DOI 10.1007/s10958-019-04232-x
Journal of Mathematical Sciences, Vol. 238, No. 3, April, 2019

SYNCHRONIZATION ANALYSIS FOR A CLASS OF GENETIC OSCILLATOR NETWORKS

Q. Gao, J. Du, and X. Liu

UDC 517.9

We consider a synchronization problem for genetic oscillator networks. The genetic oscillators are modeled as nonlinear systems of the Lur'e type. Simple and verifiable synchronization conditions are presented for genetic oscillator networks by using the theory of absolute stability and the matrix theory. A network composed of coupled Goodwin models is used as an example of numerical simulation to verify the efficiency of the theoretical method.

1. Introduction

Genetic oscillator networks have recently received increasing attention of the researchers due to their wide applications in biological and biomedical sciences [1, 2]. In general, these networks can be regarded as a class of complex dynamic networks in which the nodes denote the genetic oscillators, while the inner or outer couplings denote the interactions. Circadian rhythms, cell cycle, and synthetic oscillators are typical phenomena or examples of genetic oscillators [3]. It is of great importance to study the collective dynamics of genetic oscillator networks with a hope to understand the intrinsic biological mechanisms of the rhythmic behavior of living organisms. Synchronization is a universal phenomenon and typically occurs in genetic oscillator networks [4–6]. In [7], a coupling scheme was introduced to realize synchronization of a population of cells. Until now, the problem of synchronization of genetic oscillator networks has been thoroughly investigated by experiments, numerical simulations, and theoretical analysis [8–18].

Mathematically many genetic oscillators, such as repressilators [1], the Goodwin model [19], and circadian oscillators [20] can be represented in the form of multiple additive terms each of which is, in particular, of the linear, Michaelis–Menten, or Hill forms. The genetic oscillators whose structure is described above can be expressed in the form of Lur'e systems and can be further analyzed by using the control theory pertinent to the Lur'e systems [21]. The aim of the present paper is to systemically analyze the problem of synchronization of genetic oscillator networks both by the general theoretical analysis and by numerical simulations. We first transform genetic oscillators into Lur'e-type nonlinear systems and introduce genetic oscillator networks composed of genetic oscillators with this special structure. Then we present simple criteria for the synchronization of genetic oscillator networks by using the theory of absolute stability and the matrix theory. A network consisting of Goodwin models is used as an example to confirm the theoretical results. The obtained synchronization conditions can be represented in the form of linear matrix inequalities (LMIs) [22], which can be easily verified by using the LMI toolbox in MATLAB. In addition, the established theoretical results are general and applicable to other biochemical and neural networks in which every node is a Lur'e system.

Notation: X^T denotes the transpose of a matrix X; $X > 0$ ($X \geq 0$) means that X is a positive definite (semidefinite) matrix; $X < 0$ ($X \leq 0$) denotes a negative definite (semidefinite) matrix X; I_N denotes the identity

Key Lab Ind. Comput. Control Eng. Hebei Province, Inst. Electr. Eng. Yanshan University, Qinhuangdao, 066004, China; e-mail: liuxian@ysu.edu.cn.

Published in Neliniini Kolyvannya, Vol. 20, No. 4, pp. 477–487, October–December, 2017. Original article submitted November 12, 2013; revision submitted September 15, 2016.

 1072-3374/19/2383–0236

matrix of dimension N; R_+ denotes the set of positive real numbers, and diag $(X_1, \ldots, X_n)$ and $U \otimes V$ denote

$$\begin{pmatrix} X_1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & X_n \end{pmatrix} \quad \text{and} \quad U \otimes V = \begin{pmatrix} u_{11}V & \cdots & u_{1m}V \\ \vdots & \ddots & \vdots \\ u_{n1}V & \cdots & u_{nm}V \end{pmatrix},$$

respectively.

2. Formulation of the Problem

The notion of mathematically many genetic oscillators can be formulated in the form of multiple additive terms, which are monotonically increasing or monotonically decreasing functions. We now consider a general genetic oscillator of the following form:

$$\dot{x}(t) = Ax(t) + \sum_{h=1}^{k} B_h f_h(C_h x(t)), \tag{1}$$

where $x(t) \in R^n$ denotes the concentrations of proteins, RNAs, and chemical complexes; $A \in R^{n\times n}$, $B_h \in R^{n\times m}$, and $C_h \in R^{m\times n}$ are constant matrices;

$$f_h(C_h x(t)) = \left[f_{h1}(c_{h1}^T x(t)), \ldots, f_{hm}(c_{hm}^T x(t)) \right]^T$$

is piecewise continuously differentiable on R^m; $f_{hl}(c_{hl}^T x(t))$ is a monotonically increasing or monotonically decreasing regulatory function, which is usually of the Michaelis–Menten [23] or Hill form [23], and k is an integer greater than or equal to 1. Note that all entries of $f_h(C_h x(t))$ should not be simultaneously increasing or decreasing, i.e., some of the entries are increasing, while the other entries are decreasing.

