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High-Gain Estimation of mRNA and Protein Concentrations of a Genetic Regulatory Network

D. BOUHADJRA\textsuperscript{1,2}, A. ALESSANDRI\textsuperscript{1}, P. BAGNERINI\textsuperscript{1}, A. ZEMOUCHE\textsuperscript{2}

Abstract—In this paper, we investigate the problem of state estimation for a simple one-gene regulation dynamic process involving end-product activation to rebuild the non-measured concentrations of mRNA and the involved protein. We synthesize a convenient observer structure following the high-gain methodology by combining the observer proposed in [1] based on the system state augmentation approach and the HG/LMI technique presented in [2]. The proposed design reduces significantly the value of the tuning parameter and the observer gain along with improving its sensitivity to disturbances and measurement noise. The results are compared with the standard high-gain observer to evaluate the effectiveness of the proposed design.

Index Terms—Genetic regulatory network, Robust state estimation, high-gain methodology, Lipschitz systems.

I. INTRODUCTION

During gene expression, an enormous number of genes and proteins are either directly or indirectly interrelated with one another in living cells. The mechanisms which have progressed to control the expression of genes are known as gene regulatory networks (GRNs). GRNs describe gene expression as a function of regulatory inputs specified by the interactions between proteins and genes, that is, one gene can control another gene’s expression through its product proteins called Transcriptional Factors [3].

For the purpose of gene identification and medical diagnosis or treatment, biologists and biomedical scientists are interested in knowing the exact states of GRNs [4]. However, due to unavoidable complications such as transcription or translation delays and extrinsic/intrinsic noises, the available measurement outputs of GRNs might be different from their true states. As such, the state estimation or filtering problem for GRNs has become an important topic of research that has attracted many from the scientific community [5], [6], [4], [7], [8] and [9]. To the best of authors’ knowledge, only few works have been reported in literature regarding the robust state estimation issue for GRNs. Taking this into account, we propose in this paper a robust observer that retains all the characteristics of the popular standard high-gain observers and provides additional robustness to measurements noise which can result in a significant improvement of the monitoring performances of the genetic regulation process.

In high-gain observers design methodology, the error trajectory has an exponential decay rate that can be imposed arbitrarily fast by acting on a design parameter, appearing in the observer structure, typically known as “high-gain parameter”. Such observers are widely used in control contexts where fast observation is useful in order to prevent finite escape time of the closed-loop system. It was first introduced in [10], [11], and since then it has attracted the attention of several researchers and a huge number of papers have been published on the topic (see for instance the survey [12] and references therein). Despite all the research activities about high-gain observer in output feedback control, this direction still remains active due to some open problems related to its sensitivity to output measurement noise because of the value of the tuning parameter which may be huge for higher dimensional systems having nonlinearities with large Lipschitz constants. Indeed, the higher the gain, the larger the peaking in the transient, which may cause the destabilization of the control loop if the high-gain observer is used in cascade with a feedback regulator. To reduce the peaking, various solutions have been proposed in the literature and for an overview we refer the reader to [13], [14], [15], [16], [17], [18], [19] and the references therein.

In this work we investigate a new strategy for high-gain observer design. The proposed technique is based on a combination of the observer proposed in [1] which is based on system state augmentation approach and the HG/LMI observer developed in [2]. This new design technique provides a new threshold on the observer parameter $\theta$ that guarantees exponential convergence of the estimation error and reduces the value of the observer gain. The applicability and performance of the observer is explored through a simple genetic regulatory network with a comparison to the standard high-gain observer to clearly show the superiority of the proposed technique.

