

# Synchronization of Stochastic Genetic Oscillator Networks with Time Delays and Markovian Jumping Parameters

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## Abstract

Genetic Oscillator networks (GONs) are inherently coupled complex systems where the nodes indicate the biochemicals and the couplings represent the biochemical interactions. This paper is concerned with the synchronization problem of a general class of stochastic GONs with time delays and Markovian jumping parameters, where the GONs are subject to both the stochastic disturbances and the Markovian parameter switching. The regulatory functions of the addressed GONs are described by the sector-like nonlinear functions. By applying up-to-date ‘delay-fractioning’ approach for achieving delay-dependent conditions, we construct novel matrix functional to derive the synchronization criteria for the GONs that are formulated in terms of linear matrix inequalities (LMIs). Note that LMIs are easily solvable by the Matlab toolbox. A simulation example is used to demonstrate the synchronization phenomena within biological organisms of a given GON and therefore shows the applicability of the obtained results.

## Keywords

Genetic oscillator networks; system biology; stochastic synchrony; Markovian switching; random perturbation; linear matrix inequality (LMI).

## I. INTRODUCTION

The oscillatory behavior of genetic networks, as a fundamental challenge in the research field of systems biology, has recently attracted an increasing attention, see e.g. [1, 5, 6, 10–12, 14, 29]. Generally speaking, the genetic networks are a class of complex dynamical networks since the genetic oscillators can be expressed in terms of complicated biological functions [9, 16, 17, 23]. In such kind of genetic oscillator networks (GONs), the nodes represent the genetic oscillators, while the inner or outer couplings denote the interactions. In order to research into the intrinsic biological organisms of GONs, it is of great importance to investigate the collective dynamics of coupled genetic oscillators with hope to understand the rhythmic behavior of living organisms. Synchronization, as a universal phenomenon, occurs typically in genetic networks. For example,

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in [19], a synthetic gene network in *Escherichia coli* has been shown to have two features: the system acts as a relaxation oscillator and uses an intercell signaling mechanism to couple the oscillators and induce synchronous oscillations. A coupling scheme has been proposed that leads to synchronous behavior across a population of cells, and an analytical treatment of the synchronization process has been conducted. Up to now, the synchronization motion analysis problem for genetic oscillator networks has attracted considerable research attention. In [11,14,16,17], the synchronization problem in genetic networks has been thoroughly investigated via experiments (e.g. synchronization of cellular clock in the suprachiasmatic nucleus in genetic networks), numerical simulation (e.g. biological networks of identical genetic oscillators) as well as theoretical analysis (i.e., synchronizability of coupled nonidentical genetic oscillators).

It has been demonstrated experimentally that the networks states or oscillatory expression are significantly affected by the inherent state delay due primarily to the slow processes of transcription, translation, and translocation or the finite switching speed of amplifiers. From the synthetic biology viewpoint, it is necessary to address the time-delay effects in the mathematical models, and then a more accurate state values of the biological oscillators could be obtained from oscillatory expression measurements [22,26,30]. Note that the stability analysis issue of genetic regulatory networks with either constant or time-varying delays has recently been a research focus, see [30] and references therein. It is worth mentioning that a novel approach named ‘delay-fractioning’ has been exploited in many reported results in order to achieve less conservative delay-dependence conditions, see e.g. [20,27,28,35].

Biological data promises to enhance the fundamental understanding of life at the molecular level, from regulation of gene expression and gene function to cellular mechanisms, and may prove useful in medical diagnosis, treatment, and drug design. Substantial effort is being made to build models to analyze microarray data. It is evident that genetic networks are always affected by the random fluctuations [1,3,13,21,25,26,29,31]. Therefore, to have an accurate prediction of the dynamical behaviors of genetic oscillators, it is important to consider the random effects including intrinsic and intrinsic noise perturbations [1,3,25,26,29]. Also, as shown in [7,8,13], in gene regulatory networks, the transition from one state to the next usually takes place in accordance with certain transition probabilities, which forms a homogeneous Markov chain with finite state space. Subsequently, the dynamics of the so-called Markovian genetic regulatory networks, which are subject to mode switching (or jumping), has been thoroughly investigated in [7,8]. It should be pointed out that, up to now, the control and filtering problems for Markovian jumping systems have already been widely studied [4,18,33,34]. Recently, the stochastic synchrony study has been carried out for genetic networks in [32], where an adaptive filtering approach is elegantly developed to estimate uncertain delayed genetic regulatory networks. However, the stochastic synchrony problem for *Markovian* delayed genetic networks of specific structures has not gained adequate research attention yet, and this constitutes the main focus of this paper.

In this paper, we aim to make one of the first attempts to investigate the synchronization problem for stochastic GONs with Markovian jumping parameters and time delays so as to exhibit more realistic characteristics of the GONs, where the regulation functions are assumed to be sector-like, and the intrinsically stochastic fluctuation is a scalar Brownian motion. The main results obtained are illustrated through a numerical simulation example. The rest of this paper is organized as follows. Section II introduces the model formulation and some preliminary works. In Section III, by utilizing the approach of ‘delay-fractioning’ and a

novel matrix functional method, stochastic analysis is conducted to obtain delay-dependent sufficient criteria described by linear matrix inequalities (LMIs) [2] that can be easily checked by using standard numerical software. Section IV illustrates the obtained results and Section V concludes the paper.

**Notations:** Throughout this paper,  $\mathfrak{R}^n$  and  $\mathfrak{R}^{n \times m}$  denote, respectively, the  $n$  dimensional Euclidean space and the set of all  $n \times m$  real matrices.  $P > 0$  means that matrix  $P$  is real, symmetric and positive definite.  $I$  and  $0$  denote the identity matrix and the zero matrix with compatible dimensions, respectively; and  $\text{diag}\{\dots\}$  stands for a block-diagonal matrix,  $\text{col}\{\dots\}$  denotes a matrix column with blocks given by the matrices in  $\{\dots\}$ . If  $A$  is a matrix, the notation  $\lambda_{\max}(A)$  means the largest eigenvalue of  $A$ . The superscript “ $T$ ” stands for matrix transposition and the asterisk “ $*$ ” in a matrix is used to represent the term which is induced by symmetry. The Kronecker product of matrices  $Q \in \mathfrak{R}^{m \times n}$  and  $R \in \mathfrak{R}^{p \times q}$  is a matrix in  $\mathfrak{R}^{mp \times nq}$  and denoted as  $Q \otimes R$ . We let  $\mathcal{C}([-h, 0]; \mathfrak{R}^n)$  denote the family of all continuous functions  $\varphi$  from  $[-h, 0]$  to  $\mathfrak{R}^n$  with the norm  $|\varphi| = \sup_{-h \leq \theta \leq 0} \|\varphi(\theta)\|$ , where  $\|\cdot\|$  is the Euclidean norm on  $\mathfrak{R}^n$ . Moreover, let  $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t \geq 0}, \mathcal{P})$  be a complete probability space with a filtration  $\{\mathcal{F}_t\}_{t \geq 0}$  satisfying the usual conditions (i.e., the filtration contains all  $\mathcal{P}$ -null sets and is right continuous). Denote by  $L_{\mathcal{F}_0}^p([-h, 0]; \mathfrak{R}^n)$  the family of all  $\mathcal{F}_0$ -measurable  $\mathcal{C}([-h, 0]; \mathfrak{R}^n)$ -valued random variables  $\xi = \{\xi(\theta) : -h \leq \theta \leq 0\}$  such that  $\sup_{-h \leq \theta \leq 0} \mathcal{E}\{|\xi(\theta)|^p\} < \infty$ , where  $\mathcal{E}\{\cdot\}$  stands for the mathematical expectation operator with respect to the given probability measure  $\mathcal{P}$ . Sometimes, the arguments of a function will be omitted in the analysis when no confusion arises.