Assumption 1. *The nonlinear functions $f_{hl}(\cdot)$, $h = 1, 2, \ldots, k$, $l = 1, 2, \ldots, m$, satisfy the following slope restrictions:*

$$\gamma_{hl} \le f'_{hl}(\sigma) \le \delta_{hl} \quad \forall \sigma \in R, \quad h = 1, 2, \ldots, k, \quad l = 1, 2, \ldots, m. \tag{2}$$

Remark 1. For monotonic increasing functions, we have $\gamma_{hl} = 0$ and $\delta_{hl} > 0$, whereas for the monotonically decreasing functions, we get $\gamma_{hl} < 0$ and $\delta_{hl} = 0$. Setting

$$\varphi_{hl}(\sigma) = \frac{df_{hl}(\sigma)}{dt},$$

we can rewrite the restrictions in (2) in the form

$$\gamma_{hl} \le \frac{\varphi_{hl}(\sigma)}{\dot{\sigma}} \le \delta_{hl} \quad \forall \sigma \in R, \quad h = 1, 2, \ldots, k, \quad l = 1, 2, \ldots, m. \tag{3}$$

System (1) describes numerous well-known genetic systems, such as the repressilator [1], the Goodwin model [19] and the circadian oscillator [20]. It can be written as follows:

$$\dot{x}(t) = Ax(t) + BF(Cx(t)), \tag{4}$$

where

$$B = [B_1, \ldots, B_k], \quad C = \left[C_1^T, \ldots, C_k^T\right]^T, \quad F(Cx(t)) = \left[f_1^T(C_1x(t)), \ldots, f_k^T(C_kx(t))\right]^T,$$

and the components

$$f_{hl}\left(c_{hl}^T x(t)\right), \quad h = 1, 2, \ldots, k, \quad l = 1, 2, \ldots, m,$$

of $F(Cx(t))$ satisfy (2). Equation (4) has the form of a Lur'e system and can be investigated by using the classical Lur'e-system method in the control theory.

Remark 2. Note that the nonlinearities introduced in [8, 17] have a specific form and their number is equal to two. However, these nonlinearities can be more general and their number can be greater than two, as long as (3) is satisfied.

Note that the description of these nonlinearities differs from the description presented in [8, 17]. Equation (4) includes more than two ($k > 2$) nonlinearity vectors whose structure is simpler than the structure presented in [8, 17].

We now consider a genetic oscillator network formed by N identical genetic oscillators

$$\dot{x}_i(t) = Ax_i(t) + BF(Cx_i(t)) + \sum_{j=1}^{N} G_{ij} Dx_j(t), \quad i = 1, 2, \ldots, N, \tag{5}$$

where $x_i(t) \in R^n$ is the vector of state of the ith genetic oscillator, $D \in R^{n\times n}$ is a constant matrix linking coupled variables, G_{ij} is positive if the oscillator j is directly linked to the oscillator i; otherwise, G_{ij} is equal to zero and

$$\sum_{j=1, j\neq i}^{N} G_{ij} = -G_{ii}, \quad i = 1, 2, \ldots, N.$$

The matrix $G = (G_{ij}) \in R^{N\times N}$ indicates the connection topology, direction, and coupling strength. It is supposed to be irreducible.

Definition 1. *The genetic oscillator network (5) is said to be synchronous [24] if*

$$\lim_{t\to\infty} \|x_i(t) - s(t)\| = 0, \quad i = 1, 2, \ldots, N, \tag{6}$$

where $\|\cdot\|$ is the Euclidean norm and $s(t) \in R^n$ is a solution of an individual genetic oscillator

$$\dot{s}(t) = As(t) + BF(Cs(t)). \tag{7}$$

The synchronization state $s(t)$ satisfies the relation

$$\dot{s}(t) = As(t) + BF(Cs(t)) + \sum_{j=1}^{N} G_{ij} Ds(t) \tag{8}$$

due to the fact that

$$\sum_{j=1, j\neq i}^{N} G_{ij} = -G_{ii}.$$

The main aim is to study the synchronization problem for the genetic oscillator network (5) and derive the LMI-based sufficient conditions guaranteeing that the network is synchronous.

3. Methods and Results

We define the synchronous error as follows: $e_i(t) = x_i(t) - s(t)$. Subtracting (7) from (5), for the dynamics of the synchronous error, we get

$$\dot{e}_i(t) = Ae_i(t) + B\eta(Ce_i(t); s(t)) + \sum_{j=1}^{N} G_{ij} De_j(t), \quad i = 1, 2, \ldots, N, \tag{9}$$

where

$$\eta(Ce_i(t); s(t)) = F(Ce_i(t) + Cs(t)) - F(Cs(t)) = \left[\eta_{11}\left(c_{11}^T e_i(t); s(t)\right),\right.$$

$$\left.\ldots, \eta_{1m}\left(c_{1m}^T e_i(t); s(t)\right), \ldots, \eta_{k1}\left(c_{k1}^T e_i(t); s(t)\right), \ldots, \eta_{km}\left(c_{km}^T e_i(t); s(t)\right)\right]^T.$$