II. MATHEMATICAL MODELING OF GENETIC REGULATION PROCESS

There are different classes of genetic regulatory models, namely, thermodynamic, Boolean, Bayesian and differential equation-based models. In differential equation based-models, the regulatory networks can be modeled by differential equations, in which a set of molecules such as mRNAs and proteins interact by explicit rules defined in terms of rate equations. The concentrations of mRNAs, proteins and other elements of the system are are represented by time-dependent variables with values contained in the set of non-negative real numbers. Regulatory interactions take the form of functional and differential relations between the concentration variables. More specifically, gene regulation is modeled by reaction-
rate equations expressing the rate of elements of the system in the following form:

\[
\frac{dx_i}{dt} = f_i(x), \quad x_i \geq 0, \quad 1 \leq i \leq n,
\]

where \( x \) is the vector of concentrations of proteins, mRNAs, or small metabolites, and \( f_i \) a usually nonlinear function. Then, by specifying the function \( f \) we get equations of the form [20]:

\[
\begin{align*}
\frac{dx_1}{dt} &= \kappa_{1n} H(x_n) - \gamma_1 x_1, \quad x_1 \geq 0, \\
\frac{dx_i}{dt} &= \kappa_{i,i-1} x_{i-1} - \gamma_i x_i, \quad x_i \geq 0, \quad 1 \leq i \leq n
\end{align*}
\]

The parameters \( \kappa_{1n}, \kappa_{2n}, \ldots, \kappa_{n,n-1} \) are all strictly positive and represent production constants and \( \gamma_1, \ldots, \gamma_n \) represent degradation constants and are also strictly positive. The reaction-rate equations express a balance between the number of molecules appearing and disappearing per unit time. In the case of \( x_1 \), the production term involves a nonlinear regulation function \( H : \mathbb{R} \rightarrow \mathbb{R} \) ranging from 0 to 1. In common use, the function \( H \) is given as

\[
H^+(x_j, \theta_{ij}, m) = \frac{x_j^n}{x_j^n + \alpha_{ij}^m},
\]

\[
H^-(x_j, \theta_{ij}, m) = 1 - \frac{x_j^n}{x_j^n + \alpha_{ij}^m},
\]

corresponding to the activation and inhibition cases, respectively. The parameter \( \alpha \) gives the threshold for the regulatory influence of the concentration of the metabolite on the target gene, whereas the steepness parameter \( m \) is a measure of the collective effect of groups of metabolite molecules defining the shape of the Hill curve.

A. Simple gene regulation process

A simple example of a kinetic model for the genetic regulation process is given in Figure 1, going back to the work by Goodwin [21] and [22]. The end-product of a metabolic pathway co-inhibits the expression of a gene coding for an enzyme that catalyzes a reaction step in the pathway. This gives rise to a negative feedback loop involving mRNA concentration \( x_1 \), the protein concentration \( x_2 \), and the metabolic concentration \( x_3 \).

Let \( x_1, x_2 \) and \( x_3 \) be the concentrations of the messenger RNA (mRNA) \( a \), protein \( A \) and metabolite \( K \), respectively. Then, the corresponding Tyson’s model [20] is written under the form:

\[
\Gamma_{biology} : \begin{cases} 
\dot{x}_1 = \kappa_1 H(x_3) - \gamma_1 x_1 \\
\dot{x}_2 = \kappa_2 x_1 - \gamma_2 x_2 \\
\dot{x}_3 = \kappa_3 x_2 - \gamma_3 x_3 \\
y = x_3
\end{cases}
\]

where \( H \) is the nonlinear regulation function ranging from 0 to 1. \( \kappa_1, \kappa_2 \) and \( \kappa_3 \) are production constants, \( \gamma_1, \gamma_2 \) and \( \gamma_3 \) degradation constants, and \( H \) the nonlinear regulation function.

System (3) is considered to be a good model for the simplest type of allosteric regulation in biochemistry, i.e., the inhibition or activation of an enzyme or protein by a small regulatory molecule that interacts with the enzyme at a site (allosteric site) other than the active site at which catalytic activity occurs.

III. BACKGROUND RESULTS ON HIGH-GAIN OBSERVER

In this section we introduce some background results on high-gain observer which will be essential in the development of the proposed technique.

