i.e., $0 \leq g_i(s)/s \leq \kappa_i \ \forall s \neq 0$, and $g_i(0) = 0, i = 1, 2, \ldots, n$, which is equivalent to $g^T(y)[g(y) - Ky] \leq 0$ with $K = \mathrm{diag}\{\kappa_1, \kappa_2, \ldots, \kappa_n\}$. Moreover, it should be pointed out that this sector-like condition described by (10) is more general than those that have been used in [13], [14], and [24], where the derivative for each component of the regulatory function is assumed to be the same, which is unrealistic. In our description, such a restriction is removed.

Remark 3: Usually, various fixed-point theorems, such as Brouwer's fixed-point theorem, Schauder's fixed-point theorem, and the contraction mapping principle, can be exploited to prove the existence of equilibrium points of the addressed GRNs. For example, under Assumption 1, it is not difficult to ensure the existence of an equilibrium point of the system [see (7)] by using Brouwer's fixed-point theorem. In the sequel, we shall analyze the globally asymptotic stability of the equilibrium point, which in turn implies the uniqueness of the equilibrium point.

Before stating the main results, we introduce the following useful definitions and lemmas.

Definition 1: Let the equilibrium point of the nominal system of Σ'' be stable in the sense of Lyapunov. The nominal system of Σ'' is said to be globally asymptotically stable if

$$\lim_{t \to +\infty} \left\{ |m(t) - m^*|^2 + |p(t) - p^*|^2 \right\} = 0.$$

Definition 2: The uncertain system Σ''' is said to be globally asymptotically robustly stable if system Σ'' is globally asymptotically stable for all admissible uncertainties.

Lemma 1 (Schur's Complement) [34]: Given any real matrices Ω_1, Ω_2, and Ω_3, where $\Omega_1^T = \Omega_1$, and $\Omega_2 > 0$, then

$$\Omega_1 + \Omega_3^T \Omega_2^{-1} \Omega_3 < 0$$

if and only if

$$\begin{bmatrix} \Omega_1 & \Omega_3^T \\ \Omega_3 & -\Omega_2 \end{bmatrix} < 0.$$

Lemma 2 [31]: Assume that D, E are real matrices with appropriate dimensions, and $H(t)$ is a real matrix function satisfying $H^T(t)H(t) \leq I$. Then, for any positive scalar ε, the following inequality holds:

$$DH(t)E + (DH(t)E)^T \leq \varepsilon E E^T + \varepsilon^{-1} D^T D.$$

Lemma 3 (Jensen's Inequality) [6]: Given a positive-definite matrix $P \in \mathfrak{R}^{n \times n}$ and a scalar $\pi > 0$ for any vector $x(t) = \mathrm{col}\{x_1(t), x_2(t), \ldots, x_n(t)\}$, we have

$$\int_{t-\pi}^{t} \dot{x}^T(\omega) P \dot{x}(\omega) d\omega \geq \frac{1}{\pi} \left[x(t) - x(t-\pi)\right]^T P \left[x(t) - x(t-\pi)\right]. \tag{11}$$

III. Main Results

In this section, we aim to establish the general robust stability results for the uncertain GRN with and without noise perturbations. A Lyapunov functional method is developed based on the idea of "delay fractioning" proposed in the literature. To estimate the upper bound of the time delays for stability, we partition τ and σ into several equal components, that is, $\tau = \Sigma_{i=1}^r \tau_i$ with $\tau_i = \tau/r$, and $\sigma = \Sigma_{i=1}^r \sigma_i$ with $\sigma_i = \sigma/r$, where r

is a positive integer denoting the number of fractions. Our main results are delay dependent, which are formulated in terms of LMIs to ensure the robustly asymptotic stability of the proposed uncertain GRNs with and without noise perturbations.

A. Robust Stability Analysis of GRNs Without Noise Perturbations

In this section, a theorem is presented to give the stability condition for uncertain GRNs Σ''' without noise perturbations. Some corollaries are then obtained for the special case when there are no parameter uncertainties.

Theorem 1: Given any integer $r \geq 1$, the uncertain system Σ''' is globally asymptotically robustly stable with time delays $\tau \in (0, h_1]$, $\sigma \in (0, h_2]$ if there exist matrices $P_i > 0$, $S_i > 0$, and $\Gamma = \mathrm{diag}\{\gamma_1, \gamma_2, \ldots, \gamma_n\} > 0$, any matrices $X_j^{(i)}$, $Y_j^{(i)}$, and $Z_j^{(i)}$ ($i = 1$, 2 and $j = 1, \ldots, r$), and positive scalars ε_k ($k = 1, 2, \ldots, 8$) satisfying

$$\begin{bmatrix} X_j^{(i)} & Y_j^{(i)} \\ * & Z_j^{(i)} \end{bmatrix} > 0 \quad \Xi = \begin{bmatrix} \Xi_1 & \Xi_2 \\ \Xi_2^T & \Xi_3 \end{bmatrix} < 0 \qquad (12)$$

where $\Xi_1 = \Sigma_{k=1}^{2} \Xi_{1k}$, $\Xi_2 = \Omega_1^T \Phi$, and

$$\begin{aligned}
\Xi_3 =& -\mathrm{diag}\{\varepsilon_1 I_n, \varepsilon_2 I_n, \varepsilon_5 I_n, \varepsilon_6 I_n, \varepsilon_3 I_n, \\
& \varepsilon_4 I_n, \varepsilon_7 I_n, \varepsilon_8 I_n\} \\
\Xi_{11} =& W_{P_1}^T \tilde{P}_1 W_{P_1} + W_{P_2}^T \tilde{P}_2 W_{P_2} + W_\Gamma^T \tilde{\Gamma} W_\Gamma + \Lambda_{P_1}^T \tilde{P}_1 \Lambda_{P_1} \\
& + \Lambda_{P_2}^T \tilde{P}_2 \Lambda_{P_2} + \Omega_2^T \Psi \Omega_2 \\
\Xi_{12} =& U_1^T \mathcal{X} U_1 - U_2^T \mathcal{X} U_2 + V_1^T \mathcal{Y} V_1 - V_2^T \mathcal{Y} V_2 \\
& + Q_1^T \mathcal{S}_1 Q_1 + Q_2^T \mathcal{S}_2 Q_2
\end{aligned}$$

$$W_{P_1} = \left[\begin{array}{c} -A \quad 0_{n,(4r+3)n} \quad B \\ \hline I_n \quad 0_{n,4(r+1)n} \end{array}\right]$$

$$W_{P_2} = \left[\begin{array}{c} 0_{n,rn} \quad D \quad 0_{n,(r+1)n} \quad -C \quad 0_{n,2(r+1)n} \\ \hline 0_{n,2(r+1)n} \quad I_n \quad 0_{n,2(r+1)n} \end{array}\right]$$

$$\tilde{P}_i = \begin{bmatrix} 0 & P_i \\ P_i & 0 \end{bmatrix} \quad \tilde{\Gamma} = \begin{bmatrix} 0 & \Gamma \\ \Gamma & -\Gamma \end{bmatrix}$$

$$W_\Gamma = \left[\begin{array}{c} 0_{n,(3r+2)n} \quad \frac{\sqrt{2}}{2}K \quad 0_{n,(r+2)n} \\ \hline 0_{n,4(r+1)n} \quad \sqrt{2} I_n \end{array}\right]$$

$$\Lambda_{P_1} = \left[\begin{array}{c} -A \quad 0_{n,rn} \quad -I_n \quad 0_{n,(3r+2)n} \quad B \\ \hline 0_{n,(r+1)n} \quad I_n \quad 0_{n,3(r+1)n} \end{array}\right]$$

$$\Lambda_{P_2} = \left[\begin{array}{c} 0_{n,rn} D \quad 0_{n,(r+1)n} \quad -C \quad 0_{n,rn} \quad -I_n \quad 0_{n,(r+1)n} \\ \hline 0_{n,3(r+1)n} \quad I_n \quad 0_{n,(r+1)n} \end{array}\right]$$

$$U_1 = \left[\begin{array}{c} I_{rn} \quad 0_{rn,(3r+5)n} \\ \hline 0_{rn,(r+1)n} \quad I_{rn} \quad 0_{rn,2(r+2)n} \end{array}\right]$$

$$U_2 = \left[\begin{array}{c} 0_{rn,n} \quad I_{rn} \quad 0_{rn,(3r+4)n} \\ \hline 0_{rn,(r+2)n} \quad I_{rn} \quad 0_{rn,(2r+3)n} \end{array}\right]$$

$$V_1 = \left[\begin{array}{c} 0_{rn,2(r+1)n} \quad I_{rn} \quad 0_{rn,(r+3)n} \\ \hline 0_{rn,3(r+1)n} \quad I_{rn} \quad 0_{rn,2n} \end{array}\right]$$

