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SYNCHRONIZATION ANALYSIS FOR A CLASS OF GENETIC OSCILLATOR NETWORKS*

СИНХРОНІЗАЦІЙНИЙ АНАЛІЗ ДЛЯ КЛАСУ МЕРЕЖ ГЕНЕТИЧНИХ ОСЦИЛЯТОРІВ

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

Розглянуто задачу синхронізації мереж генетичних осциляторів. Ґенетичні осцилятори моделюються нелінійними системами типу Лур'є. Умови синхронізації, які є простими та які можливо перевірити, отримано для мереж генетичних осциляторів із використанням теорії абсолютної стійкості та теорії матриць. Мережа, що складається зі зв'язаних моделей Ґудвіна, використовується як приклад для числових обчислень, які підтверджують ефективність теоретичного методу.

1. Introduction. Genetic oscillator networks have recently received an increasing attention for their wide applications in biological and biomedical science [1, 2]. In general, they can be viewed as a class of complex dynamical 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 the genetic oscillators [3]. It is of great importance to investigate the collective dynamics of genetic oscillator networks with hope to understand the intrinsic biological mechanisms for the rhythmic behavior of living organisms. Synchronization is a universal phenomenon and occurs typically in genetic oscillator networks [4 – 6]. In [7], a coupling scheme has been introduced to make synchronization of a population of cells. The synchronization problem of genetic oscillator networks has been thoroughly investigated by experiment, numerical simulation and theoretical analysis until now [8 – 18].

Mathematically many genetic oscillators such as the repressilator [1], the Goodwin model [19] and the circadian oscillator [20] can be represented in the form of multiple additive terms, each of which particularly is of linear, Michaelis – Menten or Hill forms. Genetic oscillators with above structure can be expressed in the form of Lur'e systems and can be further analyzed by using the control theory pertinent to Lur'e systems [21]. The intention of this paper is to systemically examine synchronization of genetic oscillator networks by general theory analysis and numerical simulation. We first transform genetic oscillators into nonlinear systems of Lur'e type and introduce genetic oscillator networks composed of genetic oscillators with this special

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structure. Then we present simple criteria for synchronization of genetic oscillator networks by using absolute stability theory and 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. Besides, the established theoretical results are general and applicable to other biochemical and neuronal networks with each node being a Lur'e system.

Notations: X^T denotes the transpose for 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 an identity matrix of dimension N; R_+ denotes the set of positive real numbers; $\mathrm{diag}\,(X_1, \ldots, X_n)$ and $U \otimes V$ denote

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

2. Problem formulation. Mathematically many genetic oscillators can be formulated in the form of multiple additive terms, which are monotonic increasing or decreasing functions. We 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; $A \in \in R^{n\times n}$, $B_h \in R^{n\times m}$, $C_h \in R^{m\times n}$ 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 monotonic increasing or decreasing regulatory function and usually is of the Michaelis – Menten [23] or Hill form [23]; k is an integer greater than or equal to 1. Note that all entries of $f_h(C_h x(t))$ should not be increasing or decreasing simultaneously, that is, some of entries can be increasing while others can be decreasing.

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

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

Remark 1. For monotonic increasing functions, $\gamma_{hl} = 0$ and $\delta_{hl} > 0$, whereas for monotonic decreasing functions, $\gamma_{hl} < 0$ and $\delta_{hl} = 0$. Setting $\varphi_{hl}(\sigma) = \dfrac{df_{hl}(\sigma)}{dt}$, the restrictions in (2) are turned into

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

System (1) contains many 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 $f_{hl}\left(c_{hl}^T x(t)\right)$, $h = 1, 2, \ldots, k$, $l = 1, 2, \ldots, m$, of $F(Cx(t))$ satisfy (2). Equation (4) is of the form of Lur'e system and can be investigated by using the classical Lur'e system method in control theory.

Remark 2. Note that the nonlinearities introduced in [8, 17] are of a specific form and the number of them is two. However, the nonlinearities here can be more general and the number of them can be greater than two as long as (3) is satisfied.

Notice that the description of the nonlinearities is different from that in [8, 17]. Equation (4) includes more than two ($k > 2$) nonlinearity vectors with a simpler structure than that given in [8, 17].

We consider a genetic oscillator network composed of 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 state vector of the ith genetic oscillator, $D \in R^{n\times n}$ is a constant matrix linking coupled variables, G_{ij} is positive if oscillator j is linked to oscillator i directly, otherwise G_{ij} equals zero, $\sum_{j=1,j\neq i}^{N} G_{ij} = -G_{ii}$, $i = 1, 2, \ldots, N$. The matrix $G = (G_{ij}) \in \in R^{N\times N}$ 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

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

due to $\sum_{j=1,j\neq i}^{N} G_{ij} = -G_{ii}$. The main purpose is to deal with the synchronization problem of the genetic oscillator network (5), and derive LMI-based sufficient conditions that guarantee the network to be synchronous.

