Global Dissipativity for Stochastic Genetic Regulatory Networks With Time-Delays

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ABSTRACT Genetic Regulatory Networks (GRNs) play an important role for the development and evolution of biological systems. On the basis of the development for DNA microarray technologies, a profound study for GRNs becomes possible at genome scale. In this article, the global dissipativity and corresponding attractive set for the GRNs with stochastic disturbances and time-delays are investigated based on Lyapunov theory. Stochastic disturbances are considered into both the feedback regulation process and the translation process for reflecting the inherent noise perturbations on a foundation of factual knowledge. Through the resort to the several appropriate Lyapunov-Krasovskii Functionals (LKFs) combining with Itô’s formula and different inequality techniques, some corresponding sufficient conditions and the attractive set are obtained for the GRNs in linear matrix inequality form, which are easy to verify by the numerical software. Finally, one three-node GRN is proposed and analyzed to illustrate the validity of the proposed results by using the Field-Programmable Gate Array (FPGA) hardware simulation tool.

INDEX TERMS Global dissipativity, inequality techniques, LKFs, stochastic GRNs.

I. INTRODUCTION

Researches have shown that many diseases (such as cancer) cause by the faults of the interactions among DNAs, mRNAs, and proteins at the molecular level of the corresponding cell lines. The regulatory mechanism of the interactions is named Genetic Regulatory Networks (GRNs), which have an important position for the development and evolution of biological systems. Based on the development of DNA microarray technologies, the research for GRNs becomes possible at genome scale [1], [2]. Over the past ten years, many new and powerful techniques from theoretical analysis and experimental investigation have been used to establish the GRNs model.

Some mathematical models combining with molecular biology have been established to provide a framework for studying the dynamic characteristics of GRNs [3], for example Boolean network [4], [5], Bayesian network [6], [7], Differential Equation Model (DEM) [8]–[21], master equation model [22], [23], and so on. Subsequently, massive results have been proposed to the GRNs model based on DEM, e.g. stability analysis [10]–[12], state estimation [13]–[15], filter design [16], [17], synchronization and control [18], [19], etc. Among those results, the stability play an important role for the research of GNRS, and have attracted more attention.

However, the concentrations of mRNAs and proteins are not always approach the equilibrium points, or the points will not be stable. In some cases, they will reach and stay a bounded region far from the equilibrium points. This dynamic characteristic is called dissipativity proposed by Belgian scientist I. Prigogine in the 1970s and has found applications in many complex systems such as chemical reactions, fluid, electronic circuits, biological system. The dissipativity of various nonlinear systems have been researched as in [24]–[29]. In [24], the authors defined the concepts of global dissipation for a general class of Neural Networks (NNs) and shown that the Hopfield network and cellular NNs with or without time
delays were dissipative systems. The dissipativity analysis for NNs with different conditions were studied in [25]–[27], such as stochastic, distributed delay and markovian jump. References [28] and [29] respectively discussed the dissipative control problem for nonlinear systems with time-varying delays and randomly occurring uncertainties. The controller based on the passivity can save time and cost in the control process [28], and is used to the aircraft flight control systems [29]. To the authors’ knowledge, the problem of dissipativity for GRNs have not been researched, it remains essential and challenging. The solution of this problem is of great significance to the study of dynamic performance and control analysis for the system of mRNAs and proteins. The recent methods related to the dissipativity provide some solution thoughts for this problem.

Generally, time-delay is inevitable in the GRNs owing to the slow reaction processes of transcription, translation and the finite switching speed of the amplifier. A variety of results for GRNs with time-delay have been obtained as described in [10]–[12], [14], [19], [20], [30], [31]. The sufficient criteria have been derived in terms of LMIs for delayed GRNs by applying Lyapunov stability theory, where the delay is allowed to be constant in [10]. Furthermore, a sufficient criterion on robust stability stability has been proposed in [11] for a class of GRNs with time-delay by using a delay fractioning approach. Mixed time-delays were presented for GRNs in [12] and time-varying delays were studied in [15]. Random sensor delays were studied for the state estimation problem of nonlinear dynamical networks by Lyapunov functional approach and linear matrix inequality (LMI) technique in [14], [30].

On the other hand, the stochastic noises is also be discussed during the modeling because it generates from internal or external environment fluctuations in the process of gene regulation [9], [11], [13]. The state estimation, filtering and stability of stochastic GRNs respectively were obtained in [13]–[15], [21]. In those systems, the influence of time-delay and stochastic noises on the dynamic characteristics of the system is analyzed, and many abundant phenomena and practical results are obtained. For describing the system among DNAs, mRNAs, and proteins more accurately and show the law of development and change, the delays and noises must be fully considered on system modeling.

