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Finite-time stochastic synchronization of genetic regulatory networks

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ABSTRACT

This paper is concerned with the finite-time synchronization for a class of stochastic genetic regulatory networks (GRNs). The purpose of the addressed problem is to design a controller that can synchronize the concentration of the mRNA and the protein of GRNs in finite time with probability. Based on the recent finite-time stability theorem of stochastic nonlinear systems, sufficient conditions are first established for ensuring the finite-time stochastic stability of synchronization error in probability. Then, the gain parameters of the controller are obtained by solving a linear matrix inequality and the robust finite-time synchronization is guaranteed for GRNs with uncertain parameters. Compared with the previous references, a continuous finite-time controller is designed to achieve the synchronization objective and a constructive method that may accelerate the convergence is discussed. Finally, two numerical examples are given to illustrate the effectiveness of the proposed design method.

1. Introduction

It is known that, gene expression is a gene-to-protein process mainly consisting of transcription and translation. The mechanisms that genes encode proteins and some of which in turn regulate gene expression is called the Genetic Regulatory Networks (GRNs). In order to perform the multitude of functions necessary to survive, cells must be able to regulate the expression pattern of their genes [1], which is generally completed through GRNs – intricate webs of interactions between regulatory elements controlling protein production. The GRNs actually act as a complex dynamical system because a great number of genes and proteins either directly or indirectly interact with one another by activation and repression [2,3]. Clarifying the complex dynamics of GRNs not only is essential for the understanding of the rhythmic phenomena of living organisms, but also has many potential applications in bioengineering fields. For example, the authors in [4] investigated the synchronization of cellular clock in the suprachiasmatic nucleus by an experimental method. In recent years, due to great progress in genome sequencing, GRNs have emerged as a new research area of biological and biomedical sciences, and considerable attention has been contributed to theoretical analysis and experimental investigation on GRNs [5–9].

To better understand the regulatory mechanisms of gene networks, both quantitatively and qualitatively, biologists and mathematicians construct system models that can be studied in detail [10]. Research shows that, the stochastic fluctuations for the GRNs might occur at various stages such as transcription, translation, transport, and chromatin remodeling which stem from either probabilistic chemical reactions or random variations. Therefore, state-dependent stochastic noise should be recognized as an indispensable character that has to be taken into account when modeling GRNs [9,11]. Recently, the stochastic differential equation (SDE) has been employed to describe the molecular fluctuation in GRNs [12]. Moreover, parameter uncertainties are arguably becoming another challenging issue that impact on the model quality. It is very likely that the parameters of the built model identified from the experimental data will unavoidably vary from time to time, which largely reduces the practical significance of the aforementioned dynamical models built by the SDE [13–15]. Therefore, it is needed to estimate the unknown network states based on some available known systems such that the error system converges to zero in the mean square sense [9,11,13–16].

This paper aims to provide some theoretical results for studying the synchronization of GRNs with noise perturbations and uncertain parameters by the control theory approach. There exist many reasons why the synchronization issue of GRNs should be studied heavily, only three ones among them are shown here because of the space constraints. Firstly, synchronization is a basis

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to understand an unknown dynamic system from one or more well-known dynamic systems, which means two or more systems asymptotically share a common dynamic behavior. Secondly, because naturally occurring GRNs are generally much more complicated, the study of synchronization among GRNs is important for the understanding of the rhythmic phenomena of living organisms at both molecular and cellular levels [3]. Thirdly, in cellular physiology, we need to focus on how proteins produce and how gene networks are regulated, which could be better understood by considering the synchronization of GRNs. We hope to synchronize the complex GRNs by some relatively simple systems which nevertheless display rich dynamical behaviors and provides some opportunity to test theoretical results of genetic regulation.

Generally, synchronization can be induced by external forcing or by coupling, and many types of synchronization have been presented in the past decades [17]. Similarly, there have a large number of experimental and theoretical works studying the synchronization in genetic networks [18,19]. Unfortunately, almost all the discussions in the existing literature regarding the convergence of synchronization error do not consider the convergence speed, even though we eagerly want to synchronize network states as quickly as possible in practical applications. In order to achieve faster synchronization and to realize synchronization in finite time rather than merely asymptotically [20], an effective method is to use finite-time techniques, which are demonstrated to have better robustness and disturbance rejection properties [21].

Recently, many kinds of finite-time issues have attracted particular research interests, and there have been some results on finite-time stabilization, convergence, synchronization, consensus [21–30]. Normally, the term of $u(t) = -h\,\mathrm{sign}(\delta(t))|\,\delta(t)|^{\alpha}$, $0 \le \alpha < 1$ was introduced in the above references, where $\delta(t)$ denotes the error and h the gain. For the different values of parameter α, such techniques can generally be divided into two types: (i) continuous (when $0 < \alpha < 1$) [31–33] and (ii) discontinuous (when $\alpha = 0$) [34–36]. In this paper, the first type of $u(t)$ will be introduced into the design of the *finite-time stochastic synchronization* (FTSS) for GRNs, and another one will be discussed to optimize the synchronization speed.

Motivated by the above questions, in this paper, in order to realize the FTS of the stochastic GRNs, a continuous controller is addressed. Compared with [31–33], the difference of this paper lies in the following three aspects. First, based on the finite-time stability theorem of stochastic nonlinear systems [22–24], a new finite-time controller is proposed for GRNs with noise perturbations. Moreover, in contrast to [31–33], the FTS in this paper is guaranteed by constructing a suitable Lyapunov functional and the obtained conditions are easier to be satisfied. Second, the gain parameters of controller can be designed by solving a linear matrix inequality and the robust finite-time stochastic synchronization (RFTSS) for GRNs with parameter uncertainties can be realized as well. Finally, in order to explore the upper bound of the settling time as small as possible, we further discuss the relationship between the settling time and the parameter α, including the situation of $\alpha = 0$.

