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# On sampled-data control for stabilization of genetic regulatory networks with leakage delays \*



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#### ABSTRACT

The leakage delay has large impacts on the dynamical behavior of genetic regulatory networks (GRNs) and can bring tendency to destabilize systems. This paper is concerned with the stabilization of genetic regulatory networks with leakage delays. Some novel conditions for stabilizing the GRNs are obtained based on Lyapunov method. The sampled-data controller is designed by solving linear matrix inequalities (LMIs). Two numerical examples are given to demonstrate the effectiveness of the theoretical results

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#### 1. Introduction

In 1999, Hood first proposed the concept of systems biology. Sine then, systems biology has been one of the hottest topics. It attracted a lot of scientists and engineers from biology, mathematics, computer science, etc. [1–4]. With the development of systems biology, many complex life phenomena can be interpreted by the molecular interaction. This motivates scientists to model these interactions as network [5,6]. A lot of biology networks have been constructed such as genetic regulatory networks, metabolic networks, transcriptional regulatory networks, signalling networks and so on [7,8]. Among them, genetic regulatory network is a kind of dynamical network, which describes complex interactions between genes (mRNA) and its product (proteins). The study of GRNs has important science value, which can help scientists to understand many important and complex phenomena of living cells. Nowadays, some theoretical results have been used in some engineering applications [9]. Generally, based on different aims and applications, there are two GRNs models: discrete model such as the Boolean network model [10,11] and continuous model such as differential equation model [12–14].

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As we all know, stability of dynamical systems is one of the most important topics. The stability of GRNs has important biology meaning. Many significant results have been published [15–17]. Because the process of transcription and translation of proteins needs time, time delay should be taken into consideration in modelling GRNs. Moreover importantly, it is often a factor to cause system instability. There exist many types of time delays such as discrete delays [18], continuous delays [19], random delays [20], and mixed delays [21]. Many interesting and valuable conclusions concerning GRNs with delay have been reported.

In practical applications, leakage delay (or forgetting delay), which has been found in the negative feedback term of neural network system, is also a kind type of delay. Gopalsamy [22] firstly investigated the stability of the BAM neural networks with constant leakage delays. Further, Liu [23] discussed the global exponential stability for BAM neural networks with time-varying leakage delays, which extends and improves the main results of Gopalsamy. The robust stability of Markovian jump stochastic neural networks with leakage delays was investigated [24]. In [25], the authors considered sampled data state estimator for Markovian jumping neural networks with leakage time-varying delays. In [26], the authors discussed the global asymptotic stability for genetic regulatory networks with leakage delay. They pointed out that biological networks can show changes in the dynamic behaviors or instability due to the increase of leakage delay (see Remark 1). This means that the effect of leakage delay cannot be ignored because it can bring tendency to destabilize systems. This observation can be illustrated by the following example.

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**Remark 1.** Consider the following genetic regulatory networks:

$$\begin{cases} \dot{m}(t) = -Am(t - \rho_1) + Wf(p(t - \tau_1(t))) + I, \\ \dot{p}(t) = -Cp(t - \rho_2) + Dm(t - \tau_2(t)), \end{cases}$$
 (1)

where

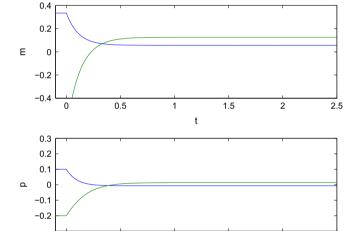
$$A = \begin{bmatrix} 9 & 0 \\ 0 & 8 \end{bmatrix}, \quad W = \begin{bmatrix} -1.5 & 0 \\ 1 & 2 \end{bmatrix},$$

$$C = \begin{bmatrix} 8 & 0 \\ 0 & 9 \end{bmatrix}, \quad D = \begin{bmatrix} -0.9 & 0 \\ 0 & 1 \end{bmatrix}, \quad I = \begin{bmatrix} 1 \\ 2 \end{bmatrix},$$

$$f = [f_1, f_2]^T, f(s) = s^2/(1+s^2), \tau_1(t) = 0.01 | \sin t|, \tau_2(t) = 0.01 | \cos t|.$$

When  $\rho_1 = \rho_2 = [0, 0]^T$ , in other words, there is no leakage delay, system (1) is stable (see Fig. 1). However, when  $\rho_1 = \rho_2 = [0.2, 0.2]^T$ , system (1) becomes unstable (see Fig. 2).