Motivated by the circumstance, our main interest is to investigate the global dissipativity in mean for the GRNs with stochastic disturbances and time-delay. By using of inequality technique and the stochastic Itô’s formula, some criteria are proposed to ensure the dissipativity of the system. The key advantages of this paper lie in that the dissipativity of GRNs are defined and theoretically analyzed for two different concentrations variables of mRNA and proteins which is different with NNS. When deriving the dissipativity results of GRNs, we met the following three questions: i) The existing definitions are not fully applicable for GRNs. ii) How to deal with two different concentrations variables of mRNA and proteins in one model? iii) How to save the time of of the simulation processing? To solve the mentioned questions, the contributions of this letter are listed as: 1) The definitions of globally dissipative in mean and corresponding globally attractive set for GRNs are first given. 2) Inequality conditions are established for the GRNs model considered the concentrations of mRNA and protein as a whole, which is different with other network models. 3) The Field-Programmable Gate Array (FPGA) hardware simulation tool was used to improve the processing speed.

The model description and preliminaries are formally presented in the Section II. The dissipativity criterions are proposed in Section III. In Section IV, one example is presented to demonstrate the validity of the proposed methods based on the Field-Programmable Gate Array (FPGA) hardware tool which can deal with the data faster and more efficiently. Finally, the conclusion is shown in Section V.

Notations: In this paper, \( \mathbb{R}^n \) and \( \mathbb{R}^{n \times m} \) respectively are the n dimensional Euclidean space and the set of all \( n \times m \) real matrices; The superscript \( T \) stands the transpose; 0 and I denote, respectively, zero matrix and unit matrix; diag(\{…\}) is for a block-diagonal matrix; For real symmetric matrices \( X \) and \( Y \), \( X \geq Y \) (or \( X > Y \)) shows that \( X - Y \) is real, symmetric and positive definite (or semi-definite); The symbol \( * \) stands symmetric blocks in the LMIs; \( (\Omega, \mathcal{F}, \mathbb{P}) \) indicates a complete probability space, and \( \mathbb{E}(\cdot) \) denotes the expectation; At last, if not specified, the matrices have appropriate dimensions.

II. PRELIMINARIES

In this paper, consider a GRNs model based on DEM by the following equations [9], [10]:

\[
\begin{aligned}
\dot{m}_i(t) &= (-a_i m_i(t) + \sum_{j=1}^{n} b_{ij} f_j(p_j(t - \tau))dt + b_{0i}, \\
\dot{p}_i(t) &= (-c_i p_i(t) + d_i m_i(t - \sigma))dt, \\
\end{aligned}
\]

(1)

where \( m_i(t), p_i(t) \in \mathbb{R} \) respectively are the concentrations of mRNA and proteins of the \( i \)th gene at time \( t; \tau \) and \( \sigma \) represent the inter- and intra-node delays which are non-negative constants; \( a_i, c_i \) denote the degradation rates of mRNA and proteins, respectively; \( d_i \) denotes the translation rate; The function \( f_j(\cdot) \) represents the feedback regulation for the proteins during the transcription, which commonly is nonlinear function with a form of monotonicity; \( \bar{\tau} = \max(\tau, \sigma) \), \( \psi_i(t) \in C([-\bar{\tau}, 0]; \mathbb{R}) \) are the initial conditions for the GRNs.

Usually, \( f_j(s) \) is chosen as the Hill form with \( f_j(s) = (s/\beta_j)^{h_j}/(s/\beta_j)^{h_j} \), where \( h_j \) denotes the Hill coefficient and \( \beta_j > 0 \) a constant. \( b_{0i} = \sum_{j \in V_0} a_{ij} \) and \( V_0 \) is the set of all transcription factors which are regressors of the gene \( i \); Define coupling matrix \( B = (b_{ij}) \in \mathbb{R}^{n \times n} \). More detailed definition for this GRNs model (1) can be found in [9], [10] and the references cited therein.
Rewriting the model (1) into matrix form:
\[
\begin{align*}
    x_m(t) &= -Ax_m(t) + Bg(x_p(t - \tau)) + B_0, \\
    x_p(t) &= -Cx_p(t) + Dx_m(t - \sigma),
\end{align*}
\]
(2)

