# STATE ESTIMATION FOR GENE REGULATORY NETWORKS WITH SAMPLED OUTPUT MEASUREMENTS AND TIME-VARYING DELAYS

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### *ABSTRACT*

*This paper investigates the H∞ state estimation problem for gene regulatory networks (GRNs) with time-varying delays and Markovian jumping parameters. The system output, which is used by the estimator, is assumed to be sampled and held during a sampling period. To deal with the time-varying delays, each delay function is limited to certain lower and upper bounds. By using Lyapunov-Krasovskii functionals, sufficient conditions for the stochastic stability of augmented GRN/Estimator networks are derived. Then, the estimator gains are synthesized from the derived stability conditions. Furthermore, we investigate how to design the estimator in presence of disturbance. All stability conditions are formulated in the form of linear matrix inequalities which can be easily solved by numerical methods. The obtained conditions are dependent on both the lower and upper bounds of delays. At the end, some simulation results are presented to demonstrate the effectiveness of the proposed method.*

### *KEYWORDS*

*Gene regulatory networks, Markovian jump parameters, time-varying delay, sampled data state estimation, Linear Matrix Inequality.*

## 1. INTRODUCTION

Gene regulatory networks (GRNs) are biochemically dynamical systems describing the regulatory interactions between DNA, RNA and proteins. GRNs play an important role in cells' response to environmental stimuli and performing their complicated biological functions.

In recent years, the modelling and stability problem of gene networks has attracted many researchers in diverse disciplines (see for example [1-5]). To describe the mechanism of gene regulations, different classes of mathematical models have been proposed. These models can be divided into three main categories, i.e., the Boolean models, the differential equation models and hybrid models. In Boolean models, each gene is considered to be in one of two logical states, ON or OFF. The logical state of each gene is determined as a function of relevant gene states ([6, 7]).In the differential equation models, the variables describe the concentration of mRNAs and proteins as continuous values ([2], [8]).In addition to Boolean and differential equation models, there are hybrid models which combine the properties of two previous models [9].

The existence of switching mechanisms in gene networks is a well-known fact [10], [11].By taking into account the stochastic behaviour of gene networks, authors in [12], [13] and [14] have modelled the switching mechanisms in GRNs by means of finite state Markov chains. In order to increase the accuracy, [15] and [16] have proposed Markovian jump GRNs with emphasis on quantitatively describing of gene regulation.

Several recent studies such as [17], [18] and [19] have shown that the time taken for gene expression to be completed is not negligible in the dynamics of GRNs. The synthesis of proteins by the ribosome is also time-consuming. As stated in [20-23], these delays are assumed to be time-varying functions in GRN dynamics. In [24, 25], the conditions for stochastic stability of GRNs with time-varying delays have been established using free weighting matrix technique. Authors in [26] have applied integral inequality approach to reduce the conservatism of linear matrix inequalities. Recently, the stochastic stability of GRNs random delays are investigated in [27, 28]. The obtained linear matrix inequalities are dependent on delay probability distributions.
From the viewpoint of biology, obtaining the gene network state components including the concentration of mRNA and protein is of a high importance. In [29], the problem of filtering has been investigated for nonlinear gene regulatory networks where time delays are supposed to be deterministic and constant. The stochastic switching mechanisms in GRN parameters, however, have not been considered in the model. Authors in [23] have proposed a robust estimator for uncertain Markovian jump gene regulatory networks with time-varying delays.

In general problems of filtering, state estimation and control, the necessary outputs of the system usually are available in sampled form. It mainly rises from the discrete nature of measurement techniques as well as digital processing via computer systems. There are many works associated with the sampled data systems in the literature such as [30, 31] and references therein. [32] studies the problem of $H\infty$ filtering for GRNs with sampled output based on input delay approach. Although there are no delays and Markovian switching considered in GRN dynamic. To the best knowledge of authors, the problem of state estimation and filtering of Markovian jump GRNs when output are sampled and held in a sampling period and the expression and translation delays are considered is not fully investigated.

In this paper, we aim to design a state estimator considering the sampled nature of the measurements. We also solve the problem of estimator design with respect to the presence of external disturbances. The delays are considered to be time-varying and limited by upper and lower bounds. The final stability conditions are also dependent on the bounds of delays and the upper amount of sampling interval time. Appropriate Lyapunov-Krasovskii functionals are used to find a sufficient condition in terms of linear matrix inequalities assuring the stochastic stability and the disturbance attenuation of the mixed GRN/estimator dynamics. By employing some free-weighting matrices and using some LMI techniques, we obtain less conservative delay dependent stability criteria. The estimator gains are then synthesized from the stability conditions which are all expressed in the terms of linear matrix inequalities. Finally, simulation examples are provided to show the effectiveness of our approach.

This paper is organized as follows: Section II describes the model of Markovian jump Gene regulatory networks and the estimator structure and gives some preliminaries; Section III presents the main results on stability and the estimator design, section IV gives some simulation examples and finally Section V concludes the paper.

## 2. SYSTEM DESCRIPTION AND PRELIMINARIES

Gene regulatory networks are modeled by differential equations as follows [2]:

$$\begin{aligned} \dot{m}(t) &= Am(t) + Bf\left(p(t)\right) + l \\ \dot{p}(t) &= Cp(t) + Dm(t) \end{aligned} \tag{1}$$

in which

$$m(t) = [m_1(t), m_2(t), ..., m_n(t)]^T,\ p(t) = [p_1(t), p_2(t), ..., p_n(t)]^T,$$
$$A = diag(-a_1, -a_2, ..., -a_n), C = diag(-c_1, -c_2, ..., -c_n),\ \ D = diag(d_1, d_2, ..., d_n),\ \ l = [l_1, l_2, ..., l_n]^T$$
$$and \quad f(t) = [f_1(t), f_2(t), ..., f_n(t)]^T.$$

where $i=1,2,\ldots$,n. $m_i(t)$ , $p_i(t) \in R$ are the concentrations of mRNA and protein of $i$th node. $a_i$ and $c_i$ are degradation rates of mRNA and protein, $d_i$ is constant, $f_i(x) = \frac{(x/\beta)^H}{1+(x/\beta)^H}$ is a monotonically increasing function, and $B = (B_{ij}) \in \mathbf{R}^{n\times n}$ is the coupling matrix of the gene network ([2,3,8]). $l_i$ is defined as a basal rate and is defined as: $l_i = \sum_{j\in V_{i1}} \alpha_{ij}$ , in which $V_{i1}$ is the set of repressors of gene $i$. Vectors $m^*$, $p^*$ are said to be the equilibrium point of system (1) if they satisfy $Am^* + Bf(p^*) + l = 0$ and $Cp^* + Dm^* = 0$. For convenience, we always shift an intended equilibrium point $(p^*, m^*)$ to origin by letting $x(t) = m(t) - m^*$, $y(t) = p(t) - p^*$.

Additively, in this paper like many others in the literature of dynamic GRNs, we consider external fluctuation as additive disturbances. In gene networks, there are also time delays in transcription, translation and translocation processes. Moreover, Markovian jumping parameters are common in modelling of GRNs. So we consider shifted-to-origin Gene regulation network with time delay, Markovian jumping parameters and disturbances of the following form:

$$\begin{aligned} \dot{x}(t) &= A(r(t))x(t) + B(r(t))g\left(y(t-\tau(t))\right) + F_1(r(t))\omega(t) \\ \dot{y}(t) &= C(r(t))y(t) + D(r(t))x(t-\sigma(t)) + F_2(r(t))\omega(t) \\ z(t) &= \begin{bmatrix} z_x(t) \\ z_y(t) \end{bmatrix} = \begin{bmatrix} H_1(r(t))x(t) \\ H_2(r(t))y(t) \end{bmatrix} \end{aligned} \tag{2}$$

where $F_1, F_2$ are input matrices and $\omega(t)$ is the input disturbance which belongs to $L_2[0,\infty)$. The nonlinear function $g(.)$ is defined as $g\left(y(t)\right) = f\left(y(t)+p^*\right) - f\left(p^*\right)$. Moreover, since $f$ is a monotonically increasing function with saturation, for all $a,b \in \mathbf{R}$ with $a \neq b$ , it satisfies:

$$0 \le \frac{f(a) - f(b)}{a-b} \le k \tag{3}$$

When $f$ is differentiable, the above inequality is equivalent to $0 \le df(a)/da \le k$ . From the relationship of $f(.)$ and $g(.)$ , we know that $g(.)$ satisfies the sector condition $0 \le g(a)/a \le k$ ,or equivalently:

