Neurocomputing 151 (2015) 737–744

Contents lists available at ScienceDirect

Neurocomputing

journal homepage: www.elsevier.com/locate/neucom

Sampled-data state estimation for genetic regulatory networks with time-varying delays

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ARTICLE INFO

Article history:
Received 18 April 2014
Received in revised form
4 October 2014
Accepted 6 October 2014
Communicated by S. Arik
Available online 23 October 2014

Keywords:
Genetic regulatory networks
Sampled-data
State estimation
Feedback regulation
Time-varying delays

ABSTRACT

This study examines the sampled-data state estimation problem for genetic regulatory networks (GRNs) with time-varying delays. Instead of the continuous measurements, the sampled measurements are used to estimate the true concentration of mRNAs and proteins of the GRNs. By changing the sampling period into a bounded time-varying delay, the error dynamics of the considered GRN is derived in terms of a dynamical system with time-varying delays. Sufficient conditions are derived such that the augmented system governing the error dynamics is globally asymptotically stable. The design of the desired state estimator is proposed by constructing a suitable Lyapunov–Krasovskii functional (LKF), and the design procedure can be easily achieved by solving a set of linear matrix inequalities (LMIs). Finally, the proposed method is validated through the numerical simulation which shows the effectiveness the our results.

1. Introduction

During the past few years there are significant progress in the area of gene engineering, neural networks and other biological sciences. The mechanisms that have evolved to regulate the gene expression are known as *genetic regulatory networks* (GRNs), here the expression of a gene is regulated by its products. Because the biological characteristics depend on coding information stored in genes, which greatly influences the biological propagation, inheritance and variation. In recent years, GRNs have become an important area in biological and biomedical sciences and received great attention among the researchers, see [4,6,10,22,23,29]. One of the main aim in systems biology has been to understand the gene functions and regulations at the system level. GRNs structured by networks of regulatory interactions between DNA, RNA and proteins have played a key role in biological systems as they explain the interactions between genes (mRNA) and proteins. Mathematical modeling and simulation tools help to understand how complex GRNs, composed of many genes and their intertwined interactions, control the functioning of living systems. They provide a framework to unambiguously describe the network structure and to infer predictions of the dynamical behavior of the system [7]. For instance, how proteins are synthesized from genes as transcription factors binding to regulatory sites of other genes, and how they interact with each other and with other substances in the cells to perform complicated biological functions. With the appearance and development of DNA microarray technology, it is possible to measure gene expression levels on a genomic scale and furthermore analyze the gene regulatory network. Based on the statistic thermodynamics and biochemical reaction principle [25], a GRN can be described by a group of nonlinear differential [9,10]. In GRNs, mRNAs and proteins may be synthesized at different locations (i.e., nucleus and cytoplasm, respectively); thus, transportation or the diffusion of mRNAs and proteins between these two locations results in sizable delays.

The study of GRN has got the interest of many researchers, many notable researches have proposed different kinds of mathematical models to describe GRN. So far, there are two basic methods concerning GRN modeling: Boolean method and dynamical system method using ordinary differential [2,5]. In Boolean models, the expression of each gene in the network is assumed to be either ON or OFF, no intermediate activity levels are ever taken into consideration, and the state of a gene is determined by the Boolean function of the states of other related genes [2]. While in the differential equation model, variables which describe the change rates of the concentration of gene products, such as mRNAs and proteins, are continuous values. The differential equation model excels the Boolean model for

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http://dx.doi.org/10.1016/j.neucom.2014.10.029
0925-2312/

its more secured accuracy. Time delays arise frequently in many dynamical systems such as economic systems, chemical processes, and neural networks [11]. It is well known that time delays in GRNs caused by transcription, translation, and translocation processes because of the slow reaction process may cause oscillation, divergence, and instability of the networks. Thus, GRNs with time delays have been extensively studied, and many important and interesting results have been proposed in terms of all sorts of methods [22,36]. GRN models are also unavoidably affected by modeling uncertainties, including parametric error. In [26], the authors studied sufficient conditions for the stochastic stability of the genetic networks with disturbance attenuation. In [21], simple delay-independent and delay-dependent conditions for disturbance analysis are developed for a class of GRNs. Theoretical analysis and experimental investigation on GRNs have increasing attention, and a large amount of important results making significant contributions for understanding both static and dynamic behaviors of biological systems can be found in [6,12,15,19,36] and references therein.