## II. PROBLEM FORMULATION AND PRELIMINARIES

Let  $r(t)$  ( $t \geq 0$ ) be a right-continuous Markovian chain on a probability space  $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t \geq 0}, \mathcal{P})$  taking values in a finite state space  $\mathbb{S} = \{1, 2, \dots, m\}$  with generator  $\Pi = \{\pi_{ij}\}$  given by

$$P\{r(t + \Delta) = j \mid r(t) = i\} = \begin{cases} \pi_{ij}\Delta + o(\Delta), & \text{if } i \neq j, \\ 1 + \pi_{ij}\Delta + o(\Delta), & \text{if } i = j. \end{cases}$$

Here  $\Delta > 0$ , and  $\pi_{ij} \geq 0$  is the transition rate from  $i$  to  $j$  if  $j \neq i$  while

$$\pi_{ii} = -\sum_{j \neq i} \pi_{ij}.$$

Among many models of genetic networks, the differential equation model is one of the mostly adopted ones. A general delayed genetic oscillator network could be described by the following vector form [16, 17]:

$$\frac{dy(t)}{dt} = Ay(t) + \sum_{i=1}^l B_i f_i(y(t)) + \sum_{i=1}^l C_i g_i(y(t - \tau)), \quad (1)$$

where  $l$  is a positive integer and  $y(t) = \text{col}\{y_1(t), y_2(t), \dots, y_n(t)\} \in \mathfrak{R}^n$  represents the concentrations of proteins, mRNAs and chemical complexes;  $A, B_i, C_i$  ( $i = 1, 2, \dots, l$ ) are matrices in  $\mathfrak{R}^{n \times n}$ ;  $f_i(y(t)) = \text{col}\{f_{i1}(y_1(t)), f_{i2}(y_2(t)), \dots, f_{in}(y_n(t))\} \in \mathfrak{R}^n$  and  $g_i(y(t - \tau)) = \text{col}\{g_{i1}(y_1(t - \tau)), g_{i2}(y_2(t - \tau)), \dots, g_{in}(y_n(t - \tau))\} \in \mathfrak{R}^n$  are monotonic genetic regulatory functions which are usually taken as the Hill form. The scalar  $\tau > 0$  denotes the translation time delay in the translation process.

As discussed in the introduction, the genetic oscillators in biological networks are tightly coupled between each other, and both the stochastic perturbations [1, 3, 13, 21, 25, 26, 29] and Markovian jumping parameters

[13] are playing important roles in generating the network dynamics. Therefore, we consider the following coupled GONs consisting of  $N$  genetic oscillators with Markovian jumping parameters and time delays:

$$\begin{aligned} dx_k(t) &= \left[ A(r(t))x_k(t) + B(r(t))f(x_k(t)) + C(r(t))g(x_k(t-\tau)) + \sum_{l=1}^N w_{kl}\Gamma_{r(t)}x_l(t) \right] dt \\ &\quad + \sigma_k(x_k(t), x_k(t-\tau), t, r(t))d\omega(t), \\ x_k(t) &= \phi_k(t), \quad r(t)|_{t=0} = r_0 \in \mathbb{S}; \quad t \in [-\tau, 0], \quad k = 1, 2, \dots, N \end{aligned} \quad (2)$$

where  $x_k(t) = \text{col}\{x_{k1}(t), x_{k2}(t), \dots, x_{kn}(t)\} \in \mathfrak{X}^n$  is the state vector of the  $k$ th genetic oscillator representing the concentrations of proteins, mRNAs and chemical complexes, which are of limited values; For  $r(t) = i \in \mathbb{S}$ ,  $A(i)$  includes the degradation terms and all the other linear terms of the  $k$ th genetic oscillator;  $B(i)$ ,  $C(i)$  are known matrices in  $\mathfrak{X}^{n \times n}$ ;  $f(x_k(t)) = \text{col}\{f_1(x_{k1}(t)), f_2(x_{k2}(t)), \dots, f_n(x_{kn}(t))\} \in \mathfrak{X}^n$  and  $g(x_k(t-\tau)) = \text{col}\{g_1(x_{k1}(t-\tau)), g_2(x_{k2}(t-\tau)), \dots, g_n(x_{kn}(t-\tau))\} \in \mathfrak{X}^n$  are usually monotonic functions satisfying the sector-bounded conditions that will be given later;  $\phi_k(t) \in L_{\mathcal{F}_0}^p([-h, 0]; \mathfrak{X}^n)$  is the initial condition of  $x_k(t)$ .

The matrix  $\Gamma_{r(t)} = [\gamma_{kl,r(t)}]_{n \times n}$  is a matrix linking the state variable of the  $l$ th genetic oscillator in the genetic network mode  $r(t)$  if  $\gamma_{kl,r(t)} \neq 0$ ; and  $W = [w_{kl}]_{N \times N}$  is the coupling matrix that represents the coupling topology, direction, as well as the coupling strength of the genetic network. The definition is given as follows: if there is a link from the  $k$ th oscillator to the  $l$ th oscillator ( $k \neq l$ ), then  $w_{kl}$  equals to a positive constant denoting the coupling strength of this link; otherwise  $w_{kl} = 0$ ;  $w_{kk} = -\sum_{k=1, k \neq l}^N w_{kl}$ . Note that many real-world genetic oscillator networks are sparse, and therefore reducible near a tree topological structure. In this paper, however, we are looking into the synchronization problem for a genetic oscillator network from a theoretical viewpoint. In such as case, we suggest that the presence of irreducible dependencies among the genes is likely to identify direct regulatory interactions mediated by a transcription factor binding to a target genes promoter region, although other types of interactions may also be identified.