From (2), it is easy to see that the components of $\eta(Ce_i(t); s(t))$ satisfy the sector conditions

$$\gamma_{hl} \leq \frac{\eta_{hl}\left(c_{hl}^T e_i(t); s(t)\right)}{c_{hl}^T e_i(t)} = \frac{f_{hl}\left(c_{hl}^T e_i(t) + c_{hl}^T s(t)\right) - f_{hl}\left(c_{hl}^T s(t)\right)}{c_{hl}^T e_i(t)} \leq \delta_{hl} \tag{10}$$

for all $c_{hl}^T e_i(t) \neq 0$, $i = 1, 2, \ldots, N$, $h = 1, 2, \ldots, k$, $l = 1, 2, \ldots, m$ and $t \in R_+$. Inequality (10) is equivalent to

$$\left[\eta_{hl}\left(c_{hl}^T e_i(t); s(t)\right) - \gamma_{hl} c_{hl}^T e_i(t)\right]\left[\eta_{hl}\left(c_{hl}^T e_i(t); s(t)\right) - \delta_{hl} c_{hl}^T e_i(t)\right] \leq 0. \tag{11}$$

We denote

$$e(t) = \left[e_1^T(t), \ldots, e_N^T(t)\right]^T, \quad S(t) = \left[s^T(t), \ldots, s^T(t)\right]^T,$$

$$\eta[(I_N \otimes C)e(t); S(t)] = \left[\eta^T(Ce_1(t); s(t)), \ldots, \eta^T(Ce_N(t); s(t))\right]^T.$$

As a result, the error dynamical subsystems in (9) are reduced to

$$\dot{e}(t) = (I_N \otimes A + G \otimes D)e(t) + (I_N \otimes B)\eta[(I_N \otimes C)e(t); S(t)]. \tag{12}$$

The error dynamical system (12) can also be regarded as a Lur'e system. Thus, if (12) is absolutely stable, then the genetic oscillator network (5) is synchronous. In what follows, the absolute stability criteria for (12) are deduced by using the theory of absolute stability and the matrix theory. These criteria guarantee the simultaneous synchronization of the genetic oscillator network (5). Denote

$$\Gamma = \text{diag}\,(\gamma_{11}, \ldots, \gamma_{1m}, \ldots, \gamma_{k1}, \ldots, \gamma_{km}) \in R^{km \times km}$$

and

$$\Delta = \text{diag}\,(\delta_{11}, \ldots, \delta_{1m}, \ldots, \delta_{k1}, \ldots, \delta_{km}) \in R^{km \times km}.$$

Theorem 1. *Suppose that G is symmetric and μ_i, $i = 1, \ldots, N$, are its eigenvalues. The genetic oscillator network (5) is synchronous if there exist positive-definite matrices $P_i \in R^{n \times n}$, $i = 1, \ldots, N$, and positive-definite diagonal matrices $\Lambda_1 \in R^{km \times km}$ and $\Lambda_2 \in R^{km \times km}$ such that the following LMIs are true:*

$$\begin{bmatrix} \Sigma_1 & \Sigma_2 & \frac{1}{2}(A + \mu_i D)^T C^T (\Gamma + \Delta)\Lambda_2 \\ \Sigma_2^T & -\Lambda_1 - B^T C^T \Gamma \Lambda_2 \Delta C B & \frac{1}{2} B^T C^T (\Gamma + \Delta)\Lambda_2 \\ \frac{1}{2}\Lambda_2(\Gamma + \Delta)C(A + \mu_i D) & \frac{1}{2}\Lambda_2(\Gamma + \Delta)CB & -\Lambda_2 \end{bmatrix} < 0, \tag{13}$$

$$i = 1, \ldots, N,$$

where

$$\Sigma_1 = P_i(A + \mu_i D) + (A + \mu_i D)^T P_i - C^T \Gamma \Lambda_1 \Delta C - (A + \mu_i D)^T C^T \Gamma \Lambda_2 \Delta C (A + \mu_i D),$$

$$\Sigma_2 = P_i B + \frac{1}{2} C^T (\Gamma + \Delta)\Lambda_1 - (A + \mu_i D)^T C^T \Gamma \Lambda_2 \Delta C B.$$