$$V_2 = \left[\begin{array}{c} 0_{rn,(2r+3)n} \quad I_{rn} \quad 0_{rn,(r+2)n} \\ \hline 0_{rn,(3r+4)n} \quad I_{rn} \quad 0_{rn,n} \end{array}\right]$$

$$\mathcal{X} = \begin{bmatrix} X^{(1)} & Y^{(1)} \\ * & Z^{(1)} \end{bmatrix} \quad \mathcal{Y} = \begin{bmatrix} X^{(2)} & Y^{(2)} \\ * & Z^{(2)} \end{bmatrix}$$

$$Q_1 = \left[\begin{array}{c} I_{rn} \quad 0_{rn,(3r+5)n} \\ \hline 0_{rn,n} \quad I_{rn} \quad 0_{rn,(3r+4)n} \end{array}\right]$$

$$Q_2 = \left[\begin{array}{c} 0_{rn,(2r+2)n} \quad I_{rn} \quad 0_{rn,(r+3)n} \\ \hline 0_{rn,(2r+3)n} \quad I_{rn} \quad 0_{rn,(r+2)n} \end{array}\right]$$

$$\mathcal{S}_i = \begin{bmatrix} S^{(i)} & -S^{(i)} \\ * & S^{(i)} \end{bmatrix}$$

$$\Omega_1 = \left[\begin{array}{c} I_n \quad 0_{n,4(r+1)n} \\ \hline 0_{n,(r+1)n} \quad I_n \quad 0_{n,3(r+1)n} \\ \hline 0_{n,2(r+1)n} \quad I_n \quad 0_{n,2(r+1)n} \\ \hline 0_{n,3(r+1)n} \quad I_n \quad 0_{n,(r+1)n} \end{array}\right]$$

$$\Omega_2 = \left[\begin{array}{c} I_n \quad 0_{n,4(r+1)n} \\ \hline 0_{n,rn} \quad I_n \quad 0_{n,(3r+4)n} \\ \hline 0_{n,(r+1)n} \quad I_n \quad 0_{n,(3r+3)n} \\ \hline 0_{n,2(r+1)n} \quad I_n \quad 0_{n,(2r+2)n} \\ \hline 0_{n,3(r+1)n} \quad I_n \quad 0_{n,(r+1)n} \\ \hline 0_{n,4(r+1)n} \quad I_n \end{array}\right]$$

$$\Phi = \left[\begin{array}{c} P_1 M_1 \quad P_1 M_1 \quad 0_{n,6n} \\ \hline 0_{n,2n} \quad P_1 M_1 \quad P_1 M_1 \quad 0_{n,4n} \\ \hline 0_{n,4n} \quad P_2 M_2 \quad P_2 M_2 \quad 0_{n,2n} \\ \hline 0_{n,6n} \quad P_2 M_2 \quad P_2 M_2 \end{array}\right]$$

$$\begin{aligned}
\Psi =& \ \mathrm{diag}\left\{(\varepsilon_1 + \varepsilon_5) N_1^T N_1, (\varepsilon_2 + \varepsilon_4) N_2^T N_2, h_1 S_1, \right. \\
& \left. (\varepsilon_3 + \varepsilon_7) N_1^T N_1, h_2 S_2, (\varepsilon_2 + \varepsilon_6) N_2^T N_2 \right\} \\
X^{(i)} =& \ \mathrm{diag}\left\{X_1^{(i)}, X_2^{(i)}, \ldots, X_r^{(i)}\right\} \\
Y^{(i)} =& \ \mathrm{diag}\left\{Y_1^{(i)}, Y_2^{(i)}, \ldots, Y_r^{(i)}\right\} \\
Z^{(i)} =& \ \mathrm{diag}\left\{Z_1^{(i)}, Z_2^{(i)}, \ldots, Z_r^{(i)}\right\} \\
S^{(i)} =& -\frac{r}{h_i}(I_r \otimes S_i), \qquad i = 1, 2.
\end{aligned}$$

Proof: Based on Lemma 1, since $\Xi_3 < 0$, (12) is equivalent to $\Xi_1 - \Xi_2 \Xi_3^{-1} \Xi_2^T < 0$. To prove the theorem, we choose a novel Lyapunov–Krasovskii functional candidate as follows:

$$V(t) = V_1(t) + V_2(t) + V_3(t) \qquad (13)$$

where

$$\begin{aligned}
V_1(t) =& \, x^T(t) P_1 x(t) \\
& + \sum_{k=1}^{r} \int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau} \begin{bmatrix} x(s) \\ \dot{x}(s) \end{bmatrix}^T \begin{bmatrix} X_k^{(1)} & Y_k^{(1)} \\ * & Z_k^{(1)} \end{bmatrix} \begin{bmatrix} x(s) \\ \dot{x}(s) \end{bmatrix} ds \\
V_2(t) =& \, y^T(t) P_2 y(t) \\
& + \sum_{k=1}^{r} \int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma} \begin{bmatrix} y(s) \\ \dot{y}(s) \end{bmatrix}^T \begin{bmatrix} X_k^{(2)} & Y_k^{(2)} \\ * & Z_k^{(2)} \end{bmatrix} \begin{bmatrix} y(s) \\ \dot{y}(s) \end{bmatrix} ds \\
V_3(t) =& \int_{-\tau}^{0} \int_{t+\beta}^{t} \dot{x}^T(\alpha) S_1 \dot{x}(\alpha) d\alpha d\beta \\
& + \int_{-\sigma}^{0} \int_{t+\nu}^{t} \dot{y}^T(\mu) S_2 \dot{y}(\mu) d\mu d\nu
\end{aligned}$$

with $r \geq 1$ (number of fractions) being an integer.

Considering the derivatives of $V_i(t)$ $(i = 1, 2, 3)$ along the trajectory of system Σ''', we have

$$\begin{aligned}
\dot{V}_1(t) =& 2x^T(t)P_1\dot{x}(t) + \begin{bmatrix} x(t) \\ \dot{x}(t) \end{bmatrix}^T \begin{bmatrix} X_1^{(1)} & Y_1^{(1)} \\ * & Z_1^{(1)} \end{bmatrix} \begin{bmatrix} x(t) \\ \dot{x}(t) \end{bmatrix} \\
&- \begin{bmatrix} x(t-\tau) \\ \dot{x}(t-\tau) \end{bmatrix}^T \begin{bmatrix} X_r^{(1)} & Y_r^{(1)} \\ * & Z_r^{(1)} \end{bmatrix} \begin{bmatrix} x(t-\tau) \\ \dot{x}(t-\tau) \end{bmatrix} \\
&- \sum_{l=1}^{r-1} \left(\begin{bmatrix} x\left(t-\frac{l}{r}\tau\right) \\ \dot{x}\left(t-\frac{l}{r}\tau\right) \end{bmatrix}^T \begin{bmatrix} X_l^{(1)} - X_{l+1}^{(1)} & Y_l^{(1)} - Y_{l+1}^{(1)} \\ * & Z_l^{(1)} - Z_{l+1}^{(1)} \end{bmatrix} \right. \\
&\left. \times \begin{bmatrix} x\left(t-\frac{l}{r}\tau\right) \\ \dot{x}\left(t-\frac{l}{r}\tau\right) \end{bmatrix} \right) \\
=& 2x^T(t)P_1\left[-A(t)x(t) + B(t)g\left(y(t-\sigma)\right)\right] + \begin{bmatrix} \mathcal{X}(t) \\ \dot{\mathcal{X}}(t) \end{bmatrix}^T \\
&\times \begin{bmatrix} X^{(1)} & Y^{(1)} \\ * & Z^{(1)} \end{bmatrix} \begin{bmatrix} \mathcal{X}(t) \\ \dot{\mathcal{X}}(t) \end{bmatrix} - \begin{bmatrix} \mathcal{X}\left(t-\frac{\tau}{r}\right) \\ \dot{\mathcal{X}}\left(t-\frac{\tau}{r}\right) \end{bmatrix}^T \\
&\times \begin{bmatrix} X^{(1)} & Y^{(1)} \\ * & Z^{(1)} \end{bmatrix} \begin{bmatrix} \mathcal{X}\left(t-\frac{\tau}{r}\right) \\ \dot{\mathcal{X}}\left(t-\frac{\tau}{r}\right) \end{bmatrix}
\end{aligned} \tag{14}$$

