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Exponential Stability of the Genetic Regulatory Networks with Delay on Time Scales

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***Abstract*—Genetic regulatory networks with delay on time scales is considered in this paper. Some sufficient conditions are obtained to ensure the existence and exponential stability of a unique equilibrium of Genetic regulatory networks. The approaches are based on constructing Lyapunov functionals, the theory of calculus on time scales and the well-known Brouwer's fixed point theorem. The obtained results are general and can be applied to corresponding continuous-time and discrete-time genetic regulatory network.**

Keywords- genetic regulatory networks; exponential stability; fixed point theorem; on time scales

I. INTRODUCTION

Genetic regulatory networks is a combination of a great number of genes and gene products interacted directly or indirectly with each other in living cells which make up a dynamic networked complex system. The dynamic behaviors of the genetic regulatory networks in living organisms become an important new area of research and received increasing attention over past few years [1], [2], [3], [4] and [10]. In addition, time delays are unavoidable in the actual evolution of the gene system, especially in the transcription and translation process. It is well-known that time delays may result in oscillation and instability of the genetic regulatory networks system. Therefore, several important results for genetic regulatory networks with time-delays have been reported in the existing literatures [5], [6]. Robust exponential stability for a class of stochastic genetic networks with uncertain parameters has been reported in [7]. According to literature [8], we know the gene interactions are characterized either in a discrete-time form or in a continuous-time case, and the topologies of the gene networks are described either deterministically or fully stochastically.Recently, the exponential stability of continuous-time and discrete-time cellular neural networks with delays has been considered in [9]. However, to the best of our knowledge, there are few investigations dealing with the stability analysis of genetic regulatory networks with delay on time scales in the existing literature. It is significant to study the genetic regulatory networks on time scales [11] which can unify the continuous and discrete situations.

Motivated by recent results [12], [13], we consider the following differential genetic regulatory networks model with delay on time scale:

$$\begin{cases} m_i^{\Delta}(t) = -a_i m_i(t) + \sum_{j=1}^{n} \omega_{ij} g_j(p_j(t-h)) + u_i, \\ p_i^{\Delta}(t) = -c_i p_i(t) + d_i m_i(t-\tau), i = 1, 2, \cdots, n. \end{cases} \tag{1}$$

$t \in \mathrm{T}$, where $m_i(t), p_i(t)$ are the concentrations of mRNA and protein of the ith gene at the time t, respectively. The parameters $a_i > 0, c_i > 0$ denote, respectively, the degradation rates of the mRNA and the protein. d_i is the translation rate. If transcription factor j is an activator of gene i, $w_{ij} = \alpha_{ij}$; if there is no link from node j to node i, $w_{ij} = 0$; if transcription factor j is a repressor of gene i, $w_{ij} = -\alpha_{ij}$. Where $\alpha_{ij} > 0$ is a bounded constant representing the dimensionless transcriptional rate of the transcription factor j to the ith gene. u_i is defined as a basal rate, $u_i = \sum_{j \in V_{i1}} \alpha_{ij}$ and V_{i1} is the set of all the j which is a repressor of gene i. The nonlinear function $g_j(\cdot) : \mathbb{R} \to \mathbb{R}$ represents the feedback regulation of the protein in the transcription process with $g_j(x) = (x/\beta_j)^{H_j} / (1 + (x/\beta_j)^{H_j})$, H_j where is the hill coefficient, β_j is a positive constant.

II. PRELIMINARIES

Definition 1: A time scale T is an arbitrary nonempty closed subset of $\mathbb{R}$. The forward and backward jump operators $\sigma, \rho : \mathrm{T} \to \mathrm{T}$ and the graininess $\mu : \mathrm{T} \to \mathbb{R}^+$ are defined, respectively, by $\sigma(t) := \inf\{s \in \mathrm{T} : s > t\}$,

$$\rho(t) := \sup\{s \in \mathrm{T} : s < t\},\ \mu(t) := \sigma(t) - t.$$

Definition 2: These jump operators enable us to classify the point t of a time scale as right-dense, right-scattered, left-

dense,left-scattered depending on whether σ(t)=t, σ(t)>t, ρ(t)=t and ρ(t)<t , respectively for any $t \in \mathrm{T}$.

