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Stochastic stabilization of genetic regulatory networks

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ABSTRACT

This paper is concerned with the stochastic stabilization for genetic regulatory networks. Based on the Lyapunov stability theory in combination with certain convex algorithm, we obtain the sufficient condition under which the unstable genetic regulatory network can be stabilized by using Brownian motion. Finally, a numerical illustrative example is provided to show the effectiveness and correctness of the proposed method.

1. Introduction

In the past few years, the genetic regulatory networks have been widely applied in many fields such as biomedical sciences, engineering sciences and so forth. Up to now, numerous efforts have been devoted to this field and accordingly, the research of genetic regulatory networks has been greatly improved. Quite a lot of mathematical models, such as Boolean networks [2], Bayesian networks [1], differential equation models [3,4], stochastic master equation models, have been proposed to provide a framework for integrating data and gaining insights into the dynamic behavior of genetic regulatory networks. Among these models, the differential equation model has been playing a vital role, which has been widely used to characterize the gene regulation process.

The differential equation model of genetic regulatory networks was originated in [3]. Since then, an increasing number of researchers [5,6,7,24,25] have started to study the genetic regulatory networks described by the differential equation models, resulting in a multitude of research fruits available in the literature. These genetic regulatory networks under consideration include but are not limited to discrete genetic regulatory networks [8], continuous genetic regulatory networks [8], delayed genetic regulatory networks [9,15,16,18,19], uncertain genetic regulatory networks [10], impulsive genetic regulatory networks [11,20], switched genetic regulatory networks [12,21] and stochastic genetic regulatory networks [9,10,17,26]. In [10], the author has considered the stochastic stability of genetic regulatory networks with mixed delays, where sufficient conditions have been established to guarantee the globally asymptotical stability by means of the linear matrix inequality (LMI) technique in combination with the Lyapunov functional method. Furthermore, the author investigated the mean-square asymptotical stability of stochastic genetic regulatory networks and discusses the stochastic stability of stochastic delayed genetic regulatory networks. In [9], the author has firstly given a definition of robust stability for uncertain genetic regulatory networks and then derived the sufficient conditions for the proposed stability by the unified utilization of Ito formula, LMI method and positive Lyapunov–Krasovskii functional approach.

It is well known that noise can be used to destabilize a given stable system. However, it is worth noting that noise can also be used to stabilize a given unstable system or to make a system more stable. The literature on stabilization by noise is expensive (see [13,14,27,28,29] and the references therein). In [13–14], the author has successfully stabilized the unstable nonlinear stochastic system by utilizing the stochastic noise. Motivated by this idea, this article will make use of stochastic noise to stabilize the unstable genetic regulatory networks. The paper consists of five sections. Section 2 introduces the genetic regulatory network model and a useful lemma. In Section 3, the stochastic stabilization of genetic regulatory networks is discussed. Section 4 provides a numerical illustrative example to demonstrate the effectiveness of obtained result. Section 5 finishes this work with giving a conclusion.

2. Model description

The genetic regulatory network is generally described by

$$\begin{cases} \dot{\boldsymbol{m}}(t) = -\boldsymbol{A}\boldsymbol{m}(t) + \boldsymbol{B}f(\boldsymbol{p}(t-\sigma(t))) + \boldsymbol{\Gamma} \\ \dot{\boldsymbol{p}}(t) = -\boldsymbol{C}\boldsymbol{p}(t) + \boldsymbol{D}\boldsymbol{m}(t-\tau(t)) \end{cases} \tag{1}$$