where \( x_m(t) = (m_1(t), m_2(t), \ldots, m_n(t))^T \), \( x_p(t) = (p_1(t), p_2(t), \ldots, p_n(t))^T \), \( A = \text{diag}[a_1, a_2, \ldots, a_n]^T \), \( C = \text{diag}[c_1, c_2, \ldots, c_n]^T \), \( D = \text{diag}[d_1, d_2, \ldots, d_n]^T \), \( B_0 = \text{diag}[b_{01}, b_{02}, \ldots, b_{0n}]^T \) and \( f(x_p(t)) = [f_1(p_1(t)), f_2(p_2(t)), \ldots, f_n(p_n(t))]^T \). Then, \( x_m(t, t_0, \phi) \) and \( x_p(t, t_0, \psi) \) are the state trajectories of the GRNs (2). The initial values \( \phi(\cdot), \psi(\cdot) \in L_2^\infty([-\bar{\tau}, 0]; \mathbb{R}^n) \) which is the family of all \( \mathcal{F}_0 \)-measurable \( \overline{C}([-\bar{\tau}, 0], \mathbb{R}^n) \)-valued random variables \( \phi = \{\phi(s) : -\bar{\tau} \leq s \leq 0\} \) satisfying \( \sup_{s \in [-\bar{\tau}, 0]} \mathbb{E}(|\phi(s)|^2) < \infty \).

The following GRNs with time-delays is obtained as in [13]:
\[
\begin{align*}
    dx_m(t) &= x[-Ax_m(t) + Bg(x_p(t - \tau))dt + u(t)] \\
    &\quad + \omega(t, x_m(t), x_p(t - \sigma))d\sigma_1(t) \\
    dx_p(t) &= [-Cx_p(t) + Dx_m(t - \sigma)]dt + v(t) \\
    &\quad + \omega(t, x_p(t), x_m(t - \sigma))d\sigma_2(t)
\end{align*}
\]
(3)

where \( \sigma_1(t) \) and \( \sigma_2(t) \) denote one-dimensional Brownian motions; \( \omega(t, x_m(t), x_p(t - \tau)) \) and \( \omega(t, x_p(t), x_m(t - \sigma)) \) denote the noise intensity functions. \( g(x_p(t - \tau)) = [g_1(x_p(t - \tau)), g_2(x_p(t - \tau)), \ldots, g_n(x_p(t - \tau))]^T \) and \( g(x_p(t - \tau)) = f_1(x_p(t - \tau) + p_1^T - f_2(p_1^T) \), \( u(t), v(t) \) are the input vectors of the model.

**Definition 1:** The GRNs (3) is globally dissipative in mean if there exists a compact set \( S \subset \mathbb{R}^{2n} \), such that \( \forall \phi_0, \psi_0 \in L_2^\infty([-\bar{\tau}, 0]; \mathbb{R}^n), \exists \mathcal{T}(\phi_0, \psi_0) > 0 \), when \( t > t_0 + T(\phi_0, \psi_0), \mathbb{E}(x(t, t_0, \phi_0), x(t, t_0, \psi_0)) \subseteq S \), where \( x_m(t_0, \phi_0), x_p(t_0, \psi_0) \) denote the trajectories of (3) from the initial state \( (\phi_0, \psi_0) \) and initial time \( t_0 \). Then, \( S \) is a globally attractive set in mean. On the other hand, \( S \) is a positive invariant in mean, when \( \forall \phi_0, \psi_0 \in L_2^\infty([-\bar{\tau}, 0]; \mathbb{R}^n), \mathbb{E}(\phi_0, \psi_0) \subseteq S \) implies \( \mathbb{E}(x(t, t_0, \phi_0), x(t, t_0, \psi_0)) \in S \) for \( t \geq t_0 \).

**Remark 1:** The regulatory mechanism between the interactions of DNAs and proteins is different from the other nonlinear network whose dissipativity has been defined. Therefore, the existing concept can not be used directly. In this paper, for the first time, the definition of globally dissipative GRNs in mean is given according to the characteristics of the model.

In this paper, Assumption 1 and 2 for the activation functions and noise intensity functions are given as [13].

**Assumption 1:** The function \( g_i(\cdot) \) satisfies:
\[
\left\{ \begin{array}{l}
    l_i^- \leq g_i(x_i) \leq l_i^+, \\
    \forall x_i \in \mathbb{R}, \quad x_i \neq 0, \quad i = 1, \ldots, n.
\end{array} \right.
\]
where \( l_i^- \) and \( l_i^+ \) are known real constants.