In the system (2),  $\omega(t)$  is a scalar Wiener process (Brownian Motion) on  $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t \geq 0}, \mathcal{P})$ , which is independent of the Markov chain  $r(\cdot)$  and satisfies

$$\mathcal{E}\{d\omega(t)\} = 0, \quad \mathcal{E}\{[d\omega(t)]^2\} = dt. \quad (3)$$

The noise intensity function vector  $\sigma_k(\cdot, \cdot, \cdot, \cdot) : \mathfrak{X}^n \times \mathfrak{X}^n \times \mathfrak{X}^+ \times \mathbb{S} \rightarrow \mathfrak{X}^n$  is Borel measurable and is assumed to satisfy the following Lipschitz condition.

*Assumption 1:* There exist constant matrices  $\Sigma_1$  and  $\Sigma_2$  of appropriate dimensions such that the following inequality:

$$[\sigma_k(u_1, v_1, t, i) - \sigma_l(u_2, v_2, t, i)]^T [\sigma_k(u_1, v_1, t, i) - \sigma_l(u_2, v_2, t, i)] \leq \|\Sigma_1(u_1 - u_2)\|^2 + \|\Sigma_2(v_1 - v_2)\|^2 \quad (4)$$

holds for all  $t > 0$ ;  $u_q, v_q$  ( $q = 1, 2$ )  $\in \mathfrak{X}^n$ ;  $k, l = 1, 2, \dots, N$ ;  $i \in \mathbb{S}$ .

*Assumption 2:* The nonlinear functions  $f(\cdot)$  and  $g(\cdot)$  satisfy the following sector-like conditions:

$$0 \leq \frac{f_i(s) - f_i(t)}{s - t} < \kappa_{1i}, \quad 0 \leq \frac{g_i(s) - g_i(t)}{s - t} < \kappa_{2i}, \quad i = 1, 2, \dots, n.$$

*Remark 1:* From Assumption 2, it is not difficult to see that

$$f^T(x)(f(x) - K_1x) \leq 0, \quad g^T(x)(g(x) - K_2x) \leq 0$$

with  $K_j = \text{diag}\{\kappa_{j1}, \kappa_{j2}, \dots, \kappa_{jn}\}$  ( $j = 1, 2$ ). On the other hand, the nonlinear functions  $f(\cdot)$  and  $g(\cdot)$  satisfying Assumption 2 are said to belong to the sector  $[0, K_1]$  and  $[0, K_2]$ , respectively.

*Remark 2:* Notice that the sector-like description of the nonlinearities has been used to model the structure and regulation mechanism of the genetic regulatory networks in many papers, see e.g. [17, 29]. Traditionally, as monotonic regulation functions,  $f(\cdot)$  or  $g(\cdot)$  usually takes the Hill form or the Michaelis-Menten form, which is a special case of the sector-like functions.

For the sake of notation simplicity, we use the matrix Kronecker product “ $\otimes$ ” to rewrite (2) in the following compact form:

$$\begin{aligned} dx(t) = & \left[ (I_N \otimes A(r(t)) + W \otimes \Gamma_{r(t)})x(t) + (I_N \otimes B(r(t)))F(x(t)) \right. \\ & \left. + (I_N \otimes C(r(t)))G(x(t - \tau)) \right] dt + \sigma(x(t), x(t - \tau), t, r(t))d\omega(t), \end{aligned} \quad (5)$$

where

$$\begin{aligned} x(t) &= \text{col}\{x_1(t), x_2(t), \dots, x_N(t)\}, \quad F(x(t)) = \text{col}\{f(x_1(t)), f(x_2(t)), \dots, f(x_N(t))\}, \\ G(x(t)) &= \text{col}\{g(x_1(t - \tau)), g(x_2(t - \tau)), \dots, g(x_N(t - \tau))\}, \\ \sigma(x(t), x(t - \tau), t, r(t)) &= \text{col}\{\sigma_1(x_1(t), x_1(t - \tau), t, r(t)), \dots, \sigma_N(x_N(t), x_N(t - \tau), t, r(t))\}. \end{aligned}$$

Before stating the main results, a definition and some lemmas are introduced here.

*Definition 1:* The genetic oscillator network (2) is said to be globally asymptotically synchronized in the mean square sense if

$$\mathcal{E} \left\{ \|x_k(t, \phi_k, r_0) - x_l(t, \phi_l, r_0)\|^2 \right\} \longrightarrow 0, \quad \text{as } t \rightarrow +\infty$$

holds for any  $\phi_k(\cdot), \phi_l(\cdot) \in L^p_{\mathcal{F}_0}([-h, 0], \mathfrak{R}^n)$ ;  $k, l \in \{1, 2, \dots, N\}$  and  $r_0 \in \mathbb{S}$ .

*Lemma 1:* [15] The Kronecker product has the following properties:

- (1)  $(\alpha A) \otimes B = A \otimes (\alpha B)$ ;
- (2)  $(A + B) \otimes C = A \otimes C + B \otimes C$ ;
- (3)  $(A \otimes B)(C \otimes D) = (AC) \otimes (BD)$ ;
- (4)  $(A \otimes B)^T = A^T \otimes B^T$ .

*Lemma 2:* Let  $\mathcal{U} = (\alpha_{ij})_{N \times N}$ ,  $P \in \mathbb{R}^{n \times n}$ ,  $x = \text{col}\{x_1, x_2, \dots, x_N\}$  where  $x_i = \text{col}\{x_{i1}, x_{i2}, \dots, x_{in}\} \in \mathbb{R}^n$  and  $y = \text{col}\{y_1, y_2, \dots, y_N\}$  where  $y_i = \text{col}\{y_{i1}, y_{i2}, \dots, y_{in}\} \in \mathbb{R}^n$  ( $k = 1, 2, \dots, N$ ). If  $\mathcal{U} = \mathcal{U}^T$  and each row sum of  $\mathcal{U}$  is zero, then

$$x^T (\mathcal{U} \otimes P) y = - \sum_{1 \leq i < j \leq N} \alpha_{ij} (x_i - x_j)^T P (y_i - y_j).$$

*Lemma 3:* [24] Let  $f$  be a nonnegative function defined on  $[0, +\infty)$ . If  $f$  is Lebesgue integrable and is uniformly continuous on  $[0, +\infty)$ , then  $\lim_{t \rightarrow +\infty} f(t) = 0$ .

The main aim of this paper to deal with the exponential mean-square synchronization problem of the genetic oscillator networks (2) or (5), and derive LMI-based sufficient conditions that guarantee the network to be exponentially synchronous in the mean-square sense for all admissible time delays, nonlinearities and stochastic disturbances.