Proof. Since G is symmetric and irreducible, 0 is its eigenvalue with multiplicity 1 and all other eigenvalues satisfy the relations

$$0 = \mu_1 > \mu_2 \geq \ldots \geq \mu_N.$$

It is possible to find an orthogonal matrix U such that $U^T G U = \mu$, where $\mu = \text{diag}\,(\mu_1, \ldots, \mu_N)$. Combining multiple LMIs in (13) into a single large LMI and applying convenient column and row permutations to the resulting inequality, we transform inequality (13) into

$$\begin{bmatrix} \Xi_1 & \Xi_2 & \Xi_3 \\ \Xi_2^T & -I_N \otimes \Lambda_1 - I_N \otimes B^T C^T \Gamma \Lambda_2 \Delta C B & \frac{1}{2}[I_N \otimes B^T C^T (\Gamma + \Delta)\Lambda_2] \\ \Xi_3^T & \frac{1}{2}[I_N \otimes \Lambda_2(\Gamma + \Delta)CB] & -I_N \otimes \Lambda_2 \end{bmatrix} < 0, \tag{14}$$

where

$$\Xi_1 = \tilde{P}(I_N \otimes A + \mu \otimes D) + (I_N \otimes A + \mu \otimes D)^T \tilde{P} - I_N \otimes C^T \Gamma \Lambda_1 \Delta C - (I_N \otimes A + \mu \otimes D)^T \times \left(I_N \otimes C^T \Gamma \Lambda_2 \Delta C\right)(I_N \otimes A + \mu \otimes D),$$

$$\Xi_2 = \tilde{P}(I_N \otimes B) + \frac{1}{2}\left[I_N \otimes C^T(\Gamma + \Delta)\Lambda_1\right] - (I_N \otimes A + \mu \otimes D)^T \left(I_N \otimes C^T \Gamma \Lambda_2 \Delta C B\right),$$

$$\Xi_3 = \frac{1}{2}(I_N \otimes A + \mu \otimes D)^T \left[I_N \otimes C^T(\Gamma + \Delta)\Lambda_2\right], \quad \tilde{P} = \operatorname{diag}(P_1, \ldots, P_N).$$

We take

$$X = \operatorname{diag}(U \otimes I_n, U \otimes I_{km}, U \otimes I_{km}).$$

Pre- and post-multiplying both sides of (14) by X and X^T, we find

$$\begin{bmatrix} \Pi_1 & \Pi_2 & \Pi_3 \\ \Pi_2^T & -I_N \otimes \Lambda_1 - I_N \otimes B^T C^T \Gamma \Lambda_2 \Delta C B & \frac{1}{2}\left[I_N \otimes B^T C^T (\Gamma + \Delta)\Lambda_2\right] \\ \Pi_3^T & \frac{1}{2}[I_N \otimes \Lambda_2(\Gamma + \Delta)CB] & -I_N \otimes \Lambda_2 \end{bmatrix} < 0, \tag{15}$$

where

$$\Pi_1 = P(I_N \otimes A + G \otimes D) + (I_N \otimes A + G \otimes D)^T P - I_N \otimes C^T \Gamma \Lambda_1 \Delta C - (I_N \otimes A + G \otimes D)^T \left(I_N \otimes C^T \Gamma \Lambda_2 \Delta C\right)(I_N \otimes A + G \otimes D),$$

$$\Pi_2 = P(I_N \otimes B) + \frac{1}{2}\left[I_N \otimes C^T(\Gamma + \Delta)\Lambda_1\right] - (I_N \otimes A + G \otimes D)^T (I_N \otimes C^T \Gamma \Lambda_2 \Delta C B),$$

$$\Pi_3 = \frac{1}{2}(I_N \otimes A + G \otimes D)^T \left[I_N \otimes C^T(\Gamma + \Delta)\Lambda_2\right], \quad P = (U \otimes I_n)\tilde{P}\left(U^T \otimes I_n\right).$$

In view of (3) and (11), the derivative of $V(e(t)) = e^T(t)Pe(t)$ satisfies the inequality

$$\dot{V}(e(t)) \le \dot{e}^T(t)Pe(t) + e^T(t)P\dot{e}(t)$$

$$-\sum_{i=1}^{N}\sum_{h=1}^{k}\sum_{l=1}^{m}\lambda_{1hl}\left[\eta_{hl}(c_{hl}^{T}e_i(t);s(t))-\gamma_{hl}c_{hl}^{T}e_i(t)\right]\left[\eta_{hl}(c_{hl}^{T}e_i(t);s(t))-\delta_{hl}c_{hl}^{T}e_i(t)\right]$$

$$-\sum_{i=1}^{N}\sum_{h=1}^{k}\sum_{l=1}^{m}\lambda_{2hl}\left[\varphi_{hl}(c_{hl}^{T}e_i(t);s(t))-\gamma_{hl}c_{hl}^{T}\dot{e}_i(t)\right]\left[\varphi_{hl}(c_{hl}^{T}e_i(t);s(t))-\delta_{hl}c_{hl}^{T}\dot{e}_i(t)\right], \quad (16)$$

where

$$I_N\otimes\Lambda_1=\operatorname{diag}(\lambda_{111},\ldots,\lambda_{1km}) \quad \text{and} \quad I_N\otimes\Lambda_2=\operatorname{diag}(\lambda_{211},\ldots,\lambda_{2km}).$$

If (15) is satisfied, then $\dot{V}(e(t))<0$. This means that (12) is absolutely stable and, hence, the genetic oscillator network (5) is synchronous.

Theorem 1 is proved.

Remark 3. The inequalities contained in (13) are LMIs. Thus, we can use the solver "feasp" from the LMI toolbox in MATLAB to compute the solution to the given LMIs.