**Assumption 2:** The function \( \omega(t, x, y) \) is assumed that exist positive semi-finite nonnegative matrices \( H_1, H_2 \) such that:
\[
\omega(t, x, y)^T\omega(t, x, y) \leq x^TH_1x + y^TH_2y, \quad \forall t \geq 0, \quad x, y \in \mathbb{R}^n.
\]

The following lemmas are introduced to get our main results.

**Lemma 1** [31]: Let \( X, Y \) and \( M \) be real matrices with \( M^2M \leq I \) and \( \varepsilon \) a scalar. Then:
\[
XMY + (XMY)^T \leq \frac{1}{\varepsilon}X^TX + \varepsilon Y^TY, \quad \forall \varepsilon > 0.
\]

**Lemma 2** [32]: The following LMI
\[
\begin{bmatrix}
    S_{11}(x) & S_{12}(x) \\
    S_{12}^T(x) & S_{22}(x)
\end{bmatrix}
> 0
\]
where \( S_{11}(x) = S^T_{11}(x), S_{22}(x) = S^T_{22}(x) \) and \( S_{12} \) with the variable \( x \), is equivalent to any one of the conditions as follows:

(i) \( S_{22}(x) > 0, S_{11}(x) - S_{12}(x)S_{22}^{-1}(x)S_{12}^T(x) > 0 \);

(ii) \( S_{11}(x) > 0, S_{22}(x) - S_{12}^T(x)S_{11}^{-1}(x)S_{12}(x) > 0 \).

**Lemma 3** [33]: Let \( \xi \) be an integrable random variable and \( \Phi : \mathbb{R} \rightarrow \mathbb{R} \) a measurable convex function with \( \mathbb{E}(\Phi(\xi)) < \infty \). Then we have: \( \Phi(\mathbb{E}(\xi)) < \mathbb{E}(\Phi(\xi)) \).

**III. MAIN RESULTS**

In this section, we firstly study the dissipativity problem for the GRNs (3) with stochastic disturbances and time delay. In particular, the criteria of globally dissipative in mean and the corresponding attractive set are obtained. Next, three corollaries are obtained under different conditions.

**Theorem 1:** With Assumption 1, 2, if there exist positive definite matrices \( P_1, P_2, Q_1, Q_2, R_1 \), and positive scalars \( \rho_1, \rho_2, \kappa \), such that:
\[
\begin{bmatrix}
    \Omega_1 & 0 & 0 & 0 & 0 & P_1B \\
    * & \Omega_2 & 0 & P_2D & 0 & 0 \\
    * & * & \Omega_3 & 0 & 0 & 0 \\
    * & * & * & \Omega_4 & 0 & 0 \\
    * & * & * & * & \Omega_5 & 0 \\
    * & * & * & * & * & -R_1
\end{bmatrix} \leq 0,
\]
(4)

where
\[
\begin{align*}
    \Omega_1 &= -P_1A - AP_1 + \rho_1H_1 + Q_1, \\
    \Omega_2 &= -P_2C - CP_2 + \rho_2H_2 + Q_2 + \kappa L^T L, \\
    \Omega_3 &= -Q_1 + \rho_2H_2, \quad \Omega_4 = -Q_2 + \rho_1H_1, \quad \Omega_5 = -\kappa I + R_1.
\end{align*}
\]

The stochastic GRNs (3) is globally dissipative in mean, and the corresponding attractive set \( S = \{x : \langle x, x \rangle \leq \min(\Omega_1, \Omega_2, \Omega_3, \Omega_4, \Omega_5) \leq \min(\Omega_1, \Omega_2, \Omega_3, \Omega_4, \Omega_5) \langle x, x \rangle \} \).
\textbf{Proof:} Consider the following radially LKF candidate:
\begin{equation}
V(t) = V_1(t) + V_2(t) + V_3(t) + V_4(t),
\end{equation}
where
\begin{align*}
V_1(t) &= x_m(t)P_1x_m(t) + x_p(t)P_2x_p(t); \\
V_2(t) &= \int_{t-\tau}^t x_m^T(\theta)Q_1x_m(\theta)d\theta + \int_{t-\tau}^t x_p^T(\theta)Q_2x_p(\theta)d\theta; \\
V_3(t) &= \int_{t-\tau}^t g^T(x_p(\theta))R_1g(x_p(\theta))d\theta.
\end{align*}