A. Standard high-gain observer

Here, we recall the basic high-gain observer as in [23]. We will consider the class of nonlinear systems in triangular form described by the following set of equations:

\[
\dot{x} = \begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \vdots \\ \dot{x}_{n-1} \\ \dot{x}_n \end{bmatrix} = \begin{bmatrix} x_2 \\ x_3 \\ \vdots \\ x_n \\ f(x) \end{bmatrix},
\]

\[
y = x_1
\]

where \( f : \mathbb{R}^n \rightarrow \mathbb{R} \) is a nonlinear function satisfying the Lipschitz property:

\[
\left| f(x_1 + \Delta_1, \ldots, x_n + \Delta_n) - f(x_1, \ldots, x_n) \right| \leq \gamma_f \sum_{j=1}^{n} |\Delta_j|. \tag{5}
\]

In a condensed form, system (4) can be rewritten as follows:

\[
\begin{cases}
\dot{x} = Ax + Bf(x) \\
y =Cx
\end{cases}
\]

where

\[
B = \begin{bmatrix} 0 & \ldots & 0 \end{bmatrix}^T, \quad C = \begin{bmatrix} 1 & 0 & \ldots & 0 \end{bmatrix}
\]

Fig. 1: An example of a genetic regulatory system involving end-product inhibition. A and C represent proteins, F and K metabolites.
and the state matrix $A$ is defined by
\[(A)_{i,j} = \begin{cases} 1 & \text{if } j = i + 1 \\ 0 & \text{if } j \neq i + 1 \end{cases}.\] (8)

Consider the following Luenberger observer:
\[\dot{\hat{x}} = A\hat{x} + Bf(\hat{x}) + L(y - C\hat{x}).\] (9)

The dynamics of the estimation error $\hat{x} = x - \hat{x}$ is then given by:
\[\dot{\hat{x}} = (A - LC)\hat{x} + B[f(x) - f(\hat{x})].\] (10)

In the high-gain methodology, we write the observer gain $L$ under the form:
\[L := T(\theta)K, \quad \theta \geq 1.\] (11)

where
\[T(\theta) := \text{diag}(\theta, \ldots, \theta^n)\] and $K \in \mathbb{R}^{n \times p}$.

In addition, the high-gain methodology focuses on the transformed estimation error
\[\hat{x} := T^{-1}(\theta)\hat{x},\] (12)

where $T^{-1}(\theta)$ is the inverse of $T(\theta)$ given by
\[T^{-1}(\theta) = \text{diag}(\frac{1}{\theta}, \ldots, \frac{1}{\theta^n}).\]

It is well-known that the dynamics of the error $\hat{x}$ is given by
\[\dot{\hat{x}} = \theta(A - KC)\hat{x} + \frac{1}{\theta^n}B\Delta f,\] (13)

with
\[\Delta f := f(x) - f(x - T(\theta)\hat{x}).\]

From the Lipschitz condition \[5\] and the fact that $\theta \geq 1$, we can show as in \[17\] that there always exists a positive scalar constant $k_f$, independent from $\theta$, such that
\[\|T^{-1}(\theta)B\Delta f\| \leq k_f\|\hat{x}\|.\] (14)

then, the following theorem is derived,

**Theorem 1 (\[23\]):** If there exist $P > 0$, $\lambda > 0$, $Y$, and $\theta \geq 1$ such that
\[A^TP + PA - CTY - YT^C + \lambda I < 0,\] (15)

\[\theta > \theta_0 = \frac{2k_f\lambda_{\text{max}}(P)}{\lambda},\] (16)

then the estimation error $\hat{x}$ is exponentially stable with
\[K = P^{-1}YT,\]

where $\lambda_{\text{max}}(P)$ is the largest eigenvalue of the matrix $P$.

**Proof:** For more details about the proof of this theorem, we refer the reader to \[23\], \[17\], \[18\].

---

**B. HG/LMI based observer**

This technique follows the standard high-gain methodology with the same state observer structure of dimension $n$. However, by exploiting the LPV/LMI technique developed in \[24\], the values of tuning parameter and observer gain are decreased. Indeed, by introducing a "compromise index" $j_0$, with $0 \leq j_0 \leq n$, the power of the proposed high-gain is limited to $j_0$ with $2j_0$ LMIs to solve instead of one single LMI as in standard high-gain observer. Lemma \[4\] introduced in the following is crucial for the HG/LMI observer design.