## III. MAIN RESULTS

Letting

$$y(t, r(t)) := [I_N \otimes A(r(t)) + W \otimes \Gamma_{r(t)}]x(t) + (I_N \otimes B(r(t)))F(x(t)) + (I_N \otimes C(r(t)))G(x(t - \tau)), \quad (6)$$

then the network (5) can be recast into the following form

$$dx(t) = y(t, r(t))dt + \sigma(x(t), x(t - \tau), t, r(t))d\omega(t). \quad (7)$$

For each  $i \in \mathbb{S}$ , Eq. (7) becomes

$$dx(t) = y^{(i)}(t)dt + \sigma(x(t), x(t - \tau), t, i)d\omega(t), \quad (8)$$

where  $y^{(i)}(t) = y(t, r(t))$  as  $r(t) = i$ .

*Theorem 1:* For a fixed integer  $d \geq 1$ , the genetic oscillator networks (2) or (5) with time-delay  $\tau \in (0, h]$  is globally exponentially synchronous in the mean square if there exist  $n \times n$  matrices  $P_i > 0$ ,  $Q_k > 0$ ,  $R > 0$ , a positive-definite matrix  $X^{(i)} \in \mathfrak{R}^{(dn+4n) \times (dn+4n)}$ , positive scalars  $\lambda^*$ ,  $e_l$  and matrices  $H^{(i)}$ ,  $M_1^{(i)}$ ,  $M_2^{(i)}$ ,  $\dots$ ,  $M_{d+4}^{(i)}$  with appropriate dimensions such that

$$P_i \leq \lambda^* I, \quad (9)$$

$$\Xi_{kl}^{(i)} = \Pi_{kl}(i) + hX^{(i)} < 0, \quad (10)$$

$$\Omega_{kl}^{(i)} = \begin{bmatrix} X^{(i)} & M^{(i)} \\ * & R \end{bmatrix} \geq 0, \quad (11)$$

where  $k = 1, 2, \dots, d$ ,  $l = 1, 2$ ,  $i \in \mathbb{S}$  and

$$\Pi_{kl}(i) = W_Q^T \tilde{Q} W_Q + \sum_{q=1}^2 (W_M^T M^{(i)} W_M^{(q)} + (W_M^T M^{(i)} W_M^{(q)})^T) + W_H^T \tilde{H}_{kl}^{(i)} W_H,$$

$$W_Q = \begin{bmatrix} I_{dn \times dn} & 0_{dn \times n} & 0_{dn \times 3n} \\ 0_{dn \times n} & I_{dn \times dn} & 0_{dn \times 3n} \end{bmatrix}, \quad \tilde{Q} = \begin{bmatrix} \mathbb{Q} & 0 \\ 0 & \mathbb{Q} \end{bmatrix}, \quad M^{(i)} = \text{col}\{M_1^i, M_2^i, \dots, M_{d+4}^i\},$$

$$W_M = I_{d+4} \otimes I_n, \quad W_M^{(1)} = [I_n \quad 0_{n \times (d+3)n}], \quad W_M^{(2)} = [0_{n \times dn} \quad -I_n \quad 0_{n \times 3n}],$$

$$W_H = \begin{bmatrix} I_n & 0_{n \times (dn+3n)} \\ 0_{n \times dn} & I_n & 0_{n \times 3n} \\ 0_{n \times (dn+n)} & I_n & 0_{n \times 2n} \\ 0_{n \times (dn+2n)} & I_n & 0_{n \times n} \\ 0_{n \times (dn+3n)} & I_n \end{bmatrix},$$

$$\tilde{H}_{kl}^{(i)} = \begin{bmatrix} (1, 1) & 0 & e_1 K_1^T + P_i B(i) & P_i C(i) & (1, 5) \\ * & \lambda^* \Sigma_2^T \Sigma_2 & 0 & e_2 K_2^T & 0 \\ * & * & -2e_1 I & 0 & B^T(i) H^{(i)T} \\ * & * & * & -2e_2 I & C^T(i) H^{(i)T} \\ * & * & * & * & hR - H^{(i)} - H^{(i)T} \end{bmatrix},$$

$$(1, 1) = \sum_{1 \leq j \leq m} \pi_{ij} P_j + \lambda^* \Sigma_1^T \Sigma_1 + P_i A(i) + A^T(i) P_i - N w_{kl} (P_i \Gamma_i + \Gamma_i^T P_i),$$

$$(1, 5) = -N w_{kl} \Gamma_i^T H^{(i)T} + A^T(i) H^{(i)T}.$$

*Proof:* Since  $\{(x(t), r(t)), t \geq 0\}$  is not a Markov process, in order to cast our model into the framework for a Markov system, let us define a new Markov process  $\{x_t, r(t), t \geq 0\}$  with

$$x_t(s) = x(t + s), \quad -\tau \leq t \leq 0.$$

Based on the idea of ‘delay-fractioning’, we consider the following novel matrix functional candidate for the genetic oscillator networks (2) or (5):

$$\begin{aligned} V(x_t, t, r(t)) &= x^T(t)(U \otimes P(r(t)))x(t) + \int_{t-\tau}^t \int_{\beta}^t y^T(\alpha, r(\alpha))(U \otimes R)y(\alpha, r(\alpha))d\alpha d\beta \\ &+ \sum_{k=1}^d \int_{t-\frac{k}{d}\tau}^{t-\frac{k-1}{d}\tau} x^T(\theta)(U \otimes Q_k)x(\theta)d\theta \end{aligned} \quad (12)$$

with  $d \geq 1$  (number of fractions) being an integer and  $U = [u_{kl}]_{N \times N}$  with  $u_{kl} = \begin{cases} -1, & k \neq l \\ N-1, & k = l \end{cases}$ . For  $r(t) = i \in \mathbb{S}$ ,  $P(r(t)) = P_i > 0$ ,  $R > 0$ ,  $Q_k > 0$ .