Definition 3: (Lakshmikantham and Vatsala [16]). For each $t \in \mathrm{T}$, let N be a neighborhood of t . Then, we define the generalized derivative (or Dini derivative), $D^{+}u^{\Delta}(t)$ to mean that, give $\varepsilon > 0$, there exists a right neighborhood $N(\varepsilon) \subset N$ of t such that

$$\frac{u(\sigma(t))-u(s)}{u(t,s)} < D^{+}u^{\Delta}(t)+\varepsilon$$

for each $s \in N(\varepsilon)$, $s > t$, where $u(t,s)=\sigma(t)-s.$

In case t is right-scattered and u(t) is continuous at t , one gets

$$D^{+}u^{\Delta}(t)=\frac{u(\sigma(t))-u(t)}{\sigma(t)-t}.$$

For simplicity, we denote C_{rd} by the set of all right-dense continuous functions. If $p(t) \in C_{rd}$ and $1+\mu(t)p(t) > 0,$ then $p(t)$ is said to be a positive regressive function. Denote R^{+} by the set of all regressive function. Next we give the definition of the exponential function and list its useful properties.

Definition 4: (Bohner and Peterson [14]). If $p \in \Re^{+}$ is a regressive function, then the generalized exponential function $e_p(t,s)$ is defined by

$$e_p(t,s)=\exp\left\{\int_s^t \xi_{\mu(\tau)}(p(\tau))\Delta\tau\right\}, s,t \in \mathrm{T},$$

with the cylinder transformation

$$\xi_h(z)=\begin{cases}\dfrac{Log(1+hz)}{h}, h \neq 0,\\ z, h=0, \qquad h=0.\end{cases}$$

Definition 5: The equilibrium $(m_i^*,p_i^*)=(m_1^*,\cdots,m_n^*,p_1^*,\cdots p_n^*)$of system (1) is said to be exponentially stable if there exist a $\xi > 0,$ $p \in R^{+}$ and $\Gamma=\Gamma(p)>0$ such that every solution $(m_1,\cdots,m_n,p_1\cdots p_n)$ of system (1) satisfying

$$\sum_{i=1}^{n}\left|m_i(t)-m_i^*\right|+\sum_{i=1}^{n}\left|p_i(t)-p_i^*\right| \le \frac{\Gamma(p)}{\xi e_p(t,0)}$$

$$\times(\sum_{i=1}^{n}\sup_{s\in[-\tau,0]_{\mathbb{T}}}\left|m_i(s)-m_i^*\right|+\sum_{i=1}^{n}\sup_{s\in[-h,0]_{\mathbb{T}}}\left|p_i(s)-p_i^*\right|), t \in \mathrm{T}_0^{+}.$$

Lemma 1: (Bohner and Peterson [15]) If $p,q \in R,$ then

(i) $e_p(\sigma(t),s)=(1+\mu(t)p(t))e_p(t,s);$

(ii) $\dfrac{1}{e_p(t,s)}=e_{\Theta p}(t,s),$ where $e_{\Theta p}(t,s)=-\dfrac{p(t)}{1+\mu(t)p(t)};$

(iii) $e_p(t,s)e_p(s,r)=e_p(t,r);$

(iv) $e_p(t,s)e_q(t,s)=e_{p\oplus q}(t,s);$

(v) $\dfrac{e_p(t,s)}{e_q(t,s)}=e_{p\Theta q}(t,s);$

(vi) $\left(\dfrac{1}{e_p(\cdot,s)}\right)^{\Delta}=-\dfrac{p(t)}{e_p^{\sigma}(\cdot,s)};$ where $\Re:=\{p\in C_{rd}:1+\mu(t)p(t)\neq 0\}.$

Finally, we state Brouwer's fixed point theorem which enables us to prove the existence of a unique equilibrium of (1).

Theorem 1: If $K \in \mathbb{R}^n$ is a bounded closed convex set.