Remark 4. Both the sector conditions (10) and the slope restrictions (3) are taken into account through the derivation of Theorem 1.

If the analyzed network is globally coupled and, hence, G has the form of a globally coupled matrix

$$G=\begin{pmatrix} -N+1 & 1 & \cdots & 1 \\ 1 & -N+1 & \cdots & 1 \\ \vdots & \vdots & \ddots & \vdots \\ 1 & 1 & 1 & -N+1 \end{pmatrix},$$

then we get the following results:

Theorem 2. *Suppose that G is a globally coupled matrix. The genetic oscillator network (5) is synchronous if there exist matrices $P_1=P_1^T>0$ and $P_2=P_2^T>0$ and diagonal matrices $\Lambda_1>0$ and $\Lambda_2>0$ such that the following LMIs are true:*

$$\begin{bmatrix} P_1A+A^TP_1-C^T\Gamma\Lambda_1\Delta C & & \\ -A^TC^T\Gamma\Lambda_2\Delta CA & P_1B+\frac{1}{2}C^T(\Gamma+\Delta)\Lambda_1-A^TC^T\Gamma\Lambda_2\Delta CB & \frac{1}{2}A^TC^T(\Gamma+\Delta)\Lambda_2 \\ B^TP_1+\frac{1}{2}\Lambda_1(\Gamma+\Delta)C & & \\ -B^TC^T\Delta\Lambda_2\Gamma CA & -\Lambda_1-B^TC^T\Gamma\Lambda_2\Delta CB & \frac{1}{2}B^TC^T(\Gamma+\Delta)\Lambda_2 \\ \frac{1}{2}\Lambda_2(\Gamma+\Delta)CA & \frac{1}{2}\Lambda_2(\Gamma+\Delta)CB & -\Lambda_2 \end{bmatrix}<0, \quad (17)$$

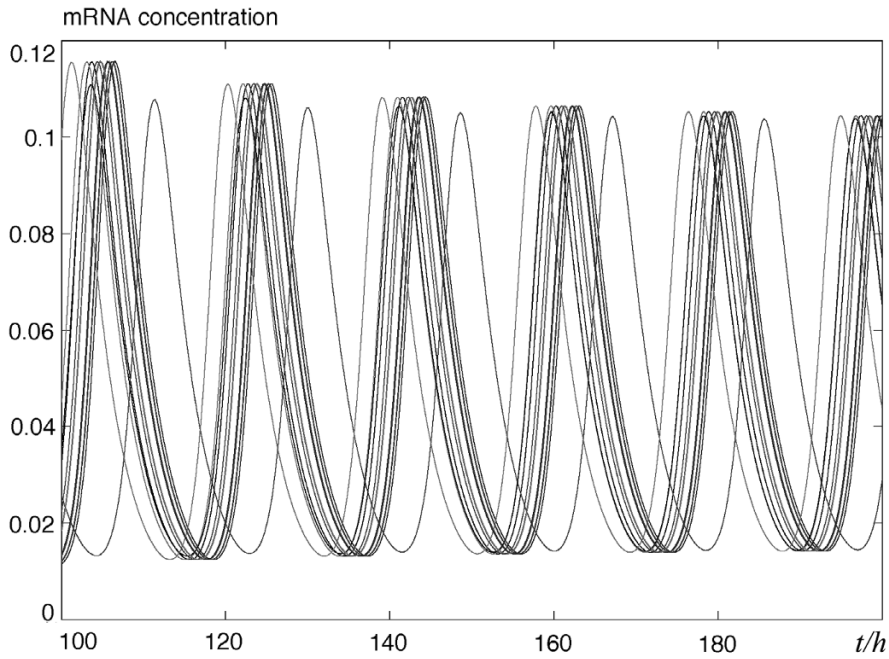

Fig. 1. Time evolution of the mRNA concentrations of 20 uncoupled oscillators.

$$\begin{bmatrix} \Omega_1 & \Omega_2 & \frac{1}{2}(A-ND)^T C^T(\Gamma+\Delta)\Lambda_2 \\ \Omega_2^T & -\Lambda_1 - B^T C^T \Gamma \Lambda_2 \Delta C B & \frac{1}{2} B^T C^T (\Gamma+\Delta)\Lambda_2 \\ \frac{1}{2}\Lambda_2(\Gamma+\Delta)C(A-ND) & \frac{1}{2}\Lambda_2(\Gamma+\Delta)CB & -\Lambda_2 \end{bmatrix} < 0, \tag{18}$$

where

$$\Omega_1 = P_2(A-ND) + (A-ND)^T P_2 - C^T \Gamma \Lambda_1 \Delta C - (A-ND)^T C^T \Gamma \Lambda_2 \Delta C (A-ND),$$

$$\Omega_2 = P_2 B + \frac{1}{2} C^T (\Gamma+\Delta)\Lambda_1 - (A-ND)^T C^T \Gamma \Lambda_2 \Delta C B.$$

Proof. If G is a globally coupled matrix, then it has two different eigenvalues, i.e., $\mu_1 = 0$ and $\mu_2 = -N$. The LMIs in (13) are reduced to the LMIs in (17) and (18).

