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Exponential convergence analysis of uncertain genetic regulatory networks with time-varying delays ☆

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ABSTRACT

This study is concerned with the problem of exponential convergence of uncertain genetic regulatory networks with time-varying delays in the case of the unknown equilibrium point. The system's uncertainties are modeled as a structured linear fractional form. Novel stability criteria are obtained by using the lower bound lemma together with Jensen inequality lemma. In order to get rid of the rigorous constraint that the derivatives of time-varying delays must be less than one, a new approach is introduced by improving Lyapunov–Krasovskii functional rather than using the traditional free-weighting matrices. Finally, numerical examples are presented to demonstrate the effectiveness of the theoretical results.

1. Introduction

Genetic regulatory networks (GRNs) govern many essential functions of living cells. The connection of molecules in such networks is the basis for biological systems. Therefore, GRNs have become an important new area of research and received great attention over past few years [1–3,7,12–16,18,23,36].

Time delay is inevitable since the processes of transcription and translation are not instantaneous in GRNs. It also can strongly affect stimulus responses. With a delay, the response of a model to a stimulus is history dependent which means the response is dependent on the values of model variables at times previous to the response. Therefore, it has been considered in many literatures [4–6,8–10,17–25,27–29,31–35]. However, except for the traditional free-weighting matrices approach, how to get rid of the rigorous constraint that the time-derivatives of time-varying delays must be less than one still need much more consideration.

Moreover, the uncertainties such as external perturbations, parameter fluctuations and data errors are inevitable in modeling GRNs. This means that one has to investigate the stability of uncertain GRNs. In practical application, the equilibrium point may be not known in uncertain GRNs, which has been raised in [21]. Besides, it is easy to see that the linear fractional uncertainty can lead to a norm bounded one which has been investigated in [4,12,18,22,24,26–29].

Motivated by the above discussion, we choose an appropriate new Lyapunov–Krasovskii functional and use the lower bound lemma together with the Jensen inequality lemma to study the exponential convergence of uncertain GRNs with time-varying delays in the case of the unknown equilibrium point. The novel Lyapunov–Krasovskii functional can make the stability criteria applicable to both fast and slow time-varying delays directly rather than using the traditional free-weighting matrices. Meanwhile, the parameter uncertainties are modeled as a structured linear fractional form. The stability criteria obtained turn out to be feasible and effective via numerical examples.

Notations: The notations used throughout the paper are fairly standard. The superscript '*T*' stands for matrix transposition; R^n

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denotes the n-dimensional Euclidean space; $R^{n\times m}$ is the set of all $n\times m$ real matrices; the notation $P>0$ means that P is a positive definite matrix; I_n and $0_{n\times n}$ represent identity matrix and zero matrix with dimension n, respectively; diag $(\cdot)$ denotes the diagonal matrix; $col\{\cdot\}$ means a column vector. In symmetric block matrices, we use an asterisk (*) to represent a term that is induced by symmetry. Matrices, if their dimensions are not explicitly stated, are assumed to be compatible for algebraic operations.

2. Problem formulation and some preliminaries

Generally, a GRN consists of a group of genes which interact and regulate the expression of other genes by proteins. A change in expression of a gene is controlled by the stimulation and inhibition of proteins in transcriptional, translational and post-translational processes. In [14], a single gene auto-regulatory genetic network with time delays containing n mRNAs and n proteins can be described by the following equations:

$$\begin{cases} \dot m_i(t) = -a_i m_i(t) + b_i(p_1(t-\sigma(t)), p_2(t-\sigma(t)), \ldots, p_n(t-\sigma(t))) \\ \dot p_i(t) = -c_i p_i(t) + d_i m_i(t-\tau(t)),\ i=1,2,\ldots,n. \end{cases} \tag{1}$$