For the function  $V : L_{\mathcal{F}_0}^p([-h, 0]; \mathfrak{R}^{Nn}) \times \mathfrak{R}^+ \times \mathbb{S} \rightarrow \mathfrak{R}^{Nn}$  given above, its infinitesimal operator  $\mathcal{L}$  [4] is defined as

$$\mathcal{L}V(x_t, t, i) = \lim_{\Delta \rightarrow 0^+} \frac{1}{\Delta} \left[ \mathcal{E} \left\{ V(x_{t+\Delta}, t + \Delta, r(t + \Delta)) | x_t, r(t) = i \right\} - V(x_t, t, i) \right]. \quad (13)$$

Then, for the stochastic process  $\{x_t, r(t), t \geq 0\}$  along the network (2) or (5), it is easy to obtain that

$$\begin{aligned} \mathcal{L}V(x_t, t, i) &= 2x^T(t)(U \otimes P_i)y^{(i)}(t) + \sum_{j=1}^m \pi_{ij}x^T(t)(U \otimes P_j)x(t) \\ &+ \text{trace}[\sigma^T(x(t), x(t-\tau), t, i)(U \otimes P_i)\sigma(x(t), x(t-\tau), t, i)] \\ &+ \tau y^{(i)}(t)^T (U \otimes R)y^{(i)}(t) - \int_{t-\tau}^t y^T(\beta, r(\beta))(U \otimes R)y(\beta, r(\beta))d\beta \\ &+ x^T(t)(U \otimes Q_1)x(t) - x^T(t-\tau)(U \otimes Q_d)x(t-\tau) \\ &- \sum_{l=1}^{d-1} \left\{ x^T\left(t - \frac{l}{d}\tau\right) [U \otimes (Q_l - Q_{l+1})] x\left(t - \frac{l}{d}\tau\right) \right\}. \end{aligned} \quad (14)$$

With the following formula

$$x(t) - x(t-\tau) = \int_{t-\tau}^t dx(\beta),$$

we have for  $r(t) = i \in \mathbb{S}$  that

$$2(\xi^{(i)}(t))^T M_U^{(i)} \left[ x(t) - x(t-\tau) - \int_{t-\tau}^t y(\beta, r(\beta))d\beta - \int_{t-\tau}^t \sigma(x(\beta), x(\beta-\tau), \beta, r(\beta))d\omega(\beta) \right] = 0, \quad (15)$$

where  $M_U^{(i)} = \text{col}\{U \otimes M_1^{(i)}, U \otimes M_2^{(i)}, \dots, U \otimes M_{d+4}^{(i)}\}$  is of appropriate dimensions and

$$\xi^{(i)}(t) = \text{col} \left\{ x(t), x\left(t - \frac{1}{d}\tau\right), \dots, x\left(t - \frac{d-1}{d}\tau\right), x(t-\tau), F(x(t)), G(x(t-\tau)), y^{(i)}(t) \right\}.$$

Considering condition (3), one has

$$\mathcal{E} \left\{ 2(\xi^{(i)}(t))^T M_U^{(i)} \int_{t-\tau}^t \sigma(x(\beta), x(\beta-\tau), \beta, r(\beta))d\omega(\beta) \right\} = 0, \quad i = 1, 2, \dots, m. \quad (16)$$

Also, by (6), for any matrix  $H^{(i)}$  with appropriate dimensions, we have

$$\begin{aligned} & 2(y^{(i)}(t))^T (U \otimes H^{(i)}) \left[ (I_N \otimes A(i) + W \otimes \Gamma_i)x(t) \right. \\ & \quad \left. + (I_N \otimes B(i))F(x(t)) + (I_N \otimes C(i))G(x(t - \tau)) - y^{(i)}(t) \right] = 0. \end{aligned} \quad (17)$$

Noticing the fact of  $UW = NW$ , it follows from Lemma 1 that

$$(U \otimes P_i)(W \otimes \Gamma_i) = (UW) \otimes (P_i \Gamma_i) = (NW) \otimes (P_i \Gamma_i), \quad \forall i \in \mathbb{S}. \quad (18)$$

Substituting (6), (15)-(16) into (14) and utilizing Lemma 2, one obtains

$$\begin{aligned} & \mathcal{LV}(x_t, t, i) \\ \leq & \sum_{1 \leq k < l \leq N} \left\{ (x_k(t) - x_l(t))^T \left[ \left( \sum_{1 \leq j \leq m} \pi_{ij} P_j + P_i A(i) + A^T(i) P_i - N w_{kl} (P_i \Gamma_i + \Gamma_i^T P_i) \right) \right. \right. \\ & \quad \left. \left. \times (x_k(t) - x_l(t)) + 2P_i B(i)(f(x_k(t)) - f(x_l(t))) + 2P_i C(i)(g(x_k(t - \tau)) - g(x_l(t - \tau))) \right] \right. \\ & + (\sigma_k(x_k(t), x_k(t - \tau), t, i) - \sigma_l(x_l(t), x_l(t - \tau), t, i))^T P_i \\ & \quad \times (\sigma_k(x_k(t), x_k(t - \tau), t, i) - \sigma_l(x_l(t), x_l(t - \tau), t, i)) \\ & + h(y_k^{(i)}(t) - y_l^{(i)}(t))^T R(y_k^{(i)}(t) - y_l^{(i)}(t)) \\ & - \int_{t-\tau}^t (y_k(\beta, r(\beta)) - y_l(\beta, r(\beta)))^T R(y_k(\beta, r(\beta)) - y_l(\beta, r(\beta))) d\beta \\ & + (\Upsilon_k(t) - \Upsilon_l(t))^T \mathbb{Q} (\Upsilon_k(t) - \Upsilon_l(t)) - \left( \Upsilon_k(t - \frac{\tau}{d}) - \Upsilon_l(t - \frac{\tau}{d}) \right)^T \mathbb{Q} \left( \Upsilon_k(t - \frac{\tau}{d}) - \Upsilon_l(t - \frac{\tau}{d}) \right) \\ & + 2(\xi_k^{(i)}(t) - \xi_l^{(i)}(t))^T M^{(i)} \left[ (x_k(t) - x_l(t)) - (x_k(t - \tau) - x_l(t - \tau)) - \int_{t-\tau}^t (y_k(\beta, r(\beta)) - y_l(\beta, r(\beta))) d\beta \right. \\ & \quad \left. - \int_{t-\tau}^t (\sigma_k(x_k(\beta), x_k(\beta - \tau), \beta, i) - \sigma_l(x_l(\beta), x_l(\beta - \tau), \beta, i)) d\omega(\beta) \right] \\ & + 2(y_k^{(i)}(t) - y_l^{(i)}(t))^T \left[ (H^{(i)} A(i) - N w_{kl} H^{(i)} \Gamma_i)(x_k(t) - x_l(t)) + H^{(i)} B(i)(f(x_k(t)) - f(x_l(t))) \right. \\ & \quad \left. + H^{(i)} C(i)(g(x_k(t - \tau)) - g(x_l(t - \tau))) - H^{(i)}(y_k^{(i)}(t) - y_l^{(i)}(t)) \right. \\ & \quad \left. + h(\xi_k^{(i)}(t) - \xi_l^{(i)}(t))^T X^{(i)}(\xi_k^{(i)}(t) - \xi_l^{(i)}(t)) - \int_{t-\tau}^t (\xi_k^{(i)}(t) - \xi_l^{(i)}(t))^T X^{(i)}(\xi_k^{(i)}(t) - \xi_l^{(i)}(t)) ds \right] \left. \right\}, \end{aligned} \quad (19)$$

where  $M^{(i)} = \text{col}\{M_1^{(i)}, M_2^{(i)}, \dots, M_{d+4}^{(i)}\}$ ,  $\mathbb{Q} = \text{diag}\{Q_1, Q_2, \dots, Q_d\}$ ,  $\Upsilon_k(t) = \text{col}\{x_k(t), x_k(t - \frac{\tau}{d}), \dots, x_k(t - \frac{d-1}{d}\tau)\}$ .