Remark 5. If the genetic oscillator network (5) is a globally coupled network, then it is necessarily to verify only two LMIs.

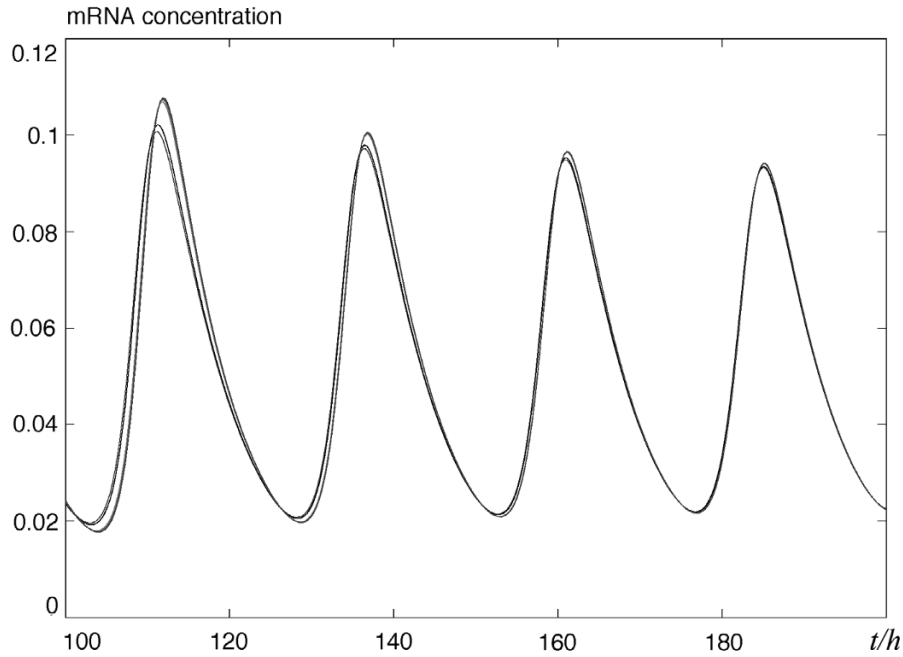

Fig. 2. Time evolution of the mRNA concentrations of 20 coupled oscillators.

4. Numerical Example

We consider a genetic oscillator network globally coupled by the classical Goodwin model [19], which describes the dynamic evolution of the coupled suprachiasmatic nucleus

$$\begin{aligned} \dot{X}_i &= k_1 \frac{1}{1+Z_i^H} - k_5 X_i + KR, \\ \dot{Y}_i &= k_2 X_i - k_6 Y_i, \\ \dot{Z}_i &= k_3 Y_i - k_7 Z_i, \\ \dot{V}_i &= k_4 X_i - k_8 V_i, \quad i = 1, \ldots, N, \end{aligned} \tag{19}$$

where the variables X_i, Y_i, and Z_i denote the concentrations of the clock gene mRNA, clock protein, and transcription inhibitor, the variable V_i denotes the evolution of the neurotransmitter, k_1, k_2, k_3, and k_4 are positive synthesis rate constants, k_5, k_6, k_7, and k_8 are positive degradation rate constants, H denotes the Hill coefficient and is a positive number, $K > 0$ denotes the coupling strength, and

