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Short communication

Passivity analysis for stochastic Markovian switching genetic regulatory networks with time-varying delays

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ABSTRACT

In this paper, the passivity problem for the stochastic Markovian switching genetic regulatory networks with time-varying delays is investigated. By applying control theory and mathematical tools, a sufficient condition for this problem is obtained and presented in terms of linear matrix inequalities (LMIs), which can be easily verified by Matlab LMI toolbox. The obtained condition provides some insight into synthetic biology and systems biology. Finally, a numerical example is given to show the effectiveness of the proposed result.

1. Introduction

Genetic regulatory networks (GRNs), structured by networks of regulatory interactions between DNA, RNA, proteins inhibiting the expression of other genes for gaining insight into the underlying processes of living systems at the molecular level, have received much research attention in recent years, and many interesting results have been reported in [1,2], and the references therein. Basically, there are two types of gene network models, the Boolean model [3], where the state converges to a terminal state via a series of state transitions that is determined by the designed Boolean rules, and the differential equation model [4], where the variables describe the concentrations of gene products, such as mRNAs and proteins, as continuous values of the gene regulation systems. Due to the slow processes of the transcription and translations, time delays are always unavoidable, therefore, considerable attention has been given on the stability of the GRNs with time delays, see [5–7].

It is worth noting that gene expression involves a series of molecular events in cells, are often subject to significant intrinsic fluctuations and extrinsic disturbances, thus gene expression is best viewed as a stochastic process [8]. The stochastic differential equation model has recently been developed to describe the molecular fluctuation in gene networks, see [9–11]. For example, in [10], the authors investigated the robust stability of stochastic GRNs with time-varying delays. In [11], the authors considered the robust stability of stochastic GRNs with time-varying discrete and distributed delays. However, the results in these two papers are conservative in some extent, since the results are only dependent on the derivative of the delay, but not on the upper bound of delay.

As is well known, most of gene networks include some kinds of switching mechanisms. For example, a bistable system can switch from one steady state to the other by increasing stimulation or inhibition or by changing other regulatory mechanisms [12]. It is noted that the switching system modeling is natural and promising in mathematically modeling the complex gene regulations, and various results have been obtained. For example, the piecewise affine (PWA) systems

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model for gene networks has been employed in [13], and the stochastic hybrid systems model has been developed in [14]. Furthermore, Markov chains have also been widely used as a generic framework for modeling gene networks. A finite state homogeneous Markov chain model has been constructed from microarray data in [15], and a novel hybrid stochastic model was recently developed for GRNs based on a Markov chain with uncertain switching probabilities in [16], and the sufficient conditions for the stochastic stability of the Markovian switching GRNs were obtained. It should be pointed out that the results are also conservative since they are only dependent on the derivative of the delays, but not the upper bound of delays. Therefore, there still leaves some room for further improvement of the stability of the stochastic GRNs with Markovian switching or without Markovian switching.

On the other hand, the theory of dissipative systems which postulates the energy dissipated inside a dynamic system is less than the energy supplied from external source often links the stability problems. Passivity is part of a broader and a general theory of dissipativeness. The main idea of passivity theory is that the passive properties of system can keep the system *internal stability*. In recent years, passivity has played an important role in synchronization [17], networked control [18], neural networks [19], etc. Although, the research on passivity has attracted much attention, little of that has been devoted to the passivity properties of the stochastic GRNs. Thus, the purpose of this paper is to investigate such an interesting problem for stochastic Markovian switching GRNs with time-varying delays.

In this paper, we deal with the passivity problem of the stochastic Markovian GRNs with time-varying delays. The definition of the stochastic passivity of the considered systems is firstly introduced, and the sufficient condition for the passivity of the systems is then given by using the Lyapunov stability theory and some stochastic analysis method. The obtained condition is both delay-dependent and delay-derivative-dependent, and therefore is less conservative than some existing stability results on the stochastic GRNs. A numerical example is finally given to show the effectiveness of the proposed results.

2. Problem formulation

In this paper, we consider the following nonlinear genetic regulatory:

$$\begin{cases} \dot{m}(t) = -Am(t) + Bf(p(t-\sigma(t))) + L, \\ \dot{p}(t) = -Cp(t) + Dm(t-\tau(t)), \end{cases} \tag{1}$$

where $m(t) = [m_1(t), m_2(t), \ldots, m_n(t)]^T$, $p(t) = [p_1(t), p_2(t), \ldots, p_n(t)]^T$, $m(t)$ and $p(t)$ are the concentrations of the mRNA and protein of the ith node at time t, respectively; $A = \mathrm{diag}\{a_1, a_2, \ldots, a_n\}$ and $C = \mathrm{diag}\{c_1, c_2, \ldots, c_n\}$ denote the degradation or the dilution rates of mRNAs and proteins; $D = \mathrm{diag}\{d_1, d_2, \ldots, d_n\}$ and $B = \{b_{ij}\} \in \mathbf{R}^{n\times n}$ are the coupling matrices, and B is defined as follows:

$$b_{ij} = \begin{cases} \bar{b}_{ij}, & \text{if transcription factor } j \text{ is an activator of gene } i, \\ 0, & \text{if there is no link from node } j \text{ to } i, \\ -\bar{b}_{ij}, & \text{if transcription factor } j \text{ is an repressor of gene } i \end{cases}$$

and the nonlinear function $f(\cdot) \in \mathbf{R}^n$ represents the feedback regulation of the protein on the transcription, which is the monotonic function in Hill form, i.e. $f_j(x) = \frac{x^{h_j}}{1+x^{h_j}}$, h_j is the Hill coefficient. The time-varying delays $\tau(t)$ and $\sigma(t)$ are assumed to satisfy $0 \leqslant \tau(t) \leqslant \tau$, $0 \leqslant \sigma(t) \leqslant \sigma$ and $\dot{\tau}(t) \leqslant \mu_1 < \infty$, $\dot{\sigma}(t) \leqslant \mu_2 < \infty$; $L = [l_1, l_2, \ldots l_n]^T$, where $l_i = \sum_{j\in I_i} \bar{b}_{ij}$ and I_i is the set of all j nodes which are repressors of gene i.

Let (m^*, p^*) be the equilibrium point of (1), it is the solution of the following equation

$$\begin{cases} -Am^* + Bf(p^*) + L = 0, \\ -Cp^* + Dm^* = 0. \end{cases} \tag{2}$$

For convenience, we shift an intended equilibrium point (m^*, p^*) of system (1) to the origin. Using $x(t) = m(t) - m^*$, $y(t) = p(t) - p^*$, it is easy to get

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

where $g(y(t)) = f(y(t) + p^*) - f(p^*)$. Since $g(\cdot)$ is a monotonically increasing function with saturation, from the definition of $g(\cdot)$, we know that $g(\cdot)$ satisfies the following condition

$$g(x)(g(x) - kx) \leqslant 0. \tag{4}$$

In fact, the system matrices of gene networks may change randomly at discrete time instances governed by Markov process. Therefore, the Markov jump system might be the suitable way to model the process of gene regulation. Considering the intracellular noises perturbations, the external gene control inputs together with the Markovian jumping parameters, a stochastic Markovian switching GRNs with time-varying delays is presented as follows