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where $\boldsymbol{m}(t)=[m_1(t), m_2(t), ..., m_n(t)]^T$, $\boldsymbol{p}(t)=[p_1(t), p_2(t), ..., p_n(t)]^T$ with $m_i(t)$ and $p_i(t)$ representing the concentrations of mRNA and protein of the ith node, respectively; $\boldsymbol{A} = diag(a_1, a_2, ..., a_n)$ and $\boldsymbol{C} = diag(c_1, c_2, ..., c_n)$ are the decay rates of mRNA and proteins, respectively; $\boldsymbol{D} = diag(d_1, d_2, ..., d_n)$ denotes the translation rate; $f(\cdot)$, which is a Hill-type monotonous saturation function, represents the feedback regulation of the proteins on the transcription; $\sigma(t)$ and $\tau(t)$ are time-varying delays; $\boldsymbol{\Gamma} = [\Gamma_1, \Gamma_2, ..., \Gamma_n]$ with Γ_i being the transcription factor of a repressor of gene I; $\boldsymbol{B} = (b_{ij}) \in R^{n\times n}$ is defined as follows:

$$b_{ij}\begin{cases} >0 & \text{if transcription factor } j \text{ is an activator of gene } i \\ =0 & \text{if there is no link from node } j \text{ to } i \\ <0 & \text{if transcription factor } j \text{ is a repressor of gene } i \end{cases}$$

Suppose system (1) has an equilibrium solution $(\boldsymbol{m}^*, \boldsymbol{p}^*)$. Letting $\boldsymbol{x(t)} = \boldsymbol{m(t)} - \boldsymbol{m}^*$ and $\boldsymbol{y(t)} = \boldsymbol{p(t)} - \boldsymbol{p}^*$, system (1) can be re-arranged as

$$\begin{cases} \dot{\boldsymbol{x}}(t) = -\boldsymbol{Ax}(t) + \boldsymbol{Bg}(\boldsymbol{y}(t-\sigma(t))) \\ \dot{\boldsymbol{y}}(t) = -\boldsymbol{Cy}(t) + \boldsymbol{Dx}(t-\tau(t)) \end{cases} \tag{2}$$

where $\boldsymbol{g(y(t))} = \boldsymbol{f(y(t) + p^*)} - \boldsymbol{f(y(t))}$ and $\mathbf{g}(\cdot)$ satisfies

$$\mathbf{g}(x)(\mathbf{g}(x) - Kx) \le 0 \tag{3}$$

with K being a constant. Obviously, system (2) admits a trivial solution.

In this paper, we shall stabilize system (2) by using Brownian motion. More precisely, we will equip system (2) with the stabilizing noises of the form $\mathbf{Mx}(t)\mathrm{d}\boldsymbol{\omega}(t)$ and $\mathbf{Ny}(t)\mathrm{d}\boldsymbol{\nu}(t)$, where $\mathbf{M} = \mathrm{diag}(M_1, M_2, \dots, M_n)^T$ and $\mathbf{N} = \mathrm{diag}(N_1, N_2, \dots, N_n)^T$, and further seek some appropriate matrices such that the equilibrium solution of stochastic differential equations

$$\begin{cases} \mathrm{d}\mathbf{x}(t) = \{-\mathbf{Ax}(t) + \mathbf{Bg}(\mathbf{y}(t-\sigma(t)))\}\mathrm{d}t + \mathbf{Mx}(t)\mathrm{d}\omega(t) \\ \mathrm{d}\mathbf{y}(t) = \{-\mathbf{Cy}(t) + \mathbf{Dx}(t-\tau(t))\}\mathrm{d}t + \mathbf{Ny}(t)\mathrm{d}\nu(t) \end{cases} \tag{4}$$

is almost surely exponentially stable.

Before discussion, we introduce the following lemma for later use.