where $\tau(t)$ and $\sigma(t)$ are the time-varying delays. $m_i(t), p_i(t)$ are concentrations of mRNA and protein of the ith node at time t, respectively. a_i and c_i are the degradation rates of the mRNA and protein, d_i is the translation rate, $b_i(\cdot)$ is the regulatory function of the ith gene. The regulatory function is of the form $b_i(p_1(t), p_2(t), \ldots, p_n(t)) = \sum_{j=1}^{n} b_{ij}(p_j(t))$, which is called SUM logic [25]. The function $b_{ij}(p_j(t))$ is a monotonic function of the Hill form, that is,

$$b_{ij}(p_j(t)) = \begin{cases} \alpha_{ij}\dfrac{(p_j(t)/\beta_j)^{H_j}}{1+(p_j(t)/\beta_j)^{H_j}} & \text{if transcription factor } j \text{ is an activator of gene } i \\ \alpha_{ij}\dfrac{1}{1+(p_j(t)/\beta_j)^{H_j}} & \text{if transcription factor } j \text{ is a repressor of gene } i \end{cases}$$

where H_j is the Hill coefficient, β_j is a positive constant, α_{ij} is the dimensionless transcriptional rate of transcription factor j to gene i, which is a bounded constant. Therefore, (1) can be rewritten into the following form:

$$\begin{cases} \dot m_i(t) = -a_i m_i(t) + \sum\limits_{j=1}^{n} w_{ij} h_j(p_j(t-\sigma(t))) + u_i \\ \dot p_i(t) = -c_i p_i(t) + d_i m_i(t-\tau(t)), \quad i=1,2,\ldots,n. \end{cases} \tag{2}$$

where $h_j(x) = (x/\beta_j)^{H_j}/(1+(x/\beta_j)^{H_j})$, $u_i = \sum_{j\in I_i}\alpha_{ij}$ is defined as a basal rate, I_i is a set of gene j which is a repressor of gene i. The matrix $W=(w_{ij})\in\mathbb{R}^{n\times n}$ of the genetic network is defined as follows:

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

Rewriting the system (2) into a compact matrix form, we obtain

$$\begin{cases} \dot m(t) = -Am(t) + Wh(p(t-\sigma(t))) + u \\ \dot p(t) = -Cp(t) + Dm(t-\tau(t)) \end{cases} \tag{3}$$

where

$$A=\mathrm{diag}(a_1,a_2,\ldots,a_n),\quad u=col\{u_1,u_2,\ldots,u_n\},\quad C=\mathrm{diag}(c_1,c_2,\ldots,c_n),$$

$$D=\mathrm{diag}(d_1,d_2,\ldots,d_n),\quad m(t)=col\{m_1(t)\ m_2(t)\ \cdots\ m_n(t)\},$$
$$p(t)=col\{p_1(t)\ p_2(t)\ \cdots\ p_n(t)\},$$

$$h(p(t))=col\{h_1(p_1(t))\ h_2(p_2(t))\ \cdots\ h_n(p_n(t))\}.$$

In the following, we always shift an intended equilibrium point (m^*, p^*) of the system (3) to the origin by letting $x(t)=m(t)-m^*, y(t)=p(t)-p^*$. Hence, the system (3) can be transformed into the following form:

$$\begin{cases} \dot x(t) = -Ax(t) + Wf(y(t-\sigma(t))) \\ \dot y(t) = -Cy(t) + Dx(t-\tau(t)) \end{cases} \tag{4}$$

where

$$x(t)=col\{x_1(t),x_2(t),\ldots,x_n(t)\}\in R^n,\quad y(t)=col\{y_1(t),y_2(t),\ldots,y_n(t)\}\in R^n,$$

$$f(y(t))=col\{f_1(y_1(t)),f_2(y_2(t)),\ldots,f_n(y_n(t))\}\in R^n,$$

the function $f_j(y_j(t)) = h_j(y_j(t)+p_j^*) - h_j(p_j^*)$.