In practice, for the high-order complex system only partial information about the gene states are available in the network outputs. For instance, the state estimation problem for GRNs to approximate the true concentrations of the mRNA and protein has been investigated in a continuous-time manner [8,14,32,33]. Robust state estimation for discrete-time stochastic GRNs with probabilistic measurement delays is discussed in [35]. In [20], the state estimation problem has been studied for a class of delayed recurrent neural networks with sampled-data that has been derived to guarantee that the dynamics of the estimation error is globally exponentially stable. The passivity based exponential state estimation of switched Hopfield neural networks is proposed in [1]. In [16], the state estimation problem has been investigated for a class of GRNs with time-varying delays and randomly occurring uncertainties. In [3], the state estimation problem has been studied for a class of discrete-time GRNs with random delays. The state estimation for delayed GRNs based on passivity theory has been discussed in [34]. More recently, in [29] Sakthivel et al. proposed the problem of robust state estimator design for a class of uncertain discrete-time GRNs with time varying delays and randomly occurring uncertainties.

It is worth mentioning that the approach to estimate the GRN states through the output sampled measurement needs less information from the network outputs, which can lead to a significant reduction of the information communication burden in the network. So, in GRNs, it is important to investigate the effect of sampling errors on the estimation of state variables by selecting the proper sampling interval. In the literature, there are some results about the state estimation problems based on sampled-data approach; in [17,27,28] the sampled-data state estimation of neural networks is discussed. Further, Lee et al. [18] studied the stochastic sampled-data control for state estimation of neural networks and Hu et al. [13] investigated the sampled-data state estimation of delayed neural networks with Markovian jumping parameters. Very recently, the sampled-data state estimation of neural networks of neutral type has been investigated in [37]. To the best of our knowledge, the sampled-data state estimation problem of GRNs has not been addressed so far.

Motivated by the above facts, in this paper, the problem of state estimation of GRNs with time varying delays using sampled measurements has been considered. Unlike previous studies, the states of the proposed GRNs were estimated using the sampled-data with sampling period. The main novelty of this paper lies in the following aspects: (1) a new sampled-data state estimation problem is addressed for delayed genetic regulatory networks. (2) Instead of continuous measurements, a set of state estimators is constructed based on the sampled measurements, a sampled-data state estimator is derived. (3) The sampling period is converted equivalently into a time-varying but bounded delay by using the input delay approach, and then the considered GRN is derived in terms of a differential equation with two different time-delays. By utilizing an appropriate LKF, Jensen's inequalities and Schur complement, the desired estimators of neuron states are designed in terms of the solution to a certain set of LMIs. Then, the estimator gains are described in terms of the solution to a set of LMIs, which can be solved by MATLAB LMI control toolbox. Finally, a numerical example and its simulations are exploited to demonstrate the usefulness and effectiveness of the presented results.

1.1. Notations

Throughout this paper, the superscripts T and (-1) stand for matrix transposition and matrix inverse respectively; $\Re^{n\times n}$ denotes the $n\times n$-dimensional Euclidean space; the notation $P>0$ means that P is real, symmetric and positive definite; I and 0 denote the identity matrix and zero matrix with compatible dimensions; diag{.} stands for a block-diagonal matrix; we use an asterisk (*) to represents a term that is induced by symmetry and sym(A) is defined as $A+A^T$. Matrices which are not explicitly stated are assumed to be compatible for matrix multiplications.