The weak infinitesimal operator is obtained following Itô formulation as:
\begin{equation}
\mathcal{L}V_1(t) = 2x_m^T(t)P_1[-Ax_m(t) + Bg(x_p(t - \tau)) + u(t)] + 2x_p^T(t)P_2[-Cp_x(t) + Dx_m(t - \sigma) + v(t)] + \omega^T(t, x_m(t), x_p(t - \tau))P_1\omega(t, x_m(t), x_p(t - \tau)) + \omega^T(t, x_p(t), x_m(t - \sigma) - \sigma)P_2\omega(t, x_p(t), x_m(t - \sigma)); \\
\mathcal{L}V_2(t) &= x_m^T(t)Q_1x_m(t) - x_m^T(t - \sigma)Q_1x_m(t - \sigma) + x_p^T(t)Q_2x_p(t) - x_p^T(t - \tau)Q_2x_p(t - \tau); \\
\mathcal{L}V_3(t) &= g^T(x_p(t))R_1g(x_p(t)) - g^T(x_p(t - \tau))R_1g(x_p(t - \tau))
\end{equation}
From Assumption 2 and the conditions of the theorem, we get:
\begin{equation}
\omega^T(t, x_m(t), x_p(t - \tau))P_1\omega(t, x_m(t), x_p(t - \tau)) \leq \rho_1[x_m^T(t)H_1x_m(t) + x_p^T(t - \tau)H_2x_p(t - \tau)]; \\
\omega^T(t, x_p(t), x_m(t - \sigma))P_2\omega(t, x_p(t), x_m(t - \sigma)) \leq \rho_2[x_p^T(t)H_1x_p(t) + x_m^T(t - \sigma)H_2x_m(t - \sigma)].
\end{equation}
It follows from Lemma 3 and the conditions of Theorem 1, we can compute the \(\mathcal{L}V(t)\):
\begin{align*}
\mathcal{L}V(t) &= \mathcal{L}V_1(t) + \mathcal{L}V_2(t) + \mathcal{L}V_3(t) \\
&\leq -x_m^T(t)(P_1A + AP_1)x_m(t) + 2x_m^T(t)P_1B \omega(t, x_m(t), x_p(t - \tau)) + x_m^T(t)(P_1D + DP_1)x_m(t - \sigma) + \rho_1[x_m^T(t)H_1x_m(t) + x_p^T(t - \tau)H_2x_p(t - \tau)] + \rho_1[x_p^T(t)H_1x_p(t) + x_m^T(t - \sigma)H_2x_m(t - \sigma)] \\
&\quad + x_m^T(t)Q_1x_m(t) - x_m^T(t - \sigma)Q_1x_m(t - \sigma) + x_p^T(t)Q_2x_p(t) - x_p^T(t - \tau)Q_2x_p(t - \tau) + g^T(x_p(t))R_1g(x_p(t)) - g^T(x_p(t - \tau))R_1g(x_p(t - \tau)) + \kappa(x_p^T(t)L^T Lg(x_p(t)g(x_p(t)))).
\end{align*}
Taking the expectation operation and using Jensen’s inequality, we obtain:
\begin{equation}
d\mathbb{E}V(t, x_m(t), x_p(t)) = \mathbb{E}L(t, x_m(t), x_p(t))dt \\
\leq (\mathbb{E}|\min(\Phi_1)\mathbb{E}|x_m^2| + \epsilon_1^2|P_1u|^2)dt \\
+ (\mathbb{E}|\min(\Phi_2)|\mathbb{E}|x_p^2| + \epsilon_2^2|P_2v|^2)dt \\
\leq 0.
\end{equation}
Where \(\mathbb{E}x_m, \mathbb{E}x_p \in \mathbb{R}^{2n} \setminus S\). It follows from Itô’s formula, we have:
\begin{equation}
\mathbb{E}V(t, x_m(t), x_p(t)) = \mathbb{E}L(t_0, x_m(s), x_p(s))ds
\end{equation}
At the same time,
\begin{align*}
\mathbb{E}V(t, x_m(t), x_p(t)) &\geq \lambda_{\min}(P_1)\mathbb{E}|x_m|^2 + \lambda_{\min}(P_2)\mathbb{E}|x_p|^2 \\
&\geq \lambda_{\min}(P_1)\mathbb{E}|x_m|^2 + \lambda_{\min}(P_2)\mathbb{E}|x_p|^2.
\end{align*}
So that exists a \(T(t_0, \varphi_0, \varphi_0) = \max\{T(t_0, \varphi_0), T(t_0, \varphi_0)\}\) such that \(\mathbb{E}x_m(t), \mathbb{E}x_p(t) \in S\). Therefore we obtain that the model (3) is globally dissipative in mean, and the corresponding attractive set of it is given. This completes the proof. \(\square\)

Remark 2: Through the proof of Theorem 1, it can be found that as soon as \(\mathbb{E}(t, t_0, \varphi_0, \varphi_0) \in S\) stays in \(S\) it enters \(S\). So \(S\) is one of positive invariant set in mean for the GRNs (3).