3. Methods and results. Define the synchronous error as $e_i(t) = x_i(t) - s(t)$. Subtracting (7) from (5), the dynamics of the synchronous error are governed by

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

where

$$\eta(Ce_i(t); s(t)) = F(Ce_i(t) + Cs(t)) - F(Cs(t)) = \left[\eta_{11}\left(c_{11}^T e_i(t); s(t)\right), \ldots \right.$$
$$\left. \ldots, \eta_{1m}\left(c_{1m}^T e_i(t); s(t)\right), \ldots, \eta_{k1}\left(c_{k1}^T e_i(t); s(t)\right), \ldots, \eta_{km}\left(c_{km}^T e_i(t); s(t)\right)\right]^T.$$

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

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

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

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

Denoting

$$e(t) = \left[e_1^T(t), \ldots, e_N^T(t)\right]^T, \quad S(t) = \left[s^T(t), \ldots, s^T(t)\right]^T,$$
$$\eta[(I_N \otimes C)e(t); S(t)] = \left[\eta^T(Ce_1(t); s(t)), \ldots, \eta^T(Ce_N(t); s(t))\right]^T,$$

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, absolute stability criteria for (12) are derived by using absolute stability theory and matrix theory. These criteria guarantee synchronization of the genetic oscillator network (5) simultaneously. Denote

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

and

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

Theorem 1. *Suppose that G is symmetrical, and μ_i, $i = 1, \ldots, N$, are its eigenvalues. The genetic oscillator network (5) is synchronous if there exist positive-definite matrices $P_i \in R^{n \times n}$,*

$i = 1, \ldots, N$, positive-definite diagonal matrices $\Lambda_1 \in R^{km\times km}$ and $\Lambda_2 \in R^{km\times km}$ such that the following LMIs hold:

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

where

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

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

Proof. Since G is symmetrical and irreducible, 0 is an eigenvalue of it with multiplicity 1 and all other eigenvalues satisfy $0 = \mu_1 > \mu_2 \geq \ldots \geq \mu_N$. An orthogonal matrix U can be found such that $U^T G U = \mu$, where $\mu = \operatorname{diag}(\mu_1, \ldots, \mu_N)$. Combining multiple LMIs in (13) into one large LMI, and applying convenient column and row permutations to the resulting inequality, (13) is transformed into

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

where

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

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

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

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 have

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

where

$$\Pi_1 = P(I_N \otimes A + G \otimes D) + (I_N \otimes A + G \otimes D)^T P - I_N \otimes C^T \Gamma \Lambda_1 \Delta C -$$
$$- (I_N \otimes A + G \otimes D)^T \left(I_N \otimes C^T \Gamma \Lambda_2 \Delta C\right) (I_N \otimes A + G \otimes D),$$
$$\Pi_2 = P(I_N \otimes B) + \frac{1}{2}\left[I_N \otimes C^T(\Gamma + \Delta)\Lambda_1\right] - (I_N \otimes A + G \otimes D)^T (I_N \otimes C^T \Gamma \Lambda_2 \Delta C B),$$
$$\Pi_3 = \frac{1}{2}(I_N \otimes A + G \otimes D)^T \left[I_N \otimes C^T(\Gamma + \Delta)\Lambda_2\right], \quad P = (U \otimes I_n)\tilde{P}\left(U^T \otimes I_n\right).$$

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

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

where $I_N \otimes \Lambda_1 = \operatorname{diag}(\lambda_{111}, \ldots, \lambda_{1km})$, $I_N \otimes \Lambda_2 = \operatorname{diag}(\lambda_{211}, \ldots, \lambda_{2km})$. If (15) is fulfilled, then $\dot{V}(e(t)) < 0$, which means that (12) is absolutely stable and accordingly the genetic oscillator network (5) is synchronous.

Theorem 1 is proved.

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

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

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

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

we have the following results.

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

$\Lambda_2 > 0$ *such that the following LMIs hold:*

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

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

where

$$\Omega_1 = P_2(A-ND) + (A-ND)^TP_2 - C^T\Gamma\Lambda_1\Delta C - (A-ND)^TC^T\Gamma\Lambda_2\Delta C(A-ND),$$

$$\Omega_2 = P_2B + \frac{1}{2}C^T(\Gamma+\Delta)\Lambda_1 - (A-ND)^TC^T\Gamma\Lambda_2\Delta CB.$$

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

Remark 5. If the genetic oscillator network (5) is a globally coupled network, only two LMIs need to be verified.