**Lemma 1 (\[24\]):** Consider a function $\Psi : \mathbb{R}^n \rightarrow \mathbb{R}^n$, then, the two following items are equivalent:

- $\Psi$ is $\gamma_f$-Lipschitz with respect to its argument, i.e.:
\[\|\Psi(X) - \Psi(Z)\| \leq \gamma_f\|X - Y\|, \quad \forall X, Z \in \mathbb{R}^n;\] (17)

- for all $i, j = 1, \ldots, n$, there exist functions
\[\psi_{ij} : \mathbb{R}^n \times \mathbb{R}^n \rightarrow \mathbb{R}\]

and constants $\gamma_{\psi_{ij}} \leq 0$, $\bar{\gamma}_{\psi_{ij}} \geq 0$, so that $\forall X, Z \in \mathbb{R}^n$,
\[\Psi(X) - \Psi(Z) = \sum_{i=1}^{n} \sum_{j=1}^{n} \psi_{ij} H_{ij} (X - Z),\] (18)

and
\[\gamma_f \leq \gamma_{\psi_{ij}} \leq \bar{\gamma}_{\psi_{ij}} \leq \gamma_f.\] (19)

and
\[\gamma_j : \mathbb{R}^n \times \mathbb{R}^n \rightarrow \mathbb{R}\]

and constants $\gamma_{\gamma_{ij}}$ and $\bar{\gamma}_{\gamma_{ij}}$, so that
\[f(x) - f(\hat{x}) = \left[\sum_{j=1}^{n} \psi_j e_n^T(j)\right] \hat{x},\] (20)

and
\[\gamma_{\gamma_{ij}} \leq \psi_j \leq \bar{\gamma}_{\gamma_{ij}}.\] (21)

where
\[\psi_j \triangleq \psi_j (x_{\hat{x}}^{j-1}, x_{\hat{x}}^{j}).\]

is defined as in Lemma \[4\]. For the sake of brevity, we use only $\psi_j$ instead of $\psi_j (x_{\hat{x}}^{j-1}, x_{\hat{x}}^{j})$.

Following (20), $\Delta f$ in (13) can be written under the following form
\[\Delta f = \sum_{j=1}^{n-j_0} \psi_j \hat{x}_j + \sum_{j=1}^{j_0} \psi_k(j) \hat{x}_k(j),\] (22)

where
\[k(j) = n - (j_0 - j),\]

$0 \leq j_0 \leq n$.
Hence, the error dynamics (13) is rewritten as follows:

\[
\dot{\tilde{x}} = \theta \left( A(\Psi^\theta) - KC \right) \tilde{x} + \frac{1}{\theta^n} B \Delta f_1, \tag{23}
\]

where

\[
\mathcal{A}(\Psi^\theta) = A + B \sum_{j=1}^{j_0} \psi_j^\theta \bar{e}_n^T (k(j)), \tag{24}
\]

\[
\Psi^\theta = \begin{pmatrix}
\psi_1^\theta \\
\vdots \\
\psi_{j_0}^\theta
\end{pmatrix} \in \mathbb{R}^{j_0},
\tag{25}
\]

\[
\psi_j^\theta = \frac{\psi_{k(j)}^\theta}{\bar{e}^{T}(j_0-j)}. \tag{26}
\]

Let us define the convex bounded set

\[
\mathcal{H}_{j_0}^\sigma = \left\{ \Phi \in \mathbb{R}^{j_0} : \frac{\bar{\gamma}_{\tau(j)}(\sigma)}{\sigma^{1+(j_0-j)}} \leq \Phi_j \leq \frac{\bar{\gamma}_{\tau(j)}(\sigma)}{\sigma^{1+(j_0-j)}} \right\} \tag{27}
\]

for which the set of vertices is defined by

\[
\mathcal{V}_{\mathcal{H}_{j_0}^\sigma} = \left\{ \Phi \in \mathbb{R}^{j_0} : \Phi_j \in \left( \frac{\bar{\gamma}_{\tau(j)}(\sigma)}{\sigma^{1+(j_0-j)}}, \frac{\bar{\gamma}_{\tau(j)}(\sigma)}{\sigma^{1+(j_0-j)}} \right) \right\}. \tag{28}
\]