$$g(a)\big(g(a)-ka\big)\le 0 \tag{4}$$

$g(.)$ is a vector function of $g_i(.)$'s in the following form:

$$g(.)=\big[g_1(.) \quad \dots \quad g_n(.)\big]^T \tag{5}$$

where $g_i(.)$'s satisfy (4) for $k=k_1,\dots,k_n$. Also define matrix $K$ as:

$$K=diag(k_1,\dots,k_n) \tag{6}$$

The output $z(t)$ is the concentration of intended genes or proteins; $r(t), t\ge 0$ is a right-continuous Markov chain on the probability space taking values in a finite state space $S=\{1,2,...,\chi\}$ with generator $\Pi=(\pi_{ij})_{N\times N}$ given by:

$$\begin{cases} P\left[r_{t+h}=i \mid r_t=j\right]=\begin{cases}\pi_{ij}h+o(h) & i\ne j\\ 1+\pi_{ii}h+o(h) & otherwi\end{cases}\\ \lim\limits_{h\to 0}\dfrac{o(h)}{h}=0 \quad , \quad \pi_{ij}\ge 0 \quad ,\pi_{ii}=-\sum_{j\ne i}\pi_{ij}. \end{cases} \tag{7}$$

For simplicity, we refer to $r(t)$ with index *i*. $\tau(t)$ and $\sigma(t)$ are time-varying delays satisfying following constraints:

$$\underline{\sigma}\le\sigma(t)\le\bar{\sigma},\ \ \dot{\sigma}(t)\le\alpha_\sigma,\ \ \underline{\tau}\le\tau(t)\le\bar{\tau},\ \ \dot{\tau}(t)\le\alpha_\tau \tag{8}$$

As previously said, the problem of GRNs state estimation for the case of time-varying delays and sampled output data has not been fully investigated. Here, we assume that the sampled signal is generated by a zero-order hold function with a sequence of hold times 0, t1,…,tk,…. So the actual measurements of mRNA/Protein concentrations used by the state estimator are:

$$\hat{z}(t)=z(t_k) \qquad t_k\le t<t_{k+1} \tag{9}$$

In which $t_k$ denotes the sampling point. Let the sampling interval to be bounded for all k, or $t_{k+1}-t_k\le\bar{d}$ for some $\bar{d}$. Define a function

$$d(t)=t-t_k \qquad t_k\le t<t_{k+1} \tag{10}$$

It can be realized that $0\le d(t)<\bar{d}$. Then, the structure of the considered estimator could be written as follows:

$$\begin{aligned}\dot{\hat{x}}(t)&=A_i\hat{x}(t)+B_i\hat{y}(t-\tau(t))+K_{1i}\big(H_{1i}x(t-d(t))-H_{1i}\hat{x}(t)\big)\\ \dot{\hat{y}}(t)&=C_i\hat{y}(t)+D_i\hat{x}(t-\sigma(t))+K_{2i}\big(H_{2i}x(t-d(t))-H_{2i}\hat{y}(t)\big)\end{aligned} \tag{11}$$

Defining $\tilde{x}(t)=x(t)-\hat{x}(t)$ and $\tilde{y}(t)=y(t)-\hat{y}(t)$, from (2) and (11) , the estimation error dynamic becomes:

$$\begin{aligned}\dot{\tilde{x}}(t) &= (A_i - K_{1i}H_{1i})\tilde{x}(t) + K_{1i}H_{1i}\left(x(t) - x(t-d(t))\right) + B_i\left(\tilde{y}(t-\tau(t)) - y(t-\tau(t))\right) \\ &\quad + B_i g\left(y(t-\tau(t))\right) + F_{1i}\omega(t) \\ \dot{\tilde{y}}(t) &= (C_i - K_{2i}H_{2i})\tilde{y}(t) + K_{2i}H_{2i}\left(y(t) - y(t-d(t))\right) + D_i\tilde{x}(t-\sigma(t)) + F_{2i}\omega(t)\end{aligned} \tag{12}$$

By defining $\bar{x}(t) = \begin{bmatrix} x^T(t) & \tilde{x}^T(t)\end{bmatrix}^T$ and $\bar{y}(t) = \begin{bmatrix} y^T(t) & \tilde{y}^T(t)\end{bmatrix}^T$ and some simple calculations, the following augmented closed loop system can be obtained:

$$\begin{aligned}\dot{\bar{x}}(t) &= \bar{A}_i\bar{x}(t) + \bar{A}_{di}\bar{x}(t-d(t)) + \bar{B}_{1i}\bar{y}(t-\tau(t)) + \bar{B}_{2i}g\left(U\bar{y}(t-\tau(t))\right) + \bar{F}_{1i}\omega(t) \\ \dot{\bar{y}}(t) &= \bar{C}_i\bar{y}(t) + \bar{C}_{di}\bar{y}(t-d(t)) + \bar{D}_i\bar{x}(t-\sigma(t)) + \bar{F}_{2i}\omega(t)\end{aligned} \tag{13}$$

in which

$$\bar{A}_i = \begin{pmatrix} A_i & 0 \\ K_{1i}H_{1i} & A_i - K_{1i}H_{1i}\end{pmatrix}, \bar{A}_{di} = \begin{pmatrix} 0 & 0 \\ -K_{1i}H_{1i} & 0\end{pmatrix}, \bar{B}_{1i} = \begin{pmatrix} 0 & 0 \\ -B_i & B_i\end{pmatrix}, \bar{B}_{2i} = \begin{pmatrix} B_{ii} \\ B_i\end{pmatrix}, \bar{D}_i = \begin{pmatrix} D_i & 0 \\ 0 & D_i\end{pmatrix}$$

$$\bar{C}_i = \begin{pmatrix} C_i & 0 \\ K_{2i}H_{2i} & C_i - K_{2i}H_{2i}\end{pmatrix}, \bar{C}_{di} = \begin{pmatrix} 0 & 0 \\ -K_{2i}H_{2i} & 0\end{pmatrix}, \bar{F}_{1i} = \begin{pmatrix} F_{1i} \\ F_{1i}\end{pmatrix}, \bar{F}_{2i} = \begin{pmatrix} F_{2i} \\ F_{2i}\end{pmatrix}, U = [I \quad 0].$$

The stochastic stability and the $\gamma$ disturbance attenuation for GRNs system are defined in two following definitions:

**Definition1**: System (13) without disturbances is stochastically stable if for any initial state in a neighborhood of origin, there exists finite positive constant $T(\bar{x}_0, \bar{y}_0, r_0)$ such that the following holds for any initial condition:

$$E\left(\int_0^\infty \left(\|\bar{x}(t)\|^2 + \|\bar{y}(t)\|^2\right)dt \mid \bar{x}_0, \bar{y}_0, r_0\right) \le T(\bar{x}_0, \bar{y}_0, r_0) \tag{14}$$

Also the mean square stability can be concluded from $\lim_{t\to\infty} E\left(\|\bar{x}(t)\|^2\right) = 0$ and $\lim_{t\to\infty} E\left(\|\bar{y}(t)\|^2\right) = 0$

Definition2: The estimator (11) is said to be an error stabilizer estimator with the $\gamma$ disturbance attenuation if the error dynamics is stochastically stable with definition 1 and there exists a constant $M(\bar{x}_0, \bar{y}_0, r_0)$, such that:

$$\left(\|\bar{x}\|_2^2 + \|\bar{y}\|_2^2\right) \stackrel{\Delta}{=} \left(E\int_0^\infty \left(\bar{x}^T(t)\bar{x}(t) + \bar{y}^T(t)\bar{y}(t)\right)dt \mid (\bar{x}_0, \bar{y}_0, r_0)\right) \le \gamma^2\left(\|\omega\|_2^2 + M(\bar{x}_0,\right. \tag{15}$$

The following lemma is used in the proof of theorems in this paper:

**Lemma1**[31]: Let $Y$ be a symmetric matrix and $H$, $E$ be given matrices with appropriate dimensions and $F$ satisfying $F^T F < I$, Then we have:

$$Y + HFE + E^T F^T H^T < 0$$

holds if and only if there exists a scalar ε > 0such that the following holds:

$$Y + \varepsilon HH^T + \varepsilon^{-1} E^T E < 0$$

# 3. MAIN RESULTS

In this section, the main results ensuring the stochastic stability of stochastic GRNs and the estimator system with Markovian jumping parameters and time-varying delays are derived and then an approach for the synthesis of the estimator gains from LMIs is introduced. First, we consider the stochastic stability problem in the following theorem.