$$\begin{aligned}
\dot{V}_2(t) =& 2y^T(t)P_2\dot{y}(t) + \begin{bmatrix} y(t) \\ \dot{y}(t) \end{bmatrix}^T \begin{bmatrix} X_1^{(2)} & Y_1^{(2)} \\ * & Z_1^{(2)} \end{bmatrix} \begin{bmatrix} y(t) \\ \dot{y}(t) \end{bmatrix} \\
&- \begin{bmatrix} y(t-\sigma) \\ \dot{y}(t-\sigma) \end{bmatrix}^T \begin{bmatrix} X_r^{(2)} & Y_r^{(2)} \\ * & Z_r^{(2)} \end{bmatrix} \begin{bmatrix} y(t-\sigma) \\ \dot{y}(t-\sigma) \end{bmatrix} \\
&- \sum_{l=1}^{r-1} \left(\begin{bmatrix} y\left(t-\frac{l}{r}\sigma\right) \\ \dot{y}\left(t-\frac{l}{r}\sigma\right) \end{bmatrix}^T \begin{bmatrix} X_l^{(2)} - X_{l+1}^{(2)} & Y_l^{(2)} - Y_{l+1}^{(2)} \\ * & Z_l^{(2)} - Z_{l+1}^{(2)} \end{bmatrix} \right. \\
&\left. \times \begin{bmatrix} y\left(t-\frac{l}{r}\sigma\right) \\ \dot{y}\left(t-\frac{l}{r}\sigma\right) \end{bmatrix} \right) \\
=& 2y^T(t)P_2\left[-C(t)y(t) + D(t)x(t-\tau)\right] + \begin{bmatrix} \mathcal{Y}(t) \\ \dot{\mathcal{Y}}(t) \end{bmatrix}^T \\
&\times \begin{bmatrix} X^{(2)} & Y^{(2)} \\ * & Z^{(2)} \end{bmatrix} \begin{bmatrix} \mathcal{Y}(t) \\ \dot{\mathcal{Y}}(t) \end{bmatrix} - \begin{bmatrix} \mathcal{Y}\left(t-\frac{\sigma}{r}\right) \\ \dot{\mathcal{Y}}\left(t-\frac{\sigma}{r}\right) \end{bmatrix}^T \\
&\times \begin{bmatrix} X^{(2)} & Y^{(2)} \\ * & Z^{(2)} \end{bmatrix} \begin{bmatrix} \mathcal{Y}\left(t-\frac{\sigma}{r}\right) \\ \dot{\mathcal{Y}}\left(t-\frac{\sigma}{r}\right) \end{bmatrix}
\end{aligned} \tag{15}$$

$$\begin{aligned}
\dot{V}_3(t) =& \tau\dot{x}^T(t)S_1\dot{x}(t) + \sigma\dot{y}^T(t)S_2\dot{y}(t) \\
&- \int_{t-\tau}^{t} \dot{x}^T(\alpha)S_1\dot{x}(\alpha)d\alpha - \int_{t-\sigma}^{t} \dot{y}^T(\mu)S_2\dot{y}(\mu)d\mu \\
\leq& h_1\dot{x}^T(t)S_1\dot{x}(t) + h_2\dot{y}^T(t)S_2\dot{y}(t) \\
&- \sum_{k=1}^{r} \int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau} \dot{x}^T(\alpha)S_1\dot{x}(\alpha)d\alpha \\
&- \sum_{k=1}^{r} \int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma} \dot{y}^T(\mu)S_2\dot{y}(\mu)d\mu
\end{aligned} \tag{16}$$

where $\mathcal{X}(t) = \mathrm{col}\{x(t), x(t-(1/r)\tau), \ldots, x(t-((r-1)/r)\tau)\}$, and $\mathcal{Y}(t) = \mathrm{col}\{y(t), y(t-(1/r)\sigma), \ldots, y(t-((r-1)/r)\sigma)\}$.

From Lemma 3, for $k = 1, 2, \ldots, r$, it readily follows that

$$\begin{aligned}
&- \int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau} \dot{x}^T(\alpha)S_1\dot{x}(\alpha)d\alpha \\
&\leq -\frac{r}{h_1}\left[x\left(t-\frac{k-1}{r}\tau\right) - x\left(t-\frac{k}{r}\tau\right)\right]^T S_1 \\
&\quad \times \left[x\left(t-\frac{k-1}{r}\tau\right) - x\left(t-\frac{k}{r}\tau\right)\right]; \\
&- \int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma} \dot{y}^T(\mu)S_2\dot{y}(\mu)d\mu \\
&\leq -\frac{r}{h_2}\left[y\left(t-\frac{k-1}{r}\sigma\right) - y\left(t-\frac{k}{r}\sigma\right)\right]^T S_2 \\
&\quad \times \left[y\left(t-\frac{k-1}{r}\sigma\right) - y\left(t-\frac{k}{r}\sigma\right)\right]
\end{aligned}$$

and then

$$\begin{aligned}
&- \sum_{k=1}^{r} \int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau} \dot{x}^T(\alpha)S_1\dot{x}(\alpha)d\alpha \\
&\leq \mathcal{X}^T(t)S^{(1)}\mathcal{X}(t) + \mathcal{X}^T\left(t-\frac{\tau}{r}\right)S^{(1)}\mathcal{X}\left(t-\frac{\tau}{r}\right) \\
&\quad - 2\mathcal{X}^T(t)S^{(1)}\mathcal{X}\left(t-\frac{\tau}{r}\right)
\end{aligned} \tag{17}$$

$$\begin{aligned}
&- \sum_{k=1}^{r} \int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma} \dot{y}^T(\mu)S_2\dot{y}(\mu)d\mu \\
&\leq \mathcal{Y}^T(t)S^{(2)}\mathcal{Y}(t) + \mathcal{Y}^T\left(t-\frac{\sigma}{r}\right)S^{(2)}\mathcal{Y}\left(t-\frac{\sigma}{r}\right) \\
&\quad - 2\mathcal{Y}^T(t)S^{(2)}\mathcal{Y}\left(t-\frac{\sigma}{r}\right)
\end{aligned} \tag{18}$$

where $S^{(i)} = -(r/h_i)(I_r \otimes S_i)$, $i = 1, 2$.

From the sector condition in Assumption 1, for any scalar $\gamma_j > 0$, one can see that

$$-2\sum_{j=1}^{n} \gamma_j g_j\left(y_j(t-\sigma)\right)\left[g_j\left(y_j\left(t-\sigma\right)\right) - \kappa_i y_j(t-\sigma)\right] \geq 0$$

which is equivalent to

$$\begin{aligned}
&2g^T\left(y(t-\sigma)\right)\Gamma K y(t-\sigma) \\
&\qquad - 2g^T\left(y(t-\sigma)\right)\Gamma g\left(y(t-\sigma)\right) \leq 0
\end{aligned} \tag{19}$$

where $\Gamma = \mathrm{diag}\{\gamma_1, \gamma_2, \ldots, \gamma_n\}$.

In view of (7), we obtain

$$\dot{x}^T(t)P_1\left[-A(t)x(t) + B(t)g\left(y(t-\sigma)\right) - \dot{x}(t)\right] = 0 \tag{20}$$

$$\dot{y}^T(t)P_2\left[-C(t)y(t) + D(t)x(t-\tau) - \dot{y}(t)\right] = 0. \tag{21}$$

Using (8), (9), and Lemma 2, for positive scalars $\varepsilon_i > 0$ $(i = 1, 2, \ldots, 8)$, we have

$$\begin{aligned} &-2x^T(t)P_1\Delta A(t)x(t) \\ &\quad\le x^T(t)\left[\varepsilon_1^{-1}P_1M_1M_1^TP_1 + \varepsilon_1N_1^TN_1\right]x(t) \quad (22)\\ &2x^T(t)P_1\Delta B(t)g\left(y(t-\sigma)\right) \\ &\quad\le \varepsilon_2^{-1}x^T(t)P_1M_1M_1^TP_1x(t) + \varepsilon_2 g^T\left(y(t-\sigma)\right) \\ &\quad\quad\times N_2^TN_2 g\left(y(t-\sigma)\right) \quad (23)\\ &-2y^T(t)P_2\Delta C(t)y(t) \\ &\quad\le y^T(t)\left[\varepsilon_3^{-1}P_2M_2M_2^TP_2 + \varepsilon_3N_1^TN_1\right]y(t) \quad (24)\\ &2y^T(t)P_2\Delta D(t)x(t-\tau) \\ &\quad\le \varepsilon_4^{-1}y^T(t)P_2M_2M_2^TP_2y(t) + \varepsilon_4x^T(t-\tau) \\ &\quad\quad\times N_2^TN_2x(t-\tau) \quad (25) \end{aligned}$$

and similarly

$$\begin{aligned} -2\dot{x}^T(t)P_1\Delta A(t)x(t) &\le \varepsilon_5^{-1}\dot{x}^T(t)P_1M_1M_1^TP_1\dot{x}(t) \\ &\quad + \varepsilon_5 x^T(t)N_1^TN_1x(t) \quad (26)\\ 2\dot{x}^T(t)P_1\Delta B(t)g\left(y(t-\sigma)\right) &\le \varepsilon_6^{-1}\dot{x}^T(t)P_1M_1M_1^TP_1\dot{x}(t) \\ &\quad + \varepsilon_6 g^T\left(y(t-\sigma)\right) \\ &\quad \times N_2^TN_2g\left(y(t-\sigma)\right) \quad (27)\\ -2\dot{y}^T(t)P_2\Delta C(t)y(t) &\le \varepsilon_7^{-1}\dot{y}^T(t)P_2M_2M_2^TP_2\dot{y}(t) \\ &\quad + \varepsilon_7 y^T(t)N_1^TN_1y(t) \quad (28)\\ 2\dot{y}^T(t)P_2\Delta D(t)x(t-\tau) &\le \varepsilon_8^{-1}\dot{y}^T(t)P_2M_2M_2^TP_2\dot{y}(t) \\ &\quad + \varepsilon_8 x^T(t-\tau) \\ &\quad \times N_2^TN_2x(t-\tau). \quad (29) \end{aligned}$$