From conditions (4) and (9), we have

$$\begin{aligned} & [\sigma_k(x_k(t), x_k(t - \tau), t, i) - \sigma_l(x_l(t), x_l(t - \tau), t, i)]^T P_i [\sigma_k(x_k(t), x_k(t - \tau), t, i) - \sigma_l(x_l(t), x_l(t - \tau), t, i)] \\ \leq & \lambda_{\max}(P_i) \left[ \sigma_k(x_k(t), x_k(t - \tau), t, i) - \sigma_l(x_l(t), x_l(t - \tau), t, i) \right]^T \\ & \quad \times \left[ \sigma_k(x_k(t), x_k(t - \tau), t, i) - \sigma_l(x_l(t), x_l(t - \tau), t, i) \right] \\ \leq & \lambda^* \left[ (x_k(t) - x_l(t))^T \Sigma_1^T \Sigma_1 (x_k(t) - x_l(t)) + (x_k(t - \tau) - x_l(t - \tau))^T \Sigma_2^T \Sigma_2 (x_k(t - \tau) - x_l(t - \tau)) \right]. \end{aligned} \quad (20)$$



Moreover, it implies from Assumption 2 and Remark 1 that

$$e_1 \begin{bmatrix} x_k(t) - x_l(t) \\ f(x_k(t)) - f(x_l(t)) \end{bmatrix}^T \begin{bmatrix} 0 & -K_1^T \\ -K_1 & 2I \end{bmatrix} \begin{bmatrix} x_k(t) - x_l(t) \\ f(x_k(t)) - f(x_l(t)) \end{bmatrix} \leq 0, \quad (21)$$

$$e_2 \begin{bmatrix} x_k(t - \tau) - x_l(t - \tau) \\ g(x_k(t - \tau)) - g(x_l(t - \tau)) \end{bmatrix}^T \begin{bmatrix} 0 & -K_2^T \\ -K_2 & 2I \end{bmatrix} \begin{bmatrix} x_k(t - \tau) - x_l(t - \tau) \\ g(x_k(t - \tau)) - g(x_l(t - \tau)) \end{bmatrix} \leq 0 \quad (22)$$

where  $e_j > 0$  ( $j = 1, 2$ ) and  $k, l = 1, 2, \dots, N$ .

Combining (20) with (22), it can be concluded that

$$\begin{aligned} \mathcal{E}\{\mathcal{L}V(x_t, t, i)\} &\leq \mathcal{E}\left\{ \sum_{1 \leq k < l \leq N} (\xi_k^{(i)}(t) - \xi_l^{(i)}(t))^T \Xi_{kl}^{(i)} (\xi_k^{(i)}(t) - \xi_l^{(i)}(t)) \right\} \\ &\quad - \int_{t-\tau}^t \mathcal{E}\left\{ (\xi_k^{(i)}(t, \beta) - \xi_l^{(i)}(t, \beta))^T \Omega_{kl}^{(i)} (\xi_k^{(i)}(t, \beta) - \xi_l^{(i)}(t, \beta)) \right\} d\beta, \end{aligned} \quad (23)$$

where  $\Xi_{kl}^{(i)}$  and  $\Omega_{kl}^{(i)}$  are defined in (10)–(11) and  $\xi_k^{(i)}(t, \beta) - \xi_l^{(i)}(t, \beta) = \text{col}\{(\xi_k^{(i)}(t) - \xi_l^{(i)}(t)), (y_k(\beta, r(\beta)) - y_l(\beta, r(\beta)))\}$ .

From condition (11), we can see that

$$\mathcal{E}\{\mathcal{L}V(x_t, t, i)\} \leq \lambda(\Xi) \mathcal{E}\left\{ \sum_{1 \leq k < l \leq N} (\xi_k^{(i)}(t) - \xi_l^{(i)}(t))^T (\xi_k^{(i)}(t) - \xi_l^{(i)}(t)) \right\}, \quad (24)$$

where  $\lambda(\Xi) = \max_{i \in \mathbb{S}} \{\lambda_{\max}(\Xi_{kl}^{(i)})\}$ .

Under condition (10), it follows readily that  $\lambda(\Xi)$  is a negative constant. Therefore, we have

$$\begin{aligned} \mathcal{E}\{V(x_t, t, i)\} - \mathcal{E}\{V(x_0, 0, r_0)\} &= \int_0^t \mathcal{E}\{\mathcal{L}V(x_s, s, i)\} ds \\ &\leq \lambda(\Xi) \int_0^t \mathcal{E}\left\{ \sum_{1 \leq k < l \leq N} (\xi_k^{(i)}(s) - \xi_l^{(i)}(s))^T (\xi_k^{(i)}(s) - \xi_l^{(i)}(s)) \right\} ds, \end{aligned} \quad (25)$$

which implies that

$$\int_0^t \mathcal{E}\left\{ \sum_{1 \leq k < l \leq N} \|\xi_k^{(i)}(s) - \xi_l^{(i)}(s)\|^2 \right\} ds \leq -\{\lambda(\Xi)\}^{-1} \mathcal{E}\{V(x_0, 0, r_0)\}. \quad (26)$$

Moreover, under Assumption 2, we can obtain  $V(x_0, 0, r_0) < +\infty$  and, subsequently,  $\sum_{1 \leq k < l \leq N} \|\xi_k^i(s) - \xi_l^i(s)\|^2$  is uniformly continuous on  $[0, +\infty)$ . Then, by using Lemma 3, we obtain

$$\mathcal{E}\left\{ \sum_{1 \leq k < l \leq N} \|\xi_k^i(s) - \xi_l^i(s)\|^2 \right\} \rightarrow 0, \text{ as } t \rightarrow +\infty. \quad (27)$$

In other words, all the subsystem in genetic oscillator networks (2) are asymptotically synchronous in the mean square sense. This completes the proof of Theorem 1.  $\blacksquare$

*Remark 3:* By taking advantage of a novel matrix functional and linear matrix inequality (LMI) techniques, the stochastic synchrony criteria have been derived in the form of LMIs for the genetic oscillator networks with time delays, Markovian switching parameters as well as stochastic disturbances. The LMI-based conditions can be readily checked by using the LMI toolbox in Matlab or other standard numerical software. An important

feature of the reported results lies in that all the conditions are dependent on the upper bound of the time-delays, which is made possible by utilizing the most updated techniques for achieving delay dependence. Note that the main criteria involve 1) the matrix  $\Gamma_i$  that links the state variable of the  $l$ th genetic oscillator in the genetic network mode  $i$ ; 2) the coupling matrix  $W$  that represents the coupling topology, direction, as well as the coupling strength of the genetic network. Therefore, the network topology does affect the dynamics of the synchronization.