$$R = \frac{1}{N} \sum_{j=1}^{N} V_j$$

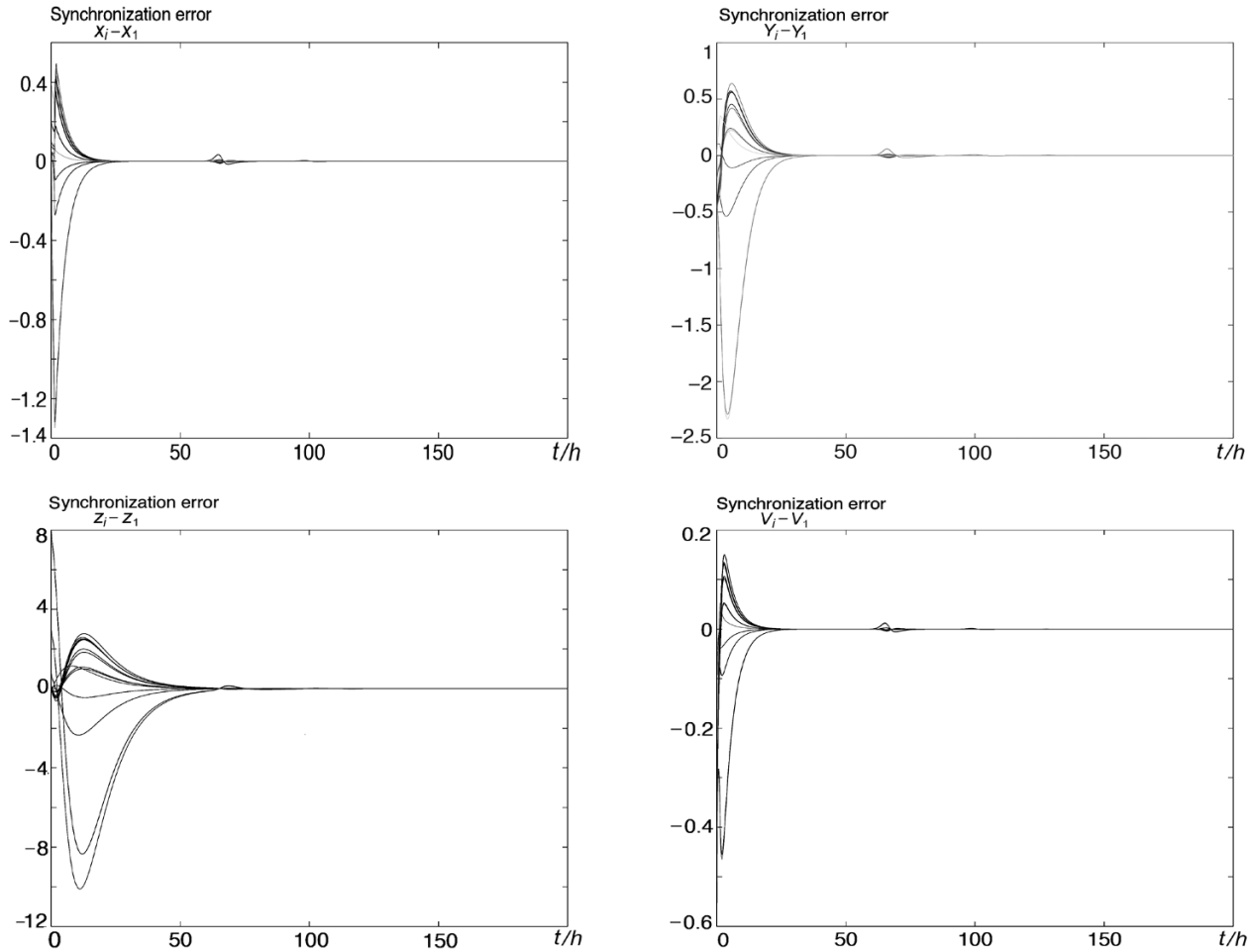

Fig. 3. Time evolution of the synchronization error between 20 coupled gene oscillators.

denotes the average neurotransmitter level and is regarded as the coupling term. The genetic oscillator network (19) can be represented in the form (5) with

$$A = \begin{pmatrix} -k_5 & 0 & 0 & K \\ k_2 & -k_6 & 0 & 0 \\ 0 & k_3 & -k_7 & 0 \\ k_4 & 0 & 0 & -k_8 \end{pmatrix}, \quad B = \begin{pmatrix} k_1 \\ 0 \\ 0 \\ 0 \end{pmatrix}, \quad C = \begin{pmatrix} 0 & 0 & 1 & 0 \end{pmatrix},$$

$$G = \begin{pmatrix} -N+1 & 1 & \cdots & 1 \\ 1 & -N+1 & \cdots & 1 \\ \vdots & \vdots & \ddots & \vdots \\ 1 & 1 & 1 & -N+1 \end{pmatrix}, \quad D = \begin{pmatrix} 0 & 0 & 0 & \frac{K}{N} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad F(Z_i) = \frac{1}{1 + Z_i^H}.$$

The parameters in (19) are chosen so that a single cell oscillator produces self-sustained oscillations with a circadian period. The values of these parameters are chosen as follows:

$$H = 12, \quad k_1 = 1.2nM \cdot h^{-1}, \quad k_2 = k_3 = 1h^{-1}, \quad k_4 = 0.7h^{-1},$$

$$k_5 = 0.25h^{-1}, \quad k_6 = 0.3h^{-1}, \quad k_7 = 0.1h^{-1}, \quad k_8 = 1.8h^{-1}.$$

In what follows, we validate the efficiency of the established theoretical method by using a network of small size with 20 genetic oscillators. We set $K = 0$. This implies that the oscillators in the network are uncoupled. In Fig. 1, we illustrate the time evolution of the mRNA concentration of 20 uncoupled oscillators with different initial conditions. It is easy to see that 20 uncoupled oscillators are not synchronous although the period of each oscillator is approximately equal to 24 h. We set $K = 0.3$. Since G is a matrix of global coupling, its eigenvalues are such that

$$\mu_1 = 0, \quad \mu_2 = \ldots = \mu_{20} = -20. \tag{20}$$

It is necessary to verify only two LMIs (17) and (18) in order to determine whether the analyzed network is synchronous. Substituting the parameters presented above in (17) and (18), feasible solutions can be obtained by using the LMI toolbox in MATLAB. This indicates that the considered network is synchronous according to Theorem 2. In Fig. 2, we show the time evolution of the mRNA concentration of 20 oscillators in the network. In Fig. 3 we illustrate the time evolution of the synchronization error between 20 coupled gene oscillators. We observe that the synchronization error between 20 coupled gene oscillators indeed approaches zero, and the analyzed network is synchronous.