Now, it follows from (14)–(29) and Lemma 1 that

$$\dot{V}(t) \le \xi^T(t)\left(\Xi_1 - \Xi_2\Xi_3^{-1}\Xi_2^T\right)\xi(t) \quad (30)$$

where $\xi(t) = \mathrm{col}\{\mathcal{X}(t), x(t-\tau), \dot{\mathcal{X}}(t), \dot{x}(t-\tau), \mathcal{Y}(t), y(t-\sigma), \dot{\mathcal{Y}}(t), \dot{y}(t-\sigma), g(y(t-\sigma))\}$, and Ξ_i $(i = 1, 2, 3)$ is defined in (12).

Furthermore, the condition in (12) indicates that there exists a positive scalar λ such that

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

which implies from the Lyapunov stability theory that the GRN in (7) is robustly globally asymptotically stable. Hence, the proof is completed. ■

For the nominal system Σ'' without parameter uncertainties, according to Theorem 1, it is not difficult to establish the following sufficient condition on the globally asymptotic stability.

Corollary 1: Given any integer $r \ge 1$, the nominal system of genetic networks Σ''' with time delays $\tau \in (0, h_1]$ and $\sigma \in (0, h_2]$ is globally asymptotically stable if there exist matrices $P_i > 0$, $S_i > 0$, $\Gamma = \mathrm{diag}\{\gamma_1, \gamma_2, \ldots, \gamma_n\} > 0$, and $\begin{bmatrix} X_j^{(i)} & Y_j^{(i)} \\ * & Z_j^{(i)} \end{bmatrix} > 0$ $(i = 1, 2$ and $j = 1, \ldots, r)$ satisfying

$$\tilde{\Xi}_1 = \tilde{\Xi}_{11} + \Xi_{12} < 0 \quad (31)$$

where

$$\begin{aligned} \tilde{\Xi}_{11} &= W_{P_1}^T\tilde{P}_1W_{P_1} + W_{P_2}^T\tilde{P}_2W_{P_2} + W_\Gamma^T\tilde{\Gamma}W_\Gamma \\ &\quad + \Lambda_{P_1}^T\tilde{P}_1\Lambda_{P_1} + \Lambda_{P_2}^T\tilde{P}_2\Lambda_{P_2} + \tilde{\Omega}_2^T\tilde{\Psi}\tilde{\Omega}_2 \\ \tilde{\Omega}_2 &= \left[\begin{array}{ccc} 0_{n,(r+1)n} & I_n & 0_{n,3(r+1)n} \\ \hline 0_{n,3(r+1)n} & I_n & 0_{n,(r+1)n} \end{array}\right] \\ \tilde{\Psi} &= \mathrm{diag}\{h_1S_1,\ h_2S_2\} \end{aligned}$$

and the other symbols have the same meaning as those defined in Theorem 1.

B. Robust Stability Analysis of GRNs With Noise Perturbations

It is now well known that the intracellular and extracellular noise perturbations are unavoidable during the modeling of genetic network models. Therefore, it would be interesting to consider the dynamics for the genetic networks with both parameter fluctuations and stochastic disturbances, and stability analysis is obviously one of the most important problems. In this section, by means of stochastic analysis theory, the globally robustly asymptotic stability conditions in the mean-square sense are obtained for the addressed uncertain stochastic GRNs.

Let us consider the GRNs with both parameter uncertainties and noise perturbations described by the following stochastic differential equations:

$$\begin{cases} dx(t) = \left[-A(t)x(t) + B(t)g\left(y(t-\sigma)\right)\right]dt \\ \qquad\quad + \rho\left(t, x(t), y(t-\sigma)\right)d\omega_1(t) \\ dy(t) = \left[-C(t)y(t) + D(t)x(t-\tau)\right]dt \\ \qquad\quad + \rho\left(t, y(t), x(t-\tau)\right)d\omega_2(t) \end{cases} \quad (32)$$

where $\omega_1(t)$ and $\omega_2(t)$ are mutually uncorrelated one dimensional Brownian motions satisfying $\mathbb{E}\{d\omega_i(t)\} = 0$ and $\mathbb{E}\{d\omega_i^2(t)\} = dt$ $(i = 1, 2)$. Furthermore, $\rho(t, x(t), y(t-\sigma))$ and $\rho(t, y(t), x(t-\tau))$ are the noise intensity functions.

Assumption 2: There exist matrices $\mathbb{U} \ge 0$ and $\mathbb{V} \ge 0$ such that

$$\rho^T(t, u, v)\rho(t, u, v) \le u^T\mathbb{U}u + v^T\mathbb{V}v \quad (33)$$

holds for all $u, v \in \Re^n$, $t > 0$.

The initial condition associated with the networks in (32) is given as follows:

$$x(t) = \phi_\omega(t) \quad y(t) = \varphi_\omega(t) \quad -\varrho \le t \le 0$$

where $\varrho \triangleq \max\{\tau, \sigma\}$; $\phi_\omega(t)$, $\varphi_\omega(t) \in L_{\mathcal{F}}^2([-\varrho, 0],\ \Re^n)$, and $L_{\mathcal{F}}^2([-\varrho, 0],\ \Re^n)$ denotes the family of all $\mathcal{F}_0$-measurable $\mathcal{C}([-\varrho, 0], \Re^n)$-valued random variables satisfying $\sup_{s\in[-\varrho,0]}\mathbb{E}\{\|\phi_\omega(s)\|^2\} < \infty$, $\sup_{s\in[-\varrho,0]}\mathbb{E}\{\|\varphi_\omega(s)\|^2\} < \infty$.

We are now in a position to analyze the problem of globally robust stability in the mean square sense for uncertain stochastic GRNs [see (32)] by using the theory of stochastic functional differential equations. We aim to establish criteria that ensure the solvability of the robust mean-square stability problem.

Theorem 2: Under Assumptions 1 and 2, for a given an integer $r \ge 1$, the genetic network in (32) with time delays

$\tau \in (0, h_1]$ and $\sigma \in (0, h_2]$ is robustly asymptotically mean-square stable if there exist positive definite matrices P_i, R_i, S_i, $Q_\alpha^{(\beta)}$, and $\Gamma = \mathrm{diag}\{\gamma_1, \gamma_2, \ldots, \gamma_n\}$, matrices $\mathcal{M}_\alpha$, $\mathcal{N}_\alpha$, and $\mathcal{T}_i$, and positive constants ℓ_i and ε_j ($i = 1, 2$; $\alpha = 1, 2, \ldots, r$; $\beta = 1, 2, 3$; $j = 1, 2, \ldots, 8$) such that the following LMIs hold:

$$P_i + h_i R_i \le \ell_i I \quad (i = 1, 2) \tag{34}$$

$$\Xi = \begin{bmatrix} \Xi_1 & \Xi_2 & \Xi_3 \\ * & \Xi_4 & 0 \\ * & * & \Xi_5 \end{bmatrix} < 0 \tag{35}$$

where

$$\Xi_1 = \mathcal{Q}_j^T \Lambda_j \mathcal{Q}_j \qquad (j = 1, 2, 3, 4)$$

$$\Xi_2 = \mathcal{W}^T \Omega$$

$$\Xi_3 = \Theta^T \Phi$$

$$\Xi_4 = \mathrm{diag}\left\{ -\frac{r}{h_1} I_r \otimes S_1,\ -\frac{r}{h_2} I_r \otimes S_2,\ -I_r \otimes R_1,\ - I_r \otimes R_2 \right\}$$

$$\Xi_5 = \mathrm{diag}\{-\varepsilon_5 I_n,\ -\varepsilon_6 I_n,\ -\varepsilon_1 I_n,\ -\varepsilon_2 I_n,\ -\varepsilon_7 I_n,\ - \varepsilon_8 I_n,\ -\varepsilon_3 I_n,\ -\varepsilon_4 I_n\}$$