Remark 3: Because of condition (12), we have \(\Omega(1, 1) < 0\), while \(\Omega(1, 0) > 0, \Omega(2, 0) > 0\) which means that \(\Omega(0, 0) > 0\). We can get that the minimum (\(\vartheta_1, \vartheta_2\)) exists such that \(\Omega(\vartheta_1, \vartheta_2) < 0\) with \(0 < \vartheta_1 < 1\) and \(0 < \vartheta_2 < 1\). Therefore, we have established a whole linear inequality conditions which is significant for the GRNs model.

Remark 4: Through adjusting the parameters \(\epsilon_1\) and \(\epsilon_2\), the radius \(r_m = |P_1u|/\sqrt{\epsilon_1\lambda_{\min}(\Phi_1)}, r_p = |P_2v|/\sqrt{\epsilon_2\lambda_{\min}(\Phi_2)}\) of the attractive set \(S\) can be minimized, respectively. To get it, the objective functions \(\Phi_1(\varphi) = (1 - \vartheta_1)(P_1A + AP_1) - \epsilon_1I, \text{ and } \epsilon_1r_m(\varphi_1) = \mathbb{E}(P_1u)/\sqrt{\epsilon_1\lambda_{\min}(\Phi_1)}(\varphi_1)\) are denoted. A medium \(\epsilon_1\) which minimize \(r_m(\varphi_1)\) is existed as in [24]. \(\epsilon_2\) can also be obtained by the same steps. Then, the minimal attractive \(S\) can be got based on those \(\epsilon_1\) and \(\epsilon_2\).

Corollary 1: In Theorem 1, let \(P_1 = P_2 = I, Q_2 = H_2, R_1 = I\), then the model (3) is globally dissipative in mean if there exist \(\rho_2, \kappa > 1\) such that:
\begin{equation}
\Omega = \begin{bmatrix}
\Omega_1 & 0 & 0 & B \\
* & \Omega_2 & 0 & D \\
* & * & -Q_1 + \rho_2H_2 & 0 \\
* & * & * & -I
\end{bmatrix} < 0,
\end{equation}
where \(\Omega_1 = -2A + H_1 + Q_1, \Omega_2 = -2C + 2H_2 + \kappa L^TL\), the global attractive set in mean is \(S = \{m, p) | |m| \leq |u|/\sqrt{\epsilon_1\lambda_{\min}(\Phi_1)}, m \in \mathbb{R}^n; \ |p| \leq |v|/\sqrt{\epsilon_2\lambda_{\min}(\Phi_2)}, p \in \mathbb{R}^n\}, \) where \(\Phi_1 = 2(1 - \vartheta_1)A - \epsilon_1I, \Phi_2 = 2(1 - \vartheta_2)C - \epsilon_2I\).
If \( \omega(t, x_m(t), x_p(t - \tau)) \equiv 0 \), then the stochastic GRNs (3) becomes the GRNs (11):
\[
\begin{cases}
\frac{dx_\Omega(t)}{dt} = [-Ax_\Omega(t) + Bg(x_p(t - \tau))]dt + u(t) \\
\frac{dx_p(t)}{dt} = [-Cx_p(t) + Dx_m(t - \sigma)]dt + v(t).
\end{cases}
\] (11)

**Corollary 2:** Under Assumption 1 and 2, if there exist positive definition matrices \( P_1, P_2, Q_1, Q_2, R_1, L \), and positive scalars \( \kappa \), such that:
\[
\Omega = \begin{bmatrix}
\Omega_1 & 0 & 0 & 0 & P_1 B \\
* & \Omega_2 & P_2 D & U \Sigma_2 & 0 \\
* & * & -Q_1 & 0 & 0 \\
* & * & * & -\kappa I + R_1 & 0 \\
* & * & * & * & -R_1
\end{bmatrix} < 0, \quad (12)
\]
where \( \Omega_1 = -P_1 A - AP_1 + Q_1, \quad \Omega_2 = -P_2 C - CP_2 + Q_2 + \kappa I L^T L \).