**Theorem 1**: The Markovian jump GRN/Estimator System (13) with zero external disturbances is stochastically stable if there exist symmetric and positive definite matrices $P_{ki}, R_k, S_k, Z_l, Q_l, \Lambda_i = diag(\lambda_{1i}, ..., \lambda_{ni})$, and matrices $X_{ji}$ ($k = 1, 2,\ l = 1, ..., 4,\ j = 1, ..., 17,\ i \in S$) satisfying the following LMIs:

$$\Phi_i = \begin{bmatrix} J_i & 0 & 0 & 0 & 0 & 0 & \Upsilon_{\lambda i} & \Upsilon_{W1i} & \Upsilon_{W2i} \\ * & \Theta_i & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & -Z_3 & -Z_3 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & -Z_3 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & -Z_4 & -Z_4 & 0 & 0 & 0 \\ * & * & * & * & * & -Z_4 & 0 & 0 & 0 \\ * & * & * & * & * & * & -2\Lambda_i & \bar{B}_{2i}^T W_{1i} & 0 \\ * & * & * & * & * & * & * & -W_{1i} & 0 \\ * & * & * & * & * & * & * & * & -W_{2i} \end{bmatrix} + N_i + N_i^T < 0, \tag{16}$$

in which

$$J_i = \begin{bmatrix} J_{xi} & 0 & 0 & P_{1i}\bar{B}_{1i} & P_{1i}\bar{A}_{di} & 0 \\ * & J_{yi} & P_{2i}\bar{D}_i & 0 & 0 & P_{2i}\bar{C}_{di} \\ * & * & -(1-\alpha_\sigma)R_1 & 0 & 0 & 0 \\ * & * & * & -(1-\alpha_\tau)R_2 & 0 & 0 \\ * & * & * & * & 0 & 0 \\ * & * & * & * & * & 0 \end{bmatrix},$$

$$\Theta_i = diag(-Z_1, -Z_2, R_1 - Q_1, R_2 - Q_2, -Q_3, -Q_4, -S_1, -S_2),\ J_{xi} = P_{1i}\bar{A}_i + \bar{A}_i^T P_{1i} + Q_1 + \sum_j \pi_{ij} P_{1j},$$

$$J_{yi} = P_{2i}\bar{C}_i + \bar{C}_i^T P_{2i} + Q_2 + \sum_j \pi_{ij} P_{2j},\ W_{1i} = \underline{\sigma}^2 S_1 + \bar{d}^2 Z_3 + (\bar{\sigma} - \underline{\sigma})^2 Z_1,$$

$$W_{2i} = \underline{\tau}^2 S_2 + \bar{d}^2 Z_4 + (\bar{\tau} - \underline{\tau})^2 Z_2.$$

and

$$\Upsilon_{\lambda i} = \left[ \left( P_{1i}\bar{B}_{2i} \right)^T \quad 0 \quad 0 \quad \left( U^T \Lambda_i K \right)^T \quad 0 \quad 0 \right]^T, \Upsilon_{W_{1i}} = \left[ \left( \bar{A}_i^T W_{1i} \right)^T \quad 0 \quad 0 \quad \left( \bar{B}_{1i}^T W_{1i} \right)^T \quad 0 \quad 0 \right]^T,$$

$$\Upsilon_{W_{2i}} = \left[ 0 \quad \left( \bar{C}_i^T W_{2i} \right)^T \quad \left( \bar{D}_i^T W_{2i} \right)^T \quad 0 \quad 0 \quad 0 \right]^T$$

$$N_i = \begin{pmatrix} \tilde{X}_i & 0 \\ 0 & 0 \end{pmatrix}, \quad \tilde{X}_i = \begin{pmatrix} \tilde{X}_{1i} \\ \tilde{X}_{2i} \\ \vdots \\ \tilde{X}_{18i} \end{pmatrix},$$

And $X_{ji}$'s are introduced at the top of the next page.

$$\tilde{X}_{ji} = \begin{cases} \left[ -X_{ji} \ \overbrace{0 \cdots 0}^{18n} \ X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ X_{ji} \ \overbrace{0 \cdots 0}^{6n} \right] & j = 1, 11, 15 \\ \left[ 0_{2n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{18n} \ X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ X_{ji} \ \overbrace{0 \cdots 0}^{4n} \right] & j = 2, 12, 16 \\ \left[ 0_{2n} \ 0_{2n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ X_{ji} \ \overbrace{0 \cdots 0}^{14n} \right] & j = 3, 7 \\ \left[ \overbrace{0 \cdots 0}^{6n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ X_{ji} \ \overbrace{0 \cdots 0}^{12n} \right] & j = 4, 8 \\ \left[ \overbrace{0 \cdots 0}^{8n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{14n} \ X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ X_{ji} \ 0_{2n} \right] & j = 5, 13, 17 \\ \left[ \overbrace{0 \cdots 0}^{10n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{14n} \ X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ X_{ji} \right] & j = 6, 14, 18 \\ \left[ X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{18n} \right] & j = 9 \\ \left[ 0_{2n} \ X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{6n} \ -X_{ji} \ \overbrace{0 \cdots 0}^{16n} \right] & j = 10 \end{cases} \tag{17}$$

-*Proof*: Consider the following Lyapunov–Krasovskii functional:

$$V\left(\bar{x}(t), \bar{y}(t), r(t)\right) = \sum_{k=1}^{5} V_k\left(\bar{x}(t), \bar{y}(t), r(t)\right) \tag{18}$$

where

$$V_{1i}(t) = \bar{x}^T(t) P_{1i} \bar{x}(t) + \bar{y}^T(t) P_{2i} \bar{y}(t)$$

$$V_{2i}(t) = \int_{t-\underline{\sigma}}^{t} \bar{x}^T(\alpha) Q_1 \bar{x}(\alpha) d\alpha + \int_{t-\sigma(t)}^{t-\underline{\sigma}} \bar{x}^T(\alpha) R_1 \bar{x}(\alpha) d\alpha + \int_{t-\underline{\tau}}^{t} \bar{y}^T(\alpha) Q_2 \bar{y}(\alpha) d\alpha$$

$$+ \int_{t-\tau(t)}^{t-\underline{\tau}} \bar{y}^T(\alpha) R_2 \bar{y}(\alpha) d\alpha + \int_{t-\bar{d}}^{t} \bar{x}^T(\alpha) Q_3 \bar{x}(\alpha) d\alpha + \int_{t-\bar{d}}^{t} \bar{y}^T(\alpha) Q_4 \bar{y}(\alpha) d\alpha$$

$$V_{3i}(t)=\underline{\sigma}\int_{-\underline{\sigma}}^{0}\int_{t+\beta}^{t}\dot{\bar{x}}^{T}(\alpha)S_1\dot{\bar{x}}(\alpha)d\alpha d\beta+\left(\bar{\sigma}-\underline{\sigma}\right)\int_{-\bar{\sigma}}^{-\underline{\sigma}}\int_{t+\beta}^{t}\dot{\bar{x}}^{T}(\alpha)Z_1\dot{\bar{x}}(\alpha)d\alpha d\beta$$
$$+\underline{\tau}\int_{-\underline{\tau}}^{0}\int_{t+\beta}^{t}\dot{\bar{y}}^{T}(\alpha)S_2\dot{\bar{y}}(\alpha)d\alpha d\beta+\left(\bar{\tau}-\underline{\tau}\right)\int_{-\bar{\tau}}^{-\underline{\tau}}\int_{t+\beta}^{t}\dot{\bar{y}}^{T}(\alpha)Z_2\dot{\bar{y}}(\alpha)d\alpha d\beta$$
$$+\bar{d}\int_{-\bar{d}}^{0}\int_{t+\beta}^{t}\dot{\bar{x}}^{T}(\alpha)Z_3\dot{\bar{x}}(\alpha)d\alpha d\beta+\bar{d}\int_{-\bar{d}}^{0}\int_{t+\beta}^{t}\dot{\bar{y}}^{T}(\alpha)Z_4\dot{\bar{y}}(\alpha)d\alpha d\beta$$