#### IV. NUMERICAL EXAMPLE

In this section, we present a numerical example to illustrate the usefulness and applicability of the developed approach in this paper.

Consider the genetic oscillator network (2) or (5) with  $N$  gene oscillators and Markovian switching between two modes. The parameters are given as follows:

$$\begin{aligned} A(1) &= \begin{bmatrix} -1.0 & 0.6 \\ 0.5 & -1.5 \end{bmatrix}, \quad A(2) = \begin{bmatrix} -1.5 & 0.5 \\ 0.4 & -2.0 \end{bmatrix}, \quad B(1) = \begin{bmatrix} 1.8 & 1.0 \\ 1.2 & 1.4 \end{bmatrix}, \\ B(2) &= \begin{bmatrix} 1.4 & 1.2 \\ 1.0 & 1.0 \end{bmatrix}, \quad C(1) = \begin{bmatrix} 2.8 & 0.5 \\ 0.3 & 1.6 \end{bmatrix}, \quad C(2) = \begin{bmatrix} 2.5 & 0.35 \\ 0.25 & 0.9 \end{bmatrix}, \\ \Sigma_1 &= \begin{bmatrix} 0.1 & 0 \\ 0.1 & 0.1 \end{bmatrix}, \quad \Sigma_2 = \begin{bmatrix} 0.1 & -0.1 \\ 0 & 0.1 \end{bmatrix}, \quad \Gamma_1 = 1.5I, \quad \Gamma_2 = I, \\ \tau &= 2.5, \quad \Pi = \begin{bmatrix} -3 & 3 \\ 4 & -4 \end{bmatrix}, \quad W = [w_{kl}]_{6 \times 6} = \begin{cases} 1, & k \neq l; \\ -5, & k = l. \end{cases} \end{aligned}$$

The nonlinear regulatory functions are of the following form

$$f_l(x_{kl}(s)) = \frac{x_{kl}^2(s)}{1 + x_{kl}^2(s)}, \quad g_l(x_{kl}(s - \tau)) = \frac{x_{kl}^2(s - \tau)}{2 + x_{kl}^2(s - \tau)}, \quad (28)$$

and it can then be verified that  $K_1 = 0.65I$  and  $K_2 = 0.48I$ .

By using the Matlab LMI toolbox, we solve the LMIs (9)–(11) to obtain a feasible solution as follows:

$$\begin{aligned} P_1 &= \begin{bmatrix} 8.7634 & -0.7823 \\ -0.7823 & 10.0816 \end{bmatrix}, \quad P_2 = \begin{bmatrix} 10.1496 & -0.9153 \\ -0.9153 & 11.5092 \end{bmatrix}, \quad Q_1 = \begin{bmatrix} 45.2497 & -10.3339 \\ -10.3339 & 57.1284 \end{bmatrix}, \\ R &= \begin{bmatrix} 0.1812 & 0.0154 \\ 0.0154 & 0.1775 \end{bmatrix}, \quad \lambda^* = 34.0188, \quad e_1 = 26.4168, \quad e_2 = 30.9079. \end{aligned}$$

Therefore, it follows from the Theorem 1 that genetic oscillator networks (2) or (5) with given parameters is globally synchronized in the mean square sense.

In order to confirm the theoretical results, the simulation study is carried out. Figs. 1–2 are plotted to show the evolution dynamics of mRNA concentrations of all the coupled gene oscillators with different random initial values. It can be seen clearly from both Figs. 1–2 and Fig. 3 that the time evolution of the stochastic synchronization error between all the coupled gene oscillators indeed approaches zero, and the expected stochastic synchrony is well achieved.

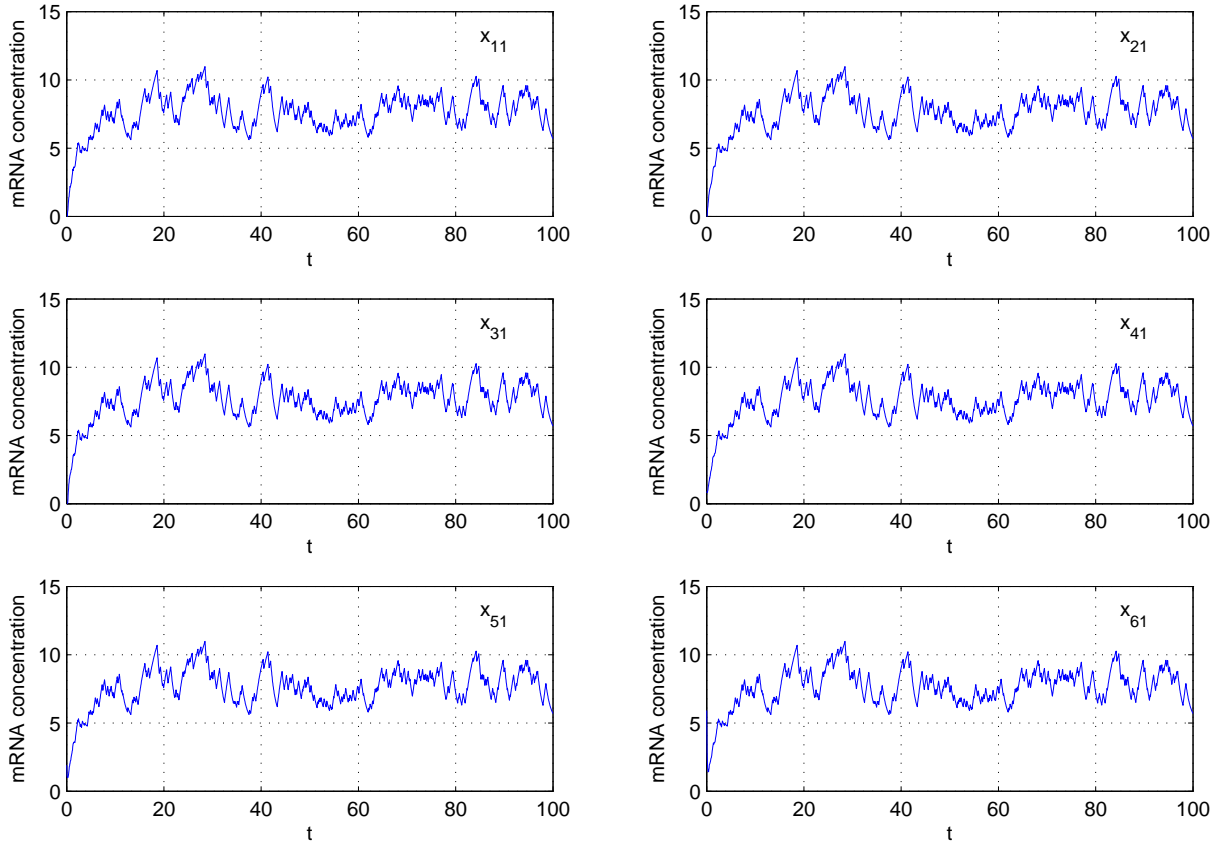


Fig. 1. Oscillation dynamics of the mRNA concentrations of  $x_{k1}(t)$  ( $k = 1, 2, \dots, 6$ ) of all coupled oscillators with different random initial values.