$$\mathcal{Q}_1 = \begin{bmatrix} \begin{array}{c} I_{rn} \quad 0_{rn,(2r+5)n} \\ \hline 0_{rn,n} \quad I_{rn} \quad 0_{rn,(2r+4)n} \end{array} \end{bmatrix}$$

$$\mathcal{Q}_2 = \begin{bmatrix} \begin{array}{c} 0_{rn,(r+2)n} \quad I_{rn} \quad 0_{rn,(r+3)n} \\ \hline 0_{rn,(r+3)n} \quad I_{rn} \quad 0_{rn,(r+2)n} \end{array} \end{bmatrix}$$

$$\mathcal{Q}_3 = \begin{bmatrix} \begin{array}{c} 0_{rn,(r+2)n} \quad I_{rn} \quad 0_{rn,(r+3)n} \\ \hline 0_{rn,(2r+4)n} \quad I_{rn} \quad 0_{rn,n} \\ \hline 0_{rn,(2r+5)n} \quad I_{rn} \end{array} \end{bmatrix}$$

$$\Lambda_1 = \begin{bmatrix} Q_1 + \mathcal{M} + \mathcal{M}^T & -\mathcal{M} \\ * & -Q_1 \end{bmatrix}$$

$$\Lambda_2 = \begin{bmatrix} Q_2 + \mathcal{N} + \mathcal{N}^T & -\mathcal{N} \\ * & -Q_2 \end{bmatrix}$$

$$\Lambda_3 = \begin{bmatrix} 0 & I_r \otimes K^T \Gamma^T & 0 \\ * & Q_3 - I_r \otimes (\Gamma + \Gamma^T) & 0 \\ * & * & -Q_3 \end{bmatrix}$$

$$\mathcal{Q}_4 = \begin{bmatrix} \begin{array}{c} I_n \quad 0_{n,(3r+4)n} \\ \hline 0_{n,rn} \quad I_n \quad 0_{n,(2r+4)n} \\ \hline 0_{n,(r+1)n} \quad I_n \quad 0_{n,(2r+3)n} \\ \hline 0_{n,(r+2)n} \quad I_n \quad 0_{n,(2r+2)n} \\ \hline 0_{n,2(r+1)n} \quad I_n \quad 0_{n,(r+2)n} \\ \hline 0_{n,(2r+3)n} \quad I_n \quad 0_{n,(r+1)n} \\ \hline 0_{n,(2r+4)n} \quad I_n \quad 0_{n,rn} \\ \hline 0_{n,(3r+4)n} \quad I_n \end{array} \end{bmatrix}$$

$$\mathcal{W} = \begin{bmatrix} \begin{array}{c} I_{rn} \quad 0_{rn,(2r+5)n} \\ \hline 0_{rn,(r+2)n} \quad I_{rn} \quad 0_{rn,(r+3)n} \\ \hline I_{rn} \quad 0_{rn,(2r+5)n} \\ \hline 0_{rn,(r+2)n} \quad I_{rn} \quad 0_{rn,(r+3)n} \end{array} \end{bmatrix}$$

$$\Theta = \begin{bmatrix} \begin{array}{c} I_n \quad 0_{n,(3r+4)n} \\ \hline 0_{n,(r+1)n} \quad I_n \quad 0_{n,(2r+3)n} \\ \hline 0_{n,(r+2)n} \quad I_n \quad 0_{n,(2r+2)n} \\ \hline 0_{n,(2r+3)n} \quad I_n \quad 0_{n,(r+1)n} \end{array} \end{bmatrix}$$

$$\Phi = \begin{bmatrix} \begin{array}{c} P_1 M_1 \quad P_1 M_1 \quad 0_{n,6n} \\ \hline 0_{n,2n} \quad \mathcal{T}_1 M_1 \quad \mathcal{T}_1 M_1 \quad 0_{n,4n} \\ \hline 0_{n,4n} \quad P_2 M_2 \quad P_2 M_2 \quad 0_{n,2n} \\ \hline 0_{n,6n} \quad \mathcal{T}_2 M_2 \quad \mathcal{T}_2 M_2 \end{array} \end{bmatrix}$$

$$\Omega = \begin{bmatrix} \mathcal{M} & 0 & \mathcal{M} & 0 \\ 0 & \mathcal{N} & 0 & \mathcal{N} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\Lambda_4 = \begin{bmatrix} \Pi^{(1)} & \Pi^{(2)} \\ * & \Pi^{(3)} \end{bmatrix}$$

$$\Pi^{(1)} = \begin{bmatrix} \Pi_{11}^{(1)} & 0 & -A^T \mathcal{T}_1^T & 0 \\ 0 & \Pi_{22}^{(1)} & 0 & D P_2^T \\ -\mathcal{T}_1 A & 0 & \Pi_{33}^{(1)} & 0 \\ 0 & P_2 D & 0 & \Pi_{44}^{(1)} \end{bmatrix}$$

$$\Pi^{(2)} = \begin{bmatrix} 0 & 0 & 0 & P_1 B \\ 0 & D^T \mathcal{T}_2^T & 0 & 0 \\ 0 & 0 & 0 & \mathcal{T}_1 B \\ 0 & -C^T \mathcal{T}_2^T & 0 & 0 \end{bmatrix}$$

$$\Pi^{(3)} = \mathrm{diag}\{\ell_1 \mathbb{V},\ h_2 S_2 - \mathcal{T}_2 - \mathcal{T}_2^T,\ 0,\ (\varepsilon_2 + \varepsilon_6) N_2^T N_2\}$$

$$\Pi_{11}^{(1)} = - P_1 A - A^T P_1 + \ell_1 \mathbb{U} + (\varepsilon_1 + \varepsilon_5) N_1^T N_1$$

$$\Pi_{22}^{(1)} = \ell_2 \mathbb{V} + (\varepsilon_4 + \varepsilon_8) N_2^T N_2$$

$$\Pi_{33}^{(1)} = h_1 S_1 - \mathcal{T}_1 - \mathcal{T}_1^T$$

$$\Pi_{44}^{(1)} = \ell_2 \mathbb{U} + (\varepsilon_3 + \varepsilon_7) N_1^T N_1 - P_2 C - C^T P_2$$

$$\mathcal{M} = \mathrm{diag}\{\mathcal{M}_1,\ \mathcal{M}_2, \ldots,\ \mathcal{M}_r\}$$

$$\mathcal{N} = \mathrm{diag}\{\mathcal{N}_1,\ \mathcal{N}_2, \ldots,\ \mathcal{N}_r\},$$

$$Q_\beta = \mathrm{diag}\left\{ Q_1^{(\beta)},\ Q_2^{(\beta)}, \ldots,\ Q_r^{(\beta)} \right\} \qquad (\beta = 1, 2, 3).$$

Proof: By setting

$$\begin{aligned} \mathfrak{x}(\alpha) &= - A(\alpha) x(\alpha) + B(\alpha) g\left(y(\alpha - \sigma)\right) \\ \mathfrak{y}(\alpha) &= - C(\alpha) y(\alpha) + D(\alpha) x(\alpha - \tau) \end{aligned} \tag{36}$$

we consider the following Lyapunov–Krasovskii functional candidate for the model in (32):

$$V\left(t, x(t), y(t)\right) = \sum_{i=1}^{5} V_i\left(t, x(t), y(t)\right) \tag{37}$$

where

$$\begin{aligned} V_1(t,x(t),y(t)) =& x^T(t)P_1x(t) \\ &+ \sum_{k=1}^{r} \int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau} x^T(s)Q_k^{(1)}x(s)ds \\ V_2(t,x(t),y(t)) =& y^T(t)P_2y(t) \\ &+ \sum_{k=1}^{r} \int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma} y^T(s)Q_k^{(2)}y(s)ds \\ V_3(t,x(t),y(t)) =& \sum_{k=1}^{r} \int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma} g^T(y(s))\,Q_k^{(3)}g(y(s))\,ds \\ V_4(t,x(t),y(t)) =& \int_{-\tau}^{0}\int_{t+\beta}^{t} \mathfrak{x}^T(\alpha)S_1\mathfrak{x}(\alpha)d\alpha d\beta \\ &+ \int_{-\tau}^{0}\int_{t+\theta}^{t} \rho^T(s,x(s),y(s-\sigma)) \\ &\times R_1\rho(s,x(s),y(s-\sigma))\,dsd\theta \\ V_5(t,x(t),y(t)) =& \int_{-\sigma}^{0}\int_{t+\beta}^{t} \mathfrak{y}^T(\alpha)S_2\mathfrak{y}(\alpha)d\alpha d\beta \\ &+ \int_{-\sigma}^{0}\int_{t+\theta}^{t} \rho^T(s,y(s),x(s-\tau)) \\ &\times R_2\rho(s,y(s),x(s-\tau))\,dsd\theta \end{aligned}$$

with $r \geq 1$ (number of fractions) being an integer.