$\Xi \in C(K,K),$ then there exists a $x^* \in K$ with $\Xi x^*=x^*.$

Throughout this paper, we make basic assumption as follows:

$$(H_1):\ g_i:\mathbb{R}\to\mathbb{R}, \left|g_i(x)-g_i(y)\right| \le L_i\left|x-y\right|,$$

$$\left|g_i(x)\right| \le M_i, \quad for\ all\ \ x,y \in \mathbb{R}.$$

III. Existence and Uniqueness of a Equilibrium

Theorem 2: Suppose (H_1) hold, then system (1) has a unique equilibrium state if

$$\sum_{j=1}^{n}\frac{\left|d_i\right|}{a_i c_i}\left|w_{ji}\right|L_i < 1, i=1,2,\cdots,n. \tag{2}$$

Proof: An equilibrium $(m_1^*, m_2^*, \cdots, m_n^*, p_1^*, p_2^*, \cdots p_n^*)$ of (1) is a solution of the system

$$\begin{cases} -a_i m_i^* + \sum_{j=1}^{n} \omega_{ij} g_j(p_j^*) + u_i = 0, \\ -c_i p_i^* + d_i m_i^* = 0, i = 1, 2, ..., n, \end{cases}$$

which leads to

$$p_i^* = \frac{d_i}{a_i c_i}\left[\sum_{j=1}^{n} w_{ij} g_j(p_j^*) + u_i\right], i = 1, 2, \cdots, n.$$

Due to the boundedness of the activations, we have

$$\left|\frac{d_i}{a_i c_i}\left(\sum_{j=1}^{n} w_{ij} g_j(p_j^*) + u_i\right)\right| \le \frac{|d_i|}{a_i c_i}\left(\sum_{j=1}^{n} |w_{ij}| M_j + |u_i|\right) = A_i.$$

Define a function $h : \mathbb{R}^n \to \mathbb{R}^n$ as follows:

$$h(x_1, x_2, \cdots, x_n) = \{h_1(x_1, x_2, \cdots, x_n), \cdots, h_n(x_1, x_2, \cdots, x_n)\},$$
$$h(x_1, x_2, \cdots, x_n) = \frac{d_i}{a_i c_i}\left[\sum_{j=1}^{n} w_{ij} g_j(x_j^*) + u_i\right].$$

Then it will follow that $h = (h_1, h_2, \cdots, h_n)$ maps the bounded closed convex set $D = D_1 \times D_2 \times \cdots \times D_n$ into itself where $D_i = [-A_i, A_i]$. By Brouwer's fixed point theorem, there exists a fixed points say p^* of h such that $p^* = h(p^*)$ or equivalently

$$p_i^* = h_i(p_1^*, p_2^*, \cdots, p_n^*) = \frac{d_i}{a_i c_i}\left[\sum_{j=1}^{n} w_{ij} g_j(p_j^*) + u_i\right],$$

we can now define $m_i^* = \frac{c_i}{d_i} p_i^*, i = 1, 2, \cdots n,$ so that $(m_1^*, m_2^*, \cdots, m_n^*, p_1^*, p_2^*, \cdots p_n^*)$ is an equilibrium of (1).

Suppose that there are two equilibrium solutions of (1) say $(m_1^*, m_2^*, \cdots, m_n^*, p_1^*, p_2^*, \cdots p_n^*)$ and $(\overline{m}_1^*, \overline{m}_2^*, \cdots, \overline{m}_n^*, \overline{p}_1^*, \overline{p}_2^*, \cdots \overline{p}_n^*)$. Then we have

$$p_i^* - \overline{p}_i^* = \sum_{j=1}^{n} \frac{d_i}{a_i c_i} w_{ij}\left[g_j(p_j^*) - g_j(\overline{p}_j^*)\right], i = 1, 2, \cdots, n.$$

Which leads to

$$\sum_{i=1}^{n}\left|p_i^* - \overline{p}_i^*\right| \le \sum_{i=1}^{n}\sum_{j=1}^{n} \frac{|d_i|}{a_i c_i}|w_{ij}| L_j \left|p_j^* - \overline{p}_j^*\right|, i = 1, 2, \cdots, n.$$

So we have

$$\sum_{i=1}^{n}\left[1 - \sum_{j=1}^{n} \frac{|d_i|}{a_i c_i}|w_{ji}| L_i\right]\left|p_i^* - \overline{p}_i^*\right| \le 0, i = 1, 2, \cdots, n.$$

(2) implies that $p_i^* = \overline{p}_i^*, i = 1, 2, \cdots, n.$ And we have $m_i^* = \overline{m}_i^*, i = 1, 2, \cdots, n.$ The proof is completed.