Since \( \bar{\gamma}_{\tau(j)} \geq 0 \) and \( \bar{\gamma}_{\tau(j)} \leq 0 \), then it is obvious that for two positive scalars \( \sigma_1, \sigma_2 \), we have the following implication

\[
\sigma_1 < \sigma_2 \implies \mathcal{H}_{j_0}^{\sigma_1} \supset \mathcal{H}_{j_0}^{\sigma_2}. \tag{29}
\]

Moreover,

\[
\lim_{\sigma \to +\infty} \left( \mathcal{H}_{j_0}^\sigma \right) = \left\{ 0 \in \mathbb{R}^{j_0} \right\}. \tag{30}
\]

On the other hand, we can show that there exists a positive real number \( k_{j_0} \leq k_f \) such that \( \Delta f_1 \) satisfies

\[
\| T^{-1}(\theta) B \Delta f_1 \| \leq \frac{k_{j_0}}{\theta^{k_{j_0}}} \| \bar{e} \|. \tag{31}
\]

Hence, the following theorem is obtained.

**Theorem 2 (\cite{2}):** If there exist \( P > 0, \lambda > 0, Y, \) and \( \sigma > 0 \) such that

\[
\mathcal{A}(\Psi^\sigma)^T P + P \mathcal{A}(\Psi^\sigma) - C^T Y - Y^T C + \lambda \Psi^\sigma \in \mathcal{V}_{\mathcal{H}_{j_0}^\sigma}, \tag{32}
\]

\[
\theta > \theta_{j_0}^{\frac{1}{1+\sigma}} = \frac{2k_{j_0} \lambda \max(P)}{\lambda}, \tag{33}
\]

then the estimation error \( \tilde{x} \) is exponentially stable with

\[
L = T(\theta) P^{-1} Y^T, \quad \theta \geq \max \left( \sigma, \theta_{j_0}^{\frac{1}{1+\sigma}} \right). \tag{34}
\]

**Proof:** For the proof, we refer the reader to [2].

**IV. IMPROVED HIGH-GAIN OBSERVER**

In this section we propose a new high-gain observer strategy which follows the popular standard high-gain methodology presented in the previous section by exploiting the HG/LMI technique developed in [2] and system state augmentation approach provided in [1].

Our key idea lies on the following assumption. If the nonlinear function \( f(.) \) in (6) satisfies the condition

\[
\frac{\partial f}{\partial x_j}(x) \equiv 0, \forall j > n - j_s \tag{34}
\]

for a given \( j_s \geq 0 \), then the Lipschitz inequality (14) becomes

\[
\| T^{-1}(\theta) B \Delta f \| \leq \frac{k_f}{\theta^{j_s}} \| \dot{\tilde{x}} \|. \tag{35}
\]

It follows that the high-gain inequality (16) becomes

\[
\theta > \left( \frac{2k_f \lambda \max(P)}{\lambda} \right)^{1+\frac{1}{\theta}} = \theta_0^{\frac{1}{1+\theta}}. \tag{36}
\]

This new threshold on \( \theta \) is significantly reduced due to the power \( \frac{1}{1+\theta} \). Indeed, instead of \( T(\theta) \theta^{-\theta} \). Therefore, the aim of this work is to transform the original system of dimension \( n \) into a system of dimension \( n + j_s \), where the new nonlinear function does not depend on \( j_s \) last components of the new state, we then construct a HG/LMI observer for the augmented system. This high-gain observer combination allows obtaining a new threshold on \( \theta \) attenuated to the power \( \frac{1}{(1+\theta)(1+\theta)} \).