It is worth noting that u is dependent on W according to the systems (2) and (3). Therefore, if we take parameter uncertainties into matrix W, u should also have uncertainties. Considering parameter uncertainties into the GRNs model (4), we give the following uncertain GRNs model:

$$\begin{cases} \dot x(t) = -(A+\Delta A(t))x(t) + (W+\Delta W(t))f(y(t-\sigma(t))) + \Delta u(t) \\ \dot y(t) = -(C+\Delta C(t))y(t) + (D+\Delta D(t))x(t-\tau(t)) \\ x_0 = x(\theta)=\varphi(\theta),\ y_0=y(\theta)=\phi(\theta),\ \forall\ \theta\in[-\omega,0] \end{cases} \tag{5}$$

where $\Delta u(t) = col\{\Delta u_1(t), \Delta u_2(t), \ldots, \Delta u_n(t)\}\in R^n$. Besides, $\varphi(\cdot)$ and $\phi(\cdot)$ are the initial functions which are continuously differentiable on $[-\omega,0]$ with $\omega=\max\{\tau_2,\sigma_2\}$. We extend $\varphi(\theta),\phi(\theta)$ on $\theta\in[-2\omega,0]$ to satisfy $\|\varphi\|_\omega = \|\varphi\|_{2\omega}$, $\|\phi\|_\omega = \|\phi\|_{2\omega}$, with $\|\varphi\|_\omega = \sup_{\theta\in[-\omega,0]}\|\varphi(\theta)\|$, $\|\phi\|_\omega = \sup_{\theta\in[-\omega,0]}\|\phi(\theta)\|$, $\|\varphi\|_{2\omega} = \sup_{\theta\in[-2\omega,0]}\|\varphi(\theta)\|$, $\|\phi\|_{2\omega} = \sup_{\theta\in[-2\omega,0]}\|\phi(\theta)\|$.

Remark 1. It is easy to see that the origin is not an equilibrium point of the system (5) due to the presence of parameters uncertainties. The equilibrium point of GRNs (5) is an unknown function about the uncertainty, which cannot be calculated. However, the GRNs (5) oscillate around the parameters of system (4) when their uncertainties are small. Therefore, we can estimate the stability for system (5) around the equilibrium point of system (4) in a small region, which is relevant to the uncertain parameter $\Delta u(t)$ [21].

In order to conduct the stability analysis for the above systems, it is necessary to make the following assumptions and lemmas:

Assumption 1. $\tau(t)$ and $\sigma(t)$ are the time-varying delays satisfying $0\le\tau_1\le\tau(t)\le\tau_2$, $\dot\tau(t)\le\tau_d<\infty$; $0\le\sigma_1\le\sigma(t)\le\sigma_2$, $\dot\sigma(t)\le\sigma_d<\infty$. $\tau_1,\tau_2,\sigma_1,\sigma_2,\tau_d$ and σ_d are some constants. Let $\tau_{12}=\tau_2-\tau_1, \sigma_{12}=\sigma_2-\sigma_1$.

Assumption 2. Due to the fact that h_j is a monotonically increasing function with saturation, from the relationship of $f(\cdot)$ and $h(\cdot)$, we know that $f(\cdot)$ satisfies the sector condition: $l_j^-\le f_j(x_j)/x_j\le l_j^+$, $j=1,2,\ldots,n$; for some constants l_j^- and l_j^+, which implies that $(f_j(x_j)-l_j^- x_j)/x_j\ge 0$, $(l_j^+ x_j - f_j(x_j))/x_j\ge 0$. Let $L_0=\mathrm{diag}(l_1^-,l_2^-,\ldots,l_n^-)$, $L_1=\mathrm{diag}(l_1^+,l_2^+,\ldots,l_n^+)$.

Assumption 3. The parametric uncertainties $\Delta A(t), \Delta W(t), \Delta C(t), \Delta D(t)$ satisfy: $[\Delta A(t), \Delta W(t), \Delta C(t), \Delta D(t)] = B\Delta(t)[H_a, H_w, H_c, H_d]$, where B, H_a, H_w, H_c and H_d are some given constant matrices with appropriate dimensions. Besides, $\Delta(t)=[I-F(t)J]^{-1}F(t)$, J are known real constant matrices of appropriate dimensions and $F(t)$ are uncertain matrices satisfying $I-JJ^T>0$ and $F(t)F^T(t)\le I$, respectively.

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