III. EXPONENTIAL STABILITY OF THE EQUILIBRIUM

Let $(m_1^*, m_2^*, \cdots, m_n^*, p_1^*, p_2^*, \cdots p_n^*)$ be the equilibrium of the system (1). Let $x_i(t) = m_i(t) - m_i^*, y_i(t) = p_i(t) - p_i^*, i = 1, 2, \cdots, n.$

Then we can rewrite the system (1) as

$$\begin{cases} x_i^{\Delta}(t) = -a_i x_i(t) + \sum_{j=1}^{n} \omega_{ij}\left[g_j(y_j(t-h) + p_j^*) - g_j(p_j^*)\right], \\ y_i^{\Delta}(t) = -c_i y_i(t) + d_i x_i(t-\tau), i = 1, 2, ..., n, \end{cases} \quad (3)$$

for all $t \in \mathrm{T}_0^+$.

It is thus sufficient to establish the stability of the trivial solution of (3) in order to establish the stability of the equilibrium $(m_1^*, m_2^*, \cdots, m_n^*, p_1^*, p_2^*, \cdots p_n^*)$ of our original system.

Theorem 3: Assume that (H_1) holds, suppose further that: (H_2): If there exist some constants $\lambda_i > 0, \xi_i > 0$ and $p \in \Re^+$ such that

$$\xi_i\left[p - a_i(1 + p\mu(t))\right] + \lambda_i |d_i| (1 + p\mu(t+\tau)) e_p(t+\tau, t) < 0,$$
$$\lambda_i\left[p - c_i(1 + p\mu(t))\right] + \sum_{j=1}^{n} \xi_j |w_{ji}| L_i (1 + p\mu(t+h)) e_p(t+h, t) < 0,$$

For all $i = 1, 2, \cdots, n,\ t \in \mathrm{T}_0^+$. Then the trivial solution of (3) is exponentially stable.

Proof: It follows the Theorem 2 that the trivial solution of (3) is a unique equilibrium of (3). Now we construct the Laypunov functional $V(t) = V_1(t) + V_2(t) + V_3(t) + V_4(t),$ where

$$V_1(t)=\sum_{i=1}^{n}\xi_i e_p(t,0)\left|x_i(t)\right|,\ V_3(t)=\sum_{i=1}^{n}\lambda_i e_p(t,0)\left|y_i(t)\right|,$$

$$V_2(t)=\sum_{i=1}^{n}\sum_{j=1}^{n}\xi_i\left|w_{ij}\right|L_j\int_{t-h}^{t}(1+p\mu(s+h))e_p(s+h,0)\left|y_j(s)\right|\Delta s,$$

$$V_4(t)=\sum_{i=1}^{n}\lambda_i\left|d_i\right|\int_{t-\tau}^{t}(1+p\mu(s+\tau))e_p(s+\tau,0)\left|x_i(s)\right|\Delta s.$$

Calculating $D^+V(t)^\Delta$ along (3), we can get

$$D^+(V_1(t)+V_2(t))^\Delta\le\sum_{i=1}^{n}\xi_i\left[p-a_i(1+p\mu(t))\right]e_p(t,0)\left|x_i(t)\right|$$
$$+\sum_{i=1}^{n}\sum_{j=1}^{n}\xi_j\left|w_{ji}\right|L_i(1+p\mu(t+h))e_p(t+h,0)\left|y_j(t)\right|, \tag{4}$$

$$D^+(V_3(t)+V_4(t))^\Delta\le\sum_{i=1}^{n}\lambda_i\left[p-c_i(1+p\mu(t))\right]e_p(t,0)\left|y_i(t)\right|$$

$$+\sum_{i=1}^{n}\lambda_i\left|d_i\right|(1+p\mu(t+\tau))e_p(t+\tau,0)\left|x_i(t)\right|. \tag{5}$$