Define a new Markov process $\left\{\bar{x}_{\rho}(t),\bar{y}_{\delta}(t),r(t),t>0\right\}$ with $\bar{x}_{\rho}(t)=\bar{x}(t+\rho)$ and $\bar{y}_{\delta}(t)=\bar{y}(t+\delta)$ $,0<\delta<-\bar{\tau}$ $,0<\rho<-\bar{\sigma}$ , the weak infinitesimal operator of the stochastic process $\left\{\left(\bar{x}(t),\bar{y}(t),r_t\right)\right\}$ is given by:

$$\mathrm{A}V\left(\bar{x}(t),\bar{y}(t),r_t\right)=\lim_{h\to 0}\frac{1}{h}\Big[E\left\{V\left(\bar{x}(t+h),\bar{y}(t+h),r_{t+h}\right)\mid\bar{x}(t),\bar{y}(t),r_t\right\}-V\left(\bar{x}(t),\bar{y}(t),r_t\right)\Big] \tag{19}$$

Based on (13) , we have:

$$\mathrm{A}V_{1i}(t)=2\bar{x}^{T}(t)P_{1i}\dot{\bar{x}}(t)+2\bar{y}^{T}(t)P_{2i}\dot{\bar{y}}(t)+\bar{x}^{T}(t)(\sum_{j}\pi_{ij}P_{1j})\bar{x}(t)+\bar{y}^{T}(t)(\sum_{j}\pi_{ij}P_{2j})\bar{y}(t)$$
$$=2\bar{x}^{T}(t)P_{1i}[\bar{A}_i\bar{x}(t)+\bar{A}_{di}\bar{x}(t-d(t))+\bar{B}_{1i}\bar{y}(t-\tau(t))+\bar{B}_{2i}g\left(U\bar{y}(t-\tau(t))\right)]$$
$$+\bar{x}^{T}(t)(\sum_{j}\pi_{ij}P_{1j})\bar{x}(t)+2\bar{y}^{T}(t)P_{2i}[\bar{C}_i\bar{y}(t)+\bar{C}_{di}\bar{y}(t-d(t))+\bar{D}_i\bar{x}(t-\sigma(t))]$$
$$+\bar{y}^{T}(t)(\sum_{j}\pi_{ij}P_{2j})\bar{y}(t) \tag{20}$$

$$\mathrm{A}V_{2i}(t)=\bar{x}^{T}(t)Q_1\bar{x}(t)-\left(1-\dot{\sigma}(t)\right)\bar{x}^{T}(t-\sigma(t))R_1\bar{x}(t-\sigma(t))+\bar{x}^{T}(t-\underline{\sigma})\left(R_1-Q_1\right)\bar{x}(t-\underline{\sigma})$$
$$+\bar{y}^{T}(t)Q_2\bar{y}(t)-\left(1-\dot{\tau}(t)\right)\bar{y}^{T}(t-\tau(t))R_2\bar{y}(t-\tau(t))+\bar{y}^{T}(t-\underline{\tau})\left(R_2-Q_2\right)\bar{y}(t-\underline{\tau})$$
$$+\bar{x}^{T}(t)Q_3\bar{x}(t)-\bar{x}^{T}(t-\bar{d})Q_3\bar{x}(t-\bar{d})+\bar{y}^{T}(t)Q_4\bar{y}(t)-\bar{y}^{T}(t-\bar{d})Q_4\bar{y}(t-\bar{d}) \tag{21}$$

$$\mathrm{A}V_{3i}(t)\le\underline{\sigma}^2\dot{\bar{x}}^{T}(t)S_1\dot{\bar{x}}(t)+\left(\bar{\sigma}-\underline{\sigma}\right)^2\dot{\bar{x}}^{T}(t)Z_1\dot{\bar{x}}(t)+\underline{\tau}^2\dot{\bar{y}}^{T}(t)S_2\dot{\bar{y}}(t)+\left(\bar{\tau}-\underline{\tau}\right)^2\dot{\bar{y}}^{T}(t)Z_2\dot{\bar{y}}(t)$$
$$-\underline{\sigma}\int_{t-\underline{\sigma}}^{t}\dot{\bar{x}}^{T}(\alpha)S_1\dot{\bar{x}}(\alpha)d\alpha-\left(\bar{\sigma}-\underline{\sigma}\right)\int_{t-\bar{\sigma}}^{t-\underline{\sigma}}\dot{\bar{x}}^{T}(\alpha)Z_1\dot{\bar{x}}(\alpha)d\alpha+\bar{d}^2\dot{\bar{x}}^{T}(t)Z_3\dot{\bar{x}}(t)$$
$$-\underline{\tau}\int_{t-\underline{\tau}}^{t}\dot{\bar{y}}^{T}(\alpha)S_2\dot{\bar{y}}(\alpha)d\alpha-\left(\bar{\tau}-\underline{\tau}\right)\int_{t-\bar{\tau}}^{t-\underline{\tau}}\dot{\bar{y}}^{T}(\alpha)Z_2\dot{\bar{y}}(\alpha)d\alpha+\bar{d}^2\dot{\bar{y}}^{T}(t)Z_4\dot{\bar{y}}(t)$$
$$-\bar{d}\int_{t-\bar{d}}^{t}\dot{\bar{x}}^{T}(\alpha)Z_3\dot{\bar{x}}(\alpha)d\alpha-\bar{d}\int_{t-\bar{d}}^{t}\dot{\bar{y}}^{T}(\alpha)Z_4\dot{\bar{y}}(\alpha)d\alpha \tag{22}$$

According to $\sigma(t)\le\bar{\sigma},\tau(t)\le\bar{\tau}$ , we have from Jensen's inequality [23] :

$$
\begin{aligned}
&-\underline{\sigma}\int_{t-\underline{\sigma}}^{t}\dot{x}^{T}(\alpha)S_{1}\dot{x}(\alpha)d\alpha-\left(\bar{\sigma}-\underline{\sigma}\right)\int_{t-\bar{\sigma}}^{t-\underline{\sigma}}\dot{x}^{T}(\alpha)Z_{1}\dot{x}(\alpha)d\alpha\leq\\
&-(\int_{t-\underline{\sigma}}^{t}\dot{x}(\alpha)d\alpha)^{T}S_{1}(\int_{t-\underline{\sigma}}^{t}\dot{x}(\alpha)d\alpha)-(\int_{t-\sigma(t)}^{t-\underline{\sigma}}\dot{x}(\alpha)d\alpha)^{T}Z_{1}(\int_{t-\sigma(t)}^{t-\underline{\sigma}}\dot{x}(\alpha)d\alpha),\\
&-\underline{\tau}\int_{t-\underline{\tau}}^{t}\dot{y}^{T}(\alpha)S_{2}\dot{y}(\alpha)d\alpha-\left(\bar{\tau}-\underline{\tau}\right)\int_{t-\bar{\tau}}^{t-\underline{\tau}}\dot{y}^{T}(\alpha)Z_{2}\dot{y}(\alpha)d\alpha\leq\\
&-(\int_{t-\underline{\tau}}^{t}\dot{y}(\alpha)d\alpha)^{T}S_{2}(\int_{t-\underline{\tau}}^{t}\dot{y}(\alpha)d\alpha)-(\int_{t-\tau(t)}^{t-\underline{\tau}}\dot{y}(\alpha)d\alpha)^{T}Z_{2}(\int_{t-\tau(t)}^{t-\underline{\tau}}\dot{y}(\alpha)d\alpha),\\
&-\bar{d}\int_{t-\bar{d}}^{t}\dot{x}^{T}(\alpha)Z_{3}\dot{x}(\alpha)d\alpha-\bar{d}\int_{t-\bar{d}}^{t}\dot{y}^{T}(\alpha)Z_{4}\dot{y}(\alpha)d\alpha\leq\\
&-(\int_{t-\bar{d}}^{t}\dot{x}(\alpha)d\alpha)^{T}Z_{3}(\int_{t-\bar{d}}^{t}\dot{x}(\alpha)d\alpha)-(\int_{t-\bar{d}}^{t}\dot{y}(\alpha)d\alpha)^{T}Z_{4}(\int_{t-\bar{d}}^{t}\dot{y}(\alpha)d\alpha)=\\
&-(\int_{t-\bar{d}}^{t-d(t)}\dot{x}(\alpha)d\alpha)^{T}Z_{3}(\int_{t-\bar{d}}^{t-d(t)}\dot{x}(\alpha)d\alpha)-(\int_{t-d(t)}^{t}\dot{x}(\alpha)d\alpha)^{T}Z_{3}(\int_{t-d(t)}^{t}\dot{x}(\alpha)d\alpha)\\
&-(\int_{t-\bar{d}}^{t-d(t)}\dot{y}(\alpha)d\alpha)^{T}Z_{4}(\int_{t-\bar{d}}^{t-d(t)}\dot{y}(\alpha)d\alpha)-(\int_{t-d(t)}^{t}\dot{y}(\alpha)d\alpha)^{T}Z_{4}(\int_{t-d(t)}^{t}\dot{y}(\alpha)d\alpha)\\
&-2(\int_{t-\bar{d}}^{t-d(t)}\dot{x}(\alpha)d\alpha)^{T}Z_{3}(\int_{t-d(t)}^{t}\dot{x}(\alpha)d\alpha)-2(\int_{t-\bar{d}}^{t-d(t)}\dot{y}(\alpha)d\alpha)^{T}Z_{4}(\int_{t-d(t)}^{t}\dot{y}(\alpha)d\alpha)
\end{aligned}
\tag{23}
$$