5. Conclusions

We propose a theoretical method for the analysis of synchronization of a class of genetic oscillator networks based on the theory of absolute stability and the matrix theory. The resulting synchronization criteria have the form of LMIs, which can be verified by using an efficient software toolbox, such as the LMI lab in MATLAB. Although the method is proposed for the genetic oscillator networks, it is also applicable to other biochemical and neural networks formed by nonlinear systems of the Lur'e type.

The present paper was financially supported by the National Natural Science Foundation of China (No. 61473245, 61004050).

REFERENCES

1. M. B. Elowitz and S. Leibler, "A synthetic oscillatory network of transcriptional regulators," *Nature,* **403**, 335–338 (2000).
2. G. Chesi and Y. S. Hung, "Stability analysis of uncertain genetic sum regulatory networks," *Automatica,* **44**, 2298–2305 (2008).
3. E. L. O'Brien, E. V. Itallie, and M. R. Bennett, "Modeling synthetic gene oscillators," *Math. Biosci.,* **236**, 1–15 (2012).
4. P. R. Sharma, P. Somani, and M. D. Shrimali, "Bio-inspired computation using synthetic genetic network," *Phys. Lett. A,* **377**, 367–369 (2013).
5. J. Wang and T. Zhou, "CAMP-regulated dynamics of the mammalian circadian clock," *Biosystems,* **101**, 136–143 (2010).
6. L. Ji, X. Yan, and N. Li, "Common noise induced synchronous circadian oscillations in uncoupled nonidentical systems," *Biophys. Chem.,* **173–174**, 15–20 (2013).
7. D. McMillen, N. Kopell, J. Hasty, and J. J. Collins, "Synchronizing genetic relaxation oscillators by intercell signaling," *Proc. Nat. Acad. Sci.,* **99**, 679–684 (2002).
8. F. Li and J. Sun, "Asymptotic stability of a genetic network under impulsive control," *Phys. Lett. A,* **374**, 3177–3184 (2010).
9. W. Zhang, Y. Tang, J. Fang, and W. Zhu, "Exponential cluster synchronization of impulsive delayed genetic oscillators with external disturbances," *Chaos.,* **21**, 6–12 (2011).

10. P. Li and J. Lam, "Synchronization in networks of genetic oscillators with delayed coupling," *Asian J. Control.,* **13**, 713–725 (2011).
11. S. Cai, Q. He, J. Hao, and Z. Liu, "Exponential synchronization of complex networks with nonidentical time-delayed dynamical nodes," *Phys. Lett. A,* **374**, 2539–2550 (2010).
12. T. Schreiber, "Constrained randomization of time series data," *Phys. Rev. Lett.,* **80**, 2105–2108 (1998).
13. A. T. Winfree, *The Geometry of Biological Time,* Springer, Berlin (2000).
14. Y. Deng, M. Ding, and J. Feng, "Synchronization in stochastic coupled systems: theoretical results," *J. Phys. A,* **37**, 2163–2173 (2004).
15. Z. Yuan, J. Zhang, and T. Zhou, "Coherence, collective rhythm, and phase difference distribution in populations of stochastic genetic oscillators with cellular communication," *Phys. Rev. E,* **78** (2008).
16. M. Osella and M. C. Lagomarsino, "Growth-rate-dependent dynamics of a bacterial genetic oscillator," *Phys. Rev. E,* **87** (2013).
17. J. Qiu and J. Cao, "Global synchronization of delay-coupled genetic oscillators," *Neurocomputing,* **72**, 3845–3850 (2009).
18. J. Lu and J. Cao, "Adaptive synchronization of uncertain dynamical networks with delayed coupling," *Nonlinear Dynamics,* **53**, 107–115 (2008).
19. P. Ruoff, M. Vinsjevik, C. Monnerjahn, and L. Rensing, "The Goodwin model: simulating the effect of light pulses on the circadian sporulation rhythm of Neurospora crassa," *J. Theor. Biology,* **209** (2001).
20. A. Goldbeter, "A model for circadian oscillations in the Drosophila period protein (PER)," *Proc. Roy. Soc. London B,* **261** (1995).
21. G. A. Leonov, D. V. Ponomarenko, and V. B. Smirnova, *Frequency-Domain Methods for Nonlinear Analysis—Theory and Applications,* World Scientific, Singapore (1996).
22. S. Boyd, L. E. Ghaoui, E. Feron, and V. Balakrishnan, *Linear Matrix Inequalities in System and Control Theory,* Soc. Industrial and Appl. Math., Philadelphia (1994).
23. C. Li, L. Chen, and K. Aihara, "Synchronization of coupled nonidentical genetic oscillators," *Phys. Biology,* **3**, 37–44 (2006).
24. G. Rangarajan and M. Z. Ding, "Stability of synchronized chaos in coupled dynamical systems," *Phys. Lett. A,* **296**, 204–209 (2002).