One of the natural solution to obtain a new system satisfying (34) is to add a set of integrators leading to the following transformation:

\[
z = \begin{pmatrix}
z_1 \\
\vdots \\
z_{n+j_s}
\end{pmatrix} = \Gamma(x) \triangleq \begin{pmatrix}
x_1 \\
\vdots \\
f(x(t))
\end{pmatrix}, \tag{37}
\]

It is easy to see that \( z \) obeys to the following dynamics:

\[
\dot{z}_i = z_{i+1}, \quad \text{for } i = 1, \ldots, n + j_s - 1, \tag{38}
\]

\[
\ddot{z}_{n+j_s} = \frac{d^2f(x(t))}{dt^2} \triangleq f\psi(z_1, \ldots, z_n), \tag{39}
\]

\[
x = \begin{pmatrix}
z_1 \\
\vdots \\
z_n
\end{pmatrix} = \begin{pmatrix}
I_n \\
0_{n \times j_s}
\end{pmatrix} z \tag{40}
\]

where \( I_n \) is the identity matrix of dimension \( n \). It is clear to see that the new system (38)-(39) satisfies the condition (34). Hence, the idea consists in constructing a HG/LMI observer for system (38)- (39) and then we deduce an estimation \( \hat{x} \) of \( x \) through (40), namely \( \hat{x} = \Phi \hat{\tilde{x}} \). Let us summarize the strategy...
in the following proposition. Let us first rewrite (38)-(39) in the condensed form:

\[
\begin{align*}
\dot{z} &= A_G z + B_G f_G(z, u) \\
y &= C_G z
\end{align*}
\] (41)

where \( A_G, B_G, \) and \( C_G \) have the same structure than \( A, B, \) and \( C, \) respectively, but with dimension \( n + j_s. \) Now we consider the following state observer corresponding to (41):

\[
\hat{z} = A_G \hat{z} + B_G f_G(\hat{z}) + L_G (y - C_G \hat{z})
\] (42)

where \( L_G \equiv \Gamma_G \Theta_G K_G, \) with \( \Theta_G(\theta) \equiv \text{diag}(\theta_1, \ldots , \theta_{n+j_s}). \)

The objective consists in determining \( \hat{z} \) converges exponentially to \( z. \) Hence, the estimated state \( \hat{x}(t) \) given by

\[
\hat{x}(t) = \begin{bmatrix} I_n & 0_{n \times j_s} \end{bmatrix} \hat{z}(t)
\] (43)

converges exponentially to \( x(t). \)

**Proposition 1:** Assume there exist \( P_G > 0, \lambda_G > 0, \) and \( \theta > 1 \) such that the following conditions hold:

\[
A_G (\Psi)'^T P_G + P_G A_G (\Psi) - C_G'^T Y_G
- Y_G'^T C_G + \lambda_G I < 0, \forall \Psi \in \mathcal{V}_{H^0}, \]
(44)

\[
K_G \equiv P_G^{-1} Y_G'^T, \quad \Theta_G(\theta) \equiv \left( 2k_{f_G} \lambda_{\max}(P_G) \right)^{-1/2},
\] (45)

where \( H^0 \) is as given in (27) with different vertices corresponding to the new nonlinear function \( f_G. \) Then \( \hat{x} \) given by (43) converges exponentially to \( x(t). \)

**Proof:** It is sufficient to prove that \( \hat{z} \) converges exponentially to \( z, \) which is ensured by the fact that we use the HG/LMI methodology on the transformed system (41). For more details on the proof we refer the reader to [2].

V. SIMULATION RESULTS

The model (3) given in section II-A has the following form:

\[
\Gamma_y : \begin{cases} 
\dot{x} = f(x) \\
y = h(x)
\end{cases}
\] (47)

Using an appropriate change of coordinate, the system is transformed into a triangular form as given in (48):

\[
\Gamma' : \begin{cases} 
\dot{\xi} = F'(\xi) = \begin{bmatrix} \xi_1 \\ \xi_2 \\ \xi_3 \end{bmatrix} = \begin{bmatrix} \xi_2 \\ \xi_3 \\ \varphi(\xi) \end{bmatrix}, \\
y = C' \xi = \begin{bmatrix} 1 & 0 & 0 \end{bmatrix} \begin{bmatrix} \xi_1 \\ \xi_2 \\ \xi_3 \end{bmatrix}
\end{cases}
\] (48)

The standard high-gain observer and the new proposed observer are designed to estimate the states of the system given by (48). For \( j_s = 1, \) we transform the system given by (48) of dimension 3 to an augmented system of dimension 4 by adding an integrator as illustrated in section IV to obtain this fourth dimensional system:

\[
\begin{cases} 
\dot{z}_1 = z_2 \\
\dot{z}_2 = z_3 \\
\dot{z}_3 = z_4 \\
\dot{z}_4 = \varphi'(\xi) \\
y = z_1
\end{cases}
\] (49)

where \( \varphi'(\cdot) \) is the new nonlinear function that does depend on the last component \( z_4. \)

In order to carry out simulations, we have used the parameters given in Table I which are not necessarily the experimental values but are consistent with the requirements of the model.