According to (4), it can be resulted that:

$$
-2\sum_{i}\lambda_{i}g_{i}(U\bar{y}(t))(g_{i}(U\bar{y}(t))-kU\bar{y}(t))\geq 0 \tag{24}
$$

or equivalently:

$$
-2g^{T}(U\bar{y}(t-\tau(t)))\Lambda_{i}g(U\bar{y}(t-\tau(t)))+2g^{T}(U\bar{y}(t-\tau(t)))K\Lambda_{i}U\bar{y}(t-\tau(t))\geq 0 \tag{25}
$$

For any $\Lambda_{i}=diag\left(\lambda_{1},\ldots,\lambda_{n}\right)>0$ .Now from (8) and ((20)-(25)) we can deduce that:

$$
\begin{aligned}
\mathrm{A}V_i(t) \le\ & \bar{x}^T(t)\left[P_{1i}\bar{A}_i + \bar{A}_i^T P_{1i} + Q_1 + Q_3 + \sum_j \pi_{ij} P_{1j}\right]\bar{x}(t) \\
& + \bar{y}^T(t)\left[P_{2i}\bar{C}_i + \bar{C}_i^T P_{2i} + Q_2 + Q_4 + \sum_j \pi_{ij} P_{2j}\right]\bar{y}(t) \\
& -(1-\alpha_\sigma)\bar{x}^T(t-\sigma(t))R_1\bar{x}(t-\sigma(t)) - (1-\alpha_\tau)\bar{y}^T(t-\tau(t))R_2\bar{y}(t-\tau(t)) \\
& + \bar{x}^T(t-\underline{\sigma})(R_1 - Q_1)\bar{x}(t-\underline{\sigma}) + \bar{y}^T(t-\underline{\tau})(R_2 - Q_2)\bar{y}(t-\underline{\tau}) \\
& - \bar{x}^T(t-\bar{d})Q_3\bar{x}(t-\bar{d}) - \bar{y}^T(t-\bar{d})Q_4\bar{y}(t-\bar{d}) \\
& - 2g^T(U\bar{y}(t-\tau(t)))\Lambda_i g(U\bar{y}(t-\tau(t))) + 2\bar{y}^T(t-\tau(t))U^T\Lambda_i K\, g(U\bar{y}(t-\tau(t))) \\
& + 2\bar{x}^T(t)P_{1i}\bar{B}_{1i}\bar{y}(t-\tau(t)) + 2\bar{x}^T(t)P_{1i}\bar{B}_{2i}g(U\bar{y}(t-\tau(t))) + 2\bar{y}^T(t)P_{2i}\bar{D}_i\bar{x}(t-\sigma(t)) \\
& + 2\bar{x}^T(t)P_{1i}\bar{A}_{di}\bar{x}(t-d(t)) + 2\bar{y}^T(t)P_{2i}\bar{C}_{di}\bar{y}(t-d(t)) \\
& - \left(\int_{t-\underline{\sigma}}^{t}\dot{\bar{x}}(\alpha)d\alpha\right)^T S_1\left(\int_{t-\underline{\sigma}}^{t}\dot{\bar{x}}(\alpha)d\alpha\right) - \left(\int_{t-\sigma(t)}^{t-\underline{\sigma}}\dot{\bar{x}}(\alpha)d\alpha\right)^T Z_1\left(\int_{t-\sigma(t)}^{t-\underline{\sigma}}\dot{\bar{x}}(\alpha)d\alpha\right) \\
& - \left(\int_{t-\underline{\tau}}^{t}\dot{\bar{y}}(\alpha)d\alpha\right)^T S_2\left(\int_{t-\underline{\tau}}^{t}\dot{\bar{y}}(\alpha)d\alpha\right) - \left(\int_{t-\tau(t)}^{t-\underline{\tau}}\dot{\bar{y}}(\alpha)d\alpha\right)^T Z_2\left(\int_{t-\tau(t)}^{t-\underline{\tau}}\dot{\bar{y}}(\alpha)d\alpha\right)
\end{aligned}
\tag{26}
$$

$$
\begin{aligned}
& - \left(\int_{t-\bar{d}}^{t-d(t)}\dot{\bar{x}}(\alpha)d\alpha\right)^T Z_3\left(\int_{t-\bar{d}}^{t-d(t)}\dot{\bar{x}}(\alpha)d\alpha\right) - \left(\int_{t-d(t)}^{t}\dot{\bar{x}}(\alpha)d\alpha\right)^T Z_3\left(\int_{t-d(t)}^{t}\dot{\bar{x}}(\alpha)d\alpha\right) \\
& - 2\left(\int_{t-\bar{d}}^{t-d(t)}\dot{\bar{y}}(\alpha)d\alpha\right)^T Z_4\left(\int_{t-d(t)}^{t}\dot{\bar{y}}(\alpha)d\alpha\right) - 2\left(\int_{t-\bar{d}}^{t-d(t)}\dot{\bar{x}}(\alpha)d\alpha\right)^T Z_3\left(\int_{t-d(t)}^{t}\dot{\bar{x}}(\alpha)d\alpha\right) \\
& - \left(\int_{t-\bar{d}}^{t-d(t)}\dot{\bar{y}}(\alpha)d\alpha\right)^T Z_4\left(\int_{t-\bar{d}}^{t-d(t)}\dot{\bar{y}}(\alpha)d\alpha\right) - \left(\int_{t-d(t)}^{t}\dot{\bar{y}}(\alpha)d\alpha\right)^T Z_4\left(\int_{t-d(t)}^{t}\dot{\bar{y}}(\alpha)d\alpha\right) \\
& + \dot{\bar{x}}^T(t)\left[\underline{\sigma}^2 S_1 + \bar{d}^2 Z_3 + (\bar{\sigma} - \underline{\sigma})^2 Z_1\right]\dot{\bar{x}}(t) + \dot{\bar{y}}^T(t)\left[\underline{\tau}^2 S_2 + \bar{d}^2 Z_4 + (\bar{\tau} - \underline{\tau})^2 Z_2\right]\dot{\bar{y}}(t)
\end{aligned}
$$

Define the vector $\xi(t)$ to be:

$$
\begin{aligned}
\xi^T(t) = & \Big[\bar{x}^T(t),\ \bar{y}^T(t),\ \bar{x}^T(t-\sigma(t)),\ \bar{y}^T(t-\tau(t)),\ \bar{x}^T(t-d(t)),\ \bar{y}^T(t-d(t)),\ \int_{t-\sigma(t)}^{t-\underline{\sigma}}\dot{\bar{x}}^T(\alpha)d\alpha,\ \int_{t-\tau(t)}^{t-\underline{\tau}}\dot{\bar{y}}^T(\alpha)d\alpha,\ \int_{t-d(t)}\dot{\bar{x}}^T(\alpha)d\alpha,\ \int_{t-d(t)}\dot{\bar{y}}^T(\alpha)d\alpha \\
& ,\ \bar{x}^T(t-\underline{\sigma}),\ \bar{y}^T(t-\underline{\tau}),\ \bar{x}^T(t-\bar{d}),\ \bar{y}^T(t-\bar{d}),\ \int_{t-\underline{\sigma}}\dot{\bar{x}}^T(\alpha)d\alpha,\ \int_{t-\underline{\tau}}\dot{\bar{y}}^T(\alpha)d\alpha,\ \int_{t-\bar{d}}^{t-d(t)}\dot{\bar{x}}^T(\alpha)d\alpha,\ \int_{t-\bar{d}}^{t-d(t)}\dot{\bar{y}}^T(\alpha)d\alpha,\ g^T(U\bar{y}(t-\tau(t)))\Big]
\end{aligned}
\tag{27}
$$