Lemma 1 [22,23]**.** *Consider the following stochastic system*

$$\mathrm{d}\mathbf{x}(t) = \{\mathbf{f}(\mathbf{x}(t), t)\}\mathrm{d}t + \sum_{i=1}^{m} G_i\mathbf{x}(t)\mathrm{d}B_i(t), \tag{5}$$

where $\boldsymbol{f}: \boldsymbol{R^d} \times \boldsymbol{R_+} \to \boldsymbol{R^d}$, which is a continuous function, satisfies local Lipschitz condition and linear growth condition as follows

$$|\mathbf{f}(\mathbf{x}, t)| \le K|\mathbf{x}|. \tag{6}$$

Suppose there exist two constants $\boldsymbol{\lambda} > \boldsymbol{0}$ and $\boldsymbol{\rho} \ge \boldsymbol{0}$ such that for $\boldsymbol{x} \in \boldsymbol{R^d}$,

$$\sum_{i=1}^{m} |G_i\mathbf{x}|^2 \le \lambda|\mathbf{x}|^2, \sum_{i=1}^{m} \left|\mathbf{x}^{\mathrm{T}} G_i\mathbf{x}\right|^2 \ge \rho|\mathbf{x}|^4$$

hold. Then, system (5) with the initial condition $\mathbf{x}(t_0)=\mathbf{x}_0 \in \mathrm{R}^d$, $t_0 \le t$ satisfies

$$\limsup_{t\to\infty} \frac{1}{t}\log|\mathbf{x}(t; t_0, \mathbf{x}_0)| \le -\left(\rho - K - \frac{\lambda}{2}\right).$$

If $\rho > K + \frac{\lambda}{2}$, the trivial solution of system (5) is almost surely exponentially stable.

3. Stochastic stabilization of genetic regulatory networks

In this section, we shall give a sufficient condition guaranteeing the almost surely exponential stability of system (4).

Theorem 1. *If*

$$\begin{cases} \left|\begin{bmatrix} \boldsymbol{Mx}(t) \\ \boldsymbol{Ny}(t) \end{bmatrix}\right|^2 \le \begin{bmatrix} \lambda_1\boldsymbol{Ix}(t) \\ \lambda_2\boldsymbol{Iy}(t) \end{bmatrix}^T \begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \end{bmatrix} \\ \left|\begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \end{bmatrix}^T \begin{bmatrix} \boldsymbol{Mx}(t) \\ \boldsymbol{Ny}(t) \end{bmatrix}\right|^2 \ge V\begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \end{bmatrix}^T \begin{bmatrix} \rho_1\boldsymbol{Ix}(t) \\ \rho_2\boldsymbol{Iy}(t) \end{bmatrix} \end{cases} \tag{7}$$

and

$$\begin{cases} \rho_1 > \lambda_1/2 \\ \rho_2 > \lambda_2/2 \end{cases} \tag{8}$$

and

$$\begin{bmatrix} -2\boldsymbol{A} + \boldsymbol{I} + \lambda_1\boldsymbol{I} - 2\rho_1\boldsymbol{I} & \boldsymbol{0} & \boldsymbol{0} & K\boldsymbol{B} \\ \boldsymbol{0} & -2\boldsymbol{C} + \boldsymbol{I} + \lambda_2\boldsymbol{I} - 2\rho_2\boldsymbol{I} & \boldsymbol{D} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{D} & -\boldsymbol{I} & \boldsymbol{0} \\ K\boldsymbol{B} & \boldsymbol{0} & \boldsymbol{0} & -\boldsymbol{I} \end{bmatrix} < 0, \tag{9}$$

then system (4) is almost surely exponentially stable.

Proof. Constructing the following Lyapunov functional

$$V(t, \boldsymbol{x}, \boldsymbol{y}) = \boldsymbol{x}^T(t)\boldsymbol{x}(t) + \boldsymbol{y}^T(t)\boldsymbol{y}(t) + \int_{t-\tau(t)}^{t} \boldsymbol{x}^T(s)\boldsymbol{x}(s)ds + \int_{t-\sigma(t)}^{t} \boldsymbol{y}^T(s)\boldsymbol{y}(s)ds,$$