Let $\mathcal{L}$ be the weak infinitesimal operator of the stochastic process $\{x_\varrho = x(t+s), y_\varrho = y(t+s) | t \geq 0, s \in [-\varrho, 0]\}$ along the trajectories of the genetic network in (32). By Itô's differential formula [11], one has

$$\begin{aligned} \mathcal{L}V_1(t) =& 2x^T(t)P_1[-A(t)x(t) + B(t)g(y(t-\sigma))] \\ &+ \rho^T(t,x(t),y(t-\sigma))\,P_1\rho(t,x(t),y(t-\sigma)) \\ &- \mathcal{X}^T\left(t-\frac{\tau}{r}\right)Q_1\mathcal{X}\left(t-\frac{\tau}{r}\right) + \mathcal{X}^T(t)Q_1\mathcal{X}(t) \end{aligned} \tag{38}$$

$$\begin{aligned} \mathcal{L}V_2(t) =& 2y^T(t)P_2[-C(t)y(t) + D(t)x(t-\tau)] \\ &+ \rho^T(t,y(t),x(t-\tau))\,P_2\rho(t,y(t),x(t-\tau)) \\ &- \mathcal{Y}^T\left(t-\frac{\sigma}{r}\right)Q_2\mathcal{Y}\left(t-\frac{\sigma}{r}\right) + \mathcal{Y}^T(t)Q_2\mathcal{Y}(t) \end{aligned} \tag{39}$$

$$\begin{aligned} \mathcal{L}V_3(t) =& \mathcal{G}^T(y(t))\,Q_3\mathcal{G}(y(t)) \\ &- \mathcal{G}^T\left(y\left(t-\frac{1}{r}\sigma\right)\right)Q_3\mathcal{G}\left(y\left(t-\frac{1}{r}\sigma\right)\right) \end{aligned} \tag{40}$$

$$\begin{aligned} \mathcal{L}V_4(t) =& \tau\mathfrak{x}^T(t)S_1\mathfrak{x}(t) - \int_{t-\tau}^{t} \mathfrak{x}^T(\alpha)S_1\mathfrak{x}(\alpha)d\alpha \\ &+ \tau\rho^T(t,x(t),y(t-\sigma))\,R_1\rho(t,x(t),y(t-\sigma)) \\ &- \int_{t-\tau}^{t} \rho^T(s,x(s),y(s-\sigma)) \\ &\times R_1\rho(s,x(s),y(s-\sigma))\,ds \end{aligned} \tag{41}$$

$$\begin{aligned} \mathcal{L}V_5(t) =& \sigma\mathfrak{y}^T(t)S_2\mathfrak{y}(t) - \int_{t-\sigma}^{t} \mathfrak{y}^T(\alpha)S_2\mathfrak{y}(\alpha)d\alpha \\ &+ \sigma\rho^T(t,y(t),x(t-\tau))\,R_2\rho(t,y(t),x(t-\tau)) \\ &- \int_{t-\sigma}^{t} \rho^T(s,y(s),x(s-\tau)) \\ &\times R_2\rho(s,y(s),x(s-\tau))\,ds \end{aligned} \tag{42}$$

where $\mathcal{G}^T(y(t)) = \text{col}\{g(y(t)), g(y(t-(1/r)\sigma)), \ldots, g(y(t-((r-1)/r)\sigma))\}$.

From Assumption 2 and the condition in (34), we have

$$\begin{aligned} &\rho^T(t,x(t),y(t-\sigma))\,(P_1+\tau R_1)\rho(t,x(t),y(t-\sigma)) \\ &\quad\leq \ell_1\rho^T(t,x(t),y(t-\sigma))\,\rho(t,x(t),y(t-\sigma)) \\ &\quad\leq \ell_1\left[x^T(t)\mathbb{U}x(t) + y^T(t-\sigma)\mathbb{V}y(t-\sigma)\right] \end{aligned} \tag{43}$$

$$\begin{aligned} &\rho^T(t,y(t),x(t-\tau))\,(P_2+\sigma R_2)\rho(t,y(t),x(t-\tau)) \\ &\quad\leq \ell_2\rho^T(t,y(t),x(t-\tau))\,\rho(t,y(t),x(t-\tau)) \\ &\quad\leq \ell_2\left[y^T(t)\mathbb{U}y(t) + x^T(t-\tau)\mathbb{V}x(t-\tau)\right]. \end{aligned} \tag{44}$$

In addition, for any matrices $\mathcal{M}_k$ and $\mathcal{N}_k$ $(k = 1, 2, \ldots, r)$, the following relationships hold:

$$\begin{aligned} &2x^T\left(t-\frac{k-1}{r}\tau\right)\mathcal{M}_k \\ &\times\left[x\left(t-\frac{k-1}{r}\tau\right) - x\left(t-\frac{k}{r}\tau\right) - \int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\mathfrak{x}(\alpha)d\alpha\right. \\ &\left.-\int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\rho(\alpha,x(\alpha),y(\alpha-\sigma))\,d\omega_1(\alpha)\right] = 0 \end{aligned} \tag{45}$$

$$\begin{aligned} &2y^T\left(t-\frac{k-1}{r}\sigma\right)\mathcal{N}_k \\ &\times\left[y\left(t-\frac{k-1}{r}\sigma\right) - y\left(t-\frac{k}{r}\sigma\right) - \int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\mathfrak{y}(\alpha)d\alpha\right. \\ &\left.-\int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\rho(\alpha,y(\alpha),x(\alpha-\tau))\,d\omega_2(\alpha)\right] = 0. \end{aligned} \tag{46}$$

Then, it follows from Lemma 2 that

$$-2x^T\left(t-\frac{k-1}{r}\tau\right)\mathcal{M}_k\int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\mathfrak{x}(\alpha)d\alpha \le \frac{\tau}{r}x^T\left(t-\frac{k-1}{r}\tau\right)\mathcal{M}_kS_1^{-1}\mathcal{M}_k^Tx\left(t-\frac{k-1}{r}\tau\right) + \int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\mathfrak{x}^T(\alpha)S_1\mathfrak{x}(\alpha)d\alpha \quad (47)$$

$$-2y^T\left(t-\frac{k-1}{r}\sigma\right)\mathcal{N}_k\int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\mathfrak{y}(\alpha)d\alpha \le \frac{\sigma}{r}y^T\left(t-\frac{k-1}{r}\sigma\right)\mathcal{N}_kS_2^{-1}\mathcal{N}_k^Ty\left(t-\frac{k-1}{r}\sigma\right) + \int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\mathfrak{y}^T(\alpha)S_2\mathfrak{y}(\alpha)d\alpha \quad (48)$$

$$\begin{aligned}&-2x^T\left(t-\frac{k-1}{r}\tau\right)\mathcal{M}_k \times\int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\rho\left(\alpha,x(\alpha),y(\alpha-\sigma)\right)d\omega_1(\alpha)\\ &\le x^T\left(t-\frac{k-1}{r}\tau\right)\mathcal{M}_kR_1^{-1}\mathcal{M}_k^Tx\left(t-\frac{k-1}{r}\tau\right)\\ &+\left(\int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\rho\left(\alpha,x(\alpha),y(\alpha-\sigma)\right)d\omega_1(\alpha)\right)^T \times R_1\left(\int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\rho\left(\alpha,x(\alpha),y(\alpha-\sigma)\right)d\omega_1(\alpha)\right)\end{aligned} \quad (49)$$

$$\begin{aligned}&-2y^T\left(t-\frac{k-1}{r}\sigma\right)\mathcal{N}_k \times\int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\rho\left(\alpha,y(\alpha),x(\alpha-\tau)\right)d\omega_2(\alpha)\\ &\le y^T\left(t-\frac{k-1}{r}\sigma\right)\mathcal{N}_kR_2^{-1}\mathcal{N}_k^Ty\left(t-\frac{k-1}{r}\sigma\right)\\ &+\left(\int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\rho\left(\alpha,y(\alpha),x(\alpha-\tau)\right)d\omega_2(\alpha)\right)^T \times R_2\left(\int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\rho\left(\alpha,y(\alpha),x(\alpha-\tau)\right)d\omega_2(\alpha)\right)\end{aligned} \quad (50)$$

whereas

$$\begin{aligned}&\mathbb{E}\left\{\left(\int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\rho\left(\alpha,x(\alpha),y(\alpha-\sigma)\right)d\omega_1(\alpha)\right)^T \times R_1\left(\int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\rho\left(\alpha,x(\alpha),y(\alpha-\sigma)\right)d\omega_1(\alpha)\right)\right\}\\ &=\mathbb{E}\left\{\int_{t-\frac{k}{r}\tau}^{t-\frac{k-1}{r}\tau}\rho^T\left(\alpha,x(\alpha),y(\alpha-\sigma)\right) \times R_1\rho\left(\alpha,x(\alpha),y(\alpha-\sigma)\right)d\alpha\right\}\end{aligned} \quad (51)$$

$$\begin{aligned}&\mathbb{E}\left\{\left(\int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\rho\left(\alpha,y(\alpha),x(\alpha-\tau)\right)d\omega_2(\alpha)\right)^T \times R_2\left(\int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\rho\left(\alpha,y(\alpha),x(\alpha-\tau)\right)d\omega_2(\alpha)\right)\right\}\\ &=\mathbb{E}\left\{\int_{t-\frac{k}{r}\sigma}^{t-\frac{k-1}{r}\sigma}\rho^T\left(\alpha,y(\alpha),x(\alpha-\tau)\right) \times R_2\rho\left(\alpha,y(\alpha),x(\alpha-\tau)\right)d\alpha\right\}.\end{aligned} \quad (52)$$