According to Newton-Leibniz formula we have:

$$
\begin{aligned}
& \int_{t-\sigma(t)}^{t-\underline{\sigma}}\dot{\bar{x}}(\alpha)d\alpha = \bar{x}(t-\underline{\sigma}) - \bar{x}(t-\sigma(t)), \quad \int_{t-\tau(t)}^{t-\underline{\tau}}\dot{\bar{y}}(\alpha)d\alpha = \bar{y}(t-\underline{\tau}) - \bar{y}(t-\tau(t)), \\
& \int_{t-\underline{\sigma}}^{t}\dot{\bar{x}}(\alpha)d\alpha = \bar{x}(t) - \bar{x}(t-\underline{\sigma}), \quad \int_{t-\underline{\tau}}^{t}\dot{\bar{y}}(\alpha)d\alpha = \bar{y}(t) - \bar{y}(t-\underline{\tau}), \\
& \int_{t-\bar{d}}^{t-d(t)}\dot{\bar{x}}(\alpha)d\alpha = \bar{x}(t-d(t)) - \bar{x}(t-\bar{d}), \quad \int_{t-\bar{d}}^{t-d(t)}\dot{\bar{y}}(\alpha)d\alpha = \bar{y}(t-d(t)) - \bar{y}(t-\bar{d}), \\
& \int_{t-d(t)}^{t}\dot{\bar{x}}(\alpha)d\alpha = \bar{x}(t) - \bar{x}(t-d(t)), \quad \int_{t-d(t)}^{t}\dot{\bar{y}}(\alpha)d\alpha = \bar{y}(t) - \bar{y}(t-d(t)).
\end{aligned}
\tag{27}
$$

In addition, there always exists the matrix $N_i$ with appropriate dimensions given in (17) so that in association with (27) we have: $N_i\xi(t)=0_{21n\times 21n}$ .Therefore, the complete derivative would be rewritten as:

$$\mathrm{A}V_i(t)=\mathrm{A}V_i(t)+\xi^T(t)\left(N_i+N_i^T\right)\xi(t)$$

On the other hand, we have:

$$\dot{\bar{x}}^T(t)W_{1i}\dot{\bar{x}}(t)=\xi^T(t)\begin{bmatrix}\bar{A}_i^T\\0_{4n}\\\bar{B}_{1i}^T\\\bar{A}_{di}^T\\0_{26n}\\\bar{B}_{2i}^T\end{bmatrix}W_{1i}\begin{bmatrix}\bar{A}_i^T\\0_{4n}\\\bar{B}_{1i}^T\\\bar{A}_{di}^T\\0_{26n}\\\bar{B}_{2i}^T\end{bmatrix}^T\xi(t),\quad \dot{\bar{y}}^T(t)W_{2i}\dot{\bar{y}}(t)=\xi^T(t)\begin{bmatrix}0_{2n}\\\bar{C}_i^T\\\bar{D}_i^T\\0_{4n}\\\bar{C}_{di}^T\\0_{25n}\end{bmatrix}W_{2i}\begin{bmatrix}0_{2n}\\\bar{C}_i^T\\\bar{D}_i^T\\0_{4n}\\\bar{C}_{di}^T\\0_{25n}\end{bmatrix}^T\xi \tag{28}$$

Now, by using Schur's complement it can be concluded that $\mathrm{A}V_i\left(\bar{x}(t),\bar{y}(t)\right)\le\xi^T(t)\Phi_i\xi(t)$. If $\Phi_i<0$ there will be some scalars $\delta_i>0$ such that:

$$\mathrm{A}V_i\left(\bar{x}(t),\bar{y}(t)\right)\le\xi^T(t)\Phi_i\xi(t)\le-\delta_i\ \xi^T(t)\xi(t),\quad\forall i\in S \tag{29}$$

A choice for $\delta_i$ could be $\delta_i=\lambda_{\min}(-\Phi_i)$. So, taking expectation from (29)we have:

$$\mathrm{E}\left(\mathrm{A}V_i\left(\bar{x}(t),\bar{y}(t)\right)\right)<-\lambda_{\min}(-\Phi_i)\mathrm{E}\left(\xi^T(t)\xi(t)\right)\le-\lambda_{\min}(-\Phi_i)\mathrm{E}\left(\left\|\bar{x}(t)\right\|^2+\left\|\bar{y}(t)\right\|^2\right),\forall i\in S \tag{30}$$

The rest of the proof is straightforward using Dynkin's formula and the Lyapunov stochastic stability theory. (See [31]).

For the disturbance attenuation purpose, the function $J_T$ is defined as follows:

$$J_T=E\left(\int_0^T\left(\tilde{x}^T(t)\tilde{x}(t)+\tilde{y}^T(t)\tilde{y}(t)-\gamma^2\omega^T(t)\omega(t)\right)dt\right) \tag{31}$$

and so the disturbance attenuation condition in *definition2* is expressed as $J_\infty<V\left(\bar{x}_0,\bar{y}_0,r_0\right)$. The term $J_T$ can be rewritten in the following form:

$$J_T=E\left(\int_0^T\left(\tilde{x}^T(t)\tilde{x}(t)+\tilde{y}^T(t)\tilde{y}(t)-\gamma^2\omega^T(t)\omega(t)+\mathrm{A}V\right)dt-E\left(\int_0^T\mathrm{A}Vdt\right)\right. \tag{32}$$

and by using Dynkin's formula:

$$J_T = E\left(\int_0^T \left(\tilde{x}^T(t)\tilde{x}(t) + \tilde{y}^T(t)\tilde{y}(t) - \gamma^2\omega^T(t)\omega(t) + \mathrm{A}V\right)dt\right) - E\left(V\left(\bar{x}(T),\bar{y}(T),i\right)\right) + V\left(\bar{x}_0,\bar{y}_0,r_0\right) \quad (33)$$

Now that the conditions for stochastic stability of the mixed GRN-estimator system are obtained, we are in a position to give the main result on the design of the state estimator for the GRN system in (2). The following theorem gives the results on stochastic stability and $\gamma$ disturbance attenuation of GRN/Estimator system.

**Theorem 2**: System (11) is a state estimator with the disturbance attenuation level of $\gamma$ for Markovian GRN system (2) if there exist symmetric and positive definite matrices $P_{11i}, P_{13i}, P_{21i}, P_{23i}, R_1, R_2, Z_1, Z_2, Q_1, Q_2, S_1, S_2, \Lambda_i = diag(\lambda_{1i},...,\lambda_{ni})$, matrices $M_{1i}$, $M_{2i}$, $X_{ji}$ ($j = 1,...,10$), scalars $\varepsilon_k > 0$ ($k = 1,...,4$) and $\mu_{1i}$, $\mu_{2i}$ ($i \in S$) satisfying the following LMIs:

$$\Psi_i = \begin{bmatrix} \tilde{J}_i & 0 & 0 & 0 & 0 & 0 & \Upsilon_{\lambda i} & P_{1i}\tilde{F}_{1i} & \tilde{\Upsilon}_{W1i} & \tilde{\Upsilon}_{W2i} \\ * & \Theta_i & 0 & 0 & 0 & 0 & 0 & P_{2i}\tilde{F}_{2i} & 0 & 0 \\ * & * & -Z_3 & -Z_3 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & -Z_3 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & -Z_4 & -Z_4 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & -Z_4 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & * & -2\Lambda_i & 0 & 0 & 0 \\ * & * & * & * & * & * & * & -\gamma^2 I & \bar{B}_{2i}^T P_{1i} & 0 \\ * & * & * & * & * & * & * & * & \Xi_i & 0 \\ * & * & * & * & * & * & * & * & * & \Delta_i \end{bmatrix} + \tilde{N}_i + \tilde{N}_i^T < 0, \quad (34)$$

in which

$$\Theta_i = diag\left(-Z_1,-Z_2,R_1-Q_1,R_2-Q_2,-Q_3,-Q_4,-S_1,-S_2\right),$$

$$T_{1i} = \begin{pmatrix} P_{11i}A_i & 0 \\ 0 & P_{13i}A_i - M_{1i}H_{1i} \end{pmatrix}, \; T_{2i} = \begin{pmatrix} P_{21i}C_i & 0 \\ 0 & P_{23i}C_i - M_{2i}H_{2i} \end{pmatrix},$$