4. Numerical example. We consider a genetic oscillator network globally coupled by the classical Goodwin model [19], which describes the dynamical evolution of coupled suprachiasmatic nucleus

$$\begin{aligned} \dot{X}_i &= k_1\frac{1}{1+Z_i^H} - k_5X_i + KR, \\ \dot{Y}_i &= k_2X_i - k_6Y_i, \\ \dot{Z}_i &= k_3Y_i - k_7Z_i, \\ \dot{V}_i &= k_4X_i - k_8V_i, \quad i = 1,\dots,N, \end{aligned} \tag{19}$$

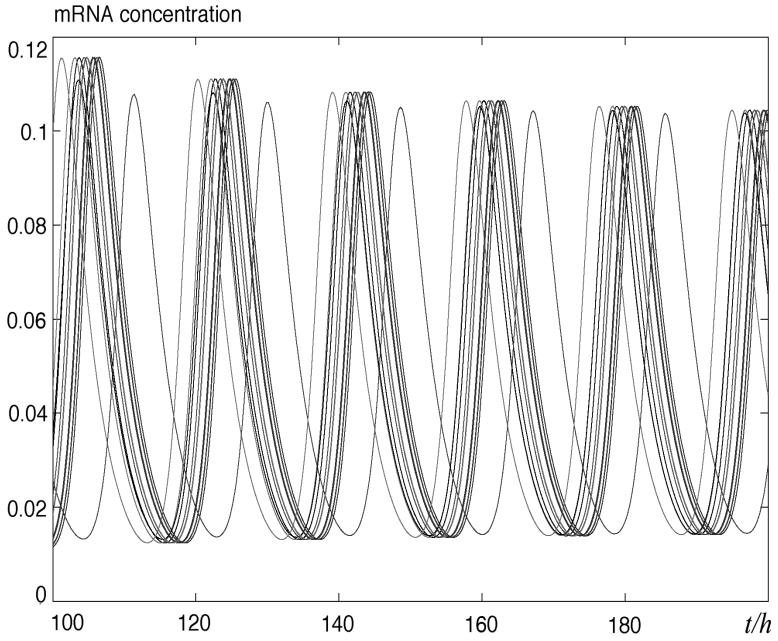

Fig. 1. Time evolution of the mRNA concentrations of 20 uncoupled oscillators.

where the variables X_i, Y_i, 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, $R = \frac{1}{N}\sum_{j=1}^{N} V_j$ denotes the average neurotransmitter level and is viewed as the coupling term. The genetic oscillator network (19) can be written in the form of (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 of (19) are chosen in such a way so that the single cell oscillator produces self-sustained oscillations with a circadian period. The values of them are taken as follows:

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

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

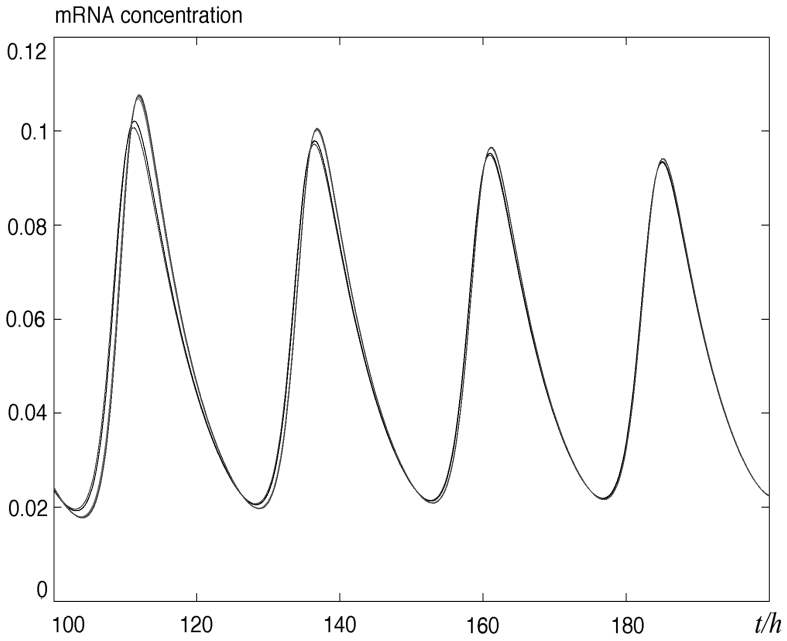

Fig. 2. Time evolution of the mRNA concentrations of 20 coupled oscillators.