we have

$$\begin{aligned} \log(V) &= \log(V_0) + O(t) \\ &+ \int_0^t V^{-1}\left(\begin{matrix} 2\begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \end{bmatrix}^T \begin{bmatrix} -\boldsymbol{Ax}(t) + \boldsymbol{B}\mathrm{g}(\boldsymbol{y}(t-\sigma(t))) \\ -\boldsymbol{Cy}(t) + \boldsymbol{Dx}(t-\tau(t)) \end{bmatrix} + \boldsymbol{x}^{\mathrm{T}}(t)\boldsymbol{x}(t) \\ -\boldsymbol{x}^T(t-\tau(t))\boldsymbol{x}(t-\tau(t)) + \boldsymbol{y}^T(t)\boldsymbol{y}(t) \\ -\boldsymbol{y}^T(t-\sigma(t))\boldsymbol{y}(t-\sigma(t)) + \left|\begin{bmatrix} \boldsymbol{Mx}(t) \\ \boldsymbol{Ny}(t) \end{bmatrix}\right|^2 \end{matrix}\right)dt \\ &- \frac{1}{2}\int_0^t V^{-2}4\left|\begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \end{bmatrix}^T \begin{bmatrix} \boldsymbol{Mx}(t) \\ \boldsymbol{Ny}(t) \end{bmatrix}\right|^2 dt \\ &= \log(V_0) + O(t) + \int_0^t V^{-1}\Bigg[2\begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \end{bmatrix}^T \begin{bmatrix} -\boldsymbol{Ax}(t) + \boldsymbol{B}\mathrm{g}(\boldsymbol{y}(t-\sigma(t))) \\ -\boldsymbol{Cy}(t) + \boldsymbol{Dx}(t-\tau(t)) \end{bmatrix} \\ &+ \begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \\ \boldsymbol{x}(t-\tau(t)) \\ \boldsymbol{y}(t-\sigma(t)) \end{bmatrix}^T \begin{bmatrix} I & 0 & 0 & 0 \\ 0 & I & 0 & 0 \\ 0 & 0 & -I & 0 \\ 0 & 0 & 0 & -I \end{bmatrix} \begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \\ \boldsymbol{x}(t-\tau(t)) \\ \boldsymbol{y}(t-\sigma(t)) \end{bmatrix} \\ &+ \left|\begin{bmatrix} \boldsymbol{Mx}(t) \\ \boldsymbol{Ny}(t) \end{bmatrix}\right|^2 - 2V^{-1}\left|\begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \end{bmatrix}^T \begin{bmatrix} \boldsymbol{Mx}(t) \\ \boldsymbol{Ny}(t) \end{bmatrix}\right|^2\Bigg]dt \\ &\le \log(V_0) + O(t) + \int_0^t V^{-1}\Bigg[\begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \\ \boldsymbol{x}(t-\tau(t)) \\ \boldsymbol{y}(t-\sigma(t)) \end{bmatrix}^T \\ &\times \begin{bmatrix} -2\boldsymbol{A} & \boldsymbol{0} & \boldsymbol{0} & K\boldsymbol{B} \\ \boldsymbol{0} & -2\boldsymbol{C} & \boldsymbol{D} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{D} & \boldsymbol{0} & \boldsymbol{0} \\ K\boldsymbol{B} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} \end{bmatrix} \begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \\ \boldsymbol{x}(t-\tau(t)) \\ \boldsymbol{y}(t-\sigma(t)) \end{bmatrix} \\ &+ \begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \\ \boldsymbol{x}(t-\tau(t)) \\ \boldsymbol{y}(t-\sigma(t)) \end{bmatrix}^T \begin{bmatrix} \boldsymbol{I} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{I} & \boldsymbol{0} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{0} & -\boldsymbol{I} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & -\boldsymbol{I} \end{bmatrix} \begin{bmatrix} \boldsymbol{x}(t) \\ \boldsymbol{y}(t) \\ \boldsymbol{x}(t-\tau(t)) \\ \boldsymbol{y}(t-\sigma(t)) \end{bmatrix} \end{aligned}$$