$$\tilde{J}_{xi} = T_{1i} + T_{1i}^T + Q_1 + \sum_j \pi_{ij}P_{1j} + \begin{bmatrix}0 & \mathrm{I}\end{bmatrix}^T\begin{bmatrix}0 & \mathrm{I}\end{bmatrix}, \quad \tilde{J}_{yi} = T_{2i} + T_{2i}^T + Q_2 + \sum_j \pi_{ij}P_{2j} + \begin{bmatrix}0 & \mathrm{I}\end{bmatrix}^T\begin{bmatrix}0 & \mathrm{I}\end{bmatrix},$$

$$W_{1i} = \underline{\sigma}^2 S_1 + \bar{d}^2 Z_3 + \left(\bar{\sigma}-\underline{\sigma}\right)^2 Z_1, \quad W_{2i} = \underline{\tau}^2 S_2 + \bar{d}^2 Z_4 + \left(\bar{\tau}-\underline{\tau}\right)^2 Z_2,$$

$$\Xi_i = \mu_{1i}\left(-2P_{1i} + \mu_{1i}W_{1i}\right), \qquad \Delta_i = \mu_{2i}\left(-2P_{2i} + \mu_{2i}W_{2i}\right),$$

$$\tilde{J}_i = \begin{bmatrix} \tilde{J}_{xi} & 0 & 0 & P_{1i}\bar{B}_{1i} & P_{1i}\bar{A}_{di} & 0 \\ * & \tilde{J}_{yi} & P_{2i}\bar{D}_i & 0 & 0 & P_{2i}\bar{C}_{di} \\ * & * & -(1-\alpha_\sigma)R_1 & 0 & 0 & 0 \\ * & * & * & -(1-\alpha_\tau)R_2 & 0 & 0 \\ * & * & * & * & 0 & 0 \\ * & * & * & * & * & 0 \end{bmatrix}.$$

And

$$\Upsilon_{\lambda_i} = \begin{bmatrix} \left(P_{1i}\bar{B}_{2i}\right)^T & 0 & 0 & \left(U^T \Lambda_i K\right)^T & 0 & 0 \end{bmatrix}^T, \tilde{\Upsilon}_{W_{1i}} = \begin{bmatrix} T_{1i} & 0 & 0 & \left(\bar{B}_{1i}^T P_{1i}\right)^T & 0 & 0 \end{bmatrix}^T,$$
$$\tilde{\Upsilon}_{W_{2i}} = \begin{bmatrix} 0 & T_{2i} & \left(\bar{D}_i^T P_{2i}\right)^T & 0 & 0 & 0 \end{bmatrix}^T, \tilde{N}_i = \begin{pmatrix} N_i & 0 \\ 0 & 0 \end{pmatrix}, \tag{35}$$

The estimator gains then are obtained from:

$$K_{1i} = P_{13i}^{-1} M_{1i}, K_{2i} = P_{23i}^{-1} M_{2i}. \tag{36}$$

*Proof*: It is easy to show by direct calculation that

$$\tilde{x}^T(t)\tilde{x}(t) + \tilde{y}^T(t)\tilde{y}(t) - \gamma^2 \omega^T(t)\omega(t) + \mathrm{A}V \le \bar{x}^T(t)\begin{bmatrix} 0 & 0 \\ 0 & I \end{bmatrix}\bar{x}(t) + \bar{y}^T(t)\begin{bmatrix} 0 & 0 \\ 0 & I \end{bmatrix}\bar{y}(t)$$
$$-\gamma^2 \omega^T(t)\omega(t) + \xi(t)^T \Theta_i \xi(t) + 2\bar{x}^T P_{1i}\bar{F}_{1i}\omega(t) + 2\bar{y}^T P_{2i}\bar{F}_{2i}\omega(t) + \bar{\sigma}\dot{x}(t)^T W_{1i}\dot{x}(t) + \bar{\tau}\dot{y}(t)^T W_{2i}\dot{y}(t) \tag{37}$$

where $\Theta_i$ is obtained with eliminating the last *4n* rows and columns of $\Phi_i$. Defining $\eta(t) = \begin{bmatrix} \xi^T(t) & \omega^T(t) \end{bmatrix}^T$ and following the same steps as we did in proof of theorem1, we have:

$$\tilde{x}^T(t)\tilde{x}(t) + \tilde{y}^T(t)\tilde{y}(t) - \gamma^2 \omega^T(t)\omega(t) + \mathrm{A}V \le \eta^T(t)\hat{\Psi}_{1i}\eta(t) \tag{38}$$

where

$$\hat{\Psi}_{1i} = \begin{bmatrix} J_i & 0 & 0 & 0 & 0 & 0 & \Upsilon_{\lambda i} & P_{1i}\tilde{F}_{1i} & \hat{\Upsilon}_{W1i} & \hat{\Upsilon}_{W2i} \\ * & \Theta_i & 0 & 0 & 0 & 0 & 0 & P_{2i}\tilde{F}_{2i} & 0 & 0 \\ * & * & -Z_3 & -Z_3 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & -Z_3 & 0 & 0 & 0 & 0 & 0 & 0 \\ * & * & * & * & -Z_4 & -Z_4 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & -Z_4 & 0 & 0 & 0 & 0 \\ * & * & * & * & * & * & -2\Lambda_i & 0 & 0 & 0 \\ * & * & * & * & * & * & * & -\gamma^2 I & \bar{B}_{2i}^T & 0 \\ * & * & * & * & * & * & * & * & -W_{1i}^{-1} & 0 \\ * & * & * & * & * & * & * & * & * & -W_{2i}^{-1} \end{bmatrix} + \tilde{N}_i + \tilde{N}_i^T < 0, \tag{39}$$

and

$$\hat{\Upsilon}_{W_{1i}} = \begin{bmatrix} \bar{A}_i & 0 & 0 & \bar{B}_{1i} & 0 & 0 \end{bmatrix}^T, \hat{\Upsilon}_{W_{2i}} = \begin{bmatrix} 0 & \bar{C}_i & \bar{D}_i & 0 & 0 & 0 \end{bmatrix}^T, \tag{40}$$

Define $T_{1i}$ and $T_{2i}$ by:

$$T_{1i}=P_{1i}\bar{A}_i=\begin{pmatrix}P_{11i} & 0\\ 0 & P_{13i}\end{pmatrix}\begin{pmatrix}A_i & 0\\ 0 & A_i-K_{1i}H_{1i}\end{pmatrix}=\begin{pmatrix}P_{11i}A_i & 0\\ 0 & P_{13i}A_i-M_{1i}H_{1i}\end{pmatrix},$$
$$T_{2i}=P_{2i}\bar{C}_i=\begin{pmatrix}P_{21i} & 0\\ 0 & P_{23i}\end{pmatrix}\begin{pmatrix}C_i & 0\\ 0 & C_i-K_{2i}H_{2i}\end{pmatrix}=\begin{pmatrix}P_{21i}C_i & 0\\ 0 & P_{23i}C_i-M_{2i}H_{2i}\end{pmatrix} \tag{41}$$

Where

$$M_{1i}=P_{13i}K_{1i}\ ,\ M_{2i}=P_{23i}K_{2i} \tag{42}$$

Now, pre and post multiply (39) by

$$V_i=diag(I_{2n\times 2n},...,I_{2n\times 2n},I_{1\times 1},P_{1i},P_{2i})$$

Finally, according to the inequalities

$$-P_{1i}^TW_{1i}^{-1}P_{1i}\le\mu_{1i}\left(-2P_{1i}+\mu_{1i}W_{1i}\right),\quad -P_{2i}^TW_{2i}^{-1}P_{2i}\le\mu_{2i}\left(-2P_{2i}+\mu_{2i}W_{2i}\right) \tag{43}$$

which are true for some constant values of $\mu_{1i}$ and $\mu_{2i}$ we can get (34). Also it requires that $\widehat{\Psi}_{1i}<0$. Then, by (38) we get:

$$J_T<V\left(\bar{x}_0,\bar{y}_0,r_0\right) \tag{44}$$

So theorem 2 guarantees the $\gamma$ disturbance attenuation for the state estimator.