In what follows, we validate the effectiveness of the established theoretical method by using a small size of network with 20 genetic oscillators. Set $K = 0$. This implies that the oscillators in the network are uncoupled. Figure 1 shows the time evolution of the mRNA concentration of 20 uncoupled oscillators with different initial conditions. We can observe that 20 uncoupled oscillators are not synchronous although the period of each oscillator is approximately 24 h. Set $K = 0.3$. Since G is a matrix of globally coupling, its eigenvalues satisfy

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

We should only verify two LMIs (17) and (18) to determine whether the considered network is synchronous. Substituting the above parameters to (17) and (18), feasible solutions could be derived by using the LMI toolbox in MATLAB. This indicates the considered network is synchronous according to Theorem 2. Figure 2 shows the time evolution of the mRNA concentration of 20 oscillators in the network. Figure 3 shows the time evolution of the synchronization error between 20 coupled gene oscillators. We can observe that the synchronization error between 20 coupled gene oscillators indeed approaches to zero, and the considered network is synchronous.

5. Conclusion. We have provided a theoretical method for analyzing synchronization of a class of genetic oscillator networks in virtue of absolute stability theory and matrix theory. The resulting synchronization criteria are of the forms of LMIs which can be verified by using efficient software toolbox such as the LMI lab in MATLAB. Although the method is proposed for genetic oscillator networks, it is also applicable to other biochemical and neuronal networks composed of nonlinear systems of Lur'e type.

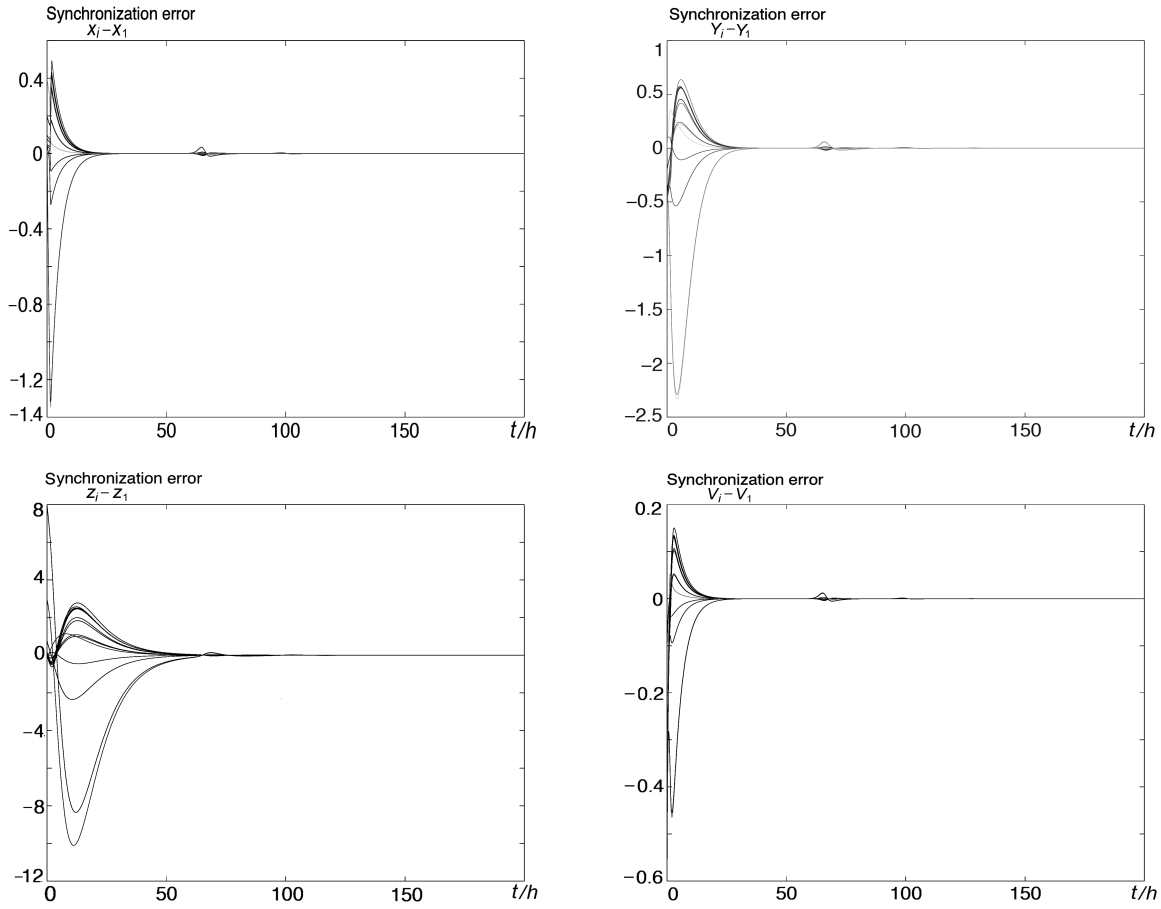

Fig. 3 Time evolution of the synchronization error between 20 coupled gene oscillators.

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