The following positive LKF candidate is considered:
\[
V(t) = V_1(t) + V_2(t) + V_3(t). \quad (13)
\]

From the proof of Theorem 1, the result can be obtained. \( \square \)

With Assumption 1 and \( g = (g_1, g_2, \ldots, g_n)^T \), we can get for any \( U = \text{diag}(u_1, u_2, \ldots, u_n) > 0 \) such that:
\[
\begin{bmatrix}
x^T \\
g(x)
\end{bmatrix}^T \begin{bmatrix}
-U & & \\
& U & \\
& & U
\end{bmatrix} \begin{bmatrix}
x \\
g(x)
\end{bmatrix} \geq 0, \quad \forall x \in \mathbb{R}^n. \quad (14)
\]
where \( \Sigma_1 = \text{diag}([l_1^{-1}, l_2^{+1}, \ldots, l_n^{+1}]), \quad \Sigma_2 = \text{diag}([\frac{l_1^{-1} + l_1^{+1}}{2}, \frac{l_2^{-1} + l_2^{+1}}{2}, \ldots, \frac{l_n^{-1} + l_n^{+1}}{2}]). \)

Different inequality technique is used to obtain the other different sufficient conditions as Corollary 3.

**Corollary 3:** Under Assumption 1,2, if there exist positive definition matrices \( P_1, P_2, Q_1, Q_2, R_1 \), positive scalars \( \rho_1, \rho_2, \) and \( U = \text{diag}(u_1, u_2, \ldots, u_n) > 0 \) such that:
\[
\hat{\Omega} = \begin{bmatrix}
\hat{\Omega}_1 & 0 & 0 & 0 & P_1 B \\
* & \hat{\Omega}_2 & P_2 D & U \Sigma_2 & 0 \\
* & * & \Omega_3 & 0 & 0 \\
* & * & * & \Omega_4 & 0 \\
* & * & * & * & -U + R_1 \\
* & * & * & * & -R_1
\end{bmatrix} < 0, \quad (15)
\]
where \( \hat{\Omega}_2 = -P_2 C - CP_2 + \rho_2 H_2 + Q_2 + U \Sigma_1, \quad \hat{\Omega}_3, \quad \hat{\Omega}_4 \) are the same definitions as in Theorem 1. The stochastic GRNs (3) with constant delays is globally dissipative in mean, and the corresponding attractive set \( S \triangleq \{(m, p)||m| \leq |P_1 u|/\sqrt{\varepsilon_1 \lambda_{\min}(\Phi_1), m \in \mathbb{R}^n, |p| \leq |P_2 v|/\sqrt{\varepsilon_2 \lambda_{\min}(\Phi_2), p \in \mathbb{R}^n}\}, \quad \Phi_1 = (1 - \theta_1)(P_1 A + AP_1) - \varepsilon I, \quad \Phi_2 = (1 - \theta_2)(P_1 C + CP_2) - \varepsilon_2 I. \)

**Proof:** Consider the same radially LKF candidate as in Theorem 1. From the proof of Theorem 1 and the conditions of Corollary 3, we can compute the \( \mathcal{L}V(t) \):
\[
\mathcal{L}V(t) = \mathcal{L}V_1(t) + \mathcal{L}V_2(t) + \mathcal{L}V_3(t)
\]
\[
\leq -x_m^T(t)(P_1 A + AP_1)x_m(t) + 2x_m^T(t)P_1 B g(x_p(t - \tau)) + 2x_m(t)P_1 u + 2x_p(t)v - x_p^T(t)(P_2 C + CP_2)x_p(t) + x_p^T(t)(P_2 D + DP_2)x_m(t - \sigma) + \rho_1 x_m^T(t)H_1 x_m(t) + \rho_1 x_p^T(t - \tau)H_2 x_p(t - \tau) + \rho_2 x_p^T(t)H_1 x_p(t) + \rho_2 x_m^T(t - \sigma)H_2 x_m(t - \sigma) + x_m^T(t)Q_1 x_m(t) - x_m^T(t - \sigma)Q_1 x_m(t - \sigma) + x_p^T(t)Q_2 x_p(t) - x_p^T(t - \tau)Q_2 x_p(t - \tau) + g^T(x_p(t))R_1 g(x_p(t)) - g^T(x_p(t - \tau))R_1 g(x_p(t - \tau)) + \begin{bmatrix} x_p(t) \end{bmatrix}^T \begin{bmatrix} -U \Sigma_1 & U \Sigma_2 \\
U \Sigma_2 & -U
\end{bmatrix} \begin{bmatrix} g(x_p(t)) \\
\rho_2 V_2^T(t) + \zeta T^T(t) \Omega_1(\theta_1, \theta_2) \zeta(t). \quad (16)
\end{bmatrix}
\]
\]

So we obtain that the model (11) is globally dissipative in mean with the corresponding attractive set \( S \). This completes the proof. \( \square \)

**Remark 5:** Up to now, we have studied the dissipativity problem for the GRNs with stochastic disturbances and time delay. Moreover, a detail algorithm is given to calculate the corresponding attraction set in terms of LMIs. It is worth noting that the presented method is based on the LMI technique. In addition, the dimension of the LMIs is related to the number of genes of GRNs. Therefore, we must face the computational burden problem when the number of genes goes up greatly. In order to deal with the computational burden issue of the proposed method, we will look for new advanced methods for handling the problem of the proposed GRNs, and the corresponding results will be presented in the future work.