## 4. Simulation Results

In this section, we examine our results to show the effectiveness of our method. As the first example, consider a Markovian jump GRN system like (2) with two operating modes and the following parameters:

$$A_1=\begin{bmatrix}-2 & 0\\ 0 & -2\end{bmatrix}, C_1=\begin{bmatrix}-2 & 0\\ 0 & -2\end{bmatrix}, B_1=\begin{bmatrix}1 & -2\\ 0.8 & 0\end{bmatrix},\ D_1=\begin{bmatrix}1 & 0\\ 0 & 1\end{bmatrix},$$
$$A_2=\begin{bmatrix}-3 & 0\\ 0 & -3\end{bmatrix}, C_2=\begin{bmatrix}-2 & 0\\ 0 & -2\end{bmatrix}, B_2=\begin{bmatrix}-1 & 0\\ 1 & 2\end{bmatrix},\quad D_2=\begin{bmatrix}-1 & 0\\ 0 & 1\end{bmatrix}$$

And

$$H_{11}=\begin{bmatrix}0.6 & 0.9\end{bmatrix},\ H_{12}=\begin{bmatrix}0.1 & 0.4\end{bmatrix},\ H_{21}=\begin{bmatrix}1 & 0.2\end{bmatrix},\ H_{22}=\begin{bmatrix}0.4 & 1.2\end{bmatrix}$$
$$F_{11}=\begin{bmatrix}0.4\\ 0.4\end{bmatrix},\ F_{12}=\begin{bmatrix}0.2\\ 0.2\end{bmatrix},\quad F_{21}=\begin{bmatrix}0.3\\ 0.3\end{bmatrix},\quad F_{22}=\begin{bmatrix}0.2\\ 0.2\end{bmatrix}$$

The regulation function is assumed to be $g(x)=\frac{x^2}{1+x^2}$. It can be easily understood that that $k=3\sqrt{3}/8$ .The transition probability rates are:

$$\Pi=\begin{bmatrix}-3 & 3\\ 1 & -1\end{bmatrix}$$

Also we take the delay derivatives equal to $\alpha_\sigma=0.4$, $\alpha_\tau=0.5$. For a given $\gamma=0.3$, by using MATLAB to solve the inequality (34) , the estimator gains for $\underline{\sigma}=\underline{\tau}=0.1$, $\bar{\sigma}=\bar{\tau}=0.8$ and the upper limit of sample time $\bar{d}=0.5$ will be as follows:

$$K_{11}=\begin{bmatrix}0.6844\\ 0.3132\end{bmatrix},K_{12}=\begin{bmatrix}0.1482\\ -0.1522\end{bmatrix},K_{21}=\begin{bmatrix}0.4144\\ 0.2525\end{bmatrix},K_{22}=\begin{bmatrix}0.2639\\ 0.1865\end{bmatrix}. \tag{45}$$

The system mode variation and the trajectories of $x_i(t), y_i(t), \hat{x}_i(t), \hat{y}_i(t)$, $(i=1,2)$ are shown in Figures 1, 2. It is clear that the estimated values by the proposed state estimator effectively converge to the the real values of mRNA/protein in an acceptable time. The disturbance input is taken to be $\omega(t)=0.3+0.3\sin(t)$. It can be noticed that with the pass of time, the error tends to zero. Therefore, the GRN-estimator system is stochastically stable in presence of disturbances. By LMIs, the minimum disturbance attenuation ratio is obtained to be 0.3. The disturbance attenuation ratio which is defined as:

$$\gamma(t)=\sqrt{\frac{\int_0^t \tilde{x}^T(t)\tilde{x}(t)+\tilde{y}^T(t)\tilde{y}(t)dt}{\int_0^t \omega^T(t)\omega(t)dt}} \tag{46}$$

is shown in Figure 3. It is obvious from Figure 3 that the disturbance attenuation ratio is always under 0.3 and the effectiveness of theorem 3 is proved.

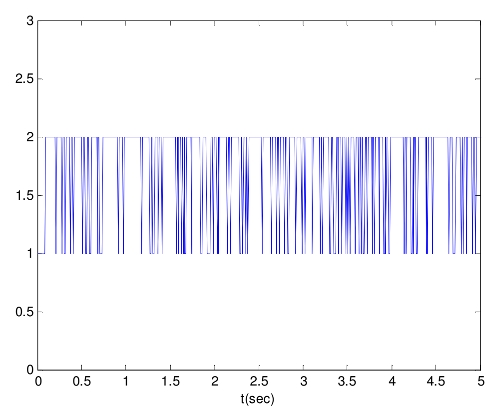


Figure 1: The variation of system mode

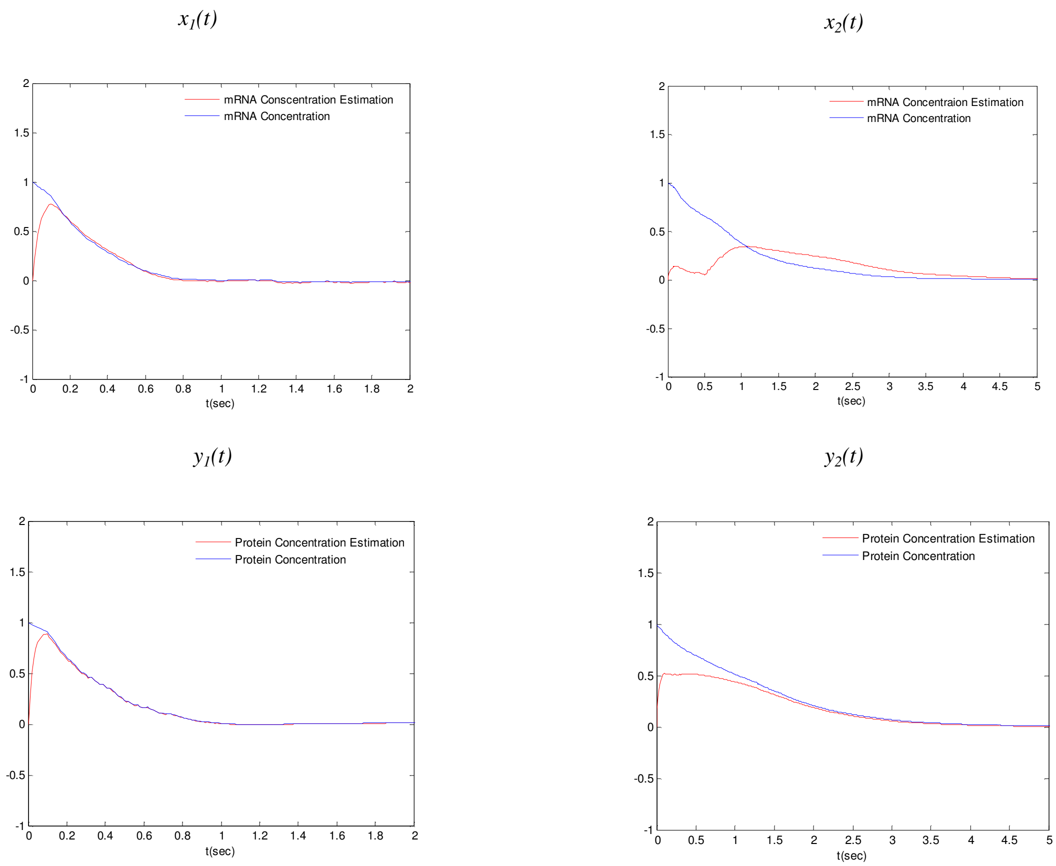


Figure 2: The real and estimated values of mRNA and Protein

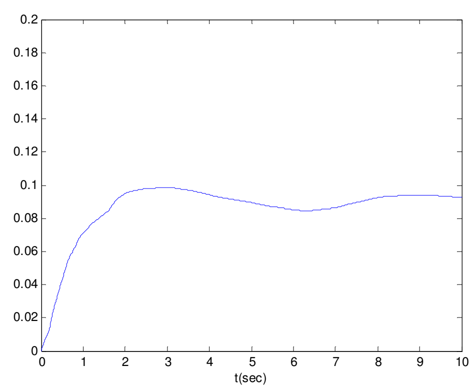


Figure 3: The disturbance attenuation ratio

## 5. CONCLUSION

State estimation with disturbance attenuation for Markovian jump gene regulatory networks including sampled outputs was considered. The sampled-data GRN system is transformed to an augmented GRN/estimator system with time-varying delays. The LMI conditions for both stochastic stability and disturbance attenuation on a certain level were developed using Lyapunov-Krasovskii functionals. Synthesizing appropriate state estimator gains via some effective LMI derivation results in the desired tracking of protein and mRNA concentrations. The simulations show that it is useful to estimate the states of these types of GRNs in presence of disturbances and parameter uncertainties which are common in cell's environment.

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