## V. CONCLUSIONS

In this paper, the stochastic synchronous analysis problem has been studied for a general array of genetic oscillator networks with Markovian switching, random perturbations as well as constant time-delays. We have established easily verifiable conditions under which the addressed delayed genetic oscillator network is asymptotically synchronization in the mean square sense in the presence of both Markovian jumping parameters and time-delays. By constructing a novel matrix functional based on the idea of ‘delay-fractioning’ and combining the stochastic analysis with the linear matrix inequality (LMI) technique, the delay-dependent synchrony criterion has been derived in the form of LMIs. A numerical example has been provided to demonstrate the effectiveness and applicability of the proposed testing conditions.

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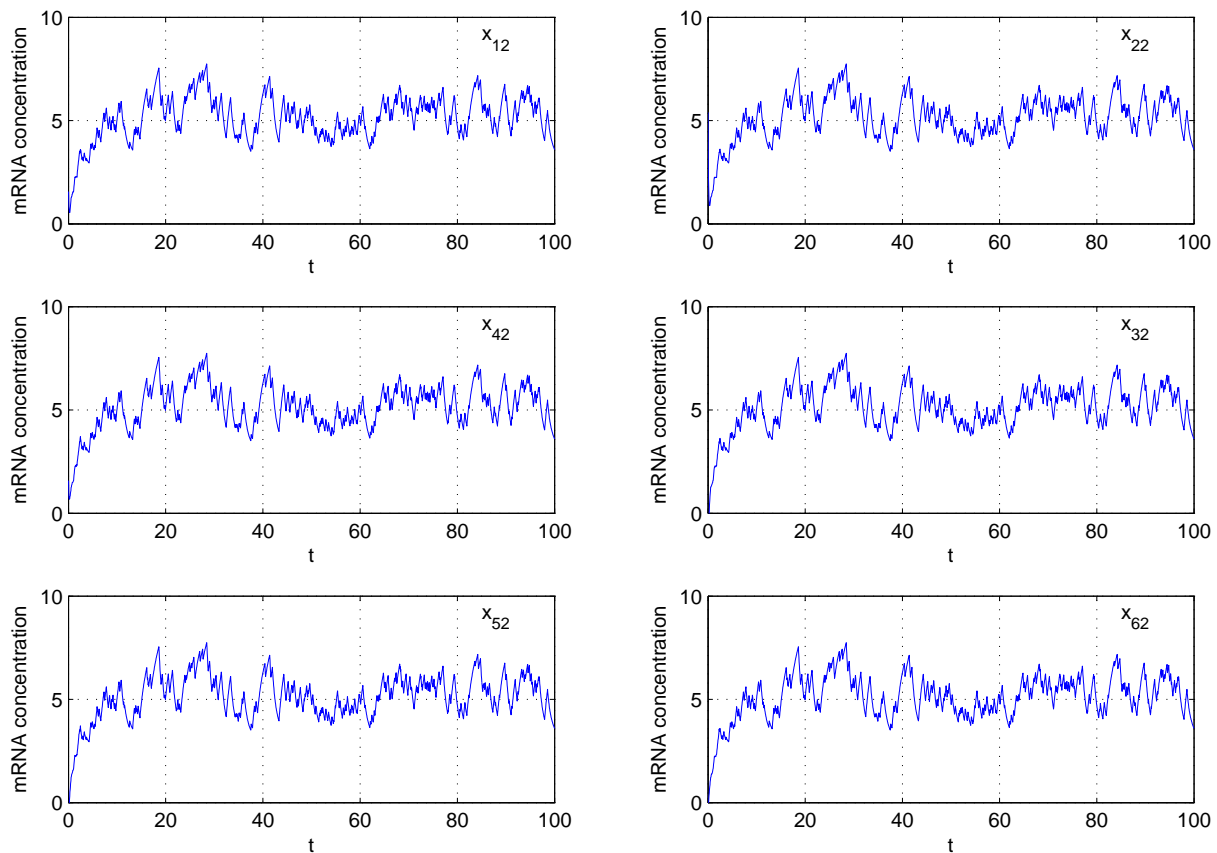


Fig. 2. Oscillation dynamics of the mRNA concentrations of  $x_{k2}(t)$  ( $k = 1, 2, \dots, 6$ ) of all coupled oscillators with different random initial values.

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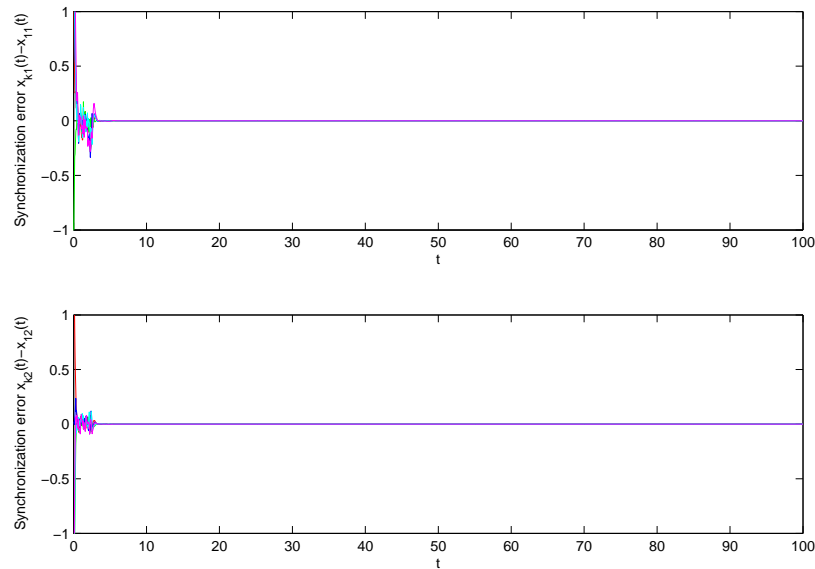


Fig. 3. The time evolution of the stochastic synchronization error between all the coupled gene oscillators.

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