**IV. NUMERICAL EXAMPLE**

In this section, an example is given to show the effectiveness and advantages of the developed theoretical results.

Consider a three-node stochastic GRNs model (3), the deterministic parameters are given as:
\[
A = \text{diag}(3, 3, 3), \quad B = \begin{pmatrix} 0.6 & 0 & 0.3 \\
0 & 0.6 & -0.1 \\
-0.4 & 0 & 0.5 \end{pmatrix},
\]
\[
C = \text{diag}(2.5, 2.5, 32.5), \quad D = \text{diag}(0.8, 0.8, 0.8),
\]
and \( \omega(t, x, y) = \text{diag}(0.25x + 0.2y, 0.3x, 0.2x - 0.15y), \) i.e. \( H_1 = 0.15I, \quad H_2 = 0.1I. \quad \tau = 1 = \sigma. \) The nonlinear function \( g(x) = \frac{x}{1+x^2} (i = 1, 2, 3; x \in \mathbb{R}), \) i.e. \( \Sigma_1 = \text{diag}(0, 0, 0), \quad \Sigma_2 = \text{diag}(0.325, 0.325, 0.325) \) and \( L = \text{diag}(0.65, 0.65, 0.65). \quad u = v = I. \)
Now, we solve the LMIs of Theorem 1 and get the following results:

\[
\begin{align*}
P_1 &= \begin{pmatrix} 14.995 & 0.260 & 0.713 \\ 0.260 & 15.613 & 0.421 \\ 0.713 & 0.421 & 15.316 \end{pmatrix}, \\
Q_1 &= \begin{pmatrix} 14.043 & 0.260 & 0.713 \\ 0.260 & 14.661 & 0.421 \\ 0.713 & 0.421 & 14.364 \end{pmatrix}, \\
\end{align*}
\]

Then, we can obtain \( \vartheta_1 = 0.836, \vartheta_2 = 0.838 \). The minimal radius of \( S \) can be got at \( \varepsilon_1 = 8.252, \varepsilon_2 = 14.804 \), i.e., \( S = \{ (m, p) | \| m \| \leq 16.721, \| p \| \leq 4.306 \} \) to assure \( \Phi_1 > 0, \Phi_2 > 0 \). An attractive set with smaller radius is given by Corollary 3.
with the initial values $m(t) = (0.6, 0.2, 0.5), p(t) = (0.4, 0.7, 0.4), t \in [-1, 0]$.

Through the simulation, the following items can be shown: 1) the model has no equilibrium point but the mRNA and protein concentrations enter and stay inside the set $S$.

2) the proposed results for the radius of attractive set can be further improved.

3) the dissipativity of the GRNs is closely correlated with the coupling coefficient $B$.

V. CONCLUSION

In this article, the dissipativity problem for GRNs with stochastic disturbances and time-delay effects was discussed by the stochastic technique, optimal algorithm and Lyapunov stability theory. The globally dissipative in mean and corresponding globally attractive set for GRNs were firstly defined based on the the concentrations of mRNA and protein. Subsequently, some novel sufficient conditions which considers the two concentrations as a whole are obtained through constructing different LKFs. Further, the results given in this paper solve the new questions and the obtained LMIs are computationally efficient which could be solved numerically by calculation software. Finally, the availability of the proposed results is offered based on a three-gen GRN and the speed of the simulation processing was improved through the FPGA hardware tool. We can see that GRNs have been discussed with the effects such as switched systems and stochastic communication protocols [12], [15]. The proposed method in this paper can be extended to deal with the dissipativity problem of those models. In particular, it can be found that the results are independent of time delays involved in the proposed system which are non-negative constants. The same conclusion for the Hopfield network and cellular NNs was first presented in [24]. The other kinds of time delays can be discussed in the future work, for example distributed delay, time-varying delay, random sensor delays, mixed time-delays and so on [12], [14], [16], [28], [30].

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FIGURE 3. Transient response of protein concentrations $x_p$ in model (11).
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