Phenomena mentioned above tell us that a large leakage delay leads to the instability of systems. So it is very important to take some control strategies to stabilize the system. Various control approaches, such as feedback control [27,28], intermittent control [29,30], impulsive control [31–34] and fuzzy logical control [35], can be adopted to ensure the stabilization of system. With the development of data communication networks and high-speed computers, the controller has been more and more scalability, reliability, flexibility, and cost

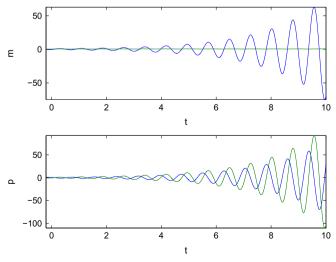


**Fig. 1.** The trajectories of state variables ( $\rho_1 = \rho_2 = 0$ ).

1.5

0

0.5



**Fig. 2.** The trajectories of state variables ( $\rho_1 = \rho_2 = 0.2$ ).

effectiveness. The sampled-data control deals with continuous system by sampling the data at discrete time based on the computer, sensors, filters and network communication. Hence it is more preferable to use digital controllers instead of analog circuits. This drastically reduces the amount of the transmitted information and improve the control efficiency. Compared with continuous control, the sampled-data control is more efficient, secure and useful [36]. In [37], the author considered the synchronization problem of coupled chaotic neural networks with time delay in the leakage term using sampled-data control. Lee [38] also investigated the synchronization problem of a complex dynamical network with coupling time-varying delays via sampled-data control. In [36], the authors introduced a discontinuous Lyapunov functional to consider the stability for linear systems by using the sampled-data control.

Motivated by the works mentioned above, in this paper, we will investigate the stabilization of genetic regulatory networks with leakage delays based on sampled-data control. To the author's knowledge, the present study is the first attempt to discuss the stabilization for GRNs with leakage delay via sampled-data control. We firstly analyze the influence of leakage delay on stability. Once the leakage delay causes the instability of system, we will take the sampled-data control to stabilize the system. By using input delay approach, which was mentioned in [37,38], we investigate the stability of GRNs under the control.

The paper is organized as follows. In the next section, the problem is formulated and some basic preliminaries, assumption, definition are given. In Section 3, an appropriate sampled-data controller is designed to ensure the stability of genetic regulatory networks with leakage delay. In Section 4, two illustrative examples are given to show the effectiveness of our results. Some conclusions are proposed in Section 5.

#### 2. Preliminaries

The genetic regulatory network is composed of a number of genes and proteins which regulate the expression of other genes. The dynamic behavior of a genetic network can be modelled by the following differential equations:

$$\begin{cases} \dot{m}_{i}(t) = -a_{i}m_{i}(t) + \sum_{j=1}^{n} \omega_{ij}f_{j}(p_{j}(t - \tau_{1}(t))) + I_{i}, \\ \dot{p}_{i}(t) = -c_{i}p_{i}(t) + d_{i}m_{i}(t - \tau_{2}(t)), \end{cases}$$
(2)

where  $a_i$  and  $c_i$  are the degradation rates of the mRNA and protein, respectively. The  $m_i(t)$  and  $p_i(t)$  denote the concentrations of mRNA and protein of the ith node at time t, respectively.  $d_i$  is the translation rate,  $\tau_1(t)$  is the feedback regulation delay and  $\tau_2(t)$  is the translation delay.  $f_j(p_j(s)) = (p_j(s)/\beta_j)^{H_j}/(1+(p_j(s))/\beta_j)^{H_j}$ , where  $H_j$  is the Hill coefficient.  $\beta_j$  is a positive constant which denotes the feedback regulation of the protein on the transcription,  $\omega_{ij}$  is defined as follows:

$$\omega_{ij} = \left\{ \begin{array}{ll} \alpha_{ij} & \text{if transcription factor } j \text{ is an activator of gene } i, \\ 0 & \text{if there is no link from } j \text{ to } i, \\ -\alpha_{ij} & \text{if transcription factor } j \text{ is a repressor of gene } i. \end{array} \right.$$

Let  $(m^*, p^*)^T$  be an equilibrium point of Eq. (2), then we will shift an intended equilibrium point  $(m^*, p^*)^T$  to the origin. The transformation  $x_i(t) = m_i(t) - m_i^*$ ,  $y_i(t) = p_i(t) - p_i^*$  change system (2) into the following compact matrix form:

$$\begin{cases} \dot{x}(t) = -Ax(t) + Wg(y(t - \tau_1(t))), \\ \dot{y}(t) = -Cy(t) + Dx(t - \tau_2(t)), \end{cases}$$

where  $A = diag[a_1, a_2...a_n]$ ,  $C = diag[c_1, c_2...c_n]$ ,  $D = diag[d_1, d_2...d_n]$ ,  $W = (\omega_{ij})_{n \times n} \in R^{n \times n}$ ,  $g_j(y(t)) = f_j(y(t) + p^*) - f_j(p^*)$ , with g(0) = 0.

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