On the other hand, for $k=1,2,\ldots,r$, one can see from the sector condition in Assumption 1 that

$$\begin{aligned}&2g^T\left(y\left(t-\frac{k-1}{r}\sigma\right)\right)\Gamma Ky\left(t-\frac{k-1}{r}\sigma\right)\\ &-2g^T\left(y\left(t-\frac{k-1}{r}\sigma\right)\right)\Gamma g\left(y\left(t-\frac{k-1}{r}\sigma\right)\right)\ge 0.\end{aligned} \quad (53)$$

With the definitions in (36), for any matrices $\mathcal{T}_1$ and $\mathcal{T}_2$, we also have

$$2\mathfrak{x}^T(t)\mathcal{T}_1\left[-A(t)x(t)+B(t)g\left(y(t-\sigma)\right)-\mathfrak{x}(t)\right]=0 \quad (54)$$

$$2\mathfrak{y}^T(t)\mathcal{T}_2\left[-C(t)y(t)+D(t)x(t-\tau)-\mathfrak{y}(t)\right]=0. \quad (55)$$

By using Lemma 2, we obtain

$$-2\mathfrak{x}^T(t)\mathcal{T}_1\triangle A(t)x(t)\le\varepsilon_1^{-1}\mathfrak{x}^T(t)\mathcal{T}_1M_1M_1^T \times\mathcal{T}_1^T\mathfrak{x}(t)+\varepsilon_1x^T(t)N_1^TN_1x(t) \quad (56)$$

$$2\mathfrak{x}^T(t)\mathcal{T}_1\triangle B(t)g\left(y(t-\sigma)\right)\le\varepsilon_2^{-1}\mathfrak{x}^T(t)\mathcal{T}_1M_1M_1^T \times\mathcal{T}_1^T\mathfrak{x}(t)+\varepsilon_2g^T\left(y(t-\sigma)\right)N_2^TN_2g\left(y(t-\sigma)\right) \quad (57)$$

$$-\mathfrak{y}^T(t)\mathcal{T}_2\triangle C(t)y(t)\le\varepsilon_3^{-1}\mathfrak{y}^T(t)\mathcal{T}_2M_2M_2^T \times\mathcal{T}_2^T\mathfrak{y}(t)+\varepsilon_3y^T(t)N_1^TN_1y(t) \quad (58)$$

$$2\mathfrak{y}^T(t)\mathcal{T}_2\triangle D(t)x(t-\tau)\le\varepsilon_4^{-1}\mathfrak{y}^T(t)\mathcal{T}_2M_2M_2^T \times\mathcal{T}_2^T\mathfrak{y}(t)+\varepsilon_4x^T(t-\tau)N_2^TN_2x(t-\tau). \quad (59)$$

Similarly, it can be obtained that

$$\begin{aligned} &-2x^T(t)P_1\Delta A(t)x(t) \\ &\quad \leq x^T(t)\left[\varepsilon_5^{-1}P_1M_1M_1^TP_1+\varepsilon_5N_1^TN_1\right]x(t) \quad (60)\\ &2x^T(t)P_1\Delta B(t)g\left(y(t-\sigma)\right) \\ &\quad \leq \varepsilon_6^{-1}x^T(t)P_1M_1M_1^TP_1x(t) \\ &\qquad +\varepsilon_6 g^T\left(y(t-\sigma)\right)N_2^TN_2 g\left(y(t-\sigma)\right) \quad (61)\\ &-2y^T(t)P_2\Delta C(t)y(t) \\ &\quad \leq y^T(t)\left[\varepsilon_7^{-1}P_2M_2M_2^TP_2+\varepsilon_7N_1^TN_1\right]y(t) \quad (62)\\ &2y^T(t)P_2\Delta D(t)x(t-\tau) \\ &\quad \leq \varepsilon_8^{-1}y^T(t)P_2M_2M_2^TP_2y(t) \\ &\qquad +\varepsilon_8x^T(t-\tau)N_2^TN_2x(t-\tau). \quad (63) \end{aligned}$$

Taking the mathematical expectation and considering (38)–(63), one has

$$\begin{aligned} &\mathbb{E}\left\{\mathcal{L}V\left(t,x(t),y(t)\right)\right\} \\ &\quad =\zeta(t)^T\left(\Xi_1-\Xi_2\Xi_4^{-1}\Xi_2^T-\Xi_3\Xi_5^{-1}\Xi_3^T\right)\zeta(t) \quad (64) \end{aligned}$$

where $\zeta(t)=\mathrm{col}\left\{\mathcal{X}(t),x(t-\tau),\mathfrak{x}(t),\mathcal{Y}(t),y(t-\sigma),\mathfrak{y}(t),\mathcal{G}(y(t)),g(y(t-\sigma))\right\}$, and Ξ_i $(i=1,\ldots,5)$ is defined in (35).

Based on the derivation conducted in Theorem 1, it follows that the uncertain stochastic model in (32) is robustly asymptotically stable in the mean square. ■

Remark 4: Similar to Corollary 1, we can obtain sufficient conditions ensuring the globally asymptotic stability of the genetic network in (32) without uncertain parameters. Furthermore, if there are no stochastic disturbances, we can further obtain specialized results, which are omitted here to save space. It is also worth pointing out that the main results in this paper can easily be extended to GRNs with time-varying delays by the same approach used in [26]. Note that we mainly focus on the effects brought by the norm-bounded uncertainty and the random fluctuations in this paper.

Remark 5: Lemma 2 is used to tackle the norm-bounded parameter uncertainties in the proof of Theorem 1. Comparing to existing literature, we apply the "delay-fractioning" approach and construct a more general Lyapunov functional to analyze the stability problem of the uncertain GRNs with time delays existing in both the translation process and the feedback regulation process. The novel delay-dependent conditions presented in Theorem 1 are formulated in the form of LMIs that can readily be solved by standard numerical software.

IV. Numerical Example

In this section, two simulation examples are presented to illustrate the effectiveness of the proposed design procedures. The examples are concerned with the synthetic oscillatory network. This kind of model has theoretically been predicted and experimentally investigated as a mathematical model of the repressilator in [5].

Example 1: In the transcriptional regulators of the model mentioned above, three repressor-protein concentrations p_i and their corresponding mRNA concentrations m_i (where $i=lacl$, $tetR$, or cl) are considered as the continuous dynamical variables. Each of the six molecular species participates in the transcription, translation, and degradation reactions. Here, we only investigate the symmetrical case in which all three repressors

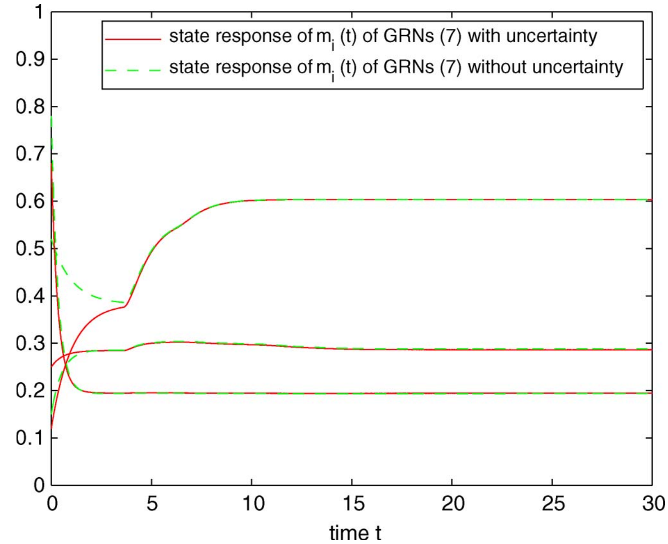

Fig. 1. mRNA concentrations.