**TABLE I: Parameters of the GRN**

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Meaning</th>
<th>Value (arb. units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \kappa_1 )</td>
<td>Production constant of mRNA</td>
<td>0.001</td>
</tr>
<tr>
<td>( \kappa_2 )</td>
<td>Production constant of protein</td>
<td>1.0</td>
</tr>
<tr>
<td>( \kappa_3 )</td>
<td>Production constant of metabolite</td>
<td>1.0</td>
</tr>
<tr>
<td>( \gamma_1 )</td>
<td>Degradation constant of mRNA</td>
<td>0.1</td>
</tr>
<tr>
<td>( \gamma_2 )</td>
<td>Degradation constant of protein</td>
<td>1.0</td>
</tr>
<tr>
<td>( \gamma_3 )</td>
<td>Degradation constant of metabolite</td>
<td>1.0</td>
</tr>
<tr>
<td>( \alpha )</td>
<td>Hill’s threshold parameter</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Table II summarizes the obtained values of the tuning parameter \( \theta \) and the observer gain \( K \) for the standard high-gain observer and the proposed observer, one can clearly see that the observer based on state augmentation approach and HG/LMI technique provides lower gain as compared to the classical high-gain observer.

**TABLE II: Simulation results for the two high-gain observers**

<table>
<thead>
<tr>
<th>Standard high-gain observer</th>
<th>Improved high-gain observer (( j_s = j_0 = 1 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \theta )</td>
<td>( K )</td>
</tr>
<tr>
<td>( 25.4906 )</td>
<td>( 9.0771 )</td>
</tr>
<tr>
<td>( 2.6928 )</td>
<td>( 3.4874 )</td>
</tr>
</tbody>
</table>

Figure 2 depicts the absolute values of estimation error \( (x_i - \hat{x}_i) \) for \( i = 1, \ldots , 3 \) under the application of additional Gaussian disturbances with zero mean and standard deviation of 0.1 at \( t = 2s \) to \( t = 4s \). We denote \( \hat{x}_{i,SHG}, \) the state estimate using the standard high-gain observer and \( \hat{x}_{i,ISHG}, \) the estimate using the improved high-gain observer proposed in section IV. From the plots, we can clearly see the convergence of the estimation error towards zero for both observers, although the standard high-gain converges rapidly but the transient performance of our proposed observer is vastly superior in particular for the estimates \( \hat{x}_2 \) and \( \hat{x}_3, \) since the smaller gain of our proposed observer makes the estimation less sensitive to the measurement noise.
activation, which aims to rebuild the non-measured concentration of one-gene regulation dynamic process involving end-product measurement delays. We have presented an effective new design technique based on HG/LMI technique and system state augmentation approach. The obtained observer ensures stability in a noise-free setting with a smaller gain as compared to the standard high-gain observer. Observer ensures stability in a noise-free setting with a smaller gain as compared to the standard high-gain observer. The remarkable assets related to this new design have been successfully addressed through an application to a simple biochemical pathway.

Fig. 2: Absolute values of estimation errors with additional measurement noise.

VI. CONCLUSION

As evolution of the high-gain observer, we have presented an effective new design technique based on HG/LMI technique and system state augmentation approach. The obtained observer ensures stability in a noise-free setting with a smaller gain as compared to the standard high-gain observer in addition to a reduced sensitivity to noise measurements. The remarkable assets related to this new design have been successfully addressed through an application to a simple one-gene regulation dynamic process involving end-product activation, which aims to rebuild the non-measured concentrations of mRNA and the involved protein.

REFERENCES