The notations in this paper are quite standard. $\mathbb{R}^n$ and $\mathbb{R}^{n\times m}$ denote, respectively, the n dimensional Euclidean space and the set of all $n \times m$ real matrices. The superscript "T" denotes the transpose and the notation $X \ge Y$ (respectively, $X > Y$) where X and Y are symmetric matrices, mean that $X - Y$ is positive semi-definite (respectively, positive definite). $\lambda_{\max}(M)$ and $\lambda_{\min}(M)$ denote the maximal and minimal eigenvalues of real matrix M respectively. Let $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\ge 0}, \mathbf{P})$ be a complete probability space with a filtration $\{\mathcal{F}_t\}_{t\ge 0}$ satisfying the usual conditions (that is, it is right continuous and contains all $\mathbf{P}$-null sets). $\mathbb{E}\{x\}$ stands for the expectation of the stochastic variable x with respect to the given probability measure $\mathbf{P}$. I and 0 represent the identity matrix and the zero matrix, respectively. $\mathrm{diag}(\cdots)$ stands for a block-diagonal matrix; matrices, if their dimensions are not explicitly stated, are assumed to be compatible for algebraic operations.

2. Model formulation and preliminaries

2.1. Network description

Consider the following genetic network, which is established as follows:

$$\begin{cases} \dfrac{dm(t)}{dt} = -Am(t) + Bf(p(t)) + J, \\ \dfrac{dp(t)}{dt} = -Cp(t) + Dm(t), \end{cases} \tag{1}$$

where $m(t) = (m_1(t), m_2(t), \ldots, m_n(t))^T$, $p(t) = (p_1(t), p_2(t), \ldots, p_n(t)))^T$ denote, respectively, the concentrations of mRNA and protein of the gene at time t, $A = \mathrm{diag}(a_1, a_2, \ldots, a_n)$ and $C = \mathrm{diag}(c_1, c_2, \ldots, c_n)$ represent the degradation rates of mRNA and protein, respectively, and $D = \mathrm{diag}(d_1, d_2, \ldots, d_n)$ is the translation rate.

The nonlinear function $f(p(t)) = [f_1(p_1(t)), f_2(p_2(t)), \ldots, f_n(p_n(t))]^T$, where

$$f_j(p_j(t)) = \frac{p_j(t)/\beta_j}{1 + (p_j(t)/\beta_j)^{H_j}},$$

with H_j being the Hill coefficient and β_j being a positive scalar. The matrix $B = (b_{ij})_{n\times n}$ is the coupling matrix of the genetic network defined as follows: if transcription factor j is an activator of gene i, then $b_{ij} = a_{ij}$; if there is no connection between j and i, then $b_{ij} = 0$; if transcription factor j is a repressor of gene i, then $b_{ij} = -a_{ij}$. Here, a_{ij} is a positive scalar that denotes the transcriptional rate of transcription factor j to gene i. $J = [J_1, J_2, \ldots, J_n]^T$ is defined as a basal rate by $J_i = \sum_{j\in V_i} a_{ij}$, where V_i is the set of repressor of gene i.

Since f_i $(i = 1, 2, \ldots, n)$ is a monotonically increasing and differentiable function with saturation, it satisfies $0 \le df_i(s)/ds \le \tilde{m}_{f_i}$, which is equivalent to

$$0 \le \frac{f_i(s_1) - f_i(s_2)}{s_1 - s_2} \le \tilde{m}_{f_i}, \quad \forall s_1, s_2 \in \mathbb{R}. \tag{2}$$

For simplicity, let $x(t) = [m^T(t), p^T(t)]^T$. Accordingly, the system (1) becomes

$$dx(t) = [\tilde{A}x(t) + \tilde{B}\tilde{f}(x(t)) + \hat{I}J]\,dt, \tag{3}$$

where

$$\tilde{A} = \begin{bmatrix} -A & 0 \\ D & -C \end{bmatrix}, \quad \tilde{B} = \begin{bmatrix} B \\ 0 \end{bmatrix}, \quad \tilde{I} = \begin{bmatrix} I \\ 0 \end{bmatrix} \quad \text{and} \quad \tilde{f}(x(t)) = f(p(t)).$$

From (2), we know that the nonlinear function $\tilde{f}(x(t))$ satisfies

$$\tilde{f}(x(t))(\tilde{f}(x(t)) - \tilde{M}_f x(t)) \le 0, \tag{4}$$

where $\tilde{M}_f = [0, M_f]$ with $M_f = \mathrm{diag}(\tilde{m}_{f_1}, \tilde{m}_{f_2}, \ldots, \tilde{m}_{f_n})$.

In this paper, we consider model (1) or (3) as the master system. The response system is

$$dy(t) = [\tilde{A}y(t) + \tilde{B}\tilde{f}(y(t)) + \hat{I}J + u(t)]\,dt + \rho(\delta(t))\,d\omega(t), \tag{5}$$

where $y(t) = [\hat{m}^T(t), \hat{p}^T(t)]^T$ and $\delta(t) = y(t) - x(t)$ is the error state, $u(t)$ is the controller, $\omega(t)$ is one-dimensional Brownian motion defined on the probability space $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\ge 0}, \mathbf{P})$, and the intensity function $\rho(\cdot)$ is the noise intensity vector satisfying the following condition:

$$\mathrm{trace}[\rho^T(\delta(t))\rho(\delta(t))] \le \|M\delta(t)\|^2, \tag{6}$$

where M is a matrix with appropriate dimensions.