are identical, except for their DNA-blinding specificities. By incorporating time delays and adjusting some parameters, the kinetics of the system is described by the following equations with the vector form:

$$\begin{aligned} \dot{m}(t)&=-A(t)m(t)+B(t)f\left(p(t-\sigma)\right)+\eta \\ \dot{p}(t)&=-C(t)p(t)+D(t)m(t-\tau) \end{aligned}$$

where $A=\mathrm{diag}\{1,2,3\}$, $C=\mathrm{diag}\{2.5,2.5,2.5\}$, $D=\mathrm{diag}\{1,1,1\}$, and

$$B=\begin{bmatrix} 0 & 0 & -0.6 \\ -0.6 & 0 & 0 \\ 0 & -0.6 & 0 \end{bmatrix}$$
$$M_1=\begin{bmatrix} 0.1 & 0.08 & 0.04 \\ 0.08 & 0.04 & -0.04 \\ 0.02 & -0.06 & 0.1 \end{bmatrix}$$
$$M_2=\begin{bmatrix} 0.2 & 0.1 & -0.15 \\ 0.1 & -0.3 & 0.05 \\ 0.15 & -0.2 & 0.1 \end{bmatrix}$$
$$N_1=\begin{bmatrix} 0.4 & 0.1 & -0.2 \\ 0.1 & 0.4 & -0.1 \\ -0.2 & -0.1 & 0.3 \end{bmatrix}$$
$$N_2=\begin{bmatrix} 0.2 & -0.3 & 0.15 \\ -0.1 & 0.2 & 0.1 \\ 0.2 & -0.2 & 0.1 \end{bmatrix}$$
$$\eta=\begin{bmatrix} 0.6 \\ 0.6 \\ 0.6 \end{bmatrix}.$$

The nonlinearities are taken as $f_j(p_j)=(p_j^2/(1+p_j^2))$ $(j=cl,lacl,tetR)$, and therefore, we have $K=\mathrm{diag}\{0.65,0.65,0.65\}$. Furthermore, $H(t)=\mathrm{diag}\left\{(1/2)\sin(4t),\cos(2.25t),\cos(1.25t)\right\}$.

By using the Matlab LMI toolbox, it can be found that the LMIs in (12) are feasible. When we set $r=1$, the time delays can be achieved as $\tau=2.5$, and $\sigma=3.6$. The simulation results of the trajectories of $m_i(t)$, $p_i(t)$ are shown in Figs. 1 and 2,

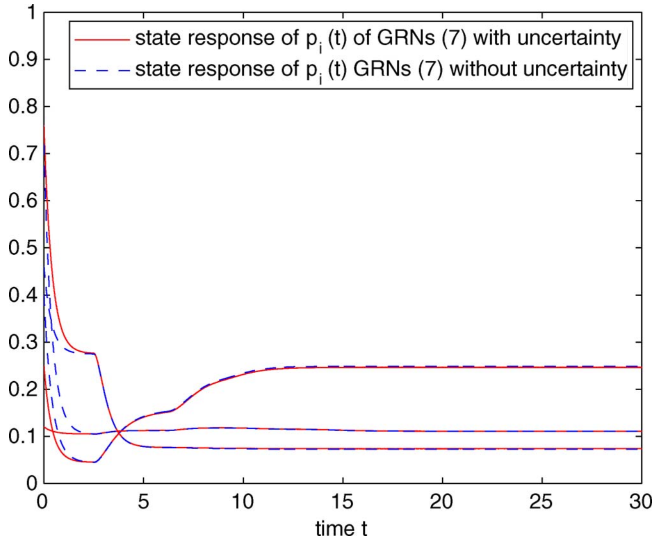

Fig. 2. Protein concentrations.

where the different initial states for system in (1) are taken as [0, 1] × [0, 1]. The simulation results further indicate that the given GRN with time delays and uncertain parameters is asymptotically robustly stable.

Example 2: In this example, we consider the uncertain genetic networks in (32) with noise disturbances with $\tau = 2$ and $\sigma = 3$, in which there are five nodes denoting the regulation factors, and the designed parameters in (32) are given by $A = \mathrm{diag}\{1, 2, 3, 4, 5\}$, $C = 2.5I$, and $D = 2I$, and the coupling matrix is given as

$$B = 0.8 \times \begin{bmatrix} 0 & 0 & -1 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 \\ 0 & 0 & -1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -1 \end{bmatrix}$$

where the coefficient 0.8 is the transcriptional rate. The parameter uncertainties satisfy $M_l = N_l = 0.25I(l = 1, 2)$ and $H(t) = \mathrm{diag}\{\sin(2t), \cos(5t), \cos(1.5t), 0.5\sin(4t), \cos(4.25t)\}$. The noise intensity vectors satisfy Assumption 2 with $\mathbb{U} = \mathbb{V} = 0.5I$. The nonlinear function is given by $f_i(s) = s^2/(1 + s^2)$ $(i = 1, 2, \ldots, 5)$, i.e., $K = 0.65I$.

By using the Matlab LMI toolbox, we can find that the LMIs in (34) and (35) are feasible (the solutions are not given here for the purpose of space saving). When we set $r = 1$, the numerical simulation results are given in Figs. 3 and 4, with the initial states randomly taken in [0, 1] × [0, 1], which further implies that the uncertain GRN with noises perturbations is globally robustly asymptotically stable in the mean square.

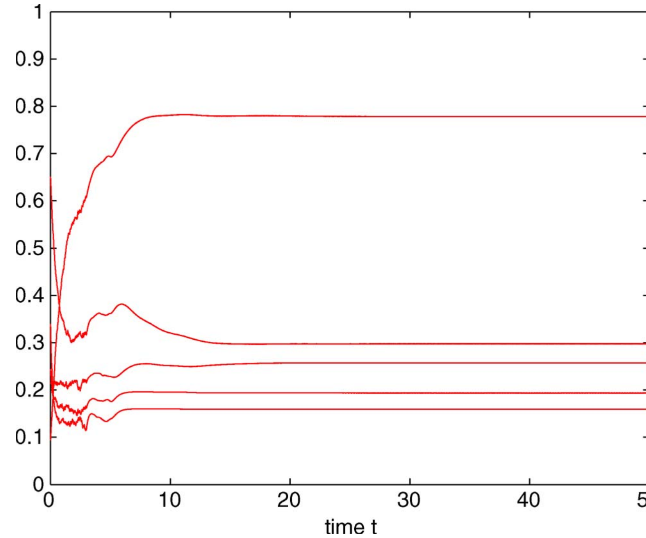

Fig. 3. State response of $m(t)$ of GRNs [see (32)].

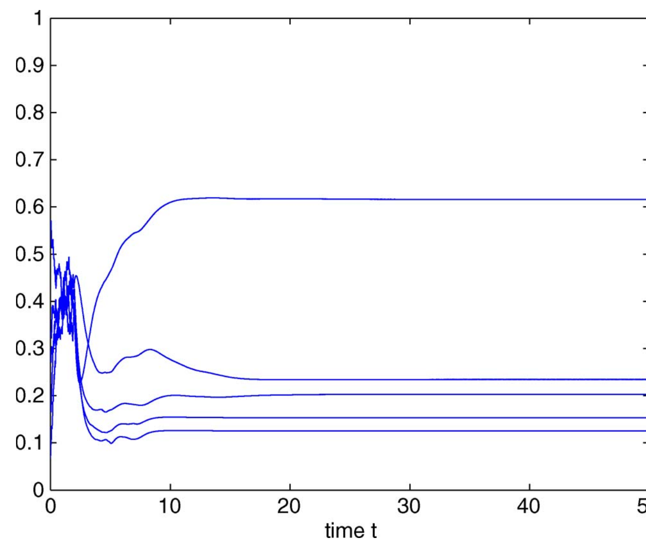

Fig. 4. State response of $p(t)$ of GRNs [see (32)].

V. Conclusion

In this paper, we have dealt with the robust stability analysis problem for GRNs with time delays, norm-bounded parameter uncertainties, and state-dependent Brownian motions. By using a Lyapunov functional approach, stochastic analysis tools, and the LMI technique, we have constructed a novel Lyapunov–Krasovskii functional and then derived sufficient conditions in terms of LMIs to ensure globally asymptotically robust stability of the addressed delayed uncertain genetic networks. Moreover, the LMI-based criteria can readily be verified by using standard numerical software. An important feature of the results reported here is that the stability condition is dependent on the upper bounds of the time delays, which is made possible by utilizing the most updated techniques for achieving delay dependence. To the best of our knowledge, the present research represents the first attempt to develop a novel computational approach specifically for the robust stability of uncertain GRNs with or without noise perturbations. In the end of this paper, two simulation examples have been exploited to illustrate the applicability and usefulness of the developed theoretical results.

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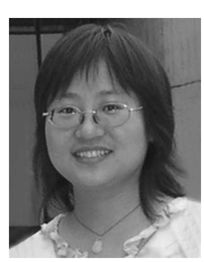

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