From (4) and (5), we can get

$$D^+V(t)^\Delta\le\sum_{i=1}^{n}\left\{\xi_i\left[p-a_i(1+p\mu(t))\right]\right.$$
$$\left.+\lambda_i\left|d_i\right|(1+p\mu(t+\tau))e_p(t+\tau,t)\right\}e_p(t,0)\left|x_i(t)\right|$$
$$+\sum_{i=1}^{n}\left\{\lambda_i\left[p-c_i(1+p\mu(t))\right]+\sum_{j=1}^{n}\xi_j\left|w_{ji}\right|\right.$$
$$\left.\times L_i(1+p\mu(t+h))e_p(t+h,t)\right\}e_p(t,0)\left|y_i(t)\right|.$$

By using (H_2), we can conclude that $V(t)\le V(0)$ for $t\in\mathrm{T}^+$. On the other hand, we have

$$V(0)=\Gamma(p)\left(\sum_{i=1}^{n}\sup_{s\in[-\tau,0]_{\mathrm{T}}}\left|x_i(s)\right|+\sum_{i=1}^{n}\sup_{s\in[-h,0]_{\mathrm{T}}}\left|y_i(s)\right|\right),$$

where $\Gamma(p)=\max\left\{\Delta_1,\Delta_2\right\}$,

$$\Delta_1=\max_i\left\{\xi_i+\lambda_i\left|d_i\right|\int_{-\tau}^{0}(1+p\mu(s+\tau))e_p(s+\tau,0)\Delta s\right\},$$

$$\Delta_2=\max_i\left\{\lambda_i+\sum_{i=1}^{n}\xi_j\left|w_{ji}\right|L_i\int_{-h}^{0}(1+p\mu(s+h))e_p(s+h,0)\Delta s\right\},$$

which means that

$$\min\left\{\xi_i,\lambda_i\right\}e_p(t,0)\left(\sum_{i=1}^{n}\left|x_i(t)\right|+\sum_{i=1}^{n}\left|y_i(t)\right|\right)\le V(t)\le V(0).$$

Thus, we finally get

$$\sum_{i=1}^{n}\left|x_i(t)\right|+\sum_{i=1}^{n}\left|y_i(t)\right|\le\frac{\Gamma(p)e_{\Theta p}(t,0)}{\min\left\{\xi_i,\lambda_i\right\}}\left(\sum_{i=1}^{n}\sup_{s\in[-\tau,0]_{\mathrm{T}}}\left|x_i(s)\right|\right.$$
$$\left.+\sum_{i=1}^{n}\sup_{s\in[-h,0]_{\mathrm{T}}}\left|y_i(s)\right|\right).$$

Therefore, the trivial solution of (3) is exponentially stable.

The proof is completed.

From Theorem 2 and Theorem 3 we can obtain the following result.

Corollary 1: Suppose (H_1) and (2) holds, and there exist some constants $\lambda_i>0,\xi_i>0$ and $p>0$ such that

$$\begin{cases}\xi_i(p-a_i)+\lambda_i\left|d_i\right|\mathrm{e}^{p\tau}<0,\\ \lambda_i(p-c_i)+\mathrm{e}^{ph}\sum_{j=1}^{n}\xi_j\left|w_{ji}\right|\mathrm{L}_i<0, i=1,2,\ldots,n,\end{cases} \tag{6}$$

$t\in\mathrm{T}_0^+$. then system (1) exists a unique equilibrium which is exponentially stable.

From Theorem 2 and Theorem 3 we can also obtain the following corollary.

Remark 1: Conditions (6) can be replaced by

$$-\xi_i a_i+\lambda_i\left|d_i\right|<0,\ -c_i\lambda_i+\sum_{j=1}^{n}\xi_j\left|w_{ji}\right|\mathrm{L}_i<0.$$

Remark 2: If the time scales $\mathrm{T}=\mathbb{Z}$ $(\mu(t)=1)$ then system (1) also includes the discrete-time delayed genetic regulatory networks model as its special cases:

$$\begin{cases} m_i(k+1)-m_i(k)=-a_i m_i(k)+u_i+\sum_{j=1}^{n} w_{ij} g_j(p_j(k-h)), \\ p_i(k+1)-p_i(k)=-c_i p_i(k)+d_i m_i(k-\tau),\ i=1,2,...,n, \end{cases}$$

where $k \in \{0,1,\cdots.\}$, h and τ are positive integers.