2. Problem formulation and preliminaries

Consider the following GRNs with time-varying delays:

$$\begin{cases} \dot{\tilde{m}}(t) = -A\tilde{m}(t)+C\tilde{g}(\tilde{r}(t-\tau(t)))+J(t), \\ \dot{\tilde{r}}(t) = -B\tilde{r}(t)+D\tilde{m}(t-\sigma(t)), \end{cases} \tag{1}$$

where $\tilde{m}(t)=[\tilde{m}_1(t),\tilde{m}_2(t),\ldots,\tilde{m}_n(t)]^T\in\mathbb{R}^n$, $\tilde{r}(t)=[\tilde{r}_1(t),\tilde{r}_2(t),\ldots,\tilde{r}_n(t)]^T\in\mathbb{R}^n$; $\tilde{m}_i(t),\tilde{r}_i(t)\in\mathbb{R}$ are the concentrations of mRNAs and proteins, respectively; $A=\mathrm{diag}\{a_1,a_2,\ldots,a_n\}$ and $C=\mathrm{diag}\{c_1,c_2,\ldots,c_n\}$ are constant matrices implying the rates of degradation; $D=\mathrm{diag}\{d_1,d_2,\ldots,d_n\}$ represents the translation rate; $B=(b_{ij})_{n\times n}$ is the coupling matrix of the genetic networks; the feedback regulation function of protein on transcription is denoted by the nonlinear function $\tilde{g}(\tilde{r}(t))=\mathrm{diag}\{\tilde{g}_1(\tilde{r}(t)),\tilde{g}_2(\tilde{r}(t)),\ldots,\tilde{g}_n(\tilde{r}(t))\}^T$, which is the monotonic function in Hill form, i.e. $\tilde{g}_i(\tilde{r}(t))=\tilde{r}^{h_i}/(1+\tilde{r}^{h_i})$ where h_i is the Hill coefficient; $J(t)=[J_1(t),J_2(t),\ldots,J_n(t)]^T$ denotes the basal rates of degradation; $\sigma(t)$ and $\tau(t)$ are the time-varying delays which satisfies

$$\begin{aligned} &0\le\sigma_1\le\sigma(t)\le\sigma_2, \quad \dot{\sigma}(t)\le\mu_1 \quad \text{and} \\ &0\le\tau_1\le\tau(t)\le\tau_2, \quad \dot{\tau}(t)\le\mu_2. \end{aligned} \tag{2}$$

where σ_1, σ_2, μ_1, τ_1, τ_2, μ_2 are known constants. The time-varying delays are assumed to be differentiable and bounded.

Let $(\tilde{m}^*,\tilde{r}^*)$ be the equilibrium point of system (1), then switch the equilibrium of system (1) to the origin by the transformation $x(t)=\tilde{m}(t)-\tilde{m}^*$ and $y(t)=\tilde{r}(t)-\tilde{r}^*$. Hence, model (1) is transformed into the following form:

$$\begin{cases} \dot{x}(t) = -Ax(t)+Bg(y(t-\tau(t))), \\ \dot{y}(t) = -Cy(t)+Dx(t-\sigma(t)), \end{cases} \tag{3}$$

where $g\{y[t-\tau(t)]\}=\tilde{g}\{\tilde{r}[t-\tau(t)]+\tilde{r}^*\}-\tilde{g}(\tilde{r}^*)$.

(**A1**) The regulation function satisfies the following assumption:

$$g(y)(g(y)-Wy)\le 0, \tag{4}$$

where $W=\mathrm{diag}\{w_1,w_2,\ldots,w_n\}$.

In high-order complex systems, it is known that only partial information about the network components are known. Therefore, in order to get the true state of the GRNs, one would need to estimate them from the available measurements. For this, we define the network measurements as follows:

$$\begin{cases} z_x(t) = Mx(t), \\ z_y(t) = Ny(t), \end{cases} \tag{5}$$