Corollary 2: Suppose (H_1) and (2) holds, and there exist some constants $\lambda_i > 0, \xi_i > 0$ and $p > 0$ such that

$$\xi_i\left[p-a_i(1+p)\right]+\lambda_i\left|d_i\right|(1+\mathrm{p})^{\tau+1}<0,$$

$$\lambda_i\left[p-c_i(1+p)\right]+(1+p)^{h+1}\sum_{j=1}^{n}\xi_j\left|w_{ji}\right|\mathrm{L}_i<0, i=1,2,\cdots,n.$$

$t \in \mathrm{T}_0^+$. then system (1) exists a unique equilibrium which is exponentially stable.

IV. Concluding Remarks

In this paper, we studied exponential stability of the genetic regulatory networks model with delay on time scales an obtained some more generalized results to ensure the existence, uniqueness and global exponential stability of the equilibrium. These results can give a significant insight into the complex dynamical structure of genetic regulatory networks model. The conditions are easily checked in practice by simple algebraic methods.

Reference

[1] L. Chen, K. Aihara, Stability of genetic regulatory networks with time delay, IEEE Trans. Circuits Syst, 2002, pp. 602-608.

[2] C. Li, L. Chen, K. Aihara, Synchronization of coupled nonidentical enetic oscillators, Phys. Biol, 2006, pp. 37-44.

[3] P.Balasubramaniam,R.Rakkiyappan,R. Krishnasamy,Stochastic stability of Markovian jumping uncertain stochastic genetic regulatory networks with interval time-varying delays, Math. Biosci, 2010, pp. 97-108.

[4] W.Zhang, J.Fang, Y.Tang, New robust stability analysis for genetic regulatory networks with random discrete delays and distributed delays, Neurocomputing, 2011, pp. 44-60

[5] X. Lou, Q. Ye, B. Cui, Exponential stability of genetic regulatory networks with random delays, Neurocomputing, 2010, pp. 759-769.

[6] Z. Wang, X. Liao, S. Guo, H. Wu, Mean square exponential stability of stochastic genetic regulatory networks with time-varying delays, Inf. Sci, 2011, pp. 792-811.

[7] G. Wang, J. Cao, Robust exponential stability analysis for stochastic genetic networks with uncertain parameters, Commun. Nonlinear. Sci, 2009, pp. 3369-3378.

[8] I. Ivanov, E. Dougherty, Modeling genetic regulatory networks: continuous or discrete?, J Biol. Syst, 2006, pp. 219-230.

[9] S. Mohamad, K. Gopalsamy, Exponential stability of continuous-time and discrete-time cellular neural networks with delays, Appl. Math. Comput, 2003, pp. 17-38.

[10] J. Hu, J. Liang, J. Cao, Stability analysis for genetic regulatory networks with delays: The continuous-time case and the discrete-time case, Applied Mathematics and Computation, 2013, pp. 507-517.

[11] S. Hilger, Analynis on measure chains-unified approach to continuous and discrete calculus, Results in Mathematics, 1990, pp. 18-56.

[12] S. Lakshmanana, Fathalla A. Rihan, Stability analysis of the differential genetic regulatory networks model with time-varying delays and Markovian jumping parameters, Nonlinear Analysis, Hybrid Syst, 2014, pp. 1-15.

[13] K.Gopalsamy, Second order neurons and learning in cohen-grossberg networks,International Joural of Neural Systems, 2006, pp. 179-189.

[14] M. Bohner, A. Peterson, Dynamic Equations on Time Scales, An introduction with applications, Birkhauser Boston, 2001.

[15] M. Bohner, A. Peterson, Advance in Dynamic Equations on Time Scales, Birkhauser Boston, 2003.

[16] V. Lakshmikantham, A. Vatsala, Hybrid systems on time scales, J. Of Comput. Appl. Math., 2002, pp. 227-235.

[17] B. Shi, X. Wang, Introductions to Functional Analysis with Application, Beijing, 2006..